

Tetrakis- and Tris(1-Methyluracil) Complexes of Pt^{II}: Formation and Properties of a Carbon-Bonded Nucleobase Species as Well as of Heteronuclear Derivatives

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The reaction of K₂PtCl₄ with an excess of 1-methyluracilate (1-MeU) in water at 60 °C leads to the formation of two major products, K₂[Pt(1-MeU-N3)₄]·10H₂O (**1**) and *trans*-K[Pt(1-MeU-N3)₂(1-MeU-C5)(H₂O)]·3H₂O (**2**). Addition of CuCl₂ to an aqueous solution of **2** yields the mixed-metal complex *trans*-[PtCl(1-MeU-N3,O4)₂(1-MeU-C5,O4)Cu(H₂O)]·H₂O (**4**). Single-crystal X-ray analysis was carried out for **1** and **4**. In both compounds, the heterometals (K⁺ in **1** and Cu²⁺ in **4**) are bonded to exocyclic oxygen atoms of the 1-MeU ligands, giving rise to intermetallic distances of 3.386(2) and 3.528(2) Å in **1** and 2.458(1) Å in **4**. The shortness of the Pt–Cu separation in **4** is consistent with a dative bond between Pt^{II} and Cu^{II}. The aqua ligand in **2** is readily substituted by a series of other ligands (e.g., 1-MeC, 9-MeGH, and CN[−]), as demonstrated by ¹H NMR spectroscopy, with ³J(¹⁹⁵Pt-¹H(6)) coupling constants being sensitive indicators. Acid–base equilibria of **1** and **2** have been studied in detail and reveal some unexpected features: **1** has a relatively high basicity, with protonation starting below pH 5, and first and second pK_a values being ca. 3.4 and 0.4, respectively. These pK_a values are markedly higher than those of related neutral 2:1 or cationic 1:1 complexes and are attributed to both charge effects (−2 charge of **1**) and a favorable stabilization of oxygen-protonated species by the arrangement of four exocyclic oxygen groups of 1-MeU ligands at either sides of the platinum coordination planes. Whereas in **2**, H⁺ affinities of the three uracil ligands are in the normal range, there is a surprisingly low acidity of N(3)H of the C5-bonded uracil with a pK_a of ≈ 12.2, which compares with 9.75 for free 1-methyluracil. This implies that the C5-bonded Pt^{II} does not induce the typical acidifying effect of a Pt^{II} metal entity when bonded to a ring nitrogen atom of a neutral nucleobase. Rather, the effect is qualitatively similar to that of a metal ion bonded to N3 of an anionic 1-MeU ligand, which likewise increases its overall basicity as compared to neutral 1-MeUH.

Introduction

Unlike mono- and bis(nucleobase) complexes of Pt^{II}, and notably those of *cis*- and *trans*-(NH₃)₂Pt^{II}, which have received considerable attention over the last three decades because of their likely relevance to the chemistry of antitumor active or inactive platinum coordination compounds,¹ tris-²

and tetrakis-nucleobase complexes³ of Pt^{II} have been studied much-less intensively. In fact, the latter compounds appear to have been primarily of academic interest, despite the fact that there is a potentially meaningful link between mono- and tris(nucleobase) complexes derived from *cis*-(NH₃)₂-Pt^{II}.^{2a–c} Apart from supramolecular,^{2d} conformational and synthetic aspects,⁴ the usefulness of these compounds as ligands for additional metal ions^{3c,5,6} has been a major point

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of interest. Related Pd^{II} compounds have likewise been studied in some cases.^{7,8} In the course of our aim of preparing and isolating the tetrakis(1-methyluracilato) complex of Pt^{II}, [Pt(1-MeU-N3)₄]²⁻ (**1**), we observed the formation of a tris(1-methyluracilato) complex, which contained differently bonded 1-MeU ligands, namely two nucleobases bonded to Pt^{II} via N3 and a third one bonded via C5, *trans*-[Pt(1-MeU-N3)₂(1-MeC-C5)(H₂O)]⁻ (**2**). Even though formation of organometallic species with metal–C5 bonds and metals being platinum, mercury, and gold has occasionally been observed before for uracil nucleobases,^{9,10} given the excess of N3-deprotonated 1-methyluracil present in aqueous solution, we consider its formation in the present case a surprise.

Here, we report on some basic properties of these two compounds, concentrating in particular on their acid–base properties and their affinity for additional metal ions.

Experimental Section

Synthesis. 1-Methyluracil (1-MeUH) was obtained as described in the literature.¹¹ K₂[Pt(1-MeU-N3)₄]·10H₂O (**1**) and *trans*-K[Pt(1-MeU-N3)₂(1-MeU-C5)(H₂O)]·3H₂O (**2**) were prepared from K₂PtCl₄ (Heraeus) and 1-MeUH as follows: To a solution of 1-MeUH (1.34 g, 10.6 mmol) in water (15 mL) was added KOH (600 mg, 10.7 mmol), and the solution was brought to dryness by rotary evaporation. K₂PtCl₄ (1.10 g, 2.65 mmol) and H₂O (7.5 mL) were added, and the resulting solution (orange-red, pH 9.5) was stirred in a stoppered flask for 18 h in a water bath (60 °C). During this time, the solution changed its color to brownish tan. This solution was brought to dryness by rotary evaporation, and the resulting solid (3.11 g) was treated three times with methanol (50 mL each). The methanol solution was brought to dryness by rotary evaporation to give a mixture (1.26 g) containing **1**, unreacted 1-MeUH, and other unidentified species. The precipitate was suspended in acetone (150 mL), then filtered, and the precipitate was washed three times with water (2 mL each) to remove a dark-brown component and finally dried in air. The compound isolated this way analyzed as K₂[Pt(1-MeU-N3)₄]·4H₂O (273 mg, 12% yield). Anal. Calcd (found) for C₂₀H₂₈K₂N₈O₁₂Pt: C, 28.4 (28.5); N, 13.3 (13.2); H, 3.3 (3.1). IR (cm⁻¹): 3750 m, 3426 vs, b, 1653 vs, 1580 vs, 1452 s, 1362 s, 1328 s, 812 m, 771 m, 593 m, 498 m. ¹H NMR (D₂O, pD 6.3, δ): 7.23 (d, ³J(¹H,¹H) = 7.4 Hz, H6), 5.44 (d, H5), 3.23 (s, CH₃). In spectra recorded at a lowfield NMR instrument (60 Mz), ¹⁹⁵Pt satellites of the H5 resonances are observed (⁴J(¹⁹⁵Pt–¹H, ca. 15 Hz). Crystals suitable for an X-ray analysis of **1**

were obtained by evaporation of an aqueous methanolic solution of **1** at room temperature. X-ray crystallography revealed the presence of 10 water molecules.

The residue of the methanol extraction of **1** (1.51 g), which consisted essentially of KCl and **2** was washed three times with water (2 mL each), leaving **2** as a light-gray solid in a yield of 440 mg (24%). Anal. Calcd (found) for C₁₅H₂₃KN₆O₁₀Pt: C, 26.4 (26.5); N, 12.3 (12.4); H, 3.4 (3.1). IR (cm⁻¹): 3435 s, b, 1657 vs, 1566 s, 1451 s, 1364 s, 1326 m, 810 m, 774 m, 628 m, 493 m. ¹H NMR (D₂O, pD 6.9, δ): 7.41 (d, ³J(¹H,¹H) = 7.4 Hz, H6(N3)), 6.46 (s, ³J(¹⁹⁵Pt,¹H) = 70 Hz, H6(C5)), 5.66 (d, ³J(¹H,¹H) = 7.4 Hz, H5), 3.34 (s, CH₃(N3)), 3.14 (s, CH₃(C5)). ¹⁹⁵Pt-NMR (D₂O, pD 7.1, δ): –3068 (s).

