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Anion Recognition and Templation in Coordination Chemistry

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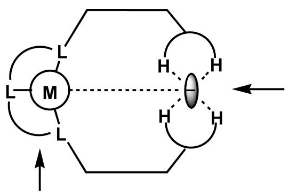
The selective recognition of anionic species by molecular receptors is an area of increasing interest due to the important roles played by anions in biological systems and the environment. An attractive approach for the recognition of anions is to use metal-based receptors, which provides some important advantages over purely organic hosts. Metallo-hosts can combine the structural and functional properties of metal centres with the recognition capabilities of organic ligands to selectively bind anionic guests. In our group we have developed different approaches for the synthesis of this type of metallo-receptors. One of these approaches is based on the use of the anion of interest as a templating agent to link together different organic and metal-containing building blocks into assemblies that have high selectivity for the templating anion. This microreview aims to give an overview of the research carried out in the author's group in this area over the past few years. Relevant examples from other groups are discussed and, where appropriate, compared to the work carried out in our group.

1. Introduction

The development of chemical receptors that can selectively recognise anionic species is a topic that has attracted increasing interest over the past few years.[1–5] This stems from the important roles that anions play in biological systems (e.g. phosphorylated metabolites, chlorides, carboxylates), the environment (e.g. cyanide and nitrate) and as building blocks in a wide range of functional materials. Initially, most anion receptors were based on organic species capable of recognising specific guests by a combination of hydrogen bonding and ion pairing. More recently, metal-based receptors have been established as a class of anion receptors which provide some important advantages over purely organic hosts by combining the structural and functional properties of metal centres with the recognition capabilities of organic ligands.[6–8] The structural and geometrical flexibility of metals can provide an excellent way of organising anion binding groups (e.g. hydrogen bonding moieties) for optimal host–guest interactions. In addition, careful choice of the metal centre can confer useful optical, electrochemical or catalytic properties to the receptor (see Figure 1).



The metallo-host binds the anionic guest by hydrogen bonding and metal–ligand interactions.

The metal centre preorganises the hydrogen bonding groups and can also interact directly with the anion.

Figure 1. Schematic representation of a metallo-host containing hydrogen bonding groups for anion recognition.

This metal–organic approach to anion binding is used by Nature in certain enzymes and receptors. For example, carboxypeptidase A (an enzyme that cleaves peptide bonds) recognises and transforms its substrate by using a combina-

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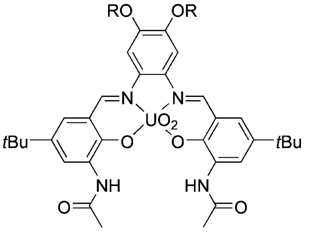
tion of hydrogen bonding (to the terminal deprotonated carboxylic acid group) and metal–substrate interactions.

A wide range of anion receptors based on analogous principles to those employed by Nature and containing metal centres as structural and/or functional building blocks have been reported over the past ten years. For example, Beer has reported extensive studies on the anion binding properties of substituted metallocenes (mainly ferrocene and cobaltocenium).[9,10] In these systems, the organometallic core imparts two important features to the receptor: structurally, it preorganises the hydrogen bonding substituents (e.g. amide and urea groups) for optimal interaction with the guest; in addition, the electrochemical properties of the metallocenes can be successfully employed as a read-out for the detection of the specific anionic guest. Also in the 1990s, Reinhoudt reported another interesting system where the structural and electrochemical properties of metal complexes were exploited for the molecular recognition and sensing of anions. In this case, complexes of $[UO_2]^{2+}$ with substituted Schiff bases were the basis for the development of electrochemical sensors for a range of anions (Figure 2).[11–14]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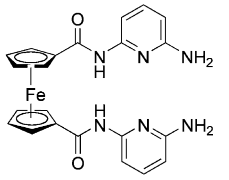
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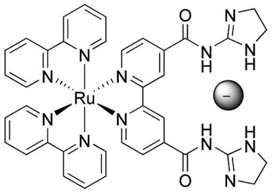
Figure 2. Metallo-hosts for anion binding containing electrochemically active metal centres for sensing.[13,15]

Metal complexes can also be used as optical labels for anion sensing. For example $[Ru(bipy)_3]^{2+}$ is highly emissive and, when one of the bipyridine ligands is substituted by a chemical receptor, the fluorescence of the complex changes in the presence of specific analytes.[16,17] With suitable substituents on the bipyridine ligand of this type of complex, it has been possible to selectively detect by optical means a range of different anions. For example, Watanabe has reported that complex **3** (see Figure 3) can selectively recognise phosphoesters and upon binding in acetone an enhancement of the luminescence of the complex is observed.[18] As was earlier reported by Beer for similar ruthenium–bipyridyl complexes, the enhanced emission is likely to arise from the more rigid structure of the complex when bound to the anion.

More recently, Gale and Loeb reported a series of receptors where square-planar platinum(II) centres were used to preorganise substituted pyridines for anion binding (see compound **4** in Figure 3).[19–21] These systems were shown to have the ability to bind a range of different anions in competitive solvents such as DMSO. Anslyn has reported another elegant example where metal centres are successfully used to preorganise hydrogen bonding groups for optimal guest binding (complexes **5** and **6**).[22] The C_3 symmetry of the resulting complex makes it an ideal receptor for anionic guests such as phosphates.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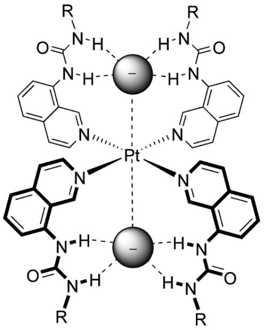
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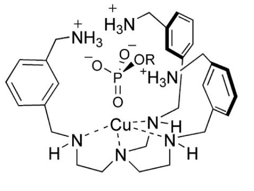
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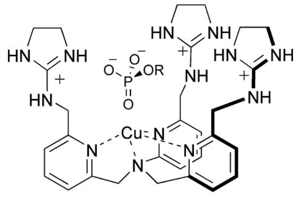
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Figure 3. Selected examples of metallo-hosts for anion binding.[18,20,22]

Several comprehensive reviews on metallo-receptors for anion binding and recognition have appeared in the literature.[6–8] The current microreview provides an overview of the studies on metal-based anion receptors carried out in the author's research group. As will be highlighted in the following section, our interest in this area started ten years ago while studying the templating properties of halides in the formation of coordination cages. This work led to the development of a wide range of metal-based receptors capable of selectively recognising specific anions. More recently, we have used anions to direct the formation of specific coordination networks, which gave rise to interesting structures with potential applications in storage and recognition. Finally, we have started developing dynamic combinatorial libraries of metallo-macrocycles by employing anions as templating agents.

