Hemicarceplex Formation With a Cyclotriveratrylene-Based Molecular Cage Allows Isolation of High-Purity ($\geq$99.0%) C_{70} Directly from Fullerene Extracts
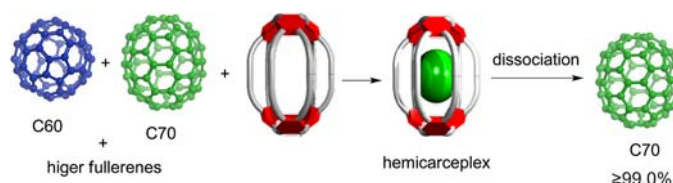
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ABSTRACT

A cyclotriveratrylene-based molecular cage that favors the formation of a room temperature isolable hemicarceplex with C_{70}, in the presence of C_{60}, has been developed. Significant differences in the association and dissociation kinetics of the molecular cage and buckyballs allowed the isolation of C_{70} in high purity ($\geq$99.0%) from a commercial fullerene extract without the need for recrystallization or HPLC.

Because of their versatile configurations and attractive properties, fullerenes, including cylindrical carbon nanotubes (CNTs) and spherical and spheroidal buckyballs, have found applications in a wide range of fields.[1] Ignoring CNTs, which lack uniform diameters or lengths, the most abundant structurally distinct species in a typical fullerene extract are two buckyballs: C_{60} and C_{70}.[2] Unfortunately, the poor solubilities of these buckyballs in organic solvents seriously complicate their isolation, purification, and practical application. Several elegant methods have been developed for the isolation of the more-abundant C_{60} from fullerene extracts;[2,3] in contrast, isolating the less symmetrical
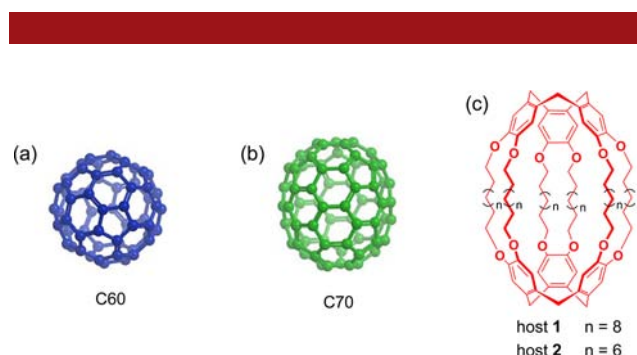

Figure 1. Chemical structures of (a) C_{60}, (b) C_{70}, and (c) CTV-based molecular cages **1** and **2**.

and photovoltaically more-interesting C_{70}[4] in high purity from the same mixtures has been less straightforward. Accordingly, relatively limited research has been undertaken to discover and expand the practical applications of C_{70}.

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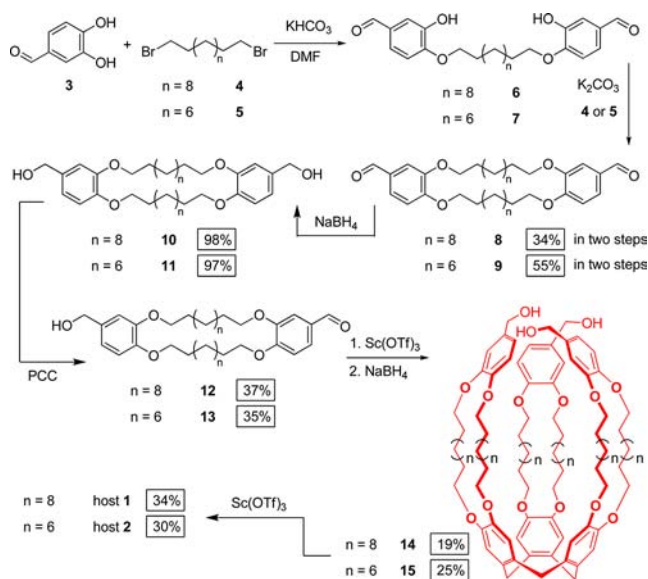
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One attractive approach for the selective isolation of C_{70} involves exploiting its host–guest complexation behavior.[5] Although a few judiciously designed synthetic host molecules do form complexes with C_{60} and C_{70} in solution,[6] using such host–guest complexes as a means of separating mixtures of buckyballs (i.e., with high degrees of selectivity and stability) remains a challenge. Unlike carcerands, which cannot release their entrapped guests, hemicarcerands allow sequestration of complementary guests (forming room temperature–isolable hemicarceplexes) as well as their release at elevated temperatures.[7] We suspected that such an approach might allow the isolation of C_{70} in high purity from fullerene extracts. Herein, we report a cyclotriveratrylene (CTV)-based molecular cage that favors the formation of a hemicarceplex with C_{70}, rather than with C_{60}, and its application to the direct isolation of high-purity ($\geq 99.0\%$) C_{70} from fullerene extracts on a scale of tens of milligrams, through a simple and concise route without the need for crystallization or HPLC.

