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Locking the dynamic axial chirality of biphenyl crown ethers through threading

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Dedication

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Abstract: This paper describes the syntheses of [2]rotaxanes comprising 23- and 26-membered biphenyl crown ethers as the macrocyclic components and secondary ammonium ions as the dumbbell-shaped components and the locking of the dynamic axial chirality of the biphenyl moieties in these structures. Chiral high-performance liquid chromatography (HPLC) revealed that our [2]rotaxane featuring the 26-membered crown ether racemized at room temperature, but the racemization of the [2]rotaxane featuring the 23-membered crown ether did not proceed at room temperature over a period of three days. After separation of the enantiomers of the [2]rotaxane incorporating the 23-membered crown ether through chiral HPLC, we studied its racemization at elevated temperature. The rate of stereoinversion in dimethylsulfoxide (a polar solvent) was faster than that in *o*-dichlorobenzene (a nonpolar solvent), and herein we discuss these kinetic parameters.

Introduction

The stereochemistry of interlocked molecules is a fascinating topic in the study of supramolecular chemistry.[1] Indeed, chiral interlocked molecules have been used as asymmetric catalysts[2] as well as hosts for the recognition of other chiral molecules.[3] Chirality can be induced through entanglement in such interlocked molecules as rotaxanes,[4–6] catenanes,[7] and so on.[8] Fixing the positional relationship between one component and the others (breaking symmetry) can generate topologically asymmetric structures without introducing covalent bonds between the components. For examples of rotaxanes, planar chiral rotaxane consisting of directional axle and macrocyclic components, [5] point chiral rotaxane arising from the position of the macrocyclic component on the axle component,[4] and helically chiral rotaxane through double threading;[6] such chirality cannot be racemized without cleavage of covalent or mechanical bonds.

Dynamic chirality can also be induced through interlocking—namely, when an interlocked structure restricts an inversion of conformation. Mitchell and Sauvage[9] reported the enantiomeric conformers—derived from restricted rotation of the macrocyclic components—of a catenane in solution at low temperature; subsequently, they achieved partial separation of its copper complex through chiral high-performance liquid chromatography (HPLC).[10] The Stoddart group[11] observed planar (rotation of a naphthyl group), axial (rotation of biphenyl and bipyridyl groups), and helical (twisted conformation of two macrocyclic rings) chiralities in a single catenane in solution at low temperature; moreover, they achieved chiral transcription by means of a bias toward a kind of dynamic chirality in response to a chiral additive.[12,13]

The absolute locking of (dynamic) chirality resulting from interlocked structures has also been investigated. For example, Ogoshi[14] synthesized a catenane and rotaxane featuring a planar-chiral pillararene macrocycle. Leigh[4a] and Saito[15] found that changes in the position of the macrocyclic component in rotaxanes could produce point and planar chiralities, respectively. Although several examples of the regulation of rates of dynamic chirality in interlocked structures have been demonstrated, only Saito[15] has systematically examined the effects of the steric features of the axle component on the rates of racemization.

In this paper, we report the effects of interlocking on the racemization of the biphenyl moieties in simple [2]rotaxanes incorporating 23- and 26-membered biphenyl crown ethers as the macrocyclic components and ammonium ions as the dumbbell-shaped components, as well as the effects of solvent on the rates of racemization (Figure 1).

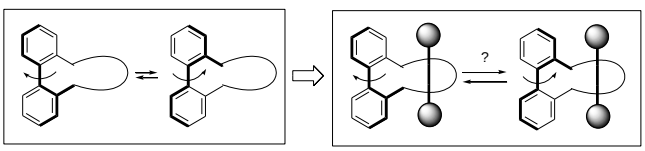


Figure 1. Schematic representation of the concept of locking dynamic axial chirality in a [2]rotaxane.