2. Anion-Templated Assemblies

The use of chemical templates to favour the formation of a specific product or assembly is a powerful approach widely used in the molecular sciences.[23,24] It is often employed in synthetic chemistry and materials science, and Nature employs it to form complex supramolecular assemblies inside the living cell. As defined by Busch *"A chemical template organises an assembly of atoms, with respect to one or more geometric loci, in order to achieve a particular linking of atoms"*.[25] In the context of synthetic organic and inorganic chemistry, this strategy not only enables the synthesis of molecules in a more efficient manner, but also aids in the preparation of assemblies that have unusual topologies, such as rotaxanes, helicates and catenanes.[26–31] A template can be considered as an entity that *contains* the required information to help organise a collection of building blocks in a specific manner. The templation process can be thermodynamically or kinetically driven. In the former, the template binds to one of the products, shifting the equilibrium so that this specific product is obtained in high yields (and selectively formed over other potential products). A kinetic template, on the other hand, operates under irreversible conditions by stabilising the transition states that lead to the formation of the desired product. Often, in the kinetically controlled reactions the template is strongly bound to the final species, acting not only as a kinetic template, but also as a thermodynamic one.

In spite of the widespread use of chemical templates, until the late 1990s there were only a handful of examples where anions had been employed as templating agents.[32–34] Initially, the lack of anion-templated processes was attributed to the more diffuse nature of anions (as compared to cations of similar size), their pH dependence, relatively high solvation free energies and also to the more complex structures they usually have (which in turn has proven to be an advantage rather than a problem). In spite of this, the past few years have seen a plethora of examples where anions successfully act as templates, showing that the *limitations* highlighted above are not as critical as first thought. Thus, several macrocycles,[35–37] helicates, rotaxanes,[38–45] catenanes[27,46] and cages[47–55] based on both organic and metal–organic systems have now been prepared by using anion-templated strategies.[56,57]

Our own work in the area of anion-templated syntheses started in the late 1990s when we were investigating a series of metal complexes with ligands possessing hydrogen bonding functionalities. More specifically, we were interested at the time in the coordination and hydrogen bonding properties of simple ligands such as those shown in Figure 4.

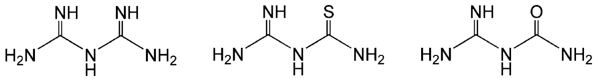


Figure 4. Selection of hydrogen bonding ligands under study.

These ligands can in principle bind to metal centres as *N*,*N*, *N*,*O* or *N*,*S* chelates. In addition, they can easily be deprotonated to generate complexes with a different set of hydrogen bonding functionalities. For example, amidinothiourea could in principle form the square-planar complexes shown in Figure 5.

A wide range of reactions between these ligands and different metal salts were investigated. In particular, the reactions between amidinothiourea (H-atu) and nickel(II) salts yielded unexpected and interesting results. As shown in Scheme 1, when NiX_2 ($X = Br^-$, I^-, AcO^-, NO_3^-, ClO_4^-) in methanol was mixed with two equivalents of amidinothiourea, the expected square-planar complex, $[Ni(atu)_2]$ (**7**), was formed.[58]

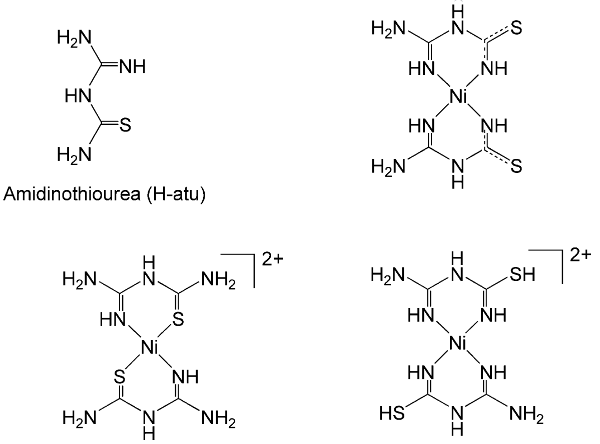
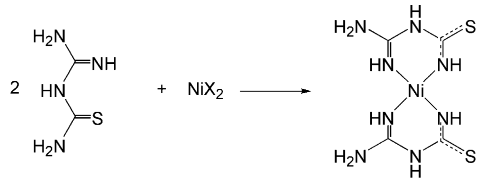


Figure 5. Amidinothiourea (H-atu) can act as either an *N*,*N* or an *N*,*S* ligand. It can coordinate as a neutral ligand (H-atu) or, when deprotonated (atu), as a mononegative ligand.



H-atu

$[Ni(atu)_2]$ (**7**)

Scheme 1. Reaction between NiX_2 ($X = Br^-$, I^-, AcO^-, NO_3^-, ClO_4^-) and H-atu. A square-planar complex is formed in which amidinothiourea acts as an *N*,*S* mononegative ligand to yield the neutral complex $[Ni(atu)_2]$.[59]

However, when the reaction was repeated with $NiCl_2$ a very different behaviour was observed: the expected square-planar complex was initially formed in solution, but this quickly rearranged to yield the unexpected hexanickel cage **8**. An X-ray crystal structure of this cage (see Figure 6) revealed that it contains an encapsulated chloride anion bound by hydrogen bonding and weak Ni···Cl interactions.

