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Palladium(II)-catalyzed intramolecular addition of arylboronic acids to ketones

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ABSTRACT

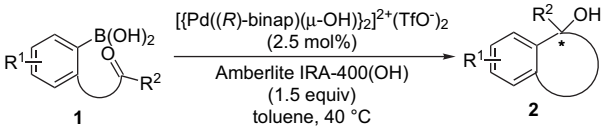
A palladium(II)-catalyzed intramolecular addition of arylboronic acids to ketones was developed. Compared to $Pd(OAc)_2$ catalysis system, cationic palladium complex with dppp as the ligand has higher catalytic activity and efficiency for wider scope of substrates. From this reaction, the normal addition product or the dehydrated product could be selectively furnished as controlled by additives. Highly optically active cyclic tertiary alcohols (up to 96% ee) can be obtained by using chiral cationic palladium complex as the catalyst.

1. Introduction

Transition metal-catalyzed Grignard-type reactions of arylboron compounds with carbonyl groups provide powerful and versatile approaches toward C–C bond formation and the synthesis of alcohols.[1–3] Several features of the chemistry make it attractive including the availability and stability of the substrates, the wide functional group tolerance as well as the potential application to asymmetric synthesis.[4] Much progress have been seen in the addition of arylboron compounds to aldehydes[1,2] and activated ketones.[3,2d] However, the successful examples of targeting simple ketones as substrates are quite limited, as is anticipated by the lesser reactivity of ketones toward the nucleophilic addition. Only recently, rhodium-catalyzed addition of arylboron compounds to simple ketones was achieved by Miura's group.[5,6]

In contrast, the corresponding reactions catalyzed by palladium are even rarer. In these reactions, aryl-transition metal complexes generated via transmetalation of arylboron compounds are reactive species as nucleophiles. Generally, compared to arylrhodium species, arylpalladium species are relatively less nucleophilic and have been involved mainly in the electrophilic reactions, such as carbon–carbon coupling reactions and the reaction with alcohols and amines.[7] Although it is uncommon for the arylpalladium species to act as nucleophiles, some examples of the direct insertion of carbon–heteroatom multiple bonds into arylpalladium intermediates have been reported by Yamamoto, Larock, and other groups.[8] Also, there are some reports about the use of palladium as the catalyst for the addition of arylboron compounds to aldehydes,[2] activated ketones,[2d] and nitriles.[9]

Enantioselective addition of arylboronic acids to ketones is a straightforward strategy for the construction of optically active tertiary alcohols.[10] After the success on Rh-catalyzed asymmetric addition of arylboronic acids to activated ketones,[3b–d] we demonstrated the chiral cationic palladium-catalyzed highly enantioselective intramolecular addition of arylboronic acids to ketones, which provided a convenient synthesis of optically active benzocycloalkanols (Eq. 1).[11]



(1)

In the process of our study on the intramolecular addition of arylboronic acids to ketones, we found that both neutral and cationic palladium complexes could catalyze this reaction and the cationic palladium complexes exhibit higher reactivity and efficiency (Scheme 1). Meanwhile, with the cationic palladium complex as the catalyst, either the normal addition product **2** or the dehydrated product **3** could be selectively furnished by the choice of additives (Scheme 1).

We report herein the full details of the development of palladium(II)-catalyzed intramolecular addition of arylboronic acids to ketones. We wish to present the effect of different kinds of palladium(II) catalysts and a full account of the scope and limitations of this reaction.

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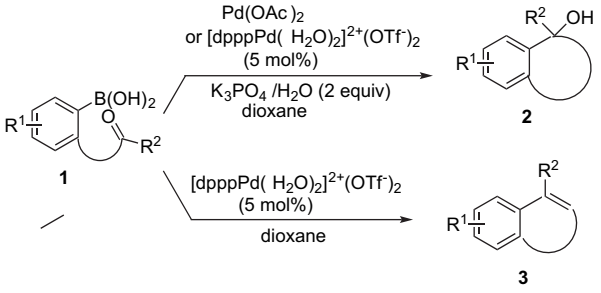


Scheme 1. Cationic palladium complex catalyzed addition of arylboronic acids to ketones.

