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Hydroaminomethylation of *n*-Alkenes in a Biphasic Ionic Liquid System

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Abstract: Hydroaminomethylation reactions were performed successfully in an imidazolium-based ionic liquid using a rhodium/sulfoxantphos system by reacting piperidine with different *n*-alkenes, affording yields higher than 95% of the resulting amine with turnover frequencies of up to 16,000 h^{-1}, along with high regioselectivity for the linear amines with l/b ratios up to 78. Additionally, facile quantitative catalyst recovery was accomplished and recycling of the catalyst and product separation was achieved by a fast phase separation after the reaction. The product distribution was monitored over time at different temperatures both in an organic solvent and in the ionic liquid in order to investigate and compare the course of the formation of (side) products and intermediates in these reactions. Furthermore, it was shown that the nature of the rhodium precatalyst has a profound effect on the activity and selectivity. Protic organic solvents and ionic liquids containing a C–H acidic bond in the imidazolium part have a beneficial effect on the hydrogenation activity of the catalyst systems.

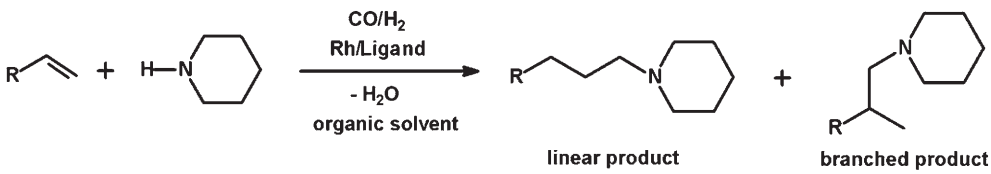
Keywords: biphasic catalysis; catalyst recycling; green chemistry; homogeneous catalysis; hydroaminomethylation; ionic liquids

Introduction

Amines are of great importance as building blocks in the chemical industry.[1] Aliphatic primary amines are especially important bulk and fine chemicals with a million ton-scale production per year. Investigations into improved access to these intermediates in terms of atom efficiency and waste reduction have received constant attention over recent years. With this goal in mind, a very interesting route is the hydroaminomethylation reaction (HAM). This reaction was first discovered in 1949 by Reppe and co-workers at BASF.[2,3] In this transition metal-catalysed one-pot cascade reaction an alkene is hydroformylated to an intermediate aldehyde which, in the presence of a primary or secondary amine or even ammonia, reacts to an imine or enamine. This imine or enamine can finally be hydrogenated to yield the amine product (Scheme 1). Good yields and high selectivities can be achieved in common organic solvents.[4–6]

Although linear and branched amines can both be formed in this HAM reaction, linear amines are the more desired products regarding current industrial applications since they can be used as building blocks for polymers. Control of the regioselectivity is therefore an important issue in this reaction. Since the regioselectivity of the hydroaminomethylation is implemented in the hydroformylation step, ligands that were developed for regioselective hydroformylation towards *n*-aldehydes, such as naphos or xantphos-type ligands, are promising candidates to be used in this reaction and are likely to give good regioselectivities.[6–8]

However, there are still substantial problems to be overcome. In the case of ammonia and primary



Scheme 1. Hydroaminomethylation of *n*-alkenes with piperidine.

amines as the substrates, the stronger nucleophilic products react preferably with the intermediate aldehyde, ultimately leading to tertiary amines. Hence, high selectivity towards primary or secondary amines is difficult to achieve. This can be partially tackled by a large excess of the starting amine or by *in situ* product separation. Several approaches, such as catalyst immobilisation and conducting the reaction in a biphasic system have been followed in order to improve the performance and selectivity in this reaction.[9–14]

One of these approaches includes HAM reactions in ionic liquids. In 1972, Parshall described the hydroformylation of ethene in molten salts. However, the melting points of these media were above 60 °C, creating some difficulties in handling these systems since they are solid at room temperature.[15] Further examples of hydroformylation in similar media or room-temperature ionic liquids (RTILs) appeared in the following decades.[16] More recent examples by Van Leeuwen et al. demonstrated the application of hydroformylation in ionic liquids,[17] and the use of sulfoxantphos as a suitable ligand system.[18] Wang et al. have recently shown the successful application of HAM in an ionic liquid-based biphasic system.[19] However, no data concerning activity, product distribution during this reaction or the influence of different parameters have been reported up to now for the HAM in ionic liquids. In addition, there is still some room for improvement of the regio- and chemoselectivity

The contributions of ionic liquids[16,20,21] to this reaction are mainly to be seen in their negligible vapour pressure, their thermal stability and their ability to form biphasic systems with a good deal of organic compounds, facilitating the product recovery and the possibility to abandon classical solvents. Another important quality of ionic liquids is the virtually unlimited number of combinations of anions and cations, offering the possibility to tailor the ionic liquid for the needs of a reaction system in a modular approach.

We have chosen the low-viscous 1-methyl-3-pentylimidazolium tetrafluoroborate [PMIM][BF_4], which is immiscible with the hydroaminomethylation products, as the reaction medium for the Rh/sulfoxantphos[22,23] system (Figure 1). A facile product recovery is therefore anticipated.

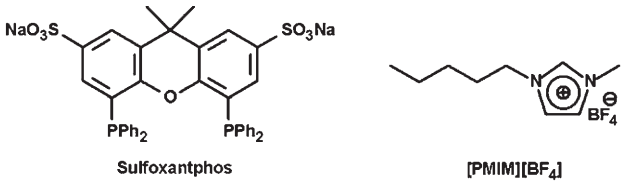


Figure 1. The water-soluble sulfoxantphos ligand and the ionic liquid [PMIM][BF_4].

We report here on detailed studies of the performance of a catalyst system in ionic liquids, giving high chemo- and regioselectivity to linear amines in the hydroaminomethylation reaction of *n*-alkenes with piperidine. We achieved effective catalyst recycling and included a method in which substrates were simply added to the reaction mixture. Additionally, the turnover frequencies were determined to get more insight into the activity of the system under different circumstances. Furthermore, the influences of the reaction time, reaction temperature and the substrate-to-rhodium (S/Rh) ratio were investigated by monitoring the product distribution during the course of the hydroaminomethylation reaction.

