Articles

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Coordination of 9-Methylhypoxanthine to [*cis*-$Pt(NH_3)_2]^{2+}$ and $[Pt(dien)]^{2+}$ As Studied by Proton NMR

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Received January 26, 1984

The reaction products of 9-methylhypoxanthine (mHyp) and [Pt(diethylenetriamine)Cl]Cl ([Pt(dien)Cl]Cl), or *cis*-$Pt(NH_3)_2Cl_2$ (*cis*-DDP), were separated by using CM-Sephadex C-25 cation-exchange chromatography and were investigated with ^1H NMR spectroscopy. The reaction was carried out at both pH 7.0 and 10.0. At pH 10, mHyp-*N1* coordination is facilitated. By studying the pH dependence of the NMR resonances, (de)protonations could be followed, providing evidence for certain structures. In the case of [Pt(dien)Cl]Cl the main products Pt(dien)(mHyp-*N7*), Pt(dien)(mHyp-*N1*), and [Pt-(dien)]$_2$(μ-mHyp-*N1*,*N7*) have been found. With *cis*-DDP the products, when an excess of mHyp is used, are predominantly *cis*-$Pt(NH_3)_2$(mHyp-*N1*)$_2$, *cis*-$Pt(NH_3)_2$(mHyp-*N1*)(mHyp-*N7*), and *cis*-$Pt(NH_3)_2$(mHyp-*N7*)$_2$, but four other minor species have also been observed. These species involve 1:1 Pt–mHyp adducts and a dinuclear product. It is shown that platinum binding to N1 of mHyp results in an increase of the pK_a of the N7 protonation. It appears possible to protonate a N1,N7-dicoordinated (bridging) mHyp below pH 1.5. The position of this added proton might be either N3 or O6.

Introduction

Soon after it was proposed that the antitumor drug *cis*-$Pt(NH_3)_2Cl_2$ (abbreviated *cis*-DDP) possibly acts by reacting with nucleobases in DNA, studies were started about nucleic acid constituents interacting with platinum compounds.[1-8] Platinum–guanosine or –inosine complexes are especially interesting[2-8] because of the known strong preference for platinum compounds for the guanine base in DNA.[1c]

It is apparent from crystal structures of compounds containing GMP (or derivatives) and platinum[2] that metal binding almost universally occurs at N7. IMP (and derivates), however, not only coordinates via the N7 but also via N1, in case the N7 is methylated.[3,4] In solution, Raman,[5] UV,[6] and NMR[7,8] spectroscopy are mostly used; of these, the latter technique yields most information and all species can be followed by their own specific resonances. ^{13}C NMR[7] is particularly useful for assigning binding sites in simple nucleobases, but ^1H NMR is used more often especially in the case of oligonucleotides.[8,9]

Summarizing these results, one can say that at neutral pH the N7 atom is the most likely binding site and in that case a lowering of the pK_a of the N1 protonation is apparent.[2c,5] At basic pH,[5a,7a,8a] however, or when the N7 is methylated,[4] N1 is the more reactive site. The consequences of N1 being singly coordinated and also of N1,N7 dicoordination are hardly known, and only a few analogue palladium complexes have been described.[10]

Therefore, we are investigating platinum–oxopurine complexes with the aim to obtain detailed information from the pH dependence of the ^1H NMR chemical shifts between pH 1 and 10.[9]

In the present study, we used 9-methylhypoxanthine (mHyp) (see Figure 1) as a simplified analogue for inosine (the sugar moiety in Ino is replaced by a methyl group). The reaction of mHyp and [Pt(dien)Cl]Cl (dien = diethylenetriamine) or *cis*-DDP (Figure 1) was performed at physiological pH (pH 7) and at a pH where N1 coordination is expected to be facilitated (pH 10). After reaction, the products were separated by using low-pressure cation-exchange chromatography. The pH dependence of the ^1H NMR chemical shift of each compound was studied, and N1 and N7 singly coordinated and N1,N7 dinuclear products are described.

Experimental Section

Starting Materials. mHyp was synthesized by oxidation[11] of the exocyclic NH_2 of 9-methyladenine.[12] *cis*-$Pt(NH_3)_2Cl_2$ and [Pt-(dien)Cl]Cl were synthesized as previously described.[13,14] The latter compound was precipitated from water with acetone, preventing the inclusion of NO_3^- anions.

