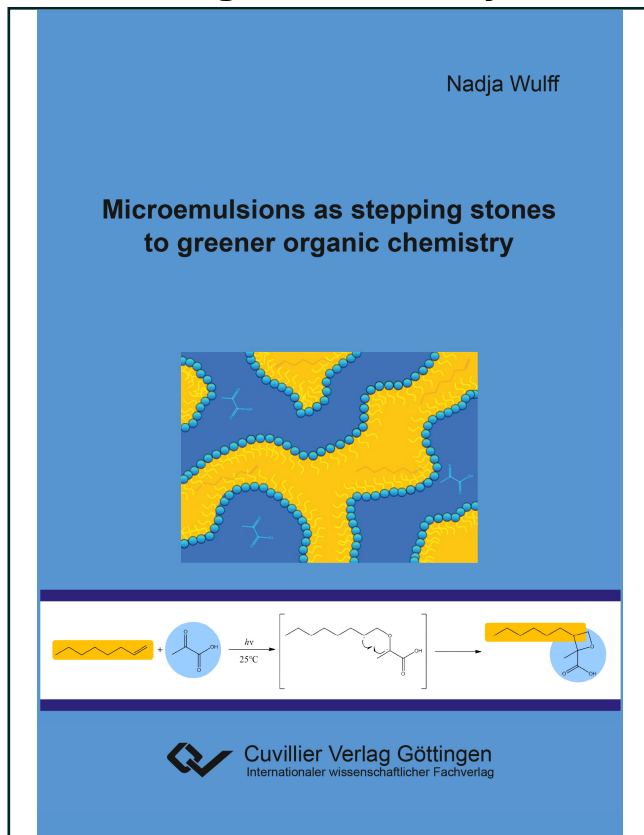




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Microemulsions as stepping stones to greener organic chemistry



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1 INTRODUCTION

In a world with high demand for specialty chemicals, such as dyes, drugs, detergents and plant protective agents, science and applied research especially in the field of organic synthesis are faced with a variety of challenges. On the way from basic raw materials to the final product the sophisticated reaction sequences, different solvent properties, incompatible reactants and further additives have to be considered. Hence, depending on the complexity of the reaction route a large number of byproducts and wastes can be generated. The likelihood of an accumulation of waste increases, if the polarity of solvents or reactants differs and thus, two immiscible phases with only a very low interfacial area form. Here, the right choice of an appropriate solvent is especially challenging: Commonly, the employed solvents are often expensive and/or toxic if both the hydrophilic or the hydrophobic reactants are to be solubilized simultaneously sufficiently well. Otherwise very poor reaction rates and product yields are obtained. Therefore, it is a crucial task to develop a methodology that minimizes these problems.

The first approach to these problems was the use of so-called phase transfer catalysts (PTC) such as cetyltrimethylammonium bromide (CTAB). By adding these catalysts in small weight fractions thermodynamically instable emulsions form providing a significantly enlarged interfacial area. As a result the modified reactions have higher product yields and the demand on very costly solvents which can dissolve both reactants can be reduced by using water and common organic solvents [1-3]. However, the main disadvantages of phase transfer catalysis are the difficulty of their separation and recovery, further a high toxicity of some catalysts, like crown ethers, and sometimes their thermal chemical stability [4].

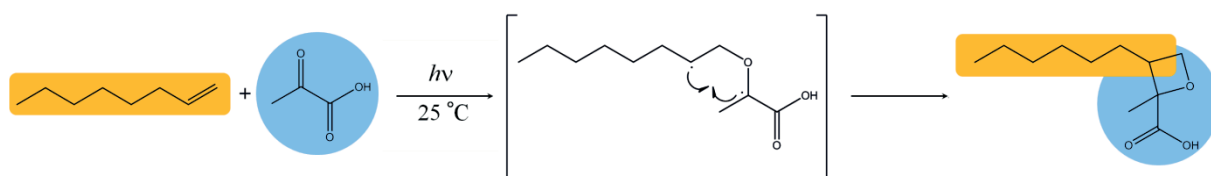
To overcome the thermodynamic instability and to ease the extraction and purification process microemulsions can be applied. Already in their infancy there was the consideration of using microemulsions as reaction media but to do so their elementary properties had to be understood. Thus, in 1954 *Schulman* and *Hoar* were the first to investigate the phenomenon of spontaneous formation of stable and isotropic water and oil emulsions, if enough cationic soap (*e.g.* CTAB) was added [5]. Later *Winsor* described the phase behavior of very similar systems in more detail and found out that the surfactant can dissolve in the water- or the oil-phase or it makes up its own phase [6]. He denoted these different states as the three *Winsor states* (I, II, III) which are still referred to when talking about water-oil-surfactant mixtures.

