

Chapter 1

General introduction

The field of homogeneous catalysis has grown dramatically over the past decade, boasting many new applications in the chemical, fine chemical, and pharmaceutical industries. Separating and recycling the catalyst, and to avoid the use of toxic and hazardous solvents are some of the main challenges in this field. Therefore, in recent years a great deal of research has been made in an attempt to solve these problems. Alternative green solvents have been used for catalysis, which also make it possible to recycle the catalyst.

The present chapter introduces the concept of homogeneous catalysis and discusses the importance of using alternative reaction media for catalysis. Water and supercritical carbon dioxide are environmentally friendly solvents, which also make it possible sometimes to recycle the catalyst. This first chapter also presents the hydroformylation reaction studied in the first part of the present thesis.

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1.1. Homogeneous Catalysis

The concept of catalyst was first introduced by Berzelius in the 19th century [1]. Subsequently, Ostwald came up with the definition that we still use today: *A catalyst is a substance that increases the rate of a chemical reaction, without being consumed or produced by the reaction* [2].

The catalyst only has a kinetic effect: it accelerates a reaction that is thermodynamically possible. A catalyst increases the reaction rates because it generates new reaction routes, which have lower activation energies (Figure 1). However, it may sometimes have an influence on the distribution of the reaction products by modifying the rates of the competitive reactions.

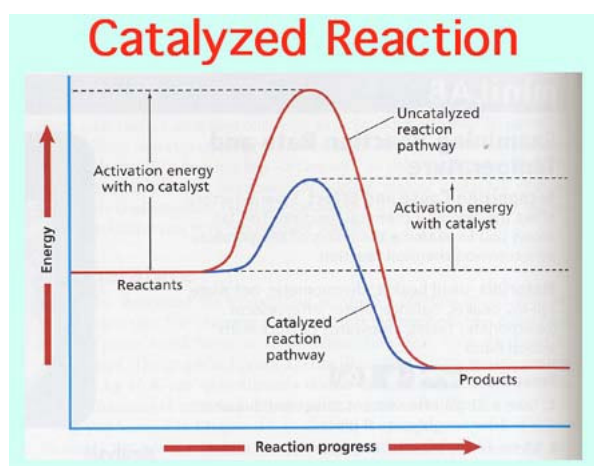


Figure 1. Effect of the catalyst on the reaction rate

Catalysts can be either *homogeneous* or *heterogeneous*. A *homogeneous catalyst* is in the same phase, normally liquid, as the reactants and products. A *heterogeneous catalyst* is in a different phase to that of the reactants, usually the solid phase, and the reactants are in the liquid or gas phase. Although, this general concept not comprises all the catalytic systems, the combination of both types of catalyst is also described. In recent years one of

the approaches that has been developed is the immobilization of the homogeneous catalyst on either solid or liquid supports, which converts the catalytic systems into multiphase systems.

Before 1938, when “oxo-synthesis” was discovered by Otto Roelen, homogeneous catalysis received only little attention [3]. Catalysis was linked to large-volume industrial chemical synthesis (ammonia synthesis, coal hydrogenation or Fischer-Tropsch synthesis). In general, catalysis was synonymous of heterogeneously catalysed reactions. Except in rare cases, such as Grignard reactants or the Mond process, organometallic compounds had no technical or commercial application. In comparison with heterogeneous catalyst, homogeneous catalysis has many advantages:

- The activity and selectivity are high.
- Reactions can be carried out in mild reaction conditions.
- Its sensitivity to catalyst poisons is low.
- There are no diffusion problems.
- The steric and electronic properties of the catalysts can be varied.
- It makes it possible to understand the reaction mechanism.

Despite of all these advantages, homogeneous catalysis has one major disadvantage: is very difficult to separate and reuse the catalytic system. Therefore, in recent years a great deal of research has been carried out to solve this problem. The most successful approach is to convert the homogeneous systems into multiphase systems. The first method was the “heterogenization” of the homogeneous catalyst immobilizing it on the surface of an organic or inorganic support [4-7]. In most cases, the activity of the immobilized system is lower than that of the homogeneous system and the supported catalyst is not as stable as expected, due to the leaching of the catalyst.

A more successful solution is to immobilize the system in a “liquid support”, from where the concept of biphasic catalysis arises. The basic principle of

biphasic catalysis is, therefore, that homogeneous catalysis is in solution in one of the phases while the reaction products are in a second phase, which is immiscible with the catalyst phase and can thus easily be separated [8].

The most developed biphasic system is probably the aqueous/organic solvent biphasic system. The catalyst is usually solubilized in water whereas the substrate and the products remain in the organic phase (Figure 2) [9]. However, the opposite approach has also been studied for water-soluble substrates [10].

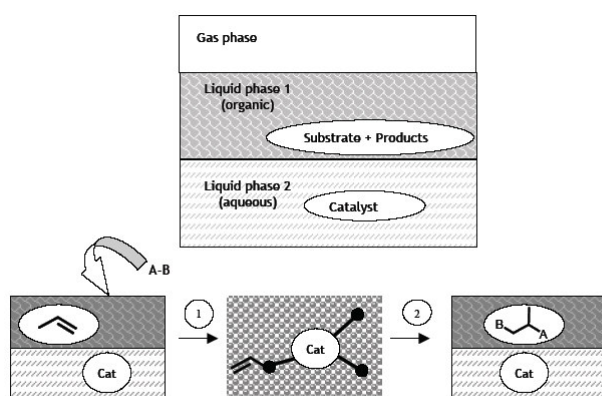


Figure 2. Schematic representation of an aqueous biphasic system.

Water is rarely used as a solvent for organic chemistry because organic compounds are not very soluble in it while some reaction intermediates are extremely reactive in it. It was rediscovered in 1980, when Breslow [11] showed that the rate of the cycloaddition of cyclopentadiene with methyl vinyl ketone in water was enhanced by a factor of more than 700 compared to the reaction in isooctane. Since then interest in the use of water as a solvent

has been growing, not only in attempt to improve reaction rates but also to improve selectivities or facilitate the separation of the catalyst.

The main advantages of using water as a solvent are the following: it is cheap, and more importantly, non-toxic; water-soluble compounds such as carbohydrates can be used directly with no need for the tedious protection-deprotection process; and water-soluble catalysts can be recycled by filtration, decantation or extraction of the other products that are insoluble in water.

Aqueous biphasic catalysis therefore requires a water-soluble catalyst to be used. The solubility of the catalysts in water is determined by their overall hydrophilic nature which may be a consequence of the charge of the complex ion as a whole, or of the good solubility of the ligands [12]. As in organometallic catalysis, phosphines also play a leading role in aqueous organometallic catalysis. Some of the neutral ligands are water soluble because of their ability to form hydrogen bonds with the surrounding water molecules. These ligands usually contains several N or O atoms, such as the 1,3,5-triaza-7-phosphaadamantane (PTA, Figure 3) tris(hydroxymethyl) phosphines, $(\text{P}(\text{CH}_2\text{OH})_3)$ or several phosphines containing long polyether chains. But the most frequently used ligands in aqueous biphasic catalysis are derived by attaching to water-insoluble tertiary phosphines ionic or polar groups, such as sulfonate, sulphate, phosphonate, carboxylate, phenolate, quaternary ammonium and phosphonium, hydroxylic, polyether, guanidino or polyamide substituents or any combination of them. Figure 3 shows some water-soluble ligands. Sulfonated phosphines are the most important ligands in aqueous organometallic catalysis since they dissolve well throughout the pH-range and are insoluble in common non-polar organic solvents. These ligands can be prepared with straightforward methods. The sulfonate group is deprotonated in a wide pH-range so its coordination to the metal need not be considered, and they are sufficiently stable under most catalysis conditions.

For these reasons the most important ligands used in aqueous catalysis in both academia and industry are the sulfonated monodentate phosphines TPPMS [13] and TPPTS [14], and sulfonated bidentate tertiary phosphines such as BINAPS [15], BISBIS [16] and BINAS [17] (Figure 3).

Apart from aqueous systems there are other possibilities of biphasic systems:

- Organic polar liquid/ Non polar organic liquid
- Ionic liquid/ Organic Liquid
- Organic perfluorinated solvent/ Organic liquid

The first of these systems is based on the immiscibility of liquids that have different polarities and it is applied by Shell in the industrial process SHOP for oligomerization of ethylene to obtain high molecular weight olefins [18]. A nickel-based catalyst is solubilized in butane-1,4-diol. The high molecular weight alkenes formed in the reaction are not soluble in the catalyst phase. Therefore, the catalyst and the products can be separated easily.

The second system uses ionic salts, which have a low melting point. They are usually known as ionic liquids and they form biphasic systems with numerous organic solvents. The system has mainly been used by academia in several organometallic-catalysed reactions [19-21].