Syntheses. The reaction between mHyp and [Pt(dien)Cl]Cl was performed with a slight excess of mHyp (1.2:1), and the one with *cis*-DDP in the ratio 2:1 (two bases to one *cis*-DDP). The (typical)

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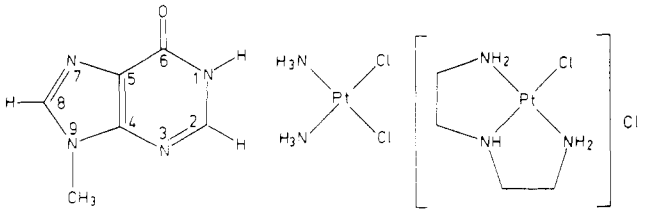

Figure 1. Schematic structures of mHyp, *cis*-DDP, and [Pt(dien)Cl]Cl.

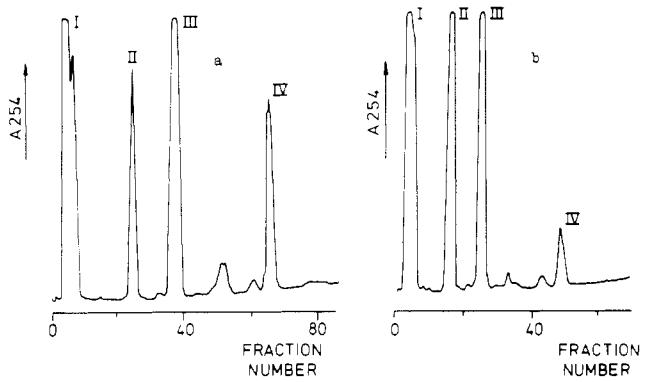

Figure 2. Elution patterns of reaction mixture of mHyp + [Pt(dien)Cl]Cl, reacted at pH 7 (a) and pH 10 (b).

5×10^{-3} mol/L mHyp reaction mixtures were stirred and brought to pH 7 or 10 with NaOH solution, directly after addition of the platinum compound. After 24 h at 50 °C in the dark, the reaction mixtures were concentrated by using a rotary evaporator. Separation was achieved by cation-exchange chromatography and elution with a linear triethylammonium hydrogen carbonate (TEAB) gradient (column 15 × 2.5 cm CM Sephadex C-25; eluent 0.0–2.0 M TEAB in doubly distilled water with a total volume of 2 L). TEAB is a volatile salt that is removed from the product by evaporation or lyophylization.

NMR Sampling. NMR samples were prepared by lyophylizing the appropriate amount of eluted solution, dissolving the residue in 1 mL of D_2O (99.8%) and lyophilizing again. Finally, the material was dissolved in 0.5 mL of 99.95% D_2O, and a 3 mM sample was obtained. A trace of tetramethylammonium nitrate was added as an internal reference. However, chemical shifts are reported relative to the sodium salt of 4,4-dimethyl-4-silapentanesulfonic acid (DSS) [$\Delta\delta$(TMA–DSS) 3.18].

NMR Measurements. NMR spectra were recorded on a Bruker WM-300 spectrometer, interfaced with an Aspect-2000 computer for data handling. The residual HDO peak was reduced by selective irradiation. The pH of the samples was adjusted by adding small quantities of concentrated NaOD or DCl solutions to the samples and was measured before and after each NMR experiment. The pH, reported as pH*, is not corrected for the deuterium isotope effect (pK_a's measured in H_2O and D_2O are virtually the same[10]). At the end of each titration experiment, the pH* was taken to 10.5. After heating the samples for about 1 h, the H8 protons were largely exchanged with D_2O, allowing their assignments.

Nomenclature. The common nomenclature for inorganic compounds is combined with the one accepted recently on nucleic acid constituents and abbreviations.[15] In formulas, the metal ion is listed first, followed by the ligands. In case of ambiguity, the coordinating atoms of the ligand are indicated (according to ref 15) after the ligand, separated by a hyphen and in italics. Bridging ligands are indicated by the prefix μ. A coordinating *cis*-$Pt(NH_3)_2^{2+}$ is indicated by the abbreviation *cis*-Pt.

