Selective Hydrogenation of Aldehydes Using a Well-Defined Fe(II) PNP Pincer Complex in Biphasic Medium

Stefan Weber,[a] Julian Brünig,[a] Veronika Zeindlhofer,[b] Christian Schröder,[b] Berthold Stöger,[c] Andreas Limbeck,[d] Karl Kirchner,*[a] and Katharina Bica* [a]

A biphasic process for the hydrogenation of aldehydes was developed using a well-defined iron (II) PNP pincer complex as model system to investigate the performance of various ionic liquids. A number of suitable hydrophobic ionic liquids based on the \( \text{N}^+\text{(Tf}_2\text{O})^-\) anion were identified, allowing to immobilize the iron (II) catalyst in the ionic liquid layer and to facilitate the separation of the desired alcohols. Further studies showed that targeted Bronsted basic ionic liquids can eliminate the need of an external base to activate the catalyst.

Introduction

The design and application of new catalysts and catalytic systems is a key driver of sustainable chemistry and a constant field of innovation. To date, the chemical industry ranging from bulk to fine chemical production relies heavily on the use of metal catalysts that are often based on rare noble metals as catalytically active site, particularly in case of homogenous catalysis. In the light of the limited abundance and the threat of a global shortage, the development of base metal catalysts relying on abundant and low cost metals with low toxicity has become an open area of research. A milestone in the development of highly active iron-based catalysts for the reduction of carbonyl groups was the implementation of pincer ligands, providing a basis for the mild and chemoselective iron-catalyzed reduction of aldehydes, ketones, imines but also of \( \text{CO}_2 \) under benign conditions and moderate hydrogen pressure. In 2014, Kirchner and co-workers developed the iron (II) pincer complex \([\text{Fe}(\text{PNPMe-Pr})(\text{CO})(\text{H})(\text{Br})] \) (I) that showed remarkable reactivity and chemoselectivity for the reduction of aldehydes. The first step of the catalytic cycle is the activation of pre-catalyst I to form a mixture of cis- and trans-dihydride complexes \([\text{Fe}(\text{PNPMe-Pr})(\text{CO})(\text{H})_2] \) (II) upon addition of dihydrogen in the presence of base, with the trans isomer being the catalytically active species (Figure 1). Key step is the regeneration of the catalytically active complex II which requires dissociation of the product alkoxide to enable coordination and heterolytic cleavage of dihydrogen. Thus, high catalytic activity was observed in the protic solvent

Figure 1. Pre-catalyst \([\text{Fe}(\text{PNPMe-Pr})(\text{CO})(\text{H})(\text{Br})] \) (I) and active species trans-\([\text{Fe}(\text{PNPMe-Pr})(\text{CO})(\text{H})_2] \) (II) used for the biphasic reduction of aldehydes in these studies.
EtOH (relative polarity 0.654) which facilitates alkoide dissociation and stabilization, while no conversion was observed in aprotic and low polarity solvents such as n-heptane (0.009).\[3]\[3]

As a result of the homogenous reaction environment in EtOH, difficulties in the separation of the formed alcohols and catalyst from the solvent ethanol arise as it is typical for homogeneously catalyzed processes. To solve these issues, a number of strategies have been developed that can balance the positive aspects of homogenous and heterogeneous catalysis.\[7]\ Biphasic catalysis, in which the catalyst resides in one of the two phases while the product is dissolved in the second phase can facilitate problems encountered with separation but maintain the high activity associated with homogenous catalysis.\[10] This concept of liquid-liquid biphasic catalysis is well established for different biphasic systems, i.e., aqueous-organic solvent mixtures, and currently applied in several industrially relevant processes such as the Rhône-Poulenc Ruhrchemie process for hydroformylation.\[10] More recently liquid ionic liquids broadened the application range for liquid-liquid biphasic catalysis, as they can avoid limitations of aqueous systems.\[11] Compatibility issues of organometallic species with water can be often overcome using ionic liquids instead. Moreover, many classical transition-metal catalyst precursors are readily soluble in ionic liquids rendering the synthesis of specially designed ligands obsolete as it would be required for aqueous, fluorinated, or supercritical fluid-based catalytic processes.\[11]

