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A rhodium-grafted hydrotalcite as a highly efficient heterogeneous catalyst for 1,4-addition of organoboron reagents to α,β-unsaturated carbonyl compounds

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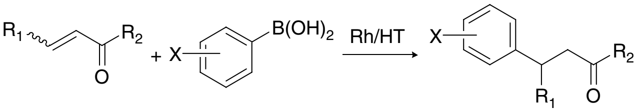
Abstract—Treatment of a hydrotalcite with an aqueous solution of rhodium trichloride results in a Rh-grafted hydrotalcite (Rh/HT) with monomeric Rh species on the surface, which successfully promoted 1,4-addition of organoboron reagents to α,β-unsaturated carbonyl compounds. Furthermore, this catalyst was reusable and was found to be applicable to a one-pot synthesis of 3,3-diarylnitrile.

Nanostructured heterogeneous catalysts with stable and well defined surface active sites, are currently receiving considerable attention, because their unique properties such as reusability and ease of handling and separation,[1] provide a means of addressing environmental and economic concerns. Hydrotalcites (HTs), which possess cation and anion exchange abilities, as well as strong surface basicity and adsorption capacity, are promising inorganic materials for the development of high-performance heterogeneous catalysts.[2–4] We recently reported new strategies for the design of solid catalysts, utilizing modified hydrotalcites for various organic reactions, such as epoxidation of olefins using hydrogen peroxide,[5a,b] oxidation of alcohols,[5c,d] and carbon–carbon bond formation, including one-pot syntheses.[5e–h]

Since carbon–carbon bond formation is one of the most important reactions in the synthetic organic chemistry, new catalytic methods are continually developed, employing not only acids and bases, but also transition metals, for efficient formation of a variety of carbon–carbon bonds. In 1997, Miyaura et al. reported a Rh-catalyzed 1,4-addition reaction of organoboron reagents to α,β-unsaturated carbonyl compounds.[6] The discovery of this new reaction triggered much research activity in the area of Rh-catalyzed carbon–carbon bond formation.[7–9] However, the homogeneous catalytic systems thus far developed often suffer from disadvantages such as requirements for toxic and expensive phosphine ligands, low catalytic activities, and tedious work-up procedures.[10] In this paper, we describe a rhodium-grafted hydrotalcite catalyst (Rh/HT) for highly efficient heterogeneous 1,4-addition of organoboronic acids to α,β-unsaturated carbonyl compounds (Scheme 1).

Preparation of the Rh/HT is as follows: the HT[11] (1.0 g), was added to 100 mL of an aqueous solution



Scheme 1. 1,4-Addition of arylboronic acids to α,β-unsaturated carbonyl compounds using the Rh/HT catalyst.

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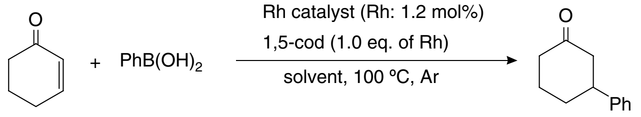
Table 1. 1,4-Addition of phenylboronic acid to 2-cyclohexene-l-one[a]



1 **2** **3**

Entry	Catalyst	Solvent	Yield (%)
1	Rh/HT	1,4-Dioxane	98
2[b]	Rh/HT	1,4-Dioxane	2
3	Rh/HT	Ethanol	98
4	Rh/HT	DME	97
5	Rh/HT	Toluene	36
6	Rh/HT	DMF	33
7	Rh/HT	*n*-Heptane	28
8	Rh/HT	THF	26
9	Rh/HT	Water	0
10	Rh/MgO	1,4-Dioxane	55
11	Rh/Mg(OH)$_2$	1,4-Dioxane	20
12	Rh/Al$_2$O$_3$	1,4-Dioxane	Trace
13	Rh/Al(OH)$_3$	1,4-Dioxane	0
14	RhCl$_3$·H$_2$O	1,4-Dioxane	0
15[c]	HT	1,4-Dioxane	0
16	None	1,4-Dioxane	0

[a] Reaction conditions: Rh catalyst (Rh; 0.012 mmol), 1,5-cyclooctadiene (0.012 mmol), 2-cyclohexene-l-one (1.0 mmol), phenyl boronic acid (1.0 mmol), solvent (2.0 mL), 100 °C, Ar, 4 h.

