

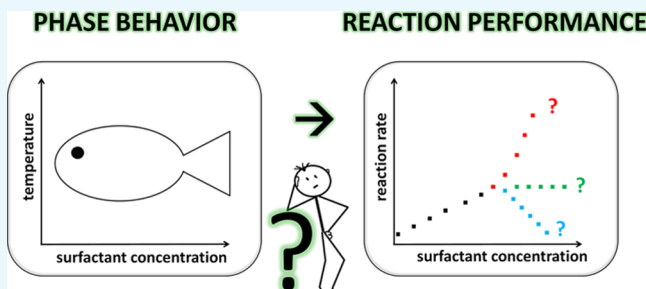
Palladium-Catalyzed Hydroxycarbonylation of 1-Dodecene in Microemulsion Systems: Does Reaction Performance Care about Phase Behavior?

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S Supporting Information

ABSTRACT: Catalysis, particularly metal-catalyzed reactions in microemulsion systems, offers a sustainable approach for organic reactions in water. However, it is still a challenging task because of the complex role of the nonionic surfactant in such a system and the interaction of the phase behavior and reaction performance. To get a profound knowledge of this role and interaction, a systematic study of the palladium-catalyzed hydroxycarbonylation of 1-dodecene in a microemulsion system is reported. The influence of the temperature, additives such as cosolvents, the catalyst concentration, and the hydrophilicity of the surfactant and its concentration has been investigated with regard to both the phase behavior and reaction performance. Interestingly, the investigations reveal that not the phase behavior of the microemulsion system but mainly the dimension of the oil–water interface and the local concentrations of the substrates at this interface, which is provided by the amount and hydrophilicity of the surfactant, control the reaction performance of hydroxycarbonylation in these systems. Moreover, it was found that the local concentration of the active catalyst complex at the interface is essential for the reaction performance. Dependent on the surface active properties of the catalyst complex, its bulk concentration, and the nature and amount of additives, the local concentration of the active catalyst complex at the interface is strongly influenced, which has a huge impact on the reaction performance.



1. INTRODUCTION

The application of biphasic catalysis represents a smart approach to perform homogeneously catalyzed reactions in an economical and ecological way. The major advantage is the possibility to separate the product from the reaction mixture and to recycle the expensive catalyst via a simple phase separation step after the reaction. In industry, the Ruhrchemie/Rhône Poulenc process was the first successful example of biphasic catalysis, where in a hydroformylation reaction, propene is converted to butanal using synthesis gas (mixture of CO and H₂). The applied rhodium catalyst is immobilized into the water phase by the water-soluble ligand TPPTS. Therefore, it can be recycled via a simple phase separation step. The rhodium leaching into the product phase is lower than 1 ppb, which equals to a loss of only 2 kg of rhodium per 2 000 000 tons of butanal.¹ Besides aqueous–organic systems, plenty of innovative biphasic media are considered as smart solvents for homogeneous catalysis, with the goal to overcome the limitations of “ordinary” biphasic systems caused by low solubility of substrates or mass transport in the aqueous phase.² An easy approach to solve this problem is the addition of cosolvents to the aqueous or organic phase, which leads to a higher solubility of the substrates in the catalyst phase and thus to a higher overall reaction performance.³ Moreover, the addition of cyclodextrins, acting as mass transfer promoters, is a promising tool to enhance the catalytic activity in aqueous

biphasic systems.^{4,5} In contrast, nonaqueous liquid/liquid biphasic systems including fluorinated biphasic systems,^{6,7} thermo-regulated organic liquid/liquid systems,^{8,9} and ionic liquids/supercritical fluids biphasic systems¹⁰ are in focus of current research. However, these systems do not meet the requirements of sustainability because of the use of often toxic solvents. Water, on the other hand, fulfills the requirements of a “green” solvent but, as already mentioned, offers only a limited solubility for many organic substrates.

A smart approach to make water applicable as a solvent for a broader range of substrates is the use of surfactants, which is reviewed in the literature for plenty of different organic transformations.^{11–13} If large amounts of the organic substrate are added to the micellar solution, microemulsion systems are obtained. Since the first introduction of the term “microemulsion” by J. H. Schulman in the 1950s, numerous publications on the formation, physical properties, and the application of microemulsions sprout up.^{14,15} Microemulsions are mixtures of two immiscible liquids, predominantly water and oil, with an amphiphile as an emulsifier. The phase behavior can be easily described by the Gibbs phase prism in which the base of this prism represents the ternary system of

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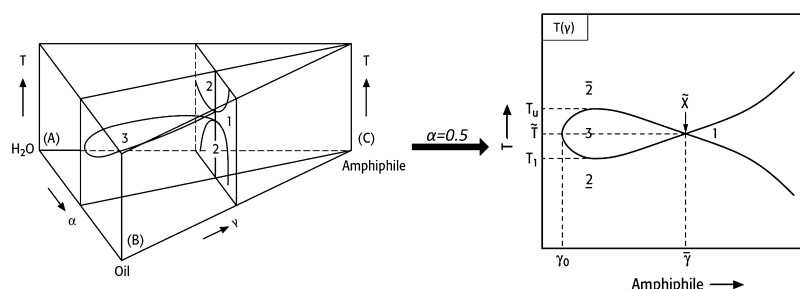


Figure 1. Gibbs phase prism for a microemulsion system consisting of oil, water, and a nonionic surfactant (left picture) and cut of the phase prism at $\alpha = 0.5$ (right picture), both taken from Schwarze et al.¹⁶

oil, water, and the amphiphile (Figure 1, left). The composition of the ternary system is characterized by the surfactant concentration γ , denoted as the mass fraction of the amphiphile to the total mass of the microemulsion system (eq 1), and the oil mass fraction α in the water–oil mixture (eq 2).

$$\gamma = \frac{m_{\text{amphiphile}}}{m_{\text{amphiphile}} + m_{\text{water}} + m_{\text{oil}}} \quad (1)$$

$$\alpha = \frac{m_{\text{oil}}}{m_{\text{water}} + m_{\text{oil}}} \quad (2)$$

The Gibbs phase prism can be reduced to Kahlweit's fish diagram, which is created by cutting the Gibbs phase prism at a fixed oil mass fraction α , as exemplarily illustrated in Figure 1 (right). The phase boundaries resemble the shape of the fish where the body of the fish represents the three-phase region of the microemulsion system. In the fish-diagram, γ_0 marks the minimal concentration of surfactant, which is needed to form a microemulsion system. The solubility of the nonionic surfactant changes with the temperature, causing the transition of the system between different phase states. At low temperatures, the nonionic surfactant is more hydrophilic and thus is mainly soluble in the water phase, forming an oil-in-water microemulsion with an excess oil phase (2Φ). In contrast, increasing the temperature leads to a water-in-oil microemulsion with an excess water phase (2Φ) caused by the higher solubility of the surfactant in the corresponding oil phase. In between, the mixture forms a three-phase region in which the middle phase is a surfactant-rich microemulsion phase. At high surfactant concentrations, the microemulsion system reaches a macroscopic one phase state. The minimal surfactant concentration, at which a one phase microemulsion is obtained, is denoted with $\tilde{\gamma}$ with the associated temperature \tilde{T} .

In general, surfactants increase the solubility of the substrate in the aqueous phase as well as the interfacial area between oil and water, which facilitates and accelerates the reaction. The applicability of surfactants for homogeneously metal-catalyzed reactions is demonstrated with numerous examples in the literature.^{17–19} Especially, the pharmaceutical industry benefits from the use of surfactants in the reaction sequence for pharmaceutical active ingredients, by avoiding toxic solvents, simplifying purification steps, and decreasing the environmental impact.²⁰ However, industrial application of surfactant-based systems as reaction media is still rare because of insufficient knowledge of the function of surfactants as promoters in biphasic catalysis.

