

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Decarboxylation of Malonic Acid in Quinoline and Related Media

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A kinetic study of the quinoline-catalyzed decarboxylation of malonic acid in organic media has been made. Two species decompose, monoanion and free acid; only the decarboxylation of the latter exhibits strong quinoline catalysis. Kinetic and other evidence lead to the postulate that the reaction proceeds by quinoline solvation of the carboxyl carbon.

Introduction

In the course of studies^{1,2} on the intermolecular carbon isotope effect in the decarboxylation of malonic acid, we observed that the decomposition was about a hundred times as fast in quinoline as in aqueous sulfuric acid. Though quinoline catalysis of decarboxylation has been employed widely, little work seems to have been done to elucidate the details of the effect.

The kinetics of the decarboxylation have been investigated for molten malonic acid³ and for the acid in aqueous solution⁴⁻⁶; in each case first-order kinetics were obtained. Hall⁵ found that monoanion and the diacid have different rates of decomposition in aqueous solution. Ogata and Oda⁶ measured the decarboxylation rates of solutions of malonic acid in xylene, aniline and dimethylaniline.

In the study to be reported here, there were four principal phases: (1) determination of the rates of decarboxylation of malonic acid and its monoanion in quinoline solution; (2) determination of the effect of varying quinoline concentration in a non-catalytic medium (here dioxane); (3) observation of the relative catalytic power of other amines; and (4) determination of enthalpies and entropies of activation where possible.

Experimental

Materials.—Malonic acid was Eastman Kodak Co. white label grade, m.p. 135°, 99.9% pure by acidimetric titration. Quinoline was purified by fractional distillation under reduced pressure (68.5°, 0.5 mm.). Pyridine was J. T. Baker purified grade. Aniline was Mallinckrodt purified grade. Dimethylaniline was purified by distillation at reduced pressure (80°, ca. 10 mm.) after being dried over barium oxide. Dimethyl- α -naphthylamine was Eastman Kodak Co. "for sulfanilamide test." Dioxane was purified by distillation from sodium wire at 100–101°. N-Ethylpiperidine (NEP) was Eastman Kodak Co. "suitable for penicillin G determination." Quinolinium nitrate was made by mixing equimolar quantities of purified quinoline and reagent grade concentrated nitric acid. The resulting solid was filtered, washed several times with ether and recrystallized from 95% ethanol.

Apparatus and Procedure.—Malonic acid was decarboxylated in various solvents and at different temperatures. The carbon dioxide evolved was measured by observing its volume in a constant pressure apparatus or its pressure in a constant volume apparatus as a function of time. The former equipment has been described elsewhere.⁷ The

latter (Fig. 1) consisted essentially of a 50-cc. reaction flask (B) fitted by means of a ball joint (N) with a rod used for crushing in the hot solvent the thin-walled glass capsule (A) containing malonic acid. This vessel was connected to a 300-cc. gas reservoir (F) which was the high pressure arm of a mercury manometer (M). The entire apparatus except the manometer tube was immersed in an oil-bath maintained within 0.02° of the desired temperature.

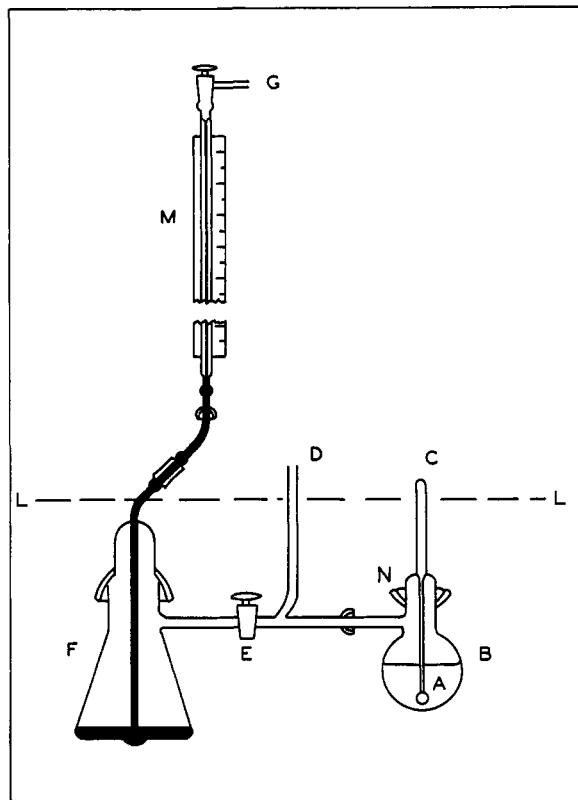


Fig. 1.—Schematic diagram of the constant volume rate measuring apparatus (letters refer to text).

