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THERMAL CONDENSATION OF SOME α-AMINOACIDS WITH PHTHALIC ACID

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ABSTRACT

The reaction kinetics of thermal condensations of glycine, DL-valine, DL-alanine and L-phenylalanine with phthalic acid are studied; the activation energy of the reactions occurring in the investigated systems is determined. Results indicate that the thermal condensation involves the formation of phthalamic acids followed by ring closure to form *N*-phthalyl-aminoacids.

The thermal behaviour of phthalic acid, glycine, DL-valine, DL-alanine, L-phenylalanine and of the corresponding *N*-phthalyl-aminoacids is also reported.

INTRODUCTION

Examples of application of thermal analysis to organic reactions have become more and more frequent as a result of the introduction of controlled atmosphere techniques.

Several workers[1–12] have prepared *N*-phthalyl-aminoacids by melting a mixture of an aminoacid with phthalic acid or anhydride. King and Kidd[11] report the mechanism of the reaction for the formation of phthalyl-DL-glutamic acid by the interaction of phthalic anhydride and L-glutamic acid in pyridine; this procedure involves the condensation of phthalic anhydride with the aminoacid followed by ring closure of the intermediate phthalamic acid.

We have carried out the thermal condensation of some *N*-phthalyl-aminoacids directely in a thermoanalyzer, by reacting the corresponding aminoacid with phthalic acid. Before starting the proper measurements, preliminarly investigations were performed for phthalic acid, for each α-aminoacid and for each *N*-phthalyl-aminoacid in order to establish their thermal behaviour under the same conditions as for the thermal condensations.

EXPERIMENTAL

Materials

Reagent grade phthalic acid, glycine, DL-valine, DL-alanine and L-phenylalanine (C. Erba R.P.) were used.

N-phthalyl-glycine (m.p. 197 °C), *N*-phthalyl-DL-valine (m.p. 106 °C), *N*-phthalyl-DL-alanine (m.p. 164 °C) and *N*-phthalyl-L-phenylalanine (m.p. 185 °C), employed as test materials were prepared as described in ref. 5 and were recrystallized several times from 10 % aqueous alcohol.

Previously ignited Al_2O_3 (C. Erba R.P.) was used as the DTA reference material.

Thermal analysis and thermal condensations

They were carried out with a Mettler vacuum recording thermoanalyzer in dynamic nitrogen atmosphere (10 l/h), at different heating rates (0.5; 1; 1.5; 2; 4 °C/min). Higher rates proved to be inappropriate because in these conditions more than one reaction takes place simultaneously.

In all experiments Pt/Pt–Rh 10 % thermocouples, 0.3 ml aluminium crucibles, and the same specimen holder (Mettler T-TD3) were employed. The following quantities were simultaneously recorded as a function of the temperature (t °C): total change in weight (TG), first derivative of the change in weight (DTG) and differential thermal analysis (DTA).

The thermal condensation reactions were performed by introducing into the thermoanalyzer, every time, a closely powdered stoichiometric mixture of each α-aminoacid and phthalic acid (different stoichiometric ratios do not affect the shape of the thermal curves in the temperature range of the condensations).

Infrared spectra

They were performed in KBr pellets using a Perkin–Elmer Model 257 spectrophotometer.

RESULTS AND DISCUSSION

Thermal behaviour of reactants

Phthalic acid

The thermal decomposition of this reactant (Fig. 1) in the 200–218 °C range gives a product, whose melting point and infrared spectrum correspond to those of phthalic anhydride. In this temperature range the TG curve shows a weight loss of a mole of water; the corresponding DTA curve, in its turn, affords two not very well separated endothermic peaks corresponding to melting (208 °C) and to water loss (218 °C). The DTA curve is not suitable for the determination of the activation energy, therefore the value of this one (see Table 1) was calculated applying Piloyan *et al.*'s[13] equation to DTG data. The phthalic anhydride is formed at a temperature higher than its melting point and it vapourizes in the range 218–244 °C as indicated by TG and by the endothermic DTA peak.

