

Chiral Recognition Abilities of New Optically Active Polyurethanes Derived from Chiral 1,3-Diols and Diisocyanates

Tohru KOBAYASHI,[†] Masa-aki KAKIMOTO*, and Yoshio IMAI*

*Takasago International Corporation, Kamata, Ohta-ku,
Tokyo 144, Japan*

**Department of Organic and Polymeric Materials,
Tokyo Institute of Technology, Ookayama,
Meguro-ku, Tokyo 152, Japan*

(Received March 4, 1993)

ABSTRACT: Optically active polyurethanes were synthesized by the polyaddition of (1*S*,3*S*)-diphenylpropanediol or (2*R*,4*R*)-pentanediol to various diisocyanates at 100°C in anisole or dimethyl sulfoxide. The obtained polyurethanes were applied to the stationary phase of high performance liquid chromatography to separate chiral compounds. The polyurethanes derived from (1*S*,3*S*)-diphenylpropanediol and aliphatic diisocyanates resolved several pairs of enantiomers of 2,2'-dihydroxy-1,1'-dinaphthyl derivatives, while those from aromatic diisocyanates showed only poor chiral recognition abilities. The wide angle X-ray diffraction studies revealed that the chiral recognition abilities were dependent on crystallinity of the polymers.

KEY WORDS Optically Active Polyurethanes / Polyadditions / Chiral 1,3-Diols / Chiral Recognition Abilities / Optical Resolution / Chiral Stationary Phase /

Resolution of racemic compounds using chiral stationary phases in high performance liquid chromatography (HPLC) is a very useful technique for both analysis of enantiomeric purity and preparation of enantiomerically pure compounds.¹ Polymeric materials such as polypeptides,² modified cellulose,³ modified amylose,⁴ polyamide derived from anti head-to-head coumarin dimer,⁵ poly(triarylmethyl methacrylate),⁶ and polyamide having 1,1'-binaphthalene-2,2'-dicarboxylic acid component⁷ have been reported as chiral stationary phases. Recently, optically active polyurethanes containing coumarin dimer component were synthesized and applied to chiral stationary phase by Chen and Lin.⁸ In most cases, however, the sources of optically active units came from naturally occurring compounds, or were obtained by the resolution of

racemates. The preparation of optically active monomers by asymmetric synthesis should be more powerful way because a variety of new types of intermediates could be obtained in both antipodes. In this article, we report the synthesis of optically active polyurethanes by the polyaddition of chiral 1,3-diols, prepared by the ruthenium-(2,2'-bis(diphenylphosphino)-1,1'-dinaphthyl) (BINAP) catalyzed asymmetric hydrogenations⁹ to various diisocyanates and its application to chiral stationary phases for HPLC.

EXPERIMENTAL

Materials

(1*S*,3*S*)-Diphenylpropanediol (>99% *e.e.*) **1a** and (2*R*,4*R*)-pentanediol **1b** (>99% *e.e.*) were prepared by the ruthenium-(*R*) BINAP

[†] To whom correspondence should be addressed.

catalyzed asymmetric hydrogenation of the corresponding β -diketones.⁹ *p*-Phenylene diisocyanate **IIa** (supplied by Tonen Sekiyukagaku Co., Inc.) and commercially available diisocyanates such as 4,4'-di(isocyanatophenyl)methane **IIb**, 1,6-diisocyanatohexane **IIc** and 1,4-diisocyanatobutane **IIg** were distilled *in vacuo* before use. The other diisocyanates were synthesized by the Curtius rearrangement of the corresponding diacyl azides.¹⁰ Macroporous spherical silica gel (LiChrospher Si 1000) was purchased from Merck Co. Its mean particle size, mean pore diameter, and mean specific surface area were 10 μm , 100 nm, and 20 $\text{m}^2 \text{g}^{-1}$, respectively. Di-*n*-butyltin dilaurate was used without purification. 2,2'-Dihydroxy-1,1'-dinaphthyl **Va** was used as received. 6,6'-Dibromo-2,2'-dihydroxy-1,1'-dinaphthyl **Vb**, 2,2'-dihydroxy-5,5',6,6',7,7',8,8'-octahydro-1,1'-dinaphthyl **Vc**, and 3,3'-dibromo-2,2'-dihydroxy-5,5',6,6',7,7',8,8'-octahydro-1,1'-dinaphthyl **Vd** were synthesized from **Va**.¹¹ Dimethyl sulfoxide (DMSO) and anisole were purified by distillation over calcium hydride and sodium metal, respectively.

