Synthesis and Characterization of Platinum(II) Complexes of L-Ascorbic Acid. Crystal Structure of Ascorbato-C^2,O^5-ethylenediamineplatinum(II) Dihydrate

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Received February 5, 1999

Reactions between diaminediaquaplatinum complexes $[Pt(N^{\cap}N)(H_2O)_2]^{2+}$ and sodium ascorbate (NaHAsc) have been studied using ^1H and ^{195}Pt NMR spectroscopy. Mixtures of platinum ascorbate species were formed involving different binding modes of the ascorbate ligand, namely, $[Pt(HAsc\text{-}O^3)(H_2O)(N^{\cap}N)]^+$, in which a single ascorbate acts as a monodentate ligand, the bis(ascorbate)platinum complexes $[Pt(HAsc\text{-}O^3)_2(N^{\cap}N)]$ and $[Pt(HAsc\text{-}O^3)(HAsc\text{-}C^2)(N^{\cap}N)]$, and $[Pt(Asc\text{-}O^2,O^3)(N^{\cap}N)]$ and $[Pt(Asc\text{-}C^2,O^5)(N^{\cap}N)]$, in which the ascorbate acts as a chelating ligand ($N^{\cap}N$ = en, *N*,*N*-dmen, *N*,*N*′-dmen, *N*,*N*,*N*′,*N*′-tmen; $HAsc^- = C_6H_7O_6^-$, $Asc^{2-} = C_6H_6O_6^{2-}$). The crystal structure of ascorbato-C^2,O^5-ethylenediamineplatinum(II) dihydrate, $[Pt(Asc\text{-}C^2,O^5)(en)]\cdot 2H_2O$, was established by X-ray crystallography. A series of diphosphineplatinum complexes of the type $[Pt(Asc\text{-}O^2,O^3)(P^{\cap}P)]$ ($P^{\cap}P$ = dppm, dppe, dppp) was prepared from the corresponding $[Pt(NO_3)_2(P^{\cap}P)]$ species. These have been characterized by elemental analysis and infrared and ^1H and $^{31}P\{^1H\}$ NMR spectroscopies.

Introduction

Diamineplatinum complexes of vitamin C (L-ascorbic acid) have received some attention because of their potential use as antitumor agents.[1−4] Apart from their biological activity, these complexes are also of interest from a chemical point of view. The *C*,*O*-bonded complex $[Pt(Asc\text{-}C^2,O^5)(cis\text{-dach})]$ (dach = 1,2-diaminocyclohexane) was the first transition metal complex of vitamin C to be structurally characterized by X-ray crystallography.[1] The structure of this complex demonstrates the importance of the C-2 binding site in metal ascorbate chemistry. A variety of monodentate and bidentate oxygen-bound, as well as carbon-bound, complexes of platinum have been reported.[2] The carbon-bound (mono)ascorbate products contain a chelating ascorbate dianion that is bound to platinum through C-2 and the deprotonated O-5 hydroxyl group. The bis(ascorbate)-platinum complexes contain one carbon-bound and one oxygen-bound ascorbate anion per platinum. Both types of complexes have demonstrated some degree of antitumor activity in standard animal tumor screens, with greater activity being found for the bis(ascorbate) species.[3,4]

A recent review shows that there have not been many reports of the isolation of solid transition metal ascorbate complexes.[5] Complexes of the general formula $M(HAsc)_n\cdot xH_2O$ ($M = Cr^{3+}$, $n = 3$, $x = 6$; $M = Mn^{2+}$, Co^{2+}, Ni^{2+}, Zn^{2+}, $n = 2$, $x = 4$), in which coordination occurs through the anionic oxygen O-3 of the ascorbate monoanion, have been characterized by electronic and infrared spectroscopies.[6−8] Titanium(IV)[9] and iron(II)[10] complexes containing ascorbate dianions coordinated through oxygen atoms O-2 and O-3 have also been characterized. The crystal structure of the first *O*,*O*-bonded ascorbate chelate complex $[Pt(O,O\text{-Asc})(PMe_3)_2]\cdot H_2O$, was published recently.[11]

In this paper we report on studies of reactions between diaminediaquaplatinum complexes $[Pt(N^{\cap}N)(H_2O)_2]^{2+}$ ($N^{\cap}N$ = en, *N*,*N*-dmen, *N*,*N*′-dmen, *N*,*N*,*N*′,*N*′-tmen) and sodium ascorbate (NaHAsc) using ^1H and ^{195}Pt NMR spectroscopy. The effect of the methyl substituents on the relative amounts and rates of formation of oxygen-bound and carbon-bound ascorbate complexes is discussed. We also report the synthesis and characterization of the diphosphineplatinum ascorbate complexes $[Pt(Asc\text{-}O^2,O^3)(P^{\cap}P)]$ ($P^{\cap}P$ = dppm, dppe, dppp). One advantage of using diphosphines as supporting ligands, instead of diamines, is that the ^{31}P chemical shifts and $^1J(Pt,P)$ coupling constants provide information about the binding modes of the ascorbate ligand.

