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PAPER

Molecular design of chiral quaternary ammonium polymers for asymmetric catalysis applications†

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Repeated reaction between a chiral quaternary ammonium dimer and disodium disulfonate gave a chiral ionic polymer, which showed excellent catalytic activity in the asymmetric benzylation of *N*-diphenylmethylene glycine *tert*-butyl ester.

Introduction

In asymmetric synthesis, chiral organocatalysts have received a considerable amount of attention in recent years as chiral organocatalysts meet the green chemistry requirements. One of the important chiral organocatalysts is optically active quaternary ammonium salt, which can be utilized in various kinds of asymmetric transformations. The development of the asymmetric quaternary ammonium catalyst was triggered by the pioneering studies of the Merck research group in 1984. They reported the α-substitution of phenylindanone derivative in the presence of cinchonine derived chiral quaternary ammonium salt. The α-alkylated product was obtained in excellent yield with high enantiomeric excess.[1,2] Inspired by the Merck results, O'Donnel group first reported the asymmetric alkylation of *N*-diphenylmethylene glycine *tert*-butyl ester using cinchona derived quaternary ammonium catalysts.[3–5] Based on O'Donnel's results, Lygo[6,7] and Corey *et al.*[8–10] independently developed highly effective catalysts for the same reaction, which were derived from cinchonidine. Furthermore, Park and Jew developed new catalysts consisting of dimeric and trimeric quaternary ammonium salts derived from cinchonidine.[11–15] They designed appropriately positioned catalytic active sites on the catalyst molecule.

Although highly efficient quaternary ammonium organocatalysts have been developed, we sometimes encounter problems in their separation from the reaction mixture mainly due to their amphiphilic properties. In comparison with transition metal catalysts, a relatively large amount of the organocatalyst is required to complete the reaction. Separation of the quaternary ammonium organocatalyst is an important process in the reaction. In order to overcome the separation issue, a number of polymer-immobilized quaternary ammonium catalysts have been prepared.[16] The first report on the asymmetric alkylation of *N*-diphenylmethylene glycine *tert*-butyl ester using crosslinked polystyrene-immobilized cinchona-derived quaternary ammonium salts was made by Hodge *et al.*[17] Improvement in the catalytic activity of the same polymeric catalyst was achieved by Najera *et al.*[18–21] Polymer-immobilized cinchona alkaloid salts with spacers were used in the same reaction.[22–24] Some other examples of immobilized cinchona ammonium salts have been developed.[25–27] In 2008 we proposed a new methodology of immobilization of quaternary ammonium salts in a polymer support.[28] Our method involves a stable ionic bond between the polymer support and catalyst. Chiral quaternary ammonium salt organocatalyst was attached to polymeric sulfonate through ammonium sulfonate linkage, which is stable enough to immobilize the organocatalyst in the polymer support.

Highly stable ionic linkage of the quaternary ammonium sulfonate made us aware of the main-chain chiral polymers containing the ionic bond between the repeating units. Reaction of bisquaternary ammonium halide and disodiumsulfonate yielded the polymeric compound containing quaternary ammonium sulfonate linkages in their main-chain.[29] In asymmetric organocatalysis, only a limited number of investigations to elucidate the use of main-chain functionalized chiral polymers have been performed.[30–32] In this article, we report the details of the synthesis of novel chiral polymers with ionic linkages between the repeating units. The catalytic activity of the chiral polymers in the asymmetric alkylation of *N*-diphenylmethylene glycine *tert*-butyl ester was also discussed.

Results and discussion

The reaction between quaternary ammonium salt and sulfonate smoothly occurred to give the quaternary ammonium sulfonate. For example, polymer-supported cinchonidium sulfonate **3** was easily prepared from the reaction of crosslinked polymer **2** possessing SO_3Na pendant groups with cinchonidine quaternary

