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The influence of universal and specific interactions on structural properties of liquid formamide

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Monte Carlo simulation of the structure of liquid formamide at 298 K was carried out. Intermolecular interactions were calculated using five different potentials. No essential changes in the spatial structure and topological properties of the network of hydrogen bonds of liquid formamide occur upon varying the electrostatic intermolecular interactions, strength of H-bonds, and temperature. Fragments of crystal structure are partly retained in liquid formamide. It was found that the network of H-bonds is structurally inhomogeneous and contains long-lived associates of closed cycles of H-bonds as well as tree-like and chain-like structures. The energy, topological, and statistical characteristics of closed cycles of H-bonds were determined.

Key words: organic solvents, formamide, structure of liquid, intermolecular interactions, hydrogen bonds, computer simulation of liquids, Monte Carlo method.

The formamide molecule contains C=O and NH_2 groups, which are the most important structural fragments of biologically active substances. In this connection intensive experimental and theoretical studies of intermolecular interactions of $HCONH_2$ molecules in the gas and condensed phases are carried out. Investigations of the structure of liquid formamide are also of importance for establishing general regularities of the formation of spatial ordering of the molecules in liquids and solutions and for revealing the extent to which specific and universal interactions between functional groups affect their energy and structural characteristics.

The space group of crystalline formamide is $P2_1/n$. The monoclinic unit cell with parameters $a = 369$ pm, $b = 918$ pm, $c = 687$ pm, and $\beta = 98°$ contains four molecules.[1—4] Each formamide molecule is simultaneously a proton donor and acceptor forming four H-bonds with neighboring molecules. The ratio of the interatomic distances indicates that the bond formed by the *cis*-H atom of the amino group is weaker than that formed by the *trans*-H atom (*cis*- and *trans*-positions of H atoms with respect to the O atom are considered). Quantum-chemical calculations[3] of the energy of interaction between two formamide molecules suggest that the *cis*-bond is ~6 kJ mol^{-1} more stable than the *trans*-bond. The apparent contradiction was explained[3] by the influence of cooperative interactions, resulting in weakening of *cis*-bonds and strengthening of *trans*-bonds in

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the formamide crystal. It is difficult to *a priori* predict the contribution of the cooperative effect to the energetics of the interaction between individual molecules of liquid formamide.

Among theoretical approaches to studying the structure of liquids, methods of computer simulation play an increasingly important role.[5] They make it possible to obtain exhaustive information on all intermolecular interactions and coordinates of particles in the model unit cell. One of the main parameters of the model is the effective potential of interparticle interactions. This potential is created to achieve agreement between the calculated structural and energy characteristics and the results of quantum-chemical studies of molecular associates and to reproduce the observed properties of a substance.

The procedure for creating the potential functions is highly sensitive to the choice of the initial molecular structure, the type of functional dependences, and the methods for consideration of cooperative interactions. To a great extent, the ambiguity of this procedure is determined by a strong dependence of the results of quantum-chemical calculations of the energy and geometric parameters of molecular associates on the calculation procedure used. Several sets of the potential functions (*e.g.*, the OPLS,[6] T,[7] and PIPF[8] sets) were created to calculate the interactions between formamide molecules.

Only for particular properties of liquid is the accuracy of their reproduction strongly dependent on the choice of the procedure for calculation of intermolecular interactions and the simulation technique. For instance, spatial ordering of liquid methanol,[9] acetone,[10] and DMF[11] molecules is determined by universal repulsive interactions (the shape of the molecules), whereas the energy, orientational, fluctuation, and dynamic characteristics are strongly dependent on specific electrostatic interactions.

Previously, it was shown experimentally[5,12—15] and theoretically[6,16,17] that cyclic dimers and chain associates are the main elements of supramolecular structure of liquid formamide. However, after comparison of quadrupole relaxation times of the nuclei, determined by NMR spectroscopy, with the results of quantum-chemical calculations of molecular associates it was suggested[18] that six-membered closed cycles of H-bonds dominate over other elements of the supramolecular spatial structure of liquid formamide and their fraction amounts to 95%. According to these calculations, H-bonds are formed by *trans*-H atoms only.

It is known[1—4] that in the crystal the molecules linked by H-bonds form the layers in which cyclic dimers formed by *cis*-bonds and hexamers formed by two *cis*-bonds and four *trans*-bonds can be singled out (Fig. 1). It can be assumed that there is a set of the most characteristic associates in the liquid phase, which is characterized by specific structural or energy parameters.

The aim of this work was to determine the structural properties of liquid formamide, to find the most stable elements of supramolecular structure, and to establish the dependences of their properties on specific interactions between the molecules and on the ratio of the strengths of the *cis*- and *trans*-bonds.

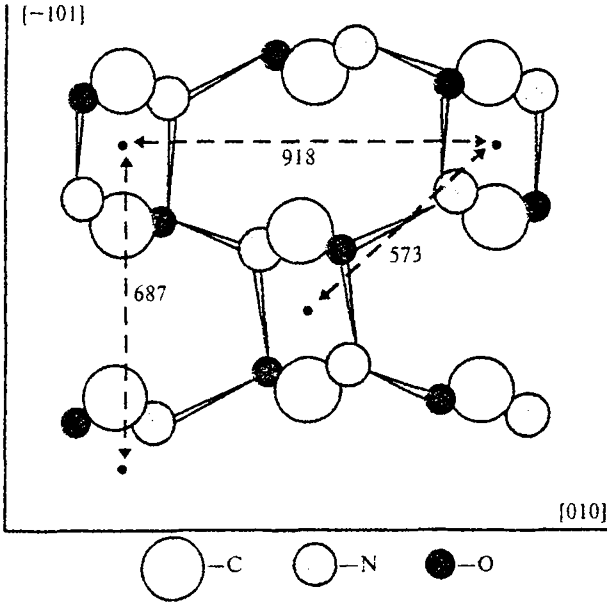

Fig. 1. Schematic view of molecular arrangement in the formamide crystal and the distances between the geometric centers of cyclic dimers, r_{22}/pm.