Recently, we reported about the special role of nonionic surfactants during catalysis in microemulsion systems for the

rhodium-catalyzed hydroformylation of 1-dodecene.²¹ It became apparent that not the phase behavior of the microemulsion system but the type of surfactant determines the reaction performance. The surfactant enlarges the interfacial area between water and oil, defining the local concentration of the substrates and the concentration of the surface active catalyst complex at the interface. As a result of these investigations, the applicability of microemulsion systems is mainly influenced by an appropriate surfactant chosen as the emulsifier. In this contribution, we want to verify these important findings for catalysis in microemulsion systems with another industrial relevant catalytic reaction: the palladium-catalyzed hydroxycarbonylation of 1-dodecene (see Figure 2).

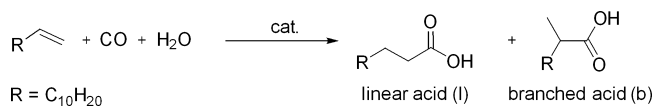


Figure 2. Hydroxycarbonylation of 1-dodecene to give the linear and branched acids.

Mortreux and collaborators were the first, who investigated the hydroxycarbonylation of alkenes in biphasic systems.^{22,23} Dependent on the reaction conditions and the catalyst system, the corresponding linear (l) and branched (b) acid can be formed, determining the l/b regioselectivity of the reaction.

In this case, water acts as both solvent and substrate, complicating the reaction system compared to the hydroformylation reaction. Hence, palladium-catalyzed hydroxycarbonylation is suitable to find a general approach for catalysis in microemulsion systems. Herein, the main focus has been set on the impact of the phase behavior of the applied microemulsion system on the resulting reaction performance.

2. RESULTS AND DISCUSSION

2.1. Effect of Temperature and Surfactant Concentration. As stated in Section 1, the phase behavior of microemulsion systems depends mainly on the temperature and the mass fractions of oil (α) and surfactant (γ). To evaluate the reaction performance in terms of the phase behavior, the oil content was fixed to $\alpha = 0.5$ and the so called Kahlweit fish diagram (Figure 3) of the microemulsion system consisting of 1-dodecene, dodecane, water, and the technical grade surfactant Marlipal 24/50 was exemplarily recorded as the benchmark system.

Marlipal 24/50 was chosen as the benchmark surfactant because of several reasons. First, the chemical structure (see the Supporting Information) is very simple, consisting of a linear alkyl chain and an oligomer of ethylene oxide. We have

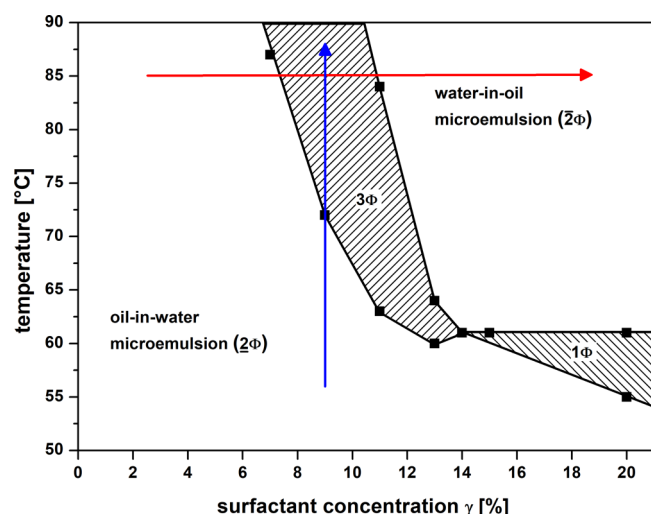


Figure 3. Phase diagram of a mixture of 1-dodecene, dodecane, water, and Marlipal (24/50) with $\alpha = 0.5$, 1 wt % Na_2SO_4 , $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.02 mmol), $\text{Pd}/\text{SX}/\text{methanesulfonic acid (MSA)}/1\text{-dodecene} = 1:4:40:110$, and mass ratio 1-dodecene to dodecane = 1:3 (red line: constant temperature, blue line: constant γ).

to mention that the surfactant is of technical grade with a certain distribution of ethylene oxide units and an apolar alkyl chain distribution. Second, no additional functional groups for example phenyl-groups exist, which could interact with the catalytic system. Third, the phase inversion temperature of the microemulsion system consisting of 1-dodecene, dodecane, water, and Marlipal 24/50 is in the middle of the investigated temperature range. Hence, Marlipal 24/50 is appropriate for our investigations. Dodecane was added as the cosolvent to the oil phase (mass ratio 1-dodecene to dodecane was 1:3) for maintaining a phase separation and for avoiding rigorous shifts of the phase diagram because of the formed product tridecanoic acid during the reaction. Additionally, 1 wt % sodium sulfate was added to microemulsion systems for destabilizing the emulsion, which empirically accelerates the time for phase separation by a factor of 4. We have to mention that the addition of sodium sulfate decreases the initial rate of hydroxycarbonylation, but the selectivity remains constant (see the Supporting Information). The impact of salts on the reaction performance and catalyst stability was investigated in detail for the palladium-catalyzed hydroxycarbonylation of propene in biphasic systems.²⁴ Nevertheless, 1 wt % sodium sulfate was used because of the enhanced phase separation. All catalyst components were added to the microemulsion system as well to observe the phase behavior for the entire reaction mixture. It has to be mentioned that the investigation on the phase behavior has been performed without carbon monoxide pressure to avoid any reaction progress. Indeed, the pressure has an impact on the phase behavior, but it can be neglected for the mild reaction pressure used in the reactions.²⁵

The investigated microemulsion system is characterized by the surfactant concentration $\tilde{\gamma} = 14\%$ and the phase inversion temperature $\tilde{T} = 61^\circ\text{C}$. An oil-in-water microemulsion with an excess oil phase (2Φ) is formed at lower temperatures. With increasing temperature, the system shifts to a water-in-oil microemulsion with an excess water phase (2Φ). In between, a macroscopically triphasic system is formed in which the middle phase is the microemulsion phase enclosed by the water-excess and oil-excess phase. Increasing the surfactant concentration

above 14%, oil and water are completely dispersed in a one phase microemulsion. Interestingly, the catalyst system follows the surfactant into the corresponding microemulsion phase because of its surface activity as seen in Figure 4, exemplarily

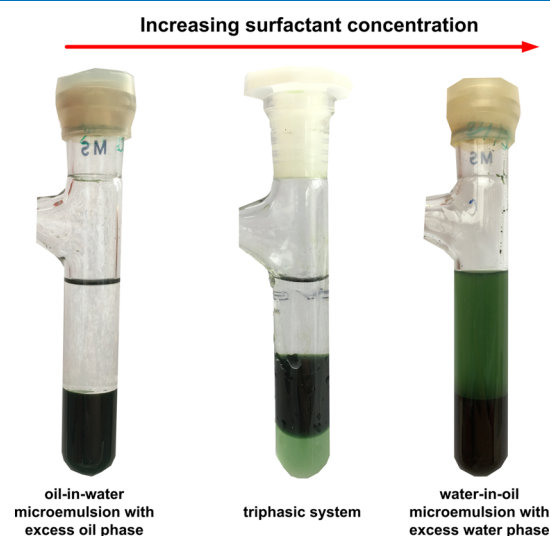


Figure 4. Pictures of the investigated microemulsion systems. Test conditions: $T = 85^\circ\text{C}$, $\alpha = 0.5$, 1 wt % Na_2SO_4 , $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.02 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene} = 1:4:40:110$, mass ratio 1-dodecene to dodecane = 1:3, Marlipal 24/50 as the surfactant, $\gamma = 4\%$ (left), $\gamma = 9\%$ (middle), $\gamma = 14\%$ (right).

recorded for an increasing surfactant concentration at a constant temperature. It is mentionable that the different phases look similar for a constant surfactant concentration with increasing temperature. The surface activity of the catalyst complex results from the surface-active ligand SulfoXantPhos, which was shown in previous publications.^{26,27} As a result, the catalyst complex behaves similar to a surfactant and the complex can be incorporated at the water–oil interface. Hence, the catalyst can be solubilized either in the continuous water phase (left picture) and the surfactant-rich phase (middle picture) or even partly in the oil phase (right picture). The change of color is due to the different catalyst complex concentrations in the different phases. Hereby, the dark greenish phases indicate a high concentration of the applied catalyst complex in the corresponding phase.

