Catalytic Asymmetric Synthesis and Optical Resolution of Planar Chiral Rotaxane

Yoshimasa Makita,[1] Nobuhiro Kihara,[2] Naohisa Nakakoji,[3] Toshikazu Takata,*[1] Shinji Inagaki,[4] Chiyo Yamamoto,[4] and Yoshio Okamoto[4]

[1]*Department of Organic and Polymeric Materials, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152-8552*
[2]*Department of Chemistry, Faculty of Science, Kanagawa University, 2946 Tsuchiya, Hiratsuka 259-1293*
[3]*Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, Sakai, Osaka 599-8531*
[4]*Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603*

(Received October 13, 2006; CL-061206; E-mail: ttaka@polymer.titech.ac.jp)

Planar chiral rotaxanes were synthesized from crown ether and secondary ammonium salt via trialkylphosphane-catalyzed acylative end-capping. Their optical resolution was achieved by chiral HPLC after acylative neutralization of the ammonium group. When optically active trialkylphosphane **2** was used as the chiral acylation catalyst, optically active rotaxane (4.4% ee) was obtained.

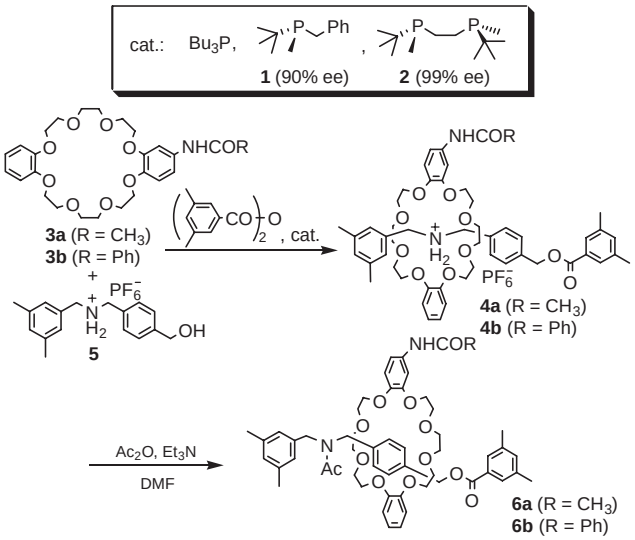
One of the most interesting features of interlocked compounds such as rotaxanes and catenanes is chirality.[1] Especially, planar chiral rotaxanes and catenanes have attracted considerable attention.[2,3] Even if the components of a rotaxane have no chirality, their combination can exhibit planar chirality. Some planar chiral rotaxanes and catenanes have been prepared using achiral components and resolved into their enantiomers by chiral HPLC separation.[2] Although chiral rotaxanes are expected to be an effective chiral source,[3m] the supply of optically active rotaxanes on a massive scale is difficult with HPLC separation.

Asymmetric synthesis is one of the most effective methods to prepare optically active compounds. Although diastereoselective preparation of some planar chiral rotaxanes has been investigated,[3c,3h] at least one equivalent of chiral auxiliary has been necessary. Further, the preparation of a chiral rotaxane that has only planar chirality is difficult. Therefore, we have focused our attention on the catalytic enantioselective synthesis of planar chiral rotaxane. We previously reported tributylphosphane-catalyzed synthesis of rotaxane consisting of crown ether and secondary ammonium salt.[4] The use of chiral trialkylphosphanes **1** and **2** instead of tributylphosphane[5] may provide a simple and effective procedure for the preparation of planar chiral rotaxanes.

Amide-substituted crown ether **3**, which has less symmetry than the parent dibenzo-24-crown-8, was used as the wheel component. The preparation of rotaxanes **4** was carried out using secondary ammonium salt **5** as shown in Scheme 1.[4]

Two racemic rotaxanes **4a** and **4b** were prepared in good yields by using tributylphosphane as the catalyst. Their structures were confirmed by comparing their spectroscopic data with those of similar rotaxanes.[4]

The optical resolution of **4** was extensively investigated using chiral HPLC; however, all attempts were unsuccessful. Under the best condition, only partial resolution of **4a** was attained by using Chiralcel OD column eluted with hexane/2-propanol (30/70). It can be deduced that two alkyl groups in the ammonium salt **4** are too similar for a chiral column to discriminate the chirality. The high polarity of **4** might also prevent



Scheme 1.

effective resolution because a highly polar eluent was necessary for **4** to elute from the column. To increase the dissymmetry of the rotaxane, the ammonium salt group was neutralized with acylative treatment to give rotaxane **6**.[4d,6] In the case of **6**, both sides of the wheel component face different functional groups, amide and ester, since the wheel moves from the ammonium station by the acylation.

