Synthesis of Optically Active Polyamides Having Axially Dissymmetric 1,1′-Binaphthalene-2,2′-dicarboxylic Acid Component and Their Optical Resolution Ability as Chiral Adsorbent for HPLC

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Optically active polyamides **4a**—**4c** were synthesized from the polycondensation of axially dissymmetric 1,1′-binaphthalene-2,2′-dicarbonyl dichloride (**2**) with 1,4-benzenediamine, 1,6-hexanediamine, and 1,10-decanediamine, respectively. CD spectra of the polyamides **4a**—**4c** are essentially the same as those of the corresponding model diamides **6a**—**6c** prepared from **2** and benzenamine, 1-hexanamine, and 1-decanamine, respectively. This similarity indicates that the conformation of the 1,1′-binaphthalene-2,2′-dicarboxamide moieties of the polyamides **4a**—**4c** in solution state are rather similar to those of the corresponding model diamides **6a**—**6c**. Several axially chiral biaryl compounds and 3,5-dinitrophenylcarbamates (3,5-DNPCs) derived from 1-aryl-1-alkanols were resolved by HPLC equipped with the columns packed the chiral stationary phases (CSPs) prepared from **4a**—**4c** adsorbed on spherical silica gel. A main control factor for the chiral discrimination seems to be the hydrogen bonding between the amide groups of the CSPs and the hydrogen-bonding sites of the atropisomeric biaryls. The donor–acceptor interaction between the binaphthalene moiety of the CSPs and the 3,5-dinitrobenzene moiety of the 3,5-DNPCs may also be important for the chiral discrimination of the 3,5-DNPCs.

A wide variety of polymeric chiral stationary phases (CSPs) have recently been developed for the separation of enantiomers by means of high-performance liquid chromatography (HPLC).[1] Some kinds of optically active polyamides have been reported to show the chiral recognition ability as the chiral adsorbents for the CSPs.[2] It is well-known that axially dissymmetric 1,1′-binaphthalene derivatives serve as highly efficient chiral inducers for a wide range of asymmetric reactions.[3] Therefore, the optically active polyamide having axially dissymmetric 1,1′-binaphthalene component in the main chain is expected to serve as the efficient chiral adsorbent of the CSP for HPLC. Although the chiroptical properties of some axially chiral polyamides have been investigated,[4] no report has dealt with the chiral recognition ability of the axially chiral polyamide. Previously, we reported a practical method for the synthesis of optically pure 1,1′-binaphthalene-2,2′-dicarboxylic acid (**1**) derivatives and their usefulness as the chiral modifiers of the packing material for HPLC.[5] In this paper, we wish to report the synthesis of polyamides **4a**—**4c** from optically pure **1** and 1,4-benzenediamine (**3a**), 1,6-hexanediamine (**3b**), and 1,10-decanediamine (**3c**). Further reported are the chiroptical properties of these polyamides and their optical resolution ability as the chiral adsorbents for the CSPs.

Results and Discussion

Synthesis of Polyamides 4a—4c and Model Diamides 6a—6c. The syntheses of the polyamides **4a**—**4c** were carried out by the method of solution polycondensation at ambient temperature in *N*,*N*-dimethylacetamide (DMAc) as shown in Scheme 1. Diamines **3a**—**3c** were reacted with the dicarbonyl dichloride **2** derived from optically pure (*S*)-**1** to yield the optically active polyamides **4a**—**4c**, respectively (Table 1). For the synthesis of **4b** and **4c**, concomitant formation of linear and/or cyclic oligomers was observed.

All the polyamides were soluble in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) and aprotic polar solvents such as *N*,*N*-dimethylformamide (DMF), DMAc, and dimethyl sulfoxide (DMSO), but insoluble in chloroform, tetrahydrofuran (THF), and usual nonpolar solvents.

