

[CONTRIBUTION FROM THE WILLIAM G. KERCKHOFF LABORATORIES OF THE BIOLOGICAL SCIENCES, CALIFORNIA INSTITUTE OF TECHNOLOGY]

THERMAL DATA. I. THE HEAT CAPACITIES, ENTROPIES AND FREE ENERGIES OF SEVEN ORGANIC COMPOUNDS CONTAINING NITROGEN

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We have recently begun in this Laboratory a systematic study of some of the thermal properties of physiologically important organic compounds. These investigations are to include studies of low temperature heat capacities and heats of combustion. The data thus obtained may be utilized to calculate the entropies and free energies of the compounds by means of the third law of thermodynamics and the fundamental thermodynamic equation $\Delta F = \Delta H - T\Delta S$. In this paper are presented the low temperature specific heat data for the following seven compounds: *d*-alanine, *l*-asparagine, *l*-asparagine hydrate, *l*-aspartic acid, *d*-glutamic acid, creatine and creatinine. We have also included the corresponding entropies and free energies calculated from these data by means of the third law of thermodynamics.

Materials

d-Alanine.—This material was placed at our disposal for this investigation by the Hoffmann-La Roche Laboratories, Nutley, New Jersey. It was subjected to several crystallizations from water by adding a large excess of alcohol. The resulting material gave theoretical values for total nitrogen. The specific rotation of the hydrochloride was, α_D^{20} 10.1°.

l-Asparagine Hydrate.—Material obtained from Merck was subjected to a number of fractional crystallizations by rapidly cooling the hot aqueous solution to prevent racemization. The Kjeldahl analysis gave the theoretical results within the error of the method. A solution, having a volume of 25 cc. at 20°, containing 10% hydrochloric acid and 2.5236 g. of the monohydrate gave the rotation α_D^{20} 27.0°.

l-Asparagine Hydrate.—The hydrated acid described above was dried in an oven at 100–110° to a constant weight.

l-Aspartic Acid.—An Eastman product was recrystallized seven times. The sample gave the theoretical values for nitrogen and free amino groups. A solution containing in 25 cc. at 20°, 2.2903 g. of this acid, and 3 mole equivalents of hydrochloric acid gave a rotation α_D^{20} 26.42°.

d-Glutamic Acid.—This material was prepared from Ajinomoto according to the method of Schmidt and Foster.¹ The final product gave the theoretical values for nitrogen and free amino groups. A solution containing in 25 cc. at 20°, 1.269 g. of the acid and 0.2483 g. of hydrochloric acid gave the rotation α_D^{20} 31.1.

Creatine.—A Pfanstiehl product was subjected to several fractional crystallizations. The final product gave the theoretical values for nitrogen.

Creatinine.—A very pure Pfanstiehl product was further purified by the methods of Edgar and Hinegardner.² The resulting product gave the theoretical values for nitrogen.

¹ Schmidt and Foster, *J. Exp. Biol. Med.*, **18**, 205 (1920–1921).

² Edgar and Hinegardner, *J. Biol. Chem.*, **56**, 881 (1923).

Method and Apparatus

In principle the method of Nernst was employed with an aneroid calorimeter to determine the "true" specific heats. The details of the method and apparatus have been described elsewhere,³ so that only a brief description is necessary.

In brief it consists of supplying a measured amount of heat electrically to a copper calorimeter which contains the substance under investigation. The change in temperature is measured by a calibrated copper-constantan thermocouple. All electrical measurements are made on a White double potentiometer in conjunction with a sensitive galvanometer. Time measurements are made with an accurately calibrated stop watch.

To promote rapid attainment of thermal equilibrium, the compound under investigation is compressed into dense pellets and these are spaced in the calorimeter by means of thin copper disks.

In view of the accuracy of the various measurements involved, the error in the specific heats is probably less than 1%.

The specific heat data in terms of the 15° calorie⁴ and with all weights reduced to a vacuum basis appear in Table I.

