Thermochimica Acta, 17 (1976) 217–229

THE THERMAL DECOMPOSITION OF BISMUTH(III) COMPOUNDS USED IN MEDICINE

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(Received 10 February 1976)

ABSTRACT

The machanisms of thermal decompositions have been studied of the following bismuth(III) salts: benzoate, salicylate, subbenzoate, subsalicylate, subgallate, iodogallate, oxalate, citrate, Na–Bi(III) tartrate and tribromophenolate using thermal and differential thermal analyses. Intermediate products of decomposition have been isolated and identified.

INTRODUCTION

Bismuth(III) compounds have been widely used in medicine. At low concentrations they elicit as astringent, anti-inflammatory and antidiarrhoeic action, whilst at higher concentrations they act as antiseptics. Since 1921, when they were first used by Sanerac and Levaditi for treatment of syphilis, they have been employed in the chemotherapy of systemic infections[1].

In this work the thermal decompositions of the following bismuth(III) compounds have been studied: benzoate, subbenzoate (Bismutyl) salicylate, subsalicylate (Bisantol), subgallate (Dermatol), iodogallate (Airol), oxalate, citrate, Na–Bi(III)tartrate (Trepol) and tribromophenolate(Xeroform).

EXPERIMENTAL

Reagents

Bi(III)subgallate (according to Polish Pharmacopoeia IV: P.Ph. IV) and the tribromophenolate (according to the Polish Official Drug Register (USL)) were manufactured by the Pharmaceutical Works "Polfa", Lodz. Bi(III)iodogallate was supplied by May Baker Ltd., Dagenham, England. The benzoate, salicylate, subbenzoate and subsalicylate were obtained by employing the method of Picon[2], whilst the oxalate and the citrate were obtained according to Godfrin[3]. The Na–Bi(III)-tartrate was prepared by refluxing a suspension of monosodium tartrate and a freshly precipitated $Bi(OH)_3$, under vigorous stirring, for 50 h. The crude product was filtered off, washed and dried in vacuo.

TABLE 1

RESULTS OF THERMAL DECOMPOSITION OF Bi(III) COMPOUNDS IN AIR

Bi(III) compound	*Decompn. stage*	*Temp. range at a heating rate of:* *5°C min⁻¹* .... *10°C min⁻¹*	*Colour of the residue*	*Composition of the residue*	*Calc.* ..... *Detd.*			
					Δm%	*%C*	*%H*	*%Bi₂O₃*
Benzoate	I	20–150 20–170	white	$(C_6H_5COO)_3Bi$	0.0 ... 0.0	44.07 ..... 44.17	2.64 .... 3.00	40.70 ..... 40.49
	II	150–530 170–600	yellow	Bi_2O_3	59.3 .... 59.5	—	—	40.70 ..... 40.55
Subbenzoate	I	20–180 20–220	white	$C_6H_5COOBi(OH)_2$	0.0 ... 0.0	23.09 ..... 23.01	1.94 .... 1.85	63.99 ..... 64.10
	II	180–360 220–380	—	$C_6H_5Bi{=}O$	17.0 .... 17.0	—	—	—
	III	360–495 380–535	yellow	Bi_2O_3	36.0 .... 38.0	—	—	63.99 ..... 63.80
Salicylate	I	20–140 20–140	white	$[C_6H_4(OH)COO]_3Bi \cdot 3H_2O \cdot 0.08$ m Bi_2O_3	0.0 ... 0.0	35.44 ..... 35.65	2.97 .... 2.86	37.98 ..... 37.90
	II	140–245 140–245	white	$[C_6H_4(OH)COO]_3Bi \cdot 0.08$ m Bi_2O_3	7.6 ... 8.0	38.36 ..... 38.91	2.30 .... 2.44	41.08 ..... 41.50
	III	245–545 245–750	yellow	Bi_2O_3	62.0 .... 62.0	—	—	37.98 ..... 37.40
Subsalicylate	I	20–230 20–230	pale-yellow	$C_6H_4(OH)COOBi(OH)_2$	0.0 ... 1.0	22.12 ..... 22.06	1.86 .... 1.97	61.29 ..... 62.12

