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Challenging metal-based transformations. From single-bond activation to catalysis and metallaquinonoids*

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Abstract: Catalytic reactions resulting from our C–X (X = H, C, O, N, halide) bond activation studies are described. Aryl chlorides can react with aluminum alkyls in preference to bromides. Using PCP-type Pd catalysts, Heck reaction with aryl iodides and bromides can proceed without involvement of Pd(0). Ru-catalyzed oxidative coupling of arenes with alkenes using O_2 was accomplished.

Using specifically designed systems, the scope and mechanisms of C–C activation in solution was studied and compared to C–H activation. C–C activation by Rh(I), Ir(I), Ni(II), Pt(II), Ru(II), and Os(II) was observed. Metal insertion into a strong C–C bond can be kinetically and thermodynamically more favorable than the competing C–H activation. Selective, single-step oxidative addition of a strong C–C bond to a metal was observed and kinetically evaluated. Catalytic C–C hydrogenolysis was demonstrated. A combination of C–C activation and C–R formation (R = aryl, silyl) resulted in unusual methylene transfer chemistry. Selective activation of aryl–O and Me–O bonds was observed. New types of interactions between metals and arenes and unusual quinonoid complexes, including quinone methides, xylylenes, methylene arenium, and a metallaquinone, were discovered. C–H and C–C agostic complexes of cationic metals, proposed as intermediates in bond activation, were isolated. Stabilization and controlled release of biologically relevant, extremely unstable, simple quinone methides, was accomplished.

INTRODUCTION

Bond activation by metal complexes forms the basis for many stoichiometric and catalytic processes. We have an ongoing interest in the development of new approaches to the activation of strong single bonds and the generation of mechanistic insight into these processes. The bonds studied in our group include C–C, C–H, C–F, C–Cl, C–O, C–N, O–H, N–H, and Si–Cl. Based on these studies, we have developed several catalytic processes as well as some unusual stoichiometric reactions. Here, we briefly review our work on the activation of C–X bonds and the catalytic generation of C–C bonds. Our studies on C–C bond activation have led to the discovery of a new family of compounds, metallaquinonoids, which will be described.

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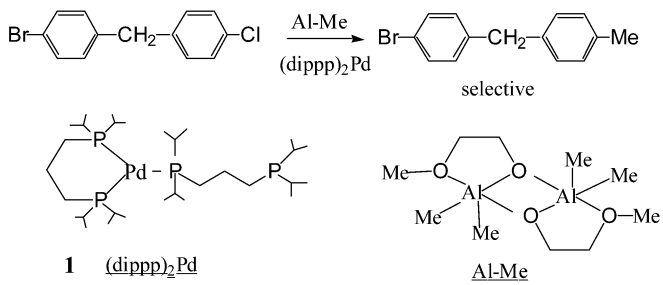
CATALYTIC REACTIONS OF ARYL CHLORIDES AND FLUORIDES

More than a decade ago, we developed the electron-rich, bulky bis-chelating phosphine palladium complexes $(dippp)_2Pd$ (dippp = 1,3-diisopropylphosphinopropane) **1** and the analogous $(dippb)_2Pd$ (dippb = 1,3-diisopropylphosphinobutane). These complexes are trigonal in solution, with one diphosphine binding in a monodentate form, and are in equilibrium with the highly nucleophilic 14e (η^2-bisphosphine)Pd(0). As a result, they undergo facile oxidative addition of aryl chlorides, by a nucleophilic aromatic substitution mechanism assisted by chloride coordination in the transition state [1].

Another interesting feature of $(dippp)_2Pd(0)$ is the *reversible* binding of CO. These features formed the basis for catalytic reactions of aryl chlorides, which at that time were limited mainly to the more reactive aryl iodides, bromides, and triflates, including various carbonylation, formylation, reduction, and vinylation reactions of aryl chlorides [2]. High yields are obtained, and the reactions can be utilized for polymerization, such as the carbonylative polymerization of aryl dichlorides with aromatic diamines to form aramides [3]. These reactions are very sensitive to chelate size, allowing control of reactivity and selectivity. For example, whereas $(dippb)_2Pd$ catalyzes the Heck reaction under the normal basic condition [2e], $(dippp)_2Pd$ catalyzes this reaction under reductive rather than basic conditions [2f]. The origin of the chelate effect has been elucidated [1b].

Recently, in collaboration with the groups of Blum and Schumann, another unique catalytic feature of $(dippp)_2Pd$ was observed, namely, the selective alkylation of aryl chlorides in the presence of aryl bromides (e.g., eq. 1) [4]. The alkylation reagents are stabilized aluminum- and gallium-alkyls, which were developed by Schumann.



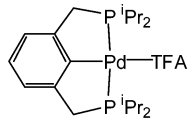
(1)

Since bromobenzene oxidative addition to $(dippp)_2Pd$ is faster than that of chlorobenzene, the selective alkylation of the chloro compound is explained by a reversible oxidative addition step under the catalysis conditions followed by a rate-determining transmetallation step. The latter may be favored with aryl chlorides as a result of a more stable 4-centered transition state involving Al···Cl bonding as compared with Al···Br.

For completeness we mention the first examples of homogeneously catalyzed activation of C–F bonds that we have developed several years ago, including hydrosilation [5a] and hydrogenolysis [5b] of hexafluoro- and pentafluorobenzene. The reactions are catalyzed by electron rich Rh(I) hydride and silyl complexes and are regioselective (with pentafluorobenzene). The mechanism was described in detail, including demonstration of each of the individual stoichiometric reactions, which is involved in the cycles. The C–F activation step involves most likely electron transfer from Rh(I) to the fluoroarene.

HECK CATALYSIS WITH PINCER PCP-PALLADIUM COMPLEXES. A NON-Pd(0) MECHANISM?

We discovered that the PCP-Pd(II) complexes **2**,**3** are excellent catalysts for Heck reactions of aryl bromides and iodides, leading to very large turnover numbers [7].



