DFT calculation of α-cyclodextrin dimers. Contribution of hydrogen bonds to the energy of formation

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The structures and energies of formation of α-cyclodextrin (α-CD) dimers formed according to the "head-to-head" (HH), "head-to-tail" (HT), and "tail-to-tail" (TT) modes, harmonic vibrational frequencies, and intensities of IR bands of the IR transitions were calculated by the DFT/PBE density functional method with full geometry optimization without symmetry restrictions. The spectral data were transformed into spectral patterns. An α-CD molecule can exist in two isomeric forms close in energy, namely, α-CD$^-$ and α-CD$^+$, with different directions of the ring intramolecular hydrogen bonds. Among the three α-CD$^-$ dimers, the highest dimerization energy (E_d/kcal mol^{-1}) belongs to the HH$^-$ (68.9), TT$^-$ (43.4), and HT$^-$ (24.8) dimers. The strength of the α-CD$^+$ dimers decreases in the series: TT$^+$ (56.7), HT$^+$ (49.4), and HH$^+$ (42.4). The energies E_H of hydrogen bonds were calculated from the low-frequency shifts of bands of stretching vibrations of the OH groups involved in the formation of these hydrogen bonds. The E_H value for each dimer correlates with E_d. A possibility of formation of intermolecular hydrogen bonds is a driving force of association of α-CD molecules in aqueous solutions.

Key words: cyclodextrins, dimers, hydrogen bonds, quantum chemical calculations, density functional theory, theoretical IR spectra.

Cyclodextrins (CDs) are cyclic oligomers of α-(D)-glucose, whose structural units are linked to each other by 1,4-glycoside bonds. Three types of CDs are most abundant. Their molecules consist of six (α-CD), seven (β-CD), and eight (γ-CD) glucose units.[1a] Cyclodextrin molecules are basket-like shaped. According to DFT calculations,[2a] the average diameter of cavities in α-, β-, and γ-CDs is 4.6, 6.0, and 7.6 Å, respectively, the basket height for all CDs is the same: 9.0 Å. Presently, CDs are widely used as water-soluble mediators of bioactive compounds and drugs, whose molecules can insert into the hydrophobic cavity of CD to form inclusion compounds.[1a] Seemingly, rather small cavity volume should prevent the insertion of large molecules; however, the cavity sizes can increase due to the ability of CD molecules to association.[1b] So-called "molecular necklaces" [3] are of special interest. They are inclusion compounds in which the "guest" is a hydrophobic polymer chemically non-bonded with CD. In this case, several CD molecules are threaded on the polymeric chain to form tubular ordered structures, whose strength increases additionally due to the interaction of the CD molecules with each other. In particular, the formation of two tubular crystalline modifications I and II was observed[3] by the interaction of α-CD with poly(ethylene glycol). In modification I the α-CD molecules are linked according to the "head-to-head" (HH)/"tail-to-tail" (TT) type (a broader part of the conic basket is considered to be the "head," and the "tail" is the more narrow part). In modification II the α-CD molecules are linked mainly by the "head-to-tail" (HT) type, and the tubular structures formed in the presence of form I contain no polymeric chain inside. The existence of such empty tubes indicates strong intermolecular interactions between α-CDs. Among them the leading role belongs to intermolecular hydrogen bonds (H bonds)[3] formed between the hydroxyl groups that frame the upper broad and lower narrow rims of the cyclodextrin basket.[2a,4] The semiempirical quantum chemical PM3 calculation showed

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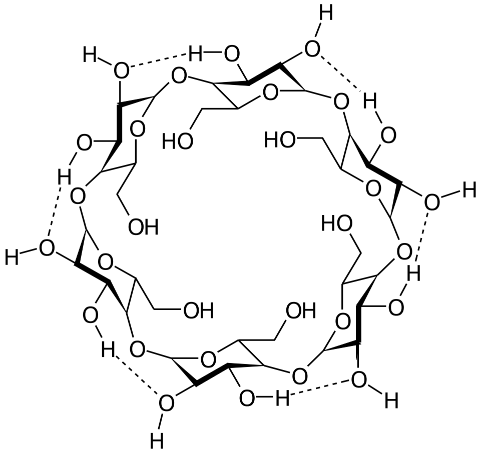
that the dimer of the HT type is more energetically favorable, because it was formed by the primary OH groups with higher proton affinity of the narrow part of the basket and the secondary OH groups of the broad part. The molecular mechanics (MM3) and molecular dynamics (AMBER* parametrization) calculations[5,6] of the α-, β-, and γ-CD dimers confirmed the higher thermodynamic stability of the HH dimers of α-CDs *in vacuo* and preference of the HT dimers in aqueous solutions. The later BLYP/6-31G(d,p)//PM3 calculations showed that the α-CD HH dimer is more preferential *in vacuo*, whereas an aqueous environment favors the stabilization of the HT and TT dimers.[7] Although the PM3 method makes it possible to calculate systems with the number of atoms up to thousand, desire to enhance the reliability of the results requires to use more accurate quantum chemical methods (in particular, density functional method (DFT)). For example, the DFT calculation[4] using the PBE functional[8] by the PRIRODA program[9] with full geometry optimization for free α-, β-, and γ-CD molecules made it possible to determine the relative thermodynamic stability of isomeric forms of these CDs. In the same work,[4] the authors used the calculated bathochromic shift of frequencies of stretching vibrations of the OH groups (ν_{OH}) involving the formation of the interglucose H bonds in the CDs to estimate the energy of these H bonds (4.5—4.9 kcal mol^{-1}). These values are realistic and allow us to hope that the energy of the intermolecular H bonds responsible for the formation of the α-CD dimers will be estimated with the same reliability and a basis for spectroscopic identification of associated CD forms will be created.

