$$i\text{-PrCH(OH)NHCH}_2\text{R} \xrightarrow{k_0} i\text{-PrCH}{=}\overset{+}{\text{N}}\text{HCH}_2\text{R} + \text{OH}^-$$

significant steric effects on K_{ca} but only very small steric effects on k_0K_{ca}, it follows that the steric strains introduced by the addition of the amines to isobutyraldehyde have been largely relieved in the transition state for loss of hydroxide ions from the adducts.

With only three reliable values of k_hK_{ca} (the maximum amount of acid catalysis observed with 2-methoxyethylamine being barely enough to double the reaction rate) little can be said about the probable importance of steric effects, but the monotonic increase of k_hK_{ca} with increasing pK_a shows that the overall process of acid-catalyzed imine formation is slowed by electron-withdrawing substituents, whose effect is seen to be much smaller than in the case of the uncatalyzed reaction. It is not surprising to find the more facile acid-catalyzed reaction (the values of k_h are around $10^8 M^{-1}$ sec^{-1}) to be a more nearly random process than the uncatalyzed reaction.

From the fact that log k_0K_{ca} and log k_hK_{ca} both increase with increasing pK_a, but with proportionality constants (*e.g.*, P in eq 2) less than 1.0, it follows that the most rapid imine formation at a given pH will take place with an amine whose conjugate acid has a pK_a in the vicinity of the given pH. The less basic amines are less reactive and the more basic amines exist to too great an extent in their protonated forms.

Experimental Section

Reagents. Gas–liquid partition chromatography showed that the 2,2,2-trifluoroethylamine was about 96% pure and that the other amines were more than 99% pure.

Kinetic Runs. Stopped-flow spectrophotometric measurements were made as described previously.[10] Each of the values of K_{ca} and K_{ic} listed in Table I is the average of 10–56 individual determinations. Each of the values of k_cK_{ca} plotted in Figure 1 is the average of the values obtained in 4–8 runs. In no set of runs was the standard deviation greater than 17%; in the average set it was 7%. The total concentration of isobutyraldehyde used ranged from 0.018 to 0.040 *M*. The total concentration of amine (including ammonium ion) ranged from 0.02 to 0.17 *M* (the higher concentrations being used in some of the runs in the more acidic solutions) except in the case of trifluoroethylamine where concentrations around 0.38 *M* were used because of the small values of K_{ca} and K_{ic}. The initial pH's of the reaction mixtures (after establishment of the carbinolamine equilibrium) were calculated from the pK_a values of Table I. These pK_a values refer to zero ionic strength but to a reaction whose equilibrium constant is independent of the ionic strength, according to the limiting form of the Debye–Hückel equation. The ionic strength in the reaction with propylamine was increased from 0.005 to 0.05, 0.31, and 0.41 *M* by added sodium chloride with an accompanying overall increase in reaction rate of about 10%. The ionic strength in the other runs, due almost entirely to the perchlorate of the amine being studied, ranged up to as much as 0.17 *M* in the more acidic solutions.

The Kinetics of Iodination of Propiolic Acid

Elizabeth Mauger[1] **and Ernst Berliner***

Contribution from the Marion Edwards Park Laboratory,
Bryn Mawr College, Bryn Mawr, Pennsylvania 19010. *Received March 29, 1971*

Abstract: The kinetics of the addition of iodine to propiolic acid and its anion were studied in water in the presence of iodide ion at varying pH and salt concentrations. The rate of the reaction can be represented by the rate law $-\text{d}(\text{I}_2)_\text{T}/\text{d}t = k_2(\text{A})(\text{I}_2) + k_3(\text{A})(\text{I}_2)(\text{I}^-)$, where A is the substrate and $(\text{I}_2)_\text{T}$ the total titratable iodine. The products of the reaction are *trans*-2,3-diiodoacrylic acid and a substance related to pyruvic acid. The amount of the latter depends on the iodide ion concentration. The first term in the rate equation corresponds to an electrophilic attack by iodine molecules. There are several mechanistic interpretations for the second term. The most attractive interpretation for this term involves a termolecular, but not synchronous, attack of iodine and iodide ion on the triple bond, with the nucleophile initiating the reaction on the free acid and the electrophile the reaction on the anion.

