Efficient Synthesis of Rotaxane Based on Complexation of Acetylene and Dicobalt Hexacarbonyl: Introduction of a Transformable Functional Group

Yuji Tokunaga,*[1] Go Ohta,[1] Yuji Yamauchi,[1] Tatsuhiro Goda,[1] Nobuhiko Kawai,[1] Takumichi Sugihara,[2] and Youji Shimomura[1]
[1]*Department of Materials Science and Engineering, Faculty of Engineering, University of Fukui, Bunkyo, Fukui 910-8507*
[2]*Faculty of Pharmaceutical Sciences, Niigata University of Pharmacy and Applied Life Sciences, Kamishinei-cho, Niigata 950-2081*

(Received April 12, 2006; CL-060437; E-mail: tokunaga@matse.fukui-u.ac.jp)

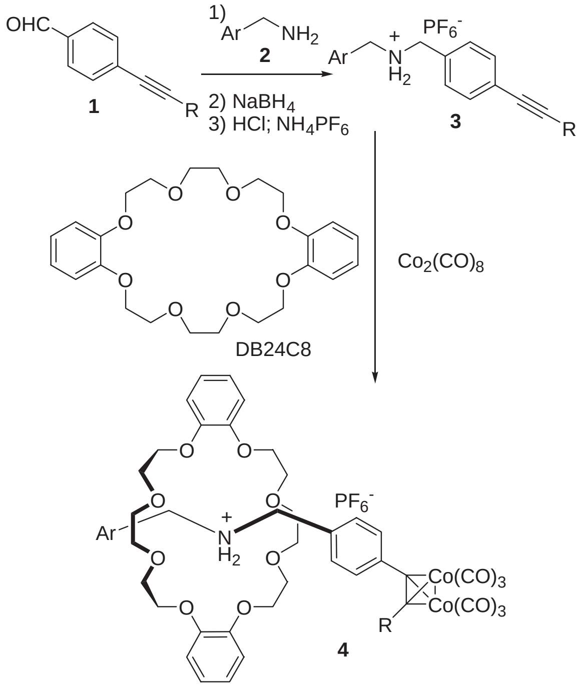
An efficient end-capping method for preparation of rotaxanes by complexation of dicobalt hexacarbonyl and acetylene moiety of the axle end is described here. The end-capping reaction of pseudorotaxanes proceeds under mild conditions and furnishes the expected rotaxanes bearing a transformable functional group in high yield.

Rotaxanes, which consist of a macrocycle and dumbbell-like axle, have received much attention as a component of molecular machines. Many methods for rotaxane synthesis have been developed, and various functionalities to rotaxanes has been introduced.[1] Recently, end-capping or clipping approaches to rotaxanes and the subsequent stopper-modification have been reported. Transformation of phosphonium groups as a stopper part of the axle into bulky alkenes by the Wittig reaction was completed by Stoddart,[2] and Leigh et al. succeeded in replacement of a mechanically interlocking auxiliary via transesterification reaction.[3] Kihara et al. also reported the exchange of a stopper part by the Tsuji–Trost allylation reaction.[4] However, these methods have been capable of each accepting only one type of reaction until now. Therefore, it might be difficult to introduce various functionalities into a main skeleton of rotaxane using the same methodology.

The use of the bimetallic alkyne complex has prevailed in the literature on organic synthesis and organometallic chemistry for a couple of decades. The complexes are commonly exploited for unique reactivity. Among these examples, the Pauson–Khand reaction,[5] a familiar reaction that employs the acetylene–$Co_2(CO)_6$ complex, is useful to construct cyclopentenone. The Nicholas reaction[6] using acetylene–$Co_2(CO)_6$ complex as a substrate is a powerful method introducing functionalities at the α-position of acetylene. Furthermore, hydrosilylation and decomplexation of acetylene–$Co_2(CO)_6$ complex[7] and a utility of the complex as a protective group of acetylene[8] have also been reported. This paper describes an efficient method for preparation of rotaxanes using acetylene–$Co_2(CO)_6$ complexation as a primary step of end-capping and the subsequent stopper-modification of rotaxane.

Self-assembly formed from secondary ammonium salt and crown ether is known to be effective for construction of rotaxanes.[1a,1b,1f,9] Synthesis of the requisite ammonium salts **3** used in this procedure begins with condensation of aldehydes **1** and benzylamines **2** to generate the corresponding imines (Scheme 1). Reduction of the imines, followed by salt formation, then produces the key intermediates, ammonium salts **3**, which possess bulky aryl groups on one end and alkyne moieties at the other.

