

Ruthenium- and Rhodium-catalyzed Carbenoid Reactions of Diazoesters in Hexaalkylguanidinium-based Ionic Liquids

Torsten Large, Tobias Müller, Helene Kunkel, Stefan Buck, and Gerhard Maas

Institute of Organic Chemistry I, University of Ulm, Albert-Einstein-Allee 11, 89081 Ulm, Germany

Reprint requests to Prof. Dr. Gerhard Maas. Fax: +49 731 5022803.

E-mail: gerhard.maas@uni-ulm.de

Z. Naturforsch. **2012**, *67b*, 347–353; received February 3, 2012

Dedicated to Professor Ernst Anders on the occasion of his 70th birthday

Hexaalkylguanidinium-based room-temperature ionic liquids were investigated as solvents for the cyclopropanation of styrene with diazoacetates catalyzed by $\text{Rh}_2(\text{OAc})_4$ or $[\text{Ru}_2(\mu\text{-OAc})_2(\text{CO})_4]_n$. While the yields of the formed cyclopropanes are much lower compared to the reactions performed in dichloromethane, the diastereomeric ratio is not significantly affected by the change of the reaction medium. Immobilization of the catalysts is only partially successful. In contrast to this intermolecular reaction, the Ru-catalyzed formation of a β -lactam by an intramolecular carbenoid C–H insertion of an α -methoxycarbonyl- α -diazoacetamide occurs in high yield, similar to the $\text{Rh}_2(\text{OAc})_4$ -catalyzed reaction. The *cis* \rightarrow *trans* isomerization of the resulting 1-*tert*-butyl-3-methoxycarbonyl-4-phenyl-azetidin-2-one is accelerated in the ionic liquid *N,N*-dibutyl-*N',N'*-diethyl-*N'',N''*-dihexylguanidinium triflate.

Key words: Diazoacetates, Cyclopropanation, C–H Insertion, Ionic Liquids, Rhodium, Ruthenium

Introduction

Ionic liquids (ILs) have recently been introduced as novel solvents for the purposes of organic synthesis [1]. Catalytic transformations have emerged as an attractive area of application [2], mainly for two reasons: a) many of the catalytically active (transition) metal salts and complexes have a good solubility in ionic liquids, and b) catalysts can be immobilized and re-used in the ionic liquid while the other components of the reaction mixture are extracted into a solvent that is not miscible with the ionic liquid.

Metal-catalyzed transformations of diazo compounds constitute an important strategy in contemporary organic synthesis [3]. Several typical transformations of diazo compounds, such as cyclopropanation, aziridination, C–H and X–H (X = O, N) insertion, and ylide formation, in the presence of copper [4–8], rhodium [4d, 9–12], palladium [13], iron porphyrin [14], or gold [15] catalysts, have been carried out in ionic liquids, mostly under the aspect of catalyst immobilization. Almost all of these studies used ionic liquids based on 1-alkyl-3-methylimidazolium ions. Afonso and coworkers briefly mentioned the rhodium-catalyzed intramolecular C–H insertion of

α -diazo- α -phosphonoacetamides in a hexaalkylguanidinium ionic liquid [16].

We have recently developed an interest in the synthesis and properties of hexaalkylguanidinium-based ionic liquids [17]. In continuation of our preceding work on carbenoid transformations of diazo compounds catalyzed by dinuclear ruthenium(I,I) complexes $[\text{Ru}(\text{CO})_2-(\mu\text{-L}_2)\text{-Ru}(\text{CO})_2]$, where L represents a bidentate acetate or amidate ligand [18, 19], we have now studied such reactions in hexaalkylguanidinium-based ionic liquids. A comparison is made with analogous rhodium-catalyzed reactions and with reactions in an imidazolium-based ionic liquid as well.

Results and Discussion

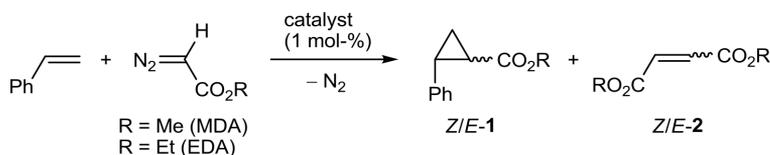
The molecular structures of the hexaalkylguanidinium-based r.t. ionic liquids used in this study are shown in Fig. 1. While $[\text{N11N22N44}]\text{OTf}$ [17], $[\text{N22N44N66}]\text{OTf}$ [17] and $[\text{N16N22N44}]\text{I}$ [20] are known compounds, $[\text{N16N22N44}]\text{OTf}$ has been synthesized from the iodide by anion exchange with silver triflate in acetonitrile. 1-Butyl-3-methylimidazolium hexafluorophosphate ($[\text{bmim}]\text{PF}_6$), a widely used ionic liquid, was taken for a comparison in some cases.

