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PMR Studies of Nickel(II)-DTPA Complexes Aqueous Solutions

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The type of coordination and conformations of the NiDTPA complexes over a wide pH range were determined. PMR and IR measurements show that only a part of the carboxylic groups coordinate to the metal ion. By deuterating the methylene groups in the acetate part of the ligand an exchange between the coordinated and uncoordinated carboxylic groups was found to be possible. Rate constants, enthalpies and entropies for the proton–deuterium isotopic exchange reaction were determined. Conversion times for the processes taking place in solutions were estimated.

Introduction

Conformational analysis of coordinated chelating ligand molecules and the structure of complexes formed in solution in the case of polydonor ligands is an important problem in modern coordination chemistry [1]. Studies on a potentially eight-donor ligand – diethylenetriaminepentaacetic acid (DTPA) – taken up by us, are an attempt to solve several problems concerning the structure, dynamics and equilibria of the complexes existing in aqueous solutions. DTPA may coordinate with the metal ions in various ways, depending on pH. As indicated in our last study on the Hg–DTPA system [2] and work by Letkeman and Westmore [3] on Cd(II) and Pb(II) complexes with DTPA, some carboxylic groups are not bound to the central ion.

For the central ions with higher coordination numbers, *e.g.* Th(IV) [7], the metal atom binds all the acetate groups (5) and (Fe(III) four of them [8]. In the Ni(II) and DTPA containing solutions one should rather expect that only some acetate groups will be linked to the metal ion. The structure where not all nitrogens are within the coordination sphere of a metal are also permissible. Studies of the Ni(II)–DTPA system by the PMR method makes it possible to determine the type of complexes appearing in solution over a broad pH range. A large chemical shift over which the spectrum is observed (180 ppm) and utilization of the relationship between the chemical shift and dihedral angle determined by the Ni–N–C and N–C–H planes [4–6] enable to describe chelate ring conformations of the diene part. This problem was insolvable for the diamagnetic systems because of diffuse lines. In order to assign the PMR lines to the respective ligand proton groups it was necessary to carry out selective deuteration.

Experimental

Preparation of Samples

For PMR measurements the samples were prepared by weighing stoichiometric portions of $NiCl_2 \cdot 6H_2O$ and DTPA (Merck). DTPA was converted into its potassium salt. $NiCl_2 \cdot 6H_2O$ was dissolved in D_2O and evaporated to dryness. The potassium salt of DTPA was treated in a similar way. This enabled to reduce the residual HDO signal. For measurements about 0.5 M solutions in D_2O were prepared. In order to obtain deuterated samples, the solution was heated up to 90 °C for several hours in a strongly alkaline medium.

For measuring the deuteration rates, a 0.1 M Ni-DPTA solution with 0.2 M excess KOD was used. The solution was heated up to a suitable temperature in a thermostat or kept in a refrigerator at about 4 °C. At certain intervals 0.25 ml samples of the reaction mixture were taken, cooled down to 6 °C and then treated with KCN in order to release the ligand and to convert the Ni(II) ion into a diamagnetic complex, $[Ni(CN)_4]^{-2}$. PMR measurements were made in the solution prepared in this way.

In order to examine the water line width, 0.1M solutions were used. In each case the pH-meter reading was converted as follows [9]:

$$pD = pH + 0.40$$

PMR and IR Measurements

NMR measurements were carried out in a JEOL-PS-100 spectrometer. All spectra are reported *vs.* DSS. The sweep width was calibrated by the sideband technique. A sweep width of 270 ppm was used. For the HDO line width, the sweep width was 0.54 for 1.08 ppm and the sweep rate was 0.2 cps/s.

In order to determine the temperature dependence of the chemical shift, methanol and glycol were used for accurate temperature measurements [10].

TABLE I. Aqueous IR Frequencies of NiDTPA complexes (cm^{-1}).[a]

pD	COOH	$NH^+CH_2COO^-$	COONi	COO^-
12.2			1595 vs	1615 sh
7.3			1995 vs	1615 sh
3.38	1730 vw	1625	1595 vs	
2.29	1725 w	1625	1595 vs	
$H_2NiDTPA$[b]	1735		1600 s	
$H(Ni_2)DTPA$ 3–5$(H_2O)_4(3H_2O)$			1590	

[a] vw, very weak; w, weak; sh, shoulder; s, strong; vs, very strong.

