THE MECHANISM OF THERMAL DECARBOXYLATION

By B. R. BROWN, M.A., D.PHIL.

(ROYAL COMMISSION FOR THE EXHIBITION OF 1851 SENIOR STUDENT, UNIVERSITY OF CAMBRIDGE)

THE frequent occurrence of decarboxylation in the degradative and synthetical procedures of organic chemistry and during the enzymic reactions of biochemistry, and the use of the decarboxylation reaction to illustrate the fundamentals of reaction kinetics in solution, are a sufficient indication of its importance. Organic chemists early recognised the value of decarboxylation and applied it as a standard method for the degradation and synthesis of molecules. Simultaneously physical chemists studied the rates of decarboxylation of organic acids in solution and used the results in the formulation of the theory of unimolecular reactions. Then came the combination of organic and physical methods with the object of elucidating the mechanism of thermal decarboxylation. This phase of the development of our knowledge of decarboxylation is outlined in this Review, but it is not out of place to notice that the success achieved in this direction is aiding the investigation of the mechanism of enzymic decarboxylation reactions.

Recent work has shown that decarboxylation can occur either by a unimolecular or by a bimolecular mechanism. Many years ago kinetic investigations made known the unimolecular decomposition of acid molecules. Within the past twenty years evidence has accumulated to substantiate this mechanism, and careful kinetic work has proved that many organic acids are decarboxylated in the form of their anions :
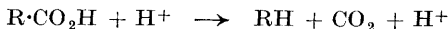
$$R{\cdot}CO_2^- \longrightarrow R^- + CO_2$$

However, some organic acids are known to be decarboxylated more readily as free acids. This effect has been interpreted [1, 2, 3] as a unimolecular decomposition of the acid in a zwitterionic form :

$$R{\cdot}CO_2H \rightleftharpoons H^+R{\cdot}CO_2^- \longrightarrow HR + CO_2$$
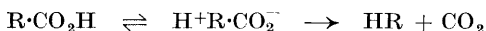
for example,
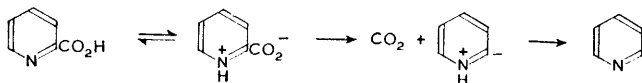
The idea that some decarboxylations take place in a bimolecular manner was first suggested in 1948 : [4]

$$R{\cdot}CO_2H + H^+ \longrightarrow RH + CO_2 + H^+$$

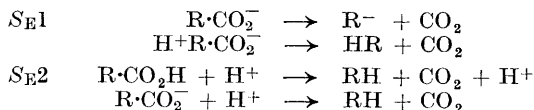[1] Pedersen, *J. Physical Chem.*, 1934, **38**, 559.
[2] Brown and Hammick, *J.*, 1949, 659.
[3] Doering and Pasternak, *J. Amer. Chem. Soc.*, 1950, **72**, 143.
[4] Schenkel and Schenkel-Rudin, *Helv. Chim. Acta*, 1948, **31**, 514.

Since then the evidence has increased sufficiently to put its occurrence beyond all doubt.

Thus the two modes of decarboxylation can be classified as uni- and bi-molecular electrophilic replacement reactions : [4, 5]

$$S_E1 \qquad \begin{aligned} R \cdot CO_2^- &\longrightarrow R^- + CO_2 \\ H^+ R \cdot CO_2^- &\longrightarrow HR + CO_2 \end{aligned}$$

$$S_E2 \qquad \begin{aligned} R \cdot CO_2 H + H^+ &\longrightarrow RH + CO_2 + H^+ \\ R \cdot CO_2^- + H^+ &\longrightarrow RH + CO_2 \end{aligned}$$

Into this scheme can be fitted the results of the many kinetic investigations which have been made. However, more evidence is needed to substantiate completely the unimolecular decomposition of some acids (e.g., malonic and β-keto-acids) in the zwitterionic form, and further kinetic studies of the S_E2 mechanism are required before the details can be clarified.

Unimolecular Mechanism (S_E1).—Three mechanisms are possible to account for the first-order kinetics of the decarboxylation of a carboxylic acid :

(1) Homolytic fission :
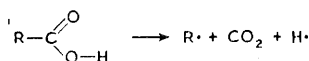
(2) Heterolytic fission :
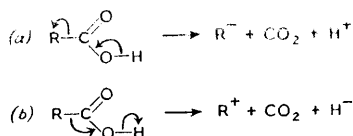
No evidence is available to support the postulation of free radicals in the thermal decarboxylation of carboxylic acids (contrast, however, photo-chemical [6] and electrolytic [7] decarboxylations, and the ketonic decarboxylation reaction [8]). Moreover, in all decarboxylations which show true first-order kinetics, the acids concerned, e.g., trichloroacetic and nitroacetic acid, contain electron-attracting substituents. The heterolytic fission of the carbon–carbon bond in an acid molecule by the mechanism 2(a) will be favoured by electron-attracting substituents. Decarboxylation by mechanism 2(b) would be hindered by these substituents. Moreover, the mechanisms 2(a) and 2(b) differ in that the intermediate products are a carbanion and a carbonium cation respectively. For the majority of acids which decompose unimolecularly neither intermediate ion has been detected. However, Muus [9] found that the rate of uptake of bromine by dibromomalonic

[5] Hughes and Ingold, J., 1935, 244.

[6] Burton, J. Amer. Chem. Soc., 1936, **58**, 692, 1645, 1655 ; 1938, **60**, 831.

