

# Simulation of the physisorption of linear molecules in $\beta$ -cyclodextrin

E. Alvira

Received: 15 May 2006 / Accepted: 20 October 2006 / Published online: 8 February 2007  
© Springer Science+Business Media B.V. 2007

**Abstract** To simulate the interaction energy between  $\beta$ -cyclodextrin and some linear molecules, a model was constructed from a simple pairwise-additive Lennard–Jones potential combined with a continuum description of the cyclodextrin cavity and of the guest molecule. Depending on the molecular length, one or two pairs of potential parameters are needed to reproduce the main features of the physisorption energy obtained by the all atoms model. From the continuum model, the relationship between the microscopic interaction energy and the macroscopic structural parameters of the molecules can also be established.

**Keywords** Continuum model · Cyclodextrin cavity · Linear guest molecule · Simulation · van der Waals interactions

## Introduction

The interactions between  $\beta$ -cyclodextrin ( $\beta$ -CD) and linear guest molecules of different sizes and compositions were previously investigated, by a model considering the interaction energy as made up of contributions from van der Waals, hydrogen-bonding and electrostatic functions, as in the AMBER force field. In these studies, the potential surfaces, energies and configurations of several inclusion complexes were obtained describing the  $\beta$ -CD and guest molecules by all atoms [1, 2]. The model presented in this work does

not consider the molecules as consisting of rigid spherical particles (atoms or assemblies of atoms) but as continuum distributions of matter (without electrical charge) [3–6], and this assumption has two advantages: it can be applied to many kind of systems and extends the information of the system, relating a microscopic property (such as the interaction energy) with macroscopic properties (such as the structural parameters of the molecules). Also, the suitability of the interaction potential proposed in this work is demonstrated by comparing the results obtained by this model for different linear molecules with those obtained by a force-field method [1, 2].

## The model

The guest-CD interaction is simulated by an average of the interaction energy, represented by the van der Waals contribution, over the uniformly distributed atoms in the CD and in the linear molecule. If we make the approximation of replacing the discrete summation by means of a continuous integration, the interaction energy  $W$  can be calculated as:

$$W(\vec{r}_0, \theta, \varphi) = \rho_{\text{CD}} \rho_{\text{mol}} \sqrt{1 + \alpha^2} \int_{-\frac{h}{2}}^{\frac{h}{2}} dl \int_0^{2\pi} dv \int_a^b V(\vec{r}_0, \theta, \varphi, l, u, v) u du \quad (1)$$

where  $\rho_{\text{CD}}$  is the superficial density of atoms in the CD cavity ( $\rho_{\text{CD}} \approx 0.73 \text{ \AA}^{-2}$ ),  $\rho_{\text{mol}}$  is the linear density of atoms in the guest molecule,  $L$  is the length of the linear molecule,  $h$  is the axial length of the CD,  $b$  the

E. Alvira (✉)  
Departamento de Física Fundamental II, Universidad de La Laguna, La Laguna, 38206 Tenerife, Spain  
e-mail: malvira@ull.es

radius of the base and  $a$  the radius of the top of the  $\beta$ -CD truncated cone ( $b \approx 5 \text{ \AA}$  and  $a \approx 4 \text{ \AA}$ ) [7],  $\alpha = -7$  ( $\alpha = h/(a-b)$ ) is a parameter derived from the geometry of the  $\beta$ -CD cavity [3] and  $V$  is a simple pairwise-additive Lennard–Jones potential. The  $Z$ -axis is collinear with the cone axis (thus the  $XY$  plane is parallel to the cone base), and the origin of the coordinates lies at the centre of mass of the cavity (which does not correspond to  $h/2$ ). For the conical surface we used a parametric representation [8, 3]:

$$\vec{r}(u, v) = u \cos v \vec{i} + u \sin v \vec{j} + \alpha(a - u) \vec{k} \quad (2)$$

For the linear molecule we also use a parametric representation [8]:

$$\begin{aligned} \vec{r}_l(\vec{r}_0, \theta, \varphi) = & (x_0 + l \sin \theta \cos \varphi) \vec{i} \\ & + (y_0 + l \sin \theta \sin \varphi) \vec{j} \\ & + (z_0 + l \cos \theta) \vec{k} \end{aligned} \quad (3)$$

where  $\vec{r}_0 = (x_0, y_0, z_0)$  is the position of the guest's centre of mass and the angles  $(\theta, \varphi) \in [0, \pi] \times [0, 2\pi]$  define the orientation of the molecule with respect to the absolute frame  $(X, Y, Z)$ .