The optical resolution of **6a** was successfully achieved using a Chiralcel OD column eluted by hexane/ethanol (85/15). Meanwhile, the optical resolution of **6b** using Chiralcel OD resulted in partial resolution. Thus, chemically bounded AD-type column was used to achieve baseline resolution with hexane/chloroform/2-propanol (60/40/2) (see Supporting Infromation). (+)-Form was first eluted using an OD column, while (−)-form was first eluted using an AD-type column. Both enatiomers of **6a** (>99% ee by HPLC analysis) were obtained by a preparative OD column. Their CD spectra (see Supporting Infromation) showed completely opposite signs, thereby indicating complete optical resolution.

For the asymmetric synthesis of **4**, chiral trialkylphosphane is necessary. Therefore, *P*-chiral phosphanes (*S*)-**1** (90% ee) and (*S*,*S*)-**2** (99% ee), which are easily prepared by (−)-sparteine-mediated desymmetrization, were used as the catalyst.[7,8]

The results of the asymmetric synthesis of **4** are summarized in Table 1. Since **1** and **2** were less active acylation catalysts than tributylphosphane, reactions proceeded slowly. When **1** was

Table 1. Asymmetric synthesis of rotaxane **4**[a]

Entry	Cat.	Wheel	Solvent	Yield /%[b]	ee /%[c]
1	Bu_3P	**3a**	$CHCl_3$	90	—
2	**1**	**3a**	$CHCl_3$	50	<0.5
3	**2**	**3a**	$CHCl_3$	48	4.4
4	**2**	**3a**	CH_2Cl_2	45	4.3
5	**2**	**3a**	benzene	10	<0.4
6	**2**	**3a**	CH_3CN	5	2.2
7	Bu_3P	**3b**	$CHCl_3$	81	—
8	**2**	**3b**	$CHCl_3$	35	−1.7

[a]Reactions of **5** were carried out at ambient temperature for 24 h in the presence of 1.4 equiv. of **3** and 0.2 equiv. of trialkylphosphane as the catalyst. When **1** and **2** were used as the phosphonium triflate, 0.2 equiv. (1 equiv. to the phosphonium salt) of triethylamine was added. Initial concentration; [**5**] = 0.33 M. [b]Isolated yield. [c]Determined after N-acylative neutralization.

used as the catalyst, little chirality was induced. However, when **2** was used as the catalyst, optically active **4** was obtained: **4a** of 4.4% ee (the error was less than 0.5%) was obtained in chloroform. In dichloromethane, **4a** of 4.3% ee was obtained. The system was heterogeneous when benzene or acetonitrile was used as the solvent, and **4a** of lower e.e. values was obtained. When **3b** was used as the wheel component, only very low chirality was induced even when **2** was used as the catalyst. Hydrogen-bonding interaction between one of the phosphane groups in **2** and the amide group on the crown ether wheel can explain the fact that **2** was the better asymmetric catalyst in the catalytic asymmetric synthesis of **4** than **1**. However, the rather low ee value indicates that such an interaction is very weak to discriminate the face of the crown ether. If a trialkylphosphane that can strongly interact with the amide group can be used as the catalyst, higher ee values are expected.

In conclusion, we have demonstrated the first catalytic asymmetric synthesis of planar chiral rotaxane. *P*-Chiral trialkylphosphanes were effectively used as the catalyst. The chiral discrimination of the rotaxane with the chiral HPLC was successfully achieved by the increment of the asymmetric nature based on the planar chirality by its N-acylation. Exploration of a more effective asymmetric catalyst and catalytic reaction is under active investigation.

We thank Professor Tsuneo Imamoto, Chiba University, for the donation of trialkylphosphanes (*S*)-**1** and (*S*,*S*)-**2**.

References and Notes

1 a) *Molecular Catenanes, Rotaxanes, and Knots*, ed. by J.-P. Sauvage, C. Dietrich-Buchecker, Wiley-VCH, Weinheim, **1999**. b) F. Vögtle, T. Dünnwald, T. Schmidt, *Acc. Chem. Res.* **1996**, *29*, 451. c) D. K. Mitchell, J.-P. Sauvage, *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 930. d) C. O. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 189. e) R. Schmieder, G. Hübner, C. Seel, F. Vögtle, *Angew. Chem., Int. Ed.* **1999**, *38*, 3528. f) C. Reuter, C. Seel, M. Nieger, F. Vögtle, *Helv. Chim. Acta* **2000**, *83*, 630. g) C. Reuter, A. Mohry, A. Sobanski, F. Vögtle, *Chem. Eur. J.* **2000**, *6*, 1674. h) C. Reuter, W. Wienand, C. Schmuck, F. Vögtle, *Chem.—Eur. J.* **2001**, *7*, 1728. i) N. P. Balsara, L. J. Fetters, N. Hadjichristidis, D. J. Lohse, C. C. Han, W. W. Graessley, R. Krishnamoorti, *Macromolecules* **1992**, *25*, 6137.

