Polyoxometalate-Based N-Heterocyclic Carbene (NHC) Complexes for Palladium-Mediated C–C Coupling and Chloroaryl Dehalogenation Catalysis


Molecular hybrids are of particular interest in catalysis, due to the interplay of joint organic–inorganic domains with very diverse functional environments. The hybrid strategy is expected to allow for fine-tuning of the stereo-electronic properties of the catalyst through a tailored choice of the interacting organic–inorganic moieties. Such a hybrid upgrade of the catalytic system can be readily accessed, through the covalent functionalization of molecular polyoxometalates (POMs).[1] Indeed, covalent POM hybrids are characterized by discrete, nanosized, multi-metal oxides as polyanionic scaffolds, which allow for anchoring on-surface organic pendants, including chiral residues.[1,2] The hybrid structures display a remarkable stability, and resist harsh catalytic conditions, enabling a multi-turnover performance and sequential recycling in ionic-liquid media exposed to MW irradiation.[3] Interestingly, the hybrid modification of the POM framework has been successfully used to expand the coordination potential by introduction of tailored organic domains. In this respect, polydentate salen-type or thiol/phosphine-terminated ligands have been immobilized on the POM surface to bind Mn, Pd or Rh ions, or to implement the stabilization of Pd0 colloids.[4–6] We present herein the synthesis, characterization, and catalytic applications of new POM-appended N-heterocyclic carbene (NHC) palladium complexes and their remarkable performance in catalyzing C–C cross-coupling and aromatic dehalogenation reactions.[7] To this end, imidazolium moieties have been successfully grafted on the defect site of the divacant Keggin polyanion [$\gamma$-SiW$_{10}$O$_{36}$]$^{8-}$. These organic domains are useful precursors of N-heterocyclic (NHC) carbenes, which are known to provide strong M–NHC bonds, thus imparting high thermal robustness and stability to organometallic intermediates in multi-turnover palladium catalysis.[9]

In addition to the specifically designed Pd binding site, such POM-based hybrids display an extended polyanionic surface. This setup is expected to contribute sterically and by virtue of electrostatic repulsions to prevent agglomeration of incipient Pd$_2^+$, which generally deteriorates the turnover efficiency of the system.[6c] The molecular nature of such composite structures is a further point of interest, offering a single-site model for extended materials. Specifically, the molecularly defined structure of the hybrid allows for selective tailoring of the active site as well as for detecting subtle changes by solution characterization techniques, including heteronuclear NMR spectroscopy and ESI-MS.

The synthetic route to Keggin-type hybrids involves the reaction of organosilane reagents with the nucleophilic oxygen atoms that border a defect site on the POM surface. Grafting strategies have been optimized in acetonitrile in which the presence of excess $n$Bu$_4$NBr promotes the solubilization of the POM by counterion metathesis (Scheme 1). Under these conditions, decoration of the lacunary POM is known to yield hybrids with two surface-anchored organosilyl (RSi-) groups, each one linked to two oxygen atoms of two edge-shared WO$_6$ octahedra.[4,10]

