Amphiphilic Resin-Supported Rhodium-Phosphine Catalysts for C-C Bond Forming Reactions in Water

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Abstract: Amphiphilic resin-supported rhodium-phosphine complexes were prepared on polystyrene-poly(ethylene glycol) graft co-polymer (1% DVB cross-linked) beads. The immobilized rhodium complexes exhibited high catalytic activity in water to promote hydroformylation of 1-alkenes, [2+2+2] cyclotrimerization of internal alkynes forming benzene rings, and 1,4-addition of arylboronic acids.
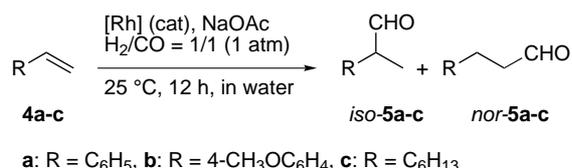
Keywords: 1,4-addition reaction of arylboron reagents; amphiphilic resin-supported catalyst [2+2+2] cyclotrimerization of alkynes; hydroformylation; rhodium

The development of organic reactions in water is becoming an important chemical research topic[1] just as organic reactions using solid-supported catalysts are gaining in popularity due to more efficient methods for product purification and catalyst recycling.[2] We have developed amphiphilic resin-supported palladium complexes with a view toward using them for catalytic reactions in water.[3] The immobilized complexes exhibited high catalytic activity as well as stereoselectivity[4] in various palladium-catalyzed organic transformations in water where the advantages of both a water-based reaction and heterogeneous catalysis have been combined in one system. Thus, for example, π-allylic substitution, carbonylation, and Suzuki–Miyaura cross-coupling have been achieved in water using a palladium complex immobilized by coordination with a triarylphosphine anchored on an amphiphilic polystyrene-poly(ethylene glycol) graft co-polymer (1% DVB cross-linked) (PS-PEG-phosphine, **1**). As part of our effort to develop wide utility of this PS-PEG phosphine ligand, rhodium-phosphine complexes bound to PS-PEG resin were prepared, and their basic catalytic abilities were examined for three types of rhodium-catalyzed carbon-carbon bond forming reactions, i.e., hydroformylation of 1-alkenes, [2 + 2 + 2] cycloaddition of internal alkynes forming benzene rings, and Michael-type alkylation of enones with arylboronic acids.

Preparation of PS-PEG-supported rhodium-phosphine complexes: Amphiphilic resin-supported rhodium-phosphine complexes[5] were readily prepared by treatment of PS-PEG-phosphine **1** with [RhCl(CO)$_2$]$_2$. Thus, a mixture of PEG-PS-phosphine **1** (loading value: ca. 0.4 mmol/g)[6] and an excess amount of [RhCl(CO)$_2$]$_2$ was agitated in dichloromethane at room temperature to give the PS-PEG resin-supported monophosphine-rhodium complex **2** quantitatively. The resin-supported bisphosphine complex **3** was obtained from the complexation performed in acetonitrile under otherwise similar conditions. Treatment of the monophosphine complex **2** in acetonitrile also gave the bisphosphine complex **3** whereby acetonitrile-promoted dissociation of the rhodium species from **2** occurred to form compound **3**. The reaction progress was conveniently monitored by gel-phase ^{31}P MAS-NMR studies of the resin beads swollen with chloroform-*d*. After formation of the complexes **2** and **3**, a narrow singlet at δ = −5 ppm observed for the starting resin phosphine **1** disappeared and was replaced by a doublet at 44 ppm with a coupling constant of 177 Hz (for complex **2**), and 28 ppm with a coupling constant of 128 Hz (for complex **3**), respectively. The remarkable low field shifts and the observation of Rh-P coupling demonstrate that the phosphine group of **1** coordinates to rhodium forming the complexes **2** and **3**.
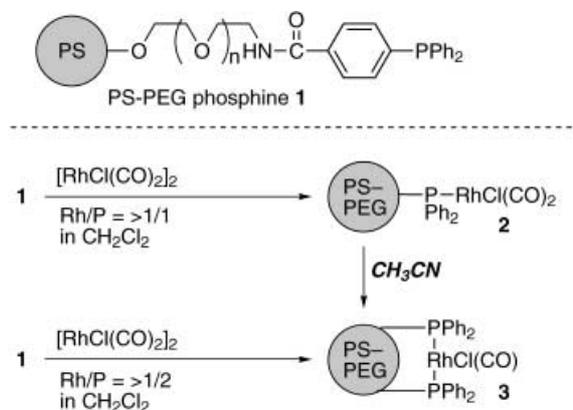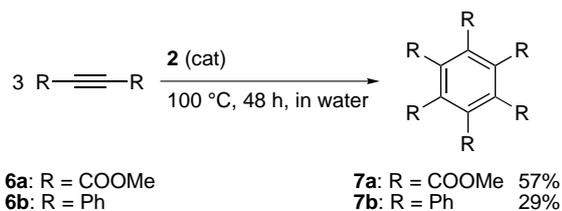

