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Synthesis of polymers containing chiral 1,2-diamine derivatives and their application to asymmetric reactions*

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Abstract: Polymer-supported chiral 1,2-diamine derivatives have been prepared. The polymers containing free 1,2-diamine moiety were applied to enantioselective hydrogenation catalyst by combination with $RuCl_2$-BINAP complex. Asymmetric hydrogenation of aromatic ketones was performed by means of the polymeric catalyst derived from these polymers to give the chiral secondary alcohols with high ee in quantitative conversion. The polymers containing 1,2-diamine monosulfonamide were applied to enantioselective transfer hydrogenation catalyst by combination with $RuCl_2$-*p*-cymene complex. Asymmetric transfer hydrogenation of aromatic ketones was performed by means of the polymeric catalyst to afford the chiral secondary alcohols. A high level of enantioselectivities up to 99 % ee was attained in neat water by using the polymeric catalyst prepared from quaternary ammonium salt-type polymer support.

Keywords: polymer support; asymmetric catalysis; hydrogenation; transfer hydrogenation; aromatic ketones; $RuCl_2$.

INTRODUCTION

Optically active 1,2-diamine and its derivatives [1] are known to be efficient chiral ligand for the catalyst of various kinds of asymmetric reactions including hydrogenation of ketones [2] and transfer hydrogenation reactions [3]. However, only limited examples of such polymeric chiral 1,2-diamines have been reported [4]. Especially chiral primary 1,2-diamine ligands have not been attached to usual cross-linked polystyrene resins. We have prepared a polymer-supported version of chiral 1,2-diamine derivatives, which were used as chiral ligands of catalyst for asymmetric reactions. We focused on the asymmetric hydrogenation of ketones by means of polymer-supported 1,2-diamine-$RuCl_2$-BINAP complex [BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl] and the asymmetric transfer hydrogenation of ketones by using polymeric 1,2-diamine monosulfonamide-$RuCl_2$-*p*-cymene complex. Sulfonated polymer supports made it possible to perform the reaction in water. The polymer networks formed a special microenvironment, which affected the reactivity and the enantioselectivity of the reaction.

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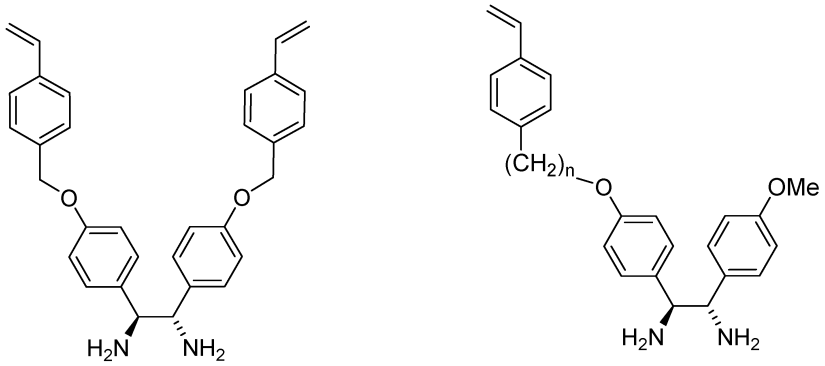
DISCUSSION

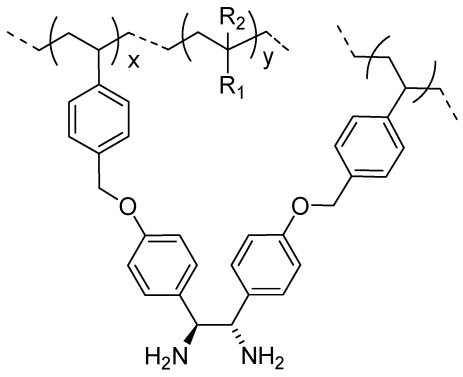
Asymmetric hydrogenation by means of the polymer-supported chiral 1,2-diamine-$RuCl_2$-BINAP complexes

