found that the acid strength of HF–$SbF_5$ solutions toward oxygen bases increases markedly with the increase in $SbF_5$ concentrations up to the 1:1 mixture.[9b,10b]

## Experimental Section

**General Methods.** Sample preparation was done under dry nitrogen, in a drybox. A.R. grade chemicals were used as purchased. GLC analyses were performed on a 1.8 m × 3 mm o.d. column, with 10% methyl silicone SP2100 on Supelcoport. Carbon-13 NMR spectra were run at 22.65 MHz on a JEOL FX-90Q instrument. All glassware was dried in the oven at 120 °C and transferred while hot to the antechamber of the drybox, which was quickly evacuated.

**Distribution Experiments.** The hydrocarbons were dried on 4A molecular sieves in the drybox. A mixture of 9:1 (v:v) pentane and heptane (integration standard) was used as inert solvent. Benzene, toluene, and mixtures of the two were dissolved in the pentane–heptane mixture in concentrations of 0.4–0.6 M. TFMSA (1 mL) was introduced into a round-bottomed flask, which was then fitted with a stopcock, covered with a rubber septum, and cooled in a −90 °C bath. A volume of the hydrocarbon solution measured to give a TFMSA to aromatics ratio of 10–25 was added from a syringe through the rubber septum, after which the stopcock was closed, and the mixture was stirred at −20 °C for equilibration (30 min). Samples were taken with a syringe through the septum and added to pentane (1.0 mL) in a vial over a pellet of NaOH. The change in the heptane-to-aromatic ratio was determined by GLC at 45 °C. In a blank experiment the pentane–heptane solution was stirred with acid as described above, and then the acid layer was quenched in water and extracted with pentane. No heptane was found in the extract.

**NMR Measurements.** The samples were prepared as described previously.[14] The order of addition of reagents was aromatic, acid, and solvent (if any) mixed in the drybox at liquid nitrogen temperature, except for $SO_2$, which was passed through a tube of $P_2O_5$, liquified, measured, and added on the vacuum line. All tubes were sealed on the vacuum line and stored in dry ice until the spectra were recorded.

# Metal-Stabilized Rare Tautomers of Nucleobases. 2.[1] 2-Oxo-4-hydroxo Form of Uracil: Crystal Structures and Solution Behavior of Two Platinum(II) Complexes Containing Iminol Tautomers of 1-Methyluracil†

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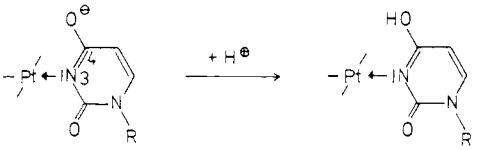
**Abstract:** A model for a metal-assisted tautomerization of the pyrimidine model nucleobase 1-methyluracil is presented which, by analogy, could account for mutagenic AT → GC or GC → AT transition in DNA. It involves initial metal binding to the N3 site of a thymine anion, followed by protonation of the exocyclic O4′ oxygen, and liberation of the rare 2-oxo-4-hydroxo tautomer which could then mispair with guanine. Three Pt(II) complexes, *cis*-$[(NH_3)_2Pt(1\text{-MeU})(1\text{-MeUH})]NO_3\cdot 2H_2O$ (**1**), *cis*-$[(NH_3)_2Pt(1\text{-MeUH})_2](NO_3)_2\cdot 3H_2O$ (**2**), and *cis*-$[(NH_3)_2Pt(1\text{-MeUH})_2][PtCl_6]\cdot 2H_2O$ (**3**) containing neutral 1-MeUH ligands in the 2-oxo-4-hydroxo tautomeric forms, have been prepared, and the crystal structures of **1** and **3** have been determined. Raman and $^1H$ NMR spectroscopies have been used to establish relevant acid–base equilibria and the protonation states of the uracil ligands in **1** and **3**. Both complexes crystallize in space group $P2_1/n$ with cell parameters $a$ = 16.181 (3) Å (**1**) and 16.019 (7) Å (**3**), $b$ = 8.340 (1) Å (**1**) and 12.415 (6) Å (**3**), $c$ = 13.744 (2) Å (**1**) and 12.513 (6) Å (**3**), $\beta$ = 97.61 (3)° (**1**) and 103.10 (6)° (**3**), $V$ = 1838.4 Å$^3$ (**1**) and 2423.7 Å$^3$ (**3**), and $Z$ = 4 (**1** and **3**). In **1**, the two 1-methyluracil ligands are oriented head-to-head, with the O4′ position of one ligand protonated and hydrogen bonded (2.52 Å) to O4′ of the anionic 1-MeU ligand. In **3**, the two rings are arranged head-to-tail. C4–O4′ distances in the 2-oxo-4-hydroxo tautomers [1.287 (7) Å, ring b of **1**; 1.302 (17) Å and 1.313 (19) Å in **3**] are only moderately longer than those in the free 2,4-dioxo tautomer yet clearly longer than the C2–O2′ bond lengths in **1** and **3**. On the basis of the X-ray results, a geometry of the hypothetical *free* 2-oxo-4-hydroxo tautomer of 1-MeUH is estimated. With respect to the normal 2,4-dioxo tautomer, the rare tautomer is expected to display major differences in internal ring angles C2 (larger by 3–4°), N3 (smaller by 8–9°), and C4 (larger by 7–8°).

The rare tautomeric forms of the naturally occurring nucleobases are of substantial interest with respect to the mechanism of spontaneous mutations, with respect to the fidelity of base pairing in nucleic acids and base mispairing, respectively,[3] and also for theoretical aspects concerning relative stabilities of tautomers.[4] While there is no doubt that under physiological conditions the normal tautomers (keto forms of pyrimidine bases, amino forms of purines) predominate to >99.99%, it is well-known that electronic excitation,[5] solvent properties,[6] and chemical modification of the nucleobase may change the tautomer equilibrium. For example, 1-methyluracil (1-MeUH), as demonstrated by spectroscopy, structural studies, and quantum-mechanical calculation,[7-9] exists almost exclusively in its diketo form I (Figure 1), exceeding the keto, iminol tautomer II by a factor of $4 \times 10^3$ to $4 \times 10^4$,[10,11] but the 5-bromo derivative contains form II in a 10-fold higher amount.[10]

**Scheme I**




As has previously been shown by us using spectroscopic methods, it is possible to stabilize a rare tautomer form of 1-

† Dedicated to Prof. Friedo Huber.

(1) For part 1, see Lippert, B.; Schöllhorn, H.; Thewalt, U. *J. Am. Chem. Soc.* **1986**, *108*, 6616.

(2) (a) Universität Ulm. (b) Universität Dortmund.

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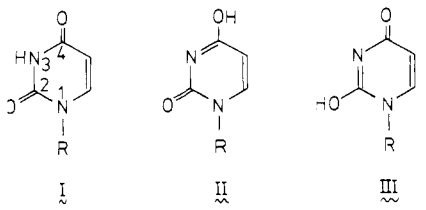

**Figure 1.** 1-Methyluracil, 1-MeUH, in its normal dioxo tautomeric form I and its two rare tautomeric forms II and III.

methylthymine[12] or uracil[13] through metal complexation. Likewise, the complexation of 2-hydroxopyridine, the minor tautomer of 2-pyridone, has been reported,[14] and there are examples that metal coordination to a neutral purine alters the site of protonation of this nucleobase.[15] The occurrence of such unusual tautomers is restricted to the respective metal-coordinated forms since, on displacement of the metal, the usual tautomer is instantaneously re-formed. However, valuable information concerning the geometry of the free tautomer can be obtained from a crystal structure of its complexed form, provided the effects of the metal on the ligand geometry are understood. A detailed knowledge of the geometry of a tautomer is, among others, of importance for quantum-mechanical calculations on the relative stability of one tautomer versus that of another.[16]

This work was performed since it provided the opportunity to estimate the geometry of the rare 2-oxo-4-hydroxo tautomer of 1-methyluracil by studying the crystal structures of two protonation products of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ (with 1-MeU = anion of 1-methyluracil, $C_5H_5N_2O_2$). In these compounds, Pt coordinates via the N3 atom of the deprotonated nucleobase, and protonation takes place at the exocyclic O4 oxygen, thus producing the platinated form of tautomer II. Protonation at O4 is a consequence of the increased basicity of this site in the metal complex as compared to neutral 1-MeUH (Scheme I) which is, for example, also reflected in the high tendency of N3-metallated uracil or thymine ligands to bind additional metals through the exocyclic oxygens.[17-19]

**Table I.** Crystallographic Data for *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(1\text{-}MeUH)]NO_3\cdot 2H_2O$ (**1**) and *cis*-$[(NH_3)_2Pt(1\text{-}MeUH)_2][PtCl_6]\cdot 2H_2O$ (**3**)

| | **1**[a] | **3**[b] |
|---|---|---|
| $f_w$ | 578.41 | 925.22 |
| space group | $P2_1/n$ | $P2_1/n$ |
| $a$, Å | 16.181 (3) | 16.019 (7) |
| $b$, Å | 8.340 (1) | 12.415 (6) |
| $c$, Å | 13.744 (2) | 12.513 (6) |
| $\beta$, deg | 97.61 (3) | 103.10 (6) |
| $V$, Å$^3$ | 1838.4 | 2423.7 |
| $Z$ | 4 | 4 |
| $d_{calc}$, g cm$^{-3}$ | 2.090 | 2.536 |
| $d_{meas}$, g cm$^{-3}$ | 2.07 | 2.54 |
| cryst size, mm | 0.3, 0.3, 0.5 | 0.2, 0.2, 0.2 |
| $\mu$, cm$^{-1}$ | 74.1 | 117.4 |
| $\theta_{range}$, deg | 2–28 | 2–26 |
| no. of unique refln | 4416 | 4755 |
| no. of refln used in the calcn | $4204F_0 > 2\sigma F_0$ | $4000F_0 > 2\sigma F_0$ |
| $R$ | 0.040 | 0.050 |
| $R_w(F)$ | 0.046 | 0.050 |

[a] **1**: $w^{-1} = \sigma^2(F) + 0.005F^2$. [b] **3**: $w^{-1} = \sigma^2(F) + 0.006F^2$.

