RESEARCH ARTICLE

Check for updates

Metallic salt-catalyzed direct indium insertion into alkyl iodides and their applications in cross-coupling reactions†

Bing-Zhi Chen,[a] Chuang-Xin Wang,[a] Zhen-Hua Jing,[a] Xue-Qiang Chu,[a] Teck-Peng Loh [ID] *[a,b] and Zhi-Liang Shen [ID] *[a]

An efficient method for the synthesis of alkyl indium reagents by means of an indium(III) or lead(II) halide-catalyzed direct insertion of indium into alkyl iodides and their applications in palladium-catalyzed cross-coupling reactions with aryl halides is developed. NMR and ESI-MS analyses indicated that rather than the formation of the commonly recognized alkyl indium sesquihalide with the formulation of $R_3In_2X_3$, the formed alkyl indium reagent in the present protocol should be a mixture of an alkyl indium dihalide ($RInX_2$) and a dialkyl indium halide (R_2InX) (both of them presumably exist as dimers).

Introduction

In recent decades, organoindium reagents[1] have been demonstrated to be intriguing and versatile organometallic compounds which usually exhibit mild reactivity, good functional group compatibility, and sometimes remarkably improved chemo- and stereoselectivity, as compared to other more reactive organometallic counterparts such as organolithium, organomagnesium, and organozinc species.[2] Normally, organoindium reagents are prepared either by the transmetallation of indium(III) halides with pre-prepared organolithium or organomagnesium reagents which display somewhat limited functional group tolerance as demonstrated by Nomura, Sarandeses, Perez Sestelo, Lee, Lei, and others,[3] or by the direct insertion of indium(0) into organic halides.[1,4] Among the various organoindium reagents prepared by the latter method, the use of more reactive allylic halides,[5] propargylic halides,[6] and α-halo carbonyl compounds[7] as substrates for direct indium insertion has been extensively investigated and used in organic synthesis, because of the easy preparation of these organoindium compounds and their good reactivity for undergoing the subsequent reactions with electrophiles. In comparison, the preparation of organoindium

reagents by using aryl halides,[8–10] alkyl halides,[11–14] benzyl halides,[15] alkenyl halides,[16] and acid chlorides[17] as substrates has mostly been developed only in recent ten years, as a consequence of the relatively poor reactivity of these organohalides and the lack of an efficient method for the activation of commercial indium metal to facilitate direct insertion. In this regard, the choice of an appropriate additive was found to greatly facilitate indium insertion. For instance, pioneered by Knochel and co-workers,[18] the research groups of Knochel,[8,15a,16] Lee,[6a–c,17] Minehan,[9] and Yoshikai[10] have disclosed that LiCl is a robust salt which substantially promotes the insertion of indium into various organic halides. In addition, our group and Lee's group have also shown that either CuX[11–13] or LiI[14] is an effective additive to boost the oxidative insertion of indium metal into alkyl halides. However, most of the previously developed methods employed stoichiometric amounts of additives to promote indium insertion into organic halides, which is not economical and does not adhere to the principles of Modern Organic Synthesis and Green Chemistry. Thus, the search for an efficient method which uses a catalytic amount of catalyst/additive to achieve the direct indium insertion into organic halides would be of great synthetic value and is more attractive in terms of economy, but has not been developed yet.[19]

On the other hand, it is generally accepted by chemists that the direct insertion of metals, such as Al, In, and Ga, into organic halides (R–X) should lead to the formation of organometallic sesquihalide with the formulation of $R_3M_2X_3$ (M = Al, In, and Ga),[8,15a,19,20] which is also considered to be an aggregated form of RMX_2 and R_2MX in a molar ratio of 1:1. However, until now this is only a conjecture of chemists and there exists no reliable evidence to support this. Thus, relevant