We recently demonstrated that I can also be conveniently immobilized on precoated silica in a supported ionic liquid phase (SILP) approach using the hydrophobic ionic liquid [C₄m2 im][N(Tf)₂].\[12] Reasonable high turnover frequencies (TOF) and turnover numbers (TON) could achieved with this catalyst system. For an extension of this approach to other SILP systems, i.e., other ionic liquids and other support materials, the wetting properties of a particular IL/support system play a key role. A strong affinity between the ionic liquid and the support surface is important both for the impregnation of the support with IL/ catalyst solution, i.e. an even thin-film coverage of the inner pore surface, and its resistance against IL/catalyst leaching. Bordes et al. have shown\[13] in a recent study of the wettability of graphite by ionic liquids, that the solid/liquid interfacial energy γSL is the best experimentally accessible parameter for the affinity of ionic liquids toward a solid surface: the lower γSL, the lower the liquid contact angle and the higher the adhesion of a liquid film on a solid surface. Since γSL depends on both the solid surface energy γSV and the liquid surface tension γLV via Young’s equation, the most suitable liquid with the strongest affinity must be found separately for each solid support material, i.e. each SILP system must be individually optimized and a pool of suitable ionic liquids must be available. For this purpose, we utilize here the iron (II) catalyzed reduction of aldehydes under biphasic conditions as model reaction and investigate reactivity, substrate dependence and catalyst recycling with a variety of different ionic liquids in order to create a pool of functional systems for their later application and optimization in SILP catalysis.

Results and Discussion

A number of critical aspects need to be considered when selecting ionic liquids for the biphasic process, including a high solubility and stability of the pre-catalyst and the active species in the ionic liquid, but also a low miscibility of ionic liquid and organic phase. Based on literature data and on our previous experience, we selected a set of hydrophobic ionic liquids based on the N(Tf)₂⁻ anion for an initial screening. Apart from the favorable physical properties in terms of viscosity, the very weakly coordination nature of N(Tf)₂⁻ should avoid ligand substitution reactions on the (pre-) catalyst while also providing a higher hydrogen gas solubility compared to other hydrophilic ionic liquids with BF₄⁻ or PF₆⁻ anion.\[14] According to these considerations, a pool of ten hydrophobic ionic liquids with different cations and variable alkyl chain length was selected as shown in Figure 2.

![Scheme 1. Catalytic reduction of 4-fluorobenzaldehyde in ionic liquid/n-heptane biphasic medium.](image)

Initial investigations on the catalytic properties were performed with 4-fluorobenzaldehyde as model substrate due to our previous research and its facile analysis via ¹H NMR spectroscopy (Scheme 1). In order to minimize the required amount of ionic liquid, the biphasic system was composed of 1.5 ml of n-heptane and 250 mg ionic liquid, which was sufficient to dissolve 0.5 mol% of the Fe-PNP pre-catalyst (S/C 200) used in all cases.

To activate the pre-catalyst 1, DBU (1,8-diaza-bicyclo [5.4.0] undec-7-ene) (5 mol%) was added, and hydrogenations were routinely run at 10 bar hydrogen pressure for 60 min reaction time. With the exception of pyridinium and picolinium-based
organometallic species are involved. The alkyl chain length showed little difference between the performance of imidazolium-based ionic liquids. Further analysis via NMR and GC-MS did not reveal any evidence for alteration of the pyridinium cation in the presence of an acidic proton in the C-2 position and the corresponding alcohol was formed as sole product in high yields (Figure 3).

Apart from undesired leaching of ionic liquid into the organic layer, the distribution of substrate, catalyst and product is a key aspect that will influence the efficiency of the reaction as well as separation of the products in biphasic catalysis. In general, the reduction of aldehydes is not an ideal situation for catalysis in organic/ionic liquid biphasic systems, as the more polar alcohol formed during the reactions is more likely to migrate to the ionic liquid phase. This unfavorable situation can be partially compensated when using a large volumetric excess of n-heptane compared to ionic liquid. We further studied concentration effects of 4-fluorobenzaldehyde 11 and 4-fluorobenzylalcohol 12 in a biphasic model system composed of ionic liquid [P4441]N(Tf2) and n-heptane similar to the ratio and condition used for catalysis. These substrates were separately added to a biphasic model system composed of 1.5 ml of n-heptane and 250 mg of ionic liquid [P4441]N(Tf2), 4, stirred for 60 min at 25 °C. 19F{1H} NMR measurements were carried out in the presence of an external standard (fluorobenzene) to quantify the distribution of substrate and product between the two phases. As expected, the less polar aldehyde 11 had a higher affinity for the organic phase compared to the product, and 0.62 mmol (corresponding to 31 %) 4-fluorobenzaldehyde 11 were found in the n-heptane layer. The more polar product 4-fluorobenzylalcohol 12 is more likely to migrate to the ionic liquids phase, and only 0.32 mmol (16 %) were detected in the organic phase of the pure model system. However, the efficiency of the ionic liquid-heptane biphasic system is evident when addressing the distribution of the Fe(II)-PNP catalyst between ionic liquid and organic phase. 51P{1H} NMR analysis of n-heptane could not detect any traces of catalyst. Moreover, ICP-MS analysis revealed an iron content of <10 ng in the organic phase which clearly shows that no leaching of the catalyst into the n-heptane solution takes place. Likewise, we did not detect DBU in the organic phase. It has to be noted that DBU is predominantly present in its protonated cationic form after activation of the pre-catalyst I and is thus immobilized in the polar ionic liquid rather than in the apolar n-heptane layer.