Measurements

IR spectra were recorded on a Shimadzu DR-8000 spectrophotometer. ¹H NMR spectra were measured on a Bruker AMX 400 spectrometer, and chemical shifts are quoted in ppm. Optical rotation measurements were obtained on a JASCO DIP-360 spectrometer. Differential scanning calorimetry (DSC) was performed with a Shimadzu thermal analyzer DSC-41M and measurements were run at a heating rate of 10°C min⁻¹ under nitrogen at a flow rate of 50 ml min⁻¹. Wide angle X-ray diffraction patterns were obtained at room temperature on a Rigakudenki RU-200 apparatus with nickel-filtered Cu-K α radiation (50 kV, 180 mA). HPLC chromatograms were obtained with a Shimadzu LC-9A chromatograph equipped with a UV detector (Shimadzu SPD-6A, peaks were detected at 254 nm).

Polymerization

A typical polymerization is described as follows.

Polyurethane IIIc. A mixture of **Ia** (2.66 g, 11.7 mmol), **IIc** (2.21 g, 11.7 mmol) and a catalytic amount of di-*n*-butyltin dilaurate (2 drops) in 30 ml of anisole were stirred at 100°C for 1.5 h under nitrogen. After the solution was cooled to room temperature, the reaction mixture was poured into methanol (200 ml). The precipitated polymer was collected by filtration, washed thoroughly with methanol, and dried *in vacuo*. The yield of the polymer was 3.41 g (71%). The inherent viscosity was 0.18 dl g⁻¹, measured at a concentration of 0.5 g dl⁻¹ in *m*-cresol at 30°C.

$[\alpha]_D^{25} - 10.4^\circ$ (*c* 0.10, DMSO).

IR (KBr); 3330, 2931, 2856, 1710, 1530, 1456, 1251, 1138, 1060, 1021, 699 cm⁻¹.

¹H NMR (DMSO-*d*₆); 1.10—1.30 (br s, 6H), 1.30—1.48 (br s, 4H), 2.20 (t, *J* = 6.7 Hz, 2H), 2.80—3.05 (br s, 4H), 5.55—5.68 (m, 2H), 6.85—7.05 (br s, 2H), 7.15—7.35 (m, 10H).

Anal. Calcd for C₂₄H₃₀N₂O₄: C, 70.22%; H, 7.37%; N, 6.82%. Found: C, 69.78%; H, 7.40%; N, 6.83%.

The other polyurethanes were synthesized by the similar procedures (Table I).

Preparation of Chiral Stationary Phase

In a flask, 10 g of macroporous spherical silica gel particles was treated with 5 ml of diphenyldimethoxysilane in 50 ml of refluxing toluene for 8 hours. After cooling to room temperature, the silylated silica gel was isolated by filtration, washed with dichloromethane, and dried *in vacuo*. The polyurethane (0.8 g) was dissolved in 8 ml of *N,N*-dimethylacetamide (DMAc). To 3.2 g of solid silica gel was added dropwise about one-tenth of the above polyurethane solution and then DMAc was removed *in vacuo*. Until all the polymer solution was added, these procedures were repeated. To the polymer-coated silica gel thus obtained was added 70 ml of methanol and packed into a stainless steel column (25 cm long

and 0.46 cm diameter) under a constant pressure of 100 kg cm^{-2} by a slurry method. Chromatograms were obtained at room temperature using a mixture of hexane and 2-propanol ($v/v=9/1$) as an eluent.

RESULTS AND DISCUSSION

Polymer Synthesis

Optically active polyurethanes **III** were synthesized by the polyaddition of chiral

1,3-diols **I** to diisocyanates **II** in anisole or DMSO as shown in eq 1. Di-*n*-butyltin dilaurate was used as a catalyst in some cases.

