[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF FORDHAM UNIVERSITY]

Effect of Solvents on the Decarboxylation of Picolinic Acid[1]

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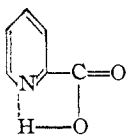
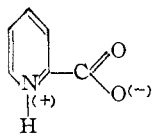
In an attempt to elucidate the decarboxylation mechanism of picolinic acid, the rates of decarboxylation of picolinic acid were determined in acid, basic and polar neutral solvents. The observed rates were found to be first order in all cases. The E and A values of the Arrhenius equation and the $\Delta H^{\ddagger}$ and $\alpha S^{\ddagger}$ values of the Absolute Reaction Rate Theory were then determined. On the basis of the data obtained a mechanism for the decarboxylation of picolinic acid is proposed and the effect of solvents on the rate of decarboxylation explained.

In an attempt to elucidate the decarboxylation mechanism of picolinic acid, the acid was decarboxylated in a series of solvents: neutral, acidic and basic. It has been shown previously[2] that methyl substitution of the pyridine ring has a pronounced effect on the rate as well as the activation energy of decarboxylation. However, from these studies no definite conclusion could be reached as to the nature of the initial reactant in the decarboxylation process. Furthermore, observations made on the rates of decarboxylation during the Hammick reaction,[3,4] did not agree with a report[5] on the rate of breakdown of picolinic acid in various solvents. Hammick[6] has shown fairly conclusively that acids of this type do not carboxylate in the free state. Therefore the problem seems to be narrowed down to the choice of which one of two reactive forms accounts for the ease of decarboxylation of this acid. The purpose of this paper then, is to show the effect of solvents on the rate and activation energy of decarboxylation and then describe a plausible mechanism.

The two reactive forms which can be proposed after ruling out the free acid are the cyclic form (I) and the zwitterion form (II).



I



II

Both of these forms increase the positive potential of the ring nitrogen, which could then exert an attraction on the carbon to carboxy pair of electrons, drawing them toward the ring and favoring relase of CO_2.

The first form is favored in the work of Doering and Pasternak[7] on α-pyridylacetic acid and similar cyclic intermediates have been proposed by Wiig,[8] Locke,[9] Muus[10] and Westheimer and Jones[11] in their work on β-keto acids.

The second form is favored by Hammick[12] in his work on quinaldinic, isoquinaldinic and picolinic acids and by Pedersen[13] in his work on β-keto acids.

It can be stated that the cyclic hydrogen bonded structure for the reactant seems more probable in the case of the β-keto acids than in the case of α-picolinic acid. In the β-keto acids the cyclic reactant would form a ring of five members excluding hydrogen as shown in III whereas, in the case of α-picolinic acid, the ring would be four membered excluding hydrogen. Furthermore, the oxygen of the β-keto acid is much less basic than the nitrogen of the pyridine ring and therefore would have less tendency to form a complete covalent bond with the hydrogen of the carboxyl group than would the nitrogen of the pyridine ring, *i.e.*, a zwitterion.

Picolinic acid was decarboxylated in various solvents over a temperature range of 165 to 185° and the rates recorded. Neutral solvents included *o*-, *m*- and *p*-dimethoxybenzene, *o*-, *m*- and *p*-nitrotoluene and *p*-cymene. Acidic solvents included phenol and *p*-nitrophenol and basic solvents included aniline, *p*-nitroaniline, N,N-diethylaniline, quinoline and tributylamine.

The rates were obtained by weighing quantitatively the amount of CO_2 evolved in measured time intervals and were found to be first order in all cases.

