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$RhCl(PPh_3)_3$/DPPF: A Useful and Efficient Catalyst for Cross-Coupling Reactions of Activated Alkenyl Tosylates with Arylboronic Acids

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Keywords: Rhodium / 1,1′-Bis(diphenylphosphanyl)ferrocene / Cross-coupling / activated alkenyl tosylates / Natural product-like compounds

A useful and effective rhodium catalyst system – [$RhCl(PPh_3)_3$/DPPF] – for the Suzuki–Miyaura cross-coupling of activated alkenyl tosylates is described. The results not only represent the first examples of the rhodium-catalyzed Suzuki–Miyaura coupling of activated alkenyl tosylates with arylboronic acids under mild conditions, but also provide an efficient route for the synthesis of some natural product-like compounds, such as furan-2(5*H*)-one, coumarin, pyrone, and quinolin-2(1*H*)-one derivatives.

Introduction

Transition-metal catalyzed cross-coupling reactions, extensively employed in a wide range of areas in organic chemistry, are arguably one of the most powerful methods for carbon–carbon bond formation.[1] While a large variety of organic electrophiles and organometallic reagents can be applied in the coupling reactions, this field is largely dominated by the use of palladium or nickel complexes as catalysts.[1] Recently, rhodium-catalyzed cross coupling reactions have attracted much attention because an electron-rich arylrhodium intermediate may undergo oxidative addition of electrophilic aromatic substrates.[2] The stoichiometric activation of aryl chlorides on a phenylrhodium complex has been realized.[3] Moreover, these rhodium catalysts have been employed in the catalytic cross-coupling of arylboron reagents with acid anhydrides,[2] aryl bromides, and electron-deficient aryl chlorides,[4] as well as in the cross-coupling of arylzinc reagents with aryl iodides.[2] Missing is a system capable of handling triflates and arenesulfonates.

Arenesulfonates are emerging as important alternatives to aryl/vinyl triflates and halides in transition metal-catalyzed cross-coupling reactions. They are often more stable and easier to handle than the corresponding triflates both in the solid state and in solution. As a direct result of these described advantages, arenesulfonates are becoming prominent substrates in cross-coupling reactions. Although tosylates are relatively unreactive compared to their halide and triflate counterparts in cross-coupling reactions, the use of arenesulfonates as electrophiles has recently witnessed remarkable progress.[5–11] Among these, the Suzuki–Miyaura[12] coupling reactions of arenesulfonates are the most attractive. Many inert, widely available arenesulfonates have been employed as coupling partners in palladium or nickel-catalyzed Suzuki–Miyaura coupling reactions including reactions performed at room temperature.[5] However, Suzuki–Miyaura couplings of arenesulfonates with boronic acids with the utilization of rhodium as a useful catalyst have not yet been disclosed. In view of their ease of preparation, increased stability, and lower expense relative to aryl triflates, as well as to broaden the application of rhodium-catalyzed cross-coupling reactions, it is of significant interest to develop general protocols for the employment of arenesulfonates in Rh-catalyzed Suzuki–Miyaura cross-coupling reactions.

With the use of a chemical genetic approach for the analysis of biological systems – the use of interfaced libraries of natural product-like molecules in connection with biological assays[13] – we became interested in the development of new approaches for the synthesis of some privileged scaffolds,[14] such as furan-2(5*H*)-one, coumarin, pyrone, and quinolin-2(1*H*)-one derivatives (Figure 1), because of their extraordinary biological activities.[15–16] The structural similarity of 4-hydroxycoumarin with 4-hydroxy-2(1*H*)-quinolone, 4-hydroxy-pyrones, and 4-hydroxy-2(5*H*)-furanones led us to envisage that their 4-tosyloxy species could be employed in transition metal catalyzed cross-coupling reactions as an ideal alternative to their corresponding triflates because of their increased stability, lower cost, and the commercial availability of their synthetic precursors. Herein, we disclose our preliminary results, which not only represent

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the first examples of the rhodium-catalyzed Suzuki–Miyaura coupling of activated alkenyl tosylates with arylboronic acids under mild conditions, but also provide an efficient route for the synthesis of 4-substituted furan-2(5*H*)-ones, coumarins, pyrones, and quinolin-2(1*H*)-ones.