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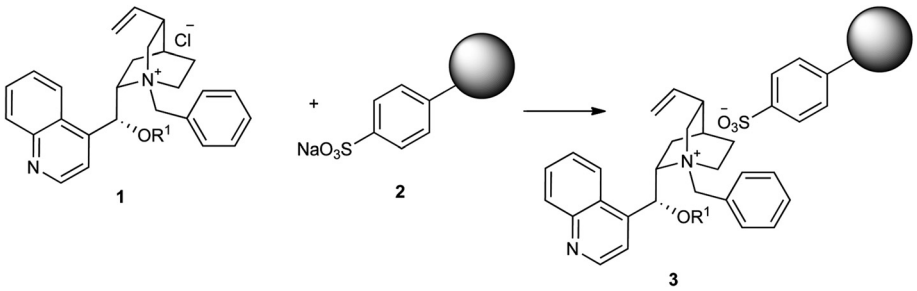
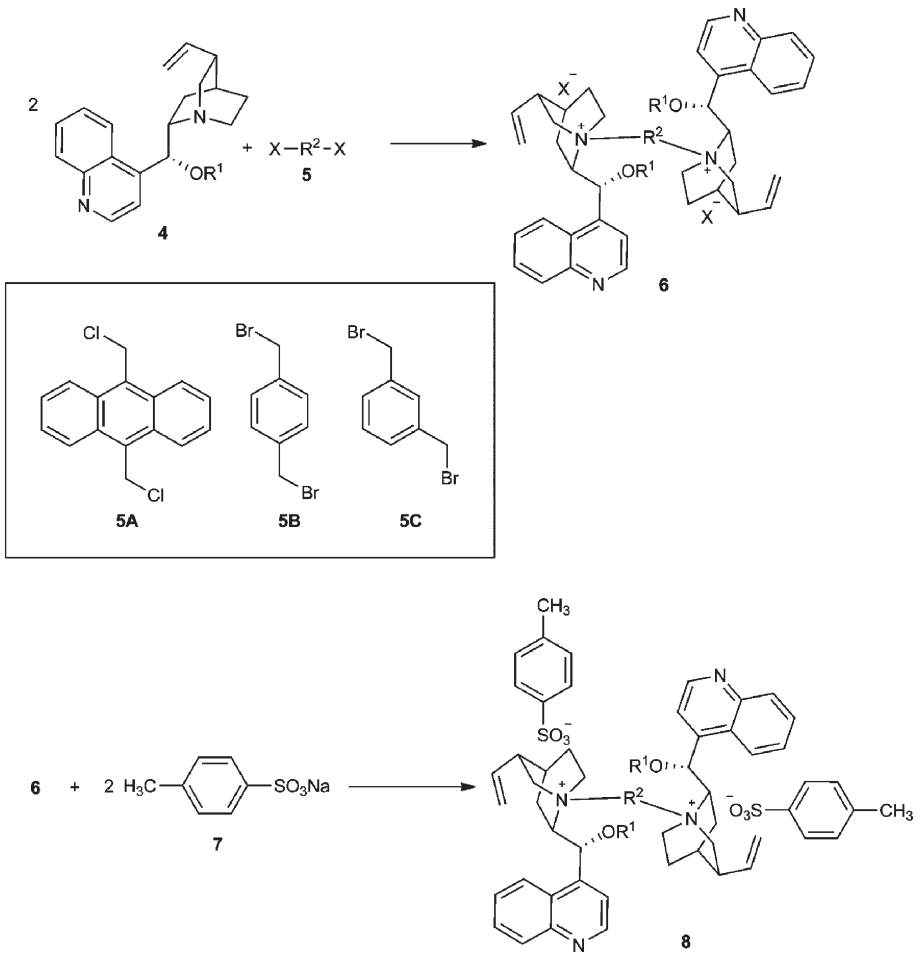
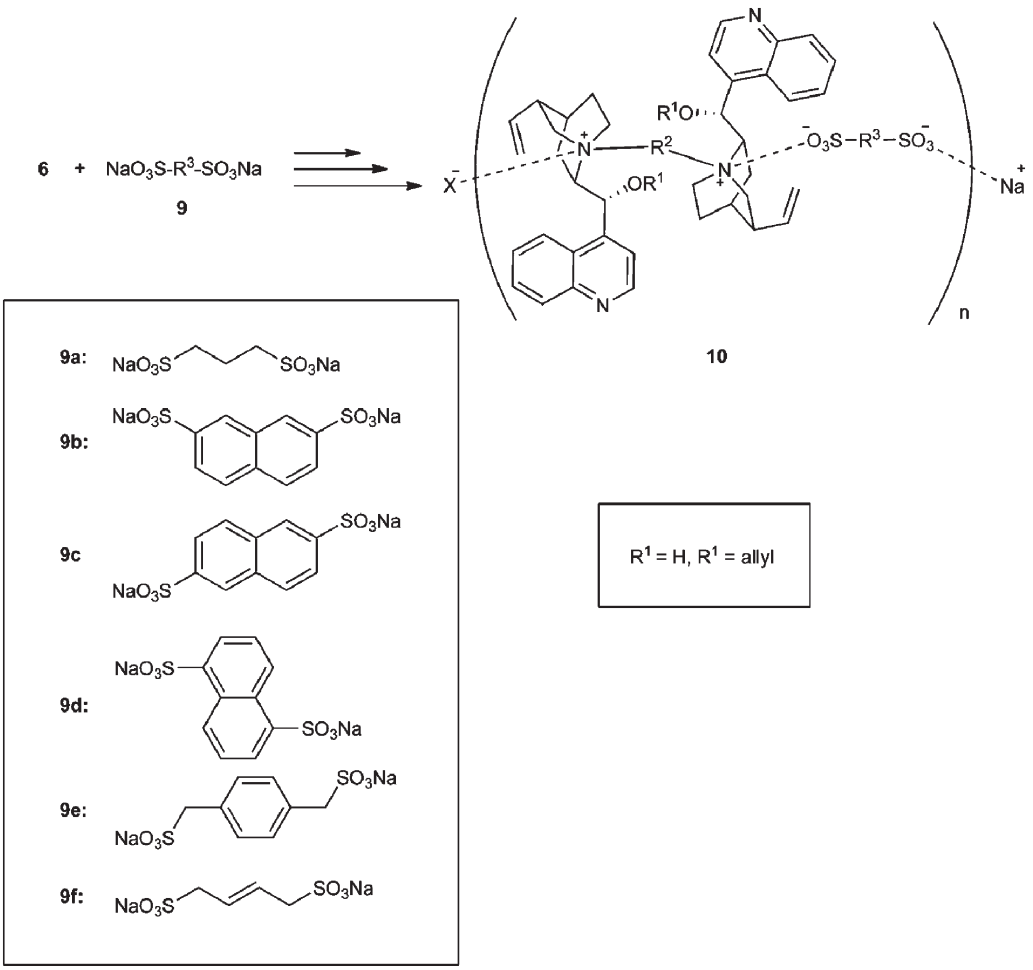


Scheme 1 Synthesis of ionically immobilized cinchonidinium salt.



Scheme 2 Synthesis of cinchonidinium sulfonate dimer.

ammonium salt **1** as shown in Scheme 1. Ionically immobilized quaternary ammonium salt was stable enough to be used as a catalyst for asymmetric reaction.[28] In order to apply this quaternary ammonium sulfonate formation reaction to polymer synthesis, we prepared dimeric quaternary ammonium halide of cinchonidine **6**. As a model reaction of polymerization, we examined ion exchange reaction between **6** and sodium toluene-4-sulfonate **7** (Scheme 2). The reaction easily occurred to give the corresponding bissulfonate **8** in quantitative conversion. If disulfonate is used instead of the sulfonate **7**, we realized that the stable ionic bond formation reaction can be utilized for the novel type of polymer synthesis. Ion-exchange reaction between bis (quaternary ammonium halide) and disulfonate may give quaternary ammonium sulfonate polymer, which contains ionic bonds between each repeating units. To the best of our knowledge, this is a new polymerization method (*ion-exchange polymerization*) for producing a chiral polymer main-chain structure, which we term "*ionic polymer*". The ion-exchange polymerization requires no catalyst and proceeds simply at room temperature, which may provide a various kinds of ionic polymers including chiral polymers. Since the chiral quaternary ammonium salts act as organocatalyst in various kinds of asymmetric transformation, the generated chiral ionic polymers should be used as catalyst for the asymmetric reactions.

