# AN INVESTIGATION OF FACTORS CONTROLLING THE FORMATION OF METAL COMPLEXES CONTAINING MACROCYCLIC LIGANDS

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LAWRENCE A. FUNKE
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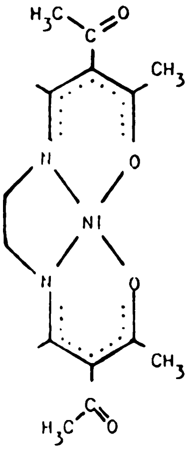
# ABSTRACT

# AN INVESTIGATION OF FACTORS CONTROLLING THE FORMATION OF METAL COMPLEXES CONTAINING MACROCYCLIC LIGANDS

By

Lawrence A. Funke

Factors controlling the condensation reaction between [3,3'-(ethylenebis(nitrilomethylidyne)]di-2,4-pentanedionato(2-)]nickel abbreviated Ni(enp), and diamines to form compounds containing macrocyclic ligands have been investigated.



Ni(enp)

The first part of this investigation was the study of the dynamic linkage isomerization, i.e., the interchange between the coordinated and uncoordinated "acetyl" groups, of Ni(enp). The interchange was followed by proton magnetic resonance spectroscopy with some of the hydrogens of the uncoordinated acetyl groups replaced by deuteriums for the purpose of "labeling." The process follows first order kinetics, with the rate constant k at 35° equal to $0.81 \pm 0.05 \times 10^{-4}$ sec$^{-1}$. The energy of activation, $E_a$, for the isomerization is $17.4 \pm 0.7$ kcal mol$^{-1}$ and the entropy of activation, $\Delta S^{\ddagger}_{298}$, is $-23 \pm 2$ eu. It is concluded that a CO group has a significant lifetime coordinated to the nickel(II) ion. The implications of this conclusion which relate to a possible mechanism for reaction of Ni(enp) with diamines to give a macrocyclic complex are discussed.

The second part of this investigation was the study of the kinetics of the hydroxide ion catalyzed ring closure reaction of Ni(enp) with ethylenediamine to form a compound containing a macrocyclic ligand. The reaction is first order in Ni(enp) and hydroxide ion and second order in ethylenediamine. Also, the rate of reaction decreases as the polarity of the solvent increases. The rate constant k at 68.2° is equal to $2.22 \pm 0.09 \times 10^{-3}$ M$^{-3}$ sec$^{-1}$. The activation energy, $E_a$, and the entropy of activation, $\Delta S^{\ddagger}_{298}$, are $10.4 \pm 0.8$ kcal mol$^{-1}$ and $-42 \pm 3$ eu. respectively. Mechanisms consistent with these results are discussed.

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By

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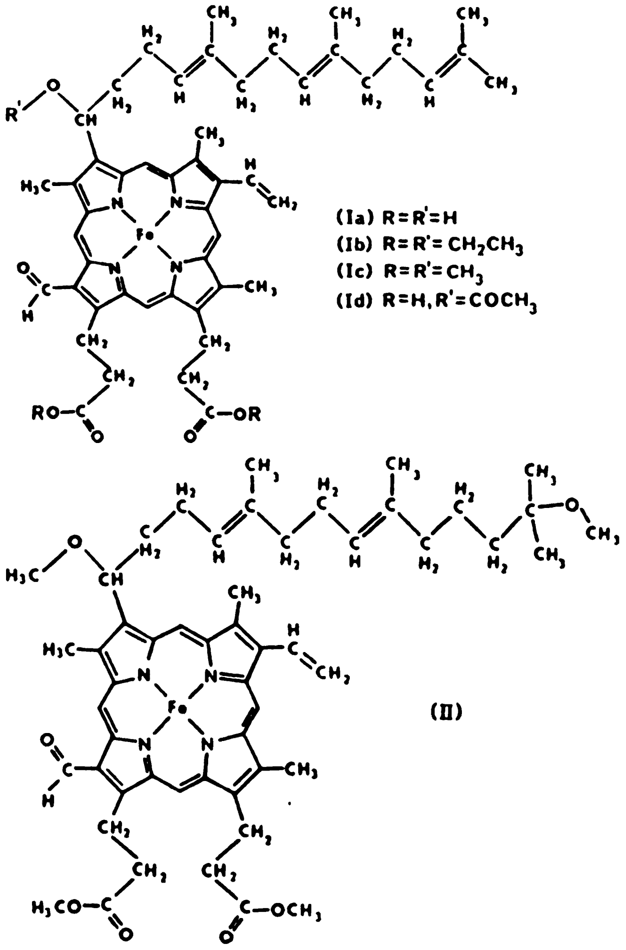
# CHAPTER I

# GENERAL INTRODUCTION

## GENERAL INTRODUCTION

Metal complexes of organic macrocyclic ligands have been known for many years. Early examples were found in the natural products, such as porphyrin and corrin ring derivatives, and in the phthalocyanines. One of the principal reasons for the current interest in complexes containing macrocyclic ligands is the possibility of relating the results of this research to biologically important molecules. Metal ions are essential for many biological systems,[1-4] and a large number of these metal ions are coordinated by macrocyclic ligands. Figure 1 shows the structure of heme a, the site of oxygen reduction in cytochrome c, and is an example of an iron(II)-porphyrin complex. Figure 2 shows the structures of vitamin $B_{12}$ and a coenzyme, examples of complexes of corrin ring derivatives. Vitamin $B_{12}$ functions in the liver and is used in the treatment of pernicious anemia and other metabolic disorders. While the therapeutic value of vitamin $B_{12}$ is known, it is not understood why it functions as it does.

Because of their structural similarity, some coordination compounds of synthetic macrocyclic ligands are being proposed as possible model systems for the study of naturally occurring compounds.[2-9] Some of the most productive research concerning model systems has been the study of synthetic dioxygen carriers. Recently, Basolo, Hoffman and Ibers[10] summarized their work in this area and Collman, et al.,[11] reported the synthesis, characterization and properties of an iron(II)-porphyrin complex which reversibly binds dioxygen. These and similar



(Ia) R=R'=H

(Ib) R=R'=$CH_2CH_3$

(Ic) R=R'=$CH_3$

(Id) R=H, R'=$COCH_3$

(II)

Figure 1. Heme a (Ia) and derivatives.

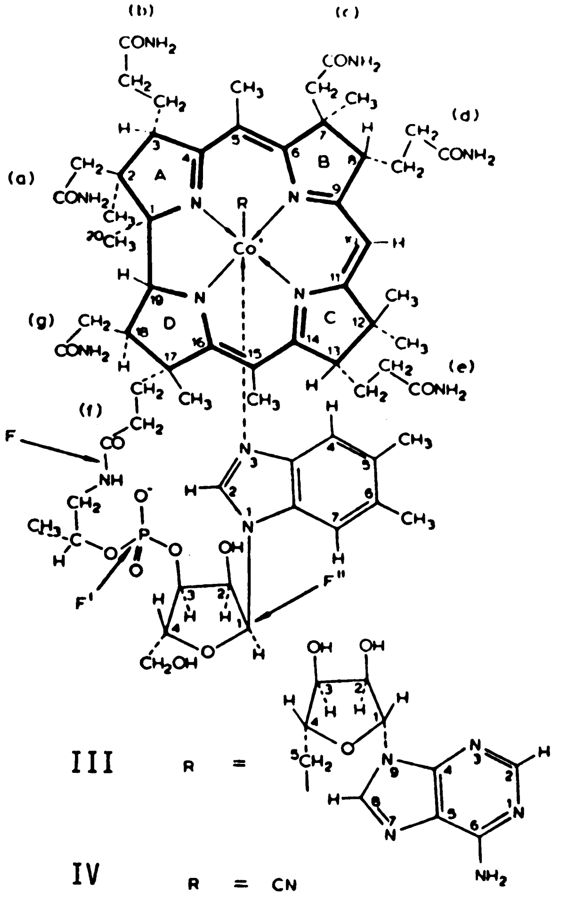


Figure 2. Structure of coenzyme $B_{12}$, 5'deoxyadenosylcobalamin, III, and vitamin $B_{12}$, cyanocobalamin, IV.

studies have greatly increased our insight into the naturally occurring dioxygen carriers.

It is only in the last two decades that a large number of new macrocyclic-ligand complexes have been prepared and investigated. Many excellent reviews of the field of macrocyclic ligands and their metal complexes are available. Busch,[12] in 1964, described the general characteristics of compounds containing macrocyclic ligands. The "kinetic template effect," the sterically orienting influence of the metal ion on the course of the formation of a coordination compound, was also discussed. Several years later, Busch[13] reviewed the synthesis, electronic structure, magnetic properties and stereochemistry of the transition metal complexes of synthetic macrocyclic ligands. At about the same time, Curtis[14] described the synthesis, physical properties and chemical reactivity of macrocyclic coordination compounds formed by the condensation of metal-amine complexes with aliphatic carbonyl compounds. Later reviews by Lindoy and Busch[9] and by Black and Hartshorn[15] discuss extensively the general considerations important in the design and synthesis of macrocyclic ligands and their complexes. The relative advantages and disadvantages of the two general synthetic approaches, namely, direct synthesis of the ligand followed by coordination to the metal ion, and "in situ" synthesis of the complex, i.e., with the metal ion already present during formation of the ligand, are discussed. Recently, Christensen, Eatough and Izatt[16] compiled a list of 221 different macrocycles and the metals bound by these ligands. The list includes macrocycles with oxygen, nitrogen, sulfur and mixed donor atoms. The size of this list indicates the wide variety of macrocyclic ligands that are now available.

Some recent studies have concentrated on the effect that various systematic changes in the macrocyclic ring structure have on the properties of the metal complexes. By the use of oxidative dehydrogenation, Hipp, et al.,[17] synthesized metal complexes with macrocycles having prescribed patterns of unsaturation. Watkins, et al.,[18] investigated the effect of varying ring size on the Mössbauer and electronic spectra and the ligand field strength of saturated tetraaza macrocyclic ligands coordinated to iron(II). Wagner and Barefield[19] studied the N-alkylation of macrocyclic secondary amine complexes of nickel(II). Chemical reactions of the new complexes and the effect of N-alkylation on the kinetic stability of the complexes and the ligand field strength of a given ligand system were discussed. Other recent work[20-24] has resulted in the development of new macrocyclic systems and of improved synthetic techniques.

A property of macrocyclic ligands that has attracted considerable attention is their ability to stabilize unusual oxidation states of metals. This ability is ascribed to the enhanced stability of the complexes of macrocyclic ligands compared to similar non-cyclic ligands,[25-27] thus enabling the macrocycles to trap metal ions in uncommon oxidation states. This enhanced stability has been termed the macrocyclic effect or multiple juxtapositional fixedness. Macrocyclic complexes of nickel(I),[28] nickel(III),[28] cobalt(I),[29] silver(II),[30,31] and silver(III),[31] have been isolated and characterized, while complexes of copper(III)[32] have been formed but are spontaneously reduced in acetonitrile. Possible applications of these complexes could include their use as oxidizing or reducing agents.

Most of the research concerned with metal complexes of macrocyclic ligands has concentrated on the study of their synthesis, properties and reactivity. Very little work to determine mechanisms of formation of these compounds has been performed. In this thesis, I will describe efforts to determine the factors controlling the formation of compounds containing macrocyclic ligands.

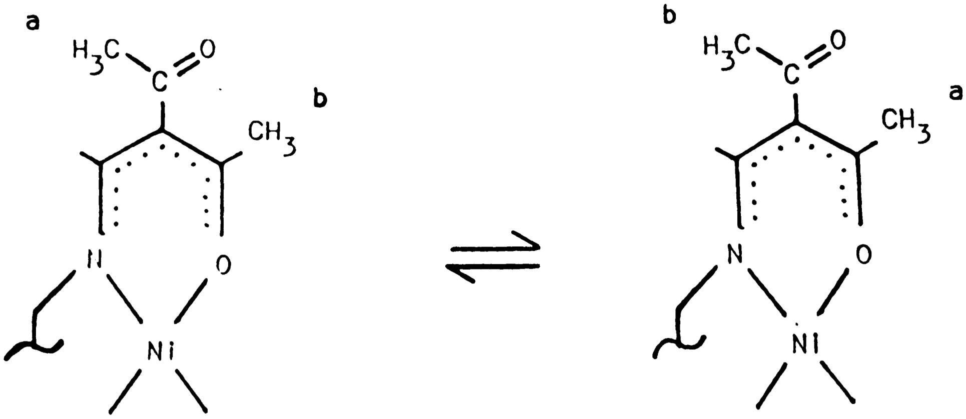
# CHAPTER II

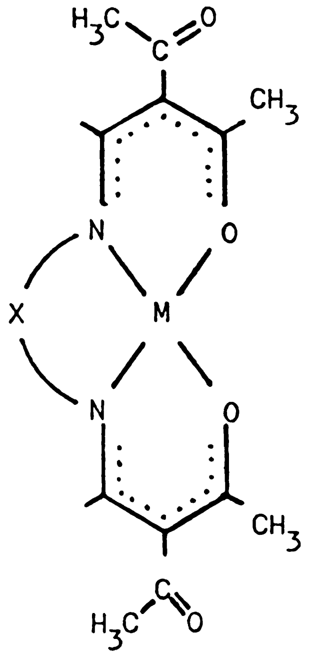
# DYNAMIC LINKAGE ISOMERIZATION OF [3,3'-[ETHYLENEBIS(NITRILOMETHYLIDYNE)]-DI-2,4-PENTANEDIONATO(2-)]NICKEL

## INTRODUCTION

Jäger has reported that reactions between complexes containing tetradentate ligands, V, and some diamines result in the formation of complexes with macrocyclic ligands,[33] VI. However, compounds similar to V, but with different substituents on the six-membered chelate ring, VII, do not undergo reaction with diamines.[5,20,34] One of the goals of this research was to determine the role of the uncoordinated CO group in the ring-closure of V to form the macrocyclic complex, VI.

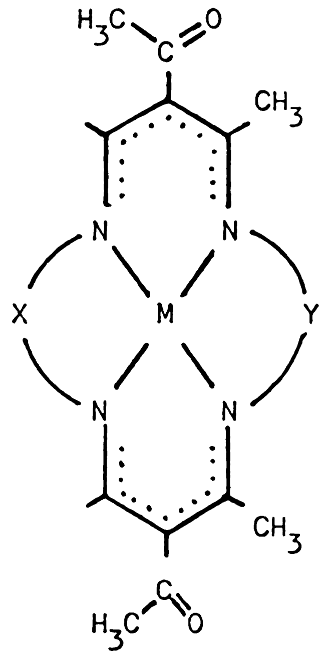
In these systems, the ring-closure may involve reaction of the amine at the coordinated CO group or at the uncoordinated CO group followed by rearrangement. Alternatively, the rate of interchange between the coordinated and uncoordinated CO groups may be sufficiently rapid that they are equivalent and thus it is not possible to determine the position of attack. This interchange process or linkage isomerization may be represented as





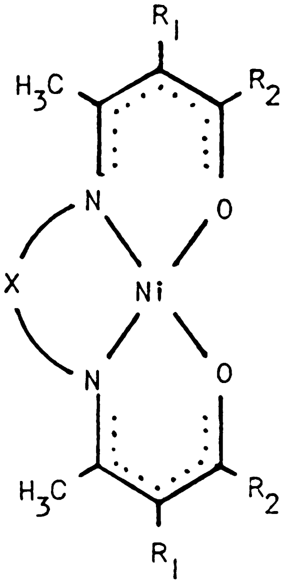
V

X = $C_2H_4$, $C_3H_6$, $C_6H_4$
M = Ni(II), Cu(II)



VI

X = $C_2H_4$, $C_3H_6$, $C_6H_4$
Y = $C_2H_4$, $C_3H_6$, $C_6H_4$
M = Ni(II), Cu(II)



VII

X = $C_2H_4$
$R_1$ = H; $R_2$ = $CH_3$, $CF_3$
$R_1$ = Br; $R_2$ = $CH_3$

In an attempt to draw some conclusions concerning the possible mechanism for the ring-closure process, we have measured the rate of interchange of the "acetyl" groups for V, X = $C_2H_4$ and M = Ni(II), over a range of temperatures from 35 to 60°.[35]

## EXPERIMENTAL SECTION

### Preparation of Materials

[3,3'-[Ethylenebis(nitrilomethylidyne)]di-2,4-pentanedionato(2-)]-nickel, abbreviated Ni(enp), was prepared as previously reported.[36] The deuterated species, Ni(enp-d), was prepared by adding 0.75 g of Ni(enp) to 40 ml of 99% MeOD (Aldrich) and adjusting the pH of the mixture to 12 with NaOH in $D_2O$. The solution was stirred at 5° for 20 days and filtered, and the residue was dried overnight at room temperature under vacuum over $P_4O_{10}$. Use of longer times and/or higher temperature resulted in a decrease in the selectivity of the deuteration, i.e. significant deuteration of the downfield methyl group as well as the upfield group occurs. If allowed to stir over extended periods of time (several months), virtually 100% deuteration of both methyl groups will occur. The conditions given above were found to yield the maximum selective deuteration, approximately 30% of the upfield methyl protons, with no other hydrogens of the ligand being exchanged for deuteriums.