Experimental

Preparation of Materials.—Picolinic acid was prepared by the oxidation[14] of α-picoline with potassium permanganate. It was recrystallized repeatedly from dry benzene. *p*-Dimethoxybenzene, *o*-, *m*- and *p*-bromoanisole, nitrobenzene, *p*-dibromobenzene, *o*-, *m*- and *p*-nitrotoluene, *p*-cymene, *p*-nitrophenol, phenol, aniline, *p*-nitroaniline, N,N-diethylaniline, quinoline and tributylamine were obtained commercially and purified by fractional distillation or recrystallization.

o-Dibromobenzene was prepared by diazotizing[15] the corresponding *o*-bromoaniline in 48% HBr and cuprous bromide. *m*-Dibromobenzene was obtained by reducing[16] the corresponding *m*-nitrobromobenzene to *m*-bromoaniline and then converting it to *m*-dibromobenzene by the same method outlined for the preparation of *o*-dibromobenzene. *o*-Dimethoxybenzene was prepared[17] by converting pyrocatechin to the *o*-dimethyl ether by refluxing in methyl alcohol and potassium hydroxide.

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m-Dimethoxybenzene was prepared by refluxing resorcinol in sodium hydroxide and dimethyl sulfate.

The Ascarite for the absorption tubes was 8–20 mesh and renewed after each experiment. The anhydrone used in the drying tubes was the same grade as in quantitative microanalysis.

Apparatus and Procedure.—The apparatus, the general procedure followed for measuring the rates of decarboxylation and the determination of the purity of the acid as well as its total decarboxylation have been described previously.[2]

In this series of experiments, 0.04 mole of the acid in 25 g. of the solvent was used in each case. The amount of carbon dioxide evolved during the time necessary for the reaction mixture to reach the temperature of the bath was recorded. This amount was then subtracted from that amount of carbon dioxide known to have been originally present in the acid. The acid present at zero time, namely, the time at which the reaction mixture reaches the temperature of the bath, could then be calculated and was designated the concentration at zero time. The log of the decrease of CO_2 in the acid *versus* time was plotted and a straight line was obtained. On the average, ten readings were taken for each experiment and, in all cases, the reaction was allowed to proceed to greater than 85% completion. Reaction rates were taken for each acid over a 20° range at approximately 5° intervals.

Results

The results tabulated in Tables I, II, III and IV were obtained by the use of the first-order equation

TABLE I

FIRST-ORDER RATE CONSTANTS FOR THE DECARBOXYLATION OF THE PICOLINIC ACID IN A SERIES OF STRUCTURALLY ISOMERIC SOLVENTS

Solvents	Temp., °C.	$k \times 10^4$, sec.	m[a]
o-Dimethoxybenzene	171.5	2.10	1.624
m-Dimethoxybenzene	171.5	2.17	1.624
p-Dimethoxybenzene	171.5	2.16	1.624
o-Bromoanisole	174.2	2.59	1.624
m-Bromoanisole	174.2	2.62	1.624
p-Bromoanisole	174.2	2.60	1.624
o-Dibromobenzene	168.5	1.52	1.624
m-Dibromobenzene	168.5	1.53	1.624
p-Dibromobenzene	168.5	1.51	1.624
o-Nitrotoluene	174.2	2.59	1.624
m-Nitrotoluene	174.2	2.84	1.624
p-Nitrotoluene	174.2	2.89	1.624

[a] m = molality in moles/1000 g. of solvent.

TABLE II

FIRST-ORDER RATE CONSTANTS FOR THE DECARBOXYLATION OF PICOLINIC ACID IN VARIOUS NEUTRAL SOLVENTS

Temp., °C.	$k \times 10^4$, sec.	m[a]	Temp., °C.	$k \times 10^4$ sec.	m[a]
p-Dimethoxybenzene			*p*-Dibromobenzene		
171.5	2.16	1.624	168.5	1.51	1.624
179.0	3.94	1.624	174.5	2.58	1.624
184.5	5.87	1.624	179.1	3.87	1.624
190.5	9.18	1.624	182.5	5.22	1.624
p-Bromoanisole			*p*-Nitrotoluene		
174.2	2.60	1.624	168.8	1.66	1.624
178.8	3.91	1.624	174.2	2.89	1.624
183.0	5.39	1.624	179.0	4.38	1.624
Nitrobenzene			*p*-Cymene		
169.0	1.75	1.624	164.5	1.34	1.624
174.6	3.06	1.624	168.3	1.94	1.624
179.0	4.71	1.624	172.8	3.15	1.624
183.0	5.82	1.624			

[a] m = molality in moles/1000 g. of solvent.

