

Polymeric Cinchona Alkaloids for the Catalytic Asymmetric Dihydroxylation of Olefins

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ABSTRACT: Three cinchona alkaloid copolymers (PMMA-BQTP, PMA-BQTP, PAN-BQTP) have been synthesized by copolymerization. Their structure was characterized by FTIR, GPC, and element analysis. The catalytic activity of these copolymers in asymmetric dihydroxylation (AD) of olefins by OsO₄ was studied. The products enantiomeric excesses (ee) and the conversion of the substrate in the dihydroxylation reactions were determined using HPLC. The effect of time, temperature, and recycle times on the reaction was also discussed. The results showed that the copolymers catalyzed the dihydroxylation

of the olefins to get diols in high optical yield. However, their catalytic efficiency was largely depended on the nature of olefins. The polymeric cinchona alkaloid can be simply recovered at the end of the reaction by centrifugation and then reused without radical change of activity or enantioselectivity. © 2008 Wiley Periodicals, Inc. *J Appl Polym Sci* 108: 845–849, 2008

Key words: asymmetric dihydroxylation; polymeric cinchona alkaloids; heterogeneous catalysis; optical active diols

INTRODUCTION

Asymmetric synthesis of optical active compounds from prochiral substrates using chiral catalyst is a major challenge in organic chemistry.¹ In recent years, several reports have appeared dealing with efficient. Osmium-catalyzed dihydroxylation of olefins is one of the most efficient methods for the preparation of vicinal diols.^{2–10} The reaction proceeds in the presence of catalytic amount of OsO₄ using cooxidant such as metal chlorates, hydrogen peroxide, *t*-butyl hydroperoxide, potassium ferricyanide, or most commonly, *N*-methylmorpholine-*N*-oxide (NMO). Although a number of processes have gained wide acceptance in this dihydroxylation, few fruitful industrial applications have been accomplished, probably because OsO₄ is highly toxic, expensive, volatile, and cannot be recovered.¹¹ Heterogeneous catalytic systems could overcome these problems¹² by using insoluble supports which offer several practical advantages over their soluble counterparts such as easy recovery and product purification.^{8,13,14} Thus, there is a continuous interest in the development of synthetically simple and efficient polymers for heterogeneous dihydroxylation of olefins.¹⁵

In view of these, we have synthesized chiral polymers, (PMMA-BQTP (poly(MA-*co*-BQTP)), PMA-

BQTP (poly(MMA-*co*-BQTP)), PAN-BQTP (poly(AN-*co*-BQTP)) and studied their catalytic activity in the dihydroxylation of olefins by OsO₄.

EXPERIMENT

Materials

Quinine and OsO₄ were obtained from Aldrich Co (Milwaukee, WI) and are used as such. Azobisisobutyronitrile (AIBN) was bought from Merck Co.

Styrene, *E*-stilbene, α -methyl-styrene, β -methyl-styrene, cyclohexene, and 1,4-benzenedicarbonyl chloride were purchased from the Shanghai Chemical Reagent Factory. Styrene, α -methyl-styrene, and cyclohexene were purified by distillation under reduced pressure. Methacrylate (MA), methylmethacrylate (MMA), acrylonitrile (AN), chloroform, benzene, and other solvents used were analytical reagent grade and were purified by standard procedures prior to use.

Instruments

IR spectra were obtained by using a Nicolet Avatar 360 FTIR spectrophotometer (KBr disk). Elemental analysis was performed on PE-2400CHN elemental analyzer. The molecular weight was measured by Waters 150C gel permeation chromatography, using THF as an eluent and polystyrene as standard sample with the column temperature of 30°C. The

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TABLE I
Copolymer Molecular Weight and PDI Data

Copolymer	Chiral monomer: second monomer (mol : mol)	M_n ($\times 10^3$)	M_w ($\times 10^3$)	M_z ($\times 10^3$)	PDI
PAN-BQTP	1 : 40	1.7	1.9	2.3	1.15
PAN-BQTP	1 : 60	1.4	2.1	2.7	1.46
PMA-BQTP	1 : 40	14.7	29.8	49.1	2.03
PMMA-BQTP	1 : 40	22.0	39.0	58.9	1.77

products of dihydroxylation were determined by Shimadzu GC-16A gas chromatograph with a 5 m \times 3 mm OV-17 column. Enantiomeric excesses of the diols were determined by Shimadzu 1671-CHA HPLC analysis using a Daicel CHIRALCEL OD column (flow rate of 0.5 mL/min, hexane/*i*-PrOH = 9/1 as eluent; UV detector). The absolute configuration was determined by the WXG-4 polarimeter.