On the basis of the phase behavior of the applied microemulsion system, the influence of temperature and surfactant concentration has been investigated in terms of reaction performance to correlate it to the phase behavior of the microemulsion system. The effect of the surfactant concentration has been investigated at a constant reaction temperature of 85°C to ensure the shift from an oil-in-water to a water-in-oil microemulsion system (see the red arrow in Figure 3). The conversion of 1-dodecene and the yield to the linear acid are shown in Figure 5. It was found that the higher the surfactant concentration, the higher is the conversion, respectively the yield to the linear acid at a given time. The yield increases from 0.3% with a surfactant concentration of $\gamma = 0.5$ to 42.6% at a surfactant concentration of $\gamma = 30\%$ after 20 h reaction time. It has to be mentioned that the addition of surfactant is generally necessary to enable the reaction because no reaction progress is observed without surfactant as the phase transfer agent. Furthermore, a critical surfactant concentration is apparently needed, in this case $\gamma > 3\%$, to

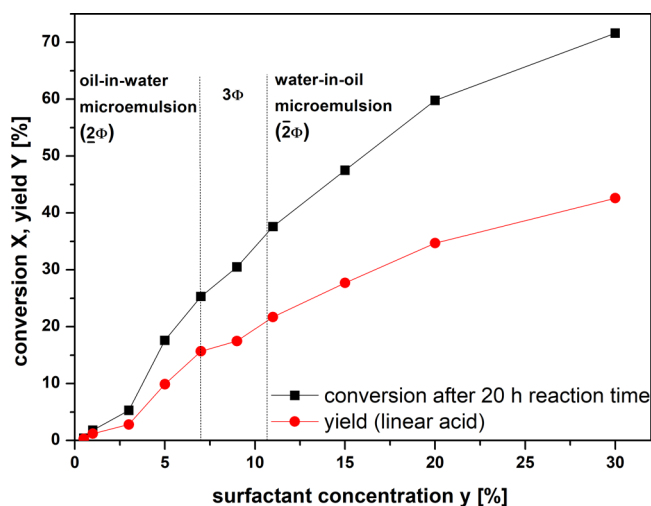


Figure 5. Effect of surfactant concentration on the hydroxycarbonylation of 1-dodecene. Experimental conditions: $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.08 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene}$ (1:4:40:110), $\alpha = 0.5$, dodecane as the cosolvent (9 g), water (12 g), Marlupal 24/50 as the surfactant, Na_2SO_4 (1 wt %), $p(\text{CO}) = 30$ bar, $T = 85$ °C, $n = 1200$ rpm, $t = 20$ h.

accelerate the reaction substantially. Below a concentration of $\gamma = 3\%$, only surfactant monomers are dissolved in the oil and the water phase, resulting only in a slow reaction progress. A further increase of the surfactant concentration leads to a strong enlargement of the interfacial area between the aqueous and organic phase. Hence, the local concentrations of the reactants, particularly water, carbon monoxide, and 1-dodecene, at the interface are increased with increasing amount of surfactant in the mixture, which results in higher reaction rates shown by higher yield and conversion.

As stated in the literature, the rate-determining step of hydroxycarbonylation is the hydrolysis step,^{28,29} thus particularly the increased amount of water at the interface may lead to the higher reaction rate with increasing surfactant concentration. Furthermore, the local concentration of the active catalyst species plays a crucial role for the reaction performance. The applied catalyst complex is negatively charged because of the ligand SulfoXantPhos. Hence, no electrostatic interaction with the neutral surfactant can be expected. Nevertheless, the catalyst complex accumulates at the water–oil interface because of its surface active properties. Thus, with an increasing interfacial area, the catalyst complex becomes more and more diluted at the interface because the overall amount of catalyst in the system remains constant. As a result, the equilibrium between active and inactive catalyst species might be shifted to a higher concentration of the active catalyst at the interface, and with that to a higher reaction rate. To confirm this assumption, we varied the catalyst concentration at a fixed surfactant concentration that is a constant interfacial area, which is shown in Section 2.3.

Interestingly, the phase behavior of the microemulsion system has no strong impact on the reaction performance of hydroxycarbonylation, which is in good agreement to the findings for hydroformylation of 1-dodecene in the same systems.²¹ The initially prepared microemulsion system changes from an oil-in-water microemulsion system at a surfactant concentration of $\gamma = 7\%$ to a macroscopically three-phase system and finally to a water-in-oil microemulsion system at $\gamma = 11\%$. No significant change in the conversion and

yield of the reaction is observed at the shift of the phase states, which would indicate a change in mass transfer conditions. This means that not the phase behavior of the microemulsion system but the interfacial area and the local concentrations of the reactants at the interface have a major influence on the reaction performance of hydroxycarbonylation. Moreover, the surfactant concentration has a minor impact on the l/b regioselectivity of the formed acid. With increasing surfactant concentration, the l/b selectivity decreases from 64:36 at a surfactant concentration of $\gamma = 3\%$ to 61:39 at $\gamma = 30\%$. Because of the increased interfacial area the isomerization of 1-dodecene takes place with an increased rate, which leads to the slightly lower l/b selectivity. It is mentionable that surfactant concentrations above $\gamma = 20\%$ are not favorable because the one phase region of the microemulsion system makes a subsequent phase separation for recycling of the catalyst system rather difficult in comparison to the other multiphase states.

Furthermore, the surfactant concentration was fixed at $\gamma = 9\%$ to investigate the effect of the temperature on the reaction (blue arrow in Figure 4). The hydroxycarbonylation of 1-dodecene was carried out at temperatures ranging from 65 to 105 °C (see Figure 6).

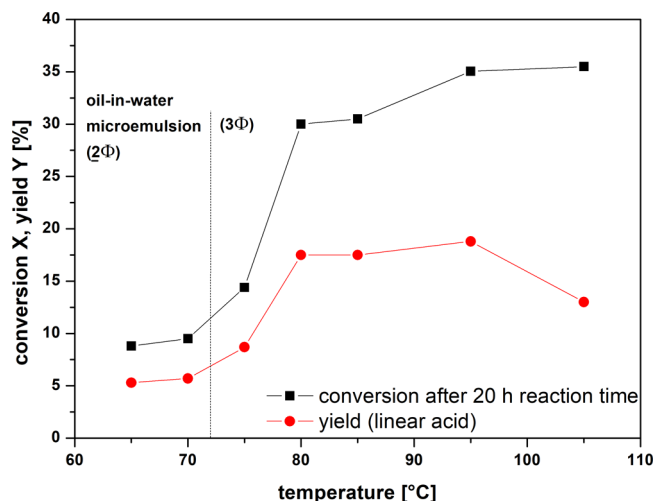


Figure 6. Effect of temperature on the hydroxycarbonylation of 1-dodecene. Experimental conditions: $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.08 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene}$ (1:4:40:110), $\alpha = 0.5$, dodecane as the cosolvent (9 g), water (12 g), Marlupal 24/50 as the surfactant, $\gamma = 9\%$, Na_2SO_4 (1 wt %), $p(\text{CO}) = 30$ bar, $n = 1200$ rpm, $t = 20$ h.

