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# Formation of Dinuclear (Head–Head, Head–Tail, $\mu$-Hydroxo) Complexes of *cis*-$(NH_3)_2Pt(II)$ with 1-Methyluracil

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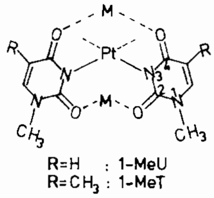
*The formation of several complexes of* cis-$(NH_3)_2$-*Pt(II) with the 1-methyluracil anion 1-MeU,* $C_5H_5N_2O_2$*, is reported:* cis-$Pt(NH_3)_2(1\text{-}MeU)Cl\cdot H_2O$, 1, *is formed on addition of 1 equivalent of HCl to an aqueous solution of* cis-$Pt(NH_3)_2(1\text{-}MeU)_2$ *on mild warming. Removal of the* $Cl^-$ *ligand from* 1 *by means of* $Ag^+$ *gives, depending upon the reaction conditions,* cis-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]^+$, 2, cis-$[Pt(NH_3)_2(1\text{-}MeU)]_2^{2+}$ *(head–tail),* 3, *and* cis-$[(NH_3)_2(1\text{-}MeU)Pt(OH)Pt(1\text{-}MeU)(NH_3)_2]^+$, 4. *Addition of* cis-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ *to* cis-$Pt(NH_3)_2(1\text{-}MeU)_2$ *leads to the head–head dimer* cis-$[Pt(NH_3)_2(1\text{-}MeU)]_2^{2+}$, *5. The formation of dimers* 3, 4, *and* 5 *is pH-dependent:* 3 *and* 5 *are favoured under acidic pH conditions, whereas* 4 *is the major species at around neutral pH.* $^1H$ *NMR, IR and in particular Raman spectroscopy have been used to differentiate between mono- and bidentate binding of 1-MeU in the various complexes. In addition, the crystal structure of the head–head dimer* 5 *($NO_3^-$ salt, monohydrate) has been performed.* 5 *crystallizes in the space group* $P2_1/c$ with $a = 10.922(2)$, $b = 15.677(3)$, $c = 14.491(2)$ Å, $\beta = 116.13(1)°$, $Z = 4$. *The structure was refined on 2864 reflections to* $R = 0.082$. *Binding of the 1-MeU ligand to the two Pt atoms occurs through N3 and O4. The non coordinating O2 oxygens participate in hydrogen bond formation with the* $NH_3$ *groups of the adjacent dimer.*

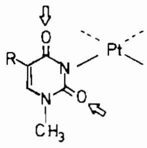
## Introduction

Bis(1-methyluracilato)*cis*-diammineplatinum(II), *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$, and its 1-methylthymine (1-MeT) analogue show a remarkable tendency to bind additional metal ions to form di-, tri- and pentanuclear complexes [1, 2] and probably even larger aggregates. This is believed to be due to both an electronic effect – Pt binding to the deprotonated N3 position increases the electron density at the exocyclic oxygens – and the favourable geometry of these oxygens for metal coordination.



Scheme 1.

Since the bis(1-MeU) and bis(1-MeT) complexes of *cis*-$(NH_3)_2Pt(II)$ are coordinatively saturated as far as the Pt is concerned, they require the presence of other metal ions to form aggregates**. In contrast, the mono(nucleobase) complexes *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]^+$ and *cis*-$[Pt(NH_3)_2(1\text{-}MeT)H_2O]^+$ have the capacity to form di- or oligomeric structures without other metal ions present. These complexes can self-associate in two principle ways: through N,O bridging of the pyrimidine-2.4-dione and through OH bridge formation.



Scheme 2.

The first possibility again is a consequence of the charge distribution in the platinated heterocycle whereas the second one is a consequence of the acidity of the coordinated aquo ligand ($pK_a$ typically between 5 and 7) and the tendency of aquo-*cis*-diammineplatinum(II) complexes to condensate with OH bridge formation in the pH range corresponding to the $pK_a$ of the aquo ligand [3, 4].

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**The possibility of aggregation through oxidation and metal–metal bond formation is not considered here.

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This paper describes the formation of various 1:1- and 2:2-complexes of *cis*-$(NH_3)_2Pt(II)$ with the 1-methyluracilato ligand, and their characterization. The head–tail dimer has previously been obtained in a different way and its crystal structure determined by Lock, Rosenberg and coworkers [5].

## Experimental

### *Preparation of Compounds*

*cis*-$Pt(NH_3)_2(1\text{-}MeU)_2 \cdot 4H_2O$ was prepared as previously described [2]. *cis*-$Pt(NH_3)_2(1\text{-}MeU)Cl \cdot H_2O$, *1*, was obtained in a similar way as the corresponding 1-MeT complex [6] after addition of 1 equivalent HCl per *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ ($c_{Pt}$ = 0.06 *M*, pH 1.7) and slow evaporation on a 40 °C waterbath. The precipitate was stirred with excess MeOH to remove neutral 1-MeUH and then briefly treated with DMF to remove any *cis*-$Pt(NH_3)_2Cl_2$ occasionally formed. Recrystallization from hot water. Yield 50–85%, depending on the extent of evaporation. Colorless microneedles, sparingly soluble in water. *Anal.* Calcd. for $Pt(NH_3)_2(C_5H_5N_2O_2)Cl \cdot H_2O$: C, 14.73; H, 3.22; N, 13.74; Pt, 47.8; Found: C, 15.02; H, 3.33; N, 13.43; Pt, 47.3.

*cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]NO_3$, *2*: 1.2 mmol *1* and 1.2 mmol $AgNO_3$ were stirred in 50 ml water for 24 h at 22 °C, filtered from AgCl, and concentrated to 3.5 ml volume by rotary evaporation at 25–30 °C. The slightly blue solution (pH 3.5) was then kept at 4 °C for 24 h. Colorless microneedles were filtered off, then washed with 1 ml water and air-dried (120 mg). *Anal.* Calcd. for $[Pt(NH_3)_2(C_5H_5N_2O_2)H_2O]NO_3$: C, 13.83; H, 3.02; N, 16.13. Found: C, 13.95; H, 3.23; N, 16.18. Slow evaporation of the filtrate at 4 °C gave two crops of greenish-yellow crystals (80 mg *3*) together with more (60 mg) of *2*.

*cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2 \cdot 3H_2O$ (head–tail dimer), *3*, was obtained in better yield when a freshly prepared solution of *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]NO_3$ was warmed to 60 °C for 30 minutes and then crystallized at room temperature. From the intensely blue solution greenish-yellow crystal plates were obtained in several crops. Yield 43%. Since the pH rises during the crystallization procedure (from 3.5 after filtration of AgCl to 5.1 after 4 days at room temperature) the pH was brought back to 3.0 after this time by addition of $HNO_3$. It is unclear at present whether the rise in pH is exclusively a consequence of the disappearance of the (acidic) aquo ligand in the condensation reaction or possibly due to release of $NH_3$. IR and Raman spectra of *3* indicate N3, O4 bridging of the 1-MeU ligands, and the determination of the cell constants by precession photographs showed *3* to be identical with the head–tail dimer previously described by Faggiani *et al.* [5].

*cis*-$[(NH_3)_2(1\text{-}MeU)Pt(OH)Pt(1\text{-}MeU)(NH_3)_2]ClO_4 \cdot H_2O$, *4*: A freshly prepared solution of *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]ClO_4$ was treated with 0.5 equivalent NaOH and the resulting solution (pH ≅ 7) allowed to crystallize at 22 °C by slow evaporation. Colorless to slightly tan plates, grown in clusters. Yield 45–60%, depending on the extent of evaporation. Moderately soluble in water. The identical compound has also been obtained by recrystallization of the corresponding $NO_3^-$ salt from an aqueous solution containing a twofold excess of $NaClO_4$. $^1H$ NMR spectra of the $NO_3^-$ and the $ClO_4^-$ salt are identical. *Anal.* Calcd. for $[(NH_3)_4Pt_2(C_5H_5N_2O_2)_2(OH)]ClO_4 \cdot H_2O$: C, 14.25; H, 3.00; N, 13.29; Cl, 4.20. Found: C, 14.44; H, 3.03; N, 13.20; Cl, 4.27.

*cis*-$[(NH_3)_2Pt(1\text{-}MeU)]_2(NO_3)_2 \cdot H_2O$ (head–head dimer), *5*: This compound has been prepared in analogy to the corresponding 1-MeT dimer [7] by combining aqueous solutions of *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ and *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ and keeping the solution (pH 3–4) in a stoppered flask for 24 h at 22 °C and 12 h at 3 °C. By then greenish-yellow crystals have formed which become bright yellow after recrystallization from water. Yield 74%. During the recrystallization procedure the formation of two modifications of *5* is observed. At 3 °C golden-yellow columns (up to 5 mm in length) form at an early stage of the crystallization which, on further concentration of the solution redissolve to give eventually yellow cubes. The column-shaped crystals are extremely fragile and rapidly lose water of crystallization when kept on air, whereas the cubes are stable on air. Elemental analyses of several samples of the columns gave poorly reproducible results, although they suggested the presence of at least 4 $H_2O$ per dimer. *Anal.* of the yellow cubes: Calcd. for $[Pt(NH_3)_2(C_5H_5N_2O_2)]_2(NO_3)_2 \cdot H_2O$: C, 14.12; H, 2.85; N, 16.47. Found: C, 14.10; H, 2.88; N, 16.49. The IR spectra (Nujol) of both modifications did not show major differences. The X-ray structure was performed with the monohydrate.

### *Apparatus*

IR spectra were recorded as Nujol mulls (CsI windows) or KBr discs on a Perkin Elmer 580 grating spectrometer. $^1H$ NMR spectra were obtained on a Jeol JNM-FX 60 in $D_2O$ with $[N(CH_3)_4]BF_4$ as internal reference. Shifts (δ scale) were calculated relative to sodium 3-(trimethylsilyl)propanesulfonate (3.1869 ppm upfield of the $[N(CH_3)_4]^+$ signal. pD values were adjusted using $CF_3COOD$ and NaOD, and determined by adding 0.4 units to the pH meter reading. Raman spectra of polycrystalline samples and aqueous solutions were recorded on a Coderg PH 1 with krypton laser excitation (647.1 nm). Calibration was achieved by means of indene. Slit widths were between 2 and 6 $cm^{-1}$.

### *Crystallography*

A crystal of *5* (dimensions approximately 0.3 × 0.25 × 0.3 mm) was sealed and mounted and the unit cell dimensions and the space group determined: $P2_1/c$, $a = 10.922(2)$, $b = 15.677(3)$, $c = 14.491(2)$ Å, $\beta = 116.13(1)°$, $Z = 4$, $V = 2227.6$ Å$^3$, mol mass 850.6, $D_c = 2.54$, $D_m = 2.54$ g cm$^{-3}$ (flotation in $CH_2I_2/CCl_4$), $\mu = 132.8$ cm$^{-1}$. The intensities of 3496 independent reflections were measured on a Syntex $P2_1$ diffractometer at room temperature (Mo-$K_\alpha$ radiation, $\lambda = 0.71069$ Å, graphite monochromator, $\omega$-scan). After Lorentz polarization and absorption corrections the structure was solved by the heavy atom method with a SHELX 76 system. The hydrogen atoms were not determined. Full matrix refinement with anisotropic temperature factors for the platinum atoms gave an R value of 0.082 (2864 reflections with $I > 2\sigma(I)$).

## Results and Discussion

### cis-*Pt(NH₃)₂(1-MeU)Cl·H₂O,* 1

Hemiprotonation of the bis(1-MeU) complex of *cis*-Pt(II) by means of HCl and slight warming gives the mixed 1-methyluracilato, chloro complex *1* and neutral 1-methylracil, 1-MeUH:

$$Pt(NH_3)_2(1\text{-}MeU)_2 + 1HCl \rightarrow$$

$$[Pt(NH_3)_2(1\text{-}MeU)(1\text{-}MeUH)]Cl$$

$$\downarrow \Delta$$

$$Pt(NH_3)_2(1\text{-}MeU)Cl + 1\text{-}MeUH$$

Formation of *1* thus is analogous to the corresponding 1-MeT compound [6]. Monodentate binding of the 1-MeU ligand through N3 is expected from the way of preparation and supported by the IR spectrum. In the double bond stretching region of the spectrum two intense bands around 1640 and 1550 cm$^{-1}$ are characteristic of $N_3$ platinum binding (*cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$, *1, 2, 4*), whereas N3, O4 bridging as with dimers *3* and *5* is recognized by the appearance of intense bands around 1650, 1520 and 1480 cm$^{-1}$. In the low frequency region of the spectrum of *1* an intense band occurs at 317 cm$^{-1}$ which is assigned to the Pt–Cl stretch. Another characteristic difference between N3 and N3, O4 binding patterns refers to the position of a sharp and intense IR band in the 600 cm$^{-1}$ range which is due to a ring deformation mode [8]. In the IR spectrum of *1* this band is observed at 595 cm$^{-1}$, very similar to *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$, *2, 4* and a series of mixed nucleobase complexes $Pt(NH_3)_2(1\text{-}MeU)X$ with X being a nucleobase other than 1-MeU. In contrast, this mode absorbs around 630 cm$^{-1}$ with the N3, O4 bridged complexes *3* and *5*.

