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# Efficient Templated Synthesis of Donor−Acceptor Rotaxanes Using Click Chemistry

William R. Dichtel,[†,‡] Ognjen Š. Miljanić,[†] Jason M. Spruell,[†] James R. Heath,*[,‡] and J. Fraser Stoddart*[,†]

*California NanoSystems Institute and Department of Chemistry and Biochemistry, University of California, Los Angeles, 405 Hilgard Avenue, Los Angeles, California 90095, and Division of Chemisty and Chemical Engineering, California Institute of Technology, 1200 East California Boulevard, Pasadena, California 91125*

Received May 4, 2006; E-mail: heath@caltech.edu; stoddart@chem.ucla.edu

The discovery of highly efficient synthetic strategies for making electrochemically switchable, mechanically interlocked compounds will facilitate their continued development as components in molecular electronic devices[1] (MEDs) and nanoelectromechanical systems[2] (NEMS). Traditionally, such compounds, incorporating cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) as the $\pi$-accepting ring component, have been synthesized[3] by "clipping" a partially formed $CBPQT^{4+}$ ring (Figure 1a) around a dumbbell or ring containing $\pi$-electron-rich recognition sites. Although this synthetic strategy has found wide application,[4] the moderate yield typical of the $CBPQT^{4+}$ clipping reaction limits its practical value to the preparation of [2]rotaxanes and [2]catenanes. Herein, we describe an alternative synthetic approach (Figure 1b,c) to donor−acceptor rotaxanes—including previously inaccessible [3]- and [4]rotaxanes. Their synthesis relies upon the efficient stoppering of their pseudorotaxane precursors.

Motivated by the use of click chemistry[5] in the synthesis of a variety of functional materials,[6−8] including an example[9] in which

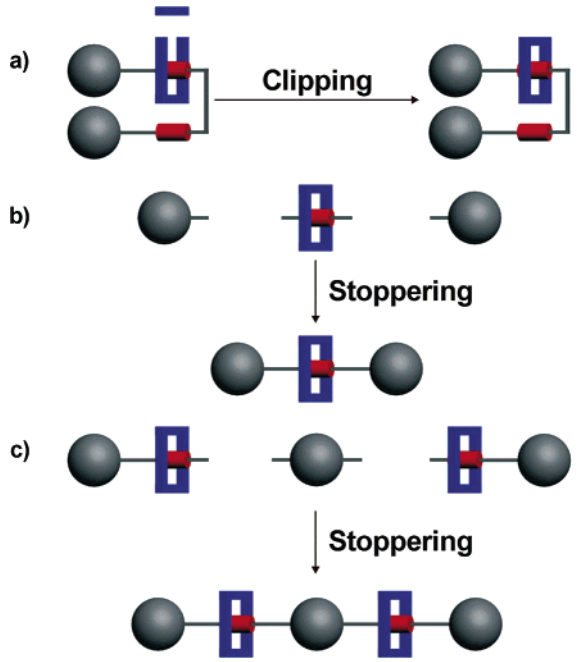
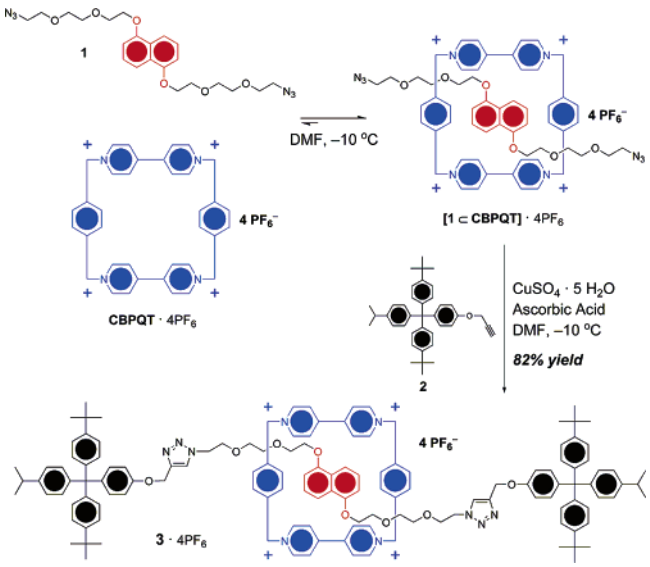



