

141. *The Mechanism of Decarboxylation. Part IV. Kinetic Evidence that the Decarboxylation of Quinaldinic and isoQuinaldinic Acids takes Place through the Zwitterion Form.*

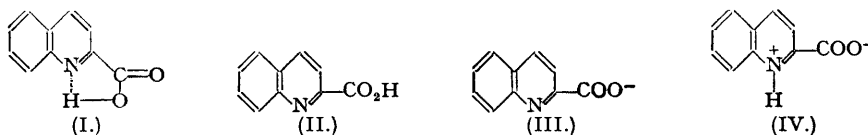
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The rates of decarboxylation of quinaldinic and isoquinaldinic acids, of sodium quinaldinate, and of the methyl betaine of quinaldinic acid have been determined in quinoline and other solvents. The kinetic data support the view that decarboxylation takes place through the zwitterion forms.

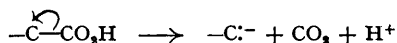
IN previous communications (Parts I, II, and III: Dyson and Hammick, *J.*, 1937, 1724; Ashworth, Daffern, and Hammick, *J.*, 1939, 809; Brown and Hammick, this vol., p. 173) evidence has been adduced in support of the view that when heterocyclic imino-acids of the

picolinic, quinaldinic, and *iso*quinaldinic type are decarboxylated, ion-radicals having cyanide ion-like structures $\left[\text{N}=\text{C} \right]^-$ are produced as intermediates. The question is now raised as to what is the actual molecular precursor of such anions.

The problem is to decide between (I), (II), (III), and (IV) as the actual species which loses carbon dioxide when quinaldinic acid decomposes in solution. The view expressed in earlier papers of this series was that it is the hydrogen-bonded form (I). A scale drawing indicates that



such hydrogen-bonding is unlikely to occur, since, though the nitrogen-oxygen distance is favourable (2.76 Å), the direction of the valencies in space is unfavourable. It is therefore concluded that the hydrogen-bonded form is unlikely to be the decarboxylating species. Evidence from the kinetics of decarboxylation of other acids shows that in almost every example the carboxyl part of the molecule is in the form of the anion, $-\text{COO}^-$, before decomposition (Pedersen, *Trans. Faraday Soc.*, 1927, **23**, 316; *J. Physical Chem.*, 1934, **38**, 559; Moelwyn-Hughes and Johnson, *Proc. Roy. Soc.*, 1940 **175**, A, 118; Trivich and Verhoek, *J. Amer. Chem. Soc.*, 1943, **65**, 1919; Verhoek, *ibid.*, 1939, **61**, 186; Muus, *J. Physical Chem.*, 1935, **39**, 343). The only exceptions appear to be the dibasic acids, oxalic and malonic (Bernouilli and Wege, *Helv. Chim. Acta*, 1919, **2**, 511; Fairclough, *J.*, 1938, 1186; Dinglinger and Schöer, *Z. physikal. Chem.*, 1937, **179**, A, 401; 1938, **181**, A, 375). This result is to be expected on general grounds, since the evidence of Part III of this series shows that the chief process in the decarboxylation of quinaldinic acid in solution is the heterolysis of the carbon-carbon bond :



which will be aided by a negative charge on the carboxyl group (cf. Schenkel and Schenkel-Rudin, *Helv. Chim. Acta*, 1948, **31**, 514). Electron-attracting substituents on the α -carbon atom will also aid this process, so that the ease of decarboxylation should increase in the order, free acid (II) < acid anion (III) < zwitterion (IV). Our experimental data for the rates of decarboxylation of quinaldinic and *iso*quinaldinic acids, of sodium quinaldinate, and of the methyl betaine of quinaldinic acid in quinoline, ethylene glycol, and acetophenone substantiate these theoretical predictions.

EXPERIMENTAL.

The rates of decarboxylation were followed where possible by determining the amount of acid remaining in solution after various time intervals, by precipitation and weighing as the insoluble copper salt (Rây and Bose, *Z. anal. Chem.*, 1933, **95**, 400). This method was found to be capable of application to *iso*quinaldinic acid as well as to its isomer.

