

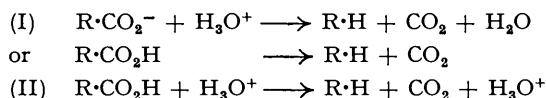
**318.** *The Mechanism of Decarboxylation. Part VI. Kinetics of the Acid-catalysed Decarboxylation of 2 : 4 : 6-Trihydroxybenzoic Acid.*

By B. R. BROWN, W. W. ELLIOTT, and D. LL. HAMMICK.

In continuation of the investigations described in Part V (Brown, Hammick, and Scholefield, *J.*, 1950, 778), the kinetics of the decarboxylation of 2 : 4 : 6-trihydroxybenzoic acid have been studied in aqueous solution. The effect of added mineral acid on the rate, *i.e.*,

$$\text{rate} = k[\text{R}\cdot\text{CO}_2\text{H}] + k_{\text{H}}[\text{H}_3\text{O}^+][\text{R}\cdot\text{CO}_2\text{H}]$$

is best interpreted on the basis of two simultaneous processes :



of which (I) can be regarded as either an  $S_{\text{E}}1$  or an  $S_{\text{E}}2$  mechanism, and (II) as an  $S_{\text{E}}2$  mechanism. The activation energy of process (I) is found to be 21,500 cal.; that of process (II) is 15,200 cal.

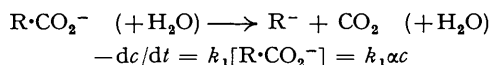
THE process of decarboxylation is essentially a replacement reaction:  $\text{H} + \text{R}\cdot\text{CO}_2\text{H} \longrightarrow \text{H}\cdot\text{R} + \text{CO}_2 + \text{H}$ ; such replacements in other molecular species (*e.g.*, replacement of halogen by OH in alkyl halides) have long been known to take place by the  $S_{\text{N}}1$  and  $S_{\text{N}}2$  processes of Hughes and Ingold (*J.*, 1935, 244), and in recent years evidence has accumulated that decarboxylation may occur by analogous  $S_{\text{E}}1$  and  $S_{\text{E}}2$  mechanisms (Schenkel and Schenkel-

Rudin, *Helv. Chim. Acta*, 1948, **31**, 514). An  $S_E1$  mechanism would require the "loosening" of the R-C bond to be the rate-determining process, with the implication of a rate unaffected by acids and facilitated by the introduction of substituents into R that *diminish* electron density at the atom  $\alpha$  to the carboxyl group (cf. Pedersen, *J. Physical Chem.*, 1934, **38**, 559; Verhoek, *J. Amer. Chem. Soc.*, 1939, **61**, 186). The rate of an  $S_E2$  process will be determined by the attack of a proton (proton acid or protonated solvent) at the  $\alpha$ -carbon atom and will show bimolecular kinetics involving "acid-catalysis" (Schubert, *J. Amer. Chem. Soc.*, 1949, **71**, 2639; Johnson and Heinz, *ibid.*, p. 2913). It will be facilitated by substituents in R that *increase* electron density at the  $\alpha$ -carbon atom (Brown, Hammick, and Scholefield, *loc. cit.*).

2 : 4 : 6-Trihydroxybenzoic acid is decarboxylated readily in aqueous solution at 50° and thus appears suitable for investigation under conditions of varying pH. It should be possible not only to establish acid catalysis, if operative, but also to determine whether the undissociated acid or the anion is the decarboxylating species.

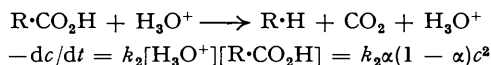
2 : 4 : 6-Trihydroxybenzoic acid may reasonably be expected to decarboxylate in aqueous solution by one or more of six mechanisms which fall kinetically into three groups :

(I) The unimolecular decomposition of the anion of the carboxylic acid, or the pseudo-unimolecular decomposition of the anion by interaction with a water molecule :

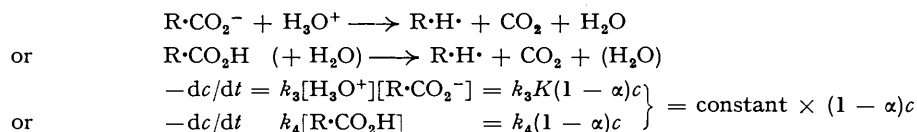


where  $c$  is the total concentration of the carboxylic acid whether dissociated or not, and  $\alpha$  is the degree of dissociation of the acid.

