COMMUNICATION

Synergistic cross-coupling catalysis: a trialkylphosphine/Pd catalyst tethered to MOF-808(Hf) is very effective for Suzuki–Miyaura coupling of problematic nucleophiles†

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Hafnium and zirconium forms of the benzene-1,3,5-tricarboxylate metal organic framework MOF-808 were prepared from aqueous solution and modified post-synthetically with 3-{(4-methoxy-phenyl)thio}propane-1-sulfonate (MPTPS) and 3-(di-*tert*-butylphosphino)propane-1-sulfonate (DTBPPS). Their ligands were stoichiometrically loaded with Pd²⁺. Pd@DTBPPS-MOF-808 is found to be a good catalyst for the Suzuki–Miyaura coupling of functionalised aryl boronic acid derivatives with aryl bromides and unactivated aryl chlorides and the MOF-808(Hf)-based catalysts show significant promise for some highly demanding cross-coupling combinations featuring electron deficient nucleophiles that suffer from poor transmetalation and significant protodeborylation. Remarkably, these led to strongly improved conversions over those based on MOF-808(Zr).

Palladium is widely used in heterogeneous cross-coupling catalysis, either as immobilised analogues of homogeneous catalytic complexes with popular ligands on high surface area solids or as supported nanoparticles.[1–15] Furthermore, there are a wide range of homogeneous Pd catalysts for Suzuki–Miyaura reactions to choose from for immobilisation[16–29] and some Pd-catalysed Suzuki–Miyaura cross-couplings are now routine. These include the use of most commercially-available aryl bromides, iodides or triflates when coupled with moderately functionalised arylboronic acids. For example, Suzuki reactions can be carried out over *ca.* 0.0025 mol% of Pd(OAc)₂ giving turnover frequencies that exceed 30 000 mol/mol catalyst/h, with the Pd readily removed after reaction.[16] While many supported Pd catalysts give TOFs far below this value, some give competitive activity: a Pd coordination complex supported on a lanthanum 2-aminoterephthalate metal organic framework (MOF) gives activity in the same range, for example.[14]

There is also a group of Suzuki–Miyaura reactions that are less routine but will work if specific catalysts and conditions are used. Examples include lightly-functionalised and non-activated aryl chlorides reacting with aryl boronic acids that are not prone to decomposition. The highly active MOF/Pd complex described in ref. 14 gives only very low yields for such substrates (*e.g.* chlorotoluene and phenylboronic acid), as does Pd(OAc)₂. In fact, reasonable scope for this type of substrate tends to require specific classes of homogeneous catalyst, with poor scope displayed by Pd nanoparticles.[2] Strongly electron-donating ligands with steric and coordinative properties that maximise the amount of mono-ligated Pd species are effective for Pd-catalysed Suzuki–Miyaura couplings of Ar–Cl, for example.[18–21,27]

Furthermore, the extensive study of the Suzuki–Miyaura reaction has revealed another group of reactions which generally fail, or for which good yields are only possible using very specific conditions that are far from ideal from an economic standpoint.[24–29] Here, we report a supported catalyst that, in addition to performing well for a substrate typically used for screening, shows promise for a class of very challenging Suzuki–Miyaura couplings that uses aryl boron nucleophiles that are known to undergo the transmetalation part of the cycle with difficulty and/or suffer from decomposition.

The implementation of immobilised organometallic catalysts faces various challenges.[30] The literature on supported cross-coupling catalysts is focussed on cross-couplings that are quite easy to accomplish with homogeneous catalysts, and so, generally, compares unfavourably with the best homogeneous examples. Nanoparticles are good catalysts for the easier Suzuki–Miyaura couplings, and readily form at the end of the reactions, making difficult recycling without leaching or gradual loss of performance. However, there is no inherent

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reason why heterogenised catalysts cannot offer enhanced reactivity, even relative to a state-of-the-art homogeneous catalyst, if the support can act synergistically. Such catalysts might circumvent limitations in the substrate scope of important reactions. In our design of heterogenised molecular catalysts we consider the support material should be robust and sufficiently porous to limit mass transport limitations; tethering different catalyst ligands to the surface should be straightforward; and the support should have functionality that acts synergistically with the tethered coordination complex. Finally, the ligand that is tethered to the support should be either commercially available or easy to make.

