Cleavage of unreactive bonds with pincer metal complexes

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Since the first reports some three decades ago, the chemistry of pincer metal complexes has seen a tremendous development with impact on materials chemistry, supramolecular chemistry, bioorganometallics, and, presumably most significantly, on (catalytic) bond making and breaking processes. The remarkable progress is due to a large extent to the well-defined nature and tunability of the pincer ligand which allows the reactivity of the metal center to be modified and eventually tailored to specific needs. This Perspective summarizes the achievements in employing pincer complexes for mediating and catalyzing the cleavage of typically unreactive bonds such as C–H, C–C, C–E, and E–H bonds, arguably one of the most spectacular applications of pincer chemistry.

Introduction

Pincer ligands have become extraordinarily useful scaffolds for directing specific reactivity patterns of metal centers for a large variety of applications, for example as highly efficient sensors, switches, and catalysts.1 Pincer ligands are typically characterized by a monoanionic E,C,E-terdentate bonding mode where C denotes a central carbamion, often an aryl anion, and E represents a neutral two-electron donor such as an amine, imine, phosphine, phosphinite, sulfide or selenide (Fig 1). In general, these ligands adopt a meridional coordination mode,2 and as a consequence, the M–C bond in pincer complexes is effectively shielded and considerably stabilized as compared to other M–C bonds. As a consequence, the high trans effect of the anionic central ligand can be fully exploited in pincer complexes.

Furthermore, the electron density at the coordinated metal center may be altered and eventually tailored by selective ligand modification, which does not affect the general bonding mode of the ligand, e.g. via introduction of electroactive groups on the aryl ring (R') or on the heteroatom E.

Various modifications have been implemented on the general pincer scaffold, including the substitution of the central carbanion by an amide (NR2) or a silyl anion.3 Similarly, the linker between the core unit and the donor arms has been changed from an sp2- or sp3-hybridized carbon to oxygen. Some of these modifications are accompanied with a significant decrease of the chemical stability of the ligand scaffold towards degradation, and ligand fragmentation has been observed in several cases.4 In part due to their high modularity, various pincer metal complexes have been developed that enable challenging bond making and breaking.5 In some cases, the rigidly chelating bonding mode has been exploited to stabilize crucial intermediates, and to provide mechanistic insights. In other cases, the variability has been crucial for imparting high catalytic activity. While significant progress in cross-coupling catalysis has been achieved and reviewed,6 perhaps the most remarkable results have been accomplished in the activation and cleavage of typically unreactive bonds, such as C–H, N–H, and O–H bonds, and also C–C and C–heteroatom bonds.

This Perspective aims to overview the most significant advances, both in terms of mechanistic understanding and catalytic performance of pincer metal complexes in cleaving such unreactive bonds. An excellent review has appeared recently on PCP iridium-catalyzed dehydrogenation of alkanes and amine boranes,7 and these reactions are thus not discussed in any depth here. Similarly, the iridium-mediated formation of carbenes from the activation of methyl ethers and amines via double α-H elimination, and ensuing catalytic applications have been summarized in a recent account.8,9

Activation of C–H bonds

Dehydrogenation of unactivated alkanes has been most efficiently performed with PCP iridium complexes as catalysts and turnover numbers up to 3000 have been achieved with optimized pincer scaffolds.7 The working mode of the catalyst has been thoroughly investigated by kinetic and theoretical studies, and concurrent isomerization reactions as well as product inhibition effects have been identified. An analogous PCP rhodium complex comprising an agostically bound methane molecule, long postulated as a crucial intermediate of the catalytic cycle, has recently been isolated and structurally characterized.10

Fig. 1. General representation of an ECE pincer ligand coordinated to a metal fragment (MX2E), including the different functions that can be regulated by appropriate ligand modifications.

chiral information
dentate constraints via chelate size electron density at metal transient H reservoir

electron density at metal physical properties (solubility, size molecular recognition sites (self-assembly)

metal-ligand bond strength
dentate constraints via substituents electron density at metal via E and substituents at E

Y$Z^+$E

M$X_2E$

R$^H$

M$X_2E$

E

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Cleavage of activated C(sp<sup>3</sup>)–H bonds

The PNP iridium(III) complex 1 activates a C–H bond of acetone stoichiometrically (Scheme 1).<sup>11</sup> In this complex, the ligand is not aromatic and comprises an exocyclic double bond. Aromatization is induced upon protonation of the benzylic position, which also transforms the anionic amide donor into a neutral pyridine system. This aromatization is reversible and deprotonation of 2 has been demonstrated to occur at the benzylic position, thus reverting the formally monoanionic PNP pincer chelate. Cooperative participation of the ligand in the C–H bond activation of acetone has been postulated, involving the addition of the C–H bond across the metal-ligand unit. Deuterium labeling studies support a stepwise process including initial oxidative C–H activation at iridium and subsequent transfer of the hydrogen to the benzylic position of the ligand with concomitant aromatization. Theoretical analyses (DFT) support the proposed mechanism and predict the tricoordinate PNP iridium complex A as a critical intermediate.

