Cooperativity between metal centers in homobimetallic Pd\textsuperscript{II}–NHC complexes: catalytic potential towards hydrodefluorination\textsuperscript{†}

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Among the several unsymmetrical bis-NHC derived distinct homo-bimetallic and mono-NHC supported Pd\textsuperscript{II} complexes studied here (1–5), the bimetallic complex 1 was noted to be the most effective catalyst for the challenging hydrodefluorination. The electron richness of the metal centers and the synergistic cooperation between the Pd\textsuperscript{II} centers (cooperativity index, \(z = 8.67\)) have been recognized to be the deciding factor for its better activity.

The term “cooperativity” fundamentally represents the augmented effect that is observed in multicOMPonent systems, typically unachievable through the mere summation of individual entities.\textsuperscript{1} Notably, numerous instances of cooperativity are observed in nature, such as the biological catalysts (enzymes), that are often regarded as quintessential, or the ultimate cooperative systems.\textsuperscript{2} These enzymes primarily rely on the collaboration of several multimetallic active sites to achieve exceptional activity and selectivity in executing intricate transformations.\textsuperscript{2,3} Throughout history, natural phenomena have served as primary sources of inspiration for various human discoveries and along this line, synthetic chemists have devised innovative methodologies to emulate these cooperative effects within the molecular systems.\textsuperscript{4} Consequently, the term “cooperativity” has become ubiquitous across various domains of chemistry, including supramolecular chemistry,\textsuperscript{5} molecular recognition,\textsuperscript{6} metal–ligand interactions,\textsuperscript{7} catalysis\textsuperscript{2,3,6,8} etc. Within the realm of cooperative catalysis, there has been considerable focus on exploring transition metal-based multimetallic catalytic systems over the past few decades.\textsuperscript{30,8} In this context, heterobimetallic catalysts, particularly those incorporating an N-heterocyclic carbene (NHC) ligand bridge, have emerged as a distinct class of catalysts, which have been extensively employed in one-pot tandem catalysis, wherein two different metals work cooperatively to enhance the overall activity compared to the equivalent catalyst systems generated from their homobimetallic or monometallic counterparts.\textsuperscript{9} However, the synthesis of these heterobimetallic complexes presents significant compatibility challenges, typically necessitating multiple synthetic steps.\textsuperscript{30–42} While heterobimetallic complexes exhibit competence in tandem reactions, we have recognized that homobimetallic complexes, which are comparatively easier to synthesize typically requiring a single step, may also possess considerable untapped potential for challenging single net transformations.

Considering the widespread usage of organofluorine compounds across various industries, including agrochemicals, paints, anticorrosive coatings, and the pharmaceutical sector, the investigation of not only C–F bond formation but also its selective activation (e.g. hydrodefluorination) has become a crucial area of study.\textsuperscript{10} However, the hydrodefluorination (HDF) process poses significant challenges due to its pronounced ionic character, leading to both thermodynamic stability as well as kinetic inertness.\textsuperscript{10a,11} While HDF has been well-explored for poly-fluorinated arenes, its application to low-fluorinated arenes and aliphatic C–F bonds remained limited.\textsuperscript{12} Additionally, efficient defluorination often necessitates high-temperature conditions along with a fluorine scavenger (e.g. hydrosilane, aluminium hydride, etc.), leading to significant inorganic waste generation.\textsuperscript{11} A more sustainable approach would be the use of H\textsubscript{2} gas (however, this poses significant safety risks)\textsuperscript{14} as a reductant or a greener alcohol, e.g. isopropyl alcohol, as a hydrogen source.\textsuperscript{15}

All the above discussions emphasize the need for advanced catalytic methods that are highly effective for the HDF of C–F bonds of low fluorinated arenes under mild conditions and thus, we wanted to explore the cooperative catalytic potential of homobimetallic systems in this particular transformation. In the past few years, we’ve developed various heteroditopic bis (NHC) ligand systems with different donors to synthesize distinct homo- and hetero-bimetallic complexes involving various transition metals and they have proven their catalytic...
merits in multiple one-pot tandem catalytic reactions, offering advantages over their equivalent systems derived e.g. from their mono-metallic counterparts. In particular, the Pd-based catalysts have shown promise in hydro-dehalogenation reactions and accordingly, herein, we disclose the very high activity of a di-Pd complex (1) in the challenging HDF of C–F bonds in fluororganic compounds that was achieved through bimetallic cooperativity, which has been studied systematically and established by the inferior activity of the analogous catalyst systems generated from the corresponding mono-metallic fragments (4 and 5).