2 a) Y. Kaida, Y. Okamoto, J.-C. Chambron, D. K. Mitchell, J.-P. Sauvage, *Tetrahedron Lett.* **1993**, *34*, 1019. b) C. Yamamoto, Y. Okamoto, R. Jäger, F. Vögtle, *J. Am. Chem. Soc.* **1997**, *119*, 10547. c) F. Vögtle, A. Hünten, E. Vogel, S. Buschbeck, O. Safarowsky, J. Recker, A. Parham, M. Knott, W. M. Müller, Y. Okamoto, T. Kubota, W. Lindner, E. Francotte, S. Grimme, *Angew. Chem., Int. Ed.* **2001**, *40*, 2468. d) N. Kameta, K. Hiratani, Y. Nagawa, *Chem. Commun.* **2004**, 466.

3 a) A. Archut, W. M. Müller, S. Baumann, M. Habel, F. Vögtle, *Liebigs Ann.* **1997**, 495. b) T. Schmidt, R. Schmieder, W. M. Müller, B. Kiupel, F. Vögtle, *Eur. J. Org. Chem.* **1998**, 2003. c) P. R. Ashton, A. M. Heiss, D. Pasini, F. M. Raymo, A. N. Shipway, J. F. Stoddart, N. Spencer, *Eur. J. Org. Chem.* **1999**, 995. d) H.-R. Tseng, S. A. Vignon, P. C. Celestre, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem.—Eur. J.* **2003**, *9*, 543. e) S. A. Vignon, J. Wong, H.-R. Tseng, J. F. Stoddart, *Org. Lett.* **2004**, *6*, 1095. f) S. J. Cantrill, M. C. T. Fyfe, A. M. Heiss, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Commun.* **1999**, 1251. g) C. P. McArdle, M. C. Jennings, R. J. Puddephatt, *J. Am. Chem. Soc.* **2002**, *124*, 3959. h) L.-E. Perret-Aebi, A. von Zelewsky, C. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem., Int. Ed.* **2004**, *43*, 4482. i) P. Mobian, N. Banerji, G. Bernardinelli, J. Lacour, *Org. Biomol. Chem.* **2006**, *4*, 224. j) A. Theil, C. Mauve, M.-T. Adeline, A. Marinetti, J.-P. Sauvage, *Angew. Chem., Int. Ed.* **2006**, *45*, 2104. k) C. D. Pentecost, A. J. Peters, K. S. Chichalk, G. W. V. Cave, S. J. Cantrill, J. F. Stoddart, *Angew. Chem., Int. Ed.* **2006**, *45*, 4099. l) Y. Tachibana, N. Kihara, Y. Ohga, T. Takata, *Chem. Lett.* **2000**, 806. m) Y. Tachibana, N. Kihara, T. Takata, *J. Am. Chem. Soc.* **2004**, *126*, 3438.

4 a) H. Kawasaki, N. Kihara, T. Takata, *Chem. Lett.* **1999**, 1015. b) N. Kihara, N. Nakakoji, T. Takata, *Chem. Lett.* **2002**, 924. c) N. Watanabe, T. Yagi, N. Kihara, T. Takata, *Chem. Commun.* **2002**, 2720. d) Y. Tachibana, H. Kawasaki, N. Kihara, T. Takata, *J. Org. Chem.* **2006**, *71*, 5093.

5 a) E. Vedejs, S. T. Diver, *J. Am. Chem. Soc.* **1993**, *115*, 3358. b) E. Vedejs, N. S. Bennett, L. M. Conn, S. T. Diver, M. Gingras, S. Lin, P. A. Oliver, M. J. Peterson, *J. Org. Chem.* **1993**, *58*, 7286. c) N. Kihara, Y. Tachibana, H. Kawasaki, T. Takata, *Chem. Lett.* **2000**, 506.

6 N. Kihara, Y. Tachibana, H. Kawasaki, T. Takata, *Chem. Lett.* **2000**, 506.

7 a) T. Imamoto, J. Watanabe, Y. Wada, H. Masuda, H. Yamada, H. Tsuruta, S. Matsukawa, K. Yamaguchi, *J. Am. Chem. Soc.* **1998**, *120*, 1635. b) Y. Yamanoi, T. Imamoto, *J. Org. Chem.* **1999**, *64*, 2988. c) I. D. Gridnev, M. Yasutake, N. Higashi, T. Imamoto, *J. Am. Chem. Soc.* **2001**, *123*, 5268.

8 Phosphanes were added to the system as the phosphonium salt to avoid oxidation, and they were used with 1 equivalent of triethylamine to regenerate the free phosphanes, see: a) M. R. Netherton, G. C. Fu, *Org. Lett.* **2001**, *3*, 4295. b) H. Danjo, W. Sasaki, T. Miyazaki, T. Imamoto, *Tetrahedron Lett.* **2003**, *44*, 3467.

9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

Published on the web (Advance View) December 16, 2006; doi:10.1246/cl.2007.162