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ARTICLE TYPE

Solvent promoted reversible cyclometalation in a tethered NHC iridium complex

James E. Wheatley,[a] C. André Ohlin[b] and Adrian B. Chaplin*[a]

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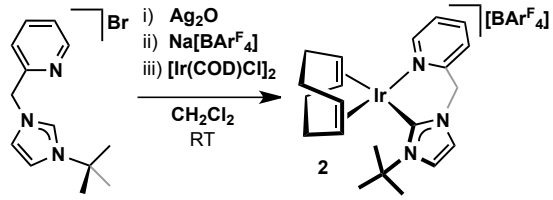
Reaction of [Ir(COD)(py–I^{t}Bu)]$^+$ (py–I^{t}Bu = 3-*tert*-butyl-1-picolylimidazol-2-ylidene) with acetonitrile results in reversible intramolecular C–H bond activation of the NHC ligand and formation of [Ir(η^2:η^1-C$_8$H$_{13}$)(py–I^{t}Bu')(NCMe)]$^+$. Coordinated COD acts as an internal hydride acceptor and acetonitrile coordination offsets the otherwise unfavourable thermodynamics of the process.

The transition metal-mediated functionalisation of alkanes is an area of contemporary importance, motivated by the desire to make effective use of these inexpensive and abundant hydrocarbons in organic synthesis and as feedstocks for the chemical industry.[1] Iridium-based complexes are of particular interest as they have been shown to promote dehydrogenation, metathesis and dehydroaromatisation reactions of alkanes.[2] The weakly interacting nature of alkanes and unfavourable entropy changes combine to make intermolecular C–H bond activation reactions exceedingly difficult to investigate.[3] However, intramolecular (alkyl) cyclometalation reactions, promoted through the chelate effect, provide convenient and valuable model systems. As a consequence of their strong σ-donor characteristics and substituent directionality, *N*-heterocyclic carbene (NHC) scaffolds are particularly well suited to cyclometalation reactions.[4] Indeed, when partnered with reactive iridium centres, NHC ligands have been shown to support a number of examples of intramolecular alkyl activation, with notable examples involving cyclometalation reactions of I^{t}Bu and IMes ligands (all irreversible, see Figure 1).[5] Similar reactivity is also found in other transition metal based systems.[6] For effective interrogation of C(sp^3)–H bond activation processes, reversibility is a desirable characteristic: in this communication, we report a system that demonstrates such reactivity.

Figure 1. Cycometalation of I^{t}Bu (left) and IMes (right).

Initially motivated to investigate chelating NHC analogues of Crabtree's hydrogenation catalyst, [Ir(COD)(py)(PCy$_3$)][PF$_6$] (**1**[PF$_6$]; COD = cyclooctadiene),[7] we prepared [Ir(COD)(py–I^{t}Bu)][BAr$^F_4$] [**2**; py–I^{t}Bu = 3-*tert*-butyl-1-picolylimidazol-2-ylidene,[8] Ar^F = 3,5-C$_6$H$_3$(CF$_3$)$_2$] using the silver-based transmetalation strategy outlined in Scheme 1, with the solid-state structure of **2** depicted in Figure 2. Despite close structural similarities to **1**[BAr$^F_4$],[9] **2** is a significantly inferior catalyst, exhibiting 40 times lower activity for the hydrogenation of cyclohexene (initial TOF 20 h^{-1} vs 830 h^{-1} with 0.1 mol% catalyst, CH_2Cl_2 solvent, 1 atm H_2 at 293 K). Consistent with this low activity, we subsequently demonstrated that, while rapid and reversible oxidative addition of dihydrogen leads to formation of [Ir(COD)(H)$_2$(py–I^{t}Bu)][BAr$^F_4$] **3**, the COD ligand in this system remains coordinated under a dihydrogen atmosphere (96 h, 1 atm H_2, CD_2Cl_2, 293 K).† Seeking to promote dissociation of the COD ligand, we turned to investigate thermolysis reactions of **2** in acetonitrile solvent. However, instead of COD loss, **2** exclusively undergoes a reversible C(sp^3)–H bond activation reaction.



Scheme 1. Synthesis of **2**.

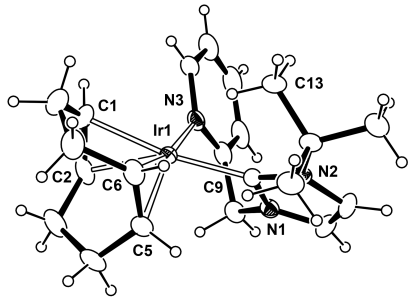
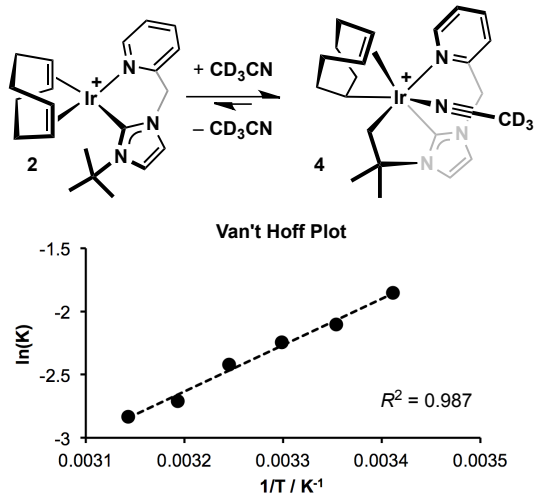


Figure 2. Solid-state structure of **2** (cation only). Thermal ellipsoids drawn at 30%. Ir1···C13 = 3.508(5) Å.

