Process Development

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Overcoming Phase-Transfer Limitations in the Conversion of Lipophilic Oleo Compounds in Aqueous Media—A Thermomorphic Approach

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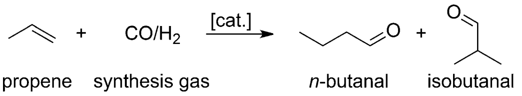
Abstract: *A new process concept has been developed for recycling transition-metal catalysts in the synthesis of moderately polar products via aqueous thermomorphic multicomponent solvent systems. This work focuses on the use of "green" solvents (1-butanol and water) in the hydroformylation of the bio-based substrate methyl 10-undecenoate. Following the successful development of a biphasic reaction system on the laboratory scale, the reaction was transferred to a continuously operated miniplant to demonstrate the robustness of this innovative recycling concept for homogenous catalysts.*

Sustainability and environmental awareness are becoming increasingly important in the chemical industry.[1] In the context of green chemistry, which aims, for example, to reduce energy use and develop new resource-efficient processes, catalysis is a key technology.[2] Essentially, reactions can be catalyzed homogeneously or heterogeneously. Although homogenous catalysis affords many advantages over heterogeneous catalysis, such as milder reaction conditions and higher selectivities,[3] only 25 % of all catalyzed processes are conducted homogeneously on an industrial scale due to the complexity of separating the product and the valuable catalyst.[4]

In addition to physical separation methods such as product distillation, homogeneous catalysts can be immobilized on solid carriers or in a liquid phase to allow for easy separation from the product.[5] One example of catalyst immobilization in liquid phases with high industrial relevance is the hydroformylation of propene (Scheme 1) in the Ruhrchemie/Rhône–Poulenc-Process (RCh-RP). In this process, the reaction takes place in an aqueous phase on a water-soluble rhodium complex containing the ligand triphenylphosphinetrisulfonate (TPPTS, Figure 3). The resulting butanals can be separated from the catalyst by simple phase separation after the reaction.[6,7] Unfortunately, this process concept is limited to the conversion of short-chain olefins due to the low water solubility of higher alkenes and therefore poor turnover frequencies (TOF) for these substrates.[6,8]

One strategy for overcoming mass transport limitations is the use of thermoregulated systems such as thermoregulated phase-transfer catalysis, microemulsions, fluorinated solvents, and polymer-bound catalysts.[9,10] One other possibility is the use of thermomorphic multicomponent solvent systems (TMS), which have several crucial advantages over other process concepts:



Scheme 1. Hydroformylation of propene.

- Thermomorphic phase behavior:
  - \- The reaction takes place without mass transfer limitations between substrate and catalyst in a single reaction phase;
  - \- The catalyst and the product can easily be separated by decantation after the reaction.
- Cheap and commercially available solvents can be used without additional surfactants, etc.
- Typically no modification of the catalyst is necessary.

TMS systems consist of at least two solvents (S_A, S_B) that have a highly temperature-dependent miscibility gap (Figure 1, $T_3 > T_2 > T_1$). These two solvents form a biphasic mixture at low temperatures. The substrate and the product (S_C) are better soluble in S_A while the catalyst occurs mainly in S_B. When heated (T_3), this mixture forms a single homogeneous liquid phase, allowing the reaction to take place without any mass transport limitations, for example, at the operation point (OP).[9,11] Cooling the mixture after the

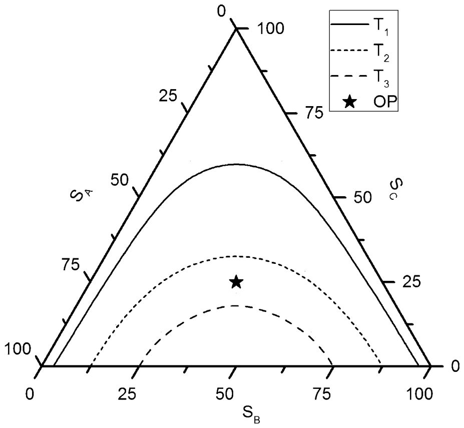


Figure 1. Ternary diagram of a TMS system.

