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Experimental and Theoretical Studies of the Propargyl-Allenylindium System

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Abstract: The transient organoindium intermediates formed in the reaction of propargyl bromide with indium in aqueous media and tetrahydrofuran were investigated by NMR spectroscopy and found to be allenylindium(I) and allenylindium(III) dibromide. The influence of solvent and methyl substitution on the propargyl-allenylindium system was also studied. The experimental observations were supported by theoretical calculations using the B3LYP/6-311+G* method.

Introduction

In recent years, indium has emerged to become a useful and intriguing metal for organic synthesis.[1] In addition to the conventional organometallic reactions in organic solvents, many indium-mediated reactions can also be carried out in aqueous media.[2] In particular, the reactions of carbonyl compounds with allyl[3] or propargyl[4] halides and indium in water have been extensively examined because they provide an efficient method of carbon−carbon bond formation, often with good regio-,[5] diastereo-[6] and enantioselectivity.[7] The reaction is particularly useful in the synthesis of carbohydrates since much of the protection−deprotection chemistry commonly required for carbohydrate chemistry is not necessary.[8] Finally, because organic solvents can be avoided, the indium-mediated reactions in water have the potential as environmentally benign processes.[9]

Despite the extensive interest, relatively little was known about the nature of the reactive organoindium intermediates in either water or organic solvents. In 1988, it was reported that allyl iodide reacted with indium in organic solvents to give the allylindium sesquiiodide (**1,** X = I).[10] The structure of **1** appeared to have been assigned solely on the basis of ^{1}H NMR spectrum (DMF-d_7) which showed two sets of allylic methylene signals at δ 1.75 (d, J = 8 Hz) and 2.02 (d, J = 8 Hz). Many investigators had subsequently used the sesquihalide structure to describe the allylindium intermediate in the indium-mediated allylation reactions in organic solvents.[11] In 1999, we showed that indium reacted with allyl bromide in water to give allylindium(I) (**2**) which was the reactive intermediate in the allylation of carbonyl compounds (Scheme 1).[12] We further showed that when allyl bromide and indium were reacted in DMF, the compounds formed could not have **1** (X = Br) as the structure. The two sets of allylic signals at δ 1.7 and 2.15 ppm were due to the formation of two allylindium compounds, one of which was allylindium(I) (**2**) identical to the species formed in aqueous media. The other allylindium compound formed in DMF was tentatively assigned to have allylindium(III) dibromide (**3**) (or its dimer), as the structure.[13]

Even less is known about the nature of the intermediates in the reactions of propargyl halides with indium even though indium-mediated propargylation reactions have also been used extensively in organic synthesis.[4,14] We did not know if indium-

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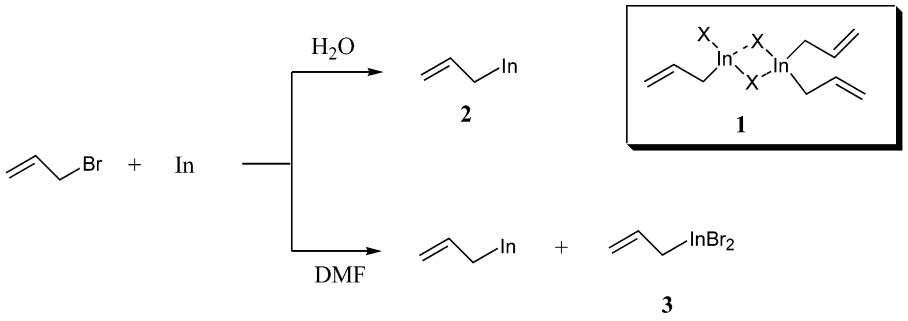
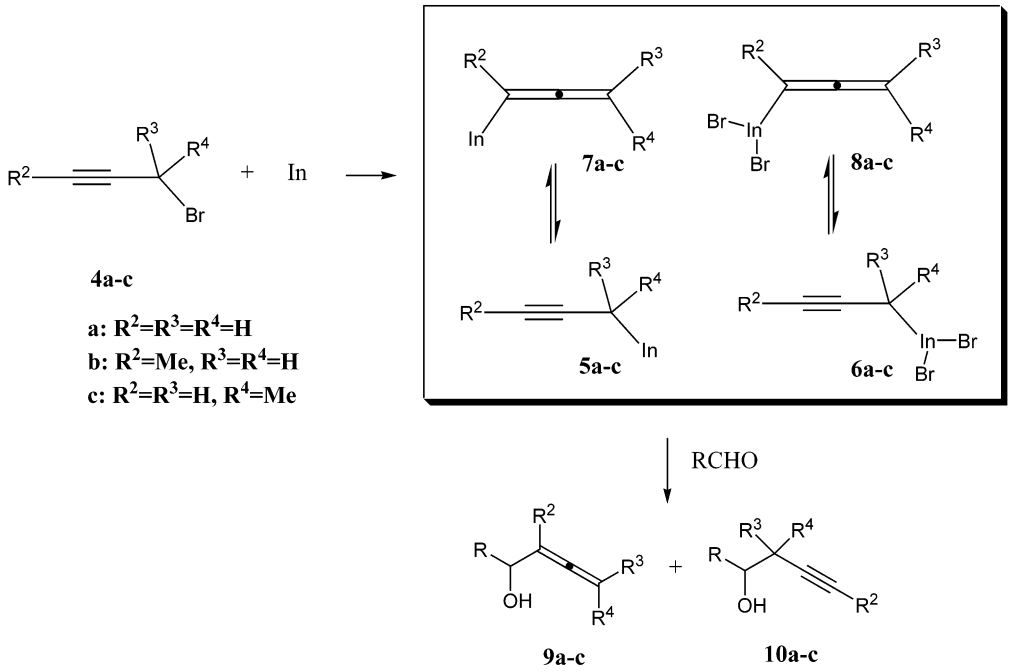
Scheme 1



Scheme 2



(I) or indium(III) species were formed in the reaction of propargyl bromide (**4**) with indium (Scheme 2), the relative equilibrium between the propargyl structures (**5**,**6**) and the allenyl structures (**7**,**8**), the role of substituent in affecting the propargyl-allenyl equilibrium, their subsequent regioselective reactions with carbonyl compounds,[4,15] and finally the role of organic solvent versus water on the nature of the reaction. This investigation set out to find answers to some of these questions.

Results and Discussions

Propargyl Bromide. Our initial effort focused on the reaction of propargyl bromide **4a** ($R^2 = R^3 = R^4 = H$) with indium in D_2O at room temperature in air without an inert atmosphere. By following the proton NMR spectra, the reaction was found to be very fast. All the starting **4a** disappeared within several minutes and no intermediate could be observed. Lowering the reaction temperature to 5 °C did not appear to slow the rate much. However, organoindium intermediate was presumed to have been formed, because when the same reaction of **4a** with indium was carried out with 4-chlorobenzaldehyde in D_2O at ambient temperature, NMR spectroscopy showed that the reaction indeed finished in 5 min to afford the homo-propargyl alcohol product **10a** ($R = 4\text{-}ClC_6H_4^-$) in high yield. To slow the process, the reaction of propargyl bromide **4a** with indium was carried out in a D_2O/THF-*d8* (1:4) media at 5 °C in air. This time we were able to observe, in the ^1H NMR spectra, the emergence of one triplet at 4.90 ppm ($J = 6.9$ Hz) and one doublet at 4.04 ppm ($J = 6.9$ Hz) (Figure 1a) after 3 min along with peaks that were assigned to propyne and allene,[16] which should be the hydrolysis products of the propargyl and allenyl organoindium intermediates **5**−**8a**. Adding 4-chlorobenzaldehyde to the reaction mixture at this stage resulted in the homo-propargyl alcohol **10a** ($R = 4\text{-}ClC_6H_4^-$, $R^2 = R^3 = R^4 = H$) but not the allenic product **9a**. We deduced therefore that in aqueous media, an organoindium intermediate was produced, and based on its proton chemical shift and coupling pattern, the structure was likely either allenylindium(I) **7a** or allenylindium(III) dibromide **8a** (Scheme 2).