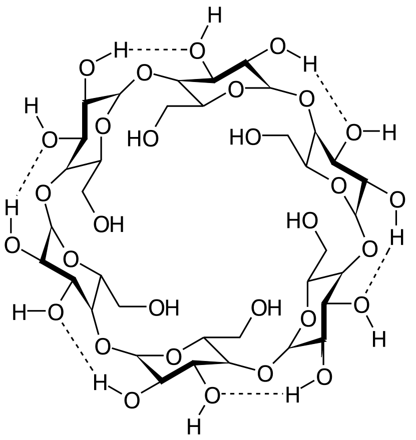
The purpose of the present work is the DFT calculation of the structures of α-CD dimers of the HH, HT, and TT types, which are the basis for tubular structures, and the energy of their formation, as well as the quantum chemical simulation of IR spectra of the dimers.

Objects of the study

An α-CD molecule consists of six glucose residues linked by 1,4-glycoside bonds. Interglucose H bonds (indicated by dotted lines in Fig. 1) impart additional stability to the α-CD basket. Each glycoside residue of α-CD contains three OH groups. For convenience let us call the OH groups in position 2 groups 2, the OH groups in position 3 will be groups 3, and the OH groups in position 6 will be groups 6. Due to the low barriers of OH-group rotation, their disordered orientations in solutions and solid phase can be infinitely numerous. Two types of ring H bonds are possible in the ordered α-CD structures.[2] Traditionally[2a] we call an α-CD "left-oriented" (α-CD$^-$) if group 3 acts as the proton donor and the O atom of group 2 of the adjacent glucose fragment is the proton donor. An α-CD in which group 2 acts as the proton donor and the oxygen atom of group 3 is the acceptor (see Fig. 1) will be named "right-oriented" (α-CD$^+$). The maximum difference in energies of these forms can be determined by the calculation of the ordered structures in which all OH groups have consistent orientation.



α-CD$^-$



α-CD$^+$

Fig. 1. Molecules of α-CDs with the left (–) and right (+) orientations of interglucose H bonds.

Our previous DFT/PBE calculations[4] showed that the α-CD$^-$ structure with the C_6 symmetry is the most thermodynamically stable monomeric CD form. The second isomeric α-CD$^+$ form, also with the C_6 symmetry, is less thermodynamically favorable: its enthalpy is by 0.5 kcal mol^{-1} higher. Evidently, this difference in energies is negligible. Nevertheless, dimers of six types can be built from these two structures: HH$^+$, HT$^+$, TT$^+$ (from α-CD$^+$) and HH$^-$, HT$^-$ and TT$^-$ (from α-CD$^-$), which can have substantially different relative energies due to different dimerization energies. In the present work, we do not consider mixed dimers and structures of monomeric α-CD forms closed from the narrow end due to the formation of ring H bonds by groups 6, because these forms are absent among more than 400 CD structures deposited with the Cambridge Structure Database.

Calculation procedure

Full geometry optimization of α-CD^+ and α-CD^- molecules and their dimers without symmetry restriction was performed as earlier[4] using the DFT/PBE method in the three-exponential basis set[10] by the PRIRODA program (version 110). The optimization was completed with the calculation of the Hessian and harmonic frequencies of normal vibrations in the mass-weighed coordinates and the intensities of IR bands. All the structures obtained were characterized by the set $3N - 6$ (N is the number of atoms in the structure) positive vibrational frequencies, which indicates that these structures belong to local minima on the potential energy surface. The ChemCraft program package[11] was used to visualize the obtained structures and IR spectra.

The dimerization energy (E_d) was calculated as a difference between the doubled values of the monomer energy (E^{CD}) and energy of the α-CD dimer (E^{dimer}) with correction to the zero-point vibration energy (ZPE)

$$E_d = 2(E_{total}^{CD} + ZPE^{CD}) - E_{total}^{dimer} - ZPE^{dimer}. \qquad (1)$$

Results and Discussion

Calculations showed that the dimerization energies range within 25—70 kcal mol^{-1}, which corresponds to 3.5—5.7 kcal mol^{-1} per each H bond. The energy values obtained are presented in Table 1.

The whole set of $3N - 6$ vibrational frequencies of α-CD (N is the number of atoms equal to 126 for the monomer and 252 for the dimer) is divided into three groups. The modes with the highest frequencies in the IR spectra (2800—3700 cm^{-1}) are highly characteristic and assigned to stretching vibrations involving hydrogen atoms ν_{C-H} (2800—3000 cm^{-1}) and ν_{O-H} (3000—3700 cm^{-1}). The vibrations with frequencies below 1700 cm^{-1} belong to the so-called "dactylograms" and are attributed to vibrations of the bonds and angles of the glucose fragments of the cage and here they are not discussed in detail.

As mentioned above, the CD molecule contains three sets of OH groups (groups 2, 3, and 6). Due to the symmetry of an α-CD molecule, the vibrational frequencies of the OH groups are very close in each set. According to this, six sets, each containing six frequencies, can be distinguished in the IR spectrum of the α-CD dimer consisting of 36 high-frequency modes. The relative error of the average frequency value in the set is 0.004 cm^{-1}, and the average difference ($2|\nu_1 - \nu_2|/(\nu_1 + \nu_2)$) between the series is 0.06 cm^{-1}. The difference of these two values by more than an order of magnitude confirms the assumption of the symmetry of the dimers. This makes it possible to believe that this division into series is statistically substantiated and, hence, one can work with sets of modes rather than with particular modes.

