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CNDO-Electrostatic Potential Maps for α-Cyclodextrin

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On the basis of electrostatic potential maps of α-cyclodextrin(α-CD), the origin of the large dipole moment of α-CD is explained. It is also pointed out that electrostatic properties inside the cavity vary dramatically depending on the conformation of the macrocyclic ring of α-CD.

Cyclodextrins(CDs) are cyclic oligosaccharides composed of at least six(1→4)-linked α-D-glycopyranosyl residues. CDs (hosts) can form inclusion complexes with various types of compounds (guests) without any covalent bonds being formed.[1-4] A central subject in the host-guest chemistry is the elucidation of the driving force for the formation of the inclusion complexes. A variety of physicochemical models for the host-guest interaction has been proposed.[1-4] However there is no general agreement as to the main force stabilizing the complexes. In the previous paper,[5] we have indicated that α-CD has a large dipole moment (12-13 D), and that the dipole moments of guest molecules studied run antiparallel to that of the host α-CD in the crystalline state. These findings suggest that electrostatic type of interaction, mainly dipole-dipole interaction, is a major factor stabilizing the complexes. In this study, we attempt to utilize electrostatic potential energy maps in order to obtain more detailed information on electrostatic properties of the CD molecule.

The electrostatic potential energy was evaluated according to Approximation II in Ref. 6, where the zero-differential approximation is retained and the nuclear attraction integrals are calculated using Roothaan's equation.[7] The geometry of α-CD was derived from the crystalline data for α-CD-guest complexes.[8,9] Thus, the potential energy maps obtained reflect electrostatic properties of the CD molecules perturbed by the corresponding guest molecules.

Figure 1 shows a potential map for the α-CD molecule complexed with p-nitrophenol(PNP). The map was drawn on the rectangular region containing the cavity axis (z-axis). A potential maximum occurs on the side of the primary hydroxyl groups (narrower rim), and a minimum on the side of the secondary hydroxyl groups (wider rim). Consequently, a potential gradient is generated along the cavity axis inside the CD-cavity. The side of the narrower rim, as a whole, has relatively large positive potentials (Fig. 2), while the other side has slightly negative ones (Fig. 3).[10] Therefore a large electronic polarization is induced in the direction of the cavity axis, explaining the large dipole moment of α-CD.[5]

The PNP molecule penetrates into the CD-cavity from the side of the nitro

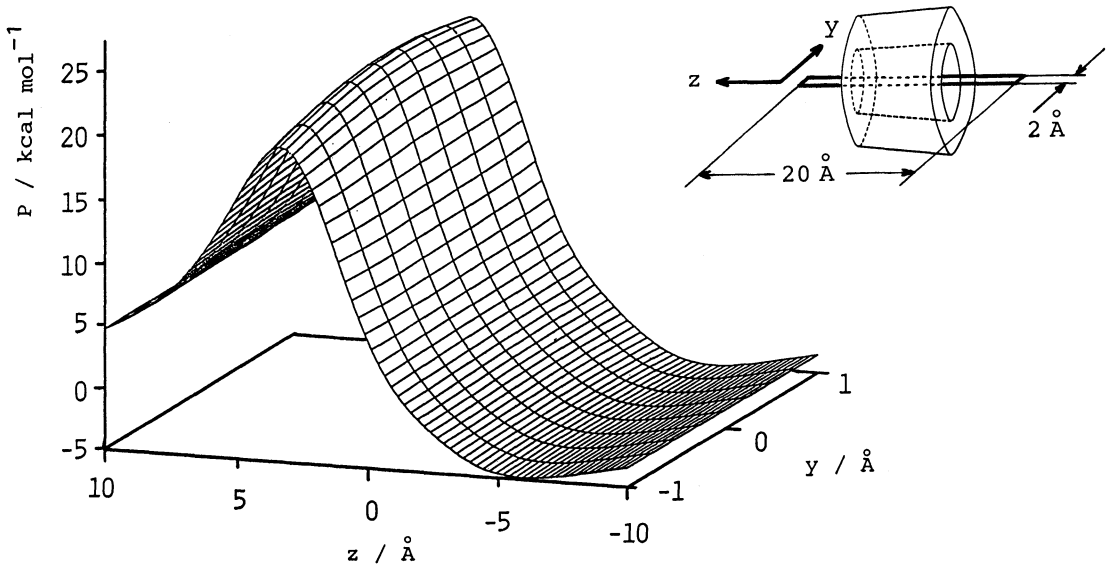

Fig. 1. A CNDO-electrostatic potential map for the α-CD complexed with PNP The z-axis is taken in accord with the cavity-one. The CD molecule is schematically represented by bucket-like shape. Potential, P, is plotted against the rectangular region(indicated by bold lines) on the y-z plane.

