QSAR & Combinatorial Science QCS

# Rotaxanes and Catenanes by Click Chemistry

**Ognjen Š. Miljanić[a], William R. Dichtel[a,b], Ivan Aprahamian[a], Rosemary D. Rohde[b], Heather D. Agnew[b], James R. Heath[b]* and J. Fraser Stoddart[a]***

[a] California NanoSystems Institute and Department of Chemistry and Biochemistry, University of California, Los Angeles, 405 Hilgard Avenue, Los Angeles, California 90095, USA, E-mail: stoddart@chem.ucla.edu
[b] Division of Chemistry and Chemical Engineering, California Institute of Technology, 1200 East California Boulevard, Pasadena, CA 91125, USA, E-mail: heath@caltech.edu

**Keywords:** Catenanes, Click chemistry, Interlocked molecules, Rotaxanes, Self-assembly, Surface chemistry

Received: June 1, 2007; Accepted: July 11, 2007

DOI: 10.1002/qsar.200740070

**Abstract**

Copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition between terminal alkynes and azides – also known as the copper (Cu)-catalyzed Azide-Alkyne Cycloaddition (CuAAC) – has been used in the syntheses of molecular compounds with diverse structures and functions, owing to its functional group tolerance, facile execution, and mild reaction conditions under which it can be promoted. Recently, rotaxanes of four different structural types, as well as donor/acceptor catenanes, have been prepared using CuAAC, attesting to its tolerance to supramolecular interactions as well. In one instance of a rotaxane synthesis, the catalytic role of copper has been combined successfully with its previously documented ability to preorganize rotaxane precursors, *i.e.*, form pseudorotaxanes. The crystal structure of a donor/acceptor catenane formed using the CuAAC reaction indicates that any secondary [$\pi\cdots\pi$] interactions between the 1,2,3-triazole ring and the bipyridinium $\pi$-acceptor are certainly not destabilizing. Finally, the preparation of robust rotaxane and catenane molecular monolayers onto metal and semiconductor surfaces is premeditated based upon recent advances in the use of the Huisgen reaction for surface functionalization.

## 1 Introduction

Since its introduction [1–3] in 2002, the copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition [4–8] between terminal alkynes and organic azides, also referred to as the copper (Cu)-catalyzed Azide–Alkyne Cycloaddition (CuAAC), has been broadly taken up by synthetic chemists and has found extensive use in the design and synthesis of new polymeric materials [9–11] as the quintessential click reaction. This explosive growth – reflected in the appearance of this Special Issue – can be attributed to the accommodating properties of the CuAAC reaction – namely, its functional group tolerance, the ease of introducing both alkyne and azide functions into organic molecules, coupled with their lack of reactivity, and its being dependent on reagents and catalysts that are commercially available and inexpensive. These benefits come with the restriction, however, of having to incorporate (a) 1,2,3-triazole unit(s) into the final structure. Nevertheless, if the functional performance of the molecule or material is relatively insensitive to this particular structural modification, then the CuAAC reaction is likely to become the method of choice for preparing many different organic compounds. The unique structural features of the 1,2,3-triazole ring – its large dipole moment, aromatic stability, and free electron pairs on nitrogen – render it a versatile building block in its own right.

The synthesis of mechanically interlocked compounds [12] places additional constraints on the reactions employed in their synthesis. Since the precursors to these mechanically interlocked compounds are held together by noncovalent bonds, other reactions performed on them must be chemically compatible with the weak interactions. In this respect, the CuAAC reaction seems to be a promising candidate since it proceeds at room temperature and can be performed in a variety of different solvents, allowing the optimization of noncovalent bonding interactions in the precursors. Indeed, beginning in 2006, several different research groups have described almost simultaneously the first examples of the application of CuAAC chemistry [13–22] in the synthesis of the best known of the mechanically interlocked molecules, the so-called rotaxanes and catenanes [12, 23]. This minireview highlights these early forays into what promises to be a fruitful area of synthesis.

It commences with an introduction to rotaxanes and catenanes, followed by some examples of rotaxane synthesis using CuAAC chemistry. This section on rotaxane synthesis will deal [24] with the preparation of (1) donor/acceptor rotaxanes, (2) cyclodextrin-based rotaxanes, and (3) copper-rotaxane complexes. We follow with a brief discussion on the preparation of donor/acceptor catenanes using CuAAC chemistry.

The molecular mechanical motion that can be electrochemically harnessed within bistable rotaxanes and catenanes has been demonstrated as enabling of various solid-state and thin film applications, including ultra-dense memories [25], nanovalves for chemical release [26], biomolecule sensing [27], and others. Robust versions of these applications require general approaches towards covalently attaching rotaxane and catenane monolayers to various surfaces. To date, strategies for assembling covalently bound bistable catenane and rotaxane monolayers have been limited in their scope. We conclude this review with a brief description of how the CuAAC reaction is being developed as a general method for constructing molecular monolayers on various substrates [9, 28], with a particular focus on the potential applications for the preparation of bistable rotaxane monolayers.

## 2 Rotaxanes and Catenanes

Rotaxanes and catenanes [12, 23] are amongst the simplest examples of mechanically interlocked molecules. These molecules are unique in that the interlocked components can be coerced through a combination of molecular design and by chemical, optical, or electrochemical, stimuli to change their orientation with respect to one another. The result is very large amplitude molecular mechanical motion that can be harnessed for tasks ranging in diversity from information storage to chemical capture and release. Finding efficient and high-yield pathways towards the preparation of catenanes and rotaxanes is thus an interesting and potentially useful endeavor.

[*n*]Rotaxanes (Figure 1A) are composed of a central dumbbell-shaped component encircled by $n-1$ trapped rings, while [*n*]catenanes (Figure 1B) contain *n* interlocked macrocycles. The prefix [*n*] indicates the number of mechanically interlocked components, regardless of their identities. The constructs shown in Figures 1A and 1B portray the [2]rotaxane and [2]catenane architectures, respectively. By way of a more complex example, a rotaxane on a central dumbbell component with four macrocyclic rings threaded onto it would be referred to as a [5]rotaxane.

