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Goetheer, E.L.V.

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Strategies for Carrier-Mediated Extractions and Reactions in Supercritical Carbon Dioxide

PROEFSCHRIFT

Ter verkrijging van de graad van doctor aan de Technische Universiteit Eindhoven, op gezag van de Rector Magnificus, prof. dr. R.A. van Santen, voor een commissie aangewezen door het College voor Promoties in het openbaar te verdedigen op dinsdag 25 juni 2002 om 16.00 uur

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Earl Lawrence Vincent Goetheer

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Voor mijn moeder
Contents

1 Introduction: Perspectives on Supercritical Fluids 1
2 Design of Fluorinated Surfactants for Use in Carbon Dioxide 13
3 Reactive Extraction with Functionalized Poly(propylene imine) Dendrimers 35
4 Functionalized Poly(propylene imine) Dendrimers as Phase Transfer Catalyst in Supercritical Carbon Dioxide 61
5 Permeation of Carbon Dioxide through a Microporous Silica Membrane at Subcritical and Supercritical Conditions 77
6 A Membrane Reactor for Homogeneous Catalysis in Supercritical Carbon Dioxide 93
7 Outlook to the Future: Micro-Heterogeneous Catalysis in Carbon Dioxide 111

Summary 121
Samenvatting 125
Dankwoord 129
Chapter 1

Perspectives on Supercritical Fluids

Abstract
A general introduction on supercritical fluids with an emphasis on carbon dioxide is given and an outline of this thesis is presented. Supercritical carbon dioxide is interesting from an economical, environmental, and technical point of view. In this thesis various approaches are described to circumvent the problems associated with the low solubility of high molecular weight and polar molecules in carbon dioxide. Different strategies are presented for carrier-mediated extraction and reaction in carbon dioxide.
Green engineering
Increasing concern regarding the dissemination of volatile organic compounds, chlorofluorocarbons, and aqueous waste streams into the environment has prompted the chemical industry to conform to more environmentally sound practices in the manufacture and processing of products. Instead of using traditional end-of-pipe approaches for environmental management, approaches that avoid the generation of wastes and pollutants, known as green engineering, can provide alternatives that are cost effective and result in significant environmental improvements.
It is evident that the Chemical Process Industry has to comply with regulatory issues, but also with the more stringent quality demands, and the need for innovative products and processes. To accomplish this, the green engineering approach alone is not enough. A closer examination needs to be done at the chemistry level. An obvious target for improvement is the use of organic solvents. The main candidates for the replacement of conventional organic solvents are water, ionic solvents, and supercritical fluids (SCFs). In this thesis the use of supercritical fluids is discussed. It is generally thought that the use of supercritical solvents provides a powerful means to achieve more efficient and cleaner processes (McHugh and Krukonis, 1994, Johnston and Lemert, 1996).

Supercritical fluids
In 1822, Baron Charles Cagniard de la Tour conducted experiments that showed that there is a critical temperature above which a substance can only be in one fluid state instead of either being a gas or a liquid (see Figure 1). Nowadays, this is called a supercritical phase. Strictly, a supercritical fluid is defined as any substance of which the temperature and pressure are higher than their critical values. In Tables 1 and 2 an overview is given of often-used organic and inorganic SCFs. The definition given above is not very well suited for a chemical engineer as the typical properties associated with SCFs are closely related to the density. For example, H₂ gas is not considered to be supercritical at room temperature and 1.23 MPa pressure because its density under these conditions is far below its critical density. Far away from the critical point a fluid ceases to display the non-ideal properties typically associated with SCFs. These properties, sometimes termed a "hybrid of those of a liquid and a gas", include the ability to dissolve solids, miscibility with permanent gases, high diffusivity, low viscosity, etc. It is the understanding of these properties, which enables chemical engineers to use these fluids to access new areas of chemistry. A more useful definition of a SCF, therefore, is "any substance of which the temperature and pressure are higher than their critical values and which has a density close to or higher than its critical density" (Darr and Poliakoff, 1999).
Table 1: Critical conditions for various inorganic solvents (Jessop and Leitner, 1999).

<table>
<thead>
<tr>
<th>Name</th>
<th>Tc (K)</th>
<th>Pc (Mpa)</th>
<th>( \rho c ) (mol/L)</th>
<th>( \mu ) (Debye)</th>
<th>Cost ($/kg)</th>
<th>Mw</th>
</tr>
</thead>
<tbody>
<tr>
<td>argon</td>
<td>151</td>
<td>4.86</td>
<td>13.3</td>
<td>0</td>
<td>6</td>
<td>39.95</td>
</tr>
<tr>
<td>carbon dioxide</td>
<td>304</td>
<td>7.38</td>
<td>10.6</td>
<td>0</td>
<td>3</td>
<td>44.01</td>
</tr>
<tr>
<td>hydrogen chloride</td>
<td>325</td>
<td>8.26</td>
<td>11.5</td>
<td>1.08</td>
<td>20</td>
<td>36.46</td>
</tr>
<tr>
<td>hydrogen bromide</td>
<td>363</td>
<td>8.55</td>
<td>0.82</td>
<td>0</td>
<td>50</td>
<td>80.91</td>
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<tr>
<td>hydrogen iodide</td>
<td>424</td>
<td>8.3</td>
<td></td>
<td>0.44</td>
<td></td>
<td>127.9</td>
</tr>
<tr>
<td>water</td>
<td>647</td>
<td>22.1</td>
<td>17.9</td>
<td>1.85</td>
<td>0.1</td>
<td>18.02</td>
</tr>
<tr>
<td>ammonia</td>
<td>405</td>
<td>11.3</td>
<td>13.8</td>
<td>1.47</td>
<td>3</td>
<td>17.03</td>
</tr>
<tr>
<td>nitrous oxide</td>
<td>309</td>
<td>7.25</td>
<td>10.3</td>
<td>0.167</td>
<td>50</td>
<td>44.01</td>
</tr>
<tr>
<td>krypton</td>
<td>209</td>
<td>5.49</td>
<td>10.9</td>
<td>0</td>
<td>3000</td>
<td>83.8</td>
</tr>
<tr>
<td>sulfur hexafluoride</td>
<td>319</td>
<td>3.76</td>
<td>5</td>
<td>0</td>
<td>50</td>
<td>146.1</td>
</tr>
<tr>
<td>xenon</td>
<td>290</td>
<td>5.83</td>
<td>8.4</td>
<td>0</td>
<td>4000</td>
<td>131.3</td>
</tr>
</tbody>
</table>

Table 2: Critical conditions for various organic solvents (Jessop and Leitner, 1999).

<table>
<thead>
<tr>
<th>Name</th>
<th>Tc (K)</th>
<th>Pc (Mpa)</th>
<th>( \rho c ) (mol/L)</th>
<th>( \mu ) (Debye)</th>
<th>Cost ($/kg)</th>
<th>Mw</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluoroform</td>
<td>299</td>
<td>4.82</td>
<td>7.5</td>
<td>1.65</td>
<td>125</td>
<td>70.01</td>
</tr>
<tr>
<td>difluoromethane</td>
<td>351</td>
<td>5.78</td>
<td>8.2</td>
<td>1.97</td>
<td></td>
<td>52.02</td>
</tr>
<tr>
<td>methane</td>
<td>190</td>
<td>4.6</td>
<td>10.2</td>
<td>0</td>
<td>80</td>
<td>16.04</td>
</tr>
<tr>
<td>methanol</td>
<td>513</td>
<td>8.08</td>
<td>8.5</td>
<td>1.7</td>
<td>18</td>
<td>32.04</td>
</tr>
<tr>
<td>ethene</td>
<td>282</td>
<td>5.04</td>
<td>7.6</td>
<td>0</td>
<td>16</td>
<td>28.05</td>
</tr>
<tr>
<td>ethane</td>
<td>305</td>
<td>4.87</td>
<td>6.9</td>
<td>0</td>
<td>100</td>
<td>30.07</td>
</tr>
<tr>
<td>dimethyl ether</td>
<td>400</td>
<td>5.4</td>
<td>5.3</td>
<td>1.3</td>
<td>15</td>
<td>46.07</td>
</tr>
<tr>
<td>ethylenediamine</td>
<td>593</td>
<td>6.28</td>
<td>4.8</td>
<td>1.99</td>
<td>200</td>
<td>60.1</td>
</tr>
<tr>
<td>propene</td>
<td>365</td>
<td>4.6</td>
<td>5.4</td>
<td>0.366</td>
<td>9</td>
<td>42.08</td>
</tr>
<tr>
<td>propane</td>
<td>370</td>
<td>4.25</td>
<td>5</td>
<td>0.084</td>
<td>10</td>
<td>44.1</td>
</tr>
<tr>
<td>n-butane</td>
<td>425</td>
<td>3.8</td>
<td>3.9</td>
<td>&lt;0.05</td>
<td>15</td>
<td>58.12</td>
</tr>
<tr>
<td>isobutane</td>
<td>408</td>
<td>3.64</td>
<td>3.9</td>
<td>0.132</td>
<td>15</td>
<td>58.12</td>
</tr>
<tr>
<td>n-pentane</td>
<td>470</td>
<td>3.37</td>
<td>3.2</td>
<td>0</td>
<td>30</td>
<td>72.15</td>
</tr>
<tr>
<td>benzene</td>
<td>563</td>
<td>4.92</td>
<td>3.8</td>
<td>0</td>
<td>30</td>
<td>78.11</td>
</tr>
<tr>
<td>n-hexane</td>
<td>508</td>
<td>3.03</td>
<td>2.7</td>
<td></td>
<td>300</td>
<td>86.18</td>
</tr>
</tbody>
</table>

Unlike the compression of a gas below its critical temperature, which normally causes the appearance of a separate liquid phase, compression of a SCF results only in an increase in the density of the SCF and not in the formation of a second liquid phase (see Figures 2 and 3). As a result of the dependence of SCF density on pressure, a continuum of densities ranging from vapor-like to liquid-like can be obtained by varying the pressure while holding the temperature constant.
Table 3: Typical physical properties of gases, SCFs, and liquids.

<table>
<thead>
<tr>
<th>Properties</th>
<th>gas</th>
<th>SCF</th>
<th>liquid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (kg/m³)</td>
<td>1</td>
<td>100-800</td>
<td>1000</td>
</tr>
<tr>
<td>Viscosity (cP)</td>
<td>0.01</td>
<td>0.05-0.1</td>
<td>0.5-1</td>
</tr>
<tr>
<td>Diffusivity (m²/s)</td>
<td>$1 \times 10^{-5}$</td>
<td>$1 \times 10^{-7}$</td>
<td>$1 \times 10^{-9}$</td>
</tr>
</tbody>
</table>

The properties of SCFs are often said to lie between those of a liquid and a gas. Although this is generally true, it is important to note that some of the properties of an SCF are more liquid-like, whereas other are more gas-like (see Table 3). Furthermore, most properties of SCFs can significantly change with relatively small changes in pressure and temperature, rendering SCFs easily tunable with respect to their qualities as a solvent and/or reactant. It is this combination of these liquid-like and gas-like properties together with the easy tunability of those properties that make SCF a promising media for chemical reactions and extractions.

![Figure 1](image1.png)

Figure 1: Upon heating of liquid carbon dioxide the supercritical phase can be reached. In the photographs above is seen that the meniscus is disappearing upon heating the solvent (clockwise).
Figure 2: Phase diagram of carbon dioxide, in which the supercritical region is the shaded area.

Figure 3: The density of carbon dioxide as a function of the pressure and temperature.

**Physical properties of supercritical carbon dioxide**
At conditions near the critical point of the SCF, small changes in the pressure result in large density changes and changes in other important physical properties of the fluid, such as
Chapter 1

viscosity, dielectric constant, and solvent strength (McHugh and Krukonis, 1994). The hydrodynamic properties of a SCF also lie between those of a liquid and a gas, imparting favorable qualities for reactions and extractions to the SCF in this respect. The dynamic viscosity of a SCF is comparable to that of a gas at the same temperature. However, the density of a SCF near its critical point is at least 2 orders of magnitude higher than that of a gas, resulting in a very low kinematic viscosity. This is very advantageous for mass transfer, since natural convection effects are inversely proportional to the square of the kinematic viscosity.

![Graph of Viscosity vs Temperature and Pressure](image)

Figure 4a: The viscosity of carbon dioxide as a function of the pressure and temperature. In this graph the viscosity of carbon dioxide can be seen to vary between liquid-like to gas-like as a function of the pressure and temperature.

The diffusivity of small organic molecules in SCFs can be considered as being gas-like, with respect to the order of magnitude. Consequently, diffusion coefficients of solutes in SCFs are gas-like too, adding to the attractiveness of SCFs with regard to processes where diffusion of a component constitutes a limiting step. Besides the density also the viscosity and diffusivity of a SCF are dependent on temperature and pressure (see Figure 4). In a SCF the viscosity increases and diffusivity decreases as the pressure is increased. An increase in temperature leads to a decrease in viscosity of the SCF (note that the opposite is true in the case of a gas), whereas the diffusivity will increase with an increase in temperature.
Figure 4b: The diffusivity of a typical solute in carbon dioxide as a function of the pressure and temperature. In this graph the diffusivity of a solute in carbon dioxide can be seen to vary between values obtained in a liquid to values obtained in a gas as a function of the pressure and temperature.

An interesting phenomenon, especially for heterogeneous catalysis and transport through porous systems is the fact that the surface tension of a liquid in equilibrium with its vapor decreases with increasing temperature and becomes zero at its critical point. Therefore, a SCF acts like a gas in uniformly filling up the available space, allowing SCFs to penetrate readily into porous solids and packed beds (Wandeler and Baiker, 1999). Carbon dioxide has a low dielectric constant (relative permittivity) of 1.01-1.67 (depending on the conditions, see Figure 5), and its polarizability (27.6 10^{-25} \text{ cm}^3) is close to that of gases such as methane, perfluoromethane, and fluoroform. The solubility parameter of Hildebrand can often be used in estimating the solubility of non-electrolytes in organic solvents. Since solvent strength is strongly correlated with density, a SCF is a highly adjustable solvent. Generally, the solubility of a given solute increases with both increasing density of the solvent and increasing vapor pressure of the solute. This is shown in Figure 5, where the solubility parameter of carbon dioxide is seen to vary over an order in magnitude around the supercritical pressure and temperature. Consequently, the solubility of a solute in a SCF increases with increasing pressure. However, it can decrease, remain constant or increase with increasing temperature depending on the predominant factor, i.e. the density of the solvent or vapor pressure of the solute. Note that the solubilities in liquids are usually larger than those in SCFs and that the dissolving power of a SCF only approaches that of a liquid solvent at high enough densities. CO₂ does not have a dipole moment, but it does have a substantial quadrupole moment that, however, operates over a much shorter distance than dipolar
interactions. Due to this quadrupole moment the solubility of a lot of components is higher in carbon dioxide than expected.

Figure 5: The Hildebrand solubility parameter ($\delta$) and the relative dielectric constant ($\varepsilon_r$) of carbon dioxide as a function of temperature and pressure (McHugh and Krukonis, 1994, Reichardt, 1988).

**Applications of SCF**

Starting in the 1960s, large efforts have been undertaken for better understanding the properties of SCFs. In Figure 6 the scientific output in articles and patents is given. The high number of patents versus articles (one to five) is a strong sign of the activity of the industry. The rapid increase in the number of articles indicates that the scientific community working on SCFs is highly active.

As a result of this a large number of possible applications have emerged, ranging from processes for extraction, reaction, and material processing to waste treatment (Perrut, 2000, Mesiano et al., 1999, Wells and DeSimone, 2001). In Figure 7 a comparison is made between the major application areas dealing with SCFs based on the number of articles. A shift in activities can be seen from the extraction and analytical applications to the reaction/catalysis type of applications (Eckert et al., 1996, Jessop and Leitner, 1999, Oakes et al., 2001).

Carbon dioxide is the most commonly used supercritical fluid. This is primarily due to its reasonable low critical temperature and pressure (304 K and 7.4 MPa), low cost, non-flammability, and non-toxicity. Examples of applications based on compressed or supercritical CO$_2$ include the extraction of caffeine, spray painting, various polymerizations, particle formation by rapid expansion from supercritical solution and precipitation with a compressed fluid anti-solvent to form microparticles and fibers (McHugh and Krukonis, 1994, Johnson and Lemert, 1996, Cooper et al., 2000). It is one of the few organic solvents that is
not regulated as VOC (volatile organic compound) by the U.S. Environmental Protection Agency (EPA). However, several other SCFs have also been used in both commercial and development processes.

![Graph showing the number of articles and patents dealing with SCF since 1957. This is based on the presence of the word supercritical in the title or abstract, according to Scifinder.]

Figure 6: The number of articles and patents dealing with SCF since 1957. This is based on the presence of the word supercritical in the title or abstract, according to Scifinder.

![Graph showing the number of articles dealing with the combination of supercritical and chromatography, extraction, reaction or catalysis, based on the presence of these words in the title or abstract, according to Scifinder.]

Figure 7: Number of articles dealing with the combination of supercritical and chromatography, extraction, reaction or catalysis, based on the presence of these words in the title or abstract, according to Scifinder.
A steady stream of emerging technologies has brought carbon dioxide all the way from a potential alternative solvent in the early 1970s to its use in industries (Adam, 2000). The most recent example is DuPont's announcement to build a 275 M$ manufacturing plant that will employ carbon dioxide technology to produce teflon and other fluoropolymers. The most promising applications of SCFs are those in which their unusual properties can be exploited for manufacturing products with characteristics and specifications that are difficult to obtain by other processes. In the case of the synthesis of fluoropolymers by DuPont the exceptional high solubility of fluorinated molecules in carbon dioxide is exploited, which is very difficult to achieve with standard solvents.

Outline of this thesis

Despite the obvious advantages of high density CO$_2$, there are still a number of issues that need to be resolved before further large-scale applications will be possible. One of the limiting factors is the fact that it is a very poor solvent for high molecular weight or hydrophilic molecules, such as amino acids, proteins, and many polymers, due to its very low values of the dielectric constant, $\varepsilon$, and polarizability per volume, $\alpha/v$. One way to make CO$_2$ suitable for dissolving these molecules is by making use of amphiphiles (surfactants) to create reverse micelles or microemulsions (in the literature there is often no clear distinction being made between the two). Additionally, economically and energetically efficient regeneration methods of high-pressure carbon dioxide are lacking. In this thesis both problems, with an emphasis on catalysis, are being addressed. Chapters 2, 3, and 4 discuss carrier-mediated processes in carbon dioxide. In Chapter 2, beside an overview of the available surfactants, guidelines are presented for the design of suitable surfactants for downstream processing of biomolecules in carbon dioxide. In Chapters 3 and 4 functionalized dendritic macromolecules are used as extractive agents and as multi-site phase transfer catalysts. These dendritic macromolecules, or so-called unimolecular micelles, provide a favorable micro-environment for anionic species, otherwise insoluble in supercritical carbon dioxide. The use of microporous silica membranes in supercritical carbon dioxide is discussed in Chapters 5 and 6 from a fundamental and a practical point of view. The fundamental aspects of transport of supercritical carbon dioxide through these membranes are described in Chapter 5. In Chapter 6 the membranes are used to retain homogeneous catalysts solubilized in supercritical carbon dioxide and a concept for a continuous homogeneously catalyzed process is proposed. The feasibility has been demonstrated using a hydrogenation reaction. Finally, Chapter 7 discusses different strategies to perform micro-heterogeneous catalysis in supercritical carbon dioxide.

The main purpose of the research described in this thesis is to enlarge the operating window of carbon dioxide. The interesting characteristics of carbon dioxide are explored, while the difficulties related to the solubility are circumvented. The methodologies presented in this
thesis are of relevance for the further development of clean chemical processes carried out in environmentally friendly high-density gases.

**Literature**

Adam, D., Clean and green … but are they mean?, Nature, 407, 938 (2000).


Chapter 1
Chapter 2

Design of Fluorinated Surfactants for Use in Supercritical Fluids

Abstract
Liquid and supercritical carbon dioxide as a replacement of organic solvents will facilitate the development of clean processes. A general disadvantage of carbon dioxide is, however, that it is a poor solvent for high molecular weight or hydrophilic molecules. A way to overcome its solubility problem is by using surfactants. In this chapter the focus is on the design and use of twin-tailed surfactants for applications in high-density carbon dioxide. The solubility in carbon dioxide of four twin-tailed surfactants with different tail lengths is studied. A clear effect of the length of the surfactant tail on the solubility can be observed. This surfactant is capable of solubilizing a large amount of water in carbon dioxide. The application of these surfactants as an extractive agent for proteins is evaluated.

Chapter 2

Introduction
Increasing concern regarding the dissemination of volatile organic compounds, chlorofluorocarbons and aqueous waste streams into the environment has prompted the chemical industry to conform to more environmentally sound practices in the manufacture and processing of products. It is generally thought, that the use of supercritical solvents provides a powerful means to achieve these goals (McHugh and Krukonis, 1994, Johnston and Lemert, 1996).

A supercritical fluid is a substance above its critical temperature and critical pressure. Unlike the compression of a gas below its critical temperature, which normally causes a phase separation and the appearance of a separate liquid phase, compression of a supercritical fluid (SCF) results only in an increase in the density of the SCF and not in the formation of a second liquid phase. As a result of this pressure dependence of the density, a continuum of densities ranging from vapor-like to liquid-like can be obtained by varying the pressure while holding the temperature constant. At conditions near the critical point of the SCF, small changes in the pressure result in large density changes and changes in other important physical properties, such as viscosity, dielectric constant and solvent strength (McHugh and Krukonis, 1994).

Carbon dioxide is the most commonly used SCF, primarily due to its reasonable low critical temperature and pressure (304 K and 7.4 MPa), its low cost, and because it is non-flammable and non-toxic. Examples of applications based on compressed or supercritical CO₂ include the extraction of caffeine, spray painting, various polymerizations, particle formation by rapid expansion from supercritical solution and precipitation with a compressed fluid antisolvent to form microparticles and fibers (McHugh and Krukonis, 1994). It is one of the few organic solvents that is not regulated as VOC (volatile organic compound) by the U.S. Environmental Protection Agency (EPA). However, several other SCFs have also been used in small and large scale operation.

One of the main disadvantages of carbon dioxide is the fact that it is a poor solvent for high molecular weight or hydrophilic molecules, such as amino acids, proteins and many polymers, because of its low dielectric constant, ε, and polarizability per volume, α/v. One way to make CO₂ suitable for dissolving these molecules is by making use of amphiphiles (surfactants) to create reverse micelles or microemulsions (in the literature there is often no clear distinction between the two). Micelles are flexible aggregates of amphiphiles that are formed above a certain temperature (Krafft point) and concentration (critical micelle concentration). Due to their structure (a hydrophobic and a hydrophilic moiety), amphiphiles tend to form aggregates as a result of self-assembly. The hydrophilic parts (often referred to as head groups) prefer to be in contact with an aqueous phase, whereas the lipophilic parts, called tails, will direct themselves towards a nonpolar phase. Depending on the continuous phase being aqueous or nonpolar, the surfactant will form micelles or reverse micelles, respectively. The spontaneous
curvature of reverse micelles corresponds to the energetically favorable packing configuration of the surfactant molecules at the interface (Pileni, 1993, Villamagna et al., 1995).

Gale et al. (1987) reported the first experimental evidence for the formation of reverse micelles in a supercritical fluid. Using sodium bis (2-ethylhexyl)-sulfosuccinate (aerosol - OT also known as AOT) it was possible to dissolve up to 10 water molecules per surfactant molecule (this ratio is the so-called $w_0$) in liquid propane at 383 K and 25 MPa. In supercritical ethane at 310 K and 25 MPa a $w_0$ of about 5 has been obtained. However, applications of reverse micellar systems in alkanes are limited due to a number of considerations, such as a relatively high critical temperature, flammability, solvent costs, and solvent toxicity (Bartscherer et al., 1995).

