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Synthesis of Chiral Crownophanes Having Two Phenolic Groups via Tandem Claisen Rearrangement and Their Chiral Recognition

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Abstract

Asymmetric crownophanes having a chiral binaphthyl unit and two phenolic hydroxyl groups were thermally synthesized from the corresponding macrocyclic ethers via tandem Claisen rearrangement. Circular dichroism (CD) spectroscopic studies and HPLC experiments confirmed that little racemization of these crownophanes occurred during the thermal rearrangement. The association constants for the interaction of the chiral crownophanes with the enantiomers of phenylethylamine, phenylglycinol, and phenylalaninol were determined by a ^{1}H NMR titration method in CD_2Cl_2. As a result, the 27 membered crownophane has some chiral recognition for phenylglycinol.

Introduction

Although the complexation of crownophanes, macrocycles containing rigid aromatic moieties and flexible oligoethylene glycol moieties, with cations have been exclusively studied [1, 2], a number of complexes between crownophanes and "neutral" molecules have also been reported in the last decades [3–5]. In most of the cases of complexation with "neutral" molecules, hydrogen bonding plays a key role. Thus the most important, often laborious work, is to place the hydrogen bonding groups, the hydrogen donor and acceptor sites, in complementary positions on the host macrocycles for the target guest molecules.

We have recently reported that 1,1′-bis(aryloxymethyl)-ethylene derivatives can twice perform the Claisen rearrangement successively, resulting in bis(hydroxyaryl) derivatives in high yields, which we call a "Tandem Claisen Rearrangement" [6]. The reaction provides a new, simple way to introduce plural, proton-donating, phenolic –OH groups into acyclic and macrocyclic compounds [7, 8]. So far, we have found that a 22-membered crownophane with two phenolic groups and tetraethylene glycol moieties, prepared via a tandem Claisen rearrangement, binds a water molecule very strongly in the tetrahedral coordination [9].

In this work, to demonstrate the versatility of this new method to prepare the host crownophanes for neutral guests, we synthesized chiral crownophanes **4**, **5**, and **6** having different ring-sizes from the corresponding macrocyclic ethers **1**, **2**, and **3** in one step via a tandem Claisen rearrangement. The crownophanes were incorporated into an axially asymmetric 2,2′-disubstituted-1,1′-binaphthyl unit as the chiral component, which generally has a rather high rotation-barrier. (e.g., 37–40 kcal/mol for 2,2′-dimethyl-1,1′-binaphthyl [10]) We will also describe the ability of enantiomer recognition of the resulting chiral crownophanes **4**, **5**, and **6** for chiral amino alcohols.

Experimental

General

^{1}H NMR spectra were measured on a Bruker Avance 500 or a Varian Gemini 300 NMR Spectrometer for solutions in $CDCl_3$ and/or CD_2Cl_2 with Me_4Si as an internal standard. CD spectra were recorded on a JASCO J-720WI. Optical rotations were measured on a JASCO DIP-1000, and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. HPLC analyses were carried out on a Eyela PLC-5D chromatograph equipped with a UV spectrophotometric detector (wavelength 254 nm) using a chiralpak AD 250 mm × 4.6 mm column. For NMR titration experiments, 0.01 M CD_2Cl_2 solutions of crownophanes were prepared accurately. The concentrations of the guest molecules were varied from 0 to 0.50 M for each experiment (total 8 measurements for each experiment). The K values were obtained by curve fitting using an equation: $\delta_{calc} = (1/2\{b - (b^2 - 4c)^{1/2}\}/[H]_0)(\delta_{HG} - \delta_H) + \delta_H$; $b = [H]_0 + [G]_0 + 1/K$, $c = [H]_0[G]_0$. (R)-phenylalaninol (Fluka 99%), (S)-phenylalaninol (Fluka 99%), (R)-phenylglycinol (Fluka 99%), (S)-phenylglycinol (Fluka 99%), (R)-1-phenylethylamine (Tokyo Kasei Kogyo 99.0%), and (S)-1-phenylethylamine (Tokyo Kasei Kogyo 98.0%) as the guest amines were all used as received.

