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Combined Reactions and Separations Using Ionic Liquids and Carbon Dioxide

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A new and general type of process for the chemical industry is developed using ionic liquids and supercritical carbon dioxide as combined reaction and separation media. In this process, the carbon dioxide pressure controls the miscibility of reactants, products, catalyst and ionic liquid, enabling fast atom-efficient reactions in a homogenous phase as well as instantaneous product recovery in a biphasic system. High reaction and separation rates can be achieved compared with the conventional fully biphasic alternative. Experimental and theoretical methods are used to find the operating conditions of the new approach. When the ionic liquid/carbon dioxide process is applied to the production of 1600 ton/year Levodopa, a medicine against Parkinson's disease, the energy consumption is reduced with 20,000 GJ per year and the waste generation is reduced with 4800 ton of methanol per year and 480 kg catalyst per year, resulting in a decrease in total operational costs of 11.3 million euros per year.

Introduction

The chemical industry is under considerable pressure to drastically reduce the huge amounts of chemical waste produced and energy consumed. Efforts to increase the resource-efficiency in chemical processing include the replacement of stoichiometric reactions by catalytic alternatives, the minimization of solvent losses and the integration of several unit operations into one process step. The main objective of this work is to find new ways to minimize waste generation and energy consumption in chemical processing using ionic liquids and carbon dioxide as combined reaction and separation media.

Ionic liquids, supercritical carbon dioxide and the 'miscibility windows' phenomenon

Ionic liquids are salts with melting points close to room temperature. They are emerging as green solvents for chemical processes, because they combine good and tunable solubility properties with negligible vapor pressures and high thermal and chemical stabilities. They are used as reaction media, where they enhance reaction rates and selectivities. It is possible to separate products from ionic liquids by extraction with supercritical carbon dioxide without any ionic liquids contamination, because the solubility of ionic liquids in carbon dioxide is negligibly low. These facts form the basis of this work, together with the recently established 'miscibility windows' phenomenon: carbon dioxide is able to force two or more immiscible phases (heterogeneous system) to form one homogeneous phase at pressure increase.

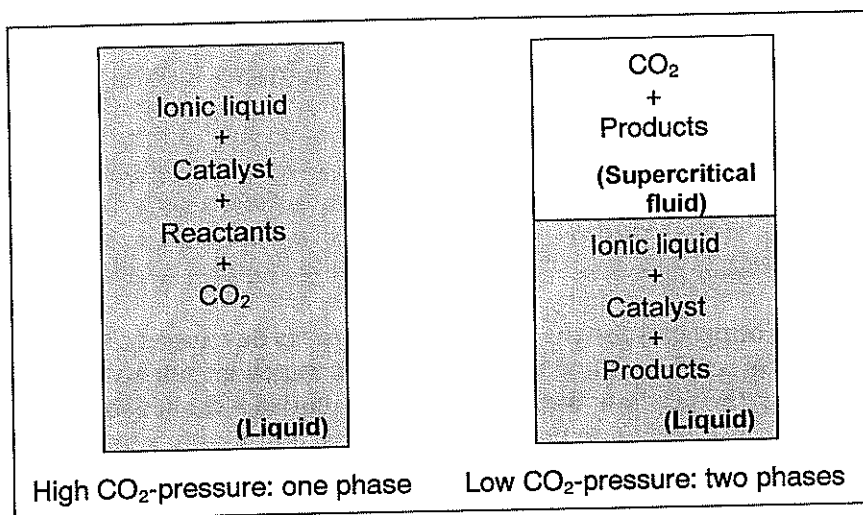


Figure 1: 'Miscibility windows' phenomenon: at high carbon dioxide pressures a homogeneous liquid phase is formed, whereas at lower carbon dioxide pressures two immiscible phases are present

Reaction in the homogeneous system

In the new process set-up, the atom-efficient reaction is carried out in the homogeneous system (~150 bar), where the reactants as well as the catalyst dissolve in the ionic liquid. The advantage of using an ionic liquid as reaction medium is that the immobilized catalyst is stabilized by the ionic liquid against oxidation, resulting in a longer lifetime of the catalyst without the need of regeneration. The advantage of adding carbon dioxide to the reaction mixture is that the solubility of many reactants is increased (higher concentrations) and/or that reactants, which are normally immiscible with pure ionic liquid, can dissolve in ionic liquid + carbon dioxide mixtures (= co-solvency effect). Therefore, it is possible to bring all components in high concentrations into one homogeneous phase. In this homogeneous system, the reaction takes place without any mass transfer limitations, which results in a high reaction rate. Moreover, the addition of carbon dioxide to the reaction mixture leads to a lower viscosity of the reaction system and a higher diffusion rate of the reactants, resulting in a further increase in reaction rate. The ionic liquid hardly expands when carbon dioxide is dissolved, because the carbon dioxide molecules occupy the cavities in the ionic liquid phase. Therefore, the reaction volume can be kept small, leading to a small equipment size.

