

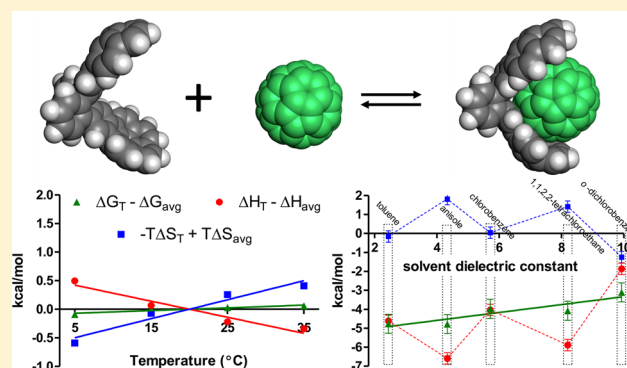
Thermodynamics of Host–Guest Interactions between Fullerenes and a Buckycatcher

Vu H. Le, Michael Yanney, Matthew McGuire, Andrzej Sygula,* and Edwin A. Lewis*

Department of Chemistry, Mississippi State University, Mississippi State, Mississippi 39762, United States

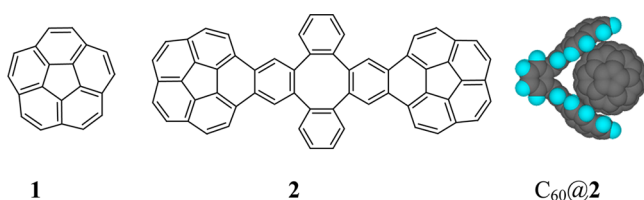
Supporting Information

ABSTRACT: ^1H NMR and isothermal titration calorimetry (ITC) experiments were employed to obtain reliable thermodynamic data for the formation of the 1:1 inclusion complexes of fullerenes C_{60} and C_{70} with the buckycatcher ($\text{C}_{60}\text{H}_{28}$). NMR measurements were done in toluene- d_8 and chlorobenzene- d_5 at 288, 298, and 308 K, while the ITC titrations were performed in toluene, chlorobenzene, *o*-dichlorobenzene, anisole, and 1,1,2,2-tetrachloroethane at temperatures from 278 to 323 K. The association constants, K_a , obtained with both techniques are in very good agreement. The thermodynamic data obtained by ITC indicate that generally the host–guest association is enthalpy-driven. Interestingly, the entropy contributions are, with rare exceptions, slightly stabilizing or close to zero. Neither ΔH nor ΔS is constant over the temperature range studied, and these thermodynamic functions exhibit classical enthalpy/entropy compensation. The ΔC_p values calculated from the temperature dependence of the calorimetric ΔH values are negative for the association of both fullerenes with the buckycatcher in toluene. The negative ΔC_p values are consistent with some desolvation of the host-cavity and the guest in the inclusion complexes, $\text{C}_{60}@C_{60}\text{H}_{28}$ and $\text{C}_{70}@C_{60}\text{H}_{28}$.



INTRODUCTION

The discovery of fullerenes and other forms of elemental carbon with curved surfaces introduced a novel aspect of supramolecular assembly based on the relatively weak dispersion forces between the convex surfaces of the conjugated carbon networks and the appropriate molecular receptors. Buckybowls, curved-surface polycyclic aromatic hydrocarbons (PAH) structurally related to fullerenes, appear to be good candidates for receptors due to the complementarity of their accessible concave surfaces with the convex surfaces of the fullerenes.^{1–6} While supramolecular assemblies of fullerenes with the smallest buckybowl corannulene (**1**) have not been detected in solution, we have shown that the efficient molecular receptors for both C_{60} and C_{70} can be constructed if at least two corannulene pincers are preorganized on a proper tether.⁷ For example, buckycatcher $\text{C}_{60}\text{H}_{28}$ (**2**) consisting of two corannulene subunits on a tetrabenzocyclooctatetraene tether was shown to form 1:1 inclusion complexes with fullerenes in both the solid state and in toluene solutions.^{8,9}



The $\text{C}_{60}@2$ inclusion complex has become a prototypical system for large dispersion-driven supramolecular systems and, as such, has been the subject of several computational studies performed at various levels of theory.^{8–14} Recently, inclusion complexes for both C_{60} and C_{70} with **2** were incorporated into the S12L test set of noncovalently bound complexes used to evaluate computational methods' performance in modeling the dispersion interactions.¹⁴ The reported theoretical gas-phase binding energies of the $\text{C}_{60}@2$ complex vary dramatically, thus emphasizing the difficulty of accurately computing the energetics of dispersion forces. Hartree–Fock based calculations as well as several commonly employed DFT functionals predict either repulsion or negligible binding energies for the assembly,¹² while the dispersion-sensitive DFT functionals predict strong gas-phase binding energies in the range -20 to -44 kcal mol⁻¹.^{9–14} Obviously, there is a need for reliable experimental data to assess the quality of the computational results. To date, the only reported thermodynamic results for the association of buckycatcher (**2**) with fullerenes are the ambient temperature Gibbs enthalpies determined in toluene- d_8 by ^1H NMR titration (-5.3 and -5.1 kcal mol⁻¹ for C_{60} and C_{70} , respectively).^{8,9} However, since the gas-phase experimental data for the thermodynamics of these inclusion complexes are not available, it is necessary to develop reliable computational

