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Iridium(III) Catalyzed Trifluoroacetoxylation of Aromatic Hydrocarbons

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Abstract

A tridentate, NNC-tb (where NNC-tb = 2-(pyridin-2-yl)benzo[h]quinoline) ligated Ir^{III} complex (NNC-tb)Ir(Ph)(4-MePy)(TFA), **11** along with analogues are very active for CH activation as evidenced by rapid catalytic H/D exchange between benzene and trifluoroacetic acid – d_1 (DTFA). The complexes were examined with a variety of oxidants for the catalytic conversion of benzene to phenyltrifluoroacetate. Herein, the synthesis and characterization of (NNC-tb)Ir complexes is described along with the reactivity of these complexes towards arenes and alkanes.

Keywords:

Catalysis, Iridium, Benzene Oxidation, C-H Activation, C-H Functionalization

Introduction

Catalytic CH activation followed by oxy-functionalization of hydrocarbons to generate alcohols using strong electrophiles has proven a viable strategy for hydrocarbon oxidation (Scheme 1).[26-32] Systems based on soft, oxidizing cations such as Hg^{II},[33-35] Pt^{II},[36-47] Pd^{II},[19, 48-51] and Au^{I}/Au^{III} [52, 53] generate oxy-functionalized products from methane at product concentrations >1 M. However, the most active systems utilize concentrated, oxidizing acids and suffer from catalyst poisoning due to the generation of product and H_2O that bind to the strongly electrophilic center.[54] This inhibition has rendered these systems impractical and provided the motivation for the development of new systems that do not suffer from such inhibition.[55]

Scheme 1. General catalytic cycle for CH activation/M-R functionalization of hydrocarbons.
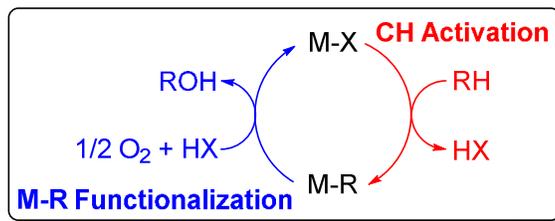
The use of less electrophilic, less oxidizing cations such as those based on Ir^{III} or Rh^{III} has been under exploration, as these species do not show sensitivities to water or product, and reactions can be carried out in non-oxidizing, relatively inert solvents such as CF_3CO_2H (HTFA).[56-59] Indeed, several reports have now shown that these weakly electrophilic cations can undergo CH activation with hydrocarbons in carboxylic acid solvents to generate M-R intermediates.[60-62] However, efficient catalysts have not been developed with these systems likely due to high energy barriers for oxy-functionalization of the M-R intermediate that is required for a complete catalytic cycle, Scheme 1.[63-66]

Recently, several groups have published examples of homogeneous catalyzed oxidations of aromatics with transition metal catalysts proposed to proceed via a CH activation mechanism (Eq. 1). For example, Sanford reported a Pd acetate complex that catalyzes H/D exchange of benzene and leads to the phenyl-ester when the system is treated with $PhI(OAc)_2$ as the oxidant.[67] Yu and coworkers reported several examples of the direct functionalization of aromatics with O_2 also using Pd catalysts.[68-70] An important thrust of our work has been the design of new homogeneous catalysts for the CH activation of alkanes and arenes. We recently reported Ir^{III} complexes bearing the ^tBu-NNC ligand (^tBu-NNC = 6-phenyl-4,4'-di-*tert*-butyl-2,2'-bipyridine) capable of undergoing CH activation with strong CH bonds such as methane and benzene.[71-74] It was shown that (^tBu-NNC)Ir(Et)(C_2H_4)(TFA) , **1**, in the presence of an oxidant, such as $NaIO_4$, gave ~6 turnovers (TON) of methyltrifluoroacetate after 3 h at 180 °C (Scheme 2). However, after 3 h, further H/D exchange or oxidation products were not observed. This is likely due to deactivation of the catalyst via pooling at higher oxidation states (e.g. Ir(IV or V) that are likely not capable of undergoing CH activation.[37]

$$\text{(1)}$$
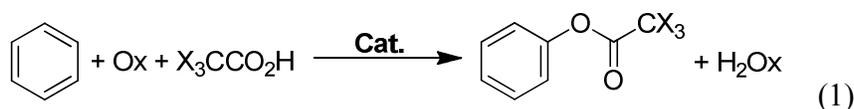
**Scheme 2.** Oxidation of methane to MeTFA by **1** in HTFA.
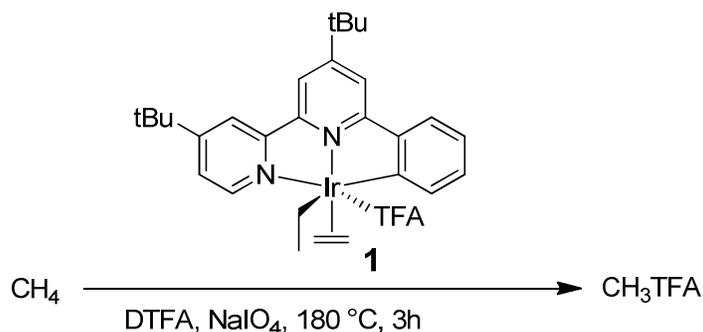
Another key issue with the (^{t}Bu-NNC)Ir system was the apparent lack of thermal stability of the (^{t}Bu-NNC)Ir systems above 100 °C that likely limited the efficiency of the system. Studies suggested that cleavage of the cyclometalated Ir-carbon bond, leading to loss/oxidation of the ligand or metal center, may have contributed to the complexes' low yield relative to the observed rates of H/D exchange and the observed loss of activity in extended run times. To address this, we investigated the use of new ligand designs to improve the stability of the catalytic system to the oxidizing and acidic reaction conditions. We also explored coupling the CH activation reaction to a functionalization reaction with potentially practical oxidants to generate phenol from benzene.

Results and Discussion

In an effort to design a more robust catalytic system, similar to the originally reported NNC system, we explored related iridium complexes with a geometrically restricted or "tied back" NNC motif. In the original report of the Ir complexes and subsequent work, it was discovered that the cyclometalled ring underwent decyclometallation as observed by incorporation of deuterium selectively in the ortho position of the phenyl ring.[74] We believe this loss of cyclometalation may be a root cause of the lack of thermal stability observed in these complexes. We postulated that fusing the phenyl ring to one of the pyridines should prevent the decyclometalation of the phenyl ring (Figure 1) as it would require loss of the chelating ligand. This led to the synthesis and study of an (NNC-tb) (NNC-tb = 2-(pyridin-2-yl)benzo[h]quinoline) ligated Ir system. The expectation was that a fused benzoquinoline motif should restrict the degrees of freedom of the cyclometalated phenyl group and lead to higher barriers for decyclometallation and higher thermal stability.

