Synthesis of Polymeric Chiral Oxazoline and Its Applications on the Asymmetric Induction

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Synopsis

A series of diastereoisomeric amino bicyclo[2,2,1]heptane derivatives was synthesized from (+)-camphor. Further treatment of aminobornanols with triethyl orthopropionate afforded chiral oxazolines, which were found to be efficient for the asymmetric induction of carboxylic acids. Synthesis and polymerization of the new chiral oxazolinebornyl methacrylate derived from aminobornanols was carried out. Effects of temperature, solvents, and molar ratio of the reagent on the polymerization of the linear chiral polymers and the synthesis of the insoluble chiral crosslinked polymers were also discussed. Aminobornanols and chiral polymers with pendant aminobornanol moieties were found to be efficient for the asymmetric induction of chiral methylalkanoic acids. Recovery of the chiral reagents, the stereoselectivity of chiral oxazolines, and the parameters governing its successful implementation and the mechanistic aspects of the processes were also investigated.

INTRODUCTION

Asymmetric reduction of prochiral carbonyl compounds by chiral hydride reagents has been the object of extensive work, and a number of methods have been reported.[1] Most work has been developed based on the use of chiral hydride reagents obtained by reaction of lithium aluminium hydride, sodium borohydride, and chiral ligands such as alkaloids,[2] amino alcohols,[3,4] chiral diols,[5,6] glucofuranose,[7] or chiral amines.[8] By use of chiral hydride reagents prepared from lithium aluminium hydride, (*S*)-(−)-2,2′-dihydroxy-1,1′-binaphthyl, and ethanol, enantiomeric excesses as high as 100% have been observed for the reduction of acetophenone.[9]

On the other hand, during the course of our synthetic investigation using the chiral (+)-camphor derivatives, we have reported convenient and efficient methods for the asymmetric reduction of aromatic ketones and other asymmetric inductions by chiral polymers with pendant chiral diols[10,11] and aminobornanol moieties.[12] This prompted us to study on the exploration of a new and efficient chiral ligand, and a series of diastereoisomeric chiral aminobornanols were synthesized (Schemes 1 and 2). Chiral oxazoline **4** and **12** were synthesized from (+)-camphor. Synthesis and polymerization of the new chiral monomer **13** was carried out. Two percent crosslinked chloromethylated polystyrene was used to derive the insoluble crosslinked chiral polymers with pendant oxazolines (Scheme 3).

