Our Deepest Condolences

At the end of July, 2008, Professor Keith Fagnou graciously accepted our invitation to author a Highlight Review in *Chemistry Letters* during his first stay in Kyoto. We received the following e-mail from him just before the deadline.

> *'I have chosen to review the different mechanisms that metals may cleave aromatic C–H bonds with a focus on those leading to successful catalysis. My hope is that this will be a very timely review and may inspire others in the catalysis.'*

Sadly, he passed away unexpectedly on November 11, 2009.

We then contacted one of his students responsible for the review as a coauthor and finally realized the completeness of the manuscript.

We are truly saddened by the loss of this tremendously talented rising star in Chemistry, and we dedicate the Highlight Review of this issue to his family, students, and all readers on the first anniversary of his passing.

Prof. Toshiaki Murai
Associate Editor of Chemistry Letters

Prof. Tamejiro Hiyama
Editor-in-Chief of Chemistry Letters

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Highlight Review

Overview of the Mechanistic Work on the Concerted Metallation–Deprotonation Pathway

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Abstract

The cleavage of aromatic C–H bonds promoted by a metal and an intramolecular base has been described over 50 years ago. Herein, discussion of selected mechanistic studies of this transformation will be presented. The basic ligand on the metal was proven to play a pivotal role in the C–H bond cleavage step and evidence of a single operative concerted metallation–deprotonation mechanism unifies the different mechanistic studies.

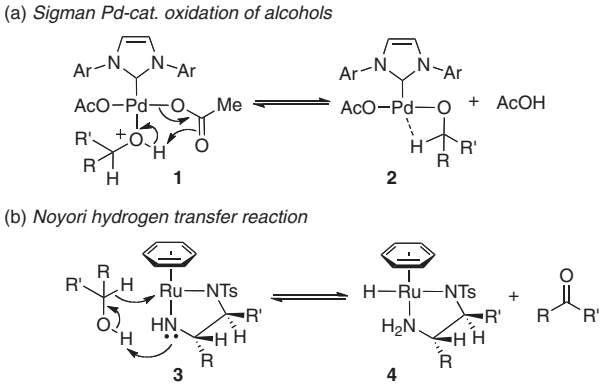
♦ Introduction

The direct functionalization of C–H bonds with transition-metal complexes has emerged in the past years as an economical and efficient alternative to the use of traditional activating-groups for the functionalization of (hetero)arenes.[1] Many mechanisms have been studied or proposed for the cleavage of C–H bonds such as oxidative addition and σ bond metathesis,[2] however, this highlight will be focusing on metal/base-promoted cleavage of aromatic C–H bonds (Scheme 1). Both experimental and theoretical studies on the various mechanisms will be covered, with an emphasis on catalytic transformations. Our hope is that this highlight will be a useful resource to understand the reaction mechanism and inspire others to further improve and extend the breadth of this transformation.

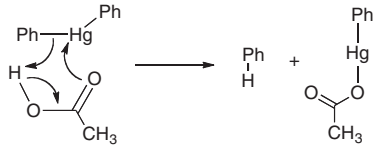
♦ Example of Deprotonation

The implication of both a metal and a base in the abstraction of a proton in an intramolecular fashion is a known process. For example, in the palladium-catalyzed oxidation of alcohol, Sigman proposed that the alcohol is deprotonated by the acetate ligand to become an X ligand and that the decomplexation of the acetic acid ligand frees a coordination site on the metal (**2**) to permit the subsequent oxidation step to occur (Scheme 2a).[3] With Noyori's ruthenium(II)-catalyzed hydrogen transfer between alcohols and ketones, it was proposed that the amido complex **3** abstracted the alcohol proton and a hydride is transferred to the metal, resulting in the formation of ruthenium(II)–hydride complex **4** (Scheme 2b).[4] With the recent development of transition-metal-catalyzed functionalizations of simple aromatic rings and alkanes,[5] C–H bond cleavage has been proposed to occur by a simultaneous metallation and

Scheme 1. Metal/base-promoted C–H bond functionalization.



Scheme 2. Examples of internal deprotonation reactions.



