Molar Heat Capacities, Thermodynamic Properties, and Thermal Stability of *trans*-4-(Aminomethyl)cyclohexanecarboxylic Acid

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The low-temperature heat capacities of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid were measured with an adiabatic calorimeter over the temperature range from (82 to 378) K. The heat capacity curve was smooth and continuous, which indicated that the compound was stable over the whole temperature range. Thermal decompositions of the compound were studied by thermogravimetry (TG) and the possible mechanism of the thermal decomposition was deduced. The energy of combustion of the compound was determined, and the standard enthalpy of combustion, $\Delta_c H^{\Theta}$, and standard enthalpy of formation, $\Delta_f H^{\Theta}$, were calculated.

Introduction

trans-4-(Aminomethyl)cyclohexanecarboxylic acid is used as a medicine to resist fibrinolysis, and it is also an indispensable protease of the cruor system of biology, which has a great effect on hemostasia of wounds.[1] There are many reports on its remarkable styptic effect. The derivatives of the compound are concerned with their dissolution kinetics, styptic mechanism, absorbing processes, and its pharmacology in the body. However, themodynamic properties such as molar heat capacities and enthalpy of formation, which are the fundamental data of a medicine, have not been reported. In this work, the low-temperature heat capacities and energy of combustion of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid were determined using a small-sample precision automated adiabatic calorimeter and a static bomb combustion calorimeter. The enthalpy of formation was derived from the energy of combustion.

Experimental Section

trans-4-(Aminomethyl)cyclohexanecarboxylic acid (CAS Registry No. 56-91-7) was supplied by Dongting Pharmaceutical Co., Ltd., People's Republic of China. The purity of the sample was determined to be 99.5 % by titration.[2]

To recrystallize the compound, the product was dissolved by hydrochloric acid and the solution was concentrated by heating on a water bath, until crystals formed. Then, acetone was added, and the solution was stirred and placed in a desiccator filled with phosphorus pentaoxide for 3 min. Finally, the product was filtered, washed by acetone twice, and dried at l05 °C. The melting point of the final product was determined to be (247 to 25l) °C by a melting-point meter (model X-5, Taike, Beijing, China), which was consistent with ref 2.

Adiabatic Calorimeter. Heat capacity measurements were performed with a small-sample automatic adiabatic calorimeter. The calorimeter consists of a sample cell, inner and outer adiabatic shields, a platinum resistance thermometer, an electric heater, two sets of differential thermocouples, and a high-vacuum can. The principle and structure of the calorimeter were described previously in detail elsewhere.[3−7] Liquid nitrogen was used as the cooling medium.

To verify the reliability of the adiabatic calorimeter, the molar heat capacities for the reference standard material α-Al_2O_3 were measured. The results showed that the deviation of our calibration data from those of NIST was within ±0.3 % in the temperature range of (80 to 400) K.

The mass of the sample for heat capacity measurements was (1.89480 ± 0.00001) g, equivalent to (12.0526 ± 0.00006) mmol on the basis of a molar mass of 157.21 g·mol^{-1}.

Thermogravimetry (TG) Analysis. A thermogravimetric analyzer (model TGA/SDTA 851e, Mettler Toledo, Greifensee, Switzerland) was used for TG measurements under high purity (99.99 %) nitrogen atmosphere with a flow rate of 60 mL·min^{-1}. The heating rate was 10 K·min^{-1}.

Combustion Reaction Isoperibol Calorimeter.[8,9] The constant volume combustion energy was determined by the precision oxygen bomb (WGR-type1, made in Changsha, Hunan). The main experimental procedures were as follows: the room temperature was regulated to (298 ± 1) K; the temperature of the outer casing water (12.0 L) bath of the oxygen bomb was controlled at (298.15 ± 0.005) K; the water (2.0 L) temperature in the calorimetric vessel was adjusted to be lower than that of the outer casing. The sample was put into the crucible that was fixed onto the support in the oxygen bomb, the determined combustion Fe wire was fixed in the bomb, the initial bomb solution (10 mL of determined distilled water) was poured into the oxygen bomb, about 2.0 MPa of oxygen was filled after the bomb had been sealed, and a constant rate of temperature change of the calorimeter was maintained when the experiment started, and the temperature was read every 30 s and recorded 20 times. At the 20th time, the compound was fired and the temperature was read every minute until the temperature changed at a constant rate. Then, the temperature was read every 30 s and recorded 20 times.

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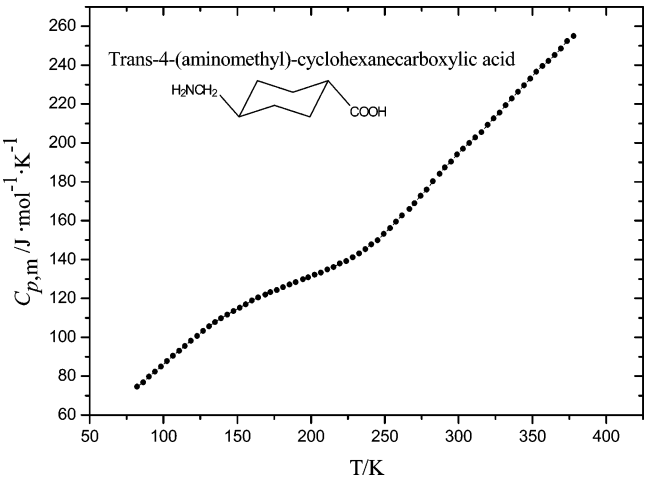


Figure 1. Experimental molar heat capacity curve of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid.

