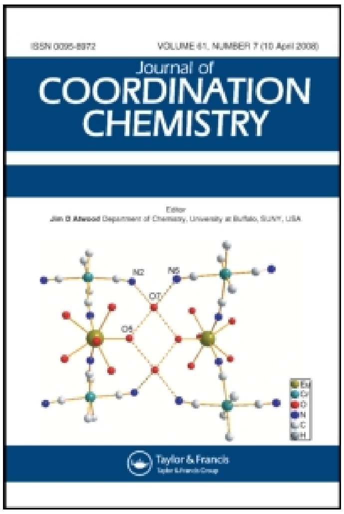

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

THE UTILITY OF HEXAAMINES FOR TEMPLATE SYNTHESIS[1]

Robert E. Hermer[a]; Bodie E. Douglas[a]
[a] Contribution from the Department of Chemistry, University of Pittsburgh, Pittsburgh, Pa.

To cite this Article Hermer, Robert E. and Douglas, Bodie E.(1977) 'THE UTILITY OF HEXAAMINES FOR TEMPLATE SYNTHESIS1', Journal of Coordination Chemistry, 7: 2, 61 — 66
To link to this Article: DOI: 10.1080/00958977708073040
URL: http://dx.doi.org/10.1080/00958977708073040

J. Coord. Chem.
1977, Vol. 7, pp. 61–66

THE UTILITY OF HEXAAMINES FOR TEMPLATE SYNTHESIS[1]

ROBERT E. HERMER and BODIE E. DOUGLAS†

Contribution from the Department of Chemistry University of Pittsburgh, Pittsburgh, Pa. 15260

(Received December 6, 1976)

NI(sen)$^{2+}$ has been found to have utility as a template for macrocycle formation. Through reaction with acetone, an unusual ligand similar to cyclam but with an ethylenediamine substituent is formed. This macrocycle abbreviated TTT (13-[[(2'-aminoethyl)amino] methyl]-5,7,7,13-tetramethyl-1,4,8,11-tetraazacyclotetradec-4-ene) is capable of sexidentate or quadridentate coordination. The coordination type is dictated by pH. The complexes Ni(TTT)$^{2+}$ and Ni(TTTH$_2$)$^{2+}$ are characterized by titration and by proton and carbon-13 nuclear magnetic resonance, electronic absorption, and infrared absorption spectroscopy.

INTRODUCTION

A tremendous amount of work on macrocyclic ligands derived from Schiff base condensation between Ni(en)$_3^{2+}$ and acetone, methyl ethyl ketone, propionaldehyde, isobutyraldehyde, butyraldehyde, etc., has been reported.[2,3] These template condensations all produce macrocycles containing four nitrogen atoms coordinated to Ni(II) in a square-planar geometry. In fact, the great majority of amine macrocycles are quadridentate, while only a few are quinquidentate or sexidentate.[4] With this in mind we investigated the utility of 1,1,1-tris(2'-aminoethylaminomethyl)ethanenickel(II), Ni(sen)$^{2+}$, as a template for macrocycle formation.

The ligand sen consists of three ethylenediamine residues bonded together by means of an alkyl group. The alkyl cap creates three secondary amine groups which when coordinated to Ni(II) are disposed at the corners of a trigonal face of the resulting octahedral complex. The connecting alkyl cap covers the trigonal face as shown in Figure 1. The three primary amine groups of the hexaamine are available for condensation with carbonyl groups of aldehydes or ketones. Acetone was chosen as the carbonyl compound most likely to produce the desired macrocycle because of its symmetry which results in only one condensation product after aldol condensation. Larger or smaller aldehydes and ketones either decrease the number of alpha hydrogens and lower reactivity or lead to more than one aldol condensation product.

The reaction between Ni(sen)$^{2+}$ and acetone should proceed in the same manner as for Ni(en)$_3^{2+}$ and acetone to produce a fourteen-membered macrocyclic ring. This was found to be the case. In an acidic acetone-methanol solution the normally purple solution of Ni(sen)$^{2+}$ was brown, an indication of macrocycle formation. Other aldehydes and ketones such as propionaldehyde (brown solution), methyl ethyl ketone (brown solution), and acetylacetone (red solution) with Ni(sen)$^{2+}$ produced solution colors indicative of macrocycle formation but isolation was hampered by polymeric oils and tars.