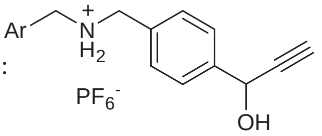
Synthesis of rotaxanes by complexation of acetylene and dicobalt octacarbonyl was investigated. Treatment of acetylene **3a** with dicobalt octacarbonyl in the presence of two equivalents of dibenzo[24]crown8 (DB24C8) afforded the corresponding rotaxane **4a**[10] in good yield. Typical results for various acetylenes **3** are shown in Table 1. High-temperature conditions and using CH_2Cl_2–CH_3CN (1:1) as a solvent, which enfeeble the hydrogen bonding between the crown and the ammonium ion, decrease the rotaxane yield (Runs 1–3). Other reactions are therefore performed at 0 °C in dichloromethane, even though the reaction mixtures are heterogeneous. The neighboring steric effects of substrates were observed. Monosubstituted acetylenes, including 2-propyn-1-ol derivative **5**,[11] give the corresponding rotaxanes in excellent yields (Table 1, Runs 1, 4, 5, and 9). In contrast, disubstituted substrates afforded products **4** in moderate yields (Table 1, Runs 6–8).[12]



Scheme 1.

The association constants of pseudorotaxanes are examined using **3a** and **3d** as axles to obtain more information on the reaction. The ^{1}H NMR titration (500 MHz, CD_3CN–$CDCl_3$ (1:1), 25 °C) of equimolar mixtures of **3** and DB24C8 (10 mM) reveals formation of pseudorotaxanes whose sharp signals are observed independently. Integrations of the complexes and ammoniums **3** afford the apparent association constants K_{exp},[13] respectively, as in eq 1. The K_{exp} of the ammonium salt **3a**, monosubstituted acetylene, is $860 \pm 190\,M^{-1}$. That of disubstituted acetylene **3d** is $1700 \pm 440\,M^{-1}$. Because these values are not related to

Table 1. Synthesis of rotaxanes by complexation of dicobalt hexacarbonyl and acetylenes[a]

Run	Axle	Product	Yield/%[b]
1	**3a**: Ar = 3,5-dimethylphenyl, R = H	**4a**	99 (61)[c]
2	**3a**: Ar = 3,5-dimethylphenyl, R = H	**4a**	66 (44)[d]
3	**3a**: Ar = 3,5-dimethylphenyl, R = H	**4a**	45 (40)[e]
4	**3b**: Ar = 4-*tert*-butylphenyl, R = H	**4b**	94 (63)[c]
5	**3c**: Ar = 9-anthryl, R = H	**4c**	89 (53)[c]
6	**3d**: Ar = 3,5-dimethylphenyl, R = CH_3	**4d**	78 (55)[c]
7	**3e**: Ar = 3,5-dimethylphenyl, R = phenyl	**4e**	77 (59)[c]
8	**3f**: Ar = 9-anthryl, R = phenyl	**4f**	78 (30)[c]
9	**5**:  Ar = 3,5-dimethylphenyl	**4g**	82 (63)[c]

[a]All new compounds were identified by ^{1}H and ^{13}C NMR, MS, and IR spectra. [b]Determind by ^{1}H NMR spectra of crude products. ( ): isolated yield. Reactions were conducted at 0 °C–room temperature using 2 equiv of DB24C8 and 1.2 equivalents of dicobalt octacarbonyl. [c]Reactions were performed at 0 °C in CH_2Cl_2. [d]A reaction was performed at room temperature in CH_2Cl_2. [e]A reaction was performed at 0 °C in CH_2Cl_2–CH_3CN (1:1).

rotaxane yields (Table 1, Runs 1 and 6), the yields depend on the reactivity of pseudorotaxanes consisting of DB24C8 and the ammonium ion, not the percentage of pseudorotaxane, that is, the difference of reactivity between the ammonium ion and the pseudorotaxane might be important.[14]

$$K_{\mathrm{exp}} = \frac{[\text{pseudorotaxane}]}{[\text{ammonium salt} + \text{ammonium ion}][\text{DB24C8}]} \qquad (1)$$

Recently, Takata et al. reported an end-capping synthesis of rotaxane using Ru-catalyzed hydrosilylation of acetylene.[15] However, they were unable to synthesize the rotaxane using acetylene **3a** as an axle part because of the neighboring bulkiness of DB24C8 of pseudorotaxane. Accordingly, the long spacer part between ammonium and the acetylene moieties needed to achieve synthesis of the rotaxane by their hydrosilylation method. This kind of rotaxane synthesis might result in the reactivity of metal complexes (catalysts) to the acetylene moiety of pseudorotaxane, and might be sensitive to the neighboring bulkiness because of large ligands of the complexes.

In conclusion, these results demonstrate that the reaction of dicobalt octacarbonyl and acetylene of pseudorotaxanes affords rotaxanes in high yields. This new technique for synthesis of various rotaxanes is being explored through our ongoing studies in this area.

This work was performed with the financial support of a Grant-in-Aid for Scientific Research on Encouraged Areas (No. 15750116) from Ministry of Education, Culture, Sports, Science and Technology, Japan.