2. Results and discussion

2.1. Neutral palladium(II)-catalyzed intramolecular addition of arylboronic acids to ketones

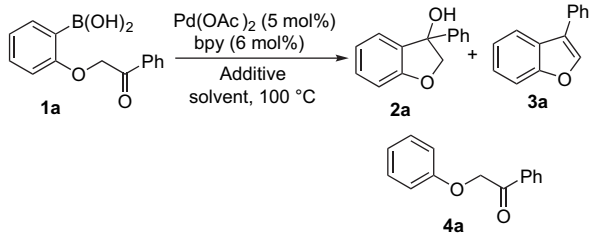
The intramolecular addition of arylboronic acids to ketones was initially studied using $Pd(OAc)_2$/bpy as the catalyst, which is effective for other palladium(II)-catalyzed reactions developed by our group.[12] Firstly, efforts were focused on optimizing the reaction conditions. The representative results are summarized in Table 1. In the presence of 5 mol % of $Pd(OAc)_2$ and 6 mol % of bpy, substrate **1a** reacted in various solvents at 100 °C to give the dehydrated product benzofuran (**3a**) in moderate to low yields (25–66%, Table 1, entries 1–5) along with the deboronated aryl ketone **4a**, which is the main side product. Moderate yield of **3a** was observed in dioxane, though the reaction required 4 to 5 days to reach completion. Additives are well known to play an important role in the transmetalation between boron and palladium.[13] Therefore, we examined the base effect on this intramolecular addition reaction. Various bases such as KOAc, KF, and K_3PO_4 could increase the reaction rate (Table 1, entries 6, 7, and 9). Interestingly, the product was changed to the normal product dihydrobenzofuranol (**2a**), which was stable enough not to dehydrate to benzofuran under these basic conditions.[14] K_3PO_4 seemed to be the most suitable base, while KOAc decreased the yield and KF required longer reaction time. Lowering the temperature led to the prolonged reaction time and the mixture of **2a** and **3a** (Table 1, entry 8). The combination of K_3PO_4 (2 equiv) and H_2O (2 equiv) resulted the desired rate enhancement and good yield (87%, Table 1, entry 9).

The effect of different palladium catalyst was investigated as demonstrated in Table 2. With KF as additive, we screened two other neutral palladium compounds $PdCl_2(CH_3CN)_2$ and $PdCl_2$. In the case of $PdCl_2(CH_3CN)_2$, longer reaction time was required (Table 2, entry 2). The yield was low while $PdCl_2$ was used as catalyst (Table 2, entry 3). In the further study, we found the ligand bpy was not necessary. Without bpy, $Pd(OAc)_2$ alone could catalyze the intramolecular addition well (Table 2, entry 4). No trace of addition product would be obtained in the absence of palladium catalyst (Table 2, entry 5).

On the basis of the above investigation, the optimal conditions for this neutral palladium-catalyzed intramolecular addition reaction are as follows: 5 mol % of $Pd(OAc)_2$, 2 equiv of K_3PO_4, and H_2O (2 equiv) in dioxane at 100 °C.

Consequently, a variety of substrates with different substituents on the ketone carbonyl was investigated to define the scope and limitation of this $Pd(OAc)_2$ catalyzed intramolecular addition. Compounds **1a–h** were easily prepared starting from the appropriate α-bromoketones and 2-iodophenol as shown in Scheme 2. After coupling of α-bromoketones with 2-iodophenol, and subsequent acetalization with ethylene glycol, **5** was obtained. Lithiation of **5** with *n*-BuLi at −78 °C, quenching with trimethyl borate,

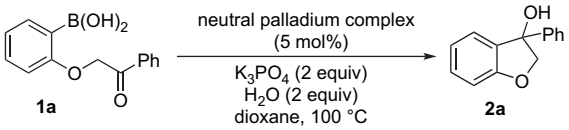
Table 1
Effect of solvents and additives on the intramolecular addition of arylboronic acids to ketones[a]



Entry	Solvent	Additive (equiv)	Time (h)	Yield[b] (%)		
				2a	3a	4a
1	HOAc/THF/H_2O (1:1:0.3)	None	108	—	25	46
2	Dioxane/H_2O (10:1)	None	72	—	41	38
3	Dioxane	None	108	—	66	12
4	DMSO	None	12	—	62	31
5	Toluene	None	12	—	50	50
6	Dioxane	KOAc (2)	12	41	—	51
7	Dioxane	KF (2)	18	73	—	10
8[c]	Dioxane	KF (2)	72	58	15	13
9	Dioxane	K_3PO_4 (2)	5	72	—	10
10	Dioxane	K_3PO_4 (2), H_2O (2)	5	87	—	5

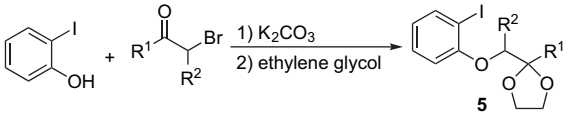
[a] All reactions were carried out with **1a** (0.2 mmol), $Pd(OAc)_2$ (5 mol %), and bpy (6 mol %) at 100 °C.
[b] Isolated yields.
[c] Reaction at 80 °C.

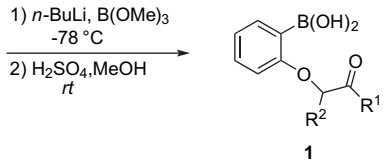
Table 2
Effect of neutral palladium(II) complexes as catalysts



Entry	Catalyst	Time (h)	Yield[a] (%)
1[b]	$Pd(OAc)_2$/bpy	18	73
2[b]	$PdCl_2(CH_3CN)_2$	72	71
3[b]	$PdCl_2$	12	57
4	$Pd(OAc)_2$	5	90
5	None	12	None

[a] Isolated yields.
[b] KF (2 equiv) was used as the additive.

