Heat capacities and thermodynamic properties of (S)-*tert*-butyl 1-phenylethylcarbamate

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Abstract An *N-tert*-butyloxycarbonylated organic synthesis intermediate, (S)-*tert*-butyl 1-phenylethylcarbamate, was prepared and investigated by means of differential scanning calorimetry (DSC) and thermogravimetry (TG). The molar heat capacities of (S)-*tert*-butyl 1-phenylethylcarbamate were precisely determined by means of adiabatic calorimetry over the temperature range of 80-380 K. There was a solid–liquid phase transition exhibited during the heating process with the melting point of 359.53 K. The molar enthalpy and entropy of this transition were determined to be 29.73 kJ mol^{-1} and 82.68 J K^{-1} mol^{-1} based on the experimental C_p–T curve, respectively. The thermodynamic functions, $[H_T^0 - H_{298.15}^0]$ and $[S_T^0 - S_{298.15}^0]$, were calculated from the heat capacity data in the temperature range of 80–380 K with an interval of 5 K. TG experiment showed that the pyrolysis of the compound was started at the temperature of 385 K and terminated at 510 K within one step.

Introduction

Protection of organic functions plays a fundamental role in the field of multi-step organic synthesis. Amine functions are wildly existed in a great amount of biologically active compounds, making its' protection a frequently existed question in synthetic and medicinal chemistry [1–4]. Lots of methods have been proposed to protect the amine group, in which *N-tert*-butyloxycarbonylation has been the most frequently applied method due to the easy of protection and deprotection, and the high stability of the N-Boc group in various synthesis conditions [5–13]. However, the thermodynamic properties of the protected compounds have been rarely reported [14].

Thermodynamic properties of a certain compound are essential for it preparation, application and theoretical research. It is well known that molar heat capacity is one of the fundamental thermodynamic properties. Many other thermodynamic properties such as enthalpy, entropy and Gibbs free energy can be obtained from the molar heat capacity [15, 16]. In this paper, the phase change properties and the thermal stability of an *N-tert*-butyloxycarbonylated organic synthesis intermediate, (S)-*tert*-butyl 1-phenylethylcarbamate (Scheme 1, $C_{13}H_{19}NO_2$, molecular mass: 221.30), were investigated by means of differential scanning calorimetry (DSC) and thermogravimetry (TG). Its molar heat capacities were determined precisely by means of adiabatic calorimetry over the temperature ranges of

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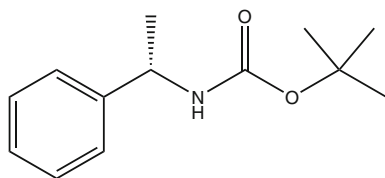
(S)-*tert*-butyl 1-phenylethylcarbamate

Scheme 1 Molecular structure of (S)-*tert*-butyl 1-phenylethylcarbamate

80–380 K. The thermodynamic properties including molar enthalpy and entropy of phase transition were determined based on the heat capacity measurement. Further more, the thermodynamic functions such as $[H_T^0 - H_{298.15}^0]$ and $[S_T^0 - S_{298.15}^0]$ were calculated from the heat capacity data in the temperature range of 80–380 K.

Experimental

Sample

The (S)-*tert*-butyl 1-phenylethylcarbamate was synthesized according to a published procedure [17]. The sample was recrystallized from CH_2Cl_2/*n*-hexane thrice prior to characterizations. The structure of the sample was confirmed by means of ^1H and ^{13}C NMR. The sample was detected by gas chromatography. GC-920 (Shanghai Analyzer Co., China) with a FID detector and a capillary column (SE-30, 30 m × 0.25 mm × 0.3 μm) was used for the detection. The carrier gas was nitrogen. The temperature of the injector and the detector was 250 °C. The oven was initially set as 80 °C for 3 min and then programmed at 5 °C/min to 180 °C where it was held for 3 min. The result showed that the purity of the sample was higher than 99.0%.

Adiabatic calorimetry

Heat capacity measurements were carried out with a high-precision automated adiabatic calorimeter which has been described in details in literatures [18–20]. Liquid nitrogen was used as cooling medium. In order to verify the reliability of the adiabatic calorimeter, the molar heat capacities of a reference standard material, α-Al_2O_3, were measured. The deviations of our experimental results from the recommended values of the National Bureau of Standards (NBS) [21] were within ±0.2% in the entire temperature range of 80–380 K.

