Circular Dichroic and Absorption Spectral Studies on Complexes of Nickel(II) with Optically Active Hydroxy Acids[1]

Leonard I. Katzin and Elsie Gulyas

Contribution from the Chemistry Division, Argonne National Laboratory, Argonne, Illinois 60439. *Received July 28, 1969*

Abstract: Circular dichroic spectra observed in the Ni(II) absorption bands are used to follow formation of, and changes in, complexes with optically active hydroxy acids. Reagents used are lactic, malic, and tartaric acids, and the lactones of the aldonic acids: arabonic, ribonic, gulonic, xylonic, galactonic, and gluconic acid. At low pH a complex with the acid anion is detected, for which the sign of the dichroism pattern correlates with the configuration at the α carbon of the ligand. With the aldonic acids, a second (1:1) chelate complex forms at higher pH by deprotonation of a hydroxyl. The sign of the dichroism correlates with configuration at the β carbon of the ligand. Both malic and tartaric acids show complexes involving one carboxyl, and both carboxyls, as a function of pH, but no hydroxyl deprotonation. Malic acid also shows evidence for a 2:1 complex. The higher-pH complex with arabonic acid has a different CD spectrum from the Ni(II) complexes of the other aldonic acids, and may represent at least partial chelation through other than the β hydroxyl.

This report continues the series of studies from this laboratory on the chemistry and spectroscopy of metal ion–ligand interactions, in which the significant tools are optically active ligands and circular dichroic spectral measurements. Previously reported investigations have dealt with interactions of α-amino acids and a series of hydroxy acids with rare earth ions,[2-4] and of the α-amino acids with Ni(II).[5] The present report relates findings with hydroxy acid–Ni(II) systems.

In the case of the rare earths, it was shown that hydroxy acid chelation occurred preferentially with a γ-hydroxyl group, forming a seven-membered ring,[2,4] but that β and probably even α chelation were also possible. At a pH that varied with the ligand, forced deprotonation of the coordinated hydroxyl could be demonstrated. It will be shown that Ni(II) chelates preferentially through a β-hydroxyl group, to give a six-membered chelate ring, and that under suitable conditions deprotonation occurs for these chelates also. Other significant deductions will also be pointed out. Relevant background details of the Ni(II) absorption spectrum and its analysis have been discussed in the report on the Ni(II)–amino acid systems,[5] and will not be repeated here.

Experimental Section

The CD and absorption spectral measurements were made on solutions in which the ligand to Ni(II) ratios ranged from about 1:1 to 3:1, and in some cases to 5:1. The pH range was from about pH 2 to (when feasible) pH 10 or 11. The techniques of recording the spectra were the same as previously described.[5]

The majority of the sugar acid ligands were available as the aldonic acid lactones. As the hydrolyzed form of the lactone was required, an equivalent amount of NaOH was allowed to react with the required amount of lactone in water for periods of from 20 min to 20 hr, as appropriate. Then 1 ml of 1 *F* $NiCl_2$ stock solution was added, and the volume adjusted to 6 ml with water, to give a solution about 0.16 *F* in Ni(II). The solutions with malic, tartaric, and lactic acids were prepared without the preliminary equilibration with NaOH.

When spectral effects of pH changes were to be determined, stepwise additions of 5 *F* NaOH (or 5 *F* HCl, when appropriate) were made to the initial solutions.

The stock solution was made from analyzed reagent $NiCl_2 \cdot 6H_2O$ (Mallinckrodt Chemical Works). Organic reagents were CP L-malic acid and D-galactonic-γ-lactone (Pfanstiehl Laboratories, Inc.), D-arabonic acid-γ-lactone and D-ribonolactone (K and K Laboratories, Inc.), gulonic lactone (Nutritional Biochemicals Corp.), glucono-δ-lactone (Matheson Co., Inc.), and analyzed reagent D-tartaric and L-lactic acids (J. T. Baker Chemical Co.). The γ-xylonic lactone was from a preparation believed to originate with J. W. E. Glattfeld.

