Inorganica Chimica Acta, *114* (1986) 127–135

The Synthesis and Characterization of 1,1-Bis(aminomethyl)cyclohexaneplatinum(II) Compounds and the Crystal Structure Determination of 1,1-Bis(aminomethyl)-cyclohexaneaquosulphatoplatinum(II) Monohydrate*

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Received August 29, 1985

Abstract

The synthesis and characterization of a number of 1,1-bis(aminomethylcyclohexane)platinum(II) complexes is described. Reaction of 1,1-bis(aminomethylcyclohexane)dichloroplatinum(II) ($LPtCl_2$) with silver sulphate and silver nitrate in water results in the isolation of the corresponding aquosulphato·monohydrate, $LPt(H_2O)SO_4 \cdot H_2O$ and dinitratoplatinum(II), $LPt(NO_3)_2$, complexes.

Treatment of aqueous solutions of these compounds with an equimolar amount of sodium hydroxide results in the formation of mixtures of hydroxo-bridged dimers and trimers. The less soluble cyclic trimeric species $[LPt(\mu\text{-OH})]_3(NO_3)_3 \cdot 2H_2O$ and $\{[LPt(\mu\text{-OH})]_3\}_2(SO_4)_3 \cdot 8H_2O$ have been isolated. The ^1H, ^{13}C and ^{195}Pt NMR spectra of the various compounds have been studied in D_2O. In particular, ^{195}Pt NMR is a valuable tool for identification of the various platinum complexes present in aqueous solution.

IR spectral data are reported. The IR spectra of $LPt(SO_4) \cdot xH_2O$ containing varying amounts of water of crystallization and/or coordination are discussed. In $LPt(H_2O)SO_4 \cdot H_2O$ the symmetry of the monodentate SO_4 ligand appears to be lowered as a result of strong hydrogen bonding to the water molecules. The crystal structure of this compound has been determined by single-crystal X-ray diffraction. The monoclinic crystal, space group $P2_1/c$, has cell dimensions $a = 13.615(9)$, $b = 7.372(1)$, $c = 14.702(2)$ Å, $\beta = 109.26(4)°$ and has four formula units in the unit cell. The structure was solved by standard methods and refined to $R = 0.0337$ based on 2671 reflections. The coordination of the metal atom is square planar with two nitrogen atoms, one oxygen of a water molecule and one oxygen of the sulfate anion being bound to platinum(II). There is extensive inter- and intramolecular hydrogen bonding.

Introduction

At present *cis*-diamminedichloroplatinum(II) finds wide clinical application in the treatment of various types of cancer [1]. Although the compound is quite effective, it also exhibits significant toxic side effects. Therefore, in recent years much emphasis has been given to the development of analogues showing high antitumor activities in combination with reduced toxicity profiles [2–4]. Chloride has been substituted for other leaving groups, such as nitrate, sulphate, oxalate and (substituted) malonate, and ammine ligands have been replaced by *cis*-di-monodentate or bidentate primary amines [2–6]. Within this framework a series of 1,1-bis(aminomethyl)cyclohexane platinum(II) compounds has been synthesized [7] which appear to exhibit high antitumor activity in various tumor systems in mice [8] and rats [9]. One representative compound of this series, 1,1-bis(aminomethyl)aquosulphatoplatinum(II) hydrate (codename TNO-6) has been selected for clinical trials [10]. Unfortunately, in contrast with the results obtained in mice and rats, this compound was found to be inferior in humans to *cis*-diamminedichloro-

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*Presented in part at the Fourth International Symposium on Platinum Coordination Complexes in Cancer Chemotherapy, see ref. 11a.

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0020-1693/86/$3.50

platinum(II), and consequently it will not find further clinical application. The present paper describes the synthesis and characterization of a number of 1,1-bis(aminomethyl)cyclohexane-platinum(II) compounds [11] and the determination of the crystal and molecular structure of 1,1-bis-(aminomethyl)aquosulphatoplatinum(II) hydrate.

Experimental

Starting Materials

K_2PtCl_4 was obtained commercially from Drijfhout, Amsterdam. 1,1-Bis(aminomethyl)cyclohexane [12] was prepared as described in the literature.

1,1-Bis(aminomethyl)cyclohexane·2HCl Salt (1)

A solution of 19.7 g (138.5 mmol) of 1,1-bis-(aminomethyl)cyclohexane in 300 ml dry toluene was cooled to 0 °C, and dry HCl gas was passed through the solution to give a colourless precipitate of the desired product in a quantitative yield (29.8 g).

1,1-Bis(aminomethyl)cyclohexanedichloroplatinum-(II) (2)

A solution of 10.75 g (50 mmol) 1,1-bis(aminomethyl)cyclohexane·2HCl (1) and 19.5 g (50 mmol) K_2PtCl_4 dissolved in 100 ml of water was heated at 95 °C. Subsequently, 4.2 g (105 mmol) of NaOH dissolved in 50 ml of water was added dropwise to the stirred solution at such a rate that the pH of the reaction mixture did not exceed 7. At the end of the addition process, the pH rose and the addition of NaOH was concluded at pH 7.5. The reaction mixture was cooled to 0 °C and the precipitate present was filtered off, washed with 100 ml of water and 25 ml of acetone and dried at reduced pressure. The crude reaction product was dissolved in 1 l of liquid ammonia and the solution thus obtained was filtered through a G3 glass filter. The clear filtrate was concentrated by evaporation of the ammonia at room-temperature. The remaining yellow solid was stirred with 100 ml of 2 N HCl, filtered off, washed with 200 ml of water and 100 ml of acetone, and dried over NaOH pellets in a vacuum desiccator to give 16.0 g (80%) of yellow-coloured product, melting point (m.p.) 304–305 °C (decomposition (dec.)). *Anal.* Calc. for $C_8H_{18}N_2Cl_2Pt$: C, 23.54; H, 4.44; N, 6.86; Cl, 17.37; Pt, 47.79. Found: C, 23.57; H, 4.60; N, 6.94; Cl, 17.20; Pt, 47.67%.

