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Interaction of Transuranium Elements with Biologically Important Molecules: Structural and Spectroscopic Study of Np(V) Complexes with Imidazole

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New Np(V) complexes with imidazole, $[NpO_2(CH_3COO)(Im)_2(H_2O)]$, $[(NpO_2)_2(C_2O_4)(Im)_6]\cdot 5Im\cdot H_2O$, and $[NpO_2(NO_2)(Im)_4]$, were synthesized. Their crystal structures were determined using X-ray single-crystal diffractometry. The crystal structures are confirmed by IR and UV−vis spectroscopic data. In all three complexes, neptunium coordinates the imidazole molecule through the nitrogen atom. These complexes are the first example of direct bonding of the imidazole molecule to the actinide atom. These results suggest that coordination of histidine residue in proteins or other imidazole-containing biologically important molecules could occur under usual biological conditions.

Introduction

The chemical characterization of the actinide species is essential for a reliable assessment of the radionuclides' migration into the geological and biological environment. Traditionally, research on actinides in biological systems has focused on routes of heavy metals into food chains. The distribution of radionuclides in primitive organisms and plants was used to estimate their mobility in the environment. However, most of these studies are limited to bulk concentration measurements or dispersion on an elemental basis and do not provide extended chemical information at the molecular level. Complex formation of the actinide species with different ligands acts on the actinides' mobility in the geological and biological environment. Translocation in plants and primitive organisms may be one factor resulting in the entrance of long-life radionuclides into the human food chain. Numerous studies have reported the binding of essential mineral nutrients such Mo, Cu, and Zn as well as toxic metal Ni to biologically important ligands.[1−4] However, the specific behavior of actinides in biological systems is not well studied,[5] and it is much more difficult to model their behavior in natural media. Moreover, the most attention has been devoted to uranium,[6−9] while there is little known about transuranium elements' interaction with biologically important molecules.[10]

The great interest in coordination properties of imidazole ($N_2C_3H_4$) is stipulated by the important role its derivatives play in coordinating metal ions in biological systems.[11] The essential amino acid histidine contains imidazole side chains. Histidine is present in various peptides and enzymes; the histidine molecule can undergo decarboxylation to histamine, which is also a common biological molecule. Being the building block of many proteins, the histidine residues are responsible for the specific binding of metal cations in addition to other side chains such as tryptophan (ring nitrogen), cysteine (thiol), methionine (thioether), serine, threonine, tyrosine (hydroxyl groups), and asparagine (car-

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bonyl group) and main chain amino and carbonyl groups. The imidazole ring moiety is part of the fused ring in the purine, which is incorporated in many biologically important molecules including alkaloids, nucleobases, nucleosides, nucleotides, RNA, and DNA.

Imidazole, which is somewhat more basic than pyridine and slightly more acidic than pyrrole, can exist in several forms depending on conditions. Under neutral conditions, the pyridine-like nitrogen N(3) possesses a pair of electrons for coordination with metal ions in the monodentate mode. In acidic solutions, the N(3) atom can be protonated to form the imidazolium cation, which can form salts with metals including f elements.[12−17] Under strongly basic conditions, the imidazole molecule can undergo deprotonation with the formation of an imidazolate anion, which can serve as a bridging ligand with two equivalent nitrogen atoms available for complexation.

In biological systems, the primary oxidation state in which neptunium will exist is 5+ and the most stable chemical form is NpO_2^+. Under physiological conditions (pH ~ 7.4), the predominant form of imidazole is the neutral molecule, the remaining part of the imidazole molecule is present in the form of an imidazolium cation, and the amount of the anionic imidazolate form in solution is negligible. Taking into account that neptunium is unlikely able to coordinate to pyrrole-like nitrogen, the coordination through pyridine-like nitrogen of histidine residue is expected in proteins. Because of this, the imidazole coordination properties are of interest as a model of transuranium element interaction with histidine side chains in proteins.