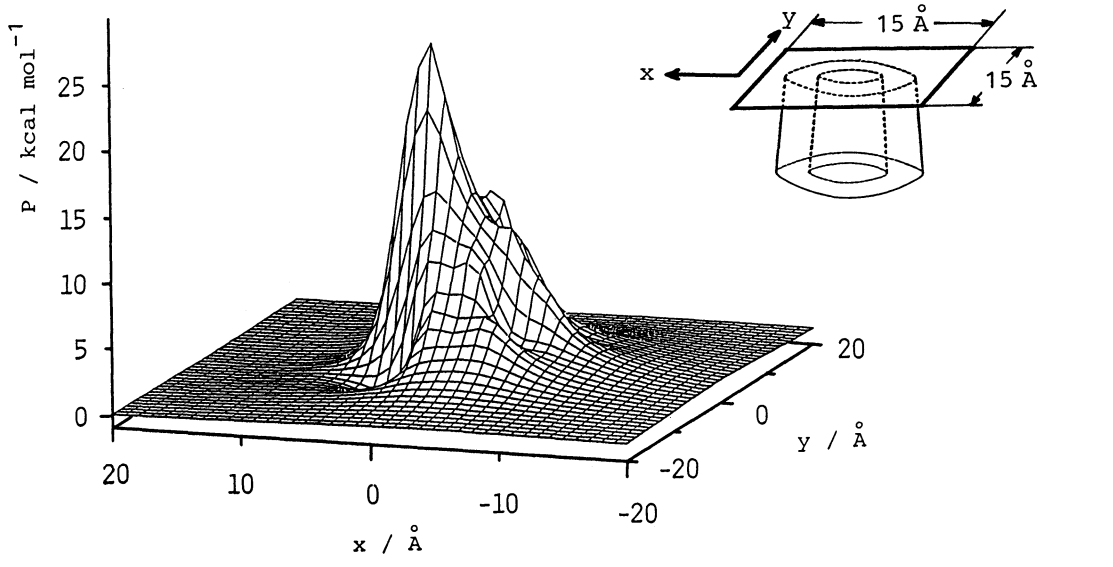

Fig. 2. A CNDO-electrostatic potential map for the narrower-rim region of the α-CD.

group.[8,11] This orientation is energetically favorable because the oxygen atoms of the nitro group generate relatively higher negative potentials, favorably interacting with the narrower-rim region of the CD molecule. The energy difference between the potential maximum and minimum is estimated as 26-27 kcal mol^{-1}, which is comparable to the depth of the potential wells generated around the lone-pairs in H_2O and HCHO.[6,12] It is, therefore, expected that on complexation the α-CD + PNP

