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ARTICLE TYPE

Iridium(I) PNP complexes in the sp^3 C-H bond activation of methyl propanoate and related esters

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The utilisation of the PNP iridium pincer complex [Ir(PNP)(COE)][BF_4] [PNP = 2,6-bis{(di-*tert*-butylphosphino)methyl}pyridine; COE = cyclooctene] in the sp^3 C–H activation of methyl propanoate and other related esters was explored. In particular, this study provides further insight into the factors that govern the regioselectivity of such reactions. These included factors such as the steric demands of the substrate, the formation of favourable ring systems as well as the electronic effects that may influence the pKa values of protons. In particular, the effects of water on the outcome of these reactions were of great interest, since earlier literature reports have shown the presence of water to promote selective C–H activation in the α-position of ketones.

The catalytic activation and functionalisation of otherwise inert sp^3 C–H bonds has been the topic of extensive research for over 25 years, and progress in this field has been well reviewed.[1-6] Sp^3 C–H activation is generally regarded as a thermodynamically uphill transformation and therefore the thermally robust pincer-type complexes have been among the most attractive and widely studied systems for promoting both stoichiometric and catalytic C–H activations.[7-9] Iridium pincer variants, in particular, are exceptionally active catalysts and have in recent years been at the forefront of many advances in this field.[7, 10-12] Selective C–H activations typically involve a single cleavage event to form products with single M–C_{sp3} bonds *via* an oxidative addition, electrophilic activation or σ-bond metathesis pathway.[13] In a contribution by Shaw[14] and other more recent reports, however, the direct formation of late transition metal carbene complexes by multiple C–H activations has been shown possible for selected substrates.[7, 11-13] Grubbs and co-workers,[7, 12, 13] in particular, have been important pioneers of such research and have shown that certain ethers undergo selective *α,α*-dehydrogenation in the presence of [Ir(PNP)$(H)_2$] [PNP = bis{2-(diisopropylphosphino)-4-methylphenyl}amide] and norbornene to generate the Ir(I) Fisher carbene complexes upon loss of hydrogen. [7, 13, 12] Geminal double C–H activations by late transition metals to generate carbenes has also been shown possible for the α-C–H bonds of cyclic ethers.[15-18] Again, PNP-type iridium pincer complexes facilitate such transformations, displaying high selectivity towards the formation of carbenes *via α,α*-C–H activation over *α,β*-hydrogen abstraction.[11, 12]

Although pincer ligands are often regarded as mere platforms to stable metal complexes, Milstein and co-workers[10] have recently shown that such ligands can cooperate in various reactions by adapting to changes at the metal centre. In iridium complexes derived from deprotonated 2,6-bis{(di-*tert*-butylphosphino)methyl}pyridine (PNP*), in particular, metal-ligand cooperations of this nature have been shown to play a decisive role in their reactivity toward sp^3 C–H activations with heated solutions of [Ir(PNP*)(COE)] in acetone giving a C-H activated Ir(I) acetonyl complex.[10] In an earlier report by the same authors, the related [Ir(PNP)(COE)][BF_4] [PNP = 2,6-bis{(di-*tert*-butylphosphino)methyl}pyridine] complex could also be employed in the selective sp^3 activation of the *β*-position of other ketones despite the greater acidity of the α-C–H bonds.[19] In the presence of water, however, the regioselectivity of these reactions could be steered to favour activations in the α-position instead. More recently, while our study was ongoing, Goldman and co-workers[20] reported that (PCP)Ir pincer complexes can also be used to promote oxidative addition of sp^3 C–O bonds in various methyl oxygenates. These include alkyl esters, where the reaction proceeds *via* an initial C–H activation followed by an α-OR migration through a cyclic transition state.

We now report our related experimental findings on the regioselectivity of C–H activation reactions involving [Ir(PNP)(COE)][BF_4] and saturated esters in both the presence and absence of water.

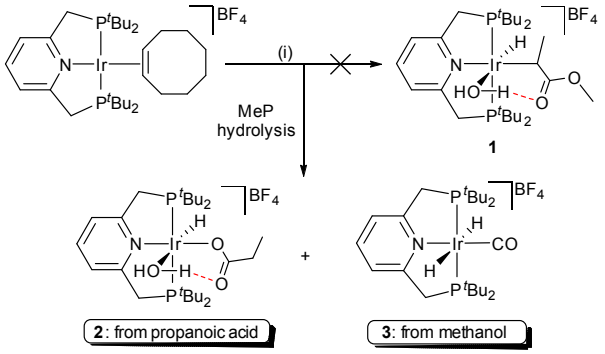
Results and Discussion

Reactions of [Ir(PNP)(COE)][BF_4] with esters in the presence of water

Inspired by the work of Milstein[19] on the effect of water on the regioselectivity of *sp*^{3} C-H activations in ketones, this study was aimed at exploring whether a similar approach can be followed for the α-C-H activation of esters such as methylpropanoate (MeP). Not suprisingly, heating a solution of [Ir(PNP)(COE)][BF_4] in a MeP / water mixture (V : V ratio 50 : 1) at 60 ^{0}C for 20 h did not give the α-C-H activated product **1**, but instead resulted in hydrolysis of the MeP ester bond to give propanoate complex **2** and the *trans*-hydrido carbonyl complex **3**

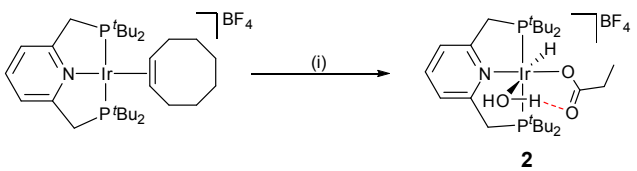
(derived from methanol) in a 1 : 3 ratio (Scheme 1). This suggests that the reaction of [Ir(PNP)(COE)][BF_4] with methanol to give **3** is favoured over the reaction with propanoic acid.

