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Rhodium catalyzed three-component reaction of aldehyde, boronic acid, and sulfonamides: a facile one-pot synthesis of diarylmethylamines

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ABSTRACT

Rhodium(I) catalyzed three-component reaction for the one pot synthesis of diarylmethylamines in excellent yields were achieved by using aldehyde, boronic acid, and sulfonamides. The use of hypervalent bis(trifluoroacetoxy)iodobenzene as an additive plays a key role in the chemo selective formation of amines instead of alcohols.

Construction of carbon–carbon and carbon–nitrogen bonds is of prime importance in organic synthesis[1] due to their prevalence in wide array of pharmaceuticals,[2] biologically active compounds,[3] natural products,[4] agrochemicals, fine chemicals, and materials.[5] The synthesis of diarylmethylamines is important because these amines are subunits of biologically significant compounds.[2] Variety of methods were reported for the synthesis of diarylmethylamines such as addition of organometallic reagent to an imine,[6] substitution of a hydroxyl group using amine nucleophiles,[7] and direct benzylic C–H amination via dehydrogenative coupling.[8] Recently, Renhua et al. reported amination of sp^3 C–H bonds via C–H activation using sulfonamides[9] and Kaneda et al. reported C–N bond formations catalyzed by a proton-exchanged montmorillonite as a heterogeneous catalyst.[10] Herein, we report rhodium-(I)-phosphine complex catalyzed three-component reaction between aryl aldehyde, boronic acid, and sulfonamide for the synthesis of diarylmethylamines.

The initial optimization studies for the one pot synthesis of diarylmethylamine were conducted by using 4-nitrobenzaldehyde, phenylboronic acid, and *p*-toluenesulfonamide as the model substrates. Various reaction parameters such as rhodium catalysts, additives, phosphorus ligands, and solvents were altered to find the best conditions. Rhodium based catalysts like bis(1,5-cyclooctadiene)rhodium(I)tetrafluoroborate (**catalyst 1**) and chloro(1,5-cyclooctadiene)rhodium (**catalyst 2**), in conjunction with phosphine ligands, 1,5-bis(diphenylphosphino)pentane (**L1**) and 1,2-bis[bis(-penta-fluorophenylphosphino)ethane (**L2**) (see Fig. 1) were tested for the reaction in the presence of additives that include silver oxide, silver carbonate, copper(II) acetate, hypervalent iodine reagent [bis(trifluoroacetoxy)iodo]benzene and [bis(acetoxy)iodo]benzene.

The reaction performed using **catalyst 1** and **L1** in the presence of silver oxide in toluene afforded the desired product diarylmethylamine in very poor yields (10%) (Table 1; entry 1). Moreover, the reaction failed when **catalyst 2** was employed under similar reaction conditions (Table 1; entry 2). The use of hypervalent iodine based [bis(trifluoroacetoxy)iodo]benzene as additive along with **catalyst 1** and **L1** improved the yield to 25% (Table 1; entry 3). In contrast, the reaction performed with **catalyst 2** under similar reaction conditions failed to furnish the desired products (Table 1; entry 4). Notably, when the reaction was conducted using **L2** instead of **L1**, excellent yield of the desired product was obtained (Table 1; entry 5). Remarkably, when the reaction was performed in the absence of bis(trifluoro-acetoxy)iodo]benzene additive, the formation of diarylmethyl alcohol in significant amount was observed [(Table 1; entry 6). The use of acetonitrile as solvent

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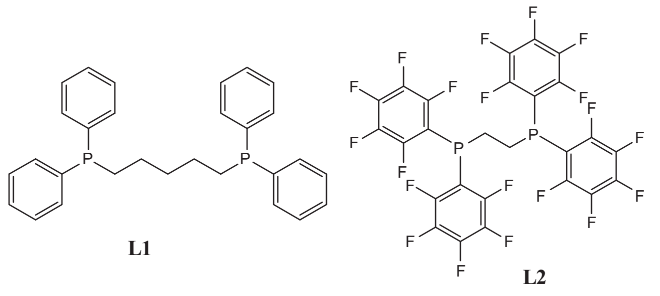
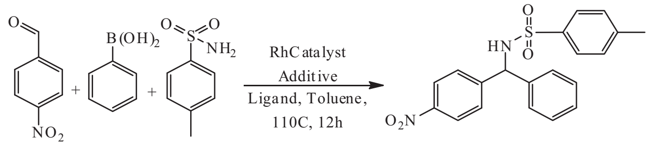


Figure 1. Phosphine based ligands.