Scheme 1. PNP iridium-mediated activation of acetone.

The propensity of these PNP-type pincer ligands in cooperating in bond activation processes has been further exploited in the Ru-catalyzed dehydrogenative coupling of alcohols (Table 1).<sup>12</sup> In the presence of primary amines, either imines or amides are formed, depending on the donor sites at the pincer ligand. With the PNP ruthenium(II) complex 3, imines are produced,<sup>13</sup> while the PNN analogue 4 affords amides.<sup>14</sup> In either system, the dehydrogenation activity of the ruthenium pincer complex is critical for high catalyst activity. Both imine and amide formation have been proposed to be sequential processes involving first dehydrogenation of the primary alcohol to the aldehyde, and subsequent reaction with the amine. Generally, a Schiff base-type reaction ensues, thus producing imines. The selectivity of complex 4 to generate amides thus implies that the carbonyl group remains coordinated when attacked by the amine, hence forming the hemiaminal within the ruthenium coordination sphere. Alternatively the hemiaminal intermediate of the Schiff base reaction may bind to the ruthenium center after being formed. In either case, an intermediate B is proposed, which can undergo a second dehydrogenation involving C–H bond cleavage to afford the amide product (Scheme 2). The mismatch in the PNN ruthenium complex between the soft metal center and the hard amine unit increases the hemilability of the pincer ligand and thus favors carbonyl coordination and hence amide formation. In contrast, the two soft phosphine donors in the PNP ligand bind stronger to ruthenium and P–Ru dissociation is disfavored. Hence, this complex releases the carbonyl intermediate rapidly and the reaction with the amine occurs as under normal Schiff base conditions to generate imines selectively. In agreement with this mechanistic proposal, secondary alcohols are less reactive and secondary amines are not incorporated at all.

Table 1. PNP iridium-catalyzed dehydrogenative coupling of alcohols

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Reagent</th>
<th>Catalyst</th>
<th>Product</th>
<th>Ref</th>
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</thead>
<tbody>
<tr>
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<td>3</td>
<td>R'O'R'</td>
<td>13</td>
</tr>
<tr>
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<td>R'O'R'</td>
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<td>R'O'R'</td>
<td>14</td>
</tr>
<tr>
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<td>R'O'R'</td>
<td>4, 5</td>
<td>R'O'R'</td>
<td>14, 15</td>
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<td>5</td>
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<tr>
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<td>R'O'R'</td>
<td>4</td>
<td>R'O'R'</td>
<td>16</td>
</tr>
</tbody>
</table>

Scheme 2. Proposed catalytic cycle for the dehydrogenative coupling of alcohols and amines to form imines or amides.

In the absence of reactive amines, homocoupling of alcohols becomes the predominant pathway with complex 4 or 5.<sup>14, 15</sup> With less bulky substituents at the pincer donor groups, esters are formed, while sterically congested metal centers as in 5 lead to the predominant formation of acetals. Efficient ester formation from alcohols requires the addition of a base.<sup>15</sup> Along similar concepts, catalytic transesterifications have been successfully accomplished upon reacting esters and
primary alcohols in the presence of complex 4.\textsuperscript{16} The PCP iridium complex 6 is an efficient catalyst for the oxidation of primary amines to nitriles (Scheme 3).\textsuperscript{17} Efficient double dehydrogenation has been achieved in the presence of tert-butylethylene as sacrificial hydrogen acceptor. Detailed mechanistic work involving a combination of competition experiments, isotope labeling studies, and kinetic analyses have identified three potential resting states of the catalyst, 6, 7, and F, which are interconnected via two pre-equilibria. Not surprisingly, a hard step is the substitution of the nitrile product from the coordination sphere of complex 7 by a new amine substrate (K \( \sim 550 \)). Subsequent reversible N–H oxidative addition is followed by \( \beta \)-hydrogen elimination to produce G as the rate-limiting step, indicated by the substantial kinetic isotope effect of 2.8(2).

### Cleavage of C(sp\(^3\))–H bonds

Cyclometalation is typically supported by initial heteroatom coordination followed by C–H bond activation.\textsuperscript{18} Since pincer ligands contain two such potential anchoring sites for metal coordination, metal-mediated activation of the C\( \text{sp}^3 \)–H bond in the ligand precursor is very common in pincer chemistry and represents one of the oldest and most frequently used strategies to introduce the metal center.\textsuperscript{19} Here, only special cases are highlighted, such as C–H bond activations that are not heteroatom-assisted or that are incomplete and allow relevant intermediates to be stabilized and investigated.

Upon coordination of a second PCP ligand to the PCP ruthenium complex 8, the agostic intermediate 9 has been isolated. This complex features one cyclometalated PCP ligand and one \( P,P \)-bidentate coordinating H–PCP ligand (Scheme 4).\textsuperscript{20} Crystallographic analysis strongly suggests an agostic interaction between the ruthenium center and the C–H bond of the non-cyclometalated ligand. In solution, NMR spectroscopy has indicated a resonance of this proton at 1.2 ppm, thus being magnetically neither a hydride nor an aryl-bound hydrogen. Extensive \( ^{31}P \) NMR spectroscopic investigations and isotope labeling experiments have revealed a dynamic behavior of this hydrogen nucleus, involving migration from the non-cyclometalated ligand to the cyclometalated one. Further evidence for such proton migration has been obtained upon introducing a substituent on one of the arene fragments (9b, \( X = Br \)), which allows the two PCP ligands and hence complexes 9 and 10 to be differentiated. Base-mediated abstraction of the fluxional proton has been unsuccessful.

