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Complexes of 4-aminopyrimidine and 4-hydroxypyrimidine with water: computed relative thermodynamic stabilities

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Abstract

Relative thermodynamic stabilities in two series of isomeric complexes of substituted pyrimidine (4-aminopyrimidine; 4-hydroxypyrimidine, 4-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. In each of the sets several relative stability interchanges are found. The interchanges are manifested in a considerable heat capacity term enhancement.

INTRODUCTION

Recently, we reported computational results on relative thermodynamic stabilities of complexes of 2-aminopyrimidine, 2-hydroxypyrimidine and their tautomers with water [1]. Such studies are important for a deeper understanding of behavior of tautomeric systems formed by substituted heterocyclic compounds, i.e. species frequently treated with respect to their importance in organic and biological chemistry, see for example refs. 2–14. The present study continues in the effort [1] and deals with the water complexes for two other systems: 4-aminopyrimidine, and 4-hydroxypyrimidine or 4-oxypyrimidine.

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THE DIMERS OF 4-AMINO-, 4-HYDROXY- AND 4-OXY-PYRIMIDINE WITH WATER

Our computational study is based on a quantum chemical description of the species [15]. The geometry optimization was performed by ab initio SCF treatment in 6-31 + + G** basis set and for numerical details we refer to ref. 15. The optimizations were followed by harmonic vibrational analysis, representing also a test of the stationary-point type. Energetics were further refined for the SCF optimal structures by means of the second order perturbation treatment (Table 1).

As can be expected in view of our previous studies [1, 11, 12], the geometry optimizations reveal more than one minimum structure for the complexes with water. Figure 1 presents the minimum-energy structures of the complexes for 4-aminopyrimidine (AP). The complexes differ in the positions of the water molecule and can be denoted with respect to the ring atom which is approached by the water molecule (APN3, APN1, APC4). As can be seen in Table 1 the structure APN3 represents the ground state of the system, and this is followed by the APN1 and APC4 structures. Figure 2 depicts five minimum energy complexes found for 4-hydroxypyrimidine (HP) and 4-oxypyrimidine (OP). The separation energy between the ground state structure OPO10 and the other low energy species HPN3 is quite small. Three further structures follow in the order HPN1, OPN1, HPC4. According to the optimizations [15], all the structures are distorted from planarity so that they exhibit C_1 symmetry.

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 4-aminopyrimidine (AP), 4-hydroxypyrimidine (HP) and 4-oxypyrimidine (OP) with water

Dimer [b]	Symmetry	ΔE/kJ mol^{-1}	$\Delta H_0^\ominus$/kJ mol^{-1}
APN3	C_1	0.0	0.0
APN1	C_1	9.97	7.75
APC4	C_1	13.53	9.82
OPO10	C_1	0.0	0.0
HPN3	C_1	1.49	1.35
HPN1	C_1	18.16	15.69
OPN1	C_1	20.50	18.67
HPC4	C_1	24.88	20.98

[a] See ref. 15 for computational details.

[b] See Figs. 1 and 2; the code following the first two letters denotes the ring atom closest to the water water molecule.

