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Dynamics of Mechanically Bonded **β**-Cyclodextrin in Isomeric Hetero[4]Catenanes

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Radial [4]catenane isomers of which the dynamics of the interlocked macrocycles are encoded by the covalent structure of the central macrocyclic backbone are described. Shuttling motion of the interlocked β-cyclodextrin was found to be dependent on both the position and interaction strength of the interlocked cucurbit[6]urils to the central macorcycle. This work demonstrates that dynamics of different mechanically bonded macrocycles in a hetero[n]catenane can be coordinated complementarily, suggesting the possible exploitation of high-order [n]catenanes as next level molecular machines in which more complex works can be performed with sophisticated intramolecular motions.

Introduction

Mechanically interlocked molecules (MIMs) are promising candidates for the construction of synthetic molecular machines such as molecular switches and molecular shuttles.[1-5] Underlying the unique potential of MIMs is the ability of the mechanically bonded components to undergo stimuli-triggered, large-amplitude intramolecular motions that is a result of the strong and flexible physical interlocking. While the incorporation of different binding motifs and the use of various kind of stimuli have been investigated in the design of various molecular shuttles and molecular switches,[2,3] most of these studies focus primarily on the thermodynamic aspect of the co-conformational switching and relatively less attention has been paid to the dynamics of the intramolecular motions of the interlocked components in MIMs.[4,5] In particular, application of a stimulus to a responsive MIM not only will change the thermodynamics and co-conformation equilibrium of a MIM, but also could change the kinetics of the intramolecular motions of the interlocked components. It is therefore fundamentally important to understand how the dynamics of the interlocked components are dependent on the structure and topology of a MIM, if the unique properties of mechanical bond are to be fully exploited in the development of MIM-based molecular machines.

On the other hand, to further advance MIM-based molecular machines to the next level of sophistication, structurally complex MIMs that are made up of interlocked macrocycles of diverse types and properties for different tasks and functions will be necessary. Although being a representative class of MIMs, catenanes reported to date are relatively simple, and [n]catenanes are highly underdeveloped when compare to [n]rotaxanes.[6] The scarcity of [n]catenane is partly because of the necessary formation of new macrocycle that adds extra challenges in the catenane synthesis.[7] Hetero[n]catenanes with multiple types of interlocked macrocycles are even rarer, as it will become much more difficult to coordinate a greater number of chemically different but compatible precursors in the simultaneous formation of both new covalent and mechanical bonds.[6d,6e,8]
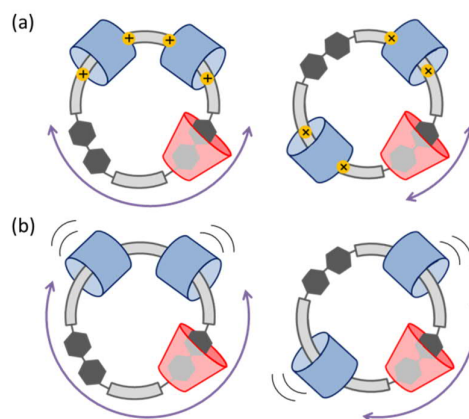
Scheme 1. Radial [4]catenanes with different sequence of recognition units on the central macrocycle. Positions of the CB[6] "roadblocks" (blue) define the shuttling path (purple arrow) for β-CD "vehicle" (red). Dynamics of the β-CD is further influenced by the protonation state of the [4]catenanes. The CB[6] are more strongly bound in the protonated form (a) than in the neutral form (b), and thus the β-CD shuttling is more accommodated in the latter.

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In this work, the synthesis and dynamics of two isomeric [4]catenanes that contains on their periphery two cucurbit[6]urils (CB[6]) and one β-cyclodextrin (β-CD) interlocked on a central macrocycle in different sequences are described. In particular, both the [4]catenanes have on their central macrocycles two each of biphenylene and diamine/diammonium that can respectively recognise the β-CD and CB[6]. Due to the different covalent sequences of the recognition units encoded in the central macrocycles, arrangement of the mechanically bonded peripheral macrocycles are also different in the isomeric catenanes, and the shuttling dynamic of the interlocked β-CD was found to be characteristic to the respective isomers (Scheme 1). Furthermore, despite the presence of a hydrophobic cavity in both the interlocked CB[6] and β-CD in the neutral forms of the [4]catenanes, only the β-CD in one of the isomers was found to be able to shuttle between the two biphenylenes. While the interlocked CB[6]s change their position on the central macrocycle only minimally when a pH stimulation is applied, shuttling dynamics of the pH-insensitive β-CD can be modulated through the interactions of the two different interlocked macrocycles.

Results and discussion

Synthesis and Characterisation of Two Isomeric Radial [4]Catenanes. Two radial hetero[4]catenanes that both contain two interlocked CB[6] and one β-CD were designed

and studied. With two CB[6] and one β-CD interlocked on the central ring, the cyclic sequence of the peripheral macrocycles are the same in the [4]catenane isomers. Yet, due to the different covalent backbone of the central macrocycle, the relative positions of the CB[6] and β-CD are different and the isomers are expected to display different dynamic behaviour. The two [4]catenanes, 4C-1 and 4C-2, were synthesised by CB[6]-mediated azide-alkyne cycloaddition (CBAAC) as shown in Figure 1 using the corresponding building blocks.[9] Stoichiometry of the β-CD (i.e. 1 eq.) has to be optimised in order to interlock only one β-CD in the presence of 2 eq. of biphenylene units in the building blocks to maximise the [4]catenane yields.[10] Having too much or too little β-CD in the reaction mixture will favour the formation of the respective [5]- and [3]catenanes. HPLC analysis of the crude product mixtures showed that both [4]catenanes were obtained in over 70% yields, with around 20% of the corresponding [3]catenanes with no interlocked β-CD as the major side-product. The two catenanes were isolated in 65% (4C-1) and 75% (4C-2) by preparative HPLC in their tetra-protonated forms as the formate salts.

