



Cite this: *Chem. Commun.*, 2017, 53, 3634

Received 9th December 2016,  
Accepted 26th February 2017

DOI: 10.1039/c6cc09807j

rsc.li/chemcomm

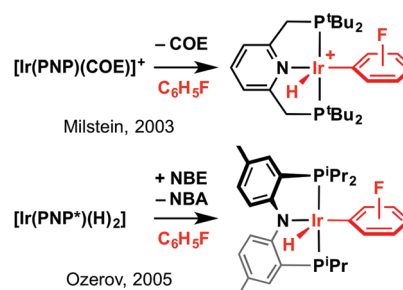
**Iridium(i) carbonyl complex [Ir(2,6-(P<sup>t</sup>Bu<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)(CO)] undergoes reversible C–H bond activation of benzene and a series of fluorobenzenes on UV irradiation. Exclusive *ortho*-selectivity is observed in reactions of fluorobenzene and 1,2-difluorobenzene.**

Epitomised by applications in the catalytic dehydrogenation of alkanes, iridium complexes of phosphine-based pincer ligands are widely recognised for their capacity to activate C–H bonds.<sup>1</sup> With fluoroaryls representing valuable synthons in organic chemistry,<sup>2,3</sup> we have targeted use of these iridium compounds for carrying out selective C–H bond activation reactions of partially fluorinated benzenes (C<sub>6</sub>H<sub>6-n</sub>F<sub>n</sub>, *n* ≤ 3).<sup>3</sup> The presence of fluorine substituents results in significantly stronger C–H bonds than benzene and, correspondingly, fluorobenzenes represent challenging substrates.<sup>3,4</sup> Previous work by Milstein and Ozerov employing neutral (PNP) and anionic (PNP\*) pincer ligands has highlighted the potential of iridium pincers, although under moderate temperature regimes (<100 °C) these systems showed poor regioselectivity in the activation of fluorobenzene (Scheme 1).<sup>5</sup> As C–H bond activation is thermodynamically favoured *ortho* to the fluorine substituents,<sup>4</sup> indiscriminate and irreversible oxidative addition reactions of transient 14 VE Ir(i) intermediates {Ir(PNP)}<sup>+</sup>/ $\{$ Ir(PNP\*)} are implicated.

We postulated that use of anionic pincer ligands bearing central aryl donors could promote selective activation of fluorobenzene substrates through increased reaction reversibility imparted by the high *trans*-influence aryl donor.<sup>6,7</sup> With a view to testing this hypothesis we selected [Ir(PCP)(CO)] **1** (PCP = 2,6-(P<sup>t</sup>Bu<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)<sup>8</sup> as a well-defined precursor for the low coordinate and formally 14 VE Ir(i) fragment {Ir(PCP)}, through

photochemically promoted dissociation of the carbonyl ligand. In this way, subsequent products of C–H bond activation would be trapped on re-coordination of the carbonyl ligand (in a closed system). Initial experiments using benzene as the substrate supported this reasoning, with [Ir(PCP)(C<sub>6</sub>D<sub>5</sub>)D(CO)] **2-d<sub>6</sub>**<sup>9</sup> generated on irradiation of a 20 mM C<sub>6</sub>D<sub>6</sub> solution of **1** at RT using a 100 W Hg arc lamp (quartz J. Young's NMR tube, Scheme 2). Following this reaction by periodic analysis using <sup>31</sup>P NMR spectroscopy, however, indicated that conversion of **1** ( $\delta_{31\text{P}}$  82.0) to **2-d<sub>6</sub>** ( $\delta_{31\text{P}}$  52.3) plateaued at 62% after *ca.* 2 h total irradiation. On the same timeframe, irradiation of independently synthesised **2** resulted in an equivalent reaction composition. In contrast, both **1** and **2** are thermally stable on extended heating at 80 °C in C<sub>6</sub>D<sub>6</sub> solution (8 h) and no isotope exchange was observed for **2** (to **2-d<sub>6</sub>**).<sup>10</sup> Together these results indicate establishment of a photostationary mixture of **1** and **2-d<sub>6</sub>**, mediated through light induced carbonyl dissociation from both species.<sup>11</sup>

To gain deeper understanding of the photolysis experiments, a series of DFT and TD-DFT calculations were performed (see ESI† for full details). In line with expectation, the computed free energy for carbonyl dissociation to form {Ir(PCP)} is a significantly endergonic process ( $\Delta G_{298\text{K}} = +194.4$  kJ mol<sup>-1</sup>). While the subsequent C–H bond activation of benzene is exothermic ( $\Delta H = -15.3$  kJ mol<sup>-1</sup>),