[a]*Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Jiangsu National Synergetic Innovation Center for Advanced Materials, Nanjing Tech University, Nanjing 211816, China. E-mail: ias_zlshen@njtech.edu.cn*
[b]*Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore. E-mail: teckpeng@ntu.edu.sg*
†Electronic supplementary information (ESI) available. See DOI: 10.1039/c8qo01244j

This journal is © the Partner Organisations 2019

Org. Chem. Front., 2019, **6**, 313–318 | 313

evidence is demanded to support or refute this surmise. In continuation of our efforts to develop indium chemistry,[21] herein we describe an efficient method for the synthesis of alkyl indium reagents *via* an indium(III) or lead(II) halide-catalyzed direct insertion of indium into alkyl iodides and their applications in palladium-catalyzed cross-coupling reactions with aryl halides. In addition, NMR analysis showed that the formed alkyl indium reagent should be a mixture of an alkyl indium dihalide ($RInX_2$) and a dialkyl indium halide (R_2InX), rather than the commonly recognized organoindium sesquihalide with the formulation of $R_3In_2X_3$.

Results and discussion

We commenced our investigation by first examining the insertion of indium into (2-iodoethyl)benzene (**1a**) in THF at 60 °C for 12 h in the presence of a variety of metallic salts (10 mol%) as reaction catalysts (Table 1). It was found that various metallic catalysts were able to catalyze the oxidative addition reaction with differing catalytic activities. Of the catalysts screened, $InCl_3$ emerged to be the most efficient catalyst for the insertion reaction to afford the desired alkyl indium reagent in 81% yield (entry 10). In addition, $CeCl_3$, $ZnCl_2$, and $PbBr_2$ were also proven to be effective catalysts for the reaction, leading to the alkyl indium reagent in relatively reduced but acceptable yields of 70%, 72% and 75%, respectively (entries 8, 9, and 15). The use of $CuBr_2$, $GaBr_3$, and PbI_2 also produced the corresponding organoindium reagent in acceptable yields ranging between 61–63% (entries 13, 14, and 17). In sharp contrast, no reaction occurred when the insertion reaction was performed in the absence of a catalyst (entry 1). It should be mentioned that a catalytic amount of metallic salt suffices to catalyze the indium insertion, and no extra manipulation regarding the pre-activation of the indium powder by using trimethylsilyl chloride and 1,2-dibromoethane is required,[8,15a] typical of the reagents used for metal pre-activation.[18,19] When the optimized reaction conditions were applied to the use of less reactive (2-bromoethyl)benzene or (2-chloroethyl)benzene as the substrate, only a trace amount of the corresponding alkylindium reagent was formed.

It should be mentioned that the formed alkyl indium reagent is relatively stable to moisture and air,[11] and thus the reaction can be directly performed in analytical grade THF (no pre-drying!) without the exclusion of air and moisture, which makes the present protocol operationally simple as compared to the preparation of other more reactive organometallic compounds (*e.g.*, RMgX, $RAlX_2$ or RZnX). In addition, the yield of the formed alkyl indium reagent can be easily calculated based on the NMR analysis of the crude reaction mixture against an internal standard after workup. As shown in Fig. 1, when the model reaction was performed by using 1.5 equiv. In and 0.75 equiv. $InCl_3$ (which might lead to the formation of 2.25 equiv. InCl) under optimized reaction conditions, the complete consumption of the starting material **1a** was observed and the formation of only one type of alkyl indium reagent (two triplet peaks **A**, Spectrum 2) was observed (86% NMR yield). We believed that the formed alkyl indium reagent should be an alkyl indium dihalide ($RInX_2$; peaks **A**) based on the following equation: $RI + InCl = RInX_2$ (X = Cl, I). In contrast, when the model reaction was conducted in the presence of 1.5 equiv. In and 0.1 equiv. $InCl_3$ under established reaction conditions (entry 10, Table 1), the generation of two types of alkyl indium species was detected on the basis of ^{1}H NMR analysis (overall 81% NMR yield, Spectrum 3), which should be the mixture of an alkyl indium dihalide
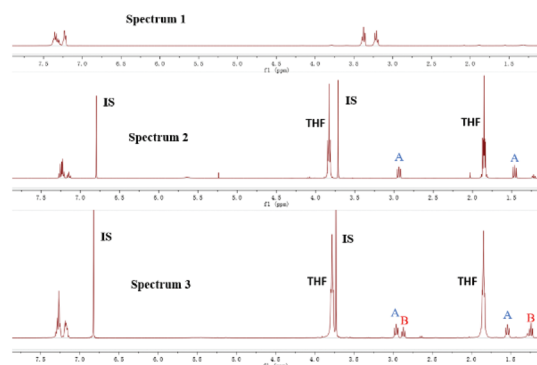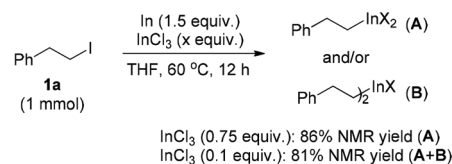
Table 1 Optimization of reaction conditions[a]