Next, we followed the reaction of propargyl bromide **4a** with indium in deuterated tetrahydrofuran alone, also in air. The reaction became quite sluggish in comparison with that in aqueous media. After 7.5 h there were still more than 50% of

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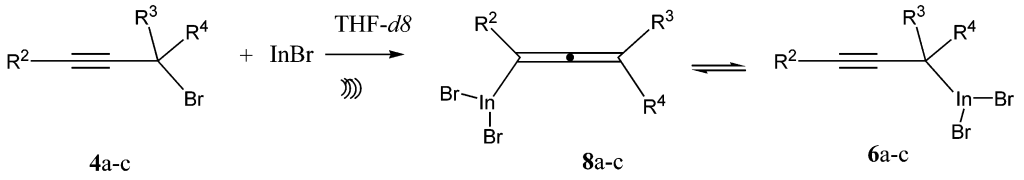
Scheme 3



the starting bromide **4a** left. Nevertheless, two sets of peaks had clearly appeared in the ^{1}H NMR spectrum, together with other peaks that resulted from allene and propyne.[16] One set of these peaks appeared at 5.03 ppm (t, $J = 6.8$ Hz) and 4.22 ppm (d, $J = 6.8$ Hz) and the another set was at 4.91 ppm (t, $J = 6.8$ Hz) and 4.02 ppm (d, $J = 6.8$ Hz). The intensity ratio of these two sets of peaks varied with time. The one at higher field started to disappear at 20 h later. After 60 h, only propyne and allene remained in the system. To shorten the reaction time in THF-*d8*, sonication was used to accelerate the reaction.[14h] Under ultrasonic irradiation, the starting propargyl bromide **4a** could be consumed within 3 h. Again, the above two sets of peaks were observed (Figure 1b), whereas, at 4.5 h, only the set of peaks at lower field could be seen (Figure 1c). Because the peaks appeared at 4.91 and 4.02 ppm in THF-*d*8 were the same as that observed in aqueous/THF-*d*8 mixture, we concluded that the two must have the same structures. The reaction of propargyl bromide with indium follows therefore the pattern found for allyl bromide.[12] Namely, in aqueous media, one reactive organoindium species was found; whereas in organic solvent, two reactive organoindium species were formed, one of which was identical to the one formed in aqueous media. Since we have showed previously that allyl bromide reacted with indium in D_2O to give allylindium(I) only, by analogy, we proposed that the set of peaks at 4.91 and 4.02 ppm has the allenylindium-(I) (**7a**) structure. By inference, the other set of peaks at 5.03 and 4.22 ppm was assigned to be allenylindium(III) dibromide **8a** (Scheme 2). We were able to confirm the indium(III) **8a** structure by the following experiment. Propargyl bromide **4a** was treated with indium(I) bromide in deuterated THF under sonication at room temperature. The reaction indeed occurred and proceeded at a reasonable rate. Only one set of peaks was observed this time and it was the same set as the lower field one (Figure 1d). Allenylindium(III) dibromide was therefore formed under such reaction conditions according to Scheme 3. Addition of 4-chlorobenzaldehyde to the system when the peaks for allenylindium(III) **8a** were maximal gave also the homo-propargyl alcohol **10a** in excellent yield.

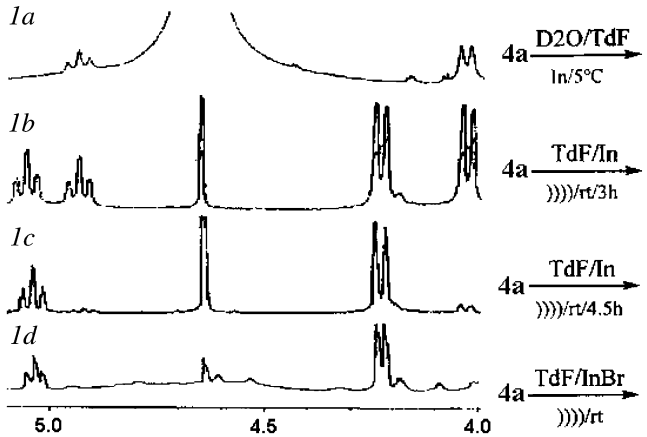


Figure 1. ^{1}H NMR spectra of organoindium species formed. (1a): Reaction of **4a** with In in D_2O/THF-*d*; (1b) reaction of **4a** with In in THF-*d* under sonication at 3 h; (1c) reaction of **4a** with In in THF-*d* under sonication at 4.5 h; (1d) reaction of **4a** with InBr in THF-*d* under sonication.

We have also investigated the ^{13}C NMR spectra of the two organoindium intermediates. In the reaction of **4a** with indium in THF-*d*8 when both **7a** and **8a** were present, the carbon spectrum showed, in addition to peaks assigned to allene, propyne and **4a**, two sets of signals at 211.54, 82.06, 64.19 ppm and 211.21, 81.47, 62.12 ppm. These signals are consistent with the two allenylindium structures **7a** and **8a**. The central allenyl carbons at 211.54 and 211.21 ppm are similar to those of allene (208.5 ppm) and allenyllithium (196.4 ppm).[17] DEPT experiments showed that the peaks at 64.19 and 62.12 ppm were from the CH_2 group. Finally, the set of 211.54, 82.06, and 64.19 ppm was assigned to allenylindium(III) dibromide **8a**, since this was the set of ^{13}C signals obtained from sample in Figure 1c when there was little **7a** left.

At the stage when all the starting **4a** was consumed (Figure 1b), the yields of the organoindium compounds **7a** and **8a** were determined to be 26% and 30% respectively by using toluene as an internal standard. On the other hand, the yields of the hydrolysis products, allene and propyne, were low (around 2.5%) at the end of the reaction. The low yields observed for allene and propyne were attributed to the volatile nature of these two compounds which could be lost during the reaction. To examine the relative reactivity of allenylindium(I) **7a** and allenylindium(III) dibromide **8a** toward electrophiles, the following experiment was carried out. At the stage when both **7a** and **8a** were present in almost equal amounts (45:55 respectively, Figure 2a), small quantity of 4-chlorobenzaldehyde (0.1 equiv) was added as a THF-*d*8 solution. After one minute, the reaction mixture was checked by proton NMR spectroscopy. The peaks corresponding to allenylindium(I) **7a** were reduced in intensity to about 30% of the initial values (Figure 2b) and signals corresponding to the coupling product **10a** could be observed (not shown). When a second aliquot of 4-chlorobenzaldehyde (0.1 equiv) was then added to the mixture, all allenylindium(I) **7a** disappeared after one minute and only allenylindium(III) **8a** could be observed (Figure 2c). Finally, when a further aliquot of 4-chlorobenzaldehyde (0.3 equiv) was added, the peaks of **8a** also disappeared completely after one minute, and the homo-propargyl alcohol **10a** was the only product in the system. This experiment therefore demonstrated clearly that while both **7a** and **8a** could react with aldehyde, the allenylindium(I) **7a** was more reactive than allenylindium-(III) dibromide **8a**.

