Inorganic Chemistry

Synthesis and Structural Studies of Gallium(III) and Iron(III) Hemicryptophane Complexes

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S Supporting Information

ABSTRACT: New gallium(III) and iron(III) endohedral complexes were obtained from a hemicryptophane ligand bearing suitable binding sites for octahedral metal coordination. The solid-state structures of the free host and of the complexes were determined by single-crystal Xray diffraction analysis. The metal ion is linked to the hydrazone nitrogen and the phenolate oxygen atoms, yielding a distorted octahedral geometry around the encapsulated metal. The two isomorphous structures of the metal complexes reveal the exclusive formation of $P\Delta/$ $M\Lambda$ enantiomeric pairs.

ryptophanes, with their spherical molecular cavity, are wellknown for their high propensity to form van der Waals host-guest complexes. Because of their essentially lipophilic character, the binding properties are restricted to neutral organic guests, rare gas, and ammonium salts.¹ Recent investigations with water-soluble derivatives allowed extension of the recognition properties of cryptophane hosts to metal ions.² The related hemicryptophane hosts have been designed to introduce endohedral functionalities in the molecular cavity, giving a ditopic character to these molecules. One of the first examples of a hemicryptophane supramolecule was based on a phosphotrihydrazone moiety and showed an affinity for aromatic guest molecules.³ From such a structure, it appeared that adding specific binding sites having an affinity for metal ions could lead to new metal hemicryptophane complexes. This has been achieved by the synthesis of several hemicryptophanes bearing suitable coordinating substituents. For instance, oxidovanadium,⁴ zinc,⁵ and copper complexes⁶ have been reported. In these structures, the metal atom is located inside the molecular cavity, leading to an endohedral complex. Some of these complexes present interesting and original catalytic properties, and the inner space of the molecular receptor behaves like a chemical reactor at the nanoscale. Similarly, proazaphosphatrane superbases⁸ and their conjugate acid azaphosphatranes⁹ have been incorporated into the cavity of a tren-hemicryptophane ligand, where the highly reactive center is encapsulated in the molecular cavity. Such supramolecular systems are obviously of prime importance in the design of new catalysts that are expected to be more robust and highly selective.

Herein, we report on the design and synthesis of a heteroditopic molecular receptor, which presents the octahedral environment for M^{3+} metal ions, and maintains the C_3 symmetry of the cyclotribenzylene (CTB) platform. Our efforts have yielded a compound that forms complexes with Ga^{III} and Fe^{III} ions, which are encapsulated into the polar part of the molecular cavity. These complexes contain a lipophilic space in close proximity to the metal ion, and the possibility to increase the length of the side chains opens the route to a new family of sizemodular molecular cavities for the simultaneous encapsulation of metal ions and neutral substrates.

The synthetic pathway that led to the hemicryptophane 1 is outlined in Scheme 1 and follows the strategy recently developed for the preparation of tren-hemicryptophane derivatives.¹⁰ The CTB 2 is synthesized in three steps from vanillyl alcohol according to the published procedure.¹¹ Selective monoallylation of 2,3-dihydroxybenzaldehyde gave compound 3,¹² which reacted with 1,4-dibromobutane in acetonitrile in the presence of K₂CO₃ to afford compound 4 in 61% yield. The CTB 2 reacted with an excess of 4 in N.N-dimethylformamide/hexamethylphosphoramide in the presence of NaOH to give the tripropenyloxy-protected compound 5 in 55% yield. Deprotection of the phenol groups in 5 was performed following the known procedure by using palladium(III) acetate/triphenylphosphine in ethanol in the presence of formic acid and triethylamine to give the precursor **6** in 70% yield. The reaction of **6** with phosphotrihydrazide $P(S)(NMeNH_2)_3^{13}$ in tetrahydrofuran led to the hemicryptophane 1 in 54% yield, which was characterized by ¹H, ¹³C, and ³¹P NMR, electrospray ionization mass spectrometry, and X-ray diffraction.

