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Mechanism of elimination of amino acid derivatives in the gas phase. Pyrolysis kinetics of ethyl picolinate, ethyl 1-methylpipecolinate and picolinic acid

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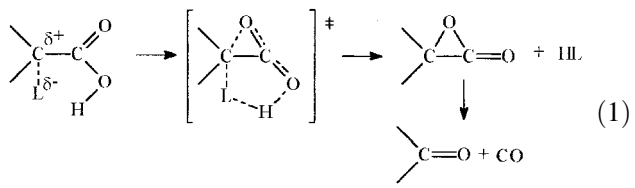
ABSTRACT: The kinetics of the gas-phase elimination of the title compounds were determined in a static reaction system over the temperature range 180.8–419.4 °C and the pressure range 15–86 Torr (1 Torr = 133.3 Pa). The reactions are homogeneous and unimolecular and obey a first-order rate law. The observed rate coefficients are represented by the following Arrhenius equations: for ethyl picolinate, $\log[k_1(s^{-1})] = (11.30 \pm 0.24) - (180.9 \pm 3.0)$ kJ mol^{-1} $(2.303\ RT)^{-1}$, for ethyl 1-methylpipecolinate, $\log[k_1(s^{-1})] = (13.36 \pm 0.31) - (209.5 \pm 3.9)$ kJ mol^{-1} $(2.303\ RT)^{-1}$ and for picolinic acid, $\log[k_1(s^{-1})] = (12.05 \pm 0.10) - (135.7 \pm 0.9)$ kJ mol^{-1} $(2.303\ RT)^{-1}$. The data from this work together with those reported in the literature confirm previous considerations that amino acids or α-nitrogen substituents of carboxylic acids undergo an extremely rapid decarboxylation process. The pyrolysis kinetics of picolinic acid, which is an intermediate of ethyl picolinate elimination, showed a dramatic fast decomposition into pyridine and CO_2 gas. The decarboxylation process of α-amino or α-nitrogen substituents of carboxylic acids differs from the decarbonylation elimination of several known α-substituted carboxylic acids in the gas phase. Copyright © 2002 John Wiley & Sons, Ltd.

KEYWORDS: gas-phase pyrolysis; kinetics; mechanism; amino acid derivatives; ethyl picolinate; ethyl 1-methylpipecolinate; picolinic acid

INTRODUCTION

Experimental determinations and *ab initio* theoretical calculations on the gas-phase pyrolyses of 2-substituted carboxylic acids[1–7] suggested a decarbonylation process as described in reaction (1). The acidic H of the COOH group assists the leaving group L for elimination, followed by the participation of the oxygen of the carbonyl to give an unstable α-lactone. This intermediate rapidly decomposes into the corresponding carbonyl compound and CO gas.



(1)

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

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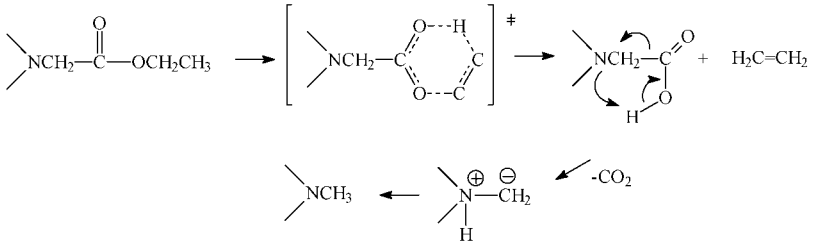
It is very difficult to displace an amino or a nitrogen derivative as a leaving substituent L in organic compounds in gas-phase elimination reactions. In addition, most simple amino acids are solids, which limits their suitability for their investigation as neutral molecules in the gas phase. However, in recent work[8] it was possible to examine the formation of neutral amino acid intermediates from the pyrolyses of their corresponding ethyl ester derivatives. The mechanism of these reactions was formulated as in reaction (2).

According to the results of the above-mentioned work,[8] neutral amino acids are very reactive species in the gas phase. This is because the N atom becomes more polarized when approaching the acidic H of the COOH group, thus causing a lowering of the energy. Therefore, a very rapid decomposition is to be expected. The nitrogen atom as a 2-substituent of carboxylic acids is not a leaving group, and decarboxylation [reaction (2)] rather than decarbonylation [reaction (1)] was obtained. The mechanistic rationalization for the fast decomposition of neutral amino acid intermediates is supported from the elimination kinetics of *N*,*N*-dimethylglycine, an intermediate of *N*,*N*-dimethylglycine ethyl ester pyrolysis. The former substrate was found to be decomposed ~96