Figure 1. Parent NNC ligand system (**^{t}Bu-NNC**) compared to the "tied back" motif (**NNC-tb**).
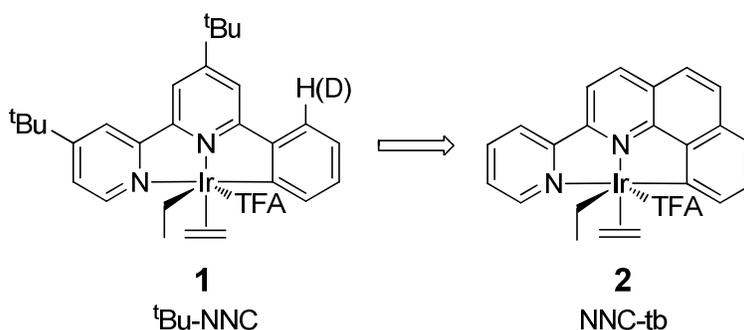
The (NNC-tb)Ir motif is readily accessible by following a similar synthetic methodology to those previously reported (Scheme 3).[71] Warming a methylene chloride solution of [Ir(COE)$_2$Cl]$_2$ with 1 eq of NNC-tb ligand[75] from -50 °C under an ethylene atmosphere, followed by stirring overnight at RT provided the six coordinate, Ir^{III} complex, (NNC-tb)Ir(Et)(C$_2$H$_4$)(Cl) (**3**) as an orange solid in 60% yield over two steps. The freely rotating ethylene ligand is observed as a singlet at $\delta = 4.1$ ppm in the ^{1}H-NMR. Replacement of the chloride is achieved by treatment with AgTFA and stirring at RT for 48 h to give (NNC-tb)Ir(Et)(C$_2$H$_4$)(TFA) (**2**). Finally, the ethyl group can be removed as ethane by stirring for 24 h at RT in neat HTFA to give (NNC-tb)Ir(C$_2$H$_4$)(TFA)$_2$ (**4**). All compounds were characterized by multinuclear NMR (^{1}H, ^{13}C, and ^{19}F), HR-MS, elemental analysis, and X-ray crystallography (Figure 2, for **3**, Figure 3, for **2**, and Figure 4 for **4**, respectively). Based on previous work with **1** in our group, heating **2** or **4** in hot HTFA should lead to loss of ethane and ethylene and generate a mixture of **5** and **6** under catalytic conditions (Scheme 3).

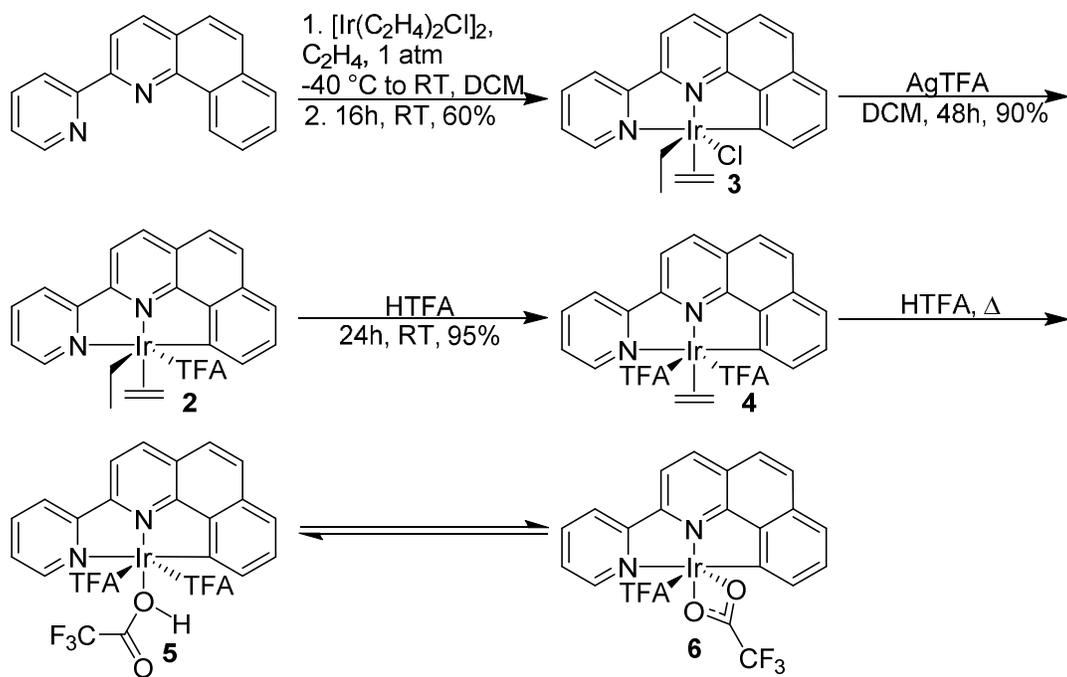**Scheme 3.** Synthesis of (NNC-tb)Ir(R)(L)(X) compounds **3-6**.

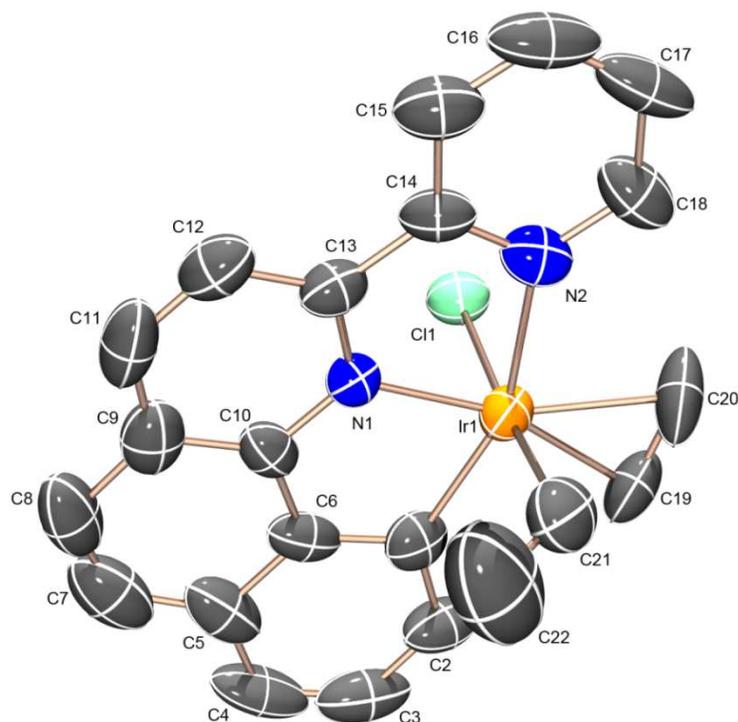**Figure 2.** ORTEP structure of (NNC-tb)Ir(Et)(C$_2$H$_4$)(Cl) (**3**) with ellipsoids at 50%.