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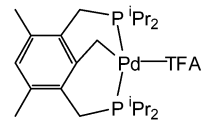

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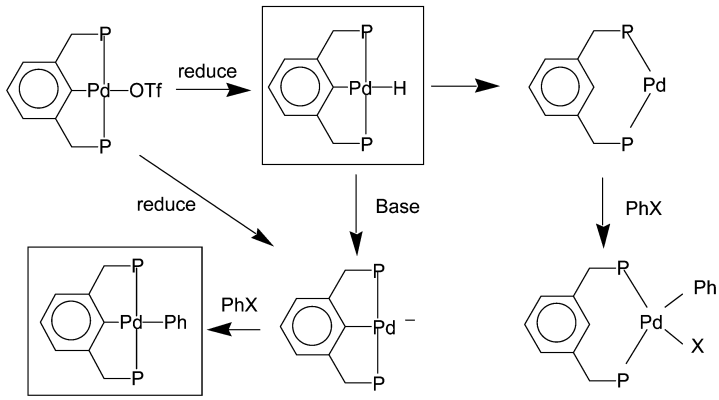
Since then, other pincer-type catalysts for this reaction have been reported. The catalysts are very stable and can function even at high temperatures, being recovered unchanged after the catalysis (except for anion exchange). Excellent catalysts based on Pd(II) complexes of metallated monophosphines were reported previously [6]. An intriguing issue is the mechanism of these reactions. Is the traditional Pd(0)/Pd(II) mechanism operative in these systems? For the metallated monophosphine complexes, this is proposed to be the case, the metallated complex being reduced to the active Pd(0) complex [8]. In contrast, we believe that the very stable, double chelated PCP-Pd complexes do not get reduced and that a non-Pd(0) mechanism is operative, possibly a Pd(II)/Pd(IV) mechanism, which was shown computationally to be feasible [9]. This is based on the following (admittedly nonconclusive) considerations. Possible modes of a Pd(0)-based mechanism with PCP-Pd, shown in Scheme 1, can be excluded.



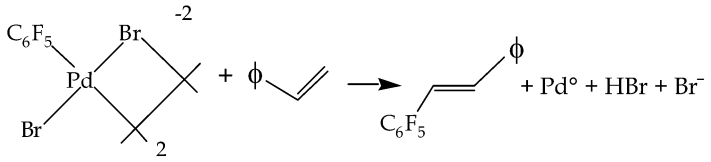
Scheme 1

PCP-Pd-H and PCP-Pd-Ph were prepared separately. The PCP-Pd-H reacts with iodobenzene to yield benzene exclusively, whereas not even traces of benzene are formed in the catalysis. PCP-Pd-Ph does not react with methyl acrylate, indicating that it is not the species undergoing insertion in the catalysis. The $\rho = 1.39$ obtained from a Hammett plot indicates that the aryl halide oxidative addition step, for which a much higher value is normally expected [1], is unlikely to be rate-determining. These observations are strongly indicative of, although they do not prove, a non-Pd(0) mechanism. Additional support for a non-Pd(0)/Pd(II) mechanism stems from the report that diene substrates or additives severely retard the catalysis by PCP-Pd, whereas traditional Heck catalysts are not adversely affected [10]. In general, we believe that a Pd(II)/Pd(IV) mechanism is quite reasonable in cases where the oxidative addition is not rate-determining. Actually, the alkene insertion step might be easier with Pd(IV) than Pd(II), due to lower back bonding to the coordinated alkene in the former case.

In addition to the PCP-type catalysts, we found that simple metallated imine Pd(II) complexes are extremely active catalysts for Heck [11a] and Suzuki [11b] reactions, although in that case the mechanism might involve generation of Pd(0).

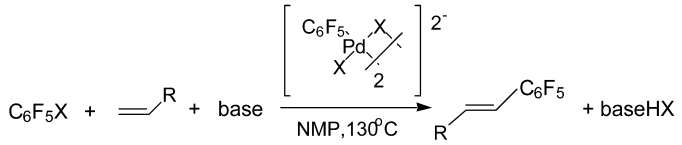
HECK CATALYSIS OF PERFLUORO-ARYL HALIDES

Insertion reactions into Rf-M (Rf = perfluoro-aryl or -alkyl) are very rare. Espinet reported such an insertion reaction (eq. 2) [12].



(2)

In collaboration with the group of Espinet, we have developed this stoichiometric reaction into catalysis of Heck reaction of perfluoroaryl halides (eq. 3) [13].



(3)

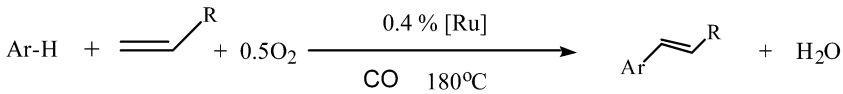
Mechanistic studies indicate that the reaction does not involve radical intermediates and that alkene coordination/insertion is rate-determining. An intuitively surprising, but on second thought, expected result is the observation that the Heck catalysis is significantly more facile with C_6F_5Br than with C_6F_5I. Alkene coordination is expected to be more difficult (for steric reasons) with the iodo complex. Indeed, reaction of styrene with the bromo palladium dimer is faster than that of the iodo analog [12].

Again, we see here an example of a selective catalytic reaction of aryl halides in which the common reactivity order of ArI > ArBr > ArCl is not followed.

OXIDATIVE COUPLING OF ARENES AND ALKENES USING O_2

Catalytic oxidative coupling of arenes with alkenes to give aryl alkenes is a highly desirable goal. Such a reaction, which does not require the utilization of a reactive substituent, and does not produce waste, may have an advantage over other methods for the preparation of aromatic alkenes, such as the well-known Heck reaction. Pd(II)-catalyzed coupling of olefins with arenes using various oxidants, mostly peroxides, is well known [14]. However, the use of peroxides and acetic acid solvent in these systems is problematic from the industrial standpoint.

We have discovered an oxidative coupling of arenes with olefins, in which O_2 can be directly used and good catalytic activity is obtained [15]. The reaction is catalyzed by Ru complexes and is facilitated by the presence of a CO atmosphere. Typical precatalysts are $[Ru(CO)_3Cl_2]_2$, $[(\eta^6\text{-}C_6H_6)RuCl_2]_2$, and $Ru(F_3CCOCHCOCF_3)_3$. Notably, the dehydrogenative coupling proceeds either under O_2 (eq. 4) or in an inert atmosphere (eq. 5). In the absence of O_2, the olefin itself serves as an oxidant, yielding the corresponding alkane. Various arenes undergo this reaction, and alkyl acrylates are the most active of the olefins tested.



