Molecular clips and tweezers with corannulene pincers

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ABSTRACT

Application of the synthetic methodology developed in our laboratory yields molecular clips and tweezers with corannulene pincers and cyclooctadiene or cyclooctatetraene tethers. These highly nonplanar systems possess a potential for binding guest molecules of various sizes. One of the clips, bis(benzocorannulene)[a,e]cyclooctadiene, exists in a 'open' chair conformation encapsulating solvating nitrobenzene in the solid state, while it is expected to prefer an internally π–π stacked twist-boat conformation in the gas phase.

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Molecular recognition of guest molecules by molecular receptors is of premium importance in self-assembly and self-organization of matter. The design and synthesis of molecular assemblies capable of such recognition is therefore a major objective of supramolecular chemistry.[1] Molecular recognition processes strongly depend on weak, noncovalent interactions, among which the π–π stacking of conjugated surfaces of arenes play an important role. A novel type of stacking of curved conjugated carbon networks has been introduced by the discovery of fullerenes and related carbon-rich materials. In this context, buckybowls, bowl-shaped polycyclic aromatic hydrocarbons with accessible concave surfaces[2] appear to be good candidates for the formation of π–π stacked supramolecular assemblies with fullerenes. Although this potential has long been recognized,[3] we only recently provided the first experimental evidence for the formation of a stable inclusion complex of C_{60} with the 'buckycatcher' (1), a molecular clip with two corannulene (2) pincers and a tetrabenzocyclooctatetraene tether.[4]

1   **2** $C_{60}@1$
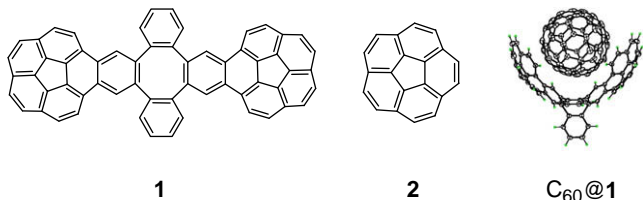
In the present Letter, we report the synthesis of a series of molecular clips[5] combining corannulene pincers and cyclooctadiene (COD) or cyclooctatetraene (COT) tethers, most notably bis(benzocorannuleno)[a,e]cyclooctadiene (3). These highly non-

planar systems exhibit clefts of various sizes and shapes with potential to bind guest molecules with geometric selectivity. In addition, conformational flexibility of their tethers allows for an adoption of conformations unavailable for the more rigid tetrabenzoCOT core of the buckycatcher 1.

3   **4**   **5**
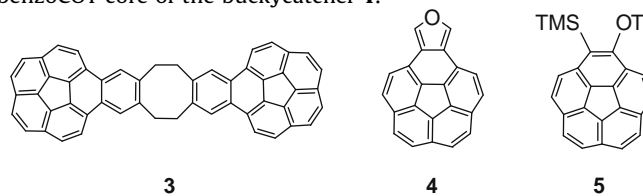
Our syntheses utilize two synthons recently introduced by us, that is, isocorannulenofuran (diene) (4) and 2-trimethylsilylcorannulenyl trifluoromethanesulfonate (5, a precursor for 1,2-didehydrocorannulene).[6] Both 4 and 5 allow for an introduction of corannulene subunits into larger molecular architectures by Diels–Alder reactions with appropriate dienophiles or dienes.

Scheme 1 presents the synthesis of molecular clip 6 with a COT tether and corannulene and benzene pincers. The synthesis starts with a Diels–Alder reaction of 4 with benzocyclobutadiene generated in situ by a standard procedure[7] which leads to the formation of two isomeric adducts, endo-7 and exo-7 (ca. 9:1) in a modest 55% yield based on consumed starting material. The isomers are separated by chromatography on silica gel and are characterized by NMR spectroscopy. In addition, endo-7 produced X-ray quality crystals and its crystal structure is shown in Figure 1. This highly nonplanar system exhibits the benzene ring of the benzocyclobutane moiety located over the convex side of the corannulene unit. The location results in a significant shielding of the four hydrogen atoms of the AA′BB′ system of the benzene ring appearing in the ¹H NMR spectrum as broad multiplets centered at 5.4 and 5.9 ppm, upfield from the usual chemical shift of aromatic protons. In con-

