N−H versus C−H Activation of a Pyrrole Imine at {Cp*Ir}: A Computational and Experimental Study

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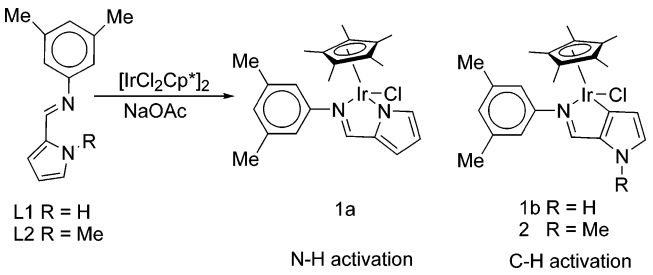
Summary: Reaction of a pyrrole imine with $[IrCl_2Cp^*]_2$/NaOAc leads to N−H activation in preference to C−H activation at the pyrrole; however, with the N-methylated ligand C−H activation occurs. Density functional calculations show that N−H bond activation is both kinetically and thermodynamically preferred to C−H activation. Both reactions occur with relatively low energy barriers by an electrophilic agostic interaction with the metal with simultaneous intramolecular hydrogen bonding with acetate leading to deprotonation via a six-membered transition state.

In 2003 we reported the facile cyclometalation of nitrogen donor ligands with $[MCl_2Cp^*]_2$ (M = Rh, Ir) or $[RuCl_2(p\text{-cymene})]_2$ in the presence of sodium acetate.[1] Subsequent density functional calculations on the cyclometalation of dimethylbenzylamine with $[Pd(OAc)_2]$[2] and $[IrCl_2Cp^*]_2$[3] showed both these reactions to proceed via six-membered transition states with significant intramolecular H bonding to coordinated acetate and some degree of agostic C−H interaction with the metal. Thus, the metal acetate provides electrophilic activation of the C−H bond and acts as an intramolecular base for the deprotonation. Other computational and experimental studies have suggested an important role for H bonding to acetate in orienting a substrate.[4] The use of carboxylate to facilitate C−H activation has also been demonstrated recently in the activation of benzene by platinum(II) complexes.[5] We report here the extension of our work to the activation of N−H bonds which provides further insight into the nature of these acetate-assisted bond activation processes.

N−H activation is an extremely important reaction in alkene amination[6] and hydrodenitrogenation.[7] For middle to late transition metals N−H activation usually occurs via oxidative addition to an electron-rich low-oxidation-state complex and such processes have been studied computationally,[8] though more recently a σ-bond metathesis pathway has also been proposed.[9] Proton transfer to a bound ligand is well-known with lanthanide metals, being a key step in hydroamination catalysis; however, these involve highly basic metal alkyls or amides.[10] Previous studies of activation of pyrrole have generally shown that N−H activation is favored over C−H activation, at least for low-oxidation-state complexes.[11] In contrast, Sames has recently reported the rhodium(III)-catalyzed arylation of pyrrole and indoles in which C−H activation is preferred over N−H activation.[12] In this case a coordinated pivalate is thought to play a key role in this process. Thus, we decided to study the cyclometalation of pyrrole imines L1 and L2, derived from pyrrole-2-carboxaldehyde, with $[IrCl_2Cp^*]_2$/NaOAc (Scheme 1). L1 has both a C−H and an N−H bond available for activation and so is an ideal system in which to assess the competition between these two processes, while L2 only has a C−H bond available. Density functional calculations have also been used to quantify the energetics of the competing N−H and C−H bond activation.

Scheme 1



Pyrrole imine L1 reacted with $[IrCl_2Cp^*]_2$ and NaOAc in dichloromethane at room temperature. The ^{1}H NMR spectrum of the product shows a 1:1 ratio of the Cp* and the pyrrole ligand. Three multiplets, each having an integration of 1H, are observed at δ 6.38, 6.78, and 7.17 in the region expected for pyrrole ring protons, suggesting formation of the N,N chelating product **1a** (the alternative C,N product **1b** would only show