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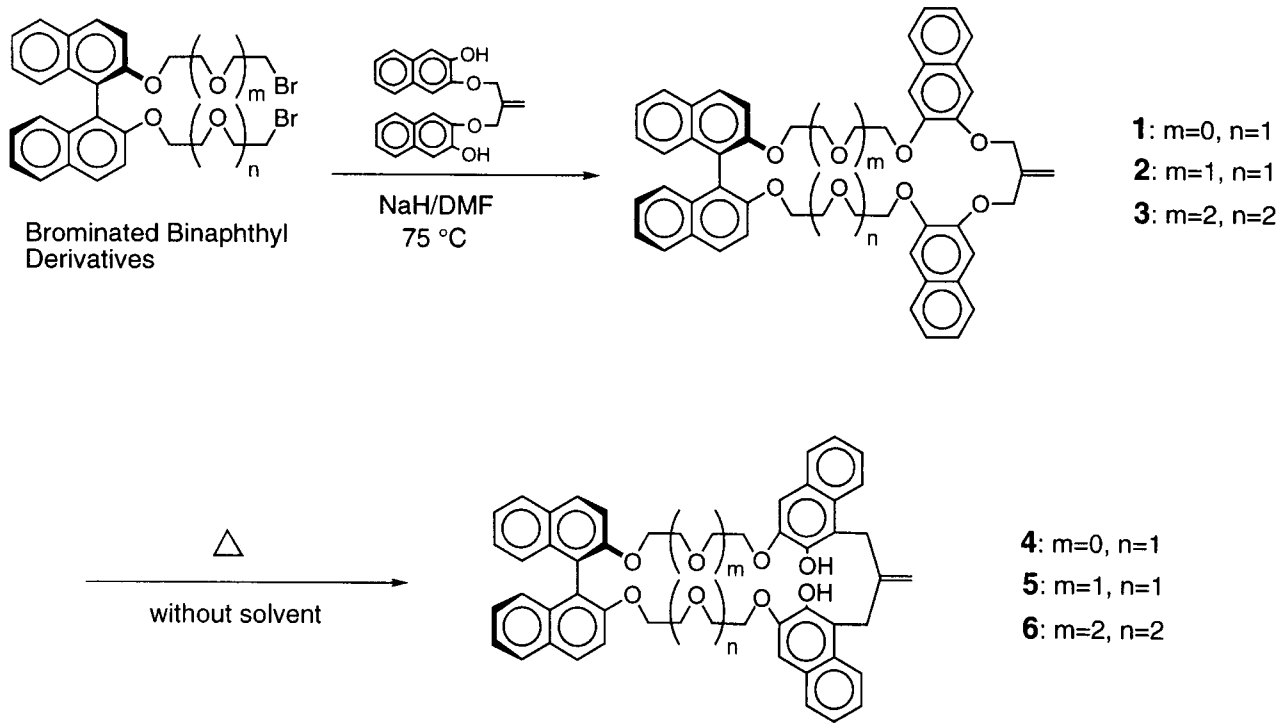

Scheme 1. Synthetic route for chiral crownophanes.

Synthesis of crownophanes

General procedure for the synthesis of brominated binaphthyl derivatives

Basically, the brominated binaphthyl derivatives were synthesized according to the method described in the literature [11]. (R)-(+)-1,1′-bi-2,2′-naphthol (1.00 equiv) was bis-etherified with the corresponding 1-chlorooligoethylene glycols protected by 3,4-dihydro-2H-pyran (3.00 equiv) by using K_2CO_3 (3.00 equiv) in DMF at 110 °C, except in the case of the crownophane **4**. For the crownophane **4**, the etherification was done in two steps: first, (R)-(+)-1,1′-bi-2,2′-naphthol (4.98 g, 17.4 mmol) was etherified with 2-(5-chloro-1-pentoxy)pyran (3.86 g, 18.4 mmol) in DMF (100 mL) solution containing K_2CO_3 (2.49 g, 18.0 mmol) at 100 °C for 12 h to give 2-[5-(pyranyl-2-oxy)-3-oxa-1-pentoxy]-2′-hydroxy-1,1′-binaphthyl (38%) as a yellow oil. Then, the mono-etherified compound (3.03 g, 6.62 mmol) reacted with 2-(2-chloro-1-ethoxy)pyran (2.22 g, 3.51 mmol) in DMF solution (80 mL) containing K_2CO_3 (1.90 g, 13.7 mmol) at 120 °C to give 2-[5-(pyranyl-2-oxy)-3-oxa-1-pentoxy]-2′-[2-(pyranyl-2-oxy)-1-ethoxy]-1,1′-binaphthyl as a yellow oil (59%).

The bromination of the resulting THP-protected compounds was done without deprotection [11]. Triphenylphosphine (19.7 mmol) was dissolved in CH_2Cl_2 (50 mL) and cooled to 0 °C. Bromine (23 mmol) was slowly added, and the reaction mixture was stirred at 0 °C for 1 h. A CH_2Cl_2 solution (15 mL) containing the THP-protected compound (3.93 mmol) was added over a period of 15 min at 0 °C and then the reaction mixture was stirred at room temperature for 12 h. CH_2Cl_2 (30 mL) was added, and the reaction mixture was washed with water (2 × 100 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was recrystallized from toluene/*n*-hexane to remove triphenylphosphine oxide. The filtrate was concentrated under reduced pressure and purified by column chromatography (silica gel, $CHCl_3$/*n*-hexane) to give the brominated compound as a yellow oil.