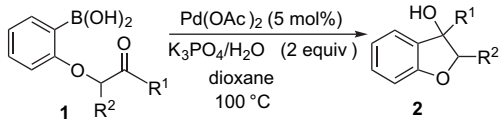




	R^1	R^2		R^1	R^2
1a	Ph	H	**1e**	4-$CF_3C_6H_4$	H
1b	4-$MeOC_6H_4$	H	**1f**	2-furyl	H
1c	2-$MeOC_6H_4$	H	**1g**	CH_3	H
1d	4-ClC_6H_4	H	**1h**	-$(CH_2)_4$-	

Scheme 2. Synthesis of substituted arylboronic acids.

Table 3
Reactions of arylboronic acids bearing different kinds of ketones[a]



Entry	1	R^1	R^2	2	Yield[b] (%)
1	**1a**	Ph	H	**2a**	90
2	**1b**	4-$MeOC_6H_4$	H	**2b**	93
3	**1c**	2-$MeOC_6H_4$	H	**2c**	91
4	**1d**	4-ClC_6H_4	H	**2d**	94
5	**1e**	4-$CF_3C_6H_4$	H	**2e**	79
6	**1f**	2-Furyl	H	**2f**	62
7[c]	**1g**	CH_3	H	**2g**	60
8[c]	**1h**	$-(CH_2)_4-$		**2h**[d]	79

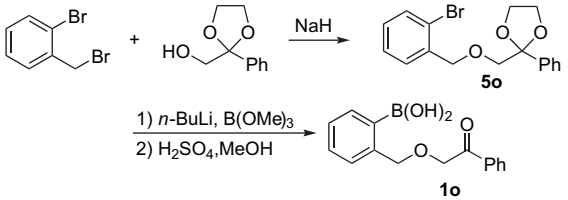
[a] Unless otherwise indicated, all reactions were performed at 100 °C using the substrate (0.2 mmol), K_3PO_4 (2 equiv), H_2O (2 equiv), and $Pd(OAc)_2$ (5 mol%) in dioxane (2 mL) under N_2.
[b] Isolated yield.
[c] H_2O (0.1 mL) was added.
[d] The stereochemistry of **2h** was determined by NOESY spectra as cis.

and then hydrolysis to remove the acetal group gave the resulting boronic acids **1a**–**h**.

With various phenylboronic acids bearing different ketones in hand, we explored the reaction scope and the results are presented in Table 3. The intramolecular arylations of either electron-donating or electron-withdrawing aromatic ketones proceeded smoothly to afford the corresponding dihydrobenzofuranol in moderate to good yields (79–94%, Table 3, entries 1–5). When *ortho*-substituted-phenyl ketone **1c** was subjected to the reaction conditions, good yield (91%) of **2c** was achieved (Table 3, entry 3). The reaction conditions were also compatible with heteroaromatic, aliphatic, and cyclic ketones, which resulted in moderate yields (60–79%, Table 3, entries 6–8). Thus, neither electronic nor steric effects of ketones appeared to play a major role on the reactivity of substrates.

Encouraged by the excellent results obtained above, we then investigated the effect of substituents on the aromatic ring of boronic acids. The starting materials **1i**–**l** were prepared according to the procedure for the substrates **1a**–**h**. 1-Naphthylboronic acid (**1i**) gave the corresponding product **2i** in a moderate yield of 79% (Table 4, entry 1). The reaction for OMe, Cl, CH_3 substituted arylboronic acids (**1j**–**l**) led to good yields (82–91%) of the desired products **2j**–**l** (Table 4, entries 2–4).

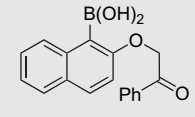
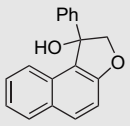
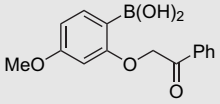
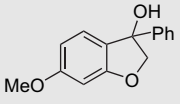
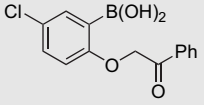
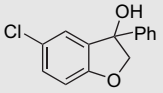
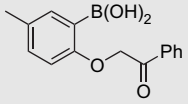
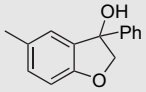
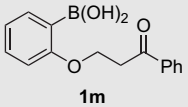
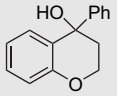
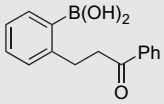
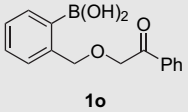
Series of dihydrobenzofuranol derivatives having been readily obtained, we decided to investigate the possibility of synthesizing other type of cycloalkanols. The substrates **1m** and **1n** were prepared according to our previously reported procedure[11] and **1o** was prepared from (2-phenyl-1,3-dioxolan-2-yl)-methanol as shown in Scheme 3.



Scheme 3. Synthesis of substituted arylboronic acids.

Under standard reaction conditions, substrate **1m** only gave a trace of desired product. When KF was used as the additive, successful cyclization of compound **1m** occurred to afford six-membered ring product **2m**, a derivative of chroman. However, the yield was low (40%, Table 4, entry 5), for compound **1m** was easily transformed to 1-phenyl-propenone. To our disappointment, substrates **1n** and **1o** did not afford the desired products under optimized conditions.

