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Kinetics and mechanisms of the gas-phase elimination of *N*-phenylglycine and its ethyl ester

Rosa M. Domínguez, Maria Tosta and Gabriel Chuchani*

Centro de Química, Instituto Venezolano de Investigaciones Científicas (IVIC), Apartado 21827, Caracas 1020-A, Venezuela

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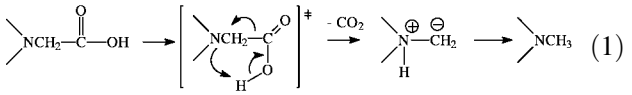
ABSTRACT: The elimination kinetics of the title compounds were determined over the temperature range 290.4–420.3 °C and pressure range 14.5–44.0 Torr. The reactions, carried out in seasoned vessels and in the presence of the free radical inhibitor toluene, are homogeneous, unimolecular and follow a first-order rate law. The rate coefficient is expressed by the following Arrhenius equation: for *N*-phenylglycine ethyl ester, log $[k_1\ (s^{-1})] = (12.13 \pm 0.38) - (193.6 \pm 4.9)$ kJ mol^{-1} $(2.303\ RT)^{-1}$; and for *N*-phenylglycine, log $[k_1\ (s^{-1})] = (12.95 \pm 0.52) - (177.4 \pm 5.8)$ kJ mol^{-1} $(2.303\ RT)^{-1}$. Both substrates yield mainly *N*-methylaniline and a small amount of aniline. *N*-Phenylglycine as a neutral amino acid decomposes 130 times faster than its ethyl ester at 380 °C. The mechanisms of these elimination reactions are presented and discussed. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: pyrolysis; elimination; kinetics; gas phase; phenylglycines

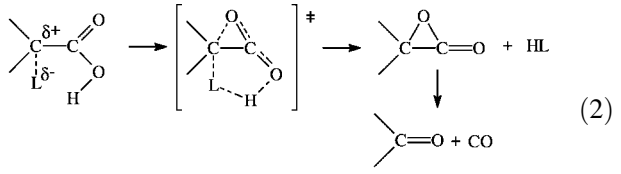
INTRODUCTION

Low molecular weight amino acids are solids and on heating sinter or decompose into amorphous materials. In addition, their insolubility in most organic solvents and high solubility as zwitterions in water are difficult to examine in gas-phase elimination reactions. However, two recent papers reported the homogeneous, unimolecular elimination of *N*,*N*-dimethylglycine[1] and picolinic acid.[2] These substrates as 2-substituted amino carboxylic acids undergo decarboxylation as shown in reaction (1).



(1)

This process of decomposition differs from the gas-phase elimination of several types of 2-substituted carboxylic acids which are found to decarbonylate[3–9] as described in reaction (2).



(2)

L = Leaving Group: Cl, Br, OH, OR, OPh, OAc.

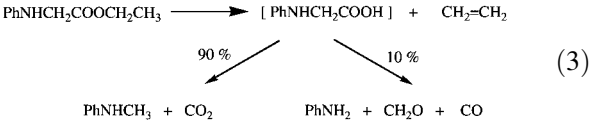
To further our understanding of the mechanistic pathways of neutral amino acid elimination in the gas phase, in the present work we studied the homogeneous, molecular pyrolysis kinetics of *N*-phenylglycine and its ethyl ester.

**Correspondence to:* G. Chuchani, Centro de Química, Instituto Venezolano de Investigaciones Científicas (IVIC), Apartado 21827, Caracas 1020-A, Venezuela.
E-mail: chuchani@quimica.ivic.ve

RESULTS AND DISCUSSION

N-Phenylglycine ethyl ester

The elimination products of this substrate described by reaction (3) requires that for long reaction times $P_f/P_0 = 3$, where P_f and P_0 are the final and initial pressures, respectively.



(3)

The average experimental P_f/P_0 values at four temperatures and 10 half-lives is 2.9 (Table 1). Additional verification of the above stoichiometry (3), up to 92% reaction, was possible by comparing the ethylene formation with the pressure increase of the substrate decomposition (Table 2).