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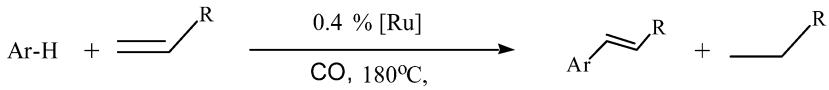
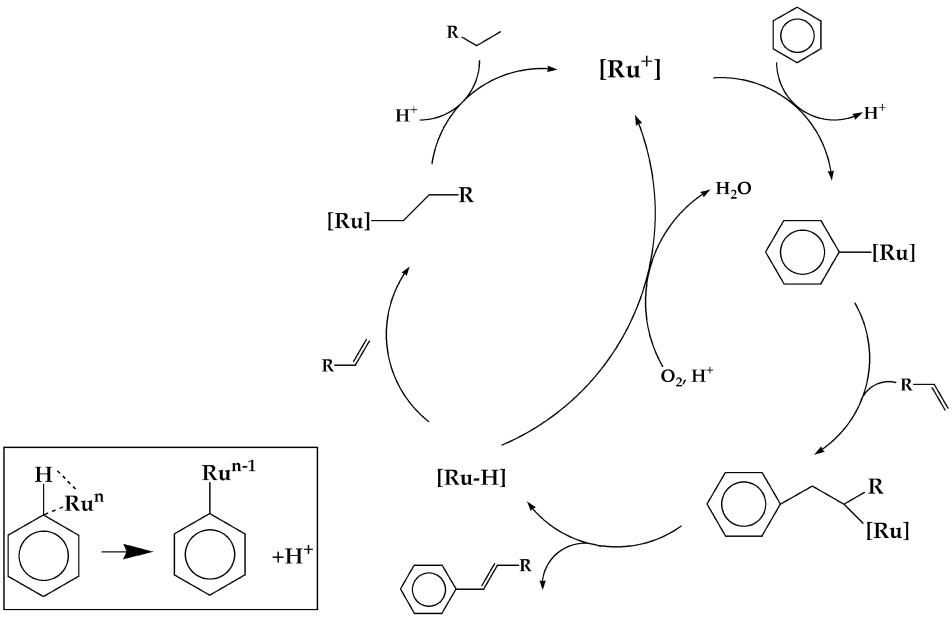


(5)

Participation of radical chain mechanisms or catalysis by metallic ruthenium was excluded. The reaction rate exhibits first-order dependence on the acrylate concentration under pseudo-first-order conditions. A kinetic isotope effect of $k_H/k_D = 2$ was measured in the reaction with methyl acrylate with C_6D_6. The reaction is mildly accelerated by electron-donating substituents on the arene ($\rho = -1.16$ for σ_p). Notably, substituent directive effects are not observed in the reaction, and an almost statistical dis-

tribution of the *para* and *meta* products are obtained. The lack of directive effects and the low ρ value suggest an electrophilic aromatic metallation mechanism, which does not involve the arene π system. One possibility is a mechanism involving deprotonation of an η^2 arene C–H bond, as demonstrated by us in the case of rhodium complexes [16].

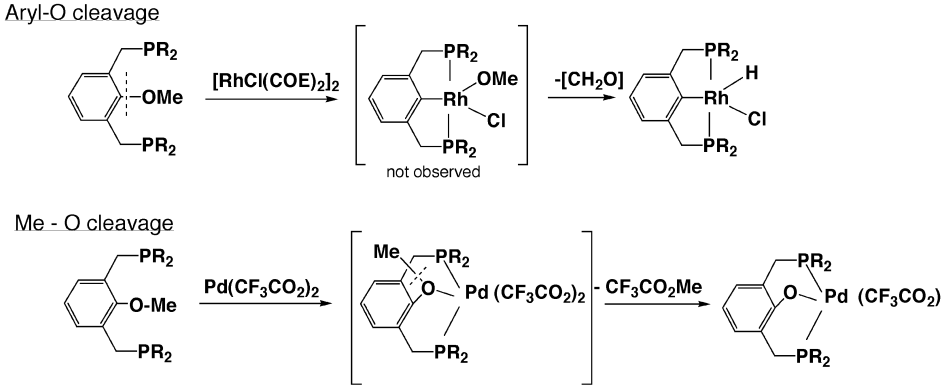
While the mechanism of the reaction is unclear, the following steps are plausible (Scheme 2); (a) electrophilic attack of the metal on a C–H bond to give a Ar-[Ru] species; (b) olefin insertion; (c) β-H elimination to yield an aromatic alkene and a Ru-H; (d) catalyst regeneration by olefin insertion into Ru-H followed by protonation (in inert atmosphere), or by oxidation when O_2 is present. CO may be required for generation and stabilization of the Ru electrophile.



Scheme 2

C–O ACTIVATION

Using a methoxy-substituted PCP system, we have observed that the C–O bonds of an aryl-O-Me system can be specifically targeted by choice of metal (Scheme 3) [17].



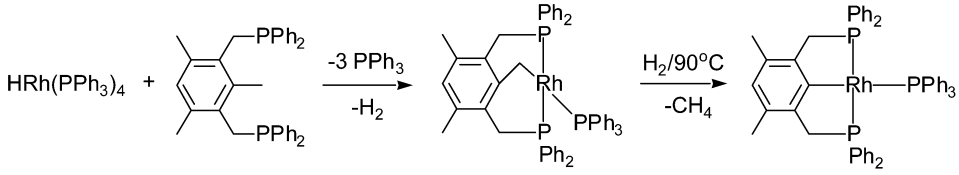
Scheme 3

Rh(I) inserts into an aryl-O bond, and Pd(II) into an alkyl-O. This is a reflection of the different mechanisms operating in these cases, a Lewis acid-type mechanism with the Pd(II) complex and a concerted oxidative addition with Rh(I). Metal complex insertion into an aryl-O bond was unprecedented prior to this work. Chelate-assisted catalytic hydrogenolysis of an amine C–N bond by rhodium was also observed [18].