[7] Fichter and Stenzl, Helv. Chim. Acta, 1939, **22**, 970 ; Fieser, Clapp, and Daudt, J. Amer. Chem. Soc., 1942, **64**, 2053.
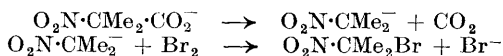
[8] See p. 145.   [9] J. Physical Chem., 1936, **40**, 121.

acid during decarboxylation was the same as its rate of decarboxylation. He interpreted this result on the basis of an intermediate mesomeric anion :
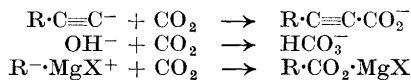

$$HO_2C \cdot CBr_2 \cdot CO_2^- \longrightarrow CO_2 + HO_2C \cdot CBr_2^- \xrightarrow{\ H^+\ } HO_2C \cdot CHBr_2$$
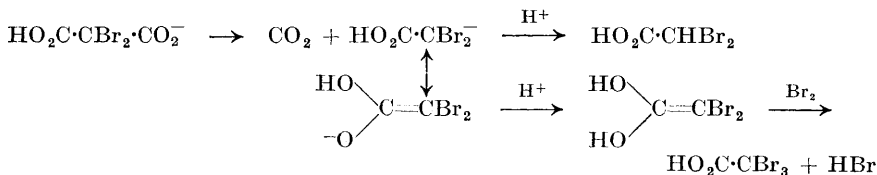
Similarly Pedersen [1] found that the rate of decarboxylation of α-nitro*iso*-butyric acid was equal to the rate of absorption of bromine during the decarboxylation, the product being bromonitro*iso*propane. Since the normal decarboxylation product, 2-nitropropane, is not brominated under the conditions used, Pedersen suggested that an intermediate anion reacted with the bromine :

$$O_2N \cdot CMe_2 \cdot CO_2^- \longrightarrow O_2N \cdot CMe_2^- + CO_2$$
$$O_2N \cdot CMe_2^- + Br_2 \longrightarrow O_2N \cdot CMe_2Br + Br^-$$

More direct evidence has been advanced by Hammick and his co-workers,[10] who have found that the intermediate products formed during decarboxylation of picolinic, quinaldic, *iso*quinaldic, and cinchoninic acids are capable of reacting with a variety of cationoid reagents (aldehydes, ketones, esters, quinoline, and aromatic nitro-compounds). An intermediate anion would react in this way :
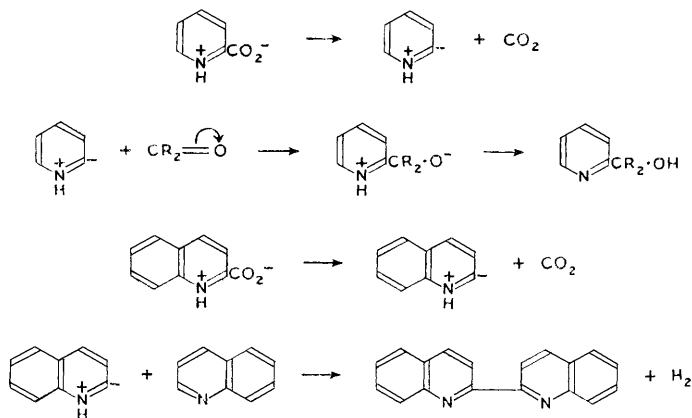

It is interesting that carboxylation as usually carried out in the laboratory is an ionic process, which involves the attachment of carbon dioxide to a negative ion, *e.g.* :

$$R \cdot C \equiv C^- + CO_2 \longrightarrow R \cdot C \equiv C \cdot CO_2^-$$
$$OH^- + CO_2 \longrightarrow HCO_3^-$$
$$R^- \cdot MgX^+ + CO_2 \longrightarrow R \cdot CO_2 \cdot MgX$$

[10] Dyson and Hammick, *J.*, 1937, 1724 ; Ashworth, Daffern, and Hammick, *J.*, 1939, 809 ; Brown, Hammick, and Thewlis, *Nature*, 1948, **162**, 73 ; Brown and Hammick, *J.*, 1949, 173 ; Brown, *J.*, 1949, 2577.

The reverse process may well be similar ; in fact under suitable conditions of temperature and concentration of carbon dioxide this type of reaction may be reversible :

$$R \cdot C \equiv C \cdot CO_2^- \quad \rightleftharpoons \quad R \cdot C \equiv C^- + CO_2$$
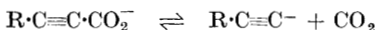
On the other hand no evidence has been advanced for the occurrence of an intermediate carbonium cation as required by the mechanism $2(b)$. The evidence for the heterolytic fission $2(a)$ is thus very strong.

However, the position of the proton at the moment of decarboxylation remains to be determined, and it is in the solution of this problem that kinetic investigations have proved invaluable. Three positions of the proton are possible :

(1) Attachment to the carboxyl-oxygen atom (decarboxylation of the acid molecule) as $2(a)$.

(2) Attachment to the solvent (decarboxylation of the acid anion) :
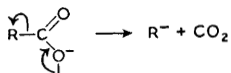
(3) Attachment to R (decarboxylation of a zwitterion) :
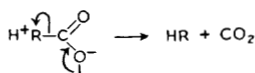
No unambiguous evidence has been recorded to indicate the decomposition of an ordinary acid molecule by a unimolecular mechanism. However, despite the empirical rule derived from the experimental results that the carboxyl group is usually in the anionic form $\cdot CO_2^-$ before decarboxylation,[2] there appears to be no theoretical reason why the fission of the carbon–carbon bond should not be simultaneous with the removal of a proton by a solvent molecule :
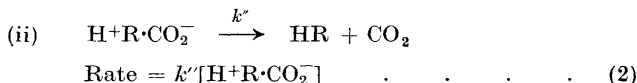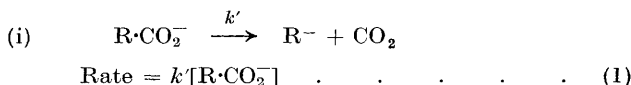

or, indeed, why the removal of the proton should not occur after the fission :
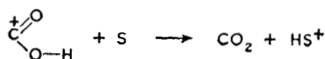
Acids which are decarboxylated by these mechanisms (malonic acid may be an example) may yet be discovered, despite the fact that the activation energy for the fission of the carbon–carbon bond is decreased by prior formation of the anion. Indeed, there is some doubt whether malonic acids and

β-keto-acids decompose as zwitterions or as hydrogen-bonded forms of the free acids.   This point is discussed later.