The results of preparation of the polymer are summarized in Table I. The yields and inherent viscosities of all the polyurethanes were 17–86% and $0.05\text{--}0.60 \text{ dl g}^{-1}$, respectively. The yields and viscosity values of the resulting polyurethanes were relatively low because of poor reactivity of the hindered secondary alcohols and instability of some

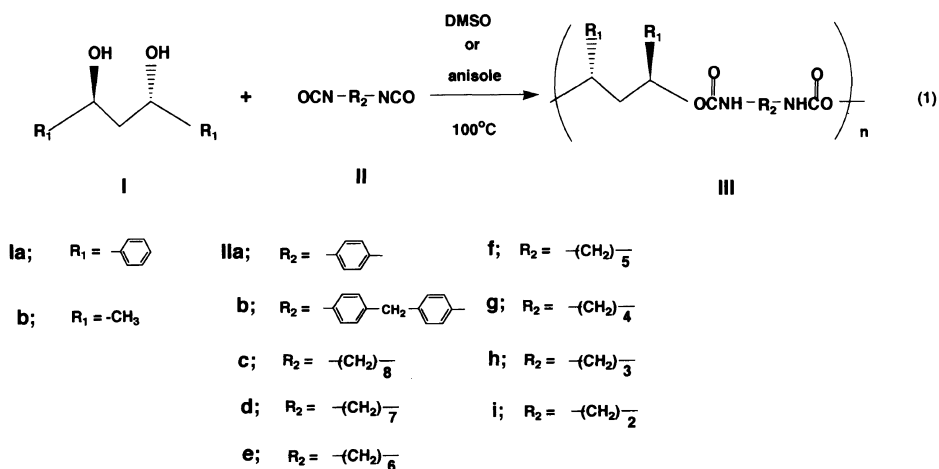


Table I. Synthesis of optically active polyurethanes

Monomers			Polymer		
Diol	Diisocyanate	Condition ^a	Code	Yield	η_{inh}^b
				%	dl g^{-1}
Ia	IIa	A	IIIa	80	0.13 ^c
Ia	IIb	A	IIIb	85	0.23 ^c
Ia	IIc	B	IIIc	83	0.15
Ia	IId	C	IIIId	71	0.18
Ia	IIe	B	IIIe	83	0.20
Ia	IIf	C	IIIIf	65	0.28
Ia	IIg	C	IIIg	67	0.18
Ia	IIh	C	IIIh	57	0.15
Ia	IIIi	C	IIIi	17	0.05
Ib	IIe	B	IIIj	86	0.60

^a The polyurethane was synthesized A) in DMSO in the absence of catalyst, B) in anisole in the absence of catalyst, and C) in anisole in the presence of a catalytic amount of di-*n*-butyltin dilaurate.

^b Measured at a concentration of 0.5 g dl^{-1} in *m*-cresol at 30°C .

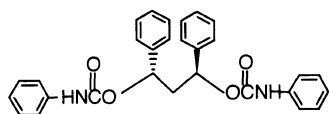
^c Measured at a concentration of 0.5 g dl^{-1} in DMAc at 30°C .

diisocyanates.

Polymer Characterization

The present polyurethanes were soluble in aprotic polar solvents such as DMAc, *N*-methylpyrrolidone, and DMSO. Table II summarizes the optical rotation values and melting points (T_m) of the polymers. The

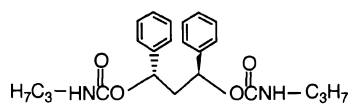
optical rotation values were in the range from -10.4° to -80.6° . We also synthesized **IVa**, **IVh**, **IVi**, and **IVj** as model compounds for polymer **IIIa**, **IIIh**, **IIIi**, and **IIIj**, respectively. The specific rotations of four model compounds were comparable to those of the corresponding polyurethanes.



