Anal. Calcd. for $C_{12}H_{15}IN_2O_2$: C, 41.64; H, 4.37; N, 8.09. Found: C, 41.96; H, 4.64; N, 8.09.

B. From 17.—A solution of **17** (145 mg., 0.50 mmole) and methyl iodide (0.20 ml., excess) in methanol (3.0 ml.) was heated in a sealed tube at 120° for 2.5 hr., then evaporated. Recrystallization of the residue from methanol–isopropyl ether gave colorless plates (0.12 g.), m.p. 195–197° dec.

This compound was identical with the above-obtained one.

1,2-Dimethyl-3-(α,β-dimethoxycarbonyl-β-hydroxyvinyl)benzimidazolium Chloride.—To a solution of **5** (0.40 g.) in water (5.0 ml.) was added 6 *N* hydrochloric acid (1.0 ml.), and the resulting solution was evaporated. The crystalline residue was recrystallized from methanol–isopropyl ether to give colorless plates (0.35 g.), m.p. 130° dec.

Anal. Calcd. for $C_{15}H_{17}ClN_2O_5 \cdot H_2O$: C, 50.21; H, 5.33; N, 7.81. Found: C, 50.35; H, 5.66; N, 8.09.

The aqueous solution of this compound was neutralized with aqueous sodium hydrogen carbonate solution then evaporated. The residue was extracted with chloroform, and the solvent was evaporated to give **5**, m.p. 238–240° dec., which was identical with above-obtained one.

1,2-Dimethyl-3-(α-methoxycarbonyl-β-hydroxyvinyl)benzimidazolium Chloride.—This compound was obtained from **6** by the same procedure as mentioned above. Recrystallization from methanol–isopropyl ether gave colorless plates, m.p. 188–190° dec.

Anal. Calcd. for $C_{13}H_{15}ClN_2O_3$: C, 55.23; H, 5.35; N, 9.91. Found: C, 55.14; H, 5.42; N, 10.03.

Neutralization of this compound by the same procedure as mentioned above reproduced **6**.

Treatment of 5 with Methanolic Hydrogen Chloride.—A solution of **5** (0.30 g.) in methanolic hydrogen chloride (10%, 3.0 ml.) was refluxed for 10 hr., then evaporated. After neutralization of the residue, the starting material (0.27 g.) was recovered.

Treatment of 6 with Methanolic Hydrogen Chloride.—This experiment was carried out by the same procedure as mentioned above. The same result, recovery of the starting material, was obtained by this treatment.

Treatment of 5 with Hydroxylamine.—To a solution of hydroxylamine hydrochloride (140 mg., 2.0 mmoles) and sodium acetate (200 mg., 2.4 mmoles) in water (1.0 ml.) and methanol (4.0 ml.) was added **5** (304 mg., 1.0 mmole). The resulting solution was allowed to stand at room temperature for 3 days. After evaporation, the starting material (280 mg.) was recovered.

Treatment of 6 with Hydroxylamine.—This experiment was carried out by the same procedure as mentioned above. The starting material was recovered unchanged by this treatment.

Attempted Oxidation of 6 with Hydrogen Peroxide.—To a solution of **6** (0.60 g.) in methanol (10.0 ml.) was added hydrogen peroxide (30%, 2.0 ml.) and the solution was refluxed for 2 hr. After evaporation, the starting material (0.50 g.) was recovered.

Oxidation of 6 with Potassium Permanganate.—To a solution of **6** (0.40 g.) in water (6.0 ml.) was added finely ground potassium permanganate with stirring at 25°, until the color of the oxidizing agent lasted for a time. Crystals separated as the reaction proceeded. At the end of the reaction, the mixture was heated to dissolve the crystalline product and filtered to remove manganese dioxide. After cooling, the product (0.20 g., m.p. 112–114°) was collected by filtration; it was identical with authentic 1,2-dimethylbenzimidazole.[5]

Attempted Reduction of 6 with Sodium Borohydride.—Sodium borohydride (50 mg.) was added to a solution of **6** (200 mg.) in water (5.0 ml.), and the solution was heated at 60° for 2 hr. The starting material (180 mg.) was recovered.

Attempted Reduction of 6 with Adams Catalyst.—A mixture of **6** (246 mg.) in methanol (20 ml.) containing platinum catalyst (prepared from Adams catalyst, 50 mg.) was treated with hydrogen at ordinary temperature and pressure. No hydrogen was absorbed during 6 hr. The starting material (240 mg.) was recovered.

