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Potential Energy of the Smoothed Surface of a Molecule in Its Interaction with a Solvent

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Abstract—A procedure was developed for calculating the potential of the smoothed surface of a solute molecule in its interaction with the solvent. The potential map of the smoothed surface was calculated for a series of molecules, including those containing various heteroatoms. A method was suggested for calculating the averaged potential of the solute molecule surface, taking into account the dynamics of solvation. The total energy of interaction of a solute molecule with the surrounding solvent was estimated.

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The energy of interaction of individual organic molecules with the surrounding condensed phase is one of the main parameters in quantitative models of solution chemistry. A solute molecule is usually considered as embedded in a cavity formed in the solvent [1, 2]. An important part of such models is estimation of the potential of the molecular surface separating the solute molecule and the solvent.

In developing an adequate mathematical description of solvation processes on the basis of the above approach, the following aspects are the most important: (1) taking into account the relative sizes of the solute and solvent molecules; (2) determining the molecular surface area and choosing a method for calculating the potential of this molecular surface; and (3) taking into account the dynamics of solvent molecules surrounding the solute molecule. It is appropriate first to consider these problems as applied to the simplest molecular systems, such as solutions of alkanes and their functional derivatives in a low-molecular-weight nonionic solvent, e.g., cyclohexane. In such systems, the major contribution to the energy of intermolecular interaction is made by dispersion forces, which significantly simplifies the construction of a mathematical model.

CALCULATION PROCEDURE

In practical calculations of intermolecular interaction, there has been a considerable success in the past decades in estimating the characteristics of adsorption of compounds on a flat uniform carbon surface in the atom–atom approximation using various forms of atomic potentials (method of atom–atom potentials) [3–6]. Application of this approach to the condensed phase (e.g., in the description of solvation) is complicated, because in this case a special algorithm should be developed for calculating the potential of a curved surface of a solute molecule taking into account the orientation of the solvent molecules. At the same time, solution of this problem by the method of atom–atom potentials would allow the use of the concepts and mathematics of this well-developed method.

In the method of atom–atom potentials, the solute and solvent molecules are considered as three-dimensional combinations of atoms with van der Waals radii. The interatomic potentials in the Buckingham–Corner form [4, 5] are believed [5] to be the best for calculating the energy of intermolecular interaction:

$$\varphi = -C_1 r^{-6} - C_2 r^{-8} + B\exp(-qr).$$

Here C_1 and C_2 are the parameters of the potentials of dipole–dipole and dipole–quadrupole dispersion attraction; B and q, parameters of repulsion forces; and r, distance between the force centers. The coefficients C_1 and C_2 are estimated with approximate Kirkwood–Müller and Margenau quantum-chemical formulas, respectively:

$$C_1 = -6mc^2 \frac{\alpha_1\alpha_2}{\alpha_1/\chi_1 + \alpha_2/\chi_2},$$

$$C_2 = \frac{46h^2\alpha_1\alpha_2}{32\pi^2 m}\left(\frac{1}{2\alpha_2\chi_1/\alpha_1\chi_2 + 1} + \frac{1}{2\alpha_1\chi_2/\alpha_2\chi_1 + 1}\right).$$

Here α is the atomic polarizability; χ, atomic diamagnetic susceptibility; m, electron weight; c, veloci-

Coefficients of the Buckingham–Corner equation for various pairs of interacting atoms

Atom 1	Atom 2	C_1, J Å^6 mol^{-1}	C_2, J Å^8 mol^{-1}	B, J mol^{-1}
C	C	1.75×10^6	2.54×10^6	1.55×10^8
C	H	6.29×10^5	1.16×10^6	2.74×10^7
H	H	2.35×10^5	5.10×10^5	7.10×10^6
C	Cl	4.39×10^6	5.96×10^6	3.99×10^8
C	O	1.09×10^6	1.59×10^6	5.95×10^7
H	Cl	1.56×10^6	2.75×10^6	6.87×10^7
H	O	3.93×10^5	7.24×10^5	1.27×10^7
Cl	O	2.75×10^6	3.72×10^6	1.52×10^8
Cl	Cl	1.11×10^7	1.39×10^7	1.03×10^9
O	O	6.83×10^5	9.93×10^5	2.51×10^7

ty of light; and h, Planck constant. The repulsion parameter B is expressed via equilibrium distance r_0 and other parameters of atom–atom potentials. The condition of balance of all the constituents of attraction and repulsion forces ($d\varphi/dr|_{r = r_0} = 0$) leads to the formula

$$B = \frac{6C_1\exp(qr_0)}{qr_0^7}\left(1 + \frac{4}{3}\,\frac{C_2}{C_1r_0^2}\right).$$

The use of this relatively sophisticated form of the intermolecular potential allows fairly adequate description from a common standpoint of the interaction of molecules both containing heteroatoms and free of them.