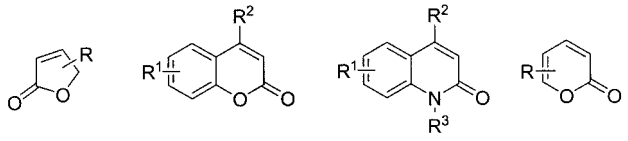


Figure 1. Some privileged scaffolds.

Results and Discussion

These tosylates were simply prepared from the corresponding 4-hydroxy species with *p*-toluenesulfonyl chloride in the presence of triethylamine (Figure 2). At the outset of our research, 4-tosyloxy-2(5*H*)-furanone (**1a**) was selected for model studies. Gratifyingly, in an initial experiment, we found that the coupling of **1a** with 4-methoxyphenylboronic acid in the presence of CsF catalyzed by RhCl(PPh$_3$)$_3$ (2 mol-%) in toluene heated at 50 °C under a nitrogen atmosphere proceeded smoothly to afford the desired product, **2a**, in 47% yield (Table 1, Entry 1). Under the same conditions, [RhCl(cod)]$_2$ and [RhCl(C$_2$H$_4$)$_2$]$_2$ proved less effective (results not shown in the Table).[17] With this promising result in hand, a number of ligands were then screened. As shown in Table 1, bidentate dppf and dppp were found to be good ligands for this coupling (Entries 2 and 3) and afforded **2a** in 82% and 72% yield, respectively. Other ligands, including PCy$_3$ and Buchwald's arylphosphanes,[5b,18] showed results that were disappointing (Entries 4–9). Further studies established that the product yields decreased with a decreasing amount of catalyst (e.g. 1 mol-%, 45% yield). Toluene was the best choice among the solvents screened (toluene, dioxane, DMF, DMSO, EtOH, and THF), and the results indicated that it was very critical for this reaction. We also found that CsF was the best base, and the reaction temperature could be lowered to 50 °C at the expense of the reaction time. The trend for the choice of solvent and base was similar to that reported by Satoh and Miura.[4] Interestingly, hydroxide bases, usually favored in palladium catalyst systems, were found to be ineffective (Table 1, Entries 20 and 21).

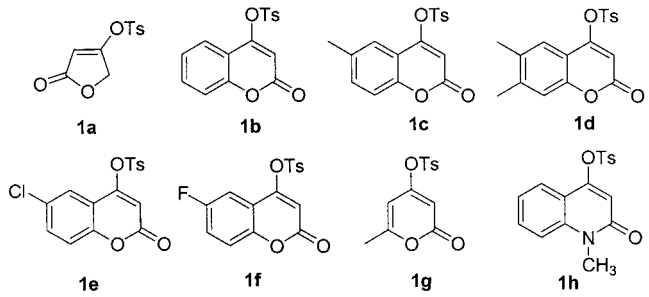
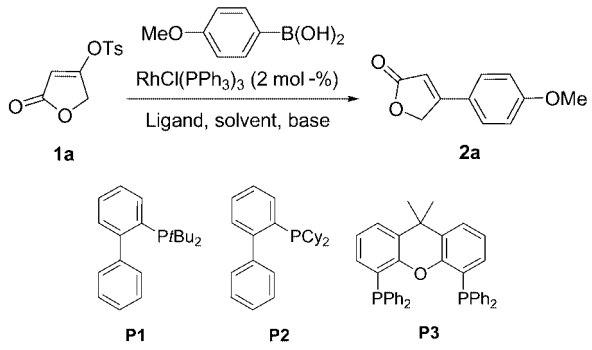


Figure 2. Tosylates.

