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THERMAL STUDIES ON SOME SUBSTITUTED AMINOBENZOIC ACIDS

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Abstract

The thermal behaviour of various substituted aminobenzoic acids (3-aminobenzoic acid (3-ABA), 4-aminobenzoic acid (4-ABA), 3-aminosalicylic acid (3-ASA), 4-aminosalicylic acid (4-ASA), and 5-aminosalicylic acid (5-ASA), as well as the 'parent' benzoic acid (BA) and salicylic acid (SA) as reference substances, and possible decomposition products: 2-aminophenol (2-AP), 3-aminophenol (3-AP) and 4-aminophenol (4-AP) in the solid state has been examined.

The various sets of isomers studied showed considerable and interesting differences. Most sublimed well before melting, generally with an increasing rate of mass loss beyond their very different melting points. The differences in behaviour of 4-ASA and 5-ASA were the most remarkable, with 5-ASA being far more stable and apparently not decarboxylating readily, while 4-*ASA* sublimed at temperatures below the melting point, becoming less stable and decarboxylating in the liquid form.

Keywords: aminobenzoic acids, aminosalicylic acids, thermochemistry

Introduction

There have been several studies of the decompositions of various substituted aminobenzoic acids in the solid state [1–10] and even more studies in solution [11–16]. In addition to their pharmaceutical uses [5, 6], such reactants are of interest because the existence of ranges of isomers allows for comparison of behaviour. They also provide promising systems for the study of the participation of melting, vaporisation, and the influence of products, on the course of decomposition of an initially-solid reactant. Carstensen and Musa [4] have reported on the decompositions of benzoic acid derivatives in the solid state: $p\text{-}XC_6H_4COOH\ (s) \rightarrow XC_6H_5\ (l) + CO_2\ (g)$. Mention is made that thermal analysis methods were not used in the study because of sublimation problems. Kornblum and Sciarrone [3] have studied the solid state decarboxylation of 4-aminosalicylic acid (4-*ASA*) and Pothisiri and Carstensen [1] the decompositions of several p-substituted salicylic acids. Wesolowski [5] has studied the kinetics and mechanism of decarboxylation of 4-*ASA* and its sodium and calcium salts in the solid

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state and in solution. A range of values for the melting point of 4-*ASA* has been reported (139–151°C). Discrepancies arise because melting is accompanied by decarboxylation, reported [5] to begin at about 110 and to continue up to 150°C, and to be accelerated by water and the product, 3-aminophenol (3-*AP*).

Experimental

Materials

Benzoic acid (BA) and salicylic acid (SA) were obtained from Unilab Saar Chem Co. 2-aminophenol (2-AP) and 3-AP were obtained from Aldrich Chemical Co. Ltd. (UK). 4-AP was obtained from Riedel-de Haën Co. Ltd. 3-Aminobenzoic acid (3-ABA) was obtained from Aldrich Chemical Co. Ltd (UK). 4-ABA was obtained from Univar Saar Chem Co. 4-Aminosalicylic acid (4-ASA) and 5-ASA were obtained from Aldrich Chemical Co. Ltd. (UK). 3-ASA was not readily available. The compounds were used without further purification.

Equipment

Thermal analyses were carried out on a Perkin Elmer Series 7 TG and DSC calibrated in standard fashion using magnetic standards (TG) and the melting of indium (DSC). The TG could be linked to a Perkin Elmer 2000 FTIR via a heated interface and a gas cell (both supplied by Perkin Elmer). Unless otherwise specified, all the samples in both DSC and TG experiments were heated in flowing nitrogen at 10 K min^{-1}. DSC experiments were carried out in three types of sample pans: (a) standard aluminium pans with lids, but uncrimped; (b) sealed aluminium pans (using a cold-welding press and the appropriate pans, supplied by Perkin Elmer); and (c) stainless-steel pressure capsules (Perkin Elmer) with copper gaskets.

Calculation of thermodynamic properties

The expected thermodynamic properties: enthalpies of formation in the solid, liquid and gaseous phases, enthalpies of melting, vaporization and sublimation, and the enthalpies of the decarboxylation reactions of the appropriate (solid) acids were calculated from tables of group contributions, according to the methods given by Domalski and Hearing [17] and the results of these predictions are given in Table 1.

