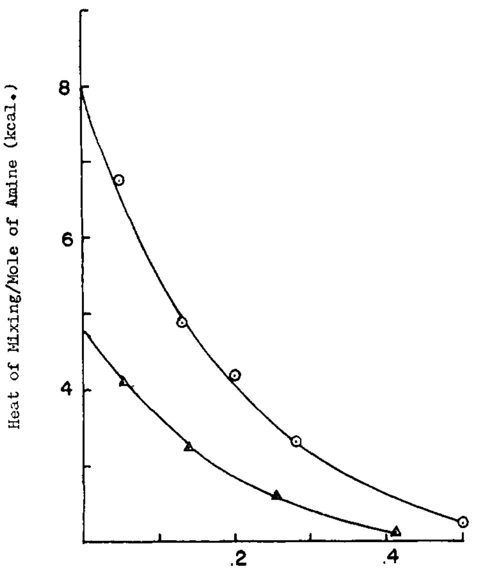

Fig. 3.—Plot of the heat of mixing for the two aromatic amines (aniline—circles, N-methylaniline—triangles) per mole of amine at various concentrations in 2-methylpyridine.

bility that aniline forms a 1:2 complex with 2-methylpyridine, both hydrogens on the aniline nitrogen being involved in the process.

In order to rule on this postulation, the n.m.r. and thermochemical data on the system N-methylaniline-2-methylpyridine were taken. The n.m.r. data are shown in Fig. 2a. Again a downfield shift of the N—H resonance is noted upon dilution with 2-methylpyridine. There is some indication of weak intermolecular interactions in N-methylaniline, however, since dilution with carbon tetrachloride produces a slight downfield shift of the N—H resonance (Fig. 2d). This shift was not due to hydrogen bonding, since the N-methyl group also displays a similar shift. Rather, this small shift may be attributed to the normal dilution effect of a nonaromatic solvent on an aromatic solute.[3]

The heat of mixing of N-methylaniline in 2-methylpyridine at infinite dilution was found to be 4.8 kcal./mole. This value is somewhat greater than one-half the value for aniline itself, a not unexpected result since it is reasonable to assume that the first hydrogen bond formed by aniline would be somewhat stronger than the second. The result does confirm the belief that at infinite dilution aniline does form a 1:2 complex with 2-methylpyridine.

Experimental

Materials.—The aniline, N-methylaniline (free of aniline and dimethylaniline), and 2-methylpyridine were Eastman Kodak White Label grade. Each was distilled before use from barium oxide through a 1-meter, vacuum-jacketed column, packed with Podbielniak "Heli-Pak." The boiling points and refractive indices agreed with the values in the literature.[6] The carbon tetrachloride was Fisher A.R. grade.

Proton Resonance Measurements.—All measurements were made with a Varian A-60 n.m.r. spectrometer (Probe temperature 28°) using tetramethylsilane as an internal standard. The results of these measurements are reported in Fig. 2, and a typical spectrum for a solution of aniline in 2-methylpyridine is given in Fig. 1.

Thermochemical Measurements.—Heats of mixing of various mixtures of aniline in 2-methylpyridine and N-methylaniline in 2-methylpyridine were carried out in a 1-pint borosilicate, stoppered, dewar flask equipped with a stirrer and a thermometer reading to 0.1°. The amounts of each component were chosen so that the final total volume approximated 26 ml. Temperature raises varied from about 1.5° for the most dilute solutions to about 7° for the most concentrated solutions of the aromatic amine in the 2-methylpyridine. Heat losses to the calorimeter were determined by the electrical method described in Mack and France.[7] The heat capacities of the individual components were taken from values in the literature,[6] and it was assumed, for the purposes of this study, that the heat capacities of the various mixtures was a linear function of the composition. A plot of the data is given in Fig. 3.

Acknowledgment.—The author wishes to acknowledge the efforts of Mr. Joe D. Hall in carrying out portions of the experimental work.

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[6] "International Critical Tables of Numerical Data," McGraw-Hill Book Co., New York, N. Y., 1930.