MOFs offer great potential as such supports.[31,32] Among the enormous number of reported structures of this chemically diverse class of materials, many zirconium (and similar hafnium) carboxylate MOFs are chemically and thermally stable and highly porous.[33] Furthermore, some show the ability to coordinate anionic ligands at their metal-oxy cluster-based

nodes when these have coordination to carboxylate much lower than the maximum. Among such materials, the benzene-1,3,5-tricarboxylate MOF-808 (ref. 34–36) is one of the most promising for a range of applications. MOF-808 was first prepared solvothermally as the Zr-form, idealised chemical formula $Zr_6O_4(OH)_4(BTC)_2(HCOO)_6$ (BTC = benzene-1,3,5-tricarboxylate).[34] MOF-808 is highly porous, chemically stable and has been prepared in Hf as well as Zr form.[35] A hydrothermal route has also been developed for its synthesis.[36] Its metal cation-centred $Zr_6O_4(OH)_4$ clusters, which are the nodes of the MOF, are coordinated by only six carboxylate groups of BTC linkers compared to the maximum possible twelve, leaving six equatorial binding sites where additional terminal ligands complete the metal cations' coordination: this is achieved in the form synthesised in the presence of formic acid as a modulator by a mixture of formate and hydroxyl ions and water molecules. The defective nature of the clusters, which possess terminal OH and H_2O ligands when not fully coordinated by terminal ligands, imparts strong catalytic
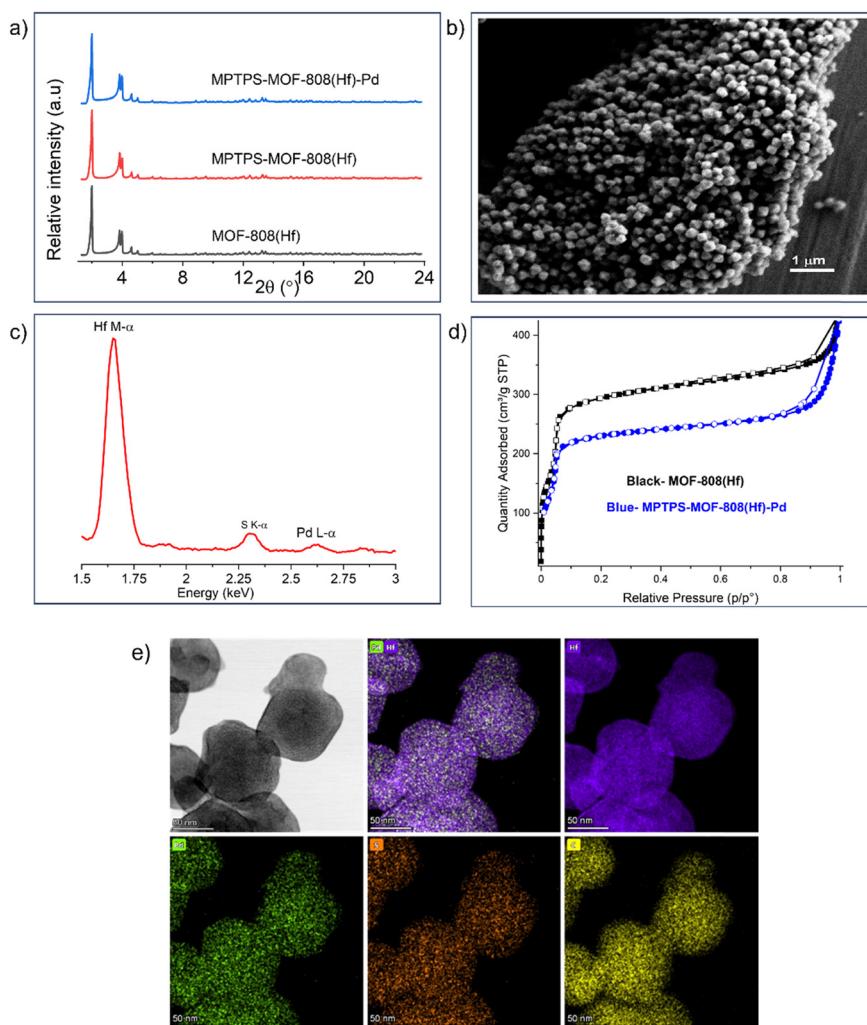

Fig. 1 a) XRD patterns of as-synthesised MOF–808(Hf), MPTPS-MOF-808(Hf) and MPTPS-MOF-808(Hf)-Pd, b) SEM of MPTPS-MOF-808(Hf)-Pd, c) EDX spectrum of MPTPS-MOF-808(Hf)-Pd, d) N_2 adsorption isotherms at 77 K of MOF-808(Hf) and MPTPS-MOF-808(Hf)-Pd and e) STEM of MPTPS-MOF-808(Hf)-Pd with associated elemental mapping.

