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The contribution of complementary hydrogen bonding to supramolecular structure†

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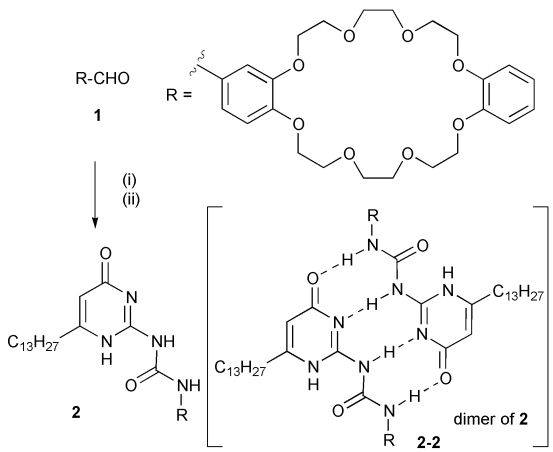
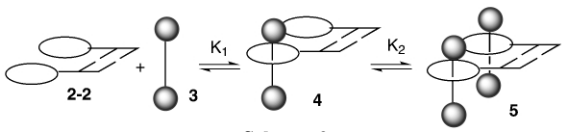
Two different types of complementary hydrogen bonding contribute to the formation and temperature dependent behavior of a pseudo[2]rotaxane dimer.

Owing to their intriguing properties and unique structures, interlocked molecules have received much attention recently from the perspective of design and synthesis.[1,2] Interlocked molecules have been developed as molecular shuttles.[3] Intermolecular interactions, including hydrogen bonding, play significant roles in forming supramolecular structures[4] as a consequence of the fact that weak interactions can lead to favorable arrangements of functional units and/or substituents. Thus, weak interactions should be the foundation of useful strategies to prepare desired supramolecular architectures. In the present report, we describe the synthesis of a novel pseudorotaxane dimer, **5** (Scheme 2) by a route which relies on the use of two different types of complementary hydrogen bonding interactions.

The preparation of pseudorotaxane dimer **5** is initiated by oxidation of the crown ether, aldehyde **1**[5] (Scheme 1) to afford the corresponding carboxylic acid. The amide obtained by Curtius rearrangement[6] of the acid, is then reacted with 2-aminopyrimidin-4-one[7a] to produce the ureidocrown ether **2**,[2] which possesses the Meijer's self-complementary 2-ureidopyrimidin-4-one motif.[7] The concentration independent downfield shifts of the urea NH protons (12.87, 12.14, and 12.06 ppm) in the ^{1}H NMR spectra (1:1 $CDCl_3$–CD_3CN) of **2** (0.5–20 mM) clearly show that this substance exists as the dimer **2**–**2** (Scheme 1).



Scheme 1 *Reagents and conditions*: (i) Jones oxidation; (ii) $(PhO)_2PON_2$, Et_3N; 6-tridecylisocytosine, py.



Scheme 2

† Electronic supplementary information (ESI) available: ^{1}H NMR spectra. See http://www.rsc.org/suppdata/cc/b1/b108922f/

The ^{1}H NMR (250 K) spectrum of a solution containing equimolar (10 mM) quantities of **2** and the bis-benzylammonium salt **3** in 1:1 $CDCl_3$–CD_3CN is shown in Fig. 1c. By comparing spectra of the precursors **2** and **3** (Figs. 1b and a, respectively) with that of the mixture, new sets of resonances are revealed, which are assigned to those of the pseudorotaxanes, **4** (2:1 complex) and **5** (2:2 complex) (Scheme 2). The benzylic and aromatic protons of the benzylammonium moieties of the pseudorotaxanes appear at 4.6 and 7.20–7.35 ppm, respectively, while resonances at 3.34–3.47 ppm and 6.76–6.92 ppm correspond to protons in the heterocyclic rings of the respective pseudorotaxanes. These chemical shift assignments are consistent with those reported previously.[8] Finally, the broad resonances at 12–13 ppm correspond to the dimeric NH protons of ureidopyrimidinone rings in the pseudorotaxanes.

