Hydroxyacetone Stearate from Bromoacetone.—Bromoacetone, 41 g. (0.3 mole), was added to a solution of triethylamine, 30 g. (0.3 mole), stearic acid, 85 g. (0.3 mole), and acetone, 100 ml., and the mixture was refluxed for 3 hr. After cooling and dilution with 2.5 l. of hexane, the solution was washed successively with water, dilute hydrochloric acid, and 1% potassium hydroxide in 40% ethanol–60% water. The organic layer was then dried with sodium sulfate and freed of traces of stearic acid by passage through a pad of Florisil. The product, recrystallized from pentane, weighed 43 g., melted at 57.5–58.5°, and was identical with the previous preparation.

Attempted Reduction of the Isopropenyl Stearate–NBS–Sodium Stearate Reaction Product (I).—A solution of 20 g. of stearic acid (0.07 mole) in 500 ml. of tetrahydrofuran (distilled from sodium under dry nitrogen) was stirred overnight with 1.6 g. of sodium shavings (0.07 g.-atom) until soap formation was complete. A solution of 10.0 g. of isopropenyl stearate (0.031 mole) in 25 ml. of dry tetrahydrofuran and 8.65 g. of NBS (0.05 mole) was simultaneously added at room temperature with stirring and the mixture was then brought to reflux temperature and held at that temperature for 3 hr. This mixture was treated with prereduced Adams' catalyst (prepared in dry THF from 5 g. of platinum oxide, discarding the supernatant solvent) and shaken overnight with hydrogen at 50 p.s.i. The mixture was filtered and the solvent removed from the filtrate under reduced pressure. The residue was dissolved in hexane and chromatographed on Florisil. Elution with hexane gave no residue. Elution with 20% benzene in hexane and 50% benzene in hexane gave 2.1 g. of *n*-octadecyl stearate m.p. 61–62°, lit.[17] m.p. 62°, identical in infrared spectrum with an authentic sample. Elution with benzene gave 0.8 g. of *n*-octadecyl alcohol, m.p. 57.5–59° (no depression with authentic sample, and identical infrared spectrum on crystal film.) Elution with 20–100% methylene chloride in benzene gave 5.7 g. of hydroxyacetone stearate, identical in melting point and infrared spectrum with an authentic sample.

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Dissociation Constants and Ultraviolet and Infrared Spectra of Pyridinesulfonic Acids[1]

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The dissociation constants of a number of pyridinesulfonic acids have been determined spectrophotometrically in water and 42% alcohol. Changes in pK_a values and changes in infrared and ultraviolet spectra are discussed in terms of structural changes.

The dissociation constants of the dimethylpyridines[4] show that the effects of methyl groups on the pK_a value are approximately additive. To see whether a similar effect operated with the sulfonic acid grouping, a number of pyridinesulfonic acids were prepared and their dissociation constants were determined from the variation of their ultraviolet spectra with hydrogen ion concentration. It was hoped to deduce the position of the sulfonic acid group in the sulfonation product[5] of 2,6-di-*t*-butylpyridine. After this work had been completed, the sulfonation product was shown independently to be the 3-sulfonic acid.[6,7] Although our data were unable to show in which direction sulfonation had occurred in the 2,6-di-*t*-butylpyridine molecule, they are of general interest and are now reported.

TABLE I

ULTRAVIOLET SPECTRA OF THE SULFONIC ACIDS OF PYRIDINE BASES[a]

Compound	In 0.1 *N* HCl λ_{max}	ϵ_{max}	In 0.1 *N* NaOH λ_{max}	ϵ_{max}
Pyridine	256			
2-Pyridinesulfonic acid	262	6,900	254	3,200
			260	3,800
			267	2,800
3-Pyridinesulfonic acid	261.5	5,060	254	2,490
			260	2,750
			267	1,970
4-Pyridinesulfonic acid	222	5,910	264	2,860
	263	5,050		
2,6-Lutidine	270			
2,6-Lutidine-3-sulfonic acid	218	5,740	268	4,330
	273	8,550	275	3,460
2,6-Lutidine-4-sulfonic acid	278.5	9,200	276	4,900
2,6-Di-*t*-butylpyridine	273			
2,6-Di-*t*-butylpyridine-3-sulfonic acid	220.5	6,580	220	11,200
	272.5	10,330	260.5	3,340

[a] Wave lengths are measured in mμ.