1-Bromo-2-Butyne. We then studied the reaction of 1-bromo-2-butyne **4b** ($R^2 = Me$, $R^3 = R^4 = H$) with indium in D_2O at ambient temperature. Again, it was not possible to observe the

(17) Reich, H. J.; Holladay, J. E.; Walker, T. G.; Thompson, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 9769.

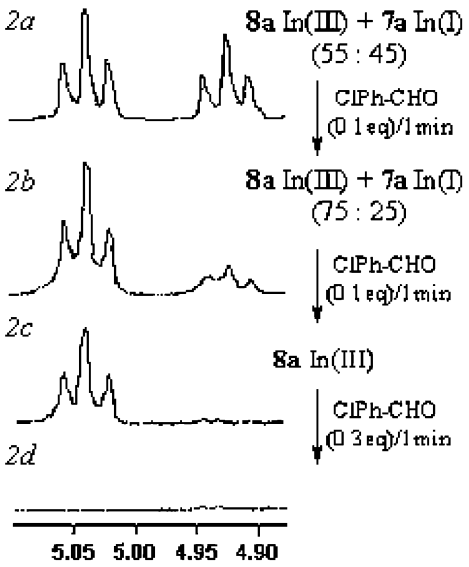


Figure 2. ^{1}H NMR spectra of organoindium species **7a** and **8a** on reactions with 4-chlorobenzaldehyde. (2a): Before addition of 4-chlorobenzaldehyde; (2b): 1 min after addition of 0.1 equiv of 4-chlorobenzaldehyde; (2c) Addition of another 0.1 eq. of 4-chlorobenzaldehyde; (2d) After addition of another 0.3 equiv of 4-chlorobenzaldehyde.

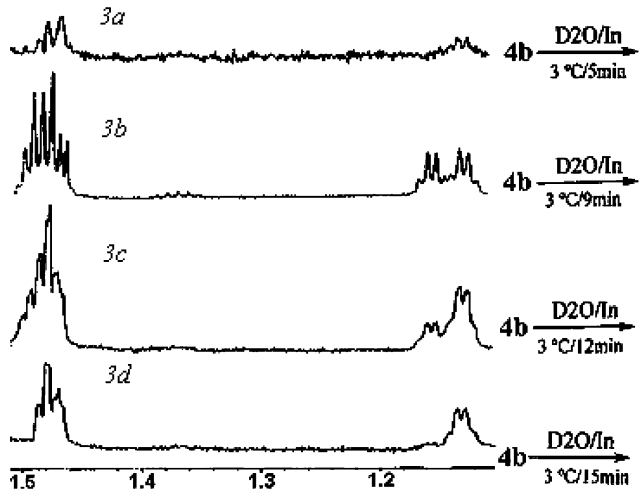


Figure 3. ^{1}H NMR spectra of organoindium species formed. (3a): Reaction of **4b** with In in D_2O at 3 °C for 5 min; (3b) reaction of **4b** with In in D_2O at 3 °C for 9 min; (3c) reaction of **4b** with In in D_2O at 3 °C for 12 min; (3d) reaction of **4b** with In in D_2O at 3 °C for 15 min.

intermediate due to the fast reaction rate. However, in this case, it became possible to follow the reaction with ^{1}H NMR spectroscopy by lowering the reaction temperature to 3 °C. By 5 min, one set of peaks appeared at 1.47 ppm (t, $J = 2.8$ Hz) and 1.14 ppm (q, $J = 2.8$ Hz) (Figure 3a). As the reaction proceeded, much to our surprise, another set of peaks at 1.49 ppm (t, $J = 2.8$ Hz) and 1.16 ppm (q, $J = 2.8$ Hz), showed up and was very close to the first set of peaks (Figure 3b). This new set of peaks then gradually declined in intensity and disappeared after 15 min (Figure 3, parts c and d). After this stage, only the first set of peaks could be seen in the proton NMR spectra. Quenching the reaction mixture by 4-chlorobenzaldehyde at the time when the two sets of peaks were of the same intensity gave allenic alcohol **9b** ($R = 4\text{-}ClC_6H_4^-$, $R^2 =$ Me, $R^3 = R^4 = H$) as the only product.[18] These results suggested that two organoindium species were formed in the aqueous media, with the second one being formed slower but also less stable to the aqueous environment. Furthermore, these transient organoindium intermediates have not the allenyl, but the propargyl structures **5b** and **6b** according to the chemical shifts and coupling pattern of the ^{1}H NMR spectra.

The reaction of 1-bromo-2-butyne (**4b**) with indium in deuterated tetrahydrofuran in air was also examined and found to be much slower than that of propargyl bromide **4a.** After 2 d vigorous stirring, the starting bromide **4b** was still largely unreacted. However, when ultrasonic irradiation was applied, the reaction was again accelerated. At 3.6 h, two new sets of peaks at 1.67 (t, 3H, $J = 2.7$ Hz) 1.40 (q, 2H, $J = 2.7$ Hz) ppm and 1.70 (br s, 3H), 1.69 (br s, 2H) ppm were noticed besides other peaks that could be attributed to 2-butyne and 1,2-butadiene, hydrolysis products of the propargyl and allenylindium intermediates.[19] We confirmed the propargylindium structures in THF-*d*8 with ^{13}C NMR spectroscopy which showed two sets of signals at 80.8, 71.9, 4.20, 3.93 ppm and 78.6, 74.0, 6.22, 3.79 ppm. Subsequent DEPT experiments showed that the carbon signals at 4.20 and 6.22 ppm were from CH_2 and those at 3.93 and 3.79 ppm were from methyl carbons. All these data pointed to propargyl structures. When the reaction proceeded to 28 h, all 1-bromo-2-butyne **4b** was gone and in the ^{1}H NMR spectra only the two major peaks at 1.69 and 1.70 ppm were still left along with some minor peaks resulted from 2-butyne and 1,2-butadiene. When excess amount of 4-chlorobenzaldehyde was added to the reaction mixture at this stage, only the allenic alcohol **9b** ($R = 4\text{-}ClC_6H_4^-$, $R^2 =$ Me, $R^3 = R^4 = H$) was obtained and no propargylic product was detected. We have also examined the reaction of 1-bromo-2-butyne (**4b**) with indium bromide in deuterated THF under ultrasound irradiation. Although the reaction was slower than that with indium, it showed nevertheless the signals at 1.69 and 1.70 ppm for the ^{1}H and 78.6, 74.0, 6.22, and 3.79 ppm for the ^{13}C NMR spectra, the same as that of the reaction of **4b** with indium at 28 h in THF-*d*8 under ultrasound. From these experiments, we concluded therefore that in organic solvent (THF), 1-bromo-2-butyne (**4b**) reacted with indium to give the propargylindium(III) dibromide **6b** and the propargylindium(I) **5b**. Compound **6b** was generated in THF from the reaction of **4b** with indium bromide. We were quite concerned that the proton chemical shifts of the two organoindium species in THF did not correspond well with those observed in aqueous media. One possibility for the difference is due to the solvent effect. We examined therefore the ^{1}H NMR spectra of the reaction of **4b** with indium in D_2O/THF-d8 (1:1). In this mixed solvent, we observed two sets of signals at 1.57 (t, 3H)/1.40 (q, 2H) and 1.61 (br d) and 1.69 (br t), intermediate in chemical shifts between those in D_2O or THF-*d*8 alone. We conclude therefore that in aqueous media, **5b** was formed first followed by the generation of **6b**, which was however hydrolyzed to give 2-butyne and 1,2-butadiene under the aqueous conditions to leave only **5b** which was also eventually hydrolyzed. At the stage when all **4b** was reacted and using toluene as the internal standard, it was possible to determine the yields of the organoindium compounds **5b** and **6b** to be 34% and 40%,