The results obtained from measurements of rates of decarboxylation indicate that some acids are decarboxylated unimolecularly as the anions only, others decompose only as zwitterions, and some show simultaneous decomposition of both ions.   Considering the two reactions :

$$(i) \qquad R \cdot CO_2^- \xrightarrow{k'} R^- + CO_2$$

$$\text{Rate} = k'[R \cdot CO_2^-] \qquad . \qquad . \qquad . \qquad . \qquad . \qquad (1)$$

$$(ii) \qquad H^+ R \cdot CO_2^- \xrightarrow{k''} HR + CO_2$$

$$\text{Rate} = k''[H^+ R \cdot CO_2^-] \qquad . \qquad . \qquad . \qquad . \qquad (2)$$

we may expect that the type of decomposition observed will be determined by the molecular structure of the acid concerned.

Some acids (*e.g.*, the trihalogenoacetic acids) cannot form zwitterions, but the negative substituents in R reduce the activation energy for the heterolytic fission of the carbon–carbon bond sufficiently to enable decarboxylation to occur at observable temperatures (compare acetic acid which does not lose carbon dioxide at 100° in water with trichloroacetic acid which is easily decarboxylated under these conditions).   The kinetic work of Verhoek and his colleagues [11, 12, 13] and of Johnson and Moelwyn-Hughes [14] has proved that trifluoro-, trichloro-, and tribromo-acetic acids decompose as the anions :

$$X_3 C \cdot CO_2^- \longrightarrow X_3 C^- + CO_2$$

The main points of the evidence are :

(1) These acids are almost completely ionised in water.

(2) The activation energies for the decarboxylation of the acids and of their sodium salts [15] in water are identical.

(3) The decarboxylation is approximately 10^7 times slower in the non-ionising solvent toluene than in water.

(4) In non-aqueous solvents (*e.g.*, ethyl alcohol) in which the acids are only slightly ionised, the rate is proportional to the concentration of the anion produced by added bases :

$$Cl_3 C \cdot CO_2 H + B \rightleftharpoons Cl_3 C \cdot CO_2^- + BH^+$$
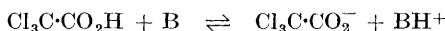
Measurements of the rate of decarboxylation of trichloroacetic acid in aqueous formamide [12] indicate that the trichloroacetate ion is solvated with water molecules before its decarboxylation.   Trifluoroacetic acid decomposes as the anion,[13] but it is much more stable than trichloro- or tribromo-acetic acid (see Table I).   This effect of the trifluoromethyl group in strengthening the adjacent carbon–carbon bond against heterolytic fission is in agreement

[11] Verhoek, *J. Amer. Chem. Soc.*, 1934, **56**, 571 ; 1945, **67**, 1062 ; Hall and Verhoek, *ibid.*, 1947, **69**, 613.   [12] Cochran and Verhoek, *ibid.*, p. 2987.
[13] Auerbach, Verhoek, and Henne, *ibid.*, 1950, **72**, 299.
[14] *Proc. Roy. Soc.*, 1940, *A*, **175**, 118.   [15] Fairclough, *J.*, 1938, 1186.
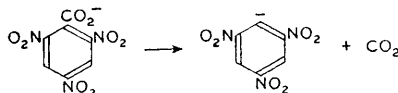
TABLE I

Activation energies for decarboxylation of trihalogenoacetic acids

| Acid.	Solvent.	E (cals.).	Ref.
$F_3C \cdot CO_2H$	Ethylene glycol	42,000	13
$Cl_3C \cdot CO_2H$	Ethylene glycol	31,600	13
$Cl_3C \cdot CO_2H$	Ethyl alcohol	31,000	11
$Cl_3C \cdot CO_2H$	Water	36,300	11, 14
$Br_3C \cdot CO_2H$	Water	32,950	14

with its general behaviour in other compounds.[16] Muus [17] investigated the rate of decarboxylation of dibromomalonic acid in aqueous solutions of varying hydrogen-ion concentration, and found that the rate of decarboxylation was proportional to the amount of primary ion present :

$$HO_2C \cdot CBr_2 \cdot CO_2^- \longrightarrow HO_2C \cdot CBr_2^- + CO_2$$
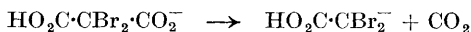
The undissociated acid and the bivalent anion are stable. Similarly Verhoek,[18] by studying the rate of decomposition of 2 : 4 : 6-trinitrobenzoic acid in alcohol, where it behaves as a weak acid, proved that it is decarboxylated only in the anionic form :

The aliphatic α-nitro-acids were studied by Pedersen,[1, 19] who found that the univalent nitroacetate ion decomposes unimolecularly, whereas the undissociated acid and the bivalent ion, $^-O_2N{=}CH \cdot CO_2^-$, are stable. There are three possibilities for a univalent nitroacetate ion :
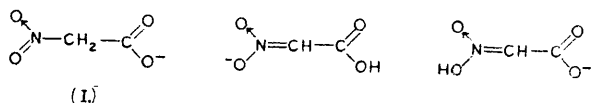
Since α-nitro*iso*butyric acid (k, 0·0448 min.$^{-1}$ in water at 17·84°) decomposes at a similar rate to nitroacetic acid (k, 0·0246 in water at 17·84°), Pedersen concluded that (I) is the ion which loses carbon dioxide because α-nitro*iso*butyric acid is capable of forming only one univalent ion, *viz.*, $O_2N \cdot CMe_2 \cdot CO_2^-$, the analogue of (I). Pedersen also found that the rate of decarboxylation was equal to the rate of reaction of an intermediate with bromine, and hence proposed the following mechanism :
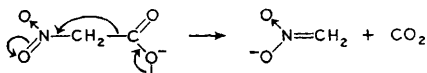
[16] Smith, *Ann. Reports*, 1947, **44**, 86.   [17] *J. Physical Chem.*, 1935, **39**, 343.
[18] *J. Amer. Chem. Soc.*, 1939, **61**, 186 ; Trivich and Verhoek, *ibid.*, 1943, **65**, 1919.
[19] *Trans. Faraday Soc.*, 1927, **23**, 316 ; *Acta Chem. Scand.*, 1947, **1**, 437.