Table I contains data on the ultraviolet spectra of the sulfonic acids measured in both acid and alkaline solutions. The strong band appearing with a maximum between 260 and 280 mμ is very probably due to a transition of a π-electron from the ground state of the molecule to an excited π-

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(1) Presented in part at the 130th National Meeting of the American Chemical Society, Atlantic City, New Jersey, September, 1956.

(2) Postdoctoral Fellow at Purdue University, 1954–1956, under Scientist's Research Project TA-01-101-3006 (EPA 151) of the International Cooperation Administration, while on leave from the National Chemical Laboratory, D.S.I.R., Teddington, Middlesex, England.

(3) Present address: Department of Medical Chemistry, Institute of Advanced Studies, the Australian National University, Canberra, A.C.T., Australia.

(4) H. C. Brown and X. R. Mihm, *J. Am. Chem. Soc.*, **77**, 1723 (1955); H. C. Brown, J. Donahue, and H. E. Podall, unpublished data; R. J. L. Andon, J. D. Cox, and E. F. G. Herington, *Trans. Faraday Soc.*, **50**, 918 (1954).

(5) H. C. Brown and B. Kanner, *J. Am. Chem. Soc.*, **75**, 3865 (1953).

(6) N. Muller and W. J. Wallace, *J. Org. Chem.*, **24**, 1151 (1959).

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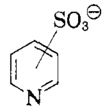
TABLE II

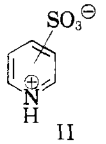
DISSOCIATION CONSTANTS OF PYRIDINESULFONIC ACIDS AT 25°

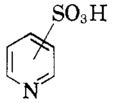
	Water					42% Alcohol				
	pK_a (obsd.)	Standard deviation of mean value	$-\Delta$pK_a	pK_a (calcd.)	pK_a (obsd.) − pK_a (calcd.)	pK_a (obsd.)	Standard deviation of mean value	$-\Delta$pK_a	pK_a (calcd.)	pK_a (obsd.) − pK_a (calcd.)
Pyridine	5.17					4.31	0.03			
2-Pyridinesulfonic acid	1.75	0.03	3.42			2.11	.04	2.20		
3-Pyridinesulfonic acid	3.22	.04	1.95			2.89	.05	1.42		
4-Pyridinesulfonic acid	3.44	.03	1.73			3.14	.03	1.17		
2,6-Lutidine	6.75					5.75	.01			
2,6-Lutidine-3-sulfonic acid	4.89	.01	1.86	4.80[a]	0.09	4.56	.02	1.19	4.33[b]	0.23
2,6-Lutidine-4-sulfonic acid	5.09	.03	1.66	5.02[a]	0.07	4.63	.04	1.12	4.58[b]	.05
2,6-Di-*t*-butylpyridine[c]	. . .	. . .	. . .	. . .	. . .	3.53	.03			
2,6-Di-*t*-butylpyridine-3-sulfonic acid	4.12	.03				2.29	.04	1.24	2.11[d]	.18

[a] Calculated from the equation $\text{p}K_a = 6.75 - 1.95B - 1.73C$. [b] Calculated from the equation $\text{p}K_a = 5.75 - 1.42B - 1.17C$. [c] This base was too sparingly soluble in aqueous solution to be measured. [d] Calcd. from the equation $\text{p}K_a = 3.53 - 1.42B - 1.17C$. B and C equal the number of sulfonate groups in the β and γ-positions of the alkylpyridine molecule.

orbital.[8] Thus it moves to longer wave lengths under the influence of both electron-attracting (SO_3^-) and electron releasing (methyl and *t*-butyl) substituents. In addition, the intensity of absorption of this π–π^* transition in the pyridinesulfonic acids approximately doubles in proceeding from alkaline to acidic media. This is a phenomenon characteristic of the protonation of the ring nitrogen of a pyridine derivative.[9] Since the pyridinesulfonic acid species present in alkaline media can only be the anion (I), the protonated species existing in the range of acidic media used in this work must be II and not III.


