

The Role of Higher Oxidation State Species in Platinum-Mediated C–H Bond Activation and Functionalization

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Abstract The Shilov system, a mixture of di- and tetravalent chloroplatinate salts in aqueous solution, provided the first indication of the potential of organotransition metal complexes for activating and functionalizing alkanes under mild conditions; the participation of higher-valent species plays a crucial role. In this chapter, we discuss the experimental and computational studies that have led to detailed mechanistic understanding of C–H activation and functionalization by both the original Shilov system and the many subsequent modifications that have been developed, and assess the prospects for practical, selective catalytic oxidation of alkanes using this chemistry.

Keywords Alkane functionalization · Hydrocarbon oxidation · Platinum

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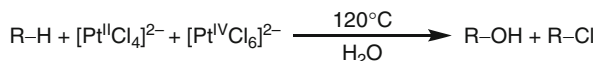
1 Introduction

Today, there are well-established examples of facile C–H bond activation by just about every transition metal in the periodic table, but the historical pride of precedence goes to platinum. The conversion of alkanes to alcohols by chloroplatinate salts, under what appeared at the time to be remarkably mild conditions, was first reported by Alexander Shilov and his coworkers around 1970. The initial triggering discovery was actually made by Garnett and Hodges [1], who examined H/D exchange in arenes catalyzed by acidic solutions of $[\text{Pt}^{\text{II}}\text{Cl}_4]^{2-}$. In itself this reaction may have seemed unremarkable, perhaps just an analog of the well-known mercuration of arenes; but the paper also mentioned (with no details) that aliphatic C–H bonds of methyl substituents on arenes, and even in cyclohexane, also exhibited some exchange. Following up on this observation, Shilov demonstrated that alkane C–H bonds undergo the exchange reaction [2] and subsequently decided (for reasons that are not completely obvious [3]) to add $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ to the system, thus obtaining a much more interesting reaction: moderately selective oxidation of alkanes to alcohols and chloroalkanes (Scheme 1) [4].

This paper and subsequent studies by Shilov and other Soviet groups – published primarily in Russian-language journals – initially attracted relatively little attention, and much of that was rather dubious: how could such “ordinary” metal complexes effect so unprecedented a transformation under near-ambient conditions? The first appearances of definitive examples of alkane activation at transition metal centers, around a decade later, did not really dispel these doubts. Activating species such as $[(\text{C}_5\text{Me}_5)(\text{PMe}_3)\text{Ir}^{\text{I}}]$, in Bergman’s pioneering work [5], were coordinatively unsaturated, often photogenerated, and very electron-rich. What correspondingly extraordinary properties do these chloroplatinate salts have to offer? Many believed that this was actually heterogeneous catalysis, with the chemistry taking place at the surface of colloidal metallic platinum, not at a discrete, soluble metal complex.

All such suspicion proved unfounded: detailed mechanistic work, carried out both by Shilov and his collaborators in the 1970s and by other groups starting in the late 1980s, has conclusively demonstrated that Shilov’s original proposal *was* correct and provided at least a partial explanation of just what is special about the Shilov system: the interplay between low-valent Pt(II) and high-valent Pt(IV) species, exploiting their differing chemical properties, is crucial in making this remarkable chemistry work.

Here, we examine the roles played by high-valent Pt complexes, not only in the Shilov system itself but also in the many subsequent examples of C–H activation that have been studied as models for and/or improvements upon the original work. To be sure, this topic has previously been addressed to some degree in general reviews of C–H activation (these are much too numerous for a complete listing, but for historical reasons we cite two by Shilov himself [6, 7]). More to the

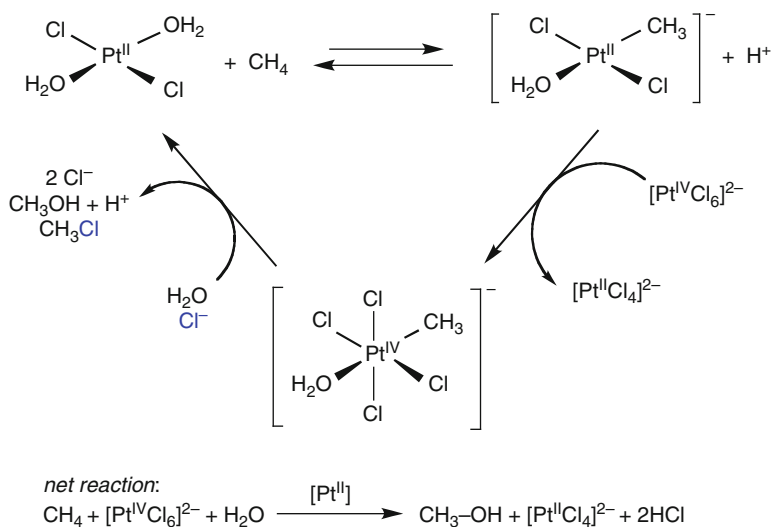


Scheme 1

point, several reviews specifically cover the Shilov and mechanistically related systems [8] and/or C–H activation chemistry of platinum [9, 10] and provide quite thorough pictures of the state of understanding at the time they were written. Hence, in the following sections, we focus on work subsequent to the last of those three reviews (2005) with an emphasis on the role of Pt(IV) in C–H bond activation and functionalization. We highlight the main developments of earlier work for background, but make no attempt at comprehensive coverage or in-depth analysis.

2 Formation and Decomposition of RPt(IV) in the Shilov System

The overall mechanism shown in Scheme 2, outlined by Shilov at an early stage in the research, has been essentially validated by all subsequent work. The reaction begins with activation of a C–H bond at a Pt(II) center. (There are examples of arene, but not alkane, activation by Pt(IV); these probably involve “classical” electrophilic routes via π -complexes and Wheland intermediates [10].) This fact seems incontrovertible since Pt(II) by itself catalyzes H/D exchange; the detailed mechanism of the activation is much less obvious, as discussed in Sect. 3. The resulting RPt(II) complex is *extremely* sensitive to electrophilic cleavage – no $[\text{RPt}^{\text{II}}\text{Cl}_x(\text{H}_2\text{O})_{3-x}]^{(x-1)-}$ species can be observed in the presence of any proton source – so using Pt(II) alone, no alkane conversion beyond isotopic exchange would be feasible. However, $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ effects oxidation to RPt(IV), which is virtually completely inert to protonolysis but quite susceptible to nucleophilic



Scheme 2

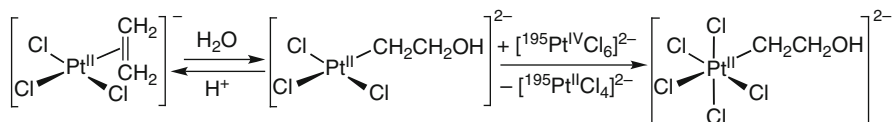
attack by water or chloride, leading to the organic products and regenerating Pt(II). The intermediacy of RPt(IV) also appears incontrovertible: species such as $[\text{MePt}^{\text{IV}}\text{Cl}_5]^{2-}$ can be synthesized independently and undergo the appropriate transformations under the conditions of the Shilov system. (Observation of an NMR signal corresponding to the latter complex, in a cooled-down solution from a methane oxidation reaction, has even been reported [11]; however, the failure to observe any such signal from a working reaction, at temperature in a pressurized NMR tube [12], casts some doubt on that claim.)

The two keys to the success of the system, then, are (1) the remarkable rapidity of the oxidation step, which can outcompete protonolysis even though the latter is too fast to measure independently; and (2) the complete “umpolung” of the C–Pt bond, from $\text{R}^{\delta-}\text{--Pt(II)}^{\delta+}$ to $\text{R}^{\delta+}\text{--Pt(IV)}^{\delta-}$, which facilitates functionalization rather than simple protonolytic reversion to alkane. In the following two sections, we discuss each of these steps.

2.1 Conversion of RPt(II) to RPt(IV)

The reaction of RPt(II) with $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ could proceed by either electron transfer or alkyl-chloride exchange; the two alternatives could be distinguished by enriching one or the other of the reactants with ^{195}Pt , if an authentic RPt(II) species were available. This experiment was eventually accomplished by two different means. First, oxidation of Zeise’s salt ($[(\text{C}_2\text{H}_4)\text{Pt}^{\text{II}}\text{Cl}_3]^-$) to $[(\text{HOCH}_2\text{CH}_2)\text{Pt}^{\text{IV}}\text{Cl}_5]^{2-}$ was shown, by kinetics analysis, to proceed via the intermediate $(\text{HOCH}_2\text{CH}_2)\text{Pt(II)}$ species [13]; then an insoluble salt of $[(\text{CH}_3)\text{Pt}^{\text{II}}\text{Cl}_3]^{2-}$, obtained by reduction in an aprotic solvent, was oxidized to $[(\text{CH}_3)\text{Pt}^{\text{IV}}\text{Cl}_5]^{2-}$ when added to a solution of $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ [14]. In both cases, the label showed up entirely in inorganic Pt(II), not RPt(IV) (Scheme 3), establishing the electron transfer route.

That finding implies it should be possible to replace Pt(IV) with any suitable oxidant and thus escape the requirement for stoichiometric consumption of Pt in the original Shilov reaction; however, there are two severe constraints on what counts as “suitable”. Oxidation of RPt(II) must be fast enough to compete with protonolysis, but the oxidant must not be so powerful as to also oxidize inorganic Pt(II), which is needed to carry out the C–H activation step. The rapidity of the oxidation step with $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ appears quite remarkable: while the absolute rate cannot be measured, the relative rate of oxidation to protonolysis can be estimated from the amounts of the corresponding products obtained when $[(\text{CH}_3)\text{Pt}^{\text{II}}\text{Cl}_3]^{2-}$ is generated transiently from nucleophilic attack of Cl^- at a methyl of $[(\text{CH}_3)_2\text{Pt}^{\text{IV}}\text{Cl}_4]^{2-}$ in an aqueous

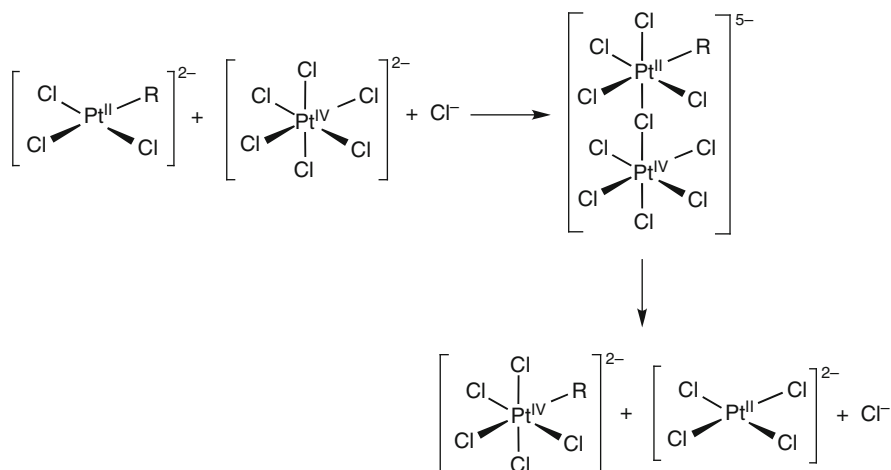


Scheme 3

solution of $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$, giving a rate constant ratio of around 20 in favor of oxidation at 95°C [15, 16]. The ratio is likely to be still higher at the Shilov operating temperature of 120°C, as a similar experiment using the insoluble $[(\text{CH}_3)\text{Pt}^{\text{II}}\text{Cl}_3]^{2-}$ salt mentioned above gave a ratio close to unity at room temperature [14, 16].