C–C ACTIVATION

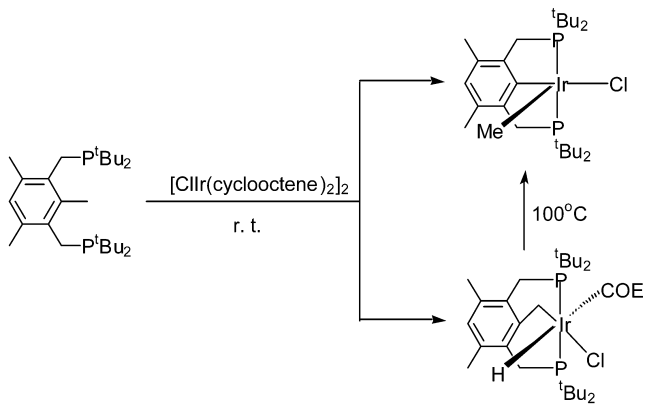
Whereas the field of C–H activation is quite developed, much less is known about the activation of strong C–C bonds. Several factors, mainly kinetic in nature, favor C–H over C–C bond activation, including the generally easier approach of the metal center to C–H bonds, their statistical abundance, and a substantially higher activation barrier for C–C vs. C–H oxidative addition due to the more directed nature of the C–C bond.

Most of the examples of C–C activation are driven by strain, by aromatization of prearomatic systems, or by the presence of a carbonyl group [19]. We have utilized PCP, PCN, and PCO-type pincer ligands in order to explore the possibility of activation of strong C–C bonds by directing the metal at them. The first example of metal insertion into an unstrained, unactivated C–C bond in solution was demonstrated using $HRh(PPh_3)_4$ [20]. Reaction of the metal complex with the *Ph*-PCP ligand (eq. 6) at room temperature resulted in H_2 elimination and formation of the kinetic C–H activation product. Reversal of the C–H activation process by heating of this product under mild hydrogen pressure, resulted in quantitative C–C cleavage and methane elimination, which provided the thermodynamic driving force for the process.



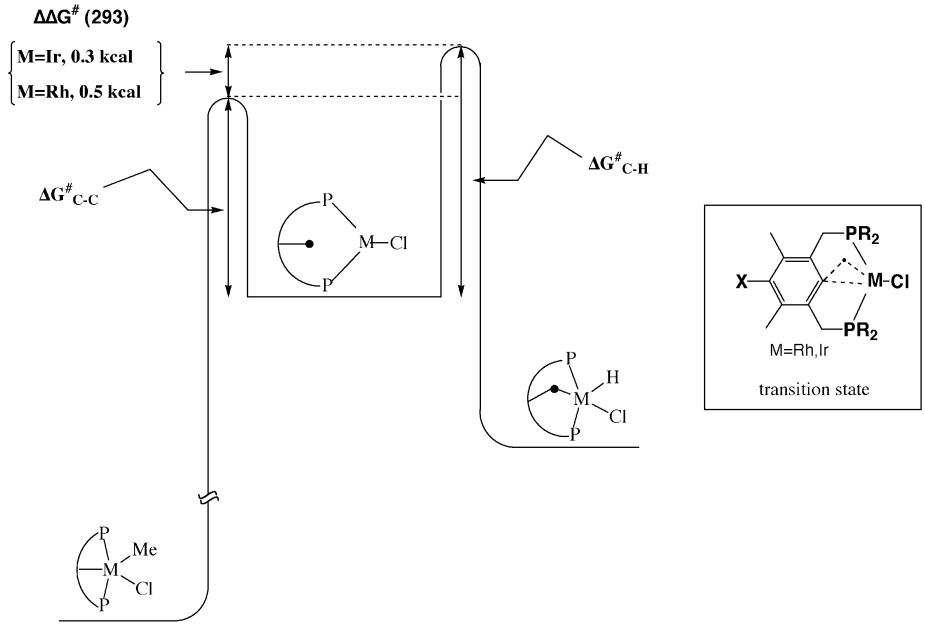
(6)

C–C activation is very sensitive to the nature of the substrate. Utilizing *Me*-PCP instead of *Ph*-PCP, the direct *Rh(I) insertion into C–C becomes thermodynamically favorable and, moreover, it is more favorable than insertion into C–H*, although 150 °C is required for the process [21]. Reaction of the bulky *t*-Bu-PCP ligand with rhodium and iridium olefin dimers at *room temperature* led to concurrent C–H and C–C activation. The C–H activation product quantitatively converted into the C–C activation product slowly at room temperature in the case of rhodium, or upon heating in the case of iridium (Scheme 4) [22].



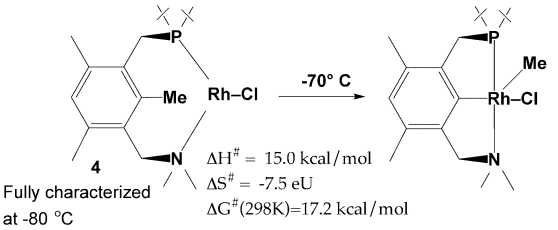
Scheme 4

Thus, iridium and rhodium insertion into the C–C bond is *thermodynamically more favorable* than its insertion into the C–H bond, as observed in the Me-PCP system. Both the C–C and C–H activation processes were shown to proceed through a common (unobserved) intermediate with the two phosphine arms coordinated to the metal center. Surprisingly, the kinetic barrier of C–C oxidative addition is slightly lower than that of C–H (Scheme 5). The similarity of the activation parameters for C–C and C–H activation processes and the fact that they are not much affected by variation in solvent polarity or by the use of *para*-substituted derivatives of the *t*-Bu-PCP ligand, indicates that *similar nonpolar transition states* are involved in both processes. The lack of substituent effect also suggests that a η^2-arene complex is not involved in the C–C activation process. Thus, the C–C bond oxidative addition in our system most probably proceeds through *a three-center nonpolar transition state similar to the one postulated for aliphatic C–H bond activation*.