The covalently linked constituent parts of both rotaxanes and catenanes are rendered inseparable by mechanical interlocking. As such, rotaxanes and catenanes are truly molecular in nature, as they conform to the definition of a molecule as an entity indivisible into simpler entities without the cleavage of a chemical bond. Both rotaxanes and catenanes are closely related to – and often synthetically derived from – [*n*]pseudorotaxanes (Figure 1C). In contrast to rotaxanes and catenanes, the components of pseudorotaxanes readily dissociate and reassociate – denying them the right to be molecules, and necessitating that these intertwined species are described as complexes or supramolecular entities.

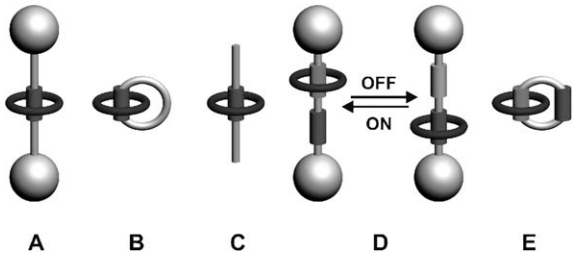



**Figure 1.** Examples of mechanically interlocked molecules and complexes: (**A**) – one-station [2]rotaxane, (**B**) – one-station [2]catenane, (**C**) – [2]pseudorotaxane, (**D**) – bistable two-station [2]rotaxane, (**E**) – bistable two-station [2]catenane. Mode of switching is shown for the bistable two-station [2]rotaxane (**D**): while the blue macrocycle is bound preferentially to the green station in the ON state, turning this station OFF forces the movement of the blue macrocycle to the red station. The bistable two-station [2]catenane operates in an analogous fashion.

A requirement for the efficient preparation of mechanically interlocked molecules under template control is a molecular recognition event between their constituent parts. Hence, each of the components present in rotaxanes and catenanes ends up having one or more recognition sites – often referred to as *stations* – that are complementary to the recognition sites located in the other component(s). Depending on the number of stations, rotaxanes and catenanes can be classified as one-station, two-station, *etc*. Two-station rotaxanes and catenanes can be either degenerate – with two identical stations – or nondegenerate with two different stations. The different stations can have very different affinities for the matching component macrocycle. Bistable [29] two-station rotaxanes and catenanes are a class of nondegenerate molecules in which the stronger binding site (station) can be turned ON and OFF reversibly, allowing the macrocycle to reside on either of the two stations, depending on the instructions that have been given to the molecule.

## 3 Preparation of Rotaxanes by a Click Chemistry Approach

The CuAAC reaction has been used to date in the preparation of four different types of rotaxanes and related complexes. Regardless of the exact chemical identities of the resulting rotaxanes, the synthetic strategies can be classified into two discrete approaches, shown schematically in Figure 2. In the first – *stoppering* – approach (Figure 2A) an [*n*]pseudorotaxane is converted into an [*n*]rotaxane by

a click reaction that attaches identical stoppers to the termini of its thread or rod component. A variant of the method "clicks" pseudorotaxanes with one pre-attached stopper, *i.e.*, hemirotaxanes (Figure 2B) onto either different stoppers – to produce a constitutionally unsymmetrical [2]rotaxane – or onto an oligovalent central core – to produce a higher order [*n*]rotaxane. The stoppering approach utilizes pseudorotaxanes and requires that the noncovalent bonding interactions between the macrocycle and the thread of the pseudorotaxane precursors are formed efficiently. The alternative, *three-point attachment* method (Figure 2C) proceeds through an intermediate in which copper(I) is coordinated simultaneously to the macrocycle and the two halves of the future dumbbell component. Since this technique relies on the defined orthogonal organization of the precursors in the tetrahedral coordination sphere of copper(I), noncovalent bonding interactions between the components of the future rotaxane are not a prerequisite and rotaxanes with only weakly interacting components can be prepared efficiently by this method.

We have used the CuAAC reaction extensively to prepare both one-station [13, 14] and switchable two-station [15, 16] donor/acceptor rotaxanes based on the cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) [30–32] as the π-acceptor ring (Scheme 1). Donor/acceptor rotaxanes based on $CBPQT^{4+}$ as the tetracationic cyclophane π-acceptor ring component have traditionally been prepared [33] by synthetic procedures that (i) create the π-donating dumbbell-shaped template, and then (ii) clip the components of the $CBPQT^{4+}$ ring around the template, to afford a rotaxane (*clipping*, Figure 2D). Although successful in a number of cases [34], this sequence of steps cannot be varied because the chemical sensitivity of the $CBPQT^{4+}$ ring to nucleophiles, bases, and strong reducing agents necessitates its introduction in the last step of the template-directed syntheses. Realizing that the $CBPQT^{4+}$ ring is tolerant of the CuAAC reaction conditions, we were able to synthesize [2]rotaxanes (Scheme 1A), starting with the preformed $CBPQT^{4+}$ ring. Thus, threading of the diazide-terminated dioxynaphthalene (DNP) derivative **1** through the cavity of the $CBPQT^{4+}$ ring provided the [2]pseudorotaxane [**1**⊂**CBPQT**]·$4PF_6$ which is stabilized by [π···π], [C–H···π], and [C–H···O] interactions [35] between the tetracationic cyclophane and DNP unit present in the thread. Clean stoppering of this intermediate with two equivalents of the alkyne-terminated stopper **2** under click conditions ($CuSO_4 \cdot 5\,H_2O$, ascorbic acid) afforded [13] the [2]rotaxane **3a**·$4PF_6$ in 82% yield. The tetrafluorinated derivative of $CBPQT^{4+}$, *i.e.*, $F_4CBPQT^{4+}$, underwent [14] the same reaction to provide the [2]rotaxane **3b**·$4PF_6$ in 37% yield, despite the ~50 times weaker binding [36, 37] between this cyclophane and DNP derivatives, relative to the $CBPQT^{4+}$/DNP pair. This result is a testament to the superiority of the CuAAC reaction over the traditional clipping method, as rotaxane **3b**·$4PF_6$ could not be prepared by the latter route [14].