Knowing that protonolysis is so fast that $[(\text{CH}_3)\text{Pt}^{\text{II}}\text{Cl}_3]^{2-}$ can never be observed in protic solvents, we can estimate that its oxidation by $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ is at least several orders of magnitude faster than the closely related exchange reaction of $[\text{Pt}^{\text{II}}\text{Cl}_4]^{2-}$ with $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ [17]. The electron-releasing properties of a methyl ligand compared to those of chloride should make the $\text{RPt}(\text{II})$ easier to oxidize kinetically as well as thermodynamically, but an effect of that size seems surprising. Presumably, the oxidation takes place via the inner-sphere “chloronium ion transfer” mechanism of Scheme 4, as was demonstrated for redox reactions of related N-ligated complexes [18], so the ability of alkyl ligands to facilitate substitution reactions may also play a role, although it does not appear that a true *trans* effect can come into play.

The mechanism of Scheme 4 (which is somewhat specific to a $\text{Pt}(\text{II})/\text{Pt}(\text{IV})$ couple or something very closely related) suggests there might be some question whether we could replace $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$; but in fact there is ample evidence that we can. A number of reports have demonstrated oxidative functionalization of aliphatic C–H bonds using catalytic $\text{Pt}(\text{II})$ and stoichiometric oxidants such as chlorine [12], hydrogen peroxide [19], peroxydisulfate [20], and the anode of an electrochemical cell [21]. Most interesting are Wacker-like systems that use catalytic amounts of an oxidant that can in turn be reoxidized by dioxygen, making the latter the stoichiometric oxidant; significant numbers of turnovers have been achieved with both $\text{Cu}^{\text{II}}\text{Cl}_2$ [22] and a polyoxometalate [23]. Recently, a microfluidic device was used for rapid screening of methane oxidation by $\text{Pt}/\text{cocatalyst}/\text{O}_2$ combinations; $\text{Fe}(\text{III})$



Scheme 4

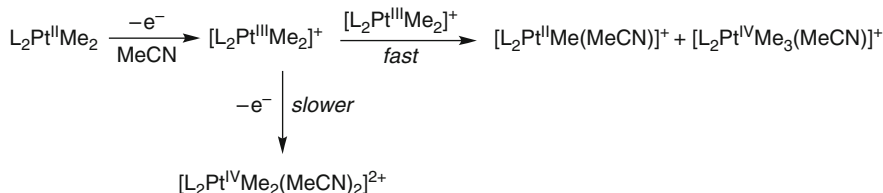
was found to be the best cocatalyst (a polyoxometallate also showed some success), giving a mixture of methanol and formic acid in up to 50 turnovers [24].

The successful use of these alternate oxidants implies that they rapidly oxidize RPt(II) while not oxidizing inorganic Pt(II). (H_2O_2 does not need to satisfy the second of these criteria: it is both an oxidant and a reductant, so a sufficient steady-state concentration of inorganic Pt(II) can be maintained, albeit at the cost of highly inefficient oxidant consumption [19].) Indeed, $\text{Cu}^{\text{I}}\text{Cl}$ has been shown to be oxidized by $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ [25], so the reverse reaction would not take place. The (relative) oxidation rates have been measured for several oxidants using the methods described above. Rather unexpectedly, $\text{Cu}^{\text{II}}\text{Cl}_2$ was found to oxidize $[(\text{CH}_3)\text{-Pt}^{\text{II}}\text{Cl}_3]^{2-}$ *faster* than $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$, by around an order of magnitude at 95°C ; $\text{Fe}^{\text{III}}\text{Cl}_3$ is somewhat less reactive [16].

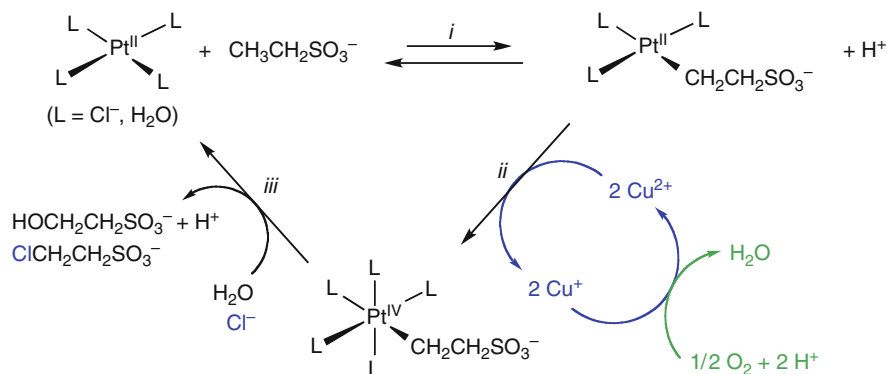
One might presume that $\text{Cu}(\text{II})$ acts as a one-electron oxidant, which would require a two-step oxidation sequence (the reaction of $\text{Cu}^{\text{I}}\text{Cl}$ with $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ appears from kinetics to be stepwise, although the results were not completely conclusive [25]), making this finding even more remarkable. Conceivably, the actual oxidant involves a cluster of $\text{Cu}(\text{II})$ centers, as has been suggested for other oxidations of Pt(II) by $\text{Cu}(\text{II})$, where the intermediacy of Pt(III) may appear unattractive [26]; similar considerations may apply to the reoxidation of Pd(0) in the Wacker system (a step that is not very well characterized mechanistically). Mixed Pt(II)–Cu(II) clusters are also known [27] and might play a part here. However, other one-electron oxidants such as $[\text{Ir}^{\text{IV}}\text{Cl}_6]^{2-}$ and $\text{Ce}(\text{IV})$, where such clustering seems most unlikely, also oxidize $[(\text{CH}_3)\text{Pt}^{\text{II}}\text{Cl}_3]^{2-}$ at rates competitive with protonolysis [16].

A two-step sequential sequence would imply an RPt(III) intermediate. Organoplatinum species in that oxidation state have been shown to be rather unstable in one system: oxidation of a (diimine) $\text{Pt}^{\text{II}}\text{Me}_2$ complex with ferrocenium affords only $\text{MePt}(\text{II})$ and $\text{Me}_3\text{Pt}(\text{IV})$ species, the result of disproportionation by methyl transfer. The two-electron oxidation products, $\text{Me}_2\text{Pt}(\text{IV})$, are observed only when electrochemical oxidation is carried out at higher potentials (Scheme 5) [28]. However, it is quite possible that the instability is largely due to the second methyl group and that a monomethyl-Pt(III) species might be sufficiently long-lived to undergo a second one-electron oxidation more efficiently.

The high reactivity of RPt(II) toward a variety of oxidants, while still unexplained, offers considerable encouragement for ultimately devising practical



Scheme 5

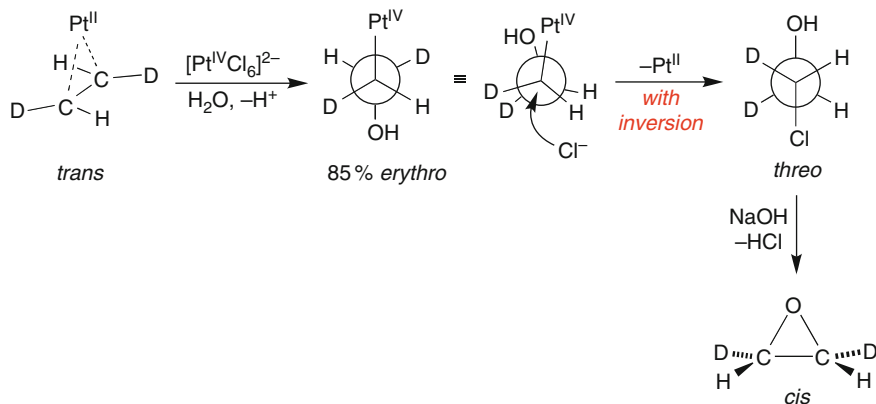


Scheme 6

applications of the Shilov chemistry. Unfortunately, O_2 by itself does not affect the needed rapid oxidation of $[\text{RPt}^{\text{II}}\text{Cl}_3]^{2-}$, although obviously it is thermodynamically competent to do so, since it reoxidizes $\text{Cu}(\text{I})$ to $\text{Cu}(\text{II})$ and the latter does oxidize $\text{RPt}(\text{II})$. (Oxidations of several N-ligated alkyl- $\text{Pt}(\text{II})$ species by O_2 have been observed; see Sect. 4.3) To date the most promising modification of the Shilov system has been the Wacker-like system of $[\text{Pt}^{\text{II}}\text{Cl}_4]^{2-}/\text{Cu}^{\text{II}}\text{Cl}_2/\text{O}_2$, which oxidizes water-soluble substrates such as ethylsulfonic acid and *p*-tolylsulfonic acid to the corresponding aliphatic alcohols and alkyl chlorides (Scheme 6), with turnover numbers in excess of 100 based on Pt [22, 29]. Of particular interest is the fact that these catalytic systems do not deactivate by precipitation of Pt metal, which is the eventual fate of virtually every experiment using the original Shilov system or most of the alternate oxidants enumerated above; instead, all of the Pt in solution is eventually converted to $[\text{Pt}^{\text{IV}}\text{Cl}_6]^{2-}$ [16, 29]. Since, as noted above, $\text{Cu}(\text{II})$ by itself is not capable of oxidizing $\text{Pt}(\text{II})$ to $\text{Pt}(\text{IV})$, there must be some stronger oxidant generated by the combination of Cu and O_2 under the reaction conditions; further mechanistic study on this catalytic combination might well prove rewarding.

