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Review

# Molecular modeling investigation of para-nitrobenzoic acid interaction in β-cyclodextrin

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ABSTRACT

Geometry optimizations of para-nitrobenzoic acid (PNBA)/β-cyclodextrin complex were carried out using MM+, PM3 and density function theory B3LYP/6-31G*. Calculations were performed upon the inclusion complexation of β-cyclodextrin (CD) with neutral (PNBA1) and anionic (PNBA2) species of para-nitrobenzoic acid. The results obtained from both methods consistently indicate that the complex of PNBA2/β-CD (B) is significantly more favorable than the others energetically. The negative enthalpy changes calculated from the statistical thermodynamic calculation suggest that both the inclusion complexation is favored enthalpy-driven process. The geometry of the most stable complex shows that the aromatic ring is deeply self-included inside the hydrophobic cavity of β-CD and also intermolecular hydrogen bonds were established between host and guest molecules. This suggests that hydrophobic effect and hydrogen bond play an important role in the complexation process.



**Contents**



## 1. Introduction

Cyclodextrins (CDs) are water-soluble oligosaccharides composed of 6 (α), 7 (ß) and 8 (γ) units of glycopyranose linked by α (1→4) bonds, arranged in a truncated cone-shaped structure as shown in Fig. 1. They are obtained by enzymatic degradation of the starch. All the polar groups are located in the exterior of a relatively hydrophobic cavity [1–4]. This amphiphilic molecular structures of CDs form easily inclusion complexes with a lot of organic, inorganic and biological compounds without covalent bond and the resultant inclusion complexes can induce modification of the physicochemical properties of guest molecules (such as water solubility and solution stability) [5,6]. The most important driving forces in the inclusion complexes are electrostatic, Van der Waals, hydrophobic interactions, hydrogen bonding, release of conformational strain, exclusion of cavity-bound energy water and charge transfer interaction [7,8]. This property of CDs to form inclusion complexes became the subject of intense theoretical studies using molecular mechanics, molecular dynamics and quantum mechanical methods because the combination of experiment and theory leads to successful results in solving structural, energetic and dynamic problems [9–23]. Para-nitrobenzoic acid (Fig. 2) is used as intermediate functional dyes, pharmaceuticals, and medicines. However, it is also one of the serious organic contaminations. It is usually difficult to treat industrial waste and living sewage. In most cases, the complicated equipments are needed

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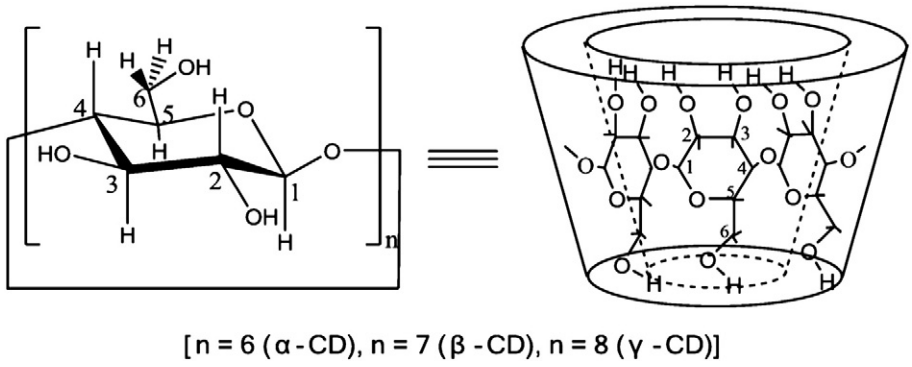


**Fig. 1.** Molecular structure of cyclodextrins.

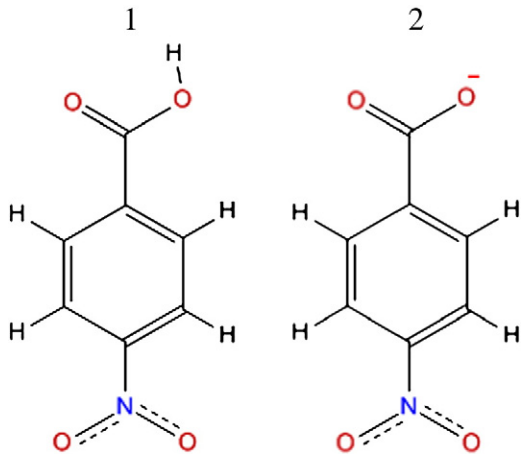


**Fig. 2.** Species form of PNBA (1 neutral and 2 anionic species of PNBA).

and cost much for the treatment of contaminations. To solve the problem, environmental scientists are striving their way to work out effective and economic methods to treat the pollutions. Cyclodextrins can increase the solubility of some contaminations reduce their toxicity, and catalyze their decomposition [24].

Recently, Zhi Fan et al. [25] have studied the encapsulation of PNBA/β-CD in the solid state and it was observed that the PNBA prefers to occupy most of the available space in the cavity, and to protrude with their polar COOH and $NO_2$ groups at hydroxyl group sides. On the other hand, the PNBA is maintained in positions to form hydrogen bonds with carboxyl groups and the surrounding hydroxyl groups.

To our knowledge, the complexation of CD with anionic specie of PNBA molecule has not yet been studied theoretically. So, the aim of this investigation is to study molecular mechanics, quantum mechanics PM3 and density function theory (DFT) methods the inclusion complex between neutral (PNBA1) and anionic (PNBA2) species of para-nitrobenzoic acid and β-CD with stoichiometry 1:1 specifically to determine its optimum geometrical structure, to describe the nature of intermolecular binding, the conformational changes of PNBA inside the β-CD cavity, the stability of the complex as well as the inclusion energetic of the formation process between the guest molecule and the host CD including thermodynamic parameters.

