Late Metal Carbene Complexes Generated by Multiple C−H Activations: Examining the Continuum of M=C Bond Reactivity

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RECEIVED ON MARCH 31, 2009

CONSPECTUS

Unactivated C_{sp^3}−H bonds are ubiquitous in organic chemicals and hydrocarbon feedstocks. However, these resources remain largely untapped, and the development of efficient homogeneous methods for hydrocarbon functionalization by C−H activation is an attractive and unresolved challenge for synthetic chemists. Transition-metal catalysis offers an attractive possible means for achieving selective, catalytic C−H functionalization given the thermodynamically favorable nature of many desirable partial oxidation schemes and the propensity of transition-metal complexes to cleave C−H bonds. Selective C−H activation, typically by

a single cleavage event to produce M−C_{sp^3} products, is possible through myriad reported transition-metal species. In contrast, several recent reports have shown that late transition metals may react with certain substrates to perform multiple C−H activations, generating M=C_{sp^2} complexes for further elaboration. In light of the rich reactivity of metal-bound carbenes, such a route could open a new manifold of reactivity for catalytic C−H functionalization, and we have targeted this strategy in our studies.

In this Account, we highlight several early examples of late transition-metal complexes that have been shown to generate metal-bound carbenes by multiple C−H activations and briefly examine factors leading to the selective generation of metal carbenes through this route. Using these reports as a backdrop, we focus on the double C−H activation of ethers and amines at iridium complexes supported by Ozerov's amidophosphine PNP ligand (PNP = [N(2-P^{i}Pr$_2$-4-Me-C$_6$H$_3$)$_2$]$^-$), allowing isolation of unusual square-planar iridium(I) carbenes. These species exhibit reactivity that is distinct from the archetypal Fischer and Schrock designations.

We present experimental and theoretical studies showing that, like the classical square-planar iridium(I) organometallics, these complexes are best described as nucleophilic at iridium. We discuss the classification of this reactivity in the context of a scheme originally delineated by Roper. These "Roper-type" carbenes perform a number of multiple-bond metatheses leading to atom and group transfer from electrophilic heterocumulene (e.g., CO_2, CS_2, PhNCS) and diazo (e.g., N_2O, AdN$_3$) reagents. In one instance, we have extended this methodology to a process for catalytic C−H functionalization by a double C−H activation-group transfer process.

Although the scope of these reactions is currently limited, these new pathways may find broader utility as the reactivity of late-metal carbenes continues to be explored. Examination of alternative transition metals and supporting ligand sets will certainly be important. Nonetheless, our findings show that carbene generation by double C−H activation is a viable strategy for C−H functionalization, leading to products not accessible through traditional C_{sp^3}−H activation pathways.
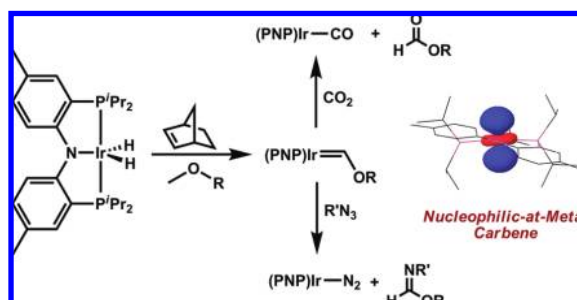
Introduction

The catalytic activation and functionalization of normally inert carbon−hydrogen bonds has been a long-standing goal of organometallic chemistry, and progress in this area has been extensively reviewed.[1] Most schemes for C−H functionalization involve an initial C−H cleavage step, which can proceed by numerous mechanisms such as

oxidative addition, electrophilic activation, or σ-bond metathesis. Irrespective of mechanism, this initial step leads to the formation of a singly bonded $M-C_{sp^3}$ species, which may be further elaborated. However, in addition to the difficulty associated with achieving catalytic turnover, this approach limits the kinds of products that may be formed to those generated by functionalizing a metal−carbon single bond. As a result, there are few successful examples of catalytic $C_{sp^3}-H$ functionalization at transition-metal centers.[2]

One approach to functionalizing the intermediate $M-C_{sp^3}$ complexes is to utilize a second C−H cleavage event, often a β-hydrogen elimination to generate alkene. This method was first introduced by Crabtree[3] and has seen major improvements in scope and efficiency with the advent of pincer-type ligands,[4] in some cases allowing the transformation to proceed in the absence of a hydrogen acceptor.[5] Nevertheless, the most common schemes employ olefins as terminal oxidants, so their utility is somewhat hampered by the fact that one olefin is simply being traded for another.[6]

One might easily envision, however, that the second C−H cleavage is not required to be a β-elimination. Instead, if α-hydrogen migration ensues, a metal carbene complex (an isomer of the metal-bound olefin) will be formed. Generation of an $M=C_{sp^2}$ species by such a route could offer new possibilities for catalytic C−H functionalization, particularly in light of the rich reactivity previously demonstrated for metal-bound carbenes.[7] We were intrigued by this possibility since, at the outset of our work, there were few examples of well-defined reactivity for any $M=C_{sp^2}$ complexes generated by multiple C−H activations.[8]