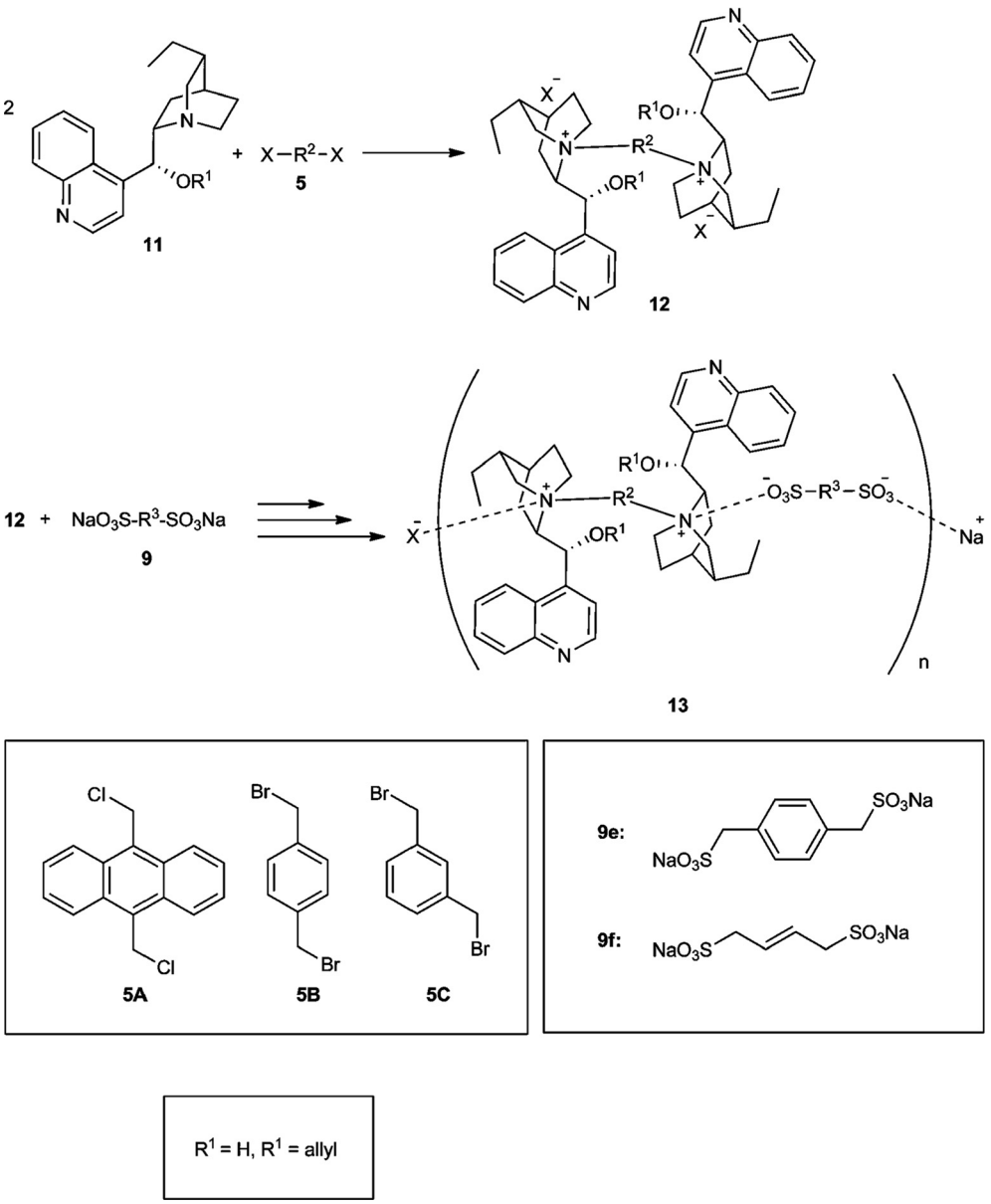


Scheme 3 Synthesis of cinchonidine derived chiral ionic polymer.

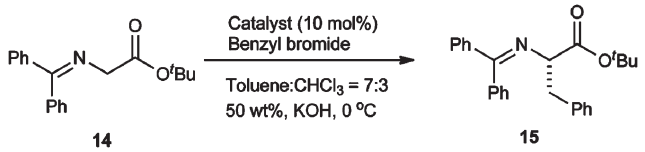
In our preliminary experiments we found that the reaction between dimeric quaternary ammonium salt **6** and 2,6-naphthalene disulfonate **9c** smoothly occurred to give the corresponding chiral polymer **10** in high chemical yield (Scheme 3).[29] As illustrated in Scheme 3, the repeated ion exchange reaction occurred to give the ionic bond between the monomers. This is the first example of the chiral ionic polymer synthesis by ion-exchange polymerization. In this study, we have synthesized various kinds of dimeric quaternary ammonium salt **6** from cinchonidine **4** and dihalides **5**. Various kinds of disulfonates **9** were used to form chiral ionic polymers **10** (Scheme 3). The effects of the structure variation of the chiral polymers on the catalytic activity in the asymmetric alkylation reaction have been investigated. The procedure of ion-exchange polymerization is very simple. A solution of the chiral ammonium dimer **6** in organic solvent was treated with the equimolar amount of disulfonate **9** in water to afford the precipitation of the ionic chiral polymer **10**. Disulfonates **9e** and **9f** were synthesized from the corresponding chlorides, while the other disulfonates are all commercially available. Secondary OH group of cinchonidine can be easily modified by ether formation. Since the *O*-allylated cinchonidine derivatives as chiral organocatalyst gave higher catalytic activities in some asymmetric reactions,[8] we synthesized *O*-allylated compounds (R^1 = allyl). The 10,11-vinyl group of cinchonidine can also be chemically modified. As a simple example, we modified the vinyl group by hydrogenation to give 10,11-dihydrocinchonidine **11**. The corresponding quaternary ammonium salt dimers **12** derived from **11** were also prepared and polymerized with disulfonates **9** to give **13** (Scheme 4). All the chiral ionic polymers obtained from the ion-exchange polymerization showed low solubility in common organic solvents except for dimethyl sulfoxide. Intrinsic viscosity [η] of the dimethyl sulfoxide solution of the polymers measured in dimethyl sulfoxide at 40 °C was in the range of 0.1 to 0.2.

