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Non-Symmetric Pincer Ligands: Complexes and Applications in Catalysis

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Pincer ligands have become ubiquitous in organometallic chemistry and homogeneous catalysis. Recently, new varieties of pincer ligands with non-symmetrical backbones and/or ligating groups, have been reported and their application in transition metal complexes has been exploited in a variety of catalytic transformations. This non-symmetric approach vastly increases the structural and electronic diversity of this class of ligand. This approach has proven benificial in a variety of ways, such as the use of a single weakly coordinating moiety, which can dissociate and thereby create a vacant coordination site to increase catalyst activity. Additionally, this provides further access to chiral ligands and complexes for assymetric induction. This perspective highlights recent, important examples of non-symmetric pincer ligands, which feature aryl or pyridine backbones, the synthesis and use of subsequent complexes in catalytic transformations, and discusses the future potential of this type of ligand system.

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Introduction

Pincer ligands, tridentate ligands that coordinate meridionally, have been used with a wide variety of transition metals – early, late and f-block – and these complexes have proven to be excellent catalyst for a variety of synthetic transformations, including hydrogenation, coupling and polymerization reactions.[1] The tridentate ligand scaffold has numerous advantages such as producing incredibly robust complexes, which are generally more stable than similar complexes featuring monodentate ligands. This allows these complexes to be used as catalysts in reactions that require high temperatures and pressures without catalyst decomposition. Additionally, the constrained geometry can increase reactivity and, thanks to the large variety of available pincer ligands, the geometries and electronics can be widely modified thus tuning the reactivity of the metal centres that feature these ligands.

Typically, pincer ligands have C_{2v} symmetry, having a central donor moiety (often an *meta*-substituted aryl or pyridine derivative) and two symmetrical substituents with coordinating groups. This symmetrical approach serves to simplify the ligand synthesis and allows for a variety of steric and electronic environments to be created. However, recently, a number of pincer ligands that lack this symmetry have been reported. This desymmetrization can be accomplished by adding substituents to the backbone of the C_{2v} pincer ligand without changing the donor groups, by changing the donor of one of the substituents, or by combining both of these techniques. This results in an enormous increase in the number of potential ligands and gives additional parameters for the tuning of the stereo-electronic properties of the ligand system. Additionally, in ligands where the donor properties of the arms are significantly different, the more labile donor can generate a free coordination site for reactivity at the metal centre while maintaining stability with the two remaining ligating moieties. This lack of symmetry also facilitates the introduction of chirality to the pincer ligand scaffold at various positions. Thus, complexes featuring enantiomerically pure pincer ligands clearly have potential for asymmetric induction during catalytic processes.

Non-symmetric pincer ligands have been around for quite some time but in the past 10 years there has been an acceleration in this area of research with several examples of non-symmetric systems reported to achieve catalytic results matching or surpassing those of comparable symmetric systems. The goal of this perspective is to highlight some of the most recent and important developments in the design, synthesis and catalytic reactivity of non-symmetrical pincer ligands, comment on the potential of this area and examine future possibilities. The quantity of excellent research in this domain precludes a thorough discussion of all known systems so herein we will concentrate on examples of systems with either central aryl rings **A** or pyridine rings **B** (Fig. 1), especially those with catalytic applications.

The non-symmetrical pincer ligands will be divided into two main categories: first, the ligands with symmetrical donor atoms (for simplicity the functionality of the donor is not considered, therefore N-donors include all amines, imines, amides etc.), primarily consisting of those with unsymmetrical substitutions to the backbone (E and R), second, those with unsymmetrical donor atoms ($L^1 \neq L^2$) both with symmetrical and non-symmetrical backbones.

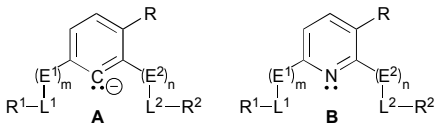
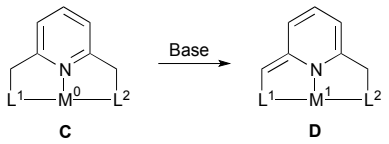


Fig. 1 Non-symmetrical aryl-based pincer ligands **A** and pyridine-based pincer ligands **B**.

1. Non-symmetric Backbones

This section will focus on examples of modifications to pincer systems of type **A** and **B** on the aryl group (R), changes of the linkers ($E^1 \neq E^2$ and/or $m \neq n$), different substituents at the L groups ($R^1 \neq R^2$), or a combination of these.

Some of the most common and widely used pincer ligands can undergo redox processes or be deprotonated in the coordination sphere of the metal, which can change the charge of the ligand, the oxidation state of the metal and/or create a non-symmetrical ligand system. This process can play an integral role in the catalytic activity of the complexes and often these complexes can be isolated. For example, complex of type **C** will give, upon deprotonation, the M(+1) complex of type **D** with a de-aromatized and unsymmetrical ligand system (Scheme 1). The importance of non-innocent ligands and cooperative effects has been reviewed elsewhere[1d, 2] but ligands which become non-symmetrical only via these processes will not be covered in this perspective.



Scheme 1 Generalized base induced de-aromatization process that many pincer complexes undergo.

There are also examples of systems that have C_s symmetry rather than the C_1 symmetry of the majority of examples that will follow. This reduction in symmetry does not occur by changing the pincer itself but rather by coordination of a metal. This change in symmetry is important and does give the potential for the synthesis of planar chiral metal complexes (vide infra). As such these important examples will be treated here.

The first such example of a bimetallic C_s symmetric complex featured an **A** type ligand ($E^1 = E^2 = CH_2$, $L^1 = L^2 = NMe_2$). Palladium and platinum chloride complexes could be reacted with $CpRu(CNMe)_3$ or $Cp^*Ru(CNMe)_3$ cations to give the bimetallic systems **E** (Fig. 2).[3] NMR and electrochemical studies indicated that the RuCp fragment had a σ-withdrawing effect on the NCN pincer ligand. The interaction between the two metal centres was also probed by synthesizing two additional bimetallic complexes, the first with a para-phenyl substituent on the NCN backbone **F**[4] and the second with an ethyl linker between the phenyl group and the aryl group of the ligand **G**.[5] In each case the RuCp moiety complexes the phenyl group and is therefore more remote from the palladium pincer group. Subsequent experimental and theoretical results further demonstrated the electron withdrawing effects of the RuCp* moiety. Initial results indicated there was no through space interaction between the two metal centres. However, theoretical and experimental results into the binding of SO_2 by the same series of CNC ligands with PtCl (in lieu of palladium) did indicate some through space interaction between the metal centres.[6]

The classical PCP pincer ligand $\mathbf{H^{iPr}}$ (**H**, R = *i*-propyl) and the sulphur analogue (with S*i*Pr groups in lieu of P*i*Pr$_2$ groups) have also been used to form bimetallic pincer complexes with RuCp and RuCp*.[7] This is again accomplished via reaction of the preformed PdCl pincer complexes with $CpRu(CNMe)_3$ or $Cp^*Ru(CNMe)_3$ cations. These species are noted to have similar properties to the NCN bimetallic systems.

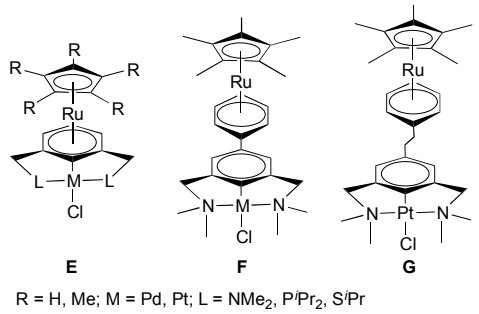


Fig. 2 First examples of bimetallic sandwich pincer complexes **E-G**.

The symmetrical POCOP system $\mathbf{F^{iPr}}$ (**F**, R = *i*-propyl) has been used to form sandwich complexes with Fe(Cp') (Cp' = 1,2,4-trimethyl-cyclopentadienide) and Ru(Cp) fragments.[8] In all cases a preformed POCOP metal complex is used and the corresponding cationic piano stool compound $[Cp'Fe(NCMe)_3]^+$ or $[CpRu(NCMe)_3]^+$ is added to form the desired sandwich complexes. POCOP Ni, Pd and Pt chloride complexes react with the ruthenium precursor to give isolable products while only $\mathbf{F^{iPr}}$IrH(Cl) has been reported to react with $[Cp'Fe(NCMe)_3]^+$ to give the corresponding bimetallic species.[8b]

A. Non-symmetric PCP ligands and complexes

Diphosphines with an aryl linker are one of the first pincer ligands and certainly one of the most prodigious. The symmetrical PCP **E** (with methylene linkers)[9] and POCOP **F** (derived from readily available resorcinol derivatives featuring ethereal linkers)[10] are the basis for a considerable number of non-symmetric systems (Fig. 3).