A first attempt focused on a divergent approach, including the covalent attachment of the triethoxysilyl-functionalized 4,5-dihydro-imidazolium bromide (1) to the divacant decatungstosilicate. The hybrid POM (2) was isolated and displayed spectroscopic data (1H, 13C, 29Si and 183W NMR, FT-IR) that are in agreement with the expected bis-functionalized structure. However, palladation of 2 met with little success (Scheme 1). Neither direct metatation using Pd(OAc)$_2$ nor transmetalation using Ag$_2$O resulted in the
formation of the desired palladium NHC complex. Similarly, base-mediated palladation with [PdCl2(CH2CN)2] in the presence of potassium bis(trimethylsilyl)amide (KHMDs) or NaH failed, as evidenced by the persistence of the 1H NMR resonance of the C2-bound protons on the dihydroimidazolium ring (δH = 8.1 ppm). Analysis of the reaction by UV/Vis spectrophotomeric titration suggests a possible electrostatic association of Pd2+ ions to the anionic POM surface. To avoid such complications, we concentrated on a convergent approach involving the immobilization of preformed palladium complexes on the POM. Hence, the trialkoxysilyl-tagged imidazolium precursor 3, containing an unsaturated heterocycle and a less hindered n-butyl substituent at the nitrogen atom, was synthesized under strictly anhydrous conditions, from (3-chloropropyl) triethoxysilane and 1-butylimidazole. Reaction of 3 with Ag2O followed by transmetallation with [PdCl2(CH2CN)2](CH3CN)2 afforded the Pd–biscarbene complex 4, as confirmed by ESI-MS, 1H and 13C NMR analyses. The absence of a resonance due to the C2-bound imidazolium proton (δH = 10.3 ppm) is corroborated by the appearance of a new signal at δC = 170.6 ppm, which is characteristic of a palladium-bound carbene carbon (see the Supporting Information, Figures S16 and S15). ESI-MS (positive mode) shows signals centered at m/z = 799.3 and 843.3, corresponding to the monochloride and monobromide cationic fragments ([C10H17N2Si(OEt)2]2PdCl)+ and ([C10H17N2Si(OEt)2]2PdBr)+, respectively (Supporting Information, Figure S17). Complex 4 was finally reacted with the divacant Keggin POM [γ-SiW10O36]8– in acetonitrile under phase transfer conditions (Scheme 1), leading to the functionalized hybrid 5 in 75% yield.

Complex 5 was characterized both in the solid state (by FT-IR spectroscopy and elemental analysis) and in solution (1H, 13C, 29Si and 183W NMR spectroscopy and ESI-MS). All spectroscopic results confirmed the proposed structure (Supporting Information, Figures S18–S23). The 183W NMR spectrum shows three resonances at −107.4, −135.8, and −142.1 ppm in 2:1:2 ratio, in agreement with the expected C3v symmetry. The 29Si NMR spectrum reveals two signals at −62.8 and −88.4 ppm with integration ratio 2:1. These results are consistent with a double substitution of the POM surface. Coordination of Pd2+ has been confirmed by X-ray photoelectron spectroscopy (XPS) of a solid sample of 5, for which the expected Pd 3d 5/2 peaks centered at 338 and 343 eV in binding energy were observed (Supporting Information, Figures S24–S26). The DFT optimized structure of 5 suggests a planar distorted coordination for Pd, with trans halide ligands and bond lengths around 2.07–2.11 (Pd–C) and 2.59 Å (Pd–Br) (Scheme 2).

Complex 5 has been tested in the palladium-catalyzed cross-coupling of aryl halides with phenylboronic acids, according to established Suzuki–Miyaura protocols (Scheme 2, path a). This reaction represents one of the key tools for selective C–C bond formation. The performance of catalyst 5 in this chemistry has been screened in 1:1 DMF/H2O mixtures and under microwave (MW)-induced dielectric heating (Table 1). This method is particularly efficient for polycharged catalysts, which behave as MW-activated molecular heat-carriers. Indeed, hybrid POMs, are known to display a remarkable thermal stability and high catalytic efficiency in MW-assisted processes.

The cross-coupling catalytic activity of 5 was initially evaluated using a representative range of aryl halides as substrates and MW irradiation at 10 W for 10–30 min (Table 1).

Under these conditions, both activated and deactivated aryl iodides react smoothly with 0.05 mol% catalyst loading, leading to the corresponding substituted biphenyl products with up to 99% yield, 1980 turnover numbers (TON), and frequencies (TOF) up to 11 880 h−1 (entries 1–4, Table 1, comparison with literature benchmarks in Tables S1 and S2 in the Supporting Information). In all reactions, the bulk temperature is kept at about 80°C by simultaneous cooling.
A C H T U N G T R E N N U N G

ylboronic acid, PhB(OH)$_2$ (1.1 equiv, 0.275 mmol), Na$_2$CO$_3$ (2 equiv, 0.5 mmol), DMF:H$_2$O = 1:1 (0.45:0.45 mL); MW irradiation: 10 W, compressed air at 30–40 psi; $T_{bulk}$=75–85°C.

Scheme 2. Cross-coupling (path a) and dehalogenation reactions (path b) catalyzed by 5 under MW irradiation. DFT optimized geometry is presented for the proposed structure of 5.