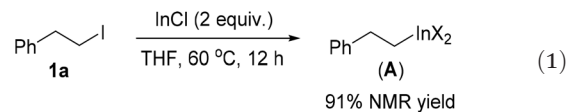| Entry	Catalyst	Yield[b] (%)	Entry	Catalyst	Yield[b] (%)
1	—	0	**10**	**$InCl_3$**	**81**
2	$TiCl_4$	15	11	$InBr_3$	50
3	$SnCl_4$	47	12	$ZnBr_2$	41
4	$PbCl_2$	32	13	$CuBr_2$	61
5	$GaCl_3$	41	14	$GaBr_3$	61
6	$CuCl_2$	41	**15**	**$PbBr_2$**	**75**
7	$AlCl_3$	45	16	ZnI_2	25
8	$CeCl_3$	70	17	PbI_2	63
9	$ZnCl_2$	72			

[a] The insertion step was performed at 60 °C for 12 h by using (2-iodoethyl)benzene (**1a**, 1 mmol), indium powder (1.5 mmol), and catalyst (0.1 mmol) in THF (2 mL). [b] The yield was determined by ^{1}H NMR analysis of the crude reaction mixture after workup by using 1,4-dimethoxybenzene as an internal standard.

Fig. 1 ^{1}H NMR spectra of substrate **1a** and the formed alkyl indium reagents by using different equivalents of $InCl_3$. **Spectrum 1**: starting material of (2-iodoethyl)benzene (**1a**); **Spectrum 2**: indium insertion by using indium (1.5 equiv.) and $InCl_3$ (0.75 equiv.); **Spectrum 3**: indium insertion by using indium (1.5 equiv.) and $InCl_3$ (0.1 equiv.); **IS**: internal standard of 1,4-dimethoxybenzene; **A**: alkyl indium dihalide ($RInX_2$); **B**: dialkyl indium halide (R_2InX).

314 | *Org. Chem. Front.*, 2019, **6**, 313–318

This journal is © the Partner Organisations 2019

(RInX$_2$; peaks **A**) and a dialkyl indium halide (R$_2$InX; two triplet peaks **B**), in the molar ratio of 10 : 3 (because the integration ratio of the two peaks **A** and **B** close to 3.0 ppm is 5 : 3). Conventionally, it is generally believed that the direct insertion of metals, such as Al, In, and Ga, into organohalides (R–X) should give rise to organometallic sesquihalide with the formulation of R$_3$M$_2$X$_3$ (M = Al, In, and Ga),[8,15a,19,20] which is also deemed to be an aggregated form of RMX$_2$ and R$_2$MX in the molar ratio of 1 : 1. However, in our case, on the basis of ^{1}H NMR analysis (Spectrum 3), no alkyl indium sesquihalide with the formulation of R$_3$In$_2$X$_3$ is formed, in view that the molar ratio of RInX$_2$ and R$_2$InX is 10 : 3 (not 1 : 1) which is in sharp contrast to the previous conjecture.[8,15a,19,20] As a result, we believed that the direct insertion of Al, In, and Ga into organohalides should lead to the formation of a mixture of RMX$_2$ and R$_2$MX, rather than the generation of organometallic sesquihalide (R$_3$M$_2$X$_3$).