Experimental Section

The diamines, silver nitrate, and sodium ascorbate were purchased from Aldrich, the diphosphines were purchased from Strem, and potassium tetrachloroplatinate was purchased from Pressure Chemical Co. NMR spectra were recorded on a Varian Unity plus 300 spectrometer operating at 300.0 MHz for ^1H, 121.4 MHz for ^{31}P, and 64.5 MHz for ^{195}Pt. ^1H chemical shifts were measured relative to the residual solvent signal, while ^{31}P chemical shifts were measured relative to external H_3PO_4. ^{195}Pt chemical shifts were measured relative to an external standard of K_2PtCl_4 in D_2O at −1624 ppm (relative to Na_2PtCl_6 at 0 ppm). Infrared spectra were recorded on a Perkin-Elmer 1600

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10.1021/ic990152z CCC: $18.00
Published on Web 11/23/1999

FTIR spectrometer. Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA.

X-ray Structure Determination. Preliminary examination and data collection were performed using a Siemens SMART CCD detector system single-crystal X-ray diffractometer using graphite-monochromated Mo Kα radiation ($\lambda = 0.710\ 73$ Å) equipped with a sealed tube X-ray source (50 kV × 40 mA), as described elsewhere.[12] Structure solution and refinement were carried out using the SHELXTL-PLUS (5.03) software package.[13]

All reactions with sodium ascorbate were performed under an atmosphere of dinitrogen to prevent oxidation. All diaminediaquaplatinum(II) complexes were prepared by the method of Dhara et al.[14] The complexes $[PtCl_2(cod)]$[15] and $[PtCl_2(P^{\frown}P)]$ (P^P = dppm, dppe, dppp)[16,17] were prepared by published procedures.

Synthesis of Complexes of the Type $[PtI_2(N^{\frown}N)]$ (N^N = en, *N,N*-dmen, *N,N′*-dmen, *N,N,N′,N′*-tmen). An aqueous solution of K_2PtCl_4 was treated with 4.1 mol equiv of KI, and the solution was stirred for 15 min at room temperature. An aqueous solution of the appropriate diamine was added dropwise to the resulting K_2PtI_4 solution, and the reaction mixture was stirred for 1−2 h. The resulting yellow precipitate was collected by filtration and washed extensively with water and ethanol. The solid was dried in vacuo. Yields were in the range 85−95%.

Preparation of Complexes of the Type $[Pt(Asc)(N^{\frown}N)]$ (N^N = en, *N,N*-dmen, *N,N′*-dmen, *N,N,N′,N′*-tmen). To a suspension of the appropriate $[PtI_2(N^{\frown}N)]$ complex (1.0 mmol) was added a solution of $AgNO_3$ (0.34 g, 2.0 mmol) in water (10 mL). The mixture was stirred at 40 °C for 2 h in a flask protected from light. The resulting precipitate of AgI was removed by filtration, and the filtrate containing $[Pt(N^{\frown}N)(H_2O)_2](NO_3)_2$ was placed in a three-necked flask fitted with a dropping funnel. A degassed solution of sodium ascorbate (0.40 g, 2.0 mmol) in H_2O (2 mL) was added via syringe to the dropping funnel and then added dropwise to the flask with stirring. At various times, aliquots of the reaction mixtures were removed by syringe and transferred to NMR tubes, and the platinum ascorbate species were identified by ^{195}Pt NMR spectroscopy. The complex $[Pt(Asc\text{-}C^2,O^5)(en)]\cdot 2H_2O$ was produced as an off-white powder (0.23 g, 50%) from the reaction of $[Pt(en)(H_2O)_2](NO_3)_2$ and sodium ascorbate. Anal. Calcd for $PtC_8H_{18}N_2O_8$: C, 20.63; H, 3.87; N, 6.02. Found: C, 20.57; H, 3.94; N, 5.93. Crystals of $[Pt(Asc\text{-}C^2,O^5)(en)]\cdot 2H_2O$ that formed from the reaction mixture were suitable for a single-crystal X-ray diffraction study.

General Procedure for the Synthesis of $[Pt(NO_3)_2(P^{\frown}P)]$ (P^P = dppm, dppe, dppp). To an acetone solution (40 mL) of $[PtCl_2(P^{\frown}P)]$ (1.0 mmol) was added silver nitrate (2.0 mmol) in water (10 mL). The mixture was stirred for 20−24 h in the dark at room temperature, and then the precipitate of AgCl was collected by filtration through Celite. The filtrate was evaporated under reduced pressure, and the products were obtained as yellow solids.

$[Pt(NO_3)_2(dppe)]$. Yellow powder. Yield (0.40 g, 56%). Anal. Calcd for $C_{26}H_{24}N_2O_6P_2Pt$: C, 43.51; H, 3.35; N, 3.91. Found: C, 43.64; H, 3.31; N, 3.81. ^{31}P NMR ($CDCl_3$): δ 33.0, $^1J_{PtP} = 3940$ Hz.

$[Pt(NO_3)_2(dppm)]\cdot H_2O$. Yellow powder. Yield (0.50 g, 72%). Anal. Calcd for $C_{25}H_{24}N_2O_7P_2Pt$: C, 41.6; H, 3.33; N, 3.88. Found: C, 41.6; H, 3.10; N, 4.06. ^{31}P NMR ($CDCl_3$): δ −68.9, $^1J_{PtP} = 3430$ Hz.

$[Pt(NO_3)_2(dppp)]$. Yellow powder. Yield (0.24 g, 33%). Anal. Calcd for $C_{27}H_{26}N_2O_6P_2Pt$: C, 44.3; H, 3.55; N, 3.82. Found: C, 43.9; H, 5.12; N, 2.38. ^{31}P NMR ($CDCl_3$): δ −13.4, $^1J_{PtP} = 3664$ Hz.

