1,3- and 1,4-Diamines. Internal H Bonding and Protonation

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Internal Hydrogen Bonding and Positions of Protonation in the Monoprotonated Forms of Some 1,3- and 1,4-Diamines[1]

Jack Hine* and Wu-Shyong Li

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Values of pK_1 and pK_2 have been determined for $N,N,2$-trimethyl-1,3-propanediamine, $N,N,2,2$-tetramethyl-1,3-propanediamine, $N,N,N',N',2,2$-hexamethyl-1,3-propanediamine, cis- and trans-2-(dimethylaminomethyl)-cyclohexylamine, 3-endo- and 3-exo-dimethylaminomethyl-2-endo-norbornanamine, o-(dimethylaminomethyl)benzylamine, and o-bis(dimethylaminomethyl)benzene. The ^{1}H nuclear magnetic resonance chemical shifts of the N-methyl and certain other hydrogen atoms in these compounds were measured in the presence of increasing amounts of added strong acid. It is concluded that the monoprotonated forms of some of the diamines exist largely as cyclic internally hydrogen-bonded species, but in other cases, such as that of monoprotonated N,N,N',N'-tetramethyl-1,3-propanediamine, such cyclization is negligible. The largest extents of cyclization are found with the monoprotonated forms of $N,N,N',N',2,2$-hexamethyl-1,3-propanediamine, o-(dimethylaminomethyl)benzylamine, and o-bis(dimethylaminomethyl)benzene, which are estimated to be 77, 93.4, and 98.6% cyclic, respectively. Also estimated are the fractions of the monoprotonated forms of the primary–tertiary diamines that are protonated at the primary and at the tertiary amino groups. These estimates and the observed overall pK values give estimated micro pK values for such specific subspecies as the tertiary-monoprotonated and primary-monoprotonated diamines.

A ^{1}H nuclear magnetic resonance (^{1}H NMR) method for determining the relative basicities of the individual amino groups of unsymmetrical diamines was described previously.[2] The micro pK_a values obtained for several ω-dimethylamino alkyl amines have since been used in studies of bifunctional catalysis of the oximation of acetone,[3] the dedeuteration of acetone-d_6,[4] and the dealdolization of diacetone alcohol[5] by the monoprotonated forms of such diamines. We have now made analogous ^{1}H NMR measurements and pK determinations on additional 1,3- and 1,4-diamines and have obtained evidence that the monoprotonated forms of some of these diamines exist to major extents as cyclic hydrogen-bonded species in which the added proton is attached to both amino groups simultaneously.

Results and Discussion

pK Values. Values of pK_1 (for the monoprotonated amine) and pK_2 (for the diprotonated amine) were determined at 35° in aqueous solution by potentiometric titration using the Davies equation for ionic activity coefficients[6] to obtain the values at infinite dilution. Table I con-

tains the results obtained for nine diamines plus literature values[2,4,7,8] for five other diamines for comparison purposes. In interpreting these results it should be noted that primary amino groups attached to saturated carbon are ordinarily significantly more basic than their N,N-dimethyl derivatives are in aqueous solution. This generalization is supported by the pK_a values listed in Table II, most of which were obtained from the literature[4,7–11] and corrected to 35° if not determined at that temperature. The only exception to this rule that we found was with the cyclohexyl compounds, where the literature value[7] at 25° and our temperature correction gave a pK_a value of 10.48 for the conjugate acid of N,N-dimethylcyclohexylamine at 35°. In view of the lack of details as to how the literature pK value had been determined we carried out a determination at 35°. The result, which is listed in Table II, shows that the N,N-dimethyl derivative is a weaker base than cyclohexylamine, albeit by a smaller amount than is found with the other pairs listed.

The most anomalous of the pK_1 values for the tertiary–primary diamines is probably that for o-(dimethylami-

Table I
Acidity Constants for Mono- and Diprotonated 1,3- and 1,4-Diamines in Water at 35°

| Diamine		pK_1	pK_2	Registry no.
$H_2NCH_2CH_2CH_2NH_2$		10.16^a	8.17^a	
$Me_2NCH_2CH_2CH_2NH_2$		9.91^b	7.67^b	
$Me_2NCH_2CHMeCH_2NH_2$		9.87	7.25	6105-72-2
$Me_2NCH_2CMe_2CH_2NH_2$		10.03	6.74	53369-71-4
$Me_2NCH_2CH_2CH_2NMe_2$		9.52^c	7.36^c	
$Me_2NCH_2CMe_2CH_2NMe_2$		9.84	5.99	53369-79-2
2-(Dimethyl-aminomethyl)-cyclopentylamines	cis	$\sim9.44^{d,e}$	$\sim7.00^{d,e}$	
	trans	9.80^d	7.59^d	
2-(Dimethyl-aminomethyl)-cyclohexylamines	cis	10.02	7.08	53369-73-6
	trans	10.29	6.70	53369-74-7
3-(Dimethyl-aminomethyl)-2-norbornamines	3-exo-2-endo	9.92	7.61	53403-34-2
	endo-endo	9.78	6.82	53369-68-9
o-$Me_2NCH_2C_6H_4CH_2NH_2$		10.07	5.86	53369-77-0
o-$C_6H_4(CH_2NMe_2)_2$		10.58	4.97	53369-80-5

[a] Interpolated between values at 30° and 40° listed in ref 7. [b] From ref 2. [c] From ref 8. [d] From ref 4. [e] Measurements made on material containing about 81% cis and 19% trans isomer.

