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Two new triazolophanes: synthesis, structures, self-assembling, and anion complexation properties

Qunpeng Duan [a,b], Wei Xia [a], Chen Lin [a,*], Yi Pan [a], Leyong Wang [a]

[a] Key Laboratory of Mesoscopic Chemistry of MOE, Center for Multimolecular Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210093, PR China
[b] Department of Material and Chemistry Engineering, Henan Institute of Engineering, 451191 Zhengzhou, PR China

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ABSTRACT

Two new triazole-based macrocyclic molecules, triazolophanes **1** and **2**, have been synthesized by the copper(I)-catalyzed cycloaddition of bis-triazole azides and bis-alkynes. The X-ray crystal structures of triazolophanes **1** and **2** revealed that both of them had an oblique-pillar cavity with the chair-like conformation in the solid state, and in their crystal structures both of them could self-assemble through intermolecular nonconventional CH···N hydrogen-bonding interactions. ^{1}H NMR titration studies indicated that triazolophane **2** could selectively and strongly bind HSO_4^-, $H_2PO_4^-$, and $HP_2O_7^{3-}$ to form 1:2 host–guest complexes in $CDCl_3$ among the tested anions.

The synthesis of novel macrocycles has received considerable attention of the chemical community due to their unique structures, properties, and applications in molecular recognition, sensing, and advanced materials.[1] The design and synthesis of new macrocycles with an appropriate cavity size, especially for those which possess predictable structures and functions as well as elegant synthesis, still remain a challenge. One family of such new architectures consists of repeat or separated aryl triazole segments, namely triazolophanes, which have traditionally been synthesized stepwise or by one-pot multi-component macrocyclization reactions.[2] For example, in 2008, Flood et al.[3] reported the synthesis and anion binding properties of [3$_4$]triazolophanes, which showed new planar macrocyclic structures comprised of four triazole units with the cavity size of about 3.8 Å. These [3$_4$]triazolophanes could encapsulate halide anions via four C–H···anion hydrogen bonds in organic solvents. In the subsequent years, triazolophanes have been successfully applied in anion recognition as anion receptors.[4] Previous studies on tetraphenylene-based triazolophanes reported by Flood demonstrated that the cavity size of the triazolophanes is important for selective anion recognition.[3b] Therefore, we envisioned that if *p*-xylylene was used as an alternative of the *N*-linked phenylenes of Flood's [3$_4$]triazolophanes (Fig. 1) in the north and south directions, two novel 'Texas-sized' molecular box-like[5] macrocyclic triazolophanes **1** and **2** with the larger size of cavity could be obtained (Scheme 1). In triazolophane **2**, considering that pyridine units have been used previously[6,7] to alter the electronic character and the size of binding sites, pyridyl groups were particularly introduced into its skeleton to replace phenylenes of Flood's [3$_4$]triazolophanes. We herein report the synthesis of two new macrocyclic triazolophanes **1** and **2** (Scheme 1) by 1,3-dipolar cycloaddition reactions using Cu(I)-catalyzed azide–alkyne cycloaddition methodology, their structures, self-assembling in the solid state, and anion complexation properties. Interestingly, triazolophanes **1** and **2** could self-assemble into microporous and string-like architectures, respectively, in the solid state. The anion binding abilities of triazolophanes **1** and **2** toward various anions were investigated by ^{1}H NMR spectroscopy, which demonstrated that triazolophane **2** could selectively and strongly bind HSO_4^-, $H_2PO_4^-$, and $HP_2O_7^{3-}$ to form 1:2 host–guest complexes in $CDCl_3$ among the tested anions (F^-, Cl^-, Br^-, I^-, AcO^-, NO_3^-, ClO_4^-, HSO_4^-, $H_2PO_4^-$, and $HP_2O_7^{3-}$), but triazolophane **1** could not strongly bind F^-, Cl^-, Br^-, I^-, and HSO_4^- in $CDCl_3$.

The synthetic approach depicted in Scheme 1 outlines the preparation of triazolophanes **1** and **2**. 1,5-Diethynyl-2,4-bis(hexyloxy)benzene **3** and 2,6-dialkynylpyridine compound **6** were prepared from commercially available resorcinol and 2,6-dibromopyridine according to the literature procedure, respectively.[7,8] *p*-Xylylene diazide **4**[9] which was readily prepared from commercially available xylene dibromide, was reacted with diethynyl compounds **3** and **6** in the presence of CuI and DBU in dry toluene

* Corresponding author. Tel.: +86 025 83592529; fax: +86 025 83597090.
E-mail address: linchen@nju.edu.cn (C. Lin).

