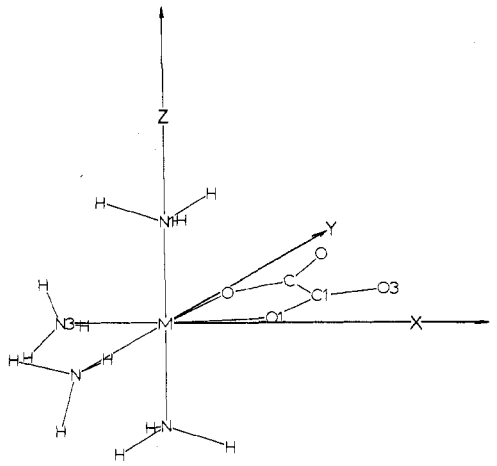

Figure 8. Details of assumed molecular structure of $M(NH_3)_4C_2O_4$ (M = Ni, Cu) used for molecular orbital calculations. Oxalate atoms and metal atom are coplanar. Metal–nitrogen and metal–oxygen distances are assumed to be 2.10 Å. Oxalate dimensions are MOC = 113°, OCO = 125°, C–C′ = 1.55 Å, and O–C = 1.25 Å.

copper case. In fact, the copper a_1 orbital places *more* of the unpaired electron density out onto the oxalate than does the nickel. If this were a dimer system, the *two* unpaired electrons in a copper dimer would seemingly be involved to a greater extent in spin polarization than the nickel electrons in the a_1 orbital; therefore this mechanism must be ruled out as the cause of the loss of interaction upon replacing nickel by copper. As advanced above, another qualitative explanation for the difference in interaction could lie in the character of the nickel b_1 ($d_{x^2-y^2}$) orbital. Our calculations have shown that of the orbitals wherein unpaired electrons reside, the nickel b_1 ($d_{x^2-y^2}$) orbital does bond *via* a $d_{x^2-y^2}$-bridge overlap which is significantly larger than is the d_{z^2}-bridge overlap. This would favor a larger exchange interaction. However, a relatively large $d_{x^2-y^2}$ coefficient in the b_1 nickel orbital, as well as small molecular orbital coefficients on the carbon for this case, seems to diminish the likelihood that the b_1 orbital is the predominant pathway of nickel exchange.

All in all, these molecular orbital calculations do not readily establish the mechanism of exchange leading to different magnetic effects for the copper and nickel systems. They do, however, seem to point out two things: (1) the character (population, energy, etc.) of the in-plane $d_{x^2-y^2}$ orbital could be of fundamental importance in determining the nature of the exchange and (2) a first-order σ-polarization mechanism is not indicated, and as such configuration interaction may be important in supporting a second-order π exchange.

We should note that as further experimental evidence of the importance of the in-plane $d_{x^2-y^2}$ orbital, a square-planar copper dimer with bis-bidentate 1,2,4,5-tetraaminobenzene bridging[43] possesses a distinct exchange interaction ($J = -12$ cm^{-1}).

Acknowledgment. We are grateful for generous support from NIH Grant HL 13652 and to Professor N. F. Curtis for telling us the results of some X-ray crystallographic work in advance of publication.

Registry No. $[Ni_2(tren)_2(N_3)_2](BPh_4)_2$, 40961-72-6; $[Ni_2(tren)_2(C_2O_4)](BPh_4)_2$, 40961-73-7; $[Cu_2(tren)_2(C_2O_4)](BPh_4)_2$, 41007-91-4; $[Cu_2(tren)_2(N_3)_2](BPh_4)_2$, 40961-74-8; $[Cu_2(dien)_2(N_3)_2](BPh_4)_2$, 40961-75-9; $[Cu_2(dien)_2(C_2O_4)](BPh_4)_2$, 40961-76-0; $[Cu_2(dien)_2(C_2O_4)](ClO_4)_2$, 21279-24-3; $Ni(NH_3)_4C_2O_4$, 15659-03-7; $Cu(NH_3)_4C_2O_4$, 40902-34-9.

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Contribution from the Department of Chemistry, Iowa State University, Ames, Iowa 50010

Stereoselectivity of *N*-(2-Pyridylmethyl)- and *N*-(6-Methyl-2-pyridylmethyl)-L-aspartic Acid Complexes of Copper(II) and Nickel(II) toward Optically Active Amino Acids

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Stability constants for a series of copper(II) and nickel(II) mixed-ligand complexes of amino acids and aspartic acid derivatives are reported. These constants indicate that the metal complexes of *N*-(2-pyridylmethyl)-L-aspartic acid and *N*-(6-methyl-2-pyridylmethyl)-L-aspartic acid coordinate the L enantiomers of alanine, phenylalanine, tryptophan, threonine, leucine, and valine in preference to their corresponding D isomers. These results are interpreted in terms of steric interactions of the α substituent of the amino acid and the pyridine residue of the aspartate derivative.

