Journal of Thermal Analysis and Calorimetry, Vol. 91 (2008) 2, 471–475

THERMOPHYSICAL PROPERTIES IN MEDIUM TEMPERATURE RANGE OF SEVERAL THIO AND DITHIOCARBAMATES

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The present study reports a DSC study of the thio- and dithiocarbamates: 3*H*-benzoxazole-2-thione (2-mercaptobenzoxazole), 3*H*-benzothiazole-2-thione (2-mercaptobenzothiazole), thiazolidine-2-thione (2-mercapto-2-thiazoline), oxazolidine-2-thione (2-mercapto-2-oxazoline) and tetrahydro-1,3-oxazine-2-thione (5,6-dihydro-4*H*-1,3-oxazine-2-thiol) in the temperature interval T=268 K and the melting temperatures. Temperatures, enthalpies and entropies of fusion are reported. No solid–solid phase transitions were observed for the compounds in the temperature interval studied. The heat capacity of the compounds as a function of temperature was measured.

Keywords: *dithiocarbamates, DSC, fusion enthalpy, heat capacity, oxazines, oxazolines, thiazolines, thiocarbamates*

Introduction

Oxazines, oxazolines, thiazolines and their benzo derivatives, such as benzoxazoles and benzothiazoles, are important heterocycles containing nitrogen and either oxygen or sulfur ring atoms [1, 2]. These heterocyclic moieties are often present as components of natural compounds [2–4], also employed in synthetic chemistry as synthetic intermediates or protecting groups [5, 6], and used in drug design [7, 8]. Importance of thioglycosyl heterocycles has recently emerged in the areas of synthetic carbohydrate chemistry and drug discovery [9]. A variety of leaving groups containing these heterocycles have been investigated [10, 11] and it has been determined that S-thiazolinyl and S-benzoxazolyl derivative possess superior glycosyl donor properties for stereoselective glycosylations [12, 13] and convergent oligosaccharide synthesis [14–16].

Thermophysical data existing in the literature for these kinds of compounds are scarce and to our knowledge, there is no previous literature reports on experimental heat capacity determination as a function of temperature of solid cyclic thio and dithiocarbamates. There are several compilations of critically evaluated calorimetrically measured heat capacities [17–20] but new data on heat capacity of important families of compounds are needed [21–23].

During the last years, we have been involved in the experimental determination of enthalpies of fusion, heat capacities and the study of polymorphism of pure organic molecules [24–28]. The present work reports the temperature, enthalpy and entropy of fusion, and heat capacities of several thio and dithiocarbamates measured by differential scanning calorimetry (DSC). The target compounds (Fig. 1) are 3*H*-benzoxazole-2-thione (2-mercaptobenzoxazole) **1**; 3*H*-benzothiazole-2-thione (2-mercaptobenzothiazole) **2**; thiazolidine-2-thione (2-mercapto-2-thiazoline) **3**; oxazolidine-2-thione (2-mercapto-2-oxazoline) **4** and tetrahydro-1,3-oxazine-2-thione (5,6-dihydro- 4*H*-1,3-oxazine-2-thiol) **5**.

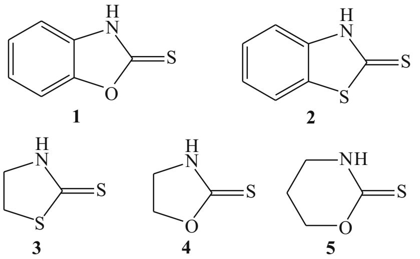

Fig. 1 Structures of the compounds studied

Experimental

Materials

Thio- and dithiocarbamates **1**–**3**, readily available from commercial sources, have been additionally purified by crystallization using acetone (**1**) or dichloromethane (**2** and **3**) as solvents. The synthesis of thiocarbamates **4** and **5** was accomplished using the corresponding amino alcohol as starting material. Thus, for the synthesis of **4**,