Reaction of Methyl Methoxalyl(1-methyl-2-benzimidazolyl)-acetate (3a) with Methanolic Hydrogen Chloride.—To a solution of **3a** (0.40 g.) in methanol (3.0 ml.) was added methanolic hydrogen chloride (10%, 1.0 ml.) under cooling in a cold-water bath. After evaporation, acetone was added to the residue to give colorless crystals (0.30 g.). Recrystallization from methyl acetate gave methyl (1-methyl-2-benzimidazolyl)acetate hydrochloride as colorless prisms, m.p. 147–149°.

Anal. Calcd. for $C_{11}H_{12}N_2O_2 \cdot HCl$: C, 54.89; H, 5.45; N, 11.64. Found: C, 54.79; H, 5.70; N, 11.66.

Neutralization of this compound gave methyl (1-methyl-2-benzimidazolyl)acetate (**24**), m.p. 66–68°.[1a,b]

Reaction of Methyl Formyl(1-methyl-2-benzimidazolyl)acetate (3b) with Methanolic Hydrogen Chloride.—This experiment was carried out by the same procedure as mentioned above. By this treatment, **3b** also gave methyl (1-methyl-2-benzimidazolyl)-acetate hydrochloride, m.p. 147–149°, which was identical with the above obtained one.

Acknowledgment.—The authors express their gratitude to Professor Emeritus E. Ochiai of the University of Tokyo and Dr. K. Takeda, Director of this laboratory, for their helpful guidance and encouragement, and their appreciation to Drs. Y. Matsui and K. Tori for their helpful discussion on the infrared and n.m.r. spectra. Thanks are also due to Messrs. I. Tanaka and K. Aono for ultraviolet and n.m.r. spectral measurements, to the members of the analysis room of this laboratory for elemental analysis, and to Mr. S. Hashimoto for his technical assistance.

Decarboxylation of Oxamic and Oxanilic Acids in Aniline[1]

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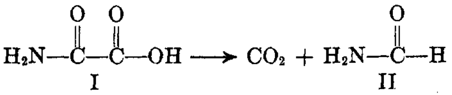
The decarboxylation of oxamic acid in aniline is complicated by a series of concurrent reactions and is not reversible as previously reported, but is accompanied by amidation and transamidation producing as final products oxanilide and formanilide.

As part of his extensive research on rates of decarboxylations in a variety of solvents, L. W. Clark has studied the decarboxylation of oxamic acid (I) in aniline,[3] *o*-toluidine,[3] quinoline,[4] dimethyl sulfoxide,[5] and triethyl phosphate.[5] In the paper on the decarboxylation of oxamic acid (eq. 1) in aniline and *o*-toluidine as solvents,[3] there are several anomalous results including unusually high and positive ΔS^* values (Table I) and the formation of a white precipitate (A) in the condenser concurrent with resorption of the gaseous CO_2 produced during the decarboxylation. Clark attributed this to reversal of the decarboxylation with formation of oxamic acid in the condenser.[3] In a later paper,[4] it was



$$\underset{\text{I}}{H_2N{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}OH} \longrightarrow CO_2 + \underset{\text{II}}{H_2N{-}\overset{O}{\overset{\|}{C}}{-}H} \qquad (1)$$

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[2] Contribution No. 1789 from the Department of Chemistry.

[3] L. W. Clark, *J. Phys. Chem.*, **65**, 180 (1961).

[4] L. W. Clark, *ibid.*, **65**, 659 (1961).

[5] L. W. Clark, *ibid.*, **65**, 1651 (1961).

TABLE I

ACTIVATION PARAMETERS FOR DECARBOXYLATION

Substrate	Solvent	ΔH^* $\left(\frac{\text{kcal.}}{\text{mole}}\right)$	ΔS^* (e.u.)	Ref.
$H_2N\overset{\overset{O}{\|}}{C}CO_2H$ (oxamic acid)	Aniline	59.7	68.0	*a*
	Quinoline	47.0	37.5	*b*
	$(CH_3)_2SO$	37.7	14.9	*c*
$C_6H_5HN\overset{\overset{O}{\|}}{C}CO_2H$ (oxanilic acid)	Aniline	49.8	46.3	*d*
	Quinoline	38.6	16.0	*e*
	Dimethylaniline	37.6	15.3	*f*
HO_2CCO_2H (oxalic acid)	Aniline	40.3	16.2	*g*
	Quinoline	38.9	15.8	*g*
	$(CH_3)_2SO$	40.6	20.7	*g*
$HO_2CCH_2CO_2H$ (malonic acid)	Aniline	26.9	−4.5	*h*
	Quinoline	26.7	−2.4	*i*
	Dimethylaniline	26.2	−6.6	*j*