Scheme 1. Preparation of PS-PEG-supported Rh-phosphine complexes **2** and **3**.

Scheme 2. Rh-catalyzed hydroformylation of alkenes in water.

a: R = C_6H_5, **b**: R = 4-$CH_3OC_6H_4$, **c**: R = C_6H_{13}

6a: R = COOMe   **7a**: R = COOMe 57%
6b: R = Ph   **7b**: R = Ph   29%

Scheme 3. Rh-catalyzed trimerization of alkynes in water.

Rhodium-catalyzed hydroformylation in water: The catalytic utilities of the amphiphilic resin-supported complexes **2** and **3** in water were first examined for the rhodium-catalyzed hydroformylation[7] of terminal alkenes where the hydroformylation was found to take place under atmospheric pressure conditions at 25 °C (Scheme 2). Thus, a mixture of styrene (**4a**) and resin-supported monophosphine-rhodium **2** (5 mol % Rh to styrene) in an aqueous solution of sodium acetate was shaken at 25 °C for 12 h under an atmospheric pressure of H_2/CO (1/1) to give a quantitative yield of the hydroformylation products iso-**5a** and nor-**5a** in a ratio of 4.3 to 1 (Table 1, entry 1). The catalytic activity of **3** was lower than that of **2** in the hydroformylation of styrene, giving a 35% yield of **5a** under otherwise similar reaction conditions (entry 2). The chemical yield of the hydroformylation product **5a** was significantly lower without sodium acetate, namely 11% (entry 3). While potassium carbonate and pyridine were effective as additives in the present catalysis in furnishing high yields of **5**, the ratios of the iso-**5**/nor-**5** were decreased to 3.1/1 (entries 4 and 5). Hydroformylation of 4-methoxystyrene (**4b**) gave a 77% yield of **5b** in an iso/nor ratio of 4.9/1 (entry 6). Octene (**4c**) also underwent hydroformylation under the same conditions to give nonyl aldehyde **5c** where the linear product nor-**5c** was obtained as the major regioisomer (entry 7).

Cyclotrimerization of alkynes forming hexasubstituted benzenes in water: Cyclotrimerization of alkynes has been thoroughly investigated with group 9 transition metals to form aromatic compounds.[8] Rhodium-catalyzed cycloaddition of dimethyl acetylenedicarboxylate (DMAD, **6a**) was examined to demonstrate the basic catalytic activity of the PS-PEG-supported complex **2** in water. Thus, when a mixture of **6a** and **2** was refluxed in water for 48 h, cyclotrimerization took place to give 57% of hexamethyl benzenehexacarboxylate.[9] Tolan (**6b**) gave 29% of hexaphenylbenzene under the same conditions. Although the chemical yields observed in the cyclotrimerization were not satisfactory, the PS-PEG resin-supported rhodium complex demonstrated its potential by realizing "aqueous switching" and "heterogeneous switching" in the reaction.

Rhodium-catalyzed 1,4-addition of ArB(OH)$_2$ in water:[10–12] Rhodium-catalyzed 1,4-addition of arylboron reagents to enones is rapidly becoming an important reaction in organic synthesis. Methyl vinyl ketone (**8**) reacted with 5 equivalents of phenylboronic acid (**9a**) in water at 25 °C in the presence of 3 mol % rhodium of the PS-PEG resin-supported complex **3** to give the methyl phenethyl ketone **10a** in 81% yield (Table 2, entry 1). The chemical yield of **10a** was improved to 93% with 5 mol % Rh of **3**. Phenylboronic acids having 4-chloro and 4-trifluoromethyl substituents (**9b** and **9c**) reacted with ketone **8** to give **10b** and **10c** in 79% and 80% yield, respectively (entries 3 and 4). Cyclohexenone (**11**) underwent the Michael-type arylation using similar conditions to give a 65% yield of 3-phenylcyclohexanone (**12**) (entry 5). Recycle experiments were examined for the reaction of **8** with **9a**. Thus, after the first run

