aqueous NaCl. The ether layer was washed consecutively with saturated NaCl solution, 2 *N* HCl, and saturated NaCl solution and dried over $MgSO_4$. After filtration, the solution was stripped of solvent to give 1.75 g of the ketone. Reduction of this ketone with $LiAlH_4$, $NaBH_4$, or $LiAl(O\text{-}t\text{-}C_4H_9)_3H$ produced exclusively *cis*-**1**-OH. The ketone is very sensitive to both acid and base. This procedure[29] was used because contact with base is kept to a minimum. The Jones, Sarett, Oppenauer, and Moffatt procedures failed.

Kinetic Runs. Buffered formolyses and acetolyses were run in solutions 0.10 *M* in sodium formate and sodium acetate, respectively. A 10-ml solution, 0.10 *M* in tosylate (*cis*-**1**-OTs), was prepared by dissolving 0.278 g (1 mmol) in 10 ml of buffered solvent already equilibrated in a bath at the desired temperature. At specific times, 1-ml portions of this solvolysis solution were pipetted into 10 ml of dioxane and the resulting solution was titrated with 0.01 *N* perchloric acid in acetic acid to a bromphenol blue end point (yellow to clear).

The acetic acid solvent mixture was prepared by refluxing acetic acid with 5% acetic anhydride for 24 hr, distilling the dried acid, and adding acetic anhydride to make the solution 1% in anhydride. Formic acid was dried by refluxing over boric anhydride for 24 hr, followed by distillation. The 0.01 *N* perchloric acid in acetic acid was prepared by mixing 70% perchloric acid, acetic acid–1% anhydride, and enough acetic anhydride to neutralize the water. This solution was then allowed to stand for 2 days before use. The indicator was a saturated solution of bromphenol blue in acetic acid–1% anhydride.

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[29] D. H. R. Barton, B. J. Garner, and R. H. Wightman, *J. Chem. Soc.*, 1855 (1964).

Catalysis of the Dedeuteration of Isobutyraldehyde-*2-d* by Linear Diamines Including 1-Dimethylamino-8-amino-2-octyne, a Bifunctional Catalyst[1a]

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Abstract: The catalytic activity of monoprotonated diamines of the type $Me_2N(CH_2)_nNH_2$ (n = 2–5) in the dedeuteration of isobutyraldehyde-*2-d* in water increases monotonically with n, *i.e.*, with the basicity of the catalysts. In 50% aqueous methanol monoprotonated hexane-1,6-diamine, undecane-1,11-diamine, and dodecane-1,12-diamine are of about equal catalytic activity. None of the preceding diamines is believed to act as a bifunctional catalyst to a major extent. The catalytic activity of 1-dimethylamino-8-amino-2-octyne (**2**) was studied in water under conditions where it existed in the monoprotonated and the diprotonated forms to comparable extents. The term in the kinetic equation that was first order in monoprotonated diamine and first order in isobutyraldehyde-*2-d* was about 7.7 times as large as would be expected, from the catalytic activities of 3-dimethylaminopropyne and 1-dimethylamino-2-butyne and other observations, in the absence of bifunctional catalysis. Therefore, the monoprotonated diamine is believed to act largely as a bifunctional catalyst by using its primary amino group to transform the aldehyde to an iminium ion and then removing the deuterium atom of the iminium ion internally by attack of the dimethylamino group. Compound **2** has an advantage over the four ω-dimethylaminoalkylamines that were studied in that it is long enough for its dimethylamino group to reach the deuterium atom in the trans isomer of the intermediate iminium ion.

Earlier papers in this series showed that, in the presence of a primary amine salt and a base, isobutyraldehyde-*2-d* may be dedeuterated by rate-controlling attack of base on the reversibly formed intermediate iminium ion.[2] It therefore seemed plausible

$$\begin{aligned} &Me_2CDCHO + RNH_3^+ \rightleftharpoons Me_2CDCH{=}NHR^+ + H_2O \\ &Me_2CDCH{=}NHR^+ + B \longrightarrow Me_2C{=}CHNHR + BD^+ \end{aligned} \qquad (1)$$

that a compound of the type B–R–NH_2 would act as a bifunctional catalyst if the divalent radical R permitted the groups B and NH_2 to have the proper relative geometric orientation. Investigation of the amino acids containing one through five methylene groups between the amino and carboxy groups gave no evidence for bifunctional catalysis.[3] It seemed possible that the failure of these catalysts to act bifunctionally was partly due to the use of the carboxylate anion group, which is known to be relatively ineffective at removing deuterons from isobutyraldehyde-*2-d*,[4] as the basic group. Hence we have studied a similar set of catalysts in which the basic group is an unhindered saturated tertiary amino group, the most effective type for isobutyraldehyde-*2-d*.[4,5] It seemed more likely, however, that the failure of the amino acid catalysts was due to the tendency of the intermediate iminium ion to have a trans configuration **1**. Models show that the R groups used would not be long enough to permit the basic group B to reach the deuterium atom in a trans iminium ion like **1**. Therefore, we have also studied