		230–300			16.3			
	II	....	—	$C_6H_4(OH)Bi{=}O$	....	—	—	—
		230–305			17.0			
		300–350			38.7			61.29
	III	....	yellow	Bi_2O_3	....	—	—	.....
		305–420			36.5			62.50
		20–60			0.0	19.55	2.11	54.17
Subgallate	I	......	yellow	$HOBi(O)_2HOC_6H_2COOH\cdot 2H_2O$	...	.....	....	.....
		20–100			0.0	20.20	2.09	53.95
		60–200	green-		11.5	21.33	1.28	59.12
	II	....		$(Bi(O)_2HOC_6H_2COOH)_2O$	....	.....	....	.....
		100–260	yellow		12.5	21.11	1.31	60.50
		240–630			45.8			54.17
	III	....	yellow	Bi_2O_3	....	—	—	.....
		290–760			46.3			53.80
		20–60			0.0	15.57	1.49	43.14
Jodogallate	I	.....	darkgreen	$JBi(O)_2HOC_6H_2COOH\cdot 2H_2O$	...	.....	....	.....
		20–60			0.0	15.77	1.39	43.82
		60–260			6.7	16.68	0.80	46.23
	II	......	greygreen	$JBi(O)_2HOC_6H_2COOH$	...	.....	....	.....
		60–280			7.5	15.89	0.75	45.50
		260–580			52.6			
	III	....	—	$(BiO)_2CO_3$	....	—	—	—
		280–700			52.0			
		700–780			56.9			43.14
	IV	....	yellow	Bi_2O_3	....	—	—	.....
		700–800			56.8			43.20
		20–60			0.0	9.56	1.07	61.79
Oxalate	I	.....	white	$(COOCOO)_3Bi_2\cdot 4H_2O$	...	....	....	.....
		20–90			0.0	9.98	1.32	60.80
		60–220			9.6	10.57	0.00	68.32
	II	......	white	$(COOCOO)_3Bi_2$	...	.....	....	.....
		90–255			9.5	10.85	0.11	67.95
		220–415			38.2			61.79
	III	....	yellow	Bi_2O_3	....	—	—	.....
		255–450			38.0			60.90

(Table continued on p. 220)

TABLE 1 (*Continued*)

Bi(III) compound	*Decompn. stage*	*Temp. range at a heating rate of: 5 °C min^{-1} .... 10 °C min^{-1}*	*Colour of the residue*	*Composition of the residue*	*Calc. ..... Detd.*			
					Δm%	%*C*	%*H*	%Bi_2O_3
		20–80			0.0	16.60	2.09	53.67
Citrate	I	......	white	$[(CH_2COO)_2C(OH)COO]Bi\cdot 2H_2O$	...	.....	....	.....
		20–100			0.0	16.60	2.48	53.40
		80–200			8.3	18.10	1.27	58.53
	II	....	white	$[(CH_2COO)_2C(OH)COO]Bi$	...	.....	....	.....
		100–250			7.5	17.77	1.98	58.67
		200–470			46.3			53.67
	III	....	yellow	Bi_2O_3	....	—	—	.....
		250–740			45.0			52.90
Na-Bi(III)-tartrate		20–60	yellowish-green		0.0	5.35	0.90	83.73
	I	......		$NaOOC(CHOBiO)_2COOBiO\cdot 3H_2O$	...	....	....	.....
		20–120			0.0	5.26	1.01	83.44
		60–240	light-brown		6.0	5.69	0.24	89.09
	II	....		$NaOOC(CHOBiO)_2COOBiO$	...	....	....	.....
		120–290			6.0	5.58	0.12	87.12
		240–700			16.3			83.73
	III	....	yellow	Bi_2O_3, Na_2CO_3	....	—	—	.....
		290–770			16.3			82.33
Tribromo-phenolate		20–260			0.0	10.66	0.37	51.71
	I	......	paleyellow	$(Br_3C_6H_2O)_2BiOH\cdot Bi_2O_3$	...	.....	....	.....
		20–300			0.0	11.11	0.53	53.00
		260–680			48.0			51.71
	II	....	yellow	Bi_2O_3	....	—	—	.....
		300–740			58.0			41.18

TABLE 2

TG HORIZONTALS, MAXIMA AND RANGES OF DTG AND DTA PEAKS OF Bi(III) COMPOUNDS

Heating rate 5°C min^{-1} in air. s = strong; m = medium; w = weak; v = very; exo = exothermic; endo = endothermic.

