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COMMUNICATION

Expanded Campestarene Hosts for Tetra- and Dinuclear Uranyl(VI) Complexes†

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The first expanded campestarenes based on a keto-enamine scaffold have been constructed using uranyl acetate as a template. Macrocycles with six and eight aryl rings in their backbone host dinuclear and tetranuclear uranium(VI) species, respectively. The complexes were characterized by SCXRD, FT-IR, UV-Vis, and NMR spectroscopy, and DFT calculations corroborated their structures.

Macrocycles have played a pivotal role in the development of supramolecular chemistry and continue to inspire new research. Schiff-base macrocycles in particular have been intensely explored owing to their ease of preparation and their ability to chelate metals.[1] They are usually prepared from the reaction of a diamine with an aromatic dialdehyde, and have been investigated for host-guest chemistry,[2–4] multimetallic cluster growth,[5–10] sensing,[11–13] and self-assembly.[13-16]

In 2011, we reported campestarenes, flat macrocycles that have 5-fold symmetry.[16] Campestarenes **1** are formed selectively in high yield *via* an *in situ* reduction and condensation approach of a single precursor, a 6-nitrosalicylaldehyde derivative (Figure 1a). These macrocycles show solvent- and temperature-dependent tautomerization between a keto-enol and enol-imine form, as shown in Figure 1b-c.[17]

The internal cavity of campestarenes, with hydroxyl and aldimine groups, appears capable of binding to ions and forming multimetallic complexes.[5,8] Unfortunately, our efforts to develop coordination chemistry with campestarenes have been frustrated by the sensitivity of the imine bonds to hydrolysis. Replacing the aldehyde with a ketone may improve the stability of the macrocycle since imines derived from ketones (i.e., ketimines) are markedly less prone to hydrolysis than aldimines.[18,19] However, the preparation of ketimines often requires harsh conditions, a catalyst, and/or azeotropic removal of water.[20]

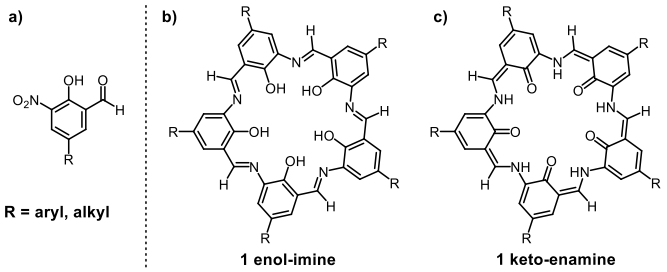

Fig 1. General structure of a) generic 6-nitrosalicyl aldehyde monomer, and the campestarene **1** in the b) enol-imine c) keto-enamine tautomers.

The linear uranyl dication is the most common form of uranium(VI) in water.[21] Its large radius, oxophilic nature, and prevalence for high coordination numbers make uranyl an attractive choice for templating large macrocycles. Although the chemistry of the uranyl ion is well-developed, there are few studies of U in macrocyclic chemistry.[22–28]

Here we report the first expanded campestarene macrocycles based on hemi-salphen ketimine ligands containing tetranuclear and dinuclear μ-OH uranyl(VI) ions in the cavity. These complexes are very stable and illustrate the use of uranyl as a template for macrocycle chemistry, with potential applications in uranium sequestration and as metallohosts.