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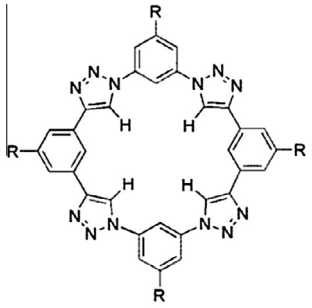
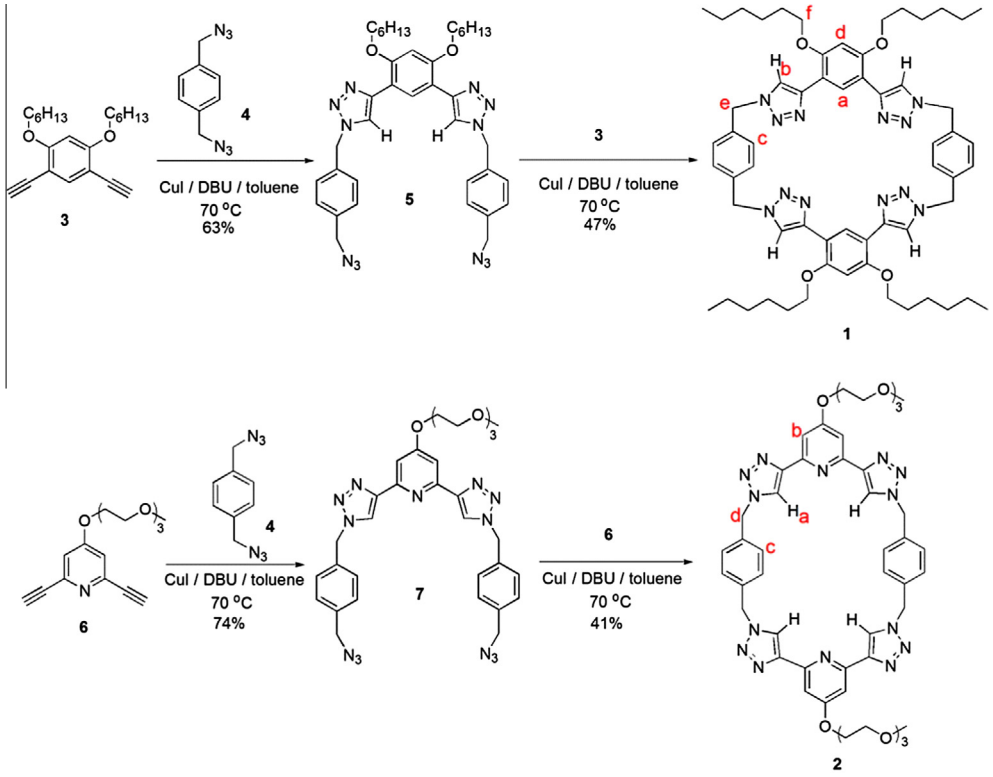


Figure 1. Structural representations of [3$_4$]triazolophanes reported by Flood et al. (R = solubilizing group).

under N_2 atmosphere at 70 °C for 14 h to afford the diazides **5** and **7**, respectively. Compounds **5** and **7** were then coupled with diethynyl compounds **3** and **6**, respectively, which underwent the cyclization by click chemistry under pseudo-high-dilution conditions to yield the final products, triazolophanes **1** (47%) and **2** (41%), respectively, as white powders. The electrospray ionization mass spectrometry (ESI-MS) and ^{1}H NMR spectra confirmed[10] the identity of the triazolophanes **1** and **2**.

Triazolophane **1** was crystallized from slow evaporation of a dichloromethane/methanol (10:1) solution. It crystallized in the monoclinic crystal system (space group, $P2_1/c$) with four molecules in the unit cell. As shown in Figure 2a, there existed four pairs of intramolecular hydrogen bonding interactions between the triazole proton H_b and the adjacent *n*-hexyloxy oxygen atoms of two phenylene moieties with the distance of 2.32–2.63 Å in the solid state of triazolophane **1**. On the other hand, in the solution of triazolophane **1**, its 2D NOESY spectrum in DMSO-d_6 also exhibited NOE contacts between the triazole proton H_b and the methylene proton H_f of the *n*-hexyl side chains, and no NOE contact between H_b and the *ortho*-phenylene proton H_a was observed (Supplementary data, Fig. S13), which supported the formation of the intramolecular hydrogen bonds in the solution as well. These intramolecular hydrogen bonding interactions play an important role in controlling the conformation of triazolophane **1**, and as shown in its crystal structure, the phenylene-bridged triazole connectivities of triazolophane **1** adopted an *anti–anti* conformation in the solid state. Moreover, as shown in Figure 2b, two macrocyclic molecules of triazolophane **1** could form a head-to-head dimer by intermolecular unconventional CH···N hydrogen bonding[11] (H28A···N5 = 2.535 Å, C28–H28A–N5 = 147.13° and H14A···N2 = 2.71 Å, C14–H14A–N2 = 150.19°), and two such dimers were interconnected through another two CH···N hydrogen bonds (H34A···N8 = 2.430 Å, C34–H34A–N8 = 150.30° and H34A···N9 = 2.731 Å, C34–H34A–N9 = 163.01°). This pattern in the solid state of triazolophane **1** infinitely repeated to self-assemble into a microporous architecture viewed along the *a*-axis (Fig. 2c).

In addition, triazolophane **2** could be crystallized from a mixture solution of chloroform and methanol (2:1). As shown in Figure 3a, triazolophane **2** adopted a chair conformation in the solid state, and its 2,6-bis(1,2,3-triazol-4-yl)pyridine (BTP) skeleton showed the *anti–anti* conformation as well. The centroid-to-centroid distance between the two parallel xylylene units in triazolophane **2** is 8.682 Å, and the vertical distance between the two pyridyl *N* atoms is 10.419 Å. In the solution, the 2D NOESY spectrum of triazolophane **2** in $CDCl_3$ (Fig. S14) showed no NOE contact between the protons on the distant pyridyl and triazolyl rings, indicating that the BTP skeletons of **2** also predominantly adopted the *anti–anti* conformation in the solution, which is in accordance with the known conformational preference of the BTP skeleton.[8] The further analysis of X-ray crystal structure of triazolophane **2** (Fig. 3b) revealed a string-like self-assembly by intermolecular unconventional CH···N hydrogen bonding interactions (H21A···N2 = 2.466 Å, C21–H21A–N2 = 171.34°, H15A···N2 = 2.606 Å, C15–H21A–N2 = 166.07°, H2A···N6 = 2.645 Å, C2–H2A–N6 = 148.63° and H22A···N3 = 2.466 Å, C22–H22A–N3 = 170.93°).



Scheme 1. Synthesis of triazolophanes **1** and **2** (DBU: 1,8-diazabicycloundec-7-ene).