Enthalpies of Formation of DNA and RNA Nucleobases from G3X Theory

Olga V. Dorofeeva*,† **and Natalja Vogt**

Chemieinformationssysteme, Universität Ulm, 89069 Ulm, Germany

The Gaussian-3X (G3X) method has been used to calculate accurate values of the gas-phase enthalpies of formation of all five DNA and RNA nucleobases: thymine, adenine, cytosine, guanine, and uracil, whose experimental gas-phase study is a difficult problem because of the low vapor pressures. Only for uracil, the published experimental value agrees well with the theoretical one. However, the revision of available experimental data on enthalpies of formation for compounds in the solid phase and enthalpies of sublimation allowed us to recommend a set of self-consistent thermochemical data for thymine, adenine, and cytosine, which lead to good agreement between experimental and theoretical gas-phase enthalpies of formation. To obtain more reliable values of enthalpy of sublimation at 298.15 K, the heat capacity values of gaseous compounds were calculated by standard statistical thermodynamics formulas using molecular parameters determined from B3LYP/6-31G(2df,p) calculations. The following values are recommended based on G3X calculations and a revision of published experimental data: $\Delta_f H^\circ_{298}$(uracil, g, 298.15 K) = (−301.5 ± 2.5) kJ·mol^{-1}, $\Delta_f H^\circ_{298}$(thymine, g, 298.15 K) = (−338.0 ± 2.5) kJ·mol^{-1}, $\Delta_f H^\circ_{298}$(cytosine, g, 298.15 K) = (−69.5 ± 3.5) kJ·mol^{-1}, and $\Delta_f H^\circ_{298}$(adenine, g, 298.15 K) = (225.7 ± 3.5) kJ·mol^{-1}. Because of a lack of reliable experimental data for guanine, the theoretical G3X value is recommended for this compound: $\Delta_f H^\circ_{298}$(guanine, g, 298.15 K) = (16.0 ± 5.0) kJ·mol^{-1}.

Introduction

It is a fundamental task to study the thermochemical properties of nucleic acid bases to understand their behavior in various biochemical processes. This paper deals with the study of five DNA and RNA nucleobases (thymine, adenine, cytosine, guanine, and uracil) by theoretical determination of the gas-phase formation enthalpy. These calculations allow us to check the reliability of not only the enthalpy of formation of the compound in the gaseous phase, $\Delta_f H^\circ_{298}$(g), but also the enthalpy of formation in the solid state, $\Delta_f H^\circ_{298}$(cr), and the enthalpy of sublimation, $\Delta_{cr}^{g} H_{298}$, used to determine the $\Delta_f H^\circ_{298}$(g) values. Besides, the values of the enthalpy of sublimation together with the enthalpy of solution allow the determination of the enthalpy corresponding to the transfer of the solute molecules from the gas state to solution (solvation enthalpy), which is important to investigate the behavior of DNA and RNA nucleobases in solution.

Over the past decade, with the improvements in both hardware performance and the development of new theoretical methods such as Gaussian-3 theory, the accurate thermochemical predictions became available even for large molecules.[1] For the 222 enthalpies of formation of small and moderate sized molecules with 2 to 10 non-hydrogen atoms, one of the latest versions, Gaussian-3X (G3X) theory, achieves the so-called thermochemical accuracy of about 4 kJ·mol^{-1}.[2] In this study, the G3X method has been used to calculate the accurate values of the gas-phase enthalpies of formation of thymine, adenine, cytosine, guanine, and uracil—molecules with 8 to 11 non-hydrogen atoms.

Although the enthalpies of formation and sublimation were determined for these compounds, there is a substantial disagreement in the measured values. These compounds are solids with high melting points (above 300 °C) and low vapor pressures, and consequently, they are elusive to gas-phase studies. One way of tackling the problem is to address it theoretically. Recently, we have calculated the enthalpies of formation of gaseous urea ($H_2N-CO-NH_2$) and two amino acids, glycine (H_2N-CH_2-COOH) and L-alanine ($H_2N-CH(CH_3)-COOH$) by the G3X method.[3] For urea and glycine, the calculated values were in good agreement with the experimental ones, whereas a large discrepancy was observed for L-alanine. One experimental value for L-alanine was 13 kJ·mol^{-1} more positive than the G3X value, and another was 38 kJ·mol^{-1} more negative. It was shown that in the former case the difference resulted from the incorrect value of enthalpy of formation in the solid state, and in the latter case the difference was determined by inaccurate adjustment of enthalpy of sublimation to the reference temperature. Thus, based on theoretical enthalpy of formation of gaseous L-alanine, we could recommend the reliable values of enthalpy of formation in the solid state and enthalpy of sublimation for this compound. In this work, the same procedure was applied to other species of biochemical interest.

