Preparation of an Ester-Substituted Triscatechol Ligand and Characterization of the Corresponding M_4L_4 Titanium(IV) Complex

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Abstract: The ester-substituted triscatechol ligand **L**-H_6 can be easily prepared in a triple imine condensation reaction. The required trisamine is prepared starting from diphenylamine and 2-bromobenzoic acid methylester. Upon coordination of titanium(IV) ions the tetrahedral M_4L_4 coordination compound is obtained, which due to the symmetry breaking substituent exists as a mixture of isomers. However, the complex can be unambiguously characterized by ESI-MS.

Key words: ligand, self assembly, coordination compound, imine, container molecule

The formation of molecules with well-defined internal space for host–guest chemistry is a challenge. Such compounds are of interest due to the features of the interior, allowing the stabilization of unusual species, or the promotion or catalysis of chemical reactions. Molecular containers can be either formed in a step-by-step covalent synthesis or more easily in self-assembly processes utilizing noncovalent interactions like hydrogen bonding, electrostatics, or metal coordination.[1]

Since several years we investigate the preparation and coordination behavior of triangular ligands, which bear chelating-metal-coordination sites at the corners (Figure 1).[2,3] With appropriate metal ions they form in a self-assembly process M_4L_4 metallosupramolecular tetrahedra exhibiting a huge internal cavity. The complexes are able to encapsulate guest molecules in their interior.[4]

Container molecules are of interest due to their ability for guest uptake. However, in order to modify the container itself, it is of interest to attach some anchor to the ligand which in subsequent studies would allow the attachment of chiral or reactive groups, catalytically active sites, or simply to interlink containers to obtain novel porous soft materials.

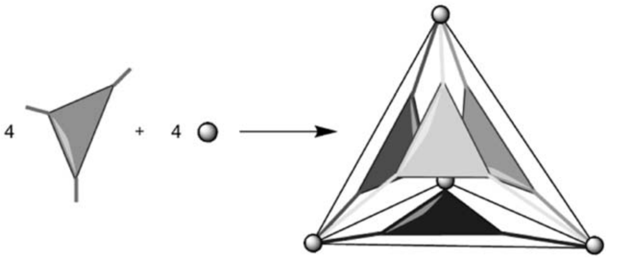

Figure 1 Schematic representation of the self-assembly of M_4L_4 container molecules from tritopic triangular ligands and appropriate metal ions

In here, the preparation of the triscatechol imine ligand **L**-H_6 is described, which forms the tetranuclear titanium(IV) complex $Na_8[\mathbf{L}_4Ti_4]$. Due to the formation of a mixture of isomers, the complex cannot be well characterized by NMR spectroscopy but ESI-MS proves to be the ideal tool for the characterization of the container.

Synthesis of the ligand **L**-H_6 starts with the copper-mediated coupling of diphenylamine (**1**) with 2-bromo methylbenzoate (**2**) in the presence of potassium carbonate and sodium sulfate in nitrobenzene as solvent at 220 °C following the protocol of Ahn.[5] After recrystallization from *n*-hexane–ethyl acetate (9:1) and column chromatography using the same solvent mixture, triaryl amine **3** is obtained in 53% yield (Scheme 1).

The triple nitration of compound **3** to obtain **4** proved to be tricky. Under mild conditions the ester-substituted unit does not react, while harsher nitrating conditions afforded overnitrated product. Finally, nitration of one equivalent of **3** in glacial acetic acid–acetic anhydride (4:1) with addition of one drop of concentrated nitric acid at 10 °C, heating to 75 °C and addition of further nitric acid (total of 3.2 equiv) afforded after chromatographic workup (silica, *n*-hexane–EtOAc = 3:1) the desired product **4** in 43%. The nitro groups of **4** are reduced using palladium on carbon in methanol under 30 bar of hydrogen atmosphere. The trisamine **5** is isolated in close to quantitative yield (98%) after simple filtration over Celite and removal of the solvent.

In our hands, imine formation of **5** with 2,3-dihydroxybenzaldehyde (**6**) in methanol did not work well on a small scale. However, condensation of 511 mg of **5** (1.5 mmol) with 628 mg of 2,3-dihydroxybenzaldehyde (**6**, 4.6 mmol) in a concentrated methanol solution at room temperature resulted in the precipitation of the product **L**-H_6 as a dark red solid in 71% yield (744 mg).[6] ^{1}H NMR shows as characteristic signals the resonance of the ester methyl group at $\delta = 3.48$ ppm and two singlets of imine protons at $\delta = 9.02$ and 8.93 ppm in the ratio 1:2. Mass spectrometry reveals the molar peak at $m/z = 709$ $[M + H]^+$.

The ligand **L**-H_6 was introduced into coordination studies with titanium(IV) ions. Therefore, l-H_6, titanoyl acetylacetonate $[TiO(acac)_2]$ and sodium carbonate are dissolved