Since 1995, a great number of researches were focused on the study of inclusion complex of cyclodextrins by semi empirical methods AM1 and PM3 to obtain electronic properties and to have

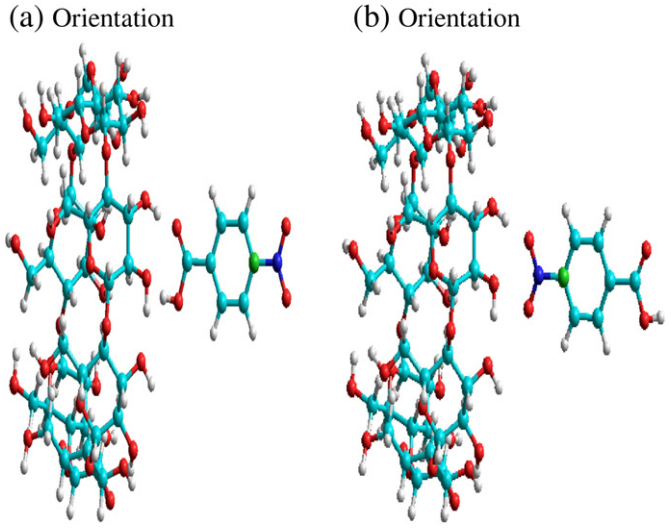


**Fig. 3.** Two possible orientations of PNBA in β-CD.

**Table 1**
The bond lengths, bond angles and dihedral angles of the crystalline β-CD and the PM3-optimized β-CD.

| | β-CD crystalline | β-CD PM3-optimized | Difference |
|---|---|---|---|
| *Bond lengths (Å)* | | | |
| $C_1$—$C_2$ | 1.527 | 1.557 | 0.030 |
| $C_2$—$C_3$ | 1.534 | 1.549 | 0.015 |
| $C_3$—$C_4$ | 1.532 | 1.557 | 0.025 |
| $C_4$—$C_5$ | 1.527 | 1.551 | 0.024 |
| $C_5$—$C_6$ | 1.534 | 1.547 | 0.013 |
| $O_5$—$C_1$ | 1.410 | 1.402 | −0.008 |
| $C_1$—$O_1$ | 1.426 | 1.412 | −0.014 |
| $C_2$—$O_2$ | 1.428 | 1.413 | −0.015 |
| $C_3$—$O_3$ | 1.431 | 1.411 | −0.020 |
| *Bond angles (°)* | | | |
| $C_1$—$C_2$—$C_3$ | 110.300 | 110.299 | −0.001 |
| $C_2$—$C_3$—$C_4$ | 109.370 | 109.056 | −0.314 |
| $C_3$—$C_4$—$C_5$ | 110.474 | 110.399 | −0.075 |
| $C_4$—$C_5$—$C_6$ | 110.518 | 111.170 | 0.652 |
| $O_6$—$C_6$—$C_5$ | 108.484 | 112.722 | 4.238 |
| $O_5$—$C_1$—$C_2$ | 110.451 | 112.449 | 1.998 |
| $O_2$—$C_2$—$C_3$ | 110.841 | 113.224 | 2.383 |
| $O_3$—$C_3$—$C_4$ | 108.285 | 111.638 | 3.353 |
| *Dihedral angles (°)* | | | |
| $C_1$—$C_2$—$C_3$—$C_4$ | −53.273 | −53.487 | −0.214 |
| $C_2$—$C_3$—$C_4$—$C_5$ | 56.087 | 54.081 | −2.006 |
| $C_3$—$C_4$—$C_5$—$C_6$ | −58.228 | −53.480 | 4.748 |
| $C_4$—$C_5$—$O_5$—$C_1$ | 62.167 | 54.940 | −7.227 |
| $C_5$—$O_5$—$C_1$—$C_2$ | −61.145 | −54.874 | 6.271 |
| $O_5$—$C_1$—$C_2$—$C_3$ | 55.214 | 53.444 | −1.770 |
| $O_2$—$C_2$—$C_3$—$C_4$ | −174.670 | −173.625 | 1.045 |
| $O_3$—$C_3$—$C_4$—$C_5$ | 175.478 | 171.268 | −13.79 |

more information about geometry of the complex. The results suggested that PM3 should be more advantageous than AM1 and give results which coincide with the experimental observations [26–38]. In 2000 some studies were carried out about the performances of AM1 and PM3 methods on CD systems. On the basis of AM1 and PM3 calculation results for some model compounds including hydroxyethyl ether and $\alpha$ (1–4) — glucobiose, it suggested that PM3 should be advantageous to AM1 in CD chemistry because PM3 can predict the O—H…O hydrogen bonds better than AM1. This proposal was supported by direct structure optimization of $\alpha$ and β-CD with AM1 and PM3, in which AM1 gave badly distorted geometries due to unreasonable hydrogen bonding, whereas PM3 reproduced the crystalline structures rather well.

In the present work, we wish to report the inclusion process of natural β-CD with neutral and anionic species of PNBA by molecular mechanics, quantum mechanics PM3 and density function theory (DFT) methods. The difference in energy was computed and the conformations of the formed stable complexes were analyzed. Our special interest is to give more information about the location of nitro and carboxylic groups compared to position of primary or secondary of hydroxyl of CD.

## 2. Computational method

All calculations were carried out using Hyperchem 7.51 [39] and Gaussian 03W version 6.0 [40] packages respectively for molecular and quantum mechanics methods.