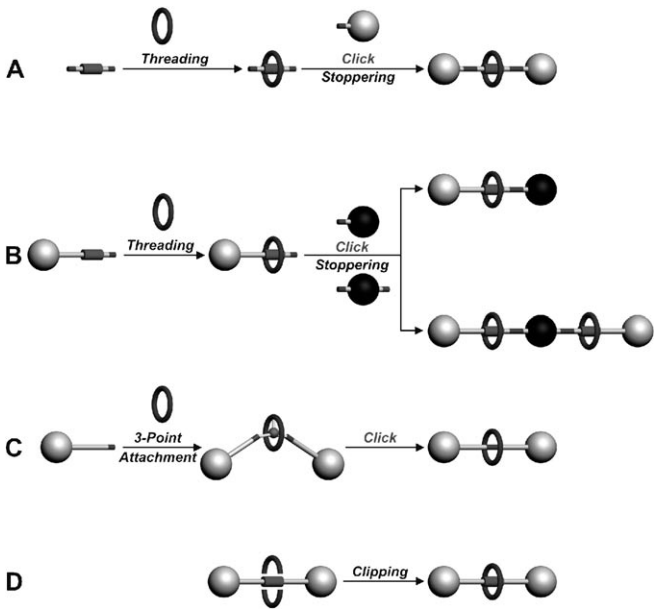
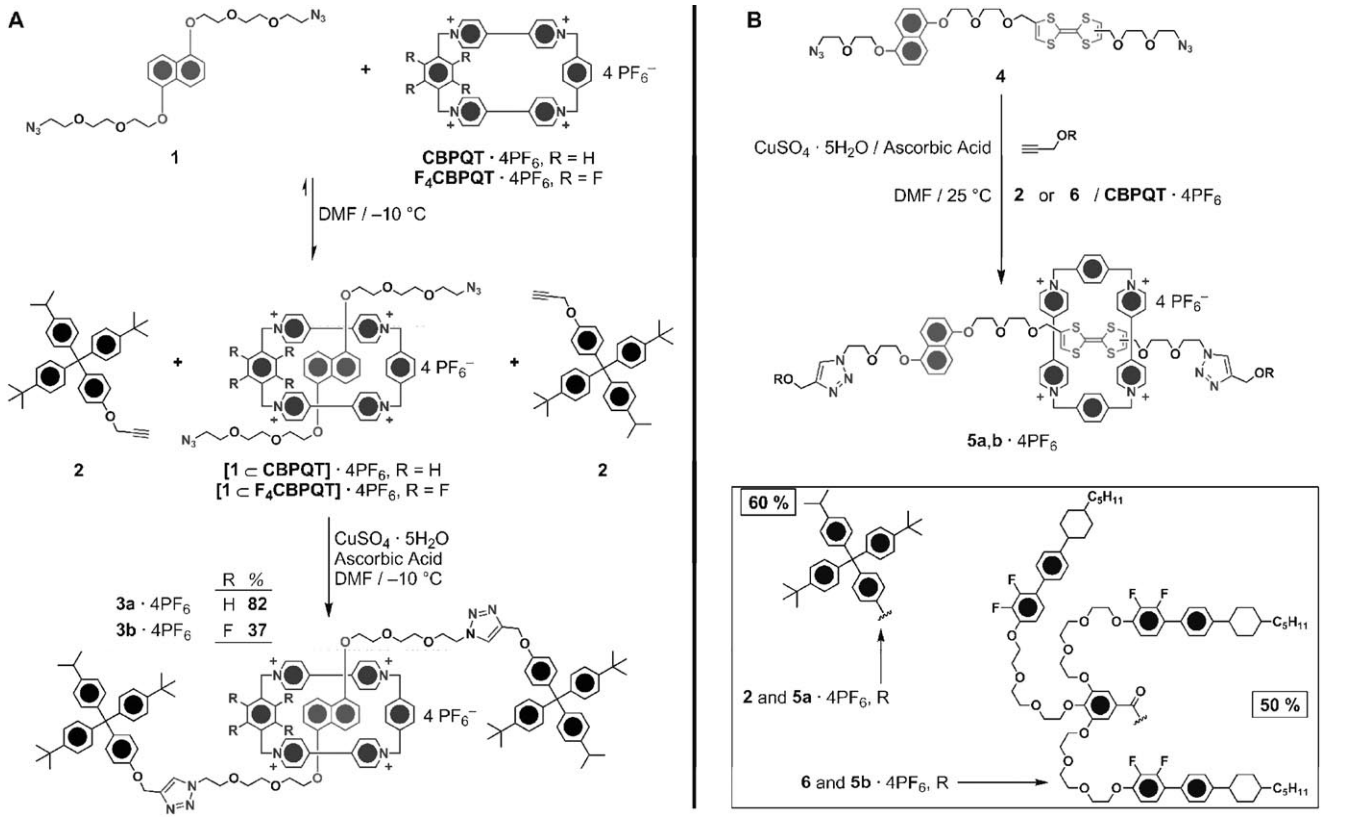



**Figure 2.** A selection of different conceptual approaches to rotaxane synthesis: (**A**) – threading forms a pseudorotaxane, which is followed by symmetrical stoppering *via* the click reaction; (**B**) – threading forms a hemirotaxane which can be either stoppered unsymmetrically, or grafted onto a central oligovalent core to produce higher [*n*]rotaxanes; (**C**) – three-point attachment organizes the macrocycle and two halves of the dumbbell in the coordination sphere of copper to provide – after the completion of click reaction – a rotaxane with only a weakly interacting macrocycle and a dumbbell; (**D**) – traditional template-directed clipping approach.