The successful application of cinchona-based quaternary ammonium salts as a chiral organocatalyst in asymmetric methylation of phenylindanone by Merck research group[1] initiated the further development of the related organocatalysts. Park *et al.*[11] first reported that chiral quaternary ammonium dimers derived from cinchona alkaloid gave higher enantioselectivity compared to the corresponding monomeric salts in the asymmetric benzylation of *N*-diphenylmethylene glycine *tert*-butyl ester **14** (Scheme 5).

We synthesized several chiral quaternary ammonium salt dimers **6**, **12** and **8**, which were applied to the same asymmetric reaction. Results of the asymmetric benzylation using these dimeric catalysts are summarized in Table 1. In case of OH free dimeric catalysts, anthryl linker A showed higher



Scheme 4 Synthesis of hydrocinchonidine derived chiral ionic polymer.



Scheme 5 Asymmetric benzylation of *N*-diphenylethylene *tert*-butyl ester.

enantioselectivities in comparison with xylyl linkers B or C (entries 1 and 2, 3, entries 4 and 5, 6, entries 13 and 14, 15, respectively). The dimeric catalysts **8** having sulfonate counter anion showed the catalytic activity similar to **6**. The asymmetric benzylation with *O*-allylated catalysts (entries 7–12) showed the opposite tendency of the catalytic activity in the same reaction. *O*-allylated catalyst having 1,3-xylyl type linker C gave the highest ee (entries 9 and 12).

Cinchonidine derived ionic polymers **10** were then used as chiral catalysts for the asymmetric benzylation reaction. Since these polymers are not soluble in both the aqueous phase and organic phase, the polymers are suspended between the two phases. In all cases, the asymmetric benzylation of glycine *tert*-butyl ester **14** smoothly occurred under reaction conditions similar to those for the dimeric catalyst. For example, the ionic polymer catalyst **10AaH** prepared from cinchonidinium dimer **6AH** and disodium 1,3-propanedisulfonate **9a** was used in the asymmetric benzylation reaction to give the corresponding chiral product **15** in 86% yield with 87% ee (Table 2, entry 1). The catalytic activity of the polymeric catalyst **10AaH** is similar to that of the corresponding dimer catalyst **6AH**. The structure of disulfonate influenced on the catalytic activity of the ionic polymer catalyst. In a series of **10AH** catalysts (entries 1–8), *trans*-butenyldisulfonate gave the highest ee (entry 8). By using **10AeH**,

Table 1 Asymmetric benzylation of *N*-diphenylmethyl glycine *tert*-butyl ester using dimeric catalyst[a]

Entry	Catalyst	Time (h)	Yield[b] (%)	ee[cd] (%)
1[e]	**6AH**	6	88	86
2[f]	**6BH**	12	91	80
3[g]	**6CH**	4	90	84
4	**12AH**	4	95	95
5	**12BH**	4	89	89
6	**12CH**	4	76	71
7[e]	**6AAllyl**	1	84	70
8[h]	**6BAllyl**	4	92	80
9[h]	**6CAllyl**	2	91	90
12[g]	**12CAllyl**	4	94	93
13	**8AH**	8	86	89
14	**8BH**	8	93	78
15	**8CH**	7	86	65

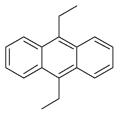
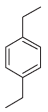
[a] The reaction was carried out with 1.2 equiv. of benzyl bromide in the presence of 10 mol% catalyst in 50 wt% aqueous KOH–toluene–$CHCl_3$ at 0 °C. [b] Determined by ^1H NMR. [c] Determined by HPLC (Chiralcel OD-H). [d] All products have *S* configuration. [e] Ref. 20. [f] Ref. 29. [g] Ref. 15. [h] Ref. 11.

the recyclability of the polymeric catalyst was examined. The polymeric catalyst was easily separated from the reaction mixture due to its insolubility. When the recovered catalyst was used for the same reaction, the polymeric catalyst showed the same catalytic activity as that obtained from the original catalyst. When *O*-allylated catalysts **10AAllyl** (entries 9–13) were used, lowering of the ee values in the asymmetric benzylation was observed.

In the series of **10BH** catalysts, enantioselectivities similar to those from **10AH** catalysts were obtained (entries 14–19). The selectivity did not decrease with the *O*-allylated catalysts **10BAllyl** (entries 20–25). Enantioselectivities obtained by using the polymeric catalyst **10B** are always higher than those obtained from the corresponding dimeric catalysts described in Table 1. Polymeric catalysts **10CH** containing meta-substituted linker gave the lower enantioselectivity in the same reaction (entries 26–31). However, interestingly, *O*-allylated catalysts **10CAllyl** showed high level of enantioselectivities in all cases (entries 32–37). This tendency was also found in the corresponding dimer catalyst series **6CH** and **6CAllyl** (Table 1). In case of *O*-allylated polymeric catalysts **10CAllyl**, slightly higher enantioselectivity compared with the corresponding dimeric catalysts **6CAllyl** was obtained. All the polymeric catalysts used were stable and no degradation of the polymers was detected during the reaction. We recovered the polymeric catalyst by simple filtration. Before and after the reaction, the intrinsic viscosity values [η] and NMR spectra of the polymeric catalyst did not change.

Chiral ionic polymers **13** prepared from 10,11-dihydrocinchonidine **11** were then used as a catalyst for the same asymmetric reaction. Polymeric catalyst **13AeH** showed an excellent catalytic activity with 95% ee (Table 3, entry 1). When the reaction temperature was lowered to −20 °C, higher enantioselectivity (97% ee) was obtained (entry 2). The reaction still occurred even at −40 °C to give the product in high conversion with high enantioselectivity (entry 3). *O*-allylated polymeric catalysts **13CAllyl** showed excellent catalytic activity with higher enantioselectivities in comparison with OH free catalysts **13CH**.