In case of pyridinium and picolinium salts, drastically lower yields (<25 %) were observed presumably due to decomposition of the catalyst in these ionic liquids. While the ionic liquid layer typically had an orange-red color after the reduction, pyridinium-based systems rapidly turned black clearly suggesting an undesired interaction between the catalyst and these particular ionic liquid cations. Further analysis via NMR and GC-MS did not reveal any evidence for alteration of the pyridinium and picolinium-based ionic liquids indicating that an unintended reduction of the ionic liquids was not responsible for the failure of the reaction. It is interesting to note that there is little difference between the performance of imidazolium-based cations [C6mim]N(Tf2) 1 and [C8mim]N(Tf2) 2. This suggests that the presence of an acidic proton in the C-2 position and the ability to form an N-heterocyclic carbene (NHC)-ligand does not interfere with the reaction as it is often observed when reactive organometallic species are involved. The alkyl chain length had limited impact on the catalytic performance and comparable yields were found for the more viscous long alkyl chain ionic liquids [C8mim]N(Tf2) 3, [P4441]N(Tf2) 4, and [N4441]N(Tf2) 5 and [N4441]N(Tf2) 7 and the corresponding short chain derivatives [C6mim]N(Tf2) 1, [P4441]N(Tf2) 4 and [N4441]N(Tf2) 6. However, from NMR analysis of the n-heptane layer it was found that leaching of these more hydrophobic ionic liquids into the organic phase took place. Such a behavior was not encountered in case of the short-chain derivatives.

Figure 3. Results of the biphasic reduction of 4-fluorobenzaldehyde with various hydrophobic ionic liquids.

We therefore expanded the pool of ionic liquids with four Brønsted basic ionic liquids to mimic typical organic bases (Figure 4). Ionic liquids with 4-(dimethylamino) pyridine (DMAP), 1,8-diazabicycloundecen-7-ene (DBU) and 1,4-diazabicyclo-[2.2.2] octane (DABCO) structural motif (13–15) were
prepared via selective alkylation of diamines and successive ion exchange. In case of the DMAP-based ionic liquid 13, crystals were grown from the intermediate chloride salt that supported its structure. This set was complemented with an amino-functionalized imidazolium derivative as $N$ reported its structure. This set was complemented with an amino-functionalized imidazolium derivative as $N$-diisopropyl-ethylamine (DIPEA) analogue (16) that has been previously used for palladium catalyzed cross coupling reactions. An interesting pattern was observed when studying the catalytic activity of $\text{Fe(PNPMe-Pr)}_2\text{CO(H)}(\text{H})\text{Br}$ in Bronsted basic ionic liquids 13–16 without additional base. The DIPEA and DABCO-based ionic liquids were not suitable and failed, indicating that the precatalyst was not activated in these ionic liquids (Table 1, entries 3–4). In contrast, excellent yields of 95 and 97% were found with DBU and DMAP analogue in a biphasic n-heptane/ionic liquid system, thereby eliminating the necessity of base addition in this reaction (Table 1, entries 1–2).

Further studies on the catalytic performance were performed with four selected ionic liquids, including $[\text{C}_4\text{m}2\text{im}]\text{N(Tf)}_2$ 2 and $[\text{P}_{4441}]\text{N(Tf)}_2$ 4 that gave the highest yields as well as the Bronsted basic ionic liquids 13 and 14. The highest TOF was found for the phosphonium-based ionic liquid $[\text{P}_{4441}]\text{N(Tf)}_2$ 4, and complete conversion was observed in only 9 min reaction time. In case of the imidazolium-based ionic liquid $[\text{C}_4\text{m}2\text{im}]\text{N(Tf)}_2$ 2 slightly longer reaction times of 12 minutes were required; however, the maximum TON was higher (Table 1, entries 5–6). In contrast, considerably lower TOF and TON values were determined for Bronsted-basic ionic liquids $[\text{C}_4\text{DBU}]\text{N(Tf)}_2$ 13 and $[\text{C}_4\text{DMAP}]\text{N(Tf)}_2$ 14 (Table 1, entries 1–2).

The lower catalytic activity might be a result of a reduced electron density on the free nitrogen in the Bronsted-basic ionic liquid cations (see Figure 5) compared to the free base.