[b] Without l,5-cyclooctadiene.

[c] HT (0.06 g) was used.

of RhCl$_3$·nH$_2$O (Rh; 2.0×10^{-3} M), and the heterogeneous mixture was stirred at room temperature for 0.5 h. The solid product was separated by filtration, then, washed thoroughly with deionized water, and dried under vacuum at room temperature, affording Rh/HT as a pink powder (Rh content: 2.0 wt %). The Rh/HT was characterized by X-ray diffraction (XRD), and X-ray absorption fine structure (XAFS). The XRD peak positions of the Rh/HT were identical to those of the parent HT. The Rh K-edge XANES spectrum of the Rh/HT was similar to that of RhCl$_3$·nH$_2$O. In Fourier transformation (FT) of k^3-weighted Rh K-edge EXAFS, the lack of peaks around 2.0–3.0 Å showed that there were no Rh–Rh or Rh–O–Rh bonds in the Rh/HT. From these results, monomeric Rh(III) species is grafted on the HT surface.

The catalytic activity of the Rh/HT for the 1,4-addition reaction of phenylboronic acid (**2**) to 2-cyclohexen-1-one (**1**) was compared with those of various solid-supported Rh catalysts (Table 1). The Rh/HT combined with 1,5-cyclooctadiene (1,5-cod) exhibited the highest catalytic activity, giving 3-phenyl-cyclohexanone (**3**) in 98% yield (entry 1), while the reaction occurred only to a slight extent in the absence of 1,5-cod (entry 2).[12] Other heterogeneous Rh catalysts, such as Rh/MgO, Rh/Mg(OH)$_2$, Rh/Al$_2$O$_3$, and Rh/Al(OH)$_3$ were found to be less active (entries 10–13). Neither the RhCl$_3$·nH$_2$O precursor (entry 14) nor the parent HT (entry 15) gave any 1,4-addition products. In the Rh/HT-catalyzed reaction, 1,4-dioxane, ethanol, and dimethoxy ethane (DME) were found to be good solvents, affording 98%, 98%, and 97 % yields of the corresponding 1,4-adduct, respectively (entries 1, 3, and 4). In contrast, THF, toluene, *n*-heptane, and DMF were poor solvents (entries 5–8), and no reaction was observed in water (entry 9).

Table 2. 1,4-Addition of organoboron reagents to α,β-unsaturated carbonyl compounds using the Rh/HT catalyst[a]

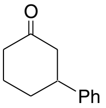
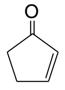
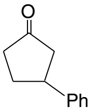
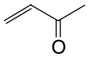
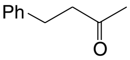
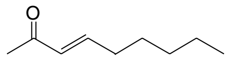
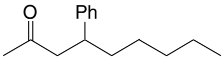
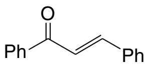
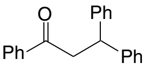
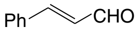
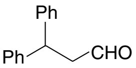
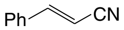
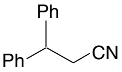
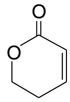
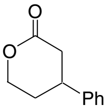
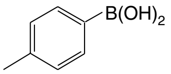
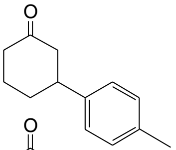
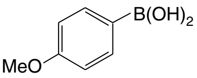
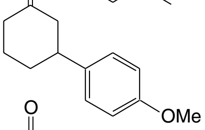
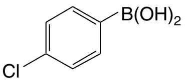
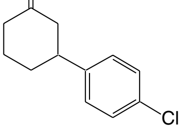
Entry	Acceptor	Donor	Product	Temperature (°C)	Time (h)	Yield[b] (%)
1	**1**	**2**		100	4	92
2[c]		**2**		150	5	75
3		**2**		100	4	92
4[c,d]		**2**		150	8	76
5[c,d]		**2**		150	24	99
6		**2**		150	4	74[e]
7		**2**		150	8	61[e]
8		**2**		100	4	61[e]