Introduction

There are few reports of stereoselectivity involving coordination of amino acidates (A^-) by complexes of labile metal ions, *i.e.*, examples in which equilibrium constants for the reactions

$$(\text{L-ligand})M^{n+} + \text{L-A}^- \rightleftharpoons (\text{L-ligand})M(\text{L-A})^{(n-1)+} \quad (1)$$

$$(\text{L-ligand})M^{n+} + \text{D-A}^- \rightleftharpoons (\text{L-ligand})M(\text{D-A})^{(n-1)+} \quad (2)$$

are different. Gillard, *et al.*,[2,3] found no stereoselective behavior for a series of bis(amino acidato)copper(II) complexes. ORD studies by Wellman, *et al.*,[4] supported this conclusion; they suggested there was little interaction between the two

(1) Fellow of the Alfred P. Sloan Foundation, 1970–1972.

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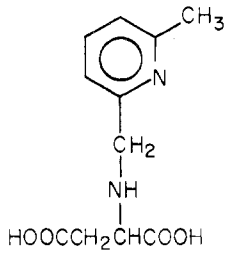
amino acids in these bis(amino acidato)copper(II) complexes. Bennett[5] reported that bis(D- or L-asparaginato)copper(II) was more stable than the corresponding (D-aspNH_2)(L-aspNH_2)Cu^{II} chelate. However, Ritsma, *et al.*,[6] found little if any difference in the stabilities of these complexes. Of all the common amino acids, histidine appears to exhibit the greatest stereoselectivity. For cobalt(II),[7,8] nickel,[8-11] and zinc(II)[8-11] the mixed (D-hist)(L-hist)M complexes were found to be more stable than the (D- or L-hist)$_2$M chelates, while copper(II) was reported[8-11] to have the opposite behavior.

In these laboratories metal complexes of amino acid derivatives have been shown to exhibit a stereochemical preference for one enantiomer of a given amino acid. The *N*-carboxymethyl-L-valinatocopper(II) [(*N*-Cm-L-Val)Cu] chelate generally formed more stable complexes with L-amino acids than with their corresponding D enantiomers;[12] *i.e.*, the formation constant for reaction 3 was larger for the L-amino acid than

$$(N\text{-Cm-L-Val})Cu + A^- \rightleftharpoons (N\text{-Cm-L-Val})(A)Cu^- \quad (3)$$

for the D isomer. This preference was later utilized partially to resolve racemic mixtures of amino acids.[13] The resolution was accomplished using column chromatography by binding the (*N*-Cm-L-Val)Cu chelate to a styrene–divinylbenzene copolymer. Recent potentiometric studies[14] indicated that the Cu(II) complexes of *N*-carboxymethyl-L-isoleucine or -L-serine and *N*-benzyl-*N*-carboxymethyl-L-alanine or -L-leucine coordinated L-valine, L-leucine, or L-threonine more strongly than their corresponding D isomers. The *N*-carboxymethyl-L-aspartic acid, -L-glutamic acid, and -D-valine chelates of copper(II) exhibited opposite preferences. We now wish to report the stereochemical preferences of the Cu(II) and Ni(II) chelates of *N*-(2-pyridylmethyl)-L-aspartic acid (*N*-pyr-L-Asp) and *N*-(6-methyl-2-pyridylmethyl)-L-aspartic acid (*N*-mepyr-L-Asp).

N-pyr-L-Asp



N-mepyr-L-Asp

Experimental Section

Preparation of *N*-(2-Pyridylmethyl)-L-aspartic Acid (*N*-pyr-L-Asp) and *N*-(6-Methyl-2-pyridylmethyl)-L-aspartic Acid (*N*-mepyr-L-Asp). These two ligands were prepared similarly. To a solution of 13.3 g (0.1 mol) of L-aspartic acid dissolved in 50 ml of 4 *N* NaOH was added with stirring 0.1 mol of 2-pyridinecarboxaldehyde or 6-methyl-2-pyridinecarboxaldehyde over a period of about 30 min. After the solution was stirred for 1 additional hr, 1.14 g of $NaBH_4$ was added in small portions. The solution was stirred until foaming ceased after which the mixture was acidified to pH 3 with 6 *M* HCl. The small amount of unreacted aspartic acid which precipitated was filtered off.

