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Hybrid Surfactants with N-Heterocyclic Carbene Heads as a Multifunctional Platform for Interfacial Catalysis

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Abstract: Processing of substrates with different solvent compatibility is a persistent problem in homogeneous catalysis, in particular when one starting compound is water soluble and the other is not. A tempting concept found in literature is micellar catalysis. However, developing catalysts, which are surfactants at the same time, stands at its beginning. We report the synthesis of a new surfactant system with a N-heterocyclic carbene (NHC) moiety as a head group. Characteristic surfactant properties such as the formation of micelles or liquid crystals is documented. The new surfactant ligand forms coordination compounds with various metals, most importantly Pd^{2+} in square planar geometry. The Pd-NHC compound as well shows surfactant features, and can be used successfully for C-C cross coupling reactions (Suzuki, Heck). The boost in catalytic activity by one order of magnitude compared to analogous, but non-amphiphilic species is reported.

Converting two reactants with different solvent compatibility, one hydrophilic the other lipophilic, is a classic problem in chemistry. Existing solutions to this problem can be divided into two categories. One method is widely known as phase-transfer catalysis.[1] One component is moved into the unfavorable phase by coordination to auxiliaries changing its solubility. Second, one may increase the chance for a reaction by providing a large interface of the immiscible phases. This can be done by creating micelles or emulsion droplets. The current state in the associated field 'micellar catalysis' was described in an excellent review article from Scarso et al. in 2015.[2] The situation becomes even more intricate, as soon as the catalysts itself is not soluble in the desired medium. Many molecular catalysts are soluble in apolar solvents due to bulky, organic ligands coordinating to the metal. The application of those compounds in polar media, ultimately water, requires extra efforts.[3] However, a major difficulty remaining is, when the catalytically active species needs to be compatible with two solvents of opposing miscibility at the same time.

Compounds, which can effectively mediate between water and an oil phase, are of course well-known: Surfactants; molecules comprising a water-soluble head and a hydrophobic tail. Arming a surfactant with catalytic properties is desired and needs the metal-containing moiety becoming its integral part, for instance as a head group.[4] A powerful approach towards the generation of metallosurfactants is the synthesis of a ligand modified by a long, hydrophobic chain, typically an alkyl group.[5] The head group becomes or remains charged after coordination of a wanted metal cation resulting in hybrid surfactants with interesting, novel properties inaccessible for pure organic compounds.[6] Good examples can be found for surfactants with magnetic heads.[7] To prepare surfactants with catalytic heads is more difficult, because one has to provide free coordination sites at the metal. So, only a few papers have been published yet.[8] A nice case was presented by Mancini and coworkers,[9] who have asymmetrically modified a porphyrin ring. After coordination to Mn^{2+} the amphiphilic compound was used for the catalytic epoxidation of alkenes with aqueous H_2O_2. Deng et al. described a Rh(I) containing surfactant, which was used for the asymmetric hydrogenation of ketones in water.[10]

Another class of highly important, catalyzed transformations is represented by C-C cross-coupling reactions. It is well-known that complexes with carbene ligands, in particular N-heterocyclic carbenes (NHC), represent powerful catalysts.[11] Since the first report of a water soluble NHC complex in 1974,[12] more attention was devoted to this subject just within the last 10 years.[13] Few examples exist on attempts to prepare an NHC system with amphiphilic properties. Mingotaud and coworkers have presented a Hoveyda's type catalyst comprising a perflourinated C_9 chain attached to Ru via a carboxylate group in 2008.[14] It is also worth mentioning the pioneering work of the Uozumi group,[15] who made a Pd-NHC pincer ligand with one side modified by two alkyl chains as hydrophobic moieties and (on the other side) two oligo glycol chains for water solubility. In several papers, the authors show that product selectivity in the Miyaura-Michael reaction can be improved in comparison to using conventional, non-amphiphilic catalysts.[16]

Surfactants with catalytic heads fill a gap between phase transfer catalysis on the one side and micellar catalysis on the other side, taking the best from two worlds. In particular a surfactant containing an NHC moiety promises to be of high potential in several C-C cross-coupling reactions like Hiyama, Kumada, Negishi, Stille, Suzuki, Sonogashira or Heck. Thus, our target (**5**) is a new class of surfactants with an NHC head group as shown in **Scheme 1**. Followed by synthesis, we will examine the capabilities of the surfactant on the complexation of different metal cations and study their surfactant features. Finally, for the Pd-containing species catalytic investigations will be performed.

