

Supertripodal ligands

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Abstract - Ligands with three-dimensional character can be synthesized in one step by conjugation of pre-assembled chelating arms to a three-dimensional framework. This approach can be applied to the synthesis of ligands incorporating a wide variety of donor groups. The specific case of a hexakis-(thioether) ligand assembled from bidentate thioether ligands and a framework derived from 1,1,1-tris(hydroxymethyl)ethane exemplifies this synthetic strategy.

Ligands with intrinsically three-dimensional cavities offer several advantages. First, owing to the macrocyclic, cryptate, and chelate effects (ref. 1), they often bind metal ions exceptionally well. Second, by enforcing spatial relationships between their donor atoms they often display substantial selectivity in their binding. On the other hand, their salient disadvantage lies in the difficulty of synthesis, which increases with the three-dimensionality of the ligand. Synthetic complexity severely constrains industrial applications of ligands with enforced three-dimensional cavities.

Historically in the synthesis of ligands such as cryptates introduction of the donor groups has been linked with incorporation of three-dimensionality into the ligand. An alternative approach, however, consists of the conjugation of pre-existing chelating arms to a three-dimensional framework (Fig. 1). One such framework is provided by the triol 1,1,1-tris(hydroxymethyl)ethane (I). This cheap starting material (<\$20/kilo) is used industrially as a cross-linking agent for polyesters. It is produced on a large scale by the base-catalyzed reaction of propionaldehyde with excess formaldehyde. Its hydroxymethyl "arms",

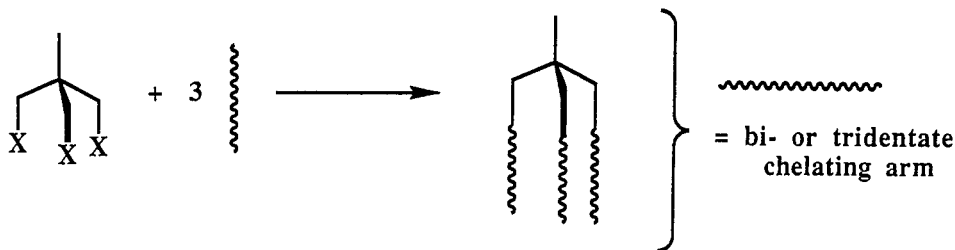


Fig. 1. Principle of the conjugation approach.

unlike those of tris(hydroxyethyl)amine, cannot undergo the "umbrella" inversion of amines; hence the framework forces the chelate arms to remain together near the metal ion. Thus this triol provides a framework for construction of ligands with intrinsic three-dimensionality, a natural "pocket".

Coupling of different chelating arms to I (or derivatives of it) yields supertripodal ligands ("podands"; ref. 2) with a wide variety of donor groups.

"Supertripodal" here refers to tripods that incorporate multidentate chelating arms; Sargeson (ref. 3) has described examples of such ligands in the synthesis of sepulchrates. Supertripodal ligands combine ease of synthesis with high binding affinity for metal ions. Together these advantages make them particularly attractive in an industrial context, where the arduous and therefore expensive routes to cryptands virtually precludes their use.

Initial work has concentrated on synthesis of hexadentate thioether ligands (refs. 4, 5) for comparison with analogous complexes of crown thioethers (refs. 6, 7). Despite the generally low reactivity of neo-pentyl halides towards

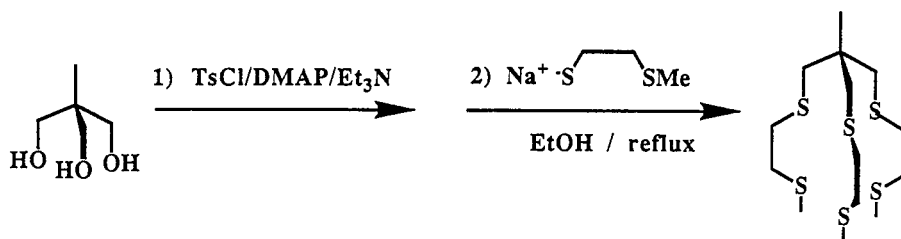


Fig. 2. Synthesis of II.

nucleophiles, treatment of 1,1,1-tris(hydroxymethyl)ethane tritosylate with three equivalents of sodium 2-methylthioethanethiolate affords II in high (76%) yield (Fig. 2). Coordination of crude II to Ni(II) in Ac_2O or MeNO_2 gives beautiful violet crystals of $[\text{Ni}(\text{II}) \cdot \text{II}]^{2+}$. Recrystallization of $[\text{Ni}(\text{II}) \cdot \text{II}]^{2+}$ followed by addition of water frees the ligand; extraction into dichloromethane and drying yields the analytically pure ligand.