Before the start of each decarboxylation, the solvent was saturated with carbon dioxide. For each run, 0.3–0.4-g. samples of malonic acid and about 12 ml. of solvent were used.

Infrared spectra were determined with a Perkin-Elmer double beam instrument. Matched cells were used, one containing the solvent and the other containing malonic acid dissolved in that solvent.

Results.—For each run the quantity of carbon dioxide evolved was plotted against time. From the smoothed experimental plots, representative points were used for the preparation of graphs of $\log_e (N_\infty - N_t)$ vs. t , where N_∞ represents the maximum yield of carbon dioxide (98% or more of theoretical in every run tested), and N_t is the amount of gas evolved at any time t . Every decarboxylation proved to be first order excepting run V-3, where two separate first-order processes operated simultaneously. The apparent first-order rate constant was in each case taken as the absolute slope of the logarithmic plot.

(1) P. E. Yankwich, R. L. Belford and Gideon Fraenkel, *THIS JOURNAL*, **75**, 832 (1953).

(2) P. E. Yankwich and R. L. Belford, *ibid.*, **75**, 4178 (1953).

(3) C. N. Hinshelwood, *J. Chem. Soc.*, 156 (1920).

(4) A. L. Bernoulli and W. Wege, *Helv. Chim. Acta*, **2**, 511 (1919).

(5) G. A. Hall, *THIS JOURNAL*, **71**, 2691 (1949).

(6) Y. Ogata and R. Oda, *Bull. Inst. Phys. Chem. Research (Tokyo)*, *Chem. Ed.*, **23**, 217 (1944); *C. A.*, **43**, 7904d (1949).

(7) E. J. Corey and Gideon Fraenkel, *THIS JOURNAL*, **75**, 1168 (1953).

The results are collected in Table I⁸ along with those obtained by Hall⁵ for aqueous decarboxylations. In Fig. 2 are shown typical plots of the original data and their logarithm-plot equivalent. Figure 3 shows k' as a function of quinoline concentration⁹ as obtained in runs V-6, 7, 8, 9 and 10.

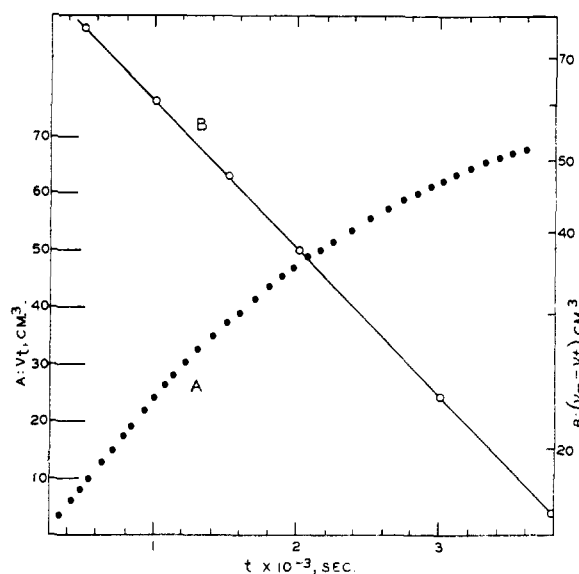


Fig. 2.—Data for a typical run, as functions of time: A, the volume of carbon dioxide evolved; B, $\log(V_\infty - V_t)$.

