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ARTICLE TYPE

Oxidative addition of ether O–methyl bonds at a Pt(0) centre[§]

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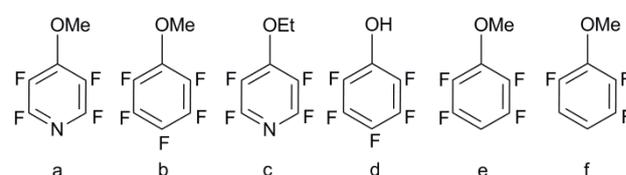
Pt(PCyp₃)₂ (Cyp = cyclopentyl) undergoes C–O oxidative addition with 2,3,5,6-tetrafluoro-4-methoxypyridine, pentafluoroanisole, 2,3,5,6-tetrafluoroanisole and 2,3,6-trifluoroanisole yielding platinum methyl derivatives. The reactions occur in preference to C–H or C–F activation.

We have shown that Pd⁰(PR₃)₂ and Pt⁰(PR₃)₂ complexes can undergo C–F oxidative addition, and the resulting square-planar Pt(II) complexes are stable to C–F reductive elimination.^{1–3} However, C–F reductive elimination is possible from 3-coordinate Pd(II)⁴ and from the metal aryl fluoride complexes in oxidation state IV.^{5–8} The related oxidative addition of ether C–O bonds appears to be missing from the literature although examples of C–O reductive elimination of ethers from Pd(II) are known.^{9,10} In contrast, C–O (ester) oxidative addition at Pt(0) has recently been described¹¹ and reductive elimination of ester C–O bonds from Pd(IV) and Pt(IV) is well known.^{12–14} We demonstrate the importance of electron withdrawing aryl groups for achieving oxidative addition of methyl aryl ethers at Pt(0) and probe the mechanism of C–O activation.

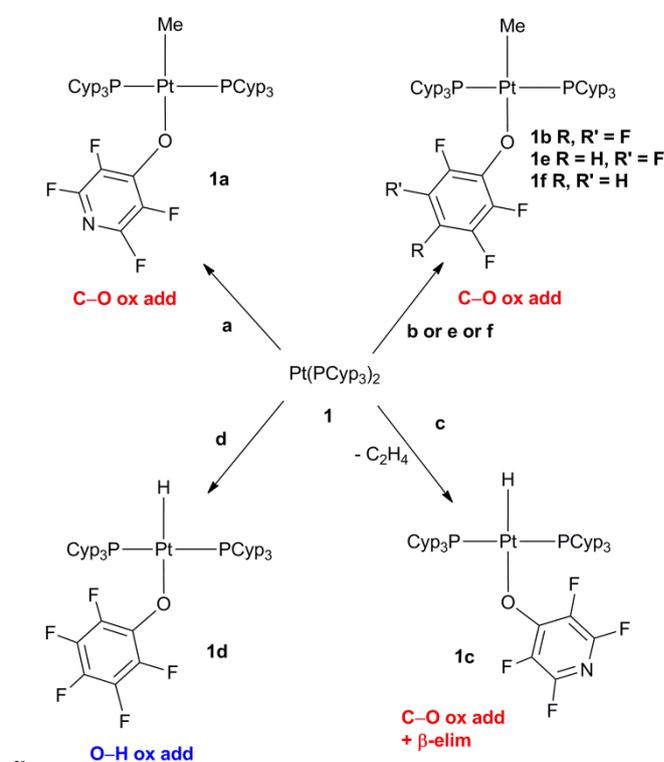
Activation of C–O bonds of ethers at transition metals, first described many years ago,^{15–17} has been rejuvenated by the work of Carmona, Paneque^{18,19} and Goldman^{20,21} who investigated the reactivity of iridium tris(pyrazolyl)borate and iridium pincer complexes, respectively. In both cases, the C–O activation was associated with initial methyl C–H bond activation (see Scheme S1 in ESI). Carmona and Paneque used methylated anisoles and demonstrated rearrangement to Ir–O metallacycles containing Ir=carbene linkages. Goldman used fluorinated anisoles and isolated the products of “simple” C–O(methyl) oxidative addition. Following the initial C–H cleavage, aryloxy migration and 1,2-hydride migration generated the product. Cross-coupling reactions involving unsupported aryl methyl ether C–O bonds have been described at nickel.^{22,23} In contrast to the iridium reactions, the cross-coupling results in cleavage of the aryl C–O bond although this bond is stronger than the O–CH₃ bond.

