Thermochimica Acta, 197 (1992) 147–160
Elsevier Science Publishers B.V., Amsterdam

Thermal analysis of different series of dipeptides

F. Rodante [a,1], G. Marrosu [a] and G. Catalani [b]

[a] *Dipartimento di Ingegneria Chimica, dei Materiali, delle Materie Prime e Metallurgia, Università "La Sapienza", via del Castro Laurenziano 7, 00161 Rome (Italy)*
[b] *Instituto Regina Elena, Viale Regina Elena 293, Rome (Italy)*

(Received 24 June 1991)

Abstract

Thermal analysis of different series of dipeptides by simultaneous TG–DSC measurements was carried out.

The thermal behaviour of these compounds was compared to that of the independent free α-amino acids contained in the dipeptides. The mutual influence of the two α-amino acids makes the dipeptides less stable than the single components.

The methyl group is the key factor in the thermal decomposition of a series of dipeptides in which each pair of dipeptides has a common component. A study of a symmetrical system shows that the thermal stability is equal in the different dipeptides by virtue of the symmetry of the system. The first fragmentation indicates where the decomposition process begins.

INTRODUCTION

α-Amino acids have been studied extensively by calorimetric analysis in both liquid and solid phases [1–21].

Many studies on dipeptides in the liquid phase have been performed, in contrast to the few that have been performed in the solid phase. This laboratory, in a first study in the liquid phase [22], investigated the influence of the structure of valine, one of the components of each dipeptide, on a number of other α-amino acids, being the second component, and the influence of the other α-amino acids on the structure of valine, using valil–valine and the individual free α-amino acids as reference structures.

In another work in the liquid phase [23], the following series of dipeptides was chosen: alanil–threonine, glicyl–threonine, seril–alanine and seril–glycine. Each group of two has a common term in the dipeptide structure: the former has threonine as the common second term, and the latter has serine as the common first term. The other α-amino acids in the

[1] Author to whom correspondence should be addressed.

dipeptide structures are α-alanine and glycine, the two simplest "standard" α-amino acids, differing only by one methyl group, to which all the differences in mutual influence found between the same and different structures can be related. Finally, a third couple, tyrosil–valine and valil–tyrosine, was studied. This couple is made up of two α-amino acids which change their positions in the dipeptides, thus giving rise to a symmetrical system.

It is well known that thermal analysis of the solid phase provides physical measurements of the thermal decomposition process for organic compounds but gives no chemical information on the process being studied. However, this technique can supply useful information on the characterization of some organic compounds with similar structures. In this manner, it was possible, in a recent work [24] to group some α-amino acids with similar structures by the shape of their thermograms, although no information concerning their thermal structure variation was given.

This present study is to determine whether thermal analysis can characterize the structural variations of dipeptides previously studied in the liquid phase [21,22] using the thermograms (in the solid phase) of the individual free α-amino acids [24]. The compounds studied in this work were: valil–valine (Val–Val), valil–leucine (Val–Leu), valil–proline (Val–Pro), valil–tyrosine (Val–Tyr), valil–tryptophan (Val–Trp), valil–lysine (Val–Lys), valil–serine (Val–Ser), seryl–glycine (Ser–Gly), seril–alanine (Ser–Ala), tyrosil–valine (Tyr–Val), glycil–threonine (Gly–Thr) and alanil–threonine (Ala–Thr). Two α-amino acids, serine and proline, were also studied.

EXPERIMENTAL AND PROCEDURE

The experimental measurements were carried out by means of a simultaneous TG–DSC, Stanton-Redcroft model 625, connected to an Olivetti 250 computer.

Instrument calibration was performed with standard indium and tin samples of known temperatures and enthalpies of fusion. For decomposition studies under dynamic conditions, the TG–DSC apparatus was set up as follows. Samples (5–6 mg) were weighed into aluminium pans placed in a nitrogen-filled dry box. In order to avoid oxidative decomposition of the samples, the TG–DSC system was flushed with nitrogen gas both below the open pan (at a flow rate of 50 ml min^{-1}) and above it (at a flow rate of 30 ml min^{-1}). In this way the gases evolved during the thermal decomposition experiment were continuously removed.

All the thermodynamic quantities were calculated using the Stanton Redcroft Acquisition system Trace, version 4.

The compounds (Carlo Erba RP) were used without further purification.

RESULTS AND DISCUSSION

The trends in thermal behaviour for the compounds examined are given in Figs. 1–14. The values of the thermodynamic quantities related to the TG and DSC measurements are reported in Tables 1–4.