Results

The characteristic dark green of aqueous Ni(II) becomes a bright, yellowish green as the cation is complexed by hydroxy acid. There is essentially no shift of the 393- and 657- nm absorption maxima, but there is an intensification. This may reach a factor of 2 at its maximum, but the ratio of the two absorption peaks stays almost constant, at around 2.8. This contrasts with the shift toward shorter wavelength, and marked drop in intensity ratio, of the amino acid and ammine complexes, with their characteristic blue color. In contrast to the spectrum of aqueous Ni(II), a weak absorption is visible in the hydroxy-acid complexes at about 280 nm. Otherwise the absorption spectrum between 250 and 700 nm is unrevealing.

Lactic acid–Ni(II) solutions with 1:1 ratio of reagent and Ni(II) show no CD at pH 2, but the start of an effect in the Ni(II) absorption region is found at pH 3. With further addition of NaOH, the Ni(II) precipitates. The solutions were more NaOH-resistant, and the CD more intense, as the ratio of lactic acid to nickel was increased, until with a ratio of 5:1, a pH between 6 and 7 could be achieved before precipitation. The CD, aside from intensity variations, has the same pattern for all of these systems (Figure 1): a strong, narrow negative dichroism with extremum at 380 nm, with perhaps a very weak positive at about 435 nm, and a strong, broad negative CD approximately centered on the absorption peak at about 663 nm.

The systems of Ni(II) with the monocarboxylic (polyhydroxylic) sugar acids have certain characteristics in common. The first signs of a complex CD show at from pH 2 (ribonic, xylonic acids) to between pH 3 and 4 (galactonic acid). All components of a given spectrum

(1) Work performed under the auspices of the U. S. Atomic Energy Commission.

(2) L. I. Katzin, *Inorg. Chem.*, 7, 1183 (1968).
(3) L. I. Katzin and E. Gulyas, *ibid.*, 7, 2442 (1968).
(4) L. I. Katzin, *ibid.*, 8, 1649 (1969).
(5) L. I. Katzin and E. Gulyas, *J. Amer. Chem. Soc.*, 91, 6940 (1969).

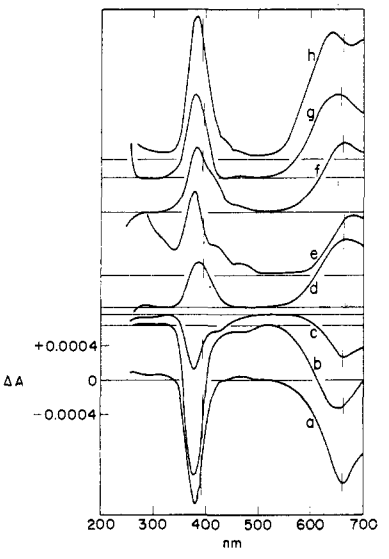

Figure 1. CD spectra of low-pH complexes of Ni(II) with hydroxy acids. Ni(II) about 0.16 *F*, 10-mm cell; dichroism in absorbancy units, scale indicated; vertical bars, location of maxima of absorption bands; (a) lactic acid, 5:1, pH 7; (b) arabonic acid, 3:1, pH 7; (c) arabonic acid, 1.1:1, pH 6; (d) gluconic acid, 2:1, pH 4; (e) galactonic acid, 3:1, pH 6; (f) xylonic acid, 1.5:1, pH 6; (g) gulonic acid, 5:1, pH 3; (h) ribonic acid, 3:1, pH 6.

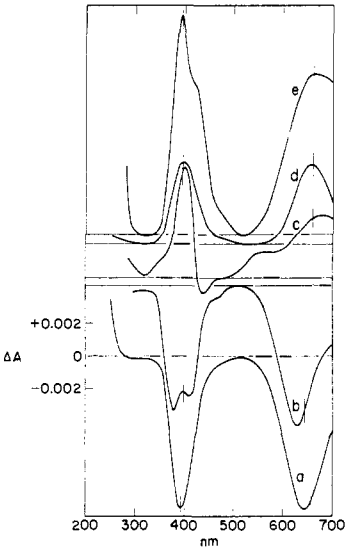

Figure 2. CD spectra of higher-pH (deprotonated) complexes of Ni(II) with hydroxy acids. Ni(II) about 0.16 *F*, 10-mm cell; dichroism in absorbancy units, scale indicated. Vertical bars, location of maxima of absorption bands; (a) ribonic acid, 1.25:1, pH 7; (b) gulonic acid, 3:1, pH 6–7; (c) arabonic acid, 1.1:1, pH 7 (scale multiplier, 0.5); (d) galactonic acid, 1.5:1, pH 7; (e) gluconic acid, 2:1, pH 7 (scale multiplier required, 0.2).

