RSC Advances

COMMUNICATION

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View Article Online View Journal | View Issue

Cite this: RSC Advances, 2013, 3, 6747 Received 5th September 2012, Accepted 11th March 2013

DOI: 10.1039/c3ra22057e

www.rsc.org/advances

Phosphonate-containing polystyrene copolymersupported Ru catalyst for asymmetric transfer hydrogenation in water[†]

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A series of phosphonate-containing copolystyrenes with chiral ligand (1R,2R)-(+)- N^1 -toluenesulfonyl-1,2-diphenylethylene-1,2-diamine were prepared by radical copolymerization. The supported Ru catalysts with excellent catalytic performances (94–98% yields, 93.9–97.8% ee and 100% chemoselectivity) in aqueous asymmetric transfer hydrogenation could be easily recycled by centrifugal separation.

In the past decades thousands of chiral homogeneous catalysts have been developed and many of them are known to be highly effective in numerous asymmetric transformations. However, the application of homogeneous catalysts in industry is limited, partly due to the problems of separation, recycling and limited stability of the catalysts.¹ One efficient way to overcome the problem of isolation of homogeneous catalysts is the heterogenization of the active catalytic molecules. To date, heterogenization is commonly achieved by non-covalent entrapment or covalent grafting of active molecules on the surface or inside the pores of a solid support,² such as organic polymers,³ silica,⁴ and magnetic nanoparticles,⁵ as it greatly simplifies the separation of the catalyst from the reaction mixture and allows the efficient recovery and reuse of expensive homogeneous catalysts. Furthermore, from the perspective of green chemistry, reactions in which water is used as a solvent have attracted a great deal of attention because water is an environmentally friendly and safe medium, which avoids the problem of pollution that is inherent with organic solvents.⁶ Although polystyrene (PS), which has good solubility in THF, dichloromethane, chloroform, benzene and ethyl acetate, is an attractive and popular organic polymer support in the field of asymmetric catalysis,⁷ it suffers from strong shrinkage and poor swelling in highly polar solvents such as water and alcohol, resulting in poor accessibility of the reactants. In order to enhance the swelling properties of the polystyrene support and the accessibility of the substrate into the catalytic site, especially in protic and highly polar media such as water, it is necessary that the polarity of the polystyrene support is modified by the introduction of highly polar functional groups.⁸

In this communication, by introducing a phosphonate group (PO_3H_2) and the chiral ligand (1R,2R)-(+)- N^1 -toluenesulfonyl-1,2diphenylethylene-1,2-diamine into the backbone of polystyrene, a novel type of phosphonate-containing polystyrene copolymer, **2ad**, bearing chiral ligands with different arm chain lengths and **2a**₁**a**₄ with different compositions (y/x) of functional groups (PO₃H₂ and NH₂), has been prepared for the first time (Scheme 1). Due to the introduction of phosphonate (PO₃H₂) and amino (NH₂) groups, the polarity of polystyrene-based supports **2a**-**d** and **2a**₁**a**₄ was strengthened to afford good solubility in alcohol and good dispersion properties in water. The supported ruthenium catalysts **3a**-**d** and **3a**₁-**a**₄ possessed mesoporous structures and excellent catalytic performances (94–98% yield, 93.9–97.8% ee and 100%



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[†] Electronic supplementary information (ESI) available: NMR, IR, GPC, SEM, AFM, GC, nitrogen adsorption-desorption isotherm plots. See DOI: 10.1039/c3ra22057e



Fig. 1 The characterization of polystyrene copolymers $2a_1-a_4$ by ³¹P NMR, AFM and nitrogen adsorption–desorption isotherm.

chemoselectivity) in the aqueous asymmetric transfer hydrogenation of aromatic ketones. Furthermore, these polystyrene-bound Ru catalysts could be easily recovered by simple centrifugal separation in quantitative yields and reused five times without a sharp loss of their catalytic properties.