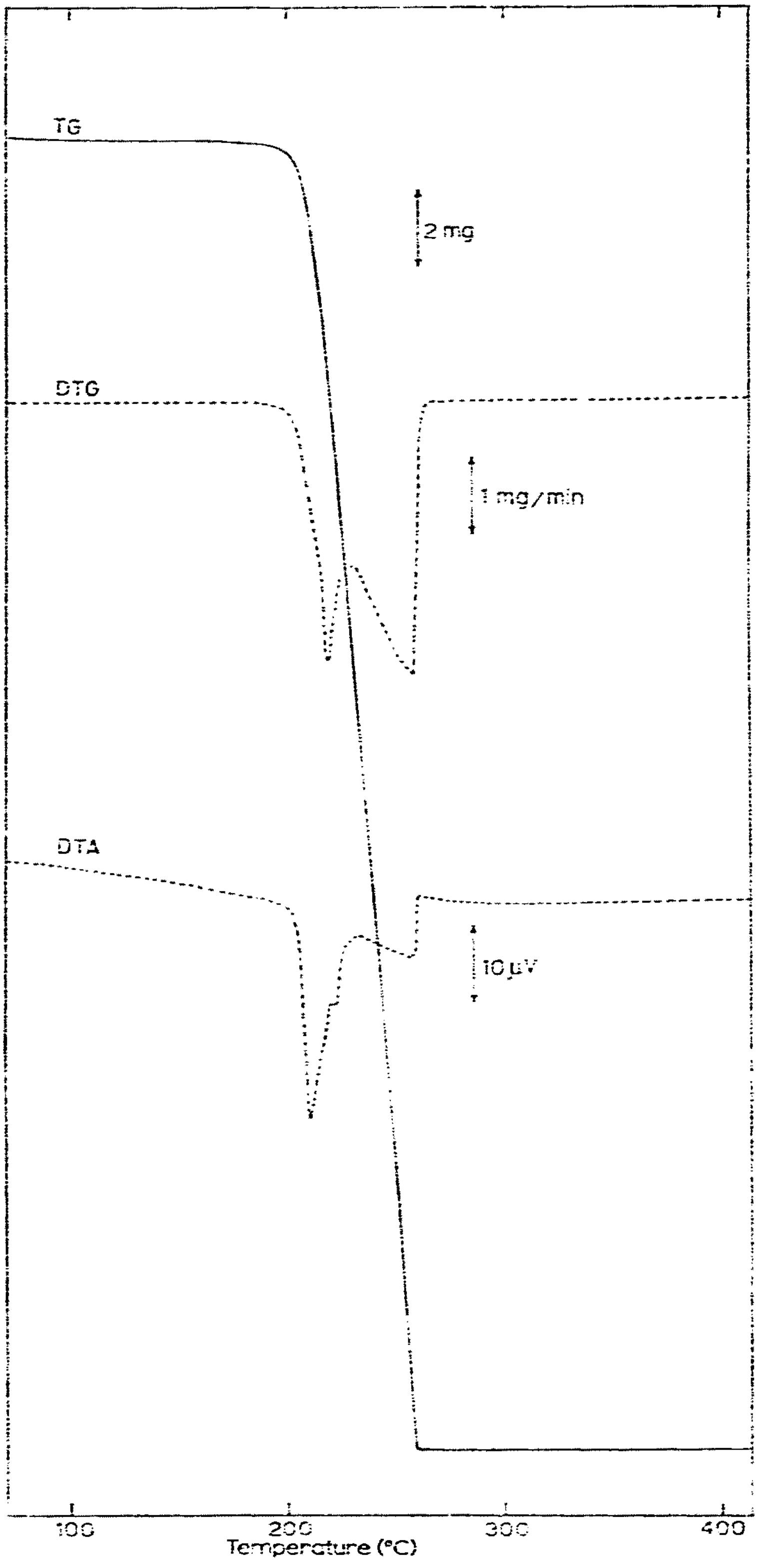


Fig. 1. Thermal analysis of phthalic acid. Weight of sample = 33.4 mg; heating rate = 4 °C/min.

TABLE 1

ACTIVATION ENERGY E_a (kcal/mole) FOUND FOR THE DEHYDRATION OF PHTHALIC ACID AND FOR THE REACTION: PHTHALIC ACID+AMINO-ACID = PHTHALAMIC ACID+H_2O

System	E_a	*Linear correlation*
Phthalic acid	29.2	0.999
Phthalic acid–glycine	32.1	0.999
Phthalic acid–DL-valine	26.4	0.998
Phthalic acid–DL-alanine	41.9	0.999
Phthalic acid–L-phenylalanine	36.5	0.998

Aminoacids

Thermal analysis curves of glycine, DL-valine, DL-alanine and L-phenylalanine give evidence that these aminoacids do not decompose respectively under 220, 275, 200 and 220°C.