[b] Results for solid compounds obtained by R. Sievers and J. Bailar [13].

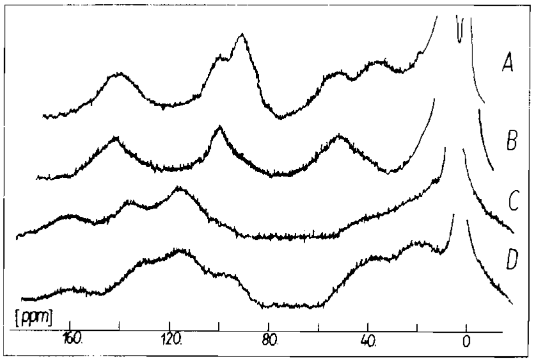

Figure 1. NMR spectra of NiDTPA solutions at pD = 3.38 (A, B) and pD = 10.0 (C, D). B and C spectra are for deuterated samples.

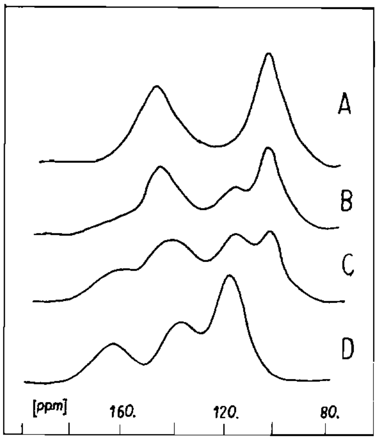

Figure 2. Comparison of NMR spectra of the deuterated samples at pD = 3.38 (A), 5.48 (B), 5.8 (C), 7.52 (D).

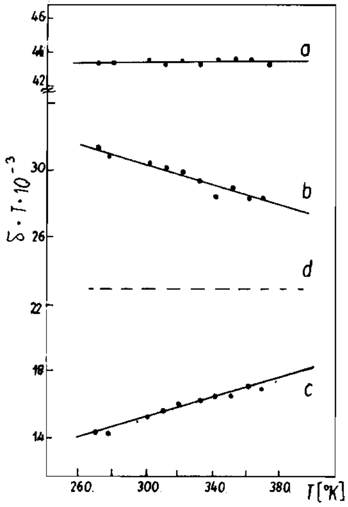

Figure 3. Temperature dependence of δT for pD = 3.38 (δ = chemical shift).

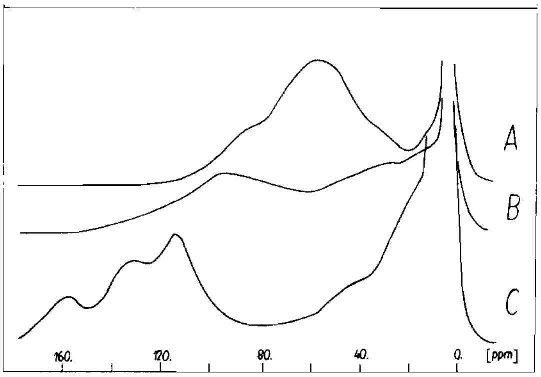

Figure 4. NMR spectrum shape dependence on temperature at pD = 9.98 for deuterated sample. (A) 353°K, (B) 333°K, (C) 303°K.

IR measurements were carried out on a Perkin–Elmer spectrometer for 0.5 *M* NiDTPA solutions in D_2O on KRS-5 plates, with the film thickness selected by trial (Table I).

Results

Typical PMR spectra at selected pD values are shown schematically in Figures 1 and 2. Since DTPA is a compound containing 18 non-labile protons, univocal assignments of all lines are very difficult to be carried out. Application of the selective deuteration suggested by Reilley *et al.* [11] simplifies the spectrum and enables to distinguish between the lines resulting from the methylene groups of the diene part and those derived from the methylene groups of the acetate part of DTPA.