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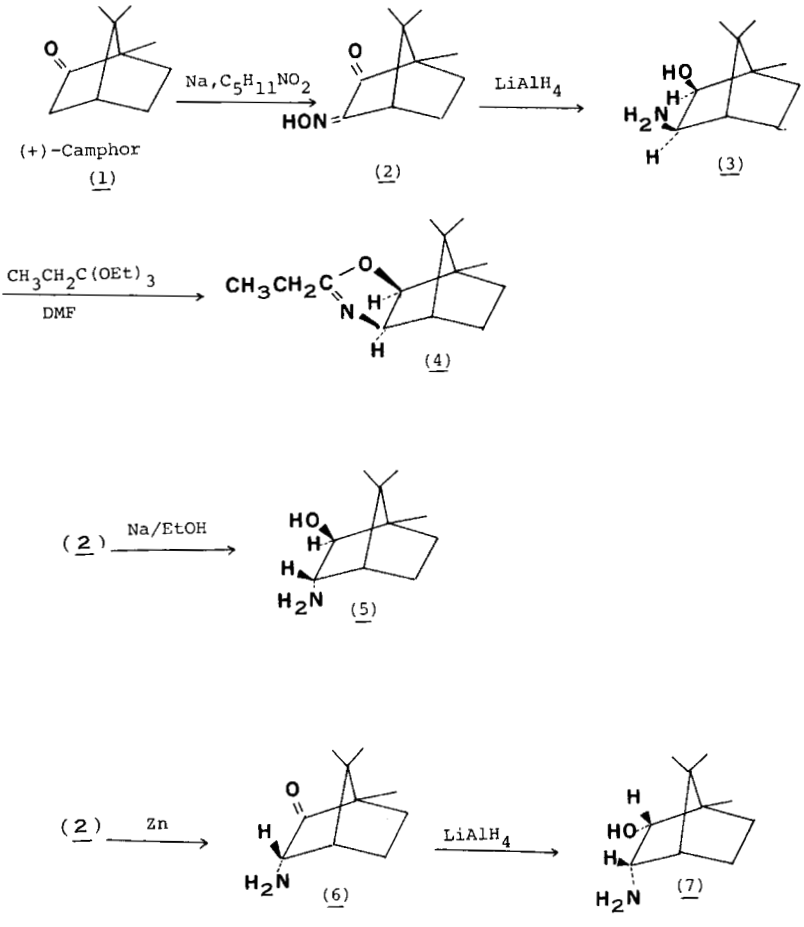
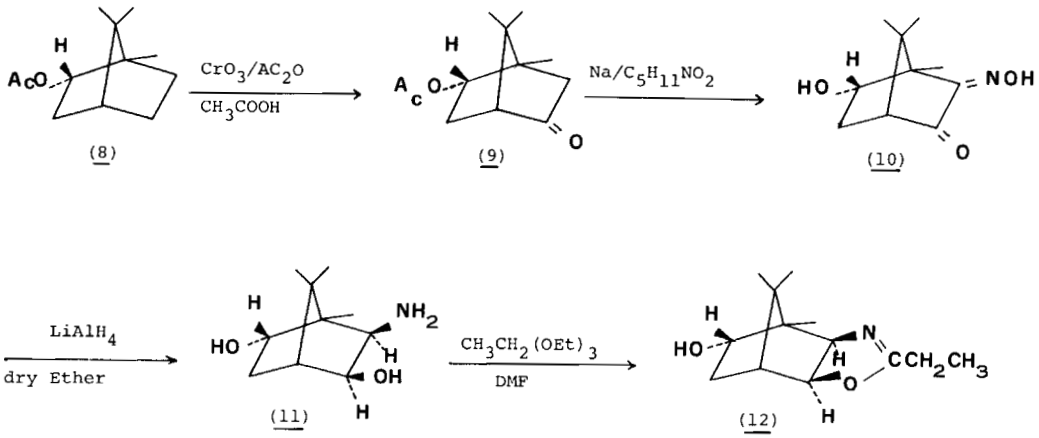
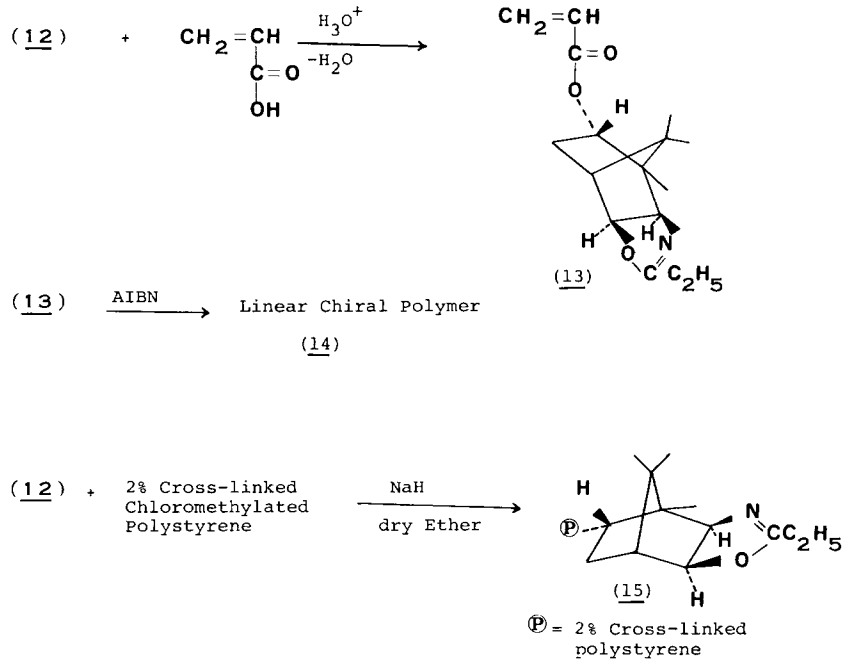


Scheme 1.



Scheme 2.



Scheme 3.