Calculation procedure

Calculations were carried out by the standard Monte Carlo method[5] in the *NVT*-ensemble. Original software was used. The conditions of the computer experiment corresponded to a density of 1.129 and 1.08 g cm^{-3} and to T = 298 and 348 K, respectively. In a cubic unit cell with an edge length of 2023 (T = 298 K) and 2053 pm (T = 348 K), 125 formamide molecules were placed. Periodic boundary conditions and spherical cutoff of the potential functions[5] were used. It was assumed that the molecules do not interact if the distance between N atoms is longer than half the edge length. In each simulation Markovian chains of length ~90 million configurations were generated. According to the conditions of the computer experiment, in two successively stored configurations each particle was moved, on the average, 40 times with a maximum possible displacement of the molecule of 10 pm and rotation by an angle of 0.1 rad. Statistical characteristics of the computer simulations corresponded to state of the art in this area of investigations.[19]

The molecular geometry shown in Fig. 2 was chosen in accord with the OPLS model.[6] The energy of universal nonelectrostatic intermolecular interactions was calculated using the Lennard-Jones potentials, while calculations of the Coulomb energy (specific interactions) were carried out taking into account the distribution of excess charges on the i, j atoms:

$$E = \sum_{i,j}(q_iq_j/r_{ij} + A_{ij}/r_{ij}{}^{12} - C_{ij}/r_{ij}{}^{6}),$$

$$A_{ii} = 4\varepsilon_i\sigma_i{}^{12}, \quad C_{ii} = 4\varepsilon_i\sigma_i{}^{6}, \quad A_{ij} = (A_{ii}A_{jj})^{0.5}, \quad C_{ij} = (C_{ii}C_{jj})^{0.5}.$$

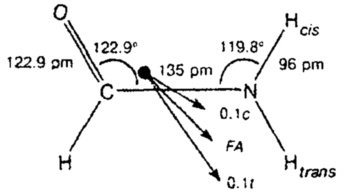

Fig. 2. Structure and geometric parameters of formamide molecule. Arrows denote the dipole moment vectors for three models and the filled circle denotes the position of the center of mass of the molecule.

The following corresponding parameters of the OPLS model (ε/J mol^{-1}, σ/pm, q/e) for the N (711, 325, −0.85), O (879, 296, −0.5), and H_{cis} and H_{trans} (0, 0, 0.425) atoms and for the C—H group (481, 380, 0.5) were used. (Hereafter the symbols H_{cis} and H_{trans} denote H atoms in the *cis*- and *trans*-positions with respect to the O atom of the molecule, respectively.)

To reveal the role of specific interactions, several independent computer experiments were carried out. In addition to the initial OPLS (*FA*) model, we considered several additional models of liquid formamide, common to which was retention of the molecular structure, the parameters of nonelectrostatic interactions, and the charges on the O and N atoms and on the C—H group. These models differ in charges (q/e) on the H atoms of the amino group: 1) the 0.05*t* model — H_{cis} (0.375), H_{trans} (0.475); 2) the 0.1*t* model — H_{cis} (0.325), H_{trans} (0.525); 3) the 0.05*c* model — H_{cis} (0.475), H_{trans} (0.375); and 4) the 0.1*c* model — H_{cis} (0.525), H_{trans} (0.325). No electrostatic interactions were considered in the *LJ* model.

Results and Discussion

It is common practice to test a created set of potential functions for agreement between the experimental and calculated characteristics of the substance. The parameters of the OPLS[5] and PIPF[7] potential functions were chosen in such a way that the calculated thermodynamic functions of amides would be the closest to the experimental ones in the framework of the *NVT*-ensemble. The internal potential energy (*E*) of formamide calculated in this work for the *FA*—OPLS model is −59.4 kJ mol^{-1}, which is in good agreement with the previously found values of −59.4 and −58.8 kJ mol^{-1} (MC[19] and MD[16] calculations, respectively, with the OPLS potential functions). The PIPF model gives an *E* value of −59.3 kJ mol^{-1}.[7] For the 0.05*c* and 0.1*c* models, the energy increases slightly to −58.3 and −59.2 kJ mol^{-1}, respectively, as the charge on the H_{cis} atom increases. In contrast to this, appreciable stabilization of the system, resulting in decrease in the energy down to −63.2 and −68.2 kJ mol^{-1}, is observed on going from the *FA* model to the 0.05*t* and 0.1*t* models, respectively. It can be assumed that essential structural transformations must occur in these cases.

Statistical errors of calculations, determined from the energy fluctuations in the configurations, did not exceed 0.02 kJ mol^{-1}. It is impossible to immediately compare other thermodynamic functions of the models using the results of our calculations for the *NVT*-ensemble. However, good agreement between the *E* values and the atom-atom radial distribution functions (RDF) we found for the *FA* model and the results obtained using other calculation procedures[6,8,16,19] indicates correctness of our calculations.

At the same time, reproduction of some thermodynamic functions using the OPLS potential functions does not imply that other experimental properties of the liquid will also be described adequately. Previously,[19] it was shown that the value of the dielectric constant for the formamide model appreciably differs from the experimental value, while the found[16] anisotropy of rotational motion is inconsistent with NMR spectroscopy data.

Macroscopic properties of a substance are always calculated using averaging over the ensemble.[20] Reconstruction of the potential functions and structural correlation functions from thermodynamic properties of the substance by numerical methods belongs to the class of ill-posed problems.[21] One of the goals of this work was to determine stable structural characteristics of liquid formamide and to establish the dependence of unstable characteristics on particular contributions of the interparticle interaction or the simulation conditions to the energy.

In contrast to physicochemical and thermochemical methods, by using "structural" methods[13,22–24] it is possible to obtain information on the spatial arrangement of the molecules in liquids from the dependences of the intensities of coherent X-ray and neutron scattering on the scattering angle. Previously,[12] attempts to find several coefficients of the expansions of correlation functions into infinite series in terms of rotationally invariant bimolecular basis functions were undertaken for liquid formamide. However, it is much easier to experimentally determine and theoretically calculate[23] the pair correlation function $G(r)$, which is the weighted sum of the atom-atom RDF $g_{ij}(r)$:

$$G(r) = \sum_{i=1}^{m}\sum_{j=i}^{m} b_{ij}\, g_{ij}(r), \tag{1}$$

$$b_{ij} = [n_i n_j (2 - \delta_{ij}) c_i c_j] / (\sum_{i=1}^{m} n_i c_i)^2, \tag{2}$$

$$g_{ij}(r) = \rho_j(r)/\rho_j. \tag{3}$$

Here m is the number of different types of atoms in the molecule, n_i is the number of atoms of type i, δ_{ij} is the Kronecker symbol, c_i is the Fourier transform of the atomic form factor for X-ray scattering (to a first approximation, it is equal to the number of electrons in the atom of type i) or the scattering length for neutron radiation (c_H = −3.739, c_D = 6.671, c_N = 9.36, c_C = 6.646, and c_O = 5.803 fm),[25] $\rho_j(r)$ is the average numerical density of atoms of type j in a spherical layer of thickness dr at a distance r from a given atom of type i, and ρ_j is the average statistical density. The function $G(r)$ includes contributions from $m(m+1)/2$ atom-atom functions.