The interaction energy  $W(\vec{r}_0, \theta, \varphi)$  depends on the configuration of the linear molecule  $(\vec{r}_0, \theta, \varphi)$ , and on its structural parameters, such as the length  $L$  and the composition and distribution of atoms on the molecule, characterized by  $\rho_{\text{mol}}$  and the  $\sigma$  and  $\varepsilon$  parameters of the Lennard–Jones potential corresponding to the interaction between the atoms of the CD and the molecule.

In order to reproduce the main features of the van der Waals interaction between  $\beta$ -CD and the linear guest molecule obtained by the all atoms method, we analysed two possibilities: the simplest case, where the interaction between the atoms is represented by one pair values  $(\sigma, \varepsilon)$  for the potential parameters, and the case where the interactions are represented by two different pairs  $(\sigma_1, \varepsilon_1)$ ,  $(\sigma_2, \varepsilon_2)$  (being  $\sigma_1 \leq \sigma_2$ ). In this last case, a new parameter,  $p$ , is required to symbolize the rate of each pair that expresses the composition of the molecule:  $0 \leq p \leq 1$ ,  $p = 0$  the interaction is represented by the values  $(\sigma_2, \varepsilon_2)$  and  $p = 1$  corresponds to the pair  $(\sigma_1, \varepsilon_1)$ . Due to the asymmetry of the guest molecule in this case, the polar angle formed with the cavity axis  $\theta$  ( $\theta \in [0, \pi]$ ) is related to the orientation of the linear molecule with respect to the cavity: if  $\theta < 90^\circ$ , the part of the molecule with values  $(\sigma_1, \varepsilon_1)$  is pointing to the top of the cone, if  $\theta > 90^\circ$  this part is pointing to the base.

## Results and discussion

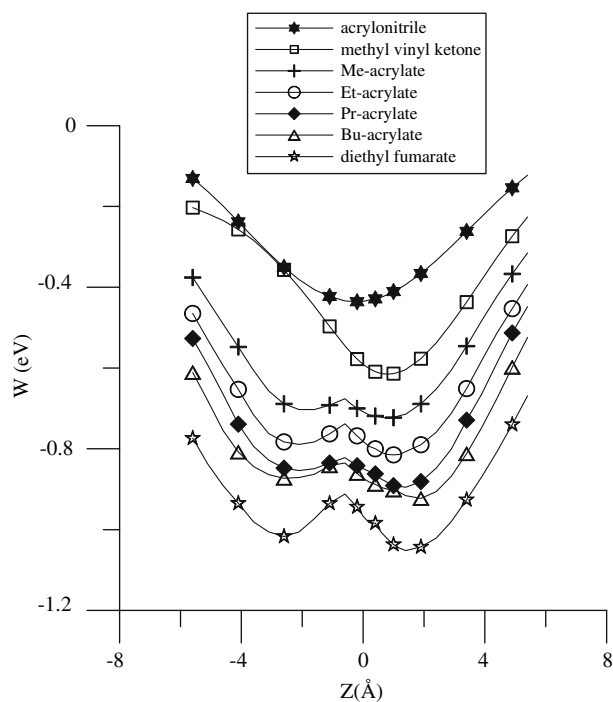
The interactions between  $\beta$ -CD and several linear molecules (acrylonitrile, methyl vinyl ketone, diethyl fumarate, methyl-, ethyl-, propyl- and butyl- acrylate) were previously investigated using a model based on the all atoms methods. The obtained results were represented in terms of potential energy surfaces, penetration potentials and inclusion complex configurations [1, 2]. The curve defined by the positions  $(X, Y)$  for every plane  $Z = \text{constant}$ , in which the potential  $W$  is minimum, characterizes the penetration trajectory and the curve joining these minima for every plane  $Z = \text{constant}$  is the penetration potential. The position and orientation of the guest molecule for which we obtain the absolute minimum potential energy gives the geometry of the guest in the inclusion complex. The potential energy surfaces were represented by partitioning the variation range of the  $Z$ -axis in the  $\beta$ -CD cavity into four parts, depending on the position of the centre of mass of the guest molecule: near the top of the cone (region I), near the centre of the cavity (regions II and III) and near the cone base (region IV).