The complexes reported here, with neutral 1-methyluracil ligands in their rare tautomer form II, are different from other metal complexes of neutral uracil and thymine which contain the metal coordinated to an exocyclic oxygen of the normal diketo tautomer I.[20]

## Experimental Section

**Preparation.** *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2\cdot 4H_2O$ (1-MeU = 1-methyluracil anion, $C_5H_5N_2O_2$) was prepared as previously described.[17a] *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(1\text{-}MeUH)]NO_3\cdot 2H_2O$ (**1**) was obtained as follows: A 1-mmol amount of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2\cdot 4H_2O$ was dissolved in 2 mL of 1 N $HNO_3$; the solution (pH 1) was centrifuged and allowed to evaporate slowly at 3 °C. After 5 days 340 mg of colorless, transparent cubes of **1** was collected, briefly dried on a filter paper, and then stored in the refrigerator to prevent loss of water of crystallization. Addition of crystal seeds of **1** to a concentrated, cooled solution in many cases increased the quality of the crystals greatly. On further evaporation of the remaining solution, long, colorless needles of a second species, *cis*-$[(NH_3)_2Pt(1\text{-}MeUH)_2](NO_3)_2\cdot 3H_2O$ (**2**), formed in varying yield (60–120 mg), which were collected and briefly dried in air. After 7–8 days at 3 °C, the solution usually was green or blue-green, and after the solution had solidified, tiny dichroic (blue and brown) crystals were detected in the solid together with larger colorless crystals, which were identified by IR as 1-MeUH, and more crystals of **2**. Redissolving the solid residue in water and slow evaporation at 3 °C or at room temperature led to a strong intensification of the blue color. Anal. Calcd for $[(NH_3)_2Pt(C_5H_5N_2O_2)(C_5H_6N_2O_2)]NO_3\cdot 2H_2O$ (**1**): C, 20.76; H, 3.67; N, 16.95. Found: C, 20.77; H, 3.61; N, 17.39. Anal. Calcd for $[(NH_3)_2Pt(C_5H_6N_2O_2)_2](NO_3)_2\cdot 3H_2O$ (**2**): C, 18.21; H, 3.68; N, 16.99; Pt, 29.58. Found: C, 18.10; H, 3.80; N, 17.46; Pt, 29.3.

*cis*-$[(NH_3)_2Pt(C_5H_6N_2O_2)_2][PtCl_6]\cdot 2H_2O$ (**3**) was prepared in two ways: (i) A 0.5-mmol amount of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2\cdot 4H_2O$ was dissolved in 10 mL of water on slight warming and cooled to 22 °C, and then 0.5 mmol of $Na_2PtCl_6\cdot 6H_2O$ was added. The yellow solution (pH 6) was brought to pH 1 by means of 1 N $HNO_3$ and the solution filtered and concentrated on a rotavapor (22 °C) to 7–8-mL volume, when precipitation started. The sample was kept at room temperature for another 15 h before being filtered from the precipitate and then washed with two 5-mL portions of ice-cold water, yield 360 mg (78%) of orange-yellow microcubes. (ii) Crystals suitable for X-ray structure analysis were obtained in 85% yield by treating a solution of *cis*-$(NH_3)_2Pt(1\text{-}$

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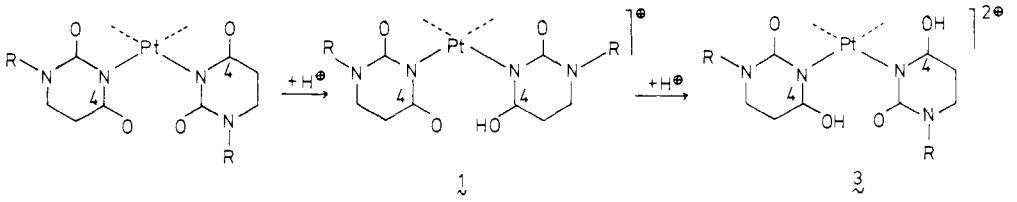
**Scheme II**



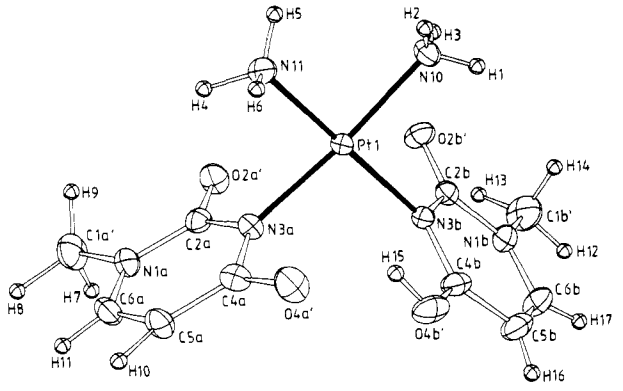


**Figure 2.** Molecular cation of *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(1\text{-}MeUH)]NO_3 \cdot 2H_2O$ (**1**) with ring b in the 2-oxo-4-hydroxo form.

MeU)$_2 \cdot 4H_2O$ with 1.3 equiv of $H_2PtCl_6$(aq) and allowing the filtered solution (pH 1.3) to slowly evaporate in air [22 °C, same concentrations as in (i)]. As early as 15 min after start, bright orange-yellow cubes appeared in the solution. The precipitate was collected on a filter after 12 h. Anal. Calcd for $[(NH_3)_2Pt(C_5H_6N_2O_2)_2][PtCl_6] \cdot 2H_2O$ (**3**): C, 12.98; H, 2.40; N, 9.09; Cl, 22.99; Pt, 42.17. Found: C, 12.98; H, 2.45; N, 8.91; Cl, 23.28; Pt, 41.9.

**Spectra.** $^1H$ NMR spectra (recorded on a JEOL JNM-FX 60 Fourier-transform spectrometer), Raman spectra (recorded on a Coderg PH 1), and IR spectra (recorded on a Perkin-Elmer 580 grating spectrometer as Nujol mulls) were obtained as described elsewhere.[12] Reported pD values were obtained by adding 0.4 to the pH meter reading. $pK_a$ values are given for uncorrected pH* because of the relationship $pK_{H_2O} = (pK_{D_2O} - 0.45)/1.015$.[21] pD values were adjusted by means of 2 N solutions of NaOD and $DNO_3$, respectively.

**Crystallography.** Crystal data were taken at room temperature (**3**) and −100 °C (**1**) on a PHILIPS-PW 1100 single-crystal diffractometer using monochromated Mo K$\alpha$ radiation ($\lambda$ = 0.71069 Å). Crystal data and other numbers related to data collection are summarized in Table I. Unit-cell parameters were obtained for the monoclinic crystals from 16 (**1**) and 19 (**3**) reflections in the range $24° < 2\theta < 32°$ and $23° < 2\theta < 37°$, respectively. The space groups $P2_1/n$ were confirmed by the successful solution and refinement in this space group. Intensity data were collected with a $\theta/2\theta$ technique [$\theta_{max}$ = 28° (**1**) and 26° (**3**)]. The reflection intensities were corrected for absorption by an empirical method using the program of Walker and Stuart[22] and for Lorentz and polarization effects.

The coordinates of the platinum atoms were found in three-dimensional Patterson syntheses. The other non-hydrogen atoms were located by subsequent $\Delta F$ syntheses. Hydrogen atoms were located for **1** only. All atoms were refined with anisotropic temperature factors. Scattering factors for neutral atoms were taken from Cromer and Mann.[23] Anomalous dispersion corrections were applied.[24] The highest peak in the final difference Fourier map was 1.2 e/Å$^3$ for **1** and 1.6 e/Å$^3$ for **3** (1.4 Å away from Pt2 and therefore of no chemical significance). The atomic parameters and equivalent isotropic temperature factors are listed in Tables II and III. The equivalent isotropic temperature factors were calculated from the $U_{ij}$ values by $U_{eq} = {}^1/_3 \sum U_{ij} a^*_i a^*_j \mathbf{a}_i \mathbf{a}_j$ ($U_{ij}$ in Å). The SHELX program package was used in these structure analyses.[25]

## Results and Discussion

**Description of the Crystal Structures.** The molecular cation of **1**, *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(1\text{-}MeUH)]^+$, is shown in Figure 2,

