DOI: 10.1002/adsc.200800362

Asymmetric Transfer Hydrogenation of Aromatic Ketones in Water using a Polymer-Supported Chiral Catalyst Containing a Hydrophilic Pendant Group

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Received: June 11, 2008; Revised: July 28, 2008; Published online: September 9, 2008

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.200800362.

Abstract: Hydrophilic polymers having pendant groups of carboxylates or sulfonates have been used as a polymer support for chiral 1,2-diamine monosulfonamides. The polymeric chiral complex prepared from the polymer-supported chiral ligand with ruthenium dichloride·*p*-cymene was used in the asymmetric transfer hydrogenation of prochiral ketones in water. The balance between hydrophilicity and hydrophobicity of the polymer support influenced both the reactivity and the enantioselectivity of the reaction in water. The chiral polymeric complex having a quaternary ammonium salt structure as the pendant group worked well in water. In most cases the polymer-supported catalyst having a quaternary ammonium sulfonate pendant group showed superior enantioselectivity compared to the corresponding non-supported model catalyst in the solution system. The polymeric catalysts can be reused without loss of catalytic activity.

Keywords: aqueous-phase catalysis; asymmetric catalysis; hydrogen transfer; immobilization; ketones; polymers

Introduction

Organic reactions in water have attracted much attention and a great number of asymmetric reactions have been performed in water.[1] Most *in vivo* organic reactions occur in an aqueous environment, and are efficiently catalyzed by enzymes. The amphiphilic property of enzymes may be one of the most important issues to promote such organic reactions in an aqueous environment. Hydrophobic substrates are efficiently incorporated into a hydrophobic pocket of the enzyme, where the reaction smoothly occurs. However, the use of water as a reaction media in usual organic synthesis is sometimes seriously restricted since most organic compounds are less soluble in water and hydrolytic degradation of reagents or catalysts inhibits the reaction. Many efforts to overcome such drawbacks have been investigated in the past several years, and a number of efficient chiral catalysts for enantioselective reactions in aqueous media has been developed.[2]

On the other hand, from the viewpoint of efficiency in organic synthesis, polymer-supported chiral catalysts are extremely useful for asymmetric reactions, mainly due to their easy separation and recycle use after the reaction. Although a considerable number of papers on the immobilization of chiral catalyst to polymer has been published so far,[3] only a limited numbers of reports on polymer-supported chiral catalysts that can be used in water have appeared.[4–13]

The combination of the 'aqueous system' and the 'recyclable catalytic system' would provide an ideal chemical process for environmentally friendly asymmetric synthesis. The first example of this combination was demonstrated by Andersson et al.[4] They developed a water-soluble poly(acrylic acid salt)-supported (2*S*,4*S*)-4-diphenylphosphino-2-(diphenylphosphinomethyl)pyrrolidine (PPM)-rhodium(II) complex, which was used for the asymmetric hydrogenation of prochiral olefins in water. Poly(ethylene glycol) is another type of typical water-soluble polymer, which has been used as polymer support for various kinds of asymmetric reactions including transfer hydrogenation,[5a] aldol reaction[5b] and alkylation[5c] in water. However, the poly(ethylene glycol)-support provides functionalities only on the end group of the polymer chain, resulting in a very low level of catalyst loading. Water-soluble polymers are not always necessary as

supporting polymers for the organic reactions in the aqueous phase. In order to produce a suitable microenvironment for organic reactions in water, the amphiphilic property of the polymer support would be rather essential. The important work of this area has been undertaken by Uozumi et al. with amphiphilic PS-PEG [polystyrene-poly(ethylene glycol)] resin-supported chiral palladium complexes, which have been successfully used for asymmetric π-allylic substitution reactions in water.[6] Hayashi et al. also reported on asymmetric 1,4-addition using a similar type of PS-PEG resin-supported chiral rhodium catalyst in water.[7] Hydrophobic substrate molecules would make a strong interaction with the PS matrix of the catalyst in water, where reaction smoothly occurs with the catalytic moiety located in the vicinity of the substrate. Another type of amphiphilic polymer is the poly(2-oxazoline)s.[8] Polymer-supported catalysts based on poly(oxazoline)s are an important example of a polymeric catalyst that can be used in aqueous media. Nuyken et al. prepared a poly(2-oxazoline) block copolymer-supported PPM-rhodium complex for the asymmetric hydrogenation of prochiral olefins in water.[9] More recently, Weberskirch et al. demonstrated that the same type of amphiphilic block copolymer-supported Co(III)(salen) complex can be employed for the hydrolytic kinetic resolution of epoxides in water.[10] Polystyrene-supported proline derivatives are also considered to be amphiphilic polymers which were used as the organocatalyst for asymmetric aldol reactions in water.[11] A different approach to polymeric chiral catalysts in water is the use of the microencapsulation technique using hydrophobic polystyrene. Kobayashi developed a microencapsulated osmium catalyst by means of cross-linked polystyrene and used it for the asymmetric dihydroxylation of olefins with phthalazine bis-dihydroquinidine [$(DHQD)_2PHAL$] in water.[12]

We have introduced a novel type of amphiphilic polymer support that consists of a polystyrene main chain and a quaternary ammonium sulfonate as its side chain.[13] We have found that such an amphiphilic polymer support behaved efficiently to provide a suitable microenvironment for asymmetric reactions. The purpose of this study focuses on the development of the polymer support that can be efficiently used in water. In order to understand the suitability of the polymer support in aqueous media we have prepared various kinds of amphiphilic polymer supports having hydrophilic pendant groups such as carboxylates and sulfonates. Enantiopure 1,2-diamine monosulfonamide as a chiral ligand was immobilized on to such an amphiphilic polymer support for use in asymmetric reactions. We chose the asymmetric transfer hydrogenation of prochiral ketones as a model reaction to evaluate the amphiphilic polymeric catalysts.