Bi(III) compound	*Decompn. stage*	*Range of TG horizontal (°C)*	*Maximum on DTG trace (°C)*	*Range of the DTG effect (°C)*	*Maximum on DTA trace (°C)*	*Range of DTA effect (°C)*
Benzoate	I	up to 150				
	II	380–400	290 vw	180–305	— endo vw	140–290
		over 530	312 w	305–325	310 endo w	290–330
			370 s	325–390	440 exo s	355–535
			428 vs	390–465	842 endo vw	830–855
Subbenzoate	I	up to 180				
	II		210 w	175–290	212 endo vw	190–240
			343 w	290–365		
	III	over 495	448 m	365–470	388 exo s	240–435
			485 w	470–500	445 exo s	435–500
					760 endo vw	740–780
					850 endo vw	835–870
Salicylate	I	up to 140				
	II		200 w	145–240	190 endo w	160–205
					— endo vw	205–240
	III	over 545	280 s	240–560	260 endo w	240–300
					380 exo m	300–420
					500 exo s	420–510
					530 exo s	510–600
					750 endo vw	745–760
					845 endo vw	830–855
Subsalicylate	I	up to 230				
	II		265 m	230–270	265 endo w	230–280
	III	over 350	300 vs	270–350	310 exo vs	280–390
					720 endo vw	695–740
					810 endo vw	800–830
Subgallate	I	up to 60				
	II		180 w	60–200	180 endo w	60–200
	III	200–240	270 m	230–340	300 exo vs	200–640
		over 630	390 w	340–490	770 endo vw	760–780
					865 endo vw	845–875
Jodogallate	I	up to 60				
	II		— vw	60–260	220 endo vw	60–250
	III		280 m	260–420	320 exo vs	250–560
	IV	580–700	540 w	420–630	770 endo vw	600–780
		over 800	760 w	650–770	820 endo vw	800–830
Oxalate	I	up to 60				
	II		120 w	80–145	120 endo m	80–170
			200 vw	145–220	210 endo vw	180–230
	III	290–360	242 vs	220–255	255 exo s	230–320
		415–620	260 w	255–290	395 exo m	365–435
			395 w	350–420	670 endo w	620–690
				over 610		

TABLE 2 (*Continued*)

Bi(III) compound	*Decompn. stage*	*Range of TG horizontal (°C)*	*Maximum on DTG trace (°C)*	*Range of the DTG effect (°C)*	*Maximum on DTA trace (°C)*	*Range of DTA effect (°C)*
Citrate	I	up to 80				
	II		—— vw	90–200	140 endo w	90–200
	III	300–350	280 vs	200–282	250 endo w	200–275
		over 470	287 vs	282–320	300 exo s	275–370
			—— vw	340–470	390 exo s	370–500
					690 endo vw	650–710
					730 endo vw	710–760
Na-Bi(III)-tartrate	I	up to 60				
	II		135 vw	60–230	140 endo m	50–220
	III	over 700	265 s	230–272	250 exo m	220–270
			280 s	272–300	290 exo s	270–430
			325 vw	300–345	700 endo vw	615–710
			375 w	345–390	760 endo m	710–790
			—— vw	390–700		
Tribromo-phenolate	I	up to 260				
	II	over 680	300 w	270–330	300 exo w	260–330
			460 vs	330–520	390 exo w	330–420
			520 vw	520–585	460 exo s	420–540
			680 w	585–690	680 endo vw	600–690
					770 endo vw	760–780

Apparatus

The thermal decomposition of the compounds was carried out on an OD-130 derivatograph (MOM, Budapest). Sample specimens (100–750 mg) were heated in Pt crucibles at a rate of 5 and 10°C min^{-1} to 950°C. As a reference, L–Al_2O_3 was employed. The sensitivities of DTA and DTG were 1/10 and 1/15, respectively.

A semimicro elemental analysis was performed using the method of Kozlowski et al.[4].

The Bi_2O_3 content of iodogallate was determined by the Langren method[5], and that of tribromophenolate by the Klissiums method[6]. In the remaining compounds the oxide content was assayed by the P.Ph. IV method[7].

Results of thermal decomposition of the compounds studied are shown in Tables 1 and 2 and in Figs. 1–5.

RESULTS AND DISCUSSION

Thermal decomposition of all of the compounds studied occurs in three stages. At the first stage, there is no loss in weight and no changes of TG, DTG and DTA, thus indicating that the given compound is quite stable. At stage II, water of crystallization or water of constitution is generally lost. This stage is characterized by an endothermic effect (cf. DTA trace in Figs. 1–5 and Table 2). At the end of this stage a small horizontal occurs, whose importance for analytical purposes is rather

