

# Inclusion Complexes of Dyes and Cyclodextrins: Modeling Supermolecules by Rigorous Quantum Mechanics

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## Abstract

The results of structure optimization and molecular dynamics simulation of host-guest  $\gamma$ -cyclodextrin-pinacyanol dye inclusion complexes are obtained by applying a density functional based tight-binding code. The results attempt to correlate UV/Vis and circular dichroism spectral data with calculated aggregate structures of the sandwich dimer, with the monomers twisted slightly against each other. The sense of twist is predetermined by the chirality of the complexing host. The UV/Vis-spectral are interpreted using the exciton model. Within this model, each excited state of the monomer generates two excitonic states in the dimer. The interaction between the two monomers results then in a Davydov splitting of the two dimer states. The opposite signs of the two dimer states can be attributed to the twist of the monomers when they interact.

## Introduction

The density functional tight-binding code (DFTB) combines the efficiency of semi-empirical quantum-chemistry and tight-binding approaches with the transferability of more sophisticated density functional methods [1]. It has been widely used to study biomolecules with atoms of different electronegativities and different bonding types, ranging from covalent and ionic bonding to hydrogen bonding and van der Waal-type interactions. We have applied this method to cyclodextrins which constitute an important family of inclusion compounds [2]. Cyclodextrins are truncated doughnut-shaped cyclic oligosaccharides consisting of  $\alpha$ -1,4 linked D-glucose units with a hydrophobic interior surface and a hydrophilic external surface [3]. Of particular interest are inclusion complexes with organic dyes. The latter are molecules with an extended  $\pi$ -electron system which interact with electromagnetic radiation in the UV/Vis range with absorption occurring when energy quanta correspond to the energy gap between the ground ( $|0\rangle$ ) and one of the excited states ( $|n\rangle$ ). The excitonic interaction between two chromophores (dimer)  $a$  and  $b$  splits the excited state ( $|n\rangle$ ) into two energy levels. The energy gap  $2V_{ab}$  which corresponds to the energy absorbed,  $D^+ - D^-$ , is called Davydov splitting [4, 5]. Dye monomer and dimer inclusion compounds in cyclodextrin cavities have been previously studied using molecular mechanics technique to investigate the stability of these complexes [6]. The chromophore of interest for our present study is pinacyanol chloride. This dye otherwise known as bis-(N-ethyl-2-quinolyl)-trimethinium chloride is shown in Figure 1. The two identical quinolyl units are connected by a trimethine bridge, CH—CHCH. The com-

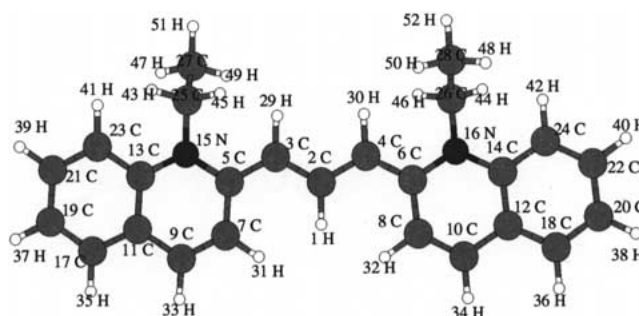


Figure 1. Pinacyanol chloride dye.

pound has received attention because of its application as a saturable absorber, mode-locker, and sensitizer in imaging technology.

In this study we present the results of the structure optimization and molecular dynamics (MD) simulation for the pinacyanol dimers in water and  $\gamma$ -cyclodextrin-pinacyanol inclusion complexes. The geometries of the complexes are followed during the optimization and analysed. The results are discussed with respect to the UV/Vis and CD spectra.

## Methods

The calculations in this paper were performed in three steps: (i) geometry optimization of the dye monomer; (ii) optimization and dynamics of the complexed dye dimer in water; (iii) optimization of the cyclodextrin-complexed dimer with some water droplets. The starting geometry for  $\gamma$ -cyclodextrin, 'SIBJAO', was taken from the Crystallographic Database [7]. The optimization of the pinacyanol dye monomer was first carried out using the conjugate gradi-

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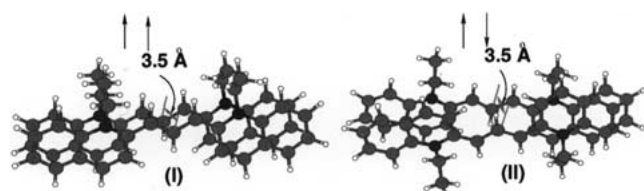


Figure 2. Dimers (I with diethyl groups placed parallel, II anti-parallel).

ent (CG) method of DFTB, with the background charge set to  $-1$  so that the whole system charge was zero. The pinacyanol dye dimer was constructed from the optimized monomer of Figure 1. To choose the starting geometry of the dye dimer and the dye dimer- $\gamma$ -cyclodextrin system, two alternatives for the relative orientation of the dye monomer are possible (although more are conceivable) [6]. These alternatives are schematically shown in Figure 2.