1,1-Bis(aminomethyl)cyclohexaneaquosulphatoplatinum(II)·H_2O (3)

1,1-Bis(aminomethyl)cyclohexanedichloroplatinum (II) (6.5 g, 15.9 mmol) was suspended in 400 ml of water. Ag_2SO_4 (4.9 g, 15.7 mmol) was added and the mixture was stirred for 5 h at 50 °C in the dark. AgCl was filtered off and the clear filtrate was concentrated by evaporation at 50 °C at reduced pressure. Evaporation to dryness resulted in the isolation of 6.15 g of a pale yellow product. Yield 85%. *Anal.* Calc. for $C_8H_{18}N_2O_4SPt·H_2O$: C, 21.29; H, 4.47; N, 6.21; O, 17.72; S, 7.10; Pt, 43.22. Found: C, 21.28; H, 4.39; N, 6.36; O, 17.23; S, 7.17; Pt, 42.90%. Upon addition of acetone to a concentrated aqueous solution (5 ml) of this product (500 mg), a pale yellow solid precipitated in quantitative yield. The solid was filtered off and dried in vacuum. The product analyzed for $C_8H_{18}N_2O_4SPt·1.5H_2O$, pointing to the original formation of $C_8H_{18}N_2O_4SPt·2H_2O$. The dihydrate readily loses water of crystallization when kept under reduced pressure at room temperature. Single crystals of $C_8H_{18}N_2O_4SPt·2H_2O$ were obtained from a vacuum-concentrated aqueous solution containing 1 g of the compound in 10 ml of water at 50 °C. The solution was cooled to +2 °C and stored for 1 month to give crystals suitable for X-ray structure determination.

1,1-Bis(aminomethyl)cyclohexanedinitratoplatinum-(II) (4)

1,1-Bis(aminomethyl)cyclohexanedichloroplatinum (II) (4.0 g, 9.7 mmol) was suspended in 30 ml of water. $AgNO_3$ (3.1 g, 18.2 mmol) was added and the mixture was stirred for 1 h at 40 °C in the dark. AgCl was filtered off and the clear filtrate was concentrated at 50 °C at reduced pressure. A colourless solid was obtained which was dried over KOH in a vacuum desiccator to give 4.17 g of **4**, m.p. 240 °C (explosive decomposition). *Anal.* Calc. for $C_8H_{18}N_4O_6Pt$: C, 20.83; H, 3.93; N, 12.14; O, 20.81. Found: C, 20.93; H, 4.10; N, 11.92; O, 20.01%.

cyclo-Tri-μ-hydroxo-tris[1,1-bis(aminomethyl)cyclohexaneplatinum(II)] trinitrate (5)

A solution of 7.8 g (17 mmol) of 1,1-bis(aminomethyl)cyclohexanedinitratoplatinum(II) in 100 ml of water was titrated with 2 N NaOH to pH 6.7 and kept at 50 °C for 2 h. During the heating period a colourless solid precipitated from the initially clear solution. The solution was cooled at 0 °C and 3.5 g of solid product was filtered off. The filtrate was kept overnight and a second crop of 0.6 g of product was obtained. The combined products were recrystallized from water to give 3.1 g of the title compound. *Anal.* Calc. for $C_{24}H_{57}N_9O_{12}Pt_3·2H_2O$: C, 22.44; H, 4.75; N, 9.81; O, 17.44; Pt, 45.56. Found: C, 22.45; H, 4.82; N, 9.74; O, 17.28; Pt, 45.76%.

Bis-[cyclo-tri-μ-hydroxo-tris[1,1-bis(aminomethyl)-cyclohexaneplatinum(II)]] trisulphate·8H_2O (6)

Silver sulphate (3.0 g, 9.6 mmol) was added to a suspension of 4.0 g (9.8 mmol) of 1,1-bis(aminomethyl)cyclohexanedichloroplatinum(II). The mixture was kept in the dark, heated at 40 °C and stirred for 5 h. AgCl was filtered off and subsequently at 50 °C 8.1 mmol of 2 N NaOH was slowly added to the filtrate over a period of 30 min. As a result, the pH of the solution rose from 2.4 to 6.0. Upon cooling to 2 °C, 2.4 g of colourless product precipitated, m.p. 250 °C (dec.). *Anal.* Calc. for $C_{48}H_{114}N_{12}O_{18}S_3Pt_6 \cdot 8H_2O$: C, 22.54; H, 5.12; N, 6.57; O, 16.26; S, 3.76; Pt, 45.75. Found: C, 22.28; H, 4.91; N, 6.45; O, 16.39; S, 3.71; Pt, 45.95%.