In this Account, we examine the generation of metal carbenes by multiple C−H activations with a focus on recent work from our own laboratory using pincer-supported iridium centers to effect this transformation. We also discuss our findings regarding the subsequent reactivity of square-planar iridium(I) carbenes, which diverges in important ways from the classical Fischer- and Schrock-type designations and instead falls nicely into a continuum of metal- and ligand-based carbene reactivity originally suggested by Roper. These findings have facilitated the discovery of several new atom- and group-transfer reactions and have allowed the development of a catalytic C−H functionalization protocol via generation of metal carbenes, clearly demonstrating the distinct reactivity available at metal−carbon multiple bonds as well as the potential value of these species in new C−H oxidation schemes.

SCHEME 1. Shaw's Chelate-Assisted Formation of an Iridium Carbene[a][9]
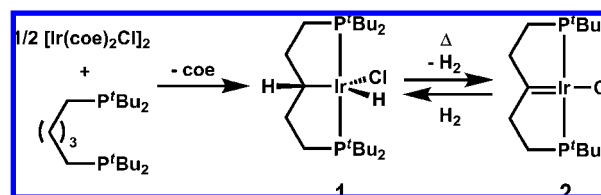

[a] coe = cyclooctene.

## Generation of Late Metal Carbenes by Multiple C−H Activations: Background

The first indication that late metals may be capable of generating carbenes by α,α-dehydrogenation came from the laboratory of Shaw, who reported that a pincer iridium complex (**1**), formed from reaction of an iridium(I) synthon with 1,5-bis(di-*tert*-butylphosphino)pentane, would release hydrogen upon sublimation to afford the pincer-type carbene complex **2** (Scheme 1).[9] This reaction is certainly helped by chelate assistance from the strong phosphine donors, stabilizing the carbene that is ultimately formed, but the finding was very important in showing that α,α-dehydrogenation and loss of H_2 to afford a stable metal carbene can be a favorable process at late metals. In fact, it was this finding that inspired much of the work we have undertaken at pincer-supported iridium centers.

Several other examples of chelate-assisted carbene formation via multiple C−H activations have been reported,[10] but the catalytic potential of this route is generally limited since the chelate assistance not only favors carbene formation but also prevents functionalization and release since the carbene must be linked to at least one strong donor that can be difficult to labilize. Thus, Carmona's 1992 report of selective double C−H activation of cyclic ethers to generate the corresponding Fischer-type carbenes was a major advance for this field.[11] The $[Tp^*]Ir(C_2H_4)_2$ complex (**3**) was shown to form heteroatom-substituted carbenes from tetrahydrofuran, 2-methyltetrahydrofuran, 1,3-dioxolane, and 1,4-dioxane (Scheme 2, $Tp^* = HB(3,5-Me_2-pz)_3^-$). For this system, competitive degradation to an allyl hydride (**4**) was inevitably observed, accounting for between 20% and 60% of the iridium-containing product. Clearly a quantitative method would be needed in order to implement this process in any catalytic cycle.

Shortly after Carmona's seminal discovery, Taube reported that reduction of $Os^{III}(NH_3)_4(CF_3SO_3)_3$ with Zn/Hg amalgam in THF affords an octahedral osmium(II) product with carbene and dihydrogen ligands.[12] This system also generates carbenes by double C−H activation of 1,4-dioxane and tetrahydropyran. Unlike $[Tp^*]Ir(C_2H_4)_2$ (**3**), Taube's system forms the

SCHEME 2. Generation of a Cyclic Carbene at Tp*-Supported Iridium(III)[11]
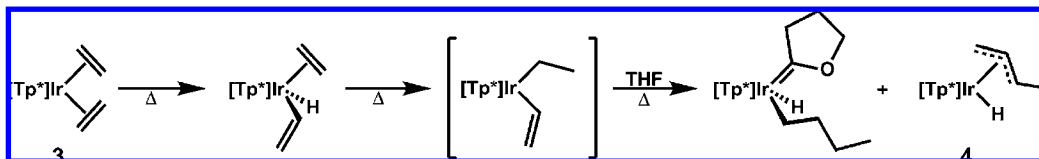
SCHEME 3. Reaction of Pincer-Supported Iridium Complexes with MTBE
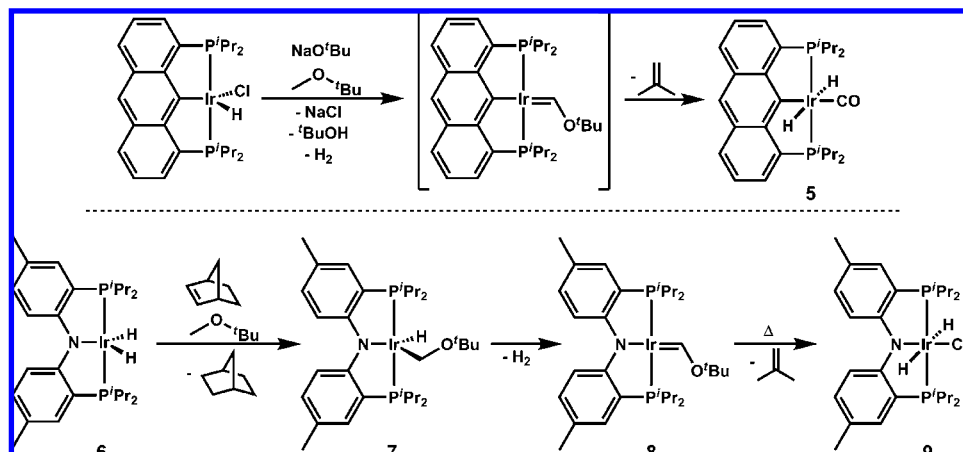
carbene in good yield (>80%), and the reaction completes in less than 1 h at ambient temperature.

