A New Protocol for Rotaxane Synthesis

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Abstract: A novel [2]rotaxane was synthesized when an aniline-bearing [2]pseudorotaxane—generated by the hydrogen bond-driven threading of a dibenzylammonium filament through the cavity of the macrocyclic polyether dibenzo[24]crown-8—was stoppered via reaction with a bulky isocyanate. Complete characterization of the [2]rotaxane was accomplished by NMR spectroscopy, mass spectrometry and X-ray crystallography. © 1999 Elsevier Science Ltd. All rights reserved.

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Rotaxanes[1] are molecular species created when a bead-like macrocycle is trapped mechanically, i.e., without the assistance of any valence forces, on a dumbbell-shaped entity. Recently, a number of protocols based on self-assembly[2] have been developed[3] for the synthesis of these mechanically-interlocked compounds. The most successful protocol has probably been the threading followed by stoppering approach,[3a] which involves (Scheme 1) the threading of a linear filament (F) through the cavity of a macrocycle (M), by virtue of noncovalent bonds,[4] to generate a pseudorotaxane (P) that is then transformed into a rotaxane (R) by reaction with a bulky stoppering reagent (S). Here, we report a novel variant of this approach, which affords a [2]rotaxane by employing, as the threading motif, the dibenzylammonium–dibenzo[24]crown-8 (DB24C8) interaction[5] and, as the stoppering reaction, urea formation[3d,6] by the addition of anilines to isocyanates. The [2]rotaxane’s structure has been verified by NMR spectroscopy, mass spectrometry and X-ray crystallography.

The protocol[7] employed to prepare rotaxane 1-O2CCF3 is depicted in Scheme 2. The one-pot reaction presumably commences with the protonation of the more basic dibenzylamine unit of 2[8] by CF3CO2H. Thereupon, the dibenzylammonium ion thus created threads through DB24C8’s cavity to form the

Scheme 1. Diagram illustrating the synthesis of a [2]rotaxane via threading followed by stoppering. The stabilizing noncovalent bonding interactions that allow the pseudorotaxane’s assembly are depicted by groups of lines between the lightly shaded portions of the filament and macroring.

hydrogen bond-stabilized[5] [2]pseudorotaxane [DB24C8-2-H]⁺, which possesses a 3,5-di-tert-
butylphenyl (dtbp) moiety that acts as a stopper in the final product 1⁺. The reaction sequence
concludes when this pseudorotaxane’s free anilino group is stoppered by nucleophilic addition
to 2,6-diisopropylphenyl isocyanate, producing a urea whose appended 2,6-diisopropylphenyl
(dipp) unit is bulky enough to prevent dumbbell extrusion from the DB24C8 macroring. The
fact that 1⁺ is stable to column chromatography demonstrates convincingly that both of the
terminal stopper groups are large enough to ensure macroring-dumbbell interlocking.

An examination of the ¹H NMR signals’ relative intensities reveals that, in 1⁺, the macroring and
dumbbell components are present in equimolar ratios. The ¹H NMR spectrum[7] also
confirms that these components are compelled to be fastened to one another mechanically. The second order multiplets observed
at δ 4.45–4.49 and 4.68–4.71 are particularly informative in this case; these resonances show[5] that it is the dumbbell’s
dibenzylammonium moiety that is encircled by the DB24C8 macroring in the interlocked molecular architecture. Conclu-
sive proof that the components are mutually interlocked with one another was provided by a T-ROESY analysis.[10,11] In this
experiment, intercomponent ROEs were observed between the α-, β- and γ-CH₃ protons of DB24C8 and the protons H⁶ and H⁷
located (vide Scheme 2) on the dtbp and p-toluidinyl (ptol) units, respectively. As expected,[13] DB24C8’s CH₃ protons become diastereotopic in the [2]rotaxane 1⁺, meaning that H⁶ and H⁷ are involved in through-space interactions only with protons
on the nearest faces of the macrocyclic polyether (Figure 1). The FAB mass spectrum of
1-O₂CCF₃ shows[7] a base peak, corresponding to the ion 1⁺, at m/z 976, thus confirming the