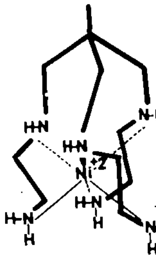

FIGURE 1 The structure of Ni(sen)$^{2+}$

A similar hexaamine 1,1,1-tris(3'-aminopropylaminomethyl)ethane,[5] spn, in the presence of Ni(II) did not undergo condensation with acetone as evidenced by the lack of color change in the blue solution. It appears that the increased size of this amine favors intermolecular polymerization with acetone rather than intramolecular condensation to form a sixteen-membered ring.

EXPERIMENTAL SECTION

Preparation of Materials. The ligands 1,1,1-tris-(2'-aminoethylaminomethyl)ethane,[6,7] sen, and

1,1,1-tris(3′-aminopropylaminomethyl)ethane,[5] spn, were prepared according to methods reported elsewhere and characterized by their NMR spectra. All solvents and $NiCl_2 \cdot 6H_2O$ were purchased from Fisher Scientific Company.

Preparation of $N^1, N^4, N^8, N^{11}, N^{13}, N'^{13}$-13-[[(2′-aminoethyl)amino]methyl]-5,7,7,13 tetramethyl-1,4,8,11-tetraazacyclotetradec-4-enenickel(II) iodide monohydrate, Ni(TTT)$I_2 \cdot H_2O$.

In 100 ml of absolute methanol was dissolved 5 g (0.020 mole) of sen, 50 ml of reagent grade acetone, and 3.5 ml of HBr (0.030 mole). To this solution in 25 ml of absolute methanol 4.8 g of $NiCl_2 \cdot 6H_2O$ (0.020 mole) was added. The mixture was refluxed overnight (16 h). Solvents were removed by a rotatory evaporator, 20 ml of H_2O was added to the residue, and a very concentrated solution of NaOH was added until the pH was twelve. The solution was washed thoroughly in many portions with 500 ml of $CHCl_3$. Then 35 ml of acetone containing 9 g of NaI (0.06 mole, excess) was added to the purple solution to yield a violet complex (8.2 g). The complex was dissolved in 60 ml of hot water, filtered, and cooled in a refrigerator. Purple crystals were filtered off and dried in a vacuum dessicator over $CaCl_2$. Yield 4.6 g, 35%. M.W. 656.5, m.p. 267°(dec.). Further recrystallization destroys the Schiff base linkage. *Anal.* Calcd. for $NiC_{17}H_{40}N_6I_2$: C, 31.07; H, 6.09; N, 12.79; I, 38.65. Found: C, 31.29; H, 5.61; N, 12.51; I, 38.33.

Preparation of $N^1, N^4, N^8, N^{11}, N^{13}, N'^{13}$-13-[[2′-aminoethyl)amino]methyl]-5,7,7,13-tetramethyl-1,4,8,11-tetraazacyclotetradec-4-enenickel(II) perchlorate, Ni(TTT)$(ClO_4)_2$.

The same procedure was used as for the preparation of Ni(TTT)$I_2 \cdot H_2O$. However, after adjusting the pH ~ 12 and washing with 500 ml of $CHCl_3$, the purple Ni(TTT)$(ClO_4)_2$ was precipitated by adding a solution of 10 g of $NaClO_4$ (0.082 mole) in 20 ml of methanol to the solution, and then recrystallized from a minimum amount of hot water. Yield 6.0 g, 50%. *Anal.* Calcd. for $NiC_{17}H_{38}N_6Cl_2O_8$: C, 34.95; H, 6.56; N, 14.39; Cl, 12.14. Found: C, 34.65; H, 6.75; 14.28;, Cl, 12.35.

Preparation of N^1, N^4, N^8, N^{11}-13-[[(2′-ammoniumethyl)ammonium]methyl]-5,7,7,13-tetramethyl-1,4,8,11-tetraazacyclotetradec-4-enenickel(II) perchlorate monohydrate, Ni($TTTH_2$)$(ClO_4)_4 \cdot H_2O$.

