Thermochimica Acta, 237 (1994) 49–53
Elsevier Science B.V., Amsterdam
SSDI 0040-6031(93)01613-8

Apparent molar heat capacities of some alkyl derivatives of 2-aminopurine, adenine and guanine in dilute aqueous solution at 25°C

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(Received 25 May 1993; accepted 22 September 1993)

Abstract

The apparent molar heat capacities $C_{p,\phi}$, and densities of adenine, 2-aminopurine, 9-methyladenine, 2,2-dimethylaminopurine, 9-ethylguanine, 2-methylamino-9-methylpurine, 2-dimethylamino-9-methylpurine, 9-methyl-2-butyladenine, and 6,9-dimethyl-8-butyladenine were determined experimentally using a differential adiabatic scanning microcalorimeter DASM-1M and an Anton Paar DMA 60/602 digital densimeter. In the series of alkylated adenines and 2-aminopurines, a linear dependence was found between the partial molar heat capacities $C_{p,2}^{\ominus}$ and the number of substituted methylene groups n_{CH_2} belonging to the skeleton of the molecule. The experimental data of the apparent molar heat capacities of 9-methyl-2-alkyladenines and 6,9-dimethyl-8-alkyladenines indicated erratic changes in $\Delta C_{p,2}^{\ominus}$ with elongation of the *n*-alkyl chain.

INTRODUCTION

It is well known that the partial molar heat capacities $C_{p,2}^{\ominus}$ of non-electrolytes in aqueous solutions also reflect the so-called "hydrophobic hydration" of solutes. In view of the essential role played by methylated purine and pyrimidine bases in the recognition processes between proteins and nucleic acids, we have undertaken systematic thermodynamic studies of these systems [1–12]. The present work is a continuation of our studies on the apparent molar heat capacities of alkylated nucleic acid bases in aqueous solution [1, 7–10]. It was found [1, 7–9] that in the case of variously methylated diketopyrimidines in aqueous solutions, the values of partial molar heat capacities at infinite dilution $C_{p,2}^{\ominus}$ are significantly higher than C_p(s) of the pure solid compounds and increase linearly with the

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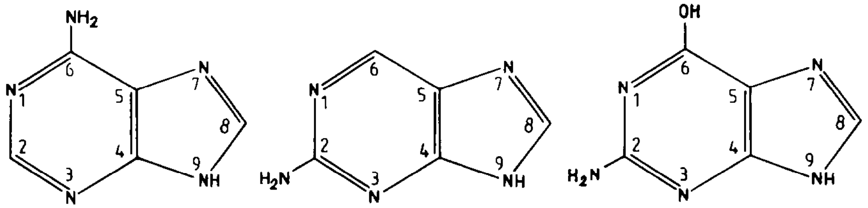
number of methylene groups $-CH_2-$ substituted, independently of the place of substitution of the latter. The determination of the $C^{\ominus}_{p,2}$ values of alkylated derivatives of adenines has also been the subject of our studies [8, 10].

The present work is an extension of our previous investigations on the $\Delta C^{\ominus}_{p,2} = f(n_{CH_2})$ relationship, supplemented by new $C_{p,\phi}$ data for alkylated adenines, 2-aminnopurines and 9-ethylguanine. Some new conclusions and relationships were revealed by increasing the number of experimental data. The structural formulae of the basic compounds are shown in Scheme 1.



Adenine
(6-Aminopurine)

2-Aminopurine

Guanine
(2-Amino-6-hydroxypurine)

Scheme 1.

MATERIALS AND METHODS

The compounds adenine, 2-aminopurine and 9-ethylguanine were Sigma commercial products of purity better than 99%. The other compounds, 9-methyladenine (99.4%), 2,2-dimethylaminopurine (99.2%), 2-methylamino-9-methylpurine (99.4%), 2-dimethylamino-9-methylpurine (99.6%), 9-methyl-2-butyladenine (98.3%), and 6,9-dimethyl-8-butyladenine (98.9%) were synthesized individually in the Laboratory of Prof. Dr. M. Dramiński (Military Academy of Medicine, Łódź, Poland), having been thoroughly purified by repeated crystallizations and repeated vacuum sublimation. Their identity and purity were checked by melting point determinations, thin layer chromatographic analyses in several solvent systems and, if necessary, by MS and ^{3}H NMR determinations. All the compounds examined were carefully dried for several days before use. All the solutions were prepared by weight using degassed and deionized distilled water. Differences in densities between the solutions under study and water obtained with a digital Anton Paar DMA 60/602 densimeter, thermostated to within ± 0.002°C. The measurements were carried out at 25°C; the uncertainty in the determination of the density was 2×10^{-6} g cm^{-3}. The heat capacities per unit volume of the solution under study were measured relative to that of water using a differential, adiabatic, scanning microcalorimeter DASM-1M. The instrument and working procedure have been described elsewhere [13]. The values of the densities d, partial molar volumes $V^{\ominus}_2$ and heat capacities $C^{\ominus}_{p,2}$ of the compounds studied, together with the $C^{\ominus}_{p,2}$ and $V^{\ominus}_2$