### Procedure for Obtaining Kinetics Data

All proton magnetic resonance (pmr) spectra were obtained with a Varian HA-100 spectrometer. TMS was used as an internal standard and chloroform-d used as solvent for recording the complete spectrum at room temperature (see Figure 4). Above room temperature, the spectra were obtained with bromoform as solvent. (No significant solvent effect on the spectrum was observed at room temperature.) Temperature was measured by using an ethylene glycol standard[37] before and after each run. The maximum temperature variation throughout a run is estimated to be ± 0.5°.

A weighed amount of Ni(enp-d) was dissolved in a known quantity of bromoform (typical concentrations approximately $5 \times 10^{-2}$ M) and the solution was then transferred to an nmr tube. The tube was capped and placed into the probe which had previously been adjusted to the selected temperature. Approximately 5 minutes were allowed for the sample to reach temperature. The timer was started and repeated scans of the methyl region of the spectrum from low to high field ($\delta \sim 2.5$ --2.25 ppm) performed. These scans began ∿ 5 Hz before the low-field peak and continued to ∿ 5 Hz after the high-field peak. Total scan time was approximately 12 seconds. For a particular scan, the time was recorded when the recorder pen reached the top of the low-field peak. Repeated scans of the spectrum were obtained until the two peaks were of equal height (see Figure 5).

## Treatment of Kinetics Data

The heights of the two $CH_3$ peaks were measured directly from the spectra and the decrease to zero of the peak height difference as a function of time was used for calculation of the kinetics of the interchange process. The data obtained at a particular temperature were treated by KINFIT, a nonlinear curve-fitting program,[38] with the

Michigan State University CDC 6500 computer. The equation for a first order process, viz., $A = A_0 e^{-k_{obs}t}$ was fitted to the data. A is the peak height difference in millimeters at time t (seconds), $A_0$ is the peak height difference at t = 0 and $k_{obs}$ is the observed first-order rate constant. Input data consisted of the experimental values of A and t and the variances in those values. Variance in t was estimated to be $\pm$ (1 sec)$^2$, and in A $\pm$ (1 mm)$^2$. (A good estimate of variance is considered to be the error in measurement squared.) $A_0$ and $k_{obs}$ are the adjustable parameters fitted to the data. The output includes both the value and the standard deviation of the parameters. After the treatment of a set of data at a particular temperature by the KINFIT program, those points which deviated considerably from the calculated A vs t curve were dropped from the data and the program was rerun. In no case was there a significant change in the value of $k_{obs}$ although the standard deviation of $k_{obs}$ decreased markedly. Figure 3 shows a computer plot from KINFIT illustrating the fit of a set of data.

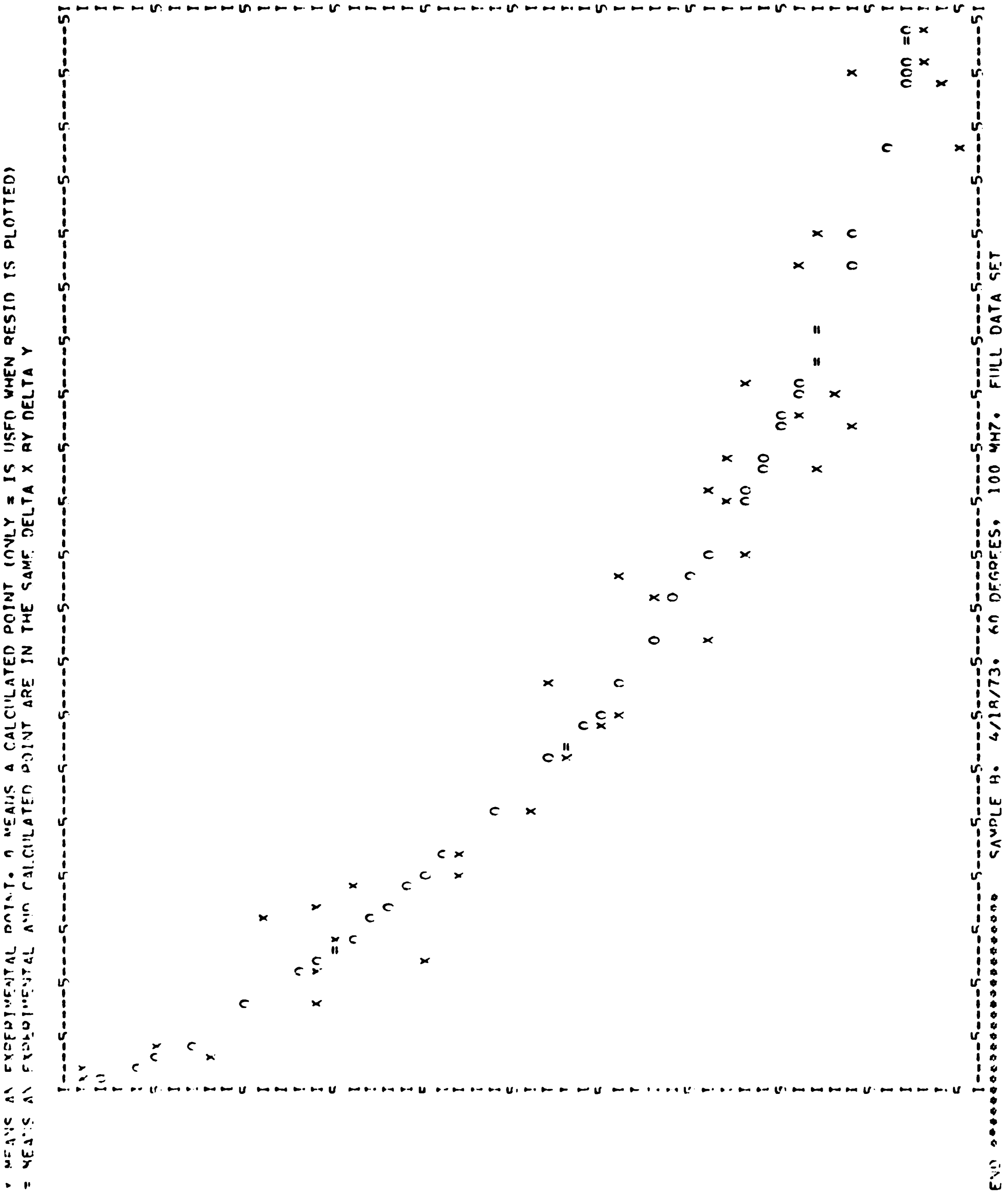
Due to convergence problems, the Arrhenius Equation,

$$k = A\ e^{-E_a/RT} \tag{1}$$

could not be used directly with KINFIT to determine the activation parameters. Instead, the rearranged equation

$$k = k_{ref}\ e^{\frac{-E_a}{R}\left(\frac{1}{T} - \frac{1}{T_{ref}}\right)} \tag{2}$$

Figure 3. Plot from KINFIT of data for linkage isomerization at 60°C.



X MEANS AN EXPERIMENTAL POINT. 0 MEANS A CALCULATED POINT (ONLY = IS USED WHEN RESID IS PLOTTED)

= MEANS AN EXPERIMENTAL AND CALCULATED POINT ARE IN THE SAME DELTA X BY DELTA Y

END ********************** SAMPLE H. 4/18/73. 60 DEGREES. 100 MHZ. FULL DATA SET

Figure 3.

was used. $T_{ref}$ is an arbitrary reference temperature and $k_{ref}$ is the rate constant at $T_{ref}$. The value of $E_a$ is independent of the choice of $T_{ref}$, as calculations using both 333°K and 308°K as $T_{ref}$ have shown. For the calculation of $E_a$, k and T were the input variables and $k_{ref}$ and $E_a$ were the fitted parameters. Variance in T was set at $\pm (1°)^2$ and variance in k was the square of the standard deviation of k. Calculation of the Arrhenius pre-exponential was made by use of the equation

$$k_{ref} = A\, e^{-E_a/RT_{ref}} \tag{3}$$

where $k_{ref}$ and $E_a$ were the parameters calculated with equation (2). Calculation of $\Delta S^{\ddagger}_{298}$ was then made by use of the equation

$$\log A = \log \left(\frac{ekT}{h}\right) + \frac{\Delta S^{\ddagger}}{2.303\ R} \tag{4}$$

## RESULTS AND DISCUSSION

The 100-MHz pmr spectrum of Ni(enp), structure V, X = $C_2H_4$, in chloroform-d at room temperature is shown in Figure 4. The resonance at δ 7.49 ppm (relative intensity 2) downfield from the internal TMS standard is assigned to the hydrogens attached to the six-membered chelate rings of the ligand in Ni(enp) and the resonance at δ 3.30 ppm (relative intensity 4) is assigned to the methylene hydrogens. The two remaining resonances (each of relative intensity 6) at δ 2.29 and 2.44 ppm are assigned to the hydrogens of the uncoordinated and

Figure 4. The 100-MHz pmr spectrum of Ni(enp) at room temperature.

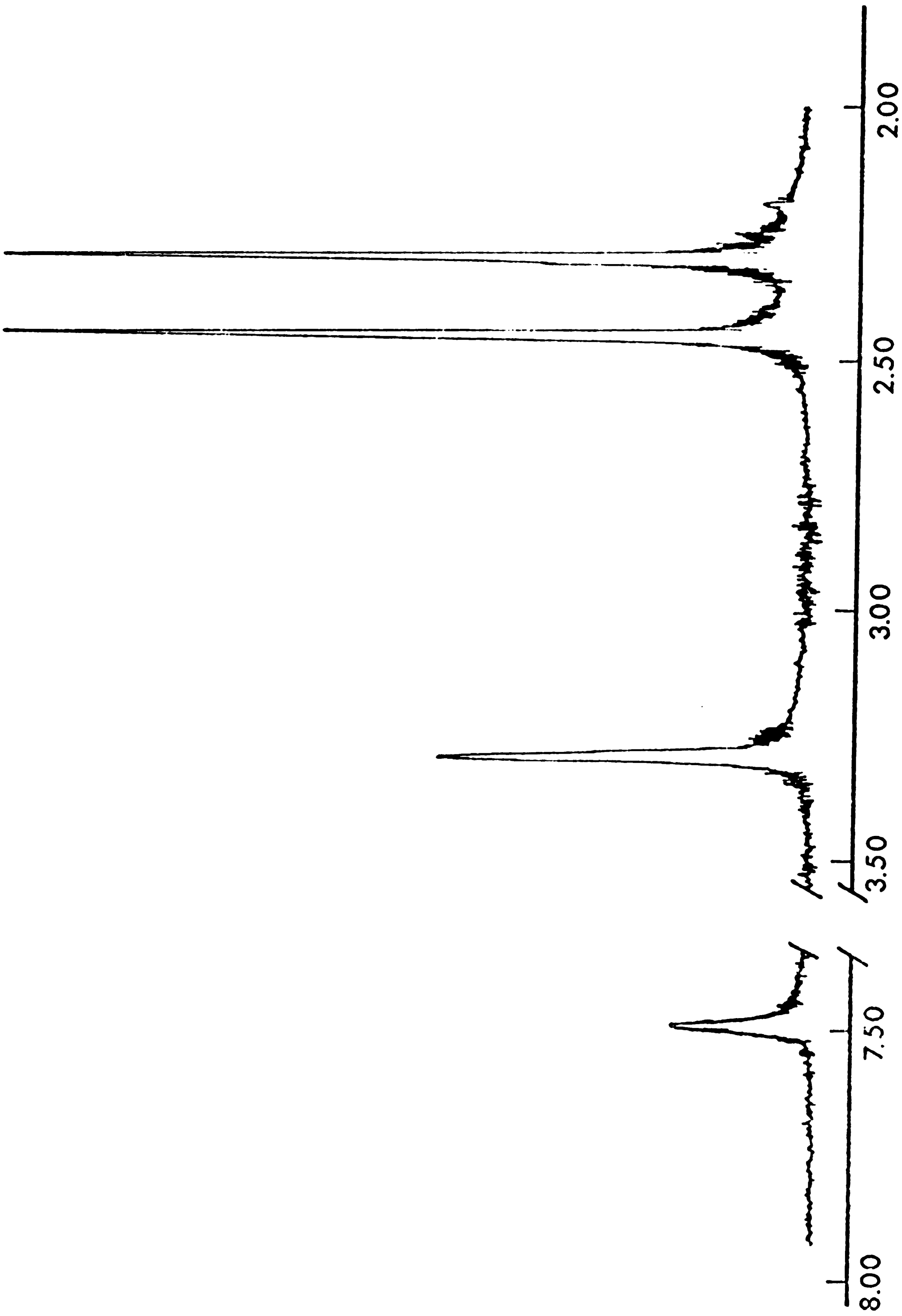
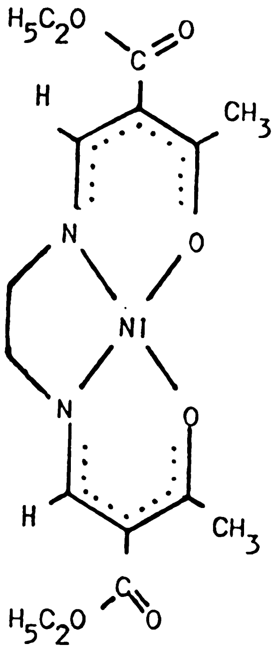


Figure 4.

coordinated $CH_3CO$ groups, respectively. These latter two assignments are made on the basis of assignments for similar compounds. In both the nickel(II) complex VIII and the macrocyclic complex derived from it by condensation with ethylenediamine, the methyl hydrogens are



VIII

observed as a singlet at δ 2.40 ppm,[39] close to the position assigned to the hydrogens of the coordinated $CH_3CO$ group in Ni(enp). In addition, Hipp and Busch[40] have reported pmr spectra of some nickel(II) complexes which contain macrocyclic ligands having uncoordinated $CH_3CO$ groups in the $\gamma$ (or 3) position of the six-membered chelate ring, VI, M = Ni(II). Resonances in the range $\delta$ 2.27--2.30 ppm were assigned to the hydrogens of the uncoordinated $CH_3CO$ groups whereas those in the region of $\delta$ 2.4 ppm were assigned to the hydrogens of the methyl groups attached to the macrocyclic ring. The assignments for Ni(enp) are consistent with these assignments.

The pmr spectrum of Ni(enp) remains unchanged in $CHBr_3$ up to 110°, above which temperature decomposition takes place. Since there is no evidence for line broadening and the methyl hydrogens remain distinguishable in the two different environments, even at elevated temperatures, linkage isomerization is not occurring rapidly, i.e., on a nmr time scale. This observation correlates with the findings of Holm, et al.,[41] for $M(triac)_3$ complexes (M = Al, Ga; triac = 3-acetylpentane-2,4-dionato). In these complexes, which contain coordinated and uncoordinated $CH_3CO$ groups, line broadening was not detected up to 180° and it was concluded that linkage isomerization is not a rapid process.

In order to measure the rate of linkage isomerization for Ni(enp), the methyl groups in the different environments were made identifiable by means of selective deuteration (see Experimental Section). The linkage isomerization was followed by monitoring the difference in peak heights for the methyl hydrogens in the partially deuterated Ni(enp-d) as it decreased to zero. Figure 5 shows the methyl region of the pmr spectrum for Ni(enp-d) at various times at 40°. A complete set of data normally consisted of between 40 and 100 such

Figure 5. Methyl region of the 100-MHz pmr spectrum for Ni(enp-d) as linkage isomerization takes place at 40°.