We used the following atomic constants (given in the order of van der Waals radius, Å [7]; polarizability α, Å^3; diamagnetic susceptibility $-\chi \times 10^6$, Å^3 [3, 8]): C, –1.75, 0.96, 12.3; H, 1.17, 0.43, 3.7; Cl, 1.8, 2.245, 33.4; O, 1.4, 0.6, 7.7. The Buckingham–Corner potential parameters of various pairs of interacting atoms, obtained from these quuantities, are given in the table. The parameter q is the same for all pairs of atoms and is equal to 3.57 Å^{-1} [3]; the interatomic potential φ is expressed in kJ mol^{-1}.

As local potential F_i of a relatively small element of the solute molecule surface we take the potential energy of the interaction (calculated by the method of atom–atom potentials) with the solvent molecule contacting with this surface element and occurring in the most favorable orientation at which this energy is maximal in the absolute value (corresponds to a minimum in the potential curve).

The directions of mutual approach of the geometric centers of molecules are defined by successively setting different polar and azimuthal angles determining the mutual arrangement of these centers. For each direction, the solvent molecule is rotated on three Euler's angles. The local potential F_i thus obtained is assigned to an element of the solute molecule surface, whose area is calculated as follows. A solute molecule is inscribed in a sphere with the radius equal to the distance from the molecular center to the most remote element of its surface. A grid is formed on the surface of this sphere by discrete variation of the polar and azimuthal angles at a given step. In the procedure used, the step of varying the angles is fixed; therefore, the elements of the sphere surface have equal area, which is taken into account in the calculations. For each solid angle obtained by variation of the polar and azimuthal angles, we find the effective area S_i of the element of the solute molecule surface, cut out by this solid angle. This area is determined by the distance of the given element from the center of the solvate molecule and the area of the corresponding element on the sphere surface. Thus, S_i limits the possible area of an element of the solute molecule surface from below. In what follows, in calculation of the molecular potential, the local potential of a surface element is taken into account with the weight proportional to the area of this surface. It should be noted that the quantities S_i and the effective area of the molecular surface ΣS_i, obtained by their summation, are of no independent significance and are required only for intermediate calculations.

The dynamic behavior of solvent molecules can be taken into account by consideration of all configurations of the system consisting of a stationary solute molecule an a probing solvent molecule approaching the solute molecule from various directions. The interaction energy, i.e., the local potential, will depend on the approach direction. Averaging the local potentials allows simulation of the dynamics of the solvation interaction. Indeed, the whole surface of the solute molecule (both the most and the least energetically favorable sections) is covered with a shell of solvent molecules. The configuration of this shell constantly changes because of thermal motion of molecules; hence, the interaction energy can be averaged. The space-and-time dynamic pattern is thus transformed into a certain averaged configuration of the mutual arrangement of the solute and solvent molecules.

Averaging the local potentials over the surface area leads to the effective potential of the smoothed molecular surface:

$$\langle F\rangle = \sum_{i=1}^{k} F_iS_i / \sum_{i=1}^{k} S_i,$$

where k is the number of division elements. This potential corresponds to the mean energy of the dispersion interaction of a solute molecule with one solvent molecule and is determined by the ratio of the sections with high and low values of the local potential.

The effective potential of a smoothed molecular surface depends on the step of variation of Euler's angles in the calculation, i.e., on the extent of the division. As this step is decreased, the absolute values of both the minimal local potential $F_{\min}$ and the effective potential $\langle F \rangle$ increase (e.g., for *n*-hexane in cyclohexane at a step of 20° $\langle F \rangle$ is –14.6 kJ mol^{-1}, and at a step of 5° it is –15.3 kJ mol^{-1}). This effect is caused by finer "tuning" of the orientation of the solvent molecule to the local configuration of the solute molecule surface. However, with a decrease in the step of variation of all the angles by a factor of 2, the computation time increases by a factor of 2^5. In our opinion, a step of 10° is a reasonable compromise, as it allows fairly detailed examination of the potential distribution on a personal computer within acceptable time.