We suspected that structural complementarity between two covalently linked CTV units and the spheroidal fullerenes would provide sufficient binding affinity in solution to abrogate the need for additional stabilizing aromatic units in the linkers.[6a,b,8] In theory, we could select linkers of a suitable length to allow the smaller C_{60} to freely enter and exit the host cavity while restricting the passage of the larger C_{70} under the same conditions. To minimize the energy cost of structural reorganization during the guest binding event, we chose zigzagging alkyl chains as spacers linking the two CTV units, giving suitably preorganized hosts for complexation with C_{70} (Figure 1).

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Scheme 1. Synthesis of Molecular Cages **1** and **2**

The molecular cage **1** was synthesized from 3,4-dihydroxybenzaldehyde (**3**) and 1,12-dibromododecane (**4**) in seven steps (Scheme 1). The selective alkylation of the dibromide **4** at the most-acidic phenol group (para position) of the benzaldehyde **3** gave a crude dialdehyde **6**, which we used directly in the subsequent macrocyclization reaction to produce the dialdehyde **8** (34% yield, two steps). NaBH$_4$-mediated reduction of both formyl groups in the dialdehyde **8**, followed by PCC-mediated oxidation of one of the hydroxyl groups of the resulting diol **10**, afforded the alcohol **12**. We synthesized the triol **14** through Sc(OTf)$_3$-catalyzed condensation of three units of the alcohol **12** into a CTV[9] and subsequent NaBH$_4$-mediated reduction of the resulting trialdehyde. The molecular cage **1** was isolated in 34% yield after another Sc(OTf)$_3$-catalyzed condensation of the triol **14**. The molecular cage **2** was synthesized from aldehyde **3** and 1,10-dibromodecane (**5**) through procedures similar to those used for the synthesis of the molecular cage **1**.

The ^{1}H NMR spectrum of an equimolar mixture (3 mM) of the host **1** and C_{60} in CDCl$_2$CDCl$_2$ displays (Figure 2b) a new set of signals corresponding to their complex, suggesting that the rates for guest entry into and exit from the internal cavity of **1** are slow on the time scale of ^{1}H NMR spectroscopy at 400 MHz. When mixing the host **1** with a commercial fullerene extract, the same complex appeared initially; after heating the solution at 323 K for 48 h, however, a new set of signals appeared for another complex. The ^{1}H NMR spectrum of an equimolar mixture of pure C_{70} and the host **1** heated at 333 K for 48 h in CDCl$_2$CDCl$_2$ displayed the same set of signals (Figure 2d). Unlike the complex $C_{60}@\mathbf{1}$, which was not sufficiently stable for isolation through column chromatography at ambient temperature, the complex $C_{70}@\mathbf{1}$ could be purified