Table 4
Reactions of arylboronic acids bearing different substituents on the aryl ring[a]

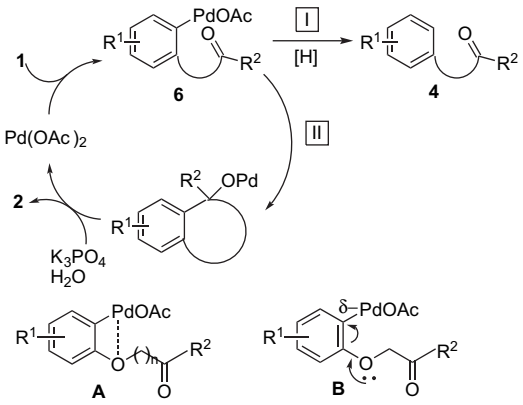
Entry	Substrate	Product	Yield[b] (%)
1	 **1i**	 **2i**	79
2	 **1j**	 **2j**	91
3	 **1k**	 **2k**	82
4[c]	 **1l**	 **2l**	90
5[d]	 **1m**	 **2m**	40
6	 **1n**	None	—
7	 **1o**	None	—

[a] Reactions were carried out at 100 °C using the substrate (0.2 mmol), K_3PO_4 (2 equiv), H_2O (2 equiv), and $Pd(OAc)_2$ (5 mol%) in dioxane (2 mL) under N_2.
[b] Isolated yield.
[c] H_2O (0.1 mL) was added.
[d] KF (2 equiv) was used as the additive.

From the structure of the substrates, it was found that the only difference of the neighboring atom of arylboronic acid between **1a**–**m** and **1n**–**o** was the change of oxygen to carbon atom. This results reflects that the neighboring oxygen in the substrates have a pronounced effect on the success of this $Pd(OAc)_2$ catalyzed intramolecular addition.

A plausible explanation for this role of oxygen atom is shown in Scheme 4. The arylpalladium intermediate **6**, formed by the transmetalation of $Pd(OAc)_2$ with substrate **1**, could partition into two competitive pathways: (i) protonolysis to generate the deboronated aryl ketone **4** (pathway-I) or (ii) addition to intramolecular ketones to yield the desired product **2** (pathway-II). As a hypothesis, the neighboring oxygen atom seemed to be helpful for the addition step (pathway-II), accounting for its ability to coordinate to the palladium atom (mode A)[15] or its electron-donation character (mode B) to increase the nucleophilicity of the arylpalladium species.[16] The coordination of the oxygen to the palladium

atom could stabilize the species **6** and bring the carbonyl group nearer to the metal atom. All of these could facilitate the addition of arylpalladium species **6** to ketones.



Scheme 4. Role of oxygen atom in this reaction.

Thus, by utilizing $Pd(OAc)_2$ as the catalyst, intramolecular addition of arylboronic acids to ketones could be achieved. However, the substrates were limited to those having a neighboring oxygen atom in the arylboronic acid and the catalytic system need to be improved.

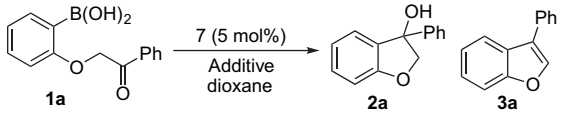
2.2. Cationic palladium complex $[Pd(dppp)(H_2O)_2]^{2+}(TfO^-)_2$ (7) as the catalyst

With the aim of improving the efficiency and generality of this intramolecular reaction, we turned our efforts to other palladium catalysts. Among kinds of Pd(II) catalysts, cationic Pd(II) complexes have great advantages over analogous neutral ones mainly in two dimensions: (1) vacant coordination site for substrates or reagents and (2) stronger Lewis acidity. Cationic palladium complexes have exhibited high reactivity in many kinds of reactions.[17]

Initially, cationic palladium complex $[Pd(dppp)(H_2O)_2]^{2+}(TfO^-)_2$ (**7**)[18] was chosen as the catalyst to examine the intramolecular 1,2-addition of **1a** (Table 5). To our delight, upon heating at 100 °C for 5 h in the presence of 5 mol % of **7** in dioxane, **1a** underwent addition smoothly to afford dihydrobenzofuran (**3a**) in extremely high yield (quantitative, Table 5, entry 1). In contrast, with $Pd(OAc)_2$ as the catalyst under the same condition, almost five days were required (Table 1, entry 3). With K_3PO_4 (2 equiv) and H_2O (2 equiv) as additives, dihydrobenzofuranol (**2a**) could be obtained selectively in high yield (85%, Table 5, entry 2). The presence of K_3PO_4 and H_2O is critical for the formation of dihydrobenzofuranol. Without K_3PO_4 and H_2O, only dihydrobenzofuran was formed (Table 5, compare entries 1 and 2, 3 and 4, 7 and 8, 10 and 11). A prolonged reaction time would favor the formation of dihydrobenzofuran (Table 5, compare entries 8 and 9). Thus, 80 °C seemed to be the most suitable temperature. Even at room temperature, **1a** could afford the addition product in moderate yield within a couple of hours (Table 5, entries 10 and 11). A slightly lower yield was observed when $[Pd(dppe)(H_2O)_2]^{2+}(TfO^-)_2$ (5 mol %) was used as the catalyst (Table 5, entry 6).