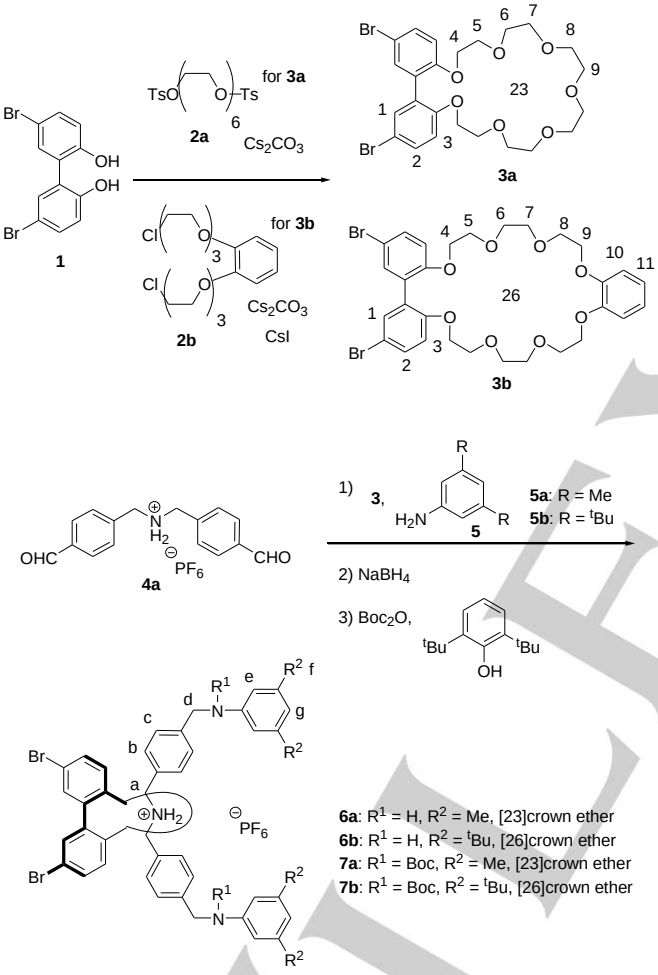
Results and Discussion

Synthesis of [2]rotaxanes 6 and 7

Scheme 1 displays our approach for the preparation of the [2]rotaxanes **6** and **7** possessing 23- and 26-membered biphenyl crown ether rings, as the macrocyclic components and secondary ammonium ions as the axle components. Cyclization of the biphenol **1**[13,16] and the ditosylate **2a**[17] or the dichloride

2b[18] in the presence of Cs_2CO_3 gave the 23- and 26-membered biphenyl crown ethers **3a** and **3b**, respectively. The reactions of the crown ethers **3**, the formylammonium salt **4**,[19] and the arylamines **5**,[20] through thermodynamic covalent chemistry,[21] followed by sodium borohydride–mediated reduction of the imino groups, afforded the [2]rotaxanes **6a** and **6b**, respectively, in their singly protonated forms. The [2]rotaxanes **6a** and **6b** were converted to the hydrophilic [2]rotaxanes **7a** and **7b**, respectively, through selective acylation of their aniline moieties,[22] allowing separation of their enantiomers through chiral HPLC.

The mass spectra of the Boc-[2]rotaxanes **7a** and **7b** featured peaks at *m/z* 1252.45 (calcd. 1252.45) and 1512.66 (calcd. 1512.66), respectively, corresponding to the species that had lost their PF_6^- anions, confirming their interlocked structures.



Scheme 1. Synthesis of the Boc-[2]rotaxanes **7**.

NMR spectral study of the dynamic chirality of the macrocycles 3 and the Boc-[2]rotaxanes 7

In the ^{1}H NMR spectrum (20 °C, 600 MHz, $CDCl_3$) of the 23-membered macrocycle **3a** (Figure 2a), the pairs of signals of the aliphatic protons were partially separated (e.g., the signals of the H_4 protons appeared at 4.03–4.07 and 4.08–4.12 ppm). Because the rate of rotation of the biphenyl moiety was slow on the NMR spectroscopic time scale, the geminal protons become chemically nonequivalent. Heating a solution of **3a** in DMSO-d_6 up to 125 °C led to peak broadening, with the two broad signals of the protons H_4 coalescing, finally these peaks overlapped at 127 °C. The rate of rotation of the biphenyl unit (k_c) 366 sec^{-1} was calculated from $\Delta\delta$ values of the signals at 120 °C (Figure S1).

We also recorded variable temperature (VT) NMR spectra of the crown ether **3b** possessing a 26-membered ring. The 4H signals, which appeared in the ^{1}H NMR spectrum at 3.53–3.60 ppm in DMSO-d_6 at 25 °C (Figure S2), broadened upon increasing the temperature. These two sets of signals coalesced at 110 °C. From the $\Delta\delta$ values at 90 °C, k_c of the crown ether **3b** in DMSO-d_6 was calculated to be 381 sec^{-1} at 110 °C.

In the ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of the [23]crown-rotaxane **6a** (Figure 2b), the signals of the aliphatic protons of the macrocyclic component appeared at 3.02–4.24 ppm, with the signals of protons H_4 and H_5 separated significantly (at 3.98 and 4.20 ppm for H_4; at 3.65 and 3.87 ppm for H_5). In addition, the signals of the diastereotopic benzylic protons H_a in the axle component were split in two (3.73 and 3.94 ppm). In contrast, the signal of the diastereotopic protons H_d appeared as a singlet at 4.35 ppm. With the macrocyclic component encircling the dialkylammonium center, it is likely that only protons H_a would be influenced by the axially chiral biphenyl unit of the macrocyclic component. The signals of the [23]crown-Boc-rotaxane **7a** were similar to those of **6a**, except for those of the protons H_d, H_e, and H_g, neighboring the aniline moieties, which shifted to low-field (Figure 2c). The signals of the diastereotopic protons H_d appeared as a pair of doublets in the ^{1}H NMR spectrum of **7a**. We suspect that N-acylation led to loss of the conformational flexibility of **7a**.

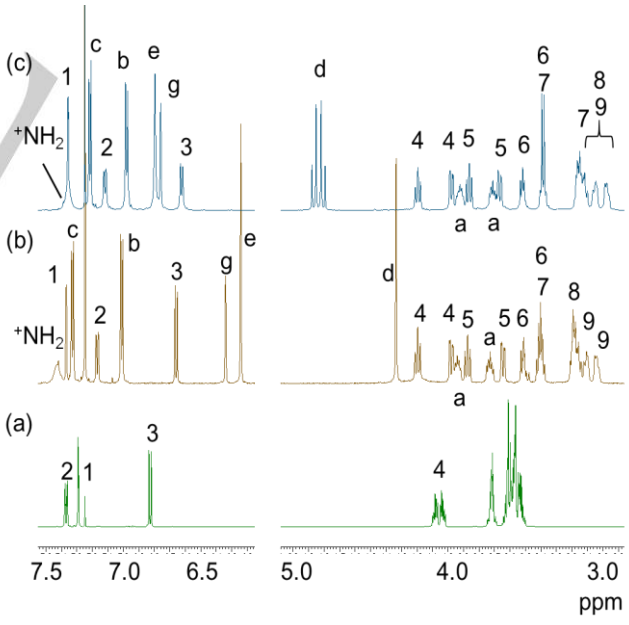


Figure 2. Partial ^{1}H NMR spectra (600 MHz, $CDCl_3$) of (a) the biphenyl[23]crown ether **3a**, (b) the [23]crown-[2]rotaxane **6a**, and (c) the [23]crown-Boc-[2]rotaxane **7a**.