More than 130 commercially available surfactants have been tested by Consani and Smith (1990) for the formation of reverse micelles in supercritical carbon dioxide (scCO$_2$). The fact that the majority of the amphiphiles evaluated were found to have minimal solubility in CO$_2$, can be attributed to the poor CO$_2$ - hydrophobic interaction or the overwhelming favorable water - hydrophilic and hydrophobic - hydrophobic associations. This suggests that hydrophobic tail - tail interactions outweigh CO$_2$ - tail interactions in these systems. Nonionic surfactants, on the other hand, appeared to be able to exhibit reasonable solubilities in CO$_2$ at moderate pressures. To date, little is known about the relative contributions of different interactions, including van der Waals interactions, polar interactions, particularly quadrupole - dipole and quadrupole - quadrupole interactions, and Lewis acid-base interactions to the solubility (O'Neill et al., 1998a). Micelle-micelle interactions, which govern the phase behavior of certain systems at relatively low surfactant and water concentration, are also of importance. Upon an increase in water content, phase separation occurs when the micelles become large enough such that the attractive interactions cause them to coalesce to form a microemulsion-droplet rich phase ("liquid") and a microemulsion-droplet depleted phase ("gas"). Three possible mechanisms of attractive micelle - micelle interactions governing this type of phase behavior have been proposed for supercritical fluids.

1) Inter-droplet van der Waals interactions between the hydrocarbon tails and the aqueous cores of the droplets (Tingey et al., 1990). These inter-droplet interactions are dependent on the temperature, droplet radius, hydrocarbon tail length, and the nature of the continuous solvent phase.

2) Another attractive force is due to overlap of the tails and the entanglement between two micelles which leads to strong, very short-range interactions (Lemaire et al., 1983).

3) A solvent exclusion effect is proposed where small solvent molecules penetrate the micelle tails leading to a higher density layer of solvent around the micelle (a clustering effect) (Peck and Johnston, 1993). This mechanism involves two micelles moving together, displacing solvent molecules from the tail region into the bulk solvent. This leads to an increase in their molecular volume and a net effective attractive force between the two micelles (Jackson and Fulton, 1996).
Chapter 2

The reverse micellar phase behavior in SCFs like ethane and propane is remarkably different from that in “normal” nonpolar liquids. Increasing the fluid pressure causes the amount of solubilized water to increase, indicating that the higher molecular weight structures are better solvated by the denser fluid phase. The phase behavior of these systems may be attributed in part to packing constraints of the surfactant molecules and the solubility of large micellar aggregates in the SCF phase. By changing pressure and/or temperature, a tool is available to manipulate the reverse micelles. This applies not only to the size of the micelle, but also to the uptake of solutes in the micelle.

Applications of surfactants in scCO₂ for the downstream processing of biomolecules

CO₂ - surfactant formulations open the way to a whole spectrum of novel processes, including dispersion and emulsion polymerizations, extractions, and the preparation of drug carriers. In Table 1 some applications of surfactants are listed.

Table 1: Applications of surfactants in scCO₂.

<table>
<thead>
<tr>
<th>Application</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>Downstream processing</td>
<td>Johnston et al., 1996, This Chapter</td>
</tr>
<tr>
<td>Environmental separations</td>
<td>Yazdi et al., 1996, 1997</td>
</tr>
<tr>
<td>Enhanced chromatography</td>
<td>Jiménez-Carmona et al., 1998</td>
</tr>
<tr>
<td>Industrial cleaning</td>
<td>Dahmen et al., 1998</td>
</tr>
<tr>
<td>Dispersion polymerization</td>
<td>O'Neil et al., 1998b</td>
</tr>
<tr>
<td>Emulsion polymerization</td>
<td>McClain et al., 1996</td>
</tr>
<tr>
<td>Polymer shaping</td>
<td>Sparacio and Beckman, 1997</td>
</tr>
<tr>
<td>Enzymatic catalysis</td>
<td>Holmes et al., 1998</td>
</tr>
<tr>
<td>Dry cleaning</td>
<td>Jureller et al., 1997, DeSimone et al., 1998</td>
</tr>
<tr>
<td>Formation of materials via phase separation</td>
<td>Mawson et al., 1997</td>
</tr>
<tr>
<td>Enhanced oil recovery</td>
<td>Irani et al., 1990</td>
</tr>
<tr>
<td>Heterogeneous reactions</td>
<td>Jacobsen et al., 1999, Chapter 7</td>
</tr>
</tbody>
</table>

In this chapter the emphasis will be on downstream processing of biomaterials. In the past two decades, the production of biochemicals has increased tremendously. The technology for separating biological products from the media in which they are produced, however, has not kept pace with the advances in synthesis and production (Stephanopoulos, 1993). The concentration of the product in the medium from which it must be recovered is a key issue for the costs involved. Very dilute streams lead to extremely high purification costs (Figure 1). This is mainly due to the fact that the separation of biochemicals usually requires a large
number of different steps, which are performed consecutively, often being batch-type, and in small-scale operations like column chromatography and filtration. An efficient and scaleable bioseparation process is fluid - fluid extraction with reverse micelles. The ability to extract a wide range of polar solutes, including proteins, from dilute complex aqueous solutions with reverse micelles in an organic solvent has been studied extensively (Pires et al., 1996, Dekker et al., 1989, Göklen and Hatton, 1985). The dominant interaction for the protein uptake by ionic surfactants is the electrostatic interaction between the anionic headgroup of the surfactant and the positive charge of the protein at a pH lower than the isoelectric point. Besides losses of the organic solvent, the disadvantage of using reverse micelles as extractive agents is that high amounts of salts are produced in the different neutralization steps involved. One way to circumvent these problems is using supercritical fluids instead of organic solvents (Fulton and Smith, 1993).

![Diagram of biomolecules and concentration](image)

**Figure 1:** Relation between the price of biomolecules and the concentration of the biomolecules in the starting material (Haggin, 1988).

Several research groups have demonstrated the principle of extracting proteins using reverse micelles in supercritical carbon dioxide. The group of Johnston (University of Texas at Austin) was the first to extract bovine serum albumin (MW=66 200 Da) with a perfluoropolyether (Johnston et al., 1996). With the help of a labeled protein, it was shown that the thermodynamically stable aqueous domains in the CO₂ continuous phase have a polarity that is nearly the same as that of bulk water. The group of Beckman (University of Pittsburg) was able to extract _subtilisin Carlsberg_ with surfactants based on perfluoropolyethers. After recovery of the enzyme, only 20% of the activity was lost (Ghenciu et al., 1998). The affinity extraction of avidin was also investigated in CO₂. The specificity of
the extraction was based on avidin-biotin bioaffinity. In order to accomplish the extraction of avidin, biotin-functional fluoroether surfactants were employed. Two different extraction procedures were followed: one based on the formation of an inverse emulsion and a second one based on the formation of a three-phase emulsion. Moreover, it was demonstrated that a hydrophilic spacer between the tails and the biotin headgroups increases the extraction efficiency by a strong binding of avidin to biotin (Ghenici et al., 1997). As an alternative, DeSimone and coworkers (University of North Carolina at Chapel Hill) extracted bovine serum albumin with a block copolymer composed of fluorinated acrylates and polyethylene glycol segments (DeSimone et al., 1998).

In Figure 2 a tentative scheme for downstream processing is suggested, in which the regeneration of the surfactant is achieved by changing pressure and/or temperature. By changing the operating conditions water is withdrawn from the interior of the reverse micelle and precipitation of the protein will occur. It has already been shown that this method of precipitating a protein from reverse micelles (removing water from the interior of the reverse micelle) works in organic solvents using a molecular sieve (Gupta et al., 1994). Using this regeneration procedure, a general drawback associated with many supercritical processes can be circumvented, namely the energy-intensive procedure of a complete pressure release followed by recompression to supercritical conditions. It is anticipated that only a minor shift in pressure or temperature will be required for the process described above.

![Diagram](image_url)

Figure 2: Tentative process scheme for downstream processing with reverse micelles in CO₂.
Important for the stability of the protein and for the extraction efficiency is the pH of the aqueous phase. Over the temperature range of 298 – 343 K and the pressure range of 7 – 20 MPa, the pH of water in contact with scCO$_2$ ranges between 2.80 and 2.95 (Toews et al., 1995). Furthermore, carbon dioxide forms reversible complexes with the free amine groups at the surface of the protein, which potentially leads to denaturation of fragile proteins (Kamat et al., 1995, Zagrobelny and Bright, 1992). This implies that process conditions will have to be chosen carefully, and that extraction using scCO$_2$ might only be suited for specific biomolecules. The desired biomolecules will have to be able to endure a low pH, and should have a sufficiently rigid structure to withstand the temporary chemical modification by carbon dioxide.

**Design of surfactants suited for scCO$_2$ applications**

Three criteria can be identified for surfactants to be able to form water-containing reverse micelles in CO$_2$:

1. The tail(s) should be highly “CO$_2$-philic”, which requires a low cohesive energy density. Strong CO$_2$ - tail interactions favor solubilization in CO$_2$, bending of the interface around water, and weak micelle - micelle interactions.
2. To the head group at least two tails should be attached or the tail should be branched to create the right curvature.
3. The head group should form hydrogen bonds with water as a driving force for aggregation. Otherwise, the surfactant may prefer to form a condensed phase instead of reverse micelles in CO$_2$.

Hoefling et al. (1992, 1993) have synthesized surfactants with favorable tail - CO$_2$ interactions. For this purpose, functional groups characterized by low solubility parameters, low polarizability parameters and possessing Lewis bases such as dimethyl siloxanes, hexafluoropropylene oxides, and fluoroalkyl groups were chosen. The synthesized surfactants displayed relatively high solubility in CO$_2$ at moderate pressures. Solutions of several surfactants in CO$_2$ were able to extract thymol blue, a hydrophilic dye, from an aqueous solution. Subsequently, a repeating fluorinated ether functional group (hexafluoropropylene oxide) has been incorporated into a polymer to increase the solubility in CO$_2$ (Harrison et al., 1994). Poly-(hexafluoropropylene oxide) is the most CO$_2$-philic soluble polymer observed to date, and surfactants with perfluoroalkyloxypolyether tails exhibit extremely high carbon dioxide solubility (Singley et al., 1997). Calculations on systems containing CO$_2$ and fluorocarbons indicate that the CO$_2$ molecules orient around the CF$_2$ segments by sandwiching the positively charged CO$_2$ carbon between two negatively charged fluorine atoms (Cece et al., 1996).

CO$_2$-philicity of the tail of the surfactant can be enhanced by incorporating groups in the tail with a low solubility parameter, low polarizability and/or electron donating capabilities (considering the fact that CO$_2$ is a weak Lewis acid) (Diep et al., 1998, Meredith et al., 1996).
For the CO₂-philic part of a surfactant poly(propylene oxide), fluoroalkyl, fluoroether, fluoroacrylates, siloxane and acetylenic alcohols can be used (Figure 3).

Figure 3: Groups used for increasing solubility of surfactants in CO₂. ① = acetylenic alcohols (Wilkinson et al., 1998), ② = poly (propylene oxide) (Johnston et al., 1997), ③ = poly (hexafluoro-propylene oxide) (Singley et al., 1997), ④ = poly (1,1-dihydroperfluoro-octylacrylate) (DeSimone et al., 1994), ⑤ = siloxane (Hoefling et al., 1992).

The ability to form reverse micelles in CO₂ depends on the molecular geometry (Figure 4a) and the presence of water (Figure 4b). One way to illustrate the importance of the molecular geometry, is by making use of the R ratio, which compares on a qualitative basis the balance of the individual cohesive energies, $A$, of the functional groups present at the interface. This ratio can be used to predict whether micelles or reverse micelles will be formed:

$$R = \frac{A_{lc} - A_{cc} - A_{ll}}{A_{bw} - A_{ww} - A_{hh}}$$

where $A_{lc}$ stands for the interaction between the lipophile and CO₂, $A_{cc}$ is the CO₂ - CO₂ interaction, $A_{ll}$ is the lipophile - lipophile interaction, $A_{bw}$ is the hydrophile - water interaction, $A_{ww}$ is the water - water interaction and $A_{hh}$ is the hydrophile - hydrophile interaction. The cohesive energy $A_{bw}$ and $A_{lc}$ promote the miscibility of the amphiphilic compound with the aqueous region and the CO₂ region, respectively. Both $A_{hh}$ and $A_{ww}$ oppose miscibility with water and, likewise, both $A_{cc}$ and $A_{ll}$ oppose miscibility with CO₂. Therefore, $R < 1$ yields

20
micelles in water, $R > 1$ yields reverse micelles in CO$_2$, and $R = 1$ yields surfactant residing primarily in a middle phase in equilibrium with the aqueous and CO$_2$ phase, respectively.

Figure 4a: Molecular geometry of an ideal surfactant for the formation of a reverse micelle in organic solvents (Pileni, 1993) or supercritical fluids.

Figure 4b: Schematic picture of a reverse micelle in organic solvent or supercritical fluids. Type 1 is the water layer associated with the headgroup of the surfactant. Type 2 is the water layer, which resembles bulk water.
Experimental

Materials - Perfluorobutyl, hexyl, octyl and decyl-iodide and 1,3 di-bromobenzene were supplied by Aldrich. Copper bronze (also supplied by Aldrich) was activated by HCl prior to use. The solvents dimethylsulfoxide (DMSO) and diethylether were of analytical grade, and demineralized water was used throughout.

Bovin serum albumin (BSA) and BSA labeled with fluorescein isothiocyanate (12 mol/mol) were purchased from Sigma and were used without further purification.

Surfactant synthesis - Dialkyl benzyl sulfuric acids based on perfluoroalkyliodide and 1,3 dibromobenzene were synthesized using copper-mediated cross coupling. The relatively mild conditions employed here yield the desired product in high yield, with only the 1,3-product being observed. The methodology used is similar to the methodology used by Van den Broeke et al. (2001). For a schematic diagram of the total synthesis route see Figure 5.

\[
\begin{align*}
2 \cdot CF_3-(CF_2)_n-I & \quad + \quad \text{Copper bronze} \\
& \quad \text{DMSO} \quad 388 \ K \\
& \quad \text{Br} \quad \text{Br} \\
\text{n} & =4,6,8 \ or \ 10 \\
\end{align*}
\]

1. fuming sulfuric acid
2. NaCl

\[
\begin{align*}
\text{Na}^+ & \quad \text{O}^- \quad \text{SO}_4^2- \\
& \quad \text{Br} \quad \text{Br} \\
& \quad \text{CF}_3-(CF_2)_n-\text{CF}_3 \\
\end{align*}
\]

Figure 5: Synthesis scheme of the twin-tailed fluorinated surfactants.

For the perfluorooctyl twin-tailed surfactant, F8, the synthesis route is given in more detail below. Into a 100 mL three-necked flask equipped with a thermometer, stirrer and a condenser with a nitrogen gas inlet, copper bronze powder (4 g), C_8F_17I (3 g) dibromobenzene (0.64 g) and DMSO (40 mL) were added. The reaction mixture was heated to 388 K under a nitrogen atmosphere and an exothermic reaction was observed. The temperature was carefully controlled between 388 and 398 K. After 8 hours an additional amount of 2 g of copper bronze and 2 g of C_8F_17I were added. After 48 hours the reaction mixture was cooled to room temperature and diethylether (20 mL) and water (30 mL) were added. The mixture was stirred and centrifuged. The organic layer was subsequently washed several times with water and was dried over anhydrous MgSO_4. Upon evaporation of the solvent, the product (2.1 g) was obtained in 86% yield as yellow oil.

1,3 di-perfluoroalkylbenzene (2 g) was added slowly to stirred fuming sulfuric acid (5 g) at 433 K. Initially, two layers were present, whereas after 28 h reaction time only one single
layer was present. Pipetting the material onto ice water (15 mL) followed by salting out with solid sodium chloride (1 g), resulted in precipitation of a gray solid (2.0 g, 90 % yield) which failed to dissolve upon heating.

The synthesis of the other surfactants, with 4, 6 and 10 carbon atoms per tail, was carried out using the same procedure. These surfactants are named F4, F6 and F10, respectively.

*Phase behavior* - The microemulsion phase stability was determined by visual observation using a stirred high-pressure optical cell (Figure 6). This cell with a variable volume between 18 and 30 mL is equipped with two sapphire windows, a stirrer bar, Pt 100, heating jacket and a movable piston. The sample composition is defined in terms of surfactant concentration and a water-to-surfactant molecular ratio, \( w_0 \), which is a measure of the solubilization capacity of the microemulsion.

![Diagram of high-pressure setup](image)

*Figure 6: Experimental setup for high-pressure applications.*

*Dynamic light scattering* - High-pressure CO\(_2\) dynamic light scattering measurements were performed in a 2 mL high pressure viewing cell equipped with three sapphire windows (placed at 90° angles), a Pt 100 and a heating jacket (see Figure 7). A 30 mW He-Ne laser (Melles Griot 05-LHP-991, \( \lambda_0 = 632.8 \text{ nm} \)) was used as the light source. The diffused light at a fixed angle of 90° was detected and analyzed using a Coulter N4 plus dynamic light scattering apparatus. The concentration of the surfactant was 1·10\(^{-2} \text{ mol/L} \), while the ratio between water and surfactant molecules was varied between 10 to 25.
**Protein extraction** - The extractor used was the same high-pressure vessel as used in the phase behavior studies. This vessel was loaded with the surfactant and the aqueous solution of the protein. After addition of carbon dioxide until the desired pressure was reached, the mixture was stirred for 30 min. The extraction was followed by UV-vis spectroscopy (Spectronic Genesys 5). The initial volume ratio of water to carbon dioxide was 1:3. The initial concentration of the protein in the aqueous phase was $1.2 \cdot 10^{-3}$ mol/L and the concentration of the surfactants was $1 \cdot 10^{-2}$ mol/L in the CO$_2$ phase. This means that initially 1 protein molecule was present per 25 molecules of surfactant.
Results and discussion
According to the principles stated above a twin-tailed fluorinated surfactant was expected to be the most ideal surfactant. The two tails are required to allow for the correct curvature. The fluor atoms are responsible for the good solubility in carbon dioxide and for the steric repulsion between the micelles. The surfactants have been designed for the extraction of large biomolecules. Due to the relatively low pH caused by the scCO₂, the biomolecules are protonated in the aqueous phase. Therefore, the surfactant needs to have an anionic headgroup to allow for favorable electrostatic interactions between the headgroup of the surfactant and the surface of the protein. The anionic headgroup used in this study is a sodium sulfonate group. A phenyl group is used as the spacer between the twin-tailed perfluoroalkyl groups and the anionic headgroup (see Figure 8).

Phase behavior - The surfactants have been evaluated on the basis of two criteria: solubility and extraction capacity. The surfactants F4, F6 and F8 appear to be insoluble in carbon dioxide. Upon addition of a very small amount of water the solubility increases readily. This is probably due to the increased shielding of the anionic headgroup by the water molecules. Practically, this is a very good indication for the formation of surfactant assemblies in carbon dioxide. In Figure 9 it can be seen that the water to surfactant ratio is crucial for the phase behavior. The pressure required to solubilize aggregates with a $w_0$ of 25 is considerably higher than the pressure required to solubilize aggregates with a water to surfactant ratio of 10. Furthermore, the larger the surfactant, i.e. a higher fluorine fraction, the lower the pressure required to solubilize a certain amount of water in carbon dioxide.

Figure 8: Space-filling representation of the 1,3 bis-perfluoroocetyl benzyl sulfonate (F8) surfactant.
Figure 9: Cloud point measurements of perfluoroocetyl (F8) and perfluorodecyl (F10) twin-tailed surfactant for different water to surfactant ratio \(w_0\) at a surfactant concentration of 0.04 M.

The cloud point pressure increases with increasing \(w_0\) at a fixed temperature, which has also been observed for microemulsions formed in the presence of perfluoropolyether surfactants. This behavior is indicative of swelling of micelles with added water, which in turn strengthens attractive micelle-micelle interactions. Thus, higher pressures are required to increase tail-solvent interactions \(A_{\ell}\) to prevent phase separation \((R \approx 1)\).

Dynamic light scattering (DLS) is commonly used to measure hydrodynamic diameters of micelles, emulsions, and latexes from several nanometers up to 1-2 \(\mu\)m. DLS requires low concentrations of the dispersed phase to avoid the effects of multiple scattering and droplet-droplet interactions on the measured droplet size. Yates et al. (1997) have used DLS to obtain the size of micellar structures in supercritical xenon, ethane, and propane.

From DLS experiments at 29.5 MPa CO\(_2\) and 293 K it follows that the radius of the aggregates of F8 with a \(w_0\) equal to 25 is around 4 - 5 nm in diameter. With a \(w_0\) of 10 the radius obtained for the same surfactant is around 2 - 3 nm in diameter (see Figure 10). There is hardly any difference between the F8 aggregates compared with the aggregates of F10 at the same \(w_0\). The area per surfactant molecule is approximately equal to 90 Å\(^2\) (at a \(w_0\) of 10) and 110 Å\(^2\) (at a \(w_0\) of 25), respectively. These relatively high values in comparison with standard reverse micelles in conventional organic solvents is also found in molecular simulations (Salaniwal et al., 2000, 2001a and 2001b). The size of the F8 aggregates is comparable to the size of aggregates of twin-tailed hybrid surfactants used by Guo et al. (1992). The size of the aggregates, using the surfactants made by Guo, is measured to be in the order of 4 - 7 nm in diameter, using small angle neutron scattering measurements (SANS) (Eastoe et al., 1996). In conclusion the interaction between the headgroup of the surfactant in
this configuration is rather low and that there is no close packing of the tails. The last conclusion could be expected due to the low cohesive energy density of the fluoroalkyl groups.

![Graph showing weight distribution vs size](image)

Figure 10: Dynamic light scattering results for F10 at a $w_o$ of 10 and 25 at 298 K and 29.5 MPa carbon dioxide.

From these SANS experiments it can be concluded that amphiphilic molecules behave very differently at the CO$_2$ - water interface as compared to the behavior of surfactants at organic - water interfaces (Dong et al., 2002). The interfacial area occupied per surfactant molecule in water-in-CO$_2$ microemulsions is usually much larger than in water-in-oil microemulsions. The unusually large areas have been attributed to the lower interfacial tension of the CO$_2$-water interface of about 20 mN/m (at moderate pressures), as compared to 40 - 50 mN/m, which is generally observed in conventional oil - water systems. From the analysis of the probability distribution of the interfacial height and width (molecular modeling) it follows that there is a sharp CO$_2$ - water interface at the molecular level (daRocha et al., 2001) and not a relatively diffuse interface layer. Another factor that contributes to the larger areas occupied by surfactant molecules is the more intensive penetration of CO$_2$ molecules into the tail region of the surfactant monolayer due to the small size of the molecules, as compared to the size of conventional organic solvent molecules.

Protein extraction - Serum albumins are transport proteins, with the capability to bind a variety of small molecules: fatty acids, amino acids, steroids, and calcium ions, as well as numerous pharmaceuticals. Bovine serum albumin (BSA), with a molecular mass of 66 200 Da, consists of 581 amino acids in a single polypeptide chain. Stabilized by 17 disulfide
bridges, BSA folds into a shape that can roughly be described as an equilateral triangle with sides of about 8 nm and a thickness of about 3 nm. This is in the same order as the size of a reverse micelle with a $w_0$ of 25. BSA has an isoelectric point of 5.2 and it is known that it can undergo conformational changes at both low and high pH (Vasilescu et al., 1999). At the conditions studied, BSA is stable and the majority of the groups on the surface of the protein are protonated providing a good interaction between the protein and the head group of the fluorous surfactants.

The extraction behavior of BSA is studied using the dye-labeled version of this protein. The dye used for labeling the BSA, fluorescein isothiocyanate, is pH sensitive. In Figure 11 the UV-vis spectra of the dye-labeled BSA is given for three different environments: water at neutral pH, water at pH 2.5, and the dye-labeled BSA in a surfactant-water aggregate in high-density carbon dioxide. The spectrum obtained in carbon dioxide is quite similar with the spectrum obtained in a water phase with pH 2.5. This indicates that during the extraction with high-density carbon dioxide the BSA proteins experience an aqueous surrounding with a relatively low pH. The low pH found in the interior of the micelles is consistent with the pH found in water / perfluoropolyether surfactant aggregates (Niemeyer and Bright, 1998). The exact position of the BSA molecule in respect to the geometry of the host (reverse micelle) is difficult to elucidate.