[7] E. Mack and W. G. France, "A Laboratory Manual of Physical Chemistry," D. Van Nostrand Co., New York, N. Y., 1934, p. 153.

The Nucleophilicity of Amines

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Studies of the basicity[1] toward protons and nucleophilicity[2] toward alkyl halides of phosphines and the corresponding basicity of amines[3] have recently appeared in the literature. From these studies, several conclusions as to the probable nucleophilic behavior of amines toward alkyl halides may be reached. First, the spatially more demanding reaction of an amine and an alkyl halide will make the steric effect of substituents on the amine comparable in magnitude to the inductive effect. Second, all other factors being equal, the nucleophilicity of amines of the same inductive effect will be in the same order as their basicities, 1° > 2° > 3°.[3] Third, those amines with aryl substituents will be abnormally weak nucleophiles through operation of the mesomeric effect.

Although many investigations of the Menschutkin reaction have been reported in the literature, none of the kinetic studies of the nucleo-

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[1] W. A. Henderson, Jr., and C. A. Streuli, *J. Am. Chem. Soc.*, **82**, 5791 (1960).

[2] W. A. Henderson, Jr., and S. A. Buckler, *ibid.*, **82**, 5794 (1960).

[3] H. K. Hall, Jr., *ibid.*, **79**, 5441 (1957).

philicity of amines are extensive enough to test the above conclusions. The effect of varying the alkyl halide[4] and the solvent[5] have been investigated in detail, but only fragmentary reports involving variation of the amine[6] are to be found. Moreover, there are not enough data available for any one set of conditions (solvent, alkyl halide, and temperature) to afford a compilation of results. Therefore, we have made a study of amine nucleophilicity as evidenced by the rate of the reaction run under

$$R_1R_2R_3N + C_2H_5I \xrightarrow[35^\circ]{\text{acetone}} R_1R_2R_3NC_2H_5^+ + I^- \quad (1)$$

conditions identical with those used in the case of phosphines.[2]

Kinetics were followed by the same conductometric method, whereby the rate of production of ammonium and iodide ions was determined from the conductivity of the reaction mixture and that of standard solutions of the salts. The reactions were followed to not more than 0.4% of completion, and the data were interpreted using the equation

$$kt = \frac{x}{ab} \quad (2)$$

the derivation of which from the second order rate equation has been previously described.[2]

In two cases, the results obtained by the conductometric method were checked titrimetrically. The reaction rates of triethylamine and phenyldiethylamine were followed over the range 0–70% of completion by a Volhard titration of the iodide ion produced, as described in the Experimental. The rate constants thus obtained agree within 8% with those determined conductometrically.

The only rate constant which may be compared directly with those in the literature is that for triethylamine ($k = 1.82 \pm 0.01 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$). Data obtained by Tommila and Kauranen[5d] for the same reaction using a titrimetric technique when extrapolated to 35° yield the value $1.29 \pm 0.15 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$.

The reaction in the case of tertiary amines is quite simple. However, in the case of primary and secondary amines, the situation is complicated by the possibility of further reaction according to the equations

$$R_2NH + EtI \longrightarrow R_2NEtH^+ + I^- \quad (3)$$

$$R_2NEtH^+ + R_2NH \longrightarrow R_2NEt + R_2NH_2^+ \quad (4)$$

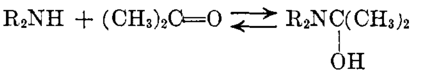
$$R_2NEt + EtI \longrightarrow R_2NEt_2^+ + I^- \quad (5)$$

Since the starting amine is always present in more than 200-fold excess and is, moreover, a slightly stronger base than the alkylated amine,[3] the equilibrium in equation 4 lies far to the right. This necessitates the use of the hydroiodide of the starting material rather than the product as the standard in preparing conductivity *vs.* concentration curves.

The possibility then exists that reaction by equation 5 will affect the kinetic results. However, since R_2NEt is present in concentrations less than 0.5% that of R_2NH and is, as will be seen, less reactive, its contribution to the rate constant may be ignored.