Results and Discussion

The hydroaminomethylation reaction was first investigated in [PMIM][BF_4], applying the Rh/sulfoxantphos system and 1-octene and piperidine as the substrates. Formation of a biphasic system was observed, facilitating the product recovery enormously. In addition, a good activity and selectivity could be obtained (Table 1). Furthermore, it was confirmed in a glass autoclave that the catalytic system was not only biphasic

Table 1. Hydroaminomethylation of 1-octene in IL; recycling experiments and comparison to hydroaminomethylation in toluene/MeOH.[a]

Entry	Cycle	S/Rh	Conversion [%]	Conversion 1-octene [%]	Isomerised octene [%]	Selectivity (amine) [%]	l/b
1	1	1150	94.4	99.2	4.8	98.6	52.1
2	2	2750	96.2	99.7	3.5	99.2	27.3
3	3	8850	86.1	96.9	10.8	93.7	11.8
4[b]	4	8850	92.3	99.1	6.8	82.5	2.5
5[c]	-	1150	94.4	99.3	4.9	87.3	62.0

[a] *Conditions:* 1-octene 7–25 mmol, piperidine 8–29 mmol, ionic liquid [PMIM][BF_4] 8 mL, [$Rh(cod)_2BF_4$] = 0.02–0.09 mol %, L/Rh = 3.8, T = 125 °C, $p(CO/H_2$ [1:2]) = 36 bar (cold pressure), t = 17 h.
[b] t = 90 h.
[c] Solvent: toluene/MeOH (1:1) 8 mL.

at room temperature, but also at the reaction temperature (125 °C). Although the regioselectivity was slightly lower in the IL compared to the Rh/xantphos system in toluene/MeOH (Table 1, *cf.* entries 1 and 5), the selectivity to the amine was improved. The conversion in the IL was comparable to that in toluene/MeOH and a higher S/Rh ratio could be used without formation of considerable amounts of aldol condensation products and *N*-formylpiperidine, which were the main side products in the reaction performed in toluene/MeOH.

Using the sulfonated system in the ionic liquid, the product layer could be completely removed, new substrates were added to the IL and the reaction was performed again. In this way the catalyst could be reused several times keeping conversion and especially chemoselectivity at a high level, while only the regioselectivity decreased considerably (Table 1, entries 1–4). In this case the drop in regioselectivity is attributed to partial oxidation of the ligand during phase separation, since the complete reaction mixture was removed from the autoclave for this purpose. As shown in Table 1, it is important to distinguish between total conversion (column 4), which is the conversion of all alkenes (1-octene and internal alkenes) and conversion of solely 1-octene (column 5). The latter is the conversion of only 1-octene present in the reaction mixture at that time. By the time this conversion of 1-octene reaches 99%, only the remaining internal alkenes can be reacted, leading to more branched product.

To overcome the problem of ligand oxidation, two possible solutions were investigated. In the first case, the product layer was removed from the autoclave by syringe under a flow of argon leaving the IL-catalyst solution in the autoclave. New deoxygenated substrate was immediately added and the reaction was performed again. In the second approach the layer separation was avoided completely and new substrates were simply added to the reaction mixture at the end of the preceding reaction.

Both options gave very satisfying results. Table 2 shows the results of recycling the catalyst solution by adding new and even different substrates using the same catalyst solution. In this procedure new alkene was added without removing the product layer in between the runs (Table 2, entries 1–3). After the third reaction was complete the product layer was removed and analysed. The catalyst solution in the IL was used again and the same procedure of simply adding new substrate was followed for entries 4 and 5 (Table 2). Conversion, chemo- and regioselectivity were in the same range for the different alkenes. However, in the case of lower conversion of around 89% (Table 2, entry 5), the results suggested an increased chemoselectivity of up to 97.3% to the amine. The decrease in regioselectivity for entry 5 might be due to the fact that a small amount of internal octenes, which were formed by isomerisation in the first run, remained in the IL leading to a lower l/b ratio in the end.

The results of the recycling experiments, in which only the product layer and not the catalyst solution was removed from the autoclave after the reaction, are summarised in Table 3. Again, conversion and chemo- and regioselectivity were very satisfying. The low chemoselectivity in entry 3 (Table 3) is merely due to a certain amount of incompletely hydrogenated enamine, which can be regarded as a reaction intermediate of the product. After the final run, the catalyst solution was removed from the autoclave and extracted with Et_2O. The ether extract was analysed (Table 3, entry 4) for comparison with the result from the product layer analysis (Table 3, entry 3). Both results are identical, indicating that analysis of the reaction mixture can be performed both *via* direct analysis of the product layer as well as after extraction of the IL phase.

The product phase in these recycling experiments was investigated for rhodium and phosphorus leaching by means of ICP-OES. It turned out that the amount of Rh was close to the detection limit (<0.09%) while the P leaching was determined to be 0.45%. Furthermore, the solubility of a PMIM-sulfoxantphos species in the organic layer was determined by means of NMR spectroscopy. Traces of the ionic liquid could be detected by ^{1}H NMR and ^{19}F NMR

Table 2. Hydroaminomethylation of *n*-alkenes in IL; recycling experiments by addition of different substrates without phase separation.[a]

Entry	Cycle	S/Rh	Substrate	Conversion [%]	Conversion 1-alkene [%]	Isomerised alkene (%)	Selectivity (amine) [%]	l/b
1	1	1800	1-octene	96.4	99.6	3.2	90.8	35.1
2	2	4500	1-decene	88.4	95.8	7.4	96.5	44.4
3	3	4500	1-hexene	92.7	95.9	3.2	92.4	33.5
4	4	3600	1-dodecene	87.8	96.1	8.1	96.8	20.0
5	5	3600	1-octene	89.1	99.5	11.7	97.3	18.1

[a] *Conditions:* alkene 10–22 mmol, piperidine 12–25 mmol, ionic liquid [PMIM][BF_4] 7 mL, [$Rh(cod)_2BF_4$] = 0.02–0.06 mol%, L/Rh = 4.5, T = 125 °C, p(CO/H_2 [1:2]) = 36 bar (cold pressure), t = 18 h.

Table 3. Hydroaminomethylation of *n*-alkenes in IL; recycling experiments with phase separation in the autoclave.[a]

Entry	Cycle	Substrate	Conversion [%]	Conversion 1-alkene [%]	Isomerised alkene [%]	Selectivity (amine) [%]	l/b
1	1	1-octene	92.8	99.2	6.4	99.0	27.7
2	2	1-hexene	94.1	97.2	3.1	93.4	38.3
3	3	1-octene	89.8	97.9	8.1	79.8	32.7
4[b]	3	1-octene	89.7	98.2	8.5	79.9	33.1

[a] *Conditions:* alkene 19–24 mmol, piperidine 22–28 mmol, ionic liquid [PMIM][BF_4] 7 mL, [Rh(cod)$_2$$BF_4$] = 0.03 mol %, L/Rh = 3.7, S/Rh = 4000, T = 125 °C, p(CO/H_2 [1:2]) = 36 bar (cold pressure), t = 17 h, analysis of product layer.
[b] Analysis of extraction layer (Et_2O) after extraction of IL phase.

spectroscopy, suggesting IL leaching, while the ^{31}P NMR spectrum did not reveal any ligand leaching. Apparently, a small amount of the IL was dissolved in the product phase whereas almost no Rh and ligand P leaching could be detected.