To assign specific resonances to the protons in the individual pseudorotaxanes **4** and **5**, ^{1}H NMR spectra of solutions containing non-equimolar mixtures of **2** and **3** were recorded at low temperature. Inspection of the ^{1}H NMR spectrum (250 K) of a mixture of 5 mM **2** and 10 mM **3** (Fig. 1d) revealed the presence of two sets of signals corresponding to both **5** and **3**. By referring to the ^{1}H NMR spectra of **2**, **3**, and a 1:1 mixture of these substances, it is possible to assign several resonances for the protons of **5**. In addition, low temperature ^{1}H NMR spectroscopic analysis of 1:1 and 1:2 mixtures of **2** and **3**

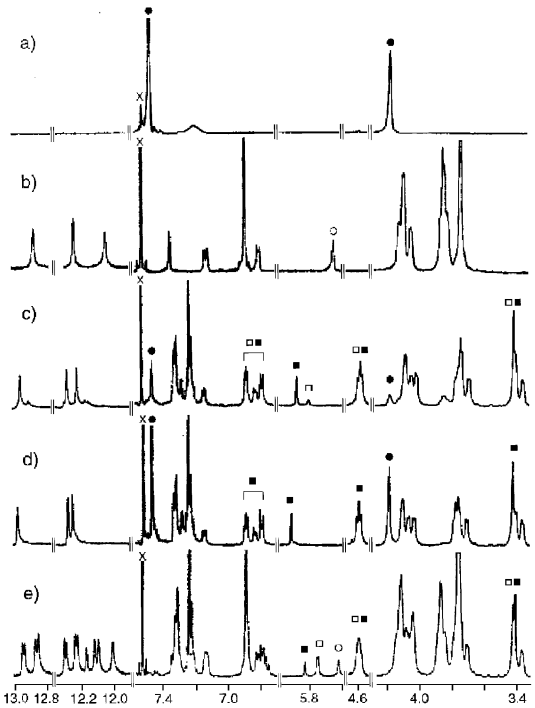


Fig. 1 ^{1}H NMR spectra of **2**, **3**, and mixtures of **2** and **3** recorded at 500 MHz in $CDCl_3$–CD_3CN (1:1) at 250 K. (a) **3**, (b) **2**, (c) a 1:1 mixture of **2** (10 mM) and **3** (10 mM), (d) a 1:2 mixture of **2** (5 mM) and **3** (10 mM), (e) a 2:1 mixture of **2** (10 mM) and **3** (5 mM). ○; 5H-ureidopyrimidinone of **2**–**2**, ●; **3**, □; **4**, ■; **5**, ×; solvent.

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enabled determination of the association constants of the 2:1 pseudorotaxane **4** (K_1 = [**4**]/[**2**–**2**][**3**]) and 2:2 pseudorotaxanes **5** (K_2 = [**5**]/[**4**][**3**]). The calculated values of K_1 and K_2 at 250 K are 9800 and 2200 M^{-1}, respectively.

Next, the ^{1}H NMR spectrum of a 2:1 mixture of **2** and **3** in 1:1 $CDCl_3$–CD_3CN was analyzed in order to identify resonances that correspond to the 2:1 pseudorotaxane **4**. The ^{1}H NMR (250 K) spectrum of this mixture (Fig. 1e) contains three sets of signals corresponding to **4**, **5**, and the precursor dimer **2**–**2**. Noteworthy are the resonances at 5.62, 5.75, 5.76, and 5.83 ppm which are characteristic of the 5H-ureidopyrimidinone protons. Aiding in this assignment is the comparison of a region of this spectrum (Fig. 2b) with the same region of the spectrum of a solution containing a 4:1 mixture of **2** and **3** (Fig. 2a).