**Table II.** Positional Parameters and Temperature Factors (Å$^2$) for **1**

| atom | *X* | *Y* | *Z* | $U_{11}$ |
|---|---|---|---|---|
| Pt1 | 0.3780 (1) | 0.4935 (1) | 0.3738 (1) | 0.025 (1) |
| N10 | 0.4830 (2) | 0.3547 (4) | 0.3803 (3) | 0.034 (3) |
| N11 | 0.3260 (2) | 0.3311 (5) | 0.4588 (3) | 0.036 (3) |
| N1a | 0.2008 (2) | 0.7961 (5) | 0.4778 (3) | 0.037 (3) |
| C1a′ | 0.2010 (4) | 0.8987 (8) | 0.5643 (5) | 0.059 (6) |
| C2a | 0.2758 (3) | 0.7327 (5) | 0.4599 (3) | 0.033 (4) |
| O2a′ | 0.3411 (2) | 0.7646 (4) | 0.5120 (2) | 0.044 (3) |
| N3a | 0.2747 (2) | 0.6298 (4) | 0.3810 (3) | 0.031 (3) |
| C4a | 0.2038 (3) | 0.5989 (6) | 0.3194 (4) | 0.038 (4) |
| O4a′ | 0.2096 (2) | 0.5093 (4) | 0.2453 (3) | 0.053 (4) |
| C5a | 0.1274 (3) | 0.6688 (6) | 0.3386 (4) | 0.043 (5) |
| C6a | 0.1296 (2) | 0.7636 (6) | 0.4190 (4) | 0.041 (4) |
| N1b | 0.5384 (2) | 0.8226 (5) | 0.2568 (3) | 0.040 (4) |
| C1b′ | 0.6146 (4) | 0.9090 (8) | 0.3012 (5) | 0.064 (7) |
| C2b | 0.5011 (2) | 0.7259 (5) | 0.3205 (3) | 0.033 (4) |
| O2b′ | 0.5306 (2) | 0.7067 (4) | 0.4051 (2) | 0.041 (3) |
| N3b | 0.4272 (2) | 0.6489 (4) | 0.2823 (2) | 0.028 (3) |
| C4b | 0.3951 (3) | 0.6695 (6) | 0.1872 (3) | 0.039 (4) |
| O4b′ | 0.3257 (2) | 0.6020 (4) | 0.1534 (2) | 0.049 (3) |
| C5b | 0.4370 (3) | 0.7639 (7) | 0.1245 (3) | 0.048 (5) |
| C6b | 0.5062 (4) | 0.8385 (7) | 0.1614 (4) | 0.052 (6) |
| N20 | 0.6109 (3) | 0.3196 (7) | 0.1875 (4) | 0.061 (6) |
| O20 | 0.5708 (5) | 0.4292 (9) | 0.2097 (6) | 0.147 (11) |
| O21 | 0.6839 (3) | 0.3012 (6) | 0.2182 (4) | 0.085 (6) |
| O22 | 0.5784 (4) | 0.2207 (10) | 0.1263 (5) | 0.121 (9) |
| O30 | 0.0764 (3) | 0.5220 (4) | 0.0935 (5) | 0.064 (5) |
| O31 | 0.7550 (5) | 0.5242 (6) | 0.3864 (5) | 0.093 (8) |
| H1 | 0.5171 (0) | 0.3748 (0) | 0.3386 (0) | |
| H2 | 0.4669 (0) | 0.2571 (0) | 0.3768 (0) | |
| H3 | 0.5328 (0) | 0.4122 (0) | 0.4224 (0) | |
| H4 | 0.2889 (0) | 0.4001 (0) | 0.5009 (0) | |
| H5 | 0.3647 (0) | 0.2598 (0) | 0.4939 (0) | |
| H6 | 0.2819 (0) | 0.2736 (0) | 0.4191 (0) | |
| H7 | 0.2199 (0) | 1.0230 (0) | 0.5449 (0) | |
| H8 | 0.1258 (0) | 0.9179 (0) | 0.5595 (0) | |
| H9 | 0.2370 (0) | 0.8347 (0) | 0.6185 (0) | |
| H10 | 0.0578 (0) | 0.6560 (0) | 0.3169 (0) | |
| H11 | 0.0819 (0) | 0.8235 (0) | 0.4286 (0) | |
| H12 | 0.6275 (0) | 0.9594 (0) | 0.2409 (0) | |
| H13 | 0.6186 (0) | 0.9672 (0) | 0.3751 (0) | |
| H14 | 0.6465 (0) | 0.8019 (0) | 0.3022 (0) | |
| H15 | 0.3023 (0) | 0.5175 (0) | 0.1922 (0) | |
| H16 | 0.4026 (0) | 0.7624 (0) | 0.0603 (0) | |
| H17 | 0.5400 (0) | 0.8903 (0) | 0.1238 (0) | |

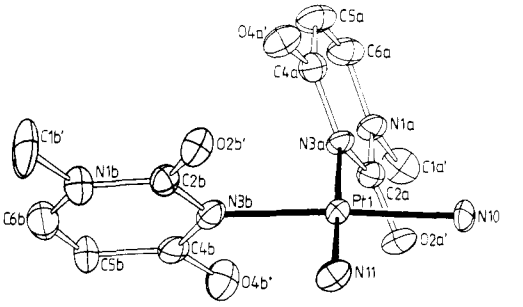


**Figure 3.** Molecular cation of *cis*-$[(NH_3)_2Pt(1\text{-}MeUH)_2][PtCl_6] \cdot 2H_2O$ (**3**).

and the cation of **3**, *cis*-$[(NH_3)_2Pt(1\text{-}MeUH)_2]^{2+}$, is depicted in Figure 3. Interatomic distances and angles are listed in Tables IV and V, respectively, and conformational parameters for both compounds are given in Table VI. The coordination geometries about the Pt centers in **1** and **3** are approximately square-planar,

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**Table III.** Positional and Thermal Parameters (Å) of **3**

| atom | X | Y | Z | U |
|---|---|---|---|---|
| Pt1 | −0.0607 (1) | 0.0125 (1) | 0.1565 (1) | 0.031 (1) |
| N10 | 0.0562 (7) | −0.0353 (9) | 0.1391 (10) | 0.037 (4) |
| N11 | −0.1080 (8) | −0.1387 (10) | 0.1234 (10) | 0.041 (4) |
| N1a | −0.3022 (8) | 0.0491 (13) | 0.2387 (13) | 0.056 (5) |
| C1a′ | −0.3482 (13) | −0.0024 (22) | 0.3115 (20) | 0.089 (10) |
| C2a | −0.2200 (9) | 0.0151 (13) | 0.2349 (13) | 0.043 (5) |
| O2a′ | −0.1880 (8) | −0.0574 (10) | 0.2977 (10) | 0.056 (4) |
| N3a | −0.1801 (7) | 0.0654 (10) | 0.1649 (10) | 0.038 (4) |
| C4a | −0.2178 (11) | 0.1420 (13) | 0.0934 (14) | 0.052 (6) |
| O4a′ | −0.1779 (9) | 0.1799 (11) | 0.0255 (12) | 0.036 (4) |
| C5a | −0.3034 (11) | 0.1789 (16) | 0.0964 (16) | 0.059 (7) |
| C6a | −0.3398 (11) | 0.1276 (16) | 0.1712 (16) | 0.058 (6) |
| N1b | 0.0506 (8) | 0.3233 (9) | 0.1605 (10) | 0.040 (4) |
| C1b′ | 0.0794 (11) | 0.3910 (13) | 0.0771 (16) | 0.055 (6) |
| C2b | 0.0192 (9) | 0.2237 (11) | 0.1278 (13) | 0.038 (4) |
| O2b′ | 0.0196 (7) | 0.1886 (8) | 0.0375 (8) | 0.046 (3) |
| N3b | −0.0121 (7) | 0.1588 (9) | 0.2022 (9) | 0.033 (3) |
| C4b | −0.0095 (9) | 0.1960 (12) | 0.3007 (12) | 0.039 (4) |
| O4b′ | −0.0413 (8) | 0.1330 (10) | 0.3655 (9) | 0.058 (4) |
| C5b | 0.0265 (13) | 0.3002 (14) | 0.3361 (15) | 0.060 (7) |
| C6b | 0.0553 (13) | 0.3600 (14) | 0.2643 (14) | 0.058 (6) |
| Pt2 | 0.3635 (1) | 0.2060 (1) | 0.1173 (1) | 0.036 (1) |
| Cl1 | 0.4736 (2) | 0.3239 (3) | 0.1095 (3) | 0.044 (1) |
| Cl2 | 0.4366 (2) | 0.1620 (3) | 0.2936 (3) | 0.050 (1) |
| Cl3 | 0.4339 (3) | 0.0718 (3) | 0.0479 (3) | 0.063 (1) |
| Cl4 | 0.2952 (3) | 0.2532 (5) | −0.0592 (3) | 0.073 (1) |
| Cl5 | 0.2560 (3) | 0.0859 (4) | 0.1297 (4) | 0.069 (1) |
| Cl6 | 0.2918 (3) | 0.3406 (4) | 0.1872 (5) | 0.070 (1) |
| O20 | 0.1442 (11) | 0.0552 (10) | 0.4735 (12) | 0.078 (6) |
| O21 | 0.2542 (16) | 0.1703 (21) | 0.4026 (18) | 0.168 (13) |

**Table IV.** Interatomic Distances (Å) and Angles (deg) of Cation **1**

(A) Pt Coordination Sphere

| | | | |
|---|---|---|---|
| Pt1–N10 | 2.047 (4) | N11–Pt1–N3b | 176.9 (2) |
| Pt1–N11 | 2.042 (5) | N3a–Pt1–N3b | 93.7 (2) |
| Pt1–N3a | 2.035 (4) | N10–Pt1–N11 | 90.1 (2) |
| Pt1–N3b | 2.039 (4) | N10–Pt1–N3a | 174.8 (2) |
| | | N10–Pt1–N3b | 89.9 (2) |
| | | N11–Pt1–N3a | 86.5 (2) |

