Rhodium-catalysed 1,4-addition of diarylindium hydroxides to α,β-unsaturated carbonyl compounds

Tomoya Miura and Masahiro Murakami*

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Diarylindium(III) hydroxides react with α,β-unsaturated carbonyl compounds in the presence of a rhodium catalyst to afford the 1,4-addition products in high yield. This reaction demonstrates the utility of diarylindium(III) hydroxide as an aryl source with rhodium catalysts.

The transmetalation between a main-group organometallic reagent and a transition metal catalyst is an important method to endow the original organometallic reagent with a different character of reactivities toward organic substrates. Indeed, a number of metal-mediated synthetic reactions involve the transmetalation as a key elementary step.[1] Recently, the rhodium-catalysed addition reactions of organometallic reagents to unsaturated functionalities have emerged as a new and useful method for the formation of carbon–carbon bonds under mild conditions.[2] An organorhodium intermediate generated by transmetallation from various organometallics like organo-boron, -silicon and -tin is reactive enough to add to α,β-unsaturated carbonyl compounds in a 1,4-fashion.[3]

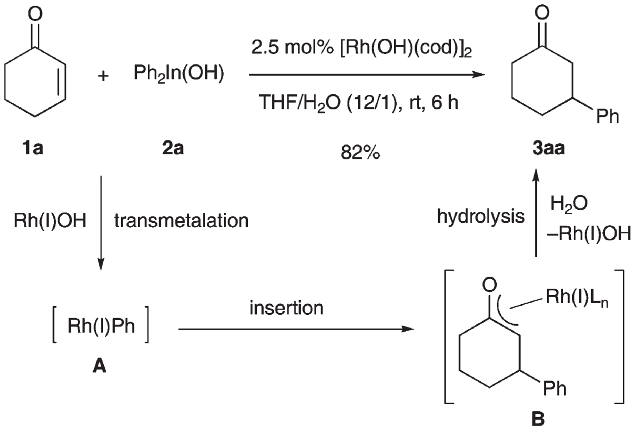
On the other hand, organoindium(III) reagents have attracted much attention as a carbon nucleophile source due to their high chemoselectivity and low toxicity.[4] In addition, organoindium(III) reagents have a synthetic advantage in that they are readily prepared from conventional organo-lithium and -magnesium reagents and then directly employed in an ensuing reaction without a need of anhydrous conditions because of their stability in aqueous media. These desirable properties led us to examine the rhodium-catalysed reaction of organoindium(III) reagents with unsaturated organic functionalities. Herein, we report the rhodium-catalysed 1,4-addition reaction of organoindium reagents to α,β-unsaturated carbonyl compounds in aqueous media, together with its extension to an asymmetric version.[5,6] This reaction demonstrates the utility of diarylindium(III) hydroxide as an aryl source with rhodium catalysts.

Initially, diphenylindium hydroxide (**2a**) was prepared by treatment of phenylmagnesium bromide (2.0 equiv.) with indium trichloride (1.0 equiv.) in THF at room temperature for 30 min followed by hydrolysis (10 min).[7] A THF solution of cyclohex-2-en-1-one (**1a**, 1.0 equiv.) and $[Rh(OH)(cod)]_2$ (0.05 equiv. in Rh) (cod = cycloocta-1,5-diene) were added successively to the resulting reaction mixture, which was further stirred for 6 h at room temperature. The 1,4-addition product **3aa** was isolated in 82% yield after aqueous workup (Scheme 1).[8] Formation of the Heck-type unsaturated product or the 1,2-addition product to the carbonyl group was not observed. The reaction pathway is assumed to proceed as follows: the transmetalation between organoindium reagent **2a** and a rhodium catalyst produces the arylrhodium intermediate **A**. Then, 1,4-addition of **A** to cyclohex-2-en-1-one (**1a**) occurs to afford the rhodium enolate **B**, which is hydrolysed by water to afford the product **3aa** and hydroxorhodium(I).

When diphenylindium chloride was used instead of diphenylindium hydroxide in dry THF, **3aa** was obtained in *ca.* 10% yield, although most of **1a** was consumed. These contrasting results can be explained by assuming that anionic ligands play an important role in transmetalation of the Rh(I) species with an indium(III)-phenyl linkage, and that a hydroxide anion is preferred over a chloride anion in terms of the electron-donating ability, as with the case of arylboronic acids.[9]

Results of the 1,4-addition of diarylindium hydroxides **2a–2e** to various α,β-unsaturated compounds **1a–1j** (**1** : **2** = 1 : 2) are summarised in Table 1.† The catalytic process worked well with a sterically and electronically diverse array of diarylindium hydroxides **2b–2e** to give the corresponding products **3ab–3ae** (entries 1–4). Reactions of enones **1b–1g**, including cyclic enones, afforded the β-phenylated ketones **3ba–3ga** in good yield (entries 5–10). Next, the 1,4-addition of **2a** to α,β-unsaturated esters, amides and nitriles was examined to expand the scope of the reaction. The reaction with methyl crotonate (**1h**) was also successful (entry 11). Crotonamide (**1i**) and crotononitrile (**1j**), whose reactivities are relatively low, afforded the products in moderate yield (entries 12 and 13).

