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Synthesis of [2]Rotaxanes by the Catalytic Reactions of a Macrocyclic Copper Complex

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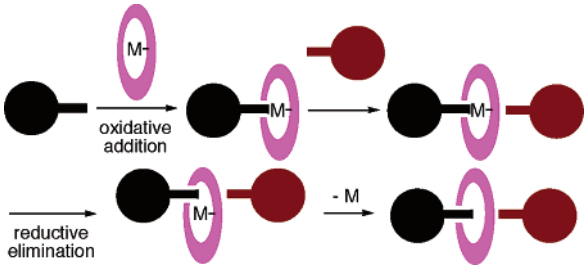
ABSTRACT

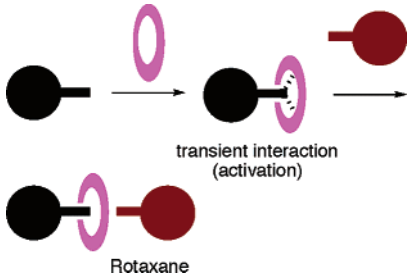


We synthesized [2]rotaxanes by the reactions catalyzed by a macrocyclic Cu(I)–phenanthroline complex. The catalytic site was located inside the ring component so that the rotaxane could be selectively formed. A C–S bond-forming reaction and oxidative dimerization of alkyne was utilized for the efficient synthesis of a new series of [2]rotaxanes.

The rotaxanes are an important class of interlocked compounds, and various synthetic methods have been developed. Among them, the template method has been widely utilized. Interactions such as metal−ligand bonds, hydrogen bonds, and ionic interactions and hydrophobic interactions have been extensively utilized for this synthetic method.[1] These transient bonds were used to keep the precursors of the components in the desired position so that the rotaxanes could be isolated in good yields by the end-capping reactions. A large number of rotaxanes have been synthesized by this method.

Recently, a new strategy has been developed for the synthesis of rotaxanes. Thus, the localization of the site of the reaction inside the ring component leads to the efficient formation of the rotaxanes (Scheme 1). For example, Vögtle et al. achieved the synthesis of rotaxanes by the anion template method.[2] In these reactions, the anion that was used for the nucleophilic reaction was "trapped" inside the macrolactam. Subsequent reaction with various electrophiles resulted in the formation of the corresponding rotaxanes in good yields. A further extension of this type of synthesis is the application of a catalytic reaction. Leigh and co-workers

Scheme 1. "Trapping" Synthesis of [2]Rotaxanes



(1) Reviews: (a) Schill, G. *Catenanes, Rotaxanes, and Knots*; Academic Press: New York, 1971. (b) *Molecular Catenanes, Rotaxanes and Knots*; Dietrich-Buchecker, C. O., Sauvage, J. P., Eds.; Wiley-VCH: New York, 1999. (c) Sauvage, J. P. *Acc. Chem. Res.* **1990**, *23*, 319−327. (d) Hoss, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 375−384. (e) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2828. (f) Jäger, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930−944. (g) Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1959−1976. (h) Sauvage, J. P. *Acc. Chem. Res.* **1998**, *31*, 611−619. (i) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643−1663.

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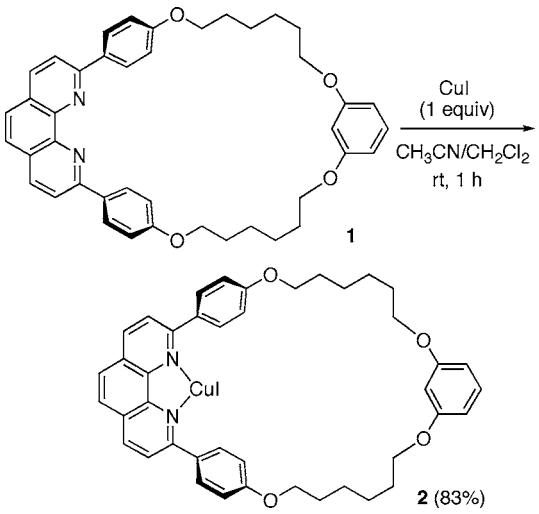
reported the synthesis of rotaxanes by the Cu(I)-catalyzed reaction.[3] In their study, the catalytic site of the reaction was located inside the ring, which led to the efficient synthesis of a rotaxane by the 1,3-cycloaddition of an organic azide with a terminal alkyne. A substoichiometric amount of Cu source was sufficient under some reaction conditions since the Cu source could be transferred among the cyclic components.

We have been interested in the possibility of the synthesis of the rotaxanes by the fixation of the reactive moiety inside the ring component. Especially, catalytic reactions are very attractive since a large number of reactions are currently available. In this paper, we report the synthesis of [2]-rotaxanes by the catalytic reactions of a macrocyclic Cu-(I)−phenanthroline complex.

