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Complexes of 2-aminopyrimidine, 2-hydroxypyrimidine and their tautomers with water. Relative thermodynamic stabilities

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Abstract

Relative stabilities in two pairs of complexes of tautomers of substituted pyrimidine (2-aminopyrimidine and 2-iminopyrimidine; 2-hydroxypyrimidine and 2-oxypyrimidine) with water have been computed. Description of the isomers is based on ab initio SCF calculation, with energetics corrected by the second-order perturbation treatment. The relative stabilities are evaluated in terms of partition functions constructed from the calculated dimeric parameters. Complexes of 2-hydroxypyrimidine and 2-oxypyrimidine with water were found to coexist at higher temperatures. However, the overall heat capacity can be enhanced by about 3%, at most, by the isomeric interplay. The relation to non-equilibrium situations is discussed.

INTRODUCTION

Tautomeric systems formed by substituted heterocyclic compounds have frequently been studied with respect to their importance in organic and biological chemistry, see for example refs. 1–11. In addition to the pure species, their molecular complexes should also be taken into consideration, e.g. their complexes with water. This study deals with two tautomeric systems; 2-aminopyrimidine + 2-iminopyrimidine, and 2-hydroxypyrimidine + 2-oxypyrimidine, and studies their dimers with water.

THE DIMERS OF 2-AMINO-, 2-IMINO-, 2-HYDROXY-, AND 2-OXY-PYRIMIDINE WITH WATER

The geometry optimization was performed by abinitio SCF treatment in 6-31++G** basis set; numerical details are presented elsewhere [12, 13].

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TABLE 1

The relative MP2/6-31++G** potential energy ΔE and ground-state energy $\Delta H_0^\ominus$ terms[a] for the dimers of 2-aminopyrimidine (AP) or 2-iminopyrimidine (IP) and 2-hydroxypyrimidine (HP) or 2-oxypyrimidine (OP) with water

Dimer[b]	Symmetry	ΔE/kJ mol^{-1}	$\Delta H_0^\ominus$/kJ mol^{-1}
AP	C_1	0.0	0.0
IP	C_1	67.21	70.56
HP	C_1	0.0	0.0
OP	C_1	9.04	9.02

[a] See ref. 13 for computational details. [b] See Figs. 1 and 2.

The optimization was followed by harmonic vibrational analysis, representing also a test of the stationary-point type. The energetics were refined for the SCF optimal structures by means of the second-order perturbation treatment (Table 1).

The geometry optimization leads to one complex with water molecules for each considered species. Figure 1 presents the minimum-energy structures of the complexes of 2-aminopyrimidine (AP) and 2-iminopyrimidine (IP) with water, while Fig. 2 presents the minimum-energy structures for the complexes of 2-hydroxypyrimidine (HP) and 2-oxypyrimidine (OP). In the amino/imino system, the amino form is considerably more stable than the IP dimer with water (Table 1). In the hydroxy/oxy system, the HP and OP complexes with water are separated by less than 10 kJ mol^{-1}. It should be realized that the structures in Figs. 1 and 2 are not planar: a few atoms, at least one, are substantially distorted from the plane (for such a non-planarity, see also refs. 14 and 15).

THE RELATIVE STABILITY COMPUTATION

Let us deal with a simplified situation first, i.e. with the equilibrium two-membered isomeric mixture. Then we can avoid consideration of all the other species. The relative populations w_i of n different isomers in their equilibrium mixture can be expressed [16] in molecular terms in the form

$$w_i = \frac{q_i \exp[-\Delta H_{0,i}^\ominus/(RT)]}{\sum_{j=1}^{n} q_j \exp[-\Delta H_{0,j}^\ominus/(RT)]} \tag{1}$$

where q_i denote partition functions of the isomers and $\Delta H_{0,i}^\ominus$ their ground-state energies (potential energy terms ΔE_i are corrected for zero-point vibrations). The partition functions are constructed in the usual approach of the rigid-rotor and harmonic-oscillator approximation because