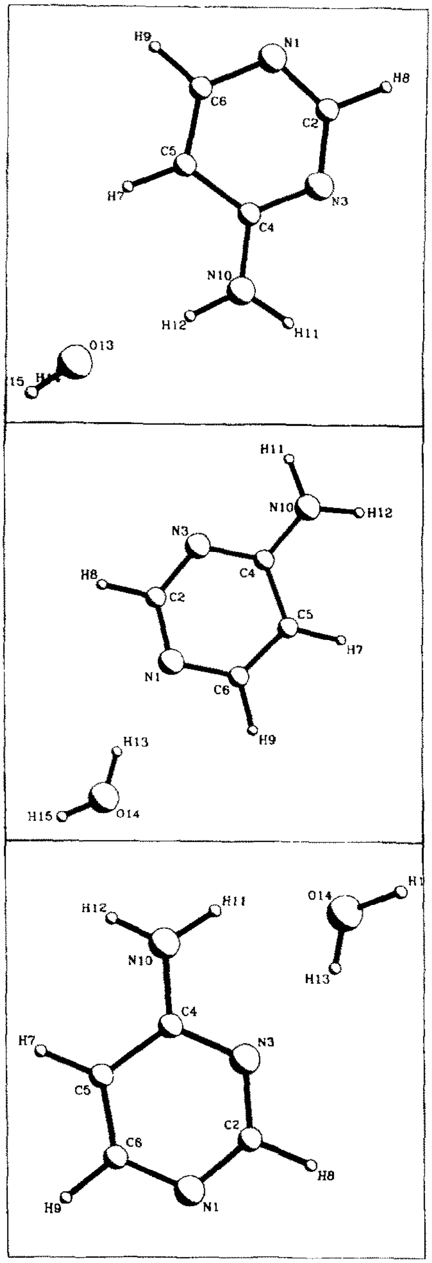

Fig. 1. Minimum energy structures of the complexes of 4-aminopyrimidine with water; from the top they are APC4, APN1 and APN3.