Scheme 3. Representation of the mechanism proposed in 1955 for the acetolysis of diphenylmercury(II).

intramolecular deprotonation mechanism. For consistency, we have chosen in this highlight to refer to this mechanism as a concerted metallation–deprotonation (CMD), although some authors have used other names such as internal electrophilic substitution (IES)[6] and ambiphilic metal–ligand activation (AMLA).[2b,7]

♦ Early Evidences of the Concerted Metallation–Deprotonation Pathway

To the best of our knowledge, the earliest proposal of a CMD mechanism was made by Winstein and Traylor in 1955 for the acetolysis of diphenylmercury in acetic acid (Scheme 3).[8] Interestingly, before Roberts and co-workers published an

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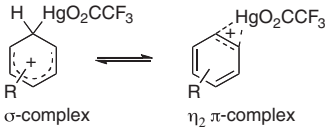


Scheme 4. Olah's description of the arene mercurium ion intermediate complexes.

elegant mechanistic study on the subject,[9] there were no in-depth kinetic studies performed on the mechanism of the mercuration of simple arenes. Earlier mechanistic proposals suggested an S_EAr mechanism based on the electrophilic character of mercury.[10] The rate law derived from these kinetic analyses of the mercuration of benzene (eq 2) showed that the arene and the electrophilic mercuric salt combined rapidly and reversibly to form an intermediate, followed by an irreversible proton transfer yielding the final product (eq 1). Based on large observed primary kinetic isotope effects (KIEs) (ca. 6.0–7.0), the proton transfer step was determined to be rate limiting.[11]

The structure of the intermediate was initially assumed to be a σ-complex, but in 1976, Olah and co-workers studied the nature of this intermediate by NMR spectroscopy and concluded that the species formed was a weakly bonded complex, which he proposed to be rapidly exchanging σ-complex and η_2 π-complex (Scheme 4).[12]

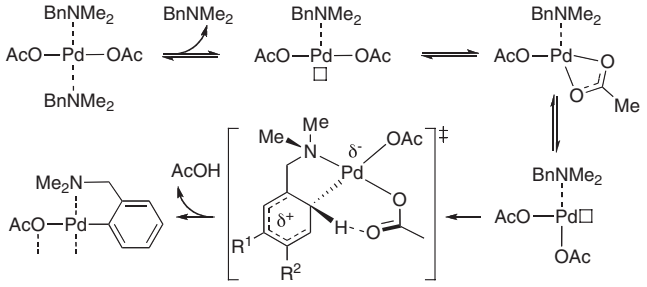
$$HgX_2 + ArH \overset{K_1}{\rightleftharpoons} Int \overset{k_2}{\rightarrow} ArHgX + HX \quad (1)$$

$$k_{obs} = \frac{k_2 K_1 [ArH]}{1 + K_1 [ArH]} \quad (2)$$

Roberts and co-workers isolated equilibrium constant (K_1) and rate constant (k_2) values and observed rates (k_{obs}) from the rate law (eq 2), in order to examine the two steps individualy.[9] They showed that the intermediate was indeed a π complex rather than a σ complex, based on the experimental free energy of formation. In the second step of the reaction (k_2, eq 1), the discrete KIEs of the reaction indicated that the C–H bond was cleaved at that step. The negative $\Delta S^{\ddagger}$ for the second step corresponded to a very organized transition state while the reaction exhibited no rate enhancement upon the addition of base, suggesting that an intramolecular proton transfer was occurring. This data was consistent with a simultaneous C–H bond cleavage and a C–Hg bond formation mechanism as proposed by Winstein and Traylor in 1955, although Roberts could not completely rule out the S_EAr mechanism.

♦ *Directed Metallation of Arenes*

In the seminal publication on palladium-catalyzed formation of biphenyl in 1968, Davidson and Triggs recognized the strong resemblance that existed between the palladation and mercuration of benzene.[13] The first types of palladation reactions that were studied in detail were cyclometallation reactions, mainly using nitrogen-based ligands to direct the reaction.[14] The initial mechanistic studies were performed soon after their discovery in the 1960's.[15] These studies established that the choice of palladium source was crucial for reactivity. It was found that palladium(II) acetate was generally the best source of palladium, since the acetato ligand is believed to play multiple roles in



Scheme 5. Mechanism of cyclometallation of DMBA-H with palladium.

cyclometallation reactions.[16] It facilitates the solvolysis of the reaction intermediates due to its larger effective volume compared to chloride. It also enhances the electrophilicity of the palladium(II) center due to the reversible ability of acetate to act as a bidentate or monodentate ligand, and potentially act as an intramolecular base for deprotonation.[16c]