(18) (a) Zhang, L.; Huang, Y.; Huang, Z. *Tetrahedron Lett.* **1991**, *32*, 6579. (b) Masuyama, Y.; Watabe, A.; Ito, A.; Kurusu, Y. *Chem. Commun.* **2000**, 2009.

(19) The deuterated tetrahydrofuran contained 5−10% water; and the existence of 2-butyne and 1,2-butadiene as hydrolysis products were confirmed by comparison of their NMR data with authentic sample and literature data. See Friedel, R. A.; Retcofsky, H. L. *J. Am. Chem. Soc.* **1963**, *85*, 1300.

respectively. Similar to the results of propargyl bromide **4a**, the yields observed for the hydrolysis products, 2-butyne and 1,2-butadiene, were only around 5% at the end of the reaction, presumably due to the volatility of these compounds.

The relative reactivity of **5b** and **6b** toward aldehyde was also tested in the same manner as that for **7a** and **8a**. At the stage when both the indium(I) **5b** and indium(III) **6b** were in almost equal amount, 0.1 equiv of 4-chlorobenzaldehyde was added to the mixture as a THF-*d*8 solution. After 3 min, NMR spectroscopy showed that most of the indium(I) intermediate **5b** had reacted while the indium(III) **6b** was still present. A further quantity of 0.3 equiv of 4-chlorobenzaldehyde was then added in one portion and this time, all the organoindium intermediates disappeared in 2 min concomitant with the formation of *E*-1-(4-chlorophenyl)-2, 5-dimethyl-2,5,6-heptatrien-1-ol as the only product according to proton NMR spectroscopy.[14h] The results are therefore similar to that of **7a** and **8a** in that the reactions between organoindium intermediates **5b** and **6b** with aldehyde were fast processes, and the organoindium(I) intermediate **5b** was a more reactive species than the indium(III) intermediate **6b**.

3-Bromo-1-Butyne (4c). The reaction of **4c** ($R^2 = R^3 = H$, $R^4 = Me$) with indium in aqueous media was also found to be fast. In a mixed solvent of D_2O/THF-*d*8 (4:1) and at low temperature (3 °C), the reaction system became a gellike mixture within one minute and therefore, was difficult to be monitored by NMR spectroscopy. Nevertheless, using equal amounts of THF-*d*8 and D_2O, the reaction gave much better results. At 30 s, three new sets of peaks clearly showed up in the ^{1}H NMR spectra and one set was assigned to be 1,2-butadiene that should be the hydrolysis product. The other two sets of peaks were at 4.98 (m, 1H), 4.46 (m, 1H), 1.56 (m, 3H) and 4.84 (m, 1H), 4.34 (m, 1H), 1.50 (m, 3H), respectively, and were consistent with the allenic structure. When 4-chlorobenzaldehyde was added to the mixture at this stage, 1-(4-chlorophenyl)-2-methyl-3-butyne-1-ol **10c** ($R = 4\text{-}ClC_6H_4^-$, $R^2 = R^3 = H$, $R^4 = Me$) was the only product observed. When the ratio of THF-*d*8 to D_2O was changed to 3:2, the NMR spectra of the mixture could be observed more clearly.

The reaction of 3-bromo-1-butyne **4c** with indium in deuterated tetrahydrofuran under ultrasonic irradiation was then carried out and found to be slower than that of propargyl bromide **4a**, but faster than 1-bromo-2-butyne **4b.** At 6 h, three new sets of peaks showed up again in the ^{1}H NMR spectra and one set of them was attributed to 1, 2-butadiene. The other two sets of peaks, which appeared around 4.88 (m, 1H), 4.40 (m, 1H), 1.61 (m, 3H) and 5.00 (m, 1H), 4.62 (m, 1H), 1.55 (dd, $J = 6.9$, 3.3 Hz, 3H), respectively, were similar to those observed in aqueous media reaction and consistent with the allenylindium structure. Adding 4-chlorobenzaldehyde to the mixture resulted in the propargylic alcohol **10c** ($R = 4\text{-}ClC_6H_4^-$, $R^2 = R^3 = H$, $R^4 = Me$). We deduced therefore that the allenylindium species **7c** and **8c** have been generated in THF-*d*8 as well as in aqueous media. Their ^{13}C NMR spectra, at 209.9, 83.8, 73.2, 14.2 ppm and 210.3, 82.9, 75.8, 14.0 ppm and the subsequent 2D-NMR experiments including COSY, HSQC, and HMBC, further confirmed the allenic structures of these two organoindium species. When the reaction was left to proceed further under sonication, the set of peaks that was at higher field in proton NMR disappeared gradually and eventually only that set of peaks at lower field could be observed. This was the set of signals generated when 3-bromo-1-butyne (**4c**) was reacted with indium bromide in deuterated THF under ultrasound irradiation, thus confirming its allenylindium(III) **8c** structure. The other set of peaks at higher field in ^{1}H NMR spectra was assigned therefore to have the allenylindium(I) **7c** structure.

Theoretical Calculations

Ab initio and density functional calculations were carried out with the GAUSSIAN 98 program to study structures and relative stabilities of allenylindium(I, III) and propargylindium(I, III).[20] All geometries were first fully optimized by the HF/6-31+G* method and then further optimized by the B3LYP/6-311+G* method.[21] The Lanl2dz basis set with Effective Core Potentials (ECP)[22] was used for indium and bromide in all calculations. Vibration frequencies were calculated for each structure, based on which free energies were calculated. As far as we are aware, there have been no previous theoretical studies on the structures and reactivities of organoindium compounds.

Propargyl/allenyl indiums. B3LYP/6-311+G* geometric optimization of propargylindium(I) (**5a**) and allenylindium(I) (**7a**) led to only one structure, which is a π-complex of allenylindium(I) (**7a-Pi**).[23] Propargylindium(III) dibromide (**6a**) and allenylindium(III) dibromide (**8a**) were calculated to be stable in σ-complexes with the B3LYP method. Allenylindium-(III) dibromide (**8a**) is calculated to be more stable than propargylindium(III) dibromide (**6a**) by 6.5 kcal/mol at the B3LYP method. Recently, Reich provided evidence that some allenyl-propargyllithium compounds may adopt localized or bridged structures depending on the solvent used.[24] We therefore also calculated structures **5-8a(H_2O)** with one water molecule coordinated to the indium atom. As shown in Figure 4, a σ-complex is obtained for each structure. The coordination of the water molecule reduces the energetic preference of the allenylic form of both In(I) and In(III) species somewhat. In any case, the calculations clearly suggest that allenylindium should be much more stable than propargylindium for these unsubstituted propargyl/allenyl systems, in agreement with the experimental observation.