At this point the two ligand solutions were worked up differently. The *N*-pyr-L-Asp solution was evaporated to dryness under vacuum on a steam bath. The resulting solid was partially dissolved in water and after filtration the solution was evaporated to dryness. The residue was treated with a small amount of CH_3OH and heated until no additional solid dissolved. The hot solution was filtered and the filtrate was evaporated under a stream of air until the product began to crystallize. Additional fractions of the product were obtained on further evaporation. The first fractions give the purest product; they were recrystallized by dissolving them in hot methanol and cooling to 10°: mp 181–183° dec; $[\alpha]^{25}D$ +13.15° (*c* 2, 5 *M* HCl); yield 60%.

Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.56; H, 5.39; N, 12.50; O, 28.54. Found: C, 53.57; H, 5.33; N, 12.50; O, 28.51.

The *N*-mepyr-L-Asp reaction solution was allowed to stand at room temperature for several hours whereupon a precipitate containing the product and some aspartic acid separated. Several fractions of the product were obtained by evaporating the solution under vacuum. After recrystallization from CH_3OH, a 44% yield of the product resulted: mp 184–185°; $[\alpha]^{25}D$ + 18.9° (*c* 2, 5 *M* HCl).

Anal. Calcd for $C_{11}H_{14}N_2O_4$: C, 55.45; H, 5.92; N, 11.76; O, 26.86. Found: C, 55.34; H, 6.01; N, 11.80; O, 26.74.

Amino Acid Ligands. D- and L-alanine (Ala) and D- and L-leucine (Leu) were purchased from Mann Research Laboratories, and the D and L isomers of phenylalanine (Phe), threonine (Thr), tryptophan (Try), and valine (Val) were purchased from Aldrich Chemical Co. The amino acids were of the highest purity available and were used without further purification. All amino acid solutions were standardized by potentiometric (pH) titration. Due to the decomposition of aqueous solutions of D- and L-tryptophan, solutions were prepared and standardized the day of use.

Metal Solutions. Baker analyzed $Cu(NO_3)_2 \cdot 3H_2O$ and $Ni(NO_3)_2 \cdot 6H_2O$ were used in the preparation of metal ion solutions. These solutions were standardized *via* ion-exchange techniques.[15] Aliquots of the metal solutions were passed through Dowex 50W-X8 strongly acidic cation-exchange resin, and the effluent solutions were titrated with standardized sodium hydroxide.

Potentiometric Measurements. A Corning Digital 112 Research Model pH meter was used to determine hydrogen ion concentrations in all potentiometric titrations, which were carried out in a double-walled cell of 50-ml capacity. The temperature of all solutions was maintained at 25.00 ± 0.05° by circulation of thermostated water through the outer jacket of the cell. The titration vessel was fitted with Corning glass and calomel extension electrodes, a microburet delivery tube, and a nitrogen inlet tube. The solutions were stirred with a magnetic stirrer, and stirring was stopped prior to making pH readings. Ionic strengths of all solutions were maintained at 0.10 *M* by the addition of an appropriate amount of 1.0 *M* potassium nitrate. All titrations were performed in triplicate.

The glass electrode was calibrated in terms of $-\log [H^+]$ (pH_c) according to the procedure of Rajan and Martell[16] using HCl, acetic acid, and NaOH solutions. For the acetic acid titration, the actual hydrogen ion concentrations ($-\log [H^+]$) were calculated from values tabulated by Harned and Owen.[17]

Standardized perchloric acid was added to solutions of *N*-pyr-L-Asp and *N*-mepyr-L-Asp (5.0×10^{-3} *M*) in order to determine the protonation constants of these ligands. All protonation constants of the ligands and the formation constants of the metal complexes were calculated using Bjerrum's method.[18] Only data from 20 to 80% of a buffer region were used in the calculations and all calculations were performed on an IBM 360-65 digital computer.

The mixed-ligand amino acid complexes were formed by bringing together in solution the metal ion (5.0×10^{-3} *M*), the auxiliary ligand (*N*-mepyr-L-Asp or *N*-pyr-L-Asp, 5.0×10^{-3} *M*), and the amino acid