In the years following Taube's paper, the generation of carbenes by double C−H activation was shown to be a more general phenomenon, and Bergman (Ir),[8a] Bercaw (Pt),[13] Caulton (Ru, Os),[14] and Crabtree (Ir)[15] all published examples of systems capable of forming heteroatom-substituted carbenes by multiple C−H cleavage events. Carmona also reported variants of the original [Tp*]Ir(C$_2$H$_4$)$_2$ system that could generate heteroatom-substituted carbenes cleanly from a large number of ethers and amines.[16]

Formation and Decomposition of Pincer-Supported Iridium Carbenes

Against this backdrop, we noted that although pincer-supported iridium complexes had been extensively utilized in α,β-dehydrogenation schemes (affording olefins), few investigations had been performed regarding the dehydrogenation of heteroatom-containing substrates by these complexes.[17] Thus, we began our studies by examining the reactivity of *tert*-butyl methyl ether (MTBE) with pincer-type 14-electron iridium(I) species, which could be generated by reductive dehydrogenation or dehydrohalogenation. For MTBE, β-hydrogen elimination would be precluded by the presence of oxygen at the β-position, allowing α-migration to be favored. Using (^{iPr}Anthraphos)Ir, which contains a standard PCP donor set, we noted that a series of facile C−H and C−O bond cleav-

age events led to the formation of *trans*-(^{iPr}Anthraphos)Ir-(CO)(H)$_2$ (**5**) with release of isobutylene (Scheme 3, top).[18]

However, utilizing the amidophosphine PNP ligand developed by Ozerov and co-workers,[19] we cleanly isolated the iridium(I) carbene (PNP)Ir=C(H)O^tBu (**8**) as a kinetic product (Scheme 3), an electronic and structural relative of Fryzuk's amidophosphine-supported iridium methylidene.[20] A combination of experimental and computational studies have indicated that carbene generation proceeds by a fast C−H oxidative addition to afford the observable hydrido alkyl intermediate (PNP)Ir(H)(CH$_2$O^tBu) (**7**),[21,22] followed by slow α-hydrogen migration and release of dihydrogen to generate the final product **8** (Scheme 3).[23] A single-crystal X-ray diffraction (XRD) structure of carbene **8** revealed that, although the carbene and amide ligands are canted slightly out of the square plane, they are precisely aligned with each other to allow a push−pull interaction between the filled pπ orbital of the amido donor and the empty pπ orbital of the *tert*-butoxymethylidene ligand, and it seems likely that this interaction contributes at least partially to the stabilization of **8** relative to the unobserved (^{iPr}Anthraphos)Ir=C(H)O^tBu.

Thermolysis of carbene **8** led to formation of a *trans*-dihydrido carbonyl (**9**), similar to the Anthraphos system, leading us to formulate a mechanism for decarbonylation of MTBE via an iridium *tert*-butoxymethylidene for both systems (Scheme 4). The regioselective nature of the decarbonylation, which exclusively afforded the *trans*-dihydrido isomer, was attrib-

SCHEME 4. Mechanism of MTBE Decarbonylation at (^{iPr}Anthraphos)Ir and (PNP)Ir via an Alkoxycarbene
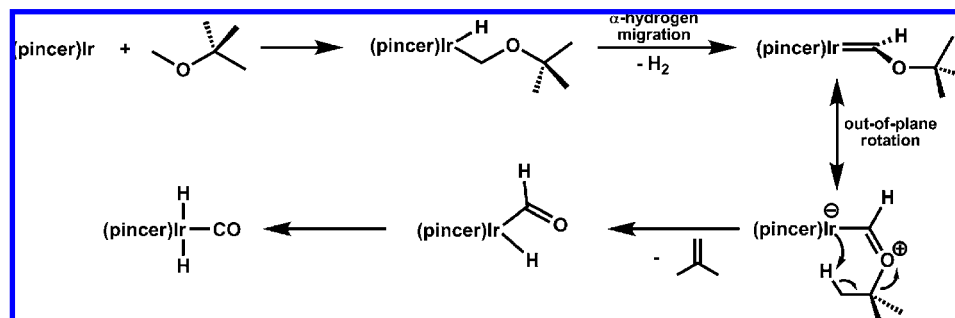
uted to formation of an iridium(III) hydrido formyl species by elimination of isobutylene, followed by stereoselective α-hydrogen migration from the formyl ligand to iridium, a step with considerable literature precedent.[24] This hypothesis was supported by the quantitative formation of the same dihydrido carbonyl upon reaction of (PNP)IrH$_2$ with formaldehyde.[18,25]