2.2 Formation of R-X from $\text{RPt}(\text{IV})$

Stoichiometrically, the liberation of RX from $\text{R-Pt}(\text{IV})\text{-X}$ amounts to reductive elimination; however, mechanistically, there are issues. Does the reaction proceed directly from six-coordinate $\text{Pt}(\text{IV})$, or is prior dissociation of a ligand required? There have been extensive studies on the mechanism of reductive elimination from $\text{Pt}(\text{IV})$ in general, especially with regard to C–C bond formation, where preformation of a five-coordinate intermediate is required, although some (kinetically more favored) C–H eliminations from $\text{Pt}(\text{IV})$ appear to proceed directly



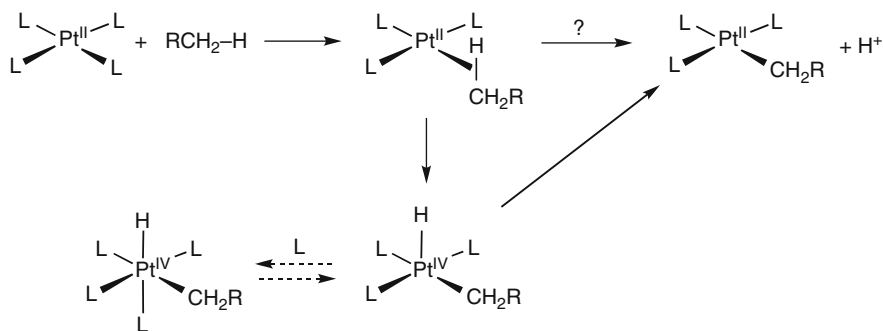
Scheme 7

from the six-coordinate state. This topic has been well reviewed [30] and is not further considered here.

For RX generation, there is the additional question of whether the C–X bond is formed via “straightforward” intramolecular reductive elimination, or by nucleophilic attack by external X^- . Model studies, such as Goldberg’s classic work with $(\text{dppe})\text{Pt}^{\text{II}}(\text{X})(\text{Me})_3$ complexes ($\text{X} = \text{I}$ or OR), all point toward external nucleophilic attack on a five-coordinate intermediate [31, 32]. Early work on the actual Shilov intermediate, $[(\text{CH}_3)\text{Pt}^{\text{IV}}\text{Cl}_5]^{2-}$, strongly supports external nucleophilic attack; for example, in the presence of added bromide, methyl bromide forms faster than the substitution of Br^- for Cl^- in the coordination sphere [33]. A later study demonstrated that Walden inversion accompanies formation of 2-chloroethanol from $[(\text{HOCH}_2\text{CH}_2)\text{Pt}^{\text{IV}}\text{Cl}_5]^{2-}$ (Scheme 7), a clear sign of nucleophilic displacement; it also provided evidence from kinetics that nucleophilic attack takes place at a five-coordinate intermediate, $[\text{RPt}^{\text{IV}}\text{Cl}_4]^-$ [13]. One implication of these findings, if they are indeed universal, is that a catalytic alkane functionalization scheme via any similar route will have to generate a $\text{Pt}(\text{IV})$ intermediate with at least one readily dissociable ligand – most probably in the position *trans* to the strongly labilizing R group – which may place additional constraints on viable candidates for such a catalyst.

3 Does C–H Activation in the Shilov System Involve $\text{Pt}(\text{IV})$ Intermediates?

Oxidative addition is the most common mode of reaction of C–H bonds with low-valent transition metal centers; but $\text{Pt}(\text{II})$, especially with hard ligands such as chloride and water, does not appear to be particularly low-valent or electron-rich. Hence, alternate mechanisms have been considered as perhaps more probable, the



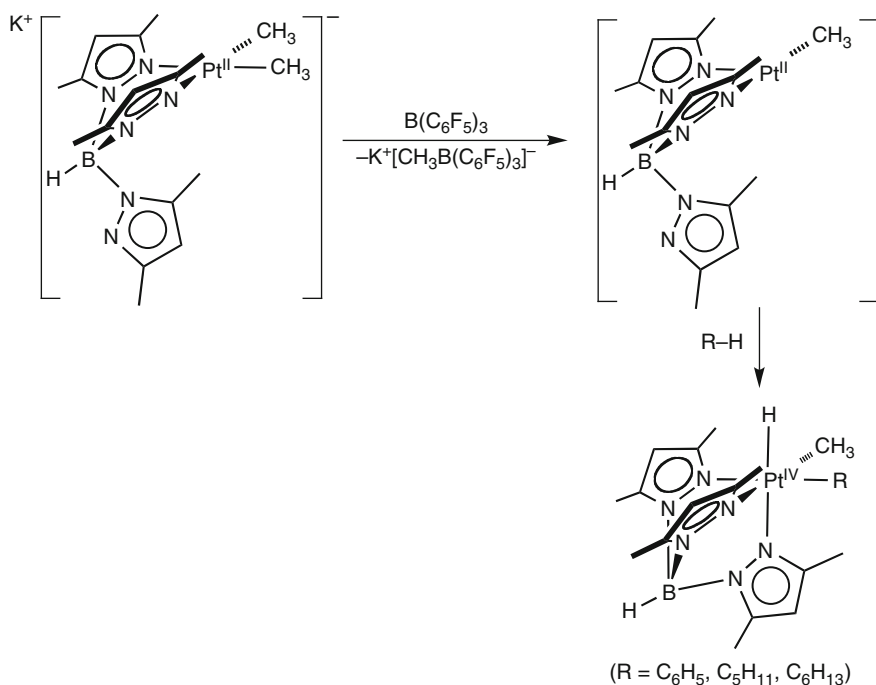
Scheme 8

most common being direct deprotonation of an alkane sigma complex, by analogy to the known acidity of dihydrogen sigma complexes. The two main alternatives (including the intermediacy of a sigma complex in the oxidative addition route, implicated in a very large number of studies on a variety of metal complexes), are shown in Scheme 8; other variants, such as something akin to the sigma bond metathesis mechanism common for d^0 complexes, could also be envisioned. Shilov's earliest papers postulated oxidative addition, on no particular grounds [2]; later he appeared to have changed his mind in favor of the sigma complex deprotonation route, again with no clear reason stated [11]. Another early paper proposed an "S_E2-mechanism with base assistance" [34]; most likely it would have been described as deprotonation of a sigma complex, but the possibility of the latter had not been recognized at the time.

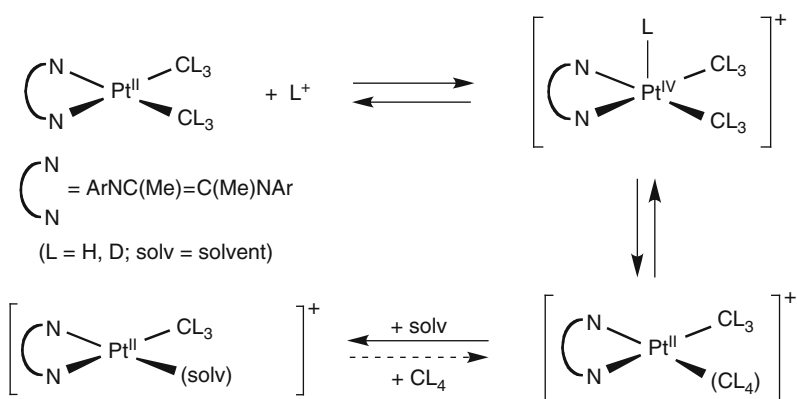
Of course, we now know that RPt(IV) hydrides can be isolated from reactions of alkanes at Pt(II) under the right circumstances, as first demonstrated by Goldberg (Scheme 9); here, the ambidentate nature of the Tp ligand facilitates stabilization of six-coordinate Pt(IV) [35]. However, assessing the generality of that route, and its applicability to cases where RPt(IV)H is *not* observable, is far from straightforward. It should be noted that there is a huge body of work, of which we can only scratch the surface, that bears on this question; we recommend that readers interested in a deeper exploration consult the afore-mentioned reviews (particularly the 2006 review by Lersch and Tilset [10], which is specifically devoted to this topic).

3.1 Studies on Protonolysis of R–Pt(II)

The daunting prospects of achieving direct experimental support for either alternative in the actual Shilov system, given the instability of the RPt(II) species formed, led us to an indirect approach involving study of protonolysis of ligand-stabilized RPt(II) complexes, models for the microscopic reverse of C–H activation. Depending on the choice of ligand L, solvent, and reaction temperature, we



Scheme 9



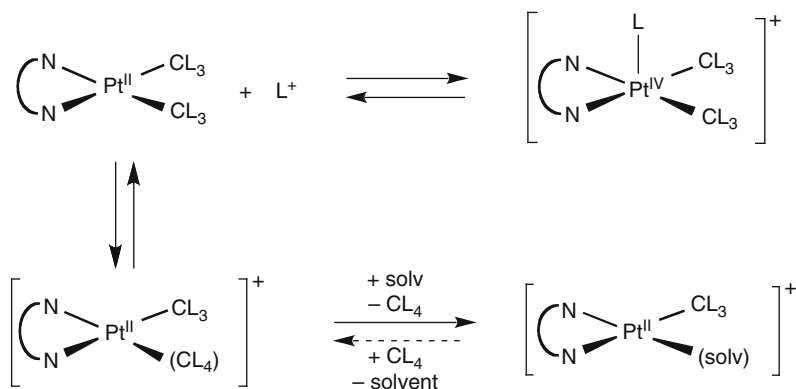
Scheme 10

observed (by NMR) a metastable $\text{RPt}^{\text{IV}}\text{H}$ prior to loss of methane; use of deuterated solvent often resulted in extensive H/D scrambling in the liberated alkane and, in some cases, the RPt^{IV} group as well [36]. Similar results have since been obtained for a number of other systems [10]. These results strongly support the mechanism shown in Scheme 10, involving protonation at Pt,

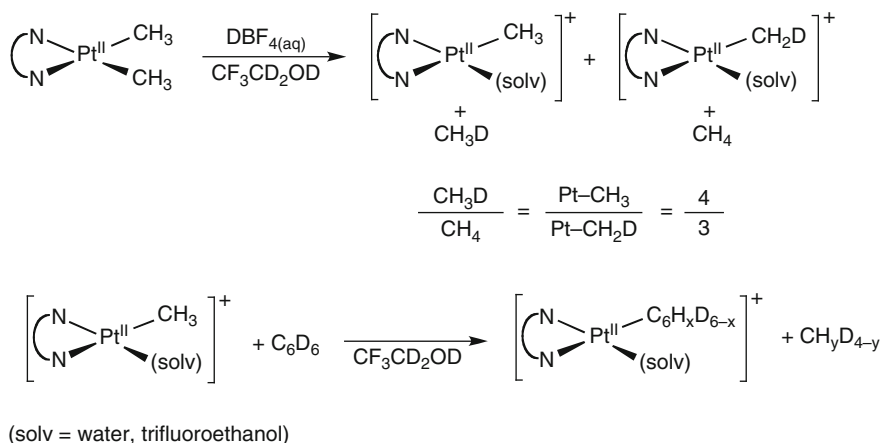
reductive coupling to form a sigma alkane complex, and dissociation of alkane; the reversibility of the first two steps accounts for the observed isotopic exchange, with the extent depending on the relative rates of the various processes. The principle of microscopic reversibility implies that C–H activation follows the oxidative addition route.

