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Chirality Transfer in Imidazolium Camphorsulfonate Ionic Liquids through Ion Pairing Effects

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Abstract: The paper describes our studies on ion pair interactions in ionic liquids (IL) using an asymmetric hydrogenation reaction as probe. Three different ionic liquids carrying prochiral keto-functionalized cations were hydrogenated in the presence of their chiral, enantiomerically pure counter-ion using an achiral heterogeneous ruthenium catalyst. For the hydrogenation of *N*-(3′-oxobutyl)-*N*-methylimidazolium camphorsulfonate (**2**), *N*-(3′-oxobutyl)imidazolium camphorsulfonate (**4**) and *N*-(5′-oxohexyl)-*N*-methylimidazolium camphorsulfonate (**6**) we found a strong dependency of the enantiomeric excess (*ee* in the cation) on the polarity of the solvent, the concentration of the IL and the structure of the IL. The highest *ee* values of up to 94% were found for the hydrogenation of **2** in ethanol. Interestingly, we observed that the *ee* (and consequently the strength of ion pair interaction) had a pronounced maximum for a certain concentration of the IL in the solvent depending on the nature of the solvent and on the substrate. Remarkably, the concentration leading to the maximum *ee* could be rationalized by independent determination of the degree of dissociation which was obtained by a combination of diffusion-ordered NMR spectroscopy and conductivity measurements.

Keywords: chirality transfer; diffusion-ordered spectroscopy; hydrogenation; ion pairing; ionic liquids; NMR spectroscopy

Introduction

Understanding the nature of cation–anion interactions in ionic liquids is a topic of high relevance to explain ionic liquid properties as well as their interaction with dissolved substances. Among reported studies dealing with this topic, most are theoretical studies in which the ion pair interactions are calculated by molecular modelling.[1–16] Experimental investigations have been published on mass spectrometric analyses[17,18] and the investigation of physico-chemical properties of either ionic liquid mixtures[19] or solutions of polar molecules in ionic liquids.[20] Most recent publications on the topic have focussed on NMR spectroscopy,[21–25] FT-IR and Raman spectroscopy.[26,27]

A few examples are known in which cation–anion interactions and ionic liquid transition state interactions have been studied by monitoring the selectivity of reactions. Chiappe et al. studied, for example, the bromination of alkynes[28] and revealed that the structure of the ionic liquid under investigation had a strong influence on the transition state, the reaction order and therefore the rate of *syn*- and *anti*-addition products. Similar findings concerning the ionic liquid's influence on the reaction selectivity were made for the C- *vs.* O-alkylation of sodium β-naphthoxide with benzyl halides[29] and for Diels–Alder reactions.[30] So far – to the best of our knowledge – only two publication describe the degree of ion pair interaction in camphorsulfonate ionic liquids and both link this interaction to the *endo*/*exo* stereoselectivity of a Diels–Alder reaction.[31,32]

The interest in chiral ionic liquids (CILs) has increased significantly in recent years. The first example of an ionic liquid with a chiral anion was reported in 1999 by Seddon's group in a study dealing with lactate ionic liquids.[33] Further ionic liquids with chiral anions were prepared later by the groups of Ohno,[34] Machado,[35] and Leitner,[36] derived from 19 natural amino acids, (*S*)-10-camphorsulfonate and (*R*)-1,10-bi-

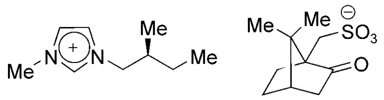


Figure 1. "Doubly chiral" ionic liquid as published 2005 by Machado's group.

naphthylphosphate, and borate anions based on L-(−)-malic acid, respectively. Chiral cations are also accessible from the chiral pool. However, usually multi-step syntheses are necessary. For example, our group has introduced in 2002 oxazolinium cations prepared from amino acids in a four-step synthesis as well as hydroxyammonium salts derived from the corresponding amino alcohol by the Leuckart–Wallach reaction.[37] Besides amino acids and amino alcohols, chiral cations have been also synthesized by alkylation of imidazole or imidazoline with chiral alkylation agents.[38]

Examples of ionic liquids with chirality in both ions are very rare to date. The first examples of this kind of a "doubly chiral" ionic liquid was 1-methyl-3-[(*S*)-2′-methylbutyl]imidazolium (*S*)-camphorsulfonate, (Figure 1) published by Machado's group in 2005.[39] Only very recently, the groups of Luo and Cheng published a new combinatorial approach to doubly chiral ionic liquids by ring opening of chiral cyclic sulfates and cyclic sulfamidates and subsequent reaction with chiral acids like tartric acid, lactic acid or camphorsulfonic acid.[40]