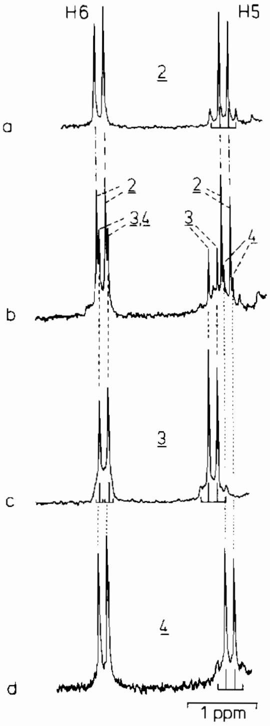


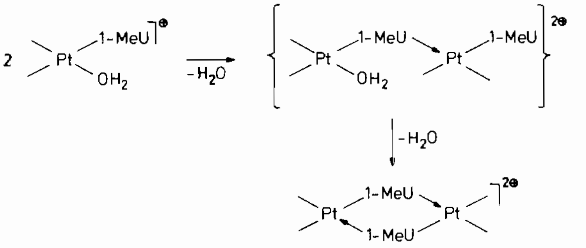
Fig. 1. $^1H$ NMR spectra (H5, H6 region) of (a) freshly dissolved *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]NO_3$, *2*, in $D_2O$ (0.1 *M* Pt, pD = 3); colorless solution; (b) spectrum (a) after 15 min at 60 °C and 20 h at 22 °C. The sample is slightly blue, pD = 3.9; (c) head–tail dimer *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2$, *3*, after isolation. Yellow solution, pD = 5; (d) $\mu$-hydroxo dimer *cis*-$[(NH_3)_2(1\text{-}MeU)Pt(OH)Pt(1\text{-}MeU)(NH_3)_2]NO_3$, *4*, after isolation. Colorless solution, pD = 8.

### *cis-[Pt(NH₃)₂(1-MeU)H₂O]⁺ and its Condensation Products, Head–Tail and μ-Hydroxo Dimers*

Treatment of *1* with 1 equivalent of $AgNO_3$ in water and cautious concentration gives *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]NO_3$, *2*, as a colorless, crystalline material. Although the presence of a coordinated aquo group could not unambiguously be deduced from IR and Raman spectra, there is indirect evidence from the vibrational spectra for this formulation: firstly, both IR and Raman spectra show the typical absorptions of ionic $NO_3^-$ (Ra 1046vs, 711w; IR 1380vs, 827w, 1760w). Secondly, besides the above mentioned IR bands characteristic of monodentate N3 coordination of Pt to 1-MeU, the Raman spectrum (solid state) of *2* exhibits all the 1-MeU ring modes at positions typical of N3 platinum binding (*vide infra*). On the same basis of arguments we have recently postulated the presence of an aquo ligand in the 1-methylcytosine complex *cis*-$[Pt(NH_3)_2(1\text{-}MeC)H_2O](NO_3)_2$ and verified this by X-ray crystallography [9].

If an aqueous solution of *2* is kept at room temperature for some time or slightly warmed, the monomeric complex undergoes condensation reactions with formation of at least two new complexes *3* and *4*. This reaction can be followed using $^1H$ NMR spectroscopy (Fig. 1). Both newly formed compounds have been isolated and identified.

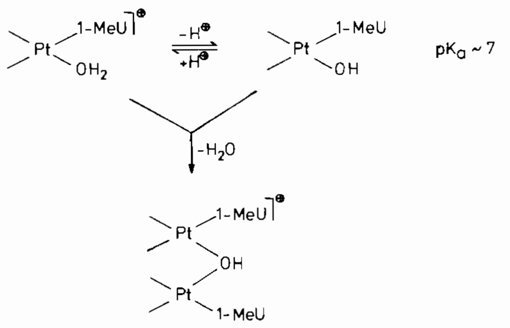
*3* is the dimer *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2$ with the 1-MeU ligands arranged in head–tail fashion, bridging the two Pt centers through N3 and O4. The identity of *3* has been established by determining the crystal cell parameters. They proved to be the same as those described by Lock, Rosenberg and coworkers for the head–tail dimer [5]. Formation of *3* thus occurs as follows:



Scheme 3.

Interestingly, in the related 1-methylthymine system two crystalline modifications of head–tail dimers have been isolated and the structures determined [10, 11].

The second complex, *4*, is a dinuclear compound with two *cis*-$Pt(NH_3)_2(1\text{-}MeU)$ moieties bridged by a hydroxo group. The 1-MeU ligands are bound to platinum in a monodentate fashion through N3. Formation of *4* according to



Scheme 4.

agrees with the finding that its yield reaches a maximum at a pH corresponding to the $pK_a$ value of the aquo ligand of *2* (Fig. 2). Formulation of *4* as a 1:1 adduct of $Pt(NH_3)_2(1\text{-}MeU)OH$ and $[Pt(NH_3)_2(1\text{-}MeU)H_2O]^+$ can be ruled out since this could not explain the existence of individual NMR signals for *4* and *2*. The slight upfield shift of the H5 and H6 resonances of *4* relative to *2* may be due to a ring current effect and indicative of a stacked arrangement of the two 1-MeU ligands in *4* (Fig. 3). As has been pointed out by us before, two nucleobases linked by a *cis*-$(NH_3)_2Pt(OH)Pt(NH_3)_2$ moiety could be oriented in two extreme ways, with no base overlap or with base stacking [12].