There are several caveats that must be kept in mind. First, of course, these studies were carried out on models, not the “real” Shilov system; conceivably, the use of stabilizing ligands could alter the mechanism. Some evidence against that possibility is provided by the observation of H/D exchange in the deuteryolysis of transiently generated $[(\text{CH}_3)\text{Pt}^{\text{IV}}\text{Cl}_5]^{2-}$ in CD_3OD (but not in D_2O , possibly because the loss of methane, which proceeds by associative displacement, may be considerably faster in the presence of the better ligand water), suggesting that the mechanisms are closely related [36]. On the basis of isotope distributions, Zamashchikov also argued for the intermediacy of an ethyl-Pt(IV) hydride in the loss of ethane accompanying decomposition of $[(\text{CH}_3)_2\text{Pt}^{\text{IV}}\text{Cl}_4]^{2-}$ [37]; his analysis relied on the (questionable) assumption of no isotope effect on alkane sigma complex stability.

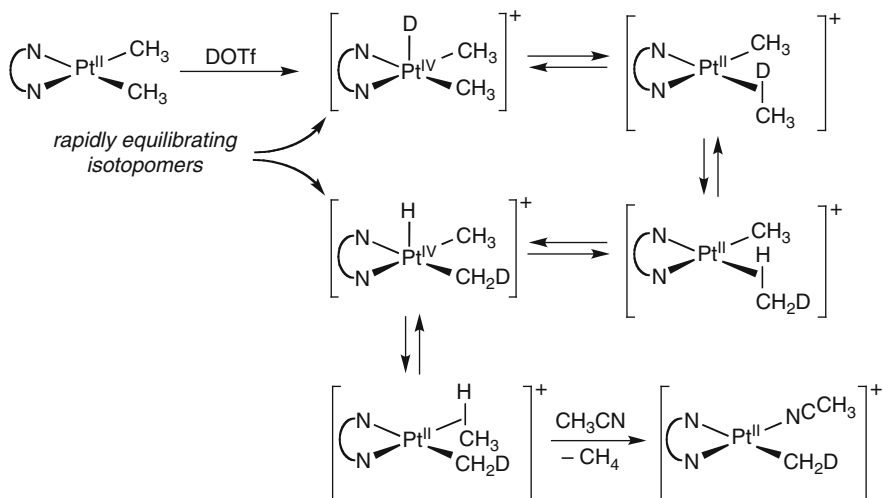
Another possibility is that the observed RPt(IV)H species do not actually lie on the main pathway. One could imagine a situation such as that shown in Scheme 11, where RPt(IV)H is formed reversibly but has nowhere else to go; protonolysis (and isotope exchange) proceed only via direct protonation of the Pt–C bond. This seems extremely unlikely, given the ample evidence of facile interconversion between M(R)(H) and $\text{M}(\eta^2\text{-RH})$ for the vast majority of C–H activation systems, but it is hard to exclude rigorously for the Shilov system. However, it can be ruled out for some of the model systems. Consider, for example, the two reactions shown in Scheme 12: the isotopic scrambling in the protonolysis (top) reaction [38] might conceivably follow the scenario of Scheme 11, but that in the benzene activation [39] clearly could not. Further support is provided by the reaction shown in Scheme 13, where the ratio of RPt(II) to RPt(IV)H products decreased with



Scheme 11



Scheme 12



Scheme 13

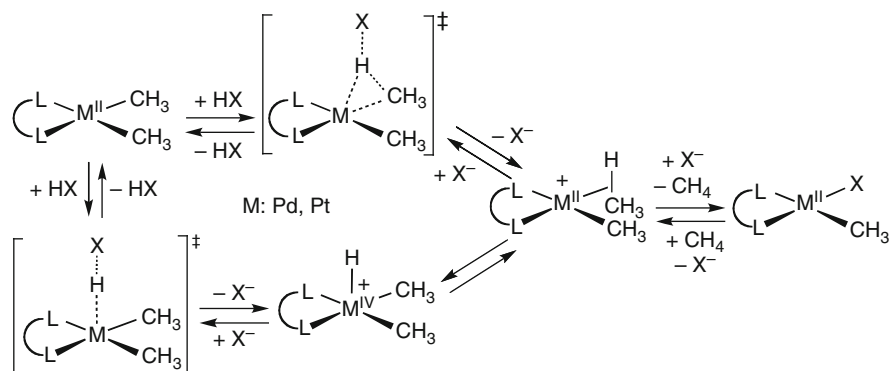
increasing amounts of trapping ligand MeCN. Such a result is consistent with reductive coupling of RPt(IV)H to $\text{Pt(II)}(\eta^2\text{-RH})$ competing with trapping, but not with the latter being the sole relevant intermediate on the protonolysis pathway [40].

A good deal of work has been invested in determining KIEs for protonolysis of metal alkyls, including those of Pt(II) , but definitive mechanistic conclusions have proven very hard to attain: there are just too many complications, as discussed by a number of commentators and well summarized in an earlier review [10]. Indeed, one of the leading researchers in this field, toward the end of a major paper surveying KIE and other experiments, comes close to giving up on the possibility

of distinguishing between the alternative mechanisms: “In conclusion, the similarity of the energy profiles . . . describing the coordinate reaction for a rate determining proton transfer to the substrate, suggests that, under these circumstances, any discussion of the site of proton attack risks becoming semantic in nature [41]”.

A more recent observation, however, may offer new opportunities: protonolysis of one particular Pt(II) complex, (COD)Pt^{II}Me₂, along with that of several related alkyl-Pd(II) species, was found to exhibit an abnormally large KIE, around 18 at room temperature [42]. Such a value is normally associated with the presence of a large tunneling component, a conclusion also supported by the large temperature dependence of the KIEs. No Pt(IV) hydride species could be detected on protonation at low temperature, nor was any H/D exchange observed, in contrast to the earlier studies on analogs with N-centered ligands; the KIE for one example of the latter, (tmeda)Pt^{II}MeCl, is normal in both room temperature value (around 4.4) and temperature dependence [43]. These results suggest, as a working hypothesis, that the appearance of KIEs, characteristic of tunneling, might be signaling a mechanistic switch: the earlier cases, with N- and P-centered ligands, proceed via protonation at metal to give RPt(IV)H, but the initial site of protonation in (COD)Pt^{II}Me₂ is the Pt–C bond to directly form an alkane complex, which loses alkane without ever going through a Pt(IV) species. This is consistent with the greater electron-withdrawing power of the π -accepting bis(olefin) ligand, in comparison to the stronger donor amine and phosphine ligands, as well as with the fact that abnormal KIEs are also observed with the Pd analogs, for which the tetravalent state will be less accessible.

Theoretical studies also agree with this proposal. DFT calculations on the above two examples indicate that the lowest-energy pathways for the two alternative mechanisms are those shown in Scheme 14. For (COD)Pt^{II}Me₂, the overall barrier calculated for the top pathway, protonation at Pt–C, is lower than that for the bottom one, protonation at Pt ($\Delta G^\ddagger = 26.9$ and 32.5 kcal/mol respectively), whereas for (tmeda)Pt^{II}MeCl, the reverse result is obtained (30.1 and 29.0 kcal/mol, respectively) [43]. To be sure, the differences are not large (especially for the latter case)



Scheme 14

and complicated by a number of features common to computational studies of this class of reaction (see following section), but the overall pattern is at least suggestive.

No experimental results for the actual Shilov system point clearly in any direction. Analysis of the methane obtained when $[\text{MePt}^{\text{IV}}\text{Cl}_5]^{2-}$ was reduced in a mixture of $\text{H}_2\text{O}/\text{D}_2\text{O}$ indicated a KIE around 9 at 0°C , a borderline number, and one whose interpretation is made more difficult by the possible involvement of so-called fractionation factors [36]. Further study, perhaps making use of the $[\text{MePt}^{\text{II}}\text{Cl}_3]^{2-}$ salt described above, might be worthwhile, although complicated by the necessarily heterogeneous reactions of this insoluble material.

3.2 Computational Studies on the Shilov System

Given the difficulty of obtaining direct experimental evidence as outlined above, computation would seem the obvious way to go. A useful and thorough review of computational studies on C–H activation has recently appeared [44]. However, there are problems here too, arising in particular from the fact that the reaction involves ionic species in water. Handling solvation often challenges computational chemists, especially when, as here, one may need to take into account hydrogen-bonding interactions of solvent molecules with coordinated ligands as well as more general effects. The first computational study to tackle the Shilov system recognized and devoted particular attention to these difficulties. For the actual C–H bond cleavage step, their DFT calculations predicted that two different mechanisms were very close in energy: the oxidative addition route via $\text{RPt}(\text{IV})\text{H}$ and a sigma bond metathesis-like mechanism in which an H atom of a coordinated methane transfers directly to an adjacent chloride. These are closely related to the reverse processes corresponding to the bottom and top mechanisms in Scheme 14, respectively; the calculations actually showed a small preference for the oxidative addition route, but the authors tended to prefer the other, although not definitively [45].

