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Designing Chiral Quaternary Ammonium Polymers: Novel Type of Polymeric Catalyst for Asymmetric Alkylation Reaction

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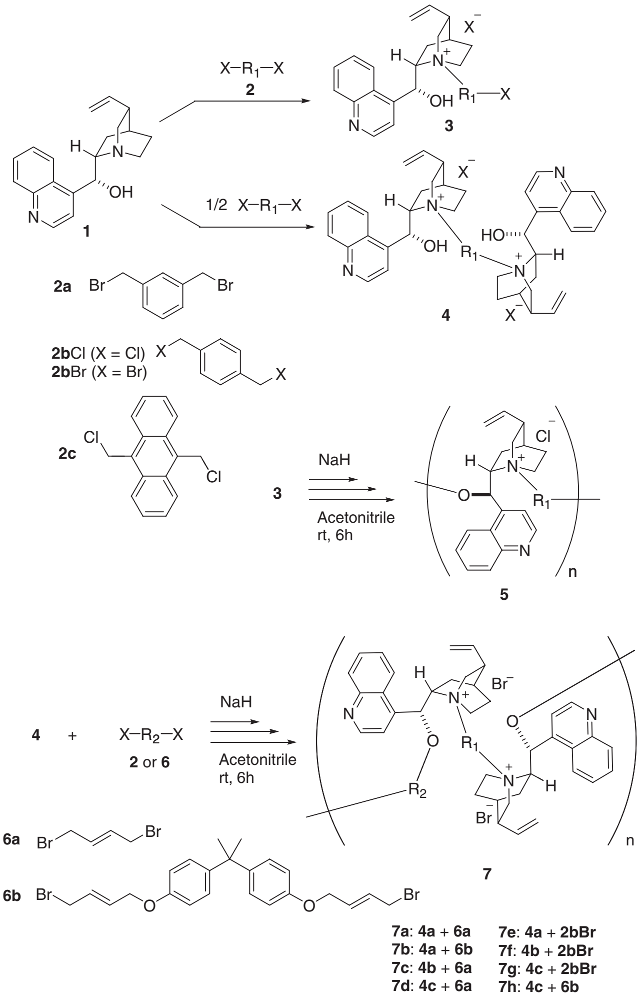
Optically active polymers containing chiral quaternary ammonium salt structure in their main chain have been prepared by simple polycondensation reaction. These polymers were used as catalyst for asymmetric alkylation of *N*-diphenylmethylidene glycine *tert*-butyl ester.

Since the first preparation of quaternary ammonium ionene polymers by Gibbs and co-workers in 1933,[1] various types of polymers containing quaternary ammonium structure in the main chain have been prepared.[2–5] They have many potential uses in biomedical applications including DNA-transfer agents,[6] multifunctional gelators,[7] and antimicrobial applications.[8,9] Another application of cationic polymers was self-assembled supramolecular complex formation followed by use as a polymer-immobilized catalyst for organic reactions.[10]

Low molecular weight quaternary ammonium salts have been efficiently used as organocatalysts in a variety of organic reactions.[11] Moreover, a number of chiral quaternary ammonium salts have been developed as chiral organocatalysts for asymmetric transformation. Some were attached to a side chain of a polymer-support, which were used in asymmetric reactions such as hydrocyanation of imines,[12] the Diels–Alder reaction,[13] aldol reaction,[14] epoxidation,[15] the Darzens condensation,[16] and alkylation.[17] We have also developed polymer-immobilized chiral quaternary ammonium salt.[18] In these all examples, monomeric chiral catalyst was attached to achiral sterically irregular polymer backbones. Compared with these pendant type catalysts, the polymers having chiral quaternary ammonium structure in their main chain have not been prepared and used as catalyst for the asymmetric reactions. To our knowledge, there has been no report on the preparation of such optically active quaternary ammonium polymers having main chain chirality. We now report the synthesis of a novel type of chiral quaternary ammonium polymers and their use in asymmetric alkylation of *N*-diphenylmethylidene glycine *tert*-butyl ester.