Table 1
Optimization of one-pot synthesis of diaryl methylamine through a three component reaction of aldehyde, boronic acid, and sulfonamide[a]



Entry	Catalyst	Additive	Ligand	Yield[b] (%)
1	**Catalyst 1**	Ag_2O	**L1**	10
2	**Catalyst 2**	Ag_2O	**L1**	n.d.
3	**Catalyst 1**	$PhI(OCOCF_3)_2$	**L1**	25
4	**Catalyst 2**	$PhI(OCOCF_3)_2$	**L1**	n.d.
5	**Catalyst 1**	$PhI(OCOCF_3)_2$	**L2**	95
6	**Catalyst 1**	–	**L2**	10[c]
7	**Catalyst 1**	$PhI(OCOCF_3)_2$	**L2**	70[d]
8	**Catalyst 1**	$PhI(OCOCF_3)_2$	PPh_3	n.d.
9[e]	$RhCl_3$	$PhI(OCOCF_3)_2$	**L2**	n.d.
10	**Catalyst 1**	Ag_2CO_3	**L2**	n.d.
11	**Catalyst 1**	$Cu(OAC)_2$	**L2**	n.d.
12	**Catalyst 1**	–	**L2**	n.d.[f]
13	–	$PhI(OCOCF_3)_2$	**L2**	n.d.[g]
14	**Catalyst 1**	$PhI(OCOCH_3)_2$	**L2**	35
15	**Catalyst 1**	$PhI(OCOCF_3)_2$	**L2**	n.d.[h]
16[i]	$Rh(acac)_3$	$PhI(OCOCF_3)_2$	**L2**	n.d.

[a] Reaction conditions: 1.0 mmol of aldehyde, 2.0 mmol of boronic acid, 1.0 mmol of sulfonamide, 2.0 mol % of catalyst, 25.0 mol % of additive, 3.0 mol % of ligand and 2 mL of toluene.
[b] Isolated yields.
[c] Diarylmethyl alcohol was isolated.
[d] Acetonitrile was used instead of toluene.
[e] 5 mol % of rhodium trichloride was used as catalyst.
[f] Molecular oxygen used as an additive.
[g] Imine was isolated.
[h] 1 mmol of imine and 2 mmol of boronic acid were used.
[i] 2 mol % of $Rh(acac)_3$ was used as catalyst.

considerably reduced the product yield (Table 1; entry 7). When the reaction was performed using triphenylphosphine as ligand, no desired product was observed (Table 1; entry 8). In a similar way, the reaction also failed when conducted in the presence of either $RhCl_3$ or $Rh(acac)_3$ catalysts under similar reaction conditions (Table 1; entries 9 and 16). Moreover, the use of additives like silver carbonate and copper(II) acetate in the reaction failed to give the desired diarylmethylamine product (Table 1; entries 10 and 11). Besides, the reaction carried out by molecular oxygen as an additive did not proceed to furnish the desired product, (Table 1; entry 12).

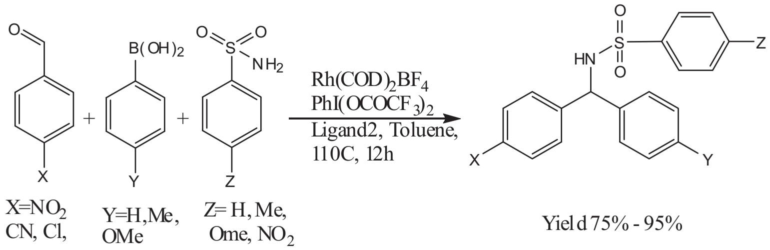
When the reaction was performed by using [bis(trifluoroacetoxy)iodo]benzene as additive in the absence of catalyst, considerable amount of imine was isolated (Table 1; entry 13). However, the reaction carried out in the presence of [bis(acetoxy)iodo]benzene under similar reaction conditions, afforded the desired amine in moderate yields (Table 1; entry 14). Notably, no product was observed when the reaction was carried out with imine and boronic acid as substrates under standard reaction conditions (Table 1; entry 15). Therefore, among various optimization studies listed in Table 1 the most promising result was shown to be Table 1; entry 5.

