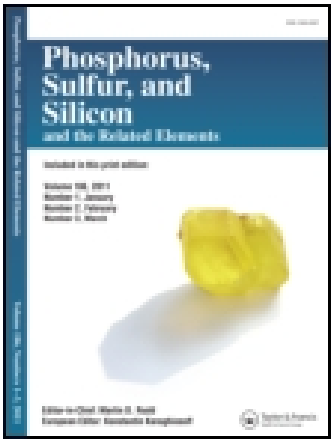


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Thiazolium-Tethering Rotaxane-Catalyzed Asymmetric Benzoin Condensation: Unique Asymmetric Field Constructed by the Cooperation of Rotaxane Components

Yuya Tachibana [a], Nobuhiro Kihara [b], Kazuko Nakazono [a] & Toshikazu Takata [a]

[a] Department of Organic and Polymeric Materials, Tokyo Institute of Technology, Tokyo, Japan

[b] Department of Chemistry, Faculty of Science, Kanagawa University, Hiratsuka, Japan

Published online: 27 May 2010.

To cite this article: Yuya Tachibana, Nobuhiro Kihara, Kazuko Nakazono & Toshikazu Takata (2010) Thiazolium-Tethering Rotaxane-Catalyzed Asymmetric Benzoin Condensation: Unique Asymmetric Field Constructed by the Cooperation of Rotaxane Components, Phosphorus, Sulfur, and Silicon and the Related Elements, 185:5-6, 1182-1205, DOI: 10.1080/10426501003773589

To link to this article: http://dx.doi.org/10.1080/10426501003773589

Phosphorus, Sulfur, and Silicon, 185:1182–1205, 2010

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426501003773589

THIAZOLIUM-TETHERING ROTAXANE-CATALYZED ASYMMETRIC BENZOIN CONDENSATION: UNIQUE ASYMMETRIC FIELD CONSTRUCTED BY THE COOPERATION OF ROTAXANE COMPONENTS

Yuya Tachibana,[1] Nobuhiro Kihara,[2] Kazuko Nakazono,[1] and Toshikazu Takata[1]

[1]*Department of Organic and Polymeric Materials, Tokyo Institute of Technology, Tokyo, Japan*

[2]*Department of Chemistry, Faculty of Science, Kanagawa University, Hiratsuka, Japan*

Asymmetric benzoin condensation of aromatic aldehydes with two kinds of optically active rotaxanes possessing thiazolium salt moieties was studied. A binaphthyl group as the chiral auxiliary was introduced in either the wheel or the axle component of the rotaxanes. Rate of the catalytic benzoin condensation of benzaldehyde with a rotaxane catalyst without the binaphthyl moiety was compared with its axle component to understand the effect of wheel component. Among several solvents used, methanol was the best solvent, which showed the highest yield (98%) of benzoin in the presence of 5 mol% of either the rotaxane and the axle catalysts. The benzoin condensations of aromatic aldehydes catalyzed by the chiral rotaxanes were studied in detail and found to give optically active benzoins with 0–32% e.e. in 5–92% yield depending on the structure of the rotaxane and the reaction conditions employed. From the results, two intrarotaxane chirality transfers are confirmed: (i) through-space chirality transfer from wheel to axle and (ii) through-bond chirality transfer controlled with an achiral wheel. Because these asymmetric reaction fields are specific to the rotaxane structure, the importance and possibility of the "rotaxane field" as a particular reaction field are demonstrated.

Keywords Asymmetric benzoin condensation; binaphthyl; rotaxane

INTRODUCTION

Rotaxane is a unique molecular system possessing spatially independent components of a wheel and axle, which can act cooperatively because they are connected by interlocking, so-called "mechanical bonding." Therefore, rotaxane skeleton has been utilized as a key structure of a variety of supramolecular systems such as molecular switches, molecular

Received 10 January 2009; accepted 2 February 2009.

Dedicated to Professor Naomichi Furukawa on the occasion of his 70th birthday.

N.K. is thankful for the Grant-in-Aid for Encouragement of Young Scientists (11750750) from the Ministry of Education, Science, Sports, and Culture. He is also grateful for the grants from The Association for the Progress of New Chemistry, The Japan Securities Scholarship Foundation, the Iketani Science and Technology Foundation, and the Yazaki Memorial Foundation for Science and Technology.

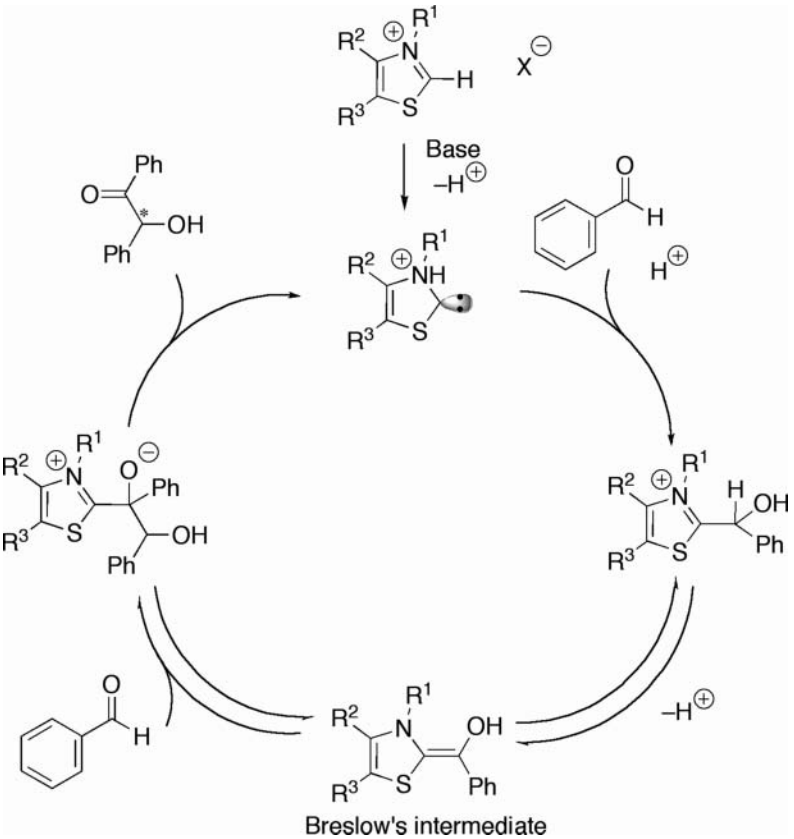
Address correspondence to Toshikazu Takata, Department of Organic and Polymeric Materials, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152-8552, Japan. E-mail: ttakata@polymer.titech.ac.jp

machines, and so on.[1] We have also reported various rotaxane-based supramolecular systems[2] including through-space photoinduced electron transfer system for the artificial photosynthetic system,[3] molecular switch, and molecular motor. Furthermore, we have found the unusual stabilization of a functional group placed on the axle component by the presence of the wheel component.[4] Thus the rotaxane system can provide a quite fascinating scaffold for the construction of functionalized supramolecular systems such as catalysts utilizing the unique characteristics of the "rotaxane field." We envisioned the significance of a novel asymmetric field constructed by the cooperation of rotaxane components, which prompted us to consider the benzoin condensation from the reaction mechanism involving controllable reactive intermediate as suggested by Breslow.[5] We have recently succeeded in developing the first rotaxane catalysts for the asymmetric benzoin condensation.[6] This article describes the synthesis and characteristics of the chiral rotaxane catalysts in detail.

RESULTS AND DISCUSSION

Design of Rotaxane Catalyst for Benzoin Condensation

Breslow's mechanism (Scheme 1) reveals that the stereoselectivity of product benzoin in typical benzoin condensation is determined at the step of the addition of second



Scheme 1 Catalytic cycle of benzoin condensation.

benzaldehyde to the catalyst–substrate adduct, so-called Breslow intermediate.[5] Namely, the stereochemistry of both the initial benzaldehyde adduct, thiazolinilydene benzyl alcohol, and the attack of second benzaldehyde at *re* or *si* face of the adduct undoubtedly determines the stereochemistry of the benzoin. Therefore, the substituents of the thiazolium moiety would control the direction of the second addition to benzaldehyde.

Many asymmetric catalysts such as thiamine **1** for the benzoin condensation have appeared so far, as shown in Figure 1. The first research on the asymmetric benzoin condensation was presented by Sheehan and Hunnemann in 1966 employing the chiral thiazolium salt (+)-**2** as the catalyst precursor,[7] although the observed enantiomeric excess of the benzoin was as low as 2%. Using modified thiazolium salts such as **3**, Sheehan and Hara could obtain the benzoin with 52% e.e. and 6% chemical yield.[8] Since these reports, various chiral thiazolium salts have been synthesized as the catalysts for the asymmetric benzoin condensation, although the enantioselectivity was not as high (1–57%).[9] Thiazolium salt **3** seems to be the best catalyst among those reported so far, which gave satisfactory enantioselectivity (47–57% ee) and chemical yield (20–30%).[10] A new type of thiazolium salt catalysts having C_2-symmetry was also studied (Figure 1, **4**).[11] On the other hand, rather high enantioselectivity (86% ee) was achieved with triazolium salts[12–14] such as **5**[12] and **6**[13] due to the advantageous introduction of two *N*-substituents around the reaction center. This might suggest that the enantioselectivity can be enhanced by the groups spatially arranged around the reaction center, in addition to the *N*-substituent, in the rotaxane catalyst system in which components are combined through space.

Prior to the design of asymmetric rotaxane catalysts, the effect of the presence of the wheel component on the reaction rate was studied, because the reaction might be severely

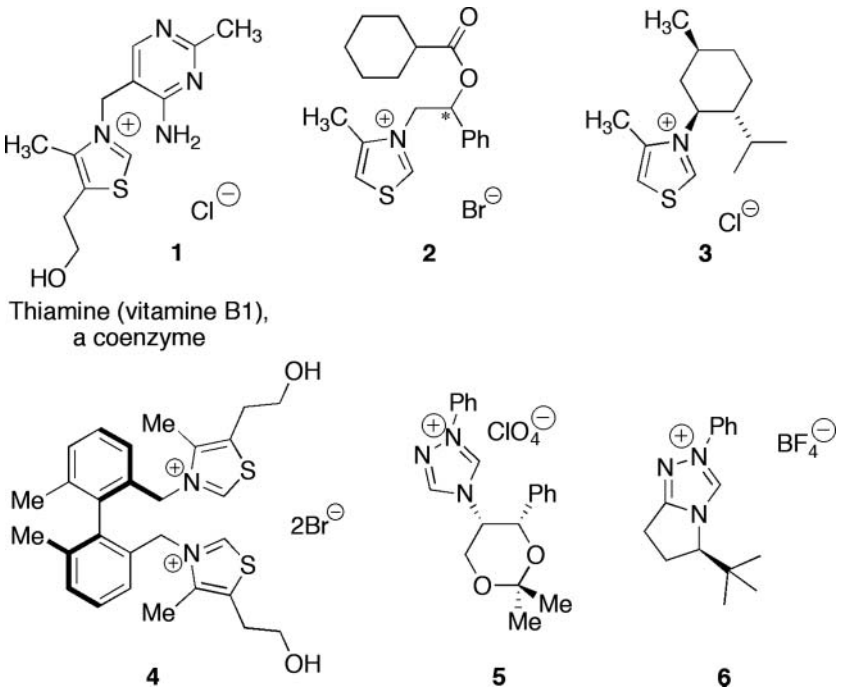
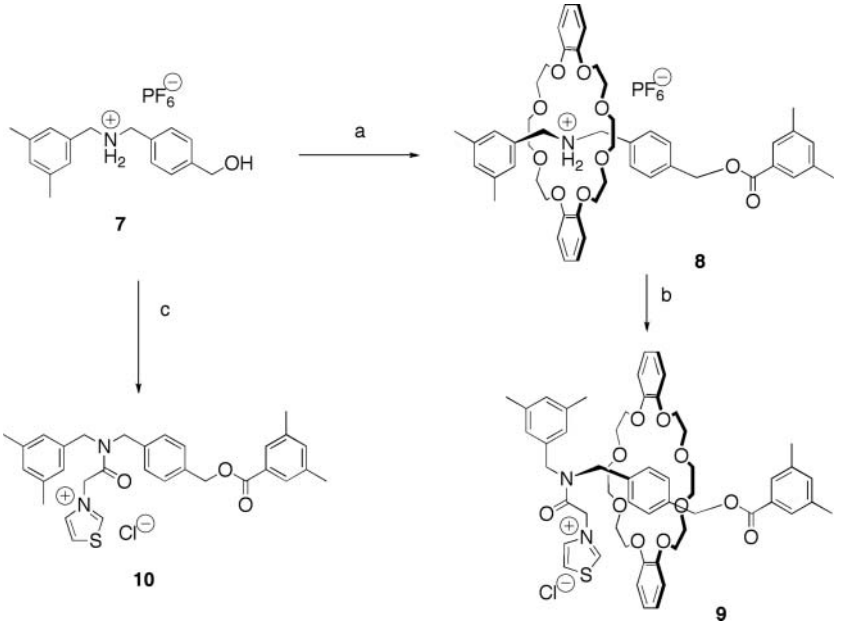


Figure 1 Chiral thiazolium and triazolium salts for the enantioselective benzoin condensation.