However, it was not until 1959 when the term microemulsion was first used by *Schulman* [7] to classify such systems that require surfactants and cosurfactants for their formulation. In the following years, *Shinoda* was the first who demonstrated the temperature dependence of the different *Winsor states* of microemulsions. Furthermore, he introduced non-ionic instead of ionic surfactants for the formulation of microemulsions, thereby eliminating the need of cosurfactant to induce phase transitions [8-13]. A very interesting property, especially with regard to following applications, though in the beginning not being considered as such, was the discovery of *Shinoda* and *Friberg* of the ultra low interfacial tension within the Winsor III region [14]. Finally, since 1983 *Kahlweit* and *Strey* investigated the phase behavior of microemulsions of different types extensively in a very detailed and revealing way and *Strey* gave conclusive proof that all microemulsion characteristics can be traced back to their ultra low interfacial tension and the related membrane properties [15-29]. The fascination on microemulsion properties continued to grow and thus, the resolution of the nanostructure of microemulsions was targeted since the 1990ies. Via scattering methods like small angle neutron scattering (SANS) [30-36], imaging methods like freeze fracture electron microscopy (FFEM) [37-41] and self-diffusion NMR [42-45] the microstructure of microemulsions was enlightened step by step. Based on the fundamental investigations of the workgroups mentioned as well as from several others, now there was enough knowledge on microemulsions to recognize their high application potential.

Thenceforth, the research on microemulsions for specific applications has exponentially multiplied and by sophisticated implementation of their fundamental properties a complete revolution regarding chemical and industrial processes started. Amongst the most important properties is the ultra low interfacial tension and the related solubilization capacity of microemulsions making one of their earliest applications in detergency industry. Their outstanding ability to simultaneously solubilize hydrophobic soils like greases as well as hydrophilic components as pigments or proteins predestines them to be very attractive cleaning agents [46]. A further industrial application which utilizes the advantage of the ultra low interfacial tension is enhanced oil recovery, where the amount of crude oil that is extracted from an oil field can be increased [47-50]. However, not only the ultra low interfacial tension of microemulsions is of great interest but also their tunable nanostructure. Hence, among others, *Eastoe et al.* investigated microemulsions as template material for the chemical synthesis of nanoparticles [51-56] as well as for tunable nanomagnets [57]. Another possible template strategy is the use of microemulsions or emulsions for polymerization

processes [58-63]. Furthermore, the composition and temperature sensitive nanostructure represent a promising carrier system for cosmetic active ingredients due to their numerous advantages over already existing conventional formulations [64]. For example, they are the basic material for several sunscreens [65]. Pharmaceutical research deals with the ability of microemulsions as potential and specific drug deliverer [66-71]. Combining solubilization capacity and tunable nanostructure and taking thermodynamic stability into account, in the fuel and combustion research microemulsions are suitable media to reduce exhaust emissions and guide us to a cleaner and greener future [72-75]. Furthermore, microemulsions are used in other fields of green applications as agriculture [76, 77] and food [78-81] but in the nearest past organic synthesis in microreactors became one of the rising stars among microemulsion applications.