For complex **2**, the magnetically equivalent phosphorus atoms are observed as a sharp singlet at δ 49.6 in the $^{31}P\{^1H\}$ NMR spectrum. In contrast, the *tert*-butyl groups on either side of the equatorial plane are chemically inequivalent giving rise to two distinct virtual triplets in the ^1H NMR spectrum. Similarly, the CH_2–P groups give rise to two doublets of virtual triplets at δ 1.31 and δ 1.36, respectively, displaying large geminal couplings of $^2J_{H-H}$ = 17.5 Hz and smaller couplings of $J_{H-P} + J_{H-P'}$ = 8.0 Hz to phosphorus. A diagnostic hydride resonance is detected as a broad triplet, owing to coupling to phosphorus, at δ -29.1. In the $^{13}C\{^1H\}$ NMR spectrum, the relatively low field chemical shift of the carbonyl group resonance (δ 181.0) is consistent with no coordination through this functionality and hence unidentate binding of the propanoate ligand; an observation that supports the proposed structure in which water occupies the 6th coordination site.



Scheme 1 [Ir(PNP)(COE)][BF_4] with MeP in the presence of water. Conditions: (i) MeP, water, 60 ^{0}C, 20 h.

To confirm these assignments complex **2** was prepared independently by the facile reaction of damp propanoic acid with [Ir(PNP)(COE)][BF_4] at 60 ^{0}C for 20 h (Scheme 2). Spectroscopic data collected for the product of this reaction were in good agreement with those obtained earlier. It must be noted, however, that minor differences between the characteristic chemical shifts exist and that these were ascribed to solvent effects. The structure of **2** could also be confirmed crystallographically (Fig. 1). A crystallographic discussion as well as a table with selected bond lengths and angles (Table S1) can be found in the ESI. Of note is the hydrogen binding between one H atom of the coordinated water and the carbonyl O atom of the propanoate ligand.



Scheme 2 Formation of [Ir(PNP)(H){OC(O)CH_2CH_3}][BF_4] by the reaction of [Ir(PNP)(COE)][BF_4] with (i) propanoic acid, 60 ^{0}C, 20 h.

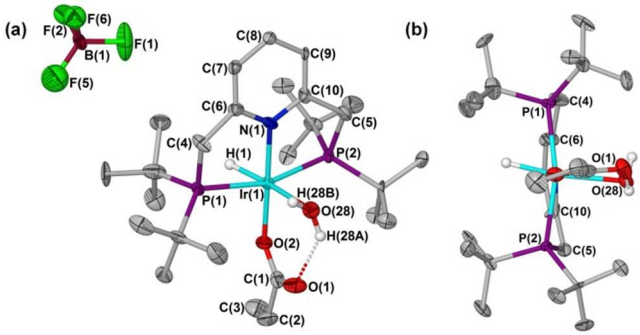


Fig. 1 (a) Molecular structure of **2** showing the numbering scheme. Thermal ellipsoids set at 50 % probability and hydrogen atoms (with the exception of the hydride and water protons) and solvent molecule are omitted for clarity; (b) side view of the structure (BF_4 omitted).

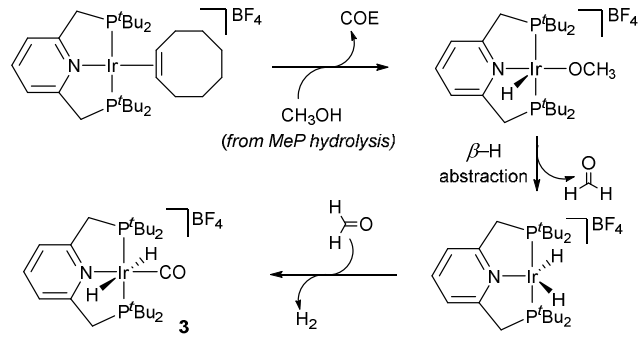
The phosphorus atoms of the *trans*-hydrido carbonyl complex **3** are magnetically equivalent resonating as a singlet at δ 68.8 in the $^{31}P\{^1H\}$ NMR spectrum. In the ^1H NMR spectrum, complex **3** gives rise to a single virtual triplet at δ 1.40 ($J_{H-P}+J_{H-P'}$ = 14.6 Hz) corresponding to the *tert*-butyl groups and another at δ 3.85 ($J_{H-P}+J_{H-P'}$ = 8.0 Hz) for the methylene groups, indicating a complex with C_{2v} symmetry. Similarly, the mutually *trans* hydrides are observed as a triplet at δ -6.77 ($^2J_{H-P}$ = 12.6 Hz) which integrates as two protons. All these values are in good agreement with those reported for the analogous $[PF_6]^-$ complex, [Ir(CO)$(H)_2$(PNP)][PF_6].[21]

Solid state infrared data reveal a strong absorption in the carbonyl region at 2010 cm^{-1} confirming the presence of the CO ligand. Furthermore, the high frequency of this vibration is consistent with limited metal to ligand π-back-donation, serving as further evidence for the presence of an Ir centre in the higher formal oxidation state of +3. The identity of **3** could also be verified by single crystal X-ray diffraction. A discussion of the structure (Fig. S2) and a table with selected bond lengths and angles (Table S2) can be found in the ESI.