Experimental Data

The enthalpy of formation of the compound in the gaseous phase can be obtained experimentally from the enthalpy of formation in the solid state and the enthalpy of sublimation

$$\Delta_f H^\circ_{298}(\mathrm{g}) = \Delta_f H^\circ_{298}(\mathrm{cr}) + \Delta_{cr}^{g} H_{298} \tag{1}$$

For all five compounds, the $\Delta_f H^\circ_{298}$(cr) and $\Delta_{cr}^{g} H_T$ values were measured experimentally by different authors (see Table 1) and,

---

* To whom correspondence should be addressed. E-mail: dorofeeva@phys.chem.msu.ru. Phone: +7(495)9394021. Fax: +7(495)9391308.

† Current address: Department of Chemistry, Moscow State University, Moscow 119991, Russia.

10.1021/je800977n CCC: $40.75

Table 1. Enthalpies of Formation ($\Delta_f H°$) and Heat Capacities (C_p°) in Both Crystalline and Gaseous Phases and Enthalpies of Sublimation ($\Delta_{cr}^{g}H$) of Uracil, Thymine, Cytosine, Adenine, and Guanine from Experiment and Theory[a]

$\Delta_f H°$(cr, 298.15 K)	$\Delta_{cr}^{g}H(T_{av})$	C_p°(cr, 298.15 K)	C_p°(g, 298.15 K)	$\Delta_{cr}^{g}H$(298.15 K)	$\Delta_f H°$(g, 298.15 K), kJ·mol^{-1}			
kJ·mol^{-1}	kJ·mol^{-1}	J·K^{-1}·mol^{-1}	J·K^{-1}·mol^{-1}	kJ·mol^{-1}	exptl	calcd (G3X) this work	Δ[b]	ref
Uracil, $C_4H_4N_2O$								
−429.6 ± 0.6	122.9 (440 K)	119.6		126.5± 2.2	−303.1 ± 2.3	−303.6	0.5	4
		120.5						5
−424.4 ± 2.5								6
−429.4 ± 0.8				126.5	−302.9 ± 2.3		0.7	7
	120.5 ± 5.2 (426 K)							8
	121.7 (425 K)							9
	130.6 ± 4.0 (520 K)			131.0± 5.0				10
	120.5 ± 1.3 (403 K)							11
	127.0 ± 2.0 (439 K)			128.0± 2.0				12
	129.4 ± 4.0 (405 K)			130.8				13
				130.8± 1.4				14
	125.3 ± 0.2 (425 K)							15
−429.6 ± 0.6[c]	125.0 (422 K)[d]	131.8[e]	107.2 ± 2.0	128.1	−301.5 ± 2.5		2.1	this work
Thymine, $C_5H_6N_2O_2$								
−462.8 ± 1.1	120.7 (440 K)	153.6		134.1± 4.2	−328.7 ± 4.3	−342.5	13.8	4
		151.4						17
−462.8 ± 0.8				134.1	−328.7 ± 4.2		13.8	7
				138.0±10.0				18
	124.4 ± 1.3 (403 K)							9, 11
	125.7 ± 3.6 (411 K)			131.3± 4.0				19
	135.8 ± 0.4 (330 K)							15
−462.8 ± 1.1[c]	122.6 (422 K)[f]	150.2[g]	132.2 ± 2.0	124.8	−338.0 ± 2.5		4.5	this work
Cytosine, $C_4H_5N_3O$								
−235.4 ± 0.9	149.9 (458 K)			176.0±10.0	−59.4 ± 10.0	−71.5	12.1	21
−221.3 ± 2.3								6
−221.3 ± 2.0				176.0	−45.3 ± 10.0		26.2	7
	150.6							8, 9
				167.0±10.0				19
	147.2 ± 2.6 (453 K)			155.0± 3.0				20
	151.7 ± 0.7 (515 K)							22
	167.7 ± 0.5 (365 K)							15
−221.3 ± 2.3[h]	149.6 (475 K)[i]	132.6[j]	120.4 ± 2.0	151.8	−69.5 ± 3.5		2.0	this work
Adenine, $C_5H_5N_5$								
91.0								24
		143.1						25
96.0 ± 0.9								24, 26
		147.0						27
96.9 ± 1.3								28
96.9 ± 1.2				108.8	205.7 ± 8.5	225.3	−19.6	7
	108.7 ± 8.0							29, 26, 30
	126.4							8, 9
	127.2 ± 1.9 (420 K)							31
	140.4 (420 K)							32
	130.0 ± 2.0 (330 K)							15
96.9 ± 1.3[k]	127.2 ± 1.9 (420 K)[l]	142.7[m]	129.9 ± 4.0	128.8	225.7 ± 3.5		0.4	this work
Guanine, $C_5H_5N_5O$								
−188.7								24
		156.9						25
−183.8 ± 0.9								24, 26
		160.7						34
	186.2							8, 9
	168.3 ± 0.6 (365 K)							15
			150.8 ± 4.0			16.0		this work