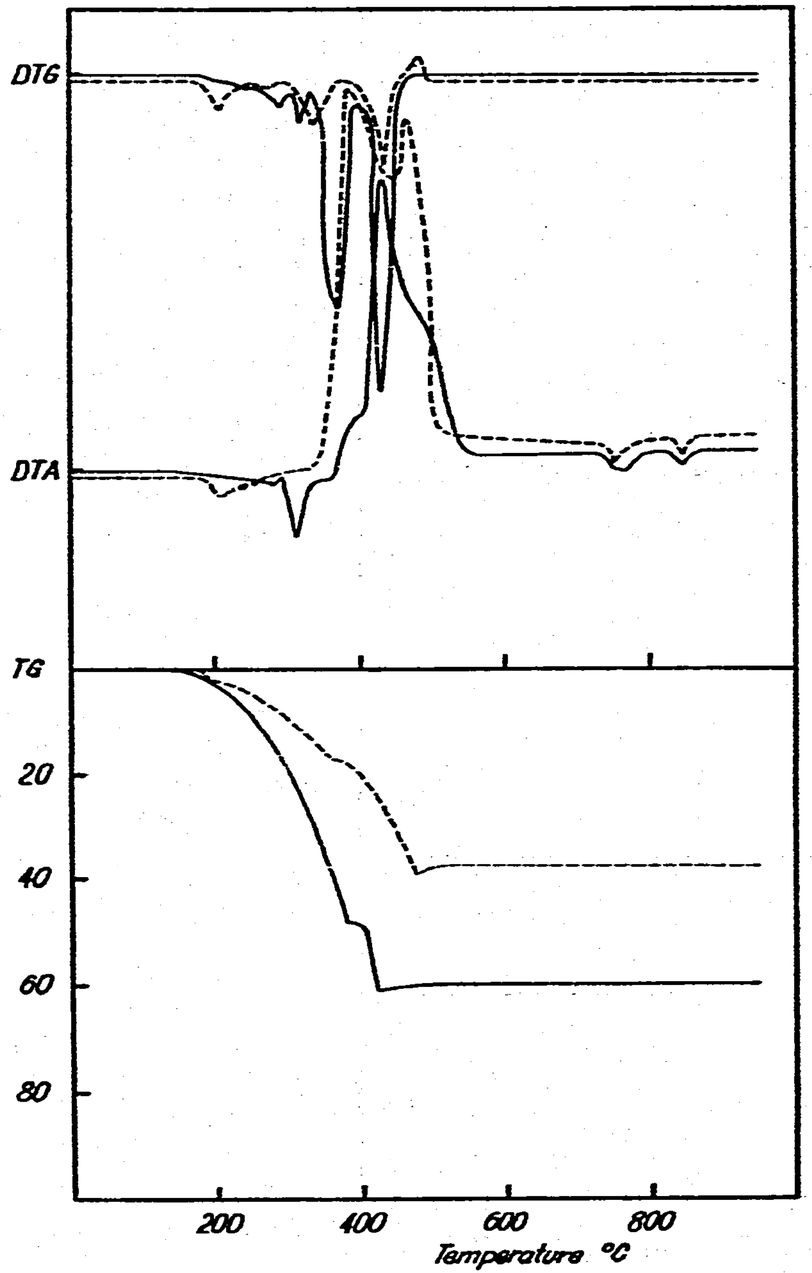

Fig. 1. TG, DTG and DTA traces of bismuth(III)benzoate, $(C_6H_5COO)_3Bi$ continuous line and of bismuth(III)subbenzoate, $C_6H_5COOBi(OH)_2$, dashed line. Heating rate 5°C min^{-1}, sample weights 300 and 200 mg, respectively.

doubtful. At stage III combustion of organic groups of the compounds takes place. The heat of combustion overweights that due to liberation of volatile products and hence the net effect of this stage is exothermic, as shown by the DTA trace (cf. Figs. 1–5 and Table 2). The final decomposition products of all the compounds