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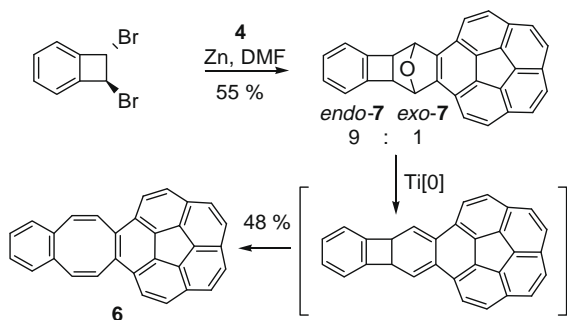
Scheme 1. The synthesis of 6.
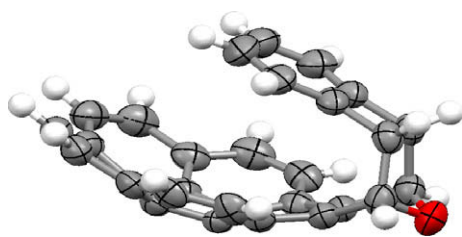
Figure 1. Crystal structure of endo-7.

trast, the analogous protons in exo-7 appear as sharp AA′BB′ multiplets centered at 7.2 and 7.3 ppm.

Both exo-7 and endo-7 can be deoxygenated with low-valent titanium to form $C_{30}H_{16}$ hydrocarbon 6 in a modest 48% yield, presumably through the dihydrobiphenylene intermediate (Scheme 1). The target 6 has not been characterized crystallographically but it is expected to form a clip with corannulene and benzene pincers located on the tub-shaped COT tether.

Scheme 2 summarizes our synthetic approaches to molecular clips with more flexible 1,5-COD subunits. Thus, isofuran 4 reacts at rt with an excess of the reactive ynes generated by dehydrobromination of a mixture of dibromocyclooctadienes[8] producing a mixture of two major adducts, 8 and 9, with isolated yields of 10% and 78%, respectively. The adducts were separated by chromatography and were characterized by the usual spectroscopic methods. In addition, 8 was characterized by X-ray crystal structure determination which shows an interesting arrangement of the cyclooctadiene ring with six carbon atoms being almost coplanar and lying in a plane approximately perpendicular to the average plane of the corannulene subunit (Fig. 2).

Both 8 and 9 are deoxygenated to the hydrocarbons 10 and 11 in high yields by reflux in benzene with $Fe_2(CO)_9$.

Treatment of the bromide 11 with tBuOK leads to the reactive dienophile 12 which in turn adds to isofuran 4 to produce 13. Deoxygenation of this endoxide with diiron nonacarbonyl gives bis(benzocorannulene)cyclooctadiene (3), a $C_{52}H_{28}$ molecular clip with a flexible COD tether and two benzocorannulene pincers.

An alternative synthetic route to 3 utilizes the 1,2-didehydrocorannulene precursor 5 and difurane 14, which can be synthesized in one step from commercially available dipropargyl ether.[9] A double Diels–Alder addition of corannulyne to 14 yields a mixture of two isomeric products, presumably syn- and anti-15. The separation of the products was not attempted but the reaction mixture was reduced with low-valent titanium to produce 3 as a white solid in a moderate yield of ca. 60% (Scheme 2).