Table 1. Suzuki coupling catalyzed by 5 under MW-irradiation (Scheme 2, path a). In all reactions: aryl halide, ArX (0.25 mmol), phenylboronic acid, PhB(OH)$_2$ (1.1 equiv, 0.275 mmol), Na$_2$CO$_3$ (2 equiv, 0.75 mmol). DMF:H$_2$O = 1:1 (0.45:0.45 mL); MW irradiation: 10 W, compressed air at 30–40 psi; $T_{bulk}$=75–85°C.

<table>
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<th>Entry</th>
<th>X</th>
<th>R$_1$</th>
<th>$%$ loading</th>
<th>product</th>
<th>t (min)</th>
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<tr>
<td>1$^{[a]}$</td>
<td>I</td>
<td>-COCH$_3$</td>
<td>0.05</td>
<td>99</td>
<td>10</td>
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<tr>
<td>2</td>
<td>I</td>
<td>H</td>
<td>0.05</td>
<td>85</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>I</td>
<td>-CH$_3$</td>
<td>0.05</td>
<td>80$^{[i]}$</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>I</td>
<td>-OCH$_3$</td>
<td>0.05</td>
<td>95$^{[i]}$</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>Br</td>
<td>-COCH$_3$</td>
<td>0.1</td>
<td>99</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>Br</td>
<td>-NO$_2$</td>
<td>0.1</td>
<td>93$^{[i]}$</td>
<td>10</td>
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<td>7$^{[a]}$</td>
<td>Br</td>
<td>H</td>
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<td>87$^{[i]}$</td>
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<tr>
<td>14$^{[a]}$</td>
<td>Cl</td>
<td>-CH$_3$</td>
<td>1</td>
<td>33$^{[i]}$</td>
<td>60</td>
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</table>

[a] Under analogous conditions, the coupling reaction catalyzed by 4 proceeds with 32% yield. [b] ArX (0.25 mmol), PhB(OH)$_2$ (1.3 equiv, 0.32 mmol), Na$_2$CO$_3$ (3 equiv, 0.75 mmol). [c] Biphenyl (1–7%) and dehalogenation products observed in traces. [d] Biphenyl (4%) and acetophenone (14%) were detected. [e] Biphenyl (18%) was detected. [f] Biphenyl (9%) and toluene (6%) were detected.

with compressed air. Control experiments performed with iodobenzene and phenylboronic acid indicate no coupling products in the Pd-free reaction, nor in the presence of the imidazolium-functionalized POM 2. It is worth noting that the POM-free NHC complex 4 deactivates rapidly under analogous catalytic regime, thus yielding poor conversion and turnover efficiency (see note [a] in Table 1). Addition of Na$_2$CO$_3$ (2 or 3 equivalents) is an essential prerequisite of the catalytic protocol, in agreement with the generally accepted mechanism involving a reactive borate anion for the transmetallation step.[29] Coupling of aryl bromides is readily achieved by increasing the catalyst loading to 0.1 mol %, with similar yields and reaction time (yield up to 99%, TON = 990, TOF = 5940 h$^{-1}$, entry 5, Table 1). A remarkable 87% yield of 4-methylbiphenyl was obtained after 30 min irradiation when using the unactivated 4-bromotoluene as substrate (TOF = 1740 h$^{-1}$, entry 8, Table 1).[23]

The POM-based system was also effective in coupling aryl chlorides, which are known to be poorly reactive but synthetically highly appealing.[22,23] An increased catalyst loading (1.0 mol %), and a larger excess of phenylboronic acid and Na$_2$CO$_3$ (1.3 and 3 equivalents with respect to aryl chloride), were pivotal for ensuring reactivity. Under such conditions, 4-chloroacetophenone gave the corresponding coupling product in 98% yield when subjected to MW irradiation for 30 min (TON = 98, TOF = 196 h$^{-1}$, entry 9, Table 1).[24] ortho-Substituted 2-chloroacetophenone was converted only sluggishly, presumably due to sterics factors (entry 10, Table 1). The POM residue may be sufficiently bulky to hamper the oxidative addition and/or transmetallation step of the catalytic cycle.[25] Other activated aryl chlorides reacted with less success, as for 4-chloronitrobenzene, affording a significant amount (18%) of biphenyl originating from homo-coupling together with 38% of cross-coupled 4-nitro biphenyl (entry 12, Table 1). In this case, the selectivity of the process did not improve upon increasing the amount of base.[26]