The effects of temperature, solvents, and molar ratio of the reagents on the polymerization of the chiral linear polymers and the synthesis of the insoluble chiral polymers were also discussed. Application of the aminobornanols on the asymmetric induction of methylalkanoic acids was carried out (Scheme 4) and was found to be efficient for the asymmetric synthesis. Recovery of the chiral reagents, the stereoselectivity of chiral oxazolines, and the parameters governing its successful implementation and the mechanistic aspects of the processes were also investigated.

EXPERIMENTAL

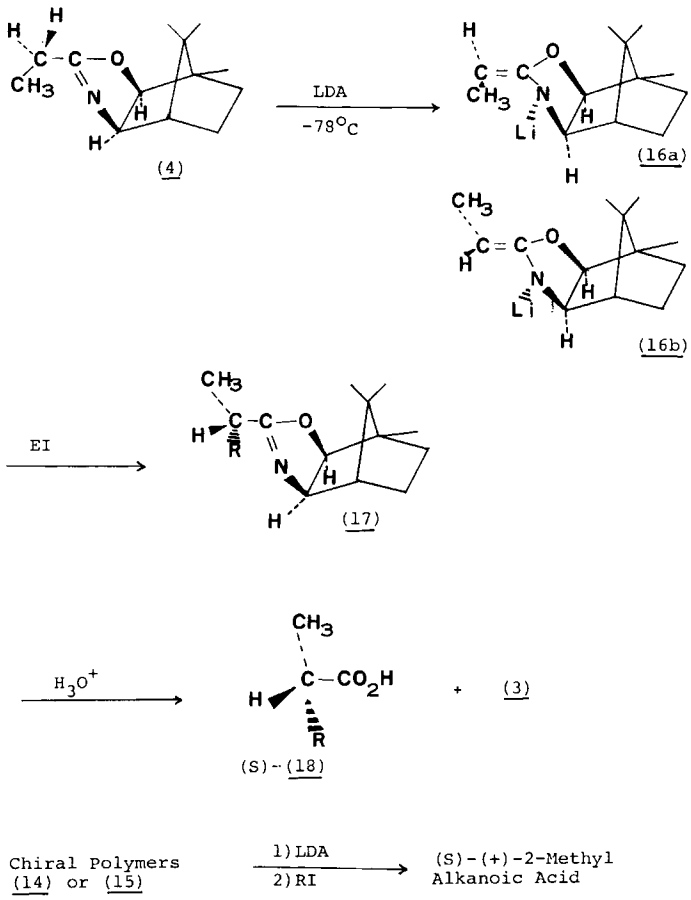
General

Sodium hydride (60 wt % in oil) and chloromethylated polystyrene (6 mmole of Cl/g, crosslinked with 2 mole % of divinyl benzene) used were commercially available ones. Organic solvents were dried over sodium wire. Reactions involving air-sensitive compounds were carried out under an inert gas atmosphere. For the evaporative bulb-to-bulb distillation, a Sibata Tube Oven was used.

Lithium diisopropylamide (LDA) was routinely prepared by adding, at 0°C, 1.0 equiv. of *n*-butyllithium (2.3 *M* in hexane) to 1.05 equiv. of diisopropylamine.

Spectroscopic Measurements

IR spectra were recorded on a Hitachi 260-30 grating IR spectrophotometer, and NMR spectra were recorded on a Bruker-100 ^{1}H-NMR high-resolution



Scheme 4.

NMR spectrometer. Optical rotation was measured with JASCO DIP-360 automatic digital polarimeter. Molecular weight measurements were done at 50°C in tetrachloromethane (CCl_4) solution with a Corona-117.

3-Hydroxyiminobornane-2-One (2)

(+)-Camphor (95 g, 0.62 mol) in dry ether (300 mL) was added to sodium (15.2 g) in an ice-bath. Isoamyl nitrite (78 g, 0.67 mol) was then added dropwise to the stirred solution, the temperature being kept below 5°C. An orange-yellow color was formed during the reaction. After the mixture was stirred for 2 h, water (300 mL) was added carefully. The aqueous layer was extracted with ether to remove unreacted (+)-camphor, then neutralized with acetic acid in an ice-bath to yield a yellow product. The yellow crystalline solid was filtered and then recrystallized from methanol, giving 36 g (0.2 mol) (32%) pure product (**2**); m.p. = 153°C, $[\alpha]_D^{20}$ = 179.1 (c = 0.22, $CHCl_3$):

