

Oligopolydentate ligands for helices and metallacycles

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Abstract: Oligopolydentate ligands contain two distinct metal binding sites separated by a spacing group. They are able to form metalla-macrocylic compounds in which the metal ions are an intrinsic part of the cycle. The cycles may be twisted about the metal-metal axis to give helical complexes. The use of different metal ions in templating the formation of the helices is discussed together with the properties of the complexes. More rigid ligands can give rise to the formation of metallacycles with internal cavities which are potential receptor sites.

Macrocylic ligands may be regarded as prototypical examples of highly structured ligands, in which the structure of the ligand is sufficiently constrained to influence, often dramatically, the properties of the complexed metal and the resulting complexes. Such ligands frequently display selectivity in their complexation properties, and may modify the redox chemistry of the complexed metal. The complexes often show high thermodynamic and kinetic stability. The relationship between metal and macrocycle is however symbiotic - the metal can change the properties of the coordinated ligand, and moreover, may play a vital rôle in templating the synthesis of the ligand. My intention in this paper is to show how many of the general ideas of macrocylic coordination chemistry expressed above may be carried over to slightly different systems, in which the metal is an intrinsic part of the cycle. The complexes will contain at least two metal ions, bridged by at least two ligands to form the macrocylic unit. In helical complexes, the cycle is twisted around the helical axis, which is generally the metal-metal axis, and consequently there is no internal cavity; if the ligand is too rigid to allow such twisting, a macrocycle with an internal cavity, and thus a potential receptor site, may be generated.

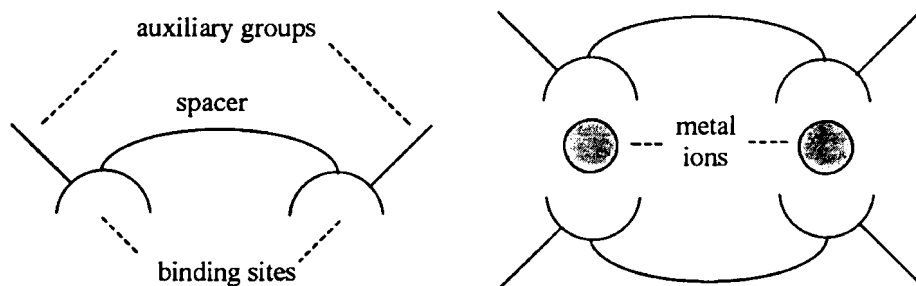


Fig.1 General features of ligands used (left) and of a metallacycle (right)

The general features of the ligand systems used are shown in Fig. 1 and the specific ligands referred to are shown in Fig. 2.

The ligands contain at least two metal binding sites which are separated by a spacing group which must be sufficiently structured to ensure that the different binding sites cannot complex the same metal, and this is the origin of the convenient, if ugly, denomination "oligopolydentate". The auxiliary groups are generally simple organic functionalities which may be added as spectroscopic probes or to improve ligand solubility; they may however dramatically influence the properties of the complex.