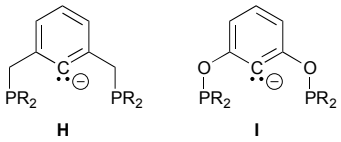
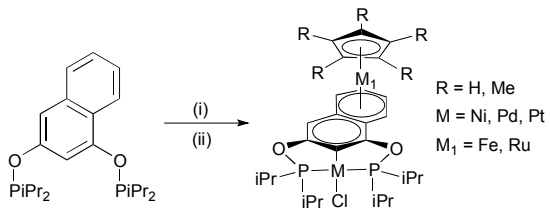


Fig. 3 PCP ligands **H** and POCOP ligands **I**.

An excellent example of a simple and effective unsymmetrical modification to this well-known backbone is the POCOP ligand **1** (Fig. 4), which is very easy to synthesize from naphthoresorcinol, base, and phosphine chloride.[11] Addition of $NiCl_2$, $PdCl_2$ or $PtCl_2$ to $\mathbf{1^{iPr}}$ leads directly to the desired metal chloride pincer complexes, which can be isolated. Like the symmetrical pincers discussed above, addition of $[CpRu(NCMe)_3]^+$ or $[Cp^*Ru(NCMe)_3]^+$ leads directly to bimetallic sandwich complexes, with the caveat that the resultant species are in fact planar chiral (Scheme 2).[12] The reaction is entirely regioselective, only forming the sandwich complex with the unsubstituted aryl ring of the napthyl moiety for steric reasons. Bimetallic ferrocene-like derivatives were also accessible by mixing the pincer complex with ferrocene in the presence of $AlCl_3$ and subsequent quenching with $[PF_6][NH_4]$. The isolated iron

sandwich Ni, Pd, and Pt complexes all display the same regioselectivity. Finally, bimetallic Cr/Ni, Pd or Pt complexes were available from the reaction of the corresponding pincer complex and $[Cr(C_{10}H_8)(CO)_3]$ to give the $Cr(CO)_3$ piano stool-type complexes, again regioselectively.[12] Methods to isolate the enantiopure bimetallic complexes are currently under investigation. Pincer **1** with phenyl groups (**1^{Ph}**) has also been reported and while similar monometallic complexes are almost certainly possible, only the the **1^{Ph}**NiCl complex has been reported by refluxing $NiCl_2$ and the ligand in toluene.[11] This species is the only complex with a type **1** ligand to be used in catalytic reactions (vide infra). In these cases it is important to note that POCOP nickel complexes are rare[10b] and the ability to synthesize them from a commercially available and inexpensive precursor such as $NiCl_2$ is a particular advantage. Bimetallic species with **1^{Ph}** have not been reported and may not be viable because of competitive coordination reactions with the aryl groups at the phosphines.[7]

PCP ligands **H** can be modified in perhaps the most obvious way; by having different groups on the phosphines themselves ($R^1 \neq R^2$). This has been done first by having one PPh_2 and either a P^tBu_2 or P^iPr_2 substituent **2**.[13] Unfortunately, while the chemistry has reasonable yields and is rather straightforward, it is much more arduous, requiring up to 11 steps (though no purification is required between some steps), a far cry from the simplistic synthesis of symmetrical versions. However, once synthesized they readily ligate to metals as expected. In both cases reaction of the pincer with $PdCl_2$(COD) gave the expected **2**PdCl complexes. It is interesting to note that, as yet, no examples of POCOP ligands with $R^1 \neq R^2$ have been reported, which can most likely be attributed to the synthetic complications.



Scheme 2 Synthesis of bimetallic POCOP sandwich complexes.

PCP ligands can also be made non-symmetrical at the position *alpha* to the phosphine (on the methylene bridge, $E^1 \neq E^2$). A single methyl group can be added on only one of the methylene linkers to create not only a non-symmetric ligand but a chiral one as well. Like with other PCP ligands, the synthesis begins from α,α'-dibromo-*m*-xylene. The subsequent four-step synthesis has a very good overall yield and the resultant ligand **3** reacts with $PdCl_2$(COD) to give the desired **3**PdCl pincer complex.[14] The reported synthetic methodology unfortunately yields a mixture of stereoisomers that were unresolved but serves as an excellent proof of concept and there is the potential to use this methodology to make a variety of non-symmetrical pincer ligands. This type of modification is obviously not possible in the case of POCOP **I**.

The inability to put differing groups at the phosphine means any non-symmetrical substitution to POCOP **I** has to be done at an even more remote position. Substitution at the 3-position of the aryl ring is possible and rather simple if the appropriate resorcinol derivative can be obtained. Just such a ligand **4** can be made, for example, from 4-*n*-dodecylresorcinol, Ph_2PCl or $^iPr_2PCl$, and triethylamine.[15] Once synthesized the corresponding pincer Ni, Pd, and Pt chloride complexes were synthesized from $NiCl_2$, $PdCl_2$(COD) and *cis*-$(Me_2S)_2PtCl_2$, respectively. The advantage observed in this case seemed to be that the long aliphatic chain resulted in complexes that are more soluble. Zargarian also reported the synthesis of two other non-symmetrical POCOP ligands with –OMe and –COOMe substituents at the 3-position of the resorcinol group (**4**, R = ^{i}Pr, R' = OMe or COOMe). This was part of a study into the effects of various substitution patterns on the corresponding POCOPNiBr complexes, which included spectroscopic and electrochemical investigations.[16] The nature and position of the substituent did in fact affect the ability of Ni to metallate the central aryl system and changed the redox potentials of the complexes themselves. However, the substituents had a negligible impact on the geometries of the metal centres. Obviously this type of remote substitution only eliminates the symmetry of the system and does not create chiral complexes but does result in two phosphinite moieties, which are magnetically (as seen by the ^{31}P NMR spectroscopy) and certainly electronically slightly different and demonstrates the potential to fine tune these ligand systems via substituent choice. Interestingly, no 3-substituted aryl groups have been used in the backbone of ligands of type **H**.

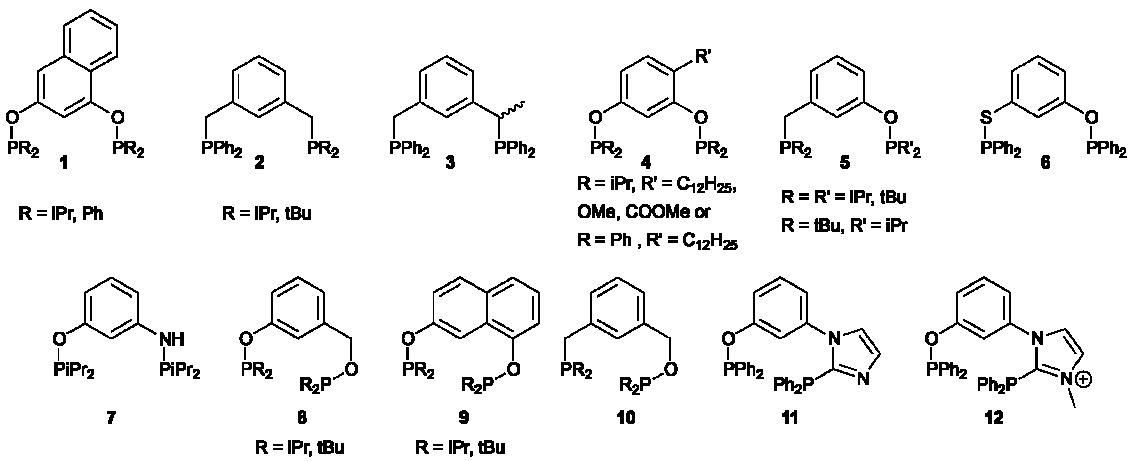
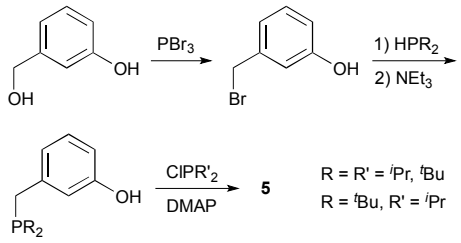


Fig 4 Examples of non-symmetrical PCP ligands.

Perhaps the most obvious change to the actual backbone elements, rather than just modification of the substituents, is the combination of the PCP and POCOP backbones ($E^1 \neq E^2$) and in 2003 Eberhard et al reported the synthesis of the PCOP ligand **5** (R = ^{t}Bu, R' = ^{i}Pr) and the corresponding **5**PdCl complex.[17] Goldman and co-workers have also used PCOP ligands and have synthesized versions that have either *tert*-butyl or *iso*-propyl groups on both sides (using a slightly modified protocol).[18] They subsequently reported **5**IrHCl complexes and iridium(I) complexes of **5** with labile ethylene or H_2 saturating the coordination sphere. The synthesis of ligands **5** is only slightly more difficult than either PCP or POCOP syntheses but remains quite easy, at only three steps from the commercially available 3-hydroxybenzyl alcohol (Scheme 3). This obviously allows for facile modification of the phosphine used at both positions giving this system the potential for extensive modification of steric and electronic parameters at the donor moieties.



Scheme 3 Original method for synthesis of PCOP ligands **5**.