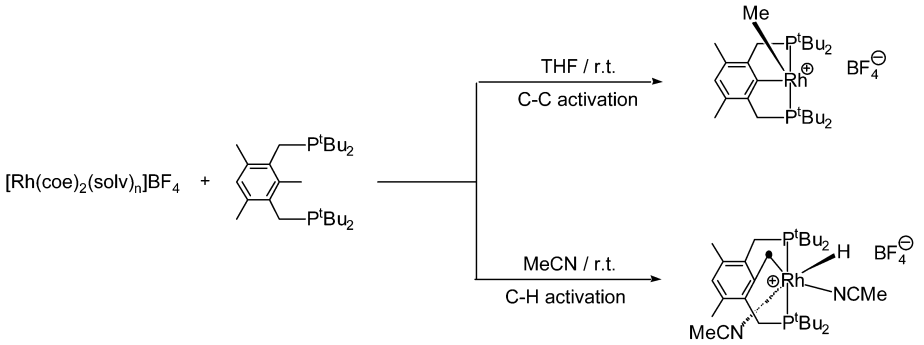
Scheme 5

Unique preference for C–C activation was demonstrated with the PCN system [23]. Upon reaction of a PCN ligand with rhodium cyclooctene dimer at room temperature or below, exclusive C–C activation took place and no C–H activation products were observed. We believe that this is due to a more favorable orientation of the metal vis-à-vis the C–C bond in this system. Remarkably, C–C activation was observed here even at –70 °C. This has enabled the observation and full spectroscopic characterization at –80 °C of the actual intermediate that undergoes the metal insertion process, complex **4** (eq. 7) [23b]. It is a chelated 14e complex, which contains no coordinated solvent molecules. Using the $^{13}CH_3$-labeled complex, we have observed no interaction between the methyl group and the metal. Kinetic studies at various temperatures have led to the activation parameters $\Delta H^{\#}$ = 14.99 kcal/mol, $\Delta S^{\#}$ = –7.45 eU and $\Delta G^{\#}$ (298) = 17.21 kcal/mol, which are compatible with a concerted oxidative addition mechanism of the C–C bond cleavage and establish that the activation barrier for this single step process in a preorganized system is quite low and enthalpy-controlled. This study represents the first direct observation and kinetic evaluation of metal insertion into a strong C–C bond.



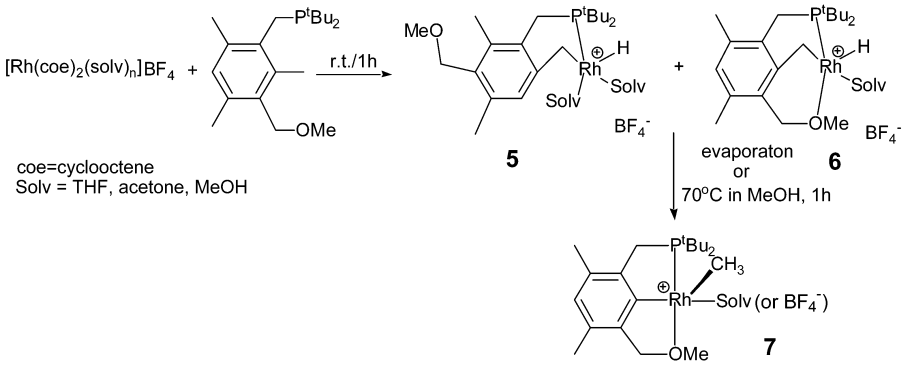
(7)

We have described so far C–C activation by *neutral* Rh and Ir complexes. Utilizing a *cationic* PCP rhodium system, we have observed that the reaction can be driven toward the *exclusive* activation of C–C or C–H bond at room temperature by *solvent choice* (Scheme 6) [24]. This remarkable selectivity is explained in terms of the different coordination abilities of the solvent molecules. The C–C activation process, which is sterically more demanding than the C–H one, is preferred in the case of the less coordinating THF, whereas in acetonitrile the active cationic intermediate is likely to be sterically more encumbered because of coordinated nitrile molecules and as a result it undergoes C–H activation. The observed products are both the kinetic and thermodynamic ones in the employed solvents. This unique selectivity, together with the reversible interconversion of C–C and C–H activation products by solely varying the reaction solvent, indicates that a remarkable degree of control over metal insertion into strong C–H vs. C–C bonds is possible.



Scheme 6

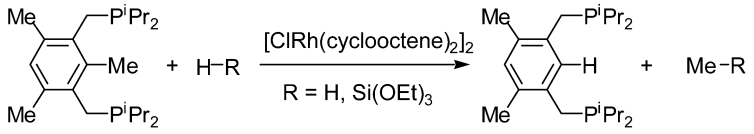
More understanding of the factors that control C–C vs. C–H activation was gained by studying the new PCO ligand system (Scheme 7) [25]. Reaction with the cationic Rh(I) precursor at room temperature results in two kinetically favored C–H activation products **5** and **6**. Upon heating these products at 70 °C, the thermodynamically favored C–C activation takes place. Interestingly, solvent evaporation under vacuum at room temperature also results in C–C activation. This is a result of stabilization of the C–C activated product **7** by BF_4^- coordination, as shown by X-ray, whereas coordination of the anion to the C–H activation product is less favorable. Our studies clearly show that the methoxy moiety, although being a relatively weak ligand, plays a critical role in the C–C bond activation process. This demonstrates the fundamental importance of a high degree of order for C–C activation. Theoretical calculations by Martin have shown that cationic 14-electron Rh(I) complexes are key intermediates in both C–H and C–C activation and that the chelating effect facilitates C–C activation both kinetically and thermodynamically. A comparison of the transition states for C–C and C–H activation indicates that specific steric requirements are important for achieving metal insertion into the C–C bond. Another significant finding is that coordination of solvent molecules (e.g., methanol) to the cationic Rh(I) center significantly lowers the kinetic barrier of C–H as well as C–C activation.



Scheme 7

Other aryl-C bonds can also be activated. When the CH_3 group between the phosphine arms of the *t*-Bu-PCP ligand is changed for CF_3, selective oxidative addition of the very strong Ar-CF_3 takes place in the reaction of the ligand with Rh(I). No $ArCF_2$-F activation product was observed [26]. With a PCP ligand containing an Ar-Et group, only sp^3-sp^2 C–C activation was observed [27].

