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Empirical and ab initio Computation of the Thermochemical Parameters of Amino Acids: I. Monoamino Carbonic Acids and Monoamino Dicarbonic Acids and Their Amides

E. V. Sagadeev[a], A. A. Gimadeev[a], D. V. Chachkov[b], and V. P. Barabanov[a]

[a]*Kazan State Technological University, ul. K. Marksa 68, Kazan, 420015 Tatarstan, Russia*
e-mail: sagadeev@list.ru

[b]*Kazan Scientific Center, Russian Academy of Sciences, Kazan, Tatarstan, Russia*

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Abstract—Using different computation methods main thermochemical characteristics of ten standard L-α-amino acids of monoamino carbonic and monoamino dicarbonic series were obtained.

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In a wide class of derivatives of the three-coordinated nitrogen atom the amino acids have special significance that cannot be overestimated. Amino acids are, in essence, basis of the animate nature on the earth because an interchange of a certain sequence of the amino acids (genetically coded) forms a primary protein structure. Their practical significance is also large: amino acids and their derivatives have extensive applications as pharmaceuticals, components of various cosmetics, and also as additives in agriculture etc. [2, 3].

It is no wonder that the amino acids as a class of organic compounds are an attractive subject of investigations in the course of several tens of years. A study of various aspects of the thermochemistry of these compounds is of special interest. In particular, an understanding and follow-up modeling of real processes in biological systems, a protein biosynthesis, phosphorylation, necessitate an elucidation of values of energy parameters for the amino acids [4].

However, despite an importance of the compounds of this class, we can conclude on the basis of a literature data that thermochemistry of the amino acids in comparison with other classes of organic nitrogen compounds is studied poorly.

In our study for a computation of standard thermochemical characteristics of ten L-α-amino acids we used Cohen and Benson increment method [10, 11] that gave good results at the examination of thermochemical characteristics of organic compounds of other classes [5–9].

An array of increments of nitrogen-containing group for the standard enthalpy of formation in the gas phase was computed on the basis of an analysis of experimental data (Table 1), including those of [10]. The obtained group increments of nitrogen-containing fragments of molecules in the enthalpy of formation are presented in Table 2. The increment computation was performed with the last version of Enthalpy computer program [20]. The increments were designated according to the notation of group contribution suggested by Benson and Bass [21]: for example, C–(CO)(N)$(H)_2$ was the carbon atom in glycine **I** bonded to carboxyl group, nitrogen atom, and two hydrogen atoms; CO–(C)(N) + N–(CO)$(H)_2$ was the amide fragment NH_2CO- in asparagine **IX** or glutamine **X**.

Using the computed (Table 2) and [1] group increments for the enthalpy of formation the values of ΔH^0_{form}(gas) of the amino acids listed in Table 1 were computed by Enthalpy computer program [20].

By the same empirical computation method the standard enthalpies of formation of amino acids in

Table 1. Experimental and computed enthalpies of formation and sublimation for L-α-amino acids, kJ mol^{-1}

Comp. no.	Compound	Formula	ΔH^0_{subl}, kJ mol^{-1}		ΔH^0_{form}, kJ mol^{-1}			
			experiment	calculation	gas phase		crystal state	
					experiment	calculation	experiment	calculation
Monoamino carbonic acids								
I	Glycine	$C_2H_5O_2N$	138.1[a]	138.1	–390.5[a]	–390.0	–528.6[a]	–528.1
II	Alanine	$C_3H_7O_2N$	144.8[a]	139.7	–414.7[a]	–415.9	–559.5[a]	–555.6
III	Valine	$C_5H_{11}O_2N$	162.8[b]	149.2	–	–466.1	–618.0[c]	–615.3
IV	Leucine	$C_6H_{13}O_2N$	150.6[b]	157.9	–	–486.8	–646.8[c]	–644.7
V	Isoleucine	$C_6H_{13}O_2N$	120.1[b]	157.9	–	–486.8	–640.7[d]	–644.7
VI	Phenylalanine	$C_9H_{11}O_2N$	154.0[b]	159.3	–	–302.0	–460.6[e,i]	–461.3
Monoamino dicarbonic acids and their amides								
VII	Aspartic acid	$C_4H_7O_4N$	–	185.8	–	–786.7	–973.3[f]	–972.5
VIII	Glutamic acid	$C_5H_9O_4N$	–	194.5	–	–807.4	–1003.3[g]	–1001.9
IX	Asparagine	$C_4H_8O_3N_2$	–	200.6	–	–590.5	–789.0[f]	–791.1
X	Glutamin	$C_5H_{10}O_3N_2$	–	209.3	–	–611.2	–825.5[h]	–820.5