More recently, Ziegler has examined the effect of the detailed structure of the Pt species participating in C–H activation (which is, of course, not known from any definitive experimental results). The calculated transition state for C–H activation leads to the intermediate resulting from the oxidative addition mechanism; it is not clear whether the methodology used would have identified and compared any alternatives. For species $[\text{Pt}^{\text{II}}\text{Cl}_x(\text{H}_2\text{O})_{4-x}]^{(x-2)-}$, the rate-determining step was always found to be coordination of methane by ligand displacement, rather than the actual C–H activation itself [46] (contrary to the findings of the earlier study [45]). Replacing chloride with other anionic ligands leads to a decreased barrier for methane coordination (and hence for the overall reaction) as the ligand becomes a stronger *trans* director; but for really strong ones, such as cyanide, the C–H activation barrier increases and becomes rate-limiting [47]. A subsequent study examined the effect of neutral ligands (alcohols, amines, and phosphines) and reached a similar conclusion [48].

These latest results imply that direct study of the kinetics of C–H activation in the original Shilov system to probe the participation of Pt(IV) would be not only extremely difficult, as has already been remarked, but also largely irrelevant, since that step is apparently rarely, if ever, rate-determining. Indeed, most of the mechanistic studies, as well as of the attempted approaches to a more practical alkane functionalization catalyst, have been directed at ligand-substituted Pt(II) complexes, the subject of the following sections.

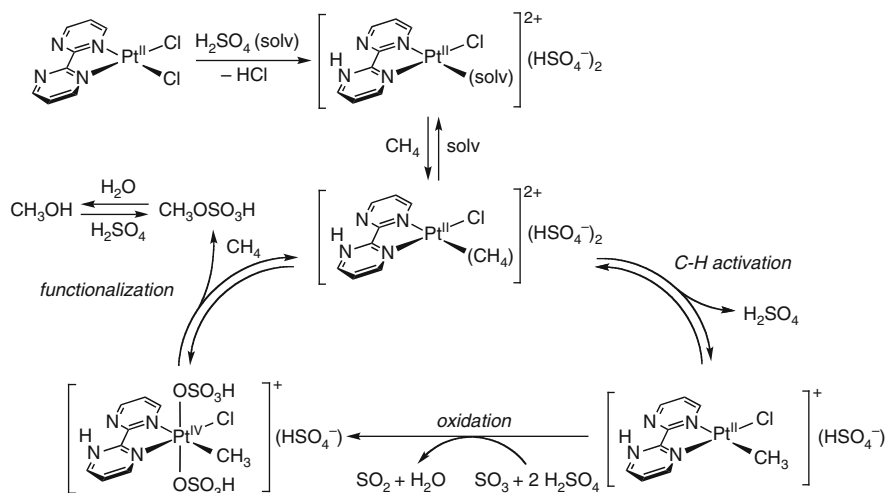
4 Pt(IV) in Alkane Activation and Functionalization by Ligand-Substituted Complexes

In the discussion of mechanistic studies of protonolysis, the microscopic reverse of C–H activation, it was noted that the requirement for complexes bearing stabilizing ligands raises a potential issue: to be comfortable with the implicit assumption that these species *really* do model the Shilov system, one should show that they can themselves effect C–H activation. The first such demonstration was achieved using $[(\text{tmeda})\text{Pt}^{\text{II}}\text{Me}(\text{C}_5\text{F}_5\text{N})]^+$, which reacts with benzene at 85°C to give methane and the corresponding phenyl complex, taking advantage of the weakly coordinating (and hence readily displaced during alkane coordination) pentafluoropyridine ligand [49]. A large number of related examples followed, of which the cationic complexes $[(\text{diimine})\text{Pt}^{\text{II}}\text{Me}(\text{TFE})]^+$ (TFE = $\text{CF}_3\text{CH}_2\text{OH}$) [50] have perhaps been the most fruitful in terms of mechanistic study, while $(\text{bipym})\text{Pt}^{\text{II}}\text{Cl}_2$ (bipym = bipyrimidine) [51] is unquestionably the most encouraging in terms of potential practical applicability. Again, we have space only to highlight a small fraction of this work.

4.1 The Catalytica System

Following up on their earlier report of surprisingly selective mercury-catalyzed oxidation of methane to methyl bisulfate by sulfuric acid (which was also the reaction medium) [52], Periana and coworkers discovered that a bipyrimidine complex of Pt(II) worked even better, generating the same product in over 70% yield – a remarkable achievement, given that “selective” oxygenation of methane to methanol or derivatives thereof rarely surpasses yields of a few percent. A mechanism closely akin to that of the Shilov system was proposed (Scheme 15), with SO_3 replacing Pt(IV) as the oxidant to convert RPt(II) to RPt(IV) ; whether the initial C–H activation involved an RPt(IV)H intermediate or not was left an open question [52].

As with the Shilov system (even more so, given the conditions: typically around 200°C in fuming sulfuric acid!), a direct experimental assault on the mechanism



Scheme 15

seems unattractive; but several groups have addressed the problem through computational studies, on both the actual bipym catalyst and the simplified analog $(\text{NH}_3)_2\text{Pt}^{\text{II}}\text{Cl}_2$. Perhaps not too surprisingly, the conclusions depend on the structure of the activating complex, which is not known experimentally; besides the question of whether chloride remains attached to Pt or is replaced by bisulfate, there is the further issue of whether the free N centers of the bipym ligand are un-, singly, or doubly protonated, and whether the bisulfate ligand (if present) is further protonated to become coordinated sulfuric acid, in such a strongly acidic medium. One study found that the oxidative addition path is slightly favored if the precursor methane complex is $[(\text{bipym})\text{Pt}^{\text{II}}\text{Cl}(\text{CH}_4)]^+$, whereas a deprotonation route is substantially favored if it is $[(\text{bipym})\text{Pt}(\text{OSO}_3\text{H})(\text{CH}_4)]^+$. The authors came down in favor of a nonoxidative route via $[(\text{bipymH}_2)\text{Pt}^{\text{II}}(\text{OSO}_3\text{H})]^{3+}$ [53]. Another group argued that the methane-activating complex has a chloride, not a bisulfate ligand, and an unprotonated bipym, but agreed that the deprotonation route is preferred, avoiding a discrete Pt(IV)–H intermediate [54]. More recent calculations by that group, however, seem to prefer the oxidative addition route [55]. Both groups, as well as another [56], find that the barrier to coordination of methane is higher than that for C–H activation, as in most of the findings for the Shilov system itself (see above). An attempt to assess the probable effect of protonation of a free N in bipym by comparing the reactivity (for H/D exchange) of the N-methylated complex was thwarted by the facile demethylation observed under reaction conditions [57].

There appears to be considerable residual uncertainty about the detailed course of C–H activation – probably not too surprising, in view of the difficulty of dealing with solvation and related issues in this far-from-innocent medium. It is perhaps more important to note that all of these studies indicate that – in *contrast*

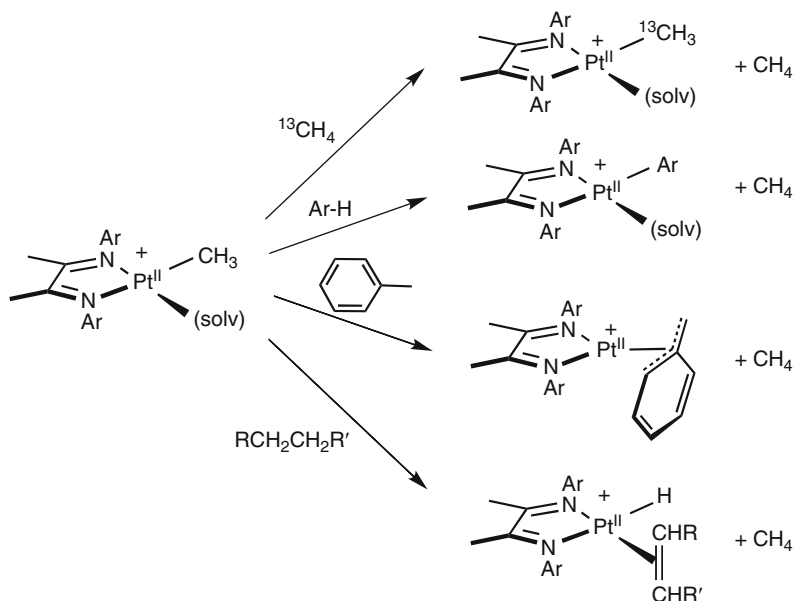
to the original Shilov system – oxidation of RPt(II) to RPt(IV) is rate-limiting, although the calculated relative barrier heights can depend to a significant extent on the exact nature of the catalytic intermediates; as might be expected, protonation of a ligand makes oxidation considerably more difficult [56]. Such sensitivity to positive charge has also been observed in related experimental studies: $[(\text{diimine})\text{Pt}^{\text{II}}\text{Me}(\text{solvent})]^+$ is much more difficult to oxidize than the corresponding neutral $(\text{diimine})\text{Pt}^{\text{II}}\text{Cl}_2$, despite the fact that replacing Cl with Me generally makes oxidation much more favorable [18]. The prediction that oxidation is the slow step also accords with the experimental observations that H/D exchange is much more pronounced for the Catalytica system and that $(\text{NH}_3)_2\text{Pt}^{\text{II}}\text{Cl}_2$ is actually *more* active, at least initially, than the bipym catalyst [52], since all the calculations suggest that the bis(amine) catalyst is more readily oxidized to Pt(IV). Unfortunately, it is much less stable, decomposing within minutes under reaction conditions (one set of calculations [58] even indicates that methane coordinates by displacing an ammonia ligand, which would be expected to be detrimental to stability). Because one of the drawbacks to the Catalytica system that make it uncompetitive with existing technology for converting methane to methanol (via syngas) is the low rate, these findings suggest an approach to optimization, by designing ligands that improve access to Pt(IV) without sacrificing the stability to harsh reaction conditions imparted by bipym. Unfortunately, to date no such combination has been developed.

Lowering the barrier for C–H activation *should* give an improved H/D exchange catalyst; following leads provided by computation, Periana showed that a Pt(II) picolinate complex catalyzes exchange between C_6H_6 and CF_3COOD at 70°C , about 300 times faster than the original bipym-based complex [59]. It is worth remarking, though, that the observation of aromatic H/D exchange in the presence of a combination of a metal complex and an acid does *not* necessarily demonstrate that C–H activation is taking place at the metal; it is at least conceivable that simple acid-catalyzed exchange could be involved, resulting from lowering the $\text{p}K_{\text{a}}$ of the acid by coordination to the metal. Only rarely have explicit tests of such a possibility (for example, by changing the acid strength of the D source [60]) been carried out.