N-phthalyl-aminoacids

The first thermal transformation for *N*-phthalyl-glycine, *N*-phthalyl-DL-valine, *N*-phthalyl-DL-alanine and *N*-phthalyl-L-phenylalanine was the melting observed respectively at 195, 111, 162 and 184°C; they all begin to decompose, with weight loss, respectively at 200, 160, 184 and 212°C.

Thermal condensations

The shape of TG and DTG curves (Figs. 2–5) indicates that all the aminoacid–phthalic acid mixtures begin to react between 120–140°C namely at a lower temperature than that required to convert phthalic acid into phthalic anhydride and to decompose the aminoacids. In any case the weight loss, amounting on the whole to two moles water, at low heating rates, occurs in two steps; the first one corresponds to 0.4–0.7 moles. Therefore the thermal condensation involves two consecutive reactions which became simultaneous when the first one rises the 40–70%. The slope variation of TG curves at the first step indicates an induction period preceding the beginning of the second reaction. All attempts to separate completely the two reactions were useless even in isothermal conditions at the starting temperature of the first reactions.

DTA curves deviate from the base line in the same temperature range of DTG curves and afford always a single peak due to the sum of the enthalpic effects of the two reactions and of the melting of the reaction mixture. This last was observed with the aid of a Kofler hot stage microscope.

All investigated systems, after loss of two moles of water, give thermal condensation products whose m.p. and infrared spectra are the same as that obtained with the relative *N*-phthalyl-aminoacids prepared as test materials.

To calculate the activation energy of the first reaction Piloyan *et al.*'s[13] equation was applied to DTG data; the obtained values are reported in Table 1.