Finally, fluorous biphasic catalysis (FBS), was introduced by Horváth and Rabai in 1994 [22]. It is based on the fact that perfluorinated alkanes, ethers and tertiary amines are not very soluble in such organic solvents as aromatic, aliphatic alcohols, acetone, tetrahydrofuran, etc. The catalyst should be soluble in the perfluorinated phase, so the catalyst should be modified increasing the affinity of it for the solvent. The most effective way of doing so is to introduce perfluorinated groups into the ligand structure. Gases are also highly soluble in perfluorinated solvents, especially oxygen, so perfluorinated solvents are particularly attractive for the oxidation processes.

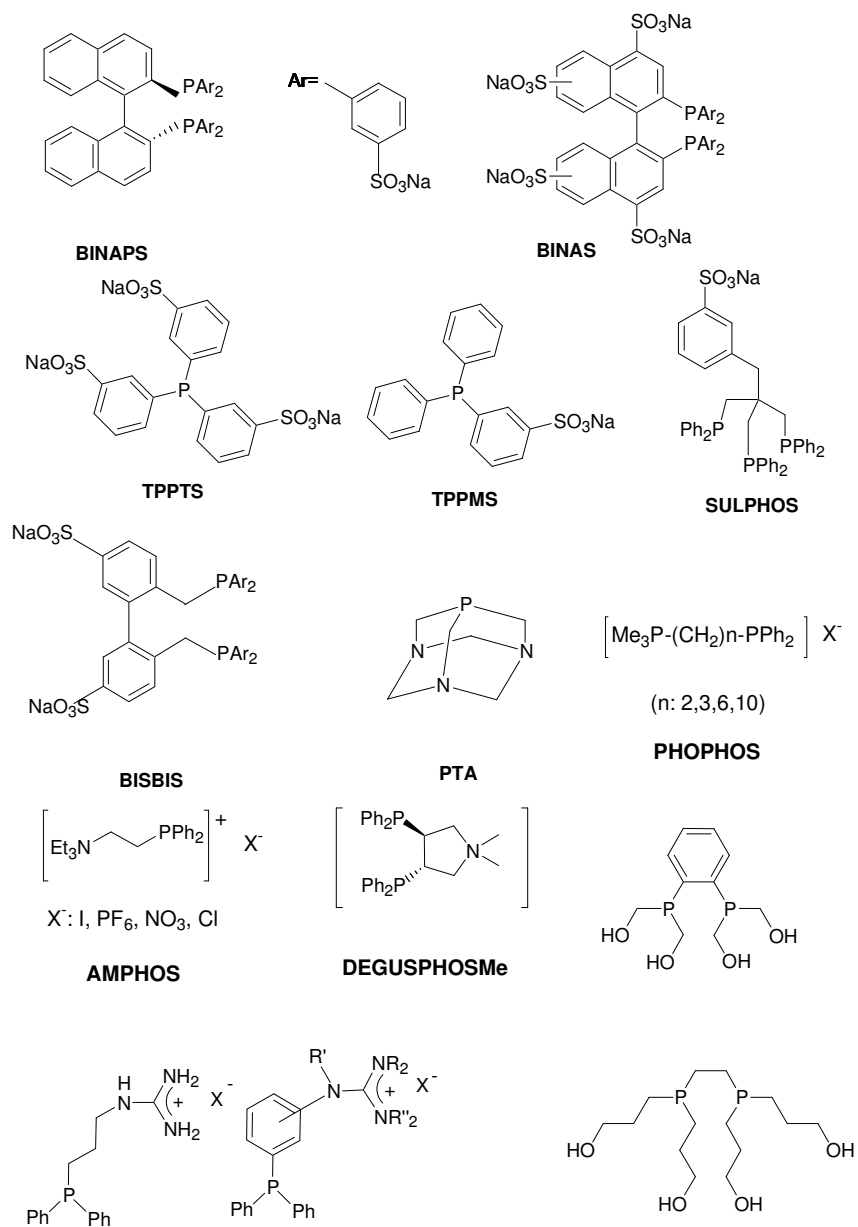
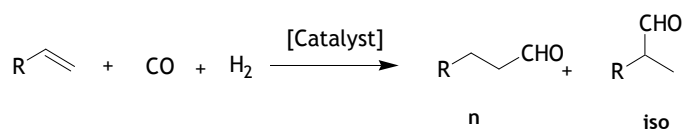


Figure 3. Water-soluble ligands

1.2. Hydroformylation

Hydroformylation is the largest volume homogeneous catalytic process that uses organometallic catalysis in industry [3]. Hydroformylation (Scheme 1) is the reaction of an alkene with carbon monoxide and hydrogen to obtain linear (n) and branched aldehydes (iso).



Scheme 1

Depending on the substrate, it is more interesting to obtain one regioisomer than the other. In the hydroformylation of long chain alkenes the linear aldehyde is the desired product, since they make it possible to synthesize alcohols that are used as intermediates for detergents and plasticizers. In the asymmetric hydroformylation of vinylarenes, however, the branched aldehyde is the desired product since it is a model precursor for the synthesis of arylpropionic acids, which are important anti-inflammatory drugs such as ibuprofen or naproxen [3, 23].

Hydroformylation (the oxo-process) was discovered by Otto Roelen in 1938 in Ruhrchemie AG. The original process used cobalt carbonyl catalyst as a catalyst. The conditions were harsh, as the reactivity of cobalt was low [24, 25]. Subsequently, cobalt catalyst was modified with tertiary phosphines, such as PBU_3 (Shell, 1964). The process proceeded at lower temperatures and pressures but still suffered from low n/iso selectivity [26]. The second generation processes use rhodium catalysts associated with arylphosphines. The first industrial process came on stream in 1974 in Celanese [27], followed by Union Carbide (1976) [28] and the Mitsubishi Chemical Corporation (1978) [29], all of which used triphenylphosphine as a ligand.

Mechanism

The common accepted mechanism for hydroformylation using PPh_3 as a ligand is depicted in Figure 4. This is the so-called dissociative mechanism, based on the mechanism proposed by Heck and Breslow [30] for cobalt-catalysed hydroformylation [23].

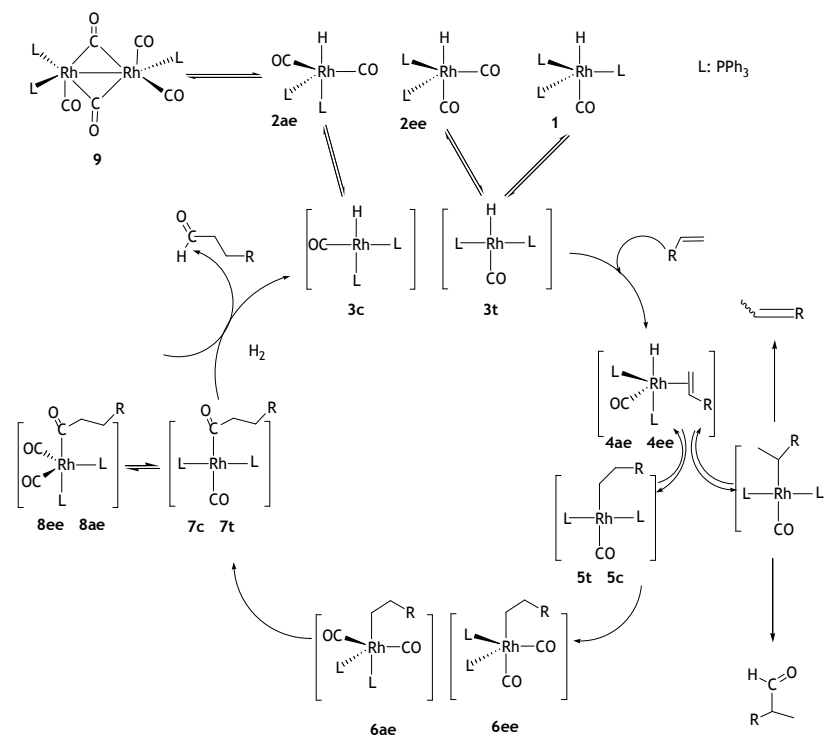


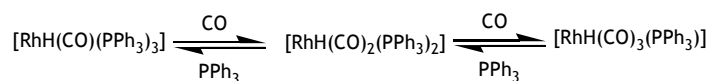
Figure 4. Simplified catalytic cycle for hydroformylation of propene $\text{L} = \text{PPh}_3$ [23].

The starting complex is $[\text{RhH}(\text{L})_3\text{CO}]$ (**1**) which under pressure of carbon monoxide forms the complexes **2ae** and **2ee**, containing the phosphine ligands in equatorial positions (ee) or axial-equatorial positions (ae). The dissociation of one phosphine ligand leads either to the square-planar complex **3c** or **3t**, which have phosphines on *cis* or *trans*, respectively. Coordination of the

alkene gives the species **4ae** or **4ee**. The migratory insertion of the hydride into the alkene gives the square-planar complexes **5** is the step that determines the regioselectivity of the system. A β -elimination of hydride in species **5** leads to isomerization when higher alkenes are used, or it can react with carbon monoxide to form trigonal bipyramidal complexes **6**. A second migratory insertion of CO into complexes **6** leads to the formation of acyl complexes **7**, and the reaction of these species with CO forms the saturated acyl intermediates **8**. Reaction of **7** with H_2 gives the aldehyde product and regenerates the unsaturated species **3**. The reaction with H_2 involves an oxidative addition and a reductive elimination.

