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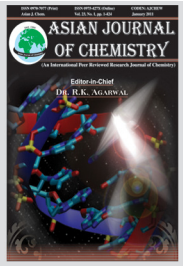

Thermal Analysis of a CRF_1 Compound $C_{22}H_{28}N_4O_2$ *via* a Temperature Modulated Differential Scanning Calorimetry

JING JI ZHANG*, TIAN QI WANG, HAN BO BAO, LIANG LIANG WANG, JUN YAO and WEN QIANG SUN

Department of Materials Science and Engineering, China Jiliang University, Hangzhou 310018, P.R. China

*Corresponding author: E-mail: zjjtongji@gmail.com

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Using a temperature modulated differential scanning calorimetry (TMDSC), thermal analysis of a new compound $C_{22}H_{28}N_4O_2$ were studied in the temperature range from T = 198 to 569 K. There existed three stages in the relationship of heat capacity and temperature. The heat capacity steadly increased with temperature increasing in the first stage (198-347 K) and third stage (384-569 K). Their relationship of molar heat capacity and temperature were fitted to the polynomials. Other thermodynamic functions, such as (H_T - $H_{298.15}$ K) and (S_T - $S_{298.15}$ K) could be calculated by the numerical integral of the heat-capacity polynomial. An endothermic process in the second stage (348-384 K) also was found and the peak in the heat capacity curve was corresponding to fusion process.

Key Words: Differential scanning calorimetry, Heat capacity, Thermal decomposition.

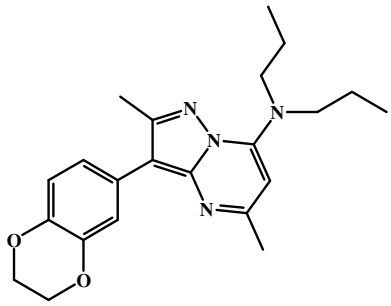
INTRODUCTION

It is well known that depression had great dangers to people's health and their contacts in the world[1]. There was a lot of pain and suffering caused by depression, to the patient and their relatives. The cost in human suffering could not be estimated. Many efforts have been developed to cure the disease. But there are still not effective and ideal treatments while some drugs also had some side effects[2]. Therefore, many researches had been developed to find faster acting, safer and more effective treatments for depression. CRF_1 antigonists is regarded as a new kind of antidepressant, which shows a fast action in clinical trials and animal models. The research of CRF_1 antagonists[3-5] properly helped us to find new fast-action and highly effective antidepressants. Hence, many antidepressants were synthesized afterward.

In the present work, the low-temperature heat capacity of a new CRF_1 compound $C_{22}H_{28}N_4O_2$ had been measured over the temperature range from 198 to 569 K and its thermal properties were calculated.

EXPERIMENTAL

The sample was synthesized in our laboratory and its formula is shown in Fig. 1. Its purity was higher than 99 %. The sample mass of $C_{22}H_{28}N_4O_2$ (m.w. 380) used for heat capacity measurement was 5 mg, which was equivalent to 0.0132 mmol.



[3-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-dipropyl-amine

Fig. 1. Molecular formula of the CRF_1 antidepressant

The heat capacity measurements were carried out by temperature modulated differential scanning calorimetry (TMDSC) on a Q1000[6] from TA instruments under N_2 atmosphere, in a temperature range from 190 to 570 K, at a heating rate of 10 K min^{-1}. The experiment was similar to the previous paper[7].

RESULTS AND DISCUSSION

Low temperature of heat capacity: There exist three stages of the stable phase of solid, the solid-liquid transition and the stable phase of liquid in the heat capacity curves of Fig. 2. Their molar heat capacity values (198-347 K) and third stage (384-569 K) steadly increases with temperature increasing. From simple calculation and modeling, the molar heat

TABLE-1
EXPERIMENTAL MOLAR HEAT CAPACITIES OF (3-(2,3-DIHYDRO-BENZO[1,4]DIOXIN-6-YL)-2,5-DIMETHYL-PYRAZOLO(1,5-a)PYRIMIDIN-7-YL)-DIPROPYL-AMINE

Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})	Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})	Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})	Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})	Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})	Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})
198	503.50	254	552.90	310	581.7800	402	786.8533	458	834.6067	514	895.2800
199	513.76	255	551.38	311	582.9200	403	788.1200	459	835.4933	515	897.5600
200	523.64	256	549.86	312	582.5400	404	789.2600	460	836.0000	516	899.5867
201	531.24	257	549.10	313	582.9200	405	790.6533	461	836.7600	517	901.3600
202	538.46	258	547.96	314	584.0600	406	791.7933	462	831.0600	518	901.9933
203	544.92	259	547.20	315	585.9600	407	792.9333	463	833.9733	519	903.6400
204	550.24	260	546.44	316	587.4800	408	793.9467	464	835.7467	520	905.4133
205	555.56	261	546.06	317	588.6200	409	794.3267	465	837.2667	521	907.3133
206	559.74	262	545.68	318	590.1400	410	796.1000	466	838.2800	522	908.8333
207	563.54	263	544.92	319	591.2800	411	796.4800	467	839.1667	523	910.7333
208	567.34	264	544.92	320	592.8000	412	797.7467	468	839.9267	524	912.0000
209	570.38	265	544.54	321	595.8400	413	798.6333	469	840.8133	525	911.8733
210	573.04	266	544.16	322	596.6000	414	799.7733	470	841.8267	526	912.7600
211	575.32	267	543.78	323	597.3600	415	800.4067	471	842.5867	527	914.5333
212	577.60	268	543.78	324	598.8800	416	801.4200	472	842.8400	528	915.9267
213	579.50	269	543.40	325	600.7800	417	801.9267	473	843.0933	529	917.4467
214	580.64	270	543.78	326	597.3600	418	802.9400	474	843.3467	530	919.0933
215	581.40	271	543.78	327	600.7800	419	803.8267	475	843.4733	531	915.4200
216	582.92	272	543.78	328	603.0600	420	804.2067	476	843.3467	532	917.7000
217	583.68	273	543.78	329	605.3400	421	805.3467	477	843.4733	533	919.6000
218	584.06	274	544.16	330	606.8600	422	805.7267	478	843.6000	534	921.1200
219	584.44	275	544.16	331	608.3800	423	807.1200	479	843.9800	535	922.1333
220	585.20	276	544.16	332	609.9000	424	808.0067	480	844.4867	536	923.1467
221	585.20	277	544.16	333	611.4200	425	809.0200	481	845.2467	537	924.1600
222	585.20	278	544.16	334	612.5600	426	810.0333	482	846.2600	538	925.0467
223	585.20	279	544.54	335	614.0800	427	810.9200	483	847.5267	539	925.5533
224	584.82	280	544.92	336	615.6000	428	811.5533	484	848.9200	540	925.9333
225	584.44	281	545.68	337	620.1600	429	812.1867	485	849.9333	541	926.5667
226	583.68	282	546.06	338	621.3000	430	813.2000	486	850.6933	542	927.5800
227	583.68	283	546.82	339	617.8800	431	813.5800	487	851.7067	543	928.7200
228	583.30	284	547.58	340	620.5400	432	814.0867	488	852.3400	544	929.8600
229	582.54	285	548.34	341	629.6600	433	814.9733	489	853.4800	545	930.1133
230	582.16	286	549.48	342	631.5600	434	815.6067	490	854.4933	546	929.8600
231	581.40	287	550.24	343	634.2200	435	815.7333	491	855.7600	547	930.4933
232	581.02	288	551.38	344	636.7682	436	817.3800	492	857.1533	548	931.8867
233	580.26	289	552.52	345	640.6800	437	817.8867	493	857.7867	549	933.7867
234	579.50	290	553.28	346	645.1059	438	818.9000	494	858.4200	550	934.8000
235	578.36	291	554.8	347	647.7659	439	819.9133	495	859.6867	551	935.5600
236	577.22	292	555.56	384	769.6267	440	820.9267	496	861.4600	552	936.9533
237	576.46	293	556.32	385	769.5000	441	821.3067	497	862.6000	553	937.4600
238	574.94	294	557.84	386	770.5133	442	822.1933	498	863.9933	554	938.2200
239	573.80	295	558.98	387	771.0200	443	823.3333	499	865.6400	555	938.8533
240	572.66	296	562.40	388	772.0333	444	823.9667	500	867.2867	556	939.3600
241	571.52	297	562.02	389	772.5400	445	824.7267	501	868.9333	557	940.1200
242	569.62	298	563.16	390	773.1733	446	825.2333	502	870.2000	558	941.0067
243	568.10	299	563.54	391	774.6933	447	818.6467	503	872.3533	559	941.5133
244	566.20	300	564.68	392	775.5800	448	821.5600	504	873.8733	560	942.6533
245	564.68	301	566.20	393	777.3533	449	823.9667	505	876.2800	561	942.7800
246	563.16	302	567.34	394	777.9867	450	825.3600	506	878.6867	562	944.6800
247	562.02	303	568.86	395	778.8733	451	827.2600	507	881.2200	563	945.4400
248	560.50	304	570.76	396	779.6333	452	828.7800	508	883.3733	564	946.4533
249	559.36	305	572.28	397	780.7733	453	829.5400	509	885.7800	565	947.7200
250	557.84	306	574.18	398	781.6600	454	830.5533	510	888.0600	566	948.4800
251	556.32	307	576.08	399	782.5467	455	831.6933	511	888.8200	567	949.6200
252	555.18	308	577.98	400	784.3200	456	832.8333	512	890.9733	568	950.0000
253	554.04	309	581.02	401	785.0800	457	833.5933	513	893.3800	569	951.6467