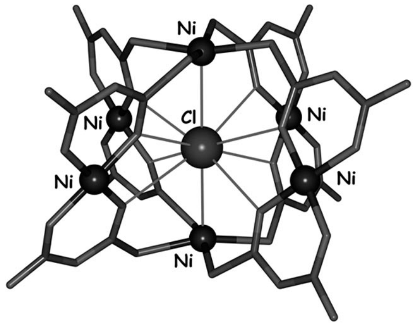
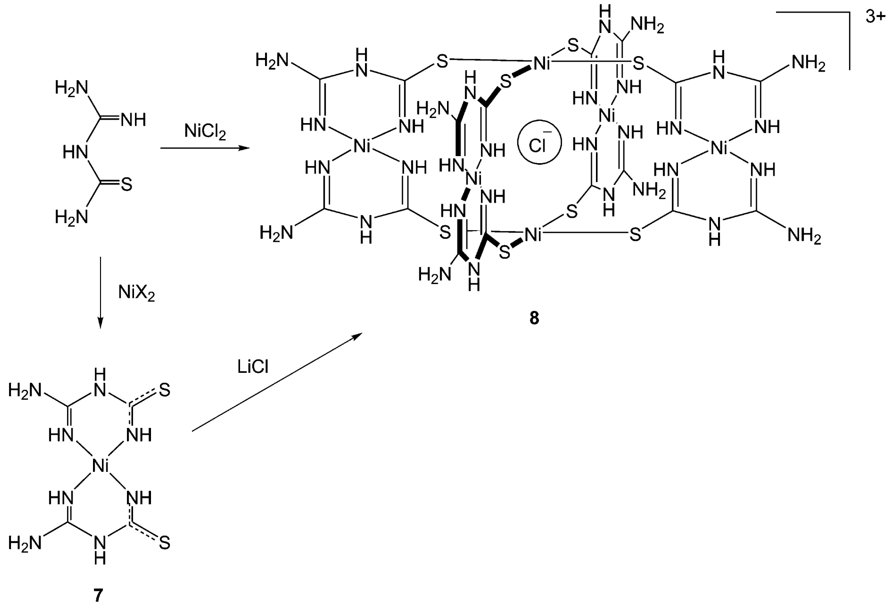


Figure 6. Molecular structure of the hexanickel complex $[Ni_6(atu)_8{\subset}Cl]Cl_3$ (**8**).[58]

These structural features and the fact that the cage only formed with $NiCl_2$ (but not in the presence of other anions) suggested that the chloride anion was acting as a templating agent. Indeed, when the chloride anion was added to mixtures of NiX_2 and amidinothiourea (where X is different



Scheme 2. Reaction scheme showing the formation of the hexanickel cage $[Ni_6(atu)_8{\subset}Cl]Cl_3$ from $NiCl_2$ and H-atu or by conversion of $Ni(atu)_2$ upon addition of a chloride salt.

from chloride), the formation of the cage was induced (see Scheme 2). An interesting feature of the templating process that yields $[Ni_6(atu)_8{\subset}Cl]X_3$ is a dramatic colour change from orange to dark green. Considering the very high selectivity of this process for the chloride anion, more recently we have successfully used the templated formation of the cage as a chloride sensor.[60]

Besides being highly sensitive to the presence of the correct anion, the formation of the cage demonstrated to be also dependant on the solvent employed. When the reaction was carried out in mixtures of acetone/methanol (instead of pure methanol), the bromide anion also acted as a template, and the hexanickel cage was formed (as confirmed by X-ray crystallography and spectroscopic characterisation in solution). This highlights the fine balance between the solvating properties of the medium and the strong hydrogen bonding interactions between the cage and the encapsulated anion.

Once the templating role of these two halides was established, it was of interest to determine whether mixed-metal cages could be formed. Therefore, the reactions between $[Ni(atu)_2]$, which is formed in situ from $Ni(ClO_4)_2$ and H-atu, and different palladium(II) salts were carried out in methanol/CH_2Cl_2. Mixed-metal cages were successfully prepared in the presence of $[PdX_2(RCN)_2]$ (X = Cl, Br) but not when using other counterions such as triflate or acetate.[59]

The formation of these cages was confirmed by mass spectrometry and X-ray crystallography. Similarly, by using platinum(II) complexes it was possible to prepare analogous Ni–Pt cages with four $[Ni(atu)_2]$ units and two platinum(II) centres bringing them together by means of Pt–S bonds (see Figure 7).

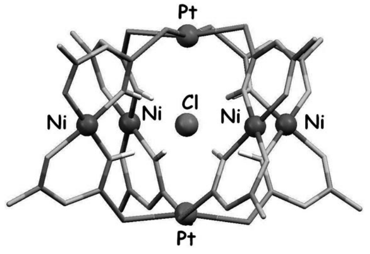
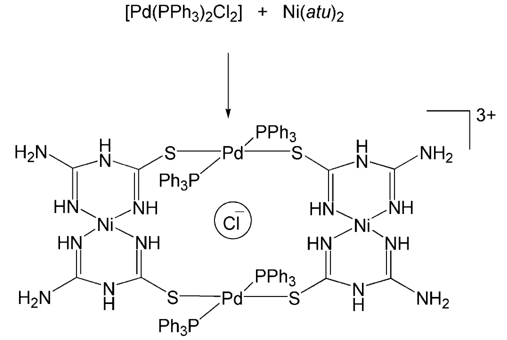


Figure 7. Molecular structure of the mixed-metal cage assembly $[Ni_4Pt_2(atu)_8{\subset}Cl](ClO_4)_3$ (**9**).[60]

Considering the high selectivity of these supramolecular assemblies for chloride and bromide ions, we then considered the possibility of preparing more “open” systems based on the same building blocks, which could allow for easy exchange of the anionic guests. In turn, this could be used for the development of molecular receptors for specific anions. Having demonstrated that Ni–Pd mixed-metal cages can be prepared, we went on to investigate the reaction between $[Ni(atu)_2]$ and $[Pd(PPh_3)_2X_2]$ (see Scheme 3).[61] The rationale for using this palladium(II) complex was that the phosphane ligands could coordinate in the *trans* position, preventing coordination of two $[Ni(atu)_2]$ units. This in turn would generate a metallo-macrocycle with a more “open” structure for guest exchange than the cages described above. As is shown in Scheme 3, when this reaction was carried out in the presence of the chloride anion (X = Cl), the expected metallo-macrocycle, $[Pd_2Ni_2(atu)_4(PPh_3)_4Cl]Cl_3$ (**10**), was formed. This compound was spectroscopically and structurally characterised (see Figure 8) to confirm the presence of the chloride guest inside the macrocycle.