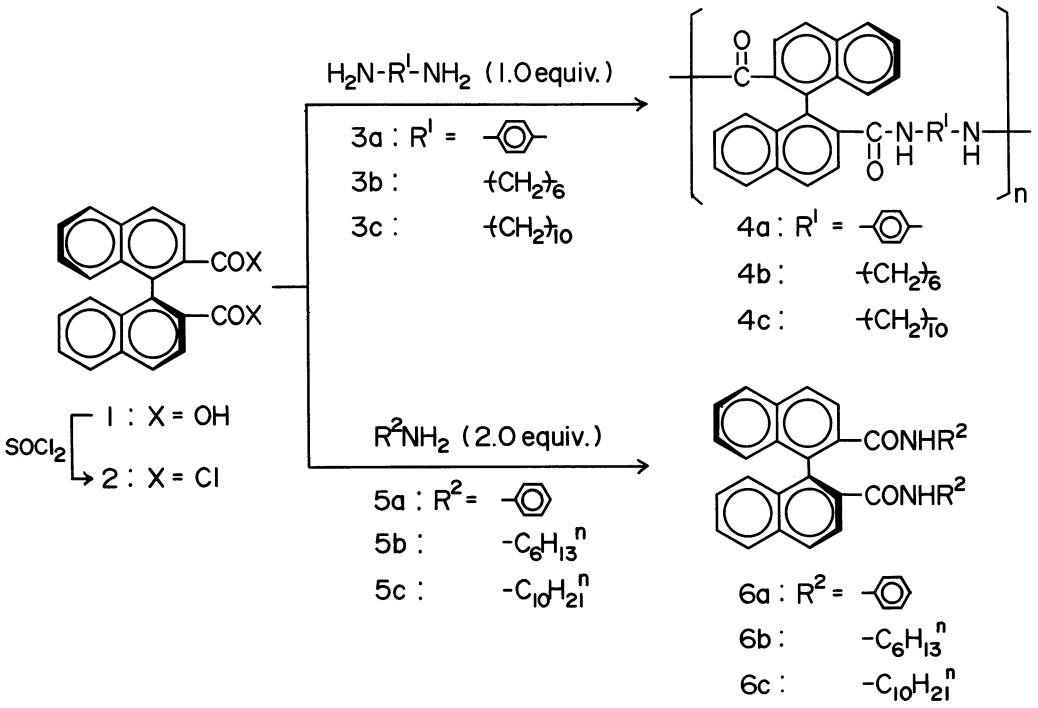
Model diamides **6a**—**6c** were prepared by condensation of **2** with benzenamine (**5a**), 1-hexanamine (**5b**), and 1-decanamine (**5c**) in benzene at reflux temperature, respectively (Table 1).

Comparison of the Chiroptical Properties of the Polyamides 4a—4c to the Corresponding Diamides 6a—6c. As shown in Table 1, the mean residue rotations ($[m]_D$) of **4b** and **4c** were comparable to the molar rotations ($[\phi]_D$) of the corresponding model diamides **6b** and **6c** in DMAc solution. CD spectra of **4b** and **4c** in both DMAc and HFIP were almost comparable to those of **6b** and **6c**, respectively, as shown in Figs. 2 and 3. In contrast, the mean residue rotation of **4a** was rather

Table 1. Synthesis of Polyamides (**4a**—**4c**) and Diamides (**6a**—**6c**)

	Yield / %	$\bar{M}_n$[a]	$\bar{M}_w/\bar{M}_n$[a]	$[m]_D$[b] for **4a**—**4c** ($[\phi]_D$[c] for **6a**—**6c**)
4a	84	20000	1.92	−2.1°
6a	95			−70.5°
4b	59	27000	1.49	−48.9°
6b	83			−71.7°
4c	27	26000	1.48	−59.4°
6c	94			−64.0°

a) Determined by GPC calibrated with polystylene standards. b) Mean residue rotation. Measured at ca. 0.024 (repeating unit mol) dm^{-3} in DMAc at ambient temperature. c) Molar rotation. Measured at ca. 0.024 mol dm^{-3} in DMAc at ambient temperature.



Scheme 1.