One of the first detailed mechanistic studies on the reactivity of palladium toward C–H bonds was made by Ryabov and co-workers on the *ortho*-palladation of *N*,*N*-dimethylbenzylamine (DMBA-H).[17] An analysis of the reaction kinetics and the observation of certain reaction intermediates by NMR allowed for the establishment of the reaction profile (Scheme 5). The negative slope of the Hammett plot ($\rho = -1.6$) indicated that the palladium(II) had an electrophilic character. The KIE (k_H/k_D) of 2.2 and the negative calculated entropy of activation ($\Delta S^{\ddagger} = -60\,cal\,K^{-1}\,mol^{-1}$) of $Pd(OAc)_2$[DMBA-H] were suggestive of a highly ordered and compact transition state in which the leaving proton is abstracted intramolecularly by acetato ligand (Scheme 5).

Arguably, the way Ryabov depicted the transition state in Scheme 5 can be interpreted as the deprotonation of a Wheland intermediate although there is no mention in the paper of the formation of such an intermediate. Nonetheless, in a later mechanistic study on the cyclopalladation of primary benzylamines, Ryabov stated that "*the transition state of the* [*ortho*-palladation of *N*,*N*-dimethylbenzylamine] *process involved concerted formation of the palladium–carbon and cleavage of the C–H bond with a nucleophilic assistance by the coordinated acetate.*"[18] While this statement does not elude to the formation of a charged intermediate, Ryabov's proposed transition state likely took into account the development of a small positive character at the transition state, as suggested by the negative slope of the reaction's Hammett plot.

More recently, a computational study on the mechanism of a *N*,*N*-dimethylbenzylamine system was reported by Davies, Donald, and Macgregor.[19] The results showed that the most accessible route proceeds via an agostic C–H interaction (**6**, Figure 1) followed by an acetate-assisted six-membered cyclic transition state. The agostic interaction polarizes the C–H bond and results in an enhancement of the acidity of the *ortho*-proton, which can then be readily deprotonated by the acetate base.[20]

Hydrogen bonding between the acetate oxygen and proton orients the base for the C–H bond cleaving step and also increases the electron density of the C–H bond which in turn further favors the agostic interaction.[21] The combination of these effects leads to a nearly barrier-less proton transfer

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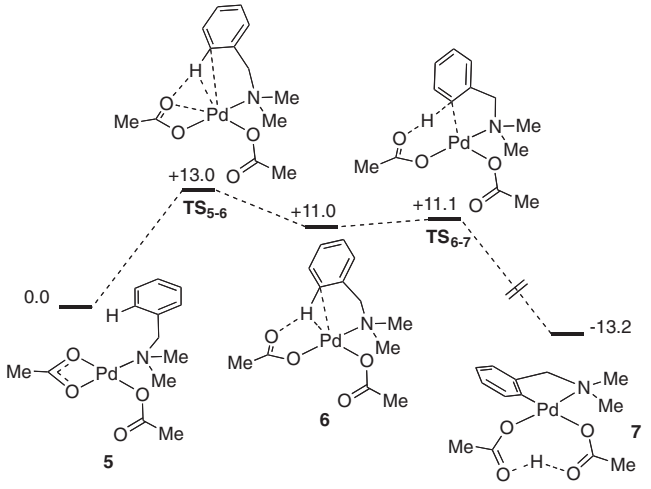


Figure 1. Computed reaction profile of DMBA-H with $Pd(OAc)_2$. Values in kcal mol^{-1}.

($\Delta E_A = +0.1$ kcal mol^{-1}) to yield the thermodynamically favorable palladacycle **7** (Figure 1). The calculated atomic charges for the species **5** to **7** showed very little if any evidence for the contribution of a Wheland intermediate. Also, the calculated KIE ($k_H/k_D = 1.2$) obtained with this mechanism does not contradict the experimental value found by Ryabov ($k_H/k_D = 2.2$).[17] In addition to palladium–acetate-promoted cyclometallation, Davies showed that other transition-metals, such as $[RuCl_2(p\text{-cymene})]_2$, $[RhCl_2Cp^*]_2$ and $[IrCl_2Cp^*]_2$, in combination with an acetate base reacted to form cyclometallated products by the same mechanism when reacted with *N*,*N*-dimethylbenzylamine.[7,22]

The mechanistic work of Roberts on the mercuration of benzene and Ryabov's work on the cyclometallation of benzylamine constitute the early examples of the CMD mechanism using stoichiometric amount of metal. In the following sections, the focus of the discussion will be directed toward catalytic transformations.

