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Interaction of Transuranium Elements with Biologically Important Ligands: Structural and Spectroscopic Evidence for Nucleotide Coordination to Plutonium

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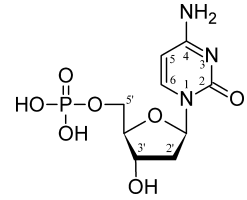
The first complex of a transuranium element (tetravalent plutonium) with nucleotide (deoxycytidinemonophosphate, dCMP) was synthesized and structurally characterized. The crystal structure of $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8](NO_3)_4 \cdot 2H_2O$ consists of complex cations $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8]^{4+}$, NO_3^- anions, and water molecules. There are two crystallographically independent Pu atoms in the structure, both having similar surroundings. Each of the Pu atoms is coordinated by three O atoms of phosphate groups belonging to three different $(HdCMP)^-$ anions, two bidentate nitrate anions, and two water molecules. The crystal structure is confirmed by IR and UV/vis/near-IR spectroscopic data.

Ion metals are able to form complexes with various bioligands: amino acids, azoles, nucleosides, nucleotides, etc. Nucleotides (or phosphoric acid ethers of the nucleosides) contain a nucleobase, ribose, or deoxyribose group, as well as one, two, or three phosphate groups.[1] Nucleotides occur in all biological objects and play an important role in metabolic processes. Adenosine, guanosine, thymidine, and cytidine monophosphates are the most important nucleotides found in nature. The understanding of the radionuclide interaction with biological systems on the molecular level is of great importance. In addition to the ability of these ions, like other heavy metals, to modify or block the functioning of biomolecules, their ionizing emission directly impacts the molecule of nucleic acid, resulting in its damage. At the same time, there are very few data on the interaction of actinides with biologically important molecules in the literature. The majority of research on actinide interaction with biomolecules is devoted to the UO_2^{2+} ion. This may be attributed to the lower radioactivity of uranium and to the usability of the uranyl ion as a fluorescent mark under a cytological study of DNA and RNA damage.[2] Data on the interaction of biomolecules with transuranium elements are almost absent.[3]

Chart 1. Structure of 2′-Deoxycytidine-5′-monophosphate (Deoxycytidylic Acid, H_2dCMP)



We present here the results of the study of Pu^{IV} interaction with 2′-deoxycytidine-5′-monophosphate (Chart 1). We were able to synthesize a Pu^{IV} complex with deoxycytidinemonophosphate (dCMP), $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8](NO_3)_4 \cdot 2H_2O$ (**1**), as a single crystal[4] suitable for structure determination using X-ray diffractometry.[5] IR and vis/near-IR (NIR) spectra of **1** were also measured and studied.[6] The crystal structure of the compound consists of complex cations $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8]^{4+}$ (Figures 1 and S1 in the Supporting Information), NO_3^- anions, and water molecules. There are two crystallographically independent Pu atoms in the structure, both having similar surroundings (Figures S2 and S3 in the Supporting Information). Each of the Pu atoms

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(1) Blackburn, G. M.; Gait, M. J.; Loakes, D.; Williams, D. M. *Nucleic Acids in Chemistry and Biology*; The Royal Society of Chemistry: Cambridge, U.K., 2006.

(2) (a) Nielsen, P. E.; Hiort, C.; Sonnichsen, S. H.; Buchardt, O.; Dahl, O.; Norden, B. *J. Am. Chem. Soc.* **1992**, *114*, 4967–4975. (b) Wittberger, D.; Berens, C.; Hamman, C. J.; Westhof, E.; Schroeder, R. *Mol. Biol.* **2000**, *300*, 339–352.

(3) (a) Neu, M. P.; Matonic, J. H.; Ruggiero, C. E.; Scott, B. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 1442–1444. (b) Moll, H.; Geipel, G.; Bernhard, G. *Inorg. Chim. Acta* **2005**, *358*, 2275–2282.