Here we report the reactions of Pt⁰(PCyp₃)₂ **1** (Cyp = cyclopentyl) with 2,3,5,6-tetrafluoro-4-methoxypyridine, pentafluoroanisole, 2,3,5,6-tetrafluoroanisole and 2,3,6-trifluoroanisole and show that Ar^FO–CH₃ oxidative addition occurs in preference to C–H or C–F oxidative addition. We also compare reactions with pentafluorophenol and 2,3,5,6-tetrafluoro-4-ethoxypyridine (Scheme 1). These reactions offer competition between C–F, C–H, C–O and O–H activation.

The thermal reaction of **1** in the presence of tetrafluoro-



Scheme 1. Substrates

Scheme 2. Reactivity of **1**

methoxypyridine **a** (1 eqv, hexane, 60 °C, 2 days) generated one product quantitatively (Scheme 2). The colourless crystalline material was characterised by multinuclear NMR spectroscopy, LIFDI mass spectrometry²⁴ and X-ray crystallography. ¹H NMR spectroscopy shows a triplet resonance at δ 0.89 with ¹⁹⁵Pt satellites ($J_{PH} = 6.3$, $J_{PtH} = 83.8$ Hz) with integration 3H relative to cyclopentyl protons and no signals to higher field. The ¹⁹⁵Pt-¹H HMQC spectrum shows that this resonance correlates with a platinum triplet at δ -4060. The ¹H peaks of the tricyclopentylphosphine also show cross-peaks to the platinum resonance. The ³¹P{¹H} NMR spectrum gives a singlet at δ 22.3

with Pt satellites (J_{PtF} 2962 Hz). The ^{19}F NMR spectrum shows two sets of inequivalent fluorines at δ -168.3 (m, F *meta* to N) and at δ -99.0 (m, F *ortho* to N) in a 1:1 integration ratio. $^{13}\text{C}\{^1\text{H}\}$ NMR spectroscopy reveals a triplet at δ -34.3 with ^{195}Pt satellites ($J_{\text{PC}} = 7$ Hz, $J_{\text{PtC}} = 695$ Hz) which correlates with the ^1H NMR resonance at δ 0.89. This pair of correlated resonances is consistent with a methyl group bound to platinum (a methoxy group would be expected at lower field with small couplings to Pt). Compound **1a** was therefore assigned as *trans*-Pt(PCyp₃)₂(CH₃)(OC₅F₄N). Colourless crystals were grown by slow diffusion of hexane into a concentrated benzene solution. The crystal structure was determined and confirmed the nature of **1a** (Figure 1) demonstrating conclusively that the Ar^FO-CH₃ bond of the ether undergoes selective oxidative addition at the Pt(0) centre (Scheme 2).

The reaction of **1** with pentafluoroanisole **b** proceeded analogously to that with tetrafluoromethoxyppyridine generating **1b** as the only product (Scheme 2). The product **1b** exhibits similar spectroscopic features to those for **1a** and was therefore assigned as *trans*-Pt(PCyp₃)₂(CH₃)(OC₆F₅). A crystal structure of **1b** (crystals grown from hexane) confirmed its identity (Figure 1). The Pt-O and Pt-C bond lengths for **1a** are 2.1586(15) and 2.044(2) Å, respectively. The Pt-O-C angle is 130.10(15)° and the torsional angle of the ring C(3)-C(2)-O(1)-Pt is 21.2(3)°. The corresponding Pt-O and Pt-C bond lengths for **1b** are 2.1306(15) and 2.047(2) Å, while the Pt-O-C angle is 126.78(14)° and the torsional angle is 27.3(3)°.

Goldman showed that the kinetic isotope effect (KIE) for oxidative addition of pentafluoroanisole ($k_{\text{OCH}_3}/k_{\text{OCDF}_3}$) to the iridium pincer complexes is 4.3 ± 0.3 providing strong support for initial C-H bond activation.^{20, 21} We synthesised **a-d₃** and investigated the reaction of **1** with a mixture of **a** and **a-d₃** in hexane. The reaction was performed with a 10-fold excess of each substrate with the consequence that no heating was required to generate a mixture of **1a** and **1a-d₃**. The ^{31}P NMR spectrum and the ^{195}Pt NMR spectrum showed clear isotopic shifts to low field of 0.17 ppm (35.3 Hz) and 14.2 ppm (1527 Hz), respectively. Determination of the initial substrate ratio by mass spectrometry and the product ratio by quantitative $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy yielded a kinetic isotope effect $k_{\text{H}}/k_{\text{D}}$ of $1.11 \pm 10\%$.

