

Asymmetric hydrogenation of methyl pyruvate in the continuous gas phase using Supported Ionic Liquid Phase (SILP) catalysis

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ARTICLE INFO

Article history:

Received 12 September 2012

Received in revised form 3 April 2013

Accepted 18 April 2013

Available online 26 April 2013

Keywords:

Asymmetric hydrogenation

Gas phase

Methyl pyruvate

Supported catalyst

SILP catalyst

Ionic liquid

ABSTRACT

Based on the recently reported asymmetric hydrogenation of methyl acetoacetate in a continuous-flow, gas phase reaction using Supported Ionic Liquid Phase (SILP) catalysis, this study deals with the even more challenging asymmetric reduction of the α -keto ester methyl pyruvate. Different support materials, ligands and ionic liquids were screened to identify an optimized Ru-based SILP catalyst. With Ru-BINAP dissolved in the ionic liquids 3-hydroxypropylpyridinium bis(trifluoromethylsulfonyl)imide on silica 100, stable catalyst performance could be obtained for more than 50 h time-on-stream. At 95 °C and with a residence time in the reactor of less than 3 s a stable product yield of 80–84% was obtained with moderate but stable enantiomeric excess of 26–30%.

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1. Introduction

Chiral molecules, pharmaceuticals and agrochemicals produced via multistep synthesis are often relatively small scale but high value products. In order to shorten “time to market” the level of development in the applied production process is often rather limited and typical standard procedures using multipurpose batch equipment is frequently applied in these productions. The associated massive use of solvents is considered the biggest contributor to waste in pharmaceutical production. Associated to the excessive solvent use, energy consuming work-up procedures and downstream processing has to be applied [1,2].

The use of continuous flow techniques offers huge potential to intensify these production processes, especially in the field of asymmetric catalysis, with improved heat and mass transfer, easier scale-up, on-demand reaction analysis and even continuous automated on-stream optimization of reaction parameters [3]. Therefore, a lot of recent publications have focused on the field of asymmetric reactions in continuous flow, some of which have been reviewed by Mak et al. [4] besides the intensification of enantioselective transformations by the use of continuous flow processes, the immobilization and recyclability of homogeneous and

heterogeneous asymmetric catalysts has been a major interest of the scientific community in the recent years [5–7].

Especially covalent tethering of active homogeneous catalysts to various support materials and immobilization by electrostatic interactions has resulted in highly stable catalyst systems capable of reuse. While immobilized catalysts often show lower catalyst leaching, their activity and stereoselectivity is generally lower than in the respective homogeneous systems, with a few exceptions [6]. Furthermore, the majority of immobilization techniques require multistep synthesis to prepare the immobilized catalyst system [8]. Easy and cost effective immobilization of highly elaborated transition metal complexes remains a critical issue for potential industrial applications of asymmetric catalysis [9,4,10].

A particularly easy technique of catalyst immobilization that has shown limited applicability in liquid systems due to leaching issues is the adsorption of homogeneous catalysts and liquid catalyst solutions on solid support material. This technique, however, appears very promising when combined with alternative media – more precisely ionic liquids or supercritical fluids. In Supported Ionic Liquid Phase (SILP) materials a homogeneous catalyst is dissolved in a thin film of ionic liquid immersed on a highly porous support material [11,12]. The resulting, macroscopically solid SILP compound is easy to handle and combines the advantages of homogeneous and heterogeneous catalysis [13]. SILP catalysts have shown excellent stability and recyclability in various types of reactions, especially when applied in gas phase reaction set-ups. The scope of successful SILP catalyzed gas phase reactions includes hydroformylation [14], methanol carbonylation [15], hydroamination [16], hydrogenation

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[17] and ultralow temperature water–gas shift reaction [18]. Just recently, we demonstrated that even reactions with demanding selectivity problems like asymmetric hydrogenation could be realized in gas phase using SILP catalysts [19]. In this earlier publication by Öchsner et al. we showed the successful enantioselective hydrogenation of the β -ketoester methyl acetoacetate. The proposed mechanism of BINAP-Ru catalyzed hydrogenation of β -keto esters includes the coordination of the ester group toward the Ruthenium center [20]. During this coordination step both carbonyl groups of the β -keto esters experience the chiral coordination sphere of the Ru catalyst resulting in a high enantiomeric excess. However, for α -keto esters the two carbonyl groups point toward opposite directions, thus leading to a different coordination within the catalytic cycle compared to the β -keto esters and therefore to a much lower enantioselectivity of the hydrogenation reaction.

In the present paper, we want to extend the scope of continuous-flow, gas phase asymmetric hydrogenation to these more sophisticated α -ketoester substrates. In detail, the asymmetric hydrogenation of methyl pyruvate (MPY) to methyl lactate (ML) is investigated. Asymmetric hydrogenation of MPY to ML has been identified in the past as a particularly demanding task for batch-wise operated homogeneous transition metal catalysis. Typically enantioselectivities between 80% and 88% could be realized at temperatures up to 50 °C [21–29]. Heterogeneous systems applying platinum contacts with a chiral modification by cinchonidine or quinine (see Fig. 1) showed comparable [30–32] or even better [33,34] activities and selectivities when used in a slurry reaction system.

In 2003, Arx et al. [35] observed for the first time moderate enantioselectivities (25–51% ee) in the continuous gas phase hydrogenation of α -keto esters using heterogeneous chirally modified supported platinum catalysts. However, a decrease of ee was observed during operation and even the complete loss of enantioselectivity was encountered due to partial hydrogenation of the cinchonidine ring system at elevated temperatures. At temperatures above 50 °C, the adsorption mode of the modifier changed and even desorption took place limiting the use of such systems for hydrogenation reactions under harsher conditions [32].

