

Enthalpies of Sublimation and Vapor Pressures of Adenine, 1-Methyladenine, 2-Methyladenine, 3-Methyladenine, and 8-Methyladenine

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Vapor pressure and the enthalpies of sublimation of adenine, 1-methyladenine, 2-methyladenine, 3-methyladenine, and 8-methyladenine are presented. The obtained values of the enthalpy of sublimation are discussed together with literature values for the alkylated derivatives of adenine.

Introduction

In this paper we report results of studies of solute–solvent interactions of nucleic acid bases with their liquid environment. To achieve complete knowledge of the mechanism of interaction between nucleic acid bases and water and thus the spatial organization of polynucleotide chains, an explanation of the contributing effects of pairing and stacking interactions between both purine and pyrimidine bases in aqueous solutions is of great importance. The method of screening the functional groups on the skeleton of the base by methyl and others alkyl groups is used to eliminate some direct interactions between certain polar and apolar atoms of the skeleton with the hydration shell. Our choice of investigated compounds was justified by this method. The objective of our study was to determine the solute–solvent interaction enthalpies for alkyl derivatives of uracyl, thymine, cytosine, and adenine.

Vapor pressures and enthalpies of sublimation of adenine and methyl derivatives of adenine presented in this study not only enlarge the information set of thermodynamic properties of this group of compounds but also, what is no less important, enables one to discuss them together with the previously determined sublimation enthalpy values of adenine and uracyl alkyl derivatives.

Experimental Section

Adenine, 1-methyladenine, and 3-methyladenine were purchased from Sigma (Lots 10H77025, 114H5017, 85H4055); 2-methyladenine and 8-methyladenine were synthesized by M. Draminski's group at the Military Medical Academy (Łódź, Poland) according to standard methods and purified by repeated crystallization and vacuum sublimation. The purities of the substances as well as their melting temperatures were determined using a DSC 910 Du Pont differential scanning calorimeter with a Thermal Analyzer 1090. The purities were better than 99.8%. Prior to measurements the substances were heated at (120–140) °C in order to remove traces of water and volatile impurities.

The vapor pressure measurement and successive determinations of molar enthalpies of sublimation were carried out by means of the Knudsen effusion method, using an apparatus described earlier (Kamiński and Szlaski, 1986).

The vapor pressure was calculated according to the relation

$$P = (m/taW)(2RT/M)^{1/2} \quad (1)$$

where a is the surface area of the effusion hole, m is the mass of the substance sublimed in time t , T is the temperature of the measurement, R is the gas constant, W is the Clausing coefficient, and M is the molar mass of substance. For calculation purposes, the assumption was made that M is equal to the molar mass of the monomer. The existence monomers was confirmed by E1 mass spectra analysis made by means of an AMD-604 (AMD GmbH, Harsted, Germany) double-focusing mass spectrometer with BE geometry (electron energy 70 eV, acceleration voltage 8 kV, source temperature 200 °C).

The Clausing coefficient, which characterizes the resistance of the stream of vapor during its passage through the effusion hole, is given by the equation (Freeman and Searcy, 1954)

$$W = 0.0147(L/r)^2 + 0.349(L/r) + 0.9982 \quad (2)$$

where r is the radius of the effusion hole and L is the height of the effusion hole (thickness of the tantalum membrane). The value of the molar enthalpy of sublimation $\Delta_s^g H_m$ calculated at mean temperatures within the experimental temperature range was determined by the least-squares method using the following equation:

$$\ln(p/p^\circ) = -A/T + B \quad (3)$$

Here $A = \Delta_s^g H_m/R$ and $B = \text{constant}$. Vapor pressure measurements were carried out with the use of tantalum membrane of thickness 0.024 mm and an effusion hole of the diameter equal to 1.0094 mm, and $W = 1.01485$.