A bistable two-station donor/acceptor [2]rotaxane **5a**·$4PF_6$ has also been constructed using this particular stoppering approach (Scheme 1B) of **4** by **2** in the presence of **CBPQT**·$4PF_6$ in 60% yield [15]. The reversible translocation of the $CBPQT^{4+}$ ring that can be induced in bistable rotaxanes of donor/acceptor type by electrochemical stimuli constitutes the basis of their application in molecular mechanical devices [38] – such as molecular muscles [39, 40] and valves [26] – and as components of high-density memory circuits [25, 41]. It was satisfying to discover that the electrochemical switching process in **5**·$4PF_6$ was unaltered [15] by the introduction of the two 1,2,3-triazole rings into the donor dumbbell, as shown by cyclic and differential pulse voltammetry. Very recently, the liquid-crystalline (LC) bistable rotaxane **5b**·$4PF_6$ was prepared [16] in 50% yield by clicking the fork-like mesogenic stopper **6** onto the pseudorotaxane [**4**⊂**CBPQT**]·$4PF_6$. The bistable [2]rotaxane **5b**·$4PF_6$ exhibits – over the temperature range from +10 to ~+150°C, at which point **5b**·$4PF_6$ starts decomposing – an LC smectic A phase which is a birefringent, viscous fluid state, as observed by polarized optical microscopy. The extended structure of **5b**·$4PF_6$ is layered, with the mesogenic units forcing the [2]rotaxane molecules into a parallel arrangement. The inter-layer separation of




**Scheme 1.** Synthesis of one-station (**A**) and bistable two-station (**B**) donor/acceptor [2]rotaxanes employing the CuAAC reaction. [2]Pseudorotaxanes, terminated at both ends of the π-donor thread with azide groups, are converted into [2]rotaxanes by simultaneous attachment of identical stoppers onto both termini.

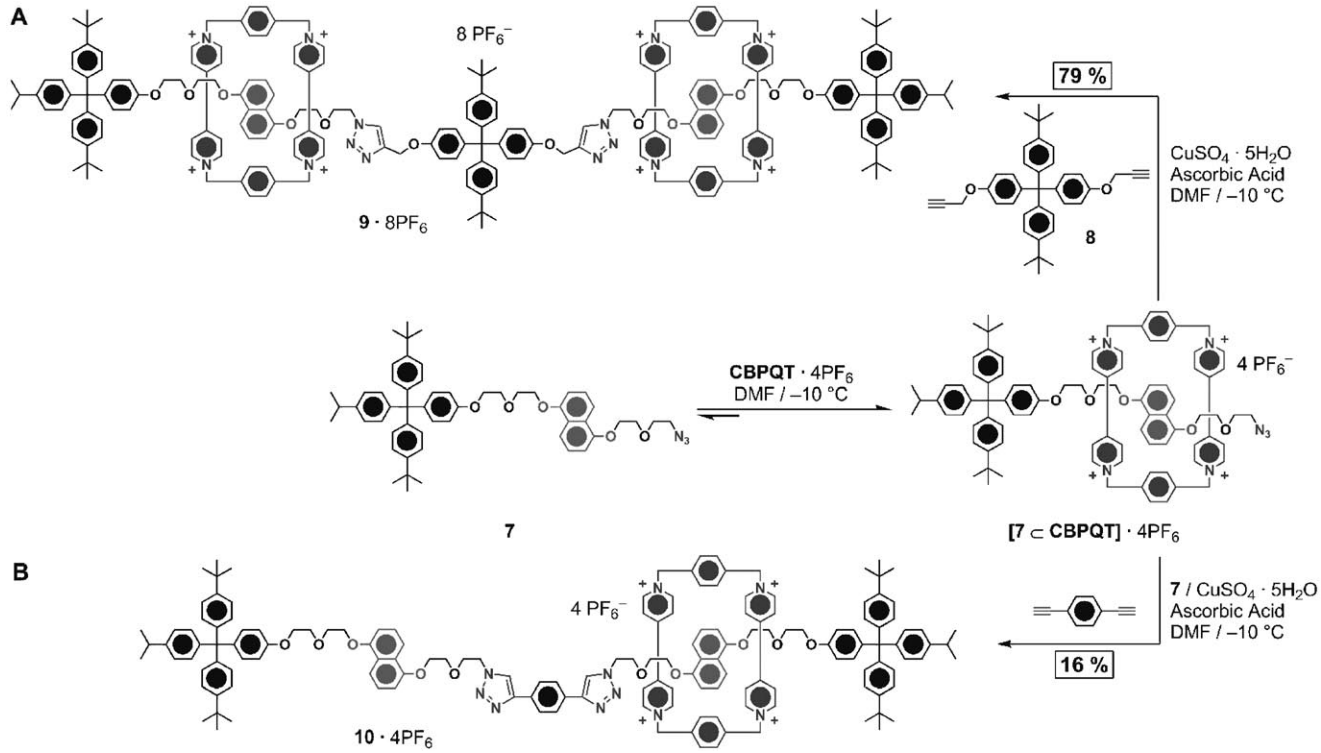
8.3 nm correlates well with the dimensions of **5b**·4PF$_6$ in its extended conformation [16].

The moderate yields observed in the clipping approach in donor/acceptor [2]rotaxanes drop to single-digits (9%) in the template-directed synthesis of a palindromic [3]rotaxane [39, 40]. The click chemistry approach, by contrast, appears not to suffer from this problem as two equivalents of the pseudorotaxane [**7**⊂**CBPQT**]·4PF$_6$ were "clicked" (Scheme 2A) onto the bivalent central core **8** to provide the palindromic [3]rotaxane **9**·8PF$_6$ in 79% yield [13]. Using two equivalents of the DNP-thread **7** (relative to **CBPQT**·4PF$_6$) and the sterically less bulky 1,4-diethynylbenzene as the central component, [2]rotaxane **10**·4PF$_6$ was isolated (Scheme 2B) in 16% yield [14]. Since this molecular shuttle features a single CBPQT$^{4+}$ ring and two degenerate DNP donor sites, we were able to probe the energy barrier to the translational motion of the CBPQT$^{4+}$ ring across the triazole-benzene-triazole spacer. From VT-NMR spectroscopic measurements, this barrier was estimated to be 15.5(±0.1) kcal·mol$^{-1}$ – that is, on a par with molecular shuttles containing tetraethyleneglycol and triphenylene spacers [42] – confirming that the 1,2,3-triazole rings do not hamper the shuttling of the CBPQT$^{4+}$ ring, either electronically or sterically to any significant extent. Finally, as a proof of the applicability of the CuAAC reaction in the construction of even higher-order rotaxanes, a branched [4]rotaxane (not shown here) was synthesized by "clicking" [**7**⊂**CBPQT**]·4PF$_6$ onto the central triyne, tris-1,3,5(4′-ethynylphenyl)benzene, in a very good yield (72%) [13].