To the best of our knowledge, asymmetric hydrogenation of α -keto esters has never been realized in homogeneous reaction

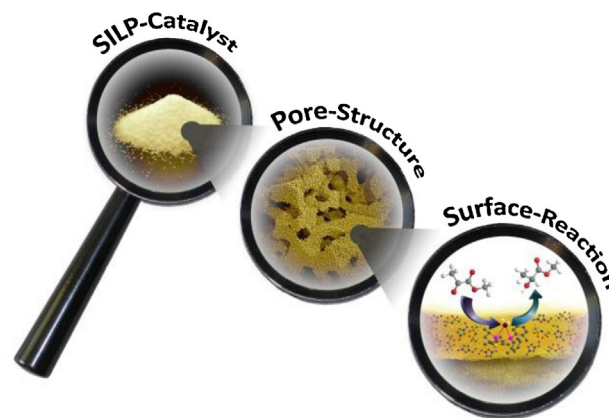


Fig. 2. Supported Ionic Liquid Phase (SILP) catalyst.

systems using a continuous-flow gas phase operation mode so far. The present publication demonstrates such a process using Ru-based SILP catalyst systems (see Fig. 2). Obvious advantages of carrying out such reaction in continuous gas-phase contact is the very simple and efficient immobilization of the catalyst complex in a liquid matrix of negligible vapor pressure that avoids any additional synthetic effort of chemical ligand modification or surface anchoring.

2. Experimental

2.1. Chemicals

The ruthenium precursor [bis(2-methylallyl)(1,5-cyclooctadiene)ruthenium(II)] as well as methyl pyruvate (94%), methanol (99.9%, <50 ppm H₂O) and acetone (99.9%, <50 ppm H₂O) were purchased from Acros Organics. The phosphine ligands (L) (R)-(+)-2,2'-Bis(diphenylphosphino)-6,6'-dimethoxy-1,1'-biphenyl 97% (MeO-BIPHEP), (R)-(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) 98%, R-(−)-1,13-Bis(diphenylphosphino)-7,8-dihydro-6H-dibenzo[f,h] [1,5] dioxin (TUNEPHOS) 97%,

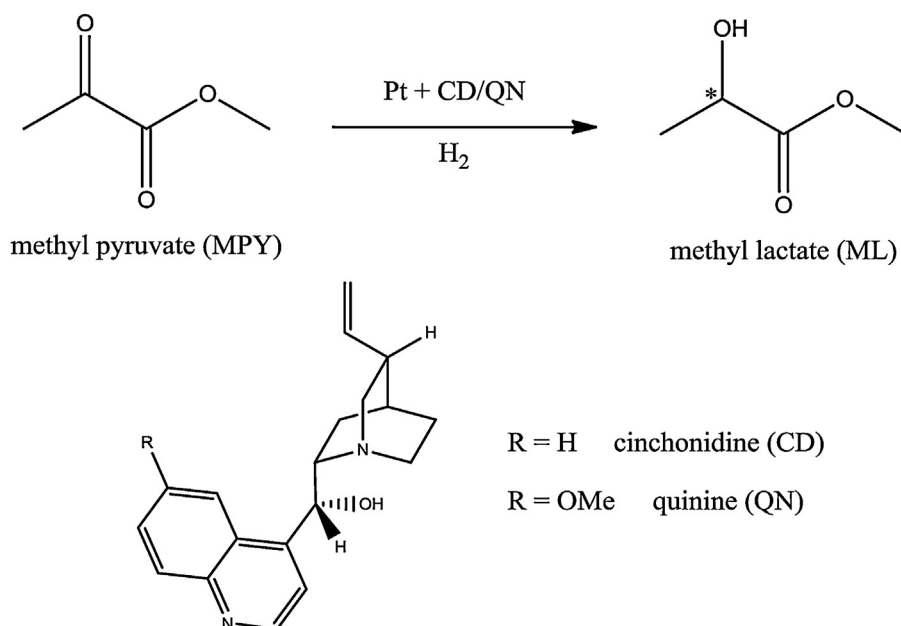


Fig. 1. Chiral modifier cinchonidine.

(R)-(+)-5,5'-Bis(diphenylphosphino)-4,4'-bi-1,3-benzodioxole (SEGPPOS) 98%, and (+)-{4-[(1R,4S)-3-(Diphenylphosphino)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl]-2,5-dimethyl-3-thien-3-yl}bis(3,5-dimethylphenyl)phosphine (catASium T3) 95% were purchased from Strem Chemicals. The monodentate ligand 4-phenyl-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]phosphine (phenylphosphine) was provided by the group of M. Beller [36] (Leibniz-Institut für Katalyse, University of Rostock) and 3-(2,5-(2R,5R)-dimethylphospholanyl)-4-di-o-tolylphosphino-2,5-dimethylthiophene was provided by Evonik Degussa GmbH [37]. The hydrobromic acid (48%) was purchased from Fluka. As support materials, calcinated silica gel 100 (particle size 0.2–0.5 mm, pore volume $0.98 \text{ cm}^3 \text{ g}^{-1}$, BET surface area $359 \text{ m}^2 \text{ g}^{-1}$, Merck KgaA), aluminum oxide 90 (particle size 0.063–0.2 mm, pore volume $0.28 \text{ cm}^3 \text{ g}^{-1}$, BET surface area $148 \text{ m}^2 \text{ g}^{-1}$, Merck KgaA) and activated carbon (pore volume $0.997 \text{ cm}^3 \text{ g}^{-1}$, BET surface area $1698 \text{ m}^2 \text{ g}^{-1}$, Blücher). The ionic liquids 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide [EMIM][NTf₂] 99% ($\text{H}_2\text{O} < 500 \text{ ppm}$, $\text{Cl}^- < 100 \text{ ppm}$, Merck KgaA), 1-ethyl-3-methylimidazolium trifluoromethanesulfonate [EMIM][OTf] 99% ($\text{H}_2\text{O} < 100 \text{ ppm}$, $\text{Cl}^- < 100 \text{ ppm}$, Merck KgaA) and 1-ethyl-3-methylimidazolium hexafluorophosphate ($\text{H}_2\text{O} < 100 \text{ ppm}$, $\text{Cl}^- < 100 \text{ ppm}$, Merck KgaA) were used for the preparation of the SILP materials as purchased. In addition, the ionic liquids tetraethylammonium bis(trifluoromethylsulfonyl)imide [Et₄N][NTf₂], butylpyridinium bis(trifluoromethylsulfonyl)imide [BPyr][NTf₂], 3-hydroxypropyl pyridinium bis(trifluoromethylsulfonyl)imide [PrOHPr][NTf₂] and 1-butyl-3-methylimidazolium hydrogensulfate [BMIM][HSO₄] were synthesized in analogy to literature procedures [38–40]. For the continuous gas phase experiments helium (purity: 4.6, Linde AG) and hydrogen (purity: 5.0, Linde AG) were used.

