

NOTES

Chromatographic Resolution of Enantiomers by High Performance Liquid Chromatography Chiral Stationary Phase Composed of Optically Active Polyurethanes

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

*Central Research Laboratory, Takasago International Corporation,
Hiratsuka, Kanagawa 254, Japan*

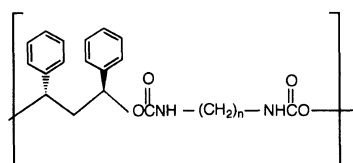
** Department of Organic and Polymeric Materials,
Tokyo Institute of Technology, Meguro-ku, Tokyo 152, Japan*

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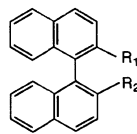
The optical resolution of racemic compounds using chiral stationary phases in high performance liquid chromatography (HPLC) is an important technique for analysis of enantiomeric purity and separation of enantiomerically pure compounds.^{1,2} The previous paper reported the preparation of

optically active polyurethanes from (1*S*,3*S*)-diphenylpropane-1,3-diol and various diisocyanates.³ A preliminary experiment was also demonstrated in their chiral recognition abilities to 2,2'-dihydroxy-1,1'-binaphthalene derivatives using HPLC technique, and it was found that a shorter methylene unit of



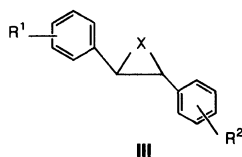
Ia : n=3

Ib : n=2



II

	R ¹	R ²
a	OH	OH
b	OH	OCH ₃
c	OCH ₃	OCH ₃



III

	R ¹	R ²	X
a	H	H	O
b	<i>p</i> -Me	H	O
c	<i>p</i> -Et	H	O
d	<i>p</i> -iPr	H	O
e	<i>m</i> -Me	H	O
f	<i>p</i> -Me	<i>p</i> -Me	O
g	<i>m</i> -Me	<i>m</i> -Me	O
h	<i>p</i> -Cl	H	O
i	<i>p</i> -F	H	O
j	H	H	S

[†] To whom correspondence should be addressed.

polyurethanes gave better optical resolution.

Hydrogen bonds between the stationary phase and substrate should play an important role in chiral recognition. Thus, substrates possessing acidic hydrogen such as binaphthols are more readily separated. In this paper, 1,1'-binaphthalenes **II** with different numbers of acidic hydrogen and *trans*-stilbene oxides **III** which can make hydrogen bond with acidic hydrogen were applied as substrates for chiral separation using optically active polyurethanes **I** with two and three methylene units as the stationary phase.

EXPERIMENTAL

Polyurethanes **Ia** and **Ib** were synthesized from (1*S*,3*S*)-diphenylpropane-1,3-diol and 1,3-diisocyanatopropane and 1,2-diisocyanatoethane, respectively.³ Inherent viscosities of **Ia** and **Ib** were 0.15 dl g⁻¹ and 0.05 dl g⁻¹, measured at a concentration of 0.5 g dl⁻¹ in *m*-cresol at 30°C. The stationary phases of HPLC were prepared from polymer-coated silica gel (polymer, 20 wt%) and packed into a stainless steel column (25 × 0.46 (i.d.) cm) by the slurry method.³ The plate numbers of the columns bearing **Ia** and **Ib** for 1,3,5-tri-*tert*-butylbenzene were about 680 and 420, respectively, with hexane-2-propanol (9:1, v/v; 1.0 ml min⁻¹) as the eluent. Dead volumes (V_0) of the columns bearing **Ia** and **Ib** were 4.26 ml and 3.48 ml, respectively, as estimated with 1,3,5-tri-*tert*-butylbenzene.

2-Hydroxy-2'-methoxy-1,1'-binaphthalene **IIb** and 2,2'-dimethoxy-1,1'-binaphthalene **IIc** were prepared from 2,2'-dihydroxy-1,1'-binaphthalene **IIa** with iodomethane and potassium carbonate in acetone. All *trans*-stilbene oxides except **IIIa** and **IIIj** were synthesized by epoxidation of the corresponding *trans*-stilbenes with *m*-chloroperbenzoic acid. Compound **IIIj** was derived from **IIIa** as described in the literature.⁴

RESULTS AND DISCUSSION

Table I shows chiral recognition abilities of polyurethanes **Ia** and **Ib** to three binaphthalene derivatives **IIa—IIc** having different numbers of acidic hydrogens. The column coated with **Ia** resolved only **IIa** which had two acidic hydrogens, while **IIb** could separate **IIa** and **IIb**. Dimethoxy substituted binaphthalene **IIc**, having no acidic hydrogen, could not be resolved even by **Ib**. The number of hydroxyl groups greatly influenced the efficiency of chiral resolution. Although such difference in chiral recognition ability between **Ia** and **Ib** is not clearly understood, the packing of polyurethanes in crystalline region seems to decide the difference.