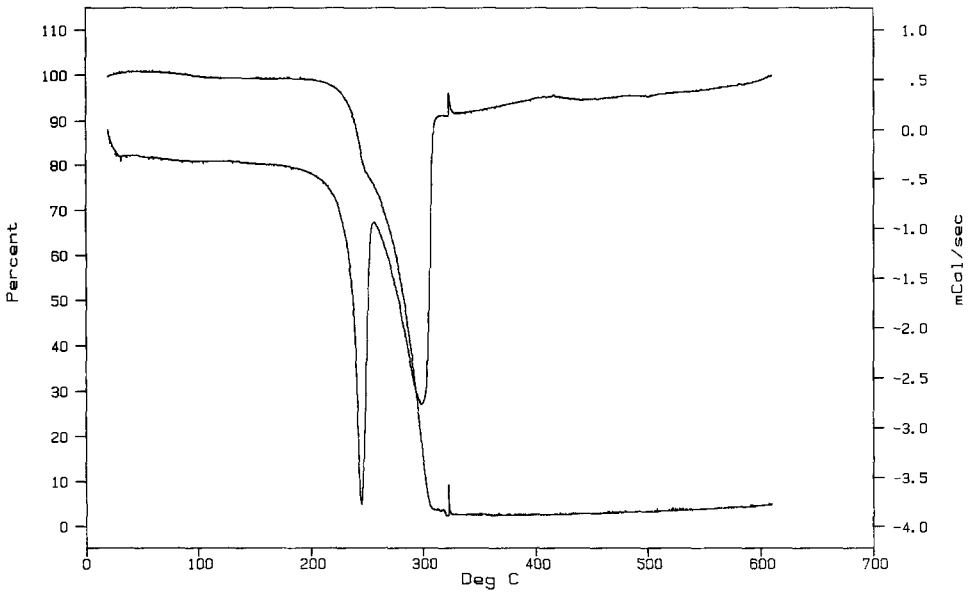

Fig. 1. DSC and TG curves of valil–valine.

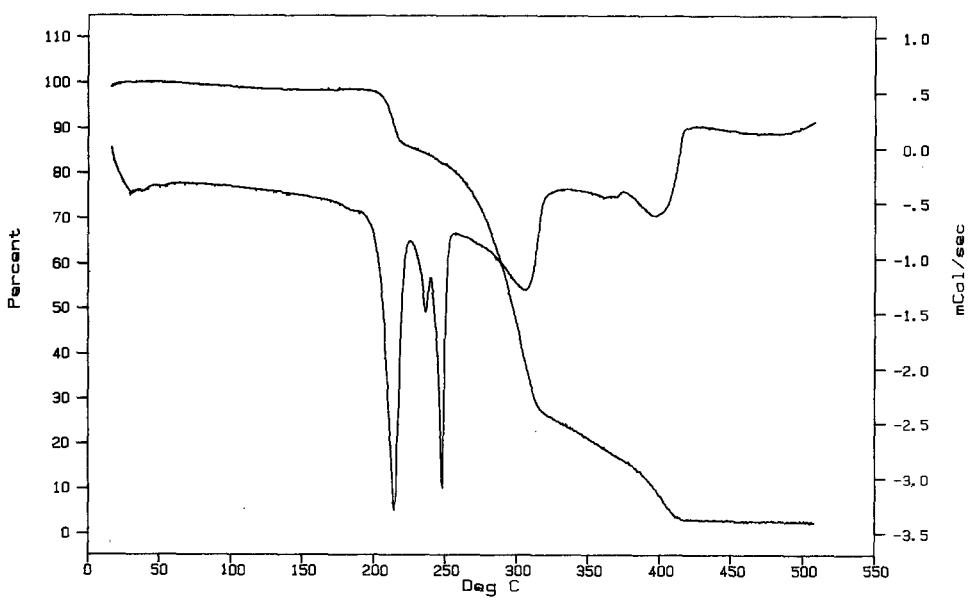

Fig. 2. DSC and TG curves of valil–serine.

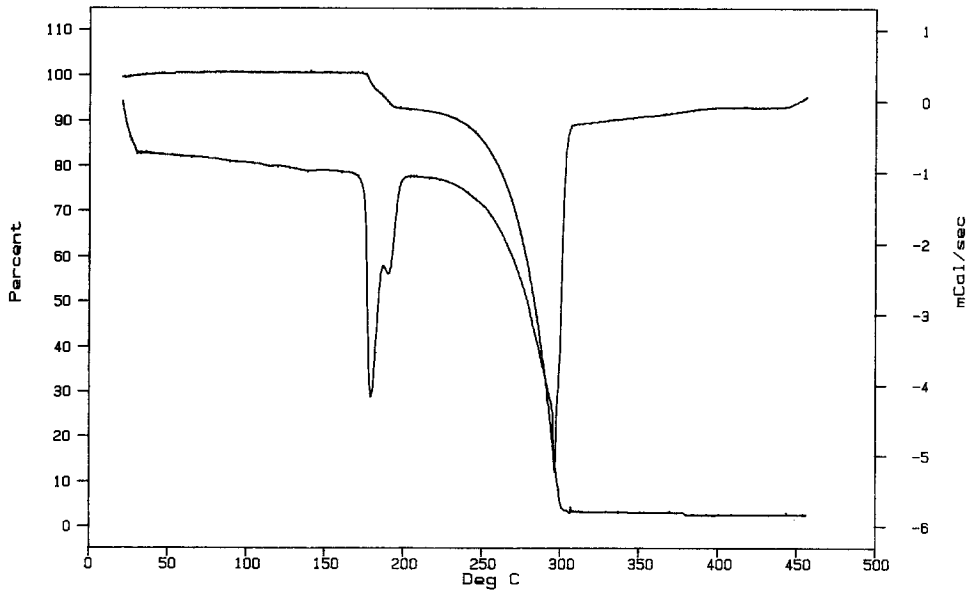

Fig. 3. DSC and TG curves of valil–leucine.