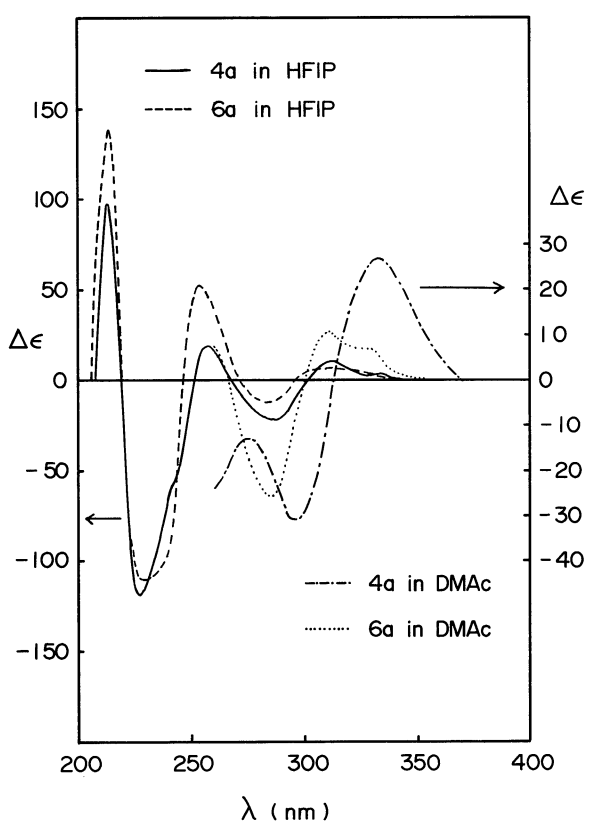


Fig. 1. CD spectra of polyamide **4a** and model diamide **6a**.

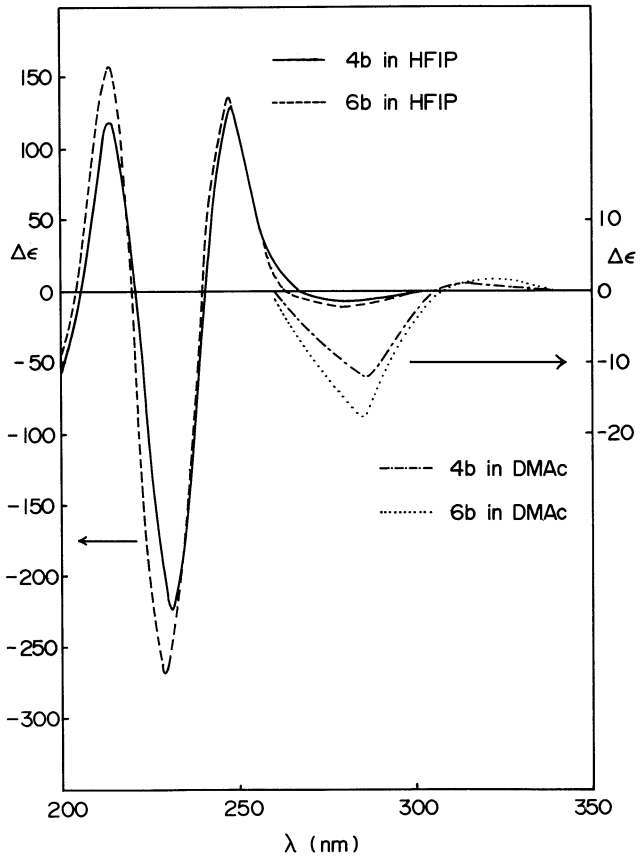


Fig. 2. CD spectra of polyamide **4b** and model diamide **6b**.

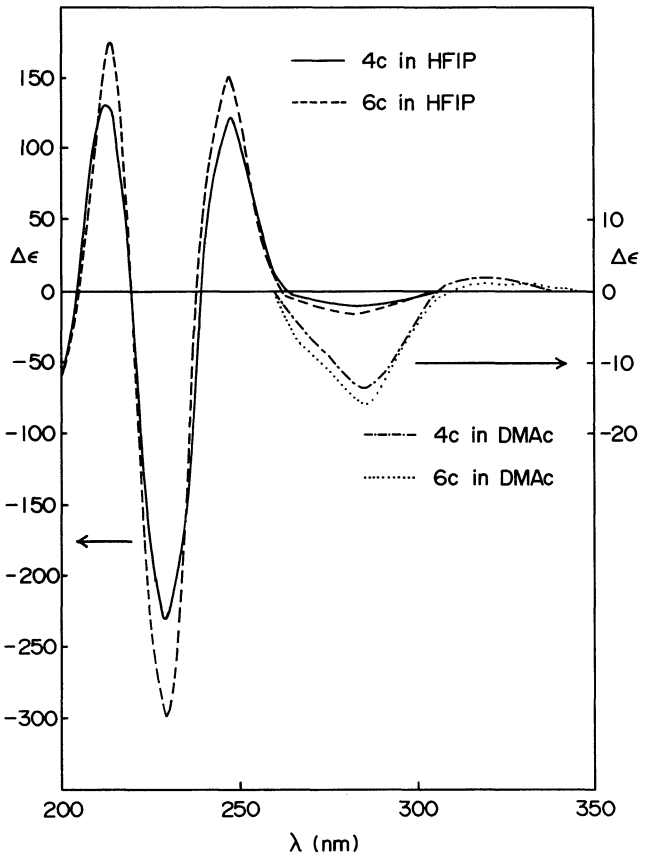


Fig. 3. CD spectra of polyamide **4c** and model diamide **6c**.