![Scheme 3. PCP iridium-catalyzed dehydrogenation of primary amines.](image)

![Scheme 4. Agostic interaction in a PCP ruthenium complex.](image)
Apart from these mechanistic insights involving intramolecular C–H bond activation of the pincer ligand itself, numerous studies report on intermolecular activation of C(sp²)–H bonds. A PNP ruthenium polyhydride complex has been shown to cleave aromatic C–H bonds reversibly. This reactivity pattern has been employed for catalytic H/D exchange using C₆D₆ as deuterium source.

Ligand cooperativity as evidenced in PNP and PNN pincer complexes is an attractive concept, and it is tempting to consider similar reaction patterns in the PNP iridium system used by Grubbs and coworkers for the formation of carbene complexes from methyl ethers and amines. In PCP iridium-catalyzed alkyne dehydrogenation, however, all mechanistic evidence obtained thus far suggests a different reaction pathway that does not invoke de- and re-aromatization of the aryl ligand. In addition, a number of ligand scaffolds that lack the possibility to reversibly de-aromatize are known to activate C–H bonds. For example, the PNP iridium complex 14 comprising oxo-linkers between the pincer arms and the central pyridine unit would generate a highly reactive oxonium species upon dearomatization (Fig 2). Isotope exchange within the metal-bound aryl or methyl group of 14 is promoted by protic reagents such as CD₃OD or D₂O and includes the formation of a protonated complex 15, which has been fully analyzed. Transient formation of a π-bound benzene ligand (from 15a) or an agostically bound methane complex (from 15b) and subsequent site exchange would account for the observed H/D substitution process. Stoichiometric C–H activation of benzene with PNP rhodium complexes that contain silicon substituents at the central amide, and with iridium complexes comprising a monoanionic PSIP pincer ligand presumably occurs without ligand participation either.

Activation of C–C bonds

While C–C bond formation is a mature field, most notably due to the significant advances in metal-mediated cross-coupling reactions, the reverse process, i.e. C–C bond cleavage, is still at its infancy. Pincer complex formation has been used as a driving force to entail alkyl-aryl C(sp³)–C(sp³) bond cleavage. Mechanistic investigations on the C–C bond activation process and also on its microscopic reverse, viz. C–C bond formation, provided insights into the intimate steps of the bond cleavage process and several crucial intermediates have been stabilized due to the unique steric and electronic impact of the pincer-type ligands.

Mechanistic investigations

Phosphine-containing PCP, PCN, and PCO pincer ligands have been used in combination with rhodium and iridium to study mechanistic aspects of C–C bond cleavage, while NCN platinum systems allowed for the stabilization of intermediates during C–C bond formation. In rhodium(I) and iridium(I) chemistry, an oxidative addition pathway for C–C bond activation has been discussed extensively, while a substitution process has been put forward for platinum(II) complexes (Scheme 6). Theoretical considerations support this general picture, yet it should be noted that despite the difference in terminology, the overall reaction coordinate of both substitution and oxidative addition are highly similar. Distinction often requires evoking minor differences in metal-ligand and ligand-ligand interactions.

Upon combining these seemingly different concepts, a detailed and comprehensive model of the pincer-metal mediated C–C bond activation process emerges (Scheme 7). Many intermediates of this process have been characterized spectroscopically, and often also crystallographically. Two conclusions are probably most relevant: firstly, the intrinsic step of C–C bond making and breaking appears to be highly similar in oxidative addition and substitution-type reactions. Secondly, mechanistic investigations on C–C bond formation and on C–C bond cleavage provide a converging picture, which suggests a common reaction coordinate.
The stability of the intermediates is highly dependent on the nature of the metal center and the donors E, and an intermediate in one M/E set may become a transition state in a different metal/ligand combination. For example, in NCN platinum chemistry (E = NMe₂), intermediates J and L have been characterized, while structure K is supposed to be the transition state in between. Complexes of type K are more stable in PCP rhodium complexes and have been isolated as an intermediate of C–C bond activation. Likewise, the coordination compound I has been postulated as a short-lived intermediate in PCP rhodium complexes. Upon changing the donor array to a PCN pincer ligand, this species is sufficiently stable to be characterized.

