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LETTERS TO THE EDITOR

Influence of *N*-Metylation Effect on the Dissolution Enthalpy of Glycoluryl in Water

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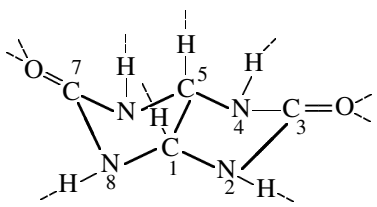
The glycolurils which relate to 2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diones, the bicyclic bis-carbamides of octane series, are known as perspective biologically active compounds which meet successful application as low toxic pharmacological preparations [1, 2]. This fact dictates necessity to reach information on thermodynamic properties of aqueous solutions of these compounds.

Earlier [3, 4] we have shown that 2,4,6,8-tetramethyl-bis-carbamide (TM*b*CA), or *mebicar*, on dissolving in water shows small endothermic effect ($\Delta_{sol}H_2^{\infty}$ –3.67 kJ mol^{-1}) despite the presence in its molecule of the same number of CH_3 groups as in hydrophobically hydrating tetramethylcarbamide (TMCA: $\Delta_{sol}H_2^{\infty} \cong$ –24.53 kJ mol^{-1} [5]). Accounting for this observation we suggest that the problem how the process of *N*-methylation affects enthalpy characteristics of dissolving in water protonated (that is, unsubstituted) glycoluril of bis-carbamide series (see the scheme) is also significant. The glycoluril bis-carbamide (*b*CA) is much more hydrophilic than TM*b*CA but is scarcely dissolving in water (5×10^{-3} mol per 1000 g of H_2O at 298.15 K, or less).

These circumstances give rise to consider *b*CA as a perspective nitrogen-containin (carbamide) fertilizer with low ability of washout from soil, but simultaneously they restrict studying structural-thermodynamic properties of aqueous solutions of this compound and features of hydration of its molecules.



Molecule of biscarbamide and possible orientations of H-bonding with surrounding water.

Using a method of precise calorimetry we succeeded in estimation of $\Delta_{sol}H_2^{\infty}$ value for *b*CA in H_2O at 298.15 K. The results of our measurements are listed in the table. They show that the *b*CA → TM*b*CA transition is characterized by a significant (by ~23 kJ mol^{-1}) strengthening in hydration of glycoluril. In addition, *N*-methylation of carbamide (CA → TMCA) increases exotermicity of its dissolution, even by almost 40 kJ mol^{-1} [5]. This fact inspires a conclusion that nature of hydration of *b*CA, a typical hydrophilic CA, is whole defined by the ability of donor and acceptor centers of glycoluril molecule to specific (through H-bonds) interaction with the molecules of water surrounding. However, when *b*CA is subjected to hydration, together with raised significance of configuration factor (as a result of

Numerical values of integral $\Delta_{sol}H_2^m$ (m_2 is molal concentration: moles of *b*CA per 1 kg of H_2O) and infinity $\Delta_{sol}H_2^{\infty}$ values of molar dissolution enthalpy (kJ mol^{-1}) of biscarbamide (2) in water (1) at 298.15 K[a]

$m_2 \times 10^3$	$\Delta_{sol}H_2^m$	$m_2 \times 10^3$	$\Delta_{sol}H_2^m$	$m_2 \times 10^3$	$\Delta_{sol}H_2^m$
1.61	26.67	1.90	26.66	2.02	26.66
1.78	26.66	1.92	26.67	2.11	26.67
1.84	26.66	1.96	26.67	2.22	26.66
$\Delta_{sol}H_2^{\infty}$ 26.66 (±0.01) kJ mol^{-1}					

[a] The $\Delta_{sol}H_2^{\infty}$ values are obtained by averaging the data on $\Delta_{sol}H_2^m$ (the halfwidth of confidence interval is given in parentheses [6]).

conformational structure of glycoluril, see scheme) becomes significant also the contribution of hydrophobic component of this process (due to existence of "nodal" methine groups in its molecule).

In experiments we used bidistilled water and a sample of *b*CA ("Automatized Technologies" company, Vologda, Russia), purified after its synthesis by washing in diethyl ether followed by recrystallization from chloroform and ethanol. Content of main substance in the preparation was (according to the Sertificate of Quality) 99.0 wt% or higher, mp 277±3°C (decomp.), pH of 10% water suspension 6.8±0.2. The $\Delta_{sol}H_2^m$ measurements were performed at 298.15± 0.005 K on an isoperibolic calorimeter (ampoule type, the vessel capacity ~60 cm^3), its constructional features have been described earlier [7]. The error in a single measurement of thermal effect was 0.2% or less.

Thus, by the method of dissolution calorimetry we measured the value of standard dissolution enthalpy of the bis-carbamide, 2,4,6,8-tetraazabicyclo[3.3.0]-octane-3,7-dione) in water at 298.15 K: $\Delta_{sol}H_2^\infty$ 26.66±0.01 kJ mol^{-1}. The fact of significant (by ~23 kJ mol^{-1}) strengthening of hydration of the studied glycoluril at its *N*-methylation.

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