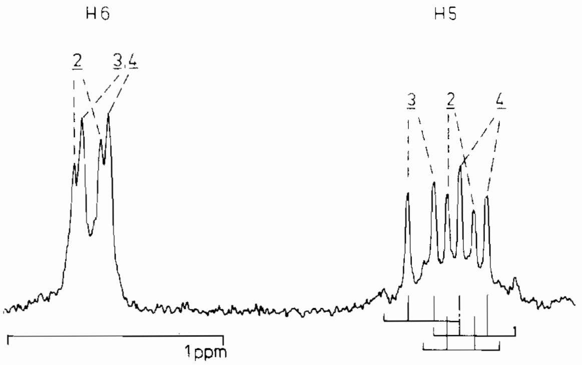


Fig. 2. H5, H6 resonances of a mixture of *2*, *3*, *4*. The spectrum was recorded 17 h after addition of 0.5 equiv. NaOD to a solution of *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]^+$. pD = 7, 30 °C. Signals of *2* actually represent averaged resonances of *cis*-$[Pt(NH_3)_2(1\text{-}MeU)H_2O]^+$ and *cis*-$Pt(NH_3)_2(1\text{-}MeU)OH$. Signals of the μ-hydroxo dimer *4* increase at the expense of *2* and *3* if the sample is warmed to 60 °C. Coupling between H5 and the $^{195}Pt$ isotope is observed for all three compounds.

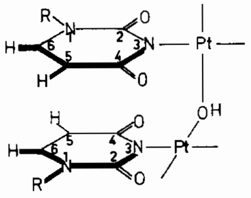


Fig. 3. Possible arrangement of the 1-MeU ligands in the μ-hydroxo dimer *4*, leading to stacking of the two heterocycles.

Besides the crystalline species *3* and *4* there is also a non-crystalline material being formed in a solution of *2* as long as no base is added. This material is extremely water-soluble and of intense blue colour. We are presently studying its relationship to the 'platinum pyrimidine blues'.

## *Head–Head Dimer*

### *Formation*

The head–head dimer *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2$, *5*, has been prepared by reaction of *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ with *cis*-$[Pt(NH_3)_2(H_2O)_2]$-

TABLE I. Atomic Parameters and Temperature Factors (Å$^2$) for Head–Head Dimer *5*.

| Atom | x/a | y/b | z/c | U |
|---|---|---|---|---|
| Pt1 | 0.4480(1) | 0.0566(1) | 0.6325(1) | a |
| Pt2 | 0.4100(1) | 0.1576(1) | 0.7886(1) | a |
| N11 | 0.6168(21) | 0.1012(13) | 0.6256(16) | 0.030(5) |
| N12 | 0.5665(21) | −0.0422(14) | 0.7239(16) | 0.032(5) |
| N21 | 0.5980(23) | 0.2056(14) | 0.8716(17) | 0.037(5) |
| N22 | 0.4282(24) | 0.0820(15) | 0.9056(18) | 0.041(6) |
| N1A | −0.1195(22) | 0.1135(14) | 0.4436(16) | 0.033(5) |
| C11A | −0.0794(33) | 0.1961(20) | 0.4964(24) | 0.049(8) |
| C2A | 0.2438(25) | −0.0763(15) | 0.5768(18) | 0.025(5) |
| O2A | 0.3236(18) | −0.1150(11) | 0.5527(13) | 0.031(4) |
| N3A | 0.2753(18) | 0.0016(11) | 0.6284(13) | 0.017(4) |
| C4A | 0.1921(24) | 0.0389(15) | 0.6625(19) | 0.026(5) |
| O4A | 0.2183(19) | 0.1101(12) | 0.7065(14) | 0.038(4) |
| C5A | 0.0629(27) | −0.0023(18) | 0.6462(21) | 0.036(6) |
| C6A | 0.0373(33) | −0.0778(21) | 0.5968(25) | 0.050(8) |
| N18 | 0.2003(21) | 0.2092(13) | 0.3719(16) | 0.032(5) |
| C11B | 0.1331(34) | 0.1873(22) | 0.2606(26) | 0.052(8) |
| C2B | 0.2739(25) | 0.1409(16) | 0.4342(19) | 0.029(6) |
| O2B | 0.2901(19) | 0.0716(12) | 0.4007(14) | 0.038(4) |
| N3B | 0.3343(19) | 0.1535(12) | 0.5400(14) | 0.020(4) |
| C4B | 0.3234(29) | 0.2314(18) | 0.5800(22) | 0.038(7) |
| O4B | 0.3768(18) | 0.2453(11) | 0.6776(13) | 0.033(4) |
| C5B | 0.2542(28) | 0.2966(18) | 0.5111(21) | 0.034(6) |
| C6B | 0.1903(30) | 0.2838(19) | 0.4063(23) | 0.044(7) |
| N10 | 0.6320(22) | 0.1722(14) | 0.1572(17) | 0.034(5) |
| O11 | 0.7080(22) | 0.2053(14) | 0.2388(16) | 0.051(5) |
| O12 | 0.6075(26) | 0.2078(16) | 0.0767(20) | 0.070(7) |
| O13 | 0.5808(25) | 0.1025(16) | 0.1559(19) | 0.067(6) |
| N20 | 0.8240(27) | 0.0362(17) | 0.0349(21) | 0.048(6) |
| O21 | 0.8457(25) | −0.0046(16) | 0.1112(19) | 0.069(7) |
| O22 | 0.9101(37) | 0.0883(23) | 0.0296(27) | 0.112(11) |
| O23 | 0.7108(28) | 0.0298(17) | −0.0401(21) | 0.076(7) |
| O30 | 0.8653(31) | 0.0572(18) | 0.8205(23) | 0.084(8) |

[a] Anisotropic temperatures $U_{ij}$ were obtained from $\beta_{ij} = 2\pi^2 b_i b_j U_{ij}$ where $\beta_{ij}$'s occur as a temperature effect from $\exp[-(\beta_{11}h^2 + \ldots + 2\beta_{12}hk + \ldots)]$ and $b_i$ and $b_j$ are the reciprocal lattice vectors. For Pt(1), $U_{11}$ = 0.0261(5), $U_{22}$ = 0.0184(5), $U_{33}$ = 0.0193(5), $U_{12}$ = 0.0015(4), $U_{13}$ = 0.0125(4), $U_{23}$ = 0.0029(3), for Pt(2), $U_{11}$ = 0.0378(6), $U_{22}$ = 0.0214(6), $U_{33}$ = 0.0177(5), $U_{12}$ = 0.0040(4), $U_{13}$ = 0.0125(4), $U_{23}$ = 0.0012(4).