The heterometallic (Pt, Hg)-derivative of **1**, Hg[Pt(1-MeU-N3)₄]·7H₂O (**3**) was obtained by stirring **1** (200 mg, 0.2 mmol) with one equiv of Hg^{II} acetate in water (30 mL). The solution was reduced to a volume of 3 mL by rotary evaporation. A colorless precipitate of **3** (126 mg, 52%) was filtered off and washed with water (1 mL). Anal. Calcd (found) for C₂₀H₃₄HgN₈O₁₅Pt: C, 23.5 (23.5); N, 11.0 (11.1). IR (cm⁻¹): 3434 m, b, 3082 w, 1648 s, 1574 s, 1492 m, 1459 s, 1377 s, 1344 m, 1254 w, 1164 w, 820 m, 787 m, 730 w, 615 w, 508 m, 475 m, 451 w. ¹H NMR (D₂O, pD 5.9, δ): 7.32–7.43 (m, H6), 5.58–5.65 (m, H5), 3.29–3.30 (m, CH₃(N3)).

trans-[Pt(1-MeU-N3)₂(1-MeU-C5)CuCl(H₂O)]·H₂O (**4**) was prepared as follows: To a solution of **2** (1.00 g, 1.5 mmol) in water (300 mL) was added CuCl₂ (250 mg, 1.5 mmol) at room temperature. The colorless solution instantaneously turned yellow and was subsequently cooled at 6 °C. Within 30 min, a tan precipitate had formed in solution. It was filtered off and washed with water (10 mL). The yield was 91%. Anal. Calcd (found) for C₁₅H₂₁ClCuN₆O₈Pt (dihydrate): C, 24.9 (24.9); H, 2.9 (2.8); N, 11.6 (11.8). IR (cm⁻¹): 3468 s, b, 3182 m, b, 1706 s, 1627 vs, 1524 vs, 1476 s, 1452 s, 1429 m, 1349 vs, 1310 m, 809 m, 762 m, 706 m, 508 m.

Brown crystals of **4** suitable for X-ray crystallography, which analyzed as a monohydrate, were obtained from a solution of **2** and was CuCl₂ kept at room temperature rather than at 6 °C.

K₂[Pd(1-MeU-N3)₄]·8H₂O (**5**) was obtained as a pale-yellow precipitate upon mixing 1-MeUH (630 mg, 5 mmol) and KOH (280 mg, 5 mmol) in water (10 mL) and adding K₂PdCl₄ (327 mg, 1 mmol). Within 1 min, precipitation of **5** started from the yellow solution (pH 10.7). After 2 h of stirring at room temperature, the precipitate was filtered and washed with ice water. Recrystallization from H₂O at 50 °C gave **5** as yellow needles in 94% yield. Anal. Calcd (found) for C₂₀H₃₆K₂N₈O₁₆Pd: C, 29.0 (28.7); H, 4.4 (4.4); N, 13.5 (13.1). ¹H NMR (D₂O, pD 10.6, δ): 7.22 (d, ³J(¹H,¹H) = 7.4 Hz, H6), 5.40 (d, H5), 3.28 (s, CH₃). Raman (cm⁻¹): 796, 642, 593. It is likely that the actual water content of **5** is higher, considering previous findings,⁸ which gave an elemental analysis with 8.5 water molecules, although X-ray crystallography revealed the presence of 10 water molecules.

Ag₂[Pd(1-MeU-N3)₄]·9H₂O (**6**) was prepared by dissolving **5** (415 mg, 0.5 mmol) in water (20 mL, 50 °C, subsequently cooled to room temperature, pH 10.1) and adding AgNO₃ (169 mg, 1 mmol) to the clear, yellow solution. After 5 h at room temperature, the solution was filtered and allowed to evaporate at 3 °C. Pale-yellow cubes were isolated in 25% yield. Anal. Calcd (found) for Ag₂C₂₀H₃₈N₈O₁₇Pd: C, 24.4 (24.1); H, 3.9 (3.9); N, 11.4 (11.4); O, 27.6 (27.7); Ag 21.9 (21.8).

Zn[Pd(1-MeU-N3)₄]·7.5H₂O (**7**) was prepared from **5** (200 mg, 0.27 mmol), dissolved in water (10 mL), and ZnSO₄·7H₂O (200 mg, 1.4 mmol) was added. The colorless precipitate that formed within a short period of time was filtered, washed with water, and

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dried in air. The yield was 26%. Anal. Calcd (found) for $C_{20}H_{35}N_8O_{15.5}PdZn$: C, 29.8 (29.8); H, 4.4 (4.4); N, 13.9 (13.7); Zn, 8.1 (8.1).

$Co[Pd(1-MeU-N3)_4] \cdot 2H_2O$ (**8**) was prepared in a way analogous to **7** and was isolated as a purple, microcrystalline material in 31% yield. Anal. Calcd (found) for $C_{20}CoH_{24}N_8O_{10}Pt$: C, 34.2 (34.1); H, 3.5 (2.9); N, 16.0 (15.8). The discrepancy between the calculated and found values for hydrogen was due to the loss of water of crystallization after weighing (value in agreement with anhydrous compound).

Spectroscopy and Other Measurements. 1H NMR spectra of **1–3** in D_2O were recorded on a Varian Mercury 200 FT (internal TSP as reference), and the ^{195}Pt NMR spectrum of **2** was recorded on a Bruker DRX 300. IR spectra (KBr pellets) were taken on a Bruker IFS 28. UV spectra were measured on a Varian Cary 100, and elemental analyses (carbon, hydrogen, and nitrogen) were performed on a Leco CHNS-932 elemental analyzer. The acid–base titrations were carried out with a pH meter (inoLab pH Level 1) with a glass electrode (SenTixMic). pD values (in D_2O) were obtained by adding 0.4 to the pH meter reading.¹² For strongly alkaline solutions (pH > 11), pD values were not measured with the glass electrode but, rather, calculated values of weighed amounts of NaOH, dissolved in D_2O , were taken to adjust the desired pD. The pK_a values (in D_2O) were determined by plotting 1H NMR chemical shifts of nonexchangeable protons versus pD. The resulting curves were analyzed by a Newton–Gauss nonlinear least-squares curve-fitting procedure,¹³ and the pK_a values obtained this way for D_2O were then converted into pK_a values valid for water.¹⁴ pK_a values (in H_2O), determined by UV spectroscopy, were obtained by recording aqueous solutions of **2** at different pH values and plotting absorptions at 290 nm versus pH.

X-ray Crystallography. Intensity data of **1** and **4** were collected on an Enraf–Nonius KappaCCD diffractometer¹⁵ using graphic-monochromated Mo $K\alpha$ radiation ($\lambda = 0.7107 \text{ \AA}$) at low temperature, 150 K. None of the crystals showed evidence of crystal decay during data collection. For data reduction and cell refinement, the programs *DENZO* and *SCALEPACK* were used.¹⁶ The structures were solved by standard conventional direct methods and refined by full-matrix least-squares based on F^2 using the *SHELXTL-5.1* program.¹⁷ The positions of all of the non-hydrogen atoms of the main structure were deduced from difference Fourier maps and were refined anisotropically. Because of the special kind of disorder for the 1-MeU ring(C) in **1**, the N(1C) nitrogen and C(5C) carbons were treated as a single atom, and the C(1C) and C(1) carbons were treated as a half atom. Actually, the N(1C) and C(5C) atoms are occupied by 50% N(1C) and 50% C(5C) each. Hydrogen atoms were generated geometrically and given isotropic thermal parameters equivalent to 1.2 or 1.5 times those of the atom to which they were attached, except the hydrogen atom on C(5C) was not generated because of the half-occupancy methyl group. All of the calculations were performed using the *WinGX System*, version

Table 1. Crystallographic Data for **1** and **4**

	1	4
formula	$C_{20}H_{40}N_8O_{18}PtK_2$	$C_{15}H_{19}N_6O_8ClPtCu$
fw	953.85	705.42
cryst syst	monoclinic	monoclinic
space group	$P2(1)/n$	$P2(1)/n$
unit cell dimensions		
<i>a</i> (Å)	13.033(3)	7.8740(16)
<i>b</i> (Å)	20.015(4)	14.403(3)
<i>c</i> (Å)	13.697(3)	24.386(5)
β (deg)	91.55(3)	90.67(3)
<i>V</i> (Å ³)	3571.6(3)	2765.4(1)
<i>Z</i>	4	4
<i>T</i> (K)	150	150
D_{calcd} (Mg/m ³)	1.705	1.687
μ (mm ⁻¹)	4.239	5.962
$R1^a$, $wR2^b$ [$I > 2\sigma(I)$]	0.045, 0.097	0.048, 0.076
R indices (all data)	0.088, 0.104	0.157, 0.089

$$^a R1 = \sum ||F_o| - |F_c|| / \sum |F_o|. \quad ^b wR2 = [\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]]^{1/2}.$$