Table 1. Reaction of 4-tosyloxy-2(5*H*)-furanone **1a** with 4-methoxyphenylboronic acid catalyzed by RhCl(PPh$_3$)$_3$.[a]

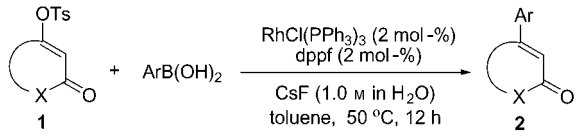


Entry	Ligand	Solvent	Base	Yield [%][b]
1	none	toluene	CsF	47
2	dppf	toluene	CsF	82
3	dppp	toluene	CsF	72
4	bpy	toluene	CsF	n.r.
5	P(*o*-tolyl)$_3$	toluene	CsF	58
6	PCy$_3$	toluene	CsF	trace
7	P1	toluene	CsF	45
8	P2	toluene	CsF	27
9	P3	toluene	CsF	n.r.
10	dppf	DMF	CsF	n.r.
11	dppf	DMSO	CsF	n.r.
12	dppf	dioxane	CsF	n.r.
13	dppf	THF	CsF	n.r.
14	dppf	EtOH	CsF	n.r.
15	dppf	toluene	KF	53
16	dppf	toluene	Cs_2CO_3	42
17	dppf	toluene	K_2CO_3	50
18	dppf	toluene	Na_2CO_3	58
19	dppf	toluene	K_3PO_4	29
20	dppf	toluene	LiOH	n.r.
21	dppf	toluene	NaOH	n.r.

[a] Reaction conditions: 4-tosyloxy-2(5*H*)-furanone (**1a**, 0.25 mmol), (4-methoxyphenyl)boronic acid (2.0 equiv.), RhCl(PPh$_3$)$_3$/ligand (1:1, 2 mol-%), solvent (4.0 mL), base (1.0 mL, 1.0 M in H$_2$O), 50 °C, 12–24 h. [b] n.r.: no reaction. Isolated yield based on 4-tosyloxy-2(5*H*)-furanone (**1a**).

Thus, with the optimized catalyst system, a variety of activated alkenyl tosylates were examined in the Rh^{I}-catalyzed cross-coupling reaction with arylboronic acids; the results are summarized in Table 2. In most cases, the activated alkenyl tosylates reacted efficiently with both electron-rich and electron-poor arylboronic acids to afford the corresponding coupling products in good to excellent yields. The failure of **1a** in the coupling with thiophene-2-boronic acid was possibly due to the deactivation of the catalyst by sulfur (Entry 4). Substituted 4-tosyloxycoumarins showed broad generality when coupled with various arylboronic acids, and substrates with electron-withdrawing groups provided better results. For example, an almost quantitative yield was obtained (99%) when 6-fluoro-4-tosyloxycoumarin (**1f**) reacted with 4-fluorophenylboronic acid (Table 2, Entry 16). 4-Tosyloxypyrone (**1g**) was also a good partner in this coupling reaction and excellent yields were obtained with various arylboronic acids (Entries 17–20), whereas reactions of 4-tosyloxyquinolin-2(1*H*)-one (**1h**) afforded moderate yields (Entries 21–22).

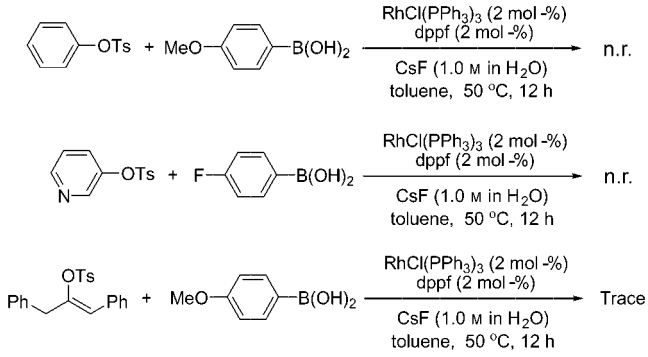
Table 2. Reaction of arenesulfonates **1** with arylboronic acid catalyzed by $RhCl(PPh_3)_3$.[a]