The influence of parameters such as temperature, reaction time, and S/Rh ratio was investigated as presented in Table 4. Obviously, when applying larger S/Rh ratios, the conversion is expected to decrease to some extent at a given reaction time, corresponding to the intrinsic kinetics. However, the S/Rh ratio does not affect the conversion and selectivity to a large extent at T = 125 °C and 18 h reaction time, showing that the catalyst is fast (Table 4, entries 1–3). As expected, the reaction time has a large influence on the l/b ratio. A key point here is the fact that the hydroformylation rate of 1-alkenes is much higher than the rate for internal alkenes, formed by slow isomerisation throughout the course of the reaction. The conversion of the 1-alkenes is always virtually complete (> 99 %) after 18 h (Table 4, entries 1–4). This effect of the reaction time on the l/b ratio is well documented for the hydroformylation of terminal alkenes where isomerisation plays a role.[24] The internal alkenes, accumulating during the reaction, are especially converted at high conversion (longer reaction time) thereby lowering the l/b ratio in time. This effect is also present in the hydroaminomethylation as depicted in Figure 2. Therefore, shortening the reaction time and lowering the reaction temperature will most probably lead to higher l/b ratios because of the decreased isomerisation rate under these conditions.

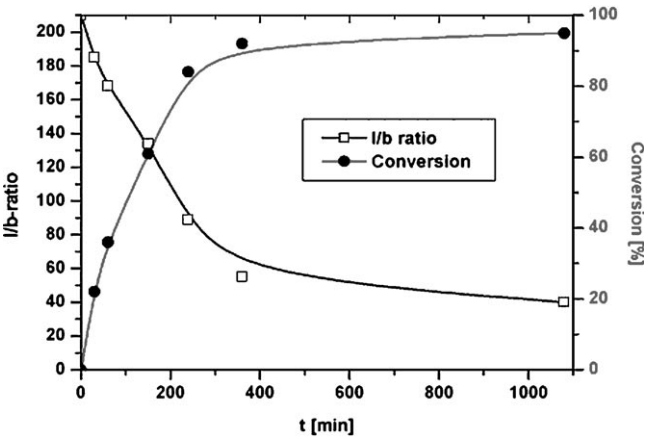


Figure 2. Conversion and l/b ratio of a hydroaminomethylation reaction over time.

Accordingly, the reaction temperature mainly affects the regioselectivity. Lowering the reaction temperature from T = 125 °C to T = 110 °C leads to an increased l/b ratio (Table 4, cf. entries 1 and 4), caused by the slower isomerisation of 1-octene at lower tem-

Table 4. Hydroaminomethylation of 1-octene in IL; effects of different parameters on activity and selectivity.[a]

Entry	Cycle	T [°C]	S/Rh	t [h]	Conversion [%]	Conversion 1-octene [%]	Isomerised octene [%]	Selectivity (amine) [%]	l/b
1	1	125	750	18	94.3	99.4	5.1	94.9	28.1
2	-	125	3750[b]	18	93.2	99.2	6.0	97.7	30.2
3	-	125	4700[b]	18	92.7	99.1	6.4	96.0	29.5
4	2	110	750	18	94.1	99.3	5.2	93.4	44.8
5	3	110	750	6	90.1	96.7	6.6	76.0(87.7)[c]	68.5
6	4	110	750	6	91.2	97.7	6.5	65.6(78.9)[c]	72.8
7	5	110	750	4	89.2	95.4	6.2	46.7(77.3)[c]	78.4

[a] *Conditions:* 1-octene 18 mmol, piperidine 21 mmol, ionic liquid [PMIM][BF_4] 6 mL, [Rh(cod)$_2$$BF_4$] = 0.13 mol %, L/Rh = 4.0, p(CO/H_2 [1:2]) = 36 bar (cold pressure).
[b] [Rh(cod)$_2$$BF_4$] = 0.025 mol %.
[c] Enamine reaction intermediate included in calculation.

perature and the higher hydroformylation rate of 1-octene compared to the internal isomers. As expected, limiting the conversion by shortening the reaction time has a profound effect on the regioselectivity. A high l/b ratio of 78 after only 4 h reaction time was observed (Table 4, entry 7), while the conversion of 1-octene is actually only slightly lower.

Strikingly, the amine selectivity dropped even to 46.7% upon recycling, as shown in entries 5–7 of Table 4. However, this effect is partially due to the fact that the intermediate enamine, being the only other major component in the reaction mixture besides linear amine and aldol condensation product, is not included as a product in the calculation of amine selectivity, but as a nitrogen-containing side product. Possibly, the reaction rate of the hydroformylation reaction is fast in comparison to that of the condensation reaction and hydrogenation of the enamine, leading to an accumulation of aldehyde, which could account for the considerable amount of aldol product formed. Another possibility might be the accumulation of water formed during the reaction in the IL (Scheme 1) leading to a higher reaction rate of the aldol condensation upon recycling the catalyst. Removing the water by evaporation under reduced pressure after several catalytic runs might solve this problem.