New Cu(I)−phenanthroline complex **2** was prepared in 83% yield by the reaction of macrocyclic phenanthroline **1**[4] with CuI (Scheme 2). Among various Cu-catalyzed reactions,

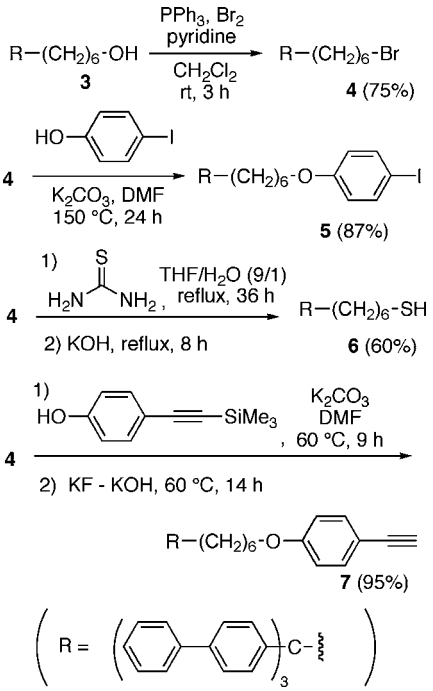
Scheme 2. Synthesis of Macrocyclic Cu(I)−Phenanthroline Complex **2**



we chose two reactions for the synthesis of [2]rotaxanes. The C−S bond-forming reaction of alkylthiol with iodoarenes would proceed in the presence of **2**, since it has been recently shown that the reaction of aryl iodide with thiol proceeded in the presence of CuI and neocuproine.[5] As the second reaction, the oxidative homocoupling reaction of alkynes (Glaser coupling, Hay coupling)[6] was selected since the catalytic activity of various Cu complexes has been reported.

For the synthesis of a stable [2]rotaxane, a precursor with a large and stable blocking group was required. We chose the tris(4-biphenyl)methyl group[4] as the blocking group and prepared the precursors which were suitable for the synthesis of the rotaxanes. The syntheses of an iodoarene (**5**), thiol (**6**), and alkyne (**7**) are summarized in Scheme 3. Thus,

Scheme 3. Synthesis of the Precursors for the Axle Components



alcohol **3**[7] was brominated and reacted with 4-iodophenol to yield an iodoarene **5**, which would be an adequate precursor for the C−S bond-forming reaction. Other precursors such as thiol **6** and alkyne **7** were prepared by standard methods in good yields.

We carried out the synthesis of [2]rotaxanes utilizing the reactions catalyzed by the macrocyclic complex **2**. The C−S bond-forming reaction was examined, and the result is shown in Scheme 4. The reaction of the iodide **5** with thiol **6** proceeded in the presence of **2** and KO*t*-Bu as a base, and rotaxane **8** was isolated in 27% yield. In this reaction it was necessary to use an excess of **5** as well as **6**, and a significant amount of the cross-coupled product **9** was also isolated. Since the complete dissociation of Cu species from **2** was observed when the reaction was completed, the formation of **9** might be explained by the progress of the reaction that was catalyzed by the dissociated Cu species.

We also examined the oxidative homocoupling of alkyne **7** in the presence of **2**. In this reaction, I_2 turned out to be a

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(3) Aucagne, V.; Hänni, K. D.; Leigh, D. A.; Lusby, P. J.; Walker, D. B. *J. Am. Chem. Soc.* **2006**, *128*, 2186−2187.