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1388–6150/$20.00

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2-aminoethanol was reacted with CS_2 in the presence of triethylamine in methanol at 0°C followed by the treatment with 30% H_2O_2 in accordance with the published procedures [29, 30]. Thiocarbamate **4** was obtained in 73% yield. The reaction of 3-aminopropanol with CS_2, as described for the synthesis of **4**, afforded thiocarbamate **5** in 62% yield. The synthetic derivatives **4** and **5** were then purified by crystallization using a mixture of dichloromethane and hexane (**4**) or toluene (**5**) as solvents. The characterization and spectral data for compounds **4** and **5** were essentially the same as reported previously [29]. All samples were carefully dried under vacuum at 50°C. Determination of purities, assessed by GC and DSC by the fractional fusion technique [31] indicated that the mole fraction of impurities in the compounds was less than 0.002, 0.001, 0.001, 0.006 and 0.001 for **1**, **2**, **3**, **4** and **5**, respectively.

The standards used for DSC calibration were hexafluorobenzene, 99.9% purity, supplied by Aldrich; benzoic acid, NIST standard reference sample 39j; and high-purity indium (mass fraction: >0.99999), tin and synthetic sapphire, supplied by PerkinElmer.

Calorimetry

A differential scanning calorimeter (PerkinElmer, Pyris 1) equipped with an intra-cooler unit was used to monitor purity, to study the fusion process, the possible existence of phase transitions in the solid samples, and to measure the heat capacity of all compounds. Temperature and power scales were calibrated [32–34] at heating rates of 0.04 and 0.17 K s^{-1}. The temperature scale was calibrated by the melting temperature of the high-purity reference materials: hexafluorobenzene, benzoic acid, tin and indium [35]. The power scale was calibrated with high-purity indium [35].

Curves of samples hermetically sealed in aluminium pans were recorded in a nitrogen atmosphere. All the pans with the samples were weighed on a Mettler AT21 microbalance with a detection limit of $1\cdot10^{-6}$ g, before and after the experiments to confirm that no product had volatilized.

After calibration, several runs with high-purity benzoic acid and indium as reference materials [35] were performed under the same conditions as the experimental determinations. The accuracies for the temperatures and enthalpies of fusion were calculated as the percentage deviation of the experimental data with regard to the values given in the literature [35] being in all the cases lower than 0.2 and 2.0% for temperature and enthalpy determinations, respectively [28].

For determination of temperature and enthalpy of fusion, a heating rate of 0.04 K s^{-1} was used. For each solid compound, six or seven samples weighing 1–2 mg were recorded. A fresh sample was used for each run. All compounds showed thermal stability in the fusion process.

Different scans were performed on heating, cooling and second heating, to determine the possible existence of phase transitions or polymorphism in the samples over the temperature range from T=268 K to their respective melting temperature at heating rates of 0.04 and 0.17 K s^{-1}.

Heat capacities were determined by the ‘scanning method’ following the experimental methodology previously described [36–38] with synthetic sapphire (α-aluminum oxide) as reference material [35–37]. DSC is a commonly accepted method for the quantitative determination of heat capacities and it has been proven as a suitable technique to obtain reliable and accurate values [39, 40]. To check the experimental method, heat capacity experiments were made with benzoic acid and synthetic sapphire as reference materials [35] in the temperature intervals T=268–360 and 268–410 K, respectively [28]. The relative percentage error of our measurements in comparison with those reported in the literature is lower than 2% [28].

The mass of sapphire used in each run was 0.030345 g. For heat capacity determinations, four to six fresh samples weighing 10–25 mg were scanned for each solid compound in the temperature range from 268 K to its melting temperature at 0.17 K s^{-1}. The complete temperature ranges for determination of the heat capacities were divided in intervals of approximately 40 K, overlapping by 5 K from one interval to another. The estimated uncertainty of the molar heat capacities is less than 2%. The experimental results for the compounds were fit to a third order polynomial in temperature.

Results and discussion

The fusion temperatures and enthalpies and the calculated entropy of fusion of the compounds are given in Table 1. The uncertainties were taken as the standard deviation of the mean. T_{fus} were taken as DSC onset temperatures.

