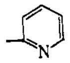
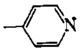
TABLE I

N-METHYL-N-ALKYL HYDROXYLAMINES

$RCH{=}CH_2 + CH_3NHOH \longrightarrow RCH_2CH_2N(CH_3)OH$

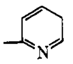
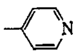
Compound No.	Compound R	Yield, %	Solvent	M.p., °C.	Empirical formula	Calcd., %	Found, %
I	$-CONH_2$	60.5	Methanol	94–95[a]	$C_4H_{10}N_2O_2$	N 23.71	23.41
II	$-SO_2C_2H_5$	49	Water	106[b]	$C_5H_{13}NO_3S$	C 35.91	36.50
						H 7.38	8.31
						N 8.37	8.30
III		79	*c*	108–109[d]	$C_9H_{15}IN_2O$[e]	C 36.73	36.88
						H 5.13	5.41
						N 9.52	9.82
IV		83.5	*c*	78[f]	$C_8H_{12}N_2O$	C 63.13	63.24
						H 7.95	8.05
						N 18.41	18.10

[a] Recrystallized from methanol. [b] Recrystallized from benzene. [c] No solvent was employed. [d] Boiling point at 1.8 mm.; n^{25}D 1.5275. [e] Analyzed as the methiodide, m.p. 113–114°. [f] Recrystallized from ligroin.

TABLE II

N,N-DIALKYL HYDROXYLAMINES

$2RCH{=}CH_2 + NH_2OH \longrightarrow RCH_2CH_2N(OH)CH_2CH_2R$

Compound No.	Compound R	Yield, %	Solvent	M.p., °C.	Empirical formula	Calcd., %	Found, %
V	$-SO_2C_2H_2$	88.5	Water	134–135[a]	$C_8H_{19}NO_5S$	N 5.11	4.78
VI		61.5	*b*	110–111[c,d]	$C_{14}H_{17}N_3O$	N 17.27	16.88
VII		62	Methanol	148–149[c,e]	$C_{14}H_{17}N_3O$	N 17.27	17.26

[a] Recrystallized from methanol. [b] No solvent was employed. [c] Recrystallized from benzene. [d] Lit.[10] m.p. 105–106.5°. [e] Lit.[10] m.p. 143–144°.

N,N-Dialkyl Hydroxylamines (General Procedure).—To 0.2 mole of N-methylhydroxylamine hydrochloride or hydroxylamine hydrochloride in 100 ml. of methanol or water, as indicated (Tables I and II), was added 0.1 mole of anhydrous sodium carbonate, followed by 0.15 mole of the vinyl compound. The reaction proceeded quite rapidly and, in the case of I, the sodium chloride was removed by filtration after stirring for 30 min. Evaporation of the methanol gave the product. The water-insoluble sulfones II and V separated during the course of the reaction and were filtered off. To prepare compounds III, IV, VI, and VII, the hydroxylamine hydrochlorides were added either directly or to a methanolic solution of the vinylpyridines and the products were extracted with chloroform from the reaction mixture after it had been neutralized by the addition of aqueous sodium bicarbonate.

Reaction of Divinyl Sulfone and Methylhydroxylamine.—To 20 g. (0.24 mole) of N-methylhydroxylamine hydrochloride in 100 ml. of water was added 13 g. (0.12 mole) of anhydrous sodium carbonate with ice cooling. Then 11.8 g. (0.1 mole) of divinyl sulfone was added dropwise and the mixture was stirred for 30 min. The crude product which had separated was filtered off and recrystallized from ethanol, yielding 15.7 g. (74%) of bis-(2-N-methylhydroxylaminoethyl) sulfone (VIII), m.p. 166–167°; λ_{max} (KBr) 3.18 (OH), 7.83 and 8.7 (SO_2) μ.

Anal. Calcd. for $C_6H_{16}N_2O_4S$: N, 13.19. Found: N, 12.93.

Reaction of Divinyl Sulfone and Hydroxylamine.—Six grams (0.05 mole) of anhydrous sodium carbonate was added to a solution of 6.9 g. (0.1 mole) of hydroxylamine hydrochloride in 200 ml. of water. Then 11.8 g. (0.1 mole) of divinyl sulfone was added dropwise with vigorous stirring. The stirring was continued for 30 min. and the separated solid was then collected. This consisted of 12.9 g. (85.5%) of 4-hydroxytetrahydro-1,4-thiazine 1,1-dioxide (IX), m.p. 192–193° dec.; λ_{max} (KBr) 2.98 (OH), 7.85 and 8.88 (SO_2) μ.

Anal. Calcd. for $C_4H_9NO_3S$: C, 31.77; H, 5.99; N, 9.26. Found: C, 31.74; H, 6.19; N, 9.35.