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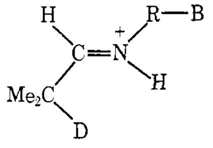
[1] (a) This work was supported in part by Public Health Service Grants AM 06829 MCB and AM 10378 from the National Institute of Arthritis and Metabolic Diseases. Address correspondence to The Ohio State University. The material related to catalysis by acetylenic amines was abstracted largely from the Ph.D. Dissertation of J. L. Lynn, Jr., 1971. This paper is part XII of the series "Catalysis of α-Hydrogen Exchange." For part XI, see (b) J. Hine, J. C. Kaufmann, and M. S. Cholod, *J. Amer. Chem. Soc.*, **94**, 4590 (1972). (c) National Institutes of Health Predoctoral Fellow (No. FO1 GM38177), 1967–1970.

[2] J. Hine, B. C. Menon, J. Mulders, and J. P. Idoux, *J. Org. Chem.*, **32**, 3850 (1967), and references cited therein.

[3] J. Hine, B. C. Menon, J. Mulders, and R. L. Flachskam, Jr., *ibid.*, **34**, 4083 (1969).

[4] J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *J. Amer. Chem. Soc.*, **87**, 5050 (1965).

[5] J. Hine and J. Mulders, *J. Org. Chem.*, **32**, 2200 (1967).



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diamine catalysts with longer chains between the two amino groups.

Results

Four diamines of the type $Me_2N(CH_2)_nNH_2$, where n was 2, 3, 4, and 5, were studied as catalysts.[6] The transition state in the rate-controlling step for bifunctional catalysis would be made up of one molecule of aldehyde, one molecule of diamine, and one proton. Therefore the pH of the reaction solutions was chosen so that the diamine existed largely in the monoprotonated form. The buffers used were sterically hindered tertiary amines that have been found[4] to be such poor catalysts for the deuterium exchange of isobutyraldehyde that they would not interfere significantly with catalysis by the diamines. From the pK values for the diamines,[8] it was seen that 1,1′,1′′-nitrilotri-2-propanol was a suitable buffer for 2-dimethylaminoethylamine, 1,1′-(ethylimino)di-2-propanol was suitable for 3-dimethylaminopropylamine, and 2-(diisopropylamino)ethanol was suitable for the other two ω-dimethylaminoalkylamines. The first-order rate constants observed are listed in Table I.

Table I. Catalysis of the Dedeuteration of Isobutyraldehyde-*2-d* by ω-Dimethylaminoalkylamines[a]

Diamine	[Diamine]$_t$,[b] M	[Buffer]$_t$,[b] M	pH	10^5k_{obsd}, sec^{-1}
$Me_2N(CH_2)_2NH_2$[c]	0.067	0.102	8.10	1.9
(pK_1 = 9.30,	0.132	0.112	8.05	3.1
pK_2 = 5.98)	0.132	0.208	8.10	3.7
	0.134	0.189	8.11	3.6
	0.135	0.089	8.18	4.0
	0.135	0.258	8.17	4.5
	0.137	0.214	7.85	3.8
	0.152	0.199	7.57	3.4
$Me_2N(CH_2)_3NH_2$[d]	0.131	0.145	8.79	15
(pK_1 = 9.91,	0.132	0.144	8.99	16
pK_2 = 7.67)	0.132	0.150	9.07	16
	0.132	0.398	8.98	18
	0.133	0.223	9.03	18
$Me_2N(CH_2)_4NH_2$[e]	0.116	0.168	9.90	25
(pK_1 = 10.17,	0.116	0.171	9.90	23
pK_2 = 8.44)	0.135	0.196	9.81	27
$Me_2N(CH_2)_5NH_2$[e]	0.129	0.171	9.93	39
(pK_1 = 10.44,	0.129	0.175	9.93	39
pK_2 = 9.07)	0.129	0.196	9.97	36

[a] In aqueous solution at 35°, $[Me_2CDCHO]_0 = 0.12$ M. [b] Total concentration regardless of state of protonation or imination. [c] 1,1′,1′′-Nitrilotri-2-propanol buffer. [d] 1,1′-(Ethylimino)di-2-propanol buffer. [e] 2-(Diisopropylamino)ethanol buffer.

