[12] The stereochemical outcome of the reaction was established through analysis with ^{1}H NMR spectroscopy. In addition, compound **11** was identical in all respects to the same compound prepared through an independent route which afforded a crystalline derivative.
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Activation, Tuning, and Immobilization of Homogeneous Catalysts in an Ionic Liquid/Compressed CO_2 Continuous-Flow System[**]

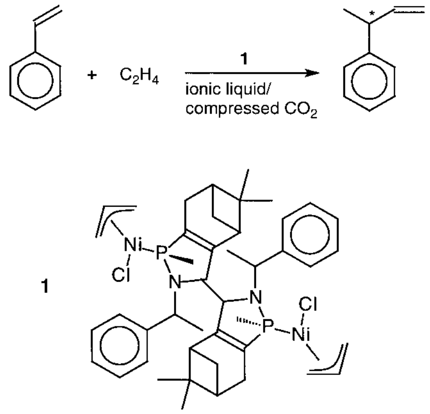
Andreas Bösmann, Giancarlo Franciò, Edo Janssen,
Maurizio Solinas, Walter Leitner,* and
Peter Wasserscheid*

Dedicated to Professor Ernst-Gottfried Jäger
on the occasion of his 65th birthday

The quest for new strategies to immobilize organometallic catalysts is one of the major challenges in homogeneous catalysis. Ionic liquids (ILs) are emerging as excellent solvents for transition metal catalysts. In many applications they are used for multiphasic reaction systems because of their miscibility gap with the reaction products.[1] Supercritical carbon dioxide ($scCO_2$) is also of increasing interest because it combines an environmentally benign character with favorable physico-chemical properties for chemical synthesis.[2, 3] Catalyst separation schemes have been devised on the basis of the tuneable phase behavior of $scCO_2$ (CESS process).[4] We report here a new continuous-flow catalytic system based on the combination of these two solvents systems, which are at the extreme ends of the volatility and polarity scale. We provide convincing evidence that the interplay of their complementary properties offers new intriguing possibilities for catalytic synthesis.

Recently, the research groups of Brennecke and Beckman described the phase behavior of biphasic systems consisting of an IL and supercritical CO_2.[5] They demonstrated that $scCO_2$ is highly soluble in some ILs, while the same ILs show no detectable solubility in the $scCO_2$ phase. Moreover, it was found that $scCO_2$ can be used to extract high-boiling organic substances from ILs without any cross-contamination of the extract with the IL. Intrigued by these pioneering studies, we and others[6, 7] started to explore this unique phase behavior for homogeneous catalysis. While our investigations were in progress, Jessop et al. used $scCO_2$ to isolate the products of a catalytic hydrogenation that was carried out in an IL.[6a] Baker, Tumas, and co-workers conducted catalytic hydrogenations of, for example, 1-decene directly in a biphasic reaction mixture consisting of the IL 1-*n*-butyl-3-methylimidazolium (BMIM) hexafluorophosphate and $scCO_2$. The ionic catalyst solution could be re-used in up to four consecutive batch experiments.[6b]

We demonstrate here that the combination of a suitable IL and compressed CO_2 can offer much more potential for process optimization than just a simple protocol for batchwise catalyst recycling. By using this unusual biphasic system we were able to activate, tune, and immobilize Ni-catalyst **1** in a continuous flow system for the hydrovinylation of styrene (Scheme 1).



Scheme 1. The hydrovinylation reaction and the Wilke's catalyst **1**.

Hydrovinylation is the transition metal catalyzed codimerization of alkenes with ethene to yield 3-substituted 1-butenes.[8] This powerful carbon–carbon bond forming reaction can be achieved with high enantioselectivity using Wilke's complex **1** as a catalyst precursor.[9] In conventional solvents pre-catalyst **1** needs to be activated with a chloride-abstracting agent, for example, the highly flammable $Et_3Al_2Cl_3$.[8, 9] Some of us reported the use of complex **1** in liquid and supercritical CO_2 after activation with alkali salts of weakly coordinating anions such as Na[BARF] (BARF = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate).[10] In a first set of experiments we aimed to identify suitable ILs that would allow the activation of **1** for the enantioselective hydrovinylation of styrene in the presence of compressed CO_2 (Table 1).[11]

The synthesis of the ILs comprising the bistriflic amide anion ($(CF_3SO_2)_2N$, Tf_2N) and the cations 1-ethyl-3-methyl-

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[*] Dr. P. Wasserscheid, Dipl.-Chem. A. Bösmann
Institut für Technische Chemie und
Makromolekulare Chemie der RWTH Aachen
Worringer Weg 1, 52074 Aachen (Germany)
Fax: (+49) 241-8888-177
E-mail: wasserscheidp@itmc.rwth-aachen.de
Priv.-Doz. Dr. W. Leitner, Dr. G. Franciò, E. Janssen,
M. Solinas
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr (Germany)
Fax: (+49) 208-306-2993
E-mail: leitner@mpi-muelheim.mpg.de