The decision to use acetone as the solvent for the kinetic study was a difficult one since it was recognized at the outset that, in the case of primary amines, imine formation was probable (equation 6) and that secondary amines might also react with the solvent (equation 7). Nevertheless, acetone was used in order to maintain conditions strictly comparable to those used in the earlier work on phosphines.[2]

$$RNH_2 + (CH_3)_2C{=}O \rightleftharpoons RN{=}C(CH_3)_2 + H_2O \quad (6)$$



$$R_2NH + (CH_3)_2C{=}O \rightleftharpoons R_2N\underset{\displaystyle OH}{\underset{|}{C}}(CH_3)_2 \quad (7)$$

Some difficulty, in truth, was experienced in the case of primary amines. It was found that imine formation took place on long standing (one or more hours) of the amine solutions, as shown by a lowering of the rate constant with time. This was avoided by using freshly prepared solutions, as described in the Experimental. Imine formation during the kinetic run itself is negligible since the run time is very short (one to five minutes).

No such reaction of secondary amines with the solvent was observed under the experimental conditions. The results of the investigation substantiate the predictions made earlier, and are presented in Table I.

A Taft plot of phosphine nucleophilicity exhibits minor deviations from linearity, departures which may be ascribed to steric effects, while amines show considerable scatter. In the sterically more demanding case of amine nucleophilicity, where the transition state is more constricted through the smaller size of nitrogen and the shorter carbon–nitrogen bond length, it is to be expected that the steric effects will assume an importance equal to or surpassing that of the inductive effect in determining the rate of reaction with an alkyl halide. This large steric effect is demonstrated by the fact that the sterically less hindered triethylamine and trimethylamine are 3.5 and 130 times more reactive than tripropylamine and tributylamine (although their inductive effects are virtually the same), while

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[4] (a) N. Menschutkin, *Z. physik. Chem.*, **5**, 589 (1890); (b) J. W. Baker, *J. Chem. Soc.*, 1128 (1933); (c) R. W. D. Preston and H. O. Jones, *ibid.*, 1930 (1912).

[5] (a) N. Menschutkin, *Z. phys. Chem.*, **6**, 41 (1890); (b) J. A. Hawkins, *J. Chem. Soc.*, 1171 (1922); (c) H. G. Grimm, H. Ruf, and H. Z. Wolff, *Z. phys. Chem.*, **13B**, 301 (1931); (d) E. Tommila and P. Kauranen, *Acta Chem. Scand.*, **8**, 1152 (1954); (e) E. F. Caldin and J. Peacock, *Trans. Faraday Soc.*, **51**, 1217 (1955); (f) E. M. Kosower, *J. Am. Chem. Soc.*, **80**, 3257 (1958).

[6] (a) G. Vavon and L. Bourgeois, *Compt. rend.*, **202**, 1593 (1936); (b) R. P. Larsen and C. A. Kraus, *Proc. Nat. Acad. Sci., U. S.*, **40**, 70 (1954); (c) V. S. Hunig and M. Kiessel, *J. prakt. Chem.*, [4] **5**, 224 (1958); (d) E. R. A. Peeling and B. D. Stone, *Chem. Ind.* (London), 1625 (1959).

TABLE I

$$RR'R''N + C_2H_5I \xrightarrow[(CH_3)_2CO\ 35.00°]{k_2} RR'R''NC_2H_5^+ + I^-$$