(4) **Safety note!** *^{239}Pu is a high-specific-activity α-particle-emitting radionuclide. This research was conducted in a radiological facility with appropriate analyses of hazards and implementation of controls for the safe handling and manipulation of radioactive materials.* The single crystals of $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8](NO_3)_4 \cdot 2H_2O$ were obtained during isothermal evaporation at 20 °C of a solution containing plutonium(IV) nitrate and deoxycytidilic acid (H_2dCMP) in the molar ratio 1:1. About 5 mg (0.016 mmol) of H_2dCMP was dissolved in 1 mL of H_2O, and then 1.6 mL of a 0.01 M solution of plutonium nitrate in 2.45 M HNO_3 was added. A tetravalent plutonium stock solution was purified by an anion-exchange technique and assayed using UV/vis/NIR spectroscopy to verify the oxidation state purity and solution concentration. The Pu^{IV} oxidation state was estimated by an absorption maximum at 470 nm.

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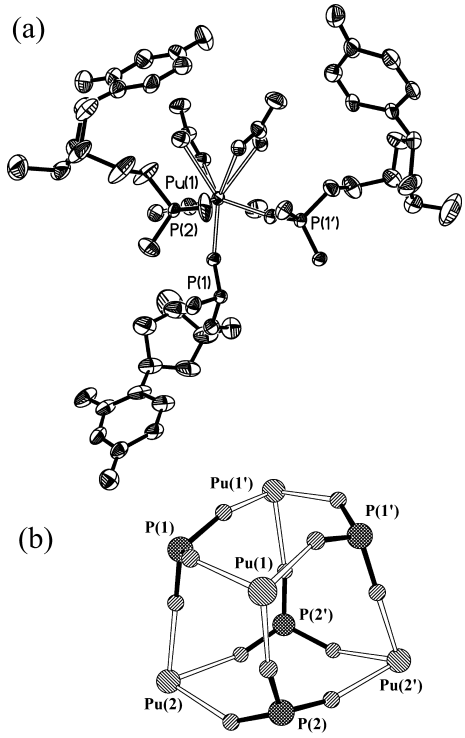

Figure 1. Structure of complex **1**: (a) surroundings of the Pu(1) atom; (b) cubanelike structure formed by Pu atoms and phosphate groups. Protons were omitted for clarity.

is coordinated by three O atoms of phosphate groups belonging to three different $(HdCMP)^-$ anions, two bidentate nitrate anions, and two water molecules, with Pu−O distances equal to 2.167(6)−2.238(5), 2.493(6)−2.565(6), and 2.360(10)−2.441(8) Å, respectively (Table S1 in the Supporting Information). Both $(HdCMP)^-$ anions play the role of tridentate bridging ligands coordinating to three different Pu atoms by O atoms of phosphate groups (Figures S4 and S5 in the Supporting Information). As a result, a cubanelike structure is formed. The four-nuclear cations $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8]^{4+}$ are linked by hydrogen bonds in which N atoms of cytosine rings play the role of donors.

The IR spectrum in the 2000−500 cm^{-1} range contains a large number of highly resolved bands corresponding to vibrations of the cytosine ring and the sugar−phosphate backbone of the dCMP ligand (Figure S6 in the Supporting Information). In the 4000−2000 cm^{-1} region, where vibrations of OH, NH_2, NH, and CH groups could be expected, the intensive diffuse absorbance band is observed with a number of peaks. The positions of the peak maxima were refined by the band deconvolution using a curve-fitting method with a Lorentzian function. In the 1800−1100 cm^{-1} region, the main vibrations of the cytosine base and the sugar ring are observed. The observed high-energy shift of ν(C═O) and ν(C═N) stretching vibrations with respect to values specific for the isolated cytosine[7] is the result of N(3) atom protonation. A similar frequency shift is observed in the spectrum of protonated pyridine $C_6H_5NH^+$. As a result, the spectrum of the Pu complex in the 1800−1100 cm^{-1} region is almost equal to the spectrum of solid cytidine isolated from an acidic solution.[8] The protonation does not impact vibrations of the aromatic ring of cytosine, which are observed at 1540 and 1442 cm^{-1}, values close to the frequencies of pyrimidine ring vibrations.[9] In the 1100−600 cm^{-1} region, the vibrations of the phosphate group are observed; because of phosphate coordination by the Pu atom, the frequencies are lower as compared to the spectrum of the free ligand or $CH_3OPO_3^{2-}$ anion of C_{3v} symmetry (in the latter case, the frequencies are equal to 1115 and 1090 cm^{-1}). In the spectrum of **1**, the $\nu(PO_4)$ stretching vibrations are exhibited by a split band at 1028−948 cm^{-1}.