General Procedure for Preparation of $[Pt(Asc)(P^{\frown}P)]\cdot xH_2O$ (P^P = dppm, dppe, dppp). An aqueous solution (5 mL) of sodium ascorbate (0.40 g, 2.0 mmol) was added dropwise to a stirred, degassed solution of $[Pt(NO_3)_2(P^{\frown}P)]$ (1.0 mmol) in acetone (30 mL) at room temperature. Evaporation of the reaction mixture after 24 h produced a yellow solid, which was washed with water, followed by ether. The products were dried in vacuo.

$[Pt(Asc\text{-}O^2,O^3)(dppm)]\cdot H_2O$. Yield 0.40 g, 52%. Anal. Calcd for $C_{31}H_{30}O_7P_2Pt$: C, 48.24; H, 3.89. Found: C 48.06; H 3.92. ^{1}H NMR ($CDCl_3$): δ 4.43 (2H, m, PC*H*$_2$), 4.32 (1H, t, $^3J_{HH} = 6$ Hz, *H*5), 3.83 (2H, d, $^3J_{HH} = 6$ Hz, *H*6,*H*6′), 4.56 (1H, d, $^3J_{HH} = 6$ Hz, *H*4), 7.5−8.0 (20H, m, C$_6$*H*$_5$). ^{31}P NMR: δ −62.1 (d, $^2J_{PP} = 21$ Hz, $^1J_{PtP} = 3000$ Hz), −62.4 (br, $^1J_{PtP} = 3086$ Hz).

$[Pt(Asc\text{-}O^2,O^3)(dppe)]\cdot H_2O$. Yield 0.47 g, 60%. Anal. Calcd for $C_{32}H_{32}O_7P_2Pt$: C, 48.91; H, 4.08. Found: C 49.04; H 4.07. ^{1}H NMR ($CDCl_3$): δ 2.39 (4H, m, PC*H*$_2$), 3.39 (1H, t, $^3J_{HH} = 6$ Hz, *H*-5), 3.71 (2H, d, $^3J_{HH} = 6$ Hz, *H*6, *H*6′), 4.49 (1H, d, $^3J_{HH} = 6$ Hz, *H*4), 7.5−8.0 (20H, m, C$_6$*H*$_5$). ^{31}P NMR: δ 29.2 (d, $^2J_{PP} = 10$ Hz, $^1J_{PtP} = 3670$ Hz), 32.7 (d, $^2J_{PP} = 10$ Hz, $^1J_{PtP} = 3366$ Hz).

$[Pt(Asc\text{-}O^2,O^3)(dppp)]\cdot H_2O$. Yield 0.50 g, 63%. Anal. Calcd for $C_{33}H_{34}O_7P_2Pt$: C, 49.56; H 4.26. Found: C, 49.50; H, 4.16. ^{1}H NMR ($CDCl_3$): δ 2.12 (2H, m, PCH$_2$C*H*$_2$), 2.50 (4H, m, PC*H*$_2$), 2.82 (1H, t, $^3J_{HH} = 6$ Hz, *H*5), 3.57 (2H, d, $^3J_{HH} = 6$ Hz, *H*6, *H*6′), 4.30 (1H, d, $^3J_{HH} = 6$ Hz, *H*4), 7.5−8.0 (20H, m, C$_6$*H*$_5$). ^{31}P NMR: δ −11.8 (d, $^2J_{PP} = 32$ Hz, $^1J_{PtP} = 3464$ Hz), −8.9 (d, $^2J_{PP} = 32$ Hz, $^1J_{PtP} = 3205$ Hz).

Results and Discussion

The diaminediaquaplatinum(II) cations were prepared as shown in eqs 1−3. Further treatment of the $[Pt(N^{\frown}N)(H_2O)_2]^{2+}$

$$K_2PtCl_4 + 4KI \rightarrow K_2PtI_4 + 4KCl \quad (1)$$

$$K_2PtI_4 + N^{\frown}N \rightarrow [PtI_2(N^{\frown}N)] + 2KI \quad (2)$$

$$[PtI_2(N^{\frown}N)] + 2AgNO_3 \rightarrow [M(N^{\frown}N)(H_2O)_2](NO_3)_2 + 2AgI \quad (3)$$

(N^N = en, *N,N*-dmen, *N,N′*-dmen, *N,N,N′,N′*-tmen)

cations with sodium ascorbate generated the diamineplatinum ascorbate complexes $[Pt(Asc)(N^{\frown}N)]$, based on the method described by Hollis et al.[18] The introduction of varying numbers of methyl groups on the nitrogen atoms of the diamine ligands allowed us to examine the effects of such substituents on the binding modes of the ascorbate ligand.

NMR Spectroscopy. Reactions of the diaminediaquaplatinum complexes with 2 mol equiv of sodium ascorbate were studied by multinuclear NMR spectroscopy. ^{195}Pt NMR data for the platinum ascorbate species that were formed are summarized in Table 1, and the proposed structures for the ascorbate complexes are shown in Scheme 1. The assignments of the complexes were based on the consistent observation that displacement of a water molecule by ascorbate causes a high-frequency shift of the ^{195}Pt resonances of 60−70 ppm per ascorbate ligand.[2] Thus, ^{195}Pt resonances of diamineplatinum complexes with two oxygen donor ligands occur between −1600 and −1900 ppm. In contrast, the ^{195}Pt resonances associated with complexes with one carbon and one oxygen donor occur between −2500 and −2800 ppm.[2]