Calibration and test measurements were performed on benzoic acid of mole fraction 0.9999 obtained from the Polish Committee for Standardization, Measures and Quality Control (Warsaw, Poland). The measurements made as was reported previously (Kamiński and Zielenkiewicz, 1996) for six temperatures in the intervals 303.7 K to 313.6 K, 300.2 K to 306.3 K, and 299.0 K to 308.6 K gave the following values of molar enthalpy of sublimation: (90.7 ± 0.8) kJ·mol⁻¹, (89.3 ± 0.5) kJ·mol⁻¹, and (89.8 ± 0.8) kJ·mol⁻¹, respectively. They are close to the values reported in other paper (Kamiński and Zielenkiewicz, 1996).

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Table 1. Experimental Vapor Pressures, Mass of the Sublimed Substance, and $\Delta \ln p/p^\circ$ ^a Obtained from Eq 3

<i>T</i> /K	<i>m</i> /mg	<i>p</i> /Pa	$10^2 \Delta \ln p/p^\circ$	<i>T</i> /K	<i>m</i> /mg	<i>p</i> /Pa	$10^2 \Delta \ln p/p^\circ$
Adenine 1 (<i>t</i> = 18 000 s)							
405.98	1.112	0.012 83	-0.052	424.55	7.745	0.090 53	0.033
410.42	1.859	0.021 37	-0.004	429.14	11.740	0.129 60	-0.045
415.29	2.230	0.037 34	-0.059	433.75	17.685	0.208 95	0.001
419.92	4.968	0.057 75	0.034	438.24	26.024	0.309 06	-0.016
Adenine 2 (<i>t</i> = 23 400 s)							
400.29	1.022	0.008 92	-0.077	419.98	6.442	0.057 61	-0.003
406.07	1.603	0.014 10	0.054	424.68	10.072	0.090 58	-0.019
410.26	2.389	0.021 12	0.067	429.26	15.203	0.137 45	-0.021
415.35	4.221	0.037 54	-0.014	434.21	22.831	0.207 61	0.007
1-Methyladenine 1 (<i>t</i> = 18 000 s)							
442.69	1.232	0.013 99	-0.057	456.40	3.429	0.039 55	0.043
445.54	1.439	0.016 40	0.027	459.11	4.361	0.050 45	0.016
448.26	2.011	0.022 99	-0.077	461.83	5.830	0.067 64	-0.061
450.98	2.202	0.025 25	0.050	464.54	7.041	0.081 93	-0.041
453.74	1.636	0.030 32	0.093				
1-Methyladenine 2 (<i>t</i> = 28 800 s)							
445.56	2.304	0.017 50	0.052	467.46	14.479	0.112 68	-0.078
451.03	3.669	0.028 05	0.029	472.87	20.552	0.160 86	-0.031
456.43	6.061	0.046 61	-0.047	478.16	29.036	0.228 53	0.003
461.84	9.372	0.068 87	-0.015	483.54	39.003	0.310 45	0.080
2-Methyladenine 1 (<i>t</i> = 18 000 s)							
412.43	1.282	0.014 06	0.007	428.19	4.575	0.051 11	0.013
415.23	1.645	0.018 10	-0.009	430.17	5.457	0.061 11	-0.013
420.76	2.592	0.028 71	-0.011	433.64	7.144	0.080 32	-0.017
424.49	3.504	0.038 98	-0.014	435.55	8.335	0.093 92	-0.027
426.34	3.844	0.042 85	0.039	437.45	8.904	0.100 55	0.026
2-Methyladenine 2 (<i>t</i> = 28 800 s)							
420.89	4.147	0.028 70	-0.001	431.81	10.084	0.070 70	-0.013
424.42	5.601	0.038	-0.013	433.63	11.430	0.080 31	0.002
426.36	6.363	0.044 33	0.015	435.55	13.342	0.093 95	-0.003
428.18	7.358	0.051 37	0.015	437.45	15.257	0.107 70	0.007
430.03	8.731	0.061 10	-0.009				
3-Methyladenine 1 (<i>t</i> = 23 400 s)							
391.84	1.671	0.013 74	0.005	407.81	6.864	0.057 56	-0.018
394.66	2.226	0.018 37	-0.028	410.59	8.515	0.071 66	-0.002
397.26	3.185	0.026 43	-0.158	413.37	10.601	0.089 51	0.006
402.17	4.075	0.033 94	0.025	417.09	14.025	0.118 96	0.026
404.99	5.453	0.045 57	-0.025	418.96	17.105	0.145 41	-0.023
3-Methyladenine 2 (<i>t</i> = 18 000 s)							
394.66	1.714	0.018 38	-0.026	404.99	4.197	0.045 59	-0.029
399.38	2.452	0.026 46	0.033	407.82	5.291	0.057 69	-0.013
402.17	3.137	0.033 96	0.029	410.61	6.553	0.071 69	0.005
8-Methyladenine 1 (<i>t</i> = 23 400 s)							
424.49	2.401	0.020 54	0.032	443.71	8.921	0.078 04	-0.020
428.18	3.011	0.015 88	0.058	446.37	10.392	0.090 89	-0.004
431.82	4.148	0.035 80	-0.020	449.20	12.017	0.105 78	0.022
435.49	5.221	0.045 25	-0.009	451.90	14.231	0.125 64	0.002
438.20	6.572	0.057 14	-0.064	454.67	16.315	0.144 49	0.046
440.91	7.817	0.068 17	-0.065				