seem to be of the same sign (Figure 1). A titration at around pH 7 results in a second complex form, with a CD (Figure 2) several times more intense than that of the lower-pH form (pH 6–7 for gulonic acid). The $\Delta\epsilon/\epsilon$ for the higher-pH form of the ribonic acid complex, for example, is 4.7×10^{-3} for the 395-nm peak, and 11.2×10^{-3} for the peak in the red. The various components for this CD spectrum are most generally of uniform sign, not necessarily the same as that of the low-pH form, but occasionally complexities are seen under the conditions of the measurement. In general, the CD spectra for both forms are independent of ligand ratio, from about 1.2:1 to even 5:1, but there are

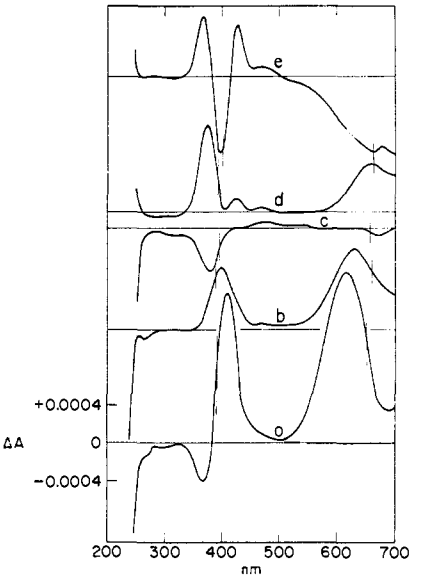

Figure 3. CD spectra of dicarboxylic acid complexes of Ni(II). Ni(II) about 0.16 *F*, 10-mm cell; dichroism in absorbancy units, scale indicated; vertical bars, location of maxima of absorption bands; (a) malic acid, 5:1, pH 4; (b) malic acid, 1:1, pH 4; (c) malic acid, 5:1, pH 2; (d) tartaric acid, >5:1 (Ni(II) *ca.* 0.12 *F*), pH 2; (e) tartaric acid, 1:1, pH 3 (scale multiplier required, 2.5).

some intensity and pH-stability effects which are attributable to variations in degree of complexing at equilibrium. Further changes are seen generally at quite high pH (10–11 or higher), but gulonic acid shows a change at about pH 9 which is but slowly reversed on addition of acid, and is one of the complications in working with ligand–Ni(II) ratios near 1:1. The high-pH systems were not further investigated.

The dicarboxylic acid, malic acid, is the hydroxy homolog of aspartic acid. At pH 2, the systems with Ni(II) show a weak negative dichroism at 380 nm, particularly with higher ratios of malic acid to Ni(II). At about pH 3 all systems show a different CD, with titration of the acid (Figure 3). For the 1:1 ratio of ligand to Ni(II) this is a positive CD, with one maximum at 400 nm, and another broader one at about 640 nm. With 2:1 and higher ratios of ligand, the spectrum takes on the complex structure of a negative extremum at 370 nm, a strong positive at 412 nm, and a strong positive at about 610 nm, going essentially to zero at about 670 nm. The high-ratio systems are only a little less pH sensitive than the 1:1 system, pH 5–6 being about as high as could be achieved before precipitation intervened.

At pH 2, 1:1 tartaric acid–Ni(II) has a faint positive CD in the 400-nm region. With 3:1 ligand–Ni(II) ratio, the CD at pH 2 becomes strong enough to recognize as similar to the gluconate "acid" form, though much weaker (Figure 3). At both ligand ratios, the systems titrate starting at pH 3, to yield a very intense multicomponent spectrum (Figure 3). This may be resolved into three positive components at 380, 425, and 480 nm, and an intense negative component at 400 nm. The peak of a broad negative band apparently coincides with the absorption peak at about 660 nm. This spectrum is stable to pH change until the onset of precipitation at about pH 6. Ratios as high as 5:1 show no new spectral features.

