# Uranyl sequestration: synthesis and structural characterization of uranyl complexes with a tetradentate methylterephthalamide ligand[1]

Chengbao Ni,[a] David K. Shuh,[a] Kenneth N. Raymond[a,b]∗

Uranyl complexes of a bis(methylterephthalamide) ligand (**LH₄**) have been synthesized and characterized by X-ray crystallography. The structure is an unexpected [Me₄N]₈[L(UO₂)]₄ tetramer, formed via coordination of the two MeTAM units of **L** to two uranyl moieties. Addition of KOH to the tetramer gave the corresponding monomeric uranyl methoxide species [Me₄N]K₂[LUO₂(OMe)].

The uranyl ion (UO_2^{2+}) is the most common species for uranium under oxidizing conditions and *in vivo*.[2-4] During the past few decades, various approaches have been used to the design of uranyl-selective chelators: several multidentate ligands based on phosphonic ligands,[5-8] siderophore-based units (Scheme 1),[9] or a combination of both[5-11] have been identified as effective. Studies by Durbin, Raymond, and coworkers have evaluated the efficacy of multidentate ligands containing catechol derivatives, 3-hydroxy-*N*-methyl-2-(*1H*)-pyridinone (Me-3,2-HOPO), and 1-hydroxypyridin-2-one (1,2-HOPO) binding units. Several of these ligands are orally active decorporation agents and effective in reducing UO_2^{2+} in both kidneys and skeleton (removal efficiency in the sequence MeTAM > CAM(S) > CAM(C) > Me-3,2-HOPO > 1,2-HOPO).[9, 12-14] Of the ligands evaluated, the 5LiO-(Me-3,2-HOPO) and 5Li-CAM(S) ligands were identified as low or non-toxic ligands with high efficiency.[14] Subsequently, tetradentate bis-Me-3,2-HOPO ligands for uranyl sequestration have been intensely studied.[15-18] It has been shown that 2Li (such as ethylene and thiophene) linked ligands[15-17] exhibit the most planar coordination mode about UO_2^{2+} and that the 4Li ligand binds the most strongly to UO_2^{2+} in all bis-Me-3,2-HOPO ligands.[18] Pellet-Rostaing and coworkers have reported uranyl sequestration studies of a series of water soluble five-carbon linked bis-CAM(S) ligands[10] as well as calixarene ligands incorporating two CAM(S) or 1,2-HOPO units.[11] They showed that the efficiency of the bis-CAM(S) ligands depends on the rigidity and steric hindrance of the spacers and that the combination of calixarene and CAM(S) or 1,2-HOPO features

different uranyl affinities at different pH.[10, 11]
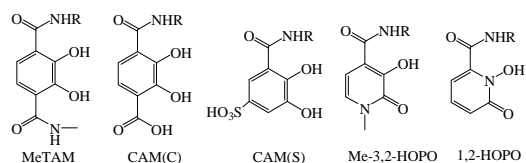
Scheme 1 Siderophore-based binding units.

Despite the fact that the MeTAM unit binds more strongly to UO_2^{2+} than CAM(S) or HOPO,[9] uranyl sequestration studies with MeTAM ligands have attracted less attention, due primarily to the very severe toxicity associated with the earlier 3Li-(MeTAM) and 4Li-(MeTAM) ligands.[14] In addition, the diprotic nature of MeTAM gives the corresponding uranyl complex -2 (or more) charge, which greatly complicates the crystallization process for structural analysis. Given these issues, the strong binding affinity of MeTAM makes this class of ligands attractive for nuclear waste remediation. Due to the low-toxicity and improved solubility of the 5LiO backbone as shown by previous studies with the 5LiO-(Me-3,2-HOPO) ligand,[14] we prepared the MeTAM analog 5LiO-(MeTAM) (**LH₄**, Scheme 2) to study the structures of its uranyl complexes. Herein, we describe the synthesis and characterization of the uranyl complexes with **L**. X-ray crystallography has revealed that [**LUO₂**]$^{2-}$ forms an unexpected tetramer [**L(UO₂)**]$_4^{8-}$, in which the two MeTAM units of each **L** bind to two UO_2^{2+} ions. The addition of KOH changes the preferred coordination nature of the tetramer to give the corresponding uranyl methoxide species [**LUO₂(OMe)**]$^{3-}$ with the two MeTAM units of **L** binding to the same uranyl moiety.
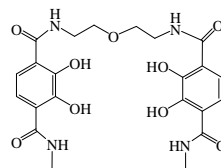
Scheme 2. The 5LiO-(MeTAM) ligand (**LH₄**).

