Platinum-catalyzed 1,4-Addition of Arylboronic Acids to *β*-Substituted *α*,*β*-Unsaturated Ketones

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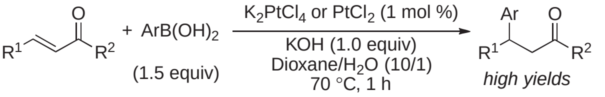
Platinum salts represented by K_2PtCl_4 were found to catalyze the 1,4-addition of arylboronic acids to β-substituted α,β-unsaturated ketones to give high yields of β-arylated ketones. The reaction is completed in 1 h in the presence of 1 mol % of the catalyst in dioxane/H_2O at 70 °C.

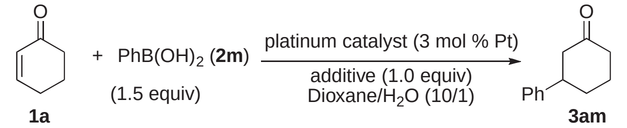
Catalytic 1,4-addition of organoboronic acids to α,β-unsaturated ketones and other electron-deficient olefins has been attracting considerable attention owing to its high utility in organic synthesis.[1] The reaction was first reported by Miyaura et al. in 1997 to be catalyzed by a rhodium complex,[2,3] and the rhodium-catalyzed 1,4-addition reactions have been extended successfully to catalytic asymmetric reactions by use of rhodium catalysts bearing chiral phosphine or diene ligands.[4,5] Palladium–phosphine complexes were also found to be active catalysts for the 1,4-addition of arylboronic acids.[6] More recently, the 1,4-addition was reported to be catalyzed by nickel[7] and ruthenium[8] complexes. Another new entry into the 1,4-addition catalyst group is platinum. A platinacycle generated by ortho-platination of tri(2,4-di-*tert*-butylphenyl)phosphite was reported by Bedford et al.[9] and by Hu et al.[10] to catalyze the 1,4-addition of phenylboronic acid to chalcone. Here, we report that the 1,4-addition of arylboronic acids to α,β-unsaturated ketones is efficiently catalyzed by simple platinum salts such as K_2PtCl_4 and $PtCl_2$ under mild conditions without any additional ligands (eq 1).



(1)

In the first set of experiments, we examined several platinum salts and complexes (3 mol %) for their catalytic activity toward the addition of phenylboronic acid (**2m**) to 2-cyclohexen-1-one (**1a**) (Table 1). It was found that K_2PtCl_4 is an efficient catalyst, giving a quantitative yield of 1,4-addition product **3am** in the presence of KOH (1 equiv) in dioxane/H_2O (10/1) at 70 °C for 4 h (Entry 1). The catalytic activity of K_2PtCl_4 is so high that the catalyst loading can be reduced to 1 mol % and the reaction time can be shortened to 1 h while maintaining the high yield of **3am** (Entry 2). The use of KOH is important for the present reaction. It can be replaced by NaOH or K_3PO_4, but the 1,4-addition did not take place without base additives (Entries 4–7). $PtCl_2$ and platinum/olefin complexes, $[PtCl_2(C_2H_4)]_2$ and $PtCl_2$(cod), are as catalytically active as K_2PtCl_4 (Entries 8–11). A lower yield (70%) of **3am** was observed in the presence of $PtCl_2(PPh_3)_2$ (Entry 11). The catalytically active species may be a phosphine-free platinum complex generated by dissociation of PPh_3 from $PtCl_2(PPh_3)_2$, considering that the reaction is not catalyzed by other platinum/phosphine complexes where the phosphine dissociation is less probable (Entries 12–14).

Table 1. Platinum-catalyzed 1,4-addition of phenylboronic acid (**2m**) to 2-cyclohexen-1-one (**1a**)

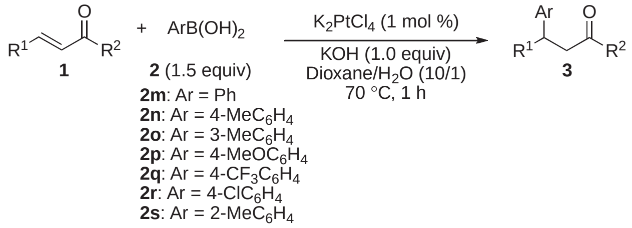


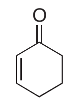
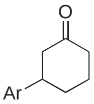
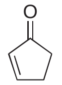
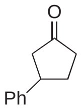
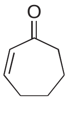
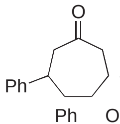
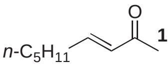
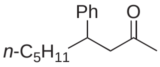
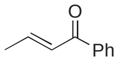
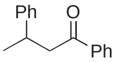
Entry	Catalyst	Additive	*T* /°C	Time /h	Yield/%[a] **3am**
1	K_2PtCl_4	KOH	70	4	>98
2[b]	K_2PtCl_4	KOH	70	1	>98
3	K_2PtCl_4	KOH	30	24	>98
4	K_2PtCl_4	—	70	4	0
5	K_2PtCl_4	NaOH	70	4	>98
6	K_2PtCl_4	K_3PO_4	70	4	>98
7	K_2PtCl_4	NEt_3	70	4	0
8	$PtCl_2$	KOH	70	4	>98
9	$[PtCl_2(C_2H_4)]_2$	KOH	70	4	>98
10	$PtCl_2$(cod)	KOH	70	4	>98
11	$PtCl_2(PPh_3)_2$	KOH	70	4	70
12	$PtCl_2(PEt_3)_2$	KOH	70	4	0
13	$PtCl_2$(dppe)	KOH	70	4	0
14	$PtCl_2$(binap)	KOH	70	4	0
15	$Pt(dba)_2$	KOH	70	4	55

[a] Determined by ^1H NMR using an internal standard ($MeNO_2$).
[b] In the presence of 1 mol % of K_2PtCl_4.