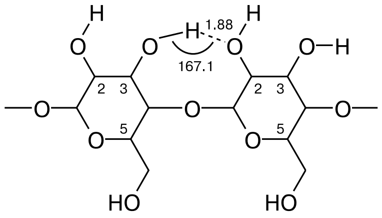
The elements of the α-CD^- and α-CD^+ structures are schematically shown in Fig. 2, and the average values of the geometric parameters of the interglucose H bonds are given in Table 2. In α-CD^- the H bond is slightly longer and the O—H...O angle by 4° less deviates from 180° (at which the H bond energy is considered to be maximum) compared to those in the α-CD^+ structure. These small values result, most likely, in the above mentioned low difference between the energies of the both forms of an α-CD molecule.

The fragments of the calculated IR spectra of α-CD^- and α-CD^+ are presented in Fig. 3. The bands at 3600 cm^{-1} are assigned to ν_{OH} of free hydroxyl groups 2 and 6. The intense band at ~3380 cm^{-1} corresponds to

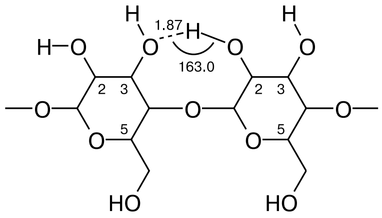
Table 1. Total energies (E_{total}), zero-point vibration energies (ZPE), and dimerization energies (E_d) calculated by the DFT/PBE method

Structure	$-E_{total}$	ZPE	E_d /kcal mol^{-1}
	au		
α-CD^-	3660.9061	1.0044	0
α-CD^+	3660.9053	1.0159	0.5*
HH^-	7321.9221	2.0209	68.9
HT^-	7321.8518	2.0112	24.8
TT^-	7321.8813	2.0155	43.4
HH^+	7321.8780	2.0112	42.4
HT^+	7321.8893	2.0149	49.4
TT^+	7321.9008	2.0156	56.7

* Difference in energies of two ordered α-CD forms.



α-CD^-



α-CD^+

Fig. 2. Scheme of formation of interglucose H bonds in an α-CD molecule; the length (Å) and angle (deg) for the H bond are presented here and in Figs 6 and 7.

Table 2. Ratio of the modulus of the difference between the principal moments of inertia to their sum (ΔM), the ellipticity of the baskets (ε), and the lengths of the O—H (r_{OH}) and H bonds (r_H)

Structure	ΔM	ε	r_{OH}/Å			r_H/Å		
			2	3	6	2	3	6
α-CD$^-$	$3\cdot10^{-4}$	1.0003	0.977	0.987	0.974	—	1.875	—
HH$^-$	$3\cdot10^{-5}$	1.0001	0.989	0.993	0.996	1.860	1.930	1.771
			0.988	0.993	0.996	1.860	1.930	1.772
HT$^-$	$6\cdot10^{-5}$	1.0006	0.949	0.959	0.959	—	1.814	1.866
			0.953	0.963	0.950	2.509	1.812	—
TT$^-$	$6\cdot10^{-3}$	1.0204	0.977	0.987	1.000	—	1.90	1.73
			0.977	0.984	1.000	—	2.1	1.71
α-CD$^+$	$1.5\cdot10^{-3}$	1.0001	0.990	0.978	0.974	1.870	—	—
HH$^+$	$2\cdot10^{-4}$	1.0006	1.000	0.992	0.974	1.763	1.807	—
			1.000	0.992	0.974	1.763	1.806	—
HT$^+$	$1.3\cdot10^{-4}$	1.0003	0.989	0.978	0.991	1.878	—	1.858
			1.006	1.005	0.974	1.681	1.666	—
TT$^+$	$1.3\cdot10^{-4}$	1.0007	0.990	0.978	1.009	1.838	—	1.658
			0.989	0.978	1.002	1.902	—	1.611

Note. The relative error of the O—H bond lengths for averaging of all the dimers under study is $5\cdot10^{-4}$, and its maximum value is $6\cdot10^{-3}$. The relative error of the H bond lengths for averaging is $3\cdot10^{-3}$, and its maximum value is $1\cdot10^{-2}$.

ν_{OH} of secondary OH groups 3 in the broad part of the cavity. These groups participate in the formation of the interglucose H bonds. The IR spectrum of α-CD$^+$ is similar. However, OH groups 3 and 6 are free in this case, whereas OH groups 2 are H-bonded.

When H bonds are formed, the vibrational frequencies of the OH groups involved in the H bonds undergo the bathochromic shift. This shift correlates[12] with the energy of the H bond (E_H), which can be calculated by the formula

$$E_H = (1/3)(\Delta\nu_{OH} - 40\ \text{cm}^{-1})^{0.5}, \qquad (2)$$

where

$$\Delta\nu_{OH} = \nu_{OH}{}^{\text{free}} - \nu_{OH}{}^{\text{bonded}} \qquad (3)$$

is the long-wavelength shift of the vibrational frequency of the OH group, whose H atom participates in the H bond. The highest of all the found frequencies (ν_{OH}) non-bonded through the H bond ($\nu_{OH}{}^{\text{free}} = 3683\ \text{cm}^{-1}$) was chosen as a frequency of the free OH group relative to which all bathochromic shifts were calculated.