Materials.—Quinaldinic acid was recrystallised once from toluene and twice from benzene; colourless needles, m. p. 156–157°. The acid was dried at 100° before use. Its hydrochloride, prepared by crystallising the acid from concentrated hydrochloric acid, separated from alcohol as colourless needles, m. p. 195° (decomp.). Sodium quinaldinate was twice recrystallised from water and dried at 100°. The methyl betaine of quinaldinic acid (Mills and Hamer, *J.*, 1922, **121**, 2008) separated from alcohol as almost colourless prisms, m. p. 142–145° (decomp.). *iso*Quinaldinic acid was twice recrystallised from benzene and dried in a vacuum at room temperature; colourless plates, m. p. 161°.

Commercial quinoline was distilled in steam, and then distilled at atmospheric pressure and finally under reduced pressure; b. p. 142°/50 mm. Quinoline hydrochloride crystallised from an anhydrous mixture of alcohol and ether in the form of colourless hygroscopic needles, which were kept over phosphoric oxide in a vacuum. Acetophenone was purified by freezing, followed by distillation, b. p. 155°/255 mm. Ethylene glycol was distilled, b. p. 113°/29 mm.

Apparatus.—Temperature control was obtained by immersing the reaction vessels (glass or silica test-tubes) in a lagged vapour bath containing a suitable liquid boiling under reflux at the prevailing atmospheric pressure. Temperatures constant to $\pm 0.1^\circ$ could be maintained for at least 2 hours. The bath liquids (water, toluene, pyridine, acetic acid, *s*-tetrachloroethane, bromobenzene, cyclohexanol, *p*-dichlorobenzene, limonene, and aniline) were distilled at atmospheric pressure, and fractions boiling over a range less than 1° at the temperatures given were used to construct the Arrhenius plots.

The reaction tubes, which were open to the air, each contained 5.00 ml. of a solution of the acid. The tubes were removed from the vapour bath at suitable time intervals, and the decarboxylation stopped by cooling to room temperature.

Method of Analysis.—The acid solutions (of normality $N/10$ to $N/2$ in quinoline or acetophenone) were washed out of the reaction tubes with ether, extracted with two lots of $N/5$ -sodium hydroxide

acidified with $N/5$ -sulphuric acid, and precipitated hot with $m/10$ -copper sulphate. The precipitates were collected on weighed Gooch crucibles, washed with hot water, and dried at 100° to constant weight.

Results.—The kinetic data obtained fitted first-order equations of the type $\log_{10}(a-x) = \log_{10}a - 0.434kt$, where a is the initial weight of copper salt and $(a-x)$ is the weight of salt after time t (secs.). These equations, and hence the rate constants k , were obtained by the method of least squares. The values of $\log_{10}(a-x)$ calculated from these equations were compared with those observed. The maximum deviation was 2.5%. The data from two typical runs are collected in Table I. A plot of

TABLE I.

Decarboxylation of quinaldinic acid in quinoline (at 160.7°).

(I) In silica reaction tubes.

t (secs.)	0	1140	2640	4380
$-\log_{10}(a-x)$ (obs.)	0.851	0.952	1.075	1.217
$-\log_{10}(a-x)$ (calc.)	0.855	0.949	1.074	1.218

$$k = 1.90 \times 10^{-4} \text{ (sec.}^{-1}\text{)}.$$

(II) In glass reaction tubes.

t (secs.)	0	615	1710	2820	4395
$-\log_{10}(a-x)$ (obs.)	0.941	1.010	1.074	1.166	1.306
$-\log_{10}(a-x)$ (calc.)	0.944	0.994	1.083	1.173	1.301

$$k = 1.87 \times 10^{-4}.$$

TABLE II.

Effect of temperature.

Quinaldinic acid in quinoline.

T , $^\circ\text{K}$.	429.2	433.9	451.2	457.6
10^4k	1.25	1.89	9.95	16.5

Quinaldinic acid in acetophenone.

T , $^\circ\text{K}$.	419.8	429.7	434.4	446.6
10^4k	1.31	3.32	5.95	18.7

*iso*Quinaldinic acid in acetophenone.*

T , $^\circ\text{K}$.	373.4	383.8	388.7	391.5
10^4k	1.73	5.51	9.89	13.1

* From this reaction phenyl-1-isoquinolylmethylcarbinol was isolated in 34% yield; colourless prisms from alcohol, m. p. $102-103^\circ$ (Found: C, 81.8; H, 6.1; N, 5.4. Calc. for $C_{17}H_{15}ON$: C, 81.9; H, 6.0; N, 5.6%). Padbury and Lindwall (*J. Amer. Chem. Soc.*, 1945, **67**, 1268) record m. p. $93-95^\circ$.

