Nucleobase–Metal Complexes

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Inverting the Charges of Natural Nucleobase Quartets: A Planar Platinum–Purine Quartet with Pronounced Sulfate Affinity**

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The formation of four-stranded nucleic acid structures like those in DNA and RNA is closely connected with the existence of guanine tetrads (G_4). In G_4 four purine bases are interconnected by eight hydrogen bonds, and the structure is further stabilized by a central cation.^[1] The negative charges of the phosphate groups are located at the periphery of this motif. Similar tetrads consisting of uracil^[2] or thymine^[3] are based essentially on the same principle. The significance of tetrastranded DNA concerning its function in the telomeres as well as in regulatory regions of the DNA is presently the subject of intense investigations.^[4]

Here we describe a non-natural quartet of 9-methylpurine, which differs from the natural nucleobase quartets in that cationic *trans*- $(NH_3)_2Pt^{II}$ moieties are located at the periphery of the quartet and an anion is trapped in the center (Scheme 1). The hydrogen bonds in the natural-base quartets



Scheme 1. G = guanine, Pu = 9-methylpurine, $M^{2+} = trans - [(NH_3)_2 Pt^{II}]^{2+}$.

are replaced by coordinative Pt-nucleobase bonds in the artificial quartet, and the overall negative charge of the natural quartets is changed to positive in the artificial one. At

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the same time we report on the corresponding molecular triangle, the analogy of which to natural purine triplets is less obvious. As we have shown in a number of cases,^[5] simultaneously N1- and N7-coordinated purine bases can behave as bridging ligands forming 90° angles. Complexes with linear coordinating metal ions M such as *trans*-(NH₃)₂Pt^{II}, Ag⁺ or Hg²⁺ lead to diverse architectures containing right angles, for example, rectangles of the type *cyclo*-(*N1*-M-*N1*,*N7*-M-*N7*)₂ (Scheme 2).



Scheme 2. Possible architectures of purine-metal complexes.

Using unsubstituted 9-methylpurine (Pu), we have now succeeded in preparing a molecular square with the coordination sequence cyclo-(N1-Pt-N7)₄. This compound, all-trans- $[\{(NH_3)_2Pt(\mu-N1-Pu-N7)\}_4]^{8+}$ (2), forms spontaneously from the 1:1 complex trans- $[(NH_3)_2Pt(Pu-N7)(H_2O)]^{2+}$ (1). Observation of the product formation by ¹H NMR spectroscopy shows that several molecules of 1 condense to form short chains, which undergo complete reaction at room temperature over five days to yield two distinct cyclic complexes (Scheme 3). Besides the molecular square 2, a molecular triangle of composition all-*trans*-[{(NH₃)₂Pt(μ -N1-Pu-N7)}₃]⁶⁺ (3) is formed. In both compounds, the Pu ligands are symmetrically equivalent and hence in the ¹H NMR spectrum only a single set of signals can be observed for the respective species. According to signal integration, the formation of 3 is preferred over formation of 2 (2/3 = 0.6:1). The situation changes when the reaction is carried out in the presence of sulfate, which acts as a template. In $100 \text{ mM} \text{ Na}_2 \text{SO}_4$, formation of 2 is preferred, and the 2/3 ratio increases to 2.5:1. In addition, the presence of sulfate anions speeds up the reaction, such that product formation is complete within three days at room temperature.

Crystallization of **2** and **3** proved to be difficult, and only very small crystals could be obtained, which have the composition **2**-(ClO₄)₈·6H₂O (**2a**) and **3**-(PF₆)₆·6H₂O (**3a**), respectively.^[6] The cations of **2a** and **3a** are shown in Figure 1. In both compounds the purine ligands and the Pt^{II} atoms are essentially coplanar, and the ammine ligands are perpendicular to this plane. Pt–N distances are normal. In **2a**, the distances between the Pt^{II} atoms on opposing sides of the square are 9.03(1) Å (Pt1–Pt1a) and 9.09(1) Å (Pt2–Pt2a). The square has outer diagonals of 17.07(4) Å (C9a–C9aa) and 17.24(6) Å (C9b–C9ba). The diagonals in the center are Communications









Figure 1. Cations of 2a and 3a with atomic numbering.

6.08 Å (H6a–H6aa) and 6.24 Å (H6b–H6ba). The N1-Pt-N7 angles deviate slightly from the ideal angle of 180° and measure 176.8(5)° (N1b-Pt1-N7a) and 177.4(5)° (N1aa-Pt2-N7b), respectively. As a consequence, the angle between the Pt^{II} atoms coordinated to the N1 and N7 sites of a purine ligand likewise deviate from the ideal 90°–88.1° in purine a and 85.1° in purine b. In the crystal structure, the cations are packed on top of each other in a slightly staggered manner with a stacking distance of 7.5 Å. Some of the perchlorate anions, which display pronounced positional disorder, are located between the cations yet appear not to be firmly fixed to these.