[a] Data of [12]. [b] Data of [13]. [c] Data of [14]. [d] Data of [15]. [e] Data of [16]. [f] Data of [17]. [g] Data of [18]. [h] Data of [19]. [i] DL form.

crystal state were obtained on the basis of data reported in [22] analogously by Enthalpy program [20] (Table 1). Good correlation between experimental data and computed values of the enthalpies of formation of all compounds is established.

Experimental definition of a heat of sublimation, another important thermochemical characteristic of the amino acids, causes significant technical difficulties [23] and empirical methods of computation are insufficient [24–26]. Thus we used the following thermodynamic equation [23] for computation of the heat of sublimation:

$$\Delta H^0_{subl} = \Delta H^0_{form}(gas) - \Delta H^0_{form}(cryst),$$

where ΔH^0_{form}(gas) is the heat of formation of a compound in the gas state; ΔH^0_{form}(cryst) is the heat of formation of a crystal substance in the standard state; ΔH^0_{subl} is heat of sublimation under standard conditions (T = 298 K). Thus we computed the heat of sublimation of all amino acids listed in Table 1. Only in case of valine **III** and isoleucine **V** (Table 1) we obtained an incomplete correlation of the compared characteristics while for the other compounds of Table 1 the correlation between experimental and computed values of the heat of sublimation are quite good.

Table 2. Group increments X_i for computation of heat of formation for compounds in gas phase (kJ mol^{-1}) and a standard deviation

Group increment	X_i, kJ mol^{-1}	σ
C–(CO)(N)(H)$_2$	–18.1	0.17
C–(C)(CO)(N)(H)	–1.8	0.01
CO–(C)(N) + N–(CO)(H)$_2$	–195.8	0.10

Incomplete correlation between experimental and computed value of ΔH_{subl} in the case of valine **III** may be attributed to a fault of its experimental measurement since this compound possesses the largest value of the heat of sublimation (162.8 kJ mol^{-1}) in the series of amino acids despite compounds with significantly larger chemical structure and molecular weight exist in this series. Therefore we can conclude that experimental value of the heat of sublimation of valine **III** in Table 1 is evidently too high.

On the contrary in the case of isoleucine **V** too low experimental value of the heat of sublimation (120.1 kJ mol^{-1}) was found in comparison with our computed value (157.9 kJ mol^{-1}). The discrepancy between the experimental value of ΔH_{subl} of isoleucine **V** and the calculated figure was apparently due to the measurements in [13] carried out at the temperature 455 K instead of standard temperature 298 K. Evidently the higher measuring temperature of the heat of sublimation the lesser value of the heat of sublimation [23].

Hence the computed value of the heat of sublimation for valine **III** and isoleucine **V** presented in the Table 1 should be considered as the more reliable.

During our studies we performed an ab initio computation of the thermochemical characteristics of all amino acids listed in Table 1. We executed quantum-chemical computations of the heat of formation of the amino acids by Gaissuan 98 program [27] for gas phase when each molecule was not subjected to influences of adjacent molecules (unfortunately the modern quantum-chemical methods of an investigation in liquid or solid phase are still unreliable). The computation was executed with overall optimization of the all geometric parameters of the molecules. A correspondence of the found structures to energy minima was proved by positive characteristic values of Hesse matrix.

