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**A concise review on nano-emulsion formation by the
Phase Inversion Composition (PIC) method**

Short running title: A review on nano-emulsification by PIC method

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ABSTRACT

Nano-emulsion formation by the phase inversion composition (PIC) method is reviewed. The relationship between phase behavior and nano-emulsion formation is revised with emphasis on the key role of phase transitions involving changes in the sign of the curvature of the surfactant layer (inversion) via zero-average-curvature structures such as bicontinuous microemulsions or lamellar liquid crystalline phases. The different low-energy methods that can be involved in a nano-emulsification process at constant temperature are also discussed.

KEY WORDS: Nano-emulsions, Phase Inversion, PIC method, Phase behavior

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INTRODUCTION

Nano-emulsions are non-equilibrium nano-droplet systems (Rodriguez-Abreu and Vila, 2014) with multiple applications. Low-energy nano-emulsification methods have brought increasing attention in the last years as they are advantageous because of their high efficiency, simplicity and yield (McClements and Jafari, 2018; Roger, 2016; Solans and Solè, 2012). In those methods, the droplet size is mainly determined by the physicochemical properties of the emulsion system (i.e. it is independent on the external energy input) (McClements and Jafari, 2018; Roger, 2016; Solans et al., 2012; Tadros et al., 2004). As a consequence, nano-emulsions can be generated using simple equipment (e.g. standard stirrers at rather low speed), and formulated with thermo- and mechano-sensitive molecules.

When low energy emulsification is triggered by inversion of the surfactant spontaneous curvature, the process is known as “phase inversion” (Lin et al., 1975; Shinoda and Saito, 1969). Inversion of the surfactant spontaneous curvature from negative to positive or vice versa can be induced by a change in temperature, as in the so-called phase inversion temperature (PIT) method (Shinoda and Saito, 1969), or by changing the composition at constant temperature during emulsification, as in the so-called phase inversion composition (PIC) or emulsion inversion point (EIP) method (Lin et al., 1975).

In contrast to the phase inversion temperature (PIT) method which is only possible with surfactants systems that are thermoresponsive (e.g. alkyl ethoxylates), the PIC method can be in principle used with all type of surfactants and with thermolabile molecules. The emulsification procedure by the PIC method is the addition, at constant temperature, of one of the components (water for oil-in-water emulsions) to the mixture of the rest of components (namely, oil and surfactant for oil-in-water

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emulsions). This procedure is similar to that of self-emulsification; however, the mechanisms are different, since in self-emulsification there is no change in the surfactant spontaneous curvature. Moreover, self-emulsification, especially if it is performed without surfactant (as in the “Ouzo” effect), leads to nano-emulsions with very low oil volume fraction which is a drawback for certain applications (Bouchemal et al., 2004).

Publications on basic aspects of nano-emulsion formation by inversion methods are scarce in the recent years. Most of the research effort on nano-emulsions reflected in the literature lately deals with applications in drug and gene delivery (Bonferoni et al., 2019; Chircov and Grumezescu, 2019; Leitner et al., 2020; Sánchez-López et al., 2019), foods (Espitia et al., 2019; Komaiko and McClements, 2016), cosmetics (Yukuyama, 2016), pesticides (Yan et al., 2019), polymerization (Wang et al., 2018) and nanoparticle synthesis (Mendelson-Masey et al., 2017; Meruga et al., 2018).

The focus of this review is on oil-in-water (O/W) nano-emulsion formation by the phase inversion composition (PIC) method. The relationship between phase behavior and nano-emulsion formation is revised with emphasis on the key role of phase transitions in which the interfacial curvature is inverted and self-organized bicontinuous microemulsions or lamellar liquid crystalline phases are crossed in the emulsification path. The different low-energy methods that can be involved in a nano-emulsification process at constant temperature are also discussed.