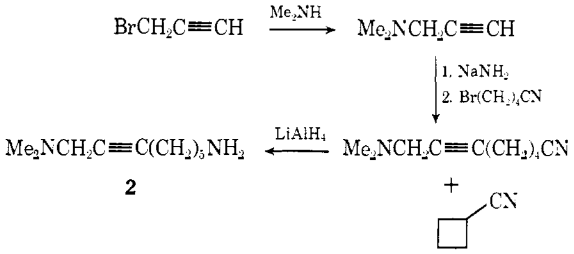
The catalytic activity of hexane-1,6-diamine, undecane-1,11-diamine, and dodecane-1,12-diamine was also studied. The latter two were so insoluble in water, even in the presence of a mole of acid per mole of diamine, that the kinetics were studied in 50% aqueous methanol. The results are shown in Table II.

Table II. Catalysis of the Dedeuteration of Isobutyraldehyde-*2-d* by the Monohydrochlorides of Some α,ω-Diaminoalkanes[a]

Diamine	[Diamine]$_t$,[b] M	"pH"[c]	10^5k_{obsd}, sec^{-1}
$H_2N(CH_2)_6NH_2$	0.150	9.54	3.7
$H_2N(CH_2)_{11}NH_2$	0.150	9.53	3.6
$H_2N(CH_2)_{11}NH_2$	0.154	9.59	4.4
$H_2N(CH_2)_{12}NH_2$	0.152	9.56	4.6
$H_2N(CH_2)_{12}NH_2$	0.153	9.59	4.6

[a] In 50% aqueous methanol at 35°. $[Me_2CDCHO]_0 = 0.027$ M. [b] Total concentration regardless of state of protonation or imination. [c] As measured by a pH meter calibrated for aqueous solutions.

The synthesis of 1-dimethylamino-8-amino-2-octyne (**2**) started with the transformation of propargyl bromide to 3-dimethylaminopropyne. This was accomplished in dimethylamine solution near 0°, although it has been done previously in ethanol in a sealed tube at 100°.[9] Treatment of the sodium salt of 3-dimethylaminopropyne with 5-bromovaleronitrile gave some of the desired 1-dimethylamino-7-cyano-2-heptyne, but it gave a larger amount of cyclobutyl cyanide. The final product was obtained by lithium aluminum hydride reduction of the dimethylaminocyanoheptyne.



The pK values for 3-dimethylaminopropyne, 1-dimethylamino-2-butyne, and **2** were determined by potentiometric titration at 35° and are listed in Table III.

Table III. Acidity Constants of the Conjugate Acids of Three Acetylenic Amines in Water at 35°

Acid	pK
$HC{\equiv}CCH_2NHMe_2^+$	7.27 ± 0.02
$MeC{\equiv}CCH_2NHMe_2^+$	7.98 ± 0.02
$Me_2NCH_2C{\equiv}C(CH_2)_5NH_3^+$[a]	10.12 ± 0.05
$Me_2\overset{+}{N}HCH_2C{\equiv}C(CH_2)_5NH_3^+$	7.55 ± 0.02

[a] This is the pK of the monoprotonated form of the diamine, which contains a small fraction of material protonated at the tertiary amino group instead.

Rate constants for the dedeuteration of isobutyraldehyde-*2-d* in the presence of the two monoamines are listed in Table IV, and those for the reaction in the presence of **2** in Table V. Ultraviolet measurements on solutions similar to those described in Table V showed that not more than 3% of the aldehyde was transformed to imine at equilibrium.

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(6) A brief description of this study appeared in a communication.[7]

(7) J. Hine, M. S. Cholod, and J. H. Jensen, *J. Amer. Chem. Soc.*, **93**, 2321 (1971).

(8) J. Hine, F. A. Via, and J. H. Jensen, *J. Org. Chem.*, **36**, 2926 (1971).

(9) J. P. Guermont, *Mem. Serv. Chim. Etat (Paris)*, **40**, 147 (1955); *Chem. Abstr.*, **52**, 2737a (1958).

Table IV. Kinetics of the Dedeuteration of Isobutyraldehyde-*2-d* in the Presence of 3-Dimethylaminopropyne and 1-Dimethylamino-2-butyne[a]

Amine	[B], *M*	[BH$^+$], *M*	pH	$10^5 \cdot k_{obsd}$, sec^{-1}
HC≡CCH$_2$NMe$_2$	0.0840	0.1004	7.29	5.81
	0.1713	0.2004	7.30	11.5
	0.3434	0.4008	7.30	23.6
MeC≡CCH$_2$NMe$_2$	0.0867	0.0813	8.06	12.3
	0.1601	0.1626	8.05	24.3
b	0.0840	0.0852	8.02	45.5[b]

[a] In water at 35°. [Me$_2$CDCHO]$_0$ = 0.054 *M*. [b] 0.1688 *M* *n*-butylammonium chloride also present.