smaller than the molar rotation of **6a**. CD spectrum of **4a** at wavelength longer than 260 nm in DMAc was somewhat different from that of **6a**, while the spectrum at wavelength shorter than 260 nm in HFIP was almost comparable to that of **6a** (Fig. 1).

It is known that the Cotton effects derived from the ^1B_b transition of the naphthalene chromophores in 1,1′-binaphthalene derivatives appear at wavelength shorter than 260 nm; the Cotton effects are supposed to reflect the conformation of the binaphthalene skeletons more closely than those derived from other transitions of the naphthalene chromophores.[6] Thus, the similarity of the CD spectra of **4a**—**4c** at wavelength shorter than 260 nm to those of the corresponding model diamides **6a**—**6c** suggests that the conformations of the 1,1′-binaphthalene-2,2′-dicarboxamide moieties of the polyamides in the solution state are similar to those of the model diamides. It seems that the differences of the chiroptical properties between **4a** and **6a** at wavelength longer than 260 nm are attributed to the differences of transition properties between the 1,4-bis(acylamino)benzene chromophore of the polyamide **4a** and the (acylamino)benzene chromophore of the model diamide **6a**.

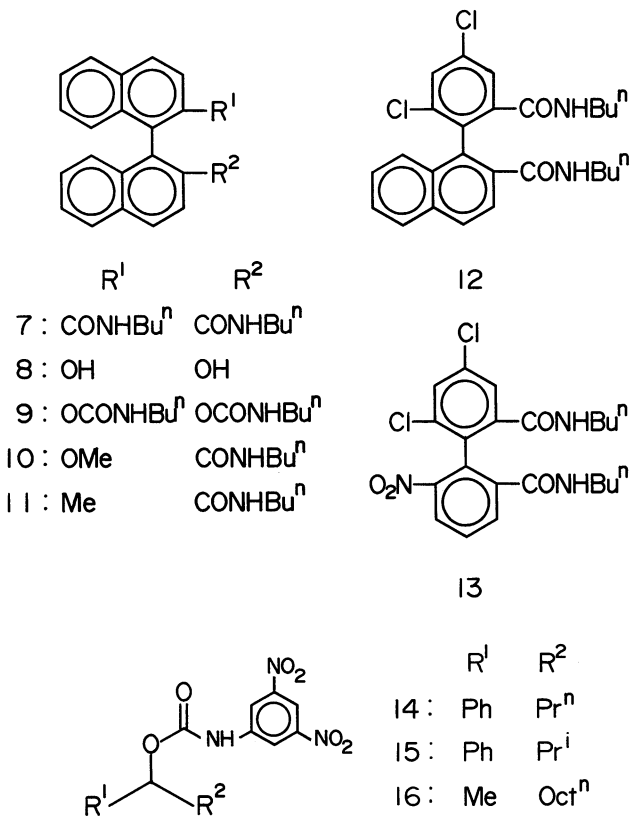
Chiral Recognition Ability of Polyamides 4a—4c as the Chiral Adsorbents for the CSPs. To investigate the chiral recognition ability of the polyamides **4a**—**4c**, CSP-4a—CSP-4c were prepared by coating spherical, macroporous silica gel with DMAc solutions of **4a**—**4c** using a conventional technique.[7] Polyamides **4a**—**4c** are constituted of amide linkages which can function as hydrogen-bonding site and bulky binaphthalene moieties which can serve as π-electron-donor group. Thus, dia-

Table 2. Chromatographic Resolution of Racemates **7**—**16** by CSP-4a—CSP-4c Packed Columns