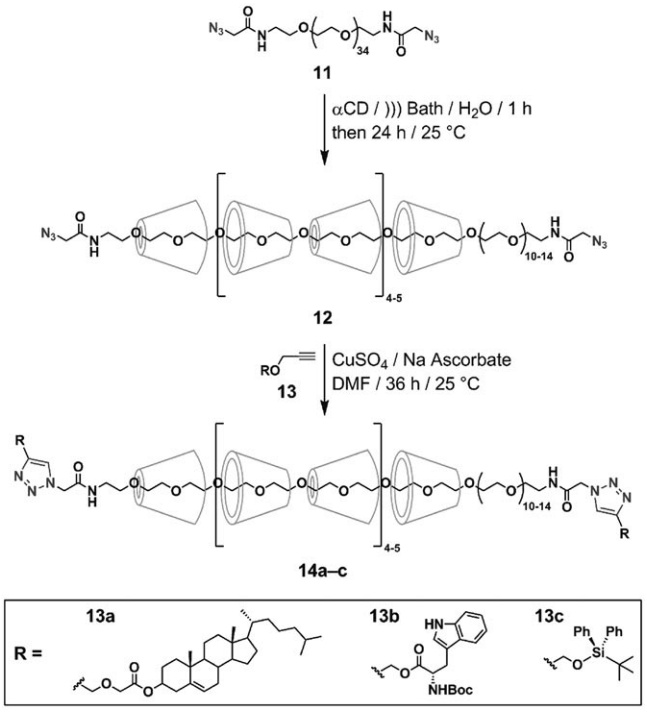
A formal [1]rotaxane self-complex in which the CBPQT$^{4+}$ ring and the DNP-containing thread are both mechanically interlocked and covalently linked, has been prepared by clicking the thread **7** onto the CBPQT$^{4+}$ ring functionalized with a terminal alkyne [14].

In the realm of oligorotaxanes based on α-cyclodextrin (αCD), Thompson and coworkers [17] have used the CuAAC reaction to attach cleavable end groups onto a central [*n*]pseudorotaxane core. Starting with the polyethyleneglycol (PEG1500) bisazidoacetate (**11** in Scheme 3), threading of it by αCD molecules formed the [*n*]pseudorotaxane **12** as an insoluble white powder. Once isolated, the pseudorotaxane was subjected to the alkyne-functionalized end-capping reagents **13a**–**c** in the presence of copper(I) as a catalyst. Insolubility of **12** called for the use of sonication, shaking, and microwave irradiation to ensure the completion of the click reaction with **13a**–**c.** Since the resulting oligorotaxanes **14a**–**c** proved insoluble as well, direct investigation by spectroscopy provided little information about their structures. By turning instead to atomic




**Scheme 2.** Synthesis of a degenerate two-station donor/acceptor [3]rotaxane (**A**) and a degenerate molecular donor/acceptor shuttle (**B**) using the CuAAC reaction to graft the hemirotaxane [**7**⊂**CBPQT**]·4PF$_6$ (along with, in the case of **10**·4 PF$_6$, an excess of **7** onto bivalent central cores **8** (A) and 1,4-diethynylbenzene (B).

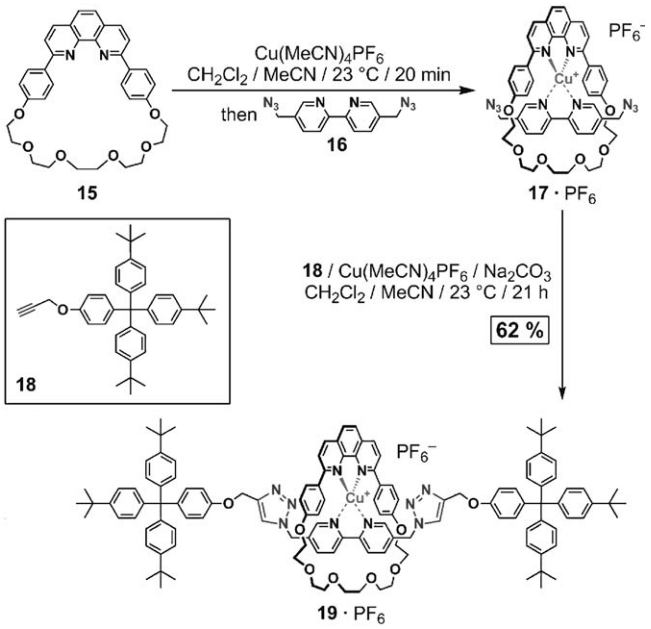



**Scheme 3.** Synthesis of rotaxanes with acid- (**13a**), base- (**13b**), and fluoride- (**13c**) cleavable groups, based on the αCD/PEG recognition motif, using CuAAC.

force microscopy and gel-permeation chromatography, the authors were able to estimate the coverage of PEG thread with αCD at 59, 69, and 61% for **14a**, **14b**, and **14c**, successively. These percent coverages correspond to approximately ten αCD units on a single polyrotaxane molecule. Exposure of polyrotaxanes **14a** and **14b** to conditions under which their end groups are cleavable – that is, acidic hydrolysis of vinyl ethers in **14a** and basic hydrolysis of esters in **14b** – resulted in clean removal of the stoppers with the generation of insoluble pseudorotaxanes. Subsequent decomplexation of the pseudorotaxanes produced αCD and slightly modified PEG threads, both of which were soluble in water. The end group cleavage reactions could be monitored *via* turbidity measurements. Interestingly, rotaxane **14c** did not undergo fluoride-mediated deprotection under aqueous conditions.