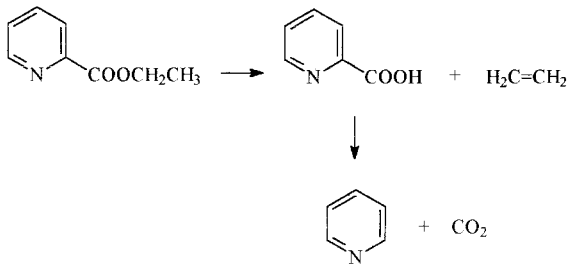
(2)

times faster than the latter at 400 °C.[8] This means that *N*,*N*-dimethylglycine decomposes rapidly at the working temperature of the corresponding ethyl ester. Consequently, the gas-phase elimination of neutral amino acids is expected to occur at very low temperatures. To further our knowledge of the mechanistic pathway of the gas-phase elimination of α-amino or α-nitrogen substituents of carboxylic acids, this work was initiated to examine the gas-phase pyrolysis kinetics of ethyl picolinate and ethyl 1-methylpipecolinate. In addition to these substrates, picolinic acid, which may be an intermediate in ethyl picolinate elimination, was examined in order to determine the extent of decomposition of α-nitrogen substituents of carboxylic acids.

RESULTS AND DISCUSSION

Ethyl picolinate

The elimination reaction of ethyl picolinate [reaction (3)] demands $P_f/P_0 = 3.0$, where P_f and P_0 are the final and initial pressures, respectively. The average experimental P_f/P_0 value at four different temperatures and 10 half-lives is 2.9 (Table 1). Additional confirmation of the stoichiometry, up to 75% decomposition, was obtained by comparing the pressure measurements with the quantitative analyses of ethylene formation (Table 2). Elimination reaction (3) is homogeneous (Table 3), since no significant variation in the rate coefficients was obtained in these experiments when using both clean Pyrex and seasoned Pyrex vessels with a surface to volume ratio of 6.0 relative to both clean Pyrex and seasoned Pyrex normal vessels. The effect of different proportions of toluene inhibitor is shown in Table 4. Therefore, this elimination reaction is molecular and not free radical in nature. No induction period was observed. The rate coefficients are reproducible with a standard deviation of not greater than 5% at a given temperature.



(3)

The first-order rate coefficients for ethyl picolinate, 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). The rate coefficient, at a given temperature, is measured at each reaction time, and after a significant number of lectures obtained, the average k value is estimated within ±5% standard deviation. A plot of $\log(3P_0 - P_t)$ vs time t gave a good straight line up to 75% decomposition. The variation of the rate coefficients with temperature and the

Table 1. Rate of final (P_f) to initial pressure (P_0) of the substrate

Substrate	Temperature (°C)	P_0 (Torr)[a]	P_f (Torr)[a]	P_f/P_0	Average
Ethyl picolinate	380.3	26	74	2.84	2.95
	391.2	30.5	90	2.95	
	399.9	29	88	3.00	
Ethyl 1-methylpipecolinate	414.1	57	172	3.00	2.93
	381.1	65	197	3.00	
	389.6	71.5	210	2.93	
	401.1	64.5	184	2.85	
	419.4	45	132	2.93	
Picolinic acid	190.8	26.5	49.5	1.87	1.86
	199.7	30	56	1.87	
	210.2	37.5	68.5	1.83	
	220.3	40.5	75	7.85	

[a] 1 Torr = 133.3 Pa.

Table 2. Stoichiometry of the reaction

Substrate	Temperature (°C)	Parameter	Value				
Ethyl picolinate	370.0	Time (min)	6	12	21	39	59
		Reaction (%) (pressure)	13.26	25.30	42.60	58.94	76.15
		Ethylene (%) (GC)	13.56	25.25	43.35	58.87	76.76
Ethyl 1-methylpipecolinate	379.0	Time (min)	7	14	23	37	65
		Reaction (%) (pressure)	15.65	30.60	51.40	63.46	81.10
		Ethylene (%) (GC)	15.59	30.00	48.75	61.65	82.32
Picolinic acid	199.7	Time (min)	4	7	10	13	16
		Reaction (%) (pressure)	24.2	38.0	49.6	59.6	68.3
		Pyridine (%) (GC)	24.4	40.1	47.7	58.7	65.9

Table 3. Homogeneity of pyrolysis reactions

Compound	S/V (cm^{-1})[a]	$10^4\ k_1$ (s^{-1})[b]	$10^4\ k_1$ (s^{-1})[c]
Ethyl picolinate at 399.9 °C	1	19.90	19.90
	6	19.76	19.91
Ethyl 1-methylpipecolinate at 401.1 °C	1	12.48	12.43
	6	12.47	12.45
Picolinic acid at 199.7 °C	1	11.42	11.58
	6	12.35	11.70

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

Table 4. Effect of free radical inhibitor on rates[a]