In (I), the monomers are aligned parallel (highest possible symmetry  $C_{2v}$ ), in (II) they are antiparallel ( $C_{2h}$ ). In the latter, there is less steric repulsion of the ethyl groups since they are on opposite sides of the complex. The initial distance between two monomer units was taken to be  $3.5 \text{ \AA}$ , which is close to the distance between the neighbouring layers in graphite. The arrangements (I) and (II) were allowed to relax in a simulation box containing eighty molecules of water. For the complexed dimer, the cyclodextrin ring was located at the central portion of the methine chain of the dye, and the total system was then optimized with a few droplets of water molecules. The geometry and relative orientation of the two monomers in the uncomplexed dimer and the dimer included in cyclodextrin was followed during the calculation by measuring the dihedral angles N15-C5-C3-C2 and N16-C6-C4-C2 of each monomer unit and the angles between the planes of the dimer which is the twist of the planes with dihedral angles (C21-C22-C22'-C21') or (C19-C20-C20'-C19') (the prime (') on the labeled atom indicates the second identical monomer unit in the dimer; we make reference to Figure 1 for labeling the atoms). This twist was set to zero (by placing the monomers parallel to each other) at the start of the relaxation and changed in response to the CG relaxation. MD simulation were performed at a fixed temperature,  $300 \text{ K}$ , with a time step of  $0.5 \text{ fs}$  starting from the optimized geometry of step (ii) above to see the evolution of the twists of the planes of the dimer in the simulation box of water. There are little noticeable changes in this structure after the CG relaxation as can be seen at the beginning of the plot in Figure 7 with the average twist of  $2.4^\circ$  in the anti-parallel uncomplexed dimer in water. Parallel uncomplexed dimer (not shown) also shows similar behaviour during the MD simulation.

### Computational results

After the relaxation, the pinacyanol monomer has a twisted geometry, (symmetry  $C_2$ ) with both dihedral angles N1-C5-C3-C2 and N16-C6-C4-C2 equal to  $173^\circ$ . This twist confirms the non-planar geometry of the isolated unit of pinacyanol dye in its ground state as shown in Figure 3.

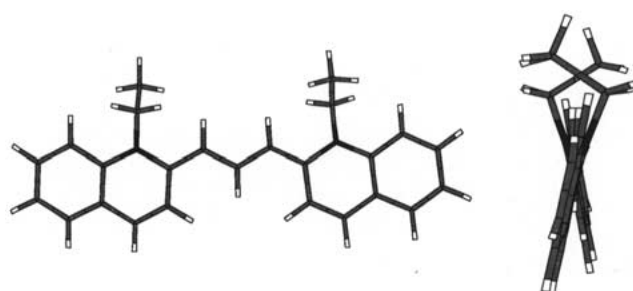


Figure 3. Geometry of the pinacyanol dye after optimisation (left: front view, right: side view).

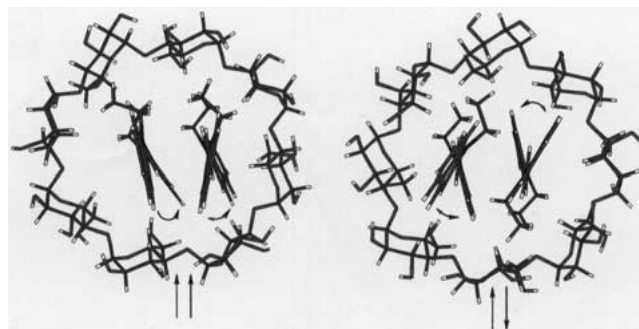


Figure 4. Geometry of the pinacyanol dimer-cyclodextrin complexes after relaxation, showing that the monomers in the anti-parallel dimer are more twisted than in the parallel dimer as schematically indicated by the arrows. Water molecules are not shown.

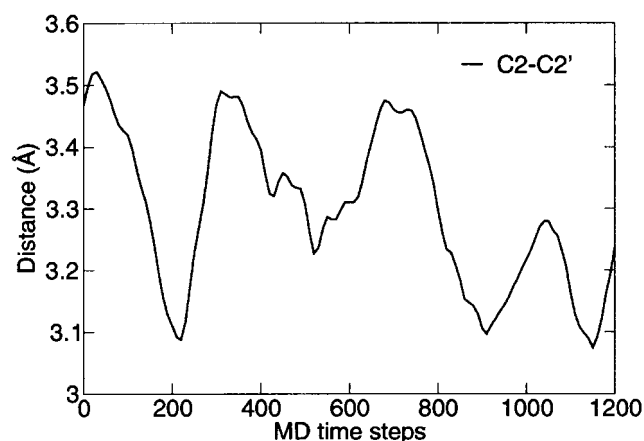


Figure 5. Plot of the distance between the centers of the monomer units in the uncomplexed parallel dimer.

