ordination sphere about Ru to 6. For the pz-capped species in acid solution particularly on oxidation, there is ambiguity about the state of protonation. OTs represents toluenesulfonate; pz, pyrazine.
(10) J. R. Pladziewicz and H. Taube, *Inorg. Chem.*, **12**, 639 (1973).
(11) This notation represents a formal assignment of oxidation state and does not necessarily imply that the species are valence trapped.
(12) N. S. Hush, *Prog. Inorg. Chem.*, **8**, 391 (1971).
(13) M. J. Powers, R. W. Callahan, D. N. Salmon, and T. J. Meyer, *Inorg. Chem.*, **15**, 894 (1976).
(14) J. K. Beattie, N. S. Hush, and P. R. Taylor, *Inorg. Chem.*, **15**, 992 (1975). References to related work appear here, except for the following.[15]
(15) T. C. Strekas and T. G. Spiro, *Inorg. Chem.*, **15**, 1974 (1976).
(16) G. M. Tom and H. Taube, *J. Am. Chem. Soc.*, **96**, 7827 (1974).
(17) H. Taube, *Proc. N.Y. Acad. Sci.*, submitted for publication.

Contribution from the Department of Chemistry,
Seton Hall University, South Orange, New Jersey 07079

Splitting of Hematin Dimers in Nonaqueous Solution

DAVID OSTFELD* and JANE A. COLFAX

Received July 8, 1977

The splitting of the dimer μ-oxo-bis[tetraphenylporphineiron(III)] by imidazole (HIm) and imidazolium chloride ($H_2Im^+Cl^-$) to form the bis(imidazole)iron(III) tetraphenylporphine cation was studied. In dichloromethane/nitromethane the reaction was observed to obey the rate law: $k_{obsd} = (k_1[HIm] + k_2[HIm][H_2Im^+])/(1 + K_1[HIm])$. This corresponds to a rapid equilibrium, with $K_1 = 220\ M^{-1}$, in which the μ-oxo dimer (hematin) reacts to form an adduct with imidazole. The actual splitting of the dimer then occurs by one of two kinetically indistinguishable routes. In one of these the hematin itself is split, with a rate constant equal to $(k_1[HIm] + k_2[HIm][H_2Im^+])$. In this route the imidazole adduct is unreactive. However, in the second path it is the imidazole adduct which is cleaved, with a rate constant of $(k_1 + k_2[H_2Im^+])$. The imidazole adduct is shown to resemble the adducts previously observed between the bis(imidazole) complex and either 1,10-phenanthroline or imidazole. The nature of the adduct is discussed.

Introduction

Oxo-bridged dimers of iron(III) complexes have long been known.[1] However, it was only recently that porFe^{III}–O–Fe^{III}por (por = porphyrin) (hematin) was found to be an oxo-bridged dimer and not a simple iron(III) porphyrin hydroxide.[2,3] The great stability of this dimer is a dominant feature in the chemistry of the iron porphyrins. In order to better understand why the dimer is so stable, it is first necessary to know the mechanism by which it dissociates.

Most μ-oxo dimers have been prepared and studied in aqueous solution. Their hydrolysis reactions can be described by a two-term rate law[4]

$$\text{rate} = (k_1 + k_2[H^+])[\text{dimer}] \quad (1)$$

The acid-catalyzed path, which has by far the larger rate constant, is presumed to involve the protonation of the oxo bridge followed by a rapid addition of water and cleavage of the dimer. The non-acid-catalyzed path is thought to involve the addition of a water molecule to form the unstable di-μ-hydroxo species, which rapidly comes apart.

Just such a two-term rate law has been observed for the hydrolysis of a hematin dimer in aqueous solution.[5,6] Intermediates involving iron atoms bridged by two hydroxide ions (or a hydroxide and a water molecule) have been proposed.[5] However, other studies found no evidence for them.[6]

Particularly interesting is the work of Hambright,[7] in which cyanide is present. The cleavage of hematin by HCN begins with a rapid equilibrium in which a hematin molecule reacts with a single cyanide anion. The hematin/cyanide adduct, which was spectrally observed, is then cleaved according to the rate law

$$\text{rate} = (k_1[H^+] + k_2[H^+][CN^-]^2)[\text{hematin}] \quad (2)$$

One path is simple acid hydrolysis, which is observed in any acidic aqueous solution. However, the other path involves the cyanide in a manner which cannot easily be explained. Cyanide was an interesting choice as the anion, since cyanide is a stronger complexing agent than most anions used in studies of this sort.

