DEVELOPMENT OF CO\textsubscript{2}-ASSISTED SEPARATION TECHNIQUES FOR THE BIOMASS CONVERSION SECTOR

by

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A thesis submitted to the Department of Chemistry
In conformity with the requirements for
the degree of Doctor of Philosophy

Queen's University
Kingston, Ontario, Canada
(September, 2022)

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Abstract

Using current technologies, obtaining chemicals from biomass is typically less environmentally friendly than from petroleum. In many cases, the most significant part of the environmental impact of biomass conversion is caused by the energetic requirements for separating intermediates or products from water. Water removal, via distillation and other drying processes, can account for up to 80% of the total energy consumption of certain biomass conversions. Unless the environmental and energetic costs of separating water from organic products can be lowered, bio-derived products will struggle to be greener and cheaper than fossil-derived products.

Carbon dioxide-assisted separations might be an alternative to promote more energetically efficient separations, especially in recovering low-volatility hydrophilic organic molecules from water. The techniques developed take advantage of previously described separations triggered by CO₂. Two new methods are proposed: high pressure switchable water (HPSW) and solvent-assisted high pressure switchable water (SA-HPSW). These methods operate from the synergy between switchable water, CO₂ expansion of liquids and liquid-liquid extraction while overcoming some drawbacks observed when those three techniques are performed separately. The ionogens used in HPSW and SA-HPSW were also recovered via reverse osmosis. In addition, the ionogens used in HPSW were also applied as a catalyst in a Baylis-Hillman type reaction. After conversion, the addition of CO₂ aided the recovery of the desired product, highlighting the dual effect HPSW might have in organic reactions in water. Considerations were also made regarding the energy consumption of the processes, and comparisons were drawn with distillation.

This work was focused on biomass products considered in commercial applications. HPSW promoted the separation of acetone (one of the components of the acetone-butanol-ethanol process), isopropanol, and ethyl lactate. SA-HPSW was evaluated for ethanol recovery (which can be obtained via fermentation of sugars). Unfortunately, high energy consumption was calculated for the distillation required to purify the ethanol even after SA-HPSW had already been performed.
SA-HPSW was also explored in the recovery of 1,4-butanediol, ethylene glycol, propylene glycol and 1,5-pentanediol, which are being explored as replacements for petroleum-derived chemicals. Finally, considerations were made regarding optimizations necessary to decrease the energy requirements for both HPSW and SA-HPSW.
Acknowledgements

Para Mãe (In Memoriam)

First, and foremost, I would like to thank my supervisor, Dr Philip Jessop. Philip, I am very grateful for the opportunity you gave me; your guidance and support allowed me to explore exciting research challenges and grow as a professional inside and outside the lab. I also want to thank you for your tireless editing throughout my entire degree. I am a better writer because of you. Coming to Queen's and working with you opened my world to so many exciting opportunities.

At the Jessop lab, I met more than fellow chemists; I made friends I will take for life. Dr Sarah Ellis and Jaddie Ho, you have both taught me so much; without your constant incentive and care, I don't know how I would have been able to do everything I did in 4 years, especially outside the lab. I had a great experience at Queen's, which was only possible due to the many people I've met through amazing initiatives. Thank you to the 2019 and 2020 QGCS executives, the Bonds for Success team, and the QC-IDEAS members; being part of these groups changed me and made me a better person. And to all the other friends I made through my journey at Queen's, thank you for sharing this experience with me.

I want to thank all the staff members of the Department of Chemistry at Queen's University, especially Jessica Bright and Michelle Boutillier; your help, even before my degree started, made my time at Queen's so much easier.

I am also grateful for the financial support I've received from Queen's, the Department of Chemistry and from Mr. Huntley M. Sinclair and his family through the Huntley Macdonald Sinclair Tuition Fellowships. Thank you for supporting international students.

I would also like to show appreciation for my loving fiancé, Laura. You are always here for me; your support and love make everything possible. I wouldn't be here without you.
Finally, I would like to thank my family and friends back in Brazil. You have always believed in me, and your love sees no distance. It seems unreal that the “silly” aspirations from tio Eduardo (even if he was thinking about a different kind of doctor) are materializing.
Statement of Originality

I hereby certify that all the work described within this thesis is the original work of the author. Any published (or unpublished) ideas and/or techniques from the work of others are fully acknowledged in accordance with the standard referencing practices. The contributions from collaborators are clearly noted below. All the work was performed under the supervision of Dr Philip Jessop.

In Chapters 1 and 2, part of the discussion was obtained from the published paper: I.T. Cunha, H. Yang, P.G. Jessop, High pressure switchable water: an alternative method for separating organic products from water, Green Chemistry (2021) 23, 3996-4007. https://doi.org/10.1039/d1gc01113h.


In Chapters 3 and 4, the energy consumption data for the different distillation setups was obtained by Muflih A Adnan and Dr Md Golam Kibria from the Schulich School of Engineering at the University of Calgary. Analyses were also performed with the support of Dr Cao Thang Dihn from Queen's University.


Igor Tadeu da Cunha, August 2022
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<th>Abbreviation</th>
<th>Full Form</th>
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</thead>
<tbody>
<tr>
<td>1,4-BD</td>
<td>1,4-Butanediol</td>
</tr>
<tr>
<td>CP</td>
<td>Cloud pressure</td>
</tr>
<tr>
<td>CXL</td>
<td>CO$_2$-expanded liquid or CO$_2$-expansion of liquids</td>
</tr>
<tr>
<td>DABCO</td>
<td>1,4-Diazabicyclo[2.2.2]octane</td>
</tr>
<tr>
<td>DEAE</td>
<td>N,N-Diethylethanolamine</td>
</tr>
<tr>
<td>3DMAP</td>
<td>3-Dimethylamino-1-propanol</td>
</tr>
<tr>
<td>DMEA</td>
<td>N,N-Dimethylethanolamine</td>
</tr>
<tr>
<td>EDEA</td>
<td>N-Ethyl-diethanolamine</td>
</tr>
<tr>
<td>EG</td>
<td>Ethylene glycol</td>
</tr>
<tr>
<td>EL</td>
<td>Ethyl lactate</td>
</tr>
<tr>
<td>EWG</td>
<td>Electron-withdrawing group</td>
</tr>
<tr>
<td>GHG</td>
<td>Greenhouse gas</td>
</tr>
<tr>
<td>GHS</td>
<td>Globally Harmonized System</td>
</tr>
<tr>
<td>3HMNPAME</td>
<td>3-Hydroxy-2-methylene-3-(4-nitrophenyl)propanoic acid methyl ester</td>
</tr>
<tr>
<td>HMTETA</td>
<td>N,N,N',N''N'''-Hexamethylenetetramine</td>
</tr>
<tr>
<td>HPSW</td>
<td>High pressure switchable water</td>
</tr>
<tr>
<td>IS</td>
<td>Internal standard</td>
</tr>
<tr>
<td>$K^*_{a1}$</td>
<td>Combined dissociation constant for dissolved CO$_2$(aq) and H$_2$CO$_3$(aq)</td>
</tr>
<tr>
<td>$K_{aH}$</td>
<td>First dissociation constant for protonated ionogen</td>
</tr>
<tr>
<td>$K_{aH2}$</td>
<td>Second dissociation constant for protonated ionogen</td>
</tr>
<tr>
<td>$K_{aH3}$</td>
<td>Third dissociation constant for protonated ionogen</td>
</tr>
<tr>
<td>KB</td>
<td>Kirkwood-Buff</td>
</tr>
<tr>
<td>$K_H$</td>
<td>Henry’s law constant</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>$K_w$</td>
<td>Dissociation constant of water in pure water</td>
</tr>
<tr>
<td>LC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Lethal concentration that kills 50 percent of a test population</td>
</tr>
<tr>
<td>LCA</td>
<td>Life cycle assessment</td>
</tr>
<tr>
<td>LCSP</td>
<td>Lower critical solution pressure</td>
</tr>
<tr>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>Lethal dose that kills 50 percent of a test population</td>
</tr>
<tr>
<td>log P</td>
<td>Base 10 log partition coefficient</td>
</tr>
<tr>
<td>MAC</td>
<td>Methyl acrylate</td>
</tr>
<tr>
<td>MDEA</td>
<td>N-Methyldiethanolamine</td>
</tr>
<tr>
<td>4-NBA</td>
<td>4-Nitrobenzaldehyde</td>
</tr>
<tr>
<td>$P_{CO_2}$</td>
<td>Pressure of CO&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td>1,5-PD</td>
<td>1,5-Pentanediol</td>
</tr>
<tr>
<td>PET</td>
<td>Polyethylene terephthalate</td>
</tr>
<tr>
<td>PG</td>
<td>Propylene glycol</td>
</tr>
<tr>
<td>PMDETA</td>
<td>N,N,N',N'',N''-Pentamethyldiethylenetriamine</td>
</tr>
<tr>
<td>PTA</td>
<td>Purified terephthalic acid</td>
</tr>
<tr>
<td>RO</td>
<td>Reverse osmosis</td>
</tr>
<tr>
<td>SA-HPSW</td>
<td>Solvent-assisted high pressure switchable water</td>
</tr>
<tr>
<td>SA-SW</td>
<td>Solvent-assisted switchable water</td>
</tr>
<tr>
<td>SO</td>
<td>Salting-out</td>
</tr>
<tr>
<td>SW</td>
<td>Switchable water</td>
</tr>
<tr>
<td>TEA</td>
<td>Triethanolamine</td>
</tr>
<tr>
<td>THEED</td>
<td>N,N,N',N'-Tetrakis(2-hydroxyethyl)ethylenediamine</td>
</tr>
<tr>
<td>TMBDA</td>
<td>N,N,N',N'-Tetramethyl-1,4-butanediamine</td>
</tr>
<tr>
<td>TMEDA</td>
<td>N,N,N',N'-Tetramethylethylene-1,2-diamine</td>
</tr>
<tr>
<td>TMPDA</td>
<td>N,N,N',N'-Tetramethyl-1,3-propanediamine</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>TMTAD</td>
<td>2,6,10-Trimethyl-2,6,10-triazaundecane</td>
</tr>
<tr>
<td>VOS</td>
<td>Volatile organic solvents</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>H-Bonding donating ability</td>
</tr>
<tr>
<td>$\beta$</td>
<td>H-Bonding accepting ability</td>
</tr>
<tr>
<td>$\delta$</td>
<td>Chemical shift</td>
</tr>
<tr>
<td>$\pi^*$</td>
<td>Polarizability</td>
</tr>
<tr>
<td>$\rho$</td>
<td>Density</td>
</tr>
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</table>
Chapter 1

Introduction

1.1 Rationale and significance

The United States, Brazil and Canada have been expanding their use of biomass in the production of fuels and chemicals to reduce petroleum utilisation. In addition, investments have been made in order to create and foster new technologies capable of replacing fossil fuels and petrochemicals.\textsuperscript{1-3} Brazil and the United States (US) have a strong commitment to the production of ethanol from sugarcane and corn, respectively.\textsuperscript{4-6} Adding to such long-term efforts, new investments have been made in order to foster the production of chemicals from second-generation biomass, such as agricultural waste, bagasse, and glycerine, among other feedstocks.\textsuperscript{7-9} These transformations result in the production of valuable chemicals, such as diols, organic acids and fertilisers, which are utilised in the polymer, fuel and agriculture sectors. Therefore, there is a great interest in developing energetically efficient technologies for converting biomass into valuable chemicals and fuels.

Using current technologies, chemical production from biomass is typically less environmentally friendly than petrochemical production. In many cases, the largest part of the environmental impact of biomass conversion is caused by the energetic requirements for separating intermediates or products from water.\textsuperscript{10} Water removal is necessary before, during, and/or after biomass conversion to products because (i) some biomass, such as algae, is grown in water, (ii) biomass contains water, (iii) dehydration reactions are used to reduce the oxygen/carbon (O/C) ratio of bioderived compounds, and (iv) many biomass conversion reactions, such as those catalysed by acids, enzymes, or microorganisms, are performed in water. However, the energy required to remove small amounts of products from the aqueous media via conventional means, such as distillation, negates the environmental benefits of biomass conversions. Close to 80% of
the energy consumed is associated with distillation or other drying processes in some biomass conversions. In contrast, removing significant quantities of water is rarely required to produce chemicals from fossil fuels. Thus, if humanity is ever to attain a truly sustainable society based upon products from renewable feedstocks, new lower-energy methods must be found to separate organic products from water.

Alternative purification processes to remove water from organic mixtures are available, but some issues hinder their adoption. Drying agents, membrane-assisted separations and precipitation assisted by salts (i.e. salting-out) are examples of separations that avoid using heat in chemical separations. However, these alternative separations have some drawbacks. Drying agents generate excessive amounts of solid waste that either needs to be disposed of or recycled, which is energy-intensive. Membrane-assisted processes such as reverse osmosis (RO) or nanofiltration present issues related to the pressures required, membrane fouling, and scalability issues. Finally, salting-out (SO), a process that relies on adding a salt (kosmotrope) to the aqueous media to drive products out, produces even more contaminated aqueous media. As a result, high-energy post-separation waste treatments are necessary, and every separation cycle requires the addition of more kosmotrope, resulting in high material and energy consumption. The US Department of Energy has highlighted developing new technologies for separating organic products from water as a priority. Therefore, there is a need for new methods for separating organic solutes from water that minimise the overall energy consumption of biomass conversion processes that are scalable, and that can be widely applied.

Biomass production of chemicals is becoming the norm, not only because of societal pressure but because, if we are to attain a truly sustainable society, our sources of raw materials need to be more renewable. Seeing this scenario and the importance of sustainable and circular production of chemicals, I focused efforts on developing separation techniques that a priori should require less energy than distillation and still promote reliable separations. CO2 was selected to
achieve this goal, and two techniques capable of recovering hydrophilic organic products from aqueous mixtures were developed. These techniques are high pressure switchable water (HPSW) and solvent-assisted high pressure switchable water (SA-HPSW).

1.2 Production of chemicals from biomass

Due to the growing demand for chemicals (e.g., polymers, solvents, fuels) and the concerns of society regarding CO₂ emissions and climate change, efforts have been made to replace petroleum-based chemicals and fuels. At the forefront of these efforts, biomass conversion (e.g. sugarcane, corn, cellulose, lignin) to value-added chemicals has been extensively explored.28-39 The importance of biomass has not only been highlighted by researchers and environmentalists but also by government agencies such as the US Department of Energy.40 Among the chemicals of interest, ethanol, furfural, hydroxymethylfurfural (HMF), and some sugars such as xylitol are at the forefront.40 In addition, the production of other chemicals such as methanol and diols has also been explored using, for example, electrochemical conversions and biocatalyzed (enzymatic and fermentation) strategies.11,13,41 This section will briefly explore some historical aspects, production methods, and applications for some of these products. However, the main focus is the strategies and challenges faced in efficiently separating these products from their reaction media.

1.2.1 Ethanol

Bioethanol has become one of the driving forces for a more sustainable fuel grid. The accelerated production of bioethanol in Brazil started back in the 1980s,4 while in the United States (US),42 the boom occurred in the early 2000s. In both countries, this increase in production was driven by changes in legislation and government incentives, especially after major oil crises.4,42 In Brazil, the government heavily invested in and subsidised the creation of bioethanol production plants. As a result, the light vehicle fleet evolved from cars only able to run on gasoline to vehicles
capable of using only ethanol and nowadays to more modern flex-fuel motors able to accept any combination of gasoline and ethanol, with most cars in Brazil being produced with a flex-fuel engine.\textsuperscript{4} For the US, some of the driving forces were the price reduction in fuels when using gasoline-ethanol blends, the implementation of the Clean Air Act, and the fluctuation in oil demand and prices.\textsuperscript{42} Independent of the motivations behind adopting bioethanol as a fuel source for Brazil and the US, the benefits of having a more sustainable fuel grid have had a significant impact across the globe.

Bioethanol production differs slightly among countries, especially when considering the sugar source, but the primary process adopted is the microbiological fermentation of sugars yielding ethanol as a product dissolved in water.\textsuperscript{4,6} This particular route is also referred to as first-generation bioethanol.\textsuperscript{43} The process relies on yeast cells that convert the sugars into ethanol, energy, cellular biomass, CO\textsubscript{2} and other products. Considering the volume of bioethanol production, many yeast strains have been bioengineered to maximize the production of ethanol in the process.\textsuperscript{44-46} The main feedstocks used in the production of first-generation bioethanol are corn (corn starch as the sugar), used in the US, and sugarcane (composed of sucrose, glucose and fructose), the primary feedstock in Brazil.\textsuperscript{4,6,43} Although sustainable sources of sugars, both corn and sugarcane are an integral part of the supply chain for the production of food for many countries. As such, there is a rising concern about utilising resources such as land, water and fertilizers in the production of fuels instead of food. New technologies have been developed to address such concerns by using waste and other feedstocks that do not compete with the food supply chain.\textsuperscript{43} The bioethanol produced using such sources is named second-generation bioethanol. In fact, some of the feedstocks used in such processes are the waste of the corn and sugarcane industries, such as corn stover or husk, and sugarcane bagasse.\textsuperscript{43} The adaptability of bioethanol production in terms of feedstocks and conversion processes are some of the key factors that contributed to the growth of bioethanol production.
Although slight differences are present in the process of production of first-generation bioethanol, there is a general procedure used, and the main operations performed can be translated to different feedstocks. The process starts by converting the raw material (corn or sugarcane) into a fermentable mixture. When sugarcane is used, the juice is obtained from the plant. At the same time, for corn, the raw material is crushed and submitted to steam treatment. In both cases, water is added to the mixture before fermentation. The next step is the addition of the yeast and the fermentation. Shorter fermentation times are used in Brazil (6-12 h), compared to the US (54-72 h). However, higher concentrations of ethanol are obtained in the US conversion: 12-18% v/v in comparison to 7-12% v/v in the Brazilian process. Once the fermentation is complete, the solid residues are separated from the liquid mixture containing the ethanol, which at this point is called raw wine, using centrifugation. The raw wine is then submitted to distillation (usually performed in a three-column setup) and the ethanol obtained goes through a dehydration process, due to the ethanol-water azeotrope, to obtain the anhydrous ethanol. Regarding the solids recovered after centrifugation, there is a difference in the processes performed in Brazil and the US. There is a recycling step in Brazil where the yeast is recovered and reused; however, the same does not occur in distilleries in the US. The main reason for this difference is the composition of the solid component obtained after centrifugation. Due to the solid nature of the raw material used during fermentation, the resulting solid residue contains too many solid residues from the corn to allow yeast recovery. Figure 1.1 presents a block flow diagram illustrating the process described above. As can be seen, the processes share many characteristics; it is worth noting that the distillation performed at the end of the process is performed in a relatively diluted mixture, which directly impacts the energy consumption of the transformation performed.
The process starts with feedstock cultivation, the most common cases being sugarcane and corn. Once the feedstock is transported to the fermentation facility, different techniques are performed to prepare the raw material and extract the sugars that will be converted into ethanol. In this stage, water is also added to the system. The next step involves the addition of yeast and other fermentation components (e.g. buffers, nutrients). The mixture obtained after fermentation is called raw wine, which is processed to remove any solids and recover yeast, which might be recycled in sugarcane processes. The final step is removing water via distillation and other dehydration processes to obtain anhydrous ethanol as the final product. Adapted from Franceschin et al.
Bioethanol plays a vital role in the transition to a more sustainable society; as such, developing technologies that amplify its positive impact on the environment is crucial. In 2021 the annual ethanol production used exclusively for fuel reached 27.3 billion gallons, a little less than the highest production observed in 2019, when 29.3 billion gallons were produced. The US accounts for 55% of the global production, with Brazil being responsible for 27% of the total world production. Energy consumption represents the second-highest cost in ethanol production, and it is primarily associated with distillation and other processes requiring heat. Considering such large production volumes, the energy consumption of bioethanol plants not only has an economic impact on the fuel produced but also on the environmental footprint of the process. As a result, new technologies that address this hurdle in bioethanol production are urgently needed. Bioethanol, among other sustainable fuel sources, has the potential to transform the way we produce and consume energy. However, efforts are still necessary to decrease the economic and environmental impact of its production.

1.2.2 The acetone, butanol, ethanol (ABE) process

The acetone, butanol, and ethanol (ABE) process was among the most valuable bioconversions developed, with a sizeable exploration in the 1900s. The importance of the ABE process is associated with the production of 1-butanol, a versatile chemical that, due to its properties, can compete with petroleum-based products. 1-Butanol can be used in gasoline blends, has lower vapour pressure, is less corrosive, absorbs less moisture and has a higher energy content than ethanol. The ABE process was first developed in 1913. Up to this day, it relies on the conversion of sugars and starches to the mixture, which can have product distribution controlled based on the fermentation conditions. Bacteria from the Clostridium genus are usually the preferred microorganism to enhance the production of 1-butanol. Additionally, this microorganism can be modified to increase conversions and even achieve the production of other products such as
organic acids. This versatile transformation has been changing the way we produce valuable chemicals since the First World War and among others, it holds the key for a more sustainable society.

Like other fermentation processes, the ABE process operates in a simple fashion where microorganisms consume sugars and convert them, among other things (e.g. cellular biomass, energy), to the product of interest. However, in the ABE process, a major issue is the poisonous character of 1-butanol to the bacteria promoting the conversion.\textsuperscript{48, 49, 51} This results in low concentrations (2-4 wt% of total products dissolved in water) of the obtained products, which hinders an efficient recovery of 1-butanol, acetone and ethanol produced.\textsuperscript{48, 49} As a result, when the product mixture is submitted to distillation, the largest portion of the energy required is associated with heating and evaporating water, a solvent that presents very poor thermal properties (large specific heat capacity and heat of vaporization in comparison to organic solvents). In addition, water-organic azeotropes (1-butanol-water at 92.7 °C and ethanol-water at 78.2 °C) are formed during distillation, compromising the product recovery efficiency.\textsuperscript{49} In some cases, up to 4 distillation columns are required in series to obtain a desirable separation of the 1-butanol from ethanol and acetone.\textsuperscript{49} This corresponds to energy requirements of up to 79.5 MJ kg\textsuperscript{-1} starting from a 0.5 wt% solution of 1-butanol in water for a 99.9 wt% final 1-butanol concentration.\textsuperscript{49} Strains are being developed to improve the resistance of the bacteria to the products obtained, but the separation will still remain a challenge even if more resistant microorganisms are developed.\textsuperscript{48} Although simple, the ABE process faces challenges when it comes to the final mixture composition and the recovery of the desired products.

Aiming to address the separation challenges faced by the ABE process, research is being conducted to evaluate the efficiency of \textit{in situ} and other non-thermal separation techniques. Some of these techniques are: (i) adsorption, (ii) liquid-liquid extraction, (iii) reverse osmosis (RO), and (iv) pervaporation. Adsorption will be described in more depth in the next paragraph. In contrast,
liquid-liquid extraction, RO and pervaporation will be described in the following sections due to their broader application in multiple conversions. All these techniques present a relative set of optimal conditions, but some of their drawbacks impede their broader application.

Adsorption is a relatively simple process that uses solid porous particles capable of adsorbing one component of a mixture to the detriment of the other components. Different adsorbents have been tested for the selective recovery of 1-butanol, such as activated carbon, zeolites, and polymeric resins.\textsuperscript{39, 51} Although some of them were able to selectively adsorb 1-butanol from acetone, butanol, and ethanol mixtures, they present some drawbacks: (i) the absorbents have a maximum adsorption capacity which requires that the adsorbed component be removed, and the adsorbent regenerated via an increase in temperature, displacement with steam or other solvent assisted methods; (ii) bacteria can adhere to the surface of the adsorbent decreasing its efficiency and regeneration; and (iii) desorbing the product from the adsorbent can be quite challenging and require multiple steps, which diminishes the applicability of adsorbents.\textsuperscript{39, 51}

### 1.2.3 Other biomass products of interest

The biomass products discussed in this section were selected due to their relevance as replacements for petroleum-based chemicals and their aqueous production process associated with challenging product recovery. They are ethylene glycol (EG), propylene glycol (PG), 1,4-butanediol (1,4-BD), and ethyl lactate (EL).

Ethylene glycol (EG) is mainly known for its application in the production of polyethylene terephthalate, or PET for short, for packaging and fibres. The global demand for PET reached 29 million metric tons in 2021, and the forecast is that this demand will continue to increase in the upcoming years.\textsuperscript{52} The current production route uses fossil ethylene and para-xylene, which are catalytically converted to EG and purified terephthalic acid (PTA).\textsuperscript{41} Polymerization is the next step in the process. Aiming to move away from non-renewable fossil-based feedstocks, companies
are investing in sustainable sources of EG from cellulosic biomass, bio-oil and sugars (usually obtained from sugarcane or corn stover).\textsuperscript{41} Companies such as Coca-Cola have agreements with EG and PTA producers (e.g. JBF Industries ltd) that provide them with bio-based chips that can be used in the production of bottles, and other packaging materials.\textsuperscript{41, 53, 54} Some of the EG production plants from JBF Industries are located in the south of Brazil, Taiwan and India.\textsuperscript{41, 53} The most efficient route to obtain bio-based EG starts with sugars that are converted to ethanol via fermentation, the ethanol can then be converted to ethylene over an acid catalyst via a water elimination reaction, and finally, oxidation of the ethylene yields EG with yields above 90\%.\textsuperscript{41}

Considering the commercial nature of EG, limited information is available regarding specific conditions in which the reactions are conducted. The desire to obtain chemicals from sustainable sources, especially when considering polymeric applications, stimulates the growth of EG production from biomass. However, as demonstrated by other substrates like ethanol, the challenges with the purification of the final product are among the barriers this process faces.

Regarding propylene glycol (PG), the high solubility in water, low toxicity and viscosity drive the application of this diol in a variety of consumer products. PG is safe for human consumption, and it finds use in antiperspirants, lotions, eye drops, food flavourings, and bulking agents in oral and topical drugs.\textsuperscript{13} Other applications include the production of polyester resins, engine coolant and anti-freeze.\textsuperscript{13} Similar to other products discussed, PG is primarily made from petroleum-based starting materials, in this case, propylene oxide. The push for more renewable feedstocks in chemical industries sparked the development of an alternative route to producing PG from glycerol over mixed-metal catalysts via hydrogenolysis.\textsuperscript{13, 55, 56} Glycerol is a desirable starting material due to its large production as a byproduct in biodiesel production. The precise mechanism for the formation of PG from glycerol is still a matter of debate, but there is strong evidence that the reaction proceeds via hydrogenolysis.\textsuperscript{56} Sharma \textit{et al.} performed this reaction starting with an aqueous solution (80 wt\%) of glycerol that was put in contact with a Cu:Zn:Cr:Zr catalyst and
submitted to hydrogenolysis at 240 °C and 40 bar of H₂.\textsuperscript{56} The product purification was performed via distillations to remove water, methanol and glycerol.\textsuperscript{56} Considering the elevated boiling points (B.P.) and low vapour pressures for both PG (B.P. 188 °C, 0.08 mmHg at 20 °C) and glycerol (B.P. 290 °C, 0.003 mmHg at 50 °C), recoveries via distillation are very energetically inefficient, which compromises the overall reaction energy balance.

1,4-Butanediol (1,4-BD), similar to its other diol counterparts, is a building block for many specialty chemicals, solvents and polymers.\textsuperscript{13} The push for renewable sources of 1,4-BD comes from major players such as Nike and Invista, with an annual demand of up to 2.5 million tons from various sources.\textsuperscript{13, 57} Companies like BASF, Cargill and others are meeting that demand.\textsuperscript{13} The commercial process was first demonstrated in 2013 by Genomatica in partnership with DuPont. Since that year, BASF has taken over the license to produce biobased 1,4-BD on a large scale. In 2015, a collaboration between Genomatica and Cargill started accelerating the production, and many other companies are investing in new plants, such as Myriant and BioAmber.\textsuperscript{13} The primary process utilizes commodity sugars, and biocatalysis is the main route to obtain 1,4-BD.\textsuperscript{13, 58} There are a couple of routes for the conversion: direct production via fermentation or catalytic upgrading of fermentation intermediates.\textsuperscript{13} Both processes take place in water and require distillation to remove the reaction media and other byproducts (e.g. methanol, propanol, butanol, acetal and other diols).\textsuperscript{59} Similar to other biocatalyzed processes, the initial sugar loading (20 g/L) and, consequently, the final product concentration of 1,4-BD (14 mM) are quite low.\textsuperscript{57} LCA calculations performed by Forte \textit{et al.} demonstrated that one of the biggest issues in the process is the heat required in the water evaporation and product purification, especially the supply which comes from fossil sources.\textsuperscript{58} The authors comment that replacing the fossil heat source with a renewable energy supply might help address the issue, but that still might have some drawbacks.\textsuperscript{58} Overall, identifying strategies that decrease energy consumption might be a more viable and lasting strategy. Similar to other bio-based technologies, the production of 1,4-BD from renewable resources can contribute
to a lower carbon footprint in chemical processes. The implementation of a biorefinery strategy where byproducts are used in other processes is also valuable not only in the production of bio-based 1,4-BD. When analysing biomass conversions it is important to note that the overall environmental impact of the process needs to account not only for the feedstock source, but also the other technical aspects of the production, such as processing of byproducts, separations and energy sources. 1,4-BD has a large demand and a range of applications; on one hand, this demonstrates the positive impact that bio-based processes can have; on the other hand, the large production volumes also correspond to large impacts when inefficient processes are in place, diminishing the positive impact that a renewable substrate might have.

Ethyl lactate (EL) is one of the few biodegradable solvents available that can be produced entirely from renewable resources (i.e. ethanol and lactic acid). Beyond being a renewable solvent, EL exceeds the properties (high boiling point, low vapour pressure and low surface tension) and performance (high solvency power) of traditional solvents used in industrial applications such as toluene and methyl ethyl ketone. The current route to produce EL uses ethanol obtained by the fermentation of sugars, and lactic acid which is also obtained from the fermentation of sugars such as glucose, sucrose, maltose or lactose. The reaction to produce EL is quite simple, ethanol and lactic acid are mixed, and an acid catalyst is added to promote the esterification yielding EL, and water as a byproduct. The reaction takes place in an aqueous solution; both dissolved acids (e.g. sulfuric acid) and heterogeneous acid catalysts (e.g. Amberlyst 15) can be used; and the reaction mixture is usually heated to temperatures varying from 25-95 ºC depending on the catalyst used. The currently utilised patented methods allow the esterification to reach equilibrium, and the ethyl lactate is removed via distillation. The thermodynamic limitation of the equilibrium esterification prevents high yields. In order to overcome such constraints, in-line recovery methods for the EL are being explored, such as reactive distillation and membrane-based separations, such as pervaporation. However, both processes have some drawbacks: reactive distillation requires large
amounts of energy; while membrane processes suffer from issues related to the stability and durability of the membranes used. The increased production of ethanol combined with the remarkable properties of EL as a solvent represent a move towards a more sustainable production process, but better alternatives need to be implemented to address the separation of EL from the reaction media, and consequently improve the yields of the reaction.

1.2.4 Environmental impact of current separation technologies applied to biomass conversion

Throughout the previous discussions regarding molecules of interest obtained from biomass materials or biocatalysis, a key issue was prevalent: the excessive energy consumption to separate the products from water. This issue was associated with the use of distillation as the primary strategy to recover the products. The mixtures obtained after each process presented low concentrations of products dissolved in water. The complexity of the product mixture obtained was also a challenge for the most part. In some of the cases presented, strategies are being developed to introduce in situ separations to improve the energetic efficiency of the processes. However, as discussed, some of these strategies have limitations in their implementation. As a result, these sustainable processes present an energy imbalance between the energy used to produce the molecules and the energy obtained when they are used for fuels that diminishes their benefits to the environment.

The excess energy associated with distillation and drying techniques to remove water can make biomass conversions 10 to 15 times more energy-intensive than petroleum-based chemical conversions. To illustrate this disparity, Figure 1.2 compares the energy consumption for ethylene production from biomass sources versus fossil routes (naphtha cracking). As seen, 5 times more energy is required in the process that uses ethanol. This energy inefficiency is directly linked to the distillation step needed to purify the ethanol obtained in the first part of the process. The energy required to remove water from the system accounts for more than 80% of the total energy added to
the system. On the other hand, using biomass substrates to promote the conversion can offset some of the energy penalties of the process. As a result, the greenhouse gas (GHG) emissions for the biomass processes are reduced to the point that the CO₂ captured by the biomass feedstocks during its growth results in a “negative” emission starting point for these conversions. Considering that more CO₂ is captured than released during the growth of the biomass feedstock, the saving on emissions can be used to offset the emissions caused during the separation steps required (due to the energy consumption of the processes) to recover the products obtained in the biomass conversions. This can potentially promote an overall CO₂-neutral emission if the CO₂ captured during the biomass growth is used to balance the CO₂ emitted during energy production. As a result, the key to making biomass conversions a genuinely sustainable process is to find energy-efficient replacements for distillation.
Figure 1.2 Comparison between the energy required in the production of ethylene via ethanol as an intermediate and the conventional process via naphtha cracking. The sugarcane process requires a large amount of energy associated with water removal. In blue is the energy necessary to cultivate the biomass or to extract the oil from the reservoir (too small to be seen clearly). In green is the energy during the conversion of raw material to intermediate, and in red is the conversion of intermediate to the final product. Adapted from reference 10.
1.3 Traditional separations of organic solutes from water

This section will focus on separation techniques already being explored in biomass conversions, either on an industrial scale or that have received attention from the academic community.

1.3.1 Distillation

Distillation is the most important separation method of components from homogeneous mixtures utilized in industry.\textsuperscript{11,61} However, the environmental impact of distillation decreases its attractiveness. “Distillation accounts for approximately 2,400 TBtu/yr, consuming roughly the same amount of energy as all the other separation processes combined”.\textsuperscript{11} Distillation of organic solvents utilizes large amounts of energy. The energy consumption is even greater when water is used as a solvent. This energy penalty is intrinsically associated with the large enthalpy of vaporization for water (2,256 J/g) when compared to the same parameters for organic solvents (e.g. 335 J/g for hexane, 501 J/g for acetone). In addition to its relatively high specific heat capacity (4.1813 J/g.K) when compared to solvents such as acetone (2.15 J/g.K), ethanol (2.30 J/g.K ) or toluene (1.72 J/g.K). Furthermore, when considering the production of low volatility or high boiling point chemicals, the energy penalty is even higher.\textsuperscript{11} In systems with a mixture of low volatility starting material with low volatility products, or a combination of multiple products and byproducts with low volatility, separation via distillation might not even be an option. This directly impacts the biomass sector, which relies heavily on reactions taking place in water, especially when considering biocatalytic systems.\textsuperscript{13} The energy penalty resulting from separating organic products from water in large-scale biomass conversion diminishes the environmental benefits of biomass as a chemical feedstock.\textsuperscript{10} Inventing processes that do not require heat could result in ten times more energy-efficient separations.\textsuperscript{12} Unless lower-energy methods are found for water removal, biomass as a feedstock for organic products will remain economically and environmentally uncompetitive.
with fossil fuels as a feedstock. The following paragraphs will provide more insight into the energetic impact of distillation in biomass conversions.