To evaluate the rotation of the biphenyl moiety in **7a**, we heated its solution in DMSO-d_6 and recorded ^{1}H NMR spectra (Figure S3). We observed chemically nonequivalent signals,

suggesting slow rotation of the biphenyl moiety, in the ^{1}H NMR spectra recorded at temperatures of up to 125 °C. Thus, the rotation of the biphenyl moiety in **7a** was inhibited by the presence of the axle component, with the signals of the [23]crown ether broadening only at temperatures above 100 °C (Figure S1).

We also subjected the [2]rotaxane **7b**, incorporating the [26]crown ether, to VT NMR spectroscopy (Figures 3 and S4). In the spectra of **7b**, the signals of the aliphatic protons became broad at temperatures above 100 °C, but coalescence of these signals did not occur at temperatures below 125 °C, consistent with the inhibiting effect of the threading of the axle-shaped component [recalling that the signals of the [26]crown ether **3b** coalesced at 125 °C (Figure S2)].

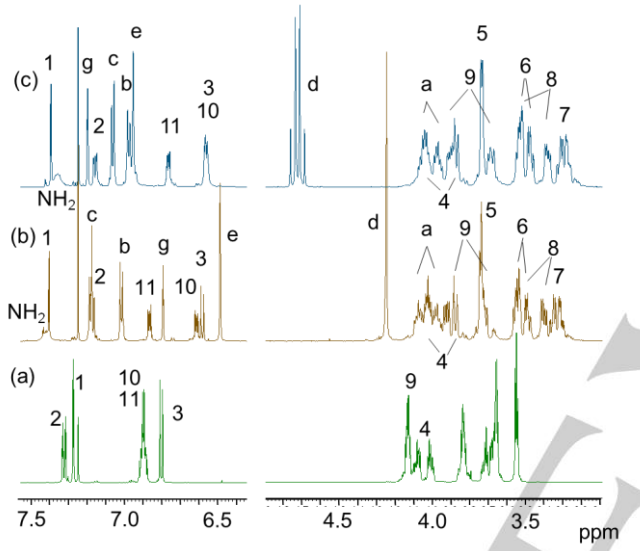


Figure 3. Partial ^{1}H NMR spectra (600 MHz, $CDCl_3$) of (a) the biphenyl[26]crown ether **3b**, (b) the [26]crown-[2]rotaxane **6b**, and (c) the [26]crown-Boc-[2]rotaxane **7b**.

Chiral HPLC separation of the enantiomers of the [2]rotaxanes 7

We separated the enantiomers of the [23]crown-Boc-rotaxane **7a** through chiral HPLC using CHIRALPAK IA-3 as the stationary phase (Figure S10). Two peaks of equal area appeared in the HPLC chromatogram of **7a**. After separation of these enantiomers, we prepared their solutions in several solvents and monitored them through chiral HPLC at room temperature. The enantiomeric excess in each solution did not change after three days at room temperature. We then heated the solutions of chiral **7a** at 60–90 °C to monitor the racemization process. Because the heating resulted in decomposition of **7a**, we could not estimate the exact rate of racemization.

The enantiomers of the [26]crown-Boc-rotaxane **7b** were partially separated using the same chiral stationary phase (Figure S11). The chromatograms of **7b** revealed evidence for interconversion of the enantiomers during HPLC analysis.[23] Namely, the two usual peaks and a plateau peak were present in the chromatograms; the ratio of the peak areas was dependent on the retention time, and changed with respect to the flow rate. We roughly integrated the three peaks, assigning the two peaks and the plateau to the non-racemized and racemized species, respectively. The plot of the concentrations of the non-racemized products provided a first-order curve. We obtained the racemization rate constant *k* from the slope of the straight line of the plot of ln[(peak area of enantiomers)/(all area)] with respect to time (*t*); we calculated a half-life (τ) of 0.54 h (Figure 4).

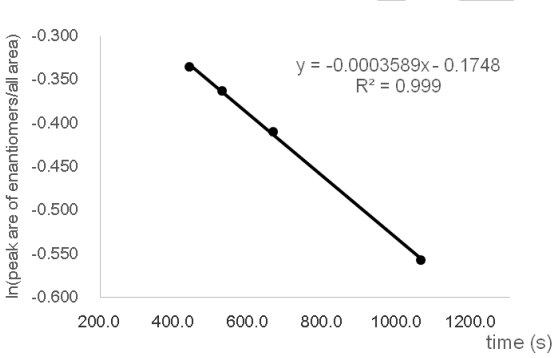
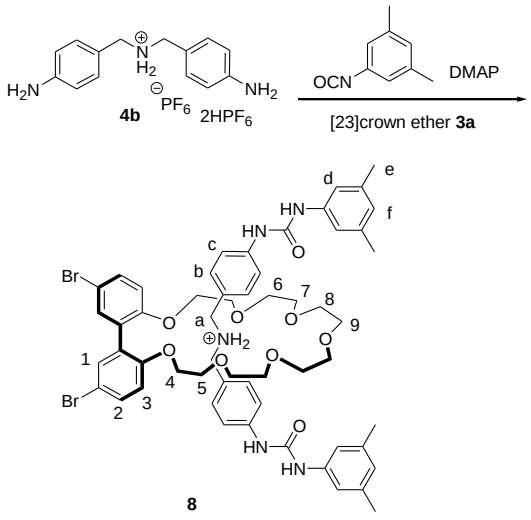


