Computational Studies of Intramolecular Carbon−Heteroatom Bond Activation of N-Aryl Heterocyclic Carbene Ligands

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Received November 15, 2007

Density functional theory calculations have been performed on intramolecular C(aryl)−X bond activation reactions in model N-heterocyclic carbene (NHC) complexes of the type $Ru(NHC)(PH_3)_2(CO)$, where NHC = 1-(C_6H_4-2-X)imidazol-2-ylidene (I(*o*-C_6H_4X), X = H, CH_3, F, OH, NH_2, OCH_3, and CF_3). In all cases C(aryl)−X activation is found to be thermodynamically favored, and the largest barrier to reaction is computed to be +21.3 kcal/mol when X = CH_3. As C(aryl)−CH_3 bond activation has been observed experimentally for a Ru−NHC complex (Jazzar, R. F. R.; Macgregor, S. A.; Mahon, M. F.; Richards, S. P.; Whittlesey, M. K. *J. Am. Chem. Soc.* **2002**, *124*, 4944), this suggests that a wide range of heteroatom-substituted N-aryl NHC ligands may be susceptible to intramolecular bond activation and potential ligand degradation. The computed exothermicity of C(aryl)−X activation follows the trend X = NH_2 < CH_3 < H < OH ≈ OCH_3 < CF_3 < F, while the barriers vary as X = H < F < OH ≈ OCH_3 < CF_3 < NH_2 < CH_3. Both series reflect the promotion of C(aryl)−X activation by the formation of stronger Ru−X bonds in the product. However, the ability of heteroatom ligands to stabilize the Ru(0) reactants through chelation can disfavor C(aryl)−X cleavage and explains the low exothermicity and high barrier associated with C(aryl)−NH_2 activation. For X = OCH_3 C(aryl)−O bond activation was found to be favored kinetically over O−C(alkyl) activation, although the latter process yields an extremely stable aryloxide product. The arrangement of coligands around the metal can significantly affect C(aryl)−X bond activation, and when X is a π-donor, this process is promoted by a trans CO ligand. These insights suggest not only possible ways to control unwanted C(aryl)−X activation in heteroatom-subtituted N-aryl NHC ligands but also factors that may promote such reactions in catalytic processes where this step is desirable.

Introduction

The last 10 years have seen a rapid increase in the use of N-heterocyclic carbenes (NHCs) as supporting ligands in transition metal homogeneous catalysis.[1−4] As with phosphines, NHCs promise control of metal center reactivity through variation in the nature of the ligand substituents. For NHCs this is often achieved at the N1/3 positions, and in most cases to date, hydrocarbyl alkyl or aryl groups have been employed. Recently, however, considerable interest has focused on synthesizing NHCs with a heteroatom group incorporated into the N1/3 substituent. In many cases, the heteroatom then provides an additional coordination group, allowing the NHC ligand to act as a multidentate/hemilabile ligand. A wide array of these NHC−X (X = O, N) donor chelating ligands are now available.[5] In this paper the focus will be on N-aryl-substituted NHCs,[6,7] and within this class examples with −OH[8] and −SH[9] groups are known. Deprotonation then yields anionic C,O or C,S donor chelates, which in several cases are chiral. Even in the absence of direct chelation the introduction of a heteroatom group can

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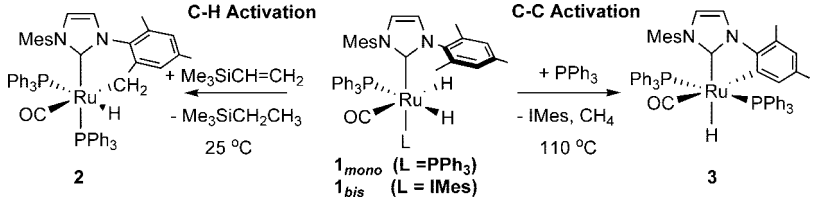
10.1021/om701151g CCC: $40.75
Publication on Web 02/14/2008

Scheme 1



significantly affect reactivity. For example, fluorinated analogues of Ru(SIMes)(PCy_3)(=CHPh)Cl_2 (SIMes = 1,3-dimesitylimidazolin-2-ylidene) give enhanced rates for olefin metathesis, a fact attributed to the ability of the fluoro substituents to stabilize the metal center during catalyst activation.[10]