Asymmetric synthesis in which the solvent is the source of chiral information is possible. However, up to now few convincing examples have been reported, and the enantioselectivities achieved in this way have been small to moderate in most cases.[41] These findings are in very good agreement with our own former work showing that the strong interaction between the ionic liquid's cation and anion makes chirality information hardly transferable within the system to uncharged molecules and transition states.[42] However, we and others realized that chiral anions like α-methoxy-α-trifluoromethylphenylacetate (deprotonated Mosher's acid) do strongly interact with the chiral cation of a CIL.[43] These ion pair interactions could be verified by ^{19}F NMR spectroscopy using a racemic mixture of Mosher's acid sodium salt as substrate in an enantiomerically pure ephedrinium bis(trifluoromethylsulfonyl)imide ionic liquid. In this context it is not surprising that the best results of solvent-induced chirality transfer reported so far were obtained by Leitner and co-workers using a chiral anion-containing ionic liquid for an aza-Baylis–Hillman reaction[36] and for a homogeneous Rh-catalyzed hydrogenation.[44] For the aza-Baylis–Hillman reaction an ionic transition state was postulated in which the Brønsted acidic, chiral anion is incorporated as a kind of organocatalyst.

While chirality transfer in ionic liquids is a very young field of research, reports on chiral recognition have been published already many years ago. In 1931 it was reported that diastereoselective interactions between a configurationally labile charged metal complex and a chiral counter ion can induce stereoselectivity at the metal center (Pfeiffer effect).[45] In the past years a number of papers have been published in high-ranked journals that have applied chiral recognition effects successfully in organocatalysis,[46] Brønsted acid-catalyzed reactions,[47] homogeneous metal-catalyzed reactions,[48] and especially phase-transfer catalysis.[49] Chiral recognition has been proven by 1D- and 2D-NMR studies with chiral ions and racemic counter-ions.[50] In most of these studies it was found that chiral recognition is stronger in less polar solvents with low dielectric constants.

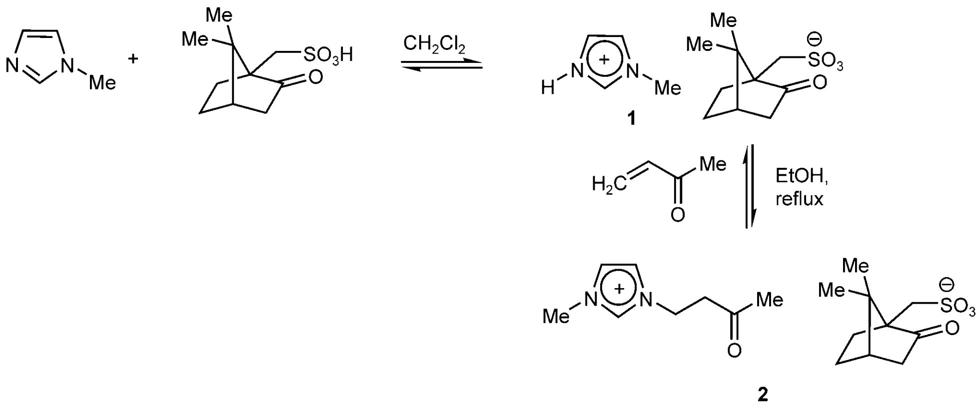
In this paper, we expand on our previous communication[51] describing the hydrogenation of [*N*-(3′-oxobutyl)-*N*-methylimidazolium] [(+)-camphorsulfonate], an ionic liquid consisting of a pro-chiral, keto-functionalized cation and an enantiomerically pure, chiral counter-ion. At the time, it was found that the hydrogenation with the achiral Ru catalyst led to a significant enantiomeric excess of the hydroxy-functionalized product cation. The working hypothesis of this previous paper was that this chiral induction is caused by the intimate ion pair interaction in the ionic liquid. Chiral poisoning effects on the surface of the heterogeneous Ru catalyst were excluded by control experiments using the same anion but hydrogenating the neutral substrate acetophenone.[51]

The focus of this paper is to highlight the effects of the reaction medium and the ionic liquid concentration on the ion pair formation and thus on the enantiomeric excess. Furthermore, we report the results from an independent investigation of the so-called degree of ion dissociation that was derived from the determination of self-diffusion coefficients and electric conductivities. For different concentrations the degree of ion dissociation is compared to the conditions showing the best asymmetric induction in the hydrogenation catalysis.

