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Short Communications

STUDY OF THE THERMAL PROPERTIES OF DERIVATIVES OF SULFONAMIDES

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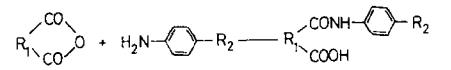
Thermal analysis of acid derivatives of sulfonamide was performed between room temperature and 600°. The tested substances were obtained by fusing and also by synthesis in boiling acetone. Information was obtained on the thermostabilities of these compounds and on the thermal decomposition processes they undergo.

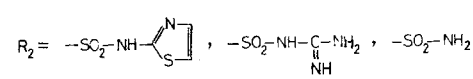
Acyl derivatives of sulfathiazole have found application in medicine for curing certain diseases of the alimentary canal [2–4] and as inhibitors on the oxidation of ammonium salts to nitrates in soil [1].

The reaction of dicarboxylic acid anhydrides with aromatic amines gives N-acyl derivatives. Low-temperature synthesis is usually described by reaction (I).



(I)

$R_1 = -Ph- \;,\; -CH_2-CH_2- \;,\; -CH=CH-$



Synthesis at high temperature leads to intermolecular reactions (cyclization) and further uncontrolled reactions. In this work, method chosen according to scheme (I) was tested.

The following acids were obtained:

1. Phthalylsulfathiazole (PST)
2. Phthalylsulfaguanidine (PSG)
3. Phthalylsulfanilamide (PSA)
4. Succinylsulfathiazole (SST)
5. Succinylsulfaguanidine (SSG)
6. Succinylsulfanilamide (SSA)
7. Maleylsulfathiazole (MST)
8. Maleylsulfaguanidine (MSG)
9. Maleylsulfanilamide (MSA)

The above acids were heated and thermally tested. The results can be useful for identification purposes. TG curves for some sulfonamide derivatives were obtained in earlier work [5].

Experimental

Reagents

Sulfathiazole, sulfaguanidine, sulfanilamide (Polfa–Poland); phthalic anhydride (POCh–Poland); succinic anhydride (APOLDA–DDR); maleic anhydride (Reachim).

Synthesis

The conditions for the preparation of the sulfonamide derivatives and the subsequent thermal testing are given in Table 1. All substances obtained were purified from starting materials by washing with water and methanol. To shorten the duration of the synthesis by the fusion method, higher reaction temperatures than those described in the literature were used. The substances obtained were compared with products synthesized in organic solution.

Purity testing of substances

The purities of substances were checked by paper chromatography; the eluents described in the literature for determination of sulfonamides were used [16–20]. The substances were dissolved in NaOH, HCl, methanol or formamide solution and detected with the Erlich reagent. No other substances were found by chromatography.

Thermal analysis

The thermal analysis of the synthesized substances was performed on a MOM (Budapest) derivatograph. Samples of 100–150 mg were heated in corundum crucibles, from ambient temperature to 600° within 50 minutes; the reference substance was Al_2O_3. DTA, DTG and TG curves were obtained. The thermal changes and the decomposition points observed in the DTA and TG curves are summarized in Table 2.

The calculated mass decreases for the investigated substances and the presumed water and acetone contents of the samples are presented in Table 3.

The melting points determined in the classical way in a capillary tube were compared with the temperature found from the DTA curve.

Results and discussion

Thermal investigations of nine acid derivatives of sulfonamides, as well as the sulfonamides used for their synthesis, were performed. The sulfonamide derivatives were obtained by fusion of sulfonamides with dicarboxylic acid anhydrides; four acids were synthesized in boiling acetone solution (Table 1, Nos 1, 2, 4, 9).

Table 1 Method of preparation of acide derivatives of sulfonamides

No	Compound	Substrate	Method		Symbol of compound	Notices
			known	used		
1	Phthalylsulfathiazole acid (PST)	ST + PA	a) fuse of substrates at 85–145°C [6] b) fuse of substrates at 100–120°C 15 kg/cm^2 [7] c) in organic solvent [8, 9]	a) fuse of substrates at 190–200°C, 30 min b) of acetone solution 60 min.	PSTm PSTa	ST added to molten PA
2	Phthalylsulfaguanidine acid (PSG)	SG + PA	–	a) fuse of substrates at 160–180°C, 30 min. b) of acetone solution 60 min.	PSGm PSGa	SG added to molten PA
3	Phthalylsulfanilamide acid (PSA)	SfA + PA	–	fuse of substrates at 160–170°C, 20 min.	PSA	PA added to molten SfA
4	Succinylsulfathiazole acid (SST)	ST + SuA	a) fuse of substrates at 75–100°C 1000–1500 kg/cm^2 [10, 11] b) in organic solvent [8, 9]	a) fuse of substrates at 120–130°C, 30 min. b) of acetone solution 60 min.	SSTm SSTa	ST added to molten SuA
5	Succinylsulfaguanidine acid (SSG)	SG + SuA	–	fuse of substrates at 125°C, 60 min.	SSG	SuA added to molten SG
6	Succinylsulfanilamide acid (SSA)	SfA + SuA	in organic solvent [12, 13]	fuse of substrates at 125–130°C, 15 min.	SSA	SfA added to molten SuA
7	Maleylsulfathiazole acid (MST)	ST + MA	in organic solvent [14]	fuse of substrates at 110°C, 15 min.	MST	ST added to molten MA
8	Maleylsulfaguanidine acid (MSG)	SG + MA	–	fuse of substrates at 70–100°C, 15 min.	MSG	SG added to molten MA
9	Maleylsulfanilamide acid (MSA)	SfA + MA	in organic solvent [15]	a) fuse of substrates at 170–175°C, 15 min. b) of acetone solution 60 min.	MSAm MSAa	MA added to molten SfA