Table II
Acidity Constants for Primary Ammonium Ions and Their *N,N*-Dimethyl Derivatives in Water at 35° [a]

R	$pK_{RNH_3^+}$	Ref	$pK_{RNHMe_2^+}$	Ref
Me	10.31	7	9.58	7
Et	10.32	7	9.79 [b]	7
n-Pr	10.24	8	9.79 [b]	7
n-Bu	10.27	7	9.80	4
i-Bu	10.15	9	9.71 [b]	7
t-BuCH₂	9.83 [c]	7	9.52 [b,d]	8
Cyclopentyl	10.31	9		
Cyclohexyl	10.30	9	10.24	e
MeOCH₂CH₂	9.09	10	8.96	4
MeO(CH₂)₃	9.83	9	9.14 [b]	8
HC≡CCH₂	7.87	9	7.27	11
PhCH₂	9.00	9	8.70 [b]	8
o-MeC₆H₄CH₂	8.90 [c]	8		
2-*endo*-Norbornyl	10.03	e		

[a] Unless otherwise noted, these values were determined at 35° or corrected to 35° using an experimentally determined value of $\Delta H°$. [b] Corrected to 35° from 20° or 25° using a $\Delta S°$ value of −11.7 eu. The standard deviation of the 12 values of $\Delta S°$ for monoprotonated, electrically neutral tertiary amines (diamine data being statistically corrected) listed in a recent compilation[9] from this average value was 3.3 eu. [c] Corrected to 35° from 16–25° using a $\Delta S°$ value of −0.8 eu estimated from values for similar primary amines. [d] Obtained in a study in which a pK_a value for neopentyl-ammonium ions was obtained that was about 0.4 log unit lower than that found by other workers. [e] Determined in the present investigation.

nomethyl)benzylamine. The data in Table II show that benzylammonium ion has a pK_a of only 9.00 and this value is decreased by an ortho methyl substituent. If replacing a hydrogen atom on this ortho methyl group by a dimethyl-amino group has the same effect on the basicity of the primary amino group that replacing a hydrogen on carbon-4 of *n*-butylamine by an amino group does,[7] the pK_a of *o*-(dimethylaminomethyl)benzylammonium ions would be about 8.7. The basicity of the tertiary amino group may be estimated analogously to be enough to make the total pK_1 of the monoprotonated diamine about 8.9. The observed value of 10.07 shows that this diamine is about 15 times as basic as would be expected from data on related compounds. Other less pronounced anomalies include the relatively large pK_1 values for the 2-(dimethylaminomethyl)-cyclohexylamines and for *N,N*,2,2-tetramethyl-1,3-propanediamine. These anomalies seem qualitatively explicable in terms of stabilization of the monoprotonated diamines by an internal hydrogen bond such as that in **1**.

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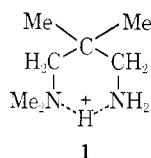
In order to have compounds for which the interpretation of ¹H NMR data would be particularly simple we studied the *N',N'*-dimethyl derivatives of the primary–tertiary diamines in three of the cases in which such compounds would have two equivalent dimethylamino groups. The pK_1 values for two of these compounds, *N,N,N',N'*,2,2-hexamethyl-1,3-propanediamine and *o*-bis(dimethylaminomethyl)benzene, also point to cyclic hydrogen-bonded structures for the monoprotonated species.

¹H Nuclear Magnetic Resonance Measurements. The ¹H NMR method for estimating the relative basicities of the two amino groups in unsymmetrical diamines involves

measuring the chemical shift, as a function of the extent of protonation of the diamine, of some hydrogen atom(s) in the diamine.[2] The most reliable results are expected when the hydrogen atom whose shift is being measured is much nearer one amino group than the other. In all the cases studied previously measurements were made on the *N*-methyl protons of dimethylamino substituted primary amines. For such cases we may derive eq 1, in which δ_{obsd} is

$$\delta_{obsd} = f_d \delta_d + f_m \delta_m \tag{1}$$

the observed chemical shift of the methyl protons in the solution in question, f_m is the fraction of the diamine that is monoprotonated and f_d is the fraction diprotonated in that solution, δ_d is the chemical shift in the diprotonated species, and δ_m is the chemical shift in the average monoprotonated species. If the monoprotonated species consists solely of diamine protonated only at the tertiary amino group and diamine protonated only at the primary amino group, the value of δ_m may be expressed as shown in eq 2,

