

Chapter 15

C-H Bond Activation at Pt(II): A Route to Selective Alkane Oxidation?

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A hypothetical catalytic cycle for the selective oxidation of alkanes to alcohols by dioxygen may be based on the activation to C-H bonds at Pt(II) centers, coupled with additional known organoplatinum chemistry. Mechanistic studies on the C-H activation process offer guides for designing potential for catalytic species.

Introduction

The selective functionalization of alkanes has been identified, in an oft-cited review article,¹ as one of the Holy Grails² of C—H bond activation research. The activation (under mild conditions) of alkane C—H bonds had itself long been considered a challenging goal; but the last two decades, inspired in large part by Halpern's recognition that the problem has more to do with thermodynamics — designing a system such that the product of C—H activation is sufficiently stable to observe — than with the kinetic inertness of alkanes,³ have generated a wealth of examples, well represented by the contents of the present volume.

The practical value of direct functionalization of alkanes lies in their abundance and low cost as feedstocks. Just to cite one example, 1,4-butanediol

(BDO), used in polymers and other applications (over 300,000 metric tons per year in the US alone), is currently produced by the condensation of acetylene with formaldehyde followed by hydrogenation or by the hydroformylation of allyl alcohol — both routes involving expensive precursors. The cost of the acetylene plus formaldehyde in the first route (not counting the hydrogen) is about 32¢ per pound of BDO. If it could be made instead by direct oxidation of butane, the cost of the latter is only about 6¢/lb BDO — a substantial difference. Another example would be a low-cost method for conversion of methane to a liquid product, leading to potentially huge improvements in utilization of remote natural gas deposits.⁴

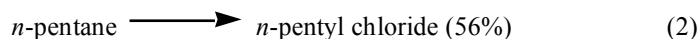
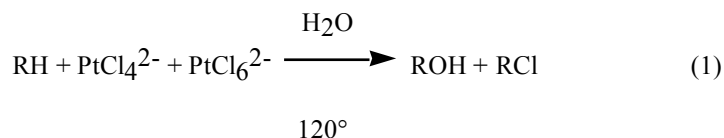
To be sure, organometallic C—H activation is not the only approach to this problem; but the main alternatives do not appear all that attractive, at least for finding general solutions. It is difficult to imagine achieving selective oxidation of butane to BDO by traditional high-temperature heterogeneous catalysis, since the product will inevitably be much more reactive than the starting material. That is not to say that *no* selective heterogeneously catalyzed alkane oxidations are possible — indeed, the oxidation of butane to maleic anhydride is an important currently practiced example. That reaction can be carried out with excellent selectivity, in large part because reactivity is significantly determined by C—H bond strength, and the C—H bonds of maleic anhydride (in contrast to those of BDO, for example) are stronger than those of butane. But in that case the chemistry is dictating the choice of product, not us. Obviously, we would prefer to be able to have it the other way around.

Biological and biologically-inspired routes are also the subjects of intense interests, especially the methane monooxygenase enzymes found in methanotrophic bacteria that oxidize methane to methanol with high selectivity.⁵ But there are serious obstacles to the economic application of biological catalysts to large-scale industrial processes such as these;⁶ and while much progress has been made towards designing artificial mimics, we are still far from a practical catalyst for selective oxidation of methane or other alkanes. Hence our attention returns to organometallic C—H activation as a more fruitful realm for exploration, at least in the short term.

However, successful elaboration of alkane *activation* into practical schemes for alkane *functionalization* has remained, tantalizingly, just out of reach, primarily because of an inherent dilemma. Most of the organometallic systems demonstrated to effect C—H bond activation are rapidly destroyed under oxidizing conditions that would be needed for the sorts of conversions described above; while most of the transformations that *would* be compatible with such species, such as dehydrogenation or carbonylation, are thermodynamically uphill at the temperatures where the species are stable. There are some intriguing examples of non-oxidative reactions that evade thermodynamic restrictions, such as dehydrogenation⁷ and borylation;⁸ it remains to be demonstrated whether either could ultimately be the basis of a practical process. We have chosen to take the other tack, and investigate organometallic C—H activation by oxidation-tolerant systems.