TABLE I
SPECIFIC HEATS

<i>d</i> -Alanine: Crystalline							
Temp., °K.	84.4	89.2	96.2	104.2	111.7	119.5	134.6
C_p per g.	0.121	0.127	0.135	0.146	0.154	0.163	0.180
Temp., °K.	149.2	165.4	179.9	200.1	219.9	239.8	260.0
C_p per g.	0.194	0.209	0.222	0.241	0.258	0.275	0.292
Temp., °K.	275.1	276.3	281.2	289.6	296.8		
C_p per g.	0.306	0.306	0.310	0.318	0.324		
<i>l</i> -Asparagine							
Temp., °K.	85.1	89.3	95.4	102.5	110.8	119.8	134.7
C_p per g.	0.109	0.114	0.120	0.128	0.136	0.145	0.158
Temp., °K.	149.9	170.3	190.4	208.8	230.3	252.1	276.2
C_p per g.	0.171	0.188	0.204	0.219	0.236	0.254	0.273
Temp., °K.	282.1	290.2	296.5				
C_p per g.	0.277	0.284	0.289				
<i>l</i> -Asparagine Hydrate							
Temp., °K.	90.4	94.1	108.3	140.1	169.4		
C_p per g.	0.120	0.125	0.141	0.175	0.206		
Temp., °K.	199.9	239.3	276.2	286.2	296.7		
C_p per g.	0.236	0.274	0.309	0.317	0.328		

³ Parks, THIS JOURNAL, 47, 338 (1925).

⁴ The factor 0.2390 was used for converting joules to calories.

TABLE I (Concluded)

l-Aspartic Acid								
Temp., °K.	88.2	91.7	98.2	109.1	123.8	139.6	159.9	179.9
C_p per g.	0.112	0.116	0.123	0.133	0.146	0.159	0.175	0.190
Temp., °K.	199.8	220.3	249.4	278.1	283.2	287.3	293.9	
C_p per g.	0.205	0.220	0.242	0.262	0.266	0.269	0.274	
d-Glutamic Acid								
Temp., °K.	90.8	95.3	101.6	108.4	117.1	130.4	145.4	159.8
C_p per g.	0.114	0.119	0.126	0.133	0.141	0.153	0.166	0.177
Temp., °K.	179.6	200.3	220.4	250.2	275.9	280.3	286.2	294.6
C_p per g.	0.192	0.210	0.224	0.246	0.266	0.269	0.274	0.281
Creatine								
Temp., °K.	86.9	91.8	97.2	112.9	126.6	140.3	159.8	179.8
C_p per g.	0.123	0.128	0.134	0.150	0.164	0.176	0.193	0.212
Temp., °K.	200.6	220.4	239.7	258.6	277.2	282.3	289.7	296.3
C_p per g.	0.230	0.248	0.265	0.280	0.295	0.300	0.306	0.312
Creatinine								
Temp., °K.	86.8	90.0	95.1	104.9	115.8	130.2	149.9	170.7
C_p per g.	0.124	0.128	0.134	0.143	0.154	0.166	0.181	0.196
Temp., °K.	189.7	210.6	229.5	275.8	282.6	289.8	296.5	
C_p per g.	0.210	0.226	0.240	0.276	0.281	0.287	0.292	

Discussion

Entropies of the Compounds.—Using the data in Table I we have calculated the molal entropies at 298.1°K. for these compounds. In these calculations we have used the extrapolation method of Kelley, Parks and Huffman⁵ to calculate the entropy at 90°K. For the entropy change between 90 and 298°K. the usual method of graphical integration was employed. The results of these calculations appear in Table II; column 2 is the entropy increment from 0 to 90°K., column 3 the entropy change between 90 and 298°K. from the experimental values, and column 4 the entropy at 298°K.

TABLE II
ENTROPIES OF THE COMPOUNDS

Substance	S_{90}	$\Delta S_{90-298.10}$	$S_{298.10}$
d-Alanine	8.88	22.77	31.6
l-Asparagine	11.90	29.84	41.7
l-Asparagine hydrate	13.57	37.46	51.0
l-Aspartic acid	12.21	29.28	41.5
d-Glutamic acid	13.00	32.73	45.7
Creatine	13.31	31.99	45.3
Creatinine	13.38	26.66	40.0

In several cases we are now able to determine the effect of substituting an amino group for hydrogen and the hydroxyl group in the molecule. If

⁵ Kelley, Parks and Huffman, *J. Phys. Chem.*, **33**, 1802 (1929).

we consider succinic acid, aspartic acid and asparagine, we find that the last two may be derived from the first by the successive change of a hydrogen and an hydroxyl to amino groups. The entropies of these compounds at 298° are, respectively, 42.0, 41.5 and 41.7 E. U.⁶ Since the extreme difference in these values is within the probable error, we feel justified in stating that there is no change in the entropy of a compound for substitutions of this type.

In two cases we have been able to obtain the effect of lengthening the carbon chain. We find a difference of 5.5 E. U. between *d*-alanine and glycine⁷ and a difference of 4.2 E. U. between glutamic acid and aspartic acid. These effects are of the same order of magnitude as found by Parks and Huffman and their collaborators in studies of various organic compounds.