The formation of complex **3** from methanol and PNP iridium complexes is a well known conversion that proceeds *via* a stereoselective decarbonylation pathway. The mechanism for this transformation is given in Scheme 3 and involves an initial O–H activation of methanol to give the methoxy hydrido complex [Ir(PNP)(H)(OMe)][BF_4] which can undergo further *β*-hydrogen abstraction to generate the dihydrido complex [Ir(PNP)$(H)_2$][BF_4] upon liberation of formaldehyde. In the final step, this dihydrido complex reacts with formaldehyde to reductively eliminate dihydrogen together with activation of the remaining aldehyde C–H bond to afford the *trans*–dihydrido carbonyl complex **3** stereoselectively. In this step, association of formaldehyde to the Ir(III) centre is thought to precede the reductive elimination of dihydrogen.[21]

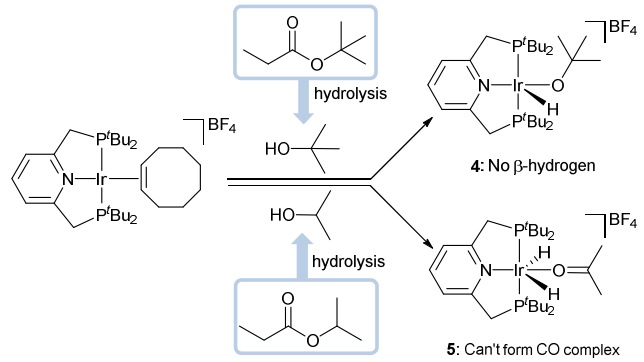
To rule out the existence of other possible pathways of decarbonylation, the reactions of [Ir(PNP)(COE)][BF_4] with *tert*-butyl propanoate and isopropyl propanoate in the presence of water were also performed. For these esters, hydrolysis would result in the formation of propanoic acid together with *tert*-butanol and isopropanol, respectively. Although these alcohols can undergo initial O–H activation to give hydrido alkoxy Ir(III) complexes, neither one of these complexes is able to participate in further decarbonylation reactions to afford CO complexes

(Scheme 4). For *tert*-butanol, further activation following the initial formation of the hydrido methoxy complex, is hampered by the absence of any *β*-hydrogens. Similarly, although in the case of isopropanol the generated hydrido isopropoxy complex can undergo further *β*-hydrogen abstraction to afford the dihydrido acetone complex **5**, the absence of another *β*-hydrogen inhibits subsequent reductive elimination of dihydrogen and further decarbonylation.



Scheme 3 Mechanism for the formation of complex **3** from [Ir(PNP)(COE)][BF_4] and methanol.

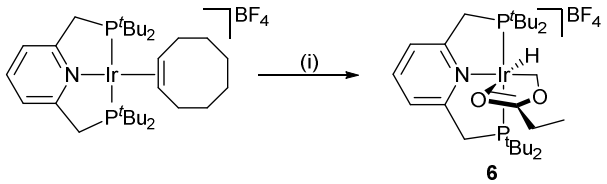
As anticipated, reactions of [Ir(PNP)(COE)][BF_4] at 60 ^{0}C with either *tert*-butyl propanoate or isopropyl propanoate in the presence of water did not lead to the formation of [$IrCO(H)_2$(PNP)][BF_4] (**3**). Instead, spectroscopic characterisation of the isolated reaction products indicated quantitative conversion of [Ir(PNP)(COE)][BF_4] to the propanoate complex **2** for both substrates, with no evidence for the formation of any of complexes **3**, **4**, [Ir(O^{i}Pr)(H)(PNP)][BF_4] or **5**.



Scheme 4 Reaction scheme to illustrate that reactions between [(PNP)(COE)][BF_4] and *tert*-butanol or isopropanol cannot afford the carbonyl complex, [Ir(PNP)(CO)$(H)_2$][BF_4].

