benzene (400 ml) and the crude products collected by filtration. These products were crystallized from acetonitrile–ethanol. The unreacted starting materials precipitated first and the desired adducts were recovered from the mother liquors by crystallization. The yields, reaction times, and analyses are listed in Table I.

Decomposition of III to N-Benzylideneaniline (IX).—The adduct III (2.0 g) was sublimed at 190° (0.1 mm). The sublimate was crystallized from hexane to yield N-benzylideneaniline, mp 43–44°, identical in every way with an authentic sample.

Anal. Calcd for $C_{13}H_{11}N$: C, 86.2; H, 6.1; N, 7.7. Found: C, 85.5; H, 6.4; N, 7.4.

Registry No.—III, 13144-99-5; IV, 13168-31-5; IV diacetyl derivative, 13145-00-1; V, 603-40-7; V diacetyl derivative, 13145-01-2; VI, 13145-02-3; VII, 602-56-2; IX, 538-51-2; 2,4′-diamino-4″-chlorotriphenylmethane, 13145-08-9; 4,4′-diamino-4″-chlorotriphenylmethane, 13145-09-0.

Catalytic Effects of Substituted Pyridines and Quinolines on the Reaction of Phenyl Glycidyl Ether and Benzoic Acid

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Received December 21, 1966

The catalytic effect of methyl-substituted pyridines and quinolines on the reaction between phenyl glycidyl ether and benzoic acid in xylene was studied at various temperatures and comparative catalytic coefficients were evaluated for these catalysts. The reaction rates decrease from pyridine to 2-picoline, from 2-picoline to 2,6-lutidine, and from quinoline to 2-methylquinoline. Introduction of a methyl group into the 3 or 4 position of pyridine increases the rate, while substitution in the 2 position decreases the rate. This should be due to a steric hindrance, which does not seem to be additive, of larger size than in the reaction of methyl iodide with 2-alkylpyridines and of smaller size than in the reaction of boron trifluoride with these bases. A deviation from a linearity between the rates and the pK_a values can be interpreted neither by a nucleophilicity of the pyridines, by an electrophilicity of their conjugated acids, nor by a linear combination of these two factors. This hindrance might be related to steric strains primarily in the activated complex and secondly in molecular addition compounds in the reaction process.

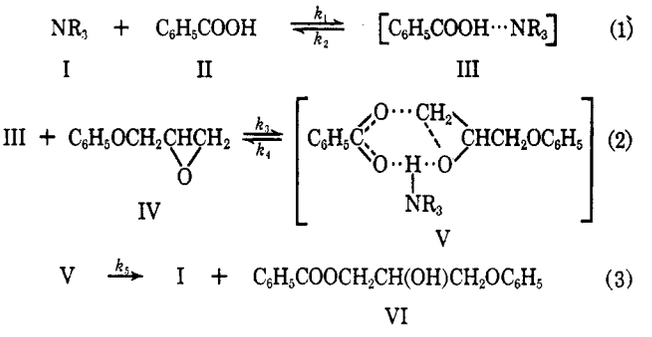
Pyridine catalyzes the solvolyses of acetic anhydride[1-3] and tetramethylphosphorodiamidic chloride,[4] whereas 2-picoline and 2,4- and 2,6-lutidines, which are stronger bases, have no effect on those reactions. This phenomenon has been ascribed to steric requirement of nucleophilic attack by the bases on the electrophiles. Subjection to steric hindrance is one of the criteria which might be considered to characterize nucleophilic as opposed to general base catalysis.

Recently, however, some reactions which are considered to proceed by general base or acid catalysis are found to be subjected to steric hindrance. Gutsche and his co-workers[5] have found that the aldol condensation is promoted by pyridine but hardly by 2,6-lutidine. Covitz and Westheimer[4] have shown that the hydrolysis of methyl ethylene phosphate, mutarotation of glucose, and inversion of menthone are dependent on steric requirement by substituted pyridines used as catalyst.