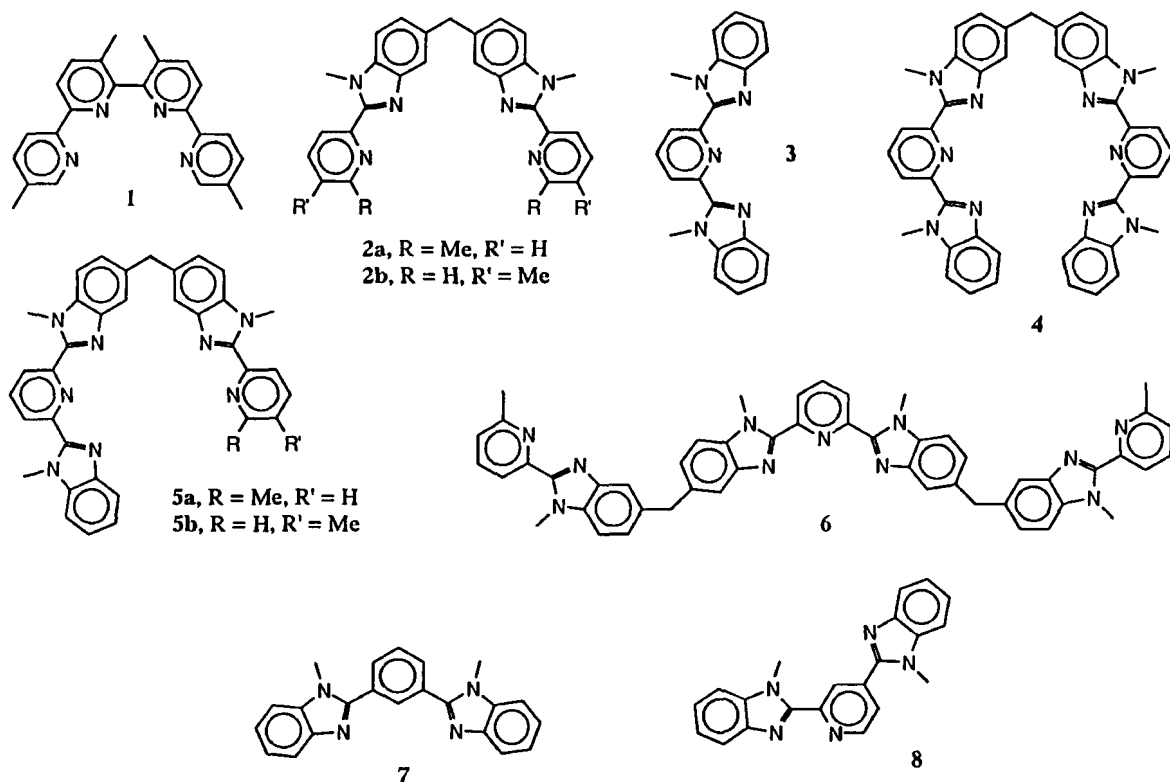


Figure 2.

HOMONUCLEAR HELICAL COMPLEXES.

The aesthetic appeal and the biological importance of helical molecules have long attracted the interest of chemists, and since the recognition by Alfred Werner of the helical nature of complexes such as tris(ethylenediamine)cobalt(III), coordination chemists have been aware of the possibility of synthesising such compounds. Many helical complexes were synthesised by chance, but frequently were not recognised as such, and the beginning of intense activity in this field may be associated with the observation by Lehn and Sauvage that the complex $[\text{Cu}_2(\mathbf{1a})_2]^{2+}$ possesses a double helical structure (1). Since then Lehn has developed syntheses of a wide variety of helical systems based on oligobipyridyls (2), while Constable and Potts have exploited the potential of polypyridyl ligands (3). The ligand 2 is a good example of the structured ligands referred to above: the two bidentate sites are separated by a spacer, and the methyl groups on the pyridyl may be regarded as auxiliary groups. The hydrogen atoms at position 4 of the benzimidazole groups repel each other and prevent the ligand adoption a planar conformation. If this ligand is reacted with a metal ion showing a preference for octahedral geometry, such as cobalt(II), then the metal ion can bind three bidentate ligand groups, and with a stoichiometry of $[\text{Co}_2(\mathbf{2})_3]^{4+}$ the coordination requirements of both ligand and metal are satisfied. The combination of the helical nature of the metal-trisbidentate ligand unit, and the flexibility of the ligand lead to a triple helical structure (4) shown in Fig. 3.

Fig. 3 Schematic drawing of $[\text{Co}_2(\mathbf{2})_3]^{4+}$ (left) and space filling representation (right).

If the metal used has a tetrahedral coordination preference such as Cu(I), then a double helix of stoichiometry $[\text{Cu}_2(2\text{a})_2]^{2+}$ is obtained, while a metal with no fixed preference such as Zn(II) gives the triple helix at high ligand:metal ratios and a double helix at lower ligand:metal ratios (5). Metal templating is also possible with higher coordination numbers: Eu(III) forms a nine-coordinate complex with three tridentate ligands **3** and by linking two such tridentate ligands together to obtain **4**, one may prepare a triple helix containing two europium ions (6).

An initially surprising observation was that the complex $[\text{Co}_2(2\text{a})_3]^{4+}$ was not oxidised to the cobalt(III) complex in solution. Close examination of the crystal structure suggested that this was due to steric interactions between the methyl groups on the pyridyl moieties which prevent the reduction of Co-N bond lengths associated with oxidation of high spin Co(II) to low spin Co(III), and this was confirmed by shifting the methyls to the 5 position (ligand **2b**); the complex $[\text{Co}_2(2\text{b})_3]^{4+}$ is readily oxidised (7). This modification also increased slightly the stability of the cobalt(II) triple helix, which is now sufficiently stable to be formed virtually quantitatively even at 10^{-6} M concentrations, showing the very high thermodynamic stability of such systems. The preparation of a cobalt(III) helix was significant in that for the first time a kinetically stable helix was available. The resolution of the enantiomers was carried out, but showed disappointingly that the optical rotation and circular dichroism of the complexes were not significantly greater than that of simple mononuclear systems (8). Reduction of the enantiomerically pure cobalt(III) triple helix afforded the equivalent cobalt(II) helix whose racemisation kinetics were studied (9). Although cobalt(II) is generally regarded as a labile metal ion, the half-life for racemisation of $[\text{Co}_2(2\text{b})_3]^{4+}$ in aqueous solution is more than 13 hours at room temperature. Comparison with the published rate constant for racemisation of $[\text{Co}(\text{bipy})_3]^{2+}$ (10) and a mononuclear complex with a similar coordination sphere to $[\text{Co}_2(2\text{b})_3]^{4+}$ (11) shows that the racemisation rate is reduced by a factor of about 10^6 , implying considerable kinetic stability for such systems.