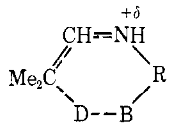
Table V. Kinetics of the Dedeuteration of Isobutyraldehyde-*2-d* in the Presence of 1-Dimethylamino-8-amino-2-octyne[a]

[BH$^+$],[b] *M*	[BH$_2$$^{2+}$],[b] *M*	pH	$10^5 k_{obsd}$, sec^{-1}
0.0222	0.0291	7.68	18.7
0.0298	0.0202	7.93	23.5
0.0496	0.0556	7.83	46.7
0.0643	0.0379	8.04	57.5

[a] In water at 35°. [Me$_2$CDCHO]$_0$ = 0.054 *M*. [b] Stoichiometric concentrations, neglecting the disproportionation of about 1% of the BH$^+$ to B and BH$_2$$^{2+}$.

Discussion

Catalysis by the Saturated Diamines. Bifunctional catalysis of the type we are seeking would involve, in the rate-controlling step, a cyclic transition state like **3**.



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In a series of catalysts of the type Me$_2$N(CH$_2$)$_n$NH$_2$, the bifunctional catalytic efficiency should be low when *n* is so small that the ring is strained and also when *n* is so large as to reduce greatly the probability that the dimethylamino group spends much time near the deuterium atom. We hoped that the smallest ω-dimethylaminoalkylamine that could form a relatively unstrained cyclic transition state would be a considerably better catalyst than those in which the primary and tertiary amino groups were separated by much longer or shorter polymethylene chains. A study of the same four catalysts in the dedeuteration of acetone-*d*$_6$ showed that 3-dimethylaminopropylamine was more than twice as effective as any of the others.[7] The data in Table I show no such phenomenon in the present case.

From the catalysis constants for water, hydroxide ion, and the buffers, it may be shown that in no case should the total amount of reaction due to the attack of these bases on isobutyraldehyde-*2-d* contribute as much as 5% to the overall reaction. Comparison with previous observations[4] shows that no significant amount of acid catalysis would be expected. Thus more than 95% of the reactions must be due to simple basic catalysis by the amino groups of the unprotonated or monoprotonated diamines or to reaction *via* intermediate iminium ions. The catalytic efficiency may be seen to increase monotonically with increasing basicity of the catalyst. Since the monoprotonated amines are in all cases the principal species present, since the monoprotonated amines are 62–79% protonated at their primary amino groups,[8] and since an unhindered tertiary amine is more effective at removing deuterons from isobutyraldehyde-*2-d* than is an unhindered primary amine of comparable basicity,[4,5,10] most of the simple basic catalysis would be expected to arise from the species of the type Me$_2$N(CH$_2$)$_n$NH$_3$$^+$. In fact, if we obtain second-order rate constants by dividing the first-order rate constants in Table I by the total concentration of diamine and plot their logarithms *vs.* the p*K* values of the diprotonated diamines, a reasonably straight line is obtained.[11] The slope of such a plot (0.3), being lower than the values obtained with families of simple bases (~0.5),[4] suggests that significant amounts of catalysis *via* iminium ion formation may also be occurring, especially with the less basic diamines. The approximate linearity, however, was believed to constitute strong enough evidence against really efficient bifunctional catalysis to discourage us from a more detailed kinetic study.

Examination of molecular models indicated that the chain between the two amino groups in undecane-1,11-diamine and dodecane-1,12-diamine should be long enough to permit these compounds to act as bifunctional catalysts *via* transition states like **2** even with a trans orientation of the carbon–nitrogen double bond in the intermediate iminium ion. The observations in Table II that these two catalysts do not differ significantly from each other or from hexane-1,6-diamine in their activity make it seem unlikely that bifunctional catalysis is of major importance with any of these compounds, however.

Basicity of 2 and Its Monoprotonated Derivatives. The basicity of **2** must be the sum of the basicities of its two amino groups. As a first approximation, the primary amino group would be expected to be about as basic as a typical long-chain unsubstituted primary alkylamine, and the tertiary amino group would be expected to be about as basic as 1-dimethylamino-2-butyne. *n*-Butylamine appears to be the longest chain unsubstituted primary amine upon which enough reliable measurements have been made to permit the calculation (by interpolation between data at 20 and 40°)[12] of the pK_a value (10.27) at 35°. Since butylamine is 200 times as basic as 1-dimethylamino-2-butyne, the first p*K* of the diamine (10.12) must be almost entirely due to its primary amino group. The decrease in p*K* relative to *n*-butylamine is most reasonably attributed to the electron-withdrawing carbon–carbon triple bond separated by five methylene groups from the primary amino group. The observed Δp*K* (0.15) is not much larger than the increment (0.125) that would be calculated by the method of Clark and Perrin.[13]

[10] J. Hine, J. Mulders, J. G. Houston, and J. P. Idoux, *J. Org. Chem.*, **32**, 2205 (1967).