Figure 3. ORTEP structure of (NNC-tb)Ir(Et)(C$_2$H$_4$)(TFA) (**2**) with ellipsoids at 50%.
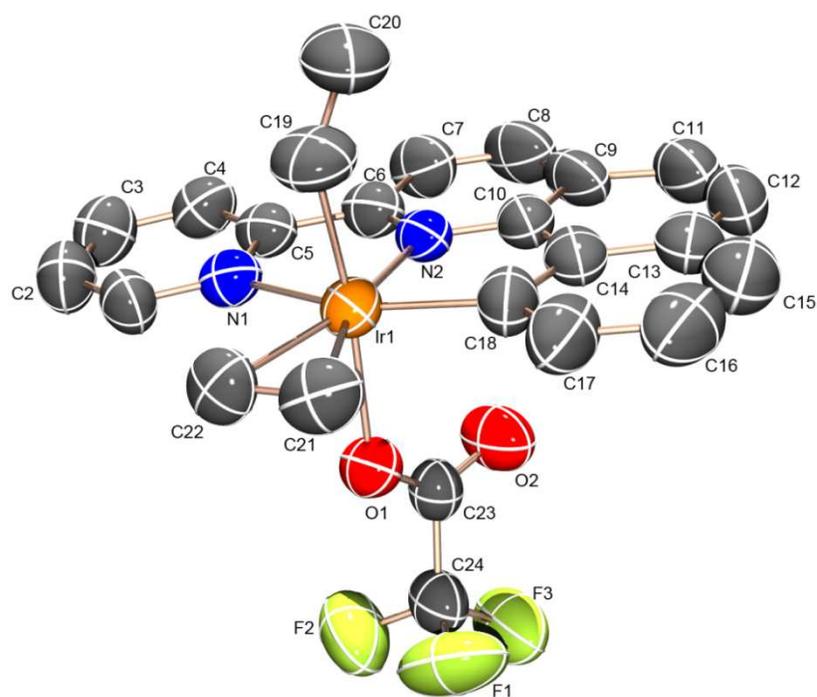
Figure 4. ORTEP structure of (NNC-tb)Ir(C$_2$H$_4$)(TFA)$_2$ (**4**) with ellipsoids at 50%.
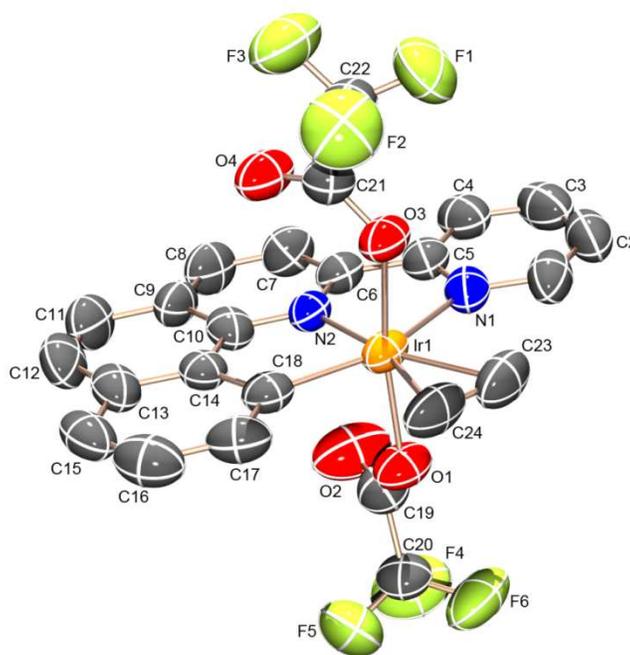
Analysis of the crystal structures for complexes **2-4** revealed increasing electrophilic character leading to a tightly bound ethylene as the electron-withdrawing TFA groups are added. Substitution of the Cl for TFA leads to an increase in the electrophilicity at the metal center as evidenced by the decreased C=C bond length (Table 1). Back donation from filled Ir π-orbitals would be expected to increase the C=C bond length. The observed decrease in C=C bond length in moving from complex **3** to the more electron deficient complex, **2**, is consistent with less back-bonding and more characteristic of a bound ethylene rather than a metalocyclopropane. In all cases, the bound ethylene is in plane with the NNC ligand in the crystal structures. The C=C bond length of coordinated ethylene in complex **3** is 1.386(16) Å, slightly longer than the C=C distance of 1.335 Å of free ethylene[76] and shorter than a typical C-C single bond (1.54 Å). The bond distance is more closely resemblant of a delocalized C-C bond, such as that of benzene (1.394 Å). The C=C bond distances in complexes **2** and **4** are 1.377(13) and 1.341(14) Å, respectively. Successive substitution of the TFA ligand on the iridium center results in a decrease

of the C=C bond length across a range of ~0.045 Å. The structural data is consistent with an appreciable electrophilic iridium center and a coordinated ethylene, which is consistent with solution NMR data for complexes **2-4**. The Ir-C distances are not particularly sensitive to changes in ligands on Ir and vary from 2.163(9) to 2.188(8) Å (Table 1).

Table 1. Comparison of the C=C and Ir-C bond lengths (Å).

Entry	Complex	C=C	Ir-C
1	Ethylene	1.335	–
2	(NNC-tb)Ir(Et)(C_2H_4)(Cl) (**3**)	1.386(16)	2.179(10), 2.180(10)
3	(NNC-tb)Ir(Et)(C_2H_4)(TFA) (**2**)	1.377(13)	2.163(9), 2.172(8)
4	(NNC-tb)Ir(C_2H_4)(TFA)$_2$ (**4**)	1.341(14)	2.182(8), 2.188(8)

Complex **2** was then examined for the CH activation reaction with a variety of hydrocarbons. H/D exchange reactions between hydrocarbons and deuterated DTFA revealed the system is active for aromatic sp^2 C-H bonds (Figure 5). Heating a 0.5 M solution of benzene in DTFA containing 5 mM of **2** at 150 °C for 3 h followed by GC-MS analysis showed 25% of the CH bonds had been converted to CD bonds (Table 2). With these positive results, reactions with benzylic and aliphatic CH bonds were examined (Figure 5). For example, heating a stirred solution of DTFA containing 5 mM **2** for 2 h at 180 °C under 500 psi of CH_4 led to H/D exchange between methane and the DTFA solvent. Analysis of the gas phase of the reaction mixture indicated that ~5% of the CH_4 was converted to 5.1% CH_3D, 0.1%, CH_2D_2, 0.0% CHD_3, and 0.0% CD_4. In comparison, **1** was shown to give ~30% conversion of CH_4 to 21.2% CH_3D, 6.6% CH_2D_2, 1.3% CHD_3, and 0.6% CD_4, under comparable conditions. It is important to note that the reaction mixtures remained completely homogeneous post reaction, in all cases, suggesting that catalyst decomposition is unlikely. Additionally, control reactions show that no

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background H/D exchange is observed between solvent and methane in the absence of either

catalyst. This would suggest that the H/D exchange is the result of reversible CH activation.

Thus, the generation of $(NNC-r)Ir(CH_3)X_2$ intermediates is plausible, where X is TFA or HTFA.

Table 2. H/D exchange of benzene and DTFA at 150 °C for 3 h catalyzed by **2**.

Run	C_6H_6	C_6H_5D	C_6H4D_2	$C_6H_3D_3$	$C_6H_2D_4$	$C_6H_1D_5$	C_6D_6	TOF $(x10^{-2} s^{-1})$	TON
Background No Catalyst	95.2	4.6	0.1	0.0	0.0	0.0	0.0	—	7
1	40.5	11.0	6.4	6.7	9.1	13.7	12.6	2.80	302
2	43.2	10.5	5.9	6.0	8.1	13.1	13.2	2.72	293

Figure 5. H/D exchange results using **2** in DTFA.
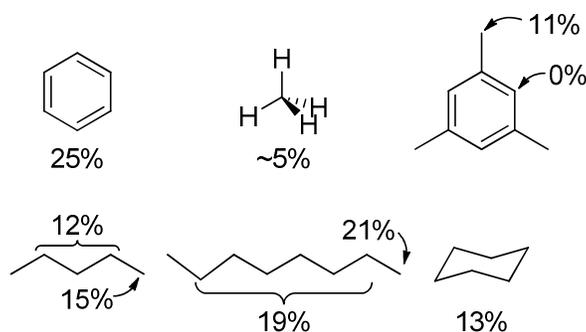
In addition to methane, complex **2** also catalyzes H/D exchange with other alkanes and

arenes such as *n*-octane, cyclohexane, mesitylene, and *n*-pentane in trifluoroacetic acid based on