The homogeneity of reaction (3) was examined by carrying out several runs in a vessel with a surface-to-volume ratio of 6.0 relative to that of the normal vessel, which is equal to 1.0 (Table 3). The elimination may be said to be homogeneous since no significant effects on the rates were obtained in clean and seasoned Pyrex vessels.

Toluene, a free radical inhibitor, used in different proportions had no effect on the rates (Table 4). No induction period was observed on plotting pressure

Table 1. Ratio of final pressure (P_f) to initial pressure (P_0)

Substrate	Temperature (°C)	P_0 (Torr)[a]	P_f (Torr)[a]	P_f/P_0	Average
N-Phenylglycine ethyl ester	390.6	26.6	71.6	2.7	2.9
	402.3	24.8	73.8	3.0	
	411.6	21.3	67.3	3.1	
	420.3	28.1	80.1	2.9	
N-Phenylglycine	319.6	32	62	1.9	1.9
	330.2	21.5	41.5	1.9	
	340.5	21	40	1.9	

[a] Torr = 133.3 Pa.

Table 2. Stoichiometry of the reaction[a]

Substrate	Temperature (°C)	Parameter[b]	Value			
N-Phenylglycine ethyl ester	411.5	Time (min)	2.5	6.5	10.5	14.5
		Reaction (%) (pressure)	28.2	67.6	77.3	92.0
		Ethylene (%) (GC)	31.2	64.2	74.4	92.6
N-Phenylglycine	309.0	Time (min)	3	5	6	8
		Reaction (%) (pressure)	21.4	32.1	37.5	46.4
		N-Methylaniline(%) (GC)	17.2	26.9	30.3	39.2
		Aniline (%) (GC)	2.2	4.0	4.7	5.7
		Sum (%) (GC)	19.4	30.9	35.0	44.9

[a] Maximum error ± 0.5.
[b] GC, gaschromatography.

Table 3. Homogeneity of pyrolysis reactions

Substrate	S/V (cm^{-1})[a]	$10^4\ k_1$ (s^{-1})[b]	$10^4\ k_1$ (s^{-1})[c]
N-Phenylglycine ethyl ester at 402.3 °C	1	15.26	14.27
	6	14.89	15.07
N-Phenylglycine at 320.9 °C	1	23.95	22.27
	6	23.80	22.76

[a] S = surface area; V = volume.
[b] Clean Pyrex vessel.
[c] Vessel seasoned with allyl bromide.

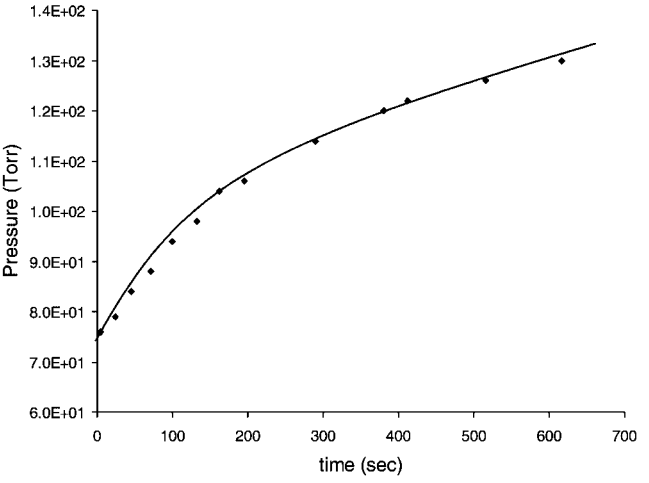


Figure 1. Pressure against time for *N*-phenylglycine ethyl ester at 420.4 °C

Table 4. Effect of free radical inhibitor toluene on rates

Substrate	Temperature (°C)	P_s[a] (Torr)	P_i[b] (Torr)	P_i/P_s	$10^4\ k_1$ (s^{-1})
N-Phenylglycine ethyl ester	402.3	34.6	—	—	15.26
		25.2	58	2.3	14.68
		24.5	112	4.6	15.04
		24.1	146	6.1	14.87
N-Phenylglycine	319.6	38	—	—	—[c]
		44	64	1.4	21.49
		22.5	83	3.7	20.48
		32	130	4.1	20.32
		21	102	4.9	20.58

[a] P_s, pressure of the substrate.
[b] P_i, pressure of the inhibitor.
[c] The k-value decreases rapidly.