Entry	1	$ArB(OH)_2$	Product	Yield [%][b]
1	**1a**	4-$OMeC_6H_4B(OH)_2$	**2a**	82
2	**1a**	$C_6H_5B(OH)_2$	**2b**	50
3	**1a**	2-$ClC_6H_4B(OH)_2$	**2c**	93
4	**1a**	thiophene-2-$B(OH)_2$	**2d**	–
5	**1b**	$C_6H_5B(OH)_2$	**2e**	60
6	**1b**	4-$OMeC_6H_4B(OH)_2$	**2f**	88
7	**1b**	4-$FC_6H_4B(OH)_2$	**2g**	88
8	**1c**	$C_6H_5B(OH)_2$	**2h**	61
9	**1c**	4-$OMeC_6H_4B(OH)_2$	**2i**	70
10	**1c**	4-$FC_6H_4B(OH)_2$	**2j**	78
11	**1d**	$C_6H_5B(OH)_2$	**2k**	74
12	**1e**	$C_6H_5B(OH)_2$	**2l**	79
13	**1e**	4-$FC_6H_4B(OH)_2$	**2m**	95
14	**1f**	$C_6H_5B(OH)_2$	**2n**	91
15	**1f**	4-$MeC_6H_4B(OH)_2$	**2o**	89
16	**1f**	4-$FC_6H_4B(OH)_2$	**2p**	99
17	**1g**	$C_6H_5B(OH)_2$	**2q**	98
18	**1g**	4-$MeC_6H_4B(OH)_2$	**2r**	93
19	**1g**	4-$ClC_6H_4B(OH)_2$	**2s**	93
20	**1g**	4-$FC_6H_4B(OH)_2$	**2t**	99
21	**1h**	$C_6H_5B(OH)_2$	**2u**	51
22	**1h**	4-$FC_6H_4B(OH)_2$	**2v**	50

[a] Reaction conditions: arenesulfonate **1** (0.25 mmol), arylboronic acid (2.0 equiv.), $RhCl(PPh_3)_3$/dppf (1:1, 2 mol-%), toluene (4.0 mL), CsF (1.0 mL, 1.0 M in H_2O), 50 °C, 12 h. [b] Isolated yield based on arenesulfonate **1**.

Other substrates, such as aryl, heteroaryl, and standard vinyl tosylates, were employed in the optimized reaction conditions. However, the results were disappointing (results shown in Scheme 1). It seems that only activated alkenyl tosylates were effective under these conditions.



Scheme 1. Reactions of other tosylates.

Conclusions

In summary, we have described a useful and effective rhodium catalyst system for the Suzuki–Miyaura cross-coupling of activated alkenyl tosylates. These results not only represent the first examples of the rhodium-catalyzed Suzuki–Miyaura coupling of activated alkenyl tosylates with arylboronic acids under mild conditions, but also provide an efficient route for the synthesis of furan-2(5*H*)-one, coumarin, pyrone, and quinolin-2(1*H*)-one derivatives, which could be directly used for biological assays.

Experimental Section

General Procedure for the Rh^I-catalyzed Suzuki–Miyaura Coupling of Arenesulfonates with Arylboronic Acids: A mixture of the activated alkenyl tosylate (0.25 mmol), arylboronic acid (2.0 equiv.), $RhCl(PPh_3)_3$ (2 mol-%), and DPPF (2 mol-%) was added into a reaction tube under a nitrogen atmosphere. Toluene (4.0 mL) and aqueous cesium fluoride (1.0 mL, 1.0 M solution) were then added. The reaction mixture was stirred at 50 °C. After the reaction was completed as monitored by TLC, the organic phase was separated and purified directly by flash chromatography (silica gel) to afford the corresponding product.

Supporting Information (see also the footnote on the first page of this article): All the products are known compounds. The characterizations of these compounds are identical with the literature reports.[19–29] For details, please see Supporting Information.

Acknowledgments

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