NMR and GC-MS analysis. With *n*-octane and *n*-pentane, exchange is observed at all positions

with a small preference for the primary position. This is not surprising, as activation of stronger,

primary CH bonds is consistent with other reports on CH activation systems.[77-79] This selectivity

can be attributed to the stronger M-C bonds formed from scission of primary, sp[3] CH bonds as a

main driving force for the observed regioselectivity. Secondary CH bonds lead to a weaker M-C

bond, which disfavors formation of the internal M-C intermediate. Furthermore, these results are

also persuasive evidence against an exchange mechanism involving radicals. The lack of

observed H/D exchange on the sp^2 CH bond of mesitylene is the result of an extraordinarily fast background reaction between DTFA solvent and mesitylene (likely the result of electrophilic aromatic substitution reactions with the methyl groups stabilizing the carbocation intermediates). This extraordinarily fast background reaction makes further H/D exchange at this position difficult to detect. In comparison to **1**, the observed rates of H/D exchange catalyzed by **2** are typically equivalent within error for benzylic CH bonds and slower for aliphatic hydrocarbons. A possible reason for this disparity will be dicussed later in this manuscript.

Recently, we utilized a method that allows for distinguishing between rate limiting steps of CH bond coordination or cleavage.[80] If the system was following typical Schultz-Flory behavior, $C_6D_1H_5$ should build up followed by gradual increase in $C_6D_2H_4$. Given that higher isotopologues of benzene are observed, it would suggest that multiple CH activation events are occuring. H/D exchange reactions between C_6H_6 and DTFA were monitored by sampling the liquid phase by GC-MS analysis after neutralization of the acid and extraction with diethyl ether. Heating 5 mM solutions of **2** in a 0.5 M solution of benzene in DTFA and sampling the reaction over 3 h led to parallel incorporation of deuterium (Figure 6). The parallel incorporation of deuterium is suggestive of CH bond coordination as the rate determining step for the CH activation reaction of benzene and can be modeled by the hypothetical energy diagram shown in Figure 7.

Figure 6. Benzene H/D exchange catalyzed by **2** monitored over 3 h at 100 °C.
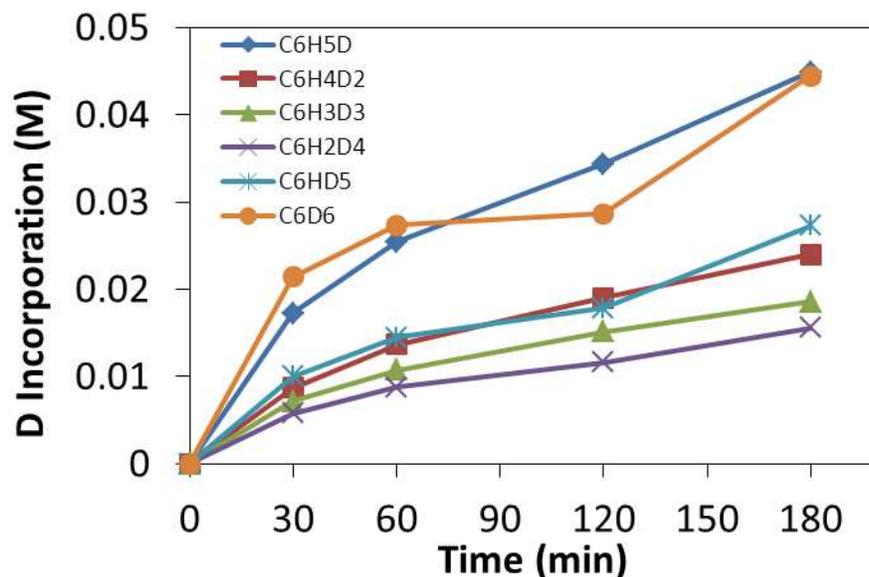
Figure 7. Representative energy diagram for CH activation that leads to parallel incorporation.
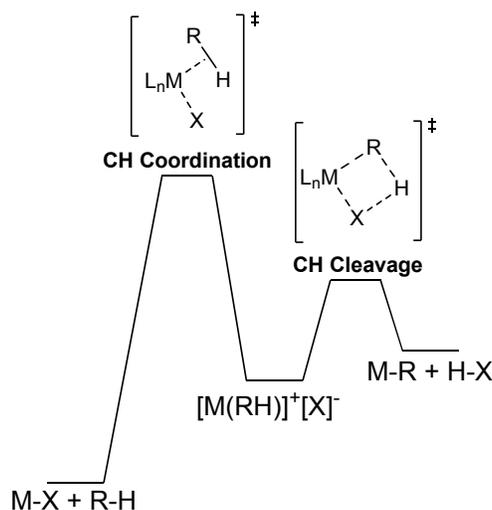
In moving to the "tied back", NNC-tb ligand, we expected the system to become more stable

to the reaction conditions. We found it perplexing, therefore, that our new complex, **2**, exhibited

less activity for H/D exchange with aliphatic hydrocarbons than did the parent complex, **1**. This

led us to question the lability of the bound ethylene in **2**. However, to avoid any complications

by the inclusion of the ethyl ligand, we choose to use complex **4** instead of **2** to examine the

lability of only ethylene. Previously, it was reported that NNC ligated Ir complexes underwent

facile loss of ethylene under similar conditions.[74, 81, 82] The loss of ethylene from **4** (Eq. 2) was

monitored by preparing a 15 mM solution in HTFA in a sealed J-Young NMR tube under argon.

The NMR tube contained a coaxial insert containing 1,3,5-trimethoxybenzene in DMSO-D_6. The

NMR tube was heated at 100 °C and monitored over 5 days by ^{1}H NMR (See SI). Monitoring of

the ethylene signal at 4.9 ppm revealed that loss of the ethylene from **4** was in fact much slower

than in previously developed (tBu-NNC)Ir complexes. A $T_{1/2}$ = ~1000 min was observed for the

loss of the Ir-ethylene signal.
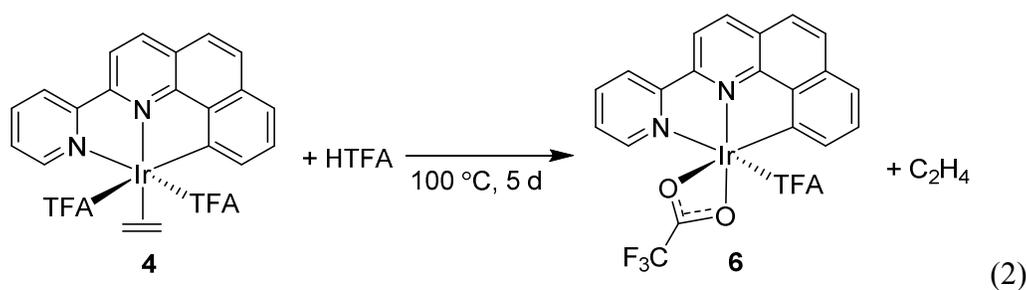
In an effort to improve catalytic CH activation in this system, we designed Ir complexes that

were based on the NNC-tb ligand, but did not have a bound ethylene. Previous work in our group

has shown that heating NNC ligated Ir complexes (**7**) in neat hydrocarbon such as benzene led to

a bridging Ir dinuclear species (**8**).[83] Treatment of the chloride dinuclear species, **8,** with a

coordinating amine base such as pyridine gave rise to the formation of a mononuclear complex

