ACCOUNTS
of chemical research

Direct Functionalization of M—C (M = Pt^{II}, Pd^{II}) Bonds Using Environmentally Benign Oxidants, O_2 and H_2O_2

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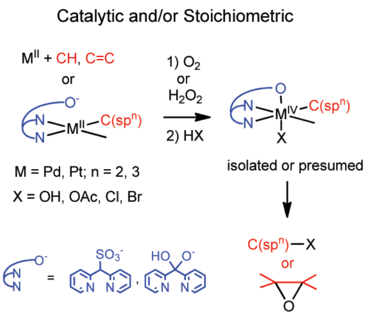
RECEIVED ON JULY 22, 2011

CONSPECTUS



Atom economy and the use of "green" reagents in organic oxidation, including oxidation of hydrocarbons, remain challenges for organic synthesis. Solutions to this problem would lead to a more sustainable economy because of improved access to energy resources such as natural gas. Although natural gas is still abundant, about a third of methane extracted in distant oil fields currently cannot be used as a chemical feedstock because of a dearth of economically and ecologically viable methodologies for partial methane oxidation. Two readily available "atom-economical" "green" oxidants are dioxygen and hydrogen peroxide, but few methodologies have utilized these oxidants effectively in selective organic transformations. Hydrocarbon oxidation and C—H functionalization reactions rely on Pd^{II} and Pt^{II} complexes. These reagents have practical advantages because they can tolerate moisture and atmospheric oxygen. But this tolerance for atmospheric oxygen also makes it challenging to develop novel organometallic palladium and platinum-catalyzed C—H oxidation reactions utilizing O_2 or H_2O_2.

This Account focuses on these challenges: the development of M—C bond (M = Pt^{II}, Pd^{II}) functionalization and related selective hydrocarbon C—H oxidations with O_2 or H_2O_2. Reactions discussed in this Account do not involve mediators, since the latter can impart low reaction selectivity and catalyst instability. As an efficient solution to the problem of direct M—C oxidation and functionalization with O_2 and H_2O_2, this Account introduces the use of facially chelating semilabile ligands such as di(2-pyridyl)methanesulfonate and the hydrated form of di(2-pyridyl)ketone that enable selective and facile M^{II}—C(sp^n) bond functionalization with O_2 (M = Pt, $n = 3$; M = Pd, $n = 3$ (benzylic)) or H_2O_2 (M = Pd, $n = 2$). The reactions proceed efficiently in protic solvents such as water, methanol, or acetic acid. With the exception of benzylic Pd^{II} complexes, the organometallic substrates studied form isolable high-valent Pt^{IV} or Pd^{IV} intermediates as a result of an oxidant attack at the M^{II} atom. The resulting high-valent M^{IV} intermediates undergo C—O reductive elimination, leading to products in high yields. Guidelines for the synthesis of products containing other C—X bonds (X = OAc, Cl, Br) while using O_2 or H_2O_2 as oxidants are also discussed. Although the M^{II}—C bond functionalization reactions including high-valent intermediates are well understood, the mechanism for the aerobic functionalization of benzylic Pd^{II} complexes will require a more detailed exploration.

Importantly, further optimization of the systems suitable for stoichiometric M^{II}—C bond functionalization led to the development of catalytic reactions, including selective acetoxylation of benzylic C—H bonds with O_2 as the oxidant and hydroxylation of aromatic C—H bonds with H_2O_2 in acetic acid solutions. Both reactions proceed efficiently with substrates that contain a directing heteroatom. This Account also describes catalytic methods for ethylene dioxygenation with H_2O_2 using M^{II} complexes supported by facially chelating ligands.

Mechanistic studies of these new oxidation reactions point to important ways to improve their substrate scope and to develop "green" CH functionalization chemistry.

I. Introduction and Background

The development of catalytic oxidation reactions targeting a more efficient use of hydrocarbon resources[1] and/or employing environmentally benign and inexpensive oxidants, specifically hydrogen peroxide[2] and oxygen,[3,4] are important trends in modern organic synthesis. The use of water as a medium for catalysis is another trend in this direction.[5]

10.1021/ar200191k

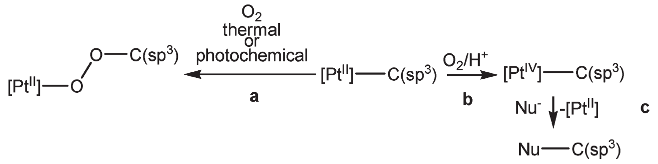
Palladium compounds have found widespread use in catalysis of organic reactions, but most of these reactions utilize traditional or waste-producing inorganic and organic oxidizing agents. The development of "greener" organometallic catalytic transformations involving platinum and palladium complexes requires the knowledge of the reactivity of their organometallic compounds toward water, oxygen, and/or hydrogen peroxide. In this Account, some novel M–C bond (M = Pd^{II}, Pt^{II}) functionalization reactions involving O_2 and/or H_2O_2 will be considered. These reactions may become a part of catalytic hydrocarbon functionalization involving platinum and palladium in the oxidation states +2 and +4. Though the latter oxidation state is common in organoplatinum chemistry, organopalladium(IV) compounds are relatively rare.[6–8] Especially rare are Pd^{IV} monohydrocarbyls having just one Pd–C bond. Palladium(IV) monohydrocarbyls can be viewed as potential intermediates in a variety of catalytic hydrocarbon oxidative functionalization reactions. Our latest developments of monohydrocarbyl palladium(IV) chemistry in water are presented in part IV of this Account. This Account does not cover our work dealing with transfer dehydrogenation chemistry utilizing sacrificial hydrogen acceptors and based on the application of Pt^{II} di(2-pyridyl)borate complexes.[9–12] Also not covered are aerobic C–H oxidation reactions involving Pd^{II}/Pd^{0} couple.[3,13–15]

II. Selective Functionalization of Pt^{II} Alkyl and Pt^{II} Olefin Complexes with O_2

The development of catalytic systems for selective hydrocarbon oxidation with O_2 requires the discovery of new reactions allowing facile M–C bond functionalization. Most of the known M–C bond functionalization reactions involve mediators that "shuttle" electrons between O_2 and low valent metal species. The use of mediators in catalytic aerobic C–H functionalization is known,[16–20] but, typically, the presence of mediators leads to poorly controllable reaction selectivity that may result, for instance, from accumulation of peroxides in reaction mixtures as well as conversion of the Pt^{II} species responsible for the activation of the organic substrate to catalytically inactive Pt^{IV} compounds.[21] This consideration is one of the important reasons which caused our interest to mediatorless oxidation.