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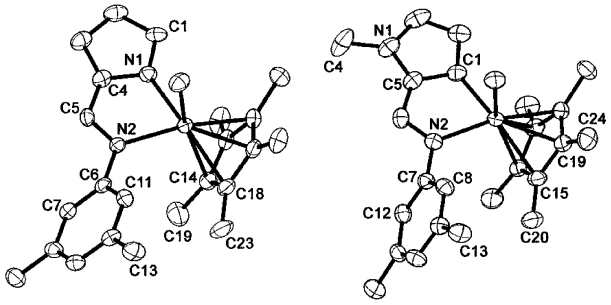

Figure 1. X-ray structures of **1a** and **2**. Selected bond lengths (Å) and bond angles (deg) are as follows. **1a**: Ir−N(1), 2.069(3); Ir−N(2), 2.123(3); N(1)−Ir−N(2), 76.4(1). **2**: Ir−C(1), 2.019(5); Ir−N(2), 2.094(4); C(1)−Ir−N(2), 77.7(2). All H atoms have been omitted for clarity.

two doublets in this region). The absence of a ν(N−H) band in the infrared spectrum is also consistent with the deprotonation of the N−H group and coordination of the pyrrole nitrogen to the metal. Hence, in this case N−H activation seems to be preferred to C−H activation.

To test whether C−H activation was indeed possible with this system, reaction of the N-methylated pyrrole imine L2 with $[IrCl_2Cp^*]_2$ and NaOAc was attempted. The C−H activated product **2** was obtained in good yield. The ^{1}H NMR spectrum shows only two doublets at δ 6.41 and 6.78 due to the pyrrole ring protons, confirming that cyclometalation has occurred and that activation of a pyrrole C−H bond is also energetically accessible in this system.

The X-ray structures of **1a** and **2** have been determined and are shown in Figure 1 with selected bond lengths and angles. The structures are very similar, though the Ir−N distances in **1a** are slightly longer than the corresponding Ir−N and Ir−C distances in **2**. In both complexes there is some distortion in the Cp* ligand with two long Ir−C bonds trans to the pyrrolide nitrogen or metalated carbon, as found in other cyclometalated complexes.[1]

Our previous work on cyclometalation using $[IrCl_2Cp^*]_2$ identified a key role for intermediates of the type $[Ir(substrate)(\kappa^2\text{-}OAc)Cp^*]^+$. Bond activation then proceeds via intramolecular proton transfer to one arm of the OAc ligand, and the most accessible route always features a six-membered transition state.[3] This is the basis of the present study, where density functional calculations[13] have been used to assess the energetics of N−H vs C−H bond activation for the model substrate $HN{=}CHNC_4H_4$.

Two forms of the precursor complex $[Ir(HN{=}CHNC_4H_4)(\kappa^2\text{-}OAc)Cp^*]^+$, **3** and **4**, were located which differ in the orientation of the pyrrole moiety (see Figure 2). **3** is slightly more stable and exhibits H bonding between the pyrrole N−H and the OAc ligand (N−H···O = 1.92 Å). As such, **3** is perfectly set up for N−H bond activation, and this proceeds in one step via $\mathbf{TS_{3-5}}$ (E = +16.8 kcal/mol). The geometry of $\mathbf{TS_{3-5}}$ reflects a displacement of the proximal OAc arm from the metal center by the approaching N−H bond. The N−H···O distance also decreases to 1.53 Å, and a slight elongation of the N−H distance to 1.10 Å is computed. However, the activating N−H bond remains remote from the Ir center, with Ir···N and Ir···H distances in excess of 2.5 Å.

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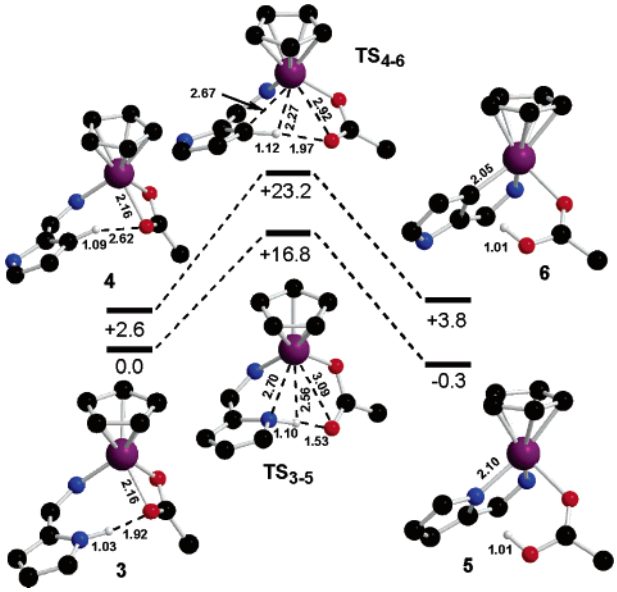

Figure 2. Computed reaction profiles (kcal/mol) for N−H (lower) and C−H activation in $[Ir(HN{=}CHNC_4H_4)(\kappa^2\text{-}OAc)Cp]^+$. Nonparticipating H atoms are omitted for clarity, and distances are given in angstroms.