In **3a**, the distances between the Pt^{II} atoms are in the range of 5.91(1)-6.00(1) Å, while the distances between the C9 atoms are between 12.67(2) and 12.73(3) Å. The N1-Pt-N7 angles in **3a** deviate markedly from the ideal 180° and are in the range of 168.8(5)–170.8(4)°. The angles between the Pt^{II} atoms coordinated to the N1 and N7 sites of a purine ligand deviate strongly from 90° and range between 67.8° and 70.8°.

Of the six hexafluorophosphate anions in 3a, one is located above and another below the center of each cation, and the C_3 axis of the anion points towards the cation. The other face of the PF_6^- anion is oriented toward a purine ligand of a parallel cation. This leads to a helical arrangement of the cations in the structure, making it chiral (Figure 2). The distance between the planes of the cations is 7.6 Å.

Both compounds show a pronounced affinity for sulfate anions. The binding of SO_4^{2-} was monitored by concentration-dependent ¹H NMR spectroscopy, where the concentration of



Figure 2. Section of the packing pattern of **3** a. The PF_6^- anions are layered between the cations, thereby producing a helix.

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the anion was varied, while the concentration of the respective cyclic compound was kept constant. In $[D_6]DMSO$, **2** shows a new signal set upon addition of nBu_4NHSO_4 . The resonances of the H6 protons and those of the ammine ligands are strongly shifted towards low field, whereas the other signals of the purine ligands are scarcely influenced (Figure 3). In D₂O, the H6 signals shift downfield with increasing concentrations of Na₂SO₄ (Figure 4). The influence on the other resonances of the purine ligands is only very weak, and the resonances of the protons of the ammine ligands cannot be observed because of isotope exchange with the solvent.



Figure 3. ¹H NMR spectra of **2** recorded in $[D_6]DMSO$. The uppermost spectrum was recorded in the absence of sulfate ions, the spectra below with increasing amounts of nBu_4NHSO_4 : a) no HSO_4^- , b) 0.1 equiv HSO_4^- , c) 0.5 equiv HSO_4^- , d) 1.0 equiv HSO_4^- , e) 3.0 equiv HSO_4^- . Upon addition of sulfate a host–guest complex forms, which displays a new set of signals indicating the slow exchange of the sulfate ions. While the signals assigned to H6 and to the protons of the ammine ligands are strongly low-field shifted, the other resonances are only weakly affected. This is consistent with the view that the sulfate is trapped in the center of the molecular square and that the NH₃ ligands are involved in hydrogen bonding with sulfate.



Figure 4. Change of the chemical shifts $\Delta \delta$ of the H6 signals of 2 (\Box) and 3 (Δ) in D₂O with increasing amounts of Na₂SO₄. In both cases the perchlorate salts (**2a** and **3b**) where used, since perchlorate ions appear to be only weakly bound to the cations. The solid lines where obtained by a least-squares fitting procedure,^[7] which yielded the association constants discussed in the text. Concentrations of the host molecules were 0.40 mm **2** and 0.47 mm **3**.

The concentration dependence of the H6 signals can be used to determine the association constants.^[7] For the binding of sulfate in D₂O, we have found association constants of $(7.2 \pm 1.2) \times 10^4 \text{ L mol}^{-1}$ for **2** and $(9.9 \pm 0.6) \times 10^3 \text{ L mol}^{-1}$ for 3. These values indicate very strong sulfate binding in water and are in the range known for very strong anion receptors such as aza crown ethers and cryptands.^[8,9] We are currently performing experiments to investigate the selectivity of 2 and **3** for different anions. These studies will be accompanied by DFT calculations in order to elucidate the mode of anion binding in more detail. Preliminary results suggest that the anion is trapped by 2 by means of multiple hydrogen bonds, with the S atom residing in the center of the cavity. In addition to the general aspect of sulfate binding, the templating effect of this anion during the formation of the square 2 is noteworthy, as is the topical issue of factors influencing equilibria of metallosupramolecular assemblies.^[10] Finally, 2 represents the first example of a true purine square with four metal entities at the periphery and alternating N1,N7 coordination. Previously described cases of metal-containing purine quartets displayed rectangular shapes^[5a,e] as a consequence of pairwise N7,N7 and N1,N1 metal binding. Another point of interest is whether these cationic nucleobase squares are capable of interacting with natural tetrastranded nucleic acid structures.[11]

Experimental Section

Preparation of *trans*-[(NH₃)₂Pt(9MePu-*N7*)Cl]ClO₄ (**1a**): A solution of Pu^[12] (134 mg, 1.00 mmol) in 5 mL of 2.4 M HClO₄ was added at once to *trans*-[(NH₃)₂Pt(OH)Cl]·H₂O^[13] (300 mg, 1.00 mmol). The mixture was stirred for 5 min, then the yellowish precipitate was filtered off and washed with ca. 20 mL of 1M NaClO₄ and 2 mL of H₂O. The product was dried under vacuum. Yield: 275 mg, 55.2 %; white powder. C,H,N analysis calcd (%): C 14.5, H 2.4, N 16.9; found: C 14.2, H 2.4, N 16.7. ¹H NMR: (D₂O, pD 2.4): δ = 9.56 (s, H6), 9.12 (s, H2), 9.09 (s, H8), 4.06 ppm (s, CH₃).