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Scheme 3. Formation of a metallo-macrocycle from [Ni(atu)$_2$] and [Pd(PPh$_3$)$_2$Cl$_2$].[61]

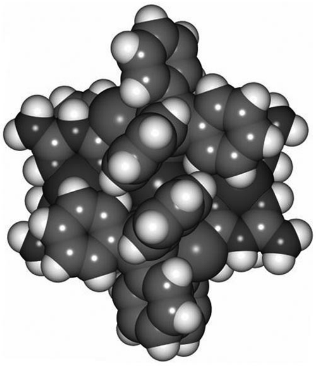


Figure 8. X-ray crystal structure (space-filling representation) of metallo-macrocycle [Pd$_2$Ni$_2$(atu)$_4$(PPh$_3$)$_4$Cl]Cl$_3$ (**10**).[61]

To confirm the templating role of the anion, the reaction was also carried out with [Pd(PPh$_3$)$_2$](OTf)$_2$. This reaction did not yield a metallo-macrocycle but the monopalladium complex [Pd(PPh$_3$)$_2$(atu)](OTf)$_2$ (**11**) resulting from *N*,*S* bidentate coordination of the atu ligand transferred from [Ni(atu)$_2$] to the palladium(II) centre. However, addition of chloride (or bromide and iodide) ions to this mixture yielded the expected metallo-macrocycle with the halide at its centre. This is in contrast to the behaviour observed in the formation of the hexametallic cages discussed before, in which only chloride (and bromide in the presence of aprotic solvents) ions act as templates. It is likely that the more open structure of the metallo-macrocyles is able to accommodate larger anions such as iodide.

Qualitative ^{31}P NMR spectroscopic studies of these macrocycles in solution indicated that the encapsulated anions can indeed be exchanged. These studies also suggested that the metallo-macrocycle has the following order of halide anion selectivity: Br > Cl > I. This is consistent with the X-ray crystallographic results for the three metallo-macrocycles: in the solid state, the better host–guest fit between the cage and the halide is indeed with the bromide anion.

The discussion so far has mainly focused on the interactions between anions and the NH groups of the ligands, which are directed toward the centre of the cage/macrocycle. However, the amidinothiourea ligands in these assemblies also have the potential of interacting with anions using their “external” hydrogen bonding groups. Indeed, close inspection of some of the crystal structures of these systems indicated that in the solid state the metallo-macrocycles can assemble into more complex infinite arrays, as shown in Figure 9.[62]

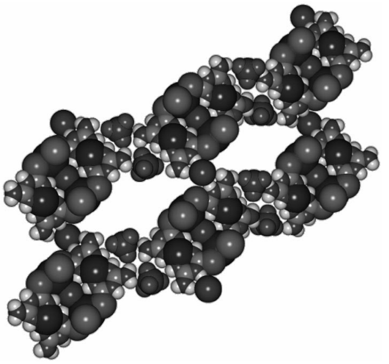


Figure 9. Section of the solid-state structure of [Pd$_2$Ni$_2$(atu)$_4$(PPh$_2$Py)$_4$Cl](Cl)(ClO$_3$)$_2$ (**12**).[62]

In this solid state assembly, the Pd–Ni metallo-macrocycles form regular two-dimensional hydrogen bonded sheets. These are produced by a combination of N–H···O and N–H···Cl hydrogen bonds between the atu ligands of the metallo-macrocycle and the non-encapsulated ClO$_4^-$ and Cl$^-$ counteranions (the overall charge of these metallo-macrocycles is +4; therefore, in addition to the encapsulated halide anion, three more counteranions are required – which are located outside the macrocyclic assembly).

3. From Templation to Recognition

Although the metallo-macrocycles and cages prepared by using the amidinothiourea ligand yielded interesting supramolecular assemblies and demonstrated the important templating role that anions can have, their potential use in molecular recognition is somewhat limited by the size and hydrogen bonding pattern of the [Ni(atu)$_2$] units. Therefore, new ligands that could yield more flexible metallo-receptors were designed. Two different general approaches, inspired by the coordinating and hydrogen bonding properties of [Ni(atu)$_2$], were investigated. The first type of ligand was based on molecules with only one coordinating group rather than two as is the case in [Ni(atu)$_2$]. In this case, upon coordination to square-planar metal centres, it was expected that a more open structure than the cages and macrocycles described in the previous section would form. More specifically, the thiol–urea ligands shown in Figure 10 were designed. The second type of ligand was based on compounds with two coordinating groups, as is the case in [Ni(atu)$_2$], containing a hydrogen bonding spacer (such as urea and amide groups) and having the versatility to change its length, geometry and flexibility (examples are ligands

L^4–L^6 in Figure 10). Upon coordination to square-planar metal centres, it was expected that these ligands would yield macrocycles and cages with a wider range of sizes and geometries. In the next two sections, some of our more recent results obtained by using these two general types of ligands are briefly described.

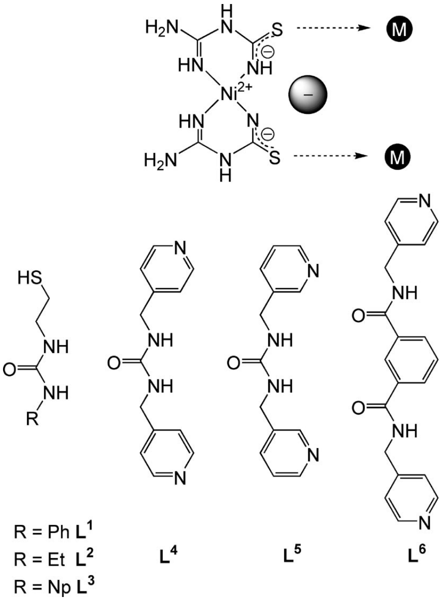
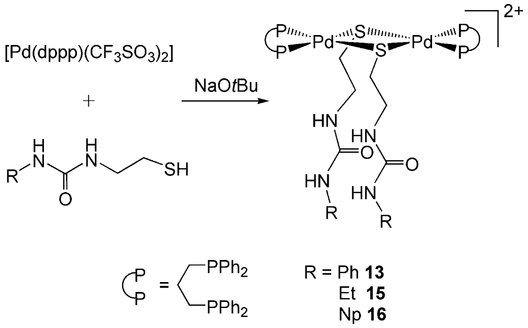


Figure 10. Selection of ligands designed on the basis of the coordinating and hydrogen bonding properties of the $[Ni(atu)_2]$ unit. **L^1–L^3** contain only one coordinating thiol group and a urea group as the hydrogen bonding unit. **L^4–L^6** are bidentate ligands [bis(pyridyl)] having a urea or amide group incorporated in the spacer group.