In the alternative intermediate, **4** (E = +2.6 kcal/mol), the C(3)−H bond is directed toward the OAc ligand (C−H···O = 2.62 Å) and so allows for C−H activation at this position via $\mathbf{TS_{4-6}}$ (E = +23.2 kcal/mol). In $\mathbf{TS_{4-6}}$ the distance between the transferring H and the Ir center is shorter (2.27 Å) and that to the accepting OAc oxygen is longer (1.97 Å) than in $\mathbf{TS_{3-5}}$. Thus, the balance between H bonding (to O) and an agostic interaction (to Ir) shifts in the two transition states, with more H bonding in $\mathbf{TS_{3-5}}$ reflecting the more acidic nature of the N−H bond compared to the C−H one. In neither transition state is there much elongation of the X−H bond being activated. Similarly the Ir···H distances are very long (>2.25 Å), implying very little oxidative character in the transition state. These results differ from the σ-bond metathesis transition states located in a ruthenium system where C−H and N−H distances of 1.463 and 1.326 Å were calculated along with short Ru···H contacts below 1.9 Å.[9,14] Most importantly, in the present study $\mathbf{TS_{3-5}}$ is 6.4 kcal/mol more stable than $\mathbf{TS_{4-6}}$, indicating a kinetic preference for N−H over C−H bond activation. In addition, product **5** is 4.1 kcal/mol more stable than **6** and so N−H bond activation is also thermodynamically preferred.[15]

We have interpreted acetate-assisted C−H bond activation as an electrophilic mechanism involving intramolecular deprotonation. In the activation of pyrrole the lower pK_a of the N−H bond is expected to facilitate deprotonation; hence, N−H activation is expected to be kinetically favored over C−H activation. It is perhaps surprising, given its nonpolar nature, that the barrier to activation of a C−H bond is only 6.4 kcal/mol greater. We propose that these results reflect the synergic nature of acetate-assisted X−H activation, where both X−H···O H bonding and X−H···M agostic interactions reinforce each other to facilitate the bond activation process. Thus, for the more

(14) Similar σ-bond metathesis transition states were obtained in the present study by considering the reactions of $(Ir(HN{=}CHNC_4H_4)(\kappa^1\text{-}OAc)Cp^*]^+$. H transfer to the remaining coordinated oxygen entailed activation barriers (relative to **3**) of 21.2 kcal/mol (N−H activation) and 31.3 kcal/mol (C−H activation). See the Supporting Information for details.

(15) Experimentally, the observed products form via displacement of HOAc by Cl^- and calculations on models of these species indicate the N−H bond activation product is the more stable one by 9.1 kcal/mol.

acidic N−H bond significant H bonding creates a more electron-rich N−H bond that is better able to undergo an agostic interaction with Ir. For the C−H bond the agostic interaction increases the acidity, leading to more efficient C−H···O H bonding. Both interactions thus work synergistically to break the X−H bond.

The rather small difference in activation energies for acetate-assisted N−H and C−H activation may account for the different selectivities observed by Sames with a rhodium(III) carboxylate.[12] In that case the pyrrole is not constrained by chelation and an η^2 bonding mode may be possible (as indeed suggested by Sames). Such an interaction may constrain the geometry to provide a hydrogen bond to the C−H. Our work demonstrates that under these conditions the activation of a C−H bond can readily occur.

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Supporting Information Available: Text giving experimental procedures and spectroscopic details, CIF files and tables giving crystallographic data, atomic coordinates, thermal parameters, and bond distances and angles for **1a** and **2**, tables giving computed Cartesian coordinates and energies of all stationary points, and text giving the full ref 13. This material is available free of charge via the Internet at http:/pubs.acs.org.

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