The unrecrystallized Ni(TTT)$(ClO_4)_2$ (~9.9 g) dissolved in 125 ml of methanol containing 4 ml of 70% $HClO_4$ was stirred in an ice bath until a yellow powder precipitated. (Sometimes oil separates, seeding may be necessary). The crude Ni($TTTH_2$)$(ClO_4)_4$ (6.4 g) was recrystallized from a minimum amount of hot methanol. The yellow crystals were removed by filtration, washed with cold methanol and dried on the filter. Yield 4.72 g, m.p. 218°C, M.W. 803.06. *Anal.* Calcd. for $NiC_{17}H_{42}N_6Cl_4O_{17}$. C, 25.43; H, 5.27; N, 10.46; Cl, 17.65. Found: C, 25.62; H, 5.31; N, 9.89; Cl, 17.14.

Physical Measurements. Electronic absorption spectra were measured on a Cary Model 14 recording spectrophotometer using a tungsten source. The $Ni(TTT)^{2+}$ complex required saturated spectrophotometric grade methanol solutions in 5 cm quartz cells for measurements. The $Ni(TTTH_2)^{4+}$ complex in the same solvent required 1 cm quartz cells with concentrations of approximately 10^{-2} M. All measurements were performed at room temperature.

Infrared spectra were measured using a Beckman IR–8 grating spectrophotomer capable of scanning the the spectral region 4000–625 cm^{-1}. Spectra were generally obtained from KBr discs except for perchlorate salts which were recorded as Nujol mulls.

Carbon-13 nuclear magnetic resonance spectra were recorded on a Jeol Inc. JNM FX–60 ^{13}C–^1H high performance NMR spectrometer operating at 15.030 MHz in the ^{13}C mode. The instrument was used in the broad band random noise ^1H decoupling mode. Since there can be no significant ^1H–^{13}C or ^{13}C–^{13}C coupling for proton decoupled (noise modulated) spectra obtained from complexes synthesized from ligands containing only the natural abundance of ^{13}C, no splittings of resonances associated with single carbon atoms are observed. The spectra were obtained using spectral windows of 5000 Hz and 2500 Hz, covered by 4096 addresses in the Fourier transform spectrum. The sample was placed in 8–10 mm coaxial tubes manufactured by Wilmad Spectroscopic Suppliers Inc. Benzene (δ = 128.7 ppm downfield from TMS) was used as the external standard in an outer coaxial tube arrangement.

Proton magnetic resonance spectra were obtained on a 60 MHz Varian Associates A-60D Analytical NMR spectrometer using DSS in D_2O as the internal reference.

The magnetic moments were determined by the NMR method devised by Evans[8] and modified by Rettig.[9]

The pH measurements were performed on a Corning Model 101 pH meter. During titration it was necessary to wait up to two hours between base additions in order to attain equilibrium and stable pH readings. A constant ionic strength was maintained at 0.10 M by addition of $NaClO_4$.

Analyses. Elemental analyses were performed by Chemalytics, Inc., Tempe, Arizona and by Integral Microanalytical Laboratories Inc., Raleigh, North Carolina.

Results and Discussion

As reported in the experimental section, the reaction between sen and acetone in the presence of nickel(II) chloride produces the macrocycle abbreviated TTT (13-[[(2′-aminoethyl)amino]methyl]-5,7,7,13-tetramethyl-1,4,8,11-tetraazacyclotetradec-4-ene). This ligand possesses the unusual ability to function as a sexidentate (octahedral coordination) or a quadridentate (square-planar coordination) ligand similar to the behavior exhibited by tris(2-aldoximo-6-pyridyl) phosphine nickel(II) perchlorate.[10] In the latter complex the ligating properties are solvent dependent whereas the TTT ligand properties depend on pH. Shown in Figure 2 are the structural forms of $Ni(TTT)^{2+}$ (high pH) and $Ni(TTTH_2)^{4+}$ (low pH).

To determine the principal species at various pH values, a 1.13×10^{-3} M solution of $Ni(TTTH_2)(ClO_4)_4$ was titrated with 1.04×10^{-1} M KOH standardized against potassium hydrogen phthalate. The solution was kept at constant ionic strength (0.10M) by addition of proper amounts of $NaClO_4$. The titration curve showed two equivalence points attributed to the following equilbria:

equivalence point

$$Ni(TTTH_2)^{+4} \rightleftharpoons Ni(TTTH)^{+3} + H^+ \qquad pH = 5.94$$

$$Ni(TTTH)^{+3} \rightleftharpoons Ni(TTT)^{+2} + H^+ \qquad pH = 8.37$$

The deprotonation of the secondary amine group in the uncoordinated arm of the yellow square-planar macrocycle $Ni(TTTH_2)^{4+}$ occurs first. Previous studies[7] on the ligand sen have shown that the primary amino groups are more basic than the secondary ones. The same is thought to be true for $Ni(TTT)^{2+}$. The second equilibrium represents the deprotonation of the primary amine.