Phosphonate-containing polystyrene copolymers 2a-d and 2a1 a_4 were prepared, respectively by simple radical copolymerization of 1-phosphonate styrene with styrenes 1a-d, bearing chiral amino groups with different arm chain lengths, and styrene 1a under different molar ratios in THF at 80 °C for 24 h and in the presence of BPO as a radical initiator. The chemical compositions (y/x) in polystyrene copolymers 2a-d (y/x = 3.66-4.08) and 2a₁-a₄ (y/x =0.21-5.72), regulated by altering the amount used of 1-phosphonate styrene, could be determined by quantitative ³¹P NMR. The structural distribution of phosphonate groups (PO₃H₂) in the polystyrene backbone could be also elucidated by ³¹P NMR (Fig. 1). Compared to ³¹P NMR of 1-phosphonate polystyrene at 12.5 (q), 5.1 (s), 1.0 (s) and 0.0 ppm (s), the new and wide ³¹P NMR peak of $2a_1-a_4$ emerged in the range of δ 20–35 ppm beside the same sharp four peaks as 1-phosphonate polystyrene, which resulted from the ³¹P absorption of the chain segment copolymerized by monomer 2a with 1-phosphonate styrene. GPC analysis showed that the weight-average molecular weights (M_w) of copolymers 2a**d** and $2a_1-a_4$ were between 759.5 and 974.1 kDa and the PDI values were between 1.06 and 1.28, which may be not accurate since monodispersed polysaccharide standards were used for calibration while the copolymers 2a-d and $2a_1-a_4$ are brush polymers. The isotherm plots of $2a_1-a_4$ were linear to the P/P_0 axis at a relatively low P/P_0 range (0–0.8) and convex to the P/P_0 axis at a high P/P_0 range (0.8–1.0), which were beyond the classic definitions.⁹ From the calculated data, the pore size distributions (PSDs) of as-synthesized $2a_1-a_4$ suggest the existence of 0.8-8 nm irregular micropores with 0.7-1.3 nm average pore diameters (Fig. 1). As expected, the surface areas, average pore diameters and pore volumes of $2a_1-a_4$ increased from 3.3 to 8.3 m² g⁻¹, 0.7 to 1.7 nm and 4.6 to 8.3 × 10⁻³ cc g⁻¹, respectively, as the loading amount of 1-phosphonate styrene in the copolystyrene backbone was increased.

Taking into account the intimate relationship between the physical surface properties of the support and its catalytic performance, polystyrene copolymers $2a_1-a_4$ were well characterised by SEM, TEM and AFM to understand their surface morphologies and particle sizes in different existential states. As a representative example, after being well-dispersed in water (1 mg sample in 5 mL of H₂O), the AFM image of copolymer $2a_3$ efficiently reflected its surface morphology in water, which seemed to simulate the "true" state of $2a_3$ in the aqueous catalytic system. Among the statistically analyzed 265 particles for $2a_3$, 90% of particle sizes were in the range of 10 to 130 nm (Fig. 1). The SEM images showed that the insoluble aggregates with particle sizes of 1–5 µm dispersed in THF and could be considered to mirror the surface morphology of $2a_3$ in the solid state.¹⁰

Upon the immobilization of $[RuCl_2(p-cymene)]_2$ into polystyrene copolymers $2a_1-a_4$, the chemical composition, porous structure and surface morphology were characterized by DTG, SEM, AFM, XPS and nitrogen adsorption-desorption isotherms and some of them are shown in Fig. 2. Some nanopores (0.8-8 nm) disappeared, especially at 6.4 nm for $2a_1-a_4$, which demonstrated that the $[RuCl_2(p-cymene)]_2$ particles were trapped inside those nanopores. It is particularly worth noting that four



Fig. 2 The comparative XPS, AFM and nitrogen adsorption–desorption isotherms of support 2a₃ and its supported catalyst 3a₃.

Table 1 The catalytic performances of 3a-d and 3a1-a4 in the asymmetric transfer hydrogenation of acetophenone^a