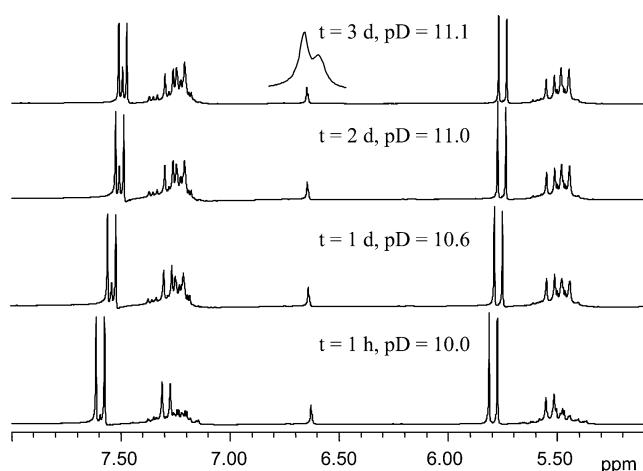


Figure 1. Lowfield sections of 1H NMR spectra of reaction mixtures of K_2PtCl_4 and 1-MeUH (5 eq) and K_2CO_3 (5 eq) in D_2O (pD 10–11) at different times.

1.64.¹⁸ Relevant crystal data and data collection parameters are summarized in Table 1.

Results and Discussion

Formation of **1 and **2**.** The reaction of K_2PtCl_4 with a five-fold excess of $K^+(1-MeU)^-$ (obtained from KOH and 1-MeUH or in situ from K_2CO_3 and 1-MeUH) in D_2O , pD 10–11, has originally been followed by 1H NMR spectroscopy. New resonances start to appear within the first hour of the reaction (Figure 1) and display the following features: First, in addition to the averaged resonances of free 1-MeUH/1-MeU⁻, a series (3–4 sets) of new H5 and H6 doublets are observed, which are in the typical range of N3-bonded 1-MeU ligands, namely at 7.2–7.4 ppm (H6) and 5.4–5.6 ppm (H5). Because of partial isotopic exchange of the H5 proton of the 1-MeU, the H6 doublets are converted into pseudo-triplets, with the third resonance growing in the center of the respective doublet and the H5 doublets losing intensity. Second, at ca. 6.6 ppm, two singlets grow in. As will be shown below, the new resonances contain those of $[Pt(1-MeU-N3)_4]^{2-}$ (**1**) and of species containing C5-bonded

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Table 2. Selected Bond Distances (Angstroms) and Angles (Degrees) for **1** and **4**

1			4		
Pt1–N3A	2.037(7)	Pt1–N3C	2.033(6)	Pt1–Cu1	2.4584(11)
Pt1–N3B	2.054(7)	Pt1–N3D	2.032(7)	Pt1–Cl1	2.387(2)
K1–O1	2.968(11)	K2–O4C	2.745(7)	Pt1–N3	2.020(6)
K1–O2	2.848(8)	K2–O4D	2.719(6)	Pt1–N3A	1.999(7)
K1–O2A	2.691(7)	K2–O3	3.084(9)	Pt1–C5B	2.006(7)
K1–O2B	2.718(7)	K2–O4	2.883(7)	Cu1–O1W	1.974(6)
K1–O2C	2.697(8)	K2–O4A	2.724(7)	Cu1–O4	1.902(6)
K1–O2D	2.717(7)	K2–O4B	2.711(6)	Cu1–O4A	1.901(6)
Pt1···K1	3.528(2)	Pt1···K2	3.386(2)	Cu1–O4B	2.265(7)
N3A–Pt1–N3B	178.2(3)	N3B–Pt1–N3C	88.6(2)	Cu1–Pt1–Cl1	93.66(7)
N3A–Pt1–N3C	91.3(2)	N3B–Pt1–N3D	91.1(2)	Cu1–Pt1–N3	86.8(2)
N3A–Pt1–N3D	88.9(2)	N3C–Pt1–N3D	177.9(3)	Cu1–Pt1–N3A	86.6(3)
O1–K1–O2	101.0(3)	O2–K1–O2C	148.1(3)	Cu1–Pt1–C5B	88.4(2)
O1–K1–O2A	74.4(3)	O2–K1–O2D	79.3(2)	Cl1–Pt1–N3	89.5(2)
O1–K1–O2B	157.5(3)	O2A–K1–O2B	115.5(2)	Cl1–Pt1–N3A	91.5(2)
O1–K1–O2C	91.9(3)	O2A–K1–O2C	75.1(2)	Cl1–Pt1–C5B	177.9(2)
O1–K1–O2D	128.6(3)	O2A–K1–O2D	71.8(2)	N3–Pt1–N3A	173.4(3)
O2–K1–O2A	136.4(3)	O2B–K1–O2C	72.7(2)	N3–Pt1–C5B	90.3(3)
O2–K1–O2B	85.5(2)	O2B–K1–O2D	73.6(2)	N3A–Pt1–C5B	89.0(3)
O4C–K2–O4D	121.0(2)	O2C–K1–O2D	114.8(3)	Pt1–Cu1–O1W	162.6(2)
O4C–K2–O3	55.0(2)	O4D–K2–O4A	75.9(2)	Pt1–Cu1–O4	88.6(2)
O4C–K2–O4	147.6(2)	O4D–K2–O4B	77.97(19)	Pt1–Cu1–O4A	88.2(2)
O4C–K2–O4A	75.1(2)	O3–K2–O4	92.7(2)	Pt1–Cu1–O4B	88.54(17)
O4C–K2–O4B	74.9(2)	O3–K2–O4A	108.3(2)	O1W–Cu1–O4	90.9(3)
O4D–K2–O3	171.7(2)	O3–K2–O4B	93.8(2)	O1W–Cu1–O4A	89.6(3)
O4D–K2–O4	90.66(19)	O4–K2–O4A	123.5(2)	O1W–Cu1–O4B	108.8(3)
O4–K2–O4B	108.7(2)	O4A–K2–O4B	120.9(2)	O4–Cu1–O4A	171.0(3)
				O4–Cu1–O4B	88.8(3)
				O4A–Cu1–O4B	99.5(3)

1-methyluracil ligand(s), for example [Pt(1-MeU-*N3*)₂(1-MeU-*C5*)X]ⁿ⁻, and, in addition, others of different Pt:1-MeU stoichiometries, which were not analyzed, however. It is, of course, to be expected that the formation of **1** with its 1:4 stoichiometry proceeds via 1:1, 1:2, and 1:3 complexes. Similar arguments apply for the 1-MeU-*N3* resonances of the second species. We note that ¹H NMR spectra recorded with samples containing K₂CO₃ and 1-MeUH, as shown in Figure 1, differed in detail from those obtained with samples containing K⁺(1-MeU)⁻. Possibly this is a result of partial coordination of CO₃²⁻ to platinum. Similarly, the concentration of K⁺ present in solution had an effect on the chemical shift of the resonances at around 6.6 ppm (below).