Pritchard and Long[6] examined the nucleophilic activity of various hindered amines toward propylene oxide in buffered aqueous solutions, while Swain[7] showed that "specific oxonium ion catalysis" for ethylene oxide reactions is observed only at so low buffer concentrations that neither the undissociated buffer acid nor the buffer base participates detectably.

In a previous paper,[8] we suggested and discussed that a hydrogen-bonded complex (III) of a tertiary amine (I) and benzoic acid (II) would play an important role for the tertiary amine catalyzed reaction of phenyl glycidyl ether (IV) and benzoic acid (see Scheme I). If an activated complex or a transition species is of the type V in Scheme I, its stability may be affected by steric requirement.

SCHEME I



Because an appropriate choice of substituents and their position permits one to vary, simultaneously or independently, both the donor tendency of the N-ring atom and the steric requirements of the molecule, substituted pyridines appear to be especially suited to the investigation of the factors which influence the stereochemistry of the transition-state species or the activated complex. This paper reports a catalytic effect of the pyridines on the reaction of phenyl glycidyl ether (PGE) and benzoic acid (BA) in xylene.

Experimental Section

Materials.—Reagent grade PGE was dried over calcium hydride for several days and distilled at reduced pressure. The fraction boiling at 103° (6 mm) was collected for use. Reagent grade benzoic acid was recrystallized from its aqueous

(1) (a) S. L. Bafna and V. Gold, *J. Chem. Soc.*, 1406 (1953); (b) V. Gold and E. G. Jefferson, *ibid.*, 1409 (1953); (c) V. Gold and E. G. Jefferson, *ibid.*, 1416 (1953).
(2) A. R. Butler and V. Gold, *ibid.*, 4362 (1961).
(3) S. L. Johnson, *J. Phys. Chem.*, **67**, 495 (1963).
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(5) C. D Gutsche and R. S. Buriks, *ibid.*, **84**, 3775 (1962).
(6) J. G. Pritchard and F. A. Long, *ibid.*, **79**, 2365 (1957).
(7) C. G. Swain, *ibid.*, **74**, 4108 (1952).
(8) H. Kakiuchi and Y. Tanaka, *J. Org. Chem.*, **31**, 1559 (1966).

TABLE I

THIRD-ORDER RATE CONSTANTS AT VARIOUS TEMPERATURES, ARRHENIUS PARAMETERS, AND HEAT AND ENTROPY OF ACTIVATION FOR REACTION OF PGE AND BA IN XYLENE[a]

Base	k'' × 10³, l.² mole⁻² sec⁻¹ 96°	108°	118°	E_A, kcal/mole	Log A	ΔS^*_{298}, eu	ΔH^*_{298}, kcal/mole	ΔG^*_{298}, kcal/mole	pK_a (25°)
Isoquinoline	8.71	17.8	31.3	16.5	7.76	−27.0	15.3	23.3	5.46[b]
3-Picoline	7.25	15.0	27.3	17.0	7.97	−26.0	15.8	23.5	5.68[c]
4-Picoline	6.78	14.2	25.8	17.1	7.97	−26.0	15.9	23.6	6.02[c]
Pyridine	6.27	12.9	24.0	17.1	8.01	−25.8	15.9	23.6	5.17[c]
2,4-Lutidine	5.72	12.1	21.9	17.3	8.05	−25.6	16.1	23.7	6.79[d]
2-Picoline	5.23	11.0	21.0	17.7	8.25	−24.7	16.5	23.9	5.97[c]
4-Methylquinoline	4.80	10.3	17.3	17.8	8.27	−24.6	16.6	23.9	5.20[e]
Quinoline	4.23	9.24	17.2	18.1	8.38	−24.1	16.9	24.1	4.80[e]
2-Methylquinoline	2.76	6.48	12.9	19.8	9.22	−20.2	18.6	24.0	5.42[e]
2,6-Lutidine	1.87	4.70	9.44	20.6	9.52	−18.8	19.4	25.0	6.75[c,d]

[a] The initial concentrations of PGE, BA, and the amine are 0.500, 0.500, and 0.0200 M, respectively. [b] A. Albert and J. N. Phillips, *J. Chem. Soc.*, 1294 (1956). [c] Reference 14b. [d] Reference 14c. [e] Reference 14d.