Reactions of [Ir(PNP)(COE)][BF_4] with esters in the absence of water

In the absence of added water, the reaction of [Ir(PNP)(COE)][BF_4] with MeP at 60 ^{0}C for 20 h resulted in the selective sp^3 C–H activation of the methoxy protons to give the hydrido complex **6**, in which the 6th coordination site is filled by coordination of the carbonyl oxygen atom (Scheme 5). It is possible that precoordination of the carbonyl functionality precedes the activation event, fixing the substrate in close proximity to the metal centre and thereby governing the regioselectivity of the reaction to give the methoxy C-H activated product. Although the *α*–methene protons represent the most acidic protons in MeP (pK_a ~ 25),[22] C–H activation in this *α*–position would lead to a structure where additional stabilisation *via* carbonyl coordination would necessitate the formation of a strained four membered ring system. Activation in the *β*–position is therefore postulated to be driven by the formation of the highly favoured, more stable, five membered ring structure. The preference for activation of the methoxy over the methyl protons is not surprising, since the pK_a value of the methoxy protons can be expected to be considerably lower than that of the methyl protons owing to the presence of a neighbouring, electron withdrawing oxygen atom. This postulation is, however, in contrast with mechanistic proposals reported for the activation of methyl acetate in the presence of [IrH(PCP)(TBV)] (where PCP = κ^3-C_6H_3-2,6-[$CH_2P(^tBu)_2]_2$ and TBV = 3,3-dimethyl-1-butenyl), for which DFT calculations suggested precoordination of the ester C=O functionality to play no particular role in the reaction pathway.[20]



Scheme 5 Formation of the methoxy activated complex **6** by the reaction of [Ir(PNP)(COE)][BF_4] with MeP under water free conditions; (i) MeP, 60 ^{0}C, 20 h.

Complex **6** is remarkably stable both in solution and the solid state provided that an inert, anhydrous environment is maintained. Comparable to the literature example of a C–H activated ketone complex, [Ir(H)(PNP){$CH_2CH_3C(O)CH_2CH_3$-κ^2C,O}][BF_4][19] the *tert*-butyl groups on either side of the equatorial plane are chemically inequivalent and are observed as two distinct virtual triplets at δ 1.21 and 1.24 in the ^{1}H NMR spectrum of **6**. Similarly, the PNP methylene protons on the same carbon are inequivalent giving rise to two distinct doublets of virtual triplets δ 3.57 and δ 3.71, respectively, owing to a large geminal coupling and a smaller coupling to the two phosphorus atoms. The activated methoxy group gives rise to a triplet that integrates to two protons at δ 6.46 ($^3J_{H\text{-}P}$ = 9.5 Hz), while the hydride is observed as a triplet at δ -23.77 ($^2J_{H\text{-}P}$ = 14.6 Hz). From a two dimensional HMQC ^{1}H/^{31}P{^{1}H} NMR correlation, Fig. 2), it is evident that both these resonances correlate with a singlet at δ 42.1 in the ^{31}P{^{1}H} NMR spectrum. Despite rigorous drying of the MeP prior to use, contamination of complex **6** with minor amounts of complexes **3** and **2** was always observed, as can be seen by the additional signals in the 2D ^{1}H/^{31}P{^{1}H} NMR spectrum (Fig. 2).

Surprisingly, reactions of [Ir(PNP)(COE)][BF_4] with either isopropyl propanoate (^{i}PrP) or *tert*-butyl propanoate (^{t}BuP) under the same reactions conditions did not result in the formation of any *α*- or *β*-C–H activated products, with the final reaction mixture comprising solely of the unaltered starting materials.

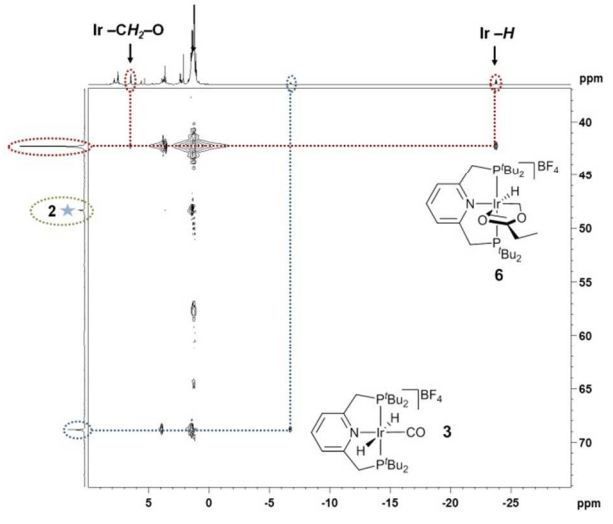


Fig. 2 2D HMQC $^{1}H/^{31}P\{^{1}H\}$ spectrum recorded for the methoxy activated complex **6**, contaminated by small amounts of **3** and **2**, clearly showing the correlation of the triplets at δ 6.77 (Ir-C*H*$_2$-O) and δ -23.77 (Ir-*H*) in the ^{1}H NMR to the phosphorous resonance at δ 42.1.

It is possible that precoordination of the carbonyl moiety to the Ir centre is a prerequisite for successful C–H activation and that the increased steric requirements of the isopropyl and *tert*-butyl groups prevent such coordinations. Alternatively, the lack of reactivity may suggest that the *β*-protons in these esters are simply not acidic enough to undergo C–H activation in the presence of [Ir(PNP)(COE)][BF_4]. Although this complex has been employed in the successful activation of C–H bonds in both the *α*- and *β*-positions of 2-butanone and 3-pentanone, protons in the *α*-position of ketones are known to have much lower pK_a values when compared to those of esters [$(CH_3)_3CC(O)CH_2CH_3$→ pK_a 21 *vs.* $CH_3CH_2CO_2CH_3$→ pK_a 25].[19, 22, 23]

Attempts to functionalise MeP *via* C-H activation

Preliminary attempts to functionalise the activated methoxy group of complex **6** demonstrated no productive reactivity towards ethene. In initial reactions the methoxy activated complex was generated *in situ* by heating a solution of [Ir(PNP)(COE)][BF_4] in MeP to 60 ^{0}C in a stainless steel autoclave pressurised with ethene (30 bar) for 15 h. Analysis of the isolated mixture, however, did not reveal the formation of any organic products. The reaction was subsequently also performed by reacting a solution of pre-formed **6** in MeP with ethene under the same conditions used for the *in situ* attempt. However, this reaction still did not result in the production of functionalised MeP or any other interesting products, with the final complex product mixture comparable to that isolated from the *in situ* experiment.