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models capable of assessing the solvent contributions to the enthalpy and entropy effects on the association thermodynamics in solution. In the first such attempt, Zhao and Truhlar calculated the entropy contribution to the gas-phase formation of $C_{60}@2$ based on the rigid rotator-harmonic oscillator model and concluded that while the calculated binding energy of the assembly is $26.4 \text{ kcal mol}^{-1}$ ($\Delta E = -26.4 \text{ kcal mol}^{-1}$) the gas-phase Gibbs free energy of association is only ca. -7 kcal mol^{-1} . In addition, the association of C_{60} with **2** in solution results in a considerable loss of the solvent-accessible surfaces which further reduces the exergonicity of the process.¹⁰ In a more comprehensive study, Grimme applied a similar approach combining dispersion-corrected DFT calculations for the gas-phase binding energies with the COSMO-RS continuum solvation model for the solvation free enthalpy assessment and evaluating the remaining rotational–vibrational enthalpic/entropic contributions based on the harmonic frequency calculations.¹¹ A series of inclusion complexes (including the $C_{60}@2$ and $C_{70}@2$ complexes) were studied, and the calculated ΔG values in solutions were reported to differ on average by only 2 kcal/mol from the available experimental data. Considering the simplicity of the model, the accuracy of the results is quite impressive, but a closer inspection of the results reveals some limitations to this approach. As an example, Grimme's model predicts overbinding of both C_{60} and C_{70} by buckycatcher (**2**) in toluene by ca. $3\text{--}4 \text{ kcal mol}^{-1}$, significantly more than the average error for the studied pool of inclusion complexes.¹¹ Obviously, a larger set of precise experimental thermodynamic data is needed to assess the accuracy of the computational methods as well as to improve the theoretical models used to describe solvation in weakly bound inclusion complexes.

Herein, we report the results of our study of the energetics of complexation of C_{60} and C_{70} with buckycatcher by both isothermal titration calorimetry (ITC) and ^1H NMR titration. The use of the ITC method allowed us to obtain a complete set of thermodynamic parameters (K_a (or ΔG), ΔH , and $-T\Delta S$) for the formation of $C_{60}@2$ and $C_{70}@2$ complexes in a number of solvents and at a number of different temperatures. We also repeated some of the earlier NMR titrations at lower concentration and at three temperatures for a better comparison with the ITC results. The heat capacity changes, ΔC_p , for formation of the $C_{60}@2$ and $C_{70}@2$ inclusion complexes in toluene were also obtained from the temperature dependence of the calorimetric enthalpy changes.

MATERIALS AND METHODS

Sample Preparation. C_{60} and C_{70} were obtained from SES Research (Houston, TX). The buckycatcher (**2**) was synthesized in our laboratory according to the procedure we previously reported.⁸ Anhydrous toluene, chlorobenzene, and *o*-dichlorobenzene were obtained from Sigma-Aldrich (St. Louis, MO). Anhydrous 1,1,2,2-tetrachloroethane and anisole were obtained from VWR (Radnor, PA). Toluene- d_8 and chlorobenzene- d_3 were obtained from Cambridge Isotope Laboratories (Tewksbury, MA).

NMR Titrations. ^1H NMR titrations were performed according to the procedure reported previously^{8,9} but at lower concentrations of fullerenes and **2** and with careful temperature control. The spectra were recorded on Bruker (Billerica, MA) AVANCE III 600 and 850 MHz spectrometers in toluene- d_8 and chlorobenzene- d_3 at 288, 298, and 308 K. Several proton signals on the corannulene subunits of **2**

exhibited measurable changes in chemical shift upon complexation with either C_{60} or C_{70} . If necessary, the overlapping peaks of some of these protons were deconvoluted using SpinWorks 3 NMR software (Kirk Marat, University of Manitoba) in order to extract the precise chemical shift values. The association constant K_a was determined using eq 1

$$\Delta\delta = \frac{L(1 + K_a X + K_a Y) - \sqrt{L^2(1 + K_a X + K_a Y)^2 - 4K_a^2 XY L^2}}{2K_a Y} \quad (1)$$

where $X = [\text{fullerene}]_{\text{total}}$, $Y = [\mathbf{2}]_{\text{total}}$, and $L = \Delta\delta_{\text{max}}$ (i.e., $\Delta\delta$ at 100% complexation). Values of K_a and L were obtained from the nonlinear regression using the curve-fitting tools of Origin v.8.5 (Northampton, MA).

Isothermal Titration Calorimetry. ITC experiments were performed using a Microcal-GE (Northampton, MA) VP-ITC. Titrations were typically done at temperatures ranging from 278 to 323 K and involved overfilling the ITC cell with ~ 1.5 mL of fullerene solution (C_{60} or C_{70}) and adding as many as 20 injections ($14 \mu\text{L}$ each) of the titrant solution of **2**. Typically, three replicate measurements were performed. The raw calorimetric data were corrected for the heat of dilution of **2** and fullerenes by subtracting the heats from the appropriate blank titrations even though these heats were negligible in comparison to the binding interaction heats. The corrected ITC titration results were fit with a nonlinear regression algorithm using the CHASM ITC data analysis program developed in our laboratory and assuming a 1:1 inclusion complex model.¹⁵

Atmospheric Pressure Photoionization Mass Spectrometry. APPI-MS experiments were carried out on a Bruker (Billerica, MA) MicrO-TOF-Q mass spectrometer. Data acquisition was set to operate in positive ion mode. All experiments were performed in 99.99% anhydrous toluene. The fullerene solutions were prepared at a concentration of approximately $100 \mu\text{M}$, while the solutions of the buckycatcher were prepared at a concentration as high as $300 \mu\text{M}$. The APPI-MS samples were prepared by mixing the solutions to yield a mixture containing a 2-fold excess of **2**. The MS capillary voltage was set to +4500 V, dry N_2 gas flow was adjusted to 12 L min^{-1} at 453 K, and the samples were directly infused into the MS by using a kD Scientific syringe pump set to a flow rate of $200 \mu\text{L/h}$. Data processing was performed by using the Bruker Daltonics Data Analysis program.

RESULTS

Upon the addition of C_{60} or C_{70} to a solution of the buckycatcher, several proton NMR peaks of **2** exhibit measurable changes of their chemical shifts. The Job plot constructed for one of the corannulene pincer protons is shown in Figure 1. Following the changes in chemical shift and using the method of continuous variation, the maximum change in chemical shifts is observed at or near a mole fraction, $[2]/([2] + [C_{60}])$, of 0.5. This is consistent with a saturation stoichiometry of 1:1 for formation of the $C_{60}@2$ complex. Similar results were obtained for other protons exhibiting measurable chemical shift changes upon titration. Using the same Job plot analysis, the 1:1 stoichiometry was also determined for the formation of the $C_{70}@2$ complex in deuterated toluene and chlorobenzene.