X-ray Crystal Structure of 1. K₂[Pt(1-MeU-*N3*)₄]·10H₂O (**1**) was eventually prepared on a preparative scale. Selected interatomic distances and angles are given in Table 2. K₂[Pt(1-MeU-*N3*)₄]·10H₂O **1** crystallizes in the monoclinic system *P2*₁/*n* and is very similar to the corresponding Pd^{II} compound previously reported by Mizutani and co-workers.⁸ Like in the latter, the four 1-MeU ligands are bonded to platinum via their N3 sites in a square-planar fashion. Pt–N distances range from 2.032(7) to 2.054(7) Å. There is a difference, however, between the two compounds, and this refers to the fact that in the palladium complex the four nucleobases are arranged *head-head-head-head* (*hhhh*), whereas in the here reported platinum compound one of the four 1-MeU ligands (ligand C in Figure 2) is adopting two different orientations. In 50% of the molecules, it is in the same direction as are the three other ligands (*hhhh*), and in 50% it is rotated to give a *hhth* arrangement (*t* = tail, cf. Experimental Section). As far as the exocyclic oxygen atoms are concerned, this feature has relatively minor consequences only. At either side of the platinum coordination plane, the exocyclic oxygens

atoms form a rim built of four oxygen atoms, with O···O distances between 3.18(2) and 3.42(5) Å (sides) and between 4.55(6) and 4.76(1) Å (diagonals). O···O···O angles are 88.4(2)–91.0(2)°. As in the palladium complex,⁸ all eight of the exocyclic oxygens act as donor atoms for the two potassium ions, with O–K bond lengths of 2.691(7)–2.745(7) Å. Both potassium ions, K1 and K2, extend their coordination spheres to coordination numbers 6 and 7, respectively. Thus, K1 has two additional H₂O ligands (O1, O2), one of which (O2)

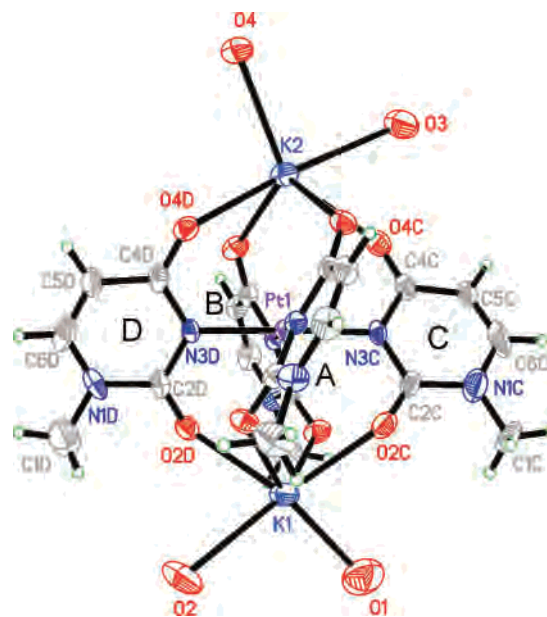


Figure 2. Section of the solid-state structure of K₂[Pt(1-MeU-*N3*)₄]·10H₂O (**1**) with atom numbering scheme. Note that the 1-MeU ligand C adopts two different orientations, corresponding to a rotation of this ligand about the N3C–C6C vector. For simplicity, only one orientation is shown.

bridges to K2 of an adjacent molecule (O2–K2', 3.15(1) Å), and similarly, K2 has two water molecules (O3, O4). Distances between these water molecules and the potassium ions vary between 2.848(8) and 3.084(9) Å.

Within the cation, the three metal ions K1, Pt1, K2 are close to linear, the angle at Pt1 being 179.59(5)°. Intermetallic distances are 3.386(2) Å (Pt–K2) and 3.528(2) Å (Pt1–K1). Again, these distances are similar to those of the palladium analogue. They are shorter than Pt–K distances in *trans*-K₂[PtI₂(1-MeU-*N3*)₂]·6H₂O (3.688(3) Å), in which each K⁺ is bonded to a O4 and O2 site of the two 1-MeU ligands.¹⁹

Molecules of **1** are arranged in a zigzag fashion, with the water molecule O2 at K1 connecting individual molecules (Figure 3). Thus, four full molecules of water are connected with each PtK₂ unit, and the six remaining water molecules (O1W–O6W) form a hydrogen-bonded array of water clusters (Supporting Information). Of these six water molecules, two (O5W, O6W) are disordered over two positions, which are very close, however.

Acid–Base Equilibria of 1. The ¹H NMR spectrum of isolated **1** in the neutral-to-weakly acidic pD range is very simple, consisting of two doublets assigned to H6 at 7.23 ppm (Figure 4) and H5 at 5.44 ppm (³*J* = 7.4 Hz) as well as a singlet for the N(1)CH₃ group at 3.23 ppm. There is no sign whatsoever for a second rotamer, as seen in the solid-state structure, being present in solution. At a strongly alkaline pD, this simplicity is retained. When going to a lower pD, the H6 and H5 resonances of **1** become complex, however, displaying multiple doublets (e.g., four at a pD 4.1) of different relative intensities. We interpret this feature in terms of protonation of the 1-MeU ligands at the exocyclic oxygen atoms and the formation of different rotamers of partially protonated 1-methyluracil ligands (Scheme 1). This view is supported by the fact that there is a clear time dependence in the appearance of these resonances. The species formed at acidic pD represent platinated forms of the rare oxo, hydroxo tautomers of 1-methyluracil.²⁰ Upon prolonged storage of samples of **1** at strongly acidic pD (<2), displacement of 1-MeUH from **1** takes place, consistent with previous findings on 1:1 and 1:2 complexes of Pt^{II} with 1-MeU.²⁰ Resonances of free 1-MeUH occur at 7.60 (H6) and 5.80 ppm (H5) and are clearly outside the range of resonances of **1** (Supporting Information).

Our initial attempt to determine p*K*_a values of protonated forms of **1** by pD-dependent ¹H NMR spectroscopy was hampered by the fact that the various protonated rotamers of **1** covered a relatively broad chemical shift range. Nevertheless, it was clearly obvious that the center of the H(6) doublets, for example, underwent a downfield shift below pD 5, indicative of proton binding. We subsequently resorted to UV–vis spectroscopy as a means of establishing p*K*_a values of (averaged) protonated forms of **1**. As a result (Figure 5), two protonation steps of [Pt(1-MeU-*N3*)₄]²⁻

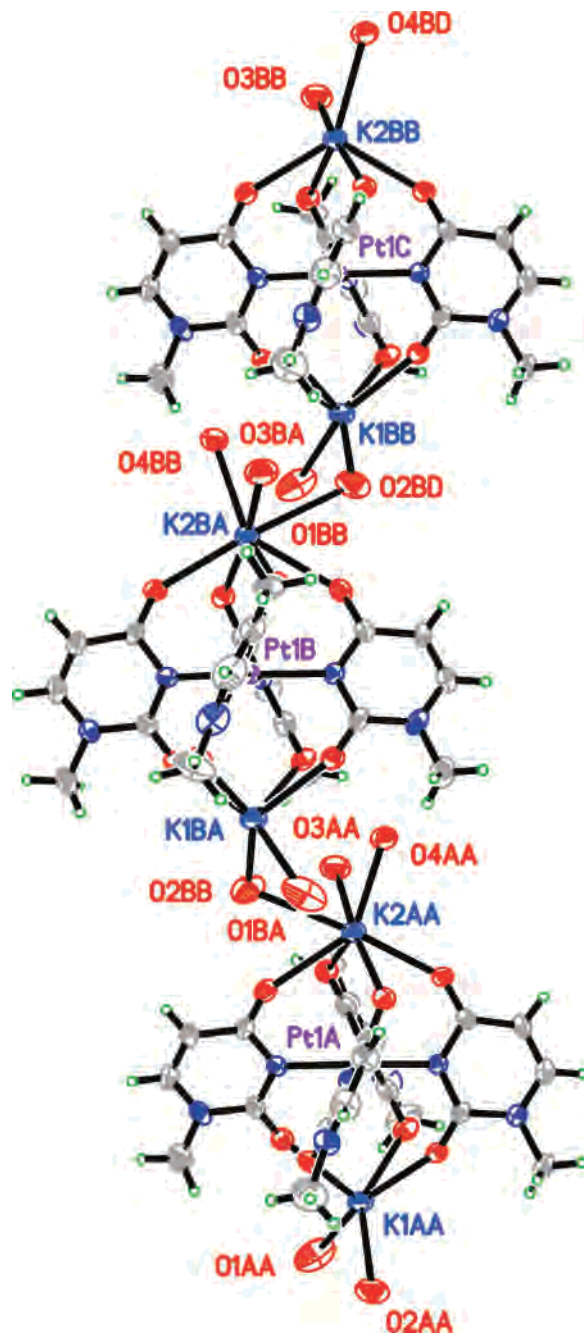
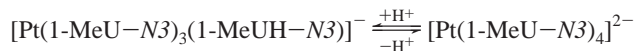


Figure 3. Zigzag arrangement of **1** with bridging aqua ligands. The other six water molecules in the crystal lattice are not shown.

