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# Unexpected C−C Bond Cleavage and C−C Bond Formation Observed in the Reaction of a Cationic Iridium Complex with Heteroatom-Substituted Cyclopropanes

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Metal-mediated cyclopropane activation, by reaction at either C−H or C−C bonds, is a potentially convenient and direct process to obtain useful C3 moieties for organic synthesis.[1,2] Both types of reaction are known to occur at late metal centers, but the factors that control the favored mode of attack in a particular case are still not clear. We wish to report a series of substituted cyclopropane activation reactions at a Cp*LIr(III) center (Cp* = pentamethylcyclopentadienyl, L = $PMe_3$). Although the products are superficially similar (allyl complexes), a detailed mechanistic study reveals that certain types of heteroatom substituents shift the initial activation process dramatically from the previously observed C−H to a new C−C bond activation pathway. In addition, the new pathway exhibits, on the way to products, an unusual series of mechanistic steps, including overall methyl migratory insertion which has been very rarely observed at Cp*LIr centers.[2c,3]

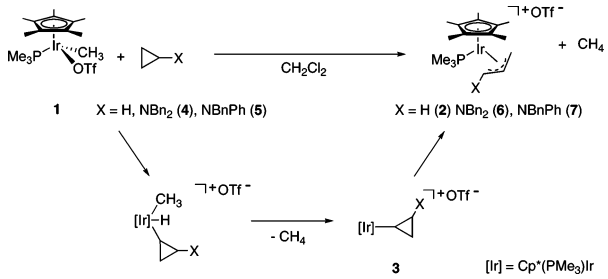
Previously, Cp*($PMe_3$)Ir($CH_3$)OTf (**1**) (OTf = $OSO_2CF_3$) was reported by our group to activate cyclopropane, yielding $\pi$-allyl complex **2** (Scheme 1).[2c] Subsequent kinetic isotope effect (KIE) experiments demonstrated that this reaction has a $k_H/k_D = 3.8 \pm 0.3$.[4] This indicates that the reaction might proceed by initial C−H bond activation, followed by extrusion of methane, to afford cyclopropyliridium complex **3**, which parallels extensive C−H bond activation studies by our group with complex **1**.[3]

With the intent of exploring the scope of this reactivity and isolating model intermediates, several heteroatom-substituted cyclopropanes were examined. Treatment of complex **1** with *N*,*N*-dibenzylcyclopropylamine (**4**) or *N*-benzyl-*N*-phenylcyclopropylamine (**5**) furnished [Cp*($PMe_3$)Ir($\eta^3$-$C_3H_4NBn_2$)][OTf] (**6**) and [Cp*($PMe_3$)Ir($\eta^3$-$C_3H_4NBnPh$)][OTf] (**7**), respectively, analogous to the product observed with parent cyclopropane. We assume that these reactions proceed by the well-precedented pathway illustrated in Scheme 1.

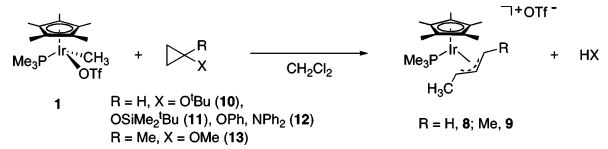
In contrast to the results summarized above, alkoxy and siloxy-substituted cyclopropanes produced unexpected products. Instead of methane loss, alcohol is eliminated to form [Cp*($PMe_3$)Ir($\eta^3$-$C_3H_4CH_3$)][OTf] (**8**) (Scheme 2). Interestingly, reaction of *N*,*N*-diphenylaminocyclopropane (**12**) with **1** also eliminates secondary amine $Ph_2NH$ rather than methane to afford methyl-migrated product **8**. Apparently, cyclopropanes bearing better anionic leaving groups favor heteroatom elimination to furnish the unexpected methyl-migrated products.

