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The Conformations of Nickel(II) Complexes with edda-Type Optically Active Polyamino Carboxylic Acids in Aqueous Solutions

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Circular dichroism (CD) and proton magnetic resonance (PMR) spectra of nickel(II) complexes containing a series of ethylenediamine-*N*,*N*′-diacetic acid(H_2edda)-type optically active quadridentate ligands were measured in aqueous solutions. The epro complex which is an edda-type optically active ligand containing L-proline residues is found to exhibit the same CD spectrum as complexes of other edda-type ligands containing L-alanine, L-valine, L-phenylalanine, and L-serine residues. The CD and PMR spectra of the mixed complexes of these edda-type ligands having an oxalate ion was also measured. From the CD and PMR spectral data, it is concluded that these complexes stereospecifically take the *Δ-s-cis* form in solution. The large contact shift observed for the a protons of the amino acidate moieties indicates that the substituent groups become axial to the chelate plane.

In a previous paper,[1] we reported the preparation and solid state character of nickel(II) complexes having a series of ethylenediamine-*N*,*N*′-diacetic acid (H_2edda)-type optically active polyamino carboxylic acids, as is shown in Fig. 1;[2] the stretching frequencies of the coordinated carboxylate groups and the thermal stability suggested that the structure of the edda-type complexes in the solid state is different from that of bis(amino acidato) complexes. In this paper, we wish to report the circular dichroism (CD) and proton magnetic resonance (PMR) spectra measured in order to obtain information about the structure of the nickel(II) complexes with the edda-type optically active ligands in aqueous solutions.

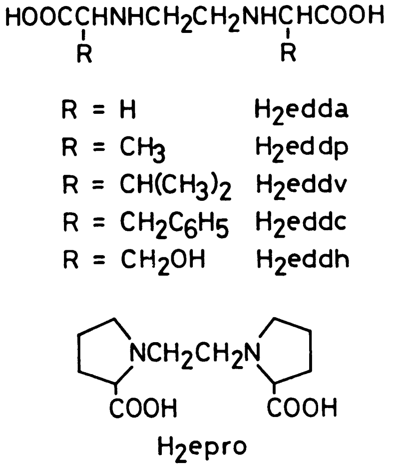

Fig. 1. The edda-type polyamino carboxylic acids. Except for H_2edda these acids possess two asymmetric carbon atoms with the *S* configuration.

Since the investigation of Milner and Pratt,[4] PMR studies have been found to be very useful for the conformational analysis of chelate rings in paramagnetic nickel(II) complexes.[5-9] However, most of subsequent work has involved optically inactive nickel(II) complexes. As is well-known, CD is an effective technique for the conformational analysis of optically active complexes. The combination of PMR and CD should lead to a more detailed understanding of the stereochemistry of paramagnetic nickel(II) complexes with optically active ligands.

Cobalt(III) complexes containing edda and its analogs have been extensively studied.[10-13] Schoenberg *et al.*,[14] have prepared cobalt(III) complexes with eddp, which is an optically active edda-type acid (see Fig. 1), and obtained the *Δ-s-cis* and *Λ-s-cis* isomers as main products and a small amount of the *Δ-uns-cis* isomer.[15,16] Since the yields of the two *s-cis* isomers were nearly equal, the stereospecificity of eddp does not appear to be very large. In the case of the nickel(II) ion, however, eddp-type quadridentate ligands may form only the most stable isomer in solution due to the labile characteristic of the nickel(II) ion. Thus, there is the possibility of displaying their essential stereospecificity by forming labile complexes. One of the purposes of this paper is to clarify this problem. Especially, the epro ion has two pyrrolidinyl groups in its interior (Fig. 1) and hence is expected to coordinate to a metal ion with a large stereospecificity. Even for the copper(II) ion, the epro ion is reported to coordinate with an *uns-cis* configuration.[3] The conformations of the nickel(II) complexes with these edda-type ligands are discussed on the basis of the CD and PMR spectra.

Experimental

Materials. The edda-type optically active polyamino carboxylic acids shown in Fig. 1 and their nickel(II) complexes were prepared as described in a previous paper.[1] Mixed ligand complexes of these acids having an oxalate ion were prepared by adding an amount of sodium oxalate two times in excess to the complex solutions.[17] Sodium 3-(trimethylsilyl)-1-propanesulfonate (TMS*) was used as an internal reference for the chemical-shift measurements for the PMR.