Asymmetric transfer hydrogenation of prochiral ketones is one of the most powerful methodologies for the production of optically active secondary alcohols.[14] Among the various chiral catalysts reported for the asymmetric transfer hydrogenation, the most significant to date is the Ru(II) complex with optically active *N*-toluenesulfonyl-1,2-diphenylethylenediamine (TsDPEN) developed by the Ikariya and Noyori groups.[15] Some polymeric versions of the catalysts were also developed for the same reaction.[16] The first example of the polymer-supported 1,2-diamine monosulfonamide as a chiral ligand of an asymmetric transfer hydrogenation catalyst was reported by Lemaire and co-workers in 1997.[16a] They synthesized the polystyrene-supported chiral monosulfonamide by radical polymerization of (*S*,*S*)-**12** with styrene and divinylbenzene in CH_2Cl_2. The corresponding polymeric chiral Ru(II) complex in 2-propanol/triethylamine gave 84% *ee* with 23% yield after two days at 70 °C.

In the past several years, the effectiveness of the use of water as the sole solvent for the asymmetric transfer hydrogenation has been proved.[17,18] Polymeric chiral catalysts immobilized on PEG[5a] or silica[19] have also been prepared and used for the same reaction in water. However, polystyrene-based polymers have not been used because of their high hydrophobicity. We have designed a novel amphiphilic polymer support that consists of cross-linked polystyrene having carboxylate and sulfonate derivatives as hydrophilic pendant groups. A chiral catalyst attached to these amphiphilic polymers may be efficiently used in aqueous media. We have found that the amphiphilic polystyrene-supported chiral 1,2-diamine monosulfonamides were excellent chiral ligands for asymmetric transfer hydrogenation catalysts.[13] Although introduction of the sulfonate moiety into reagents and catalysts is a typical way to facilitate the reaction in aqueous media,[20] to the best of our knowledge, there has been no report on the use of sulfonated polymer-supported chiral catalysts in water. In this article, we describe the details of our study on the asymmetric transfer hydrogenation of aromatic ketones by using the amphiphilic polymer-supported chiral catalyst in water.

Results and Discussion

Preparation of Novel Polymer-Supported Chiral 1,2-Diamine Monosulfonamides

As shown in Figure 1 we have prepared various kinds of cross-linked polymer-supported 1,2-diamine monosulfonamides (*R*,*R*)-**1**–**9**. We first prepared enantiopure 1,2-diamine monosulfonamide monomer (*R*,*R*)-**12** from (*R*,*R*)-1,2-diphenylethylenediamine (*R*,*R*)-**10** and *p*-styrenesulfonyl chloride **11** (Scheme 1). Radical

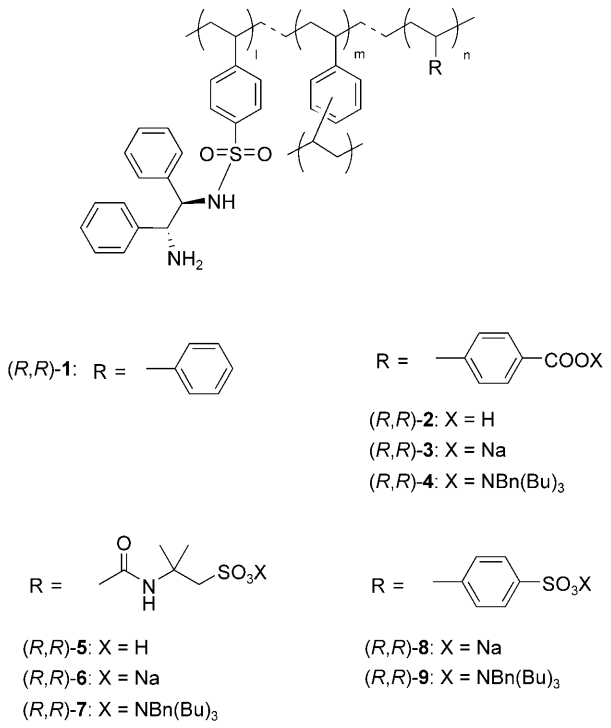
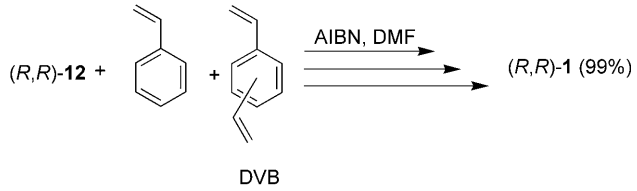


Figure 1. Polymer-supported chiral 1,2-diamine monosulfonamides.

