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Construction of new [2]pseudorotaxanes by hydrogen bonding assembly of macrocyclic tetrathiolactam with amides and an ester

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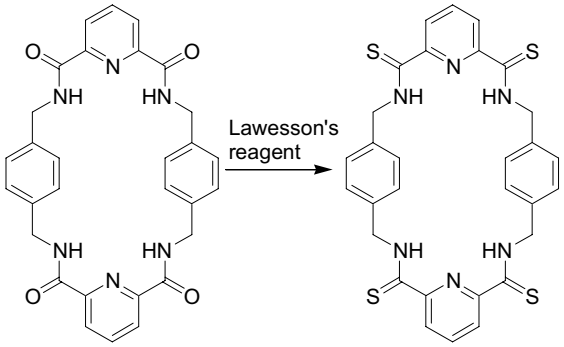
Abstract—Thionation of a macrocyclic tetralactam gave a new macrocyclic tetrathiolactam. [2]Pseudorotaxanes constructed from the macrocycle with diamides and a diester as a neutral guest have been prepared by a facile threading process. Molecular structures and hydrogen bonding association properties of the [2]pseudorotaxanes were characterized by X-ray crystallography and ^{1}H NMR spectroscopy.

Polylactams, macrocyclic amides, have received intense interest due to their ability to include anions and organic molecules.[1,2] Therefore, tetralactams have been widely used as the wheel component for preparation of interlocked or mechanically bonded molecules such as rotaxanes, pseudorotaxanes, and catenanes.[2] However, to our knowledge, isolation and solid state characterization of [2]pseudorotaxanes constructed from the tetralactams with neutral organic molecules have not been reported.[3] The strength of the hydrogen bonding ability of the macrocyclic amides can be conveniently modulated by thionation of the tetralactams,[4] whereas construction of the interlocked molecules using hydrogen bonding interaction of thioamide-based compounds has been limited. Bowman–James's and our groups have recently demonstrated that thionation of polylactams enhances hydrogen donor ability of the N–H protons in the cavity of macrocycles and improves affinity toward anions.[5] These results prompted us to examine utility of the polythiolactams to provide new mechanically linked molecules such as rotaxanes and pseudorotaxanes. We here report preparation of new [2]pseudorotaxanes by a facile threading process from tetrathiolactam, **1**, with diamides and a diester; molecular structures and hydrogen bonding association properties of the [2]pseudorotaxanes are also characterized by X-ray crystallography and ^{1}H NMR spectroscopy (Scheme 1).

In the previous paper, we have determined the molecular structures of the related tetrathiolactam, 3,6,14,17,23,24-hexaazatricyclo[17.3.1.1^{8,12}]tetracosa-1(23),8(24),9,11,19,21-haxaene-2,17,13,18-tetrathione, **3**, and its Cl^- complex,[5a] and the crystallographic data indicate that the cavity of **3** seems to be somewhat too small to include Cl^-. We therefore attempted thionation of larger macrocyclic tetralactam, **2**, which has been utilized to the wheel component of rotaxanes.[2g,h] Chemical transformation of **2** to **1** was carried out in a manner analogous to that in the previous



2 **1**

Scheme 1. Preparation of tetrathiolactam.

Keywords: Macrocycle; Thioamide; Thionation; Pseudorotaxane; Hydrogen bond.

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report.[5,6] The structure of **1** was confirmed by NMR and FAB-mass spectroscopy and elemental analysis.[7]

The crystal of **1** was obtained from a DMSO solution. A crystallographic analysis of **1** (Fig. 1)[8] reveals that **1** adopts an approximately C_{2h} conformation and solvates with one molecule of DMSO, which serves as a hydrogen bond acceptor. The macrocyclic system is also stiffened by four intramolecular hydrogen bonds between the thioamide N–H protons and pyridine imine nitrogens (N_{py}). This feature has been also observed with **3**.[2i,5]

The macrocycle **1** is insoluble in chloroform and dichloromethane, whereas the solubility of **1** increased markedly in the presence of amides, indicating that addition of amides would disrupt inter- and intramolecular hydrogen bonds of thioamide group of **1**, and the carbonyl group of amides interacts with the N–H group of **1**. In the ^{1}H NMR spectrum of **1** in $CDCl_3$ in the presence of *N*,*N*,*N*′,*N*′-tetramethylfumaramide, **4**, (ca. 10 equiv), the signal attributed to the N–H proton in the thioamide group was detected at δ 11.12.