Under the conditions using K_2PtCl_4 as a catalyst and one equiv (to enone **1**) of potassium hydroxide in dioxane/H_2O at 70 °C for 1 h, several arylboronic acids **2m**–**2s** were found to add to 2-cyclohexen-1-one (**1a**) to give the corresponding 1,4-addition products **3am**–**3as** in high yields (Table 2,[11] Entries 1–9). In addition to the unsubstituted phenyl group (**2m**), those substituted with electron-donating groups, 4-methyl (**2n**), 3-methyl (**2o**), and 4-methoxy (**2p**), were successfully introduced in the presence of 1 mol % of the K_2PtCl_4 catalyst (Entries 1–4). Although the yields for phenyl groups substituted with electron-withdrawing groups, 4-trifluoromethyl (**2q**) and 4-chloro (**2r**), are not high, owing mainly to the hydrolysis of the arylboronic acids under the reaction conditions, the yields were greatly improved by use of an excess amount (3 equiv to enone **1a**) of the boronic acids (Entries 5–8). The addition of phenylboronic acid (**2m**) took place in high yields under standard conditions (1 mol % of K_2PtCl_4 and 1.5 equiv of **2m**) for linear β-substituted α,β-unsaturated ketones, **1d** and **1e** (Entries 12 and 13), as well as some other cyclic enones, **1b** and **1c** (Entries 10 and 11). Interestingly, the 1,4-addition catalyzed by K_2PtCl_4 was observed only with aromatic boronic acids, not with olefinic boronic acids such as 1-heptenylboronic acid. This is mainly due to the hydrolysis of the alkenylboronic acid.

Table 2. Platinum-catalyzed 1,4-addition of arylboronic acids **2** to α,β-unsaturated ketones **1**: scope

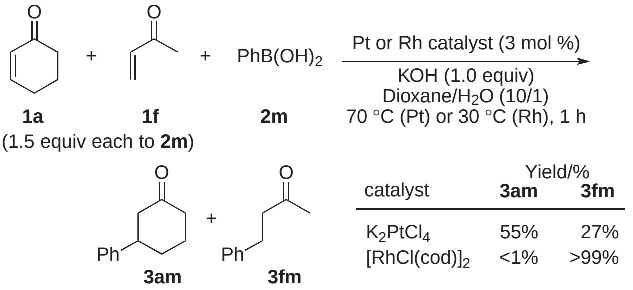


Entry	1	2	Product	Yield/%[a]
1	 **1a**	**2m**	 **3am** **3am** (Ar = Ph)	94
2	**1a**	**2n**	**3an** (Ar = 4-MeC$_6$H$_4$)	90
3	**1a**	**2o**	**3ao** (Ar = 3-MeC$_6$H$_4$)	93
4	**1a**	**2p**	**3ap** (Ar = 4-MeOC$_6$H$_4$)	89
5	**1a**	**2q**	**3aq** (Ar = 4-CF$_3$C$_6$H$_4$)	58
6[b]				94
7	**1a**	**2r**	**3ar** (Ar = 4-ClC$_6$H$_4$)	38
8[b,c]				78
9[b]	**1a**	**2s**	**3as** (Ar = 2-MeC$_6$H$_4$)	88
10	 **1b**	**2m**	 **3bm**	85
11	 **1c**	**2m**	 **3cm**	96
12	 **1d**	**2m**	 **3dm**	87
13	 **1e**	**2m**	 **3em**	96

[a]Isolated yield. [b]The reaction was carried out with 3.0 equiv of ArB(OH)$_2$. [c]In the presence of 3 mol % of the catalyst.

It is remarkable that the present platinum-catalyzed reaction exhibits high reactivity toward β-substituted enones. It makes a striking contrast with the rhodium-catalyzed reaction where β-substituted enones are much less feasible than β-unsubstituted ones for the 1,4-addition. Thus, a competition reaction of a 1:1 mixture of 2-cyclohexen-1-one (**1a**) and 3-buten-2-one (**1f**) with **2m** in the presence of K$_2$PtCl$_4$ catalyst gave **3am**, which results from **1a**, as a major product,[12] while exclusive addition to **1f** forming **3fm** was observed in the reaction catalyzed by [RhCl(cod)]$_2$/KOH, which is one of the standard rhodium catalyst systems[3] (Scheme 1).

In summary, we have developed a platinum-catalyzed 1,4-addition of arylboronic acids to β-substituted α,β-unsaturated ketones. In the presence of potassium hydroxide in dioxane/H$_2$O, the 1,4-addition was efficiently catalyzed by a small amount (1 mol %) of K$_2$PtCl$_4$ or PtCl$_2$ to give high yields of the corresponding β-arylketones.



catalyst	Yield/% 3am	Yield/% 3fm
K$_2$PtCl$_4$	55%	27%
[RhCl(cod)]$_2$	<1%	>99%

Scheme 1. Comparison of substrate selectivity between the platinum and rhodium catalysts for the addition to **1a** and **1f**.

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References and Notes

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11 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/.
12 The competition reaction of **1d** and **1f** under the same reaction conditions gave the corresponding 1,4-phenylation products **3dm** and **3fm** in 31% and 65% yields, respectively.

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