Separation in the heterogeneous system

The separation is carried out in the heterogeneous system (~100 bar). Application of the 'miscibility windows' phenomenon (pressure release) results in the instantaneous formation of a second phase out of the homogeneous liquid system (spinodal demixing). The light phase consists of supercritical carbon dioxide with dissolved products (and reactants in case of incomplete conversion), but does not contain any ionic liquid, because carbon dioxide cannot dissolve ionic liquid. The heavy phase consists of ionic liquid with dissolved catalyst and some remaining products (and some remaining reactants in case of incomplete conversion). These phases can be separated from each

other, and the pressure of the light phase is further decreased, leading to precipitation of the product (as a liquid or as a solid) out of the carbon dioxide. In this way, pure product is obtained without any detectable ionic liquid or catalyst (and no reactants when the reaction is complete). The catalyst remains in the ionic liquid phase and can be easily recycled, without negatively affecting the activity and enantioselectivity. Also, the carbon dioxide can be recompressed and reused. The essential advantage of using instantaneous demixing instead of conventional extraction with carbon dioxide is the higher rate of product separation from the ionic liquid (no diffusion limitations). Another advantage of the novel process set-up is that the energy-consumption is low. Energy is only required for recompressing the carbon dioxide, but no energy-intensive distillation step is needed. Compared to the conventional separation processes, the energy consumption in the novel process set-up can be decreased by 50-80%.

Safe process

It should be noted that the use of ionic liquids and carbon dioxide as combined reaction and separation media is safe for health and environment. Ionic liquids cannot evaporate. Therefore, they cannot lead to emissions into the atmosphere. Moreover, ionic liquids cannot be inhaled and most of them are non-flammable. Also, carbon dioxide is non-flammable and non-toxic.

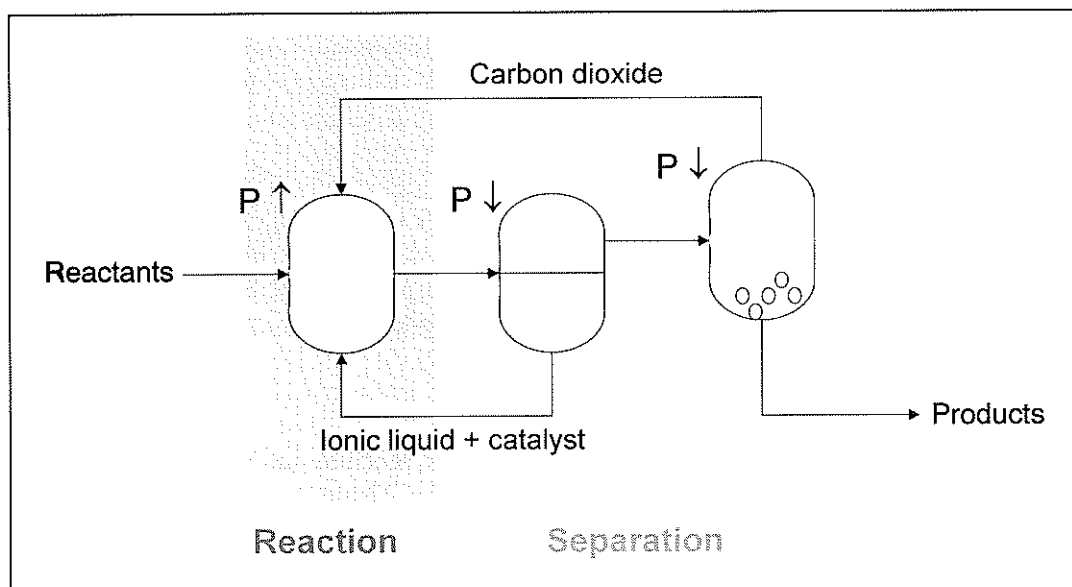


Figure 2: Novel process set-up. At high pressure the reaction is carried out in a homogeneous phase (complete conversion is assumed). The product is separated from the ionic liquid in the biphasic system that is formed at lower CO₂ pressure. Finally, the product is separated from the CO₂ by further pressure release.

Application of the novel process set-up

The novel approach to combine reactions and separations using ionic liquids and carbon dioxide is applied to the enantioselective rhodium-catalyzed hydrogenation of methyl (*Z*)- α -acetamidocinnamate in the 1-butyl-3-methylimidazolium tetrafluoroborate (ionic liquid) + carbon dioxide system. This reaction is related to the most important step in the production of Levodopa (a medicine against Parkinson's disease).