The simultaneous TG–DSC system is a very useful tool for investigating organic compounds because it combines, in a single run, weight loss and heat exchange processes, so that transformations which occur even with small weight changes (chemical reactions, decompositions, vaporization and

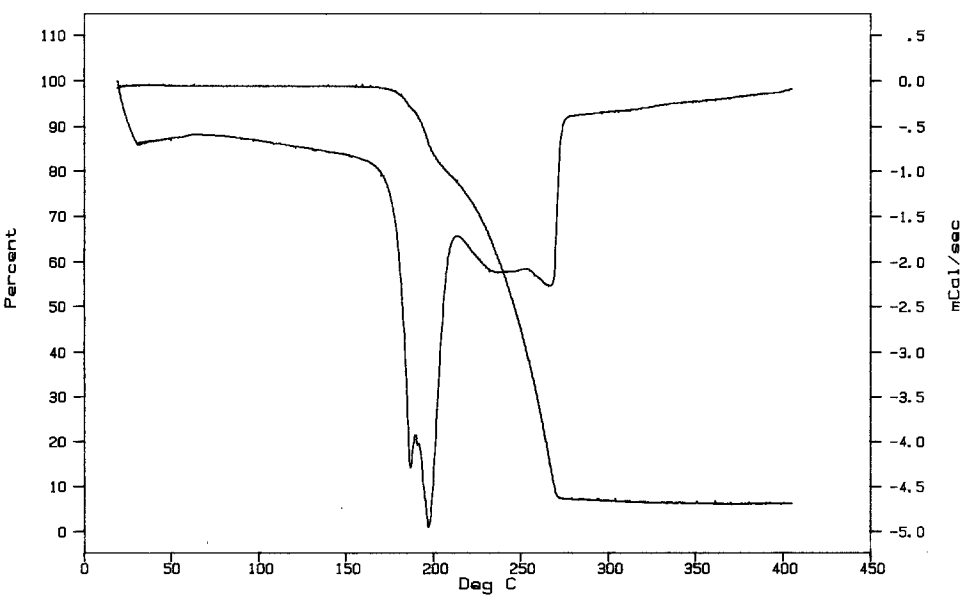

Fig. 4. DSC and TG curves of valil–proline.

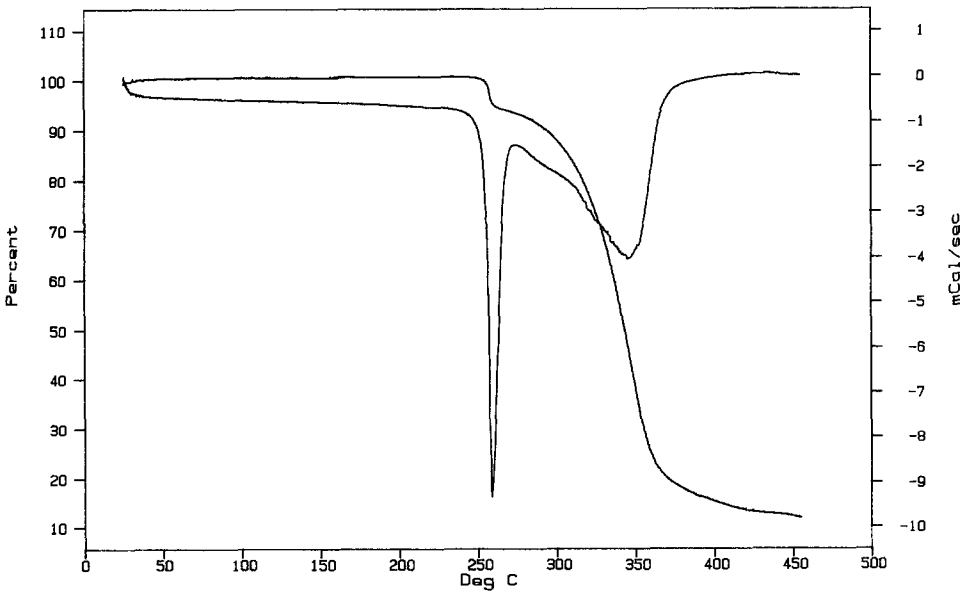

Fig. 5. DSC and TG curves of valil–lysine.

oxidation processes) can be distinguished from those which occur without weight change (melting, crystallization and polymorphic changes).

The quantities that were used to characterize the compounds were the initial temperature of decomposition (T_i) and the total enthalpy of decomposition ($\Delta H^{\ominus}$) [8,24].

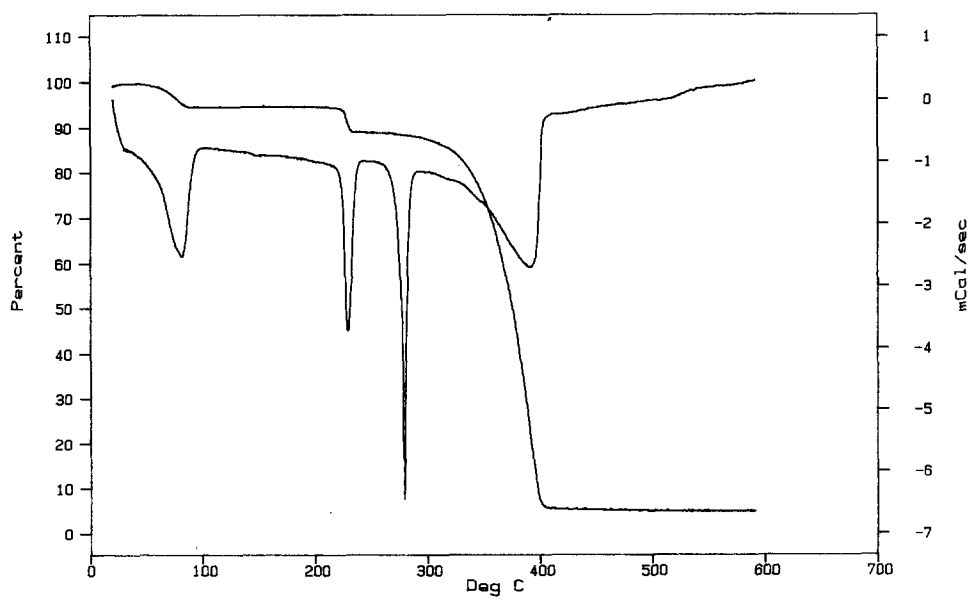

Fig. 6. DSC and TG curves of valil–tyrosine.