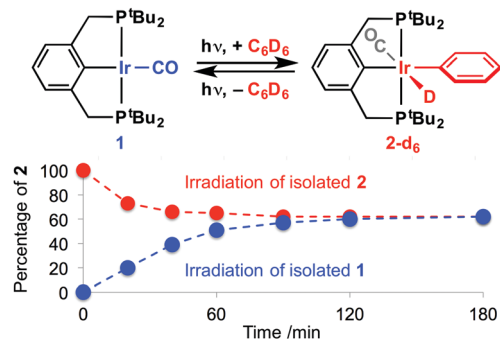


**Scheme 1** C–H bond activation of fluorobenzene using Ir-pincers. PNP = 2,6-(P<sup>t</sup>Bu<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>N, PNP\* = (4-Me-2-(Pr<sub>2</sub>P)C<sub>6</sub>H<sub>3</sub>)<sub>2</sub>N<sup>-</sup>, COE = cyclooctene, NBE = norbornene, NBA = norbornane.

Department of Chemistry, University of Warwick, Gibbet Hill Road, Coventry CV4 7AL, UK. E-mail: a.b.chaplin@warwick.ac.uk; Web: <http://go.warwick.ac.uk/abchaplin>, [www.twitter.com/chaplinlab](http://www.twitter.com/chaplinlab)

† Electronic supplementary information (ESI) available: Full experimental and computational details, NMR, IR and UV-vis spectra, TD-DFT analysis of **1** and **2**, and optimised geometries in xyz format. CCDC 1520522–1520525. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6cc09807j





Scheme 2 UV-promoted interconversion between **1** and **2** ( $[\text{Ir}] = 20 \text{ mM}$ , RT).

the Ir(III) product lies thermodynamically further uphill from **1** ( $\Delta G_{298\text{K}} = +238.0 \text{ kJ mol}^{-1}$ ). Such energetics are characteristic of an unfavourable equilibrium reaction, although one that would be offset by the use of the substrate as the solvent.<sup>12</sup> Re-coordination of the carbonyl ligand counteracts the unfavourable thermodynamics ( $\Delta G_{298\text{K}} = -95.0 \text{ kJ mol}^{-1}$ ), however, **2** is still calculated to be  $+141.3 \text{ kJ mol}^{-1}$  higher in free energy than **1** +  $\text{C}_6\text{H}_6$ . Together these results are consistent with the lack of any thermal reaction observed for either **1** or **2** in  $\text{C}_6\text{D}_6$  and highlight the important promoting role of UV-irradiation in the formation of **2** (and reformation of **1**). In this context, analysis of **1** by TD-DFT identified a number of singlet-singlet electronic transitions between 195 and 235 nm (*i.e.* UV) that can be attributed to carbonyl dissociation. A representative example is shown in Fig. 1 (full details provided in ESI†). Similar excitations are also calculated for **2** between 190 and 260 nm, suggesting that it would be difficult to selectively enact the UV-promoted dissociation of carbonyl from either **1** or **2**.<sup>13</sup>

To further explore this C–H bond activation chemistry, 20 mM solutions of **1** in fluorobenzene, 1,2-difluorobenzene, and 1,3,5-trifluorobenzene were irradiated for a total of 8 h at RT (Scheme 3). Similar to that observed in benzene, analysis by  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectroscopy indicated formation of photostationary mixtures composed of **1** and Ir(III) products of C–H bond activation **3**; as the minor and major components, respectively. Supporting our hypothesis, and contrasting with reactions of analogous PNP and PNP\* systems (*vide supra*), C–H bond activation of fluorobenzene (**3a**) and 1,2-difluorobenzene (**3b**) proceeded with exclusive *ortho*-selectivity. Both possible rotamers of each isomer are formed, although in disparate proportions (Scheme 3).

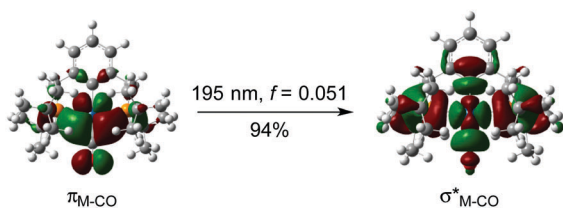
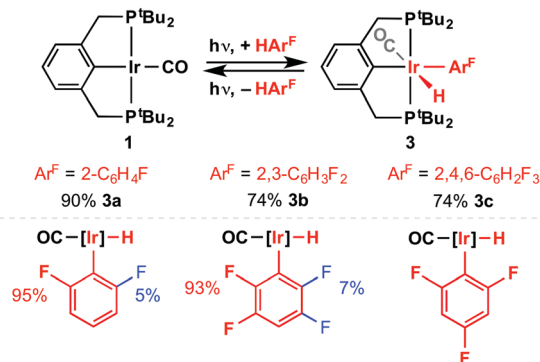


Fig. 1 Representative electronic excitation related to carbonyl dissociation from **1**; wavelength, oscillator strength ( $f$ ) and % contribution of the represented natural transition orbitals (rendered with an orbital isosurface value of 0.02).



