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A Homogeneous, Recyclable Rhodium(I) Catalyst for the Hydroarylation of Michael Acceptors

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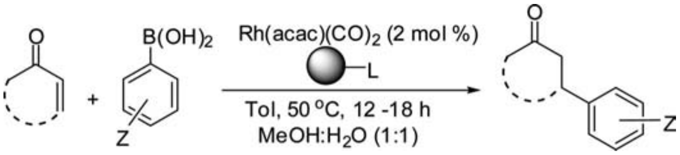
ABSTRACT



A robust and practical polymer-supported, recyclable biphephos rhodium(I) catalyst has been developed. Control of polymer molecular weight allowed the tuning of solubility such that the polymer-supported catalyst is soluble in nonpolar solvents and not soluble in polar solvents. Thus, catalytic addition of aryl- and vinylboronic acids to enones occurs under completely homogeneous conditions and catalyst recycle can be achieved by simple precipitation and filtration.

A recent survey reveals an extreme rise in the market price of rhodium such that it is by far the most expensive transition metal (28 172 USD/mol).[1] Since rhodium catalysts have wide-ranging utility in organic synthesis,[2−4] extensive attention has been paid to the development of methods for the recycle of the costly rhodium catalyst.[5] Immobilization of the catalyst on solid supports like silica[6] leads to a heterogeneous catalytic system that facilitates recycle, but ultimately reduces the catalytic efficiency and/or selectivity in synthetic transformations. Since homogeneous catalysts are often more selective than heterogeneous catalysts and are not impeded by mass-transfer effects that reduce activities of heterogeneous catalysts, the development of recyclable, *homogeneous* supports is expected to provide more synthetically tunable and practical catalysts. Here we report the design and development of a homogeneous polymer support and its successful application to the rhodium-catalyzed 1,4-additions of aryl- and vinylboronic acids to enones. Exploiting the property of the polymers' differential solubility, phase trafficking by simple precipitation with an antisolvent can be used to recover and reuse the catalyst without appreciable loss of catalytic efficiency.[7]

Previously, several research groups[5,8] have developed polystyrene supports that facilitate the recycle of rhodium

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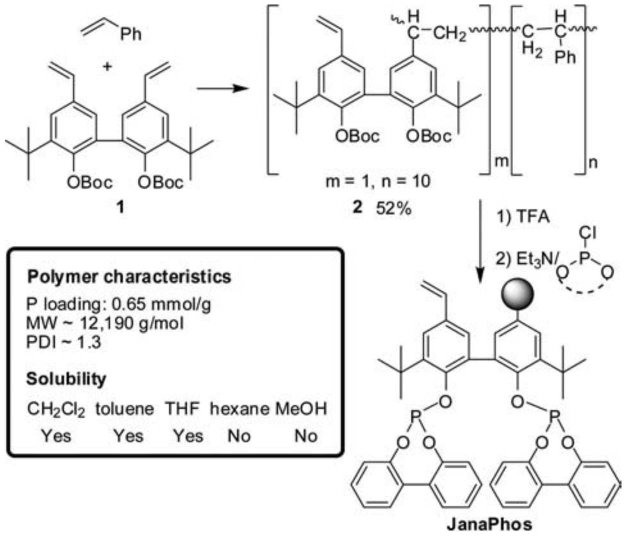
catalysts. However, the typical polymer supports suffer from serious limitations like insolubility, gel formation, tedious procedures to swell the polymer, and limited loading of the phosphorus ligand in the polymer backbone (e.g., 0.17 mmol/g).[5b] Many of these issues relate to the fact that polymers that are purchased commercially, or are prepared by conventional radical polymerization of styrene, have high molecular weight and/or broad molecular weight distribution. Thus, they have poor solubility properties. The slower kinetics of reactions catalyzed by gel-phase or solid-phase catalysts have important practical effects as well. For instance, the conjugate addition of arylboronic acids to enones suffers from competing hydrolysis of the costly boronic acids: the slower the catalyst is, the more hydrolysis occurs. Thus, when a heterogeneous polystyrene-supported catalyst is used for the conjugate addition, a 4−5-fold excess of boronic acid is required.[5] We hypothesized that problems such as this could be solved by synthesis of soluble polymer-supported rhodium catalysts that have a narrow molecular weight distribution yet can be readily recycled by precipitation and filtration. In addition to molecular weight control, it was important to design a polymer support that could bind Rh in a bidentate fashion. Such binding was expected to better site-isolate the rhodium catalysts as well as prevent leaching of rhodium from the polymer.