As systematic quantum-chemical examination of the thermochemical characteristics of L-α-amino acids was carried out for the first time we had to test for the start the applicability of quantum-chemical methods. It was known from the literature (e.g., [28, 29]) that hybrid method of the density functional theory (DFT) B3LYP [30-32] for small organic molecules results in values of the thermochemical characteristics that sufficiently good correlate with experimental data. But in our case an error of given method at a computation of ΔH^0_{form} of amino acids was significant (Table 3). Even using an extended range of B3LYP/6-311++G(df,p) [33, 34] at the computation of the heat of formation of the amino acids relative error in a series of compounds (in comparison with results of an additive calculation) was equal to 8.4–40.3%. Hence we computed H^0_{form} of compounds by several other methods (Table 3).

Calculations according to MP2 method [35, 36] in different basies result in unrealistic values of the heat of formation of the amino acids: therefore also taking into account the laboriousness of the procedure we rejected further the application of MP2. We tested relatively new DFT method PW91PW91 [37] with different basises however its results poorly correlated with ΔH^0_{form} obtained by additive scheme (Table 1, 3). Using hybrid method B3PW91 [38] we obtained significantly better correlation; thereby an accordance of computed results with the data calculated by the additive scheme (Table 1, 3) was distinctly improved at a basis enlargement. So the relative error in the compound series (in comparison with the data of the additive computation) was 0.7–12.3%.

The best correlation with the result computed by the additive scheme we obtained employing G2 [39] and G3 [40] methods. These computation schemes were elaborated by Curtiss et al. specifically for maximum exact computation of the thermochemical characteristics of molecules. The values of the heat of formation for the examined amino acids were computed only for glycine **I** and alanine **II** because of laboriousness of these schemes. We intend to perform this computation in further investigations.

Thus we obtained the most reliable results of the thermochemical parameter computation using the group increment method, B3PW91/6-311++G(3df,3pd) method, and the computation schemes G2 and G3.

The approach presented in this paper may be applied further to the computation of the thermo-

Table 3. Results of ab initio computations of the heat of formation for L-α-amino acids , kJ mol^{-1}

Comp. no.	$-\Delta H^0_{form}$(gas), kJ mol^{-1}										
	B3LYP/ 6-31G(d)	B3LYP/ 6-311++ G(df,p)	B3PW91 /6-31G(d)	B3PW91/ 6-311++ G(df,p)	B3PW91/ cc-pVTZ	B3PW91/ 6-311++ G(3df,3pd)	PW91PW91/ 6-31G(d)	PW91PW91/ 6-311++ G(df,p)	PW91PW91/ 6-311++ G(3df,3pd)	G2	G3
I	340.5	357.2	351.8	373.1	384.5	403.8	529.6	530.9	561.3	401.0	391.8
II	360.9	367.9	379.7	393.4	407.5	427.9	585.9	574.4	608.5	433.0	424.1
III	384.9	372.8	419.4	418.6	438.8	461.4	684.0	646.8	689.3	–	–
IV	400.4	380.3	443.2	435.9	459.3	483.2	733.9	685.3	732.2	–	–
V	392.8	371.5	435.4	427.5	450.7	474.7	728.3	678.6	725.5	–	–
VI	196.8	180.2	287.5	287.0	311.2	339.2	684.0	634.5	686.1	–	–
VII	684.3	694.0	722.6	743.7	762.5	794.7	1051.1	1035.9	1086.2	–	–
VIII	702.9	703.7	749.6	763.6	785.8	818.9	1105.3	1077.7	1132.1	–	–
IX	500.8	522.4	532.6	563.9	579.6	612.6	859.3	856.2	904.0	–	–
X	514.3	527.4	555.0	579.0	598.5	632.0	907.9	892.7	944.8	–	–

chemical characteristics of amino acids of various structures.

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