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       Supporting information for this article is given via a link at the end of the document.

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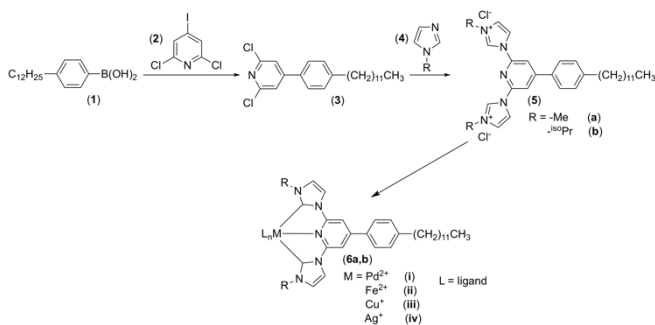
Scheme 1. Synthesis of the NHC surfactants.

The synthesis of (**5**) is described in detail in the experimental section. First, 2,6-dichloro-4-iodopyridine (**2**) was coupled to the alkyl-substituted phenylboronic acid (**1**) by means of Suzuki coupling, followed by the nucleophilic substitution of the chlorine substituents in (**3**) with a N-substituted imidazole (**4**). Because the flexible alkyl chain prevents growing single-crystals and characterization by X-ray diffraction methods, electron-spray ionization mass spectrometry (ESIMS) has proven to be a valuable method for hybrid surfactants.[7b, 17] The ESIMS patterns of (**5a,b**) are shown in **Supporting Information Fig. S1**.

Because of its molecular architecture with the two mono-cationic heads separated by the pyridine spacer (**5**) is expected to be a surfactant with so-called gemini characteristics.[18] The surfactant character can indeed be confirmed by concentration dependent surface tension measurements shown in **Fig. 1a**. The critical micelle concentration (cmc) of **5a** is 54 mg/l (7.9×10^{-5} mol/g). This is roughly one order or magnitude lower compared to a classical surfactant such as CTAB (cetyltrimethyl ammonium bromide; 9.2×10^{-4} mol/g), which we assign to the twofold charge and the larger head preventing a dense packing on the air/water interface. **5b** has a cmc in a similar range to **5a**, but the saturation value for surface tension γ ($\approx$ 40 mN/m) is higher than for a conventional surfactant. The iso-propyl groups in **5b** presumably prevent an effective occupancy of the aqueous interface. This assumption can be confirmed by calculation of the surface excess Γ and the minimum area per molecule at the air/water interface (A_m(**5a**) = 16.0Å^2, A_m(**5a**) = 24.6Å^2) from the concentration dependent γ curves (see **Supporting Information Fig. S2**).

The size of the aggregates in water at low concentration was determined by dynamic light scattering (DLS) (**Fig. 1b**). Because there is always some uncertainty in the absolute value of micellar aggregates derived from DLS, transmission electron microscopy (TEM) under cryogenic conditions (**Fig. 1c**) was also applied. Such objects with a dimension of 5 nm fit well to conventional, spherical micelles and considering the molecular extension of one surfactant molecule is 2.4 nm (see **Supporting Information Fig. S3**). At higher concentration we have also observed the formation of liquid crystalline phases (LCs) as indicated by birefringence patterns found in polarization microscopy (**Fig. 1d**). The structure of the LCs was clarified by small-angle X-ray scattering (SAXS) shown in **Fig. 1e**. The noted pattern for **5a** is characteristic for a lamellar phase (L_α) with a layer-to-layer distance of 4.9 nm. Because the head group of **5b** is more bulky, the packing