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Table I. Amino Acid Protonation (log K_a) and Formation Constants (log K_x) of Mixed-Ligand Complexes with Copper(II) and Nickel(II) Chelates of *N*-(2-Pyridylmethyl)-L-aspartic Acid and *N*-(6-Methyl-2-pyridylmethyl)-L-aspartic Acid

		log K_x							
		N-pyr-L-Asp				*N*-mepyr-L-Asp			
Amino acid	log K_a	Cu(II)	Δ	Ni(II)	Δ	Cu(II)	Δ	Ni(II)	Δ
L-Phe	9.13 ± 0.02	3.93 ± 0.01	0.10	3.54 ± 0.02	0.10	5.17 ± 0.01	0.46	3.67 ± 0.02	0.12
D-Phe	9.15 ± 0.01	3.83 ± 0.01		3.44 ± 0.02		4.71 ± 0.02		3.55 ± 0.02	
L-Try	9.43 ± 0.01	4.94 ± 0.01	0.11	4.02 ± 0.02	0.09	5.66 ± 0.01	0.37	4.25 ± 0.01	0.20
D-Try	9.41 ± 0.01	4.83 ± 0.01		3.93 ± 0.02		5.29 ± 0.01		4.05 ± 0.01	
L-Val	9.58 ± 0.01	3.99 ± 0.02	0.06	3.67 ± 0.01	0.08	4.97 ± 0.02	0.13	3.60 ± 0.01	0.13
D-Val	9.57 ± 0.01	3.93 ± 0.02		3.59 ± 0.02		4.84 ± 0.01		3.47 ± 0.01	
L-Thr	9.02 ± 0.01	3.84 ± 0.01	0	3.76 ± 0.02	0.04	4.83 ± 0.01	−0.05	3.94 ± 0.02	0.06
D-Thr	9.02 ± 0.01	3.85 ± 0.02		3.72 ± 0.02		4.88 ± 0.01		3.88 ± 0.02	
L-Leu	9.68 ± 0.01	4.12 ± 0.02	0	3.73 ± 0.02	0	4.99 ± 0.02	0.04	3.67 ± 0.01	0.04
D-Leu	9.69 ± 0.01	4.13 ± 0.02		3.74 ± 0.02		4.95 ± 0.02		3.63 ± 0.01	
L-Ala	9.76 ± 0.01	4.04 ± 0.01	0	3.73 ± 0.02	0	5.10 ± 0.01	0.06	3.83 ± 0.01	0.04
D-Ala	9.78 ± 0.01	4.03 ± 0.02		3.72 ± 0.01		5.04 ± 0.01		3.79 ± 0.01	

(5.0×10^{-3} *M*) followed by adjustment of pH to the equilibrium region. Stability constants were calculated on the basis of eq 1 and 2.

Visible Spectra. In order to measure visible spectra simultaneously with pH, a potentiometric titration cell was constructed with inlet and outlet tubes. The experimental solution was circulated from the titration cell to a flow-through quartz cell (Precision Cells, Inc., Hicksville, N. Y.) by means of a peristaltic pump (Manostat, New York, N. Y.). All spectra were recorded on a Beckman DB-G grating spectrophotometer. The cell compartment of the instrument was maintained at the same temperature as that of the potentiometric cell by the circulation of the thermostated water from the same water bath. All measurements of equimolar (0.013, 0.0087, 0.0065 *M*) metal-ligand solutions were taken at 25.00 ± 0.05° and an ionic strength of 0.10 *M*.

Results

Potentiometric Titration. Protonation constants of the amino acids are listed in Table I. In all cases values for the D and L isomers of any one amino acid are equivalent within experimental error. The values obtained here compare favorably with those in the literature.[19]

Due to the close similarity to that of *N*-pyr-L-Asp only the titration curve of *N*-mepyr-L-Asp is shown (Figure 1). The curve consists of a low-pH buffer zone terminated by a sharp inflection at $a = 1$ mol of base/mol of ligand, followed by a second buffer region with a weak inflection at $a = 2$. The logarithms of the protonation constants of *N*-mepyr-L-Asp and *N*-pyr-L-Asp are $\log K_1 = 8.68 \pm 0.01$, $\log K_2 = 3.72 \pm 0.01$, $\log K_3 = 2.72 \pm 0.01$ and $\log K_1 = 8.72 \pm 0.01$, $\log K_2 = 3.63 \pm 0.02$, $\log K_3 = 2.23 \pm 0.01$, respectively. No value was obtained for K_4, *i.e.*

$$H_3L^+ + H^+ \overset{K_4}{\rightleftharpoons} H_4L^{2+}$$

The values of $\log K_2$ and $\log K_3$ obtained by including H_4L^{2+} in the charge and mass balance equations were identical with those values obtained by excluding H_4L^{2+}.

Due to their similarity with titration curves of *N*-pyr-L-Asp, only those of *N*-mepyr-L-Asp with Ni(II) and Cu(II) are shown (Figure 1). The metal-ligand curves consist of a low-pH buffer zone terminated by a sharp inflection at $a = 2$. In the case of the Cu(II) curves a second buffer zone at high pH is observed, indicating metal chelate hydrolysis.