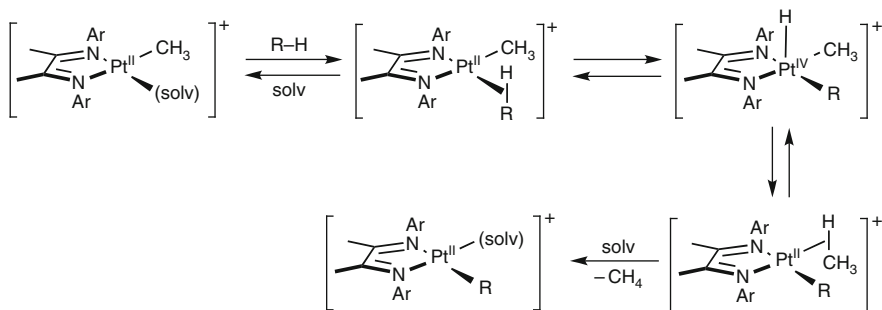
Another limitation is the fact that the reaction requires fuming sulfuric acid; the catalyst is deactivated by even small amounts of water (a reaction byproduct). One explanation, based on calculations, is that the presence of SO_3 is required because H_2SO_4 is not a competent oxidant [56]; another suggests that coordination of methane is much more facile when it occurs via displacement of a protonated H_2SO_4 ligand rather than water [55]. The introduction of an ionic liquid cosolvent has been proposed to circumvent the problem; experimental [61] and theoretical [62] studies (not including the bipym ligand in either case) have been reported for that approach, which shows some modest improvement in stability to water, but with no clear indication of why it works. (Still another economic hurdle is the cost of carrying huge quantities of sulfuric acid through a multistep process; there does not appear to be any way to fix that through better understanding of mechanism.)

4.2 Stoichiometric C–H Activation at Ligated Pt(II)

As noted above, a good deal of mechanism-oriented work has been carried out on C–H activation reactions of $[(\text{diimine})\text{Pt}^{\text{II}}\text{Me}(\text{TfE})]^+$, which as shown in Scheme 16 can lead to a variety of products: isotopic methyl exchange with $^{13}\text{CH}_4$ [63]; aryl complexes with arenes [39, 50]; η^3 -benzyl complexes with alkyl-substituted arenes [38, 64]; and cationic olefin hydride complexes with linear or cyclic alkanes [65]. Studies strongly indicate a common basic mechanism (Scheme 17), in which the C–H activation step proceeds via oxidative addition to give an RPt(IV)H intermediate – demonstrated, for example, by the isotopic exchange shown in Scheme 12 above.



Scheme 16



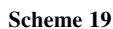
Scheme 17

For the latter, one *could* invoke instead a sigma bond metathesis-like mechanism (also described as a sigma-complex-assisted metathesis, or σ -CAM), in which H or D passes from Ar–H to R without ever *completely* breaking all C–H bonds, thus avoiding a discrete Pt(IV)–H intermediate. Calculations suggest such a process might be favorable for the case of activation of benzene by a phenyl complex, where the isotopic scrambling takes place between two aryl groups, although in such a case the involvement of *p* orbitals at *both* sites was thought to play a key role; for alkane activation, the oxidative addition pathway would be more likely [66]. It might be noted that a Pt(IV) hydride can be observed (stabilized by coordination of acetonitrile as a sixth ligand) during low-temperature protonolysis of a diphenyl complex [67]. Calculations accompanying experimental study of the gas-phase reaction of $[(\text{bipy})\text{Pt}^{\text{II}}\text{Me}]^+$ with $\text{C}_6\text{D}_x\text{H}_{6-x}$ showed no strong preference for either of the two mechanisms [68].

In any case, it is usually formation of the sigma complex $\text{Pt}(\text{II})(\eta^2\text{-R-H})$ and *not* the actual C–H activation that is rate-determining; interconversion between the sigma complex $\text{Pt}(\text{II})(\eta^2\text{-R-H})$ and $\text{RPt}(\text{IV})\text{H}$ is typically quite rapid. Only for the formation of aryl complexes of sterically undemanding diimine ligands is there evidence for rate-determining C–H activation, presumably because of the better coordinating ability of arenes [39]. In the large majority of cases – in particular, all that involve aliphatic C–H bonds – formation of a sigma complex by displacement of coordinated solvent is the slow step. (Formation of an alkyl-Pt(IV)H has been calculated to be the most energetically demanding step in the case of intramolecular benzylic C–H activation, but there the formation of the sigma complex is relatively much more favorable, as an agostic interaction [69].) Hence, while a wide array of interesting mechanistic complexities and subtleties are revealed in these studies, they are mostly unrelated to the behavior of the Pt(IV) intermediates.

More recently, C–H activation has been extended to inorganic Pt centers, better analogs of the original Shilov system, although the chemistry is limited to substrates that lead to π -stabilized products – η^3 -benzyls, η^3 -allyls, or other chelated alkene-hydrocarbyls. Dicationic $[(\text{diimine})\text{Pt}^{\text{II}}(\text{TFE})_2]^{2+}$ reacts with ethylbenzene (but not toluene!) and other arenes and olefins as shown in Scheme 18 [70]; a similar set of transformations can be effected by the dimers $[(\text{diimine})\text{Pt}(\mu_2\text{-OH})_2]^{2+}$ [71]. The reactions are generally considerably slower than the corresponding reactions of $[(\text{diimine})\text{Pt}^{\text{II}}\text{Me}(\text{TFE})]^+$, reflecting tighter binding of TFE to the dicationic Pt(II) center, which slows coordination of the C–H bond by ligand displacement. One might expect the C–H activation step to be slower as well, assuming that the oxidative addition route continues to operate; however, there is no evidence that it ever becomes rate-limiting. Hence, again, this chemistry does not provide much access for probing the detailed involvement of high-valent Pt.

Vedernikov has made extensive use of ambidentate (or “semilabile”) ligands to modulate interconversion of Pt(II) and Pt(IV) species, exploiting the same principle as the $(\kappa^2\text{- or } \kappa^3\text{-Tp})\text{Pt}$ example discussed earlier, where a dangling arm in a Pt(II) precursor coordinates to and stabilizes a Pt(IV) product. A dimethyl-Pt(II) complex of a sulfonated dipyridyl ligand not only undergoes facile H/D exchange with deuterated solvent, but can be converted to a stable Pt(IV) hydride in a nonpolar

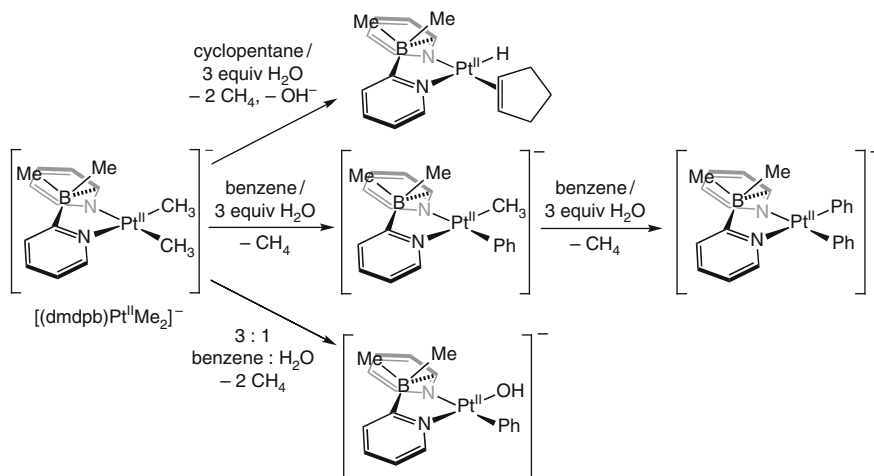


While C–H activation has not been reported for complexes based on dmpps, it has been observed with a dimethyldi(2-pyridyl)borate ligand, even though it lacks the

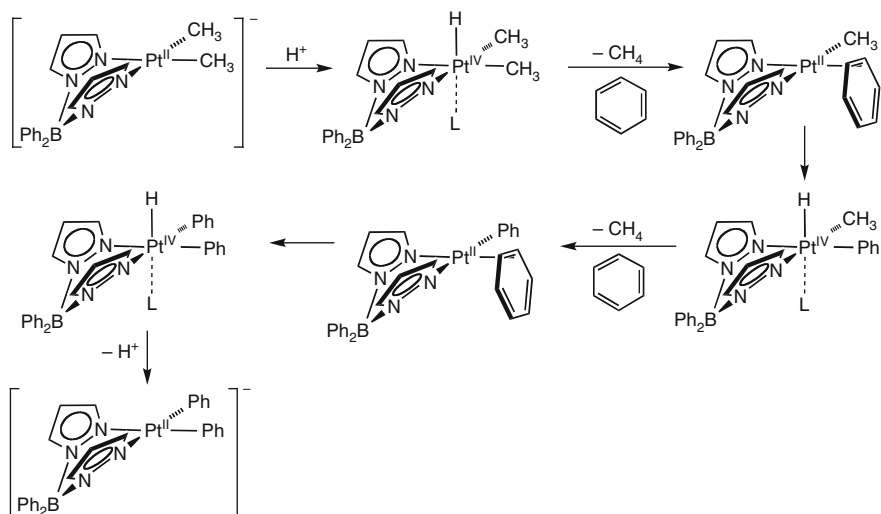
potentially coordinating extra arm: in the presence of small amounts of water, $[(\text{dmdpb})\text{Pt}^{\text{II}}\text{Me}_2]^-$ reacts with benzene or cycloalkanes to afford the products shown in Scheme 20. The reaction is thought to proceed via protonation to Pt(IV) H followed by reductive coupling, loss of methane, and activation of C–H by the resulting Pt(II) center; in the absence of an appended ligating group, the Pt(IV) intermediates are probably stabilized by coordination of hydroxide. That proposal is supported by the fact that the reaction rate is highly dependent on the counterion, being much faster for the Na^+ than $^n\text{Bu}_4\text{N}^+$ salt [73]. Perhaps the most interesting aspect of the dpms and dmdpb systems is their support of facile oxidation by O_2 , which is covered in the next section.

Structurally related species that exhibit C–H activation include the bis(pyrazolyl) borate complex in Scheme 21, for which (as in the above dmdpb system) protonation (or methide abstraction) generates an intermediate that reacts readily with benzene [74]; the bis(azaindolyl)methane complex in Scheme 22, which activates both aromatic and benzylic C–H bonds [75, 76] (some stable Pt(IV) complexes based on the same architecture have also been isolated and shown to undergo reductive elimination of MeX [77]); and complexes based on anionic bidentate ligands such as 2-(2'-pyridyl)indolide [78]. Intramolecular C–H activation was observed for one example of a series of *N*-heterocyclic carbene complexes of Pt(II); distortions induced by steric crowding appear to influence reactivity strongly [79].

