Atom-Efficient Metal-Catalyzed Cross-Coupling Reaction of Indium Organometallics with Organic Electrophiles

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Received December 7, 2000

Abstract: The novel metal-catalyzed cross-coupling reaction of indium organometallics with organic electrophiles is described. Triorganoindium compounds (R_3In) containing alkyl, vinyl, aryl, and alkynyl groups are efficiently prepared from the corresponding lithium or magnesium organometallics by reaction with indium trichloride. The cross-coupling reaction of R_3In with aryl halides and pseudohalides (iodide **2**, bromide **5**, and triflate **4)**, vinyl triflates, benzyl bromides, and acid chlorides proceeds under palladium catalysis in excellent yields and with high chemoselectivity. Indium organometallics also react with aryl chlorides as under nickel catalysis. In the cross-coupling reaction the triorganoindium compounds transfer, in a clear example of atom economy, all three of the organic groups attached to the metal, as shown by the necessity of using only 34 mol % of indium. The feasibility of using R_3In in reactions with different electrophiles, along with the high yields and chemoselectivities obtained, reveals indium organometallics to be useful alternatives to other organometallics in cross-coupling reactions.

Introduction

Transition metal-catalyzed cross-coupling reactions of organometallic compounds with organic electrophiles represent one of the most powerful methods for the construction of C−C bonds, especially between unsaturated carbons.[1] In recent years, the synthetic scope of this kind of reaction has been continuously expanded by the use of new organic electrophiles, catalysts, and organometallics. Hitherto, several organometallic nucleophiles have been useful in the palladium- or nickel-catalyzed reactions, particularly tin organometallics (Stille reaction),[2] organoboron compounds (Suzuki reaction),[3] and zinc or zinc−copper organometallics.[4] Other organometallic species have also been of use in synthesis.[5]

The development of new cross-coupling reactions with high degrees of conversion of the organometallic species, high chemo- and stereoselectivity, and the ability to form C−C bonds between all of the different carbon types (sp^3, sp^2, and sp) is still of great interest. In addition, the minimization of side-product formation[6] and the choice of processes with little or no risk associated to humans or the environment are major contemporary concerns.[7] A number of organometallic species used in cross-coupling reactions have shown limitations concerning the use of alkyl (sp^3) organometallics as coupling partners, the toxicity associated with the metal, or undesirable side reactions. The transfer of only one of the organic substituents attached to the metal has also been a significant handicap, this problem has sometimes been overcome by using mixed organometallic species[2,3] or catalytic amounts of the metal.[8] The discovery of an organometallic nucleophile of general use, regardless of the nature of the organic electrophile, is a worthwhile goal.

As part of a project aimed at finding new organometallic compounds that would be useful in organic synthesis, we recently discovered the palladium-catalyzed cross-coupling reaction of indium organometallics with vinyl and aryl triflates or iodides.[9] Here, we report in full the novel metal-catalyzed cross-coupling reactions of a wide array of triorganoindium compounds (R_3In, R = alkyl, alkenyl, alkynyl, aryl) with a variety of organic electrophiles, such as aryl halides and triflates, vinyl triflates, benzyl bromides, and acid chlorides (eq 1).

$$R_3In + 3\,R'{-}X \xrightarrow[\text{THF}]{\text{Pd or Ni catalyst}} 3\,R'{-}R \qquad (1)$$

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10.1021/ja004195m CCC: $20.00

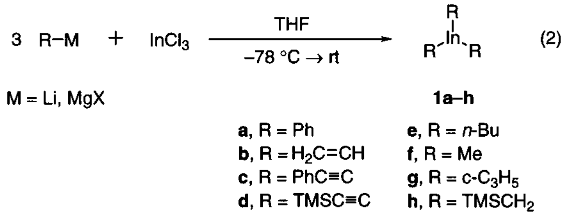
Results and Discussion

Indium Organometallics. Group 13 organometallics have in boron the most representative element, although aluminum also has useful synthetic applications. Indium has also warranted the attention of organic chemists in recent years. The apparent low toxicity[10] associated with indium as well as other interesting chemical properties, such as low nucleophilicity and heterophilicity or similarities with magnesium, zinc, and tin, makes indium organometallics attractive reagents for organic synthesis.[11]

