ISSN 1070-3632, Russian Journal of General Chemistry, 2011, Vol. 81, No. 4, pp. 701–703. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © E.V. Sagadeev, A.A. Gimadeev, D.V. Chachkov, V.P. Barabanov, 2011, published in Zhurnal Obshchei Khimii, 2011, Vol. 81, No. 4, pp. 609–611.

Empirical and *ab initio* Calculations of Thermochemical Parameters of Amino Acids: III.[1] Non-Standard Amino Acids: Monoaminomonocarboxylic, Monoaminodicarboxylic, and Diaminomonocarboxylic Acids

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, Tatarstan, 420015 Russia*
e-mail: sagadeev@list.ru

[b] *Kazan Branch of the Interdepartmental Supercomputer Center, Russian Academy of Sciences, Kazan, Tatarstan, Russia*

Received March 25, 2010

Abstract—The main thermochemical parameters of sixteen non-standard L-α-amino acids of monoamino-monocarboxylic, monoaminodicarboxylic, and diaminomonocarboxylic series were calculated using complex computational methods.

DOI: 10.1134/S107036321104013X

To date, there are over one hundred and seventy amino acids of various structures [1, 2]. Of these, twenty standard amino acids are involved in protein biosynthesis. The remaining non-standard (non-protein) amino acids exist in biological organisms in the free or bound form. They are involved in various biochemical processes, but almost never are a part of protein [2, 3]. Non-standard amino acids are quite diverse in their chemical structure. Often they are the derivatives of some standard amino acids. For example, collagen contains a non-standard amino acid 5-hydroxylysine **XVI** (see the table), which is a derivative of the standard amino acids lysine [3]. Ornithine **XIV** and citrulline **XV** (see the table) are important intermediates in the synthesis of the amino acid arginine [3], etc.

Analysis of the published data shows that the number of experimental and theoretical research in the field of thermochemistry of unusual amino acids is minimal. In the the table we collected almost all published thermochemical data for these classes of compounds. It should be noted that the experimental values of enthalpies of formation of amino acids in the gas phase are totally absent in the literature. Therefore, in continuation of the previously initiated studies on the calculation of thermochemical parameters of amino acids [9, 10], we calculated the thermochemical characteristics of sixteen non-standard *L*-α-amino acids. For this purpose we used the calculation method described in detail in [9, 10].

The calculation by the additive scheme of formation enthalpies of amino acids in the crystalline state and in the gas phase was performed using the program Enthalpy [11] on the basis of the published [12-14] and calculated by us earlier [9, 10] group contributions. The results of these calculations are listed in the table. Analyzing the results, one can see that there is a good agreement between the experimental and the calculated enthalpy values of all compounds.

Similar to [9, 10], sublimation enthalpies of amino acids were calculated from the difference in the formation enthalpies of compounds in the gas phase and in the crystalline state. Analysis of the data in the table shows that in both cases the correspondence between the experimental and calculated values of sublimation enthalpies of the compounds is not sufficient.

So, in case of butyrine **I** and norvaline **II** we observe that the experimental values of sublimation enthalpy (131.8 and 121.1 kJ mol^{-1}) are low compared with our calculated values (148.4 and 157.0 kJ mol^{-1},

[1] For communication II, see [1].

Calculated and experimental enthalpies of formation and sublimation for non-standard *L*-α-amino acids, kJ mol^{-1}