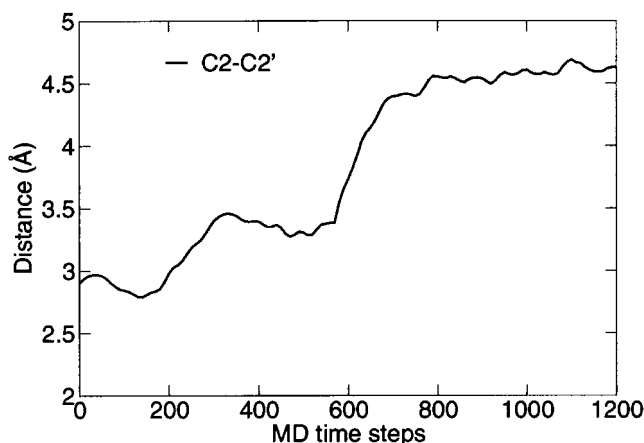


Figure 6. Plot of the distance between the centers of the monomer units in the uncomplexed anti-parallel dimer.

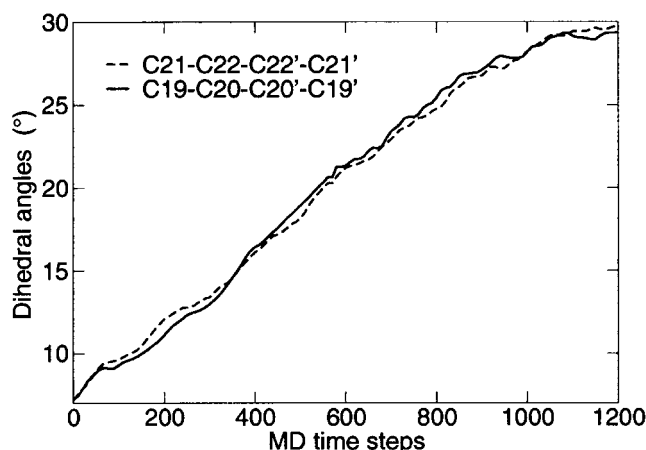


Figure 7. Plot of the dihedral angles (C21-C22-C22'-C21' and C19-C20-C20'-C19') between the monomer units in the uncomplexed anti-parallel dimer as a function of time.

The calculated twist with DFT/B3LYB and a 6-31G\*\* basis is 172° (K. Kolster, unpublished). In the dimer, these dihedral angles change both in water and in the cavity of cyclodextrin, with the anti-parallel arrangement in which there is less steric repulsion showing a larger change (from 180°) inside the cavity of the cyclodextrin. See Figure 4 where the average dihedral angles of each monomer unit of the dimer is shown to be equal to 168.0° in the parallel dimer and 162.9° in the anti-parallel dimer. By comparing these angles with the uncomplexed dimer in water, which shows an average of 172.1° and 175.4° for parallel and anti-parallel dimer respectively, these angles indicate little change with respect to the optimized isolated monomer unit of Figure 3. MD simulation of 600 fs carried on the uncomplexed parallel and antiparallel dimers shows a twist in the planes of the monomers. This twist of the monomers against each other is measured by the dihedral angles C21-C22-C22'-C21' and C19-C20-C20'-C19'. The twist shows an increase with MD time in both the uncomplexed parallel and anti-parallel dimer. Only the parallel dimer result is shown in Figure 7 since they both show similar behaviour. The evolution of the distance between the monomers during the MD are respectively shown in Figures 5 and 6 for both types of uncomplexed dimer in water. The monomers in arrangement (I) move closer with an average distance (C2-C2') equal 3.25 Å at the end of

CG relaxation. This distance fluctuates non-uniformly during the 600 fs MD simulations as shown in Figure 5. The non-uniform fluctuation is due to the steric repulsion of the ethyl groups leading to instability of the average distance. The monomers in arrangement (II) move closer at the end of CG relaxation with average distance 2.85 Å and during the 600 fs MD simulation, it fluctuates non-uniformly at the beginning of first 800 MD time steps (400 fs) and then equilibrates at an average distance of 4.45 Å at the rest of 200 fs simulation period as shown in Figure 6.

## Conclusion

The geometry linked fluctuations suggest the specific mode of interaction between the monomer units of the pinacyanol dye. This interaction as measured by the twist between the planes of the monomer units as calculated from C21-C22-C22'-C21' and (C19-C20-C20'-C19'), and also the dihedral angles of each monomer units both in the complexed and uncomplexed dimer can be related to the experimental observation of the UV/CD spectra of the chromophores in which there is a split of the excited states of the monomer units as described in the first section.

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