$$^a \Delta p = p(\text{calc}) - p(\text{exp})/p^\circ.$$

Results and Discussion

In Table 1 the following data are listed: vapor pressures at temperature *T*, masses of sublimed substances *m*, and $\Delta \ln p/p^\circ$ increments calculated from eq 3 using experimentally determined vapor pressure values. For adenine, 1-methyladenine, 2-methyladenine, and 3-methyladenine two series of measurements were carried out (marked in Tables as 1 and 2) in a similar temperature range and sublimation time *t*. In Table 2 are collected the values of *A* and *B* coefficients from eq 3 calculated respectively for series 1 and 2 and the ΔT temperature range, for which the measurements were carried out. In Table 3 are given the values of the mean enthalpy of sublimation $\Delta_s^g H_m$ calculated on the basis of the results of 1 and 2 series of measurements and the values of sublimation enthalpies of methyl derivatives of adenine (Zielenkiewicz et al., 1987,

1994; Kamiński and Zielenkiewicz, 1987; Kamiński, 1992) with the methyl group located on N⁶, N⁹, C²N⁹, and N⁶C⁸N⁹. On the basis of this set of collected values of sublimation enthalpies, the increments of sublimation enthalpy $\delta \Delta_s^g H_m$ were determined as results of the substitution of the hydrogen atom by a methyl group.

It can be noted that the average value of the enthalpy of adenine 140.4 kJ·mol⁻¹ obtained in this work differs significantly from the value 127.2 kJ·mol⁻¹ previously reported (Zielenkiewicz et al., 1984) obtained by means of the low-temperature quartz resonator method. Other values of the enthalpies of sublimation cited in the literature (Clark et al., 1965; Yanson et al., 1974) range from 109 to 126 kJ·mol⁻¹. This means that results of the enthalpy of sublimation obtained using different methods are significantly scattered. Therefore in Table 3 the increments δ