By comparing the expansions obtained for different types of irradiation and isotope substitution of the atoms in the molecules and by using the differences in the b_{ij} values, in some simplest cases one can find the $g_{ij}(r)$ functions. However, errors of scattering intensity measurements and the lack of adequate procedure for data processing[22—24] make it impossible to calculate with certainty not only the coefficients of expansion of the binary correlation function over bimolecular functions, but also the atom-atom RDF even for liquids with relatively simple molecular structure, *e.g.*, water.[24]

The formamide molecule has a complex structure; therefore, it is hardly possible to reconstruct the shape of the atom-atom RDF by analyzing the behavior of the $G(r)$ functions determined with errors. This problem also belongs to the class of ill-posed mathematical problems[21] and is reduced to the solution of an ill-posed system of nonlinear equations on an unknown class of functions. The $G(r)$ dependences found from experimental data on scattering intensities and calculated using formula (1) for the 0.1*c* and 0.1*t* formamide models are shown in Fig. 3. For the *FA*, 0.05*c*, and 0.05*t* models the curves are intermediate and are not shown here. The coordinates of the hydrogen atom of the C—H group, which is not considered explicitly in the OPLS model, were determined from the molecular geometry.[3,4] Tabulated experimental values[12] of intermolecular contributions to the differential cross section of coherent neutron scattering, $S(k)$, for liquid formamide were transformed using the formulas

$$H(k) = S(k)/(\sum_{i=1}^{m} n_i c_i)^2,$$

$$G(r) = 1 + [1/(2\pi^2\rho r)] \sum_{0}^{k_{max}} kH(k)\sin(kr)\mathrm{d}k, \qquad (4)$$

where k is the wave vector. Because of large errors of experimental determination of the amplitude of coherent scattering by H atoms, we report here the results for partially or fully deuterium-substituted formamide molecules.

We failed to calculate the $G(r)$ function using a universal procedure because of the lack of initial $H(k)$ values (in the case of X-ray scattering). The shapes of the curves are determined using different procedures for data processing.[2,13,22—24] In some instances[2,13] the integrand in formula (4) is multiplied by the modifying function:

$$M(k) = \{[\sum_{i=1}^{m} n_i c_i^2(0)]/[\sum_{i=1}^{m} n_i c_i^2(k)]\}\exp(-ak^2),$$

whereas in some other instances[23,24] this does not occur, thus making comparison of the results much more difficult. We calculated the $G(r)$ functions from the atom-atom RDF by formula (1) ignoring the $c(k)$ dependence and using no modifying functions.

As follows from the plots shown in Fig. 3, the observed interatomic distances in liquid formamide and the shape of the experimental curves for neutron scattering are, on the whole, adequately reproduced by the functions calculated using the data of computer simulation. Qualitative comparison of experimental[2,13,23] and theoretical dependences characterizing X-ray scattering also revealed no significant distinctions in their behavior. Therefore, it can be concluded that varying the electrostatic part of the interaction potential does not lead to essential changes in the shape of the $G(r)$ curves and that the results of computer simulation do not contradict the experimental data.

Among ten atom-atom RDF $g_{ij}(r)$ shown in Fig. 4, the most sensitive to changes in the potential functions are those RDF that characterize the spatial arrangement of O atoms (g_{CO}, g_{NO}, g_{OH}, and g_{OO}), whereas the shapes of the other six RDF remain virtually unchanged. The behavior of the $G(r)$ curves can be easily explained using the results obtained. For instance, the peak at ~200 pm (see Fig. 3) corresponds to coordination to the O and H atoms participating in the intermolecular H-bonds (see Fig. 4, *g*). Peculiarities of the behavior of the $G(r)$ functions at $r \approx 300$ pm are due to

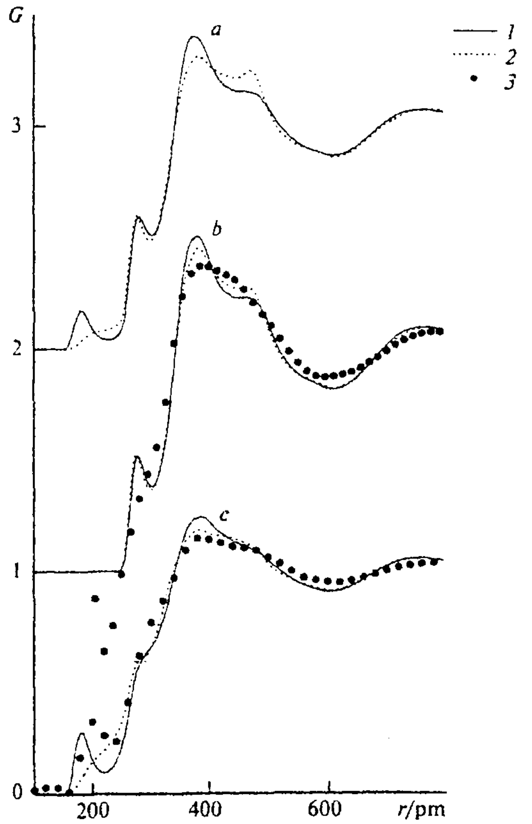

Fig. 3. Pair correlation functions ($G(r)$) for X-ray scattering (*a*) and for neutron radiation in an H/D-mixture of molecules with a zero coherent scattering length (*b*) and in deuterated formamide (*c*), calculated using formulas (1) and (2) for the 0.1*c* (*1*) and 0.1*t* (*2*) models or calculated by formula (4) using tabulated experimental $H(k)$ values[12] (*3*).

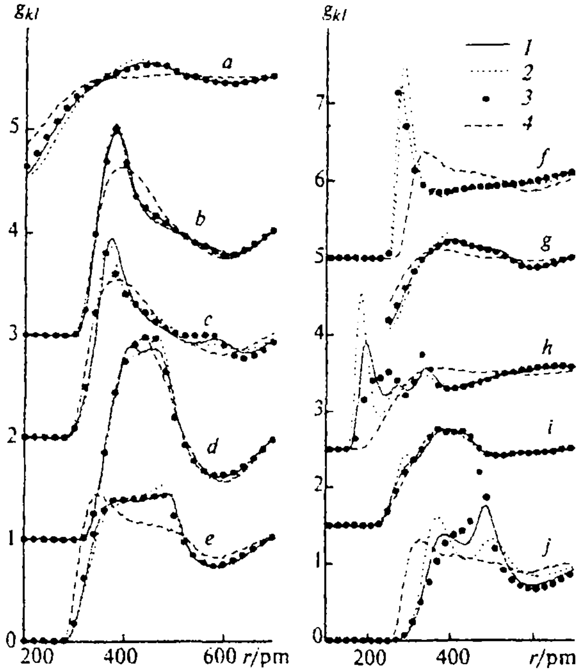

Fig. 4. Radial distribution functions ($g_{kl}(r)$) of the atoms in liquid formamide with kl = HH (*a*), NC (*b*), CO (*c*), CC (*d*), NN (*e*), NO (*f*), NH (*g*), OH (*h*), CH (*i*), and OO (*j*), calculated using the *FA* (*1*), 0.1*c* (*2*), 0.1*t* (*3*), and *LJ* (*4*) models. For clarity, the plots are shifted along the ordinate axis.

the g_{ON} maximum. Obviously, at large r values the shapes of curves are determined by the overlap and mutual amplification or by damping of oscillations of all the atom-atom RDF.