[2]Pseudorotaxanes, **7**–**9**, were obtained from reactions of **1** with threads (**4**–**6**) in chloroform and successive reprecipitation from acetonitrile/acetone, respectively[9] (Scheme 2). In the ^{1}H NMR spectrum of **7**, broad signals were observed at room temperature, whereas the signals for **7** were well separated at −50 °C (Fig. 2), in which the signal attributed to the N–H proton of thio-

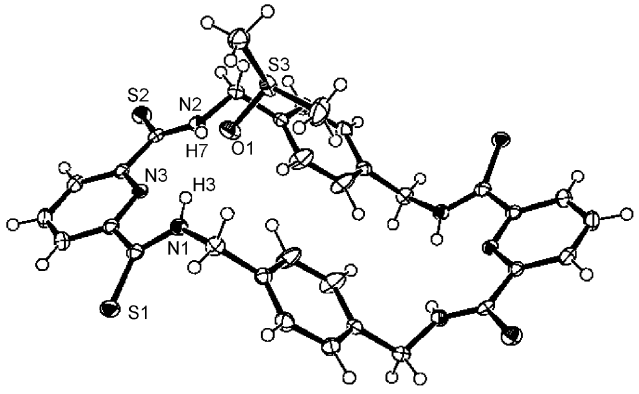
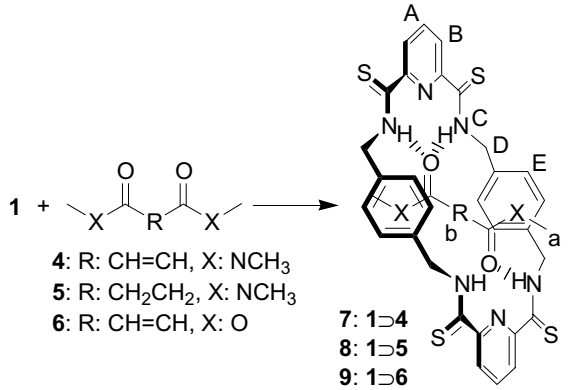


Figure 1. X-ray crystal structure of **1** (obtained as **1**·DMSO) with thermal ellipsoids drawn at the 50% probability level.



Scheme 2. Preparation of [2]pseudorotaxanes.

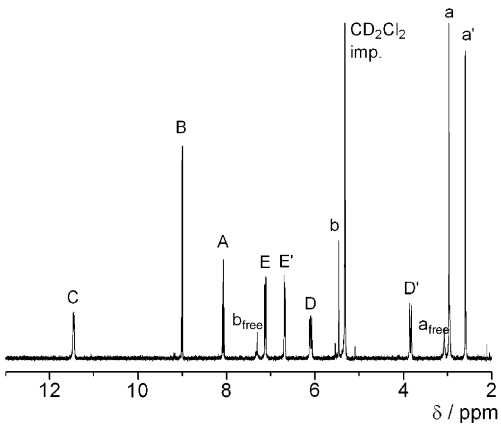


Figure 2. ^{1}H NMR spectrum of **7** (400 MHz, CD_2Cl_2, 223 K). The letters correspond to the assignments shown in Scheme 2.