Racemate	Eluent[a]	CSP-4a			CSP-4b			CSP- 4c		
		k_1'[b]	α[c]	R_s[d]	k_1'	α	R_s	k_1'	α	R_s
7	A	2.76(*S*)[e]	1.76	0.40	0.97	1.56	0.94	0.98(*S*)[e]	1.55	0.96
	B	—[f]			—[f]			5.92	1.86	2.36
8[g]	A	1.86	1.0		0.78	1.0		0.65	1.0	
9	A	0.33	1.48	0.17	0.18	1.34	0.29	0.16	1.46	0.33
	B	—[f]			1.03	1.52	0.88	0.80	1.54	1.26
10	A	2.18	1.0		0.34	1.0		0.38	1.0	
	B	—[f]			1.74	1.15	0.29	0.91(*S*)[e]	1.17	0.55
11[g]	A	0.47	1.0		0.15	1.0		0.17	1.0	
12	A	1.08	1.58	0.39	0.49	1.40	0.67	0.52	1.36	0.53
	B	—[f]			5.42	1.74	0.96	2.52[h]	1.57	1.46
13	A	1.39	1.0		0.44	1.20	0.35	0.44(*S*)[e]	1.17	0.25
	B	—[f]			5.42	1.44	0.78	2.67[h]	1.29	0.78
14	A	1.46	1.0		0.49	1.0		0.60(*S*)[e]	1.20	0.27
	B	—[f]			8.09	1.32	0.41	5.15	1.32	0.71
15	A	1.06	1.0		0.24	1.0		0.54	1.32	0.56
	B	—[f]			8.38	1.41	0.86	4.98	1.43	0.94
16[g]	A	0.48	1.0		0.19	1.0		0.26	1.0	

a) A, 2-propanol/hexane=10/90, Flow rate=1.0 ml min^{-1}; B, 2-propanol/hexane=1/99, Flow rate=1.0 ml min^{-1}. b) Capacity factor of the enantiomer eluting first=(retention volume of enantiomer—void volume of column)/(void volume of column). c) Separation factor=(k' of more retained enantiomer)/(k' of less retained enantiomer). d) Resolution factor=2×(distance between the peaks of more and less retained enantiomers)/(sum of band width of two peaks). e) Absolute configuration of the enantiomer eluting first. f) The capacity factor of the racemate was so large that no clear peak of the racemate was observed. g) This racemate couldn't be resolved even by use of eluent B. h) Flow rate=0.5 ml min^{-1}.

stereomeric interactions via π–π interaction and hydrogen bonding are expected between the CSPs and racemates which have an electron-accepting aromatic group and a hydrogen-bonding site. Table 2 shows the results of the HPLC analyses of such racemates **7**—**16**. Figure 4



Structure of racemates.

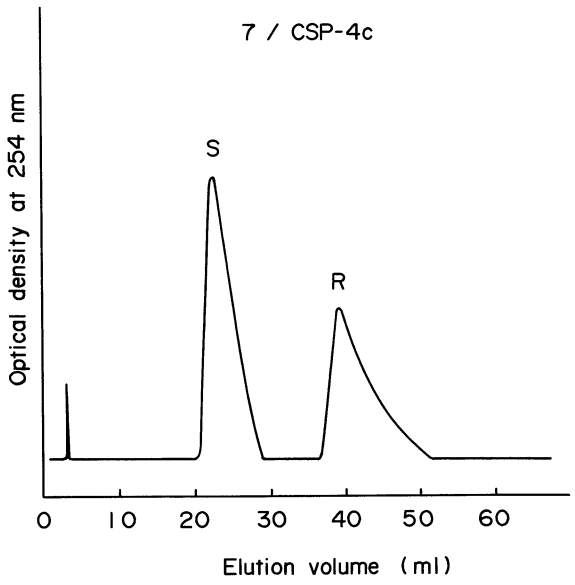


Fig. 4. Chromatographic resolution of racemate **7** on CSP-**4c** column. Column: 25×0.46 (i.d.) cm, eluent: 1% 2-propanol in hexane, flow rate: 1.0 ml min^{-1} at room temperature.