The kinetics of iodination of sodium phenylpropiolate are characterized by a three-term rate equation in which the three terms correspond, respectively, to an iodide ion catalyzed termolecular reaction of iodine, a reaction of free iodine, and one which possibly involves the hydrated iodine cation.[2] We now report the results of a study of the iodination of propiolic acid, HC≡C—COOH, and its sodium salt. As before, reaction was conducted in water and in the presence of iodide ion, at varying pH and salt concentrations.

Results

Under all conditions which were investigated, the rate is given by $-\text{d}(\text{I}_2)_\text{T}/\text{d}t = k_\text{obsd}(\text{A})(\text{I}_2)_\text{T}$, where $(\text{I}_2)_\text{T}$ is the total titratable iodine, (A) the concentration of the acid or anion, and k_obsd is the observed second-order rate constant. The constant k_obsd remains constant over a fourfold variation in the concentrations of either of the reactants. The reaction has a strong dependence on salts, which accelerate the rate in all cases.

The Effect of Iodide Ion. The effect of iodide ion on the rate of iodination of the acid was studied in five sets of runs, in which the concentration of iodine was held constant, but in which the iodine to iodide

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[1] Taken in part from the Ph.D. Dissertation of E. Mauger, Bryn Mawr College, May, 1970; United States Steel Fellow in Chemistry, 1967–1968; National Science Foundation Trainee, 1968–1970.

[2] M. H. Wilson and E. Berliner, *J. Amer. Chem. Soc.*, **93**, 208 (1971).

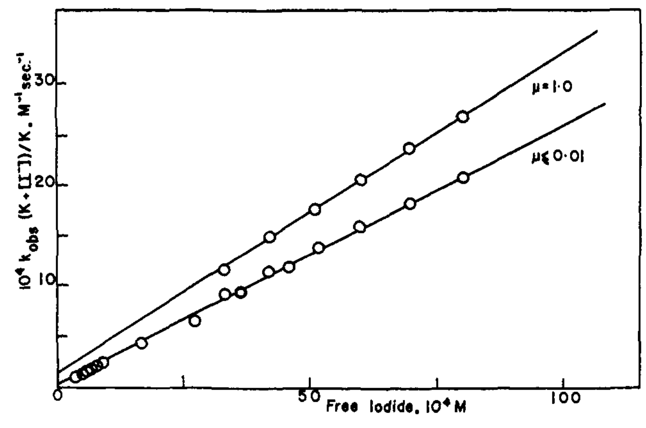

Figure 1. Dependence of the rate on iodide ion concentration.

ratio was varied as much as fivefold. The total iodide ion concentration was varied from 1.0 *M* to 5 × 10^{-4} *M*. At a high concentration of iodide ion (0.05–1.00 *M*), the reaction exhibits only an ionic strength effect. This effect is almost eliminated when the ionic strength is maintained at 2.05 *M* with sodium perchlorate. Under these conditions the rate increases by 2% when the iodide ion concentration is increased from 0.150 to 0.550 *M*. In the iodide ion range from 5 × 10^{-2} *M* to 5 × 10^{-4} *M* a linear relationship is obtained when k_{obsd} is plotted against $(I^-)K/(K + I^-)$, where *K* is the dissociation constant of the triiodide ion (1.55 × 10^{-3} at 30°), and I^- the concentration of free iodide ion (Figure 1). At high iodide ion concentration the above term reduces to *K*, and the reaction is independent of iodide ion. The kinetic dependence on iodide ion is consistent with a rate law of the form

$$-\mathrm{d}(I_2)_T/\mathrm{d}t = k_2(A)(I_2) + k_3(A)(I_2)(I^-) \qquad (1)$$

From the slope and intercept of the line, k_2 is obtained as 0.26 × 10^{-4} l./(mol sec) and k_3 as 0.26 l.²/(mol² sec).