High-resolution ESI-MS spectrum of the tetra-protonated forms of 4C-1 and 4C-2 showed a molecular ion peak at m/z = 1118.9616 and 1118.9427, respectively, which correspond to the [4]catenanes in their +4 charge state, and the isotopic patterns are also consistent with that of $C_{184}H_{252}N_{58}O_{75}^{4+}$ ([M+4H]$^{4+}$). In the ^{1}H NMR (500 MHz, D$_2$O, 298 K) spectrum of
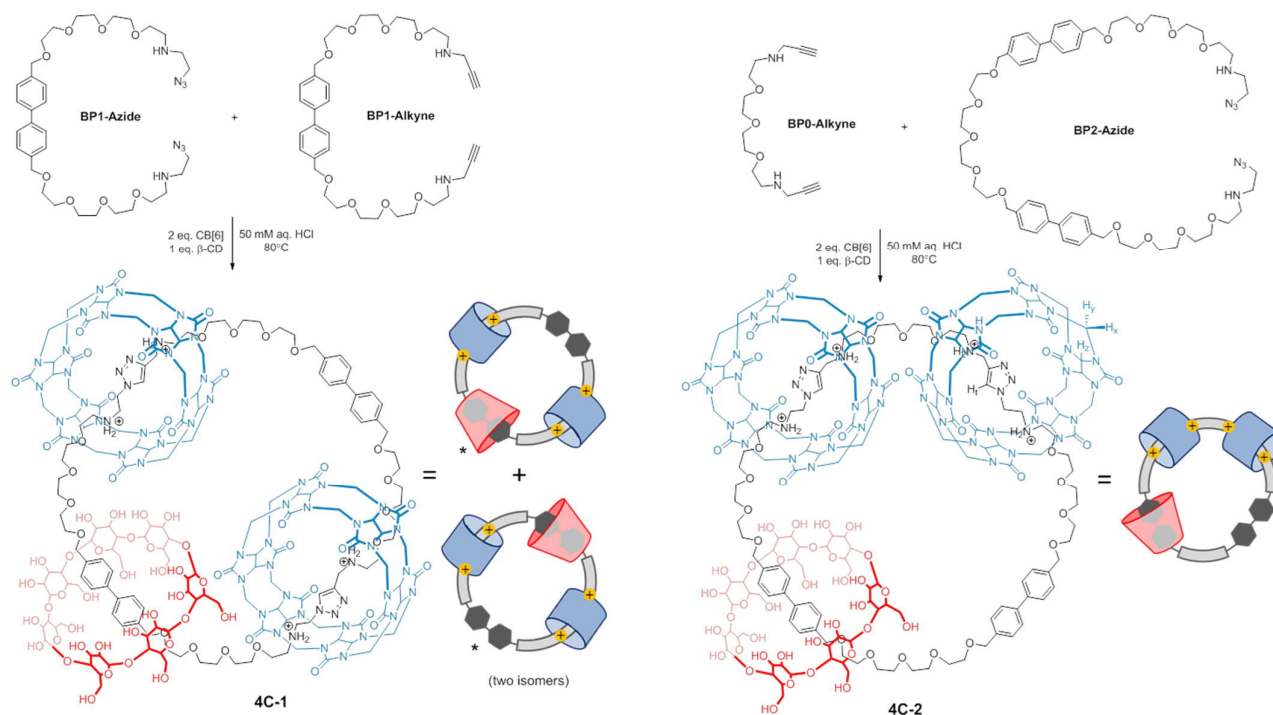

Figure 1. Synthesis of radial [4]catenanes 4C-1 and 4C-2. For 4C-1, due to the strong binding of CB[6] on the central macrocycle, the peripheral macrocycles are not exchangeable and the [4]catenane was obtained as two isomers. The biphenylene derived from the diazide building block is marked with *.
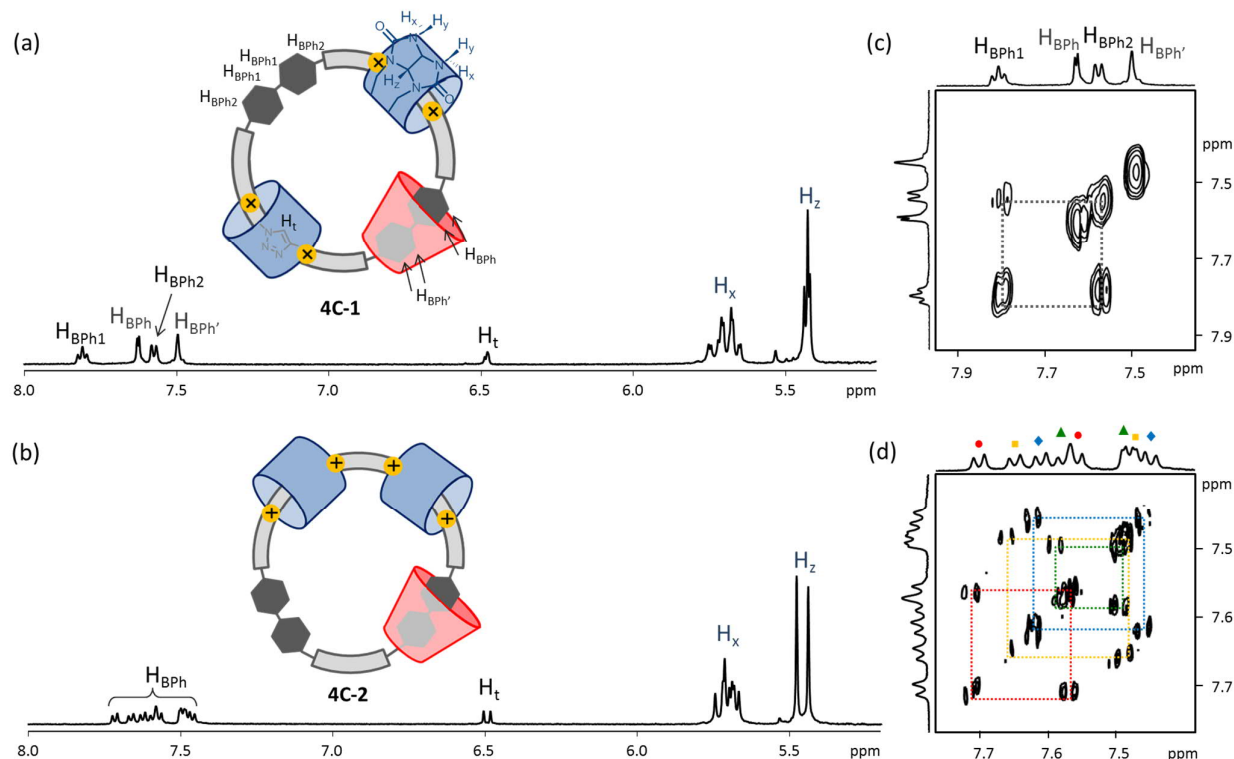
Figure 2. Partial ^{1}H NMR spectra (500 MHz, D$_2$O, 298 K) of (a) 4C-1 and (b) 4C-2 and the corresponding 2D COSY spectrum (c and d) of the aromatic region (7.3–7.9 ppm) showing the resonances of the biphenylene aromatic signals. The peaks labelled in the same colour in (d) represent protons in the same aromatic ring of the biphenylene and no further assignment is made because of the complexity in chemical shift change due to the shuttling β-CD.

