Structure Visualization of 4-DASPI–Cucurbituril Supramolecular Complex to Predict the Solvatochromic Shift of Absorption Spectrum

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Abstract

The study of supramolecular "host-guest" complexes in solutions is of fundamental and practical significance. The structures and formation enthalpy of supramolecular complexes for the 4-DASPI dye with two cavitands (cucurbit[6]uril and cucurbit[7]uril) have been obtained by the TDDFT quantum chemistry method with a camb3lyp basis. It was shown by visualization of the structures that the size of cucurbit[6]uril is too small and doesn't allow the dye chromophore to penetrate into the cavitand cavity while the dye stays in the ground state, but the formation of an external complex is possible. On the contrary, formation of an inclusion complex with the cucurbit[7]uril is energetically favorable, and the dye chromophore penetrates into the cavity. Visualization of the complex structure allows us to determine the chromophore position relative to the given cavitand cavity, and thus we can predict the changes in the dye spectra due to complexation. The theoretical results of the work are in good correlation with the experiment.

Keywords: organic dye, cavitand, supramolecular complex, inclusion complex, solvatochromic shift, heat of complex formation.

1. Introduction

The term "supramolecular chemistry" was introduced by J.-M. Lehn as "chemistry beyond the molecule". This interdisciplinary field of science standing at the intersection of chemistry, physics and biology describes formation of complexes as the result of association of two or more chemical particles bound together by non-covalent intermolecular forces. The main objects of supramolecular chemistry are molecular ensembles and devices. Such ensembles are constructed spontaneously under the acting of intermolecular forces. The supramolecular self-organization and self-assembly are the terms that describe the process of building such ensembles or complexes [1].

The study of supramolecular host-guest complexes in solutions is of fundamental and practical importance. For example, a protein molecule can be considered as a "host" molecule possessing an active center (site) that binds a small molecule-ligand ("guest") by noncovalent bonds. The study of the binding energy of a protein's active center to specific ligands is important in drug design. In addition to proteins, there are cavitands, which also have active sites. These organic molecules are often significantly smaller than proteins and have a binding center in the form of a nano-cavity.

The inclusion complexes in which a cavitand plays the function of the host molecule are interesting to research for a variety of reasons. On the one hand, relatively small cavitand molecules are easier to model than proteins, and they are useful for studying certain regularities of

binding of a "host" molecule to a "guest" molecule. On the other hand, the cavitands have unique chemical applications due to their ability to coordinate ions in solutions, trap tiny molecules, and operate as a type of nano-container. They also can be used for building molecular machines [2].

Studies of supramolecular cavitand-dye complexes have the special interest, since the interaction between "host" and "guest" in such a system is significantly manifested in the spectral characteristics of the system. The dye molecule properties are characterized by intensity of absorption and fluorescence spectra lying in the optical range wavelength region. The chromophore is the optically active component of the dye molecule that determines its spectrum properties. The electron density of the chromophore is affected by the molecular environment, which has an effect on the spectrum. When a dye molecule is placed in solution, a change in the maximum of the spectrum occurs, which is known as a solvatochromic shift. The positioning of the dye chromophore in the cavitand cavity also causes a reorganization of the dye spectrum: the spectral line shifts, and its width and intensity change.

If the cavitand is added to a water solution of the dye then its spectrum changes. That means there is the interaction of the dye and cavitand by supramolecular complex formation, because the dye spectrum varies with the change of dye's molecular environment. In our case, there is a shift in the maximum of the absorption spectrum due to a change in the distribution of electron density in the chromophore.

The structure of the supramolecular cavitand-dye complex can be determined by quantum-chemical computations. If the dye chromophore is placed into the cavitand cavity as a result of complex formation, the dye spectrum changes, as previously described. On the contrary, if the chromophore does not enter the cavity, the dye spectrum doesn't change. Therefore, visualization of the structure of the complex obtained by quantum-chemical methods allows us to assume before the experiment whether the spectrum will change during the formation of the complex [3].