Discussion

The relevant spectroscopy of the Ni(II) complexes was discussed in connection with the amino acid systems,[5] and will not be further reviewed here. It is interesting, from the standpoint of differential intensity, that the transition to the Γ_3, $\Gamma_4(^1G)$ upper state, at about 280 nm, which is not visible in the spectrum of aqueous Ni(II), reaches observable intensity in the complexes with the hydroxy acids. Though not remarked on in the amino acid report,[5] it could also be seen in the spectra of the complexes with serine.

The CD in the 400-nm region for the polyhydroxylic acid complexes shows the contribution of the transition to the octahedral $\Gamma_4(^3P)$ upper state around 410 nm, but it is not clear whether this has two components as in the case of the amino acid complexes. The indication is that there may well be two, but of the same sign, rather than the different signs that the amino acid complexes showed. What is new in the CD spectrum is a definite component that corresponds to the transition to the $\Gamma_5(^1D)$ upper state, at 450–470 nm. In one system, arabonic acid–Ni(II) above pH 7, there apparently is a unique CD contribution from the transition to the $\Gamma_4(^1G)$ upper state, slightly below 350 nm. With one or two special exceptions, which will be discussed below, the CD spectrum of a hydroxy acid complex with Ni(II) seems to be uniform in sign, rather than showing overtly components of both signs, as in the case of the amino acid complexes. Nevertheless, the differences in shape, extremum location in reference to the absorption maximum, etc., make it clear that the same spectral components are involved. This points up again the variations, between different complexes of a metal ion, of the relations of sign and intensity between different components of its CD spectrum.

The rare earths[2,4] showed one CD spectrum for complexing with a polyhydroxylic acid in the mildly acid region, which was replaced by a second, much more intense spectrum subsequent to hydroxyl deprotonation at pH 7 or so. The sign pattern of the neutral-region complex of the rare earth systems was correlated with the configuration at the γ carbon. The CD of the acid-region complex of Eu(III) showed correlation with the γ configuration, while in the case of Pr(III) the sign of the CD for the acid-region complex correlated with the configuration at the α carbon. The CD of the Ni(II) complexes with the hydroxy acids also show configuration correlation, as seen in Table I. In this case, the sign of the acid complex CD correlates with the configuration at the α carbon, as with Pr(III), but the sign of the intense neutral-region complex correlates with the configuration at the β carbon, which is different from the rare earth cases. The systems which are ambiguous (primarily because of nonuniform CD sign) will be discussed in detail further below.

In the case of the Pr(III) complexes, the γ chelation deduced for the neutral-region complexes led to the inference that the acid complexes were also γ chelated. The overt γ carbon correlation for the acid complexes of Eu(III) seemed corroborative. It is reasonable therefore to apply the same argument to the Ni(II) complexes with the aldonic acids, and to consider them β chelated even in the acid-region complex. Lactic acid has but a single α-hydroxyl group, so cannot form a β chelate. The CD of the Ni(II)–lactate complex (at high ratio) is noticeably different from the 1:1 complexes with the polyhydroxylic carboxylates, as it effectively shows only a single, strong 380-nm component in the 400-nm region. This difference by itself could be that between α chelation and β chelation, but it could also be a difference between nonchelation and β chelation, or even between mono and bis complexation. It is suggestive that, at 1:1 stoichiometry, arabonic acid, like the other polyhydroxylics, definitely shows two components in the 400-nm-region CD, but at 3:1 ratio has a CD like lactic acid (Figure 1). An infrared study of ion effects on hydroxy-acid OH vibrations[6] has suggested that lactic acid interacts strongly with Ni(II), possibly through chelation.

Table I. Correlation of CD Sign with Configuration of Ligand Hydroxyl, Ni(II)–Hydroxy Acid Systems

Reagent acid	CD sign, Ni(II) complex		–CHOH– configuration at carbon indicated		
	Low pH	Higher pH	α	β	γ
Lactic	Neg		L		
Ribonic	Pos	Neg	D	D	D
Arabonic	Neg	( )[a]	L	D	D
Xylonic	Pos	Pos	D	L	D
Gluconic	Pos	Pos	D	L	D
Galactonic	Pos	Pos	D	L	L
Gulonic	Pos	Neg	D	D	L[b]
Malic	Neg	( )[a]	L		
Tartaric	Pos	( )[a]	D	L	

[a] CD spectra not comparable to majority; see text and Figures 2 and 3. [b] Configuration in Figure 1, reference 2, erroneous.