(II) The bimolecular attack of a solvated proton on the  $\alpha$ -carbon atom of the undissociated acid :



(III) The bimolecular attack of a solvated proton on the  $\alpha$ -carbon atom of the anion of the acid, or the unimolecular decomposition of the undissociated acid or the pseudo-unimolecular decomposition of the acid by interaction with a water molecule :



where  $K$  is the dissociation constant of the acid.

These three mechanisms should be distinguishable by the effect of added mineral acid. Thus, according to mechanism (I) the rate of reaction should be retarded by added hydrochloric acid since  $\alpha$  will decrease; according to mechanism (II) the rate will be markedly increased by the addition of acid since both  $[H_3O^+]$  and  $[R\cdot CO_2H]$  will be increased; according to mechanism (III), however, the rate will be only slightly increased since the term  $(1 - \alpha)$  increases only slightly with added acid.

#### EXPERIMENTAL.

The decarboxylation was followed by removing samples of the acid solution with a pipette. Each sample was treated with excess of cold standard potassium hydroxide solution, which effectively stops the reaction, and the excess of alkali was back-titrated with standard hydrochloric acid. The indicator used was methyl-red and the titration was carried to a definite pink tint (pH *ca.* 4). A small correction was then applied (0.05 ml.) to allow for the change from the true end-point to pH 4. This correction was determined by means of a Cambridge pH meter. By this means it was not found necessary to remove dissolved carbon dioxide, which buffers the solution at pH *ca.* 6, since sharp end-points were obtained.

Temperature control to within 0.05° was ensured by means of a water thermostat. All volumetric instruments were standardised by weight at the temperature at which they were required to function.

In Table I the rate constants are given at various temperatures and at various concentrations of hydrochloric acid. In col. 3 the rate constants are those calculated assuming that mechanism (I) controls the rate, col. 4 those assuming mechanism (II), and col. 5 those assuming that mechanism (III) controls the rate. All reactions were carried out at constant ionic strength, 1.08N. with respect to HCl and KCl, in order to standardise salt effects.

TABLE I.

Temp., ° K.	Concn. of added HCl, N.	Coeff. × 10 <sup>3</sup> , sec. <sup>-1</sup> (I)	Coeff. × 10 <sup>3</sup> , 1. mol. <sup>-1</sup> sec. <sup>-1</sup> (II)	Coeff. × 10 <sup>3</sup> , sec. <sup>-1</sup> (III)	Temp., ° K.	Concn. of added HCl, N.	Coeff. × 10 <sup>3</sup> , sec. <sup>-1</sup> (I)	Coeff. × 10 <sup>3</sup> , 1. mol. <sup>-1</sup> sec. <sup>-1</sup> (II)	Coeff. × 10 <sup>3</sup> , sec. <sup>-1</sup> (III)
323.0	nil	—	135	1.09	318.2	nil	—	68.3	0.613
—	0.0458	2.94	23.9	1.19	—	0.0346	1.45	19.4	0.750
—	0.0476	3.11	23.5	1.21	—	0.0417	1.79	17.6	0.794
—	0.0541	3.87	23.5	1.30	—	0.0484	2.09	15.7	0.780
—	0.0714	4.95	18.5	1.34	—	0.0550	2.28	14.3	0.822
—	0.0853	6.18	15.4	1.35	—	0.0613	2.54	13.1	0.791
—	0.1145	8.89	12.9	1.53	—	0.0680	2.83	11.6	0.808
—	0.1474	11.5	10.3	1.57	—	0.0742	3.16	10.9	0.832
—	0.1783	16.4	10.0	1.76	—	0.0804	3.43	10.0	0.826
312.95	nil	—*	42.2	0.356	—	0.0866	4.13	10.5	0.924
—	0.0346	0.80	11.1	0.421	—	0.1000	4.73	9.5	0.948
—	0.0412	0.91	9.9	0.436	—	0.1162	5.62	8.2	0.960
—	0.0553	1.26	7.7	0.441	—	0.1218	6.02	7.5	0.948
—	0.0671	1.86	7.9	0.497	—	0.1278	5.65	7.7	0.997
—	0.0795	2.26	6.8	0.550					
—	0.0973	2.80	5.6	0.552					
—	0.1091	2.92	5.0	0.550					
—	0.1260	3.90	4.8	0.608					

\* If mechanism (I) is assumed to control the rate, a linear logarithmic plot is not obtained in the absence of added mineral acid.

TABLE II.