During the past decade, indium has been extensively applied in allylation and related reactions under Barbier conditions in aqueous media[12] or in organic solvents.[13] On the other hand, the use of triorganoindium species (R_3In) has been limited thus far to the uncatalyzed cross-coupling reaction with electron-deficient alkenyl chlorides[14] and to our recently developed nickel-catalyzed 1,4-conjugate addition to electron-deficient olefins.[15]

Indium organometallics are readily accessible by different methods: (a) reaction between an organic halide and indium metal,[16] preferably using Rieke indium,[17] (b) transmetalation between an organomercury compound and indium metal,[18] and (c) metathesis reaction of lithium, magnesium, sodium, aluminum, or zinc organometallics with indium halides.[19]

In this study, triorganoindium compounds (R_3In) were prepared as solutions in THF by reaction of $InCl_3$ with readily available organolithium or Grignard reagents.[20] By following this method, we were able to access a wide range of triorganoindium compounds including aryl, vinyl, alkynyl and alkyl, derivatives (**1a**−**h**, eq 2). With the indium organometallics in hand, we proceeded to explore their reactivity in metal-catalyzed cross-coupling reactions toward organic electrophiles.



Cross-Coupling Reaction of Indium Organometallics with Aryl Electrophiles. Aryl halides and pseudohalides (such as triflates) are among the most common electrophiles in metal-catalyzed cross-coupling reactions.[1,2] For our initial studies on the participation of triorganoindium compounds in this kind of reaction, we chose as coupling partner 4-iodotoluene (**2**, Table 1). We found that reaction of triorganoindium reagents (R_3In) with 4-iodotoluene (1:1 ratio) in THF at reflux in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$, afforded the corresponding cross-coupling products in quantitative yields after short reaction times (1−4 h). Further experimental research showed that the amount of R_3In could be reduced to a 3:1 ratio of **2**/R_3In, keeping the yields still near to quantitative, a result that suggests that all three of the organic groups attached to indium are transferred. Moreover, the reaction proceeds in similar yields when other palladium(II) or palladium(0) complexes [$Pd(CH_3CN)_2Cl_2$, $Pd(PPh_3)_4$, $Pd_2(dba)_3$, $Pd(dppp)Cl_2$] are used, and with just 1 mol % loading.

On using 4-iodotoluene as the electrophile, all of the triorganoindium compounds (**1a**−**h**) afforded the coupling products in excellent yields (82−96%, Table 1) with just 34 mol % of R_3In and 1 mol % of $Pd(PPh_3)_2Cl_2$. The cross-coupling reaction efficiently transfers alkyl, both primary and secondary, vinyl, and alkynyl groups. Interestingly, the reaction with triphenylindium provides biphenyl **3a** in high yield (96%). In all of these reactions we also proved that, in contrast with all other metals employed in cross-coupling reactions, the triorganoindium compounds transfer to the electrophile all three groups attached to indium.

These initial results reveal indium organometallics to be powerful reagents in metal-catalyzed cross-coupling reactions. Boron or aluminum, which are in the same group as indium, can only transfer one group, as other metals used in cross-coupling reactions such as tin or zinc do. This extraordinary efficiency has only previously been observed by Nomura,[14] some years ago, for the addition of trialkylindium reagents to chloroalkenes and, more recently, in cross-coupling reactions of some boron compounds.[21]

After the first series of reactions using aryl iodide **2**, we studied the reactivity of indium organometallics with aryl triflate **4** (Table 2). Aryl triflates are an important family of electrophiles