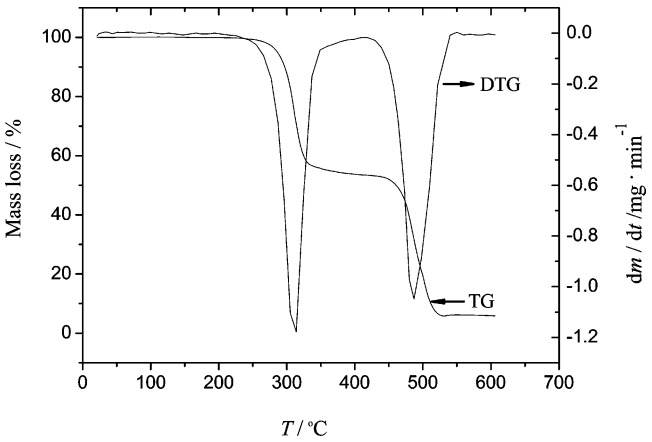


Figure 2. TG/DTG curve of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid under nitrogen atmosphere.

The fittings and the inside wall of the bomb were washed by quadratic distilled water. Then the bomb solution (including the washing solution) was transferred completely to a cone bottle. It was titrated to the final point of phenolphthalein using the standard solution of NaOH (0.1 mol·L^{-1}). Then, the corrected enthalpy of nitric acid was obtained on the basis of the results.

The energy equivalent of the calorimeter was calculated according to the equation

$$w = \frac{Qa + Gb + 5.893c}{\Delta T} \quad (1)$$

where w (J·K^{-1}) is the energy equivalent of the calorimeter; Q (J·g^{-1}) is the combustion enthalpy of benzoic acid (99.9 %); a (g) is the mass of the determined benzoic acid; G (6700 J·g^{-1}) is the enthalpy of combustion of Fe wire for ignition; b (g) is the mass of actual Fe wire consumed; 5.893 (J·mL^{-1}) is the summation of the enthalpy of formation, $\Delta_f H_{(HNO_3)}$, and the enthalpy on dilution, $\Delta_{dil} H_{(HNO_3)}$, of nitric acid, when the nitric acid was titrated by 1.0 mL of NaOH (0.1 mol·L^{-1}); c (mL) is the volume of consumed NaOH (0.1 mol·L^{-1}) solution; and ΔT is the corrected value of the temperature rise. The correct value of the heat exchange was calculated by the figure of Reynolds temperature corrected.[10]

Results and Discussion

Heat Capacity. Low-temperature molar heat capacities of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid were measured by the adiabatic calorimeter over the temperature range from (82 to 378) K (Figure 1 and Table 1). The heat capacity data are fitted to the following polynomial in reduced temperature (X) by means of the least-squares fitting.[11]

Table 1. Experimental Molar Heat Capacities of the Compound (M = 157.21 g·mol^{-1})

T/K	$C_{p,m}$/J·K^{-1}·mol^{-1}	T/K	$C_{p,m}$/J·K^{-1}·mol^{-1}	T/K	$C_{p,m}$/J·K^{-1}·mol^{-1}
82.12	74.70	181.09	125.84	282.51	180.30
86.25	76.89	185.38	127.19	286.62	184.12
90.28	79.76	189.63	128.43	290.75	187.46
94.31	82.40	193.83	129.90	294.85	190.40
98.35	85.00	198.09	130.84	298.94	194.15
102.41	87.81	202.43	132.24	303.01	197.05
106.49	90.49	206.76	133.38	307.17	200.02
110.60	93.05	211.06	134.92	311.37	202.88
114.62	95.54	215.33	136.11	315.53	205.54
118.68	98.24	219.57	138.00	319.67	209.32
122.78	100.67	223.88	139.22	323.79	212.66
126.81	103.29	228.26	141.19	327.88	215.68
130.90	105.64	232.59	143.17	331.96	219.46
135.04	107.88	236.84	145.38	336.09	222.93
139.12	109.84	240.99	147.84	340.27	226.39
143.27	111.62	245.16	149.97	344.44	229.61
147.47	113.47	249.36	153.29	348.60	233.13
151.62	115.25	253.50	156.23	352.73	236.69
155.73	116.97	257.64	159.56	356.85	239.65
159.91	118.97	261.72	162.66	360.96	242.26
164.15	120.50	265.90	166.00	365.13	245.30
168.36	122.02	270.14	168.94	369.37	248.57
172.53	123.18	274.32	172.81	373.63	252.41
176.78	124.40	278.44	176.02	377.94	254.98