At the outset, homobimetallic Pd complex (1) was synthesized from [L1–H]Br2 in a single step (Scheme 1). Its formation was confirmed through various analytical tools, including multinuclear NMR, ESI-MS, and elemental analysis. The precise molecular structure was verified through single-crystal XRD studies (Fig. S13, ESI†).

The complexes 2–4 were recently reported by us and the complex 5 was prepared using a modified literature procedure (Fig. 1). After synthesizing the di-Pd complexes 1–3, we evaluated their activity in the hydrodefluorination (HDF) of aryl fluorides, using fluorobenzene as a model substrate (Table 1). The best catalytic result was achieved with the precatalyst 1 (0.5 mol%), using NaO'Bu (1 equiv.) at 100 °C in 1-propanol (working both as a solvent and hydrogen source) for 12 h (96%, entry 1). Under the same conditions, catalyst 2 exhibited slightly lower activity (84%, entry 2), while a significant drop in the activity was observed for complex 3 (52%, entry 3). It is worth mentioning that there are only limited reports available for the HDF of fluoroarenes employing isopropyl alcohol under alkaline conditions. Subsequently, the catalytic performance of 1 was compared to a mixture of its corresponding mono-metallic equivalents 4 and 5 (Fig. 1) that effectively mimics the local coordination environment around the Pd-centric centers in complex 1 (entry 6). Intriguingly, this combination of 4 and 5 proved to be ineffective, exhibiting significantly reduced activity (only 22% product). These results conclusively illustrate the presence of a cooperative interaction between the two Pd centers linked via the NHC ligand in complex 1, thus enhancing its catalytic activity establishing it as a superior catalytic system compared to scenarios where discrete metal complexes are used (entries 1 vs. 6). Furthermore, other commercially available Pd-catalysts, e.g. [Pd(PPh3)4] and Pd/C (entries 9–10), reported for HDF reactions, were also tested and both of them were noted to be inefficient under our standard conditions.

Table 1 Hydrodefluorination of fluorobenzene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat.</th>
<th>Cat. (mol%)</th>
<th>Conv. (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0.5</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>0.5</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>0.5 + 0.5</td>
<td>22</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>—</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>[Pd(PPh3)4]</td>
<td>1</td>
<td>Trace</td>
</tr>
<tr>
<td>10</td>
<td>Pd/C</td>
<td>3</td>
<td>10</td>
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* Reaction conditions: C6H5F (0.1 mmol), NaO'Bu (0.1 mmol), catalyst (0.5–1 mol%), iPrOH. Without base. Conversions were determined by GC–MS using mesitylene as an internal standard.

A modest downfield shifts in the 13C NMR signals were noted in 2 from that of 1 (149.5 vs. 148.1/164.5 ppm). This could be understood from the fact that pyridine being a better donor than 3-Cl-Py results in a relatively weaker interaction between the PdII and CImNHC (1.935 Å in 1 vs. 1.983 Å in 2, Fig. S11, ESI†) justifying the slightly downfield shifted 13C PdII-CNHC signals in 2 as compared to 1. On the other hand, a stark difference in the catalytic activity was observed between 1 and 3, and the only difference between them is the presence of 1,2,4-triazole in 3 while imidazole in 1. To understand this activity difference between the catalysts, first of all, it is well-established that the activation of a C–X (X = halogen) bond by a Pd-catalyst typically entails oxidative addition and thus, an electron-rich metal center favors this process. Along this line, imidazolylidene (ImNHC, present in 1) is known to be a stronger σ-donor than 1,2,4-triazolylidene (1,2,4-TzNHC, present in 3). Hence, this difference confirms electron-rich traits to
the PdII-center in 1 than that of 3, which possibly yields significantly enhanced catalytic activity of 1. To understand these electronic differences, detailed analyses of both 13C NMR resonances (Fig. 2b) and theoretical calculations were then conducted. Firstly, a marginal difference in the chemical shift values of the 13C PdII–CNHC signals for the BzNHC between the complexes 1 and 3 was observed. However, a substantial disparity of 8.1 ppm was evident between the ImNHC and the 1,2,4-TzNHC moiety. Furthermore, the upfield shift in the 13C NMR resonances of a M–CNHC signal is known to be directly associated with the electron richness of the metal center. Therefore, the above differences in chemical shift values are in perfect agreement with the catalytic performance of our complexes 1–3 (Table 1).