[a] Ref. 3. [b] Ref. 4. [c] Ref. 5. [d] Ref. 7. [e] L. W. Clark, *J. Phys. Chem.*, **65**, 1460 (1961). [f] L. W. Clark, *ibid.*, **65**, 2271 (1961). [g] L. W. Clark, *ibid.*, **61**, 699 (1957): The ΔS^* and ΔF^* values for the decarboxylation of oxanilic acid in quinoline are in error in this paper. The correct values are $\Delta S^* = +5.8$ e.u. and $\Delta F^* = 32.4$ kcal./mole. [h] L. W. Clark, *ibid.*, **62**, 79 (1958). [i] L. W. Clark, *ibid.*, **62**, 500 (1958). [c] L. W. Clark, *ibid.*, **61**, 1575 (1957).

found that, when CO_2 was bubbled into formamide (II), there was no reaction, but, when CO_2 was bubbled into formamide and aniline, oxamic acid was produced. We have reinvestigated these observations and report here the results of our research on the products formed during the decarboxylation of oxamic acid in aniline at ~150°.

Results

Initial experiments confirmed Clark's observations. It was found that CO_2 gave the white solid A when passed through a mixture of formamide and aniline. The melting point of A was found to be ~100° which supported our doubts about it being oxamic acid (m.p. 210°). In one experiment of this kind, fractional distillation of the solvent, aniline, permitted isolation and unambiguous identification (mixture melting points and infrared spectrum) of formanilide. When aniline and formamide were purified before use and the CO_2 was dried, A was not formed, but formanilide could still be identified as a product.

Two kinds of decarboxylation experiments were carried out. In those utilizing volumetric measurement of evolved gas, both mercury and Clark's entraining liquid (20% Na_2SO_4 and 5% H_2SO_4 in H_2O)[6] were used in the gas burets with the results shown in Table II. Important observations are that more gas than the theoretical volume corresponding to decarboxylation was evolved in two cases and we did not observe complete disappearance of the evolved gas. Vacuum distillation of the solution left a solid, identified as oxanilide, in the distilling pot. With both entraining liquids, A was formed in the condenser above the reaction vessel. In these experiments, formanilide could not be obtained pure, but vapor phase chromatography and the infrared spectrum of the residual liquid after distilling off aniline and filtering off oxanilide showed formanilide to be present.

TABLE II

AMOUNTS OF GAS EVOLVED IN DECARBOXYLATION OF OXAMIC ACID IN ANILINE[a]

Run	Entraining liquid	Gas initially in system	Max. vol. of gas obsd. (STP),[b] ml.	Final vol. of gas (STP),[b] ml.	Theor. vol. of CO_2 (STP), ml.
1	Mercury	CO_2	28	17	46.4
2	20% Na_2SO_4 5% H_2SO_4	CO_2	63	16	47.0
3	20% Na_2SO_4 5% H_2SO_4	N_2	64	20	46.6

[a] Amounts of oxamic acid and aniline used for each run are given in Table IV. [b] The values from the runs given in Table IV have been corrected to standard temperature and pressure.

The second kind of experiment in decarboxylation was designed to avoid gas resorption and measure the amount of CO_2 produced. Dry nitrogen was passed through a decarboxylating solution of oxamic acid in aniline in order to remove the CO_2 evolved which was evaluated by difference weighing of an ascarite absorption tube through which the exiting gas passed. The amount of oxanilide formed was also determined by isolation and weighing with the results shown in Table III.

TABLE III

PRODUCTS OF "DECARBOXYLATIONS" IN ANILINE AT 150°

Acid	Concn. of acid, *M*	% yields	
		Oxanilide	CO_2
Oxamic	0.013	22	81
Oxamic	0.013	12	64
Oxanilic	0.007	5	86

Since the production of oxanilide might proceed through the intermediacy of oxanilic acid, this was decarboxylated in the same way and the amounts of CO_2 and oxanilide were evaluated as for oxamic acid (Table III).