We have prepared various kinds of polymer-supported chiral 1,2-diamine as polymeric chiral ligand of the Ru complex. Cross-linked polymer-supported chiral 1,2-diamine **3** was prepared by copolymerization of the corresponding chiral 1,2-diamine monomer **1** [5] with achiral monomer such as styrene and methacrylate (Schemes 1 and 2) [6,7]. Since the chiral monomer **1** has two vinylphenyl groups, polymerization resulted in the cross-linked structure. The obtained polymers were insoluble in organic solvent. We also prepared the chiral 1,2-diamine polymers **4** bearing spacer arm between polymer main chain and chiral 1,2-diamine moiety [8]. Another polymer **5** having branched structure was also prepared from the corresponding branched monomer and styrene. Chiral 1,2-diamine moiety would be placed in the core of the dendritic structure of **5** (Scheme 3). Chiral monomer **2** having a single vinylphenyl group was prepared. Pendant type of chiral 1,2-diamine polymer **6** was prepared by terpolymerization of **2**, styrene, and divinylbenzene (Scheme 4).

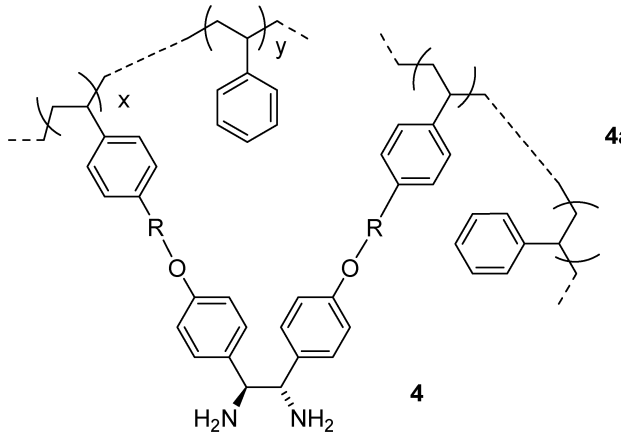


1 **2**

Scheme 1 Chiral 1,2-diamine monomer.



3a: R_1 = Ph, R_2 = H
3b: R_1 = CO_2Me, R_2 = Me
3c: R_1 = CO_2Bu, R_2 = Me



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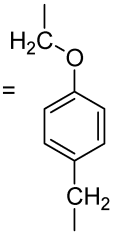
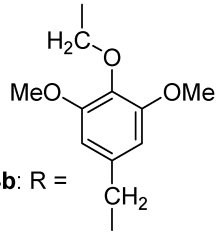
4a: R =

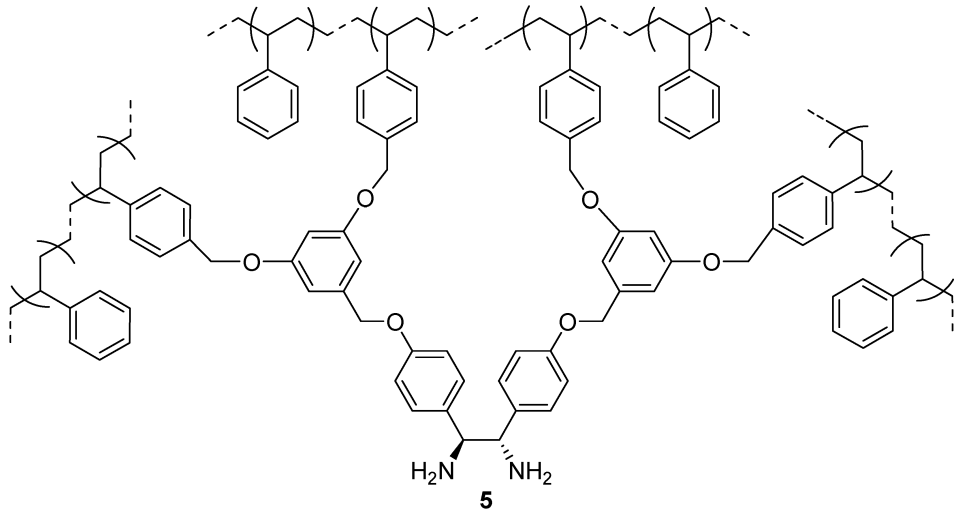


4b: R =



4c: R = —$(CH_2)_4$—

Scheme 2 Chiral 1,2-diamine polymer.



