Computer simulation and spectroscopic study of inclusion complexes of cyclodextrins with luminescent porphyrins

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Abstract. Here we report a computational study of the structure, thermodynamic and spectroscopic properties of 1:1 and 2:1 inclusion complexes of luminescent porphyrins in β-cyclodextrin. Semiempirical PM6 (Parametric Method 6) calculation allowed the optimization of the structure of the complexes, showing that the inclusion in the CD cavity changes significantly the porphyrin ring planarity for the 2:1 complexes. Thermodynamic calculations evidenced that the inclusion complex formation is slightly endothermic and that it is a non-spontaneous process in the absence of water molecules. Finally the calculated spectra were found to be in very good agreement to previously reported experimental ones.

1. Introduction

Organic and organo-inorganic molecular materials with functional properties are commonly useful as sensitive elements in sensors and smart devices [1]. However the application of functional molecules face some limitations related to the dependence of the desired properties on the solid-state structure, not to mention the limited stability and difficulties in construction of devices [2]. For instance, the application of functional molecules in solid devices it is not possible if those molecules aggregate prior to deposition with loss of property. Thus structural evaluation of potential functional elements is an important step in the study of advanced materials.

A class of compounds useful in sensor and other devices, having spectroscopic, catalytic, and biological interest are the porphyrins, macrocyclic species derived from the porphine ring [3]. Porphyrins are common in nature, playing a significant role in biological processes such as dioxygen transport and activation and electron- and energy transfer [4]. Their biological function depends on the nature of the axial ligands as well as on the presence of a metal ion coordinated to the porphyrin center. Furthermore, the supramolecular approach may be used to assemble different building blocks rendering sophisticated porphyrin supermolecules with important catalytic, photochemical and electrochemical properties. In this context we can mention the tetraruthenated H2(3-TRPyP) porphyrins with luminescent and electrocatalytic properties, which were previously described by Araki and co-workers [5]. Those systems have been obtained by attaching four [RuII(bipy)2Cl] groups to the pyridyl substituents of meso-tetra(4-pyridyl)porphyrin and meso-tetra(3-pyridyl)porphyrin and its metallated derivatives [6]. These compounds display a rich electrochemistry and versatile catalytic and
photochemical properties, associated with the ruthenium–bipyridine and metalloporphyrin complexes [7].

In general porphyrins exhibit aggregation behavior in solution, which can be prevented by inclusion complex formation with cyclodextrins [8]. Complex formation takes place by non-covalent interactions, which form the basis of a sustainable approach widely employed in materials preparation due to the low energy cost and waste minimization [9]. Cyclodextrins (CD’s) are cyclic oligosaccharides able to form inclusion complexes by the accommodation of nonpolar molecules inside its hydrophobic cavity, in a process that modifies important properties of the guest species [10]. Water solubility, reactivity, stability, and optical properties are among the properties that can be controlled by inclusion in CD’s. One common target of this field is the modulation of spectroscopic properties by CD inclusion, which in this case is the basis of sensing process [11] A range of intermolecular interactions may be present in supramolecular structures, which can be evaluated currently by theoretical methods. Until the 1990’s the use of those methods to the study of supramolecular systems has been limited due to the large size of the supermolecules as well as the fact that such systems are often studied in aqueous solution [12]. This has made computational studies very time consuming and force the use of assumptions which were not always realistic. Nowadays novel theoretical methods have been developed allowing the suitable application to large systems such as those studied here [13]. However, significant limitations remain on theoretical studies, especially those related to the explicit consideration of the presence of water molecules owing to the large size of the macromolecular systems [13].

Thus the objective of the present work was to simulate the structure of inclusion complexes of tetraruthenated H2(3-TRPyP) porphyrins with cyclodextrins, as well as the spectroscopic and thermodynamic properties, pointing out the possibility of formation of those species using the semiempirical PM6 computational method. The calculated absorption spectra were compared to experimental data reported previously [5-7]. Previous efforts have been described for device construction employing those porphyrins.