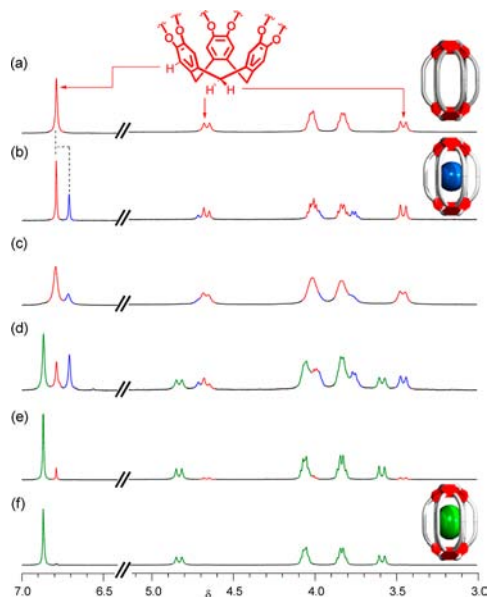(9) Brotin, T.; Roy, V.; Dutasta, J.-P. *J. Org. Chem.* **2005**, *70*, 6187–6195.

Figure 2. Partial ^{1}H NMR spectra (400 MHz, CDCl₂CDCl₂, 298 K) of (a) the free host **1**; (b) an equimolar mixture of **1** and C₆₀ (3 mM); (c) a mixture (0.5 mL) of **1** (2 mg) and fullerene extract (10 mg); (d) the solution in (c) after heating at 323 K for 48 h; (e) an equimolar mixture of **1** and C₇₀ (3 mM) after heating at 333 K for 48 h; and (f) the purified hemicarceplex C₇₀@**1**.

Figure 3. Partial ^{13}C NMR spectra (100 MHz, CDCl₂CDCl₂, 298 K) of (a) an equimolar mixture of **1** and C₆₀ (2.5 mM); (b) the free host **1**; (c) free C₇₀; and (d) the purified hemicarceplex C₇₀@**1**. The descriptors (c) and (uc) refer to the complexed and uncomplexed states, respectively, of the components.

chromatographically (SiO₂; CH₂Cl₂/hexanes, 3:2). An electrospray ionization (ESI) mass spectrum of the purified C₇₀@**1** revealed an intense peak at m/z 2569.3 corresponding to the ion [C₇₀@**1**]⁺. The good match between the observed and calculated isotope patterns of this ion supports the successful synthesis of the hemicarceplex C₇₀@**1**.

The ^{13}C NMR spectrum of the isolated complex C₇₀@**1** displays (Figure 3d) all five signals belonging to C₇₀, shifted upfield by 0.6–1.2 ppm relative to those of the free fullerene (Figure 3c), suggesting encapsulation of spheroidal C₇₀ within the cavity of **1**. The same trend in upfield shifting of the signals of C₆₀ within its complex with the host **1** in the ^{13}C NMR spectrum (Figure 3a) of their equimolar mixture (2.5 mM) implied that the spherical fullerene could also be positioned favorably within the cavity of this host in the complex. The signals in the ^{1}H NMR spectra of equimolar mixtures (4 mM) of the host **2** and the guests C₆₀ and C₇₀, respectively, in CDCl₂CDCl₂ were shifted only negligibly, even after heating the mixture at 333 K for 48 h, suggesting that neither guest could enter the cavity of host **2** by penetrating its smaller openings.

Cram defined the free energy for the formation of a hemicarceplex and the activation energy required for a guest to enter the cavity of a hemicarcerand as the intrinsic and constrictive binding energies, respectively.[10] We used ^{1}H NMR spectroscopy to monitor the dissociation of the hemicarceplex C₇₀@**1** at 298 K in CDCl₂CDCl₂ until

equilibrium had been reached, obtaining an association constant (K_a) for the hemicarceplex of 4200 M⁻¹ and its association rate constant (k) of 0.026 M⁻¹ s⁻¹ (Figure 4). The intrinsic and constrictive binding energies for the hemicarceplex C₇₀@**1** were, therefore, 4.9 and 19.7 kcal mol⁻¹, respectively. Although we could not isolate the complex C₆₀@**1**, its association in CDCl₂CDCl₂ was sufficiently slow to allow ^{1}H NMR spectroscopy to be used to determine its rate constant by monitoring the initial host−guest mixture; accordingly, we determined the equilibrium constant and the association rate constant of complexation to be 500 M⁻¹ and 0.164 M⁻¹ s⁻¹, respectively, corresponding to a free energy and an activating energy of complexation of 3.7 and 18.5 kcal mol⁻¹, respectively. Thus, the physical barrier encountered by the more sizable C₇₀ was greater than that of C₆₀ when entering the cavity of the host **1** through the openings formed by the alkyl linkers, and the binding of the host **1** to C₇₀ was stronger than that to C₆₀.