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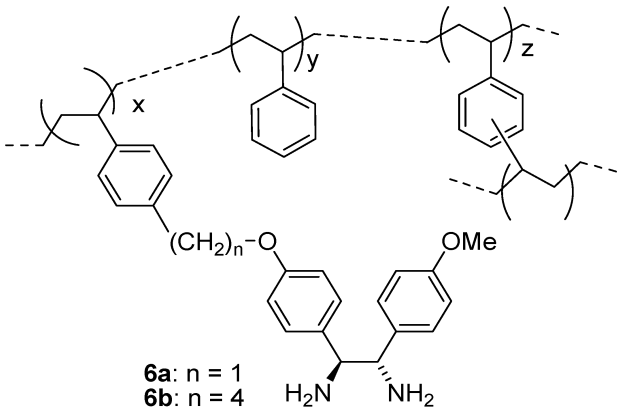
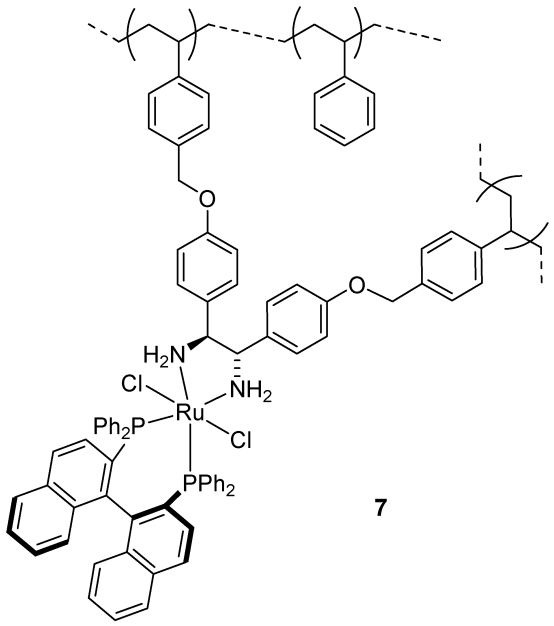
Scheme 3 Dendritic polymer-supported 1,2-diamine.



Scheme 4 Polymer-supported 1,2-diamine (pendant type).

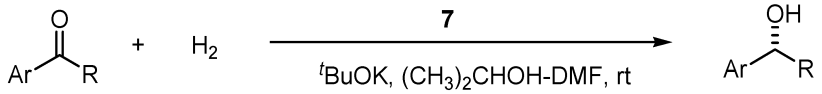
These cross-linked chiral 1,2-diamine polymers were then treated with $RuCl_2$-BINAP complex to form the polymer-supported Ru complex. The structure of **7** represented the polymeric complex prepared from **3a** (Scheme 5). The polymer color change to dark red indicated the formation of the polymeric complex. Gel-phase ^{31}P NMR spectra of the polymer complex showed the peak at 46.3 ppm, which attributed to the P atom in the Ru complex and confirmed the structure of the 1,2-diamine-$RuCl_2$-BINAP complex on the polymer **7**.



Scheme 5 Polymer-supported 1,2-diamine-$RuCl_2$-BINAP complex.

We have then used the polymeric chiral complex **7** for the asymmetric hydrogenation of aromatic ketones (Scheme 6). We have found that the reaction smoothly occurred by means of the insoluble polymeric catalyst when a mixed solvent of 2-propanol and dimethylformamide (DMF) (1:1) was used. The corresponding secondary alcohol was obtained in quantitative yield. For example, the asymmetric

hydrogenation of acetophenone was performed by using the complex prepared from **3a** and $RuCl_2$-BINAP to give chiral 1-phenylethanol in quantitative yield with 77 % ee (Table 1, entry 1). When 2,2'-bis(di-3,5-xylylphosphino)-1,1'-binaphthyl (xylBINAP) was used instead of BINAP, 96 % ee was obtained with the same catalyst (entry 2). The increase of the 1,2-diamine content in the polymer resulted in the increase of the cross-linking degree. The polymeric catalyst prepared from higher cross-linked polymer gave somewhat lower enantioselectivity (entries 3 and 4). Other several aromatic ketones were asymmetrically hydrogenated to give the chiral alcohol in quantitative yield with a high level of enantioselectivities (entries 5–8). Of various kinds of polymeric chiral ligands **3**, the copolymer **3c** obtained from butyl methacrylate as a comonomer gave the best result in the same reaction (entry 10). Another type of polymeric chiral ligand containing the longer spacer arm between the polymer main chain and 1,2-diamine moiety also resulted in high reactivity (entries 11–14). Dendritic structure like polymer **5** showed somewhat lower reactivity mainly due to its less flexibility of the 1,2-diamine moiety at the core in the dendritic polymer (entry 15). On the other hand, polymeric chiral ligand **6** prepared from monomer **2** has a relatively flexible structure of the pendant chiral 1,2-diamine, which resulted in the highly active catalyst (entries 16 and 17). The obtained enantioselectivity (80 % ee) using **6** was the same as that obtained from the low-molecular-weight counterpart in solution system.



