A Conjugate Addition of Arylboronic Acids to α,β-Unsaturated Carbonyl Compounds Catalyzed by 2β-CD-[Rh(OH)(cod)]$_2$ or [RhCl(cod)]$_2$ in a Single Aqueous Medium

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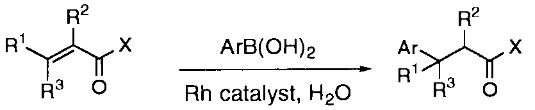
The rhodium-catalyzed conjugate addition of tolylboronic acid to α,β-unsaturated ketones, esters or amides was carried out in water. [RhCl(cod)]$_2$ and 2β-cyclodextrin-[Rh(OH)(cod)]$_2$ complexes were found to catalyze the reaction efficiently in a single aqueous medium.

Various rhodium(I) complexes catalyze the 1,4-addition of organostannanes[1] and organoboronic acids[2] to α,β-unsaturated carbonyl compounds or the Grignard-type addition to aldehydes[3,4] in an organic solvent or a mixture of an organic solvent and water. The reaction provides a convenient method for the asymmetric carbon-carbon bond formation.[5–7] We report here a new addition reaction of arylboronic acids that smoothly occurs in a single aqueous medium for both liquid and solid α,β-unsaturated carbonyl compounds (eq 1).[8]



(1)

X= alkyl, aryl, OR, NHR

The addition of p-tolylboronic acid (1.5 equiv) to 2-cyclohexenone in water was carried out in the presence of various catalysts to optimize the reaction conditions (Table 1). The rhodium(I)-cyclooctene (coe) (entry 1), -ethylene, and -norbornadiene (nbd) (entry 3) complexes were not effective, but addition of 1,5-cyclooctadiene (cod) (1–3 equiv to Rh) resulted in a quantitative conversion of the enone within 6 h at 90 °C (entries 2 and 4). Analogously, various cationic and neutral rhodium complexes possessing a cod ligand were found to exhibit excellent catalyst activity (entries 5–9). Although rhodium-phosphine complexes have been investigated extensively to extend the reactions to asymmetric synthesis,[5–7] a small and less-donating cod is the best ligand for achieving a high turnover number of the catalyst (TON). Under analogous conditions at 100 °C in water, [RhCl(cod)]$_2$ (0.001 mol%) exhibited 46000 TON in the addition of p-tolylboronic acid to methyl vinyl ketone and 24000 TON for the addition to 2-cyclohexenone.

Table 1. Effect of catalyst[a]

Entry	Rh complex	Ligand (equiv)	Temp (°C) /Time (h)	Yield/%
1	[RhCl(coe)$_2$]$_2$[b]	none	90/6	0
2	[RhCl(coe)$_2$]$_2$[b]	cod (3)	90/6	91
3	[RhCl(nbd)]$_2$[c]	none	90/6	0
4	[RhCl(nbd)]$_2$[c]	cod (1)	90/6	93
5	[Rh(cod)(MeCN)$_2$]BF$_4$[d]	none	90/6	84
6	[Rh(cod)$_2$]BF$_4$[d]	none	90/6	93
7	Rh(acac)(cod)[d]	none	90/6	86
8[e]	[RhCl(cod)]$_2$[d]	none	90/6	99
9[e]	[RhCl(cod)]$_2$[d]	none	50/6	93
10[e]	2β-CD-[RhCl(cod)]$_2$[d,f]	none	50/6	87
11[e]	2β-CD-[RhCl(cod)]$_2$[d,f]	none	25/16	42
12[e]	2β-CD-[Rh(OH)(cod)]$_2$[d,f]	none	50/6	99
13[e]	2β-CD-[Rh(OH)(cod)]$_2$[d,f]	none	25/16	73
14	Rh(acac)(coe)$_2$[b]	TPPMS[g] (2)	90/6	5
15	Rh(acac)(coe)$_2$[b]	TPPTS[h] (2)	90/6	8

[a] A mixture of 2-cyclohexenone (1.0 mmol) and p-tolylB(OH)$_2$ (1.5 mmol) was stirred for 6 h in the presence of Rh complex (3 mol%) and ligand (0–9 mol%), unless otherwise noted. [b] coe=cyclooctene. [c] nbd=norbornadiene. [d] cod=1,5-cyclooctadiene. [e] 1 mol% of catalyst was used. [f] β-CD=β-cyclodextrin. [g] TPPMS=Ph$_2$(m-NaO$_3$SC$_6$H$_4$)P. [h] TPPTS=(m-NaO$_3$SC$_6$H$_4$)$_3$P.

It was previously reported by Harada that [RhCl(cod)]$_2$ smoothly reacts with β-cyclodextrin (CD) to give a 1:1 inclusion complex.[9] The reaction provided a simple method for conversion of metal complexes to water-soluble catalysts. The complex indeed accelerated the reaction significantly, thus achieving 87% yield at 50 °C and 42% at 25 °C (entries 10 and 11). We previously proposed that the catalytic cycle involves (a) transmetalation between ArB(OH)$_2$ and a RhOH complex yielding an Ar-Rh species, (b) insertion of an alkene into the Rh-C bond, (c) finally, hydrolysis of a rhodium enolate intermediate with water giving a 1,4-addition product and a Rh(OH) species. In good agreement with this hypothesis, a change of rhodium precursors from [RhCl(cod)]$_2$ to [Rh(OH)(cod)]$_2$ further accelerated the reaction. A new (hydroxo)rhodium-β-cyclodextrin complex[10] prepared from β-cyclodextrin and [Rh(OH)(cod)]$_2$ catalyzed the reaction at lower reaction temperature than that of the RhCl complex, achieving a quantitative yield at 50 °C and 73% yield at 25 °C (entries 12 and 13). On the other hand, addition of Ph$_3$P (2 equiv) to Rh(acac)(coe)$_2$ or water-soluble triarylphosphine such as TPPMS and TPPTS resulted in low yields (entries 14 and 15).