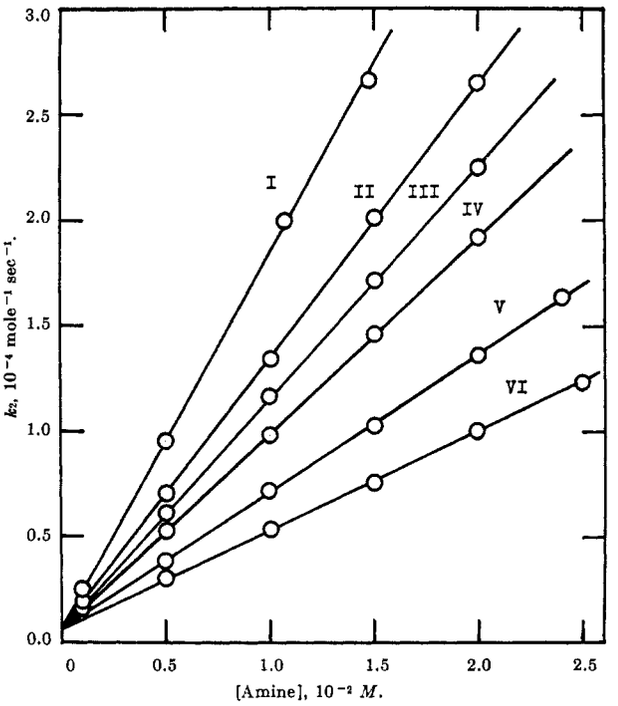

Figure 1.—Effect of initial concentration of pyridines [amine] on the observed second-order rate constant k_2 in the reaction of PGE and BA in xylene at 108° (the initial concentrations of PGE and BA are 5.00 × 10^{-1} M): I, isoquinoline; II, pyridine; III, 2-picoline; IV, quinoline; V, 2-methylquinoline; VI, 2,6-lutidine.

solution and dried over phosphorus pentoxide. The pyridines, quinolines, and isoquinoline were all reagent grade and purified before use. 2,6-Lutidine and 2- and 3-picolines were purified by the procedure of Butler and Gold[9a] and the others were distilled after refluxing with barium oxide.[9] Xylene (mixed isomer) was shaken successively with sulfuric acid and aqueous sodium bicarbonate solution, dried with calcium chloride, and then fractionally distilled. The fraction boiling at 137–139° was collected for use.

Reaction Procedure.—Reaction apparatus, procedure, and analytical methods of epoxide and acid for kinetic measurements have been described in previous papers.[5,10] A reaction flask containing BA and the solvent was heated to a desired temperature and to this were added solutions of PGE and of an amine preheated to the same temperature. The time was measured from the moment of mixing an amine in all cases. The reaction mixtures were stirred by bubbling dry nitrogen gas and for analysis the aliquots (3 or 4 ml) of the reaction mixtures were taken out at convenient intervals. The acid and epoxy contents of the sample were determined by the direct neutralization method[11,12] and by the method of Durbetaki.[13] The initial concentrations of PGE, BA, and the amine were 5.00 × 10^{-1}, 5.00 × 10^{-1}, and 0.5–2.0 × 10^{-2} M, respectively. The temperature of the reaction mixtures was kept in as constant as ±0.2°.

Results

The product (VI) was produced in yield of 80–90% of theoretical and the disappearance of benzoic acid was completely accounted for by the appearance of ester and hydroxyl groups by infrared spectrum analysis. As in the previous paper,[8] the reaction of PGE and BA in the presence of pyridines, quinolines, or isoquinoline at various temperatures was in good agreement with second-order kinetics.