IVa

$[\alpha]_D^{25} -41.8^\circ$ (c 0.11, CHCl_3)

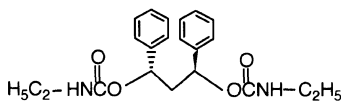
mp 194-196°C



IVh

$[\alpha]_D^{25} -10.0^\circ$ (c 0.10, CHCl_3)

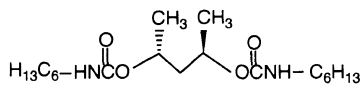
mp 146-147°C



IVi

$[\alpha]_D^{25} -10.0^\circ$ (c 0.11, CHCl_3)

mp 156-158°C



IVj

$[\alpha]_D^{25} -49.0^\circ$ (c 0.10, CHCl_3)

mp 118-119°C

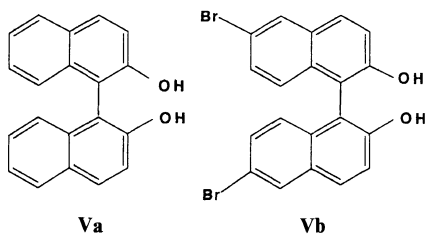
Compound **IVa**, **IVh**, **IVi**, and **IVj**

The endotherms due to melting points of the polymers were observed by the DSC measurements in case of the polyurethanes from aliphatic diisocyanates, while the polyurethanes from aromatic diisocyanates showed no melting points.

Chiral Recognition Abilities of Polyurethanes

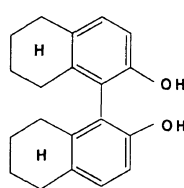
The chiral recognition abilities of these

polyurethanes were investigated by using them as chiral stationary phases of HPLC. As racemates to be resolved, we chose 2,2'-dihydroxy-1,1'-dinaphthyl derivatives **V** which are, once resolved, very important class of compounds for chiral crown ethers^{11,12} and chiral ligands of metals for asymmetric reactions.¹³



Va

Vb



Vc

Vd

Table II. Optical rotation values and melting points of polyurethanes

Polymer	IIIa	IIIb	IIIc	III d	IIIe	III f	IIIg	IIIh	IIIi	IIIj
$[\alpha]_D^a$ (degree)	-35.7	-71.6	-10.8	-10.4	-14.7	-13.4	-12.0	-12.9	-21.5	-80.6
T_m^b (°C)	— ^c	— ^c	173	163	148 ^d	215	228	223	232	214

^a Measured in DMSO at 25°C.

^b Determined by DSC in nitrogen at a heating rate of 10°C min⁻¹.

^c No endotherms were observed.

^d An exothermic peak was observed just after this endothermic peak.

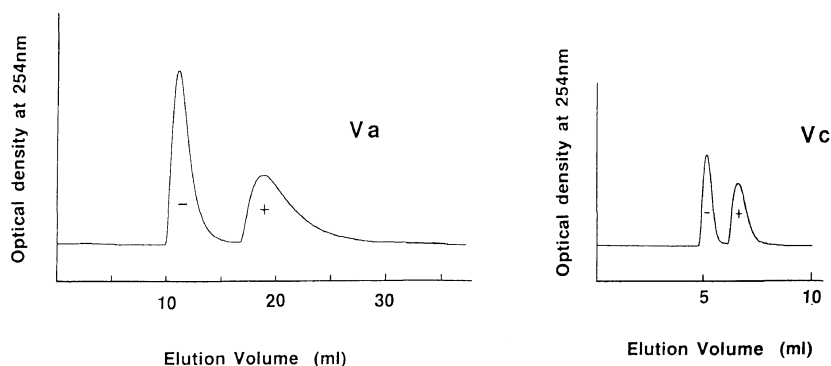


Figure 1. Chromatographic resolution of **Va** and **Vc** on the columns of **IIIg** and **IIIi**, respectively.

The chiral recognition abilities were evaluated by k_1' , α , and R_s .

$$k_1' = V_1/V_0, \quad \alpha = k_2'/k_1',$$

$$R_s = 2 \times (V_2 - V_1)/(W_1 + W_2)$$

k_1' , capacity factor for less retained enantiomer; k_2' , that for more retained enantiomer; V_1 , retention volume of less retained enantiomer; V_2 , that for more retained enantiomer; V_0 , dead volume; α , separation factor; R_s ; resolution factor; W_1 , band width of first peak; W_2 ; band width of second peak.