Substrate	Temperature (°C)	P_s[b] (Torr)	P_i[c] (Torr)	P_i/P_s	$10^4\ k_1$ (s^{-1})
Ethyl picolinate	380.3	31	–	–	6.82
		40	18	0.5	6.81
		52	40	0.8	6.70
		60	88	1.5	6.83
		26	76	2.9	6.80
		38	128	3.4	6.73
Ethyl 1-methylpipecolinate	401.1	68	–	–	12.74
		64.5	34	0.5	12.71
		70	75	1.1	12.49
		58	88	1.5	12.93
		43	90	2.1	12.70
Picolinic acid	199.7	32	–	–	11.28
		44	66	1.5	11.42
		33.5	81.5	2.4	11.17
		30	107	3.0	11.58

[a] Cyclohexene or toluene inhibitor.
[b] P_s = pressure of the substrate.
[c] P_i = pressure of the inhibitor.

Table 5. Variation of the rate coefficients with initial pressure

Substrate	Temperature (°C)	Parameter	Value			
Ethyl picolinate	391.2	P_0 (Torr)	15	25	31	62
		$10^4\ k_1$ (s^{-1})	11.57	11.71	11.57	11.55
Ethyl 1-methylpipecolinate	419.4	P_0 (Torr)	45	66	80	86
		$10^4\ k_1$ (s^{-1})	36.78	36.62	36.70	36.86
Picolinic acid	210.2	P_0 (Torr)	17	29	36	45
		$10^4\ k_1$ (s^{-1})	23.89	24.51	24.36	24.21

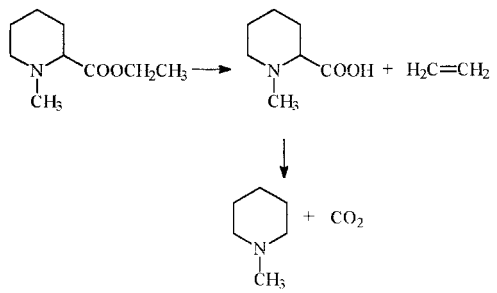
Table 6. Temperature dependence of the rate coefficients

Substrate	Parameter	Value						
Ethyl picolinate	Temperature (°C)	349.7	359.6	370.7	380.3	391.2	399.9	414.1
	$10^4\ k_1\ (s^{-1})$	1.35	2.30	4.00	6.81	11.59	19.88	33.84
Rate equation: $\log[k_1\ (s^{-1})] = (11.30 \pm 0.24) - (180.9 \pm 3.0)$kJ mol^{-1} $(2.303\ RT)^{-1}$; $r = 0.9993$								
Ethyl 1-methylpipecolinate	Temperature (°C)	364.6	371.4	381.1	389.6	401.1	409.4	419.4
	$10^4\ k_1\ (s^{-1})$	1.51	2.57	4.38	7.46	12.71	21.60	36.70
Rate equation: $\log[k_1\ (s^{-1})] = (13.36 \pm 0.31) - (209.5 \pm 3.9)$kJ mol^{-1} $(2.303\ RT)^{-1}$; $r = 0.9991$								
Picolinic acid	Temperature (°C)	180.8	190.9	199.7	210.2	220.3		
	$10^4\ k_1\ (s^{-1})$	2.75	5.93	11.58	24.40	48.69		
Rate equation: $\log[k_1\ (s^{-1})] = (12.05 \pm 0.10) - (135.7 \pm 0.9)$kJ mol^{-1} $(2.303\ RT)^{-1}$; $r = 0.9998$								

corresponding Arrhenius equation is given in Table 6 (90% confidence limits from a least-squares procedure).

Ethyl 1-methylpipecolinate

The molecular elimination of this substrate, described in reaction (4), requires that $P_f/P_0 = 3.0$. The average experimental P_f/P_0 values at four different temperatures and 10 half lives is 2.93 (Table 1). The stoichiometry of reaction (4), up to 80% decomposition, was satisfactorily verified by comparing the percentage decomposition of the substrate from pressure measurements with that obtained from the gas chromatographic (GC) measurement of the product ethylene (Table 2).



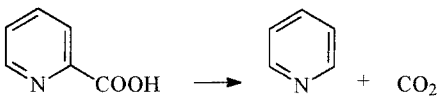
(4)

The reaction can be said to be homogeneous since no significant effects on the rates were obtained on using both clean Pyrex and seasoned Pyrex vessels with a surface to volume ratio of 6.0 relative to the normal clean and seasoned Pyrex vessels in these experiments (Table 3). The presence of different proportions of toluene, an effective free radical inhibitor, had no effect on the rates and no induction period was obtained (Table 4). The rates are reproducible with a standard deviation not greater than 5% at a given temperature.