The design of new NHCs with heteroatom functionalities therefore holds great promise for future applications in catalysis. One potential difficulty, however, is that such species may be prone to NHC-based reactions that lead to ligand degradation. The noninnocent behavior of NHCs has been widely recognized,[11] with examples ranging from NHC loss via unexpected dissociation[12] or reductive elimination[13] to reactions that fundamentally alter the structure of the ligand.[14] Within this last category are intramolecular bond activation (or cyclometalation) reactions, and in most cases these have involved C−H activation.[15–18] A well-characterized example of this occurs when Ru(IMes)(PPh_3)$_2$(CO)$(H)_2$ (**1**$_{mono}$, IMes = 1,3-dimesitylimidazol-2-ylidene) reacts with alkenes to give **2** (Scheme 1).[19] However, intramolecular activation of a C(aryl)−C(sp^3) bond in the closely related bis-NHC complex Ru$(IMes)_2$-(PPh_3)(CO)$(H)_2$ (**1**$_{bis}$) has also been reported, yielding **3**. Given that these Ru systems are susceptible to intramolecular bond activation (so that even a strong C(aryl)−C(sp^3) bond can be cleaved), we speculated that similar NHC ligands featuring C(aryl)−X groups (X = F, OR, NR_2, etc.) might also be vulnerable to degradation processes via intramolecular C(aryl)−X bond activation.

In previous work we used density functional theory (DFT) calculations to model C(sp^3)−H and C(aryl)−C(sp^3) bond activation in **1**$_{mono}$ and **1**$_{bis}$.[20] These processes rely on the removal of H_2 to form reactive Ru(0) species, and for **1**$_{mono}$ alkene hydrogenation at 25 °C readily yields 16*e* Ru(IMes)-(PPh_3)$_2$(CO), **4**. Kinetically accessible C(sp^3)−H activation can then occur to give **2**. Alternatively, H_2 may be lost thermally, and for sterically hindered **1**$_{bis}$ this combines with facile PPh_3 dissociation to give 14*e* Ru$(IMes)_2$(CO). At higher temperatures C(sp^3)−H activation becomes reversible, allowing C(aryl)−C(sp^3) cleavage to be accessed. The C−C activated species is then trapped irreversibly by H_2 and PPh_3 to give **3**. These studies highlighted two key points: (i) the high reactivity of Ru(0) species toward intramolecular bond activation; (ii) the ready

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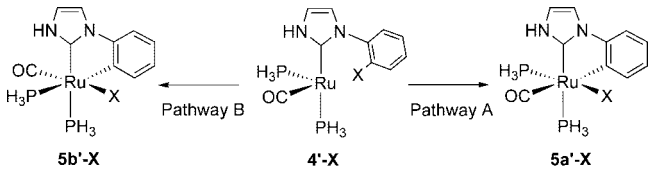
Scheme 2



formation of such species under conditions that are highly relevant to catalysis.[4,21]

In this paper we have used DFT calculations to investigate a variety of C(aryl)−X bond activations in N-aryl NHCs bearing heteroatom functionalities. Our calculations are based on Ru(I*o*-C_6H_4X)$(PH_3)_2$(CO) (**4′-X**, see Scheme 2), models of intermediate **4** formed from $\mathbf{1}_{mono}$ via alkene hydrogenation. We have previously shown that ligand steric bulk plays only a minor role in the energetics of intramolecular bond activation, and so these small models should provide a good assessment of reactivity trends.[20]

As well as the implications for NHC ligand stability, the model reactions in Scheme 2 also provide fundamental information on the activation of normally unreactive C(aryl)−X bonds. Although cyclometalation involving C(aryl)−H activation[22] is common and many examples are also known for C(aryl)−F activation,[23] few instances involving C(aryl)−O[24] or C(aryl)−N[25] bonds have been reported. Recently, however, Kakiuchi and co-workers have reported the Ru-catalyzed functionalization of aryl-ethers[26] and -amines.[27] These processes are closely related to the Murai reaction[28] and are thought to proceed via chelation-assisted C(aryl)−O/N bond activation. In one case the C(aryl)−O cleavage product has been isolated.[29] Computational studies on the Murai reaction have suggested a key role for a 16*e* intermediate of the form $Ru(PPh_3)_2$(CO){O=C(R)Ph}, which features an O-bound ketone.[30] This species is closely related to model **4′-X**, and both systems will produce five-membered metallacycles upon C(aryl)−X activation. Our model studies should therefore provide information of relevance to the development of these and related catalytic systems.

Computational Details

All DFT calculations were run with Gaussian 03[31] using the BP86 functional. Ru and P centers were described with the Stuttgart RECPs and associated basis sets (denoted "SDDALL" in G03)[32] with a set of d-orbital polarization functions on P ($\zeta = 0.387$).[33] 6-31G** basis sets were used for all other atoms.[34] All stationary points were fully characterized via analytical frequency calculations as either minima (all positive eigenvalues) or transition states (one imaginary eigenvalue), and IRC calculations were used to confirm the minima linked by each transition state. Reported energies include a correction for zero-point energies.