During the production of anhydrous bioethanol, multiple processes to remove water are necessary, amounting to an unbalanced energetic process compared to the ethanol fuel produced. The mixture obtained at the end of fermentation is called wine. The average ethanol concentration for processes starting with sugar plants is 10-12 %v/v. In comparison, a maximum of 18 %v/v is obtained from starchy starting materials.\(^\text{43}\) Starting from such a dilute product mixture represents high energetic consumption to achieve a 95.5 wt%, which is the azeotrope composition for an ethanol-water system (the most concentrated mixture that distillation can achieve). In addition, to achieve such purity, two distillation stages are required. These stages focus on removing methanol, high alcohols, and other volatile compounds such as aldehydes and ethyl lactate.\(^\text{43}\) However, 95.5 wt% is still not enough to obtain anhydrous ethanol, which is the grade required when using ethanol in a blend with gasoline.\(^\text{43}\) To obtain the anhydrous ethanol, molecular sieves are used to remove the remaining water in industrial processes. The energetic cost of the distillation stages applied can not only impact the environmental benefits of using ethanol as a biofuel but also the economics of the process.\(^\text{6}\) Therefore, a separation technology that could at least reduce the amount of water before distillation could considerably improve the overall bioethanol production process.

The ABE process suffers from very similar issues faced by the bioethanol preparation: diluted final mixtures, formation of multiple azeotropes between water and the products, and numerous distillation steps. These processes account for a drastic energy penalty to the overall conversion of sugars to acetone, butanol and ethanol.\(^\text{48,49,51}\) In addition, the toxicity of 1-butanol to the microorganisms used in biocatalysis incentivises implementing in situ separations that do not disturb the process and increase the conversion yield.\(^\text{51}\) The ABE mixtures usually only contain 2 wt% of products with the amount of acetone, 1-butanol, and ethanol obtained varying according to the microorganisms used.\(^\text{51}\) When it comes to recovering the products from this diluted mixture,
up to five distillation columns might be required.\textsuperscript{49} In addition, the formation of both an ethanol-water (78.1 °C, and 4 wt% of water) and butanol-water (at 91.7-92.4 °C, and 38 wt% of water) azeotrope is also an issue. At the moment, strippers are used to remove water (with ca. 23 wt% water content) from the butanol-rich phase and to recover any leftover butanol (up to 9.5 wt% butanol in the mixture) from the water-rich phase.\textsuperscript{49} All these issues combined make butanol production economically uncompetitive with petrochemical production.\textsuperscript{51} As a result, to achieve a competitive process, processes capable of either promoting \textit{in situ} product recovery or concentrating the product mixture are urgently needed.

The concentration of the product mixture is not the only factor that impacts the energy consumption generated by distillation. The products previously discussed in this section, for the most part, were highly volatile and presented low boiling points, except for 1-butanol, which presents a higher B.P., 118 °C. Considering that aspect, distillation, although energy-intensive, is still an option for product recovery. However, when considering bioproducts with lower volatiles and higher boiling points, for example, ethylene glycol (B.P. 197 °C), propylene glycol (B.P. 188 °C) and 1,4-butanediol (B.P. 230 °C), distillation might not be a viable option. Although the water might be removed via distillation, other impurities, and starting materials, which might also present high boiling points and low volatility, impede the purification via this route. An example is the production of PG via glycerol, a molecule that presents low volatility and a high B.P. (290 °C).\textsuperscript{56} If unreacted glycerol is still mixed with the PG, other steps such as solvent extraction followed by distillation might be required. However, systems like this, requiring extraction with organic solvents, suffer from issues related to the risks associated with flammability, smog formation, and toxicity of the solvent selected for the extraction.\textsuperscript{62-69} Therefore, alternative separations need to be developed, especially focused on low-energy processes that can remove most, if not all, of the water present in the system, but that can also be effective with very dilute mixtures.
1.3.2 Salting-out

Salting-out (SO) is a method used to remove solutes from water, which takes advantage of adding salts (kosmotropes) to the aqueous phase. The principles governing the effectiveness of SO are related to the water structure in the liquid phase and how the salts added to the water affect the interactions between the molecules present in the system. Studies have shown that water in the liquid state has a highly organized structure (held together by H-bonding) and that ions added to the solution can disrupt such structure.\textsuperscript{70, 71} The first studies describing such disruption were performed by Hofmeister in 1888, who divided common ions into kosmotropes and chaotropes.\textsuperscript{71} Ions in solution are surrounded by a hydration shell containing 10-15 water molecules, and this hydration layer is surrounded by the other water molecules.\textsuperscript{70, 71} The studies demonstrated that kosmotropes have stronger interactions with the water molecules in the hydration layer than the other molecules in the system have with the hydration layer. As a result, the kosmotropes have the ability to remove the water molecules from the hydration shell. By doing so, the organic solute molecules that, in the absence of the kosmotrope, would be separated from each other due to the hydration layer can now have better interactions.\textsuperscript{72} If these molecules are slightly hydrophobic, they will tend to aggregate and create a separate organic layer.\textsuperscript{72} This phenomenon is called the hydrophobic effect, depicted in Figure 1.3. This effect takes advantage of variations in the free energy of the system, especially the entropy of the system, before and after the addition of a kosmotrope. The water molecules surrounding the solute form a cage-like structure, this organized structure reduces the overall entropy of the system. Once the kosmotrope is added, this structure is disrupted and the solute molecules start associating with each other. As a result, the water molecules are liberated from the solvation shell, increasing the entropy the system. This effect is enhanced by the combination of electronic repulsion caused by the addition of the kosmotrope and the attractive forces between molecules of the organic solute.\textsuperscript{72} In addition, kosmotropes can maximize the H-bonding among water molecules, decreasing the interaction of the water molecules with organic
solutes.\textsuperscript{71} By taking advantage of the addition of kosmotropes, the hydrophobic effect is enhanced, allowing for the recovery of organic solutes from aqueous solutions.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.3.png}
\caption{Depiction of the hydrophobic effect taking place once a kosmotrope (purple balls) is added to a solution containing organic molecules (orange hexagons) dissolved in water (blue). The kosmotropes have stronger interactions with the water molecules of the hydration shell of the organic solutes. This disrupts the organic molecules' separation layer, favouring their agglomeration. As a result, the environment around the solute molecules becomes more hydrophobic, promoting the formation of a separate liquid phase (yellow).\textsuperscript{72} Reproduced from reference 72.}
\end{figure}

On the other hand, some salts and molecules have the opposite effect, and they cause salting-in or improved solubility of organic solutes in aqueous solutions. These species are called chaotropes.\textsuperscript{70-72} Chaotropes have weaker interactions with the water molecules in the hydration layer compared to the other molecules in the system.\textsuperscript{71} They also disrupt the H-bonding of the water molecules; as a result, the water molecules can have stronger interactions with other solutes dissolved in the solution.\textsuperscript{71} As a result, the solubility of the organic solute in the aqueous solution is enhanced, and promoting phase separation is harder. Molecules that present a chaotropic effect are also referred to as hydrotropes.\textsuperscript{73, 74} The main issue is that distinguishing prior to experimentation if a molecule will behave as a kosmotrope or a chaotrope is not always feasible,
and it is also dependent on the organic solute being removed. The general understanding is that small, multiply charged anions with a high charge density are prone to behave as kosmotropes. On the other hand, anions or cations that are larger or have diffused charge density tend to act as chaotropes, a behaviour that extends to uncharged hydroropic molecules. Avoiding or reversing the salting-in effect some molecules or ions might have is key to achieving separation.

SO does not solve the issue of energy consumption, and it also presents other drawbacks. The issue with SO is that by adding an external kosmotrope, the aqueous solution gets more contaminated in each separation cycle. Due to the permanent changes caused by adding salts to the solution, its ability to be reutilized, regenerated and even disposed of can be diminished or eliminated entirely. In order to recover or purify the water and the salts used during the SO, large amounts of energy would be required either via distillation or other water purification strategies such as reverse osmosis (RO) or pervaporation. These processes also have issues related to the composition and concentration of the SO mixture. Nonetheless, the positive impact that kosmotropes can have in separating organic solutes from aqueous solutions is highly desirable. An efficient system would require a kosmotrope that can either be easily separated from the aqueous solution or allow the aqueous solution to be reused.

1.3.2.1 Kirkwood-Buff (KB) theory of solutions

Kirkwood-Buff (KB) theory of solutions is a comprehensive theory that accounts for all the possible interactions taking place in the mixture. The KB theory of solutions, developed in 1951, addressed the issues encountered by the Hofmeister theory and provided numerical and mechanistic insight into the interactions between molecules in solutions. Such information can help identify appropriate molecules or combinations of molecules capable of promoting an efficient phase separation. Due to its statistical formality, KB theory relies on thermodynamic data to describe macroscopic changes in the mixture. Based on KB theory, a strongly favourable
organic solute-hydrotrope interaction effectively increases the solubility of the organic solute in the aqueous solution.\textsuperscript{77} To be effective, the solute-hydrotrope interaction needs to be stronger than the self-association of the hydrotrope molecules.\textsuperscript{77} As such, the hydrotrope molecules need to effectively surround the solute, improving its solubility in the aqueous solution. The same effect was not explained by Hofmeister’s theory, which only considered the impact of the changes caused by the hydrotrope on the water structure, especially the hydration shell. In KB theory, the solute-hydrotrope interaction directly affects the solute solubility. As a result, disruptions to the hydrotrope will directly impact the solubility of the solute. This aspect of the solute-hydrotrope interaction is valuable when considering switchable systems,\textsuperscript{73, 78} in which the mixture is expected to have two different behaviours upon the addition and removal of a trigger. Beyond the hydrotrope-solute interaction, the KB theory also accounts for the interactions between the solvent molecules and the interactions of the solute with the solvent. The information obtained from KB theory will be handy when dealing with the systems presented here, where additives have a switchable behaviour, and the interaction of the species in the solution will affect whether separation occurs.

1.3.3 Membrane-assisted separations

Many studies have been performed to adapt membrane-assisted separations such as RO and pervaporation to the challenges that sectors such as biomass conversions face.\textsuperscript{26} Membrane-assisted separations can benefit from relatively low energy requirements compared to other techniques, making them a desirable alternative for product recovery. However, membranes are prone to fouling when applied in mixtures containing multiple components, such as the reaction media utilised in conversions catalysed by a microorganism, the conventional approach in biomass conversions.\textsuperscript{27} This section will present the general operation, specific benefits and drawbacks for a couple of separations utilizing membranes: reverse osmosis (RO) and pervaporation.
1.3.3.1 Reverse Osmosis

Reverse osmosis (RO) has been the most widely used membrane separation process, which can be designed to operate under different conditions and with different mixtures.\textsuperscript{24} The process taking place in RO is quite simple. High pressure is applied to the feed solution, where the components of interest are dissolved; the pressure needs to be high enough to overcome the osmotic pressure of the feed solution. In most cases, water is forced through a semipermeable membrane capable of allowing the diffusion of water and blocking any other components in the mixture.\textsuperscript{79} Usually, an RO membrane consists of a polyester, cellulose acetate or composite support coated with an active layer responsible for the membrane selectivity. To improve efficiency, multiple membrane layers are stacked together with permeate channel, spacer and other layers between each membrane layer.\textsuperscript{24, 79} Extensive research has been performed into the membranes used, and most of the efficiency is associated with improvements made to the membranes.\textsuperscript{24} The membrane and pressures can also be adjusted to allow for the diffusion (membrane flux) of other components of the mixture. An effective process will take advantage of a selective membrane, low operating pressures, and a relatively simple feed solution. The RO step should require less energy than distillation. This is due to the fact that compressing the gas used in the process is less energy-intensive than heating mixtures containing large quantities of water. However, the concentration and composition of the feed solution will highly impact the energy required during the RO separation. RO has a proven track record of being used in various applications and effectively promoting water removal from mixtures.

On the other hand, how RO operates and the complexity of the mixtures can impact the effectiveness of this technique. The high pressures used in RO lead to several limitations. The first one is associated with the purity of the retentate (the mixture that remains in the RO system) and the permeate (the recovered solution). Higher pressures allow more of the solution to pass through the membrane; however, the permeate will contain more of the product, which is undesirable. The selectivity of the membrane is compromised with the higher pressures. In addition, depending on
the pressures and membrane composition and substrate, there is a risk of rupture of the membrane. In addition, high pressures can also lead to high levels of membrane fouling, which is the blockage of the pores by particles in the feed mixture. Considering that mixtures obtained after fermentation might contain a large concentration of dissolved solids, this can impact the separation efficiency. Although filtration steps might be efficient in removing unwanted large particles, the smaller particles and dissolved solids can increase membrane fouling and decrease separation efficiency. In these cases, more pre-treatment steps to recover the membrane activity and selectivity are required, increasing the operating costs of the RO system. Furthermore, the membrane's selectivity to specific species is also crucial when recovering particular products, especially if they present a chemical structure and molecular size similar to water molecules. Although very selective membranes have been developed in the past years, when considering the chemical similarities of the products being recovered via RO from the aqueous solution (e.g. acetone, ethanol, methanol), there can be a prohibitive selectivity issue. The permeate might contain water and the desired product to be collected in the retentate. Finally, there is also the issue of solute concentration. Due to the high osmotic pressure for these mixtures, the RO pressures required are quite high, which circles back to the mentioned problems. As a result, when considering the application of RO for biomass conversions, some of the issues related to selectivity, osmotic pressure and fouling can impede a reliable application of this separation on scale.

1.3.3.2 Pervaporation

Pervaporation is another technique available for separating organic products from water. Similar to RO, it relies on selective membranes, but it also has the added benefit of vaporising the solute or solvent to enhance the separation. In the pervaporation system, there are two phases, a liquid (the fermentation broth) and a vapour (concentrated product) phase, separated by a semi-permeable membrane. During pervaporation, one or more components in a liquid mixture
preferentially absorb on one side of the membrane, diffuse through the membrane thickness, and desorb and evaporate at the opposite membrane surface. This preferential sorption, diffusion and evaporation sequence is the basis for separating species by pervaporation.\textsuperscript{84} Pervaporation has been shown to improve processes like the ABE process by promoting the recovery of components, like 1-butanol, which can be toxic to the microorganism performing the biomass conversion at specific concentrations.\textsuperscript{51} Similar to RO, there is an extensive body of research being conducted to adapt to the different mixture compositions.\textsuperscript{51, 84} Pervaporation has proven benefits over other separation techniques, and the simplicity of the method is a positive factor for its application.

As it occurs during RO, the membrane selection becomes one of the key factors in the efficiency of the separation; in addition, the energy costs associated with vaporization also play a crucial role. The membranes used in pervaporation need to selectively allow for the recovery of the products obtained during fermentation while other, very similar components might also be present in the system.\textsuperscript{51} In addition, due to the vaporization character of the technique, two major issues arise: (i) the products being recovered need to present high volatility and low boiling points; otherwise, if the water needs to be vaporized, the energy consumption can be as high as distillation, diminishing the benefits of a low-energy separation;\textsuperscript{51} (ii) this separation might not be able to be implemented in line with the fermentation, since many biological systems are sensitive to changes in the fermentation broth, which would require additional steps for microorganism removal.\textsuperscript{51} In addition, considering the presence of cells and other components produced during fermentation, membrane fouling is once again an issue that can impact separation efficiency.\textsuperscript{51} Similar to RO, the membrane flux will also be affected by the concentration and composition of the fermentation broth. Therefore, the issues pertaining to membrane-assisted separations associated with the energy costs resulting from the vaporization of the product mixture or solvent can impact the development of low-energy efficient separation.
1.3.4 Liquid-liquid extraction (LLE)

Liquid-liquid extraction (LLE) is a technique that relies on partition coefficients and phase separation to allow for the recovery of products from aqueous mixtures in biomass conversions and extractions. LLE occurs when two immiscible or poorly miscible liquids are put in contact and products partition between the two liquid phases depending on their hydrophilicity and hydrophobicity.\(^5\) Considering the requirement for a two-liquid phase system, an efficient separation will occur with more hydrophobic products being extracted from the aqueous phase. This can be a challenge for some biomass conversions, especially when hydrophilic alcohols or diols need to be extracted. The product distribution also depends on the mass transfer from one phase to the other.\(^5\) Mass transfer is impacted by viscosity; as such, a less viscous product mixture is desired, which can be a challenge considering the complex nature of fermentation broths. Additionally, to recover the product, either the extraction solvent or the product must be removed via distillation, requiring one of these two components to be volatile and present a low boiling point. This ensures that the energy consumption of the process is reduced compared to the direct distillation of the aqueous product mixture. LLE has been applied for the product recovery in the ABE process,\(^\text{51}\) and ethanol fermentation.\(^\text{86}\) Studies for the recovery of 1-butanol from the ABE aqueous mixtures focused on identifying suitable solvents that would be selective, have low toxicity and could be recovered and reused.\(^\text{51}\) In ethanol fermentation, a pilot plant was constructed to evaluate the feasibility of continuous ethanol production assisted by LLE for product recovery.\(^\text{86}\) A immobilized yeast system was used, and the concentration of by-products after each extraction cycle in the reaction broth did not impact the overall conversion.\(^\text{86}\) LLE was demonstrated as a possible solution for product recovery during biomass conversion, although some constraints are present. An efficient LLE would rely on high selectivity, a large partition of the product between the two phases, low toxicity extraction solvents, volatile products and solvents, and a recyclable extractant; if these parameters are met, a reliable product recovery might be achieved using LLE.
There are some key aspects that LLE need to present to promote an effective product recovery, and other issues must be addressed if LLE is to be applied in biomass conversions. However, for the ethanol fermentation, the by-product concentration was not an issue for the conversion, in processes where the by-products might be toxic to the microorganisms, the same would not be expected. The fermentation broth would have to go through other purification processes to allow for continuous production. Toxicity is not only an issue for by-products. If the extraction solvent is toxic to the microorganisms, steps before the LLE need to be implemented to avoid contact between the microorganism and the extractant. Conventional solvents used during LLE usually present high flammability, which poses a risk to the environment and the safety of workers and locations around extraction plants. The partition coefficient also plays a crucial role in extraction efficiency. Considering the hydrophilic nature of many of the biomass conversion products previously discussed (e.g. ethanol, EG and 1,4-BD), it is expected that these molecules would have a stronger interaction with the aqueous media than with the extraction solvent. This directly impacts the extraction efficiency of LLE. One alternative would be using very hydrophilic or polar extraction solvents, which would have a greater ability to interact with hydrophilic solutes better than water. However, these solvents are usually water-miscible. Other physical properties also impact the efficiency of LLE. Most remarkably, the stability, viscosity, and thermal properties of both, the extracting solvents and the product. It was demonstrated that recycling the extraction solvent is crucial for an economically viable process. This is directly linked to the extraction solvent and its thermal properties. The solvent needs to be able to withstand the high temperatures, as well as high volatility and low boiling point, to decrease the energy consumption of the process. In addition, the boiling points of extracting solvents and products must be different enough so that the fractions recovered during distillation are not contaminated by either component. All these demands for an efficient LLE extraction can considerably impact this separation cost, feasibility and long-term viability, impacting its large-scale implementation.
1.4 Alternative separations of organic solutes from water

As has been highlighted in the previous sections, there is a need for more efficient and less energy-dependent separations of organic products from water during biomass conversions. The US Department of Energy also emphasized this as a priority.\textsuperscript{11} The following sections will highlight some efforts to develop separations that use CO\textsubscript{2} as a separation trigger.

1.4.1 Switchable Water

Switchable water (SW) is a recently developed water/organic separation strategy.\textsuperscript{73, 78, 90-92} Switchable water (SW) is the generic name for aqueous solutions of soluble ionogens to which a trigger is applied, changing the properties of the solutions. These changes allow for the reversible expulsion of solutes dissolved in the solution. SW systems rely on the property changes induced by salt formation. Such changes might be directly related to the ionic strength changes taking place when the ionogen switches from its neutral form to an ionic/protonated form. In addition, the changes in the ionogen-solute interactions are also crucial to promoting the expulsion of solutes from a solution.

1.4.1.1 The chemistry behind CO\textsubscript{2}-responsive molecules

SW uses water-soluble ionogens, amines that convert from a neutral state to an ionic state when CO\textsubscript{2} is introduced into the aqueous solution. Upon addition of CO\textsubscript{2} (1 bar) to the system, carbonic acid forms and protonates the ionogen, generating bicarbonate salts (eqn (1), where $n$ is the average number of protonated nitrogen atoms per molecule of ionogen B). The pH of pure water, once 1 bar of CO\textsubscript{2} is introduced, is about 3.94 (22 °C, 1 bar of CO\textsubscript{2}), which corresponds to a concentration of CO\textsubscript{2} around 0.03 M.\textsuperscript{93} The transformation of the ionogen from neutral to charged state triggers changes in the properties of the solution, such as increases in the ionic strength (IS),
the density, the viscosity and a decrease in the solubilising ability.\textsuperscript{78} These changes decrease the solubility of organic solutes in the aqueous phase by a factor of up to 100 fold.\textsuperscript{73}

\[ B + nCO_2 + nH_2O \rightleftharpoons [BH_n^{n+}][HCO_3^-]_n \]  \hspace{1cm} (Eqn. 1)

As eqn (1) demonstrates, the reaction between the amines and CO\textsubscript{2} is nothing more than an acid-base process; however, due to the use of CO\textsubscript{2} as the trigger, the amines used need to have very specific structures. When considering primary and unhindered secondary amines, the main issue when CO\textsubscript{2} is present is that in addition to the formation of bicarbonate salt, an additional reaction produces carbamate salts.\textsuperscript{94} Carbamates can also disrupt the interactions between the organic molecules and water. However, converting carbamates back to the amine form requires considerably higher temperatures, energy, and time compared to the conversion of bicarbonate salts back to the neutral amine, which diminishes the energetic gains of using SW instead of distillation.\textsuperscript{94}

As a result, for SW separations, tertiary or bulky (especially around the nitrogen site) secondary amines are preferred. When CO\textsubscript{2} is added to aqueous systems containing these amines, bicarbonate is the predominant product.\textsuperscript{78, 94} These amines can be regenerated more easily by slightly increasing the temperature, replacing CO\textsubscript{2} with another gas (e.g. air, N\textsubscript{2} or an inert gas), or a combination of both.\textsuperscript{94} However, not all tertiary or bulky secondary amines have an effective switchable behaviour. As one might expect, the amine's basicity will also play a crucial role in this process.\textsuperscript{94} In this thesis, basicity will be quantified using the pK\textsubscript{aH} of the amines, which is the pK\textsubscript{a} of the protonated form of the amine. The original water-amine solution, as expected, will have a basic pH. If the amine is too basic, the base will be largely protonated even before CO\textsubscript{2} is added, and a switchable behaviour will, therefore, not be observed.\textsuperscript{94} On the other hand, if the amine is not basic enough, the addition of 1 bar of CO\textsubscript{2} would not be enough to generate a sufficient decrease
in the pH to significantly protonate the amine, consequently compromising the bicarbonate formation and, by extension, the efficiency of the separation.\textsuperscript{94} As a result, the pK\textsubscript{aH} of the amines should fall into a range where once CO\textsubscript{2} is added, at least 95\% of the basic sites are protonated, but not be so basic that more than 5\% of the basic sites are protonated under air.\textsuperscript{94} The amine concentration will also impact the % protonation obtained. Depending on the pK\textsubscript{aH} of the amines, different concentrations might be required.

In addition, one could envision using polyamines which present multiple protonatable sites (e.g. di-, tri-, tetra-amines) as ionogens.\textsuperscript{91} The use of polyamines allows for more pronounced changes in the state of the aqueous solution once CO\textsubscript{2} is added. By using polyamines, lower concentrations can be used while still achieving significant changes in the ionic strength of the aqueous solution and its solubilizing ability.\textsuperscript{91, 94} However, the different protonatable sites must have a very similar pK\textsubscript{aH}, otherwise once CO\textsubscript{2} is introduced to the system, not all the sites would become protonated and switch. The distance between the protonatable sites and the groups connected to the nitrogen will directly impact the pK\textsubscript{aH} of each site.\textsuperscript{91, 94} Note that the two pK\textsubscript{aH} values of a diamine will never be identical, no matter how long the chain between them. It was found that in amines with more than four carbons between the nitrogens, the difference between the two pK\textsubscript{aH} is a minimum of 0.6.\textsuperscript{91} If the nitrogen atoms are connected by a chain of 4 or fewer carbon atoms, then the ΔpK\textsubscript{aH} is greater than 0.6 because, the protonation of one site inhibits the protonation of the other sites. To summarize, an ideal amine ionogen would have multiple protonatable sites with relatively similar pK\textsubscript{aH}; the amine would have to be tertiary or bulky secondary with not too strong or too weak basic sites; be miscible in water at all states; and be easily converted back to its unprotonated state once CO\textsubscript{2} is removed.

The selection of CO\textsubscript{2} as the ideal trigger for SW was based on multiple factors. There are numerous advantages when utilizing CO\textsubscript{2} in comparison to other triggers: (i) CO\textsubscript{2} is traceless, meaning that it will not contaminate the solution after its removal; (ii) the ionogen changes with
CO₂ are readily reversible upon CO₂ removal, easily achieved by bubbling the system with a different gas and/or with mild heating;⁷⁸, ⁹⁴-⁹⁶ (iii) there is potential for the utilization of waste CO₂ and waste heat to promote the ionogen switching; (iv) compressing 1 kg of CO₂ takes ten times less energy than distilling 1 litre of water;⁹⁷ (v) the ionogens utilized in SW are commercially available, and some have low toxicity; and (vi) CO₂ as a trigger does not require the solution to be either transparent or electrically conductive. Therefore, CO₂ is a very appealing trigger for SW systems compared to light, voltage, pH (non-switchable acids/bases) or heat.

The CO₂-switchable behaviour of amine ionogens can be pretty valuable for separating products from aqueous mixtures after synthetic procedures. The introduction of CO₂ to the system disrupts the interactions taking place between products and water and promotes their precipitation, if solid, or the formation of a separate liquid organic phase. The product can be recovered, and by simply removing the CO₂, the ionogen switches back to its neutral state, allowing the solution to be used for another synthesis.

The discussions in this section focused on using CO₂ as the trigger for SW, but other systems take advantage of different triggers with particular applications, benefits and drawbacks. These triggers present unique mechanisms and require specific molecules or ionogens. Currently, polymeric and solid-state systems are being designed to respond to changes caused by light/radiation, pH, voltage and heat.⁹⁸ The response promoted by these triggers ultimately results in changes to the shape of the polymers, and the properties of the polymer are affected. However, these systems face some challenges when considering: (i) the ability of the molecule to respond to such stimuli; (ii) their toxicity; (iii) their synthetic pathway; (iv) the accumulation of salts – for systems that use acid-base neutralizations – which increase the contamination of the aqueous solution, and limit the reuse of the aqueous solution; (v) for voltage systems, the localized changes to the surroundings of the electrode, diminish their application to bulky solutions; and (vi) the energy penalty to heat aqueous solutions can be a detriment to heat-triggered changes. Therefore,
selecting a trigger able to promote easily reversible changes to the ionogen state while avoiding the previously mentioned drawbacks is a key factor when developing a robust and reliable SW system.

1.4.1.2 Application of SW

As mentioned, the phenomenon of SW can be used in a process for the separation of an organic compound from water (Figure 1.4). To the water/organic compound mixture, one adds the ionogen. Subsequent addition of CO$_2$ gas to the system converts the ionogen to its bicarbonate salt, triggering the organic compound precipitation if solid or, if liquid, its separation in the form of an “organic-rich” liquid phase.$^{73}$ Once the organic solute is removed by either filtration or decantation; the aqueous solution can be easily decarbonated by steam stripping or by adding a non-ionic gas, such as air, N$_2$, or Ar, with or without an increase in temperature.$^{78,91}$ This converts the ionogen back to its neutral state. If desired, the ionogen can be recovered from the decarbonated water by filtration if the neutral ionogen is insoluble or by RO if soluble. After recovery, the ionogen is used again for another cycle. Notably, the RO step does not require high pressures because the osmotic pressure of the neutral ionogen solution is low - much lower than the osmotic pressure of the charged form of the ionogen.$^{99,100}$ The ability of the ionogen to switch between two states facilitates its recovery and re-use and is, therefore, a considerable improvement over the kosmotropes typically used in salting-out (SO). In addition, the ionogen re-use significantly decreases material and energy requirements, major issues when applying SO.
Figure 1.4 A process in which an organic compound is separated from water using an SW ionogen. The change of B into its ionic form raises the ionic strength of the water and disrupts the interactions taking place between the solute and water, forcing out the organic solute. Once the organic component is separated, the aqueous solution can be decarbonated (CO$_2$ can be re-used). The amine can be recovered and concentrated by reverse osmosis (reducing the amount of water) and be reused post-synthesis. Reproduced with permission from Cunha et al.$^{101}$

A variation from the SW process previously shown where the aqueous base solution is used as the reaction media (Figure 1.5) could represent energy savings and a reduction in material consumption. Suppose the reaction took place in an aqueous environment, and the presence of the ionogen did not interfere with the transformation occurring. In that case, the aqueous solution obtained after adding CO$_2$ could be simply deprotonated and re-introduced for a new synthesis. The elimination of the RO step decreases the overall energy requirements for the separation and reduces the amount of waste generated since a “recovered water” stream would not be formed. In this particular scenario, the presence of a hydrophilic catalyst that would remain in the aqueous phase
and could be reused was also considered. If a more hydrophobic catalyst is used, an additional step to separate the catalyst from the reaction product would be required.

**Figure 1.5** A process in which a reaction product is separated from an aqueous reaction media also containing a catalyst (cat) and SW ionogen. The addition of CO$_2$ to the system triggers the separation of the product. Once the product is separated, the aqueous solution can be decarbonated (CO$_2$ can be re-used). The aqueous media containing the SW ionogen and the reaction catalyst can be re-introduced for a new reaction.

As a separation method, SW presents many advantages compared to other separation techniques, but this method also has its limitations. On the positive side, SW avoids boiling and evaporating water and, therefore, likely consumes less energy than distillation. On the negative side, issues arise due to: i) the basicity of the amines, which limits the range of ionogens that can be used; ii) residual water and possibly ionogen in the organic-rich phase obtained after separation; and iii) the inability of SW to separate hydrophilic solutes from water.

The efficiency and the environmental impacts of SW are a function of the choice of amine that serves as the ionogen. As one might imagine, adding and removing an atmosphere of CO$_2$ triggers a relatively small pH change, limiting the range of amines that can be effectively used.
Amines with insufficient basicity are far from completely protonated in water under a CO$_2$ atmosphere, causing two problems: a) contamination of the organic phase with unprotonated amine and b) insufficient changes to the repulsive interactions between species in solution, which compromises the quality of the separations. Poor choice of ionogen can cause ionogen retention in the aqueous phase to be as low as 60%, which means that up to 40% of the ionogen contaminates the organic phase. These issues could be addressed by utilising either higher basicity amines or diamines instead of monoamines. Either type of amine produces higher % protonation and as a result, remains in the aqueous phase and promotes more significant changes in the solubility of the organic solute. Previous data showed that the diamines could be recovered up to 99% depending on the concentration and amine applied. There are advantages to using monoamines, especially when the amines' toxicity is considered. In order to address the protonation issue, higher pressures of CO$_2$ could be employed, which would cause more considerable pH changes in the aqueous solution.

A high-quality separation of organic product from the water will generate a product phase that contains very little water. This is especially difficult if the organic product is a hydrophilic organic. In this case, additional purification steps might be required, increasing the material and energy costs, especially if distillation is required. As a result, incomplete separations can drastically impact the efficiency of SW.

Finally, for systems in which the organic product is quite hydrophilic (e.g. ethanol, acetone and diols), SW ionogens cannot salt out the solute from the water even in their ionic form. Previously published data showed that with THF, a solvent that is only moderately hydrophilic, applying SW to promote separations could only remove 87% of the THF in the best scenarios. To date, there have been no reports of the successful utilisation of SW to separate ethanol, acetone and other hydrophilic alcohols or diols from aqueous solutions. The limitations of SW diminish its
applicability to biomass conversions that usually result in very low concentrations of highly hydrophilic organic products in water.

The switchable nature of the aqueous environment in SW was previously explored not only to remove dissolved products but also to improve the solubility of the same molecules in water. The ionogens applied in SW present a hydrotropic effect, which means they can increase the solubility of a particular molecule in water. However, the effect is lost due to the switchable nature of the ionogens in the presence of CO₂. This behaviour can be a great tool when considering the application of SW as a reaction media. In the absence of CO₂, the solution can dissolve large quantities of organic substrates, a state that is maintained throughout the reaction. However, once the complete conversion is achieved, the simple addition of CO₂ to the system allows the recovery of the product without needing a tedious and complex separation protocol. Previous work tested different organic molecules in an SW system. The results demonstrated that the presence of a neutral ionogen in the aqueous phase increased the solubility of moderately hydrophobic solutes in water compared to their solubility in pure water. The ionogen in its neutral state behaved as a hydrotrope, as expected. However, when CO₂ was introduced to the system, the ionogen was protonated, disrupting the solute-ionogen interaction. This resulted in the expulsion of the solutes from the aqueous phase (Figure 1.6). In prior reports using Kirkwood Buff solvation theory and molecular dynamics simulations, it was shown that the reduction in solubility of organic solutes in SW that occurs when the ionogen becomes protonated is best explained not by ionic strength arguments or chaotrope/kosmotrope theory but rather by the ionogen-solute interactions changing from attractive to repulsive. The hydrophobic solutes present unfavourable interactions with the protonated ionogen, disrupting the hydrotrope-solute interaction. Therefore, being able to trigger changes to the ionogen in solution and reverse such changes is essential to promote the expulsion of dissolved solutes and enable the reuse of aqueous solutions as reaction media.
Figure 1.6 Utilizing N,N,N',N'-tetramethyl-1,4-butanediamine (TMBDA) as an ionogen/hidrotrope for SW, the solubility of caffeine in water was considerably improved over a range of concentrations, following the KB theory predictions. However, when TMBDA was protonated, the caffeine-TMBDA interaction was disrupted to such an extent that the caffeine was almost completely expelled from the aqueous solution.73 Reproduced with permission from reference 73.