Structural investigation of $[\text{Ni} \cdot \text{II}]^{2+}$ shows that II coordinates with minimal strain. Bond angles at the quaternary carbon atom between chelate arms show slight expansion from tetrahedral angles (Fig. 3) (111°). Conversely, bond angles between the apical carbon atom and the three chelate-bearing arms (e.g., $\angle \text{C2-C1-C11}$) deviate from T_d values in the opposite direction (107°). Indeed, extensive splaying of the chelate arms would lead to unacceptable $\text{H} \cdots \text{H}$ interactions with the apical methyl group. Thus the structure of the framework

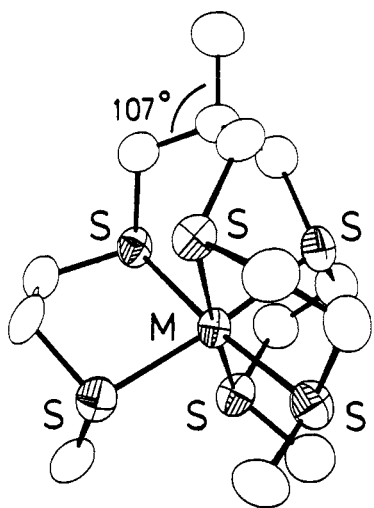


Fig. 3. Structure of a representative $[\text{M} \cdot \text{II}]^{n+}$ chelate (here $\text{M} = \text{Ni}(\text{II})$).

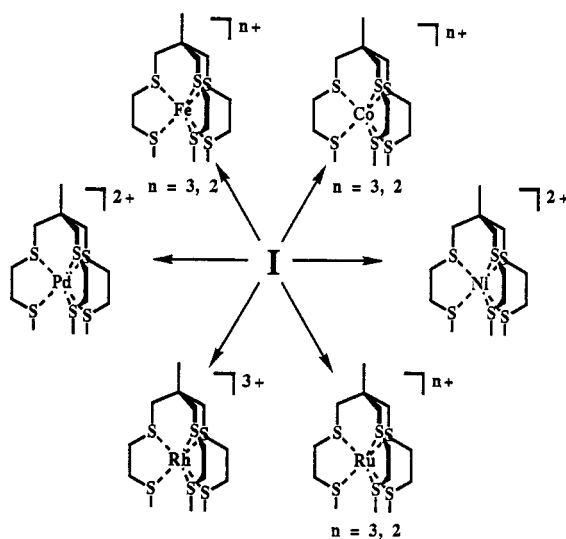


Fig. 4. Coordination chemistry of supertripod II.

to some extent forces the chelating arms toward the metal ion, and thereby improves the stability of the resulting complex.

Procedures analogous to those used to prepare the corresponding crown thioether complexes readily yields other $[M \cdot II]^{m+}$ complexes ($M = Co(II), {}^3Co(III), Fe(II), Pd(II), Ru(II), Rh(III)$) (ref. 8) (Fig. 4). In view of the structural diversity of the platinum metal complexes of crown thioethers (refs. 6, 9) the structures adopted by these compounds attract especial interest. While work to date has focused upon hexadentate thioethers attached to I, a similar procedure affords ligands based upon donor groups such as thiolates, hydroxamates, amines, and carboxylic acids. The same approach clearly can also be extended to use of frameworks other than I.

This work shows that attachment of chelating arms to a three-dimensionally articulated framework can make superligands from simple precursors in a single step. Application of this potentially general strategy can simplify synthesis of ligands that combine high affinity with selectivity. Extension of the conjugation approach affords ligands with a wide variety of other donor groups. The approach combines the advantages of other three-dimensional ligands (e.g., cryptates, sepulchrates) with the ease of synthesis of non-cyclic ligands (e.g., EDTA, NTA). Moreover, the resulting ligands can be readily fastened to polymeric supports, or attached to chains that modify the solubility of the ligand (e.g., oligomethylene sulfonates to confer water solubility). Furthermore such modification can be carried out without affecting the binding properties of the remote chelating site.

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