Relationship between phase behavior and O/W nano-emulsion formation by the PIC method

The protocol to produce O/W nano-emulsions using the PIC method typically involves adding water, generally slowly or stepwise, over a mixture of the other components (namely, oil and surfactant) at constant temperature. Although, as mentioned above, the PIC method is not restricted to poly(oxyethylene)-type nonionic surfactants but can be extended to e.g. ionic surfactants (Kini et al., 2012; Solè et al., 2012), most of the research dealing with basic aspects of nano-emulsions has been performed with this type of surfactants. Therefore, the emulsion systems considered in this section are mainly composed of water, poly(oxyethylene)-type nonionic surfactant(s) and oil. When poly(oxyethylene)-type nonionic surfactant(s) are used in the PIC methods, a water-in-oil (W/O) microemulsion is generally formed when water is first added to the oil-surfactant mixture. With the increase of water content, poly(oxyethylene) chains of the surfactant become increasingly hydrated, and the interfacial spontaneous curvature goes from negative to zero in average forming bicontinuous microemulsion or lamellar liquid crystalline structures. This transition would also imply a decrease in the effective surfactant packing parameter at the interfacial layer, from values higher than one in reverse structures (W/O microemulsions) to values near one for planar structures, e.g. lamellar phases (Israelachvili et al., 1977). With further increase of water content, these structures are no longer stable and separate into metastable nano-emulsion O/W droplets. The changes in curvature discussed here can also be rationalized using models such as the NAC-HLD equation of state developed by Acosta (Acosta et al., 2003; Acosta, 2008). This model relies on the hydrophilic–lipophilic difference (HLD) and the PIT concepts to estimate the net–average

curvature (NAC) and then predict the phase behavior from formulation parameters. However, a further discussion on the application of models to the PIC method is out of the scope of this review.

Surfactant mixtures are relevant since they are present in most commercial products. There are various articles in the literature on the phase behavior and nano-emulsion formation in mixtures of non-ionic surfactants (Bonferoni et al., 2019; Fernandez et al., 2004; Gupta et al., 2017; Hessien et al., 2011; Koroleva et al., 2018). Studying homogeneous, high purity surfactants allows a more general and molecular level insight. In an earlier report (Forgiarini et al., 2001a), mixtures of homogeneous tetraethylene glycol monohexadecyl ether ($C_{16}E_4$) and hexaethylene glycol monododecyl ether ($C_{12}E_6$) were used and the relationship between phase behavior and nano-emulsion formation by the PIC in the system water/($C_{12}E_6 + C_{16}E_4$)/decane was addressed for the first time. Nano-emulsion formation in this system is further illustrated in Fig. 1 and 2.

Fig. 1 shows the pseudo ternary phase diagrams of the system with surfactant mixing ratios ($W1 = C_{16}E_4 / (C_{12}E_6 + C_{16}E_4)$) equal to 0.2 and 0.4 for surfactant/oil (S/O) weight ratios lower than 50/50, at 25°C. Fig. 1a corresponds to the system with $W1 = 0.2$. Two single phase regions are observed: an Om (W/O microemulsion), along the oil-surfactant axis, and a lamellar liquid crystalline phase ($L\alpha$). The $L\alpha$ phase is formed for water concentrations between 25wt% and 30wt% up to a S/O of 25/75. The isotropic liquid region along the oil-surfactant axis, Om, is formed at water concentrations up to 5wt%. The diagram also shows several multiphase regions: along to the water-decane axis there is a biphasic region in which an aqueous bluish phase (W_m) and excess oil (O) coexist ($W_m + O$), and in between the aqueous vertex and the lamellar liquid crystalline phase there is a ($L\alpha + Om$) region. Nano-

emulsions are formed in this system at a (W/O) ratio equal to 90/10 by dilution of oil-surfactant mixtures along the paths indicated by dashed lines, resulting in phase inversion transitions.

The phase diagram with $W1=0.4$ is shown in Fig. 1b. In this system, three single phases are formed, $L\alpha$, O_m and bicontinuous micro-emulsion (D) phase. The $L\alpha$ phase is formed at water concentrations between 25wt% and 44wt%, solubilizing a maximum of 56% decane. The O_m phase solubilizes about 10% water at S/O ratios higher than 20/80. The D phase is formed at S/O ratios higher than 35/65 and water concentrations between 56wt% and ca. 90wt%. Additionally, there are several multiphase regions: W_m+O , $L\alpha+O_m$ regions, and at compositions between $L\alpha$ and D regions, a $(D+L\alpha)$ zone. Again, nano-emulsions can be prepared in this system at a (W/O) ratio equal to 90/10 by dilution of oil-surfactant mixtures along the paths indicated by dashed lines, that pass through phase inversion transitions.

