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Functionalized Metallated Cavitands via Imidation and Late-Stage Elaboration

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Abstract

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 (PPh$_3$=NR) reagents, π-conjugated pyrene, redox active ferrocene and polymerizable norbornene 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.

Keywords

calixarene; cavitand; late-stage functionalization; supramolecular

Introduction

Metallated 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, metallated 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 metallated 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 metallated cavitands that are adaptable to construct complex architectures are likely to find utility. Direct late-stage functionalization of metallated cavitands mitigates the synthetic uncertainties in preparing complex ligands. However, this approach is rarely
explored as a consequence of the lability of metallated cavitands and difficulties of their isolation from complex mixtures. Herein, we report a strategy to access a diversity of functionalized metallated cavitands through the formation of metal-imido complexes and subsequent elaborations.

Calixarenes represent an important class of macrocyclic compounds with numerous applications in sensing and supramolecular chemistry. The multiple phenol groups of this scaffold are capable of chelating early transition metals, and hence calixarenes are supporting ligands for metallated cavitands, among the metallated cavitands, tungsten (VI) calix[4]arene complexes have displayed considerable utility as a result of their stability and established coordination chemistry. 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. Although these methods can be used to create ligating groups to assemble metallated 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 elaboration 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)2Cl2 or a calixarene tungsten (IV) olefin adduct, both of which are not readily accessible. We recently found that simple imido ligands can be incorporated by a direct imidation of the tungsten-oxo calixarene complexes using iminophosphorane reagents. A diversity of these reagents were directly prepared from the corresponding anilines using PPh3/iPr2Et2/C2Cl6 (Scheme 2, a) or by reacting arylazides with triphenylphosphine (Scheme 2, b). We found 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. It is noteworthy that the two methods in Scheme 2 are complimentary. For instance, anilines 1a–d 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 favourable interactions with carbon-based nanomaterials, such as carbon nanotube and graphene (2a,b). Attachment of redox active ferrocene moieties creates electrochemically responsive materials (2c,d). A polymerizable norbornene moiety was examined with the aim to produce polymers appended with metallated 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 t-Bu-calixarene and WOCl₄. The subsequent addition of various
iminophosphorane reagents (2a–h) 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 by product 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).

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.[15] To enable facile access to dinuclear metallated cavitands, we first prepared
iminophosphoranes 2i and 2g using method (b) as shown in Scheme 4, and tested their
performance in accessing dinuclear 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). 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 SI).

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 transition-metal catalyzed reactions employing mild reaction conditions
might be compatible with these metal cavitands.[16] However, our initial attempts with
palladium-catalyzed Suzuki and Stille coupling reactions failed.[17] Interestingly,
Sonogashira coupling using an organic base was very efficient[18] and we also found the
copper-catalyzed azide alkyne cycloaddition (also known as click reaction) proceeded
smoothly in aqueous solution (Scheme 5).[19] Given the wide applications of these coupling
reactions in synthetic chemistry and material science, these late-stage elaborations will allow
facile incorporation of metallated 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,[20] and the corresponding product 4m represents as the first example of metallated calixarene cavitand with a substituent on the methylene bridge. The pyrene-functionalized calixarene was also prepared for potential use as a molecular tweezer.[21] As illustrated in Scheme 6, these modified calixarenes were smoothly transformed to the corresponding tungsten cavitands under our reaction conditions.

**Conclusions**

In summary, we have developed an efficient strategy to access functionalized metallated cavitands. The functional groups could be either introduced by a direct imidation of tungsten-oxo calixarene complex using various iminophosphorane reagents or by a late-stage elaboration of the imido ligands of the metallated 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 via Sonogashira reaction and copper-catalyzed 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 metallated cavitands.

CCDC 1405018 (for 4a:CH₃CN), 1405019 (for 4c:CH₃CN), 1405069 (for 4d:CH₃CN), and 1405020 (for 4i:2CH₃CN) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif)

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

**Acknowledgments**

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**References**


11. Tungsten calixarene phenylimido complex is known to be in equilibrium between monomer and dimer in solution. See ref 9b.


Figure 1.
X-ray crystal structures of tungsten cavitands.
Scheme 1.
Functionalized calixarenes and metallated cavitands.
Scheme 2.
Preparation of functionalized iminophosphorane reagents.
Scheme 3.
Preparation of functionalized tungsten cavitands through imidation.
Scheme 4.
Preparation of dinuclear tungsten cavitands and X-ray crystal structure of 4i:2CH₃CN.
Scheme 5.
Late-stage elaboration of tungsten-imido cavitands.
Scheme 6.
Late-stage elaboration of tungsten imido cavitands.