The initial structures of both species of PNBA were constructed by module builder of Hyperchem then optimized with B3LYP method at

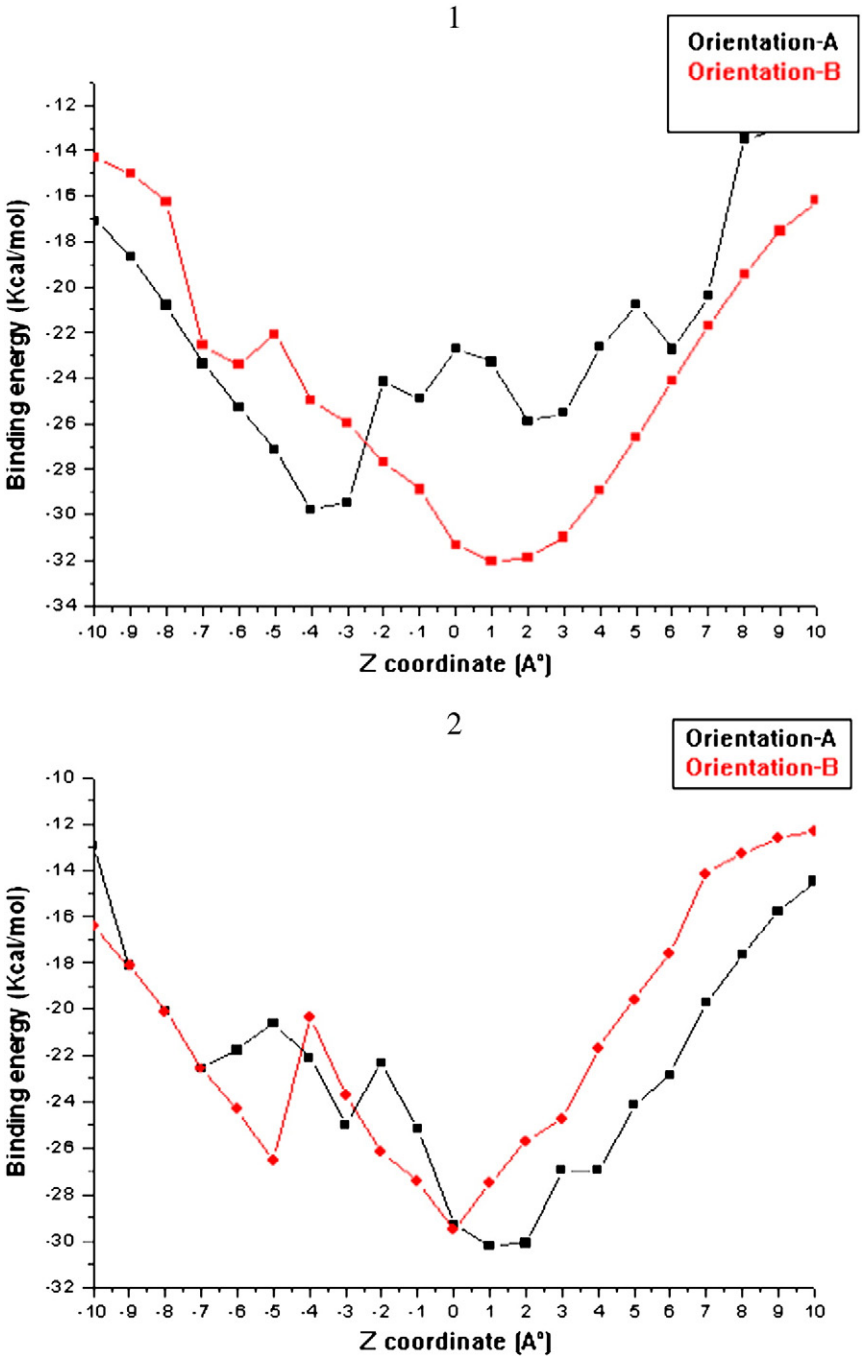


**Fig. 4.** Binding energies of the inclusion complexation of neutral and anionic species of PNBA into β-CD at different positions (Z) and for both orientations (1 neutral and 2 anionic species of PNBA).

6-31G* level (the charge −1 for anionic specie and 0 for neutral specie of PNBA).

The initial structure of β-CD is built with CS Chem3D Ultra (version 10, Cambridge software) from the crystal structure [41] and fully optimized by PM3 method without imposing any symmetrical restrictions.

For the construction of PNBA/β-CD complex, the glycosidic oxygen atoms of β-CD were placed onto the XY plane; their center was defined as the origin of the coordinate system. The primary hydroxyl groups were oriented pointing towards the positive Z axis. The guest molecule placed on the Z axis was allowed to approach the β-CD cavity from the large rim at a distance of 10 Å which separates the β-CD equatorial plane and the reference atom (C-6) in PNBA (Fig. 3).The inclusion process emulation was then achieved along the Z axis to −10 Å with a step of 1 Å .The generated structures at every step were minimized keeping the movement of the reference atom (C-6) and the β-CD structure totally restricted, and to obtain optimal complex geometry, each derived complex was completely optimized without any restriction using the MM+ force field, considering the conjugate gradient Polak–Ribiere algorithm with a Root Mean Square gradient of 0.01 kcal/mol.

Two possible orientations were considered (as shown in Fig. 3). Carboxylic group (COOH) orientated to the center of mass of β-CD, namely A orientation. Nitro group (NO2) orientated to the center of mass of β-CD, namely B orientation.

So, the most stable complexes found by MM+ calculations were re-optimized by PM3 semi empirical method under no constraints. We calculated the harmonic vibration frequencies at PM3 theory level to confirm that the PM3-optimized geometries correspond to a true minimum on the potential energy surfaces.

Because of the computation of Density Functional Theory (DFT) levels is prohibitively expensive in treating such large molecular systems, we just proceed to single point energy calculations to the PM3 optimized geometries using the density functional theory (DFT) at the level of B3LYP/6-31G*, which considers the electron correlation and high precision of energy calculations [42,43].

To quantify the interaction between host and guest in the optimized geometries, we have evaluated binding (ΔE binding) energy, which was calculated by subtracting the sum of the energy of individual free host and guest molecules to the energy of the inclusion complex (using the following formula (1)):

$$\Delta E_{\text{binding}} = E_{\text{complex}} - (E_{\text{CD}} + E_{\text{PNBA}})_{\text{isolated}}. \quad (1)$$

## 3. Result and discussion

### 3.1. Reliability of PM3 method

The experimental structural parameters of the crystalline β-CD [41] and those of the PM3 optimized data of β-CD are summarized in Table 1.