Metalation of the PCP ligand precursor 16 with a rhodium(I) salt results in C–aryl–Calkyl and C–alkyl–H bond activation (Scheme 8). Both processes are thermodynamically and kinetically very similar and subtle changes in the ligand parameters hence strongly affect the reaction outcome. For example, PPh₂ donors induce C–H bond cleavage to afford 17. Only at elevated temperatures and under H₂ atmosphere, C–C bond activation is observed. In contrast bulky P(η₅-C₅H₅)₂ donors promote C–C bond activation already at room temperature and the aryl complex 18 is the exclusive metalled product. Similarly, replacing one phosphine donor by a harder NEt₂ group or employing less basic phosphinite donors results in fast and exclusive C–C bond cleavage at room temperature and below. These outcomes indicate that steric rather than electronic effects play a dominant role for the thermodynamic preference of C–C over C–H activation. Steric congestion has been suggested to force the metal orbitals into a rigid orientation that is directed towards the C–C bond. Moreover, the C–H bond activation is reversible while the C–C activation is not, unless chemically induced, e.g., by phosphine-induced metal dissociation. The higher bond dissociation energies required for C–C bond activation as compared to C–H bond breaking is evidently compensated by the higher M–aryl bond strength and the formation of two five-membered rather than six-membered metalacycles.

Kinetic investigations of these reactions have identified the coordination compound M, i.e., an analogue of I (cf Scheme 7), as a common intermediate of both, C–H and C–C bond cleavage. Remarkably, formation of this intermediate, and not C–H or C–C bond activation is rate-determining. While displacement of a weakly bound olefin ligand in the rhodium precursor [RhCl(olefin)]₂ may be fast, formation of the 8-membered metacycle in M is obviously less favored, especially due to the possible formation of di- and polymeric coordination compounds. With appropriate donor groups, the postulated coordination complex akin to M has been characterized in solution at low temperature. When using kinetically less reactive platinum(II), the bidentate diphosphine coordination is even further stabilized.

The transoid bidentate chelation of the donor groups in M is pivotal for entailing C–C bond activation. When using monophosphine ligand precursors that lack a second donor group, C–H bond activation occurs selectively and no C–C bond cleavage has been observed. With the related PCO pincer ligand precursor 19, C–H activation is kinetically preferred at room temperature (Scheme 9). However, this reaction is not selective and produces a mixture of 20 and 21, indicating that both C–H bonds in ortho position to the phosphine are activated. Upon heating, C–C bond activation takes place exclusively at the position ortho to both the O and P donor groups to afford 22. These reactivity patterns illustrate the reversibility of C–H bond activation process, and more importantly, that bidentate ligand bonding is essential for C–C but not for C–H bond activation. Furthermore, these conclusions provide a rationale for the inherent difficulties encountered when probing catalytic or intermolecular C–C bond activation. Undoubtedly, though, the potential to accomplish and (thermally) trigger the activation of such otherwise unreactive bonds illustrates the extraordinary potential of pincer-type chelation for tuning unique metal-mediated processes.

Scheme 7. Postulated mechanism of C–C bond making and breaking within a pincer scaffold.

Scheme 8. Reversible C–H and irreversible C–C bond activation in rhodium complexation of PCP ligand precursors.
The activity of the rhodium center in intermediate M towards C–C bond cleavage is strongly associated with its tricoordinate 14e configuration. Consequently, the bond activation process reveals a strong solvent dependence. In coordinating MeCN, stabilization of the rhodium center and the formation of square-planar complexes depletes the concentration of the 14e intermediate, and C–H bond activation becomes the predominant reaction pathway. Conversely, less coordinating solvents such as tetrahydrofuran favor C–C bond cleavage.

Similarly, substitution of the metal center from rhodium to iridium, ruthenium, or platinum has direct consequences. While activation of the C–C bond in the PCP ligand precursor 16 occurs smoothly at room temperature with rhodium(I), only C–H bond activation is observed with the iridium(I) homologue. Substantial heating is required to direct the course of the reaction towards C–C bond activation. These results underline the increasing stability of Ir–hydride species compared to their Rh analogues, and presumably also the higher nucleophilicity ascribed to the rhodium(I) center.

The strong influence of the metal on the C–C vs C–H bond activation selectivity is further illustrated in osmium(II)-mediated C–C bond cleavage. Exposure of [OsCl₂(PPh₃)₃] to the hydroxy-functionalized PCP ligand precursor 23 containing basic PPr₃ donors induces Caryl⁻Calkyl bond cleavage and yields complex 24, when the reaction is performed in the presence of H₂ (Scheme 10). In the absence of H₂, the quinone methide 25 is formed selectively as a result of C–H bond activation. A dynamic process has been suggested that involves interconversion of the quinone methide 25 to its arenium tautomer N, resulting from insertion of the exocyclic olefin into the Os–H bond. An analogous product has been trapped upon addition of CO. A subsequent shift of the methyl group to osmium followed by hydrogenation of intermediate O has been postulated to account for the formation of complex 24, thus suggesting the quinone methide 25 to be an early intermediate in the direct formation of 24 from 23.