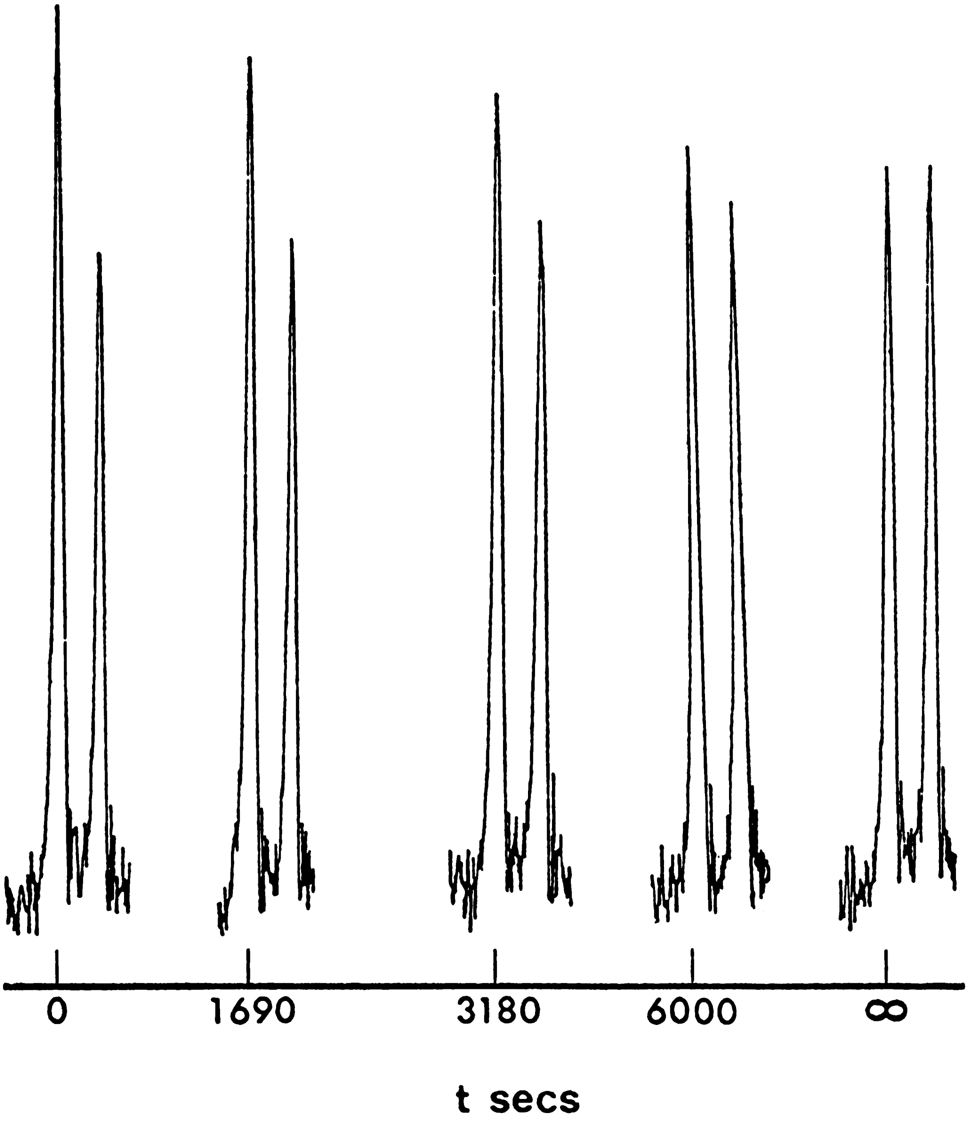
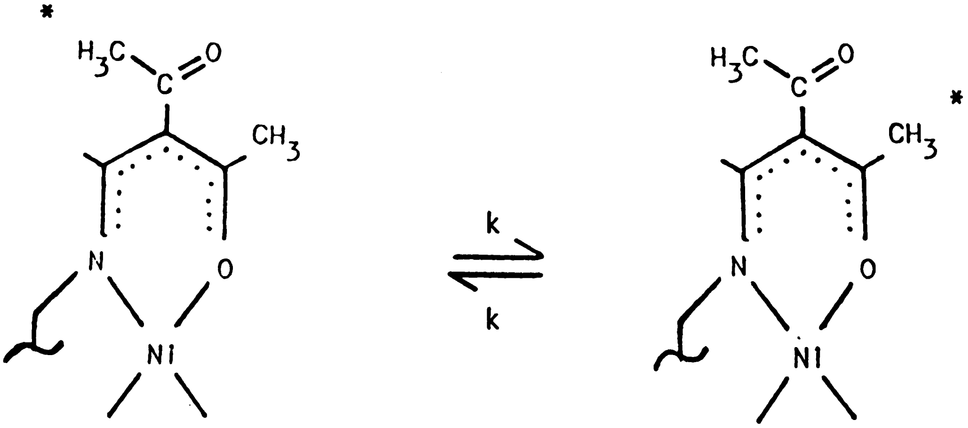


Figure 5.

scans of the methyl region. It should be noted that at no temperature was the total amount of deuteration decreased, thus ruling out any exchange with the solvent. In addition, there was no evidence of exchange between added, undeuterated, ligand and deuterated coordinated ligand.

For the linkage isomerization, represented by the following scheme (where the asterisk signifies labeling by deuterium),



L M

we can write

$$\frac{d(L)}{dt} = -k[(L) - (M)] \tag{5}$$

and

$$\frac{d(M)}{dt} = k[(L) - (M)] \tag{6}$$

Now, A, the experimental peak height difference, is proportional to [(L) - (M)]. Thus,

$$\frac{dA}{dt} = \frac{d[(L) - (M)]}{dt} \tag{7}$$

$$\frac{dA}{dt} = \frac{d(L)}{dt} - \frac{d(M)}{dt} \tag{8}$$

Substituting (5) and (6) into (8),

$$\frac{dA}{dt} = -k[(L) - (M)] - k[(L) - (M)] \tag{9}$$

$$\frac{dA}{dt} = -2k[(L) - (M)] = -2kA \tag{10}$$

Therefore,

$$\frac{dA}{A} = -2k\ dt \tag{11}$$

$$\ln A = \ln A_0 - 2kt \tag{12}$$

$$A = A_0\ e^{-2kt} \tag{13}$$

As noted in the Experimental Section, the expression

$$A = A_0\ e^{-k_{obs}t}$$

was used for treatment of the data. Equating this expression to (13), we observe that

$$k = k_{obs}/2 \tag{14}$$

The data obtained for the isomerization were treated as described in the Experimental Section. The isomerization is a first-order process and values of the first-order rate constants, k, obtained over the temperature range 35--60°C are listed in Table 1. A plot of log k <u>vs</u> 1/T°K is shown in Figure 6. From these data, the energy

Table 1. Temperature Dependence of the Rate Constants for Linkage Isomerization

| Temp, °K | $10^3/T$, °K$^{-1}$ | $k \times 10^4$, sec$^{-1}$ |
|---|---|---|
| 308 | 3.24 | 0.81 ± 0.05 |
| 313 | 3.20 | 1.20 ± 0.08 |
| 317 | 3.15 | 1.64 ± 0.09 |
| 320 | 3.12 | 2.47 ± 0.17 |
| 325 | 3.08 | 3.42 ± 0.38 |
| 329 | 3.04 | 4.99 ± 0.44 |
| 333 | 3.00 | 6.0 ± 0.5 |

of activation for the isomerization, $E_a$, is 17.4 ± .7 kcal mol$^{-1}$, and log A, 8.24. From the log A value, $\Delta S^{\ddagger}_{298}$ is 23 ± 2 eu.

Figure 6. Plot of -log k *vs* 1/T°K for linkage isomerization.

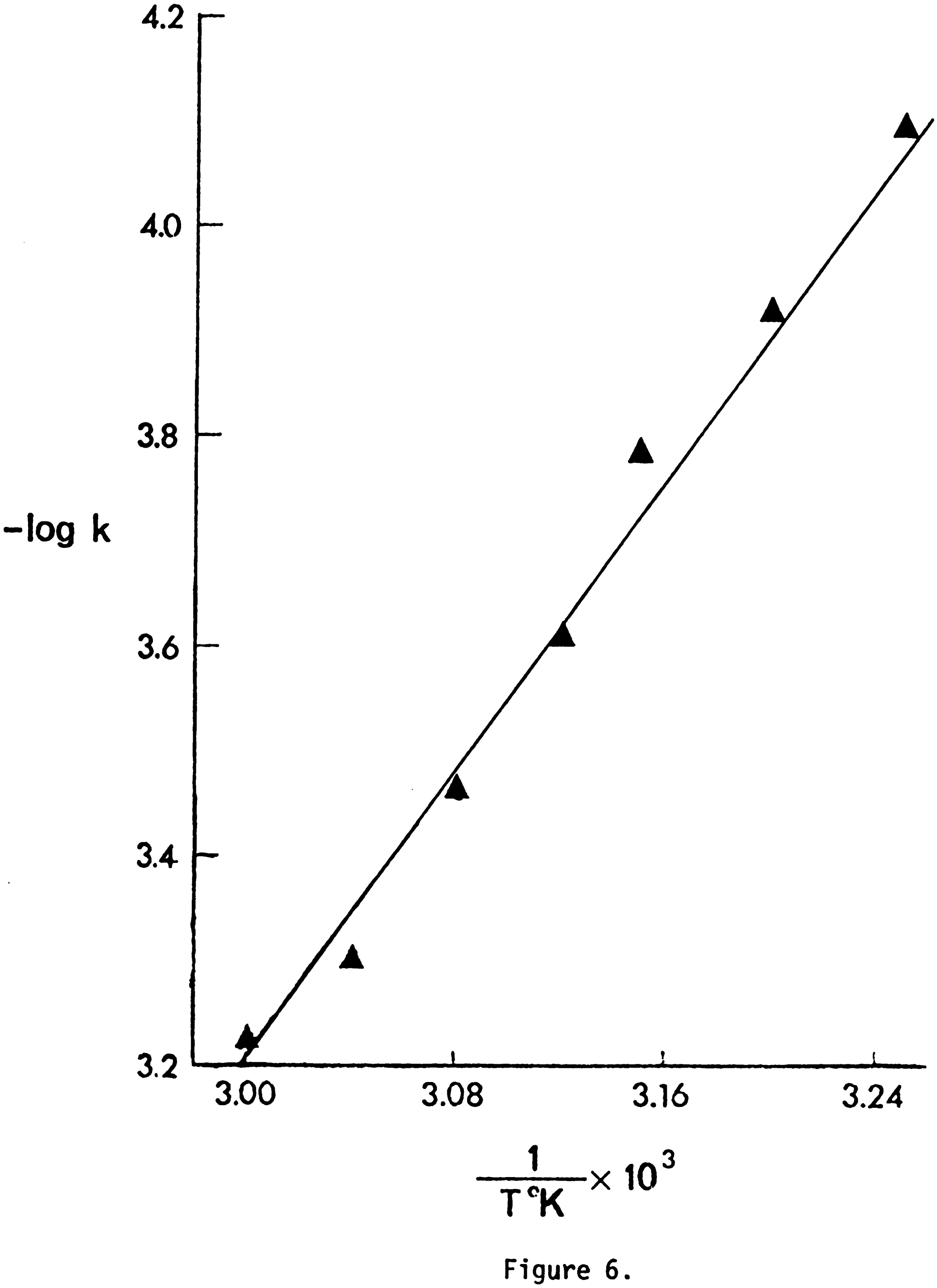


Figure 6.

The fairly large negative value of $\Delta S^{\ddagger}_{298}$ indicates that a symmetric intermediate is produced in the linkage isomerization process, which involves rotation about a $\mathrm{C}\overset{\cdots}{-}\mathrm{C}$ bond of the ligand. We suggest that, in this symmetric intermediate, "coordination" of both oxygens to the nickel(II) occurs. Fay[42] has observed linkage isomerization of triac in $\mathrm{Co(triac)_3}$ and $\mathrm{Co(acac)_2(triac)}$. He obtained $E_a$ and $\Delta S^{\ddagger}_{298}$ values of 39.6 ± 1.6 kcal $\mathrm{mol^{-1}}$ and 28 ± 4 eu and 39.9 ± 1.8 kcal $\mathrm{mol^{-1}}$ and 28 ± 5 eu, respectively. In these cobalt complexes, the linkage isomerization is proposed to proceed via a five-coordinate intermediate produced by Co—O bond rupture followed by rotation about a $\mathrm{C}\overset{\cdots}{-}\mathrm{C}$ bond within the resulting unidentate ligand and Co—O formation. This mechanism is consistent with the observation of a large positive value for $\Delta S^{\ddagger}_{298}$. The cobalt(III) ion is six-coordinated in these complexes and a mechanism involving reduction of the coordination number of the cobalt(III) ion is reasonable for the linkage isomerization. However, for Ni(enp), the nickel(II) ion is four-coordinated and a mechanism invoking association of both CO groups with the nickel(II) ion during the isomerization is both plausible and in agreement with the observed negative value for $\Delta S^{\ddagger}_{298}$.

The preexchange lifetime, $\tau$, i.e., the lifetime of a particular configuration prior to the isomerization taking place, can be obtained from the rate constant by $\tau = 1/k$. For Ni(enp-d) in bromoform, $\tau$ varies from $12.4 \times 10^{3}$ sec at 35° to $1.66 \times 10^{3}$ sec at 60°. From this information, it is possible to draw some conclusions concerning the ring-closure reaction of Ni(enp) with amines. Reactions of CO groups with amines proceed via nucleophilic attack of the amine at the carbon atom of the CO group. As noted previously, there is no evidence for exchange with free ligand. Therefore, a process in which dissociation of the complex occurs, followed by ring closure of the free ligand and then coordination of the macrocycle to the nickel(II) ion, is unlikely. In Ni(enp), there are two potential reaction sites, the carbon of the coordinated acetyl group and that of the uncoordinated acetyl group. Since the linkage isomerization is slow and a particular configuration of the ligand has a significant preexchange lifetime, the nickel(II) ion will have a significant effect on the electron density within the ligand. Coordination will result in decreased electron density at the carbon of the coordinated CO group due to its electron-withdrawing nature. Thus the carbon atom of the coordinated CO will be the preferred site for nucleophilic attack by amines in the ring closure process. Attempts to confirm this conclusion by reaction of Ni(enp-d) with amines were not successful however, since very rapid exchange of the deuteriums of the uncoordinated acetyl groups occurred in the presence of amines and the macrocycle obtained was nondeuterated.

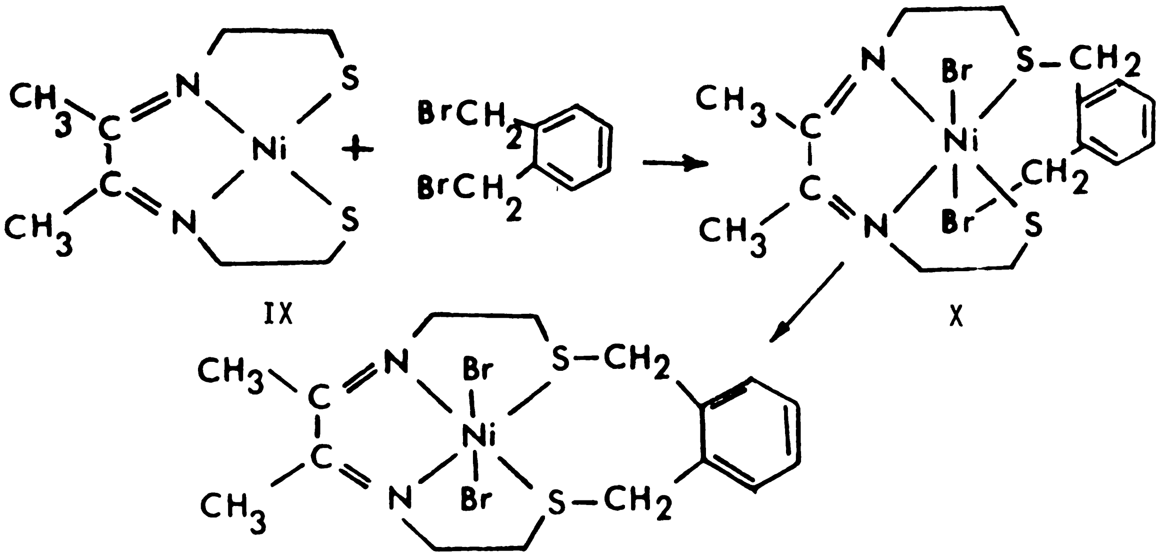
# CHAPTER III

# KINETICS AND MECHANISM OF THE RING CLOSURE OF [3,3'-[ETHYLENEBIS(NITRILOMETHYLIDYNE)]-DI-2,4-PENTANEDIONATO(2-)]NICKEL TO FORM A COMPOUND CONTAINING A MACROCYCLIC LIGAND

## INTRODUCTION

In the General Introduction, it was noted that the synthesis, properties and reactivity of a large number of macrocyclic complexes have been studied, while little work has been performed to determine mechanisms of their formation. In one of the few reported studies of this type, Hurley, Robinson and Trotz[43] investigated the stepwise formation of nickel phthalocyanine by the isolation of several intermediate products that are formed on the way to the final complex. However, no kinetics data or activation parameters were determined.