Synthesis of chiral copolymer

1,4-bis(9-*O*-quininyl)terephthalate, the chiral monomer A (BQTP) was synthesized as described in the literature.¹⁶

The copolymers C (PMA-BQTP), B (PMMA-BQTP), and D (PAN-BQTP) were synthesized by the same method as reported earlier.¹⁷ A solution of chiral monomer (BQTP, 1 mmol), second monomer (MA or MMA or AN, 40 mmol), and AIBN (0.1%) as initiator in dry benzene was refluxed for 72 h under dry nitrogen atmosphere at 70°C. After completing this reaction, the solution was poured into petroleum ether. The precipitate was filtered, washed with ethanol for three times, and dried under vacuum to give product.

The copolymer molecular weight and polydispersity index (PDI) was shown in Table I. Element analysis data were shown in Table II. The elemental analysis calculated: PAN-BQTP (1 : 40) C, 69.73%; H, 6.22%; N, 20.80%; PMA-BQTP (1 : 40) C, 59.44%; H, 7.12%; N, 1.30%; PMMA-BQTP (1 : 40) C, 62.47%; H, 7.96%; N, 1.15%.

Typical procedure for asymmetric dihydroxylation reactions

$K_3Fe(CN)_6$ (3.0 g, 9.0 mmol), K_2CO_3 (1.24 g, 9.0 mmol), and copolymer B (0.1 g) were dissolved in *t*-BuOH/ H_2O (1 : 1, 20 mL) at room temperature,

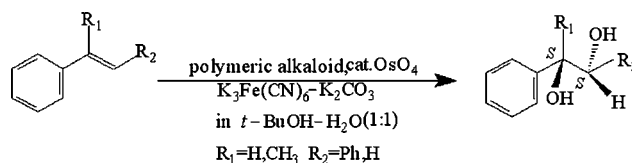
followed by addition of 1% OsO_4 solution (0.30 mL, 0.012 mmol). The solution was cooled to 0°C and the olefin (3.0 mmol) was added. The mixture was stirred vigorously at 0°C for 72 h. Na_2SO_3 (0.57 g, 4.5 mmol) was added and the mixture was allowed to warm to room temperature and stirred for 2 h. CH_2Cl_2 (10 mL) was added to the reaction mixture, and after separation of the layers the aqueous phase was further extracted with CH_2Cl_2 (5 mL \times 3). The combined organic phase were dried by anhydrous Na_2SO_4 and then concentrated by evaporation. The product was obtained after column chromatography and characterized (analyzed) by GC and HPLC (see reaction Scheme 1). The copolymer- OsO_4 complex was separation from the aqueous phase by filtration and then reused.

RESULTS AND DISCUSSION

Characterization

The polymers B, C, and D were obtained by radical copolymerization of cinchona alkaloid derived monomers with MMA, MA, and AN, respectively. These polymers were continuously extracted with ethanol to avoid the presence of non reacted chiral monomers or soluble chiral oligomers and then characterized by FTIR and elemental analysis. FTIR spectral data of copolymer are shown in Figure 1. As seen in the IR spectra of BQTP, C=N peaks appeared at 1510 cm^{-1} and the C=O peaks appeared at 1725 cm^{-1} . And the C-N (—N<) peaks appeared at 1358 cm^{-1} . In the spectra of three copolymers, C=N peaks appeared at 1510 cm^{-1} and the C=O peaks appeared at 1720 cm^{-1} . The stretching vibration of C—N (—N<) bonds of copolymer occurred at 1387, 1373, and 1365 cm^{-1} in B,C, and D, respectively. It were different because the backbone of the polymer was influenced by the other mono-

TABLE II Elemental Analysis Data			
Compound	C%	H%	N%
PAN-BQTP (1 : 40)	68.43	6.02	22.14
PMA-BQTP (1 : 40)	60.02	7.22	0.93
PMMA-BQTP (1 : 40)	61.23	7.85	0.78



Scheme 1 Asymmetric reduction reaction scheme.

