hyde, 5.0 g. (0.059 mole) of cyanoacetic acid and 0.1 g. of piperidine acetate in 75 ml. of acetonitrile at reflux for four hours. The reaction was carried out in a flask surmounted by a Soxhlet extractor charged with barium oxide. The acetonitrile was removed by distillation under reduced pressure and the residue was extracted with sodium bicarbonate solution. Acidification and recrystallization of the resulting solid from ethanol-water afforded 2.9 g. (38.7%) of pure acid, m.p. 208–209° (lit.[16] 208°).

Mesitylidenecyanoacetic acid was prepared by heating a mixture of 4.45 g. (0.30 mole) of mesitaldehyde, 5.1 g. (0.60 mole) of cyanoacetic acid, 1.5 ml. of piperidine and 15 ml. of dry pyridine at 70°. The reaction mixture was poured into dilute hydrochloric acid and the solid which precipitated was purified by extraction with sodium bicarbonate, acidification and recrystallization of the material so obtained from ethanol. After two recrystallizations the product had m.p. 193.2–195.5°. A third recrystallization failed to change the m.p.

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.30; H, 6.24; N, 6.56.

Benzylidenemalonic acid, m.p. 195–196, was prepared by the method of Claisen and Crismer.[17]

Reaction Products.—Ethyl hydrogen benzylidenemalonate (3.0 g.) was heated in pyridine solution under kinetic conditions until decarboxylation was complete and the product isolated by pouring the reaction mixture into cold dilute hydrochloric acid, extracting with ether and distilling the liquid obtained in the extract through a semi-micro column. There was obtained 1.85 g. (77%) of ethyl cinnamate, b.p. 98–99° (0.5 mm.), n^{20}_D 1.5597. It is apparent from the refractive index that the product obtained was the pure *trans* isomer (lit.[18] n^{20}_D 1.5598 for ethyl *trans*-cinnamate, n^{20}_D 1.545 for ethyl *cis*-cinnamate).

By the same procedure there was obtained from 5.0 g. of benzylidenecyanoacetic acid 3.35 g. (89.9%) of a mixture of 65% *trans*- and 35% *cis*-cinnamonitrile, b.p. 86–89° (0.7 mm.), n^{20}_D 1.5968 (lit.[3] n^{20}_D 1.6032 for *trans*-cinnamonitrile and n^{20}_D 1.5849 for *cis*-cinnamonitrile).

The same products of decarboxylation were isolated from runs in which thioacetic acid was used as catalyst. In the case of the cyano acid IB the yield of nitrile obtained was low (45%) due to reaction of the nitrile once formed with thioacetic acid.

Kinetic Data.—The apparatus and procedure used for measuring rates of decarboxylation have been described previously.[2] The only modification made in the present work was the agitation of the reaction mixture by vigorous and constant *vibration* rather than by shaking.

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[17] L. Claisen and L. Crismer, *Ann.*, **218**, 131 (1883).

[18] K. v. Auwers and E. Schmellenkamp, *Ber.*, **54**, 631 (1921).

URBANA, ILLINOIS

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

The Ionization and Dissociation of Certain Weakly Acidic Substances in Pyridine

BY ELIAS J. COREY

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A study has been made of the behavior of certain phenols and carboxylic acids in pyridine. 2,6-Dinitro-3,4-xylenol (I) and 2,5-dinitrophenol (II) are partially ionized in pyridine solution in contrast to the extremes, *p*-nitrophenol (not appreciably ionized) and 2,4,6-trinitrophenol (essentially completely ionized). Solutions of I and II contain as ionic species both dissociated ions and pyridinium–phenoxide ion-pairs. Carboxylic acids have been shown to be only slightly ionized and dissociated in pyridine.

The nature and relative amounts of the species which result when weakly acidic compounds—phenols, carboxylic acids, etc., are dissolved in pyridine have not been determined previously despite the frequency with which reactions involving solutions of acids in pyridine are carried out.[1]

In connection with an investigation of decarboxylation reactions in pyridine[2] we have determined in an approximate way the fate of several acidic substances in this solvent.

Results and Discussion

From the data in Table I it is apparent that *p*-nitrophenol is not appreciably ionized in pyridine and that 2,4,6-trinitrophenol is completely ionized. The dinitrophenols are intermediate and the acidities of these substances in pyridine parallel qualitatively the pK_a values in water.

The behavior of 2,6-dinitro-3,4-xylenol (I) and that of 2,5-dinitrophenol (II) were investigated in detail since I and II are moderately ionized in pyridine and are potential indicators for the study of colorless acids.