$C_{10}H_{15}O_2N$(181)	Calc.	C 66.30	H 8.28	N 7.73
	Found	C 66.24	H 8.12	N 7.70

cis,exo-3-Amino-2-Hydroxybornane (3)

3-Hydroxyiminobornan-2-one (**2**) (9.5 g, 52.5 mmol) in dry ether (120 mL) was added dropwise to lithium aluminium hydride (5.5 g, 145 mmol) in dry ether (250 mL). The mixture was heated under reflux for 30 min and then treated with 2 *N* HCl (76 mL). The ether layer was dried over anhydrous magnesium sulfate and evaporated in vacuo to give 7.5 g (42.3 mmol, 80.5%) pure product; m.p. = 200°C (Ref. 13, 198–200°C); IR (neat): 3350 cm^{-1} (OH); 1060, 1100 cm^{-1} (C—N); ^1H NMR ($CDCl_3$): δ = 3.4 (d; 2-H), 0.95 (s; 3 H, 1-CH_3), 1.02 (s; 6 H, 7-CH_3):

$C_{10}H_{19}OH$ (169)	Calc.	C 71.00	H 11.24	N 8.28
	Found	C 70.87	H 11.29	N 8.25

(4*R*, 5*S*)-2-Ethyl-4,5-Bornan-2-Oxazoline (4)

cis,exo-3-Amino-2-hydroxybornane (**3**) (15.7 g, 93 mmol) and triethyl orthopropionate (21 g, 120 mmol) in 40 mL of 1,2-dichloroethane was heated under reflux for 10 h. After the reaction, an orange-yellow solution was formed. The solvent was removed, leaving an oil that was distilled in vacuo to give an oily product (9.72 g, 47 mmol). IR (neat): 1660 cm^{-1} (C=N). ^1H NMR ($CDCl_3$): δ = 0.8–1.02 (m, 9 H, 3 CH_3), 2.1–2.4 (m, 5 H, $CH_3CH_2C{=}N$):

$C_{13}H_{21}ON$ (207)	Calc.	C 75.36	H 10.14	N 6.76
	Found	C 75.42	H 10.10	N 6.74

trans,endo-3-Amino-*exo*-2-Hydroxybornane (5)

Sodium was added to 3-hydroxyiminobornane-2-one (**2**) (6 g, 33.1 mmol) dissolved in absolute ethanol until the solution was saturated. The hot mixture was evaporated on a rotary evaporator to remove all unchanged ethanol and left a yellow-brown solid. This was cooled and treated with dry ether to separate the product (**5**) from the sodium ethoxide. The ether layer was then worked up to yield pure *trans,endo*-3-amino-*exo*-2-hydroxy bornane (**5**) (3 g, 17.8 mmol) m.p. = 193°C from light petroleum (b.p. 60–80°C), ^1H NMR ($CDCl_3$): δ = 6.94 (d, 2-H), 6, 60 (d, 3-H), 8.44 (m, 4-H):

$C_{10}H_{19}ON$ (169)	Calc.	C 71.0	H 11.20	N 8.28
	Found	C 71.17	H 11.32	N 8.25

cis,endo-3-Amino-2-Hydroxybornane (7)

The procedure employed was that reported by Duden and Pritzkow[14] and van Tamelen and Judd[15]; m.p. 170°C (from pentane) (Ref. 15, 172°C). ^1H NMR ($CDCl_3$): δ = 3.63, (d, 2-H), 3.45 (2d, 3-H), 0.95–1.02 (m, 9 H, 3 CH_3):

$C_{10}H_{19}ON$ (169)	Calc.	C 71.0	H 11.24	N 8.28
	Found	C 71.04	H 11.22	N 8.34

5-Oxo-6-Hydroxyiminoborneol (10)