Monitoring the product distribution over time (Figure 3), the influence of the temperature and the reaction time was studied in more detail and the hydroaminomethylation reaction was performed in toluene/MeOH as well as in the IL at $T=110\,^{\circ}C$ and $T=125\,^{\circ}C$. During the reaction in the organic solvent, samples were taken from the reaction mixture *via* a capillary and analysed by GC.[25] It was found that the hydroaminomethylation in organic solvent was fast at both temperatures, although the reaction was faster at $T=125\,^{\circ}C$. At the latter temperature a transient accumulation of enamine was observed implying that the hydrogenation of the enamine was slower than the hydroformylation and condensation reaction. For the reaction in organic solvent at $T=110\,^{\circ}C$ the rate of hydrogenation seems to be more in balance with the hydroformylation, since no accumulation of enamine

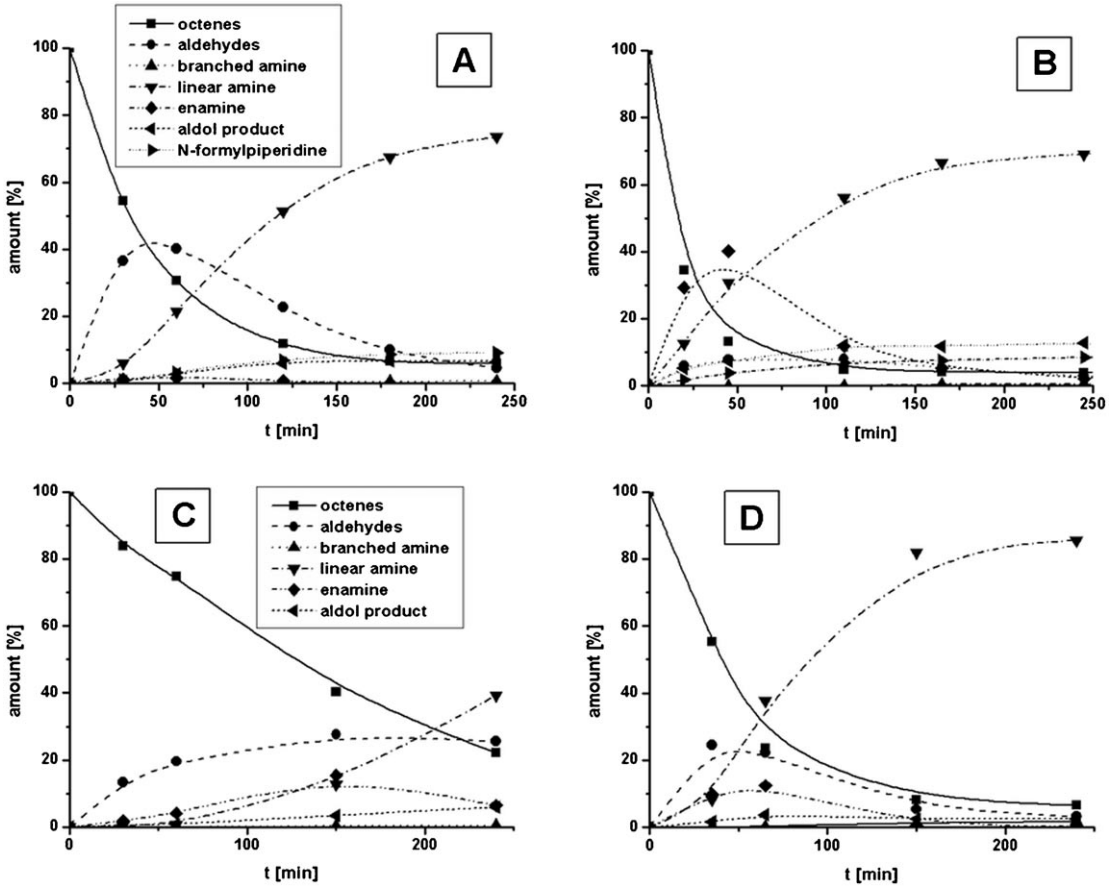


Figure 3. Product distribution during the hydroaminomethylation reaction of 1-octene. **A:** toluene/MeOH; 110 °C; **B:** toluene/MeOH; 125 °C. *Conditions:* 1-octene 9 mmol, piperidine 11 mmol, toluene/MeOH (1:1) 4 mL, $[Rh(cod)_2BF_4]=0.1$ mol%, S/Rh = 1000, L/Rh = 4.0, $p(CO/H_2\ [1:2])=36$ bar (cold pressure). **C:** IL; 110 °C; **D:** IL; 125 °C. *Conditions:* 1-octene 13 mmol, piperidine 15 mmol, ionic liquid [PMIM][BF_4] 4 mL, $[Rh(cod)_2BF_4]=0.1$ mol%, S/Rh = 1050, L/Rh = 4.0, $p(CO/H_2\ [1:2])=36$ bar (cold pressure).

was observed. However, at this temperature a transient accumulation of aldehyde was observed, which indicates that the condensation reaction is slower than the hydroformylation reaction. An advantage of performing the reaction at a lower temperature is that less aldol side product is formed.

The reaction in the IL turned out to be slower, in particular at $T=110\,^{\circ}C$. Nevertheless, the results concerning the selectivities for the hydroaminomethylation in the IL were in general better than in toluene/MeOH. The chemoselectivity was higher since the formation of aldol condensation products was suppressed in the IL and the formation of *N*-formylpiperidine, which is known to be a problem for HAM in the presence of methanol,[6] was completely absent. Conversions and regioselectivities were comparable to the results obtained in toluene/MeOH. At a reaction temperature of $T=110\,^{\circ}C$, the regioselectivity could even be improved, and remained excellent in the recycle runs.

The reason for the reproducibly slow reaction progress at $T=110\,^{\circ}C$ could be mass transfer limitation due to viscosity effects and a consequently lower concentration of synthesis gas in the ionic liquid layer. However, upon doubling the stirring rate, no increase in conversion of octene was observed while more enamine and aldol condensation product were found at the expense of the linear amine (Figure 4). A clear conclusion concerning the stirring rate and mass transfer limitations in these systems cannot be drawn from these results at the moment. More research on this specific topic is currently in progress.

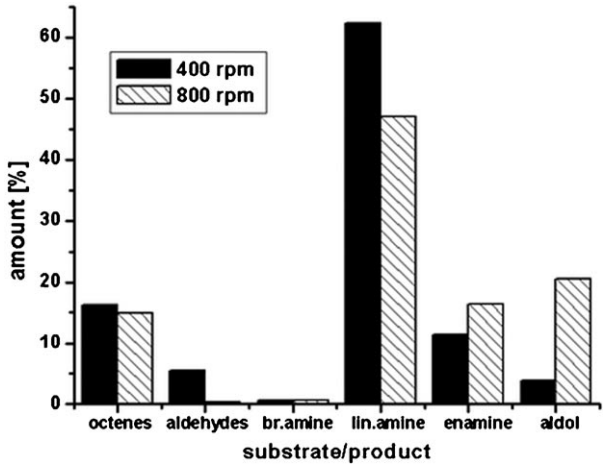
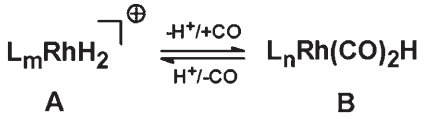


Figure 4. Product distribution of the hydroaminomethylation reaction of 1-octene in IL at two different stirring rates. *Conditions:* 1-octene 13 mmol, piperidine 15 mmol, ionic liquid [PMIM][BF_4] 4 mL, [$Rh(cod)_2BF_4$]=0.1 mol%, S/Rh=1100, L/Rh=4, $T=110\,^{\circ}C$, $t=6$ h, p(CO/H_2 [1:2])=36 bar (cold pressure).