![Figure 4. Bronsted-basic ionic liquids for the biphasic reduction of aldehydes. The inset displays the X-ray structure of the intermediate $[\text{C}_4\text{DMAP}]\text{Cl}$ (see ESI for more details).](image)

![Figure 5. Molecular orbital description of the non-binding HOMO orbitals of the alkaline ionic liquid cations. The bold numbers represent the corresponding $N$(Tf)$_2$-based ionic liquids.](image)

### Table 1. Yields and kinetic data for the biphasic reduction of 4-fluorobenzaldehyde in selected conventional and Bronsted-basic ionic liquids.

| Entry | Ionic liquid$^{[b]}$ | Yield [%]$^{[c]}$ | TOF [h$^{-1}$]$^{[d]}$ | TON$^{[e]}$ |
|-------|---------------------|------------------|----------------------|-----------|
| 1     | $[\text{C}_4\text{DMAP}]\text{N(Tf)}_2$ 13 | 98 | 800 | 220 |
| 2     | $[\text{C}_4\text{DBU}]\text{N(Tf)}_2$ 14 | 97 | 480 | 240 |
| 3     | $[\text{C}_4\text{DABCO}]\text{N(Tf)}_2$ 15 | <1 | n.d. | n.d. |
| 4     | $[\text{P}_{4441}]\text{N(Tf)}_2$ 16 | <1 | n.d. | n.d. |
| 5     | $[\text{P}_{4441}]\text{N(Tf)}_2$ 13 | >99 | 1332 | 793 |
| 6     | $[\text{C}_4\text{DBU}]\text{N(Tf)}_2$ 14 | >99 | 1008 | 1258 |

$^{[a]}$ Performed with 2 mmol aldehyde and 0.5 mol % pre-catalyst in 250 mg n-heptane for 60 min. Yield determined via $^1$F NMR spectroscopy of organic and ionic liquid phase using fluorobenzene as external standard; $^{[b]}$ performed with 2 mmol aldehyde and 0.5 mol % pre-catalyst in 250 mg ionic liquid/1.5 ml n-heptane. TOF reported as amount of substrate [mmol]/amount of catalyst [mmol]×reaction time for full conversion [h]; $^{[c]}$ performed with 20 mmol aldehyde and 0.05 mol % pre-catalyst in 250 mg ionic liquid/1.5 ml n-heptane for 80 h. Maximum TON reported as amount of product [mmol]/amount of catalyst [mmol]; $^{[d]}$ 5 mol % DBU added.

### Table 2. Computational analysis of the basicity of the nitrogen atoms of the cations and the corresponding bases. The bold numbers represent the corresponding $N$(Tf)$_2$-based ionic liquid.

| Cation/base | $q_N$ [e] | $r_N$ [Å] | PA [eV] | SASA [Å$^2$] |
|-------------|-----------|-----------|----------|--------------|
| $[\text{C}_4\text{DMAP}]^+$ (13) | −0.147 | 1.66 | 10.30 | 2.0 |
| DMAP | −0.323 | 1.51 | 11.21 | 1.5 |
| $[\text{C}_4\text{DBU}]^+$ (14) | −0.213 | 1.19 | 9.54 | 0.7 |
| DBU | −0.396 | 1.19 | 11.07 | 0.7 |
| $[\text{C}_4\text{DABCO}]^+$ (15) | −0.507 | 1.11 | 11.06 | 11.8 |
| DABCO | −0.635 | 1.22 | 11.97 | 11.4 |
| $[\text{P}_{4441}]\text{N(CH}_2\text{)}_2\text{mim}^+$ (16) | −0.840 | 1.57 | 11.50 | 0.0 |
| DIPEA | −0.836 | 1.50 | 12.06 | 0.0 |

Although the actual values of the partial charge $q_N$ in Table 2 are generally not an ideal measure for the basicity of the nitrogen atoms,$^{[22,23]}$ relative trends for the basicity can still be observed when altering moieties of the compound. Except for the isopropyl amine compounds the charge density of the alkaline nitrogen is reduced by roughly 0.15e in the cationic compound compared to the pure base which probably corresponds to lower basicities of the charged compounds. This fact is confirmed by the respective proton affinities (PA) in Table 2. Lower proton affinities are usually correlated with lower basicity of the nitrogen atoms.$^{[22,23]}$

However, arguments solely based on the Bronsted basicity cannot explain the failure of the compounds 15 and 16 as the
alkaline nitrogen atoms in these compounds should have a higher basicity compared to those in 13 and 14. The flexibility of the electron cloud at the alkaline nitrogen is characterized by its polarizability $\alpha_N$. Consequently, the ability to donate the lone pair to a Lewis electron acceptor should scale with the atomic polarizability on the nitrogen. Unfortunately, the nitrogen polarizabilities in Table 2 show no clear trend.

The majority of Lewis acid-base reaction involve $n \rightarrow \sigma^*$ or $n \rightarrow \pi^*$ molecular orbital interactions. The corresponding non-bonding HOMO of the alkaline ionic liquid cations are depicted in Figure 5. In contrast to the other cations, the $n$-orbital of $[\text{C}_4\text{DABCO}]^{+}$ has a deformed shape for a non-bonding molecular orbital which may indicate less effective interaction with the $\sigma^*$ or $\pi^*$ molecular orbital of the Lewis acid and thereby reducing the obtained yield in Table 2.