The uranyl complex [Et₃NH]₂[**L**UO₂]·2H₂O was prepared by reaction of UO₂(NO₃)₂·6H₂O with **L**H₄ in the presence of a slight excess of Et₃N and isolated as a brown solid.† [Et₃NH]₂[**L**UO₂]·2H₂O is highly soluble in MeOH or H₂O. Attempts to crystallize the complex as the [Et₃NH]⁺ salt from various solvents were unsuccessful. By replacing [Et₃NH]⁺ with Me₄N⁺, red crystals readily formed with slow diffusion of Et₂O into a MeOH/DMF (50:1) solution of the uranyl complex.

The solid state structure of [**L**UO₂]²⁻ is a tetramer (Fig.1); [Me₄N]₈[**L**(UO₂)]₄ crystallizes in space group *I4₁/acd* with a large unit cell (*ca.* 42,300 Å³). There is one [**L**(UO₂)]²⁻ moiety in the asymmetric unit and there are eight tetramers in the unit cell.† As shown in Fig. 1, [**L**(UO₂)]₄⁸⁻ has a helical structure, in which the ligands adopt a bridging coordination mode with two TAM units in each **L** coordinated to two uranyl ions. Uranyl complexes in which the bis-CAM or bis-Me-3,2-HOPO ligands show a bridging coordination mode have been reported; however, this has only been observed in ligands with either very rigid backbones[17, 19] or very long linker lengths.[16] Considering the moderate length and high flexibility of the 5LiO backbone and the fact that the closely related 5Li-(Me-3,2-HOPO) ligand forms a monomeric uranyl complex,[15] the bridging coordination of **L** in [**L**(UO₂)]₄⁸⁻ is surprising. The fifth position of the uranyl ions in the tetramer is occupied by an amide oxygen atom, due probably to ligand distortion which brings the amide oxygen atom in the vicinity of the uranyl ion.
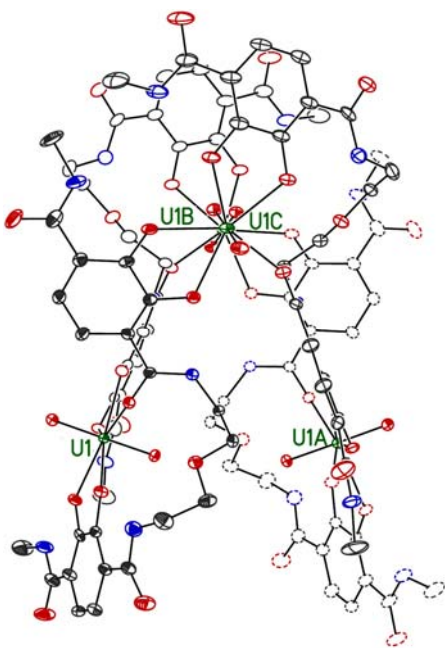

Fig. 1. Crystal structure of [**L**UO₂]₄⁸⁻ (30% probability) without hydrogen atoms. The four ligands are presented in four different ellipsoid formats. Carbon atoms are grey, nitrogen atoms blue, oxygen atoms red, and uranium atoms green**.**