Table 5. Variation of rate coefficients with initial pressure

Substrate	Temperature (°C)	Parameter	Value			
N-Phenylglycine ethyl ester	411.6	P_0 (Torr)	18	25	31	34
		$10^4\ k_1\ (s^{-1})$	24.72	24.80	24.39	24.80
N-Phenylglycine	309.0	P_0 (Torr)	14.5	21	32.5	38
		$10^4\ k_1\ (s^{-1})$	11.04	11.52	11.30	11.28

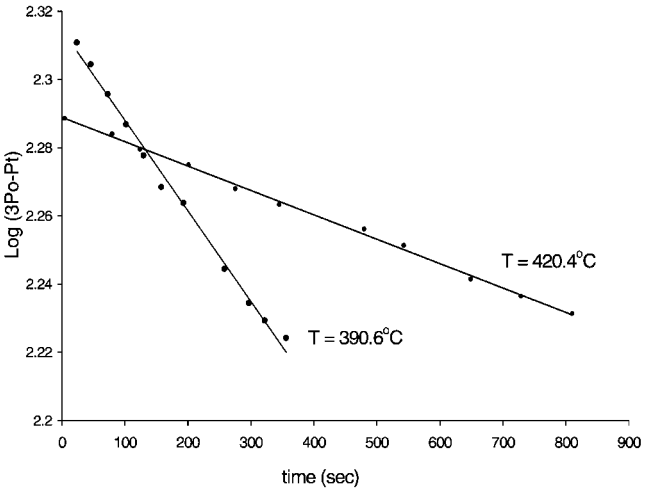


Figure 2. Plot of $\log(3P_0 - P_t)$ vs time for *N*-phenylglycine ethyl ester at two temperatures

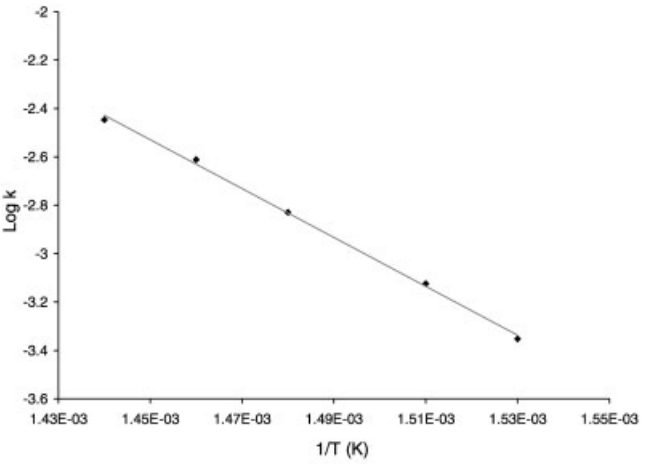


Figure 3. Arrhenius plot for *N*-phenylglycine ethyl ester

against time t (Fig. 1). The rate coefficients are reproducible with a relative standard deviation of <10% at a given temperature, and the precision of manometric measurements is ± 0.5 mm.

The first-order rate coefficients of the substrate, calculated from $k_1 = (2.303/t)\log [2P_0/(3P_0 - P_t)]$ were found to be independent of the initial pressure (Table 5). A plot of $\log(3P_0–P_t)$ against time t gave a good straight line up to 92% decomposition (Fig. 2). The temperature dependence of the rate coefficients is shown in Table 6. The results in Table 6 lead, by using the least-squares procedure and 90% confidence coefficients, to the Arrhenius graphs (Fig. 3) and equations shown.