Effect of Acids and Buffers. The addition of increasing amounts of hydrochloric or of perchloric acid (up to 0.15 *M*) increases the rate. This is an ionic strength effect, because catalysis is eliminated when an HCl–NaCl buffer at constant ionic strength (μ = 1.0 *M*) is used. The effect of acetic acid–sodium acetate buffers is analogous to that observed in the iodination of phenylpropiolic acid.[2] Three sets of buffers were used, each at a constant ionic strength and each spanning the same pH range, roughly from pH 4.5 to 6. The rates decrease with increasing hydrogen ions, but the decrease is least in a 0.25 *M* buffer and most in a 1.00 *M* buffer. This behavior is best attributed to a medium effect, caused by the acetic acid, and not to a true pH or general acid dependence.[2] The results with phosphate buffers were similar. At high concentrations of buffer (μ = 0.55–1.55 *M*) and in the approximate pH range 4–7, the rate increases with pH and with increasing concentration of disodium hydrogen phosphate. This effect also diminishes with a decrease in total buffer concentration and is ascribed to a marked dependence of the rate on the divalent ion.[3] At lower concentrations of buffers, and at pH lower than 4, there is observed a small but definite increase in rate with increasing hydrogen ion concentration (Figure 2). While it is difficult to disentangle completely salt effects from pH effects, this effect appears to be real at low ionic strength.

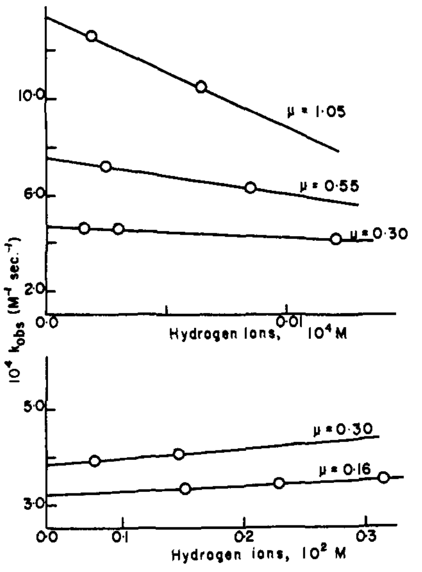

Figure 2. Dependence of the rate on phosphate buffers.

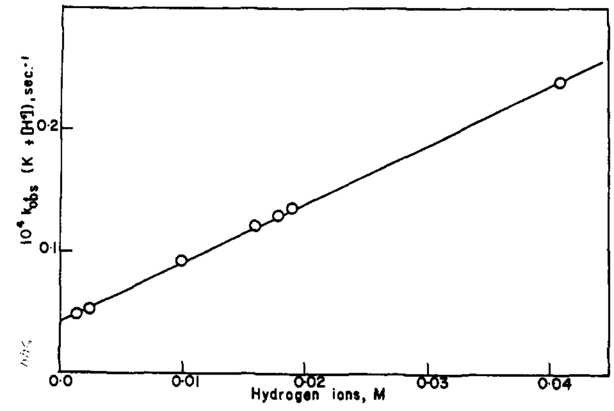

Figure 3. Dependence of the rate on hydrogen ion concentration.

Iodination of Sodium Propiolate. A comparison of the rates of iodination of propiolic acid and its sodium salt shows that at the same ionic strength the acid is more reactive than the anion. Because propiolic acid is a fairly strong acid (K_D = 1.41 × 10^{-2}), solutions of the acid in water are considerably dissociated, and the rate constants k_{obsd} quoted for propiolic acid must be composite, unless one of the two species reacts very much faster than the other. It is possible to obtain rate constants for the reactions of the anion and the acid from a plot of the observed rate constants as a function of pH by making use of eq 2

$$k_{obsd}[K_D + (H^+)] = k_A K_D + k_{HA}(H^+) \qquad (2)$$

Rate constants k_{obsd} were measured over the pH range 2.88–1.39, obtained by the addition of small amounts of HCl or $HClO_4$ (0.005–0.05 *M*) (Figure 3). The ionic strength is sufficiently low that catalysis probably cannot be attributed to an effect of ionic strength. From eq 2, k_A is calculated to be 3.00 × 10^{-4} and k_{HA} = 4.8 × 10^{-4} l./(mol sec); the acid reacts 1.6 times faster than the anion.