From Table 1, which clearly shows that the PM3 structural parameters of β-CD are well reproduced compared with the experimental data. The differences of the bond-length (−0.020–0.030 Å), bond-angle (−0.001 to3.353°) and dihedral-angle (−13.79 to 6.271°) are very small, indicating that the PM3 method has highly computational efficiency, it permits the modeling of large systems beyond the capacity of ab-initio method, and the precision is comparable to that of ab-initio with medium-sized basis set [44–47].

**Table 2**
Binding and complexation energies (kcal/mol) at the minimum energy for both orientations (neutral specie of PNBA).

| | PNBA1 | β-CD | PNBA1/βCD (A) | PNBA1/βCD (B) | PNBA2 | PNBA2/βCD (A) | PNBA2/βCD (B) |
|---|---|---|---|---|---|---|---|
| *MM+* | | | | | | | |
| $E_{bending}$ (kcal/mol) | 22.41 | 229.22 | 221.81 | 219.52 | 20.76 | 222.06 | 219.72 |
| $\Delta E_{bending}$ (kcal/mol) | | | −29.77 | −32.06 | | −27.87 | −30.21 |
| E interaction | 23.54 | 231.57 | 224.45 | 222.82 | 21.33 | 223.16 | 221.07 |
| ΔE interaction | | | −30.66 | −32.29 | | −29.75 | −31.83 |
| VDW | 10.95 | 106.46 | 97.45 | 95.57 | 9.82 | 98.03 | 95.79 |
| ΔVDW | | | −19.96 | −21.84 | | −18.25 | −20.49 |
| $E_{deformation\ (PNBA)}$ | | | −0.29 | −0.36 | | −0.25 | −0.31 |

**Table 3**
Thermodynamic parameters of the complexes A and B (neutral and anionic species of PNBA) calculated by PM3 method and the single point energies of them calculated by B3LYP/6-31G*.

| | PNBA1 | βCD | PNBA1/β-CD (A) | PNBA1/β-CD (B) | PNBA2 | PNBA2/β-CD (A) | PNBA2/β-CD (B) |
|---|---|---|---|---|---|---|---|
| *PM3* | | | | | | | |
| E[a] (kcal/mol) | −71.18 | −1457.1 | −1538.08 | −1536.48 | −109.47 | −1588.45 | −1599.76 |
| ΔE[b] (kcal/mol) | | | −9.80 | −8.20 | | −21.88 | −33.19 |
| EHOMO[c] (eV) | −7.82 | −10.39 | −8.16 | −8.15 | −7.92 | −8.20 | −8.25 |
| ELUMO[d] (eV) | −0.36 | 1.46 | −0.28 | −0.29 | −0.38 | −0.30 | −0.33 |
| EHOMO − ELUMO (eV) | −7.46 | −11.85 | −7.88 | −7.86 | −7.54 | −7.90 | −7.92 |
| H° (kcal/mol) | 100.87 | −667.31 | −644.93 | −664.27 | −37.01 | −723.51 | −698.28 |
| ΔH[e] (kcal/mol) | | | −78.49 | −97.83 | | −19.19 | −6.04 |
| G° (kcal/mol) | 54.31 | −788.48 | −779.75 | −802.48 | 43.87 | −857.76 | −828.25 |
| ΔG[e] (kcal/mol) | | | −45.58 | −68.31 | | −113.15 | −83.64 |
| S° (kcal/mol-Kelvin) | 88.61 | 406.38 | 452.17 | 463.54 | 95.842 | 450.25 | 435.89 |
| ΔS[e] (kcal/mol-Kelvin) | | | −42.82 | −31.45 | | −54.97 | −69.33 |
| *B3LYP/6-31G** | | | | | | | |
| E[a] (kcal/mol) | −392174.9 | −2681832.2 | −30741107.5 | −3074101.3 | −391930.17 | −30731762.4 | −3073774.9 |
| ΔE[b] (kcal/mol) | | | −100.4 | −94.8 | | 0 | −12.53 |

[a] E is the total optimized energy.
[b] ΔE is the binding energy upon complex:$\Delta E_{binding}$ = E complex − $E_{PNBA}$ − Eβ-CD.
[c] Energy of the highest occupied molecular orbital.
[d] Energy of the lowest unoccupied molecular orbital.
[e] $\Delta A = A_{complex} - A_{PNBA} - A_{\beta\text{-}CD}$; A = H,G.

### 3.2. Force field calculations

In this study we have considered only the inclusion compounds in molar proportion 1:1 formed between one molecule of β-CD and one of PNBA species abbreviated PNBA1/β-CD (A), PNBA1/β-CD (B), PNBA2/β-CD (A), PNBA2/β-CD (B), (1 and 2 represent neutral and anionic species of PNBA respectively).

The graphical representation of the energy changes involved during the inclusion passing process of PNBA in β-CD at different position Z for both orientations are illustrated in Fig. 4.

The first remark is that all binding energies are negative which demonstrate that the inclusion process of PNBA in β-CD is thermodynamically favorable. Second, the curves show several local minima, where the lowest minimum energy is precisely located at Z value of −4 Å and −2 Å respectively for neutral and anionic species of PNBA for A orientation. For the B orientation the energy minimum is located at Z values of 1 Å and 2 Å respectively for neutral and anionic species of PNBA.