By definition (formula (3)), the $g_{ij}(r)$ function is proportional to the average atomic density in a spherical layer of thickness dr. As a rule, the atoms within this layer are distributed anisotropically at small r values. Based merely on knowledge of the $g_{ij}(r)$ dependences, it is impossible to unambiguously establish the regularities of spatial arrangement of the molecules. This information is insufficient to describe the spatial structure of liquid systems in which no relatively strong interactions occur. In these cases it is impossible to use models in order to reduce a great variety of molecular configurations to two or three most characteristic ones.

Previously,[10,11] it was shown by the analysis of supramolecular structures that the spatial structure of aprotic solvents (acetone, DMF), determined by the molecular shape and by the action of steric and packing factors, is close to the structure of a randomly close-packed system of "soft spheres." It was expected that this regularity would not be valid if strong directed intermolecular interactions occur. However, the results of simulation of liquid methanol and solutions of charged particles in methanol showed[9,26] that in these cases the spatial structure is also determined by universal interactions (by packing of methyl groups of the molecules).

Among liquids, water possesses several specific properties. For instance, low density explicitly contradicts the principle of close molecular packing. Nevertheless, by choosing an appropriate shape of the model molecule it has been possible to correctly reproduce[27,28] specific structural properties[29,30] of liquid water. It was shown that in this case the spatial ordering also is first of all determined by the molecular shape and by packing factors.

If the principle of close molecular packing is valid for a liquid, interpretation of experimental radial distribution curves or calculations using computational methods of statistical physics should be performed with a randomly close-packed system of soft spheres as an initial approximation. Electrostatic interactions should be considered as perturbations affecting mutual orientation of the molecules.

Like water molecules, formamide molecules are capable of forming four strong directed H-bonds. However, topological properties of the networks of bonds in condensed states of water and formamide are strongly different. To answer the question of the role of packing factors in forming the spatial structure of liquid formamide, let us first consider the results of analysis of the RDF behavior. Exclusion of electrostatic intermolecular interactions leads to appreciable changes in the behavior of six out of the ten atom-atom RDF (see Fig. 4), which, at first glance, indicates essential differences in structural properties of the *FA*, 0.1*c*, 0.1*t*, and *LJ* formamide models. However, comparison of the $g_{cm}(r)$ functions characterizing the spatial distribution of the centers of mass of the molecules (Fig. 5, *a*) shows that they are virtually independent of specific interactions. Maxima of the functions are at multiple distances of the diameter of the molecule and the first coordina-

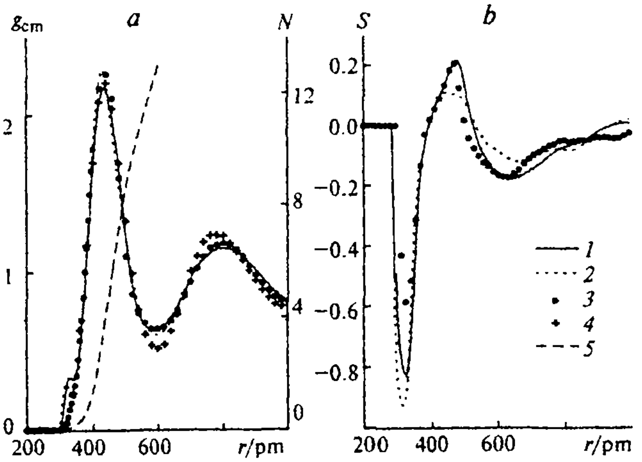

Fig. 5. *a*. Radial distribution functions for the centers of mass ($g_{cm}(r)$) of formamide molecules (*1*—*4*) and the dependence of the average number of particles (*N*) in a sphere of radius r on r (*5*). *b*. Dependence of the average cosine of the angle between the dipole moment vectors (*S*) on the distance (r) between the centers of mass of the molecules. Calculations using the *FA* (*1*, *5*), 0.1*c* (*2*), 0.1*t* (*3*), and *LJ* (*4*) models.

tion sphere contains ~12 neighbors. Such behavior of the functions is characteristic[31] of simple liquids or of a system of randomly close-packed spheres.

The dipole correlation function, *S*(*r*), which reflects the dependence of the average cosine of the angle between the dipole moment vectors on the distance between the centers of mass for a pair of molecules, is shown in Fig. 5, *b*. The *S*(*r*) function calculated in the framework of the *FA* model is in good agreement with the previously obtained results,[16] thus indicating correctness of our simulation. It was shown[19] that the behavior of this function is strongly dependent on the procedure used in computer experiments. Therefore we were interested in more objective characteristics, *viz.*, in relative changes in the function, that occurred upon the redistribution of charges on the H atoms of the amino groups of the molecules.

The module of the molecular dipole moment as well as the angle between its direction and the axis of the C—N bond increase as the charge on the *trans*-H atom increases (see Fig. 2). These parameters for different models are as follows: 3.93 D and 25.3° (0.1*c*); 4.12 D and 30.3° (0.05*c*); 4.33 D and 34.9° (*FA*); 4.57 D and 39.0° (0.05*t*), and 4.83 D, 47.3° (0.1*t*) ($1\ \mathrm{D} = 3.336 \cdot 10^{-30}$ C m). For the model with polarizable PIPF potential functions the average molecular dipole moment in the liquid phase was[8] 4.72 D, while the experimental value determined in the gas phase was 3.73 D. On the average, the angle between the vectors of induced and permanent dipole moments does not exceed 20°. Cooperative interaction causes appreciable polarization of the molecule and strengthening of *trans*-bonds in the liquid, which is in agreement with the results[3] of calculations of the ratio of the strengths of *cis*- and *trans*-bonds in the formamide crystal. Thus, the 0.05*t* and 0.1*t* formamide structures with asymmetric charge distribution correspond to a greater extent to the polarization model.