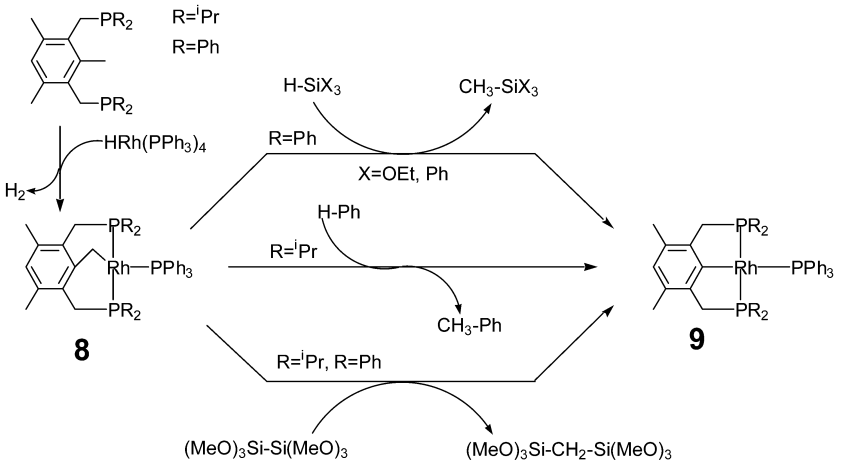
The first example of *catalytic* cleavage of an unstrained, strong Ar-C bond by a metal complex in solution was obtained using a PCP-type substrate and Rh(I) catalyst, with hydrogen or silanes (eq. 8). More than 100 turnovers were observed in the case of H_2, and a mechanism was proposed [28].



(8)

METHYLENE TRANSFER

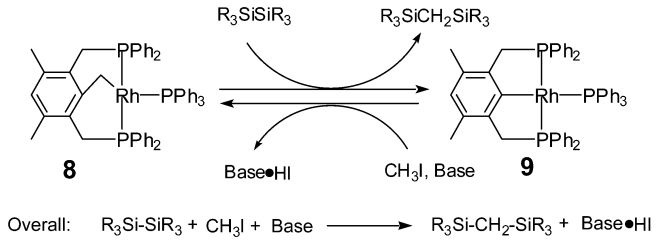
An interesting development of the C–C activation work is *the methylene transfer reaction*. If the C–C inserted metal center is capable of binding and activating additional substrates, the result could be selective insertion of the CH_2 group into another chemical bond. Indeed, the methylene group in the "methylene-bridged" complexes **8** can be abstracted not only by H_2 but by a variety of reagents. The CH_2 group was inserted into Si–H, Si–Si, and aromatic C–H bonds (Scheme 8) [29], representing a con-



Scheme 8

ceptually new process in organometallic chemistry and an unusual combination of reactions involving C–C cleavage, methylene transfer, and selective incorporation into other bonds.

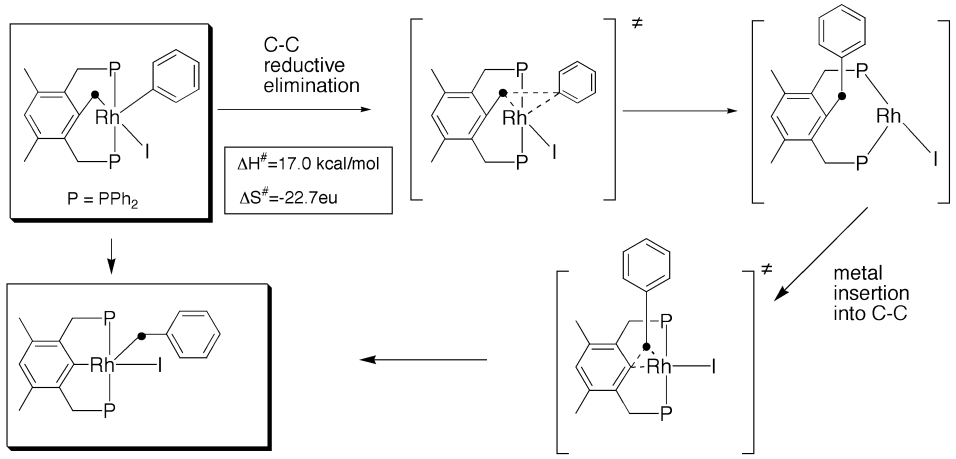
Interestingly, the methylene group can be regenerated by treatment of the "methylene-depleted" complex **9** with methyl iodide and a base, representing a two-step process in which a CH_2 group is extruded from MeI and selectively incorporated into a Si–Si bond (Scheme 9).



Scheme 9

A possible mechanism for the methylene group transfer involves substrate oxidative addition, C–C bond cleavage by a three-coordinate Rh(I) species, and, finally, product release by reductive elimination.

We have recently observed an *intramolecular* methylene transfer process in which the transferred methylene moiety remains connected to the metal center, enabling the direct observation and characterization of several stages in the process, involving a unique combination of C–C reductive elimination and C–C cleavage reactions (Scheme 10) [29b]. The rate-determining step of this reaction is the C–C reductive elimination rather than the C–C activation step.



Scheme 10

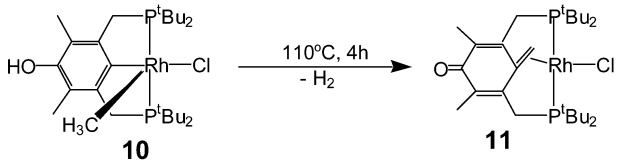
While the discussion in this review is limited to Rh and Ir complexes, we have observed C–C activation using PCP systems also with several other metals, including Pt(II) [30], Ru(II) [30b], and Os(II) [31].

METALLAQUINONOIDS

PCP-quinone methide complexes

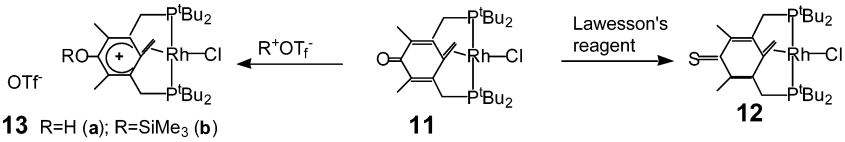
Our work on C–C activation has led to the discovery of an unusual family of compounds, the metallaquinonoids [32].