Phenylpropiolic acid also decomposes as its anion.   Fairclough [15] measured the rate of decarboxylation of the sodium salt in water at various temperatures.   It has not been determined whether the undissociated acid is also unstable under the same conditions.

On general electronic grounds it can be predicted that the activation energy for decarboxylation of a zwitterion will be less than that for the corresponding acid anion.   Hence k'' will usually be greater than k' [in equations (1) and (2)].   Moreover, the structure of the anion may not be favourable for its decarboxylation, yet the formation of a zwitterion may sufficiently reduce the activation energy for decomposition to be observed, even though the zwitterion concentration is very small.   The heterocyclic α-imino-acids, picolinic, quinaldic, and *iso*quinaldic acids, probably decompose only in the form of their zwitterions :


(II.)   (III.)
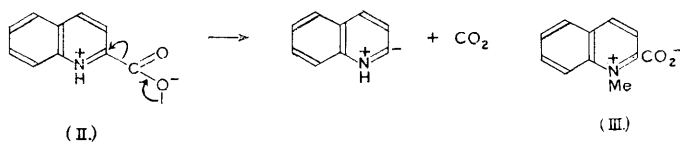
Brown and Hammick's kinetic results [2] show that the anion of quinaldic acid is stable under conditions which decompose the free acid.   Since the methylbetaine of the acid (III) decomposes very easily it is concluded that the analogous zwitterion (II), and not the undissociated acid, undergoes decarboxylation.   Recently Doering and Pasternak [3] have suggested that α-methyl-α-2-pyridylbutyric acid decomposes as its zwitterion :
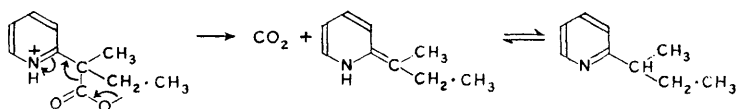
since it is stable in strongly acidic or basic solution, and racemisation occurs during decarboxylation of the active acid in neutral solution.   4-Pyridylacetic acid also decomposes in neutral aqueous solution, and these authors suggest a similar decomposition of its zwitterion :

It seems likely that thiazole-2-carboxylic acid and 2-thiazolylacetic acid, which are decarboxylated by a S_E1 mechanism,[20] decompose through their zwitterions :
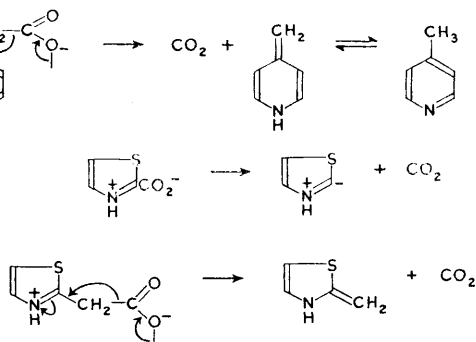
[20] Schenkel and Schenkel-Rudin, *Helv. Chim. Acta*, 1948, **31**, 924 ; Schenkel and Mory, *ibid.*, 1950, **33**, 16.

TABLE II

Activation energies for decarboxylation of thiazole acids

Acid.	Solvent.	E (cals.).
Thiazole-2-carboxylic . . .	Quinoline	20,200
Thiazole-5-carboxylic . . .	Quinoline	38,600
2-Thiazolylacetic	Quinoline	7,630
4-Thiazolylacetic	5 : 6-Benzoquinoline	29,200
5-Thiazolylacetic	5 : 6-Benzoquinoline	24,000

Thiazole-4- and -5-carboxylic and 4- and 5-thiazolylacetic acids are decarb-oxylated less rapidly than the 2-isomers, and probably as the anions. A comparison of activation energies confirms this view, since those for thiazole-2-carboxylic and the analogous acetic acid are significantly smaller than the others (see Table II).

It is to be expected that for some acids $k'[\mathrm{R \cdot CO_2^-}]$ and $k''[\mathrm{H^+ R \cdot CO_2^-}]$ [of equations (1) and (2)] will have comparable values, and that decarboxylation of both the anion and the zwitterion will then occur. β-Keto-acids can be placed in this class. The relative rates of decomposition of the anions and of the undissociated acids for several β-keto-acids have been

TABLE III

Relative rates of decomposition of β-keto-acids and their anions in water

Acid.	Relative k.		Temp.	Ref.
	Acid.	Anion.		
Acetoacetic	53	1	$37°$	21
$\alpha\alpha$-Dimethylacetoacetic	180	1	18	22
Camphor-3-carboxylic . . .	34	1	98	23
Dihydroxymaleic	1	40	20	24
Acetonedicarboxylic	1	2·5	50	25
Malonic	10	1	90	26

measured (see Table III). Since $\alpha\alpha$-dimethylacetoacetic acid, which cannot exist in an enolic form, is readily decarboxylated, Pedersen [1] concluded that the keto-forms of β-keto-acids are unstable, and he suggested that undis-sociated β-keto-acids decompose as zwitterions :

$$\mathrm{CH_3-C-CH_2-C} \begin{matrix} O \\ O^- \end{matrix} \longrightarrow \mathrm{CH_3-C=CH_2} + \mathrm{CO_2}$$
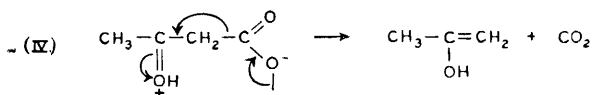
[21] Widmark, *Acta Med. Scand.*, 1920, **53**, 393.