parameter is slightly larger,[19] and the tendency to forming structures with higher curvature can be seen from the occurrence of a hexagonal phase (**see Supporting Information Fig. S4**).
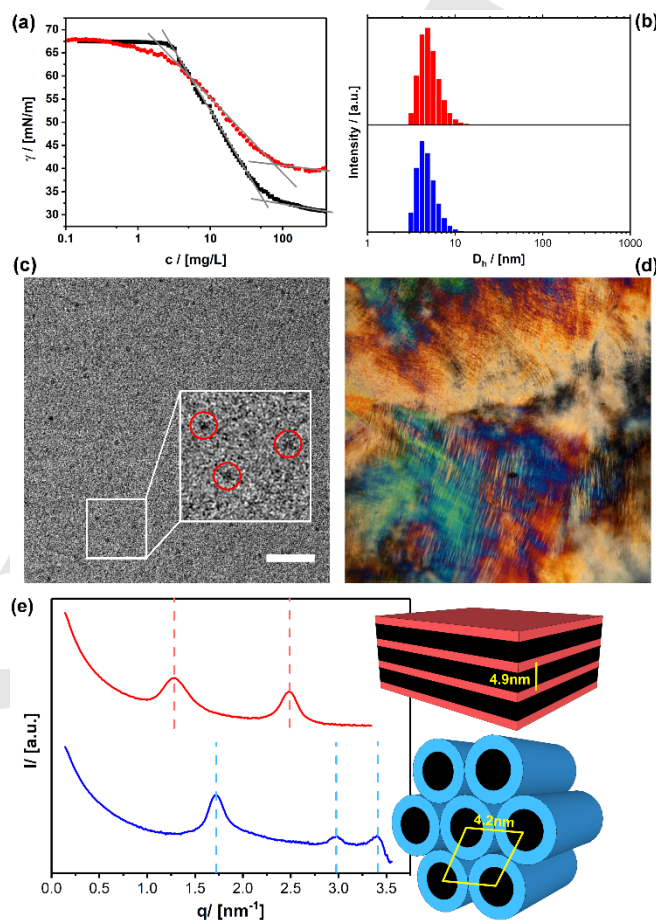

Figure 1. Amphiphilic behavior of surfactants with NHC head group **5**. (a) Surface tension measurements (**5a** (black squares); **5b** (red circles)). (b) Size distribution ($D_H \cong$ hydrodynamic diameter) derived from DLS measurements for **5b** (red) and **6bi** (blue). Cryo-TEM micrograph (c) of a micellar solution of **5a** (scale = 100 nm). Polarization microscopy image (d) and SAXS pattern (e; red line) of a liquid crystalline phase of **5a**. The SAXS pattern after coordination of Pd^{2+} (**6ai**) is also shown. The vertical lines tell the patterns expected for a lamellar phase Lα (red) and a hexagonal phase P6/mm (blue).

The true functionality of the surfactants with NHC head group is their ability to coordinate to metal centers resulting in the compounds **6,b(i-iv)** (see **scheme 1**). Among other methods summarized in **Supporting Information Fig. S5** crucial information is delivered by ESIMS shown in **Fig. 2**. The precise agreement between the experimental data and the patterns expected for the molecular ions [6a,bi]$^+$ proves the successful synthesis of the Pd^{2+} containing compounds. The proper binding of Pd could also be confirmed by shifts in infrared spectroscopy (IR) signals involving the vibrations of the pyridine and imidazolium rings. The generation of the carbene species was confirmed by characteristic changes in ^{1}H-NMR spectroscopy, most importantly the absence of the imidazolium proton at $\delta =$ 10.8 ppm. For a d^8-configuration as in Pd^{2+} in general a square