1:1 complex stoichiometry was also detected in the gas phase by APPI mass spectrometry experiments. Figure 2 shows the

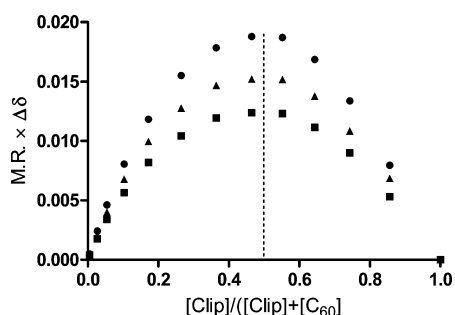


Figure 1. Job plot constructed from NMR titrations of **2** with C_{60} in toluene. Values of the [molar ratio $\times \Delta\delta$] are plotted vs the mole fraction of **2** at 288 K (\bullet), 298 K (\blacktriangle), and 308 K (\blacksquare).

APPI mass spectra obtained for each of the following chemical species in toluene: C_{60} , C_{70} , the buckycatcher **2**, and the $C_{60}@2$ and $C_{70}@2$ 1:1 inclusion complexes.

Panels A, B, and C of Figure 2 show the APPI mass spectra for solutions containing the single chemical species, C_{60} , **2**, and C_{70} , respectively. Panels A and C show only a single peak, e.g., the $C_{60}^{+1\cdot}$ and $C_{70}^{+1\cdot}$ parent fullerene radical cations, respectively. Panel B exhibits a spectrum with two notable m/z peaks with masses of 748.2 (major) and 1497.5 $g\ mol^{-1}$ (minor), corresponding to the monomeric buckycatcher and its self-associated dimer. The APPI mass spectrum for a mixture containing an excess of **2** (ca. 2:1) in addition to C_{60} is shown in panel D. The four peaks observed have m/z values of 720.0, 748.2, 1469.2, and 1497.5 $g\ mol^{-1}$. The peaks represent the radical cations of the free C_{60} , the free **2** (monomer), the 1:1 $C_{60}@2$ complex, and the buckycatcher dimer (2_2). Similarly, the APPI mass spectrum obtained for a mixture containing an excess of **2** (again ca. 2:1) and C_{70} shows four peaks with m/z values of 748.2, 840.0, 1497.5, and 1588.2 g/mol (Figure 2E). The peaks represent, respectively, the free **2** (monomer), the

free C_{70} parent anion, the buckycatcher dimer (2_2), and the 1:1 $C_{70}@2$ complex.

Isothermal titration calorimetry experiments were performed, wherein a dilute solution of the titrant (**2**) was added to a dilute solution of the fullerene titrate. A typical ITC thermogram for the addition of **2** to C_{60} in toluene at 298 K is shown in Figure 3. The solid line through the data points represents a nonlinear regression fit of the data to a thermodynamic model for the formation of a 1:1 inclusion complex. This analysis of the ITC data yields a complete set of thermodynamic parameters (K_a (or ΔG), ΔH , and $-T\Delta S$) for the formation of the fullerene@**2** complexes.

The thermodynamic data for the formation of the $C_{60}@2$ and $C_{70}@2$ complexes in toluene, chlorobenzene, and *o*-dichlorobenzene at 298 K are listed in Table 1. Similar thermodynamic data for the formation of these complexes in other solvents and at other temperatures are given in the Supporting Information (see Tables S1, S2, S3, and S4). The association constants at 298 K as determined in the ITC experiments are relatively weak, ranging from $K_a = 4600\ M^{-1}$ for the formation of $C_{70}@2$ in toluene to $K_a = 200\ M^{-1}$ for the formation of $C_{70}@2$ complex in *o*-dichlorobenzene. Two general trends are observed in these data. First, the association constants for C_{70} with buckycatcher (**2**) are typically greater than those for formation of the $C_{60}@2$ complexes. Second, complex formation becomes less favorable as the solvent becomes a better solvent for either the fullerene or the buckycatcher (**2**), resulting in a significant reduction in K_a for the formation of the fullerene@**2** complex in *o*-dichlorobenzene as compared to chlorobenzene and toluene. As seen in Table 1, at 298 K, the favorable free energy change, ΔG , for complex formation is principally the result of a favorable change in enthalpy, ΔH . With only one exception, $C_{70}@2$ in toluene at 278 K, the entropy term, $-T\Delta S$, for formation of the fullerene@**2** complexes is smaller than the enthalpy change in

