Dynamic Covalent Chemistry in Rotaxane Synthesis. Slipping Approach to [2]Rotaxane Utilizing Reversible Cleavage–Rebondage of Trityl Thioether Linkage

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A [2]rotaxane was synthesized in a high yield from a dumbbell-shaped *sec*-ammonium salt having trityl thioether and 3,5-di-*t*-butylphenyl groups at the both ends and dibenzo-24-crown-8-ether, through the slipping, utilizing the reversible cleavage–rebondage of the trityl thioether linkage.

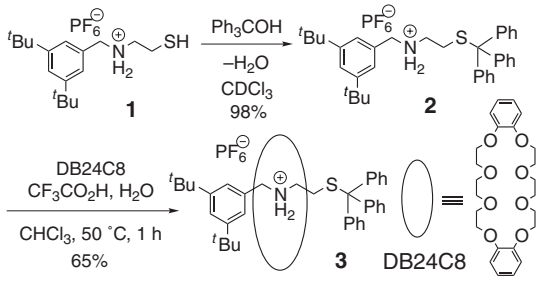
The noncovalent syntheses of supramolecular complexes are generally carried out under thermodynamic control, whereas the traditional covalent syntheses of organic molecules are usually kinetically controlled. Recently, chemists have re-noticed some advantages of covalent bonds in supramolecular chemistry, i.e. "dynamic" covalent bonds that can be formed and broken reversibly under thermodynamic control.[1] Dynamic covalent chemistry has proved to provide a new powerful protocol especially for the synthesis and functions of mechanically or topologically interlocked molecules such as catenanes and rotaxanes.[2]

We have recently succeeded in the synthesis of [3]rotaxanes and the first synthesis of poly[3]rotaxane utilizing dynamic nature of disulfide linkage as a dynamic covalent bond.[3] Here we wish to describe the utilization of trityl thioether bond[4] as a dynamic covalent bond for the synthesis of a [2]rotaxane based on *sec*-ammonium-crown ether motif.[5]

An equimolar mixture of an axle **1** possessing terminal thiol group[6] (0.070 mmol) and trityl alcohol (0.070 mmol) in $CDCl_3$ (0.70 mL) was allowed to stand at room temperature for 24 h. Trityl thioether **2** was isolated by chromatographic purification using preparative HPLC (63% yield) or using alumina column (acid-free form of **2**, 98% yield).[7] A solution of a mixture of **2** (0.10 M), dibenzo-24-crown-8 ether (DB24C8, 0.12 M), and trifluoroacetic acid (0.50 M) in chloroform containing a trace amount of water was heated at 50 °C for 1 h. The corresponding [2]rotaxane (**3**) was isolated in 65% yield.[8] The reversible cleavage–rebondage process of the trityl thioether bond must be involved in this rotaxane formation, because both the trityl and 3,5-di-*t*-butylphenyl groups are so large that the axle cannot intrude the cavity of DB24C8. Thus, **3** was formed in a "slipping" way.

A single crystal suitable for X-ray study was grown from chloroform and hexane. The X-ray crystallographic analysis revealed the interlocked structure of **3** (Figure 1).[9] The centrally located ammonium group of the dumbbell component participates in hydrogen-bonding interaction with the oxygen atoms of DB24C8 moiety. No special interaction was observed between the thioether group and the wheel component. It should be noted here that the thioether group is surrounded by the trityl group and the DB24C8 component.

Details of the syntheses of **3** were studied by ^{1}H NMR.



Scheme 1. Synthesis of [2]rotaxane (**3**) by slipping approach.

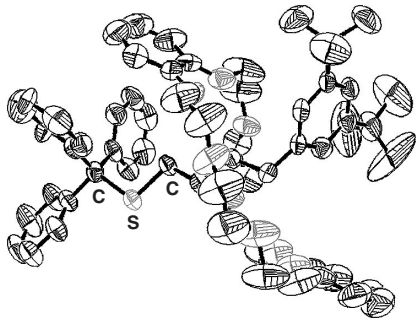


Figure 1. An ORTEP drawing of the X-ray crystal structure of [2]rotaxane (**3**). Solvent molecules and hydrogen atoms are omitted for clarity.

When an equimolar amount of **1** (0.070 mmol) was added to a solution of trityl alcohol (0.070 mmol) in $CDCl_3$ (0.70 mL), most part of **1** was not dissolved. However, the mixture gradually became a clear pale yellow homogeneous solution within 24 h. The ^{1}H NMR spectrum clearly showed that trityl thioether formation was completed to yield **2** almost quantitatively. To that solution was added a slight excess (0.080 mmol) of DB24C8. The reaction mixture was allowed to stand at room temperature and the reaction progress was monitored (Figure 2). The rotaxane formation proceeded despite the absence of trifluoroacetic acid. This is probably because the sec-ammonium salt group of **2** worked as an acid catalyst for the reversible cleavage–rebondage process, although its acidity was low. After the reaction was carried out in the same condition for 44 h, **3** was isolated by preparative GPC in 32% yield (Table 1). Prolonged reaction period resulted in 97% isolated yield in 192 h. Since the major driving force for the rotaxane formation would be the exothermic hydrogen-bonding interaction, the yield of **3** can be lowered at higher temperatures (50 °C), as shown in Table 1 (Entries 4–6). Solvents with high donor numbers are known to prevent hydrogen-bonding interaction.[10] Therefore, pseudorotaxanes prepared from *sec*-ammonium salt and crown ether motif get disassembled into their