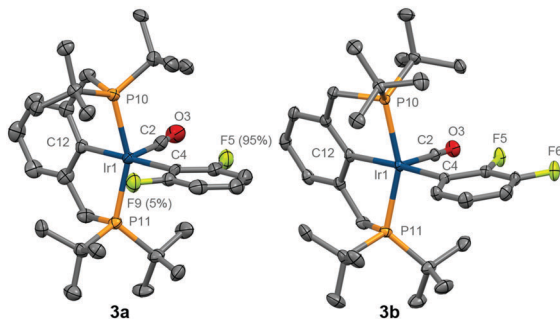
Scheme 3 UV-promoted C–H bond activation of fluorobenzenes (top;  $[\text{Ir}] = 20 \text{ mM}$ , 8 h, RT). Major rotamers depicted in red, minor rotamers depicted in blue (bottom).

Consistent with these observations and manifestation of the “*ortho* fluorine effect”,<sup>4</sup> the alternative regioisomers of **3a** ( $>10 \text{ kJ mol}^{-1}$ ) and **3b** ( $>18 \text{ kJ mol}^{-1}$ ), and their respective 5-coordinate precursors  $[\text{Ir}(\text{PCP})(2\text{-FC}_6\text{H}_4)\text{H}]$  ( $>24 \text{ kJ mol}^{-1}$ ) and  $[\text{Ir}(\text{PCP})(2,3\text{-F}_2\text{C}_6\text{H}_3)\text{H}]$  ( $>26 \text{ kJ mol}^{-1}$ ), are calculated to be significantly higher in free energy. As for the formation of **2** from **1**, computed reaction free energies suggest the formation of **3** occur outside of thermally accessible regimes and instead are presumably driven through nuanced differences in the photo-physical properties of **1** and **3**. Moreover, increasingly favourable overall reactions correlate with number of fluorine substituents:  $\Delta G_{298\text{K}}/\text{kJ mol}^{-1} = +141.3$  (**2**),  $+128.1$  (**3a**),  $+121.0$  (**3b**),  $+119.1$  (**3c**).

With the above in mind and to independently verify their structures, analytically pure samples of **3** were isolated through dehydrohalogenation of  $[\text{Ir}(\text{PCP})\text{HCl}]$ <sup>14</sup> using  $\text{K}[\text{O}^t\text{Bu}]$  in the respective fluorobenzene at  $75^\circ\text{C}$ , followed by reaction with carbon monoxide (yield = 32–54%). The structures of these new compounds, and for comparison **2**,<sup>9</sup> were fully verified in solution by  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  and  $^{31}\text{P}$  NMR, IR and UV-vis spectroscopy, and in the solid-state by X-ray crystallography (**3a**, **3b** – Fig. 2; **2**, **3c** – ESI†). Notable spectroscopic markers include low frequency hydride resonances at  $\delta -9.07$  (**2**),  $-8.86/-9.68$  (**3a**),  $-8.88/-9.66$  (**3b**),  $-9.46$  (**3c**) that show  $^3J_{\text{PH}}$  coupling of *ca.* 17 Hz, and  $^{31}\text{P}$  resonances at  $\delta 51.1$  (**2**),  $54.5/51.7$  (**3a**),  $54.7/52.2$  (**3b**),  $54.0$  (**3c**) in  $\text{C}_6\text{D}_{12}$  solution (data for major rotamers underlined). The structures of major rotamers of **3a** and **3b**, bearing the fluorine atoms proximal to the carbonyl ligand, were definitively established in solution through NOESY experiments and corroborated in the solid-state (Fig. 2). Likewise, the hydride resonances of the minor rotamers show characteristic  $^1J_{\text{FH}}$  coupling of *ca.* 10 Hz. The observed relative conformational preferences are also reproduced *in silico* (see ESI†). Complexes **3** are thermally stable on extended heating at  $80^\circ\text{C}$  in  $\text{C}_6\text{D}_6$  solution: after 8 h,  $<5\%$  **1** is formed and for **3a** and **3b** the ratio of rotamers was unchanged, as determined *in situ* by  $^{31}\text{P}$  NMR spectroscopy.