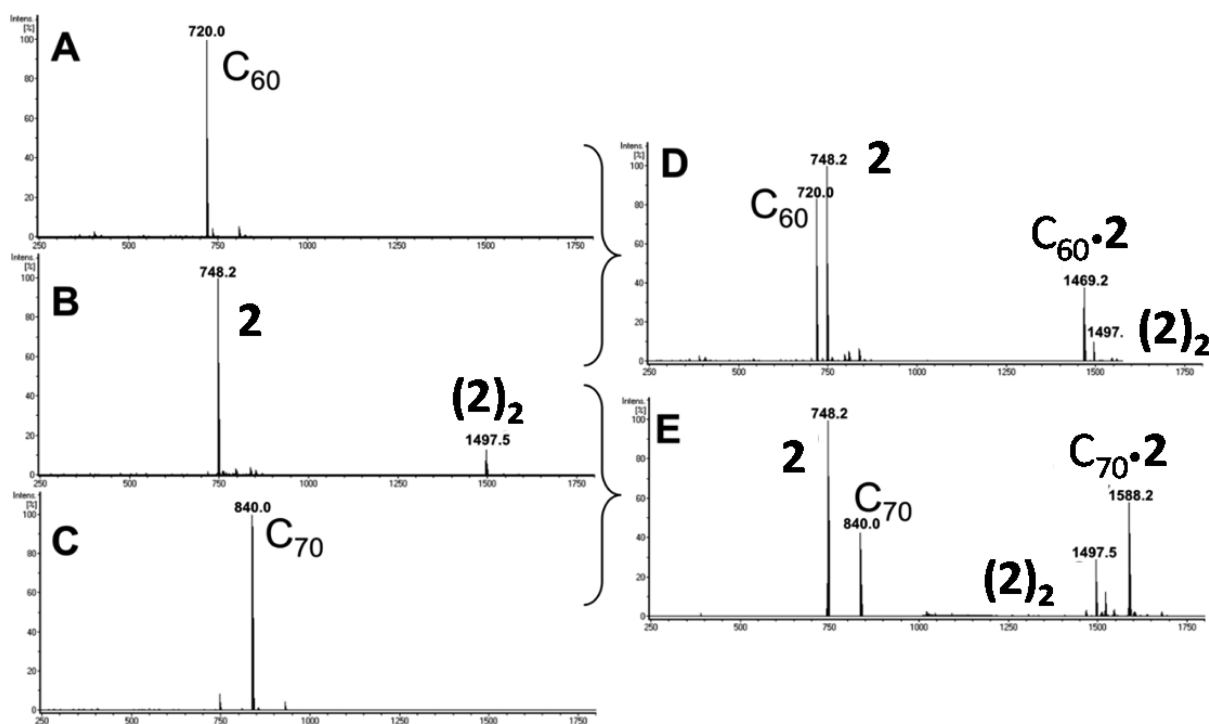


Figure 2. APPI mass spectra for toluene solutions containing C_{60} (A), **2** (B), C_{70} (C), and the mixtures of **2** with C_{60} (D) and C_{70} (E).

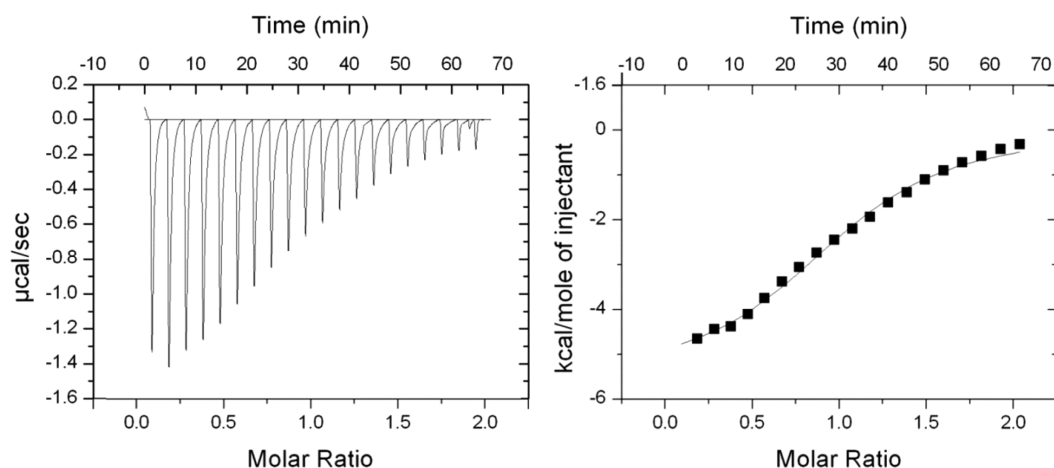


Figure 3. ITC data for the titration of **2** into C_{60} . The left panel shows the baseline-corrected raw ITC signal for a typical titration experiment in which 20 separate injections of dilute **2** titrant solution ($[2] = 0.7$ mM in toluene, injection volume = $14 \mu\text{L}$) were made into the ITC cell filled with the a dilute C_{60} solution ($[C_{60}] = 70 \mu\text{M}$ in toluene). The right panel shows ΔH for each injection (■) along with the best-fit nonlinear regression line (—) for a 1:1 inclusion complex model.

Table 1. Summary of the Thermodynamic Parameters Obtained from Fitting the ITC Titration Data Obtained at 298 K to a 1:1 Inclusion Complex Model^a

	toluene		chlorobenzene		<i>o</i> -dichlorobenzene	
	C_{60}	C_{70}	C_{60}	C_{70}	C_{60}	C_{70}
K_a	3200 ± 150	4600 ± 170	800 ± 10	900 ± 30	200 ± 20	200 ± 10
ΔG	-4.77 ± 0.03	-4.99 ± 0.02	-3.98 ± 0.01	-4.06 ± 0.02	-3.11 ± 0.09	-3.11 ± 0.03
ΔH	-4.61 ± 0.11	-2.95 ± 0.04	-4.03 ± 0.04	-3.76 ± 0.06	-1.87 ± 0.06	-1.97 ± 0.06
$-T\Delta S$	-0.16 ± 0.12	-2.04 ± 0.06	0.04 ± 0.04	-0.29 ± 0.07	-1.25 ± 0.15	-1.15 ± 0.06

^aValues for ΔG , ΔH , and $-T\Delta S$ have units of kcal mol^{-1} , and the errors listed are the standard deviations for a minimum of three replicate ITC titrations.