In addition to the electrostatic and energetic properties as well as the molecular orbitals discussed so far, steric reasons may also play a role for the interaction of the catalyst with the base. As visible from the solvent accessible surface (SASA) of the alkaline nitrogen in Table 2 the nitrogen of $[\text{C}_4\text{DMAP}]^+$ is more accessible compared to $[\text{C}_4\text{DBU}]^{+}$ which may explain the higher TOF and TON values in Table 1. In contrast, the alkaline nitrogen atom in $[\text{Pr}(\text{N})_{\text{CH}_3}]\text{mim}^+$ and DIPEA seems to be sterically more hindered, thereby prohibiting any contact of the nitrogen and the catalyst.

After identifying the most suitable ideal liquid for the biphasic reaction set-up, we addressed substrate scope and application range for a set of (hetero-)aromatic and aliphatic aldehydes (Figure 6). To separate product and catalyst, the heptane phase was simply removed via decantation. Although the product was obtained in high purity without traces of starting material, catalyst, base or ionic liquid, evaporation of n-heptane gave the product 4-fluorobenzylalcohol only in poor yield of 12%. To increase the yield, the catalyst containing phase was successively extracted with diethyl ether to collect any remaining product. This resulted in an improved isolated yield of 93%. While we did not observe any leaching of the iron-based catalysts due to its extremely low solubility in diethyl ether, the increased solubility of phosphonium-based ionic liquid $[\text{P}_{4441}]\text{N(Tf)}_2$ 4 resulted in trace contamination of the diethyl ether extract. Consequently, an additional filtration step over a batch of silica was performed to remove traces of ionic liquids and to obtain a pure product. This extraction with diethyl ether was routinely performed in the substrate screening to provide reliable results, since all products and - in case of uncomplete reaction – aldehyde starting materials could be extracted with diethyl ether.

In general, good to excellent yields were achieved for aromatic systems, even in the presence of coordinating groups. Similar results were found for the heterocyclic substrates pyridine-2-carboxaldehyde, furfural and thiophene-2-carboxaldehyde with high isolated yields, whereas the reduction failed with $N$-methyl-pyrrol-2-carboxaldehyde aldehyde. This is in accordance with our previous observations using ethanol as solvent, indicating an unfavorable interaction between the Fe(II) PNP catalyst and pyrrolo-based heterocycles. The reduction of aliphatic aldehydes was more challenging and gave variable results. While the branched long-chain aliphatic aldehyde 2-ethylhexanal was not reduced, moderate yields were observed with octanal. Moderate to high yields were obtained for selected unsaturated aldehydes. It is particularly worth noticing that the chemoselective behavior for the reduction of aldehydes was preserved in the biphasic set-up, since unsaturated aldehydes such as the challenging $\alpha,\beta$-unsaturated substrates cinnamic aldehyde and citral were selectively reduced to unsaturated alcohols that are of particular importance for the flavor and fragrance industries.

Apart from the benefits of simple product separation, liquid-liquid biphasic catalysis also offers a powerful tool for catalyst recovery and recycling. However, initial attempts to recover the Fe(II) PNP catalyst after product extraction failed. Independent of the ionic liquid, we did not observe any conversion when fresh starting material was added. Further studies on long-term stability of the catalyst in ionic liquids showed that the activated dihydride species is considerable less stable (see ESI Figure 1). $^{31}\text{P}({^1}\text{H})$ NMR spectroscopy indicated the rapid formation of several intractable decomposition products when the pre-formed dihydride complex was kept in $[\text{P}_{4441}]\text{N(Tf)}_2$, 4. This is a considerable difference and drawback compared to pre-catalyst I, which is stable in $[\text{P}_{4441}]\text{N(Tf)}_2$, 4 even for one week according to $^{31}\text{P}({^1}\text{H})$ NMR spectroscopy. It was however possible to show a certain reusability of the catalyst immobilized in $[\text{P}_{4441}]\text{N(Tf)}_2$, 4 via a semi-continuous addition of substrate (Figure 7). After 10 min reaction time a fresh batch of 4-fluorobenzaldehyde (2 mmol) was added to prevent decomposition of the active. With this strategy, the catalyst remained active for four consecutive runs and a total of 5.2 mmol starting material can be converted. Similar experiments with the Brønsted-basic ionic liquids $[\text{C}_4\text{DMAP}]\text{N(Tf)}_2$ 13 and...
catalytic activity due to partial decomposition of the Fe(II) and reuse of the catalyst for three runs, although losses in the catalyst containing ionic liquid allowed for a certain recovery for the use of supported catalysts, the facile separation of the phase could be detected. Hydrogenation of a set of aliphatic derivatization of the ligand, and no leaching in the organic base, the necessity of an addition extractions step with diethyl ether in order to obtain high isolated yields of the formed system. A customized single-element (Merck, Roth) standard was used for the calibration.