		H₃C、NH
	3a-d, 3a ₁₋₄	
$_{R} \sim 1$	HCO ₂ H/Et ₃ N	

Entry	Cat.	R	S/C	Solvent	Conv. $(\%)^b$	Yield (%) ^c	(% ee) ^d
1	3a	Н	660	H ₂ O	100	98	97.2 (R)
2	3b	Н	660	H ₂ O	100	98	96.8 (R)
3	3c	Н	660	H ₂ O	100	98	95.1 (R)
4	3 d	Н	660	H ₂ O	100	97	95.0 (R)
5	3a ₁	Н	660	H ₂ O	100	98	96.7 (R)
6	$3a_2$	Н	660	H_2O	100	98	96.8 (R)
7	$3a_{3}(3a)$	Н	660	H ₂ O	100	98	97.2 (R)
8	3a4	Н	660	H_2O	100	98	97.8 (R)
9	3a ₃	Н	660	MeOH-H ₂ O ^e	100	98	97.2 (R)
10	3a ₃	Н	660	MeOH	100	99	97.6 (R)
11	3a ₃	Н	660	$CHCl_3$	93.8	91	97.2 (R)
12	3a ₃	Н	660	DMF	95.2	92	96.3 (R)
13	3a ₃	Н	660	THF	94.8	90	96.9 (R)
14	3a ₃	Н	2.0×10^3	H_2O	99.2	97	97.2 (R)
15	3a ₃	Н	3.3×10^{3}	H_2O	90.1	87	97.4 (R)
16	3a ₃	Н	6.6×10^{3}	H_2O	44.2	40	97.3 (R)
17	3a ₃	<i>p</i> -Br	660	H_2O	100	97	95.1 (R)
18	3a ₃	<i>m</i> -Br	660	H_2O	100	97	96.2 (R)
19	3a ₃	o-Br	660	H_2O	100	98	95.8 (R)
20	3a ₃	p-NO ₂	660	H_2O	100	96	87.1 (R)
21	3a ₃	m-NO ₂	660	H_2O	100	97	82.8 (R)
22	3a ₃	<i>p</i> -Cl	660	H_2O	100	97	95.2 (R)
23	3a ₃	<i>m</i> -Cl	660	H_2O	100	98	96.1 (R)
24	3a ₃	o-Cl	660	H_2O	100	97	95.8 (R)
25	3a ₃	p-CH ₃	660	H_2O	99.2	95	97.9 (R)
26	3a ₃	m-CH ₃	660	H_2O	100	98	97.6 (R)
27	3a ₃	o-CH ₃	660	H_2O	100	96	93.9 (R)
28	3a ₃	p-OCH ₃	660	H_2O	100	94	96.9 (R)
29	3a ₃	o-OCH ₃	660	H_2O	100	96	-92.3 (S)
30	3a ₃	m-OCH ₃	660	H_2O	100	96	97.3 (R)

^{*a*} Reaction conditions: cat. (1.5 wt% Ru, 9 mg, 1.3×10^{-3} mmol), acetophenone (0.1 mL, 0.86 mmol), HCO₂H–Et₃N (0.5 mL, v/v = 1 : 3), 50 °C, 6 h. ^{*b*} Monitored by GC. ^{*c*} Isolated yield. ^{*a*} Determined by chiral GC, chiral Cyclodex-B (30 m × 0.25 nm × 0.25 µm, Supelco). ^{*e*} v/v = 1 : 1.

typical nanopores inside 2a₁-a₄, at about 0.6-0.7, 1.0-1.3, 1.8-2.4 and 3.2-4.0 nm, were reconstructed (Fig. 2 (3)). Those nanopores provided the diffusional channels for substrates to smoothly access the catalytic sites in the catalytic process. In order to cast light on the immobilized [RuCl₂(*p*-cymene)]₂ particles, support 2a₃ and its supported Ru catalyst 3a₃ (1.5 wt% Ru) were scanned by XPS as a pair of comparative examples. As expected, some N_{1s} electron binding energies of 2a3 increased from 399.8 to 401.1 eV eV increment after the immobilization with 1.3 $[RuCl_2(p-cymene)]_2$ particles (Fig. 2 (1)). However, there were only 0.1–0.4 eV changes for S_{2p} , O_{1s} and P_{2s} binding energies. Therefore, it was concluded that the $[RuCl_2(p-cymene)]_2$ particles successfully complexed with some of the amino groups. Due to the coordination reaction between $[RuCl_2(p-cymene)]_2$ and the amino groups, the AFM images showed the change of surface morphology in length, width and height owing to the interaction force among supported Ru catalyst particles. The mean length of supported Ru catalyst 3a3 decreased from 390.0 nm to 179.7 nm. However, the mean height and width slightly increased from 0.6 and 112.5 nm to 1.9 and 138.6 nm, respectively (Fig. 2 (2)).

Aqueous transfer hydrogenation of aromatic ketones was used as a model reaction to investigate the catalytic performances of supported Ru catalysts 3a-d and $3a_1-a_4$.¹¹ Due, in part, to good solubility in MeOH and good dispersion properties in H₂O, phosphonate-containing copolymer-supported Ru catalysts 3a-d



Fig. 3 The conversion and enantioselectivity of acetophenone in the overall catalytic process.