We present here experimental results from single-crystal X-ray diffraction as well as optical and IR spectroscopies for complexes of Np(V) with imidazole, $[NpO_2(CH_3COO)(Im)_2(H_2O)]$ (**1**), $[(NpO_2)_2(C_2O_4)(Im)_6]\cdot 5Im\cdot H_2O$ (**2**), and $[NpO_2(NO_2)(Im)_4]$ (**3**). These results clearly demonstrate that imidazole is able to coordinate to the neptunium atom in a monodentate fashion. Because of this, we can conclude that the binding of the imidazole moieies of different biologically important molecules to NpO_2^+ is possible under natural and physiological conditions.

Experimental Section

Caution! *^{237}Np 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.*

Samples Preparation. Hexavalent neptunium-237 stock solution was prepared by a technique that included anion-exchange purification from possible inorganic admixtures followed by precipitation of the oxalate of tetravalent Np in order to avoid any organics. Dissolution and destruction of the oxalate complex were carried out in concentrated nitric acid; then, the solution was evaporated up to wet salts and dissolved in distilled water. The reduction of hexavalent to pentavalent neptunium was performed by adding a $NaNO_2$ solution (2M). Then, an excess of concentrated NH_4OH was added to precipitate NpO_2OH, which was used as a neptunium precursor for the synthesis of compounds **1** and **2**. The precipitate was centrifuged and washed with distilled water five times.

Table 1. Crystal Data and Details of Final Refinement Calculations for Compounds **1**−**3**

compound	**1**	**2**	**3**
a, Å	15.6132(12)	9.7602(4)	8.0715(4)
b, Å	10.5746(8)	10.8928(5)	8.0920(5)
c, Å	7.9019(7)	23.8816(12)	14.5070(8)
α, deg	90	101.988(3)	101.547(3)
β, deg	90	94.976(3)	104.552(3)
γ, deg	90	104.996(2)	95.024(3)
V, *Z*	1304.63(17), 4	2372.37(19), 2	889.01(9), 2
space group	$Cmc2_1$	$P\bar{1}$	$P\bar{1}$
no. of reflns	2511	34563	22922
no. of unique reflns	1623	14095	49431
$2\theta_{max}$	60	66	60
R, $wR(F^2)$	0.026, 0.075	0.026, 0.060	0.050, 0.135

For the synthesis of **1**, NpO_2OH was dissolved in 0.5 M acetic acid. Compound **1** was obtained during isothermal evaporation at 22 °C of a mixture containing a solution of Np(V) acetate and imidazole with a Np/imidazole molar ratio of 1:1.

Compound **2** was isolated from the solution containing Np(V) tartrate (obtained by dissolution of NpO_2OH in L-tartaric acid) and imidazole at a ratio of 1:1 during isothermal evaporation at 26 °C.

Compound **3** was obtained by the following procedure. $NaNO_2$ was added to the $NpO_2(NO_3)_2$ solution in water. Np(VI) instantly reduced to Np(V). Then, imidazole dissolved in water was added. The Np/Na/imidazole molar ratio was equal to 1:5:5.

Single-Crystal X-Ray Crystallography. The data were collected on Bruker KAPPA APEX II and Bruker Smart diffractometers with CCD area detectors using graphite monochromated Mo Kα (λ = 0.71073 Å) radiation. Single crystals of 1–3 were mounted on a glass fiber and transferred to the goniometer for data collection. The crystals were cooled to 100 K under a cold nitrogen gas stream. The structures were solved using the SHELXTL software package, and the absorption corrections were made with SADABS. The structures were refined by full-matrix least-squares on F^2. All of the non-hydrogen atoms were readily located, and their positions were refined anisotropically. Hydrogen atoms were also easily located and refined isotropically. Main crystal data and details of final refinement calculations are presented in Table 1.