(R)-(+)-17-Methylene-2,3:4,5-di(1,2-naphtho)-13,14,20,21-di(2,3-naphtho)-1,6,9,12,15,19,22-heptaoxacyclotetracosa-2,4,13,20-tetraene (**1**)

The mixed DMF (20 mL) solution of 2-(2-bromo-1-ethyloxy)-2′-(5-bromo-3-oxa-1-pentyloxy)-1,1′-binaphthyl (1.05 g, 1.81 mmol) and 2-methylene-1,3-bis(3-hydroxy-naphthyl-2-oxy)propane (0.674 g, 1.81 mmol) was added dropwise to a DMF solution (100 mL) containing NaH (0.140 g, 5.84 mmol) as a base at 75 °C, followed by the addition of potassium iodide (0.071 g, 0.48 mmol). The reaction mixture was stirred at 75 °C for 14 h. After removing the solvent under reduced pressure, the residue was dissolved in $CHCl_3$ (100 mL), washed with water (3 × 100 mL), and dried ($MgSO_4$). After it was concentrated under reduced pressure, the residue was purified by column chromatography (silica gel, $CHCl_3$/AcOEt 95 : 5) to give **1** (32%) as a white solid: ^{1}H-NMR (CD_2Cl_2, 500MHz) δ 3.52 (4H, s), 3.94 (2H, m), 4.02–4.04 (3H, m), 4.16 (2H, m), 4.36 (1H, m), 4.73–4.89 (4H, m), 5.39 (1H, s), 5.44 (1H, s), 6.85 (1H, s), 7.02–7.09 (3H, m), 7.17–7.20 (3H, m), 7.26–7.38 (9H, m), 7.49 (1H, m), 7.56 (1H, m), 7.69–7.84 (6H, m); FT-IR (KBr): 1623, 1256, 1117; FAB-MS (pos): m/z 754 (M^+). Anal.calcd (found) for $C_{50}H_{42}O_7$: 79.56 (79.36); 5.54 (5.39).

(R)-(+)-17-Methylene-2,3:4,5-di(1,2-naphtho)-13,14,20,21-di(2,3-naphtho)-1,6,9,12,15,20,22,25-octaoxacyclotetracosa-2,4,13,20-tetraene
(2)

According to the same procedure as described for the synthesis of (**1**), this was prepared from 2-methylene-1,3-bis(3-hydroxynaphthyl-2-oxy)propane and 2,2′-bis(5-bromo-3-oxa-1-pentyloxy)-1,1′-binaphthyl, and purified by silica gel column chromatography (two columns: $CHCl_3$/AcOEt 9 : 1 and $CHCl_3$) to give **2** (31%) as a white solid: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.37–3.39 (4H, m), 3.46–3.59 (4H, m), 3.82–3.92 (4H, m), 3.99–4.04 (4H, m), 4.89 (4H, q), 5.45 (2H, s), 7.05 (2H, s), 7.10–7.40 (14H, m), 7.63–7.72 (4H, m), 7.77 (4H, t); FT-IR (KBr): 3054, 1624, 1258, 1117; FAB-MS (pos): m/z 798 (M^+).

(R)-(+)-20-Methylene-2,3:4,5-di(1,2-naphtho)-16,17,23,24-di(2,3-naphtho)-1,6,9,12,15,18,22,25,28,31-decaoxacyclotriaconta-2,4,16,23-tetraene
(3)

According to the same procedure as described for the synthesis of (**1**), this was prepared from 2-methylene-1,3-bis(3-hydroxynaphthyl-2-oxy)propane and 2,2′-bis(8-bromo-3,6-dioxa-1-octyloxy)-1,1′-binaphthyl, and purified by silica gel column chromatography (two columns: $CHCl_3$/AcOEt 9 : 1 and $CHCl_3$) to give **3** (43%) as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.09–3.19 (4H, m), 3.34–3.47 (8H, m), 3.74–3.80 (4H, m), 3.94–4.06 (4H, m), 4.19–4.22 (4H, m), 4.87 (4H, s), 5.47 (2H, s), 7.08–7.35 (16H, m), 7.59–7.61 (2H, m), 7.65–7.67 (2H, m), 7.74–7.81 (4H, m); FT-IR (KBr): 3054, 1625, 1257, 1116; FAB-MS (pos): m/z 886 (M^+).