I


II


III

The pK_a values obtained are summarized in Table II. The results show that the sulfonate grouping in any position of the nucleus decreases the basicity of the nitrogen atom of the pyridine nucleus; the decrease in basicity is greater the closer the sulfonate grouping is to the nitrogen atom. This is to be expected if the inductive effect of an electron attracting group is operative.

The effects of substituents on the ionization of aromatic acids and bases are approximately additive,[10] so that the introduction of a sulfonate group into the β-position of an alkylpyridine would be expected to produce a decrease in pK_a of the parent base similar to that found in the pair pyridine–3-pyridinesulfonic acid—*viz.* 1.95 pK_a units in water. Likewise, two β-sulfonate groupings might be expected to cause twice this depression. Hence the pK_a of a 3-pyridinesulfonic acid can be predicted from an equation of the type

$$\text{p}K_a\,(\text{calcd.}) = \text{p}K_a\,(\text{parent pyridine base}) - 1.95\,B$$

where B is the number of sulfonate groups in β-positions in the pyridine nucleus. A similar equation can be deduced for predicting the effects of γ-sulfonate groups and both equations can be combined into the general equation

$$\text{p}K_a\,(\text{calcd.}) = \text{p}K_a\,(\text{parent pyridine base}) - 1.95B - 1.73\text{C}$$

where C represents the number of γ-sulfonate groups in the molecule. It is applicable to measurements made in aqueous solutions; the comparable equation for 42% alcohol is

$$\text{p}K_a\,(\text{calcd.}) = \text{p}Ka\,(\text{parent pyridine base}) - 1.42B - 1.17\text{C}$$

The data in Table II show that these equations do reproduce the pK_a values to within 0.23 unit. In the 2,6-lutidine series, the difference pK_a (obsd.) −pK_a (calcd.) is always positive and is about the same for the two lutidinesulfonic acids in water. In the mixed solvent, however, this difference becomes smaller for the 4-acid but greater for the 3-acid so that the pK_a for 2,6-lutidine-3-sulfonic acid has a value 0.23 unit above that predicted.

In the 2,6-di-*t*-butylpyridine series, only the results for 42% alcohol as solvent can be considered, since it is impossible to obtain a pK_a value in water for the parent compound by direct measurement, owing to its limited solubility. Again the observed pK_a value for the 3-sulfonic acid is greater than the calculated value; hence those effects already operating in the case of 2,6-lutidine-3-sulfonic acid were present in the 2,6-di-*t*-butyl analogue.

The pK_a values for the 3- and 4-pyridinesulfonic acids can be substituted into the Hammett equation using Jaffé's value[11] ($\rho = 5.685$) of the reaction constant for the ionization of pyridine bases. This

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[8] S. F. Mason, "Recent Work on Naturally Occurring Nitrogen Heterocyclic Compounds," Special Publication No. 3, The Chemical Society, London, 1955, p. 144.

[9] H. P. Stephenson and H. Sponer, *J. Am. Chem. Soc.*, **79**, 2050 (1957).

[10] H. C. Brown, D. H. McDaniel, and O. Häfliger, "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, ed., Academic Press, Inc., New York, 1955, p. 591.

[11] H. H. Jaffé and G. O. Doak, *J. Am. Chem. Soc.*, **77**, 4441 (1955).

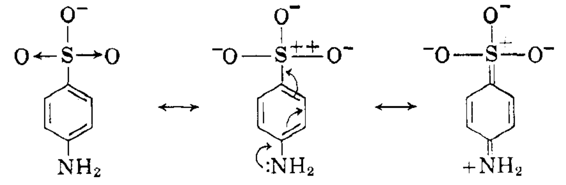
TABLE III

CORRELATION OF INFRARED SPECTRA IN BENZENE AND PYRIDINE SERIES

Arrangement substituents in benzene hydrocarbon	No. of adjacent hydrogen atoms	Characteristic bands in infrared[14c]	Corresponding sulfonic acid	Bands in infrared
1,3	3	12.35–13.33 μ and 13.79–14.71 μ	3-Pyridine	12.23 μ and 14.60 μ
1,4	2	11.63–12.50 μ	4-Pyridine	12.25 μ
1,2	4	12.99–13.61 μ	2-Pyridine	13.00 μ
1,2,3,4	2	11.63–12.50 μ	2,6-Lutidine-3-	11.72 μ
1,2,3,5	1	11.11–11.63 μ	2,6-Lutidine-4-	11.74 μ
1,2,3,4	2	11.63–12.50 μ	2,6-Di-*t*-butylpyridine-3-	12.25 μ

leads to values of 0.343 and 0.304 for the substituent constants of the SO_3^- group in the 3- and 4-positions of pyridine, respectively.