HETERONUCLEAR HELICAL COMPLEXES

A general problem in the synthesis of heteronuclear complexes is the introduction of selectivity, which allows the complexation of a metal in one specific site. In helical systems it is possible to introduce selectivity on the basis of coordination number preference. Thus two bidentate-tridentate ligands **5a** taken together can offer a tetrahedral (bis-bidentate) and an octahedral (bis-tridentate) site. Note that the auxiliary methyl group in **5a** militates against the bidentate unit acting as an octahedral (tris-bidentate) site. Reaction of two equivalents of **5a** with one equivalent of Fe(II) (octahedral preference) and Ag(I) (tetrahedral preference) gives the heteronuclear double helix $[\text{FeAg}(5\text{a})_2]^{3+}$ (12). If the methyl group is shifted to give **5b**, the bidentate unit may now form an octahedral site, and a mixture of an octahedral metal ion (Fe(II) or Zn(II)), a lanthanide ion (Ln) with three equivalents of **5b** forms the triple helical complex $[\text{MLn}(5\text{b})_3]^{5+}$ (13). For both these systems, equilibrium studies in solution with UV-visible spectroscopy, nmr, and electrospray mass spectroscopy show clearly that the heteronuclear complex is formed with high selectivity.

On the basis of these arguments, one would expect that two bidentate-tridentate-bidentate ligands **6** would offer two tetrahedral and one octahedral sites, and a complex of stoichiometry $[\text{FeAg}_2(6)_2]^{4+}$ is indeed isolated in high yield (12). Following the arguments given above, a double helical structure would be expected, but the crystal structure determination of this complex gave another surprise. After coordination of the iron in the central, octahedral site to give $[\text{Fe}(6)_2]^{2+}$, the four bidentate arms must be arranged to form the tetrahedral sites. A helical structure requires that the tetrahedral sites are formed by one bidentate unit from each ligand, but it is equally possible to form the tetrahedral sites from two bidentate units of the same ligand, to give a catenate structure in which the two cycles are interlocked (Fig. 4). An interesting feature of such a system is its chirality: since each cycle is itself helical, and may be assigned P or M helicity, the combination of the two cycles may be the homochiral (P,P or M,M) or the meso (P,M) forms. In fact the crystallisation of $[\text{FeAg}_2(6)_2]^{4+}$ as its perchlorate salt gave two distinct crystalline forms, which were revealed to be a racemate of the homochiral form, and the meso form respectively (14).

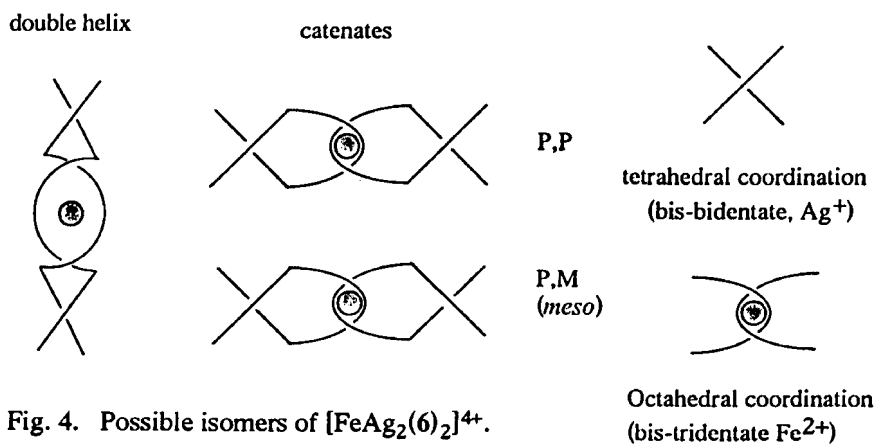


Fig. 4. Possible isomers of $[\text{FeAg}_2(6)_2]^{4+}$.

METALLACYCLES WITH CAVITIES

The chemistry of metallacycles, in which the metal is an intrinsic component of the macrocycle, is attracting increasing attention, notably in the works of Fujita and Goodgame (15). In the introduction it was mentioned that helical complexes may be regarded as twisted macrocycles - consequently we might imagine that macrocycles with cavities could be produced by untwisting a helix. An interesting example of this is shown in Fig 5 which shows how the double helical complex $[\text{Cu}_2(3)_2]^{2+}$ (16) may be untwisted to give the non-helical metallacyclic complex $[\text{Cu}_2(7)_2]^{2+}$ (17) by simple replacement of the bridging pyridine by a phenyl group.