TABLE 1

Partial molar volumes and heat capacities at 25°C

Compound	n_{CH_2}	m [a]	d [b]	$V_2^{\ominus}$ [c]	$C_{p,2}^{\ominus}$ [d]
Adenine (Ade)	0	4.22	0.997211	96.4	228.6 ± 3.0
2-Aminopurine (n^2Pu)	0	6.44	0.997326	91.9	226.1 ± 3.7
9-Methyladenine (m^9Ade)	1	9.39	0.997397	112.0	315.9 ± 5.5
2,2-Dimethylaminopurine ($m_2^{2,2}n^2Pu$)	2	3.37	0.997175	125.4	429.8 ± 4.1
2,9-Dimethyladenine ($m_2^{2,9}Ade$)	2	17.6–64.6		127.2 [e]	557.7 [e]
9-Ethylguanine (e^9 Gua)	2	2.06	0.997151	128.7	433.8 ± 3.5
2-Methylamino-9-methylpurine ($m_2^{2,9}n^2Pu$)	2	7.17	0.997321	125.2	455.4 ± 6.3
6,8,9-Trimethyladenine ($m_3^{6,8,9}Ade$)	3	23.2–34.7		141.1 [f]	628 [e]
2-Dimethylamino-9-methylpurine ($m_3^{2,2,9}n^2Pu$)	3	6.09	0.997262	142.1	559.6 ± 2.5
9-Methyl-2-ethyladenine (m^9e^8 Ade)	3	28.3		139.3 [f]	577 [e]
6,9-Dimethyl-8-ethyladenine ($m_2^{6,9}e^8$ Ade)	4	11.5		157.4 [f]	664 [e]
9-Methyl-2-propyladenine (m^9p^2 Ade)	4	11.0		155.2 [f]	638 [e]
9-Methyl-2-butyladenine (m^9b^2 Ade)	5	3.28	0.997151	172.7 [f]	713.0 ± 3.0
6,9-Dimethyl-8-propyladenine ($m_2^{6,9}p^8$ Ade)	5	15.5–33.8		174.2 [f]	777.1 [f]
6,9-Dimethyl-8-butyladenine ($m_2^{6,9}b^8$ Ade)	6	3.02	0.997140	189.1 [f]	753.2 ± 4.1

[a] Molality in mmol kg^{-1}. [b] Density in g cm^{-3}. [c] Partial molar volume in cm^3 mol^{-1}. [d] Partial molar heat capacity in J K^{-1} mol^{-1}. [e,f] Partial molar volumes and heat capacities from refs. 8 and 10.

values for the alkylated adenines determined previously [8, 10], are reported in Table 1. The measured apparent molar heat capacities $C_{p,\phi}$ were determined at concentrations of 2.1–9.4 mmol kg^{-1}. The maximum concentration investigated was quite low due to the limited solubility of the compounds, which made it impossible to establish the relationships $V_\phi = f(m)$ and $C_{p,\phi} = f(m)$. It was assumed that due to very low concentrations of the compounds studied, the determined apparent molar volumes V_ϕ and heat capacities $C_{p,\phi}$ are identical to the partial molar qualitites $V_2^{\ominus}$ and $C_{p,2}^{\ominus}$. However, the very low signal/noise ratio in the $C_{p,\phi}$ measurements caused relatively high errors. The authors are not aware of any calorimetric method allowing a higher precision of $C_{p,\phi}$ determination.