Amine	Sum σ^*	Number of runs	K_2 (l. mole^{-1} sec.$^{-1}$)[a]
$(CH_3)_3N$	0.00	4	$6.53 \pm 0.07 \times 10^{-3}$
$(C_2H_5)_3N$	−0.30	3	$1.82 \pm 0.01 \times 10^{-4}$
		3	$1.67 \pm 0.03 \times 10^{-4}$[b]
$(n\text{-}C_3H_7)_3N$	−0.34	4	$4.71 \pm 0.07 \times 10^{-5}$
$(n\text{-}C_4H_9)_3N$	−0.39	4	$5.57 \pm 0.05 \times 10^{-5}$
$(C_6H_5)N(CH_3)_2$	0.60	4	$5.47 \pm 0.03 \times 10^{-6}$
$(C_6H_5)N(C_2H_5)_2$	0.40	3	$1.76 \pm 0.04 \times 10^{-7}$
		3	$1.83 \pm 0.06 \times 10^{-7}$
$(NCCH_2)N(C_2H_5)_2$	1.51	3	$7.49 \pm 0.08 \times 10^{-7}$[l]
$(NCCH_2CH_2)N(C_2H_5)_2$	0.60	3	$7.42 \pm 0.03 \times 10^{-6}$
$HN(C_2H_5)_2$	0.29	4	$4.79 \pm 0.12 \times 10^{-4}$
$HN(n\text{-}C_3H_7)_2$	0.26	3	$3.47 \pm 0.04 \times 10^{-4}$
$HN(n\text{-}C_4H_9)_2$	0.23	4	$3.58 \pm 0.02 \times 10^{-4}$
$HN(CH_2CH_2CN)_2$	2.09	4	$6.89 \pm 0.49 \times 10^{-6}$
$HN(CH_2CN)_2$	2.91	3	$2.30 \pm 0.42 \times 10^{-7}$
$H_2N(n\text{-}C_3H_7)$	0.87	3	$1.30 \pm 0.04 \times 10^{-3}$
$H_2N(n\text{-}C_4H_9)$	0.85	4	$1.26 \pm 0.05 \times 10^{-3}$

[a] Unless otherwise stated, kinetics followed by conductance. [b] Kinetics followed by titration.

there is only a sixty-fivefold decrease in rate for diethylcyanomethylamine as compared to tripropylamine and tributylamine (a difference attributable to the very considerable electron-withdrawing power of the cyanomethyl group).

The decrease in reaction rate on increasing the substituent sizes is less for secondary amines than for tertiary, as is shown by the lesser difference in rate between the secondary ethyl- and propylamines and the tertiary.

Further increases in chain length beyond three carbons have little, if any, effect on the rate, as may be seen by comparing the reactivities of the butyl- and propylamines. The limited series triethylamine through triamylamine was investigated by Larsen and Kraus,[6b] who reached the same conclusion.

It is to be expected, by analogy with the nucleophilicity of phosphines[2] and the basicity of amines,[3] that branched chain substituents would markedly lower reactivity. While no attempt has been made to demonstrate this point, it is supported by the semiquantitative work of Hünig and Kiessel,[6c] who found *i*-propyl- and *i*-butylamines to be much less nucleophilic than the corresponding *n*-alkylamines.

The reactivity toward ethyl iodide of a series of amines of roughly comparable inductive effect is in the order primary > secondary > tertiary. This is the same order as that for the basicity of amines,[3] but the opposite of that for the basicity[1] or nucleophilicity[2] of phosphines. Hall suggested that the amine basicity series reflects the increased solvation requirements of the (charged) protonated amine over those of the (uncharged) conjugate base. Substitution of alkyl groups for protons in the base should result in a progressive increase in steric hindrance to solvation, and a consequent decrease in basicity, as one goes from primary to secondary to tertiary amines.

The same argument couched in terms of solvation of the transition state explains the nucleophilicity series encountered here. The small change is necessitated by the fact that the nucleophilicity data reflect a kinetic phenomenon while the basicity data concern an equilibrium.

Hall's correlation[3] of pK_a for amines with the sum of the σ^* values holds only for alkyl amines. It is found that aryl amines fall below the basicity predicted for them on the basis of the inductive effect alone by 1 to 4 pK units. A similar decrease in reactivity is found in the nucleophilicity of aryl as opposed to alkyl amines. This is shown by the extremely low nucleophilicity of phenyldiethylamine as compared to diethylaminopropionitrile, an amine with substituents of similar inductive and steric effects. The only other aryl amine employed in this study, phenyldimethylamine, exhibits a nucleophilicity very close to that of diethylaminopropionitrile. This fortuitous result is occasioned by two large and opposite effects: the acceleration resulting from the low steric requirements of the methyl groups and the retardation of the phenyl group.