2.2. Catalyst preparation

The applied general procedure to prepare the SILP materials has been published in the literature [14]. The Ru-SILP catalysts were prepared in situ similar to literature procedure [41] from one equivalent of [bis(2-methylallyl)(1,5-cyclooctadiene)ruthenium(II)] and two equivalents of the bidentate phosphine ligands (four equivalents in case of the monodentate phosphine ligand). The chemicals were placed in a Schlenk flask under argon atmosphere and dissolved in 5 mL of dry acetone (5 mL). A methanolic solution (0.29 M) of hydrobromic acid (0.33 mL) was added and the solution was stirred 30 min at room temperature. The solvent was removed under high vacuum over 1 h at 30 °C. In this procedure the Ru-complex RuLBr_2 was obtained as a brown solid powder. For the preparation of the catalytic SILP material, RuLBr_2 was dissolved in 15 mL dry and degassed methanol and the porous support material and the ionic liquid were added. The mixture was stirred under argon for 90 min and subsequently the solvent was removed by means of a high vacuum treatment. The final SILP catalyst was obtained as a yellow to brown powder.

2.3. Continuous gas phase experiments

Fig. 3 shows the continuous gas phase rig applied in this work. The heart of the rig forms the tubular reactor of 30 cm length ($V_{\text{reactor}} = 35 \text{ mL}$). Helium and hydrogen were fed into the rig via mass flow controllers (MFC (A) and (B), Bronkhorst F-201CV-200-RAD-11-V and F-201CV-200-RAD-33-V). The carrier gas helium was used to evaporate the substrate MPY in a CEM (controlled evaporation and mixing) unit (E) (Bronkhorst). The liquid substrates MPY and MeOH were taken from reservoirs at room temperature and fed into the CEM-unit via LIQUI-flows (C and D) (C: Bronkhorst L13-RAD-11-K-10S, D: Bronkhorst L13V02-RAD-11-K-10S). The

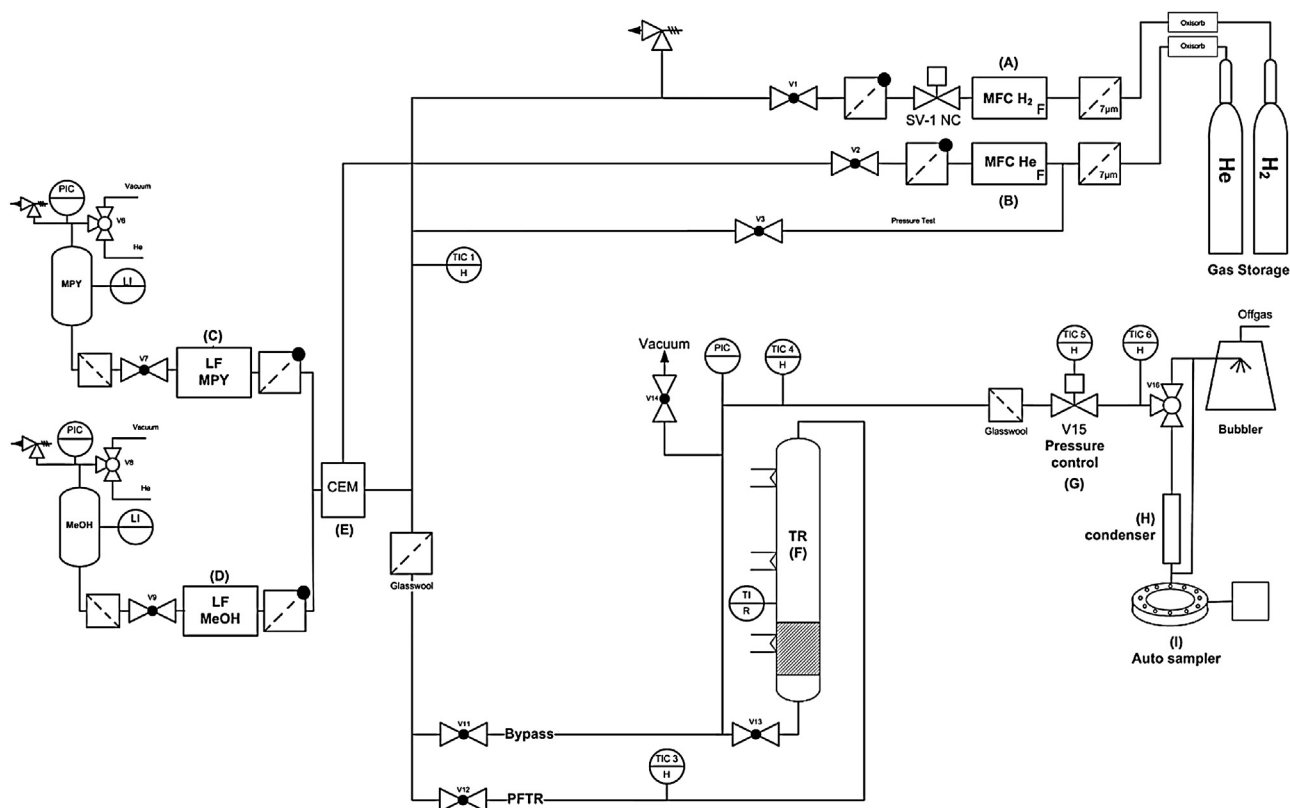


Fig. 3. Flow scheme of the applied continuous asymmetric hydrogenation reactor.

pressure was adapted by means of a backpressure regulator valve (G). A condenser unit and an autosampler ensured proper sampling at regular time intervals.

The obtained samples were diluted with diethyl ether and analyzed using gas chromatography (Varian 3900, Lipodex E column, 25 m inner diameter: 0.25 mm, temperature program 80 °C for 20 min isothermal, 80 °C → 200 °C, 10 °C/min, 200 °C for 10 min isothermal, carrier gas: 0.4 mL/min helium, detector: FID, 250 °C).