Regioselectivity

In the hydroformylation of 1-alkenes two regioisomers can be obtained. The regioselectivity of the catalyst based on PPh_3 varies from 70 to 92 % to linear aldehyde [23]. Selectivity is highest at high concentrations of PPh_3 and low CO pressures. This can be easily explained if the species formed under syn gas pressure and at room temperature (Scheme 2, Figure 4) are taken into account. Species with more coordinated phosphine ligands create more steric hindrance around the metal, which favours the formation of linear alkyl intermediate **5**. Moreover, an increase in the partial pressure of CO favours the dissociation of phosphines and the formation of branched alkyl intermediates.



Scheme 2

Brown and Kent studied the different intermediates formed with $[RhH(CO)_2(PPh_3)_2]$ by NMR [31]. They observed that the major specie $[RhH(CO)_2(PPh_3)_2]$ is a mixture of two isomers, the equatorial-equatorial (ee) and the axial-equatorial (ae) with a ratio of 85% and 15%, respectively (Figure 5).

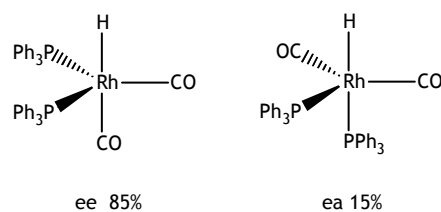


Figure 5

The reaction of these two isomers with styrene leads to the formation of the intermediates $[\text{Rh}(\text{acyl-branched})(\text{CO})(\text{PPh}_3)_2]$ major (Figure 6a) and $[\text{Rh}(\text{acyl-linear})(\text{CO})_2(\text{PPh}_3)_2]$ minor (figure 6b). As the time progresses the major acyl specie is depleted partly by isomerization of $[\text{Rh}(\text{acyl-branched})(\text{CO})(\text{PPh}_3)]$ to linear-acyl and partly by an increase in the concentration of the iso-aldehyde. The isomerization occurs slowly so that it is unlikely to contribute to the product isomer distribution. Using 1-octene and 1-decene as a substrates only the isomers $[\text{Rh}(\text{acyl-linear})(\text{CO})_2(\text{PPh}_3)_2]$ were detected.

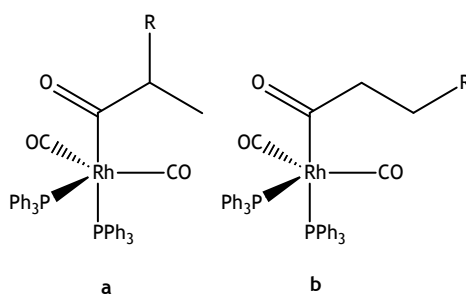


Figure 6

Other important aspects in the rate and selectivity of hydroformylation are the steric and electronic properties of the ligands. The electronic properties of phosphorus ligands have been studied by looking at the stretching frequencies of the coordinated carbon monoxide ligands in complexes such as $[\text{NiL}(\text{CO})_3]$ or $[\text{CrL}(\text{CO})_5]$ in which L is the phosphorous ligand [32]. The electronic parameter for phosphorous ligands (χ) was defined by Tolman as

the difference in IR stretching frequencies between the complex $[\text{NiL}(\text{CO})_3]$ and the reference complex $[\text{Ni}\{\text{P}(t\text{-Bu})_3\}(\text{CO})_3]$.

The cone angle, θ , introduced by Tolman classifies the phosphorous monodentate ligands by their steric hindrance. The cone angle is defined as the apex angle of a cylindrical cone centred 2.28 Å from the centre of the P atom and just touching the van der Waals radii of the outermost atoms of the molecule (Figure 7).

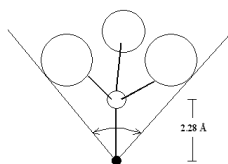
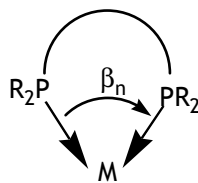


Figure 7. Diagrammatic representation of the Tolman cone angle, θ

In rhodium-catalysed hydroformylation of lineal alkenes with monophosphines PR_3 it has been observed that an increase in the cone angle induces better linear aldehyde selectivities. On the other hand, when the ligand has a very large cone angle linear aldehyde regioselectivity decreases, because the steric hindrance only allows species with one coordinated ligand to form.

Bidentate phosphorous ligands provide greater control of regioselectivity because the stability of the bidentate coordination means that much fewer species are formed than with monodentate ligands [33]. The steric effect of bidentate ligands is defined by the bite angle (β_n) which Casey and Whiteker [34] defined as the preferred ligand-metal-ligand angle formed when a bidentate ligand coordinates to a metal centre (Figure 8).

Figure 8. Bite angle, β_n .

Casey et al. studied how the bite angle affected the hydroformylation of 1-hexene catalysed by rhodium complexes. They observed that the bite angle in the intermediate $[\text{RhH}(\text{CO})_2(\text{P-P})]$ has considerable influence on the selectivity of the reaction. When BISBI, which has a bite angle of 113° and coordinates in a bis-equatorial fashion, was used as a ligand (Figure 9) the *n*/*iso* ratio obtained was 66, whereas using dppe (Figure 9) (bite angle = 90°), which coordinates in a axial-equatorial fashion, gave a *n*/*iso* ratio of 2.1. But, it is not only steric effects that lead to this high *n*/*iso* observed for diequatorial chelates. Electronic effects also play a role. The electronic interaction between two equatorial ligands is stronger than between axial-equatorial ligands. For example, back bonding from the rhodium to the alkene ligand in the equatorial plane may be stronger for bisequatorial complexes because of the strong donor phosphines in the equatorial plane. Moreover, the hydride is *trans* to CO in a bisequatorial complex so it may be more acidic than the hydride formed with dppe as a ligand since this is *trans* to a phosphine (Figure 9).

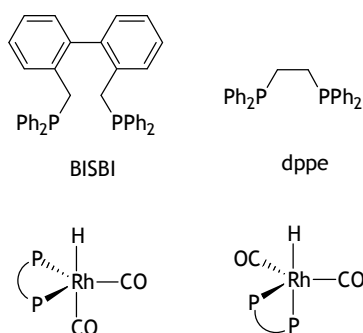


Figure 9

Phosphites

Phosphites were considered as a ligands for rhodium-catalysed hydroformylation in the late sixties, but triphenylphosphine turned out to be the ligand of choice [33]. Interest in phosphites began anew in the eighties after van Leeuwen and co-workers discovered that bulky monophosphites gave very high rates [35, 36]. Phosphites are easier to prepare than phosphines although they are more sensitive to side-reactions such as hydrolysis, alcoholysis or the Arbuzov reaction. The first example of phosphites being used in rhodium-catalysed hydroformylation was reported by Pruett and Smith of the Union Carbide Corporation, in the hydroformylation of 1-octene and methyl methacrylate [37]. Their results showed a high tendency to form the linear aldehyde.

Ligands with electron-withdrawing substituents increase the reaction rates because of a facile CO dissociation and strong alkene association. Although steric effects generally determine the relative stability of the primary and secondary alkyl complexes, electronic effects also play an important role in the regioselectivity. For diphosphine ligands electron-withdrawing substituents resulted in an increased preference for bisequatorial coordination of the phosphorous donors [38, 39]. Since phosphites have a much higher χ value than phosphines, a high preference for bisequatorial coordination is anticipated.

Because of phosphorous ligands are large, phosphites and phosphines creates more steric bulk in the rhodium complex and, the steric hindrance hamper the alkene addition. Therefore, in general, one would expect low reaction rates increasing the steric hindrance around the metal. However, van Leeuwen and Roobeek reported the use of the very bulky tris(ortho *tert*-butylphenylphosphite) as ligand and found high reaction rates in the hydroformylation of so-called unreactive alkenes such as 1,2- and 2,2-dialkylalkenes [35]. The high reactivity of these systems is explained by the exclusively formation of monoligated rhodium phosphite complexes confirmed

by *in-situ* IR and NMR studies [40]. The mechanism proposed for rhodium-catalysed hydroformylation using bulky phosphites is depicted in Figure 10.