Interestingly, the reaction of the unactivated 4-chlorotoluene turned out to yield 33% of the desired product, with concurrent homocoupling (< 9%) and dehalogenation to toluene (< 10%).[27] Catalytic dehalogenation was previously reported as a parallel reaction in Suzuki coupling; however, few papers provide details on this topic.[28] Such reaction is of major importance from an environmental point of view, in particular with regards to the degradation of highly toxic halogenated organic compounds.[29]

The proposed mechanism of palladium-catalyzed dehalogenation involves the oxidative addition of the aryl halide to the Pd$^{II}$-NHC intermediate, and the formation of a Pd$^{II}$-hydride species, generated by a strong base such as an alkoxide.[29,30] In line with this proposal, the dehalogenation reaction is strongly promoted upon changing the base from Na$_2$CO$_3$ to nBu$_4$NOH.[31] Under conditions that are otherwise identical to the Suzuki protocol, catalytic dehalogenation of aryl chlorides was readily accomplished (Scheme 2, path b). In the presence of nBu$_4$NOH as the base, 4-chloroacetophenone and phenyl boronic acid, dehalogenated acetophenone was formed as the major product (63% yield), together with 4-acetylbiphenyl in 35% yield. The competitive dehalogenation reaction has thus been investigated in
more detail. Highest selectivities were achieved when using two equivalents of nBu4NOH in DMF, under MW irradiation (Table 2). Under these conditions, a formate ion is sur-

Table 2. Dehalogenation of aryl chlorides (ArCl), catalyzed by 5 under MW-irradiation (Scheme 2, path b).

<table>
<thead>
<tr>
<th>Entry</th>
<th>ArCl</th>
<th>ArH Yield [%]</th>
<th>t [min]</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>4-chloroacetophenone &gt;99</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2-chloroacetophenone     57</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3-chloroacetophenone     86</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4-chloronitrobenzene &gt;99</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>4-chlorophenol           12</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4-chlorotoluene          43</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1-chloronaphthalene      87</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

[a] ArCl (0.25 mmol), nBu4NOH 30H2O (2 equiv, 0.5 mmol), 5 (1 mol%; 0.0025 mmol), DMF (0.5 mL); MW-irradiation: 10 W, compressed air at 30 psi; Tsub = 80–95°C. [b] After 3 cycles (2 × 30 min + 1 × 60 min).

Acknowledgements

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Keywords: carbenes · homogeneous catalysis · palladium · polyoxometalates

[14] UV/Vis spectrophotometric titration (λ < 450 nm), of 2 upon addi- tion of [Pd(OAc)2] in DMSO and incubation at 50°C for 4 h and at 100°C for 30 min indicates a 1:1 Pd2+/2 association stoichiometry.
Average TON and TOF values in the range 1100–1900 and 314–543 h\(^{-1}\), respectively, have been reported for classic NHC ligands employed in the homogeneous Suzuki coupling of deactivated aryl bromides: N. Marion, O. Navarro, J. Mei, E. D. Stevens, N. M. Scott, S. P. Nolan, *J. Am. Chem. Soc.* **2006**, *128*, 4101–4111.


Ligand 2 in combination with [Pd(Ac)\(_2\)] (1 equiv) was found to be inactive with chloroaryl substrates, thus confirming the superior performance of the POM-based NHC ligand in this chemistry.


FT-IR analysis of pre-catalyst 5 (5 mm in DMF) after incubation with nBu₄NOH·30H₂O (5 equiv) under microwave irradiation for 1 h and subsequent precipitation with water shows retention of the main spectral features associated to the POM scaffold, with bands at \(\tilde{\nu} = 946\) (w), 883 (s), 825 (w), 741 cm\(^{-1}\) (s), indicating that the POM support is stable under catalytically relevant reaction conditions.


Thermal and photoredox carbon–halogen bond cleavage by POM catalysts has been reported to proceed by radical mechanisms (D. Sattari, C. L. Hill, *J. Am. Chem. Soc.* **1993**, *115*, 4649–4657); under the condition explored, no reaction was observed with the Pd-free complex 2.