Ultimately, we have been able to synthesize a well-characterized polymer having comparatively low molecular weight and a narrow molecular weight distribution ($\sim 1.2 \times 10^4$, PDI = 1.3, Scheme 1).[9] Control of the molecular weight and distribution was achieved by adopting a living free radical polymerization technique that is mediated by the stable nitroxyl radical, TEMPO.[9] Conducting the copolymerization of the functional monomer **1** and styrene (1:10 ratio) at 123 °C produced a functional polymer whose ligand incorporation into the polystyrene backbone was estimated at 10% from the ^{1}H NMR spectrum. Interestingly, end group analysis of the vinyl region of the ^{1}H NMR spectrum suggests that the polymer is not cross-linked under these conditions. In other words, a single alkene in the bis-alkene **1** undergoes polymerization. The resulting polymer was deprotected and the phosphite ligands introduced onto the polymer backbone. The result is a polymer-supported Biphephos derivative that we call JanaPhos.[10] If incorporation of the phosphite into the polymer was perfect, one would expect a P-loading of 1.10 mmol/g and thus the ligand loading would be 0.55 mmol/g. Estimation of the P loading by ^{31}P NMR spectroscopy shows that the P-loading is 0.65 mmol/g. This value was further confirmed by ICP-OES analysis of the polymer, indicating that the polymer can support 0.32 mmol of rhodium per gram of polymer.[11]

Scheme 1. Synthesis of Polymer-Supported Ligand



Polymer characteristics

P loading: 0.65 mmol/g
MW ~ 12,190 g/mol
PDI ~ 1.3

Solubility

CH_2Cl_2	toluene	THF	hexane	MeOH
Yes	Yes	Yes	No	No

The polymer-supported phosphite is quite soluble in tetrahydrofuran, dichloromethane, and toluene (e.g., 60 mg/ml in toluene), but is insoluble in methanol. Thus, it is recovered quantitatively by simple precipitation with MeOH and filtration.

Next, we turned our attention to the examination of the supported rhodium complexes in catalytic hydroarylations of enones. The typical experimental procedure is straightforward and simple to operate. A mixture of enone (1 mmol) and arylboronic acid (1.3 equiv) was placed in a round-bottomed flask and a toluene solution (3 mL) containing $Rh(acac)(CO)_2$ and JanaPhos was added to it under an inert atmosphere. Finally, a solution of methanol and water (1:1, 0.5 mL) was added to it via syringe and the resulting reaction mixture was heated at 50 °C. As can be seen from Table 1, enals, aliphatic enones, chalcones, and cyclic enones all give high yields of hydroarylation products with our ligand.[12] Importantly, these high yields are obtained when using just 1.3 equiv of boronic acid partners; related reactions with polymer-supported rhodium catalysts require 4−5-fold excess of boronic acids.[5] In fact, our recyclable catalyst performs as well as, or better than, typical small-molecule catalysts which typically utilize 1.3−10 equiv of boronic acid.[2a,5]

It is important to note that the MeOH/H_2O cosolvent used in the hydroarylations was not enough to cause precipitation of the catalyst. In fact, the use of water as a cosolvent has a marked positive effect on the reaction yield; in the absence of protic cosolvent, the hydroarylation of cyclohexenone proceeds to only 35% conversion after 15 h.

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(9) Since our functional monomer proved to be equally active toward polymerization as styrene, the PDI is expected to be similar to that reported for pure polystyrene: Dollin, M.; Szkurhan, A. R.; Georges, M. K. *J. Polym. Sci., Part A* **2007**, *45*, 5487.