(R)-(+)-17-Methylene-2,3:4,5-di(1,2-naphtho)-13,14,15,19,20,21-bis[1,3-(2-hydroxynaphtho)]-1,6,9,12,22-pentaoxacyclotetracosa-2,4,14,19-tetraene
(4)

1 (0.06 g, 0.0795 mmol) was heated at 160 °C for 2 h under vacuum to give a yellow solid. The crude product was purified by gel-permeation chromatography (JAIGEL-1H and 2H, $CHCl_3$) to give **4** (72%) as a white solid. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 3.41–3.43 (4H, s), 3.78 (2H, s), 3.92 (1H, s), 3.99 (1H, s), 4.01–4.02 (2H, m), 4.10 (2H, m), 4.21–4.25 (3H, m), 4.43 (1H, m), 4.50 (1H, s), 4.79 (1H, s), 5.91 (1H, s), 6.81 (1H, s) 6.86 (1H, s), 7.07–7.09 (2H, m), 7.21–7.39 (12H, m), 7.46 (1H, m), 7.56 (1H, m), 7.70–7.76 (3H, m), 7.85–7.87 (2H, m), 7.93 (1H, s), 8.04 (1H, s); FT-IR(KBr): 3510, 1621, 1268, 1122; FAB-MS (pos): m/z 754 (M^+). Anal. Calcd (found) for $C_{50}H_{42}O_7$+0.5H_2O: C, 78.62(78.54); H, 5.67(5.50).

(R)-(+)-17-Methylene-2,3:4,5-di(1,2-naphtho)-13,14,15,19,20,21-bis[1,3-(2-hydroxynaphtho)]-1,6,9,12,22,25-hexaoxacycloheptacosa-2,4,14,19-tetraene
(5)

2 was heated at 150 °C for 4 h under vacuum to give **5** quantitatively as a brown solid. Analytically pure material was obtained by column chromatography (silica gel, $CHCl_3$/AcOEt 9 : 1) to provide **5** as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.17–3.30 (4H, m), 3.34–3.39 (4H, m), 3.80–3.87 (2H, m), 3.93 (4H, s), 4.01–4.09 (6H, m), 4.55 (2H, s), 6.69 (2H, s), 7.06–7.12 (4H, m), 7.18–7.23 (2H, m), 7.27–7.40 (8H, m), 7.69–7.80 (6H, m), 7.89–7.92 (2H, m); FTIR (KBr): 3448, 1624, 1270, 1116; FAB-MS (pos): m/z 798 (M^+); Anal. Calcd (found) for $C_{52}H_{46}O_8$ + 0.5H_2O: C, 77.30 (77.47); H, 5.86 (5.58)

(R)-(+)-20-Methylene-2,3:4,5-di(1,2-naphtho)-16,17,18,22,23,24-bis[1,3-(2-hydroxynaphtho)]-1,6,9,12,15,25,28,31-octaoxacyclotriaconta-2,4,17,22-tetraene
(6)

3 was heated at 150 °C for 4 h under vacuum to give **6** quantitatively as a brown solid. Analytically pure material was obtained by column chromatography (silica gel, $CHCl_3$/AcOEt 9 : 1) to provide **6** quantitatively as a white solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.05–3.18 (4H, M), 3.20–3.35 (4H, m), 3.45–3.48 (4H, m), 3.51–3.70 (4H, m), 3.95 (4H, s), 4.06-4.10 (4H, m), 4.12–4.24 (4H, m), 4.47 (2H, s), 7.04–7.07 (2H, d), 7.10 (2H, s), 7.16–7.21 (4H, m), 7.24–7.32 (6H, m), 7.33–7.36 (2H, d), 7.67–7.72 (4H, m), 7.80–7.83 (4H, m); FTIR (KBr): 3448, 1620, 1270, 1123; FAB-MS (pos): m/z 886 (M+); Anal. Calcd (found) for $C_{56}H_{54}O_{10}$ + H_2O: C, 74.32 (74.50); H, 6.24 (6.03).