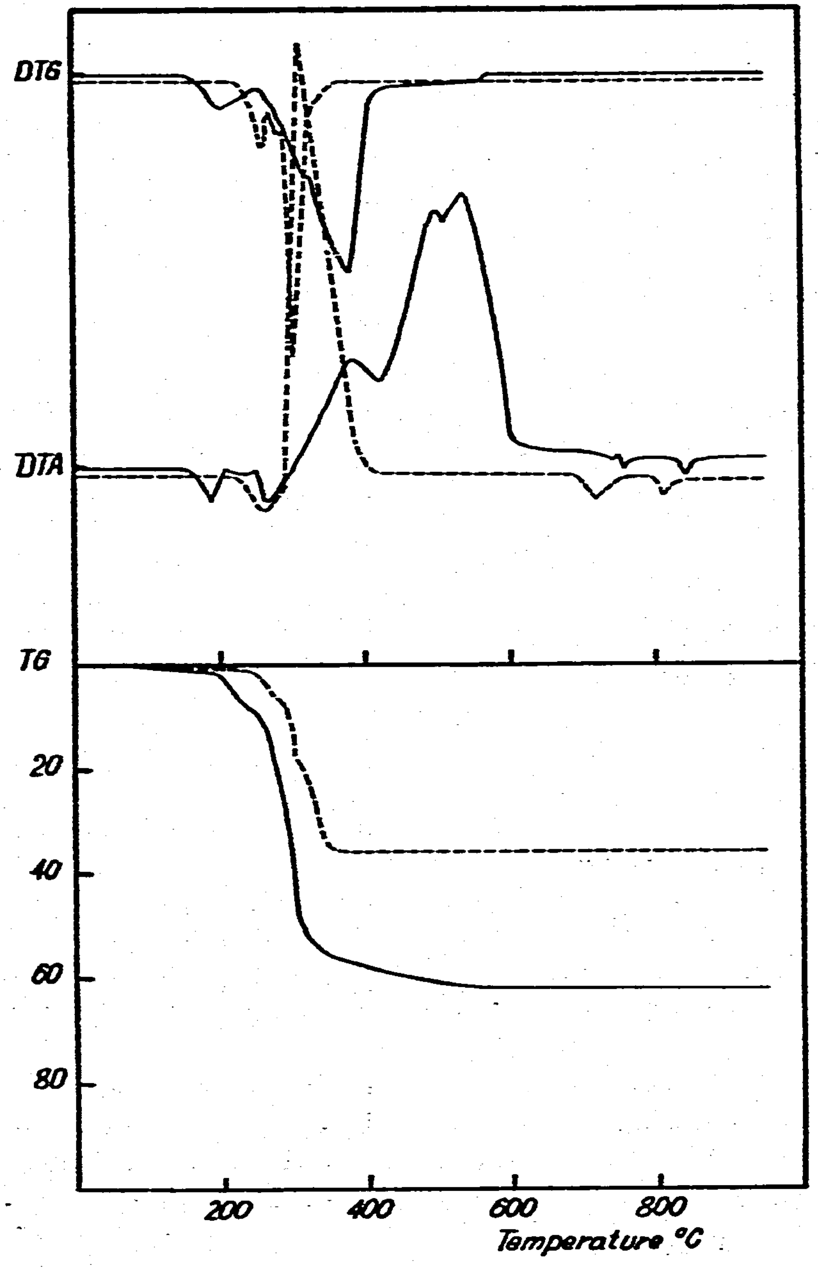

Fig. 2. TG, DTG and DTA traces of bismuth(III)salicylate, $(C_6H_4(OH)-COO)_3Bi \cdot 0.08\ m\ Bi_2O_3 \cdot 3H_2O$, continuous line and of bismuth(III) subsalicylate, $C_6H_4(OH)COOBi(OH)_2$, dashed line. Heating rate 5°C min^{-1}, sample weights 250 and 100 mg, respectively.

studied is Bi_3O_2. A horizontal corresponding to this oxide is expecially useful for analytical purposes. At still higher temperatures, characteristic endothermic DTA peaks occur which are probably due to polymorphic transformations of Bi_2O_3 (Table 2).