Sulphate Titration of 4

Reaction of sulphate ion with 1,1-bis(aminomethyl)cyclohexane diaquoplatinum(II) was studied by the addition of microliter quantities of a 1.69 M solution of Na_2SO_4 in D_2O to 2.4 ml of a 35 mM solution of **4** in D_2O. After allowing the system to come to equilibrium (2 days), ^{195}Pt and ^{13}C NMR data were obtained.

Chloride Titration of 4

Reaction of chloride ions with 1,1-bis(aminomethyl)cyclohexane diaquoplatinum(II) was studied by the addition of microliter quantities of a 1.33 M solution of NaCl in D_2O to 1.5 ml of a 44 mM solution of **3** in D_2O. After allowing the system to come to equilibrium (<1 h), ^{195}Pt NMR data were obtained.

Apparatus

IR spectra were recorded in KBr or in nujol mulls using KBr disks on a Perkin Elmer 577 infrared spectrometer. The infrared study of **3** as a function of the state of hydration of the compound was carried out using a Bruker 113 v FT-IR spectrometer. NMR spectra were run on Bruker WM-360 widebore, Bruker WP-200 and Bruker WH-90 DS spectrometers. The operating frequencies (in MHz) for the various nuclei were: Bruker WM-360, ^{1}H 360.13, ^{13}C 90.56, ^{195}Pt 77.25; Bruker WP-200, ^{195}Pt 43.02; Bruker WH-90 DS, ^{1}H 90.02, ^{13}C 22.63. All spectra were determined in D_2O at constant temperature (298 K). ^{1}H and ^{13}C chemical shift data are referenced to external TMS. ^{195}Pt chemical shifts are reported relative to external Na_2PtCl_6 in D_2O (1 g/ml). In the ^{195}Pt NMR studies, the concentrations of the Pt(II) sulphato and nitrato compounds **3** and **4** typically were in the range of 40–80 mg/ml. NMR chemical shift data are collected in Table I.

X-ray Diffraction Data

X-ray diffraction data of compound **3** were collected on an Enraf-Nonius CAD4F diffractometer for a light-yellow transparent crystal glued on top of a glass fiber. Unit cell dimensions, their corresponding standard deviations, and a complete data set were obtained via previously described standard procedures using Zr-filtered Mo Kα-radiation [13]. The crystal data and details of the data collection and structure refinement are summarized in Table II. The intensity of one reflection was monitored every hour of X-ray exposure time (total 17.3 h). There was no indication for decay during the data collection. The data were subsequently corrected for absorption, with an empirical method [14] (correction ranging from 0.784 to 1.338) and for Lorentz and polarization effects, and averaged into a unique set of data in the previously described way [13].

Structure Determination and Refinement

The structure was solved by standard Patterson and Fourier techniques and subsequently refined on *F* by blocked full-matrix least-squares techniques. Hydrogen atoms were located from a difference Fourier map. All positional parameters, anisotropic thermal parameters for the non-hydrogen atoms and one overall isotropic temperature factor were refined. Weights and an empirical extinction correction were introduced in the final stages of the refinement. Convergence was reached at $R = 0.0337$ for 2671 observed reflections. A final difference Fourier showed no significant features apart from some residual density near Pt. The final refined positional parameters are listed in Table III. Neutral scattering factors were taken from ref. 15 and corrected for anomalous dispersion effects [16]. All calculations

TABLE I. NMR Chemical Shift Data for a Number of 1,1-Bis(aminomethyl)cyclohexaneplatinum(II) Complexes[a]

Compound	δ ^{1}H			δ ^{13}C					δ ^{195}Pt	
	7,8-CH_2	2,6-CH_2	3,4,5-CH_2	7,8-C	1-C	2,6-C	4-C	3,5-C	δ	Δν½ (Hz)
L·2HCl[b]				44.5	35.9	30.8	25.8	21.3		
$[LPt(OH_2)_2]^{+2}$[c,d]	2.34	1.35	1.44	53.0	38.9	33.7	28.3	23.2	−1864	770
$[LPt(SO_4)(H_2O)]$	2.37 2.38	1.35	1.44	53.4 53.0	38.9	33.8 33.7	28.3	23.2	−1835	770
$[LPt(Cl)(H_2O)]^{+}$[d]									−2066	660
$[LPt(\mu\text{-}OH)]_2^{+2}$[d,e]	2.34	1.29	1.41						−1471	400
$[LPt(\mu\text{-}OH)]_3^{+3}$[d,e]	2.39	1.34	1.44						−1731	400

[a] Data collected in D_2O. [b] pH 5.5. [c] pH < 3.0. [d] NO_3^- or $SO_4^{=}$ salt. [e] pH > 3.8.