$(NO_3)_2$ in analogy to the corresponding 1-methylthymine complex [7]. Its formation can be followed using $^1$H NMR spectroscopy (Fig. 4). If no base is added (pH 3–4), the dimer is formed within 20 h at 22 °C almost quantitatively besides some unidentified blue product. If the pH is higher than 5 (after addition of NaOH), the reaction at 22 °C is slow and incomplete. Within 6 days only *ca.* 20% of the dimer *5* is formed which suggests that OH successfully blocks Pt from further reaction at O4 of the 1-MeU ligand, probably through formation of OH bridged oligomers of the type *cis*-$[Pt(NH_3)_2OH]_n^{n+}$ (n = 2, 3) [3].

### *Crystal Structure*

Atomic parameters of the head–head dimer *5* are listed in Table I, selected structural details are given in Table II, and the dimer cation is shown in Fig. 5. It consists of two *cis*-$Pt(NH_3)_2$ moieties bridged by two 1-MeU ligands through N3 and O4. The 1-MeU ligands are arranged in head–head fashion. There are close structural similarities between *5* and the respective 1-MeT complex [7], but also differences. The similarities refer to the intramolecular Pt–Pt distance (2.937(1) Å in *5*, 2.909(3) Å in the 1-MeT compound), the tilt angle of the Pt coordination planes (34.1° in *5*, 29.5° in the 1-MeT compound), and the slight displacement of the Pt atoms from the coordination planes towards each other (*ca.* 0.1 Å in both cases). Differences between the two structures are observed for the twist angle between the Pt coordination planes about the Pt–Pt vector (25.3° in *5*, *ca.* 1° in the 1-MeT complex) and in particular for the intermolecular structural

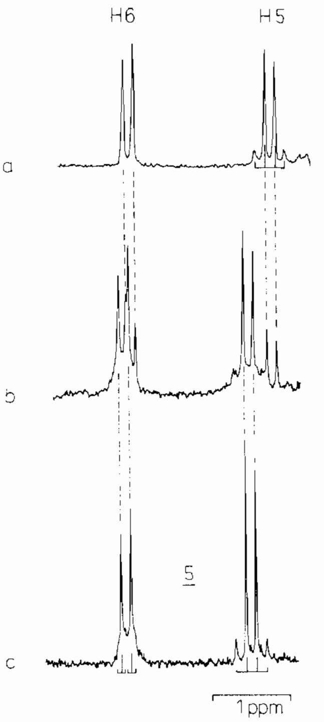


Fig. 4. $^1$H NMR spectra (H5, H6 region) of (a) a 1:1-mixture of *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ and *cis*-$[Pt(NH_3)_2(D_2O)_2](NO_3)_2$ immediately after combination. Colorless solution, 0.1 *M* each, pD = 3.5; (b) spectrum (a) after 4.5 h at 22 °C. The sample is slightly blue, pD = 3.3. Within 20 h signals due to *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ have almost completely disappeared. The sample is dark blue by then; (c) head–head dimer *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2$, *5*, after isolation. Yellow solution, pD = 5.5.

parameters. While in the 1-MeT structure the dimers are well separated (closest intermolecular Pt–Pt contact 5.6 Å), there is considerable hydrogen bonding between pairs of centrosymmetrically related dimer cations in *5* (Fig. 6). Hydrogen bonding occurs between the $NH_3$ groups and the non-coordinating O2 groups of adjacent cations, giving rise to an intermolecular Pt–Pt separation (Pt1–Pt1′) of about 4.8 Å. Similar hydrogen bonding interactions between $NH_3$ and O2 groups have also been observed in the head–tail dimer *cis*-$[Pt(NH_3)_2(1\text{-}MeT)]_2(NO_3)_2$ [11], although adjacent Pt atoms approach each other much more closely there (*ca.* 3.9 Å). The hydrogen bonding pattern of dimer *5* is contrasted by the one found in the related complex with α-pyridone instead of 1-methyluracilate as ligand [13]. The head–head dimer *cis*-$[Pt(NH_3)_2(\alpha\text{-pyridone})]_2(NO_3)_2$ crystallizes in such a way that hydrogen bonding occurs between $NH_3$ groups and the *coordinating* oxygens of adjacent cations, leading to a short intermolecular Pt–Pt distance of *ca.* 2.9 Å. A similar arrangement, though with somewhat larger Pt–Pt separations (3.25 Å), is observed in a derivative of the here described head–head dimer *5*, in the heteronuclear $Pt_4$, Ag complex [1].

It is interesting to follow the other changes in intermolecular cation arrangement when going from *5* to the mentioned $Pt_4$, Ag compound *cis*-$[Pt_4(NH_3)_8(1\text{-}MeU)_4Ag]^{5+}$: Ag binding to the four O2 sites of the two dimer cations shown in Fig. 6 causes a) an increase of the Pt1–Pt1′ separation, and b) a sliding motion of the two dimer units so that the five metals become colinear [1]. Since the center of symmetry between the two dimers is preserved while

TABLE II. Selected Structural Details of *5* (Distances in Å, Angles in deg).

| | | | |
|---|---|---|---|
| (a) Distances and angles around Pt1, Pt2 | | | |
| Pt1–Pt2 | 2.937(1) Å | | |
| Pt1–N11 | 2.015(21) | Pt2–N21 | 2.013(22) Å |
| Pt1–N12 | 2.078(21) | Pt2–N22 | 2.005(24) |
| Pt1–N3A | 2.051(17) | Pt2–O4A | 2.040(18) |
| Pt1–N3B | 2.045(19) | Pt2–O4B | 2.025(17) |
| N11–Pt1–N12 | 87.9(8)° | N21–Pt2–N22 | 91.2(9)° |
| N11–Pt1–N3A | 174.0(8) | N21–Pt2–O4A | 178.8(8) |
| N11–Pt1–N3B | 90.8(8) | N21–Pt2–O4B | 90.0(8) |
| N12–Pt1–N3A | 90.7(8) | N22–Pt2–O4A | 88.4(8) |
| N12–Pt1–N3B | 178.4(8) | N22–Pt2–O4B | 171.8(8) |
| N3A–Pt1–N3B | 90.5(7) | O4A–Pt2–O4B | 90.3(7) |
| (b) Tilt angle of Pt coordination planes | | | |
| N11, N12, N3A, N3B/N21, N22, O4A, O4B | | 34.1° | |
| (c) Torsion angle about the Pt–Pt vector | | | |
| N11, Pt1, Pt2/Pt1, Pt2, N21 | | 25.2° | |