In order to refine our results, we re-optimized each previous energy minimum structure, this time without restraint and adding the circling process adopted for each orientation, lead to structures with better stability whose different energetic characteristics are summarized in Table 2. The quantification of the interaction between PNBA and β-CD in these most stable geometries is represented by the energetic term E interaction which was calculated using Eq. (2).

$$E\,interaction = E\,complex - \left(E^{sp}_{\beta-CD} + E^{sp}_{PNBA}\right) \quad (2)$$

In this equation, $E^{sp}_{ß\text{-}CD}$ and $E^{sp}_{PNBA}$ correspond respectively to the single point energy of the β-CD and PNBA in the optimized complex. While the deformation energy of each component (host or guest) can be obtained by the difference between the single point energy of the component in the optimized complex and its energy when it is optimized in free form (Eq. (3)) [48]:

$$DEF\,(component) = E(component)^{opt}_{sp} - E\,(component)\,opt \quad (3)$$

The results summarized in Table 2 for the most stable structures obtained by MM+ study confirm that the binding energy is in favor of neutral and anionic species of PNBA for B orientation respectively of 2.29 kcal/mol and 2.34 kcal/mol. Moreover, the similarity in the magnitude of the energetic contribution of VdW interaction and the interaction energy is an indication that the driving forces responsible of the stability of the inclusion PNBA/β-CD complexes are VdW interaction.

On the other hand, the results of the investigation of deformation energy reported in Table 2 demonstrate that the PNBA (in neutral and anionic species) molecule for B orientation requires slightly more energy than that of the A orientation (in neutral and anionic species) in order to adapt its structure to bind within the cavity of β-CD as indicated by the DEF [PNBA] of about −0.31 and −0.36 kcal/mol respectively. This can be supported by the fact that flexibility of the guest structure is one of the important structural requirements for β-CD upon complexation.

### 3.3. Semi empirical and quantum mechanical calculations

Unfortunately, molecular mechanics methods do not treat explicitly the electrons [49]; therefore they cannot predict electronic properties of molecules. Also, it may not accurately describe the geometries or energetic of intermolecular interactions if a force field for a molecule is not available or not very well defined. Hence, to verify the reliability of our approach and to be consistent with experiment we have used quantum mechanical methods.

Semi-empirical (PM3) calculations were performed starting from the structures of minimal binding energy obtained in the previous MM+ study. Table 3 shows the calculated binding energy ($\Delta E_{bending}$) of PNBA complexed with ß-CD. The negative binding energy ($\Delta E_{bending}$) changes upon complexation clearly demonstrate that ß-CD can form stable complexes with PNBA. The B orientation in PNBA2/β-CD is the most favored for the two species of PNBA according to PM3 calculations. The same result is also obtained with the B3LYP/6-31G* single point calculation in which the energy difference becomes 12.53 kcal/mol.

In this case, one H bond (Fig. 5d) was formed between oxygen (O11) of $COO^-$ and H135 of secondary hydroxyl of β-CD positioned at 1.75 Å. H-bond lengths shorter than 3.0 Å which just falls in the reported data [50].

Thus, the complex formed by neutral PNBA prefers the encapsulation of carboxylic group (COO) in β-CD cavity. This orientation is preferred by 1.60 kcal/mol. The A and B orientation in neutral specie does not seem to be stabilized by such an interaction (Fig. 5a and b).

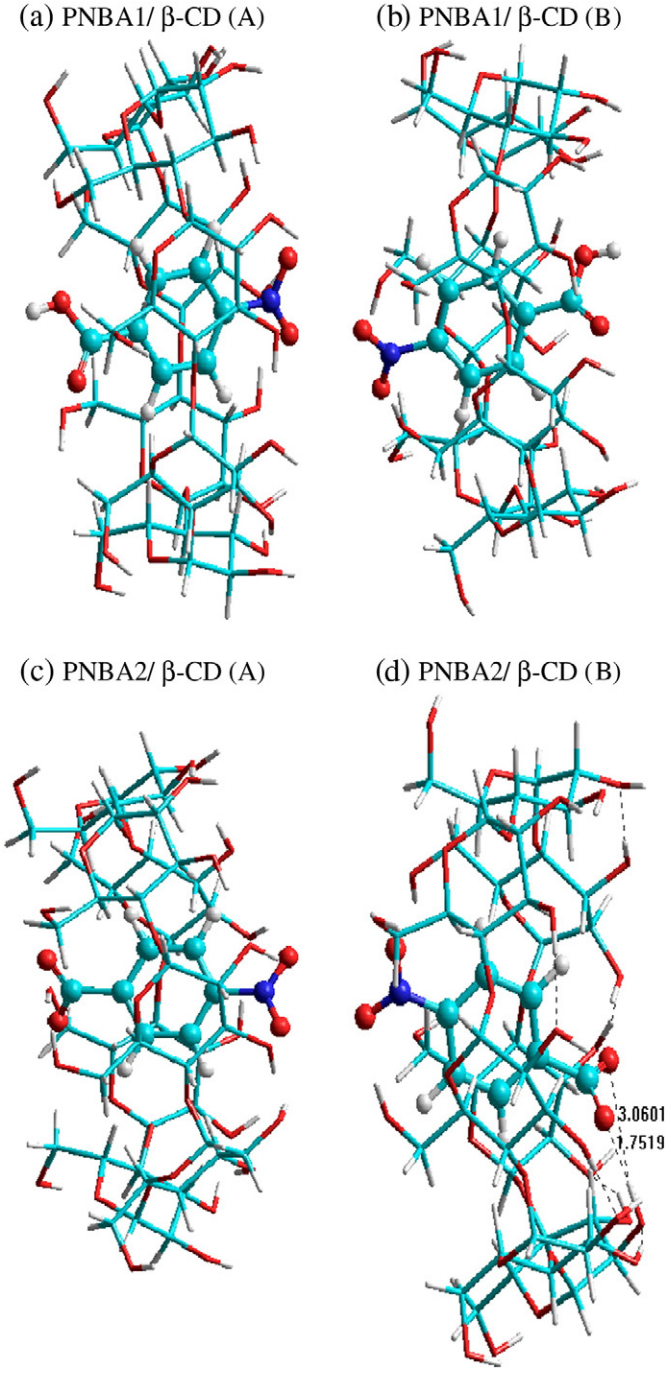


**Fig. 5.** Structures of the energy minimum obtained by the PM3 calculations.

**Table 4**
Milliken charges of the atoms of PNBA (neutral PNBA1 and anionic PNBA2 species, charge transfer of the complexes A and B calculated by B3LYP/6-31G* (and PM3) method.