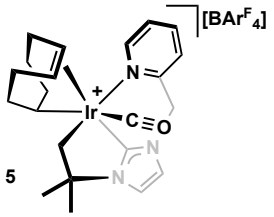
Reaction of **2** with CD_3CN resulted in the formation of the iridium(III) complex [Ir(η^2:η^1-C$_8$H$_{13}$)(py–I^{t}Bu')(NCCD$_3$)][BAr$^F_4$] **4**, where the *tert*-butyl substituent of the NHC has undergone intramolecular C–H bond cleavage (Scheme 2). In this reaction, the COD ligand acts as an internal hydride acceptor forming a chelating alkenyl–alkyl ligand with the coordination sphere completed by acetonitrile. The solution structure of **4** was comprehensively determined by NMR spectroscopy, utilising NOESY, COSY and heteronuclear correlation experiments.

Complex **4** is C_1 symmetric and exhibits distinctive 2H diastereotopic resonances for the $IrCH_2$ and $pyCH_2$ methylene protons at δ 3.40/2.93 ($^2J_{HH}$ = 11.3 Hz) and 5.31/5.12 ($^2J_{HH}$ = 15.3 Hz), respectively, together with two 3H methyl resonances at δ 1.52 and 1.38. NOE interactions of the methylene and 6-pyridal resonances with the COD ligand strongly support adoption of the py–I^{t}Bu' ligand in a *mer* conformation with the alkenyl–alkyl orientated as shown in Scheme 2 (see ESI for further details). In the $^{13}C\{^1H\}$ NMR spectrum, the coordinated carbene (δ 168.0), alkene (δ 95.4, 80.4), methylene (δ 16.6) and methine (δ 6.1) groups were all readily identified. Significantly, the cyclometalation is reversible resulting in dynamic equilibrium mixtures of **2** and **4** (1:3 at 293 K). Variation of temperature allowed the thermodynamic parameters for this reaction to be determined {K = [**4**]/([**2**][CD_3CN]), ΔH = -31 ± 2 kJ·mol^{-1}, ΔS = -120 ± 5 J·mol^{-1}·K^{-1}}, with the large and negative entropy of reaction fully consistent with acetonitrile coordination. At 293 K formation of **4** is slow and ca 2 weeks are required to reach equilibrium, although the reaction can be accelerated markedly by heating (ca 2 days to equilibrium at 308 K).

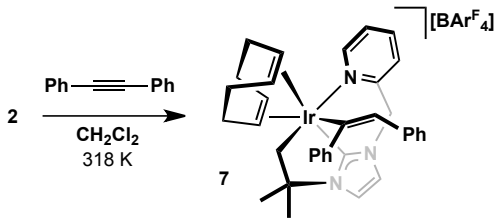


Scheme 2. Cyclometalation of **2** leading to reversible formation of **4** ([BAr^F_4]$^-$ anions omitted).

Highlighting the important promoting effect of acetonitrile solvent, **2** was completely stable to extended (96 h) heating in both CD_2Cl_2 (i.e. non-coordinating solvent) and $(CD_3)_2SO$ (i.e. strongly coordinating solvent) at 308 K. Likewise, redissolving equilibrium mixtures of **2** and **4**, formed from CD_3CN solution, in CD_2Cl_2 resulted in rapid and quantitative reversion of **4** to **2** (< 2 h at 293 K) – a reaction presumably promoted by the high trans effect of the coordinated methine group. As a consequence of the facile retro-cyclometalation of **4** in the absence of acetonitrile, we have so far been unable to isolate **4** free from **2**. Preliminary computational studies further highlight the stabilising role of acetonitrile coordination. In line with the experimentally derived value, the calculated enthalpy for the reaction of **2** with acetonitrile to give **4** is significantly exothermic (–18.8 kJ·mol^{-1}). Replacing the acetonitrile ligand with CH_2Cl_2 (+58.9 kJ·mol^{-1}), DMSO (κ_O, +3.3 kJ.mol^{-1}; κ_S, +17.8 kJ·mol^{-1}), or simply removing this ligand altogether (+43.4 kJ·mol^{-1}) in **4** all lead to positive enthalpies of reaction.