Results and Discussion

Reaction of [Pt(dien)Cl]Cl with mHyp. In Figure 2 the elution patterns of the reaction mixtures of mHyp with [Pt(dien)Cl]Cl at pH 7 (Figure 2a) and at pH 10 (Figure 2b) are shown, achieved by elution with 0–2 M TEAB on a CM Sephadex C-25 column. Under the neutral elution conditions

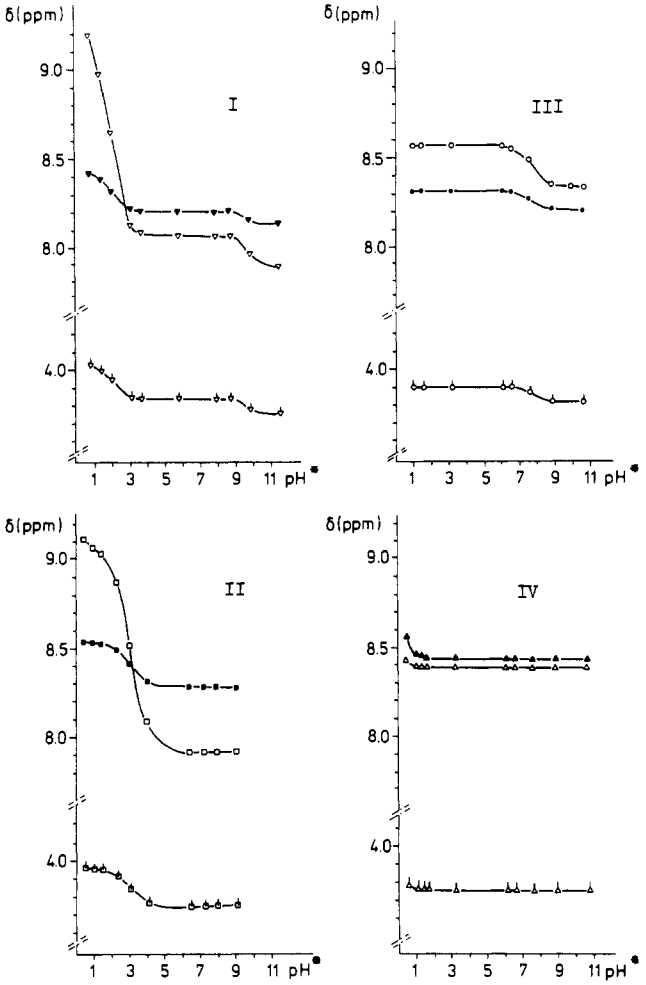

Figure 3. Chemical shift (δ) vs. pH* profiles for the Pt(dien) reaction products: open symbols, H8; closed symbols, H2; symbols with stick, H_3–C9. Peak, symbol, species: I, ▽, mHyp; III, ○, Pt(dien)(mHyp-*N7*); II, □, Pt(dien)(mHyp-*N1*); IV, △, $[Pt(dien)]_2$(μ-mHyp-*N1*,*N7*).

used, the N1 of mHyp is protonated, unless this position is occupied by platinum. Thus, each possible species has a different charge: unreacted mHyp has a zero charge and will be eluted as peak I, Pt(dien)(mHyp-*N1*), having a charge 1+, as peak II, Pt(dien)(mHyp-*N7*), having a charge 2+, as peak III, and $[Pt(dien)]_2$(μ-mHyp-*N1*,*N7*) as peak IV (charge 3+). The few small remaining peaks do not contain purine bases and were therefore not investigated further.

As can be seen directly from the elution pattern from the reaction at pH 7 (Figure 2a), the N7 product largely predominates, whereas the N1 and the dinuclear species are present in smaller amounts. When the reaction is performed at pH 10 (Figure 2b), the N1- and the N7-bound products are formed in approximately equal amounts together with only a small amount of dinuclear species. This indicates no large preference for the formation of the dinuclear product under these conditions.

The three possible Pt(mHyp) adducts are now identified, and with "free" mHyp as a reference, the pH dependence of the chemical shifts can be studied (Figure 3). From these results, conclusions can be drawn about the influence of platinum binding on mHyp protonation equilibria.

As can be seen in Figure 3-I, "free" mHyp exhibits its N1 deprotonation at pH* 9.5 and its N7 protonation, with the characteristic large H8 chemical shift change, at pH* 2. Coordination of a platinum at N7 prohibits protonation at that site and also results in the well-known lowering of the pK_a of the N1 (de)protonation[2c,5] by approximately 1.5 pK units

(15) IUPAC-IUB Joint Commission on Biochemical Nomenclature, Recommendations (1982): *Eur. J. Biochem.* **1983**, *131*, 9–15.