Effect of Methyl Substituent on Allenyl-In/Propargyl-In Equilibrium. The calculated structures and relative energies of methyl substituted propargyl-In (**5b**, **6b**, **5c**, **6c**) and allenyl-In (**7b**, **8b**, **7c**, **8c**) are given in Figure 5. For the In(I) **5b** and **7b** species, the B3LYP method only leads to the **7b**-π structure. Water complexation leads to a more stable γ-methylpropar-

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(24) Reich, H. J.; Thompson, J. L. *Org. Lett.* **2000**, *2*, 783.

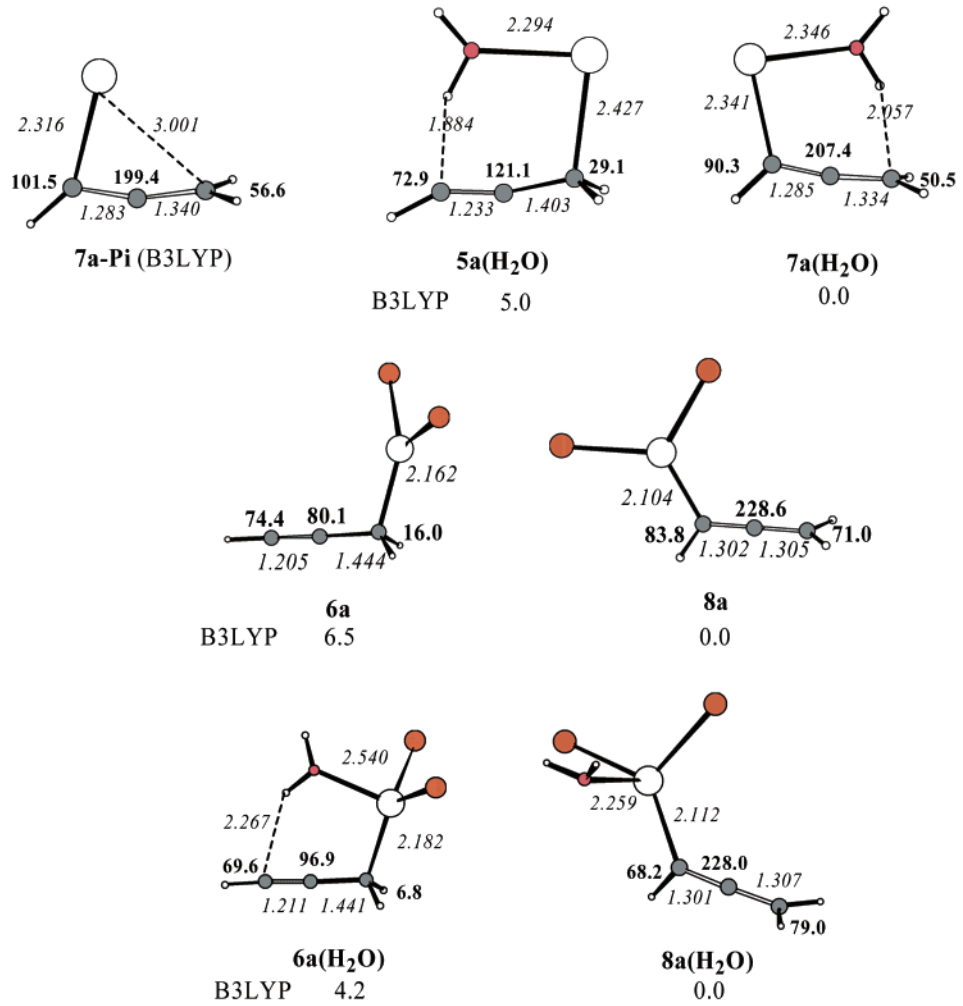

Figure 4. Calculated structures of propargylindium(I) (**5a**), allenylindium(I) (**7a**), propargylindium(III) dibromide (**6a**), and allenylindium(III) dibromide (**8a**) as well as their water complexes, **5-8a(H$_2$O)**. Calculated B3LYP (italic) bond lengths are in angstrom. Calculated relative free energies are in kcal/mol. Carbon chemical shifts are in bold numbers.

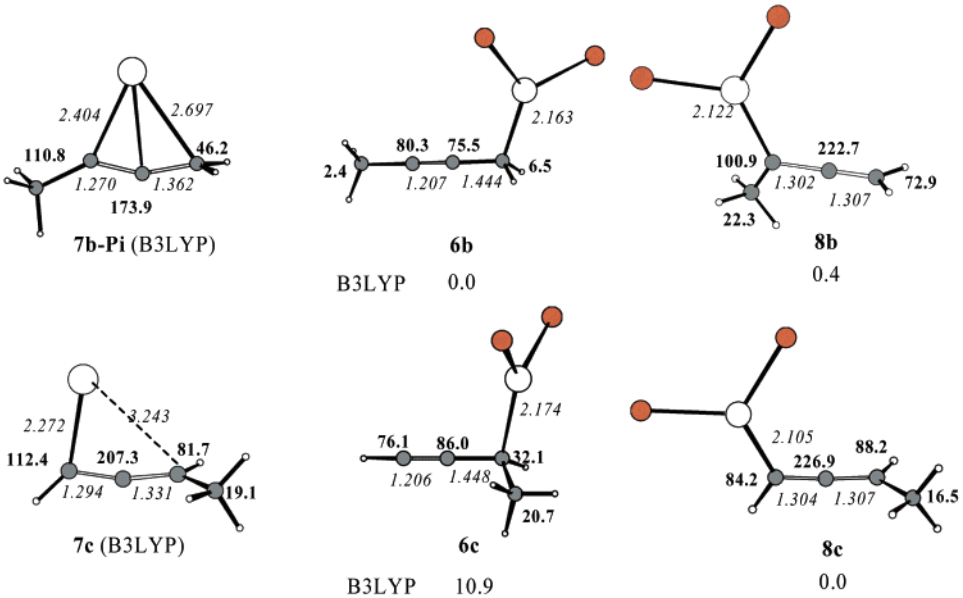

Figure 5. B3LYP calculated structures of methyl substituted allenylindium(I) (**7b**, **7c**), propargylindium(III) dibromide (**6b**, **6c**), and allenylindium(III) dibromide (**8b**, **8c**). Calculated B3LYP (italic) bond lengths are in angstrom. Calculated relative free energies are in kcal/mol. Carbon chemical shifts are in bold numbers.

gylindium(I) σ-structure (see Supporting Information). For the In(III) dibromide species, the B3LYP method gives stable σ-complexes of propargylic and allenylic forms, with the propargylic **6b** more stable than the allenylic **8b**. On the other

