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Editorial
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Ligand Design Virtual Issue

It is important to stress from the outset that this ACS Select Virtual Issue has nothing to do with protein binding and enzyme chemistry, where the terms "ligand design" and "drug design" are almost synonymous.[1] The articles chosen herein describe innovative arrays of donors that can bind to one or more metal ions to generate complexes that display some noteworthy properties, such as new reactivity patterns or intriguing structural features. Coordination chemistry has evolved in truly remarkable ways because of new kinds of ligands, new arrangements of donor atoms, and controlled geometries, in other words, as a result of *ligand design*. For example, the introduction of stable N-heterocyclic carbenes (NHCs) has changed the way people think about ligand choices.[2] In this ACS Select Virtual Issue, some recent ligand designs will be highlighted that not only are fascinating but also, in certain cases, evoke a paradigm shift in our thinking about coordination chemistry.

Why is there interest in ligand design? It is now accepted that small changes in the sterics and electronics in a ligand structure can result in dramatic changes in reactivity patterns of otherwise nearly identical complexes.[3] So, to answer the question, one can generate diverse chemistry by simply making changes in the ligand set. It would be wonderful if we could predict what the resulting reactivity patterns would be for a given set of donor atoms on a particular metal center. However, we are not there yet, although computationally, this should be surmountable in the not too distant future. For now, we still tend to operate on a "try it and see" approach.

For the purposes of this issue and expediency, non-innocent, redox-active, and cooperative ligands are excluded. The entire area of research on ligands that act in concert with the metal center to effect a transformation would make a great subject for another Virtual Issue. Rather, this collection will focus on multidentate arrays of donor atom systems that allow unusual geometries, provide platforms for small-molecule activation, and also can engage in catalytic transformations. There is no doubt that many worthy ligand designs may have been overlooked; we accept full responsibility for these omissions and hope to see them highlighted elsewhere.

Homogeneous catalysis has made great strides because of innovative ligand designs. For example, from Wilkinson's catalyst using PPh_3 as the ancillary ligand for the hydrogenation of alkenes to chiral bidentate phosphines such as binap[4] for the asymmetric synthesis of amino acid precursors, ligand designs have gone hand-in-hand with process optimization. As was already mentioned, NHCs are de rigeur in terms of ancillary ligands in catalysis, and in alkene metathesis, Grubbs' NHC systems are standard in organic laboratories across the world.[5] While catalyst systems are not the focal point herein, it is clear that the impetus for new, stable, and efficient homogeneous catalysts relies heavily on ligand design.

The inspiration that biology has had on inorganic chemistry has also impacted ligand design. Models for active sites of metalloenzymes continue to help us understand how they operate, and these models require ligand designs that allow particular metal environments to be simulated. This aspect has been nicely illustrated by the Virtual Issue on Models of Metalloenzymes (http://pubs.acs.org/page/vi/2013/models-of-metalloenzymes.html).

In this seventh Virtual Issue that follows the most recent on Inorganic Chemistry Driving the Energy Sciences (http://pubs.acs.org/page/vi/2015/InorgChemEnergySci.html), 25 articles were chosen to highlight advances in ligand design from recent issues (mostly from 2014 to 2015) of the leading American Chemical Society journals *Inorganic Chemistry*, *Organometallics*, and *Journal of the American Chemical Society*. This online ACS Selects Virtual Issue makes these articles available in a single collection along with their synopses for comprehension by the nonspecialist. The findings described in the selected articles illustrate the breadth of the field and show how innovative ligand designs are opening up new ways to activate small molecules by metal complexes, in both stoichiometric and catalytic modes. More importantly, designing new multidentate ligands has provided a creative outlet for many research groups to try to tailor metal complexes to engage in new reactivity patterns and new structural motifs.

Using the key word "pincer" in a search on the ACS Web site reveals hundreds of articles involving various aspects of ligand design. Of all of these articles, the following two papers exemplify the range of reactivity patterns that one can expect from these tridentate, meridionally bound PCP- or PCN-type donor sets. Goldman et al. have just published[6] a study of the gas-phase dehydrogenation of *n*-alkanes by ethylene or propylene using solid-phase IrPCP pincer complexes. This intriguing catalytic process has been studied kinetically and computationally, and the findings show how the structure of the ligand affects the rate; also of interest is that this heterogeneous solid–gas process favors the α-olefin products more than was found for similar homogeneous solution-phase processes. In a second contribution, Guan et al.[7] describe a Ni–POCOP system with stereogenic phosphorus centers and show that the *meso* and *rac* diastereomers, after separation, are configurationally stable enough even at 110 °C to be used in asymmetric catalysis.

