ORGANIC LETTERS

2011
Vol. 13, No. 23
6148–6151

Supramolecular Shuttle Based on Inclusion Complex between Cucurbit[6]uril and Bispyridinium Ethylene

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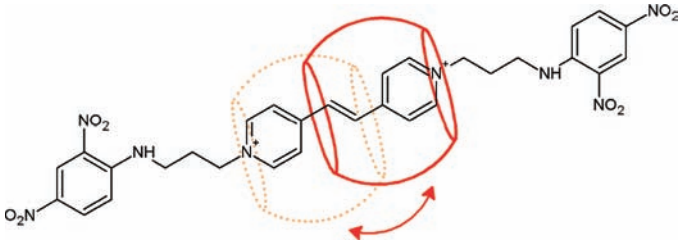
Received September 4, 2011

ABSTRACT



Cucurbit[6]uril (CB6) and bispyridinium ethylene form a stable inclusion complex. A rotaxane derived from this complex was prepared in which a CB6 wheel shuttles along an axle in an NMR time-resolved regime.

Cucurbiturils (**CBn**) are macrocyclic compounds which are utilized as supramolecular hosts for positively charged and neutral guests.[1] 1,1′-Dimethyl-4,4′-bipyridinium (methylviologen, **1**) and its extended analog, *trans-N,N*′-dimethyldipyridyliumylethylene (bispyridinium ethylene, **2**) (for structures, see Figure 1), represent common guests in the supramolecular chemistry of cucurbituril. These host−guest complexes are used for the construction of various advanced supramolecular systems. Despite several advantages of bispyridinium ethylene derivatives compared to the viologen derivatives, interaction of the former group of guests with **CBn** is significantly less explored. For instance, both **1** and **2** form charge transfer complexes with hydroxynaphthalenes, which are stabilized inside the **CB8** cavity. The ternary complexes based on **2** are, however, more stable in comparison with those in which **1** is used.[2] Similarly to **1**, two molecules of **2** (or its diamine analog) are able to be simultaneously included in the **CB8** cavity, but in the latter case, selective photodimerization takes place.[3] **CB7** forms 1:1 complexes with viologen as well as with bispyridinium ethylene derivatives (or its diamine analogs), although only in the latter case the irradiation of the complexes is followed by the transformation of the *trans* to *cis* isomer, which is

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10.1021/ol2023888
Published on Web 11/08/2011

stabilized inside the **CB7** cavity.[4] Due to its small cavity, **CB6** was reported to form a complex in which **CB6** engulfs only one aromatic ring of methylviologen.[5,6]

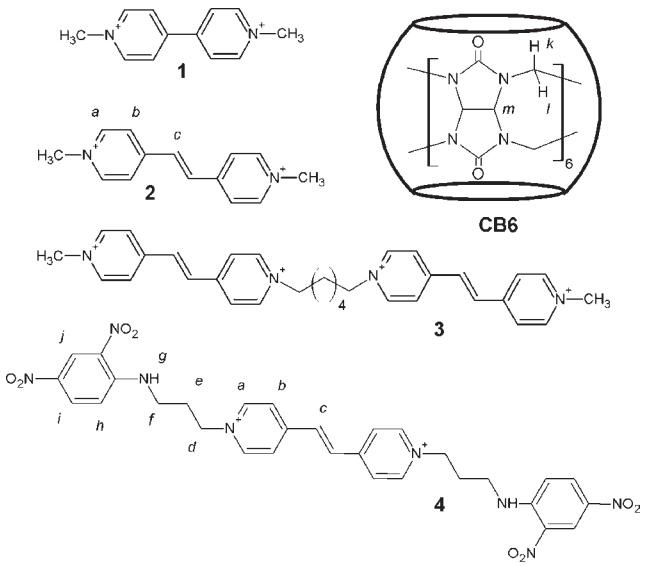

Figure 1. Structures of the guests.

It is rather surprising that, to the best of our knowledge, there is not a single example of complexation studies between **CB6** and any bispyridinium ethylene derivative **2**. Therefore, we decided to investigate the host–guest interaction between **CB6** and guest **2** and prepare supramolecular systems derived from this complex.