Although attempts were made to evaluate the yield of formanilide, it was very difficult to determine accurately the amount of formanilide in the large amount of aniline needed as solvent to get homogenous reaction. When aniline was removed by vacuum distillation, formanilide apparently codistilled since it could not be isolated from the pot residue although it was shown to be present (above). Since formamide was earlier shown to go to formanilide in aniline solution under the conditions used with oxamic and oxanilic acids, the amount of CO_2 should also represent the amount of formanilide produced in these reactions and CO_2 can be estimated with much more accuracy than formanilide.

The melting point of A (~100°) indicated that this material was not oxamic acid (m.p. 210°); this was confirmed by an infrared spectrum of A clearly different from that for oxamic acid. An examination of the infrared spectra of materials which could possibly be A revealed that ammonium bicarbonate has the same infrared spectrum.

Discussion

Our earliest results on heating formamide in aniline in the presence of CO_2 indicated that transamidation would take place under the conditions used in this study

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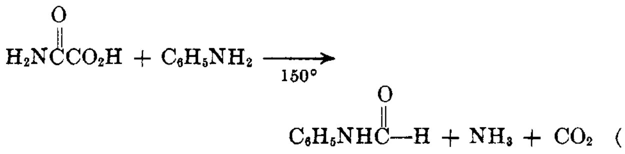
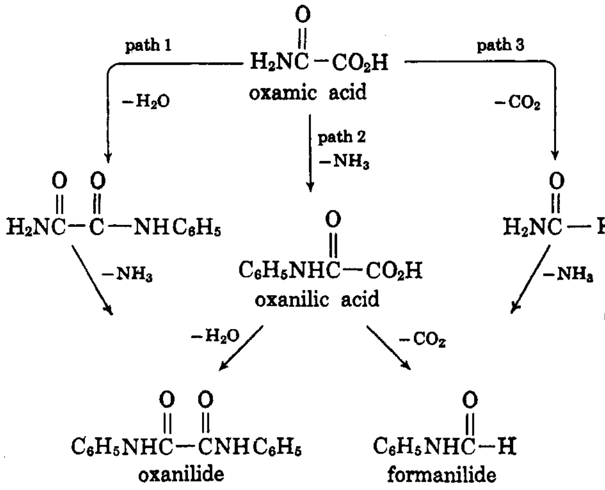
(6) L. W. Clark, *J. Phys. Chem.*, **60**, 1150 (1956).



$$H_2N\overset{O}{\overset{\|}{C}}CO_2H + C_6H_5NH_2 \xrightarrow[150^\circ]{} C_6H_5NH\overset{O}{\overset{\|}{C}}{-}H + NH_3 + CO_2 \quad (2)$$

so that at the very least eq. 1 should be replaced by eq. 2. However, further complexity was soon apparent when oxanilide was isolated as one of the products of "decarboxylation" of oxamic acid in aniline, and gravimetric analysis of the CO_2 produced showed that there was less than 100% decarboxylation (Table III). Therefore, amidation must also be occurring and all three paths shown in eq. 3 may be involved in the reactions of oxamic acid in aniline at ~150°. Since oxanilic acid was shown (Table III) to undergo about 90% decarboxylation and 10% amidation, some reaction through path 1 is required to give the product ratio observed for oxamic acid. The rate constant given by Clark for the "decarboxylation" of oxamic acid[3] is about one-half that for oxanilic acid[7] at 152° in aniline; thus oxanilic acid is a permissible intermediate in these reactions. However, the data in Table III indicate that the observed product ratios could be obtained if *decarboxylation* were occurring by way of path 2 or path 3 alone or both simultaneously. As each of these pathways of decomposition of oxamic acid presumably has a different activation energy, one would expect product ratios to be temperature dependent; temperature was only roughly controlled in these studies.