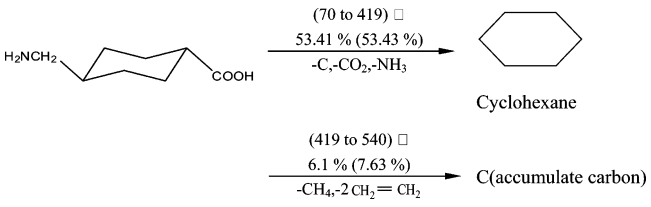
In the temperature range of (82 to 378) K

$$C_{p,m}(\text{J·K}^{-1}\text{m·L}^{-1}) = 142.7597 + 73.7745X + 84.9162X^2 + 26.8116X^3 - 120.4903X^4 - 10.0990X^5 + 58.4568X^6 \quad (2)$$

where $X = (T/\text{K} - 230)/148$ and T is the absolute temperature. The correlation coefficient of the fitted curve, R^2, is 0.9998.

In the whole temperature range, the curve of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid is roughly smooth, indicating that the compound is stable.

TG/DTG Analysis. The TG/DTG curves of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid are shown in Figure 2. It can be seen from the TG/DTG curves that three steps exist in the process of the thermal decompositions. The possible mechanism of the thermal decomposition was deduced as follows:



Energy of Combustion. The calorimeter was calibrated with benzoic acid of 99.9 % purity. The energy of combustion of benzoic acid was −26478 J·g^{-1} at 298.15 K.[12] The results of calibrated experiments are listed in Table 2.

The method for determining the combustion energy of the complex is the same as the calibration of the calorimeter with benzoic acid. The combustion energies of the samples are calculated according to the formula

$$\Delta_c E = \frac{w\Delta T - Gb - 5.893c}{a} \quad (3)$$

Table 2. Calibrated Experimental Results for the Energy Equivalent of the Calorimeter Using Benzoic Acid[a]

	mass of benzoic acid a	corrected ΔT	correction for nitric acid q_N	correction for the combustion of wire q_c	energy equivalent of calorimeter W
expt	g	K	J	J	J·K^{-1}
1	0.6167	1.620	11.97	61.64	10125.06
2	0.5676	1.490	10.77	72.36	10142.31
3	0.5162	1.355	10.17	60.97	10139.55
4	0.4808	1.262	11.97	66.33	10149.70
5	0.5793	1.521	14.36	61.64	10134.59
6	0.6803	1.780	11.97	69.68	10165.52

[a] $W = (10142.79 \pm 12.86)$ J·K^{-1}.

Table 3. Experimental Results for the Combustion Energies of *trans*-4-(Aminomethyl)cyclohexanecarboxylic Acid

	mass of compound a	corrected ΔT	correction for nitric acid q_N	correction for the combustion of wire q_c	energy of combustion $\Delta_c E$
expt	g	K	J	J	J·g^{-1}
1	0.5265	1.588	24.53	60.30	30431.00
2	0.5384	1.627	26.92	66.33	30477.47
3	0.5375	1.623	25.73	60.97	30465.21
4	0.5603	1.688	27.28	64.32	30393.41
5	0.5537	1.671	25.73	63.65	30448.30
6	0.5396	1.629	23.93	64.32	30456.55
mean					30445.32 ± 23.21

where $\Delta_c E$ denotes the constant volume combustion energy of the samples and a is the mass of the samples. The other symbols have the same meanings as in eq 1. The energies of combustion of the compound are listed in Table 3.

Standard Combustion Enthalpies and Standard Enthalpies of Formation. The standard combustion enthalpies of the compound, $\Delta_c H^{\ominus}$, refer to the combustion enthalpy change of the following ideal combustion reactions at 298.15 K and 101.325 kPa:

$$C_8H_{15}O_2N(s) + \frac{43}{4}O_2(g) \rightarrow 8CO_2(g) + \frac{15}{2}H_2O(l) + \frac{1}{2}N_2(g) \quad (4)$$

The standard combustion enthalpy of the complex is calculated from the combustion energy by eqs 5 and 6

$$\Delta_c H = \Delta_c E + \Delta nRT \quad (5)$$

$$\Delta n = n_g(\text{products}) - n_g(\text{reactants}) \quad (6)$$

where n_g is the total amount (in moles) of gas present as products or as reactants, $R = 8.314$ J·K^{-1}·mol^{-1}, and $T = 298.15$ K.

The standard enthalpy of formation of the compound, $\Delta_f H$, was calculated by Hess's law according to the thermochemical equation

$$\Delta_f H = 8\Delta_{f,CO_2(g)}H + 15/2\Delta_{f,H_2O(l)}H - \Delta_c H \quad (7)$$

The $\Delta_c H$ and $\Delta_f H$ of the compound were determined to be (4791.88 ± 3.65) kJ·mol^{-1} and (499.93 ± 4.99) kJ·mol^{-1}, respectively.

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