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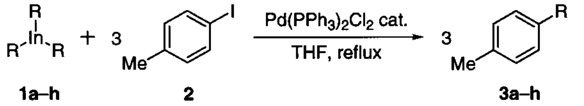
Table 1. Results of the Palladium-Catalyzed Cross-Coupling Reaction of Triorganoindium Compounds (**1a**−**h**) with 4-Iodotoluene (**2**)[a]



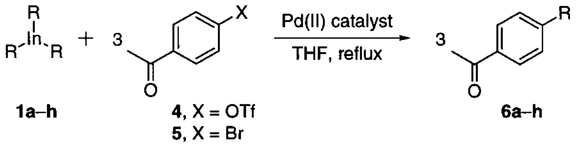
entry no.	R	*t* (h)	product	yield (%)[b]
1	Ph (**1a**)	1	**3a**	96
2	CH_2═CH (**1b**)	0.5	**3b**	89
3	PhC≡C (**1c**)	0.5	**3c**	90
4	TMSC≡C (**1d**)	1	**3d**	93
5	*n*-Bu (**1e**)	4	**3e**	82
6	Me (**1f**)	1	**3f**	85
7	*c*-C_3H_5 (**1g**)	3	**3g**	92
8	TMSCH_2 (**1h**)	2	**3h**	93

[a] Reactions were conducted in THF at reflux using 34 mol % of R_3In and 1 mol % of $Pd(PPh_3)_2Cl_2$. [b] Isolated yield based on the electrophile added.

in palladium-catalyzed cross-coupling reactions[22] due to their ease of preparation from readily available phenols and to the possibility of transforming the C−O bond into a C−C bond. The reaction of indium organometallics (**1a**−**h**) with aryl triflate **4**, in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$ (1 mol %), afforded the cross-coupled products in excellent yields (Table 2, entries 1−8). The reaction with triphenylindium (**1a**), trimethylindium (**1f**), tri-*n*-butylindium (**1e**), or tricyclopropylindium (**1g**) afforded the corresponding products in 89−96% yields. The use of other palladium catalysts, such as $Pd(PPh_3)_4$, led to similar yields. The reactions of vinyl and alkynyl indium reagents in the presence of $Pd(PPh_3)_2Cl_2$ as a catalyst gave lower yields (35−60%), with the starting triflate **4** being recovered. In these cases the use of a more reactive palladium catalyst, such as $Pd(dppf)Cl_2$[23] (1 mol %), improved the yields markedly (89−93%). In all cases, the reactions were carried out using just 34 mol % of the triorganoindium reagent, and the results are consistent with the transfer of all three groups attached to the indium. Furthermore, the reaction is chemoselective since nucleophilic addition to the carbonyl group was not detected.

Following the studies of the reactivity of indium organometallics in cross-coupling reactions with aryl halides and pseudohalides, the next electrophile to be assessed was 4′-bromoacetophenone (**5**). Aryl bromides are commonly used in cross-coupling reactions due to their ease of preparation and high stability. Aryl bromides usually have lower reactivity than the analogous iodides, with the choice of catalyst being particularly important in this case.[1,2] The metal-catalyzed cross-coupling of triorganoindium reagents (**1a**−**h**) with **5** (3:1 ratio Ar−Br/R_3In), using $Pd(PPh_3)_2Cl_2$ as the catalyst (1 mol %), afforded the corresponding coupled products in high yields (91−94%) and short reaction times (1−3.5 h, Table 2, entries 9−16). With vinyl-, alkynyl-, or cyclopropylindium reagents the yields were lower than in the corresponding cases in which $Pd(PPh_3)_2Cl_2$ was used as the catalyst, a situation similar to that occurring in the case of triflate **4**. However, when $Pd(dppf)Cl_2$ was employed, the yields were improved (Table 2, entries 10−12 and 15). As in the reaction with aryl triflate **4**, the reaction proceeds with high chemoselectivity since the products from nucleophilic addition to the carbonyl group were not detected by ^1H NMR spectroscopy.

