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Bis-corannulene Receptors for Fullerenes Based on Klärner's Tethers: Reaching the Affinity Limits

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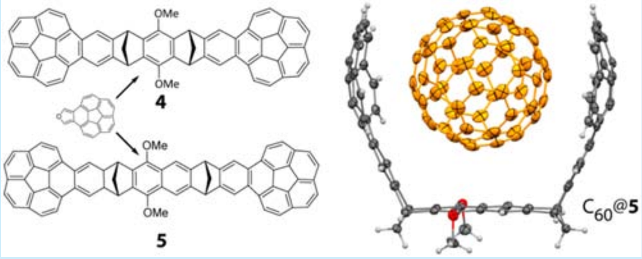
Supporting Information

ABSTRACT: Bis-corannulene receptors **4** and **5** with Klärner's tethers prepared by the Diels−Alder cycloaddition form inclusion complexes with C_{60} and C_{70}, as evidenced by ^{1}H NMR titration. While **4** exhibits affinity toward fullerenes comparable to the previously reported corannulene-based receptors, **5** exceeds the performance of the former systems by ca. 2 orders of magnitude and, in addition, shows an enhanced preference for C_{70} over C_{60}. The X-ray crystal structure of C_{60}@**5** and DFT calculations indicate that the tether in **5** not only preorganizes the pincers into a proper topology of the host but also contributes to the dispersion-based binding with the fullerene guests.



Discovery of the novel allotropic forms of elemental carbon (e.g., fullerenes and carbon nanotubes) introduced a novel motif in supramolecular chemistry based on $\pi-\pi$ stacking of curved networks of sp^2-hybridized carbon atoms. Buckybowls, the curved-surfaced polycyclic aromatic hydrocarbons structurally related to fullerenes, were quickly recognized as potential hosts for supramolecular assemblies with fullerenes due to the complementarity of the concave surfaces of the former with the convex faces of the carbon cages, provided that the dispersion-based intermolecular binding energies are strong enough.[1] Computational studies of the model dimer of the smallest buckybowl corannulene (**1**) indicated that the gas-phase binding energies of the $\pi-\pi$ stacked bowl-shaped conjugated carbon networks are substantial and quite comparable to the binding of the planar aromatic systems of the same size.[2] On the other hand, the lack of evidence for the existence of stacked dimers of **1** or the prototypical ball-in-socket C_{60}@**1** complex in solution suggested that the binding in these assemblies was not sufficiently strong to override the expected solvation and/or entropy penalties associated with the formation of a supramolecular assembly, leading to the conclusion that the attractive force of the concave−convex interaction is not significant.[3] However, in 2007, we reported that a molecular receptor **2** with two corannulene pincers preorganized on a proper tether efficiently binds fullerenes.[4] Buckycatcher (**2**) forms stable inclusion complexes with both C_{60} and C_{70} in organic solvents and in the solid state. Since then, a handful of molecular receptors with two or three corannulene pincers have been reported.[5] NMR titrations indicated that these receptors exhibit affinities toward fullerenes quite similarly to that of **2**. Interestingly, the reported tridental receptors with corannulene pincers located on conformationally flexible tethers do not show any improvement upon their fullerene complexation efficiency, as compared to the bis-corannulene analogues.[5a,c] This finding underscores the importance of the pincer preorganization on a relatively rigid tether if the high affinity for a given guest is desired. Very recently, we demonstrated that a fine-tuning of the tether topology of a bidental receptor results in the formation of "buckycatcher II" (**3**) with the affinity toward fullerenes, which is over 1 order of magnitude higher than that of **2** or the other reported corannulene-based receptors.[6] In addition to the usual 1:1 C_{60}@**3** inclusion complex, a remarkable trimeric C_{60}@$(\mathbf{3})_2$ assembly was detected in solution and was also characterized by X-ray crystallography in the solid state.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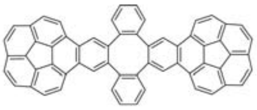
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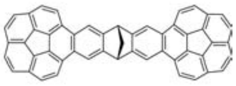
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The pursuit for molecular receptors with properly preorganized corannulene pincers led us to the tethers introduced some time ago by Klärner.[7] These molecular scaffolds allow for the preparation of molecular clips and tweezers with *syn* pincer topology by Diels−Alder cycloaddition reaction. In this account, we report the preparation of two bidental molecular receptors **4** and **5** with benzocorannulene pincers preorganized on Klärner's scaffolds. ^{1}H NMR titration shows that while **4** exhibits the affinity toward fullerenes comparable with that of buckycatcher **2**, **5** binds both C_{60} and C_{70} with the association constants higher by more than 2 orders of magnitude than **2** and over 1 order of magnitude higher than buckycatcher II (**3**).