TABLE III.

Acid.	Solvent.	E (cals.) (± 1000).	$\log_{10} PZ$ (from k in sec. $^{-1}$).
Picolinic	Quinoline	36,600	13.72
Quinaldinic	Quinoline	36,100	14.49
Quinaldinic	Acetophenone	37,400	15.58
<i>iso</i> Quinaldinic	Acetophenone	32,800	15.45

TABLE IV.

Test for heterogeneous catalysis.

Quinaldinic acid in quinoline. Temperature 160.7° .

Nature of vessel.	Added solid.	10^4k .	Nature of vessel.	Added solid.	10^4k .
Glass	None	1.87	Silica	Silica powder	1.99
Silica	None	1.90	Silica	"AnalaR" KCl	1.84
Silica	Glass wool	1.85			

TABLE V.

Effect of hydrogen chloride on the decarboxylation of quinaldinic acid in quinoline at 160.7° .

	Moles of HCl per mole of acid.	10^4k .
Quinaldinic acid only	0	1.87
Quinaldinic acid hydrochloride	1	1.90
Quinaldinic acid plus quinoline hydrochloride	7.8	2.23
		2.26
		3.18

It will be observed that the rate does not increase linearly with $[\text{HCl}]$, a definite falling off being evident.

$1/T$ and $\log k$ (from Table II, together with the data of Schenkel and Klein, *Helv. Chim. Acta*, 1945, **28**, 1211, for picolinic acid in quinoline) gives the results collected in Table III.

Decarboxylation of the Methyl Betaine of Quinaldinic Acid in Quinoline at 145.8° (Rough Manometric Technique).—A solution of the betaine in quinoline (ca. 0.2 g. in 5 ml.) was placed in a reaction tube, which was immersed in the vapour bath and attached to a mercury manometer. The rate of carbon dioxide evolution was followed by reading the pressure at suitable time intervals. No correction for the solubility of carbon dioxide in quinoline was made, and the reaction was so fast that only the last few units % could be followed with much accuracy. The rate constant obtained is therefore only a rough minimal value:

Average k (mean of two) = 33×10^{-4} (sec.⁻¹).

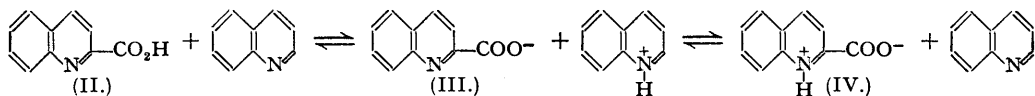
k by extrapolation for quinaldinic acid at 145.8° = 0.58×10^{-4} .

DISCUSSION.

In Table III the E and PZ values (of the equation $k = PZ \cdot e^{-E/RT}$) found for quinaldinic and isoquinaldinic acids are compared with those of Schenkel and Klein (*loc. cit.*) for picolinic acid (in their paper the quoted E values are in error by a multiplying factor of 2). Picolinic and quinaldinic acids have, within the experimental error (± 1000 cal.), the same activation energy, which is unaffected by change of solvent. The activation energy for isoquinaldinic acid in acetophenone is less than that for quinaldinic acid in the same solvent by 4600 cal., which is outside the experimental error. This result is to be expected if heterolysis of the carbon-carbon bond to yield carbon dioxide and a negative ion is the rate-determining step, since the carboxyl group in isoquinaldinic acid is between *two* electron-accepting groups—the nitrogen atom and the benzene ring—both of which will facilitate decarboxylation.

The evidence of Table IV shows that the decarboxylation of quinaldinic acid in quinoline is a purely homogeneous reaction, the rate being independent of the nature of the vessel and of the presence of solids, both polar and non-polar.

