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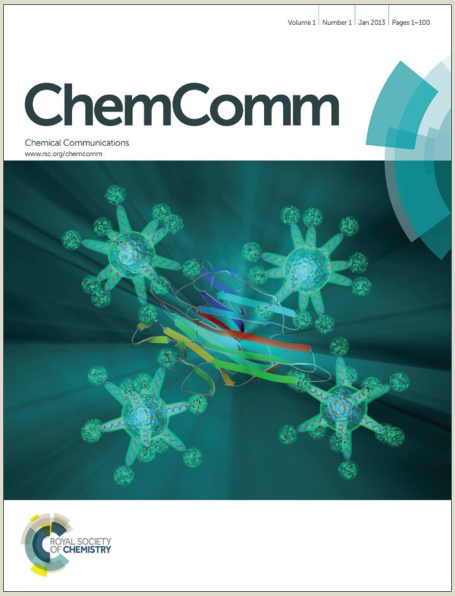

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ARTICLE TYPE

Tailor-made N-Heterocyclic Carbenes for Nanoparticle Stabilization

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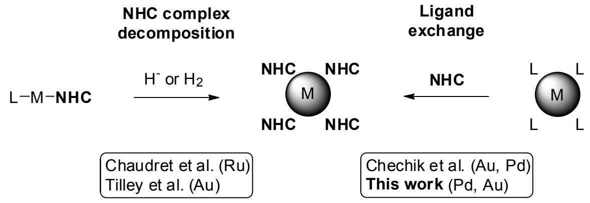
N-heterocyclic carbenes (NHCs) represent a leading class of ligands in organometallic chemistry, but have been rarely exploited as stabilizers for metal nanoparticles (NPs). We report the first example of NHC stabilized Pd-NPs that demonstrate long term stability. These NHC Pd-NPs were synthesized by a facile ligand exchange protocol using rationally designed long chained NHCs (LC-NHCs). Furthermore, we demonstrate that the surface modification of Pd-NPs results in significant chemoselectivity in a model reaction.

In recent years nanoparticles (NPs) have become increasingly important in medicine, material chemistry and catalysis.[1] They are particularly important in catalysis due to their high surface area and the metal-metal-interactions within the NP, which can open up new reaction pathways. The major challenge in the application of NPs is stabilization to avoid agglomeration which is typically achieved by ligands such as thiols, amines, disulfides, thioethers or phosphines.[2] During the last 20 years N-heterocyclic carbenes (NHCs) established themselves as a leading class of ligands in organometallic chemistry.[3] NHCs are neutral electron-rich ligands, which often form very strong metal ligand bonds. These properties would also be very attractive for the stabilization and activation of NPs, but it is unclear if these characteristics can be extrapolated from molecular complexes to NHC-NP adducts as NHCs have rarely been exploited in nanoparticle chemistry.[4] There are three seminal examples of structurally defined NHC-stabilized metal NPs with limited utility: Chaudret et al.[4a] and Tilley et al.[4b] could prepare NHC-stabilized Ru- and Au-NPs by the selective degradation of the corresponding metal complexes, whilst Chechik et al. investigated a ligand exchange approach (Scheme **1**).[4c] Chechik et al. could demonstrate that the exchange of thioethers by NHCs on the surface of Au- and Pd-NPs is possible but their resulting NP systems lacked stability and aggregated within hours. Very recent work introduced NHC stabilized Ag-[4e] and Pt-NP,[4f] and the application of NHC stabilized Ru- and Pt-NP in the hydrogenation of aromatics[4d] and nitroaromatics[4f] was demonstrated. Herein we report the first example of NHC Pd-NPs that demonstrate long term stability by rational design of novel micelle inspired long chained NHCs (LC-NHCs). Furthermore, we demonstrate that the surface modification results in significant chemoselectivity in a model reaction. Our data suggest that this is not merely an effect of catalyst deactivation.