Amine.	10 <sup>4</sup> <i>a</i> (mol./l.)	10 <sup>3</sup> <i>k</i> <sub>4</sub> (sec. <sup>-1</sup> )	Amine.	10 <sup>4</sup> <i>a</i> (mol./l.)	10 <sup>3</sup> <i>k</i> <sub>4</sub> (sec. <sup>-1</sup> )
<i>p</i> -C <sub>6</sub> H <sub>4</sub> Me·NH <sub>2</sub> ...	nil	2.90	Ph·NHMe .....	7.8	3.14
	1.5	3.05		12.0	3.35
	10.4	3.34		19.5	3.70
	17.0	3.62			
			Ph·NMe <sub>2</sub> .....	7.0	3.10
				11.2	3.40
				17.0	3.64

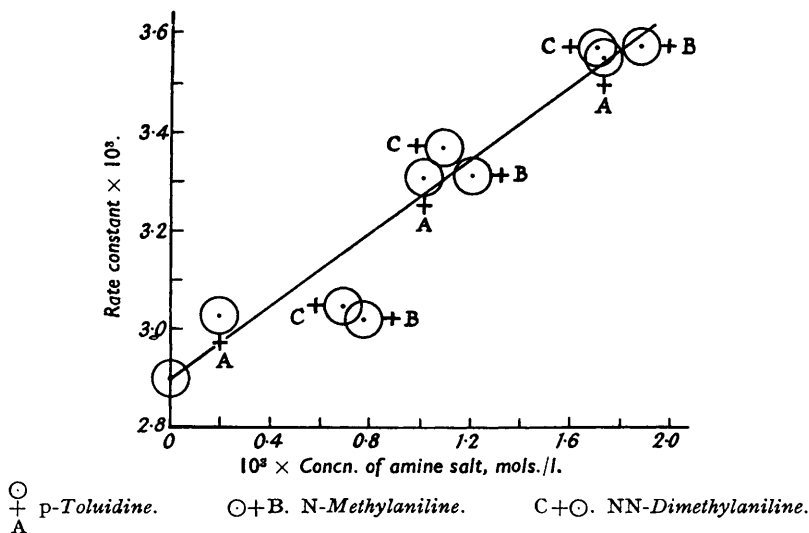
Temp., 333.2° K. *c*, ~ 0.004M.

The rate constants obtained in the presence of various aromatic amines are given in Table II and Fig. 1. They have been calculated by assuming that mechanism (III) alone controls the rate:

$$-dc/dt = k_4[R\cdot CO_2H] = k_4(1-a)(c-a)$$

where *a* is the concentration of added amine and *c* is the total concentration of carboxylic acid, *i.e.*, free acid plus amine salt of the acid. The values of *c* were determined experimentally by titration against standard barium hydroxide, bromocresol-purple being used as indicator (p*K* 6.3) after the dissolved carbon dioxide had been removed in a stream of nitrogen.

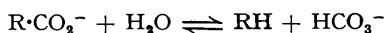
FIG. 1.



## DISCUSSION OF RESULTS.

From Table I it will be seen that cols. 3 and 4 do not provide a constant value for the rate constant and hence mechanisms (I) or (II) cannot be held to control the rate of reaction. The rate constants in col. 5 increase, at all three temperatures, by about 50% over the range 0—0.12*N*-HCl. This increase is too large and too regular to be due to experimental error and therefore mechanism (III) cannot be considered to be the rate-controlling step. Therefore, since no single assumption as to the mechanism provides a true rate constant, the actual decomposition must be composite. One of the components of the reaction must be mechanism (II), the bimolecular attack of a proton on the undissociated acid, since mechanism (III) cannot account for the magnitude of the catalytic effect of added hydrogen ions and mechanism (I) would be inhibited by added hydrogen ions. Either or both of mechanisms I and III may, however, contribute to the total effect.

In order to estimate the magnitude of the contribution of mechanism (I), the reaction was carried out at pH *ca.* 7, where only mechanism (I) can operate appreciably. It is known that the anion is decarboxylated according to the equilibrium equation :



the equilibrium constant at 50° being 0.11 (Hallstrom, *Ber.*, 1905, **38**, 2288). Employing this value of the equilibrium constant and also by the method of initial rates we find that this reaction, which is extremely slow at 50°, cannot contribute more than 0.25% to the total reaction in acidic solution. This contribution to the composite decomposition is within the experimental error and has been ignored.

We now proceed with the assumption that the second component must be mechanism (III). The total reaction may be thus expressed by the differential equation

$$-dc/dt = k_2[H_3O^+][R\cdot CO_2H] + k_4[R\cdot CO_2H]$$

where  $k_4$  may equal  $k_3K$  (see p. 1385).