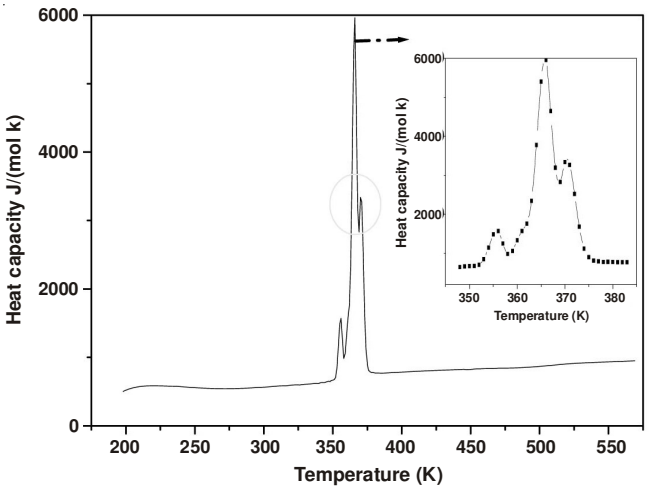


Fig. 2. Experimental molar heat capacities ($C_{p,m}$) curve of the compound $C_{22}H_{28}N_4O_2$ as a function of the temperature (K)

capacities of these stages comply with the following polynomial equations of heat capacities ($C_{p,m}$) against the reduced temperature by means of the least square method:

$$C_{p,m}\ [J/(mol\ k)] = 543.860\text{-}19.524x + 168.696x^2 + 72.844x^3 - 138.378x^4 \quad (1)$$

$R^2 = 0.97$ at temperature (198-347 K).

$$C_{p,m}\ [J/(mol\ k)] = 845.341 + 91.173x + 64.390x^2 + 1.467x^3 - 55.229x^4 \quad (2)$$

$R^2 = 0.99$ at temperature (384-569 K).

Based on eqns. 1 and 2, the molar heat capacities can be calculated and detailed molar heat capacity values are listed in Table-1. For example, the heat capacity of the sample at 298.15 K was calculated to be 557.893 J mol^{-1} K^{-1}. From Fig. 2, it is also found that an obvious endothermic process in the second stage appear and their heat capacity in this stage quickly soared because of solid-liquid transition.

Thermodynamic functions of the compound: Using the polynomial representing heat capacity and the relationship between thermodynamic functions and heat capacity, the thermodynamic functions relative to the reference temperature of 298.15 K could be calculated in the temperature ranges from 198 to 564 K with an interval of 10 K, according to the followed thermodynamic relationships and the values of thermodynamic function $H_T - H_{298.15}$, $S_T - S_{298.15}$ are listed in Table-2 with the interval of 10 K.

$$H_T - H_{298.15} = \int_{298.15}^{T} C_{pm}dT$$

$$S_T - S_{298.15} = \int_{298.15}^{T} \frac{C_{pm}dT}{T}$$

Conclusion

Using a temperature modulated differential scanning calorimetry, the low-temperature heat capacities of a new compound $C_{22}H_{28}N_4O_2$ were collected and their thermal properties were analyzed, including phase transition and thermodynamic functions. The analysis results will prove good to practical application of the CRF_1 compound in future.

TABLE-2
THERMODYNAMIC FUNCTIONS OF (3-(2,3-DIHYDRO-BENZO-[1,4]DIOXIN-6-YL)-2,5-DIMETHYL-PYRAZOLO(1,5-a)-PYRIMIDIN-7-YL)-DIPROPYL-AMINE

Temp. (K)	$C_{p,m}$ (J mol^{-1} k^{-1})	H_T-$H_{298.15}$ (KJ mol^{-1} k^{-1})	S_T-$S_{298.15}$ (J mol^{-1} k^{-1})
198	503.53000	-50.35300	-205.85800
208	567.32400	-51.05920	-203.98700
218	584.06800	-46.72540	-182.58000
228	583.30400	-40.83130	-156.18000
238	574.94000	-34.49640	-129.25800
248	560.53600	-28.02680	-102.94800
258	547.96000	-21.91840	-78.97750
268	543.78800	-16.31360	-57.70130
278	544.16000	-10.88320	-37.80280
288	551.38600	-5.51386	-18.81880
298	563.16400	0	0
308	577.98600	5.77986	19.07932
318	590.14400	11.80288	38.33575
328	603.06000	18.09180	57.84552
338	621.30000	24.85200	78.25274
348	648.53300	32.42665	100.59400
358	Melting temperature		
384	769.62760	66.18797	195.13900
394	777.98700	74.68675	217.26060
404	789.26560	83.66215	240.18930
414	799.77380	92.77376	262.94160
424	806.00760	101.55700	284.23050
434	815.60780	110.92270	306.62780
444	823.96700	120.29920	328.54040
454	830.55340	129.56630	349.66300
464	835.74700	138.73400	370.06040
474	843.34700	148.42910	391.40580
484	848.92000	157.89910	411.71770
494	858.42080	168.25050	433.88020
504	873.87300	180.01780	459.20280
514	895.28000	193.38050	488.04400
524	912.00000	206.11200	514.73280
534	921.12000	217.38430	537.28930
544	929.86000	228.74560	559.64550
554	938.22000	240.18430	581.76210
564	946.45320	251.75660	603.79930

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