[a] Uncertainties for experimental data are those given by the authors of the original works. [b] Difference between experimental and calculated values. [c] Ref 4. [d] For $\Delta_{cr}^{g}H$(422 K), the average value from refs 4 and 11−13 is recommended. [e] Ref 16. [f] For $\Delta_{cr}^{g}H_m$(422 K), the average value from refs 4 and 11 is recommended. [g] Ref 20. [h] Ref 6. [i] For $\Delta_{cr}^{g}H_m$(475 K), the average value from refs 20−22 is recommended. [j] Ref 23. [k] Ref 28. [l] Ref 30. [m] Ref 33.

as is seen from Table 1, there is an appreciable difference in the results of these measurements, especially for the enthalpy of sublimation (up to 20 kJ·mol^{-1}). Because of this, it is difficult to obtain the unambiguous $\Delta_f H_{298}^{\circ}$(g) values for these species. The goal of this work is to recommend the reliable $\Delta_f H_{298}^{\circ}$(g) values based on the results of theoretical calculations and analysis of experimental $\Delta_f H_{298}^{\circ}$(cr) and $\Delta_{cr}^{g}H_T$ values available in the literature.

The accuracy of the experimental $\Delta_f H_{298}^{\circ}$(g) values is often devaluated by the approximate adjustment of the enthalpy of sublimation to 298.15 K. If the heat capacities of the solid and gas phase, $C_{p,298}^{\circ}$(cr) and $C_{p,298}^{\circ}$(g), are known, the enthalpies of sublimation measured at high temperatures can be adjusted to $T = 298.15$ K according to the equation

$$\Delta_{cr}^{g}H_{298} \approx \Delta_{cr}^{g}H_T + [C_{p,298}^{\circ}(\mathrm{cr}) - C_{p,298}^{\circ}(\mathrm{g})](T - 298.15) \quad (2)$$

If the $C_{p,298}^{\circ}$(g) values are unknown, the empirical corrections are often used to adjust the enthalpy of sublimation to 298.15

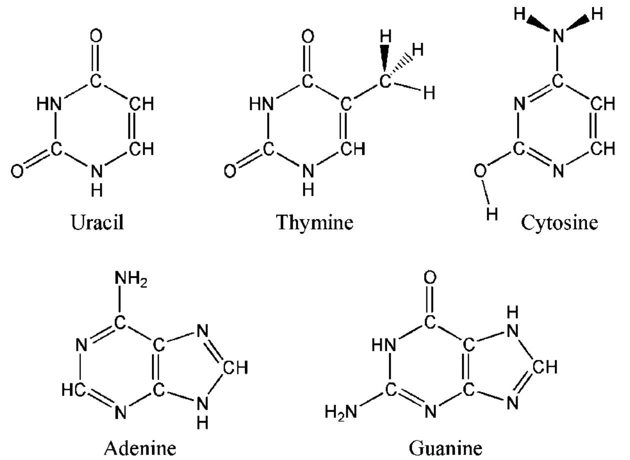


Figure 1. Structure of the most stable gas-phase tautomers of DNA and RNA nucleobases.

K.[30] In this work, the $C^{\circ}_{p,298}$(g) values were determined by quantum-chemical calculations that let us improve the $\Delta^{g}_{cr}H_{298}$ values in a number of cases.

Theoretical Calculations

The enthalpies of formation of uracil, thymine, cytosine, adenine, and guanine in the gaseous phase were calculated from the G3X energies using the atomization energy method.[35] This method involves the use of experimental enthalpies of formation of gaseous atoms at 0 K and thermal corrections for elements in their standard states; the corresponding values were taken from ref 36. All quantum-chemical calculations were performed with the Gaussian 03 suite of programs.[37] The G3X energy calculations were performed for the most stable conformers shown in Figure 1. Cytosine and guanine exist in various low-energy tautomeric forms. A correction for the mixture of these forms to the enthalpy of formation was estimated from the conformational energy differences obtained from CCSD(T)/aug-cc-pVDZ calculations.[38,39] Its value is equal to 1.3 kJ·mol^{-1} for cytosine and 1.4 kJ·mol^{-1} for guanine.

It is known that direct calculation of enthalpies of formation from quantum chemical atomization energies is often the subject of systematic errors arising from insufficient treatment of electron correlation and incompleteness of the basis sets. Application of G2 theory to larger molecules indicated a tendency for accumulation of these errors, whereas the moderate level of theory combined with isodesmic bond reaction energies yielded more accurate thermochemistry for larger molecules.[40,41] However, more recently it was shown that the accumulation of errors has been markedly reduced in the G3 theory.[42] Thus, one would expect that the uncertainty of $\Delta_f H^{\circ}_{298}$(g) values calculated in this work does not far exceed that observed for the enthalpies of formation of molecules with 2 to 10 non-hydrogen atoms.[2]

The systematic errors can be significantly reduced by using the isodesmic reactions,[43] in which the number of bonds of each type is conserved on both sides of the reaction. An isodesmic reaction leads to more accurate results if the enthalpies of formation of reference compounds are determined with high accuracy and if it is possible to chose the reaction with good group balance, where the next nearest neighbor interactions are also conserved. In this work, the method of isodesmic reactions was used to check the reliability of the G3X enthalpy formation of thymine since only for this molecule it is possible to chose a well-balanced reaction. The electronic energies for all species in this reaction were calculated at the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G(d,p) level. These energies corrected by the B3LYP/6-31G(d,p) zero-point energies, and the changes in enthalpy from (0 to 298) K were used to calculate the enthalpy of formation from isodesmic reactions.