Using a phenol-type PCP ligand, C–C activation at room temperature leads to complex **10**. Unexpectedly, upon heating this complex at 110 °C, *hydrogen* is evolved and the quinone-methide complex **11** is formed [33]. The mechanism of this unusual reaction probably involves protonation of the metal at the vacant position *trans* to the methyl group followed by a 1,2 shift of the electrophilic methyl group to the arene. β-Hydride elimination would then lead to the quinone methide complex **11** (eq. 9).



10 **11** (9)

Quinone methides (QMs) (compounds in which one of the oxygen atoms of a quinone is replaced by a methylene or a substituted methylene group) are of much interest [34]. They are involved in the biosynthesis of the natural polymers melanin and lignin, and several antitumor drugs are believed to generate a QM moiety as the active form. However, QMs are very unstable due to aromatization to the zwitterionic compound, which is capable of self-condensation or reactions with electrophiles and nucleophiles. So far, no "simple" QM was isolated except when the QM moiety is part of a fused aromatic system with little contribution of the QM form. The stability of **11** is due to formation of a strong metal–olefin bond even at the expense of loss of aromaticity. Due to this stability, selective modification of both the metal center and the carbonyl part of the molecule are possible, with no aromatization taking place. For example, using Lawesson's reagent, the carbonyl oxygen was replaced with sulfur [33], yielding the *first* thioquinone methide **12** (Scheme 11).



13 R=H (**a**); R=SiMe$_3$ (**b**) **11** **12**

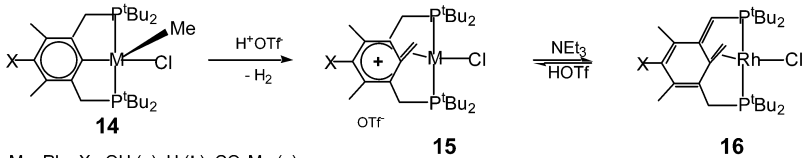
Scheme 11

Methylene arenium metal complexes

Interestingly, reaction of the red QM complex **11** with strong electrophiles (HOTf, Me_3SiOTf) leads to the green methylene arenium complexes **13** (Scheme 11) [35]. The crystal structure of **13a** and its spectroscopic properties clearly indicate that it is an unprecedented example of the methylene arenium form of a benzyl cation stabilized by complexation.

Remarkably, the drive to form these complexes is very high, even at the expense of aromaticity. Thus, when the methyl rhodium complexes **14** (as well as the iridium complex **14e**) were reacted with a slight excess of triflic acid, hydrogen (not the expected methane!) was evolved and the green methylene arenium complexes **15** were formed in quantitative yields (Scheme 12) [36]. The proposed mechanism of this process, supported by kinetic studies, involves the formation of the corresponding M(V) intermediate (by protonation *trans* to the apical methyl group), which then undergoes C–C reductive elimination, followed by β-hydrogen elimination and evolution of H_2. This procedure yielded a series of methylene arenium complexes having various substituents *para* to the *ipso*-carbon. Interestingly, the methylene arenium complexes are stable even in the absence of stabilizing substituents on the arenium moiety. As a result of localization of the positive charge inside the ring, the rhodium complexes **15b**,**c** are strong C–H acids and are deprotonated with weak bases such as NEt_3 to give xylylene complexes **16** [36].

A stable difluoromethylene arenium complex was formed by C–C activation of an aryl-CF_3 PCP ligand followed by fluoride abstraction with a Lewis acid [26a].

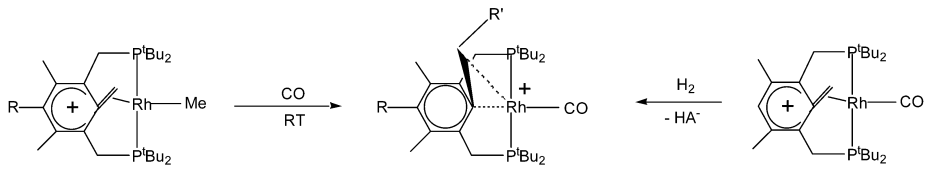


Scheme 12

It is noteworthy that the methylene arenium form is clearly preferred over the benzylic Rh(III) form in which the positive charge is localized at the metal center. This occurs at the expense of aromaticity in the latter form, even when electron-withdrawing substituents are present on the ring.

σ-Arenium vs. agostic metal complexes. Relevance to electrophilic bond activation

Reactions at the metal center can lead to aromatization. Migratory insertion reactions of hydride [36] and alkyl [37] ligands in carbonyl Rh(I) complexes give the corresponding aromatic compounds **17** (Scheme 13). The formulation of **17** as cationic agostic C–C rather than s-arenium complexes is clearly evident from ^{13}C NMR and single crystal X-ray analyses. This can be compared with a diamino pincer platinum complex for which an arenium structure was reported [38].

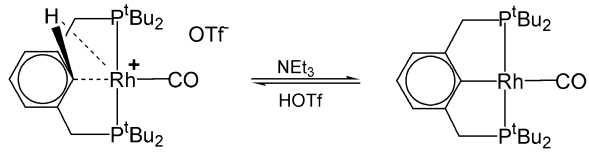


Scheme 13

The C–C agostic complex **17a** was obtained also upon reaction of the corresponding ligand with $[Rh(C_2H_4)CO(solv)_x]^+$. C–C activation was not observed since the $[RhCO]^+$ center is too electron poor to overcome the thermodynamic barrier for this process. **17** can be viewed as an "arrested" transition state towards C–C cleavage.

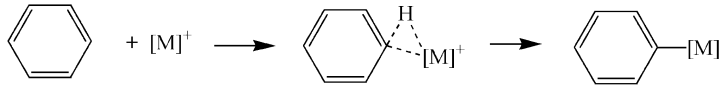
A similar reaction with a ligand, which has an *ipso*-C–H, resulted in the C–H agostic complex **18** (Scheme 14) [16]. Multinuclear NMR data and an X-ray structure indicate a strong interaction between the metal center and the C–H bond, while there is negligible contribution, if any, of the σ-arenium form. Similar results were obtained with an analogous ligand containing methoxy substituents at the *p*- and *m*-positions, showing no significant substituent effect on the spectroscopic properties. Had there been positive charge localized in the aromatic ring even to a minor extent, a large difference between the two systems would have been expected. Density functional calculations, performed by Martin, fully confirmed the agostic representation. The agostic proton in **18** is highly acidic, and it undergoes slow exchange with excess D_2O. It can be easily deprotonated by weak organic bases (NEt_3, collidine) to give **19** (Scheme 14).