3.1 Palladium Dimers with Urea-Containing Thiolato Ligands

Ligands **L^1–L^3** have been employed to prepare a range of dinuclear palladium(II) complexes in which the thiolato group bridges the two metal centres while the urea moiety is "free" to interact through hydrogen bonds with potential guests (see Scheme 4).[63]



Scheme 4. Reaction scheme for the synthesis of dipalladium complexes.

As these thiols are easily synthesised, it is possible to prepare a range of ligands with slightly different spacer groups (between the thiol and the urea) and with different substituents on the urea group. This, in turn, provides an easy way to tune the binding properties of the resulting metal complexes. In addition to the above, thiolates are good ligands for a range of different metals (e.g. palladium, platinum and gold); this opens the possibility of preparing a range of complexes with different geometries. Although we have only reported products resulting from the reactions between these ligands and palladium so far (see below), we are currently exploring analogous chemistry with other metals such as platinum and gold. Once the thiols were prepared by the synthetic procedure shown above, their reactions with $[Pd(dppp)(OTf)_2]$ were carried out to afford the expected dinuclear complexes with bridging thiolato–urea groups (see Scheme 5). The formulation and structure of several of these compounds were confirmed by X-ray crystallography.[64] An interesting feature of these complexes is that the thiolato–urea ligands are positioned on the same side of the Pd_2S_2 plane; they are thus ideally preorganised to bind anionic guests. As is shown in the solid-state structure of one of these compounds (Figure 11), the N–H groups of the ureas form hydrogen bonding interactions with the anions (in this case triflates).

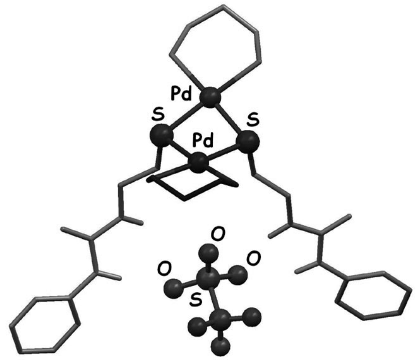


Figure 11. Molecular structure of $[Pd_2(dppp)_2\{\mu\text{-}SCH_2CH_2NHC(=O)NHPh\}_2](OTf)_2$ (**13**) (the phenyl groups on the dppp ligands and hydrogen atoms have been omitted for clarity).[63]

In the process of investigating these complexes, we came across an interesting compound in which the urea groups were shown to interact (in the solid state) with a sodium cation (the origin of which could be traced back to the NaO*t*Bu used to deprotonate the thiol) and an extra triflate. As can be seen in the crystal structure of this compound (see Figure 12), the sodium cation interacts with the oxygen atoms of the urea and its aromatic substituents. This forces the N–H groups to "point outwards" and interact with two of the triflate anions. Although this has not been investigated further, there is current interest in finding systems that can selectively interact simultaneously with specific anions and cations. Further work in this are could lead to the development of such systems based on these dipalladium compounds.

Once the overall structure of the dipalladium metallo-hosts was established, it was of interest to explore their anion-binding properties in solution. Titrations of the metallo-hosts in DMSO solution were carried out and monitored by ^1H NMR spectroscopy. From these studies,

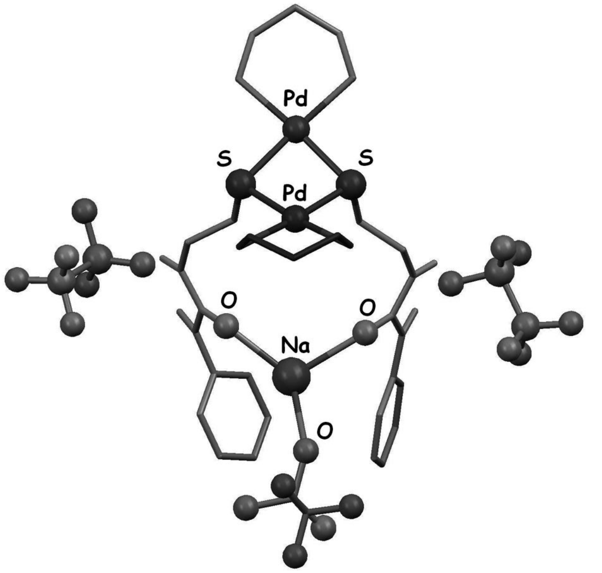


Figure 12. Molecular structure of $\{[Pd_2(dppp)_2\{\mu\text{-}SCH_2CH_2NHC(=O)NHPh\}_2](OTf)_2\}[NaOTf]$ (**13**·NaOTf) showing the interaction between the sodium ion and the oxygen atoms of the urea groups (the phenyl groups on the dppp phosphane ligands have been omitted for clarity). Most hydrogen atoms have been omitted for clarity.[63]