Reactions of $[Pt(en)(H_2O)_2](NO_3)_2$ with Sodium Ascorbate. The ^{195}Pt NMR spectrum of $[Pt(en)(H_2O)_2]^{2+}$ shows a single peak at −1920 ppm. When sodium ascorbate was added, three new peaks appeared in the ^{195}Pt NMR spectrum at −1838, −1788, and −1720 ppm that we have assigned to $[Pt(HAsc\text{-}O^3)(en)(H_2O)]^+$, $[Pt(HAsc\text{-}O^3)_2(en)]$, and $[Pt(Asc\text{-}O^2,O^3)(en)]$, respectively.[2] These three oxygen-bound ascorbate species predominated during the first 4 h of reaction. After 4 h, two

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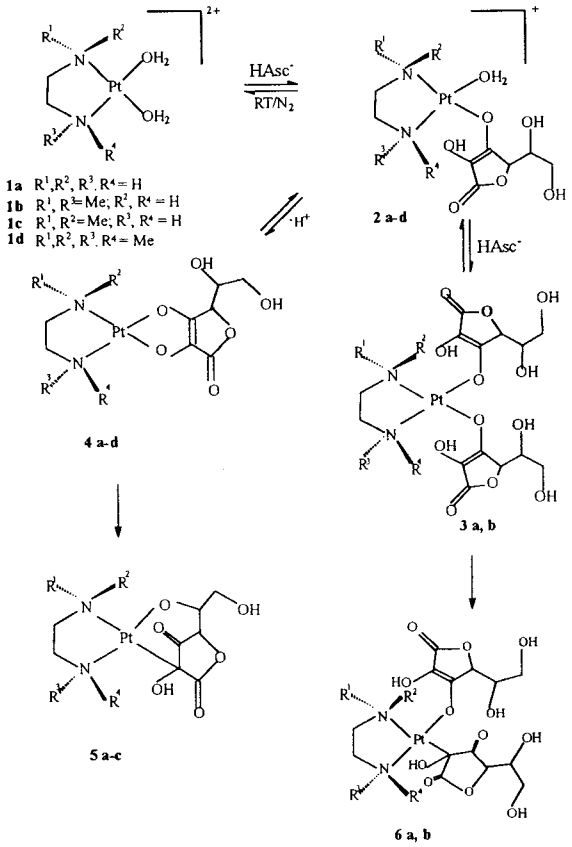
Table 1. ^{195}Pt NMR Data for Diamineplatinum Ascorbate Complexes

complex	^{195}Pt chemical shift[a]	complex	^{195}Pt chemical shift[a]
[Pt(en)$(H_2O)_2]^{2+}$, **1a**	−1920	[Pt(*N*,*N*′-dmen)(C^2,O^5-Asc)], **5b**	−2677
[Pt(en)(O^3-HAsc)$(H_2O)]^+$, **2a**	−1838	[Pt(*N*,*N*′-dmen)(C^2,O^5-Asc)], **5b**′	−2687
[Pt(en)(O^3-HAsc)$_2$], **3a**	−1788	[Pt(*N*,*N*′-dmen)(C^2-HAsc)(O^3-HAsc)], **6b**	−2755
[Pt(en)(O^2,O^3-Asc)], **4a**	−1720	[Pt(*N*,*N*′-dmen)$(H_2O)_2]^{2+}$, **1c**	−1858
[Pt(en)(C^2,O^5-Asc)], **5a**	−2648	[Pt(*N*,*N*′-dmen)(H_2O)(O^3-HAsc)$]^+$, **2c**	−1793
[Pt(en)(C^2-HAsc)(O^3-HAsc)], **6a**	−2680	[Pt(*N*,*N*′-dmen)(O^2,O^3-Asc)], **4c**	−1650
[Pt(*N*,*N*′-dmen)$(H_2O)_2]^{2+}$, **1b**	−1970	[Pt(*N*,*N*′-dmen)(C^2,O^5-Asc)], **5c**	−2641
[Pt(*N*,*N*′-dmen)(H_2O)(O^3-HAsc)$]^+$, **2b**	−1914	[Pt(tmen)$(H_2O)_2]^{2+}$, **1d**	−1814
[Pt(*N*,*N*′-dmen)(O^3-HAsc)$_2$], **3b**	−1880	[Pt(tmen)(O^3-HAsc)$(H_2O)]^+$, **2d**	−1728
[Pt(*N*,*N*′-dmen)(O^2,O^3-Asc)], **4b**	−1785	[Pt(tmen)(O^2,O^3-Asc)], **4d**	−1611
[Pt(*N*,*N*′-dmen)(O^2,O^3-Asc)], **4b**′	−1790		

[a] Chemical shifts are relative to external K_2PtCl_4 at −1624 ppm in D_2O. Estimated error in shifts is ±2 ppm.