ST – sulfathiazole, SG – sulfaguanidine, SfA – sulfanilamide, PA – phthalic anhydride, SuA – succinic anhydride, MA – maleic anhydride

Table 2 Thermal decomposition data for tested sulfonamides

Compound	Process temperature, °C	Loss in weight	Temperature of thermal decomposition, °C
ST	endothermic at 170–185	–	250
	endothermic at 205–220	–	
PSTm	exothermic at 70	–	300
	endothermic at 200–230	loss	
	endothermic at 265–280	–	
PSTa	endothermic at 200–230	loss	270
	endothermic at 270–280	–	
SSTm	endothermic at 105–145	loss	210
	endothermic at 180–210	–	
SSTa	endothermic at 100–140	–	200
	endotherimc at 175–200	–	
MST	endothermic at 200–240	loss	240
SG	endothermic at 100–150	loss	250
	endothermic at 190–200	–	
PSGm	endothermic at 135–170	loss	320
	endothermic at 240–285	–	
PSGa	endothermic at 80–130	loss	300
	endothermic at 160–190	loss	
	endothermic at 240–260	–	
SSG	endothermic at 100–130	loss	230
	endothermic at 200–230	–	
MSG	endothermic at 80–140	loss	230
	endothermic at 190–200	loss	
SfA	endothermic at 120–150	–	270
	endothermic at 175–180	–	
MST	endothermic at 160–175	–	290
	endothermic at 200–230	loss	
	endothermic at 240–265	loss	
SSA	endothermic at 205–225	–	320
	endothermic at 270–295	–	
MSAm	endothermic at 200–220	loss	290
MSAa	endothermic at 200–220	loss	300

The DTA and TG curves of compounds prepared by fusion or synthesized in solution were compared. The shape of the DTA curve of the compound obtained by fusion is different from that of the same compound prepared in acetone solution. This difference is only slight and exists in the temperature range of the synthesis (from the boiling point of acetone to the temperature of fusion used in the synthetic method).

Table 3

Compound	Temperature range, in °C	Loss in weight, %	Calculated wt loss, % of the water and acetone		Melting temperature, °C	
			%	formula	measured conventionally	from the DAT curve
ST	–	–	–	ST	199–203	205
PSTm	200–230	4.0	4.3	PST · H_2O	265–270	265
PSTa	200–230	6.0	6.7	PST $\frac{1}{2}$A *	240–250	265
SSTm	105–145	2.5	2.5	SST · $\frac{1}{2}H_2O$	185–190	175
SSTa	100–130	5.0	4.8	SST · H_2O	150–160	165
MST	200–240	8.6	9.2	MST · 2 H_2O	215–218	210
SG	100–150	7.4	7.75	SG · H_2O	190–193	190
PSGm	80–160	3.0	2.4	PSG · $\frac{1}{2}H_2O$	260–265	260
PSGa	80–130	6.2	7.1	PSG $\frac{1}{2}$A *	220–230	240
	150–180	4.1	4.4	PSG · H_2O		
SSG	100–130	1.9	1.9	SSG · $\frac{1}{2}H_2O$	205–210	190
MSG	80–140	9.0	10.3	MSG · 2 H_2O	205–210	190
SfA	–	–	–	SfA	164–167	165
PSA	190–265	10.4	10.1	PSA · 2 H_2O	300–310	240
SSA	–	–	–	SSA	210–216	205
MSAm	200–260	11.4	11.7	MSA · 2 H_2O	192–195	200
MSAa	200–260	12.0	11.7	MSA · 2 H_2O	193–198	200

* A – acetone

At temperatures higher than that of the synthesis by fusion, the shapes of the DTA curves of the compounds obtained by fusion or in solution are similar. The changes in the DTA curves might be due to intramolecular rearrangements taking place at higher temperatures.

From the similar shapes of the DTA curves at temperatures higher than those used in the syntheses, it may be seen that the compounds undergo the same changes, which is proof of their identity.

Thus, from the evidence of the DTA curves it can be suggested that the samples prepared by the fusion method differ only slightly from those obtained in acetone solution. To explain this, further identification studies are necessary.

The TG curves of compounds synthesized in acetone solution show a double mass decrease as compared with samples obtained by fusion, this being due most probably to the higher water and acetone contents (Table 3). The water originates from the washing of the substance with water in the purification process; dehydration resulting from chemical reactions at higher temperatures is also possible.

The melting points of the studied substances were determined from the DTA curves and compared with those measured in a capillary tube (Table 3). The melting points are very close to the decomposition points for most of the studied compounds, and for MSA they are even identical (Table 2); this is why determination of the melting point by the classical method is difficult for the majority of the substances. The TG curves of ST, SQ, SA and PST sulfonamides are presented in [5]. These curves were recorded for small samples (2 mg), using a special apparatus. They are similar to the TG curves given in the present work, obtained from larger samples (> 100 mg).

The DTA and TG curves for the synthesized acid derivatives of sulfonamides and for the sulfonamides used in the synthesis are quite different. This fact can be of use for the identification of these compounds, for the detection of solvent molecules, or for the determination of the degree of thermal change.

In this way it is possible to determine the technological criteria in the preparation of drugs, e.g. the temperature of drying or of tableting.

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