The progress of the reaction of **1** with two eqv **b** at 50° C was monitored in situ by ^{31}P NMR spectroscopy in protio solvents. The half-life of **1** proved to be ca. 3 times shorter in THF than in hexane ($t_{1/2}$ 200 and 620 min, respectively). An intermediate was detected in the early stages of reaction in both solvents which declined with time. It exhibited a ^{31}P resonance with $J_{\text{PtP}} = 3956$ Hz characteristic of Pt(0) (δ 26.9, s, in THF) and five distinct ^{19}F resonances, consistent with a provisional assignment as Pt(PCyp₃)₂(η^2 -C=C-C₆F₅OMe) (see ESI).

Complex **1**, dissolved in hexane, also reacted with tetrafluoroethoxyppyridine **c** (1.1 eq, 60° C), but the ^1H NMR spectrum showed this time that the principal product is a platinum hydride (δ -24.6, t $J_{\text{PH}} = 13.1$ Hz, $J_{\text{HPt}} = 1234$ Hz). The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum shows a singlet resonance at δ 46.2 ($J_{\text{PtP}} = 2940$ Hz). The complex exhibits a ^{195}Pt resonance as a triplet of doublets at δ -4704 with corresponding coupling constants. The ^{195}Pt - ^1H HSQC spectrum links the hydride and the cyclopentyl resonances at δ 1.85 to the ^{195}Pt resonance at δ -4704. The ^{19}F

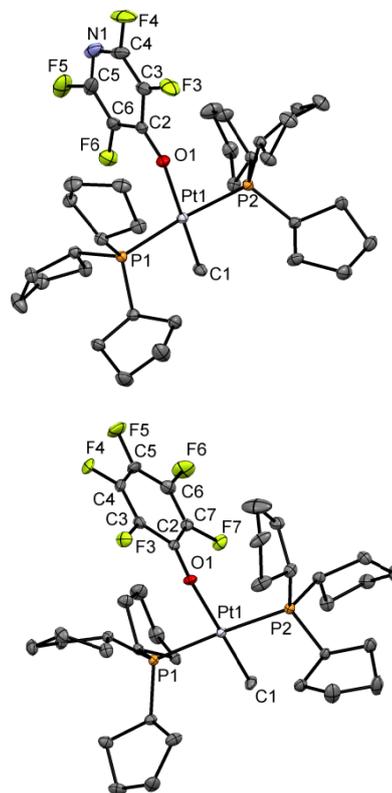
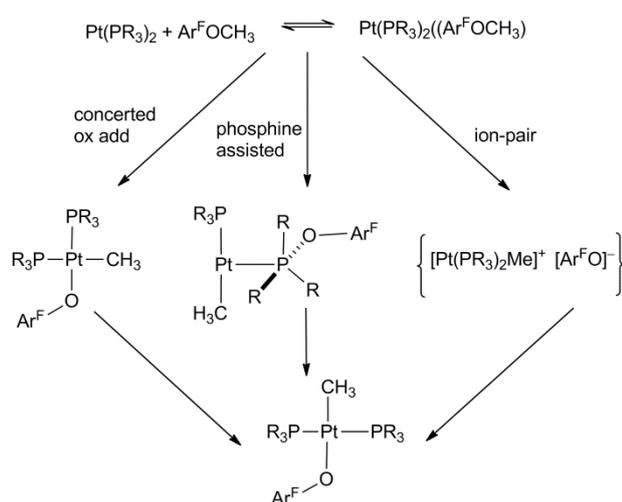


Figure 1. Molecular structure of **1a** (above) and **1b** (below). H atoms omitted. Anisotropic displacement parameters shown as 50% ellipsoids.

NMR spectrum shows two multiplets at δ -99.3 (m, F *ortho* to N) and -169.8 (m, F *meta* to N). Evidence for free C₂H₄ was obtained when the reaction was performed in C₆D₆ and monitored in situ by its ^1H NMR resonance at δ 5.2. Complex **1c** was assigned as *trans*-Pt(PCyp₃)₂(H)(OC₃NF₄), in keeping with the similar results obtained by Goldman.^{20, 21} The X-ray structure of a crystal of **1c** was consistent with the formulation but suffered from disorder both in the cyclopentyl rings and the OC₆F₅ group.