Results and discussion

Synthesis of chiral crownophanes

All crownophanes were synthesized from enantiomerically pure (R)-(+)-1,1′-bi-2,2′-naphthol as the starting material (Scheme 1). The binaphthol was first etherified with the appropriate 1-chlorooligoethylene glycols protected by 3,4-dihydro-2H-pyran. In the case of crownophane **4**, the etherification was made stepwise: first the binaphthol was etherified with *O*-protected monochloro ethylene glycol at 100 °C, followed by the etherification with *O*-protected monochloro diethylene glycol at 120 °C, while the binaphthol for crownophanes **5** and **6** was bis-etherified in a batch by using K_2CO_3 as a base at 110 °C [11]. The resulting THP-protected compounds were brominated with triphenylphosphine and bromine, without deprotection [11]. The cyclisation reaction of the brominated compounds with a 2-methylene-1,3-bis(3-hydroxynaphthyl-2-oxy)propane proceeded in the presence of NaH under conditions of moderate dilution (10^{-2} M) to give the [1 + 1] cycloadducts, macrocyclic polyethers **1**, **2** and **3** as the main products (**1**: yield 32%; **2**: 31%; **3**: 43%). The optical rotations are $[\alpha]_D^{29} = +18°$ for **1** (c = 0.22, CH_2Cl_2), +46° for **2** and +36° for **3** (c = 0.67, CH_2Cl_2). The final compounds **5** and **6** were obtained almost quantitatively via a tandem Claisen rearrangement of the precursors **2** and **3**, respectively, without solvent at 150 °C for 4 h under vacuum. For the macrocycle **1**, the thermal rearrangement proceeded very slowly under this condition. So, the reaction temperature was increased to 160 °C, at which the rearrangement was

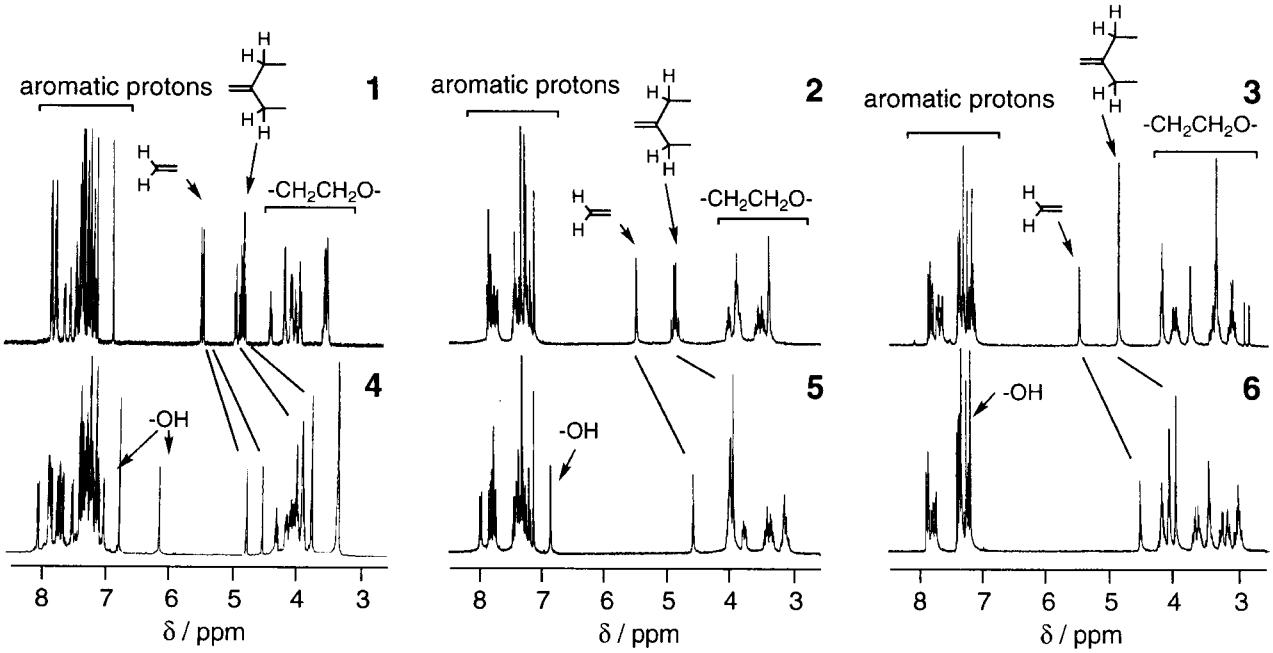

Figure 1. ^{1} NMR spectra of crownophanes **1–6** in $CDCl_3$.

