

BPC 01088

VITAMIN C INTERACTION WITH COBALT-AMMINE CATIONS

SYNTHESIS, SPECTROSCOPIC AND STRUCTURAL CHARACTERIZATION OF COBALT-PENTAMMINE AND COBALT-TETRAMMINE SUGAR COMPLEXES CONTAINING L-ASCORBATE ANION

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Received 18th June 1986

Accepted 11th July 1986

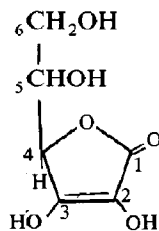
Key words: Cobalt-amine; L-Ascorbate; ¹³C-NMR; Fourier transform infrared spectroscopy; Electron absorption spectroscopy

Interaction between $[\text{Co}(\text{NH}_3)_5\text{Cl}]\text{Cl}_2$, $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]\text{Cl}$ and L-ascorbic acid has been investigated in aqueous solution and solid complexes of the type $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]\text{Cl}_2 \cdot \text{H}_2\text{O}$ and $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]\text{Cl}_2 \cdot \text{H}_2\text{O}$ have been isolated and characterized by ¹³C-NMR, FT-IR and electron absorption spectroscopy. Spectroscopic and other evidence suggested that the sugar anion binds monodentately in the $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]^{2+}$ cation via the ionized O3 oxygen atom and bidentately in $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]^{2+}$ through the O1 and O4 oxygen atoms, resulting in a six-coordinate geometry around the Co(III) ion. The intermolecular sugar hydrogen-bonding network is perturbed upon sugar metalation and the sugar moiety shows a similar conformation to that of the sodium ascorbate compound in these series of cobalt-amine complexes.

1. Introduction

Vitamin C interaction with metal ions plays an important role in the reversible oxidation of ascorbic acid in living cells. Apart from its biological importance, ascorbic acid has several potential binding sites (scheme 1) for metal-complex formation. It has been demonstrated [1] how the O1, O2, O3 and O4 oxygen atoms of the ascorbate anion are involved in metal-ligand bondings. Although it was suggested that ascorbate-metal chelate formation is weak in aqueous media [1,2], recently a unique way of coordination via C2 and O5 has been found through X-ray diffraction measurements [3] in the new anticancer drugs formed between Pt(II) amine compounds and ascorbate

anion. In the present work, we describe the synthesis and characterization of the two cobalt-amine-ascorbate complexes both in solution and in the solid state, using ¹³C-NMR, Fourier transform infrared and electron absorption spectroscopy, that have not been reported previously. Furthermore, a correlation between the spectral changes and the coordination sites used by the ascorbate anion has been established here.



Scheme 1. L-Ascorbic acid.

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2. Experimental

2.1. Materials

L-Ascorbic acid was purchased from Aldrich Chemical Co. and was converted to the sodium salt. All other chemicals were of reagent grade and used as supplied.

2.2. Synthesis of cobalt-ammine-ascorbate complexes

[Co(NH₃)₅Cl]Cl₂ (pink) and [Co(NH₃)₄Cl₂]Cl (bluish violet) were synthesized and recrystallized according to standard methods [4,5]. Cobalt-ammine-ascorbate complexes were prepared by the addition of sodium ascorbate (1 mmol) to a solution of cobalt-pentammine (1 mmol) in H₂O (25 ml) or sodium ascorbate (2 mmol) to a solution of cobalt-tetrammine (1 mmol) in H₂O (25 ml). The solution pH was adjusted to 7 by the addition of NH₄OH or NaOH solution and was heated at 60°C for 30 min. After the solution changed to a deep red color, it was removed from the hot plate and cooled down to room temperature. The insoluble polynuclear compound formed (brown) was filtered off and the filtered solution was then added dropwise to 100 ml methanol; the solution was refrigerated overnight and the precipitate formed was filtered off, washed with acetone several times and dried over CaCl₂. The analytical data showed a composition of [Co(NH₃)₅ascorbate]Cl₂ · H₂O and [Co(NH₃)₄ascorbate]Cl₂ · H₂O. The compounds are soluble in water and not in other common organic solvents and were recrystallized from a water/methanol mixture.