Table 1. Rhodium- and ruthenium-catalyzed cyclopropanation of styrene in ionic liquids or CH₂Cl₂ (see Scheme 1)^a.

Entry	Solvent	Diazoacetate ^b	Temperature (°C)	Yield of Z- + E-1 (%)	Ratio Z-1 : E-1	Yield of 2 (%)	Reference
Catalyst: [Ru₂(μ-OAc)₂(CO)₄]_n (1 mol-%)							
1	CH ₂ Cl ₂	MDA	20	95	38 : 62		[18a]
2	[N11N22N44]OTf	MDA	40	30	34 : 66	not determ.	this work
3			60	49	34 : 66	21	“
4			80	57	35 : 65	14	“
5	[N16N22N44]I	MDA	40	45	34 : 66	n.d.	“
6	[N16N22N44]OTf	MDA	40	22	42 : 58	15–18	
7	[bmim]PF ₆	MDA	22	39	43 : 57	20	“
8			40	47–52	42 : 58	12–14	“
Catalyst: [Rh₂(μ-OAc)₄] (1 mol-%)							
9	CH ₂ Cl ₂	EDA ^c	22	92	40 : 60		[21]
10	[N11N22N44]OTf	EDA	40	38	43 : 57	11	
11	[bmim]PF ₆	EDA	27	88	10 : 90	12	[10]
12			27	42	42 : 58		this work
13			50	49	41 : 59	10	this work
14	[hmim]PF ₆ ^d	EDA	50	quant.	38 : 62	n.d.	[12]
15	[bmim]PF ₆	MDA	27	56	38 : 62	11	this work
16			50	58	39 : 61	17	this work

^a A mixture of diazoester (1 mmol) and styrene (2 mmol) was gradually added to a solution of styrene (3 mmol) in the solvent (3 mL);

^b MDA = methyl diazoacetate; EDA = ethyl diazoacetate; ^c 0.5 mol-% of catalyst was used; ^d hmim = 1-hexyl-3-methylimidazolium.



Scheme 1. Cyclopropanation of styrene with diazoacetates.

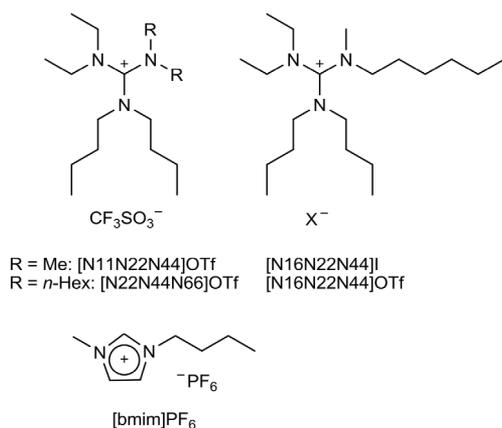


Fig. 1. Ionic liquids used in this study.

Catalytic cyclopropanation of styrene with diazoacetates

The catalytic cyclopropanation of styrene with methyl or ethyl diazoacetate (Scheme 1) affords 2-phenylcyclopropanecarboxylates **1** and usually the dialkyl fumarates and maleates **2** as by-products. This benchmark reaction has been used in the past to evaluate the effectiveness and efficiency of virtually all available catalysts. For this reaction and with the struc-

turally related dinuclear complexes [Ru₂(μ-OAc)₂(CO)₄]_n and Rh₂(OAc)₄ as catalysts, we have now checked the suitability of hexaalkylguanidinium ILs as novel reaction media. A solution of the diazoacetate in styrene was added gradually to the IL containing styrene and the catalyst. The reactions were allowed to go to complete consumption of the diazo compound. After extraction of the organic products into diethyl ether, the product yields and the diastereomeric ratios of cyclopropanes **1** were determined from the ¹H NMR spectra as well as by GC of the crude product mixtures. The results are shown in Table 1, together with some data from the literature.

For both the rhodium- and the ruthenium-catalyzed reactions, the cyclopropane yields obtained in ionic liquids as reaction media fall far behind those of the reactions in dichloromethane. This may be due in part to the limited solubility of the catalysts in the ionic liquids. At the given concentration, Rh₂(OAc)₄ was found to be only partly dissolved even at 50 °C in both the guanidinium ILs and in [bmim]PF₆. [Ru₂(μ-OAc)₂(CO)₄]_n is a coordination polymer which is insoluble in all solvents without Lewis base character. However, we had observed earlier that it is easily depolymerized when exposed to an alkyl diazo-