We proposed that the key step, elimination of isobutylene, was promoted by a high-lying Lewis-basic Ir(d_{z^2}) orbital upon 90° rotation of the carbene unit (Scheme 4). This type of behavior would be consistent with the well-known Lewis basicity of square-planar, d^8 organometallic complexes.[26] It would also indicate that, in contrast to the early metal Fischer carbenes that are electrophilic at carbon, the reactivity of these low-valent, coordinatively unsaturated complexes would be dominated by a high-lying, nucleophilic Ir(d_{z^2}) orbital. It was this finding that guided further reactivity studies (vide infra).

Although MTBE was an ideal test substrate due to the presence of a single site for directed C−H activation with no possibility for β-elimination, the facile decomposition of the carbene at elevated temperatures and a desire to extend the generality of the α,α-dehydrogenation led us to examine the dehydrogenation of a series of ethers by (PNP)Ir.[22] *sec*-Butyl methyl ether (SBME), *n*-butyl methyl ether (NBME), and *tert*-amyl methyl ether were found to generate alkoxycarbenes under conditions similar to those employed for MTBE. This result is consistent with previous observations of high selectivity for methyl C−H activation in the presence of methylene or methine protons.[27] The observation of carbenes as sole products from C−H activation of SBME and NBME shows that either (PNP)Ir exhibits a high affinity for the less encumbered H−CH$_2$O bonds or, if methylene of methine C−H activation is accomplished, such a pathway is unproductive.[28]

A carbene complex was also obtained by α,α-dehydrogenation of tetrahydrofuran (THF) at (PNP)Ir. Although this result shows that β-elimination may be avoided in some cases, only α,β-dehydrogenation to afford vinyl ethers was observed for

SCHEME 5. Dehydrogenation of TMEDA at (PNP)Ir^a
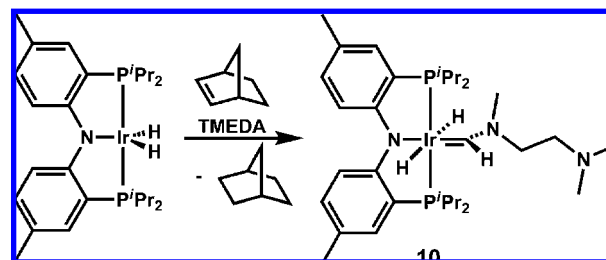
^{a} TMEDA = *N,N,N′,N′*-tetramethylethylenediamine.

1,4-dioxane and diethyl ether.[22] Compared with the results of Carmona,[29] Taube,[12] and Bercaw,[13] who obtained carbenes from these substrates, these findings highlight the subtle factors that can influence α- versus β-elimination and stabilization of carbene versus alkene.[30]

These early results, combined with reports from Carmona[29] and Crabtree,[15] led us to consider whether square-planar aminocarbene complexes might be accessed by a similar double C−H activation approach. As predicted, exposure of (PNP)IrH$_2$ (**6**) to norbornene (1 equiv) in the presence of methyl amines led to generation of iridium carbene complexes (Scheme 5, TMEDA as substrate).[31] However, in these cases, six-coordinate iridium(III) *trans*-dihydrido aminocarbene complexes were formed rather than the square-planar iridium(I) carbenes observed for methyl ethers. Although reversible isomerization to *cis*-dihydrido isomers could be thermally induced, loss of H$_2$ from the *cis*-dihydrido aminocarbenes was not observed. Thus, we proposed that the reluctance of these complexes to lose dihydrogen is related to the more strongly donating nature of the aminocarbenes, which confers a greater basicity to the iridium center. This formulation is supported by single-crystal XRD analysis and NMR spectroscopy, which show a significant amount of N → C π-donation and indicate that the aminocarbene complexes are best represented by the two limiting resonance structures provided in eq 1.

