Inversion and Proton Exchange at Asymmetric Nitrogen Centers in Palladium(II) Complexes[1]

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Abstract: The proton magnetic resonance spectra of mixed tetragonal Pd(II) complexes of *N,N'*-dimethyldiaminoethane (dmen) and five aliphatic amines and bipyridyl were analyzed over the pH range 7–13.5. Rate constants for hydrogen exchange of these and three additional complexes containing the asymmetric H–N–CH_3 system were determined from the pH of methyl doublet collapse. At a higher pH methyl peak coalescence occurs due to rapid inversion of the asymmetric nitrogen. Both processes are first order in complex and hydroxide ion concentrations. The second-order exchange rate constants vary from 0.35×10^4 to 160×10^4 sec^{-1} M^{-1} for dmen complexes of aliphatic amines to 1.3×10^7 sec^{-1} M^{-1} for the dmen complex of bipyridyl. For the same set of complexes the second-order inversion rate constants range from 0.15×10^2 to 3.0×10^2 sec^{-1} M^{-1} to a high value of 1.2×10^4 sec^{-1} M^{-1} for the bipyridyl complex. The ratio of the second-order exchange to inversion rate constants displays a smaller variation from 160 to 550 for the dmen complexes of aliphatic amines to a high value of 4300 for the bipyridyl complex. These values are similar to those found for Pt(II) complexes. These results are consistent with both exchange and inversion processes taking place through a common deprotonated intermediate. For basic amine complexes reprotonation of the deprotonated intermediates by water is diffusion controlled with a suggested rate constant of $10^{9.1}$ sec^{-1}. Use of this constant permits an estimate of the apparent absolute rate constant for inversion about nitrogen in Pd(II) complexes from 1×10^6 to 8×10^6 sec^{-1}. This paper presents a comprehensive mechanism including the roles of general base catalysts and amine hydrate intermediates in the exchange and inversion reactions for free and bound amines over the entire pH range.

Inhibition of inversion at the amine nitrogen to permit resolution of optical isomers may be accomplished experimentally by several methods. The nitrogen atom may be completely tetrasubstituted, or if one of the substituents is a proton, highly acidic solutions will slow deprotonation and hence inversion. Most simply, complexation of the amine with an inert transition metal ion will inhibit inversion, even if the complex contains an exchangeable hydrogen at the amine nitrogen. Substitution of an alkyl group or a proton by a transition metal ion lowers the exchange rate of nitrogen-bound hydrogens and inhibits inversion of the metal-bound nitrogen so that the resolution of optical isomers is possible in neutral solutions.[2] Both exchange and inversion processes have been found to be proportional to the hydroxide ion concentration, consistent with a deprotonated intermediate. For three cobalt(III)[2] and one platinum(IV)[3] amines the ratio of observed second-order rate constants for exchange to inversion is 7×10^3 to 3×10^5, while for a wide variety of platinum(II) amines a smaller ratio of 10^2 to 5×10^3 has been found.[4,5] For complexes of all three transition metal ions, many proton exchanges take place for each nitrogen inversion. This paper reports results for proton exchange and inversion of amine nitrogens with selected tetragonal palladium(II) complexes so that further comparisons are possible with an additional transition metal ion. In addition a comprehensive analysis is presented for hydroxide ion deprotonations and the reverse reprotonation reaction for uncomplexed and complexed amines as basicity of the exchangeable hydrogen is varied over eight powers of ten. The final discussion concerns the significance of general base catalysts and intermediate amine hydrates in exchange and inversion reactions of complexed amines.

Experimental Section

The Pd(II) complexes were prepared from orange-yellow Pd(en)Cl_2 and from Pd(dmen)Cl_2 synthesized in the same manner as the former compound.[6] In a typical preparation, 1 mmol of Pd(en)Cl_2, prepared from $PdCl_2$ (Alfa Inorganics), is added to 1 mmol each of sarcosine and NaOH in 5 ml of water, and the mixture is allowed to react for 2 hr to yield a solution exhibiting an absorption maximum at 305 nm, consistent with the three nitrogen and one oxygen donor system[7] of Pd(en)(sar)$^+$.

Readings of pH were taken near 25° on a Beckman Model GS pH meter equipped with a miniature combination electrode. All (OH^-) are calculated from pH meter readings and $pK_w = 14.00$. Proton magnetic resonance spectra were run on a Varian HA-100 spectrometer using an external TMS lock. Samples, usually 0.2 M in complex concentration, were allowed to equilibrate in the probe at 27° for at least 5 min before a spectrum was recorded. Boric acid buffers at 0.1 M concentration were employed from pH 7.5 to 10.2; their presence did not effect the line shape. Ionic strength of 1 M was controlled with KCl. The growth of singlet peaks in the deuterium exchange experiment was followed in H–R mode by setting the sweep time on the linear sweep unit at about 20 sec and the sweep input time on the time average computer (CAT) at about 250 sec so that about 12 spectra appear as a function of time on the chart paper printout of the CAT memory contents. For computer-generated pmr spectra, doublet collapse formulas 9.42 and 9.43 and two-peak coalescence formulas 9.28–9.31 of Emsley, Feeny, and Sutcliffe[8] were utilized. Examples of computer-generated curves are illustrated in Figures 2 and 3.