In a high-dilution experiment using 1500 ml. of water, the same compound was obtained as the only product.

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[16] M. F. Schostakovskii, E. N. Prilezhaeva, V. A. Azovskaya, and G. V. Dmitrieva, *Zh. Obshch. Khim.*, **30**, 1123 (1960); *Chem. Abstr.*, **55**, 414 (1961).

The Rate of Reaction of Piperidine with Piperonal in Methanol

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Although secondary amines cannot react with aromatic carbonyl compounds to form uncharged aldimines or ketimines, cations of the type $ArCH{=}\overset{+}{N}R_2$ (I) exist and may be intermediates in reactions catalyzed by piperidine or other secondary amines.[2] Having already studied the kinetics of ammonia[3] and primary amines[4] with aromatic aldehydes, we attempted to detect a reaction between piperidine and piperonal in methanol to form I or its tetrahedral precursor, $ArCH(OH)NR_2$ (Ia).

The ultraviolet absorption at the λ_{max} of piperonal (312 mμ) did indeed decrease in the presence of piperidine. Since no peak appeared at the higher wave length expected for I (in analogy with a protonated Schiff base[5]), this species was not present in appreciable quantity, though it might be formed in more acidic solutions. Moreover, the reaction was readily reversed by water. These observations suggested that

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[1] National Science Foundation Research Participant, 1962.

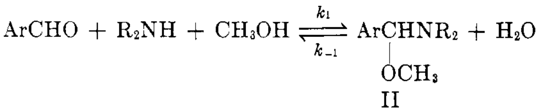
[2] M. L. Bender and R. Breslow, in "Comprehensive Biochemistry," M. Florkin and E. H. Stotz, Ed., Elsevier Publishing Co., New York, N. Y., 1962; N. J. Leonard and J. V. Pankstelis, *J. Org. Chem.*, **28**, 3021 (1963).

[3] R. K. McLeod and T. I. Crowell, *ibid.*, **26**, 1094 (1961).

[4] R. L. Hill and T. I. Crowell, *J. Am. Chem. Soc.*, **78**, 2284 (1956); G. M. Santerre, C. J. Hansrote, Jr., and T. I. Crowell, *ibid.*, **80**, 1254 (1958).

[5] T. I. Crowell and D. W. Peck, *ibid.*, **75**, 1075 (1953).

the methoxyamine II, the known product in similar systems in the presence of potassium carbonate,[6] was being produced.



$$\mathrm{ArCHO} + \mathrm{R_2NH} + \mathrm{CH_3OH} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\substack{|\\ \mathrm{OCH_3}\\ \mathrm{II}}}{\mathrm{ArCHNR_2}} + \mathrm{H_2O}$$

$$K_1 = \frac{k_1}{k_{-1}} = \frac{[\mathrm{II}][\mathrm{H_2O}]}{[\mathrm{ArCHO}][\mathrm{R_2NH}]} \qquad (1)$$

Equilibrium Constant.—The equilibrium constant K_1 was calculated from both ultraviolet and infrared spectrophotometric determination of piperonal. The values obtained at 25.0° were $K_1 = 2.4 \pm 0.1$ for eight runs over a range of 0.045–0.45 M piperidine and 0.50–1.21 M water (ultraviolet); $K_1 = 1.9 \pm 0.5$ for seventeen runs, 0.12–1.2 M piperidine, 0.14–0.36 M piperonal, and no added water (infrared). The data are consistent with the net reaction (1). Increasing the already high pH by adding sodium methoxide did not change the equilibrium constant. This seems to eliminate the concentration of the conjugate base of Ia as an important variable. Typical results are shown in Table I.

TABLE I

EQUILIBRIUM CONCENTRATIONS[a] IN METHANOL AT 25°

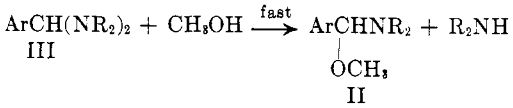
[ArCHO][b]	[R$_2$NH]	[H$_2$O]	[II][c]	K
9.2×10^{-5}	0.0232	0.05	9.2×10^{-5}	2.2
10.0×10^{-5}	0.091	0.50	4.4×10^{-5}	2.4
12.3×10^{-5}	0.091	1.21	2.1×10^{-5}	2.3
4.9×10^{-5}	0.453	0.51	9.5×10^{-5}	2.2
0.0132	1.067[c]	0.139[c]	0.139	1.4
0.0336	0.134[c]	0.104[c]	0.104	2.4
0.0280	0.276[c]	0.124[c]	0.124	2.0
0.0689	0.468[c]	0.276[c]	0.276	2.4

[a] Moles per liter. [b] Measured by ultraviolet (first four runs) or infrared (last four runs). [c] Calculated assuming reaction as in eq. 1.