The procedure suggested for calculating the local potentials gives a map of distribution of the dispersion interaction potential over the solute molecule surface. It should be noted that the cyclohexane molecule is very convenient for probing the molecular surface potential. This is a compact molecule with a relatively narrow range of variation both of the distance from the center to the surface R_s and of the local potential F_i (in interaction with a probe carbon atom). For cyclohexane, R_s ranges from 4.1 to 5.4 Å, and the range of variation of F_i does not exceed 2 kJ mol^{-1}. To compare, for *n*-hexane containing the same number of C atoms R_s varies from 3.5 to 6.9 Å, and F_i, within 2.7 kJ mol^{-1}.

RESULTS AND DISCUSSION

The calculation procedure suggested allows detailed description and visualization of some effects of intermolecular interaction. Typical maps of the potential energy distribution in interaction of cyclohexane with molecules of alkanes and haloalkanes are shown in Fig. 1. As seen from these data, the arrangement of sections with the maximal (in the absolute value) potential on the molecular surface is consistent with the qualitative chemical views on localization of sites with the strongest dispersion interaction.

The dependence of $\langle F \rangle$ of *n*-alkanes on the number of C atoms (Fig. 2a) can be accounted for as follows. As seen from Fig. 2b, with an increase in the length of the carbon chain the maximal (in the absolute value) local potentials rapidly approach a certain constant level. This fact is caused by relatively small contribution of solute atoms remote from the contact point to the total energy of intermolecular interaction, because of the short range of dispersion forces. As the alkane chain length is increased, the number of surface elements with the limiting value of the local potential increases, causing the observed trend.

Let us consider how the averaged potential is affected by heteroatoms in the solute molecules. First, it should be noted that $\langle F \rangle$ depends in a complex manner on the surface area of the solute molecule and on the Buckingham–Corner potential of the interacting atoms (which are closely correlated with each other). In turn, the surface area depends on the number, kind, and mutual arrangement of the heteroatoms in the solute molecule. As a result, relatively simple dependences are observed only for structurally related molecules, e.g., in the series of *n*-alkanes. Even in the series of beanched alkanes, the dependence of $\langle F \rangle$ on the number of carbon atoms shows appreciable scatter, with the points lying below the curve for *n*-alkanes, which suggests higher intensity of dispersion interaction in the branched compounds.

The correlations observed in the homologous series of chlorinated methanes, chloroalkanes, and ethers are plotted in Fig. 3. It is seen that, at equal other conditions, the chlorine atom makes a larger contribution to the dispersion interaction than does the oxygen atom (compare chloroalkanes and ethers). At the same time, the contribution of the chlorine atom is comparable with that of the methyl group (compare chlorinated methanes and chloroalkanes).

The averaged potential allows us to estimate the intensity of interaction of solute molecules with the surrounding solvent. To do this, it is necessary to know the mean area occupied by the solvent molecule on the curved surface of the solute molecule. As shown above, the cyclohexane molecule has a compact shape and relatively uniform distribution of the potential over the surface; therefore, to a first approximation, it can be assumed that the area occupied by the cyclohexane molecule on the surface of different solute molecules will be approximately equal (we denote it as σ). This fact allows us to calculate the mean number of solvent molecules fully covering the surface of the solute molecule. According to the procedure developed in [9], the effective boundary is represented as a smoothed surface covering the solute molecule and bounding the volume inaccessible to solvent molecules. From the averaged potential and mean number of solvent molecules fully covering the surface of the solute molecule, the energy E_s of inter-