2. Calculation details
All calculation were carried out at the restricted Hartree-Fock level (RHF) by using PM6 [14] semiempirical method implemented in the MOPAC 2007 software. COSMO (Conduct-like Screening Model) [15] solvation model was used (the relative permittivity was set 78.4) in order to take into account the effects of water. β-CD initial geometry was taken from the “Cambridge Structural Database” (CSD) with R-factor <5%, which indicates the high quality of the single crystal. The initial estimate of the porphyrin and of 1:1 and 2:1 (CD:porphyrin) inclusion complexes structures were generated from MM3 calculation in the Cache Worksystem 6.1. To estimate the charge transfer (induction) in the complexes, the individual net atomic charges obtained in calculation were summed up for estimation of the charge of the molecular fragments; β-CD and porphyrin. The electronic excited state calculations have been performed with the intermediate neglect of differential overlap/spectroscopic parametrization–configuration interaction singly replacements (INDO/S-CIS) method [16] implemented within the ZINDO program. The inclusion complex was held in the positions determined by each method. The line broadening of the calculated single transition energies and the intensities obtained from oscillator strengths were taken into account by fitting them to a Lorentzian line shape function with a half-maximum band width of 20–40 nm, which properly allows the comparison between the calculated and the observed absorption electronic spectra.

3. Results and Discussion
In figure 1 we show the molecular structure for β-CD modeled from crystallographic data and for H2(3-TRPyP). A previous study described the simulation of this structure using MM2 molecular mechanics method which is faster than more rigorous, time-consuming quantum mechanical methods. They employed ruthenium parameters described by Norrby and co-workers [17] and had to test the
method in simpler systems. Here we used PM6 quantum semiempirical method, which originally contains ruthenium parameters, finding a molecular structure for H2(3-TRPyP) that compared well to that described by Araki and co-workers [5]. In this structure, each Ru(bipy)Cl⁺ groups present at opposite corners of the porphyrin ring are oriented above the ring plane while the other two are oriented below the plane.

![Figure 1](image1.png)

**Figure 1.** Minimum-energy structures calculated with PM6 semiempirical method for β-cyclodextrin (a) and for H2(3-TRPyP) porphyrin (b), showing for the latter a front view and a side view from the ring.

Inclusion complexes with 1:1 and 2:1 CD:porphyrin stoichiometry, the latter more commonly observed for CD:porphyrin systems, were simulated and the minimum structures are shown in figure 2. Molecular modeling has shown that formation of both complexes is possible (thermodynamic study will be presented later) and that the porphyrin structure remains unchanged for the 1:1 complex, in contrast to the 2:1 complex for which the structure changes considerably. This can be more properly observed in the superposition of structures of the free and complexed porphyrin in both stoichiometries, figure 3. In the 2:1 complex, the planarity of the porphyrin ring is affected.

![Figure 2](image2.png)

**Figure 2.** Front view and view from the porphyrin ring plane
In order to better evaluate the structural changes upon complexation the porphyrin structures were superimposed fixing the positions of the hydrogen atoms of the porphyrin ring. Superposition of the porphyrin structures in the 1:1 complex simulated in the vacuum and considering a continuum medium with the water dielectric constant (implicit solvent consideration) shows that the orientation of only one Ru(bpy)Cl\(^+\) group changed significantly, with slight changes for other two groups and only one of the remaining unchanged in vacuum. The consideration of the implicit water medium had no effect on the porphyrin conformation.

When the porphyrin structures are superimposed for 2:1 complex, which is the dominating stoichiometry for porphyrin CD complexes, the orientation of all Ru(bpy)Cl\(^+\) changed significantly, in addition to a loss of planarity for the porphyrin ring. In this case the implicit solvent consideration was not possible for the complexes due to the high number of atoms. It is worth mentioning that this change is not reflected on the spectroscopic properties, which were preserved as we will see later.
The calculation of thermodynamic functions was also carried out using PM6 method. Table I shows the values of the final charges of the supermolecules after complex formation showing that there is charge transfer interaction between guest and host in the inclusion complex, where the porphyrin transfers charge to CD. This fact contributes for the stability of the inclusion complex. Also, when the calculation is carried out in water, the 1:1 complex has an increase in the porphyrin-CD charge-transfer degree. These observations suggest that the presence of water contributes to the complex formation.

**Table I: Final charge* for molecules in the inclusion complex**

|            | \(H_2(3\text{-TRPyP})\) | \(\beta\text{-CD}\) |
|------------|-------------------------|---------------------|
| In vacuum  | + 4.0259                | - 0.0259            |
| COSMO      | + 4.0331                | - 0.0331            |

*PM6 – net atomic charge. The initial charge of the porphyrin is +4.