The Shilov System

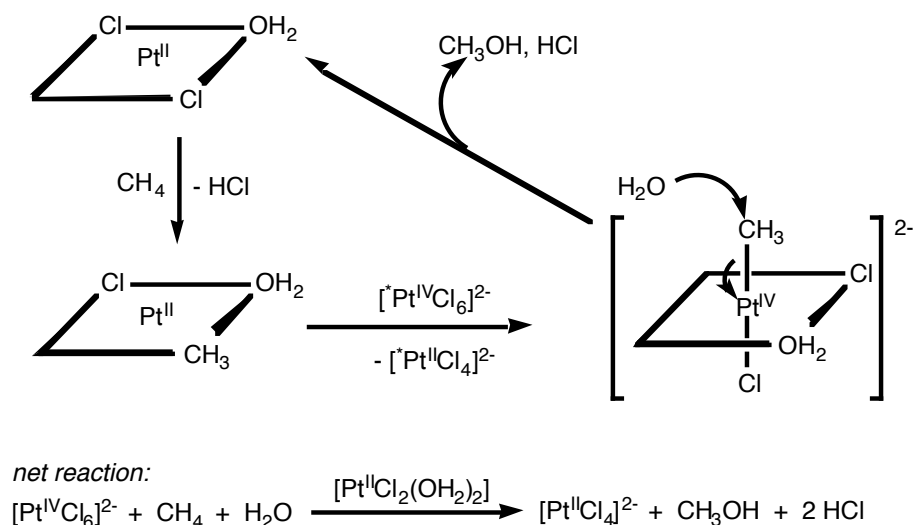
The reaction shown in Eq. 1 was first reported about 30 years ago by Shilov and coworkers, following earlier reports of platinum salt-catalyzed H/D exchange in alkanes.⁹ This system presents a number of features that appear quite promising for our goals. In particular, the complexes tolerate oxidizing conditions, including dioxygen itself, and directly produce oxygenated products. Furthermore, selectivity patterns are quite different from those exhibited by heterogeneous catalysts and other radical-based pathways: there is some preference for terminal oxidation, and reaction products are frequently less reactive than the hydrocarbons they are derived from. Some illustrations are depicted in Eqs. 2-4 (9b,10,11).



On the other hand, there are severe practical limitations to this system. First and foremost, the reaction is not catalytic in platinum; or more precisely, it is *both* stoichiometric and catalytic in platinum. A variety of studies¹⁰ have established the three-step mechanism shown in Scheme 1, consisting of i) electrophilic displacement of a proton from R—H by Pt(II), generating RPt(II); ii) oxidation of RPt(II) to RPt(IV) by $[\text{PtCl}_6]^{2-}$, and iii) nucleophilic cleavage of the C—Pt bond by H₂O or Cl⁻ (only the former is shown), affording ROH or RCl respectively, and regenerating Pt(II) as the nucleofuge. That sums up to a net overall reaction in which one equivalent of Pt(IV) is consumed per equivalent of alkane oxidized, while Pt(II) acts as catalyst (and co-product). Scheme 1 would seem to suggest that an alternate oxidant might be substituted for Pt(IV), and indeed there has been some limited success along these lines, using electrochemistry,¹¹ heteropolyacids,¹² or O₂/Cu(II)¹³ to recycle the catalyst; but in all such cases only a limited number of turnovers could be achieved before the system inactivates.

Furthermore, the reaction is fairly slow, and inefficient. And lastly, the catalytic species eventually precipitate as metallic platinum, because the Pt(II)-Pt(0) redox potential is very close to that of the Pt(IV)-Pt(II) couple. This turns out to be a double whammy: not only does activity for alkane oxidation die out with loss of

soluble catalyst, but the metallic platinum is known to be an excellent catalyst for overoxidizing the desired alcohol products,¹⁴ so selectivity suffers as well.



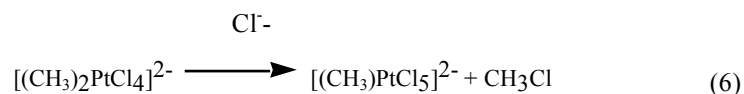
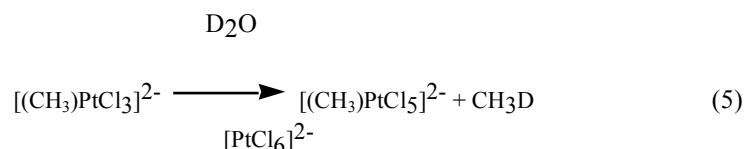
Scheme 1. Mechanism of Shilov System.