Results and Discussion

C(aryl)−X Bond Activation in 4′-X (X = H, F, OH, NH_2, and CH_3). In principle, C(aryl)−X bond activation in **4′-X** may occur such that X is placed trans to either PH_3 (pathway A, yielding products **5a′-X**, Scheme 2) or CO (pathway B, giving **5b′-X**). These two pathways were found to originate from two slightly different forms of the reactant, **4a′-X** and **4b′-X**, respectively, which are close in energy but differ in the orientation of the I*o*-C_6H_4X moiety. For X = H or CH_3 pathway A was found to give the more stable products, while pathway B was preferred for X = F, OH, or NH_2. In order to have a consistent set of results with which to compare the energetics of C(aryl)−X bond activation, we shall focus initially on the results obtained for pathway A. This choice is based on the observation that cyclometalated species such as **2** and **3** are derived from this route; however, similar trends emerge from the results based on pathway B. The most important differences between pathways A and B will be considered after the discussion of general trends.

Figure 1 gives details of the stationary points involved in C(aryl)−X bond activation along pathway A. For **4a′-H** a structure featuring a strong agostic interaction between Ru and one ortho-C−H bond (Ru···H = 1.80 Å; C2−H = 1.24 Å) was located, indicating significant preactivation of this bond to undergo cleavage. No nonagostic isomer of **4a′-H** could be located. Indeed, although a transition state for C(aryl)−H bond activation was located, incorporation of zero-point energy corrections caused the energy of this species to drop below that of the reactant. C(aryl)−H activation is also reasonably exo-

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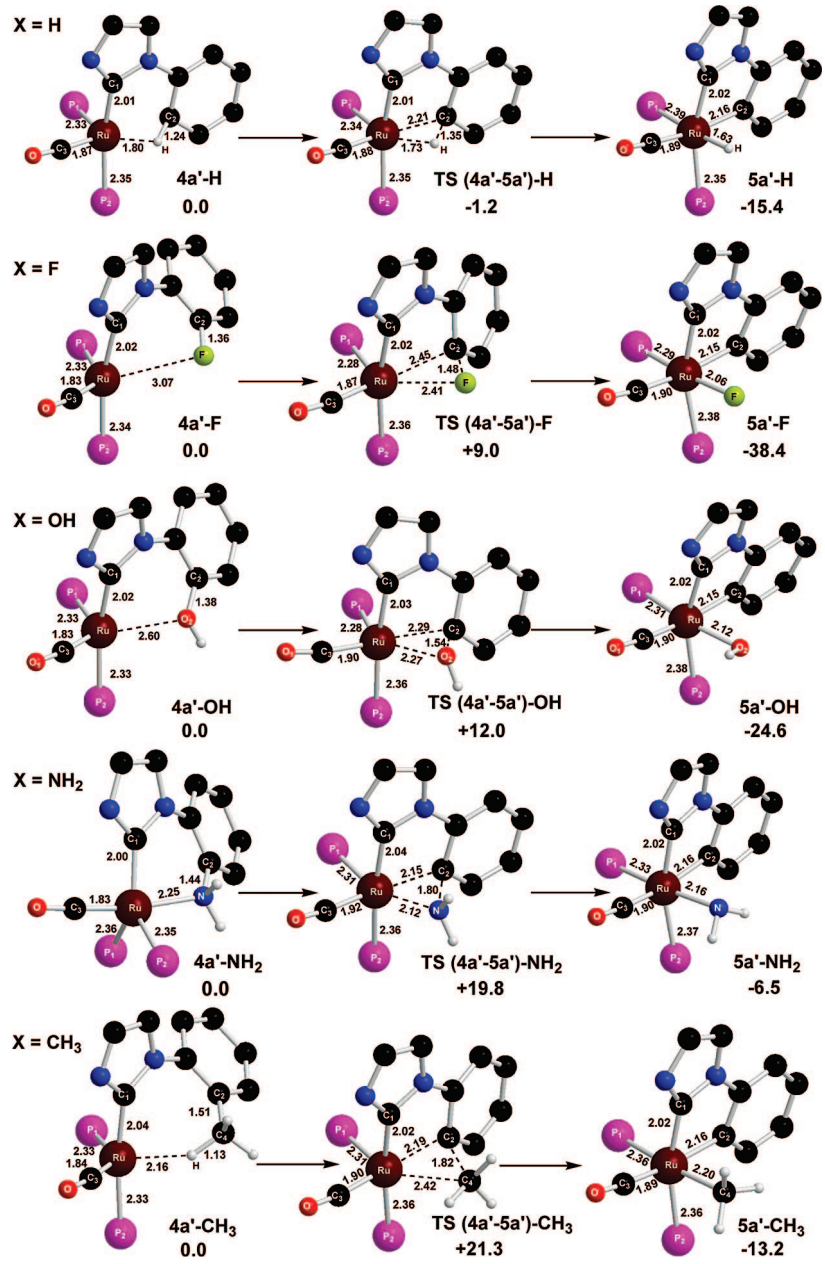