| Atoms | PNBA1 | PNBA1/β-CD (A) | PNBA1/β-CD (B) | PNBA 2 | PNBA2/β-CD (A) | PNBA2/β-CD (B) |
|---|---|---|---|---|---|---|
| $C_1$ | (0.140) 0.052 | 0.053 (0.122) | 0.067 (0.112) | 0.020 (0.075) | −0.007 (0.086) | 0.012 (0.092) |
| $C_2$ | (0.011) −0.001 | 0.058 (0.060) | 0.045 (0.059) | −0.034 (0.022) | 0.030 (0.017) | 0.006 (0.020) |
| $C_3$ | (−0.106) 0.056 | 0.095 (−0.049) | 0.096 (−0.067) | 0.067 (−0.036) | 0.099 (−0.027) | 0.110 (−0.006) |
| $C_4$ | (0.094) 0.103 | 0.062 (0.076) | 0.054 (0.059) | −0.034 (0.022) | 0.011 (0.023) | −0.008 (0.021) |
| $C_5$ | (0.142) 0.126 | 0.051 (0.122) | 0.064 (0.107) | 0.020 (0.075) | 0.007 (0.079) | 0.012 (0.085) |
| $C_6$ | (−0.357) 0.230 | 0.397 (−0.370) | 0.388 (−0.365) | 0.307 (−0.457) | 0.370 (−0.453) | 0.369 (−0.439) |
| N | (1.215) −0.027 | −0.022 (1.227) | −0.022 (1.312) | 0.054 (1.317) | −0.008 (1.321) | −0.020 (1.247) |
| N=O | (−0.590) −0.206 | −0.281 (−0.585) | −0.260 (−0.587) | −0.333 (−0.635) | −0.334 (−0.650) | −0.322 (−0.622) |
| N=O | (−0.594) −0.206 | −0.274 (−0.580) | −0.276 (−0.597) | −0.334 (−0.635) | −0.335 (−0.616) | −0.304 (−0.611) |
| C | (0.424) 0.403 | 0.446 (0.427) | 0.424 (0.426) | 0.383 (0.451) | 0.261 (0.469) | 0.267 (0.427) |
| C=O | (−0.321) −0.368 | −0.391 (−0.389) | −0.398 (−0.392) | −0.558 (−0.599) | −0.503 (−0.629) | −0.520 (−0.600) |
| C=O | (−0.059) −0.161 | −0.151 (−0.054) | −0.169 (−0.065) | −0.558 (−0.599) | −0.535 (−0.565) | −0.529 (−0.605) |
| Charge transfer | 0.000 (0.000)) | 0.043 (0.004) | 0.013 (0.001) | −1.000 (−1.000) | −0.924 (−0.945) | −0.927 (−0.990) |

The PNBA prefers to occupy most of the available space in the cavity of β-CD, which is in good agreement with experimental results [25].

The geometries of the studied complexes found by PM3 method showed that PNBA species were deeply included in β-CD especially for B orientation in PNBA2/β-CD.

Besides, the gap ($E_{LUMO} - E_{HOMO}$) is an important stability index [51], and chemicals with larger ($E_{LUMO} - E_{HOMO}$) values tend to have higher stability, therefore, the B orientation in PNBA2/β-CD and A orientation in PNBA1/β-CD are significantly more favorable than the A orientation in PNBA2/β-CD and B orientation in PNBA1/β-CD by ($E_{LUMO} - E_{HOMO}$) values.

### 3.4. Thermodynamic parameters

To investigate the thermodynamics of the binding process, the statistical thermodynamic calculation was carried out at 1 atm and 298.15 K by PM3. The thermodynamic quantities, the enthalpy change (ΔH), the thermal Gibbs free energy (ΔG) and entropy contribution (ΔS) are given in Table 3. The complex reactions of PNBA with β-CD are exothermic judged from the negative enthalpy changes. And the negative enthalpy changes suggest that both the inclusion processes are enthalpically favorable in nature. In addition, it can be seen that the entropy change (ΔS) of A and B orientation in two species are also both negative, this indicates that the formation of the complex becomes an enthalpy-driven process. The four complexation reactions have negative ΔG values and are therefore spontaneous processes, implying that binding interactions are favored. Certainly, since the inclusion reactions happen in aqueous solution, the influence of water molecules on the inclusion process should be very important. However, because of the limitation of our computer, it can hardly calculate the interactions of cyclodextrin systems in aqueous solution. Therefore, the values of thermodynamics calculated have no absolute meaning.

### 3.5. Charge transfer

Liu and Guo suggest that charge transfer interactions play a relevant role in the stabilization of their inclusion complexes [51]. The Milliken charges of the heavy atoms of PNBA1 and PNBA2, charge transfer of complexes PNBA1/β-CD and PNBA2/β-CD are summarized in Table 4 by B3LYP/6-31G* and PM3 methods. The data show that the β-CD molecule accepts the electron from PNBA, and the charge transfer of PNBA2/β-CD in B orientation (PM3: 0.0927 e, B3LYP/6-31G*: 0.990 e) is the largest of all complexes.