In contrast to other corannulene-based molecular clips synthesized in our laboratory, 3 has a very limited solubility in organic solvents. Its solubility is significantly lower than that of the larger and less flexible buckycatcher 1. To address this problem, we
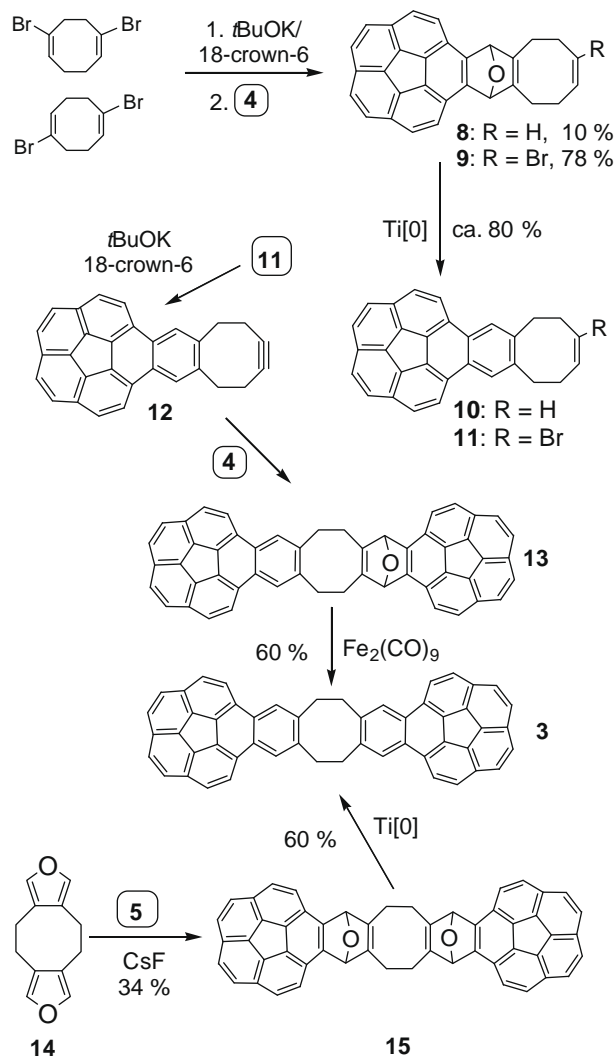
Scheme 2. Synthesis of 3 by two alternative routes.
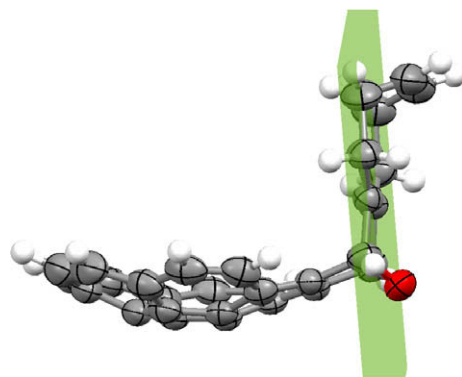
Figure 2. Crystal structure of the adduct 8. A mean plane defined by six carbon atoms of the COD ring is shown.

studied the conformational behavior of 3 by both Molecular Mechanics (MM) and Density Functional (DFT) calculations. The conformational space of a simpler analog of 3, 5,6,11,12-tetrahydrodibenzo[a,e]cyclooctene (16), has been thoroughly studied by both theory and experiment.[10] Based on these studies, we considered three possible conformations of the central cyclooctadiene ring in 3, that is, twist boat (TB), chair (C), and twist (T). Figure 3

presents the optimized geometries and relative energies of the conformers calculated at the highest level of theory applied by us, the B97-D method with the TZVP basis set.[11] This level of theory has been demonstrated to give satisfactory results for systems exhibiting weak dispersion interactions, including π–π stacking. For comparison, the relative energies of the three conformers of the dibenzo analog **16** calculated at the same level of theory are also presented in Figure 3.

16
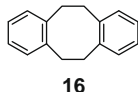
Previous low-temperature NMR studies reveal the existence of two conformers of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclooctene (**16-TB** and **16-C**) in comparable amounts.[10] Accordingly, theoretical studies predict the energies of the two conformers to be quite similar, with the twist **16-T** conformer having significantly higher energy which precludes its detection by NMR experiment.[10] Our computational results are in line with the previous studies, predicting the major conformer observed experimentally (**16-TB**) to be the most stable with **16-C** being only slightly higher in energy by ca. 0.2 kcal/mol. The **16-T** is found to be significantly higher in energy than the two other conformers. In stark contrast to **16**, the **TB** conformation of **3** is predicted to be very strongly favored over the remaining conformations by ca. 8 kcal/mol. We are convinced that this is not an artifact of the theoretical model used since the strong preference for **3-TB** is also predicted by all the MM models we used for the preliminary studies. Apparently, the presence of the large benzocorannulene pincers located on a flexible cyclooctadiene tether introduces the possibility of a strongly stabilizing intramolecular π–π stacking interaction in the **TB** conformation. Recent theoretical studies of the model corannulene dimer give an estimation of the binding in the concave–convex stacked assembly at ca. 18 kcal/mol which is large enough to compensate for the energy penalty due to distortion of the tether.[12] The two corannulene pincers in **3-TB** are clearly in an arrangement maximizing van der Waals attraction with the shortest nonbonding carbon–carbon distances between 3.44 and 3.94 Å.