In conclusion, we have demonstrated that selective C–H bond activation reactions of fluorobenzenes can be achieved under mild conditions using photolysis of  $[\text{Ir}(2,6\text{-}(\text{P}^t\text{Bu}_2\text{CH}_2)_2\text{C}_6\text{H}_3)(\text{CO})]$  **1** as a means to generate the reactive





**Fig. 2** Solid-state structures of **3a** (occupancy of disordered fluorine substituents in parenthesis) and **3b**. Thermal ellipsoids at 50% probability level; hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: **3a**, Ir1–C2, 1.931(6); Ir1–C4, 2.159(5); Ir1–C12, 2.115(5); Ir1–P10, 2.3394(15); Ir1–P11, 2.3474(15); C2–Ir1–C12, 83.8(2); C4–Ir1–C12, 178.2(2); P10–Ir1–P11, 155.84(5). **3b**, Ir1–C2, 1.928(2); Ir1–C4, 2.150(2); Ir1–C12, 2.111(2); Ir1–P10, 2.3511(6); Ir1–P11, 2.3397(6); C2–Ir1–C12, 89.07(9); C4–Ir1–C12, 173.63(8); P10–Ir1–P11, 157.41(2).

14 VE Ir(i) fragment  $\{\text{Ir}(2,6\text{-}(\text{P}^t\text{Bu}_2\text{CH}_2)_2\text{C}_6\text{H}_3)\}$  in solution. This work not only showcases the ability of iridium pincer complexes to mediate challenging C–H bond activations, but more generally highlights a potentially useful catalyst design principle that we hope will stimulate the development of new organic transformations employing partially fluorinated benzenes as building blocks.

We gratefully acknowledge financial support from the Swiss National Science Foundation (S. A. H.), EPSRC (J. E.-K.), Royal Society (A. B. C.) and University of Warwick. Crystallographic data was collected using a diffractometer purchased through support from Advantage West Midlands and the European Regional Development Fund. We also thank the Scientific Computing Research Technology Platform at the University of Warwick for providing high-performance computing facilities.

## Notes and references

- (a) K. Krogh-Jespersen, M. Czerw, K. Zhu, B. Singh, M. Kanzelberger, N. Darji, P. D. Achord, K. B. Renkema and A. S. Goldman, *J. Am. Chem. Soc.*, 2002, **124**, 10797–10809; (b) R. Ghosh, X. Zhang, P. Achord, T. J. Emge, K. Krogh-Jespersen and A. S. Goldman, *J. Am. Chem. Soc.*, 2007, **129**, 853–866; (c) W. H. Bernskoetter, P. S. White, K. I. Goldberg and M. Brookhart, *J. Am. Chem. Soc.*, 2009, **131**, 8603–8613; (d) J. Choi, A. H. R. MacArthur, M. Brookhart and A. S. Goldman, *Chem. Rev.*, 2011, **111**, 1761–1779; (e) J. Choi, D. Y. Wang, S. Kundu, Y. Choliy, T. J. Emge, K. Krogh-Jespersen and A. S. Goldman, *Science*, 2011, **332**, 1545–1548.
- For representative examples see: (a) M. Lafrance, C. N. Rowley, T. K. Woo and K. Fagnou, *J. Am. Chem. Soc.*, 2006, **128**, 8754–8756;