$$\delta_m = f_t \delta_t + f_p \delta_p \tag{2}$$

in which f_t and f_p are the fractions of monoprotonated diamine that are tertiary protonated and primary protonated, respectively, and δ_t and δ_p are the respective chemical shifts in these two species. In eq 1 and 2 all chemical shifts are downfield from that in the unprotonated diamine. Since f_d and f_m may be calculated from the amount of strong acid used in making up the diamine solution and from the pK values for the diamine, values of δ_d and δ_m may be obtained from eq 1 (or an equivalent expression) using δ_{obsd} values for diamine solutions with various amounts of added acid. However, in order to obtain a value for f_t or f_p it is necessary to estimate δ_t and δ_p. To do this it was first assumed that δ_d is equal to $\delta_p + \delta_t$ (eq 3). This fol-

$$\delta_d = \delta_p + \delta_t \tag{3}$$

lows from the assumption that protonation of the primary amino group has the same effect on the chemical shift of the *N*-methyl hydrogen atoms when the tertiary amino group is protonated as when it is not. This assumption may be a good approximation when the molecular geometry of the diamine is not significantly affected by either monoprotonation or diprotonation. It is very similar to assuming that the chemical shift of the *N*-methyl hydrogen atoms of a symmetrical ditertiary amine is affected in the same way by protonation of the distant amino group when the nearby amino group is protonated as when the nearby amino group is not protonated. If this latter assumption is correct the chemical shift of the *N*-methyl hydrogen atoms (or any hydrogen atom) of a symmetrical diamine will be a linear function of the average extent of protonation of the diamine. If the assumption is significantly in error a plot of the chemical shift vs. the extent of protonation will show a break at 1.0 proton per molecule of diamine. Hence the validity of eq 2 was tested by making such plots for *N,N,N',N'*-tetramethylethylenediamine and *N,N,N',N'*-tetramethyl-1,3-propanediamine. The plots were both linear within the experimental error and it was concluded that the monoprotonated forms of these two diamines did not exist to a significant extent as cyclic hydrogen-bonded species and that eq 2 was probably a good approximation for the primary–tertiary diamines, at least in the cases where there were two and three methylene groups between the two amino groups.[2]

Since we concluded on the basis of pK determinations that the monoprotonated forms of *o*-bis(dimethylaminomethyl)benzene and *N,N,N',N'*-2,2-hexamethyl-1,3-propanediamine[2] existed largely as species in which the added
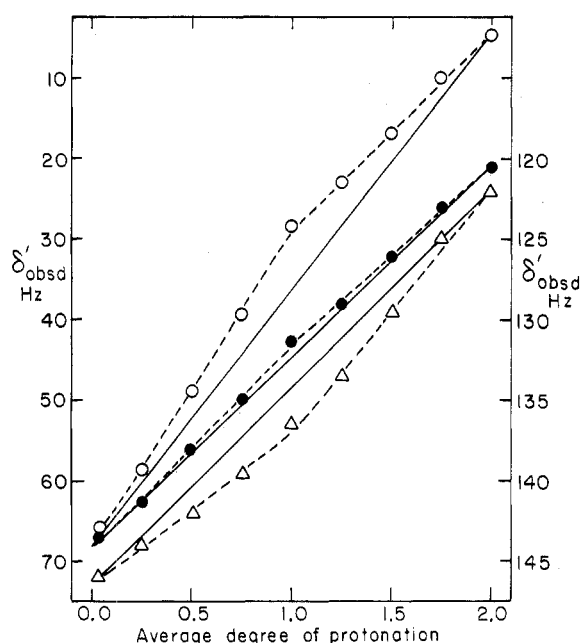
Figure 1. Plots of chemical shifts upfield from internal methanol vs. degree of protonation: O, methylene protons (shifts on left-hand scale); ●, N-methyl protons (shifts on left-hand scale); △, C-methyl protons (shifts on right-hand scale), of $N,N,N',N',2,2$-hexamethyl-1,3-propanediamine in aqueous solution.

proton was bonded to both amino groups simultaneously, we have studied the ^{1}H NMR spectra of these compounds as a function of the extent of protonation in aqueous solution. The latter diamine gave the more informative results. Plots of the chemical shifts of the N-methyl, the C-methyl, and the methylene hydrogen atoms vs. the average number of protons added to the diamine molecule are shown in Figure 1. Each set of data was fitted by the method of least squares to eq 4, which is a modified version of eq 1 in which

$$\delta'_{obsd} = \delta_0 - f_m\delta_m - f_d\delta_d \qquad (4)$$

δ'_{obsd} is measured upfield from the internal standard methanol and δ_0 is the upfield chemical shift of the unprotonated diamine relative to this standard. The experimental points agree well with the dashed lines which were constructed from the optimum values of δ_0, δ_d, and δ_m obtained. The solid lines, which are straight lines connecting the ends of the dashed lines, are drawn to show how much the plots deviate from linearity. These deviations show that δ_m is more than half as large as δ_d for the N-methyl and methylene protons but less than half as large for the C-methyl protons. Neither the absolute nor the relative magnitudes of the various chemical shifts could be reproduced by calculations based on the equation of Schweizer and co-workers,[12,13] in which we took the protonated amino groups as having unit positive charges located at the nitrogen atoms and then assumed various plausible molecular geometries. Improved agreement could be obtained by assuming that the effects of the charges were attenuated to varying degrees by the dielectric constant in the vicinity, but we did not go so far as to carry out a Kirkwood–Westheimer treatment to obtain an effective dielectric constant.[14] The fact that the protonation of a tertiary amino group has a much larger effect on chemical shifts of nearby hydrogen atoms than does protonation of an analogous primary amino group[2] suggests that much of the charge on a protonated amino group is dispersed via hydrogen bonding onto surrounding water molecules. This will seriously complicate any quantitative interpretation of the effect of protonation of amino groups on chemical shifts.