In organic [46, 82, 83] and bioorganic [84] reactions as well as in enzymatic catalysis [85-90] they gained attention as reaction media, because it was found that micellar and microemulsion solutions have a profound effect on reaction rates [91]. Among organic reactions photochemical induced transformations represent an especially interesting discipline, because the overlap of colloid chemistry and photochemistry in surfactant systems is highly valuable [92]. Well-known reactions ranging from photoinduced conformational changes as cis-trans isomerizations [93-96] to the synthesis of photocleavable microcapsules [97], photooxygenation reactions [98], photolysis [99] and polymerizations [100] are performed in microemulsions. However, most of the reactions need photosensitive surfactants or the reaction itself is destructive but until now, nobody synthesized amphiphiles in a microemulsion from simple photosensitive starting material. Thus, the idea was born to make use of the beneficial characteristics of microemulsions to synthesize a surfactant with very simple reactants in a microemulsion via UV irradiation. To demonstrate this the well-known photochemical induced [2+2] cycloaddition, the *Paternò-Büchi* reaction, was to be studied in a microemulsion as model reaction.



One product of the *Paternò-Büchi* reaction of 1-octene and the photosensitive pyruvic acid is 3-hexyl-2-methyloxetane-2-carboxylic acid and is hence the fusion of a hydrophobic

hydrocarbon tail and a hydrophilic head. Thus, it can be regarded as a surfactant. As such it is expected to influence the phase behavior of the microemulsion system significantly when it is build in situ in a microemulsion. In short, for the first time a microemulsion that generates its own cosurfactant would be created. Simultaneously, this constructive model reaction is a first step towards the realization of an universal broadband solvent. In contrast to that, currently more than 60 different solvents are used in the chemical industry during syntheses. However, due to growing environmental awareness and the ecological impact of these solvents the industry needs to change and procure such universal solvents. Newsworthy studies predict that in 20 years only 10 wide-ranging broadband solvents will be applied [101] and microemulsions are promising alternatives due to the unique possibilities they offer.

Hence, the usage of common microemulsions as an universal solvent can be seen as a significant step towards a greener chemistry. To go even one step further, the microemulsion can be formulated not only with commonly used petro based surfactants which lack biodegradability but the surfactant can be chosen both non-toxic and produced from renewable resources.

This approach gains even more significance considering the annual global production of surfactants being about 18 million tons. At first glance thankfully, a quarter of these is already produced from renewable oil originating from bamboo, palm kernel and coconut. Though this seems sustainable, often environmental issues like monoculture and rainforest-deforestation go with the production cycle ruining the balance. Nevertheless, there exists the so-called group of biosurfactants which is produced by microorganisms both from renewable and sustainable resources such as organic agricultural wastes like straw, shells and husks.

To reach this aim, the *Fraunhofer Institute for Interfacial Engineering and Biotechnology* in Stuttgart works intensively to promote the replacement of petro based surfactants by biosurfactants like the glycolipids mannosylerythritollipids (MELs) and cellobioselipids (CLs). These surfactants in particular are non-toxic, sustainable, biocompatible, antimicrobial and completely biodegradable. Thus, the institute focuses on optimizing the biotechnological production of MELs and CLs using different smut fungi (*Ustilago maydis* and *Pseudozyma*). Until now, different MELs have been produced with a yield up to 100 g/l and CL with a yield of up to 30g/l [102]. For the optimization of the biosurfactants and the fermentation process they pursue different approaches: Enzymatic modification of the produced biosurfactants,

optimization of the bioprocessing and scale up as well as genetic modification of specific metabolic pathways of the applied microorganisms, so that they can be used in cosmetics, detergents or other fields of interest. However, till now there exists no comprehensive knowledge on their efficiency as surfactants, thus, their characteristic properties need to be investigated and understood.

1.1 Task description

As described above microemulsions are suitable reaction media for organic and inorganic reactions. For this work the possibility of performing a *Paternò-Büchi* reaction in a microemulsion was selected. To formulate a suitable microemulsion model system the effects of the selected reactants, pyruvic acid and 1-octene, individually on the characteristic phase behavior of the microemulsion were to be determined first. Then combining these findings all reaction partners were to be added to a single microemulsion. Subsequent irradiation with UV light was to be varied with regard to exposure time and the influence of the potentially forming product on the phase behavior and the reaction progress traced. Furthermore, not only the irradiation intensity was a potential tuning parameter for the reaction but also the microstructure itself. Thus, the reaction was to be performed at different surfactant mass fractions and microstructures. The nature of the microstructure before and after the photochemical reaction was to be determined to see the influence of the newly formed amphiphilic product. To this end the structure was to be determined by small angle neutron scattering (SANS) and freeze fracture electron microscopy (FFEM). To complete the picture, parameters like pH and conductivity were to be monitored during the exposure.