After investigating the kinetic and thermodynamic behavior of the hemicarceplex C₇₀@**1**, we turned our attention to applying this system to the direct isolation of C₇₀ from fullerene extracts. The isolation process involved three steps (see Supporting Information (SI) for the flowchart): (i) *Formation of the hemicarceplex*—A CHCl₂CHCl₂ (5 mL) solution of the fullerene extract (300 mg, SES Research) and the hemicarcerand **1** (50 mg) was heated at 313 K for 16 h; the organic solvent was evaporated under reduced pressure, and the solid residue was suspended in CH₂Cl₂ (40 mL); the solid fullerenes were filtered off. (ii) *Isolation of the hemicarceplex*—The filtrate was concentrated, loaded onto a short column of SiO₂ (5 g), and eluted with CS₂ (50 mL) to remove any uncomplexed and/or dissociated fullerenes; the hemicarceplex C₇₀@**1** and the free hemicarcerand **1** were then isolated by eluting the column with mixtures of CH₂Cl₂ and hexanes (3:2, 250 mL) and CH₂Cl₂ and

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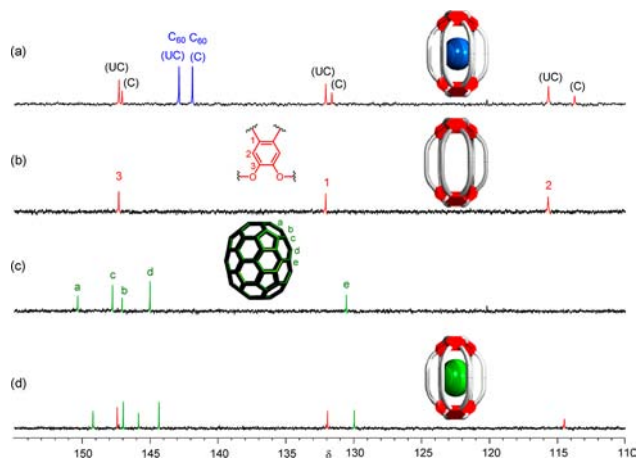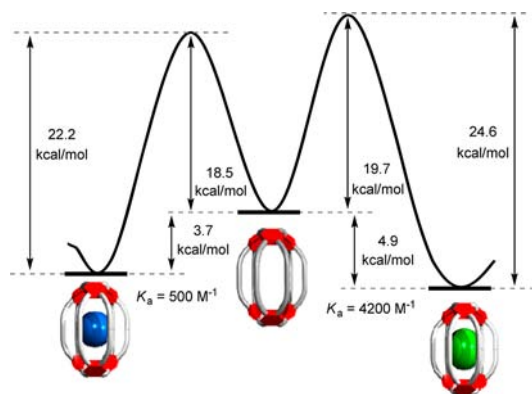
Figure 4. Constrictive and intrinsic binding energies for the complexation of C_{60} and C_{70} with the host **1** in $CDCl_2CDCl_2$.

MeOH (98:2, 50 mL), respectively. (iii) *Dissociation of the hemicarceplex*—The hemicarceplex $C_{70}@\mathbf{1}$ (33.1 mg) obtained after concentrating the appropriate eluate from the previous step was dissolved in toluene (10 mL), and then the solution was heated at 303 K for 12 h. The hemicarcerand **1** precipitated as a white solid, and the toluene solution, which contained mainly free C_{70} and the hemicarceplex $C_{70}@\mathbf{1}$, was removed via pipet after centrifugation; another charge of toluene (5 mL) was added to wash the white solid, and then the mixture was centrifuged again. The residue obtained after concentrating the combined toluene phases was suspended in CH_2Cl_2 (5 mL), in which the hemicarceplex $C_{70}@\mathbf{1}$ is highly soluble, forming a red precipitate of C_{70}, which was collected through centrifugation. The solid C_{70} was then resuspended in CH_2Cl_2 (5 mL), centrifuged, separated from the solvent, and dried; the purity of the isolated C_{70} (6.5 mg), determined through HPLC analysis, was 99.0%.