(continued on facing page)

TABLE II. *(continued)*

| | | | |
|---|---|---|---|
| (d) Deviations of Pt atoms from least squares coordination planes | | | |
| Δ Pt1 | −0.063 Å | Δ Pt2 | +0.081 Å |
| (e) Nearest intermolecular Pt–Pt separation | | | |
| Pt1–Pt1′ | 4.798(1) Å | | |
| (f) Possible intermolecular hydrogen bonds between $NH_3$ and O2 | | | |
| N11–O2A′ | 2.938 Å | N12–O2B | 2.902 Å |
| N11–O2B′ | 2.977 | | |
| N11′–O2A | 2.938 | N12′–O2B | 2.902 |
| N11′–O2B | 2.977 | | |
| Pt1–N11–O2A′ | 129.1° | | |
| Pt1–N11–O2B′ | 93.6 | | |
| Pt1–N12–O2B′ | 94.4 | | |

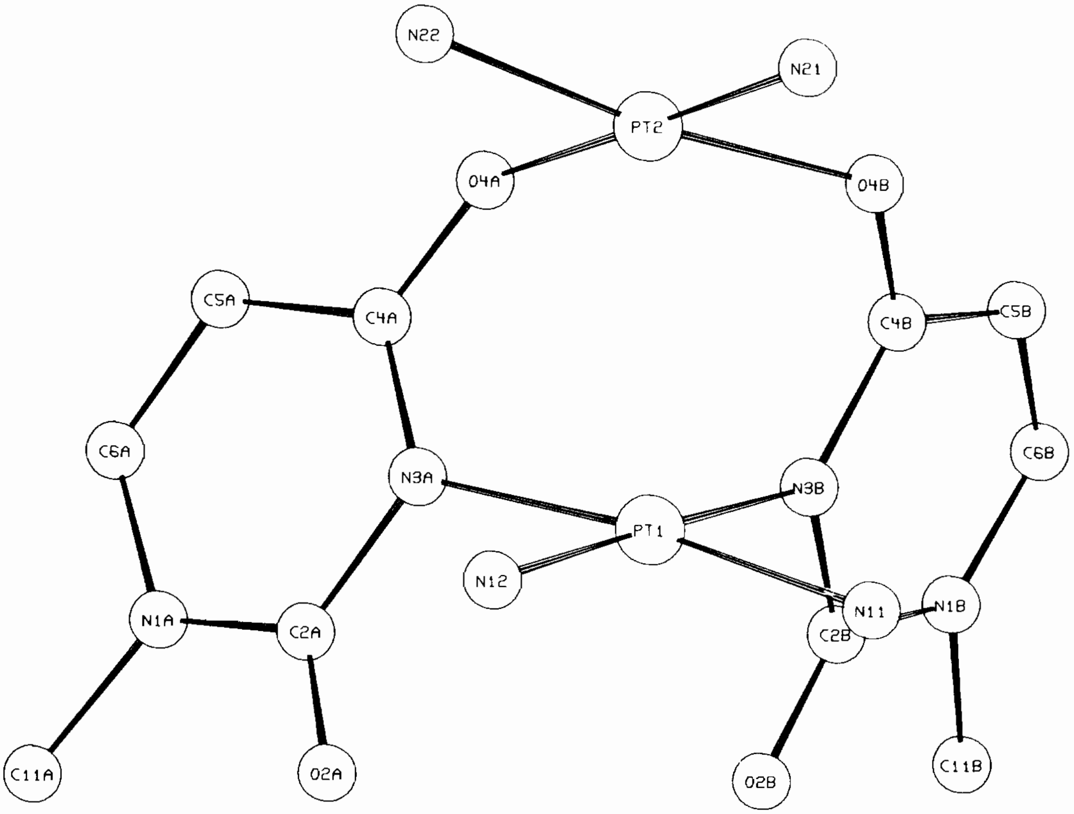


Fig. 5. View of the dimer cation *5*, *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2^{2+}$ with the 1-MeU ligands arranged in head–head fashion.

the $Ag^+$ is inserted, the plane through the four O2 atoms becomes substantially tilted relative to the Pt1 coordination plane when going from *5* (tilt angle 2.8°) to the $Pt_4$, Ag complex (tilt angle 17.7°).

### $^1H$ *NMR Spectra*

Chemical shifts of compounds *1–5* in $D_2O$ are listed in Table III. All compounds exhibit $^1H–^1H$ coupling between H5 and H6 resonances of the 1-MeU ligand ($^3J \cong 7.3$ Hz) and $^{195}Pt–^1H$ coupling

TABLE III. $^1$H NMR Shifts (δ, ppm) of 1-MeU Ligands in Compounds *1–5* ($D_2O$, 30 °C, 0.02–0.1 *M* Pt).

| | H6 | H5 | N-$CH_3$ | pD |
|---|---|---|---|---|
| *1* | 7.42 | 5.68 | 3.36 | 5 |
| *2* | 7.46 | 5.70 | 3.38 | 2–7 |
| | 7.54 | 5.78 | 3.40 | 1 |
| | 7.43 | 5.69 | 3.37 | 12 |
| *3* | 7.43 | 5.88 | 3.39 | 1–7 |
| *4* | 7.42 | 5.65 | 3.34 | 3–12 |
| *5* | 7.43 | 5.86 | 3.39 | 1–7 |