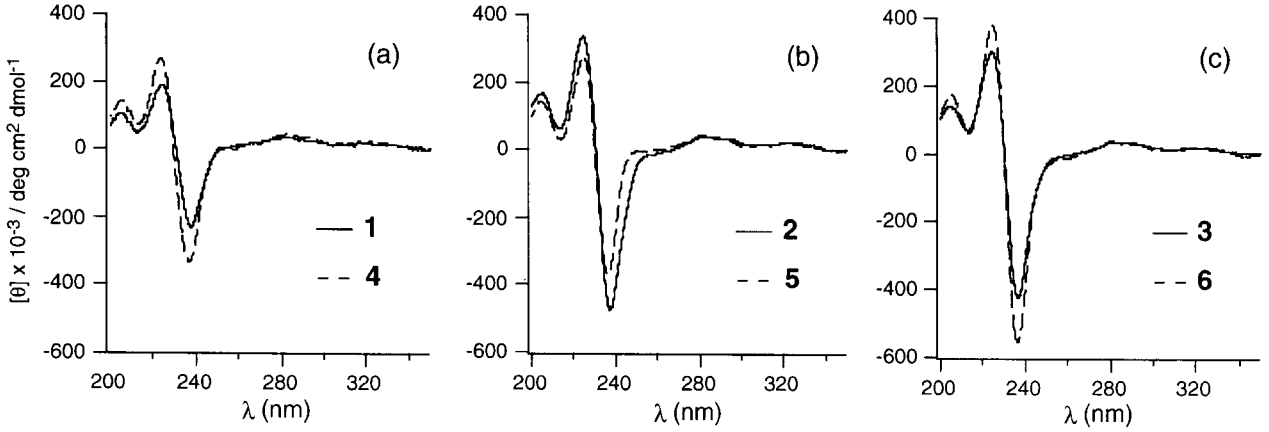

Figure 2. CD spectra of crownophanes before and after the tandem Claisen rearrangement: (a) **1** and **4**; (b) **2** and **5**; and (c) **3** and **6** in acetonitrile at r.t.

completed after 2 h. The optical rotations are $[\alpha]_D^{29}$ = +78° for **4** (c = 0.22, CH_2Cl_2), +57° for **5** and +9.3° for **6** (c = 0.67, CH_2Cl_2).

^{1}*H NMR spectra of crownophanes before and after tandem Claisen rearrangement*

Figure 1 shows ^{1}H NMR spectra of macrocyclic ethers **1**, **2** and **3** before and after the tandem Claisen rearrangement. Unsurprisingly, the complicated line-shapes of the peaks in the aromatic and –CH_2CH_2O– regions for all crownophanes were observed because of the asymmetric rigid binaphthyl moieties. The line shape of the peak around 4.8 ppm, due to the sp^3 methylene protons of the isobutenyl moiety being a AB quartet for the smaller crownophanes **1** and **2**, while a singlet for the larger one, **3**, indicating that the smaller macrocyclic polyethers are more rigid, thereby affording a slow rotation rate of the methylene moieties on the NMR time scale. Besides, both the sp^3 and the sp^2 methylene peaks of the isobutenyl moiety for compound **1** are split into two kinds of peaks around 4.8 and 5.4 ppm, respectively. This might suggest that the isobutenyl moiety for **1** are affected asymmetrically in terms of ring current effect.

After the tandem Claisen rearrangement of macrocyclic ethers **1**, **2**, and **3**, there are peaks changed in chemical-shifts and line-shapes, and new peaks appeared due to the phenolic protons in the NMR spectra. The peaks based on the isobutenyl unit shifted upfield significantly, attributed to the formation of *C*-isobutenyl bonds from *O*-isobutenyl bonds. Interestingly, the sp^3 methylene peaks of the isobutenyl group, except one on the mono ethylene-oxide side of compound **4**, around 4.0 ppm, changed in the line shape from a quartet to a singlet, although the number of member rings remained unchanged even after the tandem Claisen rearrangement, indicating that the flexibility of the macrocycles is enhanced somewhat after the Claisen rearrangement. It is noteworthy that there are two peaks due to phenolic protons in the ^{1}H NMR spectrum of compound **4**, the difference in the chemical shift is ca. 0.9 ppm. This

Table 1. Association constants (K_a) for crownophanes-chiral amines in $CDCl_3$ at r.t.

Host	Guest	K_a/M^{-1}	
		(R)-isomer	(S)-isomer
4	Phenylglycinol	4.9	5.4
	Phenylalaninol	7.7	8.8
	Phenylethylamine	0.8	0.5
5	Phenylglycinol	12	6.9
	Phenylalaninol	6.3	7.4
	Phenylethylamine	2.7	1.9
6	Phenylglycinol	ND[a]	ND[a]
	Phenylalaninol	ND[a]	ND[a]
	Phenylethylamine	ND[a]	ND[a]

[a] ND represents not determined because no significant chemical shift was observed upon adding the guest molecule.

shows that the exchange of protons between the phenolic groups is very slow on the NMR time scale at room temperature, and they exist under a significantly different magnetic environment.