Results and discussion

Thermal behaviour of the reference acids

Figure 1 shows representative DSC and TG curves (obtained under the experimental conditions described above) for benzoic (BA) and salicylic acids (SA). The DSC curves (uncrimped aluminium pans heated in flowing nitrogen at 10 K min^{-1}) show the melting endotherms of BA and SA at 115–120°C and 158–162°C, respectively.

Table 1 Calculated thermodynamic properties [17]

	Enthalpy changes/kJ mol^{-1}							
	formation				melt	vap.	sublim.	decarb.
	solid (*s*)	liquid (*l*)	gas (*g*)					
salicylic acid	–591.13	–579.86	–493.61	11.27	86.25	97.52	32.02	
benzoic acid	–386.35	–374.34	–294.75		12.01	79.59	91.6	41.84
phenol	–165.6	–156.56	–96		9.04	60.56	69.6	n/a
2-aminobenzoic acid	–401.73	–380	–290.61		21.73	89.39	111.12	39.3
3-aminobenzoic acid	–411.73	–390	–290.61		21.73	99.39	121.12	49.3
4-aminobenzoic acid	–415.73	–392	–290.61		23.73	101.39	125.12	53.3
3-aminosalicylic acid	–606.51	–585.52	–489.47		20.99	96.05	117.04	29.02
4-aminosalicylic acid	–616.51	–595.52	–489.47		20.99	106.05	127.04	39.02
5-aminosalicylic acid	–620.51	–597.52	–489.47		22.99	108.05	131.04	43.02
2-aminophenol	–183.98	–174.22	–91.86		9.76	82.36	92.12	n/a
3-aminophenol	–183.98	–174.22	–91.86		9.76	82.36	92.12	n/a
4-aminophenol	–183.98	–174.22	–91.86		9.766	82.36	92.12	n/a
benzene (*l*)		49						
aniline (*l*)		31.1						
CO_2 (*g*)	–393.51							

1. No correction was given for the different isomers of aminophenol
2. Decarboxylation of the acids is assumed to be of the form
RCOOH (*s*)→RH (*s*)+CO_2 (*g*) with the product having the appropriate isomeric form

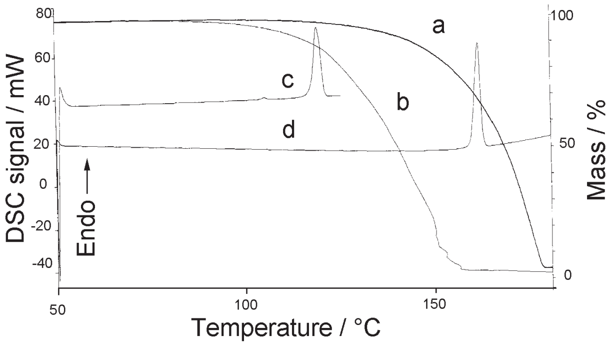

Fig. 1 Representative TG curves for a – salicylic acid (SA) and b – benzoic acid (BA) and DSC curves for c – BA and d – SA; all heated in flowing nitrogen at 10 K min^{-1}: uncrimped aluminium pans for DSC and open platinum pans for TG

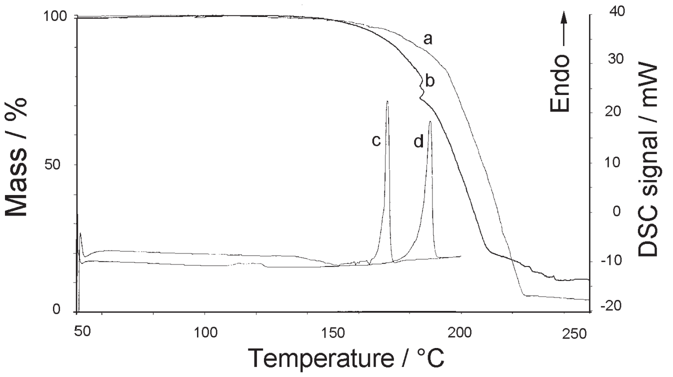

Fig. 2 Representative TG curves for the aminobenzoic acids: a – 4-ABA and b – 3-ABA and DSC curves for c – 3-ABA and d – 4-ABA; heated in flowing nitrogen at 10 K min^{-1} under the experimental conditions described above

The TG curves (open platinum pans heated in flowing nitrogen at 10 K min^{-1}) gave single-stage mass losses for both compounds. The onset of the mass loss for BA (at 10 K min^{-1}) is at about 85 and, by 158°C, 98% of the original mass has been lost by evaporation/decomposition. For SA, the mass loss starts at about 130 and is almost complete (96%) at about 178°C.