TABLE III

FIRST-ORDER RATE CONSTANTS FOR THE DECARBOXYLATION OF PICOLINIC ACID IN ACIDIC SOLVENTS

Temp., °C.	$k \times 10^4$, sec.	m[a]
Phenol[b]		
170.0	0.60	1.624
174.0	1.03	1.624
p-Nitrophenol		
169.0	0.22	1.624
173.5	0.34	1.624
179.2	0.75	1.624
182.6	1.04	1.624

[a] m = molality in moles/1000 g. of solvent. [b] Phenol was measured at only two temperatures because of its low boiling point.

TABLE IV

FIRST-ORDER RATE CONSTANTS FOR THE DECARBOXYLATION OF PICOLINIC ACID IN BASIC SOLVENTS

Temp., °C.	$k \times 10^4$, sec.	m[a]	Temp., °C.	$k \times 10^4$, sec.	m[a]
Aniline[a]			Quinoline		
168.5	1.21	1.624	169.2	1.04	1.624
173.6	1.89	1.624	173.5	1.67	1.624
177.0	2.43	1.624	178.5	2.56	1.624
p-Nitroaniline			Tributylamine		
174.0	1.76	1.624	168.5	0.92	1.624
177.0	2.48	1.624	173.5	1.79	1.624
182.0	3.69	1.624	179.0	3.17	1.624
			182.5	4.87	1.624
N,N-Diethylaniline					
169.5	1.73	1.624			
174.0	3.23	1.624			
179.0	4.61	1.624			
182.8	6.21	1.624			

[a] Aniline showed a lag in the rate after half time; not shown by any other solvent. Complete rates were taken twice.

$k = (1/t) \ln a/(a - x)$ for each separate reading of a particular experiment. The k values varied only a few parts per thousand and the average value was taken as the k representative of that temperature. The a of the equation represents the carbon dioxide initially present at zero time in the acid compound and the $a - x$ the amount present at time t. That the rates are of first order, is shown not only by an agreement of the k values when calculated for each reading by the equation, but also by plotting the log of the decrease of CO_2 in the acid compound *versus* time.

The ortho and meta isomers of dimethoxybenzene, bromoanisole, dibromobenzene and nitrotoluene did not show any appreciable change in rate, as compared to that calculated for the para isomers, as shown in Table I.

The activation energies were calculated from the Arrhenius equation by the method of least squares for the 5° intervals from the lowest temperature for each acid to the highest shown in Tables II, III and IV. The values shown for the activation energies in Table V are the average values for the 20° range used. The average deviation of the mean activation energy from those obtained for the 5° intervals over the 20° range was of the order 300 cal.

TABLE V

ACTIVATION ENERGIES IN THE $\text{LOG}_{10} A$ FACTORS OF PICOLINIC ACID IN VARIOUS SOLVENTS

Solvents	E, kcal./mole	$\log_{10} A$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$, cal./deg./mole
Neutral				
p-Dimethoxybenzene	31.1	15.63	30.2	−8.2
p-Bromoanisole	33.6	16.85	32.7	−2.5
Nitrobenzene	35.1	17.64	34.2	+1.0
p-Dibromobenzene	35.8	17.95	34.7	+1.9
p-Nitrotoluene	36.0	18.07	35.2	+3.0
p-Cymene	40.2	20.2	39.3	+12.8
Acidic				
Phenol[a]	51.6	25.21	50.5	+35.7
p-Nitrophenol	46.8	23.46	45.9	+23.2
Basic				
Aniline[b]	32.3	16.07	31.4	−6.11
p-Nitroaniline	36.9	18.32	36.0	+4.2
N,N-Diethylaniline	37.7	18.88	36.8	+6.7
Quinoline	37.8	18.73	36.9	+6.1
Tributylamine	44.6	22.10	43.7	+21.4

[a] Rates taken at only two temperatures. [b] Low rates but small increase with temp.