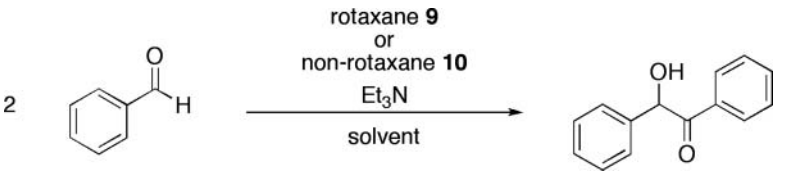
disturbed by the presence of the "big" wheel component when the thiazolium salt group is introduced in the axle component, at which the thiazolium salt group is placed for the synthetic requirement. For this purpose, two new thiazolium salt catalysts, i.e., achiral rotaxane catalyst **9** having thiazolium salt moiety at the axle component and non-rotaxane catalyst **10** (axle catalyst) were prepared to compare their catalytic activity. Scheme 2 illustrates the synthetic routes of these catalysts. The precursor rotaxane **8** was synthesized



Scheme 2 Preparation of rotaxane **9** and non-rotaxane **10** catalysts. (a) DB24C8, 3,5-dimethylbenzoic anhydride, Bu_3P, CH_2Cl_2, r.t., 81%; (b) 1. Chloroacetic anhydride, Et_3N, DMF, 40°C, 48 h, 76%; 2. thiazole, NaI, r.t., 3 d; 3. Amberlite IRA-400 (Cl-type), 92% (2steps); (c) 1. Chloroacetic anhydride, THF, –40°C, 16 h, 74%; 2. 3,5-dimethylbenzoic anhydride, Bu_3P, CH_2Cl_2, r.t., 8 h, 84%; 3. thiazole, NaI, r.t., 3 d; 4) Amberlite IRA-400 (Cl-type), 99% (2 steps).

in 81% yield from hydroxy-functionalized *sec*-ammonium salt **7**, dibenzo-24-crown-8-ether (DB24C8), 3,5-dimethylbenzoic anhydride, and catalyst tributylphosphane, according to the threading followed by the end-capping method.[15] Introduction of thiazolium salt moiety into the rotaxane axle was carried out at the ammonium nitrogen atom of the rotaxane axle by *N*-chloroacetylation[16] followed by the substitution with thiazole, because of the easy modification in addition to the prompt neutralization of the ammonium moiety. The yield of the chloroacetylation was 76%, while that of the thiazolium introduction was 92%. Final rotaxane catalyst **9** was obtained in 92% yield by the counter anion exchange with Cl^-. By a similar treatment of the hydroxy-functionalized *sec*-ammonium hexafluorophosphate **7** with chloroacetic anhydride, 3,5-dimethylbenzoic anhydride for the OH-acylation, thiazole, and Amberlite IRA-400 (Cl-type), the non-rotaxane catalyst **10** was obtained in 62% overall yield.

When the benzoin condensation of benzaldehyde (0.40 M) with two catalysts **9** and **10** (10 mol%) was carried out in the presence of triethylamine (20 mol%) in methanol at 50°C, benzoin was obtained as the product in a high yield (Scheme 3). The reaction rate



Scheme 3 Benzoin condensation catalyzed by rotaxane **9** and non-rotaxane **10**''.

was evaluated by plotting the yield of benzoin vs. time, as shown in Figure 2, where the reaction progress was monitored by ^{1}H NMR.

Although the initial rate of the condensation with the non-rotaxane catalyst **10** was two times larger than that with rotaxane catalyst **9**, the yield of benzoin reached ca. 80% within 3 h in each case. This result suggests that the crown ether wheel certainly controls the reaction kinetically due probably to the sterically bulky group positioned near the reaction center, but the degree of the rate degradation is not so serious, indicating the possible enantioselectivity during the benzoin condensation with chiral rotaxane catalyst.

Enantioselectivity is often affected by not only the sterically asymmetric field, but also the weak interactions such as π-stacking and hydrogen bonding, especially in supramolecular system. Since the weak interaction is strongly influenced by the property of the reaction medium solvent such as donor number and solvent polarity, effect of the solvent is one of the important issues to be settled. Furthermore the solvent-dependency of the rotaxane structure and the component mobility is also of importance for the catalytic event: The wheel component, when the axle component is fixed, can take both circum rotation and translation on the axle by Brownian motion, which is usually favored in a polar solvent. So we examined the effect of solvent in the benzoin condensation with the rotaxane catalysts (Table I). Whereas methanol or water is generally used as the solvent, it is known that deuterated solvents accelerate the reaction by heavy atom effect, as previously reported.[17] In fact, deuterated methanol used in the condensations with **9** and **10** resulted in the formation of higher yield of benzoin (83% vs. 76 or 77%, Table I, entries 1 and 7) than methanol

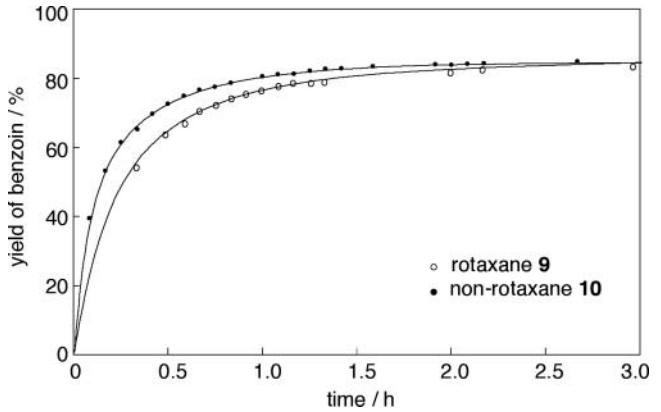


Figure 2 Plot of the yield of benzoin (%) vs. time (h) for the benzoin condensation with rotaxane **9** and non-rotaxane (axle) **10**. The reaction was carried out with benzaldehyde (0.40 M), Et_3N (0.08 M), and thiazolium salt (0.04 M) at 50°C in methanol-d_4 (0.07 mL). Initial rate of the benzoin condensation and isolated yield after 3 h: V_{int} (rotaxane **9**) $= 9.0 \times 10^{-2}$/M $\cdot$ min^{-1}, (82%), V_{int} (non-rotaxane **10**) $= 4.3 \times 10^{-1}$/M $\cdot$ min^{-1}, (82%).

Table I Effect of solvent and concentration on the yield of benzoin[a]

Entry	Cat.	(Mol%)	Solvent	Benzaldehyde/M	Yield/%
1	**9**	10	CD_3OD	0.40	83
2		10	CH_3OH	0.40	77
3		5	CH_3OH	0.80	98
4		5	DMSO	0.80	97
5		5	CH_2Cl_2	0.80	48
6		5	CH_3CN	0.80	55
7	**10**	10	CD_3OD	0.40	83
8		10	CH_3OH	0.40	76
9		5	CH_3OH	0.80	98
10		5	DMSO	0.80	98
11		5	CH_2Cl_2	0.80	34
12		5	CH_3CN	0.80	51

[a]The reaction was carried out using benzaldehyde, Et_3N (20 mol%), and thiazolium catalyst at 50°C in solvent (0.70 mL) for 24 h.

(entries 2 and 8). DMSO was a good solvent similar to methanol (entries 4 and 10). Both dichloromethane and acetonitrile afforded low yield of benzoin independent of the kind of catalyst used (entries 5, 6, 11, and 12). Thus, methanol or DMSO was concluded to be a suitable solvent. Since such a polar solvent was chosen as effective solvent, to inhibit the intermolecular interaction, but intramolecular supramolecular interaction may be still alive between the rotaxane components, which can cooperatively produce an asymmetric field.

This result seems to indicate that such a rotaxane can possesses a good asymmetric reaction field with some significant steric effects around the catalytic center.

Meanwhile, the effect of the concentration on the yield of benzoin was consistent with the reaction mechanism shown in Scheme 1: Higher concentration of the catalyst combined with lower concentration of the substrate (77% or 76%, entries 2 and 8) gave lower yield of benzoin than lower concentration of the catalyst combined with higher concentration of the substrate (98%, Table I, entries 3 and 9) did in either catalyst system.

On the basis of the above results in addition to the previous results, we have designed two types of chiral rotaxane catalysts having the thiazolium moieties on their axle components (**13** and **16**) for the asymmetric benzoin condensation. C_2 chiral binaphthyl group was chosen as a chiral auxiliary from the viewpoint of its stable chirality and spatially wider asymmetric field. The binaphthyl group was arranged at the wheel for **13** or axle component for **16**. In the case of the chiral wheel-containing rotaxane **13**, free circumrotation and translation of the wheel would construct an effective asymmetric field around the thiazolium moiety, while the spatially restricted asymmetric field placed near the bulky binaphthyl end-cap would limit the direction of second attack of substrate by the presence of the DB24C8 wheel capable of undergoing translation on the axle. MM2 calculation results of the Breslow's intermediates that are expected to be formed in the benzoin condensation also suggest the construction of potential asymmetric fields around the reaction centers of these rotaxane catalysts as shown in Figure 3. For example, the chiral auxiliary binaphthyl group on the wheel seems to make an asymmetric space near the initial benzaldehyde adduct of the thiazolium in the stable structure of the Breslow's intermediate derived from **13**.