Further non-symmetric modifications to the phosphine-aryl linkers have been done as well. The ligands **6** and **7** with a PSCOP[19] and POCNP[20] backbone were readily synthesized from 3-mercaptophenol and 3-aminophenol, respectively. In the case of **6**, NEt_3 and Ph_2PCl were used while **7** required use of a stronger base (^{n}BuLi) and $^i Pr_2PCl$ was used in lieu of the diphenyl phosphine, though it is reasonable to assume that a wide variety of phosphine chlorides could be used in both cases. The palladium chloride pincer complexes for both types of ligands have also been isolated although formation of the **7**PdCl complex required addition of triethyl amine to assist the metallation process.[20] However, these results clearly demonstrate yet another route to fine-tune the electronic properties of the phosphines with limited change to the geometry. Additionally, they are readily available and easily synthesized.

The final fashion in which PCP ligands have been modified to remove their inherent symmetry is by addition of a methylene group into the backbone thus creating ligands that form one five- and one six-membered metallocycle upon ligation (m = 1, n = 2). One of the advantages is the ability to use essentially the same synthetic protocol used for POCOP ligands. Ligand **8** was synthesized from 3-hydroxybenzyl alcohol (used in the synthesis of **5**), the desired phosphine chloride and base, just as POCOP.[21] The naphthalene-derived version **9** is similarly synthesized from the dihydroxyl precursor.[22] The PCCOP ligand **10** was synthesized exactly like the PCOP ligand but beginning from 1,3-benzenedimethanol.[17] Complexes featuring ligand **8** with Pd(II), Rh(I), and Rh(III) have been reported while pincer **10** has been reported with the former (**10**PdCl) and pincer **9** with both oxidation states of rhodium.[17, 21-22]

Finally, there is a report of one of the linkers being substituted with an imidazole and imidazolium moiety (ligands **11** and **12**, respectively). The latter is prepared only after **11** has been coordinated to a NiBr moiety (by addition of methyltriflate). In both cases the complexes feature binding modes with unsymmetrical 5- and 6-membered rings just like **8**-**10**.[23]

These non-symmetric metallocycles means that the two binding P moieties, in addition to the potential electronic and steric differences, have differing amounts of ring strain,

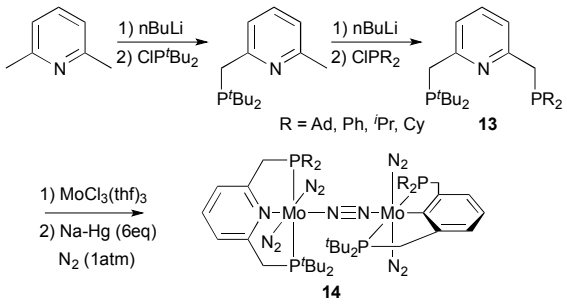
which could affect the dissociation properties of the phosphines. Additionally, the geometry of the coordination environment is changed slightly. The potential to modify these systems, especially those with short, high yield syntheses, gives further tuning possibilities. For example, if a less basic, sterically large phosphine is incorporated onto the side that forms the 6-membered ring, dissociation could be encouraged and allow for facile coordination of substrates.

While not a definitive list of non-symmetric pincers these examples demonstrate the large variability possible in one of the most classical pincer systems: PCP. Certainly the possibilities for electronically and sterically tuning of these ligands are almost endless given the variety of ways in which they can be modified. Additionally, the use of chirally pure non-symmetric pincer ligands of this type has yet to be fully exploited.

B. Other Non-symmetric ligands

The largest amount of work in aryl-linked pincer chemistry has been done with the PCP-type ligands due to the ease of access and relatively inexpensive precursors. Recently, there has been some excellent work with other systems and a few will be highlighted here. Again, they consist of symmetrical ligating atoms but with some features to remove the symmetry.

Pincers with PNP ligating moieties have also been studied quite extensively. The central aryl group is simply replaced by an *m*-pyridine linker, giving a neutral ligand that does not require any C-H activation upon ligation and obviously, with no charge, allows different oxidation states to be accessed. Work with C_{2v} symmetric systems is quite common but there are much fewer examples of non-symmetric systems. Perhaps the most important of these systems is the PNP ligands **13**, which feature unsymmetrical substituents on the phosphines themselves. The synthesis is very straightforward and consists of simple stepwise deprotonation of 2,6-lutidine and addition of the desired phosphine chloride. In all they reported four ligands each featuring one P(^{t}Bu)$_2$ ligand and a varied second phosphine PR_2 (R = Ad, Ph, ^{i}Pr or Cy) with yields between 59 and 89%, demonstrating a methodology that is efficient and flexible (Scheme 4).[24] The transition metal chemistry done with these ligands has focused primarily on molybdenum and a large variety of **13**Mo complexes have been reported. Most of them are accessed by reaction of **13** with [Mo(Cl)$_3$(thf)$_3$]. The resultant Mo(III) complex is subsequently modified to generate other Mo species. Of particular interest is the Mo(0) dinitrogen bridged complex **14** available via reduction with excess Na-Hg under a nitrogen atmosphere (Scheme 4).



Scheme 4 Synthesis of PNP ligands **13** and Mo(0) complex **14**.

The methylene linkers of the PNP backbone have also been modified though rarely unsymmetrically. The symmetrical ligand featuring amine linkers has a rich chemistry and the protons at the amine groups are ideal for applications when a protic cooperative ligand may have benefits. Kirchner and co-workers have replaced the central pyridine ring by a 2,6-pyrimidine ring and have added substituents to the ring system (exclusively at the position *para* to the coordinating nitrogen) to give the PNP ligands **15** (Fig. 5).[25] They also reported the corresponding **15**Fe(II) complexes with detailed spectroscopic and theoretical results and were able to show evidence for supramolecular assemblies formed via hydrogen bonding. They also reported that the protons at the amine linkers in the case of the symmetrical systems could be easily removed and replaced with methyl groups and that Mo(0) and W(0) complexes were accessible, which indicates that there may be potential to make similar modifications to ligands **15** and to use them in Mo and W chemistry.

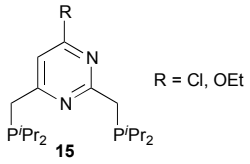
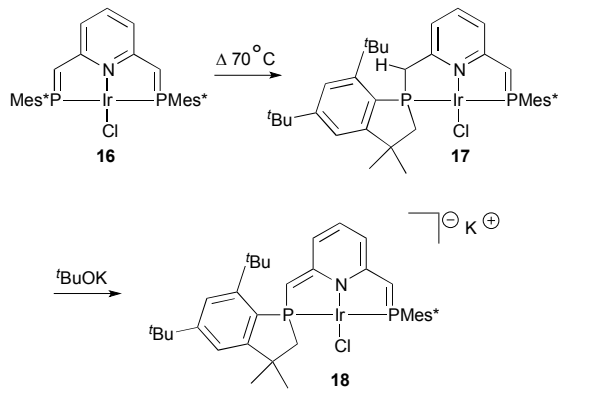


Fig. 5 PNP ligands **15.**

A rather peculiar case of loss of symmetry in a PNP ligand involves a bis-phosphaalkene. The symmetrical IrCl complex **16** can be heated to 70°C to transform it into the unsymmetrical complex **17** by intramolecular cyclization of one *tert*-Butyl group followed by proton migration (formally, the addition of the C-H across the P=C bond). This ligand now has an acidic proton, which can be removed with potassium tert-butoxide to give the dearomatized anionic complex **18**.[26] (Scheme 5) Interestingly, this complex has been reported to activate N-H bonds to form iridium amide complexes with the proton re-aromatizing the ligand. This reactivity has been extensively studied[27] but as yet no catalytic reports have appeared although such N-H bond activation could have interesting applications in catalysis.



Scheme 5 Thermal rearrangement of **16** to form non-symmetrical complex **17** and subsequent deprotonation to form anionic complex **18**.

The addition of a variety of nitrogen-based donors to a central pyridine ring has been a common motif in pincer chemistry. For example, the C_{2v} symmetric 2-6-dipyrazole-pyridines have been used as neutral NNN pincer ligands.[28] There are an ever-growing number wherein one or both pyrazole moieties have been replaced, usually by different N-heterocycles. One of the pyrazole groups has been replaced by a benzimidazole moiety to create a non-symmetric ligand of type **19** with a N-methyl-benzimidazole version also available in one additional step (Fig. 6).[29] One of the 1-pyrazole substituents of the parent ligand has also been replaced by a 3-pyrazole **20**, and an imine **21**.[30] Use of two non-pyrazoles has also been reported. The symmetric 2,6-dibenzimidazole-pyridine can be N-alkylated at only one benzimidazole (with NaH and ^{n}PrBr) to give the non-symmetric ligand **22**.[31] There are two other similar ligands featuring benzimidazole-substituted pyridines: ligand **23** with an oxazoline[31] and **24** with a benzotriazole.[32]

All of these neutral NNN pincer ligands have been reported to form a complex upon addition of $[(Ph_3P)_3Ru(Cl)_2]$, generally giving complexes of type **L**$Ru(Cl)_2(PPh_3)$ with the exception of ligands **22**[31] and **24**,[32] which gave cationic complexes [**L**$RuCl(PPh_3)_2$][Cl] and **21** (R = Me, Ar = Dipp = 2,6-diisopropylphenyl), which did not react with $[(Ph_3P)_3Ru(Cl)_2]$ but did form **21**$NiCl_2$ upon addition of dichloronickel hexa hydrate.[30b] With the exception of **19** (R = Me) and **21** all of these ligands feature acidic protons in the form of N-H groups. In the coordination sphere of Ru all of these ligands can be deprotonated to become mono-anionic with elimination of a chloride. This deprotonation strongly affects the donor properties of only one of the ligand arms, changing a neutral imine donor to an anionic amide, and thereby produces a non-symmetric electronic environment at the metal. Clearly, this indicates the potential for cooperative affects between the metal and ligand as well as generating a pincer complex with one hemi-labile arm (the imine) and one non-labile arm (the amide).