The results of experiments on the formation of supramolecular complexes of cucurbit[7]uril [5-6] (short designation CB[7]) with three types of the dyes that have the same chromophore but different lengths of the ammoniumalkyl substituent (a group of atoms attached to the chromophore) are presented in [4]. It is demonstrated that the length of the substituent influences the length of the solvatochromic shift. Modeling of the complexes' structures revealed that this effect can be connected to the chromophore displacement relative to the cucurbituril cavity. The key atom of this chromophore is a positively charged nitrogen atom. It is energetically favorable for this key atom to take a position within the cavity near one of cucurbituril's two portals, where the negative charge is concentrated.

The spectrum shift is greatest when the key atom and a considerable portion of the chromophore are inside the cavity, i.e., outside the solvent. If the substituent does not permeate the cavity due to interference, then the spectral shift is practically absent. The chromophore inclusion into the cavity of cucurbituril affects its local environment and changes the energy levels of electronic transitions in the dye molecule. In general, this effect is caused by both specific and nonspecific interactions of the chromophore with the cavity and the solvent.

Thus, calculating the structure and energy of the dye-cavitand complex, as well as visualizing the position of the chromophore relative to the cavity, can predict the presence or absence of a solvatochromic shift in a solution containing the components of the supramolecular complex.

The structure and formation energy of the inclusion complexes of cucurbit[6]uril (short designation CB[6]) and cucurbit[7]uril (Figure 1) with the dye 4-DASPI [7] are investigated in this study (the corresponding complexes are commonly denoted as 4-DASPI@CB[6] and 4-DASPI@CB[7], respectively). In our recent work [4], the dye size was varied while the cavitand was the same. Here, we investigate the complexes of the 4-DASPI with cavitands that have different diameter and the same length.

Similar to the dyes mentioned in [4], the 4-DASPI chromophore (Figure 2) has a positively charged nitrogen atom that prefers to localize around the cucurbituril portals.
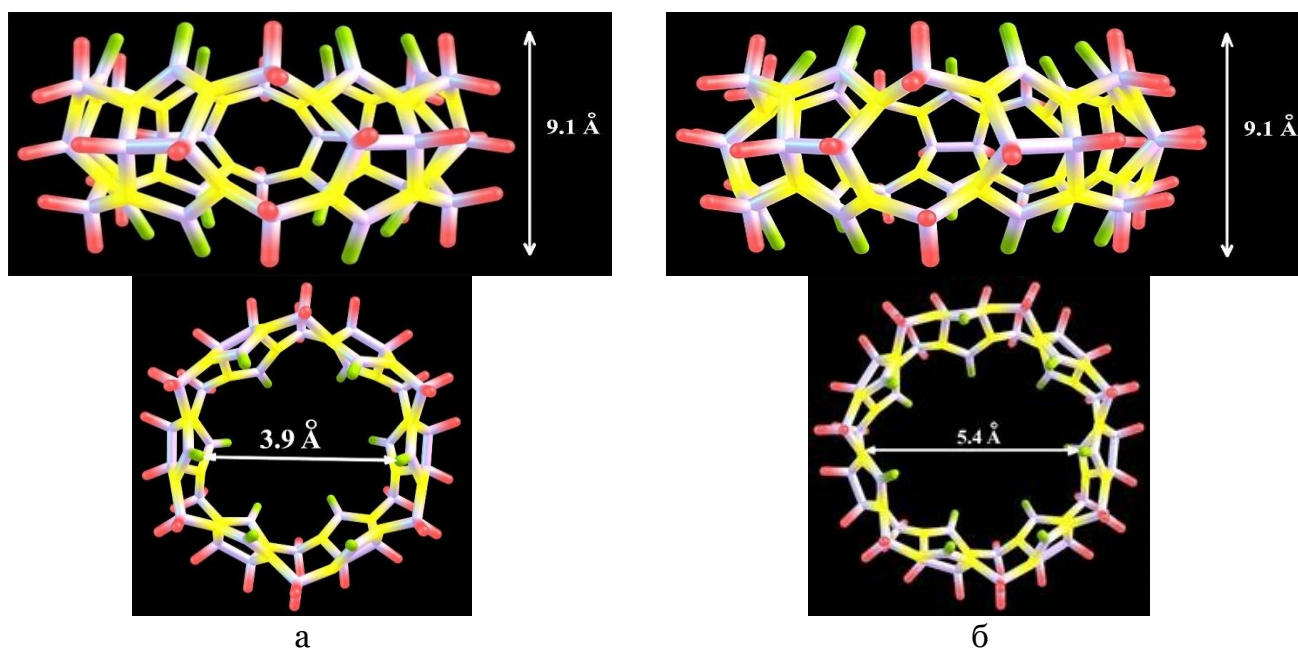
Figure 1 — Structure and size of cucurbit[6]uril (a) and cucurbit[7]uril (b) molecules