***Figure 1.*** Graphical representations of different strategies employed in the template-directed syntheses of donor−acceptor rotaxanes: (a) clipping of a macrocycle around a dumbbell; (b) double stoppering of a pseudorotaxane to form a [2]rotaxane (Scheme 1); and (c) attachment of two semirotaxanes onto a bifunctional stopper to form a [3]rotaxane (Scheme 2). An analogous approach to a [4]rotaxane is depicted in Scheme 3.

***Scheme 1***




the Cu catalyst templates rotaxane formation, we reasoned that donor−acceptor rotaxanes might be obtained by attaching alkyne-terminated stoppers to $CBPQT^{4+}$ pseudorotaxanes using the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition ("click" chemistry). The click reaction has been noted for its high regioselectivity,[5−8] tolerance of sensitive functional groups, mild reaction conditions,[10] and excellent yields. The click reaction occurs at room temperature (and below), requiring only the addition of catalytic amounts of $CuSO_4$ and ascorbic acid, all conditions which are ideal for strong binding of $CBPQT^{4+}$ to a wide variety of thread molecules containing $\pi$-donors.

This threading-followed-by-stoppering approach is complementary to clipping and has a number of advantages. Because the recognition elements are fully formed from the outset of the reaction, templation utilizes the full thermodynamic binding of $CBPQT^{4+}$ to the guest of interest. The click methodology is also much more convergent: relatively simple, modular rotaxane components are synthesized in parallel, and the mechanically interlocked structure is assembled in the final step of the reaction protocol. The general synthetic strategy (Scheme 1) involves the mixing of **CBPQT**·$4PF_6$ in DMF at −10 °C, with a 1,5-dioxynaphthalene (DNP) derivative **1** carrying azide-terminated glycol chains. Under these conditions, the equilibrium lies predominantly in favor of the [2]pseudorotaxane **[1** ⊂ $CBPQT^{4+}$**]**·$4PF_6$. A propargyl ether-functionalized stopper **2** is then added to the reaction mixture along with $CuSO_4$·$5H_2O$ and ascorbic acid. Following these mild reaction conditions, the [2]rotaxane **3**·$4PF_6$ was isolated in 82% yield. Formation of the dumbbell was not observed by thin layer chromatography.

[†] CNSI/UCLA.
[‡] California Institute of Technology.