Fig. 2 shows droplet size of emulsions with a water-in-oil (W/O) ratio equal to 90/10, prepared by stepwise addition of water to mixtures of surfactant and oil at constant temperature, 25°C, as a function of the S/O ratio. The droplet sizes were determined by Dynamic Light Scattering (DLS) using the method of cumulants. In the system with $W1=0.2$ (Fig. 2a), the droplet size decreases monotonically from 180 nm to 125 nm with increase in S/O weight ratio. At S/O ratios higher than 25/75, there is a phase transition during the emulsification process from O_m to W_m+O phases via a single $L\alpha$ phase. At lower S/O ratios, although there is no phase transition through a single $L\alpha$ phase, an $L\alpha+O_m$ is crossed during emulsification from O_m to W_m+O region.

For the system with $W1=0.4$, nano-emulsions could be formed for S/O ratios lower than 25/75 because the D phase appears at higher O/S values. The droplet size of

the resulting nano-emulsions decreases from 175 nm to 140 nm as S/O increases (Fig. 2b).

Fig. 2a and 2b show that as W1 increases (i.e. decrease of the hydrophilic surfactant content in the mixture), droplet size decreases. The explanation could lie in the fact that around the transition composition, the surfactant-water and surfactant-oil interactions are of similar magnitude as at the HLB-temperature (Shinoda et al., 1969, 1983); this temperature decreases with the increase in lipophilic surfactant content. When the HLB-temperature is very close to 25°C, the temperature at which the emulsions are prepared, minimum droplet sizes are achieved.

In the examples given for the water/(C₁₆E₄+C₁₂E₆)/decane system, it could be argued that the droplets get smaller as S/O ratio increases because the surfactant concentration also increases at the same time. However, it has been shown that surfactant concentration is not always the key factor in determining droplet size (Forgiarini et al., 2001b; Morales et al., 2003). As an example, Fig. 3 shows the droplet size as a function of total surfactant concentration (S_T) for the water/(C₁₆E₄+C₁₂E₆)/decane system with a surfactant mixing ratio W1=0.5 and a W/O ratio equal to 80/20. Nano-emulsions are formed in this system for surfactant concentrations lower than 4 wt% and higher than 6 wt%, because the D phase appears between these surfactant concentrations in this system. The droplet size decreases from 180 nm to 80 nm as surfactant concentration increases up to 4 wt%. However, at surfactant concentrations higher than 6 wt%, the droplet size increases from 100 nm to 125 nm as surfactant concentration increases. The different behavior below and above the single microemulsion D phase region can be attributed to the different phase transitions during the emulsification process.

Numerous studies have related the formation of nano-emulsions by the PIC method with phase transitions through $L\alpha$ and/or D phases (Fernandez et al., 2004; Forgiarini et al., 2001b; Heunemann et al., 2011; Maestro et al., 2008; Roger et al., 2011; Roger, 2016; Sadurní et al., 2005; Solans and Solè, 2012; Sonneviller-Aubrun et al., 2009) which coincide with those described for the PIT method (Izquierdo et al., 2004; Morales et al., 2003; Roger et al., 2010; Roger, 2016; Solans and Solè, 2012). It could be claimed that the low interfacial tensions at the transition composition are responsible for the formation of nanosized droplets. However, Forgiarini et al. (Forgiarini et al., 2001b) evidenced that in addition to interfacial tension other factors are determinant for the formation of nano-emulsions. Fig. 4 shows droplet radii of emulsions of the water/Brij 30/decane system as a function of the oil weight fraction in water, R , at a constant surfactant concentration (5 wt %) and temperature (25 °C) using three procedures: A (stepwise addition of oil to a water-surfactant mixture), B (stepwise addition of water to an oil-surfactant mixture, PIC method), and C (direct mixing of all components at the final composition). Brij 30 has a dodecyl chain with an average of 4 ethylene oxide units ($C_{12}E_4$, HLB = 9.7). On one hand, emulsification by methods A and C resulted in emulsions with sizes over 1 μm and practically independent on the oil weight fraction in water, R . On the other hand, the size of the emulsion droplets obtained by the PIC (Method B) changes significantly with R ; nano-emulsions with droplet size below 100 nm were obtained using $R = 0.2$. A correlation is observed between the values of interfacial tension between water and oil phases (also shown in Fig. 4) and droplet size of emulsions produced by the PIC method as a function of R . The lowest values of interfacial tension coincide with the lowest values of droplet size. It should be noted that these are equilibrium interfacial tensions, consequently, to a given value of R