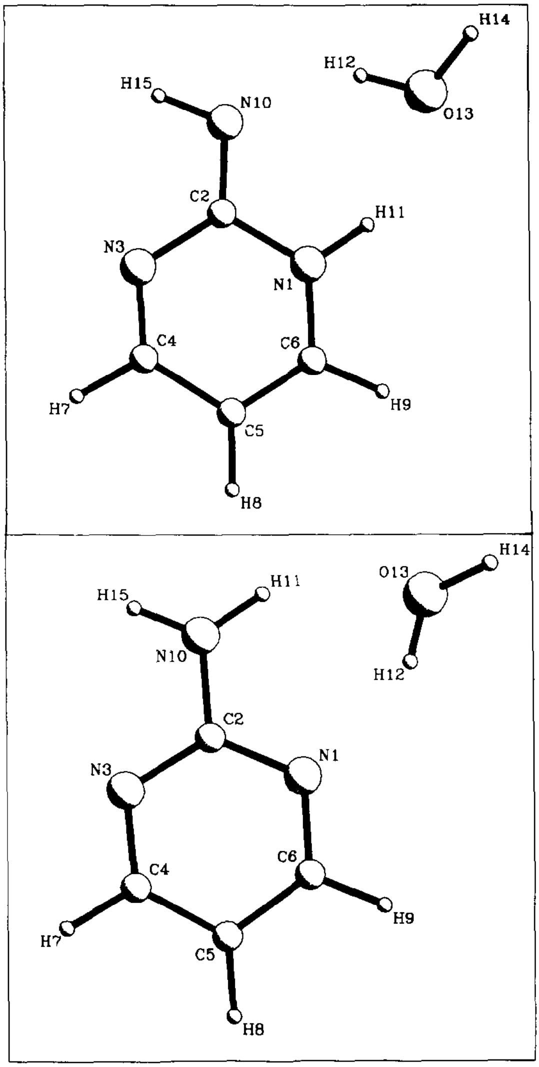

Fig. 1. Minimum energy structures of the complexes of 2-aminopyrimidine (bottom) and 2-iminopyrimidine with water.

information for a higher level description is not available from the computations.

Although all the dimeric structures exhibit C_1 symmetry (Table 1), an optical isomerism is not important for our stability computations. Because both isomers in each pair are chiral, the related chirality partition function [17] cancels out exactly.

Another approach could be considered by supposing that only dimerization, and not inter-isomeric equilibrium is reached. Then, the isomeric mole fractions would be computed from the dimerization

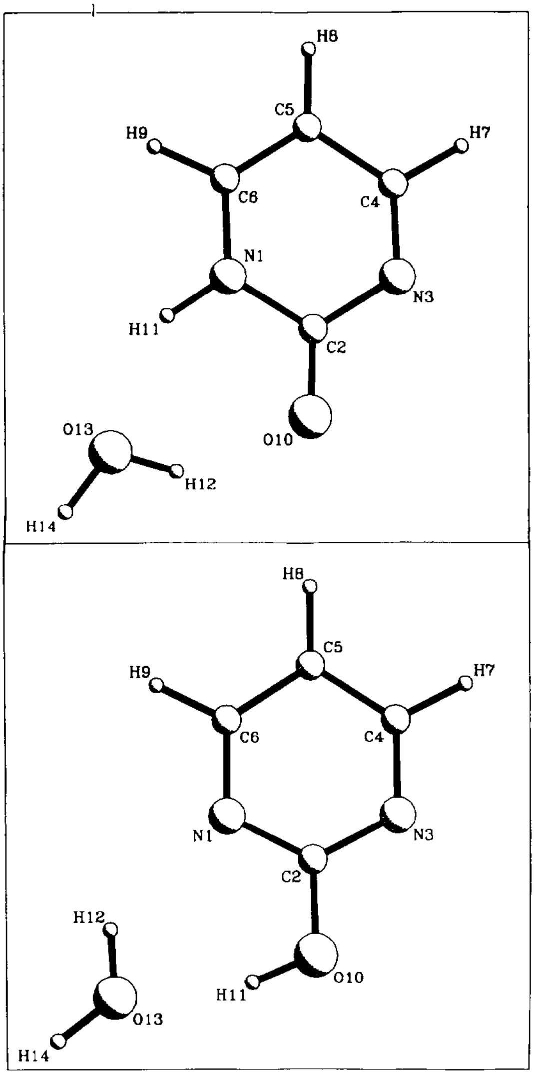

Fig. 2. Minimum energy structures of the complexes of 2-hydroxypyrimidine (bottom) and 2-oxypyrimidine with water.

equilibrium constants and the ratio between the AP and IP or HP and OP components. The ratio would be taken as a parameter from experiments and it would generally be different from its equilibrium value.