ESI-MS (electrospray ionization mass spectrometry) analysis (Fig. 2) showed that four molecular ion peaks (m/z = 546.8486, 525.0145, 1092.6893, and 1049.0214) were detected (see pages S5 and 6 in the ESI† for details) and they could be attributed to [PhCH$_2$CH$_2$InI$_2$·THF + H]$^+$ (exact mass: 546.8486; see structure **A1**) and [(PhCH$_2$CH$_2$)$_2$InI·THF + H]$^+$ (exact mass: 525.0145; see structure **B1**), and their respective dimers [(PhCH$_2$CH$_2$InI$_2$·THF)$_2$ + H]$^+$ (exact mass: 1092.6893; see structure **A2**) and {[(PhCH$_2$CH$_2$)$_2$InI·THF]$_2$ + H}$^+$ (exact mass: 1049.0212; see structure **B2**), all with the coordination of THF to indium ions. Thus, we speculated that the formed alkyl indium reagents in the reaction presumably exist in the form of dimers **A2** and **B2**, and the detected monomers **A1** and **B1** might come from the fragmentation of dimers **A2** and **B2** during ESI-MS analysis. These results, to a large extent, proved the formation of a mixture of an alkyl indium dihalide (RInX$_2$) and a dialkyl indium halide (R$_2$InX) in the insertion reaction.

We envisaged that indium monohalide (InX), instead of indium metal, might be the real species which inserts into alkyl iodides. To verify the hypothesis, we also tested the direct insertion of InCl (2 equiv.) into alkyl iodide **1a** under the same reaction conditions (THF, 60 °C, 12 h; eqn (1)). As anticipated, the reaction worked equally well to generate only one type of alkyl indium reagent (RInX$_2$) in 91% NMR yield, highly indicating that InX might be the real indium species which undergoes oxidative addition to alkyl iodides, in view that direct indium insertion into alkyl iodides could not take place in the absence of an additive or catalyst (entry 1, Table 1).

$$\text{Ph}\diagdown\diagdown\text{I} \quad \underset{\text{THF, 60 °C, 12 h}}{\overset{\text{InCl (2 equiv.)}}{\xrightarrow{\hspace{2cm}}}} \quad \text{Ph}\diagdown\diagdown\text{InX}_2 \qquad (1)$$

1a → **(A)** 91% NMR yield

ESI-MS analysis (Fig. 3) showed that two molecular ion peaks (m/z = 454.9129 and 908.8180) were detected (see page S7 in the ESI† for details) and they could be attributed to [PhCH$_2$CH$_2$InICl·THF + H]$^+$ (exact mass: 454.9130; see structure **C1**) and its dimer [(PhCH$_2$CH$_2$InICl·THF)$_2$ + H]$^+$ (exact mass: 908.8181; see structure **C2**). Thus, we surmised that the formed alkyl indium reagents in the reaction presumably exist in the form of a dimer **C2**, and the detected monomer **C1** might arise from the fragmentation of dimer **C2** during ESI-MS analysis. These results also largely corroborated the generation of an alkyl indium dihalide (RInX$_2$) in the insertion reaction.