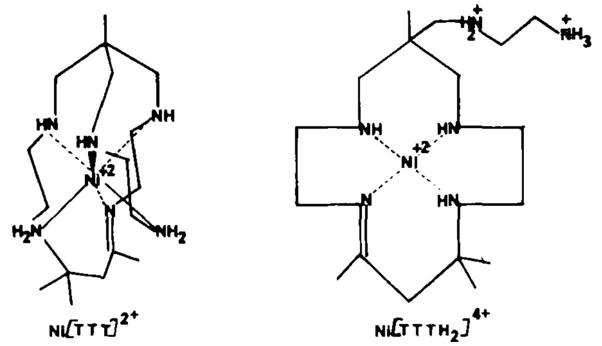

FIGURE 2 The structures of $Ni(TTT)^{2+}$ and $Ni(TTTH_2)^{4+}$

The pH of the solution is very important in determining the geometry of the complex. At low pH the ligand is quadridentate, while at high pH the ligand is sexidentate. Observation of the molar absorptivity at 22.7 kK (ϵ_{max} for the square-planar macrocycle) shows a maximum value through the first equivalence point to pH = 6.4. After pH = 6.4 the molar absorptivity drops rapidly and a new band develops at 18.8 kK (ϵ_{max} for octahedral complex). During this titration the solution turns from yellow to purple. The decrease in $\epsilon_{22.7}$ continues to zero, while $\epsilon_{18.8}$ becomes a maximum. From these data it is concluded that the yellow square-planar macrocycles, $Ni(TTTH_2)^{4+}$ and $Ni(TTTH)^{3+}$, are the sole species up to pH = 6.40. At higher pH the complex is a mixture of square-planar and octahedral species. As soon as the uncoordinated amine arm is completely deprotonated (pH = 8.37) it coordinates and forms the octahedral complex.

The octahedral geometry of purple $Ni(TTT)I_2$, which causes the complex to be paramagnetic, was verified by three magnetic moment determinations using a diamagentic susceptibility of 335.97×10^{-6}/mole calculated from Pascal's constants.[11] At 40°C the effective magnetic moment was found to be 3.08 B.M. which is consistent with its formulation as an octahedral sexidentate complex.

Electronic Absorption Spectra. The $d \rightarrow d$ transitions of Ni(II) complexes ($3d^8$) are dependent on the complex geometry as determined by the ligand. When TTT is sexidentate the octahedral field produces a triplet ground state $^3A_{2g}(F)$. After protonation of TTT the resulting quadridentate complex has a square-planar ligand field with a singlet ground state.

The electronic spectrum of the paramagnetic $Ni(TTT)^{2+}$ complex has two spin-allowed transitions in the visible region: $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$. In Figure 3 the low intensity band at 18.86 kK ($\epsilon \approx 11$) is attributed to the $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ transition while the $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ band expected at higher energy is not observed due to overlap with the charge transfer absorption band envelope beginning at 25.0 kK. The

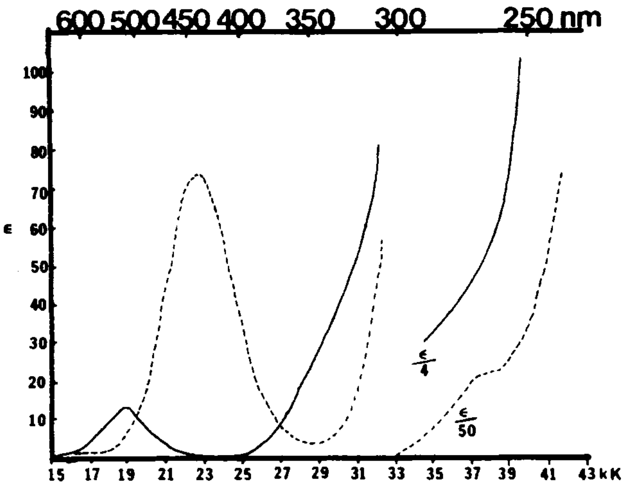

FIGURE 3 The electronic absorption spectrum of Ni(TTT)I$_2$ ——, and Ni(TTTH$_2$)(ClO$_4$)$_4$ ----.

very low intensity of the first band is typical of octahedral Ni(II) amine complexes.