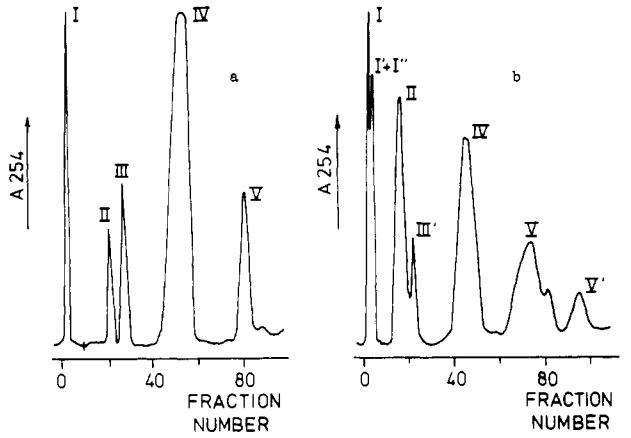

Figure 4. Elution patterns of reaction mixture of mHyp + *cis*-DDP, reacted at pH 7 (a) and pH 10 (b). The same numbers in a and b indicate same species.

(Figure 3-III). In contrast, coordination at N1 results in a change of the pK_a of the N7 (de)protonation in the opposite direction (Figure 3-II); in this case, the pK_a changes from 2 in mHyp to 3 in Pt(dien)(mHyp-*N1*). This effect is rationalized by the fact that $[Pt(dien)]^{2+}$ is much less polarizing than a proton. In $[Pt(dien)]_2(\mu$-mHyp-*N1,N7*) (Figure 3-IV) a protonation below pH 1.5 is also evident. Because both N1 and N7 are coordinated to platinum, with a less polarizing effect than protons, a protonation can now be expected that normally takes place only below pH −1. This protonation is believed to take place either at the O6 or the N3 position. Despite the latter uncertainty, the four described titration curves are a useful tool to investigate the *cis*-Pt(mHyp) adducts in the next section.

Reaction of *cis*-DDP with mHyp. Knowing how a monofunctionally binding Pt compound reacts with mHyp, we can now look at the more complicated case of *cis*-DDP. In Figure 4 the elution profiles of the 1:2 *cis*-DDP:mHyp reaction are shown. The charge of the compounds, as seen in the elution patterns, are as follows: for I, I′ and I″, zero charge; for II, III, and III′, 1+; for IV, 2+; for V and V′, 3+. Under the neutral elution condition used, mHyp is protonated at N1 unless this site is coordinated to platinum. In the former case, mHyp is neutral as a ligand; in the latter it is a 1− ion. Peak I contains "free" mHyp, whereas all other species do contain mHyp bound to *cis*-DDP. Note that the numbers used in this section and in the former on Pt(dien) compounds do not indicate the same species. The three expected reaction products are *cis*-Pt(mHyp-*N1*)$_2$ (zero charge), *cis*-Pt(mHyp-*N1*)-(mHyp-*N7*) (1+), and *cis*-Pt(mHyp-*N7*)$_2$ (2+). However, it is obvious that other species are also present.

The elution profile from the reaction at pH 7 (Figure 4a) is dominated by the large peak IV. As can be expected, and as will be shown below, this peak originates from *cis*-Pt-(mHyp-*N7*)$_2$. A possible N1–N7 adduct can be present only in a small amount because it has to be peak II or III. In that case, one expects almost no N1–N1 product. In the elution pattern from the reaction at pH 10 (Figure 4b), two peaks beside peak IV are quite large: peak I′ + I″ and peak II. As can be deduced from the analogy with the Pt(dien)–mHyp reaction, these peaks most likely contain N1-bound species. Peak I′ + I″ appears to be not "pure" in the ^{1}H NMR spectra and was therefore further separated with the use of Sephadex G-25 gel filtration. The peak with the longest retention time (I′) is likely to contain *cis*-Pt(mHyp-*N1*)$_2$, because of the adsorption properties of the aromatic ligand for the column material. The other species (I″) is *cis*-Pt(mHyp)X (X is a 1− ion such as Cl^- or OH^-).