The sample mass of (S)-*tert*-butyl 1-phenylethylcarbamate used in the heat capacity measurement was 2.19975 g, which was equivalent to 9.940 mmol based on its molar mass of 221.30 g mol^{-1}. The measurements were conducted by means of standard method of intermittently

heating the sample and alternately measuring the temperature. The heat capacities of the calorimeter cell were measured independently. The heat capacities of the sample were derived by subtracting the heat capacities of the calorimeter cell from the total heat capacities.

Thermal analysis

Differential scanning calorimetry was performed on a DSC Q1000 (TA Instruments Inc., USA) over the temperature range of 200 K to 380 K under high purity nitrogen (99.999%) with a flow rate of 50 mL min^{-1}. The heating rate was 10 K min^{-1} and the sample mass used in the experiments was 4–5 mg. The calorimeter was calibrated by Indium (99.99%).

Thermogravimetric analysis (TG) was carried out on a Cahn Thermax 500 Thermogravimetric Analyzer from room temperature to 673 K with the sample mass of 22.18 mg under nitrogen atmosphere. The heating rate was 10 K min^{-1} and the flow rate of N_2 was 100 mL min^{-1}. The equipment was calibrated by $CaC_2O_4 \cdot H_2O$ (99.9%).

Results and discussions

Heat capacities

The molar heat capacities of (S)-*tert*-butyl 1-phenylethyl-carbamate obtained from adiabatic calorimetry are shown in Fig. 1 and listed in Table 1. The figure shows that there is a phase transition existed in the experimental temperature range. The phase transition corresponds to the solid–liquid transition. The peak temperature of the phase transition is 359.87 K. No other thermal abnormality could be found in the solid phase (80–330 K) and liquid phase (362–380 K), indicating that (S)-*tert*-butyl 1-phenylethyl-carbamate is thermally stable in the corresponding temperature ranges.

The values of the experimental heat capacities can be fitted to the following polynomial equations using Origin-Pro 7.5 software:

For the solid phase over the temperature range of 80–330 K:

$$C_{p,m}^o(s) / J\,mol^{-1}\,K^{-1} = 215.885 + 111.039X + 22.260X^2$$
$$+ 19.661X^3 - 7.933X^4$$
$$- 11.638X^5 - 10.983X^6 \qquad (1)$$

where

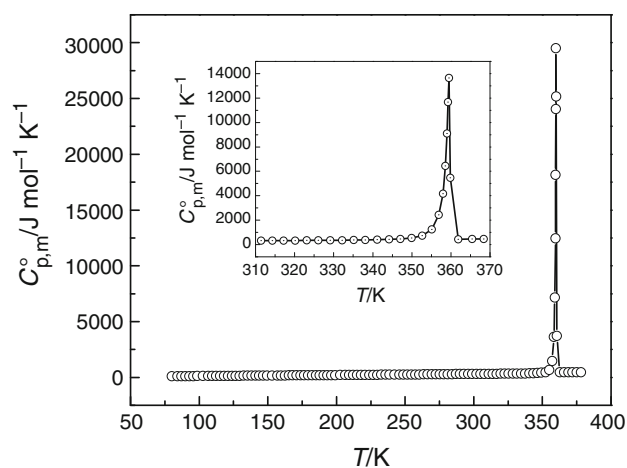$$X = \frac{T - (T_{max} + T_{min})/2}{(T_{max} - T_{min})/2} \qquad (2)$$

Fig. 1 Experimental molar heat capacities $C_{p,m}^{o}$ of (S)-tert-butyl 1-phenylethylcarbamate as a function of temperature. *Outer part* $C_{p,m}^{o}$ from 80 to 380 K, the whole experiment. *Inner part* $C_{p,m}^{o}$ from 310 to 370 K, the melting process

Table 1 Experimental molar heat capacities of (S)-tert-butyl 1-phenylethylcarbamate

T/K	$C_{p,m}^{o}$/J mol K^{-1}
80.08	100.97
84.17	105.10
87.10	108.89
89.99	112.59
92.88	116.20
95.75	119.72
98.63	123.15
102.66	126.50
106.63	129.75
109.48	132.90
112.37	136.04
115.25	139.08
118.12	142.01
120.99	144.77
123.85	147.26
126.70	149.62
129.56	152.07
132.42	154.38
135.27	156.58
138.13	158.80
140.99	161.14
143.81	163.62
146.64	166.23
149.47	168.84
153.15	171.68
156.87	174.67
159.68	177.66
162.46	180.43