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Results

Nitrogen-Bound Proton Exchange. Below pH 9.4 in H_2O the methyl signal for $Pd(en)(sar)^+$ is a doublet, the result of coupling with the N-bound proton, which is exchanging slowly with solvent protons. At pH 9.4 the methyl doublet collapses, and a comparison of computer-generated and experimental curves shows that the exchange rate is directly proportional to the hydroxide ion activity in the pH region studied. The second-order rate constant for exchange listed in Table I is calculated from

$$k_{ex} = (\pi/\sqrt{2})(J_{H-N-CH_3})/(OH^-) \qquad (1)$$

A similar treatment is accorded the next two amino acid complexes in Table I to give the tabulated second-order rate constants for exchange, k_{ex}. Despite the fact that phenylalanine is more acidic than both glycine and alanine, the Pd(II) complex of *N*-methylphenylalanine exchanges more slowly than the complexes of the other two *N*-methylamino acids. This result suggests that solvent structure or steric factors slow the exchange when the amino acid side chain is bulky. Examination of space-filling molecular models reveals that if the *N*-methyl group and the side chain adopt gauche rather than the less favored nearly cis conformations, the bulkier side chains impede hydroxide ion attack on the nitrogen-bound hydrogen, which is nearly cis to the side chain.

Table I. Second-Order Exchange and Inversion Rate Constants of Pd(II) Complexes[a]

		$k_{ex} \times 10^{-4}$	$k_{inn} \times 10^{-2}$	$r = k_{ex}/k_{inv}$
$Pd(en)(sar)^+$		52		
$Pd(en)(N\text{-}CH_3\text{–}Ala)^+$		21		
$Pd(en)(N\text{-}CH_3\text{–}Phe)^+$		6.5		
$Pd(en)(dmen)^{2+}$	I	10	1.8	550
	II	5.3	2.7	200
$Pd(NH_3)_2(dmen)^{2+}$	II	14	2.9	480
	I	11	2.9	380
$Pd(pn)(dmen)^{2+}$	I	2.8	0.8	350
	II	2.8	1.2	230
$Pd(bipy)(dmen)^{2+}$	II	1300	120	1100
	I	1300	30	4300
$Pd(gly)(dmen)^+$	I	160		
	I′	16		
	II	85		
	II′	8.5		
$Pd(GlyGly)(dmen)^0$	I	0.52	0.15	350
	II	0.55	0.22	250
	II′	0.35	0.22	160
	I′	0.35	0.15	230

[a] In units of sec^{-1} M^{-1} at 27°. For each complex the methyl doublets are listed in order of decreasing field strength.

Tetragonal complexes of Pd(II) and *N,N′*-dimethyldiaminoethane (dmen) give rise to at least two sets of methyl doublets, due to the presence of slowly interconverting *d,l* and meso isomers. A schematic representation of the pmr spectra in the methyl region for mixed Pd(II) complexes containing dmen as one ligand is shown in Figure 1. The isomer present in greatest amount (I) is assigned the *d,l* configuration on steric grounds, while the less abundant isomer (II) is presumably the meso form. In all cases $J_{H-N-CH_3} = 6.1 \pm 0.2$ Hz, with the smallest values corresponding to the highest field doublets within all systems.

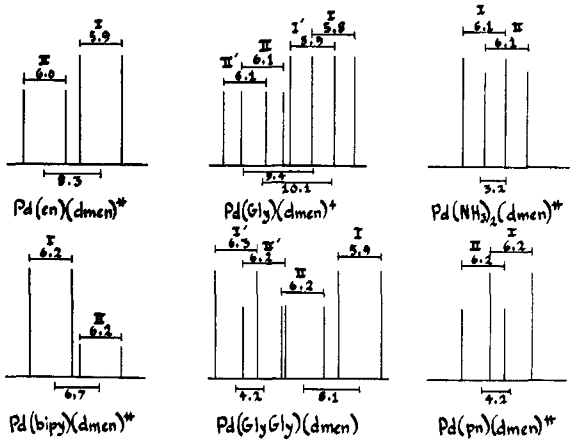

Figure 1. Representation of proton magnetic resonance spectra at 100 MHz in the methyl region for tetragonal Pd(II) complexes of *N,N′*-dimethyldiaminoethane in neutral aqueous solutions. Magnetic field strength increases to the right.

