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ВЛИЯНИЕ *ОКСО→ТИОКСО*-ЗАМЕЩЕНИЯ В МОЛЕКУЛАХ РАСТВОРЕННОЙ В ВОДЕ *N,N*-ДИМЕТИЛМОЧЕВИНЫ НА СТРУКТУРНО-УПАКОВОЧНЫЕ ЭФФЕКТЫ ГИДРАТАЦИИ В ДИАПАЗОНЕ ТЕМПЕРАТУР (278,15 – 318,15) К

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В качестве первого вклада в научное направление по исследованию термодинамических и физикохимических свойств не изучавшихся ранее водных растворов N,N-диметилтиомочевины (1,1-ДМТМ) были получены прецизионные данные по плотности растворов этого «ассиметрично-замещенного» соединения в воде между 278,15 К и 318,15 К (с шагом 10 К) при атмосферном давлении. Исходя из результатов денсиметрических измерений, были рассчитаны зависящие от температуры стандартные (парциальные при бесконечном разбавлении) молярные объемы $\bar{V}_2^o$ и расширяемости $\bar{E}_{p,2}^o$ растворенного в воде 1,1-ДМТМ. С использованием литературных данных по соответствующим объемным свойствам кислородсодержащего аналога – N,N-диметилмочевины (1,1-ДММ) – в воде, было обсуждено влияние оксо→тиоксо-замещения в 1,1-ДММ (с образованием 1,1-ДМТМ) на структурно-упаковочные эффекты, индуцированные гидратацией растворенного соединения при различных температурах. Предположено, что эффект незначительного увеличения свободного (исключенного) объема или «разрыхления» структурной упаковки гидратного комплекса при замещении 1,1-ДММ на 1,1-ДМТМ обусловлен в целом снижением термической стабильности образующихся гетерокомпонентных Н-связей. Установлен неординарный факт тождественности в изменении $\bar{V}_2^o$ как при оксо→тиоксо-замещении в изомерных N-диметилзамещенных производных мочевины, так и при соответствующих эквимолекулярных переходах от N(1,1)- к N(1,3)-метил-содержащим производным мочевины или тиомочевины в воде. Кроме того, было подтверждено ранее выдвинутое предположение о том, что каждый из функциональных >N(1)- и >N(3)-фрагментов, связанных с тиокарбонильной (>C=S)-группой молекулы алкил-замещенного производного тиомочевины, сольватируется в воде независимо, как и в установленном аналогичном случае с карбонильными (оксо-замещенными) аналогами.

Ключевые слова: *N,N*-диметилтиомочевина, *N,N*-диметилмочевина, водные растворы, гидратация, объемные молярные характеристики

INFLUENCE OF *OXO→THIOXO*-SUBSTITUTION IN MOLECULES OF *N,N*-DIMETHYLUREA AS A SOLUTE IN WATER ON STRUCTURE-PACKING HYDRATION EFFECTS BETWEEN (278.15 AND 318.15) K

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As a first step to investigating the thermodynamic and physicochemical properties of previously unstudied aqueous solutions of N,N-dimethylthiourea (1,1-DMTU), precision data were obtained on the density of solutions for this "asymmetrically substituted" compound in water between

(278.15 and 318.15) K, in 10 K increments, at the ambient pressure. Based on the results of density measurements, the temperature-dependent standard (partial at infinite dilution) molar volumes $\bar{V}_2^o$ and expansibilities $\bar{E}_{p,2}^o$ for 1,1-DMTM as a solute in water were calculated. Using the available literature data on the corresponding volume properties for the oxygen-containing counterpart, N,N-dimethylurea (1,1-DMU), in water, the influence of oxo→thioxo-substitution in 1,1-DMU, to form 1,1-DMTU, on the temperature-dependent structure-packing effects of the solute hydration was discussed. It was inferred that the effect of a slight increase in the free (excluded) volume or "loosening" of the structure packing of the hydration complex at the replacement of 1,1-DMU with 1,1-DMTM is in overall caused by a decrease in the thermal stability of the heterocomponent H-bonds formed. A non-trivial fact of the identity in changing $\bar{V}_2^o$ at both oxo→thioxo-substitution in the isomeric N-dimethyl-substituted urea derivatives, and the corresponding equimolecular transfers from N(1,1)- to N(1,3)-methyl-containing ureas or thioureas in water was established. Also, the previously advanced assumption that each of functional >N(1)- and >N(3)-fragments bonded with the thiocarbonyl (>C=S)-group of the molecule of the thiourea alkyl-substituted derivative is solvated independently in water was confirmed, as in the similar case with the carbonyl (oxo-substituted) counterparts.