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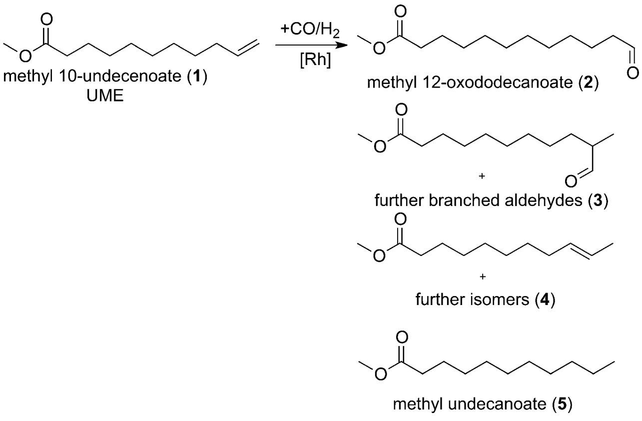
reaction (T_1) leads to the formation of two liquid phases, S_A containing the product and S_B containing the catalyst.

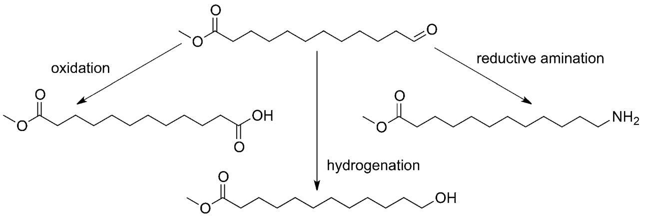
The use of TMS systems makes it easy to convert long-chain substrates that are not water soluble and recycle the catalyst readily and efficiently.[12] However, known TMS systems based on organic solvents have a limited scope when it comes to synthesizing products with a higher polarity. These products have a better solubility in the polar catalyst phase, which makes an effective separation of product and catalyst impossible.[13,14] This is why TMS systems have been used to synthesize only nonpolar products up to now.[15] The aim of this work is to extend the scope of the TMS concept to the synthesis of moderately polar and polar products.

The hydroformylation of methyl 10-undecenoate (**1**, Scheme 2) was chosen as a model reaction. Ester **1** is readily available through pyrolytic cleavage of methyl ricinoleate.[16] The desired hydroformylation product **2** can be used as a polymer precursor (Scheme 3). In addition to **2**, there are some undesired byproducts such as branched aldehydes (**3**), isomers of the substrate (**4**), and hydrogenated substrate (**5**). Research by Ternel et al. on the hydroformylation of 10-undecenenitrile has shown that the known TMS systems are not applicable for functionalizing medium-polar substrates that already contain a polar functional group due to the high solubility of the resulting products in the catalyst phase (> 90 %).[13]

As a consequence, new methods are required so that these substrates can be converted efficiently using a liquid–liquid two-phase technique. With this in mind, a new concept was developed, first on a laboratory scale, that allows for both efficient process control with high yields and selectivities as well as easy catalyst recycling. The viability of this concept was then tested in a continuously operated miniplant.



Scheme 2. Hydroformylation of methyl 10-undecenoate and observed side reactions.



Scheme 3. Possible building blocks for polymer synthesis starting from **2**.

Initially, the catalyst separation in our model reaction was tested using known organic TMS systems (Figure 2). For this purpose, a variety of polar organic solvents were tested as catalyst solvents in combination with *n*-decane as a nonpolar product solvent. $Rh(acac)(CO)_2$ was used as the catalyst precursor in combination with the Biphephos ligand (Figure 3). This catalyst complex is known for low catalyst leaching, long-term stability, and regioselectivity in favor of the linear aldehyde in the hydroformylation of 1-dodecene in TMS systems.[17] High yields of linear product (**2**) between 40 and 80 % were achieved in the hydroformylation of UME (**1**). Furthermore, a high ratio between linear and branched aldehydes (*l/b* ratio) of 99:1 was reached. As the product was highly polar, it dissolved almost exclusively in the polar catalyst phase (cp) (Figure 2), rendering the efficient separation of catalyst and product impossible.