The scope and generality of the intramolecular addition was examined using $[Pd(dppp)(H_2O)_2]^{2+}(OTf^-)_2$ (**7**) as the catalyst. Under condition A (5 mol % of **7**, 2 equiv of K_3PO_4, and 2 equiv of H_2O in dioxane at 80 °C), all substrates in hand could react smoothly to give the corresponding cycloalkanols in moderate to good yield (66–94%, Table 6). By using this method, derivatives of dihydrobenzofuranol (**2a–l**), indanol (**2n**), chromanol (**2m**), and isochromanol (**2o**) could be obtained. Especially, **2n** and **2o**, which could not be formed in $Pd(OAc)_2$ catalysis system, were obtained in good yields (83% and 82%, Table 6).

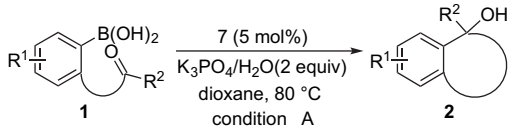
Table 5
Optimization of reaction conditions with $[Pd(dppp)(H_2O)_2]^{2+}(OTf^-)_2$ (**7**) as the catalyst[a]

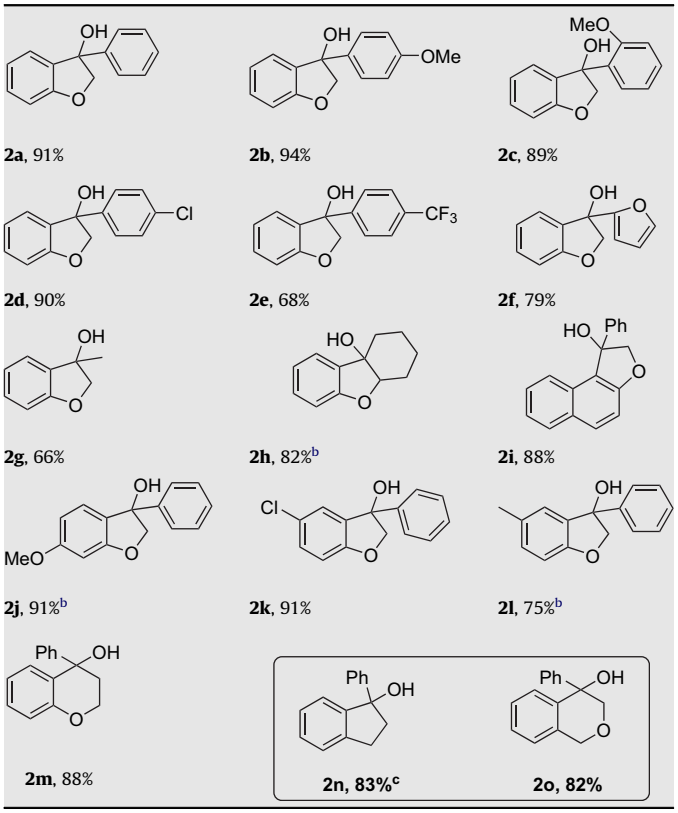


Entry	Additive (2 equiv)	Temp (°C)	Time (h)	Yield[a] (%)	
				2a	**3a**
1	—	100	5	—	100
2	K_3PO_4, H_2O	100	5	85	—
3	—	80	5	—	96
4	K_3PO_4, H_2O	80	1	91	—
5[b]	K_3PO_4, H_2O	80	1.5	65	24
6[c]	K_3PO_4, H_2O	80	2	85	—
7	—	60	5	—	95
8	K_3PO_4, H_2O	60	1	94	—
9	K_3PO_4, H_2O	60	5	—	95
10	—	25	7	12	82
11	K_3PO_4, H_2O	25	7	78	—

[a] Isolated yield.
[b] Using 2.5 mol % of **7** as catalyst.
[c] Using 5 mol % of $[Pd(dppe)(H_2O)_2]^{2+}(OTf^-)_2$ as catalyst.

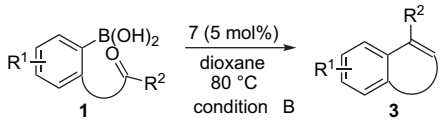
Table 6
$[Pd(dppp)(H_2O)_2]^{2+}(OTf^-)_2$ (**7**) catalyzed intramolecular addition of arylboronic acids to ketones under condition A[a]