(3)

It is clear how A is formed since all the components necessary to form ammonium bicarbonate are produced in these reactions: H_2O, CO_2, and NH_3 (eq. 4). The

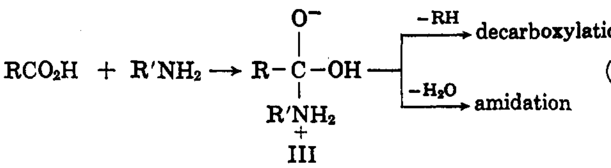
$$NH_3 + H_2O + CO_2 \rightleftarrows \overset{+}{N}H_4\,HCO_3^- \quad (4)$$

production of other gases besides CO_2 explains why the maximum volume of gas produced from oxamic acid (Table II) can be greater than that expected for 1 equiv. of CO_2. Additional H_2O required for formation of ammonium bicarbonate would be available from the aqueous entraining solution used by Clark.[6] No resorption of CO_2 takes place after the decarboxyation of oxamic acid in triethyl phosphate or dimethyl sulfoxide[5] because amidation and transamidation of oxamic acid is necessary to produce A. When the decarboxylation was carried out with mercury as the entraining solution, the final gas volume was smaller than expected (Table II). Since only ~20% of the oxamic acid reacts to give oxanilide and therefore water, most of the CO_2 evolved cannot give $NH_4^+\ HCO_3^-$ which requires a molecule of water (eq. 4). However, ammonium carbamate could also be formed (eq. 5) and this would account for the final gas volume in run 1, Table II.

$$2NH_3 + CO_2 \rightleftarrows \overset{+}{N}H_4\,H_2NCO_2^- \quad (5)$$

Examination of the activation parameters for malonic acid and oxalic acid (Table I) shows that ΔH^* and ΔS^* are not appreciably different in the various solvents, but that the ΔS^* values for the decarboxylation of oxamic acid and oxanilic acid in aniline are very high. Our results suggest that the anomalous ΔS^* values for decarboxylations in aniline (Table I) are due to complications caused by the multiplicity of reactions taking place. Probably the same difficulties cause the anomalously high ΔH^* and ΔS^* values found for decarboxylation of oxamic acid[3] in *o*-toluidine and oxanilic acid[7] in *o*-toluidine and *o*-ethylaniline. It is less clear why the ΔS^* for decarboxylation of oxamic acid in quinoline is high, but a possible explanation is that there was a small amount of secondary amine as impurity in the quinoline. It seems reasonable to conclude from the values in Table I and our results that ΔS^* should be near the 15–20-e.u. range for the *decarboxylation* of oxamic acid, oxanilic acid, and oxalic acid in aniline, quinoline, and dimethyl sulfoxide.

In the decarboxylation of malonic acid, nucleophilic catalysis was suggested to be the source of the kinetic term showing first-order dependence on quinoline.[8] Since the decarboxylation of picolinic acid shows similar solvent dependence to the decarboxylation of malonic acid, the suggestion has been made that "picolinic acid decomposes in polar solvents by a mechanism similar to that of malonic acid."[9] A first-order dependency on quinoline concentration has also been observed in the decarboxylation of N-methylpicolinic acid.[10] Nucleophilic catalysis of decarboxylation could proceed by formation of a tetrahedral intermediate (III) as is true for the hydrolysis of esters.[11] In the case of aniline as nucleophile, a tetrahedral intermediate (III, R′ = C_6H_5) could lead to amidation as well as to decarboxylation (eq. 6) so that, where it is difficult to lose RH, amidation could become important. The isolation of oxanilide in these experiments certainly means that there is nucleophilic interaction of solvent (aniline) with carbonyl groups and decarboxylation could proceed by the same pathway. In oxamic acid where two carbonyl groups are present, nucleophilic catalysis of decarboxylation could also be effective through the tetrahedral intermediate IV (eq. 7) which increases the



(6)

III

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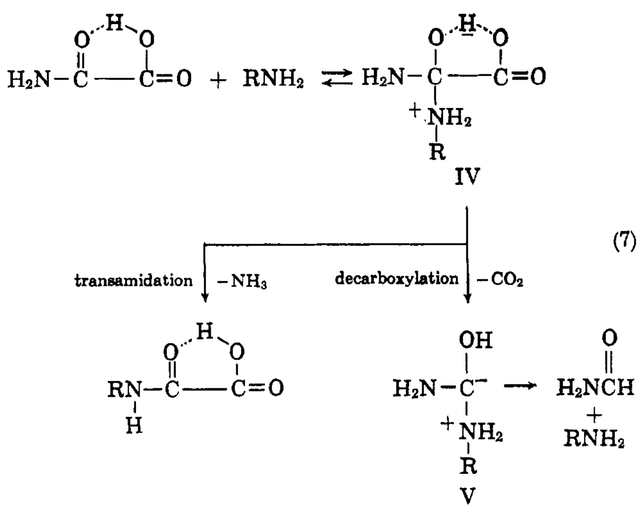
[7] L. W. Clark, *J. Phys. Chem.*, **65**, 572 (1961).

