New switchable [2]pseudorotaxanes formed by pyridine *N*-oxide derivatives with diamide-based macrocycles†

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Pyridine *N*-oxide derivatives are capable of formation of stable [2]pseudorotaxanes with diamide-based macrocycles in solution and in the solid state, and their dethreading/rethreading movements can be easily controlled by acid–base stimuli.

Pseudorotaxanes are important building blocks for syntheses of mechanically interlocked structures such as rotaxanes and catenanes which are of potential applications in construction of molecular level machines and switches.[1] In the past two decades, several elegant recognition systems with pseudorotaxane structures have been developed. For example, crown ethers form pseudorotaxanes with paraquat derivatives,[2] secondary ammonium compounds[3] and 1,2-bis(pyridinium)ethane;[4] cyclobis(paraquat-*p*-phenylene) forms charge-transfer complexes with π-electron-rich molecules such as hydroquinone,[5] tetrathiafulvalene (TTF),[6] and 1,5-dioxynaphthalene derivatives.[7] Recently, Beer and co-workers exploited the anion-templated system of isophthalamide-based compounds in the formation of interpenetrated and interlocked structures.[8]

On the other hand, pyridine *N*-oxide derivatives are interesting compounds and have been widely used as complexation ligands,[9] asymmetric catalysts.[10] Ivan Huc *et al.* have reported their pioneering work on synthetic double helices consisting of pyridine *N*-oxide units.[11] Recently, use of pyridine *N*-oxides for molecular recognition studies was also reported.[12] However, we are unaware of any of pseudorotaxanes and tunable molecular switches that have been exploited by utilizing pyridine *N*-oxide as a component. In this communication, it is demonstrated that pyridine *N*-oxide derivatives form stable [2]pseudorotaxanes with diamide-based macrocycles, plus an easily controlled dethreading/rethreading process of the resulting pseudorotaxanes under acid–base stimuli. They are therefore viable candidates for constructing interlocked supramolecular structures and related molecular machines.

The pyridine *N*-oxide derivatives and macrocycles studied in this investigation are shown in Scheme 1. The pyridine *N*-oxide derivatives **3** and **4** were synthesized from the corresponding pyridine dicarboxy acids by a simple two-step procedure (see ESI†). To simplify the spectroscopic analyses, we also synthesized a pyridine-containing new macrocycle **2** (see ESI†).

Although the pyridine *N*-oxide derivatives **3** and **4** are soluble in MeCN, Me_2CO, Me_2SO and MeOH, their solubility is very limited in $CHCl_3$ and CH_2Cl_2. However, the solubility in these chlorinated solvents can be significantly improved by addition of one or more molar equivalents of the macrocycle **1** or **2**. This observation suggested that strong intermolecular complexation of some type could occur with these systems. We observed significant shifts in the ^{1}H NMR spectra of an equimolar pyridine *N*-oxide (**3** or **4**) and macrocycle (**1** or **2**) in $CDCl_3$. The most important features of ^{1}H NMR spectrum of an equimolar mixture of **1** with **3** in $CDCl_3$ are presented in Fig. 1.

The signals of protons H_f, H_g of the macrocycle **1** and that of $H_{b'}$ $H_{c'}$ of **3** are shifted high field, and the peaks for H_α, H_β and H_γ of the ethylene glycol unit in **1** moved upfield (Fig. 1b), suggesting that hydrogen bonding (N–H···O) probably takes place between the amide N–H of **1** and the oxygen atom of the pyridine *N*-oxide **3** and between the amide N–H of **3** and the oxygen atoms of the ethylene glycol unit in **1**. All of these changes were also observed for the equimolar mixture of **1** and **4**, **2** and **3**, **2** and **4** (see ESI†). This result implies that the pseudorotaxane-like complexes would be formed between the pyridine *N*-oxide and amide macrocycle.

To quantify the affinity strength of this recognition system, the association constants are determined to be $K_{\mathbf{1}\cdot\mathbf{3}} = 2.2 \pm 0.6 \times 10^3$, $K_{\mathbf{1}\cdot\mathbf{4}} = 3.8 \pm 1.0 \times 10^2$, $K_{\mathbf{2}\cdot\mathbf{3}} = 5.5 \pm 0.4 \times 10^3$ and $K_{\mathbf{2}\cdot\mathbf{4}} = 1.8 \pm 0.2 \times 10^3$ M^{-1} for **1**·**3**, **1**·**4**, **2**·**3** and **2**·**4**, respectively, by NMR titration experiments in a mixed solvent of $CDCl_3$–CD_3OD (3 : 1 v/v) (see ESI†). The large values of K_a indicate strong interactions between the pyridine *N*-oxide and amide macrocycle. Electrospray ionization mass spectra (see ESI†) of the equimolar mixture of the pyridine *N*-oxide and amide macrocycle confirmed not only the complex formation, but also the 1 : 1 stoichiometry.