♦ *Directed Catalytic Functionalization of Arenes*

In recent years, the metal-catalyzed functionalization of unactivated arenes has become an increasingly viable alternative to classical cross-coupling reactions.[23] Electron-rich heteroarenes were the first systems to be studied in the context of catalytic transformations (vide infra). The first experimental mechanistic studies on the catalytic direct functionalization of simple arenes were mainly carried out by the groups of Echavarren[24] and Fagnou,[25] in their studies on the intramolecular formation of biaryl bonds.

During the optimization of the intramolecular direct arylation conditions, it was observed that the reaction was highly dependent on the nature of the base. Typically carboxylate bases show good reactivity whereas amines and hydroxide bases led mainly to dehalogenation.[24,25] The groups of Echavarren and Fagnou showed that intramolecular C–H bond functionalization is not significantly influenced by the electronic nature of the arene which is uncharacteristic of an S_EAr pathway

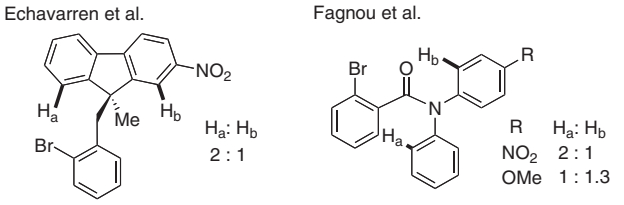


Figure 2. Selectivity observed with electronically biased substrates.

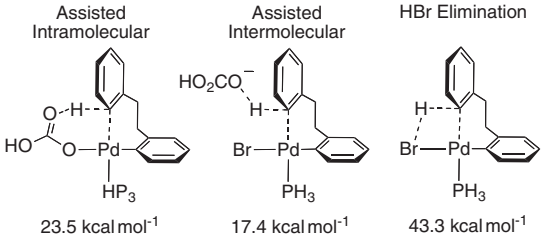
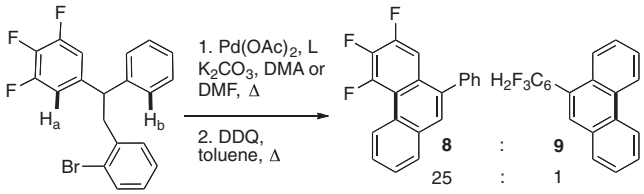


Figure 3. Mechanisms evaluated for the intramolecular direct arylation.



Scheme 6. Selectivity observed with a trifluorodiphenyl and a simple phenyl group.

(Figure 2). Large KIEs (3.5 to 6.7) were obtained from intramolecular competitions indicated that the C–H bond cleavage step is kinetically significant which is in support of the CMD mechanism.[24b,25a,25d]

Maseras, Echavarren, and co-workers evaluated by DFT three possible proton abstraction mechanisms, two of which are intra- and intermolecularly carbonate-assisted and the other being an unassisted HBr elimination (Figure 3).[26] Computationally, the intermolecular assisted pathway was favored over the intramolecular base assistance by 6.1 kcal mol^{-1}, while the HBr elimination pathway was far less accessible. The calculated ratio of product distribution (**8**:**9**) for both the intra- and intermolecular processes were in favor of the trifluorinated arene which is in agreement with the observed experimental results (Scheme 6). The computed product distribution with the intermolecular pathway more closely reflected what was observed experimentally, suggesting that this was the most likely pathway of the two (Table 1).[26]

To further support the proposed intermolecular carbonate-assisted mechanism, Maseras, Echavarren, and co-workers used bidentate ligands, such as dppm, dppe, dppf, and Xantphos, in the development of a new set of conditions for the palladium-catalyzed intramolecular direct arylation of aryl bromides.[27] Since it is unlikely that a carbonate could displace a bidentate phosphine ligand on the palladium, the intermolecular carbonate-assisted pathway is more likely to occur.[28]