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planar coordination geometry is preferred, and this can be confirmed by geometry optimization calculations performed using density functional theory (DFT) calculations (**Fig. 2**). When the coordination geometry of the metal center is different, for example octahedral as for Fe^{2+} (**6bii**) or linear as for Ag^+ (**6biv**) molecular species containing two NHC ligands are obtained (see also **Supporting information Fig. S5**). Similar coordination modes were also found in the literature for conventional, non-amphiphilic ligands.[20]
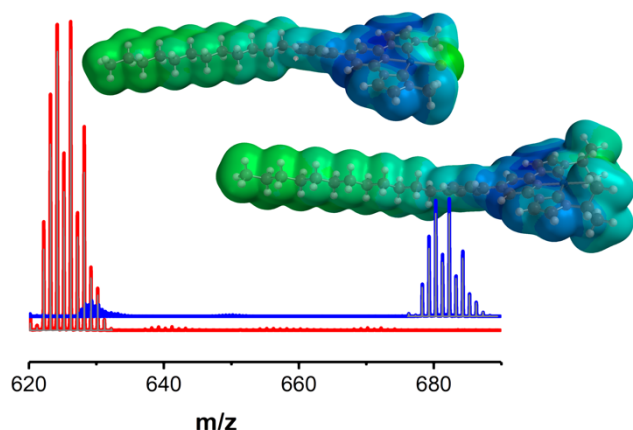

Figure 2. ESIMS spectra of the Pd-containing, hybrid surfactants **6ai** (red) and **6bi** (blue); the theoretical isotope pattern for the ions [6ai]+ and [6bi]+ is included as gray lines. The molecular structure of the surfactants determined from DFT calculations is also shown.

The self-assembly behavior of the new, hybrid surfactants **6a,bi** was investigated next. We learn from SAXS measurements (**Fig. 1e**) the presence of the metal has a marked effect on the structure of the LC phases. A hexagonal phase (P6/mm) is adopted, which is a structure encountered often for lyotropic liquid crystals formed by various amphiphiles. The periodicity of the structure has decreased slightly (4.2 nm) compared to the lamellar phase of the organic surfactant **5a**, which might be explained by the reduced repulsion of the head group, which is now only singly charged. Unfortunately, recording TEM data was hampered by the reduction of Pd in the electron beam (see **Supporting Information Fig. 6**). When we tried to examine the micellar state of **6ai**, we faced enormous problems. The compound is almost insoluble in any solvent, no matter polar or unpolar. The square planar coordination of Pd^{2+} leads to a planarization of the entire head group region of the surfactant as can be seen from **Fig. 2**. This results in an effective orientation of the four conjugated rings and induces a strong π-π interaction. Obviously one has to disturb this interaction, and this is why we have introduced the iso-propyl groups attached to the imidazolium rings in **6bi**. The iso-propyl groups introduce a bump to the molecule according to the DFT calculations (**Fig. 2**). This reduces the intermolecular head-group interaction, and as a result the surfactant becomes now soluble in polar media. The occurrence of micelles can be observed again (**Fig. 1b**). Like for the LC phases, the coordination of Pd leads to a slight decrease in the size of the self-assembled structure.
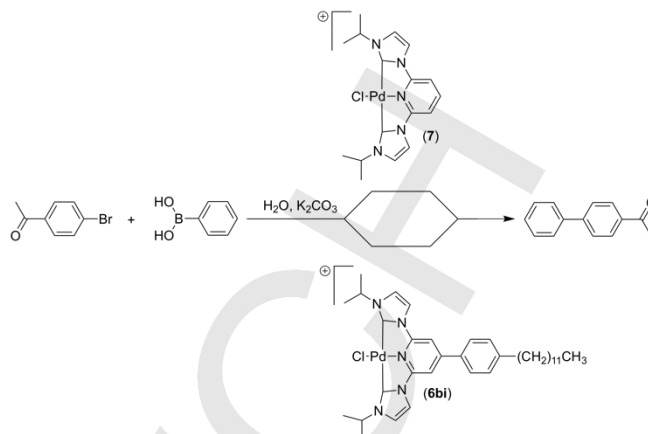
Scheme 2. Catalytic test reaction performed using **6bi** as a surfactant catalyst in comparison to a non-amphiphilic catalyst as a reference.