Aminophenols (AP)

The DSC curves for the aminophenols, 2-AP, 3-AP and 4-AP (under similar experimental conditions to those described above, but not illustrated) showed onset temperatures for melting of 118, 170 and 182°C for 3-AP, 2-AP and 4-AP, respectively. On cooling immediately after the melting endotherm and rescanning the sample, the area of the endotherm was greatly decreased, indicating decomposition with melting and/or loss of sample by evaporation. The TG curves for the aminophenols (under similar experimental conditions to those described above, but not illustrated) showed onset of mass loss at about 110°C for all three isomers. The rates of mass loss were similar for 2-AP and 3-AP, with that for 4-AP being slower. FTIR gas analysis did not indicate any significant amounts of CO_2 expected for decomposition, so evaporation must predominate and is complete for all three compounds by 200°C.

Aminobenzoic acids (ABA)

On decarboxylation, all the aminobenzoic acid isomers would give aniline (liq). The TG curves for 3-ABA (*m. p.*=171°C) and 4-ABA (*m. p.*=181–188°C) heated in flowing nitrogen at 10 K min^{-1} are similar (Fig. 2). Onset of mass loss is at about 100°C. For 4-ABA, mass loss is rapid until 95% loss at about 220°C. There is then a slow mass loss still incomplete by 420°C. For 3-ABA, mass loss is rapid until 90% loss at about 270°C. There is then a slow mass loss still incomplete by 540°C. Gas analysis by FTIR did not reveal formation of CO_2.

Aminosalicylic acids (ASA)

On decarboxylation, 4-aminosalicylic acid is expected to give 3-aminophenol, and 5-aminosalicylic acid to give 4-aminophenol. The TG curve for 4-ASA (Fig. 3) heated in flowing nitrogen at 10 K min^{-1} gives a two-stage mass loss (total 100%, with the discontinuity after about 30% mass loss at close to the reported melting point of 4-ASA (130°C). The CO_2 content, calculated from the formula of 4-ASA, is about 28.8%, i.e. close to mass loss at the discontinuity, but evolved gas analysis by FTIR shows that evolution of CO_2 occurs during the latter stage of the TG curve. The TG curve for 5-ASA (Fig. 3) gives a single-stage mass loss, total 100%) onset (under the experimental conditions described above) at about 190°C and maximum at close to 270°C, corresponding to the reported melting point of 5-ASA. Evolution of CO_2 was not detected. The DSC curve for 4-ASA (Fig. 3), under similar experimental conditions, shows several overlapping endotherms. The first (small) endotherm has onset (under these conditions) at about 110°C, the second at about 115°C and the third at

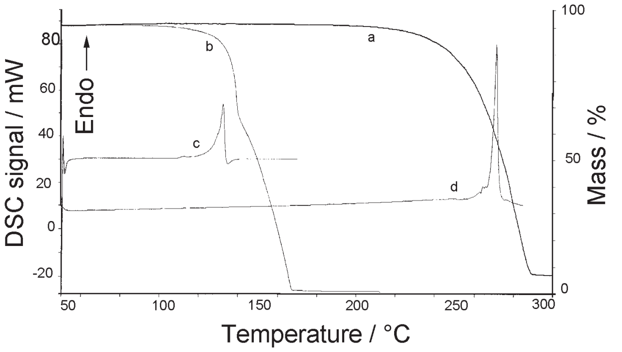

Fig. 3 Representative TG curves (open platinum pans) for a – 5-ASA and b – 4-ASA; and DSC curves (uncrimped aluminium pans) for c – 4-ASA and d – 5-ASA; heated in flowing nitrogen at 10 K min^{-1}

about 125°C, becoming complex and shifting to exothermic at about 132°C. On cooling from 155°C and rescanning the sample, a more compact complex endotherm with onset about 115°C was recorded. The expected product of decarboxylation, 3-AP, melts in the range 115–121°C.