(B) Uracil Rings

| | ring a | ring b |
|---|---|---|
| N1–C1′ | 1.464 (8) | 1.487 (8) |
| N1–C2 | 1.376 (7) | 1.386 (7) |
| C2–O2′ | 1.224 (6) | 1.208 (6) |
| C2–N3 | 1.381 (6) | 1.397 (6) |
| N3–C4 | 1.356 (6) | 1.352 (6) |
| C4–O4′ | 1.277 (7) | 1.287 (7) |
| C4–C5 | 1.424 (7) | 1.406 (8) |
| C5–C6 | 1.355 (8) | 1.323 (9) |
| C6–N1 | 1.344 (6) | 1.351 (7) |
| C1′–N1–C6 | 121.1 (5) | 122.8 (5) |
| C1′–N1–C2 | 117.5 (4) | 115.5 (5) |
| C6–N1–C2 | 121.4 (4) | 121.7 (5) |
| O2′–C2–N1 | 121.7 (4) | 122.4 (4) |
| O2′–C2–N3 | 121.0 (5) | 120.7 (5) |
| N1–C2–N3 | 117.3 (4) | 117.0 (4) |
| Pt1–N3–C2 | 117.3 (3) | 116.4 (3) |
| Pt1–N3–C4 | 119.7 (3) | 123.1 (3) |
| C2–N3–C4 | 122.0 (4) | 120.3 (4) |
| O4′–C4–N3 | 117.6 (5) | 117.6 (5) |
| O4′–C4–C5 | 123.1 (5) | 119.4 (5) |
| N3–C4–C5 | 119.3 (5) | 120.6 (5) |
| C4–C5–C6 | 117.4 (4) | 118.7 (5) |
| C5–C6–N1 | 122.4 (5) | 121.6 (6) |

with two ammonia ligands and two N3 atoms of 1-methyluracil rings binding to Pt each. Pt–$NH_3$ distances are normal,[26] and Pt–N(uracil) distances are very similar to those in related compounds.[17,18] In particular, a lengthening of the Pt–N(uracil) bond

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**Table V.** Interatomic Distances (Å) and Angles (deg) of **3**

(A) Pt1 Coordination Sphere

| | | | |
|---|---|---|---|
| Pt1–N10 | 2.041 (10) | N10–Pt1–N11 | 90.7 (4) |
| Pt1–N11 | 2.034 (10) | N10–Pt1–N3a | 89.7 (4) |
| Pt1–N3a | 2.019 (9) | N10–Pt1–N3b | 176.3 (4) |
| Pt1–N3b | 2.042 (11) | N11–Pt1–N3a | 175.5 (4) |
| | | N11–Pt1–N3b | 89.4 (4) |
| | | N3a–Pt1–N3b | 90.4 (4) |

(B) Uracil Rings

| | ring a | ring b |
|---|---|---|
| N1–C1′ | 1.505 (19) | 1.500 (25) |
| N1–C2 | 1.375 (15) | 1.376 (18) |
| C2–O2′ | 1.207 (15) | 1.218 (15) |
| C2–N3 | 1.402 (16) | 1.364 (18) |
| N3–C4 | 1.317 (16) | 1.345 (16) |
| C4–O4′ | 1.302 (17) | 1.312 (19) |
| C4–C5 | 1.444 (19) | 1.431 (20) |
| C5–C6 | 1.316 (23) | 1.385 (24) |
| C6–N1 | 1.368 (18) | 1.344 (20) |
| C1′–N1–C2 | 115.8 (10) | 118.4 (12) |
| C1′–N1–C6 | 122.9 (10) | 120.7 (13) |
| C2–N1–C6 | 121.3 (11) | 120.9 (13) |
| O2′–C2–N1 | 121.6 (12) | 118.8 (13) |
| O2′–C2–N3 | 119.9 (10) | 123.5 (12) |
| N1–C2–N3 | 118.4 (10) | 117.6 (11) |
| Pt1–N3–C2 | 120.1 (7) | 118.2 (8) |
| Pt1–N3–C4 | 119.9 (8) | 120.4 (9) |
| C2–N3–C4 | 120.0 (10) | 121.4 (11) |
| O4′–C4–N3 | 116.2 (11) | 116.0 (12) |
| O4′–C4–C5 | 123.2 (12) | 121.0 (12) |
| N3–C4–C5 | 120.6 (12) | 123.0 (13) |
| C4–C5–C6 | 119.0 (13) | 121.6 (13) |
| C5–C6–N1 | 120.0 (13) | 124.5 (14) |

(C) Anion Geometry

| | | | |
|---|---|---|---|
| Pt2–Cl1 | 2.318 (3) | Cl1–Pt2–Cl2 | 88.0 (1) |
| Pt2–Cl2 | 2.312 (3) | Cl1–Pt2–Cl3 | 90.0 (1) |
| Pt2–Cl3 | 2.296 (4) | Cl1–Pt2–Cl4 | 89.5 (1) |
| Pt2–Cl4 | 2.316 (4) | Cl1–Pt2–Cl5 | 178.7 (1) |
| Pt2–Cl5 | 2.305 (4) | Cl1–Pt2–Cl6 | 90.2 (1) |
| Pt2–Cl6 | 2.312 (4) | Cl2–Pt2–Cl3 | 90.7 (1) |
| | | Cl2–Pt2–Cl4 | 177.5 (1) |
| | | Cl2–Pt2–Cl5 | 90.7 (1) |
| | | Cl2–Pt2–Cl6 | 89.7 (1) |
| | | Cl3–Pt2–Cl4 | 89.5 (1) |
| | | Cl3–Pt2–Cl5 | 89.9 (1) |
| | | Cl3–Pt2–Cl6 | 179.5 (1) |
| | | Cl4–Pt2–Cl5 | 91.8 (1) |
| | | Cl4–Pt2–Cl6 | 90.1 (2) |
| | | Cl5–Pt2–Cl6 | 89.8 (1) |

on protonation is not observed. Unlike in the parent compound *cis*-$(NH_3)_2Pt(1\text{-MeU})_2\cdot 4H_2O$,[17a] the two heterocyclic ligands are oriented head-to-head in **1**. In **3** the two heterocyclic rings again are arranged head-to-tail, with the two 4-hydroxo groups anti to each other (Scheme II). Thus, protonation parallels binding of metal ions to the *cis*-$(NH_3)_2Pt(1\text{-MeU})_2$ moiety: In all cases studied so far by X-ray crystallography, the first metal binds simultaneously to two O4′ sites of head-to-head oriented ligands.[17b–d,i–l,18b,e,f] Only with two identical metal ions binding at the same time, e.g., with *trans*-$[(NH_3)_2Pt(1\text{-MeU})_2Ag_2]^{2+}$, do the two rings adopt a head-to-tail orientation, leading to mixed O4′,O2′ binding of the heterometals.[17f]

Bond lengths in the anionic 1-MeU (ring a) and the neutral 1-MeUH (ring b) of compound **1** do not differ significantly, but two of the angles show differences: Pt1–N3–C4 is larger in ring b ($7.6\sigma$[27]) while O4–C4–C5 is larger in ring a ($5.3\sigma$). Since these differences refer to external ring angles, any direct consequence of different charges of the two rings appears unlikely. C4–O4′ bond lengths [1.277 (7) Å in ring a, 1.287 (7) Å in ring b] are clearly longer than those of C2–O2′ (by 0.053 Å, $5.9\sigma$, in ring a; by 0.079 Å, $8.8\sigma$, in ring b). C4–O4′ bonds are also longer

(27) The esd is calculated according to $\sigma = (\sigma_1^2 + \sigma_2^2)^{1/2}$ with $\sigma_1$ and $\sigma_2$ being the errors in bond lengths and angles which are compared.

**Table VI.** Conformational Parameters of *cis*-$[(NH_3)_2Pt(1\text{-MeU})(1\text{-MeUH})]NO_3\cdot 2H_2O$ (**1**) and *cis*-$[(NH_3)_2Pt(1\text{-MeUH})_2][PtCl_6]\cdot 2H_2O$ (**3**)[a]

(A) Dihedral Angles (deg)

| | **1** | **3** |
|---|---|---|
| Pt1 coordination plane/1-MeUa plane | 88.8 | 113.5 |
| Pt1 coordination plane/1-MeUb plane | 66.4 | 119.9 |
| 1-MeUa plane/1-MeUb plane | 69.6 | 97.7 |

(B) Deviations of Atoms from Planes (Å)

| | **1**[b] | **3**[c] |
|---|---|---|
| N10* | 0.069 | −0.073 |
| N11* | −0.067 | 0.072 |
| N3a* | −0.067 | 0.073 |
| N3b* | 0.065 | −0.073 |
| Pt1 | 0.005 | −0.007 |

| | **1** | | **3** | |
|---|---|---|---|---|
| | ring a[d] | ring b[e] | ring a[f] | ring b[g] |
| N1* | −0.002 | −0.024 | 0.008 | −0.012 |
| C2* | −0.017 | 0.015 | −0.003 | 0.011 |
| N3* | 0.026 | 0.012 | −0.006 | 0.000 |
| C4* | −0.015 | −0.030 | 0.010 | −0.009 |
| C5* | −0.005 | 0.020 | −0.004 | 0.007 |
| C6* | 0.013 | 0.006 | −0.004 | 0.005 |
| C1′ | 0.015 | −0.080 | 0.073 | −0.017 |
| O2′ | −0.085 | 0.030 | −0.071 | 0.002 |
| O4′ | −0.034 | −0.079 | 0.043 | −0.047 |
| Pt1 | 0.442 | 0.181 | −0.027 | −0.050 |