CD spectra and optical purities of the crownophanes before and after tandem Claisen rearrangement

In order to investigate the influence of the thermal rearrangement on the chirality of the binaphthyls in the crownophanes, CD spectra and HPLC analysis were taken. Figure 2 shows the CD spectra of crownophanes **1–6** in acetonitrile solution. As shown in the figures, all of the crownophanes have similar, strong negative and positive Cotton effects at ca. 236 and 224 nm, respectively, which indicates a negative couplet. According to the related literature [12, 13], a negative couplet is related to the (R) absolute configuration for the 2,2′-substituted-1,1′-binaphthyls. Thus, the absolute configurations of the binaphthyl units were not affected by the thermal rearrangement. On the other hand, the enantiomer excesses of crownophanes **4**, **5**, and **6** were determined by HPLC. The e.e.'s showed high values (**4**: 96%, **5**: 91%, **6**: 93%) even after the thermal rearrangement. These facts taken together, the tandem Claisen rearrangement of the chiral crownophanes quantitatively proceeded without significant loss of enantiomeric purity.

Chiral recognition of the crownophanes for the chiral aminoalcohols

The enantiomeric recognition of the crownophanes **4**, **5**, and **6** towards chiral amines: phenylethylamine, phenylglycinol, and phenylalaninol, was investigated by a NMR titration method. The association constants of these complexes in $CDCl_3$ were obtained by the non-linear least-squares method on the basis of the ^1H NMR spectra data, and summarized in Table 1.

Unfortunately, the chiral crownophanes have not exhibited good chiral recognition for those chiral guests, overall. Even the crownophane **4** did not show significant chiral recognition, although the cavity was expected to provide a markedly asymmetric environment. However, the results offer some important information on the complex structures between the crownophanes and the aminoalcohols. First, there was no significant peak-shift upon the addition of any guests in the NMR spectra of compound **6**, which has a 33 membered ring, compared with the crownophanes **4** and **5**, which have 24 and 27 membered rings, respectively. This ring-size effect indicates that the complexation could not be formed simply by an acid-base interaction between the weakly acidic protons of the naphthol in the crownophanes and the amine of the guest molecules. Second, the crownophanes **4** and **5** have less affinity for phenylethylamine than the other aminoalcohols, suggesting that –OH groups of the guests also participate in the complexation. Finally, interestingly crownophane **5** favored the (R)-form of phenylglycinol over the (S)-form, or all the other aminoalcohols that we chose here. Indeed, upon the addition of the (R)-phenylglycinol, there were significant changes not only in the chemical shifts but also in the line shapes based on the oxyethylene protons of **5**, which we could not observe in the other complexations. To better understand the molecular interaction, 2D NOESY NMR spectra of the 1:2 mixture of **5** and (R)-phenylglycinol in CD_2Cl_2 + $CDCl_3$ were measured (Figure 3).

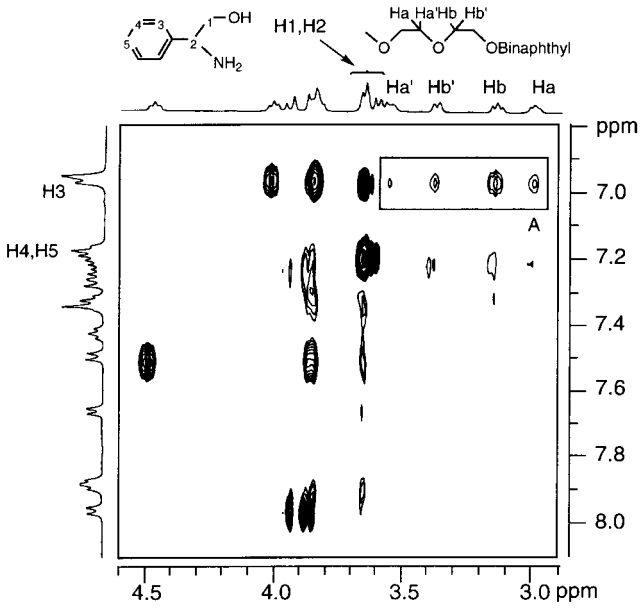

Figure 3. 2D NOESY NMR spectrum of the 1:2 mixture of **5** and (R)-phenylglycinol in CD_2Cl_2 + $CDCl_3$ at −20 °C; NOE cross-peaks (A) between the ethyleneoxy protons and the *o*-phenyl protons of the phenylglycinol.