Table 2. Comparison of Measured K_a Values for Binding of C_{60} and C_{70} to **2 as Obtained from ITC and NMR Titration Experiments**

	288 K		298 K		308 K	
	toluene	chlorobenzene	toluene	chlorobenzene	toluene	chlorobenzene
C_{60}						
ITC	4200 ± 340	1060 ± 30	3200 ± 150	800 ± 10	1900 ± 50	720 ± 40
NMR	4300 ± 350	880 ± 80	2780 ± 80	520 ± 20	2100 ± 50	340 ± 10
C_{70}						
ITC	6500 ± 230	1106 ± 100	4600 ± 170	900 ± 30	3400 ± 560	752 ± 60
NMR	5920 ± 1200	1150 ± 140	3030 ± 330	920 ± 90	2220 ± 220	690 ± 120

every instance (see the Supporting Information, Tables S1, S2, S3, and S4). The values of the entropy term ($-T\Delta S$) for the formation of the $C_{60}@2$ complex in toluene and for the formation of the $C_{60}@2$ and $C_{70}@2$ complexes in chlorobenzene are close to zero. However, the values of the entropy term ($-T\Delta S$) for the formation of the $C_{70}@2$ complex in toluene and for the formation of the $C_{60}@2$ and $C_{70}@2$ complexes in *o*-dichlorobenzene range from -1.15 to -2.04 kcal mol^{-1} . Unexpectedly, the entropy changes for the formation of the $C_{60}@2$ and $C_{70}@2$ complexes are generally either zero or favorable for complex formation with notable exceptions for both complexes in 1,1,2,2-tetrachloroethane and $C_{60}@2$ in anisole.

The association constants, K_a , for formation of the $C_{60}@2$ and $C_{70}@2$ complexes in toluene- d_8 and chlorobenzene- d_3 at 288, 298, and 308 K, determined by ^1H NMR titration, are

compared with the respective ITC determined constants in nondeuterated solvents in Table 2.

The K_a values determined by two different methods are in good to excellent agreement with one another in both toluene and chlorobenzene over the temperature range of the study. The differences between the NMR and ITC determined ΔG values for the formation of $C_{60}@2$ complexes at 288, 298, and 308 K, respectively, are -0.01 , $+0.08$, and -0.06 kcal mol^{-1} in toluene and $+0.11$, $+0.26$ and $+0.46$ kcal mol^{-1} , respectively, in chlorobenzene. Similarly, the differences between the NMR and ITC based ΔG values for the complexation of C_{70} with **2** are -0.06 , $+0.22$, and $+0.26$ in toluene and -0.03 , $+0.01$, and $+0.06$ kcal/mol in chlorobenzene at 288, 298, and 308 K, respectively.

In order to gain a deeper insight into the solvent effects on the complexation, we performed the additional ITC titrations in anisole, 1,1,2,2-tetrachloroethane, and *o*-dichlorobenzene at temperatures ranging from 278 to 323 K. The data from these

ITC experiments can be found in the Supporting Information (see Table S4). In addition, the calorimetric enthalpy changes, ΔH_{cal} , for formation of the $C_{60}@2$ and $C_{70}@2$ complexes in toluene at 278, 288, 298, and 308 K were plotted versus temperature to yield an estimate of the heat capacity change, ΔC_p , for the formation of the two fullerene•2 complexes (see Figure S1, Supporting Information). The enthalpy changes for formation of both the C_{60} and C_{70} buckyball@buckycatcher (2) complexes are linearly dependent on T over the experimental temperature range. The estimated heat capacity changes for formation of the two host–guest complexes are -0.045 ± 0.005 and -0.028 ± 0.005 kcal mol⁻¹ K⁻¹ for the $C_{60}@2$ and $C_{70}@2$ complexes, respectively. It is clear that the two ΔC_p values observed in toluene are significantly different.

DISCUSSION

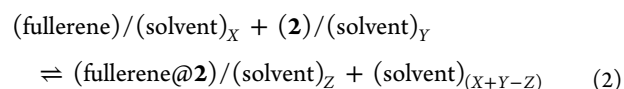
In this study, we have used ITC methods to develop a complete thermodynamic description (K_a or ΔG , ΔH , and $-T\Delta S$) for the formation of C_{60} and C_{70} fullerene•buckycatcher (2) complexes. In general, the ITC values for K_a were in good to excellent agreement with the NMR K_a data. In addition to providing values for K_a , ΔG , ΔH , and $-T\Delta S$ for formation of these dispersion complexes, the ITC experiments provided estimates for the ΔC_p values for complex formation, and evidence for an unexpected enthalpy–entropy compensation effect in the temperature dependence of the free energy change. It is important to note that the ITC experiments reported here were only possible for these relatively weak complexes because the complex stoichiometry was determined in complementary NMR experiments and because we were able to work at reasonably high concentrations for both the fullerenes and the buckycatcher. In other words, we designed ITC experiments wherein we were able to measure the heats for the formation of the complex and were able to determine the K_a values from the curvature in the titration data. These conditions were met even for the systems exhibiting K_a values as low as 200 M⁻¹.

Stoichiometric information obtained from Job plot analysis of the NMR titrations clearly suggests a saturation stoichiometry of 1:1 for both the C_{60} and C_{70} inclusion complexes (Figure 1). These results are in agreement with the previously reported crystallographic structure for the 1:1 inclusion complex of $C_{60}@2$ formed in the solid state.⁸ Also, the expected 1:1 inclusion complexes of the fullerenes and buckycatcher were observed in the APPI mass spectrometry experiments. Although formally possible, and predicted by MM calculations to be quite stable (at least in the gas phase), the 2:1 complex 3 was not detected in the APPI MS experiments. In addition, Job plots based on the NMR titration indicate that complex 3 does not exist in measurable amounts in toluene or chlorobenzene solutions, at least in the studied concentration ranges.



In addition to the expected 1:1 inclusion complexes of 2 with fullerenes, APPI experiments indicate the presence of small amounts of homodimers of the buckycatcher (Figure 2). Indeed, the dimeric head-to-head structure 4 was recently

found in the crystals of buckycatcher grown by high-vacuum sublimation and a very substantial gas-phase binding energy for the dimer was calculated by the dispersion-corrected DFT methods.^{16,17} However, as described in the Methods section, the ITC measured heat of dilution of 2 was negligible in comparison to the heats of binding to either fullerene. Also, we did not observe any measurable change in the ¹H NMR chemical shifts of 2 upon dilution in the concentration ranges studied in both deuterated toluene and chlorobenzene. We therefore conclude that the thermodynamics of association represents the formation of the solvated 1:1 fullerene@2 complex from the solvated fullerene and solvated 2. The reaction scheme for formation of the inclusion complex is shown as eq 2 below:



It is important to note that the solvation of the (fullerene@2) complex refers to the number of solvent molecules associated with the complex (Z) which would be expected to be different than the total number of solvent molecules involved in the solvation of the free fullerene and buckycatcher molecules ($X + Y$). The last term in the equation, $(\text{solvent})_{(X+Y-Z)}$, reflects the net number of solvent molecules lost, $(X + Y - Z) > 0$, upon fullerene@2 complex formation.