N-Phenylglycine

The elimination process of *N*-phenylglycine described in reaction (4) gives an average experimental value of $P_f/P_0 = 1.93$ (Table 1). Determination of the stoichiometry of reaction (4), up to 45% decomposition, was possible by comparing the percentage decomposition of the substrate from pressure measurements with the sum of the quantitative gas chromatographic (GC) analyses of the products *N*-methylaniline and aniline (Table 2).

$$\mathrm{PhNHCH_2COOH} \xrightarrow{1} \mathrm{PhNHCH_3 + CO_2} \qquad \mathrm{PhNHCH_2COOH} \xrightarrow{2} \mathrm{PhNH_2 + CH_2O + CO} \tag{4}$$

To examine the influence of the surface area on the rate of elimination, several runs were carried out in a vessel with a surface-to-volume ratio six times greater than that of the normal vessel (Table 3). The packed and unpacked clean Pyrex vessels gave slightly different kinetic results, indicating a small amount of heterogeneous reaction, while the seasoned vessels gave identical results, indicating no heterogeneous reaction within the experimental precision.

Table 6. Variation of the overall rate coefficients with temperature

Substrate	Parameter	Value					
N-Phenylglycine ethyl ester	Temperature (°C)	380.4	390.6	402.3	411.6	420.3	
	$10^4\ k_1\ (s^{-1})$	4.44	7.52	14.82	24.47	35.73	
Rate equation: $\log[k_1\ (s^{-1})] = (12.13 \pm 0.38) - (193.6 \pm 4.9)$*kJ mol*$^{-1}$ *(2.303 RT)*$^{-1}$*;* $r = 0.9990$							
N-Phenylglycine	Temperature (°C)	290.4	300.9	309.0	319.6	329.5	340.5
	$10^4\ k_1\ (s^{-1})$	3.23	6.09	11.43	20.50	36.72	70.89
Rate equation: $\log [k_1\ (s^{-1})] = (12.95 \pm 0.52) - (177.4 \pm 5.8)$*kJ mol*$^{-1}$ *(2.303 RT)*$^{-1}$*;* $r = 0.9995$							

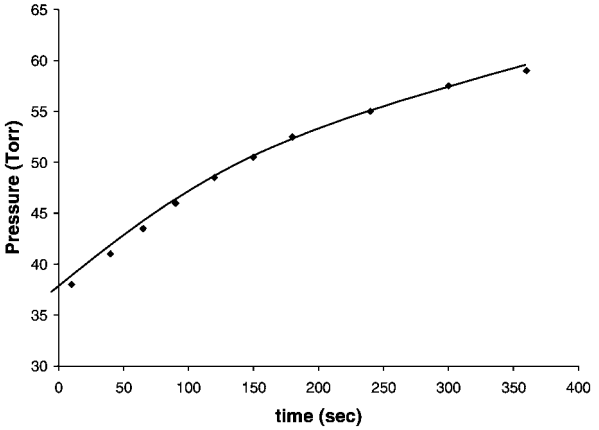


Figure 4. Pressure against time for *N*-phenylglycine at 319.7 °C

Table 7. Product distribution (%) at different extents of reaction at 309 °C

Extent of reaction (%)	Aniline	*N*-Methylaniline
19.4	13.6	86.4
30.9	13.5	86.5
35.0	13.4	86.6
45.2	12.7	87.3

Table 8. Product distribution (%) at different reaction temperatures

Temperature (°C)	Aniline	*N*-Methylaniline
309.0	13.5	86.5
319.6	13.8	86.2
330.2	12.5	87.5
340.5	14.7	85.3

Different proportions of the free radical inhibitor toluene in the elimination process are shown in Table 4. The pyrolysis experiments with *N*-phenylglycine were carried out under maximum inhibition of toluene in order to prevent any possible free radical chain reaction. No induction period was observed according to Fig. 4. The rate coefficients were reproducible with a relative standard deviation of $<10\%$ at a given temperature, and the precision of manometric measurements is ± 0.5 mm.

Details of the chromatographic analyses of the elimination products under these conditions are given in Tables 7 and 8. Within the experimental errors, the distribution of products does not vary at a given temperature as a function of extent of reaction, and varies very insignificantly as a function of temperature. In this respect, it is not unreasonable to assume that the formation of the products proceeds under kinetic control.