[a] Atoms with an asterisk define the plane. The equations refer to the basis $\langle a\ b\ c\rangle$. [b] $5.23024x + 4.10046y + 10.47950z = 6.078$ Å. [c] $-0.10695x - 3.05649y + 11.83071z = 1.827$ Å. [d] $4.01240x + 6.61096y - 8.04098z = 5.686$ Å. [e] $-9.15129x + 6.56827y + 4.31794z = 5.855$ Å. [f] $-13.72031x + 5.08779y - 1.394272z = 0.706$ Å. [g] $3.71475x + 8.51862y + 7.74521z = 1.143$ Å.

than in neutral, unplatinated 1-MeUH [1.241 (1) Å][28] but still shorter than those in hydroxopyridines [cf 1.330 (5)[29] and 1.347 (7) Å[30] in 2-hydroxopyridines; 1.340 (9) Å in a N-platinated 1-hydroxopyridine[14b]]. The rather moderate lengthening of C4b–O4b′ on proton binding and the similar C4a–O4a′ distance in the unprotonated ligand in **1** may be a consequence of the rather short hydrogen bond of the proton H15 at O4b′ to the O4a′ acceptor (O4a′–O4b′, 2.52 Å; H15–O4a′, 1.75 Å, C4a–O4a′–H15, 118°).

Bond lengths and bond angles in the two rings of compound **3** do not differ much either. Within each uracil ring, however, the C4–O4′ distances are longer than the corresponding C2–O2′ distances, $\sigma$ values being 4.2 and 3.8. Comparison of C4–O4′ distances in **3** and in *cis*-$(NH_3)_2Pt(1\text{-MeU})_2\cdot 4H_2O$ displays a trend toward longer bond lengths in **3** (0.069 Å, $3\sigma$). As to internal ring angles, N3–C4–C5 is larger in **3** (max 6.1°, $3.8\sigma$).

Apart from the strong intramolecular hydrogen bond between the protonated O4a′ position and O4b′, several additional weaker hydrogen bonds exist in **1**. The water molecule O31 is primarily connected with the nitrate anion, but the other water (O30) is associated with the cation. It accepts protons from both $NH_3$ groups (O30···N11, 3.13 Å; O30···N10, 2.99 Å) and donates protons to O4a′ (2.87 Å) and O2a′ (2.99 Å).

In **3**, both exocyclic O4 oxygens are involved in hydrogen bonding with water molecules: While O4b′ forms a very short hydrogen bond (2.49 Å) with the water molecule O21, O4a′ has a long one (3.14 Å) to the second water (O20). Both water molecules are connected by another short hydrogen bond of 2.61 Å. The hydrogen-bonding pattern in **3**, which also includes additional hydrogen bonds involving the O2′ oxygens and $NH_3$ ligands, is shown in Figure 4; a complete list of hydrogen-bonding interactions in both **1** and **3** is given in the supplementary material.

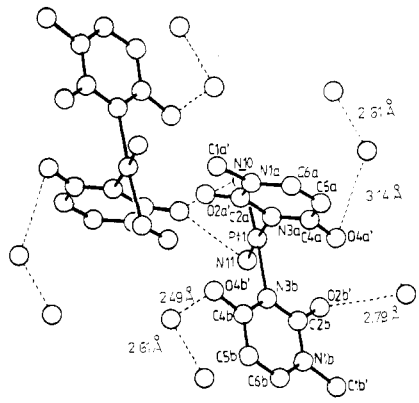


**Figure 4.** Hydrogen-bonding pattern in the crystal lattice of **3**. Only two of the four H-bonds (N10–O2a′, N11–O2a′) between the two centrosymmetrically related cations are indicated. Given distances refer to those between water molecules and O4a′, O4b′, and O2b′.

As a result of the hydrogen-bonding pattern in **3**, there is some ambiguity as to how compound **3** should be formulated best: Alternatively to the formulation of **3** as $[(NH_3)_2Pt(1\text{-MeUH})_2][PtCl_6]\cdot 2H_2O$ with two fully protonated 1-methyluracil ligands, one might, on the basis of the short distance between the two water molecules, think of describing **3** also as $[H_5O_2]^+$-$[(NH_3)_2Pt(1\text{-MeU})(1\text{-MeUH})]^+[PtCl_6]^{2-}$ with one ligand protonated and the second one acting as a hydrogen acceptor of the $H_5O_2^+$ unit. Moreover, there is the possibility of a considerable degree of proton mobility along O4a′, O20, O21, and O4b′ of the adjacent cation, leading to a situation intermediate between both extremes. In a similar situation, with a N1-platinated uracil,[31] we used this second formulation to describe the binding properties in the crystal. We are aware that the pH at which **3** was isolated (ca. 1) is not sufficient to have appreciable amounts of the doubly protonated complex *in solution* (vide infra). However, for the solid state we prefer formulation of **3** as *cis*-$[(NH_3)_2Pt(1\text{-MeUH})_2]PtCl_6\cdot 2H_2O$ essentially on the basis of the solid-state Raman spectrum of **3** (vide infra) which does not provide any evidence for two distinctly different uracil rings. Moreover, short contacts of 2.5–2.6 Å between water molecules do not automatically imply the presence of a $H_5O_2^+$ cation.[32] Finally one might argue that if a singly protonated $[(NH_3)_2Pt(1\text{-MeU})(1\text{-MeUH})]^+$ species were present in **3**, a closer similarity with **1** (e.g., head-to-head orientation of two rings) should be observed.

**Estimation of the Geometry of the Free 2-Oxo-4-hydroxo Tautomer of 1-Methyluracil.** The effect of fixation of a proton to an endocyclic N atom of a heterocycle is well understood:[33] It leads to an increase in the internal bond angle and a simultaneous decrease of the adjacent N–C–C angles so that planarity of the system is maintained. Bond lengths are little or not affected. The effect of a metal electrophile coordinating to an endocyclic N atom is generally smaller than that of a proton.[34] As to pyrimidine nucleobases, metal complexes of cytosine residues have been studied most extensively, whereas comparison of metal complexes containing deprotonated, N-bound uracil or thymine with the respective free ligand is hampered by the fact that only a single structure of the anionic ligand is available, that of N1-deprotonated thymine.[35] Complexes of thymine with N1-bound

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**Table VII.** Comparison of Molecular Dimensions of Neutral Uracil in Its Normal 2,4-Dioxo and Its Rare 2-Oxo-4-hydroxo Tautomer Form

| | normal tautomer[a] | Pt-1-MeUH[b] | free rare tautomer[c] |
|---|---|---|---|
| | (A) Internal Angles (deg) | | |
| C6-N1-C2 | 121.6 (6); 121.4 (1) | 121.7 (5) | 121.7 |
| N1-C2-N3 | 114.8 (7); 115.3 (1) | 117.0 (4) | 118.0-119.5 |
| C2-N3-C4 | 127.0 (6); 126.7 (1) | 120.3 (4) | 117.8-119.3 |
| N3-C4-C5 | 114.7 (9); 114.6 (1) | 120.6 (5) | 121.6-128.1 |
| C4-C5-C6 | 119.2 (13); 119.4 (1) | 118.7 (5) | 118.7 |
| C5-C6-N1 | 122.8 (9); 122.5 (1) | 121.6 (6) | 121.6 |
| | (B) Distances (Å) | | |
| N1-C2 | 1.379 (10); 1.378 (1) | 1.386 (7) | 1.39 (1) |
| C2-N3 | 1.373 (9); 1.378 (1) | 1.397 (6) | 1.40 (1) |
| N3-C4 | 1.383 (10); 1.385 (1) | 1.352 (6) | 1.35 (1) |
| C4-C5 | 1.440 (11); 1.441 (1) | 1.406 (8) | 1.41 (1) |
| C5-C6 | 1.338 (9); 1.352 (1) | 1.323 (9) | 1.32 (1) |
| C6-N1 | 1.380 (11); 1.370 (1) | 1.351 (7) | 1.35 (1) |
| C2-O2′ | 1.218 (10); 1.225 (1) | 1.208 (6) | 1.21 (1) |
| C4-O4′ | 1.227 (9); 1.241 (1) | 1.287 (7) | 1.29 (1) |

[a] First value refers to average value from 32 X-ray structures[43] and second one to values for 1-MeUH (2,4-dioxo form).[28] [b] Ring b of compound **1**. [c] Estimated values for free 2-oxo-4-hydroxo tautomer. Confer text.

metals [Cu,[36] enPt$^{II}$,[31] *cis*-$(NH_3)_2Pt^{II}$[37]] either show no changes in internal ring angles at all [enPt$^{II}$] or the expected trends of an increase of C6-N1-C2 [2.8°, 2.6$\sigma$, in the *cis*-$(NH_3)_2Pt^{II}$ complex], a decrease of N1-C6-C5 [4.0°, 3.6$\sigma$, in the *cis*-$(NH_3)_2Pt^{II}$ complex], and a decrease of N1-C2-N3 (1.5°, 3$\sigma$, in the Cu complex). In neither case, however, is there an effect on all three angles. With 1-methylcytosine, all internal ring angles about N3, C2, and C4 usually exhibit the expected changes on metal binding (Pt,[38] Pd,[39] Zn[40]): increase of C2-N3-C4 by 1-2.6°, decrease of N1-C2-N3 by 1-2°, and decrease of N3-C4-C5 by 2-2.7°. In many cases these changes are significant.[41]

Combining the findings from these two systems and applying them to N3-platinated 1-MeUH (ring b of **1**), one can expect that in the absence of Pt, hence in the free 2-oxo-4-hydroxo tautomer form of 1-MeUH, the internal ring angles at C2 and C4 increase by 1-2.5°, while the angle at N3 decreases to the same extent. As a result (Table VII), substantial differences in internal ring angles at N3, C4, and C2 between the normal and the rare tautomer are expected. External angles are not considered because they may be strongly influenced by hydrogen-bonding interactions. Unfortunately, the errors in bond angles of 1-methyluracil hydrobromide[42] are too large to decide whether the expected greater effect of the proton as compared to Pt on the geometry of the free tautomer indeed holds up for this case as well. Table VII also includes a comparison of bond lengths of uracil residues[28,43] and ring b of **1**. On the assumption that metal binding to an endocyclic N atom has no major effect on bond lengths within the heterocycle, bond lengths in the 1-MeUH ligand should be close to those of the free rare tautomer.