The deviations from linearity in the plots in Figure 1 may be explained *qualitatively* in terms of the formation of the cyclic hydrogen-bonded monoprotonated species, **2**, in
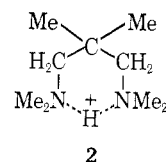
which the hydrogen bond is written as symmetrical not to imply that there is necessarily only one potential energy minimum for the hydrogen atom but to reflect the fact that the hydrogen atom would be bonded equally to both nitrogen atoms on the ^{1}H NMR time scale. It is assumed that the diprotonated amine exists largely in a conformation such as **3**, in which the positively charged nitrogen atoms
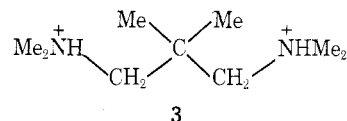
are separated as far as possible. The C-methyl hydrogen atoms are seen to be much closer to the fully positively charged nitrogen atoms in **3** than they are to the half-positively charged nitrogen atoms in **2**. This explains why diprotonation changes their chemical shift more than twice as much as monoprotonation does. The N-methyl and the methylene hydrogen atoms, on the other hand, are at the same distance from the nearer nitrogen atom in **2** as they are in **3**, but they are much nearer the more distant nitrogen atom in **2** than in **3**.

Although we regard the pK data as providing convincing evidence for the cyclic hydrogen-bonded character of most of the monoprotonated form of $N,N,N',N',2,2$-hexamethyl-1,3-propanediamine, the deviation of the plot of the chemical shifts of the N-methyl protons vs. the extent of protonation (Figure 1) from linearity is relatively small. If this is generally true for the chemical shifts of the N-methyl protons in α,ω-bis(dimethylamino) compounds, such plots may provide little evidence as to whether the monoprotonated diamines are internally hydrogen bonded or not. In view of the evidence that the plots for other types of protons are more sensitive to internal hydrogen bonding, we have studied N,N,N',N'-tetramethylethylenediamine and $N,N,-N',N'$-tetramethyl-1,3-propanediamine again, observing the chemical shifts of the N-methylene as well as the methyl protons. (The peak for the middle methylene group of the propanediamine derivative was too highly split to give reliable chemical shifts.) The data, which fit eq 4 well, gave the δ_d and δ_m values listed in Table III. The straightness of the plots of δ_{obsd} for the N-methyl hydrogen atoms vs. the extent of protonation of the diamine may be seen in the fact that the ratio of δ_d to δ_m is within the experimental uncertainty of 2.00 for both compounds. The ratio is also 2.00 for the N-methylene hydrogen atoms of N,N,N',N'-tetramethyl-1,3-propanediamine, a fact that seems highly significant since it is only 1.64 for the N-methylene protons of $N,N,N',N',2,2$-hexamethyl-1,3-propanediamine, whose monoprotonated form is believed to be largely cyclic. We take this as strong evidence for the largely acyclic character of monoprotonatedN,N,N',N'-tetramethyl-1,3-propanediamine. The ratio is 2.11 for the methylene hydrogen atoms of N,N,N',N'-tetramethylethylenediamine. The fact that this is larger than 2.00 rather than smaller than 2.00, as was observed for the methylene hydrogen atoms of a compound for which there is good evidence for the formation of a cyclic monoprotonated form, makes us suspicious of the hy-

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Table III
Values of Parameters from Eq 4 for Diamines[a]

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Diamine[b]	$\delta_d,$[c] ppm	$\delta_m,$[c] ppm	$\delta_0,$[d] ppm
$Me_2NCH_2CH_2NMe_2$	0.80	0.39	1.16
$Me_2NCH_2CH_2NMe_2$	1.18	0.56	0.90
$Me_2NCH_2CH_2CH_2NMe_2$	0.76	0.38	1.18
$Me_2NCH_2CH_2CH_2NMe_2$[e]	0.94	0.47	1.04
$Me_2NCH_2CHMeCH_2NH_2$	0.78	0.27	1.20
$Me_2NCH_2CMe_2CH_2NH_2$	0.78	0.33	1.09
$Me_2NCH_2CMe_2CH_2NH_2$	0.37	0.16	2.42
$Me_2NCH_2CMe_2CH_2NMe_2$	0.79	0.42	1.14
$Me_2NCH_2CMe_2CH_2NMe_2$	1.06	0.65	1.13
$Me_2NCH_2CMe_2CH_2NMe_2$	0.41	0.16	2.44
cis-2-Me_2NCH_2-c-$C_6H_{10}NH_2$	0.77	0.38	1.16
$trans$-2-Me_2NCH_2-c-$C_6H_{10}NH_2$	0.76	0.29	1.19
3-exo-Me_2NCH_2-2-$endo$-norbornanamine	0.79	0.40	1.20
3-$endo$-Me_2NCH_2-2-$endo$-norbornanamine	0.76	0.47	1.16
o-$MeNCH_2C_6H_4CH_2NH_2$	0.68	0.18	1.12
o-$C_6H_4(CH_2NMe_2)_2$	0.67	0.32	1.14