The experimental formulation of the complex formation problem includes adding 4-DASPI to the CB solution. Obviously, 4-DASPI is initially located outside the CB cavity. Collisions of 4-DASPI molecules with CB and interactions between them occur in solution due to thermal motion. These interactions result in the formation of inclusion complexes. The size of the energy (potential) barrier on the path of penetration of the 4-DASPI dye molecule into the CB cavity determines the possibility of complex formation.

Figure 3 shows the cavitand with the van der Waals radii of its constituent atoms.

The greater the energy barrier, the less probability of the complex formation under the effect of thermal fluctuations of energy in solution and the lower the concentration of such complexes in the state of thermodynamic equilibrium. In turn, the nature of the change in the optical spectrum of the solution is expressed by the relative number of complexes of one or more structures, since each form of complex corresponds to a specific spectral shift compared to the spectrum of the unbound dye 4-DASPI. It should be noted that the involvement of CB in the creation of the spectrum of the supramolecular complex is in the change of the dye spectrum. The intrinsic spectrum of CB is weakly represented in the considered spectral range.
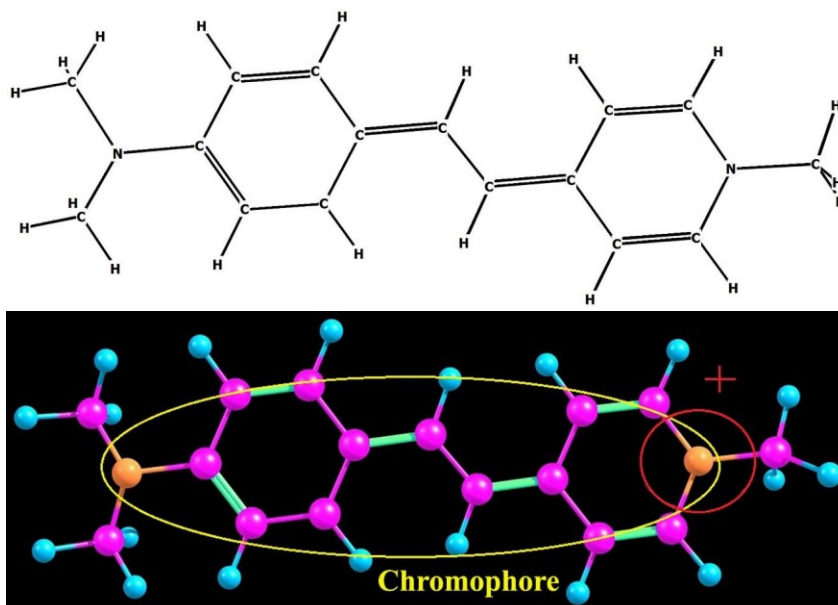
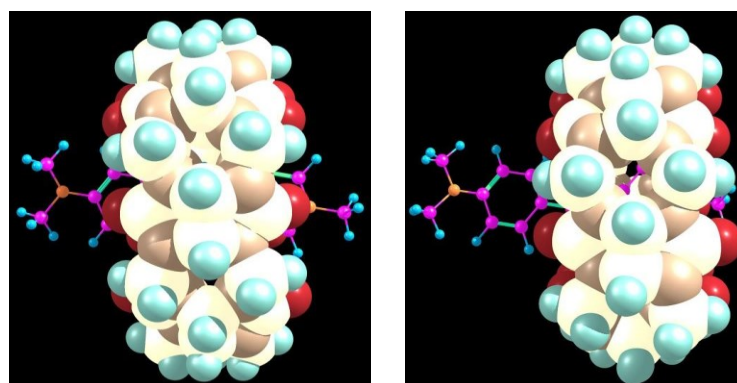Figure 2 — Structure of the dye 4-DASPI.