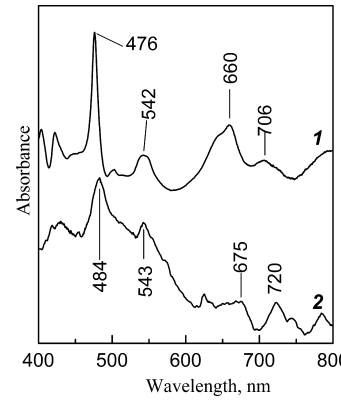

Figure 2. Electronic spectra of a Pu^{IV} stock solution in 1.5 M HNO_3 (curve 1) and solid complex **1** (curve 2).

The electronic absorption spectrum of **1** was measured in the 400−820 nm region (Figure 2). A complete list of the absorption maxima and calculated molar extinction coefficients is presented in Table 1 along with literature values for the spectrum of a Pu^{IV} solution for comparison.[10] The values of the molar absorption coefficients of **1** do not differ significantly from those of a Pu^{IV}(aq) solution. The low-energy shift of the main absorption maximum of Pu^{IV} (λ_{max} = 470 nm in a $HClO_4$ solution) is attributed to coordination of Pu^{IV} by O atoms of the dCMP phosphate group and NO_3^- anions; a similar spectrum change was observed for the Pu^{IV}

(5) X-ray data were collected on a Bruker KAPPA Apex II CCD X-ray diffractometer at 100 K using a sealed graphite monochromatic Mo Kα X-ray source. Data collection, indexing, and cell refinement were handled using *Apex 2* software. The structure was solved by direct methods and refined by full-matrix least squares on F^2.The final refinement included anisotropic displacement parameters for all non-H atoms. H atoms of water molecules were not localized. Crystal data for $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8](NO_3)_4\cdot 2H_2O$: M_r = 3105.19 g·mol^{-1}, 0.16 × 0.19 × 0.20 mm, monoclinic, *C*2, a = 26.8560(7) Å, b = 12.9317(4) Å, c = 13.5287(3) Å, β = 106.563(2)°, V = 4503.5(2) Å^3, Z = 2, ρ_{calcd} = 2.299 g·cm^{-3}, μ = 3.099 mm^{-1}, λ = 0.710 73 Å, T = 100(2) K, $2\theta_{max}$ = 60°, 13 088 reflections were collected, of which 10 993 are independent, R_{int} = 0.038, R = 0.044, wR(F^2) = 0.120.

(6) The IR and UV/vis/NIR spectra were recorded on Specord M80 and Shimadzu UV3100 spectrophotometers, respectively. The sample for the IR study was prepared in the form of a transparent NaCl disk containing 1% of the Pu complex. The sample for electronic spectrum measurement contained 5% of the complex taking into account low extinction coefficients of Pu^{IV}.

(7) Shimanouchi, T.; Tsuboi, M.; Kyogoku, Y. In *Advances in Chemical Physics*; Duchesne, J., Ed.; Interscience Publishers: London, 1965; Vol. *7*, pp 435−498.

(8) Tsuboi, M.; Kyogoku, Y.; Shimanouchi, T. *Biochim. Biophys. Acta* **1962**, *55*, 1–12.

(9) Lautie, A.; Novak, A. *J. Chim. Phys. Phys.-Chim. Biol.* **1968**, *65*, 1359–1362.

(10) Silva, R. J.; Nitsche, H. R. *Radiochim. Acta* **1995**, *70−71*, 377–396.