Experimental

General materials, methods and instruments

Reactions were carried out under dinitrogen gas (N_2, passed through a column of dichromate adsorbed on silica) using standard Schlenk, vacuum-line and cannula techniques. All glassware was flame-dried under vacuum. Triethylamine (NEt_3 Aldrich) was dried over potassium hydroxide (KOH) pellets and distilled under N_2 prior to use. Cyclooctene, silver tetrafluoroborate, 2,6-bis(chloromethyl)pyridine, *tert*-butanol, di-*tert*-butylphosphine and isopropanol were purchased from Aldrich and used as received. Propanoic acid (BDH laboratories) was dried over Na_2CO_3 and distilled under N_2 prior to use. All gases were purchased from BOC gases. $[NH_4]_3[IrCl_6]$ and isopropyl propanoate were purchased from Alfa Aesar, *tert*-butyl propanoate from Aldrich, phosphorus pentoxide from Fluka and pentane from Fischer Scientific. Methyl propanoate (supplied by Lucite International) and isopropyl propanoate were pretreated with Na_2CO_3, dried over P_2O_5, degassed by three freeze-pump-thaw cycles and finally collected by trap-to-trap distillation prior to use. *Tert*-butyl propanoate was purified using the same methodology, but with omission of the P_2O_5 step. [$\{IrCl(COE)_2\}_2$] was either prepared from $[NH_4]_3[IrCl_6]$ and cyclooctene using a literature procedure[24] or purchased from Alfa Aesar. 2,6-Bis(di-*tert*-butylphosphinomethyl)pyridine (PNP),[25] [$IrCl(COE)_2(acetone)_2$][BF_4][26] and [Ir(PNP)(COE)][BF_4][27] were prepared using standard literature procedures. Drierite was purchased from Sigma-Aldrich, dried in a furnace at 400 to 500 ^{0}C for 2–4 h and cooled under vacuum prior to use. Water was distilled and degassed by nitrogen bubbling prior to use. Toluene, tetrahydrofuran (thf), diethyl ether and hexane were dried using a Braun Solvent Purification System and degassed by additional freeze-pump-thaw cycles when deemed necessary. Methanol and ethanol were distilled under nitrogen from magnesium. Pentane and deuterated dichloromethane were purchased from Fisher Scientific and Aldrich, respectively, and were dried over phosphorus pentoxide (P_2O_5), degassed *via* three freeze-pump-thaw cycles and trap-to-trap distilled prior to use. Acetone, purchased from Fisher Scientific, was dried over Drierite (8 mesh, without indicator), degassed by three freeze-pump-thaw cycles and collected by trap-to-trap distillation prior to use.

NMR spectra were recorded on a Bruker Avance 300 FT or Bruker Avance II 400 MHz spectrometer (^{1}H NMR at 300/400 MHz, $^{13}C\{^{1}H\}$ NMR at 75/100 MHz and $^{31}P\{^{1}H\}$ NMR at 121/162 MHz) with chemical shifts δ reported relative to tetramethylsilane (TMS, ^{1}H, $^{13}C\{^{1}H\}$) or 85 % H_3PO_4 ($^{31}P\{^{1}H\}$) as external reference. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were referenced internally to deuterated solvent resonances which were referenced relative to TMS.

Solid state IR spectra were recorded using pressed KBr pellets on a Perkin Elmer Spectrum GX IR spectrometer. Elemental analysis was performed by the University of St. Andrews microanalytical service using a Carlo Erba CHNS/O microanalyser. Melting points were determined on a Gallenkamp apparatus and are uncorrected. Mass spectra were recorded either by the EPSRC National Mass Spectrometry Service Centre, Swansea on a Thermofisher LTQ Orbitrap XL high resolution instrument coupled to an Advion TriVersa NanoMate electrospray infusion system or by the Mass Spectrometry Service Centre at the University of St. Andrews using either a Micromass GCT EI/CI or a Micromass LCT ES instrument.

GC-MS chromatograms were recorded on a Hewlett Packard

6890 series GC system equipped with an Agilent J&W HP-1 general purpose column (fused silica capillary) and an HP 5973 Mass selective detector for both qualitative and quantitative analysis. Method: flow rate 1 ml min^{-1} (He carrier gas), split ratio 100:1, starting temperature 50 ^{0}C (4 min) ramp rate 20 ^{0}C min^{-1} to 130 ^{0}C (2 min), ramp rate 20 ^{0}C min^{-1} to 220 ^{0}C (15.5 min).