the charged form of 4C-1 (Figure 2a), four signals were observed for the biphenylene protons, in which two of them are spin-coupled and the other two are non-coupled as shown in the corresponding 2D COSY spectrum (Figure 2c). The two coupled signals are assigned as the free biphenylene which has a centrosymmetric local symmetry, while the two non-coupled signals are assigned as the biphenylene that is bound inside the interlocked β-CD. The four protons of the biphenylene included inside the β-CD are all inequivalent due to the symmetry of the β-CD, and therefore four doublets are expected for the biphenylene protons if the β-CD is completely static with one co-conformation or the β-CD shuttling is fast enough that the different co-conformations are fast exchanging. The two broad signals observed at 298 K for the included biphenylene are therefore suggesting that the β-CD is shuttling around the biphenylene at a rate similar to the NMR timescale, such that the biphenylene signals from the exchanging co-conformations broaden and overlap to result in the observed peaks. Because of the strong CB[6] binding at the diammonium sites (log K ~ 5-6) in the protonated form of 4C-1,[11] the two biphenylenes are not exchangeable despite the β-CD is free to shuttle. The triazole signal (H$_t$) at 6.477 ppm in the relatively upfield region when compared with those free triazoles in non-interlocked compounds is consistent with it being included inside the CB[6] cavity. The NOE cross peaks

between H$_t$ and H$_y$ of the CB[6] observed in the 2D NOESY spectrum (Figure S6) also support the close proximity of the CB[6] and the triazole. Other NOE cross peaks involving the β-CD protons, however, cannot be unambiguously assigned due to the overlapping with the resonances from the tetra(ethylene glycol). A close inspection of H$_t$ revealed that there are more than one chemical environment for the triazoles, which could be explained by the symmetry of the interlocked β-CD that renders the two triazoles chemically different and/or the presence of two 4C-1 isomers in which the β-CD stations at the two chemically different biphenylenes. Indeed, at least three signals were observed for H$_z$ of the CB[6] at 5.44 ppm, 5.43 ppm and 5.42 ppm, confirming the presence of the 4C-1 isomers with the β-CD being interlocked at the two different biphenylenes. These two isomers are considered as co-conformational isomers in which the interlocked β-CD cannot exchange between the two biphenylenes due to the strongly bound CB[6], and their interconversion would be possible if all the three peripheral macrocycles are allowed to fully circumrotate along the central macrocycle. Due to the severe overlapping of the peaks from β-CD and ethylene glycol at 3–4 ppm, these resonances cannot be unambiguously assigned and therefore further analysis of the stereochemistry of 4C-1 is not trivial.

The ^{1}H NMR (500 MHz, D$_2$O, 298 K) spectrum of the protonated form of 4C-2 (Figure 2b) is quite different to that of 4C-1. First, four sets of coupled signals were observed for the biphenylene protons, showing that the local symmetry of both biphenylenes are affected by the interlocked β-CD. Shuttling of the β-CD between the two biphenylene stations at 298 K is slow relative to the NMR timescale, as the two sharp singlets observed for H$_z$ (5.48 ppm and 5.44 ppm) and H$_t$ (6.51 ppm and 6.48 ppm) were found to coalesce at a higher temperature (see below). There could also be two stereoisomers for 4C-2 with a different β-CD orientation if the β-CD shuttling is slow, and that the chemical environment of the CB[6] and triazole could be different for these two isomers. Although it seems that the different β-CD orientations can be reflected by the slightly different chemical shift of H$_z$ as in 4C-1, the peak for H$_z$ in 4C-2 are sharp and therefore stereochemical analysis of the β-CD orientation in 4C-2 is not conclusive.[12] Nevertheless, all the observed spectral features are consistent with a [4]catenane structure. The chemical shift of the triazole H$_t$ at 6.51 ppm and the NOE cross peaks between H$_t$ and H$_y$ of CB[6] are all consistent with the CB[6] being interlocked at the triazole station similar to 4C-1 (Figure S7).

Sequence-Dependent Dynamics of the Protonated [4]Catenanes. Dynamics of the two radial [4]catenanes was first studied in their tetra-protonated forms by variable temperature (VT) ^{1}H NMR in D$_2$O. Upon increasing the temperature from 298 K to 348 K, the biphenylene signal H$_{BPh'}$ of 4C-1 resolved into two clear doublets, suggesting a faster chemical exchange of the co-conformations due to a faster β-CD shuttling at an elevated temperature (Figure 3a). A minor change in the appearance of H$_{BPh}$ was also observed, and is consistent with the faster co-conformational exchange that results in the sharpening of the overlapped peaks although these signals are not yet resolved. For the biphenylene resonances that are not included in the β-CD, only a change in the shape of H$_{BPh1}$ was observed. Peaks for the H$_z$ and H$_x$ of CB[6] were also found to have only slight changes upon increasing the temperature, suggesting that the β-CD dynamics has a small influence on the overall structure and symmetry of the [4]catenane, and that the shuttling motions of the β-CD is only confined in the region between the two tightly bound CB[6]s (Figure S11).