Ni(II) readily undergoes α chelation, as evidenced for example with the amino acids. It is striking that neutral-region complexes with the sugar acids, which for the rare earth cations involve the γ-hydroxyl, in the case of Ni(II) generally make use of the β-hydroxyl.

The pK values for dicarboxylic malic acid[7] are 3.46 and 5.10, and for tartaric acid, a bit lower. With high concentrations of these acids, at pH 2, singly charged anions and uncharged acid should predominate, hence it is reasonable that the Ni(II) complex CD apparently follows the behavior of the monocarboxylic acids (Table I). The change in the CD spectrum for 1:1 malic acid–Ni(II), which starts at about pH 2.5, is presumably the consequence of complexing through both carboxyls, which are now ionized. The dominance of the CD component at 400 nm, in the 1:1 system, at higher wavelength than the absorption maximum, as against the 380-nm component for the monocarboxylic acid complexes, is rather like the CD difference between the aspartic acid complex and the α-amino chelates.[5] Malic acid shows no CD sign attributable to a deprotonation reaction. A simple titration experiment with a 1:1 system shows that with 1.75 equiv of base per Ni(II) (seven-eighths neutralization of the acid) the pH reached is 4.0; another 0.25 equiv gives precipitation. This may be taken as confirmation that hydroxyl deprotonation is not taking place. The CD spectrum shown with higher ratios of malic acid to Ni(II) is the only evidence for any of the reagents in this series that suggests a bis complex.

The faint CD of the 1:1 tartaric acid–Ni(II) system shows a marked change even by pH 2.3, indicating onset

(6) J. D. S. Goulden, *Spectrochim. Acta*, **16**, 715 (1960).
(7) H. A. Sober, Ed., Handbook of Biochemistry, Chemical Rubber Co., Cleveland, Ohio, 1968.

of the second spectral form, and by pH 3 this has the characteristic form. The intensity relative to the malic acid CD, as well as structural differences, suggest that possibly deprotonation of one or more hydroxyls might be involved. A titration experiment shows again that but a few per cent excess base over that required to neutralize the tartaric acid brings the solution to pH 5.9, and any more alkali leads to instability and precipitation. One is therefore not dealing with hydroxyl deprotonation, and the difference from malic acid must involve the presence of the additional hydroxyl. A model of the tartaric acid molecule shows that the two hydroxyl oxygens, and one oxygen from each of the carboxyls, are capable of surrounding a hollow in which a metal ion can be readily coordinated by all four oxygens.

The Ni–tartrate CD spectrum for the pH 4–6 region can be resolved well. The positive 370-nm component ($\Delta\epsilon = 15 \times 10^{-3}$, $|\Delta\epsilon/\epsilon| = 2.6 \times 10^{-3}$) is attributable to the transition to $\Gamma_1(^1G)$. The negative 400-nm component ($\Delta\epsilon = -27 \times 10^{-3}$, $|\Delta\epsilon/\epsilon| = 2.1 \times 10^{-3}$) and the positive 425-nm member ($\Delta\epsilon = 11 \times 10^{-3}$, $|\Delta\epsilon/\epsilon| = 4.2 \times 10^{-3}$) may be presumed to have split from the original $\Gamma_4(^3P)$ upper level under C_{2v} symmetry. The transition to the $\Gamma_5(^1D)$ state appears as a CD component at about 480 nm ($|\Delta\epsilon/\epsilon| = 3.5 \times 10^{-3}$). At the 660-nm absorption peak, the CD of uniform sign has the apparent parameters $\Delta\epsilon = -14.6 \times 10^{-3}$, $|\Delta\epsilon/\epsilon| = 2.7 \times 10^{-3}$. At higher tartrate–Ni(II) ratios, the CD spectrum can be described, through the pH 2–4 range, as containing a mixture of large amounts of the "monocarboxyl" spectrum (mostly a positive peak at about 375 nm and a broad one in the 660-nm region) with the "dicarboxyl" spectrum, which seems reasonable.