[8] G. Fraenkel, R. L. Bedford, and P. E. Yankwich, *J. Am. Chem. Soc.*, **76**, 15 (1954).

[9] L. W. Clark, *J. Phys. Chem.*, **66**, 125 (1962).

[10] P. Haake and J. Mantecon, *J. Am. Chem. Soc.*, **86**, 5230 (1964).

[11] M. Bender, *ibid.*, **73**, 1626 (1951).



amount of negative charge on the carboxyl and allows decarboxylation to proceed to an ylid (V). Increasing the amount of negative charge on the carboxyl results in a faster rate in many decarboxylations,[12] and ylid intermediates have been shown to be important in several decarboxylations.[10] The same intermediate (IV) could also lose ammonia in a transamidation to give oxanilic acid (see eq. 3). Additional experimental support for nucleophilic catalysis of decarboxylations and the mechanism by which it occurs would be desirable.

Experimental

All infrared spectra were taken on a Perkin-Elmer Model 421 spectrophotometer. Analyses were done at the University of California at Los Angeles by Miss Heather King. Vacuum distillations were carried out so that aniline distilled over at 30–60°; thus, no reaction should have occurred during distillation.

Materials.—Since oxanilide was isolated in ~20% yield from the decarboxylation of oxamic acid, a possible origin was by double transamidation of oxamide as an impurity in the oxamic acid. This was checked by analysis. The results indicate less than 2% oxamide in the oxamic acid we used.

Anal. Calcd. for oxamic acid, $C_2H_3NO_3$: C, 27.0; H, 3.4; N, 15.7. Calcd. for oxamide, $C_2H_4N_2O_2$: C, 27.3; H, 4.6; N, 31.8. Found for oxamic acid used in these experiments: C, 26.8, 26.5; H, 3.2, 3.0; N, 16.0, 16.0.

Aniline was distilled at atmospheric pressure from Zn powder under nitrogen immediately before use. Formanilide and formamide were purified by vacuum distillation. Carbon dioxide was dried by dispersion through concentrated H_2SO_4. Nitrogen was purified by successively passing it through Fieser's solution (alkaline pyrogallol), concentrated H_2SO_4, and NaOH pellets.

Reaction of CO_2 with Formamide and Aniline.—Carbon dioxide, without purification, was passed through a mixture of 10 ml. of aniline and 10 ml. of formamide at 140°. The reaction was stopped when the rate of formation of white solid on the condenser slowed (approximately 1–2 hr.). The white solid, after washing with ether and chloroform, gave a variable melting point, with decomposition, 110–115°, with most of the sample melting in the 100–115° range. The solid was insoluble in ether and in chloroform but very soluble in H_2O. When the reagents were distilled before use, no solid formed in the condenser. When dry CO_2 was bubbled through 3.1 g. of distilled formamide and 50 ml. of distilled aniline at 140° for 3.5 hr., no white solid was obtained; when the solution was vacuum distilled (1 mm.), two distillate fractions were obtained: a major fraction (aniline) at 49–51° and a minor fraction at 131–135°. The minor fraction solidified on refrigeration and was recrystallized from ether–petroleum ether, m.p. 45°. It gave an undepressed mixture melting point with a known sample of formanilide. Further confirmation of structure came from its infrared spectrum taken in CCl_4 which proved to be identical from 2.5 to 18 μ with that of a known sample of formanilide in the same solvent.

Decarboxylation of Oxamic Acid in Aniline.—The decarboxylations were carried out in a three-neck, 250-ml., round-bottom flask heated in an oil bath with stirring by a magnetic stirrer. A reflux condenser, joined to the central neck of the flask, was connected to a gas buret attached to a leveling bulb filled with mercury or Clark's entraining solution (20% Na_2SO_4 and 5% H_2SO_4).[6] Oxamic acid (0.183 g.) in a glass vessel was suspended in the reaction flask, the air in the system was replaced by CO_2 or N_2, and aniline which had just been distilled was added. When equilibrium was attained, the vessel containing the oxamic acid was dropped into the aniline. Volume readings were made periodically for the first 2 hr. and the reactions were allowed to proceed for 20 to 24 hr.; selected readings are shown in Table IV. It was observed that the oxamic acid required approximately 0.5 hr. to dissolve even in 150 ml. of aniline, and, as the temperature was not controlled carefully, these results cannot be used to obtain rates. A white solid formed on the inside of the condenser and, on isolation, its properties were identical with those of the solid isolated from the formamide–aniline–CO_2 reaction. An infrared spectrum of the solid in a KBr plate was identical with an infrared spectrum of a known sample of ammonium bicarbonate. Vacuum distillation of the reaction mixture gave a solid remaining in the distilling flask, which on recrystallization from benzene had a melting point of 240–243°. The melting point of a mixture with authentic oxanilide showed no depression. The infrared spectrum in CCl_4 was identical from 2.5 to 18 μ with that of an authentic sample of oxanilide in the same solvent.