[22] Pedersen, *J. Amer. Chem. Soc.*, 1929, **51**, 2098.

[23] Bredig and Balcom, *Ber.*, 1908, **41**, 740.

[24] Franke and Brathuhn, *Annalen*, 1931, **487**, 1.

[25] Calculated by Franke and Brathuhn, ref. 24, from the results of Wiig, ref. 29.
Cf. Pedersen, ref. 22.   [26] Hall, *J. Amer. Chem. Soc.*, 1949, **71**, 2691.

It is found that the rate of decarboxylation of $\alpha\alpha$-dimethylacetoacetic acid is the same as the rate of bromination of an intermediate, which is probably the enolic form of methyl *iso*propyl ketone.   The decarboxylation of β-keto-acids is only slightly affected by secondary or tertiary amines, but is significantly catalysed by primary amines (see Table IV ;   Pedersen [27] states that Ljunggren [28] has obtained similar results for acetoacetic acid).   It is noteworthy that the exact equation which governs the catalysis of the decarboxylation of β-keto-acids by primary amines is :

$$\text{Rate} = k_0[\text{acid}] + k_1[\text{B}][\text{acid}] + k_2[\text{BH}^+][\text{acid}] + k_3[\text{B}]^2[\text{acid}]$$

where k_0, k_1, k_2, and k_3 are constants and B and BH^+ are the base and

TABLE IV

Amine catalysis of decarboxylation of β-keto-acids

Acid.	Solvent.	Temp.	Amine.	$10^4 k$.
Acetonedicarboxylic [29] .	Water	50°	None	185
		50	Quinoline	220
		50	Methylaniline	300
		50	Aniline	860
Acetonedicarboxylic [29] .	*iso*Propyl alcohol	50	None	206
		50	Acetylphenyl-hydrazine	216
		50	Pyrrole	220
		50	Dimethylaniline	300
		50	α-Naphthylamine	890
		50	Aniline	1740
		50	*p*-Toluidine	3750
		30	Phenylhydrazine	6560
Dihydroxymaleic [24] . .	Water	12	None	8·9
		12	Dimethylaniline	9·6
		12	Ethylaniline	11·0
		12	Aniline	34·7

its conjugate acid.[27, 30]   The determination of the significance of this equation awaits further elucidation of the reaction mechanism.

Westheimer and Jones [30] found that the rate of decarboxylation of $\alpha\alpha$-dimethylacetoacetic acid is virtually independent of the dielectric constant of the solvent.   Since a reaction which takes place by way of a polar intermediate should proceed more rapidly in solvents of high dielectric constant, Westheimer and Jones conclude that Pedersen's zwitterion (IV) cannot be an intermediate.   Instead, these authors suggest that it is the hydrogen-bonded form of the acid (V) which is decarboxylated.   These two views must be almost identical, since the zwitterion (IV) is very likely a

[27] *J Amer. Chem. Soc.*, 1938, **60,** 595.   [28] Dissertation, Lund, 1925.
[29] Wiig, *J. Physical Chem.*, 1928, **32,** 961.
[30] Westheimer and Jones, *J. Amer. Chem. Soc.*, 1941, **63,** 3283.
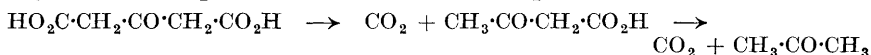
(V.)   (VI.)
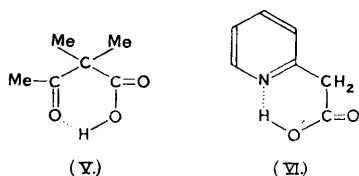
contributor to the hydrogen-bonded structure (V), because the nuclear configurations involved are identical. Similarly, the decarboxylation of 2-pyridylacetic acid may occur through a hydrogen-bonded form (VI). However, this idea cannot be extended to 4-pyridylacetic acid.[3]

Wiig [29, 31] carried out kinetic measurements on the decarboxylation of acetonedicarboxylic acid. However, his conclusions about the mechanism of the reaction are not valid.[22] That the univalent ion decomposes more rapidly than the undissociated acid is indicated by Wiig's results, which may be summarised as follows :

(1) The rate reaches a constant minimal value with increasing concentration of hydrogen ion in aqueous solution. The acid is fairly strong (K_a, 0.79×10^{-3}), and hence the effect of hydrogen ion is due to a repression of ionisation at high concentrations. A constant rate is thus attained when all the acid is in the undissociated form. The calculation of the relative rates of decarboxylation of the acid and its anion (Table III) was made by using this idea.

(2) The decarboxylation of the acid shows marked catalysis by primary amines (Table IV). However, there is also a noticeable increase of rate on addition of secondary and tertiary amines. This is to be expected if the anion is less stable than the free acid, since the addition of a base will increase the anion concentration at the expense of that of the acid.