The plots of the calculated energies of H bonds *vs.* their lengths are shown in Fig. 4. As should be expected,

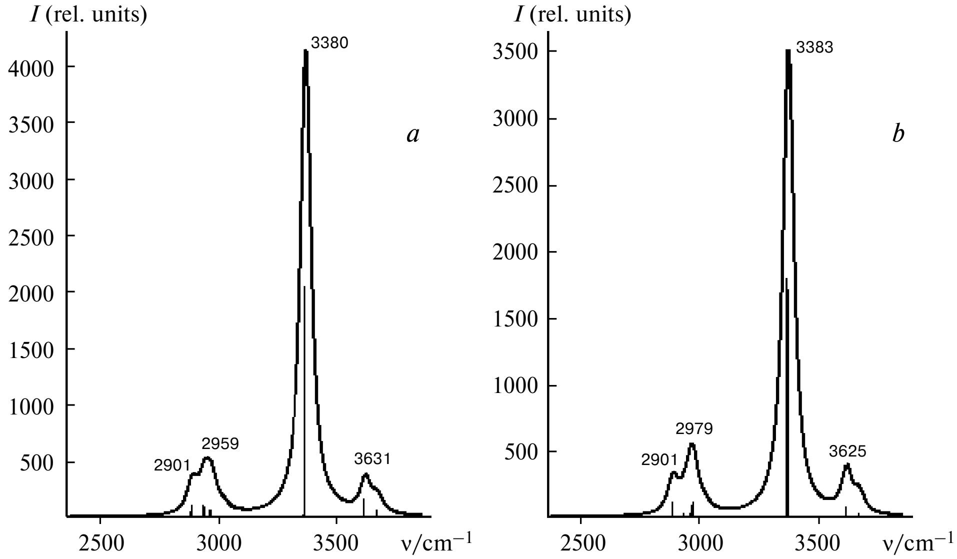


Fig. 3. Fragments of the IR spectra of α-CD$^-$ (*a*) and α-CD$^+$ (*b*) calculated by the DFT/PBE method.

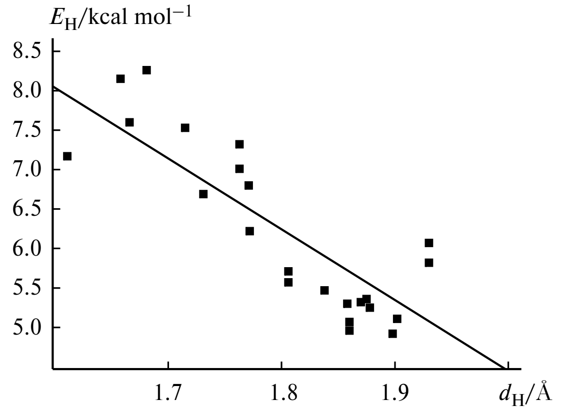


Fig. 4. Plots of the energy of hydrogen bonds *vs*. their length. Correlation coefficient is $R \approx 0.87$.

the shorter is the distance, the stronger is the bond. The general agreement of the data (correlation coefficient $R = 0.87$) is satisfactory and indicates that the chosen calculation method is appropriate.

The total energy of H bonds in the α-CD monomers and dimers can be obtained summating the $E_H{}^i$ values for all the OH groups (18 groups for the monomers and 36 monomers for the dimers). Due to the C_6 symmetry of an α-CD molecule, the calculation can be simplified going from summation over all OH groups (index *i*) to the summation over sets of groups (index *k*):

$$E_H^{CD} = \sum_{i=1}^{18}\frac{1}{3}(\Delta\nu_{OH}^i - 40\text{ cm}^{-1})^{0.5} = \sum_{k=1}^{3}\frac{1}{3}(\Delta\nu_{OH}^k - 40\text{ cm}^{-1})^{0.5}, \tag{4a}$$

$$E_H^{\text{dimer}} = \sum_{i=1}^{36}\frac{1}{3}(\Delta\nu_{OH}^i - 40\text{ cm}^{-1})^{0.5} = \sum_{k=1}^{6}\frac{1}{3}(\Delta\nu_{OH}^k - 40\text{ cm}^{-1})^{0.5}. \tag{4b}$$

Then the change in the total energy of H bonds upon dimerization is determined by the formula

$$\Delta E_H^{\text{dimer}} = 2E_H^{CD} - E_H^{\text{dimer}}. \tag{5}$$

Thus calculated $\Delta E_H{}^{\text{dimer}}$ values (Table 3) range from 25 to 132 kcal mol^{-1}. The vibrational frequencies of the OH groups and the corresponding energies of the H bonds are also given in Table 3.