Figure 1. Computed stationary points for C−X activation in **4a′-X** (X = H, F, OH, NH_2, and CH_3). Energies (kcal/mol) are quoted relative to each respective **4a′-X** species. Key distances are given in Å. All nonparticipating hydrogen atoms are omitted for clarity.

thermic ($\Delta E = -15.4$ kcal/mol), and so this process would be expected to proceed without any barrier as soon as **4a′-H** was formed. Previously, we have computed the energetics for C(sp^3)−H activation in the ortho-CH_3 group in model **4a′-CH₃** ($\Delta E^{\ddagger} = +6.6$ kcal/mol; $\Delta E = -16.0$ kcal/mol),[20] and the comparison suggests that C(aryl)−H activation will be the more likely event where competition between these two processes may exist.[35]

Unlike **4a′-H**, the structure of **4a′-F** suggests a minimal Ru···F interaction (Ru···F = 3.07 Å), and the subsequent C(aryl)−F activation has a distinct barrier of 9.0 kcal/mol. This is still small in absolute terms, and as this process is also extremely favorable thermodynamically ($\Delta E = -38.4$ kcal/mol), C−F bond cleavage should readily occur and be irreversible upon formation of **5a′-F**. For **4a′-OH** and **4a′-NH₂** an important additional feature is the increased ability of the heteroatom lone pairs to interact with the metal center, which leads to short Ru−X distances of 2.60 Å (**4a′-OH**) and 2.25 Å (**4a′-NH₂**). For **4a′-NH₂** a trigonal bipyramidal geometry is computed and the strong Ru−N interaction induces isomerization to a structure with axial amine and CO ligands.[36] C(aryl)−O activation in **4a′-OH** proceeds with a fairly modest barrier of 12 kcal/mol,

(35) With an *o*-tolyl substituent as in **4-CH₃** C(aryl)−H activation will also be favored by the formation of a five-membered ring. This factor can also reverse the preference in favor of C(sp^3)−H activation, as seen in the reactions of 1-benzyl-3-*tert*-butylimidazol-2-ylidene at Ir. The observation of C(aryl)−H activation with the 1-benzyl-3-isopropylimidazol-2-ylidene analogue, however, indicates how subtle these competition effects can be, and in this case the variable reactivity was ascribed to steric effects. See ref 15e.

(36) Alternative forms of **4a′-OH** and **4a′-NH₂** without a direct Ru−N or Ru−O interaction could also be located. The alternative form of **4a′-NH₂** featured an Ru···H−N agostic interaction ($E = +2.6$ kcal/mol), while for **4a′-OH** a species with a more open P_1−Ru−C_3 angle of 136° and a longer Ru···O2 distance of 3.77 Å was seen ($E = +1.6$ kcal/mol). In all cases, however, the most stable structures of **4a′-X** are shown in Figure 1.

Table 1. Computed Energetics for C−X Bond Activation in 4a′-X, C(aryl)−X Homolytic Bond Dissociation Energies for Ph−X Species, and Ru−X Bonds in 5a′-X (kcal/mol)

X	ΔE_{C-X}	$\Delta E^{\ddagger}_{C-X}$	C(aryl)−X	Ru−X
H	−15.4	−1.2	110.5	73.2
F	−38.4	+9.0	131.8	105.2
OH	−24.6	+12.0	113.1	73.3
NH_2	−6.5	+19.8	102.4	53.6
CH_3	−13.2	+21.3	99.9	51.1

but this increases to ca. 20 kcal/mol for C(aryl)−N activation. The energy change associated with these processes is also much more favorable for C(aryl)−O activation (−24.6 kcal/mol, cf. −6.5 kcal/mol for C(aryl)−NH_2 activation). The series is completed by C(aryl)−CH_3 activation in **4a′-CH$_3$**, and this is found to have the highest barrier of all those computed so far (21.3 kcal/mol), although this process is still reasonably exothermic (−13.2 kcal/mol).