Arenium complexes have been extensively studied earlier in NCN platinum chemistry. They are readily prepared from the solvent complex 26 and are resistant towards air and moisture. The crystal structures of several complexes show consistently that the platinum center is bound to the aryl carbon only. In all structures, the Pt⋯Caryl distance is far too large for postulating any agostic resonance structure contribution (cf K in Scheme 7). In addition, these platinum-stabilized arenium complexes readily react with nucleophiles at their ortho and para position and afford platinum-substituted cyclohexadienyl derivatives. This dearamatization process indicates that the positive charge is localized on the aromatic ring rather than on the metal center. Arenium structures have been proposed to result from a 1,2-sigmatropic shift of the alkyl group from the metal center in the (aryl)(alkyl) complex 27 to the aryl carbon in 28 (Scheme 11), thus relating structures J and L directly (cf Scheme 7).

Spectroscopic identification of this migration has been achieved by incorporating electron-donating substituents on the aryl ring (R = OH, OMe), a well-known concept in electrophilic aromatic substitution. Such a modification increases the reactivity of the ipso carbon and of the platinum center in 26 and allows (aryl)(alkyl) complexes to be stabilized with a variety of different alkyl substituents other than Me. In the case of the (benzyl)(aryl) complex 27, a color change has been observed upon formation of 28. Analysis of this transformation by UV–vis spectroscopy has revealed an isosbestic point, thus indicating the presence of an equilibrium between the two species 27 and 28 exclusively. This equilibrium implies that alkyl migration between 27 and 28, viz. the microscopic C–C bond making and breaking step, is fully reversible. Consequently the actual C–C bond formation is the exact microscopic reverse of the C–C bond cleavage process in these platinum pincer complexes.
The alky group migration has been postulated to include a 3-centered non-polar transition state reminiscent to I (cf Scheme 7). Similar transition states have been proposed in the C–C bond activation using PCP rhodium complexes. Molecular orbital considerations suggest two distinct interactions that contribute predominantly to the stability of K. One interaction (Fig 3a) is characterized by overlap of an sp³ orbital of the formally cationic alkyl group with the filled dₓ orbital of the d⁸ metal center, having predominant dₓ₂ character, and simultaneous interaction with the distorted pₓ orbital of the aryl carbon. Shuttling of the alkyl cation from the metal closer to the carbon obviously increases C–C bond overlap and thus induces a rehybridization of the pₓ orbital to an sp³ orbital, and dearomatization ensues upon C–C bond formation, leading to arenium structures. The microscopic reverse C–C bond cleavage process thus includes the metal-induced depletion of electron density in the C–C bond, a process that is favored with electrophilic metal centers such as platinum(II).

A second contribution consists of a metal dₓ electron donation into the C–C σ* orbital and leads to an agostic interaction that eventually climaxizes in an oxidative addition (Fig 3b). Stronger donor ability of the ligands E and electron-rich, nucleophilic metal centers such as ruthenium(I) or iridium(I) will thus increase the electron density in the C–C antibonding orbital (σ backbonding) and C–C bond cleavage along this reaction coordinate will be facilitated. These considerations may explain the different stability of the intermediate complexes in NCN platinum(II)-mediated C–C bond making and breaking as opposed to analogous processes at PCP iridium(I) and rhodium(I) centers. The former stabilizes arenium species due to strong C–M σ interactions with the electrophilic platinum(II), while the latter prefer an agostic bonding mode that allows the nucleophilic metal centers to be bound to a π-accepting ligand.

Scheme 11. Reversible arenium formation in NCN platinum complexes.

In agreement with this model, stabilization of an agostic complex has been achieved by appropriate modification of the donor group (29, Fig 3c). Upon substitution of one phosphine donor by a NEt₃ group, the electron density at the cationic rhodium center is reduced to such an extent that the agostic complex is moderately stable and thus does not represent a transition state anymore. The electronic balance which determines whether C–C bond activation is completed or arrested at the agostic stage is very subtle. Using [Rh(C₂H₅)₂(solvent)]⁺ rather than [Rh(CO)(C₂H₅)(solvent)]⁺ as metal precursor leads to clean C–C bond cleavage.

Methylene Transfer

Interesting synthetic opportunities emerge from reactions that are under kinetic control, leading to products from C–H rather than C–C bond activation. For example, complexation of rhodium(I) with the CH₂-PCP ligand precursor 16 bearing PPh₃ donors induces C–H bond activation and affords the benzyl complex 30 (Scheme 12). The corresponding platinum(II) complex with a coordinated [PtCl] unit—isolobal to the [Rh(PPh₃)]⁺ fragment—has been prepared even with bulky P'P'P' groups in the pincer scaffold. In these complexes, C–C bond activation has been induced by addition of H₂ or HCl. Apparently, H₂ and HCl favor reductive C–H elimination, i.e. the backward reaction from C–H bond activation and formation of the intermediate Q (Scheme 12, see also 1 in Scheme 7). Simultaneously, the activation energy for C–C bond activation is reduced, rendering C–C bond activation more favorable than C–H bond activation. The overall process from 30 to 31 may formally be considered as a CH₂ transfer to an appropriate acceptor such as H₂ or HCl, leading to the production of CH₄ and CH₃Cl, respectively. Similarly, benzene, hydroisilanes, and disilanes have been successfully employed as acceptors, providing toluene, R₃SiCH₃, and R₃Si–CH₂–SiR₃, respectively.