Preparation of 2a and trans-[{(NH₃)₂Pt(μ -N1-Pu-N7)}]- $(ClO_4)_6$ ·3H₂O (3b): A solution of 1a (199 mg, 0.400 mmol) in 15 mL of H_2O was treated with 1 mL of 1 M HNO3 and AgNO3 (67.9 mg, 0.400 mmol), and the mixture was stirred for 3 d at 45 °C in the dark. Precipitated AgCl was removed by filtration, and the solution was concentrated at reduced pressure to a volume of 5 mL. The solution was cooled to 4°C for 12 h, and the crude 2a that precipitated was isolated by filtration. Addition of 800 µL of 1M NaClO₄ to the remaining solution precipitated crude **3b**, which was isolated by filtration. The crude products were washed twice with 250 µL of H₂O and dried under vacuum. The products obtained were dissolved in 40 mL (2a) and 20 mL of H₂O (3b), respectively, and then precipitated by addition of 1M NaClO₄, filtered off, and dried under vacuum. Yields of isolated products were 38 mg (16%) of 2a and 39 mg (17%) of 3b. C,H,N analysis calcd (%): 2a: C 12.4, H 2.4, N 14.5; found: C 12.1, H 2.5, N 14.8; 3b: C 12.2, H 2.6, N 14.3; found: C 12.1, H 2.5, N 14.3. ¹H NMR: (**2**, D₂O, pD 2.0): $\delta = 10.47$ (s, H6), 9.81 (s, H2), 9.60 (s, H8), 4.22 ppm (s, CH₃); (**3**, D₂O, pD 2.0): $\delta =$ 11.44 (s, H6), 9.49 (s, H2), 9.37 (s, H8), 4.18 ppm (s, CH₃). The hexafluorophosphate salt 3a was prepared by precipitation from a solution of 3b with 0.2M solution of KPF₆ in H₂O. 3a was characterized by X-ray crystallography.

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- [6] Crystal structure data for **2a**: C_{24} H₆₀ N₂₄ O₃₈ Cl₈ Pt₄, $M_r =$ 2256.81, colorless crystals, monoclinic C2/c, a = 20.825(4), b =18.584(4), c = 16.142(3) Å, $\alpha = \gamma = 90^{\circ}$, $\beta = 98.67(3)^{\circ}$, V =6176(2) Å³, Z = 2, $\rho_{\text{calcd}} = 2.419 \text{ Mgm}^{-3}$, $\mu = 9.485 \text{ mm}^{-1}$, T =150 K. 44983 data (7069 unique, 3675 observed, $R_{int} = 0.146$, $3.08 < \theta < 27.52$ °) were collected. Final R = 0.084 ($wR_2 = 0.144$, GoF = 1.104). A major disorder of three of the four crystallographically independent perchlorate anions over two or three positions, respectively, made it necessary to use numerous constraints to fix the geometry of these ions. As a consequence, the R values are comparably poor and the assignment of crystal water molecules was not possible; the amount of crystal water given in the empirical formula therefore is based on elemental analysis data. Crystal structure data for 3a: C18 H48 N18 O6 F36 P6 Pt₃, $M_r = 2067.71$, colorless crystals, hexagonal $P6_1$, a =15.085(2), b = 15.085(2), c = 42.280(9) Å, $\alpha = \beta = 90^{\circ}$, $\gamma = 120^{\circ}$, V = 8332(2) Å³, Z = 6, $\rho_{calcd} = 2.420$ Mg m⁻³, $\mu = 7.881$ mm⁻¹, T =150 K. 29176 data (9153 unique, 7118 observed, $R_{\text{int}} = 0.068$, $3.06 < \theta < 27.49^{\circ}$) were collected. Final R = 0.046 ($wR_2 = 0.088$, GoF = 1.027). The reflections of both crystals were collected on a Nonius KappaCCD diffractometer using graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71069$ Å) and were corrected empirically (SADABS: G. M. Sheldrick, Bruker AXS Inc., Madison, WI, 2000) for absorption. The raw intensity data frames were integrated with the EVALCCD (Bruker AXS Inc., Madison, WI, 2000) program. Both structures were solved by direct methods and refined by full-matrix least-squares methods based on F^2 using the SHELXTL-PLUS (G. M. Sheldrick, Siemens Analytical X-ray Instruments, Inc., Madison, WI, 1990) and SHELXL-97 (G. M. Sheldrick, SHELXL-97, Universität Göttingen, Göttingen, Germany) programs. With the exception of the disordered perchlorate atoms in 2a and the C6b atom, two fluorine atoms of a disordered PF₆⁻ anion, and the nitrogen atoms of the ammine ligands in **3a**, all non-hydrogen atoms in the structures were refined anisotropically. The hydrogen atoms were included in geometrically calculated positions and refined with isotropic displacement parameters. CCDC-280955 and 280954 (2a and 3a) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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