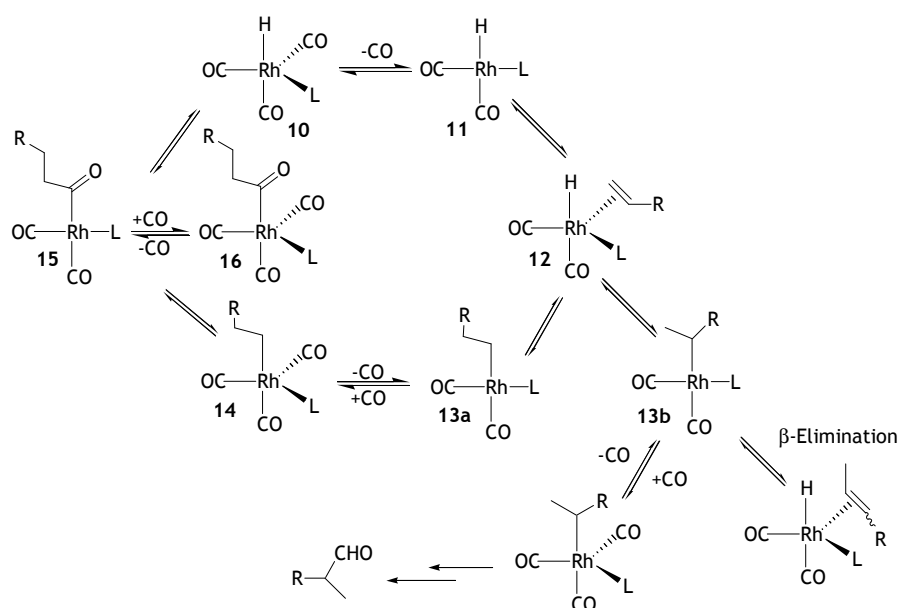


Figure 10. Mechanism proposed for hydroformylation using bulky monophosphites

As a consequence of the large cone angle of tris(ortho *tert*-butylphenyl)phosphite, the species **10** is formed under hydroformylation conditions. Since this species is electronically poor due to the presence of only one weak phosphite donor and strongly electron withdrawing carbonyls, this species easily loses CO, which leads to **11**. Alkene addition leads to species **12**, and the hydride migration results in the formation of the linear (**13a**) or branched (**13b**) alkyl intermediate. By migratory insertion these complexes give the acyl complex. However if a β -hydride elimination occurs in complex **13b** generates the isomerised alkenes. The β -elimination is faster for the

secondary alkyl intermediate than for the primary alkyl intermediate. Therefore, high isomerization rates will reduce the formation of branched acyl but not the formation of linear acyl, so high isomerization rates will reduce the formation of the branched aldehyde. As a consequence, n/iso ratios are high when the isomerization rate increases.

1.3. Hydroformylation in aqueous systems

In all homogeneous processes, the catalyst precursor is dissolved in an organic liquid phase together with the substrate and the products. The catalyst has to be recovered with special procedures, such as oxidizing the catalyst and extracting it into an aqueous phase as a salt metal. Moreover, the reaction products have to be separated from the unreacted substrate and phosphines by distillation, which may lead to further side reactions [41].

The first example in hydroformylation of recovering the catalyst without using distillation processes was in 1973, using a cobalt-modified catalyst [42]. Tris(aminoalkyl)phosphine complexes, which can be extracted from the product by an aqueous acid wash, and reextracted to the organic phase after neutralization. The economic advantages of recovering the catalyst, however, were insufficient for a low-cost metal such as cobalt. It was not until 1975 that Rhône Poulenc industries [43] patented the aqueous/organic biphasic hydroformylation of olefins, which used the trisulfonated triphenylphosphine ligand (TPPTS) (Figure 3). The first plant came on stream in 1984 in Oberhausen (Germany) and had a capacity of 100,000 t/year. Its capacity was expanded with a plant in South Korea. The Ruhrchemie- Rhône Poulenc process produces around 600,000 tones of butyraldehyde per year.

In the recent years, new hydrophilic catalysts for aqueous biphasic hydroformylation have been developed [8, 12]. Of the various ligands synthesized, the sulfonated diphosphines BISBIS, NAPHOS and BINAS (Figure 3) and the monophosphine NORBOS (Figure 11) deserve special mention. In all

cases, both activity and regioselectivity (with the exception of NORBOS) are better than for the Rh/TPPTS system (Figure 11). It is also important to notice that P:Rh ratios can be low. For all these reasons, chelating ligands are attracting more attention for future industrial use.

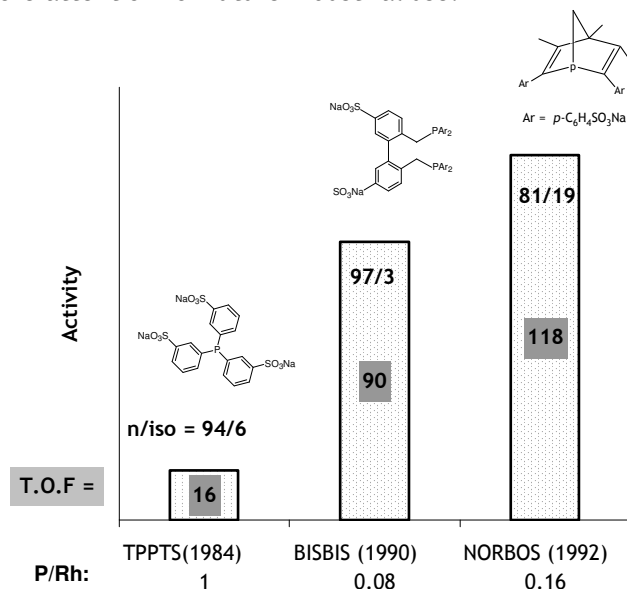


Figure 11. Results of catalysis with water-soluble rhodium-phosphine complexes. $T.O.F. = n(\text{aldehyde})n(\text{Rh})^{-1}h^{-1}$

Mechanism

The main differences between $[\text{RhH}(\text{CO})(\text{PPh}_3)_3]$ and $[\text{RhH}(\text{CO})(\text{TPPTS})_3]$ catalysts are basically that the water-soluble catalyst has lower activity and higher selectivity. The activity is lower because the solubility of alkene in water determines the rate of biphasic aqueous hydroformylation [44]. The reason for this is that the hydroformylation takes place in the aqueous phase. The higher selectivity towards the linear aldehydes may be due to the species formed. High pressure ^{13}C and ^{31}P NMR showed that the activation energy of phosphine exchange was higher for TPPTS than PPh_3 [45]. Presumably species such as $[\text{RhH}(\text{CO})_2\text{L}]$ are responsible for the formation of branched aldehydes. Looking at the general proposed mechanism for hydroformylation the

formation of these species requires the dissociation of a phosphine ligand and considering that the activation energy for phosphine exchange is higher when TPPTS is used, this results in a low concentration of $[\text{RhH}(\text{CO})_2(\text{TPPTS})]$ species. Another factor that plays a role in the selectivity of a biphasic aqueous system is the ionic strength of the aqueous phase [46]. The high excess of TPPTS used in industrial hydroformylation favours the formation of species with high content of $[\text{RhH}(\text{CO})(\text{TPPTS})_3]$ which increases the ionic strength of the media. Dissociation of TPPTS in water should be promoted due to the electronic repulsion among the sulfonate groups. Therefore, both effects should favour the formation of $[\text{RhH}(\text{CO})(\text{TPPTS})_2]$ and hence the regioselectivity towards linear aldehydes [12].

Effect of pH

The pH of the media also plays an important role in aqueous biphasic hydroformylation. In the Ruhrchemie-Rhône Poulenc process for propene hydroformylation, the pH is kept around neutral values in order to avoid acid- and base-catalysed reactions, and phosphine degradation. On the other hand it has been reported that other sulfonated phosphines can give optimal results in terms of activity at high pH values [47]. Desphande et al. found that the hydroformylation of 1-octene with TPPTS was pH-dependent and that the reaction rates were better between pH values of 10-7 [48]. It has also been shown that reaction rates of the asymmetric hydroformylation of styrene are higher at high pH values [49]. Joó et al. studied the effect of pH on Rh(I) complexes in aqueous solution [50] and investigated the reaction of $[\text{RhCl}(\text{TPPMS})_3]$ with hydrogen and carbon monoxide. At basic pHs the concentration of the complex $[\text{RhH}(\text{CO})(\text{TPPMS})_3]$, which is the precursor of the active catalytic species, were higher. At pHs lower than 5 no reaction of the complex $[\text{RhCl}(\text{TPPMS})_3]$ with hydrogen was observed. This observation may explain the high activity of these systems observed at basic pH.

Higher olefins

In spite of the success of the biphasic aqueous process in the hydroformylation of low olefins, the hydroformylation of long chain alkenes in aqueous systems is not economically viable since the low solubility of the alkene in water dramatically reduces the reaction rate. For this reason, various strategies have been developed to increase the solubility of the alkene in water.