corresponds only one value of interfacial tension. However, different values of droplet size (depending on the method of preparation) are obtained for a given R value. These results allowed concluding that low values of equilibrium interfacial tensions are required but are not sufficient to obtain nano-emulsions. Moreover, it was proposed (Forgiarini et al., 2001b) that the kinetics of emulsification may play also an important role for nano-emulsion formation. Considering the phase changes during emulsification (Fig. 5) it was clear that the change in the sign of the interfacial curvature from reverse to direct assemblies via zero-average-curvature structures (e.g. lamellar liquid crystalline and/or bicontinuous microemulsion) during emulsification is fundamental to obtain nano-emulsions. Fernandez et al. (Fernandez et al., 2004) found the same phase transitions and suggested that nano-emulsion droplet size was related to the bilayer thickness of the lamellar structure present at the inversion point. Nano-emulsions with very small droplet size (e.g. 20 nm) and high kinetic stability were obtained by Sadurní et al. (Sadurní et al., 2005) in a water/nonionic surfactant/oil system appropriate for pharmaceutical applications in which inversion from W/O microemulsions to O/W nano-emulsions proceeded via a lamellar liquid crystalline phase. Sonnevile-Aubrun et al. (Sonneville-Aubrun et al., 2009) detected by SANS a lamellar liquid crystalline phase (with zero curvature) in the very early stages of water incorporation. In the studied system, low-polydispersity nano-emulsions with a mean diameter of 100 nm were reported (Sonneville-Aubrun et al., 2009). By analysing nano-emulsification pathways, Roger et al. (Roger et al., 2016; Roger et al., 2011) concluded that during emulsification by the PIC, a reverse micellar phase swells with water and then is converted into a bicontinuous sponge phase. If more water is added, there is nucleation of oil droplets in this bicontinuous phase. Although these phase transitions coincide with

those described for the PIT method, these authors pointed out that the two methods undergo different mechanisms resulting in large differences concerning droplet size, polydispersity and as a consequence different efficiency of the emulsification method. Accordingly, the PIT method appears to be more efficient than the PIC method for a given composition, namely, by the PIT method nano-emulsions with smaller droplet sizes and narrower size distributions are obtained (Roger et al., 2010; Roger et al., 2016) while the PIC method leads to bimodal size distributions (Roger et al., 2011; Roger et al., 2016). Heunemann et al. (Heunemann et al., 2011) characterized by SANS and Cryo-TEM O/W nano-emulsions with different concentrations of oil. At a given water concentration, there is the formation of bicontinuous phase. The nano-emulsions showed two size populations, i.e. the distribution is bimodal. The ratio between populations changes with water content. It was also noted that the nano-emulsions possessed bimodal size distributions and that the relative proportion of each population depends on the amount of added water.

There is at present general agreement that the phase transitions during nano-emulsion formation by the PIC method (which are analogous to those reported by the PIT method) involve an inversion from reverse type water-in-oil (W/O) to oil-in-water (O/W) systems via zero-curvature structures such as bicontinuous microemulsions or lamellar liquid crystalline phases. However, no agreement has been reached yet on whether or not the mechanisms by which inversion is produced are the same in both methods.