The interaction of compound **2**, which is a vinylene-extended analog of methylviologen **1**, with **CB6** was investigated by using ^{1}H NMR spectroscopy (see Figure 2). Addition of 1.0 equiv of **CB6** into the solution of guest **2** in D_2O containing also 0.05 M NaCl resulted in the disappearence of the original signals and the formation of two new sets of signals. Compared to the original ^{1}H NMR signals *a* and *b*, a new resonance *b*′ deshielded by 0.63 ppm and resonances *a*″ and *b*″ shielded by 0.51 and 1.18 ppm, respectively, arose in the spectrum. In addition, signal *c* at 7.95 ppm splits into two separate signals *c*″ (overlapped by signal *b*″) and *c*′ located at 7.15 and 7.68 ppm, respectively. The ^{1}H NMR data show that **CB6** and guest **2** form a stable 1:1 inclusion complex. In this complex, the vinylene moiety of the guest is situated inside the host but the time-averaged magnetic surroundings of all guest protons of the two individual parts (′ and ″) differ as they appear as two resolved sets of signals in ^{1}H NMR spectra at 300 MHz (T = 303 K). One of the two aromatic rings is fully pulled inside the host whereas the second aromatic ring is located outside the **CB6** cavity (see Figure 2).

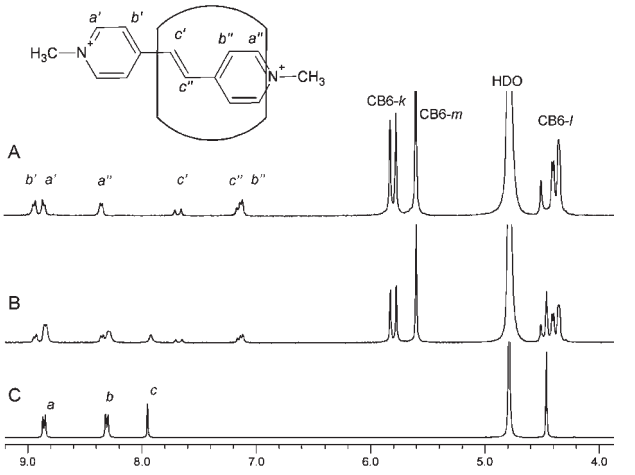

Figure 2. ^{1}H NMR spectra (300 MHz, 0.05 M NaCl–D_2O) of **2** in the absence (C) and presence of 0.5 equiv (B) and 1.0 equiv of **CB6** (A).

In contrast to the viologen guest **1**, the exchange process between free and **CB6**-bound guest **2** is slow on the NMR time scale under the experimental conditions specified above. The NMR experiments revealed that, in an equimolar mixture of **CB6** and **2**, the concentration of the free guest is insufficient to be accurately determined by ^{1}H NMR spectroscopy. This precludes the determination of the association constant by the NMR technique at the millimolar level. Therefore, UV–vis spectroscopy was used for determining the association constant. Guest **2** shows an absorption band with the maximum at 317 nm. The intensity of the absorption band decreases with the increasing amount of **CB6** in the solution. Fitting the absorbance as a function of the **CB6** concentration allowed us to obtain a value of the association constant for the 1:1 complex equal to $(2.1 \pm 0.2) \times 10^6$ M^{-1}. Due to the low solubility of **CB6** in water, the binding was measured in 0.05 M NaCl solution. Note that, under the same conditions, the association constant between **CB6** and **1** is as low as ~100 M^{-1}.[6]

Previously, it was demonstrated that although **CB6** does not fully engulf the viologen aromatic nucleus, the cavity of **CB6** is able to slip over the viologen unit.[7] This behavior was used for the construction of pseudorotaxanes and poly(pseudorotaxanes). The data presented above clearly show that **CB6** and guest **2** form a stable unsymmetrical inclusion complex. However, it was not clear if it is possible for **CB6** to slip over the double bond of guest **2**. To answer this question, we synthesized guest **3** in which two bispyridiniumethylene units are connected through a

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hexylene chain. The central hexylene unit framed by two nitrogen cations is a very good binding site for **CB6** and should be preferred by the host against the bispyridinium units.[8] Binding of **CB6** around the hexylene unit of **3** would show that the macrocycle is able to slip over the bispyridinium unit. The complexation between **CB6** and **3** was studied by ^{1}H NMR spectroscopy (see Supporting Information (SI)). All hexylene protons of the guest were shielded upon addition of **CB6** (1.0 equiv) while shielding of the aromatic part of the guest was not observed. This experiment clearly demonstrated that **CB6** is able to overcome the steric barrier presented by the bispyridinium unit and binds at the thermodynamically preferred position around the hexylene central part. The NMR spectra also indicate that the addition of 3 equiv of **CB6** results in the formation of a quaternary complex in which not only the hexylene chain but also both bispyridinium units are engulfed by one molecule of the host.