Initially, the conversion increases exponentially with increasing reaction temperature from 8% at 65 °C to 30% at 80 °C, which is typical for an Arrhenius type behavior, indicating a kinetically controlled biphasic reaction. After this, the conversion reaches unexpectedly a plateau between 30 and 35% at higher reaction temperatures. The yield of the linear acid shows a nearly similar trend but decreases in the end, resulting in a yield of only 13% at 105 °C. To understand the decreased yield, the initial rate of hydroxycarbonylation was calculated from the gas consumption at a conversion of 5%. As illustrated in Figure 7, the initial rate of hydroxycarbonylation behaves in the same way, there is an exponential increase from 2.5 to 10.5 mmol/(L·h), followed by an inflection point, and a further slightly increase of the initial rate to a critical value of 18 mmol/(L·h). Interestingly, the decline in activity cannot be

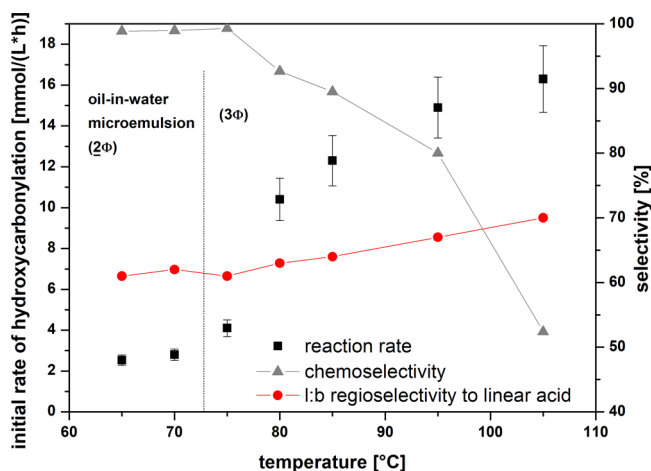


Figure 7. Effect of temperature on the initial rate and selectivity of the hydroxycarbonylation of 1-dodecene. Experimental conditions: $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.08 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene}$ (1:4:40:110), $\alpha = 0.5$, dodecane as the cosolvent (9 g), water (12 g), Marlipal 24/50 as the surfactant, $\gamma = 9\%$, Na_2SO_4 (1 wt %), $p(\text{CO}) = 30$ bar, $n = 1200$ rpm, $t = 20$ h, initial rate calculated from gas consumption at $X = 5\%$.

attributed to the change of phase behavior from an oil-in-water microemulsion to a three-phase system because this shift already happens at a temperature of 72 °C (see Figure 3). However, palladium black formation was observed as the precipitate at the reactor wall, particularly at temperatures above 100 °C, which leads to a decrease of the amount of the active catalyst. Thus, the initial rate of hydroxycarbonylation differs from the typical exponential increase and stagnates at higher temperatures. As described in the literature, palladium black formation is a specific drawback for homogeneously catalyzed reactions using palladium.³⁰ We have to mention that the reaction is not limited by mass transport at high temperatures, which was confirmed by investigations with variation of the stirrer speed, resulting in constant reaction rates.

In addition, the reaction temperature influences slightly the l/b regioselectivity to the linear acid. With increasing temperature from 65 to 105 °C, the regioselectivity of the linear acid increases from 61 to 70%. The hydrolysis step is known as the rate-determining step in the hydroxycarbonylation reaction. Because of the lower activation barrier of the hydrolysis step to the linear acid, compared to the hydrolysis step to the branched acid, hydroxycarbonylation at the terminal double bond proceeds faster.²⁹ Thus, the formation of the linear acid is enhanced with increasing temperature. Furthermore, chemoselectivity is extremely diminished from nearly 100% at 65 °C to 51% at 105 °C because an increased temperature enhances the isomerization of 1-dodecene.⁸ Considering all aspects, the phase behavior, especially the different phase states of the microemulsion system, seems to have no influence on the reaction performance of hydroxycarbonylation. To avoid the isomerization and palladium black formation, the following investigations were carried out at a reaction temperature of 85 °C.

2.2. Effect of Degree of Ethoxylation (EO). As described in the Section 2.1, the amount of surfactant is crucial for the performance of hydroxycarbonylation in microemulsion systems. To completely understand the role of the surfactant during the reaction, we investigated the influence of the surfactant chain length toward both the performance of

hydroxycarbonylation and the phase behavior. Therefore, the hydrophobicity of the surfactant was changed by varying the degree of EO from 2 to 9 (Marlipal 24/20 to Marlipal 24/90). As expected, the phase behavior is strongly influenced by the hydrophobicity of the surfactant (Figure 8). The three-phase

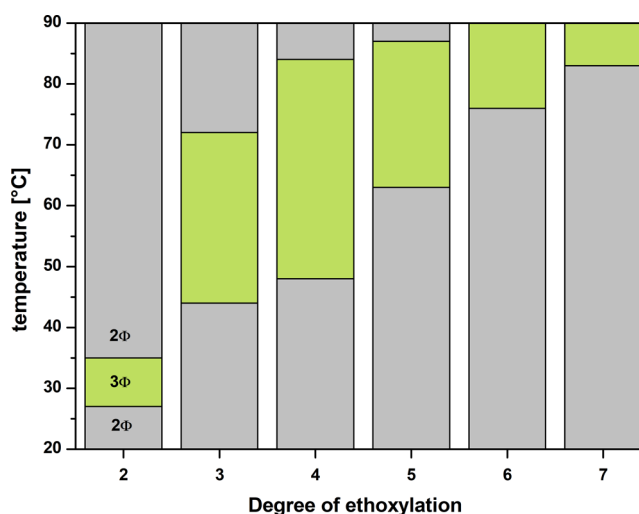


Figure 8. Phase behavior of 1-dodecene, dodecane, water, and Marlipal with different degrees of EO. Test conditions: $\alpha = 0.5$, $\gamma = 9\%$, 1 wt % Na_2SO_4 , $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.02 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene}$ = 1:4:40:110, mass ratio 1-dodecene to dodecane = 1:3.

region of the resulting microemulsion system is shifted to higher temperatures with the increasing EO number or rather decreasing hydrophobicity of the surfactant. The hydrophilic part of the surfactant, consisting of ethoxy units, undergoes a temperature-dependent conformational transformation, influencing the water solubility of the corresponding surfactant. The higher the EO number, the more temperature is needed to change the conformation of the ethoxy units. As a result of the conformational transformation, the dipole moment is reduced, resulting in a lower water solubility. Hence, the hydrophobicity of the surfactant is increased with higher EO and thus the appearance of the three-phase region is shifted to higher temperatures. The phase boundaries for the systems containing the surfactants Marlipal 24/80 and Marlipal 24/90 could not be determined because of the temperature limitation of the experimental setup.