The individual rate constants may be determined by adding such an excess of hydrogen chloride that the reaction is unimolecular or pseudo-unimolecular and the term  $(1 - \alpha)$  is virtually constant in any single run. Then by integration

$$-2.303 \log c = [k_2[H_3O^+](1 - \alpha) + k_4(1 - \alpha)]t + i$$

and hence by a plot of  $-\log c$  against time

$$\text{slope} \times 2.303 = k_2[H_3O^+](1 - \alpha) + k_4(1 - \alpha)$$

From this it follows that a plot of  $\text{slope} \times 2.303/(1 - \alpha)$  against  $[H_3O^+]$  has a slope of  $k_2$  and an intercept of  $k_4$ . In Fig. 2 this procedure has been adopted. The rate constants thus

TABLE III.

Temp. ° K. ....	312.95	318.2	323.0
$10^3 k_2$ (l. mol. <sup>-1</sup> sec. <sup>-1</sup> ) .....	1.84	2.45	3.90
$10^3 k_3 K$ or $10^3 k_4$ (sec. <sup>-1</sup> ) .....	0.359	0.67	1.04

obtained are given in Table III, and the Arrhenius energies of activation are obtained from these rate constants by Fig. 3 and tabulated in Table IV.

TABLE IV.

	Mechanism.	$E_a$ , cal.	PZ factor.
(II)	Acid + proton .....	15,200	$6.7 \times 10^7$ (l./mol. <sup>-1</sup> sec. <sup>-1</sup> )
(III)	Anion + proton .....	21,500	$2.0 \times 10^{13}$ (l./mol. <sup>-1</sup> sec. <sup>-1</sup> )
	or Acid unimolecular .....		$4.0 \times 10^{11}$ (sec. <sup>-1</sup> )

The energy of activation obtained by Brown, Hammick, and Scholefield (*loc. cit.*) for 2 : 4 : 6-trihydroxybenzoic acid in resorcinol is 13,600 cal., and the PZ factor is  $10^6$ . These values are thought to refer to the reaction between the undissociated acid and the acidic solvent and are thus to some extent comparable with the reaction between the undissociated acid and the solvated proton given above.

No great precision can be attributed to our energies of activation owing to (i) the complicated nature of the reaction; (ii) the variation in dissociation constant  $K$  with temperature being ignored and, though probably small, is not likely to be negligible; (iii) and the small temperature range allowed by considerations of solubility and speed of reaction.

FIG. 2.

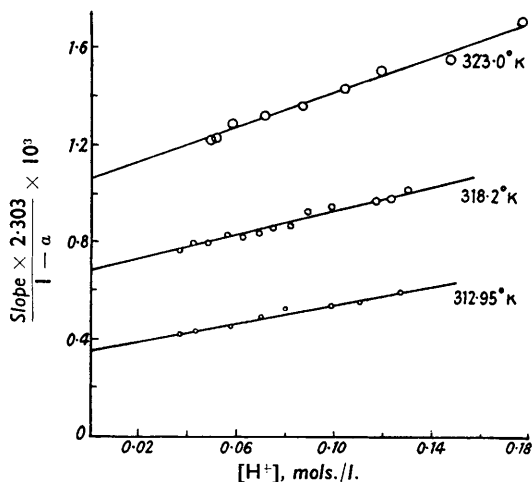
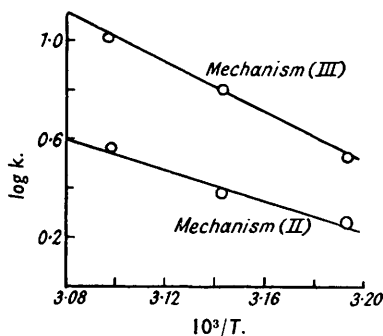
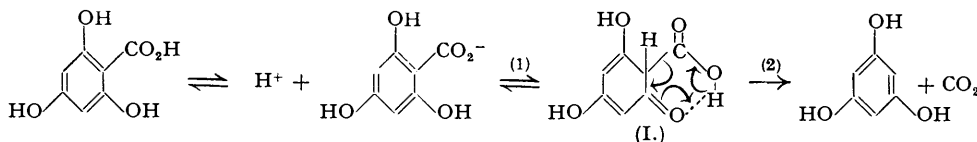


FIG. 3.