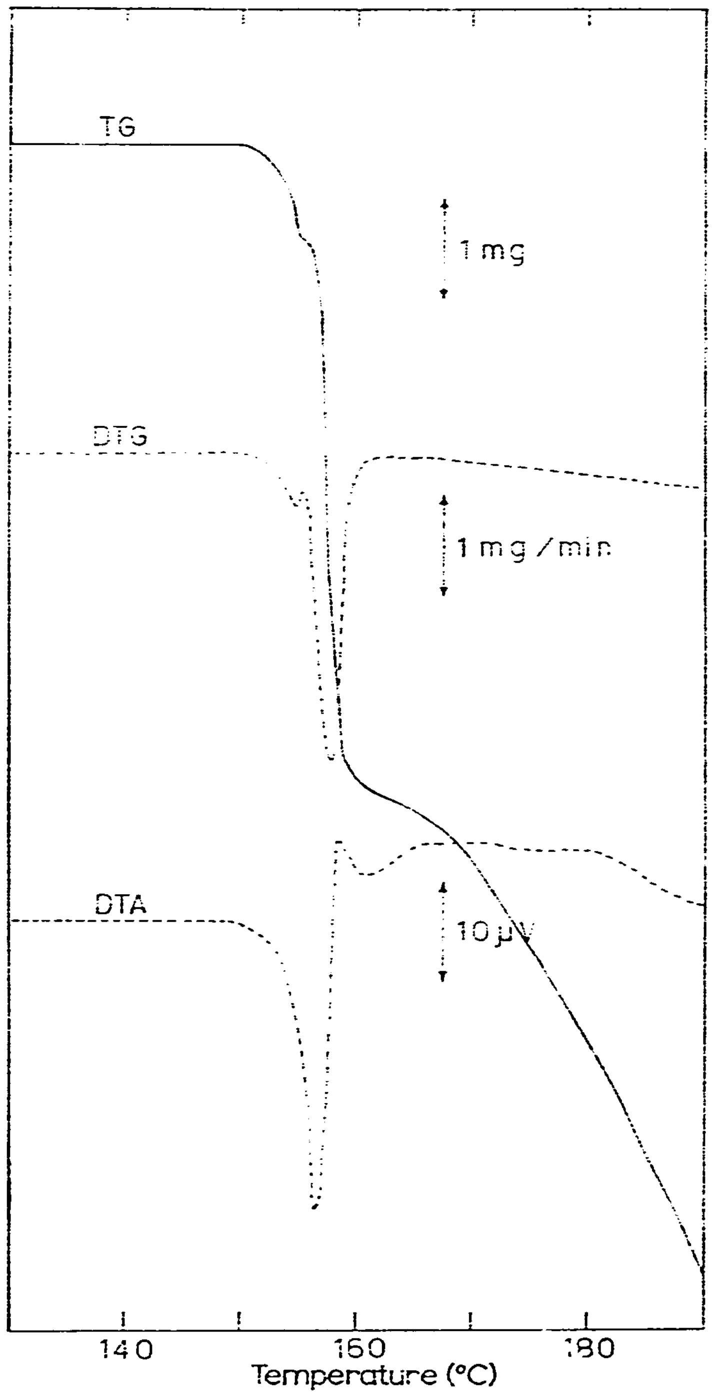


Fig. 2. Thermal behaviour of the system phthalic acid–glycine (1.1). Weight of reactant mixture = 26.0 mg; heating rate = 1 °C/min.

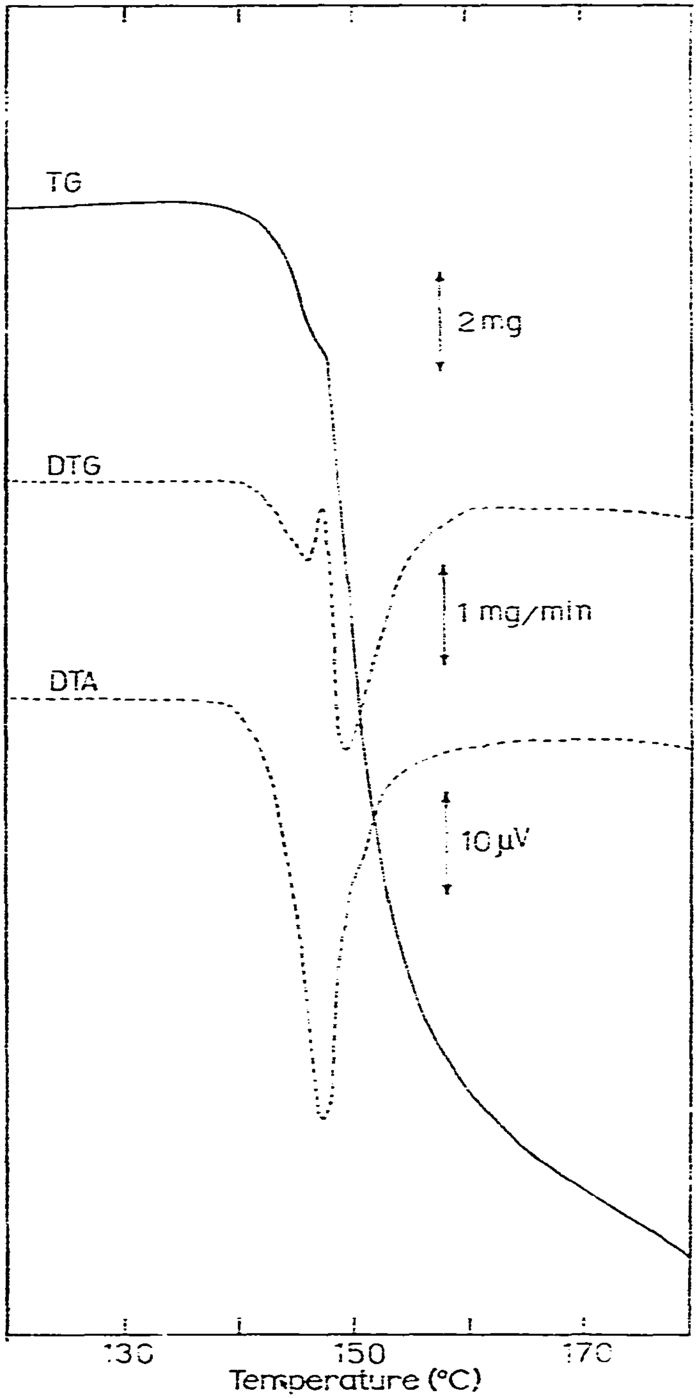


Fig. 3. Thermal behaviour of the system phthalic acid–DL-valine (1:1). Weight of reactant mixture = 146.1 mg; heating rate = 1 °C/min.