An important aspect to fully understand emulsification by phase inversion is the kinetics of the process (Hoffmann et al., 2016). This aspect which has not received enough attention could shed light on why nano-emulsions with broad size

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3 distribution are obtained in certain systems especially by the PIC method. When
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5 transient viscous phases are formed during the emulsification process, slower
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7 addition and enough shearing of the system may be needed for homogenization.
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9 Solè et al. (Solè et al., 2006) evidenced that depending on the agitation speed and
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11 the rate of water addition, the size distribution of the resulting nano-emulsions was
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13 monomodal or bimodal when a highly viscous cubic liquid crystal was formed during
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15 emulsification. If homogenization of the sample is not achieved at the phase
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17 inversion composition, not all the oil is incorporated in the transient self-assembled
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19 structure. Consequently, the fraction of oil that remains out of these structures is
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21 emulsified by mechanical energy giving rise to big and polydisperse droplets.
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23 Further evidence that the kinetics of the emulsification process is decisive on
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25 emulsion droplet size has been reported by Kaizu and Alexandridis (Kaizu &
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27 Alexandridis, 2016) using water/Pluronic-type surfactants/xylene systems which
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29 display a rich-phase behaviour. Finer and more homogeneous emulsions were
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31 obtained when lamellar structures were involved in the emulsification process.
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33 However, when other type of structures (e.g. cubic and hexagonal liquid crystalline
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35 phases) were involved in the emulsification process, parts of these structures
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37 remained as “flocs” in the final emulsions due to the higher viscosity of these phases
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39 as compared to the lamellar liquid crystalline phase.
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50 Nano-emulsification by phase inversion and/or self-emulsification

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52 The analysis of the phase behavior of the emulsion system has also allowed to
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54 understand the outcome of different emulsification procedures. Wang et al. (Wang
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56 et al., 2007; Wang et al., 2008; Wang et al., 2009) carried out what they referred to
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58 as a “two-step emulsification”. In the first step, samples were prepared in the
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bicontinuous microemulsion or lamellar liquid crystalline region. In the second step, the rest of the water was incorporated. The resulting nano-emulsions showed the same size as those obtained by the conventional PIC procedure (stepwise addition of water to surfactant-oil mixtures) (Wang et al., 2007). In the two-step process, there is a change in the curvature of the surfactant film from almost zero to positive. This means that the phase inversion from W/O to O/W structures is not strictly necessary to achieve efficient emulsification. However, to start emulsification in a single bicontinuous microemulsion or lamellar liquid crystalline phase (or any other single phase), a detailed knowledge on the phase behavior of the system is required. Indeed, Wang et al. showed (Wang et al., 2007) that in the two-step emulsification process if the initial sample did not fall in a single-phase region but in a multiphase region, further water addition in the second step resulted in opaque, larger-size emulsions instead of nano-emulsions.

Depending on the emulsion system, nano-emulsification can be achieved by a low-energy method or a combination of them (phase inversion and self-emulsification, for example). Solè et al. (Solè et al., 2012) reported the preparation of nano-emulsions using different procedures (addition of water to a microemulsion or addition of microemulsion to water, stepwise or at once) and starting from different microemulsion phases (Fig. 6). They found that by starting emulsification from W_m (O/W) microemulsions (W_m2 , W_m3 , W_m4 and W_m5), nano-emulsions with droplet sizes within the range 20–40 nm and monomodal size distribution were obtained independently of the sample and procedure used. Consequently, formation of O/W nano-emulsions from direct-type O/W microemulsion does not imply any inversion of the spontaneous curvature of the surfactant film since the trigger for emulsification is molecular diffusion (self-emulsification). However, starting emulsification from O_m

(W/O) microemulsions, nano-emulsions with monomodal size distributions and sizes coincident with those produced starting from the homologous W_m microemulsions were only obtained when the procedure used was stepwise addition of water to the microemulsion and the emulsification path crossed the W_m region (samples Om2-Om5 in Fig. 6). Then, it was concluded that the mechanism for nano-emulsification from Om region consisted in two processes: an inversion process (from Om to W_m) and a self-emulsification process (from W_m to the final O/W nano-emulsion). However, using the other emulsification procedures, coarse emulsions were obtained from all samples of the Om region. These results clearly indicated that reaching a transient equilibrium in the single-phase region W_m was the key factor to obtain nano-emulsion with minimum droplet size and narrow size distribution. Therefore, the characteristics of the W_m microemulsions are those controlling the properties of the corresponding nano-emulsions.