The changing character of the methyl region pmr spectra for $Pd(en)(dmen)^{2+}$ as the pH increases is shown in Figures 2 and 3. Below pH 10.1 the centers of the doublets for $Pd(en)(dmen)^{2+}$ are separated by 0.083 ppm. The high-field doublet, which exhibits a 50% greater intensity from 0.15 to 0.8 *M* complex, collapses at pH 10.1 and the low-field doublet at pH 10.4. Thus two different second-order exchange rate constants are calculated from eq 1 and listed in Table I. These two rate constants are unaffected by change in complex concentration from 0.1 to 0.2 *M* at constant 1 *M* ionic strength. Increasing ionic strength at constant complex concentration decreases the second-order rate constants.

A similar analysis is applicable to $Pd(NH_3)_2(dmen)^{2+}$, where the centers of the overlapping pairs of doublets are separated by only 0.032 ppm. Each doublet pair is of approximately the same intensity and the upfield doublet, which collapses at slightly lower pH, is designated as II in Table I. Extensive overlap of the doublet pair separated by 0.044 ppm in $Pd(1,3\text{-}pn)(dmen)^{2+}$ precluded determining the order of doublet collapse which occurs at pH 10.7.

The methyl region of the pmr spectra of $Pd(bipy)(dmen)^{2+}$ displays two doublets separated by 0.067 ppm, with the low-field doublet about four times more intense. Both doublets appear to collapse at pH 8.0; the low intensity of the high-field doublet makes the order of collapse uncertain.

Exchange of the N-bound protons adjacent to the methyl group in $Pd(en)(dmen)^{2+}$ was also followed near pH 7 by addition of D_2O to an H_2O solution of the complex. The growth of the singlets separated by 0.083 ppm between the doublets as the nonsplitting deuteron replaces the proton was analyzed as a reversible first-order reaction. The rate constants obtained for each isomer are about 20% less than those listed in Table I determined from collapse measurements. In the comparison no allowance has been made for possible lack of time for the samples to equilibrate thermally with the probe and for isotope effects on the pH readings, and on equilibrium and rate constants. The relatively good agreement of the rate constants determined by two different methods establishes that the exchange reaction

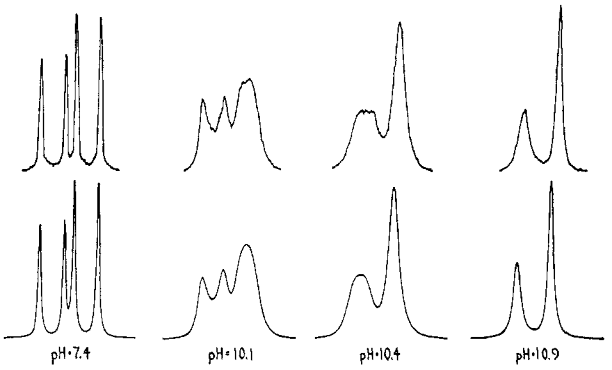

Figure 2. Experimental (above) and computer-generated (below) pmr spectra of $[Pd(en)(dmen)]^{2+}$ at pH values through the range of methyl doublet collapse.

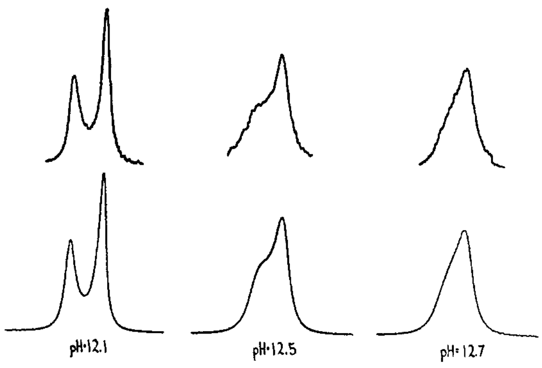

Figure 3. Experimental (above) and computer-generated (below) pmr spectra of $[Pd(en)(dmen)]^{2+}$ at pH values through the range of methyl peak coalescence.

is first order in hydroxide ion over a more than 1000-fold variation in basicity.

The Pd(II)–dmen complexes discussed thus far all have identical groups occupying the third and fourth coordination positions. This is not, however, the case with $Pd(gly)(dmen)^+$; an amine nitrogen and a carboxyl oxygen occupy these positions. This places each dmen methyl group of either the *d,l* or meso isomer in magnetically nonequivalent environments. Therefore, in contrast to the earlier cases, four methyl doublets are observed as shown in Figure 1. The lower intensity pair of doublets (II′, II) is assigned to the meso isomer, the 50% higher intensity pair (I′, I), to the *d,l* isomer. The primes designate the lower field doublet of each pair. As before, the rate constants were calculated from eq 1. The upfield doublet of each isomer collapses 1 pH unit lower than the downfield doublet; a trans-effect argument suggests slower exchange of the proton bound to the nitrogen diagonally across the coordination plane from the glycine nitrogen.