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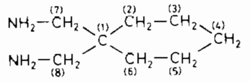


TABLE II. Crystal Data and Details of the Structure Determination

Crystal data	
Formula	$C_8H_{22}N_2O_6SPt$
Molecular weight	469.43
Crystal system	monoclinic
Space group	$P2_1/c$ (No. 14)
a (Å)	13.615(9)
b (Å)	7.372(1)
c (Å)	14.702(2)
β (°)	109.26(4)
V (Å^3)	1393(1)
Z	4
D_c (g cm^{-3})	2.238
$F(000)$	904
μ(Mo Kα) (cm^{-1})	98.3
Crystal dimensions (mm)	0.12 X 0.12 X 0.50
Data collection	
Radiation, wavelength (Å)	Mo Kα (Zr-filtered), 0.71069
θ_{min}, θ_{max} (°)	1.59, 27.5
$\omega/2\theta$ scan	$0.50 + 0.35 \tan\theta$
Reference reflections	020, (σ = 2.6%)
Total data, unique data	3256, 2938
Observed data ($I > 2.5\ \sigma(I)$)	2671
Refinement	
Number of parameters refined	231
Weighting scheme	$w^{-1} = (\sigma^2(F) + 0.000919\ F^2)/2.5496$
$R_F = \Sigma\|F_o - \|F_c\|\|/\Sigma F_o$	0.0337
$R_{wF} = [\Sigma w(F_o - \|F_c\|)^2/\Sigma w F_o^2]^{1/2}$	0.0359
Variance	2.38

TABLE III. Final Refined Positional Parameters

Atom	x/a	y/b	z/c
Pt(1)	0.05980(2)	0.18825(3)	−0.00829(1)
S(1)	−0.1266(1)	0.3235(2)	−0.1827(1)
O(1)	−0.0568(3)	0.1612(6)	−0.1390(3)
O(2)	−0.0600(4)	0.4704(7)	−0.1984(3)
O(3)	−0.1789(4)	0.3851(7)	−0.1156(4)
O(4)	−0.1998(4)	0.2597(8)	−0.2737(4)
O(5)	−0.0417(4)	0.3007(6)	0.0573(3)
O(6)	0.1458(4)	0.3975(8)	−0.1995(4)
N(1)	0.1508(4)	0.0801(8)	−0.0786(3)
N(2)	0.1749(4)	0.2199(7)	0.1205(4)
C(1)	0.3213(4)	0.1094(9)	0.0586(4)
C(2)	0.3359(6)	0.297(1)	0.0206(5)
C(3)	0.4205(7)	0.412(1)	0.0922(6)
C(4)	0.5240(7)	0.307(1)	0.1248(7)
C(5)	0.5145(6)	0.127(1)	0.1672(6)
C(6)	0.4284(5)	0.012(1)	0.0980(5)
C(7)	0.2516(5)	−0.009(1)	−0.0225(5)
C(8)	0.2752(5)	0.116(1)	0.1408(4)
H(1)	0.161(4)	0.158(4)	−0.119(4)
H(2)	0.115(4)	−0.030(4)	−0.122(4)
H(3)	0.158(4)	0.190(4)	0.178(4)
H(4)	0.201(4)	0.340(4)	0.123(4)
H(5)	0.358(4)	0.274(4)	−0.041(4)
H(6)	0.270(4)	0.367(4)	−0.009(4)
H(7)	0.432(4)	0.544(4)	0.063(4)
H(8)	0.401(4)	0.432(4)	0.148(4)
H(9)	0.580(4)	0.383(4)	0.176(4)
H(10)	0.548(4)	0.290(4)	0.070(4)
H(11)	0.585(4)	0.054(4)	0.183(4)
H(12)	0.501(4)	0.152(4)	0.236(4)
H(13)	0.453(4)	−0.026(4)	0.042(4)
H(14)	0.423(4)	−0.107(4)	0.138(4)
H(15)	0.235(4)	−0.133(5)	0.004(4)
H(16)	0.293(4)	−0.041(4)	−0.072(4)
H(17)	0.334(4)	0.176(4)	0.195(4)
H(18)	0.263(4)	−0.023(4)	0.157(4)
H(19)	−0.103(4)	0.319(4)	0.011(4)
H(20)	−0.023(4)	0.396(4)	0.092(4)
H(21)	0.173(4)	0.517(4)	−0.197(4)
H(22)	0.087(4)	0.386(5)	−0.195(4)

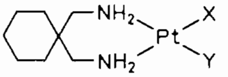
were carried out on either the in-house ECLIPSE S/230 mini-computer with the program ILIAS (An adaptation of the program SHELX-76 [17]) or on the CYBER-175 of the University of Utrecht computer center with the programs of the EUCLID package [18] (molecular geometry and illustrations).

Results and Discussion

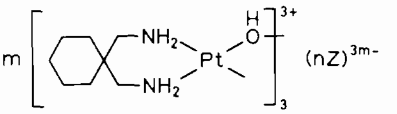
Synthesis

The 1,1-bis(aminomethyl)cyclohexaneplatinum(II) compounds described in this paper have been synthesized by reaction procedures essentially analogous to those recently reported for the synthesis of a variety of corresponding platinum complexes with ammonia, aliphatic and alicyclic amines as neutral ligands bonded to platinum [19–22]. The elemental analyses are in good agreement with the indicated formulae. Elemental analysis showed that the sulphato derivative, 1,1-bis(aminomethyl)cyclohexane aquosulphato platinum(II)·monohydrate (**3**), readily loses water of crystallization when kept at room temperature in a dry atmosphere. This phenomenon is not uncommon and has also been observed in other diaminoplatinum(II) complexes [19–21].

The μ-hydroxo bridged platinum complexes **5** and **6** have been assigned trimeric structures on the basis of both the synthetic procedure and the ^{195}Pt NMR spectral data. After accounting for the electronic effects of the diamine, the ^{195}Pt NMR parameters for the compound are in agreement with those obtained for the corresponding *cis*-diammine- [21, 23–26] and (*trans*-1,2-diaminocyclohexane)platinum(II) complexes [22].