The rate coefficients for elimination, calculated from $k_1 = (2.303/t)\log[2P_0/(3P_0 - P_t)]$, are invariable to initial pressures (Table 5), and the first-order plots of $\log(3P_0 - P_t)$ against time t gave a good straight line for up to 80% decomposition. The temperature dependence of the rate coefficients is shown in Table 6. The experimental data were fitted to the Arrhenius equation as shown in Table 6, where 90% confidence limits from a least-squares procedure are given.

Picolinic acid

The experimental stoichiometry for the pyrolysis of this substrate, as shown in reaction (5), requires $P_f/P_0 = 2.0$. The average experimental P_f/P_0 value obtained at four different temperatures and 10 half-lives was 1.86 (Table 1). It was possible to corroborate the stochiometry of reaction (5), up to 65% decomposition, by comparing the percentage decomposition of the substrate from pressure measurements with those obtained by GC analysis of the product pyridine (Table 2). The effect of the surface area in the rate of elimination was determined carried by employing a vessel with a surface to volume ratio six times greater than that of the normal vessel. The rate coefficient for formation of pyridine was unaffected in the clean Pyrex vessel and in the seasoned glass packed and unpacked vessels. The clean packed Pyrex vessel showed a very small heterogeneous effect (Table 3). Cyclohexene inhibitor had no effect on the rates (Table 4) and no induction period was observed. The rates are reproducible with a relative standard deviation of not greater than 5% at a given temperature.



(5)

The rate coefficient of this substrate was calculated from $k_1 = (2.303/t)\log P_0/(2P_0 - P_t)$ and was found to be independent of the initial pressure (Table 5). A plot of $\log(2P_0 - P_t)$ aganist time t gave a good straight line for up to 65% reaction. The temperature dependence of the rate coefficients and the corresponding Arrhenius equation are given in Table 6 (90% confidence limits from a least-squares procedure).

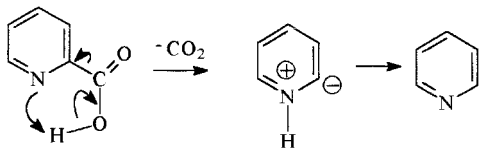
The k value of ethyl picolinate shows that it undergoes elimination slightly faster than ethyl 1-methylpipecolinate (Table 7). This small but significant difference in rate coefficients may be attributed to the aromaticity of

Table 7. Kinetic parameters for pyrolysis reactions at 360 °C

Compound	$k_1 \times 10^4$ (s^{-1})	E_a (kJ/mol)	Log[A (s^{-1})]	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta G^{\neq}$ (kJ $mol)^{-1}$
Ethyl picolinate	2.36	180.9 ± 3.0	11.30 ± 0.24	−43.1	175.6	182.1
Ethyl 1-methylpipecolinate	1.18	209.5 ± 3.9	13.36 ± 0.31	−3.7	204.2	204.8
Picolinic acid	71161	135.7 ± 0.9	12.05 ± 0.10	−28.8	130.4	134.8

the pyridine group. The delocalized π-system of pyridine must exert a greater electron-withdrawing effect than the piperidine ring. The reaction mechanism of these substrates may be explained as in reaction (2).

The homogeneous, unimolecular elimination of picolinic acid, which is produced as an intermediate in reaction (3), gives, as expected, an extremely rapid decomposition that is 2500 times faster than that for ethyl picolinate pyrolysis at 360 °C (Table 7). Consequently, neutral amino acid types of molecules must undergo a very rapid decomposition and at very low temperatures. The mechanism of picolinic acid elimination is depicted in reaction (6).



(6)

EXPERIMENTAL

Ethyl picolinate (Aldrich) and ethyl 1-methylpipecolinate (Aldrich) of >99.0% purity (GC: Porapak Q, 80–100 mesh) were employed. The quantitative analysis of the product ethylene was performed by using the same Porapak Q column. Picolinic acid (Aldrich) was shown to be 99.6% pure when analyzed by GC–MS (Saturn 2000, Varian) using a DB-5MS capillary column (30 × 0.25 mm i.d., 0.25 μm film thickness). The product pyridine, diluted with very small amount of methanol, was quantitatively analyzed by using a 2 m column of 3% OV-16 on 80–100-mesh Chromosorb Q II.

The verification of the starting materials and identification of the products were performed with a Varian Saturn 2000 GC–MS instrument with a DB-5MS capillary column.

Kinetic studies. The kinetic experiments were carried out in a static reaction system as described previously[9,10] with an Omega DP41-TC/DP41-RTD high-performance digital temperature indicator. The rate coefficients were determined from the pressure increase. 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 observed along the reaction vessel. The picolinic acid substrate was dissolved in acetic acid and injected directly into the reaction vessel with a syringe through a silicone rubber septum. The amount of substrate used for each reaction was ~0.01–0.1 ml.

Acknowledgement

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