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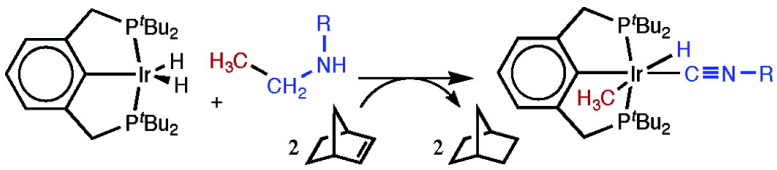

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Selective Cleavage of the C−C Bonds of Aminoethyl Groups, via a Multistep Pathway, by a Pincer Iridium Complex

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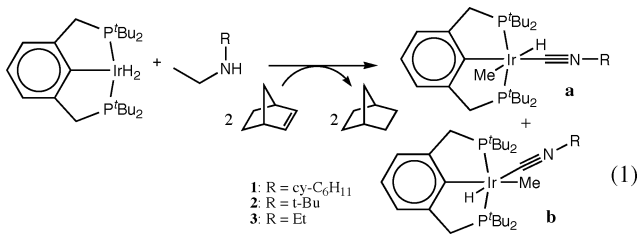
C−H and C−C bonds are the two most fundamental linkages of organic chemistry. Major efforts toward the activation of C−H bonds by soluble transition-metal complexes have reaped great rewards in recent years. The metal-mediated activation of C−C bonds has proven to be an even more challenging problem; nevertheless, significant progress in this area has been achieved via numerous approaches (or combinations thereof), including ring strain relief, aromatization, chelation, and β-alkyl elimination.[1] These successes notwithstanding, the ability to cleave "unactivated" C−C bonds, particularly with regioselectivity in a functionalized organic molecule, remains a major challenge to organic and inorganic chemists.

Among the most effective catalysts to date for the functionalization of C−H bonds, and specifically for the dehydrogenation of alkanes, are "pincer"-ligated iridium complexes.[2−5] Precursors of (PCP)Ir (PCP = κ^3-2,6-(^{t}Bu$_2$PCH$_2$)$_2$C$_6$H$_3$) can readily cleave not only hydrocarbon C−H bonds (stoichiometrically or catalytically)[6] but also the O−H bond of water[7] and the N−H bonds of anilines.[8] Herein we report the activation of an unstrained sp^3−sp^3 C−C single bond by this pincer-ligated iridium fragment; unlike the aforementioned E−H bond activations, however, this reaction is found to proceed via a multistep pathway.

As part of an effort to isolate products of the N−H addition of aliphatic amines, *N*-ethylcyclohexylamine (2 equiv) was added to a *p*-xylene solution of (PCP)Ir(NBE)[9,10] (NBE = norbornene; this complex, generated by the reaction of 2 equiv NBE with (PCP)IrH$_2$, has previously been established to act as a precursor of the 14-electron fragment (PCP)Ir). After 10 min at ambient temperature an orange solution was obtained (eq 1). A major species, **1a**, was



(1)

obtained in 91% yield, with a minor product, **1b**, in 3% yield (as determined by ^{31}P and ^{1}H NMR).[9]

The spectroscopic data indicated that products **1a** and **1b** are six-coordinate (κ^3-PCP)Ir complexes, each possessing one hydride and one methyl ligand.[11] Slow evaporation of pentane solvent yielded crystals of complex **1a**. Structure determination by X-ray diffraction[9] (Figure 1) revealed the presence of a cyclohexyl isocyanide ligand trans to the PCP carbon and a methyl group trans to a hydride. The ^{31}P and ^{1}H NMR spectroscopic data of the minor complex **1b** closely resemble those of **1a** and are all consistent with the assignment of **1b** as an isomer of **1a** with the methyl group cis to the hydride ligand.[9]

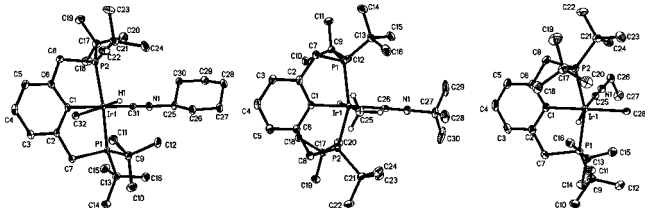


Figure 1. ORTEP diagrams of **1a**, **2a**, and **3b**. Most hydrogen atoms are omitted for clarity.

