Organoindium Reagents

DOI: 10.1002/ange.201005798

Direct Synthesis of Water-Tolerant Alkyl Indium Reagents and Their Application in Palladium-Catalyzed Couplings with Aryl Halides**

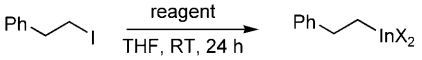
*Zhi-Liang Shen, Kelvin Kau Kiat Goh, Yong-Sheng Yang, Yin-Chang Lai, Colin Hong An Wong, Hao-Lun Cheong, and Teck-Peng Loh**

Organometallic reagents involving magnesium and zinc have found widespread applications in organic synthesis and have revolutionized the field of organometallic chemistry.[1] However, the incompatibility of organomagnesium and organozinc reagents with certain functional groups, such as carbonyl and hydroxyl, have limited their utility in organic synthesis. In comparison, the recent development of an organoindium reagent has shown that organoindium compounds exhibit great tolerance towards various functional groups, such as carbonyl, nitrile, and alcohol.[2–6] Among the many organoindium compounds, allylic indium reagent has been extensively studied by Araki, Chan, Li, Lloyd-Jones, our group, and others.[7] In recent years, Knochel,[2,3] Minehan,[4] Chupak,[5] Yamamoto,[8] and their co-workers have independently reported efficient methods for the synthesis of benzyl and/or aryl indium reagents (mainly activated by using LiCl as reaction additive). However, until now there has been no straightforward method to prepare the synthetically more useful alkyl indium reagent by using readily available alkyl halides, probably because of the low reactivity of indium and alkyl halide, which makes the direct preparation of alkyl indium reagent from alkyl halide extremely difficult.

Current methods for the synthesis of triorganoindium reagent (R_3In) suffer from drawbacks in terms of the requirement to use other reactive organometallic reagents (transmetalation of preprepared RMgX/RLi with InX_3 under anhydrous conditions and with the protection of inert gas) and thus show limited functional-group compatibility.[9] Therefore, a direct and clean method for the synthesis of alkyl indium reagent from readily available alkyl halide under mild reaction conditions and with wide functional-group tolerance is highly desirable. In connection with our recently developed radical-type alkylation reactions in aqueous media using unactivated alkyl halide and In/CuI,[10] herein we describe an efficient method for the synthesis of water-tolerant alkyl indium reagent by direct insertion of indium metal into alkyl halide with activation by CuCl at room temperature. The synthetic utility of the alkyl indium reagent was demonstrated by palladium-catalyzed coupling with aryl halide in *N*,*N*-dimethylacetamide (DMA) with great functional-group compatibility.[9,11,12]

Initially, 1-(2-iodoethyl)benzene (**1a**) was chosen as the substrate to investigate the formation of alkyl indium reagent **2a** (see Table 1) in THF at room temperature, by using CuI as reaction additive. Gratifyingly, 50% conversion from the substrate **1a** to the desired alkyl indium reagent **2a** was observed. Inspired by this promising result, various copper salts were screened to investigate their efficiency in the formation of the alkyl indium reagent **2a**.

Table 1: Optimization of reaction conditions.[a]



1a **2a**

Entry	Reagent	Yield [%][b]
1	In (2 equiv)	< 5
2	In/CuCN (2 equiv/2 equiv)	< 5
3	In/CuI (2 equiv/2 equiv)	50
4	In/CuBr (2 equiv/2 equiv)	89
5	In/CuCl (2 equiv/2 equiv)	99
6	In/CuCl (1.5 equiv/1.5 equiv)	86
7	In/CuCl (1 equiv/1 equiv)	74
8	In/$CuBr_2$ (2 equiv/2 equiv)	77
9	In/$CuBr_2$ (2 equiv/1 equiv)	88
10	In/$CuCl_2{\cdot}2H_2O$ (2 equiv/1 equiv)	93
11	In/$Cu(OAc)_2$ (2 equiv/1 equiv)	80
12	In/$CuCO_3$ (2 equiv/1 equiv)	48
13	In/$CuSO_4{\cdot}5H_2O$ (2 equiv/1 equiv)	< 5

[a] 1 mmol 1-(2-iodoethyl)benzene (**1a**, 1 equiv) was used in all the reactions. X = I and/or the anion of the copper salt. [b] The yield was determined by ^{1}H NMR spectroscopy using *p*-xylene as internal standard.