Singlet ground state diamagnetic nickel(II) complexes with four nitrogens coordinated in a square-planar array typically have a single *d*–*d* absorption band at 22.0 kK, ε ~ 100.[3] The Ni(TTTH$_2$)(ClO$_4$)$_4$ complex which can be considered a macrocycle with an amine substituent has one *d*→*d* absorption band in the visible region centered at 22.7 kK (ε = 74). In the ultraviolet region the complex has an absorption shoulder at 37.0 kK arising from the azomethine chromophore and a charge transfer band beginning at 39.0 kK.

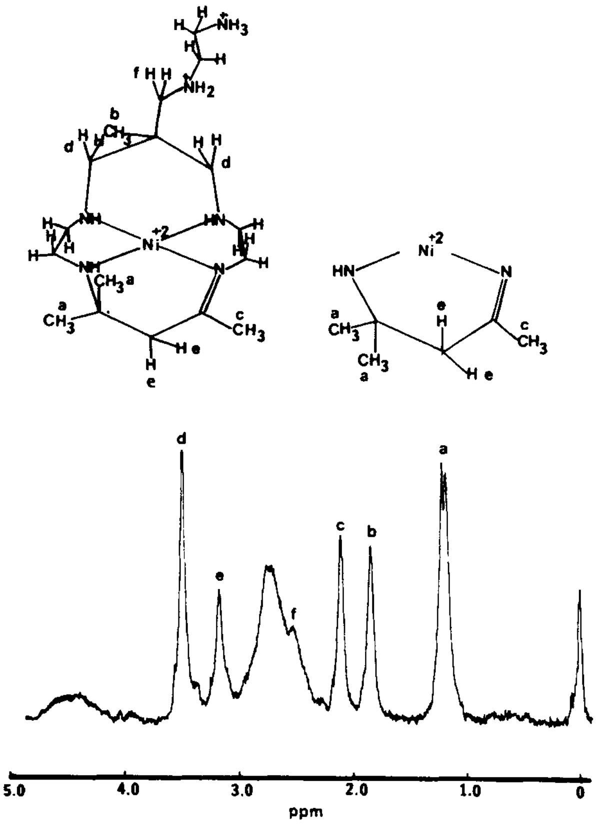

FIGURE 4 The PMR spectrum of Ni(TTTH$_2$)(ClO$_4$)$_4$ in D$_2$O vs DSS as internal standard.

Proton Nuclear Magnetic Resonance Spectrum. The PMR spectrum shown in Figure 4 of Ni(TTTH$_2$)(ClO$_4$)$_4$ supports the proposed diamagnetic square-planar macrocyclic structure. Four methyl resonances of equal intensity at δ = 1.16, 1.21, 1.78 and 2.06 ppm relative to DSS are consistent with the condensation of Ni(sen)$^{2+}$ with two molecules of acetone. The two highest field resonances labelled *a* are attributed to the gem-methyl groups which occupy one axial and one equatorial position. Overlap occurs because the two groups experience similar magnetic environments. At any moment one methyl group is equatorial while the other is axial. It is unimportant which methyl group occupies the equatorial position since both are equivalent, however, the axial sites resulting from two conformations of the six-membered rings are not equilent. The chemical shift of the axial methyl group is an average of the chemical shifts of the two axial positions. If the six-membered ring changes conformations rapidly enough only one broad resonance would be observed. Indeed at higher temperatures these peaks are expected to collapse into a single resonance.[12] Here we observe separate resonances due to an energy barrier separating the two conformations of the six-membered rings imposed by the presence of the bridging ethylene units which inhibit the flexing of the six-membered ring. The methyl resonance at δ = 2.06 ppm (c) is assigned to the imine methyl protons where typically the chemical shift is δ = 2.21 ppm.[13] This necessitates the assignment of the resonance at δ = 1.78 ppm (b) to the methyl group of the alkyl cap.

Integration of the remaining resonance peaks showed an intensity ratio of methylene protons to methyl protons of 1.67:1 compared to a theoretical value of 1.66:1. It is difficult to assign relative intensities due to specific methylene groups because of extensive splitting, peak overlap, and broadening due to quadrupolar coupling with nitrogen. The methylene resonances of the coordinated and uncoordinated ethylenediamine residues have chemical shifts in the

2.16–3.16 ppm region. The singlet from the methylene group labelled *f* appears at 2.46 ppm in the same position as the corresponding methylene protons of sen. Finally the singlets at δ = 3.23 ppm and 3.46 ppm are assigned to the methylene protons *e* and *d* respectively.