The NMR spectra were carefully assigned using a combination of DQF-COSY, HMQC, and HMBC experiments. Since at room temperature we could not observe any NOE cross-peaks between **5** and (R)-phenylglycinol, probably due to the fast exchange between the free and bound states, the measurement temperature was decreased to −20 °C, at which we could identify some intermolecular NOEs. As a result, the well-resolved NOE cross peaks were obtained between the ethyleneoxy protons and the *o*-phenyl protons of the aminoalcohol as shown in Figure 3. In addition, at this

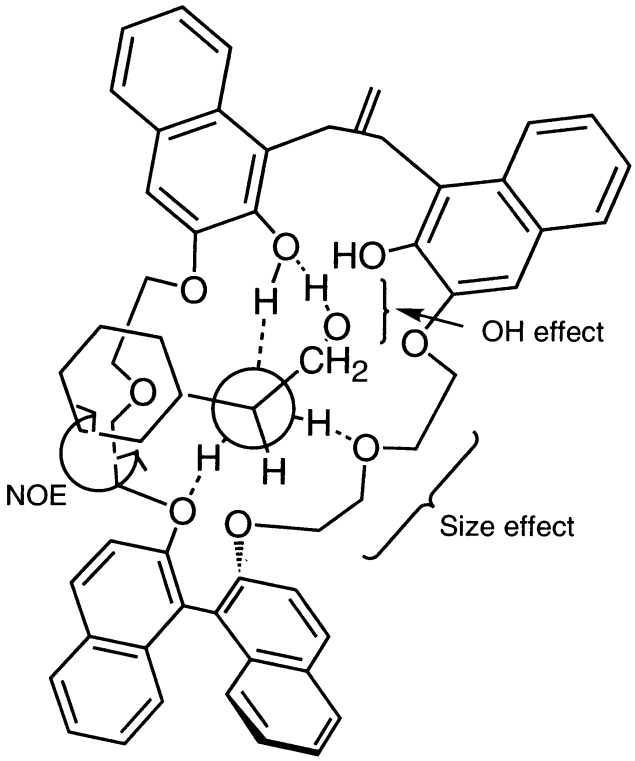

Figure 4. Predicted structure of the complex of the crownophane **5** and (R)-phenylglycinol.

temperature some relevant peaks arising from the oxyethylene protons of the crownophanes in the 1D NMR spectrum shifted to a higher field (Δ Ha: −0.36; Δ Hb: −0.22; Δ Hb′: −0.11 ppm), while the other shifted to a lower field (Δ Ha′: +0.21 ppm), compared with the corresponding peaks in the spectrum of only **5** at −20 °C. The differences in the chemical shifts could be explained by the ring current effect of the phenyl ring of the phenylglycinol. These results suggest that the phenyl ring is located near the ethyleneoxy moiety upon complexation.

Taken together, we propose a possible structure of the most favorable complex in this study, formed by crownophane **5** and (R)-phenylglycinol, as shown in Figure 4. Taking into account the fact that there was no chiral discrimination of crownophane **5** for phenylalaninols, we speculate that the enantiomer selectivity of **5** toward phenylglycinols might result not only from the asymmetric circumstances around the cavity, but also from a weak molecular interaction between the C–H of the oxyethylene moiety and the phenyl group of the guest molecule such as a CH-π interaction [14].

Conclusions

We can successfully synthesize asymmetric crownophanes having two phenolic-hydroxyl groups via a tandem Claisen rearrangement. We confirmed that there is no significant racemization during the thermal rearrangement by a combination of CD spectra and HPLC analysis. Although the crownophanes did not have good enantiomer recognition, crownophane **5** shows relatively high affinity for (R)-phenylglycinol over the (S)-isomer. The NOESY spectra of the crownophane **5**/(R)-phenylglycinol mixture reveals that the phenyl ring of the aminoalcohol is situated near the ethyleneoxy moiety in the complex.

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14. Many examples of CH-π interaction as additional stabilizing interactions for complexation has been reported. See, for example: (a) N. Nishio, M. Hirota, and Y. Umezawa: in A. P. Marchand (ed.), *The CH/π Interaction Evidence, Nature, and Consequences*, Wiley-VCH, New York (1998). Besides, we could confirm that in similar complexation, there are some [C···H] distances of 2.7–3 Å between the phenyl ring of *N*,*N*-dibenzylammonium and the oxyethylene protons of dibenzo[24]crown-8 (see Ref. [14b]), which might indicate a CH-π interaction between them, by using the Cambridge Structural Database. (b) P. R. Ashton, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, N. Spencer, J. F. Stoddart, P. A. Tasker, A. J. P. White, and D. J. Williams: *Chem. Eur. J.* **2**, 709 (1996).