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Communication

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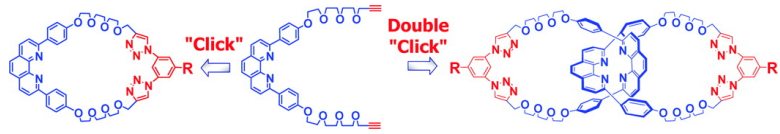

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General Method for Synthesis of Functionalized Macrocycles and Catenanes Utilizing "Click" Chemistry

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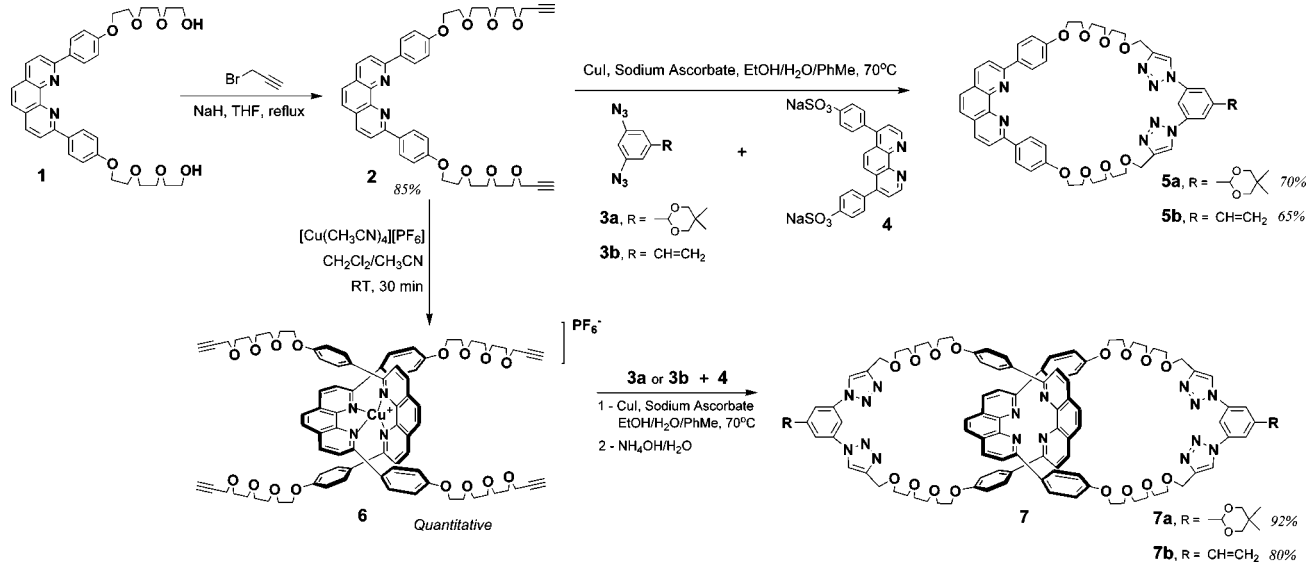
Catenanes and rotaxanes have attracted considerable attention due to their interesting chemical and physical properties, and as precursors to new materials with potential application as molecular devices for information storage and processing and as light-driven molecular machines.[1] The copper(I) template approach developed by Sauvage and co-workers[2] is a general and highly effective strategy for the preparation of catenanes, rotaxanes, and knots. This idea is based on tetrahedral coordination of a Cu(I) atom to a pair of bidentate ligands which are held in a specific orientation that directs subsequent macrocyclization and/or "stoppering" reactions that afford interlocked structures.

The biggest challenge in the synthesis of interlocked structures is ring closure of the preoriented moieties.[2a] Ether and amide linkages are most commonly utilized in synthetic routes to catenanes and rotaxanes, but product yields are generally quite low.[1] Ring-closing metathesis (RCM) has proved to be an efficient method to prepare catenanes.[3] However, the final catenanes obtained by RCM lack functional groups for further structural elaboration and therefore represent a synthetic dead end. Huisgen 1,3-dipolar cycloaddition,[4a] so-called "click" chemistry,[4b] has also been used to synthesize triazole-linked rotaxanes[4c−h] and catenanes.[5] However in these studies, which employed macrocycles,[4c−h] [2]-pseudorotaxanes,[5a] and [2]-rotaxanes[5b] obtained by classical multistep synthesis, the overall yields of the target rotaxanes and catenanes remained generally low and also lacked functional groups for further structural elaboration.

Given that "click" reactions generally proceed in high yield and show unusual tolerance toward most functional groups, we felt that by using this methodology it might be possible to improve the efficiency of the macrocyclization step while also allowing the implementation of useful functional groups into the target catenanes and rotaxanes. Our strategy (Scheme 1) employs the introduction of terminal alkyne groups into 2,9-diaryl-1,10-phenanthroline (phen) building block **1**[2c] to give *bis*-alkynyl derivative **2** for subsequent reaction with functionalized aryl 3,5-diazides.[6] For the present purpose, this approach is illustrated using acetal and vinyl moieties on the aryl 3,5-diazides. Due to the ability of **2** to complex Cu(I), which is a key component of the "click" reaction brew,[2b,4b] the biggest challenge was to prevent the formation of a phen-Cu(I) complex, which might inhibit the desired double-"click" macrocyclization. To overcome this problem, we used sulfonated bathophenanthroline **4** as an auxiliary ligand. In biological systems, **4** has been used as an additive to enhance the reaction kinetics, thereby preventing damage to substrate molecules such as peptides and proteins.[7]