The Free Energies.—We have also calculated the free energies of these seven compounds from the fundamental thermodynamic equation $\Delta F = \Delta H - T\Delta S$. The essential data are given in Table III. With the

TABLE III
THERMAL DATA AT 298.1°K.

The 15° cal. is used throughout and all weights are reduced to vacuum.

Substance	Heat of combustion at constant pressure, cal.	ΔH_{298} , cal.	ΔS_{298} , E. U.	ΔF_{298} , cal.
<i>d</i> -Alanine	387,200	-134,600	-153.5	-88,800
<i>l</i> -Asparagine	463,100	-187,100	-207.7	-125,200
<i>l</i> -Asparagine hydrate	459,400	-259,100	-254.2	-183,300
<i>l</i> -Aspartic acid	384,700	-231,300	-193.9	-173,500
<i>d</i> -Glutamic acid	542,200	-236,400	-222.3	-170,200
Creatine	555,200	-129,200	-218.2	-64,100
Creatinine	563,200	-52,800	-167.6	-2,900

exception of creatine we have used the heats of combustion as given in the "International Critical Tables"⁸ corrected to 25°. For creatine we have used the value of Emery and Benedict,⁹ since the value for creatinine appearing in the "I. C. T." is also that of these workers. Hence the results of the free energy calculations should be on a more comparable basis. These values were then employed in conjunction with 68,310 cal.¹⁰ and 94,240 cal.,¹¹ respectively, for the heats of combustion of hydrogen and graphitic carbon. The values of ΔS , the entropy of formation, were obtained by subtracting from the S_{298} values the corresponding values of the elements contained therein. We have used for the entropies of the elements the

⁶ Parks and Huffman, *THIS JOURNAL*, **52**, 4381 (1930).

⁷ Parks and Huffman, "The Free Energies of Some Organic Compounds," The Chemical Catalog Co., New York, 1932.

⁸ "International Critical Tables," Vol. V, p. 167.

⁹ Emery and Benedict, *Am. J. Physiol.*, **28**, 301 (1911).

¹⁰ Rossini, *Bur. Standards J. Research*, **6**, 34 (1931).

¹¹ Roth and Naeser, *Z. Electrochem.*, **31**, 461 (1925).

values 1.3,¹² 15.6,¹³ 22.9¹⁴ and 24.5¹⁵ E. U. per gram atom, respectively, for carbon, hydrogen, nitrogen and oxygen.

In view of the accuracy of the measurements involved, we feel that the uncertainty in the $T\Delta S$ term cannot in any case exceed ≈ 300 calories. The accuracy with which the heats of combustion of carbon and hydrogen are now known should preclude any great uncertainty due to their use even in the largest molecules considered. Consequently we feel that the accuracy of the free energy values is limited largely by the accuracy of the combustion data. A study of these values where more than one worker has burned the compound will show differences from 2000 to 4000 calories per mole.

Summary

1. The heat capacities of seven nitrogen-containing organic compounds have been measured over the temperature range 90 to 298°K.
2. The entropies of these seven compounds have been calculated from the heat capacity data.
3. The free energies of these compounds have been calculated and their accuracy was found to have been limited largely by the accuracy of the combustion data.

¹² Lewis and Gibson, *THIS JOURNAL*, **39**, 2581 (1917).

¹³ Giauque, *ibid.*, **52**, 4816 (1930).

¹⁴ Giauque, private communication.

¹⁵ Giauque and Johnston, *THIS JOURNAL*, **51**, 2300 (1929).

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DESULFURIZATION OF THIOUREAS BY BROMATE AND IODATE SOLUTIONS

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In preparing thioureas for the purpose of studying desulfurization effects on them by bromate and iodate solutions, it was observed that certain bases, though closely related, either do or do not react with phenyl mustard oil or with thiocyanic acid to yield the corresponding thioureas. For example, while *m*-nitroaniline¹ easily yields phenyl-*m*-nitrophenylthiourea, the corresponding thioureas could not be formed with ortho- or with para-nitroaniline, either by direct heating or in solvents. By direct heating the *p*-nitroaniline, however, gave thiocarbanilide and di-*p*-nitrophenylthiourea²

¹ Brückner, *Ber.*, **7**, 1235 (1874); Losanitsch, *ibid.*, **14**, 2365 (1881); Kjellin, *ibid.*, **36**, 197 (1903).

² For similar product formed by heating 3-nitrothiocarbanilide, see Elbs and Schlemmer, *J. prakt. Chem.*, [2] **27**, 480 (1883).