Keywords: *N,N*-dimethylthiourea, *N,N*-dimethylurea, aqueous solutions, hydration, volumetric molar characteristics

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INTRODUCTION

Dimethyl-substituted thioureas, like the related carbonyl- or *oxo*-containing derivatives [1-10], are among the most interesting bioactive heterofunctional compounds of the urea (U) family that perturb the water structure in different ways due to distinct interaction effects [9,11-14]. This is because the hydrogen-bonding ability of the >N−C(=S/O)−N< grouping in an aqueous medium is influenced by peculiarities of attaching each of two hydrophobic methyl substituents to nitrogen atoms [14]. According to inferences [7], rotational dynamics of water molecules, which is dominated by H bond strengths, is significantly impeded in the presence of *N,N*'-dimethylurea (1,3-DMU) and only weakly by isomeric *N,N*-dimethylurea (1,1-DMU). This difference (in the electron density distribution) directly relates to the *excluded volume* effects during a solute hydration. Restricting the excluded volume near only one of nitrogens in the hydrated 1,1-DMU molecule leads to a weaker "perturbation" of the water's rotation dynamics [5-7]. It is obvious that the similar "distribution pattern" is characteristic of equimolecular sulfur- or *thioxo*-containing *N*-dimethyl-substituted U derivatives, too. Hence, useful information on the structure-packing and interaction-related effects in aqueous solutions of interest can be derived analyzing the molar volumetric properties of each of the compared solutes over a wide temperature range.

Based on the inspection of existing literature sources, the required data on the standard (partial at infinite dilution) molar volume $\bar{V}_2^o[\equiv \bar{V}_2^\infty]$ and expansibility $\bar{E}_{p,2}^o = (\partial \bar{V}_2^o/\partial T)_p$ are available for 1,3-DMU and *N,N'*-dimethylthiourea (1,3-DMTU) [3, 8, 9, 15], as well as 1,1-DMU [1,8]. Unlike the symmetric counterpart 1,3-DMTU, any data on physicochemical and thermodynamic (including volume-related) properties for the isomer-asymmetric *N,N*-dimethylthiourea (1,1-DMTU, see in Fig. 1) as a solute in water are currently absent at all. This is largely due to the complexity of synthesizing and purifying procedures for this compound [16, 17], which is why its cost is an order of magnitude higher than that of 1,3-DMTU. Besides, there are some limitations to use of 1,1-DMTU. It is not very stable and can degrade in the presence of light or heat. This thiourea (TU) methyl-derivative is also not very soluble in water, which can limit its use in certain experiments.

Fig. 1. Structure of the *N*,*N*-dimethyl-2-thiourea (1,1-DMTU) molecule with nitrogen and carbonyl C atoms numbered (3D-version: B3LYP/6-31G*, Gaussian 09-D.01)
Рис. 1. Структура молекулы *N*,*N*-диметил-2-тиомочевины (1,1-ДМТМ) с нумерацией атомов азота и карбонильного углерода (3D-версия: B3LYP/6-31G*, Gaussian 09-D.01

Nevertheless, the structure features of 1,1-DMTU in the own solid-phase (crystalline) state were comprehensively studied [18, 19]. Unlike the "cognate" 1,1-DMU, whose molecules in the crystal are "aligned along their dipole moment vectors", 1,1-DMTU molecules are packed as centrosymmetric dimers within layer-corrugated (orthorhombic) crystalline structure [5, 19]. The latter, being formed by N–H···S=C hydrogen bonds, has in overall a denser molecular packing [19, 20]. The S atom accepts two such H bonds being less stable than N–H···C=O-bonds, since the π-bond of the *thioxo*-group is more polarizable compared to the carbonyl (*oxo*-) analogue in the 1,1-DMU molecule [14, 19, 21]. Meanwhile, based on the data from thermodynamic experiments for aqueous 1,3-DMTU and 1,3-DMU [1, 3-5, 8, 11-13, 15], it should be assumed that *oxo* → *thioxo*-substitution in the 1,1-DMU molecule during its hydration can lead to a pronounced structure-packing (volume-related) changes against the background of redistribution in the effects of solute interaction with the nearest (solvent) environment.