The X-ray structural analysis of **1**·**3** (see ESI†) clearly reveals that the pyridine ring of **3** is located in the cavity of the macrocycle **1** (Fig. 2), and is almost parallel to the planes of phenoxy rings of **1** (angles: 6.5 and 6.0°; centroid–centroid distances: 3.71 and 3.73 Å, respectively), indicating that π–π stacking interaction may exist between the pyridine ring of **3** and the phenoxy rings of the host. As expected, the oxygen atom of the *N*-oxide binds with the amide N–H and one

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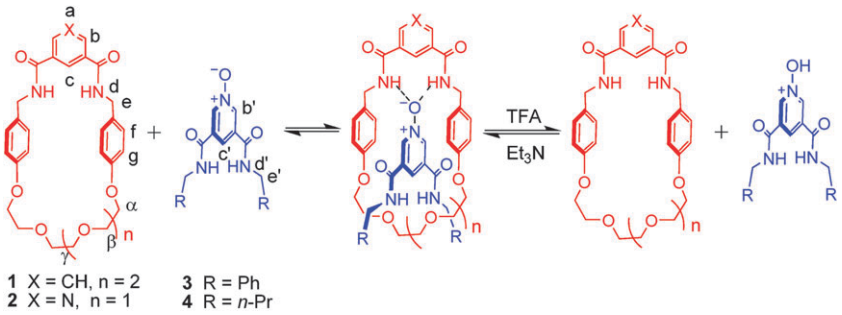
† Electronic supplementary information (ESI) available: Experimental details; ^{1}H NMR spectra for 1 : 1 complexes and for acid–base controlled dethreading/rethreading processes; association constants determination; crystal data for complexes **1**·**3** and **2**·**3**, and ESI-MS spectra of the complexes. CCDC 762537 (**2**), 762538 (**1**·**3**) and 762539 (**2**·**3**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c003118f



Scheme 1 Formation of pyridine *N*-oxide-based pseudorotaxanes and the acid–base controlled dethreading/rethreading movements.

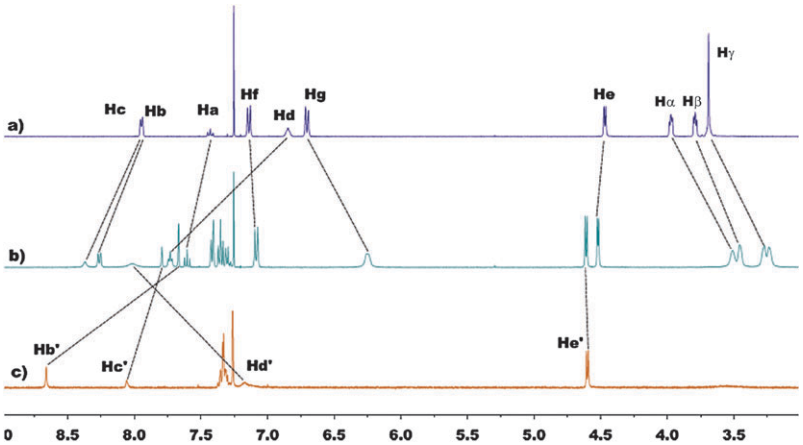


Fig. 1 Partial ^{1}H NMR spectra of (a) macrocycle **1**, (b) an equimolar mixture of **1** and **3**, and (c) pyridine *N*-oxide **3** (4 mM, $CDCl_3$, 400 MHz, 295 K).

aromatic C–H of the macrocycle **1** *via* hydrogen bondings (distances of N–H···O are 2.21, 2.27; C–H···O is 2.20 Å). There is evidence for a second hydrogen bonding interaction between the amide N–H of **3** and the polyether oxygens of the macrocycle **1** (distances of N–H···O are 2.31, 2.61 Å, respectively). These multiple and cooperative hydrogen bondings, in addition to π–π stacking interactions, make the complexes highly stable as evidenced by their *K* values. The resulting X-ray crystal structure showed unambiguously that the complexes are [2]pseudorotaxanes. The crystal structure of complex **2·3** (see ESI†) further confirmed the [2]pseudorotaxane formation of this recognition system.