Using the optimized reaction conditions in hand the scope of the reaction was evaluated for various types of substrates and the results from these studies are presented in Table 2. Among various sulfonamide substrates that were studied, we have found that the reaction proceeded smoothly, and excellent yields were obtained with various structurally diverse aldehydes and boronic acids substrates. At first, the reaction of 4-nitrobenzaldehyde with phenylboronic acid and 4-methylbenzenesulfonamide was executed in the presence of 2.0 mol % of Rh(I) catalyst bis(1,5-cyclooctadiene)rhodium(I)tetrafluoroborate (**catalyst 1**), 25.0 mol % of hypervalent iodine based additive, $PhI(OCOCF_3)_2$, and 3.0 mol % of phosphorous ligand 1,2-bis[bis(penta-fluorophenylphosphino)ethane (**L2**) in toluene at 110 °C for 12 h. This reaction gave the corresponding diarylmethylamine product in yields as high as 95% in 12 h (Table 2; entry 1). Similarly, the reaction of 4-nitrobenzaldehyde has also gave good yields (86%) for the desired product in the reaction with 4-methoxyphenylboronic acid and 4-methylbenzenesulfonamide (Table 2; entry 2). As was the case earlier, 4-nitrobenzaldehyde also smoothly reacts with *p*-tolylboronic acid, and benzenesulfonamide, and gave corresponding diarylmethylamine product in good yields of 78% (Table 2; entry 3). When the reaction was carried out using 4-nitrobenzaldehyde, phenylboronic acid, and benzenesulfonamide as substrates under optimized reaction conditions, the corresponding diarylmethylamine was obtained in good yields of 86% (Table 2; entry 4). When the reaction was carried out using 4-cyano-benzaldehyde, 4-methoxyphenylboronic acid, and 4-methylbenzenesulfonamide, an excellent yield of 93% was obtained for the corresponding diarylmethylamine product (Table 2; entry 5). For the reaction between 4-cyanobenzaldehyde, 4-methoxyphenylboronic acid, and benzene sulfonamide, an excellent yield of 89% was obtained for the corresponding diarylmethylamine product (Table 2; entry 6). The reaction between 4-cyanobenzaldehyde, 4-methoxyphenylboronic acid, and 4-nitrobenzenesulfonamide also proceeded smoothly, and gave excellent yield of 93% for the corresponding diarylmethylamine product (Table 2; entry 7). Similarly, when 4-cyanobenzaldehyde was treated with phenylboronic acid and 4-methoxysulfonamide, desired diarylmethylamine product was isolated in yields as high as 95% (Table 2; entry 8). When 4-chlorobenzaldehyde was reacted with 4-methoxyphenylboronic acid and 4-methylbenzene-sulfonamide, the corresponding diarylmethylamine product was isolated in 91% yield (Table 2; entry 9). When 6-methoxy naphthaldehyde was treated with *p*-tolyl boronic acid and benzenesulfonamide, the desired diarylmethylamine was obtained in 89% yield (Table 2; entry 10). As was the case above, 1-naphthaldehyde also smoothly reacted with phenyl boronic acid and 4-methylbenzenesulfonamide and gave good yield of corresponding product in 86% yield (Table 2; entry 11).

A plausible mechanism[11] is explained for the synthesis of diarylmethylamines in Scheme 1. In the first step, a reactive imine **5**, is formed by the condensation between amine and the aldehyde promoted by hyper-valent iodine. Then, an in situ formed Bronsted acid could protonate the imine **5** to give an even more reactive iminium ion **6**. Simultaneously, the bis(phosphine) complex of rhodium(I)tetrafluoroborate could react with the arylboronic acid to form a more nucleophilic aryl rhodium(I) complex **7**. Finally, imine and aryl rhodium(I) species can subsequently react with each other to form the desired product **4**.

In summary we have developed a general protocol for the one pot synthesis of diaryl methylamines utilizing Rh(I)/bis(phosphine) catalyzed three-component reaction of aldehyde, boronic

Table 2
Rh(I) catalyzed one-pot synthesis of diarylmethylamine using various aldehydes with boronic acid and sulfonamide substrates[a]