Interest in 1,1-DMTM and its aqueous solutions also steams from the role that the given TU derivative plays in a number of advanced chemical technologies and promising medical applications [22, 23]. In particular, 1,1-DMTM stands duty as a precursor in the synthesis of thio-/semithioglycolurils (*bis*urea derivatives), being heterocyclic compounds with a marked psychotropic or antibacterial activity *in vivo* [24-26]. The mechanism of bioactive action of 1,1-DMTU is not yet fully understood. However, in the future, this compound can be used in the development of new drugs and the study of their metabolism in the living organism.

Given the above, studying the structure-thermodynamic properties of 1,1-DMTU as a solute in water seems to be a quite important task. And, as a first step in this trend, we attempted to analyze the influence of *oxo* → *thioxo*-substitution in 1,1-DMU, to form the related 1,1-DMTU (Fig. 1), on the temperature-dependent structure-packing (volume) effects of a solute hydration based on the results of high-precision densimetric measurements [27].

MATERIALS AND METHODS

The sample of 1,1-DMTU, $(CH_3)_2NCSNH_2$ {CAS RN: 6972-05-0; molar mass: $M_2^* = 104.176$ g/mol; melting point: $T^*_{m.p.,2} = 432$ (± 1) K; manufacturer's assay: ≥ 98.0 %}, was purchased from "Shanghai Macklin Biochemical Co., Ltd" (China). Before experiments, the sample was purified by recrystallization from the predistilled rectified ethanol [11-14, 19] and dried in a vacuum chamber at ~350 K for 48 h. The product was tested by elemental composition using a «Perkin-Elmer PE 2400 CHN" automated microanalyzer. Found, %: C, 34.66; H, 7.69; N, 26.95; S, 30.70. Calculated (for $C_3H_8N_2S$), %: C, 34.59; H, 7.74; N, 26.89; S, 30.78. From here, the (Found/Theory) elemental ratio was found to be 0.994 (± 0.003) at worst (for hydrogen). The sample was then stored in a light-tight vacuum desiccator over P_2O_5. Aqueous solutions of 1,1-DMTU were prepared gravimetrically in the sealed glass flasks of a ~ 40 cm^3 volume using an "AND GH-202" analytical type balance with an uncertainty of 0.01 mg. The deionized and twice distilled (to a specific conductivity of $1.3 \cdot 10^{-6}$ S/cm) water was used for this purpose. The uncertainty in estimating the solution molality m did not exceed $3 \cdot 10^{-5}$ mol/kg.

Densities of the solutions ρ_s were measured using an "Anton Paar DMA 5000 M" (Austria) densitometer equipped with a ~2 cm^3 vibrating U-tube-shaped cell at T = (278.15 K – 318.15) K, with a step of 10 (± 0.01) K, and atmospheric pressure of p = 99.6 (± 0.8) kPa. Before each series of experiments, a standard *two-point* calibration procedure with the densities of dry air and freshly prepared water ρ_1^* was performed. All density experiments were carried out in the *isoplethal mode* being based on "a temperature scanning over the particular solution filled into the measuring cell with the repetition of the scan for next solution" [28]. With fivefold measurements, the reproducibility in $\rho_s(m)$ was up to $1 \cdot 10^{-5}$ g/cm^3. In turn, the total uncertainty in the density measurements $U_c(\rho_s)$ did not exceed $3 \cdot 10^{-5}$ g/cm^3, which is consistent with previously made conclusions regarding a similar device and experimental methodology [29]. A more detailed description of the apparatus design and the procedure for measuring ρ_s is given in works [9, 14, 28-30].

RESULTS AND DISCUSSION

The experimentally measured values of $\rho_s(m)$ for aqueous 1,1-DMTU solutions are presented in Table 1.

As mentioned above, the reproducibility in $\rho_{s,i}(m)$ did not exceed $1 \cdot 10^{-5}$ g/cm^3 at n = 5 measurements. Given this, the half-width of the confidence interval for each average-weighted experimental value

$\rho_{s,av}(m)$ was calculated using the Peters formula [31] for the root-mean-square error with the correction to Student's criterion (being $t_{0.95} = 2.78$):

$$\sigma_{\rho_s}(m) = \pm(5/4)t_{0.95} \times$$
$$\times \sum_{i=1}^{n} |\rho_{s,i} - \tilde{\rho}_{s,i}| / \left[n\sqrt{(n-1)}\right]^{-1}, \quad (1)$$

where $\rho_{s,i}$ – the solution density at a single experiment, and $\tilde{\rho}_{s,i} = \rho_{s,av}(m)$.

