A High-Yielding and Convenient Synthesis of Rotaxane Based On an Ester Forming Capping Methodology

Yuji Tokunaga,* Suzuka Kakuchi, Koichiro Akasaka, Naoki Nishikawa, Youji Shimomura, Kimio Isa,[†] and Toshihiro Seo
Department of Materials Science and Engineering, Faculty of Engineering, Fukui University, Bunkyo, Fukui 910-8507
[†]*Faculty of Education and Regional Studies, Fukui University, Bunkyo, Fukui 910-8507*

An efficient method for preparation of rotaxanes, involving hydrogen bonding guided self-assembly and diaryldiazoalkanes ester forming end-capping of pseudorotaxanes, is described. The end-capping reactions proceed under mild conditions and furnish the expected rotaxanes in excellent yields.

Recently, the design and synthesis of rotaxanes has received much attention because of the intriguing properties and unique structures of these substances.[1,2] An attractive synthetic approach to the rotaxanes takes advantage of a self-assembly phenomena to control formation of appropriate chemical bonds. A key observation made in this area was that self-assembling pseudo-rotaxanes are formed from secondary ammonium salts and crown ethers.[3] Subsequently, several techniques were developed for rotaxane synthesis, which involved sequential threading and end-capping of the pseudorotaxane skeleton.[4] Numerous end-capping methods have been investigated, including acylation of an amine[4a] or alcohol function,[4b] 1,3-dipolar cycloaddition,[4c] Wittig reaction,[4d] disulfide formation,[4e] and radical reaction.[4f] However, in some cases the yields of these processes were unacceptably low,[4a,c,f] and in others the processes are restricted to the synthesis of symmetric rotaxanes only.[4e]

Recent investigations in our laboratories have led to the development of an efficient and versatile method for the synthesis of rotaxanes. Self-assembling pseudorotaxane formation is controlled by weak intermolecular interactions between the ammonium salt thread and crown ether. It is important that these interactions be maintained under the conditions used for the capping process. The new capping methodology, uncovered in our studies, employs diaryldiazomethane esterification of a terminal carboxylic acid residue in the ammonium salt thread of a pseudorotaxane. The effectiveness of new technique is related to the high yields, mild conditions and functional group compatibility normally associated with diazoalkane esterification reactions.

The synthesis of the requisite ammonium salts **3** used in this procedure begins with condensation of primary benzylamines **1** and ester-aldehydes **2** to generate the corresponding imines (Scheme 1). Reduction of the imines, followed by ester hydrolysis and salt formation then produces the ammonium salts **3**, which possess bulky aryl groups on one end and carboxylic acid groups at the other.

NMR monitored titrations were performed to demonstrate that pseudorotaxanes are formed by interaction of the ammonium salts with crown ethers. These experiments showed that complementary hydrogen bonding between the crown ether oxygens and ammonium salt protons occurred effectively despite the existence of more acidic carboxylic acid protons in the
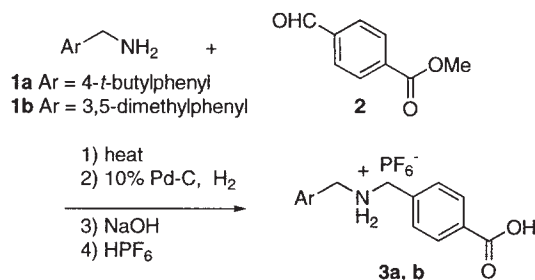
Scheme 1.

ammonium salts.[4f] The ^{1}H NMR spectrum of a 1 : 1 CDCl$_3$/ CD$_3$CN solution, containing equimolar quantities (10 mol dm^{-3}) of ammonium salt **3a** and crown ether **4a**, revealed the formation of the expected pseudorotaxane (3.52, 4.54, 4.78, and 6.70 ppm, Figure 1). The characteristic chemical shifts are consistent with those reported previously for similar complexes.[3,5] The concentration of each component in this mixture is readily determined and these are used to calculate binding constants of 1000 (mol dm^{-3})$^{-1}$ at 25 °C and 2300 (mol dm^{-3})$^{-1}$ at 0 °C. These binding constants are in the range of those for association of dibenzylammonium salts with crown ethers.[3] The agreement between the chemical shifts and binding constants of pseudo-rotaxanes, formed from ammonium salt **3a** and from dibenzyl-ammonium salts, shows that the carboxylic acid group does not interfere with the hydrogen bonding interactions.
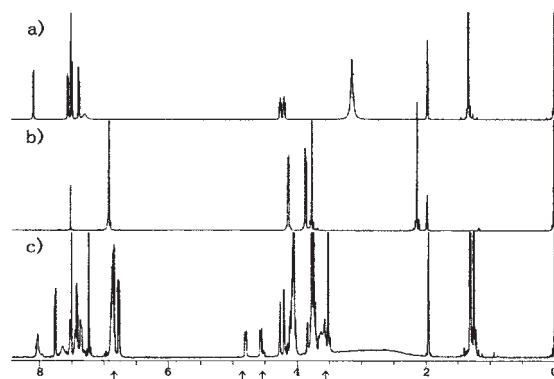

Figure 1. ^{1}H NMR spectra recorded in CDCl$_3$/CD$_3$CN (1 : 1) at 25 °C of a) **3a**, b) **4a**, and c) a 1 : 1 mixture of **3a** and **4a**.