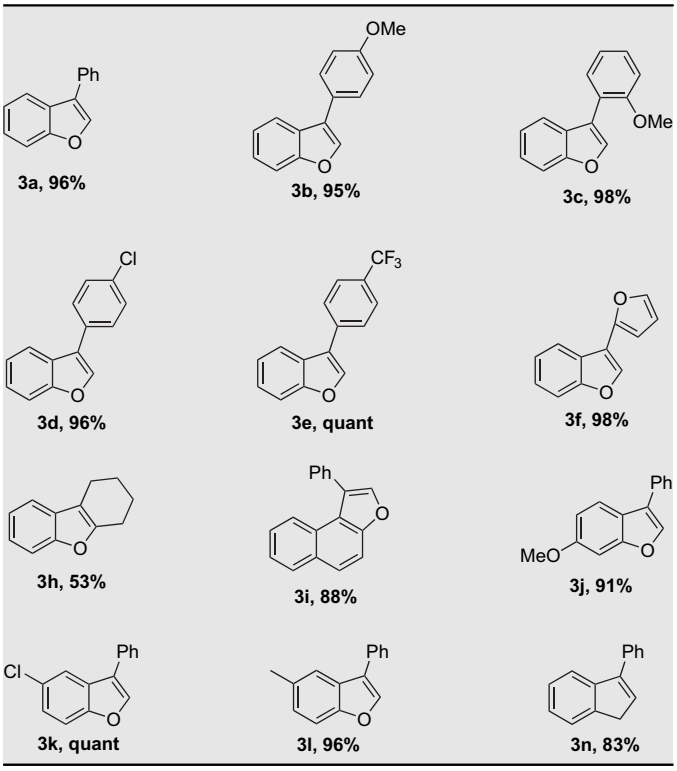




[a] Cited yields are of materials isolated by silica gel chromatography.
[b] H_2O (0.1 mL) was added.
[c] KF (1 equiv) was added as additive.

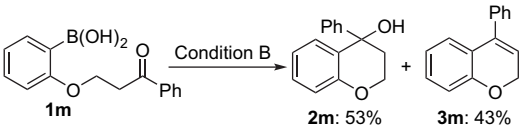
Table 7
$[Pd(dppp)(H_2O)_2]^{2+}(OTf^-)_2$ (**7**) catalyzed intramolecular addition of arylboronic acids to ketones under condition B[a]



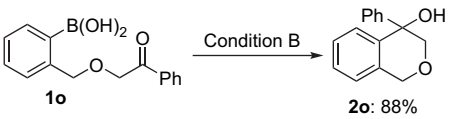


[a] Cited yields are of material isolated by silica gel chromatography.

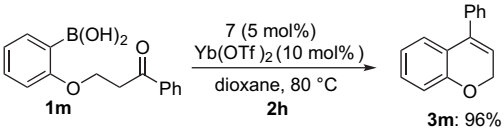
On the other hand, in the presence of 5 mol % of **7**, in dioxane at 80 °C (condition B) most substrates afforded the dehydrated products selectively in good to excellent yields (82% to quantitative, Table 7), though 1,2,3,4-tetrahydro-dibenzofuran (**3h**) was formed only in moderate yield (53%, Table 7). In case of **1m** and **1o**, poor selectivity was observed. Substrate **1m** gave 43% yield of **3m** along with 53% yield of **2m** (Eq. 2). When **1o** was subjected to condition B, no trace of dehydrated product was afforded and **2o** was produced in 88% of yield (Eq. 3). Interestingly, when 10 mol % of $Yb(OTf)_3$ was added under the condition B, substrate **1m** offered the dehydrated product **3m** selectively in high yield (96%) (Eq. 4).



(2)

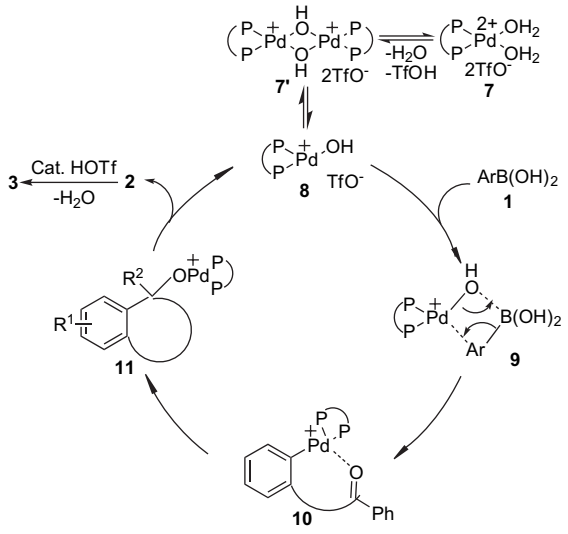


(3)



(4)

The proposed catalytic cycle is shown in Scheme 5. It has been demonstrated that interconversion exists between aquo compound **7** and the corresponding binuclear μ-hydroxo complex **7′**, which is a dimeric form of the mono-hydroxo complex **8**.[19] An equivalent amount of HOTf and H_2O should be generated when complex **8** was formed. The Pd hydroxo complex **8** was supposed to be the active catalytic species, which enable smooth transmetalation with the substrate **1** without any assistance of additive bases. Two features of intermediate **8** maybe accounted for its feasible transmetalation: cationic nature of the transition metal complex[4d,20] and the existence of the hydroxo ligand.[4a,21] After transmetalation, owing to the vacant coordination site on the cationic palladium complex, the intramolecular ketone easily coordinated to the palladium center to give intermediate **10**. High Lewis acidity of palladium center in cationic species **10** may activate the carbonyl group by coordination resulting in very smooth intramolecular 1,2-addition to produce intermediate **11**.[4a,18,21] While in $Pd(OAc)_2$ catalysis system, the analogous intermediate **6** (Scheme 4) needs the neighboring oxygen atom to assist the addition. The subsequent fast hydrolysis of **11** would afford product **2** and regenerate the catalytic active intermediate **8**. In most cases, the product **2** could dehydrate to produce **3** catalyzed by HOTf formed in situ as described above. Indeed, a control experiment showed that 5 mol % of HOTf in dioxane at room temperature did catalyze the dehydrate of **2a** to produce **3a**. Otherwise, if a base was added to neutralize the HOTf, product **2** could be isolated after reaction.