Results and Discussion

Synthesis and Properties of Prochiral Ionic Liquids

In the course of this study we have synthesized three different prochiral ionic liquids. [*N*-(3′-oxobutyl)-*N*-methylimidazolium] [(+)-camphorsulfonate] **2** was prepared as an example for a *N,N*′-dialkylated, prochiral imidazolium salt. [*N*-(3′-oxobutyl)imidazolium] [(+)-camphorsulfonate] **4** was synthesized as a representative for an N-protonated, prochiral imidazolium cation. The latter offers the option to liberate a neu-

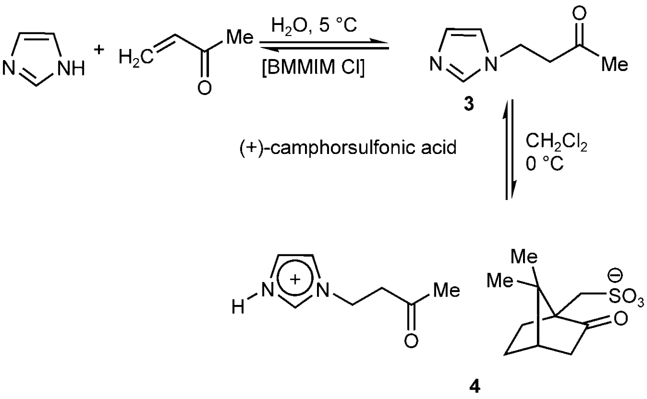


Scheme 1. Synthesis of [*N*-(3′-oxobutyl)-*N*-methylimidazolium] [(+)-camphorsulfonate] **2** *via* protonation and Michael addition of methyl vinyl ketone.

tral amino alcohol after a basic work-up of the hydrogenated ionic liquid. As an example for a different number of CH_2-spacers between the carbonyl group and the imidazolium core we synthesized [*N*-(5′-oxohexyl)-*N*-methylimidazolium] [(+)-camphorsulfonate] **6**.

In the first step of the preparation of ionic liquid **2**, 1-methylimidazole was protonated with stoichiometric amounts of the enantiomeric pure (+)-camphor-10-sulfonic acid to form the imidazolium salt **1**. Salt **1** was reacted under reflux with methyl vinyl ketone in a Michael-type addition according to our own previous work to the prochiral ionic liquid [*N*-(3′-oxobutyl)-*N*-methylimidazolium] [(+)-camphorsulfonate] (**2**).[51] Compound **2** is a highly viscous oil which is air- and temperature-stable over months (Scheme 1).

Some important physico-chemical properties of **2** and **6** have been determined and are summarized in Table 1.



Scheme 2. Synthesis of [*N*-(3′-oxobutyl)imidazolium] [(+)-camphorsulfonate] **4** *via* Michael addition of methyl vinyl ketone and subsequent protonation with camphorsulfonic acid.

In a similar manner, we synthesized [*N*-(3′-oxobutyl)imidazolium] [(+)-camphorsulfonate] (**4**) (Scheme 2). In this case the Michael addition of the side chain was performed prior to the introduction of the chiral camphorsulfonic acid anion. This approach offers the advantage of easier purification of the neutral imidazole intermediate **3** by rapid column chromatography. Once converted into an ionic liquid, purification is usually much more difficult. While the amine **3** is temperature-labile and decomposes readily at room temperature (storage at 0 °C is recommend-

Table 1. Selected physico-chemical properties of [*N*-(3′-oxobutyl)-*N*-methylimidazolium] [(+)-camphorsulfonate] **2** and [*N*-(3′-oxobutyl)imidazolium camphorsulfonate] **4**.[a]

	Vicosity[b] [mPa s]	Density[c] [g mL^{-1}]	TGA[d] Onset	T_g[e] Onset
2	1600	1.217	162 °C, 291 °C	−41 °C
6	390	1.182	317.5 °C	−37.4 °C, 13.6 °C

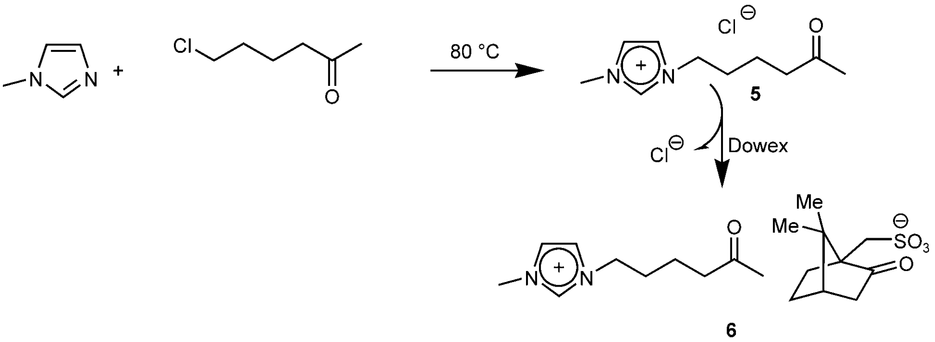
[a] All data for **2**, **6** have been obtained for samples containing 0.61% and 1.51% of water, respectively.