X-ray diffraction data of \([\text{C}_{4}\text{DMAP}][\text{Cl}], \text{CCDC entry } 1825413\) were collected at \(T = 100\) K in a dry stream of nitrogen on a Bruker Kappa APEX II diffractometer system using graphite-monochromatized Mo-K\(x\) radiation (\(\lambda = 0.71073\) Å) and fine sliced \(\eta\)- and \(\omega\)-scans. Data were reduced to intensity values with SAI\(N\) and an absorption correction was applied with the multi-scan approach implemented in SADABS.\(^{25}\) The structure was solved by the dual space method implemented in SHELXT\(^{26}\) and refined against \(P^2\) with JANA2006.\(^{27}\) Non-hydrogen atoms were refined anisotropically. H atoms were placed in calculated positions and thereafter refined as riding on the parent C atoms. A chloroform solvent molecule was modelled as disordered about three positions. Molecular graphics were generated with the program MERCURY.\(^{28}\) Crystal data and experimental details are given in Table S1 in ESI.

Quantum-chemical geometries of the compounds were optimized with GAUSSIAN09\(^{29}\) using B3LYP/6-311+G(2d,2p) and a polarizable continuum model (PCM) with the dielectric constants \(\varepsilon(0) = 14.0\) and \(\varepsilon(\infty) = 2.1\) mimicking solvation in the ionic liquids \([\text{C}_m\text{mim}][\text{NTf}_2]\) or \([\text{C}_m\text{mim}][\text{NTf}_2]\). Partial charges were determined by chelpg\(^{30}\) using \(\text{mp}897\text{XD/ aug-cc-pVTZ}/\text{PCM}\) to account for polarizable and dispersion effects. Atomic polarizabilities were obtained by applying a electric field of 0.0008 au in positive and negative \(x\)-, \(y\)- and \(z\)-direction using M06-2X/Sadlej.\(^{31}\) Computational proton affinities \(\text{PA}\)\(^{32,33}\)

\[
\text{PA} = (\text{E}(\text{A}) + \text{ZPE}(\text{A})) - (\text{E}(\text{HA}^+) + \text{ZPE}(\text{HA}^+))
\]

were evaluated from the difference of the total energy of the protonated species \(\text{HA}^+\) and the neutral species \(\text{A}\). Since the protonation adds additional vibrational degrees of freedom, both total energies were corrected for their respective zero-point vibrational energy \(\text{ZPE}\). The molecular orbitals were visualized using VMD\(^{34}\) with an iso value of 0.08. The solvent accessible surface (SASA) was calculated by VMD using a probe radius of 1.4 Å.

All ionic liquids \(1-10\) were synthesized according to standard methodologies, and analytical data was in accordance with literature. The ionic liquids were dried for at least 48 h with stirring at \(10^{-2}\) bar and \(50\) °C before use and stored under argon catalyst in the absence of hydrogen could not be avoided. Eventually, the design of targeted Brønsted basic ionic liquids can eliminate the necessity of base addition and facilitate the reaction set-up towards the future design of continuous flow processes.

**Experimental Section**

All used reagents and solvents were purchased from commercial suppliers and directly used without further purification, if not stated otherwise. Anhydrous \(\text{CH}_2\text{Cl}_2, \text{Et}_2\text{O}, \text{n-heptane, MeOH, THF}\) and toluene were dried over molecular sieve and/or via Na/K alloy and degassed via pump freezing. \(\text{H}^\text{31P}[\text{H}]\text{NMR were recorded in acetonitrile-d}_6, \text{chloroform-d}_6, \text{methylene chloride-d}_6, \text{dimethylsulfoxide-d}_6\) or methanol-d\(_6\) solution on a Bruker Avance 200 (200 MHz) or Bruker Avance 250 (250 MHz). All chemical shifts (\(\delta\)) are reported in ppm, using tetramethylsilane for \(\text{H}\), trichlorofluoromethane for \(19\text{F}\) and \(\text{H}_3\text{PO}_4\) (85 %) for \(31\text{P}\) NMR spectra. All coupling constants \(J\) are reported in Hertz (Hz).

Determination of Fe concentrations was done using an inductively coupled plasma (ICP) optical emission spectrometer PerkinElmer OPTIMA 8300 equipped with an SC-2 DX FAST sample preparation system. A customized single-element (Merck, Roth) standard was used for the calibration.