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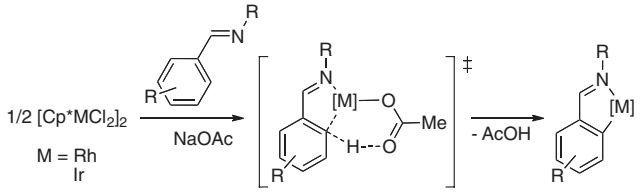
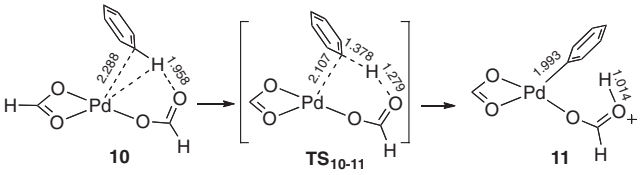
Table 1. Predicted product distribution with the different mechanisms

	ΔE_a (H_a) /kcal mol^{-1}	ΔE_a (H_b) /kcal mol^{-1}	$\Delta\Delta E_a$ /kcal mol^{-1}	Theorical ratio **8**:**9**
Assisted Intramolecular	23.5	13.2	10.3	700000:1
Assisted Intermolecular	17.4	14.4	3.0	40:1
HBr Elimination	43.3	34.5	8.8	—



Scheme 7. Reaction pathway for the functionalization of phenyl imines.



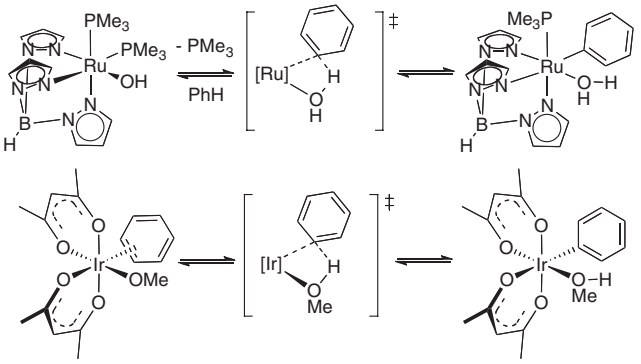
Scheme 8. Geometry changes in the palladium(II)–formate-promoted C–H bond functionalization.

Jones and co-workers studied the mechanism of functionalization of phenyl imines with $[Cp^*RhCl_2]_2$ or $[Cp^*IrCl_2]_2$ with NaOAc (Scheme 7).[29] The conclusion of these studies where in agreement with those of Ryabov (vide supra), the proton was most likely abstracted by the acetate present on the metal while a metal–carbon bond was formed.

♦ *Intermolecular C–H Bond Metallation*

In 2000, Sakaki and co-workers reported the DFT investigation of the intermolecular C–H bond metallation of benzene by Pd(κ^2-$O_2CH)_2$ to form a σ-phenylpalladium(II) formate complex and brought clarification to the overall process and its transition state (Scheme 8).[30] From previous mechanistic studies, it is known that palladium(II) acetate, when reacting with simple arenes, exhibits an electrophilic character as shown by the negative slope of the Hammett plot ($\rho^+(\sigma^+) = -1.4$ to -0.4).[31] This metallation reaction also exhibited large primary KIEs ($k_H/k_D = 4.5$–5.1).[31] Kinetics studies on the oxidative homo-coupling of benzene catalyzed by $PdCl_2$–NaOAc in acetic acid revealed that the reaction rate was independent of acetate base, although the presence of carboxylate was essential to the reactivity of the system.[32] This suggest that the proton was abstracted by the acetate on the palladium and not by an external base.

In Sakaki's computational studies, the energetic profile for the palladium(II)–formate-promoted C–H bond metallation was consistent with experimental precedent.[31] Starting from the dissociated metal complex and benzene, the initial steps of the process led to the formation of a thermodynamically favorable κ^1 π complex **10**. The C–H bond that interacts with the metal has an out-of-plane angle of 12°, which based on precedent was proven to be a κ^1 π complex instead of the commonly proposed σ complex.[20] From this intermediate, the proton can be abstracted from the arene by the distal oxygen on the formate in a six-membered cyclic transition state (**TS_{10-11}**, Scheme 8). Sakaki and co-workers also investigated the metallation of benzene using platinum(II) formate and obtained results which indicated that the platinum–benzene π complex was even more stable than its palladium analog. Consequently, the subsequent deprotonation step became less accessible, which is reflected by the greater reactivity of palladium over platinum.[30]



Scheme 9. [RuTp(OH)]- and [Ir(acac)$_2$(OMe)]-promoted metallation of benzene.

