

Functionalized Metalated Cavitands via Imidation and Late-Stage Elaboration

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Efficient methods for the preparation of functionalized metallated cavitands are described. Functional groups can be either introduced by an imidation of metal-oxo complexes or by a late-stage elaboration of the imido ligands. By using diversified iminophosphorane (PPh₃=NR) reagents, π -conjugated pyrene, redox active ferrocene, and polymerizable nor-

Introduction

Metalated cavitands with endohedral ligand affinity are of interest as a result of their selectivity provided by the precise shape of the cavity.^[1] In comparison to related macrocyclic compounds such as calixarenes, resorcinarenes or cyclodextrins, metalated cavitands often possess enhanced binding capabilities that allow for selective molecular recognition in solution.^[1,2] These receptors make use of strong directional metal-ligand interaction and hence metalated cavitands are appealing candidates for directed self-assembly and chemosensing.[1b] In addition, these systems can be considered as metalloenzyme mimics and can display unique catalytic reactivity as a result of the confined environment defined by the cavity.^[3,4] Given these striking characteristics, methods to functionalize metalated cavitands that are adaptable to construct complex architectures are likely to find utility. Direct late-stage functionalization of metalated cavitands mitigates the synthetic uncertainties in preparing complex ligands. However, this approach is rarely explored as a consequence of the lability of metalated cavitands and difficulties of their isolation from complex mixtures. Herein, we report a strategy to access a diversity of functionalized metalated cavitands through the formation of metal-imido complexes and subsequent elaborations.

Calixarenes are an important class of macrocyclic compounds with numerous applications in sensing and supramolecular chemistry.^[5] The multiple phenol groups of this scaffold are capable of chelating early transition metals, and hence calixarenes are supporting ligands for metalated cavibornene moieties were successfully introduced. Furthermore, the iodo and alkynyl groups on the imido ligands are capable of undergoing efficient Sonogashira cross-coupling and copper-catalyzed azide alkyne cycloaddition reactions, thereby providing facile access to complex architectures containing metallated cavitands.

tands.^[1a,1d,6] Among the metalated cavitands, tungsten(VI) calix[4]arene complexes have displayed considerable utility as a result of their stability and established coordination chemistry.^[7] Although some tungsten calixarene complexes were synthesized and characterized, the method to introduce these scaffolds to other platforms with various functions are limited. The examples of these compounds have largely leveraged established calixarene chemistries that focus on transformations of phenol groups on the lower rim (Scheme 1, a) or electrophilic reaction *para* to the oxygen groups.^[8] Although these methods can be used to create ligating groups to assemble metalated cavitands, greater diversity is possible by adding functionality independent of the calixarene group. To this end we have targeted direct transformations of tungsten-oxo calixarene complexes as a result of their facile preparation and inherent stability. We envisioned that various imido ligands could be directly introduced through imidation reactions and further elabora-

Previous work: functionalized calixarenes



This work: functionalized metalated cavitands



Scheme 1. Functionalized calixarenes and metalated cavitands.

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tion of the imido ligands can produce complex functional architectures (Scheme 1, b).

Results and Discussion

Tungsten calixarene imido complexes were previously prepared from air-sensitive $W^{VI}(=NR)_2Cl_2$ or a calixarene tungsten(IV) olefin adduct, both of which are not readily accessible.^[9] We recently found that simple imido ligands can be incorporated by a direct imidation of the tungstenoxo calixarene complexes by using iminophosphorane reagents.^[7c] A diversity of these reagents were directly prepared from the corresponding anilines using PPh₃/ iPr_2EtN/C_2Cl_6 (Scheme 2, a) or by reacting arylazides with triphenylphosphine (Scheme 2, b).^[10] We found that the two ortho-methyl groups on the arylimido ligand are crucial to the success of the transformation, and therefore, various functionalities were installed on the para-position of the aniline. In addition to enhancing the stability of the corresponding tungsten-imido complex, methyl groups are proposed to impart sufficient nucleophilicity to the iminophosphorane.^[11,12] It is noteworthy that the two methods in Scheme 2 are complimentary. For instance, anilines 1a-1d have low solubility in acetonitrile and the conversion to arylazides is low, whereas the alkynyl group of 1h is not compatible with the reaction conditions of method (a). To examine the scope of this method, we selected a series of functional groups that are relevant to various applications. For example, long alkyl chains and pyrene moieties are known to display favorable interactions with carbon-based nanomaterials, such as carbon nanotubes and graphene (2a and 2b).^[13] Attachment of redox active ferrocene moieties creates electrochemically responsive materials (2c and 2d).^[14] A polymerizable norbornene moiety was examined with the aim to produce polymers appended with metalated cavitands (2e). Additionally, to explore the possible elaboration of the metal cavitands at a late-stage, synthetic handles, such as iodo- and alkynyl groups were installed on the imido ligands (2f-g).