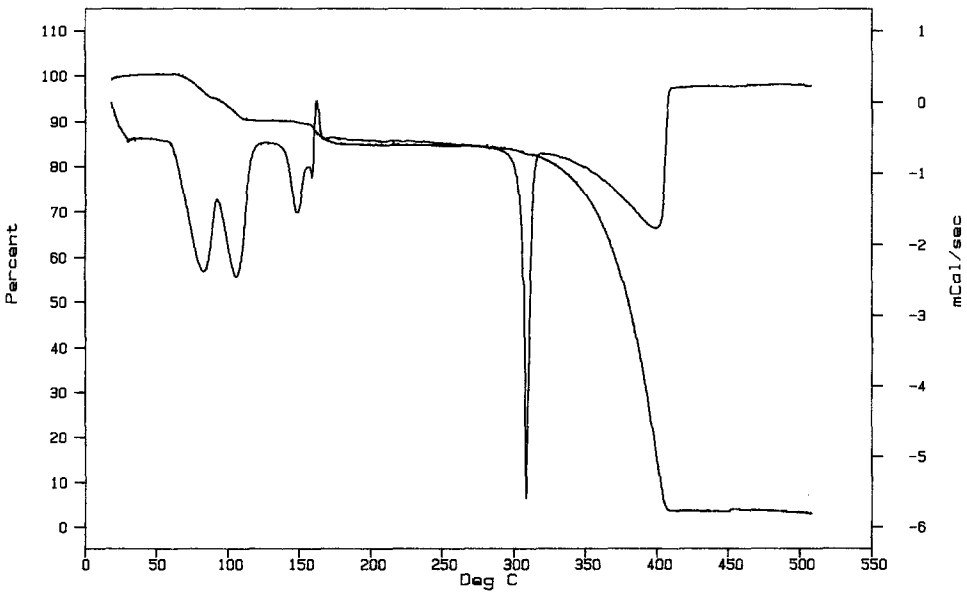

Fig. 7. DSC and TG curves of valil–triptophan.

The structure of valine–valine was used as a reference in the study of the series of dipeptides having valine as a common first term; the analysis of this compound can be carried out by comparing its thermogram with that of valine [8].

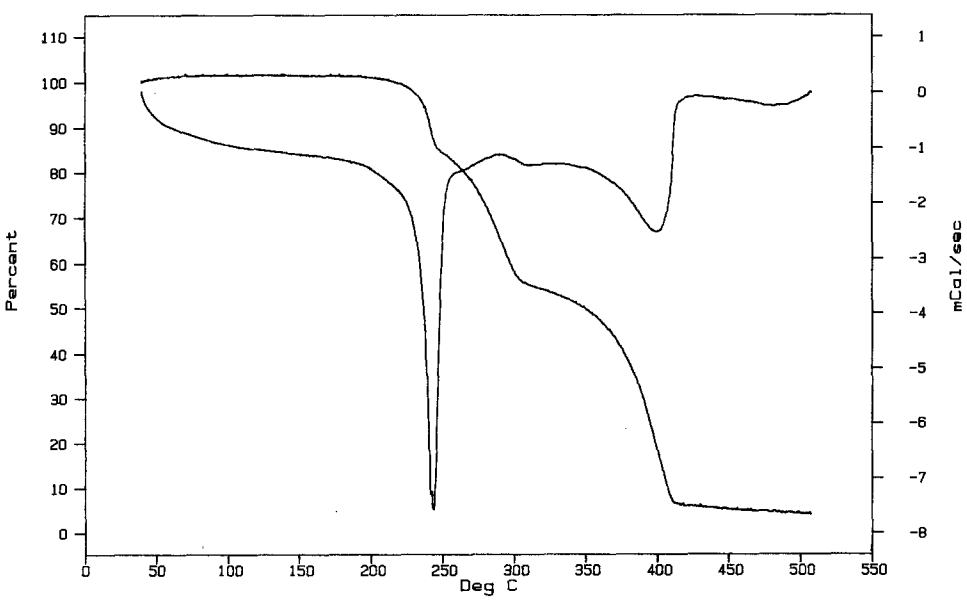

Fig. 8. DSC and TG curves of seril–alanine.