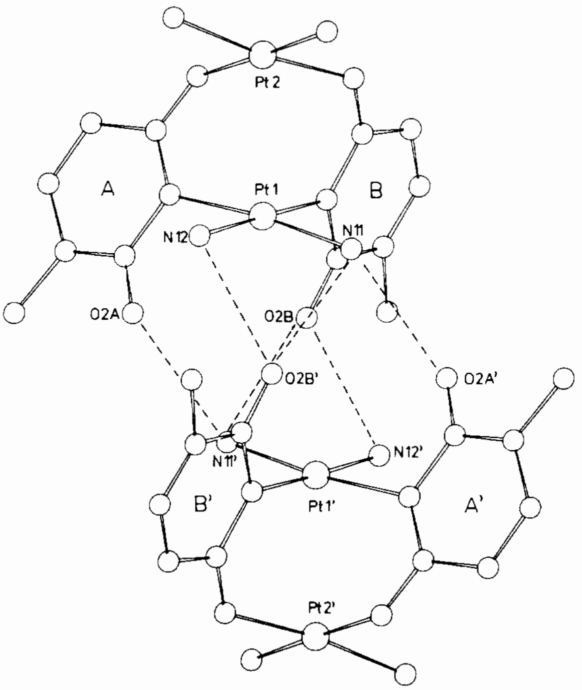


Fig. 6. Two centrosymmetrically related dimer cations of *5*. Hydrogen bonding interactions between the O2 and $NH_3$ groups of adjacent cations are indicated by broken lines.

between Pt at position N3 and H5 ($^4J$ ≅ 14.5 Hz). The H6 doublets of both dimers *3* and *5* are, unlike those of the complexes containing monodentate 1-MeU ligands, symmetrically broadened at their basis, suggesting that this is due to unresolved coupling between H6 and the $^{195}$Pt isotope at O4 ($^4J$ ≅ 5 Hz). The $^1$H NMR shifts of the head–tail and the head–head dimers are almost identical. A differentiation is possible, however, on the basis of their reactions with excess NaCl [11], giving a 1:1 mixture of *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ and *cis*-$Pt(NH_3)_2Cl_2$ in the case of the dimer *5*, but *cis*-$Pt(NH_3)_2(1\text{-}MeU)Cl$ with dimer *3*. The degradation products can readily be distinguished using $^1$H NMR spectroscopy.

The resonances of *2* undergo distinct downfield shifts below pD 2, indicating that protonation of the 1-MeU ligand takes place. The species formed, *cis*-$[Pt(NH_3)_2(1\text{-}MeUH)(H_2O)]^{2+}$, contains the neutral 1-methyluracil ligand in its unusual iminol tautomeric form, very similar to related complexes of uracil [14] or 1-methylthymine [6]. Between pH 3 and 7 the shifts of *2* are practically constant, and only in strongly alkaline medium are there very slight upfield shifts of the H5 and H6 resonances. Clearly, deprotonation of the aquo ligand of *2* to give *cis*-$Pt(NH_3)_2(1\text{-}MeU)OH$ has little effect on the resonances of the 1-MeU ligand.

The μ-hydroxo dimer *4* is stable over a wide pH range (3–12). Below pH 3 protonation of the OH group and cleavage into *2* takes place. The existence of the cation *4* even in strongly alkaline medium surprises, since one might expect immediate formation of the monomeric *cis*-$Pt(NH_3)_2(1\text{-}MeU)OH$. However, unless freshly dissolved *2* is quickly treated with an excess of base, dimer *4* always forms besides the monomeric *cis*-$Pt(NH_3)_2(1\text{-}MeU)OH$.

### *Raman Spectra*

The application of Raman spectroscopy to the differentiation of metal nucleobase complexes containing the metal bound in different way was first conclusively demonstrated by Tobias and coworkers [15]. For example, these authors showed that Hg(II) binding to N3, O4, or C5 produces distinctly different Raman spectra. More recently, Savoie *et al.* [16] have shown that binding of methylmercury to various sites of 9-methyladenine causes characteristic changes in the Raman spectrum of the ligand. Using complexes of *cis*-$(NH_3)_2Pt(II)$ with model nucleobases such as 1-methylcytosine [17], 1-methylthymine [18], and the tautomers of uracil and thymine monoanions [14, 19] we have further evaluated the usefulness of this technique. From these studies it has become evident that the Raman-intense inplane modes of planar heterocyclic rings (A′ symmetry) are sensitive for the site of metal coordination, but only slightly affected by other ligands, by hydrogen bonding, and by intermolecular coupling phenomena [20]. This refers in particular to the ring modes below *ca.* 900 cm$^{-1}$, and also to the so called ring-breathing mode of pyrimidine derivatives which frequently is the most intense Raman band of all.

### *Solution Spectra*

Raman solution spectra ($H_2O$) of 1-methyluracil, 1-MeUH, the 1-methyluracil anion, 1-MeU, of *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$, several mixed nucleobase complexes *cis*-$[Pt(NH_3)_2(1\text{-}MeU)X]^+$ (with X being a nucleobase other than 1-MeU [21]), and the head–tail dimer *3*, *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2$, have been recorded. Band positions of 1-MeUH and 1-MeU

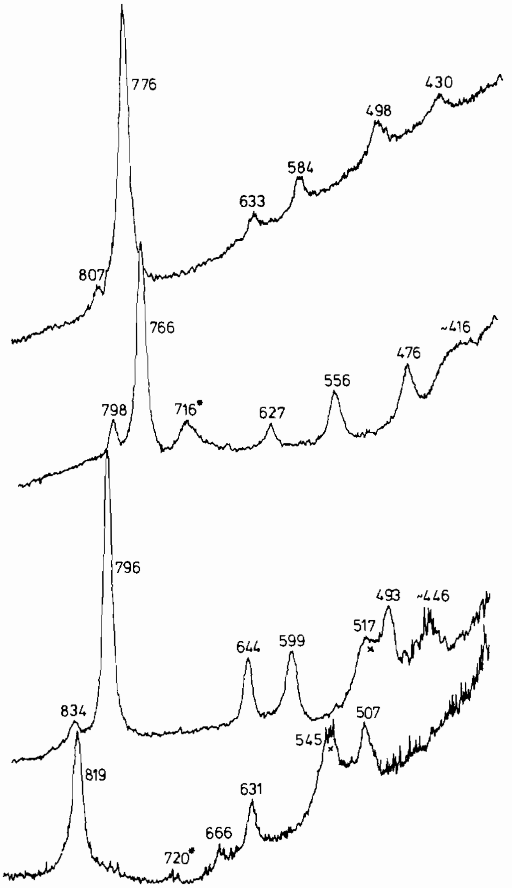


Fig. 7. Sections of the Raman solution ($H_2O$) spectra of (a) neutral 1-methyluracil, 1-MeUH. pH = 1 ($HNO_3$), identical at pH = 7; (b) sodium 1-methyluracilate, Na(1-MeU), pH = 12.5. (c) *cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$, pH = 6; (d) head–tail dimer *3*, *cis*-$[Pt(NH_3)_2(1\text{-}MeU)]_2(NO_3)_2$, pH = 5; + denotes $\nu(Pt{-}NH_3)$ modes, $^*\nu_4(NO_3^-)$. Slit width 4 $cm^{-1}$ (a), 6 $cm^{-1}$ (b–d).