Table 1

Densities of aqueous 1,1-DMTU solutions ρ_s, g/cm³, at different molalities (m) and temperatures (T) and p = 0.1 MPa

***Таблица 1.* Значения плотности водных растворов 1,1-ДМТМ ρ_s, г/см³, различной моляльности (m) при различных температурах (T) и давлении p = 0,1 МПа**

T, K	m, mol/kg (highlighted in *italics*)			
	0	*0.01503*	*0.02422*	*0.03667*
278.15	0.999965	1.000196	1.000338	1.000529
288.15	0.999101	0.999318	0.999450	0.999629
298.15	0.997047	0.997254	0.997380	0.997551
308.15	0.994035	0.994233	0.994354	0.994518
318.15	0.990216	0.990407	0.990524	0.990682
T, K	*0.05042*	*0.07370*	*0.09543*	*0.11608*
278.15	1.000740	1.001097	1.001430	1.001745
288.15	0.999827	1.000161	1.000473	1.000768
298.15	0.997739	0.998058	0.998355	0.998636
308.15	0.994699	0.995005	0.995289	0.995559
318.15	0.990856	0.991151	0.991425	0.991685
T, K	*0.14547*	*0.17215*	*0.20198*	*0.23366*
278.15	1.002194	1.002600	1.003053	1.003542
288.15	1.001187	1.001567	1.001991	1.002449
298.15	0.999036	0.999397	0.999801	1.000238
308.15	0.995942	0.996289	0.996676	0.997095
318.15	0.992055	0.992389	0.992762	0.993166

Table 2 contains values of the apparent molar volume $V_{\phi,2}(m)$ for 1,1-DMTU in its aqueous solutions. For calculation of $V_{\phi,2}(m)$, the procedure [28, 30, 32] based on the *generic* volume V_s of a binary solution (in m scale) was used:

$$V_s(m) = (1000 + M_2^* m)/\rho_s = V_1 + V_{\phi,2} m, \quad (2)$$

where $V_1 [= V_s(m \to 0)] = 1000/\rho_1^*$ (data on ρ_1^* were taken from Table 1) and M_2^* is the molar mass of 1,1-DMTU (see in the previous section). To calculate the $V_{\phi,2}(m)$ values with using Equation (2), the overall uncertainty in the density measurements of $U_c(\rho_s) \approx \approx \pm 3 \cdot 10^{-5}$ g/cm³ was taken into account.

Least squares analysis of data in Table 2 showed that the $V_{\phi,2} - m$ function at each steady-state temperature is adequately described by a first-power equation

$$V_{\phi,2}(m) = \bar{V}_2^o [\equiv V_{\phi,2}^\infty] + S_V m, \quad (3)$$

here, S_V is the "empirical slope", which can formally be considered as an adjustable parameter being the difference between the solute – solute and solute – solvent pairwise interactions in terms of volume (packing) effects [32, 33].

The parameters of Equation (3) for the system (H_2O + 1,1-DMTU) are listed in Table 3 along with the corresponding data on $\bar{V}_2^o$ and S_V for aqueous 1,1-DMU taken from our previous work [8]. Besides, Table 3 includes the $\bar{V}_2^o$ values for 1,1-DMTM predicted in [14] using two schemes for redistributing the volume contributions from N_{cis}- and/or N_{trans}-located methyl substituents (see Fig. 1):

$$\bar{V}_2^o(\text{I}) = \bar{V}_2^o(\text{1,1,3-TriMTU}) - [\bar{V}_2^o(\text{MMTU}) - \bar{V}_2^o(\text{TU})], \quad (4)$$

$$\bar{V}_2^o(\text{II}) = \bar{V}_2^o(\text{1,1,3-TriMTU}) - [\bar{V}_2^o(\text{1,3-DMTU}) - \bar{V}_2^o(\text{MMTU})]. \quad (5)$$

Table 2

Apparent molar volumes, $V_{\phi,2}$ (± 0.02), cm³/mol, of 1,1-DMTU in aqueous solutions at different molalities (m) and temperatures (T)