A Pt^{II}–C(sp^3) bond functionalization reaction can be performed via either (i) thermal[22] or photosensitized[23] O_2 insertion into Pt^{II}–C(sp^3) bond (Scheme 1, a) or (ii) an O_2 attack at the metal[24] leading to conversion of the Pt^{II} alkyl to its more electrophilic Pt^{IV} analogue (Scheme 1, b), followed by attack of a nucleophile at the platinum(IV)-bound electrophilic carbon atom (Scheme 1, c).[25]

SCHEME 1. Two Pt^{II}–C(sp^3) Bond Functionalization Strategies

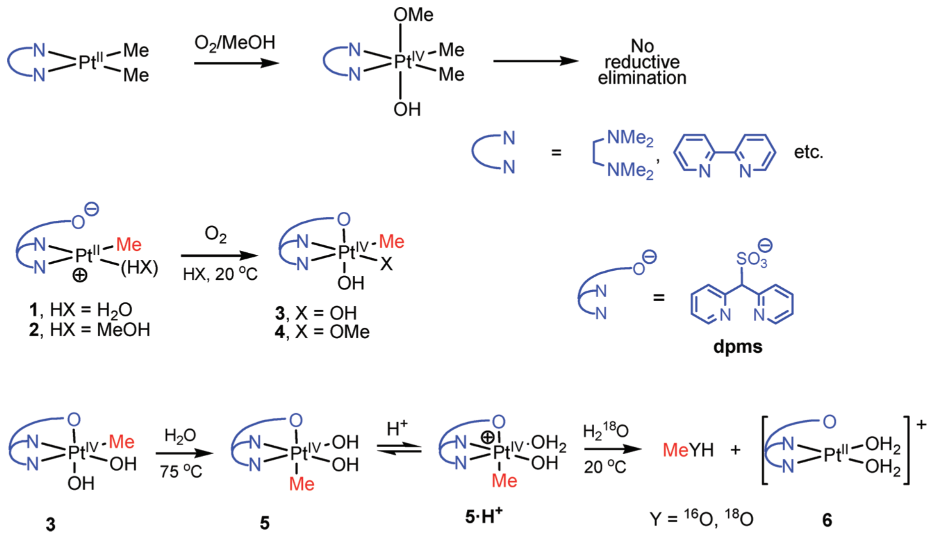


None of these strategies are efficient for Pt^{II}–C(sp^2) bonds.[26] Notably, before we began our work, the ability of organoplatinum(II) compounds to react with O_2 was only known for dimethyl Pt^{II} complexes supported by chelating bidentate N-donor ligands (Scheme 2, top).[24] Not less importantly, the N-ligated Pt^{IV} dimethyl hydroxo complexes resulting from the latter reaction are not electrophilic enough to undergo attack by most common nucleophiles which makes the M–C bond functionalization strategy (ii) described above impossible for this class of organoplatinum(II) species. Monomethyl Pt^{IV} complexes which are most relevant to the Shilov C–H functionalization chemistry[27] are reactive toward various nucleophiles as shown in Scheme 1, c, but they could not be produced by direct oxidation of Pt^{II} precursors with dioxygen according to Scheme 1, b.

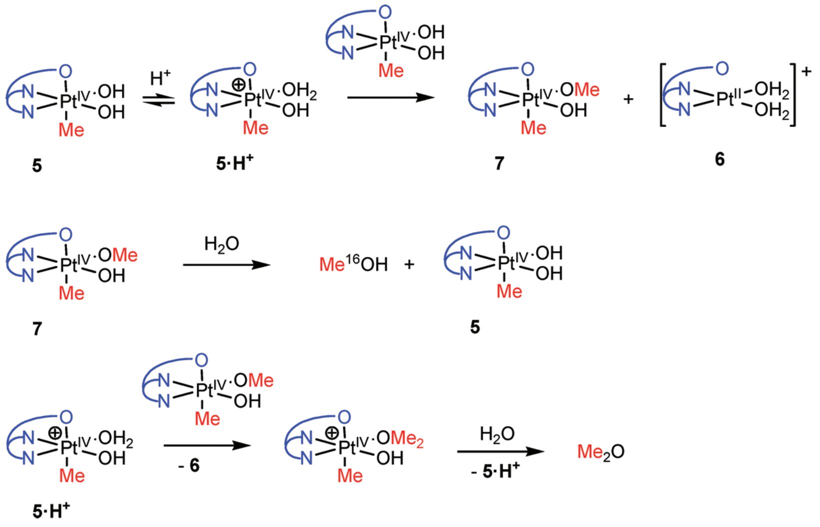
To enable facile Pt^{II}–C(sp^3) bond functionalization in platinum(II) monohydrocarbyls with O_2 as the oxidant, we proposed to use facially chelating ligands such as di(2-pyridine)methanesulfonate ligand (dpms) containing the semilabile sulfonate donor (Scheme 2).[28,29] This chelating ligand favors formation of octahedral Pt^{IV} products of oxidation by providing stabilization by the pendant sulfonate donor to the emerging high-valent platinum center. We found that the use of the dpms ligand allows for efficient Pt^{II}–C(sp^3) bond functionalization in various monoalkyl complexes. Importantly, the relatively weak coordination to the Pt^{IV} center of the semilabile sulfonate group allows for facile C–O reductive elimination from the Pt^{IV} species resulting from aerobic oxidation of their Pt^{II} precursors.