Zollinger[12] found that the pK_a of *m*-aminobenzenesulfonic acid is greater than that of the *para*-isomer. The reverse order should apply if only the inductive effect of the SO_3^- group is operative. If, however, a mesomeric effect is operating in the *para*-acid, electron attraction by the SO_3^- group is accentuated and the additional decrease caused in the basicity of the nitrogen atom in the basicity of the nitrogen atom in the anion (IV) should be, and is, reflected in the experimental data. A mesomeric effect can operate only if the sulfur atom can expand its octet of electrons and other evidence[13] favors the ability of the sulfur atom to possess such a property.



IV

The infrared spectra of the six sulfonic acids were measured using a Nujol mull technique. The 6–10-μ region of the spectra is crowded with absorption bands but from 10–14-μ the bands are fewer, well spaced out and may be used for identification purposes. All the compounds have absorption bands in the 8.0–8.5-μ and 9.26–9.90-μ regions, which Bellamy[14a] has assigned to the sulfonic acid group. The spectrum of 4-pyridinesulfonic acid resembled that of sulfanilic acid[14b] but the spectra of 2- and 3-pyridinesulfonic acids bore slight resemblance to the spectra of *o*- and *m*-aminobenzenesulfonic acids, respectively[15].

Cannon and Sutherland[16] pointed out that the infrared spectra of alkylpyridines in the 11–15-μ region closely resembled the spectra of the analogous benzene hydrocarbons formed by replacing the nitrogen atom by a C—CH_3 group. Podall[17] confirmed this correlation and tried to extend it, with less success, to the 5–6-μ region. In the case of the pyridine hydrochlorides and chloromercurates, Evans and Kynaston[18] showed that the infrared spectra in the 11–15-μ region also obeyed a Cannon-Sutherland correlation, so that the protonated nitrogen in these salts is to be regarded as a substituent. With the exception of 2,6-lutidine-3-sulfonic acid, none of the sulfonic acids absorbs in the 5–6-μ region, so that only the 11–15-μ region can be considered here.

In 3-pyridinesulfonic acid, for example, the greatest number of adjacent hydrogen atoms attached to the pyridine nucleus is 3 (and not 5 since the neutral molecule is a zwitterion and so contains a protonated nitrogen atom).

According to Sutherland's correlation, the spectrum of the 3-pyridinesulfonic acid in the 11–15-μ region should resemble that of a 1,3-disubstituted benzene. Bellamy[14] states that meta disubstituted benzenes show a characteristic band at 12.35–13.33 μ and another at 13.79–14.71 μ. The bands at 12.23 and 14.60 μ in the spectrum of the acid fall exactly within each range. A table (Table III) can thus be constructed, and it is seen that, with the exception of 2,6-lutidine-4-sulfonic acid, the spectra of the sulfonic acids obey a Cannon-Sutherland type correlation in the 11–15-μ region.

Experimental

Materials. Specimens of pyridine and 2,6-lutidine previously purified by Mihm[4] were used. 2,6-Di-*t*-butylpyridine was purified by conversion into the chloromercurates, m.p. 182–184°, from methanol.

Anal. Calcd. for $C_{13}H_{22}Cl_3HgN$: C, 31.26; H, 4.44; Cl, 21.31; N, 2.81. Found: C, 30.78; H, 4.55; Cl, 20.85; N, 3.09.

In making up a standard solution, a known weight of this chloromercurates in 42% alcohol was decomposed with hydrogen sulfide and filtered. The filtrate, containing a known quantity of 2,6-di-*t*-butylpyridine hydrochloride, was then suitably diluted.

The preparations of all but the 2,6-di-*t*-butylpyridine-3 sulfonic acid have been reported previously.[19] 2,6-Di-*t*-

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[12] H. Zollinger, W. Büchler, and C. Wittwer, *Helv. Chim. Acta*, **36**, 1711 (1953).