Because methane is not a byproduct of these eliminations, Cp*-($PMe_3$)Ir($^{13}CH_3$)OTf was used to track the position of the iridium-bound methyl in the methallyl moiety. With *tert*-butyl cyclopropyl ether **10**, the $^{13}C$ label is transferred to the terminal methyl of the allyl moiety in complex **8**, as verified by $^1H$ and $^{13}C$ NMR spectroscopy. Additional positional information was obtained by reaction of complex **1** with (1-methylcyclopropyl)(methyl) ether **13**, which yielded [Cp*($PMe_3$)Ir($\eta^3$-$CH_3C_3H_3CH_3$)][OTf] (**9**). This

***Scheme 1***




***Scheme 2***




labeling study shows the final position of the tertiary cyclopropyl carbon once complex **8** has been formed.

Although we do not observe scrambling of the $^{13}C$ label in this reaction, KIE measurements are complicated by H/D scrambling of the cyclopropyl and iridium−methyl hydrogens.[5] Cyclopropane **10** was treated with complex **1**-$d_3$, and deuterium was found not only in the methyl position of the allyl group but also in the 1 and 3 positions. Surprisingly, no deuterium was incorporated at the central carbon of the allyl in complex **8**. Control experiments revealed that H/D scrambling is an intramolecular exchange process, and the H/D composition of complex **8** is static once it is formed (see Supporting Information).

On the basis of these observations, we hypothesized that the reaction between **1** and a 1:1 mixture of siloxy ethers **11**/**11**-$d_5$ should result in an artificially large KIE for this reaction on the basis of the additional hydrogen introduced by the iridium methyl into the allyl. The $k_H/k_D$ of 1.22 ± 0.03 that we measured in this way is therefore a maximum value for this reaction. The modest magnitude of this effect, which is dramatically different from the primary isotope effects observed with arenes[3] and parent cyclopropane, argues against a C−H bond activation occurring during or before the rate-determining step. Therefore, on the basis of the type of reactivity observed for cyclopropanes with metal systems other than Cp*(L)Ir,[2d,e,i,j] the most reasonable mechanistic alternative for this reaction involves initial C−C bond cleavage to yield metallocyclobutane **14** (Scheme 3).

With the knowledge that alcohol is a product of this reaction, it was of interest to determine a mechanism for its elimination. Because the complex is cationic, it seemed unlikely that an alkoxide anion would dissociate to make a dicationic complex. Therefore, we considered the possibility that adventitious acid was involved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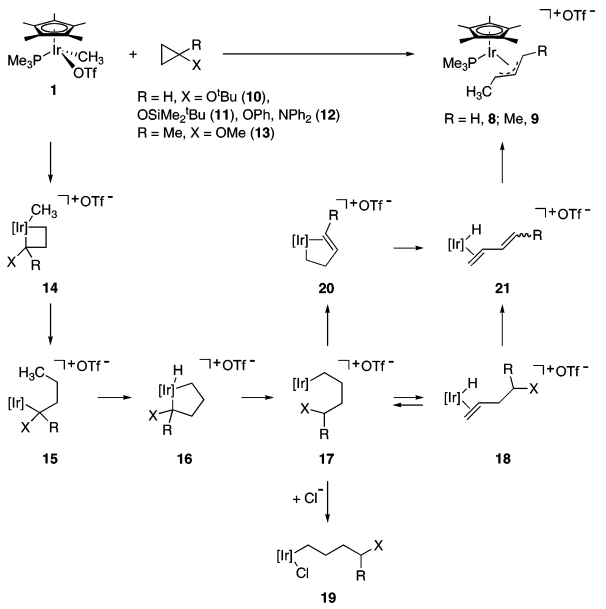
***Scheme 3***




in the ROH elimination step. To test this hypothesis, hindered 2,6-disubstituted pyridine bases were added to the reaction between **1** and cyclopropane **10**. This changed the observed product dramatically: instead of an allyl complex, a diastereomeric mixture of the thermally sensitive hydride complex **18** was observed. Further investigation revealed this complex to be a transient intermediate in the reaction of **1** and cyclopropane **10** in the absence of base as observed by NMR spectroscopy. $Cp^*(PMe_3)Ir(^{13}CH_3)OTf$ was subjected to the same basic conditions, and the $^{13}C$ carbon was tracked by $^{13}C$ NMR spectroscopy to the terminal olefinic methylene group of the carbon chain in **18**.