For the online experiments, 1.4 g of the SILP catalyst were filled into the tubular reactor (F) under helium atmosphere; the complete rig was flushed and pressurized with 10 bar helium. After an initial leak test, the rig was heated up to reaction temperature under continuous flow of 20 NmL/min helium. When the reaction temperature was reached the respective flows of helium, hydrogen, MPY and MeOH were adjusted to start the continuous experiment.

3. Results and discussion

As a consequence of transferring the hydrogenation of MPY to the described continuous gas phase reactor set-up, the reaction is carried out at elevated temperatures (up to 100 °C) with very short residence times (<3 s). Compared to standard batch experiments these reaction conditions are quite unusual for asymmetric hydrogenation. Therefore, our initial experiments aimed at identifying a stable catalyst system under these demanding conditions. For this purpose, a number of SILP materials have been prepared and screened using a range of ligands (see Fig. 4) in combination with the Ru-precursor and the ionic liquid [EMIM][NTf₂]. We were especially interested in the performance of the ligand catASium-BoT as the latter showed excellent stability in previous studies on gas phase asymmetric hydrogenation of β -keto ester methyl acetoacetate [19]. The phenylphosphine ligand represents the only monodentate ligand. This ligand is known from batch experiments to form catalytic systems of enhanced activity and enantioselectivity at higher temperatures (100–120 °C) [36]. The ligand structures Tunephos (dihedral angle 77°) [42] and Segphos (dihedral angle

65°) [43] were chosen besides BINAP (73.5°) [43] to include a variation of bite angle by means of different backbone structures.

As can be seen in Fig. 5, the various ligands applied in form of the SILP systems showed very diverse activity and stability behavior. The yields of the desired enantiomer were rather low and comparable to those obtained in gas phase reactions using chirally modified heterogeneous systems [35]. While most of the systems experienced an initial activation behavior, the SILP catalyst with catASium-T3 ligand showed very high activity right from the start. However, similar to the other ligands, the catalyst significantly decreased in activity after 20–30 h time on stream. The generally low enantiomeric excess of all ligands and the decrease over time on stream is attributed to the elevated temperatures and an associated slow degradation of the chiral ligand. As already mentioned in the introduction, the low enantiomeric excess is also an intrinsic problem of the asymmetric hydrogenation of α -keto esters. The ligand system with the best stability among the screened systems was found to be the SILP system with the BINAP ligand. TOF values of this catalyst were in the range of 15–22 mol_{ML} mol_{cat}⁻¹ h⁻¹ with a TON of 1037 after 50 h time on stream. Therefore this ligand was chosen for the following investigations.

One great advantage of continuous-flow, gas phase processes in catalysis is that detailed kinetic investigations can be carried out very efficiently. Due to the short residence time and absence of diluting solvents steady-state operation can be reached quickly allowing for very precise measurement of kinetic data for various reaction conditions within one catalytic run. In such a kinetic run (see Fig. 6) the activation energy of the SILP catalyst with BINAP was determined to be 82.6 kJ/mol. Additionally, partial reaction orders for hydrogen and MPY were found to be 0.98 and 0.6, respectively. Slightly higher enantioselectivities were obtained at lower temperatures and a visible drop in ee and a stronger deactivation was observed for temperatures above 80 °C. The activity dropped from 75% yield at 78% conversion after 40 h time on stream to about 56% yield at 60% conversion after 200 h time on stream. In the same time span the enantiomeric excess decreased from 25% ee to about 10% ee. Only minor amounts of sideproducts ($\leq 3\%$), mainly aldol, hemi-ketal and ketal byproducts were observed in all experiments.

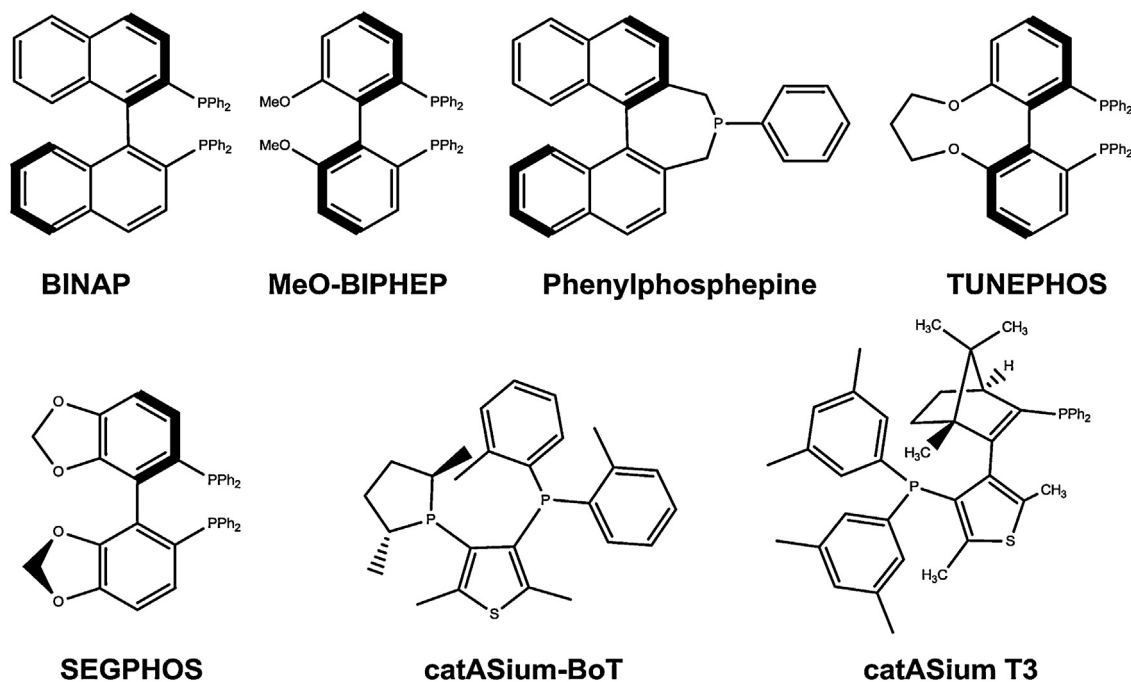


Fig. 4. Ligands screened for the asymmetric hydrogenation of MPY.