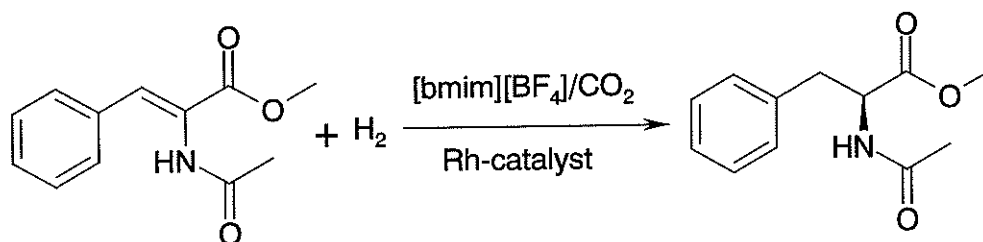


Figure 3: Rhodium-catalyzed asymmetric hydrogenation of methyl-(*Z*)- α -acetamido cinnamate in the [bmim][BF₄] + CO₂ system

Operation conditions were experimentally determined on basis of the phase behavior of the model system. Subsequently, the new production method was tested and the rate and selectivity of the reaction and separation were determined. It was found that the reaction step and the separation step could be carried out faster and more efficiently compared to the conventional production process (in methanol as solvent). Moreover, the catalyst could be reused without significantly losing its activity or selectivity.

It was demonstrated for the first time that a product can also be separated from an ionic liquid by precipitation under influence of carbon dioxide at high pressures, where the carbon dioxide acts as anti-solvent. This effect is caused by the lower solubility of the product in ionic liquid/carbon dioxide mixtures compared to the solubility in the pure ionic liquid at atmospheric conditions. After precipitation the formed crystals can be washed using carbon dioxide to obtain a purer product.

Modeling of the novel process set-up

The experimental determination of the conditions for reaction and separation in the new process set-up is very time-consuming and expensive. Therefore, an equation of state is developed that predicts the phase behavior of ionic liquid/carbon dioxide systems, which is based on the truncated Perturbed Chain Polar Statistical Associating Fluid Theory. This equation of state accounts explicitly for the dipolar interactions between ionic liquid molecules, the quadrupolar interactions between carbon dioxide molecules, and the Lewis acid-base type of interaction between the ionic liquid and the carbon dioxide molecules. Physically meaningful model pure component parameters for ionic liquids were estimated based on literature data. All experimental vapor-liquid equilibrium data are correlated with a single linearly temperature-dependent binary interaction parameter. The ability of the model to describe accurately carbon dioxide solubility in various 1-alkyl-3-methylimidazolium-based ionic liquids with different alkyl chain lengths and different

anions at pressures from 0 MPa to 100 MPa and carbon dioxide fractions from 0 mole % to 75 mole % is demonstrated.

Moreover, the limits to the operation conditions were modeled, including the long-term stability of ionic liquids with respect to high temperatures and high voltage differences. The thermal stability of ionic liquids is characterized by the height of the decomposition temperature, whereas the electrochemical stability is manifested by the width of the electrochemical window. Quantum chemical calculations were used to predict the decomposition mechanisms and products of thermal and electrochemical breakdown reactions. The activation energies of the calculated thermal decomposition reactions corresponded well with the measured decomposition temperatures and may be used to predict the decomposition temperature of an ionic liquid before it is synthesized. The electrochemical window could be correlated to the calculated difference in energy level of Lowest Unoccupied Molecular Orbital (LUMO) of the cation and Highest Occupied Molecular Orbital (HOMO) of the anion. Moreover, the electrochemical decomposition reactions of several ionic liquids on the cathode limit were successfully predicted and verified by experiments.

Economical and environmental attractiveness of the new process set-up

The use of ionic liquids in combination with carbon dioxide in chemical processes leads to economical and environmental benefits compared to conventional production processes. Reductions in the use of catalyst and volatile organic solvents lead to lower costs for raw materials and lower waste disposal costs. No expensive purification steps are required to remove catalyst residues from the product. The energy costs for pressurizing the carbon dioxide in the ionic liquid/carbon dioxide process are lower than the energy costs for evaporating the solvent in the conventional process. When the ionic liquid/carbon dioxide process is applied to the production of 1600 ton/year Levodopa, the energy consumption is reduced with 20,000 GJ per year and the waste generation is reduced with 4800 ton of methanol per year and 480 ton catalyst per year, resulting in a decrease in total operational costs of 11.3 million euros per year.

Implementation of the new process set-up

From an economical and an environmental point of view, fast implementation of the new process-set up is desired. Suggestions for the fastest implementation are made based on the cyclic innovation model, which does not represent innovation by a linear chain, but by coupled 'circles of change' that connect science and business in a cyclic manner. The most important obstacles in the implementation of the ionic liquid/carbon dioxide production process are the successful life cycle management of current production plants, the linearity of current innovation thinking and a perceived high risk of adoption. According to the cyclic innovation model, these obstacles can be overcome when developments in all cycles occur in a parallel fashion and all involved actors collaborate in coupled networks.

Conclusions and outlook

Since the 'miscibility windows' phenomenon is a general phenomenon, it is likely that the new process set-up is applicable to many industrial chemical processes. Therefore, the new process set-up using ionic liquids and supercritical carbon dioxide offers the potential to replace conventional processes with higher reaction and separation rates, but at the same time with lower energy consumption, a higher quality product and safer working conditions. It may also lead to further ionic liquid commercialization.

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