Blinn and Busch[44] studied the reaction of 2,3-pentanedionebis-(mercaptoethylimino)nickel(II), IX, with α,α'-dibromo-o-xylene and other alkyl dibromides to form a macrocyclic complex, XI. They determined that the reaction proceeds via a two-step process. The first step, the combination of one mercapto group with one end of the dibromoxylene, is the slow, rate determining step. The second step, the reaction of the remaining mercapto and bromo groups to effect ring closure, is too rapid to follow. Blinn and Busch ascribe this difference in rates to the fact that the reactive sites for the second step are already sterically oriented for the cyclization reaction. This last observation is the essence of what is called the "kinetic coordination template effect." It is also probable that precoordination of the dibromoxylene to the nickel ion occurs, as implied by the proposed structure of X. In other studies involving similar reactions, precoordination is proposed in the reaction of benzyl bromide with various mercaptoaminenickel(II) complexes[45] and in the reaction of alkyl halides with substituted 8-mercaptoquinoline complexes of nickel(II).[46,47]



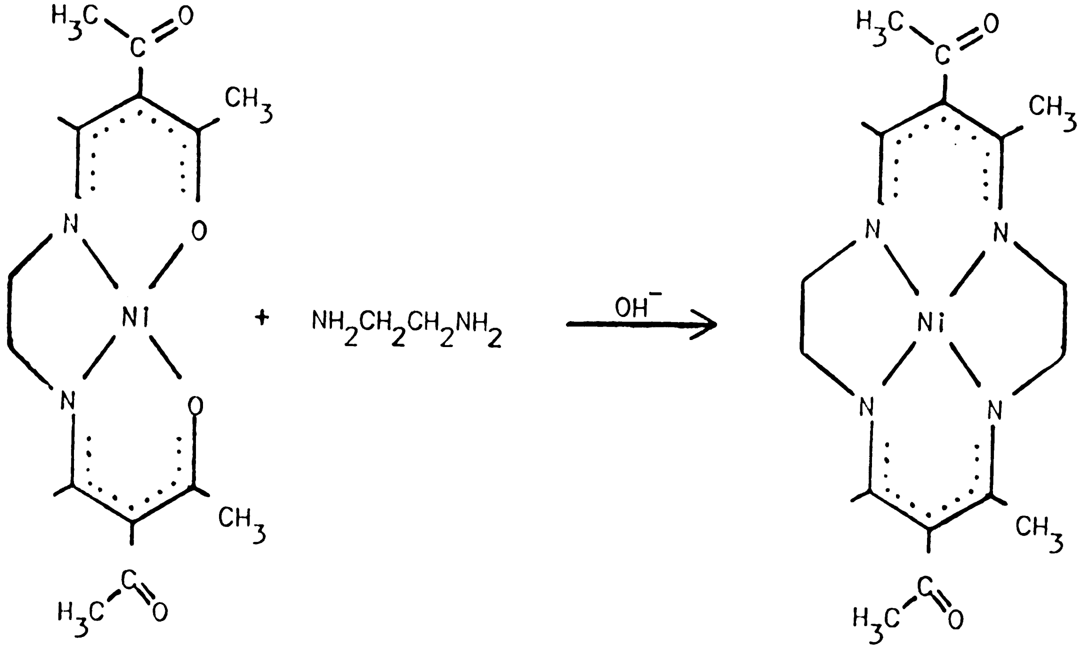
IX

X

XI

The ability of a metal ion to orient reactants so as to facilitate a certain reaction has been amply demonstrated.[12-16] In many instances the products of a particular reaction carried out in the presence and absence of a metal ion are quite different.[48-50] Leussing and coworkers, who prefer the term promnastic (matchmaker) to template, have studied the formation of Schiff bases from salicylaldehyde and glycine,[51] and salicylaldehyde and diamines.[52] They propose the formation of a ternary complex followed by condensation of the complexed ligands within the primary coordination sphere of the metal ion.

Because of the lack of mechanistic information concerning the formation of macrocyclic complexes, the investigation of the ring closure of Ni(enp), XII, with ethylenediamine to form a compound containing a macrocyclic ligand, Ni(enp-M-en), XIII, was undertaken.



XII

XIII

In order to determine the factors controlling the formation of the macrocyclic complex, the dependence of the rate of reaction on the concentrations of Ni(enp), ethylenediamine and hydroxide ion and on the solvent and temperature were studied. The course of the reaction was followed by monitoring the electronic spectra of the starting material and the product, shown in Figure 7, where 1 = Ni(enp) and 2 = Ni(enp-M-en). The decrease in the concentration of Ni(enp) and the increase in the concentration of Ni(enp-M-en) were followed by

Figure 7. Electronic Spectra of Ni(enp), (1), and Ni(enp-M-en), (2).

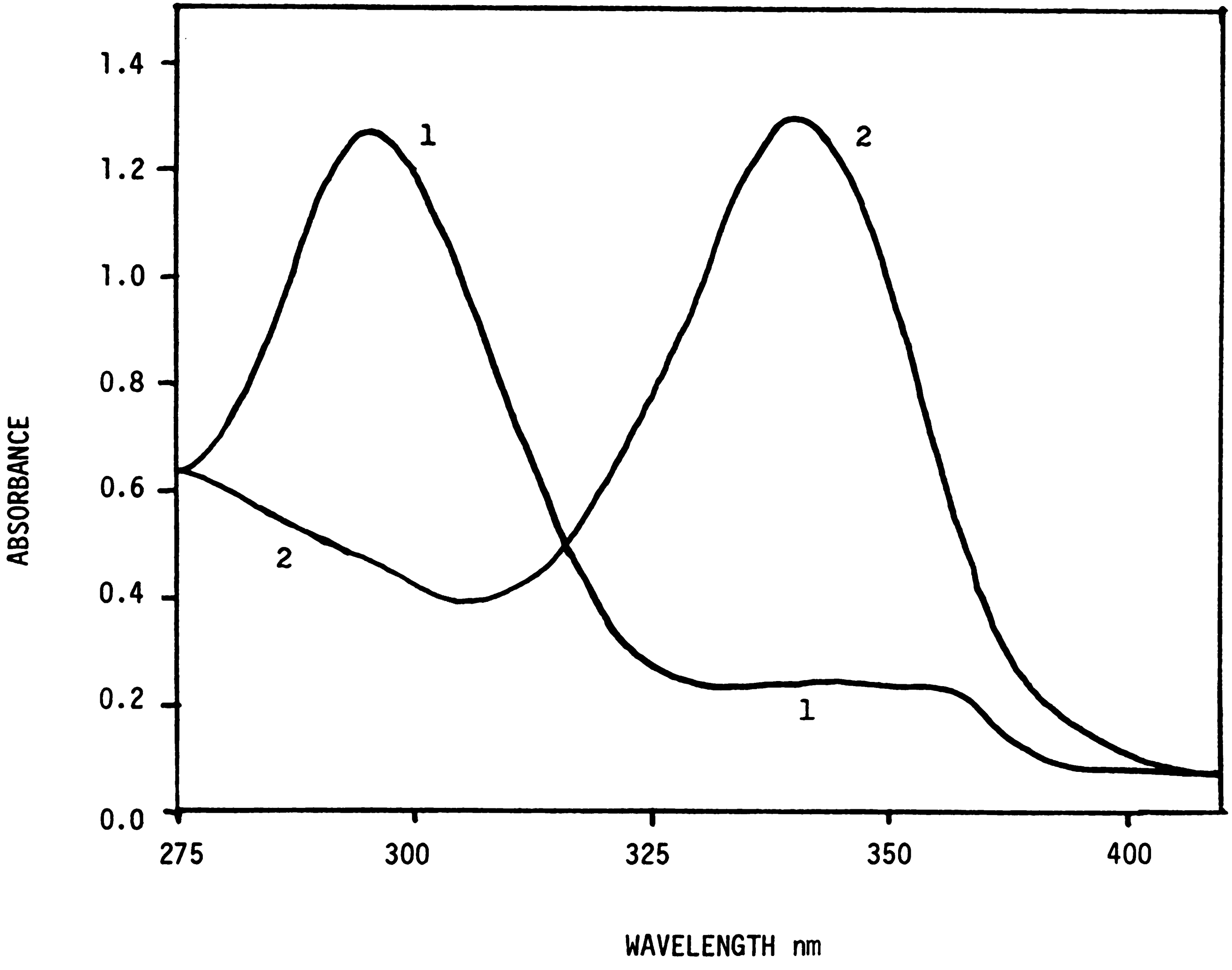

ABSORBANCE
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
275
300
325
350
400
WAVELENGTH nm
1
2
2
1

Figure 7.

monitoring the absorbances at 296 nm and 342 nm, respectively, as a function of time. The calculation of the rate constants is described in the Experimental section. A mechanism consistent with the results of this study will be presented in the Discussion.

## EXPERIMENTAL

### Preparation of Materials

[3,3'-[Ethylenebis(nitrilomethylidyne)]di-2,4-pentanedionato(2-)]-nickel was prepared as previously reported.[36]

Ethylenediamine (en) was twice distilled from sodium hydroxide under dry nitrogen and stored in a dry nitrogen atmosphere.

Tetrahydrofuran (THF) was dried by refluxing over calcium hydride, distilled from calcium hydride and then stored over molecular sieves ("Linde," type 5A).

Absolute ethanol was used as provided.

The ethanolic sodium hydroxide solution was prepared by placing the desired volume of absolute ethanol, previously degassed with dry nitrogen, in an erlenmeyer flask fitted with a connecting tube (gas adapter) and a sidearm with stopcock. The flask was placed in an ice-water bath and a flow of dry nitrogen was maintained for several minutes over the solvent. The weighed amount of reagent grade sodium hydroxide was added slowly, a few pellets at a time, over a period of several hours. The solution was constantly stirred by means of a magnetic stirrer and a continuous flow of dry nitrogen was maintained over the solution. The ice bath was kept near 0°. After complete dissolution of the sodium hydroxide the stopcocks on the sidearm and connecting tube were closed and the flask immediately taken into an inert atmosphere dry box where the solution was filtered through a medium fritted funnel. The filtrate was then placed in a clean plastic bottle, the outside of which had previously been covered with black electrical tape. The solution was removed from the dry box and stored in a refrigerator. The solution was standardized by titration with potassium hydrogen phthalate, which had previously been dried for one hour at 110°. Phenolphthalein was used as the indicator. The ethanolic sodium hydroxide was kept cold and in an inert atmosphere as much as possible in order to prevent the decomposition of the solution. It was found that if these precautions were not taken, a yellowish-brown color appeared in a few days and that the solution became progressively darker as time passed. The solution was considered unusable at the first appearance of the color.

## General Procedure for Obtaining Kinetics Data

### A. Reactions at Reflux Temperature

All reactions were carried out in a 100 ml round bottom flask fitted with the standard 24/40 ground glass joint, a 10/30 ground glass thermometer port and a sidearm with stopcock (see Figure 8). The flask was placed in a heating jacket attached to a variable voltage transformer. Stirring was provided by a magnetic stirrer and a teflon coated magnetic stir bar.

A weighed quantity of Ni(enp) was placed into the flask. (See Table 2 for the quantities of all reagents and solvents.)

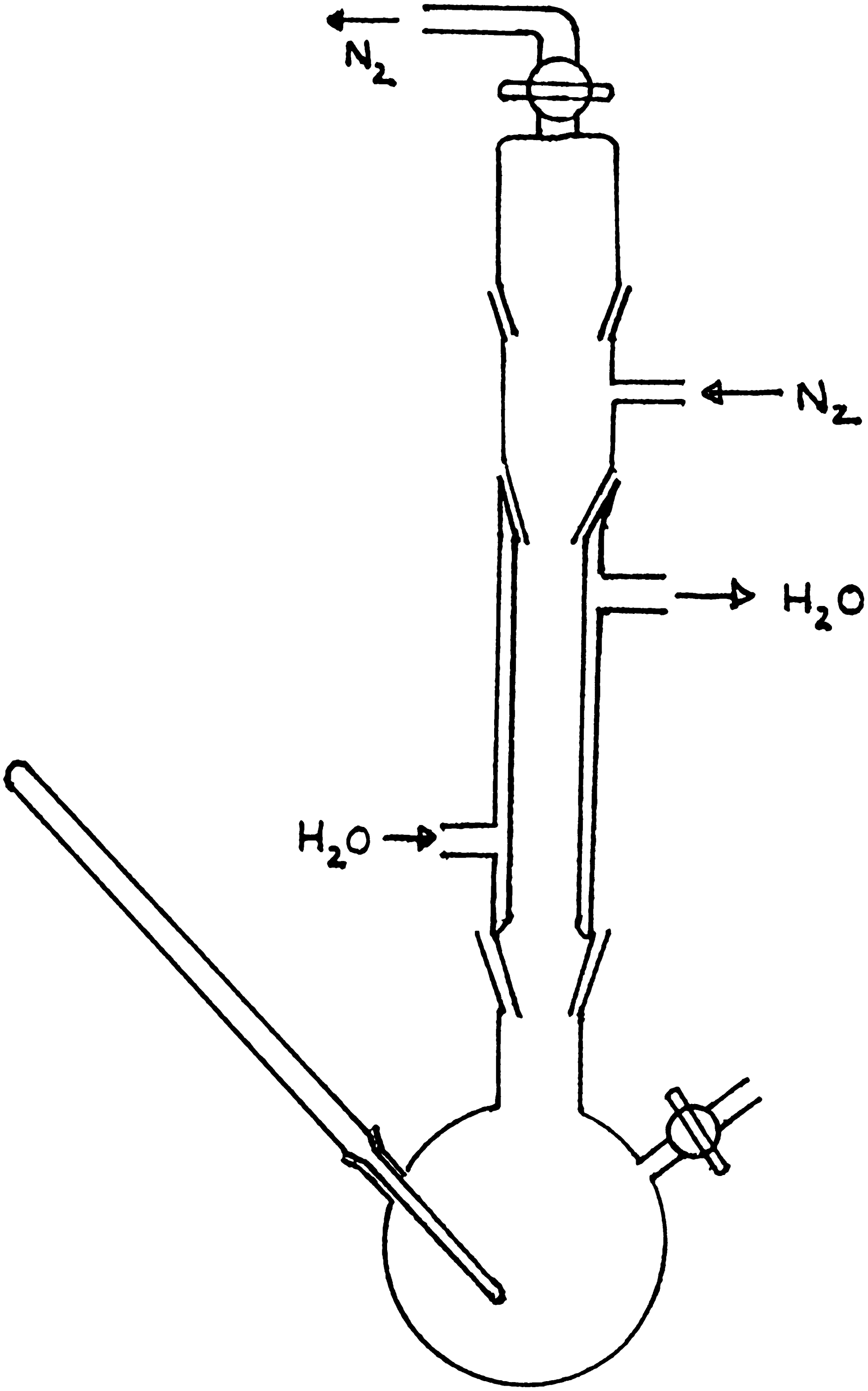


Figure 8. Sketch of the experimental apparatus.

Table 2. Experimental Conditions

| | Dependence of Rate on: | | | | |
|---|---|---|---|---|---|
| | Ni(enp) | Ethylenediamine | Hydroxide Ion | Solvent | Temperature |
| [Ni(enp)], M | vary | $5.02 \times 10^{-3}$ | $4.71 \times 10^{-3}$ | $5.02 \times 10^{-3}$ | $5.02 \times 10^{-3}$ |
| [en], M | 1.0 | vary | 0.94 | 1.0 | 2.0 |
| $[OH^-]$, M | $4.05 \times 10^{-2}$ | $4.03 \times 10^{-2}$ | vary | $3.31 \times 10^{-2}$ | $4.03 \times 10^{-2}$ |
| Temperature, °C | Reflux (69.0 ± 0.2) | 65.2 ± 0.2 | Reflux (68.7 ± 0.3) | Reflux (69.0 ± 0.4) | vary |
| $V_{Total}$, ml | 60.0 | 60.0 | 64.0 | 60.0 | 60.0 |
| $V_{THF}$, ml | 46.0 | $50.0 - V_{en}$ | 50.0 | $56.0 - V_{EtOH}$ | 42.0 |
| $V_{EtOH}$, ml | 10.0 | 10.0 | 10.0 | vary | 10.0 |
| $V_{en}$, ml | 4.0 | vary | 4.0 | 4.0 | 8.0 |
| For Results See: | Table 3 | Table 4 | Table 5 | Table 6 | Table 7 |

THF was then added to the flask followed by the absolute ethanol and then by the standardized stock sodium hydroxide solution. All of these liquids were added via a pipet. A thermometer was inserted into the thermometer port and a reflux condenser fitted to the flask. A drying tube containing Drierite, to absorb water, and Mallcosorb, to absorb carbon dioxide, was placed at the top of the condenser. The stirred solution was then heated to reflux. After the solution came to reflux and all of the Ni(enp) had dissolved, the ethylenediamine was pipetted into the solution. (The pipet was put through the top of the condenser and placed so that the tip was just below the mouth of the condenser when the amine drained into the solution.) When the solution came to reflux again, usually after less than 30 seconds, the timer was started. Samples were periodically withdrawn through the sidearm, which had been fitted with a serum cap, by means of a microliter syringe, fitted with a Chaney adapter, to assure consistent aliquot sizes. The sample aliquot was then injected into a 25 ml volumetric flask containing absolute ethanol, diluted to the mark with ethanol and stored in the dark until the spectrum was recorded or the absorbances measured. Aliquot sizes were chosen so that the total concentration of nickel complexes after dilution was about $3 \times 10^{-5}$ M.