The fragments of the calculated IR spectra of the HH$^-$, HT$^-$, and TT$^-$ dimers are shown in Fig. 5. The HH$^-$ dimer is characterized by three bands in the region of vibrations of OH groups. The band at 3423 cm^{-1} corresponds to ν_{OH} of the secondary OH groups forming intermolecular H bonds, the band at 3335 cm^{-1} is attributed to the OH groups forming the interglucose H bonds in the monomer, and the band at 3241 cm^{-1} is assigned to OH groups 6 forming two additional rings of H bonds that are absent from other structures. Just the formation of these rings result in the strong shift of the latter band corresponding to the strongest H bonds. In the HT$^-$ and TT$^-$ dimers, the bands at 3631 and 3649 cm^{-1}, respec-

Table 3. Calculated vibrational frequencies of the OH groups (cm^{-1}) and the energies of H bonds in the α-CD dimers (kcal mol^{-1})[a]

Structure	$E_H{}^{CD/dimer}$	$\Delta E_H{}^{dimer}$	Position[b]	$\bar{\nu}_{OH}$	$\Delta\nu_{OH}$	E_H
α-CD$^-$	38.7(2)	—	2	3629(2)	51	1.0(0)
			3	3382(7)	298	5.4(1)
			6	3679(0)	0	0.0(0)
HH$^-$	209.6(6)	132.3(6)	2	3419(3)	261	5.0(0)
			2	3409(2)	271	5.1(0)
			3	3336(6)	344	5.8(1)
			3	3308(1)	372	6.1(0)
			6	3292(8)	388	6.2(1)
			6	3220(27)	457	6.8(2)
HT$^-$	102.8(8)	25.5(9)	2	3626(0)	54	7.4(0)
			2	3458(3)	222	27.0(0)
			3	3372(7)	308	32.8(1)
			3	3320(35)	358	35.7(3)
			6	3675(0)	5	0.0(0)
			6	3653(0)	26	0.0(0)
TT$^-$	138(2)	60(2)	2	3653(1)	26	0.0(0)
			2	3645(6)	35	0.0(0)
			3	3510(35)	170	3.8(5)
			3	3422(13)	258	4.9(2)
			6	3240(30)	443	6.7(2)
			6	3130(50)	550	7.5(4)
α-CD$^+$	39.4(2)	—	2	3385(7)	295	5.3(1)
			3	3625(1)	54	1.3(0)
			6	3680(0)	0	0.0(0)
HH$^+$	153.6(3)	74.8(3)	2	3198(12)	482	7.0(1)
			2	3158(3)	522	7.3(0)
			3	3361(5)	319	5.6(1)
			3	3347(2)	333	5.7(0)
			6	3683(0)	3	0.0(0)
			6	3682(0)	3	0.0(0)
HT$^+$	65.9(3)	87.1(3)	2	3392(7)	288	5.3(1)
			2	3027(7)	653	8.3(1)
			3	3626(0)	54	1.3(0)
			3	3119(1)	560	7.6(0)
			6	3678(1)	2	0.0(0)
			6	3387(4)	293	5.3(1)
TT$^+$	170.8(12)	91.9(12)	2	3405(6)	275	5.1(1)
			2	3371(7)	309	5.5(1)
			3	3630(0)	49	1.0(0)
			3	3618(0)	62	1.6(1)
			6	3178(11)	502	7.2(1)
			6	3040(70)	637	8.2(5)

[a] Standard deviations of the values are given in parentheses.

[b] The position of the OH group in the glucose residue.

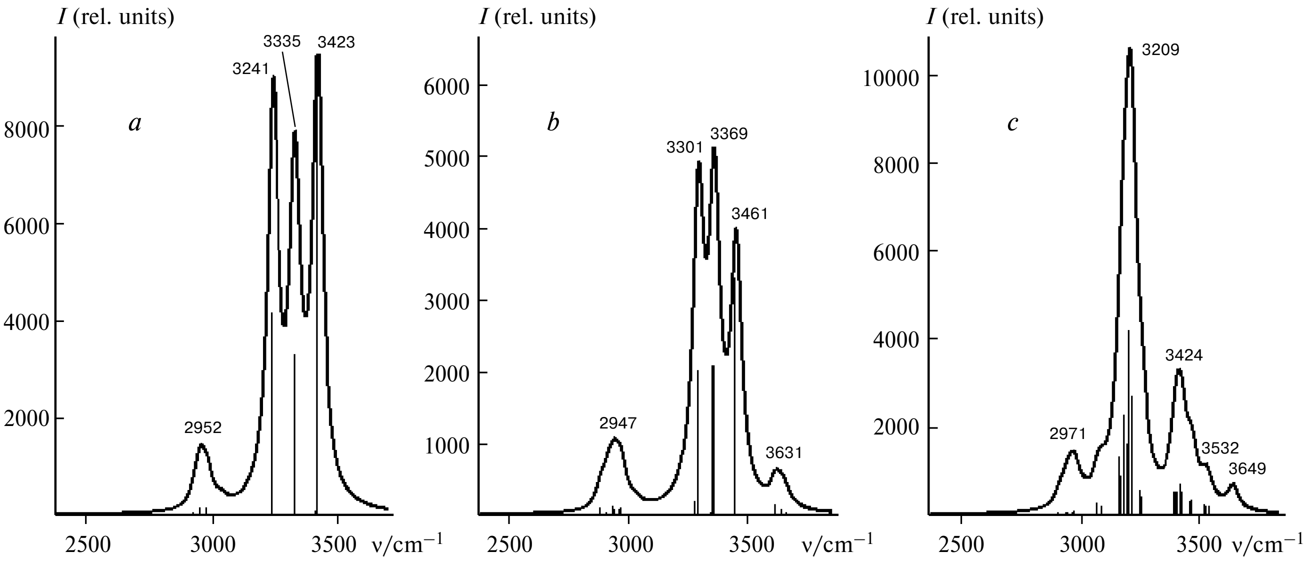


Fig. 5. Fragments of the IR spectra of the HH^- (*a*), HT^- (*b*), and TT^- (*c*) dimers calculated by the DFT/PBE method. Here and in Fig. 8 the frequencies of absorption band maxima in the spectral patterns somewhat differ from the average values of the calculated frequencies (see Table 1), because the envelope of bands of the OH groups corresponds to the band maximum in the spectral pattern.