The first strategy was to add co-solvents to the system. Adding an organic water miscible-solvent to an aqueous solution increases the mass transfer of the substrate in the aqueous phase. It has been shown that co-solvents such as ethanol, acetonitrile, methanol, ethylene glycol and acetone can enhance the rate of the hydroformylation [48, 51]. Monteil et al. [51] studied the effect of adding various co-solvents when dinuclear rhodium complexes associated with TPPTS in the hydroformylation of 1-octene were used. Ethanol was found to be the best in terms of activity although the selectivity towards linear aldehyde decreased. The addition of lower alcohols was also studied by Barhmann and Bogdanovic [52], and they found that methanol led to the highest rate increase. Similar results were found in the hydroformylation of styrene using methanol as co-solvent [49].

Adding surfactants to the system is another way of increasing the solubility of the substrate in the aqueous phase. A surfactant is a molecule that consists of two parts with opposite character. One part is hydrophilic and the other hydrophobic (Figure 12).

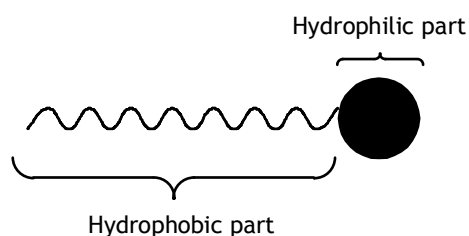


Figure 12. Schematic structure of a surfactant

Surfactants dramatically lower the surface tension of water and form aggregates like micelles in aqueous media [53]. There are many kinds of hydrophilic and hydrophobic groups of surfactants or ambiphilic compounds. Hydrocarbon chains are the most popular hydrophobic groups, fluorocarbon chains and silicon chains are also common. Surfactants are classified by their hydrophilic group. Anionic, cationic, amphoteric and neutral surfactants contain anion, cation, amphoteric ion, and nonion hydrophilic group respectively. Figure 13 shows the typical hydrophobic and hydrophilic groups of surfactants.

Depending on the concentration of the surfactants the molecules are organised in different ways. At low concentrations, surfactants will favour a surface arrangement. At higher concentrations, the surface becomes completely loaded with surfactant and any further addition must aggregate forming micelles or vesicles (Figure 14). This concentration is called the critical micelle concentration (c.m.c). It is a constant for each surfactant and depends on the solvent and temperature. In a polar solvent such as water, the hydrophilic groups are in the external part of the micelle and the hydrophobic groups will be orientated inside the micelle. These micelles are called regular micelles. In non-polar solvents, the distribution is just the opposite and these kinds of micelles are called reverse micelles.

Micelles can solubilize organic or inorganic compounds and affect their reactivity [41]. As a consequence of a gradient of polarity between the surface and the core of the micelle, a substrate can be enclosed in an appropriate environment.

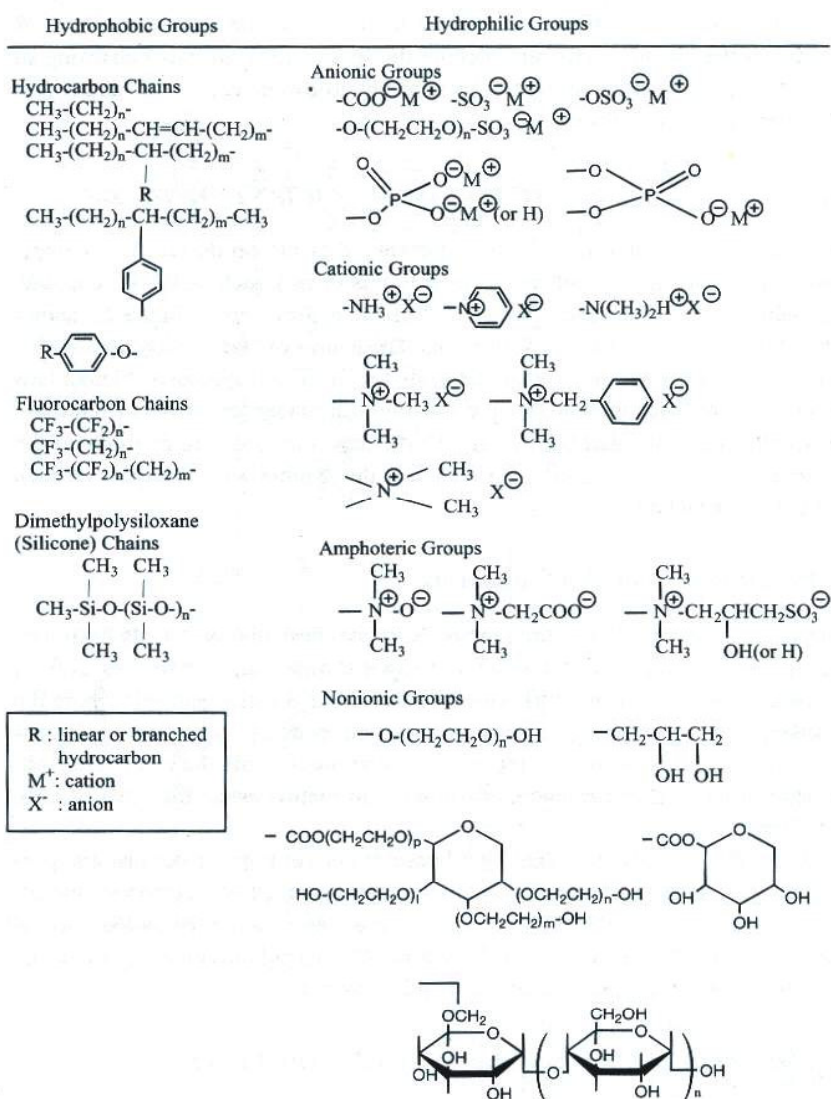


Figure 13. Typical hydrophobic and hydrophilic groups of surfactants

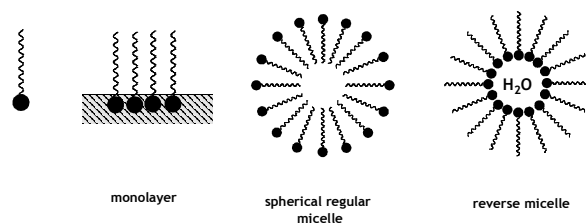


Figure 14. Self-organization of surfactants in water

Surfactants have been long used in aqueous biphasic catalysis and applied mainly to the hydrogenation and hydroformylation of alkenes. In the asymmetric hydrogenation of unsaturated amino acid derivatives catalysed by Rh(I) complexes, various studies have been made of the addition of different surfactants [54, 55, 56]. In all cases, both activity and enantioselectivity increased. It should be also pointed out that results were best when the concentration of the surfactant was above c.m.c.

Surfactants were also used in the hydroformylation of high olefins [57-61]. The hydroformylation of 1-dodecene catalysed by $[\text{RhCl}(\text{CO})(\text{TPPTS})_2]$ in water using surfactants was studied by Chen et al. [62]. They showed that conversion and regioselectivity increased when cationic surfactants were used. The influence that surfactants have on the rate of hydroformylation may depend on a combination of different factors. The addition of surfactants decreases the surface tension at the boundary of the aqueous phase and organic phase, thus producing a larger interphase area. Also, in the water-phase, the insoluble olefin is efficiently solubilized into the hydrophobic core of the micelles formed, thus favouring contact with the catalyst (Figure 15).

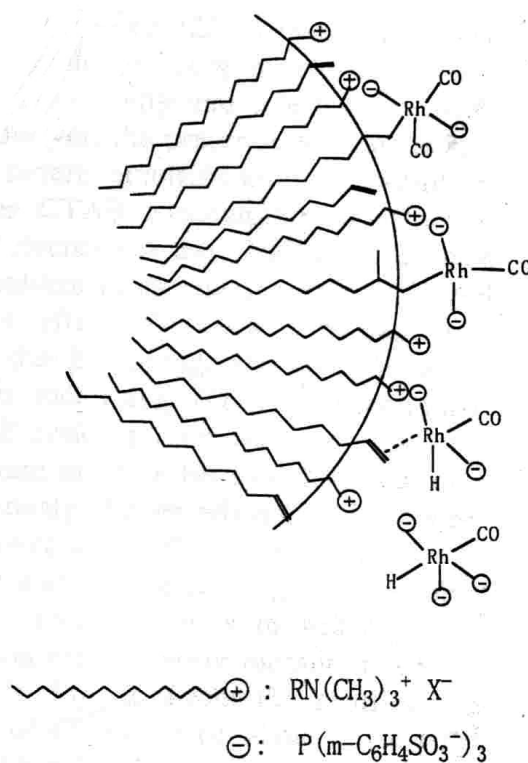


Figure 15. Interaction between the substrate and the catalyst in a micelle [62].

Cyclodextrins have also been used as mass transfer agents to biphasic reactions using water-soluble complexes [41]. Cyclodextrins are cyclic oligosaccharides composed of 6, 7 or 8 glucose units linked by a α -(1-4) glucosidic bond. As a result of their molecular structure and shape, they possess a unique ability to act as molecular containers by entrapping hydrophobic guest molecules in their internal cavity (Figure 16). The cyclodextrins have been applied to hydroformylation [63, 64], hydrocarbonylation [65] and Wacker oxidations [66].