Reactant/product mixtures

Decarboxylation of the aminosalicylic acids leads to the formation of the corresponding aminophenols. A 1:1 mol ratio mixture of 4-ASA/3-AP showed a complex overlapping endotherm, with onset about 110°C and complete by about 130°C with ΔH_{melt}=282 J g^{-1}. The calculated ΔH_{melt} from linear combination is 247 J g^{-1}. A similar mixture of 5-*ASA*/4-AP showed two endotherms. The first is sharper with onset about 170°C, *m. p.* about 179°C, and is followed by a broader endotherm, onset about 195°C and complete by about 240°C, ΔH_1=164 J g^{-1}; ΔH_2=190 J g^{-1} (Total ΔH=354 J g^{-1}). Calculated ΔH_{melt} from linear combination is 374 J g^{-1}.

Table 2 Melting and evaporation of aminobenzoic acid derivatives

Sample (*m. p.*/°C)	T_{range}/°C	ΔH_{vap}/ kJ mol^{-1}	From Table 1		ΔH/kJ mol^{-1}	
			vap.	sublim.	melt(calc.)	melt(exp.)
4-ASA (131–136)	130–150 150–180	250±40 50±5	106	127	21.0	47.9
5-ASA (270)	210–270	135±2	108	131	23.0	67.2
3-ABA (171–174)	120–170	102±2	99	121	21.7	33.7
4-ABA (183–9)	160–210	110±4	101	125	23.7	24.5
2-AP (170)	100–170	81±2	82.4	92.1	9.8	31.4
3-AP (115–120)	100–190	71±6	82.4	92.1	9.8	23.9
4-AP (181–3)	122–172	92±1	82.4	92.1	9.8	23.8
BA (120)	80–120 120–145	75±1 51±3	79.6	91.6	12.0	17.5
SA (158)	100–162	88±1	86.3	97.5	11.3	23.0

Evaporation

Between the melting and boiling points, the evaporation of many liquids from a constant surface area of sample in a suitable pan is a zero-order process [18, 19]. For isothermal evaporation this corresponds to an approximately linear mass loss with time, and for a constant heating rate and Arrhenius temperature dependence, to an exponential-type mass loss with temperature. A TG curve for benzoic acid heated at 10 K min^{-1} in flowing N_2 is shown in Fig. 1, curve b. The corresponding DTG curve (not shown) shows an increase in rate of mass loss around the melting point of benzoic acid at 122°C (the DSC curve c). Using the rate of mass loss as a measure of the zero-order rate constant, *k*, for evaporation, an Arrhenius-type plot of ln(*k*) *vs*. $1/T$ for the evaporation process (not illustrated) showed a discontinuity associated with melting. Linear regression of the high (>122°C) and low (<122°C) temperature segments gave apparent activation energies of 51±3 kJ mol^{-1} and 75±1 kJ mol^{-1}, respectively (or 80±2 kJ mol^{-1} overall). The reported enthalpy of sublimation is 89.7±0.5 kJ mol^{-1} [20]. From Table 1 above, the calculated enthalpies of vaporization and sublimation are 79.6 and 91.6 kJ mol^{-1}, respectively.

Using the above treatment as the model, the TG curves of the other samples were similarly examined. The calculated enthalpies of vaporization are given in Table 2, together with the applicable temperature ranges, and compared with the calculated values from Table 1. Also compared are the experimental enthalpies of melting, measured in sealed capsules, with the values calculated in Table 1.

Conclusions

There are considerable and interesting differences between the thermal behaviours of the various sets of isomers studied. Most of the compounds began to sublime well before melting, generally with an increasing rate of mass loss beyond the melting points, which are considerably different for the different isomers. The differences in behaviour of 4-ASA and 5-ASA were the most remarkable, with 5-ASA being far more stable and apparently not decarboxylating readily. It is interesting that 4-ASA appears to sublime at temperatures below the *m. p.*, becoming less stable and decarboxylating in the liquid form. These differences are being studied further.

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