Scheme 1. Proposed Structures of Diamineplatinum Ascorbate Complexes



new peaks were observed at −2648 and −2680 ppm due to formation of [Pt(HAsc-O^3)(HAsc-C^2)(en)] and [Pt(Asc-C^2,O^5)-(en)], respectively. The peaks due to the oxygen-bound ascorbate species diminished with time, while the peaks due to the carbon-bound species increased in intensity. An off-white precipitate was collected from the reaction mixture, whose elemental analysis was consistent with [Pt(Asc)(en)]·$2H_2O$. This *C*,*O*-bound chelate appears to be the thermodynamic product of the reaction. Our observations are consistent with those of Hollis et al. in their studies of reactions of the ^{15}N-labeled ethylenediamine complex [Pt(^{15}en)$(H_2O)_2]^{2+}$ with sodium ascorbate.[2]

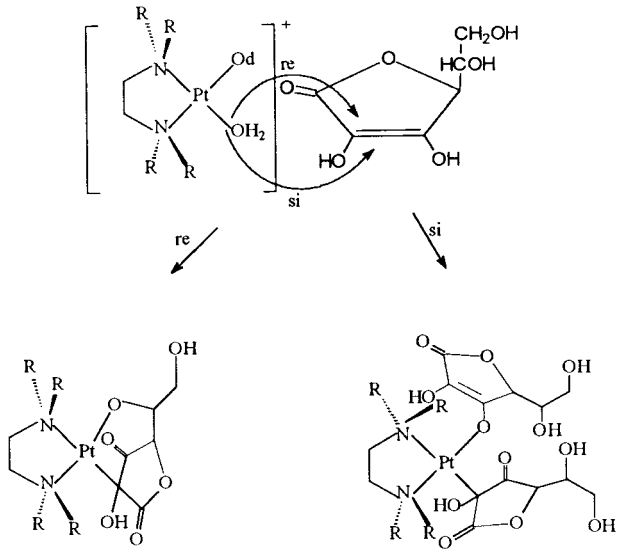
Reactions of [Pt(*N*,*N*-dmen)$(H_2O)_2$]$(NO_3)_2$ with Sodium Ascorbate. The ^{195}Pt NMR spectrum of [Pt(*N*,*N*-dmen)-$(H_2O)_2]^{2+}$ exhibits a single resonance at −1860 ppm. After addition of sodium ascorbate two new peaks appeared in the ^{195}Pt NMR spectrum at −1793 and −1650 ppm due the monodentate ascorbate complex [Pt(HAsc-O^3)(*N*,*N*-dmen)-$(H_2O)]^+$ and the chelate complex [Pt(Asc-O^2,O^3)(*N*,*N*-dmen)], respectively. The larger shift to high frequency (by 140 ppm) suggested formation of the O^2,O^3-bonded chelate rather than the bis(ascorbate) complex. The latter should appear 60−70 ppm to high frequency of [Pt(HAsc-O^3)(*N*,*N*-dmen)$(H_2O)]^+$.[2] A small peak appeared at −2641 ppm after 60 h of reaction due to formation of [Pt(Asc-C^2,O^5)(*N*,*N*-dmen)]. No other peaks were observed in this region, suggesting that the bis(ascorbate)-platinum species with one carbon-bound and one oxygen-bound ascorbate was not formed. Other workers have also reported the formation of the chelate complex [Pt(Asc-C^2,O^5)(*N*,*N*-dmen)] using ^{1}H NMR spectroscopy to monitor the reaction between [Pt$(OH)_2$(*N*,*N*-dmen)] and L-ascorbic acid over several days.[11]

Reactions of [Pt(*N*,*N*′-dmen)$(H_2O)_2$]$(NO_3)_2$ with Sodium Ascorbate. The ^{195}Pt NMR spectrum of [Pt(*N*,*N*′-dmen)-$(H_2O)_2]^{2+}$ shows a single peak at −1970 ppm. After addition of sodium ascorbate four new peaks appeared at −1910, −1880, −1790, and −1785 ppm that were assigned to [Pt(HAsc-O^3)-(*N*,*N*′-dmen)$(H_2O)]^+$, [Pt(HAsc-O^3)$_2$(*N*,*N*′-dmen)], and the two diastereoisomers of [Pt(Asc-O^2,O^3)(*N*,*N*′-dmen)], respectively. The oxygen-bound ascorbate species predominated during the first 48 h of reaction, but after this time two new peaks appeared at −2677 and −2687 ppm. These were due to the two diastereoisomers of [Pt(Asc-C^2,O^5)(*N*,*N*′-dmen)]. A peak of lower intensity was also observed at −2755 ppm, which we have assigned to the bis(ascorbate) complex [Pt(HAsc-O^3)-(HAsc-C^2)(*N*,*N*′-dmen)].

Reactions of [Pt(*N*,*N*,*N*′,*N*′-tmen)$(H_2O)_2$]$(NO_3)_2$ with Sodium Ascorbate. The ^{195}Pt NMR spectrum of [Pt(*N*,*N*,*N*′,*N*′-tmen)$(H_2O)_2]^{2+}$ consists of a single peak at −1814 ppm. After addition of sodium ascorbate, two new peaks appeared. On the basis of the difference in chemical shifts, we assigned the smaller peak at −1728 ppm to [Pt(HAsc-O^3)(*N*,*N*,*N*′,*N*′-tmen)$(H_2O)]^+$, and the more intense peak at −1611 ppm to the chelate complex [Pt(Asc-O^2,O^3)(*N*,*N*,*N*′,*N*′-tmen)]. No other peaks were observed in the spectrum even after a period of one week, suggesting that no carbon-bound ascorbate complexes were produced in this case. This observation agrees with that of Miyamoto et al., who also did not observe the formation of carbon-bound species during ^{1}H NMR studies of the reaction between [Pt$(OH)_2$-(*N*,*N*,*N*′,*N*′-tmen)] and L-ascorbic acid.[11]

The presence of methyl groups on nitrogen seems to favor formation of [Pt(Asc-O^2,O^3)(diamine)] rather than bis(ascorbate) complexes. The methyl groups also inhibit the formation of carbon-bound ascorbate complexes, presumably due to steric repulsion between the hydroxyl group (O2) and the methyl groups in a sterically crowded intermediate (Scheme 2).[11] This is evident from the decrease in the rate of formation of carbon-bound species in proceeding from the en complex (4 h of reaction time) to those of *N*,*N*′-dmen (48 h) and *N*,*N*-dmen (60 h). The difference in rate is not great, but rearrangement from oxygen-bound to carbon-bound species appears to be slower

Scheme 2. Proposed Mechanism for Formation of Carbon-Bound Platinum Ascorbate Complexes[a]



[a] Od represents an oxygen donor ligand, which might be a water, nitrate, or ascorbate monoanion.