Table 1 continued

T/K	$C_{p,m}^{o}$/J mol K^{-1}
165.28	183.19
168.12	185.91
170.98	188.47
173.82	190.56
176.53	192.61
179.34	194.49
182.25	196.45
185.07	198.34
187.87	200.36
190.66	202.38
193.40	204.67
196.26	207.19
199.19	209.82
202.77	212.40
206.29	215.13
209.17	218.03
212.13	221.13
215.04	224.32
217.89	227.89
220.80	231.36
223.80	234.81
226.77	238.10
229.70	241.26
232.68	244.14
235.72	246.68
238.70	249.57
242.21	252.11
245.72	254.54
248.66	257.01
251.58	259.58
254.49	262.44
257.38	265.62
260.33	268.97
263.36	272.38
266.38	275.81
269.36	279.43
272.33	282.92
275.28	286.52
278.21	290.23
281.12	294.34
284.03	298.07
286.91	301.78
289.87	305.22
292.88	308.28
295.89	311.16
298.89	313.81
301.88	316.16
304.85	318.51

Table 1 continued

T/K	$C_{p,m}^o$/J mol K^{-1}
307.82	320.75
310.78	323.30
313.72	325.87
316.64	328.45
319.56	331.05
322.47	333.66
325.37	336.29
328.34	338.93
331.39	345.13
334.42	351.53
337.43	357.77
340.41	366.64
343.35	383.70
346.30	414.20
349.28	419.76
352.19	476.54
354.89	662.71
357.10	1482.22
358.43	3641.82
359.08	7153.03
359.42	12463.9
359.63	18158.02
359.77	24048.84
359.87	29500.52
359.96	25189.95
360.41	3731.52
362.63	469.80
365.89	471.63
368.84	473.15
371.88	474.64
374.98	476.03
378.07	477.68

is the reduced temperature. T is the experimental temperature. T_{max} is the upper limit (330 K) and T_{min} is the lower limit (80 K) of the temperature range. So that in the solid phase (80–330 K), $X = [(T/K) - 215]/125$. The correlation coefficient of the fitting $R^2 = 0.9997$.

For the liquid phase over the temperature range of 362–380 K:

$$C_{p,m}^o(l) \, / \, \mathrm{J\,mol^{-1}\,K^{-1}} = 474.134 + 4.526X \quad (3)$$

where X is obtained according to Eq. 2 with $T_{min} = 362$ K and $T_{max} = 380$ K. The correlation coefficient of the fitting $R^2 = 0.9986$.

The temperature, enthalpy and entropy of solid–liquid phase transition

The standard molar enthalpy and entropy of the solid–liquid phase transition, $\Delta_{fus}H_m^o$ and $\Delta_{fus}S_m^o$, of the sample were calculated according to Eqs. 4 and 5:

$$\Delta_{fus}H_m^o = \frac{Q - n\int_{T_i}^{T_m} C_{p,m}^o(s)dT - n\int_{T_m}^{T_f} C_{p,m}^o(l)dT - \int_{T_i}^{T_f} H^o dT}{n} \quad (4)$$

$$\Delta_{fus}S_m^o = \frac{\Delta_{fus}H_m^o}{T_m} \quad (5)$$

where T_i is the temperature a little bit lower than the onset temperature of the solid–liquid phase transition, and T_f is the temperature a little bit higher than the terminating temperature of the transition. Q is the total energy introduced into the sample cell from T_i to T_f. H^o is the standard heat capacities of the sample cell from T_i to T_f. $C_{p,m}^o(s)$ and $C_{p,m}^o(l)$ are the standard heat capacities of the sample in solid phase from T_i to T_m and in liquid phase from T_m to T_f, respectively. n is the molar amount of the sample. The polynomials of the heat capacity obtained in "Heat capacities" section were used to calculate the standard thermodynamic functions and the results are listed in Table 2.