Fig. 3. a) Orbital interactions relevant for C–C bond activation via sigmatropic 1,2-shift of a cationic alkyl fragment along the C–M bond (electrophilic activation, electron removal from the C–C σ orbital); b) agostic interaction en route to oxidative addition (population of the C–C σ* orbital via backbonding); c) complex 27 as a structural model comprising agostic interactions.
addition of the acceptor E–R to the benzyl complex (P, Scheme 12).\textsuperscript{42} Rate-limiting C–R reductive elimination and subsequent C–C bond activation is followed by irreversible reductive E–CH\textsubscript{2}R elimination from R, thus completing the CH\textsubscript{2} transfer and affording the PCP rhodium complex 31. Notably, Rh–phosphinite complexes reminiscent of R have been shown to undergo apparent \(\alpha\)-hydrogen elimination, thus providing an alternative mechanism for the release of the CH\textsubscript{2} fragment (for R = H).\textsuperscript{43}

The absence of any products originating from double CH\textsubscript{2} insertion indicates that C\textsubscript{aryl}–C\textsubscript{alkyl} bond activation is an intramolecular process. The methylene transfer reaction can be reversed by addition of CH\textsubscript{2}I as a CH\textsubscript{2} source to complex 31, and subsequent base-promoted abstraction of HI.\textsuperscript{44} This procedure regenerates the benzyl complex 30. Similarly, SnMe\textsubscript{3} in the presence of KO'Bu has been shown to induce methylene insertion into the Rh–C\textsubscript{aryl} bond.\textsuperscript{44} Catalytic CH\textsubscript{2} transfer is thus possible and has indeed been demonstrated.\textsuperscript{45}

While the overall process is remarkable, the observed rates (10 turnovers in 48 h) require further optimization in order to become synthetically useful.

Methylene transfer to benzene requires high temperatures and long reaction times, which is in agreement with oxidative addition of the acceptor molecule as the rate-limiting step of this reaction. Consistently, the use of an aryl halide promotes fast oxidative addition to 30 already at room temperature (Scheme 13).\textsuperscript{32} The formed complex 32 undergoes a methylene transfer at slightly elevated temperatures to yield the (benzyl)(aryl) complex 31. This complex is also accessible from the PCP rhodium complex 31 via oxidative addition of substituted benzyl bromide. Reductive elimination from 33 is initiated only upon addition of a coordinating ligand such as PPh\textsubscript{3} and a carbanion R'CH\textsubscript{2} as nucleophile, presumably via transmetalation and formation of the postulated triorgano-rhodium complex S. Several competing reactions then ensue: cross-coupling of the two monodentate ligands gives complex 31 as the organometallic product. Alternatively, one of the monodentate carbanions may reductively migrate to the pincer ligand \(\text{ipso}\) carbon to produce an intermediate similar to 1 (cf Scheme 7), corresponding to a back transfer of the methylene group. Upon C–H bond activation, complexes 34 and 35 are obtained via migration of the nucleophile and the benzyl group, respectively. Variation of the substituent R at the benzylgenic has evidenced a strong electronic control.\textsuperscript{46}

Electron-releasing groups (R = OMe) increase the migration tendency and yield predominantly 35, whereas acceptors (R = CF\textsubscript{3}) migrate slower and hence produce 34 and significant amounts of cross-coupling products.

Activation of C–E bonds

The catalytic activity of pincer complexes in cross-coupling reactions implies a high potential of these complexes to activate C–B and C–Si bonds used for Suzuki-Miyaura and Hiyama-type reactions, respectively, and of course also a wealth of C–X (X = Cl, Br, I, OTf) and C–M bonds (M = Mg, Al, Sn, Zn, etc).\textsuperscript{8} Here, only strong C–E bond activation will be discussed, including cleavage and redox reactivity of C–N, C–O, and C–F bonds.

C–N bond activation

Metal-mediated C–N bond activation is little explored in pincer chemistry. Activation of a C\textsubscript{benzylic}–N bond in a pincer-type ligand precursor has been observed in the presence of [RhCl(coe)\textsubscript{2}] and H\textsubscript{2}.\textsuperscript{46} While the reaction is catalytic (up to 21 TONs), the mechanism has been postulated to not involve pincer-type metal bonding. A PNN ruthenium complex related to 1 (cf Table 1) catalytically cleaves amides to amines and alcohols under hydrogen pressure.\textsuperscript{47} This reduction is complementary to LiAlH\textsubscript{4}-mediated amide reduction. Most likely, an aromatization/dearomatization sequence of the heterocycle occurs, thus constituting the microscopic reverse of the amide synthesis discussed above (cf Scheme 2). The possibility to switch the reactivity from dehydrogenation (amide synthesis)
to hydrogenation (amide cleavage) by changing the reaction atmosphere illustrates the robustness of the pincer metal unit in these transformations.