The kinetics of the decarboxylation of dihydroxymaleic acid have been thoroughly investigated.[24, 32] Franke and Brathuhn's results [24] indicate that the acid decomposes very easily as its univalent ion, $HO_2C\cdot C(OH){:}C(OH)\cdot CO_2^-$, and behaves as a β-keto-acid (e.g., the decarboxylation is catalysed by the addition of primary amines, Table IV), and the suggestion is made that the decomposition takes place through the keto-form, presumably $^-O_2C\cdot CH(OH)\cdot CO\cdot CO_2H$. The undissociated acid is decarboxylated much less readily than the univalent ion (Table III). Though the results obtained for the two dicarboxylic acids, acetonedicarboxylic and dihydroxymaleic acid, establish that they show the same characteristics as the monobasic β-keto-acids, the detailed mechanisms have not been determined. For example, it is not known whether the decarboxylation takes place in two consecutive steps :

$$HO_2C\cdot CH_2\cdot CO\cdot CH_2\cdot CO_2H \quad \longrightarrow \quad CO_2 + CH_3\cdot CO\cdot CH_2\cdot CO_2H \quad \longrightarrow$$
$$CO_2 + CH_3\cdot CO\cdot CH_3$$

or by a simultaneous expulsion of two molecules of carbon dioxide :

$$HO_2C\cdot CH_2\cdot CO\cdot CH_2\cdot CO_2H \quad \longrightarrow \quad CH_3\cdot CO\cdot CH_3 + 2CO_2$$
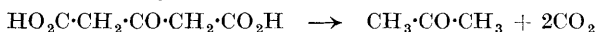
[31] J. Physical Chem., 1930, 34, 596.
[32] Locke, J. Amer. Chem. Soc., 1924, 46, 1246.

Recent investigations [26] of the effect of pH on the rate of decarboxylation of malonic acid in aqueous solution have shown that the undissociated acid decomposes about ten times as quickly as the univalent ion, $HO_2C \cdot CH_2CO_2^-$, and that the bivalent ion, $^-O_2C \cdot CH_2 \cdot CO_2^-$, does not decompose.   Malonic acid is rather similar in structure to a β-keto-acid, and hence it seems likely that the decarboxylation of the undissociated acid takes place through a similar hydrogen-bonded or zwitterion form, yielding an enolic form of acetic acid which subsequently rearranges : [33]
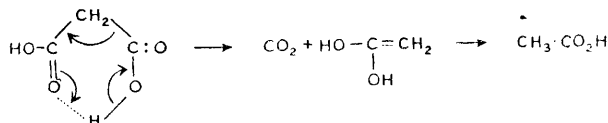

Many studies of the decarboxylation of substituted malonic acids have been made,[34] but since they all refer to simultaneous decompositions of the anion and of the acid, no analysis to obtain a reliable correlation between structure and rate of decarboxylation can be made at present.   Nevertheless, it is of interest to note than the anion, $HO_2C \cdot CH_2 \cdot CO_2^-$, of malonic acid is decarb-oxylated about ten times more slowly than the acid form, whereas for dibromomalonic acid the analogous anion, $HO_2C \cdot CBr_2 \cdot CO_2^-$, is readily de-carboxylated but the free acid is stable.   The substitution by bromine atoms has thus reduced the stability of the anion of dibromomalonic acid so much that its decarboxylation completely masks that of a zwitterion or hydrogen-bonded form, causing it to resemble the trihalogenoacetic acids in its com-pletely anionic mode of decarboxylation.   A similar, but smaller, effect is to be expected for other substituted malonic acids when the analysis can be made.   In fact the proportion of anionic and zwitterionic or acidic decom-position should be closely related to the type and amount of substitution.

Oxalic acid [35] decomposes in dioxan according to the equation :

$$HO_2C \cdot CO_2H \quad \longrightarrow \quad CO_2 + H \cdot CO_2H$$
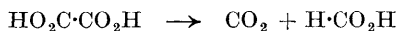
The reaction obeys a first-order kinetic equation.   In water the kinetics are similar, but subsequent decomposition of formic acid occurs :

$$H \cdot CO_2H \quad \longrightarrow \quad H_2O + CO_2$$
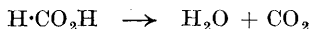
the amount of this depending on temperature.   Addition of mineral acid causes a slight increase in the reaction velocity, and a secondary salt effect has been demonstrated, indicating that undissociated oxalic acid is the chief molecular species which is decarboxylated.   The disodium salt does not decompose in aqueous solution at temperatures at which the free acid is unstable, and hence the bivalent ion, $^-O_2C \cdot CO_2^-$, is stable.   Dinglinger and Schroer [35] suggest that the mechanism of decomposition involves the move-ment of a proton from one carboxyl to the other (forming a zwitterion),

[33] King, *J. Amer. Chem. Soc.*, 1947, **69**, 2738.
[34] Bernoulli and Wege, *Helv. Chim. Acta*, 1919, **2**, 511 ; Bernoulli and Jakubowicz, *ibid.*, 1921, **4**, 1018 ; Knaus, *Tables Annuelles*, 1923—24, **6**, 1031.
[35] *Z. physikal. Chem.*, 1937, **179**, A, 401 ; 1938, **181**, A, 375.

followed by decarboxylation to yield an "enol" of formic acid, which subsequently rearranges :
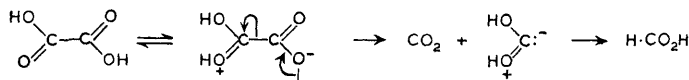

Further work on this dibasic acid is required, as nothing is known of the stability of its univalent anion, $HO_2C \cdot CO_2^-$.

Recently Arnold, Elmer, and Dodson [36] have suggested that the decarboxylation of $\alpha\beta$-unsaturated acids occurs through the $\beta\gamma$-isomers, which are known to be decarboxylated easily, yielding an olefin with a terminal double bond. The electronic mechanism proposed by these authors, and earlier by Woodward and Kornfeld, [37] is analogous to those suggested for β-keto-acids :
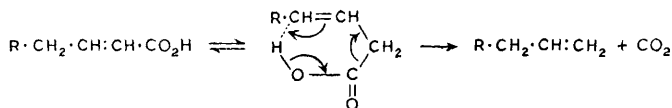
Preliminary rate studies on the decarboxylation of $\alpha\beta$-unsaturated acids which readily isomerise indicate first-order kinetics as required by the above mechanism.