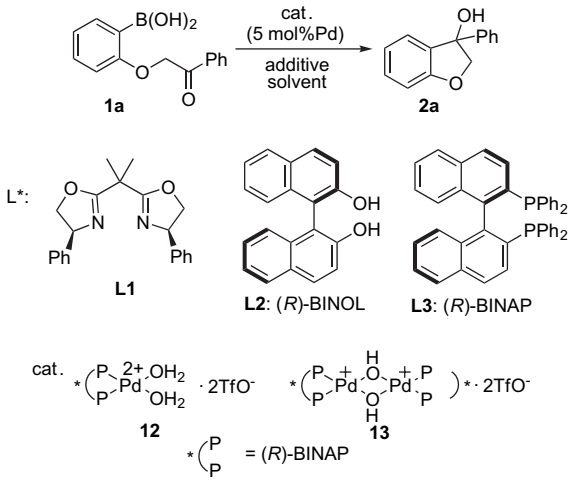
Scheme 5. Proposed catalytic cycle of the reaction.

Cationic palladium **7** has been demonstrated to be an efficient catalyst for the intramolecular addition of arylboronic acids to ketones. It can catalyze this addition reaction smoothly without the assistance of a base in transmetalation step and a neighboring oxygen atom in addition step, which indicated great advantages over $Pd(OAc)_2$ catalysis system.

2.3. Asymmetric version

Having developed successful protocols for the intramolecular addition of arylboronic acid to ketones, we turned our efforts toward the asymmetric version. The attempts at using $Pd(OAc)_2$ combined with chiral ligands to induce enantioselectivity were unsuccessful (Table 8, entries 1 and 2). Our attention was then focused on the easily prepared chiral cationic palladium complexes **12** and **13**. Unfortunately, with the catalyst **12** under the optimized reaction conditions, **2a** was formed in high yield (89%) with

Table 8
Optimization of asymmetric reaction conditions

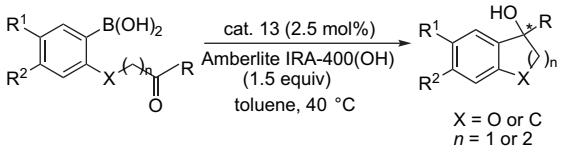


Entry	Catalyst	Solvent	Additive[a]	Temp/time (°C/h)	Yield[b] (ee[c]) (%)
1[d]	$Pd(OAc)_2$/**L1**	Dioxane	**A**	100/5	74 (0)
2[d]	$Pd(OAc)_2$/**L2**	Dioxane	**A**	100/5	88 (0)
3	**12**	Dioxane	**A**	80/1	89 (7)
4	**13**	Dioxane	**A**	80/1	77 (28)
5	**13**	Dioxane	**B**	80/2	85 (82)
6	**13**	Dioxane	**B**	40/72	83 (92)
7	**13**	CH_2Cl_2	**B**	40/5.5	81 (85)
8	**13**	MeOH	**B**	40/5.5	53 (20)
9	**13**	DMF	**B**	40/-	None
10	**13**	THF	**B**	40/9	94 (90)
11	**13**	Toluene	**B**	40/12	85 (92)
12[e]	**13**	Toluene	**B**	40/41	75 (88)
13[d]	$Pd(OTf)_2$/**L3**	Toluene	**B**	40/96	44 (78)

[a] Additive: **A**: K_3PO_4 (2 equiv), H_2O (2 equiv); **B**: Amberlite IRA-400 (OH) (1.5 equiv).
[b] Isolated yield.
[c] Determined by HPLC analysis using a Chiralcel OD column.
[d] Chiral ligand (6 mol %) was used.
[e] H_2O (2 equiv) was added.

extremely low ee (7%, Table 8, entry 3). When chiral Pd complex **13** was used instead of **12**, a slight improvement in the ee value was observed (28%, Table 8, entry 4). To our delight, while employing anion exchange resin (Amberlite IRA-400 (OH)) as the additive, we effectively furnished the cyclization product **2a** in good yield with high enantiomeric excess (85% yield, 82% ee; Table 8, entry 5). The screening of different temperature and solvents showed that the reaction proceeded smoothly at 40 °C in less polar solvents such as CH_2Cl_2, THF, and dioxane with high yield and ee value (Table 8, entries 6–11). In contrast, the results were much worse in polar solvents such as DMF and MeOH (Table 8, entries 8 and 9). Performing the reaction in DMF completely inhibited the desired intramolecular addition (Table 8, entries 9). Finally, the best result was provided in toluene at 40 °C (85% yield, 91% ee; Table 8, entry 11). Addition of 2 equiv of H_2O led to lower yield and longer reaction time as shown in entry 12. Other catalyst such as $Pd(OTf)_2$/BINAP could not give the equally good result (Table 8, entry 13).