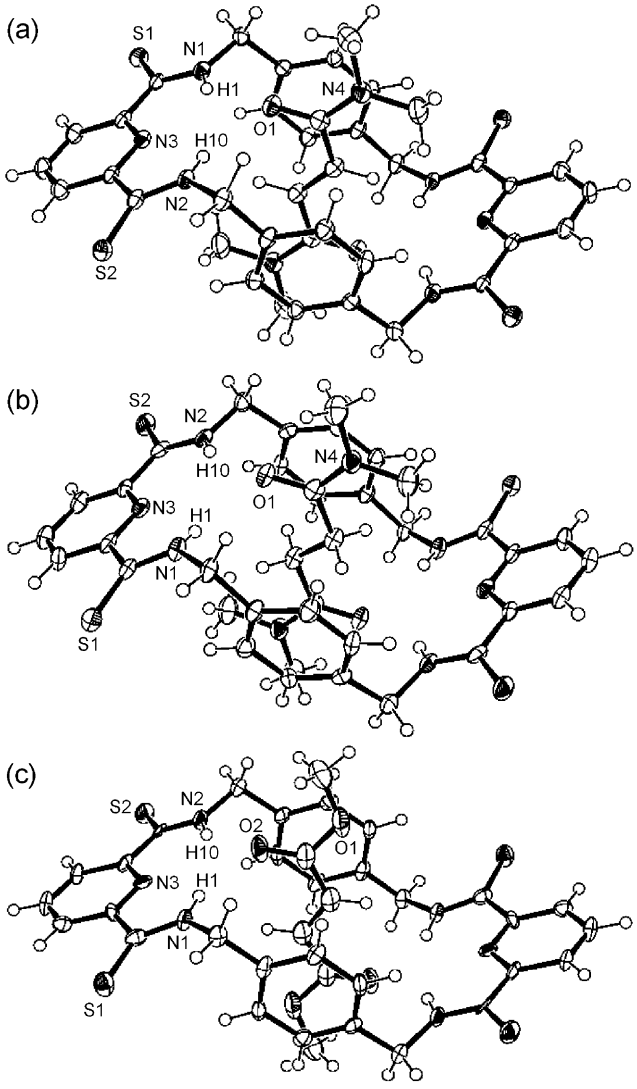


Figure 3. X-ray crystal structures of (a) **7** (**1**⊃**4**), (b) **8** (**1**⊃**5**), and (c) **9** (**1**⊃**6**), with thermal ellipsoids drawn at the 50% probability level.

amide group was detected at δ 11.46.[10] The intercomponent hydrogen bonding interaction led to a split of the proton signals (H_D and H_E),[2d,f,h] and the substantially high-field shift in the methyne protons signal (δ 5.46) of **4** compared to that of free **4** (δ 7.33) was also detected. The ratios of the signals area essentially agree with the assignment. These results indicate that **7** is thermodynamically stable like the conventional pseudorotaxanes.

The molecular structures of the [2]pseudorotaxanes **7**–**9** have been confirmed by X-ray crystallographic analysis (Fig. 3).[11–13] The crystals of **7**–**9** were obtained from slow concentration of a chloroform solution. In the solid state of **7**, the macrocycle also adopts a chair-like conformation except that the xylylene rings flip perpendicularly to the cavity, and **4** inserts approximately axially through its center. The complex stabilization is achieved via a combination of both [N–H···O=C] and [N–H···N_{py}] hydrogen bonds, and all four thioamide N–H hydrogen atoms take part in the interaction (Table 1). The π–π stacking feature between the olefin unit of **4** and the xylylene units of **1** would also assist the complexation. No intercomponent π-stacking interactions is apparent in the X-ray structure. Similar conformation and the interlocking hydrogen bonds are observed for **8** and **9** (Table 1), although **9** belongs to different molecular packing in the crystal lattice form those of **7** and **8**. The molecular structures of **7**–**9** are reminiscent of those of the rotaxanes constituted of **2** and peptides.[2g,h]

Dethreading the [2]pseudorotaxane **7** has also been examined. In the ^{1}H NMR spectrum of **7** in CD_2Cl_2, addition of tetrabutylammonium chloride ([*n*-Bu_4N]Cl) (ca. 2 equiv) led to further downfield shift in the N–H resonance of **1** (δ 12.77) and the methyne protons signal of free **4** was detected (δ 7.32) at room temperature. This reflected that strong hydrogen bond accepting ability of Cl^- induced a shift of the equilibrium toward the dethreading form.