**C–O bond activation**

The cleavage of C–O bonds has been demonstrated in stoichiometric and catalytic processes. Stoichiometric C_{aryl}–O bond scission occurs upon heating the pincer ligand precursor 36a in the presence of [RhCl(ethene)₂]₂ (Scheme 14). The PCP rhodium complex 37 is formed along with formaldehyde, and no activation of the less strong C_{alkyl}–O bond has been observed. Most conceivably, this high chemoselectivity is due to a mechanism that is related to C_{aryl}–C_{alkyl} bond cleavage (cf. Schemes 10 and 11), involving a P,P-bidentate coordination of 36a and subsequent formation of an (aryl)(methoxy) rhodium(III) intermediate that may undergo facile oxygen extrusion from oxygen transfer process reminiscent of the methylene transfer metalacycles in complex 36a.

Oxygen activation in the ethoxy PCP ligand precursor decreases oxygen on the substitution pattern at oxygen. Larger s-character of the metal center in complex nickel(II) centers, L₄E₂MH₂⁺, with harder and more electrophilic palladium(II) and iridium center, L₄E₂MH⁺, has been exploited to develop an cationic PCP iridium complex 40 in the presence of H₃SiEt₃ (Scheme 15). A variety of primary, secondary, and tertiary ethers have been successfully cleaved at room temperature. Ethers with bulky alkyl groups undergo a single C–O cleavage and give one equivalent of alkane RH and the corresponding silyl ether ROSEt₃. More basic and less bulky ethers engage in two sequential C–O bond cleavage reactions and produce two equivalents of alkane RH along with Et₃SiOSiEt₃. Mechanistic work suggests a process that involves reversible coordination of the silane to the iridium cation followed by hydride transfer from silicon to the iridium center, thus forming a silyl cation that is ether-stabilized. Subsequent C–O cleavage is promoted by the iridium dihydride intermediate, thus yielding the silyl ether and the alkane, and also regenerating the cationic complex 40. This step is rate-limiting. The oxonium species 41 as the catalyst resting state along with the known dihydride 42 has been isolated and characterized crystallographically. With less basic ethers than Et₃O, the resting state shifts forward from the oxonium salt to the silane complex T, which is also relevant to the iridium-catalyzed dehalogenation of alkyl halides.

Conversion of CO and CO₂ has been probed with a variety of pincer metal complexes, motivated at least in parts by the environmental relevance of these small molecules. The rhodium dihydride complex 43 inserts dry CO₂ into the Rh–H bond and yields a PCP rhodium complex containing a formate ligand, corresponding to a formal reduction of CO₂ (Scheme 16). The stability of the formate intermediate is strongly dependent on the nature of the metal center and on the type of pincer ligand. Changing the metal center in complex 43 to iridium affords the less stable formate complex 44 which disproportionates to a bicarbonate and a carbonyl iridium complex. Similarly, modification of the anionic fragment

**Scheme 14.** Rhodium- and palladium-mediated C–O cleavage within a pincer scaffold.

With harder and more electrophilic palladium(II) and nickel(II) centers, Lewis acid-base complexation to oxygen becomes more relevant, and consequently, C_{alkyl}–O bond activation as in monophosphine ligands is observed (38, Scheme 14). The bond cleavage selectivity is dependent on the substitution pattern at oxygen. Larger substituents decrease oxygen-metal interactions and accordingly, C–O activation in the ethoxy PCP ligand precursor 36b is less selective than in the methoxy analogue and results in both C_{alkyl}–O and C_{aryl}–O bond cleavage (9:1 ratio at 130 °C).

The ring strain imposed by the two six-membered metalacycles in complex 38 has been exploited to develop an oxygen transfer process reminiscent of the methylene transfer reaction in related complexes. Oxygen extrusion from 38 in the presence of H₂ is achieved at high temperatures (180 °C) and yields the PCP palladium complex 39 and H₂O. Similarly, the (aryl)(methoxy) rhodium(III) intermediate has been successfully employed for transferring an alkoxide. Upon performing the rhodation of the precursor 36a in the presence of HSiR₃, MeOSiR₃ has been obtained rather than formaldehyde along with complex 37.
from an alkyl moiety to an aryl anion (complex 45) transforms the formate complex into a transient, yet spectroscopically detectable intermediate that spontaneously eliminates H₂O to yield a rhodium(I) carbonyl complex. Formally, this process involves the reduction of CO₂ to CO and thus constitutes the reverse of the water-gas shift reaction. The stoichiometric oxidation of CO to CO₂ has been achieved with the platinum(IV) oxo complex 46. Concomitant reduction of the metal center affords a cationic PCN platinum(II) complex containing a carbonyl ligand. A C-bound formate complex has been obtained upon reaction of the platinum complex 47 with NaOMe. Hence formate fragments may be assembled either from CO₂ or from CO.

Scheme 16. Reactivity of pincer complexes towards CO₂ and CO.

C–F bond activation

The chemistry of the C–F bond is of high relevance, in particular for pharmaceutical applications. The bond is considered to be one of the strongest bonds and methods for C–F bond formation and scission are thus of paramount interest. Cleavage of the C–F bond has been reported in a PNP titanium complex comprising a Schrock-type carbene ligand. With fluoroarenes such as C₆H₅F₃, the C–H bond is activated selectively. Upon warming to 100 °C, C–F bond cleavage occurs via β-fluoride abstraction, resulting in a PNP–TiF complex and ortho-benzylene as side product, which has been identified by trapping experiments.