TABLE I

Compound	pK_a (25°)	Solutions in pyridine, color	Solutions in pyridine + N-ethyl piperidine Color	Change in color from pure pyridine
p-Nitrophenol	9.19	Almost colorless	Yellow	++
2,5-Dinitrophenol	5.15	Pale yellow	Yellow-orange	+++
2,6-Dinitro-3,4-xylenol	4.92[a]	Yellow	Deep yellow	+++
2,4-Dinitrophenol	4.00[b]	Deep yellow	Deep yellow	+
2,4,6-Trinitrophenol	..	Deep yellow	Deep yellow	None

[a] In 50% ethanol. pK 4.19 in 50% ethanol.

Spectra of I and II.—Solutions of (I) in pyridine exhibit bands at 360 and 430 mμ (Fig. 1). The spectrum of I in absolute ethanol is characterized by a single band at 347 mμ (log ε 3.6) which corresponds to the 360 mμ band observed in pyridine. In ethanol containing a small amount of the strong base N-ethylpiperidine absorption occurs at 425 mμ (log ε 3.79) only, and there is no band at 347 mμ. The absorption manifested in pyridine of I at 360 mμ is, therefore, attributable to the phenol (the shift $\lambda_{\max}^{\text{ethanol}}$ 347 mμ to $\lambda_{\max}^{\text{pyridine}}$ 360 mμ probably being the result of hydrogen bonding of the phenol with pyridine) and the absorption at 430 mμ to the phenoxide ion.

The spectrum of II in pyridine is analogous to that of I. Phenol absorption occurs at 360 mμ as in the case of I and phenoxide absorption is manifested at 465 mμ (Fig. 2).

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[1] In a brief communication L. E. Krohn and V. K. LaMer, THIS JOURNAL, **53**, 3563 (1931), have reported a study of the change in light absorption of indicators (*e.g.*, thymol blue) in pyridine with varying concentrations of trichloroacetic acid and diethylamine.

[2] E. J. Corey, *ibid.*, **75**, 1163 (1953).

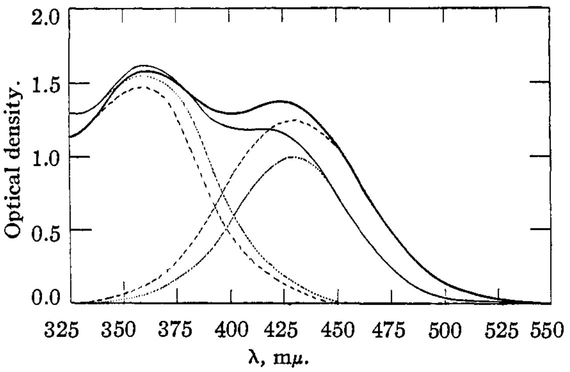

Fig. 1.—Spectrum of I (0.564 × 10^{-3} M) in pyridine: experimental curve —; estimated band envelopes, ----. Spectrum of I (0.564 × 10^{-3} M) in 42.3 × 10^{-3} M pyridinium nitrate in pyridine: experimental curve, —; estimated band envelopes, ...

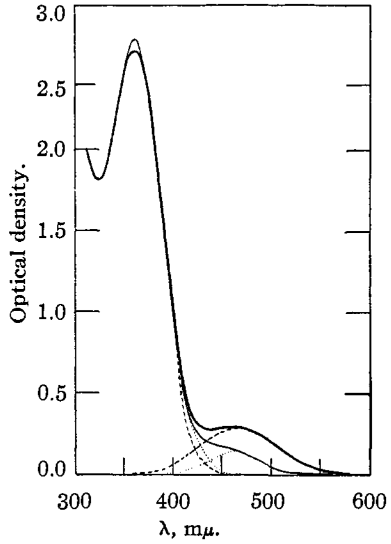

Fig. 2.—Spectrum of II (0.870 × 10^{-3} M) in pyridine: experimental curve, —; estimated band envelopes, ---. Spectrum of II (0.870 × 10^{-3} M) in 42.3 × 10^{-3} M pyridinium nitrate in pyridine: experimental curve, —; estimated band envelopes, ...

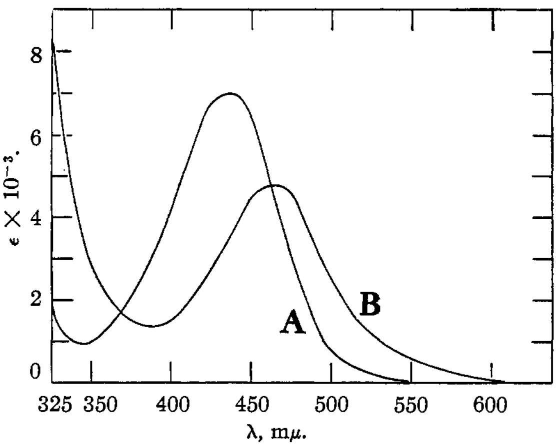

Fig. 3.—Curve A, N-ethylpiperidinium salt of I in pyridine; curve B, N-ethylpiperidinium salt of II in pyridine.