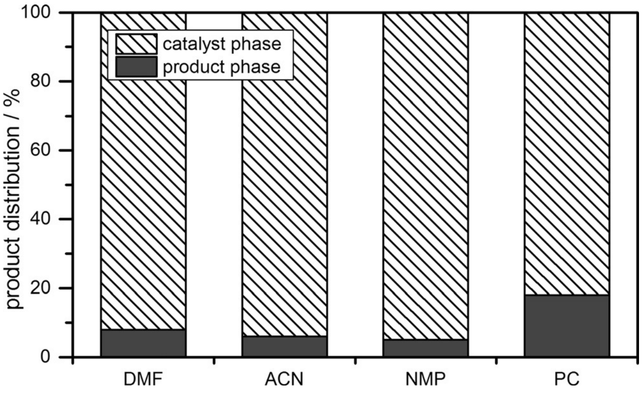


Figure 2. Product distribution when polar, organic solvents are used. Conditions: $n_{UME} = 3.9$ mmol, $n_{Rh(acac)(CO)_2} = 0.0039$ mmol, $n_{Biphephos} = 0.0195$ mmol, $p = 20$ bar, CO:H_2 = 1:1, $T_{reaction} = 90\,°C$, $T_{Separation} = 25\,°C$ $t = 2$ h, $m_{decane} = 2.1$ g, $m_{cp} = 2.1$ g; catalyst phase (cp) = DMF (dimethylformamide), ACN (acetonitrile), NMP (N-methyl-2-pyrrolidone), PC (propylenecarbonate).

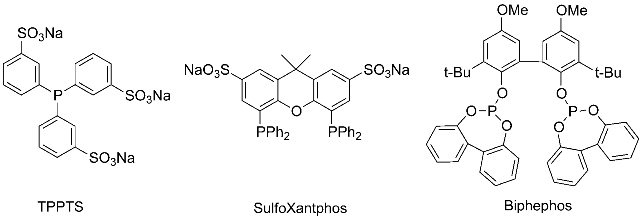


Figure 3. Molecular structure of the applied ligands.

However, several requirements needed to be fulfilled to develop a more suitable thermomorphic solvent system:

- low solubility of product **2** in the polar solvent (catalyst phase);
- high solubility of the catalyst complex in the polar solvent;
- high temperature dependence of the miscibility gap.

Using water as the polar solvent (catalyst phase) and 1-butanol as the less polar solvent (product phase) fulfilled all of these requirements. Water and 1-butanol (50:50) have an upper critical solution temperature of 106 °C. Behr et al. have already demonstrated that enzymes can be separated in a solvent system consisting of water, 1-hexanol, and methanol.[18] This work is the first to describe the use of aqueous TMS systems to separate homogeneous transition-metal catalysts from medium-polar products. Furthermore, solvents such as water and 1-butanol are preferable for continuous processes, as water is nontoxic, nonflammable, odorless, cheap, and available in great abundance. 1-Butanol is available from renewable feedstocks and is produced by biomass fermentation.[19]

A water-soluble rhodium catalyst is required for hydroformylation in aqueous solvent systems. As such, the ligand SulfoXantphos (Figure 3) was used for the investigations described in this paper. The combination of this ligand and a rhodium precursor is described as a highly selective hydroformylation catalyst in literature.[20]

The reaction system shows highly temperature-dependent behavior (Figure 4). At a reaction temperature of 140 °C and after a reaction time of 1 h, the highest yield of **2** (76 %) is observed. Branched aldehydes (**3**) (5 %), isomers of the substrate (**4**) (12 %), and the hydrogenation product (**5**) (2 %) are observed as byproducts. In contrast, lower reaction temperatures lead to a strong decrease in catalyst activity. These results clearly indicate mass transfer limitations during the reaction although the UCST of water/1-butanol is 106 °C. We find that the presence of the substrate **1** shifts the UCST towards higher temperatures, as **1** has lower polarity than the two solvents. Investigations on the phase behavior of the ternary solvent system (1-butanol/water/**1**) show a biphasic system even at a temperature of 140 °C. However, the yield of 76 % corresponds to a TOF of 1500 h^{-1}. To our knowledge, this is the highest TOF in the hydroformylation of long-chain olefins in aqueous solvent systems ever described in literature. Increasing the reaction temperature even further does not lead to better reaction performance, so that this solvent system provides all advantages of a TMS system and meanwhile ensures low energy demand by a minimum temperature change. Additionally the stability of the catalyst increases at lower reaction temperatures. Since this mixture does not form one single phase under the reaction conditions we call this a "narrow TMS system".