Table 2 Literature survey for asymmetric hydrogenation of acetophenone in water^a

Support	Reaction conditions	Efficiency	Repeatability (fifth cycle)				
Sulfonated polystyrene ¹³ Poly(ethylene glycol) ¹⁴ Silica ¹⁵ Phosphonate-containing polystyrene	HCOONa, 40 °C, 3 h HCOONa, 40 °C, 3 h HCOONa, 40 °C, 2 h, 4 mol % TBAB, HCO ₂ H–Et ₃ N (v/v = $1/3$), 50 °C, 6 h	S/C = 100, 100% conv., 97% ee S/C = 100, 99% conv., 94% ee S/C = 100, 99% conv., 96% ee S/C = 660, 99% conv., 97.8% ee	98% conv., 97–98% ee 98% conv., 94% ee 70% conv., 96% ee 90% conv., 96.6% ee				
^{<i>a</i>} Over supported $[RuCl_2(p-cymene)]_2$ catalyst.							

Downloaded by University of Limerick on 08/05/2013 17:33:02. Published on 12 March 2013 on http://pubs.rsc.org | doi:10.1039/C3RA22057E and $3a_1-a_4$ exhibited excellent catalytic conversions, enantioselectivities and chemoselectivities in protic polar solvents. As the hanging arm chain lengths increased from 3a to 3d, the enantioselectivities decreased from 97.1 to 95.0% ee owing to the successively improved flexibility (Table 1, entries 1-4). Furthermore, due to the enhanced phosphonate-containing content (y/x) from 3a₁ to 3a₄, good dispersion in water was found and the enantioselectivities increased from 96.7 to 97.8% ee (Table 1, entries 5-8). Unfortunately, the conversion of acetophenone decreased to 93-95% in aprotic polar solvents (Table 1, entries 11-13). Especially, there was good conversion (90.1%), yield (87%) and excellent enantioselectivity (97.4% ee) even at the low S/ C = 3300 (0.05 mol% Ru) (Table 1, entries 14–16). The optimized protocol was expanded to a wide variety of aromatic ketones. All of them possessed excellent conversions ($\sim 100\%$), yields (94–98%) and enantioselectivities (93.9-97.9% ee, except for the nitrosubstituted aromatic ketones) for either electron-rich or -poor and o-, m- or p-position aromatic ketones (Table 1, entries 17-30).

In particular, the used amount of Et₃N played an important role in the conversion of acetophenone. At volume ratios of Et₃N–HCO₂H < 2, the asymmetric transfer hydrogenation of acetophenone barely took place like in other pH-controlled reactions in water.¹² From the TG curves of fresh catalyst **3a**₃ and one dealing with Et₃N, the weight loss between 150 and 800 °C decreased from 90.8% to 64.2%, which demonstrated that the phosphonate moieties on the polystyrene backbone in catalyst **3a**₃ underwent deprotonation with Et₃N to form phosphonates (PO₃H⁻N⁺HEt₃) and resulted in difficult thermal decomposition. On the other hand, the formation of phosphonate acting as a surfactant was identified by the good dispersion upon adding Et₃N in the catalytic reaction. The small dosage of catalyst **3a**₃ had little influence on the used amount of Et₃N (Et₃N/HCO₂H, $\nu/\nu = 3$), and Et₃N was enough to react with formic acid as a hydrogen source.

In the overall catalytic process, the catalytic intermediates were detected using HPLC. It was found that the specifically selective hydrogenation of the C=O bond was observed without side reactions such as further hydrogenolysis of C–O and the aromatic ring. The conversions of acetophenone and the enantioselectivity of R-1-phenylethanol in the catalytic process are shown in Fig. 3.

A comparison of the present system with other reported relevant catalytic systems using $[RuCl_2(p-cymene)]_2$ as a precursor in terms of the catalyst's preparation, easiness and efficiency including the reaction time, temperature, yield, selectivity and repeatability is summarized in Table 2. The phosphonate-containing polystyrene copolymer-supported Ru catalyst, in which

hydrophilic phosphonate rendered itself dispersed in water, provided an excellent example with high S/C = 660 efficiency for the asymmetric transfer hydrogenation of aromatic ketones in water.

Catalyst $3a_3$ could be easily and quantitatively recycled by centrifugal separation and reused in five consecutive runs without a sharp loss of catalytic performance (90% conv., 86% yield and 96.6% ee in the 5th cycle).

Acknowledgements

The financial support from NSFC (grant 21071116) and CSTC (2010BB4126) is gratefully acknowledged.

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