Spectroscopy. NIR and IR spectra were measured using Shimadzu UV3100 and Specord M80 spectrometers, respectively. Samples of ~2 wt % of the solids were prepared in NaCl pellets.

Results and Discussion

Crystal Structures. The crystal structure of $[NpO_2(CH_3COO)(Im)_2(H_2O)]$ (Figure 1) shows that the neptunium atom is found in overall pentagonal bipyramidal surroundings. The pentagonal equatorial plane of neptunium consisting of three oxygen and two nitrogen atoms is planar to within 0.284 Å. The axial ONpO fragment is near linear with Np−O distances of 1.826(11) and 1.831(11) Å and an O−Np−O angle of 174(1)°. The neptunyl oxygens are disordered over two positions symmetrical about the *m* plane.

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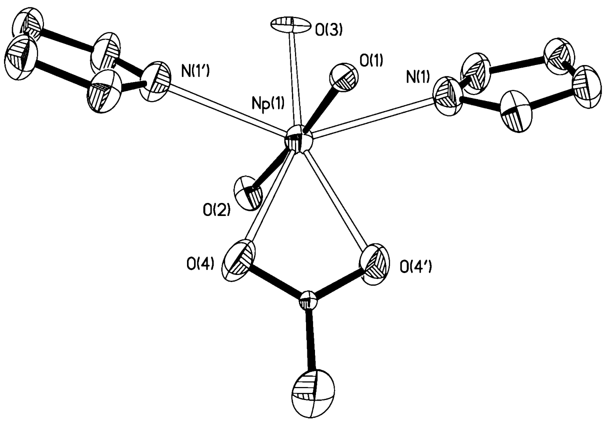

Figure 1. Fragment of the crystal structure of [$NpO_2(CH_3COO)(Im)_2(H_2O)$].

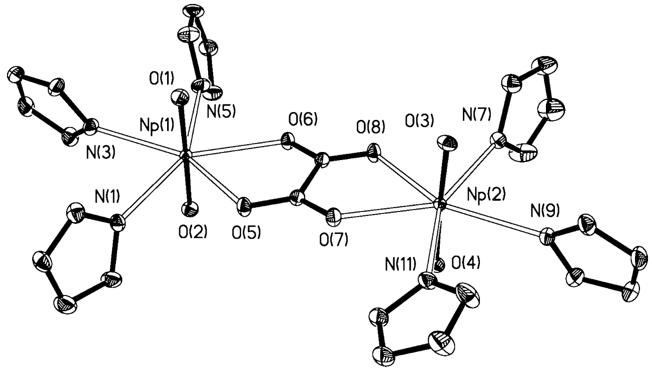

Figure 2. Complex dinuclear molecule [$(NpO_2)_2(C_2O_4)(Im)_6$] in the crystal structure of [$(NpO_2)_2(C_2O_4)(Im)_6$]·5Im·H_2O.

The acetate ligand is bidentate with Np−O distances of 2.528(4) Å. The two trans imidazole molecules are coordinated through nitrogen with a unique Np−N bond distance of 2.548(5) Å. Each near-planar (mean deviation from the plane is 0.055 Å) heterocycle ring is inclined by an angle of 42.2° to the neptunyl equatorial plane. The angle between imidazole rings is equal to 32.5°.

The crystal structure of [$(NpO_2)_2(C_2O_4)(Im)_6$]·5Im·H_2O consists of dinuclear [$(NpO_2)_2(C_2O_4)(Im)_6$] molecules (Figure 2) as well as solvated imidazole and water molecules. Two neptunium atoms in the dimer are crystallographically independent but have similar surroundings. Both neptunyl groups are near-symmetrical and linear: Np−O distances are equal to 1.832(2) and 1.850(2) Å for Np(1) and 1.824(2) and 1.860(2) Å for Np(2); O−Np−O angles are 178.54(7) and 177.06(6)° for Np(1) and Np(2), respectively. The equatorial neptunium planes are more planar than for **1** (mean deviations are equal to 0.116 and 0.111 Å) and are near coplanar (the angle between equatorial planes is 3.7°).