Table 2. Results of the Palladium-Catalyzed Cross-Coupling Reaction of Triorganoindium Compounds (**1a**−**h**) with 4′-Substituted Acetophenones **4** and **5**[a]



entry no.	R	electrophile	*t* (h)	product	yield (%)[b]
1	Ph (**1a**)	**4**	3	**6a**	95
2[c]	CH_2═CH (**1b**)		3	**6b**	89
3[c]	PhC≡C (**1c**)		1	**6c**	94
4[c]	TMSC≡C (**1d**)		1	**6d**	93
5	*n*-Bu (**1e**)		1.5	**6e**	91
6	Me (**1f**)		4.5	**6f**	91
7	*c*-C_3H_5 (**1g**)		3	**6g**	89
8	TMSCH_2 (**1h**)		1	**6h**	96
9	Ph (**1a**)	**5**	1.5	**6a**	91
10[c]	CH_2═CH (**1b**)		2.5	**6b**	94
11[c]	PhC≡C (**1c**)		1.5	**6c**	94
12[c]	TMSC≡C (**1d**)		1	**6d**	91
13	*n*-Bu (**1e**)		1.5	**6e**	91
14	Me (**1f**)		1	**6f**	94
15[c]	*c*-C_3H_5 (**1g**)		3.5	**6g**	92
16	TMSCH_2 (**1h**)		1	**6h**	94

[a] Reactions were conducted in THF at reflux using 34 mol % of R_3In and 1 mol % of $Pd(PPh_3)_2Cl_2$, except for entries 2−4, 10−12, and 15. [b] Isolated yield based on the electrophile added. [c] $Pd(dppf)Cl_2$ (1 mol %) as catalyst.

The reactivity study on triorganoindium compounds in cross-coupling reactions was continued using aryl chlorides as electrophiles, that is, 4-chlorotoluene (**7**, eq 3). Chloroarenes have generally been seen as unreactive halides in metal-catalyzed cross-coupling reactions, but the recent development of new catalysts has allowed their participation under mild conditions and with low catalyst loading.[24] Indeed, these systems have been used in Stille[25] or Suzuki reactions under palladium catalysis[24,26] and in cross-coupling reactions with Grignard[27] or organozinc organometallics under nickel catalysis.[28] In our case, indium organometallics showed low reactivity toward aryl chloride **7** under palladium catalysis, even using Buchwald or Fu catalysts.[24] However, the use of Ni(0) catalysts (5 mol %)[29] provided satisfactory yields of the cross-coupling products **3a** and **3e** (74 and 83%, respectively). As in previous palladium-catalyzed reactions, the transfer of all three groups attached to

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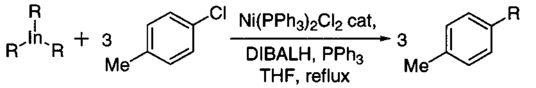
indium is also observed in nickel-catalyzed cross-coupling reactions.



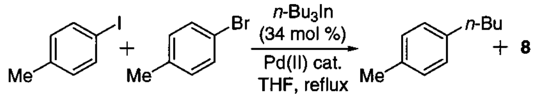
(3)