[a] At about 37° in H_2O using a 60-MHz instrument unless otherwise noted. [b] The δ values refer to the boldfaced hydrogen atoms or methyl groups. [c] Chemical shift in the diprotonated (δ_d) or the average monoprotonated (δ_m) amine downfield from that in the unprotonated diamine. [d] Chemical shift in the unprotonated diamine upfield from internal methanol. [e] At about 31° in D_2O using a 100-MHz instrument.

pothesis that this diamine also gives a cyclic monoprotonated form. Although we cannot rule out the possibility of cyclization, we can point out that the two nitrogen atoms in an ethylenediamine derivative cannot assume positions nearly as favorable for internal hydrogen bonding as those in a 1,3-propanediamine derivative can. It therefore seems possible that this rather small deviation of the ratio from 2.00 is simply a measure of the imperfection, perhaps arising from changes in the relative populations of various types of conformers, in the ^1H NMR method for measuring micro pK values and diagnosing cyclization of monoprotonated derivatives.

The ratio of δ_d to δ_m (2.09) for the N-methyl hydrogen atoms of o-bis(dimethylaminomethyl)benzene, a compound for which there is convincing pK evidence for the formation of a cyclic monoprotonated form, is also near 2.00. The interpretation of this fact, however, is even more complicated than is interpretation of the data on aliphatic diamines, because in this case one must consider the effect of cyclization on the positions of the methyl groups relative to the aromatic ring current. We have not carried through any detailed evaluation of the ring-current effect.

Estimation of Micro pK Values. We have used both the pK data and the ^1H NMR data to estimate the relative amounts of the monoprotonated primary–tertiary diamines that exist in the primary-protonated (TPH$^+$), tertiary-protonated (HTP$^+$), and cyclic hydrogen-bonded (THP$^+$) forms. In doing so we estimated the pK values associated with these individual forms, that is, the micro pK values. We expressed observed pK values in terms of additive contributions of various structural features. We first dealt with the pK_a values in Table II for the conjugate acids of monoamines of the type RNH$_2$ and RNMe$_2$ where R is a saturated hydrocarbon group larger than methyl and the values of the sum pK_1 + pK_2 for those primary–tertiary diamines in Table I in which there are three carbon atoms between the amino groups. This sum is simply the negative logarithm of the equilibrium constants for the dissociation of

the diprotonated diamine to the unprotonated diamine and two hydrogen ions. It has nothing to do with any monoprotonated form of the diamine and therefore its value is not influenced by the presence or absence of hydrogen bonding in the monoprotonated diamine. A least-squares treatment gave a contribution of 10.27 for an amine of the type RCH$_2$CH$_2$NH$_2$ or a cyclohexylamine or cyclopentylamine and a contribution of 10.22 for a 2-$endo$-norbornanamine. There is a contribution of -0.46 for such compounds if there is double branching at a β carbon atom or if there is a single branch that is eclipsed, or almost eclipsed, with the amino group [as in 3-$endo$-dimethylaminomethyl-2-$endo$-norbornanamine or cis-2-(dimethylaminomethyl)cyclopentylamine]. In the absence of such branching there is a contribution of -0.20 for a single β branch unless it is held away from the amino group with a dihedral angle of at least 120° [as it is assumed to be in 3-exo-dimethylaminomethyl-2-$endo$-norbornanamine but not in the more flexible $trans$-2-(dimethylaminomethyl)cyclopentylamine]. There is a contribution of 9.81 for an amine of the type RCH$_2$CH$_2$NMe$_2$ to which -0.07 is added for a single β branch and -0.31 for a double β branch. (Since the α-carbon–β-carbon bond is never in a ring, no complications arise from conformational rigidity.) In addition to these contributions, which apply to both the monoamines and diamines, there is a contribution of -2.52 to the sum pK_1 + pK_2 arising from destabilizing interactions between the two protonated amino groups in the diprotonated diamines. To this is added another -0.49 if the charges are held near each other by eclipsing of the C–NH$_3^+$ bond with the C–CH$_2$NMe$_2$ bond or -0.24 if the dihedral angle between these two bonds is held at about 60° [as it is assumed to be in the case of the 2-(dimethylaminomethyl)cyclohexylamines; transformation of the trans isomer to the diaxial conformer would involve much more destabilization]. From these ten parameters the 11 relevant pK_a values from Table II and the nine pK_1 + pK_2 sums from Table I may be calculated with an average deviation of 0.06 and a maximum deviation of 0.19. Every parameter had to be used to calculate more than one pK value or sum.