acetate in dichloromethane solution [18a]. In liquid [N11N22N44]OTf, complete dissolution is achieved in the presence of MDA only at 60 °C, but not at r. t. Another reason for the reduced yields could be the relatively high viscosity of the ionic liquids, which slows down the diffusion rate of the solute molecules and causes a decreased yield for the intermolecular carbenoid reaction. The viscosity of many ionic liquids decreases strongly at higher temperature. For example, the viscosity of [N11N22N44]OTf is 263 mPa s at 23 °C, and 44 mPa s at 60 °C [17]; the viscosity of [bmim]PF₆ was reported as 312 mPa s at 25 °C and 40 mPa s at 60 °C [22]. In fact, we observed an almost doubled yield of **1** for the reaction performed in [N11N22N44]OTf, when the reaction temperature was raised from 40 to 80 °C (Table 1, entries 2–4). Enhanced cyclopropane yields at higher temperature were also observed for reactions performed in liquid [bmim]PF₆ (Table 1, entries 7/8 and 12/13). On the other hand, the yield of **1** was significantly higher in [N16N22N44]I (entry 5) than in [N16N22N44]OTf (entry 6) at the same temperature, although the former is a much more viscous oil. All these observations may result from the combined influence of catalyst solubility and viscosity of the reaction medium.

For all reactions, the diastereomeric ratio *cis*-**1**:*trans*-**1** (*Z*-**1**:*E*-**1**) is found in a rather narrow range (from 34:66 to 43:57), *i. e.*, almost independent of the solvent and the reaction temperature. This is in agreement with a large body of literature data, showing that the diastereoselectivity of cyclopropanation can be controlled to some extent by the catalyst (ligands and structure) [23, 24], but not so much by the choice of solvent. Therefore, we were intrigued by a publication, in which the Rh₂(OAc)₄-catalyzed cyclopropanation of styrene in the ionic liquid [bmim]PF₆ was reported to give cyclopropanes **1** with an unusually high *trans*-selectivity of *cis*:*trans* = 10:90 (Table 1, entry 11) [10]. We cannot confirm these data; under the reported conditions, we found a diastereomeric ratio of 42:58 (Table 1, entry 12), in agreement with the general experience, the results of our ruthenium-catalyzed reactions, and another recent study [12], where [hmim]PF₆ was used as the ionic liquid. Experiments with MDA instead of EDA (entries 15 and 16) made sure that this minor change of the ester group does not affect the diastereomeric ratio, as was already known for reactions in traditional organic solvents.

In order to learn whether the ruthenium catalyst could be immobilized in the ionic liquid

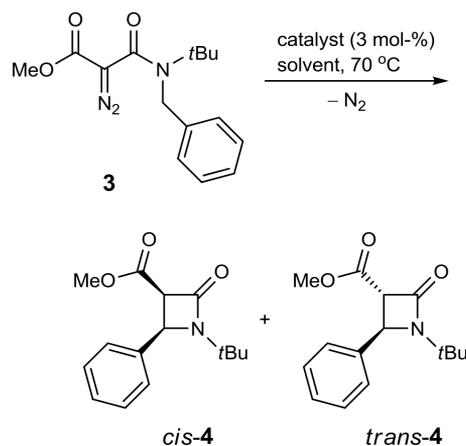
Table 2. Re-use of the Ru-catalyst/ionic liquid solution (see Table 1, entries 3 and 4).

Reaction cycle	1	2	3	4	5
<i>T</i> = 60 °C					
Yield of <i>E/Z</i> - 1 , %	49	45	37	28	22
Ratio <i>Z</i> - 1 : <i>E</i> - 1	34:66	32:68	35:65	36:64	37:63
<i>T</i> = 80 °C					
Yield of <i>E/Z</i> - 1 , %	57	36	23	20	22
Ratio <i>Z</i> - 1 : <i>E</i> - 1	35:65	42:58	39:61	38:62	39:61

[N11N22N44]OTf and the catalyst/IL combination could be re-used, we removed the organic products of the cyclopropanation reaction by several extractions with ether. The IL/catalyst combination was then re-used in five successive reaction cycles. The reactions were performed at a temperature where the catalyst was completely dissolved in the presence of the diazoester (see above). As Table 2 shows, the cyclopropane yields dropped sharply already in the second and third reaction cycle. This is partly due to leaching of the catalyst in the ether phase and partly to decomposition of the catalyst under the reaction conditions, as was indicated by a progressive dark coloration of the IL from one cycle to the next. Significant leaching has already been reported for Rh₂(OAc)₄ in [hmim]PF₆ upon extraction with ether and toluene [12].

Intramolecular carbenoid C–H insertion of an α -methoxycarbonyl- α -diazoacetamide

The rhodium- or ruthenium-catalyzed decomposition of α -diazocarbonyl **3** (Scheme 2) in toluene at 70 °C yields β -lactam **4** in high yield [19b, 25]. The lactam results from an intramolecular carbenoid C–H insertion. With the hypothesis in mind that the



Scheme 2. β -Lactam formation by intramolecular carbenoid C–H insertion.