(1)
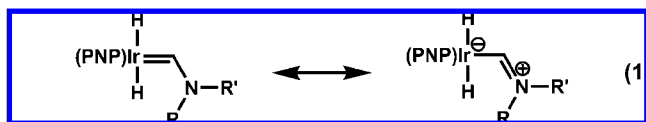
Divergent Carbene Reactivity

Based on the differences in coordination number, formal oxidation state, and frontier molecular orbitals, we expected that the iridium(I) alkoxycarbenes and iridium(III) dihydrido aminocarbenes would exhibit divergent reactivity. Exposure of the aminocarbene complex derived from TMEDA (**10**) to carbon monoxide effected a 1,2-hydride migration to generate a carbonyl adduct of iridium(III) (**11**), as shown in Scheme 6. In contrast, reaction of iridium(I) alkoxycarbene **8** with excess carbon monoxide resulted in an unusual migratory insertion of the carbene into the Ir—N bond of the PNP ligand to afford dicarbonyl complex **12** (Scheme 6).[31] Although insertion reactions of metal-bound carbenes are relatively common, this reaction represents, to the best of our knowledge, the first example of such an insertion into a metal—amide bond.[32]

With the exception of these types of ligand migration, reactivity of the carbenes with Lewis bases was generally unproductive. Such an outcome was not entirely unexpected in light of the degradation that had previously been observed for **8** and the well-established nucleophilicity of square-planar d^8 organometallics.[26] However, it was somewhat surprising that backbonding from the electron-rich iridium center reduced the electrophilicity of the carbene to such an extent that nucleophilic attack at the carbene was not observed, even for amine and alkoxide nucleophiles. This observation led us to pursue potentially new reactivity of these square-planar complexes with electrophiles.

Reaction with Heterocumulene Electrophiles

Although alkoxycarbene **8** demonstrated little productive reactivity with Lewis bases, the complex was found to exhibit a wealth of unique reactivity with electrophilic heterocumulenes. The initial discovery was somewhat fortuitous, in that CO_2 was chosen as an electrophilic C_1 synthon that also displays a rich coordination chemistry, including several examples with iridium(I).[33] Exposure of carbene **8** to an atmosphere of CO_2 led to quantitative generation of the carbonyl adduct (PNP)Ir—CO (**13**) with expulsion of *tert*-butyl formate (eq 2), a remarkable and unusual example of direct oxygen-atom abstraction from CO_2.[23,34] In light of previous results from Mayer's laboratory regarding the oxidative addition of CO_2 and other heterocumulenes,[35] we hypothesized that formation of the stable iridium carbonyl complex might also provide driving force for
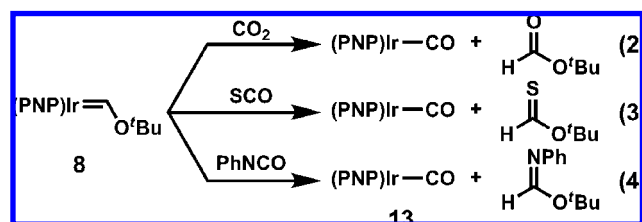
**SCHEME 6.** CO-Induced Ligand Migration at (PNP)Ir Carbenes (R = $(CH_2)_2N(CH_3)_2$)[31]
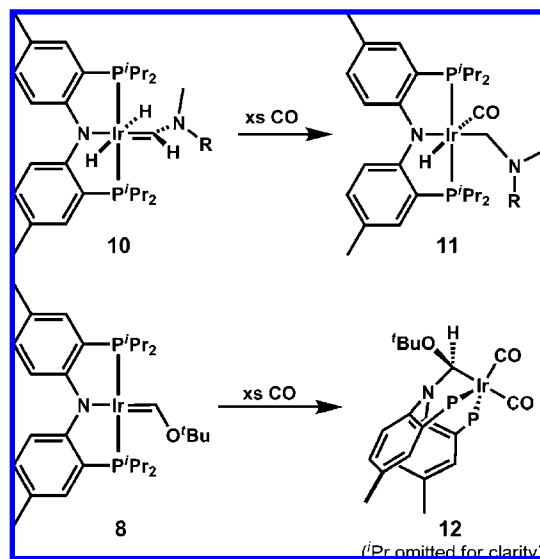
SCHEME 7. Mechanism of Oxygen-Atom Transfer from CO_2 to Carbene **8**
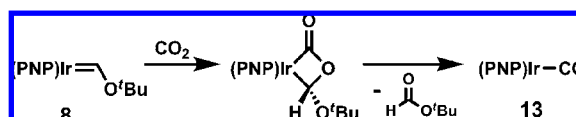
the decarbonylation of other oxygen-containing heterocumulenes. As expected, sulfur-atom and nitrene-group transfer were realized from carbonyl sulfide and phenyl isocyanate, respectively (eqs 3 and 4).

Subsequent mechanistic studies performed in our lab, as well as theoretical studies by Yates and co-workers,[21] implicated a mechanism where nucleophilic attack at CO_2 is initiated by a high-lying Ir(d_{z^2})-type orbital, followed by cyclization to form a four-membered iridalactone (Scheme 7), analogous to the metallacyclobutane demonstrated as an intermediate in olefin metathesis.[36] Subsequent retrocyclization releases the formate, generating (PNP)Ir—CO (**13**). Given our own laboratory's extensive studies into the mechanism and utility of the olefin metathesis reaction,[37] it is somewhat surprising that this "oxygen-atom metathesis" from CO_2 proceeds by a similar mechanism, but it also serves to highlight the utility of metal-bound carbenes in effecting unusual transformations, especially the scission of multiple bonds.[38] In fact, this oxygen