The observed reactivity of an aromatic C–H agostic complex is relevant to the mechanism of C–H activation of aromatic compounds, indicating that an agostic pathway (eq. 10) can be considered as an alternative to the traditional electrophilic substitution. As shown here, there is no need for substantial positive charge transfer from the metal to the aromatic ring in order to achieve "electrophilic-like" reactivity [16].



18 **19**

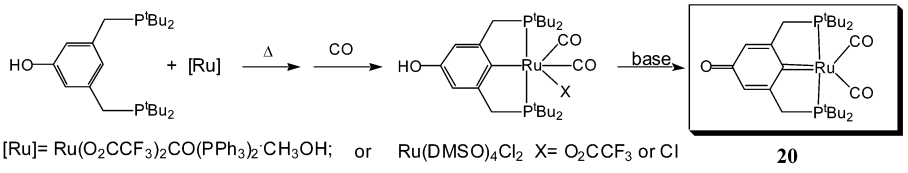
Scheme 14



(10)

Discovery of a metallaquinone

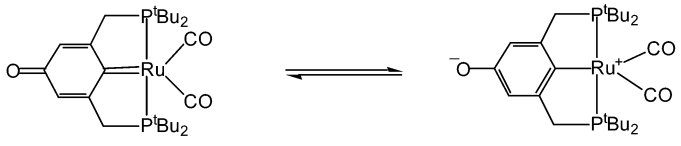
Despite the importance of quinonoid compounds, especially in biology and materials science, a metallaquinone molecule, i.e., a quinone molecule where one of the oxygens is replaced by a metal, was unknown prior to our studies. Scheme 15 oulines the synthetic pathway to the desired ruthenaquinone **20** [39].



Scheme 15

Interestingly, complex **20** is solvatochromic, being red-orange in the relatively nonpolar benzene and THF and yellow in methanol. While NMR and IR signals indicate a quinonoid system in THF or in benzene, as well as in the solid state, those signals are absent in methanol or acetone solutions. This is a result of the presence of the neutral Ru(0) metallaquinone form in nonpolar solvents and its zwitterionic Ru(II) form in polar ones (eq. 11). Thus, the metal oxidation state is solvent dependent.

DFT studies, performed by Martin, demonstrated that the metallaquinone structure is the most stable in the gas phase as well. The theoretically predicted IR spectrum of the ruthenaquinone matched well the experimental data. The electronic absorption in the visible range is assigned to an excitation from the Ru=C π-HOMO into the ring π-LUMO. Calculations show that distortion of the quinonic form to the zwitterionic form requires about 13 kcal/mol. The interesting properties of metallaquinones might open new directions in the chemistry of the quinonoid compounds, with relevance to catalysis and materials science.



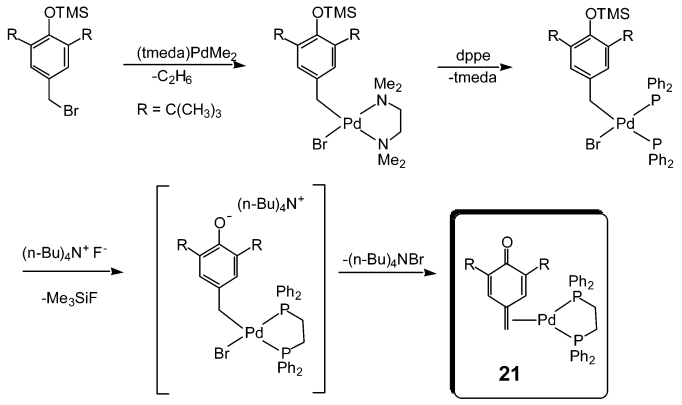
Benzene of THF Methanol or Acetone

(11)

Intermolecular quinone methide complexes

In continuation of our work on quinone methides, we prepared complexes where the p-QM moiety is *not part of the ligand system*, allowing both stabilization and controlled QM release [40]. We chose the QM derived from 2,6-di-*t*-butyl-4-methylphenol (butylated hydroxytoluene, BHT). BHT is widely used

as an industrial antioxidant to prevent deterioration of food products, and the toxicological effects of its metabolite, the quinone methide derivative BHT-QM, are of great interest. Scheme 16 outlines the synthesis of a Pd-stabilized, X-ray structurally characterized BHT-QM **21**.



Scheme 16

Complex **21** is thermally stable. It is stable even in wet methanol. Free BHT-QM would have reacted immediately with the solvent were there any dissociation equilibria of the QM. Significantly, controlled release of BHT-QM can be achieved by reaction of **21** with the electron-deficient alkene dibenzylideneacetone (DBA) resulting in clean formation of the corresponding $P_2Pd(DBA)$ complex. The unstable free BHT-QM was detected in a C_6D_6 solution by ^1H NMR immediately after its release. Substitution of the QM by DBA in methanol resulted in immediate trapping of the free QM with formation of 2,6-di-*t*-butyl-4-methoxymethylphenol. This demonstrated, for the first time, that controlled release of free QM from the metal into solution, where it is effectively trapped by nucleophiles, could be achieved. A similar approach has led to the synthesis of a stable complex of the simplest, elusive *para*-quinone methide, showing that the concept is general and practically any simple *p*-QM can be generated at the metal center [40b].

CONCLUDING REMARKS

This overview highlights the importance of fundamental understanding of bond activation in the design of new catalysis, in the generation of unprecedented structures, and in the stabilization of biologically active organic transients. Much understanding of the factors controlling bond activation has been obtained from the design of appropriate model systems. While this review is limited mainly to the activation of C–X bonds, we are also studying the activation of other bonds, such as O–H and N–H bonds, hoping to obtain insight that might lay the basis to interesting new stoichiometric and catalytic reactions.

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