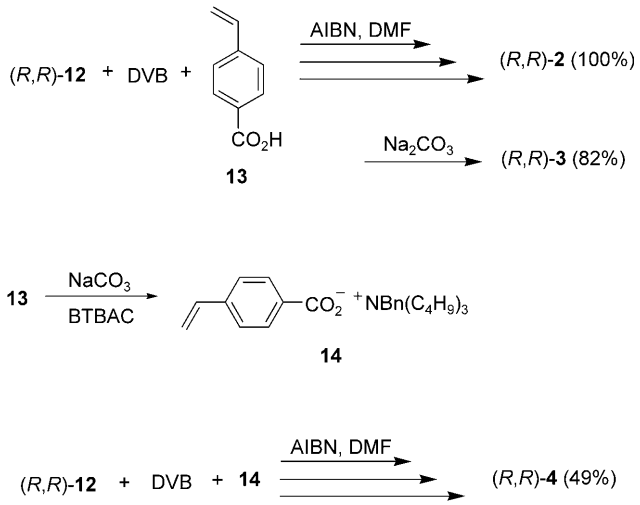
polymerization of this chiral monomer with styrene in the presence of divinylbenzene (DVB) as cross-linking agent in DMF gave the insoluble polymer-supported chiral 1,2-diamine monosulfonamide (*R*,*R*)-**1** (Scheme 2). The polymer (*R*,*R*)-**1** was well swollen in a good solvent for polystyrene such as DMF, THF and toluene. In contrast, the same polymer (*R*,*R*)-**1** was completely shrunk in water as expected from its highly hydrophobic character owing to the polystyrene main chain structure. This type of polymer would not be suitable for use in aqueous media due to the highly hydrophobicity. Since organic reactions in water are one of the important means of organic synthesis that meet green chemistry conditions, it is desirable to develop some amphiphilic polymer supports which can be efficiently used in aqueous media. In order to investigate the effect of their amphiphilic properties on the asymmetric reaction in water, we introduced novel polymer support structures including carboxylate (*R*,*R*)-**2**–**4**, alkanesulfonate (*R*,*R*)-**5**–**7** and arenesulfonate (*R*,*R*)-**8**, **9** as achiral hydrophilic pend-



Scheme 2. Preparation of cross-linked polystyrene-supported chiral 1,2-diamine monosulfonamide (*R*,*R*)-**1**.

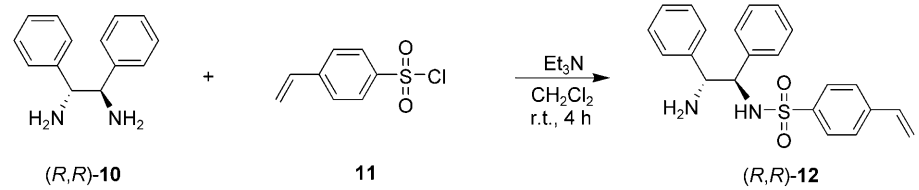
ant groups in the polymeric chiral ligands (Figure 1). These polymers were easily obtained by radical polymerization in good yield.

Polymer-supported chiral ligands (*R*,*R*)-**2**–**4** containing carboxylate derivatives were synthesized as shown in Scheme 3. Under radical polymerization



Scheme 3. Preparation of carboxylated polymer-supported chiral 1,2-diamine monosulfonamides (*R*,*R*)-**2**–**4**.

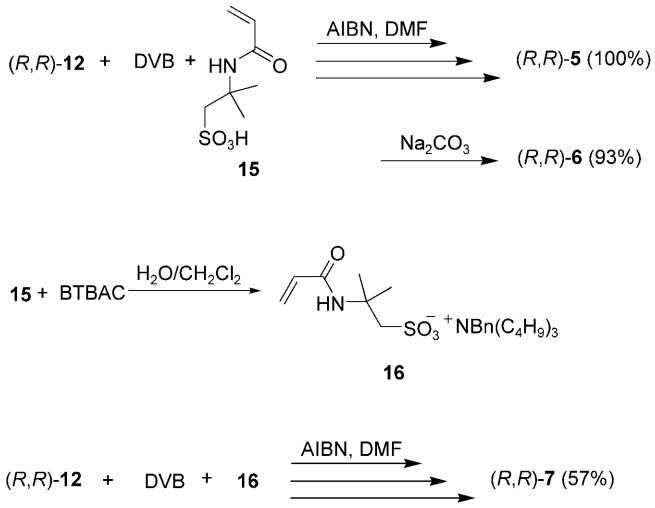
conditions in DMF, terpolymerization of (*R*,*R*)-**12**, DVB and **13** gave (*R*,*R*)-**2** in quantitative yield. Treatment of (*R*,*R*)-**2** with Na_2CO_3 in water afforded the sodium carboxylate pendant structure in (*R*,*R*)-**3**. Reaction of 4-vinylbenzoic acid **13** with Na_2CO_3 followed by an exchange reaction of sodium 4-vinylbenzoate with benzyltributylammonium chloride (BTBAC) gave the quaternary ammonium salt monomer **14**. This monomer was then polymerized with



Scheme 1. Synthesis of chiral 1,2-diamine monosulfonamide monomer (*R*,*R*)-**12**.