Having optimized the reaction conditions for the insertion step, next we applied the prepared alkyl indium reagent to palladium-catalyzed cross-coupling reactions. Toward this end, a series of aryl halides bearing various substituents were employed as coupling partners in the presence of Pd(PPh$_3$)$_4$ (5 mol%) and LiCl (2 equiv.) in dimethylacetamide (DMA)[11] at 100 °C for 24 h (Table 2). As expected, the formed alkyl indium reagent derived from substrate **1a** smoothly underwent the cross-coupling reactions to furnish the corresponding products
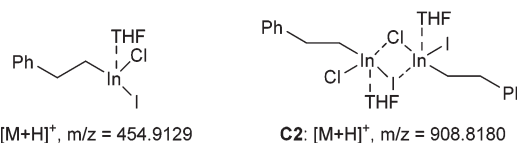

Fig. 3 Proposed structures of alkyl indium reagents formed in the InCl insertion reaction on the basis of ESI-MS analysis.
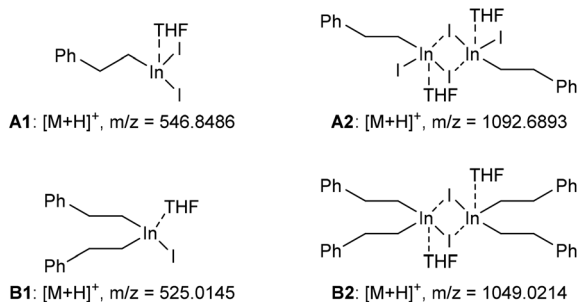
C1: [M+H]$^+$, m/z = 454.9129   **C2**: [M+H]$^+$, m/z = 908.8180

Table 2 Substrate scope study by using various aryl halides^a

2a (R = Ac), 86%	**2d**, 82%	**2e**, 86%	**2f** (X = I), 76%
2b (R = CN), 81%			**2g** (X = Br), 61%
2c (R = NO$_2$), 82%			
2h (X = I), 94%	**2k**, 54%	**2l**, 82%	**2m** (X = CH), 86%
2i (X = Br), 78%			**2n** (X = N), 89%
2j (X = Cl), 52%			

^{a} Isolated yield of the analytically pure product.

Fig. 2 Proposed structures of alkyl indium reagents formed in the InCl$_3$-catalyzed indium insertion reaction on the basis of ESI-MS analysis.

A1: [M+H]$^+$, m/z = 546.8486   **A2**: [M+H]$^+$, m/z = 1092.6893

B1: [M+H]$^+$, m/z = 525.0145   **B2**: [M+H]$^+$, m/z = 1049.0214

3a–n in moderate to good yields. In addition to aryl halides, heteroaryl iodides containing furyl (**2k**), pyridyl (**2m**), and pyrazinyl (**2n**) moieties were demonstrated to be suitable coupling partners for the reactions. Aside from more reactive aryl iodides, aryl bromides (**2g** and **2i**) and even the unreactive aryl chloride (**2j**) efficiently participated in the cross-coupling reactions to afford the expected products in moderate to good yields (52–78%). Aryl iodides **2c–e** containing a nitro group at the *para*, *meta*, and *ortho* position of the benzene ring reacted in a same manner with high efficiency to give the desired products **3c–e** in 82–86% yields. An array of important functional groups in the coupling electrophiles, including acetyl (**2a**), cyano (**2b**), nitro (**2c–e**), ethoxycarbonyl (**2f–g**), and even formyl (**2h–k**) groups, were capable of surviving the current reaction conditions completely intact, which potentially can be retained for further derivatization at a later stage.

To demonstrate the generality of the indium insertion reactions and the subsequent Pd-catalyzed cross-coupling reactions, a range of structurally varied alkyl iodides were explored as substrates (Table 3). Likewise, various alkyl iodides effectively underwent the present InCl$_3$-catalyzed direct indium insertion and the ensuing palladium-catalyzed cross-coupling with representative aryl iodide **2a**, delivering the anticipated cross-coupled products **4b–m** in moderate to good yields. Apart from primary alkyl iodides, secondary alkyl iodides **1l–m**, which normally reacted poorly in the other case,[11] worked equally well in the present protocol to give the anticipated products **4l–m** in 75–89% yields. Especially noteworthy is that versatile functional groups which are more or less sensitive to a base and a nucleophile, including chloro (**1e**), cyano (**1f**), ethoxycarbonyl (**1g**), benzoyl (**1h–i**), hydroxyl (**1j**), and OTBS (**1k**) groups, exhibited excellent compatibility with the present reaction conditions.