All species were studied with NMR spectroscopy and with the use of the pH dependence of the chemical shifts; the mHyp part was shown to be coordinated to Pt via N1, N7, or both N1 and N7. The results are summarized in Table I. Results from the NMR spectra of the four species with the most intense peaks in Figure 4b, i.e. I, I′, II, and IV, are depicted in Figure 5. As is obvious by comparison with Figure 3, peak IV (Figure 5-IV) contains mHyp, bound via N7 to platinum. The charge of the (pure) compound is 2+; thus, it is concluded that this species is *cis*-Pt(mHyp-*N7*)$_2$. By analogy, peak I′ (Figure 5-I′) contains *cis*-Pt(mHyp-*N1*)$_2$. Peak II (Figure 5-II) has a charge of 1+ and, two different mHyp's are seen in the NMR spectrum. Therefore, one is bound via N1, and

Table I. Various Species Observed in the Reaction Mixture of *cis*-DDP and mHyp, with Assignments Based upon pH Dependence of Chemical Shifts

pH 7		pH 10	
peak[a]	species	peak[b]	species
I	mHyp	I	mHyp
		I′	*cis*-Pt(mHyp-*N1*)$_2$
		I″	*cis*-Pt(mHyp-*N1*)X[c]
II	*cis*-Pt(mHyp-*N1*)-(mHyp-*N7*)	II	*cis*-Pt(mHyp-*N1*)-(mHyp-*N7*)
III	*cis*-Pt(mHyp-*N7*)X[c]	III′	*cis*-Pt(mHyp-*N1*)X[d]
IV	*cis*-Pt(mHyp-*N7*)$_2$	IV	*cis*-Pt(mHyp-*N7*)$_2$
V	(mHyp-*N7*)-*cis*-Pt(μ-mHyp-*N1,N7*)-*cis*-Pt(mHyp-*N7*)		

[a] Peak labels correspond to those in Figure 4a. [b] Peak labels correspond to those in Figure 4b. [c] X is a 1− ion such as OH^- or Cl^-. [d] X is a neutral species such as NEt_3 or H_2O.

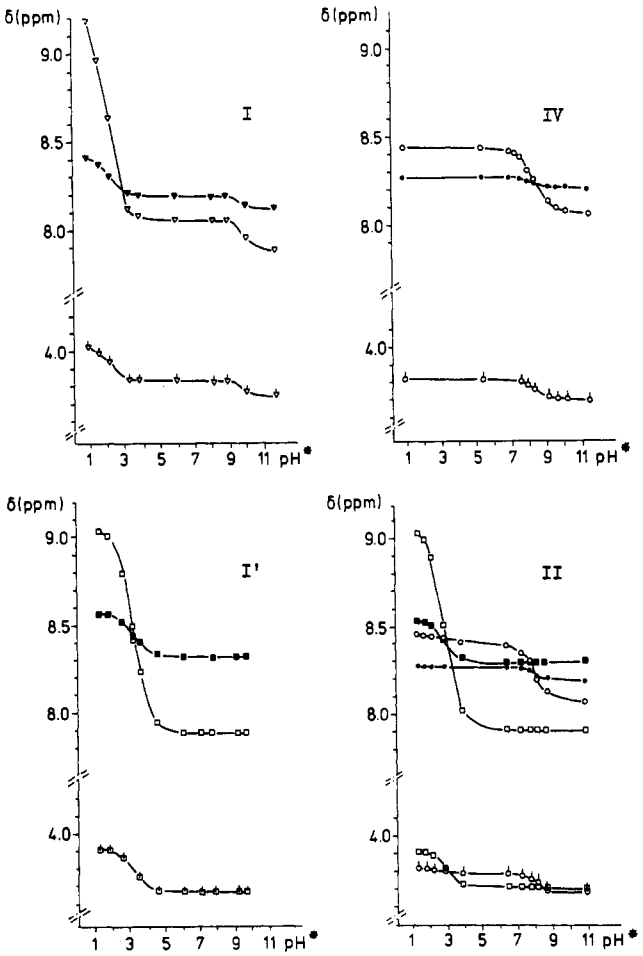

Figure 5. Chemical shift (δ) vs. pH* profiles for the *cis*-DDP reaction products: open symbols, H8; closed symbols, H2; symbols with stick, H_3–C9. Peak, symbol, species: I, ▽, mHyp; IV, ○, *cis*-Pt(mHyp-*N7*)$_2$; I′, □, *cis*-Pt(mHyp-*N1*)$_2$; II, □/○, *cis*-Pt(mHyp-*N1*)(mHyp-*N7*).