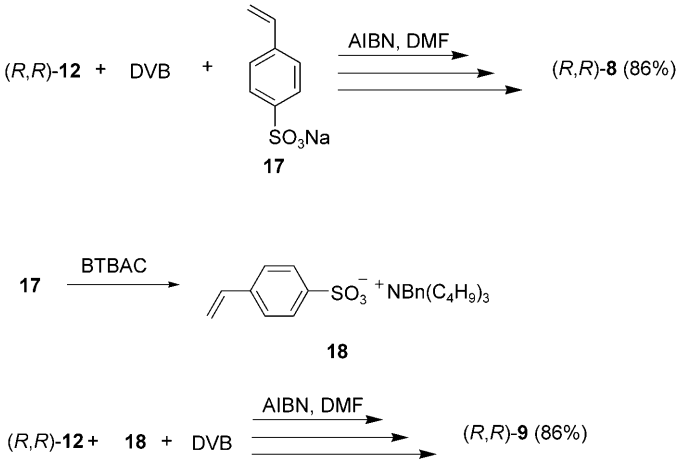
(*R*,*R*)-**12** in the presence of DVB to give the amphiphilic cross-linked polymeric chiral ligand (*R*,*R*)-**4**.

The synthesis of polymers (*R*,*R*)-**5**–**7** having alkanesulfonate pendant groups is shown in Scheme 4. Acrylamide monomer **15** having an alkanesulfonic acid moiety was copolymerized with (*R*,*R*)-**12** and DVB to



Scheme 4. Preparation of sulfonated polymer-supported chiral 1,2-diamine monosulfonamides (*R*,*R*)-**5**–**7**.

give (*R*,*R*)-**5**, which was converted into (*R*,*R*)-**6** by treatment with Na_2CO_3 in water. The reaction of **15** with BTBAC gave the quaternary ammonium salt monomer **16** of the sulfonate which was copolymerized with (*R*,*R*)-**12** and DVB to give (*R*,*R*)-**7** (Scheme 4). Polymer-supported chiral ligands (*R*,*R*)-**8** and **9** having an arenesulfonate pendant group were also prepared as shown in Scheme 5. Terpolymerization of (*R*,*R*)-**12**, DVB and sodium styrenesulfonate monomer **17** in DMF gave (*R*,*R*)-**8**. Scheme 5 also



Scheme 5. Preparation of aromatic sulfonated polymer-supported chiral 1,2-diamine monosulfonamides (*R*,*R*)-**8** and **9**.

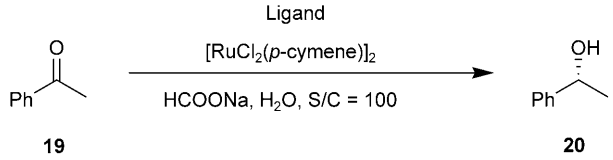
shows the preparation of (*R*,*R*)-**9** having an aromatic quaternary ammonium sulfonate pendant group by terpolymerization of (*R*,*R*)-**12**, DVB and quaternary ammonium sulfonate monomer **18** derived from **17**. In contrast to the polystyrene-supported chiral ligand (*R*,*R*)-**1**, these amphiphilic polymers were all swollen in water.

Asymmetric Transfer Hydrogenation of Acetophenone in Water

One of the most efficient catalysts for the asymmetric transfer hydrogenation of prochiral ketones is the Ru(II) complex of TsDPEN developed by Ikariya et al.[15] The reaction usually occurs under mild reaction conditions using 2-propanol or formic acid derivatives as a hydrogen source. Since the chiral Ru(II) complex is tolerant of water, it is possible to use the complex in aqueous systems. Xiao et al. demonstrated the asymmetric hydrogenation of ketones with aqueous HCOONa and the Ru-TsDPEN complex.[17,18] We have tested our amphiphilic polymers containing TsDPEN moieties for the asymmetric transfer hydrogenation in water. According to Ikariya's procedure the polymer-supported chiral 1,2-diamine monosulfonamide was treated with $[RuCl_2(p\text{-cymene})]_2$ in water at 40 °C for 1 h. The obtained polymeric complex showed an orange color which is typical of the Ru(II) complex. Although the polymer is insoluble due to its cross-linked structure, we took the ^1H NMR spectra of the polymers. The gel-phase NMR of the cross-linked polymers showed differences between the states before and after complexation. For example, after complexation, proton peaks attributed to *p*-cymene were detected. We used these polymeric chiral complexes for the asymmetric transfer hydrogenation of acetophenone.