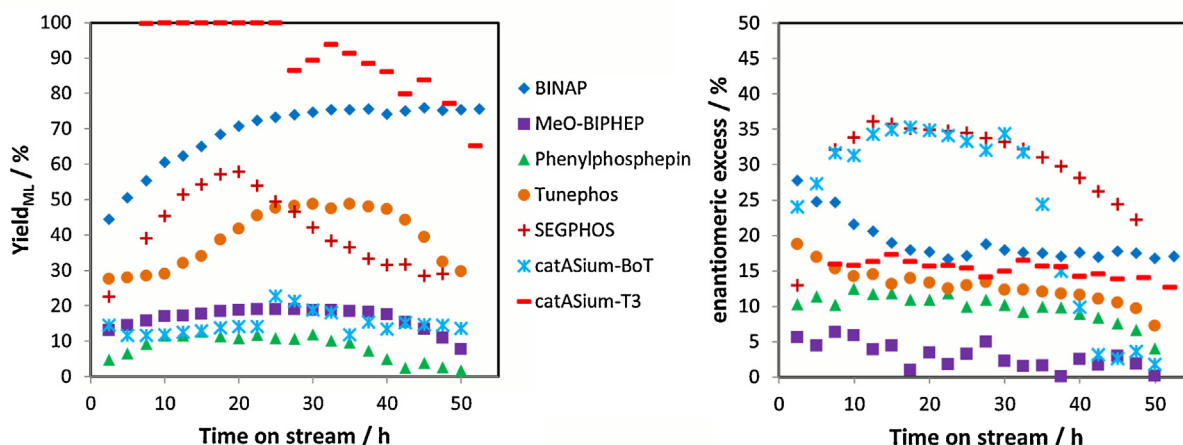


Fig. 5. Yield vs. time-on-stream profiles of the SILP catalyzed MPY hydrogenation in a continuous gas-phase reaction – variation of chiral ligand. (Reaction conditions: L/Ru = 2:1, ionic liquid = [EMIM][NTf₂], α = 0.8, silica 100 (0.2–0.5 mm), 1 wt.% Ru, 95 °C, 10 bar, 200 NmL/min He, 75 NmL/min H₂, 0.25 g/h MPY, 0.475 g/h MeOH, τ = 2.86 s).

Moreover, the formation of high-boiling aldol or ketal products could lead to a significant loss in catalytic activity and selectivity due to accumulation in the SILP pore system.

Further experiments aimed at the investigation of the influence of the support material, the ionic liquid and the ionic liquid loading. Aluminum oxide and activated carbon were investigated in addition to the silica 100 support material (see Fig. 7). While ee values were a bit higher on activated carbon, deactivation appeared after 30–40 h time on stream. Additionally leaching of the ionic liquid layer onto the glass wool below the catalyst bed was observed for both carbon supports. Therefore the adsorption of the ionic liquid layer seemed to be tighter on an inorganic support with surface oxygen and hydroxyl groups. Additionally, the observed catalytic activities seem to correlate with the pore volume and surface area of the support materials (see Section 2). Since the ionic liquid loading α (V_{IL}/V_{pore}) was kept constant, less IL is used for a support with a lower pore volume. Aluminum oxide exhibits by far the lowest pore volume ($0.28 \text{ cm}^3 \text{ g}^{-1}$) and pore surface area ($148 \text{ cm}^2 \text{ g}^{-1}$) of the support materials under investigation and therefore also experiences the lowest catalytic activity. In previous studies surface silanol groups [19], protic solvents [44] and

also acidic additives [45] were found to increase the activity in the asymmetric hydrogenation of methyl acetoacetate. These influences account for the high activity of the SILP catalyst with silica support. The lower enantiomeric excess, however, could correlate to an undesired, competitive coordination of the phosphine ligand to the silica surface. This effect was also observed for phosphine ligands in hydroformulation studies using silica supported SILP catalysts [14,46].

Since the ionic liquid constitutes the solvent in the SILP catalysts it can have a tremendous effect on activity and stability [16,17,47]. The viscosity, polarity or coordination strength of the anion can be of particular importance for the respective reaction system [13]. Fig. 8 shows activity and selectivity profiles of SILP catalysts with different ionic liquid anions. The catalytic activity and selectivity is in line with the coordination strength of the anion indicating the importance of weakly coordinating anions. Stronger coordinating anions like [OTf][−] compete with the chiral ligand when coordinating to the metal and could lead to a less active and selective system. Furthermore, a rather strong decrease in enantiomeric excess is observed for the SILP system with [EMIM][PF₆] after 30 h time on stream. This decrease could be associated to the hydrolysis

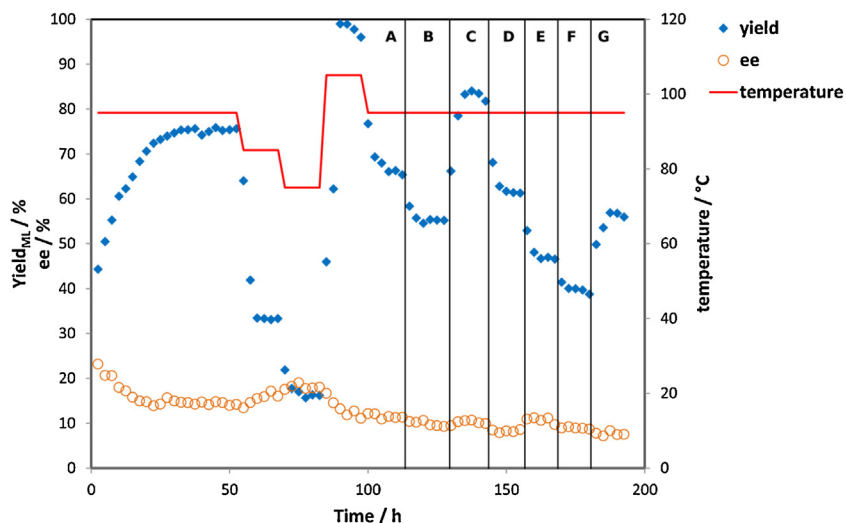


Fig. 6. Yield vs. time-on-stream profile of the SILP catalyzed MPY hydrogenation in a continuous gas phase reaction – kinetic investigation. (Reaction conditions: L/Ru = 2:1, ligand: BINAP, ionic liquid = [EMIM][NTf₂], α = 0.8, silica 100 (0.2–0.5 mm), 1 wt.% Ru, 75–105 °C, 10 bar, 200–250 NmL/min He, 75–100 NmL/min H₂, 0.25–0.75 g/h MPY, 0.475 g/h MeOH, τ = 2.84–2.86 s; partial pressures: A: p_{H_2} = 3.78 bar, B: p_{H_2} = 3.26 bar, C: p_{H_2} = 4.92 bar, D: p_{H_2} = 3.78 bar p_{MPY} = 0.028 bar, E: p_{MPY} = 0.055 bar, F: p_{MPY} = 0.082 bar, G: p_{MPY} = 0.028 bar).