Oxalate anion functions as a tetradentate bridging anion with Np−O distances in the range of 2.472(2)−2.500(2) Å. Six imidazole molecules are coordinated by neptunium atoms with Np−N distances from 2.525(2) to 2.582(2) Å. Solvated imidazole and water molecules participate in H bonds.

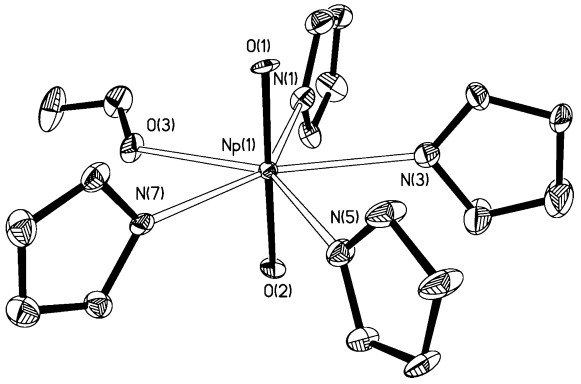

Figure 3. Crystal structure of [$NpO_2(NO_2)(Im)_4$].

In [$NpO_2(NO_2)(Im)_4$], neptunium is also found in pentagonal bipyramidal surroundings (Figure 3). The equatorial plane consists of the nitrogen atoms of four imidazole molecules and the oxygen atom of the nitrite anion. Np−N distances range from 2.542(6) to 2.546(5) Å. The nitrite anion acts as monodentate anion with a Np−O distance equal to 2.526(5) Å. The N−O distances in the nitrite ion depend on the function of the oxygen atoms and are longer for bridging oxygen (1.275(8) Å) as compared to terminating oxygen (1.237(9) Å).

The neptunyl group is almost perpendicular to the equatorial plane (angle is equal to 90.2°). The Np−O distances are equal to 1.847(5) and 1.850(5) Å; the O−Np−O angle is equal to 178.9(2)°.

IR Spectra. IR spectra of the complexes contain a large number of absorption bands corresponding to the vibrations of different functional groups. In the 4000−2000 cm^{-1} region, the most intense bands may be assigned to vibrations of coordinated imidazole. It is known that the spectrum of the parent imidazole including deiterated derivatives exhibits at least eight vibrations in the 3200−2400 cm^{-1} region, which are attributed to the stretching vibrations N(NH···N) and N(CH) and to the H bond between N(1)H and N(3) of two imidazole molecules. The coordination of the ligand by metal atoms leads to the elimination of some of the bands in the spectra of **1** and **3**. In the 3200−2400 cm^{-1} interval of the spectrum of **2**, a very broad continuum band is observed with several maxima corresponding to vibrations of both coordinated and uncoordinated imidazole molecules.

In the 2000−400 cm^{-1} region, in addition to imidazole vibrations, bands corresponding to vibrations of anions and NpO_2^+ cations are observed. The frequencies and their possible assignments are presented in Table 2. The acetate and oxalate show lower frequencies as compared to the corresponding neutral groups. The stretching vibrations, ν(NC) of the imidazole ring and ν(CC) of the oxalate ion, show a higher frequency shift. Bands at 1358, 1206, and 838 cm^{-1} are assigned to stretching and deformation vibrations. In all three spectra, the stretching frequencies of NpO_2^+ groups are about 800 cm^{-1}.

NIR Spectra. The NIR spectra of all compounds contain characteristic intense narrow peaks corresponding to f−f electronic transition. The maxima positions and extinction coefficients are presented in Table 3. There are two peaks in the spectrum of complex **2** corresponding to the presence of two crystallographically unique Np atoms in the structure.