Addition of N-ethylpiperidine to a solution of I in pyridine removes completely the phenol (360 mμ) band and promotes the phenoxide band (430 mμ) to its full intensity (Fig. 3). *When successively larger amounts of pyridinium nitrate are added to pyridine solutions of I, the intensity of the phenoxide band is reduced and rapidly reaches a definite, constant value which is significantly large.* The resulting apparent phenoxide absorption appears as a shoulder on the phenol band (Fig. 1).

The phenol II shows similar behavior (Fig. 2).

Ionization and Dissociation of I and II.—The ionization and dissociation of an acid, HA, in pyridine may be represented by the equations

$$\begin{tikzcd} n\mathrm{HA} + n\mathrm{C_5H_5N} \arrow[r, shift left, "K'"] \arrow[d, shift left] & (\mathrm{C_5H_5NH^+A^-})_n \arrow[l, shift left] \arrow[d, shift left] \\ n\mathrm{C_5H_5NH^+} \arrow[u, shift left, "K"'] & + nA^- \arrow[u, shift left, "K''"'] \end{tikzcd}$$

K' is the equilibrium constant for ionization into ion-pairs ($n = 1$) or aggregates of ion-pairs, K'' is the equilibrium constant for the dissociation of the ionized species into simple ions, and K is the overall dissociation constant. If K' is very small relative to K, the only solute species present in appreciable concentration will be HA and the dissociation products $C_5H_5NH^+$ and A^-. In the event that such a situation obtained for solutions of I and II in pyridine, the spectra observed for such solutions containing a large excess of pyridinium nitrate would be attributable to phenol only.[3] From these spectra (taken to be the spectra of the phenols free of phenoxide ions), the spectra of the N-ethylpiperidinium phenoxides and the spectra of I and II at several different concentrations in pyridine alone, one should be able to calculate values for the dissociation constants of I and II, K_{I} and K_{II}, if indeed $K \gg K'$. Actually no constants can be calculated for I and II as is indicated in Table II. It is clear, then, that the acid–base reaction under consideration involves more than simple dissociation.[4]

If K' is not very small relative to K, appreciable concentrations of ion-pairs and/or ion aggregates will exist in solution. A knowledge of the values of n involved in the acid–base reaction and the concentrations of the species involved in the equilibria would allow the calculation of K and K'_n, where K'_n is the constant K' for a given value of n.

$$K = \frac{[\mathrm{C_5H_5NH^+}][\mathrm{A^-}]}{[\mathrm{HA}]} \text{ and } K'_n = \frac{[(\mathrm{C_5H_5NH^+A^-})_n]}{[\mathrm{HA}]^n}$$

Such calculations have been carried out for solutions of I and II in pyridine on the following basis. The decrease in phenoxide-ion absorption to a constant value upon addition of successively larger amounts of pyridinium nitrate is due to repression of the dissociation of phenol to unpaired phenoxide and pyridinium ions. The residual phenoxide absorption is due to the presence of phenoxide–pyridinium ion-pairs (or their aggre-

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[3] It is unlikely that this is actually the case since there would be no ready explanation for the presence of the shoulder at wave lengths corresponding to phenoxide ion absorption.

[4] This result was anticipated on the basis of the excellent work of D. S. Burgess and C. S. Kraus [THIS JOURNAL, **70**, 708 (1948)] which indicates that completely ionic solutes such as sodium iodide and pyridinium nitrate are only partly dissociated in pyridine solution and exist mostly as ion-pairs.

gates). Obviously, the concentration of ion-pairs will not be decreased by the addition of pyridinium ions, since pyridinium ion does not appear in the expression which defines the constant K'. On the assumption that the extinction coefficients of dissociated phenoxide ions and phenoxide ions in ion-pairs are equal, it is possible to determine values for the concentration of dissociated phenoxide ions, of phenoxide–pyridinium ion-pairs and of un-ionized phenol. For purposes of making approximate calculations it was further assumed that $n = 1$, *i.e.*, the ion-pairs present are not associated. This assumption certainly seems reasonable in view of the low concentrations involved.[4] The calculated values of K and K' are recorded in Table II. The variation in the constants calculated both for I and for II at different concentrations is not much greater than that which stems from uncertainties in the estimation of band intensities.

TABLE II

Compound	I	II
K^a	1.1×10^{-8} to 3×10^{-1}	0.8×10^{-8} to 3×10^{-8}
K^b	$3.0 \pm 0.5 \times 10^{-8}$	$7.5 \pm 1 \times 10^{-4}$
K'	$3 \pm 0.5 \times 10^{-1}$	$3.3 \pm 0.5 \times 10^{-2}$
Concn. range, moles/l. $\times 10^3$	0.1885–0.942	0.500–1.74

[a] Calculated on the basis that the only ionic species present are dissociated ions, *i.e.*, no ion pairs; ($K \gg K'$).
[b] Calculated assuming both ion-pairs and dissociated ions exist in solution.