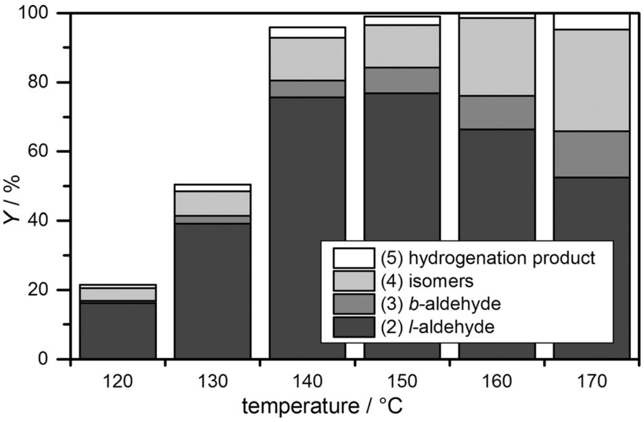


Figure 4. Temperature screening. Conditions: $n_{UME}=4$ mmol, $n_{Rh(acac)(CO)_2}=0.002$ mmol, $n_{SulfoXantphos}=0.01$ mmol, $p=20$ bar, CO:H_2 = 1:1, $t=1$ h, $m_{n\text{-Butanol}}=2.1$ g, $m_{H_2O}=2.1$ g.

In Figure 1 the narrow TMS state is evident at temperature T_2. Increasing the reaction temperature leads to a smaller miscibility gap and the components' solubility into each other is highly improved, whilst the formation of one single phase (T_3) is not achieved. The resulting product is almost completely dissolved in the 1-butanol phase and the concentration of the rhodium in this phase was at a low level of 5 ppm by weight. The distribution of the components between the two phases at 20 °C is presented in Table 1.

Table 1: Distribution of the components between polar and apolar phases.[a]

	H_2O	1-BuOH	**1**	**2**	Rh	P
product phase	18	92	99	99	5	2
catalyst phase	82	8	1	1	95	98

[a] Distribution in [%], $T_{Separation}=25$ °C

Starting with this reaction system, optimized in terms of product yield and catalyst separation, we focused on recycling the homogeneous transition-metal catalyst. As presented in Figure 5, which shows the separation of the catalyst in the aqueous phase and its reuse in a subsequent reaction run, the catalyst was successfully recovered three times.

After each separation of the catalyst and product phases, fresh substrate and 1-butanol were added prior to the initiation of another hydroformylation run. Significant deactivation of the catalyst was observed in the fourth reaction run. Among the possible explanations for this observation are the exchange of the gaseous atmosphere prior to the phase separation and the introduction of small amounts of oxygen in the reaction system. In light of this, continuously operated experiments were conducted in a miniplant consisting of a continuously stirred tank reactor (CSTR) and a phase separator.

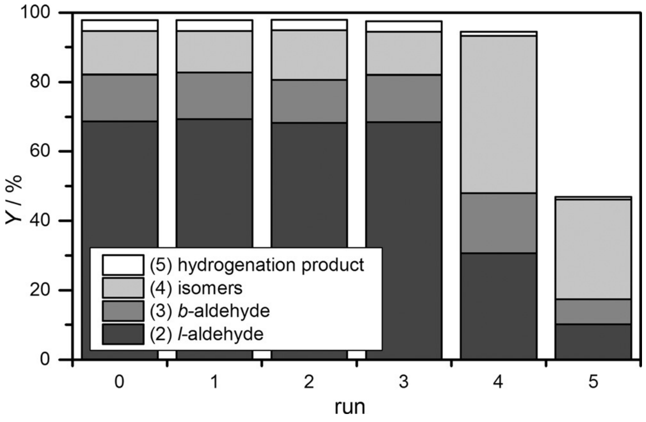


Figure 5. Hydroformylation of methyl 10-undecenoate and catalyst recycling using a batch autoclave. Conditions: $n_{UME}=70$ mmol, $n_{Rh(acac)(CO)_2}=0.035$ mmol, $n_{SulfoXantphos}=0.175$ mmol, $p=20$ bar, CO:H_2 = 1:1, $T_{reaction}=140$ °C, $T_{separation}=25$ °C, $t=1.5$ h, $m_{n\text{-Butanol}}=37.6$ g, $m_{H_2O}=37.6$ g.

At the laboratory scale, both phase separation and catalyst recycling are subject to certain limitations that can be overcome in a continuously operated miniplant. In contrast to discontinuous analyses, it is possible to separate the product from the catalyst at reaction pressure in a synthesis gas atmosphere, ensuring optimal conditions for the catalyst complex at all times. In addition, the operation of a continuous process provides the following relevant information:[21]

- long-term stability of the catalyst;
- efficiency of the catalyst recycling under process conditions;
- influence of recycling streams.