***Таблица 2.* Значения кажущихся молярных объемов, $V_{\phi,2}$ (± 0,02), см³/моль, для 1,1-ДМТМ в водных растворах различной моляльности (m) при различных температурах (T)**

m, mol/kg	Temperature: T, K				
	278.15	288.15	298.15	308.15	318.15
0.01503	88.759	89.800	90.631	91.432	92.212
0.02422	88.752	89.794	90.625	91.426	92.207
0.03667	88.743	89.786	90.618	91.419	92.201
0.05042	88.732	89.777	90.610	91.412	92.193
0.07370	88.715	89.761	90.596	91.399	92.181
0.09543	88.698	89.747	90.583	91.387	92.169
0.11608	88.683	89.733	90.570	91.375	92.158
0.14547	88.661	89.714	90.553	91.359	92.143
0.17215	88.641	89.696	90.537	91.344	92.129
0.20198	88.619	89.677	90.519	91.327	92.113
0.23366	88.595	89.656	90.500	51.310	92.096

To estimate the $\bar{V}_2^o$(I) and $\bar{V}_2^o$(II) values for 1,1-DMTM as a solute in water, the molar volume characteristics of interest from [9, 14] were used. It should be also noted here that the acronyms MMTU and 1,1,3-TriMTU in the above-specified group-contribution schemes (4) and (5) refer to *N*-monomethylthiourea and *N,N,N'*-trimethylthiourea, respectively.

According to [1, 9, 14, 32], a situation when $S_V = (\partial V_{\phi,2}/\partial m)_p < 0$ in the case of 1,1-DMTU and 1,1-DMU (see Table 3) can be attributed mainly to the

structural stabilization of aqueous clusters in the vicinity of hydrophobic (methyl) moieties of a hydrated solute molecule. This effect is conjugated to the solvent-mediated solute – solute association. However, there is still no consensus in the scientific literature regarding which thermodynamic parameters (including S_V) should be attributed to a dissolved non-electrolyte as a "structure-maker" or a "structure-breaker". As the authors [1] rightly highlighted, "molecular level solute – solvent interactions are complex and difficult to define explicitly in terms of thermodynamic properties". Suffice it to say that solutes forming strong H-bonds with water can induce both structure-promoting and structure-destroying effects depending on the state parameters of the binary aqueous system [1, 9, 14, 34].

Table 3

Standard molar volumes $\bar{V}_2^o$ of 1,1-DMTUand 1,1-DMU ([8], highlighted by *italics*) in water at different temperatures (*T*)

Таблица 3. Значения стандартных молярных объемов $\bar{V}_2^o$ для 1,1-ДМТМ и 1,1-ДММ ([8], выделены *курсивом*) в воде при различных температурах (*T*)

T, K	$\bar{V}_2^o$(± 0.03), cm³/mol		S_V(± 0.05), cm³kg/mol² *
	Experim.	Predict. [9, 14]	
278.15	88.77 *77.86*	89.25 ± 0.2 (I) 88.91 ± 0.2 (II)	-0.75 -0.80
288.15	89.81 *78.60*	89.97 ± 0.2 (I) 89.81 ± 0.2 (II)	-0.66 -0.75
298.15	90.64 *79.28*	90.68 ± 0.2 (I) 90.54 ± 0.2 (II)	-0.60 -0.72
308.15	91.44 *79.95*	91.39 ± 0.2 (I) 91.30 ± 0.2 (II)	-0.56 -0.69
318.15	92.22 *80.62*	92.07 ± 0.2 (I) 91.92 ± 0.2 (II)	-0.53 -0.66

Note: * Calculated by Equation (2) using the $V_{\phi,2}$ values from Table 2 and [8]

Примечание: * Рассчитано по уравнению (2) с использованием значений $V_{\phi,2}$ из таблицы 2 и [8]

Therefore, standard $\bar{V}_2^o[\equiv V_{\phi,2}(m \to 0)]$ values, being independent of the composition effect, are of more fundamental importance in examining the solute – solvent interaction [14, 32-36]. Comparing the data on $\bar{V}_2^o(T)$ for 1,1-DMTU summarized in Table 3, at least two obvious inferences can be drawn.

Firstly, over the temperature range between 288.15 K and 308.15 K, the experimental and predicted (with using models I and II) values of $\bar{V}_2^o$ show a discrepancy only within the limits of calculation error. At lower and higher temperatures, the discordance in the quantities compared is not as significant. This fact points to the validity of applying Equations (4) and (5) to estimate $\bar{V}_2^o$ in the case under consideration.