In a same manner, a catalytic amount of PbBr$_2$ was also able to catalyze the indium insertion into alkyl iodides, and the thus-formed alkyl indium compounds could also be successfully extended to palladium-catalyzed cross-coupling reactions with aryl iodides. As outlined in Table 4, reactions involving alkyl iodide **1a** and aryl halides **2a–c**, **2h**, and **2i** proceeded smoothly to generate the cross-coupled products in

Table 4 Substrate scope study by using PbBr$_2$ as the catalyst[a]

[a] Isolated yield of the analytically pure product.

64–89% yields. When alkyl iodides **1f**, **1h**, **1i**, and **1j** containing various functionalities (including cyano, benzoyl, and hydroxyl) were subjected to indium insertion in the presence of 10 mol% PbBr$_2$, the reactions proceeded with equal success to produce the corresponding products in 62–84% yields. In an analogous fashion, the secondary alkyl iodide of iodocyclohexane (**1l**) could be used as a substrate with equal ease, giving rise to the product **4l** in an acceptable yield of 50%.

As for the role of InCl$_3$ and PbBr$_2$, currently it is not clear.[19a,22] We speculated that the *in situ* generation of an InX (*via* the reaction of indium with metallic halide) as the key intermediate for direct insertion into alkyl iodides might be the key factor for the formation of the alkyl indium reagent.

Conclusions

In summary, we have developed an efficient InCl$_3$- and PbBr$_2$-catalyzed direct insertion of indium powder into alkyl iodides for the facile preparation of alkyl indium reagents. Upon palladium-catalyzed cross-coupling reactions with various aryl halides, a variety of cross-coupled products were obtained in moderate to good yields. The reactions, both in the insertion and cross-coupling steps, exhibit a broad substrate scope and excellent tolerance to sensitive functional groups. The reaction protocol is operationally simple which can be directly performed in analytical grade THF without the exclusion of air and moisture. Most importantly, one of the most advantageous features of the present protocol is that only a small quantity of metallic salt (10 mol%) is utilized as a reaction catalyst, which is superior when compared to previously reported methods where stoichiometric amounts of additives were employed as reaction promoters. Moreover, contrary to previous reports, NMR and ESI-MS analyses showed that the formed alkyl indium reagent should be a mixture of an alkyl indium dihalide (RInX$_2$) and a dialkyl indium halide (R$_2$InX) (both of them presumably exist as dimers), rather than the commonly recog-

Table 3 Substrate scope study by using various alkyl iodides[a]

[a] Isolated yield of the analytically pure product.

316 | *Org. Chem. Front.*, 2019, **6**, 313–318

This journal is © the Partner Organisations 2019

nized organoindium sesquihalide (or an aggregated form of $RInX_2$ and R_2InX) with the formulation of $R_3In_2X_3$. The application of the methodology for the synthesis of other types of organoindium reagents is currently being investigated in our laboratories.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1 For selected reviews regarding organoindium reagents, see: (*a*) Z.-L. Shen, S.-Y. Wang, Y.-K. Chok, Y.-H. Xu and T.-P. Loh, *Chem. Rev.*, 2013, **113**, 271; (*b*) K. Zhao, L. Shen, Z.-L. Shen and T.-P. Loh, *Chem. Soc. Rev.*, 2017, **46**, 586.