On the other hand, the β-CD is able to shuttle between the two biphenylenes in 4C-2. When the temperature increased, merging of some of the biphenylene signals was first observed up to 318 K, and the peaks were found to split again when the temperature further increased to 348 K (Figure 4a). These observations show that the rate of β-CD shuttling was slow that only one biphenylene is included inside the β-CD at 298 K. Increasing the temperature would therefore first allow the β-CD to shuttle between the two biphenylenes, and a faster exchange at an even higher temperature would help resolve the chemically inequivalent biphenylene protons to be better resolved. Consistent with the faster β-CD shuttling, merging of the two triazole signals into one single peak was observed at

328 K, and the two singlets of H$_z$ of CB[6] were also found to merge to two closely spaced signals with a Δδ of only 0.005 ppm at 348 K. Resonances of H$_x$ of CB[6] also changed from being a multiplet to two doublets (at 5.73 ppm and 5.70 ppm) as the CB[6] chemical environment became more similar. These observations are suggesting that the overall chemical environment of the two CB[6]s and triazoles are becoming more similar when the β-CD is shuttling faster at a higher temperature, and that the asymmetry of the β-CD has only a small influence on the chemical environment of the CB[6]s and triazoles. By monitoring the triazole signals, a ΔG‡ of 17.2 kcal/mol was calculated for the β-CD shuttling between the two biphenylenes, which is comparable to those observed in other (β-CD)-containing molecular shuttles that also feature a tetra(ethylene glycol) linker between the two degenerated stations.[13] Overall, the two [4]catenane isomers display very different dynamic behaviour. The mechanically bonded CB[6]s could be considered as "roadblocks" with a high kinetic barrier that define the shuttling path of the β-CD "vehicle" in the hetero[4]catenanes. More importantly, positions of the CB[6] are encoded by the covalent structure of the central macrocyclic backbone, thus the dynamics of the interlocked components of the MIMs can be easily engineered by an appropriate building block design.
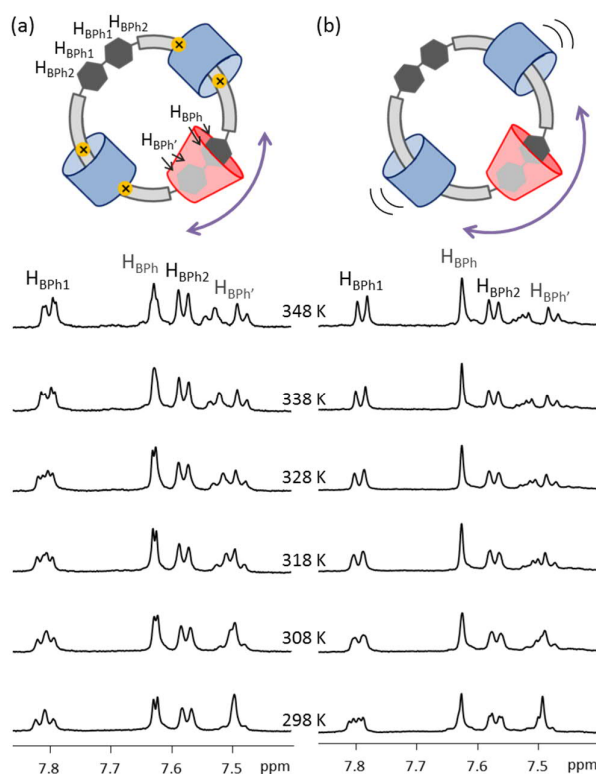

Figure 3. Partial ^{1}H NMR (500 MHz, D$_2$O) spectra showing the biphenylene aromatic resonances of (a) tetra-protonated and (b) neutral form of 4C-1 at increasing temperature. Note that H$_{BPh}$ and H$_{BPh'}$ are overlapped signals from the same aromatic ring in the biphenylene and the latter is resolved to two doublets at elevated temperatures.

Transducing the Effects of a Basic Trigger on the Interlocked CB[6] to the **β**-CD Dynamics. Since the strong CB[6] binding in the protonated form of the [4]catenanes has a large contribution from the ion-dipole interactions between the ammonium ions and the carbonyl groups on the CB[6], deprotonating the ammoniums will switch off these ionic interactions and leave hydrophobic binding as the major interactions between the interlocked CB[6]s and the central macrocycle.[14] The CB[6] and β-CD could therefore compete for the hydrophobic biphenylenes in the neutral form of the hetero[4]catenanes, and different structures and dynamics could be observed for the two isomers. In fact, a few (pseudo)rotaxanes that contain diammonium-bound CB[6] have been shown to display pH-triggered co-conformational switching with the CB[6] translocated to a hydrophobic region of the rotaxane as a result of disrupting the carbonyl-ammonium interactions.[3,5,15]