Scheme 6 Asymmetric hydrogenation of ketone.

Table 1 Asymmetric hydrogenation of aromatic ketones with polymer-supported catalyst.[a]

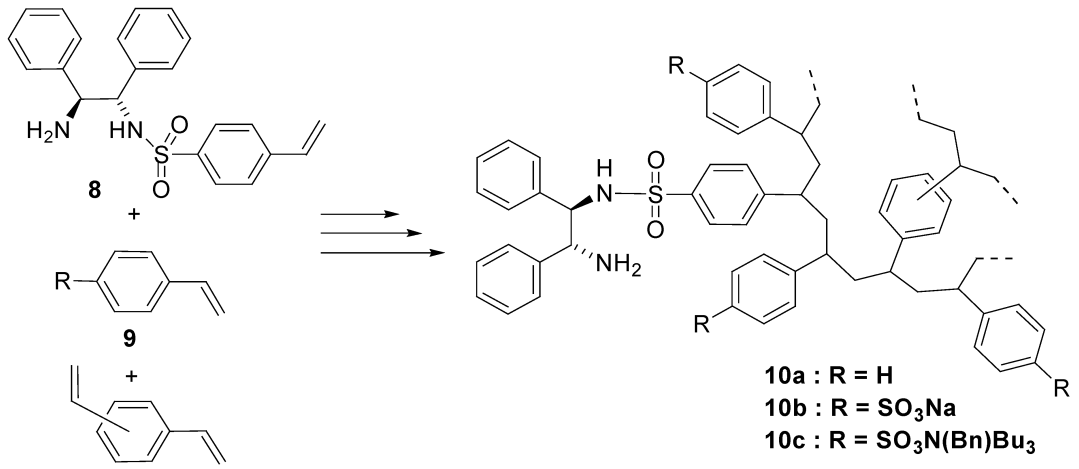
Entry	Ketone[b]	Polymeric 1,2-diamine			Conversion %	% ee
			x	*y*		
1	A	**3a**	0.05	0.95	100	77
2	A	**3a xyl**[c]	0.05	0.95	100	96
3	A	**3a**	0.10	0.90	100	75
4	A	**3a**	0.20	0.80	100	73
5	P	**3a**	0.05	0.95	100	82
6	B	**3a**	0.05	0.95	100	84
7	V	**3a**	0.05	0.95	100	88
8	N	**3a**	0.05	0.95	100	95
9	A	**3b**	0.05	0.95	100	78
10	A	**3c**	0.05	0.95	100	79
11	A	**4a**	0.05	0.95	100	77
12	A	**4b**	0.05	0.95	100	77
13	A	**4c**	0.05	0.95	100	77
14	A	**4c xyl**[c]	0.05	0.95	100	97
15	A	**5**	0.05	0.95	100	75
16	A	**6a**[d]	0.05	0.94	100	80
17	A	**6b**[d]	0.05	0.94	100	80

[a]The reactions were conducted at 1 MPa of H_2 and at room temperature with ketone (5 mmol), *t*-BuOK (1 M, 100 µl), 1,2-diamine (0.01 mmol), and BINAP-$RuCl_2$ (0.005 mmol).
[b]A: acetophenone, P: propiophenone, B: butyrophenone, V: valerophenone, N: 1-acetonaphthone.
[c]XylBINAP was used instead of BINAP.
[d]z = 0.01.

We have tested the recyclability of the polymeric catalyst. After the reaction completed, supernatant solution was easily removed with a syringe and the solvent, ketone, and hydrogen were recharged. In the case of the polymeric catalyst prepared from **3a**, the catalyst could be readily recycled and reused without significant loss of reactivity and enantioselectivity.