TABLE II. Pseudo-first Order Rate Constants for Exchange of Acetate Protons.

T, °K	Side Acetate Group	Central Acetate Group
335.8	2.16×10^{-4}	2.23×10^{-5}
317.2	5.36×10^{-5}	5.61×10^{-6}
305.9	1.90×10^{-5}	
277.1[a]	7.19×10^{-7}	

[a] Result obtained for a single measurement. The sample was kept in a refrigerator for 24 hours (about 4 °C).

TABLE III. Activation Parameters for Acetate Protons.

	E_a Kcal/mol	$\Delta H^{\ddagger}$ Kcal/mol	$\Delta S^{\ddagger}$ cal/deg/mol
Side Acetate Groups	17.1 ± 1	15.5 ± 1	−24.7 ± 3
Central Acetate Group	15.0 ± 1	16.7 ± 1	−32.0 ± 3

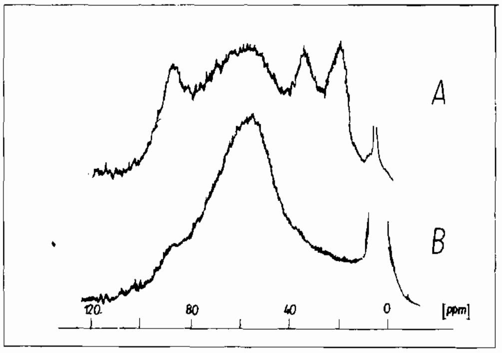

Figure 5. NMR spectra of NiDTPA solution for undeuterated (A) and deuterated samples at pD = 10.38, T = 353°K.

Essential information is provided by the dependence of the chemical shift product for particular lines on temperature. Such a relationship was examined for a sample deuterated at pD = 3.38 (Fig. 3). Because of a larger overlap of lines for samples with pD values exceeding 7 (even for deuterated systems) it was possible to carry out only a qualitative analysis of the spectrum contours (Fig. 4).

A comparison of the spectra for deuterated and undeuterated samples at 80 °C was found to be very interesting.

The acetate group lines in this spectrum are readily identifiable (Fig. 5). IR measurements in D_2O solutions make it possible to observe characteristic asymmetric stretching frequencies of the carboxylic groups related to the protonation or coordination state of that group, respectively [12]. The spectra obtained are presented in Figure 6. Assignment of shoulder band at 1615 cm^{-1} to the Ni–N–CH_2COO^- group frequency allows for Siever's and Bailar's suggestions concerning similar systems [13].

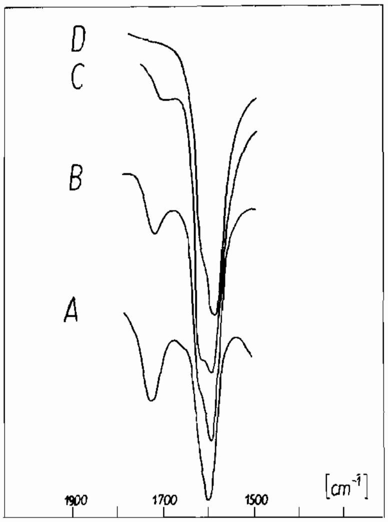

Figure 6. IR spectra of NiDTPA solutions at pD = 1.22 (A), 2.29 (B), 3.38 (C). D spectrum is obtained for all samples for pD above 7.3.

Deuteration

Because of the complexity of the NiDTPA spectrum, it was possible to observe only the resultant deuteration rate a ligand is released from the complex by the cyanide ion. Allowing for large similarities between the NiEDTA and NiDTPA structures, it was assumed that the inversion rate of side nitrogens, the interchange of acetate group sites, and the interchange of axial equatorial protons are much faster [11] than the deuteration processes.

The reaction satisfied the first order reaction equation with respect to the NiDTPA concentration. The reaction rates for the methylene groups of acetate groups at several selected temperatures are summarized in Table II. The corresponding data for the activation processes are provided in Table III. The values were found for several systems under investigation at various KOD concentrations. The values found are close to those obtained by Reilley [11] for EDTA.