1a, R = Ph **7** **3a**, R = Ph, 74%

1e, R = *n*-Bu **3e**, R = *n*-Bu, 83%

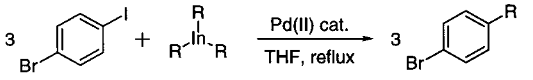
To explore the relative reactivities of triorganoindium reagents with aryl halides and triflates in palladium-catalyzed cross-coupling reactions, we carried out a number of competitive experiments. We performed the reaction of *n*-Bu_3In (34 mol %) with a 1:1 mixture of 4-iodotoluene (**2**, 100 mol %) and 4-bromotoluene (**8**, 100 mol %) in the presence of $Pd(PPh_3)_2Cl_2$ (1 mol %). We found that, after 5 h at reflux, the cross-coupling product **3e** was isolated in 80% yield, and all of the 4-bromotoluene was recovered (eq 4). When *n*-Bu_3In (34 mol %) was mixed with a 1:1 mixture of aryl triflate **4** (100 mol %) and bromide **5** (100 mol %), under the same reaction conditions as before, the coupling product **6e** was obtained in good yield, and equal quantities of the starting compounds were recovered. These results suggest that aryl iodides are more reactive than bromides and that bromides have a similar reactivity to triflates. This order of reactivity is similar to that observed with other organometallic species, and that led us to believe that the rate-limiting step in cross-coupling reactions with triorganoindium reagents is also the oxidative addition.

To study the possibility of performing a selective functionalization of polyhalogenated aryl derivatives with indium organometallics, we carried out the reactions of Ph_3In (**1a**) and *n*-Bu_3In (**1e**) with 4-bromoiodobenzene (**9**, eq 5). On using Ph_3In the cross-coupling product, 4-bromobiphenyl (**10a**), was obtained in 90% yield after 2 h refluxing, and with *n*-Bu_3In, 1-bromo-4-*n*-butylbenzene (**10e**) was obtained in 80% yield after 4 h at reflux. In both cases, reaction at the C−Br bond was not observed, suggesting that indium organometallics can be used to perform selective functionalization of polyhalogenated aryl compounds.



(4)

2 **8** **3e** (80%)



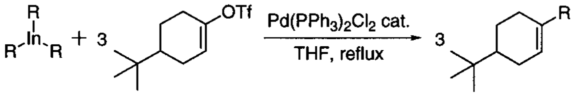
(5)

9 **1a**, R = Ph **10a**, R = Ph, 90%

1e, R = *n*-Bu **10e**, R = *n*-Bu, 80%

Cross-Coupling Reaction of Indium Organometallics with Other Electrophiles. To enlarge the scope of indium organometallics in metal-catalyzed cross-coupling reactions, we studied the reactivity toward other electrophiles, such as vinyl triflates, benzyl halides, and acid chlorides. As a representative example of a vinyl triflate we used **11** (Table 3). Vinyl triflates, which are readily available from suitable ketones, are useful organic electrophiles in cross-coupling reactions.[30] These compounds have been commonly used in natural product synthesis[31] and exhibit a similar reactivity to aryl iodides. As shown in Table 3, the cross-coupling reaction of triorganoindium compounds with vinyl triflate **11** (3:1 ratio **11**/R_3In), catalyzed by 1 mol % of $Pd(PPh_3)_2Cl_2$, afforded the corresponding products in excellent yields (89−97%) and with short reaction times (0.5−7 h). As in previous examples, the ratio of the reagents used and the yields obtained are consistent with the transfer of all three groups attached to indium.

Table 3. Results of the Palladium-Catalyzed Cross-Coupling Reaction of Triorganoindium Compounds (**1a**−**h**) with Vinyl Triflate **11**[a]



1a–h **11** **12a–h**

entry no.	R	*t* (h)	product	yield (%)[b]
1	Ph (**1a**)	1	**12a**	93
2	$CH_2{=}CH$ (**1b**)	0.5	**12b**	97
3	$PhC{\equiv}C$ (**1c**)	0.5	**12c**	95
4	$TMSC{\equiv}C$ (**1d**)	0.5	**12d**	93
5	*n*-Bu (**1e**)	1	**12e**	90
6	Me (**1f**)	7	**12f**	92
7	*c*-C_3H_5 (**1g**)	4	**12g**	90
8	$TMSCH_2$ (**1h**)	0.5	**12h**	89

[a] Reactions were conducted in THF at reflux using 34 mol % of R_3In and 1 mol % of $Pd(PPh_3)_2Cl_2$. [b] Isolated yield based on the electrophile added.