[b] 40 °C, shear rate: 1–1000 s^{-1}.

[c] 40 °C.

[d] Heating rate: 10 K min^{-1}, sample was kept at 80 °C for 30 min prior to heating, first value for **2** reflects retro-Michael reaction, second value further decomposition.

[e] Onset was determined from the heating scan, heating rate: 2 K min^{-1}, first value for **6** reflects the glass transition temperature, second value the melting point.



Scheme 3. Synthesis of *N*-(5′-oxohexyl)-*N*-methylimidazolium camphorsulfonate **6** *via* alkylation followed by anion exchange.

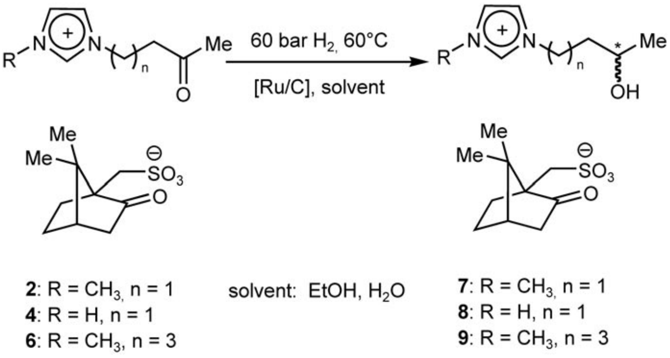
ed), the ionic liquid **4** is stable at room temperature for days if dry.

For the synthesis of **6** a different approach was chosen. First, 1-methylimidazole was alkylated with 1-chlorohexan-5-one to the corresponding chloride IL **5**. Then, the anion was exchanged for the camphorsulfonate anion using an anion exchange resin (Scheme 3).

Hydrogenation Reactions

For the hydrogenation of the prochiral keto groups of the prochiral cations in **2**, **4**, and **6** the ionic liquid was dissolved in the respective solvent and ruthenium on charcoal was applied as achiral, heterogeneous catalyst (Scheme 4). Under the reaction conditions applied here, the carbonyl group of the anion is stable. Clearly harsher conditions are necessary to reduce the anion's keto group to the corresponding alcohol.[52]

The enantiomeric excess in the respective cations of the hydrogenated ionic liquids **7**, **8**, and **9** was determined by ^{19}F NMR spectroscopy after anion exchange of camphorsulfonate *vs.* $[NTf_2]^-$ and esterification of the products with enantiomerically pure Mosher's acid chloride [α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride, MTPACl]. As reported in our previous communication this determination method has been validated by experiments with both enantiomers of Mosher's acid. Moreover, a chiral poisoning of the catalyst surface has been excluded by experiments with sodium camphorsulfonate as potential chiral poisoning agent and acetophenone as substrate. No enantiomeric excess was found in this case as already reported in our previous communication[51].



Scheme 4. Asymmetric hydrogenation of the prochiral keto-functionalized cations of the ionic liquids **2**, **4**, and **6** using a heterogeneous, achiral Ru-catalyst.

To further investigate the interplay between the chiral induction and the strength of ion pairing we investigated the hydrogenation of ionic liquids **2**, **4**, and **6** over a wide concentration range in water and ethanol. As our results indicated that ethanol is a particular interesting solvent for our specific concept, the hydrogenation of **6** was only performed in this solvent. The ionic liquid concentration was varied from 0.05 to 0.5 mol/L, the results are summarized in Table 2.