SCHEME 8. Activation of CS_2 at Carbene **8**[40]
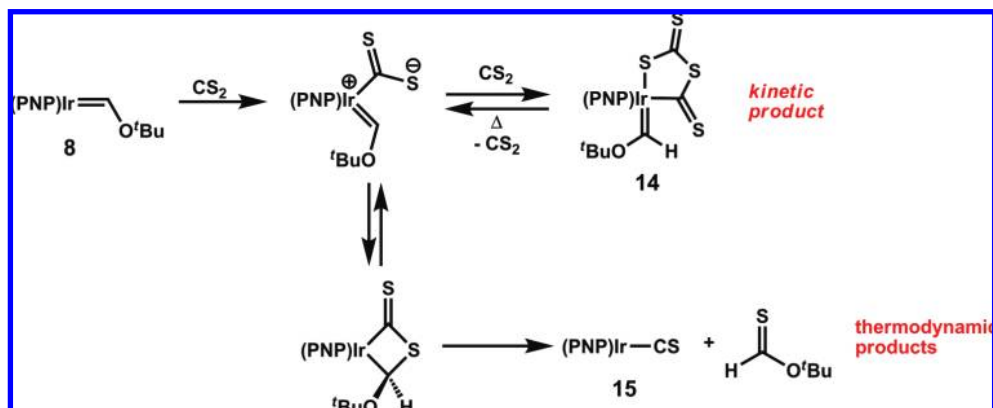
extrusion from CO_2 is formally related to Schrock's report of C=C bond formation upon reaction of a tantalum(V) alkylidene with CO_2 with generation of polymeric tantalum oxides,[39] and the different reaction outcomes are likely dictated by the differences in M=C bond polarization.

With these results in hand, we suspected that related reactivity would be observed with heterocumulenes lacking oxygen such as carbon disulfide and isothiocyanates. However, an initial test reaction, in which carbene complex **8** was exposed to an excess of CS_2, led to quantitative generation of an unusual $C_2S_4^{2-}$ adduct (**14**), where no bond formation to the carbene was observed (Scheme 8).[40] Further experiments showed this CS_2 condensation to be reversible, and extended heating of a benzene solution of **14** caused the expected sulfur-atom transfer to generate *tert*-butyl thioformate and (PNP)Ir—CS (**15**) (Scheme 8). *tert*-Butyl thioformate and thiocarbonyl complex **15** were also observed upon slow addition of CS_2 (1 equiv) to a solution of the carbene **8** at ambient temperature, showing that **14** was not an intermediate in the formation of **15** but rather a kinetic product derived from trapping a CS_2 adduct of **8** prior to dithiolactone formation and release of thioformate. Alkoxycarbene **8** reacted likewise with PhNCS, ultimately generating the isocyanide adduct (PNP)Ir—CNPh and *tert*-butyl thioformate.

These results not only highlight the variety of atom and group transfer reactivity that can be realized from the isoelectronic series of heterocumulenes but also emphasize the importance that the electron-rich, coordinatively unsaturated metal center plays in initiating reactivity. In fact, though metal carbene complexes have not previously been reported to promote the reductive condensation of heterocumulenes, this type of reactivity is often observed for electron-rich, coordinatively unsaturated metal complexes such as **8**.[41] The fact that products are observed where no bond formation to the carbene has occurred serves to cement the crucial role played by the iridium(I) center in initiating the cooperative bond scissions observed for oxygen- and sulfur-containing heterocumulenes. These findings prompted a density functional theory (DFT) investigation of the electronic structures of **8** and the isoelectronic carbonyl (**13**), thiocarbonyl (**15**), and isocyanide complexes, which confirmed the presence and importance of a high-lying (HOMO-1), nucleophilic Ir(d_{z^2}) orbital in promoting the observed reactivity, and the molecular surface of this orbital is depicted in Figure 1.[40]

Tandem Double C−H Activation-Group Transfer Oxidation of Methyl Ethers

The atom and group transfer from heterocumulenes that was effected by carbene complex **8** suggested a possible new scheme for the catalytic functionalization of methyl ethers by a double C−H activation-group transfer process. However, the disadvantage inherent in these reactions was associated with the difficulty in realizing any catalytic turnover due to the reluctance of (PNP)Ir−CO (**13**) and related complexes to serve as precursors for further C−H activation, even under forcing thermal or photolytic conditions.

In light of our previous observation that C−H activation by (PNP)Ir is not hindered by the presence of N_2, it seemed plausible that a change in oxidant from carbonyl reagents (E=C=O) to the isoelectronic diazo reagents (E=N=N) could offer a related route that circumvents unreactive carbonyl
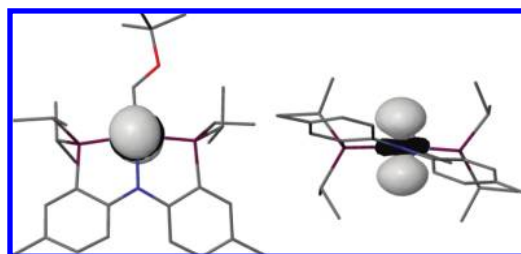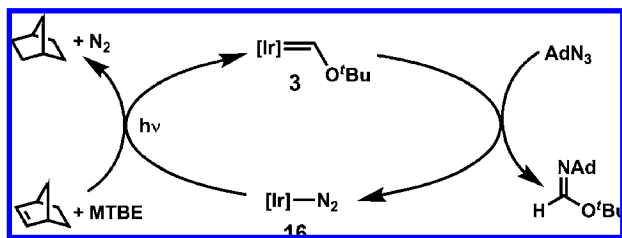

FIGURE 1. Molecular surface of Ir(d_{z^2}) orbital (HOMO-1) of carbene complex **8** (top and side views).