The heat capacities of gaseous species were calculated using a rigid-rotor harmonic-oscillator model and geometrical parameters and vibrational frequencies (scaled by 0.9854) of the B3LYP/6-31G(2df,p) optimized structures. The calculated $C^{\circ}_{p,298}$(g) values are (107.2, 132.2, 120.4, 129.8, and 150.8) J·K^{-1}·mol^{-1} for uracil, thymine, cytosine, adenine, and guanine, respectively. The uncertainty of calculated values is estimated to be 2 J·K^{-1}·mol^{-1} for uracil, thymine, and adenine and 4 J·K^{-1}·mol^{-1} for cytosine and guanine. Note that such accuracy is quite sufficient for reliable estimation of $\Delta^{g}_{cr}H_{298}$ values by eq 2 since it introduces the error of (0.3 to 0.6) kJ·mol^{-1} into the enthalpy of sublimation value.

Results and Discussion

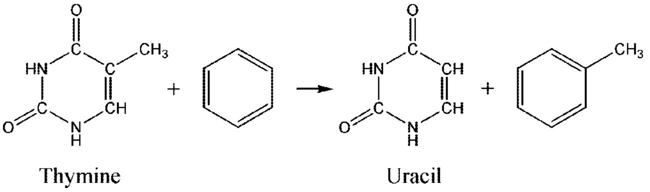
Available from the literature, experimental $\Delta_f H^{\circ}$(cr, 298.15 K), $\Delta^{g}_{cr}H$, C°_{p}(cr, 298.15 K), and $\Delta_f H^{\circ}$(g, 298.15 K) values are compiled in Table 1 together with $\Delta_f H^{\circ}$(g, 298.15 K) and C°_{p}(g, 298.15 K) values obtained in this work from theoretical calculations. Only for uracil the calculated enthalpy of formation agrees well with the experimental one. However, as seen from Table 1, for all compounds there is a substantial discrepancy in the experimental values of $\Delta^{g}_{cr}H$, which is why the different values of $\Delta_f H^{\circ}$(g, 298.15 K) may be obtained from data listed in Table 1. In this work from analysis of experimental data given in Table 1, those $\Delta_f H^{\circ}$(cr, 298.15 K) and $\Delta^{g}_{cr}H(T_{av})$ values were chosen, which lead to good agreement between experimental and calculated $\Delta_f H^{\circ}$(g, 298.15 K) values. These recommended data are given in Table 1 with reference "this work". On the basis of these experimental values of $\Delta_f H^{\circ}$(cr, 298.15 K) and $\Delta^{g}_{cr}H(T_{av})$, new experimental $\Delta_f H^{\circ}$(g, 298.15 K) values were determined in this work. The necessary $\Delta^{g}_{cr}H_{298}$ values were calculated from eq 2 using recommended values of $\Delta^{g}_{cr}H(T_{av})$ and available experimental values of $C^{\circ}_{p,298}$(cr) and $C^{\circ}_{p,298}$(g) values calculated in this work.

Uracil. For uracil, the $\Delta_f H^{\circ}_{298}$(g) value calculated by the G3X method is in excellent agreement with that determined by Nabavian et al.[4] from experimental measurements and recommended in the reference book by Pedley.[7] Another experimental $\Delta_f H^{\circ}_{298}$(cr) value,[6] as well as the $\Delta^{g}_{cr}H_{T}$ values of about 130 kJ·mol^{-1},[10,13] lead to worse agreement between experimental and calculated values. The value of $\Delta_f H^{\circ}_{298}(\text{cr}) = -424.4$ kJ·mol^{-1}[6] yields a good agreement with the G3X enthalpy of formation only for $\Delta^{g}_{cr}H_{T}$ values below 122 kJ·mol^{-1}. The value of enthalpy of formation of gaseous uracil recommended in Table 1 is based on the experimental enthalpy of formation of solid uracil[4] and enthalpy of sublimation at 422 K, which is the mean of values in refs 4 and 11 to 13. The $\Delta^{g}_{cr}H_{298}$ value is determined from eq 2 using experimental heat capacity of solid uracil[16] and the $C^{\circ}_{p,298}$(g) value calculated in this work. Note that disagreement between experimental and calculated $\Delta_f H^{\circ}_{298}$(g) values falls to 0.7 kJ·mol^{-1}, if the value of $C^{\circ}_{p,298}(\text{cr}) = 120.5$ J·K^{-1}·mol^{-1}[15] is used in the adjustment of enthalpy of sublimation to 298.15 K.