(+)-5-Oxobornyl acetate (**9**) [from (+)-camphor[16]] (18.5 g, 88.1 mmol) in dry ether (150 mL) was added sodium (5.24 g) at 0°C. Isoamyl nitrite (15.13 g, 130 mmol) was then added dropwise to the stirred solution, the temperature being kept below 5°C. After the mixture had been stirred for 4 h, water was added carefully. The precipitate was filtered off and then recrystallized from ether, giving 10.5 g (53.3 mmol) pure 5-oxo-6-hydroxyiminoborneol (**10**) m.p. 191°C (in a sealed tube); IR (neat): 3600 (OH), 1720 (C=O); and 1650 cm^{-1} (C=N):

$C_{10}H_{15}O_3N$ (197)	Calc.	C 60.91	H 7.61	N 7.10
	Found	C 60.75	H 7.67	N 7.06

cis,exo-5-Hydroxy-6-Aminoborneol (11)

5-Oxo-6-hydroxyiminoborneol (**10**) (12 g, 61 mmol) in dry ether (150 mL) was added dropwise to lithium aluminium hydride (4.5 g, 118 mmol) in dry ether (250 mL). The mixture was refluxed for 30 min and then treated with 2 *N* HCl. The ether layer was dried over anhydrous magnesium sulfate and then evaporated in vacuo to give 8.7 g (47 mmol) pure *cis,exo*-5-hydroxy-6-aminoborneol (**11**). ^1H NMR ($CDCL_3$): δ = 2.45 (m, 1 H, 6-*endo*-H), 2.82 (d, 1 H, 5-*endo*-H), 0.95–1.02 (m, 9 H, 3 CH_3).

$C_{10}H_{19}O_2N$ (185)	Calc.	C 64.86	H 10.27	N 7.56
	Found	C 64.82	H 10.24	N 7.61

(4*S*, 5*R*)-2-Ethyl-4,5-Bornyloxazoline (12)

cis,exo-5-Hydroxy-6-aminoborneol (11) (8 g, 43.2 mmol) and triethyl orthopropionate (12 g, 68 mmol) in 40 mL of 1,2-dichloro ethane was heated under reflux for 10 h. After the reaction, the solvent was removed, leaving an oil, and then was distilled in vacuo to give an oily product. The crude product was further purified by column chromatography. Yield, 4.3 g (19.3 mmol, 45%). IR (neat): 3600 cm^{-1} (OH):

$C_{13}H_{21}O_2H$ (223)	Calc.	C 69.95	H 9.42	N 6.28
	Found	C 70.02	H 0.37	N 6.31

(+)-5,6-Oxazolinebornyl Methacrylate (13)

A mixture of (**12**) (10 g, 44.8 mmol), methacrylic acid (6 g, 69.7 mmol) and *p*-toluene sulfonic acid (1.5 g) was heated in 100 mL of benzene under reflux, in the presence of hydroquinone (1.5 g). Water liberated during the reaction was removed by a Dean-Stark apparatus for 20 h. After completion of the reaction, the resulting mixture was washed with dilute aqueous sodium hydrogen carbonate solution and then with water. The oily layer was separated, dried

over anhydrous magnesium sulfate, and distilled in vacuo to yield the product (**13**). IR (neat): 1720 (C=O), 1620 cm^{-1} (C=C), $[\alpha]_D^{20}$ = +68.6 (c = 3.42, $CHCl_3$).

$C_{16}H_{23}O_3N$ (277)	Calc.	C 69.31	H 8.30	N 5.05
	Found	C 69.27	H 8.24	N 5.12

Polymerization of Chiral Monomer (13)

Polymerization of (**13**) was carried out in different solvents at 60°C for 3 h. The monomer, solvent, and AIBN were charged in this order into a polymerization tube, which was degassed in vacuo by freeze-thaw technique and then sealed off. After a polymerization time of 3 h, the tube was opened and the mixture was poured into a large excess of methanol to precipitate the polymer. The crude polymer was purified by reprecipitation using the benzene/methanol system. The conversion was calculated by gravimetry. The results of the polymerization are summarized in Table I.

Preparation of Polymeric Oxazoline (15)

To 5 g (22.4 mmol) of (**12**) in dry THF solution (50 mL) was added an excess amount of sodium hydride at room temperature and then stirred for 15 h. The reaction mixture was then reacted with 3.5 g of chloromethylated polystyrene (6 mmole of Cl/g, crosslinked with 2 mole % of divinyl benzene) at room temperature for over 7 days. After the reaction, the excess amount of sodium hydride remained was decomposed by adding water. The polymer was filtered and washed successively with water, methanol, THF, and THF/water, and again with methanol, and dried at 40°C in vacuo. The mole fraction of substituted benzyl groups in polystyrene was determined by elemental analysis. Results for the preparation of the chiral polymers are shown in Table II.