Our study of aerobic Pt^{II}–C bond oxidative functionalization started from methyl platinum(II) complexes such as **1** and **2** (Scheme 2). We found that these complexes could be readily oxidized by O_2 in water or methanol solution, respectively, under mild conditions to produce corresponding Pt^{IV} hydroxo compounds **3** and **4** in high yield.[26,30] Acid-catalyzed C–O reductive elimination from **3** allows efficient production of methanol and some of its derivatives such as dimethyl ether.[31] These reactions lead to a square planar Pt^{II} complex **6** and are accompanied by the loss of two ligands

SCHEME 2. Ligand-Enabled $Pt^{II}-C(sp^3)$ Bond Functionalization with O_2



SCHEME 3. Electrophilic Methyl Group Transfer from Cationic Pt^{IV} Species **5·H**$^+$ to Hydroxo Pt^{IV} Complex **5** and Methoxo Complex **7**

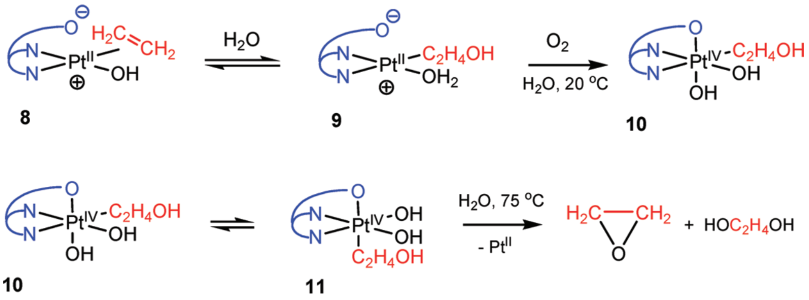


from the Pt^{IV} center available in **3** or **4**. The fastest reductive elimination rates are achieved when the alkyl and the sulfonate are *trans* to each other, as in complex **5**. This is because of the fact that sulfonate is the best leaving group present in the complex. As a result, isomerization of primary oxidation products such as **3** with the alkyl group *trans* to a pyridine residue precedes attack of a nucleophile at the electrophilic methyl ligand of **5·H**$^+$. Notably, reductive elimination of **5** performed in acidified 98% enriched ^{18}O-labeled water leads to a mixture of two isotopologous organic compounds in comparable amounts, methanol-^{18}O, which is an expected product resulting from methylation of the solvent, $H_2{}^{18}O$, with **5·H**$^+$, and methanol-^{16}O.[31] The latter methanol isotopologue is a product of a highly competitive methylation of the hydroxo ligand of complex **5** and subsequent hydrolysis of the resulting methoxo Pt^{IV} intermediate **7** (Scheme 3).

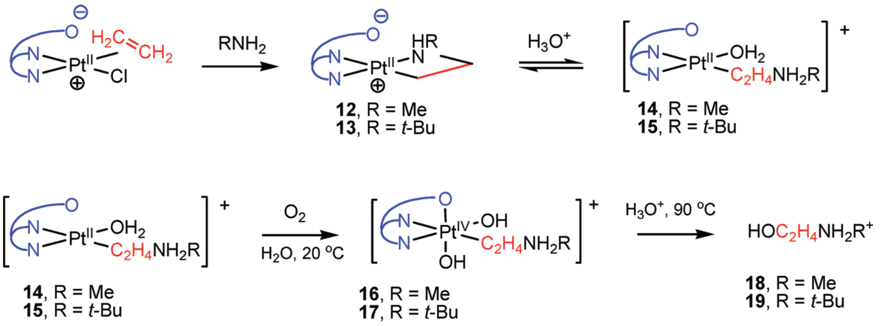
Interestingly, methoxo intermediate **7** can become to one of the major reaction intermediates in neutral aqueous solutions. This intermediate, as well as other similar methoxo species, can give rise to dimethyl ether resulting from nucleophilic attack of their methoxo ligand at the electrophilic methyl group present in **5·H**$^+$ (Scheme 3, bottom).

Aerobic oxidation of some other alkyl Pt^{II} complexes was also studied. 2-Hydroxoethyl Pt^{II} analogue of **1**, **9**, which results from nucleophilic addition of water to the ethylene ligand in complex **8**, exhibits similar $Pt^{II}-C$ functionalization chemistry (Scheme 4). Oxidation of **9** in water leads to

SCHEME 4. Aerobic Synthesis and Reductive Elimination Chemistry of 2-Hydroxoethyl Pt^{IV} Complex **10**



SCHEME 5. Aerobic Synthesis and Reductive Elimination Chemistry of 2-*N*-Alkylaminooxoethyl Pt^{IV} Complexes **15**−**17**



2-hydroxoethyl Pt^{IV} derivative **10** which, upon isomerization to the $-C_s$ symmetric isomer **11**, produces a mixture of ethylene oxide and ethylene glycol in combined high yield.[32] Ethylene glycol was presumed to result from an intramolecular nucleophilic attack by the hydroxyl oxygen of the 2-hydroxoethyl group at the Pt^{IV}−bound carbon of **11**.

2-Aminoethyl Pt^{II} complexes **14** and **15**, which can be viewed as amino analogsue of **9**, are presumed to be responsible for similar aerobic functionalization of platina(II)azetidines **12** and **13** (Scheme 5).[33] Complexes **14** and **15** form reversibly in acidic aqueous solutions of **12** and **13** which produce corresponding cationic platina(IV)azetidines **16** and **17** under an oxygen atmosphere. Reductive elimination of **16** and **17** in acidic aqueous solutions leads to ethanolamines **18** and **19**.