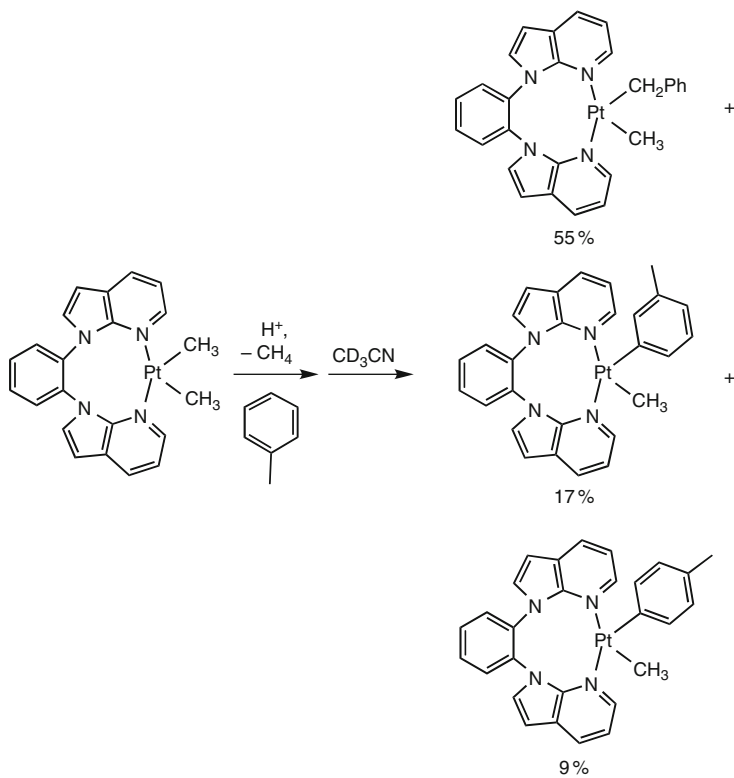
A substantial body of C–H activation chemistry can be initiated by reductive elimination from Pt(IV) species: either of ethane from stable, five-coordinate (β -diketiminate) $\text{Pt}^{\text{IV}}\text{Me}_3$ or of alkane from six-coordinate $\text{TpPt}^{\text{IV}}\text{HR}_2$. In some cases, usually involving arene activation, new stable Pt(IV) products are obtained; the course of benzene activation by the TpPt system has been examined theoretically [80]. For alkane activation, the final product is often a Pt(II)–olefin hydride



Scheme 20



Scheme 21



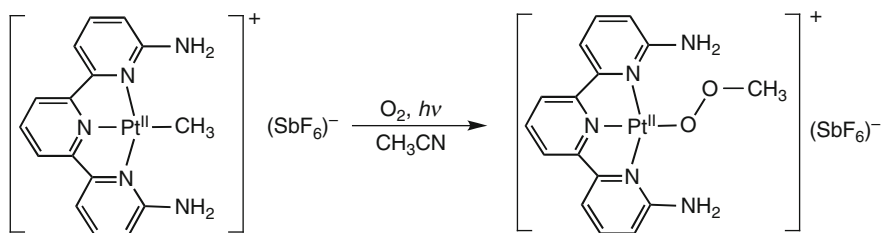
Scheme 22

complex resulting from β -hydride elimination, but there is no reason to doubt that the actual C–H activation involves oxidative addition to give an RPt(IV)H intermediate. This work has been the main topic of an earlier review [81] as well as another chapter in this volume [82] and is not examined further here.

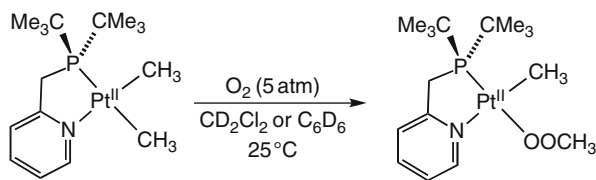
4.3 Oxidation by Dioxygen

Only a very few oxidations of inorganic Pt(II) to Pt(IV) by O_2 have been reported (reviewed in [9], as well as a more recent feature article on O_2 oxidations [83]); as noted earlier, the Shilov intermediate, $[(\text{CH}_3)\text{Pt}^{\text{II}}\text{Cl}_3]^{2-}$, is not oxidized (at least not rapidly) by O_2 either. In contrast, N-ligated complexes of alkyl- Pt(II) , especially ones having two methyl groups, show much greater reactivity toward O_2 . Presumably, this reactivity is largely a consequence of the electron-donating power of methyl substituents (as well as the N-centered ligand); unquestionably methyl substituents do foster oxidizability. For example, electrochemical oxidation of $(\text{diimine})\text{Pt}^{\text{IV}}\text{Me}_4$ (which ultimately leads to homolytic Pt-Me cleavage) is just about as easy as that of $(\text{diimine})\text{Pt}^{\text{II}}\text{Me}_2$, even though the complexes are formally Pt(IV) and Pt(II) , respectively [84].

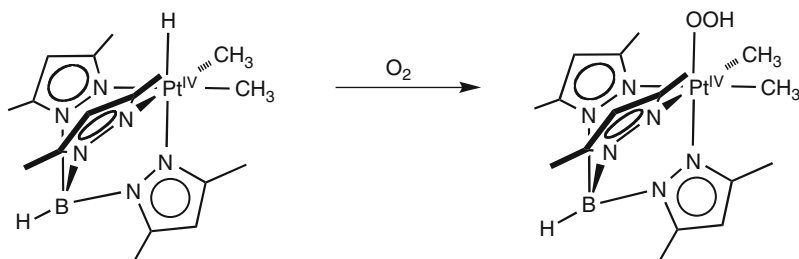
Reactions of $\text{Me}_x\text{Pt(II)}$ with O_2 can be classified into two groups: those in which O_2 inserts into a Pt-C bond and those in which Pt(IV) is generated. (A somewhat fanciful biochemical analogy would be to call these oxygenase-like and oxidase-like, respectively.) There are two well-characterized examples of the former, both light-promoted. The first (Scheme 23) involves a cationic monomethyl- Pt(II) species, which is not expected to be easily oxidized, and indeed there is no indication that any Pt(IV) species is involved; rather it appears that the terpyridine-based ligand sensitizes generation of singlet oxygen, which undergoes insertion much as an olefin might; the resulting methylperoxo complex is also light-sensitive, decomposing to formaldehyde and Pt-OH [85]. The second (Scheme 24) is much slower and probably proceeds via a radical chain pathway (the ligand in this case is unlikely to support formation of singlet O_2); again there is no evidence for participation of Pt(IV) [86]. Insertion of O_2 into a Pt(IV)-H bond is also known (Scheme 25); the



Scheme 23



Scheme 24

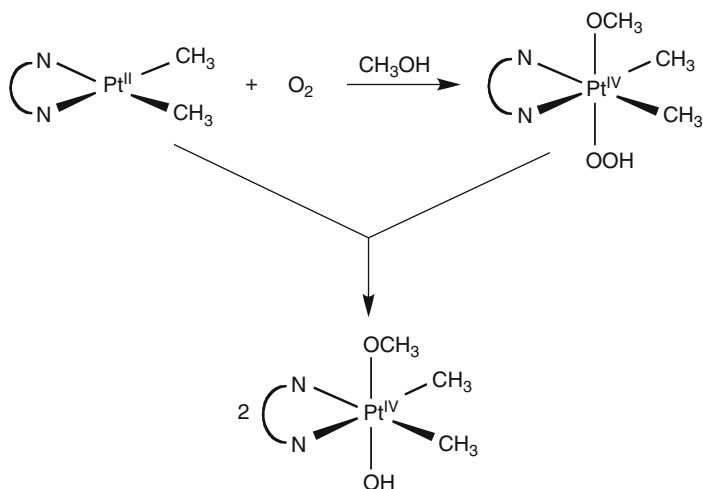


Scheme 25

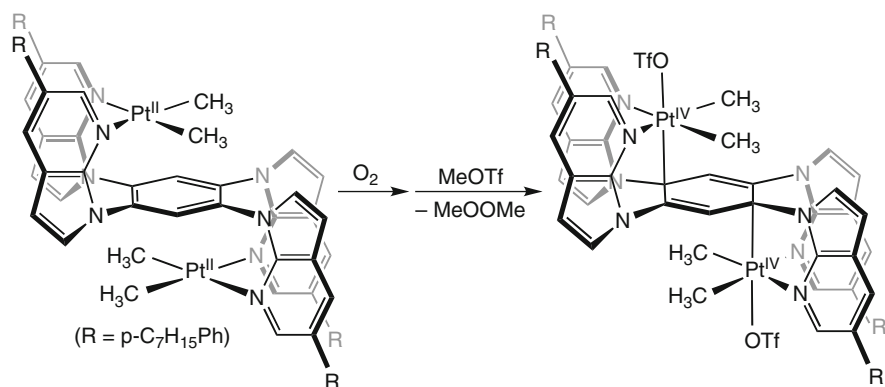
initially proposed radical chain pathway [87] has been confirmed by recent detailed mechanistic studies [88].

Oxidation to Pt(IV) by O_2 was first reported for $(\text{tmeda})\text{Pt}^{\text{II}}\text{Me}_2$ and related (phen) and (diimine) complexes; the reaction proceeds by the two-step sequence shown in Scheme 26. Neither the monomethyl $((\text{tmeda})\text{Pt}^{\text{II}}\text{MeCl})$ nor the diphenyl $((\text{tmeda})\text{Pt}^{\text{II}}\text{Ph}_2)$ analog reacts with O_2 . The mechanism of formation of intermediate Pt(IV)–OOH is not clear; observation (under some conditions) of highly colored species suggests a radical pathway, although (in contrast to the above insertion reactions) there does not appear to be any effect of light [89, 90]. A dimeric Pt(II) complex of a related ligand has recently been reported to react with O_2 ; while the product was not clearly characterized, it reacts further with MeOTf to produce dimethyl peroxide and a new Pt(IV) dimer (Scheme 27) [91]. $(\text{Me}_3\text{TACN})\text{Pt}^{\text{II}}\text{Me}_2$ is oxidized by (moist) air to give a cationic Pt(IV) hydroxo complex, $[(\text{Me}_3\text{TACN})\text{Pt}^{\text{IV}}(\text{OH})\text{Me}_2]^+$ [92].