Asymmetric Synthesis of the Methylalkanoic Acids

Oxazoline was metalated in THF using lithium diisopropylamide (1.05 equiv.) at the indicated temperature and allowed to stir for 30 min. The alkyl iodide

TABLE I
Polymerization of the Chiral Monomer (**13**)[a]

Solvent	Conv. in %	$[\alpha]_D^{20}$[c/(cg m^{-1})][b]	M 10^{-4} [c]	$\bar{P}n$[d]
Benzene	43.0	+68.5 (2.42)	2.47	90
$CHCl_3$	34.2	+70.2 (3.21)	2.86	104
Toluene	38.6	+68.7 (2.58)	2.64	96
THF	57.2	+67.9 (3.46)	2.95	107
THF	72.1	+69.1 (3.21)	3.32	120

[a] At 60°C for 3 h, M = 1.4 mol/dm^3; AIBN = 9.8 mmol/dm^3.
[b] In $CHCl_3$.
[c] At 50°C in CCl_4.
[d] Number-average degree of polymerization.
[e] At 70°C for 4 h.

TABLE II
Synthesis of the Chiral Polymer Containing Oxazolines (**15**)

Entry	Molar ratio[a] (**12**)/PS[b]	Temp. (°C)	Time (days)	Products: Content of (**12**) moieties in mmol/g	Products: Degree of functionalization (%)[d]
1	1 : 1	25	24	3.12	52.0
2	2 : 1	25	14	3.41	56.8
3	4 : 1	25	14	3.27	54.5
4	2 : 1	25	7	2.42	40.3
5	2 : 1	40	14	3.63	60.5
6	2 : 1	50	14	3.72	62.0

[a] Molar ratio of bornyl oxazoline (**12**) to chloromethylated polystyrene in THF.
[b] Chloromethylated polystyrene (6 mmole of Cl/g, with 2 mole % divinyl benzene in the feed).
[c] Calculated from elemental analysis.
[d] Mole fraction of benzyl groups substituted with the chiral oxazoline.

(1.05 equiv.) was added during 15–20 min and the solution maintained at the indicated temperature for 4 h, although the reactions were complete after 30 min. Hydrolysis with 4 *N* HCl solution at 95°C for 3 h gave (*S*)-(+)-2-methylhexanoic acids.

The low molecular model compound can be recovered by distillation in vacuo. Chiral crosslinked polymers can be recovered by simple filtration technique after the reaction. Linear chiral polymers can also be reprecipitated from methanol and then recovered by filtration.

RESULTS AND DISCUSSION

Three diastereoisomers of the aminobicyclo[2,2,1]heptane derivatives were prepared as shown in Scheme 1. The configuration of the aminobornanols was examined by ^{1}H NMR spectroscopy.[13] Isomer (**3**) could be obtained easily and in relatively good yield by reduction of the oxime (**2**) with lithium aluminium hydride. A further treatment of *cis,exo*-3-amino-2-hydroxybornane (**3**) with triethyl orthopropionate afforded a chiral oxazoline, 3-hydroxyiminobornan-2-one (**4**), which was found to be efficient for the asymmetric induction of a chiral carboxylic acid (Scheme 4). We were also able to obtain *trans,endo*-3-amino-*exo*-2-hydroxybornane (**5**) in good yield by the direct reduction of the 3-hydroxyiminobornan-2-one (**2**) with sodium ethanol.

To investigate the catalytic ability of the polymers containing chiral oxazolines to the asymmetric induction, the bornyl oxazoline (**12**) was prepared as shown in Scheme 2. Refluxing of chiral oxazoline (**12**) with methacrylic acid afforded a new chiral monomer (**13**). The free radical polymerization of the chiral monomer (**13**) was carried out in various solvents at different temperature for a certain period. Results of the polymerization are summarized in Table I. The conversion seems to be affected by the kind of solvents. On the other hand, the optical rotation of the resulting polymers does not seem to be influenced by the kind of solvents.