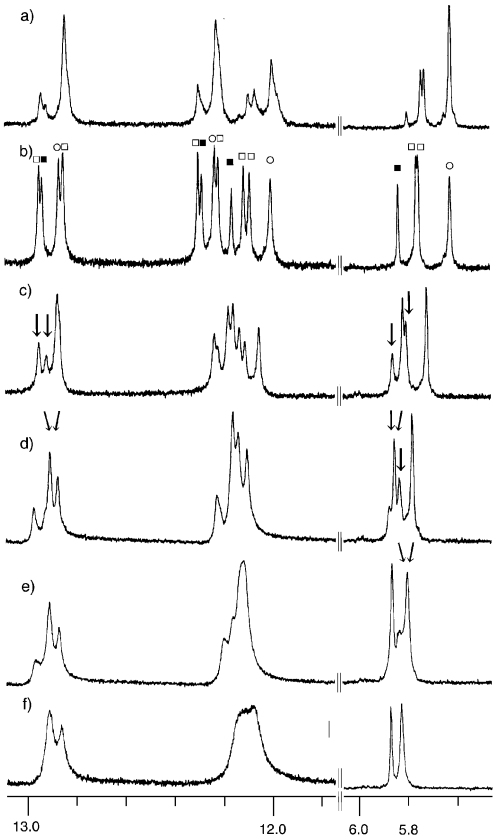

Fig. 2 ^{1}H NMR spectra of mixtures of **2** and **3** recorded at 500 MHz in $CDCl_3$–CD_3CN (1:1). (a) 4:1 mixture of **2** (10 mM) and **3** (2.5 mM) at 250 K, (b) mixture of **2** (10 mM) and **3** (5 mM) at 250 K (identical with Fig. 1e), (c) 280 K, (d) 287 K, (e) 296 K, and (f) 310 K. ○; **2**–**2**, □; **4**, ■; **5**.

The temperature dependent evolution of the spectrum of a 2:1 mixture of **2** and **3** is shown in Figs. 2b–f. In the range 250–280 K, the amount of pseudorotaxane formed decreases with increasing temperature. Several resonances, attributable to the protons in the hydrogen bonded dimer **2**–**2** (5.62 and 12.88 ppm at 250 K) and pseudorotaxane **4** (5.76 and 12.86 ppm at 250 K), remain unchanged at 280 K while signals for protons in the 5H-pyrimidinone ring of **5** (5.83 and 12.95 ppm at 250 K) and **4** (5.75 and 12.96 ppm at 250 K) are broadened at the elevated temperature. Also, the broad resonances of **5** merged into those of **4** (5.76 and 12.86 ppm) when the temperature is raised above 287 K (Figs. 2c and d). Finally, signals for **2**–**2** at 5.62 ppm and for **4** at 5.75 ppm overlap at > 296 K, and two signals appear at 12.8–13.0 ppm at 310 K (Figs. 2e and f).[9] Resonances for the benzylic protons of the bis-benzylammonium salt **3** and pseudorotaxanes **4** and **5** do not significantly change over this temperature range.

When viewed together, these observations lead us to conclude that the equilibrium processes of hydrogen bonded dimer and rotaxane formation occur slowly at low temperatures. As the temperature is raised, reversible association of the ureidopyrimidinones becomes fast on the NMR time scale.[10] Variable temperature ^{1}H NMR experiments were performed on a 2:1 mixture of **2** and **3**. Resonances for the 5H-ureidopyrimidinone protons are observed at 5.82 ppm (without associated **3**) and 5.87 ppm (with associated **3**) at 310 K. Variable temperature NMR studies of 1:2, 1:1 and 4:1 mixtures of **2** and **3** were carried out in an analogous fashion. The chemical shifts of the 5H-ureidopyrimidinone protons for **3**, with and without associated **3**, at 310 K are observed for the 1:2 mixture at 5.88 and 5.90 ppm, for the 1:1 mixture at 5.85 and 5.89 ppm, and for the 4:1 mixture at 5.82 and 5.86 ppm, respectively.

In conclusion, we have synthesized the pseudorotaxane dimer **5** and the 2:1 complex **4**, which serves as an intermediate in its formation. The architecture of **5** takes advantage of two complementary non-covalent hydrogen bonding motifs. NMR analysis has shown that the temperature dependent dynamics of the reversible processes involved in pseudorotaxane formation are governed by non-covalent hydrogen bond interactions. The controlled, sequential non-covalent introduction of guests on the crown ether grouping reduces the symmetry of dimers.[11] This results in the exchange of non-equivalent resonances, a phenomenon which enables assignment of resonances in the homo- and heterodimers.

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Notes and references

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9 The resonances corresponding to each species were not well-matched respectively, and with increasing temperature the resonances for the 5H ureidopyrimidinone protons were shifted. Although these results are unclear as yet, it is considered that secondary interactions operating at low temperature cause these observations.

10 To confirm the reversible association rate, variable temperature ^{1}H NMR investigations were carried out on a mixture of **2** and *N*-[(butylamino)carbonyl]-6-tridecylisocytosine[7*a*] in $CDCl_3$ and $CDCl_3$–CD_3CN. See supplementary information†.

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