The energetics of C(aryl)−X bond activation are summarized in Table 1. Computed values for ΔE_{C-X}, the overall energy change associated with C(aryl)−X activation, follow the trend X = NH_2 < CH_3< H < OH < F. To a first approximation, variation in ΔE_{C-X} will be determined by the energy required to break the C−X bond in **4a′-X** compared to the energy released by Ru−X bond formation in **5a′-X**. To model the former we have computed the C(aryl)−X homolytic bond strengths for the free substituted benzenes, Ph−X, while the Ru−X bond strengths in **5a′-X** have been computed directly via Ru−X homolysis. The values obtained are also displayed in Table 1[37] and indicate that both the C(aryl)−X and Ru−X bond strengths follow the trend X = CH_3 < NH_2 < H < OH < F, which, with the exception of the relative positions of NH_2 and CH_3, follows the same pattern computed for ΔE_{C-X}. This indicates that C(aryl)−X bond activation in **4a′-X** is usually most thermodynamically favorable when the strongest C−X reactant bonds are being broken. This initially counterintuitive result is explained by the fact that the Ru−X bond strengths are more sensitive to the nature of X. Thus the strongest Ru−X bond (Ru−F) is over 54 kcal/mol stronger than the weakest bond (Ru−CH_3), whereas the equivalent range in the C(aryl)−X bonds is only 32 kcal/mol. The changes in the Ru−X bonds therefore considerably outweigh those in the C(aryl)−X bonds. Similar results have in fact been reported before for H−X activation[38] and for a range of C−H activation processes.[39] In the present systems the one exception to this pattern occurs for C(aryl)−N activation in **4a′-NH$_2$**, which in terms of the above analysis has an anomalously low exothermicity. In this case this apparent discrepancy is derived from the extra stabilization of the reactant, which features strong N → Ru σ-donation through the nitrogen lone pair.

The computed activation barriers, $\Delta E^{\ddagger}_{C-X}$, follow the trend X = H < F < OH < NH_2 < CH_3. Of these processes, C−H activation has been most widely studied, and it is well-known that the spherical, nondirectional nature of the H 1s orbital greatly facilitates activation by allowing efficient interaction with the metal-based orbitals without the need for significant distortion.[40] For the remaining **4a′-X** species the steady increase in $\Delta E^{\ddagger}_{C-X}$ along the series is reflected in later transition state geometries, with shorter Ru−aryl distances and greater elongation of the C(aryl)−X bonds. The fact that C(aryl)−CH_3 activation has the highest barrier is particularly significant in the context of the stability of N-aryl NHC ligands, since despite being the least kinetically accessible process, C(aryl)−CH_3 has been observed experimentally (cf. **1** → **3**, Scheme 1). The implication is that C(aryl)−X activation in related ligands will occur more readily, making heteroatom-functionalized N-aryl NHCs susceptible to ligand-based degradation reactions.

The factors that determine the trend in $\Delta E^{\ddagger}_{C-X}$ are less clear. Setting aside the distinct case of C(aryl)−H activation, for the other C(aryl)−X bonds an approximate correlation can be seen between lower values for $\Delta E^{\ddagger}_{C-X}$ and the formation of stronger Ru−X bonds in the product. Thus the strength of the Ru−X bond being formed seems to play a role in determining both the kinetics and thermodynamics of C(aryl)−X activation and, in both cases, dominates the opposing trend seen in the C(aryl)−X bonds. An additional factor that plays a role in the barrier height is the presence of any X → Ru σ-donation in the reactant. This is most obvious for C(aryl)−N activation in **4a′-NH$_2$**, where the calculated barrier of 20 kcal/mol is much higher than might be expected from interpolation of the results for X = F, OH, and CH_3. This increased barrier reflects the need to disrupt the Ru−N bond before C−N activation can take place. A similar factor has been invoked to account for the relatively high barriers computed for the oxidative addition of amine N−H bonds.[41]

C(aryl)−X Bond Activation in Related Systems (X = CF$_3$, OCH$_3$). We have extended our studies to two further species, **4a′-OCH$_3$** and **4a′-CF$_3$**. The I*o*-$C_6H_4OCH_3$ ligand in **4a′-OCH$_3$** is a model for OCH_3 derivatives first introduced by Lappert[6] and recently extended by Grubbs.[10d] **4a′-OCH$_3$** also offers the possibility of competition between C(aryl)−O activation and O−C(sp^3) activation, in a similar way to that seen for phosphine-based pincer ligands of the type 1-OCH_3-2,6-$\{R_2PCH_2\}_2C_6H_3$.[42] **4a′-CF$_3$** is a model for fluorinated analogues of IMes, and although such species are not yet known, they might be interesting synthetic targets due to the highly electron-withdrawing character of perfluoro substituents. C(aryl)−CF_3 bond activation has also been observed in phosphine-based pincer ligands.[43]