1.4.2 Solvent-assisted switchable water (SA-SW)

Considering the challenges faced by SW, a new method combining LLE and SW was developed: the solvent-assisted switchable water (SA-SW) method. As previously discussed, one of the main issues when considering the application of LLE for separating hydrophilic solutes from water using hydrophilic solvents is the high miscibility of the solvents in water. Furthermore, as observed with the caffeine behaviour in the SW system, when a large concentration of TMBDA (Figure 1.6) is used, the solubility ratio of caffeine in water with and without CO₂ can change up to 50. With these observations in mind, one of the collaborators of the Jessop group successfully demonstrated that 1,3-propanediol (1,3-PDO), obtained after fermentation of crude glycerol and
corn steep liquor could be separated from the aqueous media. The system used isopropanol as the extraction solvent and TMBDA as the ionogen in the SA-SW separation. SA-SW operates in a very similar fashion to the conventional SW. To the aqueous mixture containing 1,3-PDO, TMBDA (at approximately 4.0 molal) and isopropanol (1:1 mass ratio to water) were added. The addition of CO₂ to this new aqueous mixture promoted the formation of an isopropanol-rich phase which contained part of the 1,3-PDO initially dissolved in the mixture. 1,3-PDO was a very challenging system, considering its hydrophilicity ($\log K_{OW} = -1.09$) and the low loading (3 wt%) in the original aqueous mixture. However, its successful recovery demonstrated that by applying a solvent, isopropanol, with an average $\log K_{OW} (-0.16)$ in combination with high concentrations of ionogen, even hydrophilic organics can be recovered from an aqueous media.

Applying SA-SW in the recovery of 1,3-PDO was a step forward when compared to separations applying other kosmotropes, but some issues still need to be overcome. The recovery results obtained for 1,3-PDO (publication under submission) using SA-SW presented some benefits compared to separations utilising a combination of SO and LLE. Considering that in SO separations, the aqueous media is permanently contaminated by the kosmotrope, generating additional waste streams that need to be treated. Therefore, using an SW ionogen, which could potentially be recovered and reused, decreases the negative impact caused by separations in the overall biomass conversion. On the other hand, analyses of the isopropanol-rich phase obtained after one extraction cycle using SA-SW brought attention to some aspects that need to be addressed: (i) around 37 wt% of the 1,3-PDO initially dissolved in the aqueous phase was dissolved in the isopropanol phase. This is a lower value than previously published data using different recovery strategies. The recovery could be improved if a multistage extraction was adopted. (ii) The isopropanol-rich phase was contaminated with TMBDA. This potentially results from low % protonation of TMBDA at 1 bar of CO₂. At high concentrations of ionogen, not all the basic sites are protonated at the pH achieved after adding CO₂. To address this issue, higher pressures of CO₂
could be considered, which would produce a more considerable pH variation in the system. (iii)

The isopropanol phase was also contaminated with water. As discussed, using a hydrophilic solvent which is also miscible in water can be an issue since the same intermolecular interactions between isopropanol and 1,3-PDO are also taking place between isopropanol and water. Using a less hydrophilic solvent that is still miscible with water could be a solution, but the extraction efficiency of 1,3-PDO might also suffer from that change. As a result, finding a high-efficiency ionogen-extraction solvent combination is still a challenge, but considering that 1,3-PDO, a very hydrophilic molecule and present in very low concentrations in aqueous media, was still recovered using SA-SW demonstrates the potential of CO$_2$-assisted separations.

1.4.3 CO$_2$-assisted expansion of liquids (CXL)

CO$_2$ expansion of liquids (CXL) is an alternative method that also relies on CO$_2$ to trigger the separation of organic solutes from aqueous solutions.$^{103}$ Dissolving CO$_2$ into organic solvents quite literally promotes a volumetric expansion in the liquids, which is the reason why they are called “expanded” liquids. To dissolve CO$_2$ in a solvent, it is necessary to overcome the intermolecular forces between the solvent molecules.$^{104}$ Expanded liquids combine the benefit of having a traditional organic solvent with the properties of a compressed gas such as CO$_2$.$^{103}$ On the other hand, noncompressible gases (i.e., those having critical temperatures far below the temperature of the experiment) are generally incapable of expanding solvents.$^{103}$ Considering that the CO$_2$ pressure can be controlled, a gamut of tunable solvents can be generated based on the pressure and solvent combination.$^{103}$ Enhancement of mass transfer and solubilizing properties make CXL a great solvent alternative for some processes in industry, such as catalysis, extractions and separations.$^{103}$ Generating a CXL is quite simple but requires special equipment due to the high pressures of CO$_2$ used. Beyond generating tunable solvents, CXL can also facilitate the separation of organics from water due to the difference in solubility of CO$_2$ between organic solvents and
water. By taking advantage of the changes promoted by adding high pressures of CO$_2$ to a solution, separations can be achieved, and the organic solvent has its properties changed, which can be very beneficial in many circumstances.

1.4.3.1 CO$_2$ behaviour in different solvents

Carbon dioxide has different behaviours according to the solvent to which it is being added; these solvents can be divided into groups according to their ability to dissolve CO$_2$. Organic solvents can dissolve larger quantities of CO$_2$ compared to water and other hydrophilic molecules and materials.\textsuperscript{103} Jessop and Subramaniam created a classification that divided different solvents into classes according to their ability to dissolve CO$_2$.\textsuperscript{103} The Class I liquids present a poor capacity to dissolve CO$_2$, their properties are not significantly impacted by the addition of the gas, beyond acidity.\textsuperscript{103} The flagship of this class is water, which also includes polyols such as glycerol and other diols.\textsuperscript{103} For this class, the \% volumetric expansion observed is minimal, as well as the wt\% of CO$_2$ capable of being dissolved; for example, water only contains 4.8 wt\% of CO$_2$ at pressures around 70 bar.\textsuperscript{103} Class II liquids present the highest property changes once CO$_2$ is added. This class encompasses the majority of the traditional organic solvents, which present moderate to high hydrophobicity.\textsuperscript{103} Examples of solvents in this class go from methanol and acetone, more hydrophilic molecules, to hexanes and other hydrophobic liquids.\textsuperscript{103} The amount of CO$_2$ dissolved in these liquids is so large that drastic changes are observed in their volume, density, polarity, and many other physical properties.\textsuperscript{103} For example, at 70 bar of CO$_2$, the volumetric expansion of 1,4-dioxane is 954\%, with the liquid containing about 79 wt\% of CO$_2$ dissolved in it.\textsuperscript{103} Finally, Class III liquids can only moderately dissolve CO$_2$; as such, the volumetric and property changes are less pronounced.\textsuperscript{103} This class is dominated by ionic liquids, liquid polymers and crude oil. Due to this, some properties might present a greater degree of changes than others.\textsuperscript{103} For example, some properties such as viscosity change significantly while others, such as polarity, do not.\textsuperscript{103} In this
class, although large amounts of CO\textsubscript{2} might be dissolved (on a mol\% basis), the volumetric expansion is not as pronounced.\textsuperscript{103} PEG-400 can have up to 63 mol\% (or 16 wt\%) of CO\textsubscript{2} dissolved at 80 bar of pressure; however, the volumetric expansion is only 25\%.\textsuperscript{103} Although the CO\textsubscript{2} mol\% solubility for PEG-400 is similar to some of the organic solvents in Class II, the expansion is much smaller because volumetric expansion is related to wt\% of dissolved CO\textsubscript{2}. As can be expected, such discrepancies in the amount of CO\textsubscript{2} dissolved in different liquids and the property changes promoted by such differences stimulate the use of CXL as a separation technique for organics dissolved in water.

1.4.3.2 Property changes promoted by CO\textsubscript{2} expansion

The property changes observed when CO\textsubscript{2} at moderate to high pressures is added to organic solvents can be significant, virtually changing the behaviour or solvents in some scenarios. The presence of CO\textsubscript{2} has been previously shown to decrease the viscosity of organic solvents as well as to increase their diffusion coefficient.\textsuperscript{103, 105} In addition, the volume expansion caused by the addition of CO\textsubscript{2} to organic solvents directly decreases the density of the solvent.\textsuperscript{103, 105} Some of these property changes will be discussed in further detail.

Polarity and H-bonding capacity are highly impacted once CO\textsubscript{2} is dissolved into the solvents, especially those which are part of Class II.\textsuperscript{103, 104, 106} In order to measure solvent polarizability ($\pi^*$) and H-bonding ability (both accepting ($\beta$) and donating ($\alpha$) ability), which are part of the Kamlet-Taft solvent parameters, solvatochromic dyes are used.\textsuperscript{103, 106} Measurements of $\pi^*$ obtained for solvents before and after CXL demonstrated a considerable decrease in polarity.\textsuperscript{106} Table 1.1 presents $\pi^*$ values for some solvents of interest, which might also be obtained via biomass conversions. As can be seen, for all the solvents displayed, the polarity decreased once CO\textsubscript{2} was added. In addition to experiments using solvatochromic dyes, dipole moment and dielectric constants can also be measured or simulated to identify the changes taking place with the bulk
solvent polarity under an increase in the CO\textsubscript{2} pressure.\textsuperscript{105} Measurements were made of methanol, and a sharp drop in the dielectric constant from approximately 35 at 40 bar to 15 at 60 bar of CO\textsubscript{2} at 35 °C.\textsuperscript{105} This result is expected, considering that spaces are occupied by CO\textsubscript{2} molecules which are non-polar, disrupting the polar environment previously observed in solvents like methanol. Furthermore, as CO\textsubscript{2} is added to the solvents, the space between molecules starts being filled by CO\textsubscript{2} molecules, disrupting the network of H-bond interactions.\textsuperscript{107} As seen in Table 1.1 for all the solvents presented, the H-donating ability decreases once CO\textsubscript{2} is introduced to the system, demonstrating a decrease in the overall polarity of the solvents. Therefore, the addition of CO\textsubscript{2}, a non-polar molecule, to solvents (especially those in Class II) promote a decrease in the polarity which can be associated with CO\textsubscript{2} occupying spaces in between the molecules and disrupting H-bond networks and other polar interactions taking place.

**Table 1.1** Kamlet-Taft solvatochromic parameters for solvents of interest in biomass conversions both neat and CO\textsubscript{2}-expanded.\textsuperscript{106}

<table>
<thead>
<tr>
<th>Solvent</th>
<th>α</th>
<th>β</th>
<th>π*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>0.08</td>
<td>0.48</td>
<td>0.71</td>
</tr>
<tr>
<td>Ethanol</td>
<td>0.86-0.98</td>
<td>0.75-0.83</td>
<td>0.51-0.54</td>
</tr>
<tr>
<td>Methanol</td>
<td>0.93-1.14</td>
<td>0.66-0.74</td>
<td>0.58-0.60</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>0.76</td>
<td>0.84-0.93</td>
<td>0.48</td>
</tr>
<tr>
<td>Acetone (50 bar of CO\textsubscript{2}, 25 °C)</td>
<td>0.28</td>
<td>0.48</td>
<td>0.43</td>
</tr>
<tr>
<td>Ethanol (50 bar of CO\textsubscript{2}, 25 °C)</td>
<td>0.54</td>
<td>-</td>
<td>0.29</td>
</tr>
<tr>
<td>Methanol (50 bar of CO\textsubscript{2}, 25 °C)</td>
<td>0.64</td>
<td>-</td>
<td>0.37</td>
</tr>
<tr>
<td>Isopropanol (50 bar of CO\textsubscript{2}, 25 °C)</td>
<td>0.61</td>
<td>-</td>
<td>0.34</td>
</tr>
</tbody>
</table>
Due to the difference in the extent of changes promoted by adding CO\(_2\) to different solvents, a miscible pair of liquids might eventually become immiscible upon the preferential expansion of one of the liquids in the solution. Considering that CO\(_2\) preferentially dissolves in Class II and III liquids, promoting more pronounced changes in polarity and H-bonding on liquids of Class II, the addition of CO\(_2\) to a solution containing two or more liquids from a different class might trigger their separation.\(^{103}\) The pressure in which the liquid-liquid phase separation occurs is known as lower critical solution pressure (LCST).\(^{103}\) The liquid that preferentially dissolves CO\(_2\) will undergo more significant expansion and an increase in its polarity, disrupting the liquid-liquid interactions in the system and promoting eventual phase separation. Pairs of liquids that behave in this manner include water/organic, IL/organic, and IL/water binary mixtures.\(^{103}\) In addition, such behaviour could also be used to separate solutes into a particular liquid phase once CO\(_2\) is added to the solution. For example, a solute dissolved in water/alcohol mixtures will partition between the two liquid phases when immiscibility is triggered by the addition of CO\(_2\).\(^{103}\) As expected, the pressure of CO\(_2\) will have a strong influence not only on the formation of two immiscible phases but also the partitioning of a solute that might be dissolved in the water/alcohol mixture.\(^{103}\) The changes in miscibility promoted by CXL will be further explored in a discussion regarding the separation of organic products dissolved in water.

1.4.3.3 CXL applied to the separation of organics from water

At elevated CO\(_2\) pressure, organic liquids can dissolve more CO\(_2\) than water can, which afford them more noticeable property changes. Considering the application of CXL for organic liquid separations from aqueous solutions, two other fundamental changes will be discussed. First, the polarity of organic liquids is highly affected by the addition of CO\(_2\). As demonstrated by measurements of the Kamlet-Taft \(\pi^*\) parameter (see Table 1.1), which refers to solvent polarity and polarizability, the addition of CO\(_2\) causes drastic decreases in solvent polarity with increases
Due to this change in polarity, the miscibility of organic solvents with water is decreased. Second, the dissolved CO$_2$ triggers a phase separation by stabilising the liquid organic phase (Figure 1.7). The organic liquid phase can be decanted at pressure. The aqueous phase, which will still contain some of the organic compound, can be decompressed to remove the CO$_2$ and be directed to further treatment as waste or be re-used as the media for further biomass extractions or conversions.

Figure 1.7 The phase changes observed upon expanding a mixture of two miscible liquids (water and organic) past a lower critical solution pressure (LCSP). At this point, adding CO$_2$ triggers an initial separation (CO$_2$ dissolved in organic liquid). The system can be equipped with a dip-tube. Upon separation, the organic phase can be decanted using the dip-tube. The water-rich phase can be decarbonated (CO$_2$ can be re-used) and either be directed as waste or be re-used in the synthesis. Reproduced with permission from Cunha et al. The minimum CO$_2$ pressure required to trigger a liquid-liquid phase split in an organic/water solution of a certain composition is called the cloud pressure (CP). The lowest point on a plot of CP vs liquid phase composition is the lower critical solution pressure (LCSP), the lowest CO$_2$ pressure capable of producing a L-L phase separation.
The CO$_2$ pressures required for CXL separations can be high, especially when hydrophilic solutes are the target. For example, the LCSP is 26 and 80 bar for water/acetone and water/methanol mixtures, respectively.\textsuperscript{103} For ethanol/water mixtures, however, no liquid-liquid phase separations are observed even at very high pressures.\textsuperscript{108} For the mixtures that do exhibit an LCSP, that pressure is insufficient to give good separation.\textsuperscript{109-111} The composition of the organic-rich and water-rich phases are almost identical near the LCSP, only significantly differentiating at higher pressures: above 50 bar for acetone/water solutions.\textsuperscript{109} Overall, the phenomenon of organic/water phase separation caused by CXL is academically interesting but of limited industrial appeal due to the high pressures required and the poor separations obtained.

### 1.5 High pressure switchable water (HPSW)

While CXL and SW both have disadvantages when used alone, it is possible that if the two methods were used simultaneously, they might operate synergistically, resulting in lower pressure requirements and better separations. It was hypothesised that the combination of SW and CXL, which I have named high pressure switchable water (HPSW), might be able to: i) promote cleaner phase separations with reduced contamination of each liquid with the other; ii) decrease the LCSP while increasing the repulsive interactions between ionogen and solute; iii) utilise less basic ionogens, which are therefore likely to be less harmful, less expensive and easier to restore to their unprotonated state; and iv) utilise ionogens with multiple basic centres, which can generate more strongly repulsive interactions with solutes but are not adequately protonated under 1 bar of CO$_2$. If this hypothesis is correct, the drawbacks presented by each technique individually would be overcome, and a more efficient separation would be achieved even when hydrophilic products needed to be separated.

Biomass production of chemicals is becoming the norm, not only because of societal pressure but because, if we are to attain a truly sustainable society, our sources of raw materials
need to be improved. However, the current biomass conversions still suffer from an unfavourable energetic imbalance that diminishes its benefits to the environment. HPSW could represent a shift in the production of chemicals from biomass, allowing for more efficient separations, at least in terms of energy consumption. Technologies such as HPSW not only fulfil the role of expanding the science behind CO₂ utilization but could cause a positive shift in the way we recover products from mixtures.

1.6 Solvent-assisted high pressure switchable water (SA-HPSW)

Throughout the development of the SA-SW and the HPSW separations, some observations sparked the development of the SA-HPSW. The rationale behind SA-HPSW is very similar to the one used for HPSW. In addition to combining SW ionogens with high-pressures of CO₂ used in CXL, an extraction solvent was added to the system. The addition of the extraction solvent follows the principles behind LLE, in which an immiscible solvent is added to an aqueous solution to promote the extraction of the desired product. However, as expressed in the discussions about LLE, the products obtained during the biomass conversions discussed are, in its majority, very hydrophilic and tend to have stronger interactions with the aqueous media than with the immiscible solvent. SA-HPSW, by taking advantage of the property changes caused by the expansion of liquids with CO₂, uses a water-miscible organic solvent that, once exposed to CO₂, expands and creates a separate liquid phase which contains the product. The organic solvents utilized in SA-HPSW start by having more favourable intermolecular interactions (H-bonding and dipole-dipole) with the product than the solvents used in a traditional LLE. By starting from a single-phase and promoting a separation upon adding CO₂, I envision more efficient product recoveries taking place. In addition, the range of solvents that could be used is expanded because the requirement for an immiscible liquid with water is overcome by the phase separation caused by the HPSW step in the process. Therefore, the SA-HPSW system could be highly beneficial to: (i) particularly hydrophilic
products that HPSW could not separate; or (ii) to products that do not expand upon the addition of CO₂, as is the case for liquids in Class I and III of the CXL classification. A key aspect that will be evaluated is the energy consumption for the purification of the organic stream obtained after the SA-HPSW separation. The impact of adding an assisting solvent will be considered as well. SA-HPSW not only could take advantage of the HPSW technique but also could expand the scope of products that can be recovered, adding another CO₂-switchable technology to the methods available for separations in the most diverse biomass conversions.

1.7 Life Cycle Assessment (LCA) and other green metrics

A quantitative analysis is required to confirm that HPSW and SA-HPSW are greener than distillation. The utilization of HPSW and SA-HPSW was postulated as a less energy-intensive and greener approach for separating organic molecules from aqueous solutions. However, quantifying that difference is necessary to determine if these techniques require less energy than distillation. The best method to quantify the multiple parameters that differentiate these new separations proposed from distillation is life-cycle assessment (LCA).

LCA was developed in the 1980s to address the issues pertaining to the life cycle of products and to create means to compare if a particular product was better than others in terms of its environmental impact. This method consists of quantifying the environmental impact of multiple parameters for each option (each of several competing processes, or several competing products, for example). Various impacts such as smog formation, toxicity, and resource depletion, among others are taken into consideration to create a matrix that can be used to compare the different options. LCAs cannot generate a single number that defines if one method is better than the other. They are used to create a comparison between the two or more options based on the impacts analysed. The option that generates the minimum impact in the selected areas is considered the greenest option. As a result, one option might be regarded as greener with respect
to one set of impacts (e.g. global warming, acid rain) but not with respect to others (e.g. ecotoxicity, eutrophication). There are also different methods of approaching and quantifying each impact. One method known as cradle-to-grave takes into consideration all the steps from the moment in which resources are extracted to the point of disposal or recycling of the product. A different approach, known as cradle-to-gate, considers the steps from the point of resource extraction to the moment the product leaves the company property and thus ignores the use and disposal stages. LCAs can provide meaningful insight into the overall impact of a particular product or process, providing insightful information for contingency points that should receive more attention and could benefit from further improvements.

Preparing a comprehensive LCA is a laborious task requiring data for all the processes and chemicals being used, including their origin and production processes. As a result, considering this project’s scope, our attention was directed to the energy comparison between the direct distillation of aqueous mixtures containing our products of interest versus all the steps involved in separating the same mixture through HPSW or SA-HPSW, with an emphasis on steps that require heat addition. The calculations (via the process simulation software, ASPEN) presented here accounted for the separation, further purification and recovery of the ionogens used during the separations. I envision that my approach should require less energy than the current methods in terms of energy consumption. In addition, recycling the ionogens also allows for a more circular process, which has been receiving significant attention from different fields. Therefore, a preliminary analysis of the energy consumption for HPSW and SA-HPSW will guide any efforts in terms of optimizations that need to be made to the separations.
Chapter 2
High pressure switchable water (HPSW) applied to the separation of acetone from water

2.1 Introduction

The production of acetone via the acetone-butanol-ethanol (ABE) process has not only a rich historical context but also is one of the most relevant fermentation processes to date. The ABE process was one of the first large-scale industrial fermentation processes developed, and the production volume was only smaller than the production of bioethanol. However, due to the inability of the fermentation process to economically compete with petrochemicals processes, in the 1960s, there was a decrease in the production of chemicals via this biotechnology route. This scenario shifted in the early 2000s, with researchers focusing on improvements related to strains capable of promoting higher conversions and the implementation of more efficient product separation technologies capable of improving the yields and economics for this fermentation. As a result, the ABE process is once again receiving attention from the academic community in the search for more sustainable ways to produce chemicals which are essential in many areas (e.g. fuels, cosmetics, antibiotics).

There is still much more to be developed in the ABE process, the product separation being the bottle-neck for the competitiveness of this process with petroleum-based conversions. Aiming to develop low-energy separation processes for bioconversion processes such as the ABE process, I have explored high pressure switchable water (HPSW), a novel method that relies on CO₂. The study presented here looks at using HPSW as an alternative chemical separation for removing acetone from water to determine whether the combination of switchable water (SW) and CO₂ expansion of liquids (CXL) can improve upon the performance and weaknesses of those two
techniques when applied individually. On the one hand, the use of SW, which employs 1 bar of CO₂, cannot promote the separation of acetone from aqueous solutions due to the high hydrophilicity of this molecule. Furthermore, only fairly basic amines can be used as ionogens in SW due to the small pH drop that 1 bar of CO₂ causes in aqueous solutions. On the other hand, when CXL is applied by itself, the pressure required to promote a liquid-liquid phase separation between acetone and water is relatively high (26 bar). In addition, once CXL is applied to this system, the two phases obtained at 26 bar present almost the same composition. This issue can only be overcome once 50 bar or more of CO₂ is added to the solution; still, the acetone-rich phase contains a considerable amount of water. I hypothesize that by combining both methods, the higher pressures of CO₂ employed in association with more efficient amines containing multiple protonatable sites can be the key to promoting separations with purer liquid phases (low contamination of water in the acetone-rich phase and vice-versa) and at lower pressures than those required for CXL. HPSW might hold the key to a low-energy and efficient separation of hydrophilic organics from water, representing a step forward in the replacement of petroleum by sustainable raw materials and a more circular economy.

2.1.1 A guide to the HPSW separation

In this section, the steps involved in the HPSW separation will be described, considering the novelty of the technique. Figure 2.1 presents the process in its entirety, and each dotted box corresponds to a specific part of the process. The diagram illustrates not only the separation of acetone from water but also the purification of the acetone-rich phase and the steps necessary to recover the amine (denoted as B).
Figure 2.1 Diagram representing the separation of acetone from an aqueous solution via the HPSW technique. The dotted boxes divide the different steps involved in this circular process. The diagram presents the separation of acetone from the aqueous solution once CO$_2$ is added to the system (green dotted box, step 2); the further purification of the acetone-rich phase (yellow dotted box, step 3); and the steps necessary to recover the amine, denoted as B (represented in the dark and light blue dotted boxes, steps 4 and 5).
**Step 1 (red dotted box)** – Considering the nature of the HPSW, meaning high pressures of CO$_2$ being used, step 1 involves transferring the aqueous solution containing acetone to a vessel capable of withstanding the high pressures used. Before this transfer, the ionogen must be added to the aqueous mixture. In this work, “synthesis product” was used to identify the solution containing only acetone and water. However, efforts are being made to promote phase separation using product mixtures obtained after biocatalyzed processes. The vessel is equipped with a dip-tube that allows for recovery of both liquid phases generated. In addition, the high-pressure vessel used here was equipped with a glass window, allowing for the visual observation of the phase separation. Neither the window nor dip-tube would be required in larger-scale separations; this apparatus would need to be modified for larger volumes.

**Step 2 (green dotted box)** – Once the product mixture, also containing the amine, is transferred to the high-pressure vessel. CO$_2$ is added to the vessel until the appropriate pressure is achieved, meaning the pressure required to achieve the phase separation desired. The combination of the amine protonation and the high pressure of CO$_2$ promotes liquid-liquid phase separation. Both the protonated amine and the molecules of CO$_2$ are responsible for disrupting the interaction taking place between acetone and water, which is crucial for phase separation. There is also a vapour CO$_2$-rich phase that contains some of the acetone and water dissolved in it. This work only focused on the composition of the liquid phases obtained after adding CO$_2$.

**Step 3 (yellow dotted box)** – The acetone-rich phase can be collected using the dip-tube. As will be noted in this Chapter, the acetone-rich phase still contains some water and trace amine dissolved in it. As a result, further purification to obtain acetone as a pure product will be required. In this case, I opted to purify this phase via distillation. Calculations (via the process simulation software, ASPEN) were made to determine the energy required to obtain pure acetone. Considering that the acetone would only contain small amounts of water, I hypothesized that this distillation step would require considerably less energy than distillation using the initial “synthesis product”
solution. A more comprehensive discussion will be presented later in the energy discussion section (Section 2.4).

**Step 4 (dark blue dotted box)** – The water-rich phase containing the protonated amine, most of the water and some of the acetone, can also be collected and submitted for further processing. The first step involves removing the CO$_2$ and, consequently, deprotonating the amine. This can be achieved by passing an inert gas through the solution and gently heating (no more than 60 °C) the system or by steam stripping. In this work, the CO$_2$ being removed was not recovered, but commercial systems available allow for recovery of the CO$_2$ that could then be used in a new separation. In addition, waste heat from other processes can be used for steam stripping, improving the overall energy consumption of the separation. These strategies would ensure a better energy and material balance for the separation.

**Step 5 (light blue dotted box)** – The final step involves the recovery of the amine added so that a new separation can take place. In this work, due to the soluble nature (in water) of the amines used, reverse osmosis (RO) was the technique selected to promote water removal and consequently concentrate the amine (conc. B) to be reused in a new separation. In addition, if possible, there is also an interest in reusing the water in a new synthesis process. However, such reuse would have to consider the eventual presence of residual amine, and possible by-products when a real fermentation product mixture is used. Furthermore, the concentrated amine solution would also contain some of the initial water, which needs to be accounted for in a new separation cycle.

Throughout all the steps taking place in the HPSW, considerations about mass and energy losses also need to be considered. However, such considerations are more relevant for process engineering. Therefore, the focus of this work was to demonstrate that a synergistic effect will occur once the principles of SW and CXL are operating in an aqueous solution containing a hydrophilic organic dissolved.
2.2 Materials and Methods

2.2.1 Materials

Chemicals were used as received. The following amines were obtained from commercial sources (Sigma-Aldrich, TCI, Fisher): N,N,N',N'-tetramethylethylene-1,2-diamine (TMEDA), N,N,N',N'-tetramethyl-1,3-propanediamine (TMPDA), N,N,N',N'-tetramethyl-1,4-butanediamine (TMBDA), N,N,N',N''-pentamethyldiethylenetriamine (PMDETA), 2,6,10-trimethyl-2,6,10-triazaundecane (TMTAD), N,N,N',N'',N''-hexamethyldiethylenetriamine (HMTETA), triethanolamine (TEA), N-methyldiethanolamine (MDEA), N,N-dimethylethanolamine (DMEA), N,N,N',N'-Tetrakis(2-hydroxyethyl)ethylenediamine (THEED), N-ethylidithanolamine (EDEA), N,N-diethylethanolamine (DEAE), 3-dimethylamino-1-propanol (3DMAP) and imidazole. The water:acetone mixtures were prepared using acetone (HPLC 99.9%, Fisher) and water with a conductivity of 18.2 MΩ obtained from a Milli-Q® purification system (Synergy UV). For the 1H NMR spectroscopy, d6-DMSO (Cambridge Isotope Laboratories) was used as the solvent. For the quantification of ionogen during RO, acetonitrile 99.9% (Acros) was utilized as internal standard.

2.2.2 Evaluation of the efficiency of ionogens for phase separation (HPSW setup)

Phase behaviour was observed using a phase monitor from Supercritical Fluid Technologies Inc (Figure 2.2). The instrument consisted of a stainless-steel vessel (which has a 100 mL internal volume) attached to a thermocouple and a pressure gauge. The vessel was also equipped with two zirconia windows. A microscope CMOS camera (Veho, Discovery VMS-004 Deluxe) connected to a computer was placed facing one of the windows allowing real-time observations of the phase behaviour in the sealed vessel. A needle valve regulated the CO2 addition, and the pressure was adjusted by a piston that was able to change the internal volume of the vessel. The vessel temperature (40 °C) was controlled with a heating mantle. The solutions remained under agitation thanks to a magnetic stir bar.
Figure 2.2 (A) Diagram representing the phase monitor used in this thesis, (B) front view and (C) top view of the phase monitor used in the evaluation of the ionogens. The sample is loaded into the vessel via the opening in the top (sample scoop). Once the transfer is complete, the vessel can be closed and pressurized with CO$_2$. The CCD camera facing one of the windows allows for observations of phase behaviour with a variation of internal pressure. There are two mechanisms to change the pressure inside the vessel, adding or removing CO$_2$, or changing the internal volume using the adjustable piston.
Solutions with a fixed molar ratio of acetone:water, typically 50:50 and the desired amine concentrations (concentrations are stated relative to the mass of water added) were prepared prior to being added to the phase monitor. Experiments were performed in triplicate, and the cloud pressures (CP) are presented as averages. The CP was obtained by adding the solutions to the phase monitor and slowly increasing the CO$_2$ pressure until cloudiness, or the formation of a separate liquid phase could be visually identified. To ensure that the pressure being recorded was correct, the pressure was slightly raised and decreased for a few cycles. The visual behaviour of the system was used to confirm the pressure being recorded for CP.

2.2.3 Evaluation of TMBDA efficiency over a range of acetone:water ratios

TMBDA was selected as the model ionogen to evaluate the pressures required for separations over a range of acetone:water ratios. For these experiments, the phase behaviour was obtained using the same setup described to evaluate the efficiency of individual ionogens. For this set of experiments, the concentration of TMBDA was fixed at 0.80 molal based on the mass of water added to prepare the acetone:water mixtures.

2.2.4 Measurements of the composition of the water-rich phase by GC-FID

Compositions of liquid mixtures under pressure were determined by gas chromatography of samples collected in a high-pressure liquid level sight gauge (hereafter referred to as the “sight gauge”) manufactured by Inferno Manufacturing Co. (modified 11A-TL-B model, T316 stainless steel, with a pressure rating of 345 bar at 38 °C, 36.5 mL internal volume), equipped with a stainless steel dip-tube. The sight gauge was kept at a constant temperature (40 °C) in a water bath. The solutions were maintained under agitation due to a magnetic stir bar added and controlled by a magnetic stir plate. To maximise the stirring, the vessel was placed on its side (horizontal position).
Solutions of acetone and water with 50:50 mass ratio (approximately 10 g of water and 10 g of acetone) and fixed concentrations of ionogen based on the number of protonatable nitrogens were prepared and pressurised to 20 and 50 bar of CO$_2$ in the sight gauge. Upon phase separation, samples of the water-rich phase were obtained, and the acetone concentration was measured by GC-FID as described below.

The sight gauge was attached to a pressure gauge, and the dip-tube was positioned to allow sampling exclusively of the water-rich phase (Figure 2.3). The dip-tube was externally connected to a needle valve. The valve was connected to a round bottom flask maintained under liquid N$_2$ and capped with a rubber septum to minimise loss of sample by expansion when the sampling was being performed. The samples obtained were analysed on a GC-FID (Perkin-Elmer, Clarus 680 equipped with an auto-sampler), replicates were obtained for each sample, and the results presented are the averages. The FID chromatograms were obtained using a 30 m CP-Volamine capillary column. The injector was maintained at 270 °C, 1 µL samples were injected, and a 1:150 split ratio was applied. The column was maintained at 40 °C for 2 min, ramped to 250 °C at 40 °C/min ratio and then maintained at 250 °C for 2 min. The He carrier gas flow at 1.00 mL/min was maintained for the entire run. The detector was kept at 270 °C. The experiments were carried out in duplicate.
The setup contains a ball valve that allows CO$_2$ to flow, a needle valve that controls the flow of CO$_2$, a pressure gauge that allows for pressure readings, a pressure (P) release valve that allows the gauge to be depressurized, a burst disk, an inlet valve connected to the sight gauge, and a dip-tube that allows for sampling of liquid phases, which is also connected to a needle valve. The temperature is controlled using a water bath (acrylic container). The sample is loaded into the sight gauge. Once the transfer is complete, the vessel can be closed and pressurized with CO$_2$. Upon phase separation, samples of the water- and acetone-rich phases can be obtained and collected in the RBF, immersed in liquid N$_2$ (to avoid sample loss).
The acetone concentration of the samples was determined using a calibration curve obtained with known acetone:water mixtures that had not been exposed to CO$_2$. To guarantee the reliability of the data obtained, acetone:water mixtures containing the same composition of the calibration curve points were also obtained at 20 bar of CO$_2$ utilising the sight gauge. The measured acetone concentration of the pressurised samples was within 4% of the true value. In order to determine the mass of acetone still dissolved in the water-rich phase, measurements of the height of the water-rich phase were obtained prior to sampling using a cathetometer. The relationship between height and internal volume on the sight gauge is known. By combining the volume measurements with the concentration obtained by GC-FID, the amount of acetone still dissolved in the water-rich phase was estimated.