An application of the CuAAC reaction in the preparation of a copper(I)-rotaxane (Scheme 4) complex was reported by Sauvage and coworkers [18] in early 2006. In their protocol, macrocycle **15** is first exposed to stochiometric amounts of Cu(MeCN)$_4$PF$_6$, followed by treatment with **16** to give the pseudorotaxane precursor **17**·PF$_6$. This Cu(I) complex is fairly labile, because of the poor steric protection provided by ligand **16**, and is expected to exhibit much faster relative motion of components than the more stable sterically encumbered counterparts. Synthetic convenience, however, lies on the side of the sterically en-

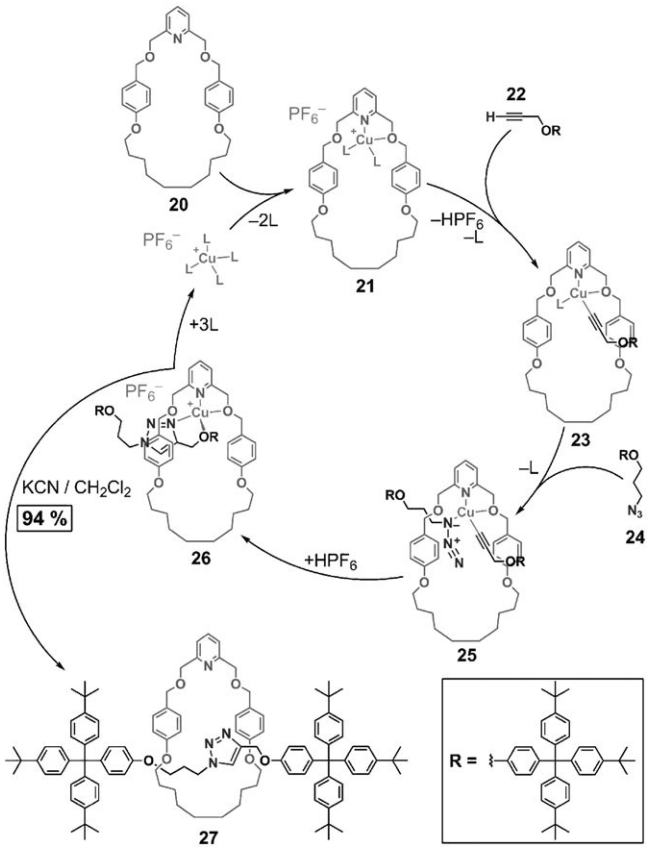
  




**Scheme 4.** Preparation of the Cu(I)-rotaxane complex **19**·$PF_6$ by click chemistry.

cumbered metal-pseudorotaxanes which are robust and can be stoppered using a variety of alkylation protocols. The more labile complexes such as **17**·$PF_6$ demand more tolerant reaction conditions, a requirement which is satisfied by the CuAAC reaction. Thus, **17**·$PF_6$ reacted with stopper **18** under CuAAC conditions [50 mol-% of $Cu(MeCN)_4PF_6$, $Na_2CO_3$] to provide the copper-rotaxane complex **19**·$PF_6$ in 62% yield after careful chromatography. The authors did not comment on any attempts at decomplexation.

Leigh and coworkers [19] have combined (Scheme 5) the catalytic properties of copper(I) complexes creatively with their ability to preorganize ligating rotaxane precursors in the tetrahedral coordination sphere of Cu(I). Thus, exposure of the starting macrocycle **20**, adorned with both pyridine (stronger) and oxymethylene (weaker) ligating sites, to $Cu(MeCN)_4PF_6$ gives intermediate **21.** This complex is able to undergo double exchange of its MeCN ligands – first for the terminal alkyne **22**, and then for the azide **24** – to give **25** which contains all three components of the future [2]rotaxane. The ensuing CuAAC reaction takes advantage of the mutual orientation of the reacting components to form the interlocked complex **26.** This complex is stable in the absence of competing ligands for copper – the free [2]rotaxane **27** is liberated only after demetallation with stoichiometric amounts of KCN. Optimal yields of rotaxane **27** (94%) were obtained using a fivefold excess of **22** and **24** relative to that of **20.** The synthesis was also rendered catalytic in copper (20 mol-% loading) through the use of pyridine as a competing ligand. However, although the conversion in this case was virtually complete, the isolated yield was a rather moderate 38%.

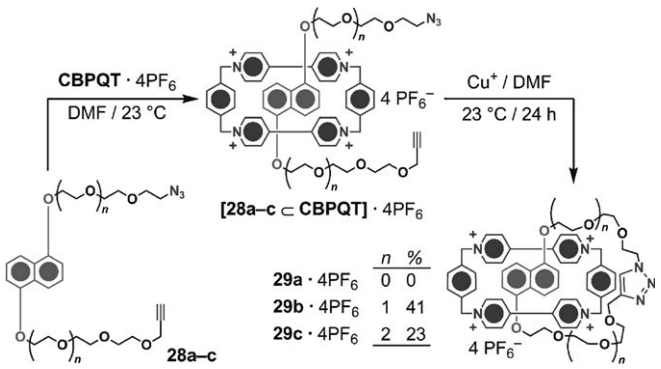



**Scheme 5.** Proposed mechanistic cycle for the preparation of rotaxanes with weakly interacting components using click chemistry.