Interestingly, norbornene and *cis*-cyclooctene analogues of hydroxo ethylene complex **8**, **20**, and **21**, are not susceptible to external nucleophilic attack by water or hydroxide (Scheme 6). In basic solutions, they exist as anionic platina(II) oxetanes, **22** and **23** (not all isomers that form are shown), that are products of intramolecular olefin hydroxyplatination.[34] The aerobic oxidation of **22** and **23** can be highly stereoselective and leads to derived platina(IV)oxetanes **24** and **25** in high yield. In turn, C−O reductive elimination from platina(IV)oxetanes **24** and **25** furnishes the corresponding olefin oxides **26** and **27** in high yield in various solvents and in the solid phase in the absence of any external nucleophiles. A very rare direct intramolecular $C(sp^3)$−O elimination mechanism was proposed for these $C(sp^3)$−O reductive elimination reactions.

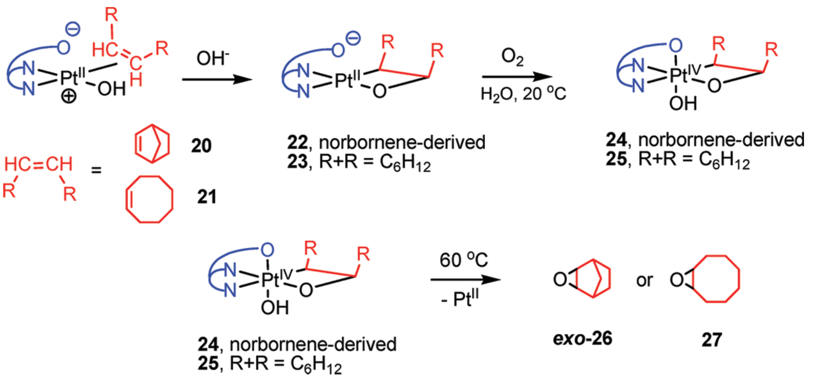
The aqueous chemistry of organometallic (dpms)Pt^{II} complexes and oxygen presented above is very attractive because of its high efficiency and selectivity. However, this chemistry has serious limitations when it comes to its applications in catalytic hydrocarbon oxidation. These limitations are mostly related to severe inhibition by water of hydrocarbon coordination to the metal.[34,35] We presume that development of next generation ligands might help overcome this problem.

In summary, functionalization of Pt^{II}−$C(sp^3)$ bonds in protic media with O_2 as the only oxidant becomes possible when semilabile facially chelating ligands are used. Importantly, no mediators are required in these reactions.

III. Aerobic Functionalization of Pd^{II} Benzyl Complexes

Oxidative heteroatom-directed C−H functionalization catalyzed by palladium(II) complexes has gained significant attention.[36] Before our work molecular oxygen was not used as oxidant in these reactions. Similar to organoplatinum(II) chemistry, one of the challenges of palladium-catalyzed C−H oxidation is to enable selective aerobic Pd^{II}−C bond functionalization. Importantly, we found that ligands of the dpms family

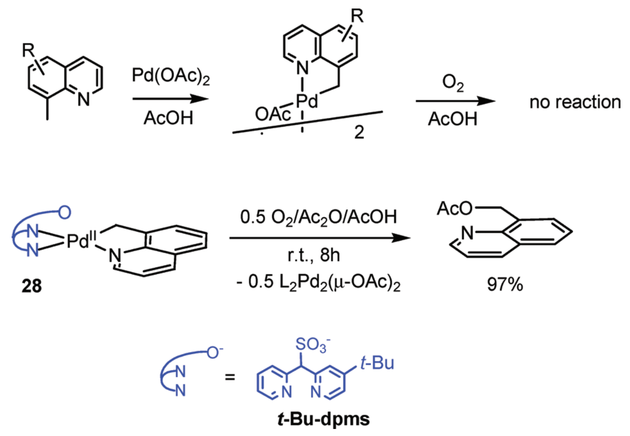
SCHEME 6. Aerobic Synthesis and Reductive Elimination Chemistry of Platina(IV)oxetanes **24** and **25**



can be useful in aerobic functionalization of benzylic palladium(II) complexes.[37] For instance, products of cyclopalladation of various substituted 8-methylquinolines are inert toward O_2 in acetic acid/acetic acid anhydride solution, whereas efficient and selective oxidation of palladacycles such as **28** is possible at 20 °C where the 4-*tert*-butyl substituted dpms ligand is attached to the metal (Scheme 7). Although the reaction scope is currently limited to palladacycles of benzylic type, this oxidation reaction can be used in catalytic C−H functionalization chemistry.[37] The use of acetic anhydride is required to protect the resulting alcohol against overoxidation by converting it into acetic acid ester which is virtually unreactive toward the palladium catalyst.

A report on $Pd^{II}-C(sp^3)$ bond functionalization in bipyridyl-supported dimethylpalladium(II) complex via dioxygen insertion into the metal−carbon bond to form methylperoxo palladium(II) complex has been published.[22] According to this report, the oxidation reaction is proposed to follow a radical chain mechanism and to include Pd^{III} intermediates. A similar mechanism of $Pd^{II}-C$ bond functionalization might be operational in our system, where the facially chelating dpms ligand provides some partial stabilization to Pd(III) transients. Understanding this reaction mechanism might lead to modification of the ligand platform and expansion of the substrate scope of this reaction by including also alkyl and aryl palladium(II) complexes.