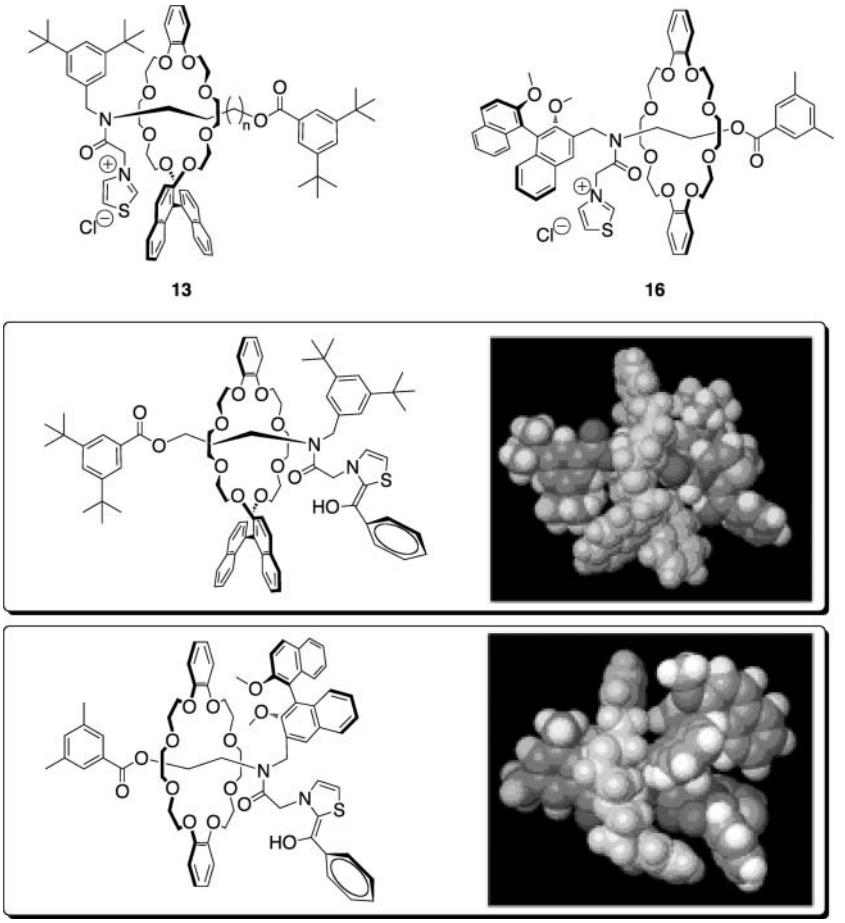
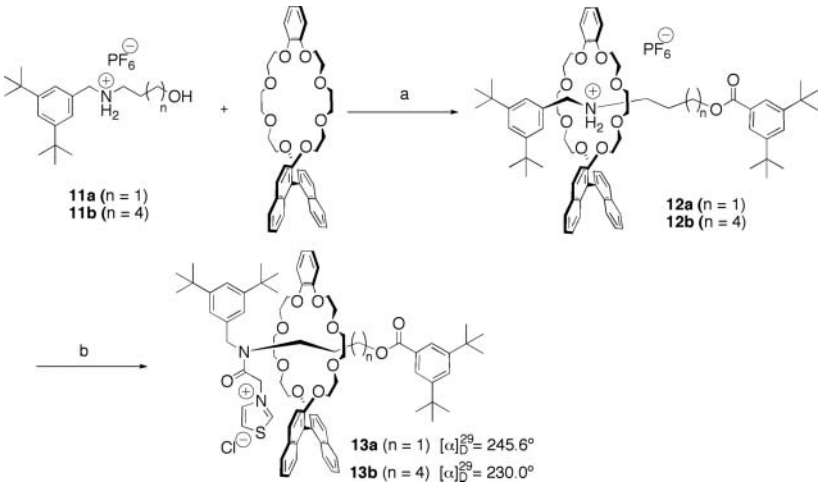


Figure 3 MM2 calculated structures of Breslow's intermediates **13Bi** and **16Bi** that are expected to be formed during the benzoin condensation catalyzed by the rotaxane catalysts **13** and **16**.

Synthesis of Optically Active Rotaxane Catalysts

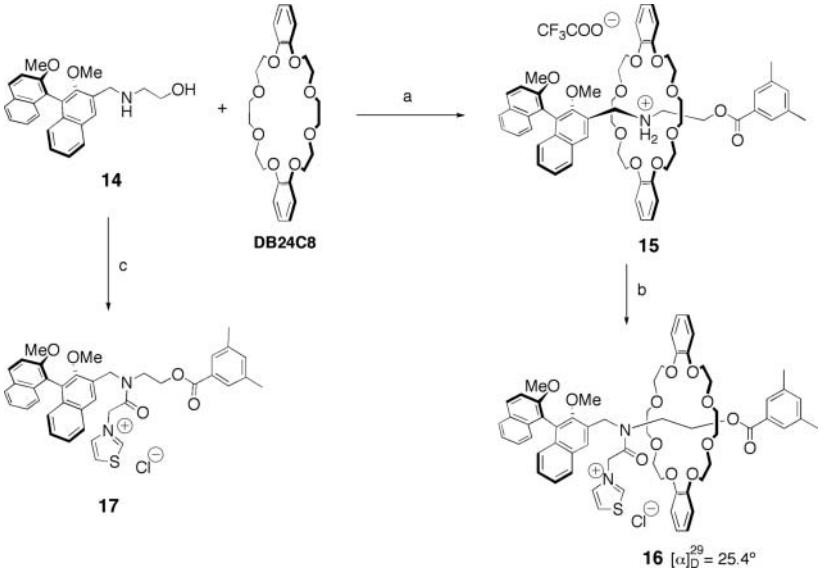
Synthetic routes of the optically active rotaxane catalysts are illustrated in Schemes 4 and 5. The chiral wheel of rotaxane **13** was synthesized from (*R*)-1,1′-bi(2-naphthol) according to the typical crown ether synthetic method (Scheme 4). Synthesis of the *sec*-ammonium salt axle part having both bulky end and hydroxy group at the termini **11** was carried out according to our previous report.[18] Trimethylene and hexamethylene chains were used as the spacers of the axle part. A mixture of the wheel component and the *sec*-ammonium salt was treated with 3,5-di-*tert*-butylbenzoic anhydride in the presence of a catalytic amount of tributylphosphane (10 mol%) at room temperature for 3 h to afford 20% ($n = 1$) and 71% ($n = 4$) yields of ammonium-type rotaxane **12**. Chloroacetylation followed by the reaction with thiazole of **12** resulted in the formation of thiazolium chloride rotaxane **13a** and **13b** in 52% and 64%, yields, respectively after the counter anion exchange with chloride ion using an ion exchange column. Low yield of shorter alkyl chain type rotaxane



Scheme 4 Synthesis of rotaxane **13** having the optically active wheel component and thiazolium salt group on the axle. (a) 3,5-Di-*tert*-butylbenzoic anhydride, Bu_3P, CH_2Cl_2, r.t., 3 h, 20% (**12a**), 71% (**12b**); (b) 1. Chloroacetic acid, Et_3N, DMF, 50°C, 24 h, 88% (n = 1), 92% (n = 4); 2. Thiazole, NaI; 3. Amberlite IRA-400 (Cl-type) 52% (**13a**, 2 steps), 64% (**13b**, 2 steps).

12a in the end-capping process is attributed to the steric hindrance of the crown ether wheel, as reported previously.

The structures of the rotaxane catalysts **13** were confirmed by specific rotation along with ^{1}H NMR, ^{13}C NMR, IR, and MS spectra in addition to elemental analysis. Figure 4



Scheme 5 Synthesis of rotaxane catalyst **16** having the optically active end-cap and the thiazoium salt on the axle. (a) 3,5-Dimethylbenzoic anhydride, Ti(*i*-OPr)$_4$, TfOH, CH_2Cl_2, r.t., 6h, 75%; (b) 1. Chloroacetic acid, Et_3N, DMF, 40°C, 24 h, 94%; 2. Thiazole, NaI, 100°C, 24 h; 3. Amberlite® IRA-400 (Cl-type), 50% (2steps); (c) 1. Chloroacetic anhydride, THF, –40°C, 15 h, 87%; 2. 3,5-Dimethylbenzoic anhydride, Bu_3P, CH_2Cl_2, r.t., 11 h, 79%; 3. Thiazole, NaI, r.t., 24 h, 99%.

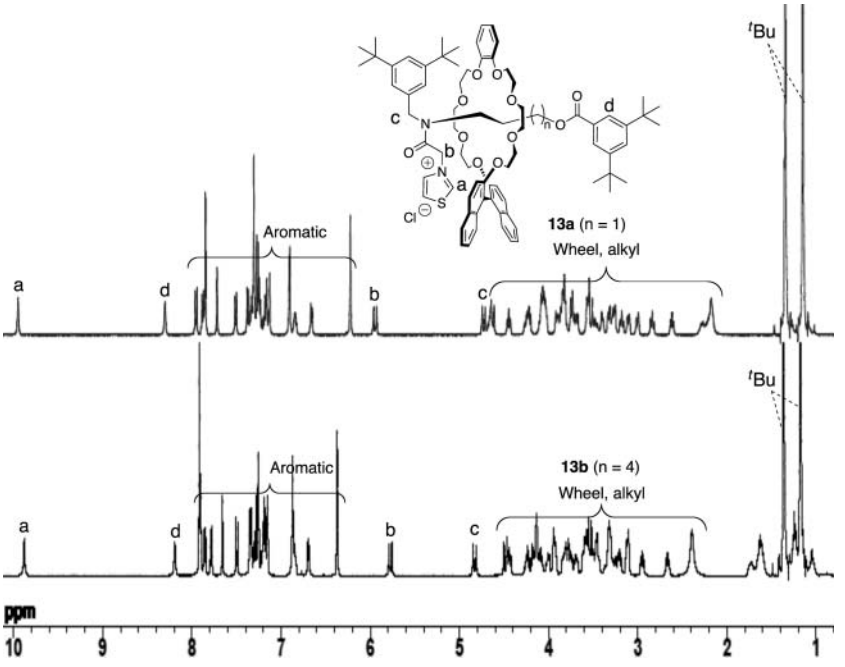


Figure 4 ^{1}H NMR spectra of chiral wheel-type rotaxane **13a** (n = 1, upper) and **13b** (n = 4, bottom) (500 MHz, $CDCl_3$, 298 K).

shows ^{1}H NMR spectra of two rotaxane catalysts **13a** and **13b**. Although both spectra are considerably too complicated to enable the detailed assignment of all signals, several characteristic signals confirm the structures of them. Namely, a thiazolium methine proton signal *a* appeared around 10 ppm due to its high acidity, while an aromatic proton signal *d* of di-*tert*-butylphenyl ring was at 8.2 ppm. Methylene signal *b* at the thiazolium linking was split probably because of the diastereotopic protons Ha and Hb. Chemical shift difference between two *b* protons of **13a** or **13b** would depend on the degree of asymmetry based on the spatial distance difference from the binaphthyl group: *b* proton signals of **13a** appeared to have a more pronounced chemical shift difference than those of **13b** because the binaphthyl group on the wheel of **13a** comes to the thiazolium group nearer than those of **13b** due to the difference of the methylene spacer length. Other spectroscopic data and elemental analysis data were clearly consistent with the proposed structure of **13**. The optical purity of **13** should be ca. 98%, since the optical purity of the starting optically active crown ether was 98% by HPLC determination using a chiral column.

The chiral axle-type rotaxane **16** was synthesized from chiral binaphthyl-functionalized axle part **14**,[17] by a procedure similar to that employed for **13** (Scheme 5). Pseudorotaxane formed in situ from **14** and DB24C8 by the assistance of trifluoromethanesulfonic acid, which was subjected to the end-capping reaction with 3,5-dimethylbenzoic anhydride in the presence of titanium tetraisopropoxide (10 mol%), giving the chiral axle-type rotaxane catalyst **16** in 75% yield.[19] Trifluoromethanesulfonic acid usually works as a very effective catalyst in the end-capping reaction with acid anhydride for the terminal OH acylation. However, no catalysis of trifluoromethanesulfonic acid was confirmed in the preparation of **16**, although the reason why it was not effective is unclear at present time.

The corresponding reference compound **17** without wheel component was also prepared from **14** by a similar method to that for **16** from **15**.

The structures of the rotaxane catalyst **16** and the axle catalyst **17** were similarly confirmed by ^{1}H NMR, ^{13}C NMR, IR, MS spectra, and specific rotation along with elemental analysis. ^{1}H NMR spectra of **16** and **17** are shown in Figure 5. Similarly to the case of the assignment of **13**, signals *a* and *d* in the down-field area were quite consistent with the structures of them, although most signals of **17** including *a* and *d* were split due to the *syn* and *anti* structures caused by the amide moiety. Since the split signal was not observed with **16**, the amide structure would be fixed as *syn* or *anti* probably because of the presence of the crown ether wheel. Diastereotopic protons signals *b* and *c* of both catalysts also support the proposed structures. All signals of **17** other than those of the aromatic region could be assignable, as shown in the spectrum. Other spectroscopic data and elemental analysis data were clearly consistent with the proposed structures of **16** and **17**. Optical purity of these catalysts should be ca. 98% for the same reason as **13**.