In Table 5, we report the bond distances, bond angles and the most interesting dihedral angles of PNBA molecule before and after complexation in β-CD obtained from PM3 and B3LYP/6-31G* calculations for the most stable structure in B orientation of PNBA2/β-CD. It is evident that in β-CD, the geometry of PNBA is completely altered. The alteration is significant in dihedral angles, which, indicates that PNBA must adapt a specific conformation to form a more stable inclusion complex. The intermolecular hydrogen bonds also play pivotal role for the conformational exchange. The calculation dihedral angle (O11—C10—C3—C4) was changed to −17.3° and

**Table 5**
Geometrical parameters of PNBA before and after inclusion in β-CD, bond distances (Å), angle (°) and dihedral angles (°) calculated by PM3 and B3LYP/6-31G* methods.

| Bond lengths (Å) | PNBA PM3//B3LYP/6-31G* | PNBA2/CD (B) PM3//B3LYP/6-31G* |
|---|---|---|
| C1—C2 | 1.337/1.334 | 1.405/1.403 |
| C1—H133 | 1.100/0.911 | 1.051/1.050 |
| C2—H14 | 1.100/0.981 | 1.050/1.049 |
| C2—C3 | 1.337/1.334 | 1.408/1.408 |
| C3—C10 | 1.351/1337 | 1.473/1.470 |
| C10—O11 | 1.208/1.204 | 1.231/1.230 |
| C10—O12 | 1.335/1.331 | 1.231/1.220 |
| C3—C4 | 1.337/1.335 | 1.407/1.406 |
| C4—H15 | 1.100/0.985 | 1.051/1.050 |
| C4—C5 | 1.337/1.321 | 1.404/1.404 |
| C5—H16 | 1.100/1.100 | 1.049/1.047 |
| C6—N7 | 1.266/1.258 | 1.419/1.418 |
| N7—O8 | 1.316/1.302 | 1.277/1.277 |
| N7—O9 | 1.316/1.301 | 1.276/1.274 |
| *Bond angles (°)* | | |
| H13—C1—C2 | 120.0/118.0 | 119.1/118.7 |
| C1—C2—H14 | 120.0/118.0 | 119.1/118.9 |
| C1—C2—C3 | 120.0/118.0 | 120.7/119.4 |
| C2—C3—C10 | 120.0/118.0 | 120.8/119.5 |
| C3—C10—O11 | 120.0/118.0 | 120.8/118.2 |
| C3—C10CO12 | 120.0/118.0 | 120.9/118.6 |
| C10—C3—C4 | 120.0/118.0 | 120.6/120.9 |
| C3—C4—H15 | 120.0/118.0 | 120.3/118.0 |
| H15—C4—C5 | 120.0/118.0 | 119.1/118.3 |
| C4—C5—H16 | 120.0/118.0 | 120.1/118.1 |
| C5—C6—N7 | 120.0/118.0 | 120.5/118.4 |
| C1—C6—N7 | 120.0/118.0 | 120.9/118.2 |
| C6—N7—O8 | 120.0/118.0 | 121.1/118.1 |
| C6—N7—O9 | 120.0/118.0 | 121.1/120.2 |
| *Dihedral angle (°)* | | |
| H13—C1—C2—H14 | 0.0/7.1 | 0.2/0.1 |
| C1—C2—C3—C10 | 180.0/120.0 | 179.4/176.1 |
| H14—C2—C3—C10 | 0.0/0.0 | −0.7/−0.5 |
| C2—C3—C10—O11 | 180.0/118.0 | 166.0/161.2 |
| C2—C3—C10—O12 | 0.0/23.1 | −17.3/−14.4 |
| O11—C10—C3—C4 | 0.0/−6.0 | −14.3/−11.8 |
| O12—C10—C3—C4 | 180.0/120.0 | 162.1/159.2 |
| C10—C3—C4—H15 | 0.0/0.9 | −0.2/−0.2 |
| C3—C4—C5CH16 | 0.0/118.0 | 179.2/165.2 |
| H15—C4—C5—C6 | −180.0/120.0 | −179.3/−175.1 |
| C4—C5—C6—N7 | 180./120.0 | 179.1/178.0 |
| C5—C6—N7—O8 | 0.0/0.7 | 3.1/2.9 |
| C5—C6—N7—O9 | −180.0/120.0 | −174.4/−168.2 |

− 14.4° for the B orientation in PNBA2/β-CD respectively based on PM3 and B3LYP/6-31G* calculations.

## 4. Conclusion

The complexation of neutral (PNBA1) and anionic (PNBA2) species of para-nitrobenzoic acid with β-CD was studied by force field MM+, semi-empirical PM3 and single point DFT calculations. The result suggests that the complexation of the PNBA2/β-CD in B orientation is significantly more favorable than the others. We note that the aromatic ring for each species of PNBA is totally embedded in β-CD cavity. In addition, the statistical thermodynamic calculations suggest that the formation of the inclusion complex is an enthalpy-driven process. We can note also that the results show that PM3 is a good feasible quantum mechanics method in the study of CD complexation. From this study we suggest the complexation of anionic specie of PNBA because it forms the most stable complex.