Therefore, it seems reasonable to conclude that solutions of I and II in pyridine at the concentrations studied contain (1) un-ionized phenol, (2) dissociated phenoxide and pyridinium ions and (3) phenoxide–pyridinium ion-pairs.

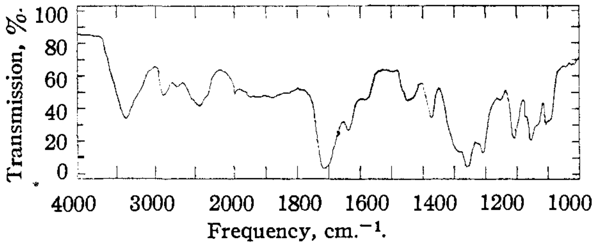

Fig. 4.—Infrared spectrum of III in pyridine.

Dissociation of Carboxylic Acids in Pyridine.—The phenoxide-ion absorption of solutions of II in pyridine (c 1.887 × 10^{-4} M) was decreased to about the same extent by 0.55 × 10^{-4} mole/l. of pyridinium nitrate as by 582 × 10^{-4} mole/l. of ethyl hydrogen isopropylidenemalonate (III) (pK 3.36 in water). Using the K'' found by Burgess and Kraus for the dissociation of pyridinium nitrate (0.5 × 10^{-4}) the dissociation constant, K, for III is found to be $\sim 2 \times 10^{-8}$. One may also estimate from the value of K'' for tetrabutylammonium acetate[4] that K' for III is *ca.* 10^{-4}.

$$(CH_3)_2C{=}C(X){-}COOH \qquad \text{III, } X = COOC_2H_5 \quad \text{IV, } X = CN$$

These values are in agreement with the infrared spectrum of a solution of III in pyridine. There is strong carbonyl absorption at 1710–1725 cm.$^{-1}$ due to the carboxyl and ester carbonyl groups, but little or no absorption at 1600 cm.$^{-1}$, the frequency at which strong absorption by carboxylate ions usually occurs. The carboxylate-ion band also is absent from the spectra of other carboxylic acids (acetic acid, (pK 4.73 in water), the cyano acid IV (pK 3.04 in water) which were studied.

Experimental

Materials.—The pyridine, b.p. 115.5–115.8°, used in the present work was obtained by distillation of Mallinckrodt Analytical Reagent pyridine through a 30-cm. column packed with stainless steel helices.

Pyridinium nitrate was prepared from pure pyridine and concentrated nitric acid. The solid so obtained was washed with ice-water, *t*-butyl alcohol and ether and dried *in vacuo* over phosphorus pentoxide.

The N-ethylpiperidine ("suitable for penicillin G determination") was obtained from Eastman Kodak Co.

2,6-Dinitro-3,4-xylenol, m.p. 126–127°, was prepared by the method of Datta and Varma.[5] The ionization constant in 50% alcohol was determined by titration with 0.05 N sodium hydroxide in 50% alcohol using a glass electrode.

2,5-Dinitrophenol, m.p. 106–107°, was made by the nitration of *m*-nitrophenol.[6]

Spectra.—The spectra in the visible of pyridine solutions were determined by means of a Cary recording spectrophotometer model 11 using a 1-cm. all-quartz cell.

The infrared absorption spectra[7] were obtained with a Perkin-Elmer model 21 double beam spectrophotometer using 0.1-mm. matched, sodium chloride cells. The space occupied by the acid in pyridine was compensated for by using in the solvent cell a sample of pyridine diluted with the necessary amount of carbon tetrachloride (for 30 mg./ml. of III in pyridine: 20 volumes of pyridine diluted to 20.3 volumes with carbon tetrachloride).

Calculations.—The extinction coefficients for the phenoxide ions of I and II were calculated from the spectra of the N-ethylpiperidinium phenoxides (Fig. 3). The intensities of phenoxide absorption for solutions of I and II in pyridine alone were found by graphical separation of the overlapping phenol and phenoxide-ion bands (Figs. 1 and 2). Concentrations of phenoxide ion were calculated from the equation $C = D/k$, where k is the extinction coefficient for the phenoxide ion and D is the optical density.

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[5] R. L. Datta and P. S. Varma, *ibid.*, **41**, 2039 (1919).
[6] H. H. Hodgson and E. W. Smith, *J. Chem. Soc.*, 2268 (1931).
[7] Determined by Miss Helen Miklas and Mrs. Rosemary Hill.