Asymmetric transfer hydrogenation of aromatic ketones by means of polymer-supported chiral 1,2-diamine monosulfonamide-$RuCl_2$-*p*-cymene complexes in water

One of the most effective catalysts for asymmetric transfer hydrogenation of ketone is 1,2-diamine monosulfonamide Ru(II) complex developed by Ikariya and Noyori [9]. This reaction can be performed in water under vigorous stirring condition [10,11]. However, only a few research groups have focused on asymmetric reaction using polymer-supported catalyst in water [12]. We have synthesized polymer-supported chiral 1,2-diamine monosulfonamide ligand **10** by copolymerization of the corresponding 1,2-diamine monosulfonamide monomer **8** with styrene derivatives **9** (Scheme 7). Polymeric chiral ligand **10** was treated with $RuCl_2$-*p*-cymene complex to give the corresponding polymer-supported complex. Styrene-based polymer **10a** gave the chiral complex, which was used for the asymmetric transfer hydrogenation of acetophenone in water. Sodium formate was a choice of the hydrogen source for the reaction in water. Unfortunately, the reaction with **10a** did not occur mainly due to the highly hydrophobic nature of the polymeric catalyst derived from polystyrene-based ligand **10a** as expected (Table 2, entry 2). Then we changed the structure of the polymer support to those having more hydrophilic property.



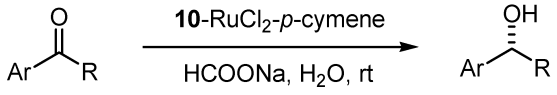
Scheme 7 Sulfonated polymer-supported chiral 1,2-diamine monosulfonamide.

Table 2 Asymmetric transfer hydrogenation of aromatic ketones in water.[a]

Entry	Ketone[b]	Polymer **10**		Temperature °C	Conversion %	% ee
		Degree of cross-linking %	R			
1[c]	A		–	28	52	94
2	A	5	H **10a**	40	0	–
3	A	5	SO_3Na **10b**	40	97	92
4	A	5	SO_3Na **10b**	18	10	91
5	A	0	$SO_3N(Bn)Bu_3$ **10c**	40	100	98
6	A	5	$SO_3N(Bn)Bu_3$ **10c**	40	100	98
7	A	5	$SO_3N(Bn)Bu_3$ **10c**	20	100	98
8	A	10	$SO_3N(Bn)Bu_3$ **10c**	40	100	98 (94)[f]
9	P	10	$SO_3N(Bn)Bu_3$ **10c**	40	91[d]	96 (86)[f]
10	C	10	$SO_3N(Bn)Bu_3$ **10c**	40	90[d]	99 (91)[f]
11	N	10	$SO_3N(Bn)Bu_3$ **10c**	40	97[e]	97 (87)[f]

[a]Reaction was performed in water 15 h.
[b]A: acetophenone, P: propiophenone, C: *p*-chloroacetophenone, N: 1-acetonaphthone.
[c]*N*-(p-toluenesulfonyl)-1,2-diphenylethylenediamine (TsDPEN) was used. See ref. [11].
[d]Conversion after 2 h.
[e]Conversion after 13 h.
[f]Date in the parenthesis were obtained by using the low-molecular-weight catalyst in water reported in the lit. [10].

Introduction of the sulfonate pendant group onto the polymer is one of the most straightforward ideas to prepare a new polymer support having hydrophilic property. Surprisingly, although sulfonated polystyrenes have been widely used as ion exchange resin, these polymers have not been used for such application, including chiral catalyst support material. We have tried to prepare chiral ligand attached to sulfonated polystyrene. First, we chose cross-linked polystyrene-support-bearing sodium-sulfonated pendant group. Sodium styrenesulfonate is a commercially available monomer, which could be copolymerized with chiral ligand monomer **8** and a cross-linking agent such as divinylbenzene under radical polymerization conditions. The obtained polymer **10b** was well swollen in water. $RuCl_2$-*p*-cymene complex prepared from **10b** was then used for the asymmetric transfer hydrogenation of acetophenone (Scheme 8). The reaction with this polymeric catalyst smoothly occurred to give the corresponding alcohol in 97 % yield with 92 % ee at 40 °C (Table 2, entry 3). However, the yield decreased when the reaction temperature was lowered (entry 4). In order to improve the reactivity and the selectivity, we have then introduced quaternary ammonium salt structure into a pendant group of the polymer support. We have found that the polymeric $RuCl_2$-*p*-cymene complex derived from **10c** was very active in water to give the alcohol product in quantitative yield with high enantioselectivity (98 % ee, entry 5). The enantioselectivity obtained by using **10c**-derived catalyst was superior to that obtained from the low-molecular-weight counterpart in solution system.