Because of the hydrophobic character of aromatic ketones using the non-supported Ru(II)-TsDPEN complex, vigorous stirring is necessaryfor the reaction to proceed in water. Under such conditions the corresponding enantioenriched secondary alcohol **20** was obtained in 52% conversion with 94% *ee* (Table 1, entry 1).[2g] A very low conversion (6%) was attained when the reaction was conducted in water without stirring (entry 2). When the Ru(II) complex prepared from polystyrene-supported chiral ligand (*R*,*R*)-**1** was used, only a miserable conversion was obtained after longer reaction times as expected from the strong hydrophobicity of the polymeric catalyst (Table 1, entry 5). Vigorous stirring gave no positive effect in the case of hydrophobic (*R*,*R*)-**1**. In order to reduce the hydrophobic property of the polystyrene support, we have introduced the carboxylic acid moiety in the side chain of the polystyrene support. Preparation of chiral polymers (*R*,*R*)-**2**–**4** containing a carboxylate

Table 1. Asymmetric transfer hydrogenation of acetophenone **19** in water.[a]



19 **20**

Entry	Ligand	Polymer-support[b]	Temperature [°C]	Time [h]	Conversion[c] [%]	*ee*[d] [%]	Configuration
1[e]	TsDPEN	–	28	1	52	94	*R*
2[f]	TsDPEN	–	32	2	6	94	*R*
3[g]	TsDPEN	–	40	24	30	94	*R*
4[h]	TsDPEN	–	40	0.5	84	95	*R*
5	(*R*,*R*)-**1**	polystyrene	40	17	7	86	*R*
6	(*R*,*R*)-**2**	H	40	43	1	–	*R*
7	(*R*,*R*)-**3**	Na	40	20	2	–	*R*
8	(*R*,*R*)-**4**	Q	40	20	50	96	*R*
9	(*R*,*R*)-**5**	H	40	2	23	92	*R*
10	(*R*,*R*)-**6**	Na	40	2	34	92	*R*
11	(*R*,*R*)-**7**	Q	40	2	100	96	*R*
12	(*R*,*R*)-**8**	Na	40	15	92	91	*R*
13	(*R*,*R*)-**8**	Na	18	15	10	91	*R*
14	(*R*,*R*)-**9h**	Q	40	3	100	98	*R*
15	(*R*,*R*)-**9h**	Q	18	18	100	98	*R*
16[f]	(*R*,*R*)-**9h**	Q	32	2	38	98	*R*
17[i]	(*R*,*R*)-**9h**	Q	40	26	66	95	*R*
18[j]	(*R*,*R*)-**9h**	Q	40	24	54	97	*R*

[a] Unless otherwise noted reactions were carried out using 1 mmol of **19**, 5 equiv. of HCOONa, and an S/C ratio of 100 in 2 mL of water.
[b] H: polymer having free acid pendant group. Na: polymer having Na salt pendant group. Q: polymer having quaternary ammonium salt pendant group.
[c] Determined by GC analysis.
[d] Determined by HPLC with Chiralcel OD.
[e] Ref.[2g]
[f] Reaction was performed without stirring.
[g] Reaction was performed using sodium benzoate as an additive.[h] Reaction was performed using benzyltributylammonium *p*-toluenesulfonate as an additive. [TsDPEN]:[Additive] = 1:9.
[i] Reaction was carried out using a 0.1 M solution of acetophenone in 2-propanol. Acetophenone:Ru:ligand:KOH = 100:1.0:1.5:20.
[j] S/C = 1000.

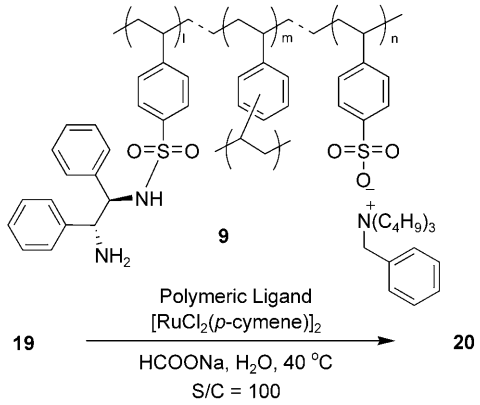
structure is shown in Scheme 3. We have examined these carboxylated polymer-supported chiral ligands [(*R*,*R*)-**2**–**4**] for the same reaction in water. Although (*R*,*R*)-**2** was smoothly suspended in water, almost no reaction occurred (entry 6). Even when a more hydrophilic polymer-supported chiral ligand [(*R*,*R*)-**3**] possessing the sodium salt structure in the side chain was used, the polymeric catalyst remained completely inactive in water (entry 7). In the model reaction using the TsDPEN-derived complex, we found that the reaction was strongly hindered when sodium benzoate was added to the reaction mixture. The yield of the alcohol decreased to 30% even after longer reaction time (24 h) at higher temperature (40 °C) in the presence of sodium benzoate (entry 3), although the reason for the retarding effect is not clear at this moment. On the other hand, the use of the polymer-supported chiral ligand (*R*,*R*)-**4** having the quaternary ammonium salt of benzoic acid as pendant group improved the reactivity in the same reaction (entry 8). By using (*R*,*R*)-**4**, (*R*)-phenylethanol was obtained in 50% yield with 96% *ee*.