Besides the shift in the phase behavior, it was found that the number of EO groups of the surfactant has a strong impact on the conversion and yield of hydroxycarbonylation (Figure 9). In general, the higher the EO number, the higher is the conversion or rather the yield of the acid. The yield of the linear acid reaches a maximum of 34% after 20 h reaction time with Marlipal 24/90 as the surfactant. It is notable that the applied surfactants do not differ in their chemical structure. Consequently, the difference in the reaction performance is caused by physical effects, particularly the local concentrations of the substrates at the interface. The density of the surfactant film at the oil–water interface might be the reason. With the increasing number of EO, the thickness of the surfactant film increases, leading to an enhanced adsorption of the reactants to the interface. Hence, the reactants are more accumulated at the oil–water interface with increasing EO number, which enhances the reaction rate. Similar results were obtained for the rhodium-catalyzed hydroformylation of 1-dodecene in

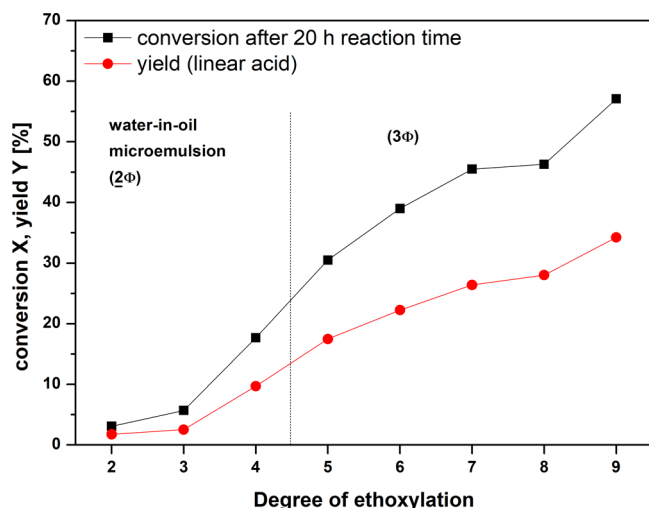


Figure 9. Effect of degree of EO on hydroxycarbonylation of 1-dodecene. Experimental conditions: $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.08 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene}$ (1:4:40:110), $\alpha = 0.5$, dodecane as the cosolvent (9 g), water (12 g), Marlupal 24/XX as the surfactant, Na_2SO_4 (1 wt %), $p(\text{CO}) = 30$ bar, $T = 85^\circ\text{C}$, $n = 1200$ rpm, $t = 20$ h.

microemulsion systems, which were recently reported by our group.²¹ Again, the phase behaviour of the microemulsion system shows no influence on the reaction performance, because no discrete changes of the conversion were observed when changing the phase state by the type of surfactant. We have to mention that the color of the reaction mixture did not change during the reaction, concluding that no palladium nanoparticles were formed.

In summary, the series of experiments confirms the assumption that the local concentrations of the reactants at the oil–water interface are crucial for the reaction performance. These concentrations are mainly determined by hydrophilicity and the amount of surfactant. The EO number of the applied surfactant controls the ability to perform as an emulsifier, which has a strong impact on the local concentrations and thus on the reaction rate for hydroxycarbonylation of 1-dodecene in microemulsion systems.

2.3. Variation of Catalyst Concentration. According to Section 2.1, the formation of inactive catalyst species depends on the local concentration of the catalyst complex at the oil–water interface. To confirm the formation of inactive catalyst species at the interface, experiments were carried out with variation of the catalyst concentration whereby the interfacial area was maintained using a constant surfactant concentration. Typically, the reaction rate increases with increasing catalyst concentration, often with a reaction order of 1.²⁸ In this case, the initial rate of hydroxycarbonylation increases in a concentration range from 0 to 8 mmol/L of palladium as seen in Figure 10 but surprisingly with a fractional reaction order of 1.8. Because the molar ratio of palladium to SulfoXantPhos to MSA remains constant at 1:4:40, we assume that the unexpected reaction order is caused by the increased concentration of MSA in this concentration range. As a result, more acidic reaction conditions are obtained with a higher amount of palladium, leading to a disproportionately high formation of the active palladium hydride species (see Figure 11) and thus to the unexpected reaction order of 1.8. Rodionova et al. investigated methoxycarbonylation of cyclo-

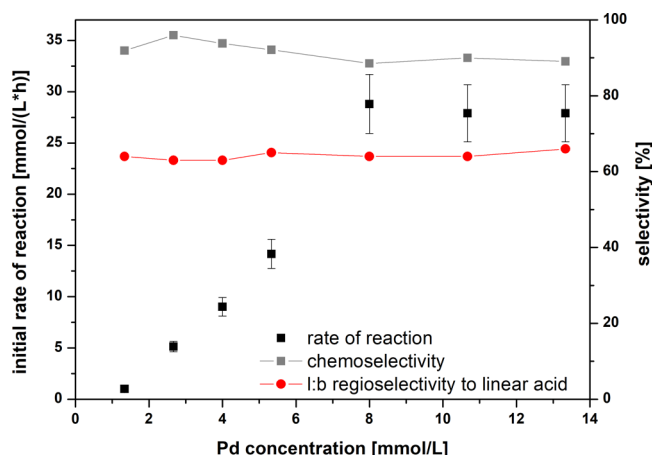


Figure 10. Effect of Pd concentration on hydroxycarbonylation of 1-dodecene. Experimental conditions: $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ as the precursor, $\text{Pd}/\text{SX}/\text{MSA}$ (1:4:40), $\alpha = 0.5$, 1-dodecene (3 g), dodecane as the cosolvent (9 g), water (12 g), Marlupal 24/70 as the surfactant, $\gamma = 9\%$, Na_2SO_4 (1 wt %), $p(\text{CO}) = 30$ bar, $T = 85^\circ\text{C}$, $n = 1200$ rpm, $t = 20$ h, $V_R = 0.03$ L, initial rate calculated from gas consumption at $X = 5\%$.

hexene and found similar results for the reaction order of the used acid as the cocatalyst.³¹

A further increase of the palladium concentration leads to a stagnation of the initial rate of reaction around 28 mmol/(L·h), indicating a catalyst inhibition because of the formation of inactive catalyst species (see Figure 11). We have to mention that variation of the stirrer speed at the highest palladium concentration shows no impact on the initial rate of hydroxycarbonylation, excluding any mass transport limitation. On the one hand, it is well-known that homogeneous palladium catalysts can form dimeric species, which are inactive for the palladium-catalyzed hydroxycarbonylation of 1-dodecene.^{32–34} We assume that high palladium and ligand concentrations lead to an enhanced formation of the inactive dimeric species, suppressing a further increase of the initial rate of hydroxycarbonylation. It has to be mentioned that the molar ratio of palladium to SulfoXantPhos to MSA remains constant at 1:4:40 for this experimental series. As a result, not only the palladium concentration is increased at the interface, but also the concentration of the ligand SulfoXantPhos, influencing the formation of the dimeric catalyst species as well. On the other hand, Mecking et al.³⁵ identified a bimolecular decomposition pathway for the active palladium hydride species forming palladium black, hydrogen, and a fully coordinated (diphosphine)₂Pd complex under reaction conditions. As a result of both deactivation pathways, the amount of the active catalyst species may stagnate at high concentrations of palladium, which would explain the observed plateau of the initial rate of hydroxycarbonylation.

In addition, the l/b regioselectivity and chemoselectivity of hydroxycarbonylation remains unchanged. Merely, isomerization of 1-dodecene takes place, which decreases chemoselectivity to 90%. As expected, the l/b regioselectivity to the linear acid is at a constant value of 64%, which confirms that an increase of the palladium concentration does not change the structure of the active catalyst species for the hydroxycarbonylation of 1-dodecene.

2.4. Modification of the Nonpolar Phase. The effect of cosolvents on the reaction performance and the phase behavior

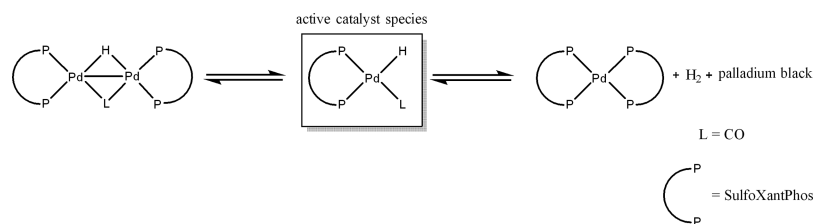


Figure 11. Possible catalyst deactivation pathways.

has also been investigated. The idea behind these experiments is to switch the phase behavior without changing the local concentrations at the oil–water interface, which should lead to similar initial reaction rates, thus verifying the previous results. As seen in Figure 12, the chain length of alkane, which has been applied as the cosolvent, affects the temperature slightly for existence of the three-phase region.