[13] W. v. E. Doering and L. K. Levy, *J. Am. Chem. Soc.*, **77**, 509 (1955).

[14] (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," J. Wiley and Sons, Inc., New York, 1960, p. 350. (b) *Ibid.*, p. 367. (c) *Ibid.*, p. 65.

[15] R. B. Barnes, R. C. Gore, V. Liddel, and V. Z. Williams, "Infrared Spectroscopy," Reinhold, New York, 1944, p. 87.

[16] C. G. Cannon and G. B. B. M. Sutherland, *Spectrochim. Acta*, **4**, 373 (1951).

[17] H. E. Podall, *Anal. Chem.*, **29**, 1423 (1957).

[18] R. F. Evans and W. Kynaston, *J. Chem. Soc.*, 1005 (1962).

[19] R. F. Evans and H. C. Brown, *J. Org. Chem.*, **27**, 1329 (1962).

butylpyridine-3-sulfonic acid was obtained by sulfonating the pyridine base in sulfur dioxide with sulfur trioxide.

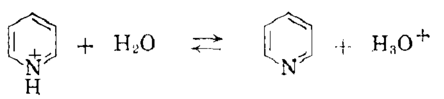
Six milliliters of sulfur trioxide was distilled in an all-glass apparatus guarded against the entry of moisture. The distillate of 7.6 g. (0.095 mole) was collected in a three-necked 100-ml. round-bottom flask which was then disconnected from the distillation apparatus and quickly fitted with a Dry Ice condenser carrying a guard tube containing anhydrite, a dropping funnel and a stopper. Sulfur dioxide, previously dried by passage through concd. sulfuric acid and phosphorus pentoxide-coated beads, was condensed in the flask until *ca.* 50 ml. of liquid had been collected. Eighteen and two tenths grams (0.095 mole) of 2,6-di-*t*-butylpyridine was now cautiously added over 1.25 hr. through the dropping funnel. The mixture refluxed for 5 hr. and was then allowed to evaporate overnight; the contents of the flask were carefully decomposed with water and the resulting slurry dissolved in 500 ml. of hot water. After neutralization with concd. aqueous barium hydroxide and filtration, the filtrate was evaporated to dryness by directing a stream of air on the surface of the hot solution and furnished 12.6 g. of solid. (Distillation of the solution was difficult owing to excessive foaming.) The precipitate of barium sulfate was extracted three times with boiling chloroform; evaporation of the chloroform from the extract yielded 8 g. of unsulfonated base. Yield of barium salt therefore was 52%. The 12.6 g. of material was dissolved in 800 ml. of hot aqueous alcohol and decomposed with the theoretical quantity (1.83 g.) of concd. sulfuric acid in 20 ml. of water. After filtration, the solution was evaporated to dryness under reduced pressure on the steam bath, and the residue recrystallized from aqueous alcohol. 2,6-Di-*t*-butylpyridine-3-sulfonic acid, white needles, m.p. 325–327° dec. (corr.), was obtained (lit.[5] m.p. 310° dec.).

Anal. Calcd. for $C_{13}H_{21}NSO_3$: C, 57.51; H, 7.78; N, 5.16. Found: C, 57.82; H, 7.98; N, 5.22.

The *S*-benzylisothiuronium derivative melted at 207–209°. (lit.[5] m.p. 216.0–216.5°).

Anal. Calcd. for $C_{21}H_{31}N_3S_2O_3$: C, 57.63; H, 7.14; N, 9.6. Found: C, 57.50; H, 7.19; N, 9.67.

Dissociation Constants. (1) **In 42% Alcohol.**—The dissociation constants were determined by studying the change of ultraviolet spectra with pH. The expression for calculating the equilibrium constant of the dissociation of the parent pyridine bases



$$\text{is } pK_a = pH + \log \frac{A_2 - A_3}{A_1 - A_2} + \log \gamma_+$$

where pK_a is the negative logarithm of the thermodynamic dissociation constant; A_1, A_2, and A_3 are the absorbances for base in acid, buffered, and alkaline solution, respectively, and γ_+ is the activity coefficient of the protonated base.[20]

The solvent was prepared by mixing, at room temperature, equal volumes of twice distilled water and 95.6% alcohol (weight %). Stock solutions for the spectroscopic measurements were made by dissolving approximately 1×10^{-3} mole of pyridine or 2,6-lutidine in 1 l. of this solvent.