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activity for acid catalysed reactions.[35,37] It has been found that formate groups on these sites can be substituted by a range of other anions, including those that can be used to support catalysts.[38]

Previously, we have shown that commercially-available sulfonated triarylphosphine ligands can replace formate groups bound to the MOF-808(Hf) clusters, generating a Lewis acidic phosphine@MOF to which rhodium or iridium complexes could be coordinated.[39] These were found to be efficient and recyclable bifunctional catalysts for the reductive amination of ketones and the hydroaminomethylation of alkenes. The hafnium form of MOF-808 was used rather than the more commonly described zirconium form because of its improved performance in reactions typically promoted by Lewis acid catalysts. Here we extend this catalyst design approach to Hf and Zr MOF-808 decorated with sulfonated thioether and trialkylphosphine ligands and subsequently complexed with Pd(II).

A thioether ligand was chosen since they have been used in Pd catalysis[40,41] and are easy to make in one step from readily available precursors. The sulfonated trialkylphosphine, di-*tert*-butyl-(3-sulfonatepropyl)phosphine[22,23] was chosen since this ligand is commercially available, and bulky electron-donating alkyl phosphines are of particularly importance in Pd catalysis. This ligand, whilst bulky at the Pd centre, is smaller than, for example, biaryl-dicyclohexylphosphines. Among the different bifunctional MOFs prepared, some were found to be capable of excellent performance in very challenging C–C bond forming reactions.

MOF-808 was prepared in both Zr and Hf form by adapting the hydrothermal method of synthesis used by Liu *et al.*[36] because hydrothermal synthesis routes are strongly favoured over those that use harmful solvents such as dimethylformamide. Details on the MOF-808 materials are given in the ESI,† Fig. S1–S3. The samples were composed of monodisperse nanocrystals with octahedral morphology, *ca.* 100 nm in dimension and single phase by X-ray powder diffraction (see Fig. 1 for Hf-example), with pore volumes (estimated from N_2 adsorption as described in the ESI†) of: MOF-808(Hf), 0.49 cm^3 g^{-1} and MOF-808(Zr), 0.78 cm^3 g^{-1}. These are reasonably close to values derived from literature data (MOF-808(Hf) 0.54 cm^3 g^{-1}; MOF-808(Zr), 0.80 cm^3 g^{-1} (ref. 34 and 39)). The difference in the specific pore volumes between Hf and Zr materials reflects the higher atomic weight of Hf than Zr. ^1H NMR of samples digested in K_3PO_4/H_2O according to a literature method[36] shows a formate-proton : BTC-proton ratio of 4 : 6, which indicated an idealised chemical formula, based on a single Zr_6- or Hf_6-cluster, of $M_6O_4(OH)_6(H_2O)_2(O_2CH)_4BTC_{6/3}$, M = Zr, Hf. Weight loss measurements during thermogravimetric analysis support this (ESI†).

MOF-808 was modified post-synthetically by anion exchange with the sulfonates, 3-{(4-methoxy-phenyl)thio}propane-1-sulfonate (MPTPS) (using the sodium salt) and 3-(di-*tert*-butylphosphino)propane-1-sulfonate acid (DTBPPS) (using the acid). An average of one ligand in four Hf_6 clusters

was added. The bulkier DTBPPS required an excess of reagent in order to achieve sufficient levels of incorporation. Full details are given in the ESI,† including ^1H NMR spectra of the digested MOFs used to quantify the ligand incorporation (Fig. S4, S5 and S11†). An example of the cluster formula of the post-synthetically modified MPTPS-MOF-808 (idealised for OH and H_2O to account for charge balance) is $Hf_6O_4(OH)_6(O_2CH)_{3.75}(H_2O)_2(BTC)_{6/3}(MPTPS)_{0.25}$.

The ligand-functionalised MOF-808 materials were loaded with Pd(II) using $Pd(OAc)_2$ in dichloromethane. A 1 : 1 Pd : ligand ratio was targeted (Scheme 1). The MOF-808 became orange during loading and ^1H NMR of the solvent after filtering the MOF detected no $Pd(OAc)_2$ (^1H NMR detection limit ≈1 mg of $Pd(OAc)_2$ from a typical reaction utilising 100 mg of $Pd(OAc)_2$).