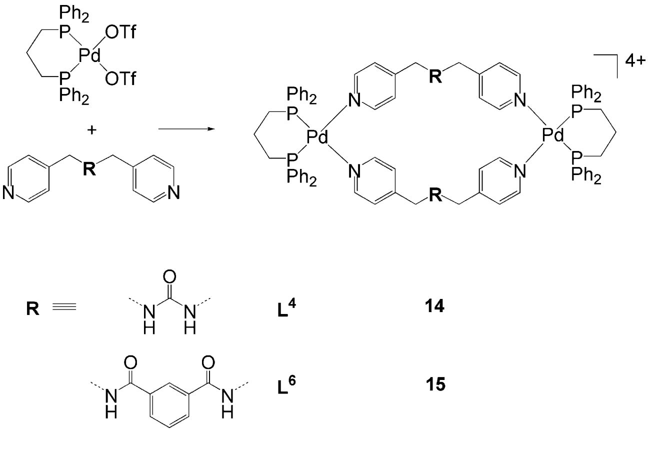
it was possible to determine the binding constants between **13** and different anions for establishing the selectivity of this metallo-host. The host–guest interactions were found to follow the trend: $H_2PO_4^- > [(PhO)PO_3H]^- > Br^- > Cl^- > HSO_4^- >> PF_6^-$ (the largest association constant was log $K_a = 3.5$ for $H_2PO_4^-$). It should be pointed out that the K_a values for the equilibrium between **13** and $H_2PO_4^-$, $[(PhO)PO_3H]^-$ and Br^- are very similar. This indicates that, although **13** binds anions reasonably well in DMSO, its selectivity is limited. Modifications to the ligands/complexes are currently being carried out to improve the selectivity of the system for specific anions.

3.2 Palladium-Based Macrocycles Having Bis(pyridyl) Ligands

As discussed in the second section of this review, an attractive approach for synthesising metallo-macrocycles is assembling simple building blocks in the presence of templating agents. If a set of building blocks can be linked in various ways, and the interaction that brings them together is reversible (e.g. labile metal–ligand bonds, hydrogen bonding, reversible covalent bonds), then a dynamic equilibrium between all the possible combinations of the molecular components can be established. This approach, known as dynamic combinatorial chemistry (DCC), can then lead to the formation of virtual libraries of compounds – named dynamic combinatorial libraries (DCL) – that are thermodynamically controlled.[65–69] The equilibrium of these virtual libraries of compounds can be modified by addition of an external guest or template. In principle, the template will favour the formation of the assembly that yields the thermodynamically most stable host–guest complex with that specific template. In this way, the added template amplifies the formation of the “best” receptor for the specific guest. This approach – pioneered by Sanders and Lehn – has already been used for the successful synthesis of metallo-macrocycles that can selectively bind specific guests. However, most of the examples of DCLs reported to date make use of cationic templates to amplify specific receptors from the library. In contrast, very few examples of anion-directed dynamic combinatorial libraries have been reported. Two elegant examples of metallo-assemblies formed by using this anion-directed DCL approach are the double helicates reported by Lehn[32] in the 1990s and the molecular triangles, squares and pentagons recently reported by Dunbar.[35,36] In both these cases, the presence of specific anions shifts the dynamic equilibrium towards the formation of a specific assembly.

Considering these ideas and our previous success in preparing metallo-cages and macrocycles by anion-templated processes, we engaged in studying systems with labile metal–ligand bonds that could generate a dynamic equilibrium. More specifically, we chose to investigate the reactions between bis(pyridyl) ligands (such as $\mathbf{L^4}$ and $\mathbf{L^6}$ – see Figure 10 in the previous section) and *cis*-$[Pd(P\text{–}P)]^{2+}$ centres. As has been demonstrated in studies by Fujita,[26] Stang[70] and others, square-planar palladium(II) centres are ideal “corners” for the synthesis of cages and macrocycles by a self-assembly processes. In spite of the vast literature in this area, there are surprisingly few studies in which the bridging ligands used to link the metal centres in the self-assembly process contain hydrogen bonding units.

We first studied the products resulting from the reactions between $[Pd(dppp)(OTf)_2]$ and the bis(pyridyl) ligand $\mathbf{L^4}$ (see Scheme 5). The reaction was carried out in CH_2Cl_2 by using a 1:1 palladium-to-ligand ratio. The combination of these reagents could in principle give a range of different cyclic and acyclic materials. Since palladium–pyridine bonds are relatively labile, it was expected that a dynamic equilibrium of different assemblies would be established (see below for more details).[71]



Scheme 5. Reaction scheme for the preparation of dipalladium macrocycles by using bis(pyridyl) ligands containing hydrogen bonding groups.

Crystals were grown from the reaction mixture, and an X-ray crystal structure analysis revealed the isolated product to be the [2+2] assembly [Pd(dppp)(**L^4**)]$_2$(OTf)$_4$ (**14**) (see Figure 13). In this assembly, the palladium centres have a distorted square-planar geometry in which two *cis* positions are occupied by the dppp ligand and the other two by the pyridyl groups of **L^4**.

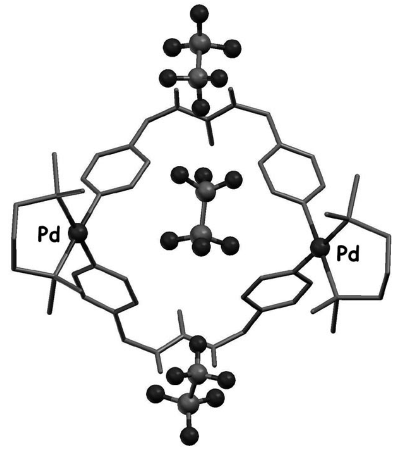


Figure 13. Molecular structure of the [2+2] metallo-macrocycle [Pd(dppp)(**L^4**)]$_2$(OTf)$_4$ (**14**) (the phenyl groups of the dppp phosphane ligands have been omitted for clarity). Three triflate anions (in "ball-and-stick" representation) interact with the central cavity of the metallo-host.[71]

Analogous [2+2] metallo-assemblies were crystallised from the reactions between [Pd(dppp)(OTf)$_2$] and **L^6** (see Figure 14) and between [Pd(dppf)(OTf)$_2$] and **L^5**. Once again, these assemblies demonstrated that the anion is indeed encapsulated by the bowl-type metallo-assemblies.[71]

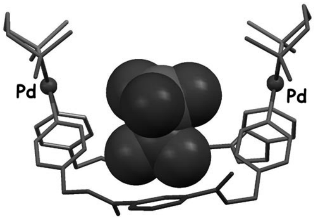
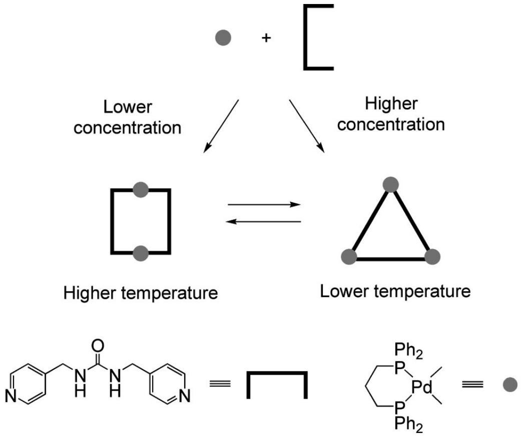