![UV-vis spectra of dye labeled BSA in three environments: water (pH=7.0), water at pH 2.5, and liquid carbon dioxide at 30 MPa and 298 K with F10.](image)

Figure 11: UV-vis spectra of dye labeled BSA in three environments: water (pH=7.0), water at pH 2.5, and liquid carbon dioxide at 30 MPa and 298 K with F10.
Figure 12: Extraction behavior of labeled BSA with perfluorooctyl (F8) and perfluorodecyl (F10) twin-tailed surfactant. The surfactant concentration is 0.03 M. The reciprocal of the extraction efficiency is defined as the number of surfactant molecules divided by the number of extracted protein molecules.

At the conditions studied the micelles filled with only water have a $w_0$ of about 30. In Figure 12 the results of the reciprocal of the extraction efficiency for the extraction of dye-labeled BSA by the F8 and the F10 surfactants are compared. The reciprocal of the extraction efficiency is defined as the number of surfactant molecules divided by the number of (extracted) protein molecules. The extraction efficiency is given as a function of the temperature for four different cases. The number of proteins extracted decreases with an increase in temperature. This is consistent with measurements in organic solvents (Dekker et al., 1991). Furthermore, at a given temperature the largest surfactant, i.e. F10, is capable of extracting more proteins per surfactant molecule. Probably, the larger $A_{lc}$ results in larger reverse micelles, which in turn result in a higher extraction capacity. There is also a clear effect of the pressure, as upon an increase in pressure more proteins are extracted for all cases. This effect is also directly related to a higher $A_{lc}$ and thus with a higher $R$ ratio. Clearly it can be stated that a good tail – carbon dioxide interaction is crucial for a successful application for protein extraction. Finding better and cheaper CO$_2$-philic groups is expected to be essential for the development of industrial downstream processing of biomolecules.

Conclusions
Four different twin-tailed fluorous surfactants have been designed and synthesized for scCO$_2$ applications. The surfactants have two identical perfluoroalkyl tails, varying in length between 4 and 10 carbon atoms. The design of this series of fluorous surfactants is based on
generic guidelines that maximize CO2-philicity on one hand, and that favor formation of reverse micelles on the other hand.

The solubility of the surfactants has been studied as a function of the pressure, temperature, tail length and the water to surfactant ratio. For the two shortest tails a low solubility is obtained. For the surfactants with a tail with 8 and 10 carbon atoms it is found that there is some water and a minimum density of CO2 required to solubilize the surfactant - water aggregates. The area per surfactant molecule in carbon dioxide is quite large compared with organic solvents. For the two surfactants with a tail with 8 and 10 carbon atoms a good solubility is possible over a wide range of conditions and the surfactant can be used to extract BSA molecules.

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Chapter 3

Reactive Extraction with Functionalized Poly(propylene imine) Dendrimers

Abstract
Functionalized poly(propylene imine) dendrimers of different generations have been used to investigate the suitability of a multi-site system as an extractive agent for anionic organic molecules. The solubility of the dendrimers depends on the functionalization. Perfluoroocetyl functionalized poly(propylene imine) dendrimers have been studied for the reactive extraction of anionic species from an aqueous phase into a carbon dioxide phase. As a comparison palmitoyl functionalized dendrimers have been studied in tetrachloromethane. These extractive agents are capable of extracting a large number of dye molecules per dendrimer, including Rose Bengal, Methyl Orange, and New Coccine. The functionalized dendrimers can be envisaged as a unimolecular (polymerized) version of the traditional low molecular weight surfactant. As compared to the extraction into a traditional organic solvent with palmitoyl functionalized dendrimers, the number of available sites and affinity of the perfluoroocetyl functionalized dendrimers appears to be lower in carbon dioxide. No evidence could be found for significant cooperative or anti-cooperative effects on the extraction equilibrium. A description is given of the extraction mechanism, based on a mass action model.

1 This chapter is based on Equilibirum and kinetics of reactive extraction with functionalized poly(propylene imine) dendrimers, E.L.V. Goetheer, M.W.P.L. Baars, L.J.P. van den Broeke and J.T.F. Keurentjes, submitted for publication


Chapter 3

Introduction

Liquid-liquid reactive extraction is an efficient, economical, and environmental-friendly method to remove cationic or anionic species from aqueous systems. Reactive extraction is used in the recovery of acids and metal ions from waste streams (Eyal and Canari, 1995). It is also used to facilitate biochemical processes, which are limited by thermodynamics, by removing acidic products or by-products from the reaction medium. An example of this is the use of a cationic reactive agent to recover carboxylic acids from fermentation streams (Bora et al., 1997). Acidic extractants can extract positively charged (metal) ions, while basic extractants, e.g. containing amine groups, are capable of extracting anionic species from the aqueous phase to the organic phase. Aliphatic tertiary and quaternary amines are being used for reactive extraction of a large variety of anionic species (Juang et al., 1997; Poposka et al., 1998).

An interesting alternative to the organic solvent used in the standard reactive extraction processes is the use of supercritical carbon dioxide. Due to the low viscosity and high diffusivity of solutes in carbon dioxide, this solvent is ideal for processes with a need for rapid mass transfer. The use of standard organic solvents limits the practical use of the aqueous phase in contrast with carbon dioxide, which is environmentally friendly and non-toxic (McHugh and Krukonis, 1994). The solubility of the extracting agents in carbon dioxide is of crucial importance. There is at this moment one study in the literature available on the use of multi-site extractants in carbon dioxide. Cooper et al. (1997) demonstrated that a perfluoroalkylether modified 4th generation poly(propylene imine) dendrimer is soluble in carbon dioxide and capable of extracting dyes from an aqueous phase. These multi-site macromolecules have some interesting features compared with the more standard single-site reactive agents. Dendrimers are a relatively new class of macromolecules (Newkome et al., 1996; Bosman et al., 1997; Scherrenberg et al., 1998). In Figure 1 the first five generations of a poly(propylene imine) dendrimer are depicted. Each generation can be seen as the building block (template) for a next generation. In this way an onion-like structure is created with the different shells corresponding to the different building blocks.

The specific feature of these dendrimers is that the solubility and other properties can be controlled by attaching appropriate endgroups (Baars et al., 1997). For example, by functionalization with perfluoroalkyl or perfluoroalkylether groups good solubility of these macromolecules in carbon dioxide is obtainable. In Figure 2 a fifth generation palmitoyl poly(propylene imine) dendrimer and a third generation perfluorooctyl functionalized dendrimer are depicted. Upon functionalization with palmitoyl groups a good solubility is possible in conventional solvents. The number of tertiary amines depends on the generation, \( N_N \), of the dendrimers, according to \( 2^N \times 2^N \). In the case of a fifth generation dendrimer there are 62 tertiary amine sites. The highly branched, monodisperse structure leads to a number of interesting structural characteristics, like globular and void-containing shapes. These configurations can be used for host-guest interactions; guest molecules are confined in the
cavities of the host system and the host-guest interactions can be related to secondary interactions, like hydrophobic, hydrogen and electrostatic interactions. The special features of the poly(propylene imine) dendrimers, in particular the high polarity and the well-defined structure with a known number of tertiary amines, make these macromolecules suited for different applications. The compact dendrimer topology is promising for controlled release and confined chemical nanoreactors. This ranges from controlled drug release, the use as reagents in diagnostic imaging and therapy, via solubilization of inorganic compounds in organic media, the dispersion of polar dyes in hydrophobic polymers, preparation of inorganic-organic hybrid nanoparticles, to the design of microreactors and catalysts (Stephan et al., 1999; Pistolis et al., 1999; Sunder et al., 1999; Chechik et al., 1999).

Figure 1: Different generations of poly(propylene imine) dendrimer, ranging from generation 1 to 5.

It has been shown that functionalized dendrimers are capable of extracting a large number of anionic dye molecules per dendrimer in organic solvents (Baars et al., 1997). SAXS measurements indicate that the localization of the guests is preferential in the interior of the dendrimer (Baars et al., 2000). The presence of the tertiary amines in the core of the
dendrimer facilitates complexation with the anionic species, predominantly by electrostatic interactions.

![Diagram of a dendrimer](image)

**Figure 2:** Fifth generation dendrimer (64 endgroups) modified with palmitoyl tails and a third generation perfluorooctyl functionalized poly(propylene imine) dendrimer (16 endgroups).

This work focuses on the understanding of the kinetics and thermodynamics of a liquid-liquid/supercritical extraction process using functionalized poly(propylene imine) dendrimers. A better understanding of the different steps at the molecular level is relevant for both reactive extraction and phase transfer catalytic processes (see Chapter 4).

**Theory**

The mechanism for anionic species to be extracted into the interior of poly(propylene imine) dendrimers is governed by the formation of ion-pairs. The complexation behavior of dissociated acids is based on ion exchange with the counterions of the positively charged tertiary amines of the dendrimer. This can be written as

\[ iA^- + jX^-R^+ \rightleftharpoons nA^- (j-n)X^-R^+ + (i-n)A^- + nX^- \]  

(1)

with \( R^+ \) being the protonated tertiary amine, \( A^- \) and \( X^- \) the counterions. The original number of counterions \( A^- \) in the bulk is indicated by \( i \), whereas \( j \) indicates the number of counterions \( X^- \) originally present in the dendrimer, and \( n \) is the number of ions \( A^- \) at equilibrium in the dendrimer. The bars refer to the dendritic system.
Crucial for the exchange is the protonation of the tertiary amines. This protonation depends on the pH of the aqueous phase. The protonation behavior of the dendrimers is governed by short-ranged repulsive interactions between ionizable sites. This leads to a two-step protonation curve. This curve has two distinct steps for a non-functionalized poly(propylene imine) dendrimer, one around a pH of 6 and another one around 9, with an intermediate plateau at two-third of the total amount of ionizable groups. This intermediate plateau is caused by the onion-like way of protonation (Koper et al., 1997, Van Duivenbode et al., 1999).

To describe the ion-exchange mechanism based on protonated tertiary amines the mass action equilibrium model has been used (Coelho et al., 1996). Besides the interaction between the amine groups and the anionic species, it can be envisaged that the complexed anionic species have an interaction with each other. This means that the extraction of an anionic compound can depend on the actual loading of the dendrimer and on the interaction energy per tertiary amine. This interaction energy can be different for tertiary amines at different locations in the dendrimer. The most general expression for the amount extracted per multi-site dendrimer, at equilibrium, is given by

\[
q_B = \sum_{i=1}^{M} \left( \frac{q_{\text{max},i} - p \cdot q_B}{c_A} \right)^p \frac{c_B}{K_i} \tag{2}
\]

with \(q_B\) the extracted amount of dye per dendrimer, and \(q_{\text{max}}\) the maximum possible number of dye molecules to be extracted by a single dendrimer. \(c_A\) is the concentration of the solute in the aqueous phase that is to be exchanged for the dye, \(c_B\) is the concentration of the dye in the aqueous phase, \(p\) is the number of electrostatic interactions between the solute to be extracted and the amine groups in a dendrimer, and \(K\) is the reaction equilibrium constant. The subscript \(i\) denotes the number of tertiary amines per dendrimer. It is noted that the reaction equilibrium constant \(K\) is a function of the temperature. In principle, it is expected that for a constant number of tertiary amines, \(M\), the maximum loading \(q_{\text{max}}\) is constant and independent of the temperature.

The transport part of the extraction process of the acid into the aqueous phase can be evaluated with the following basic transport equation

\[
N_B = -\frac{d(V \cdot c_B)}{dt} = k_c \cdot S \cdot (c_B - c_B^*) \tag{4}
\]

in which \(N_B\) is the flux of the anionic species \(B\), and \(S\) is the surface area between the two phases. The dye concentration in the water phase at equilibrium is indicated by \(c_B^*\), the mass transfer coefficient of the dye molecule in the aqueous phase is given by \(k_c\). The volume of the
water phase is given by $V_w$. The transport in the solvent phase has been studied using a similar relation.

For the anionic species A and B the following reaction equation can be written

$$B^- + \bar{A} \xleftrightarrow{k_f \over k_b} \bar{B} + A^- \tag{5}$$

with the bars indicating that the anionic species are complexed by the amine. The extraction kinetics is then given by

$$-\frac{d(q_B \cdot c_D)}{dt} = k_f \cdot S \cdot c_A^+ \cdot q_B \cdot c_D - k_b \cdot S \cdot c_B^+ \cdot q_A \cdot c_D \tag{6}$$

c_D is the dendrimer concentration and $q_A$ is the amount of counterions per dendrimer, which are not dye molecules. $c_A^+$ and $c_B^+$ are the concentrations of the counterion and the dye in the aqueous phase at the interface, respectively. In the case of equation (6) the interfacial concentration, and not necessarily the bulk concentration, determines the rate of extraction. After integration equation (6) yields

$$t = \ln \frac{\bar{k}_f \cdot q_{\max}}{(\bar{k}_f + \bar{k}_b) \cdot (q_{\max} - q_B) - \bar{k}_b \cdot q_{\max}} \tag{7}$$

with $\bar{k}_f = k_f \cdot c_A^+ \cdot S \over V_O$ en $\bar{k}_b = k_b \cdot c_B^+ \cdot S \over V_O$.

**Experimental**

*Materials* - For the organic phase tetrachloromethane was used as received from Aldrich. For details of the synthesis of the third and fifth generation palmitoyl functionalized poly(propylene imine) dendrimers the reader is referred to Baars et al. (1997). Carbon dioxide (grade 5.0) was obtained from Hoekloos (Amsterdam, The Netherlands). The perfluoro functionalized dendrimers were synthesized in-house. For the synthesis a solution of the poly(propylene imine) dendrimer in tetrahydrofuran was added to an equimolar amount of pentadecafluorooctanoyl chloride. The precipitate formed was filtered and dried in vacuo. This yielded the fluorinated dendrimer in the protonated form as a HCl-salt, as white solid. $^1$H-NMR (CDCl₃/C₆H₅COO⁻ = 99:1) indicated complete reaction of the fluorinated endgroups with the amine-endgroups of the dendritic scaffold, with $\delta$(CH₂NHCO)= 3.3 ppm.
During the extraction experiments a phosphate buffer (Aldrich) was used to maintain a constant pH. The water used in this work was deionized by a Millipore Milli-Q water system. For the dye molecules Methyl Orange, obtained from Acros Chimica, Rose Bengal, purchased from Fluka, and New Coccine, obtained from Aldrich, were used. These anionic dyes are depicted in Figure 3.

![Rose Bengal](image1.png)

![Methyl Orange](image2.png)

![New Coccine](image3.png)

Figure 3: The anionic dyes used.

*Equilibrium experiments* - The extraction equilibrium experiments were carried out in a 4 mL glass screw vessel. The extraction system is obtained by mixing 1.8 mL of an aqueous solution of the dye with 1.8 mL of 1.0·10⁻⁵ mol/L solution of a third generation or a 2.3·10⁻⁶ mol/L solution of a fifth generation poly(propylene imine) dendrimer modified with palmitoyl tails. The pH was checked with a pHM220 lab pH meter from Radiometer Copenhagen. The extractions were carried out at a temperature of 293, 313, and 333 K (± 1 K). The extraction vessels were gently shaken for at least five days before measuring the concentration of the dye in the organic and the aqueous phase. The concentrations of the organic and aqueous phase were measured using absorption spectra. Absorption spectra in the UV-vis range were recorded on a Perkin-Elmer Lambda 3 UV-vis spectrophotometer or on a Perkin Elmer Lambda 900 UV-vis-NIR spectrophotometer. For all measurements, the concentration of the extracted dye in the organic phase and the calculated concentration of the dye from the
measured concentration in the aqueous phase were within 5% deviation. Therefore, the extraction yield was determined from the absorption spectra obtained for the aqueous phase.

**High-pressure apparatus** - In the reactive extraction experiments at elevated pressures a high-pressure reactor of 80 mL was used. The volume of the reactor could be varied with a piston between 60 and 80 mL. The reactor was equipped with two opposite sapphire windows, a magnetic stirrer bar, and a Pt-100 resistance thermometer. The reactor was pressurized using an LKB HPLC pump, and the pressure was monitored by a Meyvis 802-C pressure module. Samples could be taken from the aqueous and the carbon dioxide phase with a loop, at a constant pressure provided by the piston. A high-pressure viewing cell of 2.2 mL could be attached to the high-pressure reactor to obtain UV-vis absorption spectra for both phases. During the measurements of the absorption spectra of the carbon dioxide phase great care was taken to avoid the formation of water droplets or a liquid film on the sapphire windows. The experimental set-up is schematically depicted in Figure 4. In all experiments the carbon dioxide to water volumetric ratio was equal to unity.

![Diagram](diagram.png)

**Figure 4:** The high-pressure apparatus used for the extraction of anionic dyes.

**High-pressure equilibrium experiments** - First, the perfluorooctanoyl functionalized poly(propylene imine) dendrimer was transferred into the high-pressure reactor. The reactor was then pressurized with carbon dioxide to a set-point of 30 MPa at 313 K. Using the piston a part of the content of the reactor was pumped, at constant pressure, into the high-pressure viewing-cell. In the viewing-cell 1.1 mL of an aqueous solution of Methyl Orange was present.
UV-vis absorption spectra of Methyl Orange extracted with the dendrimer into the carbon dioxide phase, were recorded with a Spectronic Genesys 5 Spectrophotometer. The extraction yield was determined by measuring the UV-vis absorbance of the carbon dioxide phase using the UV-vis extinction coefficient for aqueous solutions (Cooper et al., 1997).

*Kinetic experiments* - The kinetic experiments in tetrachloromethane were carried out in a sealed cuvet, with an interfacial area of about 1 cm², equipped with a small stirrer bar in the non-aqueous phase. The stirring was such that the organic phase was well mixed without disturbing the interface. The dye concentration in the aqueous phase is 1·10⁻³ mol/L and the dendrimer concentration is for a third generation dendrimer 5·10⁻⁶ mol/L and for the fifth generation dendrimer 1·10⁻⁶ mol/L. It was not necessary to stir the aqueous phase due to the high concentration of the dye in the aqueous phase, relative to the concentration of the dendrimer in the solvent phase. In a typical experiment, 1.6 mL of the organic phase was brought into the cuvet, subsequently 2 mL of the aqueous dye solution was gently poured on top of the solvent phase. It was possible to perform the extraction at a different temperature by using a heating jacket while measuring the absorption spectra of the organic phase. To follow the extraction rate, absorption spectra in the UV-vis range were recorded at different time intervals. The spectra were obtained with a Perkin-Elmer Lambda 3 UV-vis spectrophotometer and a Perkin Elmer Lambda 900 UV-vis-NIR spectrometer.

*High-pressure kinetic experiment* – The experiment was conducted at 313 K and 29.5 MPa in an 11 mL high pressure vessel with an interfacial area of 4.5 cm². The concentration of the dye and the third generation fluorinated dendrimer was the same as in the experiments for the third generation palmitoyl functionalized dendrimer in tetrachloromethane. The extraction was followed in time using UV-vis spectroscopy. The aqueous and supercritical carbon dioxide phase were not stirred.

Matlab (Mathworks, 1999) was used for the modeling of both the equilibrium and kinetic experiments.

**Results and discussion**

*Equilibrium experiments* – In this section first the behavior of the functionalized dendrimers in organic solvent is discussed. The pH-dependent properties of the extraction efficiency have been investigated at room temperature with the use of Rose Bengal. At a pH of 11 and 14, the solute is distributed over the two phases (dichloromethane and water), however, at a pH of 7 complete extraction is possible. Figure 5 shows that a fifth generation palmitoyl dendrimer with 62 tertiary amines extracts about 40 dye molecules at pH 7 and a high concentration of dye in the aqueous phase. This suggests that with strong dendrimer-solute interactions and every tertiary amine available for protonation a nearly 1:1 complexation between solute and tertiary amine should be possible. This pH effect on the extraction can be related to the protonation degree of the dendritic extractant. The electrostatic interactions between the solute and the dendrimer depend on both the acidity of the solute and the pH of the aqueous
medium. In the case of Rose Bengal not only electrostatic interactions play a role but also hydrophobic interactions are of importance (Miklis et al., 1997). The extraction behavior of the functionalized dendritic system has been studied for different generations using the anionic dyes Methyl Orange and New Coccine as model components. The dyes have been extracted from a buffered aqueous phase (pH = 6.4) to a tetrachloromethane phase.

Figure 5: The influence of the pH on the extraction of Rose Bengal by a fifth generation palmitoyl functionalized dendrimer in dichloromethane.

The UV-vis spectra of Methyl Orange solubilized in nonpolar solvents using functionalized dendrimers showed one peak at 420 nm for temperatures exceeding room temperature. However, when the temperature is lowered to 283 K a second peak appears (see Figure 6). Upon solubilization of Methyl Orange in a water-in-oil microemulsion the dye has two temperature dependent peaks, one at 354 and one at 416 nm (Fujieda et al., 1997). The first peak is attributed to the methyl orange monomer and the second peak to aggregates of the dye in the parallel orientation (H-aggregates) at the interface between the water phase and the oil phase. These H-aggregates have been found in the temperature range between 291 – 324 K. This suggests that the Methyl Orange is present as a monomer in the dendrimer, but at higher loading and low temperatures aggregates of the dye in the dendrimer are formed in the same manner as observed for the micro-emulsion.

In Figures 7a-d the extraction yield is given for the two dyes using a third and fifth generation dendrimer as a function of the concentration in the aqueous phase, for three different
temperatures. For all cases, a non-linear dependency is observed. Furthermore, the maximum number of dye molecules extracted per dendrimer depends on the temperature. The higher the temperature, the lower the loading per dendrimer.

Figure 6: Absorption spectra of Methyl Orange at (1) room temperature and (2) at 283 K extracted into a fifth generation dendrimer in tetrachloromethane. The spectra (3) and (4) are spectra of methyl orange in acidic water and in alkaline water, respectively.

Figure 7a: Extraction of Methyl Orange by a third generation functionalized dendrimer in tetrachloromethane. The dashed lines are based on the mass action model.
Figure 7b: Extraction of Methyl Orange by a fifth generation functionalized dendrimer in tetrachloromethane. The dashed lines are based on the mass action model.

Figure 7c: Extraction of New Coccine by a third generation functionalized dendrimer in tetrachloromethane. The dashed lines are based on the mass action model.
Figure 7d: Extraction of New Coccine by a fifth generation functionalized dendrimer. The dashed lines are based on the mass action model.

The observed temperature dependence of the extraction can be caused by a number of reasons. First of all, the electrostatic interactions become weaker upon an increase in temperature. Secondly, at higher temperatures the interior of the dendrimer will be more exposed to the solvent due to the flexible nature of the dendrimer. The third effect is that the degree of protonation of the tertiary amines decreases with an increase in temperature.

The loading of New Coccine in the dendrimer is significantly lower than the loading of Methyl Orange. This effect is independent of the generation of the dendrimer. The initial slope of the isotherm for New Coccine is very steep in comparison with the slope of the isotherm for Methyl Orange. The main reason for these effects is that New Coccine has three acidic groups, as opposed to Methyl Orange which has only one single acidic group. This can lead to the formation of more than one ion-pair per New Coccine molecule, as compared to Methyl Orange, which can form only one ion-pair. However, this does not mean that each of the three ionic groups of a New Coccine molecule interacts with a protonated tertiary amine.