The first seven of the parameters given in the preceding paragraph should be of use in estimating the basicities of the individual amino groups of the diamines. In addition two more parameters were used: one being the effect of an amino substituent on the pK_a of a dimethylammonio group three carbons away and the other being the effect of a dimethylamino substituent on the pK_a of an ammonio group three carbons away. Before evaluating these parameters let us note that K_1, the observed acidity constant for a monoprotonated diamine, may be expressed as shown in eq 5,

$$\frac{1}{K_1} = \frac{1}{K_{TPH}} + \frac{1}{K_{HTP}} + \frac{1}{K_{THP}} \tag{5}$$

where K_{TPH}, K_{HTP}, and K_{THP} are the acidity constants of the primary-protonated, tertiary-protonated, and cyclic hydrogen-bonded forms of the monoprotonated diamine (e.g., eq 6). The parameters in the preceding paragraph

$$K_{HTP} = \frac{[H^+][TP]}{[HTP^+]} \tag{6}$$

plus the two new parameters we are seeking will give estimates of K_{TPH} and K_{HTP}. These give us an estimated upper limit for K_1, i.e., a lower limit for pK_1. If a significant amount of the monoprotonated diamine exists in the cyclic hydrogen-bonded form the actual value of pK_1 should be larger than this estimate. In view of the evidence that N,N,N',N'-tetramethyl-1,3-propanediamine does not give any significant amount of cyclic species upon mono-

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Table IV
Estimated Micro pK Values for Primary–Tertiary Diamines[a]

Diamine	f_t [b]	f_c [c]	pK_{TPH}	pK_{HTP}	pK_{THP}
$Me_2NCH_2CH_2CH_2NH_2$	0.30	0	9.75	9.39	d
$Me_2NCH_2CHMeCH_2NH_2$	0.28	0.24	9.55	9.32	9.25
$Me_2NCH_2CMe_2CH_2NH_2$	0.11	0.71	9.29	9.08	9.88
trans-2-Me_2NCH_2-c-$C_5H_8NH_2$	0.33	~0.11	9.55	9.32	~8.83
cis-2-Me_2NCH_2-c-$C_6H_{10}NH_2$	0.20	0.46	9.55	9.32	9.68
trans-2-Me_2NCH_2-c-$C_6H_{10}NH_2$	0.11	0.71	9.55	9.32	10.14
3-*exo*-Me_2NCH_2-2-*endo*-norbornanamine	~0.25	~0.15	~9.70	~9.32	~9.09
3-*endo*-Me_2NCH_2-2-*endo*-norbornanamine	~0.35	~0.36	~9.24	~9.32	~9.34
o-$Me_2NCH_2C_6H_4CH_2NH_2$	0.022	0.934	8.71	8.41	10.04

[a] In water at 35°. [b] Fraction of monoprotonated diamine protonated at the tertiary amino group. [c] Fraction of monoprotonated diamine with a cyclic hydrogen-bonded structure. [d] No significant amount of cyclic hydrogen-bonded species formed.

protonation we tentatively assumed that the same was true for N,N-dimethyl-1,3-propanediamine. We further assumed that ^{1}H NMR measurements could be used as described previously to calculate the relative amounts of TPH[+] and HTP[+] present (using eq 2 with a δ_p value of 0.015 ppm).[2] That is, we accepted the previously reported pK_{TPH} and pK_{HTP} values of 9.75 and 9.39, respectively. Since the values we obtain from the parameters in the preceding paragraph are 10.27 and 9.81, this gives values of −0.52 and −0.42 for the effects of 3-dimethylamino and 3-amino substituents on the pK_a values of protonated primary amines and N,N-dimethylamines, respectively. These contributions were then combined with those from the preceding paragraph to calculate pK_{TPH} and pK_{HTP} values (which are listed in Table IV for all the compounds upon which ^{1}H NMR measurements were made) and then lower limits for pK_1 values for each of the primary–tertiary diamines with three carbon atoms between the amino groups that are listed in Table I. This lower limit was larger than the experimental pK_1 value only in the case of *cis*-2-(dimethylamino)cyclopentylamine, where it was larger by 0.17. However, since this is the amine for which the experimental pK values are probably least reliable and for which one of the poorer correlations of pK_1 + pK_2 values had been obtained, we regarded the overall agreement as satisfactory. The other seven diamines were all more basic than indicated by the estimated lower limits for pK_1, presumably because of the formation of various amounts of the cyclic hydrogen-bonded form of the monoprotonated diamine. The estimated values of K_{TPH} and K_{HTP} were used in eq 5 with the experimental values of K_1 to obtain the values of pK_{THP} listed in Table IV. From the pK values, f_t and f_c (the fraction of the monoprotonated diamine that exists in the cyclic hydrogen-bonded form), which are equal to K_1/K_{HTP} and K_1/K_{THP}, respectively, were calculated.