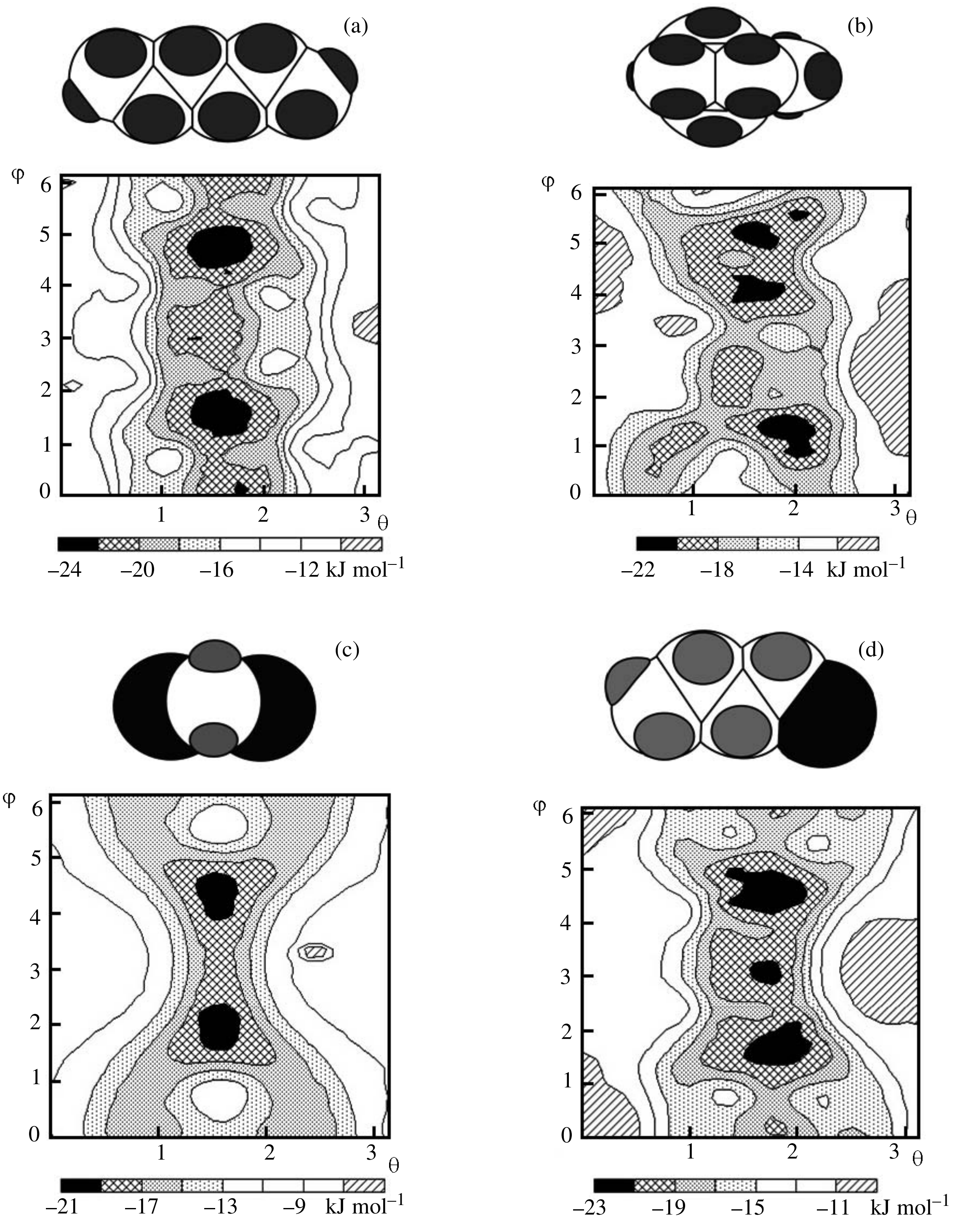

Fig. 1. Potential maps for the interaction of (a) *n*-hexane, (b) 2,2-dimethylbutane, (c) methylene chloride, and (d) butyl chloride with a probing cyclohexane molecule. The coordinates are the azimuthal and polar angles of the probe molecule center in the coordinate system associated with the main axes of the solute molecule. Isolines are drawn at 2 kJ mol^{-1} intervals.

action of the solute with the surrounding solvent can be estimated as follows:

$$E_s = \langle F \rangle S(2)/\sigma, \quad (1)$$

where $S(2)$ is the area of the solute molecule surface upon its smoothing with a probing sphere of radius 2 Å [9].