2: X, Y = Cl^-
3: X = SO_4^{2-}; Y = H_2O
4: X, Y = NO_3^-



5: *m* = 1; *n* = 3; Z = NO_3^-
6: *m* = 2; *n* = 3; Z = SO_4^{2-}

Infrared Studies

The infrared spectrum of the dichloro complex **2** shows absorption bands characteristic for the 1,1-bis(aminomethyl)cyclohexaneplatinum(II) moiety. The dinitrato complex **4** shows a series of additional bands corresponding to the presence of coordinated nitrate ligands. Depending on the presence or absence of water of crystallization, two distinct types of sulphato complexes **3** can be recognized by IR spectroscopy. FT-IR spectra have been collected on various samples containing different amounts of water of crystallization and/or water coordinated to platinum. A series of these spectra is presented in Fig. 1.

IR spectral data are reported. The IR spectra of methyl)cyclohexanePtSO$_4$H$_2$O·H$_2$O suggest the of crystallization and/or coordination are discussed.

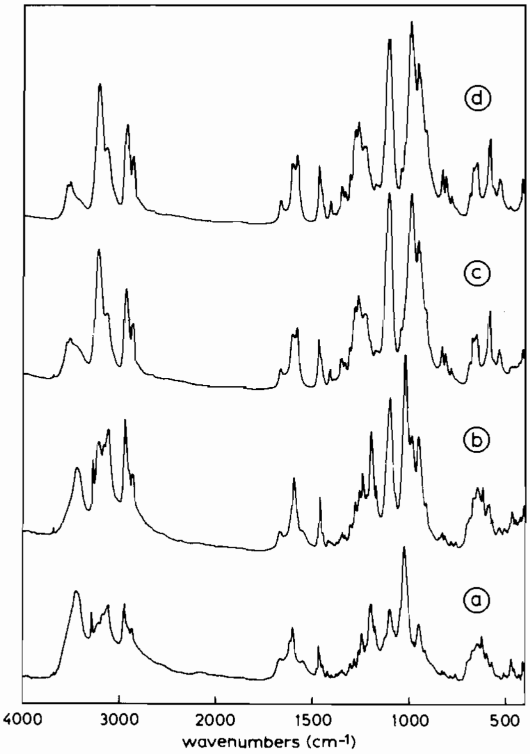


Fig. 1. FT-IR absorption spectra of LPtSO$_4$·xH$_2$O in KBr; (a) x = 2; (b) x = 1.5; (c) x = 1; (d) x = 0.

(ν_2S–O 468 cm^{-1}, ν_4S–O 590, 620, 645 cm^{-1}; ν_1S–O 945 cm^{-1} and ν_3S–O 1020, 1090, 1190 cm^{-1}). Actually, as demonstrated by X-ray crystallography, this compound contains a monodentate sulphato ligand together with one water molecule coordinated to platinum and another present as water of crystallization. Hydrogen bonding of the sulphate oxygen atoms to both types of water molecules apparently is responsible for the observed reduction of sulphate symmetry from C_{3v} to C_{2v}. The same type of monodentate sulphato ligand bonded to copper in diaquosulphato (*N,N,N′,N′*-tetramethylene diamine) copper(II) hydrate [27] has been reported to exhibit IR absorption bands at 1030, 1095 and 1170 cm^{-1}, which are essentially in the same positions as those observed for ν_3S–O of the present platinum complex.

In a dry atmosphere and/or in vacuum, the compound easily loses one molecule of water resulting in a marked change of the infrared spectrum. The IR data suggest the presence of a sulphato ligand with C_{3v} symmetry (ν_2S–O 410 cm^{-1}; ν_4S–O 580, 650 cm^{-1}; ν_1S–O 950 cm^{-1}; ν_3S–O 990, 1105 cm^{-1}). In addition, new absorption bands are present at ν 1230–1280 cm^{-1}, which, according to several authors, point to the presence of chelated [28–30] and/or bridging [31] sulphato ligands. Remarkably, further drying of the compound by heating *in vacuo* at 80 °C to a product containing 0–0.5 H$_2$O does not result in a further alteration of the infrared spectrum.

The presence of a unidentate sulphato ligand in this product seems very unlikely since the common four-coordination of platinum would not be reached.

The aforementioned results indicate that various factors, particularly sulphate–hydrogen bonding, strongly influence the appearance of the sulphato ligand infrared absorption bands in aquated metal complexes. Consequently, straightforward structural assignment of the disposition of sulphate ion on the basis of infrared data alone may not be possible. Similar phenomena have recently been described by Appleton *et al.* [21] for the IR spectra of $Pt(NH_3)_2SO_4 \cdot H_2O$ and anhydrous $Pt(NH_3)_2SO_4$. On comparison of the present data with the data presented in ref. 21, it is suggested that the former product primarily consists of $(NH_3)_2Pt(H_2O)SO_4 \cdot H_2O$. The large series of diaminoplatinumdiaquasulphates described by Gullotti *et al.* [32] are also regarded to possess a monodentate sulphato ligand in the solid state.

NMR Studies

The ^1H, ^{13}C and ^{195}Pt NMR chemical shift data of the various 1,1-bis(aminomethyl)platinum(II) species discussed in this section are presented in Table I.