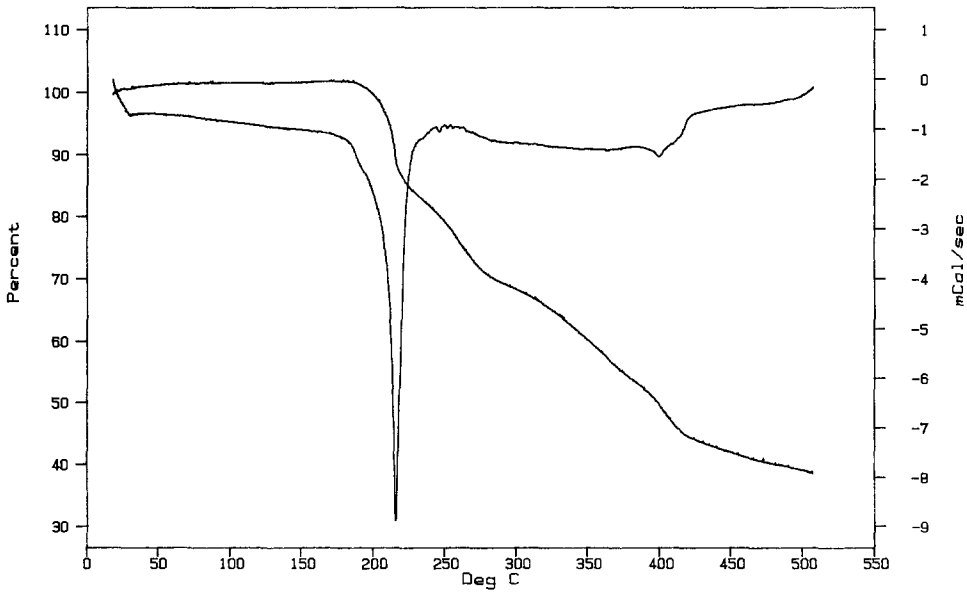

Fig. 9. DSC and TG curves of seril–glycine.

From this experimental evidence, it can be observed that for valine–valine there are two weight loss processes and two endotherms. These processes occur within the same temperature range as the decomposition of valine. The decomposition ranges which include the thermal decomposition and

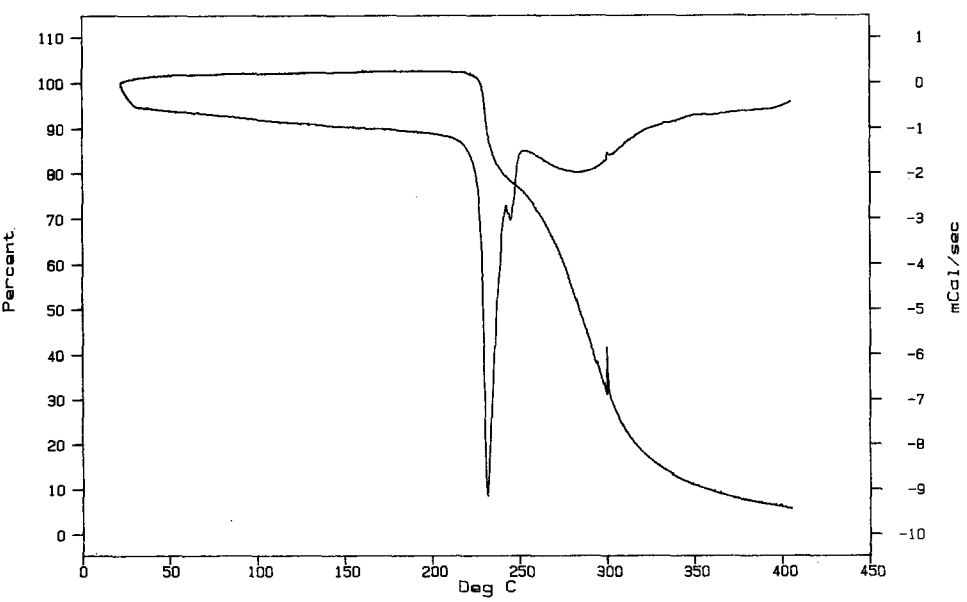

Fig. 10 DSC and TG curves of alanil–threonine.

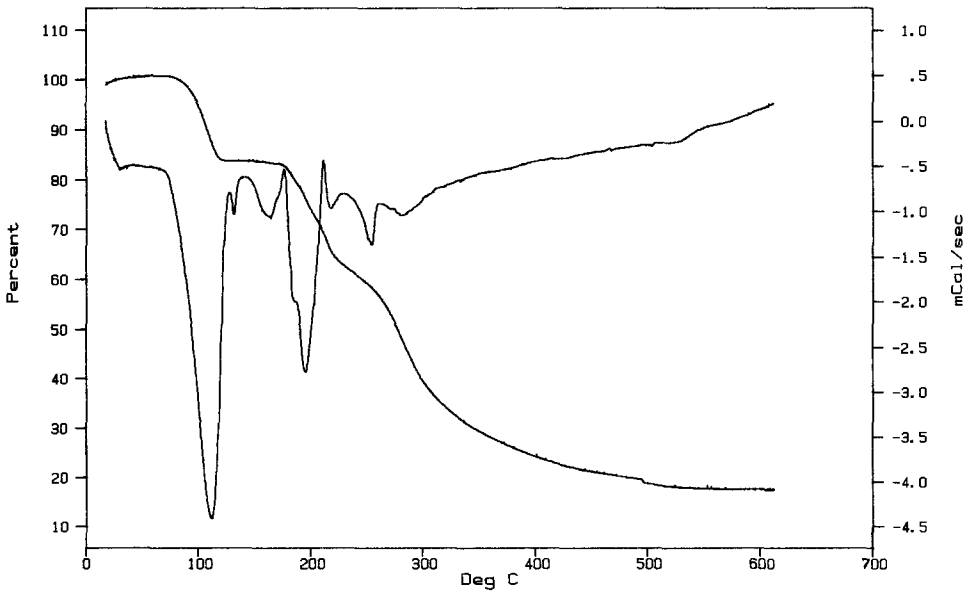

Fig. 11. DSC and TG curves of glycil–threonine.

melting of the compound are 189–258°C and 258–321°C with a weight loss ($W\%$) of 20% and 61%, respectively. Valine, however, decomposes in a single process (190–294°C) with a total weight loss of 96%.