Table 1 Temperatures, enthalpies and entropies of fusion for the compounds studied

	T_{fus}/K	$\Delta_{fus}(T_{fus})$/ kJ mol^{-1}	$\Delta_{fus}S(T_{fus})$/ J K^{-1} mol^{-1}	N[a]
1	470.0±0.1	25.0±0.1	53.1±0.3	6
2	455.9±0.2	22.3±0.2	49.0±0.4	7
3	377.0±0.1	16.8±0.1	44.6±0.4	6
4	370.6±0.3	15.9±0.1	43.0±0.3	6
5	400.2±0.1	18.4±0.1	46.0±0.3	7

[a] Number of independent experiments

The data reported of the fusion temperature in the literature, 469 K [41] for 3*H*-benzoxazole-2-thione, **1**; 453–455 [41], 454.75 [42] and 455.15 K [42] for 3*H*-benzothiazole-2-thione, **2**; 370.3–371.1 [29], 371–372 [43] and 370–372 K [44] for oxazolidine-2-thione, **4**; and 399.7–400.5 [29] and 401–402 K [44] for tetrahydro-1,3-oxazine-2-thione, **5**, are in good agreement with our values. However the value reported for thiazolidine-2-thione, **3**, 379–380 K [41] is slightly higher than our value. No solid–solid phase transitions were observed over the temperature interval from T=268 K to the corresponding melting points for any of the compounds.

Experimental curves of the heat capacity measurements as a function of temperature and the mean experimental values for all compounds are collected in Fig. 2 and in Table 2.

The coefficients of the fitted third order equation in temperature for all the compounds are collected in Table 3. The range studied for each compound is given as the last column of this table. The errors associated with the use of these correlation equations are less than 2 J K^{-1} mol^{-1} for all compounds.

As noted above, group contribution methods for the estimation of heat capacity at T=298.15 K have

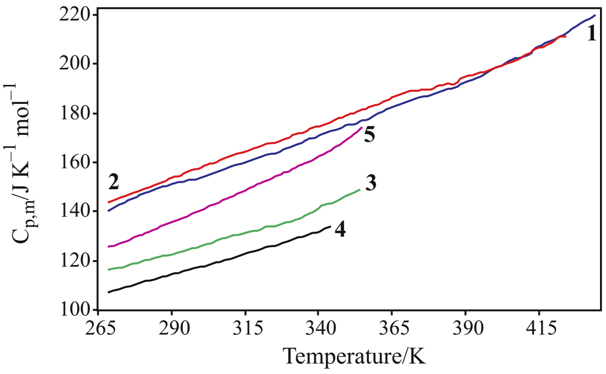

Fig. 2 Experimental curves of $C_{p,\mathrm{m}}$ *vs.* T for compounds

Table 2 Mean experimental $C_{p,\mathrm{m}}$ values

T/K	$C_{p,\mathrm{m}}$/J K^{-1} mol^{-1}					T/K	$C_{p,\mathrm{m}}$/J K^{-1} mol^{-1}	
	1	**2**	**3**	**4**	**5**		**1**	**2**
268.15	140.2	143.7	116.3	110.0	125.4	360.15	179.7	183.5
270.15	141.4	144.5	116.6	107.8	126.1	365.15	182.5	186.2
275.15	144.3	146.7	118.3	109.5	128.1	370.15	184.7	188.5
280.15	147.1	149.0	119.8	111.3	130.6	375.15	186.6	189.8
285.15	149.2	151.3	121.3	112.8	133.2	380.15	188.1	190.8
290.15	151.4	153.7	122.7	114.5	136.0	385.15	189.8	191.7
295.15	152.5	155.9	124.3	116.0	138.0	390.15	192.5	195.0
298.15	153.1	157.3	125.3	117.1	139.7	395.15	195.1	196.1
300.15	153.9	157.9	126.0	117.8	140.6	400.15	198.6	198.6
305.15	155.9	160.1	127.9	119.3	143.3	405.15	201.4	200.6
310.15	158.4	162.6	129.8	121.0	145.9	410.15	203.3	203.5
315.15	160.2	164.7	131.4	122.8	148.7	415.15	207.3	206.7
320.15	162.4	166.7	132.8	124.8	151.6	420.15	209.8	209.3
325.15	164.0	168.1	134.3	126.2	154.2	425.15	213.3	211.5
330.15	166.0	170.2	135.9	128.0	156.6	430.15	217.2	
335.15	168.5	172.6	138.3	130.1	159.4	435.15	220.1	
340.15	170.8	174.7	141.4	131.7	162.7			
345.15	173.1	177.1	143.8	134.5	165.8			
350.15	175.2	179.5	146.8		169.9			
355.15	177.1	181.4	149.6		174.3			