The Cu(II) chelate of *N*-pyr-L-Asp undergoes hydrolysis at high pH to yield [$CuLOH^-$] according to

$$CuL \overset{K_{OH}}{\rightleftharpoons} CuLOH^- + H^+ \qquad (4)$$

The value of $\log K_{OH}$ for this equilibrium was determined to be -9.38 ± 0.01. However, the Cu(II) chelate of *N*-mepyr-L-Asp undergoes hydrolysis at high pH to yield a di-μ-hydroxo dimer.[20,21] The logarithms of the formation constants of the hydrolytic reactions are $\log K_{OH} = -9.36 \pm 0.01$ and $K_D = 1.53 \pm 0.02$.

$$2CuLOH^- \overset{K_D}{\rightleftharpoons} Cu_2L_2(OH)_2^{2-} \qquad (5)$$

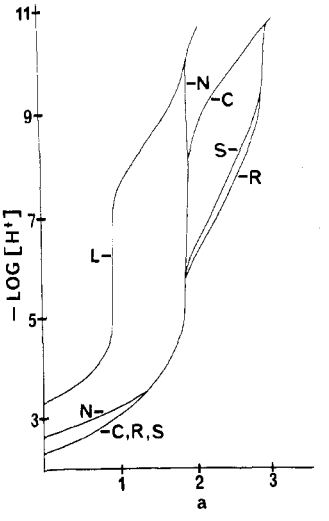

Figure 1. Potentiometric titration curves: L, 5.0×10^{-3} *M N*-mepyr-L-Asp; C, 5.0×10^{-3} *M N*-mepyr-L-Asp and Cu(II); N, 5.0×10^{-3} *M N*-mepyr-L-Asp and Ni(II); R, 5.0×10^{-3} *M N*-mepyr-L-Asp, Cu(II), and L-Try; S, 5.0×10^{-3} *M N*-mepyr-L-Asp, Cu(II), and D-Try (where *a* is moles of base per mole of *N*-mepyr-L-Asp).

The formation constants for the addition of six pairs of D- and L-amino acids to the Cu(II) and Ni(II) complexes of *N*-mepyr-L-Asp and *N*-pyr-L-Asp according to eq 1 and 2 are given in Table I. Since all the mixed-ligand titration curves are similar, only that of Cu(II) with *N*-mepyr-L-Asp and D(L)-tryptophan is shown in Figure 1. The mixed-ligand systems exhibit a low pH buffer zone terminated by an inflection at $a = 2$, followed by a second buffer zone which is terminated by an inflection at $a = 3$. The low pH region is exactly the same as that found in titrations of *N*-pyr-L-Asp or *N*-mepyr-L-Asp with Ni(II) or Cu(II), indicating that amino acidate addition to these metal chelates occurs in the higher pH buffer zone.

Visible Spectra. Absorption maxima and extinction coefficients for the Ni(II) and Cu(II) chelates of *N*-mepyr-L-Asp and *N*-pyr-L-Asp are listed in Table II (spectra are not shown). The visible spectra of equimolar solutions of Cu(II) with *N*-

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Table II. Visible Spectra of *N*-2-Pyridylmethyl-L-aspartic Acid and *N*-(6-Methyl-2-pyridylmethyl)-L-aspartic Acid Complexes of Copper(II) and Nickel(II)

	λ_{max}, nm	ϵ_{max}, M^{-1} cm^{-1}	λ_{max}, nm	ϵ_{max}, M^{-1} cm^{-1}
Cu(*N*-pyr-L-Asp)	682	78		
Ni(*N*-pyr-L-Asp)	594	3.9	364	10
Cu(*N*-mepyr-L-Asp)	702	80		
Ni(*N*-mepyr-L-Asp)	626	4.2	376	11
Cu(*N*-pyr-L-Asp)(OH)$^-$	669	72		
Cu_2(*N*-mepyr-L-Asp)$_2$(OH)$_2^{2-}$	708	166		

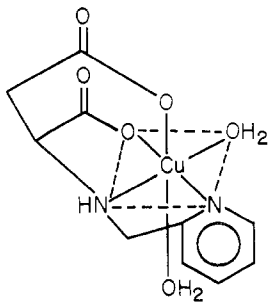
mepyr-L-Asp, Cu(II) with *N*-pyr-L-Asp, and Ni(II) with *N*-pyr-L-Asp in the low-pH buffer zone do not exhibit a shift in λ_{max} upon addition of base indicating that complex formation is complete even at low pH. Therefore, formation constants could not be obtained for these systems from the potentiometric data obtained in this study. After the inflection at $a = 2$, the visible spectra of the Cu^{II}-*N*-pyr-L-Asp solutions exhibited both a shift to higher energy and a decrease in absorbance upon addition of base. An isosbestic point was observed. After the inflection at $a = 2$, the visible spectra of Cu^{II}-*N*-mepyr-L-Asp solutions exhibited both a shift to lower energy and a slight increase in absorbance upon addition of base indicating hydrolysis. No isosbestic point was observed.