Table 3. Carbenoid formation of β -lactam **4** (see Scheme 2).

Entry	Catalyst (3 mol-%)	Solvent	Conditions ^a	Total yield of lactams ^b	Ratio <i>cis</i> - : <i>trans</i> - 4
1	Rh ₂ (OAc) ₄	toluene	70 °C/1 h	97 ^{c,d} (83 ^{d,e})	90 : 10 (89 : 11)
2	Rh ₂ (OAc) ₄	[N22N44N66]OTf	70 °C/2.5 h	98	11 : 89
3	Rh ₂ (OAc) ₄	toluene/[N22N44N66]OTf (14 : 1)	70 °C/2.5 h		82 : 18
4	[Ru ₂ (μ -sac) ₂ (CO) ₅] ₂	toluene	70 °C/1 h	94 ^c (72 ^{d,e})	91 : 9 (74 : 26)
5	[Ru ₂ (μ -sac) ₂ (CO) ₅] ₂	[N22N44N66]OTf	70 °C/2.5 h	72	3 : 97
6	Ru ₃ (CO) ₁₂	[N22N44N66]OTf	70 °C/4.5 h	66	0 : 100

^a The reactions were run up to complete consumption of the diazo compound; ^b if not stated otherwise, yields were determined by ¹H NMR analysis of the reaction mixture; ^c ref. [19b]; ^d yield of isolated product; ^e see Experimental Section for chromatographic purification.

effectiveness of an intramolecular carbenoid reaction would not be affected by the viscosity of the reaction medium as much as an intermolecular reaction, we studied the outcome of these reactions using the guanidinium-IL [N22N44N66]OTf (Fig. 1) as the solvent. The same catalysts as in our previous study [19b] were used. The results are shown in Table 3. It can be seen that replacement of toluene by the ionic liquid entails longer reaction times, although the catalysts were completely dissolved at the reaction temperature of 70 °C and in the presence of the diazo compound. Notably, as in the reaction in toluene as the solvent, the yield of the rhodium-catalyzed reaction is still almost quantitative, and the decrease in yield of the ruthenium-catalyzed reactions is much less severe than in the case of the intermolecular cyclopropanation reaction discussed above. Interestingly, the complex Ru₃(CO)₁₂, a synthetic precursor for the saccharinate complex, can also be used as a catalyst in the ionic liquid with moderate success.

The most interesting detail in Table 3 is the influence of the ionic liquid on the *cis* : *trans* ratio of the methoxycarbonyl-substituted β -lactam **4**. The initial formation of *cis*-3-alkoxycarbonyl-azetidino-2-ones in the course of the carbenoid reaction is well known [19b, 25, 26]. We have reported earlier that the *cis* : *trans* ratio depends somewhat on the catalyst, and that the amount of the *trans*-isomer increases with extended reaction times [19b]. Surprisingly, the *cis* : *trans* ratio is completely reversed in favor of a high *trans*-selectivity, when the reaction is carried out in the ionic liquid [N22N44N66]OTf. Even the addition of a small amount of this IL to toluene as the reaction medium apparently causes the amount of the *trans*-isomer to increase (entry 3). Additional experiments were made to shed light on the particular role of this ionic liquid on the isomerization *cis*-**4** \rightarrow *trans*-**4**. No isomerization occurred in CDCl₃ or C₆D₆ (25 °C/9 h), after addition of a drop of triflic acid (HOTf) or water to the CDCl₃ solution, or in toluene that contained

Rh₂(OAc)₄ (70 °C/22 h, corresponding to the reaction conditions for the formation of **4**). Partial isomerization took place during chromatography over silica gel or neutral alumina (toluene as eluent), as well as in the solid state (from 90 : 10 to a stable ratio of 68 : 32 after 150 h). The effect of the ionic liquid was confirmed on a 90 : 10 mixture of *cis*- and *trans*-**4**, which was obtained by Rh₂(OAc)₄-catalyzed decomposition of diazoamide **3** in toluene (see Experimental Section). When this mixture was dissolved in an ionic liquid, the *cis* : *trans* ratio after 2.5 h at 70 °C was 3 : 97 in [N22N44N66]OTf, 22 : 78 in 1-ethyl-3-methylimidazolium ethylsulfate, but 82 : 18 in 1-ethyl-3-methylimidazolium methanesulfonate. It appears that both the ionic liquid itself and, as the results with the two emim-based ILs show, the nature of the anion have an influence on the epimerization process. A straightforward explanation cannot be given. It is plausible that the *cis* \rightarrow *trans* isomerization of **4** is the result of an epimerization at C-3, either *via* the enol or the enolate form of the 1,3-dicarbonyl moiety. Proton catalysis does not seem to be at work, and general base catalysis by the anion of the ionic liquid can likely be excluded because the triflate-containing IL gives the highest amount of *trans*-**4** under the conditions described above, although the triflate anion is a weaker base than the ethyl sulfate and methanesulfonate anions. In this context, studies of the keto/enol equilibrium [27] and of the base-catalyzed keto/enol tautomerization [28] of 2-nitrocyclohexanone in ionic liquids compared to common organic solvents are of interest. For example, the authors have concluded that the considerable rate acceleration of the keto-enol interconversion in certain ionic liquids is not due to a special ionic liquid effect. Taking into account not only the permittivity of the solvent, but also the additional solvent parameters of dipolarity/polarizability, hydrogen bond acidity, and cohesive pressure, a reasonable linear correlation between experimental and calculated rate constants could be found for all investigated solvents [28].