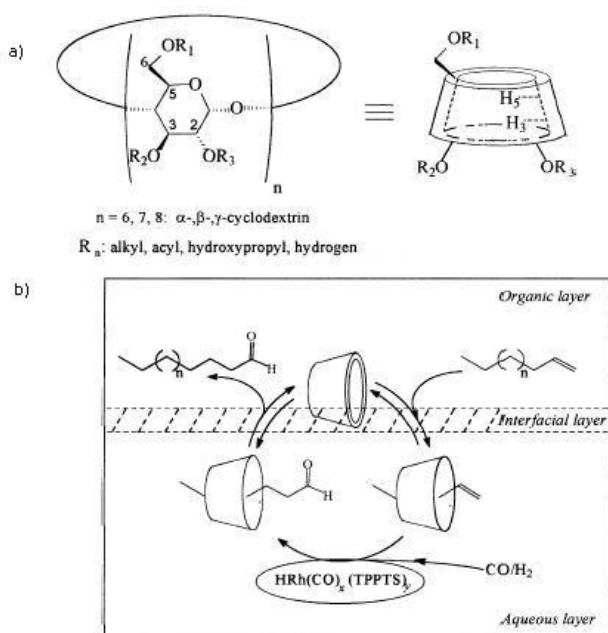


Figure 16. a) Schematic representation of the shape of cyclodextrins; b) Rhodium-catalysed hydroformylation of water-insoluble olefins in presence of cyclodextrin [63].

Dendrimers

Dendrimers (derived from the Greek words *dendron* (tree) and *meros* (part)) are highly branched macromolecules. The main difference between the linear polymers and dendrimers is that linear polymer consists of long chain molecules, like coils, crisscrossing each other. A dendrimer consists of long chains of molecules that branch out from a common center, and there is no entanglement between the individual dendrimer molecules [67].

Dendrimers have a globular configuration with monomer units branching out from the central core. The structure is highly defined and organized. The branches increase exponentially from the core to periphery (Figure 17) [68].

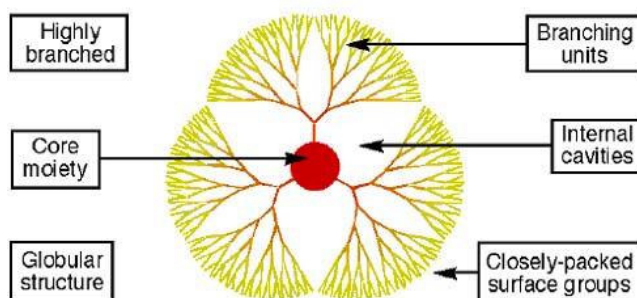


Figure 17. Dendritic structure.

The extremely regular structure of a dendrimer contributes to its nearly perfect spherical shape. Amphiphilic dendrimers have unique solution characteristics. Some amphiphilic dendrimers with ionic peripheral groups that have with hydrophobic interior structures show behaviour characteristic of unimolecular micelles [69].

Two synthetic general methods can be used to prepare dendrimers: the divergent growth method, which starts from the core and builds layers around it (inside-outwards), and the convergent growth method, which makes wedges that can be connected to a core in the last step of the synthesis (outside-inwards) (Figure 18) [70].

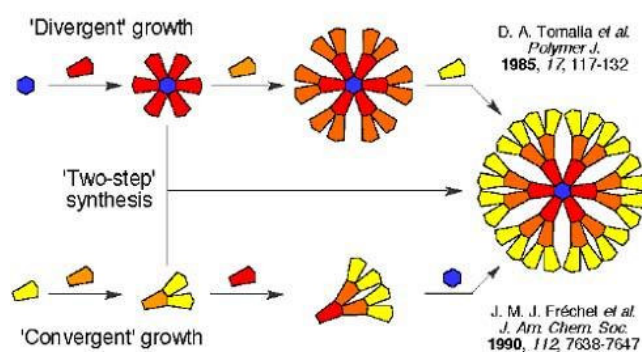


Figure 18

Dendrimers have numerous applications. For example, unsymmetrical dendrimers can form monolayers at gas-liquid interfaces or aqueous-organic interphases [67]. Amphiphilic dendrimers are useful in forming interfacial liquid membranes for stabilizing aqueous-organic emulsions. Dendrimers with carboxylate chain ends can form micelles in water. Their hydrophobic interior dissolves organic molecules that are insoluble in water.

Dendrimers with peripheral catalytic sites have been applied to transition-metal catalysis as a soluble supported catalysis [71].

1.4. Supercritical Fluids (SCF)

A supercritical fluid (SCF) is defined as a substance that is above its critical temperature (T_c) and critical pressure (P_c). The critical point represents the highest temperature and pressure at which the substance can exist as a vapour and liquid in equilibrium [72]. In the supercritical region there is only one phase, which has properties that are between those of a gas and a liquid. Figure 19 illustrates the transition from the liquid-gas region to the supercritical region (an orange “CO₂-philic” rhodium complex was added for better contrast) [73].

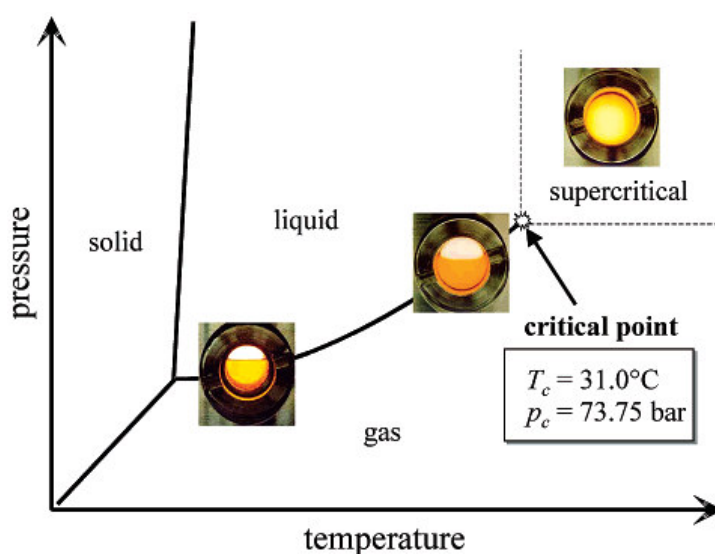


Figure 19. Schematic phase diagram of CO₂.

Supercritical fluids, especially supercritical carbon dioxide (scCO₂) has been used for decades as an extraction solvent to produce decaffeinated coffee beans, a large number of aroma products from plants and in the food industry [74, 75]. More recently, supercritical carbon dioxide has been used in other

commercial applications such as dry cleaning, metal degreasing, polymer modification and pharmaceuticals [74].

In the last decade supercritical fluids have emerged as alternative solvents for catalysis since they can replace conventional and hazardous solvents in a wide range of processes [76]. Among the different SCFs, supercritical carbon dioxide is one of the most attractive for alternative reaction media. Carbon dioxide has mild critical data ($T_c = 31^\circ\text{C}$, $P_c = 73.7$ bar), and is also truly benign and low cost. However, other SCFs such as water ($T_c = 374^\circ\text{C}$, $P_c = 217.8$ bar), hydrocarbons or fluorocarbons are also good alternative solvents for chemical synthesis [73].

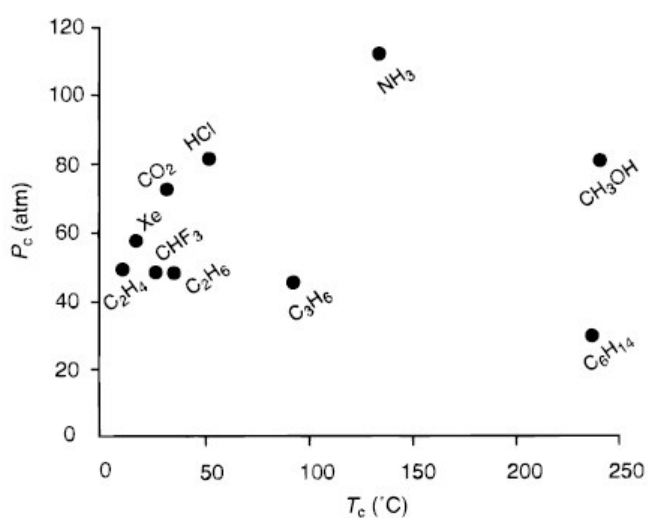


Figure 20. Critical point for selected solvents [77].