Table 1. Selected hydrogen bonds in **1**·DMSO and **7**–**9**

N–H···A	d(H···A)/Å	d(N···A)/Å	(N–H···A)/°
1·DMSO:			
N(1)–H(3)···O(1)	1.994(2)	2.852(2)	156.99(7)
N(2)–H(7)···O(1)	2.032(2)	2.889(2)	150.18(6)
N(1)–H(3)···N(3)	2.247(2)	2.638(2)	105.39(6)
N(2)–H(7)···N(3)	2.180(2)	2.633(2)	108.29(6)
7:			
N(1)–H(1)···O(1)	2.153(3)	2.917(3)	135.1(1)
N(2)–H(10)···O(1)	2.182(4)	3.078(4)	159.15(9)
N(1)–H(1)···N(3)	2.080(4)	2.654(4)	116.4(1)
N(2)–H(10)···N(3)	2.305(3)	2.648(4)	100.8(1)
8:			
N(1)–H(1)···O(1)	2.367(6)	2.939(6)	151.61(17)
N(2)–H(10)···O(1)	2.366(7)	3.046(7)	164.43(16)
N(1)–H(1)···N(3)	2.359(8)	2.676(8)	113.60(18)
N(2)–H(10)···N(3)	2.411(7)	2.657(8)	102.89(18)
9:			
N(1)–H(1) ···O(2)	2.02(1)	2.96(1)	142.4(3)
N(2)–H(10)···O(2)	2.127(11)	2.919(11)	148.7(3)
N(1)–H(1)···N(3)	2.10(1)	2.64(1)	106.9(3)
N(2)–H(10)···N(3)	2.21(1)	2.65(1)	110.2(3)

As described above, the tetrathiolactam **1** exhibits good affinity toward the amides and ester, and provides new [2]pseudorotaxanes **7**–**9** by the facile threading process. The [2]pseudorotaxanes are readily isolated and their molecular structures are characterized. The tetrathiolactam seems to be prospective host molecules, because there have been extensive studies on the amide-type supramolecules and the thionation of amide conveniently modulates the strength of the hydrogen bonding ability of the macrocycles. Further studies on preparation and organizations of other polythiolactams are in progress.

Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Center; publication numbers CCDC 233065 (**1**·DMSO), 233066 (**7**), 233067 (**8**), and 233068 (**9**).