Thymine. For thymine, the theoretical $\Delta_f H^{\circ}_{298}$(g) value is 13.8 kJ·mol^{-1} more negative than the experimental one.[4,7] It should be noted that the difference between enthalpy of sublimation at 440 K (120.7 kJ·mol^{-1}) and 298.15 K (134.1 kJ·mol^{-1}) obtained by Nabavian et al.[4] is too large. It corresponds to the value of $C^{\circ}_{p,298}(\text{g}) \approx 60$ kJ·mol^{-1} if eq 2 is used to adjust the enthalpy of sublimation to 298.15 K. As is seen, this value is nearly twice as large as that obtained by theoretical calculation. The readjustment of the enthalpy of sublimation[4] to 298.15 K using eq 2 and the $C^\circ_{p,298}$(g) value calculated in this work leads to much better agreement between experiment and theory.

The value of enthalpy of formation of gaseous thymine recommended in Table 1 is based on the experimental enthalpy of formation of solid compound[4] and the enthalpy of sublimation at 422 K, which is the mean of values in refs 4 and 11. The $\Delta^{\mathrm{g}}_{\mathrm{cr}}H_{298}$ value is obtained from eq 2 using experimental heat capacity of solid thymine[20] and the $C^\circ_{p,298}$(g) value calculated in this work.

As noted above, the method of isodesmic reactions gives reliable estimations of $\Delta_{\mathrm{f}}H^\circ_{298}$(g) values if it is possible to choose the reaction with structurally close species on both sides of the reaction and if the accurate enthalpy of formation values are determined experimentally for all reference compounds occurring in the reaction. Of all the compounds considered in this work, only for thymine the appropriate reaction may be designated. Thus the enthalpy of formation of thymine has been also calculated by the method of isodesmic reactions using the following reaction



This reaction has good group balance (the enthalpy of reaction, $\Delta_{\mathrm{r}}H^\circ_{298}$, is 4.1 kJ·mol^{-1}), and the enthalpies of formation of reference compounds are determined experimentally with high accuracy. Therefore, one might expect a reliable value of the enthalpy of formation of thymine calculated from this reaction. This calculation was used not only to check the reliability of the G3X result but also to provide a double-check on the reasonableness of the recommended $\Delta_{\mathrm{f}}H^\circ_{298}$(g) value for thymine. The calculated value of $\Delta_{\mathrm{f}}H^\circ_{298}$(thymine, g, 298.15 K) = −339.1 kJ·mol^{-1} is in excellent agreement with that recommended in Table 1 [(−338.0 ± 2.5) kJ·mol^{-1}] and agrees within its uncertainty with the G3X value (−342.5 kJ·mol^{-1}). Thus, the results for uracil and thymine suggest a high accuracy of the G3X calculations for the remaining three compounds.

Cytosine. For cytosine, the $\Delta_{\mathrm{f}}H^\circ_{298}$(g) value obtained from calorimetric measurements by Sabbah[21] is 12.1 kJ·mol^{-1} more positive than the theoretical one. The discrepancy is still more for the value recommended by Pedly,[7] who has used the other value of $\Delta_{\mathrm{f}}H^\circ_{298}$(cr) to determine the enthalpy of formation of gaseous cytosine (Table 1). The main reason of so large a difference between G3X and experimental[7,21] values of $\Delta_{\mathrm{f}}H^\circ_{298}$(g) is an inaccurate adjustment of enthalpy of sublimation from T = 458 K to T = 298.15 K. As for thymine, a large difference between the enthalpy of sublimation at (458 and 298.15) K is observed here, and that corresponds to an unreasonable value of gas-phase heat capacity of cytosine. The value of enthalpy of formation of gaseous cytosine recommended in Table 1 is based on the experimental enthalpy of formation of solid cytosine[6] and enthalpy of sublimation at 475 K, which is the mean of the values in refs 20 to 22. The $\Delta^{\mathrm{g}}_{\mathrm{cr}}H_{298}$ value is determined from eq 2 using experimental heat capacity of solid cytosine[23] and the $C^\circ_{p,298}$(g) value calculated in this work. As is seen from Table 1, the value of $\Delta^{\mathrm{g}}_{\mathrm{cr}}H_{298}$ obtained by Sabbah[21] is overestimated by 24 kJ·mol^{-1} compared to that determined in this work.