The mass action equilibrium model, equation (2), describes the multi-site extraction isotherms fairly well with a single type of tertiary amines, $i=1$. In Tables 1a and 1b an overview of the parameters obtained with equation (2) are given. For Methyl Orange an assumption of one ion-pair interaction per molecule dye has been used, $p=1$, in contrast to the description of New Coccine where the ratio of ion-pair formation per dye molecule has also been fitted. For a third generation dendrimer for both dye molecules almost the same number of interactions
between a dye molecule and the tertiary amine-groups in a dendrimer \((p^*q_{\text{max}})\) is obtained for all three temperatures. At low temperatures the maximum number of available sites is about two-third of the number of tertiary amines. The main reason for this is the intermediate plateau in the amount of protonated tertiary amines at a pH of 6.4.

The behavior of a fifth generation dendrimer is different from that of a third generation dendrimer with respect to the number of available sites. Especially at higher temperatures the maximum number of available sites for Methyl Orange is higher than for New Coccine. For almost all conditions the amount of extracted Methyl Orange per tertiary amine is larger for a fifth generation dendrimer as compared to a third generation dendrimer.

Not only the maximum number of available sites is a function of the temperature but also the reaction equilibrium constant. The affinity for the dye molecules increases with an increase in temperature except for the extraction of Methyl Orange by a fifth generation dendrimer. On the other hand the maximum number of available sites decreases with an increase in temperature (Tables 1a and 1b). Moreover, for other type of host-guest systems with adsorption on localized sites, like zeolites, often a dependency of the maximum loading on the temperature is observed (Silva and Rodrigues, 1999).

Table 1a. Equilibrium results for Methyl Orange and New Coccine based on eq (2) and \(i=1\) using at least an average of three experiments at the same conditions for the third generation palmitoyl functionalized poly(propylene imine) dendrimer. \(^{a}\): maximum number of dye molecules extracted per dendrimer

<table>
<thead>
<tr>
<th>(T) (K)</th>
<th>(q_{\text{max}}^{a}) ((\cdot))</th>
<th>(p)</th>
<th>(K) ((\cdot))</th>
<th>(q_{\text{max}}^{a}) ((\cdot))</th>
<th>(p)</th>
<th>(K) (L/mol)(^{p-1})</th>
</tr>
</thead>
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<tr>
<td>293</td>
<td>8.7</td>
<td>1</td>
<td>1.0 (10^{-3})</td>
<td>4.0</td>
<td>2.2</td>
<td>1.2</td>
</tr>
<tr>
<td>313</td>
<td>7.0</td>
<td>1</td>
<td>5.7 (10^{-4})</td>
<td>3.4</td>
<td>2.0</td>
<td>0.34</td>
</tr>
<tr>
<td>333</td>
<td>4.2</td>
<td>1</td>
<td>6.2 (10^{-4})</td>
<td>2.6</td>
<td>1.6</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Table 1b. Equilibrium results for Methyl Orange and New Coccine based on eq (2) and \(i=1\) using at least an average of three experiments at the same conditions for the fifth generation palmitoyl functionalized poly(propylene imine) dendrimer. \(^{a}\): maximum number of dye molecules extracted per dendrimer

<table>
<thead>
<tr>
<th>(T) (K)</th>
<th>(q_{\text{max}}^{a}) ((\cdot))</th>
<th>(p)</th>
<th>(K) ((\cdot))</th>
<th>(q_{\text{max}}^{a}) ((\cdot))</th>
<th>(p)</th>
<th>(K) (L/mol)(^{p-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>293</td>
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<td>1</td>
<td>1.2 (10^{-4})</td>
<td>17</td>
<td>2.3</td>
<td>2.8</td>
</tr>
<tr>
<td>313</td>
<td>33</td>
<td>1</td>
<td>5.0 (10^{-4})</td>
<td>14</td>
<td>1.9</td>
<td>0.4</td>
</tr>
<tr>
<td>333</td>
<td>28</td>
<td>1</td>
<td>5.6 (10^{-4})</td>
<td>9</td>
<td>1.4</td>
<td>6.1 (10^{-3})</td>
</tr>
</tbody>
</table>
The component that is exchanged by the dendrimer is an OH⁻ or phosphate ion, because a phosphate buffer is used. The concentration of the OH⁻ and the phosphate ions (0.05 M) is practically constant during the experiments. Extraction of inorganic anions, like the phosphate ions, may compete with the organic anions for the tertiary amine sites. Pistolis et al. (1999) found that the microenvironment inside the dendritic microcavities is considerably less polar than the bulk aqueous phase. In this case, this means that the environment created by the interior of the functionalized poly(propylene imine) dendrimer would accommodate the organic anionic molecules preferentially (see Chapter 4).

Furthermore, a comparison has been made between the model given by equation (2) with a single type of tertiary amine, \(i=1\), and with two different types of tertiary amines, \(i=2\). Consequently, for the model with two different types of amines each type of amine has a different interaction energy with the solutes. There is almost no difference between the two models for the four cases considered. Therefore, we can conclude that there is only one type of tertiary amines present in the dendrimer, and that there is not a large cooperative or anti-cooperative effect in the uptake behavior of the dyes in these dendrimers. This is in contrast with a so-called dendritic effect (Kleij et al., 2000).

**High pressure experiments** – In this section a comparison is made between the extraction of Methyl Orange into supercritical carbon dioxide and into an organic phase to study the effect of the solvent. The extraction experiments have been performed using different generations of dendrimers. Cooper et al. (1997) used functionalized poly(propylene imine) dendrimers for the extraction of anionic species from an aqueous phase to a liquid carbon dioxide phase. It was found that a fourth generation dendrimer functionalized with perfluoropolyether groups, is capable of extracting Methyl Orange to a maximum of 12 dye molecules per dendrimer at 296.5 K and 34 MPa. Of importance is, as indicated by Cooper et al. (1997), that the macromolecule has to be functionalized by CO₂philic groups like perfluoropolyethers. In the system investigated here perfluoroalkyl groups have been used as the CO₂philic groups. A critical issue is that extraction using carbon dioxide implies that without buffering the pH of the water phase is rather low, due to the formation and dissociation of carbonic acid. At 20 MPa carbon dioxide and 313 K the water phase has a pH of 2.8 (Toews et al., 1995). At these conditions all the tertiary amines are protonated, with HCO₃⁻ as the counterion. The influence of carbon dioxide as a solvent on the equilibrium extraction is threefold:

1. carbon dioxide has an influence on the micro-environment
2. carbon dioxide introduces counterions into the system
3. carbon dioxide has an effect on the pH

Essential for the comparison with an organic solvent like tetrachloromethane is to have the system at the same pH as in the extraction of Methyl Orange in carbon dioxide at 30 MPa and 313 K. A phosphate buffer has been used to control the pH and the amount of counterions used is the same as in the system at elevated pressures. In this way the first two effects can be studied.
Figure 8: UV-vis spectra of Methyl Orange in a third generation dendrimer at 313 K in carbon dioxide and in tetrachloromethane.

A slight blue shift was observed in the absorption maximum of Methyl Orange extracted in a carbon dioxide phase in comparison with the extraction in tetrachloromethane (Figure 8). In Figures 9a and 9b the equilibrium extraction results of Methyl Orange by a third and fifth generation palmitoyl functionalized poly(propylene imine) dendrimer in tetrachloromethane and a perfluorocarbon functionalized poly(propylene imine) dendrimer in carbon dioxide are given as a function of the bulk dye concentration. The extraction in tetrachloromethane is more effective than the extraction in supercritical carbon dioxide. Also, the maximum amount of extracted dye molecules and the affinity of the dye for the dendrimer depend on the solvent. The maximum loading, $q_{\text{max}}$ obtained in carbon dioxide for a fifth generation dendrimer is about 30 % lower, and for a third generation the maximum loading is 50 % lower as compared to the extractions carried out in tetrachloromethane. However, as the maximum loading should not depend on the type of counterion which has to be exchanged for the dye, the difference observed in the maximum loading between the two solvents is probably due to a change of the micro-environment inside the dendrimers. The most likely explanation is that the affinity of the dye for the dendrimers in carbon dioxide is lower than the affinity for the dendrimers in tetrachloromethane. There are two reasons for this difference in affinity. First, the affinity of the amine for the carbonate counterion is higher than the affinity for the phosphate counterion. Secondly, there can be a decrease in affinity for the ion-pair formation between Methyl Orange and the protonated tertiary amine. It can be envisaged that the molecular conformation of the macromolecule is strongly influenced by the type of
endgroups and specific non-covalent interactions that can take place between the endgroups. Therefore, the solvation of the endgroups can play a significant role in determining the tertiary structure of the dendrimers, and this can result in a change in affinity and in the maximum number of available sites.

Figure 9a: Extraction of Methyl Orange in supercritical carbon dioxide at 313 K and 30 MPa and the extraction in tetrachloromethane at 313 K. The lines through the measurements are based on the mass-action model for a fifth generation dendrimer.
Figure 9b: Extraction of Methyl Orange in supercritical carbon at 313 K and 30 MPa and the extraction in tetrachloromethane at 313 K. The lines through the measurements are based on the mass-action model for a third generation dendrimer.

Kinetic experiments - The extraction of Methyl Orange has been used to evaluate the effect of the generation number and the temperature on the transient uptake. In Figure 10a the uptake is given for a third and fifth generation functionalized poly(propylene imine) dendrimer. The kinetics of the extraction process clearly depend on the generation of the dendrimer. The uptake is faster for a third generation dendrimer than for a fifth generation dendrimer. Furthermore, the rate of extraction increases with an increase in the concentration of the dye. In Figure 10b the influence of the temperature on the extraction kinetics using a third generation dendrimer is depicted. It can be seen that the temperature has a significant effect on the kinetics: the higher the temperature, the faster the extraction.

For all kinetic experiments, the concentration of Methyl Orange in the aqueous phase is considerably higher than the concentration of the dendrimer in the organic phase. Additional experiments have been performed with a 10-fold higher dendrimer concentration, showing no effect of the dendrimer concentration on extraction kinetics. Consequently, it can be concluded that there is no mass transfer resistance for Methyl Orange in the aqueous phase.
Figure 10a: Kinetics of the extraction of Methyl Orange at 333 K for different generations of the functionalized dendrimer in tetrachloromethane (experimental data).

Figure 10b: Kinetics of the extraction of Methyl Orange by a third generation functionalized dendrimer for different temperatures in tetrachloromethane (experimental data).

In Figure 11 the extraction kinetics for Methyl Orange using a third generation fluorinated dendrimer in supercritical carbon dioxide is compared with the extraction kinetics in
tetrachloromethane using a third generation palmitoyl functionalized dendrimer. The extraction in carbon dioxide is faster than in tetrachloromethane. However, taking into account the larger surface area, the extraction kinetics for a third generation dendrimer in scCO$_2$ is quite similar to the extraction in tetrachloromethane, in spite of the less flexible tail of the perfluorooctyl functionalized dendrimer. This implies that for designing extraction processes using multi-site extractive agents the emphasis should rather be on creating large interfacial areas.

Figure 11. Extraction kinetics of Methyl Orange using dendritic extractants in supercritical carbon dioxide and tetrachloromethane at 313 K. CO$_2$ (Normalized S) denotes that the kinetics of the extraction in supercritical carbon dioxide is normalized to the available interfacial area.

For a proper understanding of reactive extraction processes based on multi-site agents like dendrimers, an adequate description of the mechanism is required. The different steps of the reactive extraction are depicted in Figure 12. A dendritic extractant is closely related with a reverse micelle. The similarity between the modified dendrimers and reverse micelles is based on the distribution of the hydrophobic and hydrophilic parts. A dendritic extractant can be seen as a unimolecular (polymerized) version of the traditional low molecular weight surfactant (Weener, 2000). This unimolecular reverse micelle has a covalently fixed macromolecular structure versus the dynamic equilibrium structure of a "classical" reverse micelle.
The description of the extraction kinetics has to take into account the mass transfer in the neighborhood of the liquid-liquid interface accompanied by reversible complexation reactions. The mass transfer involves the diffusion of the components towards and away from the interface and interfacial phenomena, including effects of the interfacial flexibility and possible deformation of the dendritic macromolecule at the water-solvent interface.

*Extraction mechanism* - For the reactive extraction with the functionalized dendrimers the following mechanism is proposed:

1. The dendrimers present in the bulk organic phase will move to the liquid-liquid interface.
2. The dendrimers will collide with and fuse at the interface and a change in conformation is observed. Ideally, the dendritic poly(propylene imine) part acts as a polar headgroup and the alkyl chains are packed together in a parallel fashion, forming a hydrophobic unit.
3. The charged dye molecules will diffuse into the dendrimer and are complexed by predominant electrostatic interaction with the basic amine groups in the dendritic interior.
4. The dendrimer will rearrange and desorbs from the interface.

In this mechanism the following assumptions are made:

- The anion is assumed to be totally dissociated as Methyl Orange has a pKa of 3.3 (Ding et al., 1998).
- There is no physical extraction because the ions are insoluble in the solvent phase.
- The ion-exchange reaction between the anion and the tertiary ammonium salt occurs at the interface, because the anion is not soluble in the solvent phase.
- Transport of the dissociated form of the organic acid or the inorganic anion is mainly by an ion-pairing mechanism.

In this mechanism the process taking place during Step 2 is the most difficult one to envisage. A reasonable explanation is that the dendrimer will adopt a highly distorted configuration at the interface. Results for the behavior of dendrimers at an air - water interface (Schenning et al., 1998; Weener, 2000) show that the dendrimer structure can change from a globular reverse micellar arrangement to a cylindrical amphoteric shape. As a result of this, the polar interior is directed towards the aqueous phase.
Figure 12: Cartoon of the uptake mechanism of dyes by a dendritic system.

In order to elucidate the processes which influence the interfacial transport rate, the reaction rate constants in equation (6) have been determined for Methyl Orange for different dendrimer generations and different temperatures. Due to the high loading of the aqueous phase by the dye, thus assuring maximum loading of the dendrimer, the back extraction can be neglected. In Table 2 the forward rate constants, $k_f$, are given for the extraction using different dendrimer generations and temperatures with the assumption that the interfacial concentration of the dye is the same as the bulk concentration.

Table 2. Kinetic results for Methyl Orange based on equation (6) using at least an average of three experiments at the same conditions.

<table>
<thead>
<tr>
<th>$T$ (K)</th>
<th>$k_f$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>293</td>
<td>2.6 $10^{-5}$</td>
</tr>
<tr>
<td>313</td>
<td>3.9 $10^{-5}$</td>
</tr>
<tr>
<td>333</td>
<td>1.1 $10^{-4}$</td>
</tr>
</tbody>
</table>

For extraction with reverse micelles a similar mechanism has been proposed (Adachi et al., 1995). The main difference with the mechanism proposed here, however, is that for the uptake
in the dendrimers the aggregation and the disintegration of the supramolecular structure is not an issue, as opposed to (reverse) micellar systems. Interpretation of the data indicates that the mass transfer of the dendrimer towards the interface is not the rate-determining step, as the mass transfer is not constant during the experiment. Furthermore, it can be concluded that the rate constant does not vary during the transient extraction experiments. Therefore, the rate-determining step of the separation is the interfacial reaction step (step 3). In the case of extraction of amino acids by reverse micelles, it has been found that the rate-limiting step is the fusion process of the micelles, in which the forward and the backward extraction rates are controlled by the interfacial processes, i.e. the solubilization and the release processes (Nishika et al., 2000). For the case of an extraction system based on tri-n-octylamine, it has been found that the rate-limiting step is the reaction of the anion with the amine at the interface (Juang and Huang, 1995). In fact, the value for \( k_r \) found in this study is quite similar to the forward rate constant found by Fröschl et al. (1995) for the reactive extraction of acetic and lactic acid by amines.

**Conclusions**

In this study the use of multi-site extraction agents for dye extraction is investigated in supercritical carbon dioxide and tetrachloromethane. Both the equilibrium amount of extracted dye and the kinetics depend on the type and concentration of the dye, the generation of the modified poly(propylene imine) dendrimer, and the temperature. In the dendrimer the basicity of the tertiary amine groups are comparable. When there is no mass transfer resistance in the aqueous phase, which is the case for the conditions studied, the reaction at the interface dominates the extraction kinetics and not the mass transfer of the dendrimer from the bulk organic phase to the interface. This is different for reverse micellar systems where the fusion of the micelles at the interface determines the kinetics. The investigated unimolecular reverse micellar systems, the modified dendrimers, in that respect more behave as a normal reactive agent. A model has been presented describing the extraction of anionic solutes by a multi-site ion-exchange mechanism.

Comparing the uptake by a third generation with that by a fifth generation dendrimer it can be concluded that the fraction of available sites (as a percentage of the total number of tertiary amines per dendrimer) does not differ considerably. The distribution coefficient is similar for both generations in the case of the extraction of an anionic species with one single anionic group. The uptake rate appears to be somewhat higher for a third generation than for a fifth generation dendrimer. Also, comparing the extraction rate using a third generation dendrimer in supercritical carbon dioxide and tetrachloromethane shows no substantial difference.

In this chapter it has been demonstrated that perfluoroalkyl functionalized poly(propylene imine) dendrimers can be used as a carrier in carbon dioxide with an high capacity for anionic organic molecules. The third generation dendrimer offers the highest capacity and uptake rate per mass of the carrier compared with a fifth generation dendrimer.
Nomenclature

$m$ number of acidic groups on the dye (-)

$N$ generation number (-)

$q_A$ amount of counterions per dendrimer, which are not dye molecules (-)

$q_B$ amount of extracted dye per dendrimer (-)

$c_D$ dendrimer concentration (mol/L)

$c_A$ concentration of the solute which serves as counterions for the dendrimer (mol/L)

$c_B$ concentration of the dye in the aqueous phase (mol/L)

$c_B^*$ equilibrium concentration of the dye in the aqueous phase (mol/L)

$c_A^+$ concentration of the counterion in the aqueous phase at the interface (mol/L)

$c_B^+$ concentration of the dye in the aqueous phase at the interface (mol/L)

$q_{\text{max}}$ maximum amount of extracted dye per dendrimer at a given temperature (-)

$K$ equilibrium constant (L/mol)$^p$-1

$p$ number of electrostatic interactions per dye molecule which interact with the amine groups in a dendrimer (-)

$N_B$ flux of anionic species B (mol/(m$^2$ s))

$S$ surface area (m$^2$)

$V_O$ volume organic phase (L)

$V_w$ volume water phase (L)

$k_c$ mass transport coefficient of the dye molecule (m/s)

$k_f$ forward rate constant (L$^2$/mol s m$^2$)

$k_b$ backward rate constant (L$^2$/mol s m$^2$)

$t$ time (s)

Literature


Chapter 4

Functionalized Poly(propylene imine) Dendrimers as Phase Transfer Catalyst in Supercritical Carbon Dioxide

Abstract
Perfluoro functionalized poly(propylene imine) dendrimers have been used as reactive extractants for anionic species and as phase transfer catalysts for two types of reactions in supercritical carbon dioxide. First, the reactive extraction of the inorganic ions permanganate and dichromate from an aqueous phase to a supercritical carbon dioxide phase has been studied using the functionalized dendrimers. The yield for these extractions is rather low, indicating that the perfluoro functionalized poly(propylene imine) dendrimers are not suited for oxidation reactions with these ions in carbon dioxide. Secondly, the poly(propylene imine) dendrimers have been used as a phase transfer catalyst for the halogen exchange reaction of benzyl chloride into benzyl bromide, and for the esterification of oxalic acid with pentafluorobenzyl bromide. In contrast with the low extraction yield for the inorganic permanganate and dichromate ions, a high reaction rate has been obtained for the halogen exchange reaction with the functionalized dendrimers as phase transfer catalysts. It is found that the rate of reaction for both cases depends on the generation number of the dendrimer. For the higher generation dendrimers, it is more difficult for the substrate to migrate from the bulk carbon dioxide phase to the interior of the dendrimer. This indicates that the mass transfer of the reagents from the solvent phase into the interior of the dendrimer determines the reaction rate for the fourth and higher generation dendrimers. A model is proposed to describe extraction and phase transfer catalysis based on the fact that the modified dendrimers combine micellar properties with that of standard phase transfer catalysts. From the different experiments it can be concluded that the perfluoro functionalized poly(propylene imine) dendrimers have great potential as multi-site phase transfer catalysts.

Introduction

A significant and recurring problem in organic synthesis is caused by water-soluble reagents used for chemically modifying water-insoluble organic substrates. In the case the synthesis is conducted as a two-phase heterogeneous process, e.g. an organic phase-aqueous phase reaction, the reaction rate is usually very low. Due to mass transfer limitations, the concentration of the reactants at the interface, where the reaction occurs, is too low for an efficient process (Varma, 1998). A number of methods are available to avoid this problem. These methods use rapid stirring, make use of a cosolvent, or employ a phase transfer catalyst. Phase transfer catalysis (PTC) is especially interesting because of the lower energy and downstream processing costs. The goal of PTC is to bring incompatible reaction agents, including the catalyst, at intimate contact (Sasson and Neumann, 1997). This allows for “micro-heterogeneously” catalyzed reactions. In this way the advantages of homogeneous catalysis, i.e. high reaction rate and high selectivity, are combined with the advantages of heterogeneous catalysis, i.e. easy separation of the catalysts from the reaction medium.

An interesting option is to combine PTC with the use of supercritical fluids, to avoid the use of organic solvents and to increase the mass transfer rate (Figure 1). Supercritical fluids (SCF) have unique properties, which make them especially suitable for phase transfer catalysis. The liquid-like densities and gas-like diffusivities and viscosities of SCF assure rapid mass transfer. Especially carbon dioxide with its rather low critical temperature and pressure ($T_c = 304 \text{ K}, P_c = 7.4 \text{ MPa}$) provides many benefits when used as a supercritical fluid (McHugh and Krukonis, 1994).

![Diagram of PTC in carbon dioxide](image)

Figure 1: Schematic representation of phase transfer catalysis in carbon dioxide. In this case $X^-$ reacts with the substrate to the product and $Y^-$. Both $X^-$ and $Y^-$ are not soluble in carbon dioxide.

One of the major problems with carbon dioxide is the low solubility of standard phase transfer catalysts, like tetra-$n$-heptylammonium bromide (Dillow et al., 1996). The solubility of the
catalyst, or more importantly, the solubility of the catalyst - substrate complex, must be as high as possible to ensure a high reaction rate. In this work, perfluoroctanoyl functionalized poly(propylene imine) dendrimers have been used to explore the possibilities of dendrimers as phase transfer catalysts in SCF. The perfluoroctanoyl functionalized poly(propylene imine) dendrimers are well soluble in carbon dioxide due to coupling of the dendrimer endgroups with the fluoro-alkyl tails. The combination of nonpolar fluoro tails with the polar interior of the dendrimer yields an inverted unimolecular micellar-like structure with a high solubility in carbon dioxide.

Dendrimers are a relatively new class of macromolecules (Bosman et al., 1999, Baars et al., 2000). The highly branched, monodisperse structure leads to a number of interesting structural characteristics, like globular and void-containing shapes. These shapes can be used for host-guest interactions; guest molecules are confined, by different type of interactions, in the cavities of the host system. The special features of the poly(propylene imine) dendrimers, in particular the high polarity and the well-defined structures with a known number of sites, make these macromolecules highly suited for extraction and reaction purposes. The presence of the tertiary amines in the core of the dendrimer facilitates complexation with anionic species, predominantly by electrostatic interactions. The number of sites depends on the generation, $N$, of the dendrimers, according to $2 \times 2^{N+1}$. In Figure 2, as an example, a third generation perfluoro functionalized poly(propylene imine) dendrimer with 14 tertiary amine sites is depicted. For the extraction of high-value species, like antibiotics, a number of options are available. An efficient method is based on fluid-fluid reactive extraction, with a single-site phase transfer catalyst (Bora et al., 1997). Functionalized dendrimers as multi-site catalysts can be an alternative for this type of separations (Baars et al., 1997). In general, multi-site phase transfer catalysts have a high activity (Balakrishnan et al., 1995).

The objective of this work is to demonstrate the potential of modified dendrimers as phase transfer catalysts in the reactive extraction of anionic species from an aqueous phase, followed by a reaction in a supercritical carbon dioxide phase.