(tBu-NNC)Ir(Ph)(Py)(Cl) (**9**, Scheme 4). Following a similar methodology, **3** was heated in neat

benzene at 160 °C for 6 h in a sealed glass vessel under vacuum. Removal of the solvent and

treatment of the residue with neat 4-methylpyridine (4-MePy) for 2 days, followed by flash

column chromatography gave (NNC-tb)Ir(Ph)(4-MePy)(Cl) (**10**) in 37% yield over two steps as

a brown powder. The use of unsubtitued pyridine led to a mixture of products that proved

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difficult to resolve by chromatography or crystalization. Specifically, ^{1}H NMR interpretations were challenging due to the nature of 21 aryl protons with 17 of them being chemically distinct and overlapping. We found that addition of the methyl group on the pyridine in the 4-position provided a means of identifying pyridine ligated Ir complexes where the methyl group is used as a reference point. Furthermore, the increased solubility of the 4-methylpyridine complex in organic solvents makes further manipulations simpler. Following isolation of **10**, stirring in DCM with 4 eq of AgTFA gave (NNC-tb)Ir(Ph)(4-MePy)(TFA) (**11**) in quantitative yield (Scheme 5).

Scheme 4. Synthesis of (^{t}Bu-NNC)Ir(Ph)(Py)(Cl) (**9**).[83]
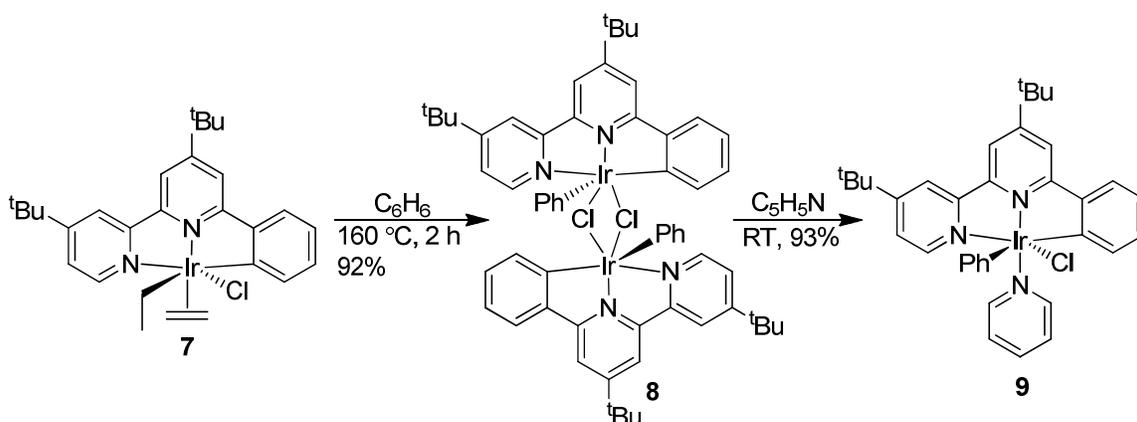
Scheme 5. Synthesis of (NNC-tb)Ir(Ph)(4-MePy)(TFA) (**11**).
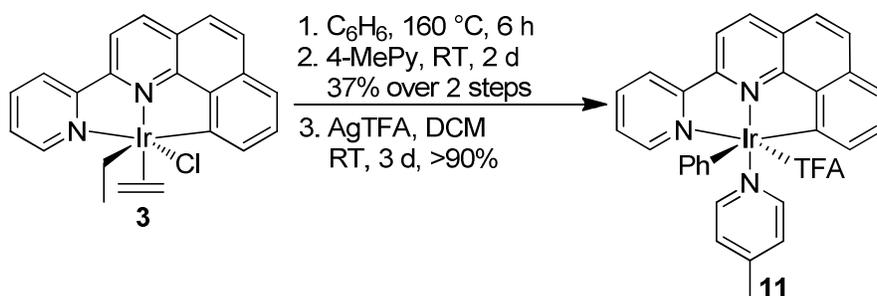
We then set out to determine if **11** was an effective catalyst for CH activation of aromatic substrates. Our group's previous work suggested that the Ir-Ph intermediates of the parent Ir(^{t}Bu-NNC) complex **1**, **8** or **9**, show similar catalytic rates to the parent compounds within

experimental error. It was our hope, in moving to the NNC-tb ligated systems, that **11** would be much more active than **2**, due to the slower loss of ethylene in the NNC-tb ligated iridium systems than those previously reported for ^{t}Bu-NNC ligated iridium systems. Therefore, we heated solutions of **11** under identical conditions to those reported for **2** (150 °C, 3 h) and found that the Ir-Ph complex led to significantly increased rates of H/D exchange between C_6H_6 and DTFA. The rate of H/D exchange was so fast that reactions did not remain pseudo-first-order with respect to benzene, preventing extraction of suitable rate data. The extraorinarly high rates of H/D exchange using **11** prompted us to compare these new complexes to some of our previously reported active CH activation catalysts.[71, 74] Our goal in development of the "tied-back" NNC was to improve stability (and hopefully enhance catalytic rates) of the parent NNC complex. Pseudo-first-order conditions for H/D exchange between benzene and DTFA catalyzed by **11** were realized by running the reaction at 75 °C for 1 h. In order to ensure that the phenyl substituent on the catalyst did not significantly contribute to the observed H/D exchange, the concentration of benzene in solution was increased to 5 M and the catalyst concentration remained at 5 mM. Control studies run with **11** in DTFA indicate that deuteration of the phenyl substituent occurs rapidly, even at room temperature, and that deuterium is incorporated into the resultant benzene (see SI). Catalysts **1**, **2**, and **11** were screened under identical conditions in order to make a direct comparison of their activity. In all three cases, the reaction mixtures remained homogeneous post reaction, suggesting that catalyst decomposition is not occurring. The results of this study indicate that **11** is approximately an order of magnitude faster than **1** and **2** (Table 3). Interestingly, there are no observed differences in rate between the "tied-back" and parent NNC complexes within experimental error. This would suggest a common mechanism for CH activation between **1** and **2**. The higher observed rate for **11** correlates well with a more

tightly bound ethylene in **2** than had been expected and it is likely that our increase in catalytic activity, when using **11**, results from the generation of a highly active Ir cation possessing open coordination sites that are not readily accessible when ethylene is present in the complex, especially at lower temperatures. Thus, slow loss of ethylene from **2** results in moderate catalyst inhibition at the start of reactions.

Table 3. Comparison of various Ir-NNC catalyst CH activation systems.
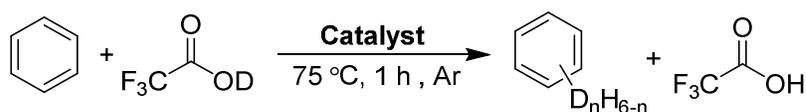
Catalyst	TON	TOF (x 10^{-3})
1	7.5 ± 0.7	2.0 ± 0.1
2	8 ± 2	2.5 ± 0.7
11	90 ± 16	25 ± 4

Conditions: 5 mM catlayst, 5 M C_6H_6 in DTFA, at 75 °C under Argon and analyzed by GC-MS after 1 h.