It should be noted that the "technical" surface area ΣS_i used for calculating $\langle F \rangle$ and the smoothed surface area $S(2)$ are calculated by different procedures and differ numerically (as noted above, ΣS_i is the lower boundary of the possible values of the molecular surface area). The extent of their difference depends on the extent of branching of the carbon skeleton, presence of heteroatoms, etc., and there surface area in formula (1) is not "automatically" reduced in going from $\langle F \rangle$ to the total energy E_s of interaction of the solute molecule with the surrounding solvent.

The macroscopic analog of E_s is the enthalpy of solvation. Solvation of many organic compounds in cyclohexane has been extensively studied [1, 2, 10], which allows us to draw correlations between the experimental and calculated quantities in this solvent. For linear and branched alkanes, the calculated values of E_s linearly correlate with the enthalpies of solvation of these compounds in cyclohexane (Fig. 4). The regression equations are statistically significant. In the case of branched alkanes, the residual variance for the straight line in Fig. 4 $S^2_{\mathrm{res}} \approx 2.8$; the F-test is $F \approx 8.9 > F^T_{(12;\,11;\,1\%)} = 4.4$. Similar pattern is observed with ethers (data not given in Fig. 4; $E_s = 0.643\Delta H - 1.82$): r^2 0.952; $S^2_{\mathrm{res}} \approx 2.7$; $F \approx 11.2 > F^T_{(3;\,2;\,10\%)} = 9.2$.

Although the procedure for calculating E_s is far from being proper (as indicated, e.g., by certain scatter of data for branched alkanes), the correlations observed in different homologous series and close slopes of these correlations reflect stable coupling of these quantities and indicate that the approach chosen shows much promise.

The calculation procedure suggested also allows us to clarify the question concerning the intensity of the dispersion interaction in alkanes (as a class of compounds important for correlation analysis): Is this quantity constant? Abramzon [11] states that the energy of intermolecular interaction per unit surface area is equal for all aliphatic hydrocarbons, i.e., their force fields are independent of the isomerism. This quantity was estimated at $\sim 2.0 \times 10^{-2}$ J m^{-2}. On the other hand, Solomonov and Konovalov [10] hold an opposite viewpoint.

According to Eq. (1), the intensity of the dispersion interaction in our designations can be written as $E_s/S(2) = \langle F \rangle/\sigma$. Since the area occupied by the cyclohexane molecule on the surface of solute molecules was assumed to be constant, the intensity is directly proportional to $\langle F \rangle$.

Our calculation [12] of the averaged potential for a series of linear and branched alkanes (trans conformations of C_5–C_{10} molecules were considered) showed that the intensity of the dispersion interaction of a solute with the hydrocarbon solvent can be approximated by a common linear equation (2):

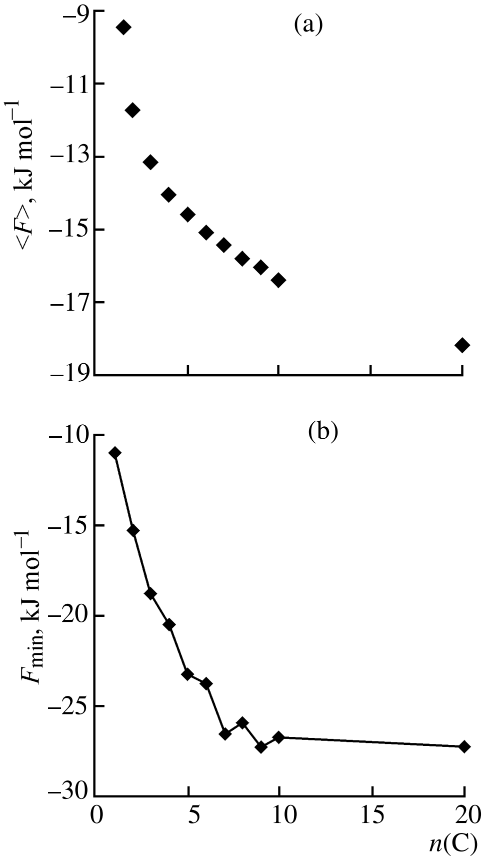

Fig. 2. (a) Effective potential and (b) maximal local potential of the surface of n-alkane molecules vs. number of C atoms.