Scheme 8 Asymmetric transfer hydrogenation of ketone.

Since polymer **10c** was well swollen in dimethylsulfoxide (DMSO), the gel-phase ^1H NMR of **10c** showed the peaks attributed to the chiral ligand and quaternary ammonium salt pendant group. After the treatment of the polymeric chiral ligand with $RuCl_2$-*p*-cymene, the gel-phase ^1H NMR spectrum confirmed the complex formation on the cross-linked polymer. Not only acetophenone, but also

other several aromatic ketones have been asymmetrically hydrogenated under the same reaction condition with the polymeric catalyst derived from **10c** to give higher enantioselectivities compared to the low-molecular-weight catalyst in water (entries 8–11). Rh and Ir complexes were also used in the same reaction. Ir-derived complex showed lower enantioselectivity and conversion.

CONCLUSION

Chiral polymeric complexes formed from **3–6** and BINAP-$RuCl_2$ efficiently performed as catalyst of asymmetric hydrogenation of aromatic ketones to give the corresponding secondary alcohols in quantitative yield with a high level of enantioselectivity. For example, asymmetric hydrogenation of acetophenone with polymer-supported chiral 1,2-diamine-$RuCl_2$-xylBINAP afforded 1-phenylethanol with 97 % ee in quantitative yield. On the other hand, the sulfonated polymer-supported chiral monosulfonamide ligands **10b** and **10c** were successfully applied to the asymmetric transfer hydrogenation of aromatic ketones in water. For example, 1-phenylethanol with 98 % ee was obtained in quantitative yield using the polymeric catalyst derived from **10c**. The polymeric chiral catalysts mentioned above facilitated the product isolation process and were recycled without loss of activity.

EXPERIMENTAL

Typical procedure for asymmetric hydrogenation of acetophenone with polymeric catalyst

A 20-ml Schlenk vessel equipped with a Teflon-coated magnetic stirring bar was charged with polymer-supported chiral 1,2-diamine (*S*,*S*)-**3** (0.01 mmol), $RuCl_2$/(*S*)-BINAP$(dmf)_n$ (4.0 mg, 0.005 mmol), and 2 ml of dry DMF. The above mixture was degassed and heated at 80 °C for 2.5 h. After removal of DMF under reduced pressure to dryness, the solid obtained was transferred to a 100-ml glass autoclave equipped with a pressure gauge and a gas inlet tube attached to a hydrogen source. Air present in the autoclave was replaced by argon. A solution of acetophenone (0.58 ml, 5 mmol) in a 1:1 mixture of 2-propanol (2 ml) and DMF (2 ml), and a 1.0 M *t*-BuOK solution in *t*-BuOH (0.1 ml), which had been degassed, were added to the autoclave. Hydrogen was then introduced into the autoclave and pressurized to 1 MPa. The reaction mixture was stirred for 1 h at room temperature. After carefully venting the hydrogen gas, the reaction mixture was diluted with ethyl acetate (10 ml) and filtered through a glass filter equipped with silica gel. The solvent was removed under reduced pressure, and the yield determined by gas chromatography (GC) was 100 %. Enantioselectivity of 1-phenylethanol was determined by high-performance liquid chromatography (HPLC) analysis using chiral stationary phase (Chiralcel OD, Daicel): hexane/2-propanol = 20:1, flow rate, 0.4 ml/min, temp. 30 °C, $t_R(R)$ = 22.8 min, $t_R(S)$ = 25.9 min.

Typical procedure for the asymmetric transfer hydrogenation

Polymer-supported chiral sulfonamide **10** (0.012 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (3.0 mg, 0.005 mmol) were added in water (2 ml). After the mixture was 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 with ether. The conversion and enantioselectivity were determined by GC and HPLC analysis, respectively.

ACKNOWLEDGMENTS

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