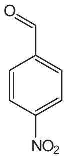
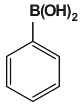
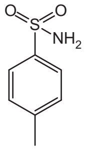
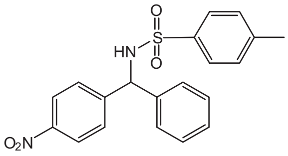
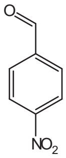
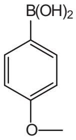
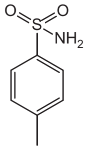
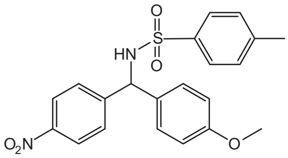
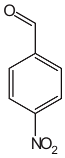
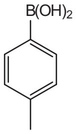
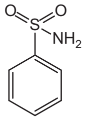
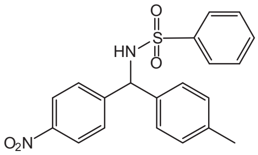
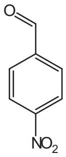
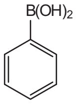
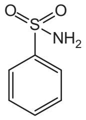
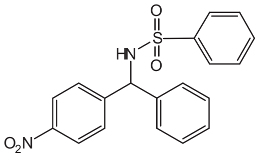
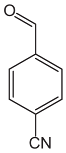
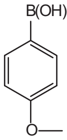
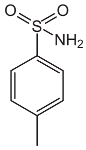
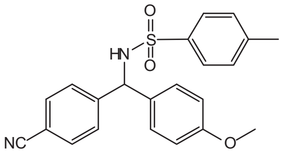
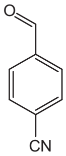
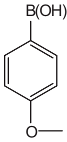
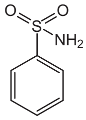
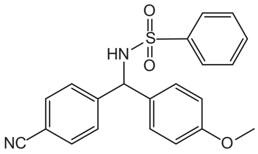
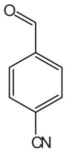
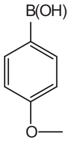
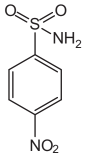
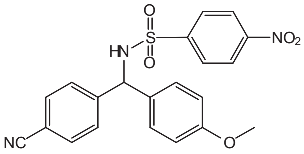
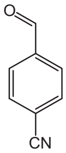
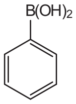
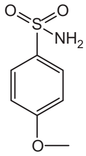
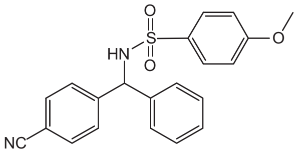
Entry	Aldehyde	Boronic acid	Sulfonamide	Diaryl amine	Yield[b] (%)
1					95
2					86
3					78
4					86
5					93
6					89
7					93
8					95

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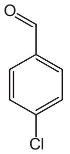
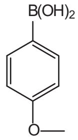
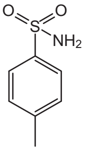
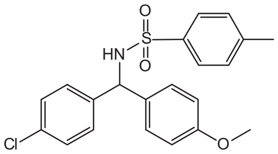
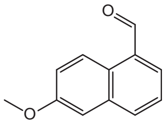
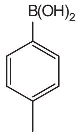
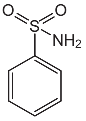
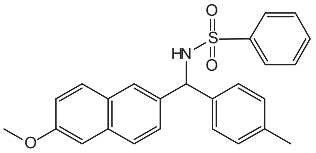
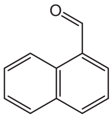
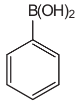
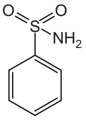
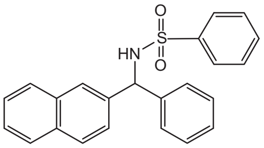
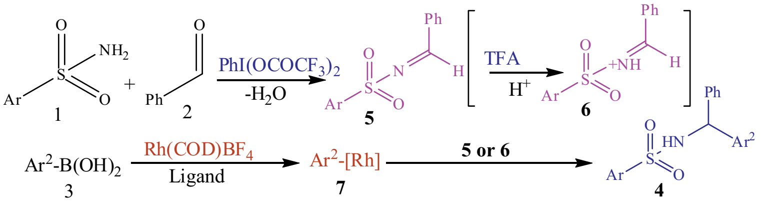
Table 2 (*continued*)

Entry	Aldehyde	Boronic acid	Sulfonamide	Diaryl amine	Yield[b] (%)
9					91
10					89
11					86

[a] Reaction condition: arylaldehyde (1.0 mmol), boronic acid (2.0 mmol), sulfonamide (1.0 mmol), Rh(COD)$_2$BF$_4$ (2.0 mol %), PhI(OCOCF$_3$)$_2$ (25.0 mol %), and ligand **2** (3.0 mol %), 2 mL toluene used as solvent.

[b] Isolated yield.



Scheme 1. A plausible mechanism for one pot synthesis of diarylmethylamine.

acid, and sulfonamide in the presence of hyper-valent based iodine reagent, PhI(OCOCF$_3$)$_2$. The protocol is applicable to a diverse range of substrate combinations with wide functional group tolerance.

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Supplementary data

Supplementary data (general procedure for synthesis, characterization data and copies of ^{1}H and ^{13}C NMR spectra of all the compounds) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.08.003.

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