The methyl region of $Pd(GlyGly)(dmen)^0$ also yields four doublets in the nmr spectrum below pH 11.4 as illustrated in Figure 1. In this case the outermost pair of doublets (assigned as I and I′) is 50% more intense than the innermost pair (assigned as II and II′). The complex exhibits an absorption maximum at 292 nm consistent with four nitrogen donors,[7] indicating that the carboxylate group is unbound. Because of overlapping of the doublets the pH of collapse is more difficult to ascertain than in the other cases. Computer-generated curves with rate constants corresponding to collapse of doublets I and II at pH 11.4 and I′ and II′ at pH 11.6 give good agreement with the experimental spectra. The rate constants are presented in Table I.

Nitrogen Inversion. The CH_2 region of sarcosine in $Pd(en)(sar)^+$ appears, below pH 9.4, as the AB portion of an ABX pmr spectrum, the X representing the slowly exchanging nitrogen-bound proton. At pH >9.4 the N-bound proton exchanges rapidly, as reported above, and the X coupling disappears so that only an AB pattern remains. Above pH 11.6 inversion of the sarcosyl nitrogen is rapid enough to cause coalescence of the AB pattern, as the methylene hydrogens no longer appear as nonequivalent. The second-order rate constant for inversion may be estimated at the pH of coalescence from

$$k_{\text{inv}} = (\pi/\sqrt{2})(\Delta\nu_{AB})/(OH^-)$$

where $\Delta\nu_{AB}$ is the chemical shift nonequivalence of the methylene hydrogens. In this case the results are uncertain owing to the possibility of competition between carboxylate groups and hydroxide ions at high pH for the fourth coordination position. Therefore the second-order rate constant of 1.1×10^4 sec^{-1} M^{-1} for this system is not included in Table I. For the same reason inversion rates were not studied in other systems involving carboxylate donors.

After collapse of the two sets of methyl doublets at pH >10.4 in $Pd(en)(dmen)^{2+}$ as described above, two singlets remain separated by 0.083 ppm, with the higher field singlet (I) about 50% more intense. This condition is illustrated by the spectra of pH 10.9 and 12.1 in Figures 2 and 3. As the pH is raised above 12.5 the two singlets coalesce because of rapid interchange between isomers I and II. Comparison of computer-generated and experimental curves indicates that the isomerization rate is first order in hydroxide ion activity. A second-order isomerization rate constant may be calculated at the pH of coalescence from

$$k_{\text{iso}} = (\pi/\sqrt{2})(\Delta\nu_{AB})/(OH^-) \qquad (2)$$

This rate constant represents the sum of the inversion rate constants for each isomer I and II, which constants are inversely proportional to their relative peak intensities. Second-order inversion rate constants calculated in this way for isomers I and II are listed in Table I.

A similar analysis is applicable to $Pd(NH_3)_2(dmen)^{2+}$, where the two singlets remaining above pH 10.1 coalesce at pH 12.1. In this case the intensities of the singlets are nearly equal, so that each inversion rate constant in Table I is half the isomerization rate constant determined from eq 2. For $Pd(pn)(dmen)^{2+}$ the two singlets remaining after doublet collapse at pH 10.7 coalesce at pH 12.7. In the case of $Pd(bipy)(dmen)^{2+}$ the singlets coalesce at pH 11.1.

For $Pd(GlyGly)(dmen)^0$, doublet collapse is complete at pH 11.6 as described. Above this pH the methyl pmr spectrum consists of four well-defined singlets in the same high, low, low, high intensity ratios as their doublet predecessors. At pH 13.4 the low-field pair of singlets I′ and II′ originally separated by 0.042 ppm coalesce. Since the high-field pair I and II are separated by 0.081 ppm, they coalesce at higher pH. The inversion rate constants in Table I are calculated from the isomerization rate constant of eq 2 by the prescription given following that equation.

Discussion

Compared to results already found for similar Pt(II) complexes,[4,5] the findings of Table I indicate that the Pd(II) complexes exhibit a greater value of k_{ex} and lesser value for k_{inv}. Though the values fall in the same range of 10^2–5×10^3 the ratio $r = k_{ex}/k_{inv}$ tends to be greater for similar Pd(II) complexes. For both metal ions complexes containing α,α'-bipyridyl or 1,10-phenanthroline give N-methyl resonances at lower field and greater values of k_{ex}, k_{inv}, and r than complexes containing nonaromatic ligands. Both tetragonal low-spin d^8 transition metal ion complexes exhibit an r value up to 100 times smaller than that for complexes of Co(III) and Pt(IV), two octahedral low-spin d^6 transition metal ions. A wider variety of metal ion complexes needs to be studied so that the effects of coordination number and geometry may be separated from number and configuration of d electrons in discussing reasons for differences in r values.