were determined, giving p*K*_{a1} of 3.4 ± 0.4 and a p*K*_{a2} of 0.4 ± 0.3. The p*K*_{a1} of 3.4 for the



equilibrium is the highest one measured to date for a Pt^{II} complex of 1-MeU. This p*K*_{a1} value compares with a p*K*_{a1} of ~1.5 for the equilibrium *cis*-[Pt(NH₃)₂(1-MeU-*N3*)(1-MeUH-*N3*)]⁺ ⇌ *cis*-[Pt(NH₃)₂(1-MeU-*N3*)₂] + H⁺ and a value of ~0.9 for the equilibrium *cis*-[Pt(NH₃)₂(1-MeUH-*N3*)(H₂O)]²⁺ ⇌ *cis*-[Pt(NH₃)₂(1-MeU-*N3*)(H₂O)]⁺ + H⁺.²⁰ The considerably higher p*K*_{a1} of **1** reflects the much-higher basicity of the anionic [Pt(1-MeU-*N3*)₄]²⁻ species as compared to neutral *cis*-[Pt(NH₃)₂(1-MeU-*N3*)₂] and cationic *cis*-

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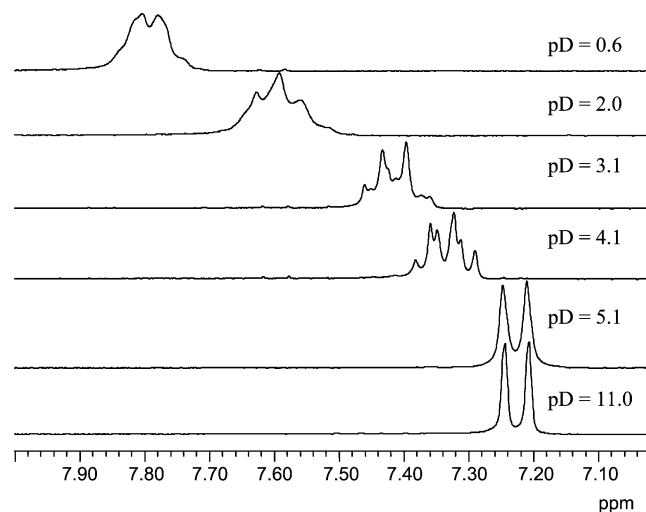
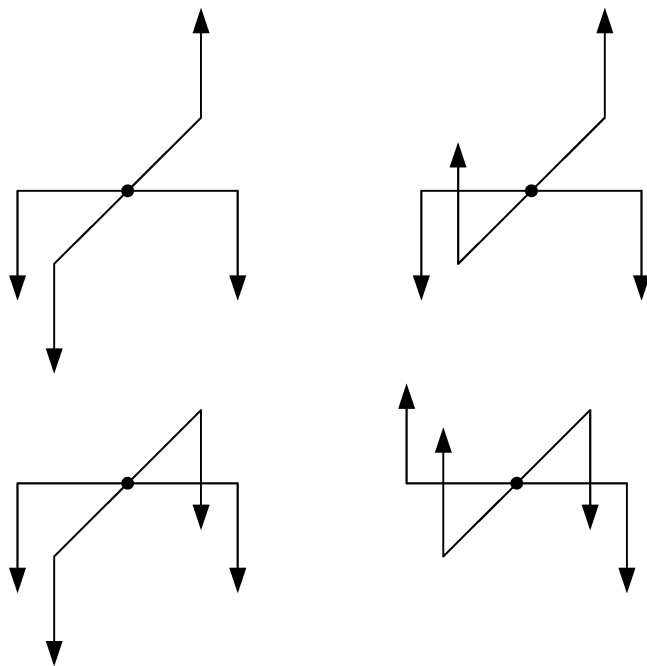


Figure 4. ¹H(6) resonances of 1-methyluracil ligands of **1** in D₂O at different pD values. Spectra were recorded ca. 1 h after pD adjustment.

Scheme 1



[Pt(NH₃)₂(1-MeU-N3)(H₂O)]⁺. Although differences in the charge of the various Pt^{II} species certainly account for differences in basicity, it is very likely that the favorable stabilization of a proton bonded to an exocyclic oxygen atom by multiple hydrogen bonding interactions with the three adjacent carbonyl oxygens adds to this effect. Considering the X-ray structure of **1**, it is even feasible that a H₃O⁺ ion rather than an isolated H⁺ may be trapped above the plane generated by four keto oxygen atoms with one or more protons dynamically disordered over the four oxygen atoms, reminiscent of a similar situation involving a NH₃ ligand of a Pt^{IV} complex and a uracil quartet.²¹ In any case, the geometrical properties of [Pt(1-MeU-N3)₄]²⁻ strongly suggest that a favorable stabilization of a protonated species by the adjacent carbonyl acceptors supports the high pK_a. It thus

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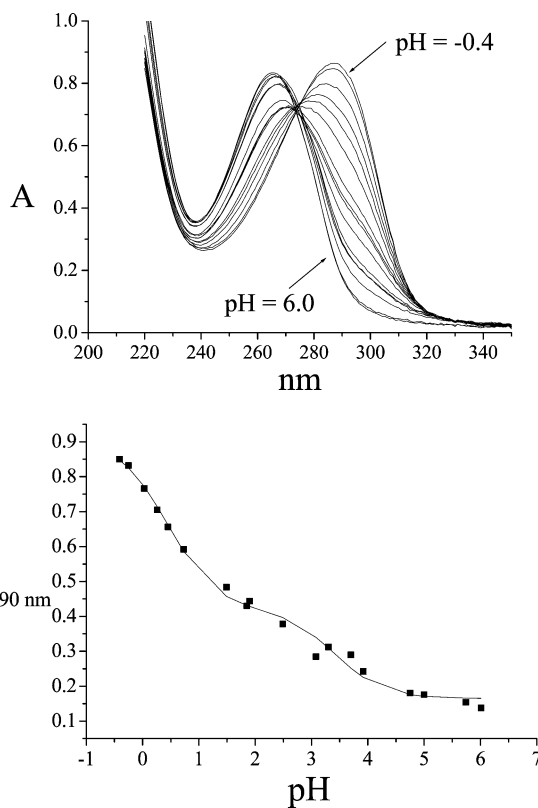


Figure 5. pH dependent UV-vis spectra of **1** (top) and pH dependence of absorption at 290 nm (bottom).

reflects similar principles as experienced with so-called proton sponges,²² albeit at a much-lower scale. Still, the effect appears to be sufficiently large to explain why aqueous solutions of K₂[Pt(1-MeU-N3)₄] (**1**) always react alkaline.²³

¹H NMR Spectra and Acid–base Equilibria of *trans*-K[Pt(1-MeU-N3)₂(1-MeU-C5)(H₂O)] (2). ¹H NMR spectroscopy provides unambiguous proof for a carbon-bonded 1-MeU ligand being present in **2** (Figure 6). Thus, the positions of the heteroaromatic 1-MeU resonances, relative signal intensities, and the fact that one of the 1-MeU ligands displays ¹⁹⁵Pt satellites of 70 Hz is consistent only with a composition of a species containing two N3-bonded 1-MeU ligands in a mutual *trans* position and a C5-bonded 1-MeU.

The pD dependence of the chemical shifts of the H6 and H5 protons of **2** is shown in Figure 7. The pK_a values are 1.3 ± 0.3 (3σ) for the N3 coordinated ligands (in protonated form, H⁺ at O4 or O2) and 1.7 ± 0.3 for the C5 coordinated one (H⁺ at O4 or O2). The value for the deprotonation of the C5-bonded 1-MeU ligand (deprotonation of N(3)H) is about 12.2 ± 0.6. The chemical shifts of *trans*-[Pt(1-MeU-N3)₂(1-MeU-C5)(H₂O)]⁻ and its deprotonated species [Pt(1-MeU-N3)₂(1-MeU'-C5)(OH)]³⁻ (with 1-MeU'-C5 representing the 1-methyluracil dianion, deprotonated at C5 and N3) vary from 0.03 ppm for the H5(N3) protons and 0.07

(22) See, e.g.: (a) Schwesinger, R. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1164. (b) Verkade, J. G. *Acc. Chem. Res.* **1993**, *26*, 483. (c) Alder, R. W. *Chem. Rev.* **1989**, *89*, 1215. (d) Raab, V.; Gauchenove, E.; Merkoulou, A.; Harms, K.; Sundermeyer, J.; Kovačević, B.; Maksić, Z. B. *J. Am. Chem. Soc.* **2005**, *127*, 15738.