Nonetheless, this is still remarkable chemistry. How do we get clean organometallic chemistry in water, a medium in which metal-carbon bonds are often quite unstable? Why is Pt(II), which is not normally considered a particularly "hot" reaction center — neither highly electron rich, as are many of the species employed in the earliest well-defined C—H activations, such as $[\text{Cp}^*(\text{PMe}_3)\text{Ir}(\text{I})]$, nor electron deficient, like the d^0 early transition metal and lanthanide complexes that effect sigma-bond metathesis of alkanes — reactive towards alkanes? And finally, if our mechanistic investigations provide some answers to these questions, can they also point out the directions we must follow to overcome the disadvantages enumerated above and achieve a practical alkane oxidation catalyst?

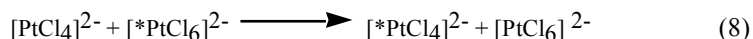
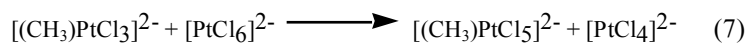
Taking the first question first: the *second* putative organometallic intermediate in Scheme 1, $[(\text{CH}_3)\text{PtCl}_5]^{2-}$, can be readily isolated and fully characterized, and is resistant to protonolytic cleavage of the Pt—C bond not only in water, but even in 1M acid.^{12,15} However, its presumed precursor, $[(\text{CH}_3)\text{PtCl}_3]^{2-}$, has never been obtained cleanly: attempts to generate it by reduction of the methyl-Pt(IV) complex with Sn(II) or other reductants in water lead to liberation of methane instead. That observation implies that the proposed electrophilic reaction of Pt(II) with a C—H bond, liberating a proton, is (not surprisingly) highly reversible. But when Shilov oxidation is carried out in D_2O , only a very small amount of deuterium incorporation in products (and unreacted substrates) is observed. Hence, the second step of Scheme

1, oxidation of (CH₃)Pt(II) to (CH₃)Pt(IV) by [PtCl₆]²⁻, must be even faster than protonolysis.

The last claim has indeed been demonstrated, even in the absence of an authentic sample of [(CH₃)PtCl₃]²⁻, by two different methods. Reduction of [(CH₃)PtCl₅]²⁻, with Cp₂Co in THF affords a solid, characterized as a mixture of [(CH₃)_xPtCl_(4-x)]²⁻ (x = 0-2), which as expected liberates methane (CH₃D) when thrown into D₂O; but if the water contains [PtCl₆]²⁻, some [(CH₃)PtCl₃]²⁻, as well as methane is produced (Eq. 5). The variation of product make with pD leads to the estimation that at room temperature the ratio of rate constants for oxidation and deuterolysis is about 3.¹⁶ Alternatively, [(CH₃)PtCl₃]²⁻, can be generated at 95 °C as the leaving group in nucleophilic displacement by Cl⁻ on [(CH₃)₂PtCl₄]²⁻ (Eq. 6), and the same partition experiment carried out,¹⁷ leading to a ratio of $k_{\text{oxidation}}/k_{\text{protonolysis}}$ of about 18. Clearly the activation enthalpy for oxidation is considerably larger than that for protonolysis, so that at the Shilov operating temperature (120 °C), oxidation will dominate completely.