## References


[1] J.C. Harrison, M.R. Eftink, Biopolymers 21 (1982) 1153–1166.
[2] O.K. Abou-Zied, A.T. Al-Hinai, J. Phys. Chem. 110 (2006) 7835–7840.
[3] J. Szejtli, Chem. Rev. 98 (1998) 1743–1754.
[4] M. Pumera, R. Matalova, I. Jelinek, J. Juza, Molecules 6 (2001) 221–222.
[5] M.V. Rekharsky, Y. Inoue, Chem. Rev. 98 (1998) 1875.
[6] K.B. Lipkowitz, Chem. Rev. 98 (1998) 1829.
[7] L. Liu, Q.X. Guo, J. Incl. Phenom. 42 (2002) 1.
[8] C. Morari, D. Bogdan, M. Bogdan, Rom. J. Phys. 50 (2005) 995.
[9] M. Fermeglia, M. Ferrone, A. Lodi, S. Priel, Carbohydr. Polym. 53 (2003) 15.
[10] P. Weinzinger, P. Weiss-Greiler, W. Snor, H. Vierstein, P. Wolschann, J. Incl. Phenom. 57 (2007) 29.
[11] E. Estrada, I. Pedrmo-Lopez, J.J. Torres-Labandeira, J. Org. Chem. 65 (2000) 8510.
[12] G. Uccello-Barretta, F. Balzano, G. Sicoli, D. Paolino, S. Guccione, Bioorg. Med. Chem. 12 (2004) 447.
[13] B. Pose-Vilarnovo, I. Pedromo-Lopez, M. Echezarreta-Lopez, P. Schroth-Pardo, E. Estrada, J.J. Torres-Lebandeira, Eur. J. Pharm. Sci. 13 (2001) 325.
[14] E. Cervello, C. Jaime, J. Mol. Struct. THEOCHEM 428 (1998) 195.
[15] J.M. Madrid, J. Pozuelo, F. Mendicuti, W.L. Mattice, J. Colloid Interface Sci. 93 (1997) 112.
[16] A.C.S. Lino, Y. Takahata, C. Jaime, J. Mol. Struct. THEOCHEM 594 (2002) 207.
[17] J.R. Grigera, E.R. Caffarena, S. de Rosa, Carbohydr. Res. 310 (1998) 253.
[18] B. Manunza, S. Deiana, M. Pintore, C. Gessa, J. Mol. Struct. THEOCHEM 195 (1997) 133.
[19] C. Yan, X. Li, Z. Xiu, C. Hao, J. Mol. Struct. THEOCHEM 764 (2006) 95.
[20] C. Yan, X. Li, Z. Xiu, C. Hao, J. Mol. Graphics Modell. 26 (2007) 420.
[21] L. Briquet, N. Staelens, L. Leherte, D.P. Vercauteren, J. Mol. Graphics Modell. 26 (2007) 104.
[22] G. Piel, G. Dive, B. Evrard, T. Van Hees, S.H. de Hassonville, L. Delattre, Eur. J. Pharm. Sci. 13 (2001) 271.
[23] D. Bodgan, C. Morari, Phys. Lett. A 366 (2007) 454.
[24] L. Bardi, A. Mattei, S. Steffan, M. Marzona, J. Chem. Technol. Biotechnol. 27 (2007) 709–713.
[25] Zhi Fan, Chun-Hua Diao, Min-Jie Guo, Du. Rong-Juan, Yuan-Fang Song, Zuo-Liang Jing, Ming Yu, Carbohydr. Res. 342 (2007) 2500–2503.
[26] A. Botsi, K. Yannakopoulou, E. Hadjoudis, J. Waite, Carbohydr. Res. 1 (1996) 283.
[27] N. Bodor, M.J. Huang, J.D. Watts, J. Incl. Phenom. Macrocycl. Chem. 25 (1996) 97.
[28] L.A. Godinez, B.G. Schulze-Fiehn, S. Patel, C.M. Criss, J.D. Evanseck, A.E. Kaifer, Supramol. Chem. 8 (1996) 17.
[29] M.J. Huang, J.D. Watts, N. Bodor, Int. J. Quantum Chem. 64 (1997) 711.
[30] N.B. Boukamel, A. Krallafa, D. Bormann, L. Caron, M. Canipelle, S. Tilloy, E. Monflier, J. Incl. Phenom. Macrocycl. Chem. 42 (2002) 269.
[31] Y. Fu, L. Liu, Q.X. Guo, J. Incl. Phenom. Macrocycl. Chem. 43 (2002) 223.
[32] A.M. Granados, R.H. de Rossi, D.A. Barbiric, E.A. Castro, THEOCHEM 91 (2002) 619.
[33] E.C. Yang, X.J. Zhao, F. Hua, J.K. Hao, THEOCHEM 75 (2004) 712.
[34] S. Chen, Q. Teng, S. Wu, CEJC 4 (2006) 223.
[35] M. Fatiha, S. Soumeya, K. Djameleddine, Asian J. Chem. 19 (2005) 217.
[36] O. Attoui Yahia, D.E. Khatmi, J. Mol. Struct. THEOCHEM 912 (2009) 38–43, 10.
[37] A.A. Rafati, S.M. Hashemianzadeh, Z.B. Nojini, M.A. Safarpour, J. Mol. Liq. 135 (2007) 153.
[38] F. Madi, et al., C. R. Chim. 10 (2009) 1016.
[39] Hyperchem, Release 7.51 for windows 2002 Hypercube. Inc.
[40] Gaussian 03, Revision B.01, M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian, Inc., Pittsburgh.
[41] T. Steiner, G. Koellner, J. Am. Chem. Soc. 116 (1994) 5122–5128.
[42] L. Liu, X.S. Li, T.W. Mu, Q.X. Guo, Monatsh. Chem. 131 (2000) 849–855.
[43] W.J. Hehre, R. Ditchfield, J.A. Pople, J. Chem. Phys. 56 (1972) 2257–2261.
[44] X.S. Li, T.W. Mu, Q. Guo, Monatsh. Chem. 131 (2000) 849.
[45] Y.J. Zheng, K.M. Merz Jr., J. Comput. Chem. 13 (1992) 1151.
[46] J.O. Morley, R.M. Morley, R. Docherty, M.H. Charlton, J. Am. Chem. Soc. 119 (1997) 10192.
[47] S. Morpurgo, M. Bossa, J. Moepurgo, J. Mol. Struct. THEOCHEM 429 (1998) 71.
[48] D.J. Barbiric, E.A. Castro, R.H. de Rossi, J. Mol. Struct. THEOCHEM 532 (2000) 171–181.
[49] T.A. Halgren, J. Comput. Chem. 20 (1999) 730–748.
[50] T. Steiner, W. Saenger, J. Am. Chem. Soc. 114 (1992) 10146–10154.
[51] L. Liu, K.S. Song, X.S. Li, Q.X. Guo, J. Incl. Phenom. Macrocycl. Chem. 40 (2001) 35–39.