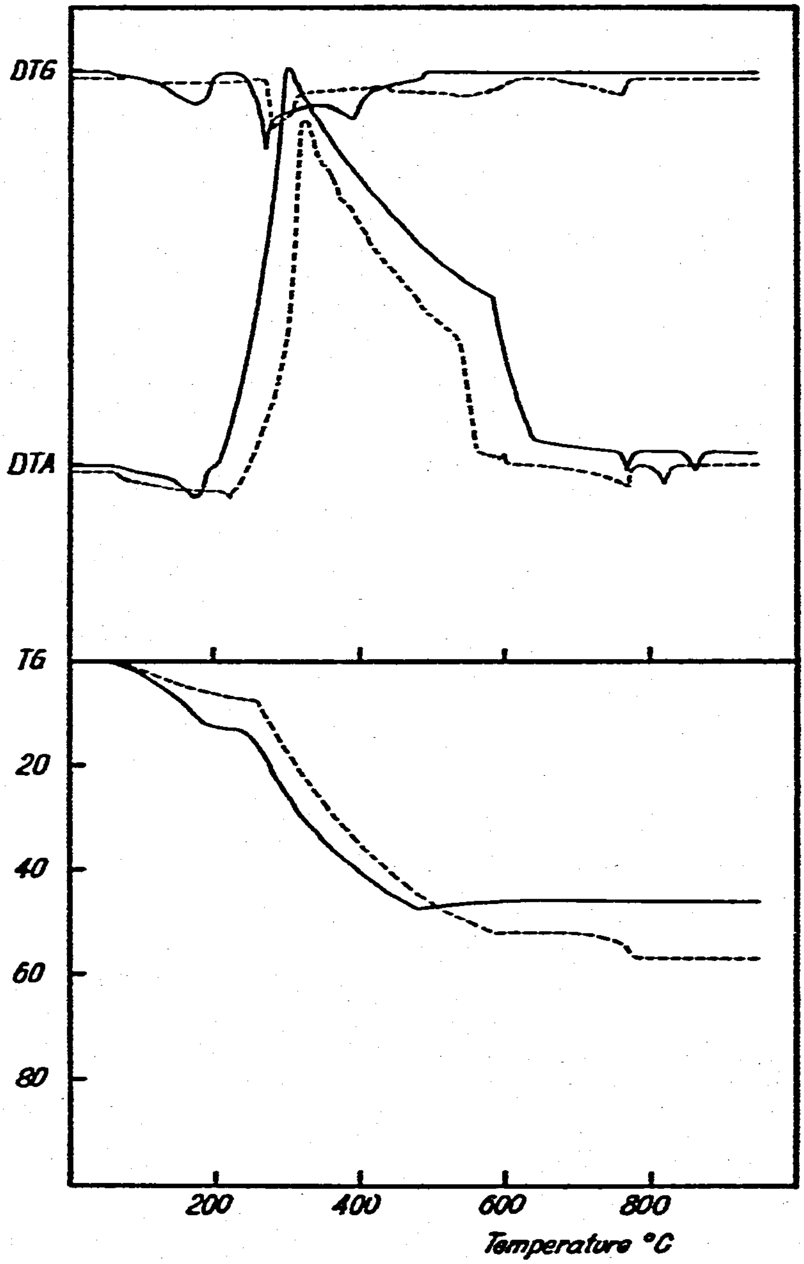

Fig. 3. TG, DTG and DTA traces of bismuth(III)gallate, $HOBi(O)_2HOC_6H_2COOH \cdot 2H_2O$, continuous line and of bismuth(III)iodogallate $JBi(O)_2HOC_6H_2COOH \cdot 2H_2O$, dashed line. Heating rate 5°C min^{-1}, sample weights 200 and 300 mg, respectively.

In order to isolate intermediate products, heating of a sample was discontinued at a proper temperature interval (cf., Table 2) and the residue was analyzed. Mean results of three determinations are listed in Table 1.

Characteristic features of thermal decomposition of individual compounds:

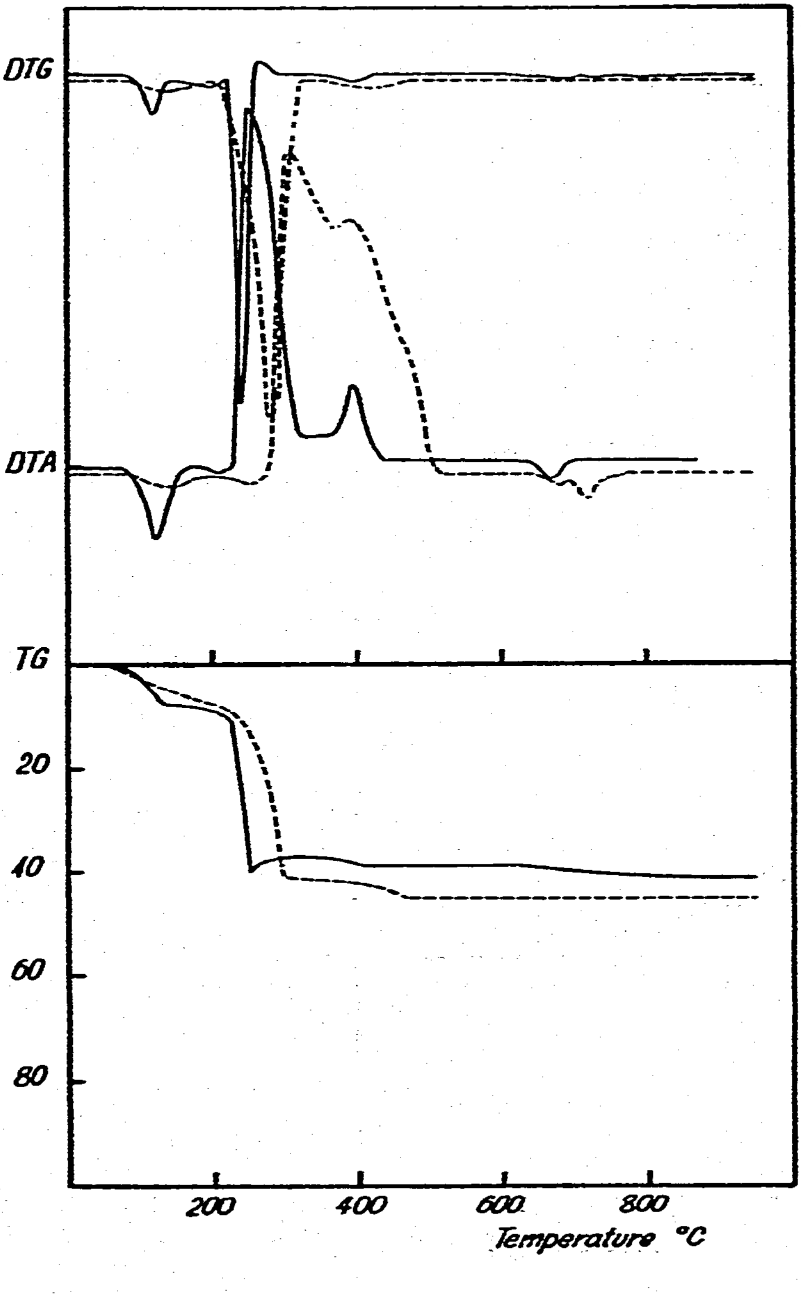

Fig. 4. TG, DTG and DTA traces of bismuth(III)oxalate, $(C_2O_4)_3Bi_2 \cdot 4H_2O$, continuous line and of bismuth(III)citrate, $[(CH_2COO)_2C(OH)COO]Bi \cdot 2H_2O$, dashed line. Heating rate 5 °C min^{-1}, sample weights 300 and 240 mg, respectively.

1. Bi(III)benzoate

Stages I and III were only distinguished during thermal decomposition of this salt (cf. Fig. 1, continuous line). A grey-green intermediate product isolated at stage III gave no characteristic infrared absorption bands. Results of elemental analyses (C, H, Bi_2O_3) indicate that the product provides a coked residue of the

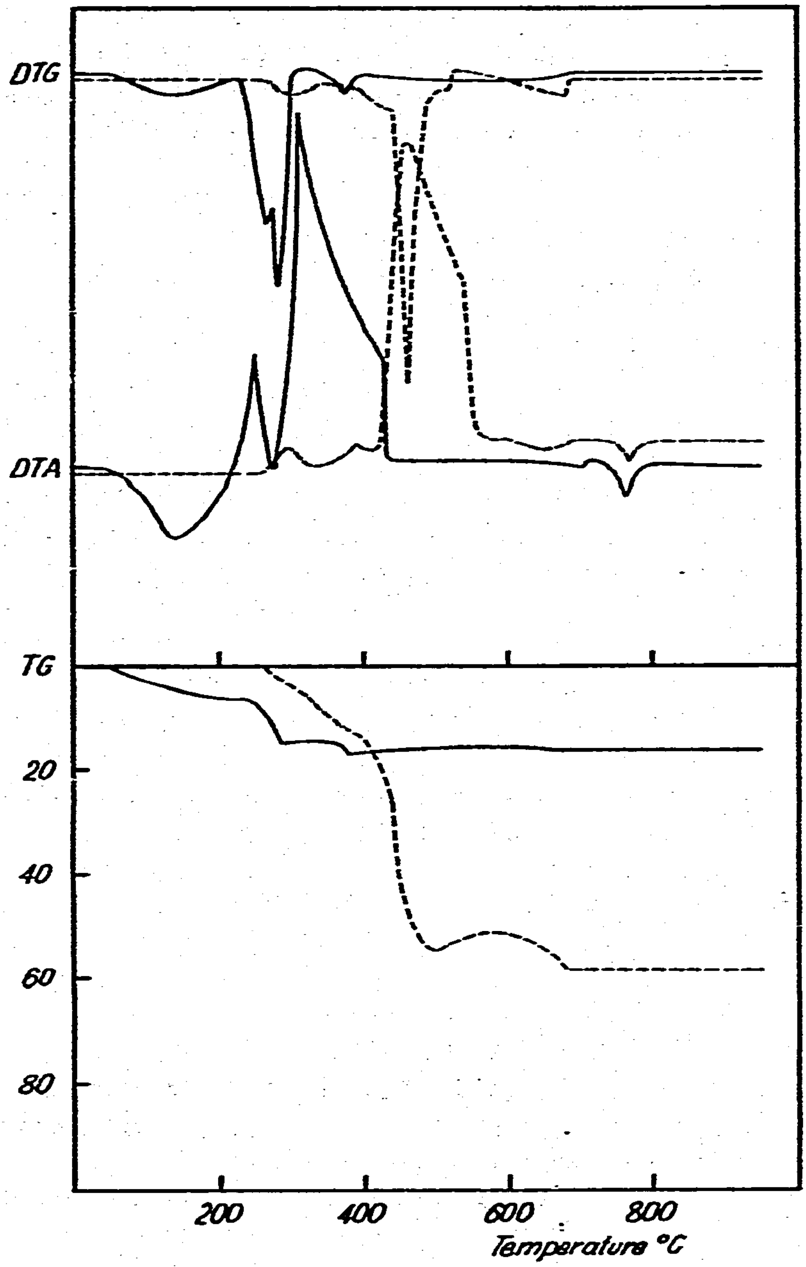

Fig. 5. TG, DTG and DTA traces of sodium–bismuth(III)tartrate, NaOOC(CHOBiO)$_2$COOBiO·3H$_2$O, continuous line and of bismuth(III)tribromophenolate, (Br$_3$C$_6$H$_2$O)$_2$BiOH·Bi$_2$O$_3$, dashed line. Heating rate 5°C min^{-1}, sample weights 700 and 200 mg, respectively.