**Qualitative description of extraction mechanism**

To extend the mechanism for reactive extraction proposed in Chapter 3 to a mechanism for phase transfer catalysis, the following points need to be incorporated:

1. Migration of the organic substrate towards the core of the dendritic molecule
2. Reaction in the dendrimer
3. Migration of the product from the core to the bulk phase

It is noted that for extraction with reverse micelles a similar mechanism has previously been proposed (Adachi et al., 1995). The main difference with the mechanism proposed here is that the aggregation and the disintegration of the micelle is taken into account, which obviously does not play a role here.
Figure 2a: A third generation poly(propylene imine) dendrimer functionalized with perfluoro-octanoyl endgroups.

$\text{CH}_2\text{Cl}_2$

$n = 8 \,(\text{Gf}2), 16 \,(\text{Gf}3), 32 \,(\text{Gf}4), 64 \,(\text{Gf}5)$

Figure 2b: Modification of a poly(propylene imine) dendrimer with perfluoro-alkyl, $n$ indicates the number of endgroups, Gf refers to the functionalized dendrimer, the number indicates the generation of the dendrimer.

An important aspect of the dendritic extraction agents is that it has a fixed number of well-defined sites, as opposed to the standard phase transfer catalysts where a large number of arrangements are possible (Kirsch et al., 1996). This difference combined with a three-dimensional micro-environment of the dendrimer makes dendritic complexes considerably less sensitive to the non-aqueous phase. For a higher generation dendrimer, the cavities are more shielded from the bulk solvent as compared to a lower generation dendrimer. As a consequence, modified dendrimers have a wider range of application as the generation number can be tuned for a given reaction.
Experimental

Materials - Potassium permanganate, potassium dichromate, potassium bromide, naphthalene, benzyl chloride, pentafluorobenzylbromide, and oxalic acid dihydrate (99 % purity) were obtained from Aldrich and were used without further purification. Carbon dioxide (grade 4.5) was obtained from HoekLoos (Amsterdam, The Netherlands). The perfluoro functionalized dendrimers were synthesized in-house. For the synthesis a solution of the poly(propylene imine) dendrimer in tetrahydrofuran was added to an equimolar amount of pentadeca-fluoroocyanoylchloride. The formed precipitate was filtered and dried in vacuo. This yielded the fluorinated dendrimer in the protonated form as a HCl-salt, as white solid. 1H-NMR (CDCl3/CF3COO⁻ = 99:1) indicated complete reaction of the fluorinated endgroups with the amine-endgroups of the dendritic scaffold, with δ(CH2NHCO)= 3.3 ppm.

High-pressure apparatus - In the reactive extraction and PTC experiments a high-pressure reactor of 80 mL was used. The volume of the reactor could be varied with a piston between 80 and 60 mL. The reactor was equipped with two opposite sapphire windows, a magnetic stirrer bar, and a Pt-100 resistance thermometer. The reactor was pressurized using an LKB HPLC pump, and the pressure was monitored by a Meyvis 802-C pressure module. Samples could be taken from the aqueous and the organic phase with a sample loop, at a constant pressure provided by the piston. A high-pressure viewing cell of 2.2 mL could be attached to the high-pressure reactor to obtain UV-vis absorption spectra for both phases. During the measurements of the absorption spectra of the carbon dioxide phase great care was taken to avoid the formation of water droplets or a liquid film on the sapphire windows.

The experimental set-up is schematically depicted in Figure 3. In Table 1 an overview is given of the experimental conditions for both the reactive extraction and the PTC experiments. In all experiments the carbon dioxide to water volumetric ratio was equal to unity.

Reactive extraction experiments - First, the perfluorooctanoyl functionalized poly(propylene imine) dendrimer was transferred into the high-pressure reactor. The reactor was then pressurized with carbon dioxide to a set-point of 15 or 30 MPa, at 313 K. Using the piston a part of the content of the reactor was pumped, at constant pressure, into the high-pressure viewing-cell. In the viewing-cell, 1.1 mL of an aqueous solution of 1·10⁻³ mol/L potassium permanganate or potassium dichromate was present. UV-vis absorption spectra of the permanganate and the dichromate, extracted with the dendrimer into the carbon dioxide phase, were recorded with a Spectronic Genesys 5 Spectrophotometer. The extraction yield was determined by measuring the UV-vis absorbance of the carbon dioxide phase using the UV-vis extinction coefficient for aqueous solutions.
Figure 3: Experimental set-up, with (1) high-pressure reactor, (2) piston, (3) HPLC pump, (4) pressure indicator and controller, (5) viewing cell. A and B refer to switching valves for taking samples from the carbon dioxide phase and the aqueous phase, respectively.

**PTC experiments** - First, the perfluorooctanoyl functionalized poly(propylene imine) dendrimer, the internal standard naphthalene, and benzyl chloride or pentafluorobenzylchloride were transferred into the high-pressure reactor. The reactor was then pressurized with carbon dioxide to a set-point of 15 MPa at 338 K. During these experiments the volume was adjusted to 60 mL using the piston. Subsequently, 40 mL water containing 2 mol/L KBr or 1·10^{-4} mol/L potassium oxalate was pumped into the reactor. At the same time the volume of the reactor was enlarged by moving the piston to assure solubility of the modified dendrimer in the carbon dioxide phase. After introducing the substrates, carbon dioxide was pumped into the reactor to a set-point of 30 MPa. To determine the yield, the samples taken from the carbon dioxide phase were analyzed by GC (Fisons Instruments MP 800) with a FID detector equipped with a DB-5 column with a length of 30 m. For the GC analysis, response factors relative to naphthalene (internal standard) were determined.
Table 1. Overview of the experimental conditions. Gf refers to perfluoroocanoyl functionalized poly(propylene imine) dendrimer, the number indicates the generation of the dendrimer.

**Reactive extraction**

<table>
<thead>
<tr>
<th>Gf5</th>
<th>Conc. Gf mol/L</th>
<th>Conc. KMnO₄ mol/L</th>
<th>Conc. K₂Cr₂O₇ mol/L</th>
<th>P MPa</th>
<th>T K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gf5</td>
<td>1·10⁻⁴</td>
<td>1·10⁻⁴</td>
<td>1·10⁻⁴</td>
<td>15, 30</td>
<td>40</td>
</tr>
</tbody>
</table>

**Halogen exchange reaction**

<table>
<thead>
<tr>
<th>Gf2</th>
<th>Conc. Gf mol/L</th>
<th>Conc. Benzyl chloride mol/L</th>
<th>Conc. KBr mol/L</th>
<th>P MPa</th>
<th>T K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gf2</td>
<td>5.1·10⁻⁴</td>
<td>0.11</td>
<td>2</td>
<td>23, 30</td>
<td>338</td>
</tr>
<tr>
<td>Gf3</td>
<td>2.2·10⁻⁴</td>
<td>0.11</td>
<td>2</td>
<td>23, 30</td>
<td>328, 338, 348</td>
</tr>
<tr>
<td>Gf3</td>
<td>4.5·10⁻⁴</td>
<td>0.11</td>
<td>2</td>
<td>23, 30</td>
<td>338</td>
</tr>
<tr>
<td>Gf4</td>
<td>1.0·10⁻⁴</td>
<td>0.11</td>
<td>2</td>
<td>23, 30</td>
<td>338</td>
</tr>
</tbody>
</table>

**Esterification**

<table>
<thead>
<tr>
<th>Gf3</th>
<th>Conc. Gf mol/L</th>
<th>Conc. Pentafluorobenzylbromide mol/L</th>
<th>Conc. Dipotassium oxalate mol/L</th>
<th>P MPa</th>
<th>T K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gf3</td>
<td>4.5·10⁻⁴</td>
<td>1·10⁻²</td>
<td>1·10⁻⁴</td>
<td>23, 30</td>
<td>338</td>
</tr>
<tr>
<td>Gf4</td>
<td>1.0·10⁻⁴</td>
<td>1·10⁻²</td>
<td>1·10⁻⁴</td>
<td>23, 30</td>
<td>338</td>
</tr>
</tbody>
</table>

**Results and Discussion**

*Reactive Extraction* - The interest in permanganate and dichromate anions for the oxidation of organic substrates has increased substantially after the observation that they could be extracted from water into relatively nonpolar solvents using phase transfer agents (Sam et al., 1972). These anions are completely insoluble in carbon dioxide, and there is yet no phase transfer agent known for extracting these compounds into carbon dioxide. However, it has been shown that KMnO₄ and K₂Cr₂O₇ are soluble in water-in-CO₂ reverse micelles (Clarke et al., 1997).

An option might be to extract these anionic components by dendritic extraction agents. The main advantage of dendritic agents is that the tertiary amine groups are all protonated due to the low pH of the aqueous phase, i.e. a pH of about 3 (Toews et al., 1995). This effectively prevents oxidation of the amine groups by the anionic species.

In this work, the possibility of extracting inorganic species like MnO₄⁻ and Cr₂O₇²⁻ from water, has been studied using a fifth generation perfluorooctanoyl functionalized poly(propylene imine) dendrimer. The modified dendrimers are well soluble in carbon dioxide without the use of a cosolvent. Initially, chloride anions are present as counter-ions to
the protonated amine groups. These counter-ions can be exchanged by other anions. However, it appears that MnO₄⁻ and Cr₂O₇²⁻ anions do not easily exchange the chloride ions. The maximum loading of MnO₄⁻ found in a fifth generation dendrimer, with 62 tertiary amine groups, is close to one molecule per dendrimer. For Cr₂O₇²⁻ this value is even lower. This is considerably lower than the extraction efficiency observed for organic anions. For Methyl Orange a maximum of around 12 dye molecules per fourth generation dendrimer has been found in carbon dioxide (Cooper et al., 1997, Chapter 3). Presumably, besides electrostatic interactions also hydrophobic interactions are relevant for the extraction, so that the environment created by the interior of the modified dendrimer preferentially accommodates organic molecules.

![Graph](image_url)

**Figure 4:** Relative UV-Vis absorption spectrum of MnO₄⁻ (continuous line) and Cr₂O₇²⁻ (dashed line) in the interior of a 5<sup>th</sup> generation perfluorooctanoyl functionalized poly(propylene imine) dendrimer.

In Figure 4 the spectra for the MnO₄⁻ and Cr₂O₇²⁻ anion complexes in the interior of the perfluorooctanoyl functionalized poly(propylene imine) dendrimer are given. The spectra obtained are essentially the same as the spectra observed in an aqueous environment and complexed with a standard phase transfer catalyst (Sam et al., 1972). Experiments using Reichardt's dye, as a solvatochromic probe for effective polarity, indicate that there is a significant amount of water present in the dendrimer core (Cooper et al., 1997). Due to the presence of the tertiary amines inside the core this water cannot be considered as bulk water. This indicates that the dendrimer core will preferentially solubilize organic anions instead of inorganic anions. This is in contrast to reverse micelles, where a high loading of inorganic...
species can be found, in the core of the dendrimers organic groups are presents (Clarke et al., 1997).

_Nucleophilic displacement_ - The application of modified dendrimers in PTC has been studied in order to extend the possibilities to extract anionic species from water into carbon dioxide. The $S_N2$ halogen exchange reaction of benzyl chloride into benzyl bromide has been investigated, see Figure 5. This model reaction is performed in a two-phase system, consisting of an aqueous phase with a large amount of KBr and a CO$_2$-phase with the functionalized poly(propylene imine) dendrimer and benzyl chloride. Relevant for this is that the benzyl chloride is not soluble in water, and that the bromide ion is not soluble in carbon dioxide. The reaction employs the reactive extraction of bromide ions from the aqueous phase to carbon dioxide phase by the dendrimers. The bromide ions are then exchanged with the chloride. The transition state of this reaction is stabilized by the positive charge of the amines.

![Chemical reaction](attachment:chem_react.png)

Figure 5: Transformation of benzyl chloride into benzyl bromide.

In Figure 6 the conversion of benzyl chloride at 328 K is given for different generations and for different concentrations of the dendrimer. The concentration of the modified dendrimer decreases with an increase in the generation. However, the concentration of the tertiary amine groups (responsible for the extraction) remains constant. Experiments have been performed at two different pressures for three different generations. For the third generation dendrimer three temperatures and two concentrations were studied. It is observed that there is no significant effect of the pressure on the reaction rate of the halogen exchange reaction. However, there is an effect of the generation of the dendrimer on the reaction rate. For the same tertiary amine concentration the fourth generation gives the lowest reaction rate, while the second and the third generation essentially give the same results. For the third generation the concentration of the dendrimer has also been doubled to $4.5 \times 10^{-4}$ mol/L, which results in a doubling of the reaction rate. By increasing the temperature the formation of benzyl bromide is sharply increased, about a factor 5 for a 20 K increase.
Figure 6: Conversion of benzyl chloride at 338 K and 30 MPa, for different concentrations of the dendrimer, Gf. The concentration of the tertiary amines is constant, $3.1 \times 10^{-3}$ mol/L, for the experiments with the Gf2, the Gf3 with the dendrimer concentration of $2.2 \times 10^{-4}$ mol/L, and with the Gf4. For the reaction with the Gf3 with a dendrimer concentration of $4.5 \times 10^{-4}$ mol/L the tertiary amine concentration is about twice as high. The reaction conditions are given in Table 1.

The dependency of the reaction rate on the dendrimer generation number can be explained by the migration of the organic substrate towards the core of the dendritic molecules. This behavior is also seen for micellar systems, where the accessibility is usually of importance. However, for standard single-site phase transfer systems the accessibility of the catalysts by the substrate is usually not an issue.

During all reactions a low amount of benzyl alcohol is formed. However, the amount of benzyl alcohol for reaction without the catalyst was clearly higher than for the cases with the catalyst. This indicates that the water present in the dendrimer reacts to a small extent with the benzyl chloride or benzyl bromide. The reaction proceeds also without a phase transfer catalyst, but with a much lower rate as compared to the reaction with the catalyst. This is due to the reaction occurring at the bulk water / carbon dioxide interface. Results from literature show that when dendrimers are used as a reactive extractant for anionic species in conventional media, the influence of the bulk solvent decreases when the generation of the dendrimer is increased (Baars et al., 1997). For the higher generation dendrimers the core of the dendritic molecule is more shielded from the bulk solvent. The effect of the generation on the reaction rate, as can be seen in Figure 6, indicates that this also holds for carbon dioxide.
can be concluded that the characteristics of the dendritic catalyst change from a regular phase transfer catalyst to a unimolecular micellar system when the generation number is increased. From a comparison with other techniques, like reactions performed in (micro)emulsions (Jacobson et al., 1999a, 1999b) and with conventional phase transfer catalysts in supercritical carbon dioxide (Ido et al., 1997), it can be concluded that the dendritic method works with a much lower catalysts concentration. Furthermore, for all experiments performed at a temperature of 338 K, a constant reaction equilibrium constant, $K$, of 0.04 has been found, being is in good agreement with literature data (Jacobson et al., 1999a). In Table 2 a comparison is made between the results obtained with the dendrimers as microreactors and synthesis carried out using an emulsion (Jacobson et al., 1999b).

Table 2. Comparison between yield of benzyl bromide obtained with dendrimers as microreactors or synthesis in emulsions.

<table>
<thead>
<tr>
<th>type</th>
<th>wt%$^b$</th>
<th>yield$^c$ %</th>
<th>yield$^d$ -</th>
<th>Ref.</th>
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<tbody>
<tr>
<td>Gf2</td>
<td>0.1</td>
<td>18</td>
<td>2.0</td>
<td>this work</td>
</tr>
<tr>
<td>Gf3</td>
<td>0.1</td>
<td>18</td>
<td>2.0</td>
<td>this work</td>
</tr>
<tr>
<td>Gf3</td>
<td>0.2</td>
<td>36</td>
<td>4.0</td>
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</tr>
<tr>
<td>Gf4</td>
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<td>11</td>
<td>1.2</td>
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</tr>
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<td>9</td>
<td>1.0</td>
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<tr>
<td>PBO-b-PEO$^d$</td>
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<td>47</td>
<td>1.6</td>
<td>Jacobson et al., 1999a</td>
</tr>
<tr>
<td>PDMS-g-PEO$^a$</td>
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<td>41</td>
<td>1.4</td>
<td>Jacobson et al., 1999a</td>
</tr>
<tr>
<td>PFPE COO NH$_4$$^a$</td>
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<td>43</td>
<td>1.5</td>
<td>Jacobson et al., 1999a</td>
</tr>
<tr>
<td>No surfactant$^c$</td>
<td>0</td>
<td>29</td>
<td>1.0</td>
<td>Jacobson et al., 1999a/b</td>
</tr>
</tbody>
</table>

$^a$ reaction conditions for synthesis in emulsion: 2M potassium bromide in the aqueous phase and 0.11 M benzyl chloride in the carbon dioxide phase. Average product yield of benzyl bromide (of \( \geq 2 \) experiments) after 5 h and 338 K for a 50/50 wt\% water/CO$_2$ phase with very intensive stirring.

$^b$ wt\%, of the modified dendrimer or the surfactant, relative to the total weight of water and carbon dioxide phase.

$^c$ yield of benzyl bromide, after 5 hours.

$^d$ yield of benzyl bromide after 5 hours normalized to the reaction without additive(surfactants or dendrimers).

Considering the differences in experimental conditions, it can be seen that the yield, after about 5 hours of reaction, for the second and third generation dendrimers is of the same order of magnitude as the yield obtained for the synthesis in an emulsion. It has, however, to be noted that the synthesis of benzyl bromide in the emulsions is faster due to better mixing and a significant difference in surface area available for exchange. This means that the total mass
transfer in the emulsion experiments (Jacobson et al., 1999b) are higher than in the experiments described in this work. A more precise comparison is difficult, because Jacobson et al. (1999a, 1999b) did not report the actual surface area.

**Esterification** - Conventional liquid-liquid extraction has several disadvantages, such as an unfavorable partitioning of highly polar components into the extraction solvent. Moreover, the extractants used often require an additional purification. This is often elaborate and tends to lead to unwanted losses of the product. A way often used in analytical chemistry to overcome these drawbacks is by utilizing extractive pentafluorobenzylation. This technique is used to concentrate and prepare anionic compounds for gas chromatography, like anions of carboxylic acids and phenols (Miki et al., 1997).

![Esterification reaction](image)

**Figure 7:** Esterification of pentafluorobenzylbromide with oxalic acid.

The esterification of pentafluorobenzylbromide with oxalic acid has been studied to demonstrate the use of the same modified poly(propylene imine) dendrimers for different reaction types. The reaction scheme is given in Figure 7. Oxalic acid has been used as a model compound for organic anionic species, having a pKa1 of 1.2. Oxalic acid at a pH of 3, i.e. the pH of the aqueous phase, is not completely protonated. Oxalic acid can therefore not be extracted by carbon dioxide without the use of dendrimers at the experimental conditions applied. In Figure 8 the conversion of oxalic acid is given as a function of time, from which the effect of the pressure and the generation can be observed. These results demonstrate that both the third and the fourth generation dendrimer are capable of catalyzing the esterification of pentafluorobenzylbromide with oxalic acid. Like in the nucleophilic displacement reaction, there is a clear effect of the generation, and no significant effect of the pressure on the reaction rate. As can be seen from Figure 8, the reaction rate strongly increases with a decrease in generation.
Figure 8: Conversion of oxalic acid in the esterification of pentafluorobenzylbromide at 23 MPa and 30 MPa, both at 338 K. The concentration of the dendrimers, Gf, is given in Table 1.

As a result of this reaction, only the di-ester of oxalic acid has been obtained. Apparently, when one of the acid groups has reacted the second one reacts very fast with the pentafluorobenzylbromide. It is likely that the mono-ester is at least partially soluble in carbon dioxide and can react further without the phase transfer catalyst.

After the reaction of oxalic acid with pentafluorobenzylbromide, the product leaves the interior of the dendritic phase transfer catalyst. The dendrimer then becomes available again for the uptake of a new oxalic acid molecule from the aqueous phase. This mechanism is crucial for the efficiency of this type of reactions.

Pentafluorobenzylolation could be applicable for concentrating of anionic species by extraction, followed by a reaction in carbon dioxide. Analysis of the perfluoralkylated organic anions can then easily be performed with supercritical CO₂ chromatography.

**Conclusions**

Perfluoro functionalized poly(propylene imine) dendrimers have been applied as phase transfer catalysts in supercritical fluids. Since dendrimers provide a unique microenvironment, it opens the way to conduct various types of reactions, like esterifications and etherifications, using phase transfer catalysis. The key issue of these reactions is the extraction step, which is mainly based on the electrostatic interactions between the dendrimer and the reagent. The poly(propylene imine) dendrimers are capable of catalyzing the halogen exchange reaction, benzyl chloride into benzyl bromide, as well as performing the
esterification of pentafluorobenzylbromide with oxalic acid. Functionalized poly(propylene imine) dendrimers are not an ideal template for inorganic anions like permanganate and dichromate ions to perform oxidation reactions in carbon dioxide, due to the low extraction yield for these anions. Moreover, it has been found that the rate of reaction strongly depends on the generation of the dendrimer. If the dendrimer generation is too high, it is more difficult for the substrate to migrate from the bulk carbon dioxide phase to the interior of the dendrimer. Catalysis with the poly(propylene imine) dendrimers is based on the polar character of the interior combined with the nonpolar exterior, and the modified dendrimers can be considered as a new type of microreactor, similar to (reverse) micelles.

**Literature**


Chapter 5

Permeation of Carbon Dioxide through a Microporous Silica Membrane at Subcritical and Supercritical Conditions

Abstract
The one-component permeation of helium, carbon dioxide, and n-butane through an alumina-supported microporous silica membrane has been studied. For carbon dioxide the permeation behavior is determined for gaseous, liquid and supercritical conditions for pressures up to 20 MPa, at various temperatures. For all conditions high carbon dioxide fluxes have been obtained. The membrane has been tested with a maximum pressure difference between the feed and the permeate side of about 2.5 MPa. At a feed-side pressure of 20 MPa and at 313 K the permeance is equal to 8.0·10^{-8} mol m^{-2} s^{-1} Pa^{-1}. The transient transport through the microporous membrane can be described with a single mass transfer coefficient. For an increase in feed-side pressure from 0.1 to 20 MPa at a temperature of 296 K the mass transfer coefficient increases by a factor of 80. The fact that carbon dioxide has a high flux through this type of silica membranes opens the way for regeneration of carbon dioxide at supercritical conditions, without the need for a depressurization/recompression cycle.

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1 This chapter is partially based on Permeation of carbon dioxide through a microporous silica membrane at subcritical and supercritical conditions, A.W. Verkerk, E.L.V. Goetheer, L.J.P. van den Broeke and J.T.F. Keurentjies, submitted to Langmuir
Chapter 5

Introduction

The permeation of supercritical carbon dioxide through inorganic membranes is interesting from both a fundamental and a practical point of view. One of the main issues in high pressure applications is the regeneration of the supercritical fluid (McHugh and Krukonis, 1994). To remove small species from supercritical fluids the system often has to be depressurized to atmospheric conditions. The subsequent recompression to supercritical conditions is the most energy consuming step (Marr and Gamse, 2000). The use of microporous inorganic membranes is a way to circumvent the depressurization. Membranes can be used to separate small species, like oils (Spricigo et al., 2001), homogeneous catalysts (Chapter 6), and micelles (Chapter 7) from carbon dioxide while maintaining supercritical conditions. The carbon dioxide will permeate through the membrane and the small species dissolved in the carbon dioxide, which have a size larger than the pores of the membrane, will be retained. In order to have a reasonable flux of carbon dioxide, the driving force for permeation through the membrane now determines the pressure drop.

Transport phenomena in microporous materials have extensively been studied for the diffusion of gaseous species in materials such as zeolites and carbon molecular sieves (Kärger and Ruthven, 1992). However, almost no studies are available dealing with the diffusion in microporous materials at supercritical conditions. Only a limited number of studies address the equilibrium adsorption in inorganic materials at elevated pressures (Vermesse et al., 1996, Humayun and Tomasko, 2000).