agree well with values in the literature [22]. There are marked changes in the positions and relative intensities of many of the 1-MeU bands on Pt coordination, differing in monodentate N3 binding (*cis*-$Pt(NH_3)_2(1\text{-}MeU)_2$ and *cis*-$[Pt(NH_3)_2(1\text{-}MeU)X]^+$) and bidentate N3, O4 binding (dimer *3*). This is to be seen particularly well in the region between 450 and 850 $cm^{-1}$ (Fig. 7). The intense band due to the ring-breathing motion of the 1-MeU at 776 $cm^{-1}$ is shifted into opposite directions on protonation (766 $cm^{-1}$) and platinum binding (796 $cm^{-1}$). N3, O4 platinum binding causes an even larger shift to higher energy (819 $cm^{-1}$), and at the same time a decrease in relative intensity. Shifts into opposite directions for protonation of 1-MeU and platinum binding to N3 or N3, O4 are also observed for the two bands around 600 $cm^{-1}$. It appears to be the rule that the 1-MeU modes in the spectral region below 850 $cm^{-1}$ absorb at higher energy in the N3, O4 bridged complexes than in the compounds containing Pt bound to N3 only.

As for the other Raman-active modes between 850 and 1700 $cm^{-1}$, these bands frequently are less intense than the low frequency modes and therefore less suitable for an immediate differentiation between N3 and N3, O4 platinum binding (*e.g.* weak Raman bands at 1210 $cm^{-1}$ with Pt–N3 complexes, yet 1194 $cm^{-1}$ with Pt–N3, O4–Pt complexes), or insensitive to the binding pattern (*e.g.* the very intense ring-stretching mode around 1244 $cm^{-1}$ in both types of complexes).

### *Solid State Spectra*

A distinct advantage of a Raman spectroscopic differentiation of metal complexes containing the metal(s) coordinated to different sites of the heterocyclic ligand is the already mentioned insensitivity of most Raman active modes towards environmental influences. At least for the bands below 850 $cm^{-1}$ the agreement between solution and solid state spectra is quite good, with respective bands differing in their positions usually by less than 5 wavenumbers. For example, in the Raman spectra of *2* and *4* 1-MeU modes are observed at around 832, 798, 647 and 597 $cm^{-1}$ thus indicating N3 coordination of Pt, whereas in the spectrum of the head–head dimer *5* these bands occur at 813, 660 and 626 $cm^{-1}$.

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## References

1 B. Lippert and D. Neugebauer, *Inorg. Chem., 21,* 451 (1982) and references cited.
2 D. Neugebauer and B. Lippert, *J. Am. Chem. Soc., 104,* 6596 (1982).
3 (a) B. Lippert, C. J. L. Lock, B. Rosenberg and M. Zvagulis, *Inorg. Chem., 17,* 2971 and references cited.
(b) J. A. Stanko, L. S. Hollis, J. A. Schreifels and J. D. Hoeschele, *J. Clin. Hematol. Oncol., 7,* 138 (1977).
4 (a) M. C. Lim and R. B. Martin, *J. Inorg. Nucl. Chem., 38,* 1911 (1976).
(b) B. Rosenberg, *Biochimie, 60,* 859 (1978).
(c) C. J. Boreham, J. A. Broomhead and D. P. Fairlie, *Aust. J. Chem., 34,* 659 (1981).
5 R. Faggiani, C. J. L. Lock, R. J. Pollock, B. Rosenberg and G. Turner, *Inorg. Chem., 20,* 804 (1981).
6 B. Lippert, *Inorg. Chim. Acta, 55,* 5 (1981).
7 B. Lippert, D. Neugebauer and U. Schubert, *Inorg. Chim. Acta, 46,* L11 (1980).
8 H. Susi and J. S. Ard, *Spectrochim. Acta, 30A,* 1843 (1974).

9 J. F. Britten, B. Lippert, C. J. L. Lock and P. Pilon, *Inorg. Chem., 21,* 1936 (1982).

10 C. J. L. Lock, H. J. Peresie, B. Rosenberg and G. Turner, *J. Am. Chem. Soc., 100,* 3371 (1978).

11 D. Neugebauer and B. Lippert, *Inorg. Chim. Acta, 67,* 151 (1982).

12 B. Lippert, ACS Symposium Series 'Chemistry and Biochemistry of Platinum, Gold and Other Chemotherapeutic Agents', American Chemical Society, in press.

13 L. S. Hollis and S. J. Lippard, *J. Am. Chem. Soc., 103,* 1230 (1981).

14 B. Lippert, *Inorg. Chem., 20,* 4326 (1981).

15 S. Mansy and R. S. Tobias, *Inorg. Chem., 14,* 287 (1975).

16 R. Savoie, D. Poirier, L. Prizant and A. L. Beauchamp, *J. Raman Spectrosc., 11,* 481 (1981).

17 R. Faggiani, B. Lippert and C. J. L. Lock, *Inorg. Chem., 21,* 3210 (1982) and references cited.

18 B. Lippert and U. Schubert, *Inorg. Chim. Acta, 56,* 15 (1981).

19 R. Pfab, P. Jandik and B. Lippert, *Inorg. Chim. Acta, 66,* 193 (1982).

20 R. Faggiani, B. Lippert, C. J. L. Lock and R. Pfab, *Inorg. Chem., 20,* 2381 (1981).

21 G. Raudaschl and B. Lippert, to be published.

22 R. C. Lord and G. J. Thomas, Jr., *Spectrochim. Acta, 23A,* 2551 (1967).