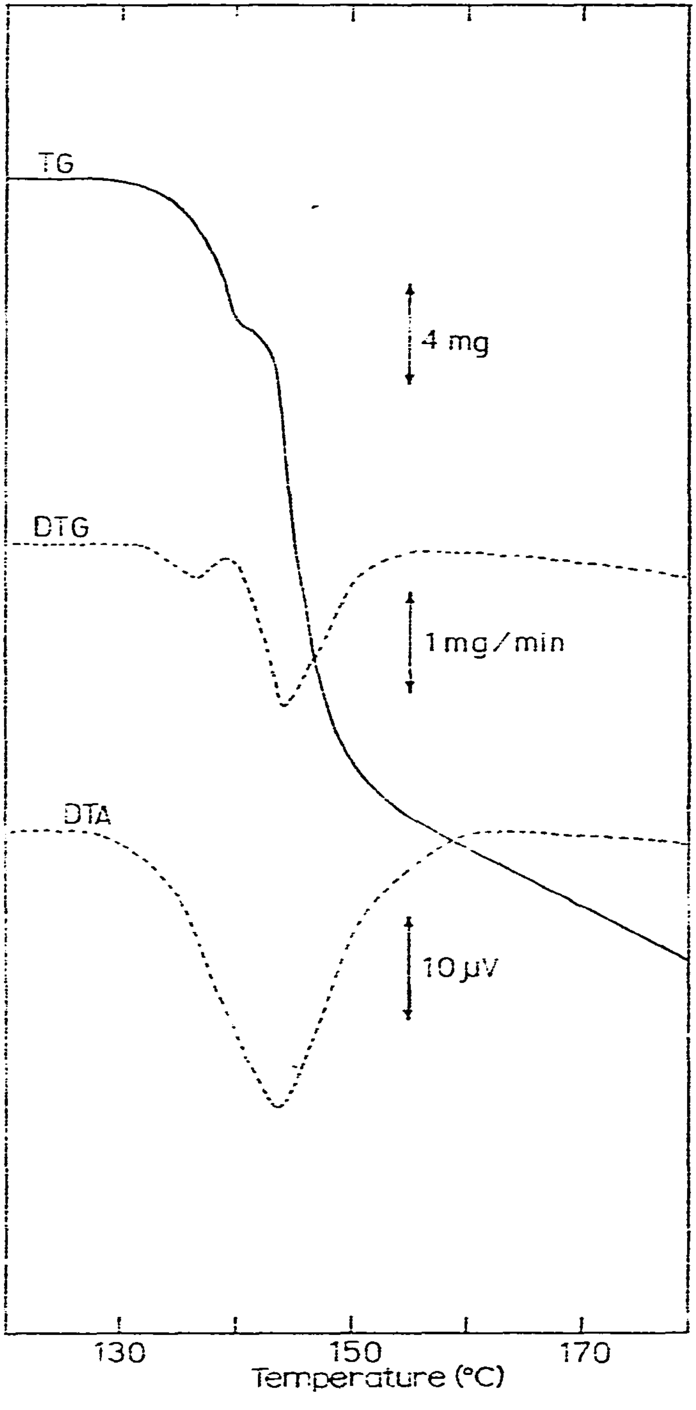


Fig. 4. Thermal behaviour of the system phthalic acid–DL-alanine (1:1). Weight of reactant mixture = 172.4 mg; heating rate = 1 °C/min.