Deprotonation of the ammoniums in 4C-1 was followed by ^{1}H NMR. The ^{1}H NMR spectrum (500 MHz, D$_2$O, 298 K) showed that two broad alkyl signals were upfield shifted to ca. 3.34 ppm with 2 eq. of NaOH and then to 3.17 ppm and 3.00 ppm with 4 eq. of NaOH (Figure S13). No further change in the chemical shift of these two peaks was observed with an extra amount of the base, indicating that 4C-1 has been fully converted to its neutral form. Similar observations have been reported in related CB[6] rotaxanes and are ascribed to an enhanced shielding of nearby methylene groups as the CB[6] translocates to a different position upon the deprotonation.[3,5] However, only a slight change in the chemical shift of the triazole signal with a Δδ of 0.07 ppm and no significant spectral change for the biphenylene protons were observed, showing that the triazole is still included in the CB[6] cavity, and that the CB[6]s did not translocate to the biphenylene although the hydrophobic inclusion could be favourable. These observations therefore suggest that the CB[6] may only slightly adjust its position with no large-amplitude translocation on the central macrocycle. Yet, the overall chemical environment of the CB[6] in the neutral form of 4C-1 seems to be different than that of the tetra-protonated form, with at least four distinct signals
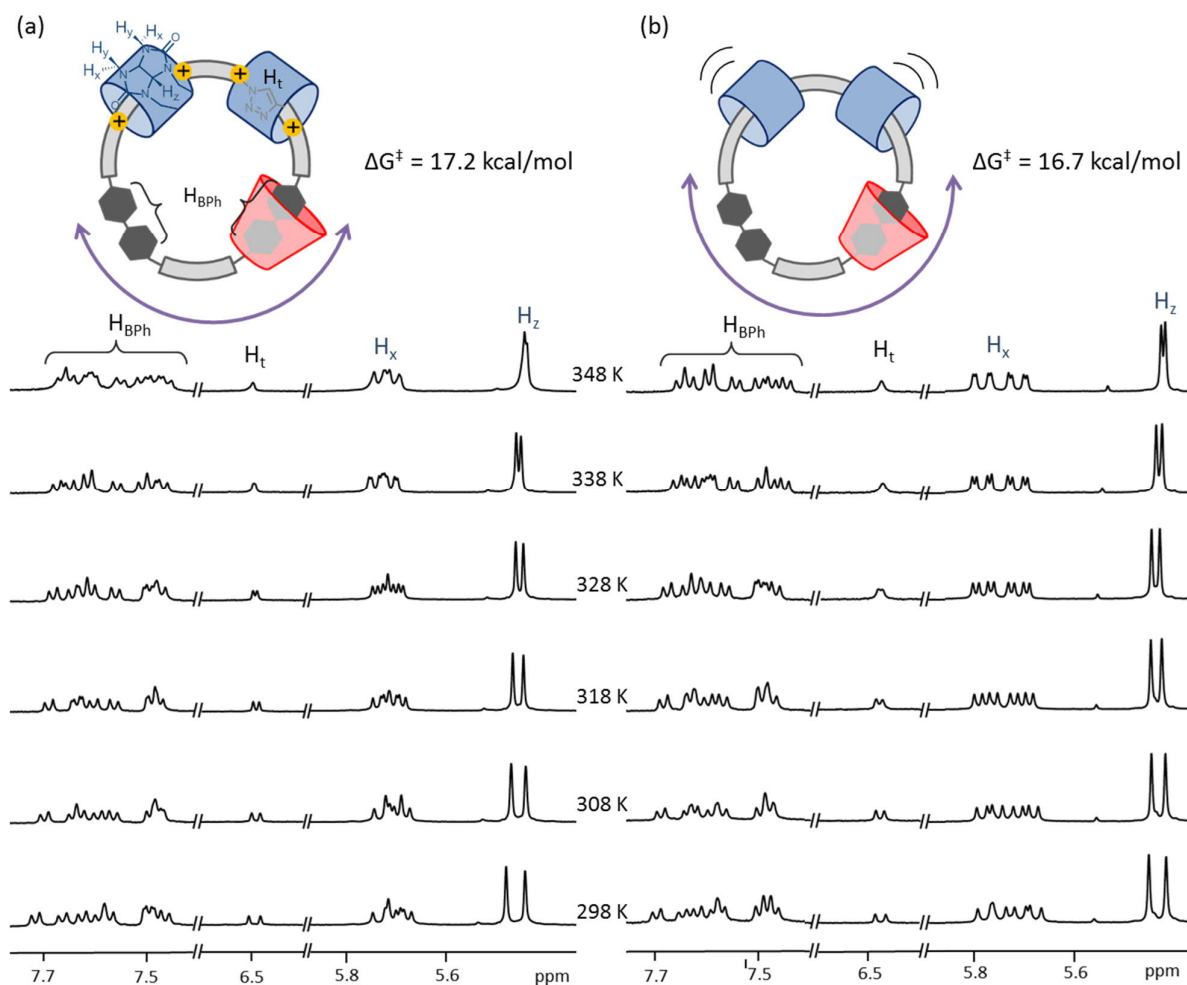

Figure 4. Partial ^{1}H NMR (500 MHz, D$_2$O) spectra showing the biphenylene, triazole and CB[6] resonances of (a) tetra-protonated and (b) neutral form of 4C-2 at increasing temperature. Energy barrier for the shuttling was calculated from the coalescence temperature of the triazole signal.

observed for H_z at ca. 5.39 ppm and a very different and more complicated multiplet pattern was observed for H_x, these spectral features are therefore suggestive of a different overall conformation for the neutral form when compared to that of the tetra-protonated form of 4C-1 (Figure S13).

The two CB[6]s are relative static with respective to the central macrocycle despite the weakening of the CB[6]-triazole interactions upon deprotonation. No noticeable change in the chemical shift of the triazole resonance was observed and the singlet remains at 6.40 ppm when the temperature was increased up to 348 K (Figure S13). Considering the larger hydrophobic surface of a biphenylene than that of a triazole, CB[6] interactions with the biphenylene are likely to be stronger than that with the triazole in the neutral form of 4C-1. The low mobility of the CB[6] could therefore be kinetic in origin,[12b] especially with the curved structure of [4]catenane, the relatively narrow opening (3.9 Å) of the CB[6] than that of β-CD (6.0 Å for the primary face and 6.5 Å for the secondary face),[16,17] and the presence of the hydrophilic tetra(ethylene glycol) linkers between the two aromatic stations. With the two CB[6] roadblocks remain on the central macrocycle, shuttling of the β-CD over the two biphenylenes is also prohibited with two sets of biphenylene signals observed up to 348 K. Similar to the tetra-protonated 4C-1, the faster β-CD shuttling at a higher temperature has led to the resolution of one of the uncoupled biphenylene signals, but the broad signal was found to be completely resolved at a lower temperature of 328 K (Figure 3b). The lower energy requires for the exchange of the biphenylene in the neutral form than that in the tetra-protonated form hence indicates the β-CD shuttling is facilitated by the deprotonation which regulates the position and tightness of the CB[6] roadblocks.

Similar modulation of the β-CD shuttling dynamics upon deprotonation was also observed in 4C-2. Addition of 4 eq. of NaOH resulted in an upfield shift of two alkyl signals to 3.17 ppm and 3.05 ppm (Figure S14), and no significant spectral changes were observed for other resonances upon deprotonation, except for the slightly better resolved multiplet of H_x and a slight upfield shift of the triazoles by ca. 0.03 ppm. These features are consistent with a slight adjustment of the CB[6] positions in the neutral form of 4C-2 as in the case of 4C-1. The triazole signals remain at ca. 6.42 ppm when the temperature was increased to 348 K, indicating that the two CB[6]s are still bound around the triazoles on the central macrocycle (Figure 4b). The fast shuttling of β-CD resulted in an averaging of the triazole chemical environment, and coalescence of the triazole signals was observed at 318 K, corresponding to a ΔG‡ of 16.7 kcal/mol that is lower than that of the tetra-protonated form, and again is suggestive of a facilitated β-CD shuttling upon deprotonation. Other spectral changes due to a faster β-CD shuttling at an elevated temperature are similar to those observed in the tetra-protonated form of 4C-2.