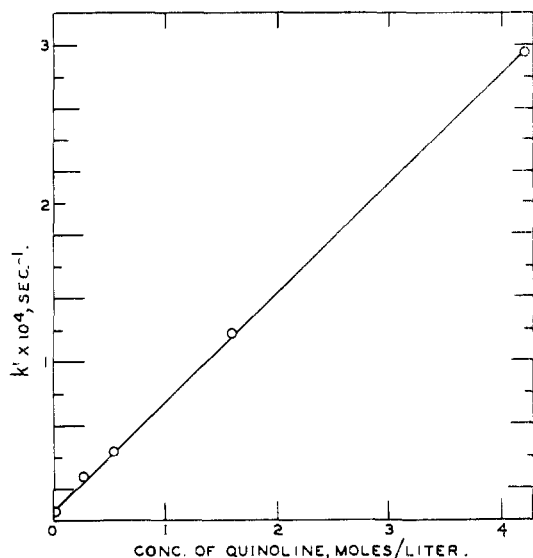


Fig. 3.—The influence of quinoline concentration on the rate of malonic acid decarboxylation (dioxane medium, 99.6°).

Thermodynamic quantities for activation were calculated from the following relations (in the notation of Glasstone, Laidler and Eyring)

$$E_{\text{exp}} = R \log(k_2'/k_1') / (1/T_1 - 1/T_2)$$

$$\Delta F^\ddagger = RT \log(RT/Nhk)$$

$$\Delta S^\ddagger = (\Delta E^\ddagger - \Delta F^\ddagger) / T$$

(8) This run was not first order due to the concurrent decarboxylation of initially equal amounts of diacid and monoanion. Apparent initial $k_1' = 3.4 \times 10^{-4}$ sec.⁻¹, apparent final $k' = 2.8 \times 10^{-4}$ sec.⁻¹.

(9) Extrapolation of this plot to the molarity of pure quinoline gives a rate constant somewhat larger than that found experimentally; this is not surprising in view of the change in nature of medium in going from pure dioxane to pure quinoline.

TABLE I

PSEUDO FIRST-ORDER RATE CONSTANTS FOR DECARBOXYLATION OF MALONIC ACID IN VARIOUS MEDIA AT VARIOUS TEMPERATURES

Run	Medium	Temp., °C.	Apparent rate constant, $k' \times 10^4$, sec. ⁻¹
P-1	Quinoline	97.5	4.06 ± 0.01
V-1	Quinoline	100.0	4.9 ± .1
P-3	Quinoline	118.7	16.2 ± .2
V-2	<i>n</i> moles quinoline + 4.5 <i>n</i> moles quinolinium nitrate	100.0	4.8 ± .1
V-3	Quinoline + (0.5 mole NEP/mole diacid)	100.0	8
V-4	Quinoline + (1.0 mole NEP/mole diacid)	100.0	2.8 ± .1
V-5	Quinoline + (5.0 moles NEP/mole diacid)	100.0	2.7 ± .1
P-2	Quinoline + (2.3 moles NEP/mole diacid)	97.5	2.10 ± .05
P-5	Quinoline + (2.3 moles NEP/mole diacid)	109.1	6.73 ± .05
P-4	Quinoline + (2.3 moles NEP/mole diacid)	118.7	18.1 ± .1
V-6	Dioxane	99.6	0.066 ± .004
V-7	0.27 <i>M</i> quinoline in dioxane	99.6	0.28 ± .02
V-8	0.53 <i>M</i> quinoline in dioxane	99.6	0.43 ± .02
V-9	1.59 <i>M</i> quinoline in dioxane	99.6	1.18 ± .02
V-10	4.24 <i>M</i> quinoline in dioxane	99.6	2.95 ± .02
V-11	Dioxane + (2.0 moles NEP/mole diacid)	99.6	1.90 ± .05
V-12	Dioxane + (5.0 moles NEP/mole diacid)	100.0	2.10 ± .05
V-13	Pyridine	100.0	4.9 ± .1
V-14	Dimethylaniline	100.0	1.30 ± .05
V-15	Aniline	100.0	1.30 ± .05
V-16	Dimethyl- α -naphthylamine	100.0	0.83 ± .07
	Water: free acid decomposition (Hall)	90	.0717
	Water: anion decomposition	90	.0071

The thermodynamic data are collected in Table II and there compared with similar figures calculated from Hall's results.