### B. Reactions at Temperatures Below Reflux Temperature

All reactions carried out at temperatures below reflux temperature were done so by placing the flask and contents in a thermostatically controlled oil bath. The temperature of the bath varied less than ± 0.05° from the set temperature. Stirring within the reaction flask was provided by an air driven, immersible magnetic stirrer and a teflon coated stir bar. The general procedure used for obtaining the kinetics data at these temperatures was the same as for those at reflux temperature up to just before the time at which the ethylenediamine was added. After the Ni(enp) had dissolved, the solution was allowed to cool to just below reflux, at which time the condenser was removed and the flask closed with a ground glass stopper. The flask was then transferred to the oil bath where it was again fitted with a reflux condenser. The condenser and flask were flushed with nitrogen for about 30 seconds and then a slow flow of nitrogen was maintained over the reaction mixture by means of adapters placed at the top of the condenser (see Figure 8). After the solution reached the desired temperature, ethylenediamine, preheated to 60° ± 1°, was injected into the solution through the sidearm via a 10 ml graduated syringe, and the timer was started. The amine was preheated because it was found that if amine at room temperature was injected into the solution, 10-15 minutes would elapse before thermal equilibrium was reestablished. With the preheated amine, a constant temperature was usually reached in less than 5 minutes. The temperature of the reaction mixture varied less than ± 0.2° once thermal equilibrium was established. The procedure for obtaining aliquots and absorbance measurements is the same as described in part A above.

### C. Physical Measurements

All spectra were obtained by use of a Unicam SP800 B spectrophotometer. Absorbances used for the calculations were obtained with a Beckman Model DB-GT Grating spectrophotometer. Both instruments were calibrated for wavelength with a holmium oxide filter. Matched quartz cells were used and absolute ethanol was used as the reference solution.

Dielectric constants were obtained at 25° with a Wissenshaftlich-Technische Werkstätten Dipolmeter Type DM-01. A calibration curve of instrument readings as a function of dielectric constant was obtained from the experimental readings and the literature values of the dielectric constants of ethanol, tetrahydrofuran, methylene chloride and 1-propanol.

### Treatment of the Kinetics Data

Reactions were followed by measuring the absorbance of the diluted aliquot solutions at two wavelengths, 296 nm and 342 nm, as a function of time. The data obtained correspond to the rate of loss of starting material, Ni(enp), and the rate of formation of product, Ni(enp-M-en), respectively. The data obtained were treated by KINFIT, a non-linear curve fitting program,[38] with the Michigan State University CDC 6500 computer. Since the ratio of amine to Ni(enp) was always very large (at least 200:1) all reactions were treated as occurring under pseudo-first order conditions. Consequently, the equation which was fitted to the experimental data was the pseudo-first order equation

$$A_t - A_\infty = (A_0 - A_\infty)e^{-k_{obs}t}$$

where $A_t$, $A_0$ and $A_\infty$ are the absorbances at time equal to t, zero and infinity respectively, t is the elapsed time in seconds and $k_{obs}$ is the pseudo-first order rate constant. Input data consisted of the experimental values of $A_t$ and t and the variances in those values. Variance in t was estimated to be $\pm$ (1 sec)$^2$ and in $A_t$ to be $\pm$ (.003)$^2$. $A_0$, $A_\infty$ and $k_{obs}$ are the adjustable parameters fitted to the data. The output includes both the value and the standard deviation of the parameters. Figures 9 and 10 show plots, from KINFIT, of the absorbance as a function of time data for a kinetics experiment, and illustrate the agreement between experimental and calculated points.

For the calculation of the activation parameters, the Arrhenius Equation

$$\ln k = \ln A - \frac{E_a}{R}\left(\frac{1}{T}\right)$$

was used, where $k = k_{obs}/[OH^-][en]^2$ (see Discussion). A plot of ln k vs 1/T was made and a least squares analysis of the data was used for the calculation of the slope ($-E_a/R$) and intercept (ln A). The energy of activation, $E_a$ was then calculated from the slope. The equation

$$\ln A = \ln \left(\frac{ekt}{h}\right) + \frac{\Delta S^\ddagger}{R}$$

was then used to calculate the entropy of activation, $\Delta S^\ddagger{}_{298}$.

## RESULTS

The rate constants, $k_{obs}$, reported in this section are the averaged values of the rate constants calculated from the absorbance

Figure 9. KINFIT plot of absorbance data measured at 296 nm as a function of time.

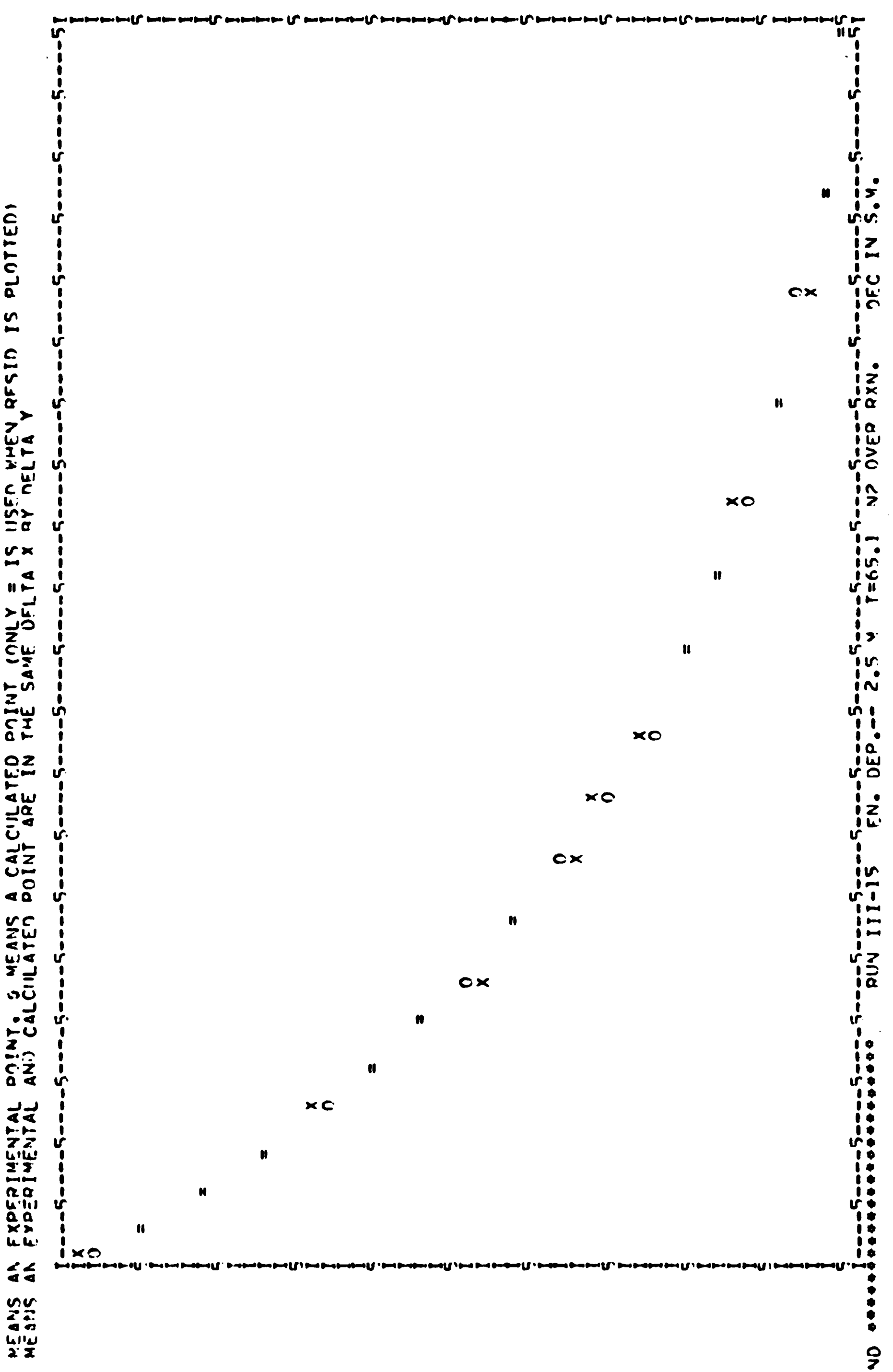
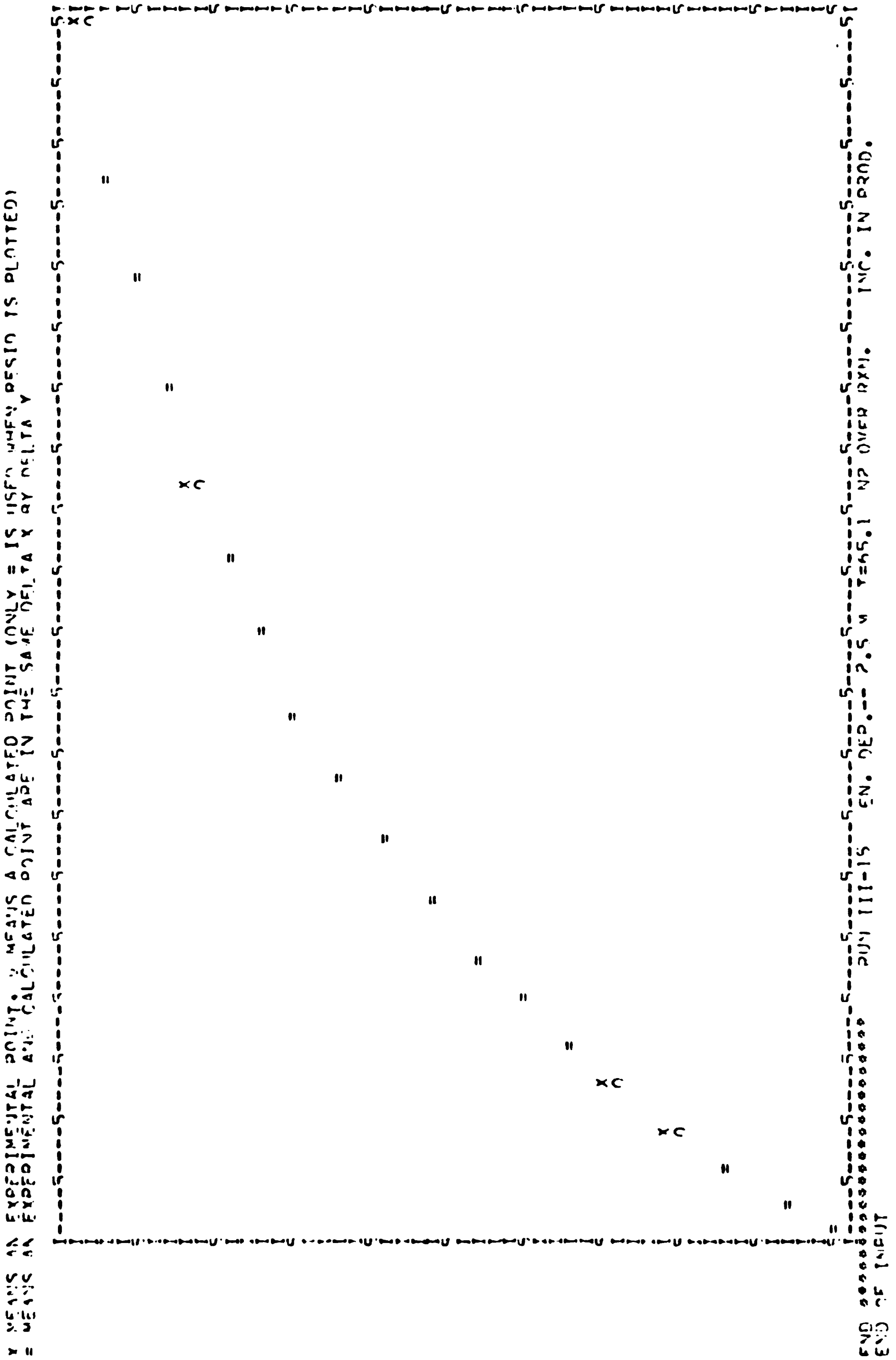

X MEANS AN EXPERIMENTAL POINT, O MEANS A CALCULATED POINT (ONLY = IS USED WHEN RESID IS PLOTTED)
= MEANS AN EXPERIMENTAL AND CALCULATED POINT ARE IN THE SAME DELTA X BY DELTA Y
END RUN III-15 EN. DEP.-- 2.5 M T=65.1 N2 OVER RXN. DEC IN S.M.

Figure 9.

Figure 10. KINFIT plot of absorbance data measured at 342 nm as a function of time.