Adenine. The only experimental $\Delta_{\mathrm{f}}H^\circ_{298}$(g) value of adenine recommended in the reference book by Pedley[7] is 19.6 kJ·mol^{-1} less than that calculated by the G3X method (Table 1). As is seen from Table 1, the experimental value[7] is based on the underestimated value of $\Delta^{\mathrm{g}}_{\mathrm{cr}}H_{298}$ which was not confirmed in subsequent investigations and so cannot be considered as reliable. The recommended experimental data, which lead to agreement between theoretical and experimental $\Delta_{\mathrm{f}}H^\circ_{298}$(g) values, are given in Table 1. The used $\Delta_{\mathrm{f}}H^\circ_{298}$(cr) value[28] seems to be accurate, and it does not differ so much from the earlier value.[24,26] For readjustment of enthalpy of sublimation to 298.15 K, the value of $C^\circ_{p,298}$(cr) = 142.7 J·K^{-1}·mol^{-1}[33] is used, which is close to those obtained earler.[25,27] Note that the accepted enthalpy of sublimation of 127.2 kJ·mol^{-1} (420 K)[31] agrees with the experimental determinations by other authors[8,15] but is substantially lower than that of 140.4 kJ·mol^{-1} (420 K) obtained later by the same authors.[32] The last value of enthalpy of sublimation results in a $\Delta_{\mathrm{f}}H^\circ_{298}$(g) value which is 13.6 kJ·mol^{-1} larger than the theoretical one.

Guanine. Experimental data on guanine are few in number. To our knowledge, there is an old measurement of $\Delta_{\mathrm{f}}H^\circ_{298}$(cr),[24,26] two determinations of enthalpy of sublimation,[9,15] and heat capacity measurements.[25,34] The use of these data together with the $C^\circ_{p,298}$(g) value calculated in this work give a discrepancy between the theoretical and experimental enthalpies of formation $\Delta_{\mathrm{f}}H^\circ_{298}$(g) from (17 to 36) kJ·mol^{-1}. Assuming experimental values of $\Delta_{\mathrm{f}}H^\circ_{298}$(cr),[24,26] a good agreement between calculated and experimental $\Delta_{\mathrm{f}}H^\circ_{298}$(g) values can result from the $\Delta^{\mathrm{g}}_{\mathrm{cr}}H_{298}$ values of about 200 kJ·mol^{-1}. Thus, we cannot recommend the reliable experimental data for this compound. New measurements of the enthalpies of formation and sublimation would be extremely valuable to check the accuracy of the theoretical calculation.

Conclusion

In conclusion, we have presented here a set of self-consistent thermochemical data for uracil, thymine, cytosine, and adenine and an accurate value of the enthalpy of formation for gaseous guanine. It has been shown that theoretical calculations could help to choose more reliable enthalpies of formation for compounds in the solid phase and enthalpies of sublimation. In some cases, the enthalpies of sublimation at 298.15 K were improved using the calculated values of $C^\circ_{p,298}$(g). The determined enthalpies of formation $\Delta_{\mathrm{f}}H^\circ_{298}$(g) of uracil, thymine, cytosine, adenine, and guanine can be used as the key values in the calculations of the enthalpies of formation of their derivatives by the method of isodesmic reactions because the G3X calculations are not yet feasible for all of these compounds.

Acknowledgment

The authors thank Prof. H.-U. Siehl and Dr. J. Vogt for assistance.

Supporting Information Available:

Complete theoretical details. Table of ideal gas thermodynamic functions. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) Raghavachari, K.; Curtiss, L. A. Quantum-Chemical Methods for Accurate Theoretical Thermochemistry. In *Quantum-Mechanical Prediction of Thermochemical Data*; Cioslowski, J., Ed.; Kluwer: New York, 2002; pp 67−98.

(2) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K. Gaussian-3X (G3X) theory: use of improved geometries, zero-point energies, and Hartree-Fock basis sets. *J. Chem. Phys.* **2001**, *114*, 108–117.

(3) Dorofeeva, O. V.; Ryzhova, O. N. Revision of standard molar enthalpies of formation of glycine and L-alanine in the gaseous phase on the basis of theoretical calculations. *J. Chem. Thermodyn*. **2009**, *41*, 433−438.

(4) Nabavian, M.; Sabbah, R.; Chastel, R.; Laffitte, M. Etude thermochimique des acides aminobenzoiques, de la pyrimidine, de l'uracile et de la thymine. *J. Chim. Phys. Phys.-Chim. Biol.* **1977**, *74*, 115–126.

(5) Kilday, M. V. Enthalpies of Solution of the Nucleic Acid Bases. 4. Uracil in Water. *J. Res. Natl. Bur. Stand.* **1978**, *83*, 547–554.

(6) Wilson, S. R.; Watson, I. D.; Malcolm, G. N. Enthalpies of Formation of Solid Cytosine, L-Histidine, and Uracil. *J. Chem. Thermodyn.* **1979**, *11*, 911–912.

(7) Pedley, J. B. *Thermochemical Data and Structures of Organic Compounds*; Thermodynamics Research Center: College Station, TX, 1994; Vol. I.

(8) Yanson, I. K.; Verkin, B. I.; Shlyarevskii, O. I.; Teplitskii, A. B. Sublimation Heats of Nitrogen Bases of Nucleic Acids. *Stud. Biophys.* **1974**, *46*, 29–44.