**2.2.5 Evaluation of the composition of the acetone-rich phase using GC-FID**

The amount of ionogen dissolved in the acetone-rich phase for TMBDA, TMTAD and 3DMAP was determined for samples obtained after separations at 50 bar of CO$_2$. The samples were collected in the high-pressure liquid level sight gauge equipped with a dip-tube. A sample of the acetone-rich phase was collected under pressure following the same procedure used for the water-rich phase. The main difference was the dip-tube position, which was placed at the correct depth to allow exclusive sampling of the acetone-rich phase. The experiments were carried out in duplicate.

The samples obtained were analysed using the same GC-FID method described above. To quantify the amount of ionogen dissolved in the acetone-rich phase, a known amount of acetonitrile (approximately 0.15 g), internal standard (IS), was added to a portion of the mixture (approximately 1.5 g) obtained from the sight gauge. The areas obtained for the ionogen and IS peaks on the GC traces were compared. The amount of ionogen dissolved in the acetone-rich phase was determined based on calibration curves.
2.2.6 Evaluation of the composition of the acetone-rich phase using NMR spectroscopy

The water:acetone ratio of the acetone-rich phase was determined by $^1$H NMR spectroscopy (Bruker 300.13 MHz spectrometer) of samples collected in the high-pressure liquid level sight gauge equipped with a dip-tube. The acetone-rich phase sample was collected following the same procedure described in the previous section. The experiments were carried out in duplicate.

A solution of acetone and water with a 50:50 mass ratio and a fixed concentration of TMBDA, TMTAD or 3DMAP was prepared and pressurised to 50 bar in the sight gauge. Upon phase separation, a sample of the acetone-rich phase was obtained. A known amount of the sample (approximately 0.10 g) was dissolved in d6-DMSO (approximately 0.80 g). The acetone:water ratio was established by comparing the CH$_3$ (s, 6H) for acetone and the singlet for H$_2$O. A calibration curve was obtained (see Appendix A). Quantification of the total mass of water in the acetone-rich phase was not possible due to phase expansion under the high pressure of CO$_2$.

2.2.7 Evaluation of ionogen recovery by reverse osmosis

The possibility of recovering and re-using selected ionogens was tested by preparing samples that simulated the composition of the water-rich phase after separation at 20 bar of CO$_2$.

Solutions were prepared utilising either TMBDA, TMTAD or 3DMAP as the ionogen. The prepared solutions were introduced to the reverse osmosis (RO) cell (Sterlitech, HP4750 Stirred Cell) using a DOW Filmtec™ BW30 flat-sheet membrane (Sterlitech). The system was sealed and submitted to N$_2$ pressures between 25 and 35 bar, depending on the amine used. The flow of liquid coming out of the cell (permeate) was monitored and collected in a graduated cylinder. Once 10 mL was collected, the cell was depressurised, and the permeate was analysed using the same GC-FID method described above. To quantify the amount of ionogen being lost during the RO, a known amount of acetonitrile, internal standard (IS), was added to a portion of the permeate solution.
coming out of the RO cell. The areas obtained for the ionogen and IS peaks on the GC traces were compared, and based on calibration curves, the amount of ionogen being lost during RO was determined.

2.3 Results and Discussion

2.3.1 Evaluation of TMBDA in the HPSW setup

Among the ionogens considered (Figure 2.4), N,N,N′,N′-tetramethyl-1,4-butanediamine (TMBDA), a switchable amine previously used in SW studies for the separation of organic solutes from water,\(^7\) was selected as the ionogen for the initial experiments testing the HPSW concept. When TMBDA was dissolved in acetone:water mixtures under 1 bar of CO\(_2\), no liquid/liquid separation was observed, even at amine concentrations as high as 3 molal (ionogen concentrations are reported relative to the mass of water). This behaviour was expected considering the greater hydrophilicity of acetone compared to the solutes previously evaluated (e.g. THF, caffeine). Following these observations, experiments were performed at higher P\(_{\text{CO}_2}\). Specifically, solutions containing 0.80 molal of TMBDA with varying amounts of acetone in water were pressurised and analysed using the phase monitor. The minimum pressure of CO\(_2\) required to initiate phase separation was recorded for each acetone/water mixture (Figure 2.5).
Figure 2.4 Amine ionogens tested as HPSW additives in this study.
Figure 2.5 Minimum CO$_2$ absolute pressure to induce liquid-liquid phase separation in solutions with different water:acetone molar fractions. The mole fractions and mass fractions of water are reported on a carbon dioxide-free and amine-free basis. For example: $x_{w^*} = x_w/(x_w + x_{ACE})$. ●: data points obtained without amine added, ▲: data points obtained with 0.80 molal of TMBDA. Error bars are presented. Reproduced with permission from Cunha et al.$^{101}$

For all of the acetone:water ratios analysed, the CO$_2$ pressure required to trigger phase separation was significantly lower when an ionogen was present (i.e. HPSW) than without an ionogen (i.e. using conventional CO$_2$-expansion, CXL). For an equimolar mixture of acetone and water, the absolute pressure required to induce a phase split using HPSW was 2.5 bar, which
corresponds to a 26 bar pressure decrease compared to CXL. The HPSW separation appears to be highly effective in acetone/water mixtures containing between 13 and 85 mol% water (between 4.5 and 63 wt% water). Even outside that range, phase separation was observed, but the $P_{CO_2}$ required rose above 20 bar.

### 2.3.2 Evaluation of various amines as ionogens for HPSW

Other ionogens were studied, aiming to improve the separations' efficiency and evaluate the impact of the properties of the ionogens on the separations. The efficiency of phase separation depends on many factors, both related to the amines used and the conditions applied. In terms of amine selection, factors such as $pK_{aH}$ ($pK_a$ of the protonated form of the amine) and ionogen structure are crucial for a successful separation. In addition, the $CO_2$ pressure directly impacts the % protonation of the basic sites available. As a result, promoting changes to the basic site environment of the ionogen can provide insightful information regarding what substituents or structures favour separations.

For this study, tertiary amines were selected because they form only bicarbonate species, rather than carbamic acids and carbamates salts, when exposed to $CO_2$ and water.\textsuperscript{100} In previous work, tertiary diamines were found to promote the most efficient separations in SW systems.\textsuperscript{78, 90, 91, 93, 121} In addition, amines with more than two protonatable basic centres also showed some potential but were not generally superior to diamines and were much more expensive. On the other hand, the amines best for HPSW may not necessarily be those that are best for SW. Due to the low pressure applied in the SW method (1 bar of $CO_2$), most of the basic sites in triamines and tetraamines were not protonated, which limited their efficacy. Similarly, tertiary alkanolamines were not very successful under 1 bar of $CO_2$ due to their low basicity. However, utilising such amines is desirable due to their lower toxicity compared to amines such as TMBDA and others.
envisioned that these somewhat less basic amines might be effective under the higher CO$_2$ pressures used in HPSW.

Many different ionogen amines are compared in Figure 2.6. The cloud pressure (CP), meaning the minimum CO$_2$ pressure required to promote phase split for a specific composition, was plotted versus the pK$_{aH}$ for the ionogens tested. The lines added to the plot have no physical meaning; they were added to help the reader see the trends for the different groups of amines. Further data regarding the ionogens tested can be seen in Appendix A. The % protonation for each basic site was also calculated from pH calculations which applied similar equations to those used in a previous paper (modifications were made to account for the number of protonatable sites in each ionogen). The equations and their derivations can be found in Appendix A, and the ionic strengths are presented in Table A2.1.
Figure 2.6 Comparison of the cloud pressure (CP) for the separation of acetone from acetone:water (50:50 molar ratio) solutions utilising tertiary diamines (TMBDA, TMPDA, TMEDA shown in green), tertiary polyamines (PMDETA, TMTAD and HMTETA, shown in red) and tertiary alkanolamines (TEA, MDEA, DMEA, EDEA, DEAE, 3DMAP and THEED, shown in blue) at 40 °C. The pK$_{aH1}$ value (monoprotonated form) was utilised to compare the basicity of the amines. The colour coding and the lines have no physical meaning, they are only present to facilitate visualization of possible trends among molecules of the same class. Reproduced with permission from Cunha et al.\textsuperscript{101}
Almost all the amines were able to promote the separation of acetone from water. With the only exception of imidazole, the amines reduced the pressure required to produce a phase separation compared to the CP observed in the absence of an amine. These results demonstrate that a synergistic effect occurs between the SW amines and the expansion of acetone promoted by CO₂. The repulsive interactions between the acetone and the protonated amines facilitated the acetone expulsion from the solution. As expected, higher CO₂ pressures were required to achieve sufficient protonation to make the ionogen-solute interactions repulsive when weaker bases (low pKₐvalues) were used. Nevertheless, some weaker amines like TMPDA, MDEA and DMEA are quite effective in HPSW, although they were earlier found to be ineffective in SW.⁷⁸,⁹¹

2.3.2.1 Evaluation of diamine ionogens

Diamines were previously shown to be very effective ionogens for the separation of organics from water,⁹¹ and therefore were the first group of ionogens tested for HPSW. However, diamines are most effective if both amine groups are protonated, and that occurs only if both pKₐ₁ and pKₐ₂ are close together. If those values are far apart, the dominant species in carbonated water will be the monocation rather than the dication. The shorter the linker between the two amine sites, the further apart the two pKᵦ values are due to electrostatic repulsion disfavouring the second protonation. Amines with unprotonated sites will tend to a) have more favourable interactions with acetone and b) potentially be removed from the aqueous phase, causing contamination of the acetone-rich phase. Previous work demonstrated that the optimal number of carbon atoms between the basic sites is 4, although shorter linkers might be tolerated at higher Pᵦ.⁹¹ These trends were corroborated in our experiments (Figure 2.6), TMBDA, with a C₄ linker, was found to be the most effective diamine. The shorter the carbon chain between the two basic sites, the lower the % protonation, which results in higher pressures required to trigger the onset of phase separation.
The decrease in the pK$_{aH2}$ value with shorter carbon chains between the basic sites significantly decreases the % protonation at the second nitrogen. For TMEDA (2 carbon chain), only 42% of the molecules in the solution at the CP are diprotonated. In comparison, TMBDA (4 carbon chain) has 98% of the molecules in solution protonated at both basic sites. The incomplete protonation hinders the ability of TMEDA to repel acetone, raises the CP, and potentially increases the amount of amine contaminating the acetone-rich phase.

2.3.2.2 Evaluation of triamines and tetraamines

Polyamines with more than two protonatable sites could be even more effective than diamines. At the most superficial level, the ionogen effectiveness can be related to the predicted ionic strength of the carbonated aqueous phase. Fully protonated polyamines should be highly effective, even at lower concentrations, because the ionic strength is a function of the square of the charge. Among the polyamines tested, TMTAD was found to be the most efficient amine, but it was no more effective than the diamine TMBDA. None of the polyamines had a degree of protonation much above 2; TMTAD had the highest at 2.3. Thus, at their CP, the polyamines behave as diammonium salts. Even if we consider acetone-ionogen intermolecular interactions rather than ionic strength, there is no reason to believe that a diprotonated polyamine should repel acetone more strongly than a diprotonated diamine. Thus, at low pressures, the polyamines offer no advantages over diamines and come with disadvantages such as higher costs for synthesis. However, at higher CO$_2$ pressures, where the degree of protonation of the polyamines should approach three or more, the quality of the separation may improve over that achievable with diamines.
2.3.2.3 Comparison between alkanolamines

Alkanolamines generally have very low toxicity, high commercial availability, and the potential to promote different ionogen-acetone interactions. For these amines, the $pK_{aH}$ impacted the % protonation achieved, but other factors such as the substituents potentially played a role (Figure 2.6). TEA, for example, has the lowest toxicity among all the amines presented here, but due to its low basicity, incomplete protonation was achieved at useful pressures of CO$_2$. The pressure required to induce separation was disappointingly high (Figure 2.6). On the other hand, the results observed for the other alkanolamines tested were more promising. The CP observed for 3DMAP and DMEA were very close to some of the polyamines tested. Although alkanolamines’ lower basicity might impact their utilisation as HPSW ionogens, their low toxicity and high hydrophilicity might be an incentive to explore these amines in HPSW systems further. Hydrophilicity is a desirable attribute in an ionogen for three reasons: greater solubility in water, lower likelihood of attractive ionogen-acetone interactions, and a lower likelihood that the ionogen will partition into the organic-rich phase.

2.3.3 Composition of the phases generated at a fixed pressure of CO$_2$

While the lowest CO$_2$ pressure required to induce a phase split is one useful measure of the effectiveness of an ionogen, it is more relevant to future applications to consider the quality of the acetone/water separation at a higher pressure. It is expected that the quality of separation obtained at the minimum pressure will be poor, so any future application would use a higher pressure. In addition, those ionogens that performed poorly in terms of having a rather high CP might perform much better at higher pressures where they might be more completely protonated. For these reasons, the ionogens were also evaluated in terms of the quality of separation that can be achieved at a fixed CO$_2$ pressure of 20 bar.
The experiments for evaluating ionogen performance at 20 bar were all performed under the following conditions. The initial water:acetone mixture was 50:50 by mass. The initial mass of acetone and water used was 10 g of each, and the concentration of ionogen (relative to the mass of water) was 0.80 molal for diamines, 0.53 molal for tri- and tetraamines and 1.60 for alkanolamines. The water-rich phase volume was calculated from the cross-sectional area of the cell, and the height of the aqueous phase was measured with a cathetometer. The aqueous phase was then removed using a dip-tube and analysed via GC-FID. The amount of acetone left in the water-rich phase was used to measure the efficacy of the ionogens. Figure 2.7 compares the amount of acetone remaining in the aqueous phase versus the pK\textsubscript{aH1} for the ionogens. The green line represents a rough correlation between the mass of remaining acetone and the pK\textsubscript{aH} of the ionogen. Note that this correlation is only observed for the amines that lack an alcohol group. In contrast, the alkanolamines exhibit no apparent correlation.

Despite their differences in terms of pK\textsubscript{aH1} and structure, the amount of acetone left in the water-rich phase was very similar for most of the alkanolamine ionogens tested. Between the most and least efficient amine, the difference in the mass of acetone left was only 0.5 g. THEED was an exception and, to a lesser extent, DEAE. The % protonation for the alkanolamines was also very similar, above 98%, except for TEA, which presented a 94% protonation and THEED, which was monoprotonated, even at high CO\textsubscript{2} pressures.
Figure 2.7 Comparison of the mass of acetone left in the water-rich phase for the separation of acetone from acetone:water (10 g of each) solutions utilising tertiary diamines (TMBDA, TMPDA, TMEDA shown as green diamonds), tertiary polyamines (PMDETA, TMTAD and HMTETA, also green diamonds) and tertiary alkanolamines (TEA, MDEA, DMEA, EDEA, DEAE, 3DMAP and THEED, shown as black circles) at 40 °C and fixed pressure of CO$_2$ (20 bar). The pK$_{aH1}$ value (monoprotonated form, at 25 °C) was utilised to compare the basicity of the amines. The colour coding and the line have no physical meaning but are shown to facilitate data analysis. Reproduced with permission from Cunha et al.$^{101}$
Turning now to the amines that lack an alcohol functional group, one finds that TMBDA, the ionogen having the lowest CP, was once again the most effective ionogen to remove acetone from the water-rich phase. At 20 bar, 68% of the acetone was expelled. Among the polyamines, TMTAD was also very effective at promoting phase separation. Regarding the other polyamines, despite the high pressures of CO\textsubscript{2} (above the CP), the % protonations observed were subpar compared to TMTAD. PMDETA presented a degree of protonation of 2.0 when the desired value was 3.0, and for HMTETA, the calculated value was 2.6 of a desired 4.0. Based on these values, it can be concluded that these particular polyamines were essentially behaving as diamines, which is not desirable. Nonetheless, TMBDA, TMTAD and TMPDA demonstrated a good efficiency in removing acetone from the aqueous solution, expelling more than 50% of the added acetone.

Aiming to evaluate the impact of higher pressures on the separation efficiency, TMBDA, TMTAD and 3DMAP were also tested at 50 bar of CO\textsubscript{2}. Analysis of the water-rich phase showed that the mass of acetone dissolved was reduced from 3.5 g to approximately 1.3 g in all the cases. For TMBDA, the remaining amount of acetone in the water-rich phase was 1.2 g, corresponding to 88% expulsion. For TMTAD, the acetone mass dissolved in the water-rich phase was 1.3 g (87% expulsion).

Analysis of the acetone-rich phase using GC-FID demonstrated that most of the ionogen added remained in the water-rich phase. For TMBDA, the mass of ionogen dissolved in the acetone-rich phase after separation at 50 bar was <0.3% of the initial mass added. For TMTAD, the mass of ionogen dissolved in the acetone-rich phase is approximately 2% of the initial mass of ionogen added. In addition, the NMR data (Appendix A) showed that for TMBDA, the H\textsubscript{2}O:acetone mass ratio in the organic phase was around 0.07, meaning that >80% of the water had been expelled from the acetone. The H\textsubscript{2}O:acetone ratio observed for TMTAD in the NMR was slightly higher, at 0.13. These results demonstrate the efficiency of TMBDA and TMTAD in working as ionogens for phase
separation; additional optimisations can be performed to decrease the pressures applied and improve phase composition.

2.3.4 Evaluation of ionogen recycling by reverse osmosis

An important requirement for practical applications of the HPSW separations is having energy-efficient recycling of the ionogens. This would reduce the environmental and economic cost and would ensure that the process has a competitive advantage over SO or distillations. In this thesis, reverse osmosis (RO) was the technique used to recover the ionogen from the water-rich phase.

TMBDA, TMTAD and 3DMAP were tested as ionogens because they present a range of molecular sizes. Table 2.1 compiles the data obtained. Solutions of ionogen, water, and acetone were prepared to simulate the water-rich phase obtained using each ionogen after phase separation at 20 bar of CO₂. GC-FID traces were obtained for the mixture being expelled from the RO cell (see Appendix A for examples of GC-FID traces obtained).
Table 2.1 Comparison of TMBDA, TMTAD and 3DMAP in RO purifications. The mass of retentate and the initial composition for solutions containing TMBDA are evaluated in terms of the % of ionogen expelled from the RO vessel. The RO was stopped after 10 mL of the mixture was collected.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ionogen</th>
<th>Pressure of \text{N}_2/bar</th>
<th>Mass of ionogen/g</th>
<th>Mass of water/g</th>
<th>Mass of acetone/g</th>
<th>Ionogen concentration(^a)/wt%</th>
<th>Mass of retentate/g</th>
<th>% of ionogen lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TMBDA</td>
<td>25</td>
<td>1.16</td>
<td>10.0</td>
<td>3.21</td>
<td>10</td>
<td>2.96</td>
<td>23%</td>
</tr>
<tr>
<td>2</td>
<td>TMBDA</td>
<td>35</td>
<td>1.16</td>
<td>10.0</td>
<td>0</td>
<td>10</td>
<td>2.07</td>
<td>10%</td>
</tr>
<tr>
<td>3</td>
<td>TMTAD</td>
<td>35</td>
<td>1.07</td>
<td>10.0</td>
<td>3.51</td>
<td>10</td>
<td>3.57</td>
<td>7%</td>
</tr>
<tr>
<td>4</td>
<td>3DMAP</td>
<td>25</td>
<td>1.65</td>
<td>10.0</td>
<td>4.11</td>
<td>14</td>
<td>2.14</td>
<td>45%</td>
</tr>
</tbody>
</table>

\(^a\)Relative to mass of water plus ionogen.
Quantification of the ionogen being lost to the filtrate was performed by comparing the count ratios obtained for the IS:ionogen against calibration curves (see Appendix A). The goal was to concentrate the ionogens as much as possible, reducing the amount of water and acetone reintroduced in further re-use cycles.

TMBDA was the first ionogen tested due to its high efficiency for phase separations. The test solution was designed to have a composition matching that of the aqueous phase obtained after phase separation. Analysis of the solution flowing out of the RO cell showed that about 23% of the initial ionogen added was lost due to passing through the membrane during RO. However, if there is no acetone in the mixture (Table 2.1 entry 2), then only 10% of the ionogen was lost. These results demonstrate the effect that acetone might have on the recyclability of the ionogens. If the HPSW stage is performed in a manner that more acetone is expelled from the mixture (such as using 50 bar of CO₂ instead of 20 bar), then the recovery of the ionogen at the RO stage should be improved.

For TMTAD, only 7% of the ionogen was lost during RO, even though acetone was present. The efficiency of TMTAD to promote acetone phase separation and the ability of this ionogen to be recovered by RO suggests that there is great potential for this ionogen to be implemented in HPSW separations.

On the other hand, for 3DMAP, the results obtained were not as promising. The smaller size of 3DMAP compared to TMBDA and TMTAD diminished the retention of this ionogen. The data obtained demonstrated that approximately 45% of 3DMAP was being expelled in the permeate from the RO cell.

In summary, further study is required to optimise the RO stage of the process. The membrane selected (BW30) is designed to recover water from solutions containing salts such as NaCl. As such, this membrane was not as selective to exclude the ionogens tested. Optimising the ionogen recovery will minimise the environmental impacts of ionogen manufacture and aqueous
waste stream cleanup. Reductions in the amount of ionogen lost could be achieved by using membranes more selective to the type of ionogens used in this work or by using polymeric ionogens rather than small molecule ionogens.

2.3.5 Comparison of the most efficient ionogens

The selection of the most suitable ionogen will have to account for various factors described throughout this Chapter. The critical properties desired are listed below:

a) low CP
b) high removal of acetone
c) low ionogen toxicity
d) low commercial price and high availability of ionogens
e) low contamination of ionogen in acetone-rich phase
f) ease of ionogen reconcentration and recycling using simple techniques such as RO

TMBDA, TMTAD and 3DMAP are compared in Table 2.2. TMTAD presents a great combination of performance, environmental and scalability factors. TMTAD can promote the removal of large amounts of acetone from the mixture. In addition, this ionogen can be almost entirely recycled from the water-rich phase. At 50 bar, the amount of ionogen lost to the acetone-rich phase is below 2% of the initial mass added. The system using TMBDA, although presenting the largest removal of acetone from the mixture, still needs to be optimised to improve ionogen recyclability. In addition, the price of this ionogen might hinder its application on a large scale unless industrial adoption of this technology leads to a lowering of the price. In the case of 3DMAP, an alkanolamine that presented a good separation efficiency has a less-than-ideal behaviour during RO, diminishing its recyclability, at least in the conditions tested. Therefore, TMTAD appears to be the ideal candidate for further development and optimisation.
The % losses of ionogen during the different stages of the HPSW separation will impact the overall economics of the process, especially when considering ionogen cost and possible improvements. To evaluate the maximum losses afforded by the process, the current industrial price for the product (acetone in this case) could be used as the basis for ionogen loss assumptions. For example, one could assume that the cost of replacing lost amine must not be higher than 1% of the selling price of the product. That would limit the amount of amine that can be lost per kg of the product obtained. Considering that any improvements made to the amine, such as using larger structures to decrease loss during the RO step, would also have to consider the 1% of the selling price of the product. As such, the search for alternative ionogens might have to rely on commercially available amines used on a large scale for other applications (lower prices are usually observed in such cases) as potential ionogens. Further evaluation of the process can be carried out using a techno-economic analysis. This analysis should take into consideration: (i) amine cost and losses, (ii) product selling price, and (iii) other operational and capital costs to implement the HPSW separation into the production process being considered.
### Table 2.2 Comparison of TMBDA, TMTAD and 3DMAP in terms of performance factors (CP value, amount of acetone removed, contamination of acetone-rich phase and ionogen recyclability), environmental (ionogen toxicity) and scalability factors (price).

<table>
<thead>
<tr>
<th>Ionogen</th>
<th>CP value</th>
<th>Amount of acetone removed</th>
<th>Ionogen toxicity&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Price&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Contamination of acetone-rich phase</th>
<th>Ionogen recyclability via RO</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMBDA</td>
<td>LOW</td>
<td>HIGH</td>
<td>4</td>
<td>$$</td>
<td>VERY LOW</td>
<td>AVERAGE</td>
</tr>
<tr>
<td>TMTAD</td>
<td>LOW</td>
<td>HIGH</td>
<td>4</td>
<td>$$</td>
<td>VERY LOW</td>
<td>HIGH</td>
</tr>
<tr>
<td>3DMAP</td>
<td>LOW</td>
<td>INTERMEDIATE</td>
<td>4</td>
<td>$</td>
<td>VERY LOW</td>
<td>LOW</td>
</tr>
</tbody>
</table>

<sup>a</sup> GHS categories assigned based on values predicted using the Toxicity Estimation Software Tool (TEST) developed by the EPA.

<sup>b</sup> H302 Category 4 means $300 < \text{LD}_{50} \leq 2000 \text{ mg kg}^{-1}$.

<sup>c</sup> H401 Category 2 means “toxic” to aquatic life, $1 < 96 \text{ hr LC}_{50} \text{ (fish)} \leq 10 \text{ mg/L}$.

<sup>d</sup> Based on the price/gram for the largest container sold by TCI for TMBDA or Sigma for TMTAD and 3DMAP.
2.3.6 Preliminary comparison to other separation methods

Throughout this study, I aimed to demonstrate the effectiveness of HPSW in comparison to energy-intensive separations such as distillation. A comprehensive LCA has been started to determine the energy required for HPSW and to find out whether HPSW is greener than distillation. Until that LCA is complete, the following qualitative comparisons can only be offered. The key problem associated with distillation is the high energy consumption due primarily to the high heat capacity of water and, to a lesser extent, the high heat of vaporisation of water. Because HPSW requires little to no heating, the energy cost of HPSW is expected to be lower than that of distillation. The primary energy costs in HPSW are the RO step, the compression of CO₂ gas, and distillation to purify the acetone-rich phase. Fortunately, the CO₂ pressures involved are much lower than those required for supercritical CO₂. HPSW would cause environmental harm due to the manufacturing of the ionogen, although that harm can be minimised by optimising the recycling of the ionogen.

HPSW is likely to be a complementary technique, rather than a direct competitor, to reverse osmosis. RO is an energy-efficient technique when it works well but is difficult for solutions where the organic solute is a very small molecule (like acetone⁸¹-⁸³) or where the solute concentration is high. In contrast, HPSW works for a small molecule like acetone, especially when the solute concentration is high. Figure 2.5 shows that the optimal solute concentration for HPSW is about 15 to 85 wt% solute.

Pervaporation is another alternative technique available for separating organic products from water. However, like RO, it has limitations; pervaporation requires either vaporisation of water (high energy cost) or the organic solute (which must therefore be volatile). HPSW requires vaporisation of neither compound and, therefore, could be a greener alternative to pervaporation, especially for mixtures involving low-volatility solutes.
Many studies have been performed to adapt membrane-assisted separations such as RO and pervaporation to the challenges that sectors such as biomass conversions face. However, membranes are prone to fouling when applied in mixtures containing multiple components, such as the reaction media utilised in conversions catalysed by a microorganism, a conventional approach in biomass conversions. In contrast, HPSW only requires a membrane when the ionogen is recovered in preparation for recycling, not when the organic solute is removed from the aqueous phase. It remains to be seen whether that results in any process advantages such as reduced fouling.

In summary, the selection of HPSW, RO or pervaporation for a particular application will have to account for factors such as mixture composition, the membrane used and solute being removed. For some systems, especially those with higher concentrations or with low volatility solutes, HPSW may be the environmentally preferable separation technique.

2.4 Preliminary energy calculations for the HPSW separation of acetone from water

A preliminary comparison between the energy consumption to recover acetone from an aqueous solution using distillation versus HPSW was obtained. The data presented here is far from exhaustive. The work focused on examining if the HPSW made energetic sense compared to a direct distillation of the aqueous solution. The calculations presented here only focused on processes involving heating. However, for a complete analysis, the energy associated with stirring, pumping, osmosis, and any potential heat recovery for both the processes also needs to be accounted for. Considering that a distillation step was still necessary after the separation of most of the acetone from the aqueous phase, if the energy required in that purification was very similar to the energy required in just a direct distillation, the use of HPSW would not make sense, at least in terms of energy consumption. The distillation data presented here was obtained via calculations using ASPEN, a process simulation software. No attempts to optimize the distillation steps for either process were made. This initial attempt at an estimate of energy consumption, although very
preliminary, is a crucial step to identifying what steps in the HPSW separation need to receive further attention and for what systems the application of HPSW is energetically viable and for what separations other techniques should be considered.

The calculations and data presented here were apply to a simple acetone-water mixture with concentrations similar to those obtained for fermentation aiming to produce acetone. The mass balance for the steps in the HPSW separation is presented in Figure 2.8. The initial acetone-water mixture has a 20 wt% concentration of acetone in water (3.75 g of acetone dissolved in 15.0 g of water). To this solution, 4.33 g of TMBDA was added (representing a 2.0 molal concentration in regards to the amount of water present), and the solution was submitted to the same separation process previously presented in this Chapter. After 40 bar of CO$_2$ was added to the system, liquid-liquid phase separation was obtained. Both the acetone- and water-rich phases were sampled using the dip-tube connected to the sight gauge in which the HPSW phase separation was performed. The height of the phases was measured and used to determine the amount of each component in the phases. All the quantifications performed followed the procedures previously described in this Chapter. To determine the composition of the acetone-rich phase, samples containing an internal standard were injected into a GC-FID. In addition, to determine the amount of water in the acetone-rich phase, Karl Fischer water titrations were performed. Similarly, the amount of acetone still dissolved in the water-rich phase was obtained via GC-FID. The difference between the initial amount of acetone added and the amount of acetone in the water-rich phase was used to determine the amount of acetone present in the acetone-rich phase. The amount of CO$_2$ was obtained based on the amine concentration (as an acid-base reaction, considering the moles of protonatable sites), and the Henry Law constants for pure water and acetone. The mass balance for the de-carbonator step was simulated based on the conditions used. Finally, an RO step was attempted to recover the amine; however, different from what was previously observed (using 0.80 molal amine solutions), a significant amount of water was not removed from the water-rich phase. The
concentration of ionogen was too high in this case, generating osmotic pressures that could not be matched by the membranes and apparatus available at our disposal (the maximum pressure safely attempted was 70 bar of N₂). Therefore, an HPSW separation was attempted to the best of our abilities, and the mass composition data obtained was used in calculations to determine the energy consumption of HPSW compared to the direct distillation of the 20 wt% acetone solution.
Figure 2.8 Schematic representation of a HPSW system in which the aqueous solution containing acetone and TMBDA is introduced to a separator which is pressurized with CO₂. The combined action of the high pressures of CO₂ and amine protonation promotes phase separation. The acetone-rich phase (top arrow from separator) is directed for further purification using distillation. The aqueous solution (bottom arrow from separator) is de-carbonated, and the amine is switched to its neutral state. Initial attempts to recover the amine using RO were unsuccessful under the conditions tested.
The phase composition obtained demonstrated that most of the acetone was recovered from the aqueous solution, and the acetone-rich phase was also relatively pure. According to the data obtained, 63% (2.36 g) of the initial acetone was recovered via HPSW, and the acetone-rich phase contained no amine, as confirmed by the GC-FID traces obtained. In addition, the acetone-rich phase only carried over approximately 2% (~0.3 g) of the total amount of water initially present in the “synthesis” solution. These results are encouraging, considering that in a purification distillation step, such a significant reduction in the amount of water present will represent a decreased amount of energy required. In addition, the absence of TMBDA (at least based on the detection limit for the GC-FID) dissolved in the acetone-rich phase is a gain in separation quality and facilitates the reuse of this particular amine in other separation cycles. Therefore, the purity of the acetone-rich phase was an indication that the energy requirements for HPSW could potentially be much smaller than a direct distillation of the “synthesis” solution.

The phase composition data were used to obtain energy requirements for the direct distillation (Scenario 1) of the “synthesis” solution and the distillation, separator and de-carbonator steps in the HPSW separation (Scenario 2). The results are shown in Figure 2.9, which compares the total energy required in the direct distillation versus HPSW. For the HPSW separation, the graph also identifies the energy contribution of each step in the process. As previously mentioned, the energy required for distillation was obtained via unoptimized calculations using ASPEN. For the energy required during the separator and de-carbonator step, only the heat was considered. Equation 2 was used to calculate the heat needed for the de-carbonator, employing the heat capacity for acetone and water. Considering that no heating was required in the separator step, the energy was set to 0 MJ/kg of acetone obtained. The values were standardized based on the energy per kg of pure acetone obtained (MJ/kg of acetone).

\[
\text{Heat} = m \ (\text{in g}) \times C \ (\text{in } J/g/°C) \times ΔT \ (\text{in } °C) \quad \text{(Eqn. 2)}
\]
Figure 2.9 Comparison of the energy required (unoptimized) to separate 1 kg of acetone via direct distillation (Scenario 1) of the “synthesis” solution versus recovering the acetone via HPSW (Scenario 2) using the compositions and conditions presented in Figure 2.8. The energy comparison only accounts for processes requiring heat. Neither the energy required for pumping, stirring and degassing nor any energy savings due to heat recovery or exchange are shown. In red, the energy needed for distillation is represented. The energy used in the de-carbonator is represented in the blue box with white dots.

Although the total energy required (based on the constraints stipulated for the calculations) in the HPSW is below the energy of direct distillation, the de-carbonator step drastically impacts the energy efficiency of the process. As expected, the distillation step required after the HPSW recovery of acetone requires 60% less energy than the direct distillation of the “synthesis” solution. This is a considerable energy improvement when comparing the two techniques. Although preliminary, these results are encouraging and support the potential of HPSW to be a viable
replacement for distillation, at least in terms of energy consumption. However, the energetic gains obtained during the separation step are completely undermined once the de-carbonation of the aqueous solution is performed. This process accounts for approximately 45% of the total energy associated with heat in the HPSW separation. Such energetic impact is directly associated with the mixture being heated from 20 to 60 °C and being predominantly composed of water (72 wt% of the water-rich phase). The high heat capacity of water (4.18 J/g.ºC) has the largest impact on the energy requirement during this step; 96% of the energy required results from the water present. However, there are possible ways of addressing this issue. For example, if the de-carbonator temperature is decreased from 60 °C to 50 °C, there is a 25% reduction in the energy required in that step. Other strategies could also be implemented to reduce the energetic impact of this step, such as using residual heat from other processes. Although the energy required for the RO step was not added to the calculations since the recovery of TMBDA was not successful for this particular scenario, future energy analysis would need to consider the energy required to recover the ionogen before reuse.