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X MEANS AN EXPERIMENTAL POINT. O MEANS A CALCULATED POINT (ONLY = IS USED WHEN RESID IS PLOTTED)
= MEANS AN EXPERIMENTAL AND CALCULATED POINT ARE IN THE SAME DELTA X BY DELTA Y
END ***************************     RUN III-15   EN. DEP.-- 2.5 M   T=65.1  N2 OVER RXN.    INC. IN PROD.
END OF INPUT
```

Figure 10.

as a function of time data obtained at the two wavelengths, 296 nm and 342 nm (see Introduction). Normally, the values of $k_{296}$ and $k_{342}$ deviated from $k_{obs}$ by less than 5%. Table 3, dependence of the rate on the concentration of Ni(enp), lists $k_{296}$, $k_{342}$ and $k_{obs}$ to illustrate the agreement between the rate constants calculated from the data obtained at the different wavelengths. All other tables list only the values of $k_{obs}$.

The slopes and intercepts of the straight lines obtained from the plots of the data were calculated by means of a least squares treatment of the data.

Concentration of Ni(enp)

The results of the experiments used to determine the dependence of the rate of reaction on the concentration of Ni(enp) are shown in Table 3.

Table 3. Dependence of the Rate on the Concentration of Ni(enp)

| [Ni(enp)] x $10^3$, M | $k_{296}$ x $10^4$, $sec^{-1}$ | $k_{342}$ x $10^4$, $sec^{-1}$ | $k_{obs}$ x $10^4$, $sec^{-1}$ |
|---|---|---|---|
| 2.51 | 1.42 ± .04 | 1.43 ± .02 | 1.43 ± .04 |
| 5.02 | 1.40 ± .06 | 1.35 ± .03 | 1.38 ± .06 |
| 7.50 | 1.56 ± .07 | 1.41 ± .03 | 1.49 ± .07 |

The pseudo-first order expression

$$\ln \frac{[\mathrm{Ni(enp)}]_t}{[\mathrm{Ni(enp)}]_0} = -kt$$

was used to calculate $k_{obs}$. Since the value of $k_{obs}$ does not vary with the initial concentration of Ni(enp), the species being monitored, a first-order reaction with respect to Ni(enp) is indicated.

Concentration of Ethylenediamine

The results of the experiments used to determine the dependence of the rate of reaction on the concentration of ethylenediamine are shown in Table 4. A plot of $k_{obs}$ vs the square of the ethylenediamine concentration is shown in Figure 11. The slope of the straight

Table 4. Dependence of the Rate on the Concentration of Ethylenediamine

| Volume of en, ml | [en], M | $[en]^2$, $M^2$ | $k_{obs} \times 10^4$, $sec^{-1}$ |
|---|---|---|---|
| 4.00 | 1.00 | 1.00 | 0.96 ± .03 |
| 6.00 | 1.50 | 2.25 | 1.74 ± .03 |
| 7.00 | 1.75 | 3.06 | 2.74 ± .05 |
| 8.00 | 2.00 | 4.00 | 2.97 ± .06 |
| 9.00 | 2.25 | 5.06 | 3.57 ± .12 |
| 10.00 | 2.50 | 6.25 | 5.12 ± .11 |

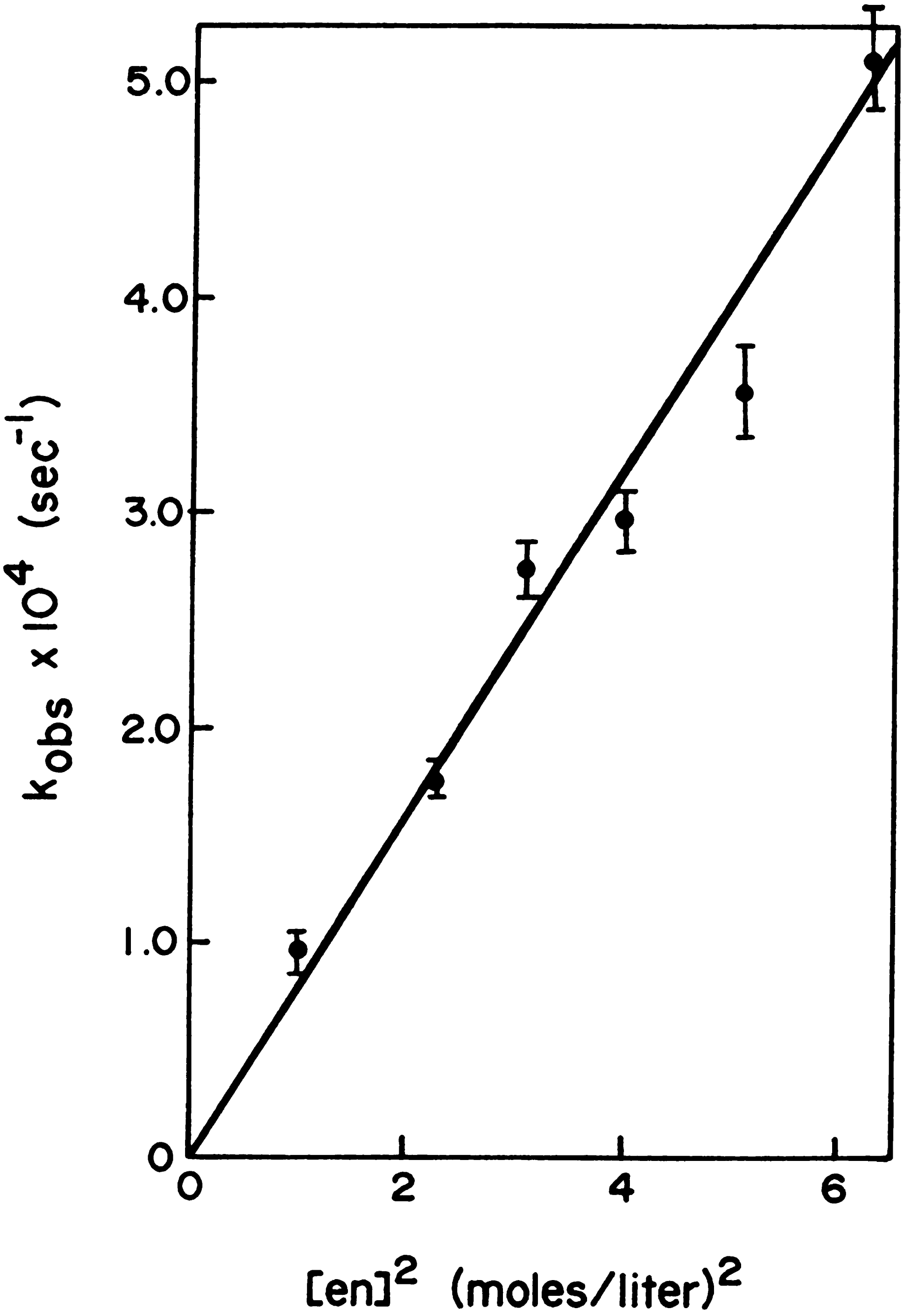


Figure 11. Dependence of the rate on the concentration of ethylenediamine.

line is 7.5 ± .5 x $10^{-5}$ $M^{-2}$ $sec^{-1}$ and the intercept is 1.5 ± 1.9 x $10^{-5}$ $sec^{-1}$, i.e., zero within experimental error. Hence, the rate of the reaction is proportional to the square of the concentration of ethylenediamine.

Concentration of Hydroxide Ion

The results of the experiments used to determine the dependence of the rate on the concentration of hydroxide ion are shown in Table 5. A plot of $k_{obs}$ vs the concentration of hydroxide ion is shown in Figure 12. The slope of the straight line is 3.41 ± .11 x $10^{-3}$ $M^{-1}$ $sec^{-1}$ and the intercept is 0.77 ± 7.5 x $10^{-6}$ $sec^{-1}$, i.e., zero within experimental error. Thus, the rate is proportional to the concentration of hydroxide ion and no reaction should occur in the absence of hydroxide ion.

Table 5. Dependence of the Rate on the Concentration of Hydroxide Ion

| $[OH^-] \times 10^2$, M | $k_{obs} \times 10^4$, $sec^{-1}$ |
|---|---|
| 1.88 | 0.73 ± .08 |
| 3.71 | 1.25 ± .08 |
| 5.66 | 1.85 ± .09 |
| 6.54 | 2.27 ± .06 |
| 7.52 | 2.41 ± .08 |
| 8.43 | 2.97 ± .08 |
| 9.30 | 3.26 ± .09 |

Figure 12. Dependence of the rate on the concentration of hydroxide ion.

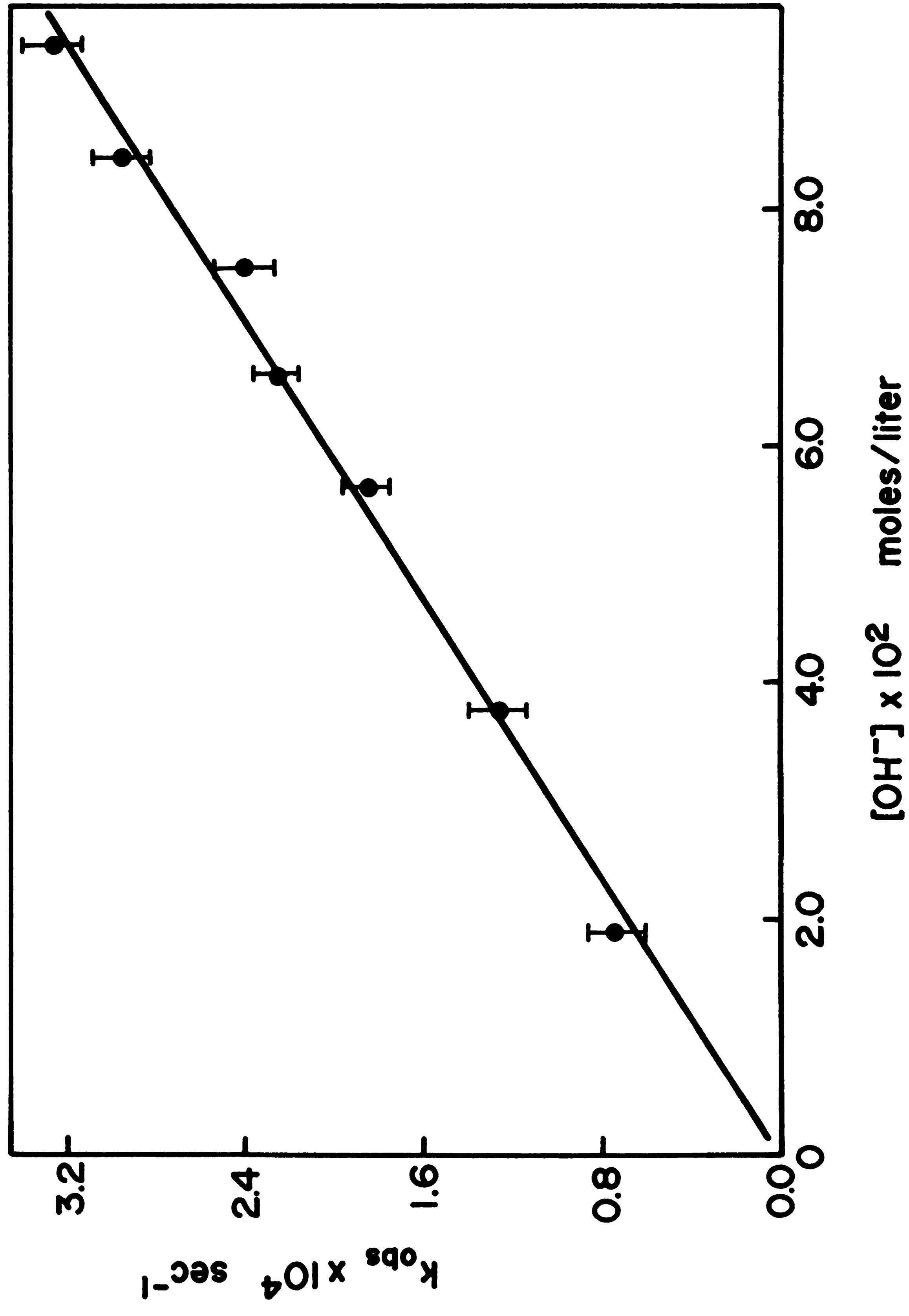

0.0
0.8
1.6
2.4
3.2
0
2.0
4.0
6.0
8.0
$[OH^-] \times 10^2$ moles/liter
$k_{obs} \times 10^4$ $sec^{-1}$

Figure 12.

## Solvent

It has been shown[53] that for a reaction between an ion and a neutral molecule the following expression may be written

$$\ln k = \ln k_0' + \frac{NZ^2e^2}{2DRT}\left(\frac{1}{r} - \frac{1}{r_\ddagger}\right)$$

where $k_0'$ is the rate constant in a medium of infinite dielectric constant, N is Avagadro's Number, Ze is the charge on the ion, r and $r_\ddagger$ are the radii of the reactant ion and the activated complex, respectively, and D is the dielectric constant. To test if this expression is applicable to the ring closure of Ni(enp), the dependence of the rate of reaction on the dielectric constant of the solvent was studied. The dielectric constant of the mixed solvent in a particular experiment was measured as described in the Experimental section. The experimental results are shown in Table 6 and a plot of ln $k_{obs}$ vs 1/D is shown in Figure 13. The slope of the straight line is

Table 6. Effect of Solvent on the Rate

| Volume of Ethanol, ml | D | 1/D | $k_{obs} \times 10^4$, sec$^{-1}$ | ln $k_{obs}$ |
|---|---|---|---|---|
| 8.0 | 9.449 | .1058 | 1.71 ± .09 | - 8.677 |
| 9.0 | 9.648 | .1036 | 1.43 ± .05 | - 8.856 |
| 10.0 | 9.895 | .1011 | 1.05 ± .07 | - 9.160 |
| 11.5 | 10.197 | .0981 | 0.92 ± .04 | - 9.296 |
| 13.0 | 10.520 | .0951 | 0.73 ± .05 | - 9.522 |
| 14.5 | 10.811 | .0925 | 0.57 ± .04 | - 9.766 |

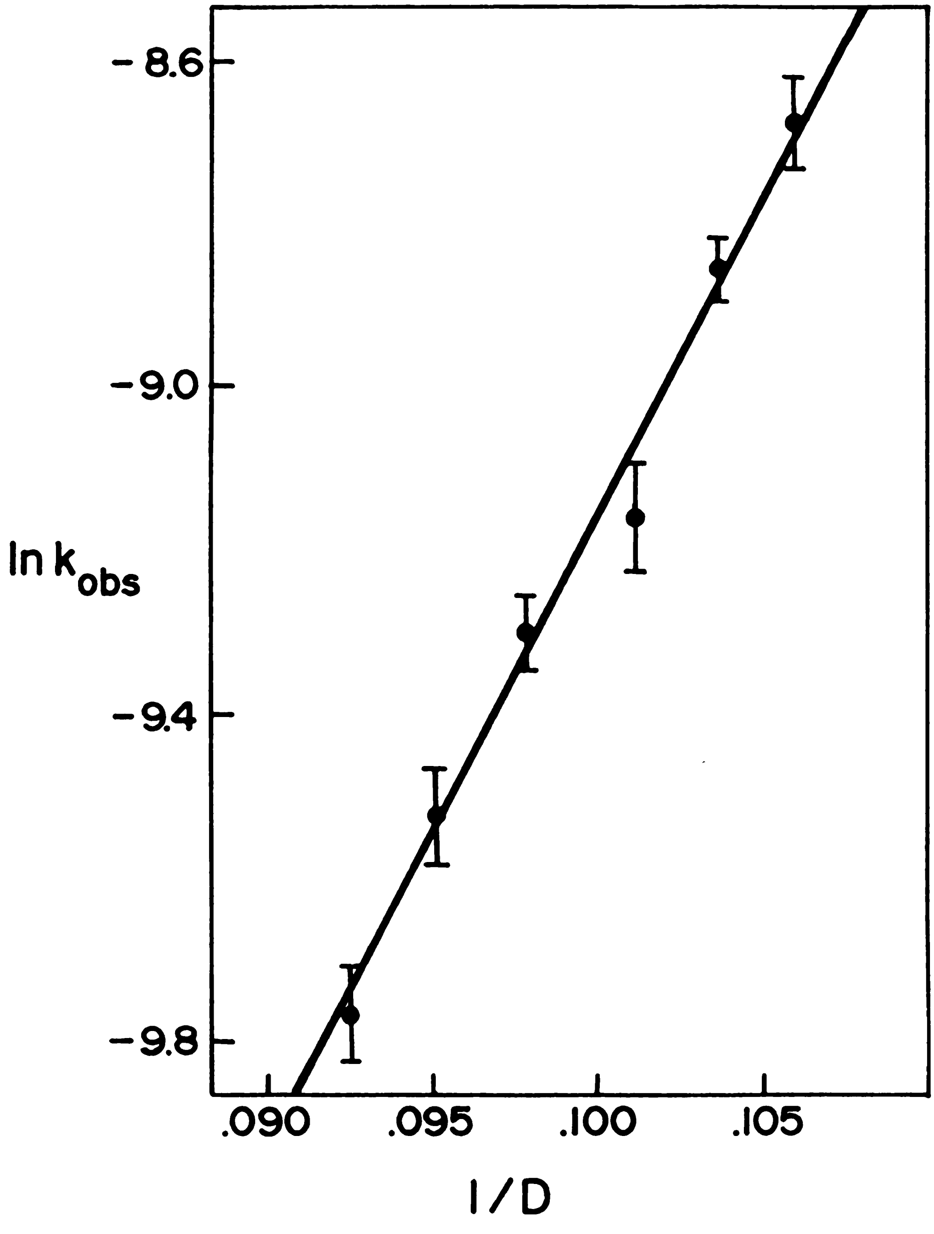


Figure 13. Effect of solvent on the rate.

71.6 ± 4.4 and the intercept is -15.2 ± .4. The data show that as the polarity of the solvent increases the rate of the reaction decreases. These results are consistent with the equation of Frost and Pearson.

Temperature

The results of the experiments used to determine the dependence of the rate of reaction on temperature are shown in Table 7, and a plot of ln k vs 1/T is shown in Figure 14. The value of the rate constant k was obtained from the pseudo-first order rate constant $k_{obs}$ by use of the equation

$$k = \frac{k_{obs}}{[en]^2[OH^-]}$$

(see Discussion). The slope of the straight line is $-5.25 \pm .41 \times 10^3$ °K and the intercept is 9.2 ± 1.2. The energy of activation, $E_a$, and the entropy of activation, $\Delta S^{\ddagger}_{298}$, were calculated as described in the Experimental section, and are 10.4 ± .8 kcal $mol^{-1}$ and -42 ± 3 eu, respectively.

Table 7. Dependence of the Rate on Temperature

| T, °C | $\frac{10^3}{T, °K}$ | $k_{obs} \times 10^4$, $sec^{-1}$ | $k \times 10^4$, $M^{-3}$ $sec^{-1}$ | ln k |
|---|---|---|---|---|
| 55.7 | 3.041 | 1.98 ± .06 | 12.3 ± .4 | - 6.702 |
| 60.2 | 3.000 | 2.36 ± .09 | 14.6 ± .6 | - 6.527 |
| 65.4 | 2.954 | 2.97 ± .06 | 18.4 ± .4 | - 6.297 |
| 68.2 | 2.930 | 3.59 ± .14 | 22.2 ± .9 | - 6.108 |

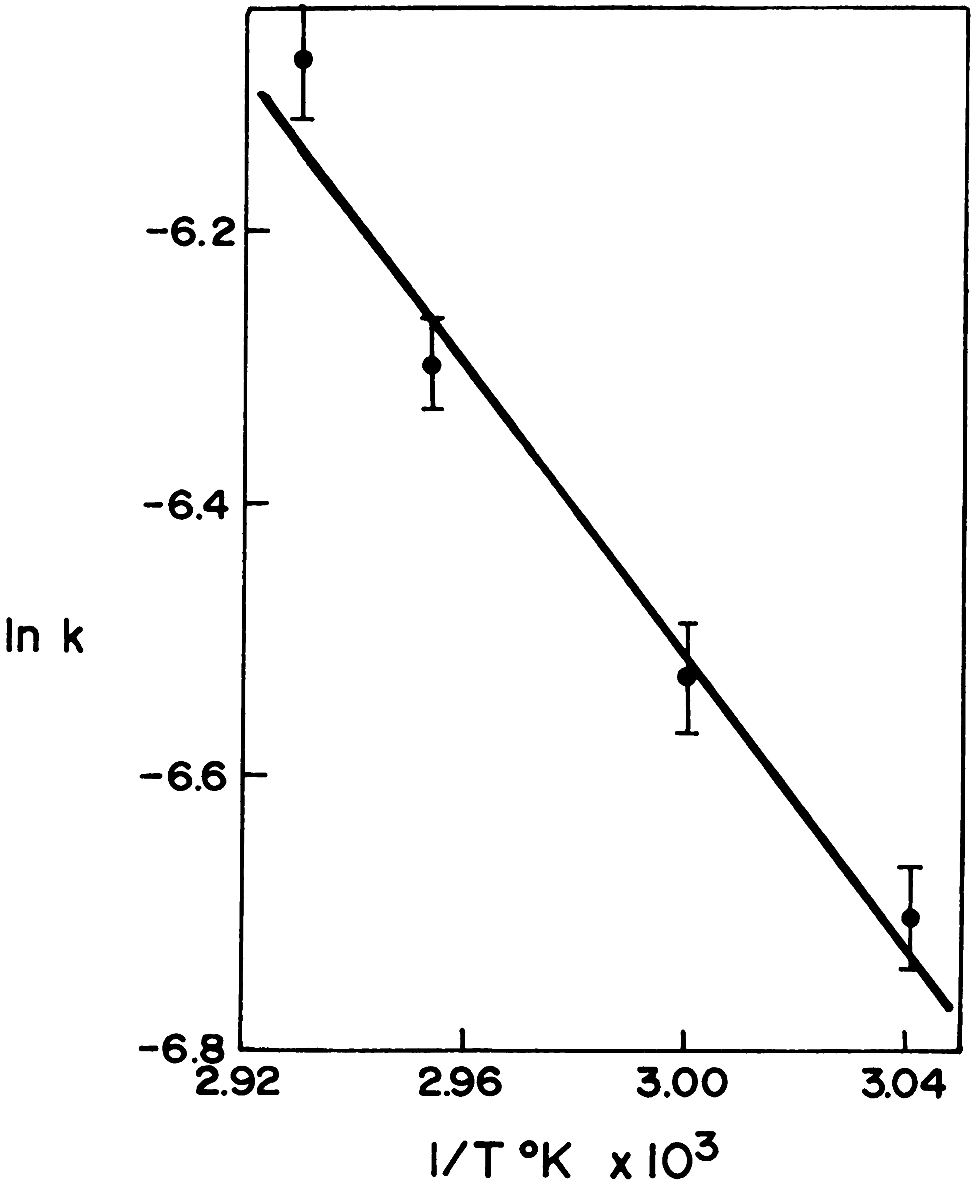


Figure 14. Dependence of the rate on temperature.

## DISCUSSION

Figure 15 shows a series of spectra obtained by following the reaction of Ni(enp) and ethylenediamine to form Ni(enp-M-en) as described in the Experimental section. These spectra illustrate that the decrease in the amount of starting material and the increase in the amount of product may be monitored as a function of time by measuring the absorbances of the sample solutions at 296 nm and 342 nm, respectively. The presence of an isosbestic point at 316 nm, as expected from the spectra of Ni(enp) and Ni(enp-M-en), Figure 7, should also be noted. The presence of an isosbestic point is normally considered to show the existence of only two uniquely absorbing species, but this interpretation is not necessarily true.[54] If an absorbing species is present only in low concentrations, its presence will not affect the appearance of an isosbestic point. Therefore, the simple series of spectra obtained from the ring closure reaction of Ni(enp) does not disprove the possibility of short-lived intermediates, but only shows that appreciable concentrations of intermediates do not build up.

The results of this investigation show there are several factors controlling the ring-closure reaction of Ni(enp) with ethylenediamine in solution. Since ring closure of the free ligand does not occur under comparable conditions, the presence of the metal ion is essential to the formation of the macrocyclic ligand. The dependence of the rate on the concentration of hydroxide ion (see Table 5 and Figure 12), as well as unsuccessful attempts to prepare Ni(enp-M-en) in its absence,

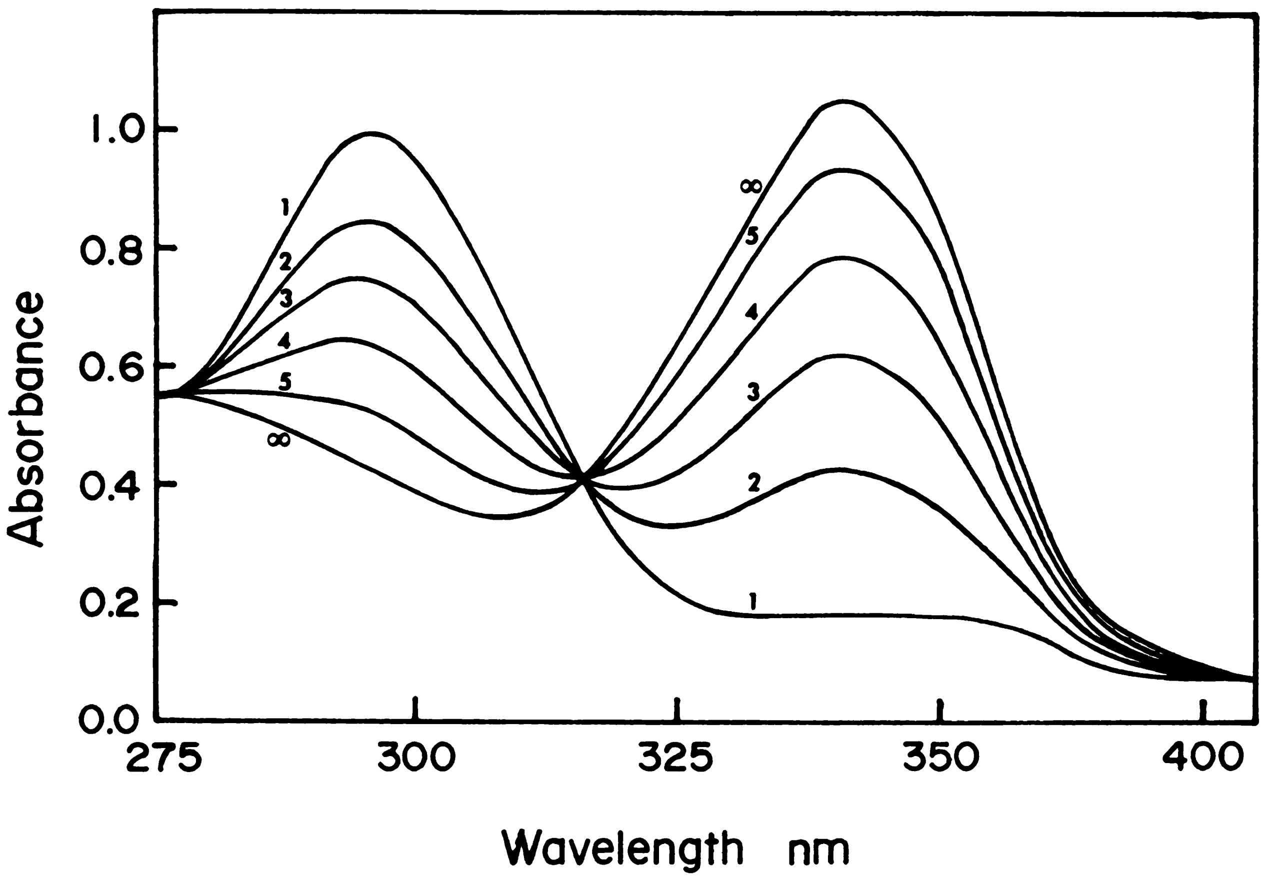


Figure 15. Series of spectra obtained by following the reaction of Ni(enp) with ethylenediamine.

show that hydroxide ion is necessary for the ring closure reaction. The effect of the solvent on the reaction (see Table 6 and Figure 13), i.e., the decrease in the rate as the polarity of the solvent increases, is also an indication of an ion-molecule reaction as the rate determining step of the reaction.[53] Laidler,[55] however, warns that equations relating rate to dielectric constant are best used as semi-quantitative formulations which allow only rough predictions to be made as to the effect of changing the dielectric constant. Therefore, no further quantitative analysis of the effect of the solvent will be presented.

As might be expected, the reaction is first order in Ni(enp). However, it is second order in ethylenediamine and these results indicate that an intermediate which involves one Ni(enp) molecule and two ethylenediamine molecules is formed. From the temperature study data, activation parameters were calculated and the energy of activation, $E_a$, and the entropy of activation, $\Delta S^{\ddagger}_{298}$, are 10.4 ± .8 kcal $mol^{-1}$ and -42 ± 3 eu, respectively. The large negative entropy change indicates the formation of a highly ordered intermediate. These values are close to the values determined by Blinn and Busch[44] for the reactions between 2,3-pentanedionebis(mercaptoethylimino)-nickel(II), IX, and alkyl bromides, described in the Introduction to this chapter. For these reactions, energies of activation between 10 and 13 kcal $mol^{-1}$ and entropies of activation between -26 and -38 eu were determined.

A mechanism consistent with these observations may be represented by the following scheme:

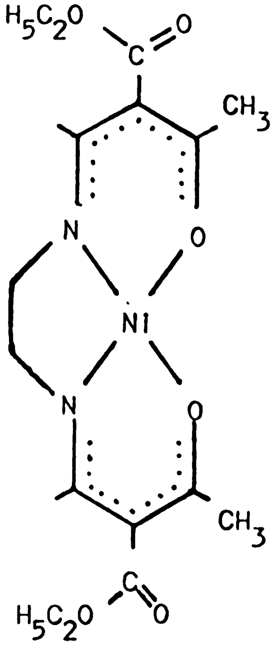
$$\mathrm{Ni(enp)} + 2\ \mathrm{en} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{A} \qquad \text{Step (1)}$$

$$\mathrm{A} \xrightarrow[\text{slow}]{k_2[\mathrm{OH}^-]} \mathrm{Ni(dang)} \qquad \text{Step (2)}$$

$$\mathrm{Ni(dang)} \xrightarrow[\text{fast}]{} \mathrm{Ni(enp\text{-}M\text{-}en)} \qquad \text{Step (3)}$$

Step (1) is a pre-equilibrium process in which an intermediate, A, probably an adduct between Ni(enp) and two ethylenediamine molecules, is formed. Step (2), a slow step, is the hydroxide ion catalyzed condensation of one of the amine groups of an ethylenediamine with one of the coordinated CO groups of Ni(enp) to form the intermediate Ni(dang). Step (3) is a fast step in which the remaining, "dangling," amine group condenses with the remaining coordinated CO of Ni(dang) to complete the ring closure and form the macrocyclic product, Ni(enp-M-en). Since Step (3) is too fast to observe, it is not possible to determine if hydroxide ion participates in the final step of the ring closure reaction.