(PCP)Ir(NBE), under the same conditions as above, reacted analogously with *N*-ethyl-*tert*-butylamine (2 equiv), yielding the new complex **2a** in 94% yield (the minor product **2b**, observed in <1% yield, slowly grew in after the initial reaction was complete). **2a** was characterized by X-ray diffraction (Figure 1). In analogy with **1a**, the methyl ligand of **2a** is trans to the hydride. Likewise, **2b** is assigned as a coordination isomer of **2a** with the methyl group cis to the hydride.

The reaction of the (PCP)Ir precursor with diethylamine proceeded in close analogy to the reactions of *N*-ethylcyclohexylamine and *N*-ethyl-*tert*-butylamine, although the former reaction proceeded more slowly and gave a significantly different product ratio. After 2 h at 45 °C, complexes **3a** and **3b** were formed in 90% yield, in a ratio of 2.0:1 (±5%), and characterized as isomers of (PCP)Ir(H)(Me)(CNEt) by ^{31}P and ^{1}H NMR spectroscopy, in analogy with **1a**, **1b**, **2a**, and **2b**. Complexes **3a** and **3b** are assigned as isomers with methyl and hydride ligands mutually trans and mutually cis, respectively. The **3a**/**3b** mixture undergoes slow isomerization to give predominantly **3b**. The X-ray structure of **3b** reveals the methyl group to be trans to the PCP carbon.[9]

All six complexes, **1a**−**3a** and **1b**−**3b**, undergo slow decomposition at 90 °C (ca. 15 h) to give the corresponding four-coordinate isocyanide complexes (PCP)Ir(CNR) and concomitant formation of methane, as observed by ^{1}H NMR.[9] (PCP)Ir(CN^{t}Bu) was further reacted with CO to give (PCP)Ir(CO),[12] liberating *tert*-butyl isocyanide.

Jensen and co-workers have reported that (PCP)IrH$_2$ can catalytically dehydrogenate secondary amines to give imines.[13] The temperature required for this dehydrogenation (200 °C) is surprisingly high; such high temperatures might be required to overcome product inhibition. Accordingly, we considered amine dehydrogenation to give imine as the initial step toward the formation of **1**−**3**. The resulting imines possess sp^2 C−H bonds; we have previously shown that vinyl and aryl sp^2 C−H bonds readily undergo oxidative addition to (PCP)Ir.[6,10] Such C−H addition in the case of the imines, if followed by methyl migration (i.e., deinsertion of isocyanide), would give the observed products **1**−**3** (Scheme 1).

Reactions of low-valent metals in which alcohols afford metal carbonyls are well established.[14] However, whereas alkyl migration from acyl ligands is commonly facile, in the case of isocyanides, alkyl migrations are only well-known in the direction of insertion.[15]

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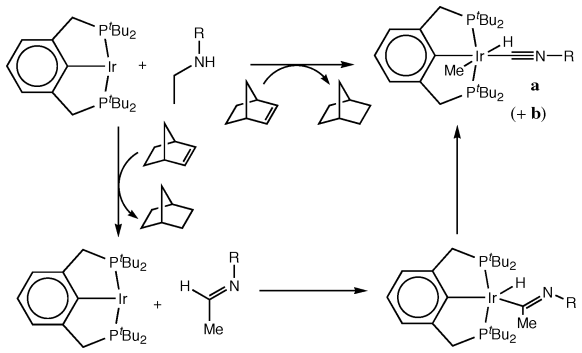
Scheme 1. Proposed Mechanism of Eq 1



We are aware of only one example of alkyl migration proceeding in the direction of isocyanide deinsertion. In a report by Caulton and co-workers[16] it was found that "RuHCl(P^iPr_3)$_2$" underwent imine C−H addition and isocyanide deinsertion. The same ruthenium fragment also dehydrogenated Me_2NH, indicating that properties favoring amine dehydrogenation and isocyanide abstraction from imines are closely related.