So far, predominantly organic and polymeric membranes have been used for supercritical separation processes (Semanova et al., 1992, Higashijima et al., 1994, Sarrade et al., 1996, Alpers et al., 1999). Polymeric membranes have the disadvantage of swelling in carbon dioxide. As a result often a hysteresis effect is observed in the amount solubilized in the polymer membrane when the pressure is changed (Sarrade et al., 1996).

Inorganic membranes can withstand harsh chemical environments, high temperatures and pressures, without a noticeable change in transport properties. Besides zeolite and carbon membranes a number of other materials are available as microporous membranes, including silica and activated alumina (Ruthven, 1984, Hsieh et al., 1988, Hassan et al., 1995, Bein, 1996, Koukou et al., 1999, Poshusta et al., 1999). Katsaros et al. (1997) studied the permeation of pure helium and pure carbon dioxide through carbon membranes with a pore size of 0.7 nm, up to pressures of 6 MPa. As a function of the pressure a clear maximum in the carbon dioxide permeance was observed between 3 and 4 MPa. For pressures above 4 MPa the carbon dioxide flux decreases.

Another group of inorganic membranes with favorable characteristics for use in supercritical applications is silica membranes. Silica has a low affinity for hydrophobic compounds, and carbon dioxide does not adsorb too well on microporous silica, as compared to silicalite-1 zeolite or microporous and activated carbons (Humayun and Tomasko, 2000). For high-pressure applications it is advantageous that the carbon dioxide is weakly adsorbed in
microporous silica membranes. In general, equilibrium adsorption in microporous materials is given by a type I isotherm (Ruthven, 1984) and this type of adsorption is characterized by a plateau at high pressures. This implies that even at high pressures the membrane material should not be saturated with carbon dioxide to have a reasonable driving force for transport across the membrane. If at both sides of the membrane the maximum amount is adsorbed, there is no driving force and hence no permeation occurs.

The objective of this work is to study the feasibility of microporous silica membranes for use in high-pressure applications. The transient permeation of pure carbon dioxide has been obtained for feed-side pressures up to 20 MPa, for three different temperatures. Results are reported for the permeation of gaseous, liquid, and supercritical carbon dioxide obtained with the same microporous silica membrane.

**Experimental**

*Silica membrane.* The microporous alumina-supported silica membrane was obtained from ECN (Petten, The Netherlands). The membrane consisted of five different layers (see Figure 1). There are four support layers, three layers of ɑ-alumina and one of γ-alumina. The selective top layer, at the outer wall of the tube, is made of amorphous silica. In Table 1 an overview is given of the dimensions of the supported membrane.

![Microporous silica membrane](image)

Figure 1: Microporous silica membrane.
Chapter 5

Table 1. Dimensions of the alumina-supported silica membrane.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value 1</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average pore diameter silica layer</td>
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<td>nm</td>
</tr>
<tr>
<td>Thickness silica layer</td>
<td>200</td>
<td>nm</td>
</tr>
<tr>
<td>Total thickness alumina support layer</td>
<td>3.1</td>
<td>mm</td>
</tr>
<tr>
<td>Length membrane</td>
<td>30</td>
<td>cm</td>
</tr>
<tr>
<td>Outer diameter membrane</td>
<td>1.4</td>
<td>cm</td>
</tr>
</tbody>
</table>

Materials - Helium (grade 5.0), carbon dioxide (grade 5.0), and n-butane (grade 2.5) were obtained from HoekLoos (Amsterdam, The Netherlands).

Setup - The high-pressure setup used to study the permeation through the silica membrane is schematically depicted in Figure 2. The silica membrane was placed in an oven (Heraeus) and the temperature was controlled with a Pt100. The membrane module could be pressurized at the feed and permeate side up to 20 MPa. To start a flux measurement the needle valve at the permeate side of the membrane was opened to create a pressure difference across the membrane. Permeation experiments were performed with a fixed pressure difference between 0.1 and 2.5 MPa, using a dead-end configuration. To obtain the mass transport through the membrane the change in pressure at the permeate side was recorded as a function of time. After closing the permeate needle valve the pressure difference across the membrane was measured with a pressure-difference meter from Druck (Smart Pressure Transmitter STX 2100).

![Figure 2: High-pressure setup used in permeation experiments.](image)

Theory on mass transport

In general, mass transport in microporous materials can be described by Fickian diffusion. The mass transport as a function of time is for a pressure-driven process given by
\[
\frac{1}{RT} \frac{dp}{dt} = \frac{dJ}{dx}
\]  \hspace{1cm} (1)

with the flux equal to

\[
J = -D \frac{dp}{dx}
\]  \hspace{1cm} (2)

In this work the mass transfer through the tubular membrane is described with the so-called linear driving force approximation

\[
\frac{dp_p}{dt} = k \left( p_f - p_p \right)
\]  \hspace{1cm} (3)

The mass transfer coefficient, \( k \), can be related to the diffusion coefficient, according to

\[
k = \alpha \frac{D}{L^2}
\]  \hspace{1cm} (4)

The results for the transient profiles will be given in terms of the normalized pressure

\[
\hat{p}(t) = \frac{p_p(t) - p_p(t = 0)}{p_f(t = 0) - p_p(t = 0)}
\]  \hspace{1cm} (5)

For a number of cases the permeance, i.e. the flux divided by the pressure difference across the membrane, is calculated from the transient permeation profiles. For a correct description of the flux the molar density of carbon dioxide at both sides of the membrane required. The molar density is obtained from the pressure with the use of the Modified Benedict-Webb-Rubin (MBWR, Reid et al., 1988) equation of state. The molar density is then used to calculate the flux, according to

\[
J = \frac{V}{A} \frac{d\rho}{dt}
\]  \hspace{1cm} (6a)

and the permeance is given by

\[
\Pi = \frac{J}{\Delta p}
\]  \hspace{1cm} (6b)

It should be noted that with the description of the mass transport with Equation (6) the actual equilibrium adsorption properties of the carbon dioxide in the silica layer are not taken into account.

**Results and Discussion**

Single-component permeation of carbon dioxide through the alumina-supported silica membrane is studied for subcritical and supercritical conditions. Carbon dioxide becomes supercritical at 304.2 K and 7.38-MPa. Transient permeation is determined for three different
carbon dioxide phases at the feed and the permeate side of the membrane, i.e. for carbon dioxide as a gas, a liquid, and in the supercritical state. Experiments have been performed with a feed pressure above the critical pressure while the permeate pressure is initially below the critical pressure. For these permeation experiments a phase transition occurs. For a temperature below the critical temperature carbon dioxide goes from the gaseous phase to the liquid phase. For a temperature above the critical temperature carbon dioxide goes from the gaseous to the supercritical phase.

Due to non-ideality effects the density of carbon dioxide changes in a non-linear way with an increase in pressure. In Figure 3 the fugacity and the density of carbon dioxide are given as a function of the pressure for the three temperatures used to study the permeation behavior.

![Graph](image.png)

**Figure 3:** Fugacity and density of carbon dioxide as a function of the pressure at 296, 313 and 358 K, respectively.

*Permeation of gaseous species* - To study the properties of the silica membrane, first the permeation of a number of gaseous species has been measured. Transient profiles of pure helium, carbon dioxide and n-butane at 296 K are compared in Figure 4. For carbon dioxide two profiles are given. The approach to equilibrium for the three gases, for almost the same pressure difference, increases in the order: carbon dioxide < n-butane < helium. The two experiments for carbon dioxide have been performed at different feed-side pressures but with almost the same pressure difference across the membrane. From the results for carbon dioxide it follows that the flux through the membrane increases with an increase in the feed pressure and hence in the density.
Figure 4: Transient permeation profiles of pure gaseous helium, carbon dioxide and n-butane at 296 K. Profiles are normalized on the pressure difference across the membrane.

The same three gases have been used to study the transport through the support, that is through a membrane without the silica layer. For the three gases, helium, carbon dioxide and n-butane, the flux through the support is at ambient conditions at least 500 times higher than the flux through the membrane with the silica top layer.

In Figure 5 the steady-state permeance of the three gaseous species is given as a function of the temperature. From the fact the helium permeance increases with an increase in the temperature it follows that the mass transport of helium through the alumina-supported microporous silica membrane is an activated process. On the other hand the fact that the permeance of both carbon dioxide and n-butane decreases with an increase in temperature indicates that another mechanism contributes to the overall mass transport through the membrane as well. Furthermore, between 295 and 375 K the permeance of n-butane is higher than the permeance carbon dioxide. This rules out the possibility of Knudsen diffusion through the silica layer, because the Knudsen diffusion coefficient is proportional to the inverse of the square root of the molecular mass.
Figure 5: Steady-state permeance of pure gaseous helium, carbon dioxide and n-butane as a function of the temperature. The pressure at the feed-side and the permeate-side were 0.2 and 0.1 MPa, respectively. The lines are a guide to the eye.

Figure 6: Transient permeation profiles of gaseous carbon dioxide for different pressure differences across the membrane. Profiles are normalized on the pressure difference and the temperature is 358 K.
Based on a comparison with other microporous membranes the mass transport through the silica membrane can be regarded as a combination of an activated Knudsen-like and an adsorption – diffusion process (Van den Broeke et al., 1999a, 1999b). The increasing flux of helium is a result of the activated transport. The decreasing trend observed for carbon dioxide and n-butane is a result of a decrease in the amount adsorbed upon an increase in temperature. The fact that there are two types of pores in the silica layer may be a result of the sol-gel preparation technique. Yoshoka et al. (2001) proposed that silica layers might consist of colloidal sol particles with intraparticle pores and somewhat larger interparticle pores between the sol particles.

To study the effect of the pressure on the permeation in more detail, a number of experiments have been performed with carbon dioxide at the same feed pressure but with a different initial pressure at the permeate side. The results for the transient permeation for a feed pressure of about 5.02·MPa are given in Figure 6. The pressure difference applied varies between 0.35 and 1.02·MPa. It can be seen that there is no effect of the permeate pressure on the transient profiles; all the normalized profiles coincide. Thus in the region investigated the flux is directly proportional with the pressure difference.

Figure 7: Transient permeation profile of carbon dioxide for temperatures above the critical temperature, and for a feed pressure above and a permeate pressure below the critical pressure.
Chapter 5

Permeation around the critical point - For applications of high-density gases there are roughly speaking two operating windows. The main operating window is, of course, at conditions clearly above the critical point. However, for some cases also near-critical conditions are required (Espinosa et al., 2000). In Figure 7 results are given for the transient permeation, in absolute pressures, for conditions where the carbon dioxide shows a phase change. Two experiments are performed at temperatures above the critical temperature, and for one experiment the temperature is below the critical temperature.

For a temperature of 313 K the pressure at the permeate side increases from 6.5 to 8.5-MPa, and at 358 K the pressure at the permeate side increases from 5.5· to 7.9-MPa. This means that for these experiments the carbon dioxide at the permeate side goes from the gaseous phase to the supercritical state. It is seen that both profiles have an inflection around 7.3-MPa. For the third experiment, performed at 296 K and with a feed pressure of 7.0-MPa and an initial permeate pressure of 5.4-MPa, a clear inflection point is seen above 6.0-MPa. For this experiment the carbon dioxide at the feed side goes from the gaseous phase to the liquid phase. At 296 K the saturation pressure of carbon dioxide is equal to 6.12-MPa. As can be seen from Figure 3, at this point the density increases from 0.21 g mL\(^{-1}\) at 6.1·MPa to 0.74 g mL\(^{-1}\) at 6.2-MPa.

It should be noted that for all experiments a reasonable rate of permeation occurs. At a temperature of 358 K it takes around 400 s to reach steady state. This is of the same order as obtained for the permeation of gaseous carbon dioxide shown in Figure 6.

![Graph showing permeation profiles](image_url)

Figure 8a: Transient permeation profiles of carbon dioxide with both the feed and the permeate pressure above the critical pressure, at a temperature of 313 K. Profiles are normalized on the pressure difference. The dashed line is a fit with Equation (3).
Permeation of CO$_2$ through a Microporous Membrane

Figure 8b: Flux of carbon dioxide as a function of the pressure difference across the membrane. Results are for different initial feed pressures at 313 K.

*Permeation at supercritical conditions* - A number of experiments have been performed at a temperature and pressure above the critical point. The transient profiles obtained at 313 K with both the feed and permeate pressure above the critical pressure are given in Figure 8a. At the supercritical conditions studied the approach to equilibrium increases with an increase in the feed-side pressure. The permeation through the membrane reaches steady state after 100 to 150 s. It should be noted that there is a relatively large change in the density for the experiment with the feed pressure of 12.49 MPa and the initial permeate pressure of 9.87 MPa, as compared to the experiments at higher pressures. The fluxes corresponding to the transient profiles of Figure 8a, and calculated with Equation (6a), are depicted in Figure 8b. From Figure 8b it follows that the flux increases more or less linearly with the pressure difference across the membrane.

*Permeance and mass transfer* - In Figure 9 the permeance of carbon dioxide at 313 K is given as a function of the feed-side pressure. The permeance is obtained from the flux given in Figure 8b at a pressure difference of 0.1 MPa. Up to the critical pressure the permeance increases linearly with the feed-side pressure. Above the critical pressure the permeance is more or less independent of the feed-side pressure.
Figure 9: Permeance of carbon dioxide as a function of the feed-side pressure of the membrane, at a temperature of 313 K.

Figure 10a: Mass transfer coefficient for carbon dioxide permeation through the silica membrane as a function of the feed pressure up to 6-MPa, at a temperature of 296, 313 and 358 K, respectively.
Figure 10b: Mass transfer coefficient for carbon dioxide permeation through the silica membrane as a function of the feed pressure up to 20 MPa, at a temperature of 296, 313 and 358 K, respectively.

The permeation results obtained with the microporous silica membrane cover a large pressure range. From the results presented in Figures 4 and 8a it follows that the permeation is a clear function of the feed-side pressure. For all cases the approach to equilibrium increases with an increase in the feed-side pressure. However, the permeation is more or less independent of the pressure difference across the membrane, as indicated by Figure 6. The fact that there is almost no effect of the pressure difference on the permeation makes a comparison of the mass transport of carbon dioxide through the silica membrane at different pressures and temperatures possible.

The mass transfer coefficient, calculated with Equation (3), is given in Figure 10 as a function of the pressure at the feed-side. It is assumed that along the length of the membrane the pressure of carbon dioxide is constant at both sides of the membrane. For the three different temperatures the mass transfer coefficient increases with the feed-side pressure. However, there is a different behavior for a pressure below or above the critical pressure. In Figure 10a it is seen that below the critical pressure the mass transfer coefficient is more or less independent of the temperature. The mass transfer coefficient first increases with the pressure and becomes constant between 3- and 6-MPa.

Above the critical pressure, see Figure 10b, the mass transfer again increases with the feed pressure, and the mass transfer coefficient also depends on the temperature. The strongest increase in the rate constant is observed for the lowest temperature. With an increase in
temperature the relative increase in the mass transfer coefficient becomes smaller. Although different mechanisms seem to contribute to the mass transport through the supported silica membrane the transient permeation of carbon dioxide can be described by a simple “rate-equation model” for a feed pressure between 0.1 and 20 MPa. When it is assumed that there is only one mechanism for mass transport, the mass transfer coefficient would increase monotonously with an increase in temperature and the amount adsorbed (Fletcher and Thomas, 1999). The result for the mass transfer coefficient at 20 MPa and 358 K corresponds with a value for the permeance of $8.0 \times 10^{-8}$ mol m$^{-2}$ s$^{-1}$ Pa$^{-1}$. The fact that carbon dioxide has a high permeance through this type of silica membranes opens the way to economically viable regeneration of liquid and supercritical carbon dioxide.

**Conclusions**

Permeation of carbon dioxide through a microporous silica membrane has been obtained at both subcritical and supercritical conditions. Over the whole pressure range, i.e. up to a feed-side pressure of 20 MPa, high carbon dioxide fluxes where obtained for relative small pressure differences across the membrane. The transient permeation through the membrane for gaseous and supercritical carbon dioxide can be described with a single mass transfer coefficient, which increases with an increase in the feed-side pressure. The results for the mass transfer coefficient combined with the results for the flux of the gaseous species as a function of the temperature indicate that different mechanisms contribute to the mass transport through the supported silica membrane.

**Nomenclature**

- $A$: surface area of membrane, m$^2$
- $D$: Fick diffusion coefficient, m$^2$ s$^{-1}$
- $k$: mass transfer coefficient, s$^{-1}$
- $L$: thickness of the membrane, m
- $J$: flux through membrane, mol m$^{-2}$ s$^{-1}$
- $p$: pressure, Pa
- $p_r$: pressure at the feed-side of membrane, Pa
- $p_p$: pressure at the permeate-side of membrane, Pa
- $\hat{p}$: normalized pressure
- $\Delta p$: pressure difference across the membrane, Pa
- $R$: gas constant, J mol$^{-1}$ K$^{-1}$
- $T$: temperature, K
- $t$: time, s
- $V$: volume of the permeate chamber, m$^3$
- $x$: space coordinate in the membrane, m
Greek
\( \alpha \) constant in Equation (4)
\( \rho \) density of carbon dioxide, g L\(^{-1}\)
\( \Pi \) permeance, mol m\(^{-1}\) s\(^{-1}\) Pa\(^{-1}\)
\( \mu \) fugacity of carbon dioxide, Pa

Literature
Chapter 5


Chapter 6

A Membrane Reactor for Homogeneous Catalysis in Supercritical Carbon Dioxide

Abstract
A method is presented for continuously operated homogeneous catalysis in supercritical carbon dioxide with in situ catalyst separation. This concept offers the advantages of benign high-density gases, i.e. the possibility of achieving high concentrations of gaseous reactants in the same phase as the substrates and catalyst, as well as easy catalyst localization by means of a membrane. For the separation of the homogeneous catalyst from the products an inorganic microporous membrane is used. The concept is demonstrated for the hydrogenation of 1-butane using a fluorous derivative of Wilkinson's catalyst, [RhCl{(C<sub>6</sub>H<sub>4</sub>-p-SiMe<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>C<sub>8</sub>F<sub>17</sub>)<sub>3</sub>}]<sub>3</sub>]. The size of the Wilkinson's catalyst is larger than the pore diameter of the silica membrane, so that the membrane retains the catalyst, while the substrates and products will permeate. Stable operation and continuous production of n-butane has been achieved at a temperature of 353 K and a pressure of 20 MPa. A turnover number of 1.2·10<sup>5</sup> has been obtained during 32 h of reaction. The retention of the catalyst has been checked using UV-vis spectroscopy and ICP-AAS; no rhodium or phosphorous species could be detected at the permeate side, indicating a retention for the catalyst in excess of 99%.

Introduction
For a large number of reactions homogeneous catalysts have a better activity and (enantio)selectivity, as compared to heterogeneous catalysts (Bhaduri and Mukesh, 2000). There are, however, two main disadvantages related to the use of homogeneous catalysis, caused by the organic solvent used as the reaction medium and the difficult separation of the catalyst from the products. With respect to the first issue, increasing concern regarding the

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dissemination of volatile organic compounds, chloro-fluorocarbons and aqueous waste streams into the environment has prompted the chemical industry to conform to more environmentally sound practices in the manufacture and processing of products. It is generally thought that the use of supercritical solvents provides a powerful means to achieve these goals (McHugh and Krukonis, 1994; Johnston and Lemert, 1996). High-density carbon dioxide has some clear advantages for both extraction and reaction purposes (Savage et al., 1995). This is due to the fact that supercritical carbon dioxide (scCO₂) has a low viscosity and that most species have a high diffusivity in scCO₂ (He, 1997). Carbon dioxide has also a reasonable low critical temperature and pressure (Tc = 304 K and Pc = 7.4 MPa), it is a cheap substance, it is non-flammable, and non-toxic.

The use of supercritical fluids (SCFs) can lead to innovating processes exploiting the unique features of high-density gases of which the complete miscibility with other gases is one of the most interesting ones (McHugh and Krukonis, 1994). This means that it is possible to obtain high concentrations of gases like hydrogen, oxygen or carbon monoxide in one single phase with the substrate. This is opposite to most liquids, which can only solubilize a limited amount of gaseous species. Therefore, reactions in SCFs can be much faster than reactions in liquids, which is especially important for reactions suffering from mass transfer limitations (Kainz et al., 1997). Furthermore, negative partial molar volumes in supercritical systems can be exploited to adjust rate constants of various reactions (Chialvo et al., 1998; Jessop and Leitner, 1999). Moreover, it has been found that in some cases the selectivity of the reaction can be significantly higher in a SCF as compared to organic solvents (Oakes et al., 2001). These aspects in combination with the high mass transfer rates observed for SCFs implies that these solvents offer specific advantages for homogeneous catalysis.

There are a number of examples of homogeneous catalytic reactions carried out in supercritical media using gaseous reactants, which clearly demonstrate the benefits of this kind of media (Koch and Leitner, 1998; Palo and Erkey, 1998). However, most of the existing homogeneous catalysts have a low solubility in scCO₂. The solubility can be increased by attaching groups with a low cohesive energy density, like perfluoroalkyl tails, to the ligands of the catalyst. As an example, a fluorous version of the Wilkinson's catalyst has been used for hydrogenation and hydroformylation reactions in scCO₂ (Kainz et al., 1997).

For the use of homogeneous catalysts it is crucial to reuse and recycle the relative expensive catalyst. In this study, the concept of homogeneous catalysis in scCO₂ using a microporous membrane to localize a homogeneous catalyst is being demonstrated. In this way the two major drawbacks associated with homogeneous catalysis are circumvented. The principle of the membrane reactor is shown in Figure 1.
Membrane Reactor

![Diagram of a membrane reactor](image)

Figure 1: Membrane reactor for continuous homogeneously catalyzed reactions in supercritical carbon dioxide.

At this moment, mainly organic membranes are being investigated for applications in carbon dioxide (Sartorelli and Brunner, 2000). However, organic membranes have several disadvantages for use in carbon dioxide, like swelling and a lack of stability. Also, composite membranes have been used. Brunner and coworkers (Sartorelli and Brunner, 2000) have used silica composite membranes with a fluorinated polymer selective top layer for regeneration of carbon dioxide. A number of inorganic membranes are now becoming available which can be used for high-pressure applications (Bein, 1996; Ismail and David, 2001; Katsaros et al. 1997; Koros and Mahajan, 2000; Tokunuga et al., 1997). Inorganic membranes exhibit physical and chemical properties that are not shown by organic membranes, including a better structural stability without the problems of swelling or compaction. Generally, they can withstand harsh chemical environments and high temperatures (Hsieh et al., 1988; Tavolaro and Drioli, 1999).

A group of inorganic membranes with favorable characteristics for use in supercritical applications are silica membranes. Silica has a high affinity for hydrophilic organic compounds while carbon dioxide does not adsorb too well on microporous silica as compared to silicalite-1 zeolite and microporous carbons. Due to these reasons a silica membrane has been used in this study.

The continuous membrane concept is demonstrated for the hydrogenation of 1-butene using a fluorous derivative of Wilkinson's catalyst, [RhCl{P-(C₆H₄-p-SiMe₂CH₂CH₂C₈F₁₇)_₃}₃]. Recently, fluorous triphenylphosphine containing a -SiMe₂CH₂CH₂-spacer has been used in the synthesis of a fluorous derivative of Wilkinson's catalyst for the hydrogenation of 1-octene under fluorous biphasic conditions (Richter et al., 2000a, 2000b). This fluorinated version of the Wilkinson's catalyst, 1, using fluorous triarylphosphines P[C₆H₄-p-SiMe₂(CH₂)₂C₆F₂n₊₁], makes it possible to tune the catalyst with respect to catalytic activity, the solubility in scCO₂, and its size. By attaching the perfluoroalkyl groups, the solubility in scCO₂ as well as the size

---

2 According to IUPAC definitions, microporous materials have pore diameters smaller than 2 nm (Sing, 1985).
of the catalyst are increased considerably. The synthesis route and the catalyst, 1, are shown in Figure 2. The size of 1, as obtained by computer modeling and verified by dynamic light scattering experiments in a fluororous solvent, is larger than 2 nm. This means that a microporous membrane will reject the Wilkinson's catalyst. Furthermore, due to the relatively hydrophilic nature of the membrane, the hydrophobic catalyst is not likely to adsorb on the surface of the membrane material.