2 P. Knochel, *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, 2005.

3 For selected examples for the preparation of triorganoindium reagents (R_3In) by a transmetallation method, see: (*a*) R. Nomura, S. I. Miyazaki and H. Matsuda, *J. Am. Chem. Soc.*, 1992, **114**, 2738; (*b*) I. Perez, J. Perez Sestelo and L. A. Sarandeses, *Org. Lett.*, 1999, **1**, 1267; (*c*) I. Perez, J. Perez Sestelo and L. A. Sarandeses, *J. Am. Chem. Soc.*, 2001, **123**, 4155; (*d*) L. Alonso-Marañón, L. A. Sarandeses, M. M. Martínez and J. Pérez Sestelo, *Org. Chem. Front.*, 2017, **4**, 500; (*e*) K. Takami, H. Yorimitsu, H. Shinokubo, S. Matsubara and K. Oshima, *Org. Lett.*, 2001, **3**, 1997; (*f*) W. Lee, Y. Kang and P. H. Lee, *J. Org. Chem.*, 2008, **73**, 4326; (*g*) L. Bouissane, J. Perez Sestelo and L. A. Sarandeses, *Org. Lett.*, 2009, **11**, 1285; (*h*) P. H. Lee, S. W. Lee and K. Lee, *Org. Lett.*, 2003, **5**, 1103; (*i*) Y. Zhao, L. Jin, P. Li and A. Lei, *J. Am. Chem. Soc.*, 2008, **130**, 9429; (*j*) L. Jin, Y. Zhao, L. Zhu, H. Zhang and A. Lei, *Adv. Synth. Catal.*, 2009, **351**, 630; (*k*) S. Bernhardt, Z.-L. Shen and P. Knochel, *Chem. – Eur. J.*, 2013, **19**, 828.

4 For selected examples for the preparation of organoindium reagents by using other methods (*e.g.*, carboindation), see: (*a*) Y. Nishimoto, R. Moritoh, M. Yasuda and A. Baba, *Angew. Chem., Int. Ed.*, 2009, **48**, 4577; (*b*) Z.-L. Shen, K. K. K. Goh, H.-L. Cheong, C. H. A. Wong, Y.-C. Lai, Y.-S. Yang and T.-P. Loh, *J. Am. Chem. Soc.*, 2010, **132**, 15852; (*c*) Y. Park, J. Min, D. Eom and P. H. Lee, *Org. Lett.*, 2015, **17**, 3934.

5 (*a*) T. H. Chan and Y. Yang, *J. Am. Chem. Soc.*, 1999, **121**, 3228; (*b*) L. A. Paquette and T. M. Mitzel, *J. Am. Chem.*

Soc., 1996, **118**, 1931; (*c*) T.-P. Loh, K.-T. Tan, S.-S. Chng and H.-S. Cheng, *J. Am. Chem. Soc.*, 2003, **125**, 2958; (*d*) C.-J. Li, D.-L. Chen, Y.-Q. Lu, J. X. Haberman and J. T. Mague, *J. Am. Chem. Soc.*, 1996, **118**, 4216; (*e*) K. Lee, H. Kim, T. Miura, K. Kiyota, H. Kusama, S. Kim, N. Iwasawa and P. H. Lee, *J. Am. Chem. Soc.*, 2003, **125**, 9682.

6 (*a*) P. H. Lee, K. Lee and Y. Kang, *J. Am. Chem. Soc.*, 2006, **128**, 1139; (*b*) P. H. Lee and K. Lee, *Angew. Chem., Int. Ed.*, 2005, **44**, 3253; (*c*) K. Lee, D. Seomoon and P. H. Lee, *Angew. Chem., Int. Ed.*, 2002, **41**, 3901; (*d*) C. Zhu, X. Zhang, X. Lian and S. Ma, *Angew. Chem., Int. Ed.*, 2012, **51**, 7817; (*e*) M. J. Lin and T. P. Loh, *J. Am. Chem. Soc.*, 2003, **125**, 13042.

7 (*a*) S. A. Babu, M. Yasuda, I. Shibata and A. Baba, *Org. Lett.*, 2004, **6**, 4475; (*b*) P. H. Lee, D. Seomoon, K. Lee and Y. Heo, *J. Org. Chem.*, 2003, **68**, 2510.