Upon dissolution of the sulphato complex **3** in D_2O, a lowering of the pD of the medium (2.2–2.4) is observed and the presence of three platinum(II) containing species is established by ^{195}Pt NMR. The two major components exhibit ^{195}Pt NMR resonances at −1835 and −1864 ppm, while the third minor component exhibits a resonance at −2066 ppm (Fig. 2a). Dissolution of the dinitrato complex **4** in D_2O resulted in two ^{195}Pt NMR active species (Fig. 2b). The chemical shift of the major and minor components in the mixture were identical to two of the components present in aqueous solutions of **3**, −1864 and −2066 ppm. Since the ^{13}C NMR spectrum of **4** exhibited a relatively simple five line resonance pattern, the major component is very likely substituted by identical ligands in the sites *trans* to the coordinated diamine group. Unsymmetrical substitution, *i.e.*, two different ligands in the aforementioned coordination sites, would be expected to lift the degeneracy of certain of the carbon resonances of the diamine yielding a spectrum having more than five lines. Due to its low concentration, ^{13}C NMR signals for the minor component were not observed. These observations and the results of previous NMR studies on *cis*-$[(NH_3)_2Pt(H_2O)_2](NO_3)_2$ [21] lead to the conclusion that the major species present in aqueous solutions of **4** is the diaquo cation $[LPt(H_2O)_2]^{2+}$. Although the solid state infrared data of **4** show the presence of bound nitrate ion, dissolution of the complex in water results in release of the weakly bound nitrate ligands and the formation of $[LPt(H_2O)_2]^{2+}$.

The identity of the high field Pt NMR resonance at −2066 ppm in the spectra of both **3** and **4** was accomplished by adding chloride ion to the NMR solution of **4**. Since addition of the ion caused a decrease in the intensity of the signal associated with $[LPt(H_2O)_2]^{+2}$ and an increase in intensity of the signal at −2066 ppm, the high field resonance was assigned to $[LPt(H_2O)Cl]^+$. Its presence in preparations of both **3** and **4** is due to incomplete precipitation of chloride ion from **2** in the synthesis of the sulphato and nitrato complexes. The ^{195}Pt NMR chemical shift of $[LPt(H_2O)Cl]^+$, is, after accounting for the differential effects of L and NH_3 on the chemical shift of Pt(II) (~300 ppm) [26], in the region expected for the chloro-aquo species [21, 24, 25]. Continued addition of chloride ion to a solution of **4** ultimately resulted in the precipitation of the dichloro complex **2**. Due to its low solubility, this compound could not be detected in solution by ^{195}Pt NMR. The spectrum obtained after addition of 0.75 equivalents of Cl^- to an aqueous solution of **4** is shown in Fig. 2c.

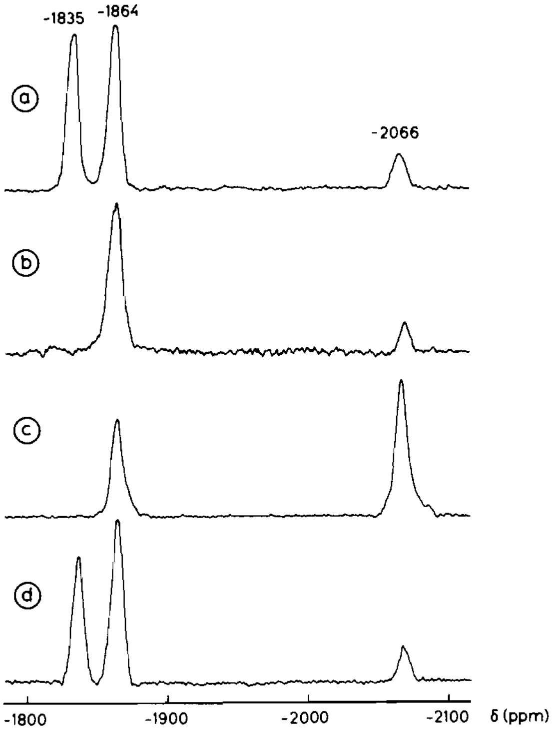


Fig. 2. Platinum-195 NMR spectra of various Pt(II) complexes in D_2O; (a) $LPt(H_2O)SO_4 \cdot H_2O$ (**3**); (b) $LPt(NO_3)_2$ (**4**); (c) Solution of **4** containing 0.75 equivalents of Cl^-; (d) Solution of **4** containing 1.1 equivalents of SO_4^{2-}.

Platinum-195 as well as ^{13}C NMR analyses of a titration of **4** with sulfate ion allowed the assignment of the lowest field ^{195}Pt NMR resonance (−1835 ppm) in **3** to $[LPt(H_2O)(SO_4)]$. Since this complex possesses non-identical ligands in the sites *trans* to the coordinated diamine, its ^{13}C NMR spectrum should be more complicated than the symmetrical substituted complex, $[LPt(H_2O)_2]^{+2}$. The data in Table I indicate that this is in fact the case, and separate resonances for [LPt(H_2O)(SO_4)] can be observed for C-2,6,7 and 8 of the diamine ligand. The assignment of the carbon resonances of the ligand L in the complexes was accomplished by comparison of spectral data with the ^{13}C NMR spectrum of 1,1-diethylcyclohexane and via calculation using Grant's rules.