Given that both **2** and **11** were competent for CH activation of benzene, we examined them for catalytic the oxy-functionalization of benzene. Catalytic functionalization was attempted using either **2** or **11** with an assortment of one and two – electron oxidants. We had particularly been interested in the use of air – regenerable oxidants, such as Cu^{II}, with the idea of using Wacker – like conditions for hydrocarbon oxidation. Unfortunately, **2** did not exhibit increased activity for benzene functionalization when compared to **1** and a maximum TON of 6.9 was achieved (see SI). Interestingly, **11** did not show any activity for benzene functionalization although it was highly active for CH activation. Attempts to stoichiometrically functionalize the phenyl substituent on **11** resulted in the formation of benzene resulting from protonolysis of the phenyl substituent. Catalytic runs were also unsuccessful. Although no TON was observed with **11** for

the oxy-functionalization of benzene, it is possible that the 4-MePy substituent is interfering with the functionalization. Further study is needed to elucidate the details of this system.

Conclusion

In our efforts to design catalysts for hydrocarbon oxidation in weakly acidic media several new Ir complexes based on the use of a cyclometalated NNC ligand have been synthesized and examined for reactions with hydrocarbons. Contrary to our expectations, ligating Ir with a "tied back" version of the NNC ligand (see complex **2**) relative to the original "non-tied back"complex did not result in increased rates of H/D exchange. Our studies have indicated that the lower rate of exchange with aliphatic substrates, such as methane, may be due to a more tightly bound ethylene in the precursor to the active catalyst and not from catalyst decomposition. The slow loss of ethylene from **2** may inhibit entrance into the catalytic cycle from the iridium pre-catalyst as two cis-coordination sites are required for CH activation. Replacement of the ethylene ligand with 4-MePy (see complex **11**) resulted in substantially increased rates of H/D exchange with benzene. Importantly, the use of oxidants, such as Cu[II], gave oxy-functionalized aryl products of benzene as either phenol or phenyltrifluoroester using complex **2**. However, the yields are low and there is a background reaction facilitated by Cu in HTFA under the reactions conditions. Unfortunately, complex **11** gave only trace amounts of oxy-functionalized products and further investigation is needed to elucidate the reason for this. Further investigations of this reaction with iridium and other metals are ongoing in our lab.

Experimental Section

General Considerations: All manipulations were carried out using an argon filled MBraun glovebox and standard Schlenk techniques using oven dried glassware (>1 h at 110 °C under

vacuum, -30 mm Hg). Methylenechloride was HPLC grade from Fisher and distilled from P_2O_5 under argon prior to use. Benzene was HPLC grade from EMD and distilled from Na/benzophenone under argon prior to use. Pentane was HPLC grade from EMD and distilled over Na/benzophenone under argon prior to use. Reagent-grade chemicals and solvents were purchased from Sigma Aldrich or Alfa Aesar and used as is unless otherwise specified. Deuterated solvents were purchased from Cambridge Isotope Inc. and degassed and stored under argon before use. Deuterated methylenechloride was further stored over 4Å molecular sieves. Deuterated trifluoroacetic acid was degassed before use by several freeze-pump-thaw cycles and stored under argon. Trifluoroacetic acid was HPLC grade from Fisher and degassed before use by several freeze-pump-thaw cycles and stored under argon. $IrCl_3 \cdot (H_2O)_x$ was obtained from Pressure Chemical. Elemental Analyses were performed by Columbia Analytical Services; Tucson, Arizona or Atlantic Microlab, Inc. of Norcross, Georgia. Electrospray Ionization (ESI) mass spectroscopy was performed at the University of Illinois Mass Spec Facility; Urbana, Illinois. Liquid phase organic products were analyzed with a Shimadzu GC-MS QP2010S equipped with cross-linked methyl silicone gum capillary column, RTX-5. Gas measurements were performed using an Agilent GasPro column. The retention times of the products were confirmed by known standards. NMR spectra were obtained on a Bruker Digital Avance III 400 (400.132 MHz for ^1H, 100.623 MHz for ^{13}C, and 376.461 MHz for ^{19}F) spectrometer. Chemical shifts are given in ppm relative to residual solvent proton resonances or to a stated internal or external standard. Liquid phase flash chromatography was performed on a Teledyne Isco Combiflash Rf and all solvents were of HPLC grade and obtained from Fisher or EMD. X-ray crystallography was performed at the Center for Nanostructured Materials located at the University of Texas at Arlington.

benzo[*h*]quinoline n-oxide: A solution of benzo[*h*]quinoline (1.8 g, 10.0 mmol) dissolved in 40 mL of CHCl$_3$ was cooled in an ice bath. To this cooled solution, MCPBA (3.0 g, 15.0 mmol) in 60 mL of CHCl$_3$ was added and the reaction stirred for 4 d at RT. The solution was washed with K$_2$CO$_3$, dried with MgSO$_4$, and concentrated *in vacuo*. The residue was washed with diethyl ether to give a crystalline solid in 65-70% yield. Characterization of the compound corresponded to that previously reported.[87]

2-chlorobenzo[*h*]quinoline: A mixture of **benzo[*h*]quinoline n-oxide** (13.8 g, 71 mmol) in 60 mL of POCl$_3$ was refluxed for 30 min. The cooled reaction mixture was poured into crushed ice, neutralized with concentrated NH$_4$OH solution, and extracted with CH$_2$Cl$_2$ (3 x 50 mL). The combined extracts were washed with water, dried over MgSO$_4$, and evaporated under reduced pressure. The residue was flash-chromatographed on silica with a gradient from hexanes to CH$_2$Cl$_2$ as the eluent to give **2-chlorobenzo[*h*]quinoline** (44-48%) as the first major fraction. Characterization of the compound corresponded to that previously reported.[87]

2-bromobenzo[*h*]quinoline: The reaction was performed in a well dried round bottom flask equipped with a reflux condenser under an argon atmosphere. To a solution of **2-chlorobenzo[*h*]quinoline** in acetic acid (60 ml) kept under reflux, ~10mL of 48% HBr was added slowly. The reaction was then refluxed for 6 h. The excess of solvent was removed in *vacuo* and the resulting product washed with a NaHCO$_3$ saturated aqueous solution, extracted into CH$_2$Cl$_2$, and dried over MgSO$_4$. The residue after removing the solvent was flash-chromatographed on silica with a gradient from hexanes to CH$_2$Cl$_2$ as the eluent to yield 55-68% of **2-bromobenzo[*h*]quinoline**. Characterization of the compound corresponded to that previously reported.[88]

2-(2'-pyridyl)-benzo[*h*]quinoline: A mixture of **2-bromobenzo[*h*]quinolone** (1.9g 7.36 mmol), 2-(tri-nbutylstannyl) pyridine (1.2eq, 3.76g, 8.83 mmol), and tetrakis(triphenylphosphine)palladium(0) (0.1eq, 850 mg, 0.74 mmol) was loaded into an oven dry Schlenk flask with a reflux condenser.[89] The solids were dissolved in dry toluene (60 mL) and refluxed under argon for 2 d. After cooling to room temperature, water was added and the mixture was concentrated under reduced pressure. Flash chromatography of the residue on silica gel, eluting with hexanes, followed by EtOAc/hexanes (1:3) gave the product (**NNC-tb**) as a white/yellow solid (1.7 g, 90%). Characterization of the compound corresponded to that previously reported.[90]