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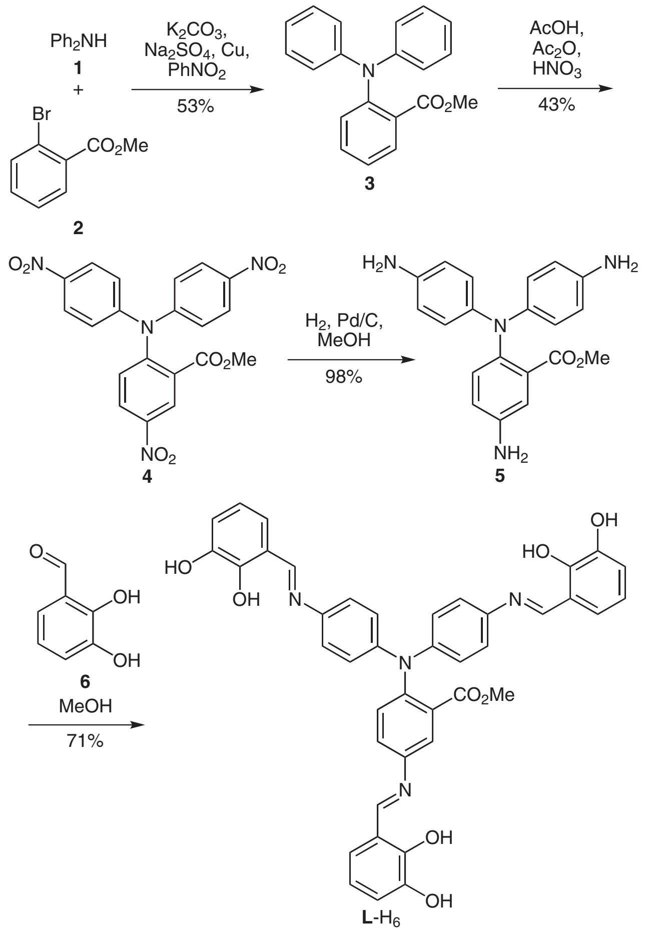

Scheme 1 Synthetic scheme for the preparation of ligand **L**-H_6

in a 1:1:1 ratio in a small amount of DMF. After 12 hours at room temperature DMF is removed, and the residue is washed with methanol. The complex $Na_8[\mathbf{L}_4Ti_4]$ is obtained in 30% yield (197 mg). Introduction of the ester reduces the symmetry of the triangular ligand leading to a series of different isomers due to different relative positions of the four esters in the complex. The four orientational isomers are indicated in Figure 2. Furthermore, the substituents can be directed towards the inside or to the outside of the tetrahedron. Consequently NMR spectroscopy is not informative in case of $Na_8[\mathbf{L}_4Ti_4]$.

Figure 3 shows a part of the ESI-MS spectrum. This analytical technique proved to be ideal for the characterization of the $Na_8[\mathbf{L}_4Ti_4]$ tetrahedron.[7] The spectrum shows solely peaks of the M_4L_4 container with varying amounts of countercations (Na^+ or H^+). The part of the ESI-MS spectrum shown in Figure 3 reveals the peaks of double, triple, or quadruple negatively charged species. The signals show the correct isotopic distribution.

In this paper we described the preparation of an unsymmetric tris(4-aminoaryl)amine **5** with an ester group at one of the aryls. Condensation with 2,3-dihydroxybenzaldehyde (**6**) affords a triangular triscatechol ligand **L**-H_6, which forms a M_4L_4 tetrahedron upon complexation of titanium(IV) ions in the presence of sodium carbonate. The pendant ester groups will be a functional unit for future work in order to add recognition or reaction sites or to link several containers.

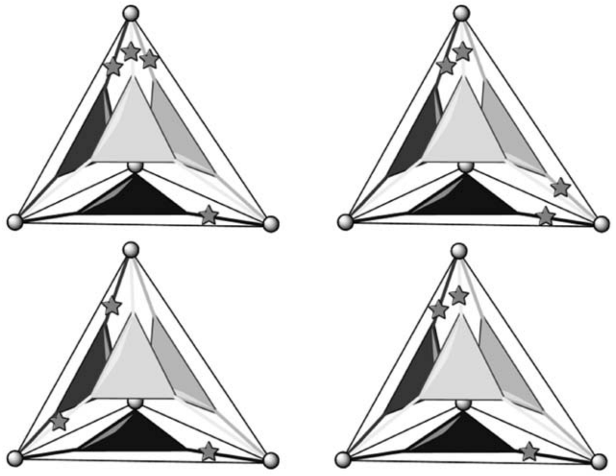

Figure 2 Orientational isomers of an M_4L_4 tetrahedron with a substituent (☆) located at one of the ligand arms

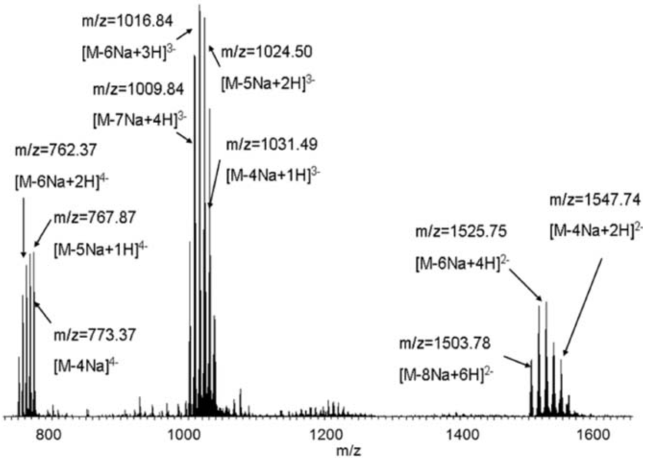

Figure 3 Part of the ESI-MS spectrum of $Na_8[\mathbf{L}_4Ti_4]$

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(6) Characterization of **L**-H_6: mp 179 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 13.36, 12.89, 9.18 (three broad signals, 6 H total, OH), 9.02 (s, 1 H, HC=N), 8.93 (s, 2 H, HC=N), 7.78–7.65 (m, 2 H, CH_{ar}), 7.40–7.32 (m, 5 H, CH_{ar}), 7.17–6.96 (m, 9 H, CH_{ar}), 6.85–6.74 (m, 4 H, CH_{ar}), 3.48 (s, 3 H, OCH_3). MS (EI, 70 eV): *m/z* = 709 [M + H]$^+$. Anal. Calcd for $C_{41}H_{32}N_4O_8$ (708.71): C, 69.48; H, 4.55; N, 7.91. Found: C, 69.39; H, 4.08; N, 8.00.

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