Figure 4. First-order plot for the racemization of the [26]crown-Boc-[2]rotaxane **7b** under HPLC conditions.

Synthesis of urea-rotaxane 8

Because we could not examine the racemization of the [23]crown-Boc-rotaxane **7a** as a result of its low stability, we synthesized the stable urea-rotaxane **8** from the ammonium salt **4b** and the [23]crown ether **3a** (Scheme 2). After treatment of **4b** with DMAP in the presence of **3a** in dichloroethane and CH_3CN (thereby deprotonating the anilinium moiety of **4b** and forming the pseudorotaxane), we obtained the rotaxane **8** through urea formation. The mass spectrum of **8** featured a signal at *m*/*z* 1110.32, corresponding to the species $[\mathbf{8} - PF_6^-]^+$ (calcd. *m*/*z* 1110.32). In the ^{1}H NMR spectrum of **8** (600 MHz, CD_3CN; Figure 5), the signals of the protons H_4 (4.05 and 4.30 ppm) and H_5 (3.69 and 3.89 ppm) of the macrocyclic component were widely separated as pairs, with the signals of the diastereotopic protons H_a appearing as sets near 3.7 and 3.9 ppm, similar to the spectral features of the [23]crown-rotaxane **6a**.



Scheme 2. Synthesis of the [23]crown-urea-[2]rotaxane **8**.

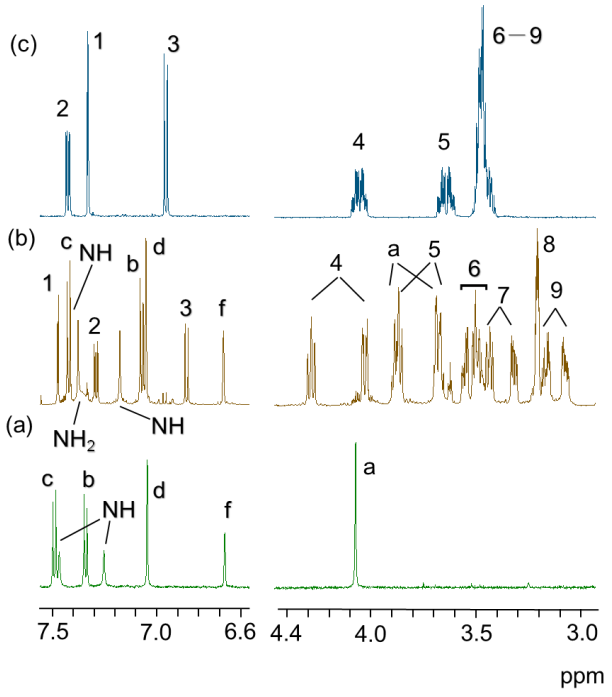


Figure 5. Partial ^{1}H NMR spectra (600 MHz, CD_3CN) of (a) the axle-shaped molecule **9**, (b) the [23]crown-urea-[2]rotaxane **8**, and (c) the biphenyl[23]crown ether **3a**.

HPLC analysis of the chiral urea-rotaxane 8

The chiral-HPLC chromatogram of the rotaxane **8** featured two peaks of equal area (Figure S12), as expected for a 1:1 mixture of its two enantiomers. After separation through CHIRALPAK IB (first fraction: 86% ee; second fraction: 94% ee), we examined the kinetics of the racemization of the urea-rotaxane **8** in DMSO and *o*-dichlorobenzene as solvents.

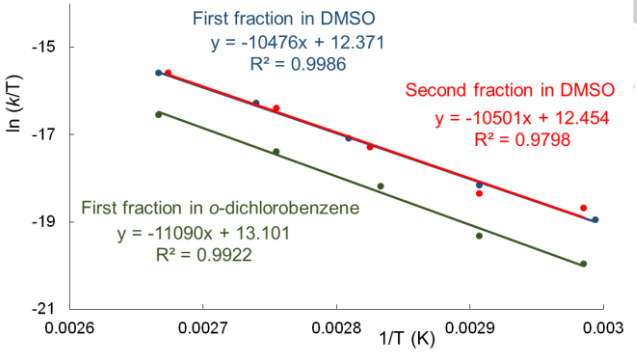


Figure 6. Eyring plots for the racemization of the [23]crown-urea-[2]rotaxane **8**. Blue: **8** (first fraction) in DMSO; red: **8** (second fraction) in DMSO; green: **8** (first fraction) in *o*-dichlorobenzene.