(NNC-tb)Ir(Et)(C$_2$H$_4$)(Cl) (3): A Schlenk bomb was loaded with 3 g (3.35 mmol) of [Ir(COE)$_2$Cl]$_2$ and then dissolved in dry/degassed pentane in the glovebox. The flask was cooled to -50 °C under argon and ethylene was bubbled through for 30 min followed by slow warming to RT. The reaction was then cooled to -50 °C and transferred by cannula to a precooled (-50 °C) Schlenk frit and washed with cold pentane (3 x 50 mL) to remove COE while under continuous ethylene pressure. The receiving flask was then changed and the system washed at RT with dry CH$_2$Cl$_2$ (3 x 30 mL) all while under ethylene pressure. To the collected filtrate solution at -50 °C, 1.72 g (2.23 mmol) of **NNC-tb** dissolved in 45 mL of dry CH$_2$Cl$_2$ was cannula transferred in. The flask was then warmed to RT and stirred for 16 h to yield a red/orange solution with a precipitate, which was evacuated to dryness on a high vac line. The reaction was then filtered over a 1 x 3" plug of silica gel first washing with ether, then EtOAc, followed by EtOAc with 10% methanol to elute the product as an orange band. There is a red/brown band that elutes with EtOAc as well as ligand/COE with diethyl ether that may be discarded. The orange residue was dissolved in DCM and crashed out in stirring pentane followed by filtration on a sintered glass

frit to give a 65% yield of **(NNC-tb)Ir(Et)(C$_2$H$_4$)(Cl)**. ^{1}H NMR (CD$_2$Cl$_2$, 400 MHz): δ 9.35 (d, *J* = 5.1 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 8.3 Hz, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 8.01 (t, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 8.9 Hz, 1H), 7.85 (d, *J* = 6.8 Hz, 1H), 7.62 (m, 4H), 4.1 (s, 4H, C$_2$H$_4$), 0.41 (m, 1H, Ir-**CH$_2$**-CH$_3$), 0.25 (m, 1H, Ir-**CH$_2$**-CH$_3$), -0.44 (t, *J* = 7.6 Hz, 3H, Ir-CH$_2$-**CH$_3$**). ^{13}C NMR {^{1}H} (CD$_2$Cl$_2$, 100 MHz): δ 163.9, 163.0, 162.3, 158.4, 153.2, 151.2, 144.8, 144.4, 135.0, 131.7, 124.9, 124.6, 122.7, 119.6, 116.2, 115.1, 65.9. HR-MS Q-Tof calc. for C$_{20}$H$_{17}$N$_2$Ir [M+H–Cl–C$_2$H$_4$]$^+$: 478.1021; found: 478.1020. Anal. Calc. for C$_{28}$H$_{36}$ClIrN$_2$: C 53.53; H 5.78; N 4.46, Cl 5.64; Found: C 53.44, H 5.67, N 4.39, Cl 5.59. X-ray: crystals were obtained by crystallization from a CH$_2$Cl$_2$ solution at -20 °C.

(NNC-tb)Ir(Et)(C$_2$H$_4$)(TFA) (2): In a 30 mL amberized vial with a magnetic stir bar, 250 mg of **(NNC-tb)Ir-(Et)(C$_2$H$_4$)(Cl)** and 102 mg (1.1 eq) of AgTFA was dissolved in 25 mL of dry DCM. The reaction was stirred in the dark for 2 d and then filtered over celite and evacuated to dryness to afford an orange-red powder. The compound was recrystallized from DCM/Pentane at -20 °C to yield 76% of **(NNC-tb)Ir(Et)(C$_2$H$_4$)(TFA).** ^{1}H NMR (CD$_2$Cl$_2$, 400 MHz): δ 9.42 (d, *J* = 5.6 Hz, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 8.12 (m, 2H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.67 (m, 4H), 4.1 (m, *J* = 19 Hz, 4H, C$_2$H$_4$), 0.51 (m, 1H, Ir-**CH$_2$**-CH$_3$), 0.36 (m, 1H, Ir-**CH$_2$**-CH$_3$), -0.48 (t, *J* = 7.6 Hz, 3H, Ir-CH$_2$-**CH$_3$**). ^{13}C NMR {^{1}H} (CD$_2$Cl$_2$, 100 MHz): δ 160.00, 153.32, 152.88, 143.39, 140.38, 139.76, 137.08, 135.47, 132.18, 131.80, 131.68, 127.82, 126.92, 123.55, 123.50, 121.35, 117.28, 111.84, 66.68 (s, Ir-**C$_2$**H$_4$), 14.83 (s, Ir-CH$_2$CH$_3$), and -14.17 (s, Ir-**C**H$_2$CH$_3$). The carbons from the –OC(O)CF$_3$ group were not observed. ^{19}F NMR {^{1}H} (CD$_2$Cl$_2$, ref. to CFCl$_3$, 376 MHz): δ -75.77. HR-MS Q-Tof calc. for C$_{22}$H$_{16}$N$_2$O$_2$F$_3$Ir [M+H$^+$–Et]$^+$: 590.0793; found: 590.0786. Elemental Analysis Calc. for

$C_{30}H_{36}F_3IrN_2O_2$: C 51.05; H 5.14; F 8.07; N 3.97; Found C 50.75; H 4.98; F 8.14; N 3.96. X-ray: crystals were obtained by crystallization from a CH_2Cl_2/ether solution at -20 °C.

(NNC-tb)Ir(C$_2$H$_4$)(TFA)$_2$ (4): In a 100 mL RBF, 232 mg of **(NNC-tb)Ir-(Et)(C$_2$H$_4$)(TFA)** was dissolved in 25 mL of HTFA. The reaction was stirred for 1 d and evacuated to dryness to give a yellow powder. The compound was purified by flash column chromatography on silica gel using a 1:1:1 mixture of hexanes:DCM:EtOAc to give 77% of **(NNC-tb)Ir(C$_2$H$_4$)(TFA)$_2$**. ^{1}H NMR (CD$_2$Cl$_2$, 400 MHz): δ 9.53 (d, J = 5.3 Hz, 1H), 8.42 (d, J = 8.3 Hz, 1H), 8.37 (d, J = 7.8 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.20 (dt, J = 7.9, 1.5 Hz, 1H), 8.01 (d, J = 8.9 Hz, 1H), 7.91 (dd, J = 6.1, 2.3 Hz, 1H), 7.76 (m, 4H), 5.02 (s, 4H, C$_2$H$_4$). ^{13}C NMR (CD$_2$Cl$_2$, 100 MHz): δ 163.8 (q, J = 36.1 Hz), 160.8, 154.8, 154.1, 153.9, 143.9, 141.0, 138.9, 135.4, 133.4, 131.9, 131.3, 128.9, 128.1, 127.2, 123.8 (t, J = 6.3 Hz), 117.7, 112.0 (q, J = 290.3 Hz), 73.1. ^{19}F NMR {^{1}H} (CD$_2$Cl$_2$, ref. to CFCl$_3$, 376 MHz): δ -75.60. HR-MS Q-Tof calc. for $C_{24}H_{16}N_2O_4F_6Ir$ [M+H]$^+$: 703.0644; found: 703.0638. Anal. Calc. for $C_{30}H_{31}F_6IrN_2O_4 \cdot H_2O$: C 44.61; H 4.12; N 3.47, found C 44.73, H 4.06, N 3.46. X-ray: crystals were obtained by crystallization from a CH$_2$Cl$_2$/n-hexane (1:1) solution at -20 °C.