In previous studies, we reported NMR titration derived K_a values for the association of both C_{60} and C_{70} with the buckycatcher (2) in toluene-*d*₈ at ambient temperatures. The reported K_a values were 8600 ± 500 M⁻¹ for formation of $C_{60}@2$ complex and 6800 ± 400 M⁻¹ for formation of $C_{70}@2$ complex, relating to ΔG of -5.3 and -5.1 kcal/mol, respectively.^{8,9} The analogous ITC determined ΔG values reported in this study are -4.8 and -5.0 kcal mol⁻¹, respectively (Table 1). Since the difference in the case of $C_{60}@2$ is larger than the expected error in the ITC experiments, we decided to repeat the NMR titrations. We speculated that any real differences in the ΔG values obtained in the ¹H NMR and ITC titrations could be attributed to the very low solubility of the fullerene@2 inclusion complexes in toluene. In an attempt to resolve the differences between the results of the previous ¹H NMR results and the current ITC results, the ¹H NMR was repeated in toluene-*d*₈ at lower concentrations for both fullerenes and 2. Also, the NMR probe temperature was better controlled throughout the NMR titrations. The latest NMR derived K_a values for the formation of $C_{60}@2$ and $C_{70}@2$ at 298 K in toluene are 2780 ± 80 and 3030 ± 330 M⁻¹, respectively, in a much better agreement with the ITC K_a values. More importantly, we now find that in toluene the buckycatcher binds C_{70} with a slightly higher affinity than it binds C_{60} (see Table 1). However, it must be noted that the small preference for binding of C_{70} in toluene (-0.2 to -0.3 kcal mol⁻¹, depending on temperature) practically disappears in the other solvents used in this study, typically exhibiting a difference in ΔG of less than ± 0.1 kcal mol⁻¹ for formation of the $C_{60}@2$ and $C_{70}@2$ complexes.

As noted in the Results section above, the entropy term, $-T\Delta S$, for formation of the fullerene•2 complexes was typically observed to be either negligibly small (e.g., C_{60} and C_{70} in chlorobenzene) or favorable for complex formation (e.g., -2.9 kcal mol⁻¹ for C_{70} in toluene at 278 K to -1.9 kcal mol⁻¹ for C_{70} in toluene at 308 K). This is rather surprising considering the strongly destabilizing entropy contributions predicted by

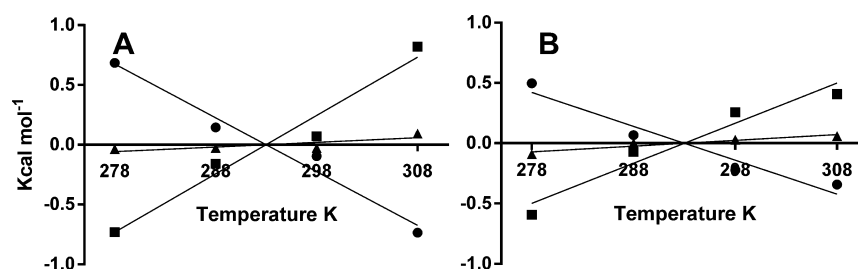


Figure 4. Normalized values for the thermodynamic parameters ($\Delta G - \Delta G_{ave}$) (▲), ($\Delta H - \Delta H_{ave}$) (●), and ($-T\Delta S + T\Delta S_{ave}$) (■) for the formation of the fullerene **2** complexes in toluene plotted at four different temperatures 278, 288, 298, and 308 K. Panel A shows the thermodynamic data for formation of the C₆₀@2 complex. Panel B shows the thermodynamic data for the formation of the C₇₀@2 complex.

the computational models for the association both in the gas phase and in toluene solution.^{10,11} A few unfavorable or positive values for $-T\Delta S$ for formation of the fullerene•**2** complexes were observed (e.g., for both fullerenes in 1,1,2,2-tetrachloroethane (ca. +1.3 kcal mol⁻¹) and for C₆₀ in anisole (+1.8 kcal mol⁻¹)). A recent paper by Barnes et al. reported small positive $-T\Delta S$ values of +0.6 to +2.5 kcal mol⁻¹ for the formation of PAH@ExBox⁴⁺ inclusion complexes in acetonitrile.¹⁸ The differences between Stoddard's work and the present study can be attributed to differences in the structure of the guest molecules (e.g., fullerenes vs PAHs), differences in the structure and charge of the host molecules (**2** vs ExBox⁴⁺), and of course the solvent, acetonitrile.

Entropy changes observed for complex formation (ΔS_{exp}) are often decomposed into a change in the configurational entropy (ΔS_{conf} , associated with the host–guest motions only) and a change in solvation entropy (ΔS_{solv}),¹⁹ as shown in eq 3. The latter term is related to motions of the solvent averaged over all possible host–guest conformations.

$$\Delta S_{exp} = \Delta S_{conf} + \Delta S_{solv} \quad (3)$$

The configurational entropy term can be estimated by summing the rotational and vibrational gas phase entropic contributions. On the basis of harmonic frequency calculations, Grimme predicted that the ΔS_{conf} should be very unfavorable for formation of the C₆₀@2 and C₇₀@2 complexes at 298 K (with $-T\Delta S$ values of +14.8 and +15.6 kcal mol⁻¹ for C₆₀ and C₇₀, respectively).¹¹ Similar entropy destabilization of the C₆₀@2 complex in the gas phase had previously been predicted by Zhao and Truhlar.¹⁰ Using the COSMO-RS solvation model to provide solvation free enthalpies, the solvation entropy, $-T\Delta S_{solv}$, contributions to the overall entropy term free energy were estimated to be -9.9 and -10.3 kcal mol⁻¹ for the formation of C₆₀@2 and C₇₀@2 complexes at 298 K, not exothermic enough to override the strongly endothermic ΔS_{conf} contribution.¹¹