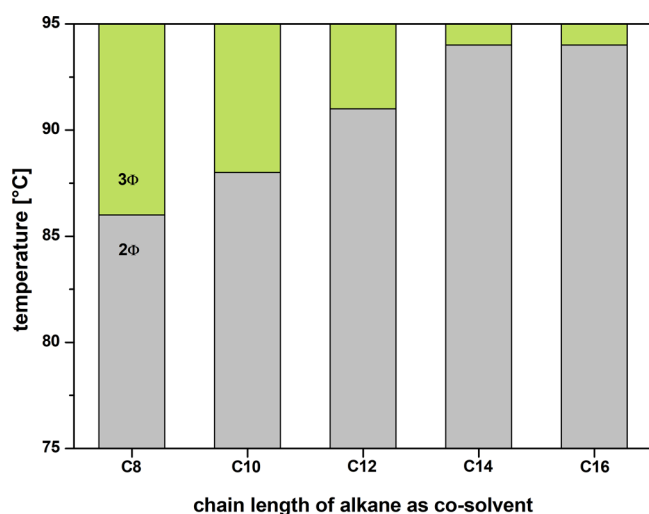


Figure 12. Phase behavior of 1-dodecene, cosolvent, water, and Marlupal 24/70. Test conditions: $\alpha = 0.5$, $\gamma = 9\%$, Na_2SO_4 (1 wt %), $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.02 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene} = 1:4:40:110$, and mass ratio 1-dodecene to cosolvent = 1:3.

As expected, with increasing hydrophobicity (chain-length) of the applied cosolvent, the phase boundaries are shifted to higher temperatures. However, the impact of changing the chain length on the phase behavior is rather low. The extension of the chain length by two carbon atoms results in a shift of the three-phase region of about 2 °C to higher temperatures. Furthermore, the slight change of the phase behavior by changing the hydrophobicity of the cosolvent shows no influence on the initial rate of hydroxycarbonylation (Figure 13), indicating no impact of the phase behavior on the reaction performance. Apparently, the local concentrations of the reactants at the oil–water interface do not differ for the applied alkanes as cosolvents despite the slight change of the phase behavior. Both chemoselectivity and l/b regioselectivity remain constant as well. The chemoselectivity is in a range of 90–95% because of isomerization of 1-dodecene. Nevertheless, the adjustment of the three-phase region by the choice of the cosolvent is crucial for a subsequent recycling procedure and product purification.

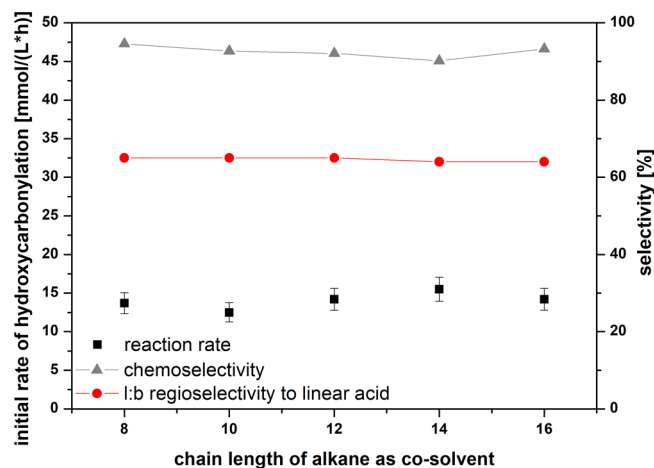


Figure 13. Effect of cosolvent on the hydroxycarbonylation of 1-dodecene. Experimental conditions: $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.08 mmol), $\text{Pd}/\text{SX}/\text{MSA}/1\text{-dodecene}$ (1:4:40:110), $\alpha = 0.5$, cosolvent (9 g), water (12 g), Marlupal 24/70 as the surfactant, Na_2SO_4 (1 wt %), $p(\text{CO}) = 30$ bar, $T = 85$ °C, $n = 1200$ rpm, $t = 20$ h, $V_R = 0.03$ L, initial rate calculated from gas consumption at $X = 5\%$.

3. CONCLUSIONS

With this contribution, the impact of nonionic surfactants on the palladium-catalyzed hydroxycarbonylation of 1-dodecene in microemulsion systems was demonstrated. Special attention was given to the interaction of the phase behavior of the microemulsion system and the reaction performance. It was found that the phase behavior does not control the reaction performance for catalysis in microemulsion systems. In contrast, the amount and type of the nonionic surfactants are crucial for catalysis in these reaction systems. First, the surfactant provides the interfacial area between oil and water. Because of the surface active properties of the applied catalyst complex, the reaction takes place at the interface. Extending this interfacial area by increasing the amount of surfactant, the reaction performance is substantially improved. Second, the hydrophilicity of the surfactant determines the local concentrations of substrates at the interface influencing the rate of hydroxycarbonylation. The presented results confirm the recently published results where the role of nonionic surfactants in the rhodium-catalyzed hydroformylation of 1-dodecene was investigated. Moreover, the concentration of the active catalyst complex at the interface has a huge impact on the reaction performance of hydroxycarbonylation. Dependent on its bulk concentration, inactive catalyst species are formed reducing the reaction performance. Consequently, the amount and chemical properties of the surfactant and the chemical behavior of the applied catalyst complex are crucial parameters to optimize the reaction performance for catalysis in microemulsion systems.

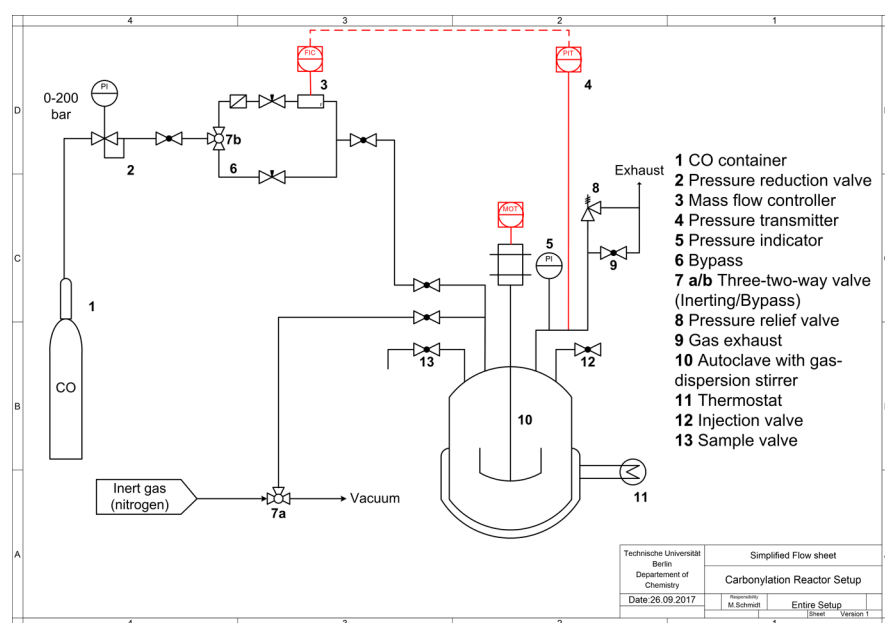


Figure 14. Experimental setup for hydroxycarbonylation.

On the basis of these results, the transfer from the lab scale into a continuously operated miniplant is currently under investigation. Hereby, the phase separation in the decanter unit and the catalyst stability is of special interest because of concentration shifts during the continuously operated reaction. In general, the three-phase region or the oil-in-water microemulsion is desirable to perform the recycling of the catalyst and the separation of the product. However, the time for phase separation is drastically reduced in the three-phase region, facilitating lower residence time in the decanter and thus the three-phase region of the microemulsion system is appropriate for recycling experiments.