Details of the bond activation reactions of **4a′-OCH$_3$** are given in Figure 2. The energetics of C(aryl)−O bond activation in **4a′-OCH$_3$** along pathway A are only marginally less favorable than the equivalent process for **4a′-OH**. Both C(aryl)−O activation processes therefore have much higher barriers than the C(aryl)−H activation computed for **4a′-H**, and this is consistent with the observation by Lappert of facile C(aryl)−H

(37) The calculated values reproduce well trends in the experimentally determined Ph−X bond dissociation energies (experimental values in kcal/mol, X = H: 112.9 ± 0.6; NH_2: 104.2 ± 0.6; OH: 112.4 ± 0.6; F: 127.2 ± 0.7; CH_3: 103.5 ± 0.6, taken from: Blanksby, S. J.; Ellison; G. B. *Acc. Chem. Res.* **2003**, *36*, 255).

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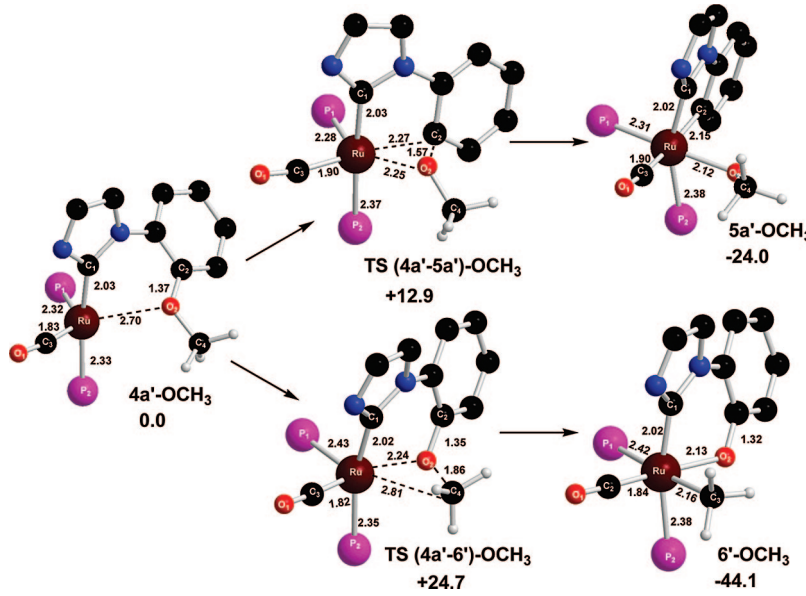

Figure 2. Computed stationary points for C(aryl)−O and O−C(alkyl) activation in **4a′-OCH$_3$**. Energies are in kcal/mol relative to **4a′-OCH$_3$**. Key distances are given in Å. All nonparticipating hydrogen atoms are omitted for clarity.

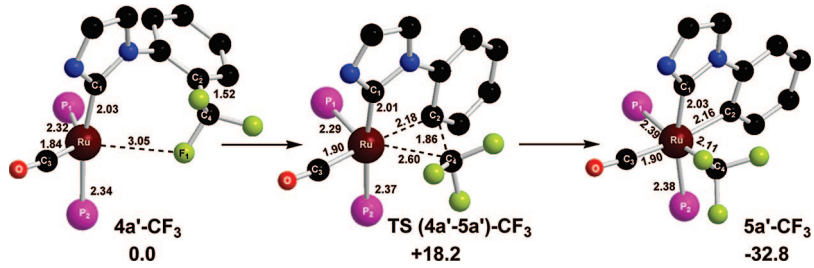

Figure 3. Computed stationary points for C(aryl)−CF$_3$ activation in **4a′-CF$_3$**. Energies are in kcal/mol relative to **4a′-CF$_3$**. Key distances are given in Å. All hydrogen atoms are omitted for clarity.