It is well-known that sonication improves the yield and reaction time of many reactions. Thus, the influence of simultaneous UV irradiation and ultrasound sonication was to be tested and analyzed in the same fashion as stated above to resolve any effect on the microemulsion based reaction.

As further new route towards green organic chemistry, the characterization of newly synthesized biosurfactants (mannosylerythritol-lipids and cellobioselipids) of the *Fraunhofer Institute for Interfacial Engineering and Biotechnology* were to be performed. These surfactants are a new class of promising glycolipid surfactants which can be used for a wide range of applications if their characteristic properties are enlightened in a complete way in comparison to common surfactants like the well-known and structurally similar bio-based alkyl polyglycosides (APGs) which are composed of a long hydrocarbon chain and a sugar-



head ($C_m G_n$). Hence, their effect on the phase behavior of a well-known microemulsion model system with regard to efficiency and hydrophilicity was to be determined. These measurements are then to be supplemented with the rheological properties (viscosity) and the surface-active properties (critical micelle concentration (cmc)).

Finally, bio-based microemulsions were to be formulated based on the knowledge of the previous investigations. These microemulsions were to be tested as green model reaction media.



2 FUNDAMENTALS

The present chapter provides a clear introduction into the principals and fundamental background which are needed to understand the techniques applied in this work. The chapter is organized as follows: In the first subchapter (2.1) microemulsions and their properties are explained. The following subchapter (2.2) deals with the large number of different classes of surfactants and their nature and origin. In the third subchapter (2.3) the theoretical basics which are necessary to understand the background of the experimental methods are given. Finally, the fourth subchapter (2.4) explains the photochemical fundamentals which are important to understand the fundamental chemistry behind the investigations of this work.

2.1 Microemulsions

Microemulsions are thermodynamically stable, macroscopically isotropic, nanostructured and self-assembly homogenous mixtures of at least three components [16, 17, 103]. Two of these three components are mutually immiscible: The polar component (A) and the non-polar component (B). The third component is an amphiphilic component (C) (*i.e.* a surfactant) and is miscible with the two other ones and thereby enables their mixing. In a ternary mixture of A, B and C the amphiphile will preferentially be adsorbed at the interface between the polar and the non-polar component. From this it results that the interfacial tension between A and B is effectively reduced by an amphiphilic film and it allows the miscibility of the two immiscible components. These ternary mixtures show an amazingly rich phase behavior in dependence of temperature and composition: One-phase microemulsion states, and two- and three-phase states are possible. This behavior is strongly related to the respective binary systems. Furthermore, a diversity of microstructures in the range between 10 to 1000 Å is found in microemulsions. It is the aim of this chapter to briefly review these relations and to allow the reader to understand the properties of the microemulsions studied in this work.

2.1.1 Phase behavior

It is almost impossible to understand microemulsions without taking the knowledge of their phase behavior into account. Therefore, it is crucial to follow up with it. It is proven that all ternary mixtures of the type water (A) – oil (B) – non-ionic surfactant (C) follow the same general pattern [9, 28, 104]. This is influenced by the interplay of the three binary systems

water – oil (A – B), oil – non-ionic surfactant (B – C) and water – non-ionic surfactant (A – C). Thus, in the following the phase behavior of binary as well as ternary mixtures is introduced. Since the influence of pressure p is weak [105] the ternary systems in this work are measured at constant pressure close to ambient pressure of 1 bar. Thus, the behavior of non-ionic microemulsions is described as function of temperature and concentration.

2.1.1.1 Binary side systems

The three binary side systems show very different phase behavior and are schematically shown in figure 2.1-1. The simplest diagram is the diagram of the binary system water – oil (A – B). Both components are immiscible and the miscibility gap extends far above the boiling point. Within the feasible temperature range (0 - 100 °C) no upper critical point of the miscibility gap is found. The binary oil – surfactant (B – C) system features a lower miscibility gap with an upper critical point cp_α , at a critical temperature T_α , typically located below 0 °C. The binary system water – non-ionic surfactant (A – C) is the most complex one as it shows two miscibility gaps. At lower temperatures a lower miscibility gap with an upper critical point, usually far below the melting point of the mixture is found. For this reason this lower miscibility gap plays no role in determining the phase behavior at experimentally accessible conditions. At higher temperatures a narrow miscibility gap with a lower critical point cp_β at the critical temperature T_β exists. The location and dimension of the critical points cp_α and cp_β are related to the behavior of the ternary system and depend on the nature of the surfactant. With increasing hydrophilicity of the surfactant the critical temperature of the miscibility gap decreases.