SCHEME 7. Aerobic Functionalization of a Benzylic 8-Methylquinoline-Derived Pd^{II} Complex **28**



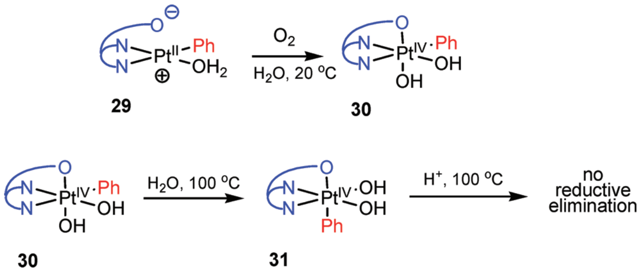
IV. Functionalization of $Pd^{II}-C(sp^2)$ Bond with H_2O_2 via Pd^{IV} Monohydrocarbyls in Water

Our attempts at oxidative functionalization of $Pt^{II}-C(sp^2)$ bond with O_2 included dpms-supported phenyl Pt^{II} complexes $(dpms)Pt^{II}Ph(HX)$ (X = OH, OMe), such as **29** (X = OH), dissolved in neat HX (Scheme 8). The reaction led to clean oxidation of these phenyl complexes to form phenyl hydroxo Pt^{IV} derivatives such as **30** which do not eliminate phenol even under relatively harsh conditions.[26] The only reaction that was observed in aqueous solutions of **30** at 100 °C was isomerization of **30** to its C_s symmetric isomer **31** featuring the sulfonate group *trans* to the phenyl ligand. The DFT calculated Gibbs activation energy for phenol elimination from **31** is about 30 kcal/mol, consistent with the observed lack of reactivity.

With the assumption that Pd^{IV} analogues containing the more oxidizing Pd^{IV} atom will be more reactive in $C(sp^2)-O$ reductive elimination, we set to use palladium compounds in oxidative $M-C(sp^2)$ bond functionalization. In 2010, when we began this work only four monohydrocarbyl Pd^{IV} complexes were known, including three monoaryl complexes (Chart 1).[38−41]

None of these complexes could be involved in reductive elimination of C−O bond. Therefore, our initial goal was to prepare new O-ligated Pd^{IV} monohydrocarbyls that would exhibit C−O elimination reactivity. To enhance the kinetic stability of these complexes we chose to use species containing two facially chelating 1,1-diaryl-1-hydroxomethoxide ligands per one palladium atom. Such ligands form readily[42−46] from the hydrated form of di(2-pyridyl)ketone, dpk, or

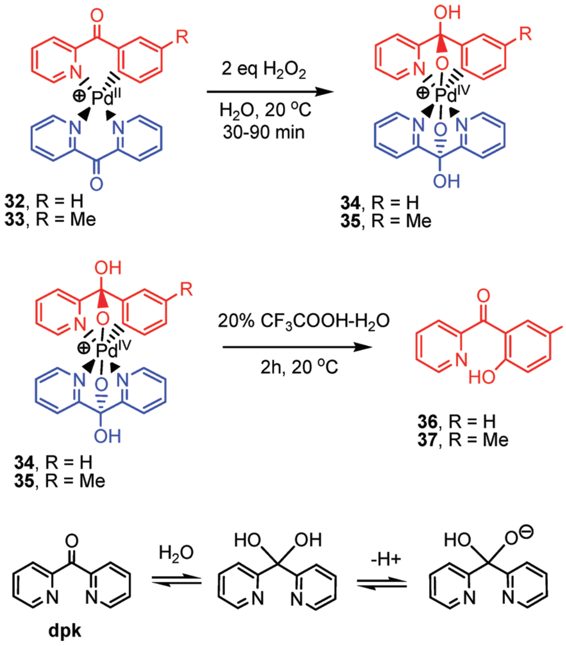
SCHEME 8. Attempted Aerobic Functionalization of a Pt^{II} Phenyl Complex **29**



the hydrated form of cyclopalladated 2-benzoylpyridine (Scheme 9, bottom). Palladium(II)-coordinated dpk ligands exist predominantly in the hydrated form in aqueous solutions.[46] The corresponding dpk derivative, 1,1-di(2-pyridyl)-1-hydroxymethoxide, was shown to stabilize octahedral Pt^{IV} and Pd^{IV} complexes.[44,45]

Complex **32** and its methyl analogue **33** were found to be stable toward O_2 in aqueous solutions; but they reacted within a few minutes with a stronger oxidant, hydrogen peroxide, to produce cleanly derived cationic Pd^{IV} monohydrocarbyls **34** and **35**, respectively.[45] Both **34** and **35** are stable in water up to 90 °C for many hours but eliminate the corresponding phenols **36** and **37** in aqueous 20% vol trifluoroacetic acid in high yield at 20 °C. The relatively high kinetic stability of **34** and **35** suggests that none of them is likely to be suitable for applications in catalytic C–H functionalization chemistry at ambient temperatures. The use of higher temperatures may be limited due to the relatively low thermal stability of hydrogen peroxide. Hence, the next step to possible catalytic chemistry involving H_2O_2 and Pd^{IV} monohydrocarbyls would be to enhance the reactivity of the Pd^{IV} species. To do so, complexes such as **38** with only one facially chelating ligand per metal atom were prepared (Scheme 10). Complex **38** which could be prepared and isolated at 0 °C was shown to reductively eliminate a $C(sp^2)$–O bond already at 20 °C. Therefore, the observed trend in reactivity of Pd^{IV} monohydrocarbyls matched our expectations: their reactivity in C–O reductive elimination increases with the decreasing number of facially chelating 1,1-diaryl-1-hydroxomethoxide ligands. One can assume that using less donating facially chelating ligands and/or sterically bulkier ligands the reactivity of derived Pd^{IV} complexes can be further enhanced. This consideration led us eventually to the discovery of catalytic $C(sp^2)$–H functionalization with H_2O_2 that is described in part V of this Account.