In comparison with the case of the soluble linear chiral polymers, a 2% crosslinked chloromethylated polystyrene was used to prepare an insoluble chiral polymer with pendant oxazolines (Scheme 3). The reaction was carried out under dry inert gas in the presence of an excess amount of sodium hydride. As can be seen from Table II, mole fraction of the substituted benzyl groups in the methylated polystyrene was affected by the amount of the reagent used, reaction temperature, and the reaction time. A higher reaction temperature contributed to a little improvement in the yield (entries 5 and 6), whereas a short reaction time gave only 40.3% yield (entry 4). The high reaction yield was attained up to 62% (entry 6).

The asymmetric synthesis of 2-methylalkanoic acids by chiral oxazoline (**4**) was carried out as shown in Scheme 4. The diastereotopic protons in (**4**) were subjected to abstraction by lithium diisopropyl-amide (LDA) affording the lithio salts (16a or 16b), which were treated at low temperature with several alkyl iodides generating the alkylated oxazolines (**17**) in 85%–92% yield (Table III). Hydrolysis in aqueous hydrochloric acid produced the 2-methylalkanoic acids (**18**) with optical purities of 37%–53%. As shown in Table III, the stereoselectivity of the asymmetric induction was affected by the alkyl iodides. The enantiomeric excess tends to increase with increasing steric requirement of the alkyl group.

The temperature of metalation was of no consequence, as seen by the data in Table IV. Regardless of the temperature at which the proton was removed, the optical yield for (*S*)-(+)-(**18**) was virtually unchanged after butylation and hydrolysis. This result suggests that the proton removal was not involved in the asymmetric induction and the alkylation must be the chiral bond-forming step.

A further study was performed to determine the optical purity of 2-methylhexanoic acid as a function of different alkylation temperatures. The results are given in Table V. From the data, it is apparent that lowering the temperature of alkylation increases the degree of asymmetric induction.

To investigate the catalytic activity of the chiral polymers with pendant aminobornanol derivatives for the asymmetric synthesis of the methylhexanoic

TABLE III
Synthetic and Optical Yield of (*S*)-(+)-2-Methylalkanoic Acids

			Methylalkanoic acids		
RI	%-(*17*)[a]	$[\alpha]_D^{20}$ (c, $CHCl_3$)	Yield (%)[a]	$[\alpha]_D^{20}$ (c, $CHCl_3$)	e.e. %[b]
Et	92	−76.2 (0.24)	72	+6.66 (0.51)	37 (S)[c]
n-Pr	87	−74.3 (0.18)	78	+7.54 (0.23)	41 (S)[d]
n-Bu	89	−68.5 (0.32)	64	+8.41 (0.32)	45 (S)[e]
$PhCH_2$	85	−57.2 (0.31)	53	+12.45 (0.27)	53 (S)[f]

[a] Distilled yields.
[b] Enantiomeric excess.
[c] Based on $[\alpha]_D^{25}$ = +18.0 (neat), Ref. 17.
[d] Based on $[\alpha]_D$ = −18.4 (neat), Ref. 18.
[e] Ref. 18, based on $[\alpha]_D$ = −18.7 (neat).
[f] Based on $[\alpha]_D$ = +23.5 (neat), Ref. 19.

TABLE IV
Effect of Metalation Temperature of (**4**) on the Optical Purity of (*S*)-(+)-2-Methylhexanoic Acid[a]

Entry	Temp. (°C)	$[\alpha]_D^{20}$ (c, $CHCl_3$)	Optical purity (%)[b]	Chemical yield (%)[c]
1	−20	+8.79 (0.12)	47	72
2	−40	+8.41 (0.41)	45	65
3	−60	+8.32 (0.37)	44	71
4	−78	+8.41 (0.32)	45	64
5	−98	+8.60 (0.34)	46	60

[a] In THF for 30 min.
[b] Based on $[\alpha]_D^{20} = -18.7$ (neat), Ref. 18.
[c] Distilled yield.

acid, both linear and crosslinked chiral polymers (**14** and **15**) were used as the asymmetric reagents, and the catalytic activity was compared with that of the low molecular oxazoline (**4**).