TABLE II

THERMODYNAMIC QUANTITIES FOR MALONIC ACID DECARBOXYLATION AT 90°

Species	Medium	ΔH^\ddagger , kcal./mole	ΔF^\ddagger , kcal./mole	ΔS^\ddagger , e.u. ¹⁰
Diacid	Quinoline	17.8	27.7	-27
Diacid	Water	30.1	29.9	+0.5
Monoanion	Quinoline	27.9	26.4	+4
Monoanion	Water	27.8	29.9	-6

The infrared spectrum of malonic acid in the presence and absence of catalytic amines gives an indication of strong interaction between the best catalysts and the carboxyl group. The data are summarized in Table III.

TABLE III

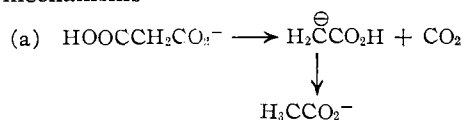
CARBONYL ABSORPTION PEAKS FOR MALONIC ACID IN VARIOUS MEDIA

Solvent	Carbonyl frequency, cm. ⁻¹
Dioxane	1730
40% dimethylaniline in dioxane	1730
Pyridine	1710
11% quinoline in dioxane	1725
22% quinoline in dioxane	1715
33% quinoline in dioxane	1715
50% quinoline in dioxane	1710
75% quinoline in dioxane	1710
Quinoline	1705

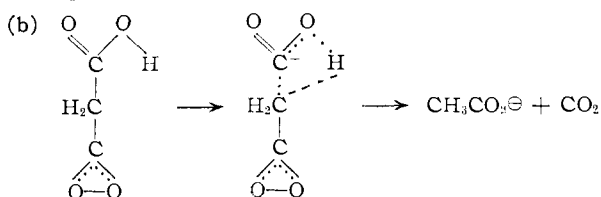
(10) We estimate the probable uncertainties in these entropies of activation as about ± 2 e.u.

Discussion

Consider first the results of some of the decarboxylation experiments near 100°. The rate of decarboxylation in quinoline solution in the presence of N-ethylpiperidine (NEP) is lower than that in pure quinoline, but has an essentially constant value when there is more than 1 mole of NEP present per mole of diacid. NEP is a strongly basic amine,¹¹ and apparently neutralizes almost completely one carboxyl hydrogen of malonic acid; the second, imperceptibly. In dioxane-NEP mixtures the reaction rates are only slightly lower than those observed in quinoline-NEP solutions. We assume therefore that these reactions in the presence of excess NEP, at least in media of low dielectric constant, involve the free hydrogen malonate ion (monoanion) and suggest the following as possible mechanisms



and, probably less likely

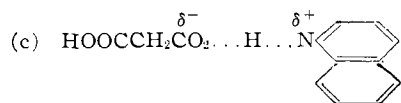


Although the rate of aqueous monoanion decarboxylation is only about one-hundredth of that in quinoline, the two reactions have essentially the same activation energies. The following equation, according to the theory of absolute reaction rates, shows that for two reactions having the same activation energy, differences in rate constant are related directly to differences in entropy of activation

$$[\Delta S^\ddagger - \Delta S^\ddagger] = R \log (k'_a/k'_b) \quad (1)$$

where k'_a and k'_b are the apparent first-order rate constants for the two processes. The difference of 10 e.u. between the entropies of activation in the two media indicates that there is in aqueous solution a greater ordering of the immediate environment of the decomposing anion incident to activation than in quinoline (or dioxane).

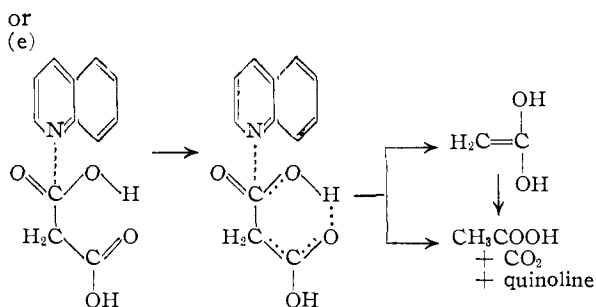
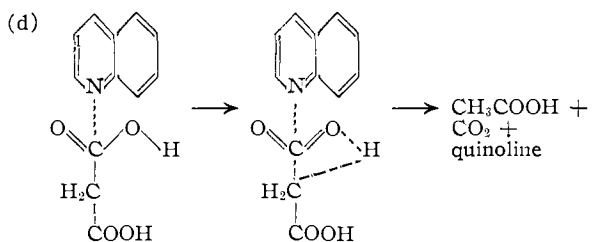
Corey¹² has shown that malonic acid is inappreciably dissociated in solvents such as pyridine and quinoline; thus one can eliminate the possibility of appreciable anion decomposition when the diacid decarboxylates in one of these pure media. Furthermore, the apparent rate constant for reaction in dioxane is a linear function of the concentration of amine. This suggests two possibilities: (1) that the reaction proceeds *via* hydroxyl association, which results in an intermediate such as c