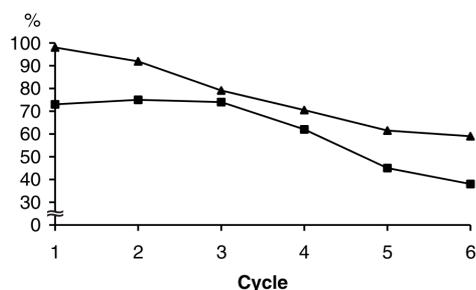


Fig. 2. Use of the catalyst/ionic liquid combination in six reaction cycles (**3** \rightarrow **4**, ionic liquid = [N22N44N66]OTf, 3 mol-% of $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$, 70 °C, 2.5 h); ■ = yield of **4**; ▲ = conversion of diazoamide **3**.

For the transformation **3** \rightarrow **4**, the possibility to reuse the catalyst immobilized in [N22N44N66][OTf] was also investigated. To this end, the reaction was carried out with 3 mol-% of catalyst at 70 °C for a fixed time of 2.5 h; after cooling, the ionic liquid was extracted ten times with pentane. This procedure was repeated in five successive reaction cycles. As indicated by a slight coloration of the pentane extracts – green in the case of $\text{Rh}_2(\text{OAc})_4$ and yellow in the case of $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$ – some leaching from the IL in the pentane phase took place with both catalysts. As the pure catalysts are not soluble in pentane, the leaching is likely caused by their complexation with the extracted β -lactam. With $\text{Rh}_2(\text{OAc})_4$, however, the yield of β -lactam **4** remained the same over all reaction cycles. This suggests that the original amount of $\text{Rh}_2(\text{OAc})_4$ was more than enough for an effective carbenoid reaction. With the ruthenium catalyst, on the other hand, the yield of **4** diminished to half of its initial value over the six reaction cycles, and a similar trend was observed for the conversion of the diazo compound (Fig. 2). These results indicate that the amount of $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$ decreased from one cycle to the next (primarily due to leaching, but to some extent also by catalyst deactivation), so that the available amount of catalyst was no longer sufficient for a fast and effective dediazonation of the diazoamide.

Conclusion

Two ruthenium- or rhodium-catalyzed carbenoid reactions – the intermolecular cyclopropanation of styrene with alkyl diazoacetates and the intramolecular β -lactam formation from 3-oxo-2-diazocarboxamides – have been performed in hexaalkylguanidinium-based ionic liquids. Compared to traditional organic solvents (CH_2Cl_2 , toluene), the yields of the in-

termolecular reaction are much lower, while the intramolecular reactions give high yields in both types of reaction media. This difference may be related to the higher viscosity of the IL hampering the effectiveness of the intermolecular carbenoid reaction.

The immobilization of the catalyst in the ionic liquid is not complete, as the recycling experiments show. Even when the ionic liquid is extracted with the very unipolar solvent pentane, leaching of both the rhodium and the ruthenium catalysts into the pentane phase (probably due to complexation to an organic product) is significant. For the ruthenium catalysts in particular, after a few cycles the amount of catalyst no longer suffices for an efficient transformation of the diazo substrate. These results suggest to modify the rhodium and ruthenium complexes used in this study by the introduction of a hexaalkylguanidinium moiety in order to increase their affinity to the ionic liquid containing the same cation type. However, in a related study [12] it was found that complexation of the dirhodium core to an imidazolium-carboxylate and use of this catalyst in [hmim]PF₆ was less efficient and could not completely suppress the leaching into the organic phase on extractive work-up.