SCHEME 9. Synthesis and C–O Reductive Elimination of Monohydrocarbyl Pd^{IV} Complexes Supported by Two Facially Chelating Alkoxide Ligands

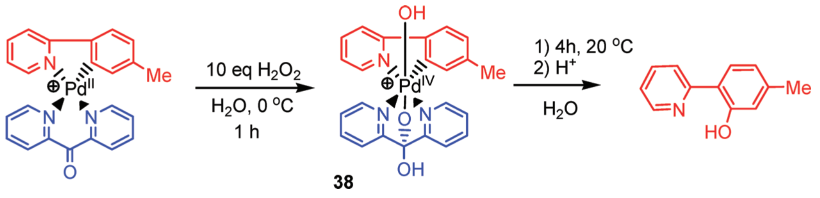


One of the remarkable properties of O-ligated Pd^{IV} monohydrocarbyls **34**, **35**, and **38** is their ability to undergo alkoxide or hydroxide ligand exchange with various HX (X = OAc, Cl, Br) in acidic media to form derived Pd^{IV} monohydrocarbyls with different Pd^{IV}–X bonds.[45] These complexes were shown to cleanly reductively eliminate corresponding Ar–X compounds under mild conditions. Interestingly, the observed rate constants for C–OH, C–Cl, and C–Br elimination from three analogous compounds $[(L)Pd^{IV}(Ar)X]^+$ (X = OH, Cl, Br) turned out to be of the same order of magnitude demonstrating only weak dependence of the reaction rates on the nature of the C–X bond being formed. These observations open up horizons for various types of oxidative C–H functionalization allowing one to introduce a great variety of functional groups into organic substrates.

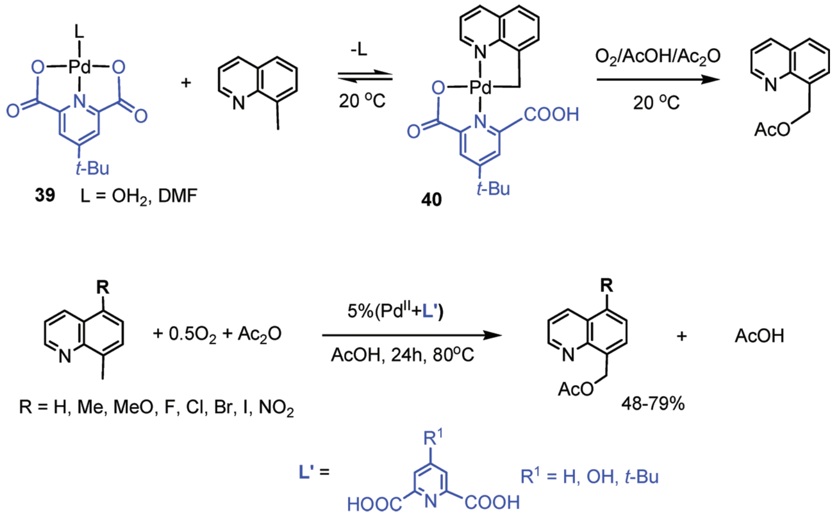
V. Catalytic C–H and C=C Functionalization with O_2 or H_2O_2 as Oxidants

The development of novel systems for catalytic hydrocarbon functionalization with O_2 or H_2O_2 as "green" oxidizing agents is one of the ultimate goals of our current work. Some of our systems for stoichiometric Pd^{II}–C functionalization with O_2 or H_2O_2 could be tuned for catalytic applications. The "tuning" here implies enabling the hydrocarbon activation step. The ability to perform both C–H bond activation and to enable Pd^{II}–C bond functionalization with O_2 has been found for palladium(II) 2,6-pyridinedicarboxylate complexes **39** (Scheme 11, top).[37] These complexes were shown

SCHEME 10. Synthesis and C—O Reductive Elimination Reactivity of Monohydrocarbyl Pd^{IV} Complexes Supported by One Facially Chelating Alkoxide Ligand



SCHEME 11. Stoichiometric and Catalytic Aerobic C—H Acetoxylation of Substituted 8-Methylquinolines



to react reversibly with 8-methylquinoline in acetic acid/acetic anhydride solution already at 20 °C to form 2,6-pyridinedicarboxylate-supported cyclopalladated 8-methylquinoline **40**. In turn, **40** reacts readily with O_2 under the same conditions to form derived organic acetate. The rate of the latter reaction is only slightly affected by addition of BHT, suggesting that it does not proceed via a free radical mechanism.

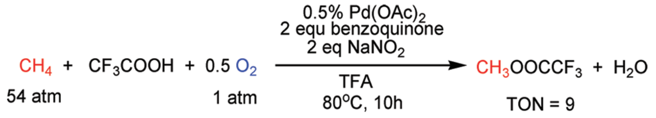
A number of 5-substituted 8-methylquinolines can be converted catalytically to corresponding 8-acetoxymethyl derivatives in 50—80% yield in the presence of 5% $Pd(OAc)_2$/5% 2,6-pyridinedicarboxylic acid system in acetic acid—acetic acid anhydride solution under an oxygen atmosphere at 80 °C. 8-Quinolylmethanols are one of the primary reaction products besides the derived acetates. The use of acetic acid anhydride allows for protection of the alcohols against overoxidation which leads to corresponding 8-quinolinecarboxylic acids and insoluble Pd^{II} bis(quinolylcarboxylates). The latter reaction is responsible for the C—H acetoxylation reaction rate decrease and lower yields of the target acetates. The catalyst used in the reaction in Scheme 11 is tolerant to the presence of various functional groups: all of the halogens, methyl, methoxy, and nitro groups. No palladium black accumulation is observed. The reaction is homogeneous as it follows from the absence of the reaction inhibition by additives of metallic mercury. The catalytically active species do not include homogeneous low valent palladium derivatives such as Pd^0 complexes as well, as it follows from the lack of the reaction inhibition by carbon tetrabromide.

Oxidative acetoxylation of 2-(*p*-tolyl)pyridine in this system is also possible; but its reaction rate is very slow, and the reaction is inefficient even at 110 °C.