## 4 Preparation of Catenanes Using the CuAAC

While the CuAAC reaction has been used successfully in the preparation of several different structural categories of rotaxanes, its use in the synthesis of catenanes [20, 21] has been limited to those containing the donor/acceptor recognition motif. Switchable donor/acceptor catenanes, based on the $CBPQT^{4+}$ π-acceptor ring, have found use as components of reconfigurable molecular switches [43] and have been proposed as the chromatic elements of electronic displays [44, 45]. As with rotaxanes, their traditional synthesis [46] involves clipping of the $CBPQT^{4+}$ ring around a preformed π-donor macrocycle in the final step. The use of the CuAAC reaction allowed us to invert the roles of the catenane components and so construct these mechanically interlocked compounds by clipping the ends of the π-donor thread around the preformed $CBPQT^{4+}$ ring. Expediently synthesized azidoalkynes **28a – c** were used (Scheme 6) as the precursors to the π-donor. Compounds **28b** and **28c** underwent clean CuAAC reactions to provide the [2]catenanes **29b**·$4PF_6$ and **29c**·$4PF_6$ in 41 and 23% yield, respectively. Interestingly, these yields were more or less independent of the concentration of the reactants, suggesting that the [2]pseudorotaxanes [**28** ⊂ **CBPQT**]·$4PF_6$,




**Scheme 6.** Synthesis of donor/acceptor [2]catenanes using click chemistry.

possess a certain level of preorganization [47] which favors catenation over polymerization. The shortest π-donor in the series, **28a**, failed to react under the CuAAC reaction conditions, presumably because of the prohibitively large distance between the reactive ends of the pseudorotaxane [20].

The crystal structure (Figure 3) of catenane **29b**·$4PF_6$ shows that the DNP/$CBPQT^{4+}$ interaction is the dominant [π···π] one, since the $CBPQT^{4+}$ ring encircles the DNP ring in preference to the triazole ring. The interlocked structure is stabilized by (a) [π···π] stacking between the DNP units in the crown ether and the bipyridinum units of $CBPQT^{4+}$ ring, (b) [C–H···π] interactions between the hydrogen atoms in the 4 and 8 position of the DNP unit and the phenylene rings in the $CBPQT^{4+}$ ring, and (c) [C–H···O] interactions between the oxygen atoms in the side chain of **29b**·$4PF_6$ and the bipyridinium α-hydrogen atoms on the $CBPQT^{4+}$ ring. Intriguingly, however, the 1,2,3-triazole moiety aligns itself with the outside face of one of the bipyridinium units of the $CBPQT^{4+}$ ring, forming an almost evenly-spaced (outer) bipyridinium-DNP-(inner) bipyridinium-triazole layer. The distance between the centroid of the triazole ring and the average plane of the inner bipyridinium unit is 3.38 Å and, as such, is very close to that of the DNP-bipyridinium separation. Additionally, the two planes are nearly parallel (7.3°) with the triazole ring being slightly offset relative to one of the two pyridinium rings. Both of these effects can be interpreted as being caused by the [π···π] stacking of the two units.

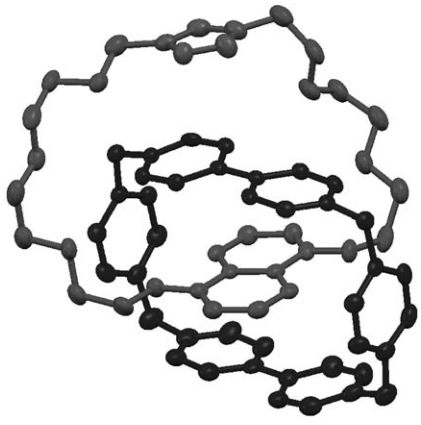


**Figure 3.** The solid-state structure of $\mathbf{29b}^{4+}$. Aside from the disordered $PF_6^-$ counterions, hydrogen atoms and solvent molecules are omitted for clarity. Thermal ellipsoids are shown at 50% probability levels. Acceptor ring shown in blue, donor thread in red, and triazole ring in purple.

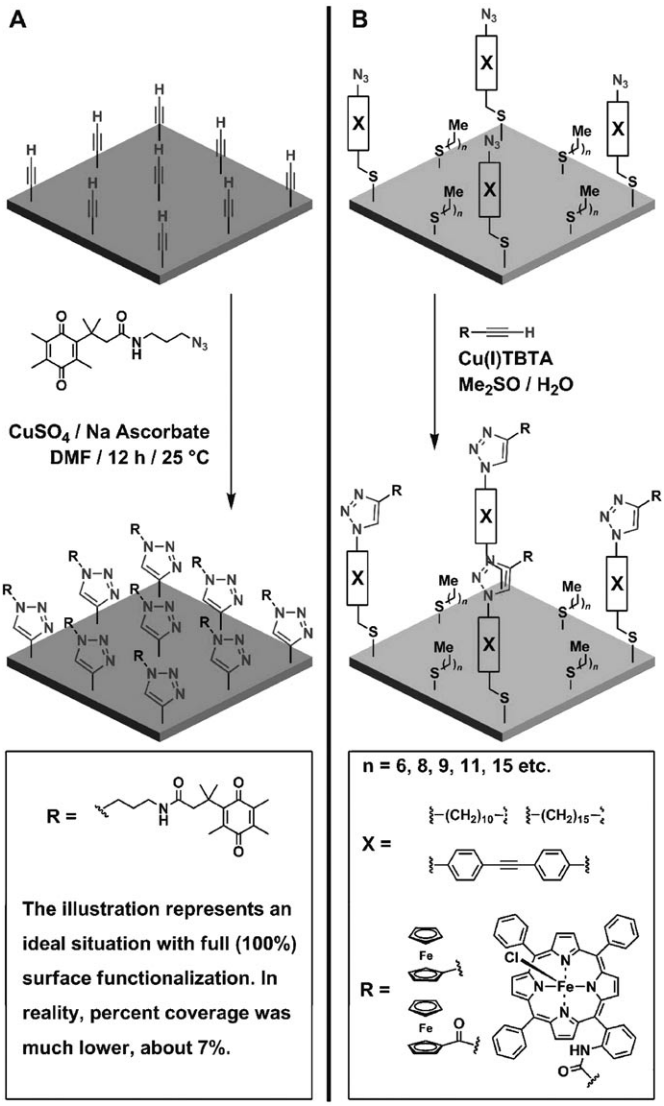
## 5 The CuAAC Reaction for Molecular Assembly and Attachment onto Surfaces