cleavage upon reaction of Ru(PPh$_3$)$_3$Cl$_2$ with the 1-phenyl-3-(2-methoxyphenyl)imidazol-2-ylidene dimer.[6b] Compared to C(aryl)−O activation, O−C(alkyl) bond cleavage in **4a′-OCH$_3$** has a much higher barrier of 24.7 kcal/mol, although the aryloxide product **6′-OCH$_3$** is extremely stable (E = −44.1 kcal/mol). Thus C(aryl)−O bond activation in **4a′-OCH$_3$** is kinetically favored, and although, in principle, O−C(alkyl) bond activation could be accessed under thermodynamic control, this would require the reversible formation of **4a′-OCH$_3$** from **5a′-OCH$_3$** with a barrier of +36.9 kcal/mol. The prediction of facile C(aryl)−O bond activation at **4a′-OCH$_3$** is consistent with selective observation of this process at Rh(I) complexes of the pincer ligand 1-OCH$_3$-2,6-{^{t}Bu$_2$PCH$_2$}$_2$C$_6$H$_3$.[42a–c] Thus C(aryl)−O bond activation appears favored (at least kinetically) at more electron-rich metal centers. In contrast, O−C(alkyl) bond activation of 1-OCH$_3$-2,6-{R$_2$PCH$_2$}$_2$C$_6$H$_3$ (R = ^{t}Bu, ^{i}Pr) has been observed at electron-deficient Ni(II) and Pd(II) metal centers for which an electrophilic pathway has been proposed. From this point of view the structure of **TS(4a′- 6′)-OCH$_3$** is interesting, as it features a short Ru···O2 contact of 2.24 Å and a very exposed CH$_3$ group (Ru···C4 = 2.81 Å, O2···C4 = 1.86 Å) that might be susceptible to anion abstraction, very much as proposed by Milstein et al. for their pincer systems.[42] C(aryl)−CF$_3$ activation in **4a′-CF$_3$** (Figure 3) is computed to be significantly more favorable thermodynamically than C(aryl)−CH$_3$ activation in **4a′-CH$_3$** ($\Delta E_{C\text{-}X}$ = −32.8 kcal/mol, cf. −13.2 kcal/mol). This is consistent with the general view that introducing fluoro substituents increases the M−CR$_3$ bond strength[44] and is confirmed by the greater computed Ru−CF$_3$ homolytic bond strength in **5a′-CF$_3$** (70.3 kcal/mol, almost 20 kcal/mol stronger than the Ru−CH$_3$ bond in **5a′-CH$_3$**). C−CF$_3$ bond cleavage is more accessible kinetically ($\Delta E^{\ddagger}_{C-X}$ = +18.2 kcal/mol, cf. +21.3 kcal/mol), and as discussed above, this lower barrier to activation is consistent with the greater product M−X bond strength.

Ligand Effects on C(aryl)−X Bond Activation. The discussion thus far has been based on pathway A (X trans to PH$_3$). Although the results for pathway B (X trans to CO) provide the same trends, the absolute values of ΔE_{C-X} and $\Delta E^{\ddagger}_{C-X}$ can vary quite dramatically. This is most apparent for **4′-F**, and so details of C(aryl)−F activation via pathway B in this species are given in Figure 4, where the relative energies of the equivalent stationary points along pathway A are shown in parentheses.

The only significant difference between **4a′-F** and **4b′-F**, the pathway B reactant, lies in the orientation of the NHC ligand, with the imidazole ring approximately bisecting the OC−Ru−P1 angle. The energies of these two alternative reactants are within 1 kcal/mol, and this small difference reflects the ease of rotation

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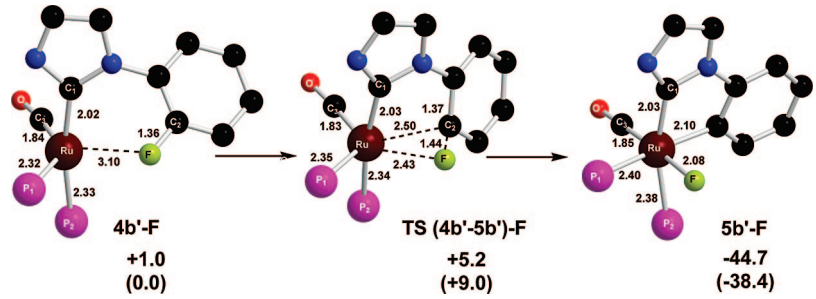
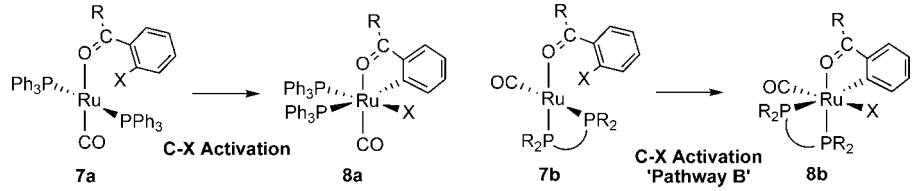


Figure 4. Computed stationary points for C(aryl)−F activation in **4b′-F** via pathway B. Energies are in kcal/mol and are relative to **4a′-F** with the equivalent pathway A data shown in parentheses. Key distances are given in Å. All hydrogen atoms are omitted for clarity.