Table 2. Selected Absorption Frequencies of IR Spectra of Np(V) Complexes

1	**2**	**3**	assignment
3508m	3526, 3458m	3528m	N(N(1)H) free
3412m	3408m		N(HOH)
3208sh			N(CH_3)
3168, 3152s	3156, 3144s	3164s	N(CH)Imd
3002, 2954, 2860, 2612w	2916, 2858, 2984, 2618w	2944, 2852, 2602w	combination bands
1644	1640		δ(HOH)
1588w	1592w	1600sh	δ(ring)
1534s	1556		N_{as} (COO^-)
1498m	1494m	1484m	N (C−N)Imd
1444s	1432s		N_s (COO^-)
		1358m	N (N=O)
		1206m	N (N−O)
1068	1056	1064s	δ (C(2)H)
		892w	N (C−C)
		838s	δ(ONO)
798s	792m	802 msh	N (NpO_2^-)
618m	632m	616s	ρ(CH)

Table 3. Peak Position and Extinction Coefficient of the Most Intense Bands in the NIR Spectra

compound	**1**	**2**	**3**
λ_{max}, nm	992	998, 1002	1001
ε, l/mol·cm	280	130, 100	215

Conclusions

The single-crystal X-ray structures of Np(V) complexes with imidazole, [$NpO_2(CH_3COO)(Im)_2(H_2O)$], [$(NpO_2)_2(C_2O_4)(Im)_6$]·$Im_5$·$H_2O$, and [$NpO_2(NO_2)(Im)_4$], have been determined; UV−vis and IR spectroscopic data are fully consistent with the X-ray structures. This is the first example of the coordination of the imidazole molecule to the actinide cation in the solid state. In contrast to uranyl compounds, where imidazole or its derivatives usually function as outer-sphere cations,[13−20] in all three neptunyl complexes, the metal atom directly coordinates more than one imidazole molecule. The only known example of imidazole ring coordination to uranyl is the complex with 1-methylimidazole, [$UO_2(CH_3COO)_2$(Me-Im)$_2$], which was derived from a nonaqueous solution,[21] namely, from ionic liquid, while all Np(V) complexes were obtained in water solutions.

Compound **2** represents an example of the in situ synthesis of oxalic acid. A similar situation was observed in the syntheses of [$(UO_2)_2(C_2O_4)(C_5H_6NO_3)_2$] and {$N(C_8H_{20})$}$_2$-[$(UO_2)_4(O)_2(C_2O_4)(H_2C_2O_3)_2$], where oxalic acid was formed during hydrothermal synthesis from L-glutamic acid[22] and 1,4-diazabicyclo[2.2.2]octane,[23] respectively. Oxalate formation was also observed under the precipitation of uranyl nitrato-oxalate from ionic liquid containing 1-butyl-3-methylimidazolium nitrate, acetone, and nitric acid.[19] The authors suggested that the oxidizing of acetone by nitric acid might be the oxalate source. The reaction of Np(V) methanesulfonate with imidazole resulted in a reduction of neptunium and in situ synthesis of the oxalate ion with the formation of Np(IV) complex (Him)[$Np(C_2O_4)(CH_3SO_3)_3(H_2O)_2$].[12]

It should be also noted that the complex [$NpO_2(NO_2)(Im)_4$] is one of the rare examples of actinide−nitrite complexation. The only other structurally characterized compound is Np(V) complex {$C(NH_2)_3$}$_2$[$NpO_2(NO_2)(NC_4O_2H_4)_2$].[24]

According to the methods used, the results clearly show that imidazole will directly coordinate to the neptunyl cation at a pH where imidazole is not protonated, for example, under natural and physiological conditions. Thus, we can expect that the coordination of histidine residues of proteins and other imidazole-containing biologically relevant molecules to neptunium is possible.

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Supporting Information Available: Complete tables of crystal and structural refinement data, atomic coordinates, bond lengths and angles, anisotropic displacement parameters, and hydrogen coordinates for compounds **1**−**3** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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