We further decided to demonstrate the potential of the stable **CB6·2** complex by the preparation of rotaxane **5** (see Figure 3 for the structure). The two-step reaction consisted of the quarternization of the pyridine nitrogen atoms by means of 3-bromopropanamine, followed by the reaction of the obtained diamine with 2,4-dinitrofluorobenzene via aromatic nucleophilic substitution in the presence of **CB6**. An initial NMR study confirmed that diamine and **CB6** form a stable 1:1 inclusion complex in which **CB6** occupied one-half of the bispyridinium units similarly to the situation described for the **CB6·2** complex. Attachment of the bulky dinitrobenzene stoppers should trap the **CB6** wheel threaded on the bispyridinium axle. This strategy was previously applied to construct rotaxane and pseudorotaxane based on the viologen axle and the **CB7** wheel.[9] However, rotaxanes based on **CB6** are almost exclusively prepared by 1,3-dipolar cycloaddition between an azide and alkyne compounds.[10]

An ^{1}H NMR spectrum of rotaxane **5** shows that the overall integral intensity of the signals corresponds to the 1:1 complex of the axle and **CB6**. However, the majority of the signals are not easily assignable (Figure 3A). The ^{1}H−^{1}H gs-DQF-COSY and ROESY NMR experiments allowed us to fully distinguish between the two chemically different parts of the rotaxane molecule **5** (see SI). Additional evidence for the rotaxane formation was obtained from an ESI mass spectrum through the observation of a signal at m/z 813.3 corresponding to the rotaxane without the two counterions (see SI).

While we were able to prove the successful preparation of rotaxane **5**, the position of the **CB6** wheel on the axle was

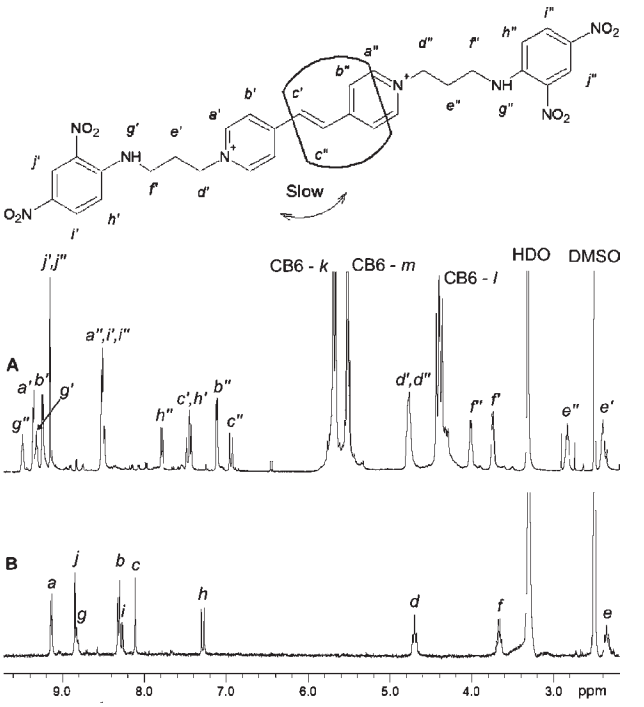

Figure 3. ^{1}H NMR spectrum (500 MHz, DMSO-d_6, 303 K) of **4** (B) and **5** (A) and a schematic representation of the shuttling mode of the **CB6** wheel.

initially difficult to predict from ^{1}H NMR spectra. To understand the supramolecular assembly of **5**, first we synthesized the rotaxane axle **4** free of **CB6**. The binding mode of the **CB6** wheel within the rotaxane was than predicted using an analogy with the **CB6·2** complex. The signal pattern of the bispyridinium moiety is identical in both cases. Both vinylene protons of the axle give rise to one singlet resonance (*c*) in the absence of the **CB6** macrocycle (see Figure 2B), similarly to free guest **2**. However, in the rotaxane this singlet splits into two doublets (*c*′, *c*″), which are significantly shielded as compared to the original singlet. This observation leads us to the conclusion that the macrocycle is located around the part of the central bispyridinium vinylene unit. Most signals of the bispyridinium ethylene arms split into two separate sets. This includes the signals of the aliphatic part (*d, e, f*), the signal of the amino group (*g*), and the signal of the aromatic proton (*h*). One set of these signals (′) approximately corresponds in position to that of the **CB6**-free axle. The ^{1}H NMR signals of the second set (″) are significantly deshielded. This indicates that the arm of the axle, which is closer to the **CB6** macrocycle, is located in the deshielding region outside the carbonyl portal of the macrocycle whereas the more distant arm of the axle is practically unaffected by the presence of the **CB6**. The conclusions drawn from the chemical shift perturbations are further supported by detected NOE interactions between the axle and the **CB6** units. The dynamically averaged methine protons (CB6-*m*) located on the outer surface of the **CB6** macrocycle can interact only with protons located