In the region of the nearest intercenter distances the molecular dipole moments are oriented mostly antiparallel and coordination increases as the *cis*-bonds are strengthened. As follows from the behavior of the *S*(*r*) curves, an increase in the charge on the *trans*-H atom leads to a decrease in the fraction of antiparallel dipole moment vectors, to an increase in the fraction of parallel dipole moment vectors, and to a decrease in the number of cyclic dimers, and it favors chain association of the molecules. In fact, the formation of cyclic dimers with participation of only *cis*-H atoms in the liquid is accompanied by specific behavior of the $g_{\mathrm{cm}}(r)$ curve at $r =$ 330 pm. Substantial overlap of the van der Waals atomic spheres is accompanied by strong repulsive interactions, which compensate for the energy gain obtained due to spatially close arrangement of charged centers in the cyclic dimer. Thus, analysis of the RDF behavior suggests that packing factors play a decisive role in the formation of the spatial molecular structure of liquid formamide.

Previously,[17] it was shown that even if we know the behavior of all atom-atom RDF or generalized functions of spatial distribution of the atomic density, it is impossible to establish the regularities of the formation of supramolecular structure of formamide. It was found that a great variety of types of molecular association exist in liquid formamide. Among supramolecular objects, chain and cyclic associates can be singled out, which determine the topological properties of the network of H-bonds.

When simulating the *I*-ensemble, in some instances it is difficult to unambiguously establish the presence or absence of an intermolecular H-bond, since it is an attribute of the vibrationally averaged *V*-ensemble. For the *I*-ensemble the choice of criteria is rather conditional, so several types of criteria for formamide are known.[6,16] Unlike the previously used energy-geometric criterion[6,17] for H-bond formation ($r_{\mathrm{OH}} < 280$ pm, $E_{\mathrm{HB}} < -18.8$ kJ mol^{-1}), in this work we assumed that two molecules form an H-bond if the distance between the O atom of one molecule and the H atom of the amino group of the other molecule is no longer than 250 pm. Artificial intramolecular charge redistribution strongly affects the bond strength and has a less pronounced effect on its geometric parameters. For this reason, the geometric criterion is more suited to the goals of this work. Some differences between the structural parameters of the network of bonds when using different criteria are of little significance. Both strong and weaker bonds in the network can be considered. The r_{OH} values were chosen after analyzing the generalized functions of the atomic density distribution.[17]

The results of calculations of the number of H-bonds for different formamide models are shown in Table 1. Theoretically, each molecule in the liquid can form four H-bonds (without considering bifurcate ones). The average number of H-bonds per molecule (n) is maximum in the *FA* model (3.43). Violation of the symmetry of intramolecular charge distribution on the H atoms of the amino group causes a decrease in the network connectivity. As should be expected, the number of bonds formed by the *cis*-H (*trans*-H) atoms (n_{cis} and n_{trans}, respectively) increases as the charge on these atoms increases. For the 0.1*c* and 0.1*t* models, each *cis*- or

Table 1. Statistical and energy characteristics of the networks of H-bonds for different formamide models

Model	n	n_{cis}	n_{trans}	$-E_2$/kJ mol^{-1}
0.1*c*	3.07	1.99	1.08	33.07
0.05*c*	3.36	1.89	1.47	27.67
FA (298 K)	3.43	1.67	1.76	23.53
FA (348 K)	3.33	1.59	1.74	21.85
0.05*t*	3.35	1.42	1.93	19.51
0.1*t*	3.05	1.03	2.02	15.70

Note. n is the average number of H-bonds per molecule, n_{cis} and n_{trans} are the numbers of bonds formed with participation of *cis*-H and *trans*-H atoms, respectively; E_2 is the average energy of H-bond formation in the cyclic dimer.

Table 2. Concentrations of closed cycles in the networks of H-bonds for different formamide models

Model	C_2 (σ_2)	C_3 (σ_3)	C_4 (σ_4)	C_5 (σ_5)	C_6 (σ_6)	C_7 (σ_7)
0.1*c*	6.85±0.05 (1.70)	5.78±0.06 (1.72)	7.46±0.07 (2.34)	7.70±0.08 (2.64)	9.65±0.11 (3.34)	12.09±0.15 (4.78)
0.05*c*	6.00±0.05 (1.74)	4.75±0.05 (1.93)	9.83±0.09 (2.76)	10.15±0.10 (3.25)	15.11±0.14 (4.49)	23.96±0.23 (7.52)
FA (298 K)	8.42±0.07 (1.94)	4.81±0.06 (1.95)	9.91±0.09 (2.81)	9.73±0.11 (3.43)	14.85±0.15 (4.45)	21.45±0.22 (6.60)
FA (348 K)	6.03±0.06 (1.62)	5.64±0.07 (2.08)	8.73±0.10 (2.82)	10.07±0.11 (3.32)	14.18±0.17 (4.77)	20.89±0.25 (7.19)
0.05*t*	4.83±0.04 (1.40)	3.56±0.05 (1.60)	6.71±0.07 (2.40)	8.68±0.08 (2.90)	13.00±0.13 (4.23)	20.45±0.20 (6.49)
0.1*t*	1.98±0.04 (1.22)	3.45±0.05 (1.69)	5.26±0.07 (2.25)	5.38±0.07 (2.39)	7.79±0.10 (3.06)	9.80±0.14 (4.10)

Note. C_i is the number of cycles per 100 molecules, σ_i is the standard deviation, and i is the number of molecules in the cycle. Listed is the confidence interval for a confidence level of 0.95.

trans-H atom participates, on the average, in one H-bond. By comparing the results symmetrically, mention may be made that the formation of *trans*-bonds is more preferable since their number is always somewhat larger than that of *cis*-bonds (*e.g.*, n_{trans} = 1.93 (0.05*t*) *vs.* n_{cis} = 1.89 (0.05*c*)). Raising the temperature favors breaking of the *cis*-bonds to a greater extent.

The network of H-bonds of formamide is a very complex association, which can be divided into more simple fragments, namely, closed cyclic and open (chain- and tree-like) molecular associates. If statistical distribution of concentrations of closed cycles in the network of bonds is considered, the existing correlations of its parameters (stable relations) will characterize the supramolecular structure of formamide. To verify the thesis on the small effect of specific interactions on the regularities of the formation of spatial structure of liquid formamide, we investigated the response of the system to changes in the intramolecular charge distribution at the supramolecular level.

It is reasonable to assume that the number of cyclic dimers in the models should vary in proportion to the changes in the strength and number of *cis*-bonds in the network. However, as follows from the data listed in Table 2, any violation of the symmetry of the charge distribution on the H atoms of the amino group results in a decrease in the concentration of dimers. The number of cyclic dimers does not increase, even though the number of *cis*-bonds increases appreciably and they become substantially energy-stabilized (see Table 1).