While pincer ligands continue to be modified in intriguing ways, particularly by changes in the backbone,[8] the donors,[9] and the linking atoms,[10] a remarkable innovative change was reported[11] by Kita and Miller in which they incorporated a crown ether onto the amine arm of a PCN pincer. This pincer crown ligand design opens up new ways to affect the reactivity at a metal center. For example, they report how the proton–deuterium exchange of an iridium(III) hydride unit is dramatically affected by the addition of various alkali-metal ions; the most dramatic affect is the addition of Li^+, which results in a 10-fold increased rate compared to Na^+. The aza-crown portion of the PCN pincer can bind in different modes, further increasing the utility of this innovative ligand design.

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Because control of sterics is straightforward in many ligand designs, understanding how steric properties influence small-molecule activation by metal complexes is possible. A particularly noteworthy example of this is the introduction of adamantyl groups on the well-established tris(pyrazolyl) (Tp) donor framework. As reported by McSkimming and Harman,[12] reduction of a $Fe^{II}Tp$ system with adamantyl units results in the stabilization of the first mononuclear iron(I) dinitrogen complex, which is unique in that the iron(I) center is high spin. Changing the substituents to the less bulky phenyl group results in a diiron system with a linear, end-on bridging dinitrogen moiety, which is well established for these kinds of systems.[13]

Novel iron(III) complexes can be stabilized by the use of trianionic tris(pyrrolide) ligands, as reported by Sazama and Betley,[14] who found that the controlled oxidation of the iron(II) "ate" complexes generated the desired iron(III) derivatives; further reaction with a diazoalkane results in an unusual antiferromagnetically coupled iron(III) "ate" complex with the coordinated diazoalkyl radical. The Veige group has also made important contributions to trianionic multidentate ligand systems; their ONO^{3-} donor set can also stabilize iron(III) systems[15] along with high-oxidation-state early-metal compounds. Ishida and Kawaguchi[16] have reported a related trianionic ONO^{3-} ligand set; in this case, vanadium nitride systems can be accessed that show nitrogen-atom-transfer reactions.

A strictly bidentate ligand that incorporates two vastly different donors has just been reported by Nakano and Nozaki.[17] By using a combination of strong and weak σ donors, namely, an NHC and an aryloxy in a chelate system that can be sterically modified, a neutral palladium(II) methyl complex has been shown to act as a very efficient copolymerization catalyst precursor that can incorporate polar monomers in a controlled fashion. The key to ligand design is the balancing of the electronic effects of the different donors and the steric effects of the NHC substituent.

The use of macrocyclic dipyridinediamine systems reported by Mirica et al.[18] has allowed for the stabilization of palladium(III) systems. The key to these ligand designs is that they provide variable donor availability via *conformational flexibility*. For example, in the square-planar palladium(II) complexes, only the pyridine donors bind to the central metal; however, upon oxidation, the palladium(III) systems adopt an octahedral geometry that is facilitated by the proximate amine donors in the macrocyclic array. The authors also note that the ease of oxidation is remarkable, a likely result of the conformational versatility of this ligand set. When this same ligand set is coordinated to nickel(III), Mirica et al. have documented[19] cross-coupling and carbon heteroatom bond formation reactions that clearly indicate the usefulness of dipyridinediamines in providing fundamental knowledge on key processes related to catalysis.

Other interesting ligand systems can also engage in different binding modes. A neutral, arene-bridged bis(diisopropylphosphine) system developed by Agapie and co-workers[20] has shown a remarkable ability to interact with one or more metals. With molybdenum(0), the central arene can bind η^2, which upon oxidation results in the loss of CO and the formation of η^6 variants that can further undergo reactions with hydride reagents and reductants. This system is active as an ammonia borane dehydrogenation catalyst. This same ligand type was shown earlier[21] to bind three nickel atoms in a triangular mode.

There have been some remarkable ligand systems specifically designed to bind to two or more metal ions. Franc Meyer's group has developed a pyrazolate-bridged ligand set with a variety of donor types. A recent report with Llobet et al.[22] describes a bipyridine-decorated pyrazolate system that can bind two ruthenium(II) systems and act as a water oxidation catalyst. It is proposed that the two Ru−oxo units act in concert to facilitate the key O−O bond-forming event. Peters' group has made a number of remarkable ligand sets based on P_3E donor arrays where E = C, Si, B, P, N. Recently, they developed[23] a strategy to use this same kind of approach but extend the system so that it can incorporate two iron(II) centers. The use of an arene thiolate unit allows the formation of a diiron complex that, under reductive conditions, can bind two terminal dinitrogen units.

Ligand systems that can bind two different metal ions have been developed by a number of groups. The Thomas group has used the phosphinoamide linker as a simple way to connect disparate metal ions such as zirconium and cobalt and generate a series of complexes that have the remarkable ability to activate small molecules, such as dinitrogen. A recent report[24] describes a versatile $Zr-CoN_2$ system that can be modified to change the nature of the Zr−Co interaction from a formal double bond to a single Co−Zr donor interaction. In this case, the phosphinoamide linker undergoes a rearrangement from bridging to nonbridging and back to bridging.