Table 2 Asymmetric benzylation of *N*-diphenylmethylene glycine *tert*-butyl ester using cinchonidine derived ionic polymer **10**[a]

Entry	R^2	Catalyst	Time (h)	Yield[b] (%)	ee[cd] (%)
1		**10AaH**	16	86	87
2		**10AbH**	22	55	74
3		**10AcH**	48	83	87[d]
4		**10AdH**	16	86	87
5		**10AeH**	12	87	88
6[f]		**10AeH**	14	88	88
7[g]		**10AeH**	14	89	88
8		**10AfH**	5	92	92
9		**10AaAllyl**	5	88	69
10		**10AbAllyl**	5	85	75
11		**10AdAllyl**	5	77	63
12		**10AeAllyl**	5	82	87
13		**10AfAllyl**	4	93	82
14		**10BaH**	7	94	88
15		**10BbH**	12	91	80
16		**10BcH**	15	92	82[e]
17		**10BdH**	8	86	85
18		**10BeH**	12	91	89
19		**10BfH**	6	94	88
20		**10BaAllyl**	5	91	86
21		**10BbAllyl**	5	88	85
22		**10BcAllyl**	20	90	91[e]
23		**10BdAllyl**	5	95	85
24		**10BeAllyl**	5	92	91
25		**10BfAllyl**	16	96	85
26		**10CaH**	12	55	61
27		**10CbH**	12	73	66
28		**10CcH**	12	75	60[e,h]
29		**10CdH**	15	76	63
30		**10CeH**	18	67	68
31		**10CfH**	16	84	69
32		**10CaAllyl**	5	88	91
33		**10CbAllyl**	6	90	92
34		**10CcAllyl**	15	86	92[e]
35		**10CdAllyl**	4.5	83	91
36		**10CeAllyl**	5.5	92	94
37		**10CfAllyl**	4	95	92

[a] The reaction was carried out with 1.2 equiv. of benzyl bromide in the presence of 10 mol% catalyst in 50 wt% aqueous KOH–toluene–$CHCl_3$ at 0 °C. [b] Determined by ^1H NMR. [c] Determined by HPLC (Chiralcel OD-H). [d] All products have *S* configuration. [e] See ref. 29. [f] The polymeric catalyst **10AeH** used in entry 6 was reused. [g] The polymeric catalyst **10AeH** used in entry 7 was reused. [h] At room temp.

Table 3 Asymmetric benzylation of *N*-diphenylmethylene glycine *tert*-butyl ester using hydrocinchonidine derived ionic polymers **13**[a]

Entry	Catalyst	Temp. °C	Time (h)	Yield[b] (%)	ee[cd] (%)
1	**13AeH**	0	4.5	97	95
2	**13AeH**	−20	7	98	97
3	**13AeH**	−40	30	97	96
4	**13AfH**	0	4	94	94
5	**13BeH**	0	4.5	96	81
6	**13BfH**	0	4	96	89
7	**13CeH**	0	4.5	88	76
8	**13CfH**	0	4	85	74
13	**13CeAllyl**	0	4.5	96	92
14	**13CfAllyl**	0	4	93	92

[a] The reaction was carried out with 1.2 equiv. of benzyl bromide in the presence of 10 mol% catalyst in 50 wt% aqueous KOH–toluene–$CHCl_3$ at 0 °C. [b] Determined by ^1H NMR. [c] Determined by HPLC (Chiralcel OD-H). [d] All products have *S* configuration.

Conclusions

We have prepared chiral ionic polymers from cinchonidine quaternary ammonium dimer and disulfonate. Repeated ion exchange reaction occurred smoothly to give the corresponding chiral ionic polymer (**10**, **13**). The synthesis of the chiral ionic polymer is simple and quantitative. The chiral ionic polymers showed excellent performance as catalyst in the asymmetric benzylation of *N*-diphenylmethylene glycine *tert*-butyl ester **14** to give phenylalanine derivative **15**. A high level of enantioselectivities up to 97% ee was obtained in this reaction with the chiral polymeric catalysts. Most of the enantioselectivities obtained with the polymeric catalyst are superior to those from the corresponding low-molecular-weight catalyst. Since the ionic polymers were insoluble in water and most of the usual organic solvent, their separation from the reaction mixture is easy and could be reused several times without loss of catalytic activity. During the reaction, the ionic polymers are stable and no change in the polymer structure was observed. The polymers used in the asymmetric reaction were quantitatively recovered as original. Various kinds of main-chain chiral polymers can be prepared by this novel strategy. This method will be applicable to the preparation of many other different chiral organocatalysts having ionic structure.

Experimental

General

All reagents were purchased from Sigma-Aldrich, Wako Pure Chemical Industries, Ltd, or Tokyo Chemical Industry Co., Ltd at the highest available purity and used as is unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) using Merck precoated silica-gel plates (Merck 5554, 60F254). Column chromatography was performed with a silica-gel column (Wakogel C-200, 100–200 mesh). Melting points were recorded using a Yanaco micro-melting apparatus and are uncorrected. ^{1}H (300 MHz) spectra were measured on a Varian Mercury 300 spectrometer. Elemental analyses were performed at the Microanalytical Center of Kyoto University. GC analyses were performed with a Shimadzu Capillary Gas Chromatograph 14B equipped with a capillary column (SPERCO β-DEX 325, 30 m × 0.25 mm). HPLC analyses were performed with a JASCO HPLC system comprising a three-line degasser DG-980-50, an HPLC pump PV-980, and a CO-965 column oven equipped with a chiral column (CHIRALCEL OD or AD, Daicel); hexane–2-propanol was used as an eluent. A UV detector (JASCO UV-975 for JASCO HPLC system) was used for peak detection. Optical rotations were recorded with a JASCO DIP-149 digital polarimeter, using a 10 cm thermostated microcell. Intrinsic viscosity [η] of each soluble sample was determined by viscosimetry, using a Ubbelohde viscometer at 40 °C in dimethyl sulfoxide (DMSO) solvent.