4. MATERIALS AND METHODS

4.1. Chemicals. The substrates such as 1-dodecene (94%), decane (94%), and hexadecane (99%) were purchased from Merck and the cosolvents such as dodecane (98%) and octane (98%) were received from ABCR. Water was obtained from VWR with the HPLC grade. Sigma-Aldrich has delivered the palladium precursor $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ with a purity of 99.9%, the cosolvent tetradecane (92%), and the cocatalyst MSA with a purity of 99.5%. SulfoXantPhos (CAS registry number 215792-51-1) was used as a ligand and was synthesized by MOLISA following a procedure described by Goedheijt et al.³⁶ It is the water-soluble analogue of the commercially available 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (XantPhos). Nonane (99%) from Sigma-Aldrich was used as the internal standard. Carbon monoxide was obtained from Air Liquide with a purity of 99.9%. The applied nonionic surfactants of the Marlipal series were provided by Sasol Germany. It is worth to mention that the surfactants are of technical grade with a certain chain length distribution. To control the ionic strength of the reaction media, sodium sulfate (Na_2SO_4) was used, which was purchased from Merck. All chemicals were used as received without further purification.

4.2. Determination of the Phase Behavior. The investigations on the phase behavior were performed in 10 mL Schlenk tubes. The cosolvent (2.25 g), 1-dodecene (0.75 g), the surfactant (Marlipal 24/XX), sodium sulfate (Na_2SO_4),

and the cocatalyst MSA were weighted into the Schlenk tube and flushed with argon. A stock solution of the precursor $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ and the ligand SulfoXantPhos was prepared in water with standard Schlenk technique and stirred overnight. The catalyst solution (3.0 g) was added to the Schlenk tube under an argon counterflow, and the tubes were closed with a septum. Afterward, the Schlenk tubes were placed into a water bath, and the phase behavior of the microemulsion system was investigated in a temperature range between 50 and 90 °C in 1 °C steps. For that, the temperature of the water bath was adjusted as desired, and then the tubes were shaken and the phase separation was observed after 10 min.

4.3. Experimental Setup for Hydroxycarbonylation.

All experiments were carried out in a 100 mL stainless steel autoclave built by Halmosi GmbH. An overview of the reactor setup is given in Figure 14. The autoclave (10) is equipped with a gas dispersion stirrer, a baffle to ensure the dispersion of the reaction mixture, and a PTFE inlay to avoid the formation of palladium black at the inner surface of the reactor wall. To maintain isobaric reaction conditions, a pressure transmitter (4) is connected with a mass flow controller (3) to the reactor. For a fast initial pressurization of the reactor with carbon monoxide, a bypass was installed (6). Additionally, the autoclave has connections for sampling (13), inertization (7a), and the injection of reactants (12) under a nitrogen counterflow. A process control system monitors all process-values and the corresponding set-values such as pressure, temperature, gas flow, and stirring speed and records the data.

4.4. Experimental Procedure for Hydroxycarbonylation. In a typical experiment, the cosolvent, 1-dodecene as the substrate, the surfactant, nonane as the internal standard (300 mg), and MSA as the co-catalyst were weighted into the PTFE inlay and introduced to the reactor. After evacuation and flushing the reactor with nitrogen three times, the catalyst solution was injected with a syringe under a nitrogen counterflow. The catalyst solution was prepared overnight, weighting $\text{Pd}_2(\text{allyl})_2\text{Cl}_2$ (0.08 mmol, 0.5 equiv) and SulfoXantPhos (0.64 mmol, 4 equiv) into a Schlenk flask using standard Schlenk technique and adding water (12 g)

through a septum. The reactor was heated up to the desired reaction temperature, pressurized with carbon monoxide, and stirred at 1200 rpm. Samples were taken at fixed time intervals, diluted with acetone, and centrifuged to precipitate the ligand from the solution. Gas chromatography (GC) analysis was performed on Shimadzu GC2010 Plus with a flame ionization detector (FID) packed with the Restek RTX5-MS column (30 m \times 0.25 mm \times 0.25 μ m). Nonane was used as the internal standard to calculate the conversion of dodecene, yields of acid, chemoselectivity, and linear-to-branched regioselectivity (l/b), expressed as the ratio of linear acid to the sum of linear and branched acids, as shown in eqs 3–6.

$$X(t) = \frac{n_{t=0}(\text{1-dodecene}) - n_t(\text{1-dodecene})}{n_{t=0}(\text{1-dodecene})} \quad (3)$$

$$Y(t) = \frac{n_{t,\text{product}}}{n_{t=0}(\text{1-dodecene})} \quad (4)$$

$$S_{\text{chemo}}(t) = \frac{Y_{\text{acid}}(t)}{X(t)} \quad (5)$$

$$S_{l/b}(t) = \frac{Y_{\text{linear acid}}(t)}{Y_{\text{acids}}(t)} \quad (6)$$

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b01708.

Information on the chemical structure of the surfactant and variation of ionic strength (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) Kohlpaintner, C. W.; Fischer, R. W.; Cornils, B. Aqueous biphasic catalysis: Ruhrchemie/Rhône-Poulenc oxo process. *Appl. Catal., A* **2001**, *221*, 219–225.
- (2) Liu, C.; Li, X.; Jin, Z. Progress in Thermoregulated Liquid/Liquid Biphasic Catalysis. *Catal. Today* **2015**, *247*, 82–89.
- (3) Schmidt, M.; Pogrzeba, T.; Hohl, L.; Weber, A.; Kielholz, A.; Kraume, M.; Schomäcker, R. Palladium catalyzed methoxycarbonylation of 1-dodecene in biphasic systems - Optimization of catalyst recycling. *Mol. Catal.* **2017**, *439*, 1–8.
- (4) Hapiot, F.; Bricout, H.; Menuel, S.; Tilloy, S.; Monflier, E. Recent Breakthroughs in Aqueous Cyclodextrin-Assisted Supramolecular Catalysis. *Catal. Sci. Technol.* **2014**, *4*, 1899.
- (5) Tilloy, S.; Bertoux, F.; Mortreux, A.; Monflier, E. Chemically modified β -cyclodextrins in biphasic catalysis: a fruitful contribution of the host-guest chemistry to the transition-metal catalyzed reactions. *Catal. Today* **1999**, *48*, 245–253.
- (6) Horvath, I. T.; Rabai, J. Facile Catalyst Separation without Water: Fluorous Biphasic Hydroformylation of Olefins. *Science* **1994**, *266*, 72–75.
- (7) Betzemeier, B.; Lhermitte, F.; Knochel, P. Wacker oxidation of alkenes using a fluorous biphasic system. A mild preparation of polyfunctional ketones. *Tetrahedron Lett.* **1998**, *39*, 6667–6670.
- (8) Behr, A.; Vorholt, A. J.; Rentmeister, N. Recyclable Homogeneous Catalyst for the Hydroesterification of Methyl Oleate in Thermomorphic Solvent Systems. *Chem. Eng. Sci.* **2013**, *99*, 38–43.
- (9) Gaide, T.; Behr, A.; Arns, A.; Benski, F.; Vorholt, A. J. Hydroesterification of methyl 10-undecenoate in thermomorphic multicomponent solvent systems-Process development for the synthesis of sustainable polymer precursors. *Chem. Eng. Process.* **2016**, *99*, 197–204.
- (10) Liu, F.; Abrams, M. B.; Baker, R. T.; Tumas, W. Phase-Separable Catalysis Using Room Temperature Ionic Liquids and Supercritical Carbon Dioxide. *Chem. Commun.* **2001**, 433–434.
- (11) Lipshutz, B. H.; Ghorai, S.; Cortes-Clerget, M. The Hydrophobic Effect Applied to Organic Synthesis: Recent Synthetic Chemistry in Water. *Chem.—Eur. J.* **2018**, *24*, 6672–6695.
- (12) Dwars, T.; Paetzold, E.; Oehme, G. Reactions in Micellar Systems. *Angew. Chem., Int. Ed.* **2005**, *44*, 7174–7199.
- (13) La Sorella, G.; Strukul, G.; Scarso, A. Recent Advances in Catalysis in Micellar Media. *Green Chem.* **2015**, *17*, 644–683.
- (14) Mason, T. G.; Wilking, J. N.; Meleson, K.; Chang, C. B.; Graves, S. M. Nanoemulsions: Formation, Structure, and Physical Properties. *J. Phys.: Condens. Matter* **2006**, *18*, R635.
- (15) Schwuger, M.-J.; Stickdorn, K.; Schomaecker, R. Microemulsions in Technical Processes. *Chem. Rev.* **1995**, *95*, 849–864.
- (16) Schwarze, M.; Pogrzeba, T.; Volovych, I.; Schomäcker, R. Microemulsion Systems for Catalytic Reactions and Processes. *Catal. Sci. Technol.* **2015**, *5*, 24–33.
- (17) Handa, S.; Lippincott, D. J.; Aue, D. H.; Lipshutz, B. H. Asymmetric Gold-Catalyzed Lactonizations in Water at Room Temperature. *Angew. Chem., Int. Ed.* **2014**, *53*, 10658–10662.
- (18) Haumann, M.; Koch, H.; Schomäcker, R. Hydroformylation in Microemulsions: Conversion of an Internal Long Chain Alkene into a Linear Aldehyde Using a Water Soluble Cobalt Catalyst. *Catal. Today* **2003**, *79–80*, 43–49.
- (19) Haumann, M.; Koch, H.; Hugo, P.; Schomäcker, R. Hydroformylation of 1-Dodecene Using Rh-TPPTS in a Microemulsion. *Appl. Catal., A* **2002**, *225*, 239–249.
- (20) Gallou, F.; Isley, N. A.; Ganic, A.; Onken, U.; Parmentier, M. Surfactant Technology Applied toward an Active Pharmaceutical Ingredient: More than a Simple Green Chemistry Advance. *Green Chem.* **2016**, *18*, 14–19.
- (21) Pogrzeba, T.; Schmidt, M.; Milojevic, N.; Urban, C.; Illner, M.; Repke, J.-U.; Schomäcker, R. Understanding the Role of Nonionic Surfactants during Catalysis in Microemulsion Systems on the Example of Rhodium-Catalyzed Hydroformylation. *Ind. Eng. Chem. Res.* **2017**, *56*, 9934–9941.
- (22) Monflier, E.; Tilloy, S.; Bertoux, F.; Castanet, Y.; Mortreux, A. New Prospects for the Palladium-Catalyzed Hydrocarboxylation of Higher Alpha-Olefins in a Two-Phase System: The Use of Chemically Modified Beta-Cyclodextrin. *New J. Chem.* **1997**, *21*, 857.
- (23) Tilloy, S.; Monflier, E.; Bertoux, F.; Castanet, Y.; Mortreux, A. A New Fruitful Development in Biphasic Catalysis: The Palladium-Catalyzed Hydrocarboxylation of Alkenes. *New J. Chem.* **1997**, *21*, 529.