After obtaining consistent results when repeating this isolation scheme another two times (isolating 7.1 and 6.7 mg of C_{70}, both in 99.1% purity; see SI), we scaled up the process 10-fold (using 3 g of the fullerene extract and 500 mg of the hemicarcerand **1**). Gratifyingly, we isolated C_{70} not only in approximately 10 times the amount (72.6 mg) but also in similar purity (99.0%). Thus, the amount of C_{70} isolated in a single purification cycle should be scalable to even greater levels if we were to apply a greater amount of the host **1**. In this large-scale experiment, the total amount of the host **1** that we recovered after chromatography and precipitation from toluene was 360 mg (72% recovery). Concentrating the CH_2Cl_2 phase obtained after dissociation of the hemicarceplex under reduced pressure allowed recycling of 96 mg of the hemicarceplex $C_{70}@\mathbf{1}$ (26%

recovery, containing 64 mg of **1**); therefore, the mass loss of the host **1** throughout the whole isolation process was approximately 15%. Because the dissociation of the hemicarceplex required no competing guests, the recycled host **1** could be used directly in a subsequent isolation cycle without the need for any specific treatment or purification process.

Dissociation of the recycled hemicarceplex under similar conditions afforded C_{70} in 92.6% purity (HPLC analysis). Notably, based on HPLC analysis, the C_{70} isolated using this method was only negligibly contaminated with C_{60} (see SI);[11] its major impurity was C_{76}. Therefore, the hemicarcerand **1** appears to also sequester C_{76} from the fullerene extract. Based on HPLC analysis of the commercial fullerene extract that we tested in this study, the ratio of C_{76}, C_{78}, and C_{84} was approximately 1:1.1:1.6 (i.e., C_{76} was a relatively minor component; see SI). Therefore, our host **1** appears to be capable of kinetically differentiating these three buckyballs through the effective formation of the hemicarceplex $C_{76}@\mathbf{1}$ under the developed experimental conditions. This result suggests that judicious extension or modification of the linkers in host **1** might allow a methodology to be developed to selectively stabilize—and, therefore, isolate—potentially photovoltaically useful higher fullerenes,[12] heterofullerenes,[13] and/or endohedral fullerenes[14] in high purity.

Although Cram first proposed, in 1995, that the internal space of a cavitand dimer might be a suitable host for C_{60},[15] hemicarcerands that can selectively imprison guests as big as C_{60} and C_{70} have never been realized previously. Significant differences in the association and dissociation kinetics for the complexes formed between the hemicarcerand **1** and various buckyballs allowed us to isolate C_{70} in high purity ($\geq 99.0\%$) from a commercial fullerene extract through selective sequestration in solution, without the need for recrystallization or HPLC. The preparation of hemicarcerands that sequester C_{70} and higher fullerenes suggests the possibility of not only isolating and stabilizing these novel molecules, their analogues, and derivatives but also applying them practically as useful photovoltaic materials by significantly increasing their solubility in less polar solvents without covalently disrupting their unique π-surfaces. We are currently working on enlarging the cavity of the hemicarcerand **1**, by elongating the linking spacers, to allow selective trapping of larger fullerenes.

Supporting Information Available. Synthetic procedures and characterization data for hemicarcerand **1** and hemicarceplex $C_{70}@\mathbf{1}$. This material is available free of charge via the Internet at http://pubs.acs.org

(11) Based on HPLC analysis, the main impurity of the commercial high purity C_{70} ($\geq 98.5\%$) was C_{60}.

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