The order of reaction with respect to the tertiary amine was determined through a series of experiments with varied concentrations of the amine (0–2.00 × 10^{-2} M) and with constant initial concentrations of PGE and BA (5.00 × 10^{-1} M). The various values of the rate constant k were plotted against the concentrations of the amine, and a straight line was obtained as shown in Figure 1. This shows that the observed second-order rate constant k was expressed as

$$k = k''[\text{amine}] + k' \qquad (4)$$

where k'' is the third-order rate constant, k' is the second-order rate constant at the zero concentration of the catalyst, and [amine] is the initial concentration of the amine. In Table I are shown the rate constants at various temperatures, the activation energies, and the frequency factors of this reaction using substituted pyridines as catalyst. The rate constants of 2- and 2,6-substituted pyridines are especially lower and their activation energies and frequency factors are correspondingly larger than the others.

The Arrhenius parameters and the enthalpies and the entropies of activation are obtained from eq 5–7

$$k = (KT/h)\exp[(\Delta S^*/R) - (\Delta H^*/RT)] \qquad (5)$$

$$\Delta H^* = E_A + (\Delta n^* - 1)RT \qquad (6)$$

$$\Delta G^* = \Delta H^* - T\Delta S^* \qquad (7)$$

(9) R. G. Pearson and F. V. Williams, *J. Am. Chem. Soc.*, **75**, 3073 (1953).
(10) H. Kakiuchi and Y. Tanaka, *Kobunshi Kagaku*, **20**, 619 (1963).
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(12) E. R. Bishop, E. B. Kittredge, and J. H. Hildebrand, *J. Am. Chem. Soc.*, **44**, 135 (1922).
(13) A. J. Durbetaki, *Anal. Chem.*, **28**, 2000 (1956).

where k, K, h, R, and T are the observed rate constant (in this case, k''), Boltzmann's constant, Planck's constant, the gas constant, and the absolute temperature, respectively, and ΔH^*, ΔS^*, ΔG^*, and Δn^* are the enthalpy, entropy, Gibbs free energy of activation, and the change of moles in activation, defined as the number of molecules of the activated complex minus the number of molecules of reactants, respectively. The parameters, enthalpies, and entropies appear in col 7–9, Table I.

The rate constants measured for over-all reaction are all accurate to ±3% or better by the agreement between duplicate determinations. These uncertainties of ±3% in the rate constants correspond to uncertainties in E_A and ΔH^* of 0.4–0.5% kcal/mole, in log A of 0.3 units, and in ΔS^* of 0.9 units. In spite of the above uncertainties, some effects of substituents of pyridines and quinolines are observed significantly.

The data in Table I reveal that there are no significant differences in the activation energies or frequency terms between the reactions with 3-picoline (E_A 17.0, log A = 7.97) and with 4-picoline (E_A 17.1, log A = 7.97). The similar identity of these quantities has been retained in the reaction of alkyl iodides with 3- or 4-monoalkylpyridines.[14a]

A methyl group in the 3 or 4 position of the pyridine nucleus causes an increase in rate of reaction with a decrease in the energy of activation (Table I). This might be attributed to the increase in the strength of the base resulting from the introduction of the methyl group. The introduction of methyl groups in the 2 and/or 6 positions also results in an increase in the basicity. 2-Picoline (pK_a 5.97) is stronger than 3-picoline (pK_a 5.68) and is almost as strong as 4-picoline (pK_a 6.02);[14b] 2,6-lutidine (pK_a 6.75) is stronger than 3- and 4-picolines and as strong as 2,4-lutidine (pK_a 6.79);[14c] 4-methylquinoline (pK_a 5.20) is almost as strong as pyridine (pK_a 5.17);[14d] and 2-methylquinoline (pK_a 5.42) is stronger than quinoline (pK_a 4.80) and 4-methylquinoline and almost as strong as isoquinoline (pK_a 5.46).[14d] Consequently, a similar increase in rate would be anticipated if the rate was proportional to the basicity of the catalyst. Nevertheless, the rates of the reaction catalyzed by 2-picoline, 2-methylquinoline, or 2,6-lutidine are not larger but smaller than pyridine, quinoline, or 2,4-lutidine, respectively.