To test the mechanistic hypothesis of Scheme 1, we reacted 2 equiv of the imine *N*-ethylideneethylamine with (PCP)Ir(NBE). Complexes **3a** and **3b** formed quantitatively within 10 min at ambient temperature. Significant further support for the intermediacy of the imine is derived from the observation that the ratio of **3a** to **3b**, obtained from the reaction with imine, was identical with that obtained from the reaction of (PCP)Ir with diethylamine (2.1:1 (±5%)).

A mechanistic alternative to the pathway of Scheme 1 may be considered in which (PCP)Ir undergoes direct addition of an imine sp^2−sp^3 C−C bond. Jun et al. have reported such additions of the C−C bond of imine groups tethered to rhodium.[17] If this were the case in the present system, the resulting iminoformyl intermediate could then undergo H migration to give products **1a**−**3a**. However, the concomitant formation of complexes **1b**−**3b**, in which the hydride is trans to the isocyanide ligand, argues strongly against such an alternative pathway (whereas the formation of both "**a**" and "**b**" isomers is entirely consistent with the pathway of Scheme 1).

The direct oxidative addition of an unstrained, untethered sp^3−sp^3 C−C bond by (PCP)Ir would undoubtedly be precluded by both unfavorable thermodynamics and, additionally, a high kinetic barrier.[18] We suspect that sp^3−sp^3 C−C addition to *any* metal center that might be generated in solution may be unlikely, if only due to competition with C−H addition. Further, even if direct C−C bond addition were to prove feasible, regioselectivity would undoubtedly be a major challenge. In the present system, the cleavage of the C−C bond is made possible by prior dehydrogenation; the regioselectivity is dictated by the dehydrogenation and perhaps, initially, by addition of the N−H bond (which is more favorable than C−H bond addition to (PCP)Ir[8]). The first examples of dehydrogenation-initiated sp^3−sp^3 C−C bond activation were reported by Crabtree for alkanes.[19] Most closely related to the present work, Jun has reported that dehydrogenation of primary amines can be followed by trans imination by rhodium-coordinated 2-amino-3-picoline to give a tethered imine group.[20] The rhodium center can then catalyze insertion of olefins into the imino C−H bond. The present system, in which an amine is converted to an isocyanide, constitutes another example suggesting that prior dehydrogenation may prove to be a general and valuable approach toward the regioselective cleavage of C−C bonds of functionalized organics.

In conclusion, we report the regioselective cleavage of the unstrained and untethered C−C bond of amines, under very mild conditions, to give coordinated isocyanides. The reaction proceeds through amine dehydrogenation, followed by sp^2 C−H addition of the imine product and subsequent methyl migration. Further study of the applicability and scope of this reaction is underway.

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Supporting Information Available: Experimental details and NMR and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Selected NMR data: **1a**, δ 0.084 (t, J_{PH} = 3.2 Hz, 3H, *CH*$_3$), −11.98 (t, J_{PH} = 15.9 Hz, 1H, Ir−*H*); **1b**, δ 0.605 (t, J_{PH} = 3.2 Hz, 3H, *CH*$_3$), −11.84 (t, J_{PH} = 16.4 Hz, 1H, Ir−*H*); **2a**, δ −0.14 (t, J_{PH} = 3.4 Hz, 3H, *CH*$_3$), −12.03 (t, J_{PH} = 16.4 Hz, 1H, Ir−*H*); **2b**, δ 0.34 (t, J_{PH} = 3.0 Hz, 3H, *CH*$_3$), −12.02 (t, J_{PH} = 16.4 Hz, 1H, Ir−*H*); **3a**, δ −0.128 (d of t, J_{PH} = 3.4 Hz, J_{HH} = 1.2 Hz, 3 H, *CH*$_3$), −11.96 (t, J_{PH} = 16.4 Hz, 1H, Ir−*H*); **3b**, δ 0.439 (d of t, J_{PH} = 4.4 Hz, J_{HH} = 1.6 Hz, 3 H, *CH*$_3$), −11.75 (t, J_{PH} = 17.8 Hz, 1H, Ir−*H*). See the Supporting Information for complete NMR data.
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