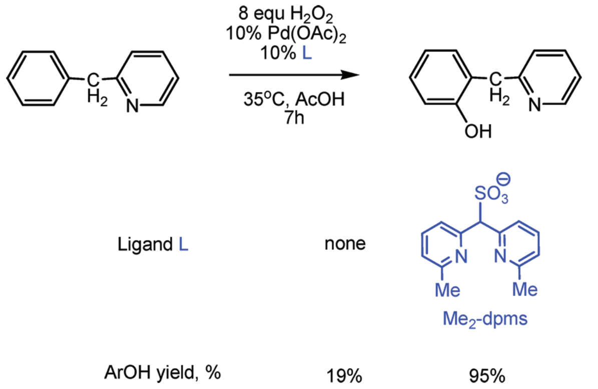
Our current studies of reactions involved in aerobic C—H functionalization are directed toward understanding their mechanisms and improving their efficiency. The most important questions to answer here are what the mechanism of Pd—C(sp^2) bond functionalization with O_2 is and what the factors are that affect the rate of this important reaction.

An example of aerobic palladium-catalyzed methane C—H functionalization with O_2 utilizing nitrogen oxides and benzoquinone as mediators is worth mentioning here. These mediators direct oxidative trifluoroacetoxylation of methane in 0.5% $Pd(OAc)_2$—$NaNO_2$—benzoquinone—trifluoroacetic acid system (Scheme 12).[20] The catalyst efficiency corresponds to nine turnovers after 10 h at 80 °C. Slow catalyst decomposition

SCHEME 12. Catalytic Oxidative Methane Trifluoroacetoxylation Utilizing O_2 as Oxidant with *p*-Benzoquinone and Nitrogen Oxides as Mediators



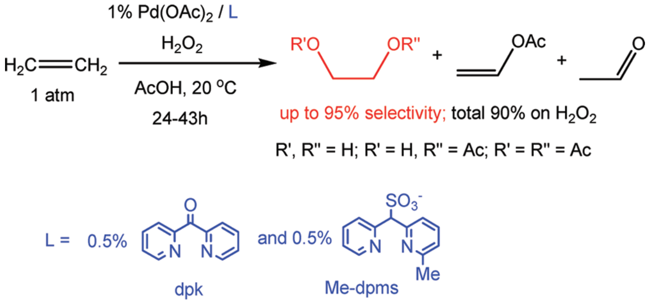
SCHEME 13. Palladium-Catalyzed $C(sp^2)$−H Hydroxylation with H_2O_2



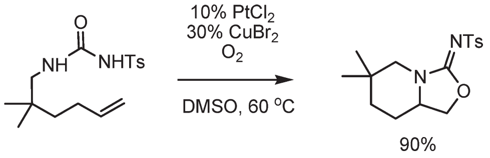
leading to precipitation of palladium black was observed, once again pointing to the importance of development of mediatorless systems.

The successful preparation of monohydrocarbyl Pd^{IV} complexes and their clean $C(sp^2)$−O reductive elimination reactivity, all enabled by facially chelating ligands, which are described in part IV of this Account prompted us to explore the potential of this system in catalytic $C(sp^2)$-H hydroxylation of 2-benzylpyridine and similar substrates with H_2O_2 in acetic acid solution. The use of a relatively bulky facially chelating bis(6-methyl-2-pyridyl)methanesulfonate, Me_2-dpms, as a ligand, in combination with 10% palladium(II) acetate at 35 °C, turned out to be more efficient than the use of $Pd(OAc)_2$ alone or the dpk−$Pd(OAc)_2$ system with the yields of corresponding phenols as high as 95% (Scheme 13).[45] Our recent study of coordination behavior in a similar system with the Me-dpms ligand (Scheme 14) and $Pd(OAc)_2$[46] suggests that even at 1:1 L:Pd ratio a significant fraction of palladium(II) acetate remains noncoordinated to the ligand and that complexes of both 1:1 and 2:1 L:Pd stoichiometry are present in solution. It is likely that palladium(II) acetate that is not coordinated to the sulfonate ligand is responsible for C−H activation of the substrate, whereas the sulfonate ligand is proposed to be transferred to the resulting palladacycle from homoleptic complex PdL_2 where L = Me-dpms. The coordinated Me-dpms ligand enables faster oxidation chemistry of the supported organopalladium(II) species.

SCHEME 14. Palladium-Catalyzed Selective and Efficient Oxidation of Ethylene with H_2O_2 in Acetic Acid Solutions



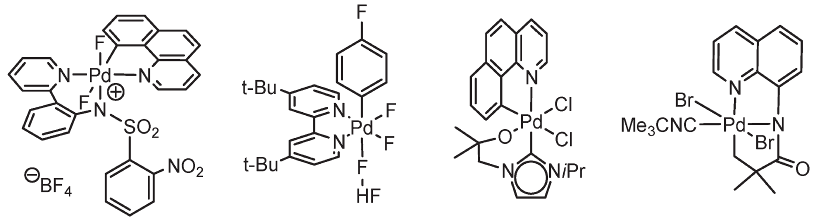
SCHEME 15. Platinum-Catalyzed Aerobic Intramolecular 1,2-Aminooxygenation Utilizing $CuBr_2$ as a Mediator



A similar mechanism of catalysis was proposed for the catalytic oxidation of ethylene in H_2O_2−AcOH system containing 1% $Pd(OAc)_2$, 0.5% dpk, 0.5% Me-dpms (Scheme 14).[46] This system was efficient for the conversion of ethylene to a mixture of glycol mono- and diacetates in up to 90% yield in H_2O_2 and up to 95% selectivity in glycol acetates at 1 atm pressure of ethylene and 20 °C. "Free" palladium(II) acetate was proposed to be responsible for coordination and activation of ethylene in reaction solutions, whereas the availability of labile dpk ligand in the system is the key condition to be met to achieve fast oxidation of 2-acetoxyethylpalladium(II) intermediate resulting from activation of ethylene with $Pd(OAc)_2$. The homoleptic complex $[Pd(dpk)_2]^{2+}$ which was shown to be the key component of the catalyst above might be the source of a labile dpk ligand necessary for faster oxidation of the 2-acetoxyethylpalladium(II) species.