Conclusions

In summary, dynamics of a pair of [4]catenane isomers that contain both mechanically bonded CB[6] and β-CD in both the protonated and neutral forms is described. The tightly bound CB[6]s were found to define the path in which the β-CD can shuttle on the central macrocycle, and therefore by strategically positioning the biphenylene and diammonium stations on the central macrocycle using appropriate building blocks, [4]catenane isomers of different dynamic properties are realized. In addition, it is shown that dynamics of the pH-insensitive β-CD can be regulated through controlling the ion-dipole interactions between the CB[6] and the central macrocycle. This work thus demonstrates the potentials and advantages of having different types of interlocked macrocycles in which their different properties can be deployed with a different role in a coordinated fashion (e.g. CB[6] as the "roadblock" for regulation and β-CD as the "vehicle" for shuttling), and that the interplay and communication between the different macrocycles could allow a higher level of control over the motions of the different interlocked components. These findings will therefore be implicated in the design and strategy of exploiting multi-component, hetero[n]catenanes as structural elements of molecular machines for more complex and complicated works.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

References

1   (a) J. P. Sauvage, Transition metal-containing rotaxanes and catenanes in motion: toward molecular machines and motors. Acc. Chem. Res., 1998, 31, 611-619; (b) J. D. Crowley, S. M. Goldup, A. L. Lee, D. A. Leigh and R. T. McBurney, Active metal template synthesis of rotaxanes, catenanes and molecular shuttles. Chem. Soc. Rev., 2009, 38, 1530-1541; (c) J. P. Collin, C. Dietrich-Buchecker, P. Gaviña, M. C. Jimenez-Molero and J. P. Sauvage, Shuttles and muscles: linear molecular machines based on transition metals. Acc. Chem. Res., 2001, 34, 477-487; (d) E. R. Kay, D. A. Leigh and F. Zerbetto, Synthetic molecular motors and mechanical machines. Angew. Chem. Int. Ed., 2007, 46, 72-191; (e) S. Kassem, T. van Leeuwen, A. S. Lubbe, M. R. Wilson, B. L. Feringa and D. A. Leigh, Artificial molecular motors. Chem. Soc. Rev., 2017, 46, 2592-2621; (f) P. R. Ashton, R. A. Bissell,

N. Spencer, J. F. Stoddart and M. S. Tolley, Towards controllable molecular shuttles. Synlett, 1992, 923-926; (g) J. D. Badjić, V. Balzani, A. Credi, S. Silvi and J. F. Stoddart, A molecular elevator. Science, 2004, 303, 1845-1849.

2 For examples, see: (a) C. J. Bruns and J. F. Stoddart, Molecular Switches and Machines with Mechanical Bonds in The Nature of Mechanical Bond: from Molecules to Machines, John Wiley & Sons, New Jersey, 2017, ch. 6, pp. 555-707; (b) R. A. Bissell, E. Córdova, A. E. Kaifer and J. F. Stoddart, A chemically and electrochemically switchable molecular shuttle. Nature, 1994, 369, 133-137; (c) A. Livoreil, C. O. Dietrich-Buchecker and J. P. Sauvage, Electrochemically triggered swinging of a [2]-catenate. J. Am. Chem. Soc., 1994, 116, 9399-9400; (d) N. Armaroli, V. Balzani, J. P. Collin, P. Gaviña, J. P. Sauvage and B. Ventura, Rotaxanes Incorporating Two Different Coordinating Units in Their Thread: Synthesis and Electrochemically and Photochemically Induced Molecular Motions. J. Am. Chem. Soc., 1999, 121, 4397-4408; (e) A. Andrievsky, F. Anuis, J. L. Sessler, F. Vögtle, D. Gudat and M. Moini, Bipyrrole-Based [2]Catenane: A New Type of Anion Receptor. J. Am. Chem. Soc., 1998, 120, 9712-9713; (f) A. Altieri, F. G. Gatti, E. R. Kay, D. A. Leigh, D. Martel, F. Paolucci, A. M. Z. Slawin and J. K. Y. Wong, Electrochemically Switchable Hydrogen-Bonded Molecular Shuttles. J. Am. Chem. Soc., 2003, 125, 8644-8654; (g) S. Saha, A. H. Flood, J. F. Stoddart, S. Impellizzeri, S. Silvi, M. Venturi and A. Credi, A Redox-Driven Multicomponent Molecular Shuttle. J. Am. Chem. Soc., 2007, 129, 12159-12171; (h) J. M. Spruell, W. F. Paxton, J. C. Olsen, D. Benítez, E. Tkatchouk, C. L. Stern, A. Trabolsi, D. C. Friedman, W. A. Goddard III and J. F. Stoddart, A Push-Button Molecular Switch. J. Am. Chem. Soc., 2009, 131, 11571-11580; (i) H. Y. Au-Yeung, G. D. Pantoş and J. K. M. Sanders, A Water Soluble Donor–Acceptor [2]Catenane that Can Switch between a Coplanar and a Gemini-Sign Conformation. Angew. Chem. Int. Ed., 2010, 49, 5331-5334; (j) A. Caballero, L. Swan, F. Zapata and P. D. Beer, Iodide-induced shuttling of a halogen- and hydrogen-bonding two-station rotaxane. Angew. Chem. Int. Ed. 2014, 53, 11854-11858.

3 (a) W. L. Mock and J. Pierpont, A cucurbituril-based molecular switch. J. Chem. Soc., Chem. Commun., 1990, 1509-1511; (b) D. Tuncel, H. B. Tiftik and B. Salih, pH-Responsive polypseudorotaxane synthesized through cucurbit[6]uril catalyzed 1,3-dipolar cycloaddition. J. Mater. Chem., 2006, 16, 3291-3296.