Bimolecular Mechanism (S_E2).—In 1948 Schenkel and Schenkel-Rudin [4] suggested that some organic acids are decarboxylated by a bimolecular electrophilic substitution mechanism :
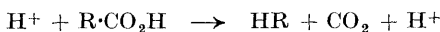
$$H^+ + R \cdot CO_2H \longrightarrow HR + CO_2 + H^+$$

in which the rate is determined by the attraction of a proton by the carboxylic acid. The kinetics are then governed by the equation :

$$\text{Rate} = k[H^+][R \cdot CO_2H] \qquad . \qquad . \qquad . \qquad . \quad (3)$$

Two possibilities arise. The proton may attack the undissociated acid molecule yielding a kinetic equation of the type shown above. On the other hand, the reaction could take place between a proton and the acid anion :

$$H^+ + R \cdot CO_2^- \longrightarrow HR + CO_2$$
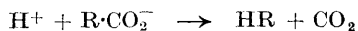
when the kinetic equation would be

$$\text{Rate} = k[H^+][R \cdot CO_2^-] \qquad . \qquad . \qquad . \qquad . \quad (4)$$

For either mechanism the rate is dependent on the attraction between the α-carbon atom of the acid and a proton. Since the formation of the anion will increase the electron density on the α-carbon atom, it may be expected that the second mechanism written above will require less activation energy than the first. However, it is possible that both mechanisms will occur, singly or simultaneously, and an analysis will have to be made for each type

[36] J. Amer. Chem. Soc., 1950, **72**, 4359.   [37] Ibid., 1948, **70**, 2508.

of acid studied.   The theory is yet in its infancy, so that, with one exception, it has not been determined whether the anion or the undissociated acid takes part.

The experiments performed have been directed towards a proof of the existence of the mechanism.   Two general methods of attack have been made, both being dependent on studies of reaction rates.   The ideal method would be to determine the exact relation between the rate of decarboxylation and the hydrogen-ion concentration, *i.e.*, to establish either of the equations (3) and (4).   So far this has only been achieved for one acid, *viz.*, mesitoic acid.[38]   However, it has been possible to show for several acids that the rate of decarboxylation increases qualitatively with increase of hydrogen-ion concentration.   Schenkel and Schenkel-Rudin [4] gave anthracene-9-carboxylic acid (VII) as an example of an acid which is decarboxylated by the S_E2 mechanism.   As evidence they cited kinetic work [39] in which it was found that the decarboxylation occurred more readily in acidic solvents (sulphuric or dichloroacetic acid) than in basic solvents (7 : 8-benzoquinoline), in direct contrast to picolinic acid [40] which is decarboxylated by a S_E1 mechanism.   Also, they pointed out that the α-carbon atom in anthracene-9-carboxylic acid has a high electron density, which favours the attraction of a proton.   Despite the fact that this was the only example quoted by Schenkel and Schenkel-Rudin in support of their theory, and even though the evidence for this particular acid was weak, it was evident that their theory of a S_E2 mechanism was plausible, and it has served as a basis for further investigations.
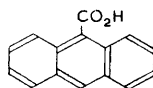
Another method of obtaining evidence for the S_E2 mechanism is to study the rates of reaction, under identical conditions, of a series of acids of the same electronic type.   This method was applied by Johnson and Heinz [41] to the decarboxylation of substituted cinnamic acids.   They found the values quoted in Table V for the rates of decarboxylation in a mixture

TABLE V

Cinnamic acids, $Ph \cdot CR' {:} CR'' \cdot CO_2H$

R'.	R''.	k (sec.$^{-1}$).
Ph	H	0·0046
CH$_3$	H	0·0022
CH$_3$·CH$_2$	H	0·00072
Ph	CH$_3$	0·00020

of water, acetic acid, and hydrogen bromide at 109°.   This order of rates can be reconciled with the electronic effects of the substituents, R' and R'',
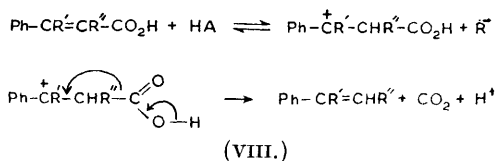
[38] Schubert, *J. Amer. Chem. Soc.*, 1949, **71**, 2639.
[39] Schenkel, *Helv. Chim. Acta*, 1946, **29**, 436.
[40] Schenkel and Klein, *ibid.*, 1945, **28**, 1211.
[41] *J. Amer. Chem. Soc.*, 1949, **71**, 2913.

on the basis of the following S_E2 mechanism, in which the first step is rate determining :

$$Ph-CR'\!\!=\!\!CR''\!-\!CO_2H + HA \; \rightleftharpoons \; Ph-\overset{+}{C}R'\!-\!CHR''\!-\!CO_2H + \overset{..}{A}\!\!\bar{\ }$$

$$Ph-\overset{+}{C}R'\!-\!CHR''\!-\!C\overset{O}{\underset{O-H}{\diagdown}} \longrightarrow Ph-CR'\!\!=\!\!CHR'' + CO_2 + H^+$$

(VIII.)

These authors assume the β-carbonium ion (VIII) to be an approximation to the transition state. Those substituents which increase its stability with reference to the reactants will thus decrease its energy level, and so reduce the activation energy of the reaction. Though the conditions under which the rates were measured did not allow the demonstration of a quantitative correlation between rates and hydrogen-ion concentration, there was definite evidence of a qualitative increase of rate with hydrogen-ion concentration. The decarboxylation of certain itaconic acids is acid-catalysed,[42] and can be regarded as occurring by a similar S_E2 mechanism :
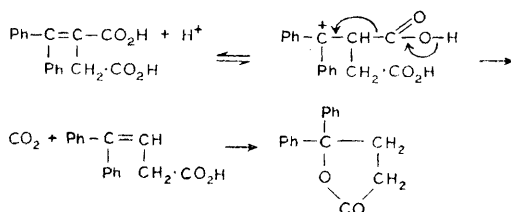
Schubert[38] investigated the decarboxylation of mesitoic acid in sulphuric acid, and demonstrated a proportionality between the pseudo-first-order constants and the concentration of the hydroxonium ion in aqueous acid containing 80—100% of sulphuric acid. The rate is therefore given by the equation :

$$\text{Rate} = k[H_3O^+][\text{acid}],$$

and hence the reaction must occur by a S_E2 mechanism of the following type :
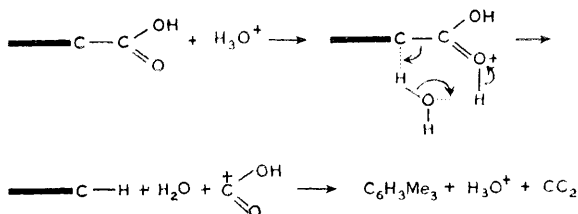