Assuming that the enantiomeric excess is a probe for the intimacy of the ionic liquid's ion pair interactions these results imply that ethanol as a quite polar solvent separates most of the ions of the ionic liquid at low concentrations forming separated ions in a way that the contact is not close enough for a very effective transfer of the chiral information to the transition state of the reaction. When increasing the concentration of IL **2**, a strong increase in chiral induction is observed indicating the formation of much closer ion pairs. At a concentration of 0.3 mol/L, an enantiomeric excess of 94% was found in the cation of IL **7**, which represents an unprecedentedly high value for this kind of ion pair induced, chiral hydrogenation. The increase of chiral induction with higher ionic liquid concentration is attributed to the formation of solvated contact ion pairs under these reaction conditions. We explain the decrease of chiral induction with an even higher ionic liquid concentration with the formation of higher ionic liquid aggregates and ion clusters in which the chirality transfer is less effective.[53,54]

Table 2. Asymmetric hydrogenation of keto-functionalized imidazolium ionic liquids **2**, **4**, and **6** – concentration variation in water and EtOH *vs. ee* in the cations of **7**, **8**, and **9** after hydrogenation.[a]

[mol/L][b]	[mol/mol]$_{EtOH}\times 10^{-3}$	[mol/mol]$_{water}\times 10^{-3}$	*ee* (EtOH) **2**	*ee* (EtOH) **4**	*ee* (EtOH) **6**	*ee* (water) **2**	*ee* (water) **4**
0.05	2.92	0.90	18%	n.d	35%	8%	n.d
0.1	5.83	1.81	55%	28%	40%	27%	36%
0.15	8.75	2.71	72%	n.d	82%	54%	41%
0.2	11.66	3.61	64%	44%	67%	42%	50%
0.3	17.49	5.42	94%	54%	45%	4%	38%
0.5	29.16	9.03	80%[49]	44%	14%	3%	36%

[a] *Conditions:* $T = 60\,°C$, $p(H_2) = 60$ bar, catalyst: Ru/C (5% Ru, 10 wt% Ru/C with respect to 2 or 4, 10 wt% with respect to 6), $t = 15$ h, conversion $X > 95\%$ in all cases.

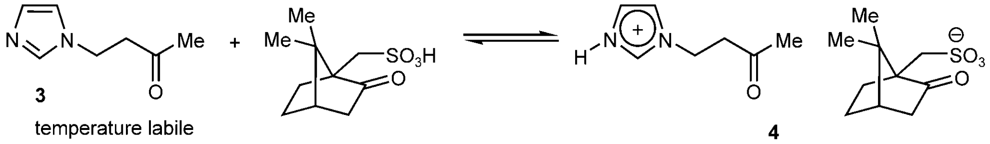
[b] IL/solvent.

In order to study the role of the solvent polarity in more detail, another set of hydrogenation experiments was carried out using water as a more polar solvent. Again, the enantiomeric excess of the reaction was monitored as a function of the ionic liquid concentration. As expected, the product ionic liquid **7** showed generally lower *ee* values when prepared in water. This can be understood from the fact that water shows in principal a higher ability to dissociate ions. For such a comparison the difference between the molar fraction (mol/mol) of the ionic liquid in the solvent and the molar concentration (mol/L) of the ionic liquid in the solvent has to be considered. The molar fraction of the ionic liquid in water is about a factor of 3 lower than in ethanol at the same molar concentration, meaning three times more solvating molecules per ion pair. Nevertheless, if comparing the *ee* values in ethanol and water at 0.1 mol/L and 0.3 mol/L, respectively, which have rather similar molar fractions of ionic liquid in the solvent, the *ee* in water is still significantly lower. The maximum *ee* was reached at a concentration of 0.15 mol/L in water and at a concentration of 0.3 mol/L in ethanol.

We were also interested to study the chiral induction in the case of the protonated salt **4** as the latter offers access to neutral amino alcohols after basic work-up. As one can see from Table 1 the enantiomeric excess of the cation of IL **8** is generally lower compared to the *N,N'*-dialkylated cation of ionic liquid **7** when obtained from the hydrogenation in ethanol. We attribute this effect to the protonation equilibrium of the starting material **4** that should weaken in average the strength of ion pair interactions (Scheme 5). In addition to that, our experiments reveal that the protonation equilibrium is shifted to its neutral form in ethanol as we found more decomposition products from the temperature-labile imidazole derivative **3** if the hydrogenation was carried out in ethanol compared to the same reaction in water.

It is very remarkable that for all ionic liquid/solvent systems under investigation the maximum chiral induction has not been observed for the highest ionic liquid concentration. We account this finding to the fact that with higher concentrations larger ion clusters are formed, which prevent the optimum arrangement of the anion, the cation and the catalytic surface during hydrogenation for optimum chirality transfer. Moreover, it is also highly noteworthy that the concentration at which a maximum *ee* is observed was found to be similar for the transformations of **2** and **4** in the same solvent, but different for the two different solvents. While the hydrogenation of **2** and **4** produced the highest *ee* in the cation at an ionic liquid concentration of 0.3 mol/L in EtOH, the same substrate ionic liquids were transformed with the highest chiral induction at an ionic liquid concentration of 0.15 to 0.2 mol/L in water.