Reaction in the Absence of Iodide Ion. In these runs rates fell off rather strongly during individual runs,

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(3) B. S. Painter and F. G. Soper, *J. Chem. Soc.*, 342 (1947).

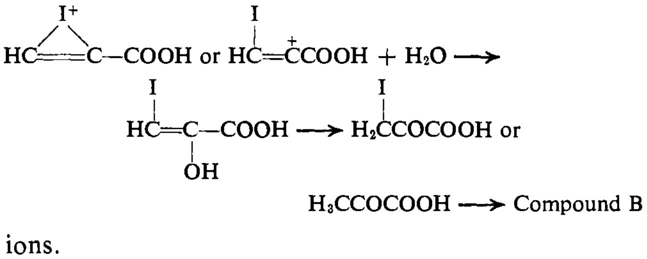
introducing large uncertainties. Nevertheless, the reaction of sodium propiolate is slightly faster than that of the acid, and the addition of HCl or $HClO_4$ decreases the rate of reaction of the acid. If it is assumed that this reaction is identical with the reaction reported as the k_2 process, then for this part of the reaction the "electrophilic" order $HC{\equiv}CCOO^- > HC{\equiv}CCOOH$ is apparently obtained.

Activation Energies. Activation parameters for the iodination of propiolic acid were determined from a plot of log k_{obsd} against $1/T$ at six temperatures between 15 and 40°. At the concentration of iodide ion used (0.05 *M*) almost all the reaction takes place by the k_3 process. The activation energy ΔE_a is 16.3 ± 0.2 kcal/mol and $\Delta S^{\ddagger} = -22 \pm 1$ eu.

Iodination of Tetrolic Acid, $CH_3C{\equiv}CCOOH$, and Its Sodium Salt. Under comparable conditions sodium tetrolate reacts about 1.6 times faster than sodium propiolate, which indicates that for the anions, the reaction is led by an electrophile. There were not sufficient data to permit the treatment in eq 2 for a determination of rate constants for tetrolic acid itself. However, an approximate analysis indicated that k_{HA} for tetrolic acid is 1.9×10^{-4} l./(mol sec), which is less than that for sodium tetrolate (4.8×10^{-4} l./(mol sec)), as expected for an electrophilic attack. Yet, tetrolic acid itself reacts more slowly than propiolic acid and the methyl group does not have an activating effect in the acid, although it does so in the iodination of the anion.

Product Isolation. Reaction products were isolated from runs with and without added iodide ion. The same two products were isolated from all reaction mixtures. The major product was *trans*-2,3-diiodoacrylic acid, identified by a comparison with an authentic sample. The minor component B, a liquid, is related to pyruvic acid, but because of the very small amounts available, positive identification could not be obtained (see Experimental Section).

It seemed likely that the compound B is a hydrate of pyruvic acid, formed from a cationic intermediate through nucleophilic attack by water, followed by ketonization as shown. The compound gives no Beilstein test, and we cannot be certain if it contains iodine, but the halogen in α-keto acids is easily reduced by halide ions.



The quantitative separation is subject to uncertainties, particularly with regard to the minor component, but the effect of iodide ion on the product ratio is large. At a 0.1 *M* concentration of iodide ion, the amount of diiodoacrylic acid is 98% and that of the ketonic product is 2%. When no iodide was initially present, 76% of diiodoacrylic acid was formed and 24% of the pyruvic acid derivative.

Discussion

The kinetics are compatible with the two-term rate eq 1. The iodination of sodium phenylpropiolate contained a third term which is possibly due to a reaction of the hydrated iodine cation, or a fast reaction of the substrate with iodine, followed by a rate-determining attack by water.[2] This term is absent in the iodination of propiolic acid over the range of iodide ion concentration studied.