The effect of pD on the water line width in the presence of NiDTPA was investigated. The relationship obtained is shown in Figure 7.

Discussion

The following complex ion structure in solutions of various pD values may be suggested (Fig. 8). Since the basic structure determining element is the diene part (N–en–N–en–N) of the ligand, considerations were carried out for a deuterated sample. The spectra at t = 30 °C were schematically summarized for the

TABLE IV. Spectral Assignments for Ni(II)DTPA Complexes at 30 °C.

Complex Species pD	Shift (ppm)	Deuterated Sample	Shift (ppm)	Undeuterated Sample
NiDTPA pD > 7	−160	N–CH$_2$ eq	−160	N–CH$_2$ eq
	−129	N–CH$_2$ eq	−129	N–CH$_2$ eq ac
	−114	CH$_2$–N–CH$_2$ eq	−114	CH$_2$–N–CH$_2$ eq
			−90	
	−35^a	N–CH$_2$, CH$_2$–N–CH$_2$ eq	−35	NCH$_2$, CH$_2$–N–CH$_2$, ac
	−15^a		−15	ax
NiDTPA pD = 3.38	−140	CHN–CH$_2$ free	−140	N–CH$_2$ free
	−101	N–CH$_2$, CH$_2$–N–CH$_2$ eq	−101	N–CH$_2$, CH$_2$–N–CH$_2$, eq
			−95	ac eq
	−50	N–CH$_2$, CH$_2$–N–CH$_2$ ax	−50	N–CH$_2$, CH$_2$–N–CH$_2$ ax
			−20	ac eq
	0	N–CH$_2$ free	0	N–CH$_2$ free, ac free

^{a}Very broad. ac, acetic CH$_2$ protons; ax, axial; eq, equatorial.

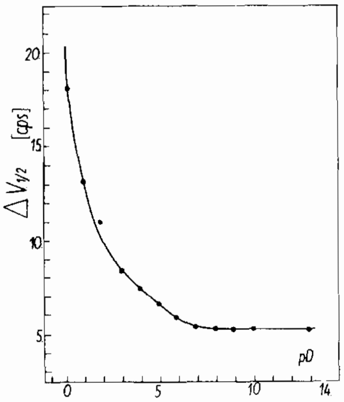

Figure 7. pD dependence of water proton line half-width.

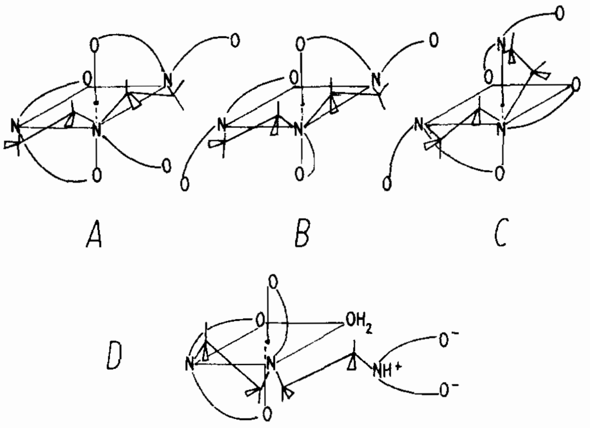

Figure 8. Probable structures of Ni(II)DTPA complexes. A, B, C: pD > 7; D: pd < 7.

NiDTPA (D) systems at pD 3.38, 9.98 and the spectra obtained by Reilley *et al.* [14] for the Ni(dien)(H$_2$O)$_4$, Ni(dien)(tach), Ni(dien)(dap) systems (Fig. 9).