The gallium and iron complexes Ga@1 and Fe@1 were obtained by treating a solution of 1 in 1,1,2,2-tetrachloroethane with $Ga(acac)_3$ or $Fe(acac)_3$, respectively (Scheme 1). Ga@1 was obtained in 70% yield as a bright-yellow solid. Similarly, Fe@1 gave a dark-blue crystalline compound in 86% yield. The diamagnetic Ga@1 complex was characterized by mass spectrometry and ¹H, ¹³C, and ³¹P NMR spectroscopy in CDCl₃. The signal of the phenolic protons disappears and the resonance of the imine protons is low-field-shifted by 0.3 ppm because of the electronic deficiency of the gallium ion, in

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Scheme 1. Synthesis of the Hemicryptophane 1 and Metal Hemicryptophane Complexes Ga@1 and Fe@1



accordance with complexation of the metal ion in the phosphorylated part of the host molecule. The Fe@1 complex was characterized by mass measurement, and its electron paramagnetic resonance (EPR) spectrum (g = 4.1; X band) is consistent with a high-spin Fe^{III} iron in an octahedral environment. The ¹H NMR spectrum shows diamagnetic signals assigned to the protons of the CTB moiety (Figure S11). This confirms that the iron ion is located in the phosphotrihydrazone core of the host molecule.

The molecular structures of the hemicryptophane 1 and both metal complexes were obtained from single-crystal X-ray diffraction studies. The solid-state structure of host 1 is shown in Figure 1. The molecule adopts a pseudo- C_3 symmetry, where



Figure 1. X-ray molecular structures of $C_7H_8@1$: (left) P- α -helix and (right) M- β -helix enantiomers (the encapsulated toluene molecule is green).

the P–S bond is oriented outward and aligned along the C_3 axis of the CTB unit. This arrangement defines a molecular cavity occupied by one toluene molecule. The linkers that bind the phosphotrihydrazone moiety to the CTB unit adopt a clockwise or anticlockwise orientation, inducing α or β helicity, which can define diastereomeric isomers due to the M or P configuration of the CTB cap (namely, the two enantiomeric pairs M- α -helix/P- β -helix and M- β -helix/P- α -helix). Interestingly, the centrosymmetric crystal of 1 contains only the M- β -helix/P- α -helix pair of enantiomers, indicating that the configuration of the CTB unit directs the helical arrangement of the linkers.

In the Ga@1 and Fe@1 hemicryptophane complexes, the metal atom is nested in the phosphotrihydrazone core and bound to the three imine nitrogen atoms and the three phenol oxygen atoms, leading to a distorted octahedral geometry of the metal center (selected bond distances and angles are given in Table S1). The P–S bond is directed outward from the molecular cavity, and the sulfur, phosphorus, and metal atoms are aligned

with the pseudo-3-fold axis of the molecule. The complexes present two stereogenic centers: the CTB unit (P or M configuration) and the octahedral coordination site (Δ or Λ configuration; Figure S15), which should lead to the existence of two diastereomeric racemates (M Δ /P Λ) and (P Δ /M Λ).

The isostructural Ga@1 and Fe@1 complexes consist of only one racemate $(P\Delta/M\Lambda)$ (Figures 2 and S16). Most likely,



Figure 2. Stereoview of the X-ray molecular structure of the Fe@1 complex (the $M\Lambda$ enantiomer is shown). Color code: C, gray; N, blue; O, red; Fe, light blue; P, magenta; S, yellow.

formation of the complex is diastereoselective because of the significant conformational strains that should occur in the M Δ /P Λ diastereomers, where nonfavorable interactions between the linking chains [O(CH₂)₄O] and the methoxy groups are expected. The octahedral metallic center and the chiral CTB unit induce a right- and left-handed helical arrangement of the O(CH₂)₄O linkers in the P Δ and M Λ enantiomers, respectively. A parallel comparison can be made with the structure of the free hemicryptophane ligand 1 described above, where the configuration of the CTB unit controls the clockwise or anticlockwise helical arrangement of the linkers.

In conclusion, we have shown that the CTB and phosphotrihydrazone moieties can be combined to lead to a hemicryptophane structure, which presents a ditopic character with polar and lipophilic binding sites inside the same molecular cavity. The new thiophosphorylated hemicryptophane 1 bearing three phenol groups is able to form octahedral metal complexes with Ga^{III} and Fe^{III} ions. NMR and X-ray diffraction studies of the complexes showed that the metal is nested inside the thiophosphorylated part of the molecule. Both metal complexes exhibit a helical structure induced by the octahedral metal center; the chirality of the CTB moiety induces exclusive formation of the P Δ /M Λ racemates.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorg-chem.5b02750.

Materials and instrumentation, synthetic procedures, NMR and EPR spectra, electrospray ionization mass spectra, crystal data, and details of structure refinement (PDF)

Crystallographic data in CIF format (CIF)

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Notes

The authors declare no competing financial interest.

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