Synthesis of 8AH

A mixture of cinchonidine dimer **6AH** (0.5 mmol, 0.43 g) in methanol (40 mL) and sodium *p*-toluene sulfonate (1.5 mmol, 0.2913 g) in water (10 mL) was stirred for 3 hours. Methanol was evaporated and the reaction mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried over $MgSO_4$. After filtration and evaporation of the solvent, the product was dried under vacuum to give a yellow solid **8AH** in 85% yield. ^{1}H NMR (d^6-DMSO, 300 MHz) δ 9.14 (d, J = 9.0 Hz, 2H), 9.07–9.05 (m, 2H), 8.87 (d, J = 9.0 Hz, 2H), 8.62–8.56 (m, 2H), 8.17 (dd, J = 1.8, 1.8, 2H), 7.97–7.80 (m, 12H), 7.31–7.27 (m, 4H), 7.23 (d, J = 3.6 Hz, 2H), 7.09 (s, 2H), 7.04–7.01 (m, 4H), 6.60 (d, J = 13.2 Hz, 2H), 5.98 (d, J = 11.4, 2H), 5.76–5.60 (m, 2H), 5.06–4.90 (m, 4H), 4.61–4.44 (m, 4H), 3.93 (d, J = 11.1, 2H), 3.30–3.22 (m, 4H), 3.02–2.89 (m, 2H), 2.25–2.16 (m, 8H), 1.94–1.84 (m, 2H), 1.68–1.51 (m, 2H), 1.38–1.30 (m, 2H). ^{13}C NMR (d^6-DMSO, 75 MHz) δ 150.3, 147.8, 145.69, 145.17, 138.4, 137.9, 123.05, 123.00, 129.83, 129.58, 128.1, 127.3, 126.5, 125.90, 125.29, 124.59, 124.48, 120.4, 116.35, 68.0, 65.2, 60.9, 54.6, 51.7, 36.7, 25.3, 24.2, 21.55, 20.8 ppm. $[\alpha]_D^{25}$ = −329.18 (c 1.0, DMSO). IR (KBr) ν 3230.18, 2949.59, 1941.00, 1660.41, 1590.02, 1509.03, 1453.10, 1180.22, 1120.44, 1032.69, 1009.55. mp: 205–207 °C. Anal. Calcd for $C_{68}H_{70}N_4O_8S_2$: C, 71.93; H, 6.21; N, 4.93. Found: C, 71.75; H, 6.17; N, 4.89.

Synthesis of 8BH

A mixture of cinchonidine dimer **6BH** (0.5 mmol, 0.42 g) in methanol (35 mL) and sodium *p*-toluene sulfonate (1.5 mmol, 0.2913 g) in water (10 mL) was stirred for 2 hours. The methanol was evaporated and the reaction mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried over $MgSO_4$. After filtration and evaporation of the solvent, the product was dried under vacuum to give a yellow solid **8BH** in 88% yield. ^{1}H NMR (d^6-DMSO, 300 MHz) δ 9.00 (d, J = 4.5 Hz, 2H), 8.29 (d, J = 8.10 Hz, 2H), 8.13 (d, J = 8.10 Hz, 2H), 7.95–7.74 (m, 12H), 7.45 (d, J = 7.8, 3H), 7.09 (dd, J = 0.6, 0.3, 3H), 6.78 (d, J = 4.2, 2H), 6.59 (s, 2H), 5.76–5.65 (m, 2H), 5.20–5.13 (m, 4H), 5.05–4.96 (m, 4H), 4.28 (s, 2H), 3.96–3.90 (m, 2H), 3.75 (d, J = 13.5, 2H), 3.50–3.42 (m, 3H), 2.73 (s, 3H), 2.27 (s, 5H), 2.20–2.02 (m, 7H), 1.87 (s, 2H), 1.36–1.28 (m, 2H). ^{13}C NMR (d^6-DMSO, 75 MHz) δ 150.3, 147.7, 145.4, 138.30, 138.29, 137.9, 134.2, 129.92, 129.80, 129.54, 128.2, 127.3, 125.5, 124.3, 123.6, 120.2, 116.3, 67.8, 64.3, 62.2, 59.3, 50.7, 36.7, 26.0, 24.1, 21.1, 20.8 ppm. $[\alpha]_D^{25}$ = −125.16 (c 1.0, DMSO). IR (KBr) ν 3207.07, 2952.48, 1942.93, 1656.55, 1589.06, 1509.99, 1461.78, 1217.83, 1172.51, 1120.44, 1032.69, 1009.55, 818.63, 777.17, 681.71, 567.93. mp: 221–223 °C. Anal. Calcd for $C_{60}H_{66}N_4O_8S_2$: C, 69.61; H, 6.43; N, 5.41. Found: C, 69.53; H, 6.40; N, 5.38.

Synthesis of 8CH

A mixture of cinchonidine dimer **6CH** (0.5 mmol, 0.42 g) in methanol (30 mL) and sodium *p*-toluene sulfonate (1.5 mmol, 0.2913 g) in water (10 mL) was stirred for 2 hours. Methanol was evaporated and the reaction mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried over $MgSO_4$. After filtration and evaporation of the solvent, the product was dried under vacuum to give a yellow solid **8CH** in 90% yield. ^{1}H NMR (d^6-DMSO, 300 MHz) δ 8.98 (d, J = 3.90