The initial condensation of the amine with Ni(enp) is proposed to occur at the coordinated CO rather than the uncoordinated CO for two reasons. From the data reported in Chapter Two, it was noted that the electron density at the carbon atom of the coordinated CO should be decreased due to the electron withdrawing nature of the nickel(II) ion, and thus be the preferred site of nucleophilic attack. Second, ring closure of the nickel(II) complex, VIII, occurs exclusively at the coordinated CO groups, as is shown by the positions of the methyl peaks in the pmr spectra of VIII and the macrocyclic complex derived from it. (See Chapter Two, Results and Discussion for details).



VIII

The rate law for the reaction scheme proposed above, if one assumes that the concentration of A is in a steady state, may be derived as follows:

$$\frac{d[A]}{dt} = k_1[\mathrm{Ni(enp)}][\mathrm{en}]^2 - k_{-1}[A] - k_2[A][\mathrm{OH^-}] = 0 \qquad (15)$$

By rearranging (15) and solving for [A],

$$[A] = \frac{k_1[Ni(enp)][en]^2}{k_{-1} + k_2[OH^-]} \qquad (16)$$

Since Step (3) of the scheme is a fast step,

$$\frac{d[Ni(enp\text{-}M\text{-}en]}{dt} = \frac{d[Ni(dang)]}{dt} = k_2[A][OH^-] \qquad (17)$$

By substituting (16) into (17),

$$\frac{d[Ni(enp\text{-}M\text{-}en)]}{dt} = \frac{k_2k_1[Ni(enp)][en]^2[OH^-]}{k_{-1} + k_2[OH^-]} \qquad (18)$$

By multiplying (18) by $\frac{1/k_{-1}}{1/k_{-1}}$ and substituting $K = k_1/k_{-1}$ into the resulting equation,

$$\frac{d[Ni(enp\text{-}M\text{-}en)]}{dt} = \frac{k_2K[Ni(enp)][en]^2[OH^-]}{1 + \frac{k_2}{k_{-1}}[OH^-]} \qquad (19)$$

where K is the equilibrium constant for Step (1), the formation of A from Ni(enp) and two ethylenediamine molecules.

At low hydroxide ion concentrations and where $k_2 << k_{-1}$, the rate law, (19), reduces to

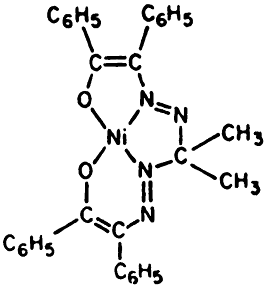
$$\frac{d[Ni(enp\text{-}M\text{-}en)]}{dt} = k[Ni(enp)][en]^2[OH^-] \qquad (20)$$

which is the experimental rate law, where $k = k_2K$ and $k_{obs} = k[en]^2[OH^-]$. Values of k at various temperatures were shown in Table 7 and vary from $2.22 \times 10^{-3}$ $M^{-3}$ $sec^{-1}$ at 68.2° to $1.23 \times 10^{-3}$ $M^{-3}$ $sec^{-1}$ at 55.7°.

The values of the individual rate constants, $k_1$, $k_{-1}$ and $k_2$ would be helpful in obtaining information about the nature of the intermediate A. The value of $k_1$ should be obtainable, since at high hydroxide ion concentrations the rate law, (19), reduces to

$$\frac{d[Ni(enp\text{-}M\text{-}en]}{dt} = k_1[Ni(enp)][en]^2 \tag{21}$$

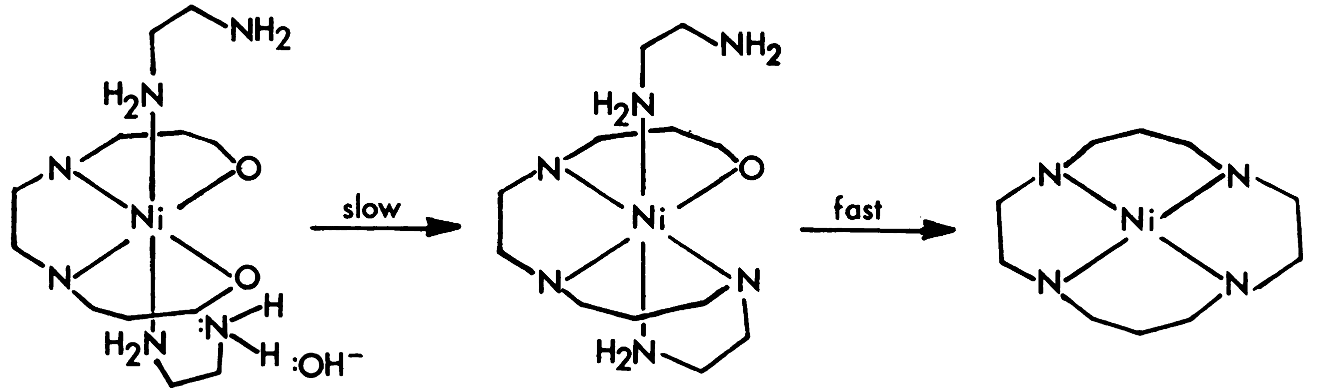
i.e., the rate becomes independent of hydroxide ion concentration and the values of $k_2$ and $k_{-1}$. Over the range of hydroxide ion concentrations studied, however, this leveling was not observed. Experiments at higher concentrations could not be performed because of the occurrence of precipitate, which appeared to be nickel hydroxide. However, in the study of the reaction of NiMMK, XIV, with 1,3-propanediamine to form a mono-condensed species, Shalhoub[56] did observe zero order dependence on the concentration of hydroxide ion at high concentrations.



XIV

If the value of the equilibrium constant K was determined the rate constant $k_2$ could also be calculated, since $k = k_2K$. However, no spectral changes which would indicate the formation of A were noted. Therefore, the data needed to calculate K could not be obtained.

Despite the inability to calculate the specific rate constants $k_1$, $k_{-1}$ and $k_2$, enough information is available to consider the nature of the intermediate A and to propose specific mechanisms for the formation of Ni(dang). One possible mechanism is shown in Figure 16. The intermediate A is Ni(enp) with an ethylenediamine molecule coordinated at each axial position. Two amines coordinate due to the greater stability of the six-coordinated, octahedral complex compared to the five-coordinated, square-pyramidal complex which would result if only one amine was coordinated to the nickel(II) ion. The next step would be the nucleophilic attack of the uncoordinated end of one ethylenediamine on the carbon atom of a coordinated CO, followed by abstraction of a proton from the amine by a hydroxide ion. Completion of this initial condensation results in the formation of an imine, with release of a hydroxide ion, to yield Ni(dang). The final step is the condensation of the unreacted end of the ethylenediamine with the remaining coordinated CO to form the macrocyclic complex, Ni(enp-M-en). As with the macrocycle formation reactions studied by Blinn and Busch,[44] the last step is a fast step, since the reactive sites are sterically oriented for the cyclization reaction. Thus, the ring closure reaction of Ni(enp) with ethylenediamine is one of only a few reported examples of the "kinetic template effect,"



A Ni(dang) Ni(enp-M-en)

Figure 16. A schematic representation of a proposed mechanism for the formation of Ni(enp-M-en). (For the sake of clarity, groups attached to the chelate rings are not shown.)

i.e., the sterically orienting influence of the metal ion on the course of the formation of a coordination compound, applied to the formation of a compound containing a macrocyclic ligand.

An alternative mechanism is similar to the mechanism just discussed in that the intermediate A is the same, i.e., Ni(enp) with ethylenediamine molecules coordinated at the axial positions. In this second mechanism, however, a hydroxide ion would abstract a proton from the coordinated end of the amine, and then nucleophilic attack of the resultant amide on the carbon atom of a coordinated CO would occur. Condensation to yield Ni(dang) followed by the fast ring closure step would complete the reaction.

Both of the proposed mechanisms are consistent with the experimental entropy of activation, $\Delta S^{\ddagger}_{298} = -42 \pm 3$ eu. The large negative entropy change indicates the formation of an intermediate that is much more ordered than the starting material. The proposed intermediate A, which is formed by the coordination of two ethylenediamine molecules to Ni(enp), is such an intermediate.

The first mechanism postulates the breaking of the nickel-nitrogen bond after the condensation of one end of the amine with a coordinated CO to form an imine linkage. The second mechanism requires the breaking of the nickel-nitrogen bond before the ethylenediamine condenses to become permanently attached to the coordinated ligand. It seems more likely that condensation would occur prior to the breaking of the bond through which the ethylenediamine molecule is attached to the nickel complex. Therefore, the first mechanism might be favored over the second mechanism.

## SUGGESTIONS FOR FUTURE WORK

More information on the role of the metal ion is needed to help to understand the mechanism of the ring closure reaction. This information can best be obtained by studying the ring closure of other compounds of the formula M(enp). The metal ions should be chosen so that a variety of electronic configurations and preferred stereochemistries are investigated. The study of the rate of ring closure of complexes containing metal ions which exhibit Jahn-Teller distortion should prove interesting, since the axial positions in these metal ions are not as available for coordination as the axial positions in metals which do not exhibit Jahn-Teller distortion. If ethylenediamine molecules coordinate at the axial positions, as proposed for the intermediate A, then the rate of reaction should be affected by this distortion. Preliminary experiments indicate that the ring closure of Cu(enp) may be studied by techniques similar to those used in the study of the ring closure of Ni(enp).

A more detailed study of the role of the amine in the ring closure reaction should be undertaken. The effect of varying the basicity of the amine on the rate of reaction could yield interesting information, although it might be difficult to distinguish between steric effects and the effects of basicity. By substituting other amines for ethylenediamine it may be possible to detect and/or isolate one or both of the intermediates proposed in the reaction scheme. Preliminary experiments show that the ring closure of Ni(enp) and Cu(enp) with 1,2-propanediamine and 1,3-propanediamine and of Ni(enp) with 1,4-butanediamine will occur.

The rates of condensation reactions, if any, between Ni(enp) and monoamines should also be studied. The entropies of activation of these reactions could prove especially useful. Since monoamines contain only one functional group, mechanisms in which one end of the amine coordinates to the nickel ion and the free end undergoes the initial condensation with a coordinated CO are not possible. Therefore, on the basis of these studies, some of the possible mechanisms for the formation of Ni(dang) may be eliminated from consideration.

# APPENDICES

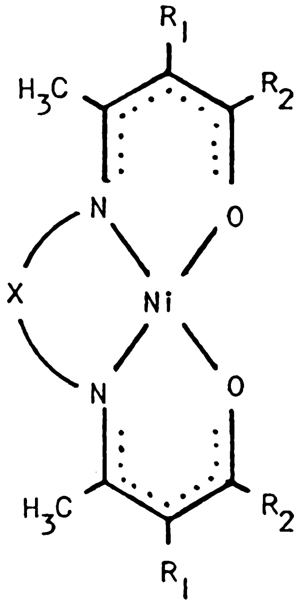
# APPENDIX A

# ATTEMPTS TO PREPARE SOME COMPOUNDS CONTAINING MACROCYCLIC LIGANDS

## ATTEMPTS TO PREPARE SOME COMPOUNDS CONTAINING MACROCYCLIC LIGANDS

### INTRODUCTION

The ring closure reactions of Ni(enp), V, X = $C_2H_4$, and Ni(enda), VIII, to form macrocyclic compounds, proceed quite readily.[33] However, it has been reported that the ring closure of Ni(baen), VII a, does not occur.[5,20] The structures of Ni(enp), Ni(enda) and Ni(baen) are very similar, except for the substituents in the $\gamma$ (or 3) position of the six-membered chelate rings. Therefore, in order to investigate the effect of various substituents attached to the six-membered chelate



VII

X = $C_2H_4$

a) $R_1$ = H; $R_2$ = $CH_3$

b) $R_1$ = Br; $R_2$ = $CH_3$

c) $R_1$ = H; $R_2$ = $CF_3$

rings on the ring closure reaction, attempts were made to prepare compounds containing macrocyclic ligands from VII. Since the groups in the $\gamma$ positions of Ni(enp) and Ni(enda) ($CH_3CO$ and $C_2H_5OCO$, respectively) are electron withdrawing, compounds containing electron withdrawing substituents attached to the chelate rings were chosen for study.

## RING CLOSURE OF Ni(baen)

Bisacetylacetoneethylenediiminonickel(II), Ni(baen), VII a, was prepared as previously reported.[57,58]

### Refluxing Ethylenediamine

Attempts were made to close Ni(baen) by using the methods employed by Jäger to form Ni(enp-M-en).[33] About 0.5 g of Ni(baen was added to 10 ml of anhydrous ethylenediamine and the solution was heated to reflux and maintained at reflux temperature for 7 days. A pink product, probably $Ni(en)_3X_2$, was filtered from the solution. The mass spectrum of this solid showed no peaks above m/e = 60 (ethylenediamine). The ethylenediamine was removed from the filtrate *in vacuo*, and a brown, tar-like substance remained in the bottom of the flask. The mass spectrum of this substance indicated the presence of Ni(baen) and ethylenediamine but no peaks corresponding to the macrocyclic complex were present.

The above procedure was repeated several times, and the length of time the solution was heated was varied between two hours and two weeks. No evidence for the formation of the macrocyclic complex was obtained from any of the experiments.