Details on post-synthetically modified MOF-808(Hf) and MOF-808(Zr) are available in the ESI,† Fig. S4–S17 and Tables S1 and S2, with selected data shown in Fig. 1 for MOF-808(Hf). Scanning Transmission Electron Microscopy (STEM) combined with elemental EDX mapping was performed on both the MPTPS-MOF-808(Hf)-Pd and DTBPPS-MOF-808(Hf)-Pd catalysts. STEM-EDS results on the Pd-phosphine-MOF-808(Hf) are shown in Fig. 1 and for other samples in the ESI† (Fig. S8 and S12). In each case, these show that both the
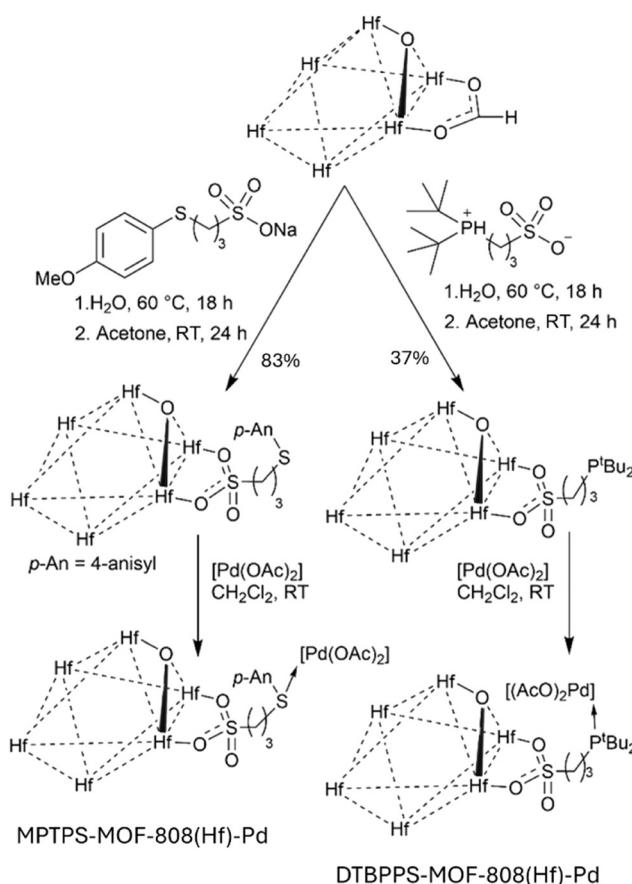
Scheme 1 Schematic representation of post-synthetic modification of MOF-808(Hf) to give catalysts. Stoichiometric metalation was performed and zirconium analogues were prepared similarly.

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tethered ligand (*via* S and P) and the coordinated Pd are distributed evenly throughout the small crystals. If these were strongly concentrated on the surface, rims of higher concentrations would be apparent. The conditions used for coordination are unlikely to reduce Pd(II) to Pd metal, but the STEM images rule out the presence of supported nanoparticles in these as-prepared materials. In the ESI,† we describe how we have decomposed the thioether-MPTPS-MOF-808(Hf)-Pd to reduce the Pd in a test alkene isomerisation reaction (section 3.1, Tables S3 and S4, Fig. S17†). STEM images of partially decomposed MPTPS-MOF-808(Hf)-Pd show the Pd nanoparticles that form in that case, even though the MOF-808 remains crystalline and microporous.

The ligand-modified and Pd-loaded MOF-808 materials were also examined by X-ray photoelectron spectroscopy (XPS). XPS is expected to give compositional information from within a few nm of the surface of the 100 nm nanoparticles. Full details and discussion of the method and results of XPS on the MPTPS-MOF-808-Pd and DTBPPS-MOF-808-Pd materials are given in the ESI† (Fig. S14–S17 and

Tables S1 and S2). The presence of the expected elements is confirmed for all four MOFs and although semi-quantitative, the Pd:Zr and Pd:Hf ratios are similar to those expected from the syntheses (1:24), and indicate there is little if any surface enrichment of the Pd. It is possible to pick out both thioether (163.6 eV) and sulfonate (168.4 eV) environments of S atoms, and Pd(II) in the spectrum of MPTPS-MOF-808(Hf)-Pd, while analysis of DTBPPS-MOF-808(Hf)-Pd shows the expected P(III) ligand (132.3 eV) bound to a Pd(II) metal centre (337.3–337.6 eV).[42–47]

Before examining challenging Suzuki-couplings, the reactivity of the catalysts was assessed. After a brief solvent and base screen (see ESI,† Table S5), IPA/water as solvent and sodium or potassium bicarbonate were chosen as standard conditions. Initial experiments were carried out with the cheaper Zr-based catalysts since we did not anticipate an advantage for using the Hf-MOFs. The Zr-based catalysts with both thioether and phosphine ligand were subjected to a high-throughput screening methodology with a selection of substrate combinations considered relevant and/or challenging for the synthesis of pharmaceuticals. Whilst

Table 1 Screening of boronic acids or ester derivatives and aryl bromides using DTBPPS-MOF-808(Zr)-Pd as catalyst

Aryl bromides		1	2	3	4	5
(isoxazole-Br)	A	71	22	24	2	67
(furan-Br)	B	82	20	66	72	54
(indole-Br)	C	47	36	57	69	68
(pyrimidine-Br)	D	70	93	100	95	64
(benzamide-Br)	E	44	86	94	89	81
(cyanofluorophenyl-Br)	F	89	38	100	84	41

Aryl bromide (1 eq.), boronic acid/equivalent (1.2 eq.), DTBPPS-MOF-808(Zr)-Pd (1 mol% Pd), Na_2CO_3 (1.5 eq.) in 2-PrOH/H_2O (70:30, 1 mL) at 66 °C for 18 h. LCMS was used to estimate the conversions, such that Conv. = (product area%)/[product area% + starting aryl bromide area% + area% of by-products associated with aryl bromide].