**Experimental**

*Materials* - Hydrogen (grade 5.0), carbon dioxide (grade 5.0), and 1-butene (grade 2.5) were obtained from HoekLoos (Amsterdam, The Netherlands). The membrane permeation experiments and the continuous membrane reactor experiments were performed with a tubular microporous silica membrane provided by ECN (Petten, The Netherlands). The membrane consisted of several support layers of α- and γ-alumina, and the selective top layer at the outer wall of the tube is made of amorphous silica (Koukou et al., 1999). The silica has a thickness of 200 nm with an average pore diameter of 0.6 nm. The membrane is 0.30 m long and has a diameter of 14 mm.

*In situ catalyst preparation* - A fluororous version of Wilkinson's catalyst, 1, was prepared in situ from one equivalent of [RhCl(COD)]₂ (COD = cis, cis-1,5-cyclooctadiene) and six equivalents of P[C₆H₄-p-SiMe₂(CH₂)₂C₆F₁₇]₃. The fluororous phosphine ligands were synthesized according to the recipe of Richter et al. (2000a, 2000b). The amounts used in the synthesis are given in Table 1. The two precursors were added to the reactor in a molar ratio of one rhodium atom per three fluororous ligand molecules. The reaction scheme for the synthesis of the fluorinated catalyst is given in Figure 2a. The reactor was flushed with carbon dioxide to remove all the oxygen. The catalyst was synthesized from the precursors by pressurizing the reactor with a mixture of carbon dioxide and hydrogen, at a temperature of 353 K and a pressure of 20 MPa. During the synthesis of the catalyst and during the hydrogenation of 1-butene, the concentration of the catalyst was measured in-line with a Spectronic Genesys 5 Spectrophotometer by following the absorption at 410 nm.
1/2 [(COD)RhCl]₂ + 3 P → \[
\begin{array}{c}
\text{Si}^\text{Me}_\text{Me} \\
\text{Me}
\end{array}
\text{(CF}_2\text{)}_8\text{F}
\]
\[3\] → COD
\[
\begin{array}{c}
\text{R}_3\text{P} \\
\text{R}_3\text{P}
\end{array}
\text{Rh} \begin{array}{c}
\text{Cl} \\
\text{PR}_3
\end{array}
\]
1

- H₂ | H₂

\[
\begin{array}{c}
\text{R}_3\text{P} \\
\text{H} \\
\text{H}
\end{array}
\text{Rh} \begin{array}{c}
\text{Cl} \\
\text{PR}_3
\end{array}

R = C₆H₄-p-SiMe₂CH₂CH₂C₈F₁₇

Figure 2a: Idealized formation of the fluorous derivative of Wilkinson's catalyst, 1, based on a fluorous triphenylphosphine derivative containing a –SiMe₂CH₂CH₂ spacer.

Figure 2b: Computational structure of 1 (MM94, Spartan 5.1.1. (SGI)).

**Batch reactor** - The homogeneously catalyzed hydrogenation of 1-butene in supercritical carbon dioxide was first performed in the high-pressure batch set-up depicted in Figure 3. The volume of the reactor could be varied with a piston between 16 and 31 mL. The reactor was equipped with two opposite sapphire windows, a heater and a Pt100 thermometer. The reactor
was pressurized using an LKB HPLC pump, and the pressure was monitored by a Meyvis 802-C pressure module. Samples were taken at a constant pressure provided by the piston. In the high-pressure reactor the precursors of the Wilkinson’s catalyst were added in a molar ratio of one rhodium atom per three fluorous ligand molecules, until a concentration of $1.3 \times 10^{-6}$ mol/L of the Wilkinson’s catalyst was obtained. The reactor is heated up to 353 K and all air is slowly removed by fluxing with carbon dioxide. For the formation of the catalyst, at $t=0$ h, the reactor is pressurized with carbon dioxide up to 10 MPa at 353 K. After the formation of the catalyst (1 μM) the hydrogenation was started by addition of 1-butene (0.02 M) and hydrogen (0.08 M), total pressure is 20 MPa. To determine the yield of the reaction, samples were analyzed by GC and GC-MS. The GC (Chrompack CP 9001) had a TCD detector equipped with a PoraPLOT Q column with a length of 25 m. The GC-MS was equipped with a 50 m CP-Al2O3/KCl column.

Figure 3: High-pressure set-up for homogeneously catalyzed batch reactions.

Permeation of supercritical carbon dioxide - The membrane permeability for high-density carbon dioxide was measured at 353 K with the high-pressure set-up depicted in Figure 4. The ceramic membrane was placed in an oven (Heraeus) and the temperature was controlled with a Pt100. The membrane set-up can be pressurized at the feed and permeate side up to 20 MPa. For a flux measurement, the needle valve at the permeate side of the membrane was opened until a trans-membrane pressure was reached varying between 1 and 3 MPa. After closing the
permeate needle valve, the trans-membrane pressure was measured with a pressure-difference meter from Druck (Smart Pressure Transmitter STX 2100).

![Diagram of membrane reactor](image)

Figure 4: High-pressure membrane reactor set-up. The function of the high pressure reactor is just for the making of the active catalyst.

**Continuous membrane reactor** - The continuous hydrogenation reaction in supercritical carbon dioxide (353 K, 20 MPa) was performed in the same high-pressure membrane reactor set-up as used for the permeation experiments, see Figure 4. The catalyst was first synthesized in situ in the high-pressure reactor, as described above. The amounts used in the synthesis are given in Table 1. The reaction was started by the addition of 1-butene and hydrogen in a molar ratio of 1:4. The substrates and the carbon dioxide were continuously supplied to the membrane module from a gas cylinder. The membrane was pressurized at the feed and permeate side up to 20 MPa with the reaction mixture, using an LKB HPLC pump. The pressure was monitored by a Meyvis 802-C pressure module. The permeate needle valve was opened to create a trans-membrane pressure varying between 0.05 and 1 MPa. The catalyst was brought into the system by flushing the feed mixture (H₂, 1-butene and CO₂) through the high-pressure reactor. To assure that no leaching of the catalyst and/or free ligand through the membrane occurred, the permeate stream was led through a high pressure viewing cell of 2.2 mL which was placed in a Spectronic Genesys 5 Spectrophotometer. The absorption was measured at 410 nm. Leaching of the catalyst and the ligand was studied in detail in a separate
retention measurement using ICP-AAS, because of the limited accuracy of UV-vis spectroscopy. The permeate stream was led through mass flow controllers (Bronkhorst) and was analyzed using GC and GC-MS. The analytical apparatuses were the same as described in the section Batch experiments.

Table 1. Concentrations used in the synthesis of 1.

<table>
<thead>
<tr>
<th></th>
<th>P-(C₆H₄-p-SiMe₂CH₂CH₂C₈F₁₇)₃</th>
<th>[RhCl(COD)]₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Batch</td>
<td>m [g] 1.9 x 10⁻³</td>
<td>m [g] 9 x 10⁻⁵</td>
</tr>
<tr>
<td></td>
<td>m [mol] 1.1 x 10⁻⁶</td>
<td>m [mol] 2.2 x 10⁻⁷</td>
</tr>
<tr>
<td>Continuous</td>
<td>m [g] 1.7 x 10⁻³</td>
<td>m [g] 1 x 10⁻⁴</td>
</tr>
<tr>
<td></td>
<td>m [mol] 1.0 x 10⁻⁶</td>
<td>m [mol] 1.8 x 10⁻⁷</td>
</tr>
</tbody>
</table>

**Results and Discussion**

*Permeation behavior* - In Figure 5 a comparison is made between the flux of gaseous carbon dioxide and 1-butene, at a temperature of 353 K and a feed pressure of 0.3 MPa. Both species permeate through the microporous membrane, and both fluxes show a linear dependency on the pressure difference across the membrane. The flux of 1-butene is a factor of 3 higher than the flux of carbon dioxide. Carbon dioxide is smaller than 1-butene with a size of 0.33 nm and 0.45 nm, respectively (Breck, 1974). However, 1-butene adsorbs stronger than carbon dioxide on silica (Verkerk et al., 2002). As a result, 1-butene permeates with a higher flux than carbon dioxide through the microporous silica membrane.

Transient permeation profiles of supercritical carbon dioxide are given in Figure 6 for different feed pressures. All the profiles are obtained for carbon dioxide in the supercritical state, i.e. pressures above 7.4 MPa. With an increase in the feed pressure the approach to equilibrium becomes faster. So, even at high pressures in combination with a low pressure difference across the membrane there is still a driving force for carbon dioxide to permeate. Consequently, at the reaction conditions the substrates (hydrogen and 1-butene), the solvent (CO₂), and the product (n-butane) will permeate through the silica membrane.
Figure 5: Flux of gaseous carbon dioxide and 1-butane at different trans-membrane pressures.

Figure 6: Transient profiles for supercritical carbon dioxide permeation through the silica membrane for different feed pressures, with $p_f$ and $p_p$ the pressure and the feed and the permeate side, respectively.
Chapter 6

Figure 7: UV-vis spectrum of I in supercritical carbon dioxide and tetrachlorocarbon.

Batch experiments - Figure 7 shows the UV-vis spectrum of the Wilkinson’s catalyst in scCO₂ and tetrachlorocarbon as a reference. The solubilized catalyst has a specific yellow color. A slight blue shift is noticeable upon solvation in carbon dioxide as compared to solvation in tetrachlorocarbon. Figure 8 shows the absorption at 410 nm during the formation of the fluorous Wilkinson’s catalyst. From the absorption spectrum it can be seen that the catalyst is formed in the scCO₂ during the first 2 h. However, after its formation the catalyst precipitates. By subsequent pressurization up to 20 MPa the catalyst dissolves again and is completely dissolved in the scCO₂ after 8 h. After complete solubilization of the catalyst, 1-butene and hydrogen are added in a molar ratio of 1:4, using 0.02 mol/L 1-butene.

Figure 9 shows a comparison between the conversion of 1-butene to n-butane obtained in the batch setup and obtained in the membrane reactor. In the batch reactor complete conversion is obtained after 100 min., which corresponds to a turnover frequency (TOF) of 9.4·10³ h⁻¹. For comparison, Deelman and coworkers (Richter et al, 2000a, b) have performed hydrogenation reactions using the same catalyst in a fluorous biphasic system, containing c-CF₃C₆F₁₁. The TOF found is in the order of 100 to1000 h⁻¹. The advantage of the high solubility of hydrogen in scCO₂ compared to the solubility of hydrogen in conventional solvents (2.7 mM in toluene, 298 K, 0.1 MPa) or fluorous solvents (6.1 mM in c-CF₃C₆F₁₁, 298 K, 0.1 MPa) leads to an increase in activity of the catalyst by at least a factor of 10, which is still rather low as compared to the ratio of hydrogen present in scCO₂ and c-CF₃C₆F₁₁. At high hydrogen
concentrations, however, it is known that the reaction rate becomes zeroth order in hydrogen (Osborn et al., 1966).

![Graph showing relative absorbance over time](image)

Figure 8: Absorbance at 410 nm of 1 in supercritical carbon dioxide as a function of time indicating the formation of 1.

**Continuous membrane reactor** - For the experiments in the continuous membrane reactor the catalyst is also prepared in situ. For pressurization the feed gas mixture is used. The catalyst concentration is equal to 2·10⁻⁶ mol/L, and in the feed 1-butene and hydrogen are present in a concentration of 0.02 and 0.08 mol/L, respectively, yielding a total pressure of 20 MPa. By changing the pressure difference across the membrane the residence time in the membrane module can be varied. In Figure 9 the conversion in the membrane reactor is given as a function of the residence time. As a consequence of the higher fluxes, i.e. shorter residence times, the conversion decreases. However, the experimental results in the batch system do not entirely agree with the results found in the continuous system. This is probably due to concentration polarization of the catalyst or absorption on the sealing material in the continuous system, so that less catalyst is present compared with the batch system.

In Figure 10 the conversion for the hydrogenation of 1-butene as performed in the membrane reactor is depicted. During the reaction at 353 K a pressure difference of 0.3 MPa has been applied, resulting in a total flux of 9.0·10⁻⁸ mol m⁻² s⁻¹ Pa⁻¹. For these conditions the residence time equals 62 min. After 3 h a constant conversion of 40% with a TOF of 4·10⁻³ h⁻¹ is obtained.
Figure 9: Conversion of 1-butene obtained in the batch and the continuous system. For the continuous experiment the reaction time is the residence time.

Figure 10: Conversion of 1-butene in a continuous membrane reactor as a function of the number of reactor volumes permeated.

Over night, the pressure of the system is reduced to 6 MPa, and the needle valve at the permeate side is closed. During depressurization the catalyst precipitates in the membrane reactor and no reaction occurs. The precipitated catalyst can be used for a new cycle by
pressurization of the membrane reactor. During the second and the third run the system is first pressurized to 20 MPa for 2 h. As a result, the catalyst dissolves again in the high-density carbon dioxide phase. At the end of the third run the conversion is about 33%, with a TOF of 3·10^3 h\(^{-1}\). This is 60% lower than obtained with the batch experiment (TOF = 9.4·10^3 h\(^{-1}\)). For the experiments performed in the continuous membrane reactor a turnover number of 1.2·10^5 is obtained in 32 h.

If leaching of the catalyst causes the decrease in conversion, the retention of the catalyst would still be well over 99%. Analysis of the permeate stream with UV-vis spectrophotometry shows, however, no permeance of the catalyst or free ligand. Additional ICP-AAS analysis of the permeate stream indicates that complete retention of the catalyst occurred. This confirms that the size of the catalysts is considerably larger than the pore diameter of 0.6 nm of the silica membrane. With respect to the deactivation, it is well know that the catalyst is susceptible to oxidation (Richter et al., 2000a, 2000b). Traces of oxygen present in the carbon dioxide or in the feed are most likely responsible for the deactivation of the catalyst.

![Diagram](image.png)

Figure 11: Proposed process concept for large-scale production.

It can be concluded that after a shutdown and start-up cycle the catalyst shows almost the same activity. This means that stable as well as flexible operation is possible using homogeneous catalysis in supercritical media, with in situ separation of the products from the catalyst.

In Figure 11 a tentative process scheme is given for large-scale operation. Of importance is the regeneration of the carbon dioxide from the products formed. This could be achieved for example by classical precipitation, adsorption, absorption, or different membrane separation step. For economic viability reasons, the catalyst concentration needs to be relatively high, the membrane area needs to be as small as possible, with a relatively high-pressure difference, thus creating a relatively short residence time. In this way the space-time yield of the membrane reactor can be maximized.
Table 2: Operation conditions for a hydrogenation reaction*.

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction kinetics</td>
<td>first order in alkene and hydrogen</td>
</tr>
<tr>
<td></td>
<td>first order in catalyst</td>
</tr>
<tr>
<td>Permeance</td>
<td>$8 \times 10^{-8}$ mol m$^{-2}$ s$^{-1}$ Pa$^{-1}$</td>
</tr>
<tr>
<td>Temperature</td>
<td>353 K</td>
</tr>
<tr>
<td>Concentration</td>
<td>0.05 mol L$^{-1}$ alkene</td>
</tr>
<tr>
<td></td>
<td>0.20 mol L$^{-1}$ hydrogen</td>
</tr>
<tr>
<td></td>
<td>variable catalyst concentration (thereby variable residence time)</td>
</tr>
<tr>
<td>Reactor volume</td>
<td>0.1 m$^3$</td>
</tr>
<tr>
<td>Minimal single pass</td>
<td>95%</td>
</tr>
<tr>
<td>conversion</td>
<td></td>
</tr>
<tr>
<td>Operation time per year</td>
<td>8000 h</td>
</tr>
</tbody>
</table>

*: reaction kinetics are derived from the batch hydrogenation experiment.

In Figure 12 the relation between the membrane surface area per volume (S/V) and the pressure difference to achieve a 95% conversion is given for the conditions given in Table 2. Four different residence times are compared and two types of modules are considered, a tubular and a capillary configuration. It is assumed that there are no mass transfer limitations due to concentration polarization, and that the permeance is linear with the pressure difference. A capillary module consists of a large number of capillaries assembled together in a module. A packing density of about 600 – 1200 m$^{-1}$ is obtained with modules containing capillaries with dimensions between tubular and hollow fibers. From Figure 12 it follows that for a given conversion the residence time depends on the catalyst concentration. The residence time is a function of the volume of the reactor and flux, so that the required surface area per volume decreases with an increase in residence time.
Figure 12: The relation between S/V and the pressure difference for given residence times (single pass conversion is fixed at 95%).

The tubular membrane used in this study has an S/V of about 400 m⁻¹. For an operation time of 8000 hours, and with a residence time of 10 minutes, a production rate of 205·10⁵ mol/year alkane can be obtained. For a given production capacity, an operation window can be defined as a function of the catalyst concentration (residence time), maximum pressure difference and available surface area per volume. However, the strength of the membrane, in terms of allowable pressure difference, the permeance through the membrane, and the regeneration method of the carbon dioxide determine the actual operating window.

Conclusions
A methodology for continuous homogeneous catalysis in supercritical carbon dioxide has been presented. A fluorous version of Wilkinson’s catalyst is used for the hydrogenation of 1-butene at a pressure of 20 MPa carbon dioxide and a temperature of 353 K. The catalyst is completely retained at the feed side of a microporous silica membrane. The retention of the catalyst and the possible free ligand is higher than 99 %, as shown by UV-vis spectroscopy and ICP-AAS.

The silica membrane investigated has some clear advantages over the membranes studied in the literature. One of the main advantages is that it is not necessary to have a high pressure difference across the membrane to obtain a substantial carbon dioxide flux.

After 32 h of operation a turnover number in the order 1.2·10⁵ has been obtained. The turnover frequencies obtained for the reaction carried out in carbon dioxide using the batch
reactor and the membrane reactor, $4.0 \times 10^3 \text{ h}^{-1}$ and $9.4 \times 10^3 \text{ h}^{-1}$, respectively, are significantly higher than the turnover frequency obtained in an organic solvent ($\text{TOF} = 100 \text{ to } 1000 \text{ h}^{-1}$).

It can be concluded that the methodology of using a membrane for localizing homogeneous catalyst in supercritical fluids will lead to various new opportunities for catalysis in supercritical fluids.

**Literature**


Sartorelli, L., and Brunner, G., Separation of extracts from supercritical carbon dioxide by means of membranes, Cd-rom proceedings 5th International Symposium on Supercritical Fluids, Atlanta GA (2000).


Chapter 7

Outlook to the Future: Micro-Heterogeneous Catalysis in Carbon Dioxide

Abstract
Homogeneous and heterogeneous catalysis in carbon dioxide offer a wide range of opportunities for more efficient and cleaner processes. However, the low solubility and the recovery of standard catalysts are two major drawbacks of homogeneous catalysis. Different approaches have been evaluated to circumvent these issues, ranging from the use of surfactants, via functionalized dendritic macromolecules, to the application of a membrane reactor.

In this chapter an alternative strategy for solubilizing catalysts in supercritical carbon dioxide by employing host-guest systems is presented. The generic character of this approach is demonstrated for catalytic oxidations using two different micro-heterogeneous systems. The first method is based on perfluoro-functionalized dendrimers as a host, the second one uses assemblies of amphiphiles. These systems lead to reasonable solubility of two different porphyrin catalysts in carbon dioxide. The catalytic activity of the two systems has been demonstrated for the oxidation of cyclohexene.

Carrier-mediated extractions and reactions
As can be seen from the previous chapters, supercritical fluids offer significant advantages as compared to traditional organic solvents. These advantages include a high miscibility with gases, variable dielectric constant, high compressibility, local density augmentation, high diffusivity, low viscosity, and variable cage strength. Both homogeneous and heterogeneous catalysis can benefit from these advantages (Table 1). Especially in the case of gaseous reactants, like oxygen, hydrogen or carbon monoxide, supercritical fluids (SCFs) are advantageous due to the possibility to have high concentrations of these reactants present in a single phase with non-gaseous reactants.

Table 1: Summary of the advantages, inherent difficulties and challenges of scCO₂.

<table>
<thead>
<tr>
<th>Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environmentally neutral</td>
</tr>
<tr>
<td>Nontoxic and nonflammable</td>
</tr>
<tr>
<td>Low viscosity and density, high diffusivity, easy adjustable by temperature and pressure</td>
</tr>
<tr>
<td>Easy to remove</td>
</tr>
<tr>
<td>Supercritical region is easily accessible (304 K, 7.3 MPa)</td>
</tr>
<tr>
<td>High miscibility with other gases (e.g. H₂, CO, O₂)</td>
</tr>
<tr>
<td>Nonpolar, weak molecular association</td>
</tr>
<tr>
<td>Thermodynamically stable, not sensitive to oxidation, and often kinetically inert</td>
</tr>
<tr>
<td>Inexpensive</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Inherent difficulties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoclave techniques are necessary</td>
</tr>
<tr>
<td>Low solubility of polar compounds, macromolecules, and organometallics in scCO₂</td>
</tr>
<tr>
<td>Phase behavior of reactants is not completely understood/known</td>
</tr>
<tr>
<td>Electrophilic properties limit the compatibility with some organic compounds (e.g. RNH₂, bases)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficient regeneration methods with a limited energy consumption are required</td>
</tr>
<tr>
<td>Number of metal directed reactions reported is small, synthetic procedures have yet to be explored</td>
</tr>
<tr>
<td>Heterogenization of homogeneous catalysts</td>
</tr>
<tr>
<td>Material processing using carbon dioxide</td>
</tr>
<tr>
<td>Combined use of carbon dioxide as solvent and reactant</td>
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</tbody>
</table>

Table 2: Activities in catalysis in supercritical carbon dioxide.
Homogeneous catalysis

<table>
<thead>
<tr>
<th>Batch</th>
<th>Continuous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jessop and Leitner, 1999</td>
<td><strong>Chapter 6</strong></td>
</tr>
<tr>
<td>Jessop et al., 1999</td>
<td>Bösmann et al., 2001</td>
</tr>
<tr>
<td>Leitner, 2000</td>
<td></td>
</tr>
<tr>
<td>Franciò et al., 2001</td>
<td></td>
</tr>
</tbody>
</table>

Carrier-mediated catalysis

- Phase transfer catalysis
  | **Chapter 4** |
  | Dillow et al., 1996 |
  | Chandler et al., 1998 |

- Host – guest strategy
  | **Chapter 7** |
  | Jacobson et al., 1999 |

Heterogeneous catalysis

<table>
<thead>
<tr>
<th>Batch/Continuous</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>- heterogeneous catalyst</strong></td>
</tr>
<tr>
<td>Hitzler et al., 1998</td>
</tr>
<tr>
<td>Baiker, 1999</td>
</tr>
<tr>
<td>Jenzer et al., 2001</td>
</tr>
<tr>
<td>Hyde et al., 2002</td>
</tr>
<tr>
<td><strong>- immobilized catalyst</strong></td>
</tr>
<tr>
<td>De Vries et al., 2002</td>
</tr>
</tbody>
</table>

* heterogenization of homogeneous catalyst upon a heterogeneous support

In Table 2 an overview is made of the approaches presented in this thesis and current activities in the field of catalysis in supercritical carbon dioxide. Homogeneous and heterogeneous catalysis in carbon dioxide offer a wide range of opportunities for more efficient and cleaner processes. However, the low solubility and the recovery of standard catalysts are two major drawbacks of homogeneous catalysis. Different approaches have been evaluated to circumvent these issues. Both fundamental and more applied aspects have been addressed. In Chapter 2 fundamental issues related to solubilization in carbon dioxide have been studied, and Chapter 5 describes the permeation behavior of liquid and supercritical carbon dioxide through microporous silica membranes.