Confirmation that with the monocarboxylic sugar acids the transition from the low-pH CD form to the second form in the neutral region actually involves a deprotonation, as postulated, is obtained with the following sort of experiment. Galactonolactone is equilibrated with a slight excess of NaOH, to full hydrolysis and neutralization. It is then mixed with Ni(II) to 1.1:1 ratio. The resulting pH is 4.75, and the CD spectrum is that of the low-pH complex, with the positive component at about 375 nm having an apparent $\Delta\epsilon$ of 4.4×10^{-3}. A similar solution but with an additional 0.5 equiv of NaOH shows the intense "neutral" CD, and a pH of only 7.15; while with a full equivalent of NaOH the pH rises only to 7.50. A proton titration is obviously in progress. With somewhat larger excess of NaOH, say another 0.5 equiv, precipitation commences.

The superficial appearance of the arabonic acid–Ni(II) system is as the sign-inverse of the tartrate system. There are differences, however, which seem to be significant. One is the early formation, during the deprotonation, of a positive peak below 350 nm, unique among the hydroxy acid–Ni(II) systems (Figure 2c), and not readily to be explained as a tail of a broad 400-nm-region CD in combination with some residual, negative low-pH form. It would appear to be a CD of the transition to $\Gamma_4(^1G)$,[5] as its relation to the peak at 400 nm does not change with further addition of alkali. Similarly, the two components apparent in the red region maintain constant relations, on further alkali addition. The behavior differs from that of the majority of the monocarboxylic acid systems, which suggests that perhaps in the case of arabonic acid a different hydroxyl than the β is involved, either alone or in addition to that hydroxyl.

The correlation of sign of CD with, on the one hand, configuration at the α carbon to which the carboxyl group is attached, and on the other, the β carbon (or for the rare earths, the γ carbon), to which the deprotonated hydroxyl group is attached, is reasonable in terms of relative binding strengths at the two points of attachment, for the low- and higher-pH forms of complex, respectively. The difference in sign between amino acid[5] and hydroxy acid ligand of the same configuration (*e.g.*, alanine and lactic acid) leaves more varied possibilities for explanation. The obvious one, of course, is the difference between amino nitrogen and hydroxylic oxygen as chelating donors. The validity of this choice may be in question because it is not definite that, with Ni(II) as the metal ion, lactic acid is in fact chelating. One may thus be comparing chelation with monodentate attachment. On the other hand, it may not matter, since chelation through a β-hydroxyl, as in the low-pH polyhydroxylic systems, is spectrally equivalent, inasmuch as the low-pH correlation with configuration at the α carbon seems to be without exception. The two slightly different forms of low-pH arabonic–Ni(II) CD noted above, if they are interpretable as chelate and nonchelate, would suggest the same thing, since no sign difference is seen. With Eu(III) complexes, the signs of the diagnostic CD components at the $^5D_1$ and $^5D_4$ upper states,[4] in the presence of lactate,[8] are the same as for the alanine chelate; the CD below 400 nm is comparable with that for the low-pH polyhydroxylic acid complexes; and the absorption spectrum is not distinguishable from those chelates, nor from the amino acid chelates. It would seem then that while alanine and lactate complexes in the rare earths show equivalent CD signs, in nickel complexes they do not. One may cite further the appearance of components of opposite signs in the 600-nm region for the Ni(II)–amino acid complexes, whereas only uniform signs are seen in the hydroxy acid systems. The implication is that, whereas in this comparison the difference between the sharing of nitrogen electrons and of oxygen electrons does not influence the sign of CD for the rare earth complex, it does influence that of the components of the Ni(II) complex spectrum.

A CD spectrum has been published for a Ni(II)–(−)-mandelic acid solution,[9] which apparently has the characteristics indicated in the present work for low-pH hydroxy acid systems. The sign of the dichroism is positive, opposite to that found here for L-lactic acid. From chemical studies, (−)-mandelic acid has been assigned to the D series of α-hydroxy acids,[10] which agrees with the correlation of the CD spectral signs. One may conclude then that substitution of the methyl group of lactic acid by the phenyl group of mandelic acid does not perturb the forces giving rise to the correlation of Ni(II) CD sign with configuration of hydroxy acid.

(8) L. I. Katzin, unpublished results.
(9) R. Larsson and B. Folkesson, *Acta Chem. Scand.*, **22**, 1970 (1968).
(10) K. Mislow, *J. Amer. Chem. Soc.*, **73**, 3954 (1951).