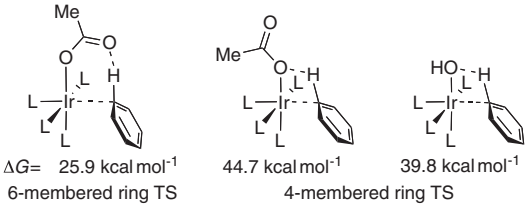


Figure 4. Comparison between acetate 6M TS and 4M TS with acetate or hydroxide ligand.

The addition of a metal to benzene has also been reported by the groups of Gunnoe[33] and Periana[34] using [Ru–OH] and [Ir–OMe] complexes respectively (Scheme 9). Both experimental and theorical mechanistic studies on these systems have shown that the metal bonds to the carbon as the proton is abstracted by the basic ligand on the metal.[6,35] Since no carboxylate bases were used in these systems, four-membered rings metallation–deprotonation transition states were proposed instead of the six-membered ring. When compared computationally, the six-membered ring transition state using iridium proved to be more easily accessible than the four-membered ring transition state with either a hydroxide ligand or the acetate (Figure 4).[36] Recently, Larrosa and co-workers showed that gold(I) combined with base could metallate arene rings, with primarily results suggesting a CMD mechanism.[37]

♦ *Catalytic Functionalization of Electron-deficient Arenes*

In 2005, Fagnou and co-workers developed a palladium-

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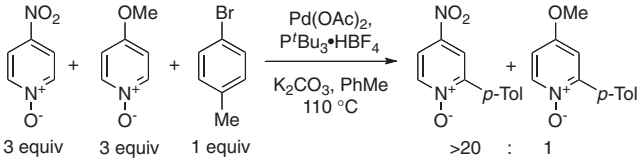
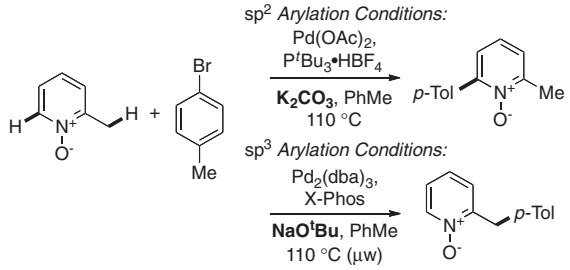


Scheme 10. Selectivity observed with electronically biased pyridine *N*-oxides.



Scheme 11. Selective arylation of picoline *N*-oxide achieved by the choice of base.

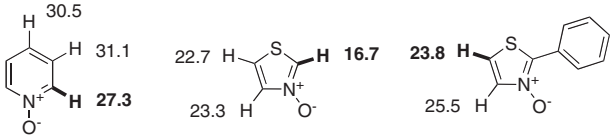
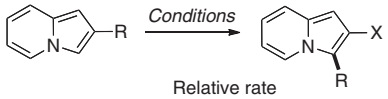


Figure 5. Calculated activation barrier for the CMD pathway. The bold bonds correspond to the experimental site of arylation. Values in kcal mol^{-1}.

catalyzed regioselective direct arylation of pyridine *N*-oxides as well as a variety of diazine and azole *N*-oxides with aryl-halides.[38] Experimentally, competition reactions showed that the electron-deficient 4-nitropyridine *N*-oxide reacts more readily than the more electron-rich 4-methoxypyridine *N*-oxide (>20:1) which is unusual considering that for direct arylation processes the palladium(II) complex is considered as electrophilic in nature (Scheme 10). A large primary KIE of 4.7 is observed with pyridine *N*-oxide.[38a] These results cannot be explained by an S_EAr mechanism. A mechanism involving heterolytic cleavage of the proton can be discarded based on studies on site-selective arylation of 2-methylazine *N*-oxides. The sp^2/sp^3 selectivity was found to be tunable with the choice of base: with K_2CO_3 the arylation occurs at the C6 position of azine *N*-oxide (Scheme 11), however using a stronger base (NaO^{t}Bu) the arylation occurs exclusively at the most acidic benzylic position.[39] The barriers of activation for each position on pyridine *N*-oxide were evaluated with the CMD pathway and the relative values for the computed transition state were consistent with the experimental regioselectivity (Figure 5).[40] Furthermore, the highly selective and sequential arylation C2 > C5 > C4 of thiazole *N*-oxide could be rationalized with this mechanism.[38c]

Fagnou and co-workers extended the intermolecular direct arylation of electron-deficient arenes to polyfluorinated arenes.[41] Experimentally, it was observed that the most electron-deficient polyfluorinated arene reacted preferentially over less electron-deficient polyfluorinated arenes. A KIE of 3.0 was observed, which is similar to the one observed with azine *N*-oxides. Furthermore, the trend of reactivity with polyfluorinated benzene