Experimental Section

N,N-Dibutyl-*N'*,*N'*-diethyl-*N''*,*N''*-dimethylguanidinium triflate ([N11N22N44]OTf) and *N,N*-dibutyl-*N'*,*N'*-diethyl-*N''*,*N''*-dihexylguanidinium triflate ([N22N44N66]OTf) were synthesized by a published procedure [17]. *N,N*-Dibutyl-*N'*,*N'*-diethyl-*N''*-hexyl-*N''*-methylguanidinium iodide ([N16N22N44]I) was obtained from Prof. W. Kanteleiner (Hochschule Aalen, Aalen (Germany)) [20]. 1-Butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF₆) was synthesized from [bmim]Cl by anion exchange with KPF₆ [29]. 1-Ethyl-3-methylimidazolium ethylsulfate and methanesulfonate were obtained from Solvent Innovation GmbH. In order to keep the water content of the ionic liquids low, they were treated at 60 °C/0.05 mbar for several hours, then stored under argon. Diazoamide **3** was prepared as published [19b].

N,N-Dibutyl-*N'*,*N'*-diethyl-*N''*-hexyl-*N''*-methylguanidinium triflate ([N16N22N44]OTf)

A solution of *N,N*-dibutyl-*N'*,*N'*-diethyl-*N''*-hexyl-*N''*-methylguanidinium iodide ([N16N22N44]I) [20] (1.09 g, 2.4 mmol) in acetonitrile (10 mL) was placed in a reaction vessel protected from light, and a solution of silver(I) trifluoromethanesulfonate (0.663 g, 2.58 mmol) in acetonitrile (5 mL) was added gradually. Precipitation of AgI re-

gan immediately, but after complete addition the mixture was stirred magnetically overnight to improve the crystallinity of the solid. The solvent was replaced by a mixture of acetonitrile and diethyl ether (25 mL, 1:4 by volume). The undissolved solid was filtered off, the solvent was evaporated (800 mbar), and the remaining ionic liquid was kept at 80 °C/0.05 mbar to remove residual volatiles. Yield: 1.08 g (93 %). The NMR spectra indicate the presence of hindered rotation in the cation: $^1\text{H NMR}$ (CDCl_3): $\delta = 0.85\text{--}0.98$ (several t, partly broadened, 9 H, CH_3 -hexyl, -butyl), 1.18–1.80 (m, 22 H, 8 CH_2 , 2 CH_3 -ethyl); 2.99, 3.00 (2 s, 3 H together, NCH_3); 2.97–3.50 (m, 10 H, 5 NCH_2). $^{13}\text{C NMR}$ (CDCl_3): $\delta = 12.69\text{--}13.90$ (all $(\text{CH}_2)_n\text{CH}_3$); 19.86 (br), 20.09 (br), 22.49, 26.46, 26.51, 27.23, 27.32, 29.41 (br), 29.57, 31.25 (CH_2); 38.35, 38.55 (NCH_3); 43.22, 43.60, 43.81, 43.86 (NCH_2CH_3), 48.86, 49.25 (br), 49.46 (NCH_2 -butyl, -hexyl); 52.90, 52.95 (NCH_2); 163.9 (CN_3), CF_3 not observed. – IR (NaCl): $\nu = 1558$ (m), 1544 (m), 1459 (m), 1442 (m), 1264 (s), 1225 (s), 1156 (s), 1032 (s) cm^{-1} . – $\text{C}_{21}\text{H}_{44}\text{F}_3\text{N}_3\text{O}_3\text{S}$ (475.65): calcd. C 53.03, H 9.32, N 8.83; found C 52.79, H 9.56, N 9.13.

Catalytic cyclopropanation of styrene with methyl diazoacetate in an ionic liquid (Table 1)

Under an argon atmosphere, the catalyst (1 mol-% relative to the diazoacetate; 4.4 mg of $\text{Rh}_2(\text{OAc})_4$, 7.1 mg of $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$) and styrene (199 mg, 2.0 mmol) were added to the magnetically stirred ionic liquid (3 mL), which was then brought to the desired temperature. A solution of methyl diazoacetate (101 mg, 1.0 mmol) in styrene (298 mg, 3.0 mmol) was gradually added *via* a syringe pump during 4 h. The reaction was allowed to continue until IR control ($\nu(\text{CN}_2) = 2115 \text{ cm}^{-1}$) indicated the complete consumption of the diazoacetate. The products were extracted with dry diethyl ether ($3 \times 10 \text{ mL}$). The ether extracts were combined, and the solvent was removed at 60 °C/800 mbar. For product analysis, the residue was dissolved in CH_2Cl_2 (3 mL) and a weighed amount of naphthalene (20–36 mg) was added as an internal standard. The mixture was analyzed by $^1\text{H NMR}$ spectroscopy (for NMR data of *cis*- and *trans*-methyl 2-phenylcyclopropane-1-carboxylate see lit. [18a] and lit. cit.) and by GC (column: Varian CP-WAX 52, 25 m \times 0.32 mm; film thickness: 1.2 μm ; helium as carrier gas, flow rate 1 mL/min). The results obtained from the two methods were in good agreement.