shows the chromatogram of the resolution of **7** on a CSP-4c column using 1% 2-propanol in hexane as the eluent. CSP-4b and CSP-4c could resolve the axially chiral 1,1'-biaryl compounds **7**, **9**, **12**, and **13**, which possessed two amide or carbamate groups, respectively. Racemate **10** which had an amide group and a methoxyl group could be resolved by CSP-4b and CSP-4c. CSP-4a could also resolve the racemates **7**, **9**, and **12**, but couldn't resolve **10** and **13**. On the other hand, none of the CSPs could resolve racemate **11** which had only an amide group as the hydrogen-bonding site. These results indicate that the presence of two hydrogen-bonding sites in a racemate is necessary for efficient chiral discrimination of these biaryl compounds. Thus, a main control factor for the chiral discrimination of biaryl atropisomers seems to be the hydrogen bonding between the amide groups of the polyamides and the hydrogen-bonding sites of the racemates. The capacity factor (k_1') and the separation factor (α) of all of the racemates decreased with a increase in the content of 2-propanol in the eluent. This result also supports the importance of the hydrogen bonding for the chiral discrimination; hydrogen bonding between the polyamides and 2-propanol in competition with the racemates should decrease the interaction between the polyamide CSPs and the racemates.

Racemate **8** couldn't be resolved by all of the CSPs despite bearing two phenolic hydroxyl groups as the hydrogen-bonding sites. This result indicates that a suitable alignment of the two hydrogen-bonding sites of a racemate is also important for efficient chiral discrimination.

Although having only one hydrogen-bonding site, 3,5-dinitrophenylcarbamates (3,5-DNPCs) **14** and **15** derived from the corresponding 1-aryl-1-alkanols were also resolved efficiently (α>1.3) by CSP-4b and CSP-4c. An important control factor of the chiral discrimination should be donor–acceptor interaction between the binaphthalene moiety of the polyamides and the 3,5-dinitrobenzene moiety of the 3,5-DNPCs.

In conclusion, we have shown here that optically active polyamides **4a**—**4c**, obtained by solution polycondensation of 1,1'-binaphthalene-2,2'-dicarbonyl dichloride (**2**) with diamines **3a**—**3c**, have chiral discriminating ability for atropisomeric biaryls **7**,**9**—**13**, and 3,5-DNPCs **14** and **15**.

Experimental

Measurements. Melting points were measured on a Yamato MP-21 and uncorrected. Microanalyses were carried out in the Microanalytical Laboratory of the Chemical Research Institute of Non-aqueous Solutions, Tohoku University. Optical rotations were obtained at room temperature (23—25 °C) using a Union Giken PM-101 polarimeter. CD spectra were measured in an 0.10 cm cell at room temperature on a JASCO J-400X spectropolarimeter. HPLC measurements were carried out on a Shimadzu LC-6A, with UV detection at 254 nm. IR spectra were measured on a Shimadzu IR-460

infrared spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL JNM-FX60 instrument. GPC measurements were carried out at 40 °C on a Tosoh HLC-8020 instrument equipped with TSK gel GMH$_{XL}$ (×2) and G2000H$_{XL}$ columns using a 5 mM LiBr solution of DMF as an eluent.

Materials. Homochiral (*S*)-1,1′-binaphthalene-2,2′-dicarboxylic acid (**1**) was prepared by a previously reported procedure[5] and converted to the bis(acid chloride) **2** by the usual method using thionyl chloride. Diamines **3a**—**3c** and amines **5a**—**5c** were purchased from Tokyo Kasei Kogyo Co., Ltd. and purified by distillation under reduced pressure (**3b**, **3c**, and **5a**—**5c**) or by recrystallization from benzene (**3a**) before use. DMAc was purified by distillation under reduced pressure over calcium hydride before use. Triethylamine was purified by distillation over calcium hydride before use. Other solvents were purified by distillation.

Preparation of Polyamides. The synthetic procedure for **4a** is representative. To a stirred solution of diamine **3a** (181 mg, 1.68 mmol) and triethylamine (343 mg, 3.39 mmol) in DMAc (14 ml) was added finely powdered dicarbonyl dichloride **2** (636 mg, 1.68 mmol) portionwise at room temperature under a nitrogen atmosphere. After stirring for 30 min, the reaction mixture was dropped into 200 ml of methanol with stirring. The resultant precipitate was collected by filtration and washed with methanol and then with acetone. Polyamide **4a** thus obtained was purified by reprecipitation from methanol and dried at 90 °C for 20 h. The polyamide weighed 580 mg (83%). **4b** and **4c** were similarly prepared (Table 1).

4a: IR (KBr) 1636, 1303, 827, and 757 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=7.0—8.1 (16H, m, Ar–H) and 10.8 (2H, br, N–H). Found: C, 79.02; H, 4.49; N, 6.86%. Calcd for $(C_{28}H_{18}N_2O_2)_n$: C, 81.14; H, 4.38; N, 6.76%.