Table 2. Relative rate for the acylation and direct arylation of C2-substituted indolizines



Conditions	Relative rate		
	X = H	Me	CO_2Et
Friedel–Craft Acylation	1.0	0.67	0.33
Direct Arylation	1.0	0.97	0.66

paralleled the computed barrier of activation with the CMD mechanism.[41a] Fagnou and co-workers recently reported that chlorinated electron-rich heteroarenes benefit from similar activation effects on C–H bond reactivity as fluorinated arenes.[42]

♦ C–H Functionalization of Electron-rich Arenes

Over the years, several pathways have been proposed for C–H bond functionalization, the S_EAr and CMD mechanisms having been the most often proposed. The mechanisms of the C–H bond cleavage of electron-rich heteroarenes are often proposed to react through a Heck-like mechanism[43] or an S_EAr mechanism, although the latter has gained more attention.[44] For instance, the regioselectivities observed in the direct arylation of electron-rich arenes, such as azoles, indolizines, and indoles, match the regioselectivity of Friedel–Crafts reactions.[44] Sames and co-workers reported a ρ value of -0.71 derived from a Hammett plot for the C2 arylation of C6 substituted indoles.[44b] In the mechanistic studies of the direct arylation of substituted indolizines, Gevorgyan and co-workers observed that the relative rate of C2 substituted indolizine arylation parallels the one under acylation conditions (Table 2). In combination with the lack of a KIE in side-by-side experiments, these results were consistent with the S_EAr mechanism.[44c] On the other hand, a one-pot competition experiment with indolizines led to a KIE of 2.1.[40] These mechanistic studies highlighted the nucleophilic character of those electron-rich heteroarenes toward palladium catalysts as an important parameter to achieve the transformation, which were attributed to the formation of palladium–arenium σ complexes.

In the previous sections of this highlight were discussed examples where similar observations were made and for which the CMD mechanism was proposed over an S_EAr mechanism. This is especially the case for studies on the mercuration of benzene[9,12] and the cyclopalladation of DMBA-H.[17,19] Moreover, the S_EAr mechanism cannot justify why 3-fluorobenzothiophene reacts preferentially over the more nucleophilic benzothiophene in a direct arylation competition reaction (Scheme 12).[40] Computationally, palladium–arenium complexes were not located for any of the heteroarenes investigated. By evaluating the energy of activation of the CMD process of multiple heteroarenes (Figure 6), CMD accurately predicted both the relative reactivities of the C2-substituted indolizines (Table 2) and the benzothiophene derivatives (Scheme 12). For a wide range of heteroarenes, the CMD pathway was able to predict the regioselectivity observed experimentally for the palladium-catalyzed direct arylation of each arenes.[40,42] Activa-

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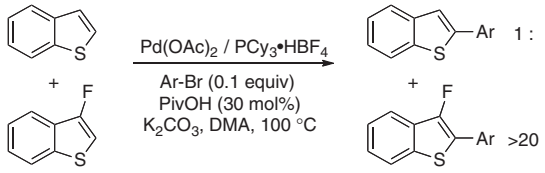

Scheme 12. Competition reaction between electronically biased benzothiophenes.

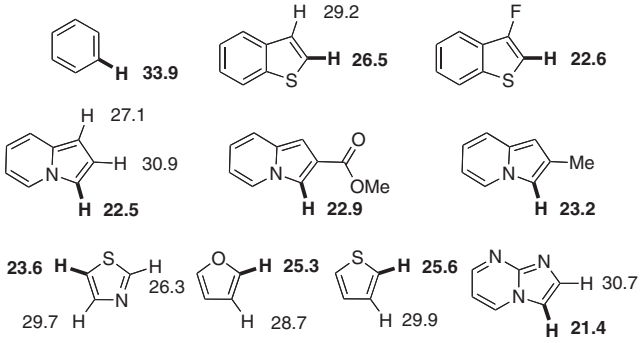

Figure 6. Calculated activation barrier for the CMD pathway. The bold bonds correspond to the experimental site of arylation. Values in kcal mol^{-1}.