Rotaxane-Catalyzed Benzoin Condensation

The benzoin condensation of benzaldehydes with rotaxane catalyst **13** was carried out as shown in Scheme 6, and the results are summarized in Table II. The condensation of benzaldehyde (1.6 M) catalyzed by **13a** (0.16 M) in the presence of triethylamine (0.32 M) in methanol was carried out for 24 h at 0°C (Table II, entry 1). The product benzoin was isolated in an excellent yield (90%) by chromatographic purification. Although the asymmetric yield of **18a** (21% e.e.) was not very high (entry 1), the e.e. of **18a** increased

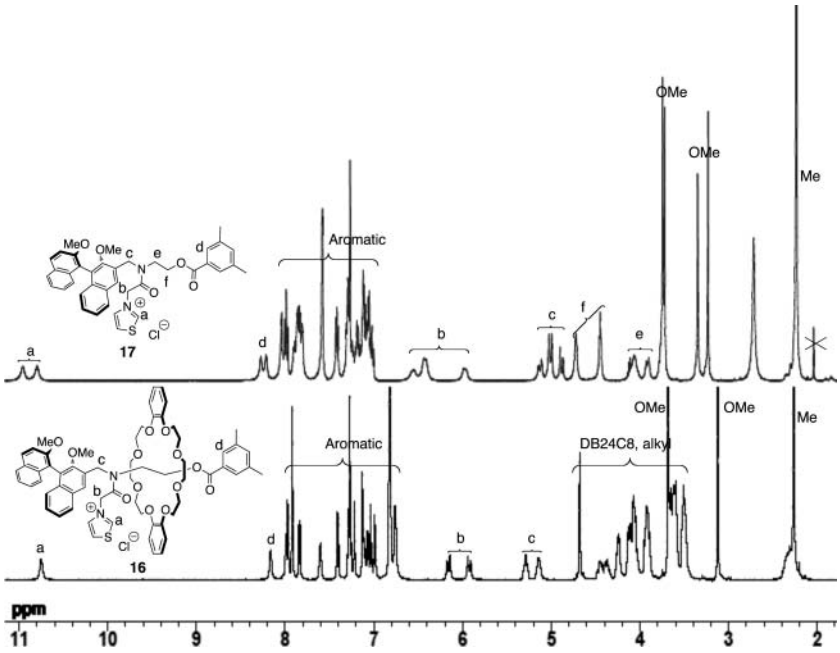
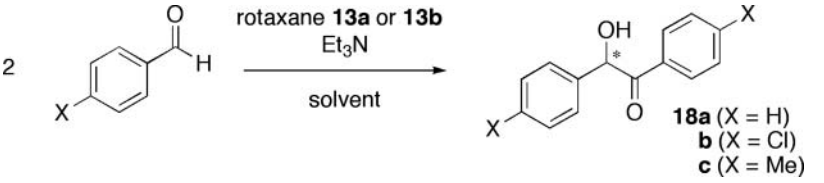


Figure 5 ^{1}H NMR spectra of chiral axle catalyst **17** (upper) and chiral axle-type rotaxane catalyst **16** (lower) (500 MHz, $CDCl_3$, 298 K).



Scheme 6 Benzoin condensation catalyzed by rotaxane **13a** and **13b**.

up to 32% (entry 2) when decreased concentration (0.016 M) of **13a** was used. The *e.e.* value of the products as determined by HPLC with a chiral column was independent of the length of the reaction period (3–24 h). The results suggest the good catalytic activity of **13a**, whereas the dependency of the e.e. value on the catalyst concentration may be indicative of the presence of two possible catalytic pathways including a stereoselection via nonsingle molecular catalysis.[20] Meanwhile no chiral induction was observed when separate dumbbell and wheel components were employed as catalyst.

The condensations at certain concentrations (0.004 M catalyst and 0.8 M substrate) were examined to characterize and compare the rotaxane catalysts **13a** and **13b** with different axle lengths. Inspection of the data of Table II (entries 1–10) revealed the through-space chirality transfer between the wheel and axle components of **13a** in terms of the formation of an optically active product. The data of Table II also show that (i) the length of the axle component slightly affects the chemical and asymmetric yields (entries 11–19); (ii) the introduction of substituents (Me and Cl) on benzaldehydes decreases the chemical

Table II Asymmetric benzoin condensation with rotaxane catalyst **13**[a]

			Aldehyde					
Entry	Cat.	(Mol%)	X	/M	Solvent	Temp./°C	Yield/%	*e.e.*/%
1	**13a**	10	H	1.6	CH_3OH	0	90	21 (*R*)
2		1		1.6	CH_3OH	0	14	32 (*R*)
3		5		0.8	CH_3OH	30	70	16 (*R*)
4		5		0.8	CH_3OH	0	34	23 (*R*)
5		5		0.8	CH_3OH	−20	17	27 (*R*)
6		5		0.8	CH_3OH	0	5	21 (*R*)[b]
7		5		0.8	DMSO	0	79	11 (*R*)
8		5	Cl	0.8	CH_3OH	0	16	18 (*R*)
9		5	Me	0.8	CH_3OH	0	10	25 (*R*)
10		5	Furfural	0.8	CH_3OH	0	39	0 (*R*)
11	**13b**	10	H	1.6	CH_3OH	0	91	12 (*R*)
12		1		1.6	CH_3OH	0	14	21 (*R*)
13		5		0.8	CH_3OH	30	73	10 (*R*)
14		5		0.8	CH_3OH	0	34	16 (*R*)
15		5		0.8	CH_3OH	−20	10	22 (*R*)
16		5		0.8	DMSO	0	81	4 (*R*)
17		5	Cl	0.8	CH_3OH	0	28	11 (*R*)
18		5	Me	0.8	CH_3OH	0	16	21 (*R*)
19		5	Furfural	0.8	CH_3OH	0	49	0 (*R*)

[a]The reaction was carried out with benzaldehyde, Et_3N (20 mol%), and catalyst in solvent (0.70 mL) for 24 h.
[b]For 3 h.

Table III Asymmetric benzoin condensation with rotaxane catalyst **16** and dumbbell catalyst **17**[a]

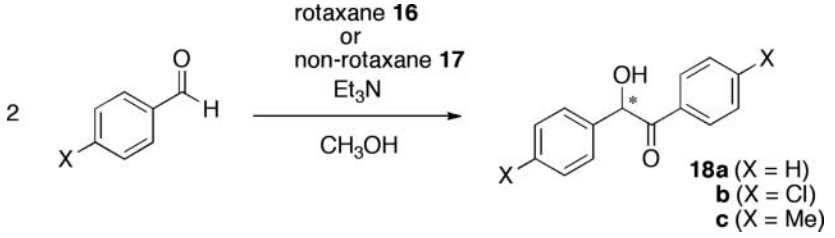
			Benzaldehyde					
Entry	Cat.	(Mol%)	X	/M	Solvent	Temp./°C	Yield/%	e.e./%
1	**16**	5	H	0.8	CH_3OH	30	82	21 (*S*)
2		5		0.8	CH_3OH	0	40	32 (*S*)
3		5		0.8	CH_3OH	–20	7	16 (*S*)
4		5	Cl	0.8	CH_3OH	0	16	18 (*S*)
5		5	Me	0.8	CH_3OH	0	22	13 (*S*)
6		5	Furfural	0.8	CH_3OH	0	19	6 (*S*)
7	**17**	5	H	0.8	CH_3OH	30	90	1 (*S*)
8		5		0.8	CH_3OH	0	65	2 (*S*)
9		5		0.8	CH_3OH	–20	56	3 (*S*)
10		5	Cl	0.8	CH_3OH	0	70	1 (*S*)
11		5	Me	0.8	CH_3OH	0	26	2 (*S*)
12		5	Furfural	0.8	CH_3OH	0	59	3 (*S*)

[a]The reaction was carried out with aldehyde (0.80 M), Et_3N (0.16 M), and thiazolium salt (0.04 M) in solvent (0.70 mL) for 24 h.

reactivity (entries 8–10, 17–19); (iii) dimethyl sulfoxide as solvent causes an increase in chemical yield and a decrease in asymmetric yield, although the degree of both yields is small (entries 7, 16); and (iv) a typical temperature effect characterized by a decrease in chemical yield and an increase in optical yield occurs as the temperature is lowered (entries 3–5, 13–15).

The molecular model studies of **13** showed that the rotation of the wheel is not free and that the binaphthyl group tends to access the thiazolium moiety to avoid the steric repulsion against the terminal bulky 3,5-di-*tert*-buthylphenyl groups of the axle. The stereoselectivity confirmed that this condensation might come from the strong influence of the crown wheel that surrounds the thiazolium moiety.

As mentioned above, a through-space chirality transfer was observed with **13**. Therefore, the rotaxane catalyst **16** having the chiral group at the end of the axle is interesting enough to evaluate the through-bond chirality transfer and to compare the degree of chirality transfer with that via through-space chirality transfer. The chirality transfer through the bond was confirmed with **16** under the same conditions (Scheme 7), although the *e.e.* values of **18** were a little lower than those of **13** as shown in Table III (entries 1–6). Interesting to note is the opposite absolute configuration of the product benzoin, which held *R* configuration when **13** was used as the catalyst while *S* configuration when **16** and **17**



Scheme 7 Benzoin condensation catalyzed by rotaxane **16** and non-rotaxane **17**.

were employed, even though the same chiral auxiliary was used. Of course it is reasonably understood because the structures of their asymmetric fields are completely different from each other. The much lower *e.e.* value of **18** with the wheel-free catalyst **17** (1–3%, Table III, entries 7–12) clearly reveals the significance of the presence of the wheel component in the stereoselection step. The role of the wheel component linked mechanically to the reaction center can be understood as one of the protections of the less stereoselective side of the asymmetric field or as one of the enhancements of the influence of the chiral environment.

Mechanism and Stereochemistry of the Enantioselective Reaction with the Rotaxane Catalysts

The initial step of the benzoin condensation is the formation of a singlet carbene by the deprotonation of thiazolium with base, as shown in Scheme 1. Then it reacts with benzaldehyde to form Breslow's intermediate (**Bi**). The second electrophilic addition of benzaldehyde to this adduct occurs under the direction control by the asymmetric field. In the case with **13**, the (*R*)-binaphthyl group accelerates the electrophilic addition of *re*-face of prochiral benzaldehyde to *si*-face of **13a**·benzaldehyde adduct (**13aBi**) as shown in Figure 6, judging from the streochemical results of the present benzoin condensation giving benzoin with *R* configuration (Table II). The addition may be assisted by the hydrogen bonding between OH group of 13aBi and carbonyl group of benzaldehyde, while one of the naphthalene plane more strongly controls the arrangement of the benzene plane of benzaldehyde by the π–π interaction between them. The other naphthalene plane may contribute to rigidify the asymmetric field by overlaying it. When the longer axle rotaxane catalyst **13b** is used, the asymmetric field is not so limited by the more free translation of the wheel component on the axle bearing the longer spacer. As a result, the degree of enantioselectivity decreases.

On the other hand, the achiral wheel component of chiral axle-type rotaxane catalyst **16** works as a steric barrier, so that the second addition of benzaldehyde to the adduct occurs mainly from the side of the binaphthyl group when the mechanism proceeds according to Figure 7. As a result, the addition favorably occurs between the *re*-face of adduct **16Bi** and *si*-face of the second benzaldehyde via the opposite fashion to that of **13**, yielding (*S*)-benzoin selectively. Because the structures of the intermediate and the transition state are

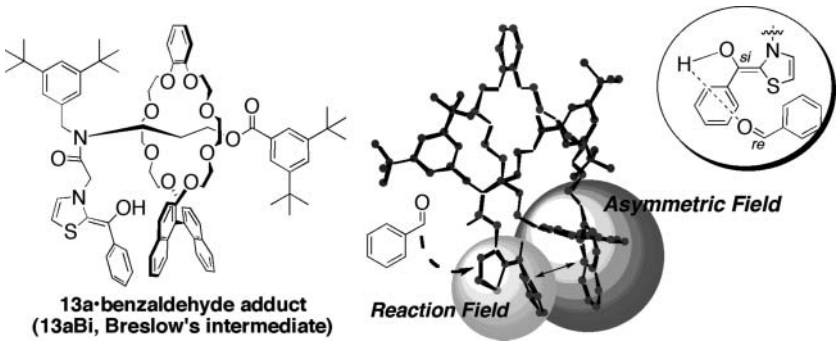


Figure 6 Mechanism of the benzaldehyde addition to **13a**·benzaldehyde adducts (**13aBi**). MM2 calculated structure of molecular model of **13a**·benzaldehyde adduct generated by MM2 calculation.