With iminophosphorane reagents in hand, we endeavored to prepare functionalized tungsten cavitands. The tungsten-oxo calixarene complex was chosen as a substrate and is readily prepared in situ from tBu-calixarene and WOCl₄. The subsequent addition of various iminophosphorane reagents (2a-2h) in refluxing toluene afforded the corresponding tungsten-imido cavitands. As shown in Scheme 3, the tungsten-imido cavitands were produced in good to excellent yields (70-84%) by this one-pot procedure. Functional groups, such as alkene (4e), alkynyl (4h), halide (4f, 4g), and ferrocene (4c, 4d) were tolerated under the reaction conditions, thereby providing access to highly diversified metal cavitands. It is noteworthy that the tungsten cavitands are stable to column chromatography using silica gel and the byproduct triphenylphosphine oxide is easily separated from the cavitand products. The structures of 4a, 4c, and 4d were unambiguously confirmed by X-ray crystallography (Figure 1).^[15]



Scheme 2. Preparation of functionalized iminophosphorane reagents.



Scheme 3. Preparation of functionalized tungsten cavitands through imidation.

Bimetallic metal cavitands are appealing building-block candidates for constructing self-assembling supramolecular polymers. A molybdenum dinuclear cavitand had been previously reported, its preparation required the use of a dimolybdenum complex precursor.^[16] To enable facile access to dinuclear metalated cavitands, we first prepared iminophosphoranes **2i** and **2g** using method (b) as shown in Scheme 2, and tested their performance in accessing di-



Figure 1. X-ray crystal structures of tungsten cavitands.

nuclear cavitands. Although the reaction was sluggish in refluxing toluene at 125 °C, we found that the use of a higher refluxing temperature (155 °C) afforded good yields of dinuclear tungsten cavitands. Both of the linear and the bent cavitands were prepared using this method. It should be mentioned that isolated tungsten-oxo complex (5) was employed in this reaction to enable a precise control of the reactant ratio. The X-ray crystal structure confirmed the linear geometry of **4i** (Scheme 4).^[15] The well-defined coordination chemistry and predictable geometry makes these dinuclear cavitands interesting building blocks to construct supramolecular assemblies with ligands that can fit into the cavitand and coordinate to the tungsten center. We have attempted the construction of supramolecular assembly by mixing 4i with N, N'-(dodecane-1,12-diyl)diformamide. The formation of assembly in both solution and solid state was confirmed by nuclear magnetic resonance (NMR) and infrared (IR) spectroscopy (Figure S1-S5 in the Supporting Information).

We next examined the feasibility of direct elaboration of the tungsten-imido cavitands. Although these cavitands are thermally stable, they tend to decompose under highly basic or acidic conditions, which poses synthetic challenges for further transformations. We envisioned that the transitionmetal-catalyzed reactions employing mild reaction conditions might be compatible with these metal cavitands.^[17] However, our initial attempts with palladium-catalyzed Suzuki and Stille coupling reactions failed.^[18] Interestingly, Sonogashira coupling using an organic base was very efficient^[19] and we also found the copper-catalyzed azide alkyne cycloaddition (also known as the click reaction) proceeded smoothly in aqueous solution (Scheme 5).^[20] Given the wide applications of these coupling reactions in synthetic chemistry and material science, these late-stage elaborations will allow facile incorporation of metalated cavitands into a variety of platforms.

Considering the availability of diverse methods to modify calixarenes, diversified architectures could be constructed by replacing one of the methylene bridges or by upper-rim functionalization of aromatic rings. To this end, we have introduced a long alkyl group at the *meso* position of calixarene,^[21] and the corresponding product **4m** represents



Scheme 4. Preparation of dinuclear tungsten cavitands and X-ray crystal structure of **4i**:2CH₃CN.



Scheme 5. Late-stage elaboration of tungsten-imido cavitands.

the first example of a metalated calixarene cavitand with a substituent on the methylene bridge. The pyrene-functionalized calixarene was also prepared for potential use as a molecular tweezer.^[22] As illustrated in Scheme 6, these modified calixarenes were smoothly transformed to the corresponding tungsten cavitands under our reaction conditions.

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Scheme 6. Preparation of functionalized tungsten cavitands.

Conclusions

In summary, we have developed an efficient strategy to access functionalized metalated cavitands. The functional groups could be introduced either by a direct imidation of a tungsten-oxo calixarene complex by using various iminophosphorane reagents or by a late-stage elaboration of the imido ligands of the metalated cavitands. Various moieties, such as π -conjugated pyrene, redox active ferrocene, and polymerizable norbornene were successfully incorporated, demonstrating the broad applicability of the current method. Furthermore, the late-stage elaboration of tungsten cavitands by Sonogashira reaction and coppercatalyzed azide alkyne cycloaddition reaction opens up opportunities for introducing these highly selective endohedral Lewis acidic receptors into various existing platforms. We expect the current strategy will promote the exploitation of new functional materials based on metalated cavitands.

Supporting Information (see footnote on the first page of this article): Full experimental procedures, characterization data and 1 H and 13 C NMR spectra.

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