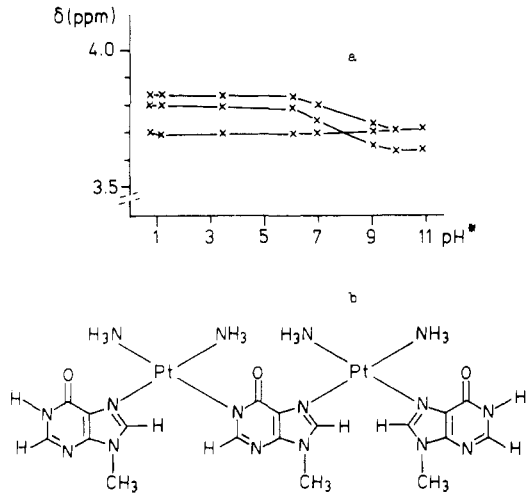

Figure 6. (a) Chemical shift (δ) vs. pH* profiles of the H_3–C9 resonances for species V (see Figure 4a). (b) Proposed structure.

one via N7, resulting in a species *cis*-Pt(mHyp-*N1*)(mHyp-*N7*).

Five minor species remain to be described: peaks I″, III, III′, V, and V′. Unfortunately, peak V′ does not contain enough material to carry out a reliable study, and only from peak V (obtained from the reaction at pH 7) could reliable NMR spectra be obtained. However, peak V from the reaction at pH 10 elutes from the column at the same ionic strength, and UV difference spectroscopy at several pH values[16] indicates that species V and V′ are the same. The pH–chemical shift profiles of its methyl signals are depicted in Figure 6a, together with the proposed structure (Figure 6b), which is deduced from the following information: (1) From the position of the peak in the elution profile one can conclude that the charge of the species is 3+. (2) From the intensity of the methyl signals it is clear that three different mHyp's are present in equal amounts. (3) From the pH–chemical shift profile it is apparent that two mHyp's are bound only via N7 because of the pK_a of the N1 (de)protonation of 7.5; the third mHyp methyl clearly exhibits the titration behavior of the mHyp in [Pt(dien)]$_2$(μ-mHyp-*N1*,*N7*), and thus species V is assigned to be the dinuclear (mHyp-*N7*)-*cis*-Pt(μ-mHyp-*N1*,*N7*)-*cis*-Pt(mHyp-*N7*).

This leaves us with peaks I″ and III′ from the pH 10 reaction mixture and peak III from the pH 7 mixture. The former two (I″ and III′) appear to contain an N1-coordinated mHyp (NMR results not shown) and must contain one other ligand (X). Because of the difference in charge (total charge of 0 and 1+ for I″ and III′, respectively), X in peak I″ has to be negative (Cl^- or OH^-) and X in peak III′ has to be neutral, i.e. NEt_3 or H_2O. The species, eluted as III in Figure 5a, also contains only one mHyp to *cis*-DDP (NMR results not shown). In contrast to peak III′, and as expected from the different pH of the reaction, this mHyp is coordinated via the N7. The concomitant X ligand must be negative because a total charge of 1+ is required.

^{1}H NMR Chemical Shift Values. In Table II the NMR chemical shifts at pH* 6.5 of the described compounds are tabulated. The four "types" of mHyp are "free" mHyp and mHyp singly coordinated to N1, to N7, and to the dinuclear N1,N7 species. The species from which no reliable NMR spectra for the base protons could be obtained are omitted. In all but the N7-coordinated compounds, the H2 protons resonate at lower field with respect to the H8.

Table II. NMR Chemical Shifts (δ) of Cis Pt and of Pt(dien) Products (pH* 6.5)

	H2	H8	H_3-C9
mHyp			
mHyp (pH* 6.5)	8.20	8.06	3.84
mHyp (pH* 10.0)	8.11	7.86	3.75
mHyp-*N7* Compounds			
cis-Pt(mHyp-*N7*)$_2$	8.27	8.42	3.81
cis-Pt(mHyp-*N7*)(mHyp-*N1*)	8.27	8.40	3.79
cis-Pt(mHyp-*N7*)X[a]	8.29	8.52	3.91
Pt(dien)(mHyp-*N7*)	8.30	8.55	3.89
mHyp-*N1* Compounds			
cis-Pt(mHyp-*N1*)$_2$	8.31	7.88	3.67
cis-Pt(mHyp-*N1*)(mHyp-*N7*)	8.30	7.91	3.72
cis-Pt(mHyp-*N1*)X[a]	8.35	7.91	3.77
Pt(dien)(mHyp-*N1*)	8.28	7.92	3.64
Dinuclear Species			
[Pt(dien)]$_2$(μ-mHyp-*N1*,*N7*)	8.32	8.17	3.82

[a] X is a 1– ion such as OH^- or Cl^-.