If the network of H-bonds of a crystal contains only two types of cycles (dimers and hexamers), various structural types of supramolecular association exist in the liquid. Concentrations of all types of cycles are rather high. Cyclic trimers are the most rare in occurrence; however, the probability of their formation increases as the *cis*-bonds are strengthened. A decrease in the network connectivity due to violation of the symmetry of charge distribution on the H atoms of the amino group results in a decrease in the concentrations of all types of cycles. This manifests itself to the greatest extent as the *trans*-bonds are strengthened and their fraction increases. Formation of *trans*-bonds favors chain association of the molecules and the formation of branched rather than network-type structures.

It can be assumed that a chain association is characteristic of liquid *N*-methylformamide, since the H atom of the amino group in the molecule is in the *trans*-position. This is also supported by the previously reported results,[8] according to which each *N*-methylformamide molecule simultaneously acts as proton donor and acceptor and participates in about two H-bonds.

It should be noted that changes in the supramolecular structure caused by raising the temperature by 50 K are no greater than those observed upon minor charge

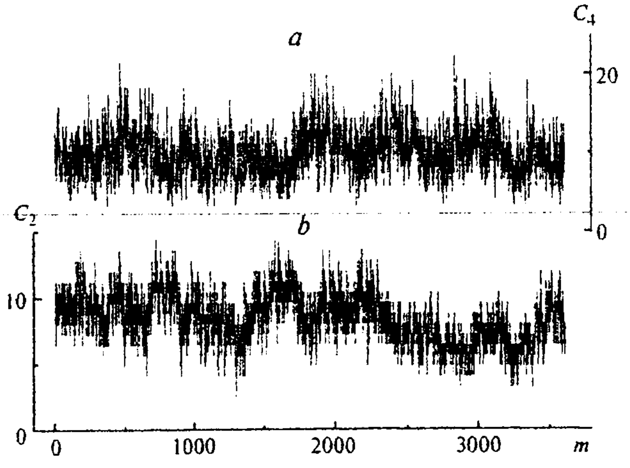

Fig. 6. Fluctuations of concentrations (C_i) of cyclic tetramers (*a*) and dimers (*b*); *m* is the number of the stored molecular configuration in the *FA* model.

redistribution. Topological properties of the network of H-bonds possess high stability toward these factors.

Two salient features manifest themselves when determining the concentrations of cycles. The results of statistical data processing showed that the distribution of cycles in molecular configurations approaches a normal distribution. Each distribution is characterized by a mean value of the measured quantity C_i and by its standard deviation σ_i. From the data listed in Table 2 it follows that these parameters are comparable in magnitude. The distributions are very broad and therefore the scatter of C_i values can be large. For instance, configurations with 2.4 cyclic dimers per 100 formamide molecules were found in the set of 3610 analyzed configurations for the *FA* model, whereas in other models the number of cyclic dimers amounted to 14.4. The number of heptamers varied from 3.2 to 56.8.

The second salient feature of the behavior of the C_i parameter is that relatively "long-lived" fluctuations are observed on some intervals of the Markovian chain. Statistical distributions of concentrations of the cycles in stored configurations are shown in Fig. 6. Low-frequency fluctuations are clearly seen against the background of high-frequency fluctuations. The fact that they are observed on the chain segments of length up to 1000 successive configurations indicates that several regions of states with low probabilities of transitions between them exist in the configuration space. In this connection mention should be made of the general problem of meeting the ergodicity condition.[5]

Structural inhomogeneity is characteristic of the description of liquid formamide at the supramolecular level. The correlation coefficients for the concentrations of cycles in the configurations (R_{ij}), which characterize the measure of linear dependence between C_i and C_j values, are shown in Table 3. The simplest cycles, dimers and trimers, were taken as a basis for calculations. Statistical estimates show that the correlation coefficients are significant at a level higher than 0.99 if $|R_{ij}| > 0.043$. A "negative" correlation between the concentrations of dimers and cycles of larger size is observed for the *FA*, 0.05*c*, and 0.1*c* models. This means that the probability of the formation of other cycles in the configuration decreases as the number of dimers increases and *vice versa*. For the 0.05*t* and 0.1*t* models, the correlation coefficient for dimers and other cycles is close to zero and is in most cases positive. It should be noted that $R_{ij} > 0$ is statistically significant at $i > 2$ and $j > 2$. Consideration of large fluctuations of concentrations makes it possible to conclude that some spatially localized fragments of the network of bonds must contain groups of cycles, whereas other fragments have an open structure. This conclusion is in agreement with the previously observed[32] structural inhomogeneity of polymer networks and with the results of previous investigations of formamide.[17]

Spatial arrangement of cycles of H-bonds is characterized by the RDF of their geometric centers defined as the arithmetic mean of atomic coordinates for *N* molecules forming the cycle (see Fig. 1). The behavior of the RDF was detailed previously.[17] It does not change essentially upon changing the criterion for the H-bond. The $G_{22}(r)$ functions characterizing the regularities of the spatial distribution of cyclic dimers in the formamide models are shown in Fig. 7. Because of the small number of cycles and, hence, larger statistical errors of the 0.1*t* model, the 0.05*t* model was chosen for comparing the behavior of the functions. The specific behavior of the $G_{22}(r)$ function at distances corresponding to the arrangement of dimers in the crystal (see Fig. 1) indicates that the models considered are quite realistic. The shape and size of the unit cell used for simulation do not correspond to the parameters of the actual monoclinic unit cell and cannot be responsible for this phenomenon.

Changes in the strength of H-bonds result in preferred stabilization of specific configurations of cycles and the first maximum of the $G_{22}(r)$ function becomes partly split into components. It can be assumed that the planar structure of the formamide molecule and its ability to form four directed H-bonds play a decisive role in the formation of the crystal structure. The average binding energy and the ratio of the strengths of the *cis*- and *trans*-bonds are likely of secondary importance and first of all determine the melting and boiling temperatures of formamide. Thus, some fragments of the crystal structure are retained in liquid formamide in addition to various other supramolecular associates.

Two types of cycles, dimers and hexamers, can be singled out in the network of H-bonds of the crystal. Melting results in destruction of the regular structure, namely, in bond break and the formation of cycles of various polymeric compositions. In the crystal, the van der Waals forces act between neighboring layers and the

Table 3. Correlation coefficients (R_{ij}) of concentrations of closed cycles of bonds in the networks of H-bonds for different formamide models

Model	*i*	R_{ij} at different *j*				
		3	4	5	6	7
0.1*c*	2	−0.19	−0.03	−0.24	−0.16	−0.23
	3		0.01	0.16	0.19	0.20
0.05*c*	2	−0.24	−0.18	−0.34	−0.22	−0.43
	3		0.14	0.21	0.19	0.31
FA	2	−0.19	−0.05	−0.28	−0.10	−0.12
	3		0.17	0.28	0.21	0.22
0.05*t*	2	−0.06	0.00	−0.03	0.01	0.00
	3		0.22	0.17	0.23	0.23
0.1*t*	2	−0.05	0.05	0.11	0.03	0.00
	3		0.23	0.18	0.21	0.24

Note. i, j are the numbers of molecules in the cycles.