There are at least two limitations to this approach for calculating the overall entropy change, ΔS_{exp} , for formation of these complexes. First, the COSMO-RS solvation model does not implicitly include solvent molecules, and even with implicit solvent molecules and molecular dynamic calculations, a quantitative assessment of solvation effects is by no means routine (e.g., see Moghaddam et al.).²⁰ Second, as reported by Grimme, this model yields free solvation energies, and the corresponding enthalpies and entropies calculated from their temperature dependence are sometimes used for analysis purposes but they do not represent the fundamental quantities.¹¹ The total entropy changes, $-T\Delta S$, as calculated by Grimme's model for the formation of the C₆₀@2 and C₇₀@2

complexes are +4.9 and +5.2 kcal mol⁻¹, suggesting a substantial destabilization entropy for both complexes in toluene at 298 K.¹¹ In contrast, the ITC determined $-T\Delta S$ values for the formation of both complexes in toluene at 298 K are both negative (-0.2 and -2.0 kcal mol⁻¹, respectively, see Table 1). These experimental $-T\Delta S$ values indicate at least modest entropic stabilization of the fullerene@2 complexes in toluene at 298 K. A reasonable assumption is that the calculated gas-phase ΔS_{conf} values are accurately estimated but the ΔS_{solv} contributions are substantially underestimated by the COSMO-RS continuum solvation model. Grimme also speculated that the calculated free energy changes, ΔG values, for formation of the C₆₀@2 and C₇₀@2 complexes in toluene are more negative than observed experimentally due to the poor performance of the COSMO-RS solvation model in predicting ΔS_{solv} for a nonpolar solute in a nonpolar solvent.¹¹

The heat capacity changes, ΔC_p , for formation of fullerene@2 complexes in toluene were determined from the slope of the linear regression lines in plots of ΔH_{cal} versus temperature from 278 to 308 K (see Figure S1, Supporting Information). The ΔC_p values for formation of both the C₆₀@2 and C₇₀@2 complexes are -0.045 and -0.028 kcal mol⁻¹ K⁻¹. These small negative values for ΔC_p indicate that the fullerene•2 complexes are somewhat less structured than the free fullerene and free **2**. The observation of a negative heat capacity change is typically attributed to the release of solvent molecules upon complex formation. In the fullerene buckycatcher system, some solvent molecules must be expelled from the interacting surfaces of the fullerene and the cleft of the buckycatcher with the net negative change in ΔC_p resulting from the net loss of solvent from the complex vs the free fullerene and free buckycatcher molecules (eq 2). Similar heat capacity effects were observed earlier for the complexation of various guests by macrocyclic cyclophane hosts in CDCl₃.²¹ The more negative ΔC_p value for formation of the C₆₀@2 complex (-0.045 kcal mol⁻¹ K⁻¹) vs the ΔC_p value for formation of the C₇₀@2 complex (-0.028 kcal mol⁻¹ K⁻¹) in toluene suggests that C₆₀ may fit better into the buckycatcher pocket and that more toluene is released in the formation of the C₆₀ complex than for formation of the C₇₀ complex.

Thermodynamic data obtained from fitting ITC experiments for the addition of **2** into either C₆₀ or C₇₀ solutions performed at several different temperature ranging from 278 to 308 K in toluene are plotted in Figure 4.

The changes in the free energy change, $\delta\Delta G$, for fullerene@2 complex formation over the temperature range 278–308 K are very small. For example, the change in the free energy change, $\delta\Delta G$, for the formation of the C₆₀@2 complex at 308 K vs 273 K is less than +0.1 kcal mol⁻¹ and less than +0.2 kcal mol⁻¹ for

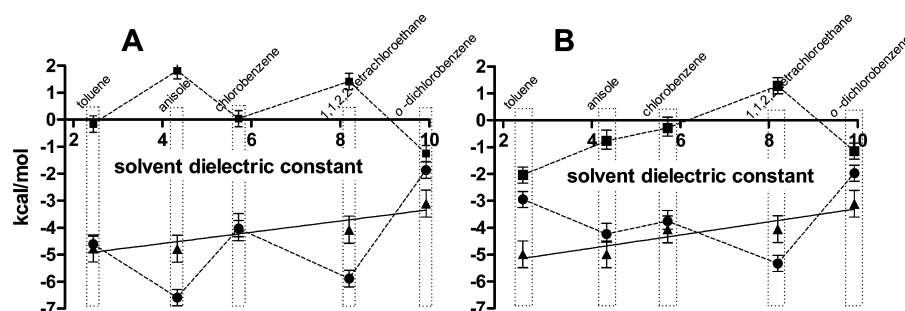


Figure 5. Enthalpy–entropy compensation for the formation of the (A) $C_{60}@2$ and (B) $C_{70}@2$ complexes, respectively. The thermodynamic parameters for fullerene@2 formation, ΔG (\blacktriangle), ΔH (\bullet), and $-T\Delta S$ (\blacksquare), are plotted as a function of solvent dielectric constant for five different organic solvents at 298 K.

formation of the $C_{70}@2$ complex at 308 K vs 273 K. Variations in the enthalpy and entropy changes for the formation of the fullerene@2 complexes are 5–10 times larger (ca. 1–1.5 kcal mol⁻¹) over the same temperature range. The changes in ΔH and in $-T\Delta S$ have opposite signs and approximately compensate one another over this temperature range, resulting in a $\delta\Delta G/\delta T$ value of almost zero. Enthalpy–entropy compensation as brought about by changes in temperature has only infrequently been observed or reported for reactions taking place in organic solvents.^{22–30} Referring to the extensive enthalpy–entropy compensation literature for reactions taking place in aqueous solution, we are not surprised by this result, since the origin of the compensation phenomenon is typically attributed to changes in solvation.^{31–41} The formation of fullerene@2 complexes must involve solvent removal from the interacting surfaces of the associated fullerene guest and the buckycatcher host pocket as well as solvent reorganization around the complex.