Samples for PMR measurements were prepared as follows. The isolated complex was dissolved in D_2O (99.75%). To reduce the size of the HDO signal, the solution was evaporated to dryness at 50 °C, and dried solid was again dissolved in D_2O. After this procedure had been repeated, the dried solid was dissolved in D_2O containing TMS*. The final concentration of each solution was about 0.02 M. In the case of complexes mixed having an oxalate ion, the complex solutions containing amount of sodium oxalate two times in excess were similarly treated. The concentration was about 0.2 M.

Measurements. Absorption spectra from the near-infrared to the near-ultraviolet regions were measured with a Hitachi EPS-3T spectrophotometer. CD spectra from 250 to 1200 nm were measured with a Jasco J-20A recording spectropolarimeter (250—1000 nm) and a Jasco J-200 grating spectropolarimeter (900—1200 nm). The PMR spectra were obtained with a Varian CFT-20 spectrometer at 80 MHz. To obtain high signal-to-noise ratios for PMR, each signal was repeatedly accumulated using a Fourier transform (FT) technique or a water-eliminated FT technique.

Results and Discussion

Figure 2 shows the absorption and CD spectra of $[Ni(eddp)(H_2O)_2]$, $[Ni(eddh)(H_2O)_2]$, and $[Ni(epro)(H_2O)_2]$ in the region of 7000 to 38000 cm^{-1}. These complexes exhibit CD curves with similar shapes, which have a large negative band in the first (lowest energy) absorption band region, two negative bands in the second absorption region, and two bands of oppsite sign in the third absorption region. The diaquanickel(II) complexes of eddv and eddc also exhibit analogous CD spectra. Of the diaquabis(L-amino acidato)nickel(II) complexes, on the other hand, it has been reported that only the L-prolinato complex exhibits a quite different CD spectrum from those of other L-amino acidato complexes in methanol[18] and water.[19] This is considered to be due mostly to the large contribution of the asymmetric secondary nitrogen atom of proline to the optical activity. Therefore, the fact that the CD spectrum of the epro complex containing the two proline residues is the same as those of other eddp-type complexes is very interesting. This will be significant in the discussion of the structure of these complexes.

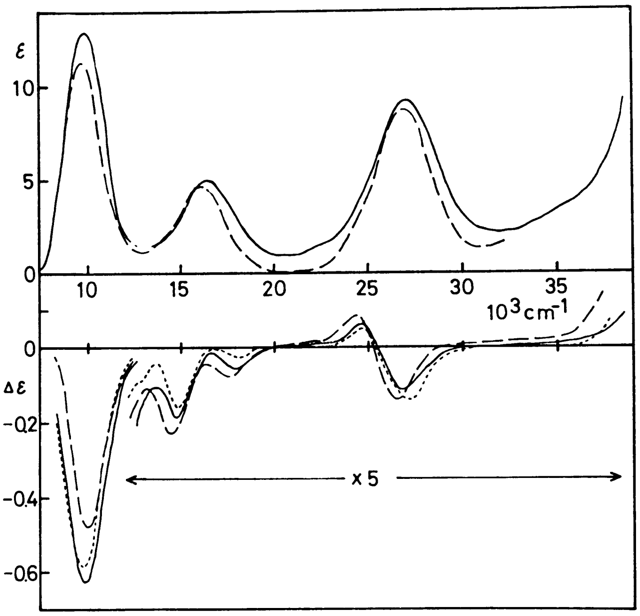

Fig. 2. Absorption and CD spectra of $[Ni(eddp)(H_2O)_2]$ (——), $[Ni(eddh)(H_2O)_2]$ (------), and $[Ni(epro)(H_2O)_2]$ (– – –) in aqueous solutions.

For the edda-type complexes, three geometrical isomers, *trans*, *s-cis*, and *uns-cis*, are possible and further there are two optical isomers of Δ and Λ for both the *s-cis* and *uns-cis* forms. Considering the asymmetry of chelate rings, the number of possible conformations increases to many more. Contributions to the CD spectrum observed for the octahedral nickel(II) complexes having edda-type optically active quadridentate ligands arise from (i) the configurational effect based on the arrangement of chelate rings around the nickel ion, (ii) the vicinal effect of the asymmetric nitrogen, (iii) the conformational effect of the central ethylenediamine(en)-type chelate ring, (iv) the conformational effect of the amino acidate chelate ring, and (v) the vicinal effect of the asymmetric carbon. Of these five effects, the contributions from the absolute configuration around the nickel ion and the asymmetric nitrogen are expected to be much more significant. Therefore, the similarity of the CD spectra observed for all the edda-type complexes suggests that these complexes have at least the same absolute configuration and an asymmetric nitrogen atom with the same configuration.