Scheme 1. Approaches for the synthesis of NHC modified NPs. L: Ligand. M: Metal

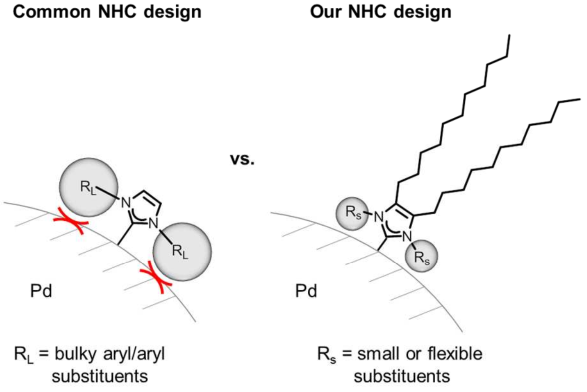


Figure 1. Comparison of different NHC designs

It is striking that currently stable NHC-NPs have only been prepared by a complex decomposition approach (Scheme 1). Preparation using a simple ligand exchange protocol would be highly desirable because this method can utilize NPs prepared using varied and established protocols providing access to various metal NPs and NP shapes.[5] We hypothesized that suitable NHCs should bear small or flexible substituents on the nitrogen atoms, to minimize steric repulsion between the NHC and the surface.[4c] Therefore, we chose small *N*-methyl substituents, or alternatively, flexible benzyl substituents which may provide additional coordination via π-surface interactions. Furthermore, we designed our NHCs with long aliphatic chains on positions 4 and 5 of the heterocycle to benefit from the steric repulsion between the NPs and provide the possibility to form protective monolayers on the surface.[2] The NHC design is illustrated in Figure 1. Notably, since we proposed that the long aliphatic chains would provide the required stabilization of the NPs, the N-substituents are still available for further modification. This would provide the possibility to fix a small functional group pointing directly to the metal surface.[4k] This characteristic is difficult to realize with conventional stabilizers such as thiols or amines.

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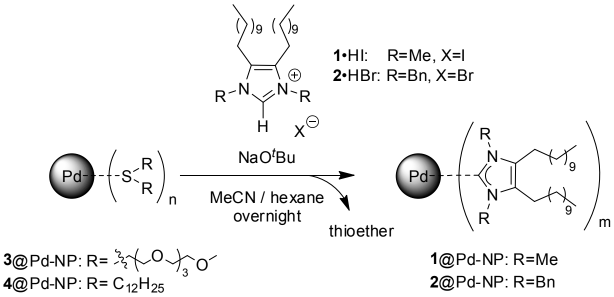

Scheme 2. Ligand exchange reaction on thioether stabilized Pd-NP with LC-NHCs.

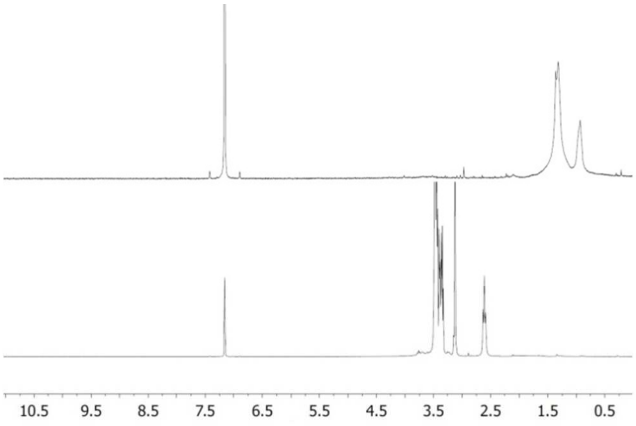

Figure 2. ^{1}H NMR spectra of **1**@Pd-NP (top) and **3**@Pd-NP. Solvent: C_6D_6.