As the stirring rate has little influence on the total conversion, it seems plausible that decreasing the reaction temperature by only 15 °C leads to a drastic decrease of the reaction rate in the IL system. For that reason several experiments with a range of different S/Rh ratios were performed and it turned out that the effect of this S/Rh ratio was much more pronounced at $T=110\,^{\circ}C$ than at $T=125\,^{\circ}C$. Especially at higher S/Rh ratios (>1200), conversions were lower than 90% after 6 h, but were reproducible in the recycle runs. In order to obtain conversions higher than 90% a reaction time of 16 h was necessary when applying an S/Rh ratio of 2800.

Given that higher S/Rh ratios lead to lower conversions after 6 h at $T=110\,^{\circ}C$, it seems probable that this also leads to higher l/b ratios because of the earlier mentioned conversion restriction. Moreover, the l/b ratio is almost constant in the recycle runs and drops only slightly after 5 recycles. Thus, performing this reaction at $T=110\,^{\circ}C$ with a reaction time of 6 h and an S/Rh ratio smaller than 1000 seems to be optimal in terms of conversion and chemo- and regioselectivity, leading to comparably good results in the recycle steps (Table 5).

In consideration of the fact that the hydroaminomethylation consists of a hydroformylation and a hydrogenation step, the cationic precursor [$Rh(cod)_2$]BF_4 is used in most hydroaminomethylation reactions for its ability to be converted to a cationic rhodium species, which is known to be a good hydrogenation catalyst [Eq. (1) **A**]. However, in hydroformylation reactions the neutral Rh precursor [$Rh(CO)_2$(acac)] is usually used because the trigonal



(Eq. 1)

Table 5. Hydroaminomethylation of 1-octene in IL; results of recycle runs at $T=110\,^{\circ}C$, $t=6$ h and S/Rh=800.[a]

Entry	Cycle	S/Rh	Conversion [%]	Conversion 1-octene [%]	Isomerised alkene [%]	Selectivity (amine) [%]	l/b
1	1	790	92.9	98.3	5.4	96.5	54.5
2	2	800	93.0	98.2	5.2	94.3	55.5
3	3	820	93.2	98.4	5.2	92.3	54.2

[a] *Conditions:* 1-octene 11 mmol, piperidine 13 mmol, ionic liquid [PMIM][BF_4] 4 mL, L/Rh=4.0, $t=6$ h, $T=125\,^{\circ}C$, p(CO/H_2 [1:2])=36 bar (cold pressure).

bipyramidal hydrido-dicarbonyl complex **B** [Eq. (1)], which is the resting state of the hydroformylation catalyst, is formed out of this Rh(I) precursor. Consequently, for the hydroformylation to take place complex **B** has to be generated when using $[Rh(cod)_2]BF_4$ as the catalyst precursor. This equilibrium shift might be induced by a base, which could be piperidine in our system. Furthermore, it might be possible that the formation of complex **B** is slower in the IL at $T=110\,^{\circ}C$ in comparison to $T=125\,^{\circ}C$. We therefore decided to test the hydroaminomethylation reaction under these conditions using a binary system consisting of both $[Rh(CO)_2(acac)]$ and $[Rh(cod)_2]BF_4$ (1:1).

Indeed, the use of this binary precatalyst resulted in a faster conversion of 1-octene (Figure 5) in comparison to the use of solely $[Rh(cod)_2]BF_4$. Yet, the most distinct difference was the fact that mainly linear amine could be obtained after 4 h reaction time while less linear amine and large amounts of aldehyde and enamine were obtained upon using solely $[Rh(cod)_2]BF_4$ (Figure 6 **A**). Even after 18 h reaction time, the regio- and chemoselectivity were excellent using the binary precatalyst (Figure 5 **A** and Figure 6 **B**), although the difference between the binary precatalyst and $[Rh(cod)_2]BF_4$ was not as pronounced as for a reaction time of 4 h. Apparently, the combination of the two rhodium precursors has an advantageous effect on the hydroaminomethylation and especially on the condensation and hydrogenation reaction, although it was expected that addition of the $[Rh(CO)_2(acac)]$ precatalyst would increase the reaction rate of the hydroformylation.

In order to investigate the effect of the binary precatalyst in more detail, the reactions {ratios $Rh^+/Rh=1:3$, 1:1 and 3:1 and solely $[Rh(CO)_2(acac)]$} were performed in toluene/MeOH while the product distribution was followed over time. Obviously, the reaction in toluene/MeOH gives much more aldol product and

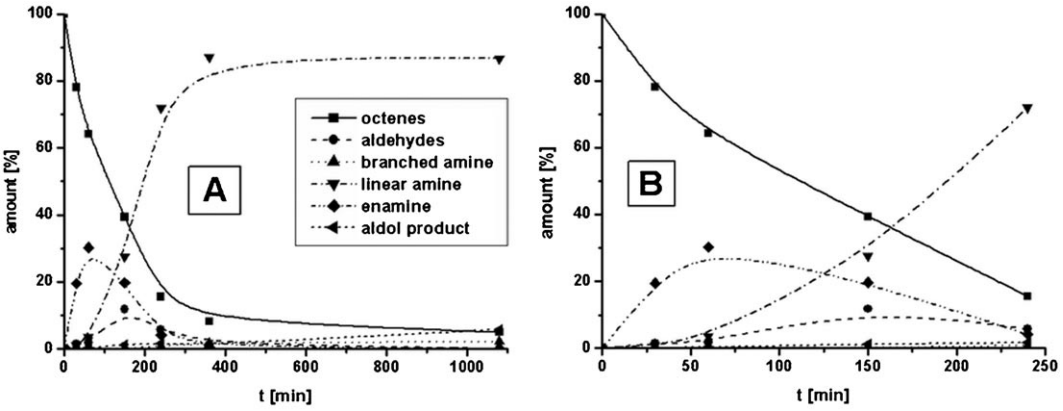


Figure 5. Product distribution of the hydroaminomethylation reaction of 1-octene in IL using a binary Rh precatalyst ($[Rh(CO)_2(acac)]/[Rh(cod)_2]BF_4$ (1:1)). The right-hand panel shows a close-up of the first 4 h of the reaction. *Conditions:* 1-octene 13 mmol, piperidine 15 mmol, ionic liquid [PMIM][BF_4] 4 mL, S/Rh = 1000, L/Rh = 4, $T=110\,^{\circ}C$, $p(CO/H_2\ [1:2])=36$ bar (cold pressure).