The spectral measurements were made with a Beckman Model DU quartz spectrophotometer, using the same matched pair of 1-cm. quartz cells throughout. The cell compartment was kept at 25.0° by circulating water from a constant temperature bath through the walls of this compartment. The spectra of the bases were measured in (a) 0.1 *N* hydrochloric acid solutions, (b) 0.1 *N* sodium hydroxide solutions, and (c) in solutions of different pH's. The latter were obtained by the use of acetic acid–sodium acetate buffers.

The solutions for measurement were prepared by mixing an aliquot volume of stock solution of base with an aliquot volume of 1 *N* hydrochloric acid, 1 *N* alkali, or buffer solution (each in 42% alcohol) and diluting with solvent; solutions for use in the blank cell of the spectrophotometer were made up in a similar manner except that solvent was substituted for the stock base solution. Absorbances were measured at five wave lengths covering the region 10 mμ on either side of the absorption maximum of the protonated form, in solutions of pH corresponding to pH = pK_a and $pK_a \pm 0.5$, respectively.

The pH values, at 25°, of the buffered base solutions, were measured with a Beckman Model G pH meter which was standardized immediately before use at pH 7.00 and pH 4.01 by the use of Beckman standard buffer solutions. The measured pH was assumed to refer only to the H_3O^+ ion; the presence of the species $C_2H_5OH_2^+$ was ignored since it was believed that in media containing more than 20 vol.% of water (as in this work), the hydrogen ions were exclusively solvated by the water.[21]

In calculating thermodynamic pK_a values, the Debye–Hückel limiting law was assumed to apply to aqueous alcohol solutions at low ionic strengths[22]; the proportion of alcohol in the mixed solvent was calculated and the dielectric constant at 25° of this medium was interpolated from the data of Åkerlöf[23].

The Debye–Hückel equation for 42% alcohol was then deduced to be

$$\log \gamma_+ = -\frac{0.9084\sqrt{\mu}}{1 + 1.993\sqrt{\mu}}$$

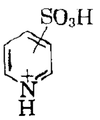
where μ is the strength of the ionic atmosphere generated by a 1:1 electrolyte.[24]

In calculating μ for sodium acetate–acetic acid buffers, it was necessary to have a value for the dissociation constant of acetic acid in 42% alcohol. A value of 2.4×10^{-6} was estimated from a plot of the data obtained by Grunwald and Berkowitz.[22]

From the spectral measurements made on each compound, fifteen estimates of its pK_a were made; mean values calculated from these data are given in Table II, together with standard deviations.

In a molecule of the pyridinesulfonic acids, there is present a strong acidic group and a weak basic group; internal neutralization will occur and the sulfonic acid is to be regarded as consisting primarily of zwitterions[25] of the type II.

In alkaline solutions, the species present was undoubtedly the anion I



V

Sulfonic acids are strong acids (pK_a, 0–2) and it is unlikely that in the range of hydrogen ion concentration studied here, the completely protonated species (V) was present in any appreciable quantity.

Consequently the equilibrium was assumed to be of the type

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[20] L. A. Flexser, L. P. Hammett, and A. Dingwall, *J. Am. Chem. Soc.*, **57**, 2103 (1935).

[21] E. A. Braude and E. S. Stern, *J. Chem. Soc.*, 1976 (1948).

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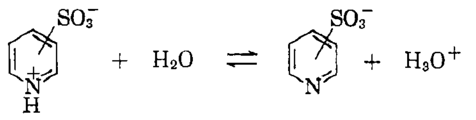
[24] A. L. Bacarella, E. Grunwald, H. P. Marshall, and E. L. Purlee, *J. Org. Chem.*, **20**, 747 (1955).

[25] W. D. Kumler, *ibid.*, **20**, 701 (1955).



The equation now applicable is

$$pK_a = pH + \log\frac{A_2 - A_3}{A_1 - A_2} - \log \gamma_-$$

where each term has the same significance as before but γ_- represents the activity coefficient of the sulfonate anion. The zwitterion is assumed to have an activity coefficient of unity.