Single crystal X-ray structure determinations

Tables containing a summary of the crystal data collection and refinement paramaters of compounds **3** and **2** can be found in Appendix 1. Data sets were collected on a Rigaku Mo MM007 (dual port) high brilliance diffractometer with graphite monochromated MoKα radiation (λ = 0.71075 Å). The diffractometer is fitted with Saturn 70 and Mercury CCD detectors and two XStream LT accessories. Data reduction was carried out with standard methods using the software package Bruker SAINT,[28] SMART,[29] SHELXTL[30] and and Rigaku CrystalClear, CrystalStructure, HKL2000. All the structures were solved using direct methods and conventional difference Fourier methods. All non-hydrogen atoms were refined anisotropically by full-matrix least squares calculations on F^2 using SHELX-97[31] within an X-seed[32,33] environment. With the exception of hydride atoms, hydrogen atoms were fixed in calculated positions. The hydrogen atoms for the water molecule and the hydride were located from a difference Fourier map. Those hydrogen atoms were refined subject to distance restraints with the hydride hydrogen atom being refined isotropically and the water hydrogen atoms using a riding model. Figures were generated with POV Ray for Windows in an X-seed environment, with the displacement ellipsoids at 50% probability level unless stated otherwise. Further information is available on request from Prof. Alexandra Slawin at the School of Chemistry, University of St. Andrews.

Synthetic procedures

Reaction of [Ir(PNP)(COE)][BF_4] with MeP in the presence of water: Formation of *trans*–[Ir(PNP)$(H)_2$(CO)][BF_4] (3) and Ir(PNP)(H)(H_2O){OC(O)CH_2CH_3}][BF_4] (2)

Water (0.60 ml) was added to a solution of [Ir(PNP)(COE)][BF_4] (0.14 g, 0.17 mmol) in methyl propanoate (2.75 g, 31.20 mmol, 3.00 ml). The mixture was heated to 60 ^{0}C for 20 h during which time a biphasic mixture consisting of an orange organic phase and a colourless aqueous phase formed. The mixture was cooled to room temperature and the two phases were allowed to separate. The organic phase was isolated and the product precipitated from this phase with the addition of hexane (20 ml). The resultant precipitate was collected, washed with diethyl ether (2 × 30 ml) and dried *in vacuo* to furnish an orange solid (0.87 g) comprising of a mixture of **3** and **2** in a 4 : 1 ratio based on ^{31}P NMR integrals. Single crystals of **3** suitable for structure determination by X-ray diffraction were obtained as yellow prisms by slow diffusion of pentane into a solution of the mixture of **3** and **2** in dichloromethane. Analytical data for compound **3**: ^{1}H NMR (300 MHz, CD_2Cl_2): δ_H = -6.77 (t, 2H, $^2J_{H\text{-}P}$ = 12.6 Hz; Ir–*H*), 1.40 (vt, 36H, $J_{H\text{-}P}$ = 7.3 Hz; C(CH_3)$_3$), 3.85 (vt, 4H, $J_{H\text{-}P}$ = 4.0 Hz; CH_2–P), 7.51 (d, 2H, $^3J_{H\text{-}H}$ = 8.0 Hz; PNP-aryl), 7.82 (t, 1H, $^3J_{H\text{-}H}$ = 8.0 Hz; PNP-aryl). ^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2): δ_P = 68.8 (s). IR (KBr): $\tilde{\nu}$ = 2954–2896 [m, sp^3 ν(C–H)], 2010 [st, ν(C=O)], 1804 [m, ν(Ir–H)], 1465–1372 [st, Ar ν(C=C)]. ES-MS: *m/z* (%) = 618 (100) [M – BF_4]$^+$. This data compare well with the literature values reported for the analogous complex [Ir(CO)$(H)_2$(PNP)][PF_6].[21]

Reaction of [Ir(PNP)(COE)][BF_4] with Propanoic acid (PA): Formation of [Ir(PNP)(H)(H_2O){OC(O)CH_2CH_3}][BF_4], 2