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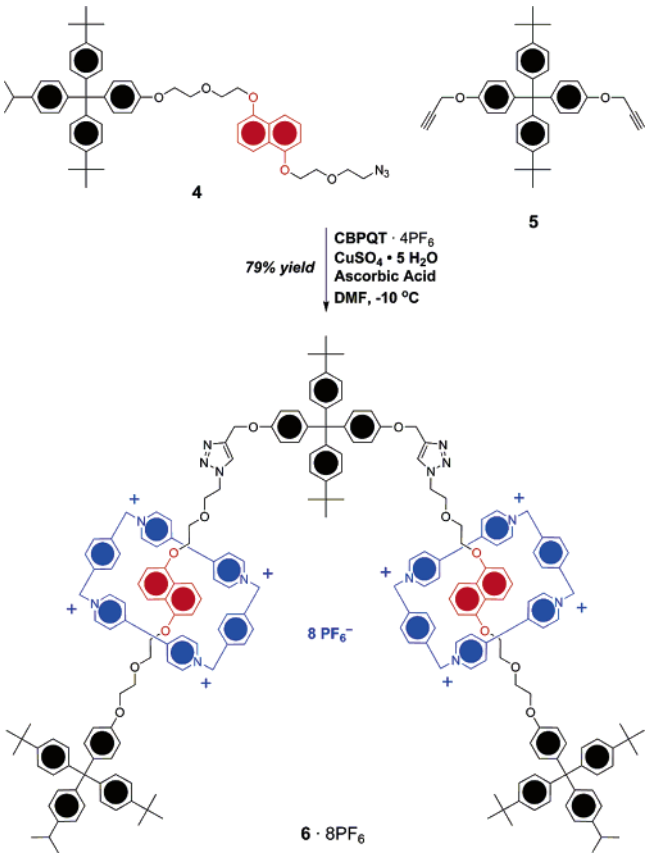
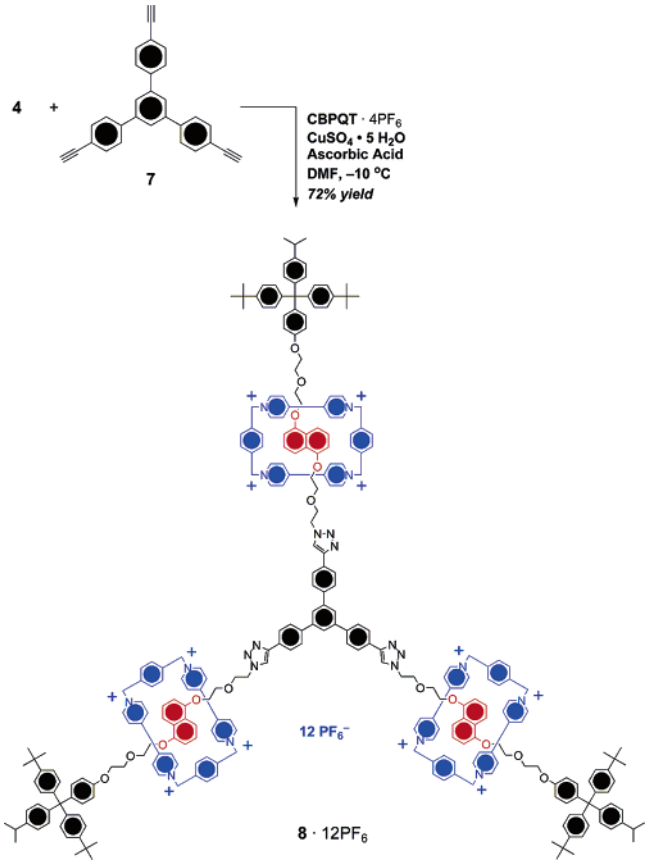
*Scheme 2*