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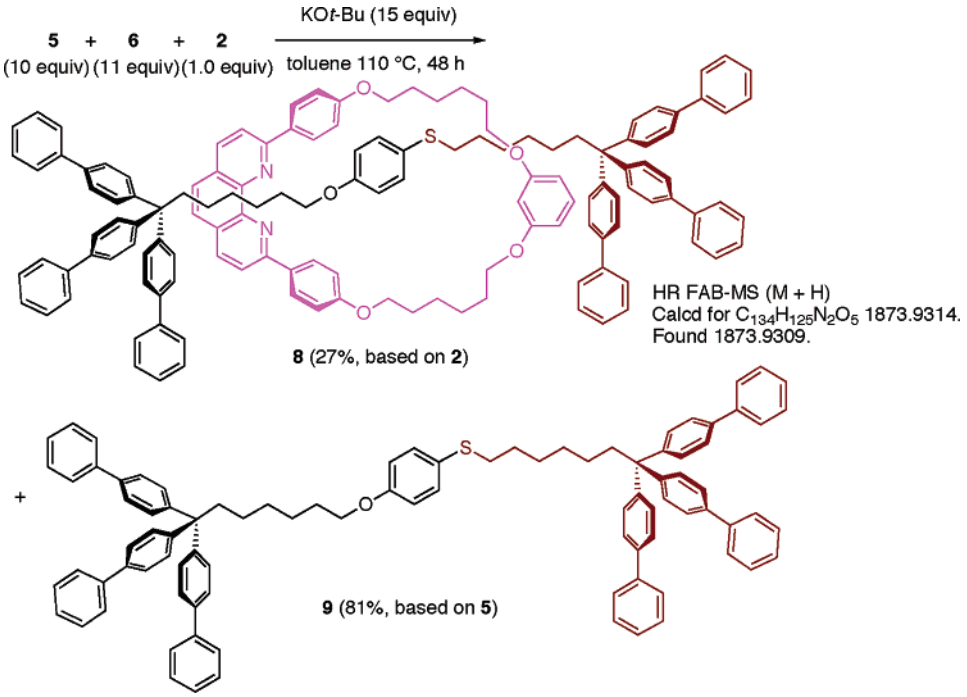
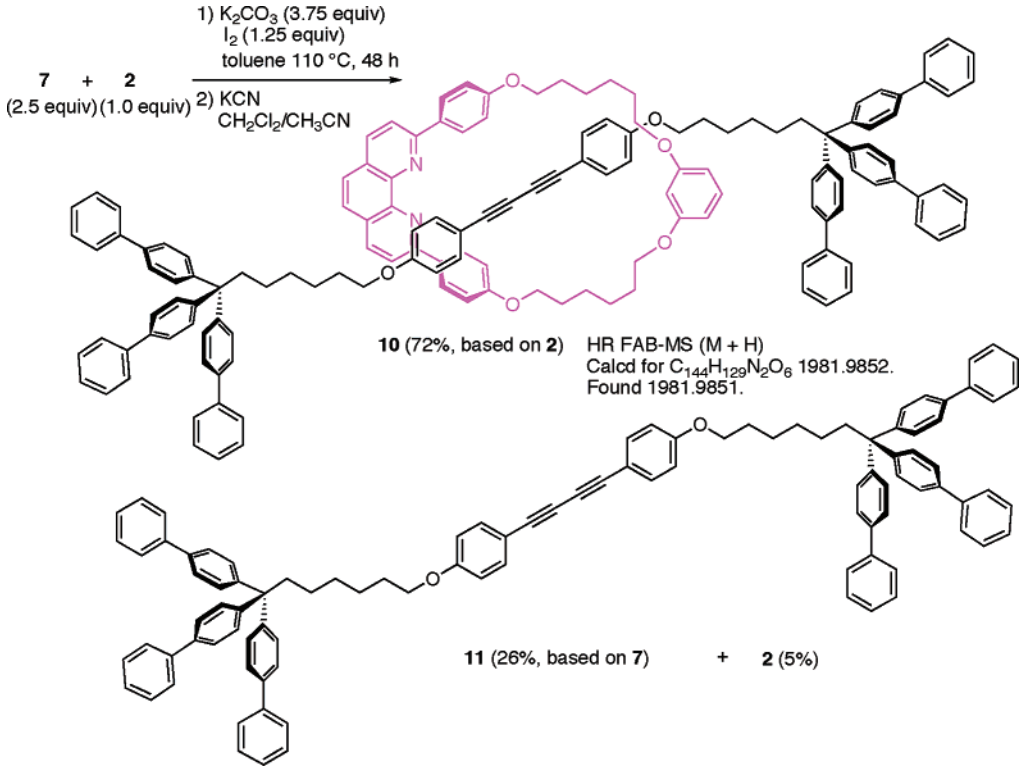
(7) (a) Liu, Q.; Burton, D. J. *Tetrahedron Lett.* **1997**, *38*, 4371−4374. (b) Batsanov, A. S.; Collings, J. C.; Fairlamb, I. J. S.; Holland, J. P.; Howard, J. A. K.; Lin, Z.; Marder, T. B.; Parsons, A. C.; Ward, R. M.; Zhu, J. *J. Org. Chem.* **2005**, *70*, 703−706.

Scheme 4. Synthesis of a [2]Rotaxane by the Cu-Catalyzed C−S Bond-Forming Reaction



good oxidant,[7] and we were pleased to find that the rotaxane **10** was isolated in 72% yield (Scheme 5). It is noteworthy that only a small excess of **7** was required for this reaction. The dissociation of the Cu species from **2** was much slower in this reaction, and it was necessary to add KCN to the reaction mixture to remove the Cu species completely from the phenanthroline complex. The observed higher yield of the rotaxane **10** might be explained in part by the