Much of the work done on metalloporphyrins has been done in nonhydroxylic solvents (e.g., benzene, chloroform) and this has prompted us to study hematin cleavage in such a medium. This could have been done using any of several different acids as the proton source, and we hope eventually to carry out such additional measurements. However, imidazolium chloride ($H_2Im^+Cl^-$) was chosen as a source of protons because the complexes of iron(III) porphyrins with imidazole (HIm) have been thoroughly studied and because the imidazole system is relatively easy to work with.

Experimental Section

Tetraphenylporphine (H_2TPP) was purchased from the Aldrich Chemical Co. and was converted to hematin using the method of Adler.[8] Imidazole (Eastman) was recrystallized three times from ethanol and then sublimed. Imidazolium chloride was prepared by bubbling hydrogen chloride through a suspension of imidazole in dry ether. Most of the ether was decanted off under dry nitrogen and the remainder was removed under vacuum. Imidazolium chloride is rather deliquescent, and operations involving it were carried out under inert atmosphere. All solvents were reagent grade and were used without further purification except that they were stored in stoppered flask over Linde 3A molecular sieves. Spectral measurements were made using a Beckman Acta-III spectrophotometer equipped with a temperature-controlled cell holder. Sample temperatures were maintained at 25.0 ± 0.2 °C.

Spectral measurements were made using a stock solution of hematin and a series of imidazole/imidazolium chloride solutions. In cases where 1,10-phenanthroline was added, weighed quantities were added to aliquots of imidazole/imidazolium chloride solution. After mixing, the hematin concentration was 5.55×10^{-5} M. All solutions were made using, as solvent, a mixture of equal parts by volume of nitromethane and dichloromethane. In each measurement 1.00 mL of the hematin solution was allowed to come to temperature equilibrium in a 1-cm Pyrex cuvette and then 1.00 mL of imidazole/imidazolium chloride solution was added rapidly. Mixing was complete within the few seconds it took to begin recording the spectrum.

Results

Hematin is converted, in solution with imidazole and imidazolium chloride, to the well-known bis(imidazole)iron(III) tetraphenylporphine cation—with chloride the presumed counterion. That this reaction goes cleanly and without

0020-1669/78/1317-1796$01.00/0

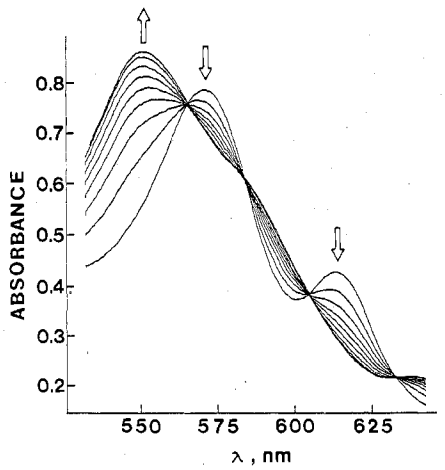


Figure 1. The effect of adding imidazole/imidazolium chloride solution to hematin in dichloromethane/nitromethane. The concentrations after mixing are [hematin] = 5.55×10^{-5} M, [imidazole] = 2.00×10^{-3} M, and [imidazolium chloride] = 8.50×10^{-4} M.

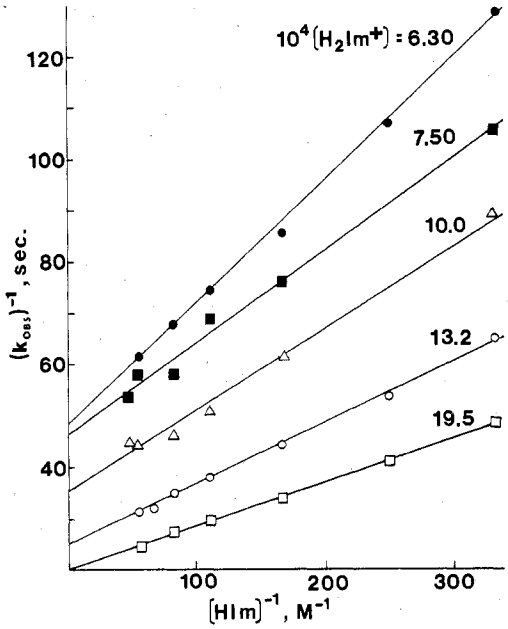


Figure 2. The effect of imidazole and imidazolium chloride on the observed rate constants for the conversion of TPPFe-O-FeTPP to TPPFe·2HIm$^+$.

significant amounts of spectrally distinguishable intermediate is shown by the isosbestic points in Figure 1.