Cinchonidine derivatives have been most frequently utilized for chiral quaternary ammonium salt formation.[19] Cinchonidine derived chiral quaternary ammonium salts **3** were synthesized from cinchonidine (**1**) and equimolar amount of dihalide **2**. Since compound **3** possesses both hydroxy and halide groups, polycondensation reaction easily occurred in the presence of NaH. Under Williamson ether synthesis conditions, one component self polycondensation of **3** readily proceeded to yield the corresponding optically active polymers **5** having quaternary ammonium structure in the main chain as shown in Scheme 1.[20]

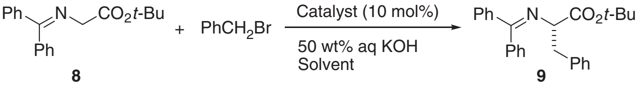
We have also prepared another enantiopure bis(quaternary ammonium salt) **4** with two hydroxy groups. Reaction of 2 equivalents of **1** with **2** exclusively yielded the quaternary ammonium dimer **4**. The control of the molar ratio between **1** and **2** clearly provided **3** and **4**, respectively. In the case of dimeric compound **4**, two component polycondensation with a dihalide **6** in a repeated Williamson reaction yielded the optically active polyether **7** containing chiral quaternary ammonium salt structure in its main chain.



Scheme 1. Preparation of chiral quaternary ammonium polymers.

In order to evaluate the catalytic activity of the chiral quaternary ammonium polymers **5** and **7**, asymmetric benzylation of *N*-diphenylmethylidene glycine *tert*-butyl ester **8** was performed with these polymers. In the first place, we used self-polycondensation polymers **5** as a catalyst for the reaction. Polymer **5** was suspended in toluene/aqueous KOH solution and alkylation of **8** smoothly occurred at room temperature to yield **9**. For example, the use of **5c** afforded the product **9** in 76% yield with 65% ee (Table 1, Run 2). Lowering the reaction temperature to 0 °C, somewhat higher enantioselectivity (72%

Table 1. Asymmetric benzylation of *N*-diphenylmethylene glycine *tert*-butyl ester by using polymeric catalyst



Run	Catalyst	Solvent[a]	Temp/°C	Time/h	Yield/%	ee/%[b,c]
1	**5b**	A	rt	15	76	57
2	**5c**	A	rt	15	76	65
3	**5c**	A	0	15	78	72
4	**5c**	B	0	15	68	62
5	**5c**	C	rt	15	70	72
6	**5c**	C	0	15	78	80
7	**5c**	C	−20	60	74	85
8	**4a**	A	rt	15	72	57
9[d]	**4a**	C	0	4	90	84
10[d]	**4b**	A	0	20	80	68
11	**7a**	C	0	15	79	75
12	**7b**	C	0	15	65	69
13	**7c**	C	0	24	87	82
14	**7d**	C	0	15	83	86
15[e]	**7d**	C	0	15	80	85
16[f]	**7d**	C	0	15	85	86
17	**7e**	C	0	15	90	76
18	**7f**	C	0	15	92	86
19	**7g**	C	0	15	79	85
20	**7h**	C	0	15	60	69

[a]Solvent A: toluene, B: CH_2Cl_2, C: toluene:$CHCl_3$ (7:3). [b]Determined by HPLC (CHIRALCEL OD-H). [c]S configuration of **9** was assigned by the relative retention times of the R/S isomers reported in the literature.[21] [d]See Ref. 22. [e]Catalyst recovered from Run 14 was used. [f]Catalyst recovered from Run 15 was used.

ee) was obtained (Run 3). Organic solvent used in the reaction also influenced the stereoselectivity. Park et al. reported that the optimal solvent condition was determined to be toluene/chloroform (v/v, 7:3) for the benzylation reaction.[23] This mixed solvent system gave better results in our polymeric catalysts (Runs 5–7). At −20 °C, the reaction of **8** and benzyl bromide in the presence of the polymer **5c** still proceeded. The higher enantioselectivity was obtained with lower reaction temperature as expected. The corresponding quaternary ammonium salt **4** as a model catalyst showed similar enantioselectivity (Runs 8–10).[22]

We then used the two component polycondensation polymers **7** as polymeric catalyst for the same reaction. In the presence of polymer **7a** prepared from **4a** and **6a** the reaction occurred to give the product **9** with 75% ee (Run 11). We prepared **7b** from **4a** and **6b** having a spacer between chiral quaternary units, which showed somewhat lower enantioselecltivity (Run 12). Higher enantioselectivities were obtained by the use of **7c** and **7d** (Runs 13 and 14). After the asymmetric benzylation, these chiral polymers could be easily separated by precipitation in hexane. The recovered polymer was reused for the same reaction. For example, **7d** was recovered and reused to give almost the same catalytic activity in the benzylation (Runs 15 and 16).

In summary, we have developed novel optically active polymers **5** and **7** with chiral quaternary ammonium repeating units. These polymers with main chain chirality efficiently performed as polymeric catalyst in the asymmetric benzylation of *N*-diphenylmethylidene glycine *tert*-butyl ester.

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