Discussion

Figure 2 shows plots of the activation energy or the logarithm of the rate constant for this reaction *vs.* the basicity of the pyridines in water. Clearly, between the basicity and the catalytic efficiency, there is no single relationship which covers all the catalysts studied here. Similar deviations from a linear relationship between the rate data and the pK_a values have been found for many other reactions.[4,6,14] Failure to observe a linearity in our system should not be due to the difference in the solvents in the two reactions,[14b] but to the difference in the steric requirements of these

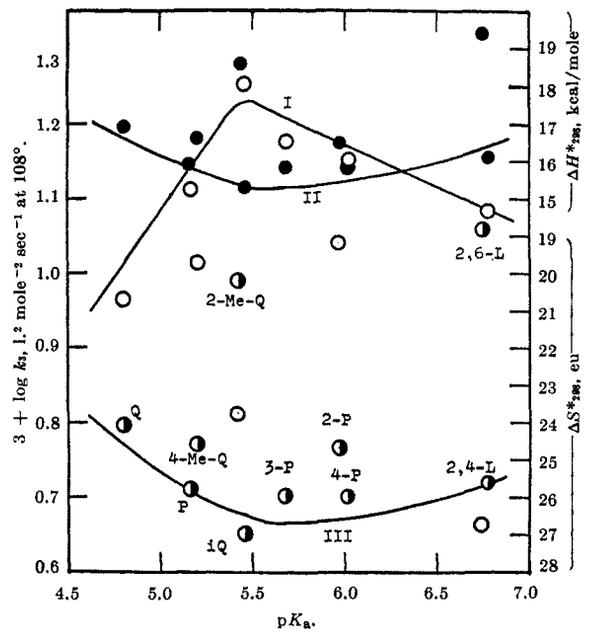


Figure 2.—The relationship between I, log k_3 (○), II, ΔH^*_{298} (●), or III, ΔS^*_{298} (◑), for the reaction of PGE and BA in xylene in the presence of various pyridines and quinolines and pK_a values of these amines.

reactions, although a slight gap remains in the complete evaluation of the catalytic coefficients through lack of knowledge of the temperature dependence of basic dissociation constants. This reaction shows steric hindrance, determined kinetically, which exceeds that in the corresponding ionizations. If the transition-state species is of type V, the steric constraint in V should be greater than it is in the corresponding pyridinium ion; otherwise the steric retardation would not be noted.

If this reaction proceeds according to Scheme I as mentioned before,[8] the observed over-all reaction constant k'' (see eq 4) may be expressed as

$$k'' = k_1k_3k_5/[k_2(k_4 + k_5) + k_3k_5C_{IV}] \quad (8)$$

Here, C_{IV} is the concentration of PGE and the k_i values (i = 1, 2, ..., 5) are the rate constants for reactions 1–3, respectively. It is difficult to interpret the values of k'' in terms of any one particular interaction; *i.e.*, there should be some factors to deviate the plots of the rate data *vs.* the pK_a values from a linearity. It can be considered, however, that this deviation is probably due to steric strains in the activated complex (V). The steric constraint in V may arise from the conflicting steric requirements of the bulky groups at the 2 and 6 positions of the pyridines with the other part of the activated complex (V). Such steric strains are not important, presumably, in the reaction of these amines with BA (reaction 1 in Scheme I).[14g,15] The strains present in this reaction may be estimated with the same assumptions as Brown and Horowitz,[14e] who evaluated the steric constraint in the reactions of the 2-alkylpyridines with boron trifluoride, methyl iodide, and methanesulfonic acid. Compared with pyridine, the activation energy of this reaction catalyzed by 2-picoline should be decreased by 0.1–0.2 kcal/mole which is caused from the polar effect of the methyl group

(14) (a) H. C. Brown and A. Cahn, *J. Am. Chem. Soc.*, **77**, 1715 (1955); (b) H. C. Brown and X. R. Mihm, *ibid.*, **77**, 1723 (1955); (c) H. C. Brown and D. Gintis, *ibid.*, **78**, 5387 (1956); (d) H. C. Brown, D. H. McDaniel, and O. Häfliger, "Determination of Organic Structures by Physical Methods," Vol. 1, F. C. Nochod and W. D. Phillips, Ed., Academic Press Inc., New York, N. Y., 1962, p 597; (e) H. C. Brown and R. H. Horowitz, *J. Am. Chem. Soc.*, **77**, 1733 (1955); (f) H. C. Brown and G. K. Barbaras, *ibid.*, **69**, 1137 (1947); (g) H. C. Brown and R. R. Holmes, *ibid.*, **77**, 1727 (1955).