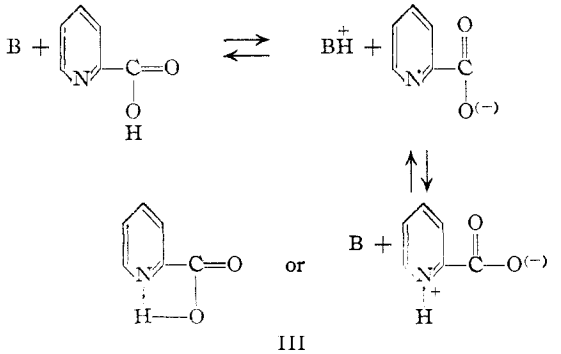
The log A factors shown in Table V were calculated using the mean activation energy and the corresponding rate constant at approximately 175°. In addition, the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values of the Absolute Reaction Rate theory as calculated from the equation

$$k = (kT/h)e^{-\Delta H^{\ddagger}/RT}\, e^{\Delta S^{\ddagger}/R}$$

are calculated.

Discussion

The data obtained indicate that the rate of decarboxylation of picolinic acid is lowered and the activation energy raised by both acids and bases. Neutral polar solvents also have a pronounced but varied effect. A theoretical explanation for the effect of acids and bases on the decarboxylation can be given by assuming that the initial reactant involved in the most facile path of decarboxylation

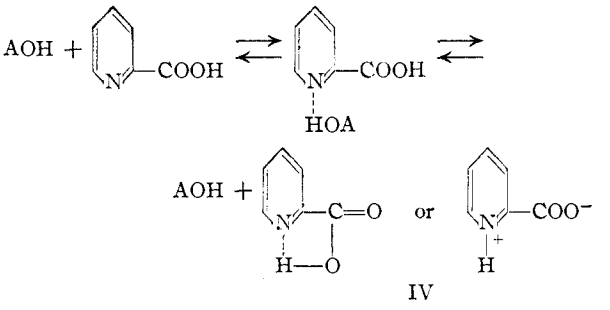


III

is either the cyclic form in I or the zwitterion form in II. The effect of neutral polar solvents on the rate and activation energy of decarboxylation is more difficult to explain.

It can readily be seen that in the case of bases, an equilibrium of the type shown in III is highly probable between the base (B) and picolinic acid. Both of the structures proposed as initial reactants would be decreased in concentration if this were the case and the rate of decarboxylation thereby decreased.

The suppression of the rate and the increase of the activation energy noted in the presence of acids is most probably due to a competition between the acidic hydrogen of the pyridine carboxyl group and the hydrogen of the acidic solvent (AOH) for the nitrogen of the pyridine ring. Thus, we would have the equilibrium shown in IV. This type of



IV

equilibrium would reduce the concentration of either form proposed as initial reactants.

The fact that the effect of neutral polar solvents on the activation energy of decarboxylation shown in Table V does not follow a definite order of increasing value with increasing polarity and the fact that *p*-cymene, a weakly polar solvent, raises the activation energy out of all proportion to its polar properties indicates that the action of the solvent on the reaction and on the initial reactants is much more complicated than at first could be predicted.

However, from a consideration of the over-all observed effect of solvents on the activation energy of decarboxylation and an analysis of the effect of solvation on the potential energies of the two forms, namely, the chelated form and the zwitterion form, we are led to favor the zwitterion as the initial reacting form and the mechanism of decarboxylation as shown.

The increase of log A with E has been observed in substituted malonic acids,[18] in halogen substituted acetic acids[19] and recently in the decomposition of peresters.[20]

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