**Raman Spectra.** Since Raman spectroscopy is a useful technique for the differentiation of heterocyclic tautomers[44] and their respective metal complexes,[13,45] it was applied in the present study

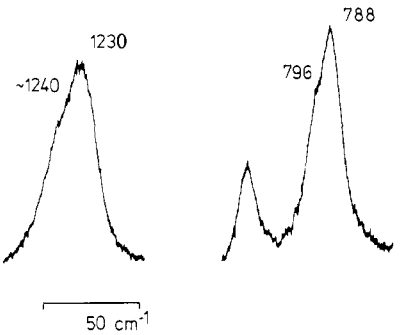



**Figure 5.** Sections of Raman spectrum (slit width 4 cm$^{-1}$) of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ in $HNO_3$, pD 0, corresponding essentially to **1**. Signals at 1230 and 788 cm$^{-1}$ are assigned to the 1-MeUH ligand and those at 1240 and 796 cm$^{-1}$ to the 1-MeU ligand (laser power 600 mW for 1230-1240-cm$^{-1}$ bands and 500 mW for 780-800-cm$^{-1}$ bands).

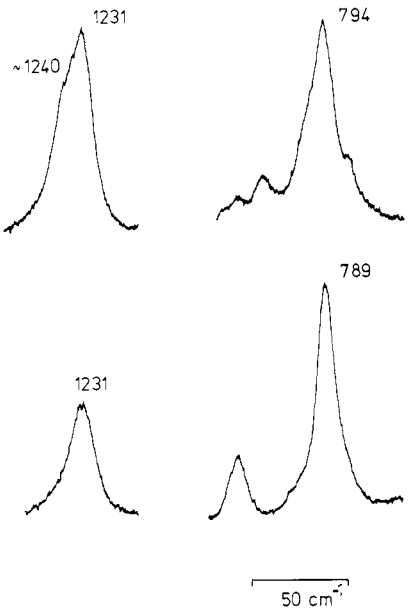



**Figure 6.** Sections of solid-state Raman spectra (ring-stretching and ring-breathing modes) of **1** (top) and **3** (bottom) (slit width 6 cm$^{-1}$ each). *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2\cdot 4H_2O$ (not shown) has single, symmetrical bands at 1242 and 793 cm$^{-1}$ for the respective modes.

to determine the state of protonation of the uracil ligands in **1** and **3**. Specifically, the two most intense uracil ring modes,[46] the ring-stretching vibration (1230-1240 cm$^{-1}$) and the ring-breathing mode (780-800 cm$^{-1}$), were examined for this purpose. The solution spectrum of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ at pH 0, which, on the basis of the p$K_a$ for the first protonation (vide infra), should mainly be due to **1**, displays two well-discernible peaks in either range (Figure 5). From comparison with the pH 6 spectrum (1240 and 796 cm$^{-1}$, symmetrical, single peaks each)[18e] we assign the signals at 1230 and 788 cm$^{-1}$ to the 1-MeUH ligand (ring b) in **1**.

The solid-state spectra of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ and of **3** (Figure 6) have single sets of Raman signals in the respective spectral ranges while that of **1**, at least for the ring stretch, displays again two components. We conclude from these observations that the two uracil ligands in **3** are practically identical, hence protonated at O4′ (cf. discussion above).

**Protonation in Solution.** Protonation of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ was followed with $^1$H NMR spectroscopy (Figure 7). Below pD 3.5, protonation of the 1-MeU ligands takes place as evident from

(36) Kistenmacher, T. J.; Sorell, T.; Marzilli, L. G. *Inorg. Chem.* **1975**, *14*, 2479.
(37) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Pfab, R. *Inorg. Chem.* **1981**, *20*, 2381.
(38) See, e.g., (a) Orbell, J. D.; Marzilli, L. G.; Kistenmacher, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 5126. (b) Faggiani, R.; Lippert, B.; Lock, C. J. L. *Inorg. Chem.* **1982**, *21*, 3210, and references cited therein.
(39) Sinn, E.; Flynn, C. M.; Martin, R. B. *Inorg. Chem.* **1977**, *16*, 2403.
(40) Beauchamp, A. L. *Inorg. Chim. Acta* **1984**, *91*, 33.
(41) We note that in one instance [N3-Pt(II) complex of unsubstituted cytosine] an increase of the C2-N1-C6 angle was observed. Confer Jaworski, S.; Schöllhorn, H.; Eisenmann, P.; Thewalt, U.; Lippert, B. *Inorg. Chim. Acta* **1988**, *153*, 31.
(42) Sobell, H. M.; Tomita, K.-I. *Acta Crystallogr.* **1964**, *17*, 122.
(43) Taylor, R.; Kennard, O. *J. Mol. Struct.* **1982**, *78*, 1.
(44) Lippert, B. *J. Raman Spectrosc.* **1979**, *8*, 274.
(45) Pfab, R.; Jandik, P.; Lippert, B. *Inorg. Chim. Acta* **1982**, *66*, 193.
(46) (a) Susi, H.; Ard, J. S. *Spectrochim. Acta, Part A* **1971**, *27A*, 1549. (b) Lord, R. C.; Thomas, G. R., Jr. *Spectrochim. Acta, Part A* **1967**, *23A*, 2551.

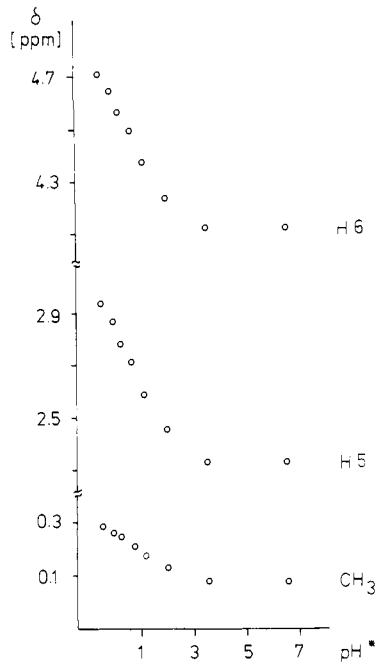



**Figure 7.** $^1$H NMR chemical shifts of 1-methyluracil resonances of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ at different (uncorrected) pH* values. Chemical shifts are relative to $NMe_4^+$.

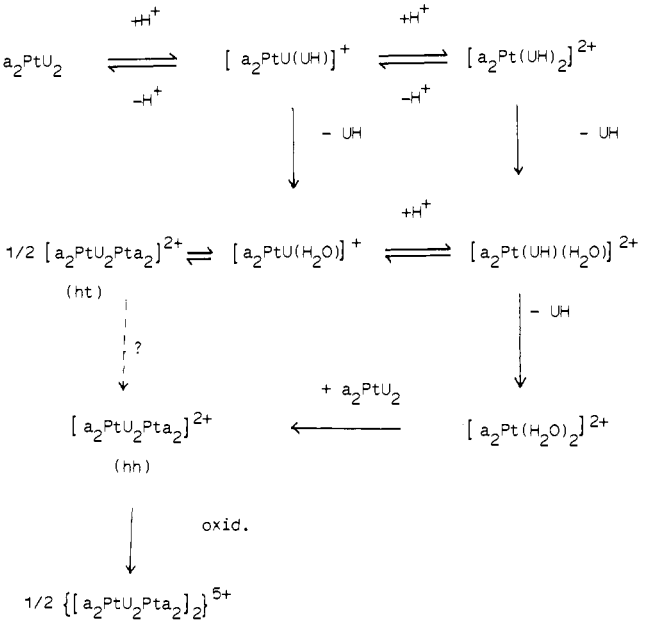
the downfield shifts of the uracil resonances. Comparison with the protonation behavior of *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(D_2O)]^+$ (not shown) and *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(1\text{-}MeC)]^+$ (1-MeC = 1-methylcytosine)[17g] reveals distinct differences: With the two latter compounds, protonation of the 1-MeU ligands starts at lower pD (2); the "titration" curve ($\delta$ shift vs pD) has a steeper inclination and displays a discrete point of inflection which gives p$K_a$ values of ca. 0.9 in both cases. H5 and H6 resonances are shifted to the same extent, by approximately 0.4 ppm in the range $0 \leq pD \leq 4$.