Table 2 (*continued*)

Entry	Acceptor	Donor	Product	Temperature (°C)	Time (h)	Yield[b] (%)
9	**1**			100	4	99
10	**1**			100	4	75
11	**1**			100	4	78

[a] Reaction conditions: Rh/HT (0.06 g; Rh: 0.012 mmol), 1,5-cyclooctadiene (0.012 mmol), acceptor (1.0 mmol), organoboron reagent (1.0 mmol), 1,4-dioxane (2.0 mL), 100 °C, Ar, 4 h.

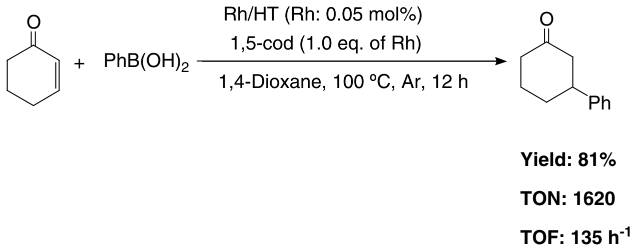
[b] Isolated yield based on acceptor.

[c] 1.5 equiv of organoboron reagent were used.

[d] Rh/HT (0.12 g; Rh: 0.024 mmol).

[e] GC yield.

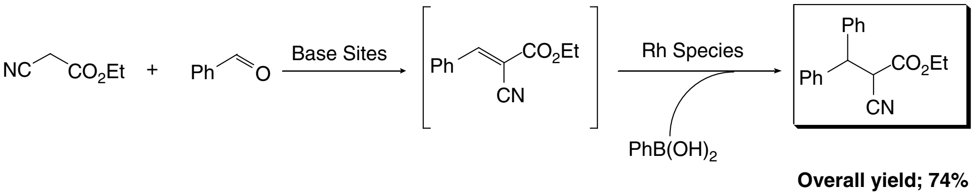
Table 2 presents a summary of 1,4-addition reaction of arylboronic acids to α,β-unsaturated carbonyl compounds in the presence of the Rh/HT catalyst and 1,4-dioxane solvent. Both aliphatic and aromatic enones were found to be good acceptors (entries 1–5); for example, methyl vinyl ketone readily reacted with **2** to give 4-phenyl-2-butanone in 92% isolated yield (entry 3). The Rh/HT catalyst system was found to be applicable to an α,β-unsaturated aldehyde and nitrile (entries 6 and 7): cinnamaldehyde reacted with **2** to give 3,3-diphenyl propanal, an important intermediate in the synthesis of quinoline synthesis,[13] without the formation of the 1,2-addition product (entry 6). Electron variation of *p*-substituted phenylboronic acids did not strongly affect product yields (entries 1, 9–11). A large-scale addition reaction of **2** to **1** using 0.05 mol % of the Rh/HT afforded **3** in 81% isolated yield[14] with a high TON of 1620 and TOF of 135 h^{-1}: these values are considerably higher than those previously reported for homogeneous reaction systems (TON; 1–100, TOF; 1–33 h^{-1})[7,15] (Scheme 2).



Scheme 2. Large scale 1,4-addition of phenylboronic acid to 2-cyclohexen-1-one catalyzed by the Rh/HT.

The spent Rh/HT catalyst was easily separated from the reaction mixture by simple filtration. The recovered catalyst was found to be reusable with retention of its high catalytic activity and selectivity; yields of over 90% were attained for at least the two catalyst-recycling reactions of **1** and **2**.[16] ICP analysis of the filtrate showed 2% leaching of Rh species during the above reactions, however, the filtrate was found not to promote the addition reaction.