The state of ionisation of quinaldinic acid in quinoline is not known quantitatively, since conductivity measurements have not been made, and for our purpose the conductivity would have to be known at the decarboxylation temperatures of 150—180°. However, the state of the acid can be predicted qualitatively with a fair degree of certainty. Since the nitrogen atoms in quinoline and in quinaldinic acid must be of roughly equal basicities, the following equilibria will obtain:

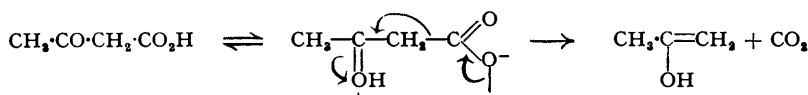
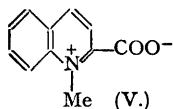


The addition of hydrogen chloride to the system (as the hydrochloride either of the acid or of quinoline) will therefore increase the concentration of species (II) (free acid) and (IV) (zwitterion), and decrease that of the quinaldinate ion (III). Table V shows that addition increases the reaction rate, one equivalent of hydrogen chloride increasing the rate constant by about 24%. Similarly, the addition of 7.8 equivalents of hydrogen chloride causes an increase of 70%. That this effect is not due to a decarboxylation mechanism involving the attack of a solvated proton on a molecule of quinaldinic acid (or on any species whose concentration is proportional to that of the acid) is supported by the fact that the rate constant is not directly proportional to the concentration of added hydrogen chloride, but falls off with increasing concentration, as would be expected for a dissociation phenomenon. That the mechanism of the decarboxylation cannot involve an undissociated acid molecule and a proton is confirmed by the first-order kinetics, since such a bimolecular process would result in a second-order equation. Hence the results indicate that one or both of the species (II) and (IV) decarboxylate more readily than does the anion (III).

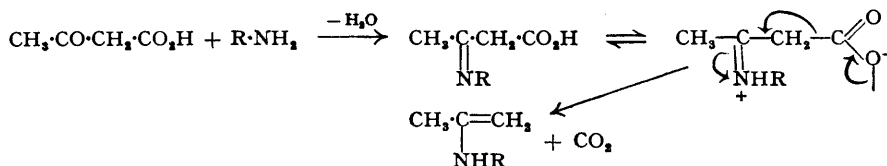
The foregoing statement is capable of confirmation by comparing the rates of decarboxylation of the acid and of one of its salts under the same conditions. As sodium quinaldinate is insoluble in quinoline, a change had to be made to a solvent capable of dissolving both the acid and its sodium salt. The choice was eventually made of ethylene glycol. In this solvent at 184.4°, the acid decomposed at an appreciable rate ($k = 20.1 \times 10^{-4}$), whereas there was no detectable decomposition of the sodium salt. It is almost certain that quinaldinic acid will be present in ethylene glycol as an equilibrium mixture of free acid, zwitterion, anion, and solvated protons. Though there appear to be no recorded conductivity measurements of salts in this solvent, it is

improbable that the salt could be present as anything but an equilibrium mixture of ion pairs and sodium and quinaldinate ions. The results obtained from a study of the addition of hydrogen chloride to a solution of the acid in quinoline are therefore confirmed, and further, it is established that while one or both of the species free acid and zwitterion decarboxylate readily, the quinaldinate ion does not decompose at all below a temperature of 184.4°.

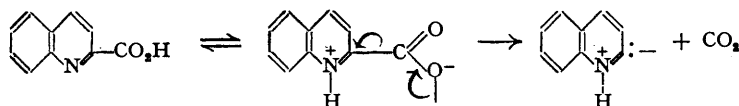
The remaining problem is to decide between the free acid and the zwitterion as decarboxylating species. This has not been done absolutely, but evidence is provided which indicates that the zwitterion is very likely the more unstable of the two. Thus it has been shown that the betaine (V), which is analogous in structure and charge distribution to the zwitterion, decarboxylates with extreme ease, measurements yielding a minimal value of 57 for the ratio k of betaine: k of acid in quinoline at 145.8°. From these considerations it can be inferred that the zwitterion loses carbon dioxide much more readily than does the ordinary form of the free acid, a view formally analogous to that of Pedersen (*J. Physical Chem.*, 1934, **38**, 559; *J. Amer. Chem. Soc.*, 1938, **60**, 595) on the normal and the catalysed decarboxylations of β -keto-acids; compare



and



with



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