RESULTS AND DISCUSSION

For the alkylated adenines and 2-aminopurines examined (Table 1), a linear relationship between $C_{p,2}^{\ominus}$ and the number of $-CH_2-$ groups attached directly to the skeleton and to the amino groups thereon was found

$$C_{p,2}^{\ominus} = a + bn_{CH_2}$$

where $a = 261.8 \pm 12.3$ J K^{-1} mol^{-1} and $b = 95.9 \pm 3.7$ J K^{-1} mol^{-1}, with a product–moment correlation coefficient δ of 0.9624. The slope of the plot $C_{p,2}^{\ominus}$ versus n_{CH_2} is similar to that obtained from the linear relationship

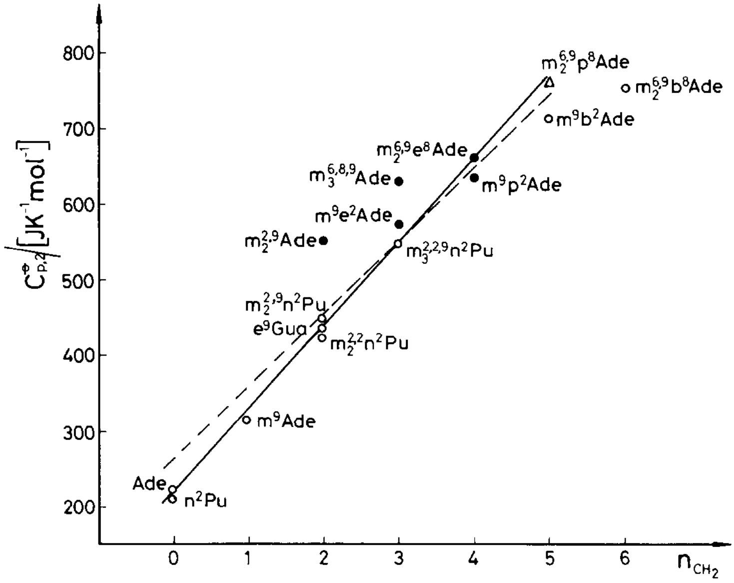


Fig. 1. Partial molar heat capacities versus number of $-CH_2-$ groups: ○, this work; ●, ref. 8; △, ref. 10; ——, the slope of the plot $b = \Delta C^{\ominus}_{p,2} = 105.6$ J K^{-1} mol^{-1}; – – –, $b = 95.9$ J K^{-1} mol^{-1}.

between partial molar heat capacities and n_{CH_2} for diketopyrimidines [1, 9] and for homologous series of alkylated aliphatic amides and hydrocarbons [14–16]. A more exact correlation of $C^{\ominus}_{p,2} = f(n_{CH_2})$ can be obtained for all the examined compounds, except the three adenine derivatives 2,9-dimethyladenine, 6,9-dimethyl-8-butyladenine and 6,8,9-trimethyladenine. In this case, in the above relationship $a = 288.8 \pm 5.7$ J K^{-1} mol^{-1}, $b = 105.6 \pm 1.8$ J K^{-1} mol^{-1} and $\delta = 0.9938$. Very similar results, $a = 228.3 \pm 10.7$ J K^{-1} mol^{-1}, $b = 105.2 \pm 2.29$ J K^{-1} mol^{-1} and $\delta = 0.9922$, were obtained for only the seven adenine derivatives. Nevertheless, the value of the increment $b = \Delta C^{\ominus}_{p,2} = 105$ J K^{-1} mol^{-1} is somewhat higher than that found [1, 9, 14–16] for other hydrophobic compounds (about 90 J K^{-1} mol^{-1}).

On closer inspection of the experimental $C^{\ominus}_{p,2}$ data of the 6,9-dimethyl-8-alkyladenines and 9-methyl-2-alkyladenines (see Table 1 and Fig. 1), there are erratic changes in $\Delta C^{\ominus}_{p,2}$ with elongation of the n-alkyl chain. The $\Delta C^{\ominus}_{p,2}$ increments calculated for successive pairs of compounds differ considerably one from another, and for $m_3^{6,8,9}$ Ade and $m_2^{6,9}e^8$ Ade, $m_2^{6,9}e^8$ Ade and $m_2^{6,9}p^8$ Ade, $m_2^{6,9}p^8$ Ade and $m_2^{6,9}b^8$ Ade, correspond to 36, 113.1 and -23.9 J K^{-1} mol^{-1}, respectively; and for $m_2^{2,9}$ Ade and m^9e^2 Ade, m^9e^2 Ade and m^9p^2 Ade, m^9p^2 Ade and m^9b^2 Ade, are equal to 19.3, 61 and 75.0 J K^{-1} mol^{-1}, respectively. This is probably a result of the different structural features of the solid compounds and solutions studied and should be the subject of further investigations.

ACKNOWLEDGEMENTS

We cordially thank Mgr. Jolanta Szemińska for her contribution to the experimental work. We gratefully acknowledge financial support from KBN Program 2 0828 91 01.

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