The process represented by k_2 almost surely involves a bimolecular attack by free iodine molecules. The available evidence points to an electrophilic attack because in the few runs that were conducted in the absence of iodide ion this term must predominate, and the anion reacts faster than the acid itself. The k_2 process contributes only very little to the total rate at moderate iodide ion concentrations and is probably solely responsible for the formation of the small amount of the pyruvic acid. Diiodoacrylic acid must also be formed in the k_2 reaction, because in the absence of iodide ion, 74% of it is produced (some of it probably by the k_3 reaction because iodide ion is produced in the formation of pyruvic acid). But at a 0.1 *M* concentration of iodide ion, when the k_3 reaction predominates, the amount of *trans*-diiodoacrylic acid increased to 98%, and that of pyruvic acid decreased to 2%. Because all of the isolated acrylic acid is the trans isomer, and because iodine is a superior neighboring group,[4] it is likely that the intermediate is a cyclic iodonium ion.

The second term in eq 1 allows for numerous mechanistic interpretations. It is represented above as a termolecular reaction of iodine, iodide ion, and the substrate. Because of the triiodide ion equilibrium, this term is equivalent to $k_3'(A)(I_3^-)$, where $k_3' = Kk_3$. The reaction could, therefore, involve a bimolecular attack by triiodide ion. Trihalide ions have repeatedly been implicated as weak electrophiles, both in aromatic[5] and olefinic[6] halogenations, and are considered to be carriers of electrophilic halogens. In the present case k_3' is 150 times as large as k_2, and the triiodide ion would have to be a considerably stronger electrophile than iodine, which is inherently unlikely. The trihalide ion could, however, also act as a nucleophile. Nucleophilic attacks by trihalide ion have been mainly discussed in connection with halogenations of α,β-unsaturated olefinic systems under conditions of acid catalysis, where attack should take place on a protonated carbonium ion.[7] If the reaction involved iodine and iodide separately, it could not only be concerted but also involve a rapid and reversible complexing of A with I_2 followed by a rate-determining attack of iodide ion. Finally, the reaction could involve a rapid and reversible nucleophilic attack by iodide ion to form a vinylic carbanion, followed by a slow electrophilic attack by iodine.[8] All these possibilities conform to the require-

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(4) R. C. Fahey and H.-J. Schneider, *J. Amer. Chem. Soc.*, **90**, 4429 (1968); A. Hassner, F. B. Boerwinkle, and A. B. Levy, *ibid.*, **92**, 4879 (1970).

(5) E. Berliner and M. C. Beckett, *ibid.*, **79**, 1425 (1957); R. P. Bell and E. N. Ramsden, *J. Chem. Soc.*, 161 (1958); R. P. Bell and D. J. Rawlinson, *ibid.*, 63 (1961).

(6) P. D. Bartlett and D. S. Tarbell, *J. Amer. Chem. Soc.*, **58**, 466 (1936); R. P. Bell and M. Pring, *J. Chem. Soc. B*, 1119 (1966); R. P. Bell and D. Dolman, *ibid.*, 500 (1968); J. H. Rolston and K. Yates, *J. Amer. Chem. Soc.*, **91**, 1483 (1969); N. Kanyaev, *Zh. Obshch. Khim.*, **29**, 841 (1959); *Chem. Abstr.*, **54**, 1249f (1960).

(7) P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 2838 (1950); R. E. Buckles and J. P. Yuk, *J. Amer. Chem. Soc.*, **75**, 5048 (1953). See also the discussions in P. B. D. de la Mare, *Quart. Rev., Chem. Soc.*, **3**, 126 (1949), and P. B. D. de la Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," Elsevier, New York, N. Y., 1966.

(8) See, for instance, S. I. Miller and R. Tanaka, *Selec. Org. Trans-*

ment that the rate-controlling transition state contain an iodine molecule and an iodide ion. All of them have been considered in connection with olefinic halogenation.[9]

A distinction cannot be made on kinetic grounds, and the chemical evidence is not overwhelming. More help is provided by a consideration of the effect of structural changes in the substrate, and of the products of the reaction. Propiolic acid reacts faster than its anion and faster than tetrolic acid, which is a "nucleophilic order" of attack, although propiolate anion reacts more slowly than tetrolate anion which is the reverse. The attack on the triple bond cannot, therefore, be designated as clearly electrophilic or clearly nucleophilic, unless separate attacking species are postulated. The effects of structural changes are small and nearly balanced. The acid catalysis observed at a pH below 4 is probably not a true catalysis. Above pH 4 almost all of the propiolic acid is present as the anion, and no catalysis was observed in this pH region. Below pH 4 more acid is present, and because the acid reacts faster than the anion, this has a semblance of an acid catalysis.

