Molecular riveting: high yield preparation of a [3]-rotaxane

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An aminothiol axle molecule is so efficient at threading through the macrocycle 24-crown-8 that iodine oxidation produces a [3]-rotaxane in record yield (84%) by literally riveting two rings together.

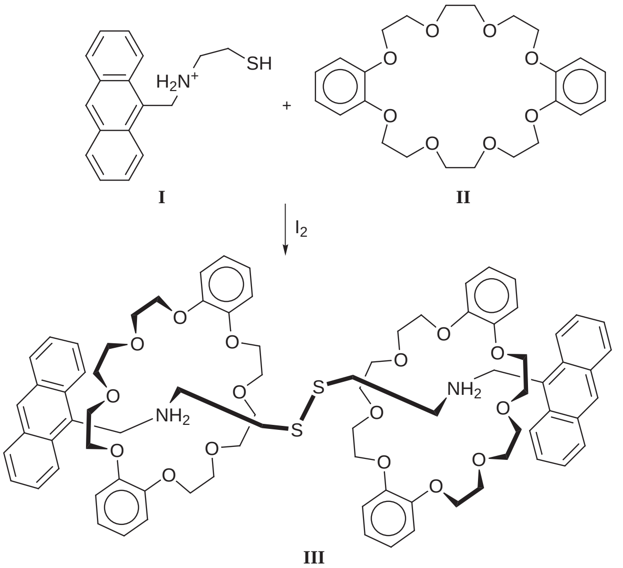
Molecular motifs incorporating mechanically interlocked molecules, such as rotaxanes, catenanes and knots, are harbingers to a virtual molecular macrame of orderly molecular entanglements that will constitute new materials for the 21st century.[1] But the preparation of mechanically interlocked molecules presents a significant challenge,[2] and the probability of success decreases as the number of interlocked molecules increases. For example, only a few [3]- and higher rotaxanes[3] have been prepared and their yields are often low, with the highest reported yield for a [3]-rotaxane being 55%.[3] Reaping the potential of the field will depend on the detailed understanding of template reactions, including such elementary processes as molecular threading, which underlies the work reported here. In on-going studies of the relationships that favor the threading of linear molecules through cyclic molecules, we have found a methodology that produces a [3]-rotaxane in record yield (84%) by literally riveting two rings together. Such high yields open the way to molecularly interlocked polymers based on rotaxane formation.

Having learned from the threading of rings onto polymers[4] that closely positioned coordination sites strongly favor rotaxane formation, we first applied a new methodology to [2]-rotaxane formation.[5] Interaction between a functional group at the terminus of the linear component and its cyclic partner positions the tip of the linear molecule for penetration into the ring and prepays the entropic price of threading. Relaying of the binding site for the cyclic molecule from the terminal to the internal functional group completes the threading process. Closely related syntheses, based on the coordination of secondary ammonium groups to crown ethers were described shortly thereafter.[3b,e,6]

The success of our relay threading and the ease with which secondary amines form pseudo rotaxanes led to the hypothesis that, for maximum threading, the internal function of the axle molecule should bind the cyclic component substantially more strongly than does the terminal function. Further guidance, specifically applicable to [3]-rotaxanes, is provided by the recent work of Stoddart and co-workers,[3e] which relies solely on the crown ether–secondary ammonium ion interaction. For closely related structures, the yields of two [2]-rotaxanes were found to be 24 and 31%, while that for the [3]-rotaxane was only 10%. It may be significant that the fractional yield of the [3]-rotaxane is approximately the square of that for a [2]-rotaxane [$0.1 \approx (0.31)^2$]. These admittedly very limited data correspond to a simple model in which the yield of the blocking reaction may be largely controlled by the preequilibrium concentration of pseudo rotaxane. In such a case, the yield of the [3]-rotaxane is likely to be limited by the product of the yields (preequilibrium concentrations) of the two required threading processes. Therefore we suggest that the preparation of a [3]-rotaxane constitutes a powerful test for the efficiency of a given methodology for molecular threading.

A secondary ammonium group provides the primary binding site in our new axle molecule and the thiol group was selected as the terminal function because (a) it should not compete significantly with the secondary ammonium group for coordination to the crown ether, (b) it should, however, exert a relatively weak, reversible attraction for the crown ether and (c) it is well suited for a number of blocking reactions. To the best of our knowledge, the formation of strong crown ether–thiol complexes has not been reported, while, on the other hand, thiols do form easily detectable hydrogen bonds with a variety of nitrogen and oxygen containing functional groups.[7] The thioammonium salt, **I**Br, was synthesized by Schiff base condensation of 9-anthraldehyde with 2-aminoethanethiol, followed by borohydride reduction.