In summary, we showed that hydrophobic ionic liquids in combination with \(n\)-heptane can be used as biphasic reaction media for the iron (II) catalyzed hydrogenation of aldehydes. The presented liquid-liquid biphasic process presents a novel and improved methodology compared to the homogenous reaction in terms of product isolation and catalyst separation. The iron (II) PNP pincer complex catalyst was efficiently immobilized in the ionic liquid phase without requiring any derivatization of the ligand, and no leaching in the organic phase could be detected. Hydrogenation of a set of aliphatic and aromatic aldehydes including unsaturated species was performed under comparatively mild conditions (25 °C, 1 h, 10 bar \(\text{H}_2\)). However, while the products were typically obtained in high purities without contamination from catalyst, ligand or base, the necessity of an addition extractions step with diethyl ether in order to obtain high isolated yields of the formed alcohols reduction the utility of the biphasic system for this particular application. Clearly, a reduced amount of ionic liquid as used in our previous study with supported ionic liquid phases (SILPs) is beneficial and can overcome this issue.\(^{31}\) As for the use of supported catalysts, the facile separation of the catalyst containing ionic liquid allowed for a certain recovery and reuse of the catalyst for three runs, although losses in the catalytic activity due to partial decomposition of the Fe(II) combination with \([\text{C}_4\text{DBU}][\text{NTf}_2]\) 14 were less successful as the catalytic activity ceased already after the first run.

**Conclusions**

![Figure 7. Cumulative turnover of 4-fluorobenzaldehyde in biphasic reaction media using \([\text{PNP}][\text{NTf}_2]\) 4, \([\text{C}_4\text{DMAP}][\text{NTf}_2]\) 13 or \([\text{C}_4\text{DBU}][\text{NTf}_2]\) 14 to immobilize the iron-based pre-catalyst \(\text{Fe(PNP)}(\text{H})(\text{Br})(\text{CO})\) (I). Performed with 2 mmol aldehyde each run and 0.5 mol % pre-catalyst in 250 mg ionic liquid/1.5 ml \(n\)-heptane.

...
Synthesis of 1-butyl-4-(dimethylamino) pyridine-1-ium Chloride ([CDBU][Cl])

N,N-Dimethylpyridinium-4-amine (11.4 g, 93 mmol) was dissolved in anhydrous acetonitrile and freshly distilled 1-chlorobutane (16.9 g, 180 mmol) was added in one batch. The reaction mixture was refluxed for four days. During the reaction, the product precipitated from the reaction mixture as colorless solid. The solid was separated from the solution via filtration, washed three times with diethyl ether and dried under high vacuum to yield [CDBU][Cl] as colorless solid (19.2 g, 96 %). 1H NMR (200 MHz, methylene chloride-d2) δ = 0.81 ppm (d, J = 5.9 Hz, 2H), 1.91–1.69 (m, 8H), 1.62 (quint, J = 15.5, 7.5 Hz, 2H), 0.98 ppm (t, J = 7.3 Hz, 3H).

Synthesis of 1-butyl-4-(dimethylamino) pyridin-1-ium bis(trifluoromethane) sulfonylimide ([CDBU][N(Tf)2])

[CDBU][Cl] (7.0 g, 32.7 mmol) was dissolved in H2O and lithium bis(trifluoromethane) sulfonylimide (10.3 g, 35.9 mmol) in H2O was added dropwise. The mixture was stirred for one hour at room temperature. The biphasic reaction mixture was extracted three times with CH2Cl2. The combined organic phases were washed repeatedly with MilliQ-grade H2O until no chloride anions could be detected. The organic phase was dried over Na2SO4, filtrated and the solvent was removed. Remaining volatiles were removed under high vacuum with stirring at 50 °C to yield [CDBU][N(Tf)2] as colorless liquid (12.9 g, 86 %). 1H NMR (200 MHz, methylene chloride-d2) δ = 0.64 ppm (d, J = 7.8 Hz, 2H), 6.92 ppm (d, J = 7.8 Hz, 2H), 4.27 ppm (t, J = 7.3 Hz, 2H), 3.16 ppm (s, 6H), 1.77 ppm (q, J = 7.5 Hz, 2H), 1.39–1.18 (m, 2H), 0.88 ppm (t, J = 7.3 Hz, 3H).

Synthesis of 1-octyl-4-diazabicyclo[2.2.2]octan-1-ium bis(trifluoromethane) sulfonylimide ([C8DABCO][N(Tf)2])

[C8DABCO][Cl] (5.0 g, 17.2 mmol) was suspended in dichloromethane. Sodium hydroxide (0.7 g, 17.2 mmol) dissolved in water and added. The biphasic system was stirred for ten minutes at room temperature. Sodium hydroxide (0.7 g, 17.2 mmol) dissolved in water and added. The biphasic reaction mixture was extracted three times with CH2Cl2. The combined organic phases were washed repeatedly with MilliQ-grade H2O until no more chloride anions could be detected. The organic phase was dried over Na2SO4, filtrated and the solvent was removed. Remaining volatile traces were removed under high vacuum with stirring at 50 °C to yield [C8DABCO][N(Tf)2] as light yellow solid (5.9 g, 39 %). 1H NMR (250 MHz, methylene chloride-d2) δ = 3.36–3.09 ppm (m, 14H), 1.8–1.68 (m, 2H), 1.46–1.20 ppm (m, 13H), 0.98 ppm (t, J = 7.1 Hz, 3H).