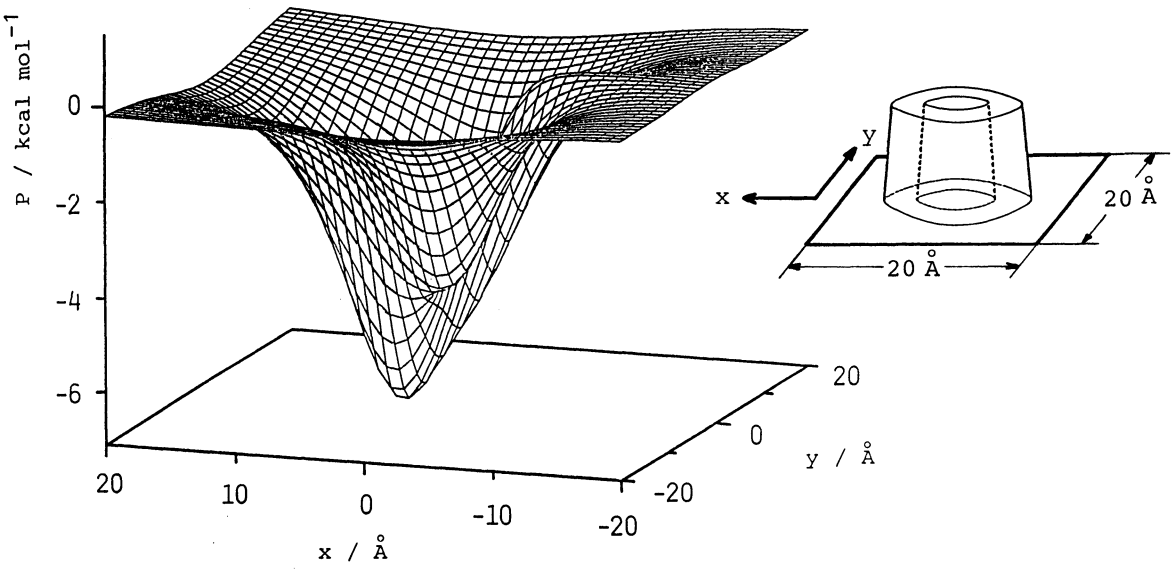

Fig. 3. A CNDO-electrostatic potential map for the wider-rim region of the α-CD.

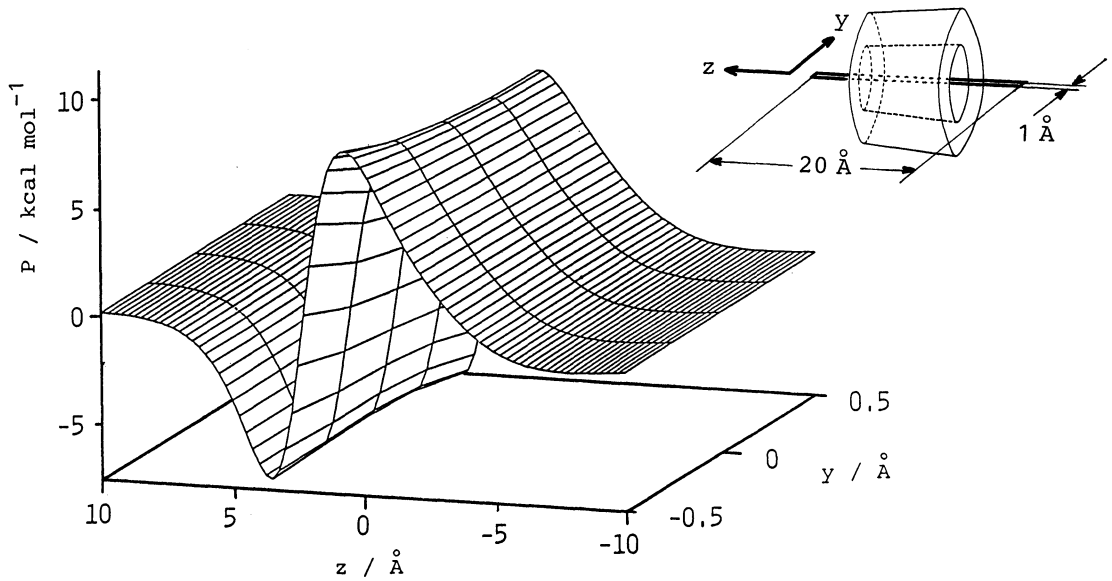

Fig. 4. A CNDO-electrostatic potential map for the cavity-inner region of the α-CD complexed with two water molecules.

system can be stabilized at least to the extent of ordinary hydrogen bonding complexes.

Figure 4 shows a potential map for the α-CD complexed with two water molecules,[13] where the sense of the potential gradient is reversed compared with that in Fig. 1. According to the X-ray diffraction data for this complex,[9] the macrocyclic ring is highly distorted. This indicates that the potential profile inside the cavity strongly depends on the conformation of the macrocyclic ring. From the above argument, in the α-CD-PNP complex the conformation of the α-CD seems to be fixed so as to optimize the electrostatic interaction. In view of this case, we can say that the conformational change of the CD-macrocyclic ring is induced towards the maximum electrostatic interaction between the host and guest molecules.

These results demonstrate that the potential map is a valuable tool for a better understanding of the nature of the CD-guest interactions. It is of great interest to apply the present method to a variety of problems concerning host-guest, and more generally donor-acceptor interactions.

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10) Positive and negative potentials correspond to the repulsive and attractive forces between the probe(positive) charge and the molecular charge distribution, respectively.
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12) According to Ref. 6, the CNDO/2 method underestimates the depth of potential wells compared with ab initio methods. Thus, one should pay main attention to the relative magnitudes rather than the absolute values of potential obtained.
13) The orientations of the guest molecules are described in Ref. 9.

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