The values of f_c and pK_{THP} for *trans*-2-(dimethylaminomethyl)cyclopentylamine and 3-*exo*-dimethylaminomethyl-2-*endo*-norbornanamine are probably rather unreliable because they were obtained from estimated lower limits for pK_1 that differed from the experimental pK_1 values by only 0.05 and 0.07, respectively. In addition, the estimated pK_1 values for the norbornanamines were based in part on parameters that also appeared in the calculation of pK_1 for relatively few other compounds. This decreases the estimated reliability of the results obtained for these compounds. In spite of such reasons for doubt, the relative values of f_c listed in Table IV are on the whole rather plau-

sible. For the three acyclic diamines the increase in f_c that accompanies methylation of the β carbon atom may be explained in the same way as the "*gem*-dimethyl effect", which has been found to encourage many cyclization reactions.[15] For the five compounds in which the H_2NC-CCH_2NMe_2 bond is part of a ring, the two smallest f_c values are for the two diamines in which the dihedral angle is about 120° such that the two amino groups are so far apart that hydrogen bonding between them is difficult. (We would have expected hydrogen bonding to be easier with the more flexible cyclopentane derivative but are not sure that either f_c value is really significantly different from zero.) The next smallest f_c value is for the endo-endo norbornyl compound, in which the dihedral angle must be near 0°. Use of molecular models shows that with such a dihedral angle it is impossible to achieve simultaneously an optimum nitrogen–nitrogen distance (which we take to be in the range 2.5–3.0 Å) and optimum C–N–N angles (which we take to be around 109°) for a cyclic hydrogen-bonded species. The two largest f_c values for cyclic diamines are for the cyclohexyl compounds, where the dihedral angle is about 60°, which is fairly nearly optimum for formation of a cyclic hydrogen-bonded species. The fact that f_c is larger for the trans than for the cis isomer may result from axial–axial interactions in the cyclic hydrogen-bonded form of monoprotonated *cis*-2-(dimethylaminomethyl)cyclohexylamine. (These cyclized monoprotonated diamines bear a certain resemblance to the decalins, where the trans is significantly more stable than the cis isomer.)

The pK_{TPH} and pK_{HTP} values for o-(dimethylaminomethyl)benzylamine were estimated as described previously. These and the experimental value of pK_1 give an f_c value of 0.934, which shows a greater extent of cyclization of the monoprotonated diamine than for any of the other primary-tertiary diamines studied. Analogous calculations on o-bis(dimethylaminomethyl)benzene, however, give an even larger f_c value, 0.986. The f_c value obtained for $N,N,N',N',2,2$-hexamethyl-1,3-propanediamine is 0.77.

In aqueous solution, where the amine and ammonio groups have the alternative of hydrogen bonding to water, the tendency for cyclization is much smaller than it is in the gas phase, where 1,3-propanediamine has been found to have a proton affinity[16] about 19 kcal/mol larger than that for a similar monoamino compound such as n-butylamine.[17] Even in solution a much larger tendency toward cyclization has been observed with the monoprotonated form of 1,8-bis(dimethylamino)naphthalene, whose pK_1

value of 12.34 shows that it is more than 800,000 times as basic as any of the less N-methylated derivatives of 1,8-diaminonaphthalene.[18]

Experimental Section

Chemicals. The synthesis and properties of the *N,N*,2-trimethyl-1,3-propanediamine, *N,N*,2,2-tetramethyl-1,3-propanediamine, *N,N,N',N'*,2,2-hexamethyl-1,3-propanediamine, *cis-* and *trans*-2-(dimethylaminomethyl)cyclohexylamine, the 3-dimethylaminomethyl-2-norbornanamines, *o*-(dimethylaminomethyl)benzylamine, and *o*-bis(dimethylaminomethyl)benzene used have been described recently.[19] The other compounds were commercial products.

p*K* Determinations. The diamines and *N,N*-dimethylcyclohexylamine were titrated with standard 0.10 *M* hydrochloric acid in aqueous solution at 35.0 ± 0.5° using a Radiometer Model 26 pH meter and type G202B and K401 glass and reference electrodes. The pH values were read to 0.001 from the meter after the stirrer had been turned off. Values obtained when 0.2–0.8 and 1.2–1.8 equiv of acid had been added were used in a computer program[20] that obtained the p*K* values that minimized the sums of the squares of the deviations of the calculated from the observed pH values, of which there were usually about 25. In no case was the standard deviation as large as 0.040. The 20-, 25-, or 30-ml samples of 0.020 ± 0.005 *M* amine solutions titrated gave ionic strengths in the range 0.003–0.016 during the first half of the titration, which largely determined the value of p*K*₁, and 0.018–0.045 during the second half, which largely determined p*K*₂. The pH was taken to be $-\log a_{H^+}$ and ionic activity coefficients were calculated from the Davies equation.[6]

The p*K* for 2-*endo*-norbornanamine was determined analogously except that 0.040 *M* amine hydrochloride was titrated with 0.10 *M* sodium hydroxide.

¹H Nuclear Magnetic Resonance Measurements. All ¹H NMR measurements were made at about 37° in H_2O using a Varian A-60A spectrometer except in the case of the measurements on the methylene protons of *N,N,N',N'*-tetramethyl-1,3-propanediamine, which were made in D_2O at about 31° using a JEOL JNM-MH-100 instrument to minimize complications arising from spin–spin splitting and overlap with other peaks. All the amines were studied at a total concentration of 0.1 *M* except in the case of *o*-bis(dimethylaminomethyl)benzene, 3-*endo*-dimethylaminomethyl-2-*endo*-norbornanamine, and the methylene proton study of *N,N,N',N'*-tetramethyl-1,3-propanediamine, where concentrations of 0.04–0.05 *M* were used. In the case of the 3-*endo*-dimethylaminomethyl-2-*endo*-norbornanamine 20% methanol was added to increase the solubility of the amine. In all other cases 0.1–0.5 *M* methanol was used as an internal reference. The concentrations of the three forms of the diamines present were calculated from the concentrations of amine and hydrochloric or perchloric acid used to make up the solutions and the p*K* values at 35°. This

resulted in values of f_m and f_d that were combined with the δ'_{obsd} values to calculate the values of δ_0, δ_m, and δ_d shown in Table III by the method of least squares.