It was noted in the Results section that fullerene@2 complex formation becomes less favorable in solvents where the solubility of the fullerene or **2** is greater, presumably underlining the importance of any desolvation penalty. To further explore the nature of this observation, ITC results obtained in five different solvents (toluene, anisole, chlorobenzene, 1,1,2,2-tetrachloroethane, and *o*-dichlorobenzene) at 298 K are compared. These thermodynamic data which can be found in Table 1 and in the Supporting Information (see Table S4) are plotted as a function of solvent dielectric constant in Figure 5. Again, we observe enthalpy–entropy compensation in which the free energy change for complex formation is less dependent on the solvent properties (e.g., polarity, hydrogen bonding, dielectric constant, etc.) than is either the enthalpy or entropy change. In fact, while the free energy changes for formation of the fullerene@2 complexes are observed to vary linearly with the solvent dielectric constant, becoming 1.5–2 kcal mol⁻¹ less favorable in *o*-dichlorobenzene than in toluene, both the enthalpy and entropy changes vary unpredictably while exhibiting a high degree of compensation. In effect, every change in ΔH is opposed by a compensating change in $-T\Delta S$. The explanation for this phenomenon must reside in the fact that complex formation proceeds with the release of solvent from the fullerene@2 complex.

While the mechanism of enthalpy–entropy compensation remains uncertain, it is obvious that there must be a linear relationship between ΔH and $T\Delta S$ for those systems where this phenomenon is observed. Linear equations, like eq 4, have been used to evaluate the degree of compensation:

$$T\Delta S = \alpha\Delta H + C \quad (4)$$

The slope, α in eq 4, approaches a value of 1.0 for perfect compensation, and C represents the inherent stability of the complex, i.e., ΔG for the reaction with $\Delta H = 0$.⁴²

As shown from the linear regression fit of the thermodynamic data in Figure 6, there is a reasonable linear correlation

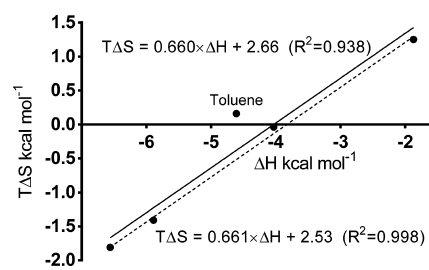


Figure 6. Plot of the $T\Delta S$ value vs the ΔH value for formation of the $C_{60}@2$ complex in five different solvents at 298 K. The data points from left to right correspond to anisole, 1,1,2,2-tetrachloroethane, toluene, chlorobenzene, and *o*-dichlorobenzene. The broken line shows the correlation for the four solvents with the toluene data omitted.

between ΔH and $T\Delta S$ ($R^2 = 0.94$), with a slope (α) of 0.660 and an intercept ($T\Delta S_0$) of 2.66 kcal mol⁻¹ for the formation of the $C_{60}@2$ complex in the five solvents sampled. If the toluene point is not included in the fit, the slope remains unchanged ($\alpha = 0.661$), the value for $T\Delta S_0$ changes from 2.66 to 2.53 kcal mol⁻¹, and the correlation coefficient for the linear fit is improved, $R^2 = 0.998$. The slope indicates that 66% of the change in enthalpy is canceled out (or compensated) by an opposite change in the entropy term. The value of α ($\alpha = 0.66$) determined here for the formation of the $C_{60}@2$ inclusion complexes is very similar to the values found by Inoue and Wada for the quinine@porphyrin receptor (0.60) and pyridine@metalloporphyrin (0.61) inclusion complexes in organic solvents.⁴² These moderate values of α have been interpreted to indicate that only moderate conformational changes are taking place in the host molecule. The positive $T\Delta S_0$ value (2.7 kcal/mol) indicates that the ΔS term for desolvation is favorable for formation of the inclusion complexes in the studied solvents. This seems to be consistent with desolvation of the buckycatcher pocket (the loss of 1–2 molecules of solvent, see our X-ray studies of the solvates of **2**)¹⁷ and the removal of some of the solvent molecules from the first coordination (solvation) sphere of the fullerene (probably another 2–4 molecules). The negative ΔC_p values discussed

earlier for the formation of the fullerene@2 complexes are consistent with the loss of 4–7 solvent molecules.

CONCLUSION

Detailed NMR and ITC titration studies provided a set of thermodynamic data for the formation of C₆₀@2 and C₇₀@2 inclusion complexes over a 30 K temperature range and in five different solvents. The formation of these host@guest inclusion complexes is typically enthalpically driven. In contrast with the predictions based on the existing solvation models, the entropy contributions are typically either stabilizing or close to zero, with the notable exception for both fullerenes in 1,1,2,2-tetrachloroethane and for C₆₀ in anisole. Enthalpy–entropy compensation effects were observed at different temperatures and in different solvents. “Better” solvents for fullerenes significantly decrease their association with the buckycatcher, an effect which is not predicted by the COSMO-RS solvation model. Relatively small but significant heat capacity effects were found with ΔC_p for formation of C₆₀@2 and C₇₀@2 complexes, –45 and –28 cal mol^{–1} K^{–1}.

The thermodynamic data for these prototypical large dispersion-driven supramolecular systems should be invaluable to the further development and fine-tuning of computational methods and models for estimating the energetics of π – π interacting systems in solution. These data will be particularly important in predicting dispersion-driven complex formation in aromatic or π bonding solvents.

ASSOCIATED CONTENT

Supporting Information

Figure showing enthalpy change plotted as a function of temperature and tables showing thermodynamic parameters and NMR results. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: asygula@chemistry.msstate.edu

*E-mail: elewis@chemistry.msstate.edu

Notes

The authors declare no competing financial interest.

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