But probably the most important advantage of using SCFs is the high miscibility of gases in these media compared to very limited solubility of gases in liquid solvents [77]. This is of considerable interest for homogeneous catalysis and in particular for those reactions in which the reactants are gases. Furthermore, the research made into SCFs extraction and purification of compounds from mixtures can be used in the separation of transition metal

complexes from the reaction products because it solves the problem of recovering the catalyst at the end of the reaction. Controlled pressure reduction can be used to precipitate the catalyst selectively, assuming that these species are less soluble than the products in the supercritical fluid at lower densities.

Homogeneous catalysis in scCO_2 first became an object of research during the last decade probably due to the low solubilizing power of carbon dioxide. ScCO_2 is a non-polar solvent so it can only be used as a solvent in a narrow range of non-polar, non-ionic and low molecular weight catalysts, reagents and substrates. This limitation can be countered by using surfactants, co-solvents or other reagents, which increase the solubility of polar or ionic compounds in scCO_2 [77].

To work with supercritical fluids is important to take into consideration experimental parameters such as temperature and pressure because they affect the density of the system. Figure 21 shows density of CO_2 as a function of pressure and temperature. For a particular temperature, an increase in the pressure leads to an increase in the density, which can range from 0.05 g/ml to 0.80g/ml. On the other hand for a particular pressure, an increase in the temperature leads to a decrease in the density. It should be pointed out that the biggest changes in the density values are produced around the critical point. These changes in density affect the ability of the fluid to dissolve substances, thus, changing pressure and temperature the solubility in SCF can be tuned. As an example, the solubility of a polar solute such as benzoic acid in scCO_2 as a function of pressure and temperature is represented in Figure 22. The isotherms intersect within a restricted region of pressure named crossover pressure, which divides the graph in two regions. Between these two regions, there is a change in the temperature dependency of the solubility.

Below the crossover pressure, an increase in the temperature decreases the solubility of compounds (Figure 22) because the SCF density decreases. Above the crossover pressure, an increase in the temperature increases the solubility of the solute because the volatility of the solute increases.

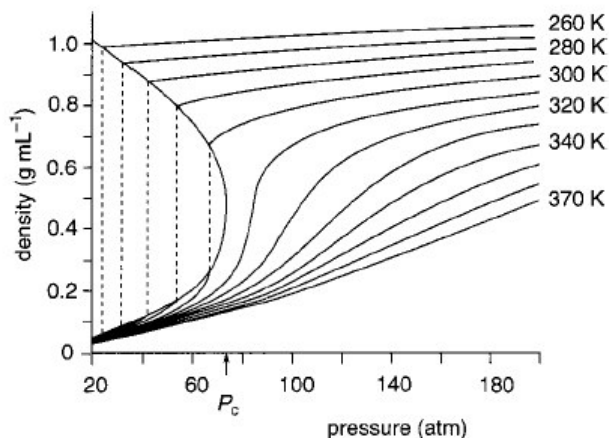


Figure 21. The density of pure CO₂ as a function of pressure and temperature [77].

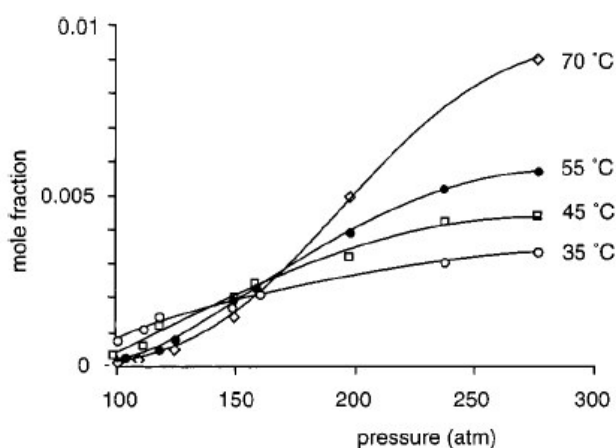


Figure 22. Mole fraction solubility of benzoic acid in scCO₂ as a function of pressure and temperature. The crossover pressure is approximately 160 atm [77].

It is also important to take into account the other density-dependent variables, such as viscosity, and the dielectric constant (ϵ). Since density depends on the pressure, these variables are also pressure-dependent. The absolute values of the variation in ϵ depend on the nature of the SCFs. For CO_2 variation of ϵ and viscosity are low (Figure 23), from 1.3 at $d_r = 1$ to 1.6 at $d_r = 2$ (reduced density (d_r) = value of density at actual point (d)/Density at the critical point (d_c)), which means that carbon dioxide remains a very non-polar solvent even for relatively large changes in pressure and temperature. For other more polar fluids, such as fluoroform and water, the same changes in density leads to drastic variations of the dielectric constant [72]

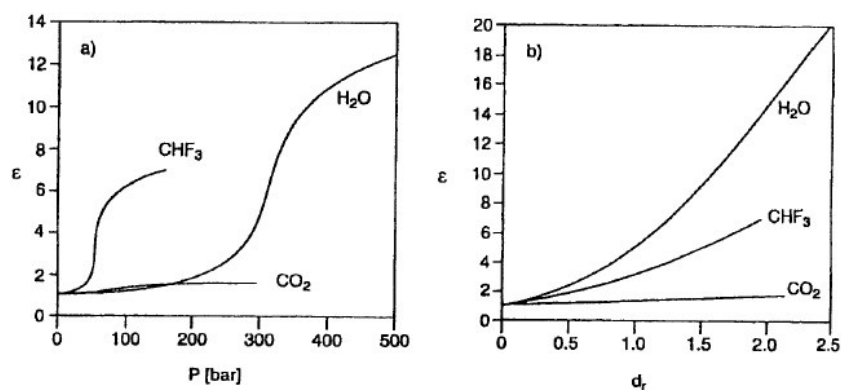


Figure 23. Variation of the dielectric constant of H_2O , CO_2 , and CHF_3 as function of pressure and reduced density [72].

Viscosity is generally lower and diffusivity higher in SCFs than in common liquid solvents. Compounds diffuse in SCFs at faster rates than in liquid solvents. However, this does not mean that SCFs do not have limitations of mass transfer.

Another important parameter is the reactivity of SCFs since they are not always inert under reaction conditions. This can be useful for some activation

processes but hazardous for uncontrolled reactions. Some of the hazardous SCFs are ethyne or 1,1-difluoro-ethene, which can polymerise under pressurization or can be explosive. Even alkanes become thermodynamically unstable at higher temperatures. But sometimes the reactivity of SCFs can be beneficial: the controlled polymerization of scC_2H_4 , for example, is an important industrial process. $scCO_2$ can be quite reactive and it inserts readily into M-H, M-R, M-OR or M-NR₂ bonds in transition metal complexes and reacts with secondary and primary amines to form carbamate salts [77].

Solubility of catalyst precursors

Supercritical carbon dioxide is a non-polar solvent so only non-polar catalysts will be soluble in it. It is known that some transition metal complexes are soluble in $scCO_2$ but there is no data for complexes that contain ligands such as phosphines, porphyrines or carbonyls. Polar complexes, ionic complexes or even non-polar complexes containing aryl groups are not soluble in $scCO_2$ [77]. Therefore, a great deal of research has been done in recent years to increase the solubility of the catalytic system. One of the first approaches was ligand modification. Ligands with aryl groups were substituted by alkyl or perfluoroalkyl groups [78, 79]. Alkyl phosphines with low molecular masses such as PMe_3 or PEt_3 are soluble in $scCO_2$ and provide active catalysts in hydroformylation [78, 80, 81]. Smart et al. [82] studied the effect of alkyl chains on the solubility of phosphorous compounds in supercritical carbon dioxide and reported that ligands with an approximate chain length of eight carbons, preferably branched, have the properties that will most likely lead to high solubility (Figure 24). Branched chains were also inserted into surfactants derived from sodium bis-2-ethyl-1-hexyl sulfosuccinate (AOT) and it has shown that a high degree of chain tip methylation increases solubility in supercritical carbon dioxide (Figure 24) [83]. The introduction of alkyl chains between six and sixteen carbons long into aryl phosphines was also studied by

Banet Osuna et al. [84] who showed that the effect is not so pronounced for aryl phosphines. The solubility of the ligands was low and decreased when the number of carbons in the alkyl chain increased. The addition of other CO₂-philic groups such as silyl or carbonyl, as substituents for aryl groups, provided often soluble systems [81,85].