A nontrivial variation of the Figure 2B concept of the threading step to form a hemirotaxane, or singly-stoppered pseudorotaxane, is for the stopper moiety to be a surface. The use of bistable [2]catenanes and [2]rotaxanes for various solid state applications has been explored by a number of groups [25–27] over the past few years, and many of those applications require the formation of catenane or rotaxane molecular films and monolayers. In fact, an actual example of using a surface as the stopper moiety for the threading step has been demonstrated by at least one [27] of these groups. Nevertheless, options for assembling bistable mechanically interlocked molecules, and other functional molecules, onto surfaces have remained limited. The Langmuir–Blodgett technique, while useful for preparing monolayers of amphiphilic bistable catenanes and rotaxanes on many different surfaces, generates only physisorbed monolayers. Conversely, covalently attached monolayers are much more robust, but have only been demonstrated for in a very few specific cases, *e.g.*, thiol-terminated pseudorotaxanes attached to Au surfaces [48]. For many of the applications involving bistable catenanes and rotaxanes, the molecule/electrode interface plays a critical role [49]. For example, the switching within [2]catenane and [2]rotaxane molecular switch tunnel junctions has been demonstrated to originate from an electrochemically driven molecular switching process only for the cases of carbon nanotube [50] and silicon bottom electrodes [43]. When metallic bottom electrodes are utilized, other, non-molecular processes dominate the junction performance [51]. The CuACC reaction is beginning to provide a much more general approach for the preparation of covalently attached molecular monolayers on a wide variety of metal, insulator, and semiconductor surfaces. Thus, although it has not yet been employed for the construction of bistable catenane and rotaxane monolayers, the relevant aspects of this chemistry are worth mentioning in this minireview. Since some of this click chemistry has been reviewed recently [9, 28], we only discuss the most relevant and recent advances.

The most relevant surfaces for assembling electrochemically switchable catenanes and rotaxanes are conducting substrates. Click chemistry has been utilized to attach molecules (Scheme 7) to gold [9, 28], graphitic sheets [52], and

nonoxidized Si [53] – all of which can serve as working electrodes within an electrochemical cell and thus permit electrochemical access to the substrate-bound molecules. For gold surfaces, Chidsey's group [54] has explored the rate of electron transfer through the 1,2,3-triazole linkage. They found that electron transfer rates can be varied from $\sim 10^5$ down to 1 $s^{-1}$, depending on the length and conjugation of the electron transfer bridge and the dilution of the triazole-containing molecule within the monolayer by alkane thiols. For molecular electronics, the unoxidized Si surface is likely to play an important role. Organic passivation of H- or Cl-terminated Si surfaces can enhance the resistance of those surfaces to oxidation [55]. The best organic passivation is achieved on the unreconstructed Si(111) surface. Even on this surface, steric interactions mean that the only two organic groups, which can be harnessed to achieve a 100% coverage, are methyl [56] and ethynyl [53, 57]. Rohde *et al*. [53] have utilized the CuACC reaction to couple (Scheme 7A) electrochemically active benzoquinones to ethynyl-terminated Si(111) and demonstrated that the surface is protected against oxidation and can be further functionalized by electrochemical reduction of the benzoquinone, a procedure which resulted in cleavage of the molecule and exposure of an amine terminus. While those results are encouraging in terms of a strategy for building molecular monolayers on Si, the CuACC reaction proceeded in low yield, forming only a 7% coverage. Alternative strategies for achieving higher surface coverages *via* the Huisgen 1,3-dipolar cycloaddition chemistry (without the Cu catalyst) have been reported by Reinhoudt's group [58]. They have utilized microcontact printing of an ethynyl-terminated molecule onto an azide-terminated $SiO_2$ surface. Although quantitative estimates for the percent coverage achieved were not obtained, qualitative analysis indicated that the surface coverage was high. Thus, the combination of these surface chemistry strategies with microcontact printing protocols may lead to a promising approach for forming robust and high coverage bistable catenane and rotaxane monolayers on a host of conducting substrates, including Si. Achieving such films would represent a significant step forward for molecular electronics.




**Scheme 7.** Functionalization of ethynylated Si-111 (**A**) and azide-terminated gold (**B**) surfaces using the CuAAC reaction.

## 6 Conclusions

Although still in its infancy, the use of the CuAAC reaction in the synthesis of mechanically interlocked molecules seems a good strategy since a range of different noncovalent recognition motives tolerate this copper-catalyzed method for the template-directed synthesis of rotaxanes and catenanes in good yields. In addition, the CuAAC reaction is also emerging as an excellent strategy for constructing molecular monolayers on different conducting substrates. We view these early developments as promising for two reasons. From a practical point of view, the use of click reaction should facilitate the synthesis of mechanically interlocked molecular compounds and thus streamline their use in functioning molecular devices and machines, as well as in other applications. It is certainly encouraging that the 1,2,3-triazole unit installed by the click reaction does not interfere with either the electrochemical switching or with the liquid-crystalline properties of bistable donor/acceptor [2]rotaxanes. Furthermore, the potential for including a variety of substrates as key reagents in the assembly of bistable donor/acceptor [2]rotaxanes may increase the robustness of a number of already demonstrated applications, and open up new ones as well.

In the context of synthetic methodology, the CuAAC reaction might well be just the tip of the iceberg when it comes to using pseudorotaxanes and other complexes as supramolecular synthons. Any reaction that is compatible

with the conditions required for efficient noncovalent bonding should mirror the CuAAC reaction in its efficiency and versatility. By exploring this notion, we have already proven [20, 21] that the oxidative homocoupling of alkynes (Eglinton coupling) [59, 60] – a reaction which also proceeds through a copper-acetylide intermediate – serves as an efficient reaction for the assembly of donor/acceptor [2]catenanes under template control. It is our expectation that our predictions will be vindicated.

## 7 Acknowledgements

The research conducted in our own laboratories has been funded by the Microelectronics Advanced Research Corporation (MARCO) and its focus centers for Functional Engineered NanoArchitectonics (FENA) and Advanced Materials and Devices (AMD), the National Science Foundation (NSF-CCF- 05204490), the Defense Advanced Research Projects Agency (DARPA), and the Center for Nanoscale Innovative Defense (CNID).

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