In Chapters 3 and 4 the focus has been on using dendritic macromolecules in reactive extraction and phase transfer catalysis. Additionally, a comparison has been made between standard solvents and carbon dioxide. In Chapter 6 an efficient methodology has been presented for localizing homogeneous catalysts facilitating continuous catalytic operation in SCF. Finally, some alternative methods, based on host - guest complexes, to improve the solubility of homogeneous catalysts are presented in this chapter. Clearly, the membrane
reactor methodology can be combined with the host – guest strategy to separate in situ the product from the catalyst.

**Host-guest strategies**

One way to increase the solubility of catalysts in SCFs is to modify existing catalysts with ligands especially designed for carbon dioxide. However, modifying conventional catalysts in this manner is often troublesome and expensive. It is more efficient to use existing catalysts, which have been optimized for more traditional organic solvents, without any chemical modification.

Two methods are evaluated for homogeneous catalysis in supercritical carbon dioxide (scCO₂), using standard catalysts that are (normally) not soluble in carbon dioxide (Figure 1). Both methods are based on the idea of non-covalent binding of homogeneous catalysts in host - guest systems, where the host is soluble in scCO₂. The first method is based on employing a macromolecular carrier. The carrier has a favorable interaction with the catalyst and assures solubility of the catalyst - carrier complex. As an example of a macromolecular carrier a functionalized dendrimer, a so-called unimolecular micelle, has been used. The second method is based on the use of surfactants to create a micro-heterogeneous system in scCO₂. In this case a reverse micelle serves as the host for the catalyst. The CO₂-philic tails of the surfactants shield the polar interior of the micelle, and a micro-environment is created where the catalyst can be active.

![Diagram of a perfluoroctyl functionalized third generation poly(propylene imine) dendrimer and a reverse micelle.](image)

Figure 1: A perfluoroctyl functionalized third generation poly(propylene imine) dendrimer and a reverse micelle.

The similarity between modified dendrimers and reverse micelles is based on the distribution of the hydrophobic and hydrophilic parts. In fact, a dendritic species can be seen as a unimolecular (polymerized) version of the traditional low molecular weight surfactant. In this
way a micro-heterogeneous environment is created, which leads to a number of advantages like increased reaction rate, the possibility to tune the environment of the catalyst, and easy separation of the catalyst from the products. The environment of the catalyst can be tuned by the type of SCF, the operating conditions (pressure and temperature), and the type of host.

In both immobilization strategies, a porphyrin catalyst (Figure 2) is used as a typical example of a class of catalysts that is normally not suited for reactions in scCO₂ due to its low solubility. Two different porphyrin catalysts have been used for the oxidation of cyclohexene with molecular oxygen. A stoichiometric amount of a sacrificial aldehyde, acetaldehyde, is used as a reductant.

In the first method a porphyrin is used with sulphonated headgroups (1; 5,10,15,20-tetrakis(4-sulfonatophenyl)-21H,23H-porphyrin manganese(III) chloride). This porphyrin has a good interaction with the protonated tertiary amines of the dendritic carrier. The carrier used is a third generation poly(propylene imine) dendrimer modified with fluorinated tails (see Chapters 3 and 4). The dendrimer has a polar interior and a periphery of CO₂-phlic tails (Figure 2).

In the second method a porphyrin is used with pyridine groups (2; 5,10,15,20-tetra(4-pyridyl)-21H,23H-porphyrin manganese(III) chloride tetrakis(methochloride)) attached to the macrocycle. The pyridine groups have a good interaction with the anionic headgroups of the 3,5-bis(perfluorooctyl) phenylsulfonate sodium salt surfactant (see Chapter 2).

**Experimental**

*Materials* - The porphyrins 5,10,15,20-tetrakis(4-sulfonatophenyl)-21H,23H-porphyrin manganese(III) chloride (1) and 5,10,15,20-tetra(4-pyridyl)-21H,23H-porphyrin manganese(III) chloride tetrakis(methochloride) (2) were purchased from Porphyrin Products Inc. Cyclohexene (99%) was purchased from Aldrich. Carbon dioxide (grade 5.0), and oxygen (grade 4.0) were obtained from HoekLoos (Amsterdam, The Netherlands). The synthesis of the surfactant and perfluoro functionalized dendrimer is described in Chapters 2 and 3, respectively.

![Figure 2: Porphyrin catalysts used for the oxidation of cyclohexene.](image-url)
Chapter 7

**Apparatus** - The high-pressure extraction is carried out in a vessel with a variable volume, between 11 and 26 mL, two sapphire windows and a magnetic stirrer bar. The reactor is a small 2.2 mL vessel also equipped with two sapphire windows and a magnetic stirrer bar. Both vessels are temperature and pressure controlled.

**Procedure** - In the case of the extraction of 1 the concentration of the carrier in pure carbon dioxide was $1 \times 10^{-3}$ mol/L and the concentration of 1 in the water phase was $2 \times 10^{-3}$ mol/L. The ratio of the aqueous phase to the carbon dioxide phase was 1 to 4. The condition for the extraction of 2 was the same as for 1 except that the concentration of the surfactant in the carbon dioxide phase was $2 \times 10^{-2}$ mol/L.

A dual reactor approach is used for the preparation and utilization of the two host-guest complexes. In the first high-pressure reactor the dendrimer or the reverse micelles have been used to extract the porphyrin catalyst from an aqueous phase to a carbon dioxide phase. The extracted host-guest complex is then transferred to a second reactor (Figure 3). In the second reactor also the substrate and coreductant are present.

To perform the reactions, the catalysts 1 and 2 were first extracted into carbon dioxide and then transferred to the second reactor vessel containing $5 \times 10^{-2}$ mol/L acetaldehyde and cyclohexene. The conditions for the extraction to perform the reaction were the same as for the extraction into pure carbon dioxide, but a mixture of carbon dioxide/oxygen has been used instead. The oxygen pressure was 0.8 MPa. After 8 h of reaction samples were taken and analyzed using GC.

Figure 3: High-pressure equipment.
Results and Discussion

High-pressure in-situ UV-vis spectroscopy is used to measure the solubility of the dendrimer - porphyrin and the reverse micelle - porphyrin complex in scCO₂, and to explore the effects of the environment on the electronic structure of the porphyrin. In Figure 4a the UV-vis spectrum of 1 attached to the dendritic carrier in a bulk phase of supercritical carbon dioxide (323 K, 30 MPa) is compared with the spectra of 1 solubilized in water.

The electronic absorption spectra are extremely sensitive, making UV-vis spectroscopy a powerful tool for elucidating information about the surrounding of the porphyrin. In particular, the Soret band of the porphyrin, a high intensity \( \pi \rightarrow \pi^* \) transition around 400 - 440 nm, shifts considerably upon binding of substrates or an axial ligand to the porphyrin, or by dimerization or distortion of the porphyrin structure. A slight blue shift of the Soret band is clearly visible, shifting from 469 to 475 nm. In Figure 4b the Soret band of 2 in the reverse micelle in scCO₂ and in water is shown. There is also a slight blue shift. The relative UV-vis spectra of both 1 and 2 in scCO₂ do not change with a change in pressure of carbon dioxide. This indicates that the pressure has not an influence on the environment of 1 and 2.

![UV-vis spectra of the porphyrin catalysts](image1)

![UV-vis spectra of the porphyrin catalysts](image2)

Figure 4: UV-vis spectra of the porphyrin catalysts; (a) 1 attached to the dendritic carrier in supercritical carbon dioxide and 1 in water; (b) 2 solubilized inside the reverse micelle in supercritical carbon dioxide and 2 in water.

Under the conditions studied, a reasonable loading of the catalyst in carbon dioxide is obtained using the two host - guest systems. The amount extracted of the porphyrin catalysts was deduced from the assumption that the extinction coefficients are similar in water and in the carrier or the micelle. In the case of the first strategy the extraction yield is 17% at 323 K and 30 MPa. However, high-pressure dynamic light scattering experiments indicate that more than one single carrier is involved in the extraction of one porphyrin suggesting a sandwhich-like structure. For the second strategy the extraction yield equals 14% at the same conditions as applied for the first strategy.
Table 3: Experimental results for the two immobilization strategies, at 323 K and 30 MPa.

<table>
<thead>
<tr>
<th>host - guest</th>
<th>% product(^{(a)})</th>
<th>TON(^{(a)})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>epoxide</td>
<td>alcohol</td>
</tr>
<tr>
<td>dendrimer - 1</td>
<td>16</td>
<td>62</td>
</tr>
<tr>
<td>reverse micelle - 2</td>
<td>13</td>
<td>67</td>
</tr>
</tbody>
</table>

(a) after 8 hours.

After obtaining the otherwise non-soluble catalysts in carbon dioxide, the catalytic activity of the micro-heterogeneous systems containing 1 and 2 has been investigated. These systems in combination with the properties of scCO\(_2\) are suited for oxidation reactions with molecular oxygen. In contrast with the work performed by Loeker et al. the background oxidation was not dominant (Loeker and Leitner, 2000). The reason for this is probably the difference in steel used for the reactors. The oxidation of cyclohexene with molecular oxygen leads to a number of different products like epoxides, alcohols and ketones. In both cases, the selectivity towards the epoxide is not very high (Table 3). However, the turnover number (TON) is in good agreement with investigations using porphyrin catalysts in traditional organic solvents (Birnbaum et al., 1995). It is interesting that the product distribution and the TON are quite similar for both systems. From these results it follows that although the unimolecular reverse micelle has a covalently fixed macromolecular structure while the "classical" reverse micelle has a dynamic equilibrium structure the two systems constitute the same micro-environment for this type of reactions.

**Future outlook and concluding remarks**

There are two main focal points for possible improvements in the area of catalysis in SCFs. The first one is related to the type of catalysis, the second issue is related to the solvent. With respect to the first issue, process concepts for large-scale application of homogeneous catalysis in SCF are lacking. From Table 2 it is clear that for a breakthrough in the use of SCF more continuously operated processes are required.

It is generally accepted that heterogeneous catalysis, is more readily applicable for continuous operation using scCO\(_2\). Especially, for fine chemicals synthesis some clear opportunities exist. Heterogenation of available homogeneous catalyst could speed-up the development of catalysis in scCO\(_2\) operated continuously. For example, methyltrioxorhenium (MTO) is
known to be a versatile catalyst suited for epoxidation, oxidation, and Diels-Alder reactions and upon activation it can also be used for metathesis (Owens et al., 2000, Herrmann, et al., 1991). A heterogeneous version of MTO can be obtained by immobilization on a silica-alumina oxide material (ASA). By heterogenation the catalyst complex (MTO/ASA) is also highly active in catalyzing ring opening metathesis reactions with norbornene as a monomer in scCO₂ (De Vries et al., 2002).

For the second issue, a logical extension of catalysis in SCF seems to be the use of expanded solvents as reaction media for catalysis. Expanded solvents combine the advantages of both SCF and traditional organic solvents. The expanded solvents can contain a large amount of carbon dioxide at rather low pressures and thereby allowing a higher solubility of gaseous reactants in the expanded solvent. This potentially leads to higher reaction rates. A second advantage is the even more tunable nature of the solvent-CO₂ combination as compared to scCO₂. For example, environmentally friendly solvents like methanol and ethanol can be made more apolar by pressurization with carbon dioxide. Moreover, the solubility of more hydrophilic or larger components is substantially higher as compared to the solubility in pure carbon dioxide.

In this thesis the potential of SCF has been demonstrated for a number of extraction and catalytic reactions and new possibilities have been proposed. In particular, different methods have been explored to immobilize, in the broadest sense, homogeneous catalysts. The different concepts presented in this work including the immobilization using a membrane or the carrier-mediated catalysis could lead to more efficient catalytic processes. The carrier-mediated catalysis, including phase transfer catalysis, and the immobilization using reverse micelles or dendritic macromolecules, offers numerous opportunities for alternative process concepts, further to be explored in the future.

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Summary

A global increase in environmental awareness has led to an ever-increasing control over the use and disposal of hazardous materials by the chemical industry. This in turn makes the chemical industry continuously searching for new and cleaner alternatives for its current processes. One obvious target area for improvements comprises the currently used organic solvents. Suitable candidates for the replacement of conventional organic solvents include supercritical fluids (SCF). Carbon dioxide is the most commonly used SCF, primarily due to its reasonably low critical temperature and pressure (304 K and 7.4 MPa), low cost, non-flammability and non-toxicity. By just employing carbon dioxide as a replacement for organic solvents, the application potential is often limited to compounds soluble in carbon dioxide. A general disadvantage of carbon dioxide is, however, that it is a poor solvent for high molecular weight or hydrophilic molecules. Different approaches to extend the application window of carbon dioxide are described. A way to overcome this solubility problem is by using surfactants. A methodology for the design and use of twin-tailed surfactants for applications in high-density carbon dioxide is presented. The solubility in carbon dioxide of four twin-tailed surfactants with different tail lengths is studied. A clear effect of the length of the surfactant tail on its solubility can be observed. This type of surfactant appears to be capable of solubilizing a large amount of water in carbon dioxide. Additionally, the use of these surfactants as extractive agents for proteins is evaluated.

A second strategy for solubilizing non-soluble components in carbon dioxide is using carriers such as perfluorooctyl functionalized poly(propylene imine) dendrimers. Upon functionalization with "CO2-philic" groups these dendrimers are soluble in carbon dioxide. The functionalized dendrimers can be envisaged as a unimolecular (polymerized) version of a micelle with traditional low molecular weight surfactants. These dendritic macromolecules are capable of extracting a large number of dye molecules from an aqueous phase to a carbon dioxide phase. A description is given of the extraction mechanism, based on a mass action model. These carriers can also be used as a phase transfer catalyst. To evaluate the usefulness of the dendrimers two types of reactions in supercritical carbon dioxide have been examined, namely the halogen exchange reaction of benzyl chloride into benzyl bromide and the esterification of oxalic acid with pentafluorobenzylbromide. It is found that the rate of reaction for both cases depends on the generation number of the dendrimer. For the higher generation dendrimers, it is more difficult for the substrate to migrate from the bulk carbon dioxide phase to the interior of the dendrimer. This indicates that mass transfer of the reagents from the solvent phase into the interior of the dendrimer determines the reaction rate for the fourth and higher generation dendrimers. A model is proposed to describe extraction and
phase transfer catalysis based on the fact that the modified dendrimers combine micellar properties with that of standard phase transfer catalysts. Homogeneous catalysis can benefit from the use of supercritical solvents, due to the high diffusivity and low viscosity, making these solvents suitable for rapid mass transfer. Especially reactions with gaseous species, e.g. hydrogen and oxygen, are of interest. The low solubility and the recovery of standard catalysts are two major drawbacks of homogeneous catalysis. Different approaches have been evaluated to circumvent these issues, ranging from the use of surfactants, and functionalized dendritic macromolecules, to the application of a membrane reactor.

Two alternative strategies for solubilizing catalysts in supercritical carbon dioxide by employing host - guest systems are presented. The first method is based on perfluoro-functionalized dendrimers as a host, the second one uses assemblies of amphiphiles. These systems lead to reasonable solubility of two different porphyrin catalysts in carbon dioxide. The generic character of this micro-heterogeneous approach is demonstrated for the catalytic oxidation of cyclohexene with oxygen.

An important issue in homogeneous catalysis is the separation of the often very expensive catalyst from the products. For this problem, a methodology is developed based on the use of microporous membranes for localizing the catalyst, thus allowing for continuous operation. The membrane reactor concept offers the advantages of benign high-density gases, i.e. the possibility of achieving high concentrations of gaseous reactants in the same phase as the substrates and catalyst, as well as easy catalyst localization by means of a membrane.

A microporous silica membrane has been evaluated for the permeation of gaseous, liquid and supercritical carbon dioxide up to 20 MPa, at various temperatures. For all conditions high carbon dioxide fluxes have been obtained. The membrane has been tested with a maximum pressure difference between the feed and the permeate side of about 2.5-MPa. At a feed-side pressure of 20 MPa and at 358 K the permeance is equal to $8.0 \cdot 10^8$ mol m$^{-2}$ s$^{-1}$ Pa$^{-1}$. The transient transport through the microporous membrane can be described with a single mass transfer coefficient. The fact that carbon dioxide has a high flux through this type of silica membranes opens the way for regeneration of carbon dioxide at supercritical conditions, without the need for a depressurization/recompression cycle.

The membrane reactor concept is demonstrated for the hydrogenation of 1-butene using a fluorour derivative of Wilkinson's catalyst. The size of the Wilkinson's catalyst is larger than the pore diameter of the silica membrane, so that the membrane retains the catalyst, while the substrates and products will permeate. Stable operation and continuous production of $n$-butane has been achieved at a temperature of 353 K and a pressure of 20 MPa. A turnover number of $1.2 \cdot 10^5$ has been obtained during 32 h of reaction.

The performed research has lead to greater insights in employing the positive properties of carbon dioxide and circumventing the difficulty of applying this as a solvent for polar and charged species. The methodology presented in this thesis will be relevant for the future
development of clean chemical processes carried out in environmentally friendly high-density gases.
Samenvatting

In de chemische procesindustrie worden veel milieubelastende chemicaîien gebruikt. Dankzij een groeiend milieubewustzijn wordt hieraan steeds meer aandacht besteed. Dit zorgt ervoor dat de chemische industrie continu bezig is met het zoeken naar nieuwe en schonere alternatieven voor huidige processen. Superkritische vloeistoffen behoren tot de kanshebbers om organische oplosmiddelen (gedeeltelijk) te vervangen. Koolstofdioxide is de meest gebruikte superkritische vloeistof, voornamelijk omdat het een redelijk lage kritische temperatuur en druk heeft (304 K en 7.4 MPa), goedkoop is, en niet-brandbaar en niet-toxisch is. Het gebruik van koolstofdioxide als een vervanger van organische oplosmiddelen is vaak beperkt tot applicaties waarbij componenten oplosbaar zijn in dit medium. Verder is het in het algemeen een slecht oplosmiddel voor polaire of hoog moleculaire componenten. In dit proefschrift werden methoden beschreven om dit oplosbaarheidprobleem te omzeilen door gebruik te maken van surfactant-systemen.

Een methodologie voor het ontwerp en gebruik van twee-staartige surfactants is opgezet. Verder is de oplosbaarheid in koolstofdioxide van vier twee-staartige surfactants met verschillende staartlengte bestudeerd. Een duidelijk effect van de staartlengte is waarneembaar. Dit type surfactant lijk geschikt te zijn om grote hoeveelheden water in koolstofdioxide op te nemen. Daarnaast is het gebruik van deze surfactants als extractiemiddel voor eiwitten geëvalueerd.

Een tweede strategie voor het oplossen van niet-oplosbare componenten in koolstofdioxide is het gebruik van dragers zoals perfluorocanoyle gefunctionaliseerde poly(propylene imine) dendrimeren. Door het functionaliseren met "CO2-minnende" groepen zijn deze dendrimeren goed oplosbaar in koolstofdioxide. Deze gefunctionaliseerde dendrimeren kunnen beschouwd worden als een unimoleculaire (gepolymeriseerde) versie van een micel, gebaseerd op de traditionele laagmoleculaire surfactants. Deze dendritische macromoleculen zijn in staat om efficiënt grote hoeveelheden kleurstof te extraheren van een waterfase naar een koolstofdioxide fase. Een beschrijving wordt gegeven van het extractiemechanisme, gebaseerd op het zogenaamde "mass action" model.

Deze dragers kunnen ook gebruikt worden als fase transfer katalysatoren. De toepasbaarheid van de dendrimeren is onderzocht voor twee verschillende type reacties, namelijk de halogeen uitwisselingsreactie van benzylechloride naar benzylbromide en de esterificatie van oxaalzuur met pentafluorbenzylbromide. De snelheid van de reactie wordt in beide gevallen bepaald door de generatie van de dendrimeren. Voor een hogere generatie dendrimeren geldt dat het moeilijker wordt voor het substraat om van de bulk koolstofdioxide fase te migreren naar de kern van de dendrimeren. Voor de extractie en fase transfer katalyse wordt een model
voorgesteld gebaseerd op het feit dat gemodificeerde dendrimeren eigenschappen hebben tussen gewone micellen en standaard fase transfer katalysatoren in. Homogene katalyse kan profiteren van het gebruik van superkritische oplosmiddelen. Deze oplosmiddelen hebben een lage viscositeit en tevens hebben de reactanten opgelost in deze media een hoge diffusiviteit, zodat er een snel matransport optreedt. Vooral reacties met gasvormige reactanten zoals waterstof, zuurstof en koolmonoxide kunnen hiervan profiteren. De lage oplosbaarheid en de terugwinning van de katalysatoren zijn belangrijke issues. Verschillende strategieën zijn geëvalueerd om deze problemen te omzeilen, zoals het gebruik van surfactants en gefunctionaliseerde dendrimeren en de applicatie van membraanreactoren. Er zijn twee alternatieve methoden voor het oplossen van katalysatoren in superkritische koolstofdioxide ontwikkeld gebaseerd op het zogenaamde "host-guest" principe. De eerste strategie is gebaseerd op het gebruik van perfluorocyaanyl gefunctionaliseerde dendrimeren als gastheer. De tweede is gebaseerd op het gebruik van surfactants. Deze beide methoden leiden tot een redelijke oplosbaarheid van twee verschillende porfyrine katalysatoren in koolstofdioxide, die zonder hulpstoffen niet oplosbaar zijn in dit medium. Het generieke karakter van deze micro-heterogene aanpak is gedemonstreerd voor de katalytische oxidatie van cyclohexeen met zuurstof.

Een belangrijk item in homogene katalyse is de scheiding van de vaak zeer dure katalysator van de producten. Voor dit probleem is een methode ontworpen, die gebaseerd is op het gebruik van microporeuze membranen voor het lokaliseren van de katalysator. Hierdoor wordt het mogelijk om reacties continu te bedrijven. Het membraanreactor concept heeft de voordelen van het gebruik van milieuvriendelijke koolstofdioxide en maakt het mogelijk om een hoge concentratie gasvormige reactanten in dezelfde fase als de andere substraten en de katalysator te hebben. Tevens heeft het de voordelen van het immobiliseren van de katalysator.

Een microporeus silica membraan is geëvalueerd voor de permeatie van gasvormig, vloeibaar en superkritisch koolstofdioxide tot 20 MPa bij verschillende temperaturen. Voor alle onderzochte condities werd een hoge koolstofdioxide flux verkregen. Het membraan is getest met een maximaal drukverschil tussen voeding en permeaat van 2.5 MPa. Bij een voedingsdruk van 20 MPa en een temperatuur van 358 K is de permeatie gelijk aan $8,0 \cdot 10^{-8}$ mol m$^{-2}$ s$^{-1}$ Pa$^{-1}$. De transiënte metingen door de microporeuze membraan kunnen beschreven worden met een enkele matransportcoëfficiënt. Het feit dat koolstofdioxide een hoge flux heeft door dit type silica membranen maakt het mogelijk om koolstofdioxide te regenereren onder superkritische condities zonder de noodzaak van een decompressie / compressie cyclus. Het membraanreactor concept is gedemonstreerd voor de hydrogenering van 1-buteen met een fluorversie van de Wilkinson katalysator. Deze katalysator is in superkritische koolstofdioxide groter dan de poriediameter van het silica membraan. Hierdoor houdt het membraan de katalysator tegen waarbij de producten, substraten en koolstofdioxide de membraan kunnen passeren. Stabiele operatie en een continue productie van n-butaan is bereikt bij een
temperatuur van 353 K en een druk van 20 MPa. Een omzettinghoeveelheid per katalysator van $1.2 \times 10^5$ is bereikt na een continue bedrijfsvoering van 32 uur.
Het voltooide onderzoek zal leiden tot een groter inzicht in het gebruik van de positieve eigenschappen van koolstofdioxide en het omzeilen van de problemen die geassocieerd zijn met het gebruik van dit oplosmiddel voor polaire en geladen componenten. De methodologieën die hier zijn gepresenteerd zullen relevant zijn voor de toekomstige ontwikkeling van schone chemische processen, uitgevoerd in milieuvriendelijke hoge dichtheid gassen.
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Earl Goetheer