molecular formula $C_4H_4O_2Bi$. A small horizontal due to this residue could, however, not be employed for analytical purposes.

2. *Bi(III)subbenzoate (Bismuthyl)*

Stage II of the decomposition of this salt consists probably in loss of one molecule of water of constitution followed by decarboxylation (cf., Fig. 1, dashed line). The differentiation of this stage is confirmed by two minima on the DTG trace and a slight inflection on the TG trace. An intermediate product formed at this stage could not be isolated owing to the lack of a clear-cut horizontal on the TG trace.

3. *Bi(III)salicylate*

The presence of a small quantity of Bi_2O_3 in this salt is due to a slow hydrolysis of the salt which occurred during its preparation (cf., Fig. 2, continuous line).

4. *Bi(III)subsalicylate (Bisantol)*

The decomposition of this salt follows exactly the pattern observed with Bismutyl (cf., Fig. 2, dashed line). The DTA trace for Bisantol was recorded by Renzo and Pirisi[8]. They identified three endothermic DTA peaks over the ranges 40–70°C (a maximum at 66°C), 170–185°C (a maximum at 175°C) and 280–330°C (a maximum at 320°C), as well as an exothermic peak over the range 340–500°C. However, these findings could not be confirmed in this work.

5. *Bi(III)subgallate (Dermatol)*

A gravimetric study of Dermatol aimed at employing the method for analyzing gallic acid has been reported by Duval[9] who found that Bi_2O_3 was the final decomposition product of the salt. The oxide was heated to 948°C. Our present study showed the decomposition of Dermatol to occur in three stages. In the infrared spectrum of an intermediate product isolated at stage II, the presence of a carboxyl group was shown by finding bands due to $\nu_{C=O}$, ν_{C-O} and ν_{O-H} at 1670 (s), 1330 (s) and 3480 (s) cm^{-1}, respectively (cf., Fig. 3, continuous line). The decomposition is terminated at about 630°C to give Bi_3O_2.

6. *Bi(III)iodogallate (Airol)*

The decomposition of Airol occurs in four stages (cf., Fig. 3, dashed line). An infrared spectrum of a residue isolated at stage II, bands due to a carboxyl group were found. The presence of an iodine atom in the molecule of Airol affects the mechanism of thermal decomposition as compared with that of Dermatol. At stage III bismutyl oxide was formed which was not defected during the decomposition of Dermatol.

7. *Bi(III)oxalate, Bi(III)citrate and Na–Bi(III)tartrate (Trepol)*

The decomposition of these salts (cf., Fig. 4, continuous line, Fig. 4, dashed line and Fig. 5, continuous line, respectively) follows a similar pattern. A horizontal formed at stage III of the decomposition of the citrate over the range 300–350°C is due to formation of a coked residue and hence is useless for analytical purposes. With Trepol, the final products consist of Bi_2O_3 and Na_2CO_3.

8. *Bi(III)tribromophenolate* (*Xeroform*)

The decomposition of the compound occurs in two stages. This is due to the presence of bromine atoms which form volatile products with Bi(III). For this reason the weight of the residue Bi_2O_3 is reduced.

CONCLUSIONS

(1) Results of this study on thermal decomposition of Bi(III)compounds used in medicine showed that thermal analysis can be useful for the determination of the number of molecules of water bound, for detecting contamination with starting reagents and for the control of the agreement of declared composition of a compound with pharmacopoeial standards.

(2) The knowledge of heating curves is useful for gravimetric analysis of a compound. For quantitative analysis of the compounds studied, a horizontal formed at the first and at the last stages of decomposition is only suitable. The remaining horizontals are of no analytical importance owing to a narrow temperature interval over which they occur or to difficulties in identification of an intermediate compound formed.

(3) Raising heating rates from 5 to 10°C min^{-1} had no essential influence on the mechanism of the thermal decomposition. As the heating rates increased, DTA and DTG peaks as well as horizontals on the TG traces, changed in the manner reported by Schultze[10].

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