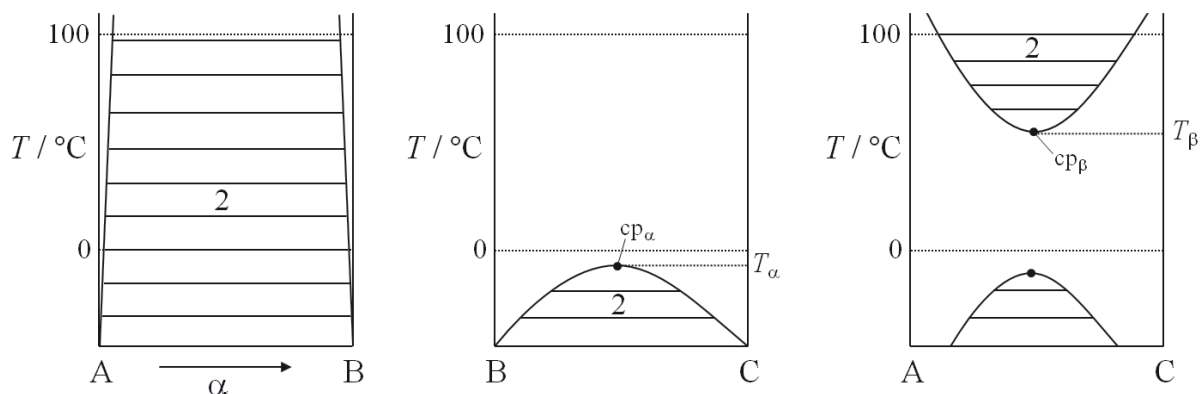


Figure 2.1-1: Schematic phase diagrams of the different binary systems. Left: Water (A) and oil (B) showing a large miscibility gap. Middle: Oil (B) and non-ionic surfactant (C) showing a lower miscibility gap with an upper critical point cp_α . Right: Water (A) and non-ionic surfactant (C) showing an upper miscibility gap with an upper critical point cp_β , as well as a lower miscibility gap with an upper critical point which is mostly below 0 °C. The dotted lines illustrate the measuring limits (based on [16]).

The phase behavior of a ternary system A – B – C relates to an interplay of the upper miscibility gap of the A – C and the lower miscibility gap of the B – C mixture. Hence, at high temperatures the surfactant will rather be dissolved in the oil whereas at low temperatures it will preferably dissolve in water. The phase behavior of a ternary system can be represented in a phase prism with the *Gibbs* phase triangle A – B – C as the base and the temperature axis as the ordinate [16, 22]. This phase prism is explained in the following subchapter.

2.1.1.2 Ternary systems

Figure 2.1-2 illustrates a schematic drawing of the phase prism for the ternary system containing water (A), an oil (B) and a non-ionic surfactant (C). It is the result of the up-folded three binary side systems using the *Gibbs* phase triangle as base. The phase behavior is strongly related to the position of the critical parameters cp_α and cp_β . Thus, the temperature dependent solubility of the surfactant in oil as well as in water strongly controls the phase sequence of the ternary system.