As shown in Table 1, most of the copper salts screened did promote the reaction at room temperature. Among them, good to excellent yields were obtained when CuCl, $CuCl_2{\cdot}2H_2O$, CuBr, $CuBr_2$, and $Cu(OAc)_2$ were employed as reaction additives. Nevertheless, only with the use of CuCl as reaction additive was the substrate **1a** fully consumed and exclusively produced the desired alkyl indium reagent **2a** in almost quantitative yield (Table 1, entry 5). ^{1}H NMR analysis ($CDCl_3$ as solvent) showed that the chemical shift of the α-CH_2 proton of **1a** moved upfield from $\delta = 3.2$ to 1.7 ppm (see the Supporting Information, pages S3 and S15), which indicated the formation of an alkyl indium reagent.[13] A

[*] Z. L. Shen, K. K. K. Goh, Y. S. Yang, Y. C. Lai, C. H. A. Wong, H. L. Cheong, Prof. Dr. T. P. Loh
Division of Chemistry and Biological Chemistry
School of Physical and Mathematical Sciences
Nanyang Technological University
Singapore 637371 (Singapore)
Fax: (+65) 6791-1961
E-mail: teckpeng@ntu.edu.sg

[**] We gratefully acknowledge Nanyang Technological University (NTU), the Ministry of Education (No. M45110000), and A*STAR SERC Grant (No. 0721010024) for the funding of this research.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201005798.

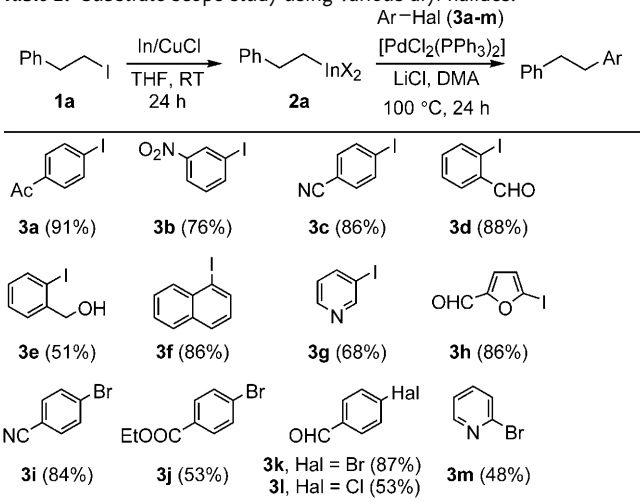
relatively low yield was obtained when the reaction was performed with a decrease in additive loading (Table 1, entries 6 and 7). A trace amount of the desired product was detected when indium was solely used under these conditions (Table 1, entry 1).

Importantly, the alkyl indium reagent **2a** is thermally stable in organic solvents (such as THF, 1,4-dioxane, and DMA) and tolerant to water,[14,15] though it may decompose completely when subjected to purification by silica-gel column chromatography. In addition, no competitive β-hydride elimination, homocoupling, or formation of ethylbenzene was observed under the optimized conditions (Table 1, entry 5). Moreover, the reaction was completely performed under an air atmosphere; no protection of the reaction with inert gas was needed. All these features make the alkyl indium reagent more convenient to prepare and easier to handle than its lithium, magnesium, and zinc counterparts. In comparison, when In/LiCl (2 equiv/2 equiv) was used as reaction promoter, which was developed by Knochel and others in the synthesis of benzyl and aryl indium reagents,[2,3] the formation of two main types of alkyl indium reagent was observed (see the Supporting Information page S3 for details of a ^{1}H NMR comparison of the two reactions using CuCl and LiCl). This further demonstrates the advantage of using CuCl as reaction additive in the generation of a single alkyl indium reagent.