When we apply the continuum model to the same molecules we observe that it can reproduce the main results of the all atoms model: the order of magnitude of the interaction energy (with an error of about 2.5%), the shape of the penetration potential, the configurations of the inclusion complexes (orientation of the linear molecule and approximate position of its centre of mass) and the main features of potential energy surfaces. Thus, in Table 1 the numerical results of the continuum model are included along with some parameters that simulate the interaction with the guest molecules  $(p, \sigma, \varepsilon)$ . Fig. 1 shows the penetration potentials obtained. The following features can be pointed out:

(a) For linear molecules with length  $L < 6 \text{ \AA}$  (acrylonitrile and methyl vinyl ketone) only one pair of potential parameters  $(\sigma, \varepsilon)$  were needed to reproduce the main features of the physisorption energy. From the results obtained by the all atoms model [1, 2], the parameters used in the simulation of acrylonitrile and methyl vinyl ketone were derived, because the role of the potential parameters in the interaction energy  $W$  is similar to that in the Lennard–Jones potential between a pair of atoms:  $\varepsilon$  governs the strength of the interaction and  $\sigma$  is related to the position of the minimum energy ( $r_{\text{min}} = 1.12 \sigma$ ) [9]. By the continuum model, the variation in the potential energy along the cavity axis was found to resemble a potential well, in agreement with the results obtained by the all atoms model.

**Table 1** Minimum of potential energy  $W$  inside the cavity for some linear molecules and parameters used in the continuum model

Guest molecule	$L$ (Å)	$p$	$\sigma_1$ (Å)	$\varepsilon_1$ (eV)	$\sigma_2$ (Å)	$\varepsilon_2$ (eV)	Position A				Position B			
							$d$ (Å)	$Z$ (Å)	$\theta$ (rad)	$W$ (eV)	$d$ (Å)	$Z$ (Å)	$\theta$ (rad)	$W$ (eV)
Acrylonitrile	4.5	-	3.0	0.003	-	-	1.3	-0.2	0.209	-0.436	-	-	-	-
Methyl vinyl ketone	4.5	-	4.2	0.0015	-	-	-	-	-	-	0.0	0.8	0.000	-0.615
Methyl acrylate	6.0	0.70	2.7	0.003	3.7	0.004	0.8	-1.6	0.314	-0.703	1.2	0.8	2.722	-0.724
Ethyl acrylate	6.5	0.75	2.7	0.003	3.7	0.005	0.9	-2.1	0.314	-0.789	1.2	1.0	2.722	-0.815
Propyl acrylate	7.5	0.80	2.7	0.004	3.7	0.005	1.1	-2.1	0.209	-0.854	1.4	1.4	2.722	-0.895
Butyl acrylate	8.0	0.90	2.7	0.004	3.7	0.009	1.2	-2.6	0.209	-0.873	1.6	1.9	2.722	-0.923
Diethyl fumarate	10.0	0.60	2.5	0.003	3.5	0.004	1.0	-2.6	0.419	-1.017	1.5	1.4	2.722	-1.052

**Fig. 1** The penetration potential obtained with the continuum model for different linear molecules

In the cases of acrylonitrile and methyl vinyl ketone, the interaction energy can also be represented by two parameter pairs such as  $(\sigma_1 = 2.3 \text{ \AA}, \varepsilon_1 = 0.005 \text{ eV})$ ,  $(\sigma_2 = 2.5 \text{ \AA}, \varepsilon_2 = 0.006 \text{ eV})$ ,  $p = 0.4$  and  $(\sigma_1 = 2.5 \text{ \AA}, \varepsilon_1 = 0.005 \text{ eV})$ ,  $(\sigma_2 = 2.7 \text{ \AA}, \varepsilon_2 = 0.006 \text{ eV})$ ,  $p = 0.5$  respectively.

(b) For linear molecules with length  $L \geq 6 \text{ \AA}$  (acrylic esters and diethyl fumarate), two pairs of potential parameters  $(\sigma_1, \varepsilon_1)$ ,  $(\sigma_2, \varepsilon_2)$  were needed to reproduce the main features of the physisorption energy obtained by the all atoms model. The penetration potential presents two minima inside the cavity (position A for  $Z < 0$  and position B for  $Z > 0$ ), separated by a potential barrier associated with a rotation of the linear molecule of about  $180^\circ$  with respect to the cavity axis. For these molecules, the parameters that simulate the

interaction with the CD  $(p, \sigma, \varepsilon)$  have a decisive influence on the depths or the positions of the minima, but the relation with them is not as direct as in the case of one pair of potential parameters.