8 Y.-H. Chen and P. Knochel, *Angew. Chem., Int. Ed.*, 2008, **47**, 7648.

9 V. Papoian and T. Minehan, *J. Org. Chem.*, 2008, **73**, 7376.

10 (*a*) L. Adak and N. Yoshikai, *J. Org. Chem.*, 2011, **76**, 7563; (*b*) L. Adak and N. Yoshikai, *Tetrahedron*, 2012, **68**, 5167.

11 Z.-L. Shen, K. K. K. Goh, Y.-S. Yang, Y.-C. Lai, C. H. A. Wong, H.-L. Cheong and T.-P. Loh, *Angew. Chem., Int. Ed.*, 2011, **50**, 511.

12 Z.-L. Shen, K. K. K. Goh, C. H. A. Wong, Y.-S. Yang, Y.-C. Lai, H.-L. Cheong and T.-P. Loh, *Chem. Commun.*, 2011, **47**, 4778.

13 S. Kim, C.-E. Kim, B. Seo and P. H. Lee, *Org. Lett.*, 2014, **16**, 5552.

14 B.-Z. Chen, M.-L. Zhi, C.-X. Wang, X.-Q. Chu, Z.-L. Shen and T.-P. Loh, *Org. Lett.*, 2018, **20**, 1902.

15 (*a*) Y.-H. Chen, M. Sun and P. Knochel, *Angew. Chem., Int. Ed.*, 2009, **48**, 2236; (*b*) L. S. Chupak, J. P. Wolkowski and Y. A. Chantigny, *J. Org. Chem.*, 2009, **74**, 1388.

16 Z.-L. Shen and P. Knochel, *Chem. – Eur. J.*, 2015, **21**, 7061.

17 D. Lee, T. Ryu, Y. Park and P. H. Lee, *Org. Lett.*, 2014, **16**, 1144.

18 For representative LiCl-facilitated Mg and Zn insertions into organic halides, see: (*a*) F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm and P. Knochel, *Angew. Chem., Int. Ed.*, 2008, **47**, 6802; (*b*) A. Krasovskiy, V. Malakhov, A. Gavryushin and P. Knochel, *Angew. Chem., Int. Ed.*, 2006, **45**, 6040.

19 For selected typical examples of metallic salt-catalyzed insertion of aluminum into organic halides, mostly in the presence of stoichiometric amounts of LiCl, see: (*a*) T. D. Blümke, Y.-H. Chen, Z. Peng and P. Knochel, *Nat. Chem.*, 2010, **2**, 313; (*b*) Z. Peng, T. D. Blümke, P. Mayer and P. Knochel, *Angew. Chem., Int. Ed.*, 2010, **49**, 8516; (*c*) T. D. Blümke, T. Klatt, K. Koszinowski and P. Knochel, *Angew. Chem., Int. Ed.*, 2012, **51**, 9926.

20 (*a*) S. Araki, H. Ito and Y. Butsugan, *J. Org. Chem.*, 1988, **53**, 1831; (*b*) M. J. S. Gynane and I. J. Worrall, *J. Organomet.*

Chem., 1974, **81**, 329; (*c*) K. Takai and Y. Ikawa, *Org. Lett.*, 2002, **4**, 1727.

21 For a review, see: (*a*) T.-P. Loh and G.-L. Chua, *Chem. Commun.*, 2006, 2739. For selected typical examples of indium chemistry developed in our group, see: (*b*) Y.-J. Zhao and T.-P. Loh, *J. Am. Chem. Soc.*, 2008, **130**, 10024; (*c*) L. Shen, K. Zhao, K. Doitomi, R. Ganguly, Y.-X. Li, Z.-L. Shen, H. Hirao and T.-P. Loh, *J. Am. Chem. Soc.*, 2017, **139**, 13570; (*d*) Z.-L. Shen and T.-P. Loh, *Org. Lett.*, 2007, **9**, 5413; (*e*) J.-F. Zhao and T.-P. Loh, *Angew. Chem., Int. Ed.*, 2009, **48**, 7232.

22 K. Takai, *Bull. Chem. Soc. Jpn.*, 2015, **88**, 1511, and references cited therein.