These preliminary results encourage the optimization of HPSW, especially focusing on the steps occurring after the separation in the pressure vessel.

Optimizations to the energy consumption of the system are not the only improvement points for the HPSW separation. The recovery of the TMBDA added to the system could not be performed due to the osmotic pressure of the final aqueous solution obtained. As previously discussed, polymers are an alternative ionogen that could be considered for HPSW. One particular scenario that could be considerably beneficial would be the use of polymers that in their unprotonated form are insoluble in water but, once CO₂ is added, can be dissolved in the aqueous solutions. If such polymers are used, the recovery of the ionogen becomes a simple matter of removing the CO₂ from the system, which is already required. After that, a filtration step would be enough to recover the ionogen for use in another cycle. Using a polymer that switches from an insoluble to a soluble state in the presence of CO₂ represents an improvement in energy
requirements. Since energy is also required to recover the ionogen via RO, eliminating that step is beneficial. In addition, replacing an RO separation with a filtration represents a simplification in the operations taking place during the separation, which is an incentive when considering large-scale processing. As a result, simple modifications to the HPSW setup can result in valuable energetic gains and stimulate the application of this separation on a large scale.

There are other avenues in which the reduction of energy consumption promoted by HPSW could also positively impact. The data presented here focused on acetone, a very volatile and low boiling point organic molecule, which means that the energy consumption during distillation might still be energetically sound as a separation. If distillation were to be applied in the separation of organic molecules with slightly lower volatilities and higher boiling points (e.g. 1-butanol and diols) than acetone, the energy required for distillation is expected to be higher. In some cases, water might be able to be removed by distillation, but if products and by-products remain, their separation might become an even more challenging issue. In these cases, HPSW could be used as a first separation process, reducing the amount of water mixed with the organic molecules. As a result, the distillation step required after the separation would potentially require less energy. The energy delta between using distillation as the only purification method versus using HPSW followed by distillation for the systems with lower volatility organics would be higher than the energy delta currently obtained for the acetone system. Therefore, it is hypothesized that the HPSW would be even more favourable in the system where lower volatility and high boiling point organics are being recovered from aqueous mixtures.

HPSW could also be considered an alternative for systems in which an azeotrope is formed at certain temperatures and compositions. One of the disadvantages of using distillation is the formation of azeotropes between water and organic molecules. This issue is usually overcome by using additional drying processes relying on molecular sieves, drying agents and other strategies that generate solid waste that needs to be treated or disposed of. In this thesis, the formation of
azeotropes between 1-butanol and water (55.5 wt% 1-butanol at 92.4 °C) and ethanol and water (95.5 wt% ethanol at 78.2 °C) was highlighted. Other systems which present azeotropes that could be considered are 1-propanol (71.7 wt% 1-propanol at 87.7 °C) and isopropanol (87.7 wt% isopropanol at 80.4 °C). HPSW has the potential to overcome this issue by promoting the recovery of organic mixtures with concentrations above the azeotrope. As a result, the issue of performing distillation in organic-water mixtures where azeotropes are formed might be addressed by HPSW; in addition, the waste generation caused by the need for drying agents after distillations might also be diminished.

2.5 Conclusions and recommendations

The separation of organic products from water is so environmentally and economically costly that biomass-derived products struggle to compete against petrochemicals. The separation of organic solutes from water is a focal point considering that such separations account for 80% of the energy consumption of the biomass conversion sector, which heavily relies on reactions taking place in water. The goal was to create a new method for separating organic products from water by combining two known techniques: SW and CXL.

A new process called high pressure switchable water (HPSW) was proposed. By combining the benefits of changing the polarity of organic liquids at high CO₂ pressures and the solute repulsion caused by protonated amines, HPSW promotes efficient acetone separation from aqueous solutions. The data obtained with a range of ionogens demonstrated that the tertiary amines TMBDA and TMTAD would be suitable choices to further explore the separation of organics from water. In addition, it was shown that less harmful alkanolamines, despite their poor performance in SW, could also be used for HPSW separations due to the higher pressures applied. Namely, methyl-substituted alkanolamines such as 3DMAP can be efficient ionogens for HPSW separations.
The data obtained also demonstrated the possibility of recovering the ionogens. For example, the first, unoptimised recovery of the TMTAD ionogen from the aqueous phase by RO gave an ionogen recovery of more than 85%. The solution mass was decreased five-fold. These results are very promising, and with further optimisations, a process that combines HPSW and RO can potentially reduce the energy impact of the separation.

Finally, the energy calculations performed for the HPSW separation demonstrated an actual reduction in energy consumption, at least in terms of heat used, when comparing it to distillation. Although the de-carbonation of the water-rich phase might still be a point of contention and improvement, the 60% reduction in the energy required in the distillation step takes place after HPSW compared to the direct distillation of the product mixture is a remarkable result. Optimizations are necessary, especially in terms of residual heat utilization and reduction of the temperature of some of the steps taking place in the HPSW separation. Nonetheless, the energy reductions observed indicate that there is a path moving forward for the utilization of HPSW as an alternative for direct distillation of product mixtures obtained after biomass conversions.
Chapter 3

Solvent-assisted high pressure switchable water (SA-HPSW): recovery of ethanol from aqueous media

3.1 Introduction

Propelled by government incentives, concerns about emissions, and the search for a reliable fuel source, ethanol has become the biofuel of choice in many countries. In Brazil, the 1970’s oil crisis sparked the start of the “Proalcool” program in 1975; from that point on, the government subsidies helped in the expansion of not only ethanol-gasoline blends but the development of a vehicle fleet capable of efficiently running on pure ethanol.\textsuperscript{4} In the European Union, the motivations were also very similar, adding to concerns regarding greenhouse gas (GHG) emissions and the desire to promote local agriculture.\textsuperscript{43} For the United States, currently the world leader in ethanol production,\textsuperscript{123} the growth was a little delayed.\textsuperscript{42} By the 2000s, the promulgation of multiple policies (state and federal) incentivizing ethanol production, price competitiveness, reformulated gasoline requirements, and improvements in ethanol's octane content accelerated the ethanol market's growth and attractiveness.\textsuperscript{42} Environmental concerns, oil supply issues and the desire to decrease the dependency on oil imports might have heavily motivated the search for sustainable fuels such as ethanol. Still, aspects associated with the raw material source for the biofuels, petroleum demand/availability, and prices for both oil and biofuels also play a significant role in the investments made in sustainable fuels.\textsuperscript{43,123} The oil crisis in the 1970s might have motivated the search for cheaper, less volatile (in terms of global market fluctuations) and abundant sources of fuel, but conflicts such as the Ukraine war raise concerns about the increase in the production of biofuels in times of limited supply of raw materials.\textsuperscript{123} In addition, the diversion of food crops to produce fuels has also been raised as a significant concern even prior to the supply issues we are currently facing.\textsuperscript{7,124} Nonetheless, the global energy crisis is still a significant driving force in
accelerating the clean energy transition, which relies on biofuels like ethanol.\textsuperscript{123} Therefore, bioethanol plays a crucial role in the transition to a more sustainable society. Bioethanol is a successful case demonstrating how societal demands, governmental incentives, and market trends can be combined to incentivise a transition to greener production and consumption of fuels and chemicals.

The fermentation of sugars yielding ethanol as a product dissolved in water is the primary strategy adopted. The processes used in ethanol production are simple and have been optimized to generate the highest yields without interfering with the microorganism responsible for the conversion.\textsuperscript{4,6} After fermentation of the sugars, an aqueous mixture containing not only ethanol but also cellular biomass, CO\textsubscript{2} and other products is obtained. This mixture is submitted to distillation; however, due to the azeotrope formed between ethanol-water (95.5 wt\% ethanol at 78.2 °C) and the need for anhydrous ethanol (≥ 99\%) for its use as a fuel, other drying processes are also required to achieve the correct ethanol grade.\textsuperscript{4,6,43} These processes primarily focused on the removal of large quantities of water considerably impact the energy requirements of bioethanol production. In fact, energy consumption represents the highest energetic cost (Figure 1.2) and the second-highest financial cost in ethanol production.\textsuperscript{6} The energy consumption of bioethanol plants has an economic impact on the fuel produced and the environmental footprint of the process. As a result, new technologies that address the hurdle of recovering ethanol from aqueous mixtures in bioethanol production are urgently needed.

Carbon dioxide-assisted technologies might be an avenue to start addressing the issue of recovering ethanol from aqueous mixtures. Attempts were made to use switchable water (SW) to separate ethanol from water. However, no phase separation was observed, even when high ionogen concentrations (4.0 molal) were used, which was attributed to the elevated hydrophilicity of ethanol (log P = -0.4). Modifications to SW were made, and an extraction solvent was added to the mixture (solvent-assisted switchable water, SA-SW). Although previously successful with a hydrophilic
dil (1,3-propanediol), SA-SW could not promote the recovery of ethanol. In addition, as demonstrated in the diol work, SA-SW presented some issues related to phase composition, amine protonation and extraction efficiency. One of the points of improvement considered for SW was the use of higher pressures of CO$_2$. As demonstrated by experiments via CO$_2$-expansion of liquid (CXL), the pressures required to recover ethanol from aqueous mixtures can be pretty high, around 100 bar, and liquid-liquid phase separation is not observed; instead, ethanol is dissolved in the CO$_2$ gas phase.$^{108}$ A combination of SW and CXL (i.e. high-pressure switchable water, HPSW) was attempted, but no liquid-liquid phase separation was observed. Considering the challenges and limitations presented by the previous techniques, modifications were made to the SA-SW to identify if ethanol could be recovered at high pressures of CO$_2$. This new technique, which I named solvent-assisted high pressure switchable water (SA-HPSW), takes advantage of the presence of an extraction solvent that can have attractive interactions with ethanol. Once this solvent is expanded at high pressures of CO$_2$, and the ionogen is protonated, an organic-rich phase is created, and I hypothesized that this phase would be able to extract the ethanol from the aqueous media. By applying high pressures of CO$_2$, some issues could potentially be overcome, such as inadequate amine protonation, high amine concentration required, and insufficient purity of phases. In this chapter, SA-HPSW will be evaluated as a strategy to recover ethanol from water. Considerations will be made regarding the separation conditions applied in SA-HPSW, post-separation purifications via distillation, and possible ways to improve the process.

3.1.1 A guide to SA-HPSW separations

In this section, the steps involved in the SA-HPSW separation will be described, considering the novelty of the technique. Figure 3.1 presents the process in its entirety, and each dotted box corresponds to a specific part of the process. The diagram illustrates the separation of
ethanol from water and the purification of the ethanol-rich phase, which could also involve the reuse of the extraction solvent, and the steps necessary to recover the amine (denoted as B).
Figure 3.1 Diagram representing a simplified version of the separation of ethanol from an aqueous solution via the SA-HPSW technique. The dotted boxes divide the different steps involved in this circular process. The diagram presents the separation of ethanol from the aqueous solution assisted by an extraction solvent and an amine (red dotted box, step 1) once CO₂ is added to the system (green dotted box, step 2); the further purification of the ethanol-rich phase (yellow dotted box, step 3); and the steps necessary to recover the amine, denoted as B (represented in the dark and light blue dotted boxes, steps 4 and 5).
**Step 1 (red dotted box)** – Because SA-HPSW requires high pressures of CO₂, step 1 involves transferring the aqueous solution containing ethanol to a vessel capable of withstanding the high pressures used. Before this transfer, the ionogen and extraction solvent must be added to the aqueous mixture. In this work, I used a “synthesis product” solution containing only ethanol and water. However, efforts are being made to promote phase separation using product mixtures obtained after fermentation and other conversion processes. The vessel is equipped with a dip-tube that allows for recovery of both liquid phases generated. In addition, the high-pressure vessel used here was equipped with a glass window, allowing for visual observation of the phase separation. Neither the window nor dip-tube would be required in larger-scale separations; this apparatus would need to be modified for larger volumes.

**Step 2 (green dotted box)** – Once the product mixture, also containing the amine and extraction solvent, is transferred to the high-pressure vessel. CO₂ is added to the vessel until the appropriate pressure is achieved, meaning the pressure required to achieve the phase separation desired. The combination of the amine protonation and the expansion of the extraction solvent by the high pressure of CO₂ promotes liquid-liquid phase separation. Ideally, ethanol would be extracted to the organic-rich phase. Both the protonated amine and the molecules of CO₂ are responsible for disrupting the interactions taking place between ethanol-water and extraction solvent-water, which is crucial for phase separation. There is also a CO₂-rich vapour phase that contains some of the ethanol, extraction solvent and water dissolved in it. This work only focused on the composition of the liquid phases obtained after adding CO₂.

**Step 3 (yellow dotted box)** – The organic-rich phase can be collected using the dip-tube. As will be noted in this Chapter, the organic-rich phase still contains some water and trace amine dissolved in it. As a result, further purification to obtain ethanol as a pure product will be required. The process used to purify the ethanol can also be used to recover the extraction solvent, which could be re-introduced for a new separation (step not shown in the figure). In this case, I opted to
purify this phase via distillation. Calculations (via the process simulation software, ASPEN) were made to determine the energy required to obtain pure ethanol. I hypothesized that this distillation step would require considerably less energy than distillation using the initial “synthesis product” solution. However, the presence of the extraction solvent, which also needs to be removed, might significantly impact the overall energy requirement for the separation. A more comprehensive discussion will be presented later in this work's energy discussion section (Section 3.4).

**Step 4 (dark blue dotted box)** – The water-rich phase containing the protonated amine, most of the water and some of the ethanol and extraction solvent (not displayed) can also be collected and submitted for further processing. The first step involves removing the CO$_2$ and, consequently, deprotonating the amine. This can be achieved by passing an inert gas through the solution and gently heating (no more than 60 ºC) the system or by steam stripping. In this work, the CO$_2$ being removed was not recovered, but commercial systems available allow for recovery of the CO$_2$ that could then be used in a new separation. In addition, waste heat from other processes can be used for steam stripping, improving the overall energy consumption of the separation. These strategies would ensure better energy and material balance for the separation.

**Step 5 (light blue dotted box)** – The final step involves the recovery of the amine added so that a new separation can take place. In this work, due to the soluble nature (in water) of the amines used, reverse osmosis (RO) was the technique selected to promote water removal and consequently concentrate the amine (conc. B) to be reused in a new separation. In addition, if possible, there is also an interest in reusing the water in a new synthesis process. However, such reuse would have to consider the eventual presence of residual amine, ethanol, extraction solvent and possible by-products when a real fermentation product mixture is used. Furthermore, the concentrated amine solution would also contain some of the initial water, which needs to be accounted for in a new separation cycle.
Throughout all the steps taking place in the SA-HPSW, considerations about mass and energy losses also need to be considered. However, such considerations are more relevant for process engineering. Therefore, the focus of this work was to demonstrate that SA-HPSW, by taking advantage of an extraction solvent (miscible in water), the presence of an ionogen and high pressures of CO$_2$, could promote the recovery of very hydrophilic organics (e.g. ethanol) from aqueous solutions.

3.2 Materials and Methods

3.2.1 Materials

Chemicals were used as received. The following amines were obtained from commercial sources (Sigma-Aldrich, TCI, Fisher): N,N,N',N'-tetramethyl-1,4-butanediamine (TMBDA), 2,6,10-trimethyl-2,6,10-triazaundecane (TMTAD), 3-dimethylamino-1-propanol (3DMAP), ethanol (absolute ≥99.8%), isopropanol (anhydrous 99.5%), acetone (HPLC 99.9%), 1-butanol (anhydrous 99.8%), acetonitrile (anhydrous 99.6%), 2-butanol (anhydrous 99.5%), cyclohexane (anhydrous 99.5%), diethoxymethane (99.7%), 1-pentanol (ACS reagent ≥99%), triglyme (ReagentPlus®, 99%). The water:organic mixtures were prepared using water with a conductivity of 18.2 MΩ obtained from a Milli-Q® purification system (Synergy UV). For the $^1$H NMR spectroscopy, d1-CDCl$_3$ (Sigma-Aldrich) was used as the solvent. For the quantifications via GC-FID and $^1$H NMR, 1,4-dioxane (anhydrous 99.8%, Sigma-Aldrich) was utilized as the internal standard. The Karl Fischer titrations were performed using Hydranal-Coulomat AK H (Fisher, Honeywell Fluka) as the titration medium.
3.2.2 Solvent-assisted high pressure switchable water (SA-HPSW) phase separation setup

Solutions of ethanol in water (20 wt%) were prepared to simulate the solution obtained after fermentation. To this aqueous solution, 0.80 molal of TMTAD (concentration is stated relative to the mass of water added) and extraction solvent (1-butanol, 1-pentanol, 2-butanol, acetone, acetonitrile, cyclohexane, diethoxymethane or isopropanol,) in a 1:1 mass ratio with the amount of water present were added. These new aqueous solutions containing all the desired components were transferred to a high-pressure liquid level sight gauge (hereafter referred to as the “sight gauge”) manufactured by Inferno Manufacturing Co. (modified 11A-TL-B model, T316 stainless steel, with a pressure rating of 345 bar at 38 °C, 36.5 mL internal volume), equipped with a stainless steel dip-tube (Figure 3.2). The sight gauge was kept at a constant temperature (40 °C) in a water bath. The solutions were maintained under agitation due to a magnetic stir bar added and controlled by a magnetic stir plate. To maximise the stirring, the sight gauge was placed on its side (horizontal position). The sight gauge was pressurised to 50 bar of CO₂. Upon phase separation, samples of the water- and organic-rich phases were obtained. The amount of ethanol and extracting solvent dissolved in the water-rich phase was determined via GC-FID. For the organic-rich phase, the amount of TMTAD extracted from the aqueous phase was determined via GC-FID, and the amount of water removed from the aqueous mixture was determined using Karl Fischer titration.
Figure 3.2 (A) Diagram representing the setup for the sight gauge, (B) photo of the sight gauge and (C) photo of the setup used in the experiments. The setup contains a ball valve that allows CO$_2$ to flow, a needle valve that controls the flow of CO$_2$, a pressure gauge that allows for pressure readings, a pressure (P) release valve that allows the gauge to be depressurized, a burst disk, an inlet valve connected to the sight gauge, and a dip-tube that allows for sampling of liquid phases, which is also connected to a needle valve. The temperature is controlled using a water bath (acrylic container). The sample is loaded into the sight gauge. Once the transfer is complete, the vessel can be closed and pressurized with CO$_2$. Upon phase separation, samples of the water- and ethanol-rich phases can be obtained and collected in the RBF, immersed in liquid N$_2$ (to avoid sample loss).
The sight gauge was attached to a pressure gauge, and the dip-tube was positioned to allow sampling from both the water- and organic-rich phases, one at a time. The dip-tube was externally connected to a needle valve. The valve was connected to a round bottom flask maintained under liquid N\textsubscript{2} and capped with a rubber septum to minimise sample loss by expansion when the sampling was being performed.

### 3.2.3 Measurements of the composition of the water-rich phase

The samples obtained from the water-rich phase were analysed on a GC-FID (Perkin-Elmer, Clarus 680 equipped with an auto-sampler), replicates were obtained for each sample, and the results presented are the averages. The FID chromatograms were obtained using a 30 m Elite-5ms capillary column. The injector was maintained at 300 °C, 1 µL samples were injected, and a 1:150 split ratio was applied. The column was maintained at 40 °C for 2 min, ramped to 300 °C at 40 °C/min ratio and then maintained at 300 °C for 2 min. The He carrier gas flow at 1.00 mL/min was maintained for the entire run. The detector was kept at 300 °C. The experiments were carried out in duplicate.

The ethanol and extraction solvent concentrations for the samples were determined using calibration curves using dioxane as the internal standard (IS). The curves (the areas obtained for ethanol, extraction solvent and IS peaks on the GC traces were used to generate the curves) were obtained with known ethanol:water or extraction solvent:water mixtures that had not been exposed to CO\textsubscript{2}. To quantify the concentration of ethanol and extraction solvent in the samples obtained for the water-rich phase, a known amount of dioxane (approximately 0.30 g) was added to a portion of the mixture (approximately 1.0 g) obtained from the sight gauge. In order to determine the mass of ethanol and extraction solvent still dissolved in the water-rich phase, measurements of the height of the water-rich phase were obtained prior to sampling using a cathetometer. The relationship between height and internal volume on the sight gauge is known. Height measurements were
obtained with the sight gauge on the vertical position. The amount of ethanol and extraction solvent still dissolved in the water-rich phase was estimated by combining the volume measurements with the concentrations obtained using the GC-FID calibration curves.

3.2.4 Evaluation of the composition of the organic-rich phase

The amount of ionogen, TMTAD, dissolved in the organic-rich phase was determined for samples obtained after separations. The samples obtained were analysed using the same GC-FID method described above, but samples from the organic-rich phase were used instead of using 1.0 g of the water-rich phase. The experiments were carried out in duplicate.

The amount of water removed by the extraction solvent and dissolved in the organic-rich phase was determined via Karl Fischer titration. The titrations were performed using a Coulometric KF Titrator without a diaphragm (Mettler Toledo, C20S). For this analysis, approximately 0.1 mL samples of the organic-rich phase were obtained with a syringe, the mass of the syringe and sample was measured, and after injection in the KF titrator, the mass of the “empty” syringe was measured, and the weight of the sample injected was obtained by difference. The amount of water was automatically determined by the KF titrator. In order to approximately determine the mass of water dissolved in the organic-rich phase, the relationship between height and internal volume on the sight gauge was again used. Considering that the mass of the organic-rich phase could not be measured and that the solvent expanded with the CO₂ addition, the relationship between the volume of the organic-rich phase and the density of the extraction solvent was used to obtain an approximate mass for the organic-rich phase. The amount of water in the samples analysed via Karl Fischer titration was extrapolated to the approximate mass of the organic-rich phase to determine the total mass of water removed from the aqueous phase by the extraction solvent.
3.2.5 Evaluation of ionogen recovery by reverse osmosis

The possibility of recovering and re-using TMTAD was tested via reverse osmosis (RO). Samples were prepared to simulate the composition of the water-rich phase after SA-HPSW separation with 1-butanol as the extraction solvent. These samples were submitted to a treatment using RO to remove the water and concentrate the TMTAD aqueous solution. The prepared solutions were introduced to the reverse osmosis (RO) cell (Sterlitech, HP4750 Stirred Cell) using a DOW Filmtex™ BW30 flat-sheet membrane (Sterlitech). The system was sealed and submitted to a pressure of 40 bar of N₂. The flow of liquid coming out of the cell (permeate) was monitored and collected in a graduated cylinder. Once the permeate flow ceased, the cell was depressurised, and the permeate was analysed using the same GC-FID method described above. To quantify the amount of ionogen lost during the RO, a known amount of dioxane, internal standard (IS), was added to a portion of the permeate solution coming out of the RO cell. The areas obtained for the ethanol, 1-butanol, amine and IS peaks on the GC traces were compared, and based on calibration curves, the amount of ethanol, 1-butanol and amine being lost during RO was determined.

3.3 Results and Discussion

3.3.1 Evaluation of different assisting solvents

The separation of ethanol via SA-HPSW was explored with different extracting solvents. Aqueous mixtures of ethanol in water (20 wt% concentration) were prepared. To these mixtures, TMTAD was added as the ionogen, with a 0.80 molal concentration (relative to the water content). The extracting solvent being tested was then added to the aqueous mixture. When acetone, acetonitrile, 1-butanol, 2-butanone, diethoxymethane or isopropanol were used as extracting solvent, a single-phase mixture was obtained under air. In the cases where cyclohexane or 1-pentanol were used as extracting solvent, a biphasic mixture was obtained under air. The mixtures were then transferred to the sight gauge so the mixtures could be pressurized with CO₂ (to an
internal pressure of 50 bar). After the addition of CO₂, phase separation was observed for monophasic systems under air, or maintained for the biphasic mixtures under air. The extracting solvents were selected due to their ability to undergo volumetric expansion once CO₂ is present. Furthermore, the H-bonding donating (α) and accepting (β) abilities of the solvents were also taken into consideration. The ACS solvent selection tool was used to select extracting solvents with varying values of partitioning coefficients (log P) obtained using the ALOGPS 2.1 tool. The environmental impact of the solvents was also considered during the selection. In addition, the solvent selection also took into consideration the possible intermolecular interaction between the solvents and ethanol to evaluate the effect of these interactions on the extraction efficiency of the solvents.

Regarding the amine selection, the results obtained via HPSW were the driving force in the selection of TMTAD. During HPSW, TMTAD presented some of the highest efficiencies in separating acetone from aqueous mixtures. In addition, during the amine recovery experiments via RO, due to its size, the highest exclusions (low contamination of permeate) were observed with TMTAD. As a result, TMTAD was selected as the amine of choice for the SA-HPSW recovery of ethanol.
Table 3.1 Evaluation of ethanol removal efficiency with a variety of extracting solvents capable of expanding under CO$_2$ (50 bar). The % removal was obtained via GC-FID. The log P obtained with the ALOGPS 2.1 tool, and the H-bonding donating (α) and accepting (β) abilities using the Kamlet-Taft parameters are also displayed.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Extracting solvent</th>
<th>Log P for the extracting solvent</th>
<th>Kamlet-Taft parameter α</th>
<th>Kamlet-Taft parameter β</th>
<th>%Wt of ethanol removed (considering initial mass)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Isopropanol</td>
<td>-0.04</td>
<td>0.76</td>
<td>0.84-0.93</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>1-Butanol</td>
<td>0.84</td>
<td>0.79</td>
<td>0.84</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>1-Pentanol</td>
<td>1.35</td>
<td>0.84</td>
<td>0.86</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>Acetone</td>
<td>-0.29</td>
<td>0.08</td>
<td>0.48</td>
<td>63</td>
</tr>
<tr>
<td>5</td>
<td>Acetonitrile</td>
<td>-0.33</td>
<td>0.19</td>
<td>0.40</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>2-Butanone</td>
<td>0.37</td>
<td>0.06</td>
<td>0.48</td>
<td>59</td>
</tr>
<tr>
<td>7</td>
<td>Diethoxymethane</td>
<td>0.84</td>
<td>0.00</td>
<td>0.45</td>
<td>49</td>
</tr>
<tr>
<td>8</td>
<td>Cyclohexane</td>
<td>3.46</td>
<td>0.00</td>
<td>0.00</td>
<td>7</td>
</tr>
</tbody>
</table>

There are indications of a dependency between the efficiency of extracting solvents and their intermolecular interactions with ethanol during SA-HPSW. As demonstrated by the data presented in Table 3.1, the ethanol removal efficiency of the extracting solvent might be linked to their α and β Kamlet-Taft parameters. There is an increase in recovery efficiency with increases in the β parameter. The trend is not as defined for α, but similarly to the β parameter, an increase in the value of α is also associated with an increase in the % recovery of ethanol. However, log P cannot be used to identify suitable extracting solvents for this particular recovery using SA-HPSW. As evidenced in the data presented, the attractive forces between the solvent and ethanol play a
crucial role in the recoveries observed. The overall trend observed was that solvents capable of promoting H-bonding with ethanol, especially alcohols, are prone to promote more efficient recoveries, as evidenced by the results obtained with 1-butanol (78% recovery), isopropanol (83% recovery) and 1-pentanol (76% recovery). The solvents with the ability to both donate and accept H-bonding are more effective than solvents that can only perform one of them, as is the case for dimethoxyethane (49% recovery), which can accept H bonds, but doesn’t have H-bonding donating protons. In cases such as cyclohexane, where the solvent has no H-bond ability and is in a separate phase from ethanol, the recovery efficiency is very low. The lack of attractive interactions and the mass transfer issues resulting from the biphasic mixture can be linked to the low recovery performance. When considering the log P, the value by itself cannot be used to identify if a solvent will be able to recover ethanol during SA-HPSW efficiently. Although a direct correlation between the values for the properties used in this study and the % recovery expected cannot be made, general trends were observed.

The behaviour of systems that start biphasic under air was further investigated to identify the impact of the ionogens and CO₂ in ethanol recovery from aqueous solutions. As evidenced by the results obtained with 1-pentanol (Table 3.1, entry 8), biphasic starting mixtures might also present efficient ethanol recovery. On the other hand, cyclohexane (also biphasic under air), which does not have hydrogen bonding capabilities, showed a very small ethanol recovery efficiency (7% recovery). Although further investigations have to be performed, mass transfer issues seemed to have been overcome by the 1-pentanol system (initially biphasic under air), a solvent that presents H-bonding ability. This might be an indication that solvents capable of performing hydrogen bonding with ethanol might be effective in extracting solvents even if they are not in the same phase as ethanol. This hypothesis was also probed via experiments using a 5 wt% mixture of ethanol in water relying on 1-butanol as the extracting solvent. At this particular concentration of ethanol, the mixture with 1-butanol is biphasic under air. A comparison between a system not submitted to CO₂
addition and a system pressurized to 50 bar was conducted. The system to which CO₂ was added had a slightly better recovery, 79%, compared to 75% observed for the system without CO₂. The major differences were in the amount of water, and TMTAD carried over to the 1-butanol phase. Without CO₂, 46 mass% of the initial water added and 75 mass% of TMTAD were mixed in the 1-butanol phase. For the system submitted to 50 bar of CO₂, these values dropped to 20 mass% for water and 1 mass% for TMTAD. This was an indication that the CO₂ was important to ensure a cleaner organic phase. Therefore, the data suggest that starting from a biphasic system might not have a large interference with the phase transfer of ethanol, as long as the extracting solvent can have strong intermolecular interactions with ethanol. In addition, CO₂ was an important element in promoting cleaner (low contamination with water and ionogen) phase separations.

A selection was made in terms of extraction solvents to further evaluate for the recovery of ethanol from aqueous mixtures via SA-HPSW. The parameters considered in the selection were: the % recovery data, the solvent properties and their environmental impact (both as a solvent and their synthesis). Among the best-performing alcohols, 1-butanol and isopropanol were selected due to their synthesis, reliability and environmental impact. In the case of 1-butanol, both ethanol and 1-butanol are produced through the ABE process. In this case, one could envision using the products of the ABE reaction to perform their recovery. However, considering the concentrations used in this study compared to those obtained via the ABE process, data would have to be obtained to determine the minimum viable amount of 1-butanol necessary to promote phase separation. In the case of 1-pentanol, the negative environmental impact of its production process was the primary reason why this solvent was rejected as a viable SA-HPSW solvent. Acetone was also selected as an extracting solvent for additional SA-HPSW experiments. The HPSW studies performed with acetone demonstrated this solvent effectively separates from water once CO₂ is present, and acetone is also one of the components in the ABE process. Therefore, acetone, 1-butanol and isopropanol were further tested in ethanol recovery via SA-HPSW.
The experiments with the selected solvents focused on identifying the complete composition of both water- and organic-rich phases. The aqueous ethanol mixtures were prepared as described in Section 3.2.2. After the addition of CO₂, samples were obtained for both the water- and organic-rich phases and composition analyses were performed using GC-FID. Table 3.2 presents the composition of the liquid phases.
Table 3.2 Composition of the water- and organic-rich phases obtained after SA-HPSW recoveries of ethanol at 50 bar of CO₂ (at 40 ºC).

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Water-rich phase</th>
<th></th>
<th></th>
<th>Organic-rich phase</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mass of ethanol / g (wt% from initial)</td>
<td>Solvent mass / g (wt% from initial)</td>
<td>Water mass / g (wt% from initial)</td>
<td>TMTAD / g (wt% from initial)</td>
<td>Mass of ethanol / g (wt% from initial)</td>
<td>Solvent mass / g (wt% from initial)</td>
<td>Water mass / g (wt% from initial)</td>
</tr>
<tr>
<td>Acetone</td>
<td>0.7 (37)</td>
<td>1.0 (12)</td>
<td>5.6 (70)</td>
<td>1.28 (99)</td>
<td>1.3 (63)</td>
<td>7.0 (88)</td>
<td>2.4 (30)</td>
</tr>
<tr>
<td>1-Butanol</td>
<td>0.4 (22)</td>
<td>0.3 (3)</td>
<td>5.3 (66)</td>
<td>1.2 (97)</td>
<td>1.6 (78)</td>
<td>7.7 (97)</td>
<td>2.7 (34)</td>
</tr>
<tr>
<td>Isopropanol&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.4 (17)</td>
<td>1.0 (10)</td>
<td>5.0 (53)</td>
<td>1.4 (94)</td>
<td>2.1 (83)</td>
<td>8.5 (90)</td>
<td>4.5 (47)</td>
</tr>
</tbody>
</table>

The initial aqueous mixtures were prepared with the ethanol concentration in water of 20 wt% (2.0 g of ethanol in 8.0 g of water). TMTAD was used as the ionogen at a 0.80 molal (relative to the mass of water) concentration (approximately 1.3 g of TMTAD). The extracting solvent:water mass ratio was 1:1. Amounts of organic, extracting solvent and TMTAD were obtained via GC-FID using dioxane as IS, and calibration for each component. Amount of water obtained via Karl-Fischer titration.

<sup>a</sup> The number in brackets refers to the wt% relative to the amount of the component initially added to prepare the mixture. As such, the number in the water-rich phase combined with the number in the isopropanol-rich phase for each component adds up to 100%. Masses and wt% are approximated.

<sup>b</sup> The initial masses used for the experiments with isopropanol were slightly different than acetone and 1-butanol due to the volume of the sight gauge. Ethanol was 2.5 g, water and isopropanol were 9.5 g, and TMTAD was 1.5 g.
The data obtained demonstrated the efficient separation of the extraction solvent and low amine contamination in the organic-rich phase. Considering the hydrophilicity and hydrogen bonding capabilities of the solvents tested, one of the main concerns was their separation from an aqueous media. However, as Table 3.2 shows, for all the solvents tested, the highest mass % of extracting solvent remaining in the water-rich phase was observed for acetone (12 wt% from initial). This demonstrates that the CO₂ expansion associated with the disruptions in the attractive interactions between the solvents and water effectively contributes to the solvent separation from water. Therefore, improvements can be attempted by changing the amine concentration, increasing the amine concentration or changing the extracting solvent:water mass ratio. The results were positive regarding the amount of TMTAD being carried over to the organic-rich phase. The highest contamination observed was 6 wt% (relative to the initial amount of TMTAD added) for isopropanol, while for the separations with 1-butanol, only 1% of the initial mass of TMTAD added to the aqueous mixture migrated to the 1-butanol phase. This indicates that the amine is being effectively protonated, which improves its miscibility and preference for the aqueous environment. The efficient ethanol recovery obtained by the extracting solvents was also matched by their efficient separation from the aqueous phase and low contamination with TMTAD.