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in the center of the **CB6** cavity. We observed this type of interaction only for (b'') and (a'') protons (see Figure 4). NOE crosspeaks between protons (CB6-*k*) and protons (a''), (b''), (b'), (c'), (c''), and (d'') indicate that these protons approach one of the **CB6** portals from either the inner or outer part. It is interesting to note significant deshieldings of the protons (g'') and (h''). This effect could be rationalized by folding of the arm ($''$) back to the carbonyl portal.[11]

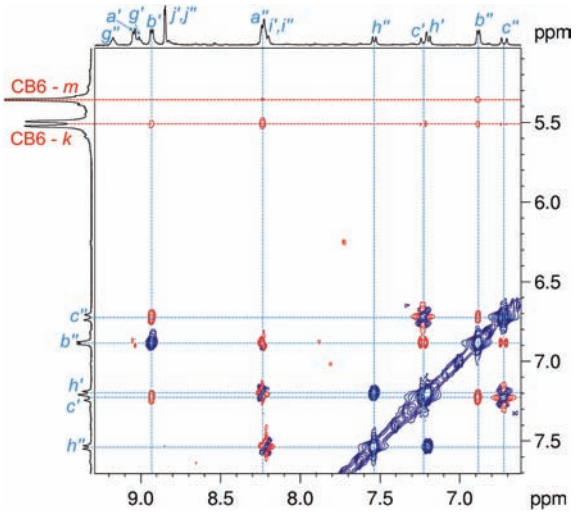

Figure 4. A portion of ^{1}H–^{1}H ROESY spectrum (500 MHz, mixing time 50 ms, DMSO-d_6, 303 K) of rotaxane **5**.

The axle of rotaxane **5** contains two identical parts with the same affinity toward **CB6**. Therefore, it can be expected that the macrocycle will slide over the central vinylene unit. The transfer between the two halves of the axle is slow on the NMR time scale, and thus it is why one can observe two sets of NMR signals corresponding to both parts of the axle. In other words, rotaxane **5** behaves as a supramolecular shuttle in which the **CB6** wheel shuttles between two identical parts of the axle. This transfer has been characterized by observing the exchange signals between ($'$) and ($''$) parts arising in the ROESY spectrum (see Figure S6 in the SI).

To obtain additional information about the dynamics of the shuttling and to characterize its energy barrier we measured several ^{1}H NMR spectra in DMSO-d_6 at various temperatures. The ^{1}H NMR signals of protons e' and e'' were well resolved and separated from other signals at 303 K, coalesced at the temperature of 355 K, and collapsed into the one signal after a subsequent heating due to the time averaging. The rate constant k of 288 s^{-1} for the sliding of the **CB6** wheel over the central bispyridinium ethylene unit was estimated at 355 K. This corresponds to the energy barrier $\Delta G^{\ddagger}$ of 71 kJ·mol^{-1} from which the rate constant of 4 s^{-1} has been estimated for a temperature of 303 K.

In conclusion, we have demonstrated that the interaction between bispyridinium ethylene **2** and **CB6** results in the formation of an inclusion 1:1 complex with a high association constant of (2.1 ± 0.2) × 10^6 M^{-1}. The stable complex has been used to construct rotaxane **5**. 1D and 2D NMR experiments revealed that, in the rotaxane **5**, the **CB6** wheel undergoes a shuttling process with a rate constant of 4 s^{-1} estimated for a temperature of 303 K.

Acknowledgment. We thank the Czech Science Foundation (P207/10/0695), Ministry of Education of the Czech Republic (MSM0021622413 and LC06030), and the projects CETOCOEN (no. CZ.1.05/2.1.00/01.0001) and CEITEC (CZ.1.05/1.1.00/02.0068) from the European Regional Development Fund for financial support.

Supporting Information Available. Synthetic procedures, characterization data, 1D and 2D NMR, ESI MS spectra of rotaxane **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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