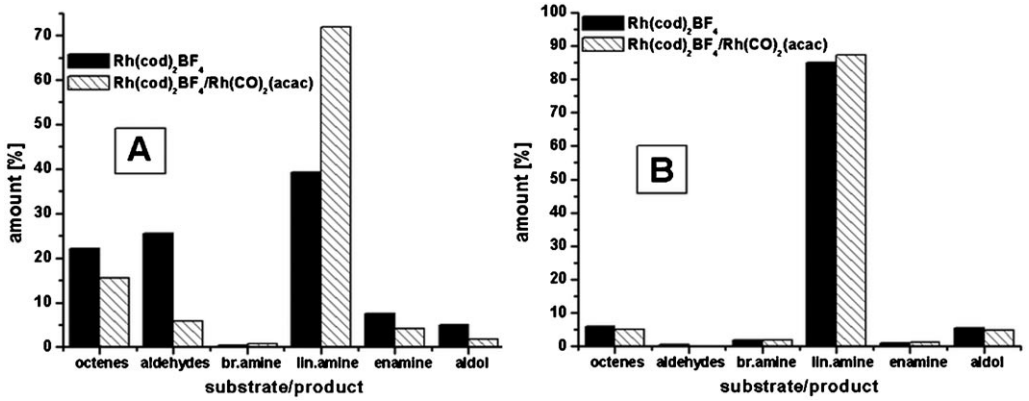
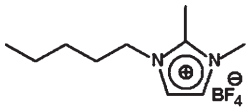


Figure 6. Comparison of the product distributions of the hydroaminomethylation reaction of 1-octene in IL using different Rh precursors: **A:** $t=4$ h; **B:** $t=18$ h. *Conditions:* 1-octene 13 mmol, piperidine 15 mmol, ionic liquid [PMIM][BF_4] 4 mL, S/Rh = 1000, L/Rh = 4, $T=110\,^{\circ}C$, $p(CO/H_2\ [1:2])=36$ bar (cold pressure).

N-formylpiperidine in comparison to the reaction in the IL because of the earlier mentioned effect of MeOH in the HAM. The reaction with the binary precatalyst (1:1) turned out to give improved results in terms of conversion and especially selectivity compared to the reaction using only $[Rh(CO)_2(acac)]$ (Figure 7). The results with this binary precatalyst even showed an optimum in terms of conversion of octenes in comparison to the results of the reactions using the binary precatalyst with the ratios $Rh^+/Rh = 1:3$ and $Rh^+/Rh = 3:1$, and solely $[Rh(cod)_2]BF_4$. However, the more $[Rh(CO)_2(acac)]$ was used in the precatalyst, the more aldol condensation product and *N*-formylpiperidine were formed, which is most likely due to the higher reaction rate of the condensation reaction. Another possibility might be that the equilibrium shifted toward the hydroformylation catalyst, slowing down the hydrogenation and in this way giving rise to more side product formation, since more aldehyde and enamine were present in the reaction mixture. For the reaction in the IL these condensation side reactions play a less important role since they are nearly absent in the first runs and thus the binary precatalyst (1:1) might be even more beneficial there.

Strikingly, in the hydroaminomethylation with $[Rh(CO)_2(acac)]$ in toluene, without MeOH, no amine product was obtained and only enamine and aldehyde were formed. It seems that MeOH or another protic solvent is necessary for the hydrogenation step to take place. We assume that the C–H acidic imidazolium part of the ionic liquid acts comparable to a protic species.[26] This hypothesis was verified performing the reaction in 1-pentyl-2,3-dimethyl-imidazolium tetrafluoroborate ($[PM_2IM][BF_4]$; Figure 8), which does not contain an acidic H and in which the hydrogenation of the enamine turned out to be very slow and thus rate-limiting. Furthermore, literature examples can be found where HAM reactions in



$[PM_2IM][BF_4]$

Figure 8. Ionic liquid $[PM_2IM][BF_4]$ without an acidic C–H bond in the imidazolium part.

aprotic solvents (THF, toluene, MTBE and anisole) turn out to show slow hydrogenation of the enamine.[6,27] Probably, this proton is necessary to shift the equilibrium depicted in Eq. (1) to the cationic Rh-(III) species, which is proposed to be the actual hydrogenation catalyst, especially since piperidine could act as a base, shifting the equilibrium towards the neutral Rh(I) species **B**. This might also explain the fact that a maximum in the amount of enamine can be observed upon using $[Rh(CO)_2(acac)]$ as a precatalyst, and the amount of *N*-formylpiperidine and aldol condensation products formed in the HAM increases following the order $[Rh(cod)_2]BF_4 < [Rh(CO)_2(acac)]/[Rh(cod)_2]BF_4$ (1:3) $< [Rh(CO)_2(acac)]/[Rh(cod)_2]BF_4$ (1:1) $< [Rh(CO)_2(acac)]/[Rh(cod)_2]BF_4$ (3:1) $< [Rh(CO)_2(acac)]$ since increasing amounts of the hydroformylation catalyst are present, slowing down the hydrogenation of the enamine and thus giving rise to more condensation products.

For the determination of the turnover frequency (TOF) the HAM of 1-octene with piperidine in the ionic liquid was performed in an autoclave equipped with a mass flow controller. The TOF at 20% conversion was determined both for the hydroaminomethylation and the hydroformylation reactions at different temperatures and pressures (Table 6). As expected, the hydroformylation of 1-octene is faster at lower pressure, since the hydroformylation reaction has a negative order in CO pressure (Table 6, entry 1). The same effect was observed for the hydroaminomethyla-