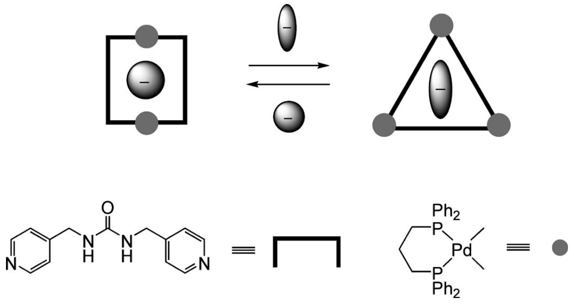
Figure 14. Molecular structure of the [2+2] metallo-macrocycle [Pd(dppp)(**L^6**)]$_2$(OTf)$_4$ (**15**) (the phenyl groups of the dppp phosphane ligand have been omitted for clarity). One of the triflate anions (shown in space-filling representation) is located in the middle of the assembly.[71]

In spite of the three solid-state structures obtained for these systems, ^{1}H NMR spectroscopic studies in solution indicated that more than one species co-existed in solution. As indicated above, in principle a 1:1 mixture of the bis(pyridyl) ligands and *cis*-[Pd(P–P)]$^{2+}$ (where P–P stands for chelating diphosphane) centres could yield macrocycles of different sizes (or even acyclic products). Several ^{1}H NMR spectroscopic and ESI mass spectrometric studies were carried out with one of the systems – [Pd(dppp)(OTf)$_2$] and **L^4** – to establish its behaviour in solution. These studies suggested that there is indeed an equilibrium between a [2+2] and a [3+3] metallo-assemblies, which can be shifted by modifying the experimental conditions; for example: (a) by a change in solvent (e.g. in DMSO, ^{1}H NMR spectroscopy provides evidence for more than one species, whereas in acetone only one of the species is present); (b) by a change in concentration (dilution experiments in DMSO confirmed that at higher concentrations the [3+3] assembly is favoured); (c) by a change in temperature. These observations are summarised in Scheme 6.



Scheme 6. Schematic representation of the influence that concentration and temperature have on the nuclearity of the system.

Once the behaviour of the system in solution was established, it was of interest to investigate whether the addition of anions to the reaction mixture would amplify the formation of one of the products. Interestingly, it was indeed demonstrated that specific anions can favour the formation of one of the metallo-assemblies; e.g. addition of several equivalents of $H_2PO_4^-$ to a DMSO solution containing a mixture of the [2+2] and [3+3] assemblies shifted the equilibrium to the formation of only one of them – the [2+2] assembly (see Scheme 7).



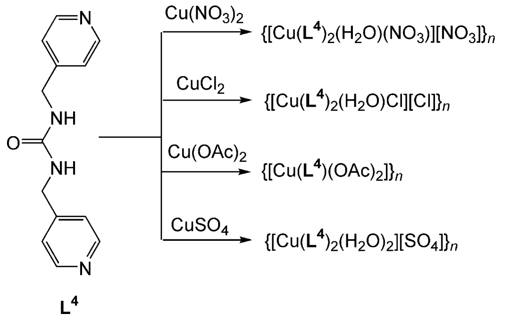
Scheme 7. Schematic representation of the change in nuclearity of the system upon addition of different anions.

Although these is still a very simple "library" of metalloreceptors, the principles have been set for the development of more complex and potentially useful dynamic combinatorial libraries based on metallo-assemblies – e.g. by mixing several hydrogen bonding ligands with *cis*-[Pd(dppp)]$^{2+}$ centres.

4. Anion Influence on the Structure of Polymeric Metal–Organic Assemblies

The same concepts of anion templation and self-assembly, employed for the synthesis of metallo-macrocycles and -cages, could in principle be used for the development of coordination networks and frameworks. These polymeric nanomaterials can have important potential applications in sensing, storage and catalysis. However, a frequent problem when synthesising this type of infinite metallo-assemblies is that, due to the relatively labile nature of metal–ligand bonds and the various potential geometries of metal centres, it is often very difficult to predict a priori the final structure of the assembly. One of the several factors that can have a great impact on the final structure of metal–organic frameworks is the nature of the counteranions present.[72] Most metal–organic networks/frameworks use metal cations with charges between +1 and +3. Therefore, the crystalline metal assembly has to compensate all the positive charges with the corresponding anionic species. This can be done by either of two approaches: using negatively charged ligands or, if the ligands are neutral, using the counteranions of the metal to balance the charges. In the latter, anions can either coordinate strongly to vacant sites on the metal centre or remain as noncoordinating counterions in the metal–organic assembly. However, even if they do not interact directly with the metal centres, noncoordinating anions can dictate the structural properties of the final assembly by preorganising the ligands (i.e. by acting as templates).

With this in mind, we studied the ability of some anions to control the formation of infinite metallo-assemblies by treating different copper(II) salts with the bis(pyridyl) hydrogen bonding ligands **L^4** and **L^5**. The reactions which have been studied and the resulting products are summarised in Scheme 8.[73]



Scheme 8. Summary of the reactions carried out between ligand **L^4** and different copper(II) salts.[73]

At the time we started our investigations, the reaction between **L^4** and $Cu(NO_3)_2$ had been previously shown to yield a coordination network with the formula $\{[Cu(\mathbf{L^4})_2(H_2O)(NO_3)](NO_3)\}_n$ (**16**).[74] In this metallo-assembly one of the nitrates is directly coordinated to the copper centres, while the other one is located outside the coordination sphere and forms hydrogen bonds with the urea groups of the ligand. We found an analogous structure when the reaction was carried out with $CuCl_2$: a non-interpenetrating grid of formula $\{[Cu(\mathbf{L^4})_2(H_2O)Cl][Cl]\}_n$ (**17**) was formed with one of the chloride atoms directly bound to the metal centre and the second one located as a free ion in the channels formed by the grids (see Figure 15).