Despite a range of over 10^3 in the k_{ex} and k_{inv} values of Table I, there is only about a tenfold variation in the ratio of the two observed second-order rate constants. This conclusion suggests common features in the mechanism of the two processes, and the following reactions provide the simplest scheme that satisfies the results.

$$>\!\!\!-\text{N:H} + \text{OH}^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} >\!\!\!-\text{N:} + \text{H}_2\text{O} \qquad (3)$$

$$>\!\!\!-\text{N:} \overset{k_3}{\rightleftharpoons} \text{:N}\!\!-\!\!\!< \text{ (invertomer)} \qquad (4)$$

Assuming a steady-state concentration for the deprotonated complex, the observed second-order rate constants for exchange at and inversion about nitrogen are given by

$$k_{ex} = k_1 \qquad (5)$$

$$k_{inv} = k_1k_3/(k_2 + k_3) = k_1k_3/k_2 \qquad (6)$$

The exchange rate is given by the sum of all general base catalyzed removals of protons from amine, with hydroxide ion usually the predominant catalyst. Owing to the back reaction the observed rate constant for racemization as determined polarimetrically is twice that for inversion. When the observed second-order rate constant for exchange is much greater than that for inversion as found for the metal ion complexes, $k_2 \gg k_3$ and the last equality in eq 6 results. The observed inversion rate is proportional to the product of the rate at which an amine nitrogen inverts and the acidity constant of the nitrogen-bound protons. The ratio of exchange to inversion second-order rate constants is given by

$$r = k_{ex}/k_{inv} = k_2/k_3 \qquad (7)$$

and is determined by partitioning of the deprotonated intermediate between reprotonation and inversion.

The relation between the rate constants for hydroxide ion removal of a proton (k_1) and reprotonation (k_2) as a function of their ratio $k_1/k_2 = K_b = K_a/K_w$ is shown in Figure 4 for several amines. Beginning on the right-hand side of Figure 4 the first 13 circles refer to imidazole and 12 aliphatic amines in Table 2 of ref 9 near 22°. It is important for our purposes that [Pt(meen)(en)Cl$_2$]$^{2+}$ yields points which, though determined at a higher temperature, fall within the limits of the noncomplexed amines as shown by the right-side pair of squares in Figure 4. For 13 uncomplexed and 1 complexed amine with $-\text{p}K_b > 2.5$ the rate of deprotonation by hydroxide ion is diffusion controlled, with an average rate constant $k_1 = 10^{10.35}$ sec^{-1} M^{-1}. In this region the first-order rate constant for reprotonation of amine increases with increasing basicity of amine. Finally, as the amine becomes more basic than hydroxide ion ($\text{p}K_b > 0$) the rate of reprotonation becomes diffusion controlled, and the second-order rate constant for deprotonation decreases with increasing amine basicity. Pairs of points for three compounds with $-\text{p}K_b < 2$ are utilized to approximate the curves in this region where there are only a limited number of examples for which two of the three quantities K_b k_1, and k_2 have been determined. The points at $-\text{p}K_b = 1.6$ and 0.6 refer to acetamidinium[10] and N-methylguanidinium[11] ions, respectively. For the latter compound $k_{ex} = 10^{9.55}$ sec^{-1} M^{-1} at 27° was determined from the pH of collapse of the methyl doublet in order to provide an additional point for Figure 4 in a critical region. No statistical corrections were attempted; their inclusion would mainly move the points along the curves in Figure 4 with no significant alterations. The set of squares on the left of the figure refer to the complex[4] Pt(bipy)(N,N,N′-tmen)$^{2+}$. Though not consistent with values for other Pt(II) complexes,[4] that of tmen offers the least ambiguity in the difficult experimental work required for determination of pK_b. In these weakly acidic complexes the general base catalyzed reaction is expected to exhibit a high Brønsted exponent so that catalysis by general bases other than hydroxide ion should be difficult to detect unless relatively high concentrations of catalysts are employed at low pH.