Rate Constants.—From four kinetic runs at room temperature and 0.03–0.8 M piperidine, $k_1 = 0.049 \pm 0.006$ l. mole^{-1} min.$^{-1}$. The piperonal concentration was 10^{-4} M so that the forward reaction was pseudo first order. Equilibrium was established in these experiments due to a small but significant amount of water in the methanol; the first-order rate constants were calculated from the initial rates and divided by the piperonal concentrations to give the second-order constant k_1. Since the twenty-sevenfold variation in piperidine concentration would lead to a change of 0.7 pH unit, it appears that the rate is insensitive to pH in the alkaline solutions studied.

The calculated value of k_{-1} referred to below, is then 0.049/2.2 or 0.022 l. mole^{-1} min.$^{-1}$ for the hydrolysis of II by dilute solutions of water in methanol.

We prepared the diamine (III) from piperonal and piperidine in benzene, according to Stewart and Hauser.[6] The rate of hydrolysis of III to piperonal was proportional to the water concentration. The second-order rate constant is 0.025 ± 0.02 l. mole^{-1} min.$^{-1}$ (nine runs, 0.025–0.25 M water). This value is so close to the calculated k_{-1} (eq. 1) as to suggest that the reaction of III with methanol to form II is rapid, followed by rate-controlling hydrolysis of II. We confirmed this by treating III with methanol. The n.m.r. spectrum of the solution showed piperonal to be absent at this stage. After one minute, methanol and piperidine were removed by evaporation. Hydrolysis and titration of the residue showed that III had lost 1 equiv. of piperidine as in eq. 2.



$$\underset{\mathrm{III}}{\mathrm{ArCH(NR_2)_2}} + \mathrm{CH_3OH} \xrightarrow{\text{fast}} \underset{\substack{|\\ \mathrm{OCH_3}\\ \mathrm{II}}}{\mathrm{ArCHNR_2}} + \mathrm{R_2NH} \qquad (2)$$

Thus methanolysis appears to be the first step in the mechanism of hydrolysis of the diamine III when the water concentration is low.

Experimental

Rate and Equilibrium Studies.—Solutions of piperonal and piperidine (freshly treated to remove pyridine[7]) were prepared in reagent-grade methanol. The water content of each component was determined by Karl Fisher titration. Ultraviolet spectra were determined on a Perkin-Elmer Spectracord. Infrared measurements of the 5.9- and 6.2-μ carbonyl peaks were made on a Perkin-Elmer Model 21, using silver chloride cells.

N,N′-(3,4-Methylenedioxybenzylidene)bispiperidine (III).—This compound, prepared by the method of Stewart and Hauser,[6] was recrystallized from isooctane, to yield white crystals, m.p. 74–78°. Hydrolysis gave 97–100% of the theoretical quantity of piperonal (ultraviolet spectrum) and of piperidine (titration). Neither the infrared nor the n.m.r. spectrum showed characteristic aldehyde absorption.

Anal. Calcd. for $C_{18}H_{26}N_2O_2$: N, 9.27. Found: N, 9.08.

Acknowledgment.—We are grateful to the National Science Foundation for a research grant and to Mrs. Winnie Faye Coyne and Mr. Robert A. Pages for n.m.r. spectra.

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[6] A. T. Stewart and C. R. Hauser, *J. Am. Chem. Soc.*, **77**, 1099 (1955). See also E. P. Burrows, R. F. Hutton, and W. D. Burrows, *J. Org. Chem.*, **27**, 316 (1962).

[7] T. E. Young and E. D. Amstutz, *J. Am. Chem. Soc.*, **73**, 4773 (1951)

Direct Formylation of Sydnones[1a,b]

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The ease with which the sydnone ring undergoes a variety of electrophilic substitution reactions led us to suggest that its reactivity was comparable to that of thiophene.[1a] We now wish to report that the direct formylation of 3-phenylsydnone (Ia) and of 3-benzylsydnone (Ib) by the Vilsmeier procedure[2] introduces the aldehyde group into the 4-position under conditions remarkably similar to those used in formylating thiophene.[3]

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[1] (a) Sydnones. IV. Part III: J. M. Tien and I. M. Hunsberger-*J. Am. Chem. Soc.*, **83**, 178 (1961). (b) Part of this work was performed at Fordham University. Supported, in part, by grants (CY-2962 and CA, 5478) from the National Cancer Institute of the Public Health Service. (c) To whom all inquiries should be sent.

[2] A. Vilsmeier and A. Haack, *Ber.*, **60B**, 119 (1927); A. W. Weston and R. J. Michaels, *Org. Syn.*, **31**, 108 (1951).

[3] W. J. King and F. F. Nord, *J. Org. Chem.*, **13**, 635 (1948).