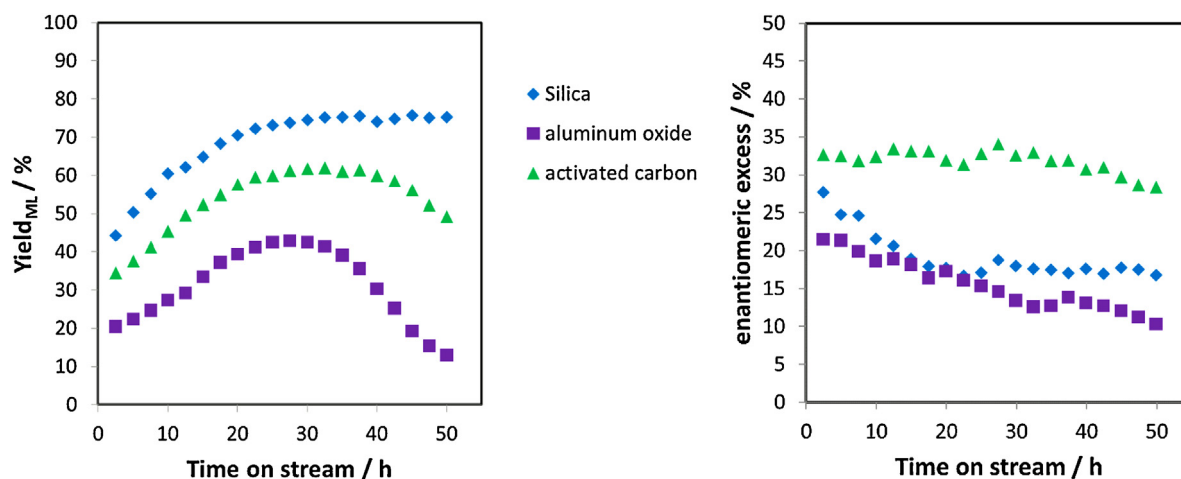


Fig. 7. Yield vs. time-on-stream profiles of the SILP catalyzed MPY hydrogenation in a continuous gas-phase reaction – variation of support. (Reaction conditions: ligand = Xantphos, L/Ru = 2:1, ionic liquid = [EMIM][NTf₂], α = 0.8, 1 wt.% Ru, 95 °C, 10 bar, 200 Nml/min He, 75 Nml/min H₂, 0.25 g/h MPY, 0.475 g/h MeOH, τ = 2.86 s).

of the anion and the production of HF, which has been observed previously [13]. Water can be formed as co-product from the side reactions aldol condensation and ketal formation. Though being rather low in all ILs under investigation, the hydrogen solubility is generally higher for [NTf₂][−] based ionic liquids compared to [OTf][−] and [PF₆][−] type ILs. This could additionally enhance the activity of the [EMIM][NTf₂] SILP catalyst [48,49].

The influence of different cations on the reactivity and selectivity was studied as well. Floris et al. [50] utilized tetraalkylammonium ionic liquids in combination with methanol and found good activities and ee values in the asymmetric hydrogenation of methyl acetoacetate. However, when varying the amount of ionic liquid from 0.2 wt.% up to 100 wt.% a dramatic decrease in activity and enantioselectivity was observed with increasing amount of ionic liquid. This observation is in line with the work of Wolfson et al. on the importance of alcoholic solvents [44] and acidic additives [45] in the asymmetric hydrogenation of β -keto esters. Alcoholic solvents and acidic additives were found to facilitate the protonation of the product and hence increase the reaction rate. These findings were taken into account for the ionic liquid cation screening. As shown in Fig. 9 the tetraethylammonium ionic liquid showed a significantly lower activity than the other ionic liquid cations under investigation. Pyridinium based ionic liquids showed similar and even better activity and better stability in terms of

enantioselectivity. More protic solvents resulted in SILP catalysts with higher activity. Particularly, this is observed for the protic ionic liquid [PrOHpyr][NTf₂], which yielded the highest activity and enantioselectivity. The protic character of the ionic liquid seems to be of similar importance as observed in systems with molecular solvents [44].

To verify the effect of increasing ionic liquid loadings on catalyst activity compared to the literature reports for liquid phase catalysis [50], the ionic liquid loading of the SILP catalysts under investigation was varied.

Fig. 10 shows the variation of the ionic liquid loading α . In contrast to the results in liquid phase asymmetric hydrogenations [50], increased amounts of ionic liquid were found to enhance catalytic activity, stability and selectivity. This stabilizing effect of higher ionic liquid loadings was also observed in our previous studies on the asymmetric hydrogenation of the β -keto ester methyl acetoacetate [19]. Obviously, in the SILP system, the ionic liquid provides a solvation layer for the asymmetric catalyst complex and a higher amount of IL stabilizes the catalyst throughout the reaction in a better way. Notably, no mass transport limitation effects were observed for high α values, which is due to the relatively slow reaction rate of the asymmetric hydrogenation reaction. Another important result of the IL loading variation is the fact that the relatively long catalyst activation time is independent on the amount