This decrease in reactivity of aryl amines as bases and nucleophiles reflects delocalization of the electron pair on nitrogen by conjugation with the phenyl ring, and consequent lowering of electron density on nitrogen. Interestingly, such conjugation is not noted in the basicity[1] or nucleophilicity[2] of phosphines. Their reactivity is predictable on the basis of the inductive effect alone.

Experimental

All amines were Eastman Kodak products of the highest purity available. Biscyanomethylamine was recrystallized from water and then from ethanol to afford material of m.p. 75.0–75.5°. All other amines were stored over potassium hydroxide pellets for 24 hr. and then were carefully fractionated using a twelve-plate column packed with glass helices. A constant-boiling middle cut of no more than 50% was collected. All amines had analyses within 0.3% for C, H, and N and showed no detectable impurities on vapor phase chromatography.

Ethyl iodide, Eastman Kodak, was dried over anhydrous magnesium sulfate and distilled, a 50% center cut being taken. This was stored under nitrogen over mercury in a brown glass bottle.

Ammonium salts were formed by adding the amine to an excess of ethyl iodide. Repeated recrystallization from ethanol or ethanol–ethyl acetate afforded salts with the melting points shown in Table II. These were analyzed for iodide, and all were within 0.3%.

Acetone was "Baker Analyzed" reagent material, and was used without further purification.

Standard solutions of ammonium salts were made up by weighing out appropriate amounts of the salts, transferring them to 100-ml. volumetric flasks, and diluting to the mark with acetone. Less concentrated solutions were made up by dilution. The conductivity was measured in a 25-ml. conductivity cell with unplatinized platinum electrodes of cell constant 0.4925. Measurements were made at 60

TABLE II

Salt	M.p., °C.
$(CH_3)_3N(C_2H_5)I$	300 (dec.)
$(C_2H_5)_4NI$	283.8–284.0
$(n\text{-}C_3H_7)_3N(C_2H_5)I$	240.0–240.4
$(n\text{-}C_4H_9)_3N(C_2H_5)I$	202–203
$(C_6H_5)N(CH_3)_2(C_2H_5)I$	135–136
$(C_6H_5)N(C_2H_5)_3I$	124–125
$(NCCH_2)N(C_2H_5)_3I$	182–183 (dec.)
$(NCCH_2CH_2)N(C_2H_5)_3I$	167–189 (dec.)

c.p.s. using an Industrial Instruments, Inc., Model RC 16 B 1 conductivity bridge.

Standard solutions of hydroiodides were made up by adding 30% hydriodic acid to an excess of the amine in acetone. The concentration of iodide was determined by Volhard titration. The effect of the water added on the conductivity of the solution was checked by measuring the conductivity of pure tributylamine hydroiodide with and without added water. Within the concentration ranges used in this investigation, no change in conductivity was noted.

Conductometric kinetic runs of tertiary and secondary amines were made as described previously.[2] Solutions 0.1 *N* or less in amine and ethyl iodide were made up in 50-ml. volumetric flasks. The two solutions were placed in a thermostatted water bath maintained within the limits 35.00 ± 0.01°. After a minimum of 30 min., 40-ml. aliquots of each solution were withdrawn with thermostatted pipets and mixed by shaking in a 100-ml. thermostatted volumetric flask. The solution was then transferred to the conductivity cell immersed in the bath. At appropriate intervals, the time and resistance were recorded.

In the case of primary amines, the amine was added directly to a thermostatted solution of ethyl iodide in acetone, and the kinetic run was made immediately after mixing in the same manner as above.