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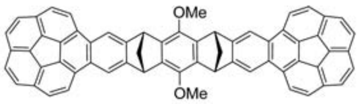

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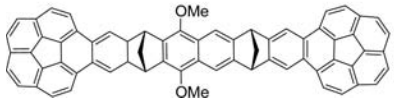

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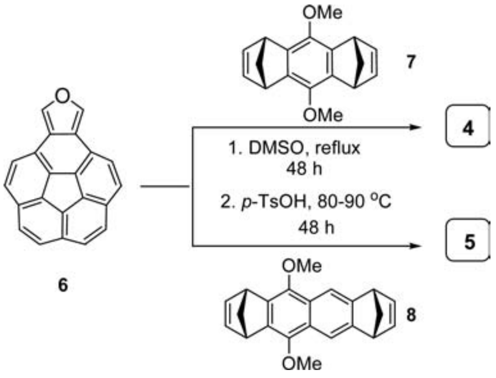
Syntheses of **4** and **5** are outlined in Scheme 1. In both cases, isocorannulenofuran **6**, a useful synthon for preparation of large conjugated systems containing corannulene subunits,[8] is employed as a diene in the Diels–Alder cycloadditions.

Scheme 1. Synthesis of Bis-corannulene Receptors 4 and 5



Klärner's dienophiles **7** and **8** were prepared according to the previously published procedures with minor modifications.[9,10] The mixtures of stereoisomeric Diels–Alder adducts produced in refluxing DMSO were subsequently dehydrated without separation by *p*-TsOH to yield **4** and **5** with modest overall isolated yields of 45 and 40%, respectively. The yields were not improved by the alternative attempts with the separation of the Diels–Alder cycloadducts followed by acid-catalyzed dehydration in solvents like diglyme, toluene, or 1,1,2,2-tetrachloroethane.

The Klärner's tethers preorganize the corannulene pincers in a *syn* fashion, resulting in a creation of large cavities able to adopt size and shape compatible guest molecules including fullerenes. Molecular modeling calculations performed with B97-D and M06-2X hybrid functionals and TZVP and QZVP* basis sets showed that in the gas-phase **4** can exist in three distinct conformations described by the relative topology of its corannulene pincers as concave–concave (**4a**), concave-convex (**4b**), and convex–convex (**4c**) interconverting through the relatively low-barrier bowl-to-bowl inversions of the corannulene fragments.[10] Four conformations of the larger clip (**5a–d**) were located by molecular modeling. The "open" concave–concave conformers **4a** and **5a** along with the lowest energy "closed" structures **4b** and **5d** are shown in Figure 2. The remaining conformers are presented in the Supporting Information.

Owing to the relatively short tether in **4**, the corannulene fragments can interact by dispersion forces which render the desired "open" conformation **4a** less stable than the "closed" **4b** by 6.2 kcal/mol. The latter conformer is stabilized by the efficient concave-convex $\pi-\pi$ stacking of the corannulene surfaces overriding the tether deformation penalty.

Analogous to the more thoroughly studied **2**[4,11] the "open" conformations **5a–c** have similar relative stabilities differing by less than 0.4 kcal/mol.[10] Somewhat to our surprise, the "closed" concave–concave conformer **5d** was also located by B97-D calculations and found to represent the global energy minimum for **5**. In this case the size of the tether allows only for limited CH–π attractive interactions between two corannulene pincers resulting in a modest preference for **5d** with the B97-D functional (1.9 kcal/mol, Figure 1).