The partial rates of product formation described in reaction (4) were determined by quantitative GC analyses of *N*-methylaniline and aniline. The temperature dependence of the rate coefficients for the formation of these products (Table 9) gives by the least-squares procedure and with 90% confidence limits the following Arrhenius equations: for *N*-methylaniline formation, $\log[k_1\ (s^{-1})] = (12.46 \pm 0.57) - (172.6 \pm 6.4)\text{kJ mol}^{-1}\ (2.303\ RT)^{-1}$, $r = 0.9993$, and for aniline formation, $\log[k_1\ (s^{-1})] = (14.85 \pm 0.38) - (208.6 \pm 4.3)\text{kJ mol}^{-1}\ (2.303\ RT)^{-1}$, $r = 0.9998$. The Arrhenius plots are described in Fig. 5. The large numbers for the kinetic parameters of aniline formation (Table 9) may be due to mechanical errors during experimental measurements. Even though $\log A = 14.85$ is not a preferred value for a five-membered cyclic transition state, it is compensated by a larger value of $E_a = 208.6\,\text{kJ mol}^{-1}$. This occurs in many examples of pyrolyses described in the literature.

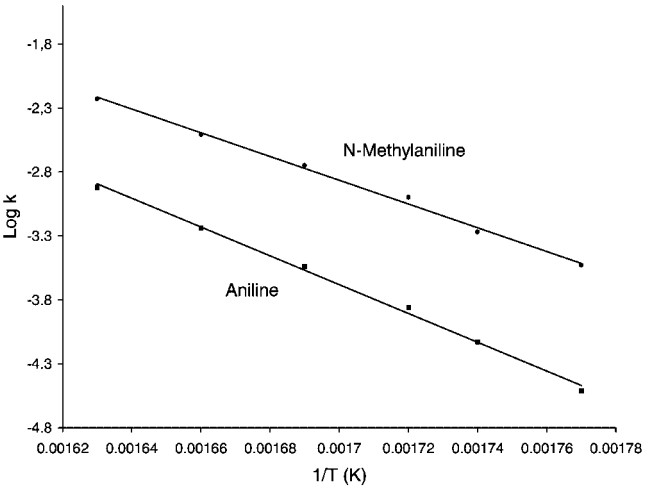


Figure 5. Arrhenius plots for *N*-methylaniline and aniline formation from *N*-phenylglycine

Table 9. Temperature dependence of partial rate coefficients of products formation from pyrolysis of *N*-phenylglycine

Product	Parameter	Value					
Aniline	Temperature (°C)	290.4	300.9	309.0	319.6	329.5	340.5
	$10^4\ k_1\ (s^{-1})$	0.31	0.74	1.39	2.88	5.69	12.10
Rate equation: $\log[k_1\ (s^{-1})] = (14.85 \pm 0.38) - (208.6 \pm 4.3)\text{kJ mol}^{-1}\ (2.303\ RT)^{-1}$; $r = 0.9998$							
N-Methylaniline	Temperature (°C)	290.4	300.9	309.0	319.6	329.5	340.5
	$10^4\ k_1\ (s^{-1})$	2.92	5.35	10.04	17.62	31.03	58.79
Rate equation: $\log[k_1\ (s^{-1})] = (12.46 \pm 0.57) - (172.6 \pm 6.4)\text{kJ mol}^{-1}\ (2.303\ RT)^{-1}$; $r = 0.9993$							

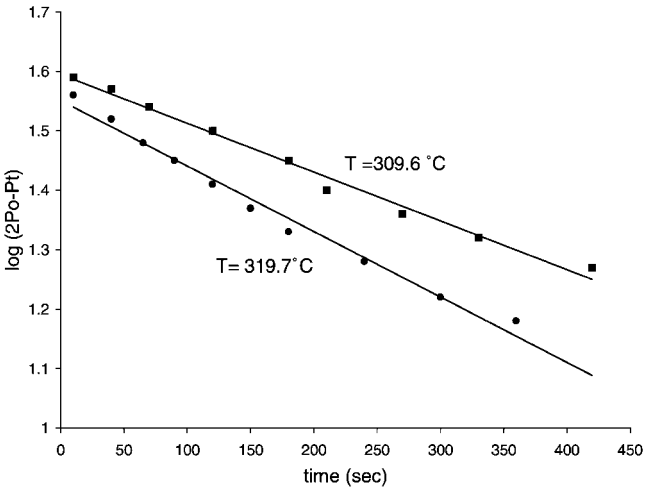


Figure 6. Plots of log $(2P_0 - P_t)$ vs time for *N*-phenylglycine at two temperatures

Therefore, comparative elimination reactions must be made through k values rather than E_a values.