SCHEME 9. Demonstrated Catalytic Cycle for Oxidation of MTBE to *tert*-Butyl *N*-Adamantylformimidate by a Double C−H Activation-Group Transfer Process

FIGURE 2. Possible interactions of metal carbenes with nucleophilic and electrophilic reagents. Adapted from ref 45.

complex **13**. Precedent for this approach comes from the seminal experiments of Collman, where a net dinitrogen-for-carbonyl ligand exchange was realized at Vaska's complex upon reaction with organic azides and loss of isocyanate.[42] As predicted, (PNP)Ir=C(H)O^{t}Bu (**8**) reacted smoothly with organic azides and nitrous oxide to release the corresponding *tert*-butyl formimidate or formate, respectively, and (PNP)Ir−N$_2$ (**16**) (eqs 5 and 6; TMS = trimethylsilyl, DIPP = 2,6-diisopropylphenyl, Ad = 1-adamantyl).[43]
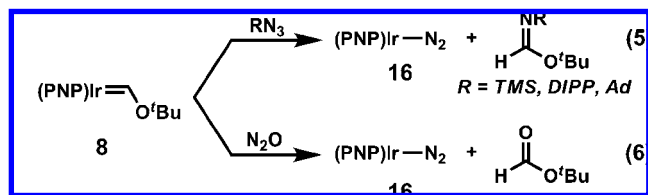
Dinitrogen adduct **16** proved to be a suitable precursor for the double C−H activation of MTBE, losing N$_2$ and regenerating carbene **8** upon thermolysis or photolysis, though thermolysis resulted in competitive degradation of **8** to *trans*-(PNP)Ir(CO)(H)$_2$ (**9**), as described above.[18] Unfortunately, neither method proved to be effective in the presence of diazo oxidants, presumably due to preferential reaction of the unobserved (PNP)Ir fragment with the oxidant. However, the feasibility of a photocatalytic scheme was initially demonstrated by a stepwise process, where sequential addition of organic azide (1 equiv) and photolysis of the resulting solution in the presence of norbornene with MTBE as solvent allowed several turnovers to be attained with a high yield of the expected formimidate (93% relative to added oxidant).[43]

Ultimately, this method was extended to a true catalytic scheme (Scheme 9) using a syringe pump to control the rate of oxidant addition and mild photolytic conditions (i.e., a bright halogen bulb). Under these conditions, with 10% catalyst loading relative to diazo oxidant, high yields (>90%) could be achieved for the tandem double C−H activation-group transfer process to convert MTBE to *tert*-butyl *N*-adamantylformimidate.[44] SBME and NBME could be converted to their corresponding formimidates, albeit less efficiently, by a
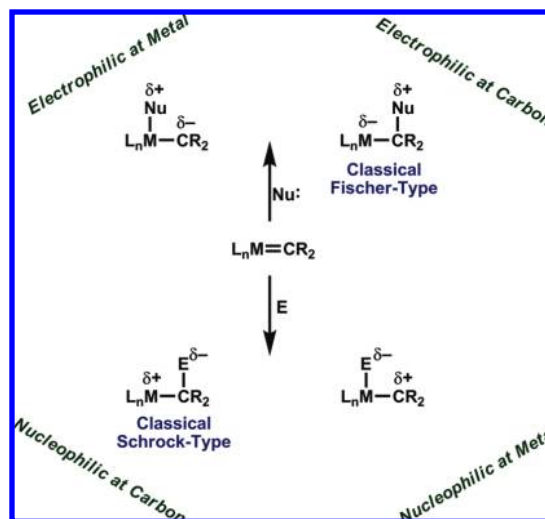
similar process. To the best of our knowledge, these reactions represent the only examples of catalytic C−H functionalization by double C−H activation to generate a M=C$_{sp^2}$ species, and they suggest that catalytic C−H functionalization chemistry may also be realized for a number of other late-metal systems previously demonstrated to generate carbenes by this type of route.