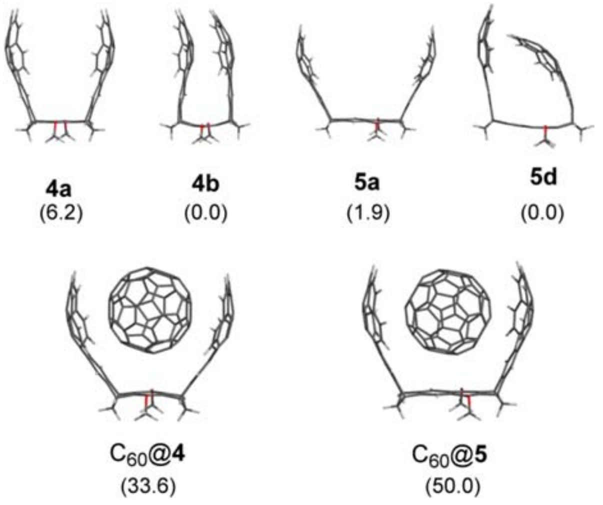


Figure 1. (Top) B97-D/TZVP-optimized structures of the concave–concave "open" conformations **4a** and **5a** and the lowest energy "closed" conformations **4b** and **5d** along with their relative energies in kcal/mol. (Bottom) 1:1 inclusion complexes of both receptors with C_{60}. The B97D/QZVP* binding energies of the complexes are given in kcal/mol.

It has to be pointed out that the "open" conformations are expected to be strongly favored by solvation due to their significantly larger solvent-accessible surfaces. However, a significant gas-phase preference for **4b** suggests that this conformation may compete with the open conformations even in solution, potentially decreasing the ability of **4** for hosting the guest molecules.

Strong affinities toward fullerenes are predicted by B97-D calculations for both **4** and **5** since the gas-phase binding energies (defined as $-\Delta E$ for the complex formation step) are quite substantial for C_{60}@**4** and C_{60}@**5** supramolecules (33.6 and 50.0 kcal/mol respectively, Figure 1). Based on these numbers, **5** is expected to be a significantly better receptor for small fullerenes than **4**. Comparison of the lowest energy structures of both isolated clips (**4b** and **5d**) with their structures in the inclusion complexes with C_{60} (Figure 1) indicates that **4** will suffer from a more severe host deformation penalty since the inclusion of the guest requires a significant change of its structure. Indeed, the calculated deformation penalty in C_{60}@**4** is ca. 6 kcal/mol higher than in C_{60}@**5**, accounting fully for the difference in the calculated binding energies of the two complexes.

For comparison, the binding energies calculated at the same computational level for C_{60}@**2**[1a,11] and C_{60}@**3**[6] are 41.8 and 42.5 kcal/mol, respectively, suggesting that **5** should be the most efficient bis-corannulene molecular receptor for fullerenes prepared to date. ^{1}H NMR titration experiment provides an evidence for the complexation of both **4** and **5** with fullerenes in toluene and chlorobenzene, as demonstrated by the changes of the chemical shifts of some protons of the clips upon addition of C_{60} or C_{70} (Figure 2). For the smaller receptor **4**, a 1:1 binding stoichiometry was determined by the Job plot analysis. The association constants K_a were calculated by non linear curve fitting of the NMR data to the 1:1 complexation model, providing the values of 2550 ± 50 and 2950 ± 110 M^{-1} for C_{60}@**4** and C_{70}@**4**, respectively (toluene-d_8, rt).[10] While large, these association constants are very similar to the ones determined previously for buckycatcher **2** and to the other bi- and tridental corannulene-based receptors reported to date,[4,5,12] but lower than that found for buckycatcher II (**3**).[6]

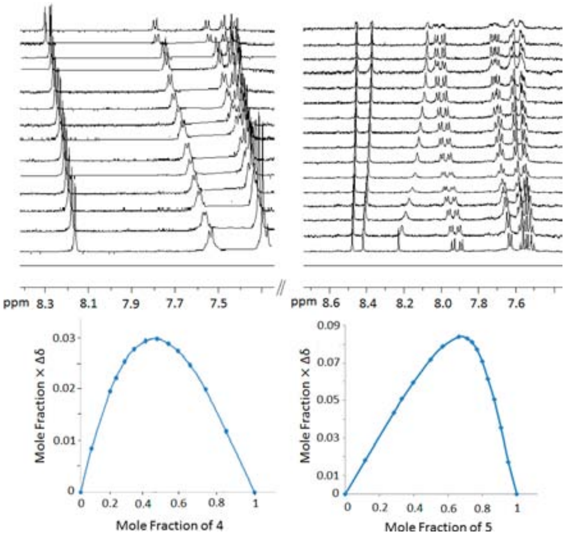


Figure 2. (Top) Partial ^{1}H NMR spectra of **4** (left) and **5** (right) with variable concentrations of C_{60}. (Bottom) Job plot constructed from the C_{60} titrations of **4** (toluene-d_8, left) and **5** (chlorobenzene-d_5, right).