The long chain imidazolium salts **1**•HI and **2**•HBr, precursor for the LC-NHCs, where synthesized in a 4 step sequence. Starting from commercially available aldehydes a sequence of benzoin condensation, oxidation, cyclization and alkylation led to the corresponding imidazolium salts.[6] Pd-NPs with weak thioether ligands as leaving group were synthesized according to Obare et al.[7] Unpolar Pd-NPs (4.0 (0.5) nm) were stabilized by didodecylsulfide (**4**). Polar Pd-NPs (4.5 (0.4) nm) were functionalized with bis(tetraethylene glycol mono-methyl ether)sulfide (**3**). The polar thioether **3** was synthesized in two steps.[6] We selected this thioether in order to be able to remove the unbound ligand after the exchange reaction by simple extraction with a polar solvent. The LC-NHC stabilized Pd-NPs were synthesized by mixing **3**@Pd-NP with the corresponding LC imidazolium salt (**1**•HI or **2**•HBr) and NaO*t*Bu in a two phase system of hexane and acetonitrile (Scheme 2). After purification the LC-NHC Pd-NP could be isolated as brown solid. It should be noted that the LC-NHC Pd-NPs are stable over four months and can be handled under air. To confirm the crucial role of the aliphatic chains, the corresponding benzannulated or unsubstituted NHCs were also tested as stabilizers. Although an exchange occurred, the resulting systems showed poor stability: storage for 12 h or exposure to air led to fast aggregation of these NPs.[6] In addition, we cross-checked the ligand exchange by using the sterically demanding NHC IPr (1,3-bis(2,6-diisopropylphenyl)-imidazolydene) and obtained similar results to the Chechik group. An exchange was observed but the resulting material quickly aggregated.[6] We also prepared an IPr analogue bearing long alkyl chains on the backbone (LC-IPr) and obtained identical results to those in the exchange reaction of IPr, strongly supporting our concept.[6] It should be pointed out that sterically demanding NHCs were successfully applied to stabilize smaller NPs (1.2 -2.2 nm) synthesized via the decomposition approach.[4a,b] It seems feasible that smaller NP with a bigger curvature tolerate bulky ligands, whilst with increasing size of the NP and thus a smaller curvature, the substitution becomes more critical. Therefore, we propose that small substituents would be preferable to enable the development of a general exchange protocol.

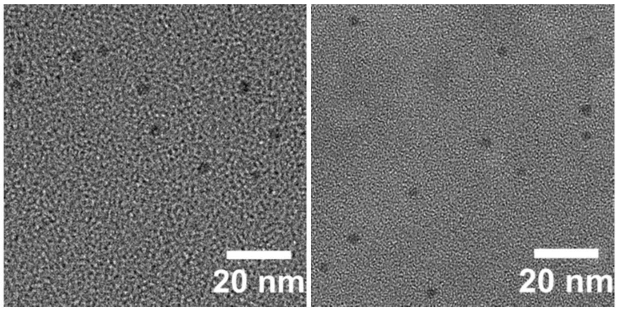

Figure 3. TEM images of **3**@Pd-NP (left) and **1**@Pd-NPs (right) (for **2**@Pd-NPs see SI).

NMR analysis of **1**@Pd-NP and **2**@Pd-NP proved that the thioether **3** was completely exchanged by the LC-NHCs, as no signals of the thioether **3** were detected and only signals of the alkyl chains of the NHCs were observed (Figure 2). The signals of the protons located close to the NP surface are not visible due to the broadening of the signals.[4a,8] When the unpolar Pd-NPs (**4**@Pd-NP) were used to perform the exchange the thioether **4** could not be completely removed leading to a mixed ligand environment (**1**•**4**@Pd-NP; ratio of **1**/**4** = 1:1 according to ^{1}H NMR). Intriguingly, in this case sharp NMR signals were observed for the NHC ligands and the binding of the NHCs to the NP surface was verified by PFG-NMR measurements.[6] Furthermore, a ^{13}C labelled analogue of **1**•HI was synthesized to investigate the binding mode of the NHC. After the exchange reaction with the **4**@Pd-NP,[9] the C1 atom of ^{13C}**1**@Pd-NPs showed a downfield shift compared to the imidazolium salt in the ^{13}C NMR spectrum (168.2 ppm (^{13C}**1**) / 136.5 ppm (^{13C}**1**•HI)). Thus, NMR indicates that the carbene is indeed the binding species.

The size of the LC-NHC Pd-NPs were analyzed by transmission electron microscopy (TEM) and dynamic light scattering (DLS). According to TEM, **1**@Pd-NPs have a narrow size distribution of 4.4 (0.5) nm indicating that no aggregation occurred during the exchange reaction. The hydrodynamic diameter of the NPs was determined by DLS. It was found to be to 5.6 nm before and after the exchange reaction.[6] TGA and elemental analysis were conducted to investigate the composition of the NPs. The NPs have a metal content of 67-72% for **1**@Pd-NP and 55-62% for **2**@Pd-NP, which is consistent with previous reports.[4a-c] In addition to that, the C:H:N ratios were in good agreement with the calculated values for the NHCs, confirming that the NPs are only stabilized by the carbenes.