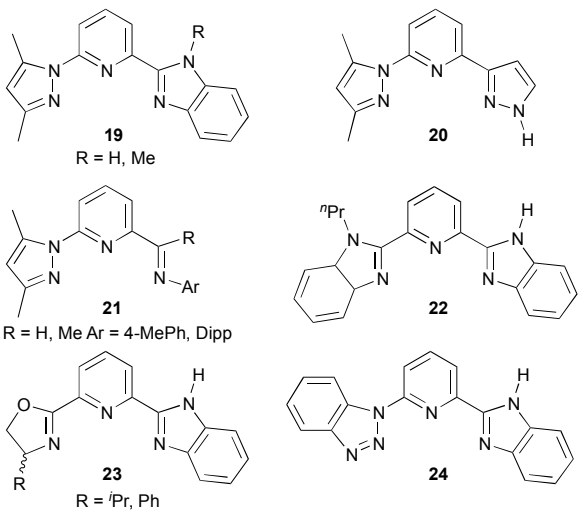


Fig. 6 Non-symmetrical NNN pincer ligands **19**-**24.**

C. Catalytic uses

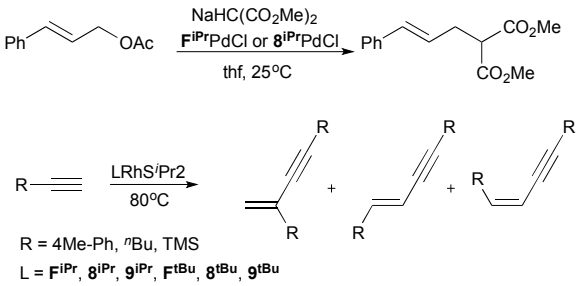
The fact that any of the above transition metal pincer complexes are catalytically active for a variety of reactions should come as no surprise. By their nature, these robust complexes are excellent catalysts, especially for reactions requiring extreme temperatures in which many other complexes decompose.

The robust character of the non-symmetrical complexes can be seen in the case of the **2^{iPr}**PdCl complex, which catalyses the Heck coupling of iodo-benzene and styrene at 180°C.[13] Mercury drop experiments indicate that the complex is doing all of the catalysis. The substrates are not particularly challenging, the catalyst loading (5 mol %) is not extremely low and the yield is good, at 80%, but not extraordinary, however, by changing from the iso-propyl ligand **2^{iPr}** to the tert-butyl substituted ligand **2^{tBu}** the reactivity and yield is reduced to zero. This indicates a very fine steric control of the reaction considering the very similar electronics of the two slightly different alkyl groups. However, direct comparison to symmetrical PCP ligands under the same conditions was not reported. The related Pd(II) complex with the POCOP ligand **4** (R = Ph, R' = $C_{12}H_{25}$) on the other hand has been compared directly to the unsubstituted parent POCOP **F^{Ph}**Pd(II) complex for both Heck and Suzuki-Miyaura coupling reactions. The non-symmetric complex was used with six substrates for both reactions with yields of 45-99%.[15] In this case the direct comparisons show that while the final yields obtained are similar the non-symmetrical catalyst reacted faster. A fact that was attributed to the increased solubility afforded by the long aliphatic substituent.

The non-symmetric POCOP ligands have not been limited to only palladium chemistry. The napthyl-based ligand **1** on a Ni(II) centre (**1**NiCl) has been used in Suzuki-Miyaura coupling. A wide variety of substrates were tested with

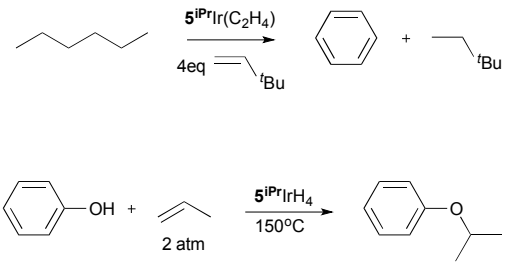
yields of 43-99% with a catalytic loading of 1 mol%.[11] While the loading is higher and the reaction times longer than that used for palladium catalysts, the move to more abundant 3d metals is an important goal for sustainable chemistry.

Palladium (II) complexes with the POCOP ligand **8^{iPr}** have also been used in catalysis.[17] The results of catalytic allylic alkylation of cinnamyl acetate with sodium dimethyl malonate using both the symmetrical POCOP **F^{iPr}**PdCl and **8^{iPr}**PdCl complexes showed that the non-symmetrical ligand produced a more active catalyst, going to completion in just 12 hours at 25°C compared to 72 hours for **F^{iPr}**PdCl (Scheme 6, top). Considering the extreme similarities of the ligating groups (phosphinites in both cases with identical substituents) the primary difference lies in the geometry of the ligation afforded by the mixed five and six membered metallocycles. The authors found the result was an increase in bite angle, which, by analogy to bidentate phophines, typically increases turnover frequency. Rhodium complexes of POCOP ligands have also been used for other catalytic coupling reactions. The complex **9^{iPr}**RhHCl was used for the coupling of aryl halides with thiols and performed well but was not as effective as the **F^{iPr}**RhHCl catalyst.[22a] Rhodium(I) isopropyl sulphide complexes of **8** and **9** have been used in the catalytic dimerization of terminal alkynes. Again similar results were obtained using the corresponding symmetrical complex with the same phosphine substituents (isopropyl substituted versions **F^{iPr}**, **8^{iPr}** and **9^{iPr}** obtained yields up to 97% and even yielded similar distributions of products) (Scheme 6, bottom). The only caveat being that **9^{iPr}** was more sluggish requiring 36 hours as opposed to three. The *tert*-butyl substituted ligands (**F^{iPr}**, **8^{tBu}** and **9^{tBu}**) had very little activity in all cases.[22b] While both results demonstrate that non-symmetric systems are active catalysts, the near identical results precludes any conclusions about the effect of unsymmetrical substitution.



Scheme 6 Catalytic reactions with ligands **8** and **9**.

One of the most striking demonstrations of the utility of non-symmetrical pincer ligands is the use of PCOP ligands. Goldman and co-workers have worked extensively with this non-symmetric pincer and the closely related C_{2v} symmetric PCP **E** and POCOP **F** ligands. The unique properties of the PCOP ligand were first observed in the dehydroaromatization of n-alkanes.[33] Pincer Ir(I) complexes were found to transform n-alkanes into a variety of mono- and/or di-substituted aromatics via successive transfer dehydrogenation reactions. Interestingly, the PCOP ligand **5** was extremely effective for these transformations and in some instances gave the highest yield and/or selectivity of the catalysts tested (Scheme 7, top). From the results it appears that the reason for the excellent performance can be attributed primarily to sterics. The bulky PCP ligand with *tert*-butyl phosphine substituents gave only trace amounts of aromatic products while a change to *iso*-propyl groups increased yields drastically. The *iso*-propyl POCOP analogue, known to be less sterically demanding than the corresponding PCP ligand,[33] also performed poorly. The PCOP ligand **5^{iPr}** appears to have a nearly ideal steric environment for this reactivity. A PCOP Ir(I) complex has also been reported to catalyse one of the rare examples of an olefin hydroaryloxylation reaction (Scheme 7, bottom).[34] Again, there is an implication that the sterics of the ligand allow it to be one of the most active catalysts for this reaction.

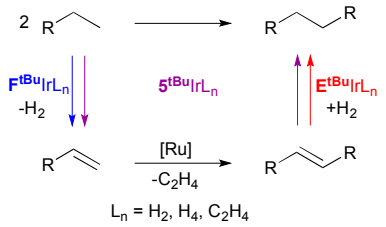


Scheme 7 Examples of reactions catalysed by **5**Ir(I) complexes.

There has been an in depth study of the use of PCOP ligands in co-catalysed alkane metathesis chemistry. In this case calculations were used to show that the combination of one phosphine and one phosphinite had the ideal electronic properties to create a more effective iridium catalyst. The alkane metathesis requires both hydrogenation and dehydrogenation steps and the calculations showed that the PCP and POCOP pincer ligands had resting states that favoured either dehydrogenated (PCP, blue) or hydrogenated (POCOP, red) products while the PCOP appeared to favour neither state (Scheme 8, purple).[18] These results were confirmed experimentally, with the PCOP complex resulting in drastically improved yields, particularly after the phosphine substituents were adjusted to provide an optimal steric environment. This is an excellent example of the power of non-symmetrical pincer ligands and their ability to tune both the electronic and steric parameters of a catalyst as well as being a triumph of rational ligand design.