With the optimized reaction conditions in hand, we continued to study the palladium-catalyzed coupling of alkyl indium reagent with aryl halide. The first palladium-catalyzed coupling of organoindium reagent involving triorganoindium complex (R_3In) was reported by Sarandeses and co-workers and the reaction was carried out in THF.[9,11] However, the palladium-catalyzed coupling of alkyl indium reagent **2a** with 4′-iodoacetophenone (**3a**) proceeded sluggishly in THF (<20% yield). After optimization of the reaction conditions by using various solvents and palladium catalysts, it was gratifying to find that the coupling reaction proceeded more efficiently at 100 °C using $[PdCl_2(PPh_3)_2]$ as catalyst, DMA as solvent, and LiCl as additive (see the Supporting Information page S4 for details of reaction conditions optimization). A good yield of 91% was obtained when the reaction was carried out under the above optimal conditions (Table 2, substrate **3a**). To demonstrate the general applicability of the alkyl indium reagent in palladium-catalyzed coupling with aryl halide, a variety of alkyl and aryl halides were screened.

As shown in Table 2, the coupling reactions of alkyl indium reagent **2a** with various aryl halides proceeded efficiently to afford the desired products in moderate to good yields. It is important to note that functional groups, including COR, NO_2, CN, CHO, and COOR, can be well tolerated in the coupling reaction, which makes the protocol more general and synthetically more useful. Especially noteworthy, substrate **3e** containing a hydroxyl group also reacted well under optimal conditions to give the product in a moderate yield of 51%. Heterocyclic halides such as 3-iodopyridine (**3g**), 5-iodofuraldehyde (**3h**), and 2-bromopyridine (**3m**) can also be used as coupling partners under the optimized conditions. Finally, it is gratifying to observe that

Table 2: Substrate scope study using various aryl halides.[a,b]



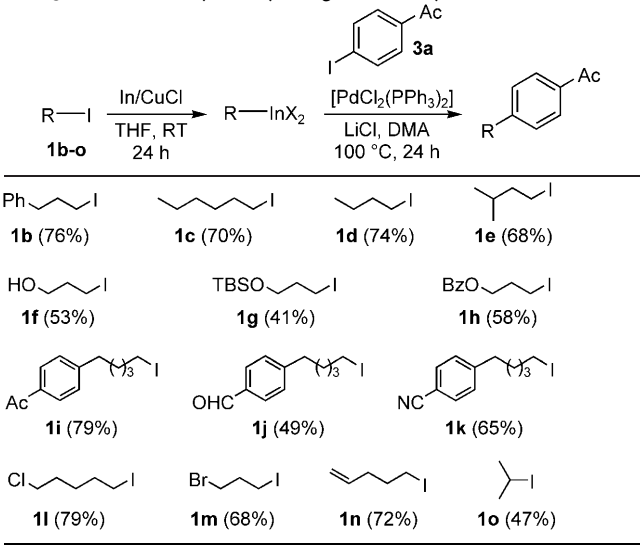
[a] See the Supporting Information for detailed reaction conditions. [b] Yield of isolated product based on **3** as limiting reagent.

aryl chloride **3l** can be employed as well leading to the desired product in 53% yield.

In addition, a range of alkyl halides was also screened to investigate the substrate scope of the reaction. All alkyl iodides can be effectively converted into the corresponding alkyl indium reagents at room temperature (>90% conversion), as indicated by crude ^{1}H NMR analysis of the first-step reaction mixture. The subsequent coupling reactions of 4′-iodoacetophenone (**3a**) with various alkyl indium reagents proceeded well to furnish the target products in moderate to good yields.

As shown in Table 3, alkyl iodides possessing functionalities such as OH (**1f**), OTBS (**1g**; TBS = *tert*-butyldimethylsilyl), COOR (**1h**), COR (**1i**), CHO (**1j**), and CN (**1k**)

Table 3: Substrate scope study using various alkyl iodides.[a,b]

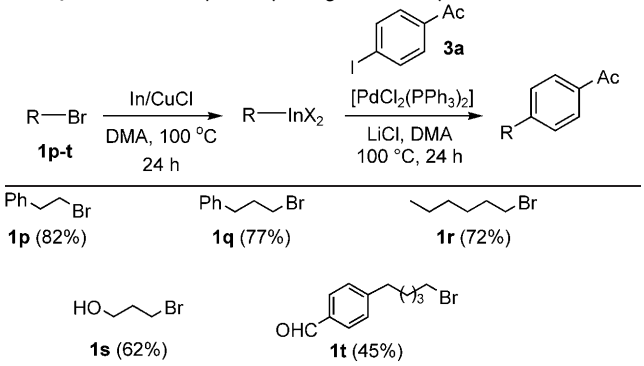


[a] See the Supporting Information for detailed reaction conditions. [b] Yield of isolated product based on **3a** as limiting reagent.