These results do not differentiate between the unimolecular decomposition of the undissociated acid and the bimolecular attack of a proton on the  $\alpha$ -carbon atom of the anion. This is due to the fundamental similarity of the two reactions from a kinetic standpoint. If the acid decomposes unimolecularly it is likely that the tautomeric keto-form will be the decarboxylating species. This acid forms a trioxime and since the keto-form would be a  $\beta$ -keto-acid, it might be expected to be readily decarboxylated. The following equilibria may therefore be possible:



Thus the difference between a unimolecular decomposition of the acid and a bimolecular reaction between a proton and an anion may depend on whether (1) or (2) is the rate-determining step. Both mechanisms would probably pass through an intermediate of structure (I). If this intermediate is very unstable then (1) will be rate determining, and the reaction will be of the  $S_E2$  type. On the other hand, if (I) is fairly stable, (2) will be the rate-determining step, and the mechanism will be of the  $S_E1$  type. For the  $S_E2$  mechanism (I) must be regarded as an activated transition state; for the  $S_E1$  mechanism (I) is regarded as the stable keto-form of the hydroxy-acid. Hence the two mechanisms probably cannot be differentiated, since they give rise to the same kinetic equation and both pass through the same intermediate. They cannot be differentiated by a primary salt effect since the activity of the intermediate complex, an uncharged species, is the same as that of the free acid. A secondary salt effect has been demonstrated but it may be shown that this is of no diagnostic significance.

However, a comparison of the effect of primary, secondary, and tertiary amines may be of some value. Pedersen (*loc. cit.*) reports that the decarboxylation of acetoacetic acid is markedly catalysed by primary amines, slightly by secondary amines, and hardly at all by tertiary amines. This was held to be due to the interaction of the keto-group with the primary amine. The decarboxylation of 2 : 4 : 6-trihydroxybenzoic is, however, catalysed equally, within the limits of experimental error, by primary, secondary, and tertiary amines (see Fig. 1). This amine catalysis may be attributed to general acid catalysis by the ammonium ions formed in acid solution, and the small magnitude of the effect may be due to the small catalytic power of the weak acid  $\text{>N}^+\text{H}$  as compared to that of  $\text{H}_3\text{O}^+$ . In the absence of specific catalysis by primary

amines, we therefore infer that mechanism (III) is probably the attack of a proton on the  $\alpha$ -carbon atom of the anion, and that the anion may be decarboxylated by a water molecule (mechanism I), an ammonium ion, and also by an oxonium ion (mechanism III). The magnitude of the catalytic effects are  $\text{H}_3\text{O}^+ > \text{>N}^+\text{—H} > \text{H}_2\text{O}$ . The experiments on the effect of added amines were carried out at high dilutions where mechanism (II) contributes less than 5% to the total reaction, since the acid is almost completely dissociated.

It is therefore concluded that 2 : 4 : 6-trihydroxybenzoic acid is decarboxylated in acidic solution by at least three mechanisms :

(I)	anion + water molecule	very slow
(II)	acid + oxonium ion	fast
(III)	anion + oxonium ion	fast

In the absence of added hydrogen chloride, (III) is the main contributor to the total reaction, but in the presence of excess of hydrogen chloride (II) and (III) are equally important.

In all the above calculations the value of the acid dissociation constant used is  $2 \times 10^{-2}$ . Ostwald (*Z. physikal. Chem.*, 1889, **3**, 253) determined  $K$  at  $25^\circ$  to be  $2.1 \times 10^{-2}$ . We, however, have worked at temperatures of  $40$ — $50^\circ$  and at high salt strength (1.08N.). On using a Cambridge pH meter at  $20^\circ$  and salt strength 1.08N., a value of  $2.0 \pm 0.3 \times 10^{-2}$  was obtained, but since this is a difficult region of acidic strength to determine accurately, this value must be regarded as approximate only. It is fortunate, however, that our deductions are largely independent of the value of the dissociation constant since  $\alpha$  varies as  $\sqrt{K}$ ;  $(1 - \alpha)$  in the presence of excess of hydrogen chloride is even less dependent on  $K$ . Indeed, even if  $K$  were as large as  $5 \times 10^{-2}$ , the above deductions as to the mechanism would hold though the actual values of the rate constants would be different. Only if  $K$  were as large as  $7 \times 10^{-2}$  would our deductions be invalid and a single mechanism, *i.e.*, (III) would hold. The effect of temperature on  $K$  should be, by analogy with other strong acids, both organic and inorganic, to decrease  $K$  with increasing temperature; such an effect would operate to the advantage of our conclusions.

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