(9) Yanson, I. K.; Teplitskii, A. B.; Sukhodub, L. F. Experimental Studies of Molecular Interactions Between Nitrogen Bases of Nucleic Acids. *Biopolymers* **1979**, *18*, 1149–1170.

(10) Bardi, G.; Bencivenni, L.; Ferro, D.; Martini, B.; Nunziante Cesaro, S.; Teghil, R. Thermodynamic Study of the Vaporization of Uracil. *Thermochim. Acta* **1980**, *40*, 275–282.

(11) Teplitskii, A. B.; Yanson, I. K.; Glukhova, O. T.; Zielenkiewicz, A.; Zielenkiewicz, W.; Wierzchowski, K. L. Thermochemistry of Aqueous Solutions of Alkylated Nucleic Acid Bases. III. Enthalpies of Hydration of Uracil, Thymine and Their Derivatives. *Biophys. Chem.* **1980**, *11*, 17–21.

(12) Brunetti, B.; Piacente, V.; Portalone, G. Sublimation Enthalpies of Some Methyl Derivatives of Uracil from Vapor Pressure Measurements. *J. Chem. Eng. Data* **2000**, *45*, 242–246.

(13) Szterner, P.; Kaminski, M.; Zielenkiewicz, A. Vapour Pressures, Molar Enthalpies of Sublimation and Molar Enthalpies of Solution in Water of Five Halogenated derivatives of Uracil. *J. Chem. Thermodyn.* **2002**, *34*, 1005–1012.

(14) Zielenkiewicz, W.; Szterner, P. Thermodynamic Investigation of Uracil and Its Halo Derivatives. Enthalpies of Solution and Solvation in Methanol. *J. Chem. Eng. Data* **2005**, *50*, 1139–1143.

(15) Barros, A. L. F.; Medina, A.; Zappa, F.; Pereira, J. M.; Bessa, E.; Martins, M. H. P.; Coelho, L. F. S.; Wolff, W.; Faria, C. A Simple Experimental Arrangement for Measuring the Vapour Pressures and Sublimation Enthalpies by the Knudsen effusion method: Application to DNA and RNA Bases. *Nucl. Instrum. Methods Phys. Res. A* **2006**, *560*, 219–223.

(16) Zielenkiewicz, W.; Kozbial, M.; Swierzewski, R.; Szterner, P. Heat Capacities of Uracil, Thymine, and Its Alkylated, Cyclooligomethylenated, and Halogenated Derivatives by Differential Calorimetry. *J. Chem. Eng. Data* **2007**, *52*, 93–97.

(17) Alvarez, J.; Biltonen, R. Nucleic acid-solvent interactions: temperature dependence of the heat of solution of thymine in water and ethanol. *Biopolymers* **1973**, *12*, 1815–1828.

(18) Ferro, D.; Bencivenni, L.; Teghil, R.; Mastromarino, R. Vapour Pressures and Sublimation Enthalpies of Thymine and Cytosine. *Thermochim. Acta* **1980**, *42*, 75–83.

(19) Burkinshaw, P. M.; Mortimer, C. T. Enthalpies of Sublimation of Transition Metal Complexes. *J. Chem. Soc., Dalton Trans.* **1984**, *75*, 77.

(20) Kilday, M. V. Enthalpies of Solution of the Nucleic Acid Bases. 2. Thymine in Water. *J. Res. Natl. Bur. Stand.* **1978**, *83*, 529–537.

(21) Sabbah, R. Thermodynamique de Composes Azotes. V. Etude Thermochimique de la Cytosine. *Thermochim. Acta* **1980**, *35*, 73–77.

(22) Zielenkiewicz, A.; Wszelaka-Rylik, M.; Poznariski, J.; Zielenkiewicz, W. Thermochemistry of Aqueous Solutions of Alkylated Nucleic Acid Bases. X. Enthalpies of Hydration of Cytosine and some Methylated, Hydroxy and Methoxy Derivatives of Cytosine. *J. Solution Chem.* **1998**, *27*, 235–243.

(23) Kilday, M. V. Enthalpies of Solution of the Nucleic Acid Bases. 3. Cytosine in Water. *J. Res. Natl. Bur. Stand.* **1978**, *83*, 539–546.

(24) Stiehler, R. D.; Huffman, H. M. Thermal Data. IV. The Heats of Combustion of Adenine, Hypoxanthine, Guanine, Xanthine, Uric Acid, Allantoin and Alloxan. *J. Am. Chem. Soc.* **1935**, *57*, 1734–1740.

(25) Stiehler, R. D.; Huffman, H. M. Thermal Data. V. The Heats Capacities, Entropies and Free Energies of Adenine, Hypoxanthine, Guanine, Xanthine, Uric Acid, Allantoin and Alloxan. *J. Am. Chem. Soc.* **1935**, *57*, 1741–1743.