The visible spectra of Ni^{II}-mepyr-L-Asp solutions, in contrast to the above, exhibited in the low-pH buffer zone a shift to higher energy in both λ_{max} values (645 to 626 nm and 382 to 376 nm) and an increase in absorbance upon addition of base. No isosbestic point was observed.

Discussion

Protonation Constants. The similarity of the K_2 values for *N*-mepyr-L-Asp and *N*-pyr-L-Asp and the difference of 0.49 log unit in the log K_3 values indicate that the K_2 values can be assigned to protonation of the aspartic acid side chain carboxylate and K_3 values to protonation of the pyridine nitrogen. Protonation of the amino nitrogen is associated with K_1.

Metal Chelates. A possible structure (I) for Cu(*N*-mepyr-L-Asp) and Cu(*N*-pyr-L-Asp) is that with the N-donor ligands and one carboxylate group coordinating in the square plane; the axial ligands will coordinate weakly or not at all. As indicated by the pH titrations and the visible spectra, Cu(*N*-pyr-L-Asp) is converted at high pH to Cu(*N*-pyr-L-Asp)(OH)$^-$, in which the OH$^-$ ligand presumably occupies the fourth position in the square plane. In contrast, Cu(*N*-mepyr-L-Asp) forms at high pH both Cu(*N*-mepyr-L-Asp)(OH)$^-$ and the di-μ-hydroxo dimer, [Cu(*N*-mepyr-L-Asp)(OH)]$_2^{2-}$. The tendency of the *N*-mepyr-L-Asp complex to give the dimer presumably arises from the reduced coordinating ability of the 2-methylpyridine group, which either dissociates or coordinates weakly to an axial site leaving two cis positions in the square plane available for hydroxo bridge formation.

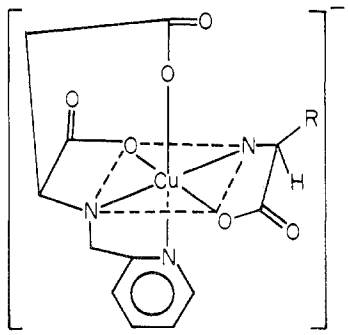


I

Martell, *et al.*,[20,21] previously noted similar structural changes in the formation of di-μ-hydroxo dimers of Cu(II) complexes of other polydentate ligands. The lack of dimer formation by Cu(*N*-pyr-L-Asp)(OH)$^-$ probably results from the stronger coordinating ability of the pyridine group which is not easily displaced from its position in the square plane. Lower stability constants for coordination of 2-methylpyridine by Cu(II) as compared to those for pyridine[22-24] support this conclusion.

The reduced coordinating ability of the 2-methylpyridine group is also manifest in the lower energy absorption maximum (Table II) in the *N*-mepyr-L-Asp complexes of both Cu(II) and Ni(II) as compared to those for their *N*-pyr-L-Asp analogs. This has previously been observed in spectra of complexes of Cu(II) with pyridine and 2-methylpyridine.[24]

Metal-Ligand-Amino Acid Complexes. Table I indicates that the addition of amino acidates to Cu(*N*-mepyr-L-Asp) is 10 times more favorable than to Cu(*N*-pyr-L-Asp). This can be explained by assuming that the amino acidates coordinate to the Cu(II) square plane (II) and that the pyridine



II

residue either dissociates or moves from the square plane to a weaker axial coordination site. The ease with which this conformational change occurs will be reflected in the stability constant for amino acidate addition. As discussed in the previous section, the hydrolysis of Cu(*N*-mepyr-L-Asp) to a di-μ-hydroxo dimer and Cu(*N*-pyr-L-Asp) to a monohydroxo monomer is a result of the relative strengths of the Cu^{II}-pyridine nitrogen bonds. Thus, the same rationale, the reduced coordinating ability of an ortho-substituted pyridine moiety and the resultant ease with which it is moved from an equatorial coordination site, is used to explain the more favorable addition of amino acidates to Cu(*N*-mepyr-L-Asp) than to Cu(*N*-pyr-L-Asp).