2.3. Physical measurements

¹³C-NMR spectra were recorded on a Bruker WP-80 instrument in ²H₂O solution. The Fourier transform infrared spectra were taken on a Digilab FTS 15D/C Fourier transform interferometer equipped with an HgCdTe detector and a KBr beam splitter and a Globar source. The spectra were taken as KCl pellets with a resolution of 2–4 cm⁻¹. The electronic spectra were measured on a Unicam Sp-1700 instrument with 10⁻³ M solution.

3. Results and discussion

3.1. NMR spectra

The ¹³C-NMR chemical shifts of free L-ascorbic acid, sodium ascorbate and the cobalt-ammine-ascorbate complexes are given in table 1. The results observed here for the free acid and its sodium salt are in good agreement with those of the literature reports [6,7]. Upon acid ionization, drastic changes occurred for the ¹³C-NMR chemical shifts of C3 (20 ppm), C2 (5 ppm), C1 (5 ppm) and C4 (3 ppm) (table 1). The considerable downfield shift of the C3 atom is related to the ionization of the OH3 group. It should be noted that the major downfield shift of C3 (20 ppm) with respect to the simple carboxylic acid (4–5 ppm) is caused by the lengthening of the C2–C3, C3–C4, C1–O1 and C2–O2 bonds in the mono-anion formed in the sodium ascorbate salt [8] and also related to the delocalization of the electron distribution throughout the enol-diol and carbonyl

Table 1

¹³C-NMR chemical shifts of L-ascorbic acid, sodium ascorbate and the cobalt-ammine-ascorbate complexes in ²H₂O solution

Compound	δ (ppm)					
	C ₁	C ₃	C ₂	C ₄	C ₅	C ₆
L-Ascorbic acid	173.79	156.07	118.51	76.87	69.66	62.80
Sodium ascorbate	178.09	176.34	113.85	79.28	70.46	63.46
[Co(NH ₃) ₅ ascorbate] ²⁺	178.83	177.56	113.63	79.94	70.66	63.56
[Co(NH ₃) ₄ ascorbate] ²⁺	181.80	176.38	112.31	83.31	70.61	63.60

groups [6]. The changes observed here are also responsible for the downfield shifts of C1, C4 and the upfield shift of C2 atoms (table 1). In the present work, the ^{13}C -NMR spectra of the $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]^{2+}$ cation showed marked similarities with the sodium ascorbate salt (table 1), indicating the coordination of the Co(III) ion through the ionized O3 atom. On the other hand, the ^{13}C -NMR spectra of the $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]^{2+}$ cation exhibited considerable downfield shifts for C1 (5 ppm) and C4 (3 ppm) compared with the spectra of the sodium salt (table 1). The spectral changes observed for C1 and C4 are indicative of cobalt ion chelate formation via O1 and O4 in the cobalt-tetrammine-ascorbate compound. Similar cobalt(III) chelate formation was concluded, on the basis of ^{13}C -NMR spectroscopy, in a series of cobalt-ammine-carboxylate complexes [9].

3.2. Fourier transform infrared spectroscopy

3.2.1. Acid OH and CH stretching vibrations

The crystal structure of L-ascorbic acid showed [10] several hydrogen-bonded OH groups that are involved in an intermolecular hydrogen-bonding network. The infrared spectra of ascorbic acid and its sodium salt have been studied by Hvoslef and Klæboe [11] and the possible assignments of the vibrational frequencies have been made. In the present work, several broad and strong absorption bands appearing in the region $3500\text{--}3000\text{ cm}^{-1}$ in the infrared spectra of L-ascorbic acid are assigned to these hydrogen-bonding OH groups. Upon acid ionization and cobalt coordination, drastic changes were observed for the OH stretching vibrations (broadening and shifting). The changes observed are due to the ionization of the O3H group and the participation of the sugar oxygen atoms in metal-ligand bondings. Similar spectral changes occurred in the spectra of D-glucuronic acid and its structurally known $\text{Ca}(\text{D-glucuronate})\text{Br} \cdot 3\text{H}_2\text{O}$ compound, where the metal coordination was found to be through the sugar OH and carboxyl oxygen atoms [12]. It should be noted that the rearrangements of the sugar hydrogen-bonding system observed upon sugar ionization, in the crystal structure of the sodium ascorbate [8] salt,