Figure 3 – Conformations of inclusion complexes of the 4-DASPI@CB[7] dye with visualization of van der Waals radii of cavitand atoms.

In the analyzed system, there are two ways of formation of the inclusion complex, depending on which side of the dye enters into the cavity. Thus, it is necessary to estimate the magnitude of the energy barriers to the formation of the complex along the possible ways. Quantum chemistry approaches can be used to make these estimations.

In this work, it is shown, the energy barrier of chromophore penetration into the cavity has a very large dependance on the cavity size The possible conformations of supramolecular complexes differ greatly for two types of the host molecule: cucurbit[6]uril (CB[6]) or cucurbit[7]uril (CB[7]). The visualization of these complexes gives the possibility to determine whether or not solvatochromic shift exists. Conclusions concerning solvatochromic shifts based on complicated visualization are compared with experimental data at the end of the work.

2. Calculation of structure and energy of supramolecular complexes

The enthalpy of complexation is a key indication of stable complex formation and can be estimated by the formula:

$$\Delta H_{Kp@CB} = H_{Kp@CB} - H_{Kp} - H_{CB}$$
$$\Delta H_{D@CB} = H_{D@CB} - H_{D} - H_{CB},$$

(1)

where $H_{D@CB}$ is the overall enthalpy of complex formation, H_D and H_{CB} represent the enthalpy of dye (D) and cucurbituril (CB), respectively. These characteristics can be determined using quantum chemistry methods.

To optimize the structures of complexes and their components, the quantum-chemical techniques PM3 and TDDFT in the ab initio molecular quantum chemistry software package GAMESS-US [8-10] were used. This software can compute a variety of molecular characteristics, ranging from basic dipole moments through frequency-dependent hyperpolarizations. The majority of calculations may be performed directly or in parallel way. At the beginning, the molecular structures were optimized by relatively fast MP3 method. Then it was corrected by a more accurate TDDFT method with the camb3lyp functional in the 6-311G (d, p) basis. The complexation energies were calculated using the TDDFT technique.

In the process of calculations of the enthalpy of interaction between CB and the dye that was positioned in different points relative to the center of mass of CB (Figure 4), multiple initial configurations of the components were used. The dye molecule was displaced along the axis going through the center of mass CB, as shown in Figure 4. Each calculation point is determined by the specific coordinate of the key atom of the 4-DASPI (positively charged nitrogen atom N) in relation to the CB cavity. Graphs given by Figures 5-6 visualize the calculated energy barrier that molecules need to overcome to form an inclusion complex.