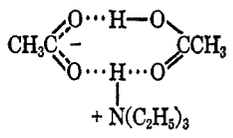
(15) P. D. Bartlett, M. Rohe, and R. M. Stiles, *ibid.*, **76**, 2349 (1954).

nearest to the nitrogen atom. As a matter of fact, a methyl group at the 2 position increased the activation energy by 0.6 kcal/mole compared with the unsubstituted pyridine. This may be due to the steric strain in the transition-state species (V) of this reaction. These strains may be evaluated for 2-picoline, 0.6, from E_A (2-picoline) − E_A (4-picoline); 2,6-lutidine, 3.9, from E_A (2,6-lutidine) − E_A (2,4-lutidine) + 0.6; quinoline, 1.6, from E_A (quinoline) − E_A (isoquinoline); 2-methylquinoline, 3.6, from E_A (2-methylquinoline) − E_A (4-methylquinoline) + 1.6 kcal/mole, where E_A (substituted pyridines) are the activation energies of this reaction in the presence of substituted pyridines. The steric constraint in this reaction catalyzed by these bases is larger than that of methyl iodide with 2-alkylpyridines while smaller than that of boron trifluoride.[14e]

Additivities in the pK_a values have been found for benzoic acid derivatives and the pyridine series.[14b,16] In this reaction, the first methyl group at the 2 position of pyridine brings about the increase of 0.6 kcal/mole in the activation energy and the second methyl groups at the 6 position of 2-picoline and at the 2 position of quinoline result in increases of 3.3 and 2.0 kcal/mole, respectively. This fact shows that the steric strain in this reaction is clearly not additive. The dispersion in this reaction rate or in the activation energy shown in Figure 2 can be interpreted neither by a nucleophilic activity of the pyridines, an electrophilic activity of their conjugate acids only, nor by a linear combination of these two factors. It may be estimated by a higher order interaction term of them or by another factor beside them.[17]

The less active amines are those having a substituent in one or both of the positions adjacent to the heterocyclic nitrogen atom and this suggests steric influence on the mechanism of the catalysis. The view that the catalysis occurs *via* some association between the hydrogen-bonded complex (III) and the whole or part of the epoxide (IV), as shown in Scheme I, is supported by other steric hindrances of α substituents on the rate and equilibria of association reaction of tertiary amines.[1b,14,17-21] The stability of the transition-state species (V) would be probably affected by the molecular structure of the pyridine and this may well explain the catalytic efficiency in this reaction.

Proton transfer from the hydrogen-bonded complex (III) to PGE (IV) through the activated complex or transition-state species (V) may be suggested from the fact that in aprotic solvents such as carbon tetrachloride or nitromethane a proton transfers from an acid to a base by forming a hydrogen bond involving additional molecules of the acid.[22] For example, the addition of triethylamine to an excess of acetic acid in carbon tetrachloride leads to the formation of the solvated ion pair $(C_2H_5)_3N^+OCOCH_3^-HOCOCH_3$, the structural formula for which is probably shown as VIIa.[23] Addi-



VIIa

tion of pyridine or 2,4-dinitroaniline to an excess of sulfuric acid in nitromethane leads to a reaction that is best represented by eq 9.[24] The major product of the

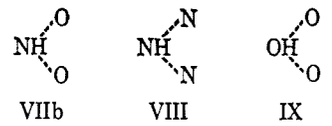
$$B + 3H_2SO_4 \rightleftharpoons BH^+OSO_3H^-2H_2SO_4 \qquad (9)$$

addition reaction of a base B with sulfuric acid, shown by eq 9, is found to be an ion pair solvated by sulfuric acid rather than a pair of free ions, even though nitromethane is a highly polar solvent.