Diaryldiazomethane esterification of the pseudorotaxanes provides a convenient route for rotaxane formation. Accordingly, complexation of ammonium salts **3** with excess crown ethers **4**[6] followed by reaction with diphenyldiazomethane gives the

expected rotaxanes **5** in high yields (Scheme 2 and Table 1).[7] The reactions were carried out in either $CHCl_3$ or $CH_3CN/CHCl_3$ (1 : 1). Although heterogeneous solutions of the pseudorotaxanes were achieved only when $CHCl_3$ was used as a solvent, the esterification reactions were high yielding in both solvent systems.
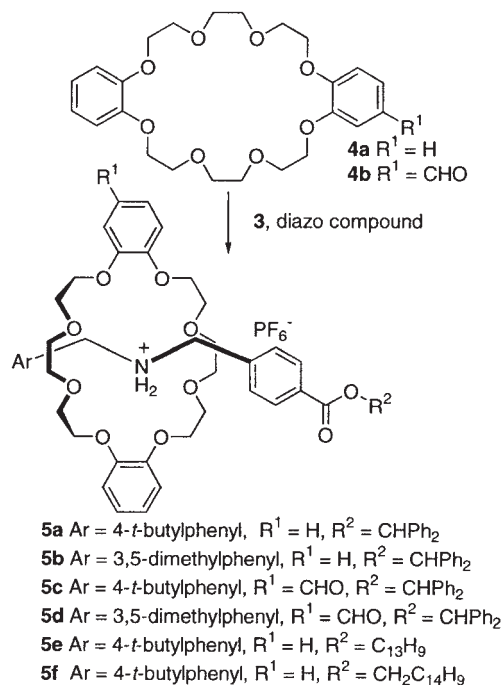
Scheme 2.

Table 1. Esterfication of pseudorotaxane

Run	Axis	Crown Ether	Solvent	Product	Yield/%[a]
1	**3a**	**4a**	$CHCl_3$-MeCN (1 : 1)	**5a**	87 (62)
2	**3a**	**4a**	$CHCl_3$[b]	**5a**	81
3	**3b**	**4a**	$CHCl_3$-MeCN (1 : 1)	**5b**	97 (83)
4	**3b**	**4a**	$CHCl_3$[b]	**5b**	97
5	**3a**	**4b**	$CHCl_3$-MeCN (1 : 1)	**5c**	81 (79)
6	**3a**	**4b**	$CHCl_3$[b]	**5c**	91
7	**3b**	**4b**	$CHCl_3$-MeCN (1 : 1)	**5d**	91 (67)
8	**3b**	**4b**	$CHCl_3$[b]	**5d**	92
9	**3a**	**4a**	$CHCl_3$-MeCN (1 : 1)	**5e**	(78)
10	**3a**	**4a**	CH_2Cl_2-MeCN (1 : 1)	**5f**	45 (38)

All new compounds were identified by ^{1}H and ^{13}C NMR, MS, and IR spectra. [a]Determind by ^{1}H-NMR spectra of crude products. ( ): isolated yield. [b]Heterogeneous.

To demonstrate the versatility of this method, 9-diazo-9*H*-fluorene was used in place of diphenyldiazomethane for the esterification process. Reaction with excess amount of this reagent proceeds to furnish the corresponding rotaxane **5e** in high yield (Scheme 2, run 9 Table 1). In a similar manner, by using 9-anthryldiazomethane, carboxyl groups in the pseudorotaxane can be efficiently transformed to 9-methylanthryl ester **5f** (run 10 Table 1).

In conclusion, the observations made in this effort show that complementary hydrogen bonding interactions between dibenzo[24]crown-8 and secondary ammonium salts results in efficient

formation of pseudorotaxanes despite the existence of carboxylic acid group in the latter substrates. In addition, the results demonstrate that esterification of the acid by using diaryldiazoalkanes affords rotaxanes in excellent yields. Thus, it appears that the conditions used for this end-capping reaction do not affect the weak interactions responsible for pseudorotaxane formation. The scope of the new technique for rotaxane synthesis is being explored in our ongoing studies in this area.

References and Notes

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7 The typical synthesis procedure: Ammonium salt **3a** (59.8 mg, 0.135 mmol) and crown ether **4b** (128.8 mg, 0.270 mmol) were dissolved in a mixture of $CHCl_3$ (13.5 ml) and CH_3CN (13.5 ml). Diphenyldiazomethane (31.4 mg, 0.162 mmol) was added to the reaction mixture under ice-bath, and the reaction mixture was stored in refrigerator (at 4 °C) for 2d. After removal of solvent, the residue was washed with toluene and ethyl acetate to provide **5c** (120 mg, 79%) as a white solid. ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.23 (s, 9H), 3.48–3.70 (m, 8H), 3.70–3.95 (m, 8H), 3.95–4.22 (m, 8H), 4.55–4.62 (m, 2H), 4.77–4.85 (m, 2H), 6.56–6.87 (m, 7H), 7.05 (s, 1H), 7.28–7.34 (m, 2H), 7.35–7.47 (m, 10H), 7.63–7.73 (br, 2H), 7.79–7.82 (m, 2H), 9.65 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 22.61, 31.15, 31.55, 34.63, 51.87, 52.48, 67.70, 67.93, 68.33, 70.00, 70.03, 70.23, 70.58, 70.80, 70.87, 77.20, 77.62, 109.85, 111.80, 112.06, 121.64, 125.74, 127.20, 128.04, 128.08, 128.23, 128.59, 128.66, 129.01, 129.69, 130.18, 130.57, 136.69, 140.02, 140.06, 146.64, 147.94, 152.73, 152.79, 164.51, 190.68. Ir ν_{max} (KBr) cm^{-1}: 2940, 1720, 1700, 1460, 1690, 560. mp 112–115 °C. HRMS Found: $m/z = 941.4773$ (M-PF$_6^-$). Calcd for $C_{57}H_{66}NO_{11}$: 941.4714.