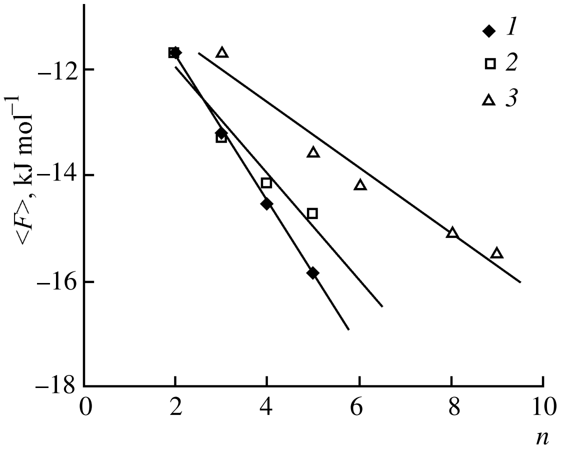

Fig. 3. Averaged surface potential as a function of the number of nonhydrogen atoms in the molecule: (*1*) chlorinated methanes, $\langle F \rangle = -1.38n - 10.36$, r^2 0.998; (*2*) chloroalkanes, $\langle F \rangle = -0.98n - 9.98$, r^2 0.952; (*3*) ethers, $\langle F \rangle = -0.63n - 10.29$, r^2 0.960. (n) Total number of carbon atoms and heteroatoms in the molecule.

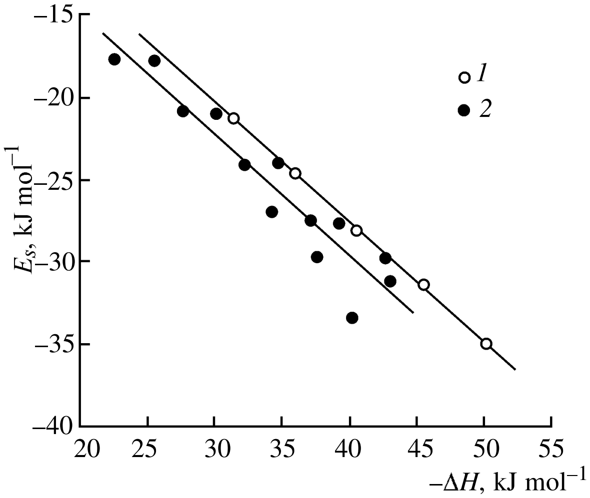

Fig. 4. Correlation between the calculated energy of interaction of a solute molecule with the surrounding solvent and the experimental anthalpy of solvation in cyclohexane: (*1*) linear alkanes ($E_s = 0.727\Delta H + 1.52$, r^2 0.9995) and (*2*) branched alkanes ($E_s = 0.735\Delta H - 0.25$, r^2 0.897). The area σ occupied by the solvent molecule on the surface of solute molecules is taken equal to 100 Å^2.

$$\langle F\rangle S(2) = -306n - 452m - 750p - 13\,320, \qquad (2)$$

where n is the total number of C atoms in the solute molecule; m, total number of branchings of the carbon skeleton; and p, number of side chains with the length exceeding C_1. The multiple correlation coefficient of this equation is $R^2 = 0.943$ (for a set of 20 compounds).

The above correlation and the values and signs of its coefficents have clear physical sense. The interaction intensity depends on the total number of C atoms in alkane molecules (first term). For linear alkanes, this is the only variable term. For branched alkanes, an additional interaction intensity appears, depending on both the total number of branchings of the carbon skeleton and on the length of side chains. This is associated with increased "spatial concentration" of C atoms in branched alkanes compared to their linear isomers. It should be noted that atoms in the side and main chains do not differ (their total number is taken into account by the first term); only a correction for the presence of side chains is made. The side ethyl substituent makes the alkane molecule more compact, under equal other conditions, which increases the effective potential of the molecular surface.

Our results show that the intensity of the dispersion interaction with the solvent depends on the isomerism of the carbon skeleton, i.e., the Solomonov and Konovalov's viewpoint [10] is confirmed. At the same time, the energy of intermolecular interaction per unit surface area, calculated by the suggested procedure, varies from 1.8×10^{-2} J m^{-2} for hexane to 1.3×10^{-2} J m^{-2} for decane, which is fairly well consistent with the estimations made in [11].

Thus, the procedure suggested for calculating the potential of the smoothed surface of a solute molecule allows calculation of the intensity of its dispersion interaction with the surrounding solvent, consideration of the dynamics of solvent molecules, and estimation of the enthalpy of solvation of a compound in cyclohexane.

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