Table 2. Crystallographic Data for the Structure Determination of **5a**

empirical formula	$C_8H_{18}N_2O_8Pt$	Z	2
		T (K)	298(2)
fw	465.33	ρ_{calcd} (Mg/m^3)	2.426
cryst syst	monoclinic	V (Å^3)	637.11(6)
space group	$P2_1$	abs coeff (mm^{-1})	11.051
a (Å)	6.1374(4)	θ range (deg)	3.15−29.58
b (Å)	16.0713(10)	no. of reflns collected	11336
c (Å)	6.7618(3)	no. of independent reflns (R_{int})	3236 (0.037)
α (deg)	90		
β (deg)	107.206(2)	$R(F_o^2)$	0.0183
γ (deg)	90	$R_w(F_o^2)$	0.0399

when one nitrogen has two methyls compared with the case where one methyl group resides on each nitrogen. When both nitrogens have two methyl substituents, rearrangement to carbon-bound ascorbates is prevented altogether.

Crystal and Molecular Structure of [Pt(Asc-C^2,O^5)(en)]·2H$_2$O. The solid-state structure of [Pt(Asc-C^2,O^5)(en)]·2H$_2$O was determined by X-ray crystallography. Data collection, structure solution, and refinement parameters are given in Table 2. The molecular structure of [Pt(Asc-C^2,O^5)(en)]·2H$_2$O is shown in Figure 1, and selected bond distances and angles are given in Table 3. The Pt atom is coordinated by the two N atoms of the ethylenediamine ligand, and C2 and O5 of the ascorbate ligand. The molecule has distorted square planar geometry with N(1)−Pt−N(2), N(2)−Pt−C(2), O(5)−Pt−N(1), and O(5)−Pt−C(2) angles of 83.31(14)°, 90.18(15)°, 90.52(13)°, and 95.98(13)°, respectively. The Pt−N distance trans to the carbon atom (2.083(3) Å) is slightly longer than that trans to oxygen (2.052(3) Å) as a result of the greater trans influence of the σ-carbon ligand. The Pt−O and Pt−C distances are 2.032(3) and 2.126(4) Å, respectively. These values compare favorably with the corresponding bond distances and bond angles in [Pt(Asc-C^2,O^5)(*S*,*S*-dach)].[1] Intermolecular hydrogen bonding occurs between O5 of one unit and OH-2 of another, with an O−H···O distance of 1.956 Å and an O−H···O angle of 157°. There is also evidence of intermolecular hydrogen bonding between O2 of one unit and OH-6 of another, with an O−H···O distance of 2.56 Å and an O−H···O angle of 152°. Two water molecules are trapped in the lattice by hydrogen-bonding interactions with the NH_2 groups.

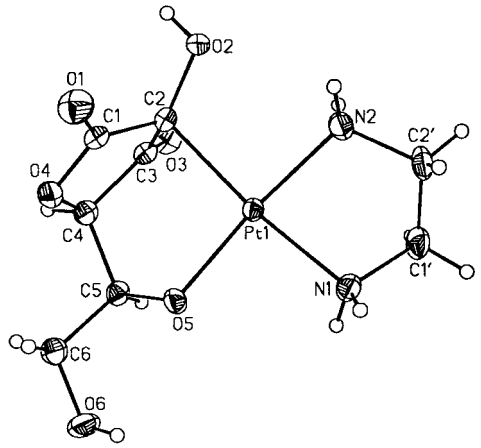


Figure 1. Molecular structure of [Pt{NH$_2$(CH$_2$)$_2$NH$_2$}(C$_6$H$_6$O$_6$)]·2H$_2$O, showing the atom-numbering scheme.

Table 3. Selected Bond Distances and Angles for [Pt(Asc-C^2,O^5)(en)]·2H$_2$O

bond distances (Å)		bond angles (deg)	
Pt(1)−N(1)	2.083(3)	N(2)−Pt−N(1)	83.31(14)
Pt(1)−N(2)	2.052(3)	N(2)−Pt−C(2)	90.18(15)
Pt(1)−O(5)	2.032(3)	N(1)−Pt−C(2)	173.45(14)
Pt(1)−C(2)	2.126(4)	O(5)−Pt−N(1)	90.52(13)
O(1)−C(1)	1.221(5)	O(5)−Pt−C(2)	95.98(14)
O(2)−C(2)	1.393(5)	C(5)−O(5)−Pt	115.8(2)
O(3)−C(3)	1.228(5)	O(2)−C(2)−Pt	112.3(2)
C(2)−C(3)	1.455(6)	C(1)−C(2)−Pt	109.3(3)
C(3)−C(4)	1.520(6)	C(3)−C(2)−Pt	87.4(3)