Synthesis of 1-(2-(diisopropylamino)ethyl)-3-methyl-imidazolium Chloride

A round bottom flask was charged with 2-(diisopropylamino)ethylchloride hydrochloride (14.01 g, 70 mmol) and 1-methylimidazole (8.9 g, 97 mmol). The mixture was suspended in anhydrous ethanol and refluxed for 2 days. The solid was collected via filtration, washed repeatedly with anhydrous THF and dried under vacuum to yield [Pr2N(CH2)2mim][Cl] as colorless solvent (17.10 g, 85 %). 1H NMR (250 MHz, chloroform-d3) δ = 7.37–3.37 ppm (m, 8H), 2.88–2.75 ppm (m, 2H), 2.13 ppm (t, J = 5.9 Hz, 2H), 1.91–1.69 ppm (m, 8H), 1.62 ppm (quint, J = 15.5, 7.5 Hz, 2H), 1.37 ppm (q, J = 7.3 Hz, 2H), 0.98 ppm (t, J = 7.2 Hz, 3H).

Synthesis of 1-(2-(diisopropylamino)ethyl)-3-methyl-imidazolium Sulfonylimide

[Pr2N(CH2)2mim][N(Tf)2] (5.0 g, 17.2 mmol) was suspended in dichloromethane. Sodium hydroxide (0.7 g, 17.2 mmol) dissolved in water and added. The mixture was stirred for one hour at room temperature. Sodium hydroxide (0.7 g, 17.2 mmol) dissolved in water and added. The mixture was stirred for one hour at room temperature. The mixture was stirred for ten minutes at room temperature. The biphasic reaction mixture was extracted three times with CH2Cl2. The combined organic phases were washed repeatedly with MilliQ-grade H2O until no more chloride anions could be detected.
organic phase was dried over Na2SO4, filtered and the solvent was removed. Remaining volatile traces were removed under high vacuum with stirring at 50°C to yield [Pr2N(CH2)2mim][NTf2], 16 as colorless liquid (7.7 g, 88%). 1H NMR (250 MHz, methylene chloride-\text{d}_2) \delta = 8.49 (s, 1H), 7.25 (t, J = 1.8 Hz, 1H), 7.15 (t, J = 1.8 Hz, 1H), 4.04 (d, J = 6.1 Hz, 2H), 3.84 (s, 3H), 2.92 (hept, J = 6.6 Hz, 2H), 2.72 (t, J = 5.5 Hz, 2H), 0.81 ppm (d, J = 6.6 Hz, 12H).

General Procedure for the Hydrogenation of Aldehydes on the Example of 4-fluorobenzaldehyde 11

All hydrogenation reactions were carried out in a 20 mL screw-cap tube with a TeCSi autoclave using a 10 mL working volume. The autoclave was charged with substrate (2 mmol), DBU (0.1 mmol) and [Pr2N(CH2)2mim][NTf2] (0.1 mmol) in a glove box and placed into the autoclave. The autoclave was equipped with a stirrer and a steel valve. The steel valve was closed and the autoclave was evacuated and flushed with argon three times. The hydrogen pressure was adjusted to 10 bar (0.01 mmol) in a glove box and placed into the autoclave. The autoclave was released. Fresh 4-fluorobenzaldehyde (2 mmol) in \text{CHCl}_3 \text{d}_2) was added and the autoclave was flushed with argon three times. The hydrogen pressure was adjusted to 10 bar (0.01 mmol) and the reaction was stirred at 25°C for 10 min. The desired hydrogen pressure (10 bar) was established and the reaction was stirred at 50°C for 60 min. The pressure was released. The organic and ionic liquid phase was separately collected and the reaction mixture was filtered over silica and the solvent was evaporated. The obtained crude products were purified by flash column chromatography to yield the desired alcohols in spectroscopically pure form.

Acknowledgements

Financial support by the Austrian Science Fund (FWF) is gratefully acknowledged (Project No. P28866-N34 and P29146-N34).

Conflict of Interest

The authors declare no conflict of interest.

Keywords: Hydrogenation · aldehydes · iron · pincer complexes · ionic liquids · biphasic catalysis

[1] a) P. Chink, R. Morris, Acc. Chem. Res. 2015, 48, 2495–2495. b) G. A. Filonenko, R. van Putten, E. J. M. Hensen, E. A. Pidko, Chem. Soc. Rev. 2018, 47, 1459–1483. c) F. Kallmeier, R. Kempe, Angew. Chem. Int. Ed. Engl. 2018, 57, 46–60.