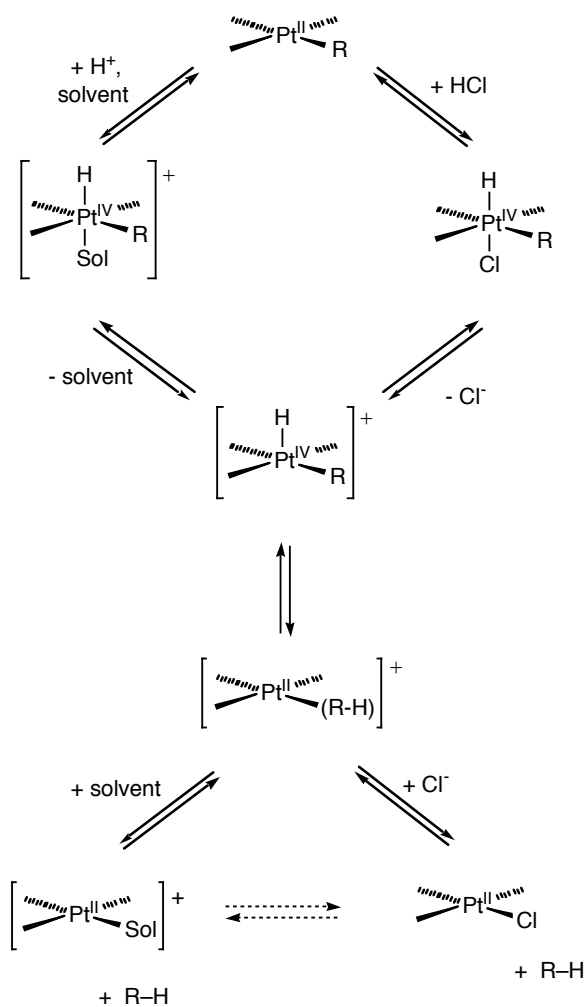


The oxidation step (ii) of the overall mechanism is therefore *remarkably* fast; since protonolysis of [(CH₃)PtCl₃]²⁻ is too fast to measure, we can place a lower limit on the rate constant for Eq. 7, which turns out to be at least three orders of magnitude faster than that of the self-exchange reaction of Eq. 8.¹⁸ Why so fast? Probably two factors are at work here: replacement of a chloride by a methyl makes oxidation of the Pt(II) center thermodynamically more favorable; and the stronger *trans* effect of the methyl ligand will accelerate formation of a chloride-bridged intermediate, required for the inner-sphere redox mechanism commonly observed in Pt(II)-Pt(IV) chemistry.



This finding suggests *part* of the answer to the second question: what is so special about Pt(II)? In analogy to Halpern's suggestion about alkane activation in general, it may be not so much the ability to effect C—H activation *per se*, but rather the mechanism whereby the product of that activation is (kinetically) protected against reversal by protonolysis. But a more complete answer, as well as leads for improving

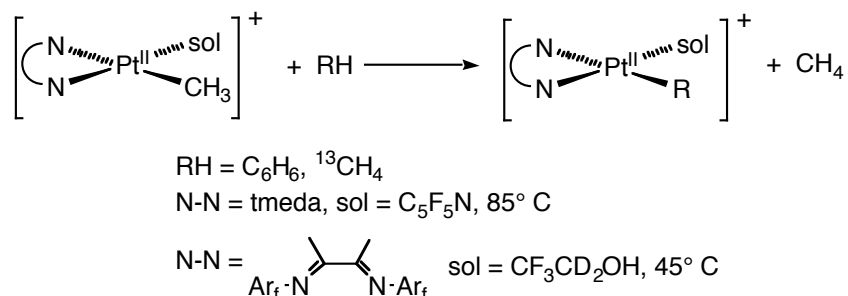
activity and moving towards a viable catalytic system, require more specific understanding of the actual C—H activation process — step i of the mechanism — and direct study of the Shilov process does not readily yield any such information. To get the details we need, we must turn to model systems.



Scheme 2. Mechanism for R-Pt protonolysis (reading down)/C-H activation (reading up)

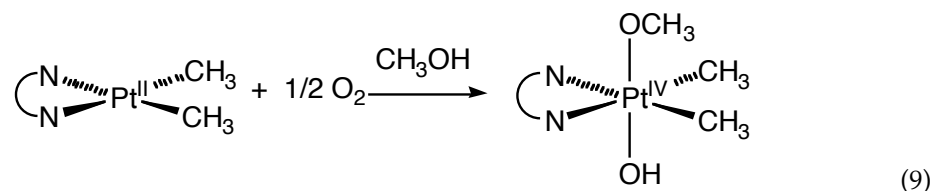
Studies on ligated Pt(II) complexes

The mechanism of Scheme 2 has been proposed to account for the results of an intensive program of experiments on the protonolysis of (tmeda)Pt(CH₃)Cl and related complexes (tmeda = N,N,N',N'-tetramethylethylenediamine); and, invoking the principle of microscopic reversibility, the same mechanism (reading bottom to top) should apply for C—H activation.¹⁹ It should be noted in particular that i) ligand substitution and dissociation plays a key role at several points, and ii) the actual C—H bond cleavage is an oxidative addition step. Subsequently it was postulated that similar complexes could carry out (stoichiometric) C—H bond activation as shown in Scheme 3, if a solvent (sol) could be found to satisfy several requirements: it must support dissolution of ionic species, coordinate relatively weakly, and not be subject itself to facile C—H activation. Two different systems were successfully designed, with sol = pentafluoropyridine²⁰ and 3,3,3-trifluoroethanol (TFE)²¹ respectively.