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Table 1. Hydrovinylation of styrene in a IL/compressed CO_2 reaction system.[11]

Entry	Ionic liquid	Conversion [%]	3-Phenyl-1-butene [%]	Isomers [%]	Oligomers [%]	*ee* (*R*) [%]
1	[EMIM][Tf_2N]	69.9	65.3	0.8	3.8	53.4
2	[EMIM][BF_4]	39.6	38.9	0.7	–	34.2
3	[EMIM][Al{$OC(CF_3)_2Ph$}$_4$]	90.5	87.5	0.7	2.3	78.2
4[a]	[EMIM][BARF]	100	63.8	26.2	10.0	89.4
5	[4-MBP][Tf_2N]	70.5	69.7	0.8	–	58.4
6	[4-MBP][BF_4]	35.5	34.8	0.7	–	44.2
7	Li[Tf_2N][b]	24.4	23.8	0.6	–	65.9
8	Na[BF_4][b]	5.0	5.0	–	–	n.d.

[a] $T = 25\,^{\circ}C$. [b] Solid salts; anion/Ni = 100/1.

imidazolium (EMIM) and 1-*n*-butyl-4-methylpyridinium (4-MBP) was carried out following a general procedure described by Bônhote et al.[12] [EMIM][BF_4], [4-MBP][BF_4], [EMIM][Al{$OC(CF_3)_2Ph$}$_4$], and [EMIM][BARF] were synthesized by treating [EMIM]Cl and [4-MBP]Cl (both purchased from Solvent Innovation GmbH, Cologne[13]) in dry acetone with Na[BF_4], Na[Al{$OC(CF_3)_2Ph$}$_4$], and Na[BARF], respectively.[14]

Catalyst **1** was activated in all IL/CO_2 systems under investigation, but the effectiveness of the activation is clearly very dependent on the nature of the IL's anion. A comparison of the results in different ILs with EMIM as the common cation reveals that the level of conversion drops in the order BARF > Al[$OC(CF_3)_2Ph$]$_4$ > Tf_2N > BF_4 (entries 1–4). This trend is consistent with the estimated nucleophilicity/coordination strength of the anions. The high activity of catalyst **1** in [EMIM][BARF] leads to a significant amount of consecutive isomerization and oligomerization, even at room temperature (entry 4).

The specific environment of the ionic solvent system appears to activate catalyst **1** beyond a simple anion-exchange reaction. This is emphasized by the observation that even the addition of a 100-fold excess of Li[Tf_2N] or Na[BF_4] in pure CO_2 lead at best to a moderate activation of **1** relative to any of the ILs with the corresponding counterions (entries 7, 8).

There is also a significant intrinsic influence of the anion on the enantioselectivity of the reaction, as revealed by comparing experiments with negligible consecutive reactions (entries 1–3; 5/6).[15] The cation of the IL also exhibits a significant influence on the performance of **1**. At comparable conversions, higher *ee* values were found with [4-MBP][BF_4] and [4-MBP][Tf_2N] than the corresponding [EMIM] salts (entries 1/5, 2/6). This first observation of a cation effect on enantioselective catalysis in ILs may open up new avenues for catalyst tuning.

The influence of the reaction conditions was assessed briefly for the system [EMIM][Tf_2N]/CO_2. Increasing the partial pressure of ethylene and decreasing the temperature was found to suppress the consecutive side reaction. A 58% conversion of styrene (styrene/Ni = 1000/1) was achieved after 1 h under 40 bar of ethylene at 0 °C, with 3-phenyl-1-butene being detected as the only product (71% *ee* of the *R* isomer).

Encouraged by these results, we evaluated the batchwise recycling of catalyst **1** in ionic liquids. The products could be readily isolated from the IL/CO_2 system by extraction with scCO_2. However, similar to what had been seen for the hydrovinylation in compressed CO_2 alone,[10] the active nickel species deactivated rapidly within three to four batchwise cycles. We speculated that this disappointing result was related mainly to the instability of the active species in the absence of substrate and that this could be avoided by continuous operation in a flow reactor.

Our continuous flow apparatus for homogeneous catalysis in IL/CO_2 systems is depicted schematically in Figure 1. The ionic catalyst solution is placed into the reactor R where it is in intimate contact with the continuous reaction phase entering from the bottom. The reaction phase is made up in the mixer from a pulsed flow of ethylene and a continuous flow of styrene and compressed CO_2.[16] Figure 2 shows the results of a lifetime study for catalyst **1** dissolved, activated, and immobilized in the system [EMIM][Tf_2N]/CO_2 by this straightforward technique. Catalyst **1** shows a remarkably stable activity over 61 h, and enantioselectivity drops only slightly over the long reaction period. The results clearly indicate—at least for the hydrovinylation of styrene with