Thermodynamic functions of the compound

The thermodynamic functions of (S)-*tert*-butyl 1-phenylethylcarbamate relative to the reference temperature of 298.15 K were calculated in the temperature range of 80–380 K with an interval of 5 K. Polynomials of the heat capacity mentioned above were applied in the calculation, and the thermodynamic relationships are as follows:

Before melting:

$$H_T^o - H_{298.15}^o = \int_{298.15}^{T} C_{p,m}^o(s)dT \quad (6)$$

Table 2 Thermodynamic parameters of (S)-*tert*-butyl 1-phenylethylcarbamate

Thermodynamic properties	Melting point T/K	$\Delta_{fus}H_m^o$/kJ mol^{-1}	$\Delta_{fus}S_m^o$/J K^{-1} mol^{-1}
Adiabatic calorimetry	359.53	29.73	82.68
DSC	359.04 ± 0.095	29.76 ± 0.115	82.90 ± 0.28

Table 3 Calculated thermodynamic functions of (S)-tert-butyl 1-phenylethylcarbamate

T/K	$C_{p,m}^{o}$/J mol^{-1} K^{-1}	$H_{m(T)} - H_{m(298.15)}$/ kJ mol^{-1}	$S_{m(T)} - S_{m(298.15)}$/ J mol^{-1} K^{-1}
80	100.2	−44.59	−240.963
85	106.3	−44.08	−234.696
90	112.3	−43.54	−228.433
95	118.3	−42.96	−222.192
100	123.7264	−42.36	−215.985
105	128.9202	−41.73	−209.822
110	133.9112	−41.08	−203.709
115	138.7293	−40.40	−197.649
120	143.4009	−39.69	−191.646
125	147.9491	−38.97	−185.699
130	152.3943	−38.22	−179.81
135	156.7546	−37.44	−173.977
140	161.0461	−36.65	−168.198
145	165.2832	−35.83	−162.473
150	169.4789	−35.00	−156.799
155	173.6453	−34.14	−151.173
160	177.7932	−33.26	−145.595
165	181.9332	−32.36	−140.061
170	186.0751	−31.44	−134.568
175	190.2283	−30.50	−129.114
180	194.4021	−29.54	−123.697
185	198.6054	−28.56	−118.313
190	202.847	−27.55	−112.961
195	207.1355	−26.53	−107.636
200	211.4793	−25.48	−102.338
205	215.8865	−24.41	−97.0617
210	220.3649	−23.32	−91.8058
215	224.9218	−22.21	−86.5673
220	229.5637	−21.07	−81.3435
225	234.2965	−19.91	−76.1318
230	239.1248	−18.73	−70.9295
235	244.0521	−17.52	−65.7343
240	249.0801	−16.29	−60.5436
245	254.2086	−15.03	−55.3553
250	259.4352	−13.75	−50.1672
255	264.7547	−12.44	−44.9774
260	270.159	−11.10	−39.7842
265	275.6363	−9.73	−34.5863
270	281.1707	−8.34	−29.3826
275	286.742	−6.92	−24.1725
280	292.3248	−5.48	−18.9557
285	297.8879	−4.00	−13.7326
290	303.394	−2.50	−8.50395
295	308.7988	−0.97	−3.27139
298.15	312.1026	0.00	0.00
300	314.0504	0.59	1.962866

Table 3 continued

T/K	$C_{p,m}^{o}$/J mol^{-1} K^{-1}	$H_{m(T)} - H_{m(298.15)}$/ kJ mol^{-1}	$S_{m(T)} - S_{m(298.15)}$/ J mol^{-1} K^{-1}
305	319.0886	2.17	7.195734
310	323.8441	3.77	12.42324
315	328.2378	5.40	17.64043
320	332.18	7.04	22.84122
325	335.5695	8.71	28.01837
330	338.2926	10.39	33.1633
335	Phase change		
340			
345			
350			
355			
362	469.6071	45.18	130.967
365	471.1159	46.75	135.3022
370	473.6306	49.37	142.4703
375	476.1452	52.01	149.5689
380	478.6599	54.66	156.5999

$$S_T^{o} - S_{298.15}^{o} = \int_{298.15}^{T} \frac{C_{p,m}^{o}(s)}{T} dT \qquad (7)$$

After melting:

$$H_T^{o} - H_{298.15}^{o} = \int_{298.15}^{T_i} C_{p,m}^{o}(s) dT + \Delta_{fus} H_m^{o} + \int_{T_f}^{T} C_{p,m}^{o}(l) dT \qquad (8)$$

$$S_T^{o} - S_{298.15}^{o} = \int_{298.15}^{T_i} \frac{C_{p,m}^{o}(s)}{T} dT + \Delta_{fus} S_m^{o} + \int_{T_f}^{T} \frac{C_{p,m}^{o}(1)}{T} dT \qquad (9)$$

where T_i is the temperature at which the melting started, and T_f is the temperature at which the melting finished. The calculated thermodynamic functions, $H_T^{o} - H_{298.15}^{o}$ and $S_T^{o} - S_{298.15}^{o}$, of (S)-tert-butyl 1-phenylethylcarbamate are shown in Table 3.