The barrier configuration presented in Figure 5 shows that there are two high energy barriers to the formation of the 4-DASPI@CB[6] inclusion complex, each of which corresponds to a specific orientation of the dye relative to CB. In the first case, the dye enters the cavity from the side of the charged N atom (left barrier); in the other, it does the same with the opposite side containing two methyl groups (right barrier). With such barrier values, the formation of an inclusion complex in solution, which occurs due to thermal fluctuations, has an extremely low probability through both of the above reaction paths.
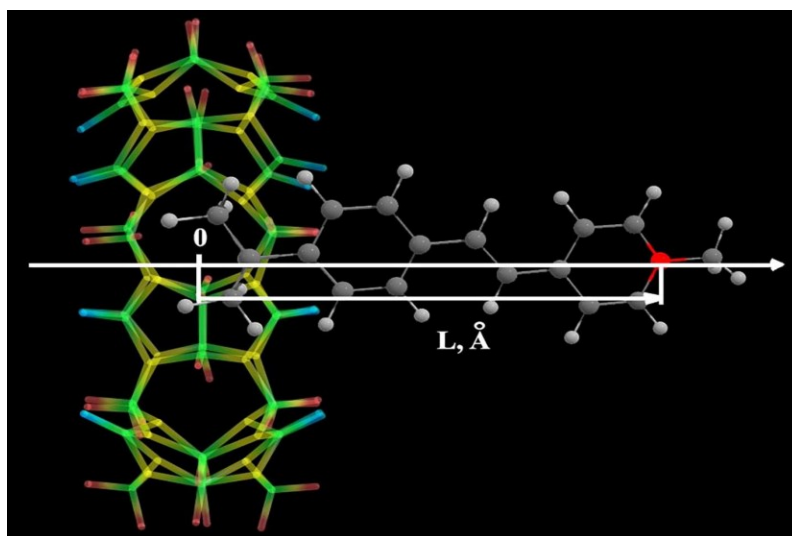

Figure 4— The coordinate axis, defining the mutual location of the dye and CB, goes through the center of mass of CB (point 0) perpendicular to its plane. The coordinate of the positively charged nitrogen atom (highlighted in red) determines the location of the dye.

On the contrary, the energy surface structure of the 4-DASPI@CB[7] complex illustrated in Figure 6 represents an open potential well. In this case, the inclusion supramolecular complex can be formed.
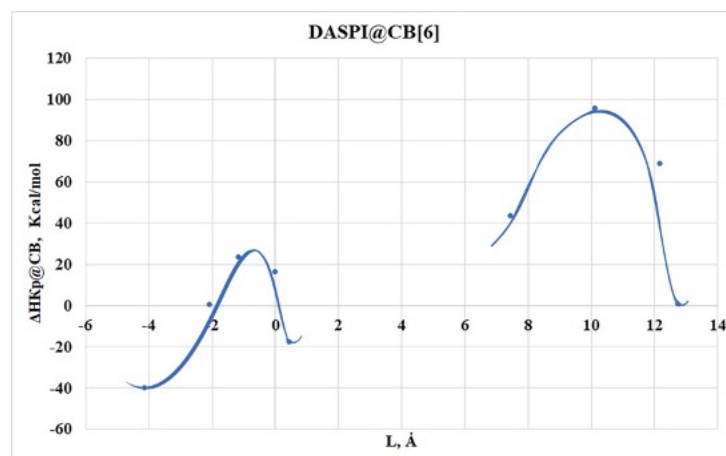
Figure 5 — Visualization of the energy barriers describing the interaction of 4-DASPI and CB[6]. Point 0 corresponds to the mass center of CB.

Indeed, as the experiment shows, the absorption spectrum of the 4-DASPI dye in an aqueous solution containing CB[6] does not change. This suggests that the chromophore does not enter the CB cavity because the potential barrier prevents the formation of the inclusion complex. On the other hand, the spectra of 4-DASPI changes dramatically in solution with CB[7]. This indicates the penetration of the chromophore into the cavity of the cavitand [11] and formation of inclusion complex.
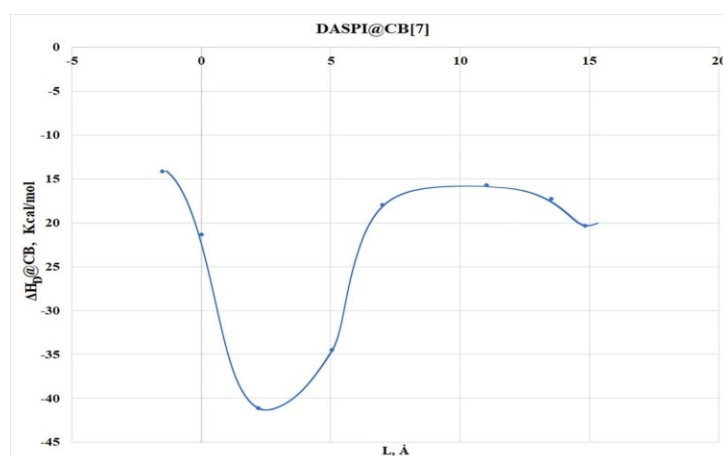

Figure 6 — Visualization of the energy barrier distribution describing the interaction of 4-DASPI and CB[7]. Point 0 corresponds to the center of mass of CB.