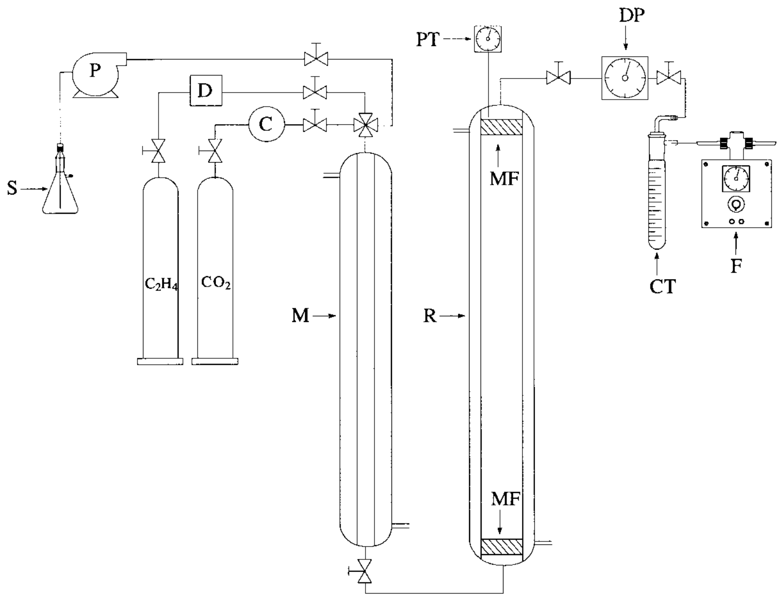

Figure 1. Schematic view of the continuous-flow reaction apparatus. The parts are labeled as follows: C: compressor, CT: cold trap, D: dosimeter, DP: depressurizer, F: flowmeter, M: mixer, MF: metal filter, P: HPLC pump, PT: pressure transducer and thermocouple, R: reactor, S: styrene.

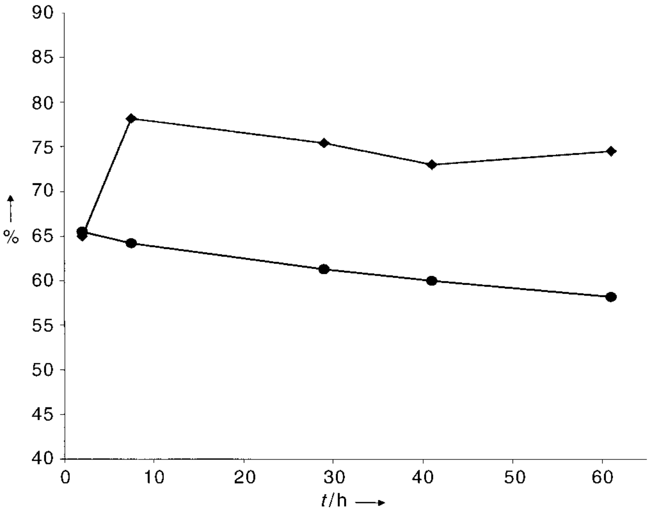

Figure 2. Lifetime study for catalyst **1** activated and immobilized in the system [EMIM][$(CF_3SO_2)_2N$]/compressed CO_2 during the hydrovinylation of styrene,(●: *ee* value; ◆: conversion).

1—that an IL catalyst solution can show excellent catalytic performance during continuous product extraction with compressed CO_2.

As a general conclusion, continuous flow systems consisting of an ionic catalyst solution and compressed CO_2 offer a new intriguing immobilization technique for homogeneous catalysis. The combination of nonvolatile ILs with nonhazardous CO_2 represents a particularly attractive approach to environmentally benign processes. The IL in combination with CO_2 provides the potential to activate and tune the organometallic catalyst. Furthermore, product separation from the catalyst is now possible without exposing the catalyst to a variation of temperature, pressure, or substrate concentration. In contrast to the use of pure IL, the compressed CO_2 greatly decreases the viscosity of the ionic catalyst solution, thus facilitating mass transfer during the catalytic reaction. Moreover, the use of CO_2 as the mobile phase enables a reactor design that is very similar to a classical fixed-bed reactor.[17] Thus, our new immobilization technique provides an attractive approach to combine the molecular design of homogeneous catalysts with the advanced process design of heterogeneous catalysis.

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[11] In a typical experiment, a stainless-steel high-pressure reactor (V = 10 mL) equipped with thick-wall glass windows, a PTFE stirring bar, and a thermocouple was charged with ionic liquid (2 mL) and ethene (0.3 g, 10 mmol) under an argon atmosphere. A dosing unit containing a styrene solution of **1** (0.3 mL, styrene/Ni = 350/1) was connected to the reactor through a ball valve and pressurized with CO_2 (7 g). The reactor was filled through another valve with CO_2 (9 g). The reaction mixture was then warmed to 40 °C, while the dosing unit was heated to 60 °C. Opening the ball valve started the reaction which was allowed to proceed for 1 h. After venting the volatiles through a cold trap, the IL was extracted with pentane, and the combined extract and trap contents were analyzed by GC-MS.

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