With increasing temperature the solubility of the surfactant (C) in water decreases, whereas at the same time its solubility in oil (B) increases. Therefore, at low temperatures and approximately equal amounts of water and oil it will separate into a water-rich (o/w) microemulsion phase coexisting with an oil excess phase. This state is called $\underline{2}$. Increasing the temperature to $T = T_l$ ($l = \text{lower}$) the former microemulsion phase splits into two phases: A water excess phase (a) and a surfactant-rich middle phase (c). This is caused by the decreasing solubility of the surfactant in water at higher temperatures. Thus, at T_l a three-phase body appears with a surfactant-rich middle phase (c) coexisting with a water (a) and an oil (b) excess phase. With further increase of the temperature the middle phase swells until its maximum at T_m ($T_m = T_l + T_u/2$) is reached. At even higher temperature T_u the three-phase body disappears and an oil-rich (w/o) microemulsion phase (b) in coexistence with a water excess phase (a) is found. This state is denoted as $\overline{2}$. The temperature-dependent progression of the phase behavior from (o/w) microemulsions to (w/o) microemulsions, namely the sequence $\underline{2} \rightarrow 3 \rightarrow \overline{2}$, is called phase inversion.

Due to the complexity of the *Gibbs* phase prism it has been proven useful to perform characteristic sections through the phase prism. Many of the properties can conveniently be accessed by performing isothermal or isoplethal sections through the phase prism. One established section through the phase prism is the $T(\gamma)$ -section which is explained in more detail in the next subchapter.

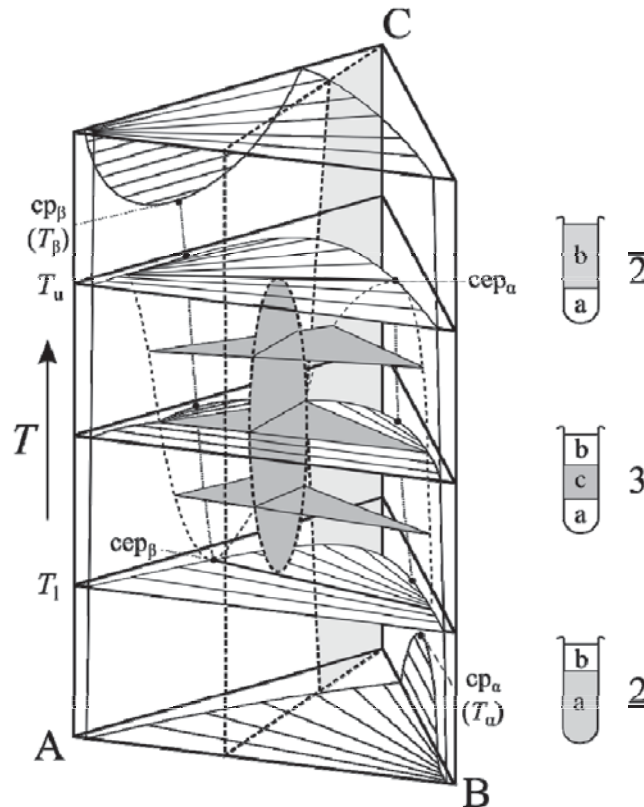


Figure 2.1-2: Schematic drawing of a *Gibbs* phase prism illustrating the temperature-dependent phase behavior of ternary systems of the type water (A), oil (B) and non-ionic surfactant (C). The test tubes at the right side show the two- and three-phase states observed at different temperatures [103].

2.1.1.3 $T(\gamma)$ -section

As already explained above, the determination of the entire phase diagram as shown in figure 2.1-2 is very complex and time-consuming. Therefore, the so-called $T(\gamma)$ -section can be performed [16, 22, 24]. This method significantly facilitates the investigation of the phase behavior. A schematic view of the section is shown in figure 2.1-3.

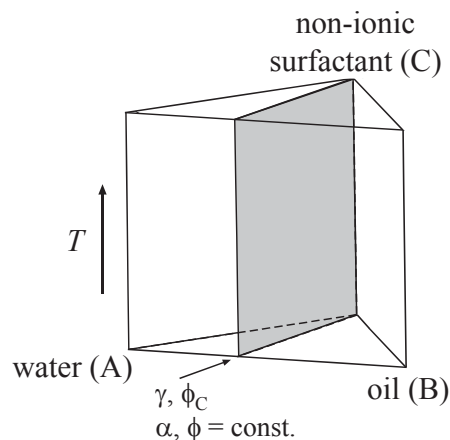


Figure 2.1-3: Schematic phase prism of a ternary microemulsion. The shaded area indicates the isoplethal method ($T(\gamma)$ -section) a common method to investigate the phase behavior of ternary systems at constant mass fraction α [104].