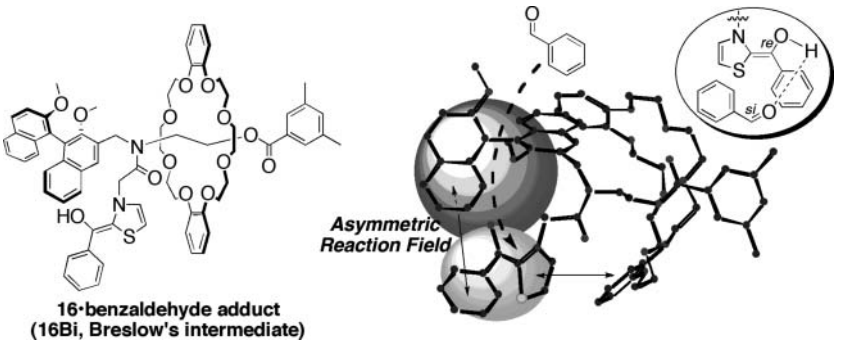


Figure 7 Mechanism of the benzaldehyde addition to **16**·benzaldehyde adducts (**16Bi**). MM2-calculated structure of molecular model of **16**·benzaldehyde adducts generated by MM2 calculation.

flexible in solution state enough to permit the amide bond rotation and the circumrotation and translation of the wheel component, the benzoin obtained with **16** has an asymmetric yield lower than that with **13**. However, the introduction of wheel component to make the rotaxane structure was very effective, and the present results emphasized the importance of the cooperation of the component in the rotaxane catalyst system.

In summary, the first rotaxane catalysis was demonstrated in this work. The results obtained here would help to clarify the fundamental features of the rotaxane structure capable of constructing a unique reaction field as exemplified in the asymmetric benzoin condensation. Study on a more precise design for the asymmetric rotaxane catalyst with higher chemical and asymmetric yields based on the guiding principle obtained here is underway.

EXPERIMENTAL

Methods and Materials

^{1}H and ^{13}C NMR spectra were recorded on JEOL GSX500 (500 MHz) and JEOL GX270 (270 MHz) spectrometers using tetramethylsilane as an internal standard. IR spectra were recorded on a Jasco FT/IR-460plus spectrometer. FAB-MS analyses were made on a Finnigan MAT TSQ-70 instrument. Melting points were measured on a Yanako MP-3 instrument. Optical rotations were measured on a Jasco DIP-1000 instrument. Preparative GPC was carried out using JAI LC-908 equipped with JAIGEL-1C and JAIGEL-2C columns. Enantiomeric excess (e.e.) was measured on a Jasco Gulliver system equipped with Daicel Chiralpak AD-H column. Acetonitrile, *N*,*N*-dimethylformamide, triethylamine, and all aldehydes were used after distillation over calcium hydride. Methanol was distilled over magnesium before use. Dichloromethane was treated with phosphorous pentoxide before distillation over calcium hydride. Other chemicals were reagent grade and used without further purification.

General Procedure for Benzoin Condensation[21]

To a solution of triethylamine and an aldehyde, a chiral thiazolium salt was added under an argon atmosphere. The reaction mixture was allowed to stand at mentioned temperature. After 24 h, the reaction mixture was evaporated to give the crude solid, which

was purified by silica gel column chromatography (eluent: dichloromethane). The product was identified as benzoin by ^{1}H NMR spectra.

Preparation of Achiral Rotaxane Catalyst 9

Rotaxane **8** was chloroacetylated by according to the literature.[16]

The *N*-chloroacetylated rotaxane (240 mg, 0.25 mmol) was dissolved in thiazole (3.0 g, 35 mmol). Then sodium iodide (38 mg, 0.25 mmol) was added to the solution, and it was stirred for 3 days. After that, it was poured into 1 M HCl (300 mL) with vigorous stirring, and the formed precipitate was combined by filtration. The precipitate was dissolved in methanol and passed through anion exchange column (Amberlite IRA-400 treated with hydrochloric acid followed by water, eluent: methanol). Thiazolium salt–thethered rotaxane **9** was obtained as white solid in 92% yield (230 mg, 0.23 mmol).

mp 209–210°C (dec.). ^{1}H NMR (500 MHz, CDCl3) δ 11.20 and 10.96 (two s, 1H), ppm. ^{13}C NMR (125.7 MHz, CDCl3) δ 166.43, 164.03, 161.41, 148.31, 148.01, 138.57, 138.00, 137.95, 137.77, 137.52, 136.59, 136.05, 134.23, 133.80, 130.49, 128.94, 128.53, 127.98, 127.65, 127.15, 126.48, 125.59, 124.62, 124.02, 120.66, 120.37, 111.51, 111.44, 69.75, 69.52, 69.45, 69.27, 67.97, 66.47, 55.69, 49.79, 49.64, 21.40, 21.33, 20.99, 20.86 ppm. IR (KBr) 2920 ($\nu_{C-H,\,as}$), 2883 ($\nu_{C-H,\,s}$), 1702 ($\nu_{C=O}$, ester), 1658 ($\nu_{C=O}$, amide), 1253 (ν_{C-O-CO}, as), 1125 ($\nu_{C-O-CO,\,s}$) cm^{-1}. FAB-MS (matrix: *m*-NBA) m/z 961.1 [M-Cl$^-$]$^+$.

Preparation of Achiral Non-Rotaxane Catalyst 10

***N*-Chloroacetylation of amino alcohol.** Amino alcohol (that is, the precursor of **7**) was previously synthesized according to the literature as the starting material. To a solution of amino alcohol (811 mg, 3.18 mmol) in THF (20 mL), a solution of chloroacetic anhydride (544 mg, 3.18 mmol) in THF (10 mL) was added at –40°C. After stirring for 16 h, the reaction mixture was washed with 5% NaOH aq. and brine. Then the organic layer was dried with magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography ($CHCl_3$, $R_f = 0.14$). *N*-Chloroacetylamide alcohol was obtained as colorless oil in 75% (493 mg, 2.36 mmol) yield.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40–7.15 (m, 4H), 6.95, 6.92 (d, $J = 6.5$ Hz, 1H), 6.82 and 6.74 (two s, 2H), 4.72–4.43 (m, 6H), 4.13 (s, 2H), 2.31 and 2.29 (d, 6H), 1.72 (br, 1H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 166.95, 166.84, 140.86, 140.45, 138.31, 137.78, 135.67, 135.06, 134.99, 134.18, 129.18, 129.12, 128.90, 127.81, 127.15, 126.83, 126.12, 125.59, 125.51, 123.90, 123.76, 123.68, 77.24, 77.16, 64.12, 64.03, 63.95, 49.97, 49.87, 49.77, 48.39, 48.31, 41.25, 41.18, 41.11, 21.03 ppm. IR (neat) 3409 (ν_{O-H}), 2918 ($\nu_{C-H,\,as}$), 2858 ($\nu_{C-H,\,s}$), 1650 ($\nu_{C=O}$) cm^{-1}.

***O*-Acylation of *N*-chloroacetylamide alcohol.** To a solution of the obtained *N*-chloroacetylamide alcohol (330 mg, 0.99 mmol) and 3,5-dimethylbenzoic anhydride (300 mg, 1.06 mmol) in dichloromethane (10 mL), tributylphosphane (25 μL, 0.10 mmol) was added at room temperature. After 8 h, the mixture was washed with 5% Na_2CO_3 aq, dried with sodium sulfate, and concentrated. The crude product was purified by silica gel column chromatography ($CHCl_3$, $R_f = 0.57$). *N*-chloroacetylamide ester was obtained as colorless oil in 84% (387 mg, 0.84 mmol) yield.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.68 (s, 2H), 7.47–7.40 (m, 2H), 7.26–7.17 (m, 3H), 6.94 and 6.91 (twos, 1H), 6.82 and 6.74 (two s, 2H), 5.35 and 5.33 (d, 2H), 4.63–4.45

(m, 4H), 4.14 (s, 2H), 2.35 (s, 6H), 2.30 and 2.29 (two s, 6H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 166.68, 166.52, 165.98, 138.19, 137.67, 137.48, 136.27, 135.78, 135.62, 135.50, 135.18, 134.20, 129.51, 129.10, 129.03, 128.85, 128.77, 128.35, 128.04, 127.94, 126.91, 126.29, 125.59, 125.55, 123.79, 123.70, 77.23, 77.16, 65.76, 65.66, 65.60, 50.15, 49.69, 48.36, 41.28, 41.21, 41.14, 20.96, 20.79 ppm. IR (neat) 2918 ($\nu_{C-H,\,as}$), 2860 ($\nu_{C-H,\,s}$), 1716 ($\nu_{C=O\ ester}$), 1658 ($\nu_{C=O\ amide}$) cm^{-1}.

The addition of thiazole to *N*-chloroacetylamide ester. To a solution of *N*-chloroacetylamide ester (360 mg, 0.78 mmol) in thiazole (1.5 mL, 21 mmol), sodium iodide (234 mg, 1.56 mmol) was added at room temperature. After 24 h, the solution was poured into a 1 M HCl (300 mL) with vigorous stirring. The formed precipitate was combined by filtration. The crude product was dissolved in methanol and passed through anion exchange column (Amberlite IRA-400 treated with hydrochloric acid followed by water, eluent: methanol). Thiazolium salt **10** was obtained as white solid. Yield 99% (446 g, 0.77 mmol).

mp 144–145°C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (s, 1H), 8.62–8.61 (m, 1H), 8.35–8.33 (m, 1H), 7.59 (d, J = 7.5 Hz, 2H), 7.43–7.29 (m, 3H), 7.29 (d, J = 7.5 Hz, 2H), 6.94–6.83 (m, 3H), 5.98 and 5.95 (two s, 2H), 5.35 and 5.31 (two s, 2H), 4.61–4.40 (m, 4H), 2.31–2.22 (m, 12H) ppm. ^{13}C NMR (125.7 MHz, DMSO-d_6) δ 165.55, 164.97, 164.85, 161.76, 138.53, 137.90, 137.71, 137.29, 136.36, 1354.94, 135.63, 135.51, 135.44, 135.03, 134.66, 134.63, 129.36, 129.00, 128.58, 128.33, 128.07, 127.85, 127.56, 126.67, 125.44, 125.03, 65.77, 65.70, 55.12, 49.63, 49.17, 48.28, 20.93, 20.72 ppm. IR (KBr) 1717 ($\nu_{C=O,\,ester}$), 1659 ($\nu_{C=O,\,amide}$), 1210 ($\nu_{C-O-CO,\,as}$) cm^{-1}. FAB-MS (matrix: *m*-NBA) m/z 513.1 [M$-$Cl$^-$]$^+$.

Preparation of Chiral-Wheel–Type Rotaxane 13a and 13b

Binaphthyl-benzo-26-crown ether: Diol precursor. To a solution of *tert*-BuOK (10.3 g, 87.2 mmol) in THF (40 mL), catechol (3.89 g, 35.0 mmol) in THF (40 mL) was added, then the mixture was refluxed for 3 h. Additionally, a solution of 2-[2-(2chloroethoxy)ethoxy]-ethanol (15.1 g, 87.5 mmol) in THF (20 mL) was added and refluxed for a further 40 h. After cooled to ambient temperature, to the reaction mixture was added 5% Na_2CO_3 aq., and it was extracted with chloroform. The combined organic layer was washed with brine, dried with magnesium sulfate, and concentrated *in vacuo*. The obtained crude product was purified by silica gel column chromatography (EtOAc:methanol = 9:1; R_f = 0.23). Diol precursor with catechol and oxymethylene groups was obtained in 57% (7.41 g, 19.8 mmol) yield as a colorless oil.