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there were one or two reactions where the thioether MPTPS-MOF-808(Zr)-Pd catalyst gave slightly better conversions than the phosphine-bearing catalyst, in many examples the phosphine is either slightly preferable or significantly preferred. The summary of the screen for the DTBPPS-MOF-808(Zr)-Pd catalyst is shown in Table 1, with that for MPTPS-MOF-808(Zr)-Pd results archived in the ESI,† Table S6.

Most studies using supported catalysts use the cheapest lightly functionalised aryl halide and aryl boronic acids, with a notable exception being ref. 9. Some of the reactions feature problematic nucleophiles. The successful coupling of 1*H*-benzimidazol-4-ylboronic acid **2** with 5-bromo-pyrimidine **D** and *N*-methyl-4-bromobenzamide **E** using just 1.2 equivalents of boronic acid is interesting since it is known that heterocycles with free NH groups, especially those that are relative acidic, can lead to the formation of dimeric heterocycle-bridged catalyst resting states.[48] Indeed, one previous report on the use of MOF-Pd nanoparticles describes benzimidazoles as catalyst poisons.[9] It is then reasonable to hypothesise that the formation of these dimeric Pd complexes with bridging heterocycles would not occur to a great extent on a coordination complex that is located within the pores of a MOF, and therefore MOFs could hold some advantage for such substrates. Good conversion for a range of more densely functionalised cross-coupling partners even without optimisation shows significant utility for this catalyst. One example of a reaction from the screen that contains functionality in both coupling partners is shown in Scheme 2. After the screen, this was carried out at both 1 mmol and 20 mmol scale. Repeating the 20 mmol scale reaction but recycling the filtered off MOF was attempted for one recycle (and no further) and gave almost identical results. This shows that the catalyst and conditions should be reasonably applicable to more functionalised substrates, and that the yields from the screening should transpose to laboratory scale synthesis.

A model reaction of Pd-catalysed cross-coupling between 3,5-bis-(trifluoromethyl)bromo-benzene and phenylboronic acid recycles 5 times with the trialkylphosphine/Hf-based Pd

Scheme 2 Suzuki–Miyaura coupling of two functionalised substrates (note reaction (i) was conducted at an oil bath temperature of 66 °C, reactions (ii) and (iii) at 70 °C). Identifying letters and numbers refer to those of Table 1. For reaction (i) the isolated yield of purified product is given, for reactions (ii) and (iii) the conversion to product measured by LCMS is given.

catalysts, with the result archived in the ESI,† section 3.2, Table S8. These experiments establish that the catalyst must be reasonably long-lived and hence should not be difficult to use. The thioether/Hf catalyst was less effective. These experiments were not designed to assess long term recyclability, which, if it can be done at all, would need a good engineering solution, rather than filtering off what are likely to be very sensitive activated catalysts. The ability to extend the use of a catalyst will be dependent on the substrate, conditions and the type of engineering approach used (*e.g.* continuous flow). Our current project searched for genuinely unusual reactivity that is of value regardless of how readily it could be recycled.

Evidence that the reaction takes place on a molecular complex bound to the MOF, rather than nanoparticles, was obtained by comparing the reactivity of three catalysts with an aryl chloride substrate (Table 2). As has been noted in a recent review,[2] nanoparticle-based catalysts generally give very low yields for any aryl chloride that does not have a strong activating group like an acetyl, nitro, formyl or trifluoromethyl. Coupling of phenylboronic acid and chlorobenzene is sometimes reported, but since both homocouple to give biphenyl, the cross-coupling yield cannot be determined unambiguously. There is only one example[4] of a deactivated aryl chloride coupling in high yield from all of the examples of nanoparticle-catalysed cross-couplings in ref. 4–12. These couplings also fail with homogeneous catalysts that are derived from modest donor ligands like thioethers or triarylphosphines. Pd catalysts derived from trialkylphosphine ligands are expected to catalyse such reactions, however.