We prepared solutions of the enantiomers of **8** in these two solvents, heated them at 61–102 °C, and monitored their racemization using chiral HPLC. We observed first-order racemization in each solvent (Figure S13 for DMSO; Figure S14 for *o*-dichlorobenzene), with the racemization in DMSO proceeding approximately twice as fast as that in *o*-dichlorobenzene near 80 °C. Eyring plots of the data for the racemization of **8** yielded straight lines (Figure 6); Table 1 lists the corresponding kinetic parameters. The data for the racemizations of both enantiomers in DMSO were good in agreement. From a comparison of the two solvents, we concluded that the racemization in DMSO was enthalpically favorable, but entropically disfavored. In the transition state, the biphenyl moiety ought to be flat, with the resulting narrow cavity of the crown ether potentially weakening (breaking) the hydrogen bond(s) (Figure 7). Therefore, upon proceeding to the transition state, energy would be needed to weaken (break) the hydrogen bonds in *o*-dichlorobenzene, the nonpolar solvent (i.e., an enthalpic cost). In contrast, because the hydrogen bond–acceptor DMSO can weaken (break) hydrogen bonds, the transition state for racemization in DMSO would be enthalpically favorable, but the complexation of the [2]rotaxane with DMSO would be associated with an entropic cost. Other possibility of the solvent effect is ion pairing. The neighboring counter anion (PF_6^-) could sterically inhibit the rotation of biphenyl unit in the rotaxane because of tight ion-pairing in nonpolar *o*-dichlorobenzene. Overall, the DMSO-assisted transition state would decrease the free energy of activation ($\Delta G^{\ddagger}$).

Table 1. Kinetic parameters of the racemizations of the crown ethers **3** and the [2]rotaxanes **7a** and **8**.

substrate	solvent	$\Delta H^{\ddagger}$ kJ/mol	$\Delta S^{\ddagger}$ J/mol K	$\Delta G^{\ddagger}$ kJ/mol	half-life h temperature
3a [23]crown	DMSO-d_6	ND	ND	ND	5.3x10^{-7} [a] (127 °C)
3b [26]crown	DMSO-d_6	ND	ND	ND	5.0x10^{-7} [a] (110 °C)
7b	Mixed solvent[b]	ND	ND	ND	0.54[c] (RT)
8	DMSO[d]	87.1	–94.6	115.3	14 (83 °C)
	DMSO[e]	87.3	–94.0	115.3	18 (81 °C)
	$C_6H_4Cl_2$	92.2	–88.6	118.6	43 (80 °C)

[a] Determined by VT NMR analysis. [b] Trifluoroacetic acid/diethylamine /hexane/$CHCl_3$, 1:1:500:500. [c] Determined by retention-time-dependent HPLC analysis. [d] First fraction of the enantiomer was used for the racemization. [e] Second fraction of the enantiomer was used for the racemization.

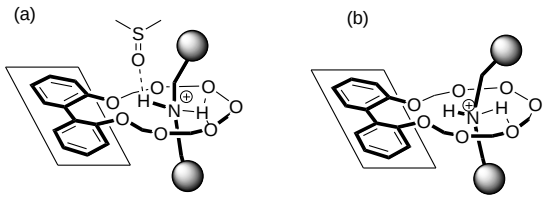


Figure 7. Proposed transition states for the racemizations of the [23]crown-urea-[2]rotaxane **8** in (a) DMSO and (b) *o*-dichlorobenzene.

Summary

We have synthesized [2]rotaxanes comprising 23- and 26-membered biphenyl crown ethers as macrocyclic components and secondary ammonium ions as dumbbell-shaped components and investigated the effects of interlocking on the dynamic axial chirality of their biphenyl moieties. VT NMR

spectra of the [23]- and [26]crown ethers **3** and the [23]- and [26]crown-Boc-[2]rotaxanes **7** revealed inhibition of racemization of the biphenyl moieties in the [2]rotaxanes, a direct result of the interlocking. The racemization of the [26]crown-Boc-[2]rotaxane **7b** proceeded at room temperature, with retention-time-dependent HPLC analysis revealing a half-life (τ) of 0.54 h under the HPLC conditions. In contrast, both enantiomers of the [2]rotaxanes **7a** and **8**, incorporating the 23-membered biphenyl crown ether as the macrocyclic component, could be isolated using chiral HPLC. Because no racemization of the [23]crown-[2]rotaxanes occurred at room temperature, we concluded that the size of the crown ether ring affected the dynamics of racemization of the biphenyl (axially chiral) unit. Racemization of the [2]rotaxane **8** in DMSO and *o*-dichlorobenzene occurred at high temperature, with DMSO enhancing the rate of racemization. The chiral HPLC monitoring provided the kinetic parameters for the racemization processes, which were enthalpically and entropically favorable in polar DMSO and nonpolar *o*-dichlorobenzene, respectively

Experimental Section

Materials and General Methods

The biphenyl **1**,[13] the ditosylate **2a**,[17b] the ammonium salt **4a**,[19b] and 3,5-di-*tert*-butylaniline **5b**[20] were prepared according to previously reported procedures. The dichloride **2b**[18] was prepared using the method described in the Supporting Information. DMF and dichloroethane were dried over 4-Å molecular sieves. Other solvents and commercially available chemicals were used as received. ^{1}H and ^{13}C NMR spectra were recorded using ECX-500II and ECA-600II spectrometers, with tetramethylsilane (TMS) as the internal standard. Mass spectra were recorded using JEOL JMS-700T (FAB) and Bruker Daltonics autoflex (MALDI) spectrometers. Infrared spectra were recorded using a Shimadzu FTIR-8600PC spectrometer. HPLC was performed using a Shimadzu LC-20AT apparatus, an SDD-M20A detector, and DAICEL CHIRALPAK IA3 (0.46 × 25 cm for analysis), IB3 (0.46 × 25 cm for analysis), IA (1.0 × 25 cm for isolation of enantiomers), and IB (1.0 × 25 cm for isolation of enantiomers) chiral columns. All reactions were performed under a positive atmosphere of dry N_2. All solvents were removed through rotary evaporation under reduced pressure. Silica gel column chromatography was performed using Kanto Chemical silica gel 60N. Thin-layer chromatography was performed using Merck Kieselgel 60PF_{254}.