Titrimetric kinetic runs were run on solutions made up as above, and kept in the thermostatted volumetric flask sealed with a rubber stopple. At appropriate intervals, approximately 4-ml. samples of the reaction mixture were removed from the flask using a syringe and long hypodermic needle. An exact 3-ml. aliquot of the removed sample was immediately quenched in 10 ml. of acetone and 10 ml. of water. The time was measured from the beginning of shaking to the instant of quenching. The aqueous acetone solution was extracted three times with 10-ml. portions of ether and then titrated by the Volhard method, as were the standard ammonium salts.

The Ultraviolet Absorption Spectra of Methazonic Acid and Its Sodium Salts

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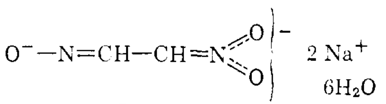
The ultraviolet absorption spectra of methazonic acid and its sodium salts have been studied in aqueous solution at various pH values.

In agreement with published values,[2a,b] the spectrum of disodium methazonate in water (Fig. 1a) has a band at 298 mμ (ϵ_{max} 17,800) which deviates slightly from Beer's law at higher concentrations (Fig. 3a). There is, however, a second, less intense, band at 220 mμ (ϵ_{max} 5400) which obeys Beer's law up to a concentration of at least 0.005% (Fig. 3b).

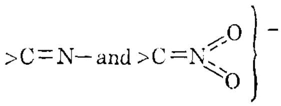
Both bands are unchanged after the solution has been left for two weeks. The structure of disodium methazonate is thought[3] to be I so that the



$$\left[O^-{-}N{=}CH{-}CH{=}N\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}\right]^- \; 2\,Na^+ \; 6H_2O$$

I

more intense band can therefore be ascribed to a $\pi\rightarrow\pi$ transition in the conjugated structures



$$>C{=}N{-} \text{ and } \left[>C{=}N\begin{smallmatrix}\nearrow O\\ \searrow O\end{smallmatrix}\right]^-$$

In 0.01 *N* sodium hydroxide, this band is displaced to longer wave lengths (Fig. 1b) and is intensified (λ_{max} 310 mμ; ϵ_{max} 18,500) suggesting that complete formation of the resonating nitroxylate ion is not attained until a pH value of about 12 units. This observation confirms that of Matthew and Kubler,[2b] who give a value for the specific extinction coefficient of methazonic acid in *N* potassium hydroxide at 310 mμ of 197.3, which corresponds to a molar extinction coefficient[4] of 20,520. These values can be compared with that of dimethyl glyoxime in 0.1 *N* sodium hydroxide (λ_{max} 270 mμ; ϵ_{max} 17,700), where the band is ascribed to a $\pi\rightarrow\pi$ transition in the two conjugated —C=N—O⁻ structures; replacement of the —N—O⁻ ion by the nitroxylate ion, which is itself a resonating structure, would account for the

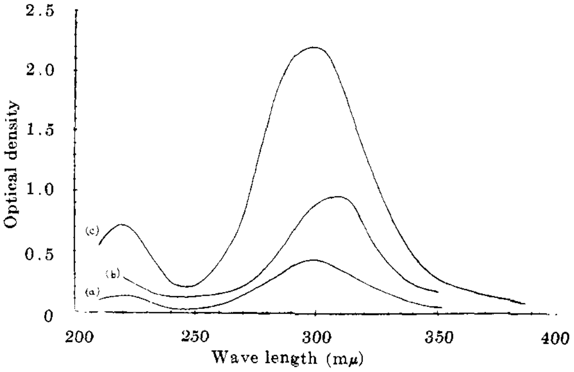


Fig. 1.—Ultraviolet absorption spectra: (a) disodium methazonate in water, 0.025 mmoles/l.; (b) disodium methazonate, in *N*/100 sodium hydroxide, 0.05 mmole/l.; (c) monosodium methazonate in water, 0.016 mmole/l.

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[2] (a) C. M. Drew, J. R. McNesby, and A. S. Gordon, *J. Am. Chem. Soc.*, **77**, 2622 (1955); (b) V. E. Matthews and D. G. Kubler, *J. Org. Chem.*, **25**, 266 (1960).

[3] D. J. Morgan, *ibid.*, **23**, 1069 (1958).