Hz, 2H), 8.28–8.22 (m, 3H), 8.11 (d, J = 8.40 Hz, 2H), 7.87–7.81 (m, 6H), 7.74–7.69 (m, 3H), 7.47 (d, J = 7.5 Hz, 4H), 7.08 (d, J = 7.2 Hz, 4H), 7.00 (s, 2H), 6.61 (s, 2H), 5.73–5.62 (m, 2H), 5.29 (d, J = 11.7 Hz, 2H), 5.17 (s, 1H), 5.11–5.05 (m, 3H), 4.94 (d, J = 10.2 Hz, 2H), 4.33 (s, 2H), 3.96–3.90 (m, 2H), 3.74 (d, J = 10.2 Hz, 2H), 2.66 (s, 2H), 2.26 (s, 5H), 2.11–2.05 (m, 3H), 1.99 (s, 2H), 1.75 (s, 2H), 1.33–1.26 (m, 2H), 1.13 (d, J = 12.3 Hz, 4H), 0.94 (d, J = 6.6 Hz, 2H). ^{13}C NMR (d^6-DMSO, 75 MHz) δ 150.2, 147.6, 145.37, 145.04, 139.69, 139.25, 138.10, 138.07, 135.1, 129.89, 129.43, 128.6, 128.19, 127.3, 125.5, 124.3, 123.5, 120.1, 116.3, 67.9, 64.3, 59.2, 50.6, 46.2, 36.8, 25.9, 24.3, 20.8, 18.9 ppm. $[\alpha]_D^{25}$ = −127.43 (c 1.0, DMSO). IR (KBr) ν 3247.54, 2512.79, 1920.75, 1640.16, 1590.99, 1570.74, 1509.03, 1460.81, 1208.18, 1118.51, 1032.69, 1009.55, 814.78, 777.17, 755.96, 683.64, 565.04. mp: 213–215 °C. Anal. Calcd for $C_{60}H_{66}N_4O_8S_2$: C, 69.61; H, 6.43; N, 5.41. Found: C, 69.55; H, 6.38; N, 5.35.

Synthesis of 12AH

A mixture of (−)-10,11-dihydrocinchonidine (3.0 g, 10.2 mmol) with 9,10-bis-(chloromethyl)anthracene (1.38 g, 5 mmol) in a mixture of 30 mL (ethanol : DMF : $CHCl_3$/5 : 6:2) was stirred at 100 °C for 6 h. After completion of reaction, the reaction mixture was cooled at room temperature. After cooling the reaction mixture to room temperature the reaction mixture was diluted with methanol (25 mL) and then added dropwise to ether (300 mL) with stirring. The solid precipitated was filtered, washed with ether (200 mL). The crude solid was reprecipitated from methanol–ether to afford 3.82 g (88% yield) of product. $[\alpha]_D^{25}$ = −229.53 (c 1.0, DMSO). ^{1}H NMR (d^6-DMSO, 300 MHz) δ 9.04–8.90 (m, 4H), 8.71–8.66 (m, 2H), 8.17–8.04 (m, 2H), 7.95–7.75 (m, 8H), 7.69–7.53 (m, 4H), 7.01 (brs, 1H), 6.58–5.41 (m, 3H), 4.69–4.38 (m, 2H), 4.00–3.41 (m, 3H), 3.20–3.11 (m, 2H), 2.20–1.93 (m, 4H), 1.75 (s, 4H), 1.52–1.37 (m, 5H), 1.31–1.02 (m, 8H), 0.75–0.70 (m, 3H), 0.55–0.519 (m, 5H). ^{13}C NMR (d^6-DMSO, 75 MHz) δ 150.1, 147.70, 147.66, 147.14, 146.0, 132.8, 129.66, 129.23, 126.9, 124.67, 124.14, 120.5, 118.8, 65.7, 59.5, 54.9, 42.6, 34.6, 25.61, 25.47, 24.3, 22.5, 17.2, 11.3 ppm. IR (KBr) ν 3170.40, 2957.30, 2560.04, 1662.34, 1590.02, 1509.03, 1457.92, 1385.60, 781.03, 758.85. mp: 181–183 °C. Anal. Calcd for $C_{54}H_{60}N_4O_2Cl_2$: C, 74.72; H, 6.97; N, 6.45. Found: C, 74.68; H, 6.83; N, 6.35.

Synthesis of 12BH

The procedure described for **12AH** was followed using (−)-10,11-dihydrocinchonidine (3.0 g, 10.2 mmol) and α,α′-dibromo *p*-xylene (1.32 g, 5 mmol), which gave **12BH** (4.12 g, 96% yield). ^{1}H NMR (d^6-DMSO, 300 MHz) δ 9.00 (d, J = 4.2 Hz, 1H), 8.36 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 9.0 Hz, 1H), 7.95 (s, 1H), 7.89 (s, 1H), 7.84 (d, J = 5.1 Hz, 2H), 7.78–7.73 (m, 1H), 6.74 (d, J = 4.5 Hz, 1H), 6.58 (d, J = 3.6 Hz, 1H), 5.28 (d, J = 12 Hz, 1H), 5.10 (d, J = 12 Hz, 1H), 4.28 (s, 1H), 3.98–3.93 (m, 1H), 3.71–3.63 (m, 1H), 3.52 (d, J = 9.9, 1H), 3.43 (d, J = 5.1, 1H), 2.14–2.07 (m, 1H), 1.99–1.83 (m, 4H), 1.35–1.28 (m, 1H), 1.24–1.05 (m, 2H), 0.71–0.66 (m, 3H). ^{13}C NMR (d^6-DMSO, 75 MHz) δ 150.15, 147.6, 145.3, 134.0, 129.81, 129.77, 129.35, 127.3, 124.3, 123.8, 120.1, 67.6, 64.0, 61.93, 61.59, 50.5, 35.8, 25.6, 24.6, 23.6, 20.8, 11.3 ppm. $[\alpha]_D^{25}$ = −95.49 (c 1.0, DMSO). IR (KBr) ν 3154.97, 2954.41, 1938.11, 1666.20, 1591.95, 1507.10, 1458.89, 1404.89, 1388.50, 1120.44, 1093.44, 1056.80, 855.28, 780.06, 758.85. mp: 227–229 °C. Anal. Calcd for $C_{46}H_{56}N_4O_2Br_2$: C, 64.49; H, 6.59; N, 6.54. Found: C, 64.55; H, 6.51; N, 6.38.