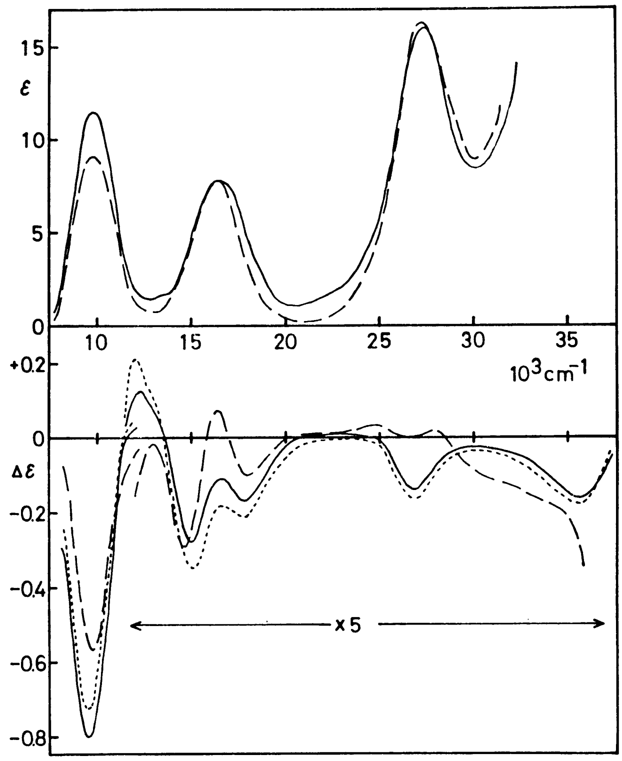

Fig. 3. Absorption and CD spectra of $[Ni(eddp)(ox)]^{2-}$ (——), $[Ni(eddh)(ox)]^{2-}$ (------), and $[Ni(epro)(ox)]^{2-}$ (– – –) in aqueous solutions.

The edda-type polyamino carboxylic acids appear primarily to have the particular character that they hardly coordinate to a metal ion in a plane.[12] For example, so far, no cobalt(III) complex with an edda-type acid in the planar configuration has been reported. Only *s-cis* and *uns-cis* isomers have actually been obtained.[10–14,20–22] This also appears to be the case for the nickel(II) complexes. The fact that the CD spectra of the nickel(II) complexes are not so greatly influenced when mixed complexes having an oxalate ion are formed (Fig. 3) indicates that these complexes are of the *cis*-type form to which the oxalate ion can coordinate without changing the configuration of the quadridentate ligands.

Among the edda-type ligands, especially the epro ion which has two pyrrolidinyl rings is expected to coordinate with large stereospecificity. Even to the copper(II)

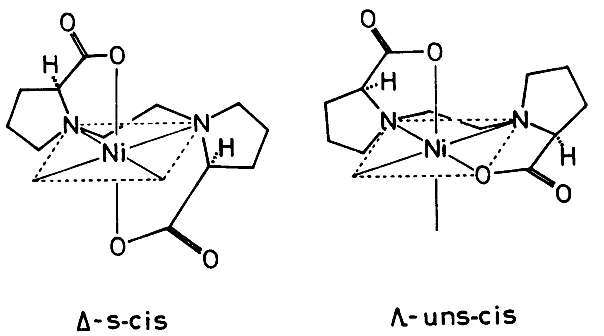

Fig. 4. Schematic drawing of the Δ-*s-cis* and Λ-*uns-cis* forms possible for the epro complex.

ion, which is generally thought to form planar complexes, epro appears to coordinate with a Λ-*uns-cis* configuration.[3] In addition, some tetraamines, which have two pyrrolidinyl groups in their interior as well as epro, do not form planar species of nickel(II) ions, but form only octahedral species.[23–25] An examination of the molecular models shows that the possible *cis* forms for epro are only two, Δ-*s-cis* and Λ-*uns-cis*, because of the rigid pyrrolidine rings. These two forms are illustrated in Fig. 4. The configuration of all the tertiary nitrogen atoms is *R*.[26] The central en-like chelate ring is a δ *gauche* in the Δ-*s-cis* form, while it appears to be an envelope in the Λ-*uns-cis* form. The epro complex will exist in either the Δ-*s-cis* or the Λ-*uns-cis* form in solution. Therefore, other eddp-type complexes are also considered to have a structures similar to either of these two forms on the basis of the similarity of the CD spectra.