[23]Crown ether 3a
A suspension of the biphenol **1** (1.05 g, 3.05 mmol), the ditosylate **2a** (1.99 g, 3.39 mmol), and Cs_2CO_3 (4.20 g, 12.9 mmol) in dry DMF (200 mL) was stirred for 72 h at 110 °C. After evaporation of the solvent, the residue was treated with dil. HCl aq. and extracted with AcOEt. The combined organic phase was washed with water and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified through column chromatography (SiO_2; CH_2Cl_2/toluene/AcOEt, 1:1:1) to afford a white solid (0.87 g, 48%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.51–3.67 (m, 16H), 3.70–3.77 (m, 4H), 4.03–4.07 (m, 2H), 4.08–4.12 (m, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 7.31 (d, *J* = 2.7 Hz, 4H), 7.39 (dd, *J* = 8.9 and 2.7 Hz, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 68.8, 69.8, 70.5, 70.7, 70.9, 112.6, 114.0, 129.2, 131.5, 133.6, 155.7 (one aliphatic carbon signal overlapping/missing). HRMS (FAB) calcd. for $C_{24}H_{31}Br_2O_7^+$ [M + H]$^+$: *m/z* 589.0431, found: 589.0427. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3009, 2925, 2872, 1496, 1485, 1452, 1290, 1271, 1246, 1129, 907. Mp: 68–73 °C (^{i}Pr_2O).

[26]Crown ether 3b
A suspension of the biphenol **1** (2.50 g, 7.27 mmol), the dichloride **2b** (3.29 g, 8.00 mmol), Cs_2CO_3 (9.57 g, 29.4 mmol), and CsI (0.38 g, 1.5 mmol) in dry DMF (250 mL) was stirred for 72 h at 110 °C. After evaporation of the solvent, the residue was treated with dil. HCl aq. and extracted with AcOEt. The organic phase was washed with water and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified through column chromatography (SiO_2; CH_2Cl_2/toluene/AcOEt, 2:1:1) to afford a colorless oil (1.06 g, 21%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.54–3.58 (m, 4H), 3.64–3.76 (m, 8H), 3.81–3.88 (m, 4H), 3.99–4.05 (m, 2H), 4.07–4.18 (m, 6H), 6.81 (d, *J* = 8.6 Hz, 2H), 6.88–6.94 (m, 4H), 7.28 (d, *J* = 2.4 Hz, 2H), 7.34 (dd, *J* = 8.6 and 2.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 68.6, 69.0, 69.6, 69.7, 70.8, 112.5, 114.0, 114.2, 121.4, 129.2, 131.4, 133.4, 148.9, 155.6 (one aliphatic carbon signal overlapping/missing). HRMS (FAB) calcd. for $C_{30}H_{35}Br_2O_8^+$ [M + H]$^+$: *m/z* 681.0693, found: 681.0713. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3011, 2930, 2874, 1595, 1506, 1485, 1452, 1255, 1128, 1059, 908, 843.

[23]Crown-[2]rotaxane 6a
A solution of the crown ether **3a** (1.04 g, 1.76 mmol) and the ammonium salt **4a** (0.773 g, 1.94 mmol) in 1,2-dichloroethane (8 mL) and CH_3CN (6 mL) was heated at 50 °C for 55 h. 3,5-Dimethylaniline (**5a**; 1.38 mL, 10.2 mmol) was added and then the mixture was heated at 50 °C for 63 h. After cooling to room temperature, the mixture was diluted with EtOH (3 mL). $NaBH_4$ (0.338 g, 8.93 mmol) was added at 0 °C and then the mixture was stirred overnight at 60 °C. The excess $NaBH_4$ was quenched with 10% HCl aq. and then the mixture was neutralized with sat. $NaHCO_3$ aq. After evaporation of the organic solvent, the aqueous phase was extracted with CH_2Cl_2. The organic phase was washed sequentially with 5% HPF_6 aq., water, and sat. NaCl aq., dried (Na_2SO_4), and concentrated. The residue was purified through column chromatography (SiO_2; CH_2Cl_2/acetone, 20:1) to give a white solid (1.03 g, 49%). ^{1}H NMR (600 MHz, CD_3CN): δ 2.11 (s, 12H), 2.89–2.94 (m, 2H), 2.98–3.02 (m, 2H), 3.04–3.11 (m, 4H), 3.15–3.20 (m, 2H), 3.30–3.35 (m, 2H), 3.36–3.42 (m, 2H), 3.45–3.50 (m, 2H), 3.61–3.65 (m, 2H), 3.69–3.76 (m, 2H), 3.79–3.85 (m, 2H), 3.88–3.95 (m, 2H), 3.97–4.02 (m, 2H), 4.18–4.24 (m, 2H), 4.25–4.30 (m, 4H), 4.80–4.91 (m, 2H), 6.21 (br s, 4H), 6.25 (br s, 2H), 6.74 (d, *J* = 8.9 Hz, 2H), 7.04–7.08 (m, 4H), 7.16 (dd, *J* = 8.9 and 2.9 Hz, 2H), 7.27–7.40 (m, 6H), 7.45 (d, *J* = 2.9 Hz, 2H). ^{13}C NMR (125 MHz, CD_3CN): δ 21.6, 47.6, 52.3, 69.5, 71.3, 71.5, 71.8, 111.9, 113.4, 115.8, 119.8, 128.3, 128.6, 130.7, 131.0, 132.8, 135.7, 139.4, 143.0, 149.4, 155.6. HRMS (MALDI) calcd. for $C_{56}H_{68}Br_2N_3O_7^+$ [M – PF_6]$^+$: *m/z* 1052.3419; found: 1052.3351. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3449, 3040, 2912, 2873, 1602, 1513, 1478, 1452, 1353, 1226, 1100, 1080, 960, 848, 558.