Optimizations are necessary to reduce the amount of water dissolved in the organic-rich phase. One of the main advantages of using SA-HPSW is being able to replace water with a more volatile organic solvent, hopefully reducing the energy requirements of the process. However, as evidenced by the organic-rich phase composition for all three solvents after SA-HPSW (Table 3.2) the amount of water still dissolved in the organic phase was quite high. These results could be rationalized considering the favourable H-bonding taking place between water, the extracting solvent and ethanol. The amount of water present in the organic-rich phase will directly impact the distillation step used to purify the ethanol afterwards. The two main issues are the energy required, since water will need to be removed, and the formation of azeotropes between the alcohols with
water (acetone does not form an azeotrope with water), which will require additional purification steps (e.g. drying agents or molecular sieves) to achieve the ethanol purity required in fuels. A more in-depth investigation of the impact of the water presence will be performed in Section 3.4. Addressing the water transfer to the organic-rich phase is quite challenging since the SA-HPSW relies on the same intermolecular bonds between solvent-ethanol during the recovery, and these interactions are causing the water phase transfer. Therefore, adjustments to the extracting solvent:water might be performed, and hydrophilic solvents that are less prone to H-bonding but could still recover ethanol (e.g. 2-butanone or diethoxymethane) might be used. These solvents previously tested were not further explored due to their recovery efficiency. This issue could be addressed by applying a multi-stage SA-HPSW extraction in which each cycle increases the amount of ethanol recovery as it is performed in conventional LLE. As a result, there are some avenues to be explored aiming to improve the ethanol recovery efficiency while reducing the amount of water carried over to the organic-rich phase.

3.3.2 Evaluation of ionogen recycling by reverse osmosis

Reusing the components of the SA-HPSW is essential if this system is to be implemented. Reverse osmosis (RO) was performed on the water-rich phases obtained after separation to identify if the ionogen would remain in the retentate phase, and what other components would also be present. Solutions of ionogen, water, extracting solvent and ethanol were prepared to simulate the water-rich phase composition obtained after the SA-HPSW for each solvent. GC-FID traces were obtained for the mixture being expelled from the RO cell (permeate).

The majority of the TMTAD present in the water-rich phase remained in the retentate phase, but the amount of water and other components being expelled was not as high as desired. For the mixtures containing acetone, only 10% (in terms of the initial mass present) of the amine was lost to the permeate phase at 30 bar of N₂. The lowest losses were observed with 1-butanol and
isopropanol. For both systems, only 4% of TMTAD was being lost to the permeate at 40 bar of N\textsubscript{2} for 1-butanol and 55 bar of N\textsubscript{2} for isopropanol. These results are on par with the results obtained in the HPSW study for the recovery of acetone.\textsuperscript{101} However, the main issue was the amount of water passing through the membrane. For the acetone system, 63% (relative to the initial mass of water) of the water initially added was recovered in the permeate. On the other hand, for 1-butanol, only 21% of the initial water present was removed, while for isopropanol, the removal was only 28%. Although no optimizations were performed in terms of the membrane or RO pressure used, these removals are still quite low. The issue of having so much water returning to the SA-HPSW step is that the % recovery is associated with the composition of the initial mixture. With an excess of water returning, the recovery of ethanol would be compromised. Therefore, RO can still be considered an efficient technique to retain TMTAD, but the concentration capabilities of this technique, for these particular systems, still need to be optimized.

In summary, changes can be attempted in order to improve the expulsion of water from the retentate phase or avoid RO altogether. One possible way to solve the water removal issue would be to increase the applied RO pressure. However, as discussed, changes to RO pressures might improve separation, but pressure increases can also decrease exclusion selectivity and damage the membranes used (ruptures or membrane fouling). Another avenue discussed in the HPSW systems would be using solid-phase ionogens (e.g. polymers) that are insoluble in water in their neutral state but, once CO\textsubscript{2} is present, dissolve in the aqueous mixture.\textsuperscript{101} In this case, instead of using RO to recover the ionogen, the polymer would be expected to precipitate after the de-carbonation step, and filtration could be used to retrieve the polymer for another use. One potential issue with polymers is the low extent of protonation they undergo once CO\textsubscript{2} is added.\textsuperscript{126} This will impact the SW portion of the SA-HPSW, which could compromise the ethanol recovery.
3.4 Preliminary energy calculations for the SA-HPSW separation of ethanol from water

The energy requirements for SA-HPSW recovery of ethanol from aqueous mixtures were roughly (non-optimized setup) compared to the energy required when distillation is applied instead. Many optimizations need to be performed. In addition, the work focused on processes involving heating and the RO step (values used based on expert advice from collaborators). A complete analysis would also require energy values for the energy associated with stirring, gas pumping, and degassing. In addition, potential heat recoveries were not considered in the analysis presented here. For SA-HPSW to be considered a viable recovery technique, one of the main requirements is that the distillation step used for purification must require considerably less energy than the direct distillation of ethanol from water. The distillation data presented here was obtained via calculations using ASPEN, a process simulation software. No attempts to optimize the distillation steps for either process were made. Although very preliminary, the analyses presented here can be used to guide research efforts in terms of what steps require more attention and optimizations to make SA-HPSW a viable separation technique to recover hydrophilic organics from aqueous mixtures.

The 1-butanol system was selected in this analysis, considering the recovery efficiency of 1-butanol and the ABE process, which produces both ethanol and 1-butanol. The data obtained for the 20 wt% ethanol aqueous solution, with a 1:1 wt% of 1-butanol:water, and TMTAD (0.80 molal) as the ionogen was used in the energy calculations. The mass balance for the steps in the SA-HPSW separation is presented in Figure 3.3. The initial ethanol aqueous mixture contained approximately 2.0 g of ethanol to 8.0 g of water. 1-Butanol (approximately 8.0 g) and TMTAD were added and the mixture was transferred to the sight gauge. After 50 bar of CO₂ was added to the system, liquid-liquid phase separation was obtained. Both the 1-butanol- and water-rich phases were sampled using the dip-tube connected to the sight gauge. The height of the phases was measured and used to determine the amount of each component in the phases. All the quantifications performed followed the procedures previously described in this Chapter. For the organic components, GC-
FID was used, and the appropriate calibration curves (Appendix C) were applied in the quantifications. Karl Fischer water titrations were performed to determine the amount of water in the 1-butanol-rich phase. The amount of CO₂ was obtained based on the amine concentration (as an acid-base reaction, considering the moles of protonatable sites), and the Henry’s Law constants for pure water, 1-butanol and ethanol. The mass balance for the de-carbonator step was simulated based on the conditions used. Finally, the unoptimized data for the RO step was also used. Therefore, an SA-HPSW separation was attempted to the best of our abilities, and the mass composition data obtained was used in calculations to determine the energy consumption of SA-HPSW compared to the direct distillation of the 20 wt% ethanol aqueous solution.
Figure 3.3 Schematic representation of an SA-HPSW separation cycle in which the aqueous solution containing ethanol, an extracting solvent (1-butanol) and TMTAD is introduced to a separator which is pressurized with CO\textsubscript{2}. The combined action of the high pressures of CO\textsubscript{2}, the amine protonation promotes phase separation, and the expansion of the extracting solvent promotes phase separation. The butanol-rich phase (top arrow from separator) is directed for further purification using distillation. The aqueous solution (bottom arrow from separator) is de-carbonated, and the amine is switched to its neutral state. Initial attempts to recover the amine using RO were also performed.
The phase composition obtained demonstrated that most of the ethanol was recovered from the aqueous solution; issues regarding the purity of the 1-butanol-rich phase and RO are also clear. The SA-HPSW separation was able to recover 80% (1.6 g) of the initial amount present. However, 34% of the water initially added to prepare the mixture is still dissolved in the 1-butanol-rich phase. Furthermore, as discussed, the RO recovery of TMTAD was unsatisfactory regarding the amount of water expelled in the permeate phase. Therefore, the purity of the 1-butanol-rich phase might be an indication that the energy required after SA-HPSW might not be as low as expected.

The next step involved the quantification of the overall energy requirement for the SA-HPSW. The phase composition data were used to obtain energy requirements for the direct distillation (Scenario 1) of the “synthesis” solution and the distillation, separator and de-carbonator steps in the SA-HPSW separation (Scenario 2). The results are shown in Figure 3.4, which compares the total energy required in the direct distillation versus SA-HPSW. For the SA-HPSW separation, the graph also identifies the energy cost of each step in the process. As previously mentioned, the energy required for distillation was obtained via unoptimized calculations using ASPEN. For the energy required during the separator and de-carbonator step, only the heat was considered. Equation 3 was used to calculate the heat needed for the de-carbonator, employing the heat capacity for ethanol, water and 1-butanol. The RO energy requirement was calculated following equation 4, which considers that 2 kWh are necessary to treat 1 m$^3$ of the mixture. The values were standardized based on the energy per kg of ethanol obtained (MJ/kg of ethanol). The ethanol purity was set to 95.5 wt% due to the azeotrope formed with water.

$$Heat = m \ (in \ g) \times C \ (in \ J/g^\circ C) \times \Delta T (in ^\circ C) \quad (Eqn. \ 3)$$

$$RO \ energy = vol \ (water \ rich \ phase \ in \ L) \times 2 \frac{kWh}{m^3} \ (energy \ for \ RO) \times 3600 \frac{kJ}{kWh} \ (conversion \ unit) \quad (Eqn. \ 4)$$
Figure 3.4 Comparison of the energy required to separate 1 kg of ethanol (84 wt% in water) via direct distillation (Scenario 1) of the “synthesis” solution versus recovering the ethanol via SA-HPSW (Scenario 2). Neither the energy required for pumping, stirring and degassing nor any energy savings due to heat recovery or exchange are shown. In red, the energy needed for distillation is represented. The energy used in the de-carbonator is represented in the blue box with white dots. Finally, the RO energy was represented by the yellow box with white xs. The values were displayed as well due to the difference in magnitude.

The energy disparity between SA-HPSW and distillation is associated with removing both water and 1-butanol from the 1-butanol-rich phase. Although the concern prior to the ASPEN calculations was the presence of water in the 1-butanol-rich phase, the data obtained demonstrated that the extracting solvent might significantly impact the heat required during SA-HPSW. The distillation calculations performed for the SA-HPSW, considered a distillation process with three
stages. The first tower was responsible for removing only 1-butanol. This solvent presents a high boiling point (117.7 °C), which results in the temperatures having to be maintained quite high in the distillation tower (125 °C). The second tower was responsible for removing the remaining 1-butanol and some water. The main issue during this stage was the loss of some of the ethanol, which compromised the overall ethanol recovery for the SA-HPSW. Finally, the third tower was used to remove enough water to generate the ethanol-water azeotrope at 95.5 wt% ethanol. Considering the > 10x disparity in the energy between the direct distillation compared to SA-HPSW, just optimizing the distillation step will not result in energy savings that will change the outcome of these calculations. Purification via distillation in the SA-HPSW needs to be replaced by a less energy-intensive technique. Regarding the other steps in the SA-HPSW separation, heating water was the main reason for the high energy requirements in the de-carbonator step. This issue could be addressed by reducing the temperature during this process. Finally, for the RO step, the energy contribution was small. Nonetheless, optimizations could still be performed, primarily focusing on the concentration of the retentate. If amines are to be used, other recovery methods could be attempted instead of RO, such as forward osmosis (FO). Alternatively, amines that are not miscible in water once deprotonated or polymeric amines could also be considered. SA-HPSW is competing with distillation, a process that has been optimized over many years and interactions. Although not as encouraging as expected, the unoptimized data obtained for the SA-HPSW recovery of ethanol provide valuable insight into what needs to be changed for this technique to be considered.

Following recommendations from collaborators, some adjustments for the SA-HPSW were explored to address the high energy requirements of this separation. The first approach would be changing the extracting solvent to a higher boiling point solvent. This modification would have to be followed by changing the distillation step in the SA-HPSW to a flash distillation or flash drum. In a flash distillation, the organic-rich stream would be partially vaporised at a certain temperature and pressure. This system which allows for extremely fast vaporizations, creates two phases: one
vapour enriched on the lowest-volatility component of the mixture, which would be ethanol in this case, and a liquid phase containing the least volatile components. That is the main reason why the larger the difference in the boiling points of the mixture components, the more likely they are to be in different phases. Preliminary experiments were performed to identify possible candidates for this modified SA-HPSW. The main issue encountered was identifying a high boiling point extracting solvent that would still promote phase separation once CO₂ was added to the system. Tests with 1,2-hexanediol (B.P. = 223 °C) and PEG-400 did not successfully promote phase separation upon adding CO₂. On the other hand, triglyme (B.P. = 216 °C), a solvent that can also promote H-bonding with ethanol, recovered 78% of the ethanol initially added, and the water-rich phase was only contaminated with 10% of triglyme. The main concern was the amount of water dissolved in the triglyme-rich phase, 32% of the initial. However, this might not be an issue if, during the flash distillation, the water remains in the liquid phase. ASPEN calculations for this modified system are currently being performed and will be published when available.

SA-HPSW might be valuable in aqueous mixtures where the product presents high boiling points. For these systems, the purification of the high B.P. product needs to be performed by completely removing any side products and water via distillation. In this case, I hypothesize that the poor thermal properties of water would have a larger impact on the distillation energy. If we could replace water with a lower boiling point and more volatile solvent (e.g. acetone, isopropanol), the energy required to purify the product might be reduced. Instead of removing water, the organic solvent would be removed instead. For these systems, the amount of water dissolved in the organic-rich phase will impact the energy required by the separation. As a result, the extracting solvent selected will have to follow in the category of partially hydrophilic and partially able to perform H-bonding to decrease the amount of water being pulled into the organic-rich phase. This might be a better avenue to explore the separations via SA-HPSW, especially considering the developments being made in the production of diols and other hydrophilic organics in aqueous media.
3.5 Conclusions and recommendations

Ethanol is among some of the most valuable chemicals for a sustainable transition produced via sugar fermentation. Ethanol production has been increasing since the 1980s, with considerable improvements to conversion efficiencies, reliability and selectivity of microorganisms, and volume. However, the same attention has not been given to the recovery of ethanol from the aqueous mixture, which is still being done via distillation. This separation process encounters issues related to the energy required due to the poor thermal properties of water and the formation of an azeotrope which requires the introduction of further purification processes. Seeing this issue and the importance of ethanol to our society, I set as my goal to create an alternative method for separating ethanol from aqueous media. By combining a well-described technique (LLE) and the recently developed HPSW, the separation of ethanol was achieved using a CO₂-assisted process, which has not been accomplished before.

This new process is called solvent-assisted high pressure switchable water (SA-HPSW). By combining the strong interactions of the hydrophilic extracting solvent with their ability to perform H-bonding with ethanol, water-miscible solvents were employed. The liquid expansion which is caused by high pressures of CO₂, which can promote phase separation of organics from water, enhanced by the presence of SW ionogens (HPSW). SA-HPSW was attempted with TMBDA, TMTAD and 3DMAP, ionogens proved to perform HPSW of acetone. TMTAD was selected for further testing due to its efficiency and possibility of being reused. The extracting solvent selection took into account the solvent polarity, H-bond ability and origin. Acetone, 1-butanol and isopropanol demonstrated the highest recovery efficiency among the solvents tested, 63, 78 and 83 wt% (from initial ethanol present), respectively.

Experiments were also performed to determine if TMTAD could be concentrated via RO after the SA-HPSW. The data obtained prove that TMTAD was primarily remaining in the retentate phase. The wt% of TMTAD in the permeate phase was as low as 4% when the 1-butanol and
isopropanol systems were tried. However, the main issue was the inadequate amount of water expelled. The same 1-butanol and isopropanol systems were only capable of removing 21% and 28%, respectively. Nevertheless, the TMTAD recovery selectivity is promising, and with further optimisations, a process that combines SA-HPSW and RO can potentially be considered.

On the other hand, calculations (unoptimized) were performed to identify the amount of energy required by SA-HPSW compared to the direct distillation of ethanol. The use of a distillation purification step (ASPEN calculations) after SA-HPSW considerably impacted the energy cost (>10x more energy was required using SA-HPSW compared to direct distillation) of this separation. Thus the initial, unoptimized version of SA-HPSW is more energy-intensive than distillation. Although preliminary, the calculations demonstrated that the purification step via distillation needs to be replaced by a different technique. Flash distillation was considered, and different solvents are being tested to evaluate if they can both promote the recovery of ethanol from the aqueous phase and decrease the amount of energy required in the separation. Ethanol aqueous solutions have been extensively investigated and optimized by other groups. One possible alternative to expanding the impact and shifting the focus on SA-HPSW would be considering the recovery of less volatile and high boiling products (e.g. diols). These systems still struggle when considering the application of distillation as the purification process, and SA-HPSW could fill this gap. Therefore, possible alternatives can overcome the issues encountered while developing SA-HPSW.

This work focused on pure ethanol-water mixtures. However, the behaviour and possible constraints of using SA-HPSW still have to be investigated via experimentation with real fermentation or other systems producing hydrophilic organics dissolved in water (e.g. electrochemical conversions and enzyme-catalyzed reactions).
Chapter 4

Expanding the scope of HPSW additives: the combination of catalysis and product recovery

4.1 Introduction

Chemical reactions capable of forming carbon-carbon (C-C) bonds are among the most important reactions in organic chemistry, and efforts are being devoted to having water as the reaction medium.\textsuperscript{128, 129} Although considered a “greener” reaction medium, as discussed in this thesis, water still has its limitations. Organic chemists are developing new catalysts, substrate combinations and methodologies to allow conventional reactions to occur in water instead of organic solvents.\textsuperscript{129} However, the product recovery techniques are still very much reliant on distillation, liquid-liquid extraction (LLE), column chromatography and other high-energy and material-intensive methods. As a result, finding alternatives for separating the products obtained from these reactions is desirable, as well as reducing the material consumption by promoting multiple steps in the reaction and even in the separation using the same reagents. Aiming to explore such concepts, a base-catalyzed reaction, namely the Baylis-Hillman reaction, was attempted using the amines used for high pressure switchable water (HPSW). The main goal was to use the amines as a base catalyst during the reaction and, upon adding CO\textsubscript{2} after the reaction, promote product recovery via a simplified, less energy-intensive and material-consuming process. Water still has an essential role to play in the replacement of organic solvents with less toxic and environmentally harmful reaction media; however, the issues associated with post-reaction product recovery still need further attention.
4.1.1 Reactions in water

To achieve more environmentally-friendly industrial processes, a critical step is replacing volatile organic solvents (VOS). VOS present issues not only in terms of toxicity to the environment (e.g. smog formation, energy consumption and water contamination) but also safety issues (e.g. flammability, which can cause explosions) to workers and communities around chemical factories.\(^{62-69, 87-89, 130}\) The main issue is that VOS are widely used in industrial processes not only in reactions but also in extractions and other separations.\(^{131-135}\) Considering all the problems associated with VOS, there is a push for change from environmental groups, researchers, industry, and even regulatory agencies, which are creating stricter regulations or even banning certain solvents.\(^{136-140}\) Other organic solvents, such as chlorinated organic solvents, are an exception in terms of flammability, but they present high toxicity.\(^{141}\) In view of VOS-related issues, water has been explored as a replacement for them, at least as a reaction medium.\(^{128, 129}\) Replacing VOS with more sustainable and less harmful solvents is vital if we are to achieve cleaner processes in the chemical industries.\(^{142-149}\)

Water is nature’s solvent and presents many properties that set it apart from organic solvents in research and industrial processes (e.g. Diels-Alder and hydroformylation).\(^{129}\) Biocatalysed reactions are a prime example of reactions that operate in water with great success, both with enzymes and other biomolecules as catalysts.\(^{129}\) In fact, the hydrophobic effect in water when organic molecules, catalysts and products are present allows for reactions that could not occur in other solvents to be achieved in water.\(^{129}\) The hydrophobicity improves the proximity of the substrates with the catalyst, improving the binding of these substrates to enzymes.\(^{129}\) In biocatalysis, the hydrophobic effect facilitates the substrate-catalyst interaction, but this effect also plays an important role when considering product recovery. In systems where the products are hydrophobic, there might be a natural phase separation from water, which simplifies the purification processes required.\(^{129}\) In addition, although detrimental in the removal of water during product purification, the high heat capacity of water (4.1813 J/g.K), when compared to organic solvents such as acetone
(2.15 J/g.K), ethanol (2.30 J/g.K) or toluene (1.72 J/g.K), facilitates temperature control by the reaction medium. Additionally, reactions starting from amino acids and carbohydrates can proceed without significant modifications in the structure of the starting materials because these molecules are water-miscible as they are. Furthermore, due to its unique physical and chemical properties, water is known for enhancing the rates of various organic reactions (e.g. Diels-Alder). Water has also demonstrated its utility in organic reactions that benefit from a biphasic system. For example, in hydroformylation, one of the largest industrial processes currently in operation, the catalysts can be designed to be soluble in water. At the same time, the starting olefins and the aldehydes obtained as products are immiscible in the aqueous media, which facilitates not only product recovery but also catalyst recyclability. Therefore, the benign nature of water, associated with its abundance and capacity to simplify and even improve some reactions encourages the exploration of this solvent as a reaction medium in organic chemistry.

Some of the same properties that make water a desirable reaction medium can also be part of the issues associated with its use. Throughout this thesis, the negative impact caused by removing water from product mixtures via distillation and other energy-intensive methods has been emphasized. The high heat capacity and enthalpy of vaporization of water are the main reasons for the expense of the purification process. This issue might be overcome by promoting the extraction of the products via LLE. However, when LLE is used, additional steps are required, such as brine washes, distillation of the extraction solvent and, in some cases, column chromatography for further purification of the desired product. During the brine washes, additional wastewater is generated, and as mentioned, purifying the wastewater can be quite costly, both environmentally and economically. As for the need for organic solvents during the extraction and column chromatography, these solvents used can be quite toxic, flammable and cause other environmental issues, diminishing the benefits of using water as the reaction media in the first place.
Therefore, overcoming the drawbacks associated with water removal at the end of reactions is a crucial step toward promoting greener organic reactions.

Considering the focus on reactions that predominantly occur in water or water-organic single-phase mixtures, an array of reaction types could be explored. The first group of reactions that could be explored are acid-catalyzed reactions. Although Lewis acids are usually unstable in water or have ligands incompatible with aqueous environments, Brønsted acid catalysts (e.g. HBF₄) are stable and can be used, for example, in the activation of imines in reactions with silyl enol ethers to afford β-amino ketones via a Mannich-type reaction.¹²⁹

Carbon-carbon bond formation is an important class of reactions in organic chemistry. These reactions, which are usually catalyzed by metal reagents, can struggle in the presence of water due to the coordination of water molecules to the metal centre, proton transfer promoted by water and overall incompatibility of the catalysts with air- and water-rich environments.¹²⁸, ¹²⁹ However, by avoiding the formation of carbanions and taking advantage of allyl halides, which are highly reactive toward metals, some developments in the allylation of carbonyl compounds and imines using Zn, Sn, Mg, and other metals have been achieved in water.¹²⁹ The formation of rings is also important in a chemist's toolbox. Pericyclic reactions, like Diels-Alder, are a very refined way to produce structures with controlled stereochemistry.¹²⁸, ¹²⁹ Diels-Alder reactions can not only proceed in water but are, in fact, accelerated by its presence and have higher endo/exo selectivity compared to the reaction in organic solvents.¹²⁸, ¹²⁹ This is associated with the hydrophobic effect in water, its polarity, and the well-structured H-bond network.¹²⁸, ¹²⁹

Finally, base-catalyzed reactions have also received significant attention. Such reactions rely on bases like amines, metal oxides, amidines and guanidines as “green bases” to promote many reactions.¹⁵¹ Among the reactions, the Baylis-Hillman, Michael and Knoevenagel reactions are very useful.¹⁵¹-¹⁵⁴ These reactions allow C-C bond formation using water or water-organic solvent single-phase systems and commercially available and cheap bases.¹⁵¹-¹⁵⁵
Considering the extent of literature focused on the use of tertiary amines to catalyze Baylis-Hillman reactions, I decided to explore how the amines used in the HPSW separations would perform as catalysts in the Baylis-Hillman reaction, and later promote product separation upon the addition of CO₂. More and more reaction protocols are being developed to allow for the use of an aqueous reaction media, this is a field that can considerably benefit from the development of strategies that mitigate the impact of product recovery on the overall environmental impact of the reactions.

Switchable water (SW) solutions (i.e. ionogen dissolved in water) have already been used as a reaction medium, and upon addition of CO₂ as the method to promote product recovery. However, in the cases previously explored, the ionogens were not used as the catalyst for the reaction. Published data is available for the hydroformylation of styrene with CO and H₂, which was performed in a solvent system containing water, N,N,N',N'-tetramethyl-1,4-butenediamine (TMBDA), which are the SW components, and tert-butanol as a co-solvent. The presence of an organic solvent and the TMBDA enhanced the solubility of the substrates during the reaction, improving the reaction rate. The catalyst system selected, [Rh(COD)Cl]₂ and the sodium salt of sulfonated triphenylphosphine (TPPTS, P(C₆H₄-m-SO₃Na)₃), had a hydrophilic character to facilitate post-reaction separation between product and catalyst. As can be seen in Figure 4.1, the system remained monophasic during the reaction, and upon the addition of CO₂, the aldehyde product and t-butanol co-solvent created a separate phase that allowed for the recycling of the catalyst and aqueous media, which was reused for another reaction. Therefore, the concept of using switchable water as a reaction medium has already been demonstrated. However, developments can still be made in which the amine is not only part of the reaction media and post-reaction product recovery but is also the catalyst in the reaction.
Figure 4.1 Schematic representation of the hydroformylation of styrene taking place in SW using a t-BuOH/water/TMBDA solvent system with a homogeneous rhodium catalyst. During the reaction, the system is monophasic; after reaction completion, CO₂ can be added, and the product and t-BuOH create a separate phase promoting the recovery of the catalyst in the aqueous phase. The aqueous system containing the catalyst can be reused for another reaction.⁹⁰ Reproduced with permission from reference 89.

This project aims to explore base-catalyzed reactions in aqueous media with product recovery facilitated by HPSW. The focus will be the Baylis-Hilman reaction of benzaldehydes with acrylates.

### 4.1.2 Baylis-Hillman reaction

The Baylis-Hillman reaction is a remarkable reaction for the formation of C-C bonds. Initially developed in 1972, this reaction only requires three components, one of them being the catalyst, which can form C-C bonds between the α-carbon in an activated alkene (bonded to an electron-withdrawing group (EWG)) and an electrophile, traditionally benzaldehyde (Scheme 4.1).
Amines catalyze the reaction with the large majority of reports using 1,4-diazabicyclo[2.2.2]octane (DABCO) as the catalyst. This coupling reaction is often performed at room temperature in a water/cyclic ether solvent mixture. The Baylis-Hillman reaction, although not much explored in the years following its development, has received much more attention recently, with a range of reviews and publications exploring its mechanism, substrate scope, catalysts and solvents. Considering the nature of the bond being formed, the reaction can be quite atom efficient, mainly if a 1:1 mole ratio of the activated alkene and electrophile are used. However, the workup required to obtain the purified product can compromise the $E$ factor (defined as the ratio of the mass of waste over the mass of product obtained) for the reaction. The reaction also creates a chiral centre when prochiral electrophiles are used as starting material, which has been explored for an asymmetric version of this reaction. As a result, the Baylis-Hillman reaction presents an exciting opportunity to explore other amines as catalysts and novel ways to promote product recovery in order to improve its $E$ factor.

Scheme 4.1 Representative conditions for the Baylis-Hillman reaction.

The mechanism behind the Baylis-Hillman reaction has also received attention. Although presenting a simple setup and outcome, the mechanism behind this reaction is still being investigated. Recent developments have demonstrated that: (i) hindered bases with high $pK_{aH}$ can be efficient catalysts in the reaction; (ii) there is a strong correlation between the rate and the $pK_{aH}$ of the amine used, with stronger bases being more appropriate catalysts; and (iii) H-bonding solvents can help in the promotion of the reaction, especially during the proton transfer step.
general mechanism was proposed based on density functional theory (DFT) calculations and experimental observation (Scheme 4.2). The first step involves a reversible Michael addition of the amine nucleophile onto the acrylate, which results in the formation of an enolate. In the second step, the enolate generated attacks the aldehyde, and the resulting molecule is a zwitterionic intermediate. The third and final step is a proton transfer, followed by the amine catalyst elimination to yield the desired product. The DFT calculations have shown that the proton transfer is the rate-determining step for this reaction and that protic solvents (e.g. water or MeOH) can accelerate this step by behaving as a shuttle to transfer the proton from the α-position to the alkoxide. The developments in understanding the mechanism behind the Baylis-Hillman reaction demonstrate the importance of basic amines and solvents such as water in the observed rates.

Scheme 4.2 Mechanism currently proposed for the Baylis-Hillman reaction.

Although many examples have been reported of the Baylis-Hillman reaction using cyclic tertiary amines like DABCO, fewer examples are available when considering the use of linear
tertiary amines. The previous reports for the Baylis-Hillman reaction catalyzed by linear amines have shown that both N,N,N',N'-tetramethylethane-1,2-diamine (TMEDA) and N,N,N',N'-tetramethyl-1,3-propanediamine (TMPDA) promote good yields (above 85%) for both acrylamides and cyclic activated alkenes, respectively. TMBDA was also explored as a catalyst for one of the reactions, presenting relatively good yields (80%). The reactions were performed in a mixture of water and cyclic ethers, dioxane for TMEDA and THF for TMPDA. In terms of reaction conditions and product purification, for both examples, an extensive workup was required using LLE, brine washes and final purification via column chromatography, which in some cases required chlorinated solvents such as dichloromethane. Such protocols are responsible for generating large quantities of waste, increasing the E factor for the reaction, and causing significant environmental impacts and health risks. A study conducted with upper-year undergraduate students found that the E factor for the Baylis-Hillman reaction performed varied from 130 to 516 with an average of 180, without considering the amount of water used. The main contribution to such a high E factor came from using organic solvents in product purification. Therefore, there are multiple avenues to improve and explore different configurations for the Baylis-Hillman reaction, aiming not only at the scope of amines used, but also in the reduction of the impact caused by the methods used in the product recovery and purification.

Herein, I will describe preliminary attempts to perform the Baylis-Hillman reaction using TMBDA or TMTAD as the catalyst during the coupling of a nitrobenzaldehyde (electrophile) and methyl acrylate (as the activated alkene). A single-phase solvent mixture of dioxane and water (1:1 v/v) was used. After the reaction completion, the system was pressurized with CO₂ following the HPSW protocol, and both the organic and the aqueous phases were characterized to identify product and catalyst distribution. No attempts were made to optimise starting material or solvent ratios. The main goal was to demonstrate that the same molecule could perform catalysis and product recovery, using CO₂ as the trigger. Therefore, by simplifying the post-reaction workup,
HPSW could be an alternative to improve the $E$ factor, energy consumption and other metrics of not only the Baylis-Hillman reaction but different base-catalysed reactions taking place in an aqueous environment.

### 4.2 Materials and Methods

#### 4.2.1 Materials

Chemicals were used as received, except for methyl acrylate (Sigma-Aldrich) which was passed through a basic Al$_2$O$_3$ column (Sigma-Aldrich) to remove the monomethyl ether hydroquinone inhibitor. The following amines were obtained from commercial sources (Sigma-Aldrich, TCI, Fisher): N,N,N',N'-tetramethylene-1,2-diamine (TMEDA), N,N,N',N'-tetramethyl-1,4-butandiamine (TMBDA), 2,6,10-trimethyl-2,6,10-triazaundecane (TMTAD). The Baylis-Hillman reactions were performed using 4-nitrobenzaldehyde (98% (GC) (4-NBA), Sigma-Aldrich) and methyl acrylate (99%, contains $\leq$100 ppm monomethyl ether hydroquinone as inhibitor) (MAC). The water:dioxane reaction media was prepared using 1,4-dioxane (anhydrous 99.8%, Sigma-Aldrich) and water with conductive of 18.2 MΩ obtained from a Milli-Q® purification system (Synergy UV). For the conventional workup, diethyl ether (anhydrous, $\geq$99.7%, Sigma Aldrich) was used for the extractions; the extract was dried over anhydrous Na$_2$SO$_4$ (Sigma-Aldrich). The acidifications were performed using HCl (ACS reagent, 37% in water, Sigma-Aldrich). Diethyl ether and ethyl acetate (anhydrous, 99.8%, Sigma-Aldrich) were used for the column chromatography. The final purification for the conventional workup was performed via column chromatography using a silica gel column (Sigma-Aldrich). For the $^1$H NMR spectroscopy, CDCl$_3$ or CD$_3$OD (Sigma-Aldrich) were used as the solvent.
4.2.2 Baylis-Hillman’s reaction setup

The reaction mixtures were prepared following this procedure unless otherwise specified.$^{158}$ 3-Hydroxy-2-methylene-3-(4-nitrophenyl)propanoic acid methyl ester (3HMNPAME) is the product of the amine-catalyzed reaction between 4-nitrobenzaldehyde (4-NBA) and methyl acrylate (MAC) in dioxane:water reaction media.$^{158}$

![Scheme 4.3 Reaction scheme for the formation of 3HMNPAME.](image)

The dioxane:water (1:1 v/v) reaction media was prepared by adding 5.0 mL of 1,4-dioxane to 5.0 mL of water in a 25 mL round-bottom flask (RBF). To the RBF containing the reaction media, 3 mmol of 4-NBA (~ 0.45 g) was added using a spatula. Following this addition, 9 mmol of MAC was added (~ 0.78 g) using a pipette. Prior to being added to the reaction mixture, the methyl acrylate was passed through a basic alumina column to remove the inhibitor. Finally, the amine was added to the reaction mixture. Experiments were performed with either 1 mmol of the following amines: TMEDA (~ 0.12 g), TMBDA (~ 0.14 g) or TMTAD (~ 0.22 g); or with an amine concentration in terms of the water content of 0.80 molal, which is the concentration used for HPSW separations, in these cases, it was used TMBDA (~ 0.58 g) or TMTAD (~ 0.81 g). After all the reagents were added to the RBF, a stir bar was also added to the RBF. The RBF was placed in an oil bath on a hotplate with a magnetic stirrer. The temperature was set to 30 ºC and measured via a thermocouple also put in contact with the oil bath. Reactions were performed for at least 15 h. During the first 10-15 min, the reaction mixture for all the different combinations attempted had a pale yellow colour, with some small pieces of the benzaldehyde slowly dissolving over time. After
that, the benzaldehyde completely dissolved, and the mixture was monophasic (clear) and pale yellow. After 15 h of reaction, the colour of the mixture changed from pale yellow to a darker yellow (clear) monophasic mixture. This final reaction mixture was then submitted to either the conventional post-reaction product recovery procedure,\textsuperscript{158} or separations using the HPSW setup; both procedures will be presented in the following sections.