Mediatorless oxidation of olefins to ketones and epoxides can also be performed with O_2 in the presence of heterovalent Pt^{II}/Pt^{III} polynuclear complexes featuring Pt^{III}−Pt^{II} bonds.[47] Some terminal linear olefins and cycloolefins could be oxidized catalytically with O_2 in biphasic 1,2-dichloroethane−water−anionic surfactant−heterovalent Pt^{II}/Pt^{III} systems with the turnover numbers ranging from 4 to 25. Epoxides are observed typically for cycloalkene substrates with the selectivity of 76% for norbornene to 92% for cyclohexene, whereas the predominant formation of ketones is observed for linear alkenes with the

CHART 1. Monohydrocarbyl Pd^{IV} Complexes Reported by Mid-2010



selectivity of 58% for 1-hexene to 99% for 1-heptene and 1-octene. The reaction mechanism is unclear: the isolated relatively stable platinum(III) alkyls did not exhibit C−O reductive elimination reactivity.

Though the major focus of our work is on mediatorless oxidation chemistry, it is worth mentioning here a recent example of an efficient platinum-catalyzed oxidative cyclization of *N*-alkenyl-*N′*-tosylureas which can be viewed as intramolecular 1,2-aminooxygenation of olefins with O_2 as oxidant and 10% $PtCl_2$ as a catalyst, 30% $CuBr_2$ as a mediator, and DMSO as a solvent. Yields of resulting pyrrolidines range from 30 to 90% (Scheme 15).[48] The reaction efficiency is strongly dependent on the amount of the mediator and the nature of solvent used.

VI. Summary

Facially chelating dipyridine ligands having a semilabile donor group, such as di(2-pyridyl)methanesulfonate (dpms) or hydrated di(2-pyridyl)ketone (dpk), can enable facile M−C bond (M = Pt^{II}, Pd^{II}) functionalization chemistry in protic media with O_2 or H_2O_2 as the oxidants. The ligands help stabilize a high valent metal center emerging as a result of the attack of O_2 or H_2O_2 at the metal. The presence of the labile sulfonate or alkoxide donor in the tripod ligand and the derived high valent metal complex is important for making subsequent C−O reductive elimination from the M^{IV} center facile. The overall reaction outcome and its efficiency depend on the nature of the hydrocarbyl and the metal involved. For instance, aryl Pt^{II} species supported by facially chelating ligands can be oxidized under O_2 atmosphere to their Pt^{IV} derivatives but no facile C−O reductive elimination from the derived Pt^{IV} aryl follows. By contrast, various Pt^{II} alkyls and Pt^{II} hydroxo olefin complexes can be converted selectively and in high yield in aqueous solutions or in other protic solvents to Pt^{IV} hydroxo derivatives that produce oxygenated organic compounds, alcohols, ethers, epoxides, or ethanolamines upon $C(sp^3)$−O reductive elimination. Palladium(II) monohydrocarbyls of benzylic type can also be made reactive toward O_2 when semilabile tripod ligands such as dpms are attached to the metal. Since oxidation of alcohols to carbonyl compounds can also be catalyzed by Pd^{II} complexes, the resulting alcohols should be protected against overoxidation, for example, by using AcOH−Ac_2O mixtures. Corresponding benzylic acetates can be prepared in high yield in such systems. Finally, cationic monohydrocarbyl Pd^{II} complexes with Pd^{II}−$C(sp^2)$ bond supported by dpk do not react with O_2 and require the use of stronger oxidizing agent, H_2O_2, to be converted to Pd^{IV} derivatives. The presence of two facially chelating alkoxide ligands makes the derived cationic Pd^{IV} monohydrocarbyls resulting from the oxidation kinetically stable in neutral aqueous solutions and in solid state, but in acidic media $C(sp^2)$−O reductive elimination to form phenols can be facile and high yielding. As the number of facially chelating ligands at the metal decreases, their reactivity increases. As a result, cationic Pd^{IV} monohydrocarbyls stabilized with one tripod semilabile alkoxide ligand are much more reactive and allow to observe C−X reductive elimination chemistry (X = OH, OAc, Cl, Br) already at 20 °C. These reactions occur with rates remarkably similar for various X, which might allow for the introduction of diverse functional groups into organic substrates under relatively mild and uniform conditions.

Modification of the systems above allowing for stoichiometric M−C bond functionalization that enables hydrocarbon coordination and activation at the metal can lead to catalytic systems utilizing O_2 or H_2O_2 as oxidants for oxidative functionalization of organic substrates. Substrates which have donor atoms directing the metal toward selective activation of specific C−H bonds can be efficiently acetoxylated with O_2−Ac_2O in the case of benzylic C−H bond donors or hydroxylated with H_2O_2 as the oxidant in the case of aromatic C−H bonds donors. Catalytic dioxygenation of a hydrocarbon substrate, ethylene with H_2O_2 in acetic acid solution can also be enabled in tripod ligand−$Pd(OAc)_2$ systems.

Future progress in the field of ligand-enabled C−H oxidation with O_2 and H_2O_2 will be, most likely, most closely related to the progress in our understanding of the mechanisms of reactions involved at hydrocarbon activation and O_2 or H_2O_2 activation steps.

The NSF (CHE-0614798) is gratefully acknowledged for the financial support of this work. Our mechanistic studies of aerobic Pd^{II}−C and C−H bond functionalization are based upon work supported as part of the Center for Catalytic Hydrocarbon Functionalization, an Energy Frontier Research Center funded by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences under Award Number DE-SC0001298. The author is also very grateful to his co-workers, whose names are cited in the references, for their invaluable contributions.

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Andrei N. Vedernikov has received his B.Sc., Ph.D., and D.Sc. degrees from the Kazan State University. He held a Professor position there in the period from 1985 to 2003. He was a Research Associate with Professor Kenneth G. Caulton at Indiana University in 2001−2003, after which period he joined the Department of Chemistry and Biochemistry of the University of Maryland, College Park, in 2003. His research interests include experimental and computational organotransition metal chemistry and catalysis.

FOOTNOTES

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