[26]Crown-[2]rotaxane 6b
A suspension of the crown ether **1b** (0.363 g, 0.530 mmol) and the ammonium salt **4a** (0.194 g, 0.490 mmol) in $CHCl_3$ (10 mL) and CH_3CN (5 mL) was stirred for 13 h at room temperature. After evaporation of the solvent, $CHCl_3$ (8 mL) and 3,5-di-*tert*-buthylaniline (**5**; 509 mg, 2.48 mmol) were added and then the mixture was stirred overnight at 40 °C. After cooling, the mixture was diluted with EtOH (4 mL). $NaBH_4$ (133 mg, 3.52 mmol) was added at 0 °C and then the mixture was stirred overnight at room temperature. The excess $NaBH_4$ was quenched with 10% HCl aq. and then the mixture was neutralized with sat. $NaHCO_3$ aq. After evaporation of the organic solvent, the aqueous phase was extracted with CH_2Cl_2. The organic phase was washed sequentially with 5% HPF_6 aq., water, and sat. NaCl aq., dried (Na_2SO_4), and concentrated. The residue was purified through column chromatography (SiO_2; toluene/THF, 7:1) to give a colorless oil (266 mg, 37%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.27 (s, 36H), 3.24–3.45 (m, 6H), 3.46–3.59 (m, 6H), 3.65–3.78 (m, 6H), 3.86–4.12 (m, 10H), 4.25 (s, 4H), 6.50 (d, *J* = 1.6 Hz, 4H), 6.59 (d, *J* = 8.9 Hz, 2H), 6.60–6.64 (m, 2H), 6.80 (t, *J* = 1.6 Hz, 4H), 6.86–6.90 (m, 2H), 7.01–7.04 (m, 4H), 7.16–7.21 (m, 6H), 7.41 (d, *J* = 2.8 Hz, 2H), 7.36–7.48 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 31.5, 34.8, 47.8, 52.0, 68.1, 69.3, 69.4, 70.3, 70.5, 71.1, 107.5, 112.2, 112.4, 113.3, 115.0, 121.6, 127.6, 127.8, 129.3, 129.4, 131.9, 134.7, 141.7, 146.7, 147.3, 151.7, 154.6. HRMS (MALDI) calcd. for $C_{74}H_{96}Br_2N_3O_8^+$ [M – PF_6]$^+$: *m/z* 1312.5559; found: 1312.5531. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3447, 3414, 2966, 2904, 2870, 1599, 1505, 1452, 1363, 1247, 1129, 1102, 1063, 956, 879, 558.

[23]Crown-Boc-[2]rotaxane 7a
A solution of the [2]rotaxane **6a** (0.304 g, 0.250 mmol), Boc_2O (700 µL, 3.00 mmol), and 2,6-di-*tert*-butylphenol (0.147 g, 0.750 mmol) in THF (10 mL) was heated at 80 °C overnight. After evaporation of the solvent, the residue was purified through column chromatography (SiO_2; CH_2Cl_2/AcOEt, 10:1) to give a white solid (0.306 g, 87%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.44 (s, 18H), 2.25 (s, 12H), 2.96–3.22 (m, 10H), 3.37–3.44 (m, 4H), 3.50–3.57 (m, 2H), 3.65–3.77 (m, 4H), 3.85–4.02 (m, 6H), 4.18–4.24 (m, 2H), 4.82 (d, *J* = 15.8 Hz, 2H), 4.88 (d, *J* = 15.8 Hz, 2H), 6.64 (d, *J* = 7.9 Hz, 2H), 6.77 (br s, 2H), 6.81 (br s, 4H), 6.97–7.02 (m, 4H), 7.13 (dd, *J* = 7.9 and 1.6 Hz, 2H), 7.21–7.26 (m, 4H), 7.31–7.43 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.3, 28.3, 51.4, 53.1, 68.5, 70.46, 70.50, 70.7, 70.9, 80.6, 113.3, 114.4, 123.9, 127.5, 127.6, 129.57, 129.64, 132.0, 134.9, 138.1, 140.2, 142.2, 154.1, 154.8. HRMS (MALDI) calcd. for $C_{66}H_{84}Br_2N_3O_{11}^+$ [M – PF_6]$^+$: *m/z* 1252.4467; found: 1252.4462. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3040, 3009, 2914, 2875, 1687, 1684, 1598, 1478,

1454, 1393, 1368, 1249, 1237, 1212, 1162, 1148, 1099, 1080, 960, 849, 558.