The strong gas-phase preference for the internally π–π stacked **TB** conformation may explain the unusually low solubility of **3** in
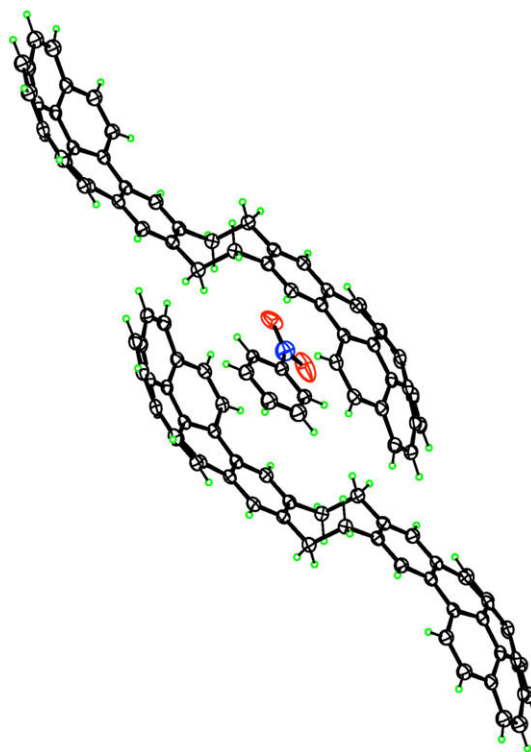
Figure 4. Crystal structure of **3***PhNO$_2$ solvate. One of four orientations of the disordered solvent molecule is shown. The second molecule of **3** is added to demonstrate the encapsulation of nitrobenzene.

common organic solvents since the solvent-accessible surface of this conformation is dramatically reduced in comparison to the usual 'open' conformations of other buckybowls. On the other hand, an interesting possibility arises that the 'open' conformations like **3-C** could become preferred in condensed phases if the solvating power of a solvent can override the gas-phase preference for **3-TB**. Due to the low solubility of **3** we were not able to address the problem by low-temperature NMR studies. Instead, we focused our attention on X-ray crystallography and, after several unsuccessful attempts, we obtained good quality crystals of a 1:1 solvate of **3** with nitrobenzene. X-ray structure determination shows that the chair conformation **3-C** prevails in the solid state of the solvate (Fig. 4). The disordered nitrobenzene molecule is encapsulated by two neighboring molecules of **3** and is in van der Waals contacts with the concave sides of the benzocorannulene pincers.

Despite the dramatic differences in the calculated relative stabilities of the conformers of **3** and **16** (Fig. 3) the solid-state conformations of the central COD rings are quite similar since **16** also prefers the chair conformation in the crystal.[13] However, **3** incorporates nitrobenzene in the solid and we believe that the solvation effects constitute a decisive factor for the preference of the chair conformation in the **3***PhNO$_2$ solvate. We are currently trying to grow X-ray quality crystals of 3 from other solvents expecting to observe the internally π–π stacked twist-boat conformer 3-TB in absence of the strongly solvating guests.

In summary, a series of highly nonplanar molecular clips with corannulene and COT or COD subunits was synthesized by application of the Diels–Alder methodology. These systems exhibit clefts of various sizes and shapes and have the potential to bind molecules based on sizes. The largest synthesized clip, bis(benzocorannulene)[*a,e*] cyclooctadiene **3**, a more flexible analog of the buckycatcher **1**, encapsulates solvating molecules of nitrobenzene in the solid and prefers the chair conformation in the solvate, even

	TB	**C**	**T**
3	0.00	8.16	11.43
16	0.00	0.24	3.47

Figure 3. B97-D/TZVP calculated minimum energy conformations of **3** and the relative energies [kcal/mol] of the twist-boat (**TB**), chair (**C**), and twist (**T**) conformers of **3** and **16**.

though it is predicted to exist in the internally π–π stacked twist-boat conformation in the gas phase.

Acknowledgments

Supplementary data

Experimental procedures, characterization of the new compounds and the details of the computational studies are provided. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 746256–746258. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.09.177.

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