- (b) H.-Q. Do and O. Daugulis, *J. Am. Chem. Soc.*, 2008, **130**, 1128–1129; (c) Y. Nakao, N. Kashihara, K. S. Kanyiva and T. Hiyama, *J. Am. Chem. Soc.*, 2008, **130**, 16170–16171; (d) X. C. Cambeiro, T. C. Boorman, P. Lu and I. Larrosa, *Angew. Chem., Int. Ed.*, 2012, **52**, 1781–1784; (e) P. Ricci, K. Krämer, X. C. Cambeiro and I. Larrosa, *J. Am. Chem. Soc.*, 2013, **135**, 13258–13261; (f) X. C. Cambeiro, N. Ahlsten and I. Larrosa, *J. Am. Chem. Soc.*, 2015, **137**, 15636–15639; (g) J. Takaya, S. Ito, H. Nomoto, N. Saito, N. Kirai and N. Iwasawa, *Chem. Commun.*, 2015, **51**, 17662–17665; (h) M. Simonetti, G. J. P. Perry, X. C. Cambeiro, F. Juliá-Hernández, J. N. Arokianathar and I. Larrosa, *J. Am. Chem. Soc.*, 2016, **138**, 3596–3606.
- (a) E. Clot, O. Eisenstein, N. Jasim, S. A. Macgregor, J. E. McGrady and R. N. Perutz, *Acc. Chem. Res.*, 2011, **44**, 333–348; (b) S. D. Pike, M. R. Crimmin and A. B. Chaplin, *Chem. Commun.*, 2017, **53**, DOI: 10.1039/c6cc09575e.
- (a) M. E. Evans, C. L. Burke, S. Yaibuathes, E. Clot, O. Eisenstein and W. D. Jones, *J. Am. Chem. Soc.*, 2009, **131**, 13464–13473; (b) E. Clot, C. Mégret, O. Eisenstein and R. N. Perutz, *J. Am. Chem. Soc.*, 2009, **131**, 7817–7827; (c) E. Clot, M. Besora, F. Maseras, C. Mégret, O. Eisenstein, B. Oelckers and R. N. Perutz, *Chem. Commun.*, 2003, 490–491.
- (a) L. Fan, S. Parkin and O. V. Ozerov, *J. Am. Chem. Soc.*, 2005, **127**, 16772–16773; (b) E. Ben-Ari, M. Gandelman, H. Rozenberg, L. J. W. Shimon and D. Milstein, *J. Am. Chem. Soc.*, 2003, **125**, 4714–4715; (c) E. Ben-Ari, R. Cohen, M. Gandelman, L. J. W. Shimon, J. M. L. Martin and D. Milstein, *Organometallics*, 2006, **25**, 3190–3210.
- D. Y. Wang, Y. Choliy, M. C. Haibach, J. F. Hartwig, K. Krogh-Jespersen and A. S. Goldman, *J. Am. Chem. Soc.*, 2016, **138**, 149–163.
- During the preparation of this manuscript the C–H bond activation of fluorobenzene using related Ir-POCOP pincer complexes has been described: L. P. Press, A. J. Kosanovich, B. J. McCulloch and O. V. Ozerov, *J. Am. Chem. Soc.*, 2016, **138**, 9487–9497.
- (a) K. Krogh-Jespersen, M. Czerw, K. Zhu, B. Singh, M. Kanzelberger, N. Darji, P. D. Achord, K. B. Renkema and A. S. Goldman, *J. Am. Chem. Soc.*, 2002, **124**, 10797–10809; (b) D. Morales-Morales, R. Redón, Z. Wang, Do W. Lee, C. Yung, K. Magnuson and C. M. Jensen, *Can. J. Chem.*, 2001, **79**, 823–829.
- M. Kanzelberger, B. Singh, M. Czerw, K. Krogh-Jespersen and A. S. Goldman, *J. Am. Chem. Soc.*, 2000, **122**, 11017–11018.
- Acid catalysed oxidative addition of C(sp)<sup>3</sup>–H bonds to **1** have, however, been reported: J. D. Hackenberg, S. Kundu, T. J. Emge, K. Krogh-Jespersen and A. S. Goldman, *J. Am. Chem. Soc.*, 2014, **136**, 8891–8894.
- Consistent with this suggestion, photolysis of 20 mM solutions of **1** and **2** in C<sub>6</sub>D<sub>6</sub> under 1 atm of CO at RT resulted in prolonged (>6 h) establishment of similar photostationary mixtures of **1**:**2-d<sub>6</sub>** (1:1.4, corresponding to 58% **2-d<sub>6</sub>**) to those obtained under an argon atmosphere (after ca. 2 h). For discussion of mechanistic pathways in related photochemical reactions of [Rh(PMe<sub>3</sub>)<sub>2</sub>(CO)Cl] see: G. P. Rosini, W. T. Boese and A. S. Goldman, *J. Am. Chem. Soc.*, 1994, **116**, 9498–9505.
- J. E. Wheatley, C. A. Ohlin and A. B. Chaplin, *Chem. Commun.*, 2014, **50**, 685–687.
- Notably using a long pass (glass) filter (<330 nm): no reaction was observed when a 20 mM solution of **1** was irradiated in C<sub>6</sub>D<sub>6</sub> for 2 h at RT, while <5% formation of **1** was observed when a 20 mM solution of **2** was irradiated in C<sub>6</sub>D<sub>6</sub> for 2 h at RT.
- C. J. Moulton and B. L. Shaw, *J. Chem. Soc., Dalton Trans.*, 1976, 1020.