tively, correspond to vibrations of free OH groups. For the TT^- dimer these are secondary OH groups, and for HT^- these are primary OH groups 3 for one α-CD molecule and secondary for another α-CD molecule. The bands at 3301 and 3369 cm^{-1} are attributed to the interglucose H bonds of the HT^- dimer, and for the TT^- dimer these are the bands at 3424 and 3532 cm^{-1}. The bands at 3461 cm^{-1} and 3209 cm^{-1} correspond to vibrations of the OH groups forming intermolecular H bonds in the HT^- and TT^- dimers, respectively. Thus, the HH^- dimer is most stable compared to other structures due to 12 additional H bonds in the tail parts of the molecules.

The schemes of the H bonded groups in the α-CD$^-$ and α-CD$^+$ dimers are shown in Figs 6 and 7, respectively. The fragments of the IR spectra of the HH^+, HT^+, and TT^+ dimers calculated in the present work are presented in Fig. 8. The calculation for the HH^+ and TT^+ dimers gives two bands at 3370 and 3194 cm^{-1} in the region of vibrations of the OH groups involved in the formation of intermolecular H bonds. The first of these bands is assigned to ν_{OH} of the groups forming the interglucose H bonds, and the second band corresponds to ν_{OH} of the groups providing joining of two α-CD monomers into a dimer. Since the last band is strongly shifted to the long-wavelength spectral region, a stronger H bond corresponds to this band (see Table 3). Three intense bands at 3392, 3120, and 3022 cm^{-1} are obtained in the region of frequencies of OH groups involved in H-bond formation by the calculation of the IR spectrum of the HT^+ dimer. Evidently, the first band corresponds to the interglucose H bonds, because its position is close to the absorption observed for the monomeric form of α-CD$^+$. The band at 3120 cm^{-1} is attributed to ν_{OH} of secondary OH group 3. The band at 3022 cm^{-1} corresponds to ν_{OH} of primary OH group 6. Such a mutual arrangement of the bands means that the primary OH group is a stronger H donor than the secondary group and, therefore, forms a stronger H bond, which is characterized by the greater long-wavelength shift of the band.

Thus, the most stable is the HH^- dimer in which each OH group participates in H-bond formation. The structures of the HT^+ and TT^+ types are less favorable. They are characterized by a strong shift of one band corresponding to the OH groups involved in the formation of intermolecular H bonds. The other dimers are less stable.

The geometry optimization of α-CD molecules performed in the present work showed that they have the C_6 symmetry, which agrees with the results of previous quantum chemical calculations.[2] The optimized dimeric structures also possess high symmetry: the HH and TT dimers have the D_6 symmetry, and the HT dimers are of C_6 symmetry. To prove the symmetry of the molecule, we used the ratio of the module of the difference in the principal moments of inertia to their sum $\Delta M = |M_x - M_y|/(M_x + M_y)$. Evidently, for symmetric structures the ΔM value should identically be equal to zero. For the α-CD monomer ΔM is $3 \cdot 10^{-4}$ and that for the dimers it is $(0.3—60) \cdot 10^{-4}$, which confirms high symmetry of these structures. Some geometric parameters of the calculated dimeric structures are presented in Table 2.

Ellipticity of CD molecules characterizes the degree to which the shape of the cross section of the CD basket differs from circle. It is calculated by the formula $\varepsilon = d_{max}/d_{min}$, where d_{max} and d_{min} are the maximum and minimum diameters of the pseudocycle formed by the