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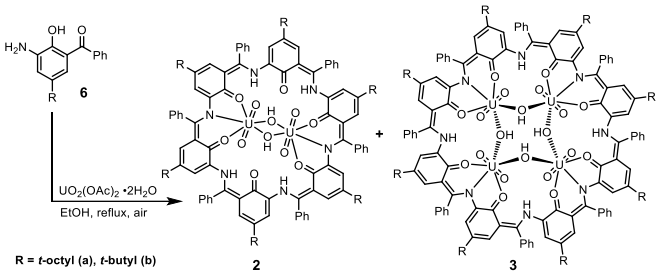
† Electronic Supplementary Information (ESI) available: Crystallographic and spectroscopic data for **2a**, **2b**, **3a**, and **3b** are given. Select ^{1}H NMR experiments, UV-Vis studies and DFT computational data and analyses. CCDC: 1862463, 1862464, 1862465, 1862466. See DOI: 10.1039/x0xx00000x

Monomers **6a-b** were prepared in three steps from the corresponding phenol derivative (Scheme S1). Bulky *p*-*t*-octyl and *p*-*t*-butyl groups were selected to prevent aggregation and enhance solubility in the target macrocycle. Although aldehyde analogues rapidly condense to give campestarenes, ketones **6** are stable in solution and as solids. We explored the use of Lewis acid catalysts (e.g., $TiCl_4$[19,29] & $Sc(OTf)_3$[30,31]) to condense **6a** into macrocycles, but only low yields of oligomeric compounds were obtained. Brønsted acid catalysis (e.g., *p*-toluenesulfonic acid in *n*-BuOH) showed only trace amounts of macrocycle by mass spectrometry (MS) after several weeks. Similar results were obtained using toluene as a solvent with azeotropic removal of water. Unable to isolate the ketimine analogue of macrocycle **1**, we turned to metal templating.



Scheme 1. Preparation of complexes **2** and **3** from monomer **6**

Marks showed that condensation of 1,2-dicyanobenzene with UO_2Cl_2 did not form the expected uranyl phthalocyanine complex, but instead resulted in a pentameric complex, with the uranium(VI) center adopting a pentagonal bipyramidal geometry inside a superphthalocyanine ligand.[27] Inspired by this work, we investigated uranyl templation with our ligand system.

Reaction of **6a** with of 0.2 eq of $UO_2(OAc)_2{\cdot}2\ H_2O$ (Scheme 1) in ethanol resulted in a dark solution. Analysis of the reaction mixture by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) MS showed the presence of two major products with *m*/*z* = 2413.2 and 3531.4. The two products, deep-purple **2a** and red **3a**, were successfully separated by column chromatography. Single crystals of both **2a** and **3a** were obtained and were analyzed by SCXRD. By increasing the proportion of UO_2^{2+} used from 0.2 to 0.5 equiv, yields improved from <1% to *ca.* 7% and *ca.* 20% for **2a** and **3a**, respectively. Importantly, high concentrations (*ca*. 150 mM) are required to form the macrocyclic complexes.

SCXRD data revealed that **2a** is comprised of a ketimine macrocycle with six arene rings in the backbone (Figure 2) hosting a dimeric $[(UO_2)_2(\mu\text{-}OH)_2]^{2+}$ species in the center, bound by two O,N,O chelating groups from the macrocycle. The compound is neutral with four ketone and two amino ligands coordinating the metal centers with two bridging μ-OH ligands. μ-OH protons could not be observed in the diffraction data, but they appear at 11.32 ppm in the ^{1}H NMR spectrum (DCM-d_2). Equatorial U-O bond lengths for the macrocyclic ligand are 2.433(4) and 2.304(3) Å, similar in length to the bridging O_μ ligands. The uranium(VI) atoms adopt a slightly distorted pentagonal bipyramidal geometry, with a long N-U bond length of 2.592(4) Å. Axial U-O bonds are 1.769(4)–1.782(4) Å, normal for $[UO_2]^{2+}$ complexes .[32]