The N7-coordinated compounds in a monobase adduct show a large downfield chemical shift change of the H8 proton by almost 0.5 ppm due to platinum binding. When, however, two mHyp's are bound, the chemical shift change of the H8 proton amounts to only 0.35 ppm. This smaller downfield shift is due to shielding by the second base. The chemical shift change of H2 upon platinum binding at N7 is—irrespective of the other ligand—between 0.07 and 0.10 ppm downfield.

In contrast to the normal behavior as given above, the H8 protons of the N1-coordinated compounds are shifted *upfield*, by 0.14–0.18 ppm. The H2 proton, though downfield shifted, exhibits a much smaller chemical shift change than in the analogous adenine compounds. Even in comparison with the deprotonated mHyp, the chemical shift changes are small (approximately 0.2 and 0.05 ppm for H2 and H8, respectively).

The bridged compound [Pt(dien)]$_2$(μ-mHyp-*N1*,*N7*) also exhibits small chemical shift changes compared to those of the free ligand (only 0.12 and 0.11 ppm for the H2 and H8 protons, respectively). This indicates that the effects of mono- and diplatinum binding are not additive in this case.

Concluding Remarks

Studying the pH dependence of the ^{1}H NMR chemical shifts appears to be a very suitable method to ascertain binding sites of platinum compounds to nucleobases. Obviously, this method can only be used because of the stability of Pt–nitrogen bonds. It is shown that, in contrast to the lowering of the pK_a of the N1 (de)protonation by platination of N7, the pK_a of the N7 (de)protonation increases by one pK unit when platinum binds at N1. This has been suggested also in 9-methyladenine platinum complexes,[17] and it is likely to originate from the less polarizing properties of $Pt(NH_3)_2^{2+}$ in comparison with a proton.

Reaction at neutral pH results in the binding of platinum compounds almost exclusively at N7, while reaction at pH 10—expectedly—facilitates N1 coordination. Besides monofunctional binding either via N7 or N1, binding to two platinums also is observed. At pH* $\leq$1.5 this bridging mHyp can even be protonated.

Effects of platinum binding at N1 on the chemical shifts at neutral pH appear to be upfield for H8 and only slightly (approximately 0.1 ppm) downfield for H2 protons.

Acknowledgment. This research was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Ad-

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vancement of Pure Research (ZWO) and by Grant MBL-83-1 from the Koningin Wilhelmina Fonds (KWF, Dutch Organization for Fight Against Cancer). C. Erkelens is thanked for his assistance at the 300-MHz NMR facility at Leiden. Experimental assistance by P. van Klaveren is gratefully acknowledged. Prof. Dr. C. Altona and Dr. G. W. Canters are thanked for carefully reading the manuscript and for helpful comments.

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Coordination Chemistry of Microbial Iron Transport Compounds. 26. Dimeric Dialkoxo-Bridged Iron(III) Complexes of Linear Dihydroxamate Ligands[1]

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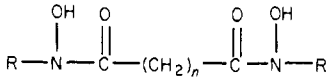
Received June 7, 1983