Figure 1 shows the examples of chromatographic resolutions of **Va** and **Vc** on the columns bearing polyurethanes **IIIg** and **IIIi**, respectively. The results of the resolution were summarized in Table III. Polyurethane **IIIa** derived from **Ia** and *p*-phenylene diisocyanate **IIa** showed chiral recognition abilities to **Va** and **Vb**, but did not resolve **Vc** nor **Vd**, which

have flexible octahydronaphthalene rings. Polyurethane **IIIb** synthesized from **Ia** and 4,4'-di(isocyanatophenyl)methane **IIb** showed chiral recognition abilities only to **Vb**, which is rather large racemate. In contrast, almost all the polyurethanes prepared from **Ia** and aliphatic diisocyanates resolved these four pairs of racemates. It is interesting to note that the polyurethanes with small methylene units (**IIIg**, **IIIh**, and **IIIi**) gave better results compared with those possessing long methylene units (**IIIc** and **III d**). These results could be explained by the densities of optically active carbon in the repeating units of the polymers.

Figure 2 shows the wide angle X-ray diffraction patterns of the polymers. The results revealed that polymers **IIIa** and **IIIb**, which showed poor chiral recognition abilities, were amorphous, whereas polyurethanes **IIIc–IIIi** derived from **Ia** and aliphatic diisocyanates were crystalline.

Table III. Chromatographic resolutions of 2,2'-dihydroxy-1,1'-dinaphthyl derivatives **V** by optically active polyurethanes^a

Polymer	Racemates											
	Va ^b			Vb ^b			Vc ^c			Vd ^c		
	k_1'	α	R_s	k_1'	α	R_s	k_1'	α	R_s	k_1'	α	R_s
IIIa	0.75	1.21	0.42	0.72	1.35	0.43	0.32	1	—	0.40	1	—
IIIb	1.03	1	—	0.79	1.29	0.38	0.25	1	—	0.30	1	—
IIIc	2.47	1.23	0.71	3.58	1.28	0.70	0.85	1	—	1.04	1	—
III d	2.48	1.29	0.88	3.45	1.37	0.86	0.57	1.31	0.61	0.67	1.25	0.47
IIIe	3.46	1.34	0.76	3.66	1.44	1.12	0.52	1.37	0.69	0.70	1.27	0.56
III f	2.48	1.61	1.23	3.48	1.72	1.32	0.55	1.73	1.36	0.44	1.17	0.31
III g	2.39	1.98	1.52	3.32	2.34	1.69	0.55	1.61	1.00	0.67	1.30	0.63
III h	1.59	1.89	1.30	2.37	2.55	1.40	0.43	1.65	1.14	0.38	1.31	0.33
III i	1.39	1.60	1.11	1.73	1.91	1.55	0.32	2.16	1.50	0.34	2.02	1.28
III j	0.79	1	—	1.32	1	—	0.33	1	—	0.36	1	—

^a Hexane/2-propanol (v/v=9/1) was used as an eluent.

^b Flow rates were 1.0 ml min⁻¹.

^c Flow rates were 0.5 ml min⁻¹.

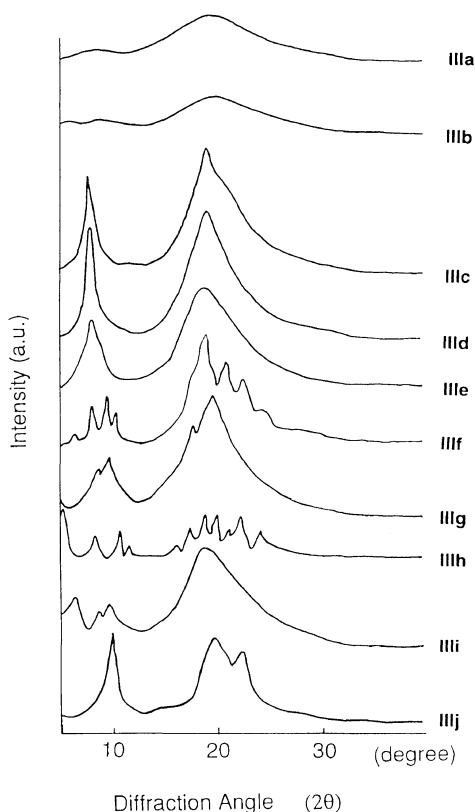


Figure 2. Wide angle X-ray diffraction profiles of polyurethanes **III**.