Table 1. Rh-catalyzed hydroformylation of alkenes in water.[a]

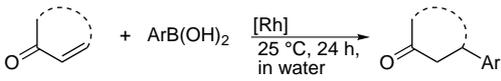| Entry	Alkene	Catalyst	Additive[b]	Product	Yield [%][c]	Ratio of iso/nor[d]
1	**4a**	**2**	NaOAc	**5a**	> 99	4.3/1
2	**4a**	**3**	NaOAc	**5a**	35	4.0/1
3	**4a**	**2**	none	**5a**	11	4.5/1
4	**4a**	**2**	K_2CO_3	**5a**	94	3.1/1
5	**4a**	**2**	pyridine	**5a**	94	3./1
6	**4b**	**2**	NaOAc	**5b**	77[e]	4.9/1
7	**4c**	**2**	NaOAc	**5c**	57	1/8.5

[a] All reactions were carried out in water at 25 °C for 12 h under CO/H_2 (1/1, 1 atm) in the presence of **2** or **3**. The ratio of alkene (mol)/catalyst (Rh equiv)/H_2O (L) = 1/0.05/10.
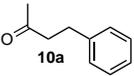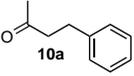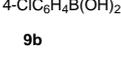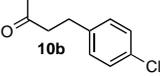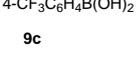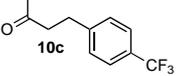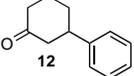[b] 0.2 M aqueous solution was used as the reaction medium.
[c] GC yield.
[d] Determined by GC analysis.
[e] Isolated yield.

Table 2. Rhodium-catalyzed Michael reaction of enones with arylboronic acids in water.[a]

Entry	Enone	ArB(OH)$_2$	Product	Yield [%][b]
1	8	PhB(OH)$_2$ 9a	10a	81[d]
2[c]	8	PhB(OH)$_2$ 9a	10a	93[d]
3	8	4-ClC$_6$H$_4$B(OH)$_2$ 9b	10b	79
4	8	4-CF$_3$C$_6$H$_4$B(OH)$_2$ 9c	10c	80
5	11	PhB(OH)$_2$ 9a	12	65

[a] All reactions were carried out in water at 25 °C for 24 h in the presence of **3**. The ratio of alkene (mol)/**3** (Rh equiv)/H$_2$O (L) = 1/0.03/4.

[b] Isolated yield.

[c] 5 mol % rhodium of **3** was used.

[d] GC yield (internal standard: naphthalene).

giving excellent yield of **10a** (Table 2, entry 2), the PS-PEG-supported rhodium complex was recovered by filtration. The recovered catalyst was successively subjected to a second and a third series of the reaction to give 85% yield (second run) and 89% yield (third run), respectively, demonstrating the practical recyclability of this catalyst. It is noteworthy that during 3 continuous recycle experiments, no deposition of rhodium metal on the glass (the so-called metal mirror) was observed. Metal leaching from the resin matrix under the reaction conditions should cause mirror formation. Although the chemical yield was only moderate, the present test reaction system is particularly interesting to us because of the possible extension to asymmetric catalysis[11] in water.

In summary, the immobilization of a rhodium complex on PS-PEG resin provided an efficient catalyst promoting a variety of rhodium-catalyzed carbon-carbon bond forming reactions in water under heterogeneous conditions. Currently, we are focusing our efforts on the development of immobilized chiral rhodium catalysts attached to PS-PEG for asymmetric catalysis in water.

Experimental Section

Preparation of PS-PEG Resin-Supported Rhodium-Monophosphine Complex 2

A Merrifield vessel was charged with 1.1 g of PS-PEG-phosphine **1** (0.37 mmol of phosphine residue), 78 mg of [RhCl(CO)$_2$]$_2$ (0.20 mmol), and 20 mL of dichloromethane under a nitrogen atmosphere. The mixture was agitated on a wrist-action shaker for 15 min. The mixture was filtered and the collected resin beads were rinsed 5 times with dichloromethane (20 mL × 10 min shaking). The resin beads were dried under vacuum at room temperature for several hours to give the pale yellow resin **2**. IR (nujol): ν = 1977 cm^{-1}; (KBr): ν = 1979 cm^{-1}; ^{31}P{^{1}H} NMR (SR-MAS, CDCl$_3$): δ = 29.2 (d, J = 128 Hz).