Thermodynamic functions such as entropy and free energy were calculated in the 273 K to 298 K temperature range for the 1:1 and 2:1 complexes, considering the chemical reactions in vacuum for the optimized structures:

\[
\beta\text{-CD} + H_2(3\text{-TRPyP}) \rightarrow \beta\text{-CD} - H_2(3\text{-TRPyP}) \\
2\beta\text{-CD} + H_2(3\text{-TRPyP}) \rightarrow [\beta\text{-CD}]_2 - H_2(3\text{-TRPyP})
\]

Table 2 shows that both from \(\Delta S\) and from \(\Delta G\), the inclusion complex formation is non-spontaneous processes in the vacuum, as negative \(\Delta S\) and positive \(\Delta G\) values were found at different temperatures for both stoichiometries. However both the charge transfer calculation and solubility increase (not shown in this work) evidence the formation of the inclusion complexes in solution. As positive \(\Delta H\) values were found, the signal of \(\Delta G\), which would determine if the process is
spontaneous, would depend on the signal and magnitude of $\Delta S$ in the equation $\Delta G = \Delta H - T\Delta S$. The positive $\Delta H$ values probably resulted from the positive charges of the porphyrins, since the presence of counterions was not considered in this calculation. Concerning the $\Delta S$, in practice, the main driving force for the formation of inclusion complexes is the entropy increase caused by the release of water molecules originally present in the CD cavity, which were not considered explicitly in this work. The entropy change becomes less negative with increasing temperature, probably reflecting an increasing dynamic disorder of the molecular structure. Thus the calculation of thermodynamic functions pointing out nonspontaneous processes in vacuum reflects the absence of explicit water molecules in the calculation, whose consideration would demand a great deal of computational resource. Also the implicit solvent consideration doesn’t yield better results and the explicit water consideration for these large systems is still too resource-consuming.

| Parameter | 1:1 complex | 298 K | 273 K | 2:1 complex | 298 K | 273 K |
|-----------|-------------|-------|-------|-------------|-------|-------|
| $\Delta H$ / kcal mol$^{-1}$ | 2.25 | 2.37 | 11.60 | 12.24 |
| $\Delta S$ / cal mol$^{-1}$ | -69.84 | -69.42 | -118.86 | -116.62 |
| $\Delta G$ / kcal mol$^{-1}$ | 21.32 | 23.06 | 44.05 | 46.99 |

Finally the results of the calculation of absorption spectra for the 1:1 complex in the vacuum and implicit aqueous medium are shown in figure 5.

![Figure 5](image_url)

**Figure 5.** Calculated absorption spectra in vacuum and implicit aqueous medium (black and blue) for the 1:1 and 2:1 in vacuum (red) inclusion complexes.

It can be observed that the consideration of implicit aqueous medium had no effect at all on the spectrum of the 1:1 complex, as it is identical to the spectrum calculated in the vacuum. The band at 270 nm is assigned to a $\pi\to\pi^*$ transition from bpy ligands; the shoulder at 298 nm to a ligand field transition of RuII ions; the band at 380 nm is the Soret band characteristic of porphyrins. An interesting point is the absence in all spectra of a metal to ligand charge transfer band at 470 nm, observed experimentally by Araki and co-workers [5-7]. A comparison to the spectrum calculated for the 2:1 complex in vacuum shows that the intensity ratio of the $\pi\to\pi^*$ bpy to the Soret transitions changed slightly probably as a result of the structure distortion. Such changes are very subtle and it can be considered that the spectroscopic properties are practically preserved upon inclusion in CD cavity, evidencing that this process will not cause limitations to potential applications.
4. Conclusions
In conclusion it can be emphasized that the theoretical semiempirical study with PM6 method for the formation of inclusion complexes of the porphyrin H2(3-TRPyP) pointed out that the porphyrin structure is considerable changed in the 2:1 CD:porphyrin stoichiometry, in contrast to the 1:1 stoichiometry. Also the thermodynamic calculation carried out in the vacuum and considering an implicit aqueous medium indicated that the process is nonspontaneous, mainly due to the lack of explicit consideration of the water molecules responsible for the entropic contribution. This is in contrast to experimental evidences (not shown) of successful formation. Calculation of absorption spectra evidenced that for the 2:1 complex, the structural distortion of the porphyrin brought about by encapsulation causes modifications of the spectral profile.

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