The non-symmetrical PNP pincers Mo(0) complexes **14** have been used in catalysis. Nishibayashi and co-workers attempted to tune the sterics of their nitrogen fixing catalyst by varying the groups at the phosphines.[24] Unfortunately,

these steric adjustments did not yield more active catalysts. The best results were obtained with the ligand **13^{Ad}**, which yielded 19 equivalents of NH_3 (compared to 23 equivalent for the symmetrical **13^{tBu}** complex) and decreased all the way to only one equivalent for the complex featuring **13^{Cy}**. These non-symmetrical systems have also been part of efforts to understand the mechanism experimentally and theoretically.[35]



Scheme 8 Sigma bond metathesis reaction. PCOP ligand **5^{tBu}** promotes dehydrogenation and hydrogenation steps equally and is more active than **E** or **F** type catlysts.

Finally, the non-symmetrical NNN systems **19**-**24** have been used at Ru(II) centres to form highly active transfer hydrogenation catalysts for ketones and aldehydes.[29b, 30-32] This includes a chiral complex featuring ligand **23**, which asymmetrically hydrogenates prochiral ketones with ee's of up to 97%.[31] The precise affects of the non-symmetric ligand on the transfer hydrogenation reaction are, as yet, not entirely clear but further studies could certainly be done to identify if non-symmetric ligands affect the results for steric or electronic reasons.

2. Non-symmetric Donors

Pincer ligands with non-symmetrical donors have recently become a small but important aspect of organometallic chemistry. This is primarily because of some of the recent catalytic results obtained using these systems. These types of systems have incredible potential as they have very different donor ligands that are forced into a *trans* conformation. These have also been the subject of considerable research into non-innocent or collaborative metal-ligand reactivity. The majority of this research has focused on pyridine-based systems with C, N, and P donors but the potential diversity is nearly endless. Herein, the focus will be on examples of PNN and CNN systems, with some discussion of relevant systems with three different donors.

A. PNN ligands and complexes

In 2005, after working with PNP ligands extensively, Milstein and co-workers reported the synthesis of the first PNN ligand **25** (Fig. 7).[36] The idea behind substituting one phosphine for an amine was an astute one based on the groups experience: the significantly more labile amine had the potential to dissociate and facilitate reactivity at the metal centre. Ligand **25** can be synthesized in three steps from 2,6-lutidine by mono-bromination, substitution with diethyl amine and finally deprotonation and addition of $^tBu_2PCl$ with an overall yield of 46% (Fig. 7). The process can be modified such that the diethyl amine can be exchanged for a variety of amines (^{t}Bu, ^{i}Pr, and Bz) though in this case the phosphine must first be added and protected with a borane before the amine is added and the phosphine is deprotected.[37]

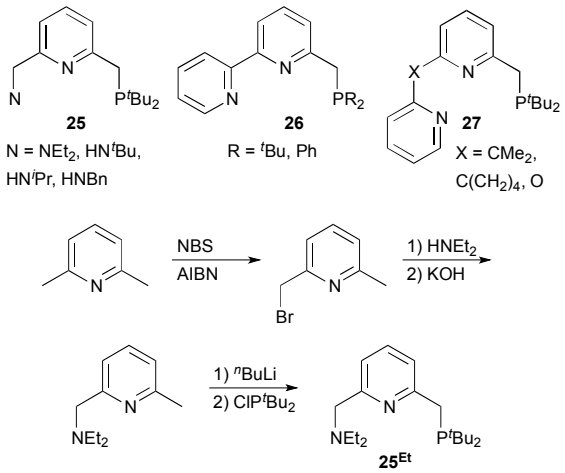
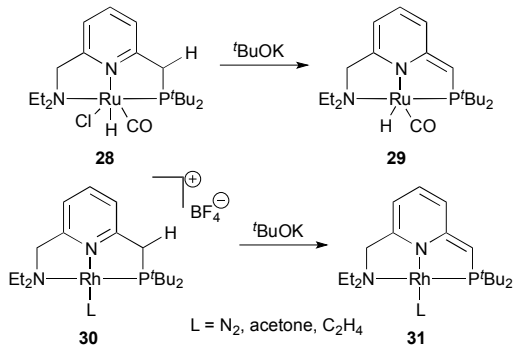


Fig. 7 Examples of PNN ligand **25**-**27** and the synthesis of the first PNN **25^{Et}**.

The amine can also be replaced by a pyridine moiety to give pincers **26** but a different synthetic process is required. In this case different phosphines have been used ($PtBu_2$ or PPh_2P).[38] The nature of the syntheses for both **25** and **26** indicates that other modifications of the phosphine and amine/pyridine substituents are possible. Milstein and co-workers also reported ligands **27** with a carbon [CMe_2 or cyclic $C(CH_2)_4$] or oxygen linker between the pyridine groups of **26**.[39]

All of these ligands have been used in Ru(II) complexes by addition of $RuHCl(CO)(PPh_3)_3$ to the free ligands. The resultant **25**-**27**RuHCl(CO) complexes can be deprotonated at the position *alpha* to the phosphine with potassium *tert*-butoxide to give complexes of type **29** (Scheme 9). This process creates an anionic pincer ligand and dearomatizes the pyridine ring, which is indispensable for metal-ligand cooperative effects.



Scheme 9 Example of dearomatization of complex **28** to form **29** (in this case with **25^{Et}**)

Cationic Rh(I) complexes **30** of pincer **25^{Et}** have been synthesized by addition of the free ligand to $[Rh(thf)_2(COE)_2][BF_4]$, $[Rh(acetone)_2(COE)_2][BF_4]$ or $[Rh(acetone)_2(C_2H_4)_2][BF_4]$.[40] In each case the 16 electron complex **30** has one labile ligand *trans* to the pyridine nitrogen, which can be easily substituted for a variety of other ligands. More importantly, these complexes can also be deprotonated with potassium *tert*-butoxide to create the neutral complex **31**.

More recently $MoCl_3(thf)_3$ was added to **25^{Et}** to give the **25^{Et}** $MoCl_3$ complex, which can be reduced with Na-Hg amalgam, in the presence of PMe_3 or PMe_2Ph and nitrogen, to the Mo(0) complexes **25^{Et}**$Mo(N_2)_2PMe_3$ and **25^{Et}**$Mo(N_2)_2PMe_2Ph$, respectively.[41] The Mo(V) nitride complex (**25^{Et}**MoNCl) has also been reported.[42] This reflects a broadening interest in these PNN ligands and indicates that PNN ligands could be used with other metals as well.

The PNN backbone has also been modified by inserting an amine linker, rather than a methylene linker, between the pyridine and phosphine. This was first accomplished in a somewhat long but reasonably efficient six-step synthesis to give the oxazoline-substituted ligand **32** (R = Me) (Fig. 8).[43] The motivating factor behind this change is the more acidic proton at the nitrogen, which could further facilitate cooperative effects. Subsequently, the oxazoline was modified (R = H) and the entire nitrogen group was changed to a pyridine **33** or an amine **34** thus giving the beginning of a library of this type of more acidic PNN pincer.[44]

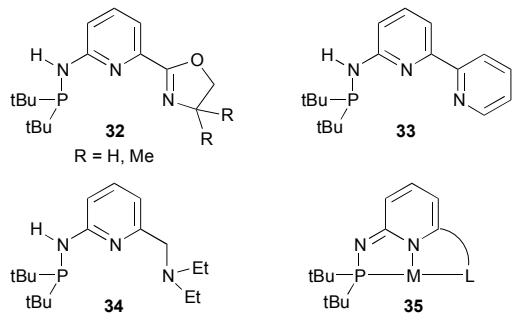


Fig. 8 PNN ligands **32**-**34** and the deprotonated metal complex of these ligands **35**.

As yet, these ligands have only been used in Ru(II) complexes. As with Milsteins ligands they have been added to $RuHCl(CO)(PPh_3)_3$ to give the **32**-**34**RuHCl(CO) complexes. As expected, these complexes can be easily deprotonated with potassium *tert*-butoxide to give the dearomatized complexes of type **35**.