The considerably larger shifts of 1-MeU resonances (ca. 0.6 ppm in the same range) on protonation of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ and the fact that no inflection point is observed suggest that the second protonation step (**1** → **3**) has some overlap with the first one. On the basis of chemical shift arguments (p$K_{a1}$ at shift of ca. 0.2 ppm), one can estimate a p$K_{a1}$ of $\simeq$1.5 for the process *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2 + H^+ \rightleftharpoons$ *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(1\text{-}MeUH)]^+$. This value is in good agreement with that determined by means of UV spectroscopy (1.4[47]) and not unexpectedly somewhat lower than in the corresponding 1-methylthymine system (2.05[12]).

The protonation process of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ is accompanied by a marked broadening of the (averaged) uracil resonances: For example, at pD $\simeq$ 0, the H6 resonance has completely lost its doublet structure (broad singlet, half width 0.3 ppm), but with increasing acidity (3 N $DNO_3$), the resonances sharpen again. A plausible explanation for this behavior might be the slowing down of ligand rotation about the Pt–N bond in **1** as a consequence of strong intramolecular hydrogen bonding (cf. X-ray results).

**Complex Decomposition.** Our earlier reports[12,17e,18e] on the labilization of the Pt–N (uracil, thymine) bond on protonation of the nucleobase is confirmed in this study. Depending on the acidity of the solution, different reaction products can be detected: In dilute $DNO_3$ solution (pD 1.6), the original $^1$H NMR resonances due to *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ and **1** (averaged) are lost with time at the expense of resonances due to the free ligand 1-MeUH, the 1:1 complex *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(D_2O)]^+$ (averaged with protonated form), and the 2:2 complex(es) (head-to-head and/or head-to-tail).[48] Formation of the dinuclear

**Scheme III**




*cis*-$[(NH_3)_2Pt(1\text{-}MeU)]_2^{2+}$ complex with head-to-head arranged 1-MeU ligands is certain since *cis*-$[(NH_3)_8Pt_4(1\text{-}MeU)_4]^{5+}$ [Pt(2.25)–1-MeU blue[49]] is isolated from an aged solution of *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ at pH 1.6 ($DNO_3$, dark blue after 3–8 days at 22 °C). Formation of the head-to-tail isomer from *cis*-$[(NH_3)_2Pt(1\text{-}MeU)(D_2O)]^+$ would, however, also be logical.[18e] For a summary, see Scheme III.

In 2–3 N $DNO_3$, formation for Pt(2.25)–1-MeU blue does not occur. Rather, besides 1-MeUH, a transient species is observed in the $^1$H NMR spectrum which has chemical shifts identical with or close to those of typical diplatinum(III) complexes of 1-methyluracil.[50] After 9 days at 22 °C, more than 95% of the original 1-MeU ligands are converted into free 1-MeUH with most of it having undergone isotopic exchange ($^2$D vs $^1$H) at the C5 position.

**Complex 3 in $Me_2SO$-$d_6$.** Displacement of 1-MeUH from **3** occurs also in $Me_2SO$. After 15 h at 22 °C, almost 50% of bound 1-MeUH is present as free 1-MeUH. After 45 h, at which time the spectrum appears not to change any further, signals of free 1-MeUH dominate the $^1$H NMR spectrum, but there are additional resonances which are assigned to $NH_4^+$ (1:1:1 triplet at 7.10 ppm, $J$ = 51 Hz), to a Pt(IV)–$NH_3$ complex (1:1:1 triplet at 5.84 ppm, $J$ = 53 Hz),[51] and, tentatively, to *trans*-$[(Me_2SO)_2Pt(NH_3)(1\text{-}MeU)]^+$ [H6, 7.36 ppm, d, $^3J$ = 7.6 Hz; H5, 5.30 ppm, d; $NH_3$, 4.11 ppm, $^2J(^{195}Pt\text{–}^1H)$ = 55 Hz] (cf. supplementary material). The approximately equal intensities of $NH_4^+$ and 1-MeU resonances of the Pt(III) complex formed are consistent with the following reaction sequence:

$$cis\text{-}[(NH_3)_2Pt(1\text{-}MeUH)_2]^{2+} \xrightarrow[-(1\text{-}MeUH)]{+Me_2SO} cis\text{-}[(NH_3)_2Pt(1\text{-}MeUH)(Me_2SO)]^{2+} \xrightarrow[-NH_4^+]{+Me_2SO} trans\text{-}[(Me_2SO)_2Pt(NH_3)(1\text{-}MeU)]^+$$

(47) Krizanovic, O.; Lippert, B. In *Platinum and Other Metal Coordination Compounds in Cancer Chemotherapy*; Nicolini, M., Ed.; Nijhoff Publishing: Boston, 1988; p 700.

(48) The two isomers are not readily differentiated on the basis of their chemical shifts; cf. ref 18d.

(49) (a) Mascharak, P. K.; Williams, I. D.; Lippard, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 6428. (b) Lippert, B.; Schöllhorn, H.; Thewalt, U. *Inorg. Chem.* **1987**, *26*, 1736. (c) ref 17d.

(50) Schöllhorn, H.; Eisenmann, P.; Thewalt, U.; Lippert, B. *Inorg. Chem.* **1986**, *25*, 3384.

(51) This interpretation is based on the characteristic pattern and the position of the $NH_3$ resonances. Confer Müller, G.; Riede, J.; Beyerle-Pfnür, R.; Lippert, B. *J. Am. Chem. Soc.* **1984**, *106*, 7999. Since we can exclude the possibility that the Pt(IV)–$NH_3$ complex is formed in a reaction between $NH_4^+$ and the $PtCl_6^{2-}$, we conclude that a redox process [oxidation of Pt(II)–$NH_3$ by $PtCl_6^{2-}$] has occurred.

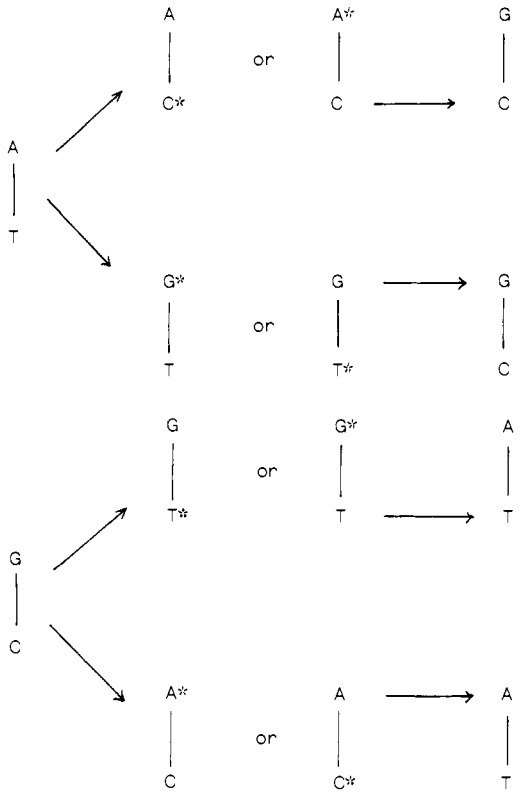



**Figure 8.** Schematic representations of base mispairing leading to transitions AT → GC (top) and GC → AT (bottom). The rare T* tautomer may either be in the template (second row from top) or be incorporated (third row from top).

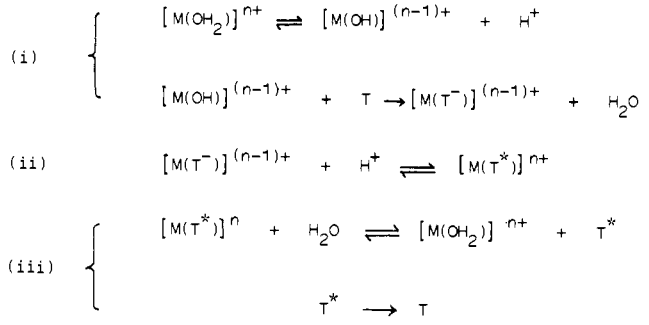
According to it, the acidic proton of the coordinated 1-MeUH ligand is utilized to shift the equilibrium

$$NH_3\text{-}Pt\text{-}Me_2SO \underset{-Me_2SO}{\overset{+Me_2SO}{\rightleftharpoons}} Me_2SO\text{-}Pt\text{-}Me_2SO + NH_3$$

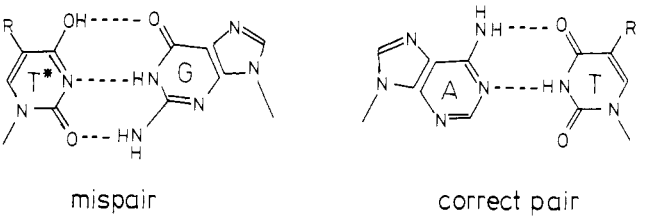
to the right by forming $NH_4^+$.[52] Once deprotonated, the uracil ligand no longer exhibits the acid lability of the 1-MeUH ligand.