The formation of platinum aryloxy hydrides can also be achieved by reaction with the corresponding phenol, as shown by reaction of **1** with pentafluorophenol **d** (300 K, 1.1 eqv in hexane) yielding **1d** as the only product which was identified as the O-H oxidative addition product Pt(PCyp₃)₂(H)(OC₆F₅). The hydride resonated at δ -24.3 (t, $J_{\text{PH}} = 13.4$, $J_{\text{HPt}} = 1178$ Hz) while the ^{195}Pt resonance appeared at δ -4696 (td, $J_{\text{PtP}} = 2964$, $J_{\text{PtH}} = 1176$ Hz).

We also investigated the importance of the number of fluorine substituents on the reactivity of **1** with methylarylethers and potential competition with C-H activation. The reaction of **1** with 2,3,5,6-tetrafluoroanisole **e** proceeds more slowly than that with **b** but yields an analogous product, *trans*-Pt(PCyp₃)₂(CH₃)(OC₆HF₄) **1e**. The reaction between **1** and 2,3,6-trifluoroanisole **f**, required excess to proceed and yielded *trans*-Pt(PCyp₃)₂(CH₃)(OC₆H₂F₃), **1f**. The rates of reaction decreased in the order **b** > **e** > **f**, as the number of fluorine substituents was reduced. There was no reaction between **1** and anisole even with excess substrate. The crystal structures of **1e** and **1f** (Figure S3) are similar to those of **1a** and **1b**. However, **1e** exhibits a contact between Pt and F(7) (2.972(1) Å) shorter than the sum of the Van der Waals radii



Scheme 3. Proposed mechanisms of C-O oxidative addition

(3.22 Å) and a torsion angle C(3)–C(2)–O(1)–Pt of $-1.00(14)^\circ$.

Our results provide some guidance on the mechanism of reaction, even though a definitive conclusion is not yet possible.

The C–H activation route appears very unlikely for $\text{Pt}(\text{PCy}_3)_2$ because of the low KIE, the difficulty of forming a carbene at Pt, and the accessibility of cyclometalated products by C–H activation as observed for $\text{CpRh}(\text{PMe}_3)$.^{25,26} Three alternative routes are consistent with a low KIE: direct oxidative addition,⁹ phosphine-assisted reaction^{2,3} and an ion-pair route⁹ (Scheme 3). In each case, initial coordination of the substrate would occur, consistent with detection of the Pt(0) intermediate in the reaction with **b**. Direct oxidative addition reaction represents the reverse of the reductive elimination reactions observed by Buchwald.^{10,27} The selectivity for breaking the O–CH₃ bond can be understood in the phosphine-assisted route because of the preference to put the electronegative O–Ar^F group on the metallophosphorane.^{2,28,29} The ion-pair route generates $[\text{Pt}(\text{PCy}_3)_2\text{Me}]^+$ with the ethers and $[\text{Pt}(\text{PCy}_3)_2\text{H}]^+$ with pentafluorophenol^{30,31} in parallel to recent C–O reductive elimination mechanisms.⁹ The increased rate in the more polar solvent, THF, lends support to the ion-pair route.

These results demonstrate selective C–O oxidative addition at fluorinated aromatic methyl ethers. The selectivity for the O–CH₃ bond in **b**, **e** and **f** in preference to the O–Ar bond matches Goldman's observations (also with fluorinated arenes). With unfluorinated Ar–O–CH₃ substrates, Paneque again observed O–CH₃ cleavage¹⁹ but Milstein observed Ar–O cleavage at $\text{Rh}(\text{PCP})$.¹⁷ The reaction of **a** at $\text{Pt}(\text{PCy}_3)_2$ contrasts with the C–F oxidative addition observed with the same substrate at $\text{Ni}(\text{PEt}_3)_2$ and with the cyclometallation product formed by C–H and C–F activation at $\text{CpRh}(\text{PMe}_3)$.^{24,25,26}

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Notes and references

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[†] Electronic Supplementary Information (ESI) available: scheme of reactions of ethers at iridium, general procedures, syntheses, HSQC of **1a** and **1c**, kinetic isotope effect including spectra, in-situ monitoring of

formation of **1b**, kinetic plot and spectra of intermediate, NMR data, crystallographic methods and data for **1a**, **1b**, **1e** and **1f**. See DOI: 10.1039/b000000x/

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