were all tolerated under the reaction conditions, and afforded the expected products in moderate to good yields. The successful use in the reaction of substrate **1f** which bears a hydroxyl group makes the method a good alternative to the use of other organometallic reagents, such as organomagnesium and organozinc reagents, because of their low tolerance to hydroxyl groups. Especially noteworthy, because of the low reactivity of alkyl bromide and alkyl chloride, dihalides **1l** and **1m** containing Cl and Br functionalities only reacted at the C–I bond while leaving the C–Cl and C–Br bonds intact. This finding indicates that the formation of alkyl indium reagent can be selectively achieved at the C–I bond, and the C–Cl and C–Br bonds can be kept for late-stage modification in organic synthesis. The use of substrate **1n** further broadened the substrate scope to alkyl halides containing an alkene functionality. As for secondary iodide, the reaction of 4′-iodoacetophenone (**3a**) with organoindium reagent derived from *i*PrI (**1o**) also proceeded as expected, albeit in a moderate yield of 47%.

However, alkyl bromide, as a result of its low reactivity relative to alkyl iodide, cannot be converted into the corresponding alkyl indium reagent under the same conditions.[16] Fortunately, when the reaction involving 1-(2-bromoethyl)benzene (**1p**) was carried out in DMA at 100°C in the presence of In/CuCl, >90% conversion of the alkyl bromide to the corresponding alkyl indium reagent was observed. Thus, several alkyl bromides were tested in the protocol to further broaden the general applicability of this method in the synthesis of alkyl indium reagent from alkyl bromide and further coupling with aryl halide. As shown in Table 4, the alkyl bromides **1p–t** can be employed for the synthesis of alkyl indium reagents as well, and the subsequent coupling reactions with aryl iodide **3a** also proceeded efficiently to furnish the desired products in moderate to good yields.

Table 4: Substrate scope study using various alkyl bromides.[a,b]



[a] See the Supporting Information for detailed reaction conditions. [b] Yield of isolated product based on **3a** as limiting reagent.

In summary, a mild, efficient, and straightforward method for the synthesis of water-tolerant alkyl indium reagent through CuCl-mediated direct insertion of indium into alkyl halide in THF at room temperature is described. The synthesis of the alkyl indium reagent is easy to handle since the reaction can be carried out under an air atmosphere and even in the presence of water. The palladium-catalyzed coupling of the alkyl indium reagent with various aryl halides proceeded efficiently in DMA to afford the desired products in moderate to good yields. The great compatibility of the alkyl indium reagent and the subsequent coupling reactions with functional groups, including COR, COOR, CHO, CN, OH, OTBS, NO_2, C=C, Br, and Cl, render this method general and useful: 1) protection of sensitive functional groups, either in the alkyl indium reagent or in the electrophile, is unnecessary; and 2) the versatile functional groups can thus be kept for late-stage modifications, which confers the method great potential for use in organic synthesis. Further studies pertaining to determination of the structure of the alkyl indium reagent and its synthetic utility in organic synthesis are currently in progress.

Experimental Section

General procedure for the synthesis of alkyl indium reagent and its palladium-catalyzed coupling with aryl halide (Tables 2 and 3): Alkyl iodide (1 mmol), indium (2 mmol), CuCl (2 mmol), and analytical-grade THF (3 mL) were added sequentially to an 8 mL sample vial. The mixture was stirred vigorously at room temperature for 24 h. After reaction, the mixture was allowed to stand for around 10 min, then the upper clear solution was carefully separated from the bottom black precipitate by a syringe. The residual precipitate was washed with THF (3 mL) and the THF layer was carefully separated by syringe. The combined organic layers were concentrated in vacuo. The residue was dissolved in DMA (3 mL) and transferred to another 8 mL sample vial. Aryl halide (0.7 mmol), LiCl (2 mmol), and $[PdCl_2(PPh_3)_2]$ (0.05 mmol, 0.05 equiv) were added to the vial sequentially. The reaction mixture was stirred at 100°C for 24 h. After reaction, the mixture was directly purified by silica-gel column chromatography with EtOAc/hexane as eluent to afford the desired product.