For the recycling experiments the ionic liquid after completed reaction was extracted with diethyl ether ($5 \times 7 \text{ mL}$). Phase separation was supported by centrifugation. Before the next reaction cycle, the ionic liquid was kept at 50 °C/40 mbar to remove traces of diethyl ether.

Catalytic decomposition of diazoamide 3 a) in the ionic liquid [N22N44N66]OTf

N-Benzyl-*N*-*tert*-butyl-2-methoxycarbonyl-2-diazoacetamide (**3**, 50 mg, 0.173 mmol) was dissolved in $[\text{N}22\text{N}44\text{N}66]\text{OTf}$ (0.5 mL), and the catalyst (3 mol-%; 2.3 mg of $\text{Rh}_2(\text{OAc})_4$; 3.7 mg of $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$) was added. The solution was heated at 70 °C until the diazo compound was consumed (2.5 h, IR control). After cooling, the ionic liquid was stirred with *n*-pentane (2 mL) for 8 min, and after phase separation the pentane layer was pipetted off. The extraction procedure was repeated nine times. The pentane extracts were combined, and the solvent was evaporated. The yield and diastereomeric ratio of *N*-*tert*-butyl-3-methoxycarbonyl-4-phenylazetidin-2-one (*cis*- and *trans*-**4**) was determined by integration of characteristic $^1\text{H NMR}$ signals (*cis*-**4**: $\delta = 4.23 \text{ ppm}$, $^3J = 6.3 \text{ Hz}$; *trans*-**4**: $\delta = 3.71 \text{ ppm}$, $^3J = 2.3 \text{ Hz}$ [19b]) (Table 3); for the determination of yields, a weighed amount of naphthalene was added as an internal reference.

b) in toluene

The reported procedure [19b] was carried out on a smaller scale and with a chromatographic work-up that avoids the partial epimerization of azetidinone **4**. A solution of diazoamide **3** (282 mg, 1 mmol) in dry toluene (2 mL) was added within 45 min to toluene (13 mL) containing the catalyst (3 mol-%; 13.3 mg of $\text{Rh}_2(\text{OAc})_4$, 21.2 mg of $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$). The mixture was heated at 70 °C for 1 h. The solvent was evaporated *in vacuo*, and azetidinone **4** was purified by threefold column chromatography over charcoal (1 g)/cellulose (2 g) using toluene as eluent. Yield of **4**, with $\text{Rh}_2(\text{OAc})_4$ as catalyst: 83 %, *cis*-**4**:*trans*-**4** = 90:10; with $[\text{Ru}_2(\mu\text{-sac})_2(\text{CO})_5]_2$: 72 %, *cis*-**4**:*trans*-**4** = 74:26.

Acknowledgement

This work was supported financially by the Bundesministerium für Bildung und Forschung (BMBF), project “Novel Ionic Liquids as Innovative Reaction Media for Technical Organic Chemistry”.

[1] P. Wasserscheid, T. Welton (Eds.), *Ionic Liquids in Synthesis*, 2nd ed., Wiley-VCH, Weinheim, 2007.

[2] a) V.I. Pärvulescu, C. Hardacre, *Chem. Rev.* 2007, 107, 2615–2665; b) P.J. Dyson, T.J. Geldbach, *Metal*

Catalysed Reactions in Ionic Liquids, Springer, Dordrecht, 2006; c) J. Muzart, *Adv. Synth. Catal.* 2006, 348, 275–295; d) Z.C. Zhang, *Adv. Catal.* 2006, 49, 153–237; e) V. Calò, A. Nacci, A. Monopoli, *Eur. J.*