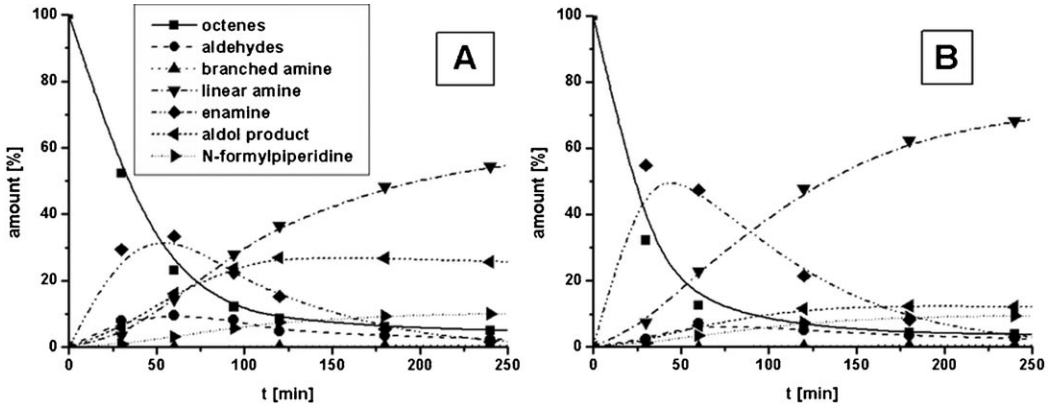


Figure 7. Product distribution of the hydroaminomethylation reaction of 1-octene in toluene/MeOH using $[Rh(CO)_2(acac)]$ (**A**) and a mixed Rh precursor ($[Rh(CO)_2(acac)]/[Rh(cod)_2]BF_4$ (1:1)) (**B**). *Conditions:* 1-octene 13 mmol, piperidine 14 mmol, toluene/MeOH 8 mL, S/Rh = 1000, L/Rh = 4, $T = 110\,°C$, $p(CO/H_2\ [1:2]) = 36$ bar (cold pressure).

Table 6. Determination of the turnover frequency (TOF) for hydroaminomethylation and hydroformylation experiments.[a]

Entry	Reaction type	T [°C]	p [bar][b]	Solvent	Rh precursor	l/b ratio	Selectivity product [%]	TOF [h^{-1}][d]
1[c]	HF	110	30	**A**	**1**	28.3	95.5	14200
2[c]	HF	110	50	**A**	**1**	26.0	93.7	8600
3	HF	110	50	**B**	**2**	36.9	96.9	9100
4	HAM	110	50	**B**	**2**	41.4	96.1	9000
5	HAM	125	30	**B**	**2**	15.2	97.9	16100
6	HAM	125	50	**B**	**2**	22.7	91.0	10300

[a] *Conditions:* 1-octene, piperidine (for HAM only), solvent 5 mL, L/Rh = 4, S/Rh = 2000-3000, t = 18 h, **A** = toluene/MeOH, **B** = [PMIM][BF_4], **1** = [$Rh(CO)_2$acac], **2** = [$Rh(cod)_2$]BF_4.
[b] Pressure at reaction temperature; CO_2/H_2 [1:2].
[c] CO/H_2 [1:1], solvent 10 mL.
[d] TOF at 20% conversion.

tion at lower pressure, probably initiated by the faster hydroformylation reaction (Table 6, entry 5). The reaction rate of the hydroformylation in the IL was comparable to the reaction rate in toluene/MeOH (Table 6, *cf.* entries 2 and 3) although a different Rh precursor was used. It was expected that the reaction using [$Rh(CO)_2$(acac)] would be faster since it is known to give a good hydroformylation catalyst. Apparently, the hydroformylation in the IL is faster or at least equally fast as the reaction in toluene/MeOH. Nevertheless, we see in Figure 3 (**B** and **D**) that this does not apply for the hydroaminomethylation. Performing the HAM at $p = 30$ bar leads to a higher chemoselectivity, but to a lower regioselectivity in comparison to the HAM at $p = 50$ bar. Since the reaction at $p = 30$ bar is faster, probably a lot of the internal alkenes react at high conversion, leading to a lower regioselectivity. The HAM at $T = 110$ °C and $p = 50$ bar (Table 6, entry 4) gives a chemoselectivity comparable to the HAM at $T = 125$ °C and $p = 30$ bar (Table 6, entry 5) and a TOF slightly lower than for the HAM at $T = 125$ °C and $p = 50$ bar (Table 6, entry 6) while the regioselectivity is better than for entries 5 and 6 (Table 6). Performing the hydroaminomethylations at $T = 110$ °C and $p = 50$ bar seems to be the preferred reaction condition for this reaction.

Conclusions

In conclusion, we have shown that hydroaminomethylation of *n*-alkenes and piperidine, giving rise to less side product formation than in toluene/MeOH, and subsequent reuse of the catalyst is possible in ionic liquids by simple phase separation without any significant leaching of rhodium or ligand to the product layer. High chemo- and regioselectivities were achieved in the recycle steps. Oxidation of the ligand was avoided by performing the phase separation in the autoclave or by simple addition of substrates after completion of the initial reaction. The influence of different reaction parameters was investigated by monitoring the product distribution in a model reaction as well as in the ionic liquid. In addition, turnover frequencies were determined. Reaction time and temperature were of great influence in terms of chemo- and regioselectivity because of conversion limitation. S/Rh ratio dependency was not observed at $T = 125$ °C, but was much more pronounced for a reaction temperature of $T = 110$ °C. A reaction temperature of $T = 110$ °C, a reaction time of 4–6 h and an S/Rh ratio smaller than 1000 were found to be the optimal reaction conditions in terms of conversion and regio- and chemoselectivity, also in the recycle steps. Applying a binary Rh precatalyst is advantageous in this reaction. Protic organic solvents or ionic liquids with a C–H acidic bond in the imidazolium part of the ionic liquid turned out to be necessary for the hydrogenation of the enamine to take place. This was explained by the equilibrium between the resting state of the hydroformylation species and the expected cationic species of the hydrogenation catalyst.

Experimental Section

All air- or water-sensitive operations were performed using standard Schlenk techniques under a purified argon atmosphere. Toluene and dichloromethane were purified over custom-made alumina columns. Ethyl acetate, piperidine, methanol and ethanol were distilled from CaH_2 and 1-hexene, 1-octene, 1-decene, 1-dodecene were purified by distillation from Na_2SO_4 and percolation over neutral activated alumina. These solvents were deoxygenated *via* the freeze-pump-thaw technique before use. Chemicals were purchased from Acros Chimica, Merck KGaA, Biosolve B.V. and Aldrich Chemical Co. 9,9-Dimethyl-2,7-bissulfonato-4,5-bis(diphenylphosphino)xanthene sodium salt was prepared according to a literature procedure.[22] Hydrogen gas (99.999%), carbon monoxide gas (99.997%) and synthesis gas [CO (99.997%)/H_2 (99.999%); 1:1] were purchased from Hoek Loos and synthesis gas [CO (99.9%)/H_2 (99.9996%); 1:2] was purchased from Praxair. Gas chroma-

tographic analyses were run on a Shimadzu GC-17 A instrument and an Ultra 2 column (25 m × 0.2 mm). GC/MS analyses were conducted on a Leco Pegasus II chromatograph with a DB-1 MS column (10 m × 0.1 mm). NMR data were recorded on a Varian Oxford 200 MHz NMR spectrometer. Gas uptake was monitored by Bronkhorst EL-Flow mass flow controllers with a range from 0 to 150 mL min^{-1}.