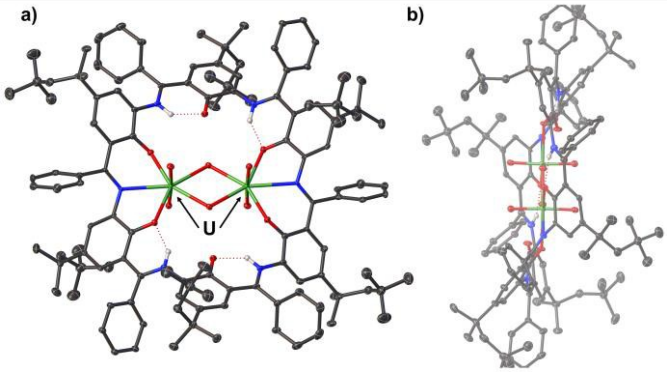


Figure 2. Solid-state molecular structure of **2a** determined by SCXRD. a) Top view and b) side view. Colors: white (H), black (C), blue (N), red (O), and green (U). Solvent molecules and non-hydrogen bonding hydrogen atoms omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

From the crystal structure, the macrocycle in **2a** adopts a chair-like conformation with vertices of *ca.* 6.5 Å (Figure S22), likely due to repulsion between the phenyl rings. This leads it to have approximately C_i symmetry in the solid state. There is intramolecular hydrogen bonding within the cavity (Figure 2a), between O2…H2N2 and O3…H3N1. The long distances between O3 and H3 imply localized hydrogen bonding, unlike campestarenes, which have a continuous network of hydrogen bonds. Interestingly, the arene groups of the macrocycle are in the keto-enamine tautomeric form, in which the proton is situated on the nitrogen atom rather than on the oxygen atom and aromaticity is lost in the aminophenol group.

C-O and C-N bond lengths (1.292(6)–1.315(6) Å and 1.312(6)–1.232(7) Å, respectively) are intermediate between single and double bonds, which implies the negative charge of the O,N,O chelate is delocalized along the arene system, common for the hemi-salphen motif.[32,33] The uncoordinated C-O and C-N bond lengths correspond to C-O double and C-N single bonds, suggesting the keto-enamine form of **2a**.[33] This was unexpected because previous investigations of campestarenes showed crystallization in the enol-imine form.[17]

DFT calculations were undertaken on simplified models **2c** (R = H, phenyl substituents removed) and **2d** (R = H) at different levels of theory *in vacuo* . Calculations on **2d** confirmed that the complex belongs to the C_i point group, is μ-OH bridged rather than μ-O, and is not planar, though the extent of the chair-like geometry is reduced compared to the SCXRD results. On the other hand, 78MWB/AVTZ/6-31g/M06 calculations on a complex including the meso-phenyl groups suggest deviation from planarity is due mainly to steric repulsion of the phenyl rings. Additionally, **2a** is more tautomerically inert than campestarenes, and exists only in the keto-enamine form.

Although **2a** is not flat in the solid state, it is fluxional in solution; ^{1}H NMR spectroscopy (DCM-d_2) shows C_{2h} symmetry. The most diagnostic signals are for the *meta* protons on the monomeric units, which appear as four doublets ($^4J_{HH}$ = 2.2 Hz) that integrate for 2 protons each, and a singlet integrating for 4

protons. Resonances at 18.59 and 17.13 ppm in DCM-d_2 are assigned to the ketimine NH protons. The singlet at 11.32 ppm is assigned to the μ-OH protons. These assignments were confirmed by H/D exchange with D_2O (Figure S19). ^{1}H NMR spectroscopy of **2a** at elevated temperatures (in 1,1,2,2-tetrachloroethane-d_2) gave improved resolution that allowed additional NMR signals to be assigned (Figure S21). A singlet at 6.87 ppm split into two doublets, consistent with the splitting pattern expected for **2a**.

The IR spectrum of **2a** shows a strong $[UO_2]^{2+}$ ν_{as} band at 907 cm^{-1} which has significant contribution from a μ-OH bending mode. The two NH bending vibrations observed at 1530 and 1515 cm^{-1}, respectively, and the absence of a C=N ν_{as} at *ca*. 1600 cm^{-1} also confirm the keto-enamine tautomeric form of **2a**.