The reaction was monitored using the rate of increase in the absorption band at 550 nm. Similar results were obtained in several instances by monitoring the disappearance of the band at 570 nm. Since the concentration of hematin was considerably less than that of imidazole or imidazolium chloride, the concentrations of imidazole and imidazolium chloride did not change appreciably during the reaction and the reaction can be considered to be first order in hematin. Plots of $\ln (A_t - A_\infty)$ against time were linear over at least 90% of the absorbance change, and rate constants were obtained from their slopes.

The relationship between k_{obsd} and imidazole concentration, shown in Figure 2, is indicative of a rapid preequilibrium involving imidazole. The reciprocals of the slopes of these lines, when plotted against the concentration of imidazolium ion, give a straight line with a nonzero intercept. This is shown in Figure 3. This indicates a two-term rate law with one term

Table I. Calculated and Observed Values for k_{obsd}

10^3[HIm], M	10^4[H_2Im^+], M	Obsd 10^3k_{obsd}, s^{-1}	Calcd 10^3k_{obsd}, s^{-1}
3.00	6.3	7.8	8.1
4.00	6.3	9.3	9.5
6.00	6.3	11.7	11.5
9.00	6.3	13.5	13.5
12.00	6.3	14.7	14.7
18.00	6.3	16.2	16.2
3.00	7.5	9.5	9.2
6.00	7.5	13.1	13.2
9.00	7.5	14.5	15.4
12.00	7.5	17.3	16.8
18.00	7.5	17.2	18.5
21.00	7.5	18.7	19.1
3.00	10.0	11.2	11.7
6.00	10.0	16.3	16.7
9.00	10.0	19.7	19.5
12.00	10.0	21.7	21.3
18.00	10.0	22.5	23.5
21.00	10.0	22.4	24.2
3.00	13.2	15.4	14.8
4.00	13.2	18.6	17.5
6.00	13.2	22.5	21.2
9.00	13.2	26.3	24.8
12.00	13.2	28.6	27.1
15.00	13.2	31.1	28.6
18.00	13.2	31.5	29.8
3.00	19.5	20.6	21.0
4.00	19.5	24.3	24.7
6.00	19.5	29.5	30.1
9.00	19.5	34.0	35.1
12.00	19.5	36.5	38.3
18.00	19.5	40.8	42.2

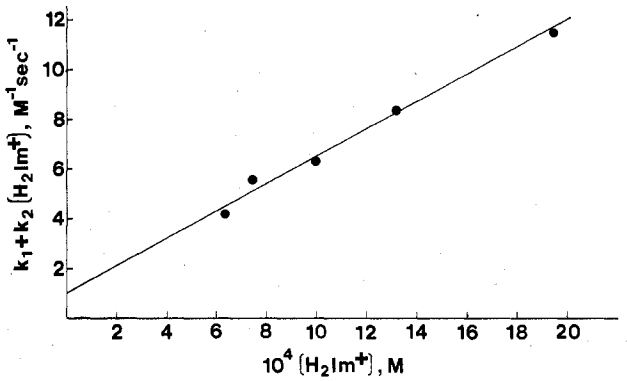


Figure 3. The dependence of the reciprocal of the slope of the lines plotted in Figure 2 on imidazolium chloride concentration.

being dependent and the other independent of acid (imidazolium chloride) concentration.

$$k_{obsd} = \frac{[HIm](k_1 + k_2[H_2Im^+])}{1 + K_1[HIm]} \quad (3)$$

This is thought to result from the rapid preequilibrium

$$TPPFe\text{-}O\text{-}FeTPP + HIm \overset{k_1}{\rightleftharpoons} TPPFe\text{-}O\text{-}FeTPP\cdot HIm \quad (4)$$

Further reaction could then proceed by either of two kinetically indistinguishable routes. In one of them the hematin itself is cleaved, with the imidazole complex being relatively unreactive.

$$TPPFe\text{-}O\text{-}FeTPP + 4HIm + 2H^+ \xrightarrow{k_1} 2[TPPFe\cdot 2HIm]^+ + H_2O \quad (5)$$

$$TPPFe\text{-}O\text{-}FeTPP + 2HIm + 2H_2Im^+ \xrightarrow{k_2} 2[TPPFe\cdot 2HIm]^+ + H_2O \quad (6)$$

Alternately this same rate law could be obtained from a

Table II. Equilibrium Constants Calculated for the Reaction

$$\text{TPPFeOFeTPP} + \text{HIm} \overset{K_1}{\rightleftharpoons} \text{TPPFeOFeTPP·HIm}$$