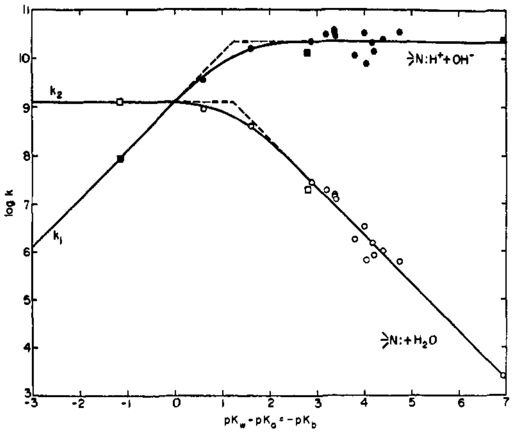

Figure 4. Logarithms of rate constants for deprotonation of substituted ammonium by hydroxide ions, k_1 (solid points), and the reverse reprotonation reaction, k_2 (open points), *vs.* logarithm of ammonium ion acidity. Circles refer to uncomplexed and squares to complexed amines as described in the text.

The points of Figure 4 fall along curves similar to those found for proton transfer reactions in other acid–

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Table II. First-Order Rate Expressions for Special Cases of Eq 13

Case	Inequalities	Inversion, k_{in}	Exchange, k_{e}	$r = k_{\mathrm{e}}/k_{\mathrm{in}}$
I	$k_{\mathrm{H}} > k_{\mathrm{HB}}(\mathrm{HB}) < fk_{\mathrm{H}}$	$k_{\mathrm{B}}(\mathrm{B})$	$k_{\mathrm{B}}(\mathrm{B})$	1
II	$k_{\mathrm{H}} > k_{\mathrm{HB}}(\mathrm{HB}) > fk_{\mathrm{H}}$	$fk_{\mathrm{H}}K_{\mathrm{a}}/(\mathrm{H}^+)$	$k_{\mathrm{B}}(\mathrm{B})$	$k_{\mathrm{HB}}(\mathrm{HB})/fk_{\mathrm{H}}$
III	$k_{\mathrm{H}} < k_{\mathrm{HB}}(\mathrm{HB}) > fk_{\mathrm{H}}$	$fk_{\mathrm{H}}K_{\mathrm{a}}/(\mathrm{H}^+)$	$k_{\mathrm{H}}K_{\mathrm{a}}/(\mathrm{H}^+)$	$1/f$

base systems.[12] Figure 4 appears to represent the first attempt to apply the principles developed for proton transfer reactions[12] to the substituted ammonium hydroxide ion reactions into the region where $\mathrm{p}K_{\mathrm{b}} > 0$. The curves are described by equations of the form

$$k_2 = l_1/(K_{\mathrm{b}} + l_1/l_2) \qquad (8)$$

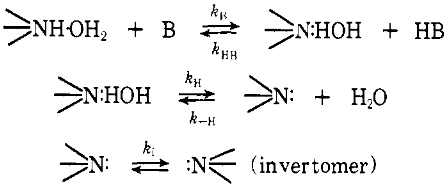
and

$$k_1 = K_{\mathrm{b}}l_1/(K_{\mathrm{b}} + l_1/l_2) \qquad (9)$$

where l_1 and l_2 refer to the diffusion-controlled limits for the rate constants k_1 and k_2, respectively. The curves in Figure 4 are constructed with $l_1 = 10^{10.35}\ \mathrm{sec}^{-1}\ M^{-1}$ and $l_2 = 10^{9.1}\ \mathrm{sec}^{-1}$.

If the results of Figure 4 may be applied to other metal ion complexes, it becomes possible to estimate the inversion rate constant k_3 for basic complexes with such positive $\mathrm{p}K_{\mathrm{b}}$ values that its value is difficult or impossible to determine. In the region where $\mathrm{p}K_{\mathrm{b}} > 0$, eq 5, 8, and 9 permit an estimate of $K_{\mathrm{b}} = k_{\mathrm{ex}}/l_2$. Independently in the same region eq 7 and 8 yield $k_3 = l_2/r$, so that the inversion rate constant varies inversely as r. With $l_2 = 10^{9.1}\ \mathrm{sec}^{-1}$ the Pd(II) complexes of Table I yield $k_3 = 0.3 \times 10^6$ and $1.2 \times 10^6\ \mathrm{sec}^{-1}$ for the deprotonated *d,l* and meso bipyridyl isomers, respectively, and from 2×10^6 to $8 \times 10^6\ \mathrm{sec}^{-1}$ for all the other complexes. In a similar calculation we estimate a range of $k_3 = 0.3 \times 10^6\text{–}20 \times 10^6\ \mathrm{sec}^{-1}$ for Pt(II) complexes and of $k_3 = 0.5 \times 10^4\text{–}20 \times 10^4\ \mathrm{sec}^{-1}$ for Co(III) complexes. For the relatively less basic octahedral Pt(IV) complex $\mathrm{p}K_{\mathrm{b}}$ may be measured so that it is possible to calculate more directly that[3] $k_3 \simeq 400\ \mathrm{sec}^{-1}$. Thus the octahedral complexes of two different metal ions with r values in the same numerical range are differentiated on the basis of their inversion rate constants k_3. For all four transition metal ions studied, log k_3 appears to decrease in proportion to increasing oxidation state of the metal ion. All these values may be compared with those of $k_3 = 0.2\text{–}2 \times 10^6\ \mathrm{sec}^{-1}$ measured for the uncomplexed but cyclic *N,N′*-dimethylpiperazine.[13]