### 4.2.3 Conventional product recovery steps

For this procedure, product recovery was performed as described by Zhao \textit{et al.}\textsuperscript{158} The reaction mixture, which was obtained after 15 h of reaction, was first slowly (dropwise using a pipette) acidified using 1.5 N aqueous HCl. The pH was monitored using pH test strips; once the pH reached 4-5, the acid addition was stopped. Once the pH was acidic, the reaction mixture changed from clear to cloudy. Next, the reaction mixture was transferred to an Erlenmeyer flask, and 30 mL of water was added to it. The product was then extracted from the aqueous phase using diethyl ether (3 x 15.0 mL). After extraction, the organic phase was pale yellow, and the aqueous phase only had a faint yellow colour. The ether phase was recovered and combined in a separate Erlenmeyer flask. The next step involved washing the ether phase with brine (2 x 25.0 mL). The organic phase was recovered and dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}. The ether solution was filtered to remove the Na\textsubscript{2}SO\textsubscript{4} and transferred to an RBF. The next step involved removing the solvent under vacuum at 60 °C. The resulting product was a yellow viscous oil.

The final purification of the crude product was performed using flash column chromatography on silica gel. The column was prepared using a diethyl ether:ethyl acetate (5:1 v/v) solvent mixture. The fractions containing the product appear as a yellow band in the column. The fractions were collected, and the solvent was removed under vacuum at 60 °C. The resulting product was still a yellow viscous oil. The product was collected and analysed using \textsuperscript{1}H NMR spectroscopy (400.30 MHz) using CDCl\textsubscript{3} as the solvent.
4.2.4 HPSW recovery of the product

The protocol used for this product recovery followed the procedure used for HPSW. The product mixtures obtained after reactions catalyzed by either TMBDA or TMTAD were transferred to a high-pressure liquid level sight gauge (hereafter referred to as the “sight gauge”) manufactured by Inferno Manufacturing Co. (modified 11A-TL-B model, T316 stainless steel, with a pressure rating of 345 bar at 38 °C, 36.5 mL internal volume), equipped with a stainless steel dip-tube. The sight gauge was kept at a constant temperature (25 °C) in a water bath. The solutions were maintained under agitation due to a magnetic stir bar added and controlled by a magnetic stir plate. To maximise the stirring, the vessel was placed on its side (horizontal position). The vessel was then pressurized to 50 bar of CO₂. The sight gauge was attached to a pressure gauge, and the dip-tube was positioned to allow sampling from both the water- and dioxane-rich phases. The dip-tube was externally connected to a needle valve. The valve was connected to a round bottom flask maintained under liquid N₂ and capped with a rubber septum to minimise sample loss by expansion when the sampling was being performed. Upon phase separation, the water-rich phase was recovered and submitted to ¹H NMR (400.30 MHz) analysis using CD₃OD as the solvent. The dioxane-rich phase was also collected, and analyses were performed by ¹H NMR spectroscopy (400.30 MHz) using CDCl₃ as the solvent, and Karl Fischer titration.

The approximate amount of the water- and dioxane-rich phases was determined based on the volume inside of the sight gauge. To obtain these values, the sight gauge was placed in a vertical position, and measurements of the height of the water- and dioxane-rich phases were obtained using a cathetometer. The relationship between height and internal volume on the sight gauge is known. As such, the volume of the phases could approximately be determined. In addition, after the dioxane-rich phase was collected, the mass of the recovered mixture was also measured.
4.2.5 Characterization of the product mixture

The reaction products were characterized by \(^1\)H NMR spectroscopy. The spectra were recorded with a Bruker Avance 400.30 MHz NMR spectrometer. For the spectra obtained for the purified product after the conventional workup and the samples of the dioxane-rich phase obtained after HPSW, the solvent was CDCl\(_3\). For the water-rich phase obtained after HPSW product recovery, the solvent used for the \(^1\)H NMR was CD\(_3\)OD.

The amount of water in the dioxane-rich phase, obtained after the HPSW separations, was determined via Karl Fischer titration. The titrations were performed using a Coulometric KF Titrator without a diaphragm (Mettler Toledo, C20S). The titration solution used was the Hydranal-Coulomat AK H (Fisher, Honeywell Fluka), which is suitable for titrating ketones and aldehydes. For this analysis, approximately 0.1 mL samples of the dioxane-rich phase were obtained with a syringe, the mass of the syringe and sample was measured, and after injection in the KF titrator, the mass of the “empty” syringe was measured, and the weight of the sample injected was obtained by difference. The amount of water was automatically determined by the KF titrator. Considering the mass of water obtained, the amount of water in the collected dioxane-rich phase was approximately determined using the mass measured for the dioxane-rich phase.

4.3 Results and Discussion

4.3.1 Evaluation of different amines as base catalysts

Using the results obtained by Zhao et al.,\(^{158}\) the reaction between 4-nitrobenzaldehyde (4-NBA) and methyl acrylate (MAC), Scheme 4.4, was selected to evaluate the behaviour of different tertiary amines. This particular aldehyde-activated alkene combination was found to be one of the highest yielding (above 89%) reactions by Zhao et al.\(^{158}\) The original reaction was initially performed using N,N,N',N'-tetramethylene-1,2-diamine (TMEDA) as the catalyst. This setup was replicated, and the reaction was also attempted with N,N,N',N'-tetramethyl-1,4-butanediamine
(TMBDA) and 2,6,10-trimethyl-2,6,10-triazaundecane (TMTAD) as catalysts. Both TMBDA and TMTAD were found to promote the best separations during the HPSW experiments with other organic molecules (Chapter 2). In addition, as previous works with quinuclidine-based catalysts demonstrated, the Baylis-Hillman reaction presents higher reactivity when more basic catalysts are used. Considering that both TMBDA (pKaH 10.3 and 8.8) and TMTAD (pKaH 10.0, 9.0 and 6.4) present higher basicity than TMEDA (pKaH 9.1 and 5.9) and DABCO (pKaH 8.7), these catalysts were expected to increase the conversions. Zhao et al. also observed this relationship between basicity and conversion when comparing the reactivity between TMEDA and DABCO, the latter having a lower conversion, for the reaction between 2-nitrobenzaldehyde and butyl acrylate. As a result, TMBDA and TMTAD have not only an impact on the HPSW separations but could also promote higher conversions due to their basicity.

Scheme 4.4 Reaction between 4-NBA and methyl acrylate catalyzed by TMEDA, TMBDA or TMTAD to promote the formation of 3HMNPAME.

The preliminary Baylis-Hillman reactions performed with 4-NBA and methyl acrylate catalysed by TMEDA, TMBDA and TMTAD provided some initial insights. Table 4.1 presents a comparison between the crude yields obtained with each of these amines. The initial results obtained seemed to corroborate literature showing that more basic amines are usually better catalysts for the Baylis-Hillman reaction. TMBDA and TMTAD, the more basic amines, presented 79% and 77% crude yields, respectively, but only 66% for TMEDA. Between TMBDA and TMTAD, the pKaH difference is very small, while TMEDA is a weaker base than TMBDA and
TMTAD. However, the crude yield obtained in the experiments with TMEDA was at least 23% lower than the isolated yield reported by Zhao et al. In addition, the expected product after the conventional workup was a yellow solid; in the reactions performed during this work, a yellow oil was obtained, which could indicate the presence of starting material and solvents still mixed with the final product (confirmed via $^1$H NMR, Figure 4.2). Further investigation needs to be performed to determine what was the cause for the lower yield, considering that the reactions conditions were replicated according to the published literature. In addition, experiments could also be performed with lower basicity amines to determine the extent of the impact of this property in the conversions observed. Although improvements to the reaction need to be attempted, the results obtained provide an initial indication that the basicity of the catalyst might impact the conversion, corroborating the published literature.

Table 4.1 Comparison between different catalysts for the Baylis-Hillman reaction between 4-NBA and MAC.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$pK_{aH1}$</th>
<th>$pK_{aH2}$</th>
<th>$pK_{aH3}$</th>
<th>Catalyst loading / mmol</th>
<th>Product recovery protocol</th>
<th>Crude yield / %</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMEDA</td>
<td>9.1</td>
<td>5.9</td>
<td>10.0</td>
<td>1.0</td>
<td>Conventional workup</td>
<td>66</td>
</tr>
<tr>
<td>TMTAD</td>
<td>9.0</td>
<td>6.4</td>
<td></td>
<td>1.0</td>
<td>Conventional workup</td>
<td>77</td>
</tr>
<tr>
<td>TMBDA</td>
<td>10.3</td>
<td>8.8</td>
<td></td>
<td>1.0</td>
<td>Conventional workup</td>
<td>79</td>
</tr>
</tbody>
</table>

The reactions were performed between 4-NBA (3 mmol) and MAC (9 mmol) in dioxane:water (1:1 v/v) reaction media at 30 °C for 15 h.
\(^1\)H NMR spectra were obtained for the product recovered after the reaction and product isolation using the conventional workup. Figure 4.2 presents these spectra for the reactions performed with 1 mmol of TMEDA, TMBDA and TMTAD. The \(^1\)H NMR spectra present peaks and matching integrations for the expected product structure (published \(^1\)H NMR data), confirming that the desired product was obtained. However, the presence of unreacted 4-NBA was also confirmed: aldehyde proton at 10.1 ppm in the \(^1\)H NMR spectrum (400.30 MHz) and aromatic multiplets around 8.1 and 8.4 ppm. In addition, solvent peaks for dioxane, diethyl ether and ethyl acetate were also observed around 3.5 and 2 ppm. Therefore, improvements need to be made during the purification via column chromatography.
Figure 4.2 $^1$H NMR spectra obtained for the reaction product between 4-NBA and MAC catalyzed by TMEDA (spectra A), TMBDA (spectra B) and TMTAD (spectra C). The spectra were obtained after product isolation and purification using the conventional workup. However, unreacted 4-NBA and solvent peaks (indicated with a *) were still present in the spectra obtained.
4.3.2 Comparison between conventional product recovery versus HPSW separation

The conventional workup to recover the product from the Baylis-Hillman reaction generates a large amount of waste. The conventional workup requires LLE, acid and brine washes and column chromatography to recover the final product. Each one of these steps requires a considerable amount of reagents and might generate waste that is hard to treat or reuse. Each step will be discussed in detail.

1) **Acidification of aqueous phase:** After the reaction is complete, the mixture is acidified to increase the catalyst solubility in the aqueous phase prior to LLE extraction. The acidification step with HCl creates issues for the recovery and reuse of the amine catalyst. A possible recovery step would rely on a strong base (e.g. NaOH) being added to the aqueous phase to deprotonate the amine. However, the salt accumulation could potentially impede the use of the aqueous phase for a new reaction. As such, the amine would need to be recovered, which can be quite challenging, as discussed in Chapter 3 of this work.

2) **LLE with diethyl ether:** This step ensures that the product can be recovered and purified. Diethyl ether is a highly flammable solvent (-45 °C flash point), besides being a peroxide and smog former. This poses a risk for workers using this solvent. However, in terms of recovery and reuse of the solvent, considering its high volatility (vapour pressure of 58.66 kPa at 20 °C) and low boiling point (34.6 °C), recovery and possible reuse of the solvent could be accomplished, which would diminish the need for fresh solvent in each synthesis.

3) **Brine washes:** The use of aqueous brine generates another stream of contaminated water that needs to be potentially treated or recycled. The brine could potentially be reused to avoid additional waste generation. However, after each cycle, the brine could be concentrated with other components, which could interfere with the following product purification steps. In addition, as discussed, recovery of water from brines is energetically costly.
4) **Column chromatography**: The final step is the isolation and purification of the product via column chromatography. This step presents many issues regarding solvent volumes used, flammability, and solid waste generation. Both diethyl ether and ethyl acetate are used. Ethyl acetate is flammable (−4 °C flash point), volatile (9.7 kPa at 20 °C) and presents a relatively low boiling point (77.1 °C), which makes this solvent a smog former and a risk for workers but also facilitates its recovery and possible reuse. On the other hand, the solid silica waste generated can pose a more complex issue, considering that purification of the silica for future cycles can be energetically and environmentally costly. An alternative for this issue could be replacing column chromatography with other processes such as countercurrent chromatography that can avoid large waste generation by using supercritical fluids such as CO₂.

Therefore, using a conventional separation and product purification process not only increases the $E$ factor for a reaction that is considered highly atom efficient, but also creates other issues related to the safety of workers and other environmental impacts.

HPSW was considered an alternative for the product recovery from the aqueous mixture because there is a potential to reuse the aqueous phase and avoid the generation of large amounts of waste (Figure 4.3). If, after the reaction with TMBDA or TMTAD as catalysts, the reaction media could be pressurized with CO₂ promoting the separation of the dioxane and the products from the aqueous media, the separation would be greatly simplified and improved in terms of energy and material consumption. In fact, considering the presence of dioxane, a solvent known to expand with CO₂, in the reaction media during the Baylis-Hillman reaction, the separation of the product could be achieved by SA-HPSW. Dioxane, which is important for the reaction, can improve product recovery by creating an organic-rich phase. Some key parameters need to be met for HPSW to be effective in this particular Baylis-Hillman reaction: (i) the product needs to be more miscible in the dioxane-rich phase than in the aqueous phase; (ii) side products and starting materials need
to remain in the aqueous phase or be easily separated from the final product; (iii) the amine needs to remain in the aqueous phase after CO₂ addition; (iv) the amount of water in the dioxane-rich phase needs to be kept as low as possible; and (v) the purification processes taking place after HPSW need to be simple and require a low amount of energy. Therefore, experiments were performed to understand if HPSW could meet the requirements specified, simplifying and reducing waste generation for this particular Baylis-Hillman reaction.
Figure 4.3 Diagram representation of a Baylis-Hillman reaction followed by product recovery using HPSW. The initial step is the catalysis promoted by amines such as TMBDA or TMTAD. Once the reaction is completed, the mixture is transferred to a high-pressure vessel and pressurized with CO₂, enabling phase separation. The organic-rich phase would ideally only contain the product and organic solvent (dioxane) and could be further purified via distillation. The aqueous phase would contain any unreacted starting material (SM), the amine and water, and after a simple decarbonation, it could be reused in a new reaction.
HPSW separation was applied after slightly modified Baylis-Hillman reactions performed with TMBDA and TMTAD as catalysts. The reactions performed prior to HPSW were slightly adjusted to ensure an efficient separation. The most significant change was the amount of amine added to the reaction media; 4.1 mmol of TMBDA or TMTAD were used in the reactions (compared to 1 mmol used in the conventional workup experiments). This change ensured an amine concentration of 0.80 molal in terms of the water content in the reaction media, which was identified as a satisfactory concentration for HPSW and SA-HPSW separations. Otherwise, the reactions were performed following the procedure previously described. Once the reaction was completed, the mixture was transferred to the high-pressure sight gauge and pressurized to 50 bar of CO2. Although the pressure used was 50 bar, the phase separation started around 15 bar. Higher pressures were used to ensure the highest protonation of the amine, which is known to improve its water miscibility, and to increase the expansion of dioxane, favouring the transfer of the organic product to that phase. The dioxane-rich phase retained the yellow colour from the product mixture. In contrast, the aqueous phase presented a faint pale yellow colour, a visual indication that the product was primarily dissolved in the dioxane-rich phase. Once phase separation was obtained, both the water and dioxane-rich phases were collected with the help of the dip-tube and characterized using 1H NMR spectroscopy.

The 1H NMR spectra obtained for the dioxane-rich phase provided an indication of the composition of the phase and conversions for the reaction. After adding CO2 to the reaction mixture, the dioxane phase was recovered for both the reactions with TMBDA (Figure 4.4) and TMTAD (Figure 4.5) as catalysts. These reactions were performed with higher catalyst loading (4.1 mmol) to facilitate the HPSW separation; this change also improved the overall reaction conversion. As observed in the 1H NMR spectra of the dioxane-rich phase for both TMBDA and TMTAD, only trace amounts of 4-NBA (limiting reagent in the reaction) were observed, indicating a high conversion to the final product. Although quantifications were not performed, the NMR
spectra are an indication that higher catalyst loadings promote higher conversion, especially when comparing these results to the crude yield obtained for the reactions using 1 mmol of catalyst. In addition, an efficient HPSW would also be confirmed by the complete transfer of the product to the dioxane phase. As confirmed via $^1$H NMR spectroscopy of the aqueous phase (Figure 4.6), peaks associated with the product or starting materials were not observed, demonstrating that the HPSW was efficient in recovering the product from the aqueous phase. On the other hand, the presence of the dioxane-rich phase also resulted in the transfer of the unreacted MAC (added in excess in this particular reaction) to the organic phase, as confirmed by the $^1$H NMR spectra. As a result, further purification steps would have to address this issue. One alternative for removing MAC from the dioxane phase post-separation would be using distillation to remove both the dioxane and the unreacted MAC. Ideally, after distillation, both dioxane and MAC would be recovered and added to a new reaction. Finally, the spectra obtained also indicate the presence of small amounts of TMTAD being transferred to the dioxane-rich phase. Considering the goal of reusing the catalyst and aiming to avoid complex purification steps after the HPSW separation, this transfer needs to be addressed in future optimizations. Due to the contamination of the dioxane-rich phase with TMTAD, unreacted 4-NBA and MAC, and water, further purification via distillation was not attempted at this time. The use of HPSW to promote product recovery was demonstrated to be a possible alternative to conventional workup proceeds, provided that the contamination of the dioxane-rich phase is addressed in future experimental setups.
Figure 4.4 $^1$H NMR spectra obtained for the dioxane-phase (spectra B) obtained after adding 50 bar of CO$_2$ to the reaction catalysed using TMBDA. Spectra A was obtained for pure MAC, and spectra C presents the $^1$H NMR for pure TMBDA. As can be observed, the dioxane-rich phase contains trace amounts of unreacted 4-NBA (limiting reagent) and the unreacted MAC (excess in this reaction).
Figure 4.5 $^1$H NMR spectra obtained for the dioxane-phase (spectra B) obtained after adding 50 bar of CO$_2$ to the reaction catalysed using TMTAD. Spectra A was obtained for pure MAC, and spectra C presents the $^1$H NMR for pure TMTAD. As can be observed, the dioxane-rich phase contains trace amounts of unreacted 4-NBA (limiting reagent), the unreacted MAC (excess in this reaction) and some of the TMTAD catalyst.
Figure 4.6 $^1$H NMR spectra obtained for the aqueous phase obtained after adding 50 bar of CO$_2$ to the reactions catalysed using TMBDA (spectra A) and TMTAD (spectra B). In the spectra obtained, the reaction product or unreacted starting materials were not detected, demonstrating the efficiency of the HPSW in separating organic molecules from aqueous environments.
The $^1$H NMR spectra (Figure 4.6) for the aqueous phase after HPSW provided insight into some aspects that need to be explored to improve the separation. As evidenced in the dioxane-rich and aqueous phase $^1$H NMR spectra, the unreacted MAC and part of the TMTAD used as catalyst were transferred to the dioxane-rich phase. The reaction selected to determine the efficiency of HPSW for product recovery required the use of excess activated alkene (i.e. MAC).\textsuperscript{158} However, many examples of other Baylis-Hillman reactions are performed using 1:1 or 1:1.5 equivalents for the aldehyde and the activated alkene.\textsuperscript{155} MAC is a molecule with a low boiling point (80 °C); as such, its removal from the dioxane-rich phase could be accomplished via distillation. In some cases, if the activated alkene is more hydrophilic, it is hypothesized that the alkene would remain in the aqueous phase. However, in cases where the activated alkenes have high boiling points, are not as hydrophilic, or when full conversion is not achieved, further purification steps would need to be introduced to isolate the product. The partition of unreacted starting materials to the dioxane-rich phase is an issue that needs to be addressed if HPSW is to be considered an efficient route to recover products from Baylis-Hillman reactions.

Although some issues related to amine transfer to the dioxane-rich phase were observed, the use of TMBDA as a catalyst seemed to avoid such problems. One of the main benefits of using HPSW and consequently amines which are known to be suitable ionogens in the separation but also possible catalysts in the Baylis-Hillman reaction is the elimination of some purification steps present in the conventional workup. It was demonstrated that both TMBDA and TMTAD were efficient catalysts for the Baylis-Hillman reaction. By applying such amines, instead of using HCl at the end of the reaction to promote acidification of the media and promoting the separation of the catalyst from the product, CO$_2$ can be used. The use of CO$_2$, a molecule that can be easily removed from the media (via steam stripping or addition of other gas), and the switchable behaviour of the amines were driving forces to employ HPSW as a recovery technique for the products from Baylis-Hillman reactions. The goal was to add high pressures of CO$_2$ to the reaction mixture, promote the
protonation of the amine, and separate the products. Once the aqueous phase was recovered, a simple de-carbonation process using heat, steam stripping or an inert gas would enable deprotonation of the amine, allowing for the aqueous phase to be reused in a new reaction (Figure 4.3). Such an approach would improve the circularity of this reaction and reduce catalyst consumption, energy use, and aqueous waste generation. It was demonstrated via the $^1$H NMR spectra for the dioxane-rich phase obtained after the reaction with TMBDA (Figure 4.4) that amine transfer was not detected. However, an unknown amount of amine was present, as indicated by the $^1$H NMR spectra for the dioxane-rich phase after reactions with TMTAD (Figure 4.5). TMTAD has one extra protonatable site than TMBDA, which is not very basic ($pK_{aH} = 6.4$). As such, this site is not completely protonated, which would decrease the hydrophilicity of TMTAD and preference to partition to the dioxane phase. This is an issue for two main reasons; first, the presence of amine in the dioxane-rich phase means that distillation could not be used to promote product purification. The need for additional purification steps directly impacts the benefits of using HPSW in the first place. Second, if amine is being lost to the dioxane phase, new reactions would require the addition of more amine to replace that lost in previous reactions. Nonetheless, the results with TMBDA demonstrated that HPSW can still be effective when higher basicity amines are chosen. In addition, HPSW, by taking advantage of CO$_2$, generates an aqueous stream that can easily be treated and reused. Compared to the conventional workup, which relies on HCl for acidification and generates an aqueous waste stream that cannot easily be recovered. Furthermore, for the Baylis-Hillman reaction, it was demonstrated in this work and the published literature that more basic amines promote higher conversions, as such, TMBDA would be a good catalyst choice.$^{156, 158, 160}$ Therefore, TMBDA was shown to be an effective catalyst and product separation trigger in the Baylis-Hillman reaction, demonstrating that HPSW might be considered as a post-reaction treatment.

The amount of water transferred to the dioxane-rich phase was determined using Karl Fischer titration. The final component in the dioxane-rich phase is water. The presence of water
will interfere with any additional purification steps, especially if distillation is the selected process to remove the solvent and any unreacted materials. Through Karl Fischer titration, the amount of water in the dioxane-rich phase for the reactions with TMBDA and TMTAD was determined to be approximately 8 wt% (~0.64 g total water in the dioxane phase) and 9 wt% (~0.84 g total water in the dioxane phase), respectively. Although not high, these values will increase the energy requirements of the distillation used to isolate the product. In addition, the water in the dioxane-rich phase might behave as a transporter for the amine increasing its partition, which could also explain the presence of TMBDA and TMTAD in that phase. One possibility to address this issue would be using more hydrophobic co-solvents in the Baylis-Hillman reaction, such as THF, which was already demonstrated as an effective reaction media. By changing the hydrophobicity of the reaction media, the partition of water, amine, and even products would be altered, and a cleaner phase separation could be obtained. Even though water contamination was still observed in the dioxane-rich phase for the HPSW post-reaction treatment, the amount of aqueous waste stream generated is considerably reduced compared to the conventional workup. In the conventional workup, multiple brine washes and drying with Na₂SO₄ are performed to eliminate water. These additional steps generate large amounts of aqueous and solid waste that must be treated after the process. As such, I hypothesize that treating the waste created in the conventional workup would result in higher energetic and environmental impacts than removing the water still dissolved in the dioxane-rich phase obtained after the HPSW workup. Therefore, although water transfer to the dioxane-rich phase is not ideal and might cause some issues, compared to the conventional workup, benefits could be observed using HPSW.

One aspect of the Baylis-Hillman reaction that remains to be addressed is using pure water as the reaction media. Amines such as TMBDA are known to behave as hydrotrpdes, improving the solubility of organic molecules in aqueous media in the absence of CO₂. As a result, the amines could improve the miscibility of more hydrophobic starting materials, ensuring that the reactions
could still occur even if only water was used as the reaction media. Using pure water could potentially improve the purification steps taking place after HPSW, eliminate the use of organic solvents, and possibly solve the issues in terms of the partition of unreacted starting materials and catalysts. If the product obtained after the Baylis-Hillman reaction was hydrophobic enough, adding CO$_2$ to the system would promote its separation. The absence of an expanded organic phase could also reduce the partition of the amine catalyst and water to the product phase. Ideally, the product phase obtained would not require additional purification steps after the separation via HPSW. But such hypotheses, especially when solid products need to be separated via HPSW, remain to be validated. In addition, the number of reports describing the use of pure water as the reaction media for the Baylis-Hillman reaction is limited.$^{162}$ However, it was found that reactions between benzaldehyde and acrylonitrile catalyzed by DABCO were greatly accelerated in water compared to usual organic solvents.$^{162}$ These results are corroborated by mechanistic studies that demonstrated that hydrogen-bond donors, such as water, activate the reaction by allowing the proton transfer step to occur via a concerted lower-energy mechanism in which one molecule of water act as a shuttle to transfer the proton (Scheme 4.2).$^{156}$ As a result, exploring Baylis-Hillman reactions in pure water followed by HPSW is a natural progression, especially considering that the amines used as catalysts can also behave as hydrotropes, improving the solubility of more hydrophobic starting aldehydes and alkenes.

4.4 Conclusions and Recommendations

The development of reactions in water is one of the pillars of promoting organic synthesis that rely on less toxic solvents and consequently generates less environmental impact. Water does have the potential to be a greener solvent than other flammable, toxic and environmentally damaging organic solvents. However, the same properties that make water a benign solvent also diminish its positive impact when the recovery of products from the aqueous media is considered.
This work aimed to start an investigation into the use of HPSW and its amines as catalysts for the Baylis-Hillman reaction and as an alternative technique for product recovery.

The data obtained demonstrated that the TMBDA and TMTAD, amines known for their efficiency in HPSW, could also increase the conversion in a model Baylis-Hillman reaction. The reaction selected used 4-NBA as aldehyde and MAC as the activated alkene in dioxane:water (1:1 v/v) reaction media. The reactions with TMBDA and TMTAD, presented 79 and 77% crude yield, which was higher than the yield obtained with TMEDA (66%), a slightly lower basicity amine. This result confirmed the previous literature that established that higher basicity amines are usually more efficient catalysts in the Baylis-Hillman reaction.

Once HPSW was used instead of conventional workup procedures, some improvements could be accomplished, but there are still issues to be overcome. By using HPSW, the amount of reagents required will potentially decrease; the environmental impact is potentially reduced, considering that some VOS are partially eliminated from the protocol; and less waste might be generated. In addition, due to the higher concentrations of amine used in the HPSW workup, the reaction conversion was considerably improved. When TMBDA was used as the catalyst, close to full conversion (trace amounts of the 4-NBA present in the \(^1\text{H} \text{NMR} \) spectra) was obtained in the modified protocol for HPSW compared to an approximate 79% yield when the published protocol was used.\(^{158}\) I envision that by taking advantage of HPSW as the workup procedure, the amount of waste generated that requires treatment would be considerably reduced. The conventional workup requires acidification with HCl, LLE, brine washes and drying over Na\(_2\)SO\(_4\) prior to product purification with column chromatography. HPSW could potentially eliminate most of these isolation steps, improving the \(E\) factor for the Baylis-Hillman reaction. Furthermore, by using CO\(_2\) as the trigger in the separation, the aqueous phase obtained after HPSW could potentially be reused in a new reaction, which is also an energetic and environmental improvement. However, as demonstrated by \(^1\text{H} \text{NMR} \) spectra obtained for the dioxane-rich phase (obtained after adding 50 bar
of CO$_2$), the product and solvent were not the only molecules recovered. The dioxane-rich phase also contained water (between 8-9 wt%), unreacted MAC, traces of 4-NBA and some amine in the case of TMTAD. Due to these contaminants, further purification of the dioxane-rich phase was not attempted in these preliminary experiments. These issues must be addressed in future experiments if HPSW is to be considered a reliable product recovery technique for Baylis-Hillman and other base-catalysed reactions in water. Therefore, I hypothesize that HPSW might be a viable route to replace a conventional workup procedure in Baylis-Hillman reactions.

Different avenues could be explored to overcome the challenges observed in this work. Exploring the use of 1:1 equivalents between the aldehyde and activated alkene could reduce the issues with the partition of unreacted starting materials if full conversion is achieved. Another alternative would be using more hydrophilic starting materials, which would remain in the aqueous phase even after the addition of CO$_2$. Higher basicity amines could potentially decrease the contamination of the dioxane-rich phase as well as improve conversions. These amines would present higher protonation once CO$_2$ is introduced to the system, which would decrease their partition to the dioxane phase. In addition, as previously mentioned, more basic amines were found to be more efficient catalysts for the Baylis-Hillman reaction. Finally, changing the hydrophobicity of the co-solvent used in the reaction media could also improve the partition of the components in the product mixture. More hydrophobic solvents would ideally be less prone to take any water or hydrophilic components in the product mixture, facilitating any purification processes required after the HPSW is performed. The attempts presented in this work are very preliminary. Further investigation and optimizations are essential if HPSW is to be considered an alternative separation technique for reactions such as Baylis-Hillman.

This study exclusively investigated the reaction between 4-NBA and MAC. In addition, the reactions performed used dioxane:water reaction media. The use of pure water as reaction medium, taking advantage of the hydrotropic effect demonstrated by the HPSW amines, is still to
be examined. It is hypothesized that this change could accelerate the reaction and also promote a cleaner product phase that could potentially avoid the need for additional purification steps. Furthermore, there is a plethora of other aldehyde and alkene combinations that could be attempted. In addition, there are different base-catalysed reactions such as aldol condensation and Michael additions that could also benefit from a product separation via HPSW. The preliminary observations of this work are promising and demonstrate that there is an avenue to use amines as catalysts in reactions taking place in water and as promoters of product separation via HPSW.
Chapter 5

Conclusions and Recommendations

5.1 Conclusions

This thesis has demonstrated the application of two new CO$_2$-assisted separation techniques to address the issue of high energy consumption in biomass conversions. Biomass conversions (e.g. sugarcane, corn, cellulose, lignin) to value-added chemicals are an essential part of the efforts being made to attain a more sustainable society. However, the energy consumption issues faced by this field due to the need to remove large volumes of water (a solvent with very poor thermal properties) can diminish the positive impact of using renewable resources in the first place. As a result, this project was set to address such an issue by taking advantage of CO$_2$ and the changes it could promote to the interactions between molecules in an aqueous system. The first approach, high pressure switchable water (HPSW), combined two previous known separations, switchable water (SW) and CO$_2$-expansion of liquids (CXL), to promote the separation of some hydrophilic organics (i.e. acetone, isopropanol, 1-propanol and ethyl lactate) from aqueous mixtures. A variation of HPSW was also developed to address the separation issues faced by highly hydrophilic organics. This variation combined HPSW and liquid-liquid extraction (LLE) using water-miscible solvents, being named solvent-assisted high pressure switchable water (SA-HPSW). Finally, an initial evaluation was performed to identify if HPSW ionogens could promote base catalysed reactions in water (i.e. Baylis-Hillman) and, upon addition of CO$_2$, promote product recovery. Although very preliminary, the results indicated that this approach could be further developed and expanded to more substrate combinations and reactions. The overall goal was to identify if the HPSW and SA-HPSW could promote more energy-efficient separations compared to traditional separations (e.g. distillation) and start an evaluation of possible avenues of application.
Society is moving towards a greener and sustainable future, where people will rely on biomass and other sustainable sources for fuels, chemicals and everyday household products. However, there is still much to be done regarding technologies supporting this transition. Therefore, it is pivotal that academia and industry invest in alternatives that address the hurdles faced by this field. This project was set to investigate issues regarding the separation of hydrophilic organic products from water which can account for up to 80% of the energy consumed in some biomass conversions. The current technologies are well-established and demonstrate efficiency for some separations. However, issues still arise from the nature of the biomass conversions (complexity of mixture, presence of solids, thermal properties of products) and the inherent properties of the separations (range of concentrations, thermal requirements, recyclability) that still need to be overcome. Developing an energetically viable and technically achievable new separation was the challenge undertaken in this thesis. Although improvements and optimizations are still required, the results demonstrated that HPSW and SA-HPSW might play an important role in producing value-added molecules from biomass.

This research developed HPSW as a new separation technique aimed at the recovery of hydrophilic organics from aqueous mixtures. The study presented here investigated the synergistic effect between SW and CXL. HPSW promoted separations of acetone, isopropanol, 1-propanol and ethyl lactate from water at pressures lower than CXL and using amines that could not previously be used in SW. The data obtained also demonstrated how HPSW expanded the range of ionogens that could be used in the separations, which is an improvement in terms of separation efficiency and reduction of toxicity since the ionogens tested presented lower toxicities than the ones previously explored in SW separations. The tertiary amines TMBDA, TMTAD and 3DMAP showed the best efficiencies among the amines tested. Furthermore, the ionogens were also recovered via reverse osmosis (RO) after promoting the separation, allowing them to be reused. The preliminary energy calculations performed for the HPSW separation demonstrated an actual
reduction in energy consumption, at least in terms of heat used, when comparing it to distillation. Optimizations are necessary to: (i) improve recovery efficiency, (ii) address the efficiency while performing RO to recover the ionogen from concentrated mixtures or mixtures containing small ionogens, and (iii) reduce the energy required in the steps following the HPSW separation. Nonetheless, the energy reductions observed indicate that HPSW might be a viable separation alternative for the recovery of hydrophilic organic products from aqueous mixtures obtained after biomass conversions.