[11] The line is essentially as good if one plots the p*K* value for the tertiary ammonio group of the diprotonated amine (*i.e.*, the conjugate acid of the specific species thought likely to be the principal catalyst). These values, at the appropriate ionic strengths (around 0.15 *N*), were used in the plot published previously.[7]

[12] D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworths, London, 1965.

[13] J. Clark and D. D. Perrin, *Quart. Rev., Chem. Soc.*, **18**, 295 (1964).

In interpreting the kinetic data obtained in the presence of **2**, we also need to have pK_a values that are measures of the basicities of the tertiary amino group in the unprotonated diamine and of the primary amino group in that form of the monoprotonated diamine that is protonated at the tertiary amino group. We have estimated these values by assuming that the basicity of the tertiary amino group in the unprotonated diamine is the same as that of 1-dimethylamino-2-butyne. (The fact that the second pK of the diamine is lower by 0.43 at zero ionic strength is attributed to the substituent effect of protonating the primary amino group.) From this estimate it follows that the monoprotonated diamine exists to the extent of $10^{-2.14}$ or 0.7% in the tertiary-protonated form and that the pK_a of the free primary amino group in this form is 9.69 at zero ionic strength.

Catalysis by 2. Catalysis of the deuterium exchange of isobutyraldehyde-*2-d* by 3-dimethylaminopropyne and by 1-dimethylamino-2-butyne was studied as model reactions for catalysis by **2**. Catalysis by water and hydroxide ions[4] in these runs may be shown to contribute no more than 0.1% to the total reaction rates. Rate constants of $6.88 \times 10^{-4}\ M^{-1}\ \text{sec}^{-1}$ for 3-dimethylaminopropyne and $14.7 \times 10^{-4}\ M^{-1}\ \text{sec}^{-1}$ for 1-dimethylamino-2-butyne were obtained. These values give a Brønsted β of 0.46 for amines of the type $XC{\equiv}CCH_2NMe_2$. (The value for unhindered pyridines is 0.49.)[4] To learn how good a catalyst **2** would be if its primary and tertiary amino groups were not in the same molecule, we figuratively cut the molecule in two. That is, we studied the catalytic activity of a mixture of *n*-butylamine and 1-dimethylamino-2-butyne. According to known and estimated rate constants, there should be no more than a 2% contribution to the reaction rate by any terms other than those in eq 2, in which

$$k_{\text{obsd}} = k_{\text{RNMe}_2}[\text{RNMe}_2] + k'_{\text{RNMe}_2}K_{\text{I}}^{\text{Bu}}[\text{RNMe}_2][\text{BuNH}_3^+] \quad (2)$$

$RNMe_2$ is 1-dimethylamino-2-butyne, k_{RNMe_2} is its known rate constant for attack on isobutyraldehyde-*2-d*, k'_{RNMe_2} is its rate constant for attack on the iminium ion $Me_2CDCH{=}N^+HBu$-*n*, and K_{I}^{Bu} is the equilibrium constant for formation of this iminium ion from the aldehyde and *n*-butylammonium ions. The value obtained for $k'_{\text{RNMe}_2}K_{\text{I}}^{\text{Bu}}$ is $2.34 \times 10^{-2}\ M^{-2}\ \text{sec}^{-1}$.

The runs using **2** as a catalyst were carried out at pH's so low that more than 99% of the primary amino groups were protonated. Under these conditions we estimate that no more than 2% of the reaction could be due to terms other than those in eq 3, in which BH

$$k_{\text{obsd}} = (k_{\text{BH}} + k_{\text{i}}K_{\text{I}})[\text{BH}^+] + k'_{\text{BH}}K_{\text{I}}[\text{BH}^+]^2 + k''_{\text{BH}}K_{\text{IH}}[\text{BH}^+][\text{BH}_2^{2+}] \quad (3)$$