^{1}H NMR (270 MHz, $CDCl_3$) δ 6.90 (s, 4H), 4.16–4.11 (m, 4H), 3.87–3.83 (m, 4H), 3.74–3.63 (m, 8H), 3.59–3.54 (m, 4H), 3.49 (s, 4H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 148.5, 121.2, 114.6, 72.3, 70.4, 70.0, 69.4, 68.6, 61.2 ppm. IR (KBr) 3400 (ν_{O-H}), 2924 ($\nu_{C-H,\,as}$), 2875 ($\nu_{C-H,\,s}$), 1255 ($\nu_{=C-O-C,\,as}$), 1126, ($\nu_{-C-O-C,\,as}$), 1058 ($\nu_{C-O-C,\,s}$) cm^{-1}.

Ditosylation. To a solution of diol derivative (7.24 g, 19.3 mmol) in cold pyridine (40 mL), a solution of *p*-toluenesulfonyl chloride (11.0 g, 57.9 mmol) in cold pyridine (40 mL) was added dropwise at 0°C. After addition, the mixture was stirred for 24 h at 0°C. The reaction mixture was poured into 6 M HCl (200 mL), and it was extracted with ethylacetate. The combined organic layer was washed with 5% Na_2CO_3 aq followed by brine. And then it was dried with $MgSO_4$, and the solvent was removed by rotary evaporator. The crude product was purified by silica gel column chromatography (EtOAc:hexane =

1:1; $R_f = 0.21$). Ditosylate was obtained in 47% yield (6.14 g, 8.99 mmol) as a colorless oil.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.65 (d, $J = 8.2$ Hz, 4H), 7.19 (d, $J = 8.2$ Hz, 4H), 6.78 (s, 4H), 4.04–3.98 (m, 8H), 3.70–3.66 (m, 4H), 3.57–3.51 (m, 8H), 3.49–3.44 (m, 4H), 2.28 (s, 6H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 148.4, 144.3, 132.4, 129.8, 129.4, 127.8, 127.4, 121.1, 114.5, 70.3, 69.3, 69.0, 68.5, 68.2, 21.2 ppm. IR (KBr) 2927 ($\nu_{C-H,\,as}$), 2872 ($\nu_{C-H,\,s}$), 1354 ($\nu_{S(=O),\,as}$), 1176 ($\nu_{S(=O),\,s}$) cm^{-1}.

Cyclization of ditosylate with (*R*)-binaphthol. To a suspension of (*R*)-(+)-binaphthol (441 mg, 1.54 mmol) and cesium carbonate (5.02 g, 15.4 mmol) in THF (40 mL), a solution of ditosylate (1.05 g, 1.54 mmol) in THF (40 mL) was added, and the mixture was refluxed for 24 h. After it was cooled to ambient temperature, 5% Na_2CO_3 was added, and it was extracted with ethylacetate. The combined organic layer was washed with brine, dried with $MgSO_4$, and then the solvent was removed under the reduced pressure. The resulting residue was purified by silica gel column chromatography (EtOAc:hexane = 3:1; R_f 0.42). Binaphthyl-benzo-26-crown ether was obtained in 69% yield (663 mg, 1.06 mmol) as colorless oil.

^{1}H NMR (270 MHz, $CDCl_3$) δ 7.83 (dd, $J = 1.3$, 8.9 Hz, 2H), 7.77 (d, $J = 8.2$ Hz, 2H), 7.41 (dd, $J = 1.6$, 8.9 Hz, 2H), 7.28–7.10 (m, 6H), 6.86 (br, 4H), 4.16–3.93 (m, 8H), 3.77 (s, 4H), 3.58–3.24 (m, 12H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 154.0, 148.6, 133.7, 129.1, 129.0, 127.5, 125.9, 125.1, 123.3, 121.1, 120.3, 115.9, 114.0, 70.6, 70.5, 69.7, 69.6, 69.4, 68.9 ppm. IR (KBr) 2924 ($\nu_{C-H,\,as}$), 2871 ($\nu_{C-H,\,s}$), 1256 ($\nu_{C-O-C,\,as}$), 1127 ($\nu_{C-O-C,\,s}$) cm^{-1}. FAB-MS (matrix: m-NBA) m/z 624.3 $[M^-]^+$. Anal. calcd for $C_{38}H_{40}O_8$: C 73.06; H 6.45. found: C 72.94; H 6.44.

Preparation of (*R*)-Chiral-Wheel-Rotaxane (12)

To a solution of ammonium salt **11** (0.70 mmol) and chiral crown ether (0.70 mmol) in CH_2Cl_2 (1.4 mL), 3,5-di-*tert*-butylbenzoic anhydride (0.84 mmol) and tributylphosphane (0.07 mmol) were added. After the reaction mixture was allowed to stand at room temperature for 6 h, the mixture was washed with 1 M hydrochloric acid, 5% sodium carbonate, and brine, then dried with $MgSO_4$, and evaporated *in vacuo* to give a crude product, which was purified by preparative HPLC (eluent: chloroform).

12a: White solid. Yield 20%, mp 96°C. ^{1}H NMR (500 MHz, $CDCl_3$) 7.87 (d, $J = 2.0$ Hz, 2H), 7.84 (d, $J = 8.5$ Hz, 2H), 7.81–7.78 (m, 2H), 7.69 (s, 1H), 7.55 (d, $J = 8.5$ Hz, 1H), 7.37–7.33 (m, 3H), 7.26–7.13 (m, 4H), 7.09 (br, 2H), 7.04 (s, 2H), 6.94 (d, $J = 8.5$ Hz, 1H), 6.86–6.81 (m, 3H), 6.76–6.74 (m, 1H), 4.32–4.10 (m, 7H), 4.04–4.00 (m, 2H), 3.77–3.67 (m, 3H), 3.63–3.49 (m, 5H), 3.39–3.17 (m, 10H), 3.03–2.93 (m, 3H), 2.00–1.85 (m, 2H), 1.37 (s, 18H), 1.17 (s, 18H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.83, 154.48, 154.15, 151.15, 146.66, 146.33, 133.59, 133.55, 130.85, 130.00, 129.94, 129.77, 129.66, 129.16, 127.97, 127.31, 126.51, 126.47, 125.08, 124.94, 124.41, 124.22, 124.09, 123.63, 123.34, 121.85, 121.77, 120.97, 118.12, 116.65, 112.42, 112.20, 71.23, 71.00, 70.82, 70.71, 70.47, 70.07, 69.69, 69.37, 68.28, 67.71, 61.44, 52.96, 45.96, 35.01, 34.76, 31.46, 31.33, 26.11 ppm. IR (KBr): 2962 (ν_{C-H}), 1717 ($\nu_{C=O,\,ester}$), 1240 ($\nu_{C-O-CO,\,as}$), 1129 ($\nu_{C-O-CO,\,s}$), 843 ($\nu_{P-F,\,as}$), 557 ($\nu_{P-F,\,s}$) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 1118.4, calcd for $[M\text{-}PF_6]^+$: 1118.7. $[\alpha]_D^{27}$ 105.4° (c = 0.100, CH_2Cl_2). Anal, calcd for $C_{71}H_{92}F_6NO_{10}P{\cdot}H_2O$: C, 66.49; H, 7.39; N, 1.09. found: C, 66.33; H, 7.41; N, 1.24.

12b: White solid. Yield 71%, mp 86–88°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, $J = 9.0$ Hz, 1H), 7.91–7.85 (m, 5H), 7.65 (s, 1H), 7.57 (d, $J = 9.5$ Hz, 1H), 7.39–7.34 (m,

3H), 7.26–7.15 (m, 7H), 6.99 (br, 2H), 6.88–6.85 (m, 4H), 4.26–4.14 (m, 8H), 4.10–4.05 (m, 1H), 4.02–3.99 (m, 1H), 3.93–3.90 (m, 1H), 3.77–3.74(m, 1H), 3.67–3.30 (m, 14H), 3.23–3.10 (m, 3H), 2.95–2.91 (m, 1H), 2.82 (br, 1H), 2.57 (br, 1H), 1.58–1.52 (m, 2H), 1.36 (s, 18H), 1.20 (s, 18H), 1.16–1.07 (m, 2H), 1.01–0.96 (m, 2H) ppm. ^{13} C NMR (125 MHz, $CDCl_3$) δ 167.07, 154.77, 154.29, 151.15, 150.92, 146.82, 146.58, 133.62, 133.49, 130.93, 129.97, 129.90, 129.87, 129.79, 129.67, 128.02, 127.92, 126.96, 126.53, 126.47, 124.99, 124.97, 124.37, 124.30, 123.54, 123.29, 121.85, 121.77, 121.66, 121.18, 118.19, 116.98, 112.45, 112.38, 71.53, 70.95, 70.82, 70.76, 70.567, 70.33, 70.16, 69.62, 69.16, 68.26, 68.11, 64.40, 53.00, 48.83, 34.94, 34.78, 31.39, 31.32, 28.44, 26.13, 25.99, 25.33 ppm. IR (KBr): 2961 (ν_{C-H}), 1714 ($\nu_{C=O,\ ester}$), 1246 ($\nu_{C-O-CO,\ as}$), 1129 ($\nu_{C-O-CO,\ s}$), 844 ($\nu_{P-F,\ as}$), 558 ($\nu_{P-F,\ s}$) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 1160.7, calcd for $[M\text{-}PF_6]^+$: 1160.7. $[\alpha]_D^{27}$ 98.0° (c = 0.100, CH_2Cl_2) Anal, calcd for $C_{74}H_{98}F_6NO_{10}P{\cdot}H_2O$: C, 67.10; H, 7.61; N, 1.06. found: C, 67.47; H, 7.75; N, 1.20.

N-Chloroacetylation of Rotaxane 12

A solution of **12** (0.131 mmol), chloroacetic anhydride (1.31 mmol), and triethylamine (0.66 mmol) in *N,N*-dimethylformamide (2.0 mL) was stirred at 50°C for 24 h. After addition of aqueous 5% sodium carbonate solution, the mixture was extracted with ethyl acetate. The organic layer was washed with a mixture of 5% sodium carbonate solution and methanol (*v/v* = 1/1), 2 M hydrochloric acid, and brine, then dried over anhydrous magnesium sulfate, and evaporated *in vacuo* to give a crude product, which was purified by preparative HPLC (eluent: chloroform).

***N*-Chloroacetylated chiral-wheel-type rotaxane 12a** White solid. Yield 88%, mp 115–117°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 1.5 Hz, 2H), 7.67 (s, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.33–7.30 (m, 1H), 7.24–7.15 (m, 7H), 7.07 (s, 1H), 6.85- 6.77 (m, 4H), 6.30 (s, 2H), 4.75 (d, J = 16.5 Hz, 1H), 4.62–4.57 (m, 1H), 4.36–4.29 (m, 4H), 4.20–4.15 (m, 2H), 4.10–4.02 (m, 3H), 3.95–3.92 (m, 2H), 3.84–3.80 (m, 1H), 3.72–3.60 (m, 4H), 3.54–3.22 (m, 9H), 3.10–3.03 (m, 2H), 2.98–2.95 (m, 1H), 2.88–2.84 (m, 1H), 2.67–2.64 (m, 1H), 2.38–2.28 (m, 1H), 2.13–2.04 (m, 1H), 1.32 (s, 18H), 1.11 (s, 18H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.27, 167.19, 154.56, 154.45, 150.65, 150.05, 148.31, 148.16, 136.33, 133.76, 133.60, 130.43, 129.41, 129.16, 129.14, 128.20, 127.63, 126.52, 125.89, 125.62, 125.34, 124.98, 123.63, 123.46, 123.63, 123.46, 123.39, 121.13, 121.00, 120.85, 120.04, 119.82, 119.30, 117.58, 115.29, 112.89, 112.40, 71.44, 71.15, 70.91, 70.58, 70.47, 70.18, 69.89, 68.79, 68.72, 68.64, 63.44, 47.99, 43.88, 42.35, 34.97, 34.63, 31.48, 27.00 ppm. IR (KBr): 2962 (ν_{C-H}), 1710 ($\nu_{C=O,\ ester}$), 1656 ($\nu_{C=O,\ amide}$), 1248 ($\nu_{C-O-CO,\ as}$), 1118 ($\nu_{C-O-CO,\ s}$) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 1193.7, calcd for [M]+: 1193.6. $[\alpha]_D^{27}$ 192.2° (c = 0.100, CH_2Cl_2). Anal. Calcd for $C_{73}H_{92}ClNO_{11}{\cdot}H_2O$: C, 72.28; H, 7.81; N, 1.15. found: C, 72.26; H, 7.52; N, 1.24.