More recently, Homs (Homs, 2016) confirmed that the characteristics of the surfactant self-assembly of the last single phase formed during emulsification determines the properties of the resulting nano-emulsions. In these investigations nano-emulsion formation was studied in water/mixed nonionic surfactant/oil systems as a function of oil/surfactant (O/S) ratio. Phase behavior studies allowed to define the different single-phase regions (W/O microemulsion, lamellar liquid crystalline phase, bicontinuous and O/W microemulsions) that could be formed during emulsification. Depending on the O/S ratio, it was shown that nano-emulsification proceeded by phase inversion, phase inversion followed by self-emulsification or by only self-emulsification.

Conclusions

Herein, we have used several representative examples to illustrate the formation of oil-in water (O/W) nano-emulsions by the phase inversion composition (PIC). When water is added stepwise over a mixture of the other components (oil and surfactant) at constant temperature, there is an inversion from reverse type water-in-oil (W/O) to oil-in water (O/W) systems via zero-average-curvature structures such as bicontinuous microemulsions and/or lamellar liquid crystalline phases. Although low values of equilibrium interfacial tensions are required for nano-emulsion formation it has been shown that they are not sufficient. The phase transitions through lamellar liquid crystalline phases and/or bicontinuous microemulsion phases play a key role not only in the formation of nanosized droplets but also in determining the size of the resulting nano-emulsions. There is at present general agreement that the phase transitions occurring during PIC emulsification are analogue to those of the PIT method. However, there is no agreement on whether the mechanisms of emulsification are the same. The kinetics of the emulsification process, especially when viscous transient phases are formed, is an aspect that has not been investigated sufficiently yet and could help understanding why bimodal or broad size distributions are obtained in certain systems. It has been shown that depending on the emulsion system, nano-emulsification can be achieved by one or a combination of low-energy methods (e.g. by phase inversion, phase inversion followed by self-emulsification or by only self-emulsification). Further research on nano-emulsions should focus on their formation using naturally occurring surfactants and essential oils. Applications in food, cosmetics and pharmaceutical fields, among others, would benefit from such developments using the PIC method as it allows preparation of

nano-emulsions in mild conditions (suitable for mechano- and thermosensitive molecules) and using simple equipment.

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Figure legends

Fig.1 Phase behavior of water/(C₁₂E₆+C₁₆E₄)/decane system at 25°C. The surfactant mixing ratio ($W_1 = C_{16}E_4 / (C_{12}E_6 + C_{16}E_4)$) is (a) 0.2 (HLB_{mix} = 11.1) and (b) 0.4 (HLB_{mix} = 10.4). W: aqueous liquid phase, D: isotropic bluish liquid phase (microemulsion), O: oil liquid phase; L α : a liquid-crystal-present region; Wm: liquid phase (O/W microemulsion); Om: isotropic liquid phase (W/O microemulsion). Dashed lines indicate the experimental emulsification paths for the preparation of nano-emulsions for a final W/O weight ratio of 90/10. Single-phase regions are marked in light grey whereas the region that was not explored is marked in dark grey (Feng and Solans, unpublished results).

Fig. 2 Droplet size of nano-emulsions prepared by PIC method as a function of S/O at 25°C in water/(C₁₂E₆+C₁₆E₄)/decane systems. The water/decane ratio is 90/10 (w/w). The surfactant mixing ratio (W_1) is (a) 0.2 and (b) 0.4 (Feng and Solans, unpublished results). The thick arrow near the water apex in the phase diagrams of Fig.1 indicates the composition region (thick grey line) corresponding to the samples in Fig.2. The boundary between nano-emulsions and microemulsions was distinguished by preparing the samples by two methods: PIT and simple mixing of all the components at once. Homogenous, isotropic and translucent samples which characteristics did not change with the preparation method and time were considered microemulsions.