Chiral *trans*-stilbene oxides **III** are useful intermediates for some organic compounds. If acidic hydrogens in the substrates are required for the chiral separation using **I**, it must be difficult to separate **III** possessing no acidic hydrogen. To prove this hypothesis, we synthesized several *trans*-stilbene oxide derivatives and checked in detail chiral recognition abilities of **Ib** to them. The chromatographic separation of **IIIa** by the column bearing **Ib** is illustrated in Figure 1, and it was concluded that **IIIa** could be separated by the column coated with **Ib**. The results of resolution of **III**

Table I. Resolution of enantiomers **IIa, b, c** on Polyurethane **Ia** or **Ib** coated silica gel column^a

Racemates	Polyurethane Ia			Polyurethane Ib		
	k_1^b	α^c	R_s^d	k_1^b	α^c	R_s^d
IIa	1.59	1.89	1.30	1.39	1.60	1.11
IIb	1.08	1	—	1.28	1.18	0.40
IIc	0.42	1	—	0.47	1	—

^a Eluent hexane-2-propanol (9:1, v/v); flow rate 1.0 ml min⁻¹.

^b Capacity factor for less retained enantiomer = (retention volume - dead volume)/dead volume.

^c Separation factor = (capacity factor for more retained enantiomer)/ k_1 .

^d Resolution factor = 2 × (distance of the two peak position)/(sum of band-widths of the two peaks).

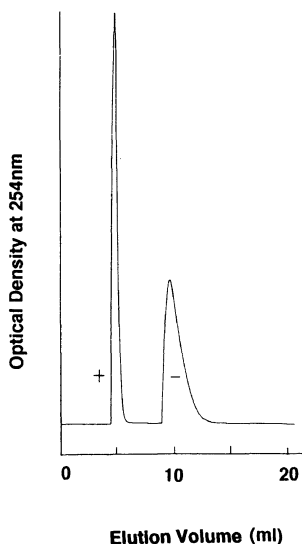


Figure 1. Optical resolution of *trans*-stilbene oxide **IIIa** on a column bearing **Ib**. Eluent, hexane-2-propanol = 9 : 1 (v/v); flow rate, 1.0 ml min⁻¹.

by **Ib** are summarized in Table II.

With increasing bulkiness of substituents on the *para*-position of phenyl rings of **III** in the order of **IIIa**, **IIIb**, **IIIc**, and **IIId**, the separation factor α and resolution factor R_s decreased. The efficiency of separation decreased in the case of *meta*-substituents of phenyl rings (**IIIe** and **IIIg**). Since *trans*-stilbene oxide **III** have no acidic hydrogen, the mechanism of separation for **III** should be different from that for **IIa** and **IIb**. It seems that stereoselective hydrogen bonding interactions between **Ib** and hydrogen accepting molecule **III** play important roles in chiral recognition. When the phenyl rings of **III** were substituted by alkyl groups, hydrogen bonding interactions should be restricted because of steric hinderance. A big difference of the chiral recognition ability was observed for **IIIh** and **IIIi**. Strong hydrogen bonding between fluorine atom of **IIIi** and

Table II. Resolution of *trans*-stilbene oxide derivatives **III** on polyurethane **Ib** coated silica gel column^a

Racemates	k'_1	α	R_s
IIIa	0.51	4.28	3.10
IIIb	1.01	3.04	2.78
IIIc	0.59	1.99	1.26
IIId	0.30	1	—
IIIe	0.23	1.69	0.71
IIIf	1.92	1.33	0.63
IIIg	0.20	1	—
IIIh^b	1.79	3.58	2.86
IIIi	1.54	1	—
IIIj	0.19	1	—

^a Eluent hexane-2-propanol (9 : 1, v/v); flow rate, 1.0 ml min⁻¹, unless otherwise noted.

^b Eluent hexane-2-propanol (5 : 1, v/v); flow rate, 3.0 ml min⁻¹.

the urethane group of **Ib** seems to prevent hydrogen bonding between oxygen of **IIIi** and **Ib** for the chiral recognition. *trans*-Stilbene sulfide **IIIj** could not be resolved by this column because of poor hydrogen bonding ability of sulfur atoms with urethane function of **Ib**.

Hydrogen donating racemates **II** and accepting racemates **III** were successfully resolved by the column bearing polyurethane **Ib**. The present results indicate that regular hydrogen bonding interactions between **Ib** and racemates are essential for efficient separation.

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