Scheme 3. Stoichiometric C-H activation by ligated Pt(II)

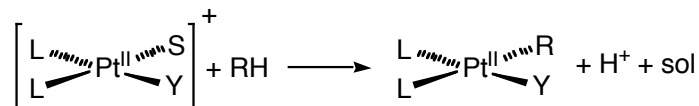
Can these ligated complexes help overcome the problems inherent in the original Shilov system? In each case the answer appears to be a somewhat qualified yes. First, with regard to replacing Pt(IV) as stoichiometric oxidant, we have found that certain Pt(II) complexes, of the form (N-N)PtMe₂, can be oxidized to Pt(IV) by dioxygen, according to Scheme 4.²² Second, with regard to rate, the reactions of Scheme 3 can be operated under substantially milder conditions — some even at room temperature²³ — than the 120 °C required for the ligand-free aqueous system. And finally, many of the ligated complexes are also more resistant to decomposition to platinum metal. The most dramatic case is Periana's bipyrimidine complex, which efficiently catalyzes oxidation of methane to methyl bisulfate by sulfuric acid (thereby providing an alternative to Pt(IV) as stoichiometric oxidant as well); here the complex is not only kinetically but thermodynamically stable relative to Pt(0), as it spontaneously reforms by heating the ligand with the metal in sulfuric acid.^{23,24}



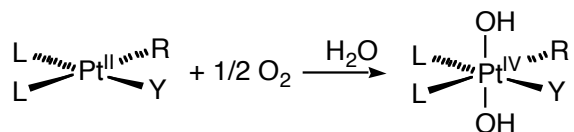
Given these findings, we can construct (on paper) a catalytic cycle for the oxidation of alkane to alcohol by dioxygen, shown in Scheme 5. Close analogs of each of the first three steps have been demonstrated for (NN)-ligated platinum complexes. The first, C—H activation, operates as in Scheme 3; the second, oxidation, can be carried out in water (using sulfonated ligands²⁵) as well as in methanol; and the third has been observed, for example, with $[\text{PtMeCl}_2(\text{H}_2\text{O})(\text{tmeda})]\text{Cl}$.¹² But no single complex has yet been found that effects all the steps, and indeed there are problems that need to be overcome with each to close a catalytic cycle. The first step would need to be a *net* alkane activation, liberating a proton as shown, rather than an alkyl exchange reaction;²⁶ oxidation would need to be fast compared to the reverse of step 1, as is the case for the original Shilov system (see above); and the third step, nucleophilic cleavage of the Pt—C bond, may well require geometric rearrangement, as studies on the Shilov mechanism¹² and related systems²⁷ strongly indicate that dissociation of a ligand *trans* to the alkyl group precedes nucleophilic attack. The fourth step amounts to simple ligand substitution and should not pose any serious problems.²⁸

Much of our recent effort has been focused on understanding the factors controlling the rate of C—H activation, so that designing a complex capable of performing the first step of the cycle productively and rapidly can be pursued rationally. We recently reported²⁹ the results of extensive studies into the reaction shown in Scheme 6, where by varying aryl groups attached to N and the backbone R groups of the diimine we were able to achieve a wide range in ligand electronic and steric character. The findings can be summarized as follows:

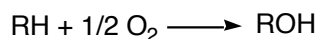
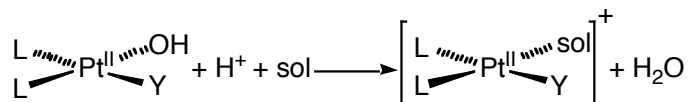
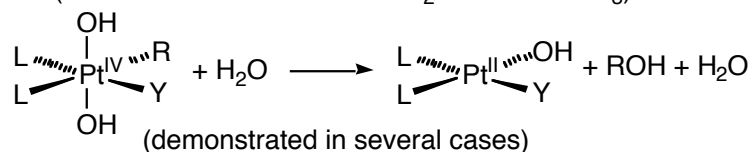
1. Complexes obtained in this manner by protonolysis with aqueous acid exist as an equilibrium mixture of aquo and solvento complexes; for all complexes, the rate is proportional to the ratio $[\text{C}_6\text{H}_6]/[\text{H}_2\text{O}]$, and more electron-rich complexes (as measured by ν_{CO} in $[(\text{N-N})\text{Pt}(\text{Me})(\text{CO})]^+$) react faster.
2. For ortho substituted aryls, the measured KIE (C_6H_6 vs. C_6D_6) is very close to 1, and complete statistical scrambling of H/D in the evolved methane and Pt-Ph is observed with C_6D_6 or $\text{C}_6\text{H}_3\text{D}_3$. In one case protonolysis of $(\text{N-N})\text{Pt}(\text{Me})(\text{Ph})$ at low temperature led to observation of a π -benzene adduct by NMR. (A related adduct has since been isolated and characterized crystallographically.³⁰)