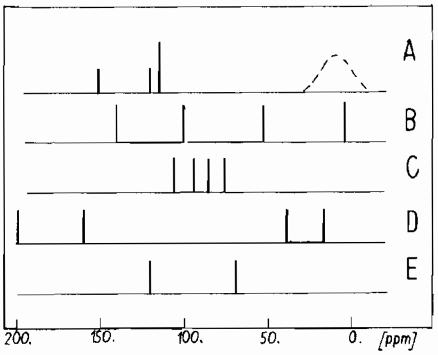

Figure 9. Schematic NMR spectra of: (a) Ni(II)DTPA complex at pD = 9.98, deuterated sample; (B) Ni(II)DTPA complex at pD = 3.38, deuterated sample; (C) Ni(II)dien complex; (D) Ni(II)dien(dpa) complex – only dien part; (E) Ni(II)dien(tach) complex – only dien part. tach = 1,3,5-cyclohexatriamine, enforces a facial coordination; dpa = dipicolinic acid, enforces a meridional coordination. C, D., E are taken from ref. 14.

A comparison of the NMR spectrum obtained with the results reported by Reilley *et al.* [14] enables to suggest a meridional coordination of the diene nitrogens. From the molecular model it can be seen that in the case of a facial coordination the steric hindrance would be very large. Therefore, the C structure is improbable in this case.

The difference in chemical shifts of the diene part of the NiDTPA in comparison with the Ni(dien)(tach) is clear when one considers more precisely the appropriate amines. In case of the NiDTPA the aliphatic protons of the diene part are localised between the ternary nitrogen atoms. In case of the Ni(dien)(tach) the appropriate protons are localised between the binary and primary nitrogens. It is known [6] that the contact shift of the Ni(II)–amine complexes with the ternary nitrogens is smaller than for the Ni(II)–amine complexes with the primary and binary nitrogens (amines act as the chelating ligands). Our results are in agreement with that regularity.

The comparison of the shape of the spectra of Ni-DTPA and Ni(dien)(tach) in spite of differences in absolute chemical shifts provided the essential conclusions about the geometry of the NiDTPA complex (see above).

It is difficult to estimate the effect of coordination through the carboxyl groups on the Ni(II)–N bond strength and hence on the magnitude of chemical shifts [15]. The magnitudes of chemical shifts in the equatorial part of the spectrum are consistent with the values found for EDTA [11] and EDDA [16].

The transition from pD10 to 3 resulting from addition of one proton, as found potentiometrically [17], is manifested by a principal structural change in the spectrum [Figures 1, 2].

At intermediate pD values (from 4 to 6) the discernible lines of both complex species of suitable life-times are found to be overlapped. The suggested assignments of spectral lines to the corresponding proton groups in the complex are provided in Table IV. The magnitudes of chemical shifts are given for 30 °C.

For pD = 10 the ratio of PMR line intensities for the equatorial protons was 1:1:2 (their axial parts were too diffuse to integrate these lines). Such a line splitting results from unequal amounts of the CH_2-COO^- groups at terminal nitrogens linked to the metal ion. This case is analogous to that found in unequivalently N-substituted ethylenediamines [18]. For such a complex structure the equatorial (observed) and axial (unvisible) N–CH_2 protons should be distinguished, respectively; it is probable that the corresponding CH_2–N–CH_2 protons are equivalent. This is in agreement with the suggested A structure.

All 5 CH_2COO^- groups may enter ineterchangeably into possible coordination sites although the probability for the terminal groups to enter is higher. This is reflected in the reaction rate constants which are one order lower for the central acetate group. Since the deuteration process requires the metal–COO bond to be present [18], the contribution of the B structure, as shown by deuteration, is lower that that of the A structure. The type of changes occurring under the influence of pD is also confirmed by the IR spectroscopy. For pD $\geqslant$ 7 (A complex) the bands found are interpreted as corresponding to the coordinated (1595 cm^{-1}) and uncoordinated (1615 cm^{-1}) groups. A decrease in pD down to 3.4 results in the formation of a band at 1625 cm^{-1}, corresponding to the R_2–NH^+–CH_2COO^- frequency which indicates that one nitrogen was released from its coordination sphere and protonated. This corresponds to the D structure of the complex. A further decrease in pD reduces the 1625 cm^{-1} line intensity resulting in the appearance and intensity increase of the 1725 cm^{-1} line. The aminodiacetate group becomes then further protonated on the COO^- groups. The structural transition A $\rightleftharpoons$ D is confirmed by the line width studies (Fig. 4). A regular increase in the half-widths for pD $\leqslant$ 7 is an evidence that water enters the first coordination sphere [19–21].