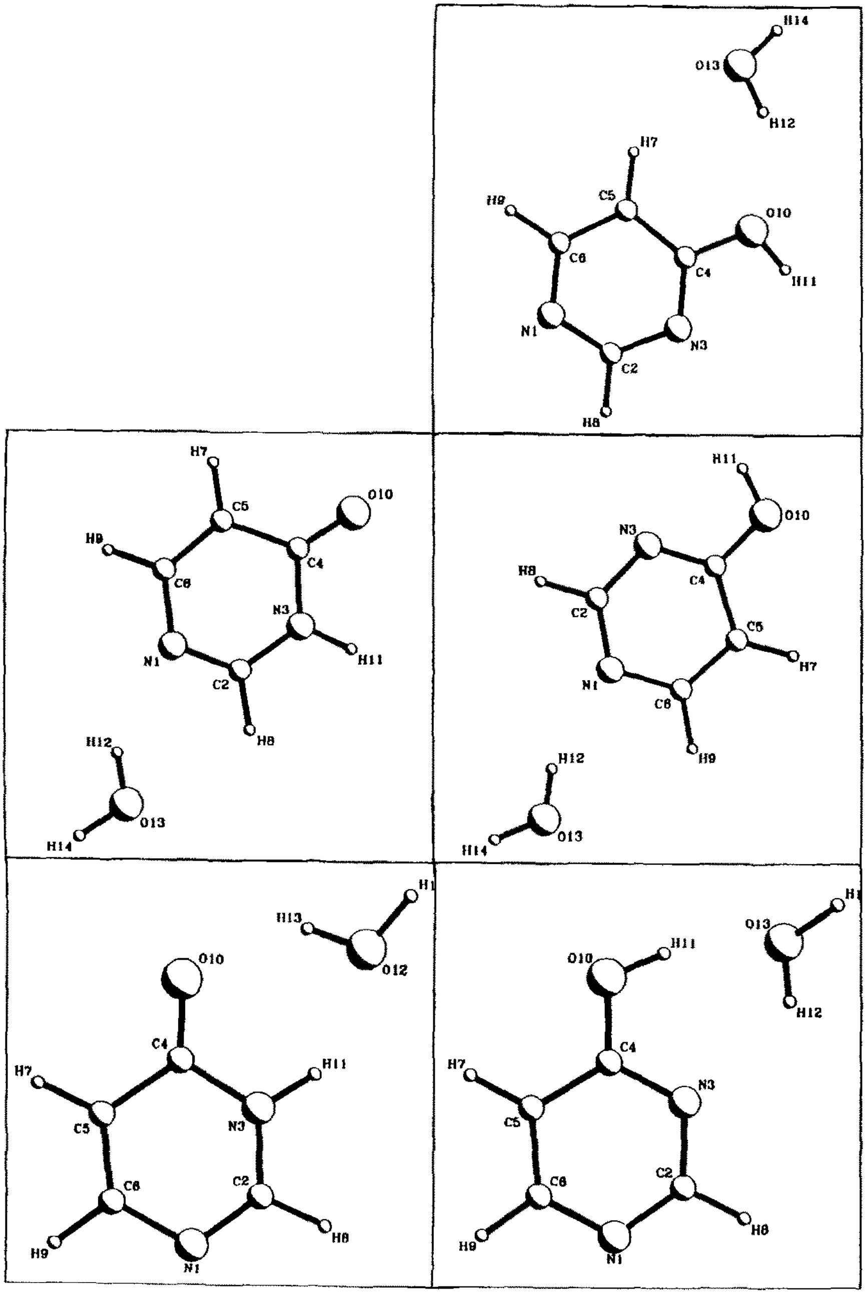

Fig. 2. Minimum energy structures of the complexes of 4-oxypyrimidine (left) and 4-hydroxypyrimidine (right) with water; from the top they are OPN1, OPN10 and HPC4, HPN1, HPN3.

THE RELATIVE STABILITY COMPUTATION

We shall deal with two different equilibrium mixtures, the three membered system of the AP complexes and the five membered system of HP/OP complexes. Relative stabilities of n different isomers can be treated in terms of the equilibrium mole fractions w_i, which are, in molecular terms, expressed [16] in the following form:

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

where q_i denotes partition functions of the isomers and $\Delta H^{\ominus}_{0,i}$ their ground-state energies (potential energy terms ΔE_i corrected for zero-point vibrations). The partition functions are constructed in the usual approach of the rigid-rotor and harmonic-oscillator approximation as 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. As all isomers in each set are chiral, the related chirality contribution to the partition functions cancels out exactly. Similarly, we do not scale the computed vibrational frequencies as the factors can cancel out in eqn. (1), especially so at higher temperatures.

RESULTS AND DISCUSSION

Table 2 presents the computed temperature dependencies of the equilibrium mole fractions for the APN3, APN1 and APC4 structures. The ground state structure APN$_3$ must be the most populated isomer in the low temperature region. However, already at room temperature the relative stabilities of the three complexes become quite close. In a very narrow temperature interval we can observe three relative stability interchanges. First, at about 343 K, APN1 and APC4 structures reach their equimolarity. Then, at 345 K, APN3 and APC4 exhibit the same concentrations. Finally, at 346 K the equimolarity exists for the APN3 and APN1 structures. It is indeed a unique coincidence. The computations indicate that around room temperature one should expect all three species in comparable concentrations.

The results for the five-membered system of HP/OP complexes are reported in Table 3. Although we present five relative stability interchanges in the temperature interval studied, some of them happen at temperatures too high to be of experimental significance. At room temperature the equilibrium mixture should consists of two major components OPO10 and HPN3, though the ground state structure is still the prevailing component.

Interchanges of relative stabilities of isomers in their equilibrium mixture

TABLE 2

The weight factors[a] w_i for the dimers of 4-aminopyrimidine (AP) with water at selected temperatures T

T/K	$w_{\mathrm{APN3}}/\%$	$w_{\mathrm{APN1}}/\%$	$w_{\mathrm{APC4}}/\%$
100	99.9	5×10^{-2}	5×10^{-3}
200	87.5	8.5	4.0
250	67.5	19.6	13.0
298.15	47.8	28.3	23.9
300	47.1	28.6	24.3
343[b]	34.0	33.0	33.0
345[b]	33.4	33.2	33.4
346[b]	33.2	33.2	33.6
350	32.3	33.5	34.2
400	22.8	35.4	41.8
500	12.9	35.6	51.5
750	5.4	32.4	62.2
1000	3.3	30.0	66.7

[a] $w_{\mathrm{APN3}} + w_{\mathrm{APN1}} + w_{\mathrm{APC4}} = 100\%$; see Table 1 for the structure coding. [b] Point of two-isomer equimolarity.