[Ir(PNP)(COE)][BF_4] (0.38 g, 0.49 mmol) was dissolved in propanoic acid (4.97 g, 67.02 mmol, 5.00 ml) to give a yellow reaction solution. This solution was heated to 60 ^{0}C for 20 h with stirring. After this period, the mixture was cooled to room temperature and reduced to dryness under vacuum. The resulting residue was washed with hexane (3 × 10 ml) and dried *in vacuo* to afford the product as a pale orange solid (0.35g, 94 %). Yellow prisms suitable for structure determination by single crystal X-ray diffraction were obtained by slow diffusion of hexane at room temperature into a dichloromethane solution of **2**. ^{1}H NMR (300 MHz, CD_2Cl_2): δ_H = -29.12 (t, 1H, $^2J_{H\text{-}P}$ = 11.6 Hz; Ir–*H*), 1.08 (t, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz; propanoate-CH_3), 1.31 (vt, 18H, $J_{H\text{-}P}$ = 7.1 Hz; C(CH_3)$_3$), 1.36 (vt, 18H, $J_{H\text{-}P}$ = 7.1 Hz; C(CH_3)$_3$), 2.27 (q, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz; propanoate-CH_2), 3.55 (dvt, 2H, $J_{H\text{-}H}$ = 17.5 Hz, $J_{H\text{-}P}$ = 4.0 Hz; CH_2–P), 3.80 (dvt, 2H, $J_{H\text{-}H}$ = 17.5 Hz, $J_{H\text{-}P}$ = 3.7 Hz; CH_2–P), 7.50 (d, 2H, $^3J_{H\text{-}H}$ = 8.1 Hz; PNP-aryl), 7.76 (t, 1H, $^3J_{H\text{-}H}$ = 8.1 Hz; PNP-aryl). ^{13}C{^{1}H} NMR (75 MHz, CD_2Cl_2): δ_C = 9.0 (s; propanoate-CH_3), 28.0 (s; propanoate-CH_2), 29.3 (bs; C(CH_3)$_3$), 36.4 (vt, $^1J_{C\text{-}P}$ = 11.7 Hz; $C(CH_3)_3$), 37.1 (vt, $^1J_{C\text{-}P}$ = 11.7 Hz; CH_2–P), 37.6 (vt, $^1J_{C\text{-}P}$ = 10.0 Hz; $C(CH_3)_3$), 122.0 (vt, $^3J_{C\text{-}P}$ = 4.5 Hz; PNP-aryl), 139.3 (s; PNP-aryl), 166.5 (vt, $^2J_{C\text{-}P}$ = 3.1 Hz; PNP–aryl), 181.4 (s; propanoate-*C*=O). ^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2): δ_P = 49.6 (s).

Reaction of [Ir(PNP)(COE)][BF_4] with *tert*-butyl propanoate (^{t}BuP) or isopropyl propanoate (^{i}PrP) in the presence of water to give [Ir(PNP)(H)(H_2O){OC(O)CH_2CH_3}][BF_4] (2)

Water (0.1 ml) was added to a suspension of [Ir(PNP)(COE)][BF_4] (0.04 g, 0.05 mmol) in *tert*-butyl propanoate (1.73 g, 13.29 mmol, 2.0 ml) or isopropyl propanoate (1.77 g, 15.20 mmol, 2.0 ml). The resulting mixture was heated to 60 ^{0}C for 15 h after which the orange mixture was cooled to room temperature and evaporated to dryness under vacuum. The obtained orange solid was analysed using standard NMR spectroscopic techniques without any further purification. Analysis of this solid indicated quantitative conversion of [Ir(PNP)(COE)][BF_4] to [Ir(PNP)(H)(H_2O){OC(O)CH_2CH_3}][BF_4] (**2**) for both ^{t}BuP and ^{i}PrP with no trace of the CO complex [Ir(PNP)$(H)_2$(CO)][BF_4] (**3**).

Reaction of [Ir(PNP)(COE)][BF_4] with MeP in the absence of water: Formation of [Ir(PNP)(H){CH_2OC(O)CH_2CH_3}][BF_4], 6

[Ir(PNP)(COE)][BF_4] (0.19 g, 0.24 mmol) was dissolved in methyl propanoate (3.66 g, 41.50 mmol, 4.00 ml) and the resulting red solution heated to 60 ^{0}C for 20 h with stirring. After this period, the orange mixture was cooled to room temperature and all volatiles removed under reduced pressure. The crude

product was washed with hexane (3 × 15 ml) and dried *in vacuo* to furnish the product as an orange solid (0.17 g, 94%). ^{1}H NMR (300 MHz, CD_2Cl_2): δ_H = -23.77 (t, 1H, $^2J_{H-P}$ = 14.6 Hz; Ir–*H*), 1.07 (t, 3H, $^3J_{H-H}$ = 7.5 Hz; MeP-C*H*$_3$), 1.21 (vt, 18H, J_{H-P} = 7.1 Hz; C(C*H*$_3$)$_3$), 1.24 (vt, 18H, J_{H-P} = 7.1 Hz; C(C*H*$_3$)$_3$), 2.38 (q, 2H, $^3J_{H-H}$ = 7.5 Hz; MeP-C*H*$_2$), 3.57 (dvt, 2H, J_{H-H} = 17.1 Hz, J_{H-P} = 4.1 Hz; C*H*$_2$–P), 3.71 (dvt, 2H, J_{H-H} = 17.1 Hz, J_{H-P} = 3.5 Hz; C*H*$_2$–P), 6.46 (t, 2H, $^3J_{H-P}$ = 9.5 Hz; MeP-OC*H*$_2$-Ir), 7.52 (d, 2H, $^3J_{H-H}$ = 7.7 Hz; PNP-aryl), 7.83 (t, 1H, $^3J_{H-H}$ = 7.7 Hz; PNP-aryl). ^{13}C{^{1}H} NMR (75 MHz, CD_2Cl_2): δ_C = 8.9 (s; MeP-*C*H$_3$), 27.2 (s; MeP-*C*H$_2$), 29.3 (bs; C(*C*H$_3$)$_3$), 29.7 (bs; C(*C*H$_3$)$_3$), 35.9 (vt, $^1J_{C-P}$ = 12.9 Hz; *C*(CH$_3$)$_3$), 37.1 (vt, $^1J_{C-P}$ = 9.7 Hz; *C*(CH$_3$)$_3$), 39.4 (vt, $^1J_{C-P}$ = 10 Hz; *C*H$_2$–P), 51.8 (vt, $^2J_{C-P}$ = 6.3 Hz; MeP-*C*H$_2$-Ir), 121.7 (vt, $^3J_{C-P}$ = 4.3 Hz; PNP-aryl), 139.3 (s; PNP-aryl), 163.1 (vt, $^2J_{C-P}$ = 2.7 Hz; PNP–aryl), 187.7 (m; MeP-*C*=O). ^{31}P{^{1}H} NMR (121 MHz, CD_2Cl_2): δ_P = 42.1 (s). IR (KBr): $\tilde{\nu}$ = 2949–2871 [st, sp^3 *ν*(C–H)], 1610 [st, *ν*(C=O)], 1466–1371 [st, Ar *ν*(C=C)], 1059 [st, *ν*(C–O)]. ES-MS: *m/z* (%) = 676 (32) [M – BF_4]$^+$, 588 (44) [Ir(PNP)]$^+$, 532 (11) [Ir(H)(PNP) - ^{t}Bu]$^+$.