The cross-coupling reactions of organometallics with benzyl halides is usually an uncatalyzed process due to the high reactivity of the halides. Nevertheless, low nucleophilic organometallics (B, Al, Sn, Zn) require palladium or nickel catalysis.[29c,32] Generally, the reactions afford high yields with unsaturated organometallics. We explored the reactivity of triorganoindium compounds with benzyl bromide (**13** Table 4). The reaction of aryl, alkenyl, and alkynyl indium organometallics with **13**, with a 3:1 ratio of **13**/R_3In in the presence of 1 mol % of Pd(dppf)Cl_2, afforded the cross-coupling products with short reactions times (1−2.5 h) in almost quantitative yields (94−96%). When the corresponding reactions were carried out with trialkylindium compounds (Me_3In, *n*-Bu_3In) the yields were lower (10−20%), and the use of more reactive catalysts, higher temperatures, or different solvents did not improve the yields.

Another important group of electrophiles in cross-coupling reactions are the acid halides. Their reactions with organometallic compounds is a useful method for the synthesis of ketones, although sometimes nucleophilic addition to the resulting ketone takes place. The addition of low nucleophilic organometallics can be promoted using suitable catalysts, generally palladium complexes.[33] The low nucleophilicity of triorganoindium com-

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(29) Ni(0) catalysts were obtained by reduction of $Ni(PPh_3)_2Cl_2$ with DIBALH or *n*-BuLi in the presence of PPh_3 as a ligand, see: (a) Lipshutz, B. H.; Bulow, G.; Lowe, R. F.; Stevens, K. L. *J. Am. Chem. Soc.* **1996**, *118*, 5512−5513. (b) Lipshutz, B. H.; Blomgren, P. A.; Kim, S.-K. *Tetrahedron Lett.* **1999**, *40*, 197−200. (c) Lipshutz, B. H.; Bulow, G.; Fernandez-Lazaro, F.; Kim, S.-K.; Lowe, R.; Mollard, P.; Stevens, K. L. *J. Am. Chem. Soc.* **1999**, *121*, 11664−11673.

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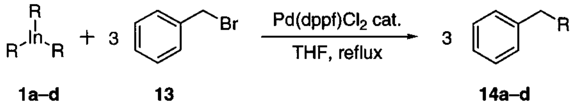
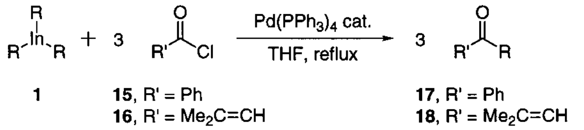
Table 4. Results of the Palladium-Catalyzed Cross-Coupling Reaction of Triorganoindium Compounds (**1a**−**d**) with Benzyl Bromide (**13**)[a]



entry no.	R	*t* (h)	product	yield (%)[b]
1	Ph (**1a**)	1	**14a**	96
2	CH$_2$=CH (**1b**)	1	**14b**	94
3	PhC≡C (**1c**)	2.5	**14c**	94
4	TMSC≡C (**1d**)	2.5	**14d**	94

[a] Reactions were conducted in THF at reflux using 34 mol % of R$_3$In and 1 mol % of Pd(dppf)Cl$_2$. [b] Isolated yield based on the electrophile added.