[26]Crown-Boc-[2]rotaxane 7b

As described above, the Boc-[2]rotaxane **7b** (white powder, 58.3 mg, 89%) was synthesized from the [2]rotaxane **6b** (51.3 mg, 35.1 μmol), Boc_2O (95.0 μL, 414 μmol), and 2,6-di-*tert*-butylphenol (21.2 mg, 105. μmol) in THF (3 mL), with purification through column chromatography (SiO_2; AcOEt). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.28 (s, 36H), 1.42 (s, 18H), 3.22–3.44 (m, 6H), 3.45–3.58 (m, 6H), 3.65–3.79 (m, 6H), 3.85–4.11 (m, 10H), 4.71 (d, *J* = 15.8 Hz, 2H), 4.76 (d, *J* = 15.8 Hz, 2H), 6.54–6.61 (m, 4H), 6.76–6.80 (m, 2H), 6.94–7.02 (m, 8H), 7.05–7.10 (m, 4H), 7.17 (dd, *J* = 8.6 and 2.6 Hz, 2H), 7.21 (t, *J* = 1.7 Hz, 2H), 7.31–7.43 (m, 2H), 7.41 (d, *J* = 2.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 28.4, 31.4, 34.8, 52.0, 53.7, 68.0, 69.2, 69.4, 70.3, 70.5, 71.0, 80.3, 112.1, 113.2, 115.1, 119.7, 120.4, 121.7, 127.5, 127.6, 129.26, 129.31, 131.9, 134.7, 140.6, 142.3, 146.5, 151.0, 154.5, 154.9. HRMS (MALDI) calcd. for $C_{84}H_{112}Br_2N_3O_{12}^+$ $[M - PF_6]^+$: *m/z* 1512.6607; found: 1512.6627. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2966, 2934, 2904, 2870, 1685, 1598, 1505, 1478, 1452, 1366, 1325, 1248, 1211, 1151, 1129, 957, 848, 558.

[23]Crown-urea-[2]rotaxane 8

A suspension of the [23]crown ether **3a** (230 mg, 0.390 mmol), the bis-ammonium salt **4b** (205 mg, 0.400 mmol), and DMAP (49.1 mg, 0.400 mmol) in 1,2-dichloroethane (1.6 mL) and CH_3CN (1.6 mL) was heated at 50 °C for 42 h. After cooling to room temperature, 3,5-dimethylphenyl isocyanate (220 μL, 1.55 mmol) was added and then the mixture was stirred for 20 h. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 (100 mL). This solution was washed sequentially with 1 M HCl aq., 5% HPF_6 aq., and water, dried (Na_2SO_4), and concentrated. The residue was purified through column chromatography (SiO_2; toluene/CH_2Cl_2/AcOEt, 2:1:1) to give a solid (150 mg, 30%). ^{1}H NMR (600 MHz, CD_3CN): δ 2.26 (s, 12H), 3.06–3.12 (m, 2H), 3.15–3.25 (m, 6H), 3.31–3.36 (m, 2H), 3.43–3.59 (m, 8H), 3.67–3.72 (m, 4H), 3.86–3.93 (m, 4H), 4.02–4.07 (m, 2H), 4.27–4.33 (m, 2H), 6.70 (br s, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 7.06–7.11 (m, 8H), 7.20 (br s, 2H), 7.31 (dd, *J* = 8.9 and 2.5 Hz, 2H), 7.33–7.43 (m, 2H), 7.40 (br s, 2H), 7.42–7.46 (m, 4H), 7.49 (d, *J* = 2.5 Hz, 2H). ^{13}C NMR (150 MHz, CD_3CN): δ 21.5. 52.1, 69.6, 71.40, 71.43, 71.5, 71.7, 72.0, 113.4, 115.9, 117.8, 119.1, 125.4, 126.0, 128.6, 131.7, 132.8, 135.7, 139.6, 140.1, 141.6, 153.4, 155.7. HRMS (MALDI) calcd. for $C_{56}H_{66}Br_2N_5O_9^+$ $[M - PF_6]^+$: *m/z* 1110.3222; found: 1110.3246. IR (KBr, ν_{max}, cm^{-1}): 3415, 3071, 2914, 2873, 1708, 1672, 1601, 1541, 1452, 1313, 1216, 1098, 1080, 960, 846, 558.

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Keywords: Rotaxane • biphenyl • axial chirality • racemization • hydrogen bond

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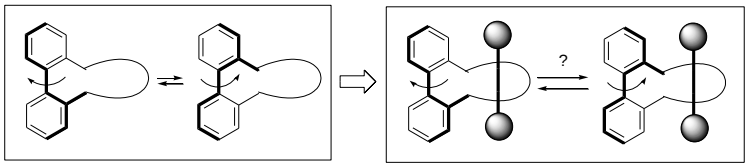

[2]Rotaxanes comprising biphenyl crown ethers as the macrocyclic components and secondary ammonium ions as the dumbbell-shaped components were synthesized. The interlocked structures inhibited racemization of the axially chiral biphenyl moieties, and the degree of locking of the dynamic axial chirality in these [2]rotaxanes dependant on ring size of the macrocycles and solvent.

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