Stoichiometric C–F bond scission in hexafluorobenzene has been accomplished with the PCP platinum(0) complex 48 at ~35 °C (Scheme 17), yielding the corresponding platinum(II) complex 49 containing a C₆F₅ ligand and NaF. A radical mechanism has been postulated, involving a one-electron transfer from the platinum center to C₆F₅, thus generating a platinum(I) intermediate and a [C₆F₅]⁺, which couple after loss of F.

Scheme 17. C–F bond cleavage by a PCP platinum(0) complex.

Activation of E–H bonds

N–H bond activation

A PCP iridium pincer complex comprising an aliphatic carbanionic moiety has been successfully employed for the activation of ammonia and hydrazine. While only stoichiometric activation has been achieved, interesting transfer reactions may emerge from metal bound amides. Related work has demonstrated the stoichiometric activation of a N–H bond of various anilines mediated by complex 3 (cf Table 1). Ligand participation via heterocycle aromatization may be a key feature also in this activation process.

O–H bond activation

Activation of the O–H bond in alcohols has been invoked in the activation of H₂ at the PNP iridium(1) complex 14b (cf Fig 2). The formation of the trans dihydride oxidative addition product implies an indirect activation process, presumably including first RO–H bond activation to form complex 15b as a transient intermediate with RO⁻ as counterion. Subsequent heterolytic H₂ activation regenerates the alcohol, albeit with a proton stemming from H₂. Rapid incorporation of deuterium upon performing the reaction in the presence of D₂O or CD₂OD support the postulated reaction pathway. Ligand assisted RO–H bond activation has been observed also in PNP platinum and palladium complexes, in which the PNP ligand is dearomatized. In this case, the hydrogen is ultimately bound to the benzylic position, inducing aromatization of the heterocycle. The activity of this type of pincer complexes towards O–H bond activation has been further expanded to develop a process that allows for effective water splitting at complex 4 (Scheme 18). The reaction includes cooperative fixation of water at the ruthenium center and the pincer ligand to give complex 50, followed by thermally induced H₂ elimination, affording the dihydroxide 51. Consecutive light-induced dissociation of H₂O₂ and disproportionation yields O₂ and H₂O. Intramolecular hydrogen transfer from the benzylic position of intermediate U to the ruthenium center and concomitant de-aromatization regenerates complex 4. Isotope labeling experiments have demonstrated that the H₂O₂ formation is an intramolecular...
process rather than a consequence of a bimolecular reaction. Even though parts of the water splitting need to be sequentially pulsed by thermal and photochemical stimulation, the possibility to split water at a single metal center provides intriguing perspectives for further developments.

![Scheme 18. Water splitting mediated by the PNP ruthenium complex 4.](image)

**Si–H bond activation**

Catalytic Si–H bond activation using the PCP iridium complexes 40 and 42 has been discussed together with C–O bond activation in ethers (cf Scheme 15). The same mechanism of silane activation has been exploited for the catalytic reduction of alkyl halides. Elegant competition experiments have uncovered a pre-equilibrium involving iridium coordination either to RX or to HSEt3. This equilibrium is responsible for the unusual preference of catalyst 40 to convert pure RBr faster than pure RCl and much faster than RI. In mixtures, however, the expected reactivity sequence RI > RBr > RCl is restored, as the pre-equilibrium is shifted to HSEt3 coordination when the better coordinating iodoalkane is present only in minor quantities. Both intra- and intermolecular Si–H activation has been observed at a platinum center bound to a PSiP pincer ligand. Mechanistic studies may unravel intriguing differences between Si–H bond activation processes and the well-understood C–H bond activation.

**Conclusions**

Pincer ligands have provided an excellent platform for tailoring the activity of metal centers towards the cleavage of strong bonds that are typically unreactive. Both stoichiometric metal-mediated reactions as well as efficient pincer metal-catalyzed processes have been disclosed, many of which lacking precedence such as room temperature C–C bond making and breaking and the complete splitting of water at a single metal center. The high steric and electronic flexibility of the pincer ligand has been pivotal for uncovering mechanistic details that also provide guidelines for general transition metal-mediated reactions. Furthermore, pincer ligands show great potential to adapt to specific needs of the coordinated metal center, as illustrated for example by reversible ligand de- and re-aromatization, and by the accommodation of metals in various oxidation states (cf platinum(0) up to platinum(IV) within the same PCP pincer scaffold). Despite the remarkable progress achieved up to now, the enormous variability in pincer chemistry—e.g. through modification of the donor groups as well as in the central unit—may pave the way for further breakthroughs in bond activation processes, thus providing exciting perspectives for organometallic chemistry, organic synthesis, and materials science.

**Notes and references**

Cleavage of unreactive bonds with pincer metal complexes

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Due to the unique flexibility and tunability of pincer ligands, organometallic pincer complexes have been successfully employed for mediating and often also catalyzing the cleavage of typically unreactive bonds,