(NNC-tb)Ir(Ph)(4-methylpyridine)(Cl) (10): In a thick-walled Schlenk bomb containing a magnetic stir bar and a resealable PTFE valve, 300 mg (0.55 mmol) of **(NNC-tb)Ir-(Et)(C$_2$H$_4$)(Cl)** was dissolved in 100 mL of dry benzene under argon. The red solution was then frozen in liq. N$_2$ and the head space was evacuated. The flask was thawed and then heated at 160 °C for 6 h in a well stirred oil bath. During the course of the reaction and upon cooling, a dark brown solid precipitated from solution. The solvent was then removed under vacuum to give a dark colored residue. In a 250 mL RBF, the residue was dissolved in 30 mL of 4-methylpyridine. The reaction was stirred for 2 d under air at RT. The solvent was then removed by rotary

evaporation to give a dark brown residue. Flash chromatography on silica eluting with Hexanes

to neat THF yielded the product as the second dark brown band in 37% yield over two steps. [1]H

NMR (CD$_2$Cl$_2$, 400 MHz): δ 9.29 (d, J = 5.0 Hz, 1H), 8.12 (t, J = 3.9 Hz, 1H), 8.08 (d, J = 8.9

Hz, 1H), 8.04 (d, J = 6.3 Hz, 2H), 7.98 (dt, J = 7.8, 1.5 Hz, 1H), 7.91 (q, J = 21.6, 8.6 Hz, 2H),

7.84 (d, J = 8.8 Hz, 1H), 7.68 (dt, J = 5.3, 1.0 Hz, 1H), 7.55 (m, 3H), 6.72 (d, J = 5.6 Hz, 4H),

6.42 (m, 3H), 2.09 (s, Ir-C$_5$H$_4$N-C**H$_3$**, 1H). ^{13}C NMR (CD$_2$Cl$_2$, 100 MHz): δ 158.6, 158.5, 155.2,

150.9, 150.4, 150.1, 149.3, 146.6, 138.9, 136.7, 136.7, 135.8, 134.8, 132.5, 132.3, 131.9, 128.7,

128.1, 126.2, 125.8, 125.6, 123.3, 123.2, 121.9, 118.2, 117.0, 21.1 (Ir-C$_5$H$_4$N-C**H$_3$**). HR-MS Q-

Tof calc. for C$_{30}$H$_{24}$N$_3$IrCl [M+H]$^+$: 654.1288; found: 654.1296. Anal. Calc. for C$_{30}$H$_{23}$ClIrN$_3$: C

55.16, H 3.55, N 6.43; found, C 54.98, H 3.42, N 6.45.

(NNC-tb)Ir(Ph)(4-methylpyridine)(TFA) (11): In a 100 mL RBF, 150 mg of (NNC-tb)Ir-

Ph.4MePy.Cl and 202 mg (4 eq) of AgTFA were dissolved in 80 mL of dry DCM. The reaction

was stirred in the dark for 3 d. The sample was then filtered over a plug of alumina with a celite

bottom and washed with DCM and then DCM/10%MeOH to elute a yellow/red band. The

solution was then evacuated to dryness. The residue was then recrystallized from DCM/pentane

at -20 °C to give >90% yield of the title product. Alternatively, the residue can be sonicated in

diethyl ether (3 x 30 mL) followed by centrifugation and decanting of the liquid to reisolate the

residue. This procedure affords purity levels of that achieved by recrystallization. ^{1}H NMR

(CD$_2$Cl$_2$, 400 MHz): δ 10.16 (d, J = 5.4 Hz, 1H), 8.17 (d, J = 7.9 Hz, 1H), 8.01 (m, 3H), 7.93 (d,

J = 8.6 Hz, 1H), 7.88 (d, J = 6.4 Hz, 2H), 7.83 (d, J = 8.5 Hz, 1H), 7.65 (dt, J = 7.2, 1.3 Hz, 1H),

7.59 (m, 3H), 6.78 (d, J = 6.1 Hz, 2H), 6.56 (m, 2H), 6.48 (m, 3H), 2.11 (s, Ir-C$_5$H$_4$N-C**H$_3$**, 3H).

^{13}C NMR (CD$_2$Cl$_2$, 100 MHz): δ 158.58, 157.31, 156.09, 155.71, 149.82, 149.75, 148.29,

145.28, 138.99, 135.50, 135.30, 134.69, 132.08, 131.62, 129.94, 129.36, 129.11, 126.61, 126.02,

125.36, 123.42, 123.18, 122.32, 118.64, 116.90, and 21.15 (Ir-NC$_5$H$_4$-**C**H$_3$). The carbons from

the –OC(O)CF$_3$ group were not observed. ^{19}F NMR {^{1}H} (CD$_2$Cl$_2$, 376 MHz): δ -75.45. HR-MS

Q-Tof calc. for C$_{26}$H$_{18}$F$_3$IrN$_3$O$_2$ [M-Ph]$^+$: 654.0981; found: 654.654.0987. Anal. Calc. for

C$_{32}$H$_{23}$F$_3$IrN$_3$O$_2$: C 52.60, H 3.17, N 5.75; found, C 52.31, H 3.26, N 5.83.

General Procedure for H/D Exchange (gases): A 4 mL high pressure stainless steel bomb

containing a glass liner with a magnetic stir bar was charged with 1.0 mL (1.31 x 10^{-2} mol) of a

CF$_3$COOD solution containing 5 mM catalyst. The flask was heated for 120 min on a

temperature controlled aluminum block maintained at 180 °C (unless otherwise mentioned). The

gas phase was sampled and analyzed by GC-MS. The percent deuterium incorporation was

determined by deconvoluting the mass fragmentation pattern for methane using a Microsoft

Excel program.[81] An important assumption is built into the program is that there are no isotope

effects on the fragmentation pattern of methane. The parent ion peak of methane is relatively

stable towards fragmentation and can be used to quantify the exchange reactions. The mass

fragmentation pattern from m/z of 12 to 21 was analyzed for each reaction and compared to

control reactions not containing catalyst. The results obtained by this method are accurate within

± 5% of deuterium incorporation or loss.

General Procedure for H/D Exchange (liquids): A 4 mL Schlenk flask with a resealable

PTFE valve and a magnetic stir bar was charged with 1.0 mL (1.31 x 10^{-2} mol) of a CF$_3$COOD

solution containing 0.5 M substrate and 5 mM of catalyst (unless otherwise mentioned). The

flask was heated for 180 min in a well stirred oil bath maintained at 150 °C for arenes and 180

°C for all other hydrocarbons. The liquid phase was sampled and analyzed by GC-MS and ^{1}H

NMR. Liquid hydrocarbon substrates were compared to control reactions not containing catalyst

and any background reactions were subtracted accordingly.

The percent deuterium incorporation into benzene when determined by GC-MS was performed by deconvoluting the mass fragmentation pattern of benzene using a Microsoft Excel program.[81] An important assumption is built into the program is that there are no isotope effects on the fragmentation pattern of benzene. The parent ion peak of benzene is relatively stable towards fragmentation and can be used to quantify the exchange reactions. The mass fragmentation pattern from m/z of 78 to 84 was analyzed for each reaction and compared to control reactions not containing catalyst. The results obtained by this method are accurate within ± 5% of deuterium incorporation or loss. All other hydrocarbons, besides benzene, were determined by ^{1}H NMR comparison of control and catalytic reactions.

H/D Exchange Over Time Leads to Parallel Incorporation of D: Following our general procedures, H/D exchange reactions were sampled at 30, 60, 120, and 180 mins and monitored by GC-MS.

Associated Content

Notes: The authors declare no competing financial interest.

Supporting Information: Synthetic data, calibration curves for GC data interpretation, labeling studies, oxy-functionalization studies, crystallographic data, and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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