refers to the monoprotonated and BH_2 to the diprotonated form of **2**. The equilibrium constants K_{I} and K_{IH} are for the formation of the iminium ions $Me_2CDCH{=}N^+H(CH_2)_5C{\equiv}CCH_2NMe_2$ and $Me_2CDCH{=}N^+H(CH_2)_5C{\equiv}CCH_2NHMe_2^+$ from aldehyde and BH and BH_2, respectively; k'_{BH} and k''_{BH} are for the attack of BH (*via* its unprotonated tertiary amino end) on these iminium ions. The rate constant k_{i} is for internal dedeuteration of the singly charged iminium ion *via* attack by its free dimethylamino group. In principle, the values of the three constants $k_{\text{BH}} + k_{\text{i}}K_{\text{I}}$, $k'_{\text{BH}}K_{\text{I}}$, and $k''_{\text{BH}}K_{\text{IH}}$ should be capable of being determined by a least-squares treatment of the data in Table V. In practice, however, the reaction is so dominated by the first of these three constants that values of the latter two cannot be determined reliably. Since $k'_{\text{BH}}K_{\text{I}}$ and $k''_{\text{BH}}K_{\text{IH}}$ refer to processes that differ only in whether an amino group 8–11 atoms from the reaction center is protonated or not, they should be approximately equal. For a better approximation, we may use the fairly linear plot of p$K_{\text{RCH}_2\text{NH}_3^+}$ *vs.* log $(k'_{\text{Py}}K_{\text{I}}^{\text{R}})$ for the equilibrium constants for the formation of iminium ions from isobutyraldehyde-*2-d* and ammonium ions of the type $RCH_2NH_3^+$ multiplied by the rate constants for dedeuteration of these iminium ions by pyridine.[2] Since the slope of this plot is −0.40, we shall assume that log $(k''_{\text{BH}}K_{\text{IH}})$ exceeds log $(k'_{\text{BH}}K_{\text{I}})$ by 0.40 of the difference in pK_a between the primary ammonio groups in the monoprotonated and the diprotonated forms of **2**. Such an assumption could not lead to highly precise results, because if it were exactly true at one ionic strength it probably would not be at another, since varying ionic-strength effects on the acidity constants and rate constants are expected. To follow the ordinary treatment of ionic strength effects on rate constants for reactions between ions[14] is, in the case of the transition state of the reaction governed by k''_{BH}, to treat two positive charges separated by 21 atoms as if they were on the same atom. Hence, we have neglected ionic strength effects on rate constants. Since the activity coefficient of a singly charged ion may be calculated from the Davies equation[15] to remain in the range 0.748 ± 0.027 over the range of ionic strengths covered by Table V, this neglect should not lead to serious error. From the average activity coefficient, we may calculate a pK_a for the primary amino group of diprotonated **2** (9.94) from which the factor 0.40 gives an estimate that $k''_{\text{BH}}K_{\text{IH}}$ is equal to $1.18\ k'_{\text{BH}}K_{\text{I}}$. Introduction of this estimate into eq 3 gives an equation with only two unknowns. A least-squares treatment of the data in Table V gives values of $7.1 \times 10^{-3}\ M^{-1}\ \text{sec}^{-1}$ and $1.85 \times 10^{-2}\ M^{-2}\ \text{sec}^{-1}$ for $k_{\text{BH}} + k_{\text{i}}K_{\text{I}}$ and $k'_{\text{BH}}K_{\text{I}}$, respectively. The rate constants in Table V may be calculated from these values with an average deviation of 2.5%.

The value of $k'_{\text{BH}}K_{\text{I}}$ is quite plausible, being 20% smaller than $k'_{\text{RNMe}_2}K_{\text{I}}^{\text{Bu}}$, the rate constant for attack of a somewhat more basic tertiary amine on a rather similar iminium ion. The value of $k_{\text{BH}} + k_{\text{i}}K_{\text{I}}$, on the other hand, seems much too large to consist of k_{BH} alone. If the point for monoprotonated **2** falls on the Brønsted plot described by the catalysis constants for 3-dimethylaminopropyne and 1-dimethylamino-2-butyne at zero ionic strength, the value of k_{BH} would be $9.3 \times 10^{-4}\ M^{-1}\ \text{sec}^{-1}$. Since $k_{\text{BH}} + k_{\text{i}}K_{\text{I}}$ is 7.7 times this large, we conclude that the $k_{\text{i}}K_{\text{I}}$ term is real. From the observed value of $k_{\text{BH}} + k_{\text{i}}K_{\text{I}}$ and the estimated value of k_{BH}, we estimate that $k_{\text{i}}K_{\text{I}}$ is about $6.2 \times 10^{-3}\ M^{-1}\ \text{sec}^{-1}$.

According to studies using molecular models, **2** may react with isobutyraldehyde-*2-d* and acid to give a trans iminium ion in which the dimethylamino group

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(14) *Cf.* J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1962, p 74.