DSC and TG analysis

The DSC curve of the sample is depicted in Fig. 2. A sharp endothermic peak corresponding to the melting process of the sample is exhibited in the figure. The melting point and the entropy of the solid–liquid phase transition could be obtained from the DSC experiment and the results are listed in Table 2. It could be seen that the thermodynamic properties of the sample obtained from DSC experiments
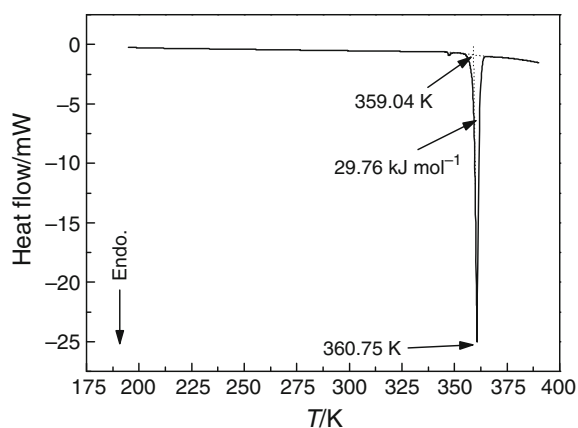
Fig. 2 DSC curve of (S)-*tert*-butyl 1-phenylethylcarbamate under high purity nitrogen with the onset temperature of 359.04 K and the peak temperature of 360.75 K
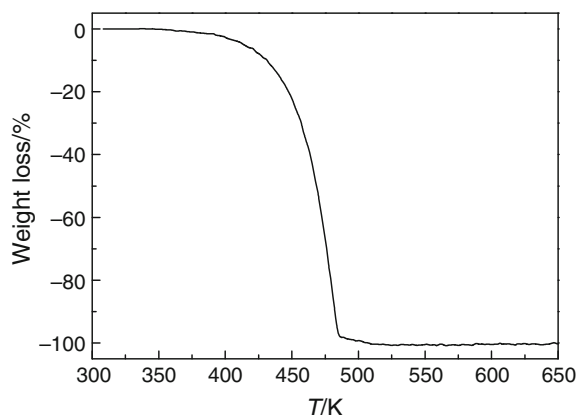

Fig. 3 TG curve of (S)-*tert*-butyl 1-phenylethylcarbamate

are agreed well with that obtained from adiabatic calorimetry. Figure 2 also shows that no other thermal abnormality exists in the experimental temperature range, which is agreed with the result of adiabatic calorimetry.

The TG curve of the sample is showed in Fig. 3. The figure shows that (S)-*tert*-butyl 1-phenylethylcarbamate is thermally stable below the temperature of 380 K. The sample starts to loss its' mass at the temperature of 385 K and the mass is totally lost within one step with the terminate temperature of 510 K.

Conclusions

An N-*tert*-butyloxycarbonylated organic synthesis intermediate, (S)-*tert*-butyl 1-phenylethylcarbamate, was prepared and investigated by means of DSC and TG. DSC experiments results indicated that the compound started to melt at the temperature of 359.04 ± 0.095 K with the phase change enthalpy of 29.76 ± 0.115 kJ mol^{-1}. TG experiment

revealed that the pyrolysis of the compound was started at the temperature of 385 K and terminated at 510 K. Furthermore, the molar heat capacities of (S)-*tert*-butyl 1-phenylethylcarbamate were precisely determined by means of adiabatic calorimetry over the temperature range of 80–380 K. The adiabatic calorimetry indicated that the melting point of the compound was 359.53 K, where as the molar enthalpy and entropy of the phase transition were determined to be 29.73 kJ mol^{-1} and 82.68 J K^{-1} mol^{-1}, respectively, from the experimental $C_p - T$ curve. The thermodynamic functions, $[H_T^0 - H_{298.15}^0]$ and $[S_T^0 - S_{298.15}^0]$, were calculated from the heat capacity data obtained from the adiabatic calorimetry in the temperature range of 80–380 K with an interval of 5 K.

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