The most attractive mechanism is a termolecular, but not synchronous, one. In the reaction of the acids, bond making to the nucleophile may precede the attachment of the electrophile in the transition state, and the carbon would attain some carbanion character without fully developing a carbanion. This accords with the well-documented susceptibility of the triple bond toward nucleophilic reagents and the great nucleophilicity of iodide ion. In the reaction of the anions the attack of the electrophile could run ahead of the attachment of the nucleophile. Such a spectrum of transition states is now envisaged for many E2 elimination reactions[10] and is preferable to postulating separate attacking species for the acid and the anion. Since the transition states would be different for the reactions of the acids and the anions, a rate comparison between the two becomes irrelevant, but *within* the acid or anion series the effect of the methyl groups would be fully accounted for. A similar suggestion has recently been made to explain a nonlinear Hammett plot in the bromide ion catalyzed bromination of substituted phenylmethylacetylenes.[11,12]

The termolecular mechanism suggested for the third-order term in the iodination of propiolic acid would not only account for the kinetics, but also for the exclusive trans addition, the absence of solvent participation, and the near balance of the structural effects. These features of the reaction combine to make this mechanism the most attractive one, even if there is no certain evidence on which to eliminate the others.

Experimental Section

Materials. Propiolic acid (Aldrich Chemical Co.) was stored under refrigeration and redistilled before use (bp 46–48° (8 mm)). Tetrolic acid (Farchan Research Laboratories) was recrystallized from ether or from ligroin–ether, mp 75.5–76.5° (lit.[13] 76°). *trans*-2,3-Diiodoacrylic acid, prepared according to the literature,[14] melted at 103.3–104.5° (lit.[14,15] 104, 106°) after two recrystallizations from carbon tetrachloride and one from cyclohexane. Sodium propiolate and sodium tetrolate were prepared from the acids with sodium ethoxide.[2] All inorganic salts used in the kinetics were reagent grade chemicals, which, except for iodine, were dried overnight at 110°.

Kinetic Measurements. The temperature for the kinetic measurements was 30.0 ± 0.05°, except in runs for the determination of the activation parameters. All stock solutions were made up at the appropriate temperatures. Reaction was followed by titration of unreacted iodine with standard sodium thiosulfate solution.[2] Most of the runs were conducted under second-order conditions, and rate constants were calculated by a least-squares computer program. A few runs were conducted under pseudo-first-order conditions. Runs were followed to 40–60% completion. Except in a very few cases, the standard deviations within one run were less than 1%. Duplicate runs agreed within a few per cent. Titration of three different samples after ten half-lives demonstrated that the additions went more than 99% to completion.

Isolation of Products. At moderate concentrations of iodine (iodine = 0.05 *M*, potassium iodide = propiolic acid = 0.10 *M*), reaction mixtures were made up in 100- or 200-ml flasks. At the end of ten half-lives a very faint color of iodine persisted in the reactions of propiolic acid, but not in those of sodium propiolate. After addition of a small amount of sodium bisulfite the products were extracted repeatedly with reagent grade ether. The recovery was about 85%, calculated on the basis of formation of diiodoacrylic acid. The diiodoacrylic acid was isolated and crystallized until pure (mp 103.3–104.5°). The combined mother liquors were evaporated to dryness and analyzed by thin-layer chromatography.

Reactions without added iodide (iodine = 0.001 *M*, propiolic acid = 0.05 *M*) were run on a 1-l. scale. About 8% of iodine remained unreacted after ten half-lives. These reaction mixtures were worked up by continuous extraction with reagent grade ether. From each of various duplicate runs the same two products were obtained. All of the product (about 500 mg) was analyzed directly by quantitative tlc. Qualitative analysis by tlc was carried out as described before.[2] The developing solvent was chloroform saturated with formic acid. The starting material remained at the origin. Product B (see text) migrated the fastest followed by the diiodoacrylic acid.