Secondly, when interpreting the experimentally obtained data in Table 3 together with those taken from [9, 34], it is worth noting the fact that the $\bar{V}_2^o(H_2O)$ value for 1,1-DMTU is equal to half of the sum of the corresponding values for TU and *N*,*N*,*N'*,*N'*-tetramethylthiourea (1,1,3,3-TetMTU) in water. Namely, (90.64 ± 0.03) and (54.74 + 126.53)/2 = (90.63 ± 0.03) cm³/mol, respectively, at *T* = 298.15 K. The same goes for the situation when the half-sum of V_2^o(TU; H_2O) and $\bar{V}_2^o$(1,3-DMTU; H_2O) is equal to the V_2^o value for hydrated MMTU: (54.74 + 91.32)/2 = (73.03 ± 0.03) and (72.96 ± ± 0.05) cm³/mol at the same temperature [9, 14]. This circumstance supports the previously substantiated assumption of *independent solvation* of *N*(1,3)-attached-to-CS moieties of the TU alkyl-derivative molecule in water [14]. A similar conclusion was reached earlier [2, 37] regarding the volume- and enthalpy-related hydration effects for the related carbonyl-containing (U) *N*-dimethyl-derivatives.

Another important feature of the binary aqueous systems discussed is an identity in changing $\bar{V}_2^o$ at the *oxo* → *thioxo*-substitution in the isomeric molecules of *N*-dimethyl-substituted U derivatives and at the corresponding equimolecular transfers ($\Delta_{tr}\bar{V}_2^o$) from *N*(1,1)- to *N*(1,3)-containing ureas or thioureas (see Fig. 2). This circumstance highlights a certain similarity of solvation processes in the standard aqueous solutions of *N*-dimethyl-substituted derivatives of U and TU. In turn, this gives us *carte blanche* to consider the structure-packing effects of 1,1-DMU hydration as a basis for discussing the volume properties of 1,1-DMTU as a solute in water.

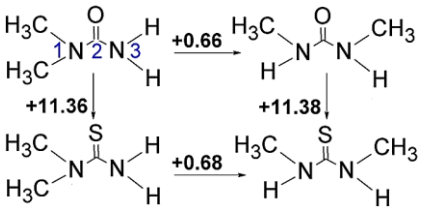

Fig. 2. A comparative scheme of changes in the standard molar volume (±0.03 cm³/mol) during *oxo* → *thioxo*- and *N*(1),*N*(1) → *N*(1),*N'*(3)-methyl-substitutions in the urea derivative molecules in water at *T* = 298.15 K (this work and Refs 9, 14)

Рис. 2. Сравнительная схема изменений стандартного молярного объема (±0,03 см³/моль) при *оксо* → *тиоксо*- и *N*(1),*N*(1)→*N*(1),*N'*(3)-метил-замещениях в молекулах производных мочевины в воде при *T* = 298,15 K (эта работа и ссылки 9, 14)

As follows from the scheme shown in Fig. 2, the H-by-CH_3 replacement on $N(1)_{cis}$- and $N(1)_{trans}$-positions of the same nitrogen atom of TU has a less pronounced effect on $\bar{V}_2^o$ than it does the attachment of two methyl groups to the $N(1,3)_{cis}$-locations of two

different nitrogens. As we have mentioned above (for aqueous 1,1-DMU [5]), this is largely due to restricting the excluded volume effect for 1,1-DMTU despite the fact that the specified molecule has the same number of *N*-sited CH_3-groups as its isomeric counterpart, 1,3-DMTU. Proceeding from the equality of transfer effects $\Delta_{tr}\bar{V}_2^o$ induced by the *oxo* → *thioxo*-substitution in the U-derivative molecules (see Fig. 2), one can also assume that the impact of 1,1-DMTU on bulk water dynamics (beyond the first hydration shell) should be larger than that of 1,3-DMTU [5]. In turn, factors influencing the occurrence of $\Delta_{tr}\bar{V}_2^o$ at such a substitution in hydrated 1,1-DMU molecules require separate consideration.

Of particular importance here are the data on *packing density* $d = V_{w,2}/\bar{V}_2^o$ [9, 14, 35], which represents the volume ($\bar{V}_2^o$) fraction in the new-formed "hydration complex" occupied by the intrinsic volume $V_{int,2}$ of a solute. The latter ($V_{int,2}$) is most often expressed through the van der Waals volume (per one mole) $V_{w,2} = v_{w,2}N_A$ [35], where $v_{w,2}$ and N_A are the molecule volume and Avogadro number, respectively. When evaluating $V_{w,2}$ for 1,1-DMTU, (= 59.0 ± ± 0.2) cm^3/mol, and 1,1-DMU, (= 53.7 ± 0.1) cm^3/mol, in our previous works [9, 14], it was postulated that these values are temperature-independent over the *T*-range in question. The values of the *d* parameter calculated using the data on $\bar{V}_2^o$ from Table 3 are presented in Table 4.