Received: September 15, 2010
Published online: December 5, 2010

Keywords: cross-coupling · indium · organoindium reagents · palladium · synthesis design

[1] P. Knochel, *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**.
[2] Y. H. Chen, P. Knochel, *Angew. Chem.* **2008**, *120*, 7760; *Angew. Chem. Int. Ed.* **2008**, *47*, 7648.
[3] Y. H. Chen, M. Sun, P. Knochel, *Angew. Chem.* **2009**, *121*, 2270; *Angew. Chem. Int. Ed.* **2009**, *48*, 2236.
[4] V. Papoian, T. Minehan, *J. Org. Chem.* **2008**, *73*, 7376.
[5] L. S. Chupak, J. P. Wolkowski, Y. A. Chantigny, *J. Org. Chem.* **2009**, *74*, 1388.
[6] For palladium-catalyzed coupling of R_3In or R_2InCl reagent with aryl halides in aqueous media, see: K. Takami, H. Yorimitsu, H. Shinokubo, S. Matsubara, K. Oshima, *Org. Lett.* **2001**, *3*, 1997. However, it should be noted that the real organoindium species involved in the reaction is R_2InOH; as stated by the authors, hydrolysis of R_3In or R_2InCl to R_2InOH was observed when R_3In or R_2InCl was subjected to water.
[7] For selected examples, see: a) S. Araki, H. Ito, Y. Butsugan, *J. Org. Chem.* **1988**, *53*, 1831; b) S. Araki, T. Shimizu, P. S. Johar, S. J. Jin, Y. Butsugan, *J. Org. Chem.* **1991**, *56*, 2538; c) C. J. Li, T. H. Chan, *Tetrahedron Lett.* **1991**, *32*, 7017; d) C. J. Li, T. H.

Chan, *Tetrahedron Lett.* **1991**, *32*, 7020; e) X. H. Yi, Y. Meng, X. G. Hua, C. J. Li, *J. Org. Chem.* **1998**, *63*, 7472; f) T. H. Chan, Y. Yang, *J. Am. Chem. Soc.* **1999**, *121*, 3228; g) G. C. Lloyd-Jones, T. Russell, *Synlett* **1998**, 903; h) S. M. Capps, G. C. Lloyd-Jones, M. Murray, T. M. Peakman, K. E. Walsh, *Tetrahedron Lett.* **1998**, *39*, 2853; i) T. P. Loh, G. Q. Cao, J. Pei, *Tetrahedron Lett.* **1998**, *39*, 1453; j) T. P. Loh, X. R. Li, *Angew. Chem.* **1997**, *109*, 1029; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 980; k) L. Paquette, T. M. Mitzel, *J. Org. Chem.* **1996**, *61*, 8799; l) W. Schmid, M. Whitesides, *J. Am. Chem. Soc.* **1991**, *113*, 6674; m) F. Bossard, V. Damabrin, V. Lintanf, P. Beuchet, P. Mosset, *Tetrahedron Lett.* **1995**, *36*, 6055.

[8] N. Fujiwara, Y. Yamamoto, *J. Org. Chem.* **1999**, *64*, 4095.

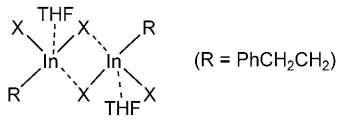
[9] For pioneering work in the synthesis of R_3In by transmetalation of preprepared RLi or RMgX with $InCl_3$, see: a) H. C. Clark, A. L. Pickard, *J. Organomet. Chem.* **1967**, *8*, 427. For pioneering work concerning the application of R_3In in organic synthesis, see: b) I. Pérez, J. P. Sestelo, L. A. Sarandeses, *Org. Lett.* **1999**, *1*, 1267; c) I. Perez, J. P. Sestelo, L. A. Sarandeses, *J. Am. Chem. Soc.* **2001**, *123*, 4155, and references therein.