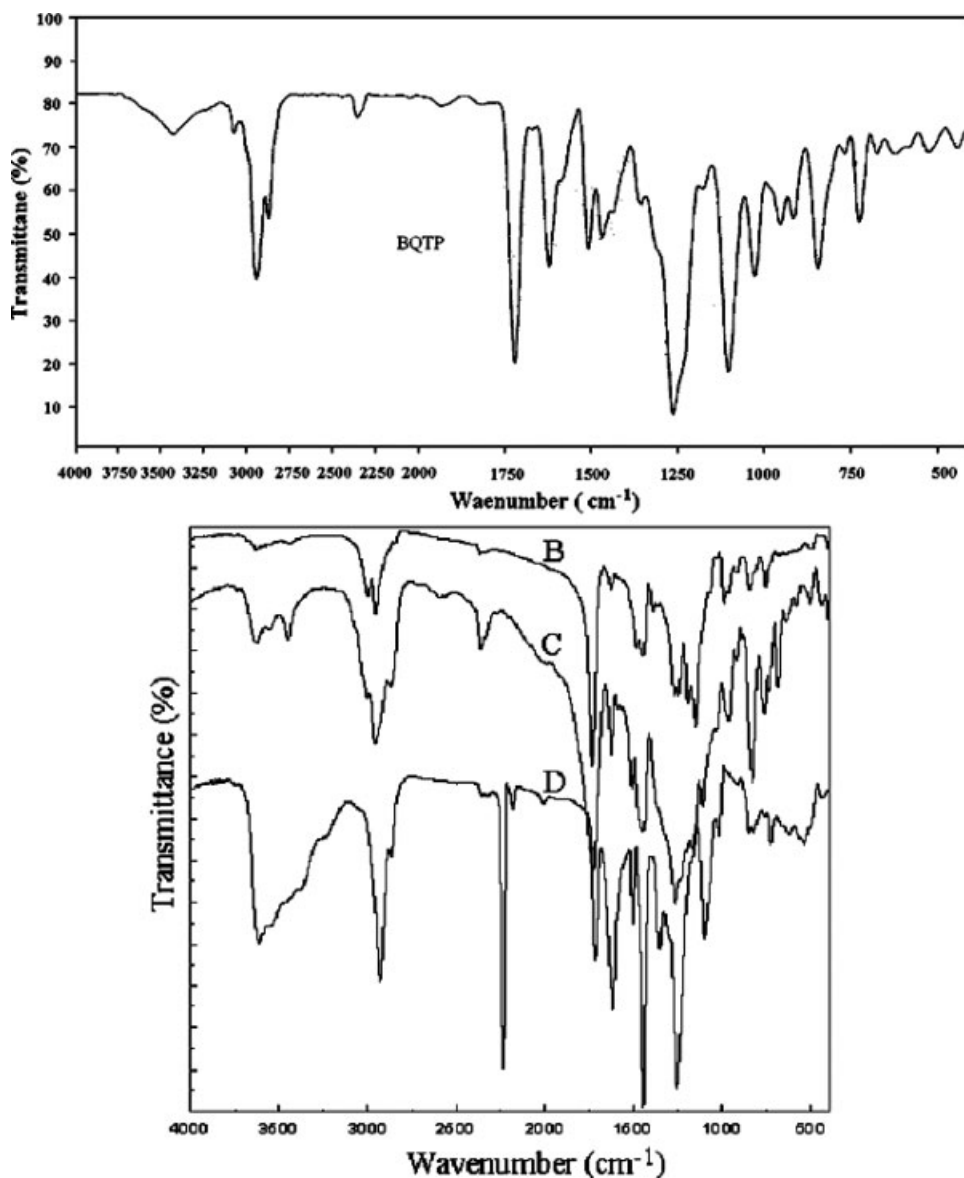


Figure 1 FTIR spectra of polymer and BQTP.

mers (MMA, MA, or AN). The FTIR results confirmed the copolymerization between BQTP groups and other monomers. The structures of the copolymers and BQTP are shown in Scheme 2.