Fig. 3 Droplet size of nano-emulsions as a function of the total surfactant concentration (S_T) by PIC method at 25°C in water/(C₁₂E₆+C₁₆E₄)/decane systems. The surfactant mixing ratio (W_1) is 0.5 and the water/decane ratio is 80/20 (w/w) ME: microemulsion (Feng and Solans, unpublished results). The boundary between

nano-emulsions and microemulsions was distinguished as indicated in the caption of Fig.2

Fig. 4 The vertical axis on the left shows the droplet size for emulsions of the water/Brij 30/decane system versus the oil weight fraction in water, R , obtained by various emulsification methods: A (oil is added dropwise to a water+surfactant mixture), B (water is added dropwise to an oil+surfactant mixture, i.e. PIC method), and C (all components are mixed for the final composition). The vertical axis on the right shows the equilibrium interfacial tension as a function of R . The surfactant concentration (5 wt %) and temperature (25 °C) are kept constant. (Adapted with permission from Forgiarini et al., 2001b. Copyright 2001 American Chemical Society.).

Fig. 5 Phase behavior of water/Brij 30/decane system at 25 °C and schematic representation of phase transitions during emulsification. Om, isotropic liquid phase (W/O microemulsion); $L\alpha$, lamellar liquid crystalline phase; D' , shear birefringent liquid phase; W_m , bluish liquid phase (O/W microemulsion); W , aqueous liquid phase; O , oil liquid phase; MLC, multiphase region including lamellar liquid crystal. (Adapted with permission from Forgiarini et al., 2001b. Copyright 2001 American Chemical Society.).

Fig. 6 Microemulsion regions (Om and W_m) in the pseudoternary water/SDS:hexanol (1:1.76)/dodecane system at 25 °C. Om and W_m denote W/O and O/W microemulsions, respectively. Solid and dashed lines indicate the experimental emulsification paths for the preparation of nano-emulsions for a final water content of 98 wt%. (Reproduced with permission from Solè et al., 2012. Copyright 2012 Elsevier)

Fig.1 Phase behavior of water/(C₁₂E₆+C₁₆E₄)/decane system at 25°C. The surfactant mixing ratio ($W_1 = C_{16}E_4 / (C_{12}E_6 + C_{16}E_4)$) is (a) 0.2 (HLB_{mix} = 11.1) and (b) 0.4 (HLB_{mix} = 10.4). W: aqueous liquid phase, D: isotropic bluish liquid phase (microemulsion), O: oil liquid phase; L_α: a liquid-crystal-present region; W_m: liquid phase (O/W microemulsion); O_m: isotropic liquid phase. Dashed lines indicate the experimental emulsification paths for the preparation of nano-emulsions for a final W/O weight ratio of 90/10. Single-phase regions are marked in light grey whereas the region that was not explored is marked in dark grey (Feng and Solans, unpublished results).

190x254mm (96 x 96 DPI)

Fig.2 Droplet size of nano-emulsions prepared by PIC method as a function of S/O at 25°C in water/(C₁₂E₆+C₁₆E₄)/decane systems. The water/decane ratio is 90/10 (w/w). The surfactant mixing ratio (W1) is (a) 0.2 and (b) 0.4 (Feng and Solans, unpublished results).

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254x190mm (96 x 96 DPI)

Fig.4 The vertical axis on the left shows the droplet size for emulsions of the water/ Brij 30/decane system as a function of the oil weight fraction in water, R , at a constant surfactant concentration (5.0 wt %) and temperature (25 °C) obtained by emulsification methods A (stepwise addition of oil to a water-surfactant mixture), B (stepwise addition of water to an oil-surfactant mixture, PIC method), and C (mixing all the components at the final composition). The vertical axis on the right shows the equilibrium interfacial tension as a function of R , at a constant surfactant concentration (5.0 wt %) and temperature (25 °C). (Adapted with permission from Forgiarini et al., 2001b. Copyright 2001 American Chemical Society.).

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Fig.6 Microemulsion regions (Om and Wm) in the pseudoternary water/SDS:hexanol (1:1.76)/dodecane system at 25 °C. Om and Wm denote W/O and O/W microemulsions, respectively. Solid and dashed lines indicate the experimental emulsification paths for the preparation of nano-emulsions for a final water content of 98 wt%. (Reproduced with permission from Solè et al., 2012. Copyright 2012 Elsevier)

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