The key comparisons are that the thioether-based MOF/Pd catalyst shows no conversion in the methylphenylboronic acid/chlorobenzene reaction (Table 2, entry 1) and neither does a sample of the same MOF that contains a significant amount of Pd nanoparticles (Table 2, entry 2). Details of this aging process and the STEM image showing the nanoparticles of this MOF are in the ESI.† It should also be noted that Pd nanoparticles supported on MOF-808(Zr) have recently been reported as catalysts by others for Suzuki–Miyaura couplings of aryl iodides and bromides. Aryl chlorides gave traces of the biaryl product (excepting PhCl + PhB(OH)$_2$, which gave 21% yield, expected primarily to be from reactant homocoupling).[12]

By contrast with the nanoparticle-containing MOF or the thioether/MOF/Pd system, DTBPPS-MOF-808(Zr)-Pd catalyst gives significant conversion (Table 2, entry 3). Surprisingly, DTBPPS-MOF-808(Hf)-Pd was even more effective (Table 2, compare entries 3 and 4, also 6 and 7). The conclusion that can be drawn from this is that DTBPPS-MOF-808(Hf)-Pd is a coordination complex during these catalytic reactions. We are aware of another MOF-supported coordination complex being reported to operate on one example of an unactivated aryl chloride cross-coupling, but Suzuki–Miyaura coupling of unactivated aryl chlorides, even using relatively reactive aryl boronic acids, is rarely achieved with heterogeneous catalysts.[1–4,13]

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Table 2 Suzuki–Miyaura coupling reactions between selected aryl chlorides and boronic acids using Pd–MOF-808 catalyst

Entry[a]	R in ArB(OH)$_2$ [compound no.]	Ar–Cl G or H	Product	Solvent	Temp. (°C)	MOF catalyst	% yield[b] product
1	R = Me, [6]	G	6-G	IPA/H$_2$O (70/30)	66	MPTPS-MOF-808(Zr)-Pd	0
2	R = Me, [6]	G	6-G	IPA/H$_2$O (70/30)	66	MPTPS-MOF-808(**Hf**)-Pd Containing Pd nanoparticles[c]	0
3	R = Me, [6]	G	6-G	IPA/H$_2$O (70/30)	66	DTBPPS-MOF-808(Zr)-Pd	48
4	R = Me, [6]	G	6-G	IPA/H$_2$O (70/30)	66	DTBPPS-MOF-808(**Hf**)-Pd	75
5	R = H, [7]	H	7-H	DMF/MeOH (95/5)	100	MPTPS-MOF-808(**Hf**)-Pd	0
6	R = H, [7]	H	7-H	DMF/MeOH (95/5)	100	DTBPPS-MOF-808(Zr)-Pd	33
7	R = H, [7]	H	7-H	DMF/MeOH (95/5)	100	DTBPPS-MOF-808(**Hf**)-Pd	85
8	R = OMe, [8]	G	8-G	DMF/MeOH (95/5)	100	DTBPPS-MOF-808(**Hf**)-Pd	99

[a] Aryl chloride (1 mmol), boronic acid (1.5 mmol), L-MOF-808(Hf)-Pd (1 mol% Pd) and base (1.5 eq.) in solvent (5 mL) for 16 h. [b] Yield is isolated yield of purified compounds. [c] See ESI† for synthesis and characterisation of MPTPS-MOF-808(Hf) supported Pd nanoparticles.

Table 3 Suzuki–Miyaura cross-coupling of 3-nitrophenylboronic acid **9** or 3-(*N*,*N*-dimethylamino)phenylboronic acid **10** with 2-bromo-6-fluorobenzonitrile **F**, using Pd–MOF-808 catalysts

Entry	Catalyst	R group	Yield (%)
1[a,b]	MPTPS-MOF-808(Zr)-Pd	NO$_2$	55
2[a,b]	DTBPPS-MOF-808(Zr)-Pd	NO$_2$	37
3[c]	MPTPS-MOF-808(Zr)-Pd	NO$_2$	32
4[c]	DTBPPS-MOF-808(Zr)-Pd	NO$_2$	27
5[c]	DTBPPS-MOF-808(Hf)-Pd	NO$_2$	76
6[b]	MPTPS-MOF-808(Zr)-Pd	NMe$_2$	95
7[b]	DTBPPS-MOF-808(Zr)-Pd	NMe$_2$	96
8[b]	DTBPPS-MOF-808(Hf)-Pd	NMe$_2$	97

[2-Bromo-6-fluorobenzonitrile **F** (1 eq.), boronic acid **9** or **10** (1.2 eq.), L-MOF-808(Hf/Zr)-Pd catalyst (1 mol% Pd), Na$_2$CO$_3$ (1.5 eq.) in 2-PrOH/H$_2$O (70:30, 5 mL) at 66 °C for 18 h]. [a] LCMS was used to estimate the conversions for this reaction as described in ESI.† [b] % isolated product after chromatographic purification. [c] 1.5 eq. of 3-nitrophenylboronic acid **9** was used.