In order to expand our concept to other cation structures and to reveal the structural sensitivity of our concept we finally investigated the same hydrogenation using IL **6** as the substrate. As shown above, **6** is characterized by a longer alkyl spacer between the center of positive charge and the pro-chiral keto functionality. Table 2 shows the results of the hydrogenation of **6** in ethanol. Again, a pronounced dependency of the product cation *ee* with the ionic liquid concentration was observed. The *ee* reached a maximum value of 82% at an ionic liquid concentration of



Scheme 5. Protonation equilibrium between the ionic liquid and the neutral oxobutylimidazole and camphorsulfonic acid.

0.15 mol/L, lower and higher IL concentrations led to significant reduction in chirality transfer.

Determination of the Degree of Ion Dissociation α

Encouraged by this interesting correlation of solvent and concentration range on the one hand and degree of chiral induction on the other hand, we aimed to determine the degree of ion dissociation in our reaction system by an independent analytical method. For this purpose, a combination of diffusion ordered NMR spectroscopy (DOSY-NMR) and electric conductivity measurements has been applied. DOSY-NMR is a very powerful tool to determine the self-diffusion coefficients of the ionic liquid's cation and anion (D_+ and D_-) independently and was applied for several ionic liquids in recent years.[55–60] In our experiments the bpp-led sequence (bipolar pulsed pairs longitudinal echo current delay) has been applied. The pulse sequence has been optimized by adjusting the duration of the field gradient $\delta/2$, the intervals between the gradient pulses Δ and the magnitude of the field gradient g (for details see Experimental Section and Supporting Information).

From the fact that anion and cation have self-diffusion coefficients in the same order of magnitude one can conclude that they either diffuse independently from each other but with the same velocity (which is rather unlikely due to their different size and shape) or that they form an ion pair. For the cation as well as for the anion, the diffusion coefficient stays constant with rising temperature (within the error of the measurement) up to a temperature limit between 20 and 30 °C. When reaching this temperature a remarkable rise of the values is observed which is strongly dependant on the ionic liquid's concentration. In a similar manner we have determined the diffusion coefficients for anion and cation of ionic liquid **2** in D_2O and for ionic liquid **6** in EtOH.

Besides the self-diffusion coefficients, we also determined the electric conductivities of ionic liquid **2** at 40 °C at different concentrations in ethanol and water and of IL **6** in ethanol (for details of the measurement and results see Supporting Information). From the self-diffusion coefficients and the conductivity data we calculated the degree of dissociation α using a modified Stokes–Einstein equation [Eq. (1)].[55] It should be mentioned here that the so-called degree of dissociation is not a measure for the number of ion pairs in solution, but reflects the order of cations and anions. The smaller the value of α, the better ordered are the ions of the whole system.

$$\sigma_D = \frac{Ne^2}{kT}\left(D_+ + D_-\right)\alpha \tag{1}$$

where σ_D = conductivity, N = cations per volume, e = electric charge, D_+/D_- = self-diffusion coefficients and α = degree of dissociation.

A very similar approach to determine the degree of dissociation of non-functionalized ionic liquids was recently proposed by Watanabe.[56]

Figure 2, Figure 3, and Figure 4 display graphs in which the degree of dissociation (α) calculated according to Eq. (1) is plotted against the IL concentration.

From a comparison of Figure 2 and Figure 3 one can find that the degree of dissociation of **2** in water is significantly higher than in ethanol. This corresponds nicely to our findings from the hydrogenation experiments and can be taken as a proof that the con-

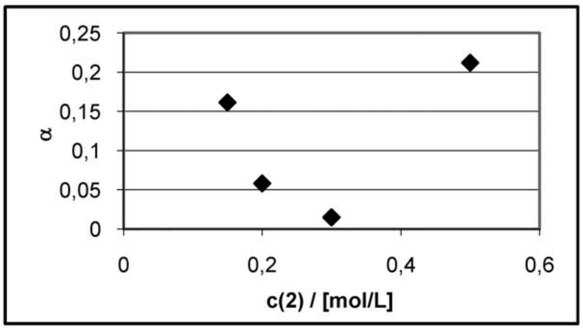


Figure 2. Degree of dissociation α as a function of the concentration of **2** in ethanol at 40 °C.