The strength of the coordination of the LC-NHCs to the NP was investigated by competition experiments by adding either an excess of a thioether or a thiol, which is known to bind very strongly to noble metal NPs.[2] After the treatment of **1**@Pd-NP

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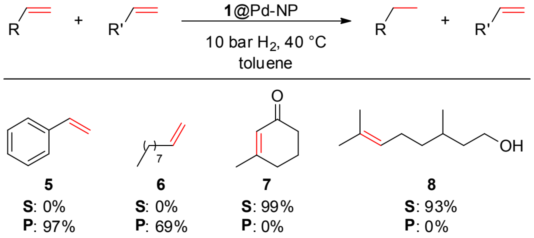


Scheme 3. Competition experiment. Conditions: Olefin (0.40 mmol), **1**@Pd-NP (0.5 mg), toluene (1 mL), hydrogen (10 bar), 40 °C, 18 h. Yields were determined by calibrated GC-FID. S: substrate. P: hydrogenation product

with excess of thioether **3** and washing, no changes in the NMR spectra could be observed, indicating no change in the composition of the ligand sphere occurred. In contrast, treating **1**@Pd-NPs with the corresponding thiol (2,5,8,11-tetraoxatridecane-13-thiol **15**)[6] the resulting Pd-NPs were extracted into the polar phase indicating that the NHCs were replaced by the polar thiol. After washing with hexane the NMR spectra showed that the Pd-NPs were functionalized with the thiol and no signals corresponding to the NHC could be observed. These experiments show that the NHC is not irreversibly bound to the NP surface and can be exchanged by a stronger ligand such as a thiol. On the other hand, weaker ligands like thioethers are not able to replace the NHCs from the surface. In terms of the generality of the developed protocol we were delighted to see that the exchange reaction was not limited to Pd-NPs. When thioether protected Au-NPs were utilized, the exchange proceeded smoothly under standard conditions yielding stable LC-NHC Au-NPs.[6]

After the successful synthesis of the LC-NHC Pd-NPs, we were interested to see whether these new NP systems are still catalytically active or the long chains of the ligand shield the active surface. Therefore, we chose the chemoselective hydrogenation of olefins as a model reaction to test if the NHC influences the activity or selectivity of the Pd-NPs.[9] Styrene (**5**), 1-decene (**6**), 3-methyl-2-cyclohexenon (**7**) and citronellol (**8**) were selected as representative substrates, because of the different reactivity of the double bonds (different degree of substitution, conjugated or non-conjugated). All substrates were submitted together to different hydrogenation condition in competition experiments, which revealed that the **1**@Pd-NPs could differentiate between the substrates by their degree of substitution (Scheme 3).[9] While styrene (**5**) and 1-decene (**6**) were fully converted, 3-methyl-2-cyclohexenon (**7**) and citronellol (**8**) remained unchanged in the reaction mixture. Interestingly, 1-decene (**6**) was not fully hydrogenated but the partial isomerization of the double bond in internal positions was observed. These disubstituted double bonds were not hydrogenated so that 1-decene (**6**) was converted to a mixture of decane and internal decenes. When **2**@Pd-NPs were applied as catalyst, the same selectivity was observed.[6]

Control experiments were conducted to ensure that the observed chemoselectivity is caused by the NHC surface modification.[6] First the competition experiment was repeated with commercial Pd/C as the catalyst. Under identical conditions no chemoselectivity was observed and all substrates were fully hydrogenated. When thioether stabilized Pd-NPs (**4**@Pd-NP) were applied as catalyst the hydrogenation proceeded with very low chemoselectivity.[6] These experiments arguably demonstrate that the NHC influences the reactivity of the Pd surface and that a strong binding between stabilizer and surface is essential. Another interesting result was obtained when **1•4**@Pd-NPs were applied, which are stabilized by a mixture of thioether **4** and LC-NHC **1**: these NPs give the same chemoselectivity as the pure **1**@Pd-NPs.[6] Keeping in mind that in the case of the mixed stabilized NPs we could prove by NMR experiments that the NHC is binding via the carbene carbon atom to the Pd-NPs and that the thioether **4** could not induce chemoselectivity, this experiment strongly indicates that the observed chemoselectivity is caused by the surface modification with the NHC ligands. The addition of a drop of mercury to a running reaction immediately suppressed any reactivity, suggesting that the mode of action is heterogeneous and no *in situ* formed homogeneous species is responsible for the observed chemoselectivity.[6,10]