(goes for Y = CH₃ with methane loss; implicit in Shilov system)



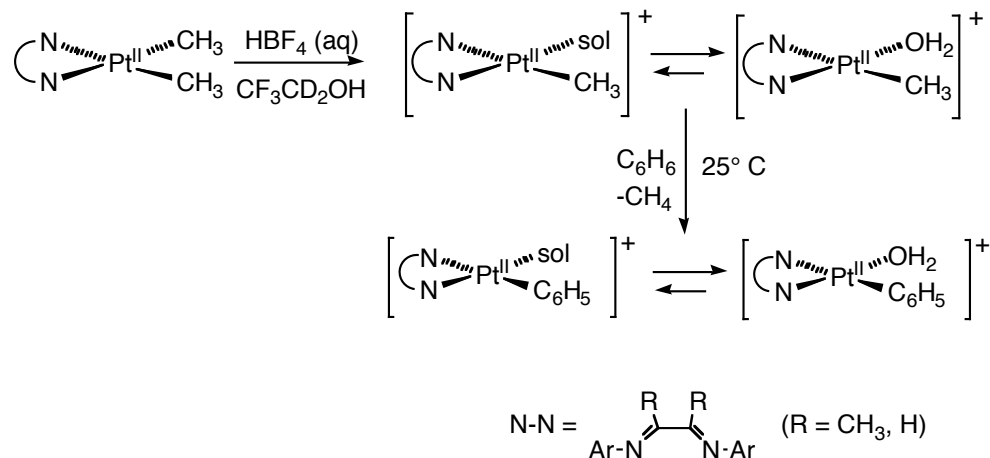
(demonstrated in MeOH and H₂O for R=Y=CH₃)



Scheme 4. Hypothetical catalytic cycle for alkane oxidation

3. For non-ortho substituted aryls, reactions 10-40 times faster than 2,6-disubstituted Ar analogs; KIEs are on the order of 2; and only partial scrambling of H/D is found.

These results imply that there is a switch in rate-determining step (rds), depending upon steric crowding. For the more crowded complexes with 2,6-disubstituted aryls, the initial π -benzene coordination is rate-limiting, leading to a KIE ~ 1 and to extensive isotopic scrambling, as the processes responsible for the latter — reversible C—H bond breaking and making — are fast compared to the rates of hydrocarbons entering and departing from the coordination sphere. In contrast, for the less hindered non-ortho-substituted aryl complexes C-H cleavage becomes the rds, signaled by a higher KIE and only partial H/D exchange.



Scheme 5. Diimine-ligated Pt complexes for C-H activation study

Surprisingly, though, the electronic effects appear to be quite similar for either rds. We interpret this in terms of a ground state effect: the electronic nature of the ligand operates primarily to affect the equilibrium between aquo and solvento complexes, with more electron-withdrawing ligands favoring the (unreactive) former. Indeed, within a group of sterically similar complexes, the equilibrium and rate constants correlate well with one another.²⁹ The electronic effect on the actual transition state for the reaction must be relatively small, then, but we cannot even tell if there is one and in which direction it lies, as it is masked by the trend in stabilization/destabilization of the aquo complexes.

An obvious way around this problem, which should at the same time lead to more reactive systems, would be to generate the methyl-Pt(II) cations by a rigorously anhydrous route. This has now been achieved by treating the corresponding dimethyl complexes with a neutral tris(pentafluorophenyl)boron reagent in TFE (Scheme 7).³¹ The reaction could in principle proceed either by methide abstraction or by protonolysis by the *in situ*-generated acid $\text{H}^+[\text{B}(\text{OCD}_2\text{CF}_3)(\text{C}_6\text{F}_5)_3]^-$; the latter must be the case, since only methane and no $[\text{BMe}(\text{C}_6\text{F}_5)_3]^-$ is observed as co-product.