For preparative tlc 20 × 20 cm glass plates were coated with 0.5 mm of silica gel G (Merck), which had been washed with ether for several hours. Up to 200 mg of residue from the combined mother liquors could be separated on each plate. The recovery factor from the plates was about 65%. The nmr spectrum of the diiodo fraction showed the presence of some product B, so that the separation on the silica gel was not complete. The amount of B present in this fraction was calculated from the areas of their respective hydrogen peaks. Because the amount of B from 1-l. runs was only about 5–10 mg, fractions from several runs were combined for analysis. Yields of the ketonic product are based on the hydrate. The quantitative results are only approximate.

Compound B gives a weak positive test with 2,4-dinitrophenylhydrazine and a strong positive test with $FeCl_3$ on a silica thin-layer plate. A redistilled sample of pyruvic acid did not migrate on the silica gel thin-layer plate used for the thin-layer chromatography under conditions where product B migrated almost as rapidly as the solvent front. Also, pure pyruvic acid gave only a faint $FeCl_3$ test. However, upon treatment of commercially obtained and redistilled pyruvic acid with water, extraction into ether, and separation on silica gel plates, under conditions identical with those used for the separation of the reaction mixtures, a fraction was obtained which is very mobile on silica gel and gives a strong positive test with $FeCl_3$. The infrared spectrum of this compound is almost identical with that of B, but not with that of pyruvic acid prior to the water–ether treatment. The nmr spectrum of compound B is identical with that of treated pyruvic acid. However, the acidic hydrogen, present in untreated pyruvic acid, is absent.

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form., **1**, 143 (1970); *Chem. Abstr.*, **74**, 63614b (1971); G. F. Dvorko and D. F. Mironova, *Ukr. Khim. Zh.*, **32**, 362 (1966); *Chem. Abstr.*, **65**, 7014 (1966), and earlier papers by E. A. Shilov and G. F. Dvorko.

(9) See de la Mare, ref 7; P. B. D. de la Mare and R. Bolton, ref 7; R. C. Fahey, *Top. Stereochem.*, **3**, 237 (1968); J. E. Dubois and E. Bienvenue-Goetz, *Bull. Soc. Chim. Fr.*, 2086 (1968).

(10) D. V. Banthorpe in "Studies on Chemical Structure and Reactivity," J. H. Ridd, Ed., Methuen and Co., London, 1966, Chapter 3.

(11) J. A. Pincock and K. Yates, *Can. J. Chem.*, **48**, 3332 (1970); *J. Amer. Chem. Soc.*, **90**, 5643 (1968).

(12) Third-order kinetic terms have been identified with termolecular reactions in the above reaction (ref 11) and in the addition of HCl to hexyne; R. C. Fahey and D. J. Lee, *ibid.*, **90**, 2124 (1968); **88**, 5555 (1966).

(13) C. J. Wilson and H. H. Wenzke, *ibid.*, **57**, 1265 (1935).

(14) B. Homolka and F. Stolz, *Chem. Ber.*, **18**, 2282 (1885).

(15) F. Kai and S. Seki, *Chem. Pharm. Bull.*, **14**, 1122 (1966).

Only one absorption peak is obtained (at τ 8.77), which is further upfield than the methyl peak in pyruvic acid itself. A similar shift in the absorption in the methyl peak is known to accompany the formation of the hydrate of the parent acid.[16] Uncertainty in the assignment of a definite structure to product B results primarily from the absence of the acidic hydrogen in the nmr spectrum. For this reason a definite structure cannot be assigned to compound B at the present time, but we are certain that it is related to pyruvic acid. Infrared spectra were taken on a Perkin-Elmer infracord, and nmr spectra on a Varian A-56/60 nmr spectrophotometer in $CDCl_3$ which contained TMS. All pH measurements were made on a Beckman Model G pH meter.

Acknowledgment. This work was supported by National Science Foundation Grant No. GP-4986, which is gratefully acknowledged.