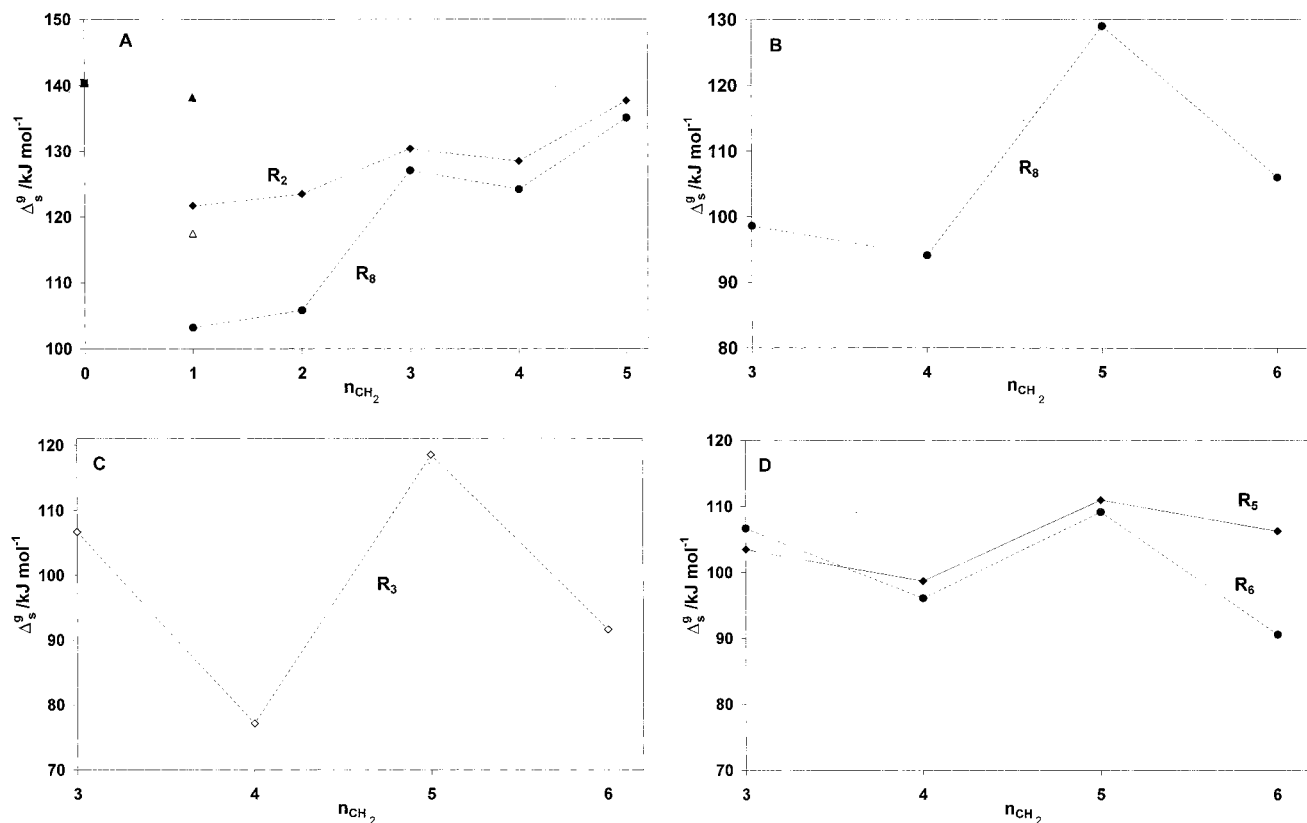


Figure 1. Plot of enthalpy of sublimation $\Delta_s^g H_m$ vs the number of methylene groups n_{CH_2} . A: \blacklozenge , 9-methyl-2-alkyladenines (Zielenkiewicz et al., 1987); \bullet , 9-methyl-8-alkyladenines (Zielenkiewicz et al., 1994; Kamiński and Zielenkiewicz, 1987); \blacksquare , adenine (this work); \blacktriangle , 1-methyladenine (this work); \triangle , 3-methyladenine (this work). B: \bullet , 6,9-dimethyl-8-alkyladenines (Zielenkiewicz et al., 1994). C: \diamond , 1,6-dimethyl-3-alkyluracils; \blacksquare , uracil (Teplitsky et al., 1980; Zielenkiewicz et al., 1994). D: \blacklozenge , 1,3-dimethyl-5-alkyluracils (Kamiński and Zielenkiewicz, 1996); \bullet , 1,3-dimethyl-6-alkyluracils (Zielenkiewicz et al., 1993). R_2 , R_3 , R_5 , R_6 , and R_8 : methyl, ethyl, propyl, and butyl groups (see Figure 3).