In [**L**(UO₂)]₄⁸⁻, the slightly lengthened U-O(oxo) distances (1.785(5) and 1.794(6) Å) than those in bis-Me-3,2HOPO or 1,2-HOPO complexes[16, 17, 20] are probably due to the presence of more negatively charged ligands. The U-O_{phenolate} distances are in the range 2.342(6) to 2.397(5) Å, comparable to the average U-O distance of 2.371(4) Å in Na₄[U(catechol)].[21] A close examination of the structure revealed that the average U-O_{phenolate}

distances to the two MeTAM units are slightly different (2.345(6) Å and 2.380(5) Å) with the shorter U-O_{phenolate} distance corresponding to the smaller torsion angle (12.9(2)°) between the MeTAM plane and the O-U-O plane. Thus, the bending of the MeTAM unit may lengthen the U-O_{phenolate} distance slightly. The U-O_{amide} distance of 2.365(5) Å in [**L**(UO₂)]₄⁸⁻ is similar to the U-O_{phenolate} distances, indicating strong interactions between uranium and the amide oxygen. Such unusually strong interactions are precedented by those between the uranyl ion and a DMF or DMSO molecule occupying the fifth position of Me-3,2-HOPO complexes.[15] The average MeTAM bite angle is 66.4(2)°, close to those in Na₄[U(catechol)][21] and Me-3,2-HOPO uranyl complexes.[15-17, 20]

The sum of the five equatorial O-U-O angles in [**L**(UO₂)]₄⁸⁻ is 360.5(2)° and the mean deviation of the six equatorial atoms (five oxygens and one uranium) from the equatorial plane is 0.078(4) Å, suggesting a good planar geometry around UO₂²⁺. Unlike the monomeric bis-Me-3,2-HOPO uranyl complexes, in which the O_{phenolate}-U-O_{phenolate} angle can be viewed as a "ligand bite angle" and depends strongly on the linker length (65.2(2)° to 94.1(1)°),[16] there is no such angle in [**L**(UO₂)]₄⁸⁻. Thus, a comparison of this angle is not applicable. Instead, comparison of the remaining three angles to the average value of 75.7°, obtained by assuming each ligand (MeTAM or HOPO) bite angle approximately 66.5°, can be employed.† In a highly relaxed uranyl coordination environment, such as with untethered binding units, the remaining angles should be close to 75.7°, as is exactly the case in the untethered uranyl complex (Pr-Me-3,2-HOPO)₂UO₂(DMF) with angles of 74.2(2), 76.8(2), and 76.1(2)°, respectively.[15] In [**L**(UO₂)]₄⁸⁻, the corresponding angles of 76.0(2), 77.1(2), and 74.6(2)° are within less than 1.5° to the average value, suggesting an equally highly relaxed uranyl coordination environment. Thus, the bridging coordination of **L** and the tetramer formation are consequences of achieving a highly relaxed and planar geometry around UO₂²⁺.
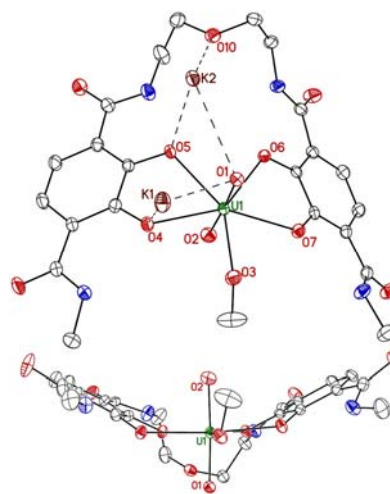
Fig. 2 Crystal structure of [**L**UO₂(OMe)]³⁻ (30% probability) without hydrogen atoms. Up: structure of [K₂**L**UO₂(OMe)]⁻; down: side view of [**L**UO₂(OMe)]³⁻.

Addition of a slight excess of KOH into a MeOH solution of [Et₃NH]₂[**L**UO₂]·2H₂O causes an immediate color change from brown to bright red. The ¹H NMR spectrum showed the appearance of a methoxide ligand at 5.54 ppm. In addition, the

amide proton signals suggested the presence of multiple species.† These observations indicate that the dominant species is the uranyl methoxide and that the methoxide ligand forms an equilibrium with other molecules, such as MeOH or DMSO, in solution.