To provide additional validation, we performed DFT calculations (ESP mapping) to estimate the total charge density for complexes 1 and 3 (Fig. 2a). Notably, there was no significant difference in the electron density around the PdII–BzNHC moiety in both the complexes (1 and 3). However, an obvious difference in electron density was detected around the PdII–CNHC signals for the BzNHC between the complexes 1 and 3. This disparity of 8.1 ppm was evident between the ImNHC and the 1,2,4-TzNHC moiety. Furthermore, the upfield shift in the 13C NMR resonances of a M–CNHC signal is known to be directly associated with the electron richness of the metal center. Therefore, the above differences in chemical shift values are in perfect agreement with the catalytic performance of our complexes 1–3 (Table 1).

Next, the substrate scope was explored and gratifyingly, the catalyst 1 exhibits remarkable activity in the HDF of diverse fluoroarenes with various functional groups, yielding good to excellent yields (Table 2). Electronic factors significantly influence the reactivity of aryl fluorides, e.g. the electron-deficient substrate, 3-fluoropyridine, achieved impressive 93% conversion in just 6 h (7a). Meanwhile, the presence of a phenyl group offered quantitative conversion in 24 h (7b). Substrates with more electron-rich groups like –OMe and –NH2 need extended reaction duration (7e–7g). These differences suggest that the rate-limiting step might be the oxidative addition of aryl fluoride, which correlates with the electron richness and hence, the activity (1 > 2 > 3) of our catalysts. Furthermore, steric hindrance also plays a role, with hindered substrates showing reduced activity (7f vs. 7g).

Although the heterocyclic substrate 7h exhibits reduced reactivity (only 29%), polyfluorinated substrates, consistently underwent HDF (7j–7m). Finally, as representative examples the products 7b and 7d were isolated in excellent yields (91–93%). Moreover,
the complex 1 was even found to be active at a lower loading of 0.1 mol%, with a moderate turnover number (TON) of 410 for the HDF of fluorobenzene. Inspired by the success with HDF of ary fluorides, we next explored a tandem reaction combining HDF with transfer hydrogenation (TH) (see ESI†). Earlier reported methods generally rely on heterobimetallic catalysts; however, our catalyst 1 exhibits decent activity in this reaction for a range of substrates (Table S1, ESI†).

Next, we investigated the efficacy of catalyst 1 in more challenging HDF of α,α,α-trifluorotoluenes, known for their inertness, and gratifyingly, it proved effective for various trifluorotoluenes (Table 3). While α,α,α-trifluorotoluene showed moderate yield under optimized conditions (11a), the catalyst performed exceptionally well with electron-deficient substrates. For example, HDF of 4-CF3-py provided a good yield of 63%, even with a lower catalyst and base loading (1 mol% and 2 equiv., respectively) in a shorter time of 24 h (11b). Furthermore, tandem HDF and TH of 4-CF3-Ph-CO-CH3 resulted in 58% yield of 11d along with 34% of the only HDF product (11d′) with total HDF of 92%. Next, HDF of 4-F-Ph-CF3 yielded two products (12% tolune and 82% 4-CF3-Ph) in just 12 h (7i, Table 2), revealing better activity of 1 towards aromatic C–F bonds. Under harsh conditions, the same trend was observed; however, slightly higher toluene formation was observed (11c and 11c′, Table 3) indicating that forging conditions are required to surge the extent of CF3 activation. For hexafluoro-m-xylene (11e and 11e′) and hexafluoro-p-xylene (11f and 11f′), selective HDF of only one trifluoromethyl group was detected, leaving the second group unaffected, regardless of the base and catalyst loading.

In summary, we have synthesized several homobimetallic PdII-NHC complexes (1–3) and among them, complex 1 was noted to be highly efficient for challenging HDF reactions exhibiting the highest activity, followed by 2 and 3, due to their differing electronic environments. Moreover, the activity of 1 surpasses that of its monometallic equivalents, attributed to cooperativity between the PdII-centers in complex 1. Intriguingly, the extent of electronic coupling between the metal centres in complexes 1–3, and accordingly, their activity is noted to be dependent on the nature of the bridging NHC donor. In essence, the present protocol involving easy synthesis, understanding of the electronic environment and cooperativity between the metal centers holds immense potential towards the development of future efficient catalyst systems.

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Conflicts of interest
There are no conflicts to declare.

Notes and references