Although other unsymmetrically substituted complexes, e.g., a dinuclear sulphato bridged species, cannot be unequivocally ruled out, the most likely product formed in the titration of $[LPt(H_2O)_2]^{+2}$ with $SO_4^=$ ion is the mononuclear species containing monodentate sulphate, *i.e.*, [LPt(H_2O)(SO_4)]. The ^{195}Pt NMR chemical shift difference observed for the aquosulphato and diaquo species (~29 ppm) is similar to that observed for the analogous *cis* diammine complexes [21]. A ^{195}Pt NMR spectrum of a solution of **4** containing 1.1 equivalents of $SO_4^=$ ion is shown in Fig. 2d.

Titration of aqueous solutions of **3** and **4** with an equimolar amount of NaOH resulted in the isolation of the μ-hydroxo-bridged trimers **5** and **6**. ^{195}Pt NMR reveals that in solution both μ-hydroxo-bridged dimeric and trimeric platinum complexes are formed with ^{195}Pt NMR resonances at −1471 and −1731 ppm, respectively. The observed resonances are almost identical to their (*trans*-1,2-diaminocyclohexane) platinum(II) counterparts [22]. The dimer and trimer are in equilibrium with one another according to: 2 trimer ⇌ 3 dimer. The equilibrium constant in D_2O at room temperature in solutions containing ~40 mM Pt was calculated from the ^{195}Pt NMR spectral data to be $K = [\text{dimer}]^3/[\text{Trimer}]^2 = {\sim}0.36$ M. The selective isolation of the trimers **5** and **6** is obviously based upon their solubility differences. As observed for the corresponding (*trans*-1,2-diaminocyclohexane)platinum species, the trimer apparently is less soluble than the dimer.

Description of the Crystal Structure

The molecular structure of *cis*-1,1-bis(aminomethyl) cyclohexaneaquosulphatoplatinum(II)·H_2O (**3**) has been elucidated by X-ray crystallography. Figure 3 shows the asymmetric unit of the structure. The monoclinic unit cell contains four such units. They combine into a two-dimensional multiple hydrogen-bonded layer (Fig. 4) perpendicular to the *a*-axis. The cyclohexane moieties are positioned perpendicular to those planes, so that two hydrogen-bonded layers (at $x = 0$ and $x = 1$) are separated by layers with cyclohexane stacking.

The coordination of the metal is square planar with bonding of two nitrogen atoms, one water molecule and one oxygen of the sulphate anion, to platinum(II). The present structure is very similar to that of diaquosulphato(*N*,*N*,*N'*,*N'*-tetramethylethylenediamine)copper(II) hydrate [27]. Selected data on the geometry are presented in Table IV*. There is a marked difference in the S–O bond length for the oxygen atom that coordinates to Pt (1.531(5) Å), as opposed to the other three that range from 1.457 to 1.478 Å. A correlation is observed between the latter three values and the number of hydrogen bonds to the sulphate oxygen atoms: the longest bond, S–O(2) = 1.478(5) Å, is involved in three hydrogen bonds, the shortest, S–O(4) = 1.457(5), in only one and the intermediate distance, S–O(3) = 1.467(5) Å, in two hydrogen bonds. This trend has been reported previously by Gorter and Engelfriet [33].

All hydrogen atoms of the N(amine) and O(water) atoms are involved in at least one hydrogen bond (Table IV); H2(N1) is involved in a bifurcated hydrogen bond to O(2) of the sulphate and O(6) of

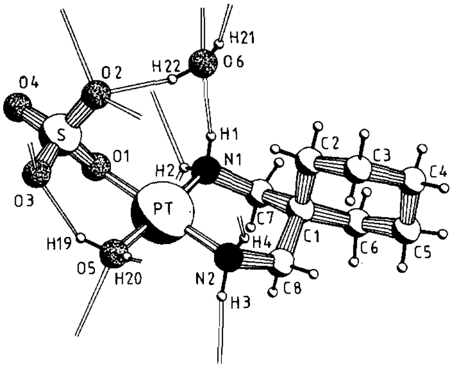


Fig. 3. PLUTO drawing of the asymmetric unit of LPt(H_2O)SO_4·H_2O (3) along with the adopted numbering scheme. The directions of the hydrogen bonds to neighbouring molecules have been indicated.

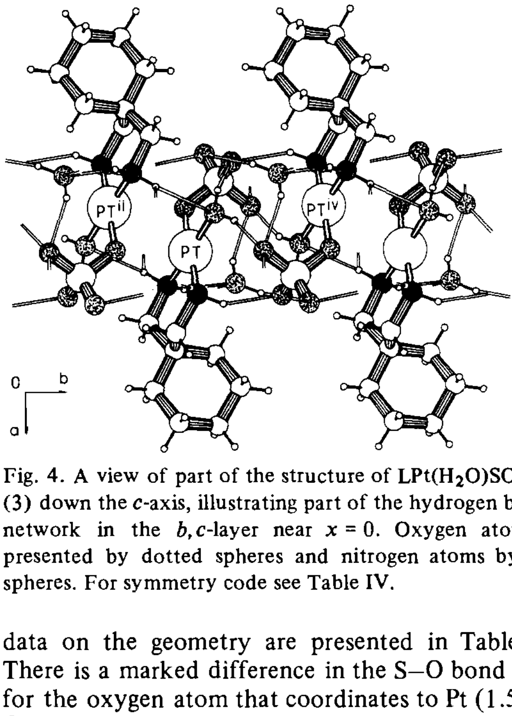


Fig. 4. A view of part of the structure of LPt(H_2O)SO_4·H_2O (3) down the *c*-axis, illustrating part of the hydrogen bonding network in the *b*,*c*-layer near $x = 0$. Oxygen atoms are presented by dotted spheres and nitrogen atoms by black spheres. For symmetry code see Table IV.