*Scheme 3*



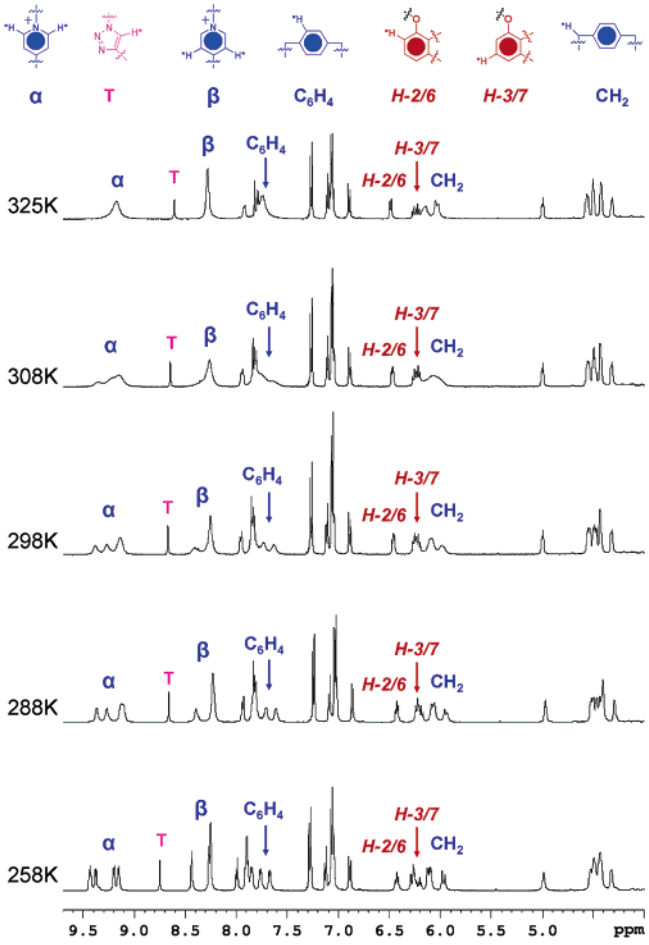




***Figure 2.*** Partial $^1$H NMR spectra (500 MHz, $CD_3COCD_3$) of **8**·12$PF_6$ recorded at different temperatures. Several diagnostic peaks are labeled, including the signals for the CBPQT$^{4+}$ α and *β* protons, and resonances for two of the three DNP protons. Slow rotation of the bipyridinium and *p*-phenylene units in the CBPQT$^{4+}$ rings is reflected in their broad proton resonances at 298 K. At lower temperatures, these rotations are slowed even further until the signals become clearly resolved. The signals for the CBPQT$^{4+}$ α and *β* protons coalesce into single, albeit broad, peaks at higher temperatures.

Encouraged by this successful proof of concept, we decided to apply this methodology to the synthesis of [3]rotaxanes. Doubly bistable [3]rotaxanes incorporating tethered CBPQT$^{4+}$ rings have been used as redox-driven molecular muscles.[11] Although actuation was achieved, clipping two CBPQT$^{4+}$ rings around the synthetically valuable palindromic dumbbell gave the desired [3]rotaxane in only 9% yield. Using the click methodology, a similar (albeit simplified) palindromic [3]rotaxane was synthesized from relatively simple precursors **CBPQT**·4$PF_6$, the stoppered DNP azide **4**, and bis-(propargyl ether) **5** in 79% isolated yield.[12]

The comparative efficiency of the click methodology is emphasized by the synthesis (Scheme 3) of the branched [4]rotaxane **8**·12$PF_6$ in 72% isolated yield after reacting **4** with tris-1,3,5(4′-ethynylphenyl)benzene[13] **7** in the presence of **CBPQT**·4$PF_6$. A clipping approach is expected to provide this [4]rotaxane in very low (<3%) yield.

The partial $^1$H NMR spectra (Figure 2) of **8**·12$PF_6$ reflect its 3-fold symmetry. The resonances for the DNP protons, which are shielded and resonate at $\delta = 6.49$ (H-2/6), 6.22 (H-3/7), and 2.75 (H-4/8, not shown) ppm, are typical for rotaxanes containing CBPQT$^{4+}$ and DNP residues. At +25 °C, rotations of the bipyridinium units and *p*-phenylene ring systems in the CBPQT$^{4+}$ rings are slow on the $^1$H NMR time scale, resulting in broadening

of the signals for the $CBPQT^{4+}$ protons. The spectrum becomes much simpler as the signals for these protons coalesce at higher temperatures. At lower temperatures, the exchange processes between all of the relevant protons slow yet further, allowing for resolution of nonequivalent proton signals. Throughout the temperature range investigated, the triazole resonance remains a sharp singlet near $\delta = 8.60$ ppm, a reasonable value for triazole protons. This observation suggests that the triazole does not compete with DNP to bind with the $CBPQT^{4+}$ ring—a hypothesis we are currently investigating more thoroughly.

During this preliminary research, it has become apparent that, as a result of using click chemistry as the covalent modification step in rotaxane synthesis, it not only renders the simple donor−acceptor [2]- and [3]rotaxanes (Schemes 1 and 2) much more accessible but it also provides the opportunity to prepare respectable quantities of more exotic mechanically interlocked compounds, such as the branched [4]rotaxane (Scheme 3). The synthesis and applications of these new materials to MEDs and NEMS will now become part of the ongoing research efforts in our laboratories.

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**Supporting Information Available:** Experimental details, spectral characterization data of all new compounds (PDF), and complete refs 1a,e and 11. This material is available free of charge via the Internet at http://pubs.acs.org.

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