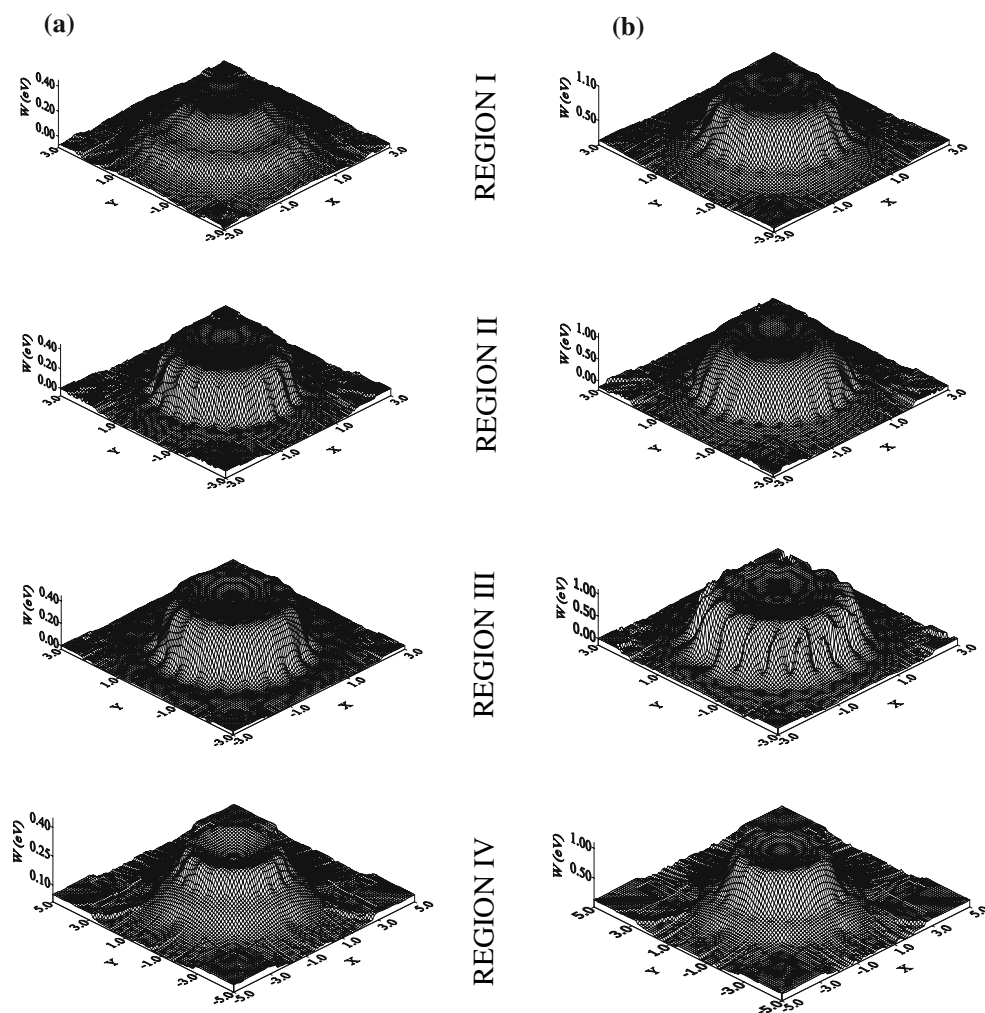
The values of  $\sigma_1$  and  $\sigma_2$  are the same for the different acrylic esters, but different  $\varepsilon_1$  and  $\varepsilon_2$  parameters have been necessary to reproduce the magnitude of the interaction energy. The parameter  $p$  increases with molecular length  $L$ . As it represents the degree to which each pair  $(\sigma_1, \varepsilon_1)$  and  $(\sigma_2, \varepsilon_2)$  expresses the composition of the molecule, it seems that the values  $\sigma_1$  and  $\varepsilon_1$  characterize the interaction between the acrylic ester and  $\beta$ -CD to a higher degree. This result together with the orientation of the guest molecule in the minima of potential energy inside the cavity [1] imply that the values  $(\sigma_1, \varepsilon_1)$  represent the interaction between the acrylic ester radical and  $\beta$ -CD.

The interaction potential for diethyl fumarate shows the highest potential barrier inside the cavity and the deepest minima of the energy. This is due to the confluence of three factors: the highest molecular length  $L$ , lowest parameter  $p$  and the difference between  $\sigma_1$  and  $\sigma_2$ .