Next we examined the alkanesulfonic acid derivatives as a hydrophilic pendant group of the polymer support. The use of the polymeric catalysts derived from this type of polymeric chiral ligands [(*R*,*R*)-**5**–**7**] gave higher yields as compared to those from carboxylated polymers (entries 9–11). In this type of polymer again that with the quaternary ammonium salt of the sulfonate as a pendant group [(*R*,*R*)-**7**] gave the best result with quantitative conversion and high level of enantioselectivity, 96% *ee* (entry 11). We then examined the polymeric chiral ligands (*R*,*R*)-**8** and **9** containing aromatic sulfonate derivatives as a pendant group on the polymer support. Even higher conversion was obtained when the catalyst was derived

from a sodium sulfonate polymer (entry 12). However, on lowering the reaction temperature to 18 °C an appreciable decrease of the conversion was observed (entry 13) with the (*R*,*R*)-**8** derived catalyst. Further higher enantioselectivity (98% *ee*) with quantitative conversion was attained by using the quaternary ammonium salt of the aromatic sulfonated polymer support (*R*,*R*)-**9h** (entry 14). It is also noted that both the enantioselectivity and conversion obtained with this polymeric catalyst are obviously higher than those obtained from the low molecular weight catalyst derived from TsDPEN in water. The polymeric catalyst could be easily separated from the reaction mixture due to its insolubility and reused for the following reaction. We have confirmed that at least five recycle uses were possible without any loss of catalytic activity of the polymeric catalyst. Under the reaction conditions of entry 14 using the catalyst derived from (*R*,*R*)-**9h** we obtained **20** in quantitative yield with 98, 97, 97, 97, and 97% *ee*s for five recycling experiments. Lowering the temperature did not severely influence the reactivity as appeared in the case of the quaternary ammonium salt polymer-support (*R*,*R*)-**9h** (entries 14, 15). More interestingly, in spite of heterogeneous conditions using (*R*,*R*)-**9h**, the reaction smoothly proceeded without vigorous stirring which was essentially required for the reaction with TsDPEN. Even with no stirring some reaction did occur in 2 h to give the chiral alcohol with 98% *ee* (entry 16), while the use of TsDPEN gave only 6% conversion without stirring (entry 2), as mentioned before. These data obtained using the polymeric catalyst obviously showed that both the reactivity and the enantioselectivity using the catalyst derived from the quaternary ammonium sulfonate polymer (*R*,*R*)-**9h** were higher than those obtained from the corresponding low molecular weight counterpart catalyst derived from TsDPEN in solution system. When 2-propanol was used as hydrogen source instead of an aqueous solution of sodium formate, a longer reaction time was required with a decrease of the enantioselectivity to some extent (entry 17). This result also revealed that the quaternary ammonium salt polymers are especially effective in water.

In order to understand the effect of catalyst loading, degree of cross-linking, and the content of quaternary ammonium pendant groups on the asymmetric transfer hydrogenation reaction, we have prepared various kinds of sulfonated polymer-supported chiral 1,2-diamine monosulfonamides (*R*,*R*)-**9** as shown in Table 2. These polymer-supported chiral ligands (*R*,*R*)-**9** with different composition (l: chiral ligand,

Table 2. Effect of the chiral ligand loading and the cross-linking degree on the enantioselective transfer hydrogenation of acetophenone **19** in water.[a]



Entry		Polymeric chiral ligand l	m	n	Time [h]	Conversion[b] [%]	*ee*[c] [%]	Configuration
1	**9a**	0.01	0	0.99	10	72	98	*R*
2	**9b**	0.10	0	0.90	3	100	98	*R*
3	**9c**	0.30	0	0.70	15	100	97	*R*
4	**9d**	0.50	0	0.50	17	100	97	*R*
5	**9e**	0.10	0.01	0.89	20	100	98	*R*
6	**9f**	0.10	0.03	0.87	20	100	98	*R*
7	**9g**	0.10	0.05	0.85	20	100	98	*R*
8	**9h**	0.10	0.10	0.80	3	100	98	*R*
9	**9i**	0.10	0.20	0.70	20	100	97	*R*

[a] Reactions were carried out at 40 °C using 1 mmol of **19**, 5 equiv. of HCOONa, and an S/C ratio of 100 in 2 mL of water.
[b] Determined by GC analysis.
[c] Determined by HPLC with Chiralcel OD.

m: cross-linking agent, n: sulfonated monomer) were applied to the reduction of **19** (Table 2). The influence of the catalyst loading (1%, 10%, 30% and 50%) was first investigated. In all cases, 97–98% enantioselectivities were constantly observed (entries 1–4). However, the composition (l, m, n) in the polymer influenced the reactivity of the polymeric catalyst. The balance between hydrophilicity and hydrophobicity of the polymer-support would be the most important factor to control the reactivity. The best composition was found to be $l=0.10$, $m=0.10$, $n=0.80$ (entry 8). The degree of cross-linking sometimes severely affects on the reactivity of the polymeric catalyst. We have used polymeric catalysts having different cross-linking degrees (entries 5–9). Interestingly, the reaction still smoothly occurred on using highly cross-linked polymer **9i**.