By using a combination of K^+ and Me_4N^+ ions, large dark red crystals of $[Me_4N]K_2[LUO_2(OMe)]$ were obtained. $[Me_4N]K_2[LUO_2(OMe)]$ crystallizes in space group *P-1* with two $[LUO_2(OMe)]^{3-}$ moeities in the asymmetric unit. The $O_{amide}\cdots K^+\cdots O_{oxo}$ interactions link $[LUO_2(OMe)]^{3-}$ moieties to form a three dimensional network in the solid state.† Similar $K^+\cdots O_{oxo}$ interactions have been observed in the solid state structures of other uranyl complexes.[3, 22-26] Interestingly, one oxo group in $[LUO_2(OMe)]^{3-}$ shows interactions with two K^+ ions (2.825(3) and 3.164(2) Å), while the other oxo group shows no such interaction. Aside from the association of K^+ ions, the most striking differences between $[LUO_2(OMe)]^{3-}$ and $[L(UO_2)]_4^{8-}$ are the coordination mode of **L** and the fifth ligand of UO_2^{2+}. In $[LUO_2(OMe)]^{3-}$, the two MeTAM units of **L** are coordinated to one UO_2^{2+} ion (Fig. 2) with a methoxide ligand occupying the fifth position. The dramatically different coordination mode of **L** is most likely due to the combined effects of the methoxide ligand and K^+ ions. The methoxide ligand is a much stronger donor (U-O(3) = 2.288(3) Å)[27] than the amide oxygen and its coordination makes the second MeTAM unit free of distortion. In addition, interactions of the K^+ ion (K2) with both the backbone oxygen (O10) and the uranyl oxo group (O1) bring the second MeTAM unit within the vicinity of uranyl ion, to which the first MeTAM unit of **L** has also been bound.

As shown in Fig. 2, $[LUO_2(OMe)]^{3-}$ shows a rather ruffled structure with large torsion angles (25.4(2) to 33.7(2)°) between the MeTAM planes and the corresponding O-U-O planes. The bent binding of the MeTAM units is partially due to the length of the 5LiO backbone, since a similarly ruffled structure with bent HOPO binding was observed in the 5Li-(Me-3,2-HOPO) uranyl complex.[15] The $K^+\cdots O_{phenolate}$ interactions further contribute to the bending because the torsion angles mentioned above are always larger for the MeTAM unit with $K^+\cdots O_{phenolate}$ interactions than those without in $[LUO_2(OMe)]^{3-}$. The sums of the equatorial angles (360.4(2) and 360.3(2)°) are close to 360° and the mean deviation of the equatorial atoms from the equatorial planes is *ca.* 0.065 Å, suggesting a similarly good planar geometry around UO_2^{2+} as the tetramer. Due to the presence of $K^+\cdots O(1)$ interaction, the U-O(1) distance is *ca.* 0.01 Å longer than the corresponding U-O(2) distance. The U-$O_{phenolate}$ distances (2.350(2) to 2.412(2) Å) and the MeTAM bite angles (65.81(8) to 66.44(8)°) are similar to those in $[LUO_2]_4^{8-}$ (see above). The remaining three equatorial angles in $[LUO_2(OMe)]^{3-}$ are in the narrow range of 65.81(8) to 78.02(9)°, which are considerably closer to 75.7° than those in the 5Li or *m*-xyl-(Me-3,2-HOPO) uranyl complexes,[15, 16] indicating a much more relaxed coordination environment around UO_2^{2+} in $[LUO_2(OMe)]^{3-}$ than those in the Me-3,2-HOPO complexes.†

In summary, we have synthesized and structurally characterized the uranyl complexes of a bis-MeTAM ligand for the first time. Structural analysis of $[L(UO_2)]_4^{8-}$ shows that the tetramer formation is governed by the highly relaxed and planar coordination geometry around UO_2^{2+}. The corresponding uranyl methoxide complex forms a monomeric salt structure with inclusion of a methoxide ligand. The results presented highlight the effect of uranyl coordination geometry in the molecular structures and will provide information for the design of uranyl sequestering agents based on the TAM unit.

Notes and references

*a*Chemical Science Division, Lawrence Berkeley National Laboratory
*b*Department of Chemistry, University of California, Berkeley, CA, 94720, USA. E-mail: raymond@socrates.berkeley.edu; Tel:+1 510-642-7219; Fax: +1 510-486-5283.