(23) pK_b = 14 - 3.4 = 10.6; pOH = 1/2(pK_b - log c); with c = 0.1 M, pOH = 1/2(10.6 + 1) = 5.8; pH 8.2; with c = 1 M, pH 8.7.

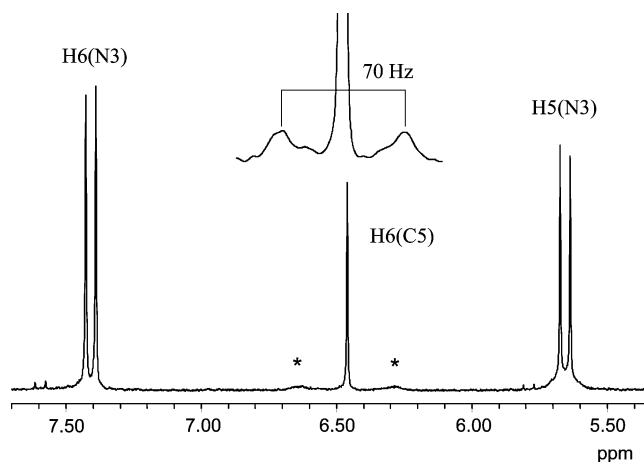


Figure 6. Section of ^1H NMR spectrum of **2** in D_2O , pD 6.9. ^{195}Pt satellites with 3J of 70 Hz for the H(6) resonances of the C5-bonded 1-MeU are indicated by asterisks.

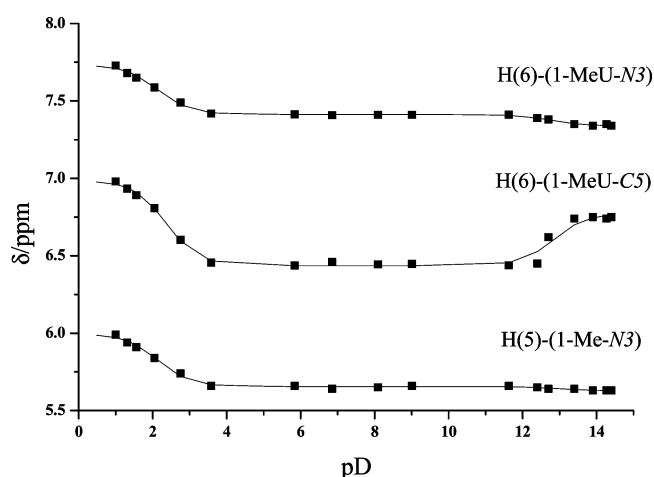


Figure 7. pD dependence of aromatic 1-MeU resonances of **2**.

ppm for the H6(N3) protons to 0.30 ppm for the H6(C5) proton. This feature is consistent with deprotonation occurring at the C5-bonded uracil ligand and suggests that the N3-bonded ligands are somewhat sensitive to this process. In contrast, the pronounced downfield shifts of all of the aromatic uracil protons at low pD values are indicative of the protonation of all three uracil ligands, with the C5-bonded one being somewhat more basic (above). A pK_a for the water ligand cannot be determined because there is no change in the chemical shift of the uracil protons in the range typical for deprotonation of $\text{Pt}^{\text{II}}\text{-OH}_2$ groups. The highfield shift of the ^{195}Pt -NMR resonance of **2** (-3068 ppm) suggests that the platinum ion is, relatively speaking, electron rich, and, consequently, the aqua ligand is expected to be less acidic than it is in cationic complexes containing nitrogen donors. For example, the pK_a of the H_2O ligand in $\text{cis-}[\text{Pt}(\text{1-MeU-N3})(\text{NH}_3)_2(\text{H}_2\text{O})]^+$ is 7.0 ± 0.1 .²⁴

The relatively high pK_a of 12.2 for the N(3)H deprotonation of the 1-MeU-C5 ligand in **2** deserves some comment. A comparison of the pK_a value of 1-MeUH (9.75)²⁵ with pK_a values of a series of 1-Me-5-X-uracil ligands with X

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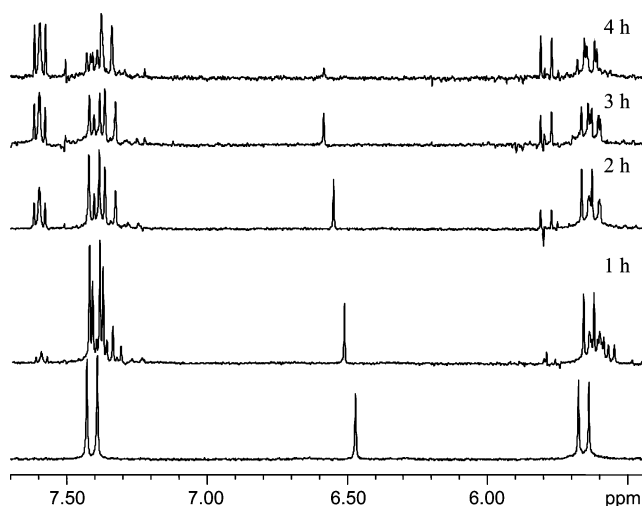


Figure 8. Decomposition of **2** at acidic pH. Samples were kept at pD 1.4 at room temperature for various amounts of time (1–4 h) and then brought back to pD ~ 7 . The three-line resonance due to H6 of free 1-methyluracil at 7.6 ppm consists of a singlet (C5-deuterated 1-methyluracil) in the center of a doublet due to 1-methyluracil derived from N3-bonded 1-MeU.

$= \text{NO}_2$ (7.20)²⁶, Br (7.84)²⁷, and CH_3 (10.1)²⁸ reveals that the $\text{trans-}[\text{Pt}(\text{1-MeU-N3})_2(\text{OH})]^-$ entity, when bonded to C5, apparently has lost its acidifying effect on the proton at N3 largely. This situation is in marked contrast to that with Pt^{II} binding to endocyclic nitrogen atoms of neutral nucleobases, where an acidification of the nucleobase is observed.²⁹ Although the negative charge of the platinum entity is likely to contribute to this effect,³⁰ it is primarily the binding mode to the deprotonated C5 position that accounts for this feature. The situation in **2** is qualitatively similar to that seen in 1-MeU-N3 ligands of Pt^{II} , which become more basic than the free, neutral nucleobase 1-MeUH when it comes to accepting a proton. Whereas 1-MeUH is protonated in strongly acidic medium only (pK_a of 1-MeUH $_2^+$ is ca. -3)^{27,31}, $\text{Pt}(\text{1-MeU-N3})$ is protonated much more readily (pK_a of $\text{Pt}(\text{1-MeUH-N3})L_n$ ranging from 0.9–3.4, depending on coligands L and charge, see above). Concerning the C5-bonded uracil ligand in **2**, it is less acidic (or conversely more basic) by $12.2 - 9.75 = 2.45$ log units. In the 1,3-dimethylxanthine/ $[\text{Ru}(\text{NH}_3)_5]^{3+}$ system, Clarke has pointed out that the C8-bonded metal entity acidifies N(9)H to a smaller extent than does the identical metal entity bonded to N7, despite the shorter distance between the metal at C8 and the proton at N9.³²

Sensitivity of C5 Ligand toward H^+ and Alkali Metal Ions. The sensitivity of both the N3- and the C5-platinum bond toward protons is evident from Figure 8. The figure shows the H6 and H5 ^1H NMR signals of **2**, measured at pD = 7.0, and after stirring **2** for 1, 2, 3, and 4 h in DNO_3

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Table 3. $^3J(^{195}\text{Pt}, ^1\text{H}_6)$ Coupling Constants and H6 Chemical Shifts of 1-MeU-C5 in *trans*-[Pt(1-MeU-N3)₂(1-MeU-C5)(X)]ⁿ⁻

ligand X ^a	$^3J(^{195}\text{Pt}, ^1\text{H})$ (Hz)	δ H6
OH ⁻	70	6.49
H ₂ O	70	6.46
1-MeC-N3	60	6.65/6.67
9-MeGH-N7	59	6.66/6.68
ND ₃	58	6.46/6.47
py-N	56	6.47/6.50
Me ₂ SO-S	51	6.74
CN ⁻	46	6.59/6.60

^a Abbreviations: 1-MeC = 1-methylcytosine, 9-MeGH = 9-methylguanine, py = pyridine, Me₂SO = *N,N'*-dimethylsulfoxide.

solution at pD = 1.4. The samples were subsequently brought to pD ~7 by means of NaOD to have a direct comparison with the starting compound. As can be seen, the intensities of both the H6 resonance of the C5-bonded nucleobase and the intensities of the N3-bonded nucleobases are decreasing with time whereas the new signals due to free 1-methyluracil (~5.8 and ~7.6 ppm) are increasing. From the relative intensities of the uracil-H6 singlet (of C5-deuterated free ligand) and the uracil-H6 doublet (of originally N3-bonded ligand) it is evident that the C5-bonded 1-methyluracil is displaced faster than the N3-bonded ones. This observation is consistent with an easier protonation of the carbon-bonded uracil ligand (cf. above).