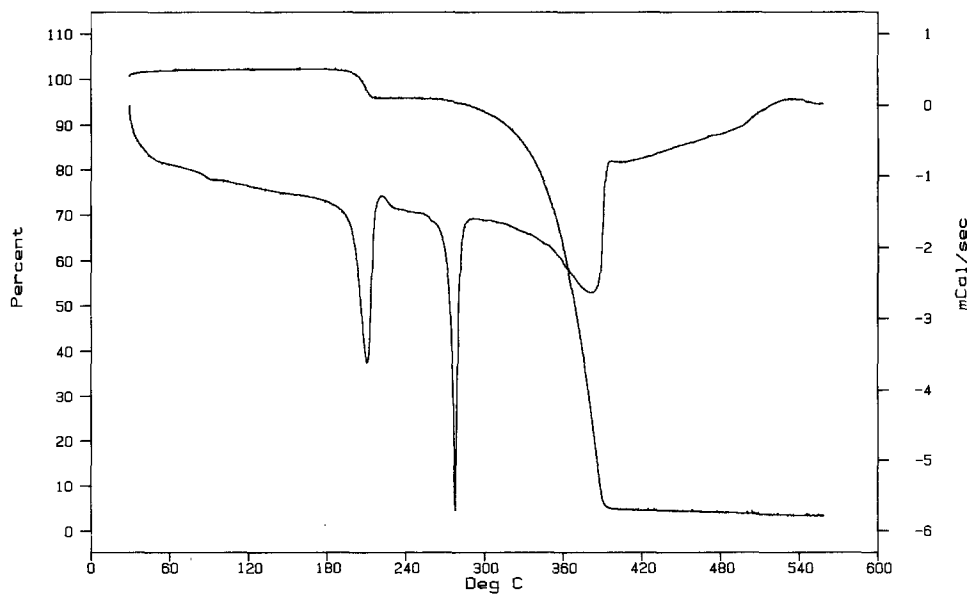

Fig. 12. DSC and TG curves of tyrosil–valine.

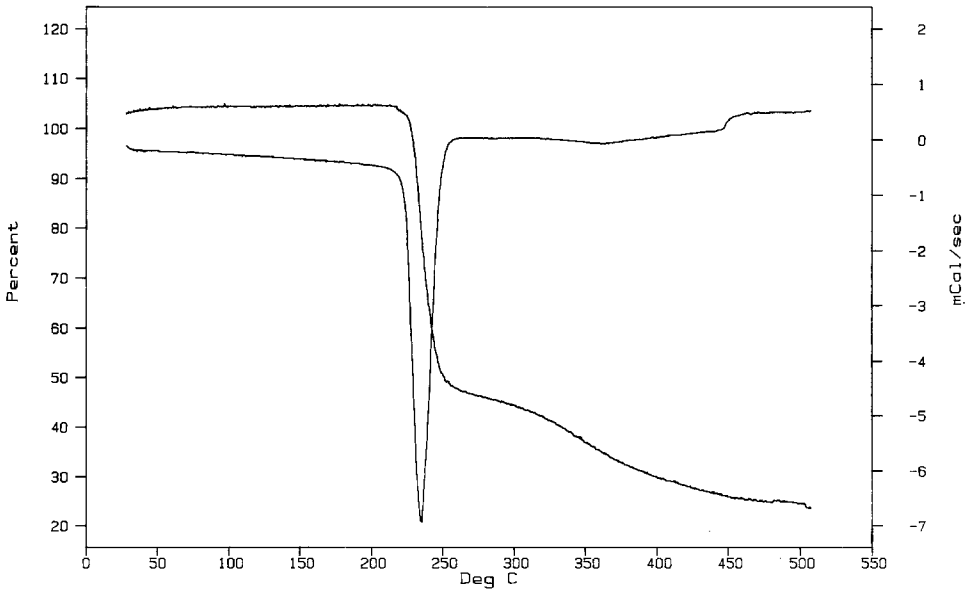

Fig. 13. DSC and TG curves of serine.

The sum of the first and second enthalpy values of the decomposition processes is 148.80 cal g^{-1} while valine has a value of 229 cal g^{-1}. The two peaks of the dipeptide at 246 and 299°C bracket the peak of valine (269.64°C). Valine, as previously observed [8], loses the carboxyl group and then the amine group.