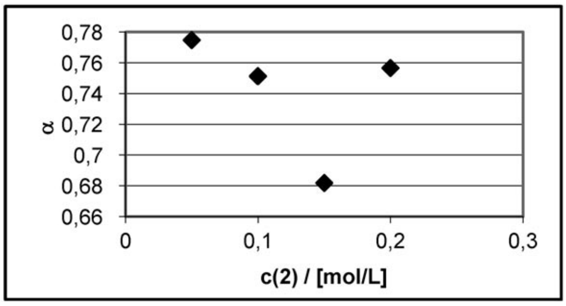


Figure 3. Degree of dissociation α as a function of the concentration of **2** in D_2O at 40 °C.

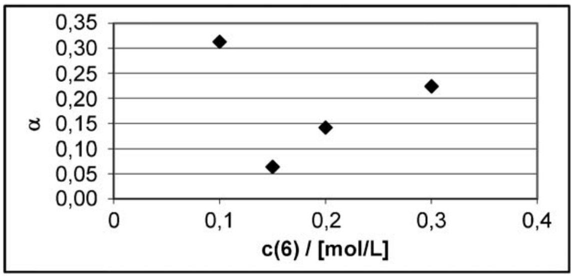


Figure 4. Degree of dissociation α as a function of the concentration of **6** in ethanol at 40 °C.

tact of the ionic liquid ions in water is not close enough to transfer the chiral information very effectively.

Very remarkably, in every example investigated, a minimum for the degree of dissociation was found in the concentration range between 0.15 and 0.5 mol/L for exactly the concentration where also the highest enantiomeric excess was found in the hydrogenation experiments. This finding strongly supports the interpretation that intense ion pair association is indeed a necessary condition for effective chiral induction in this special type of asymmetric hydrogenation.

Moreover, these results open a new and very promising way to predict the concentration range of most intense ion pair interaction also for other systems by a combination of DOSY-NMR and conductivity measurements.

Conclusions

We have shown that in the asymmetric hydrogenation of prochiral ionic liquids high enantiomeric excesses can be realized by transferring the chiral information from the enantiopure anion to the prochiral cation by intimate ion pair interactions. Although the formation of a close contact ion pair in solution is not the only prerequisite it has shown to be crucial for successful chirality transfer.

In addition, we have determined the degree of dissociation of the ionic liquid in ethanolic and aqueous solutions for different concentrations using DOSY-NMR and conductivity measurements. With these measurements we have expanded the scope of ion pair dissociation studies for the first time to highly functionalized ionic liquids. Very remarkably, the lowest value for the degree of dissociation has been found for the concentration 0.3 mol/L, where also the highest degree of chiral induction in the hydrogenation experiments was obtained. Our results may serve to predict the conditions of effective chiral induction by ion pairing in ionic liquids. In further developing chiral induction among ion pairs to a potential ionic auxiliary chemistry, this methodology may save in the future tedious screening experiments to identify the best solvents and concentration ranges for a given ionic liquid of interest.

Experimental Section

General Remarks

All syntheses were carried out under argon unless otherwise specified. Solvents for the hydrogenation reactions were of spectroscopic grade. Methylimidazole was distilled und kept under argon at −18 °C prior to use. All other chemicals were used as received. Ruthenium on charcoal (5% Ru) was purchased from Fluka. Hydrogenations were carried out in a glas liner in a 300-mL Parr autoclave equipped with a gas entrainment stirrer, a thermocouple, hydrogen inlet, and heating mantle. The conductivity was determined using a conductivity cell (LTA 1, WTW, cell constant $K=1$, platinized platinum electrode). The differential scanning calorimetry (DSC) was carried out using a Netzsch DSC 204 under N_2 atmosphere in sealed aluminum pans. The temperature stability was measured by thermogravimetric analysis (TGA) using a Netzsch TG 209. The sample was kept at 80 °C for 30 min and heated to 450 °C with a heating rate of $10\,\mathrm{K\,min^{-1}}$. The water content was determined by Karl–Fischer titration using a Metrohm 756 KF Titrator. Electrospray mass spectrometry was carried out on a Bruker Esquire 6000.