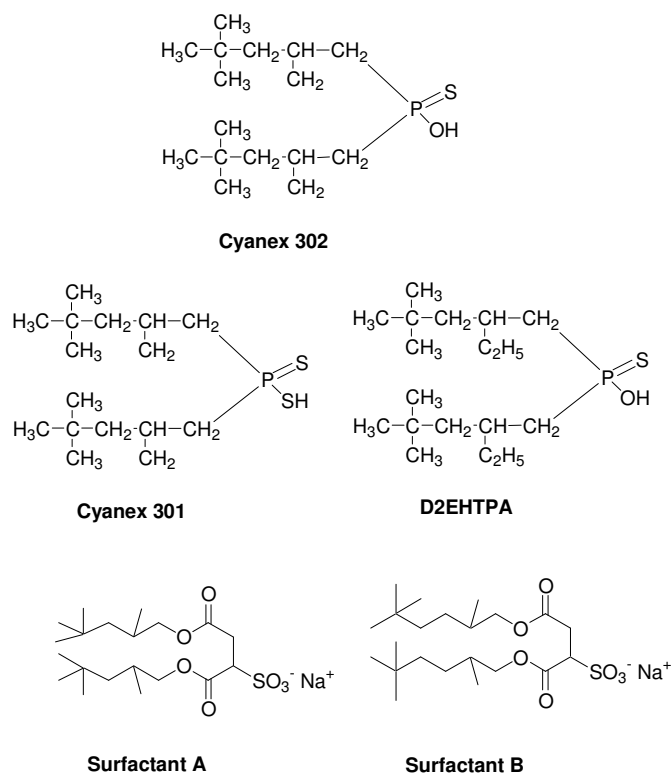


Figure 24. CO₂-philic compounds containing alkyl-branched groups

However, the most successful approach is to insert perfluorinated chains into aryl phosphines. Leitner and co-workers introduced this concept, by attaching perfluorinated alkyl chains to the ligand. These ligands contain methylene groups in the first two carbons of the aryl substituent (ponytail). The effect of this was to reduce the electrowithdrawing effect [79, 86]. Other groups [84,

87-91] have reported the use of ligands containing perfluorinated chains (Figure 25).

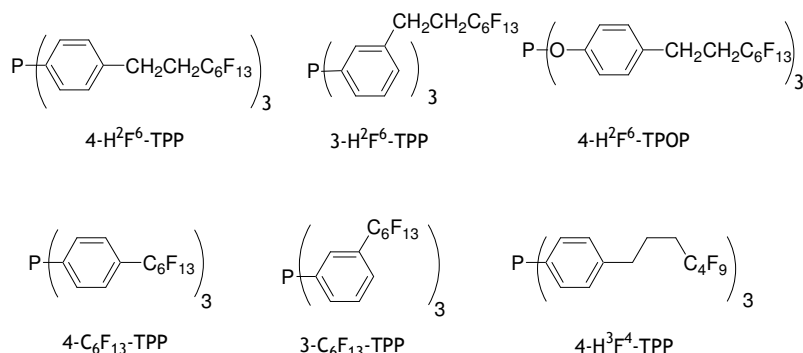


Figure 25. Perfluorinated ligands

The use of co-solvents increases also the solubility of catalyst precursors in supercritical carbon dioxide. Adding polar solvents increases the solubility of polar compounds in scCO₂. For example, the addition of 5-10% of methanol increases the solubility of transition metal complexes, which are insoluble without methanol [77]. The use of selected counterions, such as BARF (tetrakis(3,5-bis(trifluoromethyl))phenylborate) or CF₃SO₃⁻, also enhanced the solubility of transition metal complexes [92]. Finally, the use of surfactants that form reverse micelles in scCO₂ and solubilize hydrophilic compounds is another strategy that has been developed. These surfactants contain polar hydrophilic heads and CO₂-philic tails such as siloxane or fluorinated groups to increase the solubility in scCO₂ [93, 94].

Because CO₂-philic organometallic complexes are more readily available, carbon dioxide has increasingly been used as an alternative reaction medium in homogenous catalysis. The complete miscibility of gases in carbon dioxide makes it an ideal medium for catalysed reactions in which the reactants are gases. For this reason, one of the most widely studied catalysed reactions in scCO₂ is hydrogenation. The hydrogenation of carbon dioxide to obtain formic

acid was described by Jessop et al. [78]. Burk et al. [92] used BARF and CF_3SO_3^- as counteranions in their study of asymmetric hydrogenation of α -enamides with cationic rhodium complexes. They found that the catalytic systems are soluble and obtained enantioselectivities similar to the ones obtained in conventional organic solvents. Other successful examples of asymmetric hydrogenation in scCO_2 of α,β -unsaturated carboxylic acids [95] or hydrogenation of imines [96] have also been reported.

Hydroformylation has also been widely studied with scCO_2 as the reaction medium. The first example, was reported by Rathke et al. [97] for the hydroformylation of propylene with $[\text{Co}(\text{CO})_8]$ as catalyst. However, this process suffered from the drawbacks of cobalt catalysts (high pressures and temperatures). Leitner et al. [79] studied the hydroformylation of various alkenes with $[\text{Rh}(\text{cod})(\text{hfacac})]$ ($\text{hfacac} = 1,1,1,6,6,6$ -hexafluoropentane-2,4-dionate) either associated with perfluorinated phosphine ligands or as unmodified complex. The results showed that hydroformylation with the unmodified catalysts is faster in scCO_2 than in conventional solvents. The results of using CO_2 -philic ligands were similar to the ones obtained in conventional solvents with triphenylphosphine as the ligand. Furthermore, the extractive properties of carbon dioxide made it possible to extract the products of hydroformylation 1-octene from the catalyst. The aldehydes contained less than 1 ppm of rhodium and the catalyst was reused in five catalytic runs with no loss of activity and selectivity. The use of perfluorinated ligands in rhodium-catalysed hydroformylation was also studied by several groups [84, 88, 89].

Cole-Hamilton et al. [80,81] reported the use of trialkylphosphines such as PEt_3 as ligands for the rhodium-catalysed hydroformylation of 1-hexene. This kind of ligands are readily available, cheap, soluble in scCO_2 and do not involve synthesizing perfluorinated ligands, which are difficult to prepare. Ligands containing trimethylsilyl groups, $\text{P}(4\text{-C}_6\text{H}_4\text{SiMe}_3)_3$ and $\text{Ph}_2\text{P}(4\text{-C}_6\text{H}_4\text{SiMe}_3)$, were also investigated in the hydroformylation of 1-octene. Although the

complexes are not totally soluble, the activity and regioselectivity were high (80 and 82.4%, n/iso = 4.0 and 3.0, respectively) [81]. Cole-Hamilton et al. also reported the use of insoluble metal rhodium complexes in the hydroformylation of 1-hexene and 1-nonene [98]. They managed to recycle the catalyst by flushing the products formed into a second autoclave. The products contained undetectable amounts of rhodium. Recently, Leitner et al. [99] reported a cartridge catalyst that used a poly(ethyleneglycol) (PEG) modified phosphine ligand, MeOPEG₇₅₀-PPh₂. In a scCO₂ regulated reaction separation sequence they tested within other reactions the hydroformylation of 1-octene with the catalyst formed in situ from MeOPEG₇₅₀-PPh₂ and [Rh(acac)(CO)₂]. The catalyst was insoluble in scCO₂ but its activity was high and conversion reached 99% in two hours. After the reaction time, the products were separated from the catalyst by extraction with scCO₂. The products contained less than 5 ppm of rhodium and the catalyst was reused six times with no significant changes in activity and selectivity.

Supercritical carbon dioxide has also been successfully applied in carbon-carbon coupling reactions, which occur at high rates and selectivities in scCO₂ [100]. The first example was reported by Tumas et al. [101]. They studied the Heck and Stille couplings using palladium complexes associated with different phosphines. The best results were obtained with fluorinated phosphines. Couplings carried out on a solid support are of particular interest [102], reactions that use polymer supports require solvents that can swell the polymer and expose the active reaction sites. The ability of scCO₂ to plasticise polymers has been exploited in a number of applications, including polymer impregnation, formation of blends and particle formation [103]. For all these reasons, scCO₂ is an interesting alternative solvent for polymer-supported reactions.

Polymerisation reactions have also been studied in scCO₂. Amorphous low melting point fluoropolymers can be synthesized in carbon dioxide either by free radical or cationic methods. They are not very soluble in common organic

solvents, which makes it difficult for them to be synthesized. In fact, they are only soluble in chlorofluorocarbons (CFCs) and CO₂. Due to the environmental problems associated with the use of CFCs, CO₂ is an environmentally friendly option for the synthesis of these types of highly fluorinated monomers [104]. Polymerisations catalysed by metal transition complexes have also been studied in scCO₂. De Vries et al. [105] showed that the polymerisation of ethylene and 1-hexene catalysed by cationic palladium complexes in scCO₂ gave polymers with properties similar to those obtained in dichloromethane. Few studies have been made of the copolymerization of carbon monoxide with olefins in scCO₂ [106-108].

Finally, in the recent years many examples of multiphasic systems that use scCO₂ have been described. The combination of ionic liquids and scCO₂ has emerged as a new biphasic system for homogeneous catalysis. ScCO₂ is soluble in ionic liquids, and decreases their viscosity and therefore, enhances the mass transfer. Ionic liquids are not soluble in scCO₂. Hence, non-volatile compounds can be extracted quantitatively from ionic liquids with scCO₂ [109]. The biphasic system ionic liquids/scCO₂ has been applied successfully in many homogeneous catalysed reactions [110-114].

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