Knowing that aryl boronic acids with electron-withdrawing substituents can be either more difficult or very challenging indeed in the coupling reaction,[24–29] we considered a comparison of catalysts for two sterically similar but electronically different aryl boronic acids would be of particular interest. The comparison of thioether-Pd/Zr and, trialkylphosphine-Pd/Zr in the coupling of nitro-phenylboronic acid or dimethylamino-phenylboronic acid (Table 3) show that the latter undergoes cross-coupling very readily whichever catalyst is used (Table 3 entries 6–8) while under the same conditions, the nitro-phenylboronic acid generally only gives low to moderate yields. Notably, there was a significant uplift in yield if the framework metal is changed from Zr to Hf, as in DTBPPS-MOF-808(Hf), Table 3 entry 5. We have previously studied MOF-808-Hf in a variety of reactions and the Hf form tends to exhibit better

performance than the Zr form in Lewis acid-catalysed reactions.[39] Certainly hafnium(ɪv) salts have previously been used as effective Lewis acids in homogeneous catalysis.[49] However, Lewis acids are not generally used in Suzuki–Miyaura coupling and it should also be noted that MOF-808(Hf) prepared hydrothermally has been shown to show a higher ratio of Brønsted : Lewis acid sites than MOF-808(Hf) prepared solvothermally.[50] We therefore investigated whether this remarkable effect is observed for any other related Suzuki–Miyaura coupling reactions over our catalyst.

Even for the relatively limited selection of substrates shown in Table 4, the Hf-derived MOF is observed to be much more active than the Zr-derived one. 2,6-Difluorophenyl boronic acid **11** has been estimated to transmetalate more than 150 times more slowly than phenyl boronic acid **7** (ref. 27) whilst undergoing proto-deboronation much faster.

Table 4 Suzuki–Miyaura coupling reactions using low reactivity boronic acid/esters: comparison of DTBPPS-MOF-808(Zr)-Pd and DTBPPS-MOF-808(Hf)-Pd

Entry[a]	ArB(OH)₂ [compound no.]	Ar–Cl [F, G or I]	Product	Temp. (°C)	MOF catalyst	Yield[b] (%)
1	**11**	Ph-Cl **G**	**11-G**	60	DTBPPS-MOF-808(Zr)-Pd	35
2	**11**	Ph-Cl **G**	**11-G**	60	DTBPPS-MOF-808(**Hf**)-Pd	94
3	**4**	Ph-Cl **G**	**4-G**	80	DTBPPS-MOF-808(Zr)-Pd	11
4	**4**	Ph-Cl **G**	**4-G**	80	DTBPPS-MOF-808(**Hf**)-Pd	81
5	**4**	**I**	**4-I**	80	DTBPPS-MOF-808(Zr)-Pd	70
6	**4**	**I**	**4-I**	80	DTBPPS-MOF-808(**Hf**)-Pd	97
7	**5**	**F**	**5-F**	80	DTBPPS-MOF-808(Zr)-Pd	30
8	**5**	**F**	**5-F**	80	DTBPPS-MOF-808(**Hf**)-Pd	98
9	**5**	Ph-Cl **G**	**5-G**	80	DTBPPS-MOF-808(Zr)-Pd	53
10	**5**	**G**	**5-G**	80	DTBPPS-MOF-808(**Hf**)-Pd	97
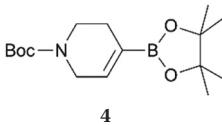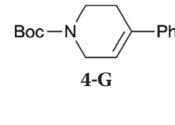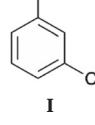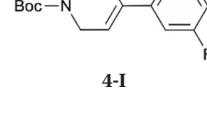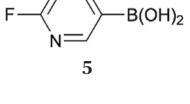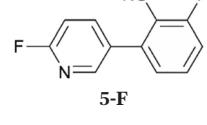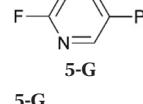
[a] Aryl halide (1 mmol), boronic acid or ester (1.2 mmol), L-MOF-808(Hf/Zr)-Pd (1 mol% Pd) and sodium carbonate (1.5 eq.) in 2-propanol/water (70 : 30, 5 mL) for 18 h at 80 °C. [b] Yield is isolated yield of purified compounds.

This leads to significant issues with most catalysts; the main solution available with aryl halides is to use special pre-catalysts of the Buchwald-type ligands at 2 mol% Pd loading. These pre-catalysts have been designed for use at low temperatures to limit degradation, although 1.5 equivalents of boronic acid are still required.[27] The coupling of chlorobenzene using just 1.2 equivalents of 2,6-difluorophenyl boronic acid 11 (Table 4, entries 1 and 2) can therefore be described as a very significant challenge and the formation of 94% product is therefore encouraging.