Equilibrium constants for the addition of amino acidates to Cu(*N*-mepyr-L-Asp) (log $K \simeq 5.0$) are similar to those observed for amino acid complexation to copper(II) nitrilotriacetate (NTA) (log $K \simeq 5.2$)[25] while those of Cu(*N*-pyr-L-Asp) are similar to those of copper(II) diethylenetriamine (dien) (log $K \simeq 4.0$).[26] These data are also consistent with the idea that amino acidate addition is dependent upon the ease of moving a donor from an equatorial site. As expected it is more difficult to remove an amino donor (dien) from a square-planar site than a carboxylate group (NTA).

Equilibrium constants for the addition of amino acidates to the Ni(II) chelates are very similar. This similarity is ex-

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pected in that unlike Cu(II) all six binding sites of Ni(II) are essentially equivalent. Molecular models indicate that structure II is favored for these Ni(II) chelates on the basis of strain. Equilibrium constants for the addition of amino acidates to the Ni(II) *N*-mepyr-L-Asp and *N*-pyr-L-Asp chelates ($\log K \simeq 3.7$) are considerably lower than those of the Ni(II) complexes of NTA ($\log K \simeq 4.7$)[25] and dien ($\log K \simeq 5.1$).[27]

The constants listed in Table I indicate that the Cu(II) and Ni(II) chelates of *N*-mepyr-L-Asp and *N*-pyr-L-Asp coordinate L enantiomers of amino acidates more strongly or equally as strongly as the D isomers except for the small opposite effect found in the Cu^{II}–*N*-mepyr-L-Asp–threonine system. The differences (Δ in Table I) between the K_X values for L- and D-amino acid enantiomers generally decrease with decreasing size of the α substituent of the amino acidate, *i.e.*, Phe > Try > Val > Leu ~ Thr ~ Ala, indicating that the stereoselectivity results from steric interactions and possibly the aromatic character of the side chain. The metal complexes of *N*-mepyr-L-Asp yield larger Δ values than those of *N*-pyr-L-Asp also indicating the importance of steric interactions.

The structure of the mixed-ligand chelate most compatible with the observed potentiometric data and steroselectivity is II. The α substituent (R) of the L enantiomer of the amino acid in II is pointing away from the bulky pyridyl residue while in the D isomer the R group is directed toward the aromatic ring. Thus, L-amino acids are bound more strongly than their D enantiomers.

Copper(II) complexes of *N*-mepyr-L-Asp exhibited the greatest amount of stereoselectivity. This is probably due to the increased crowding caused by the smaller size of Cu(II) as compared to Ni(II) and the 6-methyl group of the pyridyl group. The substantial preference of the metal chelates for the L enantiomers of Try and Phe are encouraging, and further studies are currently in progress in these laboratories.