Scheme 3



of small NHC ligands[45] and the minimal Ru···F interaction (Ru···F > 3 Å in both **4a′-F** and **4b′-F**). The greatest energetic difference between pathways A and B is seen in the products, where **5b′-F** is 6 kcal/mol more stable than **5a′-F**. In principle, the greater stability of **5b′-F** may be due to "push–pull" interactions along the trans-F−Ru−CO axis that alleviate Ru−F filled−filled dπ−pπ interactions.[46] Some support for this view comes from the computed Ru−F homolytic bond strength in **5b′-F**, which is 114 kcal/mol, 10 kcal/mol higher than in **5a′-F**. Despite this, the Ru−F bond in **5b′-F** is slightly longer (2.08 Å) than that in **5a′-F** (2.06 Å), a case of a shorter bond not necessarily equating to a stronger bond. Moreover, the computed carbonyl stretching frequency in **5b′-F** is also higher (1950 cm^{-1}) than in **5a′-F** (1942 cm^{-1}), suggesting less π-back-donation in the former case. The greater Ru−F bond strength in **5b′-F** therefore does not appear to be determined by more favorable π-interactions, but rather by σ-effects. Thus, the relative energies of **5a′-F** and **5b′-F** reflect the overall ligand trans influences, with the combination of aryl trans to PH_3 and F trans to CO in **5b′-F** being more stable than the alternative arrangement in **5a′-F**.

The preference for having F trans to CO is also apparent in **TS(4b′−5b′)-F**, which is almost 4 kcal/mol lower in energy than **TS(4a′−5a′)-F** along pathway A. Accordingly, **TS(4b′−5b′)-F** has a slightly earlier transition state geometry with longer Ru−C2 and Ru−F distances and a slightly shorter C2−F distance compared to **TS(4a′−5a′)-F**. The lower barrier for C(aryl)−F activation via pathway B is also consistent with the stronger Ru−F bond that is being formed in this case.

For the other π-donor ligands (X = OH and NH_2) similar differences between pathways A and B to those described above for X = F are computed, and full details are given in the Supporting Information. These results indicate that the energetics of C(aryl)−X activation can be significantly affected by the metal coordination environment. In the present paper, the species **4′-X** are models for potential Ru(NHC)$(PR_3)_2$(CO) intermediates in which the NHC ligand is most likely to have bulky N-aryl substituents at both the N1 and N3 positions. In such complexes C(aryl)−X activation via pathway B is unlikely on steric grounds, as the species formed would place the aryl substituent directly over a PPh_3 ligand (consider the alternative "pathway B" isomers of **2** and **3** in Scheme 1). However, less sterically demanding scenarios can be envisaged, for example, for the postulated intermediate in Murai-type C(aryl)−X activations, Ru$(PPh_3)_2$(CO){O=C(R)Ph} (Scheme 3). Calculations suggest that this takes the form of structure **7a**, in which the ketone is trans to CO.[30] However, if CO could be moved cis to the ketone, perhaps through use of a chelating diphosphine (**7b**), the equivalent mechanistic choice between pathways A and B would arise and, as a result, the possibility of a CO ligand being used to promote C(aryl)−X activation in cases where X is a π-donor ligand.

Conclusions

Density functional theory calculations have been performed to model C(aryl)−X bond activation in model Ru(*Io*-C_6H_4X)$(PH_3)_2$(CO) species (X = H, F, OH, NH_2, CH_3, OCH_3, and CF_3). The results indicate that C(aryl)−CH_3 cleavage entails the highest barrier to activation; however, given that this process has been seen experimentally in related systems the implication is that N-aryl NHC ligands bearing heteroatom substituents, X, may be vulnerable to intramolecular C(aryl)−X bond activation. C(aryl)−H and C(aryl)−F activation are predicted to be particularly facile processes. Trends in the energetics of C(aryl)−X bond activation are primarily determined by the strength of the Ru−X bond being formed, although the ability of heteroatom groups with free lone pairs can significantly stabilize the Ru(0) species against C(aryl)−X activation. The coordination environment around the metal can significantly affect the energetics of reaction. In particular, when X is a potential π-donor ligand, C(aryl)−X activation is significantly enhanced when X moves trans to a CO ligand.

Acknowledgment. We thank the EPSRC, the University of Bath, and Heriot-Watt University for support.

Supporting Information Available: Tables of computed Cartesian coordinates and energies of all species. Full ref 31. This material is available free of charge via the Internet at http://pubs.acs.org.

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