We now describe a general formulation of inversion and exchange applicable to free and bound amines over the entire range of pH. Because the observed first-order rate constant for exchange of substituted ammonium ions in solutions more acid than pH 1.5 decreases with increasing acidity, deprotonation of ammonium ions by water is divided into two steps involving the formation of an intermediate basic amine hydrate.[14–16]



$$>\mathrm{NH{\cdot}OH_2} + \mathrm{B} \underset{k_{\mathrm{HB}}}{\overset{k_{\mathrm{B}}}{\rightleftarrows}} >\mathrm{N{:}HOH} + \mathrm{HB} \qquad (10)$$

$$>\mathrm{N{:}HOH} \underset{k_{-\mathrm{H}}}{\overset{k_{\mathrm{H}}}{\rightleftarrows}} >\mathrm{N{:}} + \mathrm{H_2O} \qquad (11)$$

$$>\mathrm{N{:}} \overset{k_{\mathrm{i}}}{\rightleftarrows} \mathrm{{:}N}< \text{ (invertomer)} \qquad (12)$$

When the hydrogen ion concentration becomes great enough, the rate of the hydronium ion catalyzed reverse reaction 10 exceeds the rate of diffusion of water from amine in reaction 11. In this circumstance, $k_{\mathrm{H^+}} > k_{\mathrm{H}}$, a preequilibrium prevails in reaction 10 and reaction 11 becomes the rate-determining step for exchange. General base catalysis has not been emphasized in previous treatments of inversion and exchange. Production of an noninverting amine hydrate as opposed to dehydrated amine by general bases other than water does not appear to have been mentioned previously, and this extension is discussed at the end of this section. Only the deprotonated and dehydrated amine inverts according to reaction 12.

Application of the steady-state approximation to the hydrated and dehydrated basic amine over the pH range where protonated amine is the dominant species yields, for the observed first-order rate constant for inversion

$$k_{\mathrm{in}} = \frac{k_{\mathrm{B}}(\mathrm{B})}{1 + (1/fk_{\mathrm{H}})[k_{\mathrm{HB}}(\mathrm{HB})]} = \frac{k_{\mathrm{H_2O}}(\mathrm{H_2O}) + k_{\mathrm{N}}(\mathrm{N{:}HOH}) + k_{\mathrm{OH}}(\mathrm{OH^-})}{1 + (1/fk_{\mathrm{H}})[k_{\mathrm{H^+}}(\mathrm{H_3O^+}) + k_{\mathrm{NH}}(\mathrm{NH}) + k_{\mathrm{H_2O}}'(\mathrm{H_2O})]} \qquad (13)$$

The rate constants in the numerator of eq 13 and in the denominator brackets are catalytic coefficients for the indicated general bases and general acids, respectively. If additional general bases and acids are present, more terms need to be added to the numerator and the brackets. The observed first-order rate constant for exchange is identical with (13) with omission of the fraction $f = k_{\mathrm{i}}/(k_{\mathrm{i}} + k_{-\mathrm{H}})$. Since the rate constant for rehydration of dehydrated amine, $k_{-\mathrm{H}}$, though not known with certainty, is probably close to that for diffusion of water in the aqueous systems considered, it should be greater than the inversion rate constant, k_{i}, for amines where tunneling is not a significant contributor to the in-

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version rate. Therefore we take $f = k_i/k_{-H}$ and hence less than unity for the remainder of the discussion. A consequence of this approximation is that the product $fk_H \simeq k_ik_H/k_{-H}$ represents an equilibrium in reaction 11 so that the dehydration step is not rate limiting in inversion. If the hydration and dehydration rate constants for a free amine are about equal, the product fk_H is approximated by the inversion rate constant, k_i.

Three cases may be reduced from eq 13, depending upon whether unity is greater than both $k_{HB}(HB)/fk_H$ and $k_{HB}(HB)/k_H$, is greater than the second but not the first, or is less than both ratios. These three cases are presented in Table II along with corresponding rate expressions and ratios of first-order observed rate constants, $r = k_e/k_{in}$. Only in the last two cases, where the k_B step is not rate limiting for inversion, does the appearance of f permit an estimate of the inversion rate constant, k_i.