Since the significant performance in the asymmetric catalysis was achieved when polymer (*R*,*R*)-**9** having quaternary ammonium sulfonate pendant groups was used, we next investigated the effect of the counter cation X in the achiral sulfonate pendant group on the same reaction (Table 3). A series of polymer-supported chiral ligands (*R*,*R*)-**8b**, **9b**, **21**–**23** containing various kinds of cations were synthesized through copolymerization of (*R*,*R*)-**12** and the corresponding sulfonate monomers (Table 3). When sodium sulfonated polymer (*R*,*R*)-**8b** was used, the reaction stopped before reaching completion (Table 3, entry 1). Since the polymer was unusually swollen in water, this would cause the insufficient stirring. The catalyst derived from (*R*,*R*)-**9b** [$X=NBn(Bu)_3$], as well as the cross-linked one, gave the corresponding chiral alcohol **20** in 98% *ee* with quantitative conversion in water (entry 2). Instead of benzyltributylammonium salt, a longer tetraalkyl quaternary ammonium salt (*R*,*R*)-**21** was also effective for the reaction (entry 3). The high enantioselectivity with quantitative conversion was achieved even when the quaternary phosphonium salt of the sulfonate pendant group was employed (entries 4 and 5). It should be noted that, regardless of the kind of X, a quaternarized structure obviously plays a very important role in the polymer support providing excellent performance in water.

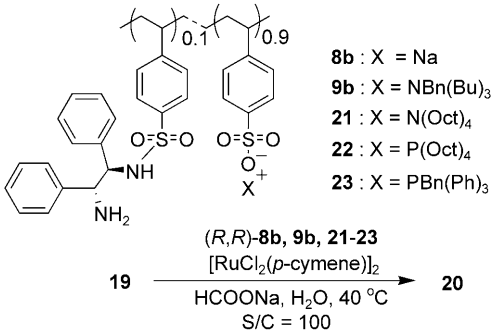
Next, we have examined the effect of transition metal precursors other than Ru(II) in the same reaction using the polymeric chiral catalyst derived from (*R*,*R*)-**9b** (Table 4). Almost the same activity was observed with the catalyst prepared from $[RhCl_2Cp^*]_2$ while the catalyst prepared from $[IrCl_2Cp^*]_2$ decreased both reactivity and enantioselectivity.

Table 4. Effect of other transition metal precursors on the enantioselective transfer hydrogenation of acetophenone **19** using polymeric catalyst derived from (*R*,*R*)-**9b** in water.[a]

Entry	Metal precursor	Time [h]	Conversion[b] [%]	*ee*[c] [%]	Configuration
1	$[RuCl_2(p\text{-cymene})]_2$	3	100	98	*R*
2	$[RhCl_2Cp^*]_2$	10	99	98	*R*
3	$[IrCl_2Cp^*]_2$	4	77	89	*R*

[a] Reactions were carried out at 40 °C using 1 mmol of **19**, 5 equiv. of HCOONa, and an S/C ratio of 100 in 2 mL of water.
[b] Determined by GC analysis.
[c] Determined by HPLC with Chiralcel OD.

Table 3. Effect of sulfonate structure on the enantioselective transfer hydrogenation of acetophenone **19** in water.[a]



Entry	Ligand	Time [h]	Conversion[b] [%]	*ee*[c] [%]	Configuration
1	(*R*,*R*)-**8b**	15	97	92	*R*
2	(*R*,*R*)-**9b**	3	100	98	*R*
3	(*R*,*R*)-**21**	10	100	98	*R*
4	(*R*,*R*)-**22**	11	100	98	*R*
5	(*R*,*R*)-**23**	10	100	97	*R*

[a] Reactions were carried out at 40 °C using 1 mmol of **19**, 5 equiv. of HCOONa, and an S/C ratio of 100 in 2 mL of water.
[b] Determined by GC analysis.
[c] Determined by HPLC with Chiracel OD.

Asymmetric Transfer Hydrogenation of Various Aromatic Ketones in Water

Encouraged by the results mentioned above, the asymmetric transfer hydrogenations of various kinds of aromatic ketones by using the sulfonated polystyrene-supported chiral catalyst (*R*,*R*)-**9** containing the quaternary ammonium salt pendant group were investigated (Table 5). Since the polymeric catalysts prepared from (*R*,*R*)-**9b** and (*R*,*R*)-**9h** showed the same catalytic activity in the case of acetophenone reduction (entries 1 and 2), we can evaluate the aromatic ketone reduction by using these polymers. Most of the aromatic ketones tested were smoothly converted into the corresponding optically active secondary alcohols with excellent enantioselectivities of up to 99% *ee* using the polymeric catalysts in water. Interestingly, in all cases the enantioselectivities obtained with the polymeric catalysts were superior to those in the model reaction[18o] using the catalyst derived from TsDPEN as shown in Table 5. To the best of our knowledge, there have been only a few reports of polymeric chiral catalysts that provided a higher enantioselectivity than those obtained from their low molecular weight counterparts.