We were delighted to find that when a highly dilute equimolar mixture of **2** and **3a** or **3b** was added dropwise (10 h) to a mixture containing CuI, sodium ascorbate (SA), 1,8-diaza[5.4.0]bicycloundec-7-ene (DBU), and phen ligand **4** in an oxygen-free 7:3:1 EtOH/H_2O/PhMe solvent mixture at 70 °C, macrocycle **5a** or **5b** were obtained in 65−70% isolated yield. In accordance with the proposed structures for **5a** and **5b**, ^{1}H NMR signals (Figure 1) are observed at δ 4.73 and 7.95 ppm for, respectively, the CH_2 group adjacent to the triazole moieties and the proton on the triazole ring (for details, see Supporting Information (SI)). In a control experiment in which the reaction was carried out under exactly the same conditions but in the absence of **4**, a complex product mixture was

Scheme 1. Synthesis of Functionalized Macrocycles and [2] Catenanes Using "Click" Chemistry



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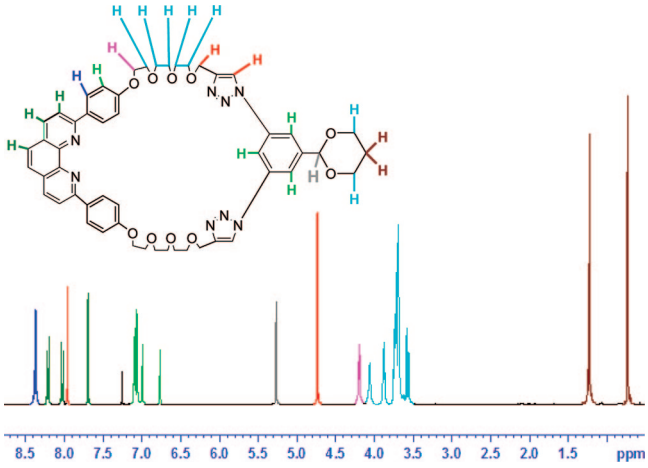

Figure 1. ^{1}H NMR spectrum of macrocycle **5a** in $CDCl_3$.

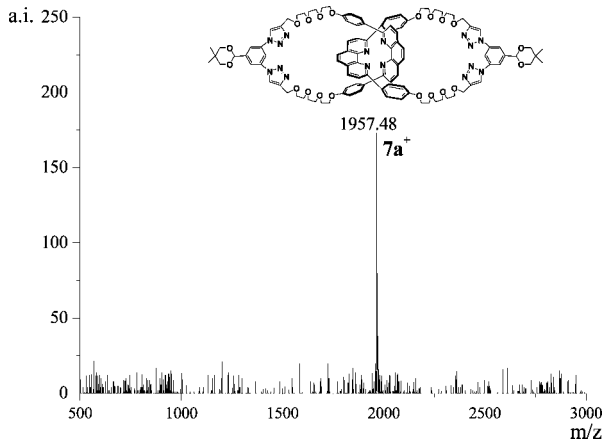

Figure 2. MALDI-TOF mass spectrum of catenane **7a**.

obtained, which yielded only 7% of the desired macrocycles **5a/5b** along with nonidentified products.

This promising result encouraged us to explore other variants of this methodology. We envisaged preparation of a difunctionalized catenane in a one-pot procedure. The reaction was carried out as follows: *bis*-dialkynyl(phen)$_2$-Cu(I) complex **6**, prepared following the general literature procedure,[2] was added to a 7:3:1 EtOH/H_2O/PhMe mixture of DBU (20 equiv), SA (2 equiv), **4** (2 equiv), and CuI (1 equiv) at 70 °C. A highly dilute solution of **3a** or **3b** (1 equiv) in 9:1 EtOH/PhMe was then added dropwise, affording the symmetrically functionalized catenanes **7a** and **7b** in 80−92% yield (see SI for experimental details). The materials obtained after the workup procedure, which involved washing with ammonium hydroxide,[4i,j] were Cu-free catenanes. Their ^{1}H NMR spectra are quite similar to those of the analogous macrocycles; however, MALDI-TOF analysis (*m/z* calculated for **7a**: 1956.86; found: 1957.48 $[M+1]^+$, Figure 2) confirmed the postulated Cu-free catenane structure. When these materials were treated with $Cu(CH_3CN)_4^+PF_6^-$ in 7:3 CH_2Cl_2/CH_3CN, the color changed to deep red, consistent with formation of the catenane (phen)$_2$Cu(I)PF_6 complex.[2] The MALDI-TOF spectrum of the Cu(I)-**7a** complex showed *m/z* 2020.08 (calculated for $C_{108}H_{116}N_{16}O_2Cu$ 2019.79; see SI).

In conclusion, a general method has been developed to prepare phen-based macrocycles and catenanes bearing functional groups, opening up possibilities for constructing architecturally interesting new materials. As part of our continuing interest in the effects of molecular topology on photoinduced electron transfer mechanisms in artificial photosynthetic systems,[8] the peripheral functional groups in these catenanes and macrocycles can be used to attach a variety of electron donor and acceptor moieties, such as porphyrins, phthalocyanines, and fullerenes. We are also exploring construction of more elaborate interlocked architectures using this approach.

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Supporting Information Available: Experimental details for preparation and spectral characterization of macrocycles and catenanes and their precursors. This material is available free of charge via the Internet at http://pubs.acs.org.

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