Preparation of PS-PEG Resin-Supported Rhodium-Bisphosphine Complex 3

A Merrifield vessel was charged with 1.1 g of PS-PEG-phosphine **1** (0.37 mmol of phosphine residue), 39 mg of [RhCl(CO)$_2$]$_2$ (0.10 mmol), and 20 mL of acetonitrile under a nitrogen atmosphere. The mixture was agitated on a wrist-action shaker for 15 min. The mixture was filtered and the collected resin beads were rinsed 5 times with dichloromethane (20 mL × 110 min shaking). The resin beads were dried under vacuum at room temperature for several hours to give the pale yellow resin **3**. IR (KBr): ν = 1961 cm^{-1}; ^{31}P{^{1}H} NMR (SR-MAS, CDCl$_3$): δ = 45.2 (d, J = 177 Hz).

Hydroformylation of Alkenes in Water;[13] General Procedure

A Merrifield vessel was charged with 80 mg of resin-bound complex **2** (loading value: 0.31 mmol/g, 5 mol % Rh), NaOAc (83 mg, 1 mmol), and 5 mL of distilled H$_2$O under a CO/H$_2$ atmosphere (1 atm). To the mixture was added alkene (0.5 mmol), and the reaction mixture was shaken on a wrist-action shaker at 25 °C for 12 h. The mixture was filtered and the resin was extracted three times with ether (5 mL × 10 min). The combined extract was dried over Na$_2$SO$_4$ and concentrated under reduced pressure to give crude **5**. The chemical yield and iso/nor ratio of the resulting aldehydes **5** were determined by GC analysis (internal standard: biphenyl).

Cyclotrimerization of Alkynes[14]

A typical procedure is given for the reaction of dimethyl acetylenedicarboxylate (**6a**). A Schlenk tube was charged with 319 mg of resin-bound complex **2** (loading value: 0.31 mmol/g, 20 mol % Rh) and 5 mL of distilled H$_2$O under a nitrogen atmosphere. To the suspension were added 61.5 μL of dimethyl acetylenedicarboxylate (**6a**; 0.5 mmol), and the reaction mixture was refluxed for 48 h. After being cooled, the mixture was filtered and the resin was extracted three times with ether (5 mL × 10 min). The combined extract was dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The crude residue was chromatographed on silica gel (eluent: n-hexane/

EtOAc = 1:1) to give hexamethyl benzenehexacarboxylate (**7a**) as a white solid; yield: 41 mg (57%).

1,4-Addition of ArB(OH)$_2$ to Enones;[15] General Procedure

A Merrifield vessel was charged with 92 mg of resin-bound complex **3** (loading value: 0.16 mmol/g, 3 mol% Rh), ArB(OH)$_2$ (2.5 mmol), and 2 mL of distilled H$_2$O under a nitrogen atmosphere. To the mixture was added **8** (41 µL, 0.5 mmol), and the reaction mixture was shaken on a wrist-action shaker at 25 °C for 24 h. The mixture was filtered and the resin was extracted three times with chloroform (2 mL × 10 min shaking). The combined extract was washed with saturated NaHCO$_3$, then dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The crude residue was chromatographed on silica gel to give the 1,4-adduct **10**.

Acknowledgements

References and Notes

[1] For examples, see: a) P. T. Anastas, T. C. Williamson, Eds.; *Green Chemistry*; ACS Symposium Series 626, American Chemical Society: Washington, DC, **1996**, and references cited therein; b) C.-J. Li, T.-H. Chan, *Organic Reactions in Aqueous Media*; Wiley, New York, **1997**; c) P. A. Grieco, (Ed.), *Organic Synthesis in Water*, Kluwer Academic Publishers, Dordrecht, **1997**; d) W. A. Herrmann, C. W. Kohlpaintner, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1524.