Table IV

Rate of Evolution of Gas from Oxamic Acid in Aniline

Run 1[a]		Run 2[b]		Run 3[c]	
Time, min.	Vol., ml.	Time, min.	Vol., ml.	Time, min.	Vol., ml.
0	0	0	0	0	0
7	1	14	14	13	11
15	3	22	24	24	27
25	4	33	34	34	42
50	10	42	41	45	52
65	13	64	51	56	60
78	17	79	56	67	62
135	26	99	57	74	61
185	28	206	47	95	57
1200	19	1100	15	900	25

[a] Oxamic acid (0.1844 g.) in 50 ml. of aniline at 144°; mercury entraining fluid; CO_2 initially in system. [b] Oxamic acid (0.1873 g.) in 110 ml. of aniline at 148°; aqueous 20% Na_2SO_4–5% H_2SO_4 as entraining fluid; CO_2 initially in system. [c] Oxamic acid (0.1852 g.) in 150 ml. of aniline at 150°; aqueous 20% Na_2SO_4–5% H_2SO_4 as entraining fluid; N_2 initially in system.

Product Distribution in the Decarboxylation of Oxamic and Oxanilic Acids.—The following changes were made in the apparatus: nitrogen was passed through the reaction mixture by means of a through-joint in the third neck of the flask; the reflux condenser was attached to a tube containing anhydrone which was connected to a tube containing ascarite. The system was allowed 2 hr. to attain equilibrium. The ascarite tube was then weighed and reconnected to the system; the reaction was started (the system was continuously flushed with nitrogen). After 20–24 hr. at about 150°, the ascarite tube was reweighed and the increase in weight was assumed to be equal to the weight of CO_2 evolved. In these decarboxylations, little or no white solid formed on the condenser and none was observed at the end of the reaction period.

The reaction mixture was vacuum distilled almost to dryness; the precipitated oxanilide was washed with ether and chloroform, air dried, and weighed.

This same procedure was used to determine the amounts of CO_2 and oxanilide formed by reaction of oxanilic acid in aniline.

Formanilide was identified by distilling the reaction mixture down to 5 ml. and adding ether to precipitate the dissolved oxanilide. The precipitated oxanilide was washed with ether and the washings were added to the original ether solution. The ether was removed, the residue was dissolved in benzene, and HCl gas was passed in to remove aniline as the hydrochloride. This process had to be repeated two or three times to remove most of the aniline. The benzene was removed and the residue was diluted to a known volume with carbon tetrachloride. Formani-

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(12) B. R. Brown, *Quart. Rev.*, **5**, 131 (1951).

lide was shown to be present by a comparative infrared spectrum with authentic formanilide in CCl_4. All the bands in the spectrum of formanilide were present in the spectrum of the residue, and they indicated formanilide to be the major component of the residue. There were also impurity bands probably due to decomposition products from aniline.

The presence of formanilide in the reaction mixture was further confirmed by vapor phase chromatography as follows. The last 5 ml. of residue was treated with ether to remove dissolved oxanilide, the ether was removed, and the remaining aniline solution was passed through 20% S.E. 30 silicone oil on firebrick at 220°. Although the base line became unsteady after peaks corresponding to aniline and formanilide were observed (probably owing to oxidation products of aniline), the presence of a peak due to formanilide was confirmed by its enhancement on adding formanilide to the solution.

Aliphatic β-Chlorovinyl Aldoximes[1a]

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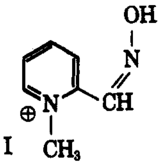
A number of aliphatic β-chlorovinyl aldehydes have been converted to their oximes. Infrared, ultraviolet, and n.m.r. spectral data verify the proposed structures. The β-chlorine atom of the conjugated aldehydes was found to be more stable toward replacement when a substituent other than hydrogen was also in the β-position. These compounds appear where possible to be mixtures of *cis* and *trans* isomers detectable by n.m.r.