The better resolution abilities of the polyurethanes from aliphatic diisocyanates rather than those from aromatic diisocyanates could be explained by the assumption that the functional groups in a regular conformation in the crystalline part give a regular interaction between polyurethanes and 2,2'-dihydroxy-1,1'-dinaphthyl derivatives, as observed in optically active polyamides.⁵ Hydrogen bond interaction between functional groups of the polyurethanes and hydroxyl groups of 2,2'-dihydroxy-1,1'-dinaphthyl derivatives seems to be responsible for the resolution, because dimethyl ether of 2,2'-dihydroxy-1,1'-dinaphthyl could not be resolved by any columns prepared in this series. The polyurethanes derived from (2*R*,4*R*)-pentanediol **Ib** and 1,6-diisocyanatohexane **IIf** could not resolve any racemates even though it had some degree of crystallinity. This result suggested that π - π interaction between the polymers and the racemates was also important for the resolution.

CONCLUSIONS

The optically active polyurethanes from the

chiral 1,3-diols and various diisocyanates were successfully prepared. The polyurethanes from **Ia** and aliphatic diisocyanates showed good chiral recognition abilities to 2,2'-dihydroxy-1,1'-dinaphthyl derivatives, while both the polyurethanes from aromatic diisocyanates and the polyurethane from **Ib** and **Ile** gave poor results. Hydrogen bond interaction between polymer functional groups and hydroxyl groups of 2,2'-dihydroxy-1,1'-dinaphthyl derivatives is responsible for the resolution. The chiral recognition abilities of the polymers were dependent on existence of crystallinity.

REFERENCES

1. a) S. G. Allenmark, *Chromatographic Enantioseparation. Methods and Applications*, John Wiley and Sons, New York, 1988. b) Y. Okamoto, *Chemtec*, 176 (1987).
2. a) G. Blaschke, *Angew. Chem., Int. Ed. Engl.*, **19**, 13 (1980). b) G. Blaschke, W. Broker, and W. Fraenkel, *ibid.*, **25**, 830 (1986).
3. a) A. Ichida, T. Shibata, I. Okamoto, Y. Yuki, H. Namikoshi, and Y. Toga, *Chromatographia*, **19**, 280 (1984). b) Y. Okamoto, M. Kawashima, and K. Hanada, *J. Am. Chem. Soc.*, **106**, 5357 (1984).
4. Y. Okamoto, R. Aburatani, T. Fukumoto, and K. Hanada, *Chem. Lett.*, 1857 (1987).
5. K. Saigo, T. Shiwaku, K. Hayashi, K. Fujioka, M. Sukegawa, Y. Chen, N. Yonezawa, M. Hasegawa, and T. Hashimoto, *Macromolecules*, **23**, 2830 (1990).
6. Y. Okamoto, S. Honda, I. Okamoto, H. Yuki, S. Murata, R. Noyori, and H. Takaya, *J. Am. Chem. Soc.*, **103**, 6971 (1981).
7. Y. Tamai, Y. Matsuzaka, S. Oi, and S. Miyano, *Bull. Chem. Soc. Jpn.*, **64**, 2260 (1991).
8. Y. Chen, and J-J. Lin, *J. Polym. Sci., Polym. Chem. Ed.*, **30**, 2699 (1992).
9. M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, and R. Noyori, *J. Am. Chem. Soc.*, **110**, 629 (1988).
10. Y. Iwakura, K. Uno, and K. Hayashi, "Jushukugo to Jufuka," S. Kambara, Ed., Kyoritu, Tokyo, 1958, p 140.
11. D. J. Cram, R. C. Helgeson, S. C. Peacock, L. J. Kaplan, L. A. Domeier, P. Moreau, J. M. Mayer, Y. Chao, M. G. Siegel, D. H. Hoffman, and G. D. Y. Sogah, *J. Org. Chem.*, **43**, 1930 (1978).
12. D. S. Lingenfelter, R. C. Helgeson, and D. J. Cram, *J. Org. Chem.*, **46**, 393 (1981).
13. K. Mikami, M. Terada, and T. Nakai, *J. Am. Chem. Soc.*, **112**, 3949 (1990).