When water-free methyl-Pt(II) cations, thus prepared, are reacted with benzene in TFE, we do observe the expected accelerations relative to the corresponding reactions in the presence of water. However, there is *no* statistically significant dependence of rate on the electronic properties of the diimine ligand (Table 1). Clearly, then, in the present system the latter exert an effect *solely* through manipulation of ligand substitution—specifically on the relative thermodynamic stability of the aquo complex—and not on the actual process of C—H bond cleavage.

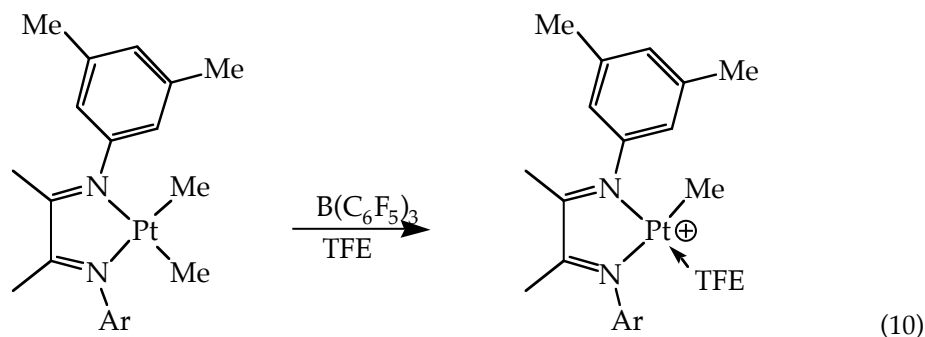


Table 1. Apparent second-order rate constants for the reaction of methyl-Pt(II) cations with benzene, in the presence and absence of water, as a function of diimine ligand.

<u>Ar group</u>	<u>k_2, 20°C, 0.05 M H_2O²⁹</u>	<u>k_2, 25°C, water-free³¹</u>
	(31)	(33)
3,5- $C_6H_3(CF_3)_2$	$8.4(8) \times 10^{-4} M^{-1}s^{-1}$	$1.3(3) \times 10^{-2} M^{-1}s^{-1}$
3,4,5- $C_6H_2(OMe)_3$	$4.0(4) \times 10^{-3} M^{-1}s^{-1}$	$1.6(2) \times 10^{-2} M^{-1}s^{-1}$
3,5- $C_6H_3R_2$	$6.2(6) \times 10^{-3} M^{-1}s^{-1}$ ^a	$1.6(2) \times 10^{-2} M^{-1}s^{-1}$ ^b

^a R = *t*-Bu. ^bR = Me.

Conclusion

Can a practical route to selective alkane oxidation be based on this Pt(II) chemistry? *Collectively*, the complexes we have studied effect all the individual steps that would be needed for catalysis, with dioxygen as the terminal oxidant. We now need to construct a *single* complex that will perform them all, closing a catalytic cycle, and at the same time get reaction rates up to practical levels, while still maintaining (or, better, improving upon) the selectivity patterns that have been demonstrated for the original Shilov system. The recent findings reported above highlight the central role played by ligand substitution processes — at least comparably important to that of actual C—H bond breaking — in regulating C—H activation reactions. Fortunately we appear to have considerable control over those

processes by manipulating ligand steric and electronic properties, solvent, and other reaction parameters. Whether that will be sufficient to overcome the remaining obstacles, and put all the pieces together, remains to be seen.

Acknowledgments

We thank all those — students, postdocs, colleagues, collaborators — who have previously and/or are currently contributing to this program: Lily Ackerman, Tom Baker, Christoph Balzarek, Jeffrey Byers, Charles Carter, Andy Herring, Mike Freund, Matt Holtcamp, Lars Johansson, David Lyon, Gerrit Luinstra, Rebekah Main, Jonathan Owen, Seva Rostovtsev, Joseph Sadighi, John Scollard, Shannon Stahl, Mats Tilset, Lin Wang, David Weinberg, and Antek Wong-Foy. We thank BP for ongoing support.

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² Actually we had been laboring under the impression that there is only *one* Holy Grail; but a scholarly source (the same one quoted in reference 1) provides textual evidence that the plural may in fact be appropriate: (Graham Chapman, as King Arthur) "Go and tell your master that we have been charged by God with a sacred quest. If he will give us food and shelter for the night, he can join us in our quest for the Holy Grail." (Michael Palin, in an outr-r-r-rageous French accent) "Well, I'll ask him, but I don't think he'll be very keen--he's already got one, you see?" (Chapman) "Are you *sure* he's got one?" (Palin) "Oh yes, it's very nice."

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