The oxidative coupling of the thiol groups of two pseudo rotaxane molecules provided a very convenient route for [3]-rotaxane formation (Scheme 1). Complexation of **I** with excess crown ether **II** and subsequent oxidation of the resulting complex with a small excess of iodine gave the [3]-rotaxane triiodide, $\mathbf{III}(I_3)_2$, in remarkably high yield (84%) (Scheme 1). The high yield synthesis proceeds as follows: 9-anthrylmethyl(2-mercaptoethyl)ammonium bromide (**I**) (0.347 g, 1 mmol) and dibenzo-24-crown-8 (**II**) (1.344 g, 3 mmol) were dissolved at room temperature in the presence of air in a mixture of MeOH (7 ml) and $CHCl_3$ (10 ml). I_2 (0.381 g, 1.5 mmol) in $CHCl_3$ (10 ml) was slowly added over 10 min. Crystallization began after standing for 30 min. After 12 h the reaction mixture was refrigerated for 1 h and then filtered. The resulting brown crystalline product was washed with MeOH and dried in air. Larger iodine concentrations resulted in the formation of a highly crystalline adduct, $\mathbf{III}(I_3)_2\cdot 1\tfrac{1}{2}I_2\cdot 2MeOH$. The mechanics of this molecular riveting reaction are closely analogous to the familar macroscopic riveting process, *i.e.* the rivet is inserted in



Scheme 1

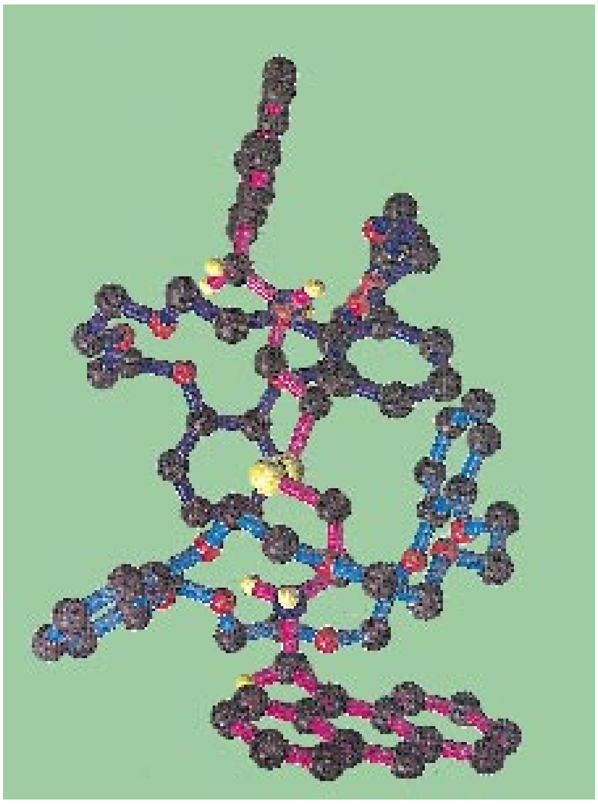


Fig. 1 Structure of the cationic [3]-rotaxane

holes in two parts that are subsequently joined together when the rivet is made complete with massive heads at each end. Referring back to the model described above, if the yield of this reaction were determined by the pseudo rotaxane preequilibrium, the pseudo rotaxane must be present in an equilibrium concentration exceeding 90%.

The crystal structure‡ of the [3]-rotaxane (Fig. 1) confirms the threading of the crown ether and clearly shows the axle–torus interactions. These include H-bonds between the amine nitrogen and the oxygen atoms of the crown, as well as [N^+–C–H···O] interactions between the methylene group adjacent to the anthryl unit and the crown ether oxygens.

The substantially higher yield obtained for **III** compared to all other rotaxanes based on secondary ammonium salt–crown ether partners, as well as the data obtained for polymeric rotaxanes,[4] strongly supports the relay threading hypothesis. Clearly, the close proximity of two binding sites on the axle molecule and the relative coordinating abilities of those two sites play important roles in facilitating these threading reactions. Further, this process of linking two molecules together by a highly efficient reaction gives promise of much new chemistry. For example, we suggest that molecular riveting will ultimately be used to produce new families of polymers and films.

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Notes and References

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‡ *Crystal data* for **3**: $2[C_{82}H_{98}N_2O_{16}S_2]4[I_3]3[I_2]4MeOH$, M = 5204.0, triclinic, space group $P\bar{1}$, a = 15.805(1), b = 16.0197(5), c = 19.7166(5) Å, α = 95.999(5), β = 102.880(5), γ = 94.478(5)°, U = 4813.23(7) Å^3. T = 180(2) K, Mo-Kα radiation, λ = 0.71073 Å, Z = 1, D(cal) = 1.679 mg m^{-3} μ(Mo-Kα) = 3.283 mm^{-1}. Siemens SMART three-circle system with CCD area detector. 21 986 reflections measured, 14 644 unique [R(int) = 0.0414]. Absorption correction by psi-scan. The crystals are weakly diffracting; one anthracene unit is disordered between two positions; three of the iodine positions in the polyiodide anion are incompletely occupied; and, of the two MeOH molecules in the asymmetric unit, one has a disordered oxygen position. Refinement on F^2 was accomplished using SHELXL 96 (Sheldrick, 1996) with 1049 parameters. R1 [for 8361 reflections with $I > 2\sigma(I)$] = 0.0980, wR2 (all reflections) = 0.3091. Goodness-of-fit on F^2 = 0.943. CCDC 182/873.

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