The X-ray analysis[12] of a single crystal of the [2]rotaxane 1-O₂CCF₃ reveals that there are
two crystallographically independent molecules in the asymmetric unit. Apart from the relative
orientations of the i-Pr and t-Bu groups, the dumbbell’s conformation is essentially the
same in both molecules. However, different geometries are adopted by the DB24C8 macroring
in each of the [2]rotaxanes, resulting in slightly modified intramolecular hydrogen bonding
interactions. The [2]rotaxane architecture displayed in Figure 2 is stabilized by hydrogen
bonds involving both NH₂⁺ hydrogen atoms and one of the adjacent dtbp–CH₃ hydrogen atoms,
Figure 2. Molecular structure of one of the pair of independent [2]rotaxanes present in the crystals of 1•2CCF₃. Hydrogen bonding distances and angles [X–O], [H–O] distances (Å), [X–H–O] angles (°): (a) 2.85, 2.01, 156; (b) 2.89, 2.16, 137; (c) 3.31, 2.36, 171; (d) 2.89, 2.03, 159; (e) 2.86, 1.98, 164. The other independent molecule has an additional [C–H–O] hydrogen bond (f) which occurs between the asterisk-labeled oxygen atom and one of the ptol–CH₂ hydrogen atoms. The hydrogen bonding distances and angles for this second molecule are: (a) 2.91, 2.11, 147; (b) 3.01, 2.23, 145; (c) 3.41, 2.51, 157; (d) 2.76, 1.92, 163; (e) 2.91, 2.02, 168; (f) 3.25, 2.41, 147.

whereas one of the ptol–CH₂ hydrogen atoms is also utilized in its crystallographically independent congenner. The −O₂CCF₃ anion forms a pair of hydrogen bonds to the urea unit of each independent rotaxane’s cationic dumbbell component. Despite the apparent overlaying of one of the crown ether’s catechol rings with the central ptol ring of the dumbbell component in both independent molecules, the interplanar separations are too large to represent any significant stabilizing π–π interactions (the ring centroid–ring centroid distances are 4.48 and 4.54 Å, respectively, in the two molecules). There are no major inter-[2]rotaxane interactions.

In conclusion, we have developed a new one-pot protocol for the synthesis of urea-containing [2]rotaxanes that relies on the stoppering of [2]pseudorotaxanes—generated when an aniline-bearing dibenzylammonium filament threads through the crown ether DB24C8—by bulky isocyanates. It is not unreasonable to conjecture that this protocol can be extended to the synthesis of rotaxanes (i) comprised of more than two components, i.e., [2+n]rotaxanes, or (ii) containing other functional groups formed by nucleophilic addition to isocyanates, e.g., carbamates. We are also fascinated by the proposition that rotaxanes such as 1⁺ can function as elementary molecular devices. Experiments are underway in our laboratories to see if 1⁺ acts as an acid–base controlled molecular switch wherein the DB24C8 component relocates itself to hydrogen bond with the urea moiety when the dibenzylammonium unit is deprotonated by treatment with base.

References and Notes
X-Ray quality single crystals were obtained when a CH₂Cl₂ solution of 1.02CCF₃ was layered with C₆H₁₄. Crystal data for pKₐs: R₂NH₂ + 11, ArNH₃ + 3.5 (March, J.).

Experimental procedure: Solid DB₂₄C₈ (1.41 g, 3.15 mmol) was added to a stirred solution of 2 (0.34 g, 1.05 mmol) in anhydrous CH₂Cl₂ (5 mL). After addition of HO₂CCF₃ (81 µL, 1.05 mmol) and 5 min stirring, the solution was treated with a single portion of 2,6-diisopropylphenyl isocyanate (1.13 mL, 5.25 mmol). The reaction mixture was stirred for a further 5 d at 25 °C, then the solvents were removed in vacuo. The remainder was purified by column chromatography (SiO₂; gradient elution from n-hexane/CH₂Cl₂).

ν-H'), 3.52-3.58 (m, 4H; (CH₃)₂CH), 3.78-3.85 (m, 4H; β-H'), 4.07-4.17 (m, 8H; α-H'/β-H'), 4.45-4.49 (m, 2H; α-H'/γ-H'), 4.68-4.71 (m, 2H; dtbq-CH₂), 6.79-6.94 (m, 8H; α-O₂CCF₃H₂), 7.10 (d, J 8.5 Hz, 2H, β-H'), 7.14 (d, J 8 Hz, 2H, H₁), 7.21-7.26 (m, 1H; m- or p-dppH₁), 7.28 (d, J 1.5 Hz, 2H, H₁), 7.35 (t, J 1.5 Hz, 1H, o-(Bu)-dtbqH), 7.44 (d, J 8.5 Hz, 2H; o-NH-to'H), 7.53 (tr s, 2H, NH₂), 8.97 (s, 1H, dpp-NH), 10.16 (s, 1H, pto-NH; 13C NMR (100 MHz, CDC₁₅, 27 °C): δ 23.5, 24.4, 28.6, 31.5, 34.9, 52.9, 53.1, 63.1, 63.8, 70.2, 70.3, 112.8, 118.4, 122.0, 122.4, 122.9, 123.3, 123.7, 127.1, 129.7, 131.6, 133.2, 143.2, 147.4, 147.6, 151.4, 155.7; FABMS: m/z 976 (100%)[M-O₂CCF₃]⁺, C₆₁H₈₂F₃N₃O₁₁ (1090.3): calcd C 67.20, H 7.58, N 3.85; found C 66.68, H 7.55, N 3.58.

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