(26) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic Press: New York, 1970.

(27) Kilday, M. V. Enthalpies of Solution of the Nucleic Acid Bases. 1. Adenine in Water. *J. Res. Natl. Bur. Stand.* **1978**, *83*, 347–369.

(28) Kirklin, D. R.; Domalski, E. S. Enthalpy of Combustion of Adenine. *J. Chem. Thermodyn.* **1983**, *15*, 941–947.

(29) Clark, L. B.; Peschel, G. G.; Tinoco, I., Jr. Vapor Spectra and Heats of Vaporization of Some Purine and Pyrimidine Bases. *J. Phys. Chem.* **1965**, *69*, 3615–3618.

(30) Chickos, J. S.; Acree, W. E., Jr. Enthalpies of Sublimation of Organic and Organometallic Compounds 1910−2001. *J. Phys. Chem. Ref. Data* **2002**, *31*, 537–698.

(31) Zielenkiewicz, A.; Zielenkiewicz, W.; Sukhodub, L. F.; Glukhova, O. T.; Teplitsky, A. B.; Wierzchowski, K. L. Thermochemistry of Aqueous Solutions of Alkylated Nucleic Acid Bases V. Enthalpies of Hydration of N-Methylated Adenines. *J. Solution Chem.* **1984**, *13*, 757–765.

(32) Zielenkiewicz, W. Enthalpies of Sublimation and Vapor Pressures of Adenine, 1-Methyladenine, 2-Methyladenine, 3-Methyladenine, and 8-Methyladenine. *J. Chem. Eng. Data* **2000**, *45*, 626–629.

(33) Boyer, J. S.; Francis, M. R.; Boerio-Goates, J. Heat Capacity Measurements and Thermodynamic Functions of Crystalline Adenine; Revised Thermodynamic Properties of Aqueous Adenine. *J. Chem. Thermodyn.* **2003**, *35*, 1917–1928.

(34) Kilday, M. V. Enthalpies of Solution of the Nucleic Acid Bases. 6. Guanine in Aqueous HCl and NaOH, and Guanine Hydrochlorides in Aqueous HCl. *J. Res. Natl. Bur. Stand.* **1981**, *86*, 367–381.

(35) Nicolaides, A.; Rauk, A.; Glukhovtsev, M. N.; Radom, L. Heats of formation from G2, G2(MP2), and G2(MP2, SVP) total energies. *J. Phys. Chem.* **1996**, *100*, 17460–17464.

(36) Gurvich, L. V.; Veytz, I. V.; Alcock, C. B., Eds. *Thermodynamic Properties of Individual Substances*; Hemisphere: New York, 1989; Vol. I; 1990, Vol. 2.

(37) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N. ; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y. ; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision E.01; Gaussian, Inc.: Wallingford CT, 2004.

(38) Trygubenko, S. A.; Bogdan, T. V.; Rueda, M.; Orozco, M.; Luque, F. J.; Sponer, J.; Slavicek, P.; Hobza, P. Correlated ab Initio Study of Nucleic Acid Bases and Their Tautomers in the Gas Phase, in a Microhydrated Environment and in Aqueous Solution. Part 1. Cytosine. *Phys. Chem. Chem. Phys.* **2002**, *4*, 4192–4203.

(39) Hanus, M.; Ryjacek, F.; Kabelac, M.; Kubar, T.; Bogdan, T. V.; Trygubenko, S. A.; Hobza, P. Correlated ab Initio Study of Nucleic Acid Bases and Their Tautomers in the Gas Phase, in a Microhydrated Environment and in Aqueous Solution. Guanine: Surprising Stabilization of Rare Tautomers in Aqueous Solution. *J. Am. Chem. Soc.* **2003**, *125*, 7678–7688.

(40) Raghavachari, K.; Stefanov, B. B.; Curtiss, L. A. Accurate density functional thermochemistry for larger molecules. *Mol. Phys.* **1997**, *91*, 555–559.

(41) Raghavachari, K.; Stefanov, B. B.; Curtiss, L. A. Accurate thermochemistry for larger molecules: Gaussian-2 theory with bond separation energies. *J. Chem. Phys.* **1997**, *106*, 6764–6767.

(42) Redfern, P. C.; Zapol, P.; Curtiss, L. A.; Raghavachari, K. Assessment of Gaussian-3 and density functional theories for enthalpies of formation of C_1 - C_{16} alkanes. *J. Phys. Chem.* **2000**, *104*, 5850–5854.

(43) Hehre, W. J.; Radom, L.; Schleyer, P. R.; Pople, J. A. *Ab InitioMolecular Orbital Theory*; Wiley: New York, 1986.

Received for review December 18, 2008. Accepted February 9, 2009. This research was supported by the Dr. Barbara Mez-Starck Foundation (Germany) and Russian Foundation for Basic Research under Grant No. 09-03-00949.

JE800977N