B. CNN ligands and complexes

Another common non-symmetric modification of a 2,6-substituted pyridine has one amino ligating unit and an aryl group as in ligand **36** (Fig. 9). Upon coordination the aryl group *ortho*-metallates to form pincer complexes and the ligand becomes monoanionic. Generally, this type of ligand is synthesized from commercially available 2-aryl-pyridines via protection of the pyridine, cyanation of the 6-position, deprotection, and reduction to the amine (Scheme 10).[45] The process is quite straightforward and only suffers from lower yields on the final step. However, a variety of 2-aryl-pyridines can be used, which makes for a flexible approach.[46] This includes one example of the fused tricyclic 1-phenanthroline used as the backbone **37**.[47]

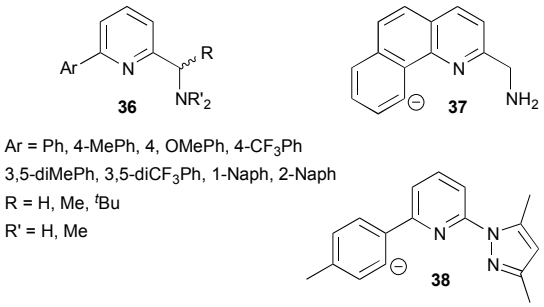
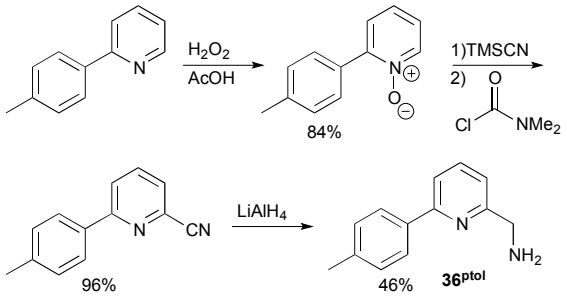


Fig. 9 CNN ligands **36**, **37** and **38**.

The most common version of this CNN ligand, with a 4-methylphenyl-pyridine unit **36^{ptol}**, has been modified by methylating the amine (R' = Me).[46a] A methyl or tert-butyl group can also be added to the methylene linker (R = Me, ^{t}Bu).[46a, 48] Of course, if this is done enantioselectively the synthetic procedure is much more complicated but excellent ee's were reported. In the case of the enantiopure methyl substituted methylene, Baratta and co-workers also reported a variety of aryl substituents as well, including, phenyl, 4-MePh, 4-OMePh, 4-CF_3, 3,5-diMe, 3,5-diCF_3, 1-napthyl, and 2-napthyl.[46b] The backboned has also been made rigid by use of a 1-phenanthroline moiety to give pincer ligand **37**.[47] The amine arm has been modified further by substitution with a 1-pyrazole to give the pincer **38**.[49]



Scheme 10 Synthesis of CNN ligand **36**^{ptol}.

Essentially, all of these ligands have been used to make Ru(II) complexes with some Os(II) complexes having also been reported. Generally, the ligand is mixed with [$RuCl_2(PPh_3)$(dppb)] [dppb = 1,4-bis(diphenylphosphino) butane] in the presence of NEt_3, which serves to promote the ortho-metallation process, to give the **L**RuCl(dppb) complexes. $RuCl_2(PPh_3)_3$ or $OsCl_2(PPh_3)_3$ has also been used with addition of a bidentate phosphine (such as dppb) to synthesize complexes of similar structures. Chiral Josiphos or Skewphos have been used with both chiral and achiral CNN ligands **36**.[46b, 48, 50]

Interestingly, an N-heterocyclic carbene (NHC) has also been used as a donor in a non-symmetric CNN pincer ligand. The 2,6-Bis(bromomethyl)pyridine, used for the symmetrical CNC pincers, serves as the starting material. Addition of a single equivalent of N-aryl imidazole followed by addition of an amine with potassium carbonate gives the CNN ligands **39** (Fig. 10).[51] Despite this two-step synthesis, there are relatively few examples. The aryl group on the NHC has been modified (Mes or Dip) and a variety of amines have been used, including several examples with pendant triethoxylsilyl groups.[52] These silyl groups have been used to immobilize the subsequent complexes on silica for recoverable catalyst. Despite the limited number of examples, these ligands have been used with a variety of metals, including Ru, Rh, Pd and Au. In lieu of an amine group Yu and co-workers have reported a series of NHC-pyrazole CNN ligands **40**-**42**.[29a, 44b, 53] While the synthesis of these ligands is not overwhelming, solubility difficulties made the selection of substituents somewhat limited. The palladium chloride complexes of **40** and **42** were reported by a simple transmetallation of the silver carbene complex. However, Ruthenium complexes of **40** and **41** were somewhat more difficult, requiring $RuCl_3$ trihydrate to be heated with the ligand precursor to 190°C in the presence of CO (1 atm). Halide exchange with KI did give pure complexes **40**$RuI_2(CO)$ and **41**$RuI_2(CO)$.

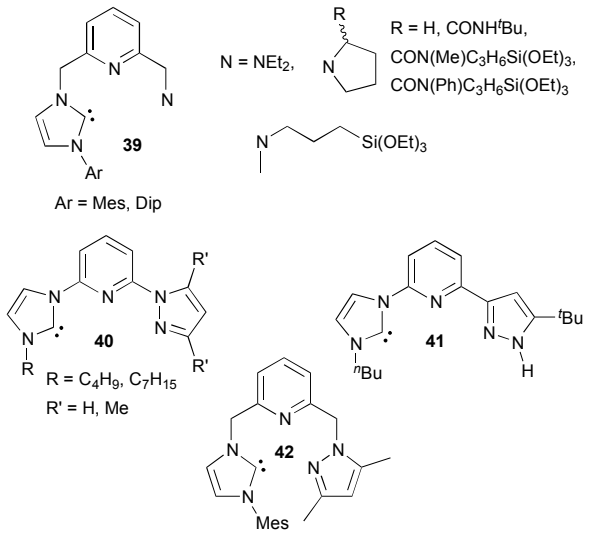


Fig. 10 NHC CNN ligands **39**-**42**.

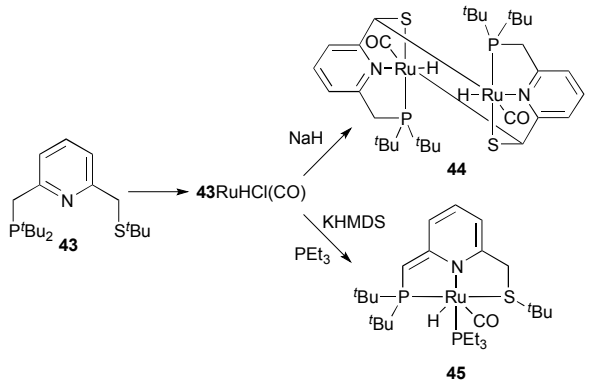
The relative paucity of examples of non-symmetrical pincers featuring NHC is somewhat surprising considering the prevalence of carbenes in organometallic chemistry. Certainly the robust carbene metal bond can be advantageous in the design of new pincer ligands. Additionally, ligands **39** can be deprotonated at the methylene between the pyridine and the NHC to allow for cooperative effects and the pyrazole of **41** can also be deprotonated.

C. Other unsymmetrical donor pincer ligands

There are a variety of other unsymmetrical donor ligands that have been reported, with two similar donor atoms (PCC, NCC, SNN etc.) or three different donor atoms (CNO, CNS, NCP, NCS, PNO, ONS etc.). However, there are several featuring aryl or pyridine linkers that are related to the current discussion.

Milstein and co-workers have reported the PNS ligand **43** by stepwise substitution of the 2,6-Bis(chloromethyl)pyridine first with a protected phosphine ($^tBu_2PBH_3Li$) and then a sulphide (^tBuSNa).[54] Upon deprotection the ligand was added to [$HRuCO(PPh_3)_3Cl$] to give the **43**RuH(CO)Cl complex. This ligand and complex are closely related to the PNN systems **25**. The thioether group, like the amino group of the PNN systems, is hemilabile, which permits an additional coordination site to be generated but unlike the amine group the thioether is not very basic. The quaternization of the pendant amine with Lewis acids may be one way in which the PNN complexes are deactivated and thus the PNS system may have some advantages. Similar to the PNN system, it has an acidic methylene proton alpha to the phosphine, which contributes strongly to the cooperative effects between the ligand and the metal centre. However, upon deprotonation with NaH the **43**RuH(CO)Cl complex eliminates the chloride but does not form the dearomatized ligand expected. In fact

the result of the deprotonation is complex **44** generated via elimination of isobutylene. The dearomatized ligand can be generated by using KHMDS in the presence of PEt_3, but rather than having an open coordination site as in other cases, gives the saturated octahedral complex **45** (Scheme 11).



Scheme 11 PNS ligand **43** and synthesis of ruthenium complexes **44** and **45**.

Odinets and co-workers have reported a series of four types of SCN pincer ligands **46**-**50** that also bears mention (Fig. 11).[55] In each case the sulphur donor is of a thiophosphoryl substituent and the nitrogen is an imine moiety, in most cases as part of a benzothiazole group. The synthesis of each is somewhat involved, consisting of five to seven steps and, because of the important differences in the backbones, the procedures vary significantly, however, this is precisely why this series of ligands is interesting. Upon addition of $(Benzonitrile)_2PdCl_2$ to each of the ligands the corresponding pincer PdCl complex is obtained. With the exception of ligands **46** and **50**, each generates non-symmetrical metallocycles: one five-membered metallocycle and one six. This creates an opportunity to study the effects of such non-symmetric metallocycles in conjunction with the non-symmetric donors, mixing the donor properties of the N and S groups with the more or less constrained ring system.