Table 4. ^{31}P{^{1}H} NMR Data for Diphosphineplatinum Nitrate and Ascorbate Complexes

complex	δ (ppm)	$^1J_{PtP}$ (Hz)	$^2J_{PP}$ (Hz)
[Pt(NO$_3$)$_2$(dppm)]	−68.9	3411	
[Pt(dppm)(NO$_3$)(OH$_2$)]$^+$	−60.8		11
	−65.7		11
[Pt(dppm)(OH$_2$)$_2$]$^{2+}$	−64.9	3060	
[Pt(Asc-O^2,O^3)(dppm)]	−62.4	3086	
	−62.1		21
[Pt(NO$_3$)$_2$(dppe)]	33.0	3940	
[Pt(Asc-O^2,O^3)(dppe)]	32.7	3366	10
	29.2	3670	10
[Pt(NO$_3$)$_2$(dppp)]	−13.4	3664	
[Pt(dppp)(NO$_3$)(OH$_2$)]$^+$	−4.1		28
	−12.7		28
[Pt(dppp)(OH$_2$)$_2$]$^{2+}$	−9.2	3435	
[Pt(Asc-O^2,O^3)(dppp)]	−8.9	3205	32
	−11.8	3464	32

Preparation of Diphosphineplatinum(II) Nitrate Complexes. We have prepared a series of diphosphineplatinum(II) nitrate complexes as shown in eqs 4 and 5. The reactions of

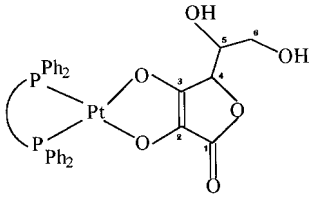
$$[Pt(cod)Cl_2] + Ph_2P(CH_2)_nPPh_2 \rightarrow [PtCl_2(P^{\cap}P)] + cod \quad (4)$$

$$[PtCl_2(P^{\cap}P)] + 2AgNO_3 \rightarrow [Pt(NO_3)_2(P^{\cap}P)] + 2AgCl \quad (5)$$

$$(P^{\cap}P = dppm, dppe, dppp)$$

[PtCl$_2$(P$^{\cap}$P)] with silver nitrate were performed in acetone−water mixtures. The ^{31}P{^{1}H} NMR spectra of the reaction mixtures suggested that [Pt(NO$_3$)$_2$(P$^{\cap}$P)], [Pt(H$_2$O)$_2$(P$^{\cap}$P)]$^{2+}$, and the mixed complexes [Pt(NO$_3$)(H$_2$O)(P$^{\cap}$P)]$^+$ were present in solution (Table 4). It is possible to isolate the dinitratoplatinum complexes by removing the precipitate of silver chloride and evaporating the filtrate after prolonged stirring (20−24 h) in the dark.

Table 5. ^{1}H NMR Data for Diphosphineplatinum Ascorbate Complexes



complex	CH_2	H-5	H-6,6′	H-4	ArH
[Pt(dppm)(Asc-O^2,O^3)][a]	4.56 m, br	4.32 br	3.83 s, br	4.43 d	7.5-8.0 m
[Pt(dppe)(Asc-O^2,O^3)][a]	2.39 m	3.39 t	3.71 d	4.49 d	7.5-8.0 m
		$^3J_{HH}$ = 6 Hz	$^3J_{HH}$ = 6 Hz	$^3J_{HH}$ = 6 Hz	
[Pt(dppp)(Asc-O^2,O^3)][a]	2.50 m	2.82 t	3.57 d	4.28 d	7.5-8.0 m
	2.12 m	$^3J_{HH}$ = 6 Hz	$^3J_{HH}$ = 6 Hz	$^3J_{HH}$ = 6 Hz	
[Pt(dppp)(Asc-O^2,O^3)][b]	3.08−3.32 m	3.85 dt	3.57 d	4.11 d	7.3−7.6 m
	2.50−2.70 m	$^3J_{HH}$ = 2, 6 H	$^3J_{HH}$ = 6 Hz	$^3J_{HH}$ = 6 Hz	

[a] Chemical shifts relative to $CDCl_3$ at 7.27 ppm. [b] Chemical shifts relative to acetone-d_6 at 2.05 ppm.

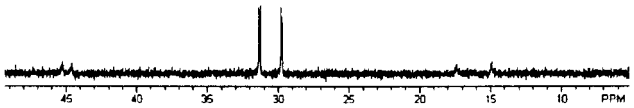


Figure 2. ^{31}P{^{1}H} NMR spectrum of [Pt(Asc)(dppe)] in $CDCl_3$.

Preparation of Diphosphineplatinum(II) Ascorbate Complexes. Reactions between the platinum nitrate complexes and 2 mol equiv of sodium ascorbate (eq 6) produced the O^2,O^3-

$$[Pt(NO_3)_2(P^{\cap}P)] + 2NaHAsc \rightarrow [Pt(Asc)(P^{\cap}P)] + H_2Asc + 2NaNO_3 \quad (6)$$