UV-Vis spectroscopy of **2a** in DCM showed an intense band at 500 nm that is reminiscent of the intense absorption band observed at ~550 nm in campestarenes.[17] Electronic spectroscopy in an array of solvents with varying dielectric constants did not result in drastic changes to the spectra. This lack of solvatochromism seems to indicate the tautomeric inertness of **2a**, in agreement with the calculations.

Complex **2b** was also prepared and structurally characterized; it showed similar properties to complex **2a**.

SCXRD of **3a** revealed that it is a tetranuclear uranium complex captured inside a ketimine macrocycle having eight aryl rings (Figure 3). The complex adopts a "saddle-like" conformation with approximate S_4 symmetry. Each of the four uranyl(VI) groups in **3a** is chelated by an O,N,O group of the macrocycle, similar to the bonding mode observed in compounds **2a** and **2b**. The uranyl groups are bridged by four μ-OH groups, the H atoms of which were able to be modeled for complex **3a**. The U-O_{ax}, U-O_{μ}, U-N, and hydrogen bond lengths are all similar to those observed in **2a** (Table S2).

Complex **3b** with terminal *t*-butyl groups was also structurally characterized by SCXRD. The solid-state structure of **3b** is very similar to **3a**, with similar bond lengths and angles.

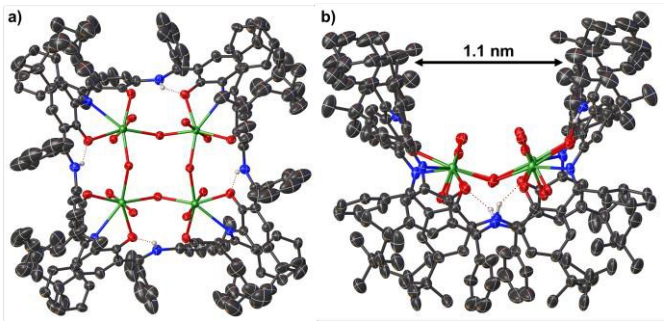


Figure 3. Crystal structure of **3a**, a) top view and b) side view. Thermal ellipsoids are shown at the 50% probability level.

The "saddle-like" structure of **3** allows for the formation of two binding pockets within the complex, the external hydrophobic one being ~1.1 nm in diameter. The internal cavity resembles a metallocrown,[34] with four oxygen atoms in alternating up-down geometry. Long U-O_{μ} bond lengths (2.315(5)–2.328(5) Å) and O_{μ}-O_{μ} distances (2.984(8) Å) creates a cavity that can potentially host a small cation, such as Li^+ or Na^+. With this in mind, host guest studies are currently being conducted. The eight arene rings in the backbone of the macrocycle adopt a bent boat-like motif, which is similar to the antiaromatic compound cyclooctatetraene (Figure S23).

While complex **3** seems to have approximate S_4 symmetry in the solid state, DFT computations at the 78MWB/AVTZ/6-31g/M06 and ωB97x levels of theory *in vacuo* confirmed this. This model with R=H and lacking the meso-phenyl groups showed a saddle-shaped geometry very close to the experimental data, suggesting that the geometry of complex **3** is less sensitive to peripheral substitution than **2**. Furthermore, computations on a model complex with μ-O bridging lacks the S_4 symmetry and has a very different geometry compared to the solid-state structure of **3** (see SI). These results confirm that the bridging groups are μ-OH.

We had difficulty interpreting the ^{1}H NMR data of **3a**, possibly because the bulky *t*-octyl groups led to slow interconversion of multiple conformations. Thus, we discuss the ^{1}H NMR data for **3b** with *t*-butyl substituent. The ^{1}H NMR spectrum of **3b** is simpler than that of **2b** owing to the 4-fold symmetry of the macrocyclic complex in solution (Figure 4). The NH protons (δ 18.45 ppm in DCM-d_2) are highly deshielded because of intramolecular hydrogen bonding. A broad resonance at 12.18 ppm is assigned to the four μ-OH ligands. The *meta* protons of the aryl groups in the macrocycle appear as four doublets ($^4J_{HH}$ = 2.3 Hz) and the *t*-butyl groups appear as two singlets at 0.79 and 0.74 ppm. The ^{1}H NMR spectrum of **3a** in DMSO-d_6 (Figure S20) has similar resonances to those shown in Figure 4 for **3b** in DCM-d_2, but the low solubility of complexes **2** and **3** in DMSO made analyses difficult.