In contrast to **4**, association of **5** with C_{60} and C_{70} goes beyond the usual 1:1 inclusion complex formation as indicated by the continuous variation plot based on the titration in both toluene-d_8 and chlorobenzene-d_5 (Figure 2). By analogy with buckycatcher II (**3**), we assume that the trimeric aggregates C_{60}@**5**$_2$ and C_{70}@**5**$_2$ are formed in addition to the 1:1 supramolecular assemblies, as described by eq 1.

$$\mathbf{5} + C_{60/70} \overset{K_1}{\rightleftharpoons} C_{60/70}@\mathbf{5} + \mathbf{5} \overset{K_2}{\rightleftharpoons} C_{60/70}@\mathbf{5}_2 \tag{1}$$

Attempts to estimate the microscopic association constants K_1 and K_2 for the receptor **5**−C_{60} pair by NMR titration in toluene-d_8 failed, presumably owing to the rather limited solubility of the supramolecular complexes and to the very high association constants in this solvent. In order to minimize the potential errors, we performed the NMR titration experiments in chlorobenzene-d_5 since, as demonstrated previously for the receptors **2** and **3**, the association constants of such receptors with fullerenes in this solvent are lowered by ca. 1 order of magnitude in comparison to toluene.[6,12] Chlorobenzene is also a better solvent for both the host and guest molecules as well as for their inclusion complexes. However, even in chlorobenzene-d_5 we were able to obtain only crude estimates for the association constants of **5** with C_{60} (ca. 5×10^4 and 8×10^3 M^{-1} for K_1 and K_2, respectively). On the other hand, much better quality fitting of the NMR titration data of **5** with C_{70} in the same solvent allowed for a more reliable estimation of K_1 and K_2 at $(2.0 \pm 0.7) \times 10^5$ and $(3.3 \pm 0.9) \times 10^4$ M^{-1}, respectively.

The limited accuracy of NMR titration experiments notwithstanding, the superior affinity of **5** toward C_{60} and especially toward C_{70} is clearly demonstrated. As reported previously, the association constant for C_{60}/buckycatcher (**2**) in chlorobenzene is 520 ± 20 M^{-1} at room temperature. Under the same conditions, the recently reported buckycatcher II (**3**) binds C_{60} with K_1 and K_2 constants of 10040 ± 1100 and 1180 ± 640 M^{-1}, respectively. Apparently, **5** binds C_{60} an order of magnitude stronger than **3** and 2 orders of magnitude stronger than **2**. The high affinity of **5** toward fullerenes predicted by the molecular modeling (vide infra) can be rationalized by a closer inspection of the calculated structure of C_{60}@**5** in which the fullerene cage is placed in the center of the doubly concaved clefts of the receptor with most of the corannulene pincer's carbon atoms being in van der Waals contact with the carbon atoms of C_{60}. In addition, there are some van der Waals contacts between the fullerene cage and the naphthalene subunit of the tether. The small receptor deformation penalty in C_{60}@**5** indicates the favorable arrangement of the pincers for the fullerene guests. Therefore, the Klärner's tether in **5** not only preorganizes the corannulene pincers into the optimal topology for the inclusion complex formation but also contributes to the dispersion-based attraction of the fullerene hosts.