### Pressure Tube

Attempts to perform the ring closure reaction of Ni(baen) with ethylenediamine at temperatures greater than the reflux temperature of ethylenediamine were carried out with the reactants placed in a glass pressure tube. For the experiments described in this section, 0.5 g of Ni(baen) and 10 ml of anhydrous ethylenediamine were placed in a pressure tube. The general procedure for preparing the pressure tube and contents for an experiment are described elsewhere.[59]

#### A. 150°

For the first of these experiments, the sealed tube was placed in an oil bath at 150° for 18 hours. After the tube and its contents were cooled to room temperature, they were frozen in liquid nitrogen and the tube was opened. After the contents of the tube melted, the mixture was filtered through a medium fritted funnel. A very small amount of solid was obtained and dried under vacuum over $P_4O_{10}$. The mass spectrum of this solid indicated the presence of a small amount of macrocyclic complex but all attempts to isolate the compound failed. The ethylenediamine was removed from the filtrate _in vacuo_, and the tar-like substance which remained was dissolved in xylene. Upon removal of the xylene, _in vacuo_, red-brown needles were obtained. The mass spectrum of this solid indicated the presence of Ni(baen) only.

#### B. 200°

The above procedure, in part A, was repeated, except the tube was placed in a Wood's Metal bath at 200° for 40 hours. However, the solution refluxed during the entire time period because the cooler, unimmersed part of the tube acted as a condenser. The procedure in part A, was again repeated except the tube was placed in a tube furnace at a temperature of 200° for 24 hours. In each experiment, a pink precipitate, assumed to be $Ni(en)_3X_2$, was obtained after filtration of the mixture. The filtrate was treated as described above in part A, and red-brown needles were obtained. The mass spectrum of this solid indicated the presence of Ni(baen) only. No evidence for the formation of the macrocyclic compound was obtained.

## Solution

Attempts were made to effect the ring closure of Ni(baen) through the use of conditions similar to those employed in the study of the ring-closure reaction of Ni(enp) (see Chapter III). To a 50 ml round-bottomed flask fitted with a sidearm and stopcock were added 0.28 g (0.001 mol) of Ni(baen), 25 ml of THF, 5 ml of 0.25 M ethanolic sodium hydroxide and 6.7 ml (0.1 mol) of ethylenediamine. The solution was heated to reflux and maintained at reflux temperature for 7 days. Periodically, about twice a day, a sample was withdrawn from the solution and the UV-visible spectrum recorded. The spectra indicated a slight decrease in the concentration of Ni(baen), but no new absorption peaks, which would indicate the formation of the macrocyclic complex, appeared. After 7 days, the solution was cooled and then filtered. A pink solid, assumed to be $Ni(en)_3(OH)_2$, was obtained. The solvent was removed from the filtrate *in vacuo*. The resultant tar-like substance was treated with xylene as described above under Pressure Tube, part A, and red-brown needles were obtained. The mass spectrum of the solid indicated the presence of Ni(baen) only.

## RING CLOSURE OF Ni(baenBr$_2$)

Bis-3-bromoacetylacetoneethylenediiminonickel(II), Ni(baenBr$_2$), VII b, was prepared as previously reported.[60]

### Refluxing Ethylenediamine

To a 50 ml round-bottomed flask were added 0.2 g of Ni(baenBr$_2$), and 10 ml of anhydrous ethylenediamine. The stirred solution was heated to reflux. Within 45 minutes, the dark solution had lightened considerably and a pink-violet precipitate had formed. The solution was filtered and the precipitate dried. The mass spectrum of the solid showed no peaks above m/e = 60 (ethylenediamine). The solid was assumed to be Ni(en)$_3$X$_2$.

### Solution

Several attempts to effect the ring closure of Ni(baenBr$_2$) with ethylenediamine were made by following the procedure previously described for the ring closure of Ni(baen) in solution (see above). The amounts of ethylenediamine and hydroxide ion were varied, but for each experiment the results were similar. In each case, the solution became considerably lighter in color and a pink solid, Ni(en)$_3$(OH)$_2$, formed. No evidence for the formation of the macrocyclic complex was obtained.

## RING CLOSURE OF Ni(btfaen)

Bistrifluoroacetylacetoneethylenediiminonickel(II), Ni(btfaen), VII c, was prepared as previously reported.[58]

### Refluxing Ethylenediamine

To a 50 ml round-bottomed flask was added 0.5 g of Ni(btfaen) and 10 ml of anhydrous ethylenediamine. The solution was heated to reflux and maintained at reflux temperature for 24 hours. The solution was cooled and filtered but no solid was obtained. With the addition of 50 ml of distilled water, a tan precipitate formed. The mixture was filtered and the residue dried. The mass spectrum of the solid indicated the presence of Ni(btfaen) only.

### Pressure Tube

A pressure tube containing 0.3 g of Ni(btfaen) and 10 ml of ethylenediamine was prepared as previously described.[59] The tube was placed in a tube furnace, which had been preheated to 200°, for two hours. The tube was removed from the furnace, cooled to 0° and opened. The mixture was filtered and a pink solid, $Ni(en)_3X_2$, recovered. No other solid could be isolated from the filtrate.

### Solution

A solution containing 0.1 g of Ni(btfaen), 25 ml of THF, 2 ml of 0.15 M ethanolic sodium hydroxide and 3.8 ml of ethylenediamine was prepared. The solution was heated to reflux and maintained at reflux temperature for 48 hours. Samples were withdrawn from the solution periodically and the UV-visible spectrum recorded. The spectra indicated some decomposition of Ni(btfaen) had occurred but no evidence for the formation of the macrocyclic complex was obtained. The mixture was cooled and was filtered. A pink solid was obtained. The solvent was removed from the filtrate *in vacuo* and 50 ml of distilled water was added. A tan precipitate formed. The mass spectrum of the dried solid indicated the presence of Ni(btfaen) only.

## CONCLUSIONS

Attempts to prepare macrocyclic compounds by the ring closure reaction of VII with ethylenediamine were not successful. Ni(baen) and Ni(btfaen) are not as reactive as Ni(enp) and decompose to $Ni(en)_3X_2$ under severe conditions. $Ni(baenBr_2)$ is less stable than Ni(enp) since decomposition occurs even under mild conditions. It is evident that substituents attached to the chelate rings of VII affect the stability of the metal complexes, but the role of these substituents in the ring closure reaction of VII is uncertain.

# APPENDIX B

# ALTERNATE METHODS OF SYNTHESIS OF COMPOUNDS CONTAINING MACROCYCLIC LIGANDS

# ALTERNATE METHODS OF SYNTHESIS OF COMPOUNDS CONTAINING MACROCYCLIC LIGANDS

## INTRODUCTION

The information obtained from the study of the factors controlling macrocyclic ligand formation has resulted in the development of alternate methods of synthesis of several metal complexes containing macrocyclic ligands. In the previously reported method of synthesis,[33] a mixture of Ni(enp) or Cu(enp) and a diamine is heated to reflux and maintained at reflux temperature for several hours. Separation of the macrocyclic product from the diamine is difficult and yields are between 20 and 40%.

In solution, the ring closure reactions of Ni(enp) and Cu(enp) occur quite readily. Isolation of the macrocyclic product from the solution is easily managed and greater yields are obtained than by the previous method of synthesis. These yields are between 45 and 76%. Details of the syntheses are given below.

## RING CLOSURE OF Ni(enp)

### Ethylenediamine

Into a 250 ml round-bottomed flask were added 0.5 g (1.5 x $10^{-3}$ mol) of Ni(enp), 100 ml of acetonitrile, 10 ml of 0.3 M (3 x $10^{-3}$ mol) of ethanolic sodium hydroxide, and 10 ml (9 g, 0.15 mol) of ethylenediamine. The solution was heated to reflux temperature and was maintained at that temperature for 90 minutes. The reaction was assumed to be complete when the absorbance peak for Ni(enp) was no longer observable in

the UV-visible spectrum. The solution was cooled to room temperature and then added to 40 ml of distilled water. A red precipitate was produced. After the water mixture was cooled to near 0°, it was filtered through a fine fritted funnel. The solid was dried overnight at 100° under vacuum and identified by its mass spectrum as the macrocyclic product, Ni(enp-M-en). Yield: 76%. (The mass spectrum also indicated the absence of Ni(enp) in the product.)

### 1,2-Propanediamine

The procedure for performing the ring closure reaction of Ni(enp) with 1,2-propanediamine and the identification of the product is the same as that described with ethylenediamine, above, except that 13 ml (11 g, 0.15 mol) of 1,2-propanediamine was used in place of the ethylenediamine and the solution was maintained at reflux temperature for 4 hours. Yield: 53%.

### 1,3-Propanediamine

The procedure for performing the ring closure of Ni(enp) with 1,3-propanediamine and the identification of the product is the same as with ethylenediamine, above, except that 13 ml (11 g, 0.15 mol) of 1,3-propanediamine was used in place of ethylenediamine and the solution was maintained at reflux temperature for 4 hours. Yield: 58%.

## RING CLOSURE OF Cu(enp)

### Ethylenediamine

Into a 100 ml round-bottomed flask were added 0.5 g ($1.5 \times 10^{-3}$ mol) of Cu(enp), 25 ml of THF, 5 ml of 0.3 M ($1.5 \times 10^{-3}$ mol) of ethanolic sodium hydroxide and 6 ml (5.4 g, 0.09 mol) of ethylenediamine. The solution was heated to reflux and maintained at reflux temperature for 15 minutes. The reaction was assumed to be complete when the absorbance peak for Cu(enp) was no longer observable in the UV-visible spectrum. The solution was cooled to room temperature and then added to 200 ml of distilled water. A purple precipitate was produced. After the water mixture was cooled to near 0°, it was filtered through a fine fritted funnel. The solid was dried overnight at 110° under vacuum and identified as the macrocyclic product, Cu(enp-M-en), by its mass spectrum. Yield: 72%. (The mass spectrum also indicated the absence of Cu(enp) in the product.)

### 1,2-Propanediamine

The procedure for performing the ring closure reaction of Cu(enp) with 1,2-propanediamine and the identification of the product is the same as with ethylenediamine, above, except that 6.5 ml (5.6 g, 0.075 mol) of 1,2-propanediamine was used in place of ethylenediamine, 15 ml of 0.3 M ethanolic sodium hydroxide was used in place of 5 ml and the solution was maintained at reflux temperature for 20 minutes. Yield: 53%.

### 1,3-Propanediamine

The procedure for performing the ring closure reaction of Cu(enp) with 1,3-propanediamine and the identification of the product is the same as with ethylenediamine, above, except that 6.5 ml (5.6 g, 0.075 mol) of 1,3-propanediamine was used in place of ethylenediamine, 15 ml of 0.3 M ethanolic sodium hydroxide was used in place of 5 ml and the solution was maintained at reflux temperature for 75 minutes. Yield: 45%.

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