Scheme 5. Synthesis of a [2]Rotaxane by Cu-Catalyzed Oxidative Coupling of **7**



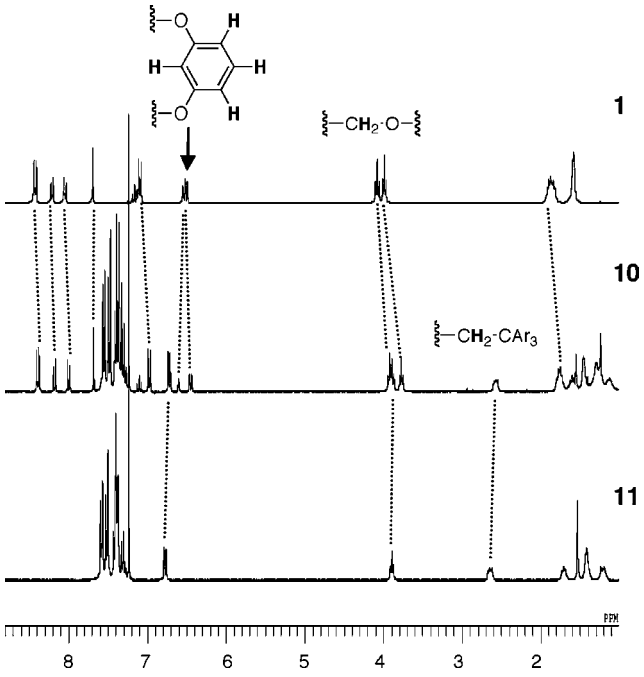


Figure 1. ^{1}H NMR spectra of **1**, **10**, and **11**

higher stability of **2** under the reaction condition shown in Scheme 5.

The structures of the rotaxanes **8**[8] and **10**[9] were fully characterized. The ^{1}H NMR spectra of **1**, **10**, and **11** were shown in Figure 1.[10] The observed shifts of the signals are in accordance with other structurally similar rotaxanes.[4] For example, the signals of the resorcinol moiety of **1** appeared at δ 6.55 and 6.51 ppm, while those of **10** appeared at δ 6.61 and 6.45 ppm. The upfield shifts of some signals were also observed. Furthermore, the observed mass spectra of **8** and **10** are strong supporting evidence for the formation of the rotaxanes.

In summary, we succeeded in the synthesis of [2]rotaxanes by the reactions catalyzed by a macrocyclic Cu(I)−phenanthroline complex. The catalytic site was located inside the ring component so that the rotaxane could be efficiently formed. Only a small excess of a precursor was required for the synthesis of a rotaxane in a good yield. The study provided a new and efficient method for the synthesis of a new series of [2]rotaxanes. Application of this reaction to the preparation of rotaxanes as well as other supramolecules will be reported in due course.

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Supporting Information Available: Detailed experimental procedures and spectral data of **2** and **4**−**11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Selected data for compound **8**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, J = 8.7 Hz, 4H), 8.16 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.4 Hz, 2H), 7.68 (s, 2H), 7.54−7.24 (m, 56H), 7.08 (t, J = 8.4 Hz, 1H), 6.92 (d, J = 8.7 Hz, 4H), 6.84 (d, J = 8.4 Hz, 2H), 6.49 (s, 1H), 6.43 (d, J = 8.4 Hz, 2H), 3.85−3.74 (m, 10H), 2.74 (t, J = 7.5 Hz, 2H), 2.61−2.41 (m, 4H), 1.83−1.35 (m, 18H), 1.35−1.00 (m, 14H); HR FAB-MS (M + H) calcd for $C_{134}H_{125}N_2O_5$ 1873.9314, found 1873.9309.

(9) Selected data for compound **10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, J = 8.7 Hz, 4H), 8.20 (d, J = 8.7 Hz, 2H), 8.01 (d, J = 8.7 Hz, 2H), 7.69 (s, 2H), 7.56 (d, J = 8.4 Hz, 12H), 7.49 (d, J = 8.4 Hz, 12H), 7.41−7.27 (m, 34H), 7.11 (t, J = 8.1 Hz, 1H), 6.98 (d, J = 8.7 Hz, 4H), 6.72 (d, J = 8.7 Hz, 4H), 6.61 (s, 1H), 6.45 (d, J = 8.4 Hz, 2H), 3.93 (t, J = 6.3 Hz, 4H), 3.90 (t, J = 7.2 Hz, 4H), 3.78 (t, J = 6.5 Hz, 4H), 2.63−2.51 (m, 4H), 1.85−1.69 (m, 8H), 1.67−1.54 (m, 4H), 1.54−1.39 (m, 8H), 1.39−1.23 (m, 8H), 1.21−1.04 (m, 4H). Anal. Calcd for $C_{144}H_{128}N_2O_6$: C, 87.24; H, 6.51; N, 1.41. Found: C, 87.43; H, 6.56; N, 1.21. HR FAB-MS (M + H) calcd for $C_{144}H_{129}N_2O_6$ 1981.9852, found 1981.9851.

(10) See the Supporting Information for the comparison of the ^{1}H NMR spectra of **1**, **8**, and **9**.