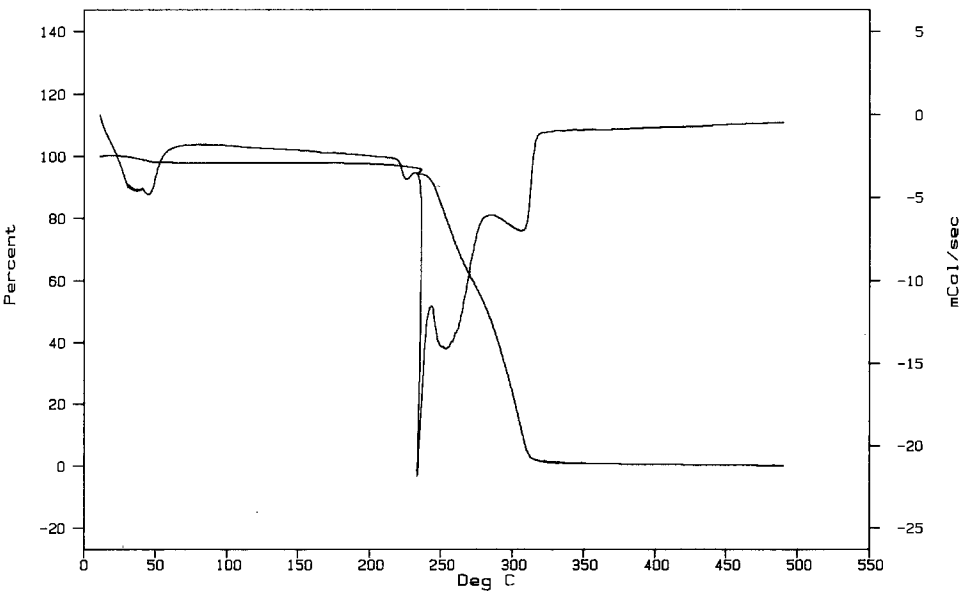

Fig. 14. DSC and TG curves of proline.

TABLE 1

Thermodynamic parameters of thermal decomposition of dipeptides from TG measurements

Compound	Stage of decomposition							
	I		II		III		IV	
	ΔT (°C)	W (%)	ΔT (°C)	W (%)	ΔT (°C)	W (%)	ΔT (°C)	W (%)
Val–Val	189–258	20.5	258–321	61.2				
Val–Ser	195–225	14.9	225–325	59.8	325–492	21.8		
Val–Leu	170–203	7.9	203–310	89.0				
Val–Pro	163–215	18.0	215–278	68.6				
Val–Lys	248–268	6.4	268–450	81.4				
Val–Tyr	54– 95	6.1	218–242	6.1	242–300	1.5	300–418	83.2
Val–Trp	59–121	10.4	295–422	81.3				
Ser–Ala	220–255	17.5	255–315	25.9	315–425	48.4		
Ser–Gly	184–230	19.0	230–500	43.3				
Ala–Thr	217–252	23.7	252–400	67.0				
Gly–Thr	70–128	17.0	179–250	25.0	250–500	40.0		
Tyr–Val	192–224	6.2	224–400	88.6				

The weight loss of the first decomposition process of valil–valine, put in a mathematical proportion with its molecular weight, acquires the value of 44.28 g related to the loss of the carboxyl group.

TABLE 2

Thermodynamic parameters of thermal decomposition of dipeptides from DSC measurements

Compound	Stage of decomposition								
	I			II			III		
	ΔT (°C)	ΔH (cal g^{-1})	Peak (°C)	ΔT (°C)	ΔH (cal g^{-1})	Peak (°C)	ΔT (°C)	ΔH (cal g^{-1})	Peak (°C)
Val–Val	189–258	48.4	246	258–313	100.4	299			
Val–Ser	195–225	48.5	214	225–256	30.3	248	325–492	49.0	396
				256–325	38.6	305			
Val–Leu	170–203	46.7	180	203–310	171.0	297			
Val–Pro	163–215	107.4	187	215–278	80.5	267			
			198						
Val–Lys	241–275	72.1	260	275–378	177.6	370			
Val–Tyr	54– 95	43.1	82	218–242	22.0	230	300–400	111.8	391
Val–Trp	59–121	96.0	83	295–319	35.9	308	319–411	108.6	399
Ser–Ala	220–255	132.0	244	318–418	162.0	400			
Ser–Gly	184–230	148.0	216						
Ala–Thr	217–252	134.0	240						
Gly–Thr	70–128	103.0	111	179–250	62.4	194			
Tyr–Val	192–224	37.8	211	289–395	128.9	382			

TABLE 3

Thermodynamic parameters of thermal decomposition of two α-amino acids from TG measurements

Compound	Stage of decomposition			
	I		II	
	ΔT (°C)	W (%)	ΔT (°C)	W (%)
Serine	213.0–269.0	57.8	269.0–500.0	21.7
Proline	218.0–330.0	95.5		

Thus, the dipeptide has the same thermal stability as valine but requires less energy for complete decomposition.

Valil–serine has three decomposition steps in the temperature range 195–422°C: the first (ΔT = 195–225°C) has a weight loss of 14.9% (with a corresponding proportional weight loss of 30.4 g) and can be related to the CH_2OH group and an endotherm process, ΔH = 48.54 cal g^{-1}; the second (ΔT = 225–325°C) has a weight loss of 59.76% and two endotherms (ΔH = 30.31 cal g^{-1} and ΔH = 38.37 cal g^{-1}); the third (ΔT = 325–492°C) has a weight loss of 21% and ΔH = 49 cal g^{-1}. Serine has two decomposition steps with T = 213–269°C (W = 57.8%) and T = 269–500°C (W = 21%).

The first decomposition step of valil–serine has the same heat amount as that of valil–valine; the second and third steps have a weight loss close to those of serine. The dipeptide is 94% decomposed at 493°C while serine is 79% decomposed at 500°C. The overall enthalpy is 166.5 cal g^{-1} lower than the enthalpies of the individual α-amino acids, confirming the decreased thermal stability of the dipeptide.

It can be concluded that valine destabilizes the structure of serine.

The first decomposition step of valil–leucine indicates a loss of one molecule of water of crystallization (18.18 g). The overall enthalpy (227.6 cal g^{-1}) is close to those of the two components and the temperature range of decomposition is contained in the temperature ranges of the decomposition processes of the components. Thus, the effect of valine on leucine seems to be weak.