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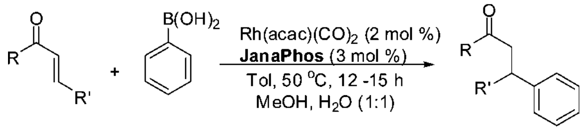
(11) Recent reaction improvements have led to phosphorus loadings of 1.06 mmol/g; however, the experiments reported in this paper utilized polymer with lower (0.65 mmol/g) phosporus loading.

(12) A control experiment wherein cyclohexenone was treated with phenylboronic acid without added $Rh(acac)(CO)_2$ and did not produce any product under identical conditions.

Table 1. Conjugate Addition of Phenylboronic Acid



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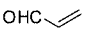
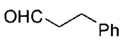
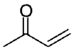
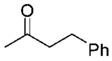
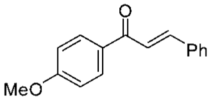
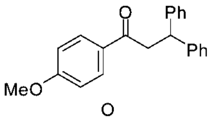
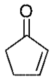
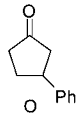
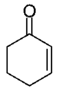
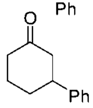
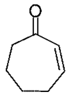
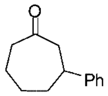
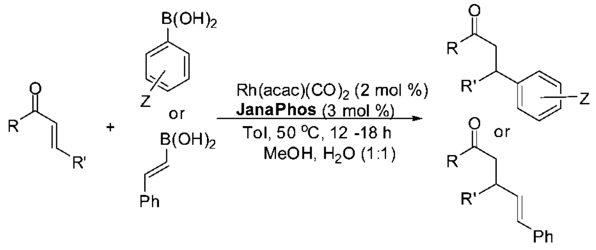
1			82
2			86
3			84
4			92
5			83
6			86

Table 2. Rh-Catalyzed 1,4-Addition of Boronic Acids



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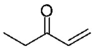
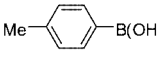
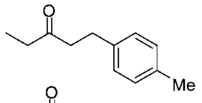
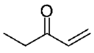
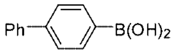
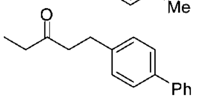
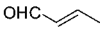
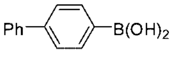
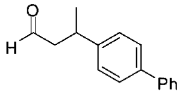
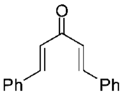
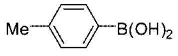
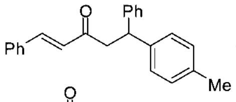
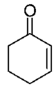
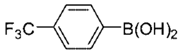
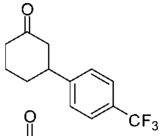
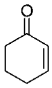
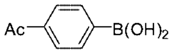
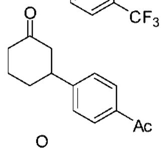
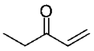
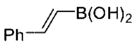
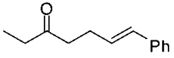
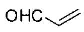
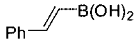
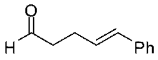
1				87
2				83
3				87
4				77
5				87
6				75[a]
7				77
8				82

[a] 2 equiv of the boronic acid was used.

Next, the scope of boronic acids that can be utilized was briefly examined. Simple aryl and biaryl boronic acids all provided good yields of arylated products with a variety of enals and enones (Table 2). Moreover, dibenzylidene acetone undergoes selective monoarylation, generating only 5% of the double-addition product (Table 2, entry 4). Lastly, vinylboronic acids were suitable reaction partners, allowing access to γ,δ-unsaturated ketones (Table 2, entries 7 and 8).

Having explored the general scope of the reaction, our attention turned to recycle of the catalyst. Here, the reaction was run as previously described. Then, upon completion of the hydroarylation, excess methanol was added to the reaction mixture and the catalyst precipitated out as a white solid (Figure 1). While the white solid is somewhat unusual for a rhodium-containing catalyst, the ^{31}P$-$^{103}Rh coupling present in the ^{31}P NMR of isolated catalyst confirms that Rh remains bound to the polymer.[13]

The catalyst was then isolated by filtration and used for subsequent reactions. It was observed that performing the filtration under air was associated with the gradual loss of catalytic activity as gauged by the yield of product (Table 3). However, filtration under an inert atmosphere allowed recycle with no appreciable loss of catalytic activity (Table 3).