There is an interesting detail of this experiment to be noted, namely the unexpected downfield shift of the H6 resonance of the 1-MeU-C5 ligand. We propose that it is a consequence of an interaction between **2** and NaNO₃ produced in solution during neutralization of the DNO₃ acidic solutions. In fact, the addition of NaNO₃ to an aqueous solution of **2** has the very same effect. Similarly, we found that other salts likewise caused downfield shifts, which were particularly pronounced in the case of LiNO₃ (Supporting Information), with shifts exceeding 0.5 ppm. It appears that the anion (e.g., NO₃⁻ vs ClO₄⁻) likewise has some effect. At the highest concentration applied (0.5 M LiNO₃), a second set of resonances, ca. 20% of those of **2**, is observed in the ¹H NMR spectrum, which we assign to a second rotamer of **2**, with resonances of 1-MeU-N3 and 1-MeU-C5 ligands in a 2:1 ratio.³³ If binding of Li⁺ via the exocyclic oxygen groups of the three 1-MeU ligands is considered, possibly with involvement of the aqua ligand of platinum as well, two different species are feasible (Supporting Information). In both cases, the H6 resonances of the 1-MeU-C5 ligands experience binding of Li⁺ to anion **2**.

Trans Influence Studies with 2. The above-mentioned 3J coupling between the ¹⁹⁵Pt isotope and H6 of the carbon-bonded 1-methyluracil ligand proved to be very sensitive on the nature of the ligand in the trans position. Thus, substitution of the aqua ligand of **2** by a series of ligands of varying trans influence not only leads to changes in the chemical shift of H6 but also to changes in coupling constants, which range from 70 to 46 Hz (Table 3). These values inversely correlate with the trans influence of the

(33) Chemical shifts (δ): 3.27 (CH₃ of 1-MeU-C5), 3.37 (CH₃ of 1-MeU-N3), 5.68 (d, $^3J = 7.2$ Hz, H5 of 1-MeU-N3), 7.20 (s, H6 of 1-MeU-C5), 7.39 (d, H6 of 1-MeU-N3).

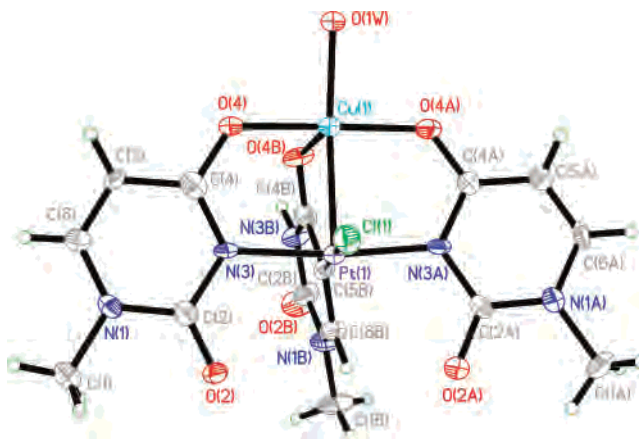


Figure 9. View of *trans*-[PtCl(1-MeU-N3,O4)₂(1-MeU-C5,O4)Cu(H₂O)]·H₂O (**4**) with atom numbering scheme.

ligand X; hence, they are larger for the oxygen donor H₂O than for the carbon donor CN⁻, with nitrogen and sulfur donors in between. A similar trend has previously been reported for C5-platinated 1,3-dimethyluracil complexes.^{10b} These and the here reported 3J coupling constants are substantially larger than those in a diplatinum(III) complex with an axially C5-bonded 1-methyluracil ligand.^{10a}

In addition to changes in chemical shifts of the various 1-MeU resonances and of $^3J(^{195}\text{Pt}-^1\text{H}_6)$ coupling constants of the 1-MeU-C5 ligand, substitution of the aqua ligand in **2** is reflected also by an increase in resonance number. This is probably due to hindered rotation of individual ligands in the derivatives of **2**. Thus, with 9-methylguanine a doubling of all three resonances (H5, H6, CH₃) of the 1-MeU-N3 ligands and of H6 of the 1-MeU-C5 ligand (each approximately 55:45) is observed, and in addition minor-to-moderate changes in chemical shifts as well as in the 3J value (ca. 59 Hz) take place (Supporting Information). The most-simple interpretation implies two different arrangements of the trans positioned 1-MeU-N3 ligands, for example, *head-head* and *head-tail* and hindered rotation. With DMSO added to an aqueous solution of **2** (pD 7.9), there is an immediate doubling of all three resonances of the N3-bonded ligands, a downfield shift of the H6 resonance of 1-MeU-C5 (6.74 ppm, $^3J = 51$ Hz), and a clear indication of the CH₃ resonances of the DMSO ligand at 3.12 ppm to which DMSO is bonded via its sulfur atom, displaying ¹⁹⁵Pt satellites of 16.6 Hz (Supporting Information). Substitution of the aqua ligand in **2** by ND₃ has a relatively minor effect on the overall appearance except in decreasing 3J coupling to 58 Hz (also Supporting Information).

Mixed Hg,Pt Compound 3. Addition of Hg(CH₃COO)₂ to an aqueous solution of **1** gave a colorless precipitate of composition Hg[Pt(1-MeU-N3)₄]·7H₂O (**3**). The ¹H NMR spectrum of **3** (in D₂O, pD 6.4) displays multiple doublets of H5 and H6 resonances of the 1-MeU-N3 ligands centered at around 5.6 and 7.4 ppm (Supporting Information). As these resonances neither coincide with those of **1** nor with free 1-MeUH, they are assigned to 1-MeU ligands, which adopt multiple mutual orientations, as is similarly seen in ¹H NMR spectra of partially protonated species of **1** (above). No detailed proposal concerning the involvement of the various