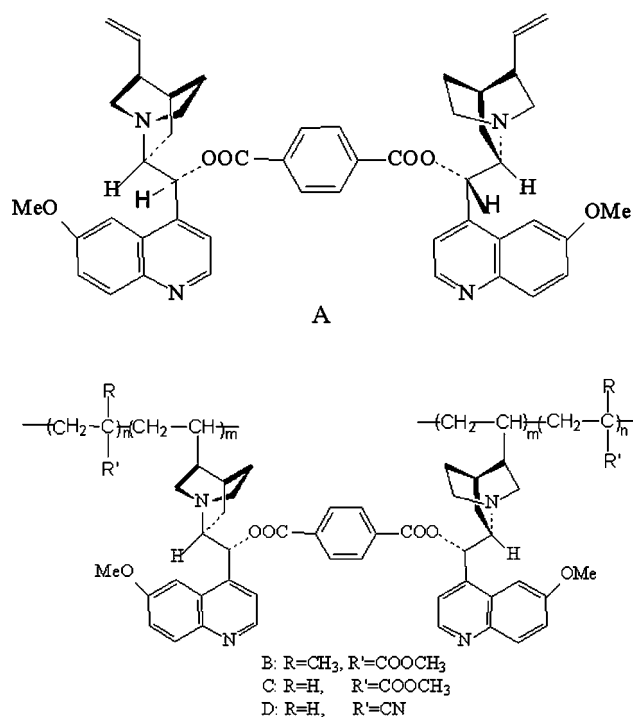
Asymmetric dihydroxylation of olefins

In the presence of polymeric cinchona alkaloids, olefin dihydroxylation using $K_3Fe(CN)_6 \cdot K_2CO_3$ as secondary oxidant was investigated by monitoring the olefin consumption. The results of the catalytic activity of polymeric cinchona alkaloids in the dihydroxylation are presented in Table III.

In the $t\text{-BuOH}/H_2O\text{-}K_3Fe(CN)_6$ system, the polymeric catalysts swelled well. The swelling may provide chiral environments similar to that of the

homogeneous catalytic system. The accessibility of the active site in the polymer matrix depends on the compatibility between the polymer support and the liquid reaction medium. It could be imagined that in a polar solvent, the compatibility would be improved by increasing the polarity of polymer support.

The enantioselectivity of the dihydroxylation was also assessed using various catalysts and substrates, and the results are summarized in Table III. As can be seen from Table I, all products gave *S* configuration. However, the extent of the asymmetric induction was greatly sensitive to polymer composition, especially R and R' which greatly affected the chemical and optical yield. Polymeric catalyst derived from PMMA-BQTP give the highest enantioselectiv-



Scheme 2 Structures of BQTP, PMMA-BQTP, PMA-BQTP, and PAN-BQTP.

ity in the asymmetric dihydroxylation of *E*-stilbene, we have reached 94% of ee.

Effect of catalytic reaction temperature

The catalytic activity of PMMA-BQTP-OsO₄ was investigated as a function of temperature. The results are shown in Figure 2. It is evident from the figure that as the reaction temperature is lowered, higher optical yield is obtained. As the mobility of polymer's chiral segments is expected to increase with rise in temperature, the asymmetric reaction may not be favored at higher temperature. At 0°C, the optical

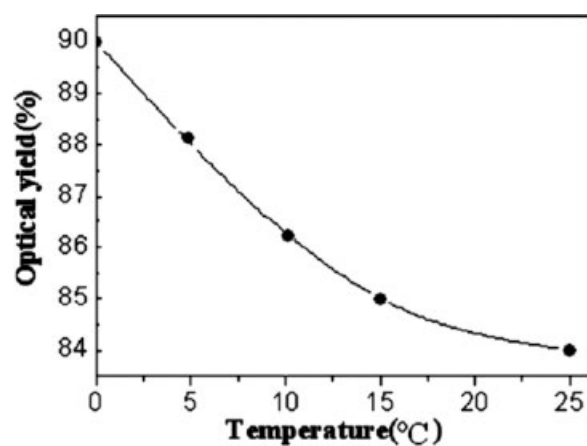


Figure 2 Relationship between the optical yield and temperature (PMMA-BQTP-OsO₄). Amount of catalyst, 100 mg; OsO₄, 0.3 mL (1%); *E*-Stilbene, 3.0 mmol; reaction time, 24 h.

yield was 1.07 times than that of 25°C. When the temperature decreased, the optical yield increased slowly.

Effect of catalytic reaction time

To further confirm the role of the chiral polymers on the kinetics and conversion of the dihydroxylation of *E*-Stilbene, the reaction was monitored by HPLC using a CHIRALCEL OD column. It was thus possible to monitor the extent of the conversion as well as its enantioselectivity, without isolation of the products. Figure 3 shows the influence of reaction time on the asymmetric dihydroxylation. It can be seen that the product and optical yields are greatly affected by the reaction time. With the reaction time increasing from 12 to 72 h, the product yield increased from 30.0 to 72% and the optical yields increased from 60 to 83.7% ee. Consequently, the best reaction time turned out to be 48 h.