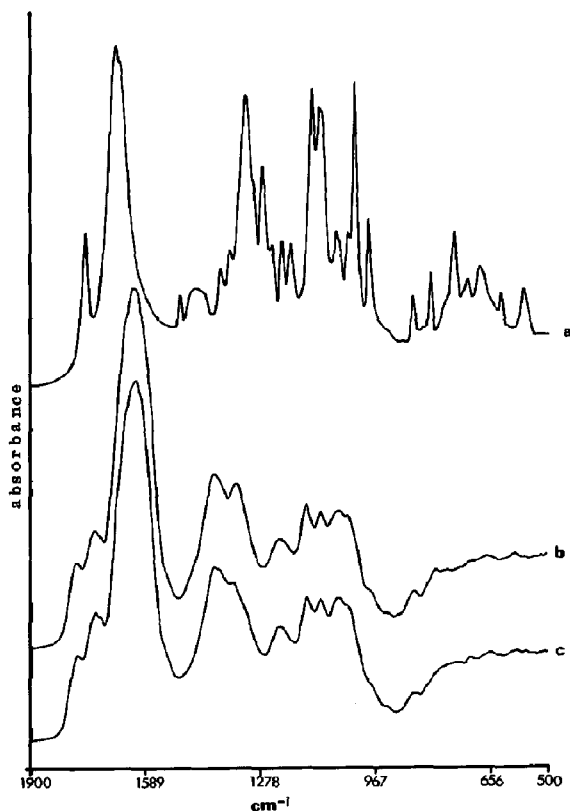


Fig. 1. Fourier transform infrared spectra of L-ascorbic acid and its cobalt-ammine complexes in the region $1900\text{--}500\text{ cm}^{-1}$ for (a) L-ascorbic acid, (b) $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]\text{Cl}_2 \cdot \text{H}_2\text{O}$ and (c) $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]\text{Cl}_2 \cdot \text{H}_2\text{O}$.

are also responsible for the spectral changes observed for the sugar OH stretching vibrations. The CH stretching vibrations of the free acid appeared at about $3000\text{--}2800\text{ cm}^{-1}$ and showed no major alteration upon cobalt coordination.

3.2.2. Acid carbonyl and ring vibrational frequencies

The $\text{C}=\text{O}$ stretching vibrations of free L-ascorbic acid [11] appeared as a strong absorption band at 1754 cm^{-1} and exhibited shifting and splitting upon cobalt interaction (fig. 1). The splitting and shifting of the $\text{C}=\text{O}$ stretching vibration towards higher (1774 cm^{-1}) and lower (1724 cm^{-1}) frequencies, in the spectra of both cobalt-tetrammine- and cobalt-pentamine-ascorbate complexes, are

due to the participation of the carbonyl group oxygen atom in metal-ligand bonding. Another strong and broad absorption band observed at 1670 cm^{-1} , in the free acid, which could be related to the C=C and C=O stretching vibrations also shifted towards lower frequencies (1612 cm^{-1}) in the spectra of the cobalt-ascorbate complexes (fig. 1). The changes observed for these absorption frequencies are also due to the participation of the carbonyl oxygen atoms in metal-ascorbate complexation. In the present study, the deuteration of L-ascorbic acid showed no considerable changes for the absorption bands at 1754 and 1670 cm^{-1} , which is consistent with the assignment of these vibrations to C=O and C=C stretching frequencies. Other absorption bands in the region $1500\text{--}1100\text{ cm}^{-1}$ in the free sugar spectrum, related to the strongly coupled CH and OH stretching vibrations [11], showed considerable changes upon complex formation (fig. 1). The major intensity changes and the shifting of these absorption bands are related to the acid ionization and the involvement of the sugar oxygen atoms in metal-ligand bonding. The C–O stretching vibrations [11] of the free acid in the region $1100\text{--}900\text{ cm}^{-1}$ showed intensity changes and shifted towards lower frequencies in the spectra of the cobalt-amine-ascorbate complexes (fig. 1). The spectral changes observed for the C–O stretching vibrations are consistent with the alteration of the C=O stretching vibrations and are indicative of the involvement of the C=O and C–O oxygen atoms in cobalt-ascorbate complex formation. Several other absorption bands with medium intensities at about $900\text{--}500\text{ cm}^{-1}$ in the spectra of the free acid that are assigned to the sugar ring C–O–C and C–C–C skeletal deformation modes [12] exhibited considerable changes upon acid metallation (fig. 1). The changes observed for these vibrational frequencies are related to the ionization of the O3H hydroxyl group and the participation of the ring oxygen atoms in metal-ligand bonding that perturbs the electron distribution of the ring system, where the vibrations are mostly localized and finally bring about ring distortion [12]. It should be noted that due to the marked similarities of the infrared spectra of $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]^{2+}$ and $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]^{2+}$ cations, it is