(c) Concerning the orientation of the guest in the inclusion complex (Table 1), the angle formed with the cavity axis is about  $24^\circ$ , similar to the angle obtained by the force-field method ( $30^\circ$ ). The main discrepancies between the intermolecular potential presented in this work and that computed by the all atoms model derive from the position of the guest's centre of mass in the configuration of the inclusion complex. In the continuum model the  $Z$  coordinate of the absolute energy minimum is nearer to the cavity centre than to the base of the cone, and, moreover, this model is only able to reproduce the position in the plane  $Z = \text{constant}$  by the distance from the cavity axis  $d$ , instead of the  $(X, Y)$  coordinates.

For guest molecules with length  $L \geq 6 \text{ \AA}$  the section of the molecule characterized by parameters  $\sigma_1$  and  $\varepsilon_1$  is pointing towards the smaller top of the conical cavity in position A; in position B this section is pointing

**Fig. 2** Potential energy surfaces for **(a)** acrylonitrile, and **(b)** diethyl fumarate



towards the larger base of the  $\beta$ -CD. Taking into account the length of the molecule and the Z coordinate of its centre of mass in positions A and B, it seems that the part of the molecule characterized by parameter  $\sigma_2$  ( $\sigma_2 > \sigma_1$ ) is included into the cavity. The parameter  $\sigma$  of the Lennard–Jones potential reflects the size of particles when they approach each other [9], therefore it can be concluded that the guest tends to introduce the atoms with bigger size into the cavity, probably to achieve maximum contact between the molecule and the internal surface of the CD cavity and then to minimize the interaction energy.

Figure 2a shows the potential energy surfaces for acrylonitrile and Fig. 2b for diethyl fumarate. The following features can be pointed out:

(a) The potential surfaces have a more corrugated shape as the size of the guest ( $L$  or parameters related with composition) increases, as in the all atoms model.

(b) The size of the regions where the energy is attractive (or repulsive) is similar for different parameters, which is a consequence of the cavity geometry and the effective structural parameters of the  $\beta$ -CD.

(c) The main discrepancy occurs in the potential surface of the region I, because the circular symmetry observed for points located at the same distance  $d$  from the cavity axis is a consequence of the continuum model, which cannot distinguish the different points  $(x_0, y_0)$  on the surface  $Z = \text{constant}$  such that  $x_0^2 + y_0^2 = d^2$ .

The agreement observed between the results obtained with the continuum and all atoms methods confirms the suitability of the parameters selected for the cavity and guest molecules.

**Acknowledgments** We are grateful to the Ministerio de Educación y Ciencia and FEDER (FIS2005–02886) for their generous financial support.

## References

1. Alvira, E., Mayoral, J.A., García, J.I.: A model for the interaction between  $\beta$ -cyclodextrin and some acrylic esters. *Chem. Phys. Lett.* **25**, 335–342 (1995)
2. Alvira, E., García, J.I., Mayoral, J.A.: Factors influencing  $\beta$ -cyclodextrin inclusion complex formation. *Recent Res. Devel. Chem. Phys.* **1**, 89–100 (2000)
3. Alvira, E.: Physisorption in cyclodextrin cavities: an analytical model. *Chem. Phys. Lett.* **267**, 221–228 (1997)
4. Peterson, B.K., Gubbins, K.E., Heffelfinger, G.S., Marini, U., Marconi, B., van Swol, F.: Lennard-Jones fluids in cylindrical pores: nonlocal theory and computer simulation. *J. Chem. Phys.* **88**, 6487–6500 (1988)
5. Derycke, I., Vigneron, J.P., Lambin, Ph., Lucas, A.A., Derouane, E.G.: Physisorption in confined geometry. *J. Chem. Phys.* **94**, 4620–4627 (1991)
6. Alvira, E., Breton, J., Delgado, V., Girardet, C.: Interaction between an atom and a mesoscopic helieoidal system. Fourier-transform analysis. *J. Chem. Phys.* **97**, 6821–6828 (1992)
7. Szejtli, J.: Cyclodextrins and their inclusion complexes. Akademiai Kiado, Budapest (1982)
8. Apostol, T.M.: *Calculus*. Editorial Reverte, Barcelona (1976)
9. Hirschfelder, J.O., Curtiss, C.F., Bird, R.B.: *Molecular theory of gases and liquids*. John Wiley and Sons, New York (1967)