Boronic pinacol esters are known to be less reactive in transmetalation than most other boron nucleophiles.[51,52] Stability to protodeboronation of pinacol esters of boron is generally relatively good relative to boronic acids, but they are used in alkenylboron derivatives since these compounds are associated with a greater tendency to undergo protodeboronation and others side reactions.[52] Once again the same consistent improvement in performance was observed for two aryl chlorides if the Hf-containing MOF, DTBPPS-MOF-808(Hf), was used relative to the Zr one.

The fluorinated pyridyl boronic acid has all the characteristics which tend to be problematic, since both the heterocycle and the fluoro-substituent are electron-withdrawing. Even unsubstituted 3-pyridyl boronic acid is known to be moderately unstable due to issues with protodeboronation.[28] Again, DTBPPS-MOF-808(Hf) gives improved results relative to DTBPPS-MOF-808(Zr). The yields observed with DTBPPS-MOF-808(Hf) are high despite the fact only a very modest excess of aryl boronic acid is used.

Given the importance of extending the scope of this important reaction, homogeneous catalysis studies continue to be devoted to this challenge. The literature reveals how challenging arylboronic acids have successfully been used with aryl diazonium salt substrates, but these more expensive and rarely commercially available electrophilic partners will not be the ideal choice for many synthetic chemists. No base is needed since the N_2 leaving group is non-coordinating and transmetalation can proceed without base.[29] This implies that if a halide can be extracted from the Pd(L)ArX intermediate, transmetalation occurs more readily. Recently, a paper appeared that utilised this concept successfully by using the combination of two homogeneous catalysts, a trimeric zinc coordination complex as a Lewis acid, and a dialkyl-arylphosphine Pd complex.[26,53] The zinc complex (ca. 80%) was combined with 2 to 5 mol% of Pd catalyst and no base was needed.[26] Whilst these conditions, particularly the amount of the Lewis acid, will not be suitable for some synthetic chemists, mechanistic investigations established that the Lewis acid plays a role in controlling the removal of halide ions from the Pd centre and hence to facilitate transmetalation. Exact proof of the role of Hf within the insoluble MOF would be a challenge experimentally, due to its heterogeneous nature and the sensitivity of the intermediates. Computationally predicting the reactivity (or even 3D environment) for each possible location of the ligated Pd centres would be a formidable task. Nevertheless,

halide extraction by Lewis acids that promotes transmetalation does operate in homogeneous catalysis and seems plausible here. Brønsted acidic and H-bond donor sites could also assist halide abstraction to some degree. Alternatively, or additionally, it is possible that either Lewis acidic sites or Brønsted acidic sites could bind the base activator. The exact impact of this is not known but could change the concentration of base activator in the local environment near the Pd centre.

The superior performance of DTBPPS-MOF-808(Hf)-Pd over DTBPPS-MOF-808(Zr)-Pd is surprising and can be of significant utility to synthetic chemists for specific Suzuki reactions. It can also be of significance from the point of view of catalyst design, because it is straightforward to prepare MOF-808 and convert it into a variety of supported catalysts. In this way Lewis acids and molecular complexes are readily introduced into catalytic reactions in a way that should limit incompatibility between catalysts.

Application of these MOFs to develop a broad-scope Suzuki–Miyaura protocol is outside the scope of our project; it is hoped the preliminary observations shown here will provoke other related studies. In addition to the specific observations from catalysis studies reported here, it is worth noting that we have very easily extended the post-synthetic modification of MOF-808 to sulfonated ligands that could be used by others in a wide range of metal catalysed bifunctional catalytic cycles. This establishes the PSM ligand exchange approach we have been developing as of significant utility for making new catalysts. The observations of a Hf super-charging effect on the Suzuki–Miyaura reactions catalysed by DTBPPS-MOF-808(Hf)-Pd can therefore be useful as a design concept in catalysis.

Data availability

Author contributions

Soneni Ndlovu: investigation, data analysis, writing – original draft and editing. Charlotte A. Lane: investigation and data analysis (alkene isomerisation). Aaron B. Naden: investigation (STEM), writing – original draft; Federico Grillo: investigation (XPS), writing – original draft. Irene Giménez-Nueno: supervision, writing – original draft and editing. Matthew L. Clarke: conceptualisation, supervision, data analysis, writing – original and revised drafts and editing, funding acquisition; Paul A. Wright: conceptualization, supervision, data analysis, writing – original draft and editing, funding acquisition.

Conflicts of interest

There are no conflicts of interest to declare.

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