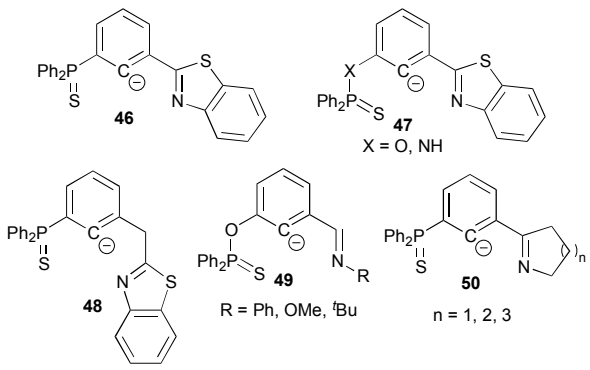


Fig. 11 SCN ligands **46**-**50**.

The PCS ligand **51** has also been reported and is available in four steps with a yield less than 73% (Fig 12). The corresponding PdCl complex was available by addition of $[Pd(MeCN)_4][(BF_4)_2]$ and workup with NaCl.[56] Three related ligands based on isovanillin have been reported. The PCN ligand **52** and the corresponding PdCl complex were available in only three steps wherein $PdCl_2$ was used as the metal source.[57] The related PCN and PCS ligands (**53** and **54**, respectively) and their Pd complex were also reported. In both cases the ligand precursors required a bromide substituent between the ligand arms to facilitate oxidative addition. The complexes were accessible in three and six steps, respectively. While these complexes have been used as catalysts (vide infra) they are mentioned here particularly because of the ability of **51** and **53** (R = ^{i}Pr to prevent competitive coordination)[7] to form planar chiral bimetallic complexes. **51**PdCl and **53**PdBr react with $[CpRu(NCMe)_3]^+$ and, in the case of **51**, $[Cp^*Ru(NCMe)_3]^+$ to give a racemic mixture of the desired complexes. The use of a chiral anion allowed selective crystallization of a single enantiomer. These results certainly open the possibility of asymmetric induction in catalytic processes using these bimetallic complexes.

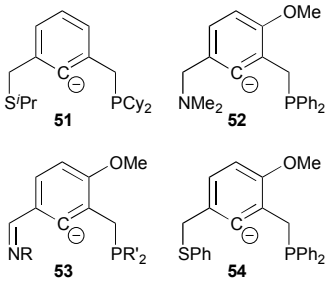


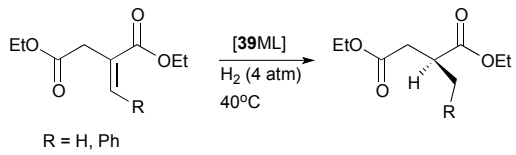
Fig. 12 Ligands **51**-**54** (R = Ph, ^{t}Bu; R' = Ph, ^{i}Pr).

D. Catalytic uses

Many of these ligands with non-symmetrical donor groups have been used to make transition metal catalysts. This includes some very classical coupling reactions. Palladium Chloride complexes of SCN ligands **46**-**50** have been used for Suzuki coupling, however, they found that, most likely, they only served as a precatalyst with the pincer ligand being eliminated to create Pd(0) species, which served as the actual catalyst.[55] Cationic palladium(II) chloride complexes of CNN ligands **40** and **42** have also been used for Suzuki reactions. The robust nature of the complexes may assist the catalytic process but temperatures of only 80°C were necessary for the coupling of a variety of aryl boronic acids with aryl bromides or iodides, with good to excellent yields based on the substrates.[53] The robust nature of the complexes did allow for heating to 120°C in order to use aryl chlorides as coupling partners with isolated yields varying widely from 30-98%. In this case

there was no report that the pincer complex decomposed to form the active catalyst.

Sanchez and co-workers have used the CNN ligands **39** with Au(III), Pd(II), Rh(I) and Ru(II). Primarily, they have focussed on using these species in the hydrogenation of alkenes and imines.[51a, 52a, 58] However, of more interest to the current discussion is the use of chiral pyrrolidine moieties. This unsymmetrical substitution and availability of stereochemically pure pyrrolidines makes the synthesis of single enantiomer ligands quite easy. To this end **39** (R = CONH^{t}Bu) was used to make complexes [**39**AuCl]$^{2+}$, [**39**RhCOD]$^+$, and [**39**PdCl]$^+$. The subsequent hydrogenation reactions of prochiral alkenes or imines then have the potential for chiral induction. Interestingly no, or low, ee % (0-18% depending on the ligand and metal) was reported at 40°C and 4 atm H_2, for a less bulky alkene (diethyl itaconate) while ee % of up to 99% was reported for the larger alkene diethyl 2-benzylidene succinate (Scheme 12).[52c, 58] The chiral pyrrolidine moiety has also been used to affix the complex to solid silica supports making recovery and reuse of the catalyst quite simple. In this case the robust nature of pincer systems should prevent leeching of the metals and subsequent loss of efficacy. This was true for four consecutive runs wherein the immobilized catalyst retained the same catalytic properties. The easily modifiable pyrrolidine opposite and NHC moiety, which creates a very strong metal bond, allows this ligand system to function as a chiral tethered catalyst without significant leeching. These complexes have also been used for other catalytic reactions. The tethered **39**Au(III) complex has been used in the three-component synthesis of propargyl amines from amines, aldahydes, and terminal alkynes, again with good recyclability. **39**Ru(II) complexes were used for the cyclopropanation of styrene with alkyl diazoacetates.[52c]



Scheme 12 Asymmetric hyrogenation of alkenes using complexes of **39**.

The importance of catalytic transformation of N_2 to NH_3 is well known and Nishibayashi and co-workers have very recently reported attempts to use non-symmetrical PNN ligands with their nitrogen fixing Mo(0) catalysts.[59] However, while the complex **25**^{Et}Mo$(N_2)_2$L (L = PMe_3 or PMe_2Ph) has stoichiometrically converted N_2 to ammonia, catalytic results have not yet been reported.[41] The related cationic Mo(V) complex [**25**^{Et}Mo(N)Cl][OTf] has been used in catalytic tests with moderate results.[42] The full elucidation of non-symmetric pincers with these systems is certainly of great interest and could assist in understanding both the nitrogen fixing process and the effects of such non-symmetric systems. Especially, as one may recall from section 1c, non-symmetric PNP systems effected reactions primarily for steric reasons, whereas the PNN systems will have a more pronounced electronic effect.

The PNN and CNN ligands discussed in this section have been used extensively in hydrogenation or dehydrogenation reactions, primarily catalysed by pincer Ru(I) complexes, with a few examples using Os(I) species.

The transfer hydrogenation of ketones and aldehydes, which does not require high pressures of hydrogen gas but rather uses a sacrificial H_2 source, are well documented. The hydrogen source, typically isopropanol, is transformed into a ketone while the substrate is hydrogenated to an alcohol (Scheme 13). Ruthenium complexes of pincers **36**-**38** have been reported to perform this reaction extremely rapidly, often within minutes, with near quantitative yields. For example, 0.005 mol% **36**^{ptol}RuCl(dppb) (dppb = $Ph_2PC_4H_8PPh_2$) in isopropanol (with 2 mol% NaOH) hydrogenated acetophenone to the corresponding alcohol (98% yield) in five minutes (at 82°C).[45, 60] Baratta and co-workers have done extensive work with this reaction to identify the mechanism, the effects of the base and to develop asymmetric transfer hydrogenation catalysts.[50, 61] Chiral induction has been achieved by introduction of a Me or ^{t}Bu group to the ligand framework (**36**, R = Me, ^{t}Bu), which they were able to isolate as a pure enantiomer, by use of chiral bisphosphine auxiliaries (Josiphos) (Fig. 13).[46a, 48] This has led to ee's of up to 95% on acetophenone and 99% with propiophenone, with catalyst loadings of only 0.005 mol% at 60°C. Similar results were obtained with osmium based catalysts. They have also worked on acceptorless dehydrogenation of ketones using **36**Ru and **36**Os catalysts.[46b, 47]

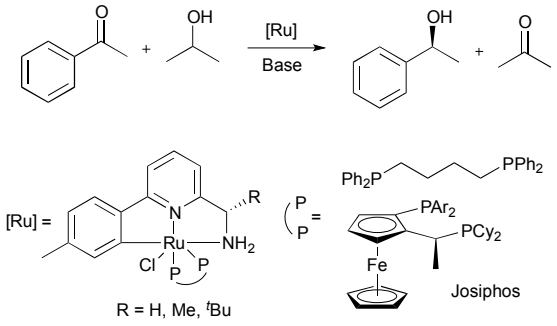
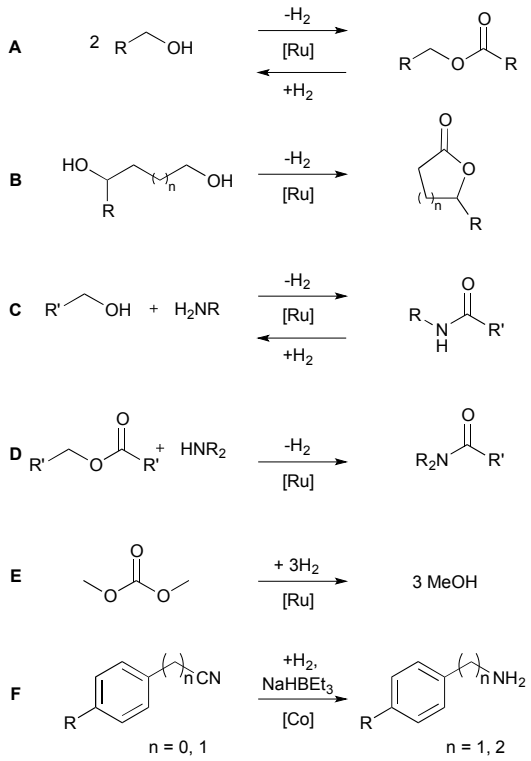


Fig. 13 Example of transfer hydrogenation reaction and an active ruthenium catalyst featuring a ligand of type **36**.