FT-IR spectroscopy of **3a/b** shows very similar patterns to **2a/b**, except with a stronger ν_{as} $[UO_2]^{2+}$ at 925 cm^{-1}. Based on the strong N-H stretch and the absence of C=N stretches, **3a** and **3b** are also in the keto-enamine tautomeric form. The UV-Vis spectra of **3a/b** are red shifted by about 10 nm relative to **2a/b**; absorption maxima for **3a** and **3b** are at 515 and 510 nm, respectively.

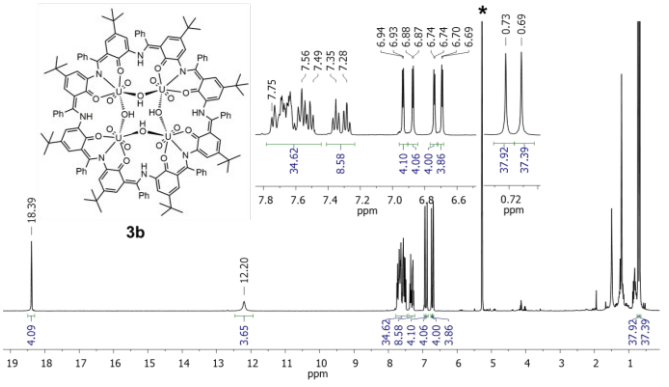


Figure 4. ^{1}H NMR spectrum of complex **3b** (DCM-d_2, 25 °C, 400 MHz). * = DCM-d_2

The $[(UO_2)_4(OH)_4]^{4+}$ motif found in **3** is rare, and only a few compounds in the CCSD have similar binding modes, most of which are purely inorganic salts of $[UO_2]^{2+}$. The only related example of a U_4 cluster was published by Thuéry, where a calix[8]arene was reacted with $UO_2(NO_3)_2{\cdot}6H_2O$ to give a macrocyclic U_4 cluster with O,O,O-tridentate environments.[35,36]

The geometry of that complex is similar to **3**, with six phenoxo ligands coordinating to a $(UO_2)_4(\mu\text{-}O/OH)_4$ cluster. In their case, the macrocycle templated the formation of the $(UO_2)_4$ cluster, in contrast with our results where the macrocycle is templated by the uranyl(VI) cation.

Complexes **2** and **3** are very stable and form under mild conditions, suggesting that the macrocycles themselves are promising candidates for uranyl sequestering agents. Attempts to demetallate **2a** or **3a** to liberate the free macrocycles were unsuccessful. The complexes are stable for several months in DCM-d_2 or DMSO-d_6.

In conclusion, we have discovered expanded campestarene macrocycles templated by uranyl(VI). The macrocycles host interesting di- and tetranuclear $[UO_2]^{2+}$ complexes in their interior. Held together with μ-OH bridges, these complexes are highly chemically and thermally stable. The smaller dinuclear system **2** is housed in a hexameric macrocyclic ligand. The larger U_4 macrocyclic complex **3** is bound within the cavity of an octameric macrocycle with a saddle-like geometry and could have interesting host-guest properties due to its large hydrophobic binding pocket along with its highly electronegative internal cavity.

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Conflicts of interest

There are no conflicts to declare.

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TOC IMAGE

Expanded campestarene macrocycles with keto-enamine structures host dinuclear and tetranuclear hydroxo-bridged uranyl(VI) clusters in their interiors.