The structure of V can be suggested from a general discussion on the stereochemistry of the hydrogen bond.[25-27] Up to now there has been no general conclusion to show whether the hydrogen bond would be rectilinear or not. It is generally assumed, however, that the hydrogen in the hydrogen bond will lie on a straight line joining the two bridged atoms if other constraining influences allow.[28] This is supported by the many examples.[25,29,30]

The evidence of crystal structures of three crystalline oximes[31] is conflicting on this point. Certain small molecules are found to show such a multiplicity of hydrogen bonding that chelate rings are formed containing two hydrogen bonds, which may well, under such constraint, depart from linearity. A six-membered ring of this kind is exemplified in crystalline urea.[32] In an electron-diffraction study of crystalline boric acid,[33] the hydrogen atoms are found to be not collinear with the oxygens, but to be displaced from this position as a result of attraction toward two oxygen neighbors.

A "shared" or "bifurcated" hydrogen bond such as that between VII and IX has been reported in the structure of sulphamic acid,[34] dicyanodiamide,[35] racemic acid hydrate,[36] and α-iodic acid,[37] respectively. The struc-



VIIb VIII IX

tural change in the pyridines used as catalyst for this reaction may result in a similar structural change in the hydrogen bond of V, whose stability therefore would be altered. Bifurcation of this kind would seem to be inherently unstable; as such the structural alteration of

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(18) R. J. Bruehlman and F. H. Verhoek, *J. Am. Chem. Soc.*, **70**, 1401 (1948).
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the hydrogen bond is considered to play an important role for the base-catalyzed reaction of PGE and BA.

Registry No.—Benzoic acid, 65-85-0; phenyl glycidyl ether, 122-60-1; isoquinoline, 119-65-3; 3-picoline, 108-99-6; 4-picoline, 108-89-4; pyridine, 110-86-1; 2,4-lutidine, 108-47-4; 2-picoline, 109-06-8; 4-methylquinoline, 491-35-0; quinoline, 91-22-5; 2-methylquinoline, 91-63-4; 2,6-lutidine, 108-48-5.

Acknowledgment.—The author is grateful to Mr. K. Tomizuka for his help with the manuscript.

Synthesis and Chemistry of Thiazolo[3,2-a]pyridinium Compounds[1]

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Received February 14, 1967

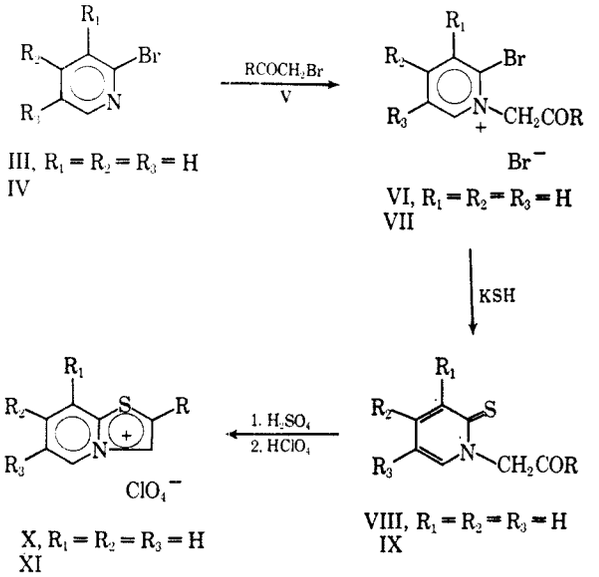
1-β-Oxoethylpyridine-2-thiones may be cyclized in sulfuric acid to yield 2-substituted thiazolo[3,2-a]pyridinium salts. The environment about position 2 appears more shielded than that about position 3 as measured either by resonance of a ring proton or of the protons of an alkyl substituent at the position. The pK_a values of the 2- and 3-carboxylic acids are the same, within experimental error.