4b: IR (KBr) 1619, 1541, 1280, 819, and 749 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=−0.1—0.9 (8H, br, CH_2), 2.4—3.2 (4H, br, CH_2–N), 6.8—8.3 (12H, m, Ar–H), and 8.6—9.2 (2H, br, N–H). Found: C, 78.40; H, 6.20; N, 6.39%. Calcd for $(C_{28}H_{26}N_2O_2)_n$: C, 79.59; H, 6.20; N, 6.63%.

4c: IR (KBr) 1643, 1538, 824, and 756 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=0.3—1.5 (16H, br, CH_2), 2.4—3.2 (4H, br, CH_2–N), 6.9—8.1 (12H, m, Ar–H), and 8.7—9.2 (2H, br, N–H). Found: C, 77.83; H, 7.17; N, 6.18%. Calcd for $(C_{32}H_{34}N_2O_2)_n$: C, 80.30; H, 7.16; N, 5.85%.

The discrepancies in these carbon analyses may be attributed to the carbonization of the binaphthalene moieties of the polyamides.[8]

Synthesis of Model Diamides. The synthetic procedure for **6a** is representative. To a stirred solution of the dicarbonyl dichloride **2** (212 mg, 0.558 mmol) in dry benzene (10 ml) were added benzenamine (**5a**) (125 mg, 1.34 mmol) and triethylamine (136 mg, 1.34 mmol) at room temperature under a nitrogen atmosphere. The solution was refluxed with stirring for 1 h and then cooled to room temperature. The reaction mixture was washed (2 M HCl (1 M=1 mol dm^{-3}), 10% Na_2CO_3, and distilled water) and dried over Na_2SO_4. Solvents were removed under reduced pressure, and the residue was purified by silica-gel column chromatography (eluent: 50% ethyl acetate in hexane) to afford the diamide **6a** in 95% yield (260 mg) as amorphous powder. Diamides **6b** and **6c** were similarly prepared as colorless glass (Table 1).

6a: IR (KBr) 1643, 1545, 1332, 755, and 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=6.80—8.10 (22H, m, Ar–H) and 8.90—9.30 (2H, br, N–H). Found: C, 82.90; H, 4.91; N, 5.69%. Calcd for $C_{34}H_{24}N_2O_2$: C, 82.90; H, 4.91; N, 5.69%.

6b: IR (neat) 1624, 1543, 1326, 1299, 824, and 756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.85—1.00 (22H, m, CH_2 and CH_3), 2.82—3.14 (4H, m, CH_2–N), and 7.05—8.08 (14H, m, Ar–H and N–H). Found: C, 80.63; H, 8.06; N, 5.47%. Calcd for $C_{34}H_{40}N_2O_2$: C, 80.27; H, 7.93; N, 5.51%.

6c: IR (neat) 1631, 1563, 1331, 1301, 825, and 756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.80—1.24 (38H, m, CH_2 and CH_3), 2.82—3.14 (4H, m, CH_2–N), and 6.96—8.04 (14H, m, Ar–H and N–H). Found: C, 81.04; H, 9.30; N, 4.41%. Calcd for $C_{42}H_{56}N_2O_2$: C, 81.24; H, 9.09; N, 4.51%.

Preparation of Packing Material and Column Packing. Macroporous silica gel (Merck, LiChrospher SI 1000: mean particle size, 10 μm; pore size, 100 nm) was silanized with dichlorodiphenylsilane according to the literature method.[7] A polyamide (ca. 0.15 g) was dissolved in 7 ml of DMAc and the silanized silica gel (3.0 g) was wetted with the polymer solution. The resultant mixture was irradiated with ultrasound for 1 min. Then the solvent was evaporated in vacuo. Obtained polymer-coated silica gel was dried in vacuo at 80 °C for 5 h and then dispersed in 30 ml of methanol with sonication during 5 min. After filtration and washing with methanol, the silica gel was dried in vacuo at 80 °C for 5 h. The chiral packing material thus obtained was packed in a stainless steel HPLC column (i. d.: 0.46 cm, length: 25 cm) by a slurry method. The plate number of the columns packed CSP-4a—CSP-4c were about 4500, 2900, and 2500, respectively, for benzene using 10% 2-propanol in hexane as the eluent at ambient temperature.

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