$10^4[H_2Im^+]$, M	K_1, M^{-1}
6.3	212
7.5	237
10.0	230
13.2	204
19.5	234
	Av 223

mechanism in which the imidazole adduct is the reactive species.

$$\text{TPPFe–O–FeTPP·HIm} + 3\text{HIm} + 2\text{H}^+ \xrightarrow{k_1} 2[\text{TPPFe·2HIm}]^+ + \text{H}_2\text{O} \quad (7)$$

$$\text{TPPFe–O–FeTPP·HIm} + \text{HIm} + 2\text{H}_2\text{Im}^+ \xrightarrow{k_2} 2[\text{TPPFe·2HIm}]^+ + \text{H}_2\text{O} \quad (8)$$

The rate constants for reactions 5–8 are, respectively, k_1[HIm], k_2[HIm][H_2Im^+], k_1, and k_2[H_2Im^+].

The k_2 step is expected and presumably involves a rapid equilibrium in which steady-state concentrations of a protonated or hydrogen-bonded hematin species are formed. The k_1 step, while appearing to resemble the non-acid-catalyzed path observed in aqueous solution, is implausible in the nonhydroxylic medium used here. Presumably the k_1 step results from the formation of small quantities of HCl by the methylene chloride. Although careful purification of the methylene chloride did not result in a noticeable decrease in the reaction rate, a slow reaction was observed between hematin and imidazole in methylene chloride and in several other chlorinated solvents which was absent in nonchlorinated solvents. Unfortunately it proved impractical to obtain quantitative data using a solvent mixture which did not contain a halogenated solvent. Values of $k_1 = 1.0\ s^{-1}$ and $k_2 = 5500\ M^{-1}\ s^{-1}$ were obtained from Figure 3.

The equilibrium to form an imidazole adduct was unexpected but clearly indicated by the data. That the imidazole adduct is spectrally indistinguishable from hematin itself is shown by the fact that the spectrum of hematin in dimethoxyethane is not altered by the presence of 0.1 M imidazole. The values of K_1 calculated from the intercepts in Figure 2 are reasonably consistent and give an average value of 220 M^{-1}, as shown in Table II.

Further measurements were made in order to obtain information on the nature of the hematin–imidazole interaction. A set of kinetic runs was made in which imidazole was 4.00×10^{-3} M and imidazolium chloride was 1.30×10^{-3} M. In addition to these reactants another compound was added to each run in order to see if it influences the rate. Since neither a weak Bronsted acid (water or methanol) nor a somewhat stronger Bronsted base (*N*,*N*-dimethylaniline or bipyridyl) had any measurable effect on the reaction rate, it was concluded that the imidazole does not interact via a hydrogen bond. Several other compounds which also had no effect on the reaction rate were mesitylene, *o*-dichlorobenzene, and nitrobenzene.

However 1,10-phenanthroline (phen) was found to strongly inhibit the reaction. As is shown in Figure 4, the reciprocal of the observed rate constant was found to have a linear dependence on the concentration of 1,10-phenanthroline.

This is consistent with the expected equilibrium

$$\text{TPPFe–O–FeTPP} + \text{phen} \overset{k_2}{\rightleftharpoons} \text{TPPFe–O–FeTPP·phen} \quad (9)$$

Assuming the phenanthroline adduct to be unreactive leads

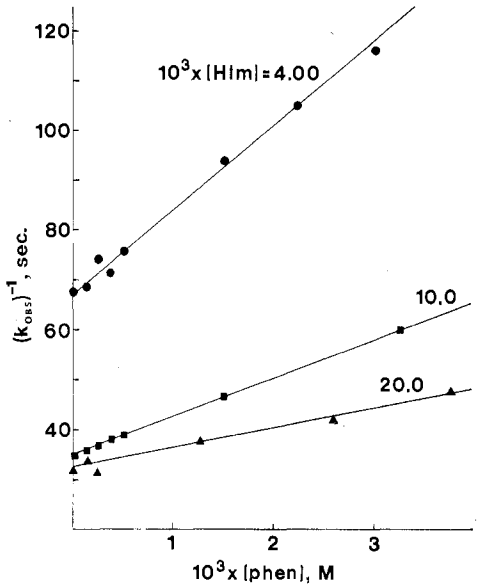


Figure 4. The effect of 1,10-phenanthroline concentration on the observed rate constant for the conversion of TPPFe–O–FeTPP to TPPFe·2HIm$^+$. After mixing [imidazolium chloride] = 1.30×10^{-3} M.