Experimental conditions were similar to those used for the parent bases; lower pH's were required and were generated with hydrochloric acid–potassium chloride solutions. It was found that Beer's law was obeyed by all the materials in both acidic and alkaline solutions in the concentration range of 5×10^{-5} to 15×10^{-5} *M*.

(2) **In Water.**—The sulfonic acids were studied in twice distilled water. The pK_a values were higher and consequently solutions of a different pH from those used under (1) were employed. Chloroacetic acid–sodium chloroacetate buffers were used for most of the solutions of low pH. A different Debye–Hückel expression was also employed, owing to the change in dielectric constant of the medium. It was

$$\log \gamma_- = \frac{-0.509\sqrt{\mu}}{1 + \sqrt{\mu}}$$

Infrared Spectra were obtained in Nujol mull using a Perkin-Elmer recording spectrometer.

Acknowledgment.—Our thanks are due to Mrs. C. S. Tang-Yeh and Mrs. S. L. Margerum for the analyses and Mrs. B. Polister for the infrared data.

Reaction of Isocyanates with Some Alkyl-Substituted Monohydroxamic Acids, Carbamoyl Derivatives of N-Acyl-O-alkylhydroxylamines. II[1,2]

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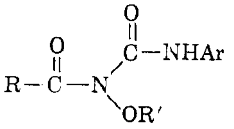
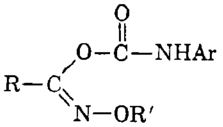
The reaction of phenyl isocyanate with hydroxamic acid esters results in the formation of an addition product which is obtained in a nearly quantitative yield when extreme care is used in the work-up. The phenyl carbamoyl group probably is attached to the nitrogen of the hydroxamic acid ester.

In 1905 Biddle[3] allowed phenyl isocyanate to react with methyl formohydroxamate and obtained a phenylcarbamoyl derivative. We have found the reaction of phenyl isocyanate and α-naphthyl isocyanate with hydroxamic acid esters to be a general reaction leading in most cases to solid derivatives in high yields.

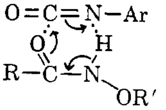
There are two possible structures for the carbamoyl derivatives. The carbamate group may be attached to nitrogen giving I or to oxygen giving II. Structure I would arise from a reaction of the isocyanate with an NH group, while structure II could occur from an enolization of the starting hydroxamic acid ester followed by the reaction of the isocyanate with the OH group of the enol form. Another mechanism for the formation of II would be by the "quasi" ring intermediate (III).



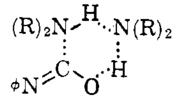
I



II



III



IV

A number of workers[4] have considered the mechanism of the reaction of isocyanates with amines and alcohols. It has been shown recently[4d] that the reaction of phenyl isocyanate with aniline can be interpreted as a termolecular reaction, intermediate IV, in which the nitrogen of one molecule of aniline acts as a nucleophile, and a hydrogen from a second molecule of aniline acts as an acid. With the hydroxamic acid esters the carbonyl oxygen could behave as a nucleophile and the hydrogen on nitrogen as a proton source as in III, to give II. On the other hand I could arise from intermediate IV, or by the enol of the hydroxamic acid ester reacting by intermediate III. More experiments will be necessary to determine which intermediate is correct.

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[2] Presented in part at the 136th National Meeting of the American Chemical Society, New York City, September 16, 1960. For paper I of this series see J. H. Cooley, W. D. Bills, and J. R. Throckmorton, *J. Org. Chem.*, **25**, 1734 (1960).

[3] H. C. Biddle, *Am. Chem. J.*, **33**, 60 (1905); H. L. Yale, *Chem. Rev.*, **33**, 209 (1944).

[4] (a) R. G. Arnold, J. A. Nelson, and J. J. Verbane, *ibid.*, **37**, 47 (1957); (b) J. W. Baker and D. N. Bailey, *J. Chem. Soc.*, 4647, 4652, 4663 (1957); (c) J. Burkus, *J. Org. Chem.*, **26**, 779 (1961); (d) K. Sauer and M. H. Kasparian, *ibid.*, **26**, 3498 (1961).