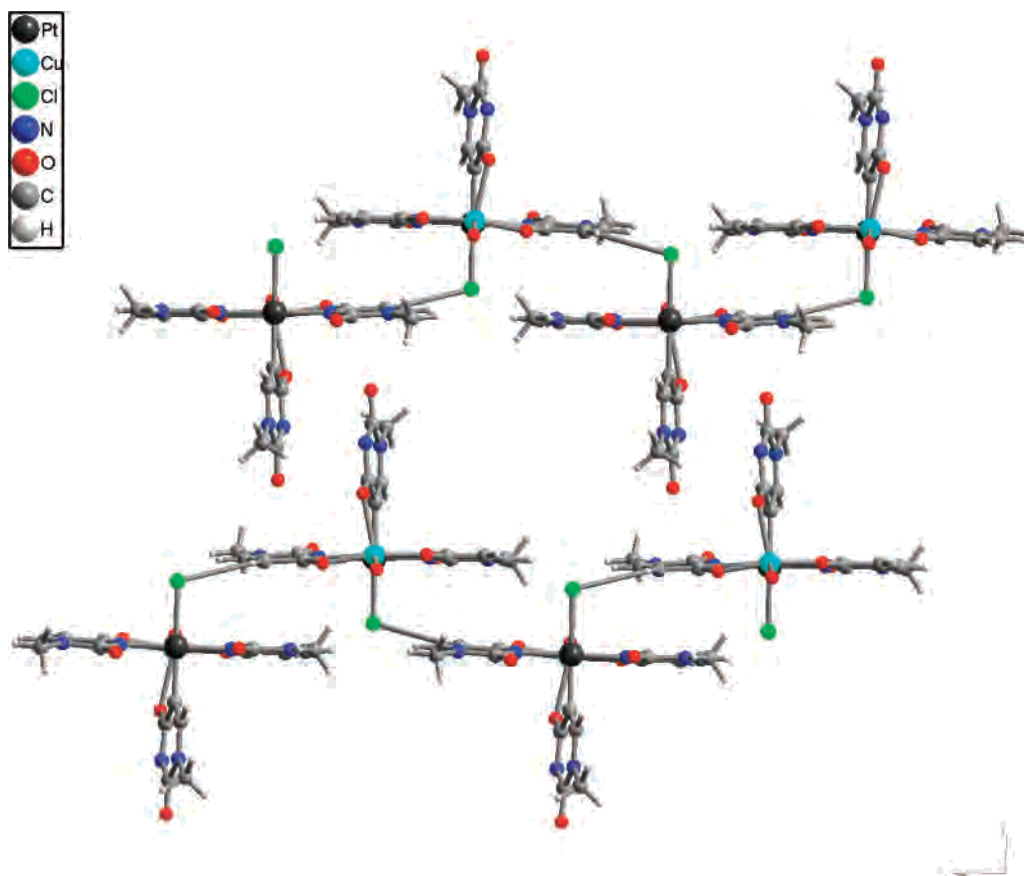


Figure 10. Packing of molecules of **4** with view along the *a* axis. All three 1-MeU ligands are involved in stacking interactions.

exocyclic oxygen atoms of the 1-MeU ligands in mercury binding can be made.

X-ray Crystal Structure of PtCu Complex 4. Although we were unable to obtain crystals suitable for the X-ray crystallography of **2**, we finally succeeded in crystallizing a Cu^{II} derivative of **2**, *trans*-[PtCl(1-MeU-*N3*)₂(1-MeU-*C5*)-Cu(H₂O)]·H₂O (**4**), that unambiguously confirms the presence of *N3*- and *C5*-bonded 1-MeU ligands. Figure 9 gives a view of the molecule. It consists of a *trans*-[Pt(1-MeU-*N3*)₂(1-MeU-*C5*)Cl]²⁻ entity to which a [Cu(H₂O)]²⁺ unit has been attached via three exocyclic O4 oxygen atoms. The platinum coordination sphere is normal as far as bond lengths and angles are concerned (Table 2). It is to be considered square-planar or, more appropriately, square-pyramidal with Cu1 in an apical position. The shortness of the Pt1–Cu1 separation of 2.4581(11) Å is clearly consistent with such a notion and qualifies it as a Pt → Cu dative bond between the filled 5 *d*_{z² orbital of Pt^{II} and the half-filled 3 *d*_{x²-y² orbital of Cu^{II}.^{34,35} The Pt–Cu bond is clearly shorter than that in 1-methylcytosinato-bridged PtCu complexes from *trans*-[Pt(a)₂(1-MeC-*N3*)₂]²⁺³⁵ or [Pt(1-MeC-*N3*)₄]²⁺⁵ (a = NH₃ or amine, 1-MeC = 1-methylcytosine) with distances ranging from 2.50 to 2.56 Å and is much shorter than that in heteronuclear Pt,Cu complexes derived from *cis*-Pt(a)₂L₂ (L = uracil, cytosine, or a related heterocyclic ligand). In the}}

latter compounds, intermetallic distances are in the range 2.63–2.98 Å.³⁶

All three nucleobases are almost perpendicular to the PtCN₂Cl coordination plane. There are no unusual distances or angles in the uracil rings. The internal ring angle at the *N3* position of the *C5*-bonded uracil amounts to 129.5(9)°, which is consistent with this site being protonated.³⁷ If deprotonated, this angle would be expected to be significantly smaller and on the order of 120°.³⁸

The coordination number of copper in **4** is five. In addition to Pt1, three carbonyl oxygen atoms (O4, O4A, O4B) and a water molecule (O1w) complete the coordination sphere. The two Cu–O bonds to the 1-MeU-*N3* ligands are short (1.90(1) Å *av*), the Cu1–O1w is intermediate (1.97(1) Å), and the Cu1–O4B bond to the 1-MeU-*C5* ligand is long (2.27(1) Å). These features, together with the angles about the copper ion, provide the impression of an essentially square-pyramidal geometry of the donor atoms about the metal, with O4B being the apical ligand. This view is further supported by more-refined analyses according to Holmes³⁹ and Reedijk,⁴⁰ which characterize the coordination geometry of copper

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as 76% square-pyramidal, 24% trigonal-bipyramidal, 87% square-pyramidal, and 13% trigonal-bipyramidal, respectively (Supporting Information).

As shown in Figure 10, molecules of **4** are oriented such that all three nucleobases become engaged in stacking interactions with the bases of neighboring molecules, the C5-bonded ligand with a C5-bonded one, and the N3 bonded ligands with N3 bonded ones. As a result, rectangular channels are formed along the *a* axis with Pt···Pt distances of 13.83 (2) Å across the diagonal and an effective area of ca. 8.0 × 5.7 Å², with the thickness of the π -aromatic system taken into account.

Heteronuclear Derivatives of K₂[Pd(1-MeU-N3)₄] (5). Compound **5** has been obtained as yellowish needles upon the reaction of K₂PdCl₄ with four equiv of KOH and an excess of 1-MeUH (5 equiv) at room temperature.⁴¹ More recently, the X-ray crystal structure of this compound, prepared in a slightly different manner, has been reported.⁸ If acidic reaction conditions are avoided, which lead to the cleavage of the Pd–N(3) bonds, heteronuclear analogues of **5**, with the alkali cation substituted by transition-metal ions, can be obtained by adding the respective metal salt (AgNO₃, ZnSO₄, CoSO₄, Cu(NO₃)₂) to a solution of **5**. Thus, the following compounds have been prepared in yields of 20–30% and were characterized by elemental analysis: Ag₂[Pd(1-MeU)₄]·9H₂O (**6**) (pale-yellow cubes), Zn[Pd(1-MeU)₄]·7.5H₂O (**7**) (colorless powder), and Co[Pd(1-MeU)₄]·2H₂O (**8**) (purple microcrystals). Cu[Pd(1-MeU)₄]aq was obtained as a green microcrystalline material, contaminated with small amounts of Cu(NO₃)₂.

Summary

The here-described tetrakis- and tris-nucleobase complexes display several interesting features. First, K₂[Pt(1-MeU–N3)₄]·10H₂O (**1**) has a remarkable affinity for protons, which is proposed to be primarily a consequence of the favorable stabilization of the protonated species by the spatial arrangement of the sets of four exocyclic oxygen atoms of the 1-MeU

ligands at either side of the platinum coordination plane. Second, *trans*-K[Pt(1-MeU–N3)₂(1-MeU–C5)(H₂O)] (**2**) is a unique example of a tris-nucleobase complex of 1-methyluracil that contains two different linkage isomers, bonded to platinum via N3 and C5, respectively. The carbon-bonded nucleobase can be considered a rare metal-stabilized tautomer of the 1-methyluracil anion, being deprotonated at C5 and still protonated at N3. The acidity of the proton at N3 (*pK*_a = 12.2) in the 1-MeU–C5 ligand is the lowest one in a series of 5-substituted 1-methyluracil ligands with X = NO₂, Br, H, CH₃. With regard to the possible consequences of a C5-platinated uracil nucleobase in RNA for base pairing, the markedly reduced acidity of the N3 proton is expected to weaken any interaction with the complementary adenine. Finally, **2** adds to the list of organometallic compounds with biomolecules and represents a truly bioorganometallic species.^{42,43} Mechanistic aspects of its formation are as of yet unclear. Compared to known examples of C–H activation by Pt^{II} complexes,⁴⁴ the mild conditions leading to the carbon-bonded **2** are noteworthy, however.

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Supporting Information Available: Figures of the arrangements of water molecules and layers between anions of **1**, H(6) resonance of 1-MeU ligands of **1** following acidification, 1H NMR spectra of **2** and **3** under various conditions, and CIF files. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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