TABLE III
Comparison of Heterogeneous AD of Olefins Using Polymeric Cinchona Alkaloids B, C, and D^a

Entry	Olefin	Copolymer						Conf ^d
		B		C		D		
		Yield (%) ^b	ee (%) ^c	Yield (%)	ee (%)	Yield (%)	ee (%)	
1	<i>E</i> -Stilbene	84	94	60	55	60	35	<i>S,S</i>
2	Styrene	80	84	65	54	70	32	<i>S</i>
3	α -Methyl-styrene	82	82	76	48	65	27	<i>S</i>
4	β -Methyl-styrene	78	90	57	56	47	38	<i>S</i>
5	Cyclohexene	60	60	36	32	30	12	<i>S,S</i>

^a Amount of catalyst, 100 mg; OsO₄, 0.3 mL (1%); olefins, 3.0 mmol; temperature, 0°C; reaction time, 72 h.

^b Isolated yields by GC.

^c % ee was determined by chiral OD column.

^d The absolute configuration was determined by the WXG-4 polarimeter.

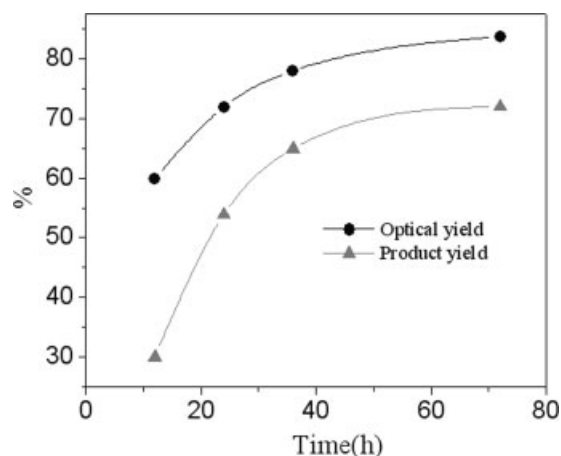


Figure 3 Relationship between the optical yield, product yield, and reaction time (PMMA-BQTP-OsO₄). Amount of catalyst, 100 mg; OsO₄, 0.3 mL (1%); *E*-Stiblene, 3.0 mmol; room temperature.

Effect of OsO₄ amount

Table IV shows the influence of the amount of OsO₄ on the reaction. It can be seen that when the OsO₄ increased, the product yield increased from 76.5 to 80.2% and the optical yield increased from 82.0 to 84.0% ee. It indicated that the asymmetric catalytic activity of PMMA-BQTP increased with increasing amount of OsO₄, but not of the same rate. When the amount of OsO₄ was more than 0.18 mL (1%), the optical yield kept stable.

Effect of catalyst recycling times

To investigate the stability of polymer-OsO₄, its recycling efficiency was tested. The results are shown in Table V. It can be seen that when polymer-OsO₄ complex was reused twice, the optical yield only decreased from 83.7 to 75.4% ee, but the product yield almost did not vary. When the reused times was more than three, the activity or enantioselectivity almost did not decrease.

TABLE IV
Relationship Between the Optical Yield and Amount of OsO₄^a (PMMA-BQTP)

Amount of OsO ₄ (ml)	ee (%)	Product yield (%)
0.05	82.0	76.5
0.11	82.5	77.8
0.13	83.0	79.4
0.18	83.8	79.7
0.33	84.0	80.2

^a Amount of PMMA-BQTP 100 mg; *E*-Stiblene, 3.0 mmol; reaction time, 72 h; room temperature.

TABLE V
Relationship Between Product Yield and Recycling Times (PMMA-BQTP-OsO₄^a)

Recycling numbers	ee (%)	Product yield (%)
1	83.7	80.1
2	75.4	79.6
3	66.2	80.2
4	65.4	78.2
5	66.1	78.5
6	65.3	79.1

^a Amount of catalyst, 100 mg; OsO₄, 0.3 mL (1%); *E*-Stiblene, 3.0 mmol; reaction time, 72 h; room temperature.

CONCLUSION

In conclusion, three chiral copolymers were synthesized and characterized. It was demonstrated that these polymer act as effective asymmetric catalyst for dihydroxylation. The advantage of chiral polymer-OsO₄ complex catalyst is that it is very easy to prepare, and could be used without radical change of optical activity. This kind of catalysts is a potentially important catalyst in asymmetric dihydroxylation. Further studies on the chiral catalytic activity of the complex catalyst with various compositions, as well as the nature of the interaction between OsO₄ and the polymers, are being carried out.

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