For a series of dihydroxamate ligands of the general formula $RN(OH)C(=O)(CH_2)_nC(=O)N(OH)R$ (H_2L) the dimeric complexes Fe_2L_3 contain pseudooctahedral tris(hydroxamato)iron(III) centers that are separated by many angstroms and are analogous to complexes of the microbial ferric ion chelating agent (siderophore) rhodotorulic acid. Certain of the synthetic Fe_2L_3 complexes display anomalous behavior in alcohol solutions, due to the formation of the μ-alkoxo-bridged species $Fe_2L_2(OR')_2$. Solution equilibria are reported for several such complexes as the ligand and alcohol are varied. Three of the alkoxo-bridged dimers were characterized in the solid state: **1** (n = 5, R = isopropyl, R′ = CH_3); **2** (n = 5, R = phenyl, R′ = CH_3); **3** (n = 5, R = phenyl, R′ = CH_2CH_3). The coupling of the $S = {}^5/_2$ iron centers has been fit by using the Hamiltonian $\hat{H} = -2J\vec{S}_1\cdot\vec{S}_2$ to give values of J (esd) of −10.92 (4), −13.25 (3), and −12.16 (2) cm^{-1} for **1**–**3**, respectively. The structure of **1** has been determined by single-crystal X-ray diffraction. The space group is $P2_1/n$ with Z = 2, such that the center of the Fe_2O_2 dimer unit lies on a crystallographic inversion center (C_i symmetry). The approximate symmetry of the complex is C_{2h} and is composed of dihydroxamate ligands that span the two iron atoms, in addition to the μ-alkoxide bridges. The Fe–O distances average 2.002 (4) (alkoxide), 2.003 (2) (N–O), and 2.038 (8) Å (C–O). The O–Fe–O bond angles average 77.72 (4) (intra-ring) and 75.42 (5)° (alkoxide). The distortion of the FeO_6 centers from octahedral symmetry results in the three trans O–Fe–O angles 163.3, 165.6, and 158.3°. Red-orange monoclinic crystals of **1** have a = 11.453 (1) Å, b = 14.986 (2) Å, c = 11.948 (1) Å, β = 119.046 (8)°, and V = 1792.8 (7) Å^3. For two formula units of **1** per cell, d(calcd) = 1.32 and d(obsd) = 1.33 (3) g cm^{-3}. Of 4122 measured reflections, 3023 were used to refine 199 variables, with resultant standard and weighted agreement factors (on F) of R = 2.7 and R_w = 3.9%.

Introduction

Rhodotorulic acid is a naturally occurring iron(III) chelating agent of microbial origin in which the two hydroxamate groups of this tetradentate ligand are separated by a maximum chain length extension of up to 10 Å.[2,3] We have prepared a series of analogous dihydroxamate ligands whose synthesis and general iron(III) coordination chemistry,[4] as well as use as synthetic analogues in studying microbial iron transport,[5] we report elsewhere. The general formula of these synthetic ligands is

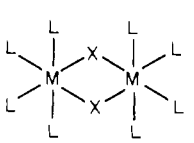


L^1: R = isopropyl, n = 5
L^2: R = phenyl, n = 5

In the following text we will designate as H_2L the free acid form of these ligands. The particular dianion designated L^1 has five bridging methylene groups in the chain (n = 5) and terminal isopropyl groups (R = i-C_3H_7). For the ligand dianion L^2, n = 5 and R = phenyl.

In the process of characterizing the iron(III) complexes of the series of dihydroxamic acid ligands for which R = i-C_3H_7 and n = 3–6, 8, and 10, it was found that compounds of stoichiometry $Fe_2L_3\cdot H_2O$ may be isolated from aqueous solutions containing the ratio Fe^{3+}:L of 2:3.[4] The compounds are dimeric in solution and appear to be polymeric in the solid state. Their physical properties are typical of ferric tris(hydroxamato) complexes such as that formed by rhodotorulic acid itself.[3] Upon dissolution in methanol, however, the iron complex with ligand L^1 (n = 5, R = isopropyl) exhibits anomalous spectroscopic and magnetic properties. All efforts to isolate the anomalous species from methanol solutions containing the ratio Fe^{3+}:L of 2:3 led ultimately to the tris(hydroxamato) complex $Fe_2(L^1)_3\cdot H_2O$. This paper describes the isolation and X-ray crystal structure of the dimeric methoxy-bridged iron(III) complex $Fe_2(L^1)_2(\mu\text{-}OCH_3)_2$, as well as the synthesis of the related complexes $Fe_2(L^2)_2(\mu\text{-}OCH_3)_2$ and $Fe_2(L^2)_2(\mu\text{-}OCH_2CH_3)_2$, and the temperature-dependent magnetic properties of these compounds. The solution chemistry of these unusual dimeric compounds, which are stable over only a narrow range of conditions, has been explored as a function of the bridging alkoxide group's basicity.

The fundamental property of spin exchange[6] in multinuclear complexes containing more than one paramagnetic center has been explored in detail[7–20] in dimeric complexes of the type



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