As a catalytic test reaction we selected the Suzuki coupling of phenylboronic acid with 4-bromoacetophenone (see **scheme 2**). As a reference we have also synthesized the non-amphiphilic coordination compound (**7**), which was used for the catalytic reaction under otherwise identical conditions. The reaction was checked by gas-chromatography (GC) (**Fig. 3**). It can be seen the surfactant compound **6bi** is superior over **7** with a conversion of over 99% within 15 minutes. It is obviously much more difficult for the non-amphiphilic catalyst to process a substrate mixture containing both, a hydrophobic (4-bromoacetophenone) and a hydrophilic (boronic acid) compound. Thus, the micellar catalysis route enabled by **6bi** leads to a substantial increase in the turn over frequency (TOF) from 2.5×10^{-3} s^{-1} for (**7**) to 3.6×10^{-2} s^{-1} (mole product per mole catalyst and second), although the catalytic center is the same. This is in a range also reported for conventional catalyst systems reported in the literature.[21] For proof of concept, we have also checked the activity of the Pd-NHC surfactants in other C-C cross-coupling reaction such as the Heck reaction (see **Supporting Information Fig. S7**).

Our study verifies that an NHC-based system with surfactant architecture opens new perspectives in micellar catalysis. The presented case is open for a multiple number of adjustments. It was already shown that (**5**) is compatible with diverse metals. Therefore, we expect that analogous complexes with Pt or Au cannot only be used for a range of other catalytic transformations e.g. hydrosilylation reactions,[22] but they are also promising in other applications like as an anti-tumor drug.[23] Further, additional substituents at the phenyl ring might help to fine-tune the catalytic activity and to adjust product selectivity. We had overcome the problem of the undesired π-π interaction by attaching isopropyl substituents to the imidazolium. We intend to use other, polar groups in the future for increasing the solubility of the surfactant in water even more. In particular a sulfonic acid group seems to be tempting aiming at acid - cross-coupling tandem catalysis.[24]
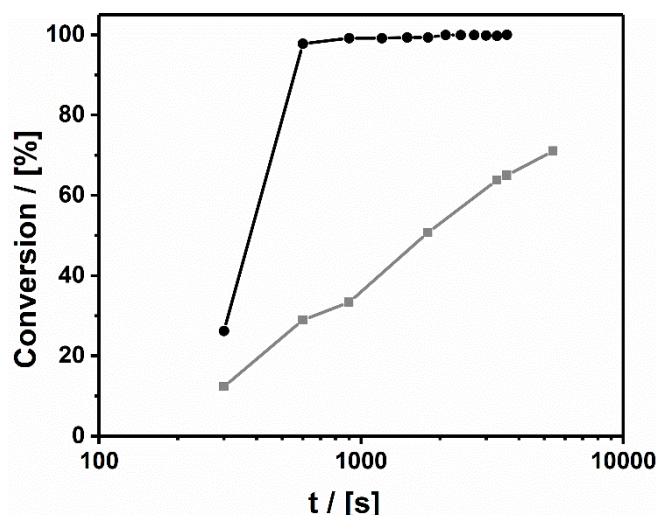
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Figure 3. Monitoring the catalytic conversion (Suzuki coupling; scheme 2) by GC-MS, using 1-butanol as an internal standard (black: amphiphilic catalyst **6bi**, grey: non-amphiphilic reference **7**).

Experimental Section

Experimental Details are given in the Suppporting Information.

Acknowledgements

Keywords: Surfactants • Self-Assembly • Homogeneous Catalysis • Cross-Coupling Reactions • Organic-Inorganic Hybrids

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Soapy catalyst in action. A organic-inorganic hybrid surfactant containing a carbene-Pd complex as a head is used for micellar catalysis bridging the gap for substrates with orthogonal solvent-compatibility.
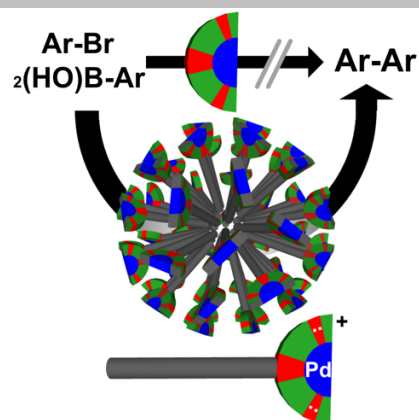
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