The PMR spectra of [Ni(eddp)$(H_2O)_2$] and [Ni(eddh)$(H_2O)_2$], and complexes of these mixed with oxalate ions in D_2O are shown in Fig. 5. The signal due to the residual HDO of the solvent is not shown. The large peak at about -5.5 ppm observed for the eddp complex is assigned to the methyl protons on the basis of its relative area. The methylene protons in the hydroxymethyl group of the eddh complex appear at -7.2 ppm. Three other broad peaks, with almost the same intensity, observed at lower fields for each complex correspond to the central ethylene protons and the α protons in the amino acidate moieties, assuming the assignments for the edda complex.[6] Since the protons of the ethylene linkage of the edda complex were found to appear at -26 and -116 ppm, the α proton of the eddp complex could be assigned to either of the two bands at -126 and -103 ppm. Similarly, the α proton of the eddh complex corresponds to either of the two peaks at -121 and -102 ppm. The other of these two peaks is assigned to the equatorial protons of the ethylene linkage. In any case, the α protons of the eddp and eddh complexes would appear at a field lower than -100 ppm. This is significant when examining the ring conformation, as will be described below.

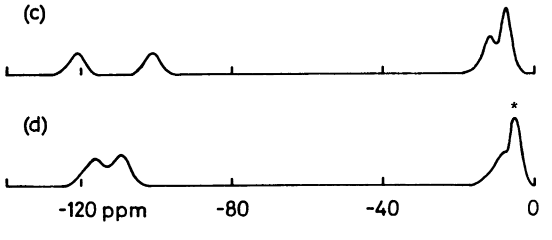

Fig. 5. PMR spectra of (a) [Ni(eddp)$(H_2O)_2$], (b) [Ni(eddp)(ox)]$^{2-}$, (c) [Ni(eddh)$(H_2O)_2$], and (d) [Ni(eddh)(ox)]$^{2-}$ in D_2O at 34 °C. The chemical shift is relative to the internal standard, TMS*. The signal from the residual HDO of the solvent is not shown. The signals with the sign (*) overlap with the signal of HDO.

The coordination of an oxalate ion appears to have some influence on the contact shifts of the ethylene and α protons (Fig. 5); in the eddh complex the signal of the equatorial proton of the ethylene moiety and that of the α proton approach each other, and in the eddp complex the two signals overlap to become a single broad band. Since the coordination of an oxalate ion does not change the configuration of the quadridentate ligand, this finding suggests that the coordinated oxalate ion might change the magnetic environment around the protons, or might even affect detailed conformations of the chelate rings.

The simplicity of the PMR spectra suggests that the eddp and eddh complexes exist not as equilibrium mixtures, but almost all in *s-cis* form. In the *s-cis* form, there is a C_2-symmetry axis passing through the central ethylene linkage and the nickel atom which makes the two chelate rings of the amino acidate equivalent. Consequently, it may be concluded that the nickel(II) complexes of edda-type optically active ligands are of Δ-*s-cis*-type absolute configuration. The CD spectra observed for mixed complexes having an oxalate ion afford some evidence to support this conclusion. As can be seen in Fig. 3, a new positive CD band emerges at higher wavenumbers in the first adsorption-band region when mixed complexes are formed. This CD pattern in the first absorption region, with negative and positive components from low wavenumbers, is characteristic of the absolute Δ configuration.[27–29] That the mixed complexes clearly indicate the Δ-type CD spectra is probably attributable to an increase in Δ-type ring pairing due to the addition of the oxalate chelate ring. That is to say, the contribution of the Δ-type configurational effect to the optical activity becomes relatively greater.

As described above, the PMR and CD spectral data indicate that these edda-type optically active ligands should stereospecifically ccordinate to a nickel(II) ion to form only the Δ-*s-cis* isomer in solution. Then, the steric factor for which ligands other than epro are forced to coordinate with the Δ-*s-cis* form must be examined. The four possible *s-cis* forms for the eddp-type complexes are depicted in Fig. 6. The symbols δ and λ represent the *gauche* form of the central en-type

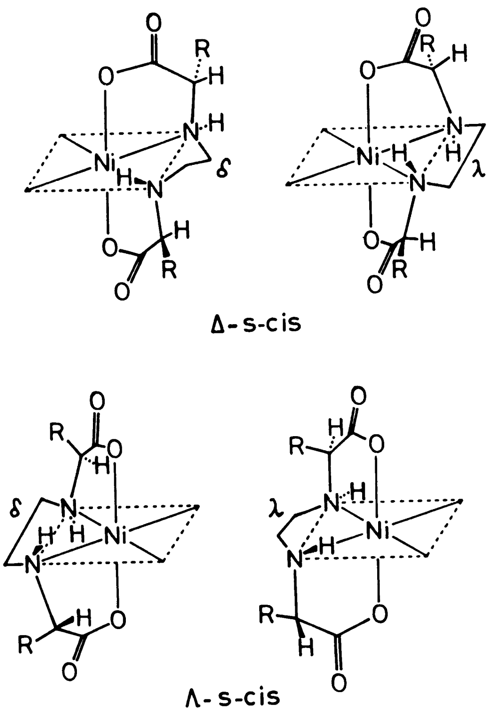

Fig. 6. Schematic drawing of the *cis*-type structures possible for the eddp-type complexes.