As noted earlier, the semilabile ligand systems introduced by Vedernikov exhibit interesting O_2 chemistry [83]. The dimethyl-Pt(II) complex, $[(\text{dmeps})\text{Pt}^{\text{II}}\text{Me}_2]^-$, is the most reactive, undergoing oxidation to Pt(IV) in minutes at room temperature in water [72]. The related monomethyl analogs $(\text{dmeps})\text{Pt}^{\text{II}}\text{Me}(\text{HX})$ react similarly but more slowly, probably because they are neutral (actually zwitterionic); it is probable that O_2 actually reacts with a small equilibrium concentration of the corresponding conjugate base $[(\text{dmeps})\text{Pt}^{\text{II}}\text{MeX}]^-$ [93, 94]. The mechanism of oxidation appears to be similar to that of the related tmeda system, involving an intermediate Pt(IV)–OOH species that oxidizes another molecule of Pt(II). In all cases, the stereochemistry of the product corresponds to addition of OH and coordination of the sulfonate arm in the original axial positions of the Pt(II) square planar complex (Scheme 28). The analogous phenyl complexes are similarly oxidized by O_2 , but more slowly [95]. $(\text{dmeps})\text{Pt}(\text{II})(\text{olefin})$ complexes also react with O_2 ; here (as in the oxidation of Zeise's



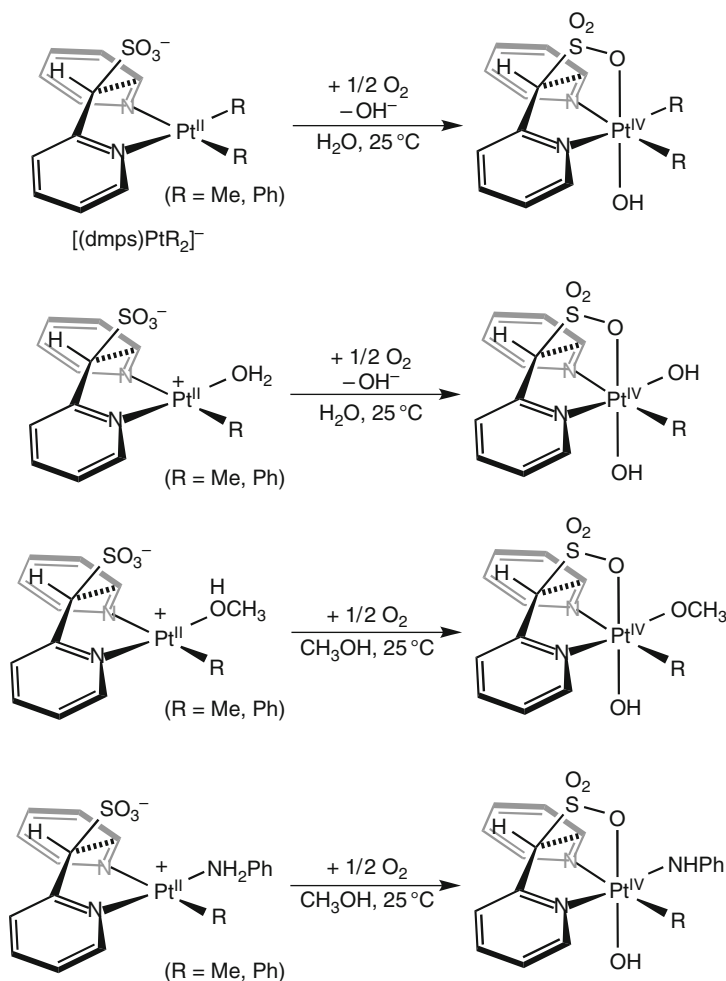
Scheme 26



Scheme 27

salt, discussed earlier), the reactive species are (2-hydroxyalkyl) $\text{Pt}(\text{II})$ complexes, and products include (2-hydroxyalkyl) $\text{Pt}(\text{IV})$, $\text{Pt}(\text{IV})$ -oxetanes, or epoxides, depending on the olefin and reactions conditions [96, 97].

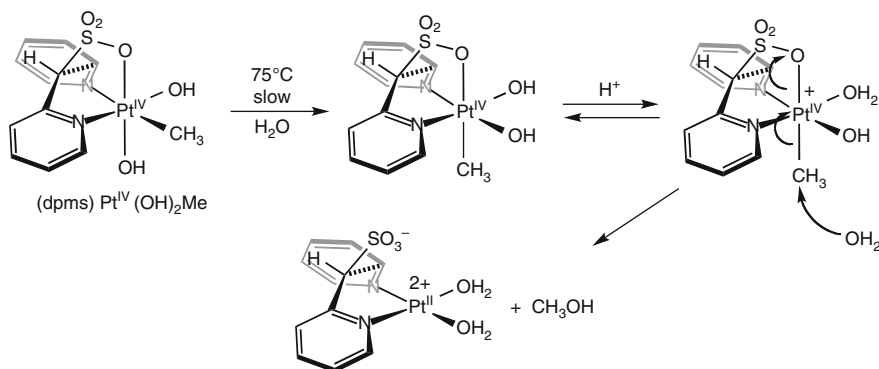
Reductive elimination of methanol, the last step in a hypothetical methane functionalization scheme, can be observed from the monomethyl- $\text{Pt}(\text{IV})$ species, but only at elevated temperature; mechanistic studies indicate that the formation of methanol is preceded by isomerization, as shown in Scheme 29 [73]. This finding is in accord with earlier studies on C–X bond formation, which require dissociation of a ligand *trans* to the alkyl group before nucleophilic attack at C in the five-coordinate intermediate. The original oxidation product has a pyridine ligand *trans* to



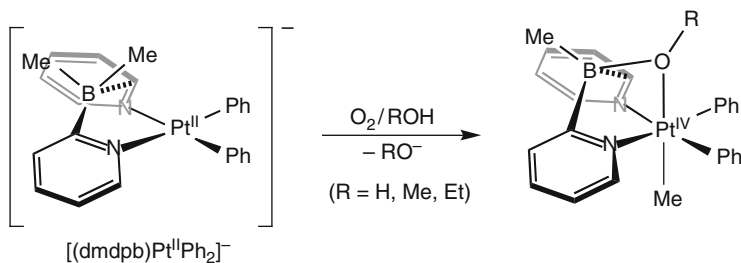
Scheme 28

methyl, strongly disfavoring dissociation. Protonation of a hydroxy ligand is also required; no methanol forms in neutral solution. Some of the C–O bond formation involves a bimolecular pathway, in which OH (or OMe, in which case some dimethyl ether is formed) coordinated to one Pt attacks a methyl group on another.

The related complex $[(dmdpb)Pt^{II}Ph_2]^-$ likewise reacts readily with O_2 in alcoholic solvent, but in a very different manner: a methyl group moves from B to Pt, leaving an opening for RO to add to B and occupy the sixth coordination site in the Pt(IV) product (Scheme 30) [98]. Presumably the absence of a potential sixth ligand in intact dmdpb (in contrast to dpms) accounts for this unexpected behavior. No C–X bond formation has been reported for this system.



Scheme 29



Scheme 30

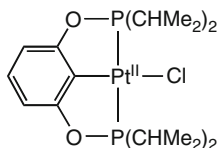
5 Conclusions and Prospects

Obviously, the main reason for interest in all of this chemistry is the potential for mild, selective, catalytic functionalization of alkanes. There have been a number of transformations based on C–H activation at Pt, including a stoichiometric dehydrogenation in a natural product synthesis [99] and some hydroarylations of olefins [100, 101]. With regard specifically to catalytic oxidative functionalization via high-valent Pt intermediates, while many examples of the individual steps that would likely be involved in such processes – activation of C–H, redox chemistry of alkyl-Pt species, formation of C–X bonds, as well as dehydrogenation – have been demonstrated and (reasonably) well understood mechanistically, finding a single system that can effect *all* of them sufficiently well to add up to a practical catalyst remains elusive. There are, of course, systems that are catalytic, but not yet practical: the original Shilov system is too slow and unstable; the catalyst in the Catalytica system is stable, but the reaction is still too slow, and there are other problems as discussed earlier. Incorporation of ligands often improves one step, but only at the cost of retarding another.

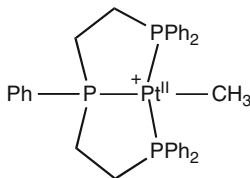
Two issues seem to be ubiquitous. First, the redox chemistry needs to be finely balanced: oxidation of RPt(II) has to be fast to compete with protonolytic cleavage and selective, so that the Pt(II) species that activates the C–H bond is not itself oxidized. Second, the RPt(IV) species has to be able to undergo facile dissociation, so that a five-coordinate intermediate needed to facilitate nucleophilic C–X bond formation is readily accessible; for complexes of multidentate ligands, this criterion will probably require the ability to isomerize easily, as in Scheme 29 above. And, of course, all of this must be achieved within the context of maintaining a Pt(II) center capable of activating the C–H bond.

Nonetheless, recent accomplishments provide ample grounds for encouragement. For example, C–H bonds can be activated by aquo- and hydroxo-Pt(II) complexes (Scheme 18). The oxidation/functionalization sequence of Schemes 28 and 29 ends by producing such a complex; while complexes of the dmfs ligand do not also effect C–H activation, it does not seem unreasonable that some other ligand might support all of the steps. One possibly promising approach is the introduction of “pincer” ligands, which have been shown to have interesting properties in C–H activations and other chemistry involving metals other than Pt. The pincer complex in Scheme 31 was shown to catalyze oxidation of 1-propanol to a mixture of 1,3- and 1,2-propanediol, using H_2O_2 as oxidant and Pt(IV) or Cu(II) as cocatalyst – an interesting result, although there are several limitations: only a few turnovers could be obtained; the combination of Cu(II) and O_2 did not work; and the pincer ligand itself is partially chlorinated under reaction conditions [102]. The cationic pincer complex $[(\text{triphos})\text{Pt}^{\text{II}}\text{Me}]^+$ shown in Scheme 32 undergoes facile protonolysis even with very weak acids, in contrast to cationic methyl complexes that lack the tridentate ligand structure; the enhanced reactivity was attributed to torsional strain [103], which (by microscopic reversibility) could conceivably be exploited to accelerate C–H activation reactions as well.

In addition, of course, many of the principles established for Pt may be (and have been) extended to other metals, Pd in particular; we do not have space to address



Scheme 31



Scheme 32

any of that comparative chemistry here. With the high level of current research activity, including the continuous introduction of novel ligand architectures, it seems highly probable that the right combination of metal, ligand, and reaction-environment will eventually pay off.

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