(15) C. W. Davies, *J. Chem. Soc.*, 2093 (1938).

may, without obvious strain, reach the deuterium atom when the molecule is in a conformation such that the carbon–deuterium bond is as nearly as possible parallel to the overlapping p orbitals of the carbon–nitrogen double bond. Thus **2** has an advantage over the four diamines of the type $Me_2N(CH_2)_nNH_2$ and hexane-1,6-diamine, none of which have long enough chains between their two amino groups to give bifunctional catalysis *via* a trans iminium ion without significant strain. The longer and more flexible chains of undecane-1,11-diamine and dodecane-1,12-diamine probably constitute a disadvantage for these compounds since they give the possibility of a larger number of catalytically unproductive conformations than in the case of **2**, which has a shorter chain and one that has four carbon atoms held rigidly collinear. The longer chain diamines would also give the possibility of a larger number of catalytically useful conformations, but the well-known difficulties encountered in cyclizations to give macrocyclic products show that this factor is ordinarily of less importance. The fact that **2** contains an unhindered tertiary amino group should tend to make it a better catalyst than the diprimary amines, but it is not clear that it makes bifunctional catalysis any more recognizable for **2**. The tertiary amino groups should increase the rate of monofunctional catalysis as well as that of bifunctional catalysis. Compound **2** was constructed as a convenient compromise between ease of synthesis and more complete rigidity of the catalyst, which, in the optimum case, should give a much more effective catalyst.

Experimental Section

Reagents. The ω-dimethylaminoalkylamines used have been described previously.[8] The α,ω-diaminoalkanes were commercial samples that were not purified further. Isobutyraldehyde-*2-d* was prepared as described previously.[4]

3-Dimethylaminopropyne. Addition of 70.5 ml (0.90 mol) of redistilled Aldrich 3-bromopropyne to 250 ml (3.8 mol) of anhydrous dimethylamine was carried out with stirring and cooling with an ice bath. During the 80-min addition, the reaction temperature rose to 25° and a white precipitate formed. After an additional 2.2 hr the excess dimethylamine was allowed to evaporate, xylene was added, and the mixture was filtered. Fractional distillation of the filtrate gave 57.3 g (76%) of 3-dimethylaminopropyne: 99% pure by glpc; bp 79–80° (lit.[9] 79–81°); ir (KBr) 3.20 ($C\equiv CH$) and 4.75 μ ($C\equiv C$); pmr (neat) δ 3.03 (d, 2, J = 2.2 Hz, CH_2), 2.40 (t, 1, J = 2.1 Hz, $C\equiv CH$), and 2.21 ppm downfield from TMS (s, 6, NMe_2). The material used in kinetic studies was refractionated to give a product bp 82.0–82.5°, 99.9% pure by glpc.

1-Dimethylamino-7-chloro-2-heptyne. To a sodamide solution prepared from 6.3 g (0.27 g-atom) of sodium and 250 ml of liquid ammonia was added 32 ml (0.30 mol) of 3-dimethylaminopropyne over a period of 15 min. After 1 hr, 30 ml (0.26 mol) of 1-bromo-4-chlorobutane was added over a period of 10 min. The solution was stirred for an additional 8 hr, 1 g of ammonium chloride was added, and the solution was allowed to evaporate overnight. The residue was taken up in water and pentane and the pentane layer extracted with aqueous hydrochloric acid. After the acid layer was washed with pentane, it was made basic with solid sodium hydroxide and extracted with pentane. Distillation of the dried pentane extracts gave 23.5 g (51%) of 1-dimethylamino-7-chloro-2-heptyne: purity by glpc $\geq$ 95%; bp 62–72° (0.45–0.49 mm); ir (KBr) 4.42 ($C\equiv C$) and 15.32 μ (CH_2Cl); pmr (neat) δ 1.75 (m, 4, $CH_2C\mathit{H}_2C\mathit{H}_2CH_2$), 2.19 (m, 8, NMe_2 and $CH_2C\mathit{H}_2C\equiv C$), 3.15 (t, 2, J = 2.1 Hz, $C\mathit{H}_2NMe_2$), and 3.54 ppm (t, 2, J = 6.1 Hz, CH_2Cl).

An attempt to replace the chlorine atom of this compound by a cyano group by refluxing with excess sodium cyanide in acetone for 24 hr gave less than 1% reaction.

1-Dimethylamino-7-cyano-2-heptyne. Alkylation of 3-dimethylaminopropyne with 30 ml (0.26 mol) of 5-bromovaleronitrile by the method described in the preceding section gave 7.16 g (17%) of 1-dimethylamino-7-cyano-2-heptyne: 99.5% pure by glpc; bp 88–98° (0.30 mm); ir (KBr) 4.43 μ ($C\equiv N$); pmr (neat) δ 1.66 (m, 4, $CH_2C\mathit{H}_2C\mathit{H}_2CH_2$), 2.10–2.56 (m, 10, CH_2CN, NMe_2, and $CH_2C\mathit{H}_2$-$C\equiv C$), and 3.13 ppm (t, 2, J = 2.2 Hz, $C\mathit{H}_2NMe_2$).