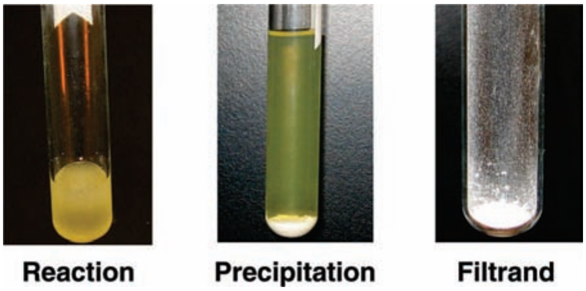


Figure 1. Recycle of catalyst.

Next, to examine the utility of the catalyst on a somewhat larger scale, the reaction of cyclohexenone with phenylboronic acid was performed on a 20 mmol scale and the product 2-phenylcyclohexanone was isolated in identical yield (83%) to the small-scale reaction (Table 1, entry 5). Thus, the ligands described herein may have practical application in larger scale reactions.

Finally, with the goal of demonstrating the broad utility of the soluble polymer-bound ligand reported herein, a variety of standard rhodium-catalyzed reactions were per-

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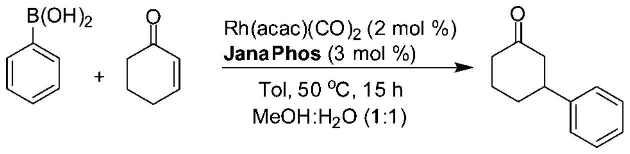
(13) See the Supporting Information for details.

Table 3. Catalyst Recycle

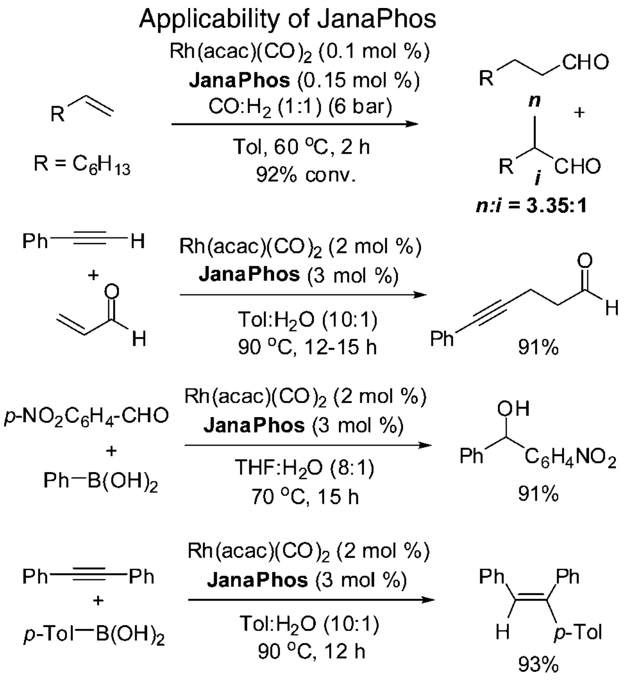


filtration under air		filtration under argon	
run	yield (%)	run	yield (%)
1	83	1	83
2	83	2	83
3	85	3	82
4	73	4	82
5	68	5	83

formed with the JanaPhos ligand (Scheme 2). As is evident from Scheme 2, good yields of product are obtained in the hydroformylation of 1-octene,[10] conjugate addition of an alkyne to acrolein,[14] arylation of an aldehyde,[4a,15] and arylation of an alkyne.[4d] Broader substrate scope studies of these reactions are ongoing and will be reported in due course.

In conclusion, we have developed a recyclable polymer-supported rhodium(I) catalyst for the efficient 1,4-addition of aryl- and vinylboronic acids to enones. In addition the catalyst is active for a number of other rhodium-catalyzed reactions, including hydroformylation. The catalyst operates under homogeneous catalytic conditions, thus avoiding typical problems associated with heterogeneous catalysts. Finally, the supported catalyst can be readily recycled by simple precipitation and filtration.

Scheme 2. Applicability of JanaPhos



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Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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