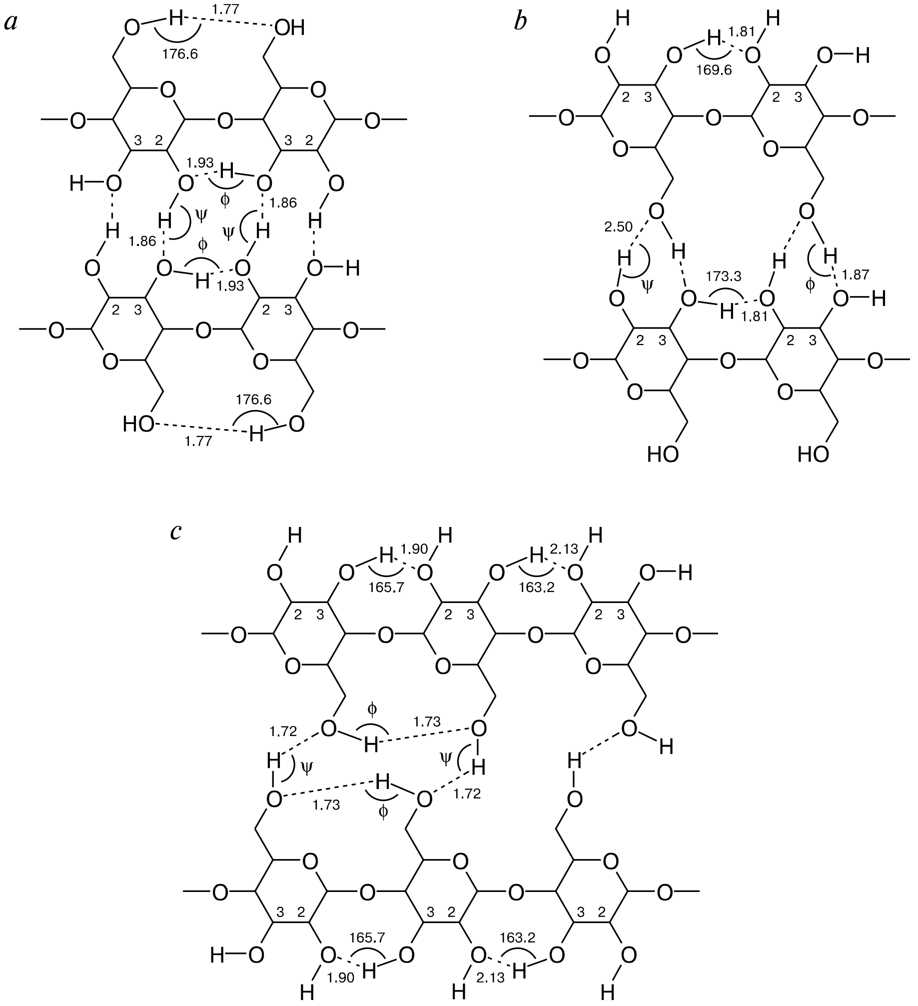


Fig. 6. Scheme of fragments of the α-CD^- dimers: HH^- dimer, $\phi = 171.6°$, $\psi = 148.4°$ (*a*); HT^- dimer, $\phi = 139.9°$, $\psi = 111.9°$ (*b*); TT^- dimer, $\phi = 166.9°$, $\psi = 163.2°$ (*c*).

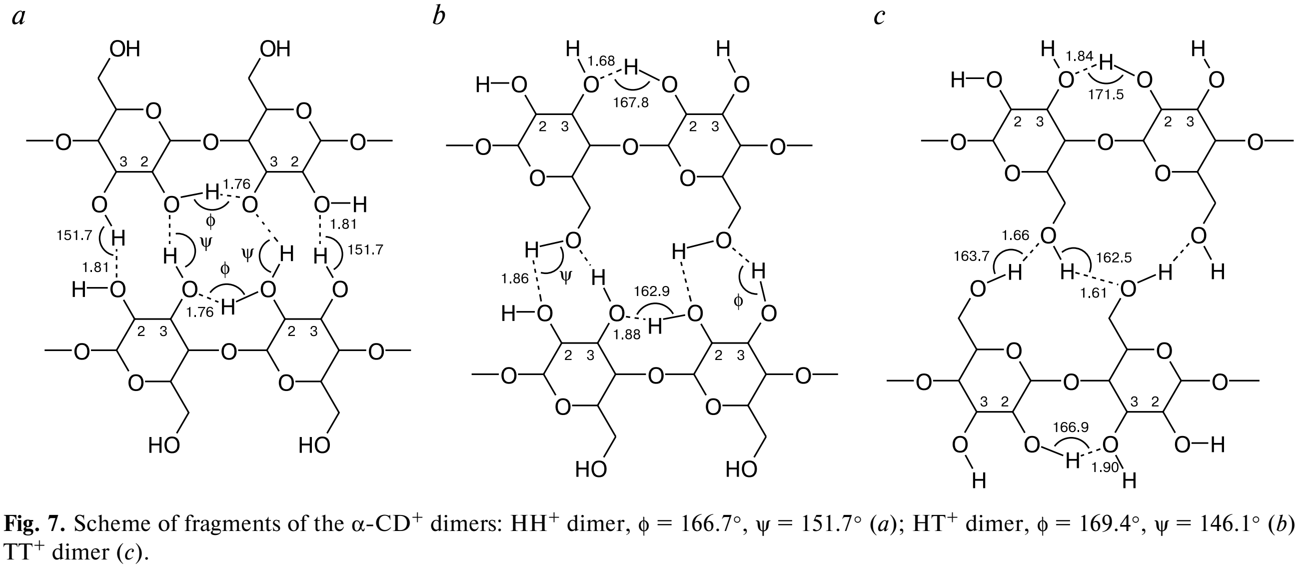


Fig. 7. Scheme of fragments of the α-CD^+ dimers: HH^+ dimer, $\phi = 166.7°$, $\psi = 151.7°$ (*a*); HT^+ dimer, $\phi = 169.4°$, $\psi = 146.1°$ (*b*); TT^+ dimer (*c*).