- Org. Chem.* **2006**, 3791–3802; f) T. Welton, *Coord. Chem. Rev.* **2004**, 248, 2459–2477; g) R. A. Sheldon, *Chem. Commun.* **2001**, 2399–2407.
- [3] M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, John Wiley & Sons, New York, **1998**.
- [4] a) J. M. Fraile, J. I. García, C. I. Herrerías, J. A. Mayoral, D. Carrié, M. Vaultier, *Tetrahedron: Asymmetry* **2001**, 12, 1891–1894; b) J. M. Fraile, J. I. García, C. I. Herrerías, J. A. Mayoral, O. Reiser, M. Vaultier, *Tetrahedron Lett.* **2004**, 45, 6765–6768; c) J. M. Fraile, J. I. García, C. I. Herrerías, J. A. Mayoral, S. Gmough, M. Vaultier, *Green Chem.* **2004**, 6, 93–98; d) L. N. Ivanova, A. N. Lobov, A. A. Fatykhov, R. M. Sultanova, S. S. Zlotskii, V. A. Dokichev, *Russ. J. Org. Chem.* **2011**, 47, 1755–1760.
- [5] D. L. Davies, S. K. Kandola, R. K. Patel, *Tetrahedron: Asymmetry* **2004**, 15, 77–80.
- [6] M. L. Kantam, V. Neeraja, B. Kavita, Y. Haritha, *Synlett* **2004**, 525–527.
- [7] M. L. Kantam, B. Neelima, C. V. Reddy, *J. Mol. Catal. A: Chemical* **2006**, 256, 269–272.
- [8] P. Rodriguez, A. Caballero, M. M. Diaz-Requejo, M. C. Nicasio, P. J. Perez, *Org. Lett.* **2006**, 8, 557–560.
- [9] P. M. P. Gois, C. A. M. Afonso, *Tetrahedron Lett.* **2003**, 44, 6571–6573.
- [10] J. S. Yadav, B. V. S. Reddy, P. Narayana Reddy, *Adv. Synth. Catal.* **2004**, 346, 53–56.
- [11] S. Muthusamy, B. Gnanaprakasam, *Tetrahedron* **2005**, 61, 1309–1315.
- [12] D. C. Forbes, S. A. Patrawala, K. L. T. Tran, *Organometallics* **2006**, 25, 2693–2695.
- [13] F. Yang, Y.-M. Zhang, W.-W. Quiu, J. Tang, M.-Y. He, *Chin. J. Chem.* **2002**, 20, 114–116.
- [14] W. Sun, F. E. Kühn, *Tetrahedron Lett.* **2004**, 45, 7415–7418.
- [15] A. Corma, I. Dominguez, T. Rodenas, M. J. Sabater, *J. Catal.* **2008**, 259, 26–35.
- [16] L. C. Branco, P. M. P. Gois, N. M. T. Lourenço, V. B. Kurteva, C. A. M. Afonso, *Chem. Commun.* **2006**, 2371–2372.
- [17] H. Kunkel, G. Maas, *Eur. J. Org. Chem.* **2007**, 3746–3757.
- [18] a) G. Maas, T. Werle, M. Alt, D. Mayer, *Tetrahedron* **1993**, 49, 881–888; b) T. Werle, G. Maas, *Adv. Synth. Catal.* **2001**, 343, 37–40; c) G. Maas, J. Seitz, *Tetrahedron Lett.* **2001**, 42, 6137–6140; d) T. Werle, L. Schäffler, G. Maas, *J. Organomet. Chem.* **2005**, 60b, 673–676; e) S. Buck, G. Maas, *J. Organomet. Chem.* **2006**, 691, 2774–2784.
- [19] a) M. Grohmann, S. Buck, L. Schäffler, G. Maas, *Adv. Synth. Catal.* **2006**, 348, 2203–2211; b) M. Grohmann, G. Maas, *Tetrahedron* **2007**, 63, 12172–12178.
- [20] W. Kantelehner, unpublished results. The compound was prepared by analogy to a published procedure; see: W. Kantelehner, E. Haug, W. W. Mergen, P. Speh, T. Maier, J. J. Kapassakalidis, H.-J. Bräuner, H. Hagen, *Liebigs Ann. Chem.* **1984**, 108–126.
- [21] A. Anciaux, A. J. Hubert, A. F. Noels, N. Petiniot, *J. Org. Chem.* **1980**, 45, 695–702.
- [22] S. Zhang, N. Sun, X. He, X. Lu, X. Zhang, *J. Phys. Chem. Ref. Data* **2006**, 35, 1475–1517.
- [23] G. Maas, *Chem. Soc. Rev.* **2004**, 183–190.
- [24] A. Caballero, A. Prieto, M. M. Díaz-Requejo, P. J. Pérez, *Eur. J. Org. Chem.* **2009**, 1137–1144.
- [25] M. K.-W. Choi, W.-Y. Yu, C.-M. Che, *Org. Lett.* **2005**, 7, 1081–1084.
- [26] A. G. H. Wee, S. C. Duncan, *Tetrahedron Lett.* **2002**, 43, 6173–6176.
- [27] G. Angelini, C. Chiappe, P. De Maria, A. Fontana, F. Gasparrini, D. Pieraccini, M. Pierini, G. Siani, *J. Org. Chem.* **2005**, 70, 8193–8196.
- [28] G. Angelini, P. De Maria, C. Chiappe, A. Fontana, S. Gasbarri, G. Siani, *J. Org. Chem.* **2009**, 74, 6572–6576.
- [29] J. Dupont, C. S. Consorti, P. A. Z. Suarez, R. F. de Souza, *Org. Synth.* **2002**, 79, 236–241.