The overall rate coefficients for *N*-phenylglycine elimination, in seasoned vessels and in the presence of toluene inhibitor, were found to be independent of the initial pressure of the substrate $\{k_1 = (2.303/t) \log [P_0/(2P_0 - P_t)]\}$ and the first-order plots, log $(2P_0 - P_t)$ vs t, are satisfactorily linear up to 45% reaction (Table 5, Fig. 6). The variation of the overall rate coefficients with temperature, at 90% confidence limits with the least-squares method, is given in Table 6. The Arrhenius plot is shown in Fig. 7.

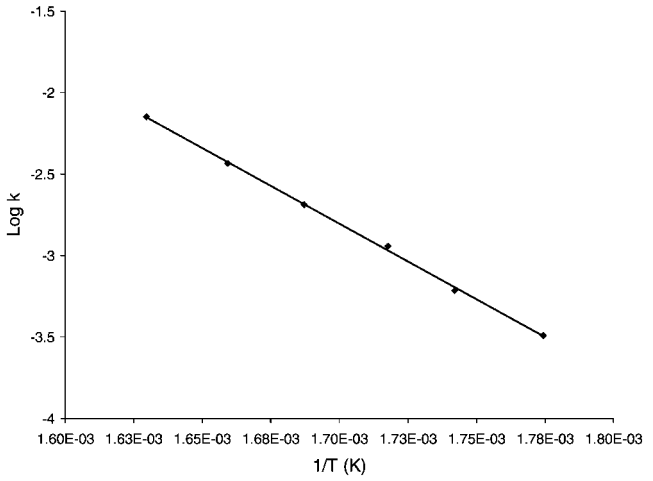
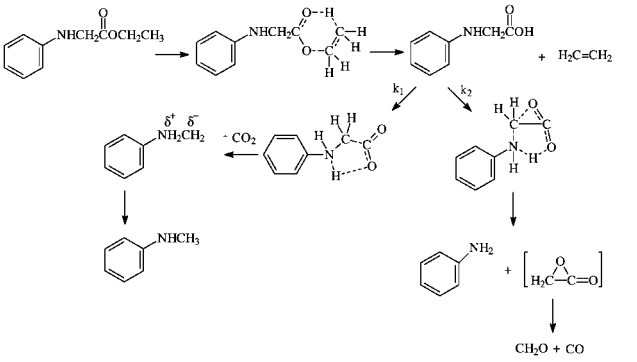


Figure 7. Arrhenius plot for the overall elimination of *N*-phenylglycine

The negative entropy of activation $\Delta S^{\ddagger}$ of these eliminations suggests a symmetrical arrangement and a possible approximation to planarity of the transition state. Log $A = 12.13$ for *N*-phenylglycine ethyl ester is a reasonable value for a six-membered cyclic transition-state mechanism, while log $A = 12.95$ for *N*-phenylglycine is acceptable for a five-membered cyclic transition state type of mechanism. The enthalpy of activation $\Delta H^{\ddagger}$ implies endothermic eliminations, whereas the free energy of activation $\Delta G^{\ddagger}$ indicates that these reactions are not spontaneous, unstable and endergonic.

The *N*-phenylglycine produced as an intermediate in reaction (3) gives an extremely fast decomposition, 130 times faster than that for *N*-phenylglycine ethyl ester at 380 °C (Table 10). This result appears to support the previous idea that neutral amino acid type molecules undergo a rapid decomposition at low temperatures.[1,2] According to the present results, together with the data in Tables 6 and 9, the overall mechanism for the elimination of *N*-phenylglycine ethyl ester together with *N*-phenylglycine may be rationalized as in reaction (5).