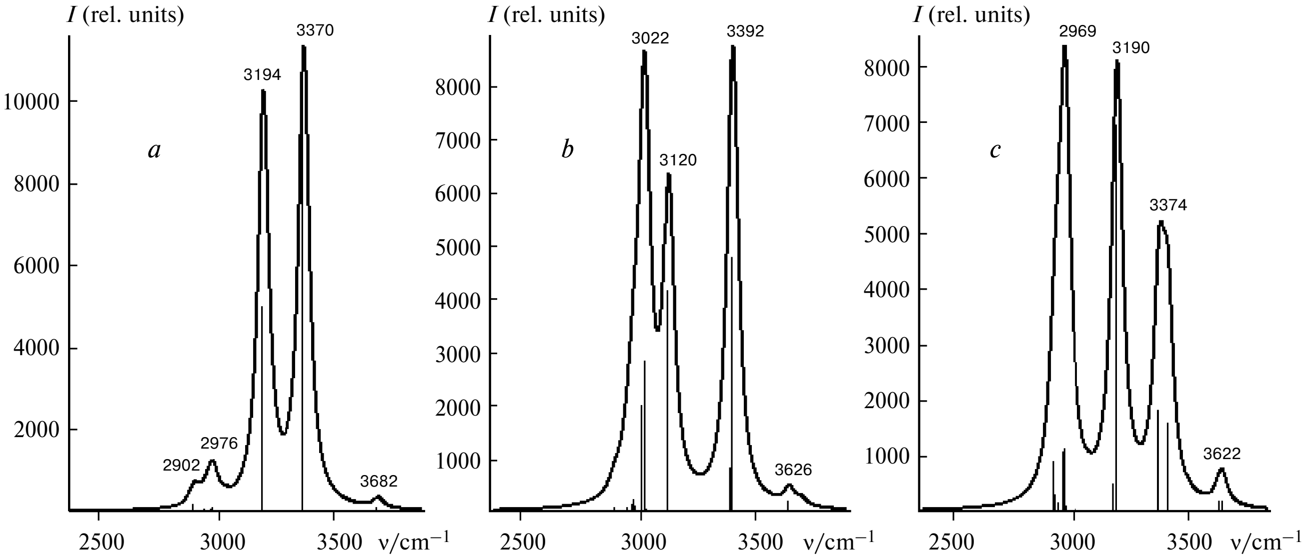


Fig. 8. Fragments of the IR spectra of the HH$^+$ (*a*), HT$^+$ (*b*), and TT$^+$ dimers (*c*) calculated by the DFT/PBE method.

interunit O atoms. The ε value is virtually the same for the monomers and dimers under study (1.001 and ~1.005, respectively). The exception is the TT$^-$ dimer (ε = 1.02); however, this value is also close to unity, and the TT$^-$ dimer structure can be considered round in the cross section and symmetric.

For the symmetric structure the corresponding geometric characteristics of the glucose residues should be the same. In this case, the average deviation of any value upon its averaging over six glucose residues of α-CD can serve as a formal estimate of symmetry. The average deviation of the O—H bond lengths in the OH groups of types 2, 3, and 6 for all the dimers studied is $5 \cdot 10^{-4}$, and its maximum value is $6 \cdot 10^{-3}$. The mean deviation of the H bond lengths is $3 \cdot 10^{-3}$ (the maximum value is $1 \cdot 10^{-2}$). The low errors confirm the symmetry of the optimized dimer structures.

The calculation of the α-CD dimers with ordered orientation of H bonds showed that they are characterized by high dimerization energies (see Table 1) and total energies of the H bonds calculated independently from the IR band frequencies (see Table 3). We found a linear correlation (Fig. 9) between these values ($R \approx 0.98$):

$$E_\mathrm{d} = 0.41\Delta E_\mathrm{H}{}^\mathrm{dimer} + 15\ \mathrm{kcal\ mol^{-1}}. \qquad (6)$$

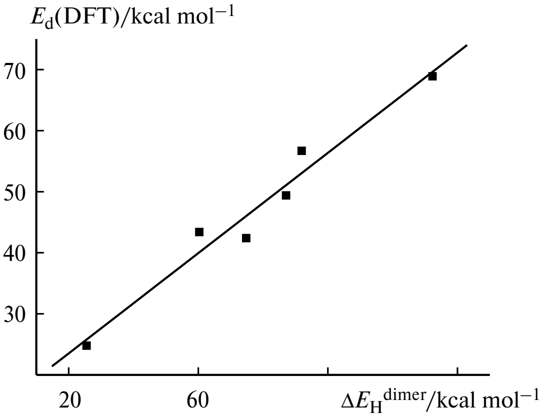


Fig. 9. Correlation between the total energy of H bonds in the dimers and the dimerization energy.

The value of the free term (15±4 kcal mol^{-1}) ranges from 22 to 60% (on the average, 35%) of the total dimerization energy. These values show how high could be the association energies of CD molecules containing a considerable number of OH groups capable of forming intermolecular H bonds in the dimers. As follows from published data,[13] at room temperature fast "flip-flop" of H bonds occurs in CD crystal hydrates. Therefore, a mixture of molecules with randomly oriented OH groups exists in an aqueous medium.[6] The energies of ordered α-CD forms calculated in the present work indicate that their stability can be rather high and explain the formation of empty tubular structures of type II, which have earlier been found experimentally.[3]

Thus, it is found that the most thermodynamically stable monomeric CD form is an α-CD$^-$ molecule of C_6 symmetry with the interglucose H bonds formed by the hydrogen atoms of the 3-OH groups and O atoms of the 2´-OH groups of the adjacent glucose units. The second isomeric form (α-CD$^+$) with the interglucose H bonds forrmed by the H atoms of the 2-OH groups and O atoms of the 3´-OH groups of adjacent glucose units. This form also has the C_6 symmetry and is by 0.5 kcal mol^{-1} less thermodynamic favorable than α-CD$^+$. Among the three α-CD$^-$ dimers HH$^-$ is characterized by the highest bond energy (68.9 kcal mol^{-1}) followed by the TT$^-$ (43.4) and HT$^-$ (24.8) dimers. The strength of the α-CD$^+$ dimers decreases in the series: TT^+ (56.7), HT^+ (49.4), and HH^+ (42.4).

The energies of the H bonds were calculated from low-frequency shifts of the bands of stretching vibrations of the OH groups involved in the formation of intermolecular H bonds. The linear correlation between E_d and E_H was found. Hence, a possibility of formation of intermolecular H bonds is a driving force of association of α-CD molecules in aqueous solutions.

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