The Carbon-13 Nuclear Magnetic Resonance Spectrum. Many times when the PMR spectrum has many broad overlapping resonances that hide fine structure the carbon-13 spectrum might be more informative. That is not the case here as evidenced by the complex carbon-13 spectrum of $Ni(TTTH_2)(CLO_4)_4$ shown in Figure 5. It is obvious that none of the carbons in this complex are equivalent. The carbon-13 chemical shifts of $Ni(TTH_2)(ClO_4)_4$ are reported in Table I.

The structure of $Ni(TTH_2)(ClO_4)_4$ necessitates 14 carbon-13 signals arising from 4 methyl, 2 quaternary, 10 methylene, and one imine carbon. The actual spectrum shows 16 signals arising from 4 methyl, 1 quaternary, 10 methylene, and one imine carbon. Four of the methylene carbons have well-resolved resonances and the rest are part of a complex multiplet.

TABLE I
Carbon-13 chemical shifts[a] of $Ni(TTTH_2)(ClO_4)_4$

methyl[b]	methylene	methylene multiplet	imine
22.31 ppm	36.20 ppm	51.70 ppm	185.19 ppm
23.53	36.42	52.20	
24.54	44.97	52.60	
25.07	47.00	52.85	
		53.65	
		54.23	
		55.13	

[a] Original data were converted using the factor $\delta_C^{C_6H_6}$ = 128.65 ppm downfield from TMS

[b] solvent is D_2O with benzene as external reference

The four methyl carbon resonances are consistent with the condensation of two moles of acetone with $Ni(sen)^{2+}$. The methyl group *b* of the alkyl cap is the most shielded because it is least affected by the deshielding amino groups relative to the other methyl carbons. It is assigned the 22.31 ppm chemical shift. The geminal methyl groups, as discussed in the PMR section occupy axial and equatorial positions.

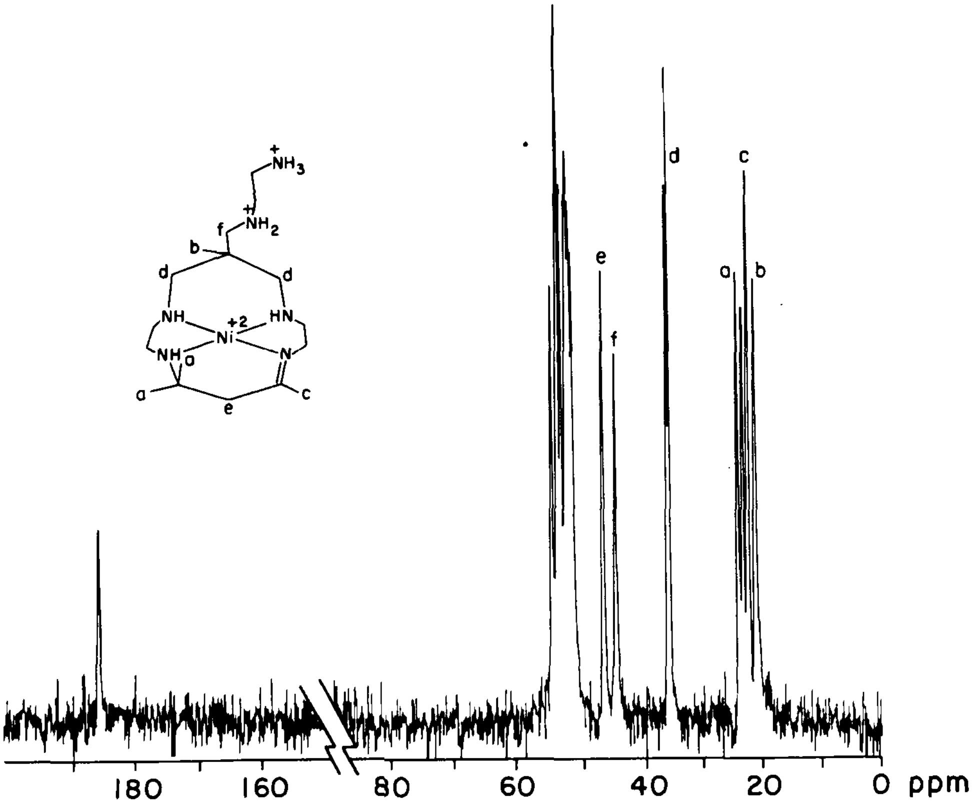

FIGURE 5 The carbon-13 NMR spectrum of $Ni(TTTH_2)(ClO_4)_4$ in D_2O.