Table 1. Experimental and Calculated ^{13}C NMR Chemical Shift of Various Organoindium Intermediates

isomeric structures	experimental	calculated for allenyl structure	calculated for propargyl structure
allenylindium(I)/		**7a(H_2O)**	**5a(H_2O)**
propargylindium(I)	C1: 81.47	C1: 90.3	C1: 29.1
(**5a/7a**)	C2: 211.21	C2: 207.4	C2: 121.1
	C3: 62.12	C3: 50.5	C3: 72.9
allenylindium(III)		**8a(H_2O)**	**6a(H_2O)**
dibromide/propargyl	C1: 82.06	C1: 68.2	C1: 6.8
indium(III) dibromide	C2: 211.54	C2: 228.0	C2: 96.9
(**6a/8a**)	C3: 64.19	C3: 79.0	C3: 69.6
α-methylallenyl-indium(I)/		**7b-Pi**	
γ-methyl-propargylindium(I)	C1: 4.20	C1: 46.2	
(**5b/7b**)	C2: 71.9	C2: 173.9	
	C3: 80.8	C3: 110.8	
	C4: 3.93	C4: -	
α-methylallenyl-indium(III)		**8b**	**6b**
dibromide/γ-methyl-	C1: 6.22	C1: 72.9	C1: 6.5
propargylindium(III)	C2: 74.0	C2: 222.7	C2: 75.5
dibromide	C3: 78.6	C3: 100.9	C3: 80.3
(**6b/8b**)	C4: 3.79	C4: 22.3	C4: 2.4
γ-methylallenyl-indium(I)/		**7c**	
α-methyl-propargylindium(I)	C1: 73.2	C1: 112.4	
(**7c/5c**)	C2: 209.9	C2: 207.3	
	C3: 83.8	C3: 81.7	
	C4: 14.2	C4: 19.1	
γ-methylallenyl-		**8c**	**6c**
indium(III)	C1: 75.8	C1: 84.2	C1: 76.1
dibromide/α-methyl-	C2: 210.3	C2: 226.9	C2: 86.0
propargylindium(III)	C3: 82.9	C3: 88.2	C3: 32.1
dibromide (**8c/6c**)	C4: 14.0	C4: 16.5	C4: 20.7

hand, the allenylic **7c** and **8c** are calculated to be more stable than the propargylic **5c** and **6c**.

In general, a methyl group, which is electron-donating and acts as steric hindrance, destabilizes a carbanion center. Specifically, in structure **8b**, the methyl group is at a sp^2 carbanion center and causes destabilization to **8b** with respect to **6b**. As a result, the propargyl-In structure **6b** is predicted to be more stable than the allenyl-In structure **8b**. Likewise, in structures **5c** and **6c**, the methyl group is at a sp^3 carbanion center. It causes a destabilization to **5c** and **6c** with respect to **7c** and **8c**. Therefore, allenyl-In structures **7c** and **8c** are predicted to be more stable than **5c** and **6c**, respectively. These calculation results are in full agreement with the experimental observations presented earlier.

^{13}C NMR Calculations. Another useful tool for structural characterization of organometallic compounds is to compare the calculated ^{13}C NMR chemical shifts with the observed values. Using the B3LYP method,[25] it has been possible to compute the theoretical chemical shifts of various organoindium structures. The calculated ^{13}C NMR chemical shifts of propargyl/allenyl indium compounds **5**−**8** are given in Figures 4 and 5 (bold numbers). The calculated values and the experimentally observed ^{13}C chemical shifts for the various organoindium species are summarized in Table 1. It is clear from the results in Table 1 that these calculations further support the experimental assignment of structures. That is, the organoindium species from the reaction of **4a** and **4c** with In are in allenyl-In forms, while those from the reaction of **4b** are in propargyl-In forms.

(25) The calculated ^{13}C NMR chemical shifts were evaluated by GIAO at the B3LYP/6-311++G** level based on the B3LYP-optimized structures: (a) London, F. *J. Phys. Radium*, Paris **1937**, *8*, 397. (b) McWeeny, R. *Phys. Rev.* **1962**, *126*, 1028. (c) Ditchfield, R. *Mol. Phys.* **1974**, *27*, 789. (d) Dodds, J. L.; McWeeny, R. Sadlej, A. J. *Mol. Phys.* **1980**, *41*, 1419. (e) Wolinski, K.; Hilton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

Discussion

Because many organoindium (III) compounds are known to be hydrolyzed by water to the corresponding hydrocarbons,[26] it was initially suggested that aqueous indium-mediated reactions may not have involved the formation of discrete organoindium intermediates.[27] It was subsequently established that, at least in the case of indium-mediated allylation reactions, allyl bromide reacted with indium in water to form a transient allylindium(I) (**1**) intermediate (Scheme 1). The conclusion that allylindium(I) was the active allylating agent in water was somewhat unexpected as most organoindium compounds have indium(III) oxidation state.[28] We were quite concerned by our previous inability to observe a discrete intermediate in the reaction of propargyl bromide with indium in water under the same conditions in which allylindium(I) was observed.[29] This raises at least two questions concerning organoindium chemistry in aqueous media. Is the formation of a transient but discrete allylindium(I) (**1**) intermediate in water a general phenomenon or is it only limited to the specific case of allylic system? Is there any particular significance regarding the oxidation state of indium which confers either stability or reactivity to the allylindium intermediate (**1**)?

It is now clear from the results in Figure 1 that a transient but discrete organoindium intermediate was also formed in the reaction of propargyl bromide and indium in aqueous media. The intermediate was much shorter lived than allylindium(I), and could only be observed in D_2O/THF-*d*8 (1:4) mixture at 5 °C (Figure 1a). The behaviors of the propargyl bromide/indium system paralleled that of the allyl bromide/indium system, however, in that two organoindium intermediates were observed in organic solvent (THF-*d*8) alone (Figure 1b), one of which was the same as the species formed in aqueous media. We were able to prove that the other species formed in THF-*d*8 was an indium(III) compound by its independent generation from the reaction of propargyl bromide and indium(I) bromide (Figure 1d and Scheme 3). The propargyl system is however more complicated than the allylic system because it can exhibit propargyl-allenyl isomerism for either the indium(I) species (**5a** and **7a**) or the indium(III) species (**6a** and **8a**). The proton NMR spectra are more consistent with the allenylic structures **7a** and **8a**. The allenylic structural assignments were confirmed by ^{13}C NMR measurements as well as computations. The observed ^{13}C NMR signals for the two intermediates at 211.21 and 211.54 ppm are consistent with the allenyl central carbons of **7a** and **8a**, and in reasonable agreement with the calculated values of 207.4 and 228.6 ppm respectively using the B3LYP method (Table 1). Calculations by either the HF or the B3LYP methods showed that between the propargylindium structures (**5a** and **6a**) and the allenylindium structures (**7a** and **8a**), the allenyl structures are the more stable irrespective whether the indium is in the +1 or the +3 oxidation states. The predominance of the allenylindium structures **7a** and **8a** is compatible with the observed regioselection in their reactions with carbonyl compounds. When either **7a** or **8a** was quenched with *p*-chloroben-

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zaldehyde, the product obtained was the homo-propargyl alcohol **10a** ($R = 4\text{-}ClC_6H_4^-$, $R^2 = R^3 = R^4 = H$). In general, propargyl/allenyl organometallic reagents react with carbonyl compounds via an S_E2' pathway. The product distribution is determined by the position of the equilibrium between the two intermediates and their relative rates of addition to carbonyl compounds (Scheme 3) with the allenylmetals leading to the homo-propargyl alcohols.[30] Theoretical calculations using the B3LYP method suggests also that water coordination with indium can affect the structures and energies of the propargyl/allenylindium systems. This role of water may be helpful in the eventual understanding of the particular ability of indium in mediating these reactions in aqueous media.