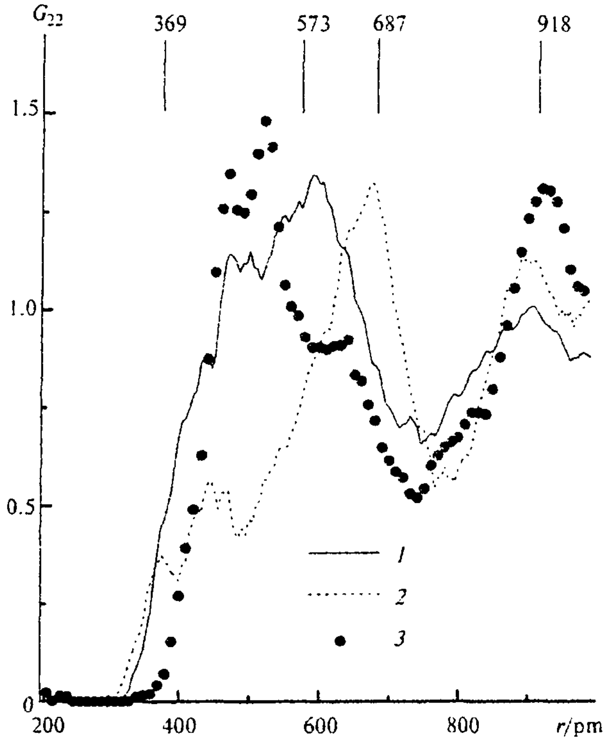

Fig. 7. Radial distribution functions of geometric centers of cyclic dimers ($G_{22}(r)$), calculated using the *FA* (*1*), 0.1*c* (*2*), and 0.1*t* (*3*) models. The intercycle distances in the formamide crystal are shown on the upper abscissa axis.

system of H-bonds consists of superimposed networks. At the same time, the liquid is characterized by intense formation of H-bonds between the layers, by the formation of a three-dimensional spatial network of bonds, by a decrease in the density, and, as a consequence, by the absence of specific details of the behavior of the $G_{22}(r)$ functions at a distance of 369 pm. It is more probable[17] that associates of cyclic dimers with an intercycle distance of ~500 pm, constituting the fragments of chain and ribbon structures, are formed in the liquid.

The above-mentioned absence of correlation between the number of cyclic dimers and the strength of *cis*-bonds in different configurations of formamide models (see Tables 1 and 2) made it possible to suggest that structural and entropy factors also have a major effect on the concentrations of other cycles. If dimers are formed only by *cis*-bonds, four topologically different structures can be defined for trimers, five topologically different structures can be defined for tetramers, *etc.* Let us denote the number of cycles belonging to each topological type per 100 formamide molecules by c_j^i, where the (i, j) indices, respectively, denote the number of *cis*- and *trans*-bonds in the cycle. For the known ratio of the number of H-bonds of one type to the number of H-bonds of the other type in the network the c_j^i values depend on *a priori* combinatorial probability of simultaneous formation of *i cis*- and *j trans*-bonds in the associate, on the average binding energy, and on the entropy factors (the probability of self-closure of the chain of bonds).

In fact, the networks of bonds of the formamide models contain mostly specific types of cycles with topological indices (i, j). The most probable types of molecular association in cyclic trimers and tetramers are shown in Fig. 8. From analysis of the plots shown in Fig. 9 it follows that, virtually for all models, the (2, 1)-cycles with two *cis*-bonds and one *trans*-bond (see Fig. 8, *b*) dominate among trimers and that there are no (0, 3)-cycles formed only by *trans*-bonds. Low formation energies of the *cis*-bonds in the 0.1*c* model favor the increase in the number of the (3, 0)-cycles (see Fig. 8, *a*). The most probable tetrameric structures are (3, 1)- and (2, 2)-cycles (see Fig. 8, *d—f*).

The formation of cycles in the system is favored by *cis*-bonds. For instance, the distribution of trimers, tetramers, and pentamers over topological types is asymmetric and is shifted toward cycles with larger numbers of *cis*-bonds (the (4, 0)-cycles are present in the networks, whereas (0, 4)-cycles are absent). Cyclic polymers differ not only in their topological indices, but also in the number of bonds formed by O atoms. The structurally different tetramers with the same topological indices (2, 2) are shown in Fig. 8, *e, f*. Extra "degrees of freedom" make a more sophisticated analysis of the supramolecular structure of the network of H-bonds much more difficult. The absence of a strong dependence of the concentrations of topologically different types of cycles on the average binding energy (see Fig. 9) indicates that the entropy and packing factors have

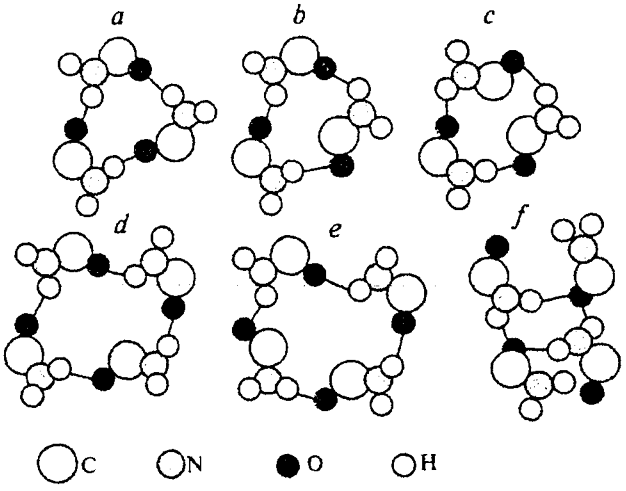

Fig. 8. The most probable types of association of formamide molecules in cyclic trimers and tetramers with topological indices (i, j) = (3, 0) (*a*); (2, 1) (*b*); (1, 2) (*c*); (3, 1) (*d*); and (2, 2) (*e*), (*f*); *i* and *j* are the numbers of *cis*- and *trans*-bonds in the cycle, respectively.

the strongest effect on regularities of the formation of the supramolecular structure of formamide.