[2] For recent reviews, see: a) B. A. Bunin, *Combinatorial Index*, Academic Press, London, **1998**; b) D. Obrecht, J. M. Villalgordo, *Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries*, Tetrahedron Organic Chemistry Series Vol. 17, Elsevier, Oxford, **1998**; c) F. Z. Dörwald, *Organic Synthesis on Solid Phase*, Wiley-VCH, Weinheim, **2000**; d) D. E. De Vos, I. F. J. Vankelecom, P. A. Jacobs, (Eds.), *Chiral Catalyst Immobilization and Recycling*, Wiley-VCH, Weinheim, **2000**.

[3] a) Y. Uozumi, H. Danjo, T. Hayashi, *Tetrahedron Lett.* **1997**, *38*, 3557; b) Y. Uozumi, H. Danjo, T. Hayashi, *J. Org. Chem.* **1999**, *64*, 3384; c) Y. Uozumi, T. Watanabe, *J. Org. Chem.* **1999**, *64*, 6921; d) H. Danjo, D. Tanaka, T. Hayashi, Y. Uozumi, *Tetrahedron* **1999**, *55*, 14341.

[4] a) Y. Uozumi, H. Danjo, T. Hayashi, *Tetrahedron Lett.* **1998**, *39*, 8303–8306; b) Y. Uozumi, K. Shibatomi, *J. Am. Chem. Soc.* **2001**, *123*, 2919–2920.

[5] For examples of amphiphilic polymer-bound rhodium complexes reported to date, see: a) D. E. Bergbreiter, Y.-S. Li, *Tetrahedron Lett.* **1997**, *38*, 3703–3706; b) A. N. Ajjiou, H. Alper, *J. Am. Chem. Soc.* **1998**, *120*, 1466–1468.

[6] a) E. Bayer, W. Rapp, in *Chemistry of Peptides and Proteins*, (Eds.: W. Voelter, E. Bayer, Y. A. Ovchinikov, V. T. Iwanov), W. de Gruter, Berlin, **1986**, Vol. 3, pp. 3; b) W. Rapp, in *Combinatorial Peptide and Nonpeptide Libraries*, (Ed.: G. Jung), VCH, Weinheim, **1996**, pp. 425; c) X. Du, R. W. Armstrong, *J. Org. Chem.* **1997**, *62*, 5678; d) O. W. Gooding, S. Baudert, T. L. Deegan, K. Heisler, J. W. Labadie, W. S. Newcomb, J. A. Porco, Jr., P. Eikeren, *J. Comb. Chem.* **1999**, *1*, 113.

[7] For recent examples of rhodium-catalyzed hydroformylation of alkenes with solid-supported catalysts, see: P. Arya, G. Panda, N. V. Rao, H. Alper, S. C. Bourque, L. E. Manzer, *J. Am. Chem. Soc.* **2001**, *123*, 2889–2890, and references cited therein.

[8] For recent reviews on transition-metal-catalyzed [2 + 2 + 2] cyclotrimerization, see: H.-W. Frühauf, *Chem. Rev.* **1997**, *97*, 523; M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49.

[9] Hexafuctionalized benzenes have recently been gaining use as a core molecule of benzene-based dendrimers; for example, see: S. Hecht, J. M. J. Fréchet, *J. Am. Chem. Soc.* **1999**, *121*, 4084–4085.

[10] M. Sakai, H. Hayashi, N. Miyaura, *Organometallics* **1997**, *16*, 4229.

[11] For a recent review, see: T. Hayashi, *Synlett* **2001**, *SI*, 879.

[12] We have recently reported that base-catalyzed 1,4-addition (Michael reaction) in a single aqueous medium using PS-PEG resin-anchored quaternary ammonium hydroxides, see: K. Shibatomi, Y. Uozumi, *Synlett* **2000**, 1643–1645.

[13] Chemical Abstracts Registry numbers of all products have been provided by the author: *iso*-**5a**, [93-53-8]; *nor*-**5a**, [104-53-0]; *iso*-**5b**, [5405-83-4]; *nor*-**5b**, [20401-88-1]; *iso*-**5c**, [7786-29-0]; *nor*-**5c**, [124-19-6].

[14] Chemical Abstracts Registry numbers of all products have been provided by the author: **7a**, [6237-59-8]; **7b**, [992-04-1].

[15] Chemical Abstracts Registry numbers of all products have been provided by the author: **10a**, [2250-26-7]; **10b**, [3506-75-0]; **10c**, [57132-19-1]; **12**, [20795-53-3].