(11) N. F. Hall and M. R. Sprinkle, *THIS JOURNAL*, **54**, 3469 (1932).

(12) E. J. Corey, *ibid.*, **75**, 1172 (1953).

or (2) that the carboxyl carbon is solvated and decarboxylates according to a scheme such as d



the latter being the more likely.

We believe that carbon solvation is more likely than hydroxyl association for several reasons: 1. At temperatures below 116° monoanion decomposition proceeds less rapidly than does the free acid decarboxylation in question; the proposed mechanism involving c, however, would represent an approach to anion formation and would not be expected to result in free acid decomposition exceeding the rate of monoanion decarboxylation. The likely mechanisms which can be written for hydroxyl association decarboxylation would differ from the postulated anionic mechanisms only in substitution of the linkage $\text{O} \cdots \text{H} \cdots \text{N}$ for O^- , a change not expected to increase the rate of the process.

2. Carbon dioxide has very high solubility in amines,¹³ probably due to weak carbon-nitrogen linkage.¹⁴ It is reasonable to expect that similar interactions exist between various amines and carboxyl carbons. Some evidence for a change in the bonding about the carboxyl carbon atom is given in Table III where it is seen that an appreciable shift of the carbonyl band from its normal frequency occurs. There is, of course, the possibility that this shift is due primarily to interaction between the amine and the hydroxyl group; Corey¹² has found that extensive hydroxyl association would occur in solvents such as pyridine and quinoline. However, dimethylaniline, which at room temperature has almost the same basicity¹¹ and probably the same ability to associate with hydroxyl as has pyridine, caused no appreciable carbonyl shift, probably because of steric hindrance to carbon solvation.

3. Near 100° both the magnitude of the intermolecular carbon isotope effect for diacid decarboxylation in quinoline and its temperature coefficient² are larger than predictions for *thermal*, *i.e.*, uncatalyzed, reaction based on the simplified model

(13) G. Just, *Z. physik. Chem.*, **37**, 342 (1901).

(14) J. H. Hildebrand and R. L. Scott, "The Solubility of Nonelectrolytes," Reinhold Publ. Corp., New York, N. Y., 1950, p. 249.

suggested by Bigeleisen.¹⁵ Those results are explained if there are presumed to operate one or more rapid reversible equilibria prior to the rate-determining step in the decarboxylation which affect the binding about the carboxyl carbon atom(s). The data in Table II indicate that the decarboxylation of the diacid in the presence of quinoline is a bimolecular process. While the isotope effect results do not permit one to reach a definite conclusion concerning the nature of the solvation equilibria, calculation² shows that proton transfer cannot be the rate-determining process; such a conclusion seems to reduce the likelihood that activation proceeds by proton shift from a solvation equilibrium such as hydrogen bonding of the carboxyl groups with solvent (quinoline) molecules.

4. Examination of models shows that steric hindrance of various amines might interfere with their catalytic ability. The relative rates of malonic acid decarboxylation in the presence of the six amines listed in Table I (runs V-13 to 16) are commensurate with the expected hindrance.

Of course, the direct evidence for the participation of the amine in the decarboxylation of the free acid consists of the dependence on the amine concentration of the rate of reaction, and the large negative entropy of activation. The latter is much

(15) J. Bigeleisen, *J. Phys. Chem.*, **56**, 823 (1952).

more negative than the value which would be expected if formation of the activated complex involved minor rearrangements of solvent molecules (*i.e.*, rearrangements which are incident to activation but not so extreme as to result in solvent concentration dependence of the reaction rate). Comparison of the thermodynamic data in Table II indicates clearly that in water and quinoline media the reaction mechanisms are very different for free acid decarboxylation, while they may be similar for that of the monoanion.