Flexing of the ring averages their environments so that two resonances of nearly equal chemical shift and intensity occur. On this basis the two geminal methyl carbons *a* are assigned chemical shifts of 24.34 and 25.07 ppm, since the resonance at 23.53 ppm is noticeably more intense. This very intense peak must be caused by a methyl carbon in an environment quite different from the other methyl carbons. The imine methyl fits this description.

The barely resolved 36.20 and 36.52 ppm signals in the methylene carbon region must result from very similar carbons and are assigned to the methylene carbons labelled *d* which are so alike that one must travel through four atoms before encountering a dissimilar group. Methylene carbon *f* of the uncoordinated amine arm should have a chemical shift similar to the methylene carbon of the alkyl cap of sen which has a chemical shift of 42.77 ppm. On this basis carbon *f* is ascribed to the peak at 44.97 ppm.

Typical values of the carbon-13 chemical shifts for chelated ethylenediamine methylene carbons in macrocyclic ligands fall in the region of 51.6 ppm.[14] Therefore, the six methylene groups of the macrocyclic backbone are responsible for the mutiplet in this region. The multiplet, however, contains seven signals. The extra signal is thought to arise from one of the quaternary carbons. The other quaternary carbon, expected to be of low intensity, is masked by the large number of peaks occurring in this region of the spectrum. Lastly we observe the low intensity imine carbon resonance at 185.19 ppm, a typical value.[14]

Infrared Spectra. The infrared spectra of $Ni(TTT)I_2$ and $Ni(sen)I_2$ are nearly identical. $Ni(TTT)I_2$ has three additional absorption bands appearing at 1647, 1353, and 1159 cm^{-1}. The sharp 1647 cm^{-1} band arises from the C=N group and was used in this work as a preliminary indicator of Schiff base formation.

Summary The $Ni(sen)^{2+}$ complex appears to be useful synthetically for template synthesis. Future work will probably give macrocyclic ligands derived from methyl ethyl ketone, propionaldehyde, and acetylacetone but procedures must be developed for the removal of polymeric products. Macrocyclic complexes derived from $Ni(spn)^{2+}$ are more unlikely because of its larger size. Since no reaction occurs with acetone, other ketones and aldehydes are expected to be even more unfavorable for macrocyclic synthesis with $Ni(spn)^{2+}$.

REFERENCES

1. Taken from the Ph.D. Dissertation of Robert E. Hermer, the University of Pittsburgh, 1976.
2. D. A. House and N. F. Curtis, *J. Am. Chem. Soc.*, **86**, 1331 (1964).
3. N. F. Curtis, *Coord. Chem. Rev.*, **3**, 3, (1968).
4. J. D. Curry and D. H. Busch, *J. Am. Chem. Soc.*, **86**, 592 (1964).
5. Synthetic procedure to be published.
6. H. Stetter and W. Bockmann, *Chem. Ber.*, **84**, 834 (1951).
7. R. W. Green, K. W. Catchpole, A. T. Phillip and F. Lions, *Inorg. Chem.*, **2**, 597 (1963).
8. D. F. Evans, *J. Chem. Soc.*, 2003 (1959).
9. M. F. Rettig cited in D. L. Ehman and D. T. Sawyer, *Inorg. Chem.*, **9**, 204 (1970).
10. J. E. Parks, B. E. Wagner and R. H. Holm, *Inorg. Chem.*, **10**, 2472 (1971).
11. A. Earnshaw, *Introduction to Magnetochemistry*, Academic Press, N.Y., 1968, page 4.
12. D. H. Williams, N. J. Rose, and D. H. Busch, *J. Am. Chem. Soc.*, **89**, 703 (1967).
13. N. J. Rose, M. S. Elder, and D. H. Busch, *Inorg. Chem.*, **6**, 1924 (1967).
14. John Cragel, Ph.D. Dissertation, University of Pittsburgh, 1975.