All of the main structural features of C_{60}@**5** predicted by molecular modeling are confirmed by X-ray diffraction study of a crystal of this complex obtained by a slow evaporation of mixed solutions of C_{60} and **5** in *o*-dichlorobenzene. (Figure 3).[10,13] In the solid state, the C_{60} guest is placed approximately in a center of the concave−concave cleft formed by two corannulene pincers. Distances between the centroid of C_{60} and the centroids of two five-membered rings of the corannulene pincers are 6.76 and 6.83 Å. Similar distances were found in the previously studied C_{60}@**2** and C_{60}@(**3**)$_2$ complexes.[4,6] However, a slightly larger separation of C_{60} from the concave face of pristine corannulene (6.94 Å) was reported by Dawe et al.[15] The carbon cage in C_{60}@**5** is ordered, and it makes 23 C···C contacts of less than 3.4 Å to the host (3.154(4)−3.384(4) Å), one of which is to one of the carbon atoms of the naphthalene part of the tether. Although each C_{60} cage is wrapped by **5** and by the solvent molecules, it still is in close contacts with three neighboring carbon cages showing 10 intermolecular C···C contacts with other C_{60} molecules in the range 3.264(4)−3.399(4) Å. The nearest centroid-centroid distances between these C_{60} molecules are 9.802, 9.876, and 10.101 Å, indicating van der Waals contacts of the carbon cages.

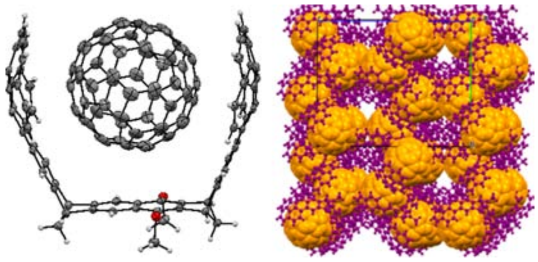


Figure 3. (Left) Crystal arrangement in C_{60}@**5**. (Right) Crystal packing pattern seen approximately along the *a* crystallographic axis. Disordered solvent (omitted for clarity) lies in the voids between complexes.

A notably higher affinity of **5** toward C_{70} as compared to C_{60} demonstrated by the NMR titrations can be rationalized by the molecular modeling study. The gas-phase binding energy calculated for C_{70}@**5** inclusion complex (52.8 kcal/mol) is 2.8 kcal/mol higher than that of C_{60}@**5**.[10] Assuming that both the solvation and entropy penalties associated with the supramolecular complex formation are comparable in the two cases, we conclude that the stronger dispersion-based attraction of C_{70} by **5** results in the more exergonic thermodynamics of the C_{70}@**5** complex formation and causes a notable specificity of the receptor for the larger fullerene.

In summary, two molecular receptors **4** and **5** with two corannulene pincers preorganized on Klärner's tethers **7** and **8**, respectively, were prepared by Diels−Alder methodology. DTF-D computational studies indicated that **5** should exhibit a significantly higher affinity toward both C_{60} and C_{70} than **4**. Indeed, ^{1}H NMR titration demonstrated that while **4** binds both C_{60} and C_{70} with similar affinity to the previously reported corannulene-based receptors, **5** appears to be the record-setting molecular clip for both studied fullerenes with the association constants higher by ca. 2 orders of magnitude. In addition to the usual 1:1 fullerene@**5** inclusion complexes, the trimeric fullerene@**5**$_2$ assemblies are also formed in toluene and chlorobenzene.[16] X-ray crystal structure determination of C_{60}@**5** along with the DFT studies provide a rationale for the efficiency of this receptor in size/shape recognition of fullerenes; the tether in **5** not only preorganizes the corannulene pincers into a favorable topology, but in addition, it contributes to some extent to the attractive dispersion interactions with the guest fullerene cages. As anticipated on the basis of the results of DFT-D calculations, **5** exhibits some preference in binding C_{70} over C_{60} owing to the stronger gas-phase binding energies of the former carbon cage with the receptor.

"Intelligent design" of efficient and specific receptors for selected guests is an important part of supramolecular chemistry with potential applications in nanotechnology and in material and separation sciences. With the preparation of **5**, we demonstrated that fine-tuning of the tether topology generates a receptor with the strongest affinity toward small fullerenes of all previously reported receptors containing two or three corannulene pincers. This exceptional affinity, anticipated a priori based on DFT-D calculations, may potentially represent the upper limit for bis-corannulene molecular clips which bind fullerenes by relatively weak dispersion interactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02666.

> Synthetic procedures, NMR and MS spectra for **4**, **5** and **8**; ^{1}H NMR titration studies; DFT calculations for the conformers of **4** and **5** and for the inclusion complexes C_{60}@**4**, C_{60}@**5**, and C_{70}@**5** (PDF)
>
> X-ray data for C_{60}@**5***1.5*o*-DCB solvate (CIF)

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Notes

The authors declare no competing financial interest.

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