Complex **18** is most probably reached by C−C reductive elimination in the initial metallacycle intermediate **14** to afford the cationic complex **15**, followed by C−H bond activation of the terminal methyl to yield **16**. Reductive elimination and $\beta$-hydride elimination would then furnish complex **18** as a mixture of alkene diastereomers. To transfer the iridium center from one end of the carbon chain to the other, we propose this C−H bond activation/reductive elimination scheme (rather than the more common chain-walking mechanism) to account for the lack of H/D scrambling into the 2-position of allyl complex **8**. Complex **17**, the proposed immediate precursor to **18**, can also be trapped with a number of nucleophiles. When chloride is used, a single isomer **19** ($Cp^*(PMe_3)Ir(C_4H_8OC_4H_9)Cl$, Figure 1) is formed. Supporting our hypothesis of acid catalysis, hydride complex **18** proceeds cleanly to allyl complex **8** when an excess of triflic acid is added, demonstrating its validity as an intermediate in the mechanism.

The fact that added base arrests this reaction at compound **18** demonstrates that C−C bond formation occurs before elimination of the alkoxy-, siloxy-, or diphenylamino-substituents (See Supporting Information for further discussion). The $^{13}C$-labeling study reveals the regiochemistry of the C−C bond formation. Finally, observing that acid is required to convert intermediate hydride **18** to allyl complex **8**, we propose elimination of the heteroatom substituent as the most probable next step.

Acid-promoted elimination of alcohol from hydride complex **18** should furnish complex **21**. Several groups have proposed analogous structures as intermediates in the hydrovinylation of ethylene by iridium(III) complexes.[6] A pathway from **17** to **21** could also go through crotyliridium(III) complex **20**. As yet, we have no evidence to rule out either pathway: both would account for the regiochemistry of the overall methyl-migration and isotope-labeling phenomena we observe.

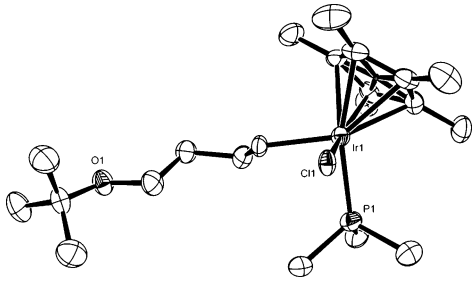



***Figure 1.*** ORTEP diagram of $Cp^*(PMe_3)Ir(C_4H_8OC_4H_9)Cl$ (**19**). Thermal ellipsoids are shown at the 50% probability level. Hydrogen atoms have been omitted for clarity.

In summary, we have shown that several heteroatom-substituted cyclopropanes react with $Cp^*(PMe_3)Ir(CH_3)OTf$ via C−C bond cleavage and formation. This is an unexpected mode of reactivity for a complex known to favor reaction by C−H bond activations and to avoid methyl-migratory insertion reactions.[2c,3] On the basis of $^2H$ and $^{13}C$ isotope-labeling studies, dependence on acid, and literature precedent, we propose the mechanism pictured in Scheme 3. Further experiments and computations directed at understanding the selectivity of these reactions and the divergent reactivities observed for amino- and alkoxy-substituted cyclopropanes are in progress.

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**Supporting Information Available:** Experimental procedures, spectral data for unknown compounds, and a comment on the difference in behavior of alkylamino- and alkoxycyclopropanes. This material is available free of charge via the Internet at http://pubs.acs.org.

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