3. Visualization of supramolecular complexes

The optimal structures of supramolecular complexes were obtained as a result of quantum-chemical computations. In the 4-DASPI@CB[6] system, only an external complex can be formed by van der Waals forces and hydrogen bonds, in which the chromophore does not penetrate to the cavity of the cavitand. On the contrary, for the 4-DASPI@CB[7] system, as indicated in the previous section, the formation of an inclusion complex is possible. The dye molecule fits freely inside the CB[7] cavity, forming a pseudo-rotaxane structure of a supramolecular complex with no covalent chemical bonds between the components. Thus, the diameter of the cavitand cavity is the crucial factor of complex formation (Figure 7).
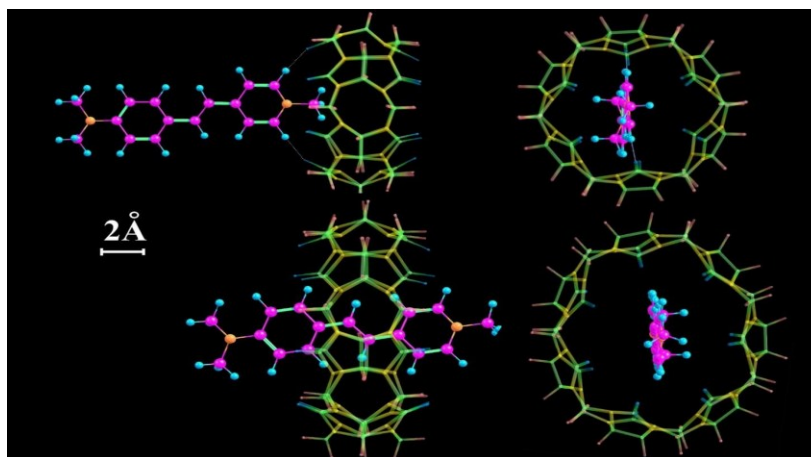
Figure 7 — Complexes of 4-DASPI dye with cucurbit[6]uril (top) and cucurbit[7]uril (bottom). The size of cucurbit[6]uril is too small to allow the dye chromophore in the ground state to penetrate the cavity.

The results of quantum chemical calculations were visualized using Chemcraft graphical software [12]. The Chemcraft application, developed in the Delphi programming environment, is good for visualization of GAMESS and Gaussian output files. The package has a user-friendly interface for viewing and evaluating computation files, as well as several utilities for creating new tasks.

4. Conclusions

It has been shown that visualization of the supramolecular complex structure optimized through quantum-chemical techniques allows to predict the presence or absence of a solvatochromic shift in the absorption spectrum associated with the complexation.

When the chromophore of a dye penetrates into the cavitand cavity (inclusion complex formation), the frequencies of electron-vibrational transitions change, and the dye spectrum shifts. The 4-DASPI@CB[7] inclusion complex is an example of such a system.

On the other hand, if the energy barrier prevents the chromophore from penetrating to the cavity, there is an external (exclusion) complex. Because the chromophore local molecular environment does not change in this scenario, the absorption spectra remain almost the same, without any shift, as it takes place in the case of the 4-DASPI@CB[6] complex.

These conclusions are supported experimentally by the fact that the absorption spectrum of the dye 4-DASPI in aqueous solution with cucurbit[6]uril does not differ from that of the free dye (the maximum of the spectrum at about 450 nm), whereas the absorption spectrum of the complex 4-DASPI@cucurbit[7]uril differs significantly from that of free 4-DASPI (the spectral maximum shifts to about 320 nm).

Acknowledgements

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