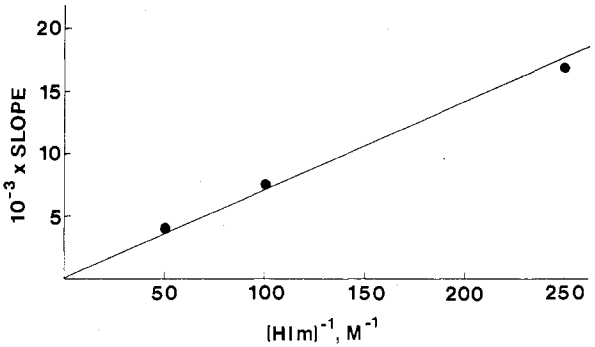


Figure 5. The dependence of the slopes of the lines in Figure 4 on the reciprocal of the imidazole concentration.

to a decrease in the observed rate as shown in the following rate law:

$$k_{obsd} = \frac{[\text{HIm}](k_1 + k_2[\text{H}_2\text{Im}^+])}{1 + K_1[\text{HIm}] + K_2[\text{phen}]} \quad (10)$$

A further check on the correctness of this rate law can be made by studying the dependence on 1,10-phenanthroline at different concentrations of imidazole. The slope of the lines in Figure 4 should be

$$\text{slope} = \frac{K_2}{[\text{HIm}](k_1 + k_2[\text{H}_2\text{Im}^+])} \quad (11)$$

Thus a plot of slope against the reciprocal of [HIm] should give a straight line which goes through the origin. This is shown in Figure 5. The slope of the line in Figure 5 can then be used to calculate K_2. This is calculated to be 580 M^{-1}.

Discussion

For reasons discussed earlier, a genuinely acid-independent process is considered unlikely in our system. Yet even a simple acid-*dependent* path (one dependent only on imidazolium ion) is not observed. This is in marked contrast to what is usually observed in aqueous solution. The rate law observed here is more similar to the second of two terms observed by Hambright in the cleavage of hematin by HCN in aqueous solution. This term was formulated as either $k_4[H^+][CN^-]^2$ or k_5-[HCN][CN^-]. By analogy to our work it appears that the

second of these formulations is the correct one.

Cyanide, however, has a greater affinity for hematin than does imidazole, and in Hambright's work all the hematin was converted immediately to the monocyano adduct. This, and not hematin, is the species which is then cleaved. This would appear to support the mechanism in which the imidazole adduct is the reactive species (eq 8).

However, the splitting of the cyano adduct with a rate proportional to $[HCN][CN^-]$ does not strictly correspond to the splitting of the imidazole adduct, since this latter reaction has a rate proportional to $[H_2Im^+]$. While there is no reason that both reactions must have similar rate laws, this would be an attractive feature. One possible explanation for this difference is that if the hematin itself is the reactive species in our system, as in eq 6, Hambright's system would have differed from ours in that the rapid reaction to form the cyanide adduct would prevent the hematin from reacting.

An adduct between hematin and either imidazole or 1,10-phenanthroline has not previously been reported. However, our observations are strikingly similar to those of Abbott.[9,10] He observed adducts between bis(imidazole)-iron(III) cation and 1,10-phenanthroline, imidazole, and 2-methylimidazole. As was the case in our measurements, other compounds studied, even similar ones such as bipyridyl and N-methylimidazole, did not form adducts.[10] Also the size of Abbott's equilibrium constants, 90 and 500 M^{-1} for imidazole and 1,10-phenanthroline, respectively,[10] are similar to those we have observed, 220 and 580 M^{-1}.

Abbott has postulated that this interaction may occur by an overlap between the two π clouds and, given the list of compounds which form adducts, this is quite plausible. However, it has been shown that significant hydrogen bonding occurs between free and complexed imidazoles when bis-(imidazole)iron(III) porphyrin is dissolved in the presence of excess imidazole.[11] Since hydrogen bonding should increase the donating ability of the imidazole ligands, this should energetically favor the bis(imidazole) complex and would thus explain Abbott's observations. However, our results cannot be explained in terms of hydrogen bonding.

For experimental reasons neither we nor Abbott's group have examined cyanide to see if it forms adducts. However, Hambright's work indicates that cyanide does behave like imidazole and 1,10-phenanthroline. It should be noted that cyanide, like the others, is unsaturated and that one molecule quickly adds to the iron porphyrin. Unlike the others cyanide does cause a small spectral change. However, this change is too small to be caused by direct interaction with the metal or by any significant change in structure.