- (24) Bertoux, F.; Monflier, E.; Castanet, Y.; Mortreux, A. Palladium Catalyzed Hydroxycarbonylation of Olefins in Biphasic System: Beneficial Effect of Alkali Metal Salt and Protective-Colloid Agents on the Stability of the Catalytic System. *J. Mol. Catal. A: Chem.* **1999**, *143*, 23–30.
- (25) Kahlweit, M.; Strey, R.; Firman, P.; Haase, D.; Jen, J.; Schomaecker, R. General Patterns of the Phase Behavior of Mixtures of Water, Nonpolar Solvents, Amphiphiles, and Electrolytes. 1. *Langmuir* **1988**, *4*, 499–511.
- (26) Schmidt, M.; Pogrzeba, T.; Stehl, D.; Sachse, R.; Schwarze, M.; von Klitzing, R.; Schomäcker, R. Verteilungsgleichgewichte von Liganden in mizellaren Lösungsmittelsystemen. *Chem.-Ing.-Tech.* **2016**, *88*, 119–127.
- (27) Pogrzeba, T.; Müller, D.; Illner, M.; Schmidt, M.; Kasaka, Y.; Weber, A.; Wozny, G.; Schomäcker, R.; Schwarze, M. Superior catalyst recycling in surfactant based multiphase systems - Quo vadis catalyst complex? *Chem. Eng. Process.* **2016**, *99*, 155–166.
- (28) Rosales, M.; Pacheco, I.; Medina, J.; Fernández, J.; González, A.; Izquierdo, R.; Melean, L. G.; Baricelli, P. J. Kinetics and Mechanisms of Homogeneous Catalytic Reactions. Part 12. Hydroalcoxycarbonylation of 1-Hexene Using Palladium/Triphenylphosphine Systems as Catalyst Precursors. *Catal. Lett.* **2014**, *144*, 1717–1727.
- (29) Roesle, P.; Dürr, C. J.; Möller, H. M.; Cavallo, L.; Caporaso, L.; Mecking, S. Mechanistic Features of Isomerizing Alkoxycarbonylation of Methyl Oleate. *J. Am. Chem. Soc.* **2012**, *134*, 17696–17703.
- (30) Papadogianakis, G.; Verspui, G.; Maat, L.; Sheldon, R. A. Catalytic Conversions in Water. Part 6. A Novel Biphasic Hydrocarboxylation of Olefins Catalyzed by Palladium TPPTS Complexes (TPPTS=P(C₆H₄-m-SO₃Na) ₃). *Catal. Lett.* **1997**, *47*, 43–46.
- (31) Averyanov, V. A.; Sevostyanova, N. T.; Batashev, S. A.; Vorobiev, A. A.; Rodionova, A. S. Kinetics and Mechanism of Cyclohexene Hydrocarbomethoxylation Catalyzed by the Pd(OAc)₂-PPh₃-p-Toluenesulfonic Acid System. *Russ. J. Phys. Chem. B* **2014**, *8*, 140–147.
- (32) Baya, M.; Houghton, J.; Konya, D.; Champouret, Y.; Daran, J.-C.; Almeida Leñero, K. Q.; Schoon, L.; Mul, W. P.; van Oort, A. B.; Meijboom, N.; et al. Pd(I) Phosphine Carbonyl and Hydride Complexes Implicated in the Palladium-Catalyzed Oxo Process. *J. Am. Chem. Soc.* **2008**, *130*, 10612–10624.
- (33) Portnoy, M.; Milstein, D. A Binuclear Palladium(I) Hydride. Formation, Reactions, and Catalysis. *Organometallics* **1994**, *13*, 600–609.
- (34) van Leeuwen, P. W. N. M.; Zuideveld, M. A.; Swennenhuis, B. H. G.; Freixa, Z.; Kamer, P. C. J.; Goubitz, K.; Fraanje, J.; Lutz, M.; Spek, A. L. Alcoholysis of Acylpalladium(II) Complexes Relevant to the Alternating Copolymerization of Ethene and Carbon Monoxide and the Alkoxycarbonylation of Alkenes: The Importance of Cis-Coordinating Phosphines. *J. Am. Chem. Soc.* **2003**, *125*, 5523–5539.
- (35) Rünzi, T.; Tritschler, U.; Roesle, P.; Göttker-Schnetmann, I.; Möller, H. M.; Caporaso, L.; Poater, A.; Cavallo, L.; Mecking, S. Activation and Deactivation of Neutral Palladium(II) Phosphinesulfonate Polymerization Catalysts. *Organometallics* **2012**, *31*, 8388–8406.
- (36) Goedheijt, M.; Kamer, P. C. J.; Van Leeuwen, P. W. N. M. A Water-Soluble Diphosphine Ligand with a Large natural Bite Angle for Two-Phase Hydroformylation of Alkenes. *J. Mol. Catal. A: Chem.* **1998**, *134*, 243.