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(16) For a recent survey of the literature on nmr spectra of pyruvic acid and its hydrate, see N. Hellström and S.-O. Almqvist, *J. Chem. Soc. B*, 1396 (1970).

The Mechanism of the Aromatization of Arene Oxides

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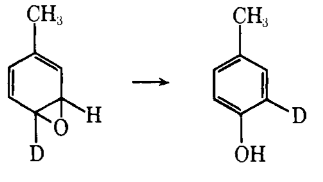
Contribution from the Department of Chemistry, University of California, Santa Barbara, Santa Barbara, California 93106. *Received March 17, 1971*

Abstract: The kinetics of the aromatization of arene oxides has been studied at 30° (μ = 1.0) between pH 2.5 and 14.0. The pH–log k_{obsd} profiles for benzene oxide (**1**) and naphthalene oxide (**2**) are characterized by a straight line of slope -1.0 in the acid region in agreement with specific acid catalysis, and a plateau in the pH >7 region indicating a spontaneous aromatization. With phenanthrene oxide (**3**) only the acid-catalyzed portion was detected. For the spontaneous aromatization the entropy of activation ($\Delta S^{\ddagger} = -25.7$), solvent deuterium kinetic isotope effect ($k_1^{H_2O}/k_1^{D_2O} = 1.33$) at pH 12, and the established requirement of the NIH shift are in accord with a mechanism involving a rate-determining 1,2-hydride shift to form an enone which rapidly tautomerizes to the phenolic product. The detailed mechanism is discussed in light of the experimental data.

The oxidation to phenolic compounds is one of the most important biological reactions of aromatic hydrocarbons (*i.e.*, conversion of L-phenylalanine to L-tyrosine and the metabolism and detoxification of aromatic hydrocarbons by hydroxylases in the liver). Since it has been suggested that this oxidation proceeds through benzene oxides[3] (**1**) in the case of benzene, and 9,10-phenanthrene oxide[4] (**3**) in the case of phenanthrene, and proved to go *via* 1,2-naphthalene oxide[5] (**2**) in the case of naphthalene, the mechanism of the rearrangement of these arene oxides is of considerable interest. Any mechanism proposed for the aromatization of the arene oxides must incorporate the features of the NIH shift.[6] Thus, 3,4-epoxy-3,4-dihydrotoluene-*4*-^2H undergoes the NIH shift [7] (eq 1) on rearrangement to



(1)

4-hydroxytoluene-*3*-^2H in both the acid and neutral regions and naphthalene oxide-*1*-^2H also undergoes this shift[8] at pH 8. Although the aromatization of arene oxides[9] has been studied in some detail, there is little or nothing known about the catalysis of the reaction. It is stated, however, that proteins and even acetamide catalyze the formation of phenol from **1**,[3] but methanolic acetamide does not catalyze the formation of naphthol from **2**.[5c]

The present study deals with the dependence of the rates of the aromatization of **1**, **2**, and **3** upon lyate species and acetamide concentration.

Experimental Section

Materials. Benzene oxide was prepared by the method of Vogel[10] from 4,5-dibromocyclohexene oxide. The epoxidation of 4,5-dibromocyclohexene followed a modification of Van Tamelen's[11] method using *m*-chloroperbenzoic acid instead of perbenzoic acid. This brought the reaction time down from 1 month to 15 hr in refluxing chloroform. 1,2-Naphthalene oxide[12] and 9,10-phenanthrene oxide[13] were prepared as previously described.

Kinetic Measurements. All experiments reported here were carried out in aqueous solution at 30° with μ = 1.0 (KCl) unless otherwise noted in the text. The rate of disappearance of **1** was followed by recording the decrease in optical density at 250 nm over the entire pH range studied. The rates of formation of 1-naphthol from **2** and 9-phenanthrol from **3** were followed at 235 and 250 nm, respectively, in the same manner. The pH was maintained by the addition of a potassium hydroxide solution controlled by a Radiometer pH-stat assembly. The reactions were followed in a thermostated, stirred cell with a 3-cm path length specifically

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