General Procedure for Hydroaminomethylation Experiments

Reactions were performed in 75-mL home-made stainless steel autoclaves. In a typical experiment, the autoclave was charged with a solution of $[Rh(cod)_2]BF_4$ (7.2 mg, 17.8 μmol; cod = 1,5-cyclooctadiene) or $[Rh(CO)_2(acac)]$ (4.6 mg, 17.8 mmol) (acac = acetylacetonate) or a combination of these Rh precursors and sulfoxantphos (55.8 mg, 71.3 μmol) or xantphos (41.3 mg, 71.3 μmol) in 4 mL of the ionic liquid or toluene/MeOH. 1-Octene (2.0 g, 18 mmol) and piperidine (1.7 g, 20 mmol) were added and the autoclave was purged three times using CO (p = 10–12 bar) to remove the remaining argon from the autoclave. Subsequently, the autoclave was pressurised with CO (p = 12 bar) and H_2 (p = 24 bar) and heated to reaction temperature. After 18 h the autoclave was cooled to room temperature in an ice bath and the gases were vented. Phase separation was immediate and the product layer was removed from the autoclave by a syringe under an argon atmosphere. The catalyst solution was ready to be used in a new catalytic run. The product layer was analysed by GC and GC/MS. In these analyses the l/b ratio could be determined within an error range of 0.05%.

Hydroaminomethylation reactions in toluene/methanol, from which samples were taken during the reaction, were conducted in a similar way as described above, in an autoclave equipped with a tailor-made sample system that consisted of a capillary with an inner diameter of 0.25 mm, combined with a 2-way and a 3-way valve.[28] The sample was taken by means of the pressure inside the autoclave. The connection between the two valves was used to collect the sample (estimated volume 50 μL). By opening the 2-way valve the sample was collected in a GC vial, diluted with MeOH/Et_2O and analysed by GC. After finishing the reaction, cooling the autoclave and venting the gases, the reaction mixture was removed from the autoclave and analysed by GC and GC/MS.

General Procedure for the Determination of the Turnover Frequency (TOF)

Typical hydroaminomethylation and hydroformylation experiments were performed as described above, except for the fact that the substrates were added *via* a dropping funnel, in home-made, automated 100-mL stainless steel autoclaves. Some hydroformylation experiments were performed with CO/H_2 (1:1) while all other experiments were conducted using CO/H_2 (1:2). After loading the autoclave, it was purged four times with synthesis gas (CO/H_2 1:2), pressurised to reaction pressure with synthesis gas (CO/H_2 1:2) and heated to reaction temperature. The reaction mixture was stirred for 10–15 min in order to saturate the solution with synthesis gas. Subsequently, the substrates were added *via* the dropping funnel, and the reaction was started. During the reaction the gas uptake was monitored by mass flow controllers (Bronkhorst; 0–150 mL min^{-1}) and the turnover frequency was calculated from the originating gas uptake curves at 20% conversion.

Synthesis of 1-Pentyl-3-methylimidazolium Tetrafluoroborate (1)

1-Methylimidazole (60 mL, 0.752 mol) was mixed with 1-bromopentane (93.20 mL, 0.752 mol). The mixture was stirred at 50 °C for 24 h. Subsequently, the liquid was diluted in acetone (100 mL) and then sodium tetrafluoroborate (85 g, 0.774 mol) was added. The mixture was stirred for 48 h at room temperature and then filtered. After evaporation of the acetone the liquid was filtered once more and washed with diethyl ether (30 mL). The remaining diethyl ether in the product was removed under vacuum afterwards; Yield: 177 g (729 mmol, 97%). ^{1}H NMR (200 MHz, CD_3OD): δ = 8.81 (s, 1H), 7.60 (s, 1H), 7.53 (s, 1H), 4.16–4.24 (t, 2H), 3.92 (s, 3H), 1.82–1.96 (q, 2H), 1.31–136 (m, 4H), 0.92 (t, 3H); ^{19}F NMR (200 MHz, CD_3OD): δ = −153.37.

Synthesis of 1-Pentyl-2,3-dimethylimidazolium Tetrafluoroborate (2)

1,2-Dimethylimidazole (7.0 g, 72.8 mmol) was mixed with 1-bromopentane (7.81 mL, 72.8 mmol) and 1,1,1-trichlorethane (25 mL) as a solvent. The mixture was stirred at 50 °C for 24 h. 1,1,1-Trichlorethane was decanted and the residue was diluted in acetone (30 mL) and sodium tetrafluoroborate (8.5 g, 77.4 mmol) was added. Further work-up was identical to the work-up for compound **1**; Yield: 17 g (66.1 mmol, 91%). ^{1}H NMR (200 MHz, D_2O): δ = 7.17–7.12 (d, 2H), 3.96–3.88 (t, 2H), 3.59 (s, 3H), 2.40 (s, 3H), 1.68–1.58 (q, 2H), 1.22–1.01 (m, 4H), 0.74–0.67 (t, 3H); ^{19}F NMR: −150.59.

ICP-OES (Inductively Coupled Plasma Optical Emission Spectrometry)

Rhodium and phosphorus leaching were analysed by means of ICP-OES. Samples were prepared by removal of the volatiles from the organic layer under reduced pressure and subsequent calcination of the residue at 500 °C over 72 h. Afterwards, the residue was dissolved in 2 mL HNO_3 (65%) and diluted with distilled water to 25 mL in a measuring flask. Before starting the measurements on the samples, a calibration curve for Rh and P was prepared. The measurements were performed with a SPECTRO CIROS^{CCD} spectrometer equipped with a free running 27.12 MHz generator at a power of 1400 W. The sample introduction was performed by a cross-flow nebuliser with a double pass Scott-type spray chamber and a sample uptake rate of 2 mL min^{-1}. The outer gas flow was 12 L min^{-1}, the intermediate gas flow was 1 L min^{-1} and the nebuliser gas flow was 1.00 L min^{-1}.

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