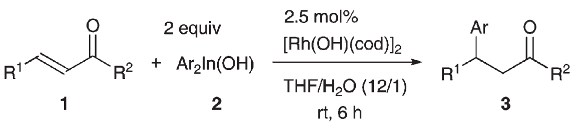
It should be noted that the use of chiral diene ligand **4**, developed by Carreira *et al.*, led to the formation of **3aa** in 97% yield with a good enantioselectivity of 94% ee (eqn 1).[10]

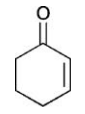
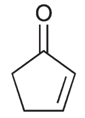
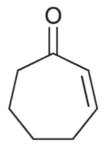
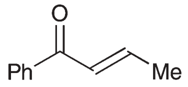
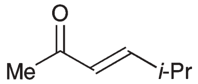
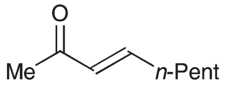
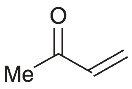
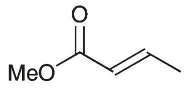
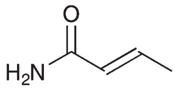
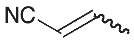


Scheme 1

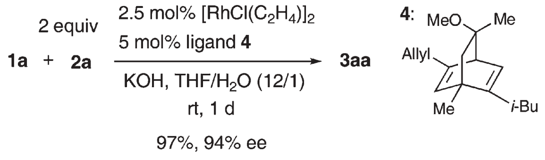
Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Katsura, Kyoto, 615-8510, Japan.
E-mail: murakami@sbchem.kyoto-u.ac.jp; Fax: +81 75 383 2748;
Tel: +81 75 383 2747

Table 1 Rhodium-catalysed 1,4-addition of diarylindium hydroxides



Entry	Substrate **1**		**2** (Ar)	Product **3**	Yield (%)[a]
1	**1a**		**2b** p-$CH_3C_6H_4$	**3ab**	94
2			**2c** o-$CH_3C_6H_4$	**3ac**	99
3			**2d** p-$CH_3OC_6H_4$	**3ad**	77
4			**2e** p-FC_6H_4	**3ae**	85
5	**1b**	 **1b**	**2a**	**3ba**	91
6	**1c**	 **1c**	**2a**	**3ca**	79
7	**1d**	 **1d**	**2a**	**3da**	88
8	**1e**	 **1e**	**2a**	**3ea**	73
9	**1f**	 **1f**	**2a**	**3fa**	85[b]
10	**1g**	 **1g**	**2a**	**3ga**	78
11	**1h**	 **1h**	**2a**	**3ha**	87
12	**1i**	 **1i**	**2a**	**3ia**	57[c]
13	**1j**	 **1j**	**2a**	**3ja**	40

[a] Isolated yields. [b] 3 equiv of **2a**. [c] **1i** remained after workup.



(1)

In summary, we have developed the rhodium-catalysed 1,4-addition of organoindium reagents to α,β-unsaturated carbonyl compounds, demonstrating the utility of diarylindium(III) hydroxide as an aryl source with rhodium catalysts.

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Notes and references

† Indium trichloride (221 mg, 1.0 mmol) was placed in an oven-dried, Ar-purged flask and dissolved with THF (1 mL). Arylmagnesium bromide (1.0 M THF solution, 2.0 mL, 2.0 mmol) was added dropwise to the solution at 0 °C. Then, the mixture was stirred at room temperature for 30 min to prepare diarylindium chloride. Water (0.5 mL) was added at 0 °C to form a white suspension. After the suspension was stirred at room temperature for 10 min, a solution of substrate **1** (0.5 mmol) in THF (3.0 mL) and $[Rh(OH)(cod)]_2$ (5.7 mg, 0.0125 mmol, 0.05 equiv of Rh) were added. The resulting reaction mixture was further stirred for 6 h at room temperature. Water (10 mL) was added, and the aqueous layer was extracted with ethyl acetate (15 mL × 3). The combined organic extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane–ethyl acetate) to give the product **3**.

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8 The product **3aa** was obtained in 62% yield and a small amount of **1a** remained when 1.0 equiv. of PhMgBr and 0.5 equiv. of $InCl_3$ were used. No reaction was observed without the rhodium catalyst.

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