Calculation of Micro p*K* Values for Primary–Tertiary Diamines. These calculations may be illustrated by the case of *trans*-2-(dimethylaminomethyl)cyclohexylamine. For p*K*ₜₚₕ we start with the p*K* of 10.27 for a cyclohexylamine (or $RCH_2CH_2NH_2$). A contribution of −0.20 is added because the primary amino group has a single β branch (not held away with a dihedral angle of 120° or more). Finally, −0.52 is added for the effect of the dimethylamino substituent three carbons away from the primary amino group. For p*K*ₕₜₚ the uncorrected value is 9.81, −0.07 is added because of the single branch β to the dimethylamino group, and −0.42 is added because of the primary amino group three carbon atoms away. The resulting p*K*ₜₚₕ and p*K*ₕₜₚ values of 9.55 and 9.32, respectively, and the experimentally determined value 10.29 for p*K*₁ (from Table I) give *K* values that leave *K*ₜₕₚ as the only unknown in eq 5. The value 10.14 thus obtained for p*K*ₜₕₚ is then used to calculate f_c, which may be seen to be equal to K_1/K_{THP}. Similarly, f_t is equal to K_1/K_{HTP} and f_p to K_1/K_{TPH}.

References and Notes

(1) This investigation was supported in part by Public Health Service Grant GM 18593 from the National Institute of General Medical Sciences.
(2) J. Hine, F. A. Via, and J. H. Jensen, *J. Org. Chem.*, **36**, 2926 (1971).
(3) J. Hine, M. S. Cholod, and W. K. Chess, Jr., *J. Am. Chem. Soc.*, **95**, 4270 (1973).
(4) J. Hine, M. S. Cholod, and R. A. King, *J. Am. Chem. Soc.*, **96**, 835 (1974).
(5) J. Hine and W. H. Sachs, *J. Org. Chem.*, **39**, 1937 (1974).
(6) C. W. Davies, *J. Chem. Soc.*, 2093 (1938).
(7) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution", Butterworths, London, 1965.
(8) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution: Supplement 1972", Butterworths, London, 1972.
(9) J. J. Christensen, R. M. Izatt, D. P. Wrathall, and L. D. Hansen, *J. Chem. Soc. A*, 1212 (1969).
(10) J. Hine, C. Y. Yeh, and F. C. Schmalstieg, *J. Org. Chem.*, **35**, 340 (1970).
(11) J. Hine, J. L. Lynn, Jr., J. H. Jensen, and F. C. Schmalstieg, *J. Am. Chem. Soc.*, **95**, 1577 (1973).
(12) M. P. Schweizer, S. I. Chan, G. K. Helmkamp, and P. O. P. Ts'o, *J. Am. Chem. Soc.*, **86**, 696 (1964).
(13) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed, Pergamon Press, Oxford, 1969, p 68.
(14) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506, 513 (1938).
(15) Cf. G. S. Hammond in "Steric Effects in Organic Chemistry", M. S. Newman, Ed., Wiley, New York, N.Y., 1956, Chapter 9.
(16) R. Yamdagni and P. Kebarle, *J. Am. Chem. Soc.*, **95**, 3504 (1973).
(17) D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Am. Chem. Soc.*, **94**, 4726 (1972).
(18) R. W. Alder, P. S. Bowman, W. R. S. Steele, and D. R. Winterman, *Chem. Commun.*, 723 (1968).
(19) J. Hine and W.-S. Li, *J. Org. Chem.*, **40**, 289 (1975).
(20) W. H. Sachs, submitted for publication in *Technometrics*.

9,9'-Dianthrylmethane Derivatives. Conjugate Rearrangements and Photocyclizations

Douglas E. Applequist* and Daniel J. Swart

Department of Chemistry, University of Illinois, Urbana, Illinois 61801

Attempted preparation of di-9-anthrylmethane and its brominated derivatives led to the discovery of incorrect structural assignments in previous work. The successful preparation of 9,9'-dianthrylmethane derivatives is reported, and the photocyclization of some of them is described.

It was earlier reported from this laboratory that 9,9'-dianthrylmethane (1a) had been prepared by catalytic hydrogenolysis of 9,9'-dianthrylcarbinol (2) using 5% palladium on carbon in ethanol.[1] The preparation has since been found unreproducible (yields of zero to 9%) and alterna-

tives have therefore been sought. A satisfactory two-step procedure has been found, the first step being reduction of 2 with a 2:1 mixture of aluminum chloride and lithium aluminum hydride in ether to give 3a, an isomer of 1a, in 94% yield, and the second step being the isomerization of 3a to