chelate ring. The substituent groups are denoted by R. The configuration of the secondary nitrogen atoms is *R* in the Δ-*s-cis* forms and *S* in the Λ-*s-cis* forms.

In the Δ-*s-cis* forms, both substituent groups are axial to the N–Ni–O chelate plane but point away from the central en-like chelate ring(*exo*), while in the Λ-*s-cis* forms, they point toward the central chelate ring(*endo*). Since the interaction between the non-bonding atoms is probably smaller in the *exo*-form than in the *endo*-form,[30] the Δ-*s-cis* form is considered to be thermodynamically more stable than the Λ-*s-cis* form. This may be the reason why these quadridentate ligands coordinate to a labile nickel(II) ion to form stereospecifically the Δ-*s-cis* isomer. For the cobalt(III) complex of eddp, however, both Δ-*s-cis* and Λ-*s-cis* isomers are obtained with almost the same yield, and hence the stereospecificity of eddp is not so large toward the inert cobalt(III) ion.[14] Thus, it can be said that the eddp-type ligands display their essential stereospecificity by forming labile nickel(II) complexes.

As has been pointed out by many other investigators,[4–7,31–33] the contact shift of the α protons in the amino acidate chelate ring depends on the relative axial-equatorial nature of the protons, that is, on the dihedral angle between the planes of the Ni–N–C and N–C–H groups; the equatorial proton appears at a very low value of the field (*ca.* −100 ppm) while the axial proton appears at a field higher than −40 ppm. The α protons of the eddp and eddh complexes are observed at fields lower than −100 ppm, indicating that the α protons are equatorial and hence the substituent groups are axial. Thus, this PMR finding supports the expectation that these complexes should be of Δ-*s-cis* form.

From an empirical correlation between the dihedral angle and the contact shift,[5] the α protons observed at about −100 ppm for the eddp and eddh complexes are considered to be on a pseudo-*gauche* form of the amino acidate chelates. Figure 7 shows the ring conformations of the two Δ-*s-cis* forms illustrated in Fig. 6 as viewed from the Ni–N bond axis. The lower amino acidate chelate ring is omitted for clarity. The δ and λ symbols represent the conformation of the central en-type chelate ring. In the case of the λ conformation, the amino acidate ring becomes a highly strained envelope and, moreover, the substituent group designated as *R* closely approaches the neighboring coordination site. Therefore, the λ form is considered to be very unstable. In the δ form, on the other hand, the amino acidate ring is pseudo-*gauche* (λ). The observed contact shift is indicative of the δ form, in fair agreement with the relative stability expected for the two forms.

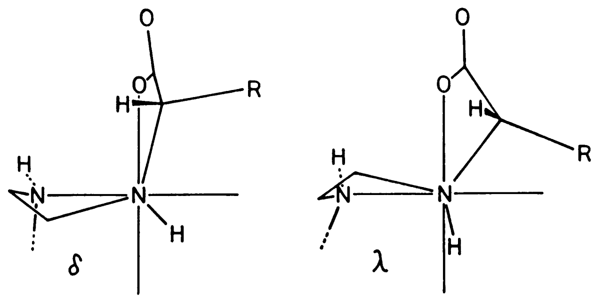

Fig. 7. The ring conformations in the Δ-*s-cis* forms as viewed from the Ni–N bond axis. δ and λ represent the conformations of the central en-type chelate ring. R designates the substituent groups. Another amino acidate chelate ring is not shown for clarity.

In conclusion, the eddp-type ligands would stereospecifically coordinate to the nickel(II) ion to form the Δ-*s-cis* isomer, in which the secondary nitrogen atoms are in an *R* configuration and the central en-type chelate ring is δ-*gauche*. This structure is exactly the same as the Δ-*s-cis* form expected for the epro complex except for the minor difference between the secondary and tertiary nitrogens. Thus, it can be said that the stereospecificity of eddp-type ligands is identical to that of epro containing L-proline residues.

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