As follows from data in Table 4, the fractional free volume expressed in terms of the $V_{w,2}/\bar{V}_2^o$ ratio slightly increases (by 4%) with the virtual *oxo* → *thioxo*-substitution in the hydrated 1,1-DMU molecule. In other words, the structure packing of the hydration complex formed by 1,1-DMTU is looser than in the case of the oxygen-containing analogue. It is interesting that a similar trend of decrease in the temperature-dependent *d* value occurs at the transfer from 1,3-DMU to 1,3-DMTU, too, with the only difference being that in this case, less densely packed (by *ca.* Δd = 0.05) aqueous structures around solutes are formed [9]. On the one hand, this fact points to more pronounced structure rearrangements in the hydration shell of the asymmetrical isomer, whose $-N(CH_3)_2$- and $-NH_2$-located groups are concurrently conjugated with the H-bond-accepting >C=S- or >C=O- fragment. On the other hand, the situation can stand duty as confirmation of conclusions [12, 13] about the determining role of the functional [N–CS(CO)–N] grouping in promoting water structuring around two methyl entities. That is, the established substitution-related packing effect (Table 4) is induced by changing in the energy hydrophilic-hydrophobic balance during the hydration process of 1,1-DMTU and 1,1-DMU.

Table 4

Packing density parameters *d* for hydrated 1,1-DMTU- and 1,1-DMU at different temperatures (*T*)

***Таблица 4.* Значения параметра плотности упаковки *d* для гидратированных 1,1-ДМТМ и 1,1-ДММ при различных температурах (*T*)**

T, K	$d = V_{w,2}/\bar{V}_2^o$ (± 0.003)	
	1,1-DMTU	1,1-DMU [8]
278.15	0.665	0.690
288.15	0.657	0.683
298.15	0.651	0.677
308.15	0.645	0.672
318.15	0.640	0.666

In our case, the hydrogen-bonding ability of the above functional grouping is modulated by the insertion of hydrophobic methyl substituents on $N(1)_{cis}$- and $N(1)_{trans}$-positions (Fig. 1) of the same nitrogen atom of the TU molecule [9, 11, 12]. In contrast to *N*-methyl-substituted ureas, the corresponding TU-derivatives have somewhat higher dipole moments with increased polarizability of the >C=S-bond [21, 38]. Therefore, the process of hydration of the [N–CS–N] grouping, accounting for the hydrogen bonds in the thiocarbohyl's region only, was found to be more exothermic compared to that of the [N–CO–N] grouping [12]. This fact is consistent with a predominant role of the sulfur atom in the hydrophilic hydration of 1,1-DMTU, while the process of 1,1-DMU solvation in water suggests a major contribution of the unsubstituted nitrogen atom to the H-bonding effects [12, 39].

It is well known that 1,1-DMU dissolves in water with the pronounced endothermic effect ($\Delta_{sov}H_2^o \approx$ ≈ 12 kJ/mol at *T* = 298.15 K) against the background of the positive and relatively large standard partial molar heat capacity $\bar{C}_{p,2}^o$ of the hydration process {≈ 235 J/(K·mol)} [2, 39]. The latter quantity directly correlates with the structure of the first hydration shell of hydrophobic moieties [13, 40-42], that is, with the effect of structuring water clusters in the nearest vicinity of them. Unfortunately, the lack of such characteristics for the 1,1-DMTM solvation in water does not yet allow us to make more substantiated inferences about the energy and interaction-related changes in the hydration complex induced by *oxo* → *thioxo*-substitution in the 1,1-DMU molecule. However, the additional useful information can be derived analyzing the standard (partial) molar expansibilities $\bar{E}_{p,2}^o$ of both compared isomeric counterparts as solutes in water.