TABLE 4

Thermodynamic parameters of thermal decomposition of two α-amino acids from DSC measurements

Compound	I Stage of decomposition		
	ΔT (°C)	ΔH (cal g^{-1})	Peak (°C)
Serine	213–269	155.6	235.2
Proline	227–318	214.7	233.7

Proline is characterized by a single decomposition process, while valil–proline shows two decomposition steps, the proportional weight loss of the first (44.12 g) being related to a carboxyl group. Taking as a reference the temperature ranges and the enthalpies of decomposition of the components of the dipeptide, it can be observed that valine destabilizes proline, decreasing the temperature range of decomposition and the overall enthalpy.

The proportional weight loss of the first decomposition step of valil–lysine (17.01 g) indicates loss of the NH_3 group. A comparison between the ranges of temperature and the enthalpy values of valine and lysine and the corresponding values of the dipeptide shows that the structure of lysine is weakened by valine. The phase transition (68–80°C) and fusion process (224–252°C) of the pure lysine [8] are lost.

The first decomposition process of valil–tyrosine (54–95°C) indicates that the proportional weight loss (18.17 g) is related to a molecule of crystallization water, while in the second (218–242°C) the proportional weight loss (17.08 g) suggests the loss of an NH_3 group. Thus, the valine structure decreases the stability of the tyrosine molecule: the dipeptide is 89% decomposed at 418°C, while tyrosine is 74% decomposed at 576°C.

It is interesting to observe the thermal behaviour of the symmetric compound tyrosil–valine: there is no crystallization water, whereas loss of an amine group does occur. Thus, there is no meaningful variation as a result of the exchange of the components.

Valil–tryptophan loses two molecules of water of crystallization in the range 59–129°C, proportional weight loss 36 g and $\Delta H = 96$ cal g^{-1}. The dipeptide structure is weakened in thermal stability: the weight loss at 422°C is 81%, while tyrosine has a weight loss of 76.25% at 500°C.

The presence of five- and six-membered rings in tryptophan and tyrosine gives rise to similar thermograms.

A thermal stability scale, referred to the initial temperature of decomposition, for the dipeptides having valine as a common first component can be written as Val–Trp > Val–Lys > Val–Tyr > Val–Ser > Val–Val > Val–Pro > Val–Leu. Dipeptides with side-chains containing an aromatic or polarized group have higher thermal stability values: the "heat" scale can be written as Val–Trp > Val–Lys > Val–Leu > Val–Pro > Val–Tyr > Val–Ser > Val–Val.

The following compounds must be now considered: seril–alanine, seril–glycine, glycil–threonine and alanil–threonine.

Seril–alanine has three decomposition steps: the first has a weight loss of 17.49% and a consequent proportional weight loss of 31 g which can be hypothesized to be the loss of a CH_2OH group: the weight losses of the second and third steps are 25% and 48.41% respectively, with $\Delta H = 162$ cal g^{-1}. The total weight loss is 92.85% in the range $\Delta T = 220$–425°C with $\Delta H = 294.00$ cal g^{-1}. Thus, the thermal stability is diminished with respect

to that of serine ($\Delta T = 213–500°C$ with a loss of 79.89% and $\Delta H = 155.6$ cal g^{-1}).

Seril–glycine has an initial decomposition step at $\Delta T = 181–230°C$ with $\Delta H = 148$ cal g^{-1} and a weight loss of 19% with a proportional weight loss of 31, which can again be related to the CH_2OH group.

Thus, the thermal stability of serine–alanine is greater than that of seril–glycine, both for the initial temperature of decomposition and for the total enthalpy of decomposition.

The proportional weight loss of the first decomposition process (45.05 g) for alanil–threonine indicates the loss of the CH_3–CH–OH group. The total weight loss at 400°C is equal to 92%.

Alanine and threonine have thermograms similar to that of the dipeptide.

Glycine–threonine loses two molecules of water of crystallization (36.34 g) at $\Delta T = 70–128°C$. A fusion process follows and then the usual two-step decomposition, in the first of which the proportional loss of weight (45.00 g) can be related again to the CH_3–CH–OH group. The thermal stability ($W = 83\%$ at 500°C) is lower than that of glycine ($W = 65\%$ at 573°C).

Thus, the thermal stability of alanil–threonine is greater than that of glycil–threonine.

CONCLUSIONS

In general, the mutual influence of two α-amino acids makes the dipeptide less stable than the single components. Moreover, in the solid phase the methyl group plays a fundamental role in the thermal stability, just as in the liquid phase it is the key factor in the mutual influence of the different dipeptide structures.

In the symmetrical system (valil–tyrosine and tyrosil–valine), the thermal stability is equal in the two dipeptides just as the enthalpy values of the dissociation processes in solution of the three functional groups (carboxyl group, amine group and hydroxyl group of tyrosine) are equal in the different dipeptides by virtue of the symmetry of the system.

The proportional weight loss indicates the first fragment of decomposition (carboxyl group, amine group and functional groups) and the beginning of the decomposition. Valil–valine and valil–proline lose the carboxyl group of the second component. Valil–serine, seril–alanine and seril–glycine lose the CH_2OH group of the serine. Valil–tyrosine, tyrosil–valine and valil–lysine lose one amine group. Alanil–threonine and glycil–threonine lose the CH_3–CH–OH group of threonine. None of these fragments were caused by breaking the amidic bond, which is revealed to be a strong bond.

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