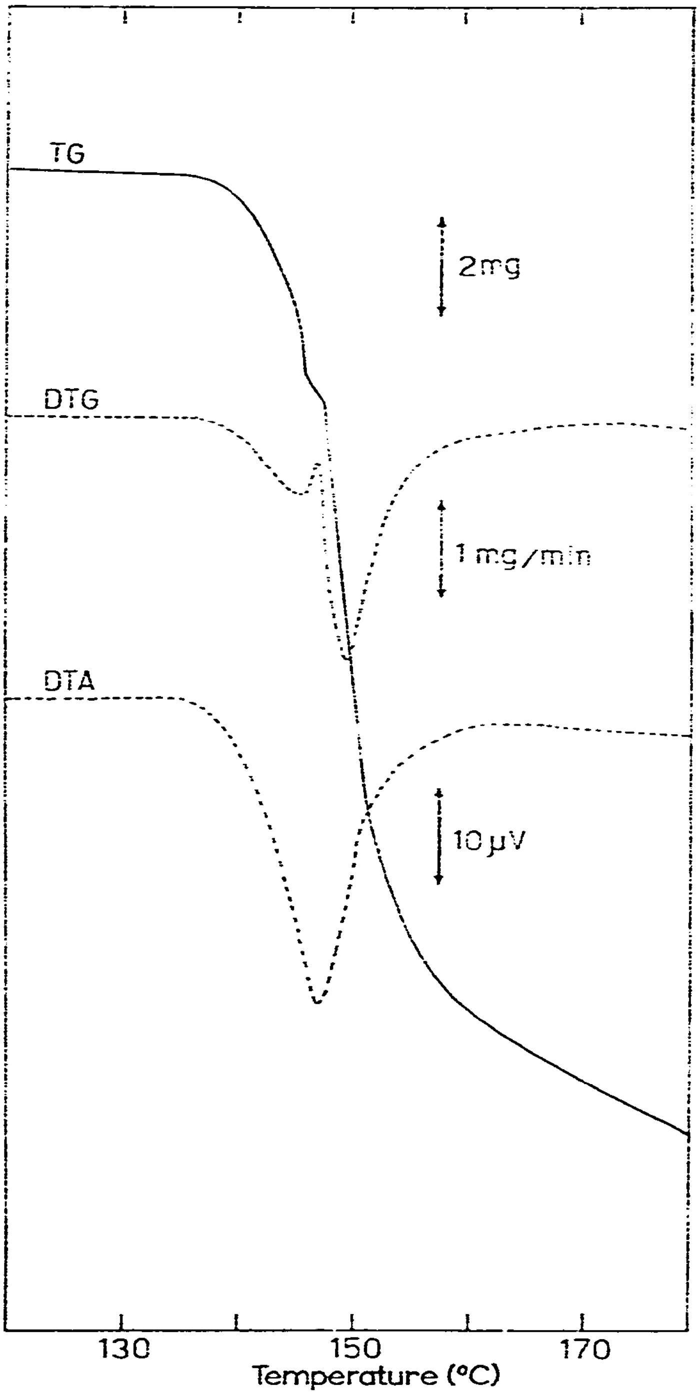
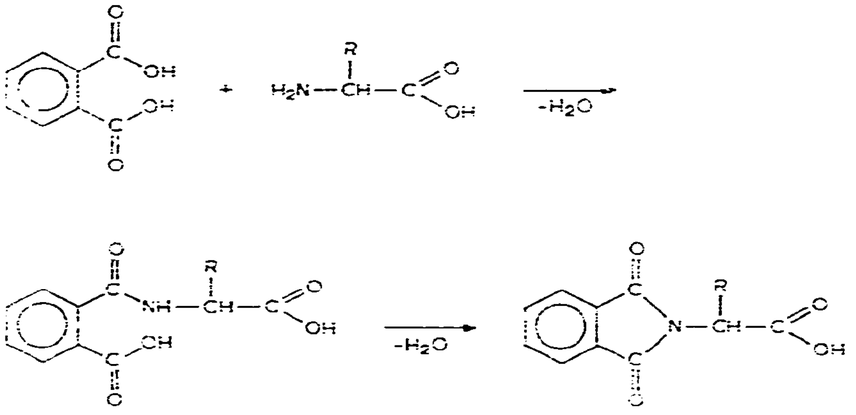


Fig. 5. Thermal behaviour of the system phthalic acid–L-phenylalanine (1:1). Weight of reactant mixture = 138.0 mg; heating rate = 1 °C/min.

The thermal behaviour of the investigated α-aminoacid–phthalic acid systems excludes the formation of phthalic anhydride and the successive condensation of this with the aminoacid; it can be explained admitting the formation of intermediate phthalamic acid followed by the ring closure into *N*-phthalyl-aminoacid:



(R = H, CH_3, $CH(CH_3)_2$, $CH_2C_6H_5$)

Over and above the first mechanism should require the activation energy of the first reaction to be independent of the nature of the aminoacid and equal to that of the formation of phthalic anhydride from the dehydration of phthalic acid. The different activation energy values we have found (see Table 1) indicate the second mechanism to be the correct one.

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