Let us consider the problem of the stability of cyclic polymers taking the *FA* model as an example. The dependences of average energies of H-bonds (E) on the number of *cis*-bonds in the cycles at $T = 298$ and 348 K are shown in Fig. 10. The E values for trimers are much higher than for the other types of cycles and are not shown here. As can be seen, in both cases the cycles with two *cis*-bonds are the most stable. Hexamers in the formamide crystal are characterized by the (2, 4) topological indices. It is this type of cycles that have the lowest energies among hexamers in the *FA* model of liquid formamide. Raising the temperature by 50 K shifts the plots along the coordinate axis by ~3 kJ mol^{-1} toward higher energies.

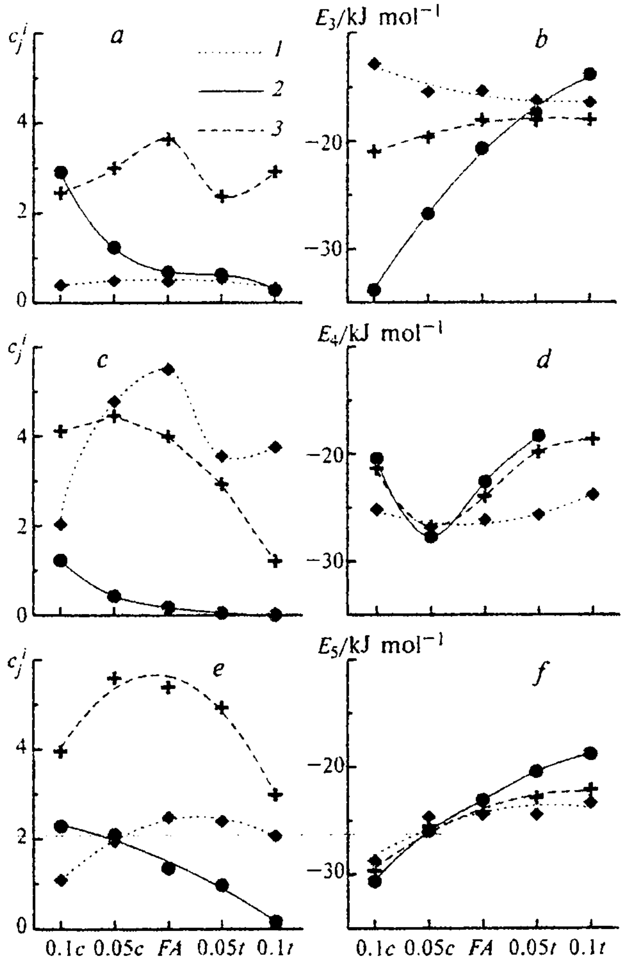

Fig. 9. Concentrations of cyclic polymers (c_j^i is the number of cycles per 100 molecules) (*a*, *c*, *e*) and corresponding average energies of H-bonds, E_k (k is the number of molecules in the cycle), (*b*, *d*, *f*) for different models of liquid formamide; $k = 3$ (*a*, *b*), $(i, j) = (1, 2)$ (*1*), (3, 0) (*2*), (2, 1) (*3*); $k = 4$ (*c*, *d*), $(i, j) = (2, 2)$ (*1*), (4, 0) (*2*), (3, 1) (*3*); and $k = 5$ (*e*, *f*), $(i, j) = (2, 3)$ (*1*), (4, 1) (*2*), (3, 2) (*3*); i and j are the numbers of *cis*- and *trans*-bonds in the cycle.

At the same time, the average energy of H-bonds in dimers increases only by ~1.5 kJ mol^{-1}, though they have a higher decomposition rate (see Table 2). Compared with other types of cycles, the energy of dimers is less sensitive, while their structure (and entropy) is more sensitive to thermally induced destabilization. For all formamide models studied, no (0, 6)-cycles were found among hexamers. Hence, the conclusion[18] that it is these structural elements that dominate in the network of H-bonds of formamide is not confirmed.

The results obtained showed that the spatial structure of liquid formamide and the topological characteristics of the system of H-bonds possess a rather high stability toward changes in specific interactions and temperature. Structural properties of condensed matter are mainly determined by universal interactions (the molecular shape) and the ability of formamide to form four directed H-bonds. The first factor determines the molecular packing, which is close to that of a closely packed system of soft spheres in the liquid phase. The second factor can be considered as a weak perturbation affecting the mutual orientation of the molecules.

Our analysis of the behavior of correlation functions revealed limitations of currently used experimental methods of studying the structure of liquids with complex molecular structure. Changes in the strength of H-bonds strongly affect the parameter of network connectivity and the number of *cis*- and *trans*-bonds; however, they have a much weaker effect on the ratio of concentrations of closed cycles of bonds and their spatial arrangement. Fragments of three-dimensional crystal structure with a more close packing of the molecules are partly retained in liquid formamide. Transition from the crystalline to the liquid state is accompanied by changes in the principle of structural organization and by the formation of a large number of various supramolecular associates.

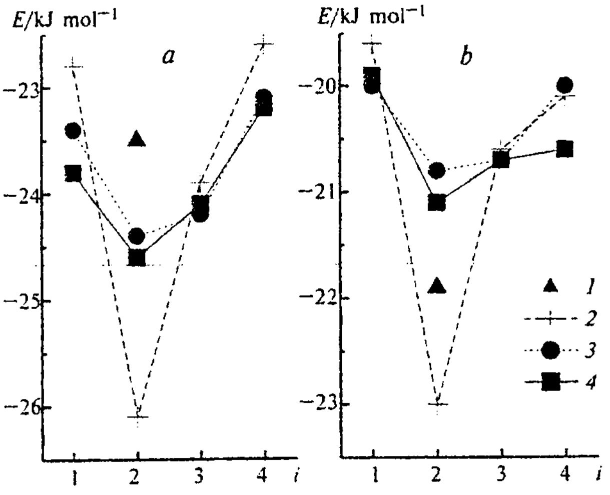

Fig. 10. Average energies of H-bonds in cyclic polymers (E) for the *FA* model at 298 K (*a*) and at 348 K (*b*): *1*, dimer; *2*, tetramer; *3*, pentamer; and *4*, hexamer; i is the number of *cis*-bonds in the cycle.

Structural inhomogeneity is characteristic of the network of H-bonds of liquid formamide. It manifests itself in the presence of both relatively long-lived associates of closed cycles of bonds and branched (chain and ribbon) associates. Strengthening of *trans*-bonds shifts the dynamic equilibrium toward open structures. Computer simulation does not confirm previously drawn conclusions that *trans*-bonds dominate over *cis*-bonds and cyclic hexamers dominate over other structural elements in the network of H-bonds of liquid formamide. The results of our study suggest that the structural properties of not only neat liquids, but also solutions are mainly determined by universal interactions, the molecular shape, steric and packing factors, and by mutual complementarity of spatial structures of the components.

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