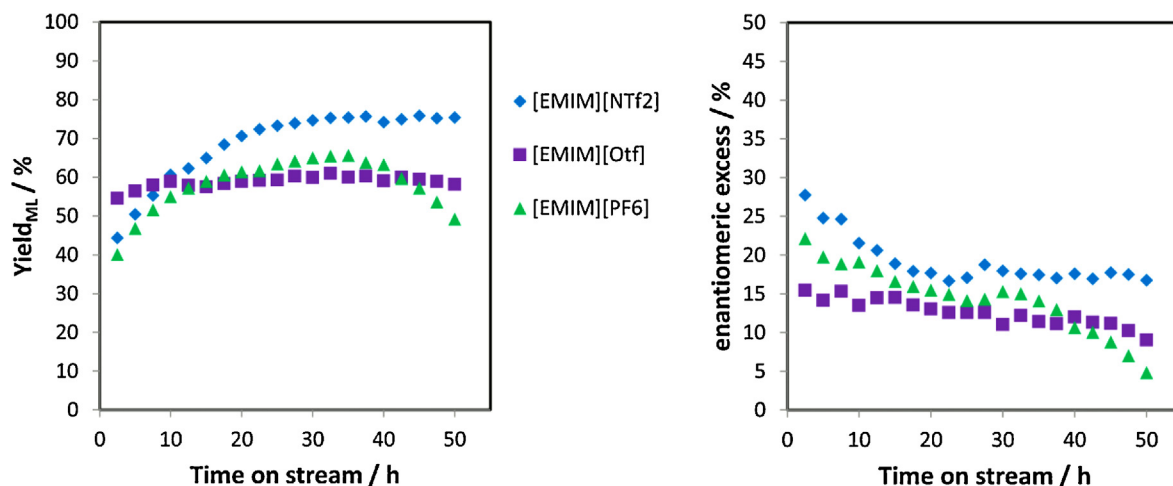


Fig. 8. Yield vs. time-on-stream profiles of the SILP catalyzed MPY hydrogenation in a continuous gas-phase reaction – variation of ionic liquid anion. (Reaction conditions: ligand = Xantphos, L/Ru = 2:1, α = 0.8, silica 100 (0.2–0.5 mm), 1 wt.% Ru, 95 °C, 10 bar, 200 Nml/min He, 75 Nml/min H₂, 0.25 g/h MPY, 0.475 g/h MeOH, τ = 2.86 s).

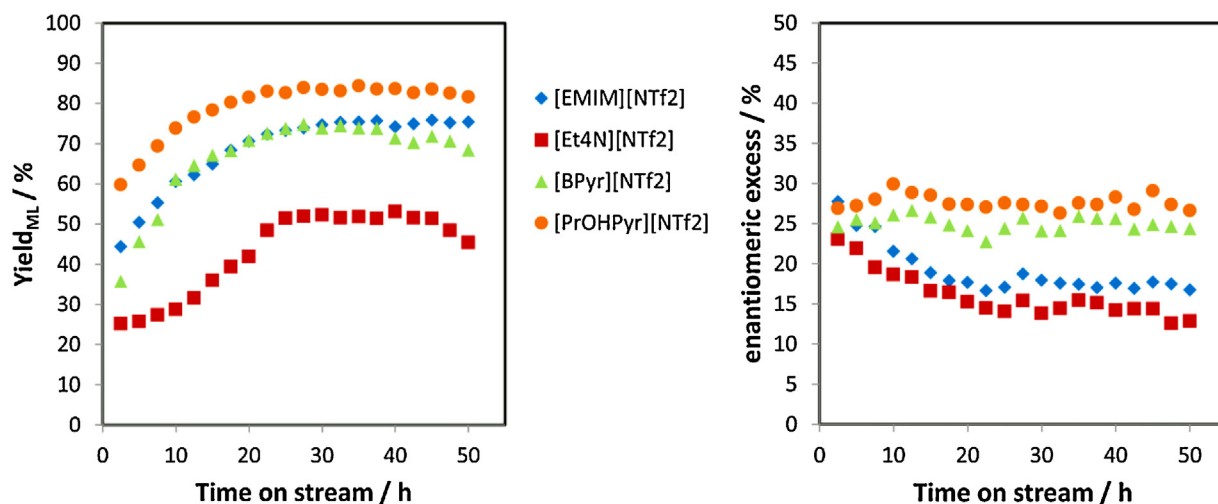


Fig. 9. Yield vs. time-on-stream profiles of the SILP catalyzed MPY hydrogenation in a continuous gas-phase reaction – variation of ionic liquid cation. (Reaction conditions: ligand = Xantphos, L/Ru = 2:1, α = 0.8, silica 100 (0.2–0.5 mm), 1 wt.% Ru, 95 °C, 10 bar, 200 NmL/min He, 75 NmL/min H₂, 0.25 g/h MPY, 0.475 g/h MeOH, τ = 2.86 s).

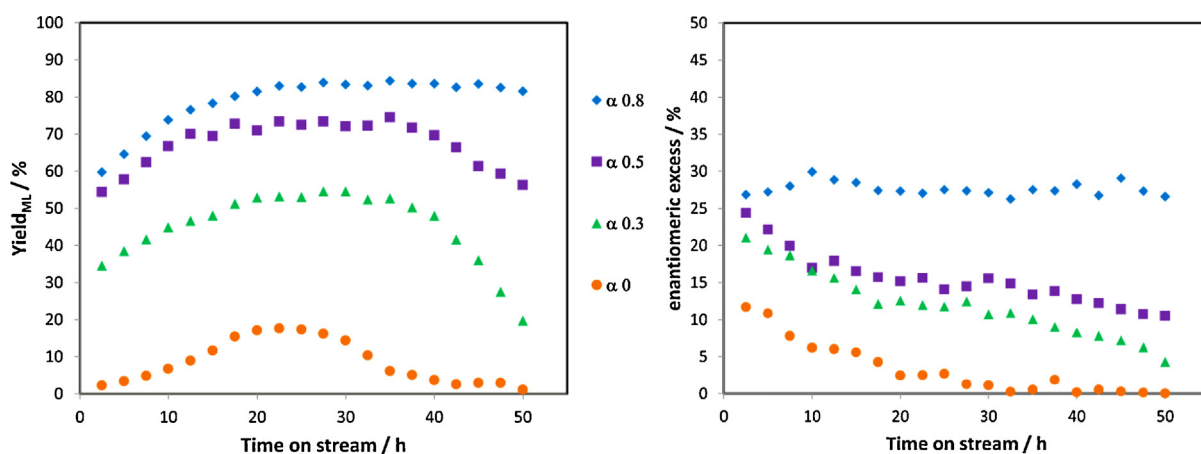


Fig. 10. Yield vs. time-on-stream profiles of the SILP catalyzed MPY hydrogenation in a continuous gas-phase reaction – variation of ionic liquid loading. (Reaction conditions: ligand = Xantphos, L/Ru = 2:1, ionic liquid = [PrOHpyr][NTf₂], α = 0–0.8, silica 100 (0.2–0.5 mm), 1 wt.% Ru, 95 °C, 10 bar, 200 NmL/min He, 75 NmL/min H₂, 0.25 g/h MPY, 0.475 g/h MeOH, τ = 2.86 s).