Acknowledgements

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7. 3,11,18,26,33,36-Hexaazapentacyclo[26.2.2.2^{13,16}.1^{5,9}.1^{20,24}]-hexatriaconta-5,7,9(36),13,15,20,22,24(33),28,30,31,34-dodecaene-4,10,19,25-tetrathione, **1**: 3,11,18,26,33,36-Hexaazapentacyclo[26.2.2.21^{3,16}.1^{5,9}.1^{20,24}]hexatriaconta-5,7,9(36),13,15,20,22,24(33),28,30,31,34-dodecaene-4,10,19,25-tetrone, **2** (150 mg, 0.28 mmol) and 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane- 2,4-disulfide, (so-called Lawesson's reagent) (1.0 g, 2.5 mmol) were suspended in toluene (40 mL), and the mixture was refluxed for 60 h under N_2. The reaction mixture was filtered and the crude product was thoroughly washed with methanol and purified by recrystallization from THF (59 mg, 35% yield). FAB-MS: m/z 599 $[M+H]^+$. ^{1}H NMR (400 MHz in DMSO-d_6): δ 11.69 (t, $J = 3.8$, 4H), 8.64 (d, $J = 5.0$, 4H), 8.12 (t, $J = 5.0$, 2H), 7.40 (s, 8H), 4.21 (d, $J = 3.8$, 8H). ^{13}C NMR (100 MHz in DMSO-d_6): δ 189.8, 149.6, 138.5, 136.1, 127.2, 126.9, 47.4. Anal. Calcd for $C_{30}H_{26}N_6S_4$: C, 60.17; H, 4.38; N, 14.03; S, 21.42%. Found: C, 60.81; H, 4.50; N, 14.08; S, 20.70%.
8. Crystallographic data for **1**·DMSO: $C_{32}H_{32}N_6OS_5$, $M = 676.94$, monoclinic, $P2_1/a$, $a = 9.362(3)$, $b = 15.157(5)$, $c = 12.572(4)$ Å, $\beta = 90.634(5)°$, $V = 1783.9(10)$ Å^3, $Z = 2$, $D_{calcd} = 1.260$ g cm^{-3}, μ(MoKα) = 3.58 cm^{-1}, $T = 113$ K, $F(0\,0\,0) = 708$, 26100 reflections measured, 4080 unique, 3037 observed ($I > 3\sigma(I)$), 236 valuables, $R1 = 0.039$, $Rw = 0.055$.
9. Pseudorotaxane, **7** (**1**⊃**4**): **1** (5.6 mg, 9.4×10^{-3} mmol) was added to a chloroform solution (5 mL) of **4** (32 mg, 0.19 mmol), and the mixture was stirred at room temperature for 24 h. After the reaction, the mixture was filtered. The filtrate was collected and the solvent was removed by evaporation. The residue was dissolved in acetonitrile (1 mL), and reprecipitation from acetone gave a yellow powder of **7** (0.7 mg, 10% yield). **7**: ^{1}H NMR (400 MHz, CD_2Cl_2, 223 K): δ 11.46 (br d, 4H), 9.01 (d, 4H), 8.07 (t, 2H), 7.12 (d, 4H), 6.69 (d, 4H), 6.09 (dd, 4H), 5.46 (s, 2H), 3.83 (dd, 4H), 2.97 (s, 6H), 2.59 (s, 6H). [2]Pseudorotaxanes **8** and **9** were prepared analogously. **8**: ^{1}H NMR (400 MHz, CD_2Cl_2, 223 K): δ 11.32 (br s, 4H), 9.04 (d, 4H), 8.05 (t, 2H), 7.20 (br, 8H), 6.25 (br, 4H), 3.93 (br, 4H), 3.1–2.9 (br, 12H), 2.6–2.3 (br, 4H). **9**: ^{1}H NMR spectrum of **9** could not be assigned because of broad signals even at 223 K.
10. The downfield shift of the N–H signal is consistent with the presence of a hydrogen-bonding interaction.
11. Crystallographic data for **7** (**1**⊃**4**): $C_{38}H_{40}N_8O_2S_4$, $M = 769.03$, triclinic, $P\bar{1}$, $a = 9.577(9)$, $b = 9.868(10)$, $c = 11.078(12)$ Å, $\alpha = 80.62(5)°$, $\beta = 79.41(5)°$, $\gamma = 66.52(4)°$, $V = 939.1(16)$ Å^3, $Z = 1$, $D_{calcd} = 1.360$ g cm^{-3}, μ(MoKα) = 2.99 cm^{-1}, $T = 113$ K, $F(0\,0\,0) = 404$, 13252 reflections measured, 3925 unique, 2919 observed ($I > 3\sigma(I)$), 255 valuables, $R1 = 0.055$, $Rw = 0.082$.
12. Crystallographic data for **8** (**1**⊃**5**): $C_{38}H_{42}N_8O_2S_4$, $M = 771.04$, triclinic, $P\bar{1}$, $a = 9.439(8)$, $b = 10.081(10)$, $c = 11.065(12)$ Å, $\alpha = 81.78(6)°$, $\beta = 79.44(6)°$, $\gamma = 65.49(4)°$, $V = 939.2(15)$ Å^3, $Z = 1$, $D_{calcd} = 1.363$ g cm^{-3}, μ(MoKα) = 2.99 cm^{-1}, $T = 113$ K, $F(0\,0\,0) = 406$, 13680 reflections measured, 3986 unique, 1810 observed ($I > 3\sigma(I)$), 256 valuables, $R1 = 0.065$, $Rw = 0.081$.
13. Crystallographic data for **9** (**1**⊃**6**)·2H$_2$O: $C_{36}H_{38}N_6O_6S_4$, $M = 778.97$, monoclinic, $C2/c$, $a = 26.58(2)$, $b = 15.661(9)$, $c = 9.716(6)$ Å, $\beta = 101.476(9)°$, $V = 3963.7(41)$ Å^3, $Z = 4$, $D_{calcd} = 1.305$ g cm^{-3}, μ(MoKα) = 2.90 cm^{-1}, $T = 113$ K, $F(0\,0\,0) = 1632$, 30236 reflections measured, 4635 unique, 2246 observed ($I > 3\sigma(I)$), 260 valuables, $R1 = 0.111$, $Rw = 0.123$.