There is a need for better antidotes against organophosphate poisoning. Compounds modeled after one of the present drugs, 2-PAM,[2] were sought because 2-PAM, although effective, is unstable over long periods in water.

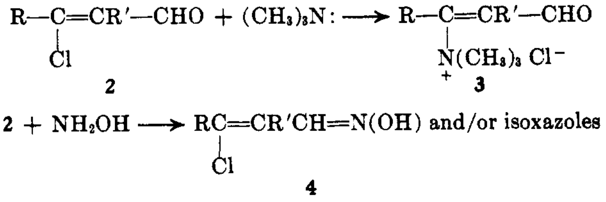


2-PAM

$$(CH_3)_3\overset{+}{N}—CR{=}CR'—CH{=}N(OH)$$

1

The attempted synthesis of compounds of type **1**, whose similarity to 2-PAM is readily apparent, is reported here. The following reaction paths were investigated.



$$\underset{\textstyle 2}{R—\underset{Cl}{\overset{|}{C}}{=}CR'—CHO} + (CH_3)_3N: \longrightarrow \underset{\textstyle 3}{R—\underset{\overset{+}{N}(CH_3)_3\ Cl^-}{\overset{|}{C}}{=}CR'—CHO}$$

$$2 + NH_2OH \longrightarrow \underset{\textstyle 4}{R\underset{Cl}{\overset{|}{C}}{=}CR'CH{=}N(OH)} \text{ and/or isoxazoles}$$

$$3 + NH_2OH \longrightarrow 1 \text{ and/or isoxazoles}$$

$$4 + :N(CH_3)_3 \longrightarrow 1 \text{ and/or isoxazoles}$$

Until very recently, β-chlorovinyl aldehydes were quite difficult to obtain but are now readily prepared through the formylation of ketones with the phosphorus oxychloride–dimethylformamide reagent.[3] In the course of our research, it was found that increasing the quantities of reactants gave yields comparable to, and in some cases better than, those reported. The products are unstable, but decomposition could be inhibited by dissolving the aldehyde in toluene containing a small amount of trimethylamine.

Treatment of these β-chlorovinyl aldehydes with trimethylamine in toluene under pressure at elevated temperatures failed to yield the expected quaternary salts. In most cases, small amounts of trimethylamine hydrochloride and varying amounts of intractable tars were formed, the unchanged β-chlorovinyl aldehydes being recovered in good yields (usually >65%). 2-Chlorocyclohexene carboxaldehyde was recovered nearly quantitatively. In a few cases dimethylamine was found to be equally unreactive.

The low reactivity of these aldehydes toward trimethylamine is in sharp contrast to the great reactivity of β-chlorovinyl ketones with trimethylamine,[4] where there apparently is less steric hindrance to attack by the trimethylamine molecule. The addition of various nucleophiles to β-chlorovinyl aldehydes has been investigated by other workers,[3e,5–7] who report the formation of both aldehyde derivatives and products arising through displacement of the β-chlorine atom.

When the chlorovinyl aldehydes prepared in this work were treated with hydroxylamine in aqueous alcohol, the corresponding oximes were usually formed (see Table I). The pure solid oxime of β-chlorocrotonaldehyde was not obtained. This is not surprising since crotonaldoxime does not easily form at room temperature.[8] 2-Chlorocycloheptene carboxaldehyde formed the oxime in a very low yield, the major product being 1-cyano-2-chlorocycloheptene.[9]

No analyses were found in the literature for the β-chlorovinyl aldehydes prepared, presumably because of their great instability. The analyses of the oxime derivatives and the gas chromatograms of the aldehydes therefore constitute a better measure of their purity than has yet been reported. The oximes were generally unstable even when purified.

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[1] (a) Financed in part by the Institute of Neurological Diseases and Blindness (under Grant NB 04088-01) and the Research Corporation; taken in part from the dissertation of A. E. Pohland. (b) Person to whom correspondence should be directed at the Division of Food Chemistry, Bureau of Scientific Research, Food and Drug Administration, U. S. Department of Health, Education and Welfare, Washington, D. C. 20204. (c) Boettcher Fellow, 1962–1963.

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