very difficult to separate the monodentately and bidentately bonded ascorbate anions. Conclusive evidence regarding the nature of the cobalt-ascorbate bonding came from the ^{13}C -NMR spectroscopic study discussed earlier (see section 3.1).

It is worth mentioning that the antisymmetric and symmetric stretching vibrations of the NH_3 and H_2O molecules in the region $3500\text{--}3200\text{ cm}^{-1}$ were overlapped by the strong and broad sugar OH stretching frequencies. Similarly, the H_2O and NH_3 bending modes in the region $1600\text{--}1650\text{ cm}^{-1}$ were also obscured by the strong and broad acid C=O and C=C stretching vibrations (fig. 1).

3.3. Electron absorption spectra

The electronic absorption spectra of $[\text{Co}(\text{NH}_3)_5\text{Cl}]\text{Cl}_2$ and $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]\text{Cl}$ have been studied in detail [5,13]. A strong and broad absorption band at 530 nm (in the visible region of the electronic spectrum of the *cis*- $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]^{2+}$ cation, related to the ${}^1\text{A}_{1g} \rightarrow {}^1\text{E}_g$ transition [5], shifted to a band maximum at 540 nm in the spectra of the $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]^{2+}$ cation. Similarly, an absorption band observed at 535 nm in the visible region of the spectrum of the $[\text{Co}(\text{NH}_3)_5\text{Cl}]^{2+}$, assigned to the ${}^1\text{A}_{1g} \rightarrow {}^1\text{E}_g$ transition [13], appeared at about 545 nm , in the spectra of the $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]^{2+}$ cation. Similar spectral changes have been observed in the visible spectra of the $[\text{Co}(\text{NH}_3)_4(\text{H}_2\text{O})_2]^{2+}$ cation upon complexation with several sugar residues [14]. It has been concluded that the cobalt-amine-sugar complexes show similar behaviour to those of the cobalt-amine-carbonato compounds while the band maxima located in the visible region shifted towards higher wavelengths on carbonate complexation [14,15].

4. Concluding remarks

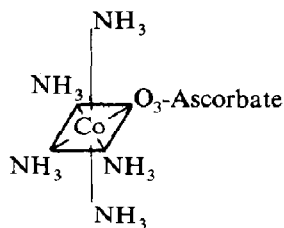
On the basis of the ^{13}C -NMR, Fourier transform infrared and electron absorption spectroscopy of vitamin C and its cobalt-amine complexes studied here, the following points can be emphasized:

- (a) The strong intermolecular acid hydrogen-

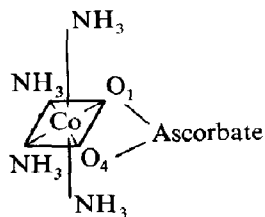
bonding network is rearranged upon sugar ionization and metallation;

(b) The ascorbate anion binds monodentately in $[\text{Co}(\text{NH}_3)_5\text{ascorbate}]\text{Cl}_2 \cdot \text{H}_2\text{O}$ via ionized O3 (scheme 2) and coordinates bidentately in $[\text{Co}(\text{NH}_3)_4\text{ascorbate}]\text{Cl}_2 \cdot \text{H}_2\text{O}$ through O1 and O4 (scheme 3) and

(c) Due to the marked spectral similarities with the sodium ascorbate salt the acid anion would have a similar conformation, in these cobalt-ammine-sugar complexes.



Scheme 2.



Scheme 3.

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