[10] For our previous work on the development of Barbier–Grignard-type alkylation reactions of imine, aldehyde, nitrone, and α,β-unsaturated carbonyl compound in aqueous media using In/CuI through a radical-type mechanism, see: a) Z. L. Shen, T. P. Loh, *Org. Lett.* **2007**, *9*, 5413; b) Z. L. Shen, H. L. Cheong, T. P. Loh, *Chem. Eur. J.* **2008**, *14*, 1875; c) Z. L. Shen, Y. L. Yeo, T. P. Loh, *J. Org. Chem.* **2008**, *73*, 3922; d) Y. S. Yang, Z. L. Shen, T. P. Loh, *Org. Lett.* **2009**, *11*, 1209; e) Z. L. Shen, H. L. Cheong, T. P. Loh, *Tetrahedron Lett.* **2009**, *50*, 1051. For a review of our previous work on indium, see: f) T. P. Loh, G. L. Chua, *Chem. Commun.* **2006**, 2739.

[11] For selected examples concerning palladium-catalyzed coupling of R_3In or other types of organoindium reagents with various electrophiles (such as aryl halide, acid chloride, benzyl halide, alkenyl halide), see: a) M. A. Pena, J. P. Sestelo, L. A. Sarandeses, *Synthesis* **2005**, 485; b) M. A. Pena, I. Perez, J. P. Sestelo, L. A. Sarandeses, *Chem. Commun.* **2002**, 2246; c) R. Nomura, S.-I. Miyazaki, H. Matsuda, *J. Am. Chem. Soc.* **1992**, *114*, 2738; d) P. H. Lee, S. Sung, K. Lee, *Org. Lett.* **2001**, *3*, 3201; e) M. A. Pena, J. P. Sestelo, L. A. Sarandeses, *Synthesis* **2003**, 780; f) B. Gotov, J. Kaufmann, H. Schumann, H. G. Schmalz, *Synlett* **2002**, 361; g) N. Jaber, D. Gelman, H. Schumann, S. Dechert, J. Blum, *Eur. J. Org. Chem.* **2002**, 1628; h) K. Lee, J. Lee, P. H. Lee, *J. Org. Chem.* **2002**, *67*, 8265; i) K. Lee, D. Seomoon, P. H. Lee, *Angew. Chem.* **2002**, *114*, 4057; *Angew. Chem. Int. Ed.* **2002**, *41*, 3901; j) K. Takami, H. Yorimitsu, K. Oshima, *Org. Lett.* **2002**, *4*, 2993; k) P. H. Lee, S. W. Lee, K. Lee, *Org. Lett.* **2003**, *5*, 1103; l) K. Takami, S. Mikami, H. Yorimitsu, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2003**, *68*, 6627; m) P. H. Lee, S. W. Lee, D. Seomoon, *Org. Lett.* **2003**, *5*, 4963; n) M. A. Pena, J. P. Sestelo, L. A. Sarandeses, *J. Org. Chem.* **2007**, *72*, 1271; o) E. Font-Sanchis, F. J. Cespedes-Guirao, A. Sastre-Santos, F. Fernandez-Lazaro, *J. Org. Chem.* **2007**, *72*, 3589; p) J. Caeiro, J. P. Sestelo, L. A. Sarandeses, *Chem. Eur. J.* **2008**, *14*, 741; q) Y. Zhao, L. Jin, P. Li, A. Lei, *J. Am. Chem. Soc.* **2008**, *130*, 9429; r) L. Jin, Y. Zhao, L. Zhu, H. Zhang, A. Lei, *Adv. Synth. Catal.* **2009**, *351*, 630.

[12] For selected recent examples associated with the development of transition-metal-catalyzed cross-coupling reactions with wide functional-group compatibility, see: a) D. A. Everson, R. Shrestha, D. J. Weix, *J. Am. Chem. Soc.* **2010**, *132*, 920; b) A. Krasovskiy, C. Duplais, B. H. Lipshutz, *J. Am. Chem. Soc.* **2009**, *131*, 15592.