4 For example, see (a) C. J. Bruns and J. F. Stoddart, The Stereochemistry of the Mechanical Bond in The Nature of Mechanical Bond: from Molecules to Machines, John Wiley & Sons, New Jersey, 2017, ch. 5, pp. 471-554; (b) A. Livoreil, J. P. Sauvage, N. Armaroli, V. Balzani, L. Flamigni and B. Ventura, Electrochemically and Photochemically Driven Ring Motions in a Disymmetrical Copper [2]-Catenate. J. Am. Chem. Soc., 1997, 119, 12114-12124; (c) F. Durola, J. Lux and J. P. Sauvage, A Fast-Moving Copper-Based Molecular Shuttle: Synthesis and Dynamic Properties. Chem. Eur. J., 2009, 15, 4124-4134; (d) S. S. Andersen, A. I. Share, B. L. C. Poulsen, M. Kørner, T. Duedal, C. R. Benson, S. W. Hansen, J. O. Jeppesen and A. H. Flood, Mechanistic Evaluation of Motion in Redox-Driven Rotaxanes Reveals Longer Linkers Hasten Forward Escapes and Hinder Backward Translations. J. Am. Chem. Soc., 2014, 136, 6373-6384.

5 (a) D. Tuncel and M. Katterle, pH-Triggered Dethreading–Rethreading and Switching of Cucurbit[6]uril on Bistable [3]Pseudorotaxanes and [3]Rotaxanes. Chem. Eur. J., 2008, 14, 4110-4116; (b) D. Tuncel, Ö. Özsar, H. B. Tiftik and B. Salih, Molecular switch based on a cucurbit[6]uril containing bistable [3]rotaxane. Chem. Commun., 2007, 1369-1371.

6 (a) G. Gil-Ramírez, D. A. Leigh and A. J. Stephens, Catenanes: Fifty Years of Molecular Links. Angew. Chem. Int. Ed., 2015, 54, 6110-6150; (b) F. Bitsch, C. O. Dietrich-Buchecker, A. K. Khemiss, J. P. Sauvage and A. Van Dorsselaer, Multiring interlocked systems: structure elucidation by electrospray mass spectrometry. J. Am. Chem. Soc., 1991, 113, 4023-4025; (c) D. B. Amabilino, P. R. Ashton, A. S. Reder, N. Spencer and J. F. Stoddart, Olympiadane. Angew. Chem. Int. Ed. Engl., 1994, 33, 1286-1290; (d) D. B. Amabilino, P. R. Ashton, S. E. Boyd, J. Y. Lee, S. Menzer, J. F. Stoddart and D. J. Williams, The Five-Stage Self-Assembly of a Branched Heptacatenane. Angew. Chem. Int. Ed., 1997, 36, 2070-2072; (e) H. Iwamoto, S. Tafuku, Y. Sato, W. Takizawa, W. Katagiri, E. Tayama, E. Hasegawa, Y. Fukazawa and T. Haino, Synthesis of linear [5]catenanes via olefin metathesis dimerization of pseudorotaxanes composed of a [2]catenane and a secondary ammonium salt. Chem. Commun., 2016, 52, 319-322; (f) S. Dasgupta and J. Wu, Template-directed synthesis of kinetically and thermodynamically stable molecular necklace using ring closing metathesis. Org. Biomol. Chem., 2011, 9, 3504-3515; (g) M. J. Langton, J. D. Matichak, A. L. Thompson and H. L. Anderson, Template-directed synthesis of π-conjugated porphyrin [2]rotaxanes and a [4]catenane based on a six-porphyrin nanoring. Chem. Sci., 2011, 2, 1897-1901; (h) S. P. Black, A. R. Stefankiewicz, M. M. Smulders, D. Sattler, C. A. Schalley, J. R. Nitschke and J. K. Sanders, Generation of a Dynamic System of Three-Dimensional Tetrahedral Polycatenanes. Angew. Chem. Int. Ed., 2013, 52, 5749-5752; (i) S. G. Roh, K. M. Park, G. J. Park, S. Sakamoto, K. Yamaguchi and K. Kim, Synthesis of a Five-Membered Molecular Necklace: A 2+2 Approach, Angew. Chem. Int. Ed., 1999, 38, 637-641; (j) S. Li, J. Huang, F. Zhou, T. R. Cook, X. Yan, Y. Ye, B. Zhu, B. Zheng and P. J. Stang, Self-Assembly of Triangular and Hexagonal Molecular Necklaces. J. Am. Chem. Soc., 2014, 136, 5908-5911; (k) T. Sawada, M. Yamagami, K. Ohara, K. Yamaguchi and M. Fujita, Peptide [4]Catenane by Folding and Assembly. Angew. Chem. Int. Ed., 2016, 55, 4519-4522; (l) J. Wu, K. C.-F. Leung and J. F. Stoddart, Efficient production of [n]rotaxanes by using template-directed clipping reactions. Proc. Natl. Acad. Sci. USA, 2007, 104, 17266-17271; (m) S.-J. Rao, Q. Zhang, J. Mei, X.-H. Ye, C. Gao, Q.-C. Wang, D.-H. Qu and H. Tian, One-pot synthesis of hetero[6]rotaxane bearing three different kinds of macrocycle through a self-sorting process. Chem. Sci., 2017, 8, 6777-6783; (n) X.-Q. Wang, W.-J. Li, W. Wang and H.-B. Yang, Heterorotaxanes. Chem. Commun., 2018, 54, 13303-13318; (o) Q. Wu, P. M. Rauscher, X. Lang, R. J. Wojtecki, J. J. de Pablo, M. J. A. Hore and S. J. Rowan, Poly[n]catenanes: Synthesis of molecular interlocked chains. Science, 2017, 358, 1434-1439.

7 (a) H. Y. Au-Yeung, C.-C. Yee, A. W. H. Ng and K. Hu, Strategies to assemble catenanes with multiple interlocked macrocycles. Inorg. Chem., 2018, 57, 3475-3485; (b) N. H. Pérez and J. E. Lewis, Synthetic strategies towards mechanically interlocked oligomers and polymers. Org. Biomol. Chem., 2020, 18, 6757-6780.