Table 5. Results of the Palladium-Catalyzed Cross-Coupling Reaction of Triorganoindium Compounds (**1**) with Acid Chorides **15** and **16**[a]



entry no.	R	electrophile	t (h)	product	yield (%)[b]
1	Ph (**1a**)	**15**	2	**17a**	89
2	PhC≡C (**1c**)		1	**17c**	94
3	Me (**1f**)		18	**17f**	97
4	Ph (**1a**)	**16**	1	**18a**	87
5	PhC≡C (**1c**)		2	**18c**	90
6	TMSC≡C (**1d**)		3	**18d**	90

[a] Reactions were conducted in THF at reflux using 34 mol % of R$_3$In and 1 mol % of Pd(PPh$_3$)$_4$. [b] Isolated yield based on the electrophile added.

pounds led us to explore their reactivity with acid chlorides (**15** and **16**, Table 5) under palladium catalyst. Ketones were obtained in good yields (87−97%) using Pd(PPh$_3$)$_4$ (1 mol %) as catalyst and a ratio of acid chloride/R$_3$In of 3:1. The results are summarized in Table 4, showing that all types of carbon groups can be accommodated. In these reactions, the tertiary alcohol resulting from double addition was not detected, and in the reaction with the α,β-unsaturated acid chloride **16**, we observed that the reaction is highly regioselective since the competitive conjugate addition was not observed (entries 4−6).

Mechanistic Insights. The mechanism for the palladium-catalyzed cross-coupling reaction of triorganoindium reagents with organic electrophiles can be explained in terms of the generally accepted mechanism for this type of reaction.[34] In accordance with our results, the rate-limiting step should be the oxidative addition. In this mechanism we must accept that both R$_2$InX and RInX$_2$ are leaving species in a catalytic cycle and both can re-enter in a new catalytic cycle and effectively transfer their organic groups. We tested this possibility by preparing *n*-Bu$_2$InCl and *n*-BuInCl$_2$ and using them in the palladium-catalyzed cross-coupling reaction with aryl triflate **4**.[20,35] The cross-coupling product **6e** was obtained in satisfactory yields (60−70%). The reason that indium is so efficient in the rapid transfer of the three organic groups attached can be explained in terms of the low bond strengths in the triorganoindium reagents and the large difference between the heats of formation of indium trialkyls and indium halides.[14,36]

Nevertheless, an alternative mechanism based on the high Lewis acid character of the indium reagents could modify the classical mechanism with the formation of a transient Pd−In complex as the step prior to the transmetalation.[37] Bimetallic complexes have been proposed by Marshall[38] in allenylindium additions to aldehydes and in cross-coupling reaction of arylboronic acids.[39]

Conclusions

In conclusion, we have developed a new and generally high-yielding metal-catalyzed cross-coupling reaction involving triorganoindium compounds. In this novel reaction triorganoindium reagents containing alkyl, vinyl, alkynyl, and aryl groups transfer, with high atom efficiency, the three organic groups to aryl, vinyl, benzylic, and acyl electrophiles in the presence of easily accessible palladium or nickel catalysts. The cross-coupling reaction proceeds in short reaction times and low catalyst loading with excellent yields and with high chemoselectivity, to provide an interesting range of compounds. These novel features make indium organometallics useful alternatives to other organometallics used in cross-coupling reactions and also mark them out as promising reagents for organic synthesis.

Experimental Section

General Methods. All reactions were conducted in flame-dried glassware under a positive pressure of argon. Reaction temperatures refer to external bath temperatures. All dry solvents were distilled under argon immediately prior to use. Tetrahydrofuran (THF) and diethyl ether (Et$_2$O) were dried by distillation from the sodium ketyl of benzophenone. Liquid reagents or reagent solutions were added by syringe or cannula. The total volume of solvent is given for these additions. Usually the compound was dissolved in 80% of the stated volume, and the flask was then rinsed with the remaining 20% of fresh solvent. Organic extracts were dried over anhydrous MgSO$_4$, filtered, and concentrated using a rotary evaporator at aspirator pressure (20−30 mmHg). Thin-layer chromatography was effected on silica gel 60 F$_{254}$ (layer thickness 0.2 mm), and components were located by observation under UV light or by treating the plates with a phosphomolybdic acid or *p*-anisaldehyde reagent followed by heating. Flash chromatography was performed on silica gel 60 (230−400 mesh) by Still's method.[40]