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Registry No. *N*-pyr-L-Asp, 41203-01-4; *N*-mepyr-L-Asp, 41203-02-5; Cu(*N*-pyr-L-Asp)$(H_2O)_2$, 41203-03-6; Ni(*N*-pyr-L-Asp)$(H_2O)_2$, 41203-04-7; Cu(*N*-mepyr-L-Asp)$(H_2O)_2$, 41203-05-8; Ni(*N*-mepyr-L-Asp)$(H_2O)_2$, 41203-06-9; Cu(*N*-pyr-L-Asp)$(OH)^-(H_2O)$, 41203-07-0; Cu_2(*N*-mepyr-L-Asp)$_2(OH)_2^{2-}$, 41203-08-1; Cu(*N*-pyr-L-Asp)(L-Phe)$^-$, 41203-09-2; Ni(*N*-pyr-L-Asp)(L-Phe)$^-$, 41203-10-5; Cu(*N*-mepyr-L-Asp)(L-Phe)$^-$, 41203-11-6; Ni(*N*-mepyr-L-Asp)(L-Phe)$^-$, 41203-12-7; Cu(*N*-pyr-L-Asp)(D-Phe)$^-$, 41203-13-8; Ni(*N*-pyr-L-Asp)(D-Phe)$^-$, 41212-29-7; Cu(*N*-mepyr-L-Asp)(D-Phe)$^-$, 41212-30-0; Ni(*N*-mepyr-L-Asp)(D-Phe)$^-$, 41212-31-1; Cu(*N*-pyr-L-Asp)(L-Try)$^-$, 41212-32-2; Ni(*N*-pyr-L-Asp)(L-Try)$^-$, 41212-33-3; Cu(*N*-mepyr-L-Asp)(L-Try)$^-$, 41212-34-4; Ni(*N*-mepyr-L-Asp)(L-Try)$^-$, 41212-35-5; Cu(*N*-pyr-L-Asp)(D-Try)$^-$, 41212-36-6; Ni(*N*-pyr-L-Asp)(D-Try)$^-$, 41212-37-7; Cu(*N*-mepyr-L-Asp)(D-Try)$^-$, 41212-38-8; Ni(*N*-mepyr-L-Asp)(D-Try)$^-$, 41212-39-9; Cu(*N*-pyr-L-Asp)(L-Val)$^-$, 41212-40-2; Ni(*N*-pyr-L-Asp)(L-Val)$^-$, 41212-41-3; Cu(*N*-mepyr-L-Asp)(L-Val)$^-$, 41212-42-4; Ni(*N*-mepyr-L-Asp)(L-Val)$^-$, 41212-43-5; Cu(*N*-pyr-L-Asp)(D-Val)$^-$, 41212-44-6; Ni(*N*-pyr-L-Asp)(D-Val)$^-$, 41212-45-7; Cu(*N*-mepyr-L-Asp)(D-Val)$^-$, 41385-45-9; Ni(*N*-mepyr-L-Asp)(D-Val)$^-$, 41212-46-8; Cu(*N*-pyr-L-Asp)(L-Thr)$^-$, 41212-47-9; Ni(*N*-pyr-L-Asp)(L-Thr)$^-$, 41212-48-0; Cu(*N*-mepyr-L-Asp)(L-Thr)$^-$, 41212-49-1; Ni(*N*-mepyr-L-Asp)(L-Thr)$^-$, 41212-50-4; Cu(*N*-pyr-L-Asp)(D-Thr)$^-$, 41212-51-5; Ni(*N*-pyr-L-Asp)(D-Thr)$^-$, 41212-52-6; Cu(*N*-mepyr-L-Asp)(D-Thr)$^-$, 41212-05-9; Ni(*N*-mepyr-L-Asp)(D-Thr)$^-$, 41212-06-0; Cu(*N*-pyr-L-Asp)(L-Leu)$^-$, 41212-07-1; Ni(*N*-pyr-L-Asp)(L-Leu)$^-$, 41212-08-2; Cu(*N*-mepyr-L-Asp)(L-Leu)$^-$, 41212-09-3; Ni(*N*-mepyr-L-Asp)(L-Leu)$^-$, 41212-10-6; Cu(*N*-pyr-L-Asp)(D-Leu)$^-$, 41212-11-7; Ni(*N*-pyr-L-Asp)(D-Leu)$^-$, 41212-12-8; Cu(*N*-mepyr-L-Asp)(D-Leu)$^-$, 41212-13-9; Ni(*N*-mepyr-L-Asp)(D-Leu)$^-$, 41212-14-0; Cu(*N*-pyr-L-Asp)(L-Ala)$^-$, 41212-15-1; Ni(*N*-pyr-L-Asp)(L-Ala)$^-$, 41212-16-2; Cu(*N*-mepyr-L-Asp)(L-Ala)$^-$, 41212-17-3; Ni(*N*-mepyr-L-Asp)(L-Ala)$^-$, 41385-46-0; Cu(*N*-pyr-L-Asp)(D-Ala)$^-$, 41212-18-4; Ni(*N*-pyr-L-Asp)(D-Ala)$^-$, 41212-19-5; Cu(*N*-mepyr-L-Asp)(D-Ala)$^-$, 41212-20-8; Ni(*N*-mepyr-L-Asp)(D-Ala)$^-$, 41212-21-9; L-aspartic acid, 56-84-8; 2-pyridinecarboxaldehyde, 1121-60-4; 6-methyl-2-pyridinecarboxaldehyde, 1122-72-1.

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Metal Complexes of 1,4,8,11-Tetramethyl-1,4,8,11-tetraazacyclotetradecane, *N*-Tetramethylcyclam

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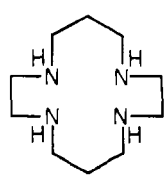
Preparations and properties of some nickel(II), copper(II), and zinc(II) complexes of the new 14-membered macrocyclic ligand 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane, II (*N*-tetramethylcyclam), are reported. Complexes of these metals are five-coordinate when a suitable anion or solvent molecule is available. Spectral data for a number of five-coordinate Ni(II) complexes are given. Nmr results on the $Zn(TMC)Cl^+$ ion indicate all four methyl groups are on the same side of the coordination plane. Qualitatively, the nickel(II) complex is kinetically labile compared to complexes of other ligands of the 14-membered class.

Investigations of metal complexes containing macrocyclic ligands has been an area of active research for several years.[1] Of the several tetradentate macrocyclic ligands known, by far the largest number of these contain 14 members and are perturbations on the simplest, 1,4,8,11-tetraazacyclotetradecane, which is commonly known as cyclam, I.[2] As a part



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of our own investigations on the redox chemistry of Ni(III) complexes of certain of these saturated 14-membered tetra-

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