(5)

N-Phenylglycine ethyl ester, as an organic ester with a C_β—H bond, pyrolyses through a six-membered cyclic transition state[10,11] to yield *N*-phenylglycine and ethylene [reaction (5)]. At the reaction temperature, the intermediate *N*-phenylglycine is unstable and decomposes rapidly through decarboxylation to *N*-methylaniline (k_1) as described for neutral type amino acid elimination in reaction (1). That is, the nucleophilicity of the N atom will abstract the acidic H of the COOH group to form a five- centered transition state, which through CO_2 elimination yields *N*-methylaniline. Surprisingly, and contrary to the idea that an amino nitrogen substituent is a difficult leaving group in the gas-phase elimination of

Table 10. Kinetic and thermodynamic parameters at 380 °C

Substrate	$k_1 \times 10^4$ (s^{-1})	E_a (kJ mol^{-1})	Log A (s^{-1})	$\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta G^{\ddagger}$ (kJ mol^{-1})
N-Phenylglycine ethyl ester	4.40	193.6 ± 4.9	12.13 ± 0.38	−27.6	188.3	206.3
N-Phenylglycine	574.3	177.4 ± 5.8	12.95 ± 0.52	−11.9	172.1	179.9

Table 11. Comparative kinetic parameters at 300 °C

Substrate	$k_1 \times 10^4$ (s^{-1})	E_a (kJ mol^{-1})	Log A (s^{-1})	Ref.
N,*N*-Dimethylglycine	7.97	176.6	13.0	1
N-Phenylglycine	5.32	172.6 ± 6.4	12.46 ± 0.57	This work

2-substituted carboxylic acids, a small amount of aniline was also obtained (k_2). This suggests that the oxygen carbonyl may assist to stabilize the $C_\alpha^{\delta+} \cdots ^{\delta-}$NHPh bond polarization in the transition state, which then decomposes to aniline and the unstable lactone as shown in reaction (2). The latter product rapidly decarbonylates to produce formaldehyde.

The recently reported gas-phase elimination of *N*,*N*-dimethylglycine[1] is found to be slightly faster in the rate of decarboxylation than *N*-phenylglycine (Table 11). This small difference may be explained by the OH bond polarization of the carboxylic group, in the sense of $O^{\delta-} \cdots H^{\delta+}$, while the nucleophilicity of the N atom of the amino acid is determinant. Since the N atom of the $(CH_3)_2N$ substituent is more nucleophilic than the N of the PhNH group for the abstraction of the acidic hydrogen, a higher rate of decarboxylation of *N*,*N*-dimethylglycine is expected [reaction (5), k_1]. The fact that *N*-phenylglycine yields a small amount of aniline, the nitrogen atom in the PhNH substituent, as an activating group of the aromatic nuclei, may delocalize its available electrons towards the benzene ring. Therefore, a bond polarization as reported above of $C^{\delta+} \cdots ^{\delta-}$NHPh favors the assistance of the oxygen carbonyl of the COOH group to the partial positive carbon and the product formation depicted in reaction (5) (k_2).

EXPERIMENTAL

N-Phenylglycine ethyl ester (Acros) of 99.5% purity (GC: 3% OV-17 Chromosorb Q II, 80–100 mesh) and *N*-phenylglycine (Aldrich) of 99.0% purity [GC–MS (Saturn 2000, Varian) DB-5MS capillary column, 30 m × 0.250 mm i.d., 0.25 μm] were used. The substrates and products *N*-methylaniline (Aldrich) and aniline (Aldrich) were analyzed with the same Varian Saturn 2000 GC–MS instrument with a DB-5MS capillary column, and ethylene gas with a column of Porapak Q, 80–100 mesh.

Kinetics. The elimination kinetics were examined in a static system described before[12,13] with an Omega DP41-TC/DP41-RTD high-performance digital temperature indicator. The rate coefficients were determined manometrically and chromatographic analyses were performed with a precision of 0.5 mm. The temperature was controlled by a Shinko DC-PS resistance thermometer controller and an Omega Model SSR280A45 solid-state relay, maintained within ±0.2 °C and measured with a calibrated platinum–platinum–13% rhodium thermocouple. No temperature gradient was detected along the reaction vessel. *N*-Phenylglycine ethyl ester was dissolved in dioxane and injected directly into the reaction vessel with a syringe through a silicone-rubber septum. The amount of substrates used for each run was ~0.05–0.1 ml.

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