Hall⁵ has shown that acid catalysis is not important in aqueous solution decarboxylation, and our data for decomposition in dioxane indicate that the dielectric constant of the medium is not an important factor in the case of the free acid as it is for the monoanion. It is therefore probable that the decarboxylation of un-ionized malonic acid is a simple thermal reaction in the absence of amine catalysts.^{3,4,16,17}

Acknowledgments.—This research was supported by the A.E.C. We are grateful for the interest and helpful suggestions of Dr. E. J. Corey. We are indebted to Miss Helen Miklas for the infrared determinations.

(16) B. R. Brown, *Quarterly Rev.*, **5**, 131 (1951).

(17) R. A. Fairclough, *J. Chem. Soc.*, 1186 (1938).

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[CONTRIBUTION FROM THE ISTITUTO DI CHIMICA GENERALE E ANALITICA OF THE POLITECNICO DI MILANO, ITALY, GATES AND CRELLIN LABORATORIES, CALIFORNIA INSTITUTE OF TECHNOLOGY, AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XVI. 1,3-Interactions and Homoallylic Resonance

BY M. SIMONETTA¹ AND S. WINSTEIN²

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Evidence from stereochemistry and reaction kinetics suggests the existence of an important 1,3-interaction between a carbonium ion center and a π -electron-containing β -substituent. A semi-empirical molecular orbital method has been used to estimate the stabilization due to π -electron delocalization in the case of a vinyl, diolefinic or phenyl group beta to a cationic carbon center. Even at the unmodified 1,3 C-C distance of 2.5 Å., a slight stabilization due to electron delocalization is found, the 1,3-overlap integrals, with proper orientation, being appreciable. Considerable compression of the 1,3-distance is more than compensated for by increase in resonance energy; the intervening methylene group is in effect a poor insulator against interaction of the unsaturated centers. The net stabilizations are estimated as *ca.* 10, 6 and 4 kcal./mole for β -dienyl, β -vinyl and β -phenyl, in accord with the rate-enhancing effects of these substituents in solvolysis.

Evidence from stereochemistry and reaction kinetics suggests the existence of an important interaction between a carbonium ion center and a π -electron-containing β -substituent such as a vinyl or phenyl group. This is true for *homoallylic* cases such as cholesteryl I³ and dehydronorbornyl V⁴ and *homobenzyl* cases such as benzylmethylcarbiny VI.^{5,6} Thus cholesteryl derivatives have enhanced

(1) Arthur A. Noyes Fellow in Chemistry. California Institute of Technology, 1951-1952.

(2) Research supported in part by the Office of Naval Research.

(3) (a) S. Winstein and R. Adams, *THIS JOURNAL*, **70**, 838 (1948);

(b) S. Winstein and A. H. Schlesinger, *ibid.*, **70**, 3528 (1948).

(4) S. Winstein, H. M. Walborsky and K. C. Schreiber, *ibid.*, **72**, 5795 (1950).

(5) S. Winstein, *Bull. soc. chim.*, **18**, 55C (1951).

(6) S. Winstein, M. Brown, K. C. Schreiber and A. H. Schlesinger, *THIS JOURNAL*, **74**, 1140 (1952).

rates of ionization,³ ascribed to delocalization of the electron cloud of the neighboring olefinic group in the rate-determining step.³ This participation of the 5,6-olefinic group in the substitution process gives rise to a non-classical ion^{3,5} which has been written as II (canonical structures IIa and IIb) with partial 3,5-bonding and weakened 5,6-bonding. This intermediate reacts³ with nucleophilic species at C₆ to yield 3,5-cyclosteroids III or at C₃ to yield cholesteryl derivatives IV with over-all retention^{3,5} of configuration from I to IV.

The concept of the hybrid allyl ion VII is familiar, but the non-classical structure II represents a hybrid structure for the next homologous case, with a methylene group interposed between the cationic center and the π -electron system; this is the reason