8 (a) D. B. Amabilino, P. R. Ashton, V. Balzani, S. E. Boyd, A. Credi, J. Y. Lee, S. Menzer, J. F. Stoddart, M. Venturi and D. J. Williams, Oligocatenanes Made to Order. J. Am. Chem. Soc., 1998, 120, 4295-4307; (b) K. Wang, C.-C. Yee and H. Y. Au-Yeung, Facile syntheses of [3]-, [4]- and [6]catenanes templated by orthogonal supramolecular interactions. Chem. Sci. 2016, 7, 2787-2792; (c) A. W. H. Ng, C.-C. Yee and H. Y. Au-Yeung, Radial Hetero[5]catenanes: Peripheral Isomer Sequences of the Interlocked Macrocycles. Angew. Chem. Int. Ed., 2019, 58, 17375-17382; (d) C.-C. Yee, A. W. H. Ng and H. Y. Au-Yeung, Control over the macrocyclisation pathway and product topology in a copper-templated

catenane synthesis. Chem. Commun., 2019, 55, 6169-6172; (e) H. Y. Au-Yeung and A. W. H. Ng, Mechanical Interlocking of Macrocycles in Different Sequences. Synlett, 2020, 31, 309-314; (f) N. D. Colley, M. A. Nosiglia, L. Li, F. Amir, C. Chang, A. F. Greene, J. M. Fisher, R. Li, X. Li and J. C. Barnes, One-Pot Synthesis of a Linear [4]Catenate Using Orthogonal Metal Templation and Ring-Closing Metathesis. Inorg. Chem., 2020, 59, 10450-10460.

9   A. W. H. Ng, C.-C. Yee, K. Wang and H. Y. Au-Yeung, Efficient catenane synthesis by cucurbit[6]uril-mediated azide–alkyne cycloaddition. Beilstein J. Org. Chem., 2018, 14, 1846-1853.

10   (a) D. Armspach, P. R. Ashton, R. Ballardini, V. Balzani, A. Godi, C. P. Moore, L. Prodi, N. Spencer, J. F. Stoddart, M. S. Tolley and T. J. Wear, Catenated Cyclodextrins. Chem. Eur. J., 1995, 1, 33-55; (b) J. Li, P. Nowak, H. Fanlo-Virgós and S. Otto, Catenanes from catenanes: quantitative assessment of cooperativity in dynamic combinatorial catenation. Chem. Sci., 2014, 5, 4968-4974.

11   (a) J. Lagona, P. Mukhopadhyay, S. Chakrabarti and L. Isaacs, The cucurbit[n]uril family. Angew. Chem. Int. Ed., 2005, 44, 4844-4870; (b) W. L. Mock and N. Y. Shih, Dynamics of molecular recognition involving cucurbituril. J. Am. Chem. Soc., 1989, 111, 2697-2699; (c) K. Kim, Mechanically interlocked molecules incorporating cucurbituril and their supramolecular assemblies. Chem. Soc. Rev., 2002, 31, 96-107.

12   (a) M. V. Rekharsky, H. Yamamura, M. Kawai, I. Osaka, R. Arakawa, A. Sato, Y. H. Ko, N. Selvapalam, K. Kim and Y. Inoue, Sequential Formation of a Ternary Complex among Dihexylammonium, Cucurbit[6]uril, and Cyclodextrin with Positive Cooperativity. Org. Lett., 2006, 8, 815-818; (b) C. Yang, Y. H. Ko, N. Selvapalam, Y. Origane, T. Mori, T. Wada, K. Kim and Y. Inoue, Dynamic Switching between Single- and Double-Axial Rotaxanes Manipulated by Charge and Bulkiness of Axle Termini. Org. Lett., 2007, 9, 4789-4792; (c) C. Ke, R. A. Smaldone, T. Kikuchi, H. Li, A. P. Davis and J. F. Stoddart, Quantitative Emergence of Hetero[4]rotaxanes by Template-Directed Click Chemistry. Angew. Chem. Int. Ed., 2013, 52, 381-387; (d) X. Hou, C. Ke and J. F. Stoddart, Cooperative capture synthesis: yet another playground for copper-free click chemistry. Chem. Soc. Rev., 2016, 45, 3766-3780; (e) J. Y. H. Man and H. Y. Au-Yeung, Synthesis of a [6]rotaxane with singly threaded γ-cyclodextrins as a single stereoisomer. Beilstein J. Org. Chem., 2019, 15, 1829-1837; (f) X. Yu, W. Liang, Q. Huang, W. Wu, J. J. Chruma and C. Yang, Room-temperature phosphorescent γ-cyclodextrin-cucurbit[6]uril-cowheeled [4]rotaxanes for specific sensing of tryptophan. Chem. Commun., 2019, 55, 3156-3159.

13   P. R. Ashton, C. L. Brown, E. J. Chrystal, K. P. Parry, M. Pietraszkiewicz, N. Spencer and J. F. Stoddart, Molecular Trains: The Self-Assembly and Dynamic Properties of Two New Catenanes. Angew. Chem. Int. Ed., 1991, 30, 1042-1045.

14   (a) W. L. Mock and N. Y. Shih, Host-guest binding capacity of cucurbituril. J. Org. Chem., 1983, 48, 3618-3619; (b) W. L. Mock and N. Y. Shih, Structure and selectivity in host-guest complexes of cucurbituril. J. Org. Chem., 1986, 51, 4440-4446.

15   D. Tuncel, N. Cindir and Ü. Koldemir, [5]Rotaxane and [5] Pseudorotaxane Based on Cucurbit[6]uril and Anchored to a Meso-tetraphenyl Porphyrin. J. Incl. Phenom. Macrocycl. Chem., 2006, 55, 373-380.

16   (a) K. Kim, N. Selvapalam and D. H. Oh, Cucurbiturils–a new family of host molecules. J. Incl. Phenom. Macrocycl. Chem., 2004, 50, 31-36; (b) J. W. Lee, S. Samal, N. Selvapalam, H. J. Kim and K. Kim, Cucurbituril homologues and derivatives: new opportunities in supramolecular chemistry. Acc. Chem. Res., 2003, 36, 621-630.

17   M. V. Rekharsky and Y. Inoue, Complexation thermodynamics of cyclodextrins. Chem. Rev., 1999, 98, 1875-1918.