Conclusions

In conclusion, we have successfully synthesized novel polymer-supported chiral 1,2-diamine monosulfonamides containing a hydrophilic functional group such as carboxylate and sulfonate. We have found that the chiral polymeric ligand having a pendant group of quaternary ammonium salt structure was highly suitable for the use in water. The amphiphilic property of the support polymers can be easily controlled by the content of quaternary ammonium salt and its structure. In this paper, we exemplified the asymmetric transfer hydrogenation of various aromatic ketones in order to emphasize the effectiveness of the amphiphilic polymers containing the quaternary ammonium salt structure as pendant group of the support polymers. By using the polymeric catalyst prepared from polymer **9**, the enantioselective reduction of aromatic ketones was achieved in water to give optically active secondary alcohols with up to 99% *ee*. Moreover, the catalyst was recycled several times without loss of the catalytic activity. We are currently investigating the usefulness of the novel amphiphilic polymer support in other asymmetric reactions in water.

Experimental Section

Preparation of Aromatic Sulfonated Polymer-Supported Chiral 1,2-Diamine Monosulfonamides (*R*,*R*)-9

A glass ampoule equipped with a magnetic stirring bar was charged with DMF (0.78 g), (*R*,*R*)-**12** (71.9 mg, 0.19 mmol), **18** (0.70 g, 1.52 mmol), divinylbenzene (25.0 mg, 0.19 mmol), and AIBN (6.5 mg, 40.0 μmol). The ampoule was sealed after three freeze-thaw cycles under liquid nitrogen. Copolymerization was carried out at 60 °C for 60 h. The ampoule was opened and the resulting mixture was poured into ether. The obtained polymer was collected on a glass filter and washed with THF and methanol and dried under vacuum; yield: 94%. ^{1}H NMR (400 MHz, DMSO-d_6, TMS): $\delta = 0.6$–1.8 (br; CH_2, CH), 2.8–3.3 (br; CH_2), 4.3–4.8 (br; CH_2 of benzyl), 6.8–7.2 (br; Ar-H of sulfonamide), 6.0–7.9 (br; Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS): $\delta = 13.4$, 18–20, 22–24, 56–62, 125–134; IR (KBr): $\nu = 1333\ cm^{-1}$ (SO_2 of sulfonamide); anal. calcd. for $C_{24.8}H_{36}NO_{2.6}S_{0.9}$: C 71.15%, H 8.67%, N 3.35%, S 6.89%; found: C 71.08%, H 8.61%, N 3.29%, S 6.86%.

Table 5. Enantioselective transfer hydrogenation of various aromatic ketones using polymeric catalyst derived from (*R*,*R*)-**9** in water.[a]

Entry	Ketone	Polymeric ligand	Time [h]	Conversion[b] [%]	*ee* [%][c] polymer	*ee* [%][c] TsDPEN[d]	Configuration
1	Acetophenone	(*R*,*R*)-**9b**	3	100	98	(94)	*R*
2	Acetophenone	(*R*,*R*)-**9h**	3	100	98	(94)	*R*
3	Propiophenone	(*R*,*R*)-**9b**	2	91	96	(86)	*R*
4	1-Acetonaphthone	(*R*,*R*)-**9b**	13	97	97	(87)	*R*
5	1-Indanone	(*R*,*R*)-**9h**	22	100[e]	98	(95)	*R*
6	4-Chloroacetophenone	(*R*,*R*)-**9b**	2	90	99	(91)	*R*
7	2-Chloroacetophenone	(*R*,*R*)-**9h**	22	100	99[f]	(89)	*R*
8	2-Methoxyacetophenone	(*R*,*R*)-**9h**	3	79	91[f]	(72)	*R*
9	2-Trifluoromethylacetophenone	(*R*,*R*)-**9h**	45	46	60[f]	(20)	*R*

[a] Reactions were carried out using 1 mmol of ketone, 5 equiv. of HCOONa, and an S/C of 100 in 2 mL of water.
[b] Determined by GC analysis, unless otherwise noted.
[c] Determined by HPLC with Chiralcel OD, unless otherwise noted.
[d] Data obtained from the literature (ref.[18o]) by using TsDPEN-derived catalyst.
[e] Determined by ^{1}H NMR.
[f] Determined by GC with β-DEX 120.

General Procedure for Asymmetric Transfer Hydrogenation

$[RuCl_2(p\text{-cymene})]_2$ (3.0 mg, 0.005 mmol) and the polymer-supported chiral 1,2-diamine sulfonamide (0.012 mmol) were added in water (2 mL). After the mixture had been degassed and stirred at 40 °C for 1 h under an argon atmosphere, sodium formate (340 mg, 5 mmol) was introduced. Ketone (1 mmol) was then added and the mixture was stirred at 40 °C for a certain period of time. After cooling to room temperature, the organic compounds were extracted twice with ether. The conversion and enantioselectivity were determined by GC and HPLC analysis, respectively. The aqueous phase was extracted from the reaction vessel, and a 0.3 M aqueous solution of benzyltributylammonium chloride (2 mL) was added to the remaining polymeric Ru catalyst and stirred for 3 min. The polymeric Ru catalyst was then reused by adding the same amount of sodium formate and ketone again.

Supporting Information

Experimental procedures, characterization, and spectra for compounds **1**–**9**, **12**, **14**, **16**, **18**, **21**–**23** are available as Supporting Information.

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan.

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