The viscosity was measured under inert gas atmosphere applying an Anton Paar Physica MCR 100 rheometer at 40, 50, 60, 80 and 90 °C. The density determination was carried out using an Anton Paar DMA 4500 density meter. NMR experiments were carried out with a Jeol ECX 400 MHz spectrometer with a 2-chanel (HF, LF)-probe. Spectra were referenced to the solvent. The procedure of bpp-led-DOSY-NMR followed published procedures.[53,54,59–62]

[*N*-(3′-Oxobutyl)-*N*-methylimidazolium] [(+)-Camphorsulfonate] (2)

A flask was charged with methylimidazole (35.35 g, 0.43 mol). Dichloromethane (250 mL) and (+)-camphor-10-sulfonic acid (100 g, 0.43 mol, 1.0 equiv.) were slowly added. After 2 h, the solvent was removed and the product was obtained as a white solid. This was dissolved in ethanol (400 mL) and methyl vinyl ketone (71.67 mL, 60.34 g, 0.861 mol, 2.0 equiv.) was slowly added. The mixture was refluxed for 3 d. After removal of the solvent the product was obtained as light brown, highly viscous oil; yield: 157.64 g (0.41 mol, 95%).

[*N*-(3′-Oxobutyl)imidazolium] [(+)-Camphorsulfonate] (4)

A flask equipped with a dropping funnel was charged with imidazole (29.31 g, 0.43 mol), 1-butyl-2,3-dimethylimidazolium chloride (11.27 g, 0.06 mol, 0.15 equiv.), and water (300 mL) and cooled to 5 °C. Methyl vinyl ketone (46.5 mL, 39.18 g, 0.56 mol, 1.3 equiv.) was slowly added. The mixture was stirred for 12 h while slowly heating up to room temperature. The resulting solution was extracted four times with dichloromethane in order to separate the product from BMMIM Cl, which remains in the water phase. The organic phase was dried over $MgSO_4$ and the solvent was removed in vacuo. The brown oil was purified by column chromatography (silica, dichloromethane/ethanol, 8/1, v/v) giving the 1-methyl-3-(2-oxobutyl)imidazol as colorless viscous liquid; yield: 38.90 g (0.28 mol, 65%).

The liquid was dissolved in dichloromethane (300 mL) and (+)-camphor-10-sulfonic acid (65.04 g, 0.28 mol, 1.0 equiv.) was added portion wise. After 2 h the solvent was removed and the ionic liquid was obtained as a light brown oil; yield: 104.02 g (0.28 mol, 100%).

[*N*-(5′-Oxohexyl)-*N*-methylimidazolium] [(+)-Camphorsulfonate] (6)

A flask was charged with methylimidazole (8.22 g, 0.10 mol) and 1-chlorohexan-5-one (14.7 mL, 0.11 mol, 1.1 equiv.) and heated to 80 °C for three days. Remaining 1-chlorohexan-5-one was distilled out of the product under reduced pressure.

A 0.1 M aqueous solution of the product ionic liquid was slowly percolated through a strong base anion exchange resin charged with (+)-camphorsulfonate. Water was removed under reduced pressure. The resulting yellow ionic liquid was chloride free according to silver nitrate test; yield: 37.92 g (0.09 mol, 91%).

Column preparation: A Dowex 1-X8 column (Cl^- form, capacity = 1.2 mmol/mL, r = 2.25 cm, h = 11 cm) was washed with 2 M NaOH until no chloride could be detected when adding silver nitrate solution. After washing to neutral pH with water the column was charged with 0.1 M camphorsulfonic acid solution and washed to neutrality again.

Hydrogenation

Prior to every hydrogenation, the hygroscopic ionic liquid was thoroughly dried at 45 °C and under reduced pressure to guarantee minimal water content. The ionic liquid was dissolved in 75 mL of the solvent and ruthenium on activated charcoal was added (5% Ru/C, 10 wt% with respect to IL **2** and **4**, 5% Ru/C, 50 wt% with respect to IL **6**). The mixture was hydrogenated in an autoclave at 60 °C, 60 bar hydrogen pressure for 16 h. After filtration of the catalyst and removal of the solvent the product was obtained as highly viscous brown oil.

Anion Exchange

The ionic liquid was dissolved in dichloromethane and an aqueous solution of 1.2 equivalents $Li[NTf_2]$ was added. After 30 min half of the water phase was replaced. The procedure was repeated twice. Drying over $MgSO_4$ and removal of the solvent led to a viscous light brown oil in up to 60% yield.

^{19}F NMR

The ionic liquid was dissolved in dry dichloromethane and reacted with enantiopure Mosher's acid chloride [α-methoxy-α-(trifluormethyl)-phenylacetyl chloride, MTPACl] and tripropylamine to drive the reaction to completion. The diastereomeric esters were analyzed by ^{19}F NMR spectroscopy.

Supporting Information

The analytical data of the products and selected examples of ^{19}F NMR spectra for the determination of the *ee* and DOSY-NMR spectra are given in the Supporting Information.

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