1. Part XX in the series "Specific Sequestering Agents for the Actinides." For Part XX, see reference 18.
2. J. G. Hamilton, *Reviews of Modern Physics*, 1948, **20**, 718.
3. S. Fortier and T. W. Hayton, *Coord. Chem. Rev.*, 2010, **254**, 197.
4. N. N. Greenwood and A. Earnshaw, *Chemistry of the Elements*, Pergamon Presss, New York, 1997.
5. T. Bailly, R. Burgada, T. Prange and M. Lecouvey, *Tetrahedron Lett.*, 2003, **44**, 189.
6. G. Y. Xu, C. H. Yang, B. Liu, X. H. Wu and Y. Y. Xie, *Heteroat. Chem*, 2004, **15**, 251.
7. M. Sawicki, J. M. Siaugue, C. Jacopin, C. Moulin, T. Bailly, R. Burgada, S. Meunier, P. Baret, J. L. Pierre and F. Taran, *Chem.-Eur. J.*, 2005, **11**, 3689.
8. R. Burgada, T. Bailly, T. Prange and M. Lecouvey, *Tetrahedron Lett.*, 2007, **48**, 2315.
9. A. E. V. Gorden, J. D. Xu, K. N. Raymond and P. Durbin, *Chem. Rev.*, 2003, **103**, 4207.
10. A. Leydier, D. Lecercle, S. Pellet-Rostaing, A. Favre-Reguillon, F. Taran and M. Lemaire, *Tetrahedron*, 2008, **64**, 6662.
11. A. Leydier, D. Lecercle, S. Pellet-Rostaing, A. Favre-Reguillon, F. Taran and M. Lemaire, *Tetrahedron*, 2008, **64**, 11319.
12. P. W. Durbin, B. Kullgren, J. Xu and K. N. Raymond, *Radiat. Prot. Dosim.*, 1994, **53**, 305.
13. P. W. Durbin, B. Kullgren, J. D. Xu and K. N. Raymond, *Health Phys.*, 1997, **72**, 865.
14. P. W. Durbin, B. Kullgren, S. N. Ebbe, J. D. Xu and K. N. Raymond, *Health Phys.*, 2000, **78**, 511.
15. J. D. Xu and K. N. Raymond, *Inorg. Chem.*, 1999, **38**, 308.
16. G. Szigethy and K. N. Raymond, *Inorg. Chem.*, 2010, **49**, 6755.
17. G. Szigethy and K. N. Raymond, *Inorg. Chem.*, 2009, **48**, 11489.
18. G. Szigethy and K. N. Raymond, *Chem. Eur. J.*, 2011, **17**, 1818.
19. P. Thuery and B. Masci, *Supramol. Chem.*, 2003, **15**, 95.
20. J. Casellato, P. A. Vigato, S. Tamburini, R. Graziani and M. Vidali, *Inorg. Chim. Acta*, 1983, **72**, 141.
21. S. R. Sofen, K. Abudari, D. P. Freyberg and K. N. Raymond, *J. Am. Chem. Soc.*, 1978, **100**, 7882.
22. C. J. Burns, D. L. Clark, R. J. Donohoe, P. B. Duval, B. L. Scott and C. D. Tait, *Inorg. Chem.*, 2000, **39**, 5464.
23. J. A. Danis, M. R. Lin, B. L. Scott, B. W. Eichhorn and W. H. Runde, *Inorg. Chem.*, 2001, **40**, 3389.
24. P. Thuery and B. Masci, *Dalton Trans.*, 2003, 2411.
25. P. L. Arnold, A. J. Blake, C. Wilson and J. B. Love, *Inorg. Chem.*, 2004, **43**, 8206.
26. P. L. Arnold, D. Patel, A. J. Blake, C. Wilson and J. B. Love, *J. Am. Chem. Soc.*, 2006, **128**, 9610.
27. I. G. Santos and U. Abram, *Inorg. Chem. Commun.*, 2004, **7**, 440.