The results of the asymmetric synthesis of (*S*)-(+)-2-methylalkanoic acid by chiral polymers (**5**) and (**6**) are summarized in Table VI. As usual, the optical yield seems to be lower when the chiral derivatives is fixed to polymeric carrier, as compared with chiral low molecular model compounds. In case of the chiral polymers, the enantioface differentiation took place effectively by raising the reaction temperature, and the highest enantiomeric excess was achieved at 10°C. This result suggests that the complex is stable at this temperature.

Results obtained in our investigation show that low molecular oxazoline (**4**) and polymeric chiral oxazolines (**14**) and (**15**) are effective for the asymmetric synthesis of methylalkanoic acids. The chiral polymers have the advantage over the low molecular model compounds in that they can be recovered quantitatively by simple filtration technique and could be reused for the further asymmetric induction without causing decrease in enantiomeric excess. The manipulation of the chiral low molecular model compound in the asymmetric synthesis is, however, complicated as compared with that of the polymers, though a higher optical yield can be obtained.

TABLE V
Effect of Butylation Temperature on the Optical Purity of 2-Methylhexanoic Acid[a]

Entry	Temp. (°C)	$[\alpha]_D^{20}$ (c, $CHCl_3$)	Optical purity (%)[b]	Chemical yield (%)[c]
1	−10	+4.67 (0.17)	25	70
2	−20	+5.24 (0.25)	28	74
3	−40	+6.36 (0.46)	34	72
4	−50	+6.92 (0.37)	37	65
5	−78	+8.41 (0.32)	45	64

[a] Treated with LDA at −78°C in THF.
[b] Based on $[\alpha]_D = -18.7$ (neat), Ref. 18.
[c] Distilled yield.
[d] Dry ice-acetone.

TABLE VI
Asymmetric Synthesis of (*S*)-(+)-2-Methylalkanoic Acids by Chiral Polymers Having Aminobornanol Derivatives[a]

Entry	Chiral polymers	RX	Temp. (°C)	Methylalkanoic acids	
				$[\alpha]_D^{20}$ (c, $CHCl_3$)	e.e. %[c]
1	**14**	Et	10	+3.78 (0.54)	21.0[d]
2	**14**	*n*-Pr	10	+6.44 (1.20)	35.0[e]
3	**14**	*n*-Bu	0	+6.92 (0.73)	37.0[f]
4	**14**	*n*-Bu	10	+7.67 (0.45)	41.0
5	**14**	*n*-Bu	20	+5.98 (0.37)	32.0
6	**15**	*n*-Bu	10	+5.05 (0.41)	27.0
7	**15**	*n*-Bu	20	+5.22 (0.53)	28.0
8	**15**	*n*-Bu	30	+3.24 (0.36)	17.3
9	**15**[g]	*n*-Bu	20	+5.25 (0.52)	28.1

[a] Linear chiral polymer (**14**) and 2% crosslinked chiral polymer were used.
[b] Alkylation temperature.
[c] Enantiomeric excess.
[d] Based on $[\alpha]_D^{25} = -18.0$ (neat), Ref. 17.
[e] Based on $[\alpha]_D = -18.4$ (neat), Ref. 18.
[f] Based on $[\alpha]_D = -18.7$ (neat), Ref. 18.
[g] By recovered chiral polymer.

CONCLUSION

Chiral oxazoline bornylmethacrylate derived from aminobornanols was synthesized and polymerized in various organic solvents at different temperatures. Aminobornanol and chiral polymers with pendant aminoboranaol moieties were found to be efficient for the asymmetric induction of chiral methylalkanoic acids. The manipulation of the chiral low molecular model compound in the asymmetric induction is complicated as compared with that of the polymers, though a higher optical yield can be obtained.

In the case of the polymers, the enantiomeric excess was found to increase with increasing reaction temperature, and it seems to reach a maximum at a certain reaction temperature. In the case of the low molecular model compounds, however, the anantiomeric excess appears to increase when lowering the temperature. The chiral polymers can be applied at significantly higher temperature as compared with those chiral low molecular weight compounds. Chiral polymers can be recovered quantitatively by simple filtration and could be reused for the further asymmetric induction without causing decrease in enantiomeric excess.

The proton removal by lithium diisopropyl amide does not seem to be involved in the asymmetric induction, and the alkylation must be the chiral bond-forming step.

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