RESULTS AND DISCUSSION

Table 2 presents the temperature evolution of the weight factors w_i for both two-membered isomeric sets. In the system of AP/IP dimers, their energy separation prevents isomer coexistence. The complex of AP with water predominates throughout. The situation in the other system is

TABLE 2

The weight factors[a] w_i for the dimers of 2-aminopyrimidine (AP) or 2-iminopyrimidine (IP) and 2-hydroxypyrimidine (HP) or 2-oxypyrimidine (OP) with water at selected temperatures T

T/K	w_i (%)		w_i (%)	
	AP	IP	HP	OP
100	100.0	1×10^{-35}	100.0	2×10^{-3}
200	100.0	2×10^{-17}	99.40	0.60
250	100.0	9×10^{-14}	98.16	1.84
300	100.0	2×10^{-11}	96.19	3.82
350	100.0	1×10^{-9}	93.65	6.36
400	100.0	2×10^{-8}	90.78	9.22
500	100.0	1×10^{-6}	84.86	15.14
750	100.0	3×10^{-4}	72.71	27.29
1000	100.0	5×10^{-3}	64.94	25.06

[a] Two different two-isomer equilibria: $w_{AP} + w_{IP} = 100\%$ and $w_{HP} + w_{OP} = 100\%$.

different. In the low-temperature region, the HP–water dimer is, of course, much more populated than the other isomer. However, at higher temperatures, the stabilities of both structures become closer. In a high-temperature limit, the ratio of both dimers is roughly 2:1.

The presence of two isomeric forms should be apparent [16] from the overall values of the thermodynamic terms, as compared to the partial values. The heat capacity term is known to be substantially influenced by the isomeric interplay. Table 3 gives this quantity in the HO/IP system. The isomerism contribution to the heat capacity exhibits the usual temperature maximum, although its height amounts to a modest value of

TABLE 3

Specification of two distinguished points[a] in the isomeric enhancement of the heat capacity of the equilibrium mixture of the dimers of 2-hydroxypyrimidine and 2-oxypyrimidine with water

Type[a]	T/K	$\delta C_{p,1}$[b]/J K^{-1} mol^{-1}	$(\delta C_{p,1}/C_p^\ominus)$/%
$\delta C_{p,1}$ maximum	428	5.57	3.37
$\frac{\delta C_{p,1}}{C_p^\ominus}$ maximum	357	5.23	3.59

[a] Maximum in the isomerism contribution to heat capacity $\delta C_{p,1}$, or maximum in the relative enhancement $\delta C_{p,1}/C_p^\ominus$ of the $C_p^\ominus$ term. [b] Isomerism contribution to the heat capacity related to the species more stable in the low-temperature region, i.e. to the 2-hydroxypyrimidine–water complex.

$5.6\,J\,K^{-1}\,mol^{-1}$. The highest relative isomeric enhancement reaches only about 3.6%.

Let us suppose that the dimerization equilibrium is obtained but the ratio of the monomeric units, AP/IP or HP/OP, possesses a generally non-equilibrium value m. Let us denote the dimerization equilibrium constant for the first and second dimer $K_{d,1}$ and $K_{d,2}$, respectively. These equilibrium constants could readily be evaluated using the quantum-chemical data. Then, a more general relation describes the ratio of the isomeric populations

$$\frac{w_1}{w_2} = \frac{K_{d,1}}{K_{d,2}} m \qquad (2)$$

If the m ratio is the equilibrium monomeric ratio, the values from eqn. (2) are identical with those of Table 2. Otherwise, one could carry out an m-parametric study, producing a whole set of isomeric populations for all relevant non-equilibrium m values. Such a treatment would be required if equilibrium between tautomeric monomers could not be established.

There are several improvements to be considered. The treatment should be refined by including anharmonicity effects. The relative energetics can still be improved by higher-order contributions. The computation deals with a gas-phase situation, not with a solution, but one can expect a cancellation in eqn. (1) concerning possible solvent effects. However, it should be realized that for the systems of the studied dimensions one cannot expect such corrections to be available in a short time period.

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