Table 2. Coefficients A and B of Vapor Pressure Eq 3

expt no.	$\ln(p/p^\circ)$		no. of pts	$\Delta T/K$	$\Delta_s^g H_m$
	B	-A			
Adenine					
1	38.4 ± 0.6	17350 ± 252	8	406–438	144.2 ± 2.0
2	36.6 ± 0.6	16560 ± 274	8	400–434	137.7 ± 2.2
1-Methyladenine					
1	33.6 ± 1.1	16770 ± 622	9	443–465	139.4 ± 5.1
2	33.0 ± 0.6	16470 ± 346	8	446–484	136.9 ± 2.8
2-Methyladenine					
1	30.9 ± 0.4	14500 ± 162	10	412–437	120.6 ± 1.3
2	31.5 ± 0.3	14770 ± 147	9	421–437	122.8 ± 1.2
3-Methyladenine					
1	31.7 ± 0.3	14110 ± 144	10	392–419	117.3 ± 1.1
2	31.8 ± 0.9	14150 ± 377	6	395–411	117.6 ± 3.1
8-Methyladenine					
1	25.4 ± 0.7	12416 ± 289	11	424–455	103.2 ± 2.4

$\Delta_s^g H_m$, resulting from the substitution of methyl groups to the adenine moiety, based only on $\Delta_s^g H_m$ values obtained by the same experimental effusion method are presented. Conclusions resulting from these data (Table 3) are methylation of adenine in position N1 changed the value of the enthalpy of sublimation by only $-2.2 \text{ kJ}\cdot\text{mol}^{-1}$ comparing to the value obtained for adenine, whereas methylation of adenine in positions C2 and N3 generated changes in the enthalpy of sublimation of $-18.7 \text{ kJ}\cdot\text{mol}^{-1}$ and $-22.9 \text{ kJ}\cdot\text{mol}^{-1}$, consecutively. The largest change in the enthalpy of sublimation value $-37.2 \text{ kJ}\cdot\text{mol}^{-1}$ was induced by substitution of a methyl group on C8. Comparison of the value obtained in this work for 8-methyladenine ($\Delta_s^g H_m = 103.2 \text{ kJ}\cdot\text{mol}^{-1}$) with the value obtained previously for 8,9-

dimethyladenine ($\Delta_s^g H_m = 105.8 \text{ kJ}\cdot\text{mol}^{-1}$) as well as values of enthalpies of sublimation determined for 2-methyladenine ($\Delta_s^g H_m = 121.7 \text{ kJ}\cdot\text{mol}^{-1}$) and 2,9-dimethyladenine ($\Delta_s^g H_m = 123.5 \text{ kJ}\cdot\text{mol}^{-1}$) proves that the increase of the number of methyl groups in the adenine skeleton does not generate an increase of the enthalpy of sublimation. On the other hand, when we compare $\Delta_s^g H_m$ values for 6,8,9-trimethyladenine and 8,9-dimethyladenine, it becomes obvious that the addition of the third methyl group to the moiety results in an increment in the value of the enthalpy of sublimation [$\delta(\Delta_s^g H_m) = -7.2 \text{ kJ}\cdot\text{mol}^{-1}$]. This means that the enthalpy of sublimation is not simply an additive quantity but depends both upon the location and number of methyl groups added independently if they are attached to the skeleton or participate in elongation of the alkyl side chains. The changes of enthalpy of sublimation observed with increasing number of methyl groups added to the adenine molecule are illustrated graphically in Figure 1, where the plot of $\Delta_s^g H_m$ vs the number of methylene groups CH_2 is presented. In Figure 1A also the values of enthalpies of sublimation of 9-methyl-2-ethyladenine, 9-methyl-2-propyladenine, 9-methyl-2-butyladenine, 9-methyl-8-ethyladenine, 9-methyl-8-propyladenine, and 9-methyl-8-butyladenine are given. Apparently the elongation of alkyl side chains in positions C2 and C8 induces a nonlinear increase of the sublimation enthalpy. This behavior is more visible for adenine derivatives alkylated in position C8 (Figure 1A) than in the case of position C2. In Figure 1B the dependence of the sublimation enthalpy on the number of CH_2 groups for 6,8,9-trimethyladenine, 6,9-dimethyl-8-ethyladenine, 6,9-dimethyl-8-propyladenine,