Some of the most important work being done using non-symmetrical pincer catalysts is the dehydrogenative coupling of alcohols to form esters. The simple, efficient and environmentally benign synthesis of esters with only hydrogen gas as a by-product is an important goal in organic chemistry. Milstein and co-workers were the first to employ non-symmetrical pincer complexes to catalyse this important reaction. Interestingly, they found that the PNN

complex **28** was more efficient than the symmetrical PNP pincer complex, giving 90% ester compared to 67% for the latter (Scheme 13, **A**).[36, 62] The increased efficiency has been attributed to the facile dissociation of the amine moiety, which allows coordination of the alcohol substrate, an important step in the catalytic process. The formation of the dearomatized complex of type **29** (a process which also occurs in the symmetrical case) is also thought to be essential to the reactivity.[37] The scope of this reaction has been investigated with a variety of primary and secondary alcohols as well as the use of diols to form lactones (Scheme 13, **B**).[63] These same pincer complexes have been used, under hydrogen gas pressure, to perform the reverse reaction and generate alcohols from esters.[62b]



Scheme 13 Examples of reactions catalysed by ruthenium and cobalt complexes featuring PNN pincer ligands **25**, **26**, and **27**.

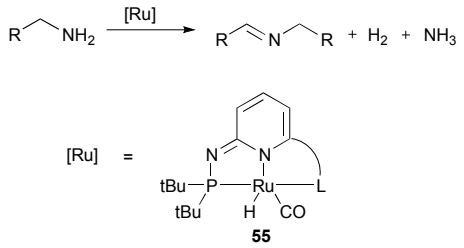
A natural extension of this chemistry is to couple two different substrates. While this is certainly possible with alcohols, the selectivity would be low and therefore give a mixture of the four possible esters that may not be easily separated. However, coupling of an alcohol with an amine has been done to give the amide product (Scheme 13, **C**).[38, 64] In this case only the amide and ester are potential products but yields of up to 99% were reported for the amide, with no traces of the ester.[65] Very recently this reaction has been reported as a rechargeable hydrogen storage system, by using ethanol and ethylenediamine as the coupling partners. Importantly, an extremely low catalyst loading (0.2 mol%) was used and no stoichiometric additives were necessary.[66]

In a reaction related to **A**, symmetrical esters (like those generated from reaction **A**, Scheme 13) can be transformed into two equivalents of the corresponding amide (Scheme 13, **D**).[67] Interestingly, in the former case only primary amines were reported to react while in the later case primary and secondary amines were used. The reverse reaction, generation of alcohols and amines from amides, has also been catalysed by ruthenium PNN pincer complexes.[39] The PNS complex **45** was also reported to couple amines and alcohols although it was not as active as PNN complexes most likely because of deactivation pathways including elimination of the ^{t}Bu group at sulphur (similar to the generation of **44**).[54]

Ruthenium complexes of **25** and **26** have also been reported to perform the hydrogenation of dimethyl carbonate, methyl carbamates and methyl formate to give three, two and two equivalents of methanol, respectively (Scheme 13, **E**).[68] Importantly, these substrates can be generated from CO and/or CO_2, thus giving an indirect path to form methanol from these abundant and inexpensive gases.

Another important result has recently been reported, wherein $CoCl_2$ complexes with ligands of type **25** and **26** have been used as catalysts for the hydrogenation of aryl and benzyl nitriles to their corresponding primary amines (Scheme 13, **F**).[69] The most efficient ligand (**25**, N = NH^{t}Bu) gave excellent yields of up to 99% for a variety of substrates with a catalyst loading of only 2 mol%. This represents the first example of hydrogenation of nitriles using a cobalt catalyst. Clearly the use of less expensive base metals for such catalytic transformations makes this a very promising result.

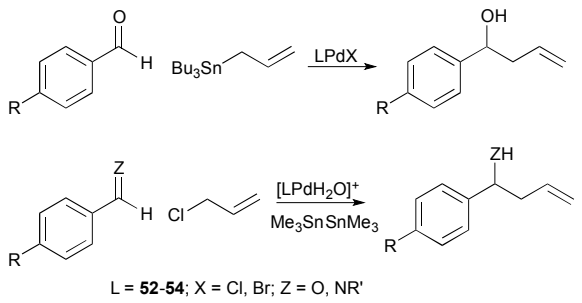
The high impact of the above-mentioned dehydrogenative coupling reactions has led to the use of other non-symmetrical pincers in this chemistry. Ruthenium complexes of ligands **32**-**34** have been used to perform both the coupling and decoupling process in Scheme 13 **A**, typically starting from the dearomatized complex of type **55** (Scheme 14).[44b, 44c] Results with all the ligands are good but it appears ligands **32** and **34** create more active catalysts. Additionally, these complexes were found to couple a variety of primary amines by dehydrogenation to form imines, ammonia and hydrogen with yields up to 93% (in the case of benzyl amine) (Scheme 14).[44a]



Scheme 14 Formation of imines from primary amines catalysed by ruthenium complexes of type **55**.

The CNN ligand **39**^{NEt2} has also been reported to form active ruthenium catalysts for the hydrogenation of esters to alcohols. In this case the **39**RuHBr(CO) was deprotonated to form the dearomatized species, which was subsequently found to hydrogenate a variety of esters.[51b]

Finally, palladium complexes of **52**-**54** have been used for the homoallylation of aldehydes with allyl(tributyl)stannane (Scheme 15, top). The PCS complex **54**PdCl performed the best, giving isolated yields up to 93%. Cationic palladium complexes [**52**-**54**Pd(H_2O)][BF_4] were also used for the tandem reaction of aldehydes or sulphonimines with allyl chorides and hexamethyldistannane (Scheme 15, bottom). Again the complex featuring **54** performed the best although yields for this more difficult reaction were expectedly lower (isolated yields of up to 71%). However, the yields afforded by complexes of **54** are less than those reported for the symmetrical SCS system. The electron withdrawing meta-OMe group may be causing this deactivation, which can be verified by synthesizing the corresponding ligands without the methoxy substituents and doing a more direct comparison.



Scheme 15 Homoallylation of aldehydes (top) and tandem coupling/homoallylation of aldehydes and sulphonimines (bottom) catalysed by palladium complexes of pincers **52**-**54**.

All of the previous examples demonstrate the utility of non-symmetric pincer ligands, especially because in many cases they perform much better than symmetrical analogues. This increased activity can often be attributed directly to one of the ligand arms being significantly more labile. Even the less active catalysts give clues as to how better catalysts can be designed. While excellent work has been done with non-symmetric groups there remains an almost endless potential for further ligand design.

Conclusions

In the vast world of pincer ligands a rather new but important group of non-symmetrical ligands has begun to grow, especially among the aryl or pyridine linked systems. Herein, the synthesis, coordination behaviour and catalytic reactivity of a number of important examples have been discussed. However, these examples only represent a fraction of the potential of this type of ligand with more examples being reported regularly.

The goal of this perspective has been to highlight some relevant examples of how the C_{2v} symmetry of aryl and pyridine-linked pincer ligand systems can be broken. This has been done by changing substituents and linkers or adding groups at any of several key positions. How these ligands have been used in catalysis, especially examples wherein the lack of symmetry may have an important effect on the activity have also been highlighted. These changes have been attributed to a variety of factors including solubility, the ability to finely tune the steric environment (e.g. use of two different substituents on the ligand arms), and the modulation of the electronics at the metal centre (e.g. use of one labile ligating group to generate open coordination sites). What is clear is that the ability to fine tune the electronic and/or steric properties of the ligand has led to excellent catalytic results some of which cannot be matched by symmetrical systems. Despite the large amount of work in this area there are clearly more modifications that can be made to the ligand system and unexplored areas for complexes and catalysts especially by moving to more earth abundant and cheaper 3d metals. However, from the given examples it is clear that these non-symmetrical systems deserve and will continue to receive considerable interest in the optimization and discovery of new, robust catalytic processes.

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Non-Symmetric Pincer Ligands: Complexes and Applications in Catalysis

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Non-symmetric pincer ligands and their complexes have become relevant in different areas of chemistry greatly increasing the pincer structural motifs known and hence their physical and chemical properties. The impact of these species in organometallic chemistry and catalysis is discussed in this perspective.