TABLE 3

The weight factors[a] w_i for the dimers of 4-hydroxypyrimidine (HP) and 4-oxypyrimidine (OP) with water at selected temperatures T

T/K	$w_{\mathrm{OPO10}}/\%$	$w_{\mathrm{HPN3}}/\%$	$w_{\mathrm{HPN1}}/\%$	$w_{\mathrm{OPN1}}/\%$	$w_{\mathrm{HPC4}}/\%$
100	86.2	13.8	3×10^{-6}	4×10^{-8}	5×10^{-9}
200	77.0	23.0	5×10^{-2}	4×10^{-3}	3×10^{-3}
250	74.6	24.9	0.4	4×10^{-2}	4×10^{-2}
267[b]	73.8	25.4	0.6	7×10^{-2}	7×10^{-2}
298.15	72.3	26.0	1.3	0.2	0.2
300	72.2	26.0	1.4	0.2	0.2
350	69.1	26.1	3.5	0.6	0.8
400	64.7	25.4	6.8	1.2	2.0
500	52.7	21.9	15.5	3.3	6.6
547[b]	46.6	19.7	19.7	4.5	9.6
704[b]	29.7	13.2	29.7	7.7	19.8
750	26.0	11.7	31.4	8.4	22.5
779[b]	24.0	10.9	32.3	8.8	24.0
839[b]	20.6	9.4	33.6	9.4	27.0
1000	14.2	6.7	35.4	10.5	33.2

[a] $w_{\mathrm{OPO10}} + w_{\mathrm{HPN3}} + w_{\mathrm{HPN1}} + w_{\mathrm{OPN1}} + w_{\mathrm{HPC4}} = 100\%$; see Table 1 for the structure coding. [b] Point of two-isomer equimolarity.

TABLE 4

Specification of distinguished points[a] in isomeric enhancement of the heat capacity of the equilibrium mixture of the dimers of 4-aminopyrimidine (AP) with water and the mixture of the dimers 4-hydroxypyrimidine or 4-oxypyrimidine (HP/OP) with water

Type[a]	T/K	$\delta C_{p,1}$[b]/J K^{-1} mol^{-1}	$\frac{\delta C_{p,1}}{C_p^\ominus} / \%$
AP–water			
$\delta C_{p,1}$ maximum	256	48.1	28.8
$\frac{\delta C_{p,1}}{C_p^\ominus}$ maximum	242	47.2	29.2
HP/OP–water			
$\delta C_{p,1}$ maximum	55	2.7	4.9
$\delta C_{p,1}$ maximum	536	35.9	16.3
$\frac{\delta C_{p,1}}{C_p^\ominus}$ maximum	50	2.6	5.0
$\frac{\delta C_{p,1}}{C_p^\ominus}$ maximum	502	35.2	16.6

[a] Maximum in the isomerism contribution to the 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 heat capacity related to the species most stable in the low temperature region, i.e. to the ground-state structure; see Tables 2 and 3.

have interesting consequences for the heat capacity term, namely its enhancement [16]. Table 4 studies this effect in both systems. The isomerism contribution to heat capacity exhibits the usual temperature maximum and in the HP/OP case there are two such maxima. In both systems the isomerism contribution to heat capacity can reach the quite high values of 48 and 35 J K^{-1} mol^{-1}. The highest relative isomeric enhancements also reaches substantial values of about 29 and 16%.

With respect to system dimensionality there are various approximative steps included. The treatment should be refined by an estimation of anharmonicity effects. The relative energetics could still be refined by higher-order contributions. The computations treat gas-phase conditions, not a solution, but one can expect a cancellation in eqn. (1) concerning possible solvent effects. Anyhow, it should be realized that, for such large systems, the corrections are unlikely to be available for some time.

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