Helping to further substantiate the structure of **4**, reaction in situ with CO (1 atm) resulted in the substitution of acetonitrile with CO and formation of [Ir(η^2:η^1-C_8H_{13})(py–I^{t}Bu')(CO)][BAr^F_4] **5**, as characterised by NMR spectroscopy and ESI-MS (m/z = 544.1953 [M]$^+$; calc. 544.1935). Spectroscopic data are similar to those of **4**, although there is a considerable downfield shift of the methine ^{13}C resonance from δ 6.1 to 22.9 in **5**, consistent with *trans* coordination of the carbonyl ligand (δ_{13C} 172.9). Alongside **5**, the bis-carbonyl complex [Ir$(CO)_2$(py–I^{t}Bu)][BAr^F_4] **6** is formed by reaction of **2** with two equivalents of CO; verified by independent synthesis of **6** from **2** under CO. While **5** is stable under CO atmosphere, removal of solvent and addition of CD_2Cl_2 results in retro-cyclometalation and predominately a mixture of **2** and **6** (no **5** observed after 12 h) – the later formed by reaction of **2** with liberated CO.



Scheme 3. Reaction of **2** with diphenylacetylene.

To help gain insight into the mechanism of the cyclometalation reaction, we targeted the reaction of **2** with diphenylacetylene, as an external hydride acceptor. This alkyne has previously been used to trap out C–H bond activation reactions of COD coordinated to iridium[10] and we wished to explore if such reactivity was important in our system. Heating **2** with a large excess of diphenylacetylene at 318 K resulted in the gradual, but irreversible, formation of the new cyclometalated complex [Ir(COD)(py–I^{t}Bu'){κ^1-C(Ph)=CHPh}][BAr^F_4] **7**, which was isolated in 61% yield after 11 days (Scheme 3). The reaction also proceeded at 293 K with stoichiometric diphenylacetylene, but was considerably slower. With the alkyne acting as a hydride acceptor, the COD ligand thus appears to only play a spectator role in the C–H activation process. Moreover, **7** is completely stable in solution for extended periods of time (1 week, CD_2Cl_2, 293 K) in marked contrast to **4**. We attribute this stability to the enforcement of octahedral geometry by the bidentate ligands (i.e. chelated donors trans to the alkyl and vinyl groups). The new complex was fully characterised in solution and the solid-state. The X-ray structure of **7** is shown in Figure 3 and further reinforces the structural assignments of **4** and **5** inferred solely from solution data. Notably, the carbene and coordinated methylene ^{13}C resonances (δ 159.9 and 18.1) are in good agreement with those found for **4** and **5**. The synthesis of **7** strongly suggests that the formation of **4** occurs via a straightforward mechanism involving initial C–H bond oxidative

addition of the *tert*-butyl substituent in **2**, which is notably held in close proximity to the metal centre [Ir1···C13 = 3.508(5) Å], and subsequent hydride insertion into the COD ligand. The intimate details of this process remain to be determined; we have gathered tentative evidence that suggestions reversible pyridine dissociation could play a role (see ESI).

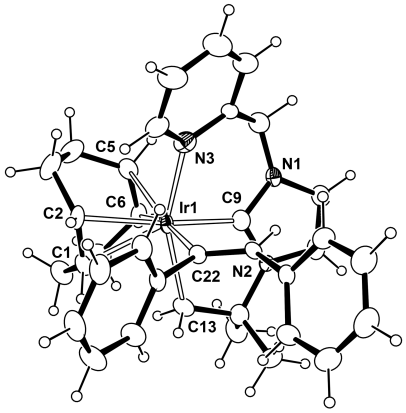


Figure 3. Solid-state structure of **7** (cation only). Thermal ellipsoids drawn at 30%. Ir1-C13 = 2.216(9) Å.

Having identifying the promoting roles of the COD ligand (internal hydride acceptor, thermodynamic) and acetonitrile solvent (thermodynamic and kinetic), we are currently working to extend these features to promote cyclometalation reactions in other systems. Notably, we have already prepared the rhodium equivalent [Rh(COD)(py–I^{t}Bu)][BAr$^F{}_4$] **8** analogously to **2** (see ESI for solid-state structure). In line with a computed reaction enthalpy of +11.9 kJ·mol^{-1}, **8** however was stable to prolonged heating in CD_3CN solution (308 K, 96 h).

In conclusion, we report on an interesting and dynamic intramolecular alkyl C–H bond activation reaction within an Ir(I) complex bearing a tethered NHC ligand. Mechanistic studies are consistent with a pathway involving direct cyclometalation of the NHC ligand and highlight the need for acetonitrile solvent or an external hydride acceptor.

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Notes and references

[a] *Department of Chemistry, University of Warwick, Gibbet Hill Road, Coventry CV4 7AL, UK. E-mail: a.b.chaplin@warwick.ac.uk*
[b] *School of Chemistry, Monash University Clayton, Victoria 3800, Australia*

† Electronic Supplementary Information (ESI) available: Full experimental details, NMR spectra and solid-state structure of **10**. See DOI: 10.1039/b000000x/. CIF have been deposited with the Cambridge Crystallographic Data Centre under CCDC 965408 (**2**), 965409 (**7**) and 965410 (**8**).

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Graphical abstract