12b: White solid. Yield 92%, mp 83–84°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 2.0 Hz, 2H), 7.86–7.82 (m, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.65–7.64 (m, 1H), 7.47–7.42 (m, 2H), 7.33–7.30 (m, 1H), 7.26–7.16 (m, 6H), 7.13 (s, 1H), 6.83–6.67 (m, 5H), 6.50 (s, 2H), 4.59 (d, J = 16.0 Hz, 1H), 4.34–4.30 (m, 1H), 4.20–4.03 (m, 8H), 3.98 (d, J = 13.0 Hz, 1H), 3.93–3.89 (m, 1H), 3.83–3.69 (m, 4H), 3.61 (d, J = 16.0 Hz, 1H), 3.59–3.55 (m, 2H), 3.49–3.34 (m, 5H), 3.26–3.19 (m, 4H), 3.12–3.09 (m, 1H), 3.00–2.92 (m, 2H), 2.84–2.81 (m, 1H), 1.58–1.50 (m, 2H), 1.37 (s, 18H), 1.17 (s, 18H), 1.13–0.89 (m, 4H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.21, 166.86, 154.58, 154.43,

150.77, 150.15, 148.31, 148.23, 136.7, 133.64, 133.61, 130.19, 129.56, 129.43, 129.28, 129.24, 128.16, 127.72, 126.69, 125.92, 125.79, 125.31, 125.08, 123.59, 123.52, 120.89, 120.84, 120.43, 120.39, 120.16, 119.63, 116.50, 115.58, 112.87, 112.63, 71.07, 70.79, 70.75, 70.62, 70.52, 70.42, 70.31, 70.18, 70.04, 69.24, 68.66, 68.43, 65.70, 48.05, 48.00, 42.18, 35.00, 34.70, 31.53, 31.48, 29.09, 28.34, 25.79, 25.55 ppm. IR (KBr): 2962 (ν_{C-H}), 1713 ($\nu_{C=O,\ ester}$), 1654 ($\nu_{C=O,\ amide}$), 1245 ($\nu_{C-O-CO,\ as}$), 1123 ($\nu_{C-O-CO,\ s}$) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 1235.6, Calcd for $[M]^+$: 1235.7. $[\alpha]_D^{27}$ 191.8° (c = 0.100, CH_2Cl_2). Anal. Calcd for $C_{76}H_{98}ClNO_{11}\cdot H_2O$: C, 72.73; H, 8.03; N, 1.12. found: C, 72.71; H, 7.72; N, 1.20.

(*R*)-Chiral Axle Rotaxane Thiazolium Salt 13

A mixture of *N*-chloroacetylated rotaxane (140 mg, 0.117 mmol), sodium iodide (175 mg, 1.17 mmol), and thiazole (0.70 mL, 9.8 mmol) was allowed to stand at 80°C for 24 h. The resulting mixture was poured into 1 M HCl (100 mL). The precipitate was collected by filtration. The crude product was dissolved in methanol and passed through anion exchange column (Amberlite IRA-400 treated by hydrochloric acid followed by water, eluent: methanol). The crude product was further purified by preparative HPLC (eluent: chloroform).

13a: White solid. Yield 52%, mp 176–177°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.95 (br, 1H), 8.30 (s, 1H), 7.95 (d, J = 9.5 Hz, 1H), 7.89–7.85 (m, 3H), 7.72 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.38–7.13 (m, 10H), 6.91–6.83 (m, 3H), 6.66 (d, J = 8.0 Hz, 1H), 6.22 (s, 2H), 5.96- 5.93 (m, 1H), 4.75–4.61 (m, 3H), 4.47–4.43 (m, 1H), 4.25–4.20 (m, 2H), 4.08–4.02 (m, 4H), 3.92–3.6 (m, 8H), 3.57–3.02 (m, 10H), 2.30–2.84 (m, 1H), 2.64–2.60 (m, 1H), 2.33–2.18 (m, 4H), 1.38 (s, 18H), 1.15 (s, 18H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.31, 163.44, 161.71, 154.50, 154.24, 150.89, 150.30, 148.34, 147.73, 136.31, 135.45, 133.65, 133.50, 129.97, 129.47, 129.36, 129.32, 128.96, 128.16, 127.67, 127.17, 126.95, 126.17, 125.89, 125.22, 124.93, 123.75, 123.63, 123.50, 122.01, 121.75, 121.05, 120.31, 119.84, 119.06, 117.27, 114.72, 112.80, 71.38, 70.65, 70.62, 70.47, 70.39, 70.18, 70.07, 69.89, 68.60, 68.22, 63.00, 54.88, 49.02, 43.62, 34.97, 34.60, 31.44, 31.42, 26.52 ppm. IR (KBr): 2961 (ν_{C-H}), 1710 ($\nu_{C=O,\ ester}$), 1662 ($\nu_{C=O,\ amide}$), 1247 ($\nu_{C-O-CO,\ as}$), 1119 ($\nu_{C-O-CO,\ s}$) cm^{-1}. FAB-MS (matrix: m-NBA) m/z 1243.6, calcd for $[M\text{-}Cl^-]^+$: 1243.7. $[\alpha]_D^{29}$ 245.6° (c 0.100, CH_2Cl_2). Anal, calcd for $C_{76}H_{95}ClN_2O_{11}S\cdot 5H_2O$: C, 66.62; H, 7.72; N, 2.04; S, 2.34. found: C, 66.88; H, 7.36; N, 2.18; S, 2.26.

13b was similarly prepared using *N*-chloroacetylated rotaxane **12b** (600 mg, 0.485 mmol). The reaction was carried out at room temperature for 24 h.

13b: White solid. Yield 64%, mp 142–143°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.88 (br, 1H), 8.19 (s, 1H), 7.91–7.90 (m, 4H), 7.86 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.5 Hz, 1H), 7.66 (s, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.36–7.15 (m, 9H), 6.87–6.85 (m, 3H), 6.69 (d, J = 7.5 Hz, 1H), 6.37 (s, 2H), 5.77 (d, J = 17.5 Hz, 1H), 4.83 (d, J = 16.5 Hz, 1H), 4.50–4.21 (m, 2H), 4.27–4.07 (m, 5H), 4.01–3.92 (m, 3H), 3.84–3.69 (m, 4H), 3.62–3.46 (m, 7H), 3.33–3.20 (m, 4H), 3.13–3.12 (m, 2H), 2.97–2.93.(m, 1H), 2.69- 2.65 (m, 1H), 2.39 (br, 3H), 1.66–1.60 (m, 4H), 1.36 (s, 18H), 1.26–1.23 (m, 2H), 1.18 (s, 18H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.20, 163.27, 161.24, 154.48, 154.26, 150.88, 150.21, 148.23, 147.96, 136.38, 35.85, 133.46, 133.39, 129.81, 129.51, 129.49, 129.43, 129.03, 128.05, 127.68, 126.91, 126.53, 126.24, 126.03, 125.18, 124.96, 123.81, 123.78, 123.46, 121.78, 121.43, 120.43, 120.29, 120.20, 119.25, 116.04, 115.22, 113.95, 112.78, 70.99, 70.82, 70.52, 70.51, 70.47, 70.38, 70.31, 70.13, 69.45, 68.79, 68.62, 65.07, 55.16, 49.05,

47.53, 34.93, 34.60, 31.43, 31.40, 29.41, 27.69, 25.95, 25.89 ppm. IR (KBr): 2961 (ν_{C-H}), 1714 ($\nu_{C=O,\ ester}$), 1658 ($\nu_{C=O,\ amide}$), 1245 ($\nu_{C-O-CO,\ as}$), 1124 ($\nu_{C-O-CO,\ s}$) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 1285.7, calcd for $[M\text{-}Cl^-]^+$: 1285.7. $[\alpha]_D^{29}$ 230.0° (c 0.100, CH_2Cl_2). Anal, calcd for $C_{79}H_{101}ClN_2O_{11}S{\cdot}4H_2O$: C, 68.05; H, 7.88; N, 2.01; S, 2.30. found: C, 68.17; H, 7.56; N, 2.14; S, 2.20.

Preparation of (*R*)-Aminoalcohol 14

Protection of (*R*)-binaphthol with MOM group. To a suspension of NaH (9.0 g, 230 mmol) in THF-DMF (2:1, 600 mL), a solution of (*R*)-(+)-binaphthol (30 g, 105 mmol) in THF (240 mL) was added dropwise at 0°C under an atmosphere of Ar gas. After 6 h stirring at 0°C, chloromethoxymethyl ether (29 mL, 580 mmol) was added to the mixture and stirred another 6 h at 0°C. Then the reaction was quenched with water, and it was extracted with dichloromethane. The combined organic layer was dried with Na_2SO_4, and the solvent was removed under reduced pressure. The obtained residue was purified by reprecipitation from CH_2Cl_2-MeOH. After filtration, a protected binaphthol was obtained as colorless needles in 73% (29 g, 77 mmol) yield.

mp 104–105°C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.95 (d, $J = 9.2$ Hz, 2H), 7.87 (d, $J = 8.1$ Hz, 2H), 7.57 (d, $J = 8.9$ Hz, 2H), 7.37–7.31 (m, 2H), 7.25–7.13 (m, 4H), 5.09 (d, $J = 6.8$ Hz, 2H), 4.97 (d, $J = 6.8$ Hz, 2H), 3.14 (s, 6H) ppm. IR (KBr) 2952 ($\nu_{C-H,\ as}$), 2900 ($\nu_{C-H,\ s}$), 1241 ($\nu_{C-O-C,\ as}$), 1147 ($\nu_{C-O-C,\ s}$) cm^{-1}.

(*R*)-3-Formyl-2, 2′-dimethyloxymethyl-1,1′-binaphthyl (formylation). To a solution of the protected binaphthol (6.00 g, 16.0 mmol) in THF (50 mL), n-BuLi in hexane (6.20 mL, 16.1 mmol) was added dropwise at 0°C, and it was kept 0°C for 3 h with stirring. After addition of DMF (1.86 mL, 24.0 mmol), it was stirred for 1 h at 0°C. The reaction mixture was washed with sat. NH_3 aq, 5% Na_2CO_3 aq and brine, then dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc:hexane = 1:5; Rf 0.30). The product was obtained as a colorless needle in 84% yield (5.42 g, 1.35 mmol).

mp 126–127°C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.56 (s, 1H), 7.99 (t, $J = 8.4$, 2H), 7.86 (d, $J = 7.8$, 1H), 7.60 (d, $J = 8.9$, 1H), 7.45–7.14 (m, 6H), 5.14–5.02 (m, 2H), 4.76–4.68 (m, 2H), 3.14 (s, 3H), 2.98 (s, 3H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 190.78, 153.60, 152.59, 136.78, 133.54, 130.87, 130.09, 129.97, 129.46, 128.89, 128.80, 127.85, 126.73, 126.65, 125.78, 125.69, 124.98, 124.10, 119.27, 116.16, 100.00, 97.74, 57.04, 56.98, 55.92, 55.86 ppm. IR (KBr) 2950 ($\nu_{C-H,\ as}$), 2892 ($\nu_{C-H,\ s}$), 1690 ($\nu_{C=O}$) cm^{-1}.

(*R*)-3-Formyl-2,2′-dihydroxy-1,1′-binaphthyl (deprotection). The formylated binaphthyl (5.39 g, 13.4 mmol) was dissolved in chloroform (100 mL). Then 12 M HCl (30 mL) and isopropanol (120 mL) were added the solution, and the mixture was stirred for 38 h at room temperature. After the reaction mixture was washed with water and brine, it was dried with Na_2SO_4, filtered, and concentrated. The obtained crude product was used in the next reaction without further purification. Yellowish solid; 95% (3.98 g, 12.7 mmol).

mp 212–213°C. ^{1}H NMR (270 MHz, CDCl3) δ 10.58 (s, 1H), 10.11 (s, 1H), 8.31 (s, 1H), 7.98–7.84 (m, 3H), 7.43- 7.19 (m, 6H), 7.08 (2H, dd, $J = 8.3, 0.7$), 5.06 (s, 1H) ppm. ^{13}C NMR (67.5 MHz, CDCl3) δ 196.31, 154.19, 151.34, 138.96, 138.89, 137.56, 133.28,

131.06, 130.32, 129.91, 129.16, 128.21, 127.68, 126.60, 124.95, 124.81, 124.32, 123.40, 122.05, 117.66, 115.05, 113.13 ppm. IR (KBr) 3468 (ν_{O-H}), 1652 (ν_{C-O}) cm^{-1}.