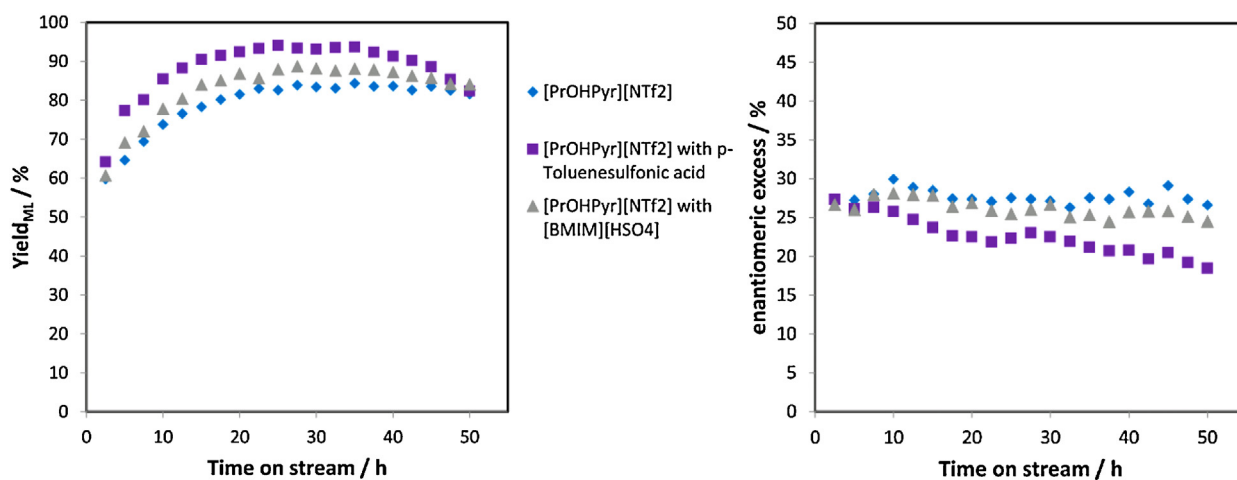


Fig. 11. Yield vs. time-on-stream profiles of the SILP catalyzed MPY hydrogenation in a continuous gas-phase reaction – addition of acidic additives. (Reaction conditions: ligand = Xantphos, L/Ru = 2:1, ionic liquid = [PrOHpyr][NTf₂], α = 0.8, acidic additive/Ru = 10/1 silica 100 (0.2–0.5 mm), 1 wt.% Ru, 95 °C, 10 bar, 200 NmL/min He, 75 NmL/min H₂, 0.25 g/h MPY, 0.475 g/h MeOH, τ = 2.86 s).

of ionic liquid loading. We assume that the extended time to full catalyst activation is linked to the low equilibrium solubility of hydrogen in the applied ionic liquid leading to a slow formation of the active species from the precursor complex.

Finally, the influence of acidic additives was investigated since activity enhancing effects of Brønsted acids had been reported for liquid phase systems [45]. For an addition of p-toluenesulfonic acid as well as for the addition of the acidic ionic liquid [BMIM][HSO₄] an increase in catalytic activity was observed, while the enantiomeric excess slightly decreased over time on stream (see Fig. 11). Though the system with p-toluenesulfonic acid achieved highest yields of about 95%, it deactivated more rapidly than the system with the additive [BMIM][HSO₄]. For the latter, yields of 88.7% and ee values of 25% were realized over more than 50 h time. Turn over frequencies were in the range of 25 mol_{ML} mol_{Ru}⁻¹ h⁻¹ resulting in an overall TON of 1100. Hence, a moderate acidity of support material, ionic liquid and acidic additives results in an active and quite stable SILP catalyst system. Moderate but quite stable enantioselectivities were obtained in the continuous-flow, gas phase asymmetric hydrogenation of the α-keto ester methyl pyruvate.

4. Conclusion

In conclusion we have successfully demonstrated the application of SILP catalysts in the gas phase asymmetric hydrogenation of α-keto esters, a substrate class that is known to be difficult to hydrogenate with high enantioselectivities. More precisely, the enantioselective hydrogenation of methyl pyruvate was demonstrated utilizing Ru-based SILP catalysts. Various ligands, support materials and ionic liquids were screened and evaluated with respect to catalyst activity, selectivity and stability. With Ru-BINAP dissolved in the ionic liquids 3-hydroxypropylpyridinium bis(trifluoromethylsulfonyl)imide on silica 100 an enantiomeric excess of 26–30% could be obtained at 80–84% yield for more than 50 h time on stream. Moreover, high degrees of pore filling are necessary to achieve reasonable enantioselectivity and good stability. Moderate acidity using silica support material and adding p-toluenesulfonic acid or 1-butyl-3-methylimidazolium hydrogen sulfate increased the product yield up to 95% yield. The reported SILP catalysts offer a simple yet very elegant way to ensure proper catalyst/product separation and allow for catalyst recycling without any need for ligand modifications.

Acknowledgements

This work was started in the context of the BMBF-sponsored network “Supported Ionic Liquid Phase catalysis” and we thank our partners LIKAT (Prof. Beller) and Evonik (Dr. Kadyrov) for ligand donations within this project. We gratefully thank the Deutsche Forschungsgemeinschaft within the Erlangen Excellence Cluster “Engineering of Advanced Materials” and the project was continued as part of the European Community’s Seventh Framework Program [FP7/2007–2013] for SYNFLOW under grant agreement no NMP2-LA-2010–246461 and this support is gratefully acknowledged. Infrastructural support was granted by the Deutsche Forschungsgemeinschaft through the Erlangen Excellence Cluster “Engineering of Advanced Materials”.

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