Comp. no.	Compound	Formula	ΔH^0_{subl} (calculated)	ΔH^0_{form} (calculated)				
				crystal state	gas phase			
				additive scheme	additive scheme	B3LYP/ 6-31G(d)	B3PW91/ cc-pVTZ	B3PW91/ cc-pVQZ
	Monoaminomonocarboxylic acids							
I	2-Aminobutyric acid (butyrine)	$C_4H_9O_2N$	148.4[a]	–585.0[b]	–436.6	–374.1	–424.7	–436.2
II	Norvaline	$C_5H_{11}O_2N$	157.0[c]	–614.4	–457.4	–387.2	–441.8	–454.6
III	Norleucine	$C_6H_{13}O_2N$	165.7	–643.8[d]	–478.1	–400.2	–459.1	–473.3
IV	2-Amnio-3-phenylbutyric acid	$C_{10}H_{13}O_2N$	161.5	–489.4	–327.9	–209.5	–324.9	–343.7
V	3,4-Dihydroxyphenylalanine	$C_9H_{11}O_4N$	209.0	–870.8	–661.8	–505.6	–652.7	–674.7
	Monoaminodicarboxylic acids							
VI	4-Methylglutamic acid	$C_6H_{11}O_4N$	194.4	–1030.6	–836.2	–712.9	–798.3	–814.7
VII	3-Hydroxyglutamic acid	$C_5H_9O_5N$	226.7	–1201.2	–974.5	–851.4	–946.4	–962.8
VIII	2-Aminoadipic acid	$C_6H_{11}O_4N$	203.2	–1031.3	–828.1	–713.8	–801.1	–818.1
IX	2-Amino-4-hydroxyadipic acid	$C_6H_{11}O_5N$	235.4	–1230.6	–995.2	–863.4	–963.9	–982.1
X	2-Aminopimelic acid	$C_7H_{13}O_4N$	211.8	–1060.7	–848.9	–728.1	–819.6	–838.0
XI	2-Amino-4-hydroxypimelic acid	$C_7H_{13}O_5N$	244.2	–1260.1	–1015.9	–883.5	–988.7	–1008.1
	Diaminomonocarboxylic acids							
XII	3-Aminoalanine	$C_3H_8O_2N_2$	207.5	–588.8	–381.3	–310.2	–372.2	–386.6
XIII	4-Aminobutyrine	$C_4H_{10}O_2N_2$	216.2	–618.2	–402.0	–314.8	–382.8	–399.0
XIV	Ornithine	$C_5H_{12}O_2N_2$	224.9	–647.6[e]	–422.7	–328.6	–400.7	–417.5
XV	Citrulline	$C_6H_{13}O_3N_3$	192.7	–825.0	–632.3	–520.3	–617.2	–639.9
XVI	5-Hydroxylysine	$C_6H_{14}O_3N_2$	265.9	–876.4	–610.5	–491.6	–584.5	–605.0

[a] Experiment 131.8 kJ mol^{-1} (*DL*-form) [4]. [b] Experiment –580.6 kJ mol^{-1} (*DL*-form) [5]. [c] Experiment 121.1 kJ mol^{-1} (*DL*-form) [6]. [d] Experiment –639.1 kJ mol^{-1} [7]. [e] Experiment –652.6 kJ mol^{-1} [8].

respectively). The reason for the observed inconsistency is due apparently to the fact that the ΔH_{subl} for both compounds was determined at elevated temperature rather than under standard conditions at 298 K. Thus, the sublimation enthalpy of butyrine **I** was determined at 409 K [4], and ΔH_{subl} value for norvaline **II** was obtained at 455 K [6]. As noted previously [9, 10], ΔH_{subl} value decreases as the determination temperature increases. Therefore, for butyrine **I** and norvaline **II** the calculated enthalpies of sublimation given in the table should be probably regarded as the most reliable.

Further, we performed *ab initio* calculations of gas-phase formation enthalpies of the amino acids. Based on the results of [9, 10] we chose the B3LYP/6-31G(d) method to calculate ΔH^0_{form} to accelerate the search for the most energetically favorable conformations of the molecules, as well as B3PW91/cc-pVTZ and B3PW91/cc-pVQZ methods. Analyzing the data in the