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*See also 'Supplementary Material'.

TABLE IV. Selected Data on the Geometry

(a) Bond distances (Å)

Pt–N(1)	2.021(5)	S–O(3)	1.467(6)	C(1)–C(8)	1.536(9)
Pt–N(2)	2.034(5)	S–O(4)	1.457(6)	C(1)–C(7)	1.530(10)
Pt–O(1)	2.059(5)	N(1)–C(7)	1.499(9)	C(2)–C(3)	1.537(12)
Pt–O(5)	2.099(5)	N(2)–C(8)	1.506(8)	C(3)–C(4)	1.539(13)
S–O(1)	1.531(5)	C(1)–C(2)	1.528(10)	C(4)–C(5)	1.492(15)
S–O(2)	1.478(5)	C(1)–C(6)	1.555(9)	C(5)–C(6)	1.531(12)

(b) Bond angles (°)

N(1)–Pt–N(2)	96.2(2)	C(7)–C(1)–C(2)	110.7(6)
O(1)–Pt–N(1)	84.2(2)	C(8)–C(1)–C(2)	113.1(6)
O(5)–Pt–N(1)	176.8(2)	C(6)–C(1)–C(8)	107.4(6)
O(1)–Pt–N(2)	179.0(2)	C(6)–C(1)–C(7)	106.9(6)
O(5)–Pt–N(2)	87.1(2)	C(6)–C(1)–C(2)	109.6(5)
O(1)–Pt–O(5)	92.6(2)	C(1)–C(2)–C(3)	114.1(7)
Pt–N(1)–C(7)	119.7(4)	C(2)–C(3)–C(4)	109.7(8)
Pt–N(2)–C(8)	119.8(4)	C(3)–C(4)–C(5)	112.4(8)
N(1)–C(7)–C(1)	113.5(6)	C(4)–C(5)–C(6)	111.7(7)
N(2)–C(8)–C(1)	116.1(5)	C(1)–C(6)–C(5)	114.2(7)
C(7)–C(1)–C(8)	108.9(5)	Pt–O(1)–S	119.8(3)

(c) Torsion angles (°)

N(2)–Pt–N(1)–C(7)	22.3(5)	Pt–N(2)–C(8)–C(1)	43.4(7)
N(1)–Pt–N(2)–C(8)	−18.0(5)	C(7)–C(1)–C(8)–N(2)	−69.5(7)
Pt–N(1)–C(7)–C(1)	−51.7(7)	C(8)–C(1)–C(7)–N(1)	73.4(7)

(d) Hydrogen bonds (Å and °)

D–H···A	D···A	D–H	H···A	Angle D–H···A
N(1)–H(1)···O(6)	2.925(8)	0.87(5)	2.10(4)	158(5)
N(1)–H(2)···O(2^{i})	3.203(7)	1.05(4)	2.49(6)	124(3)
N(1)–H(2)···O(5^{ii})	3.239(7)	1.05(4)	2.55(4)	123(4)
N(2)–H(3)···O(6^{iii})	2.933(8)	0.97(6)	1.97(6)	170(4)
N(2)–H(4)···O(3^{iv})	2.914(7)	0.95(4)	2.05(3)	151(4)
O(5)–H(19)···O(3)	2.684(7)	0.89(6)	1.88(6)	150(5)
O(5)–H(20)···O(2^{iv})	2.679(7)	0.86(4)	1.88(5)	155(4)
O(6)–H(21)···O(4^{v})	2.831(8)	0.95(4)	1.91(4)	165(5)
O(6)–H(22)···O(2)	2.858(7)	0.84(5)	2.08(5)	156(3)

Symmetry code: i = $-x, y-\frac{1}{2}, -z-\frac{1}{2}$; ii = $-x, -y, -z$; iii = $x, \frac{1}{2}-y, \frac{1}{2}+z$; iv = $-x, 1-y, -z$; v = $-x, \frac{1}{2}+y, -z-\frac{1}{2}$

the hydrate molecule that functions as a donor/acceptor bridge in the structure.

The shortest distance between two Pt atoms amounts to 3.267(1) Å, which is slightly larger than the value 3.25 Å reported in Magnus green salt.

Supplementary Material

A complete listing of the refined parameters, bond distances, angles and torsion angles and a table of the observed and calculated structure factors is available upon request from one of the authors (A.L.S.).

Acknowledgements

The authors wish to thank Mr. G. J. Rotscheid for carrying out the elemental analyses, and Mrs. E. Ch. Th. Gevers and Mr. R. Bosman for obtaining the IR spectral data and for helpful discussions concerning their interpretation. Thanks also to Dr. A.J.M. Duisenberg for collecting the X-ray data. This research was financially supported by Bristol-Myers Co., New York. The X-ray structure determination (A.L.S.) was supported in part by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for

Advancement of Pure Research (ZWO). One of us (J.C.D.) is grateful to the American Cancer Society for a Scholar in Cancer Research Award.

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