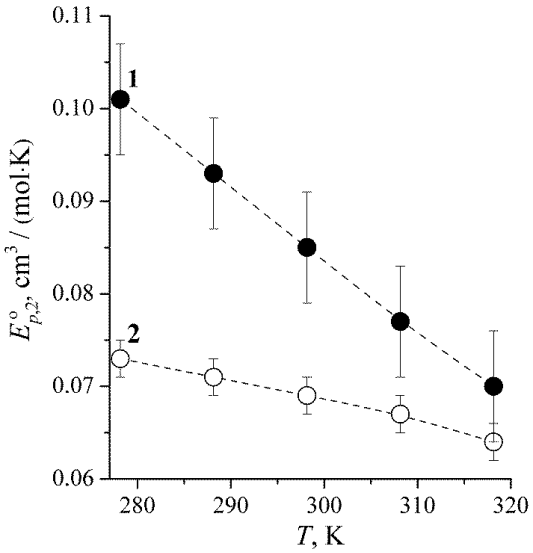

Fig. 3. Standard molar expansibilities of 1,1-DMTU (1) and 1,1-DMU (2) [8] in water as a function of temperature, with a "corridor" of errors

Рис. 3. Зависимости стандартных молярных расширяемостей 1,1-ДМТМ (1) и 1,1-ДММ [8] от температуры с «коридором» ошибок

To calculate the $\bar{E}^{o}_{p,2} = (\partial \bar{V}^{o}_{2}/\partial T)_p$ values, the $\bar{V}^{o}_{2} - T$ functions taken from Table 3 were approximated by a second-power equation [9, 14]:

$$\bar{V}^{o}_{2} = a_0[\equiv \bar{E}^{o}_{p,2}] + a_1(T-\theta) + a_2(T-\theta)^2, \quad (6)$$

where θ = 298.15 K is the average-weighted temperature. Differentiating Equation (6) with respect to $(T-\theta)$, the temperature-dependent values of $\bar{E}^{o}_{p,2}(\theta)$ for 1,1-DMTU and 1,1-DMU [8] in water were obtained and presented in Fig. 3.

As can be seen in Fig. 3, the $\bar{E}^{o}_{p,2}$ values for 1,1-DMTU are in overall markedly larger than the corresponding values for 1,1-DMU. But, the difference in $\bar{E}^{o}_{p,2}$ reduces sharply with increasing temperature. The situation with $(\partial \bar{V}^{o}_{2}/\partial T)_p$ for aqueous 1,1-DMTU is more typical for a predominant hydrophilic solute. The latter, as is well known, is characterized by the prevailing effect of the H-bonded hydration shell destruction, being weakened under the influence of temperature [9, 14, 32]. In accordance with the Hepler's relation [9, 14, 34, 43], $-\left(\partial \bar{E}^{o}_{p,2}/\partial T\right)_p = -(\partial^2 \bar{V}^{o}_{2}/\partial T^2)_p = \left(\partial \bar{C}^{o}_{p,2}/\partial p\right)_T$, the trend of changing the $\bar{E}^{o}_{p,2} - T$ function (see Fig. 3) can provide the information on a solute capability to destroy (a negative slope) or promote (a positive slope) the hydration shell structure. In the context of this conception, the process of *oxo*→*thioxo*-substitution in 1,1-DMU, to form 1,1-DMTU, is accompanied largely by a decrease in the thermal stability of forming heterocomponent hydrogen bonds. The occurring difference in the structure-breaking effect is seemingly the main reason for the relative loosening of the molecular packing of the solute hydration complex being formed at the *oxo* → *thioxo*-substitution of interest (see Table 4).

CONCLUSION

Given the aforesaid, the following basic points can be highlighted.

The previously advanced assumption that each of functional >*N*(1)- and >*N*(3)-fragments bonded with the thiocarbonyl (>C=S-)group of a thiourea alkyl-derivative molecule in water are *solvated independently* was confirmed using newly and previously obtained results on the volume properties of standard aqueous solutions of interest.

A non-trivial fact of the identity in changing the standard molar volume of a solute at *oxo* → *thioxo*-substitution in the isomeric molecules of *N*-dimethyl-substituted urea derivatives and at the corresponding equimolecular volume-related transfers from *N*(1,1)- to *N*(1,3)-methyl-containing ureas or thioureas in water was established for the first time.

It was inferred that the fractional free (excluded) volume somewhat increases with virtual *oxo* → *thioxo*-substitution in the hydrated *N,N*-dimethylurea molecule, a fact being in consistency with the effect of loosening the structure packing of the hydration complex formed.

It was found that the replacement of *N,N*-dimethylurea with its sulfur-containing analogue in water is accompanied largely by a decrease in the thermal stability of forming heterocomponent H-bonds, and the occurring difference in the structure-breaking effect is seemingly the main reason for the above loosening of the molecular packing of a solute hydration shell.

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CONFLICTS OF INTEREST

Автор заявляет об отсутствии конфликта интересов, требующего раскрытия в данной статье.

The author declare the absence of a conflict of interest warranting disclosure in this article.

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