The Continuum of M=C Bond Reactivity

Aside from providing new routes to C=E bond formation via M=C$_{sp^2}$ complexes, the reactivities that have been observed for (PNP)Ir=C(H)O^{t}Bu (**8**) serve to highlight the variety of possible pathways for reaction of metal-bound carbenes. Most descriptions of metal carbenes emphasize two limiting pathways where electrophilic or nucleophilic reactivity at C$_\alpha$ is tied to classification as either Fischer-type (coordinated singlet carbene) or Schrock-type (coordinated triplet carbene), respectively. However, the behavior we observe is more accurately described by a nucleophilic metal center that interacts with electrophilic heterocumulenes, withdrawing electron density from the coordinated carbene to allow cyclization and ultimately atom or group transfer. This "nucleophilic-at-metal" formulation fits nicely into a scheme outlined by Roper more than 20 years ago, where the interactions of metal carbenes with nucleophiles and electrophiles fall into four limiting categories that may be metal- or carbene-initiated (Figure 2).[45]

Classical Fischer-type reactivity (top right in Figure 2) is often observed for heteroatom-substituted carbenes attached to early metals with electron-withdrawing coligands and has been exploited frequently to exchange substituents on Fischer-type complexes (eq 7).[46] Nucleophilic reactivity at C$_\alpha$ (bottom

left in Figure 2) is most frequently observed for Schrock-type alkylidenes, for instance in the coordination of trimethylaluminum to a well-characterized tantalum(V) methylidene (eq 8).[47] However, nucleophilic reactivity at C_α has also been reported for heteroatom-substituted carbenes ligated to sufficiently reduced metal centers.[48] Electrophilic reactivity at the metal center is also common for high-valent alkylidenes, as demonstrated in the trapping of a titanium(IV) methylidene with phosphine ligands (eq 9).[49]
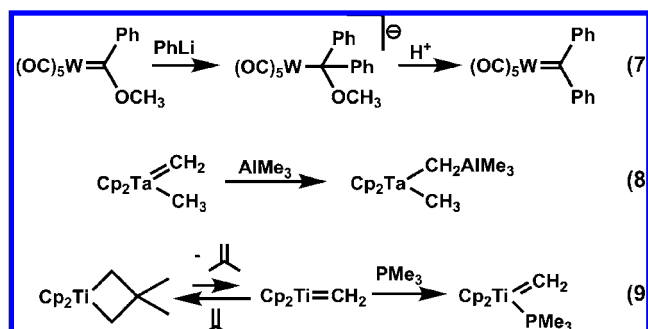
Clearly these designations are not absolute, with many complexes showing ambiphilic reactivity depending on reaction conditions. Additionally, cooperative substrate activation across metal−carbon multiple bonds, which falls somewhere between the top and bottom hemispheres of Figure 2, is clearly important in several processes such as the Wittig-type olefination of amides and esters by Tebbe's reagent, which does not occur with simple phosphorus ylides.[50]

The reactivity we have reviewed in this Account serves to complete the spectrum originally proposed by Roper (Figure 2)[45] by showing that, in some cases, a nucleophilic metal center can play a key role in initiating reactivity between these "Roper-type" metal carbenes and electrophiles. This finding is likely not limited to the (PNP)Ir system and may extend to other low-valent, coordinatively unsaturated late-metal centers. Additionally, our findings outline a pathway by which square-planar carbenes of the late transition metals may generally exhibit a strong propensity to activate multiply bonded electrophilic substrates to atom and group transfer, indicating that this somewhat underutilized class of carbene reactivity certainly warrants further investigation.

Conclusions and Outlook

We have presented results showing that pincer-supported iridium systems are effective for the α,α-dehydrogenation of certain ether and amine substrates to generate Ir=C_{sp^2} species. The square-planar alkoxycarbene complexes formed in this way react in an unusual manner with electrophilic heterocumulenes (e.g., CO_2) and diazo reagents (e.g., N_2O) to effect

atom and group transfer to the metal-bound carbene, and this reactivity has allowed the development of a new protocol for the oxidation of several methyl ethers by a double C−H activation-group transfer process. This finding represents the first demonstration of successful catalytic C−H functionalization via metal carbene generation. Additionally, we have revisited Roper's framework for understanding the reactivity of metal carbene complexes[45] and have shown that these pincer-supported low-valent, coordinatively unsaturated species are best described as nucleophilic-at-metal, a characteristic that allows them to perform the facile scission of strong C=E and N=E bonds.

Clearly much work remains if these methods are to find general application in synthetic organic chemistry. Although the scope is currently limited, the new pathways that have been unveiled may find broader utility as the reactivity of late metal carbenes continues to be explored. Examination of alternative transition metals and supporting ligand sets will certainly be important in this respect. Nonetheless, these findings show that carbene generation by double C−H activation is a viable strategy for C−H functionalization, leading to products not accessible through traditional C_{sp^3}−H activation pathways.

BIOGRAPHICAL INFORMATION

Matthew T. Whited was born in Raleigh, NC, in 1982. He received his B.S. degree from Davidson College and his Ph.D. from the California Institute of Technology as a Moore Fellow under the guidance of Jonas C. Peters and Robert H. Grubbs. He is currently a postdoctoral researcher in the laboratory of Mark E. Thompson at the University of Southern California. His research interests involve the application of inorganic and organometallic chemistry to problems of energy and organic synthesis.

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FOOTNOTES

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