In the unsubstituted propargyl/allenylindiums **5**−**8a** equilibria, both experimental and theoretical studies indicated that the allenylindium structures are the more stable. However, the equilibrium is greatly affected by substitution.[31] For the γ-methylpropargyl/α-methylallenylindiums **5**−**8b** derived from 1-bromo-2-butyne (**4b**), the equilibria are in favor of the propargylic intermediates **5b** and **6b**. On the other hand, if the methyl is substituted at a different position as in the case of α-methylpropargyl/γ-methylallenylindiums **5**−**8c**, then the equilibria are in favor of the allenyl structures **7c** and **8c**.[32] These results are consistent with the previous conclusions regarding the regioselectivity in indium-mediated allenylation and propargylation reactions. In all cases, the products have the regioselection expected from the S_E2' pathway.[4,14,32]

Conclusion

The present results, together with previous studies,[12] clearly demonstrated that transient but discrete organoindium intermediates were formed in the indium-mediated allylation and propargylation/allenylation of carbonyl compounds in aqueous media. The nature of the organoindium species formed depends on the solvent used. In aqueous media, only the organoindium(I) species were observed by NMR spectroscopy, whereas in organic solvent (THF), both organoindium(I) and organoindium(III) species were formed and observed. In the propargyl/allenyl indium system, the equilibrium is in favor of the allenylindium species. Methyl substitution affects the equilibrium. These experimental observations are consistent with theoretical calculations using the B3LYP methods, suggesting that computational methods may be helpful in the understanding of these organometallic reactions in aqueous media.

Experimental Section

General. All reagents were obtained commercially unless otherwise noted. Indium powder, propargyl bromide and 1-bromo-2-butyne were fresh commercial samples and used directly without any further purification. 3-Bromo-1-butyne was prepared according to literature procedure.[33] 4-Chlorobenzaldehyde was checked for purity by ^{1}H NMR and was recrystallized if impure. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} plastic backed plates and was visualized by dipping into a solution of ammonium molybdate (2.5 g) and ceric sulfate (1 g) in concentrated H_2SO_4/H_2O (10 mL/90 mL) and heated with a heat gun. All NMR spectra were recorded on Varian Mercury-300 (300 MHz) or Mercury-400 (400 MHz) at 20 °C. Chemical shifts for protons are reported in parts per million and referenced to residual protium in deuterated chloroform (δ 7.26), deuterium oxide (δ 4.60) or tetrahydrofuran (δ 1.73, 3.58). Carbon chemical shifts are reported in parts per million relative to the carbon resonance of the methylene groups of tetrahydrofuran-d_8 (δ 25.3, 67.4).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from Propargyl Bromide 4a and Indium in Aqueous Media. To a solution of propargyl bromide **4a** (0.5 mmol) in THF-*d*8 (0.4 mL) and D_2O (0.1 mL) at 5 °C was added in one portion indium powder (0.55 mmol). The mixture was stirred vigorously at 5 °C and examined at intervals by ^{1}H NMR. At 3 min, 4-chlorobenzaldehyde (0.25 mmol) was added to the system. After stirring for 1 h, the product was extracted into $CDCl_3$ and checked by NMR spectroscopy which indicated 1-(4-chlorophenyl)-3-butyne-1-ol (**10a**)[18a] was obtained in 30% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 4H), 4.86 (t, 1H, J = 6.2 Hz), 2.64−2.61 (m, 2H), 2.42 (s, br, 1H), 2.09 (t, 3H, J = 2.8 Hz).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from Propargyl Bromide 4a and Indium in Deuterated THF (without ultrasound). To a solution of propargyl bromide **4a** (1.0 mmol) in THF-*d*8 (0.8 mL) at ambient temperature was added in one portion indium (1.0 mmol). The mixture was stirred vigorously at room temperature and examined at times by ^{1}H NMR spectroscopy.

Procedure for the Spectroscopic Studies of Organoindium Intermediates from Propargyl Bromide (4a) and Indium in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added propargyl bromide **4a** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one portion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectroscopy. At 4.5 h, 4-chlorobenzaldehyde (0.15 mmol) was added to the mixture. After 1 h, TLC and NMR spectroscopy indicated 1-(4-chlorophenyl)-3-butyne-1-ol (**10a**) was the only product in the reaction with a yield of 40% (NMR).

Procedure for the Spectroscopic Studies of Organoindium Intermediate from 1-Propargyl Bromide 4a and Indium Bromide in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added propargyl bromide **4a** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium bromide (0.5 mmol) was then added. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectroscopy.

Procedure for Determining the Yields of Organoindium Intermediates 7a and 8a in the Reaction of Propargyl Bromide 4a and Indium in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added propargyl bromide 4a (0.5 mmol), toluene (0.17 mmol, internal standard) and THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one portion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined by ^{1}H NMR spectroscopy at 3 h when all the starting 4a had been consumed. The yields of the organoindium intermediates were determined by comparing the peak integration area of 7a or 8a with toluene.

Procedure for Determining the Relative Reactivity of Organoindium Intermediates 7a and 8a with Aldehyde. To an oven-dried NMR tube was added propargyl bromide **4a** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one portion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and examined by ^{1}H NMR spectroscopy. At time when **7a** and **8a** were almost in equal amount, 4-chlorobenzaldehyde, which was dissolved in small amount of THF-*d8*, was added in portions, and the reaction was monitored by proton NMR spectroscopy (Figure 2) at intervals specified.

Allenylindium(I) (7a): Yield, 26% in THF-*d*8; ^{1}H NMR (400 MHz, THF-*d*8) δ 4.91 (t, 1H, J = 6.8 Hz) and 4.02 (d, 2H, J = 6.8 Hz); ^{13}C NMR (75 MHz, THF-*d*8) (DEPT) δ 211.21 (C), 81.47 (CH), 62.12 (CH_2).

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Allenylindium(III) Dibromide (8a): Yield, 30% in THF-*d*8;^{1}H NMR (400 MHz, THF-*d*8) δ 5.03 (t, 1H, J = 6.8 Hz) 4.22 (d, 2H, J = 6.8 Hz); ^{13}C NMR (75 MHz, THF-*d*8) (DEPT) δ 211.54 (C), 82.06 (CH), 64.19 (CH_2).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 1-Bromo-2-butyne (4b) and Indium in Aqueous Media. To a mixture of 1-bromo-2-butyne **4b** (1.0 mmol) in D_2O (1.0 mL) at 3 °C was added in one portion indium powder (1.1 mmol). The mixture was stirred vigorously at 3 °C and examined at times by ^{1}H NMR spectroscopy. At 9 min, 4-chlorobenzaldehyde (0.5 mmol) was added to the mixture. After stirring for 1 h, the reaction mixture was extracted with $CDCl_3$ and checked by TLC and NMR spectroscopy which indicated that 1-(4-chlorophenyl)-2-methyl-2, 3-butadien-1-ol (**9b**)[18] was the only product in the reaction with a yield of 35% (NMR); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 4H), 5.10 (s, 1H), 4.92−4.90 (m, 2H), 2.17 (s, br, 1H), 1.56 (t, 3H, J = 2.8 Hz).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 1-Bromo-2-butyne (4b) and Indium in Deuterated THF (without ultrasound). To a solution of 1-bromo-2-butyne **4b** (1.0 mmol) in THF-*d*8 (1.0 mL) at ambient temperature was added in one portion indium (1.0 mmol). The mixture was stirred vigorously at room temperature and examined at times by ^{1}H NMR spectroscopy.