To study the chemically driven dethreading and rethreading movements in this system, an excess of trifluoroacetic acid (TFA, 45 equiv) was added to an equimolar solution of **1** and **3** in $CDCl_3$. Gratifyingly, the ^{1}H NMR spectrum (Fig. 3c) of the resulting mixture revealed that the protonation[13] of the pyridine *N*-oxide led to decomplexation, because the signals of the phenoxy ring protons shifted almost back to the original positions of the free macrocycle **1** (Fig. 3a). It is noted that small differences were observed for pyridine ring protons in the ^{1}H NMR spectrum due to the protonation of the *N*-oxide. This indicates that, upon protonation, the pyridine *N*-oxide no longer resides inside the cavity of the macrocycle. Deprotonation of the protonated pyridine *N*-oxide by adding an excess of triethylamine (TEA, 50 equiv.) almost recovered the ^{1}H NMR spectrum (Fig. 3d), which is similar to that of the original complex (Fig. 3b), suggesting a return of the pyridine *N*-oxide unit back inside the cavity of the macrocycle, that is to say the complex, a [2]pseudorotaxane, was regenerated. This process can be also realized for the systems of **1·4**, and **2·4** by sequential addition of TFA and TEA (see ESI†).

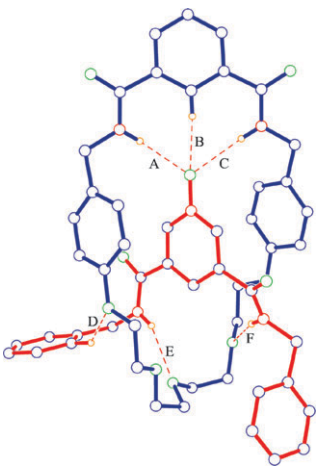


Fig. 2 Ball-and-stick views of the X-ray crystal structure of complex **1·3**. Macrocycle **1** is blue, pyridine *N*-oxide **3** is red, hydrogens are orange, oxygens are green, and nitrogen is red. Hydrogens except those involved in hydrogen bonding have been omitted for clarity.

However, this TFA/TEA stimulus does not work for the system of **2·3** (see ESI†), indicating that the complex **2·3** is too stable to achieve the protonation of the pyridine *N*-oxide by TFA. This is probably because the protonation of the pyridine ring of **2** increased the acidity of the amide and enhanced

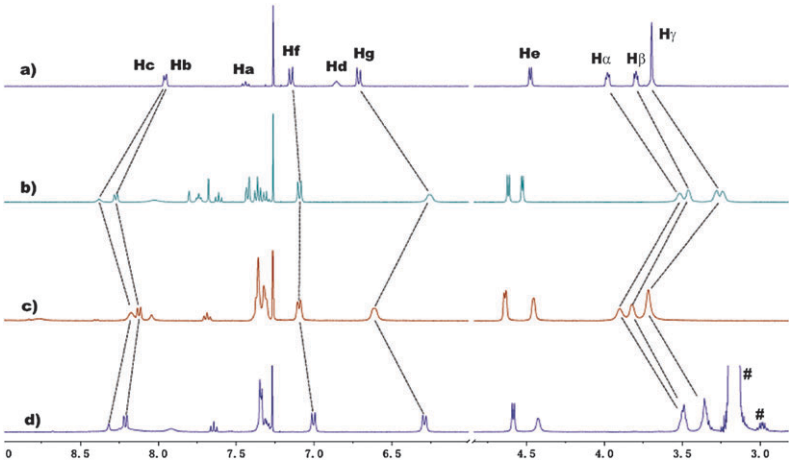


Fig. 3 Partial ^{1}H NMR spectra of (a) macrocycle **1**, (b) an equimolar mixture of **1** and **3**, (c) the mixture obtained after adding an excess of TFA to the solution in (b), and (d) the mixture obtained after adding an excess of TEA to the solution in (c) (4 mM, $CDCl_3$, 295 K, 400 MHz).

binding ability of the macrocycle. Thus, the pyridine *N*-oxide-based pseudorotaxanes can be considered to be suitable candidates for the development of acid–base-controllable[14] molecular machines and switches.

In summary, we have demonstrated that pyridine *N*-oxide derivatives, as new motifs, can form stable [2]pseudorotaxanes, which are stabilized by multiple and cooperative hydrogen bonding and π–π stacking interactions, with diamide-based macrocycles in solution and in the solid state; and the dethreading/rethreading process of the resulting [2]pseudorotaxanes is reversible under acid–base control. These findings may offer an alternative approach for constructing a variety of new supramolecular structures with interlocked [*n*]rotaxanes and [*n*]catenanes. In particular, it might be useful for development of new nanoscale molecular machines and devices.

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