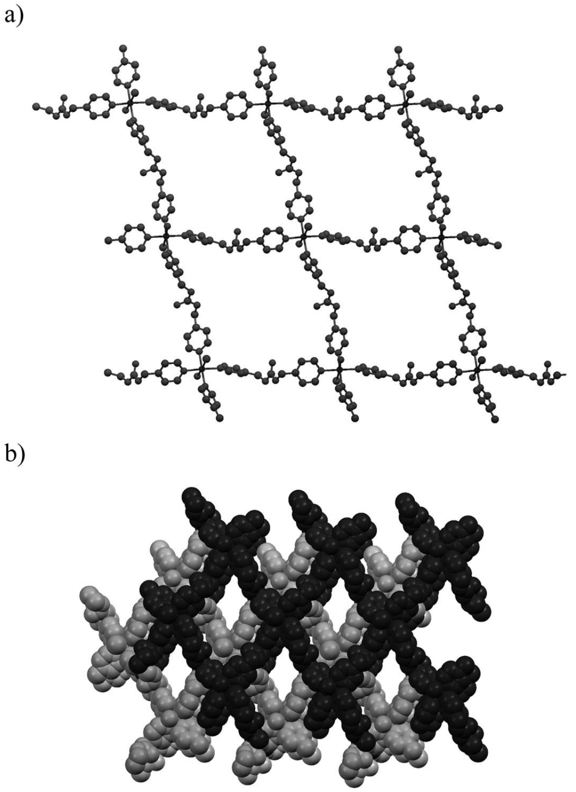


Figure 15. (a) Section of the 2D infinite assembly of metallo-squares formed by reaction between $CuCl_2$ and **L^4** (the copper centres are located at the corners of the squares); (b) The 2D assemblies of metallo-squares stack on top of each other, generating channels that are filled with solvent molecules and accommodate the free chloride counteranion (the figure represents four layers of 2D assemblies).[73]

In contrast, the reaction of $Cu(OAc)_2$ and **L^4** yielded a 2D network of copper(II) centres with the formula $\{[Cu(\mathbf{L^4})(OAc)_2]\}_n$ (**18**). The copper centres have a square-based pyramidal geometry; three independent **L^4** molecules and two acetate ligands coordinate to the metal. In this assembly, the equatorial positions of the copper centres are coordinated by two pyridine rings and two acetate anions, while the axial position is occupied by a third ligand coordinated through the carbonyl group of its urea moiety (see Figure 16). This type of coordination leads to the formation of a polymeric assembly of $Cu_2(\mathbf{L^4})_2$ rectangles.

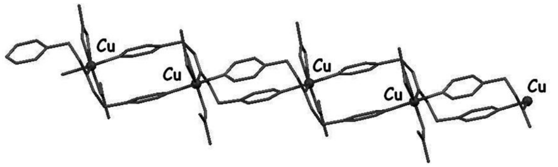


Figure 16. Partial view of the polymeric assembly of metallaboxes formed by bridging of the copper centres with **L^4** through the pyridyl (in the equatorial positions) and urea (axial position) moities of the ligand. The acetate anions are coordinated to the metal centres. Hydrogen atoms have been omitted for clarity.[73]

Yet another different assembly is obtained when the same reaction is carried out with $CuSO_4$ and ligand **L⁴**. In this case a polymeric network with the formula $\{[Cu(\mathbf{L^4})_2(H_2O)_2][SO_4]\}_n$ (**19**) is formed (see Figure 17) in which each copper(II) centre is coordinated to four independent ligands through their pyridyl groups and to two water molecules. An interesting feature of this polymeric assembly is that, in contrast to the other structures described above, the sulfate anions are not coordinated to the copper centres. Instead, they form hydrogen bonds with the urea groups of the bridging bis(pyridyl) ligand and the coordinated water molecules.

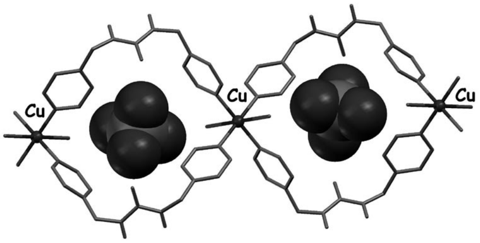


Figure 17. Partial view of the crystal structure of the assembly resulting from the reaction between $CuSO_4$ and **L⁴**. In this case, the anions are located above the macrocycles formed by coordination of four different bridging ligands to each copper(II) centre. The sulfate anions are shown in space-filling representation (most hydrogen atoms have been omitted for clarity).[73]

The four polymeric metallo-assemblies described in this section highlight the important role that anions play (either by direct coordination or by templation) in defining the overall structure of the assembly. With a better understanding of the anion–ligand and anion–metal interactions, it may be possible in the future to prepare metal–organic frameworks in a more controlled and rational fashion. This in turn, will have important implications in the widespread applications of these interesting nanoporous materials.

5. Concluding Remarks and Outlook

Metal complexes containing ligands that feature hydrogen bonding functionalities have proven to be very good molecular receptors for the selective recognition of anions. Structurally, metal centres can play an important role in organising hydrogen bonding ligands for optimal binding of anions. In addition, the Lewis acidity of metal centres can enhance the interaction between anions and metallo-hosts. The diverse properties of metals (optical, magnetic and electrochemical) are potentially very useful in the development of chemical sensors for anions.

The templating role of anions for the formation of supramolecular metallo-assemblies has also been presented. At the time that our first halide-templated metallo-cages and macrocycles were reported, only a handful of anion-templated systems had been studied previously. Since then, the area has grown considerably and a wide range of metallo-assemblies can now be prepared by using anion-templated approaches. Using anion templates, we have also explored the formation of metallo-receptors by dynamic combinatorial approaches; although our results are still preliminary, this area promises to yield interesting and novel chemical receptors for a range of different anions. Finally, the use of anions to direct the formation of specific metal–organic polymeric materials has been successfully explored to produce a range of different frameworks, some of which have nanoporous structures.

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