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Phenyllithium, *n*-butyllithium, methyllithium, (trimethylsilylmethyl)-magnesium chloride, vinylmagnesium bromide, and DIBALH were purchased from Aldrich and used after titration by known procedures.[41]

(2-Phenyl)ethynyllithium and 2-(trimethylsilyl)ethynyllithium were prepared from phenylacetylene and trimethylsilylacetylene by treatment with *n*-BuLi at −78 °C and warming to room temperature. These compounds were used immediately for the preparation of the corresponding triorganoindium compound. Cyclopropyllithium was prepared from cyclopropyl bromide by a halogen−metal exchange reaction with *t*-BuLi at −78 °C. The reaction mixture was warmed to room temperature and used immediately for the preparation of the tricyclopropylindium.

General Procedure for the Preparation of Indium Organometallics. A 25 mL round-bottomed flask furnished with a stirrer bar was charged with $InCl_3$ (0.37 mmol) and dried under vacuum with a heat gun. The mixture was cooled, a positive argon pressure was established, and dry THF (4 mL) was added. The resulting solution was cooled to −78 °C, and a solution of RLi or RMgBr (1.1 mmol, 1.0−1.8 M in hexanes, THF, or Et_2O) was slowly added (15−30 min). The mixture was stirred for 30 min, the cooling bath was removed, and the reaction mixture was warmed to room temperature.

General Procedure for the Palladium-Catalyzed Cross-Coupling Reaction. A solution of R_3In (0.34 mmol, ∼0.1 M in dry THF) was added to a refluxing mixture of the electrophile (1 mmol) and Pd catalyst (0.01 mmol) in dry THF (4 mL). The resulting mixture was refluxed under argon until the starting material had been consumed (TLC or GC), and the reaction was then quenched by the addition of few drops of MeOH. The mixture was concentrated in vacuo and Et_2O (30 mL) was added. The organic phase was washed with aqueous HCl (5%, 10 mL), saturated aqueous $NaHCO_3$ (15 mL), and saturated aqueous NaCl (15 mL), dried, filtered, and concentrated in vacuo. The residue was purified by flash chromatography to afford, after concentration and high-vacuum-drying, the cross-coupling product.

General Procedure for the Nickel-Catalyzed Cross-Coupling Reaction of Aryl Chlorides. To a solution of $Ni(PPh_3)_2Cl_2$ (0.05 mmol) and PPh_3 (0.10 mmol) in dry THF (5 mL) was added slowly a solution of *n*-BuLi in hexanes (55 μL, 0.08 mmol, 1.5 M) [or DIBALH in toluene (55 μL, 0.08 mmol, 1.5 M)] at room temperature. After 10 min, 4-chlorotoluene (1.00 mmol) was added, the resulting mixture was refluxed and a solution of R_3In (0.40 mmol, ∼0.1 M in dry THF) was added. The mixture was refluxed, until the starting material had been consumed (TLC or GC). The reaction was quenched by the addition of few drops of MeOH. The mixture was concentrated in vacuo, and Et_2O (30 mL) was added. The organic phase was washed with aqueous HCl (5%, 10 mL), saturated aqueous $NaHCO_3$ (15 mL), and saturated aqueous NaCl (15 mL), dried, filtered, and concentrated in vacuo. The residue was purified by flash chromatography to afford, after concentration and high-vacuum-drying, the cross-coupling product.

Acknowledgment. We are grateful to the Xunta de Galicia (XUGA 10305A98) and University of A Coruña for financial support. I.P. acknowledges a predoctoral fellowship from the Xunta de Galicia. We also thank Professor Dolores Pérez (Universidade de Santiago de Compostela, Spain) for critical reading of the manuscript.

Supporting Information Available: Relevant spectral data for compounds prepared (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA004195M

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[41] Brown, H. C. *Organic Synthesis via Boranes*; Wiley: New York, 1975; pp 248−249.