**Effect of Pt on Ligand Properties.** The effect of platinum on the uracil ring in terms of $H^+$ affinity (basicity) can be viewed from two points: (i) Displacement of the proton at N3 of the dioxo tautomer of 1-methyluracil by the heavy metal electrophile increases the basicity of the exocyclic O4′ oxygen markedly. Depending on the $pK_a$ of the protonated, free 1-MeUH (−3.4,[10] −3.0,[11] −2.84,[11] −3.5,[53] −2.2,[53] −2.1[53]),[54] chosen as the reference, and the $pK_a$ values of the respective protonated (O4′) and platinated (N3) ligand ($pK_{a1}$ of 1.4 in **1**, 0.9 in *cis*-$[(NH_3)_2Pt(1\text{-}MeUH)(1\text{-}MeC)]^{2+}$,[17g] and 0.8 in *cis*-$[(NH_3)_2Pt(1\text{-}MeUH)(H_2O)]^{2+}$), the magnitude of this increase in basicity of O4′ amounts to 3.9 ± 1.0 log units. The maximum seen in the case of the bis(1-methyluracil) complex probably is a consequence of the favorable intramolecular hydrogen bond between the protonated and unprotonated O4′ sites in **1** which further stabilizes this arrangement. (ii) If the acidity of the Pt(1-MeUH) moiety is referenced to the acidity of the free, rare 2-oxo-4-hydroxo tautomer of 1-methyluracil ($pK_a \simeq 5.7$[55]), the usual increase in ligand acidity on metal binding is observed. It is 4.6 ± 0.3 log units for the three 1-MeUH complexes mentioned above, which is somewhat lower than in the case of a Pt(IV) complex of the rare iminooxo tautomer of 1-methylcytosine[1] yet considerably higher than in Pt(II) complexes of the normal aminooxo tautomer of cytosine.[17g]

**Scheme IV**




**Scheme V**




## Conclusions

In this paper, structural and spectroscopic results are presented which demonstrate that the rare 2-oxo-4-hydroxo tautomer form of 1-methyluracil can be formed through metal (Pt) binding at N3 and subsequent protonation at the O4′ site. The results confirm and extend a previous study of the corresponding 1-methylthymine system, which was based on spectroscopic evidence.[12] The results are of particular interest with respect to mutagenicity mechanisms involving transitions:[56] Rare tautomers of thymine, either in the template strand or in the incoming nucleotide, may mispair with guanine and consequently alter the genetic information (Figure 8). According to our findings, a metal- (not necessarily Pt) mediated tautomerization process could involve the following steps (Scheme IV): (i) Metal coordination at N3 of a thymine (or uracil) nucleobase. With metal complexes forming readily hydroxo species at physiological pH,[57,58] alkaline conditions for metal binding are *not* required. (ii) Protonation of the metal–nucleobase complex. While the $pK_a$ determined in the case of Pt(II) may be too low to be physiologically relevant,[12] other metal complexes may be better in this respect. For example, protonation of Pd(II)–1-MeU takes place at pH 6.[59] On the other hand, Au(III) is so strongly bound to N3 of 1-MeU that significant protonation of the nucleobase occurs only below pH 0.[60] It thus appears that weak metal coordination to N3 and the resulting higher basicity of the nucleobase facilitates protonation, hence raises the $pK_a$. (iii) Cleavage of the metal–N3 bond and liberation of the rare tautomer. In our model system, we have, at present not attempted to demonstrate the occurrence of the rare tautomers of uracil and thymine, although their postulation is chemically reasonable. It probably is the higher acidity of the rare tautomer(s), compared to the preferred tautomeric form, which favors rapid interconversion to the major tautomer.[61] However, it appears possible that under aprotic conditions, which at the same

(52) (a) Beyerle, R.; Lippert, B. *Inorg. Chim. Acta* **1982**, *66*, 141. (b) Braddock, P. D.; Romeo, R.; Tobe, M. L. *Inorg. Chem.* **1970**, *13*, 1170.
(53) Gukovskaya, A. S.; Sukhorukov, B. J.; Prokop'eva, T. M.; Antonovskii, V. L. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1972**, *12*, 2682.
(54) Another value reported in the literature most likely is incorrect: Parry, E. P.; Hern, D. H.; Burr, J. G. *Biochim. Biophys. Acta* **1969**, *182*, 570.
(55) Calculated according to $K = (K_2/K_T)(1 + K_T)$ with $K_2$ (apparent constant for deprotonation of 1-MeUH) = $10^{-9.71}$ and $K_T$ (tautomer equilibrium constant) = $10^{-4}$ (ref 10).
(56) See, e.g., (a) Drake, J. W.; Allen, E. F.; Forsberg, S. A.; Preparata, R.-M.; Greening, E. O. *Nature* **1969**, *221*, 1128. (b) ref 17f.
(57) See, e.g., Burgess, J. *Metal Ions in Solution*; Horwood: Chichester, England, 1978; p 259.
(58) (a) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Rosenberg, B. *J. Am. Chem. Soc.* **1977**, *99*, 777. (b) Rochon, F. D.; Morneau, A.; Melanson, R. *Inorg. Chem.* **1988**, *27*, 10, and references cited therein.
(59) Micklitz, W.; Sheldrick, W. S.; Lippert, B., submitted for publication in *Inorg. Chem.*
(60) Micklitz, W.; Mikulcik, P.; Müller, G.; Riede, J.; Lippert, B., submitted for publication in *Inorg. Chim. Acta.*
(61) Benaude, O.; Dreyfuss, M.; Dodin, G.; Dubois, J. E. *J. Am. Chem. Soc.* **1977**, *99*, 4438.

time would reduce ionization of the rare tautomer, a 2-oxo-4-hydroxo tautomer of thymine (or uracil) might be sufficiently long lived to accomplish base mispairing (Scheme V).

In any case, the here-proposed model for a metal-assisted tautomerization of 1-methyluracil or 1-methylthymine[12] could provide a rationale for findings on the increase of GC content in bacterial DNA at the expense of AT under the influence of Cu(II),[62] although we note that there is an alternative possibility (cf. Figure 8).

Isolation of the two Pt complexes **1** and **3** containing rare nucleobase tautomers has been possible because kinetics of the complex decomposition are sufficiently slow. With Pd(II) or first-row transition elements the preparation of analogues is difficult, if not impossible. The results of the X-ray structure analysis of **1** have been used to estimate the geometry of the rare 2-oxo-4-hydroxo tautomer.

**Acknowledgment.** This work has been supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Degussa (loan of $K_2PtCl_4$).

**Registry No. 1**, 121809-96-9; **2**, 121809-97-0; **3**, 121844-93-7; 1-MeUH, 615-77-0; *cis*-$(NH_3)_2Pt(1\text{-MeU})_2$, 83350-97-4; $Na_2PtCl_6$, 16923-58-3; $H_2PtCl_6$, 16941-12-1.

**Supplementary Material Available:** Table A listing positional and anisotropic thermal parameters of **1**, Table B listing positional parameters and temperature factors for **3**, Table C listing possible hydrogen-bonding interactions in **1** and **3**, and Figure 1 showing $^1H$ NMR spectra of **3** in MeSO-$d_6$ (4 pages); tables of observed and calculated structure factors (37 pages). Ordering information is given on any current masthead page.

(62) Weed, L. L. *J. Bacteriol.* **1963**, *85*, 1003.

# DNA Oligomers and Duplexes Containing a Covalently Attached Derivative of Tris(2,2′-bipyridine)ruthenium(II): Synthesis and Characterization by Thermodynamic and Optical Spectroscopic Measurements†

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**Abstract:** Oligonucleotides having the base sequence 5′-GCA(C*)TCAG-3′ and 5′-GCAC(T*)CAG-3′ were synthesized where C* and T* equal, respectively, a chemically modified cytidine or thymidine base containing a linker arm terminating in a primary amine. The primary amine of these modified oligomers reacted specifically with the *N*-hydroxysuccinimide ester of 4-carboxy-4′-methyl-2,2′-bipyridine to form bipyridine-labeled oligomers, and these oligomers reacted with $Ru(bpy)_2(H_2O)_2^{2+}$ to give oligonucleotides with covalently attached derivatives of $Ru(bpy)_3^{2+}$. Oligonucleotides with nonspecifically bound $Ru(bpy)_2(H_2O)_x^{2+}$, where $x = 0$ or 1, were also formed, but were chromatographically separated from the former product. Duplexes of the $Ru(bpy)_3^{2+}$-labeled oligonucleotides were formed upon addition of their unmodified complementary strands and were studied by melting temperature behavior as a function of concentration and by absorption and emission optical spectroscopies. Both hybridization behavior and the spectroscopic properties of the ruthenium label itself were retained in these labeled duplexes. This work shows that it is possible to use DNA duplexes as molecular scaffolds to organize covalently attached polypyridyl-substituted transition-metal complexes and constitutes an initial step in the construction of macromolecules with specifically located, redox-active subunits.

The ability of DNA oligomers to hybridize allows a complementary probe strand to bind to a specific, target base sequence. Additionally, such probe/target hybridization can be detected by spectroscopic methods if the probe sequence is appropriately labeled. There are a number of reports of synthetic oligonucleotides that contain a covalently attached label,[1-9] and label attachment can be either to a base[1,2,9] or to a phosphate.[4-8] We have previously studied a series of oligonucleotides and duplexes with a variety of labels attached at either thymidine or cytidine.[9] However, in that study as well as in most others,[4-8] the labels were organic molecules, usually with good fluorescence properties. Examples include derivatives of pyrene,[8,9] acridine,[3-6] phenanthridine,[7] and fluorescein.[9] Very recently, Helene and co-workers attached a number of metalloporphyrins to oligonucleotides.[10] However in that study, as in many others, the labels were attached was at 3′ or 5′ terminal phosphates. Importantly, Dreyer and Dervan attached an inorganic coordination complex, Fe–EDTA, to a

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