The steps which are rate limiting in inversion and exchange are determined by the relative magnitudes of the terms in the denominator of eq 13. For most amines $k_{H^+} \simeq 10^{10}$ sec^{-1} M^{-1}, the diffusion-controlled limit for protonation of amine by hydronium ion. When $B \equiv$ free amine, eq 10 becomes symmetrical and second order in total amine in both directions with $k_N = k_{NH} = 10^7$–10^9 sec^{-1} M^{-1}. The last equality is the indicated value for symmetrical acid–base reactions in several systems.[12] The rate constant for dehydration of amine, k_H, has been found to vary from[14,15] $10^{8.4}$ to $10^{11.3}$ sec^{-1}. As shown in Figure 4 the remaining term in the denominator of eq 13, $k_{H_2O}'(H_2O)$, depends upon the basicity of the amine.

For *N*-benzyl-*N*-methylethanolamine a plot of the observed first-order rate constant for exchange[15] and inversion[16] *vs.* pH exhibits a plateau near pH 2 and an inversion reaction second order in nitrogen compound at pH >3. For this compound of pK_a = 8.4, Figure 4 shows that $k_{H_2O}'(H_2O) < 10^5$ sec^{-1}. Since[15] $k_H = 10^{9.1}$ sec^{-1}, the unity term dominates the denominator of eq 13 for both inversion and exchange and case I applies. Both reactions are general base catalyzed with water, the main catalyst at pH 2 ($k_{H_2O}(H_2O) \simeq 30$ sec^{-1}) and amine becoming the dominant catalyst at pH >3 ($k_N = 10^{7.4}$ sec^{-1} M^{-1}), accounting naturally for the second-order reaction in the latter region. The strongest general bases yield the greatest catalytic coefficients. For this compound, as for two other tertiary benzylamines,[16] f is probably relatively large (>0.1) so that case II prevails over only a limited pH region, but should set in at a higher pH for inversion. At pH <1 case III obtains as the k_{H^+} term dominates the denominator of eq 13 for both inversion and exchange. Some kind of division of reaction 3 into reactions like 10 and 11 is necessary to account for the observed[14,15] acid inhibition of exchange of unbound amines in strongly acid solutions. If the rate constant for rehydration of basic amine is equal to or greater than that of dehydration, then for two other tertiary benzylamines[16] at 25° the inversion rate constant $k_i \geq 6 \times 10^7$ sec^{-1}.

For the metal ion complexes of Pd(II), Pt(II), Co(III), and Pt(IV) different inversion and exchange rates are observed throughout the pH regions studied, eliminating case I. For complexes of the first three metal ions and other ammonium ions with pK_a > 13, Figure 4 shows that $k_{H_2O}'(H_2O) = 10^9$ sec^{-1} so that at pH >2 this term is the largest in the brackets of eq 13. Since k_H may also have a comparable value it may be necessary to include both constants in the denominator expression, defying a reduction of eq 13 into cases II and III. The choice between the two cases depends critically on whether general base catalysis occurs in the exchange reaction as shown in Table II. Though not usually intensively sought, catalyses by bases including solvent other than hydroxide ion have been mentioned in the proton exchange reaction of several metal ion complexes,[2,3] indicating that case II applies in these instances. Equilibrium is established in eq 10 predominantly *via* the water–hydroxide ion acid–base system, consistent with reaction 3 and the k_3 step rate limiting in eq 6. Case II yields the same rate-limiting steps for exchange and inversion assigned above for the Pd(II) complexes. However, division of reaction 3 into reactions 10 and 11 alters the interpretation of the inversion rate constants with the result that, if eq 10–12 rather than eq 3 and 4 apply, the k_3 values quoted in Table I need to be multiplied by k_{-H}/k_H to yield k_i.

An important question is whether formation of dehydrated basic amine is adequately described by reaction 3 and its relatives for general bases other than water or should properly be divided into the two reactions 10 and 11. Another question is whether division into reactions 10 and 11 for water as a general base is appropriate for amines in metal ion complexes. The questions asked are whether the major pathway for production of invertible amine occurs by attack of general bases at the nitrogen atom as in reaction 3 or at a bound water molecule as in reaction 10. In the former instance the inversion rate constants may be calculated as described in the first part of this section. In the event of attack at bound water the rate of dehydration of basic amine could so greatly exceed that of its reprotonation that reactions 10 and 11 might be written as a sum. However, as mentioned in the last paragraph, different numerical values of inversion rate constants are obtained by the two mechanisms unless $k_H = k_{-H}$. It does not seem possible to answer the questions posed with the data available, and since we are also uncertain as to how the ratio k_{-H}/k_H varies among the variety of free and complexed amines studied, we refrain from interpretation of inversion constant values.