The collaboration of the Love and Arnold groups has resulted in a series of papers that utilize an easily assembled pseudo "pacman" bis(macrocycle) that allows the incorporation of uranium(VI) and other metals in a controlled fashion. Most recently,[25] this system has helped their groups to make important contributions to understanding what conditions are necessary to effect reduction of the very stable uranyl ion.

Probably one of the more intriguing ligand designs that is specific for generating bimetallic complexes is the N_3P_3 donor set developed by Lu's group. With this framework, her group has recently worked with the Gagliardi group[26] to examine in detail the influence of different donor metals on the ability to tune the reactivity of a dinitrogen ligand moiety in a $M-Co-N_2$ unit. From heterobimetallic systems such as M = Al, V, or Cr to the homobimetallic M = Co, interesting differences are observed that can correlate to the different metal combinations. Moreover, Arnold's group, in collaboration with the Lu group, has shown[27] that actinide incorporation into this N_3P_3 donor set allows the further activation of a carbonyl−cobalt moiety that can subsequently be transformed photochemically to generate a heterobimetallic An−Co interaction, where An = Th, U.

There have also been ligand sets that can incorporate even more metals such as in the work by Colacio and co-workers.[28] Schiff-base-type ligands based on a phenolate ether side arm have provided Ln−Ni−Ni−Ln (Ln = lanthanide) arrays that display complicated temperature-dependent magnetic behavior for Ln = Dy, while for Ln = Gd, a significant magnetocaloric effect is observed.

The triphenylene core has been modified by the Himmel group[29] to generate trinuclear complexes using the guanidine functionality. While the hexakis(tetramethylguanidino)−triphenylene (L) moiety is itself redox-active, the neutral ligand can coordinate three metals arranged around the periphery. The $L(CuX)_3$ systems display considerable twist distortion of the central arene ring. For X = I, the three copper(I) centers can be oxidized to generate $L(CuI_2)_3$ by the addition of stoichiometric diiodine without oxidation of the ligand. Low-temperature magnetic experiments and DFT calculations show that there is magnetic superexchange for the three copper centers, which is most prevalent for $L(CuI_2)_3$. Interestingly, this ligand can also bind three nickel(II) centers to generate $L(NiCl_2)_3$ and three cobalt(II) derivatives to generate $L(CoCl_2)_3$; interestingly, the cobalt(II) centers show only small magnetic coupling, although the zero-field splitting is relatively large. The incorporation of silver(I) centers allows for aggregation and the formation of iodide-bridged coordination polymers.

A number of outstanding contributions have recently appeared from the Murray group,[30] wherein a trinucleating cyclophane system incorporates three β-diketiminato units. This array of three bidentate donors creates a unique environment in which three metal ions can interact with small molecules. In a recent article,[31] three iron centers interact with a nitride moiety in a manner that has relevance to dinitrogen activation by nitrogenase.

Ligands that incorporate the heavier members of group 15 have been reported by the Gabbaï and Limberg groups. A tetradentate stibine-based ligand[32] attached to platinum undergoes a ligand-based oxidation to add F^- ions to the stibine without binding at the soft platinum(II) center. Similarly, Limberg et al.[33] report a related system based on bismuth in which a tridentate interaction with platinum(0) and platinum(II) can be documented.

As mentioned at the beginning of this Editorial, NHCs are important donor groups that have reinvigorated coordination chemistry with their ease of synthesis, their strong donating ability, and their unique steric effects. The Hahn and Peris groups[34,35] have reported two multi-NHC assemblies that illustrate how ligand designs can be used to create unique multimetallic environments. Decorating 1,3,5-triphenylbenzene with three NHC donors has allowed the supramolecular assembly of a cylindrical framework wherein three coinage metals [copper(I), silver(I), and gold(I)] bridge the two arene tris(NHC) units. The ability to modulate the distances between the arene units is intriguing and may lead to ways to tailor the cavity size. The final paper chosen by Meyer's group[36] describes the coordination chemistry of a ferrocene unit decorated with one pyrazolyl unit on each ring, which with copper(I) and silver(I) generates a structural motif similar to the tris(NHC) units described by Hahn et al.; in this case, the ferrocene units act as the linker between the two triangular metal environments with bridging pyrazole moieties.

With the above ligand design papers, we have tried to capture some recent results that exemplify the creativity of coordination chemists in their ability to imagine multidentate ligand systems that can generate new and unusual kinds of coordination environments for one or more metal ions. There is no doubt that future ligand designs will be equally innovative and affect the way we think about small-molecule activation, homogeneous catalysis, metalloenzyme modeling, and many other areas yet to be discovered. I for one am looking forward to those "wow" moments when I read articles in the future that feature new ligand designs.

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Notes

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