The pentane layer that had been extracted with acid in the preceding procedure was dried and distilled to give 5.55 g (26%) of cyclobutyl cyanide: 95% pure by glpc; bp 41–47° (21–16 mm); ir (KBr) 4.44 μ ($C\equiv N$); pmr (neat) δ 1.74–2.62 (m, 6, $CH_2CH_2CH_2$), 2.88–3.46 ppm (m, 1, CHCN). Acid hydrolysis[16] gave cyclobutanecarboxylic acid identical with an authentic sample[17] in ir, pmr, and glpc.

Various attempts to improve the yield by changing the concentrations of reagents, the reaction time, and the reaction temperature (to −70°)[18] did not raise the yield of 1-dimethylamino-7-cyano-2-heptyne above 19%. (In the same run 51% cyclobutyl cyanide was obtained.)

1-Dimethylamino-8-amino-2-octyne (2). Addition of 11.1 g (68 mmol) of 1-dimethylamino-7-cyano-2-heptyne to a solution of 2.7 g (71 mmol) of lithium aluminum hydride (Metal Hydrides, Inc.) in 150 ml of anhydrous diethyl ether under nitrogen was carried out over 20 min. After stirring and refluxing the solution overnight, the addition of 10.8 ml of 10% sodium hydroxide caused the formation of a white precipitate. After stirring for another night the solution was filtered. Distillation of the filtrate and ether washings gave 8.74 g (79%) of **2**: $\geq$ 99.3% pure by glpc; bp 122.5–126.0° (13–14 mm); ir (KBr) 2.97 and 3.03 (NH_2), 4.42 ($C\equiv C$), and 6.25 μ (NH_2); pmr (neat) δ 1.03 (s, 2, NH_2), 1.44 (m, 6, CH_2-$C\mathit{H}_2C\mathit{H}_2C\mathit{H}_2CH_2$), 2.19 (m, 8, NMe_2 and $CH_2C\mathit{H}_2C\equiv C$), 2.63 (t, 2, J = 6.1 Hz, $C\mathit{H}_2NH_2$), and 3.16 ppm (t, 2, J = 2.1 Hz, $C\mathit{H}_2NMe_2$).

Anal. Calcd for $C_{10}H_{20}N_2$: C, 71.38; H, 11.96; N, 16.66. Found: C, 71.44 ± 0.05; H, 12.13 ± 0.06; N, 17.03 ± 0.12.

Shortening the reduction time or the time the solution stood after addition of sodium hydroxide to about an hour reduced the yields to about 50%.

1-Dimethylamino-2-butyne. Alkylation of 3-dimethylaminopropyne with methyl iodide by the method described in the preceding sections gave 48% of 1-dimethylamino-2-butyne: 99.2% pure by glpc, bp 112–115° (lit.[19] bp 114–115.5°).

p*K* Determinations. Standard solutions of the amines in water were titrated potentiometrically under nitrogen using a Beckman Research pH Meter, Model 101900 at 35°. Values of p*K* were calculated from a number of points taken between 10 and 90% of the equivalence point with allowance for the fact that hydroxide ion concentrations were not always negligible compared with amine and ammonium ion concentrations. The method used for diamines has been described previously.[8] The pH was taken as the negative logarithm of the hydrogen ion activity and activity coefficients were calculated from the Davies equation,[15] which becomes eq 4 at 35°.

$$\log f = -0.5189Z^2\left(\frac{\sqrt{\mu}}{1 + \sqrt{\mu}} - 0.2\mu\right) \qquad (4)$$

Although replacement of the constant 0.2 by 0.3 was later found to give better overall agreement with data on a large number of salts,[20] the value 0.2 gave smaller standard deviations in the p*K* values calculated from our data.

Kinetic Runs. Individual points in kinetic runs were started by injecting isobutyraldehyde-*2-d* into a sample of the catalyst solution at 35.0° and shaking. Points were stopped by addition of excess acetic acid and chloroform. The deterium content of the aldehyde in the chloroform extracts was determined by pmr measurements and first-order rate constants calculated as described previously.[4]

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(16) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, pp 292–293.

(17) For which we wish to thank Professor Paul G. Gassman.

(18) *Cf.* M. S. Newman and R. D. Closson, *J. Amer. Chem. Soc.*, **66**, 1553 (1944).

(19) V. A. Engelhardt, *ibid.*, 78, 107 (1956).

(20) C. W. Davies, "Ion Association," Butterworths, London, 1962, pp 34–38.