A process scheme of the miniplant used in these experiments is shown in Figure 6. This setup had been used successfully in the hydroformylation of 1-dodecene. A mixture of substrate **1** and the nonpolar solvent 1-butanol was fed into the reactor using a piston pump. Additionally, the synthesis gas flow was regulated by a mass flow controller. Following phase separation, the catalyst phase was recycled from the decanter to the reactor using a gear pump. In addition, the product phase was removed via the phase separator (pulsating).

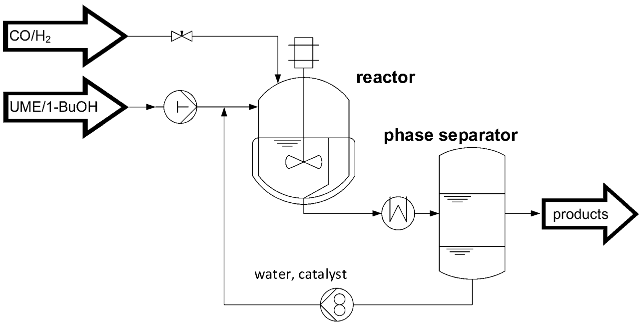


Figure 6. Process flow diagram of the miniplant for the hydroformylation of methyl 10-undecenoate.

After the startup procedure, continuous operation of the miniplant was achieved (Figure 7). A constant high yield of the linear product **2** of 73 % was achieved over a time period of 21 hours. In terms of the reaction behavior of the CSTR, the selectivity was virtually the same as that observed in previous experiments in the batch autoclave. Only the rhodium loss of 15 ppm by weight into the product stream under continuous operation is higher than that recorded for the batch separation. As the water phase decreased under continuous operation owing to its solubility in 1-butanol, catalyst leaching was likely favored. Nevertheless, stable process conditions were maintained for 21 h without interference, which demonstrates the stability of the catalyst species under process conditions.

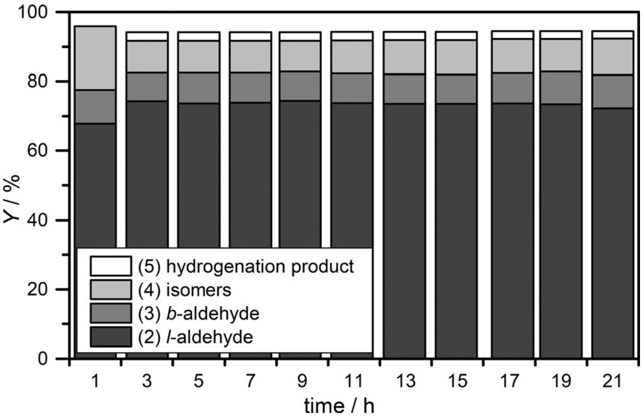


Figure 7. Continuous hydroformylation process in a miniplant. Conditions: $p = 20$ bar, CO:H$_2$ = 1:1, $T_{\text{reaction}} = 140\,°\text{C}$, $T_{\text{separation}} = 5\,°\text{C}$, $w_{n\text{-Butanol}}:w_{\text{H}_2\text{O}} = 1:1$, $m_{\text{H}_2\text{O}} = 300$ g, $m_{\text{Rh(acac)(CO)}_2} = 0.275$ mmol, $n_{\text{SulfoXantphos}} = 1.375$ mmol, $\dot{n}_{\text{UME}} = 100.4\ \text{mmol}\,\text{h}^{-1}$, $\dot{V}_{n-\text{Butanol}} = 34.4\ \text{g}\,\text{h}^{-1}$.

We have described the development of a highly integrated process for the reaction and separation of the catalyst based on an aqueous TMS system. This system is especially relevant for separating medium-polar products, as demonstrated by the hydroformylation of 10-undecenoate. The concept, which was initially explored in batch experiments, was then conducted as a continuous process in a miniplant. Furthermore, the use of green solvents (water and 1-butanol) suitable for the development of sustainable chemical processes underscores the potential for continued innovation in terms of environmentally sound chemical processes.

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Keywords: catalyst recycling · homogeneous catalysis · hydroformylation · process development · thermomorphic solvent systems

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