A comparison of the spectra for deuterated and undeuterated samples (pD = 10) at 80 °C indicates that the diffuse band corresponds to the diene part while the three distinct lines (–80, –30, –10 ppm) correspond to the methylene protons of the coordinated acetate groups which, as for EDTA [11], do not average their shifts even at such high temperatures. The lines of the uncoordinated acetate groups may coincide with the diene part of the spectrum. The processes involving a rupture of the metal–COO^- bond, then metal–N bond, inversion at the nitrogen and addition to Ni(II) result in the deuteration of all acetate groups. These processes should be fast in comparison with the deuteration processes but slow for the NMR "time window".

A basic problem is the position of free acetate groups for structure A in the spectrum at room temperature. According to Reilley's findings [11] they should be located in the 80–90 ppm region for RT. This coincides, however, with the set of lines of the diene part observed in that region. Analysis of intensities is too inaccurate to definitely assign specific line positions in the spectrum to the uncoordinated groups. Analysis of the characteristic temperature dependence of the deuterated sample spectrum presented in Figure 4 should take into account the fact that in the case of structure A rapid changes in the en ring conformation of a $\delta \rightleftharpoons \lambda$ type are rather improbable. Because of a large steric hindrance, the complex equilibria of the A $\rightleftharpoons$ C type or inversion at the central nitrogen are also rather improbable [14]. Since the axial lines are found to be shifted up field, it may be estimated qualitatively that the temperature dependence of δT on T shows a deviation from parallelism with respect to the T axis. In order to explain this deviation one should assume the existence of a rapid equilibrium between some unequally filled states of molecules. The mechanism of these processes could be analogous to the NiEDTA case [24]. The other processes like nitrogen inversion are also possible.

The spectrum for lower pD's should be analyzed. In the case of deuterated sample, a spectrum consisting of four lines is observed. According to the suggested D structure, the line located in the diamagnetic spectral region corresponds to the unbound N–CH_2 groups [5]. Allowing for the temperature dependence $\delta T = f(T)$ it was assumed that the line at a minimum field corresponds to a free methylene group in CH_2–N–CH_2 and those at about –50 and –90 ppm are connected to the chelating ring through the axial and equatorial protons, respectively (line width about 12 ppm).

It may be assumed that there is a suitable conformation equilibrium of the chelate ring which is reflected in the dependence of δT on T being deviated from parallelism to the T axis for the ring protons (Fig. 3).

The intensity ratio of the lines found is 1:1:1 (the line in the highest field coincides partly with water) which corresponds to the suggested line assignment.

The occurrence of only one line for the axial protons and one for the equatorial protons is inexplicable.

In the case of undeuterated samples one line identified with the axial acetate protons appears at −30 ppm. The equatorial acetate protons provide a line at about −95 ppm. The line in the dia-range enhances its intensity which is an evidence that the CH_2COO^- protons of the uncoordinated part of DTPA are in this position.

Electronic integration of the equatorial part gives an intensity ratio of 2:5 which confirms the coordination of 3 acetate groups and is consistent with the D structure. Using the relationship [22]

$$\frac{1}{\tau} < \Delta\nu$$

one may estimate the rates of the following processes at room temperature:

i) $NiHDTPA \rightleftharpoons NiDTPA + H^+$

ii) Intramolecular N-transition for the D structure consisting in the exchange: terminal coordinated nitrogen ⇌ terminal uncoordinated nitrogen.

In instance i) the line at −140 ppm due to the coordination of free nitrogen is divided into two components: axial (−15 to −30 ppm) and equatorial.

Since no averaging of these lines is observed for the system under investigation, $1/\tau < 2.5 \times 10^3$. For process i) the rate constant of dissociation is lower than $1/\tau$ which is in agreement with the results obtained by other authors [23].

For process ii) the averaging process should comprise the −140 and −101 as well as −140 and −50 ppm lines. Hence, $1/\tau < 3.9 \times 10^3$.

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