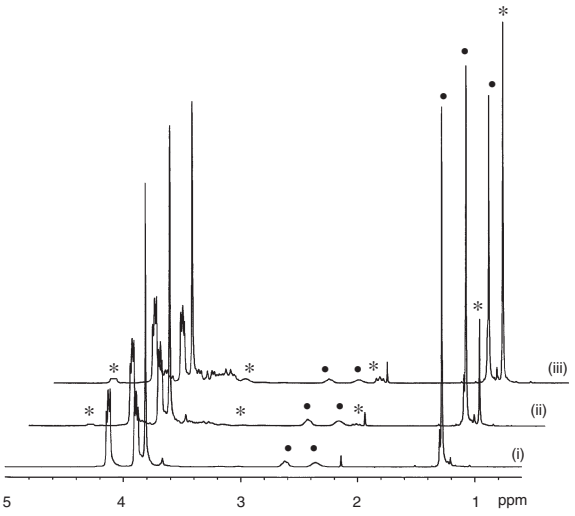
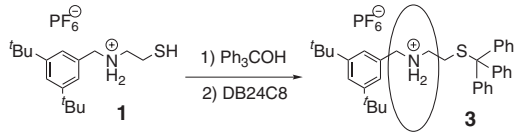


Figure 2. ^{1}H NMR spectral change (270 MHz, $CDCl_3$, rt) during the reaction of **2** and DB24C8 in (i) 0 h, (ii) 1 day, and (iii) 4 days after addition of DB24C8. • denotes the signals of dumbbell (**2**), whereas * denotes the signals of [2]rotaxane (**3**).

Table 1. Synthesis of [2]rotaxane (**3**) by slipping approach[a]



Entry	Temp/°C	Time[b]/h	Yield[c]/%
1	r.t.	44	32
2	r.t.	109	70
3	r.t.	192	97
4	50	39	63
5	50	72	70
6	50	119	81

a) Solvent: $CHCl_3$. Concentration: [**1**] 0.10 M, [Ph_3COH] 0.10 M, [DB24C8] 0.12 M. b) Reaction time after the addition of DB24C8. c) Isolated yield.

components in the solvents having highdonor numbers such as DMSO and DMF.[3b] To examine the deslipping of **3**, a DMSO-d_6 solution of **3** (0.050 M) containing a small amount of water was heated at 50 °C and the deslipping behavior was monitored by ^{1}H NMR spectroscopy. However, no change was detected at all after 20 h. Neither addition of a large excess of water (0.35 mmol) nor addition of trifluoroacetic acid (0.35 mmol) promoted the deslipping reaction. This could be attributed to the "dynamic protection" of the thioether group by the DB24C8 component, as observed in the isolation of a reactive intermediate stabilized by the rotaxane structure.[11] In principle, the formation of the thioether group in **3** could be taken as reversible, but it is virtually irreversible under the conditions as mentioned above (Scheme 2).

Thus, we could demonstrate that the trityl thioether linkage can be regarded as a dynamic covalent bond and can be a powerful tool for the rotaxane synthesis by a slipping approach.

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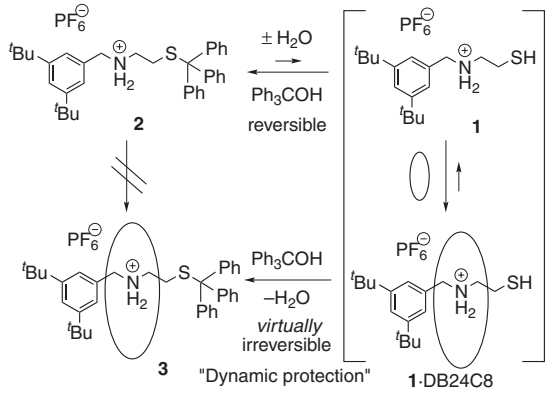

Scheme 2. Schematic diagram of the formation of **3**.

References and Notes

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7 **2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.10 (m, 18H, ArH), 3.73 (s, 2H, $ArCH_2$), 2.63 (t, $J = 7.6$ Hz, 2H, NCH_2), 2.21 (t, $J = 7.6$ Hz, 2H, SCH_2), 1.30 (s, 18H, *t*-Bu) ppm. Acid-free form of **2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, $J = 7.3$ Hz, 6H, ArH), 7.27–7.15 (m, 10H, ArH), 7.06 (d, $J = 1.5$ Hz, 2H, ArH), 3.63 (s, 2H, $ArCH_2$), 2.62 (t, $J = 6.8$ Hz, 2H, NCH_2), 2.39 (t, $J = 6.8$ Hz, 2H, SCH_2), 1.31 (s, 18H, *t*-Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 144.9, 129.6, 127.8, 126.6, 122.2, 121.0, 66.5, 53.9, 47.7, 34.8, 32.2, 31.5 ppm. IR (NaCl) $\upsilon = 2962, 1597, 1488, 1443, 1361, 742, 700\ cm^{-1}$.

8 [2]Rotaxane (**3**) was previously synthesized by the "threading-endcapping" method (Ref. 6).

9 Crystal data for **3**: $C_{62}H_{78}NSPF_6O_8Cl_6$, Mr = 1355.04, monoclinic space group $P2_1/c$ (#14), $a = 14.6475(4)$ Å, $b = 29.3480(6)$ Å, $c = 16.1942(2)$ Å, $\beta = 89.505(2)°$, $V = 6961.2(3)$ Å^3, $Z = 4$, $D_{calcd} = 1.293\ g\cdot cm^{-1}$, $m = 3.650\ cm^{-1}$, Mo Kα radiation ($\lambda = 0.7107$ Å), $2\theta_{max} = 55.0$ °C, 15565 reflections ($I > 3\sigma(I)$), $R_1 = 0.099$, $Rw = 0.107$, GOF = 1.841.

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