Under the optimized asymmetric reaction conditions, a variety of substrates including various aromatic, heteroaromatic, and aliphatic ketones could be used to afford the optically active tertiary alcohols in good to excellent yield and enantioselectivity (Scheme 6).[11]



Scheme 6. Asymmetric intramolecular addition of arylboronic acids to ketones.

3. Conclusion

We have developed a palladium(II)-catalyzed intramolecular addition of arylboronic acids to ketones. Compared to $Pd(OAc)_2$ catalysis system, cationic palladium complex **7** have higher catalytic activity and efficiency for wider scope of substrates. With using **7** as the catalyst, different products, the normal addition product **2** or the dehydrated product **3**, could be furnished selectively as controlled by additives. Though the combination of chiral ligands and $Pd(OAc)_2$ could not induce the enantioselectivity, highly optically active cyclic tertiary alcohols (up to 96% ee) can be obtained by using chiral cationic palladium complex as the catalyst.

4. Experimental section

4.1. General

All reactions were carried out in dry solvents under a nitrogen atmosphere unless otherwise noted. All solvents were dried and distilled before use according to the standard methods. The progress of all reactions was monitored by thin layer chromatography to ensure that the reactions had reached completion.

4.2. Representative procedure for the $Pd(OAc)_2$ catalyzed intramolecular addition of arylboronic acids to ketones to furnish cycloalkanols

Under nitrogen, K_3PO_4 (113 mg, 2 equiv) was added to a mixture of **1a** (73.7 mg, 0.288 mmol), $Pd(OAc)_2$ (3.4 mg, 5 mol %), and water (11 μL, 2 equiv) in dioxane (2.9 mL). The reaction mixture was stirred at 100 °C for 5 h. After the reaction was completed as monitored by TLC, the reaction mixture was quenched with H_2O and the aqueous layer was extracted with EtOAc (3×20 mL). The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 8:1) to obtain the product **2a** (55 mg, 90%).

*4.2.1. 3-Phenyl-3-hydroxy-2,3-dihydrobenzofuran (**2a**)*[22]

Oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51–6.91 (m, 9H), 4.67 and 4.49 (AB q, J=10.2 Hz, 2H), 2.54 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 142.5, 132.1, 130.6, 128.2, 127.5, 126.0, 124.4, 121.4, 110.7, 86.0, 82.5. IR (oil) ν 3437 (br), 3061, 1600 cm^{-1}. MS (m/z, EI): 212 (M^+, 100), 194, 77.

4.3. Representative procedure for $[Pd(dppp)(H_2O)_2]^{2+}(OTf^-)_2$ (7) catalyzed intramolecular addition of arylboronic acids to ketones under condition A to yield cycloalkanols

Under nitrogen, K_3PO_4 (128.1 mg, 0.6 mmol) was added to a mixture of **1a** (76.6 mg, 0.3 mmol), **7** (12.6 mg, 0.015 mmol), and water (11 μL, 0.6 mmol) in dioxane (3 mL). The reaction mixture was stirred at 80 °C for 1 h. After the reaction was completed as monitored by TLC, the reaction mixture was quenched with H_2O and the aqueous layer was extracted with EtOAc (3×20 mL). The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 8:1) to obtain the product **2a** (58 mg, 91%).

4.4. Representative procedure for $[Pd(dppp)(H_2O)_2]^{2+}(OTf^-)_2$ (7) catalyzed intramolecular addition of arylboronic acids to ketones under condition B to yield the dehydrated products of cycloalkanols

Under nitrogen, a mixture of **1a** (51.3 mg, 0.2 mmol) and $[Pddppp(H_2O)_2]^{2+}(TfO^-)_2$ (4.1 mg, 5 mol %) was stirred in dioxane (2 mL) at 80 °C for 5 h. After cooling, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 20:1) to obtain the product **3a** (37 mg, 95%).

4.4.1. 3-Phenylbenzofuran (**3a**)[23]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86–7.28 (m, 10H). IR (oil) ν 3057, 3025, 747, 697 cm^{-1}. MS (*m*/*z*, EI): 194 (M^+, 100), 166, 83.

4.5. Representative procedure for asymmetric cyclization of 1a catalyzed by 13 to furnish the optically active cycloalkanols[11]

Under nitrogen, Amberlite IRA(OH) (1.5 equiv) was added to a solution of **1a** (51.2 mg, 0.2 mmol), **13** (9.0 mg, 2.5 mol %) in toluene (2 mL). The reaction mixture was stirred at 40 °C for 12 h. After the reaction was completed as monitored by TLC, the reaction mixture was quenched with 1 N NaOH (8 mL) and the aqueous layer was extracted with EtOAc (3×15 mL). The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/EtOAc, 8:1) to obtain the product **2a** (36 mg, 85%). The ee value was determined by chiral HPLC using a Chiralcel OD-H column with hexane/isopropanol=90:10, flow=0.7 mL/min; ee: 92%; $[\alpha]_D^{20}$ −114.5 (*c* 1.00, $CHCl_3$).

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Supplementary data

Experimental procedure, characterization data, and copies of ^{1}H and ^{13}C NMR spectra for new compounds are provided. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.05.056.

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