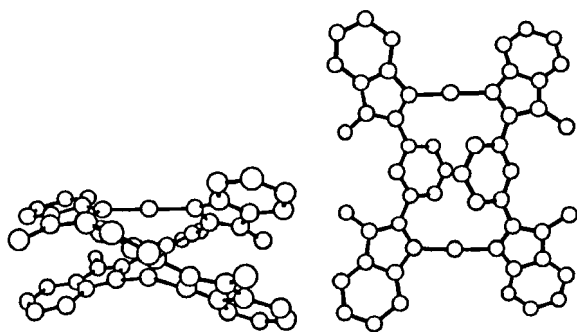


Fig. 5 The structure of $[\text{Cu}_2(3)_2]^{2+}$ may be untwisted to give the structure of $[\text{Cu}_2(7)_2]^{2+}$.

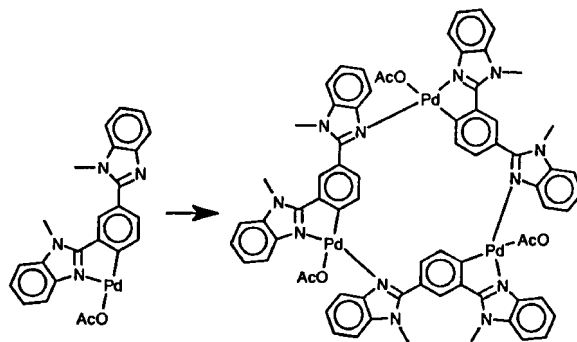


Fig. 6

In general however, internal cavities may be generated more readily by ensuring sufficient rigidity in the spacer group to prevent the second coordination site from bending back to form a helix. The ligand 7 is the starting point for the study of the formation of metallacycles and their potential as receptors. Reaction of 7 with $\text{Pd}(\text{OAc})_2$ gives a cyclometallation of the phenyl ring in position 6 (position 2 being sterically hindered), but the mononuclear product is not isolated, the trimer $[\text{Pd}_3(7\text{-H})_3(\text{OAc})_3]$ being the principal product (Fig. 6).

The postulated monomeric intermediate possesses a vacant coordination site on the metal, and a free benzimidazole ligand, but the limited conformational flexibility of the molecule (essentially limited to torsion about one phenyl-benzimidazole bond) does not allow formation of a dimer, and thus a trimer is formed. The trimer is cup-shaped (18), and the crystal structure shows a molecule of acetonitrile to be included inside the cup. The trimer is quite stable in solution, but the acetonitrile molecule is lost from the cup. It seemed plausible that an identical structure could be obtained by replacing ligand 7 by 8, which could bind palladium in a similar fashion, the carbon-palladium bond being replaced by a pyridine-palladium coordinate bond. Reaction of 8 with $\text{Pd}(\text{O}_2\text{CET})_2$ gave only the monomeric complex $\text{Pd}(8)(\text{O}_2\text{CET})_2$ with no sign of the trimer (19). The crystal structure of $\text{Pd}(8)(\text{O}_2\text{CET})_2$ showed the $\text{Pd}(8)$ unit to be essentially isostructural with the $\text{Pd}(7\text{-H})$ unit of the

trimer, so that the structural constraints necessary for trimer formation were satisfied. The trimer is in fact formed by protonation of the complex $\text{Pd}(8)(\text{O}_2\text{CEt})_2$ which labilises one of the carboxylate ligands, and leads to quantitative formation of $[\text{Pd}_3(8)_3(\text{O}_2\text{CEt})_3]^{3+}$ identified by its nmr spectrum and by electrospray mass spectroscopy.

Since $[\text{Pd}_3(8)_3(\text{O}_2\text{CEt})_3]^{3+}$ possesses both an internal cavity and a positive charge, it is a potential receptor for anions. Studies showed that the nmr spectrum of the trimer was indeed dependent on the counter ion of the acid used for protonation. Titration of the mesylate salt with perchlorate followed by nmr showed an end point corresponding to one perchlorate per trimer in DMSO solution; mesylate itself appears to be only very weakly bound by the complex. Since the nmr spectrum maintains the C_3 symmetry of the complex, the perchlorate anion must lie on the threefold axis of the complex, and this agrees with its inclusion in the cavity. This hypothesis is further supported by the electrospray mass spectrum of $[\text{Pd}_3(8)_3(\text{AcO})_3](\text{ClO}_4)_3$ in acetonitrile solution which shows the peak corresponding to $[\text{Pd}_3(8)_3(\text{AcO})_3](\text{ClO}_4)^{2+}$ to be of comparable intensity to that of the free cation, while the peak due to the species with two perchlorates is an order of magnitude less intense. These preliminary results suggest that careful design of positively charged metalla-macrocycles can offer interesting perspectives in the design of anion receptors.

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