table, one can see that the average difference between the values of ΔH^0_{form} obtained by B3PW91/cc-pVTZ compared with those of the additive calculation is 20.7 kJ mol^{-1}, while the method B3LYP/6-31G(d) gives the difference 107.1 kJ mol^{-1}, despite the fact that the average computation time of ΔH^0_{form} using B3PW91/cc-pVTZ method is only twice more than the time of B3LYP/6-31G(d) calculation. As noted earlier [10], among the used quantum-chemical DFT-calculation methods for ΔH^0_{form} of amino acid the B3PW91/cc-pVQZ method is the most accurate one. Thus, the average difference between the ΔH^0_{form} values obtained by B3PW91/cc-pVQZ and the data of additive calculation is only 8.6 kJ mol^{-1}. However, in this case the calculation time for ΔH^0_{form} of amino acids by B3PW91/cc-pVQZ grows very significantly, up to fifty times, compared with the B3LYP/6-31G(d) method. By the example of the studied classes of compounds it is interesting to note the fact that for ΔH^0_{form} of amino acids, containing in the structure phenyl fragment, the calculation method B3PW91/cc-pVTZ gives more accurate results than the method B3PW91/cc-pVQZ. For example, the difference in the values of ΔH^0_{form} of compounds **IV** and **V** obtained according to the additive calculation is 3.0 and 9.1 kJ mol^{-1} in comparison with the results obtained by B3PW91/cc-pVTZ method, and by B3PW91/cc-pVQZ method: 15.8 and 12.9 kJ mol^{-1}, respectively. This fact we have already reported [10].

Hence, the established in the present work regularities can be used further for obtaining reliable calculations of the thermochemical parameters of amino acids for which the corresponding experimental data are absent.

All quantum-chemical calculations were carried out within the program Gaussian 98 [15] in the Kazan Branch of the Interdepartmental Supercomputer Center of the Russian Academy of Sciences.

REFERENCES

1. Grinstein, G. and Vinicius, M., *Khimiya aminokislot i peptidov* (Chemistry of Amino Acids and Peptides), Moscow: Mir, 1965.
2. Greene, N., Stout, W., and Taylor, D., *Biologiya* (Biology), Moscow: Mir, 1990, vol. 1.
3. Lenindzher, A., *Osnovy biokhimii* (Principles of Biochemistry), Moscow: Mir, 1985, vol. 1.
4. De Kruif, C.G., Voogd, J., and Offringa, J.C.A., *J. Chem. Thermodynamics*, 1979, vol. 11, no. 7, p. 651.
5. Yang, X.W., Liu, J.R., Gao, S.L., Hou, Y.D., and Shi, Q.Z., *Thermochim. Acta*, 1999, vol. 329, no. 2, p. 109.
6. Svec, H.J. and Clyde, D.D., *J. Chem. Eng. Data,* 1965, vol. 10, p. 151.
7. Strepikheev, A.A., Skuratov, S.M., Shtekher, S.M., Muromova, R.S., Brykina, E.P., and Kachin, O.N., *Dokl. Akad. Nauk SSSR*, 1955, vol. 102, no. 1, p. 543.
8. Ponomarev, V.V. and Migarskaya, L.B., *Zh. Fiz. Khim.,* 1960, vol. 34, no. 11, p. 2506.
9. Sagadeev, E.V., Gimadeev, A.A., Chachkov, D.V., and Barabanov, V.P., *Zh. Obshch. Khim.,* 2009, vol. 79, no. 3, p. 464.
10. Sagadeev, E.V., Gimadeev, A.A., Chachkov, D.V., and Barabanov, V.P., *Zh. Obshch. Khim.,* 2009, vol. 79, no. 7, p. 1133.
11. Sagadeev, E.V. and Safina, Yu.G., *Zh. Fiz. Khim.,* 2002, vol. 76, no. 9, p. 1565.
12. Cohen, N. and Benson, S.W., *Chem. Rev*., 1993, vol. 93, no. 7, p. 2419.
13. Cohen, N., *J. Phys. Chem. Ref. Data*, 1996, vol. 25, no. 6, p. 1411.
14. Domalski, E.S. and Hearing, E.D., *J. Phys. Chem. Ref. Data*, 1993, vol. 22, no. 4, p. 805.
15. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, J.A., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui Q., Morokuma, K., Malick, D. K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Baboul, A.G., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, M.A., Nanayakkara, A., Gonzalez, C., Challacombe, C., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Andres, J.L., Gonzalez, C., Head-Gordon, M., Replogle, E.S., and Pople, J.A., *Gaussian 98*, Gaussian Inc. Pittsburgh PA, 1998.