Synthesis of 12CH

The procedure described for **12AH** was followed using (−)-10,11-dihydrocinchonidine (3.0 g, 10.2 mmol) and α,α′-dibromo *m*-xylene (1.32 g, 5 mmol), which gave **12CH** (4.2 g, 98% yield). ^{1}H NMR (d^6-DMSO, 400 MHz) δ 9.00 (d, J = 4.4 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 7.2 Hz, 1H), 7.95–7. 76 (m, 5H), 6.77 (s, 1H), 6.61 (s, 1H), 5.33 (d, J = 11.2 Hz, 1H), 5.13 (d, J = 11.2 Hz, 1H), 4.33 (s, 1H), 3.99 (s, 1H), 3.53–3.31 (m, 2H), 2.10–1.75 (m, 6H), 1.30–1.13 (m, 3H), 0.66 (d, J = 7.2 Hz, 3H). ^{13}C NMR (d^6-DMSO, 125 MHz) δ 149.9, 147.3, 145.0, 138.7, 134.8, 129.54, 129.16, 128.3, 127.1, 124.1, 123.6, 120.0, 67.3, 63.9, 61.91, 61.01, 50.2, 35.6, 30.5, 24.5, 23.9, 20.6, 11.0 ppm. $[\alpha]_D^{25}$ = −132.18 (c 1.0, DMSO). IR (KBr) ν 3434.60, 3200.29, 2958.27, 2875.34, 2113.60, 1933.29, 1664.27, 1590.02, 1509.03, 1458.89, 1387.53, 1116.58, 1062.59, 803.21, 778.14, 754.99. mp: 224–226 °C. Anal. Calcd for $C_{46}H_{56}N_4O_2Br_2$: C, 64.49; H, 6.59; N, 6.54. Found: C, 64.32; H, 6.55; N, 6.42.

Synthesis of disulfonate 9e

A mixture of α,α′-dibromo *p*-xylene (10 mmol, 2.64 g) in DMSO (30 mL) and Na_2SO_3 (22 mmol, 2.77 g) in H_2O (20 mL) was stirred at 100 °C for 12 hours. After completion of the reaction, the reaction mixture was filtered and filtrate was collected. The amount of solvent in the filtrate was reduced to 15 mL by pump. The concentrated solution was added into ethanol (250 mL) with stirring. The white precipitate obtained was filtered, washed with methanol, hexane and dried under vacuum to give **9e** in 98% yield. ^{1}H NMR (D_2O, 300 MHz) δ = 7.44 (s, 2H), 4.21 (s, 2H). ^{13}C NMR (D_2O, 75 MHz) δ 131.6, 56.6. IR (KBr) ν 3468, 2978, 1629.55, 1516.74, 1425.14, 1148.40, 1057.76, 969.05, 852.38, 743.42, 633.86, 533.22. Anal. Calcd for $C_8H_8Na_2O_6S_2$: C, 30.97; H, 2.60. Found: C, 31.05; H, 2.58.

Synthesis of disulfonate 9f

A mixture of *trans*-1,4-dibromo-2-butene (10 mmol 2.1390 g) in DMF (15 mL) and Na_2SO_3 (22 mmol, 2.77 g) in H_2O (15 mL) were stirred at 100 °C for 11 h. After cooling the reaction mixture to room temperature, H_2O (30 mL) and ethanol (20 mL) were added successively to the reaction mixture. The excess Na_2SO_3 precipitated was filtered out and the filtrate was collected, washed with CH_2Cl_2 (3 × 20 mL) to remove the unreacted *trans*-1,4-dibromo-2-butene. The volume of the reaction mixture was reduced by rotary evaporator and dried under vacuum to obtain the crude product. The crude product was recrystallized in ethanol–H_2O (6 : 4) mixture to give **9f** in 96% yield as a white solid. ^{1}H NMR (D_2O, 300 MHz) δ = 5.89–5.85

(m, 1H), 3.70–3.68 (m, 2H). ^{13}C NMR (D_2O, 75 MHz) δ 127.2, 54.7. IR (KBr) ν 3478.95, 1677.16, 1622.80, 1410.67, 1187.94, 1049.09, 628.68, 615.18, 597.82, 536.11. Anal. Calcd for $C_4H_6Na_2O_6S_2$: C, 18.46; H, 2.32. Found: C, 18.52; H, 2.38.

General procedure for catalytic enantioselective benzylation of *N*-diphenylmethylidene glycine *tert*-butyl ester (14) using chiral polymeric catalyst 10AeH

Chiral polymeric catalyst **10AeH** (100 mg) and *N*-diphenylmethylidene glycine *tert*-butyl ester (**14**: 0.53 g, 1.78 mmol) were added to a mixed solvent of toluene (7 mL) and chloroform (3 mL). 50 wt% aqueous KOH solution (2.5 mL) was added to the above mixture. Benzyl bromide (0.37 g, 2.14 mmol) was then added dropwise at 0 °C to the mixture. The reaction mixture was stirred vigorously for 12 h. Saturated sodium chloride solution (10 mL) was then added, and the mixture was subsequently filtered to recover **10AeH**, which was washed with water and dichloromethane several times. The organic phase was separated, and the aqueous phase was extracted with dichloromethane. The organic extracts were washed with brine and dried over $MgSO_4$. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (ether–hexane = 1 : 10 as eluent) gave (*S*)-*tert*-butyl *N*-(diphenylmethylidene)phenylalaninate (**15**) (0.60 g, 1.55 mmol, 87% yield). The enantiomeric excess (88% ee) was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane–2-propanol = 100 : 1, flow rate = 0.3 mL min^{-1}, retention time: *R* enantiomer = 27.6 min, *S* enantiomer = 47.9 min). The absolute configuration was determined by comparison of the HPLC retention time with the authentic sample independently synthesized by the reported procedure.[3]

Recycling experiment of the polymeric catalyst 10AeH. Recovered **10AeH** was dried *in vacuo* at room temperature. Benzyl bromide (0.33 g, 1.93 mmol) was added dropwise at 0 °C to a mixture of **14** (0.47 g, 1.6 mmol), chiral polymeric catalyst **10AeH** (90 mg) in toluene (7 mL) and chloroform (3 mL), and 50 wt% aqueous KOH solution (2.5 mL). The reaction mixture was stirred vigorously for 14 h. Saturated sodium chloride solution (10 mL) was then added, and the mixture was subsequently filtered to recover **10AeH**, which was washed with water and dichloromethane several times. The organic phase was separated, and the aqueous phase was extracted with dichloromethane. The organic extracts were washed with brine and dried over $MgSO_4$. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (ether–hexane = 1 : 10 as eluent) gave (*S*)-*tert*-butyl *N*-(diphenylmethylene)phenylalaninate (**15**) (0.54 g, 1.41 mmol, 88% yield, 88% ee).

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