bonded chelate complexes [Pt(Asc-O^2,O^3)(P$^{\cap}$P)] in modest yields (50−59%). Their ^{31}P{^{1}H} NMR spectra in $CDCl_3$ solution exhibit two doublets, each with ^{195}Pt satellites, indicating that the two phosphorus nuclei are nonequivalent (Figure 2). The magnitudes of the coupling constants (3000−3700 Hz) are typical of tertiary phosphino groups lying trans to oxygen donors (Table 4). The chemical shifts and coupling constants for [Pt(Asc-O^2,O^3)(P$^{\cap}$P)] (P$^{\cap}$P = dppe, dppm) agree well with those reported for [Pt(C_2O_4)(dppe)] (δ(^{31}P) 32.7, $^1J_{PtP}$ = 3628 Hz) and [Pt(C_2O_4)(dppm)] (δ(^{31}P) −63.7, $^1J_{PtP}$ = 3081 Hz), respectively.[19,20] Similarly, the chemical shifts and coupling constants for [Pt(Asc-O^2,O^3)(dppp)] (δ(^{31}P) −8.9, $^2J_{pp}$ = 32 Hz, $^1J_{PtP}$ = 3205 Hz; δ(^{31}P) −11.8, $^2J_{PP}$ = 32 Hz, $^1J_{PtP}$ = 3464 Hz) are in agreement with those measured for other [Pt(diolate)-(dppp)] complexes.[21] The ^{1}H NMR data for the ascorbate complexes [Pt(Asc-O^2,O^3)(P$^{\cap}$P)] are summarized in Table 5. Results of microanalysis of the products are consistent with the general formula [Pt(Asc)(P$^{\cap}$P)]·H_2O (P$^{\cap}$P = dppm, dppe, dppp).

Infrared Spectroscopy. We have also characterized the diamine- and diphosphineplatinum ascorbate complexes by infrared spectroscopy (Table 6). The position of the ν(C═O) band of ascorbic acid at 1754 cm^{-1} shifts to lower frequency by between 30 and 50 cm^{-1} upon coordination to platinum. There is also a low-frequency shift in the combination bands due to ν(C═C) + ν(C═O), which appear at 1660 and 1675 cm^{-1} in the free acid.[22] A single sharp band was found between 1600 and 1625 cm^{-1} in the platinum complexes. A single broad band due to ν(O−H) is observed between 3315 and 3350 cm^{-1} for each of the diamineplatinum ascorbate complexes, in contrast to free ascorbic acid where four sharp bands are observed between 3220 and 3525 cm^{-1}.[22]

Table 6. Infrared Spectral Data for Platinum Ascorbate Complexes

compound	ν(O−H), cm^{-1}	ν(C═O), cm^{-1}	ν(C═O + C═C), cm^{-1}
[Pt(Asc-C^2,O^5)(en)][a] powder	3350 br	1721 s	
		1623 s	
[Pt(Asc-C^2,O^5)(en)][a] crystals	3332 s	1727 s	
		1624 s	
[Pt(Asc-O^2,O^3)(tmen)][a]	3317 br	1707 s	1603 br
[Pt(Asc-O^2,O^3)(dppm)][b]	3400 br	1699 s	1677 s
			1653 s
[Pt(Asc-O^2,O^3)(dppe)][b]	3380 br	1700 s	1654 m
			1617 m
[Pt(Asc-O^2,O^3)(dppe)][a]	3422 br	1732 m	1618 s
[Pt(Asc-O^2,O^3)(dppp)][b]	3391 br	1700 m	1675 m
			1654 m
L-ascorbic acid[b]	3525 s	1754 s	1675 s
	3410 s		1660 s
	3315 s		
	3220 s		

[a] KBr pellet. [b] Nujol mull.

Summary. We have investigated reactions between diaminediaquaplatinum complexes and sodium ascorbate using multinuclear NMR spectrosopy. Mixtures of platinum ascorbate species were formed involving different binding modes of the ascorbate ligand. The oxygen-bound complexes [Pt(HAsc-O^3)-(H_2O)(N$^{\cap}$N)]$^+$, [Pt(HAsc-O^3)$_2$(N$^{\cap}$N)], and [Pt(Asc-O^2,O^3)-(N$^{\cap}$N)] were formed first, and then conversion to the carbon-bound species [Pt(HAsc-O^3)(HAsc-C^2)(N$^{\cap}$N)] and [Pt(Asc-C^2,O^5)(N$^{\cap}$N)] took place. Rearrangement to the carbon-bound species was inhibited by the presence of methyl groups on the nitrogens, and did not occur at all in the tetramethylethylenediamine case. The solid-state structure of [Pt(Asc-C^2,O^5)(en)]·$2H_2O$ was established by X-ray crystallography.

We have prepared a series of diphosphineplatinum nitrate complexes, which we have employed as precursors to the first platinum ascorbate complexes containing diphosphine ligands. We have characterized the ascorbate complexes by ^{1}H and ^{31}P NMR spectroscopy, as well as by elemental analysis. These data suggest that the ascorbate ligand binds to platinum as the doubly deprotonated bidentate ligand through oxygen atoms O2 and O3. It seems that steric repulsion between the hydroxyl group (O2) and the phenyl groups of the diphosphine ligands prevents the formation of C^2,O^5-chelate complexes. On the basis of the diphosphine bite angles, such steric interactions should increase

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in the order dppm < dppe < dppp for the O^2,O^3-bonded chelates. Further studies of the reactions of sodium ascorbate with diphosphineplatinum and -palladium complexes are in progress.

Acknowledgment. This work was supported through a grant from the National Science Foundation (Grant Number CHE-9508228) and a University of Missouri—St. Louis Research Award. Thanks are expressed to the NSF for grants for the purchase of NMR and X-ray instrumentation.

Supporting Information Available: Tables giving crystal data, structure refinement, atomic coordinates, isotropic and anisotropic displacement parameters, and bond lengths and angles for [Pt(C^2,O^5-Asc)(en)]·$2H_2O$. This material is available free of charge via the Internet at http://pubs.acs.org. The data have been deposited at the Cambridge Crystallographic Data Center (CCDC). Any request to the CCDC should quote the reference number 137144.

IC990152Z