[13] Currently, we propose that the structure of the alkyl indium reagent is $RInX_2$ by analogy with the aryl and benzylic indium reagents that were previously developed by Knochel. In addition, the coordination of THF with the alkyl indium reagent was also observed (see the Supporting Information for the ^{1}H NMR spectrum of the alkyl indium reagent **2a**). A slight chemical shift of THF in the ^{1}H NMR spectra was also visible (OCH_2 moved downfield from $\delta = 3.76$ to 3.86 ppm), which might be because of its coordination to the indium center. In addition, the ratio of THF to alkyl group ($R = PhCH_2CH_2$) in the ^{1}H NMR spectra is approximately 1:1 (see the Supporting Information, page S15). Furthermore, it was interesting to find that the alkyl indium reagent **2a** could decompose when THF was completely removed under reduced pressure or when it was purified by silica-gel column chromatography. Therefore, the presence of THF might play an important role in the stabilization of the alkyl indium reagent **2a** by coordinating with the indium center. Thus, the following structure was proposed for the alkyl indium reagent **2a**.



For related crystal structures of organoindium reagents with a halide bridge and five-coordinated indium center, see: a) Y. Nishimoto, H. Ueda, Y. Inamoto, M. Yasuda, A. Baba, *Org. Lett.* **2010**, *12*, 3390; b) Y. Nishimoto, R. Moritoh, M. Yasuda, A. Baba, *Angew. Chem.* **2009**, *121*, 4647; *Angew. Chem. Int. Ed.* **2009**, *48*, 4577; c) M. Yasuda, M. Haga, A. Baba, *Organometallics* **2009**, *28*, 1998; d) M. Yasuda, K. Kiyokawa, K. Osaki, A. Baba, *Organometallics* **2009**, *28*, 132. Also see reference [13c] for a similar allylic indium species, which was reported to be stabilized by the coordination of THF/pathalan with the indium center. In addition, the authors stated that removal of reaction solvents (THF and acetonitrile) may lead to the decomposition of the allylic indium species.

[14] No visible hydrolysis of the alkyl indium reagent **2a** was observed when it was stirred in THF/H_2O (1:1) for 2 h. In addition, the fact that an excellent yield (93%) was obtained for the formation of **2a** when hydrate-containing $CuCl_2 \cdot 2H_2O$ was used as reaction additive (Table 1, entry 10) also proved that the alkyl indium reagent was not sensitive to water.

[15] For reviews of organic reactions in water, see: a) C. J. Li, T. H. Chan, *Tetrahedron* **1999**, *55*, 11149; b) C. J. Li, *Chem. Rev.* **2005**, *105*, 3095; c) C. J. Li, *Chem. Rev.* **1993**, *93*, 2023; d) C. J. Li, L. Chen, *Chem. Soc. Rev.* **2006**, *35*, 68; e) D. Dallinger, C. O. Kappe, *Chem. Rev.* **2007**, *107*, 2563; f) S. Kobayashi, A. K. Manabe, *Acc. Chem. Res.* **2002**, *35*, 209; g) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751; h) C. J. Li, *Acc. Chem. Res.* **2002**, *35*, 533; i) C. J. Li, *Green Chem.* **2002**, *4*, 1; j) H. Miyabe, T. Naito, *Org. Biomol. Chem.* **2004**, *2*, 1267; k) C. I. Herrerías, X. Q. Yao, Z. P. Li, C. J. Li, *Chem. Rev.* **2007**, *107*, 2546; l) K. K. Chauhan, C. G. Frost, *J. Chem. Soc. Perkin Trans. 1* **2000**, 3015; m) G. Babu, P. T. Perumal, *Aldrichimica Acta* **2000**, *33*, 16; n) T. P. Loh in *Science of Synthesis* (Ed.: H. Yamamoto), Georg Thieme, Stuttgart, **2004**, p. 413.

[16] The following solvents were screened for the conversion of 1-(2-bromoethyl)benzene to the corresponding alkyl indium reagent: THF, 65 °C, 24 h, <5% yield; 1,4-dioxane, 100 °C, 24 h, 38% yield; DMA, 100 °C, 24 h, >90% yield; DMF, 100 °C, 24 h, >90% yield. Considering that the subsequent palladium-catalyzed coupling reaction should be carried out in DMA, this was chosen as reaction solvent for the formation of the alkyl indium reagent from alkyl bromide.