References and Notes

1 a) V. Balzai, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem., Int. Ed.* **2000**, *39*, 3348. b) R. Ballardini, V. Balzani, A. Credi, M. T. Gandolfi, M. Venturi, *Acc. Chem. Res.* **2001**, *34*, 445. c) A. Harada, *Acc. Chem. Res.* **2001**, *34*, 456; C. A. Schalley, K. Beizai, F. Vögtle, *Acc. Chem. Res.* **2001**, *34*, 465. d) J.-P. Collin, C. Dietrich-Buchecker, P. Gavina, M. C. Jimenez-Molero, J.-P. Sauvage, *Acc. Chem. Res.* **2001**, *34*, 477. e) J.-P. Sauvage, C. Dietrich-Buchecker, *Molecular Catenanes, Rotaxanes and Knots*, Wiley-VCH, Weinheim, **1999**. f) T. Takata, N. Kihara, *Rev. Heteroat. Chem.* **2000**, *22*, 197.

2 S. J. Rowan, J. F. Stoddart, *J. Am. Chem. Soc.* **2000**, *122*, 164; S. J. Rowan, S. J. Cantrill, J. F. Stoddart, A. J. P. White, D. J. Williams, *Org. Lett.* **2000**, *2*, 759; S.-H. Chiu, S. J. Rowan, S. J. Cantrill, L. Ridvan, P. R. Ashton, R. L. Garrell, J. F. Stoddart, *Tetrahedron* **2002**, *58*, 807; S. J. Rowan, J. F. Stoddart, *Polym. Adv. Technol.* **2002**, *13*, 777.

3 J. S. Hannam, S. M. Lacy, D. A. Leigh, C. G. Saiz, A. M. Z. Slawin, S. G. Stitchell, *Angew. Chem., Int. Ed.* **2004**, *43*, 3260.

4 N. Kihara, S. Motoda, T. Yokozawa, T. Takata, *Org. Lett.* **2005**, *7*, 1199.

5 For recent reviews on Pauson–Khand reaction, see: K. M. Brummonda, J. L. Kentb, *Tetrahedron* **2000**, *56*, 3263; A. J. Fletcher, S. D. R. Christie, *J. Chem. Soc., Perkin Trans. 1* **2000**, 1657; Y. K. Chung, *Coord. Chem. Rev.* **1999**, *188*, 297; T. Sugihara, M. Yamaguchi, M. Nishizawa, *Chem. Eur. J.* **2001**, *7*, 1589; L. V. R. Boñaga, M. E. Krafft, *Tetrahedron* **2004**, *60*, 9795.

6 For recent reviews on Nicholas reaction, see: K. M. Nicholas, *Acc. Chem. Res.* **1987**, *20*, 207; B. J. Teobald, *Tetrahedron* **2002**, *58*, 4133.

7 K. Kira, H. Tanda, A. Hamajima, T. Baba, S. Takai, M. Isobe, *Tetrahedron* **2002**, *58*, 6485; S. Hosokawa, M. Isobe, *Tetrahedron Lett.* **1998**, *39*, 2609.

8 For example, see: D. Seyferth, M. O. Nestle, A. T. Wehman, *J. Am. Chem. Soc.* **1975**, *97*, 7417, and references given.

9 P. R. Ashton, P. J. Campbell, E. J. T. Chrystal, P. T. Glink, S. Menzer, D. Philp, N. Spencer, J. F. Stoddart, P. A. Tasker, D. J. Williams, *Angew. Chem., Int. Ed.* **1995**, *34*, 1865.

10 See Supporting Information.

11 The ammonium salt **5** was synthesized from 3,5-dimethylbenzylamine and the corresponding aldehyde, which was obtained from terephthalaldehyde and ethynylmagnesium bromide.

12 The ^{1}H NMR spectra of crude products of disubstituted acetylenes revealed formation of the other products, which might be produced by the reaction of **3** and dicobalt octacarbonyl. On the other hand, the certain signals were not observed in ^{1}H NMR spectra of crude products of monosubstituted acetylenes.

13 F. Huang, J. W. Jones, C. Slebodnick, H. W. Gibson, *J. Am. Chem. Soc.* **2003**, *125*, 7001.

14 The association constant of the ammonium salt **3c** was also examined; the value of K_{exp} is $6400 \pm 1400\,\mathrm{M}^{-1}$.

15 H. Sasabe, N. Kihara, K. Mizuno, A. Ogawa, T. Takata, *Tetrahedron Lett.* **2005**, *46*, 3851; H. Sasabe, N. Kihara, K. Mizuno, A. Ogawa, T. Takata, *Chem. Lett.* **2006**, *35*, 212.

Published on the web (Advance View) June 10, 2006; doi:10.1246/cl.2006.766