Finally we are unable to explain why only certain molecules form porphyrin adducts. This question will have to await further work.

Acknowledgment. We wish to thank Dr. Daniel Huchital for helpful discussions and Dr. Edwin Abbott for permission to quote unpublished results. The support of the Research Corporation is gratefully acknowledged.

Registry No. TPPFeOFeTPP, 12582-61-5; HIm, 288-32-4; $H_2Im^+Cl^-$, 1467-16-9; $[TPPFe{\cdot}2HIm]^+$, 52155-41-6.

References and Notes

(1) K. S. Murray, *Coord. Chem. Rev.*, **12**, 1 (1974).
(2) I. A. Cohen, *J. Am. Chem. Soc.*, **91**, 1980 (1969).
(3) J. O. Alben, W. H. Fuchsman, C. A. Beaudreau, and W. S. Caughey, *Biochemistry*, **8**, 534 (1969).
(4) R. G. Wilkins and R. E. Yelin, *Inorg. Chem.*, **8**, 1470 (1969).
(5) E. B. Fleischer, J. M. Palmer, R. S. Srivastava, and A. Chatterjee, *J. Am. Chem. Soc.*, **93**, 3162 (1971).
(6) J. R. Sutter, P. Hambright, P. B. Chock, and M. Krishnamurthy, *Inorg. Chem.*, **13**, 2764 (1974).
(7) P. Hambright and M. K. Krishnamurthy, *J. Inorg. Nucl. Chem.*, **37**, 557 (1975).
(8) A. D. Adler, *Inorg. Synth.*, **16**, 216 (1976).
(9) E. H. Abbott and P. A. Rafson, *J. Am. Chem. Soc.*, **96**, 7378 (1974).
(10) E. H. Abbott, private communication.
(11) F. A. Walker, M. W. Lo, and M. T. Ree, *J. Am. Chem. Soc.*, **98**, 5552 (1976).

Contribution from the Department of Chemistry,
Montana State University, Bozeman, Montana 59717

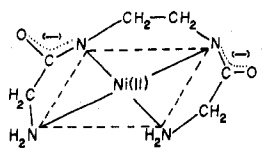
Kinetics of the Nickel(II)–N,N′-Diglycylethylenediamine Reaction with Ethylenediaminetetraacetate

ROGER PEARSON and GORDON K. PAGENKOPF*

Received October 6, 1977

The reaction of deprotonated nickel(II)–N,N′-diglycylethylenediamine with ethylenediaminetetraacetate has been studied over the pH range of 8.55–11.47. The ligand exchange reaction proceeds through two paths. The first of these is dissociative, $k_d = 2.1 \times 10^{-4}$ s^{-1}, and the second involves direct replacement by deprotonated EDTA, $k_{EDTA^{4-}} = 3.33 \times 10^{-3}$ M^{-1} s^{-1}, and monoprotonated EDTA, $k_{HEDTA^{3-}} = 8.13 \times 10^{-3}$ M^{-1} s^{-1}. The overall reaction is accelerated through reaction with bicarbonate ion to form a protonated intermediate. This complex is more reactive than $NiH_{-2}DGEN$ and the exchange reaction is initiated at a nonterminal coordination site. The reaction is retarded at higher pH values by the loss of a proton from the parent complex.

N,N′-Diglycylethylenediamine (DGEN) forms a yellow square-planar complex with Ni(II) in which both of the DGEN amide protons have been ionized.[1,2] The mode of coordination of the ligand to nickel is through the two terminal amine groups and the two deprotonated amide nitrogens. The deprotonated complex is designated by $NiH_{-2}DGEN$.



Ionization of the protons is virtually complete by pH 8. Nickel(II) also facilitates the ionization of amide protons from coordinated polypeptides and polyamides. As with DGEN the deprotonated complexes are generally formed by pH 8.[3–5]

The displacement of short-chain polypeptides from nickel(II) and copper(II) by multidenatate ligands such as ethylenediaminetetraacetate and triethylenetetramine proceeds through proton transfer limited[5–7] or direct replacement paths.[8,9] In these studies the polypeptide is believed to unwrap from the metal stepwise starting with the carboxyl terminus. When the third residue in glycylglycylglycine is replaced by L-histidine (glygly-L-his), the reactivity pattern is altered to a proton-assisted mechanism that is initiated at a nonterminal position.[10–12]

0020-1669/78/1317-1799$01.00/0