A XANES spectrum of the used Rh/HT catalyst showed retention of +3 oxidation state of the Rh species on the HT. Based on the reaction mechanism reported for homogeneous Rh catalysts,[7b] the Rh/HT-catalyzed reaction may involve the transmetalation between the rhodium hydroxide[17] and arylboronic acid to give an arylrhodium species, followed by insertion of the enone. The rhodium enolate may then undergo hydrolysis to give the 1,4-addition product and a rhodium hydroxide species. Because formation of Rh clusters was observed during the reaction in the absence of 1,5-cod, it is



Scheme 3. Three-component reaction using the Rh/HT catalyst.

thought that 1,5-cod acts as a ligand for the surface Rh species, preventing aggregation.[18] However, studies on the mechanistic details and the structure of the Rh species are in progress.

The potential versatility of the Rh/HT was demonstrated by a one-pot synthesis of 3,3-diarylnitrile from **2**, benzaldehyde, and ethyl cyanoacetate. After the completion of the aldol reaction of ethyl cyanoacetate with benzaldehyde catalyzed by surface base sites on the HT, further reaction with **2** in the same reactor afforded 2-cyano-3,3-diphenyl propionate, an important precursor of (2*R*)-3,3-diphenyl-2-methylalanine,[19] in 74% overall yield (Scheme 3).[20]

In conclusion, we have demonstrated that the Rh/HT acts as an efficient catalyst for the 1,4-addition reaction of organoboron reagents to various α,β-unsaturated carbonyl compounds in the presence of 1,5-cod. The advantages of this reaction system include (i) high catalytic activity and selectivity, (ii) applicability toward diverse sets of substrates, (iii) simple work-up and catalyst reusability, and (iv) the possibility of one-pot synthesis. This Rh/HT catalyst could act as a pivotal tool in the development of economically and environmentally friendly carbon–carbon bond forming reactions.

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11. HT $[Mg_{0.827}Al_{0.173}(OH)_{1.930}(CO_3)_{0.090}(Cl)_{0.063}\cdot 0.62H_2O]$ was obtained from Tomita Pharmaceutical Co., Ltd.
12. For recent examples of 1,4-addition reactions using Rh-diene complex catalysts; see Refs. 7c–e.
13. Karageorge, G. N.; Bertenshaw, S.; Iben, L.; Xu, C.; Sarbin, N.; Gentile, A.; Dubowchik, G. M. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5881.
14. For the large-scale reaction, **1** (12 mmol), **2** (12 mmol), Rh/HT (0.030 g, Rh: 0.006 mmol), 1,5-cod (0.006 mmol), and 1,4–dioxane (20 mL) were used. The reaction mixture was vigorously stirred at 100 °C under Ar for 12 h. After the reaction, the catalyst was removed by filtration, and the filtrate was evaporated. The crude product was purified by silicagel column chromatography (*n*-hexane/ethyl acetate, 9:1), thus affording **3** as a colorless oil (81% isolated yield).
15. During the preparation of our manuscript, a high performance homogeneous rhodium catalyst (TOF = 14,000) for the 1,4-addition of arylboroxines to α,β-unsaturated ketones was reported. See: Chen, F.-X.; Kina, A.; Hayashi, T. *Org. Lett.* **2006**, *8*, 341.
16. In each recycling experiment, 1,5-cod was added.
17. During adsorption of metal species onto the HT surface, the strong surface basicity of the HT may induce formation of metal hydroxide species; see Refs. 5e,f.

18. In FT of k^3-weighted Rh K-edge EXAFS of a recovered Rh/HT after the reaction without 1,5-cod, peaks due to Rh–Rh bonds appeared at around 2.4 Å, which suggested the formation of Rh clusters.
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20. In a three-component reaction, a mixture of benzaldehyde (1 mmol), ethyl cyanoacetate (1 mmol), Rh/HT (0.060 g, Rh: 0.012 mmol), 1,5-cod (0.012 mmol), and 1,4-dioxane (2 mL) was vigorously stirred at 60 °C under Ar for 1 h. Then, **2** (1.5 mmol) was then added to the same flask, and allowed to further react at 100 °C under Ar for 8 h. After the reaction, the catalyst was separated by filtration. The filtrate was evaporated and the crude product was purified by column chromatography using silica (*n*-hexane/ethyl acetate, 9:1) to afford a pure ethyl 2-cyano-3,3-diphenylpropionate (74% isolated yield).