Table 1. Molar Absorption Coefficients of the Pu^{IV} Ion in the Electronic Spectrum of **1**

Pu^{IV} complex		Pu^{IV}(aq)	
λ, nm	ϵ, $M^{-1}\cdot cm^{-1}$	λ, nm	ϵ, $M^{-1}\cdot cm^{-1}$
484	40	470	49
540	15	555	14.6
675	42	652	36
720	10	726	15.6

complex with ethylenediaminetetraacetic acid, where the main absorption maximum has a value of 495 nm.[11]

The coordination mode of a metal ion depends on the nature of the active centers of the biomolecules. In nucleotides or nucleotide-containing molecules, the coordinating sites are N and O atoms of the nucleobase, as well as O atoms of sugar and phosphate groups. The ability of the ion metal to link to one or another coordination site depends on the reaction conditions, nature and size of the metal ion, and surroundings of the nucleotide. For example, native DNA shows a high coordinating activity of phosphate groups because the majority of nucleobase coordination sites are shielded inside the DNA molecule and participate in hydrogen bonds. The same situation is observed in the studied Pu^{IV} complex **1**, where the metal atom is coordinated by phosphate groups only. In the complexes of d elements with nucleotides, heterocyclic N atoms of the nucleobase as well as any of O atoms of the nucleobase and sugar and phosphate groups may act as donors,[12] forming isolated or polymeric structures. In the only known uranium complex with a nucleotide (adenosinemonophosphate), the uranyl ion is coordinated by a phosphate group as well as 2′- and 3′-hydroxyl groups of sugar with the formation of isolated polynuclear anions.[13]

In conclusion, we presented here the first structural study of a transuranium element interaction with a nucleotide. The crystal structure of the Pu^{IV} complex with dCMP was determined using single-crystal X-ray diffractometry and confirmed by IR and electron spectroscopy. The results show that the phosphate group of the nucleotide is quite effective for plutonium binding. At the same time, it should be noted that, because we used acidic conditions for the synthesis to avoid hydrolysis of plutonium, the N(3) atom of cytosine underwent protonation. In these conditions, the HdCMP monoanion coordinates to the Pu atom through the phosphate group only, although under less acidic conditions, the coordination of the O or heterocyclic N atom of the cytosine base as well as the O atom of the sugar hydroxyl group could be expected.

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Supporting Information Available: Crystal and refinement data for $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8](NO_3)_4\cdot 4H_2O$ in CIF format, thermal ellipsoid representation of a $[Pu_4(NO_3)_8(HdCMP)_4(H_2O)_8]^{4+}$ cation, a list of the main interatomic distances, IR spectrum of **1**, and a list of absorption maxima in the IR spectrum and their assignments. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Boukhalfa, H.; Reilly, S. D.; Smith, W. H.; Neu, M. P. *Inorg. Chem.* **2004**, *43*, 5816–5823.

(12) (a) Pezzano, H.; Podo, F. *Chem. Rev.* **1980**, *80*, 365–401. (b) Begum, N. S.; Manohar, H. *J. Chem. Soc., Dalton Trans.* **1992**, 2277–2281. (c) Kato, M.; Sah, A. K.; Tanase, T.; Mikuriya, M. *Eur. J. Inorg. Chem.* **2006**, 2504–2513. (d) Galy, G.; Mosset, A.; Grenthe, I.; Puigdomenech, I.; Sjoeberg, B.; Hulten, F. *J. Am. Chem. Soc.* **1987**, *109*, 380–386. (e) Giori, G.; Cini, R. *Inorg. Chim. Acta* **1988**, *151*, 153–161. (f) Armentano, D.; Mastropietro, T. F.; Julve, M.; Rossi, R.; Rossi, P.; De Munno, G. *J. Am. Chem. Soc.* **2007**, *129*, 2740–2741.

(13) Szabo, Z.; Furo, J.; Csoregh, J. *J. Am. Chem. Soc.* **2005**, *127*, 15236–15247.