(*R*)-3-Formyl-2,2′-dimethoxy-1,1′-binaphthyl (methylation). A suspension of formylated binaphthol (2.18 g, 6.93 mmol) and potassium carbonate (3.87 g, 28.0 mmol) in iodomethane/DMF (1/1, 60 mL) was refluxed for 12 h. After it was cooled to room temperature, it was diluted with water and extracted with chloroform. The combined organic layer was washed with 1 M HCl and brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc:hexane = 1:10; Rf 0.20). The desired compound was obtained as yellowish solid in 95% (1.94 g, 12.7 mmol) yield.

mp 126–127°C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 10.48 (s, 1H), 8.47 (s, 1H), 7.94 (t, J = 7.6, 2H), 7.80 (d, J = 7.6, 1H), 7.39 (d, J = 9.2, 1H), 7.35–7.02 (m, 6H), 3.71 (s, 3H), 3.41 (s, 3H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 190.61, 156.41, 154.77, 137.12, 133.71, 130.98, 130.18, 130.09, 129.82, 128.88, 128.34, 127.95, 126.79, 126.03, 125.54, 125.52, 124.70, 123.67, 117.68, 113.26, 62.47, 56.47 ppm. IR (KBr) 2931 ($\nu_{C-H,\,as}$), 2837 ($\nu_{C-H,\,s}$), 1696 ($\nu_{C=O}$) cm^{-1}.

(*R*)-Aminoalcohol 14 (reduction). A solution of binaphthyl aldehyde (1.94 g, 5.67 mmol) and 2-amino-1-ethanol (328 mg, 5.67 mmol) in toluene was refluxed for 24 h with Dean–Stark trap. After the solvent was removed under reduced pressure, a yellowish oil was obtained. Then the oil was dissolved in methanol (20 mL), and sodium borohydride (1.50 g, 40.0 mmol) was added to it. The mixture was stirred for 24 h, and 6 M HCl was added to stop the generation of hydrogen gas. Then 5% NaOH aq. was added to make it basic, and it was extracted with chloroform. The combined organic layer was washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc:methanol = 9:1; Rf 0.17). The desired aminoalcohol **14** was obtained as yellowish solid in 86% (1.90 g, 4.90 mmol) yield.

mp 68–71°C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.97 (d, J = 8.6, 1H), 7.84 (d, J = 12.2, 2H), 7.82 (d, J = 14.9, 1H), 7.08 (d, J = 8.9, 1H), 7.35–7.08 (m, 6H), 4.05 (s, 2H), 3.73 (s, 3H), 3.69 (t, J = 4.9, 2H), 3.35 (s, 2H), 3.32 (s, 2H), 2.85 (t, J = 5.0, 2H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 154.83, 154.63, 133.74, 133.41, 131.83, 130.36, 129.71, 128.83, 127.76, 127.59, 126.53, 125.80, 125.12, 124.96, 124.65, 124.36, 123.49, 118.88, 113.35 60.55, 56.42, 50.43, 49.25 ppm. IR (KBr) 3316 (ν_{O-H}), 2935 ($\nu_{C-H,\,as}$), 2837 ($\nu_{C-H,\,s}$) cm^{-1}.

Preparation of (*R*)-Chiral-Axle-Type Rotaxane 15

To a mixture of (*R*)-aminoalcohol **14** (327 mg, 0.84 mmol), DB24C8 (397 mg, 0.89 mmol), and titanium isopropoxide (2.5 μL, 8.4 mmol), dichloromethane (1.2 mL) and triflic acid (112 μL, 1.27 mmol) were added at 0°C under an argon atmosphere. The mixture was stirred at 0°C for 30 min. 3,5-Dimethylbenzoic anhydride (298 mg, 1.06 mmol) was then added to the solution. After the reaction was carried out at room temperature for 6 h, the reaction mixture was washed with 5% sodium carbonate solution, 1 M hydrochloric acid, and brine, then dried over anhydrous magnesium sulfate, and evaporated *in vacuo* to give a crude product, which was purified by silica gel column chromatography (eluent: chloroform:methanol = 100:1) to give 702 mg (75%) of **15** as a white solid.

mp 96–98°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 9.5 Hz, 1H), 7.88 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.73 (br, 2H), 7.64 (s, 2H), 7.53 (d, J = 8.5 Hz, 1H), 7.47 (dd, J = 1.8, 9.3 Hz, 1H), 7.33–7.27 (m, 2H), 7.19–7.02 (m, 5H), 6.85 (br, 8H), 4.74 (br, 2H),

4.65–4.59 (m, 2H), 4.20–4.05 (m, 10H), 3.82 (br, 8H), 3.75 (s, 3H), 3.70–3.64 (m, 8H), 3.21 (s, 3H), 2.17 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.88, 154.43, 153.46, 147.01, 137.55, 134.67, 134.19, 133.20, 130.35, 130.01, 129.25, 128.51, 127.69, 127.66, 126.96, 126.81, 126.06, 124.89, 124.66, 124.32, 123.78, 123.62, 123.25, 121.32, 121.29, 120.61 (q, *J*C-F = 320 Hz), 117.51, 112.95, 112.32, 112.30, 77.20, 70.53, 70.48, 69.93, 69.88, 67.89, 67.82, 60.46, 60.07, 55.96, 48.87, 47.92, 20.64 ppm. IR (KBr): 2930 (ν_{C-H}), 1720 ($\nu_{C=O\ ester}$), 1266 ($\nu_{S=O,\ as}$), 1031 ($\nu_{S=O,\ s}$), 637 (ν_{S-O}) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 968.5, calcd for [M-$CF_3SO_3^-$]$^+$: 968.5. $[\alpha]_D^{26}$ 38.0° (c = 0.100, CH_2Cl_2). Anal, calcd for $C_{59}H_{66}F_3NO_{15}S{\cdot}H_2O$: C, 62.37; H, 6.03; N, 1.23. found: C, 62.27; H, 6.09; N, 1.36.

(*R*)-*N*-Chloroacetyl Rotaxane (*N*-Chloroacetylation of 15)

A solution of **15** (1.16 g, 1.04 mmol), chloroacetic anhydride (1.77 g, 10.4 mmol), and triethylamine (724 μL, 5.19 mmol) in *N,N*-dimethylformamide (15 mL) was stirred at 40°C for 24 h. After addition of 5% aqueous sodium carbonate solution, the reaction mixture was extracted with chloroform. The organic layer was washed with a mixture of 5% aqueous sodium carbonate solution and methanol (*v/v* = 1/1), 2 M hydrochloric acid, and brine, then dried over anhydrous magnesium sulfate, and evaporated *in vacuo* to give a crude product, which was purified by silica gel column chromatography (eluent: chloroform) to give 1.02 g (94%) of *N*-chloroacetylated rotaxane as a white solid.

mp 214–215°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 2H), 7.97 (d, *J* = 9.5 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.43–7.40 (m, 2H), 7.29–7.25 (m, 2H), 7.13–7.07 (m, 5H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.85–6.69 (m, 8H), 5.25–5.20 (m, 1H), 5.13–5.07 (m, 1H), 4.66–4.52 (m, 2H), 4.47–4.34 (m, 2H), 4.26–4.22 (m, 3H), 4.11–4.08 (m, 3H), 3.96–3.78 (m, 8H), 3.71 (s, 3H), 3.68–3.64 (m, 2H), 3.55–3.39 (m, 10H), 3.16 (s, 3H), 2.27 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.54, 166.48, 154.70, 154.43, 148.23, 148.11, 137.35, 133.99, 133.56, 132.77, 131.10, 130.67, 130.40, 129.37, 128.93, 128.78, 128.04, 127.68, 125.85, 125.37, 124.99, 124.54, 124.50, 124.02, 123.61, 123.28, 120.57, 120.50, 119.65, 113.40, 112.56, 111.86, 71.26, 71.19, 70.30, 70.26, 68.06, 68.05, 62.30, 60.05, 56.22, 45.70, 44.35, 42.66, 21.14 ppm. IR (KBr): 2918 (ν_{C-H}), 1709 ($\nu_{C=O,\ ester}$), 1658 ($\nu_{C=O,\ amide}$), 1248 ($\nu_{C-O-CO,\ as}$), 1126 ($\nu_{C-O-CO,\ s}$) cm^{-1}. FAB-MS (*m*-NBA): *m/z* 1043.4, calcd for [M]$^+$: 1043.4. $[\alpha]_D^{26}$ 42.4° (c = 0.100, CH_2Cl_2). Anal. Calcd for $C_{60}H_{66}ClNO_{13}{\cdot}H_2O$: C, 67.82; H, 6.45; N, 1.32. found: C, 68.06; H, 6.63; N, 1.47.

(*R*)-Chiral Thiazolium Rotaxane (16)

A mixture of *N*-chloroacetylated rotaxane (486 mg, 0.48 mmol), sodium iodide (672 mg, 4.48 mmol), and thiazole (1.0 mL, 14 mmol) was allowed to stand at 80°C for 48 h. The resulting mixture was poured into 1 M HCl (100 mL). The precipitate was collected by filtration. The crude products were dissolved in methanol, and the solution was passed through anion exchange column (Amberlite IRA-400 treated by hydrochloric acid followed by methanol, eluent: methanol). The crude product was further purified by silica gel column chromatography (eluent: chloroform:methanol = 10:1) to give 281 mg (56%) of **16** as white solid.

mp 172°C. (dec.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.75 (br, 1H), 8.17 (br, 1H), 7.98–7.96 (m, 2H), 7.92 (s, 2H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.30–7.26 (m, 2H), 7.22 (s, 1H), 7.13–6.98 (m, 5H), 6.82 (br, 6H), 6.76 (br, 2H), 6.16 (d, *J* = 16.0 Hz, 1H), 5.92 (d, *J* = 16.0 Hz, 1H), 5.32–5.26 (m, 1H), 5.17–5.11 (m,

1H), 4.68 (s, 2H), 4.47–4.35 (m, 2H), 4.26–4.23 (m, 2H), 4.13–4.03 (m, 6H), 3.95–3.89 (m, 4H), 3.68 (s, 3H), 3.65–3.50 (m, 12H), 3.12 (s, 3H), 2.27 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.60, 163.98, 162.03, 154.64, 154.21, 148.21, 137.50, 133.88, 133.83, 132.89, 130.56, 130.32, 129.85, 129.55, 128.90, 128.57, 127.74, 125.99, 125.40, 125.30, 125.17, 124.66, 124.39, 124.26, 124.11, 123.34, 121.26, 121.14, 119.20, 113.42, 113.39, 112.92, 71.32, 71.24, 70.41, 68.86, 68.73, 61.86, 60.00, 56.25, 55.64, 45.80, 45.10, 21.13 ppm. IR (KBr): 2919 (ν_{C-H}), 1709 ($\nu_{C=O,\ ester}$), 1664 ($\nu_{C=O,\ amide}$), 1248 ($\nu_{C-O-CO,\ as}$), 1125 ($\nu_{C-O-CO,\ s}$) cm^{-1}. FAB-MS (matrix: m-NBA) m/z 1093.1, calcd for $[M\text{-}Cl^-]^+$: 1093.5. $[\alpha]_D^{29}$ 25.4° (c = 0.100, CH $_2Cl_2$). Anal. Calcd for $C_{63}H_{69}ClN_2O_{13}S{\cdot}4H_2O$: C, 62.96; H, 6.46; N, 2.33; S, 2.67. found: C, 62.61; H, 6.24; N, 2.48; S, 2.65.

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