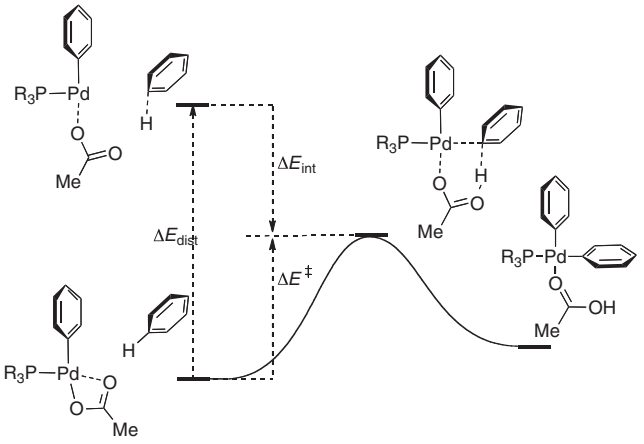

Figure 7. Representation of CMD pathway for benzene with activation-strain analysis.

tion-strain analysis was used to gain a better understanding of some of the factors that come into play in establishing the barrier of activation. In such analysis the activation barrier ($\Delta E^{\ddagger}$) is divided into two components, energetic cost (ΔE_{dist}) associated with the distortion of the substrates to reach the transition state and the energetic gain (ΔE_{int}) arising from the interaction of the substrates at the transition state (Figure 7). The trend observed from the study was that π-electron-rich arenes benefit from large ΔE_{int} stabilization, which are offset by large ΔE_{dist} values, while electron-deficient arenes do not benefit from large ΔE_{int} stabilization nor do they experience large ΔE_{dist}.

♦ Additives Used to Enhance Reactivity

The addition of a co-catalyst to direct arylation reactions has been shown to generate highly active catalysts and enhance the breadth of catalytic transformations. Larock and Sames had used stoichiometric amounts of pivalate salts in palladium and rhodium systems.[45,46] Fagnou first used pivalic acid (PivOH) as a co-catalyst in a palladium-catalyzed direct arylation reaction in order to efficiently functionalize benzene and other simple arenes.[47] The pivalate anion is believed to act as a catalytic proton shuttle from benzene to the stoichiometric carbonate base. Without this additive, very little conversion of starting material to product was obtained. The use of pivalic acid as an additive has allowed for the development of milder conditions and improved regioselectivity for many intramolecular direct arylation reactions,[26,27,48] as well as in the functionalization of electron-deficient arenes,[38c,38d,49,50] and electron-rich heteroarenes.[40,42,49a,51–53] Computationally, the influence of the pivalate anion on the benzene C–H bond cleaving transition state results in a decrease of 1.3 kcal mol^{-1} when compared to the bicarbonate anion (24.9 vs. 26.2 kcal mol^{-1}).

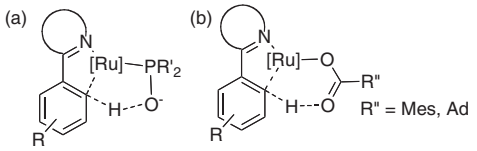

Figure 8. Other acid additives used to promote C–H bond cleavage.

Aside from pivalic acid, other additives have been used in C–H functionalization reactions. Ackermann and co-workers have used heteroatom-substituted secondary phosphine oxide (HASPO) preligand in ruthenium-catalyzed[54] and palladium-catalyzed[55] direct arylation of arenes. Presumably, the phosphine oxide acts as the intramolecular base (Figure 8a).[56] Ackermann also uses 2,4,6-trimethylbenzoic acid and 1-adamantylcarboxylic acid as co-catalyst in ruthenium- and palladium-catalyzed C–H bond functionalization reactions (Figure 8).[57,58] Furthermore, Larrosa and co-workers used *o*-nitrobenzoic acid as an additive in the palladium-catalyzed C2 arylation of indoles.[59]

♦ Concluding Remarks

Herein we have presented studies which have led to a better understanding of the metal/base-catalyzed functionalization of arene C–H bonds. Both the early work by Roberts and Ryabov have proposed a concerted metallation–deprotonation pathway instead of the S_EAr pathway. Later, computational and experimental studies on similar systems have come to the same conclusions. The pivotal role of the base on the metal, particularly carboxylate type bases, was highlighted throughout the studies. With a better understanding of the metal/base-promoted cleavage of C–H bond mechanism, our hope is to inspire further development in the C–H bond functionalization area.

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† Prof. Keith Fagnou passed away unexpectedly on November 11, 2009.

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