Table 3 Coefficients of the fitted curves

Compound	A[a]	B[a]	C[a]	D[a]	r^2	Range/K
1	–171.4	706.3	–557.4	176.1	0.999	268–435
2	–174.6	659.4	–456.0	128.2	0.998	268–425
3	–787.6	2580.8	–2513.0	845.4	0.997	268–355
4	–428.1	1454.7	–1370.7	461.4	0.999	268–348
5	–571.1	1873.1	–1761.0	598.4	0.999	268–355

[a] Parameters corresponding to an equation of the type: $C_{p,\mathrm{m}}=A+B(T/298.15)+C(T/298.15)^2+D(T/298.15)^3$

Table 4 Group values used in evaluating $C_{p,\mathrm{m}}$ at 298.15 K/J K^{-1} mol^{-1} of solids 1–5

Group		Γ_i
Tertiary aromatic sp^2 carbon[a]	C_BH	17.5
Quaternary aromatic sp^2 carbon[a]	C_BC	8.5
Cyclic secondary sp^3 carbon[a]	$–CH_{2}–_C$	24.6
Cyclic thiocarbamate[b]	$–O(C{=}S)NH–_C$	64.6
Cyclic dithiocarbamate[b]	$–S(C{=}S)NH–_C$	73.5

[a]From [45]; [b]Evaluated in this work using Eq. (1) and minimizing the function: $[C_{p,\mathrm{m}}(298.15\ \mathrm{K})_{\mathrm{expt}}–C_{p,\mathrm{m}}(298.15\ \mathrm{K})_{\mathrm{calc}}]^2/C_{p,\mathrm{m}}(298.15\ \mathrm{K})_{\mathrm{expt}}$

Table 5 Experimental and calculated heat capacities at *T*=298.15 K

Compound	$C_{p,\mathrm{m}}$ (298.15 K)/J K^{-1} mol^{-1}	
	exp.	calc.
3*H*-benzoxazole-2-thione	153.1	151.6
3*H*-benzothiazole-2-thione	157.3	160.5
Thiazolidine-2-thione	125.3	122.7
Oxazolidine-2-thione	117.1	113.8
Tetrahydro-1,3-oxazine-2-thione	133.2	138.4

been reported. Table 4 lists group values (Γ_i) evaluated previously for the contributions of the carbon fragments present in the structures of compounds **1–5** and the values estimated by group contribution is summarized in Table 5 [45]. Heat capacities are estimated using Eq. (1) where n_i refers to the number of each group listed in Table 4 and Γ_i represents its group value. The subscript *c* in Table 4 differentiates cyclic groups from their acyclic counterparts; group values for the latter have not been evaluated by this study. The calculated heat capacities at *T*=298.15 K are in good agreement with experiment. However, because of the scarcity of data for these two new groups, the group values for cyclic thio and dithiocarbamates should be considered as tentative assignments.

$$C_{p,\mathrm{m}}\ (298.15\ \mathrm{K})_{\mathrm{calc}}=\Sigma_i n_i \Gamma_i \qquad (1)$$

Acknowledgements

We acknowledge the Spanish MCyT/DGI under project BTQ2006-12745. A. V. D. thanks National Institutes of General Medical Sciences (GM077170) for financial support of this research. M. T. thanks MEC/SEUI, AP2002-0603, Spain for financial support.

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Received: January 16, 2007
Accepted: May 25, 2007

DOI: 10.1007/s10973-007-8345-8