The thiazolo[3,2-a]pyridinium cation (II) was first synthesized[2,3] by cyclization of α-(2-pyridylthio) ke-

I II

tones and -aldehyde (I). This approach to the synthesis of the thiazolopyridinium system lends itself best to the preparation of monosubstituted derivatives with substituents at position 3 (II, R = H). In connection with our study of the nmr spectrum of the thiazolopyridinium system, there was a need for a method which would afford derivatives monosubstituted at position 2 (II, R′ = H).

The new synthesis is based upon an observation by Djerassi and Pettit[4] that 2-bromo-1-phenacylpyridinium bromide (VI, R = C_6H_5) reacts with hydrosulfide ion to afford an excellent yield of 1-phenacyl-2-



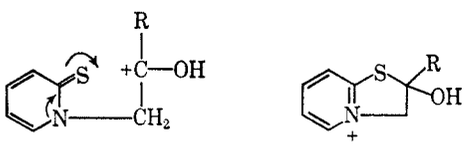
III, $R_1 = R_2 = R_3 = H$
IV

VI, $R_1 = R_2 = R_3 = H$
VII

X, $R_1 = R_2 = R_3 = H$
XI

VIII, $R_1 = R_2 = R_3 = H$
IX

pyridinethione (VIII, R = C_6H_5). From an earlier observation[5] that 1-phenacyl-2-pyridone may be cyclized in sulfuric acid to yield the 2-phenyloxazolo[3,2-a]pyridinium cation, it appeared plausible that 1-phenacyl-2-pyridinethione (VIII, R = C_6H_5) might, under the same conditions, afford the 2-phenylthiazolo[3,2-a]pyridinium (X, R = C_6H_5) cation. This prediction proved correct, for the new product had the expected composition, ultraviolet absorption, and infrared and nmr (only aromatic protons) spectra. Through use of a variety of bromomethyl ketones (V) and of bromopyridines (IV), it proved possible to prepare a variety of 2-substituted thiazolo[3,2-a]-pyridinium salts with either alkyl or aryl groups at position 2 as well as with methyl groups in the pyridine ring. In no case was there evidence that any significant portion of the thione (IX) cyclized with the loss of hydrogen sulfide to afford the related oxazolo[3,2-a]pyridinium salt. The mechanism of cyclization may be viewed as a protonation of the carbonyl oxygen atom (XII) followed by an attack of the highly nucleophilic sulfur atom on the conjugate acid. The resulting carbinol (XIII) would be expected to dehy-



XII XIII

drate readily in the concentrated acid. The results of the syntheses are summarized in Table I.

An interesting observation reported earlier[3a] was that the nmr spectrum of 2,3-dimethylthiazolo[3,2-a]-pyridinium (II, R = R′ = CH_3) perchlorate showed, in addition to aromatic resonances, a single sharp singlet (at δ 2.80 ppm) corresponding to six protons. The methyl proton resonances of the 2-methyl and 3-methyl isomers (II, R = CH_3, R′ = H, or II, R = H, R′ = CH_3) differ and occur at δ 2.84 and 2.94[6] ppm, respectively. A similar difference was shown by the methyl protons of the new 2- and 3-*t*-butyl derivatives (II, R = *t*-Bu, R′ = H, and II, R = H, R′ = *t*-Bu),

(1) This investigation was supported by Public Health Service Research Grant No. H-2170 of the National Institutes of Health.

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(3) (a) C. K. Bradsher and D. F. Lohr, Jr., *Chem. Ind.* (London), 1801 (1964); (b) C. K. Bradsher and D. F. Lohr, Jr., *J. Heterocyclic Chem.*, **3**, 27 (1966).

(4) C. Djerassi and G. R. Pettit, *J. Am. Chem. Soc.*, **76**, 4470 (1954).

(5) C. K. Bradsher and M. F. Zinn, *J. Heterocyclic Chem.*, **1**, 219 (1964).

(6) We have not been able to reproduce the value of τ 7.17 reported earlier[3b] for the 3-methyl derivative.