The additions of p-tolylboronic acid to the representative α,β-unsaturated ketones, esters and amides are summarized in Table 2.[11] Both [RhCl(cod)]$_2$ and 2β-CD-[Rh(OH)(cod)]$_2$ (0.1 mol%) were highly effective for solid and liquid α,β-unsaturated ketones and esters. The isolated yields by chromatography often exceeded 90% for the representative α,β-unsaturated

Table 2. Addition of 4-tolylboronic acid to α,β-unsaturated carbonyl compounds in water[a]

Entry	Carbonyl Compound	Catalyst (mol%)	Temp/°C	Time/h	Yield/%[b]
1	(*E*)-PhCH=CHCOPh	$[RhCl(cod)]_2$ (0.1)	90	6	95
2	(*E*)-PhCH=CHCOPh	2β-CD-$[Rh(OH)(cod)]_2$ (0.1)	50	16	94
3	(*E*)-PhCH=CHCOCH$_3$	$[RhCl(cod)]_2$ (0.1)	90	6	92
4	(*E*)-PhCH=CHCOCH$_3$	2β-CD-$[Rh(OH)(cod)]_2$ (0.1)	50	24	89
5	2-cyclohexenone	$[RhCl(cod)]_2$ (0.1)	90	6	88
6	2-cyclohexenone	2β-CD-$[Rh(OH)(cod)]_2$ (0.1)	50	6	94
7	(*E*)-PhCH=CHCO$_2$CH$_3$	$[RhCl(cod)]_2$ (0.1)	90	6	99
8	(*E*)-PhCH=CHCO$_2$CH$_3$	2β-CD-$[Rh(OH)(cod)]_2$ (0.1)	50	16	87
9	(*E*)-CH$_3$CH=CHCO$_2$CH$_3$	$[RhCl(cod)]_2$ (0.1)	90	6	49
10	(*E*)-CH$_3$CH=CHCO$_2$CH$_3$	$[RhCl(cod)]_2$ (0.1)/cod (3)	90	6	85
10	(*E*)-CH$_3$CH=CHCO$_2$CH$_3$	2β-CD-$[Rh(OH)(cod)]_2$ (0.1)	50	16	79
11	(*E*)-CH$_3$CH=CHCONHCH$_2$Ph	$[RhCl(cod)]_2$ (0.1)/cod (3)	90	6	54

[a]A mixture of α,β-unsaturated carbonyl compound (1.0 mmol), *p*-tolylB(OH)$_2$ (1.5 mmol) and a catalyst in water was stirred at the temperature and for the period shown in Table 2. [b]Isolated yields by chromatography.

ketones and methyl cinnamate (entries 1–8). However, $[RhCl(cod]_2$ resulted in low yields in the slower reaction of methyl crotonate, presumably due to decomposition of the catalyst via dissociation of the cod ligand from the metal (entry 9). It was found that an addition of cod in large excess (30 equiv to Rh) serves to keep the catalyst activity (entry 10). However, it was still not effective for solid amides such as *N*-benzylcrotonamide (entry 11).

References and Notes

1 S. Oi, M. Moro, S. Ono, and Y. Inoue, *Chem. Lett.*, **1998**, 83.

2 M. Sakai, H. Hayashi, and M. Miyaura, *Organometallics*, **16**, 4229 (1998).

3 M. Sakai, M. Ueda, and N. Miyaura, *Angew. Chem. Int. Ed.*, **37**, 3279 (1998); M. Ueda and N. Miyaura, *J. Org. Chem.*, **65**, 4450 (2000).

4 S. Oi, M. Moro, Y. Inoue, *J. Chem. Soc., Chem. Commun.*, **1997**, 1621.

5 Y. Takaya, M. Ogasawara, T. Hayashi, M. Sakai, and N. Miyaura, *J. Am. Chem. Soc.*, **120**, 5579 (1998).

6 S. Sakuma, M. Sakai, R. Itooka, and N. Miyaura, *J. Org. Chem.*, **65**, 5951 (2000).

7 T. Hayashi, T. Senda, and M. Ogasawara, *J. Am. Chem. Soc.*, **122**, 10716 (2000); T. Hayashi, T. Senda, Y. Takaya, M. Ogasawara, *J. Am. Chem. Soc.*, **121**, 11591 (1999).

8 Recently, the rhodium-catalyzed 1,4-addition of Ph$_3$Bi to unsaturated carbonyl compounds was carried out in aqueous media: S. Venkatraman and C-J. Li, *Tetrahedron Lett.*, **42**, 781 (2001).

9 A. Harada, S. Yamamoto, and S. Takahashi, *Organometallics*, **8**, 2560 (1989).

10 A reaction of $[Rh(OH)(cod)]_2$ (0.12 mmol) and β-cyclodextrin (0.24 mmol) in water (15 mL) at 40 °C precipitated a yellow complex (51%).

11 **Typical Procedure (Table 2).** A flask was charged with 2β-CD-$[Rh(OH)(cod)]_2$ (0.001 mmol) and *p*-tolylboronic acid (1.5 mmol), and flushed with argon. Water (3 mL) and an α,β-unsaturated carbonyl compound (1.0 mmol) were then added. The mixture was stirred for 6 h at 50 °C. The product was isolated by chromatography over silica gel.