Attempt to catalytically functionalise C–H activated MeP by the *in situ* generation of [Ir(PNP)(H){CH$_2$OC(O)CH$_2$CH$_3$}][BF$_4$] (6)

A solution of [Ir(PNP)(COE)][BF_4] (0.20 g, 0.25 mmol) in methyl propanoate (9.15 g, 103.85 mmol, 10 ml) was added to an autoclave under dinitrogen. The autoclave was subsequently sealed tightly, pressurised with ethene (30 bar) and heated to 60 ^{0}C for 15 h with stirring. After this period, the autoclave was cooled to room temperature, vented to the atmosphere and opened to reveal the product mixture as a yellow solution containing a brown solid. Both phases were analysed making use of standard GC-MS and NMR spectroscopic techniques. The desired product methyl 2-methylbutanoate was, however, not detected. ^{31}P NMR revealed in addition to [Ir(PNP)(H)$_2$(CO)][BF_4] (**3**), the presence of two new complexes in the form of singlets at δ 73.1 and δ 50.7. These complexes, which do not have corresponding hydride resonances, could not be assigned unambiguously.

Attempt to catalytically functionalise C–H activated MeP *via* preformed [Ir(PNP)(H){CH$_2$OC(O)CH$_2$CH$_3$}][BF$_4$] (6)

A solution of [Ir(PNP)(H){OC(O)CH$_2$CH$_3$}][BF_4] (0.21 g, 0.29 mmol) in methyl propanoate (9.15 g, 103.85 mmol, 10 ml) was added to an autoclave under dinitrogen. The autoclave was subsequently sealed tightly, pressurised with ethene (30 bar) and heated to 60 ^{0}C for 15 h with stirring. After this period, the autoclave was cooled to room temperature, vented to the atmosphere and the product mixture analysed using standard GC-MS and NMR spectroscopic techniques. As before, the desired product methyl 2-methylbutanoate was not observed and the measured ^{31}P NMR spectra were comparable to those previously obtained for the *in situ* attempt.

Conclusions

In this study the reactivity of the iridium pincer complex [Ir(PNP)(COE)][BF_4] towards the activation of C–H bonds in both the *α*- and *β*-positions of methyl propanoate, isopropyl propanoate and *tert*-butyl propanoate were explored. In the presence of water, methyl propanoate did not undergo *α*-C–H activation. Instead, hydrolysis of the ester bond led to the formation of propanoic acid and methanol which participated in further reactions with [Ir(PNP)(COE)][BF_4] to generate [Ir(H)(PNP)(H$_2$O){OC(O)CH$_2$CH$_3$}][BF_4] from propanoic acid and [Ir(CO)(H)$_2$(PNP)][BF_4] *via* methanol decarbonylation. Reactions of MeP with [Ir(PNP)(COE)][BF_4] in the absence of added water led to selective sp^3 C–H activation of the methoxy group to give [Ir(H)(PNP){CH$_2$OC(O)CH$_2$CH$_3$}][BF_4]. Under the same conditions, the related but more sterically demanding esters, isopropyl- and *tert*-butyl propanoate did not undergo sp^3 C–H activation in either of the *α*- or *β*-positions.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [Crystallographic discussion and data tables, NMR spectra and Crystallographic Information Files (CIF)]. See DOI: 10.1039/b000000x/

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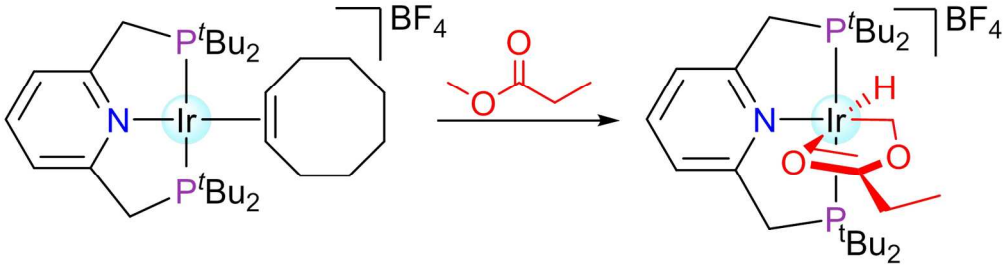

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