Table 3. Increments $\delta\Delta_s^g H_m$ (kJ·mol⁻¹) of the Enthalpy of Sublimation

compd	$\Delta_s^g H_m$	$\delta\Delta_s^g H_m(1)$	$\delta\Delta_s^g H_m(2)$	$\delta\Delta_s^g H_m(3)$	$\delta\Delta_s^g H_m(6)$	$\delta\Delta_s^g H_m(8)$	$\delta\Delta_s^g H_m(9)$
adenine	140.4						
1-methyladenine	138.2	-2.2 (1-ade)					
2-methyladenine	121.7		-18.7 (2-ade)				
3-methyladenine	117.5			-22.9 (3-ade)			
8-methyladenine	103.2					-37.2 (8-ade)	
2,9-dimethyladenine	123.5 ^a						1.8 (2, 9-2)
8,9-dimethyladenine	105.8 ^b						2.6 (8, 9-8)
6,8,9-trimethyladenine	98.6 ^c				-7.2 (6, 8, 9-8, 9)		

^a Kamiński, 1992. ^b Kamiński and Zielenkiewicz, 1987. ^c Zielenkiewicz et al., 1994.

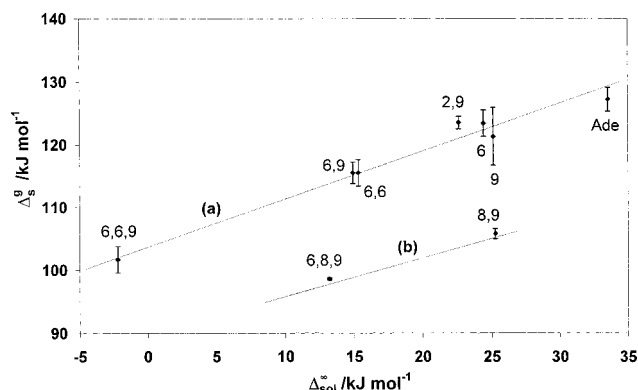


Figure 2. Enthalpy of sublimation (Kamiński and Zielenkiewicz, 1987; Zielenkiewicz et al., 1984; Kamiński, 1992) vs enthalpy of solution (Zielenkiewicz et al., 1984, 1987, 1994; Kilday, 1978) for methylated adenines. (a) Adenine and methylated adenines: 9; 6; 2,9; 6,6; 6,9; 6,6,9. (b) Methylated adenines: 8,9; 6,8,9 (see Figure 3).

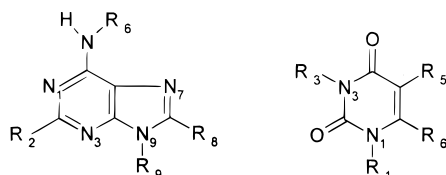


Figure 3. Structural formulae of investigated compounds.

and 6,9-dimethyl-8-butyladenine (Zielenkiewicz et al., 1994) is given. This curve (Figure 1A) is similar with the appearance of a maxima for odd number of groups CH₂ ($n_{\text{CH}_2} = 3, 5$) and a minima for even numbers of CH₂ ($n_{\text{CH}_2} = 4, 6$) groups. Similar alternation (odd-even effect) of sublimation enthalpy arising from different numbers of CH₂ groups substituted to the molecule skeleton have been observed (Teplitsky et al., 1980; Zielenkiewicz et al., 1993, 1994; Kamiński and Zielenkiewicz, 1996) for a series of alkylated uracils (Figure 1C,D). Suwińska (1995) attempted to explain the cause of the alternation effect of sublimation enthalpy values by confrontation with calculated values of molecular packing and packing energy in the crystals of 1,3,6-trimethyluracil, 1,3-dimethyl-6-ethyluracil, 1,3-dimethyl-6-propyluracil, and 1,3-dimethyl-6-butyluracil.

Comparison of the values of sublimation enthalpies of methylated adenine with the solution enthalpies of these compounds in water (Zielenkiewicz et al., 1984, 1987, 1994; Kilday, 1978) is presented in Figure 2. For adenine and six derivatives of adenine methylated in positions C2, N⁶, and N9 a linear function of $\Delta_s^g H_m$ vs $\Delta_{\text{sol}} H^\circ$ was observed

(curve a). The derivatives of adenine methylated in position C8 are located on curve b below curve a.

Diversity of changes in the values of sublimation enthalpy indicates the presence of significant structural differences in the molecule resulting from the addition of methylene groups including location of hydrogen bonds and existence of conformational changes associated with lengthening of the side chains.

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