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 1-Bromo-2-butyne (4b) and Indium in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added 1-bromo-2-butyne **4b** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one potion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectroscopy. At 19 h, 4-chlorobenzaldehyde (0.05 mmol) was added to the mixture and was found to have been 100% converted to *E*-1-(4-chlorophenyl)-2, 5-dimethyl-2,5,6-heptatrien-1-ol[14h] after overnight as checked by TLC and NMR; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (s, 4H), 5.72−5.66 (m, 1H), 5.08 (s, 1H), 4.66−4.60 (m, 2H), 2.73−2.69 (m, 2H), 2.52 (s, br, 1H), 1.71 (t, 3H, J = 3.3 Hz), 1.47−1.46 (m, 3H). In a separate experiment excess amount of chlorobenzaldehyde (0.55 mmol) was added to the system at 28 h and 1-(4-chlorophenyl)-2-methyl-2, 3-butadien-1-ol **9b**[16] was obtained in 9% yield (NMR).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 1-Bromo-2-butyne (4b) and Indium Bromide in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added 1-bromo-2-butyne **4b** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium bromide (0.5 mmol) was then added. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectrosocpy.

Procedure for Determining the Yields of Organoindium Intermediates 5b and 6b in the Reaction of 1-Bromo-2-butyne 4b and Indium in Deuterated THF. (with ultrasound). To an oven-dried NMR tube was added 1-bromo-2-butyne 4b (0.5 mmol), toluene (0.5 mmol, internal standard) and THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one potion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined by ^{1}H NMR spectroscopy at 19 h when all the starting 4b was consumed. The yields of organoindium intermediates were determined by comparing the peak integration area of 5b or 6b with toluene.

Procedure for Determining the Relative Reactivity of Organoindium Intermediates 5b and 6b with Aldehyde. To an oven-dried NMR tube was added 1-bromo-2-butyne **4b** (0.5 mmol), THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one portion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectroscopy. At the time when **5b** and **6b** were almost in equal amount, 4-chlorobenzaldehyde, which was dissolved in small amount of THF-*d8*, was added in portions, and the reaction was monitored by proton NMR spectroscopy at different intervals.

γ-Methylpropargylindium(I) (5b): Yield, 34% in THF-*d*8;^{1}H NMR (400 MHz, D_2O) δ 1.47 (t, 3H, J = 2.8 Hz), 1.13 (q, 2H, J = 2.8 Hz); ^{1}H NMR (300 MHz, THF-*d*8) δ 1.67 (t, 3H, J = 2.7 Hz) 1.40 (q, 2H, J = 2.7 Hz); ^{13}C NMR (75 MHz, THF-*d*8) (DEPT) δ 80.8 (C), 71.9 (C), 4.20 (CH_2), 3.93 (CH_3).

γ-Methylpropargylindium(III) Dibromide (6b): Yield, 40% in THF-*d*8; ^{1}H NMR (400 MHz, D_2O) δ 1.49 (t, 3H, J = 2.8 Hz) 1.16 (q, 2H, J = 2.8 Hz); ^{1}H NMR (300 MHz, THF-*d*8) δ 1.70 (s, 3H), 1.69 (s, 2H); ^{13}C NMR (75 MHz, THF-*d*8) (DEPT) δ 78.6 (C), 74.0 (C), 6.22 (CH_2), 3.79 (CH_3).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 3-Bromo-1-butyne (4c) and Indium in Aqueous Media. To a solution of 3-bromo-1-butyne **4c** (1.0 mmol) in THF-*d*8/D_2O (1 mL, v/v in different ratios) at 3 °C was added in one portion indium powder (1.0 mmol). The mixture was stirred vigorously at 3 °C and examined at times by ^{1}H NMR spectroscopy. At 3 min (THF-*d*8/D_2O v/v = 1:1), 4-chlorobenzaldehyde (0.5 mmol) was added to the system. After stirring for 1 h, the reaction mixture was extracted with $CDCl_3$ and checked by NMR spectroscopy which indicated that 1-(4-chlorophenyl)-2-methyl-3-butyne-1-ol (**10c**)[34] was the only product in the reaction; ^{1}H NMR (400 MHz, $CDCl_3$) δ (two isomers, *erythro*: *threo* = 44:56) *threo*, 7.31 (s, 4H), 4.50 (d, J = 6.4, 1H), 2.80−2.74 (m, 1H), 2.60 (s, br, 1H), 2.22 (d, J = 1.6 Hz, 1H), 1.12 (t, J = 6.8 Hz, 3H); *erythro*, 7.31 (s, 4H), 4.70 (d, J = 5.6, 1H), 2.88−2.72 (m, 1H), 2.60 (s, br, 1H), 2.14 (d, J = 1.6 Hz, 1H), 1.12 (t, J = 6.8 Hz, 3H).

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 3-Bromo-1-butyne (4c) and Indium in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added 3-bromo-1-butyne **4c** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium powder (0.5 mmol) was then added in one portion. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectroscopy. At 6 h, 4-chlorobenzaldehyde (0.15 mmol) was added to the mixture. After overnight, NMR spectroscopy indicated that 1-(4-chlorophenyl)-3-butyne-1-ol (**10c**) was the only product in the reaction.

Procedure for the Spectroscopic Studies of Organoindium Intermediates from 3-Bromo-1-butyne (4c) and Indium Bromide in Deuterated THF (with ultrasound). To an oven-dried NMR tube was added 3-bromo-1-butyne **4c** (0.5 mmol) and THF-*d*8 (0.5 mL). Indium bromide (0.5 mmol) was then added. The NMR tube was put into an ultrasound bath for sonication at ambient temperature and was examined at times by ^{1}H NMR spectroscopy.

γ-Methylallenylindium(I) (7c): ^{1}H NMR (400 MHz, THF-*d*8) δ 4.91−4.86 (m, 1H), 4.43−4.36 (m, 1H), 1.63−1.59 (m, 3H); ^{13}C NMR (100 MHz, THF-*d*8) δ 209.9, 83.8, 73.2, 14.2.

γ-Methylallenylindium(III) dibromide (8c):^{1}H NMR (400 MHz, THF-*d*8) δ 5.04−4.96 (m, 1H), 4.65−4.57 (m, 1H), 1.55 (dd, J = 6.9, 3.3 Hz, 3H); ^{13}C NMR (100 MHz, THF-*d*8) δ 210.3, 82.9, 75.8, 14.0.

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Supporting Information Available: The stable γ-methylpropargylindium(I) σ-structure and the HF computed values (pdf). This material is available free of charge via the Internet at http://pubs.acs.org.

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