At present this is the only quantitative demonstration of the dependence of the rate of a decarboxylation on hydrogen-ion concentration, and hence

[42] Johnson, Petersen, and Scheider, *J. Amer. Chem. Soc.*, 1947, **69**, 74.

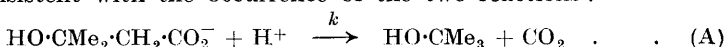must constitute the best available proof of the occurrence of the S_E2 mechanism.

Brown, Hammick, and Scholefield's kinetic investigations [43] of a series of hydroxybenzoic acids indicate that these acids, which have a high electron density on the α-carbon atom, are decarboxylated by a S_E2 mechanism. The rates of reaction under comparable conditions in resorcinol as solvent increased, and the activation energies decreased, in the order : benzoic, o-hydroxybenzoic, 2 : 4-dihydroxybenzoic, 2 : 4 : 6-trihydroxybenzoic, which is the order in which the substituents facilitate the approach of a proton to the anionoid α-carbon atom :
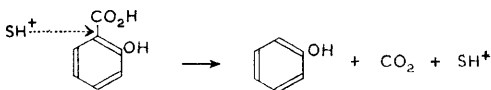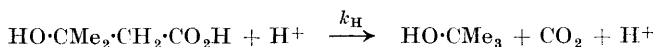

There is no reason why an acid of suitable structure should not simultaneously follow the two S_E2 equations (3) and (4) in its decarboxylation. Although the kinetic results are not very extensive and are complicated by the occurrence of salt effects, it seems probable that the decarboxylation of β-hydroxyisovaleric acid follows both reactions.[44] The observed first-order rate constants ($k_{obs.}$) at various hydrogen-ion concentrations in water are given by the equation :
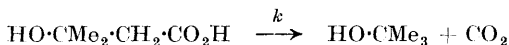
$$k_{obs.} = k + k_H[H^+]$$

which is consistent with the occurrence of the two reactions :

$$HO \cdot CMe_2 \cdot CH_2 \cdot CO_2^- + H^+ \quad \xrightarrow{k} \quad HO \cdot CMe_3 + CO_2 \quad . \quad . \quad (A)$$

and

$$HO \cdot CMe_2 \cdot CH_2 \cdot CO_2H + H^+ \quad \xrightarrow{k_H} \quad HO \cdot CMe_3 + CO_2 + H^+$$

However, it should be pointed out that (A) cannot be distinguished kinetically from an ordinary S_E1 decarboxylation of the free acid, i.e., from :

$$HO \cdot CMe_2 \cdot CH_2 \cdot CO_2H \quad \xrightarrow{k} \quad HO \cdot CMe_3 + CO_2$$

Consequently this may be an example of an acid which is decarboxylated by both mechanisms, S_E1 and S_E2, simultaneously.   Only further investigations can throw light on this problem.

The Ketonic Decarboxylation Reaction.—It has been known for a long time that by the action of heat on a mixture of sodium acetate and soda-lime, methane is produced by ordinary thermal decarboxylation of the acetate :

$$CH_3 \cdot CO_2^- \quad \rightarrow \quad CH_3^- + CO_2$$
$$CH_3^- + H^+ \quad \rightarrow \quad CH_4$$
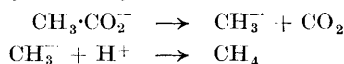
Also it is known that by distilling calcium acetate, acetone and calcium carbonate result :

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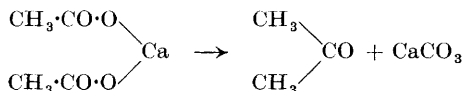
[43] *J.*, 1950, 778.   [44] Pressman and Lucas, *J. Amer. Chem. Soc.*, 1940, **62,** 2069.

The mechanism of this reaction, which involves the loss of carbon dioxide as calcium carbonate and the coupling together of the resulting fragments, has recently been investigated by Bell and Reed [45] who used the isotopic tracer method.   Barium acetate (IX) containing ^{13}C in the carbonyl group was heated with ordinary barium formate, and it was found that the residual barium carbonate retained the labelled carbon atoms, showing that the formation of acetaldehyde (which was proved not to contain the labelled carbon) occurs as follows :

(IX.)
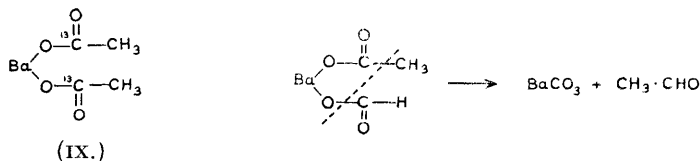
The authors suggest that the fission of the carbon–carbon bond of the acetate results in the formation of a free methyl radical, which is capable of combining with a formyl residue to yield acetaldehyde.   This mechanism which involves homolysis is consistent with the vigorous thermal conditions of the reaction.   The work of Miller, Cook, and Whitmore [46] on the varied minor products obtained in the ketonic decarboxylation reaction lends further support to a free-radical mechanism.

[45] *Nature*, 1950, **165**, 402.   [46] *J. Amer. Chem. Soc.*, 1950, **72**, 2732.