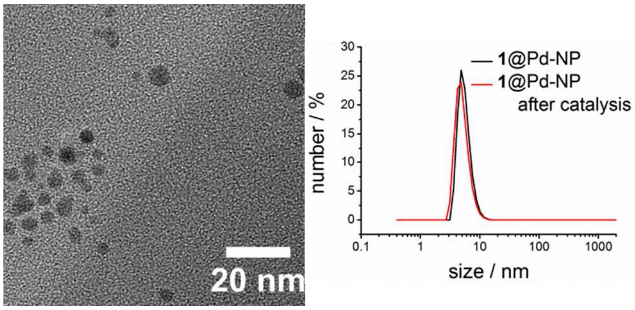
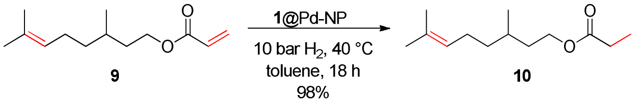


Figure 4. TEM image (left) and DLS measurement (right) of **1**@Pd-NPs after catalytic reaction (for **2**@Pd-NPs see SI).

Regarding the stability of the LC-NHC NP system, DLS and TEM analysis before and after the catalytic runs revealed that the size of the NPs remained unchanged (4.5 (0.3) nm) (Figure 4). Furthermore, when a two months old batch of Pd-NPs was used as catalyst, or the reaction was run under harsher conditions (100 °C, 20 bar) the same chemoselectivity was observed, indicating a strong interaction between ligand and surface.[9]

It is important to note that the chemoselectivity is not caused by a simple reduction of the general activity of the Pd-NP after surface modification, and that it is not necessary to stop the reaction after a certain time to prevent conversion of the higher substituted olefins. The same result for the competition experiment was obtained when the reaction was stopped after 1 h, which means that the conversion of styrene (**5**) and 1-decene (**6**) is completed rapidly and in the residual 17 h the catalyst is unable to hydrogenate the remaining olefins. In addition to this, citronellol (**8**) alone was submitted to the reaction conditions and no hydrogenation product was detected after 18 h.[6] To rule out a catalyst poisoning by starting materials, products or side products, a second portion of starting materials was added at the end of the reaction and styrene (**5**) and 1-decene (**6**) were again completely converted. The observed chemoselectivity may be caused by the site selective binding of the NHC to corners, edges and faces exhibited on the surface of the NPs. Chaudret et al. have proven in their systems that NHCs preferentially bind to low valent sites such as corners.[4a] As different sites offer different activities, a site specific binding leading to the observed chemoselectivity is feasible.

Finally the selectivity of our NP system was demonstrated by the



Scheme 4. Selective hydrogenation of 3,7-dimethyloct-6-en-1-yl acrylate (**10**).

hydrogenation of 3,7-dimethyloct-6-en-1-yl acrylate (**9**), which contains two double bonds (Scheme 4). Under standard conditions the hydrogenation processed smoothly and selectively to 3,7-dimethyloct-6-en-1-yl propionate (**10**), which was isolated in 98% yield. Again, Pd/C and the thioethers-stabilized **4**@Pd-NP gave markedly different results.[6]

Conclusions

In conclusion, we report a novel class of NHC ligands bearing long alkyl chains at their backbone, which allow for the first time the synthesis of stable NHC-modified NPs via a ligand exchange approach. Furthermore, we could demonstrate that the modification by NHCs influences the activity and selectivity of Pd-NPs in the hydrogenations of olefins. Utilizing our protocol we intend to synthesize novel NHC modified nanomaterials of different metals and shapes. The modification of the LC-NHCs will be investigated with a view to addressing challenges such as asymmetric heterogeneous catalysis.

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