There are still challenges when considering the recovery of very hydrophilic organics such as ethanol and diols, but SA-HPSW might be a starting point to solve this puzzle. SA-HPSW, a separation technique that uses extraction solvents miscible in water, promoted the separation of ethanol. Up to this point, this molecule could not be effectively recovered from aqueous phases using separations that rely on CO₂. When CXL was applied to ethanol, even at high CO₂ pressures (> 100 bar), only partial ethanol dilution occurred in the CO₂ gas phase. The aqueous phase still contained the majority of the ethanol initially added.¹⁰⁸ SA-HPSW was able to promote higher recoveries to a liquid phase, although the energy required to promote the purification of the ethanol obtained still needs to be addressed. Exploring new extraction solvent combinations (e.g. varying the boiling point) or using a different post-SA-HPSW purification method could address part of the issues observed. In addition, diols, which do not expand significantly with the addition of CO₂, could also be recovered using isopropanol as the extraction solvent. For these systems, the composition of the isopropanol-rich phase is still a hurdle that must be overcome. However, considering diols and other systems in which the volatility of the product might be low, reducing the amount of water that needs to be removed by using SA-HPSW can represent a considerable improvement in the energy requirements for the product recovery and purification. Therefore, SA-HPSW expands the range of aqueous product mixtures that can be treated by CO₂-assisted
separations, maximizing the impact that such separations might have not only in the biomass sector but also in other aqueous mixtures.

This thesis also expanded on the concept of using switchable solvents as reaction media and product recovery strategy. The preliminary results obtained with the Baylis-Hillman reaction were the first attempt to use the amines used in the HPSW as the reaction catalyst and as the trigger for product separation once CO$_2$ is introduced to the system. The reactions performed also corroborated previously reported literature demonstrating the positive effect that increases in the catalyst's basicity have on the extent of the conversion in Baylis-Hillman reactions. The data presented is still preliminary; the scope of substrates to which the system can convert and the possible reactions that could be catalyzed beyond Baylis-Hillman still need to be extensively investigated. Nonetheless, amines used for HPSW were proven to promote Baylis-Hillman catalysis, and the products were exclusively dissolved in the organic-rich phase after the addition of CO$_2$, indicating the feasibility of the process at least in the conditions tested.

5.2 Limitations and recommendations for this work

Throughout this work, it was demonstrated that HPSW and SA-HPSW could be further developed and considered for implementation in biomass conversions. The energy consumption for both techniques still needs to be improved, especially considering the processes taking place after the separation with CO$_2$ is achieved. The composition of the obtained phases is also an issue that needs to be addressed to improve the purification step. The efficiency of HPSW and SA-HPSW needs to be tested against aqueous product mixtures obtained after fermentation. Finally, the presence of the ionogens in these fermentation broths might also be considered to improve the separations' overall energy and material consumption. For the studies with real fermentation broths, the key challenges will potentially be the presence of by-products, interactions with microorganisms and enzymes, and recyclability of the fermentation media. There are many
milestones that HPSW and SA-HPSW need to achieve before being implemented in large-scale fermentations, but the knowledge gained with the findings described in this thesis will aid in the efforts being made by the student taking over this project.

As highlighted throughout this thesis, there are still many areas of improvement to be explored; in addition, there are fundamental concepts that still need to be explored. Although there is a good understanding of how the more conventional organic solvents (e.g. acetone, isopropanol, THF, dioxane, DMF) behave once CO\textsubscript{2} expansion takes place, the data available for diols and other liquids that would potentially be part of Class I in the CXL notation is limited. In addition, the direct correlation of the property changes with the increase of CO\textsubscript{2} mass\% dissolved in the organic liquid is well established. However, there is limited information as to why some organic liquids can dissolve larger amounts of CO\textsubscript{2} compared to others. Such behaviour might be associated with the expanding liquid's polarity, polarizability and H-bonding capabilities. As observed in the experiments with acetone and isopropanol, although the molecules present a very similar chemical structure and log P, their Kamlet-Taft parameters and cloud pressures (CP) differ substantially. As such, predictions of CP values could not be made using log P. The log P could only be used to identify systems that might not undergo phase separation via HPSW. For some systems, the intermolecular interactions might play a more significant role than for systems where these interactions are weaker. Kirkwood-Buff integrals (KBIs) could also help quantify the associations of the mixture's components with each other. Online tools are available, facilitating the application of KB theory to different mixtures. However, the extent to which these tools could be explored in high-pressure systems still needs to be determined. Therefore, having a better understanding of the behaviour of CO\textsubscript{2} in different organic liquids is an essential step toward increasing the application of CO\textsubscript{2}-assisted separations.
5.3 Additional opportunities for SW/biomass-based work

Considering the simplicity (in terms of components) of the systems investigated in this thesis compared to the complex nature of fermentation broths, a key aspect is to evaluate how HPSW and SA-HPSW would perform in real mixtures. As previously highlighted, products obtained after biomass conversion promoted by microorganisms impose challenges for developing alternative separation strategies. An ideal HPSW or SA-HPSW system would employ ionogens that could be added to the aqueous solution in which the biomass conversion occurs. On the one hand, the ionogens could aid conversions by behaving as a co-catalyst or even simply being the buffer for the fermentation media. In addition, the extra steps required to recover the ionogen, which can be challenging and energy-intensive, could be eliminated by reusing the aqueous phase. On the other hand, such an approach might not be adequate considering the negative impact that external molecules can have on biocatalysis viability and the challenges associated with reusing the reaction media in biocatalysis. Furthermore, issues arise from the possible toxicity of the ionogens to the microorganisms or the potential for the decomposition of the ionogens during biomass conversion. Therefore, investigating the behaviour of the ionogens in catalysis promoted by microorganisms (e.g. bacteria, yeast) or enzymes is an important avenue that needs to be explored. In addition, evaluating the impact of having the ionogen in the fermentation broth versus adding the ionogen after the fermentation also needs to be investigated.

The difference in the solubility of CO$_2$ in different organic solvents can also expand the applications of HPSW and SA-HPSW. This thesis only focused on systems where one product of interest was being recovered. Considering the complexity of fermentation broths and the presence of unreacted starting materials, being able to selectively remove one component of the mixture at a time can be quite valuable. There is a wide range of lower critical solution pressures (LCSP) observed for different organic solvents, one could envision taking advantage of that difference to selective separate an organic molecule to the detriment of the other molecules present in the
aqueous mixture. Using different pressures of CO$_2$ combined with different ionogens could allow for the selective separation of biomass products such as diols, furfural, glycerol and others from complex aqueous mixtures. Therefore, investigating if the CO$_2$ pressure and ionogen composition present a selective behaviour in multi-component aqueous mixtures would not only allow for a more valuable separation but also approximate the application of HPSW and SA-HPSW to more real mixtures.

5.4 Other future directions

Prediction power is an important requirement when considering the application of HPSW and SA-HPSW to a broader range of product mixtures. By having predictive power, the discovery of adequate combinations of CO$_2$ pressure, ionogen concentration and, if necessary, extraction solvent can be accelerated. In addition, by combining experimental data with prediction tools for thermodynamic properties, such as COnductor-like Screening MOdel for Real Solvents (COSMO-RS), which is a tool for solvent selection already being used for alkanediol-based deep eutectic solvents (DES),$^{164}$ the behaviour of the systems might be potentially predicted and adjustments can be made more easily. Considering the changes promoted by CO$_2$ expansion, data such as Kamlet-Taft solvatochromic parameters would need to be obtained for diols and other alcohols. By using such data, the chemical potentials predicted via COSMO-RS could potentially be more representative of the behaviour expected experimentally. In addition, the predictions would also need to account for the high pressures of CO$_2$ being used in the separations. Therefore, COSMO-RS and other prediction software could be powerful tools to promote the screening of extracting solvent-organic-water combinations that could potentially undergo phase separation using SA-HPSW. These prediction tools would save time and resources and help develop a library containing information about the expected behaviour of the combinations tested, guiding the selection of parameters for systems being tested for the first time.
In this thesis, an initial investigation of the energy differences between distillation, HPSW and SA-HPSW was performed; going beyond that is essential when considering the application of these separations in real mixtures. However, energy consumption associated with processes requiring heat is only one of the environmental parameters to identify if the new separations being proposed are effectively more environmentally benign than distillation. As previously discussed, the best approach to quantify the multiple parameters that differentiate the HPSW separation from distillation is life-cycle assessment (LCA). By doing so, other factors such as smog formation, toxicity, and resource depletion, among others, would also be considered. Furthermore, given the goal to explore HPSW and SA-HPSW to fermentation processes of industrial relevance, a techno-economic analysis (TEA) also needs to be performed. A TEA will evaluate the estimated capital cost, operating cost and savings if HPSW or SA-HPSW are to replace or aid in distillation or other separation techniques already in place. Determining possible energy savings, changes in environmental footprint and costs associated with HPSW and SA-HPSW is a fundamental step in applying these techniques to industrially relevant systems.

Although the discussions and systems evaluated in this thesis were focused on biomass conversions (primarily fermentation), HPSW and SA-HPSW are not limited to such systems. As demonstrated by the experiments performed in the Baylis-Hillman reaction, separations aided by CO₂ could be expanded to many scenarios where a hydrophilic organic needs to be recovered from an aqueous mixture, both as a product or as a contaminant. Although CO₂ was used as a trigger for this work, many developments are being made to use CO₂ as a feedstock in electrochemical conversions to value-added chemicals in aqueous media. Among the products obtained, methanol and ethanol are some of the desired molecules. The electrochemical systems are still being developed to promote high selectivity and conversion aiming at commercial application. Some companies, such as Air Company (in New York) and Twelve (in San Francisco), have received considerable investments to develop large-scale electrochemical conversion of CO₂.
Considering the early-stage nature of these technologies and companies, there is potential to implement and co-develop the CO₂ conversion and the separation of the products obtained. Collaborations with such start-up partners could represent an exciting way to add value to both technologies. Alternatively, certain organic molecules need to be removed from water due to their toxicity, low biodegradability or overall negative environmental impact. Among the contaminants of relevance are: (i) agriculture waste (e.g. pesticides, herbicides, fertilizers), (ii) textile waste (i.e. dyes), (iii) household waste (e.g. antibiotics and other medicines, personal care products, cleaning products), among many others. Forward Water, a spin-off company from the Jessop group, is currently taking advantage of the principles governing SW to promote forward osmosis aiming to purify contaminated waste streams. Clean and potable is a scarce asset in many countries and remote communities. As a result, finding alternatives to promote water purification is of urgent relevance. If HPSW or SA-HPSW could be modified to operate at lower pressures and still promote efficient removal of contaminants, they could potentially be considered in wastewater purification. Therefore, either by promoting the recovery of value-added chemicals or eliminating pollutants, developments made to HPSW and SA-HPSW could help fulfil the needs of people in diverse conditions.
References


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Appendix A

Additional data for Chapter 2

A1. Derivations of equations used on pH, % protonation and ionic strength calculations

A1.1. Monoamines

The derivations and equations for this scenario were previously published. The $[\text{H}_3\text{O}^+]$, % protonation and ionic strength equations obtained were:

$$[\text{H}_3\text{O}^+]^3 + [\text{H}_3\text{O}^+]^2(K_{\text{aH}} + [\text{B}]_0) - [\text{H}_3\text{O}^+](K_{\text{w}} + K_{*\text{a1}}K_{\text{H}P_{\text{CO}_2}}) - (K_{\text{aH}}K_{\text{w}} + K_{\text{aH}}K_{*\text{a1}}K_{\text{H}P_{\text{CO}_2}}) = 0 \quad (\text{Eq.1})$$

$$\% \text{ protonation} = \frac{[\text{H}_3\text{O}^+]}{[\text{H}_3\text{O}^+]+K_{\text{aH}}} \times 100\% \quad (\text{Eq.2})$$

$$I = 1/2 \sum_{i=1}^{n} c_i z_i^2 \quad (\text{Eq.3})$$

Where $K_{\text{aH}}$ corresponds to the dissociation constant for the protonated ionogen (conjugated acid of the amine), which can be obtained from published $pK_{\text{aH}}$; $K_{*\text{a1}}$ corresponds to the combined dissociation constant for dissolved $\text{CO}_2(aq)$ in the aqueous phase and the $\text{H}_2\text{CO}_3(aq)$ formed by reaction with water (for this thesis, the values were obtained from published data$^{93}$ but Cai’s equation for $\text{CO}_2$ in freshwater can be used to calculate values)$^{166}$; $K_{\text{w}}$ is the dissociation constant of water in pure water; $K_{\text{H}}$ is Henry’s law constant for $\text{CO}_2$ (also obtained from published data$^{93}$; $[\text{B}]_0$ is the initial ionogen concentration in moles of ionogen added per litre of water; $P_{\text{CO}_2}$ is the CO$_2$ pressure added; $c$ is the concentration for individual ionic species, and $z$ is the charge of each ionic species.

$$K_{\text{aH}} = [\text{B}]_{\text{aq}}[\text{H}_3\text{O}^+]_{\text{aq}} / [\text{BH}^+]_{\text{aq}} \quad (\text{Eq.4})$$

$$K_{*\text{a1}} = [\text{H}_3\text{O}^+]_{\text{aq}}[\text{HCO}_3^-]_{\text{aq}}/([\text{H}_2\text{CO}_3]+[\text{CO}_2(aq)]) \quad (\text{Eq.5})$$

$$K_{\text{w}} = [\text{H}_3\text{O}^+][\text{OH}^-] \quad (\text{Eq.6})$$

$$K_{\text{H}} = ([\text{H}_2\text{CO}_3]+[\text{CO}_2(aq)])/P_{\text{CO}_2} \quad (\text{Eq.7})$$

It should be noted that the values utilised for each constant were interpolated from the literature data for the specific temperature in which the separations were performed (i.e. $pK_{\text{aH}}$...
values) and/or were obtained for pure solutions containing just the species to which the constant refers to. The \([H_3O^+]\) and \% protonation were obtained exclusively from calculations and are therefore considered to be only approximations.

**A1.2. Diamines**

\[
[H_3O^+]^4 + [H_3O^+]^3 (2[B]_0 + K_{ah2}) + [H_3O^+]^2 (K_{ah1}K_{ah2} + [B]_0 K_{ah2} - K_w - K_{a1}K_{H2}P_{CO2})
- [H_3O^+](K_{a1}K_{H2} + K_{a1}K_{H2}P_{CO2}K_{ah2}) - (K_{a1}K_{H2}P_{CO2}K_{H2}K_{ah2} + K_{W}K_{ah1}K_{ah2}) = 0 \text{ (Eq.8)}
\]

\[
% \text{ protonation } BH^+ = \frac{([BH^+] + [BH^2+] - [B]_{aq})}{[B]_0} \times 100 \text{ (Eq. 9)}
\]

\[
% \text{ protonation } BH^2^{2+} = \frac{[BH^2^{2+}]}{[B]_0} \times 100 \text{ (Eq. 10)}
\]

Where \([B]_{aq}\) is the concentration of unprotonated ionogen species dissolved in the aqueous solution.

Derivation for Eq.8:

\[K_w = [H_3O^+][OH^-] \text{ (Eq.11)}\]

\[K_{a1} = [H_3O^+]_{aq} \frac{[HCO_3^-]_{aq} ([H_2CO_3] + [CO_2(aq)])}{[H_2CO_3] + [CO_2(aq)]} \text{ (Eq.12)}\]

\[K_{H} = ([H_2CO_3] + [CO_2(aq)])/P_{CO2} \text{ (Eq.13)}\]

\[[HCO_3^-] = K_{a1}K_{H}P_{CO2}/[H_3O^+] \text{ (Eq.14)}\]

\[K_{ah} = [B]_{aq}[H_3O^+]/[BH^+] \text{ (Eq.15)}\]

\[[B]_{aq} = K_{ah}[BH^+]/[H_3O^+] \text{ (Eq.16)}\]

\[K_{ah2} = [BH^+][H_3O^+] / [BH^2^{2+}] \text{ (Eq.17)}\]

\[[BH^2^{2+}] = [BH^+][H_3O^+] / K_{ah2} \text{ (Eq.18)}\]

Charge balance: \([HCO_3^-] + [OH^-] = [H_3O^+] + [BH^+] + 2[BH^2^{2+}] \text{ (Eq.19)}\)

Mass balance: \([B]_0 = [B]_{aq} + [BH^+] + [BH^2^{2+}] \text{ (Eq.20)}\)

Applying equations 16 and 18 to equation 20.

\[[B]_0 = K_{ah}[BH^+]/[H_3O^+] + [BH^+] + [BH^2^{2+}] / K_{ah2} \text{ (Eq.21)}\]
Multiply both sides by \([\text{H}_3\text{O}^+]\)

\[[\text{B}]_0[\text{H}_3\text{O}^+] = \text{K}_\text{alt}[\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+] + [\text{BH}^+][\text{H}_3\text{O}^+]^2/\text{K}_\text{alt2} \text{ (Eq.22)}\]

Multiply both sides by \(\text{K}_\text{alt2}\)

\[[\text{B}]_0[\text{H}_3\text{O}^+][\text{K}_\text{alt2}] = \text{K}_\text{alt}[\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+]\text{K}_\text{alt2} + [\text{BH}^+][\text{H}_3\text{O}^+]^2 \text{ (Eq.23)}\]

Isolate for \([\text{BH}^+]\)

\[[\text{BH}^+] = \frac{[B]_0[\text{H}_3\text{O}^+]\text{K}_\text{alt2}}{\text{K}_\text{alt}[\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+][\text{K}_\text{alt2}] + [\text{BH}^+][\text{H}_3\text{O}^+]^2} \text{ (Eq.24)}\]

To simplify, consider \(\text{A} = \text{K}_\text{alt}[\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+][\text{K}_\text{alt2}] + [\text{BH}^+][\text{H}_3\text{O}^+]^2\)

Applying equations 11, 14, 18, 19 and 24 to equation 19

\(\text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2}/[\text{H}_3\text{O}^+] + \text{K}_\text{W}/[\text{H}_3\text{O}^+] = [\text{H}_3\text{O}^+] + [\text{B}]_0[\text{H}_3\text{O}^+]\text{K}_\text{alt2}/\text{A} + 2[\text{BH}^+][\text{H}_3\text{O}^+]\text{K}_\text{alt2} \text{ (Eq.25)}\)

Applying equation 24 to equation 25

\(\text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2}/[\text{H}_3\text{O}^+] + \text{K}_\text{W}/[\text{H}_3\text{O}^+] = [\text{H}_3\text{O}^+] + [\text{B}]_0[\text{H}_3\text{O}^+]\text{K}_\text{alt2}/\text{A} + 2[\text{B}]_0[\text{H}_3\text{O}^+]^2/\text{A} \text{ (Eq.26)}\)

Multiply both sides by \([\text{H}_3\text{O}^+]\)

\(\text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2} + \text{K}_\text{W}] = [\text{H}_3\text{O}^+] + [\text{B}]_0[\text{H}_3\text{O}^+]\text{K}_\text{alt2}/\text{A} + 2[\text{B}]_0[\text{H}_3\text{O}^+]^2/\text{A} \text{ (Eq.27)}\)

Multiply both sides by \(\text{A}\)

\(\text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2}\text{A} + \text{K}_\text{W}\text{A} = [\text{H}_3\text{O}^+]^2/\text{A} + [\text{B}]_0[\text{H}_3\text{O}^+]^2\text{K}_\text{alt2} + 2[\text{B}]_0[\text{H}_3\text{O}^+]^3 \text{ (Eq.28)}\)

Replacing \(\text{A}\) on equation 28.

\(\text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2}\text{K}_\text{alt}\text{K}_\text{alt2} + \text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2}\text{K}_\text{alt2}[\text{H}_3\text{O}^+] + \text{K}_\text{alt}[\text{K}_\text{H} \text{P}_{\text{CO}_2}[\text{H}_3\text{O}^+]^2 + \text{K}_\text{W}\text{K}_\text{alt}\text{K}_\text{alt2} + \text{K}_\text{W}\text{K}_\text{alt2}[\text{H}_3\text{O}^+] + \text{K}_\text{W}[\text{H}_3\text{O}^+]^2 = [\text{H}_3\text{O}^+]^2\text{K}_\text{alt}\text{K}_\text{alt2} + [\text{H}_3\text{O}^+]^3\text{K}_\text{alt2} + [\text{H}_3\text{O}^+]^4 + [\text{B}]_0[\text{H}_3\text{O}^+]^2\text{K}_\text{alt2} + 2[\text{B}]_0[\text{H}_3\text{O}^+]^3 \text{ (Eq.29)}\)
Rearranging equation 29, I obtain Eq. 8

\[ [\text{H}_3\text{O}^+]^4 + [\text{H}_3\text{O}^+]^3(2[B]_0 + K_{\text{aH}2}) + [\text{H}_3\text{O}^+]^2(K_{\text{aH}3}K_{\text{aH}2} + [B]_0K_{\text{aH}2} - K_w - K_{\text{a1}}K_{\text{H}2}) \]

\[ - [\text{H}_3\text{O}^+](K_wK_{\text{aH}2} + K_{\text{a1}}K_{\text{H}2}K_{\text{aH}3} + K_{\text{aH}}K_{\text{H}2}K_{\text{aH}2}) = 0 \]

A1.3. Polyamines (3 plus protonatable sites)

For polyamines, BH\(^+\), BH\(_2\)\(^2+\) and BH\(_3\)\(^3+\) need to be considered. I did not account for BH\(_4\)\(^4+\) species because their pK\(_{\text{aH}4}\) is too low to allow for protonations even at the pressures in which the experiments were performed. As a result, the following [H\(_3\)O\(^+\)] and % protonation equations are applied.

\[ [\text{H}_3\text{O}^+]^5 + [\text{H}_3\text{O}^+]^4(K_{\text{aH}} + 2[B]_0) + [\text{H}_3\text{O}^+]^3(K_{\text{aH}2}K_{\text{aH}3} + 2[B]_0K_{\text{aH}3} - K_w - K_{\text{a1}}K_{\text{H}2}K_{\text{aH}2} + K_{\text{aH}} + K_{\text{aH}2}K_{\text{aH}3} - K_{\text{a1}}K_{\text{H}2}K_{\text{aH}3} - K_{\text{a1}}K_{\text{H}2}K_{\text{aH}2}K_{\text{aH}3}) \]

\[ - [\text{H}_3\text{O}^+](K_wK_{\text{aH}2}K_{\text{aH}3} + K_{\text{a1}}K_{\text{H}2}K_{\text{aH}2}K_{\text{aH}3} + K_{\text{aH}}K_{\text{H}2}K_{\text{aH}2}K_{\text{aH}3}) = 0 \text{ (Eq. 30)} \]

% protonation \(BH^+\) = \(\frac{([BH^+] + [BH^2_2^+])}{[B]_0} \times 100\) \text{ (Eq. 31)}

% protonation \(BH^2_2^+\) = \(\frac{([BH^2_2^+] + [BH^3_3^+])}{[B]_0} \times 100\) \text{ (Eq. 32)}

% protonation \(BH^3_3^+\) = \(\frac{[BH^3_3^+]}{[B]_0} \times 100\) \text{ (Eq. 33)}

Where \([B]_{\text{aq}}\) is the concentration of unprotonated ionogen species dissolved in the aqueous solution.

Derivation for Eq.30

\(K_w = [\text{H}_3\text{O}^+][\text{OH}^-]\) \text{ (Eq. 34)}

\(K_{\text{a1}} = [\text{H}_3\text{O}^+]_{\text{aq}} [\text{HCO}_3^-]_{\text{aq}}/([\text{H}_2\text{CO}_3] + [\text{CO}_2(aq)])\) \text{ (Eq. 35)}

\(K_{\text{H}} = ([\text{H}_2\text{CO}_3] + [\text{CO}_2(aq)]) / P_{\text{CO}_2}\) \text{ (Eq. 36)}

\([\text{HCO}_3^-] = K_{\text{a1}}K_{\text{H}}P_{\text{CO}_2}/[\text{H}_3\text{O}^+]\) \text{ (Eq. 37)}
\[
K_{\text{af}} = [\text{B}]_0/[\text{H}_3\text{O}^+]/[\text{BH}^+] \quad (\text{Eq. 38})
\]
\[
[\text{B}]_0 = K_{\text{af}}[\text{BH}^+]/[\text{H}_3\text{O}^+] \quad (\text{Eq. 39})
\]
\[
K_{\text{ah}_2} = [\text{BH}^+][\text{H}_3\text{O}^+]/[\text{BH}_2^{2+}] \quad (\text{Eq. 40})
\]
\[
[\text{BH}_2^{2+}] = [\text{BH}^+][\text{H}_3\text{O}^+]/K_{\text{ah}_2} \quad (\text{Eq. 41})
\]
\[
K_{\text{ah}_3} = [\text{BH}_2^{2+}][\text{H}_3\text{O}^+]/[\text{BH}_3^{3+}] \quad (\text{Eq. 42})
\]
\[
[\text{BH}_3^{3+}] = [\text{BH}_2^{2+}][\text{H}_3\text{O}^+]/K_{\text{ah}_3} \quad (\text{Eq. 43})
\]
\[
[\text{BH}_3^{3+}] = [\text{BH}^+][\text{H}_3\text{O}^+]^2/K_{\text{ah}_2} K_{\text{ah}_3} \quad (\text{Eq. 44})
\]

Charge balance: \([\text{HCO}_3^-] + [\text{OH}^-] = [\text{H}_3\text{O}^+] + [\text{BH}^+] + 2[\text{BH}_2^{2+}] + 3[\text{BH}_3^{3+}] \quad (\text{Eq. 45})
\]

Mass balance: \([\text{B}]_0 = [\text{B}] + [\text{BH}^+] + [\text{BH}_2^{2+}] + [\text{BH}_3^{3+}] \quad (\text{Eq. 46})
\]

Applying equations 39, 41 and 44 on equation equation 46
\[
[B]_0 = K_{\text{af}}[\text{BH}^+]/[\text{H}_3\text{O}^+] + [\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+]/K_{\text{ah}_2} + [\text{BH}^+][\text{H}_3\text{O}^+]^2/K_{\text{ah}_2} K_{\text{ah}_3} \quad (\text{Eq. 47})
\]

Multiply both sides by \([\text{H}_3\text{O}^+]\)
\[
[B]_0[\text{H}_3\text{O}^+] = K_{\text{ah}}[\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+] + [\text{BH}^+][\text{H}_3\text{O}^+]^2/K_{\text{ah}_2} + [\text{BH}^+][\text{H}_3\text{O}^+]^3/K_{\text{ah}_2} K_{\text{ah}_3}
\]

(Eq. 48)

Multiply both sides by \((K_{\text{ah}_2} K_{\text{ah}_3})\)
\[
[B]_0[\text{H}_3\text{O}^+]K_{\text{ah}_2} K_{\text{ah}_3} = K_{\text{ah}}K_{\text{ah}_2}K_{\text{ah}_3}[\text{BH}^+] + [\text{BH}^+][\text{H}_3\text{O}^+]K_{\text{ah}_2} K_{\text{ah}_3} + [\text{BH}^+][\text{H}_3\text{O}^+]^2 K_{\text{ah}_3}
\]

+ [\text{BH}^+][\text{H}_3\text{O}^+]^3 \quad (\text{Eq. 49})

Isolate for \([\text{BH}^+]\)
\[
[\text{BH}^+] = \frac{[B]_0[\text{H}_3\text{O}^+] K_{\text{ah}_2} K_{\text{ah}_3}}{(K_{\text{ah}} K_{\text{ah}_2} K_{\text{ah}_3} + K_{\text{ah}_2} K_{\text{ah}_3} [H_3O^+] + K_{\text{ah}_3} [H_3O^+]^2 + [H_3O^+]^3)}
\]

(Eq. 50)

To simplify, consider \(A = (K_{\text{ah}} K_{\text{ah}_2} K_{\text{ah}_3} + K_{\text{ah}_2} K_{\text{ah}_3} [H_3O^+] + K_{\text{ah}_3} [H_3O^+]^2 + [H_3O^+]^3)\)
Applying equations 34, 37, 41, 44 and 50 to equation 45

\[ K^*_{a1} K_{H} P_{CO2}/[H_3O^+] + K_w/[H_3O^+] = [H_3O^+] + [B]_0[H_3O^+]K_{aH2}K_{aH3}/A + 2[BH^+][H_3O^+]K_{aH2} + 3[BH^+][H_3O^+]^2/K_{aH2}K_{aH3} \text{(Eq.51)} \]

Applying equation 50 on equation 51

\[ K^*_{a1} K_{H} P_{CO2}/[H_3O^+] + K_w/[H_3O^+] = [H_3O^+] + [B]_0[H_3O^+]K_{aH2}K_{aH3}/A + 2[B]_0[H_3O^+]^2K_{aH3}/A + 3[B]_0[H_3O^+]^3/A \text{(Eq.52)} \]

Multiply both sides by \([H_3O^+]\)

\[ K^*_{a1} K_{H} P_{CO2} + K_w = [H_3O^+]^2 + [B]_0[H_3O^+]^2K_{aH2}K_{aH3}/A + 2[B]_0[H_3O^+]^3K_{aH3}/A + 3[B]_0[H_3O^+]^4/A \text{(Eq.53)} \]

Multiply both sides by \(A\)

\[ K^*_{a1} K_{H} P_{CO2}A + K_wA = [H_3O^+]^2A + [B]_0[H_3O^+]^2K_{aH2}K_{aH3} + 2[B]_0[H_3O^+]^3K_{aH3} + 3[B]_0[H_3O^+]^4 \text{(Eq.54)} \]

Replacing \(A\) in equation 54

\( (K^*_{a1} K_{H} P_{CO2})(K_{aH}K_{aH2}K_{aH3}) + (K^*_{a1} K_{H} P_{CO2})(K_{aH2}K_{aH3}[H_3O^+]) + (K^*_{a1} K_{H} P_{CO2})(K_{aH3}[H_3O^+]^2) + (K^*_{a1} K_{H} P_{CO2})[H_3O^+]^2K_{aH2}K_{aH3} + K_wK_{aH2}K_{aH3} + K_wK_{aH2}K_{aH3}[H_3O^+] + K_wK_{aH3}[H_3O^+]^2 + K_w[H_3O^+]^3 = [H_3O^+]^2(K_{aH}K_{aH2}K_{aH3}) + [H_3O^+]^3(K_{aH2}K_{aH3}) + [H_3O^+]^4(K_{aH3}) + [H_3O^+]^5 + [B]_0[H_3O^+]^2K_{aH2}K_{aH3} + 2[B]_0[H_3O^+]^3K_{aH3} + 3[B]_0[H_3O^+]^4 \text{(Eq.55)} \)

Rearranging equation 55, obtaining Eq.30

\( [H_3O^+]^5 + [H_3O^+]^4(K_{aH3} + 2[B]_0) + [H_3O^+]^3(K_{aH2}K_{aH3} + 2[B]_0K_{aH3} - K_{aH}K_{aH2}P_{CO2}) + [H_3O^+]^2(K_{aH}K_{aH2}K_{aH3} + [B]_0K_{aH2}K_{aH3} - K_wK_{aH3} - K^*_{a1} K_{H} P_{CO2}K_{aH3}) - [H_3O^+]^2(K_{aH}K_{aH2}K_{aH3} + [B]_0K_{aH2}K_{aH3} - K_wK_{aH3} - K^*_{a1} K_{H} P_{CO2}K_{aH3} - K^*_{a1} K_{H} P_{CO2}K_{aH2}K_{aH3}) - (K^*_{a1} K_{H} P_{CO2}K_{aH}K_{aH2}K_{aH3} + K_wK_{aH2}K_{aH3}) = 0 \)
### Additional data for the evaluation of ionogen efficiency

The data obtained from applying the equations previously presented is displayed in Table A2.1. The table also compares the cloud pressure (CP) for each ionogen and presents the pK$_{aH}$ values utilised in the calculations.

**Table A2.1.** The CP (absolute pressure at 40 ºC) of several tertiary amines for acetone:water (50:50 molar ratio), the % protonation and the ionic strength obtained in the presence of CO$_2$. The superscript numbers beside each amine acronym correspond to the references from which the values of pK$_{aH}$ were obtained.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amine</th>
<th>Amine concentration /molar</th>
<th>CP/ bar</th>
<th>pK$_{aH}$</th>
<th>% protonation</th>
<th>Ionic strength/ molar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No ionogen</td>
<td>n.a.</td>
<td>26.5 ± 0.3</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
</tbody>
</table>
| 2     | TMEDA$^{167}$ | 0.156 ± 0.001           | 16.3 ± 0.9 | pK$_{aH1}$ = 9.1  
|       |       |                           |         | pK$_{aH2}$ = 5.9  
|       |       |                           |         | BH$^+$ = 99.9%  
|       |       |                           |         | BH$_2^{2+}$ = 41.7%  
|       |       |                           |         | 0.29 |
| 3     | TMPDA$^{168}$ | 0.156 ± 0.001          | 6.7 ± 0.5 | pK$_{aH1}$ = 9.8  
|       |       |                           |         | pK$_{aH2}$ = 7.7  
|       |       |                           |         | BH$^+$ = 100%  
|       |       |                           |         | BH$_2^{2+}$ = 93.2%  
|       |       |                           |         | 0.45 |
| 4     | TMBDA$^{169}$ | 0.156 ± 0.001         | 2.5 ± 0.2 | pK$_{aH1}$ = 10.3  
|       |       |                           |         | pK$_{aH2}$ = 8.8  
|       |       |                           |         | BH$^+$ = 100%  
|       |       |                           |         | BH$_2^{2+}$ = 98.3%  
|       |       |                           |         | 0.46 |
| 5     | PMDETA$^{168}$ | 0.104 ± 0.001        | 6.3 ± 0.4 | pK$_{aH1}$ = 9.4  
|       |       |                           |         | pK$_{aH2}$ = 8.4  
|       |       |                           |         | pK$_{aH3}$ = 2.4  
|       |       |                           |         | BH$^+$ = 100%  
|       |       |                           |         | BH$_2^{2+}$ = 98.9%  
|       |       |                           |         | BH$_3^{3+}$ = 0%  
|       |       |                           |         | 0.31 |
| 6     | TMTAD$^{168}$ | 0.104 ± 0.001        | 3.3 ± 0.4 | pK$_{aH1}$ = 10.0  
|       |       |                           |         | pK$_{aH2}$ = 9.0  
|       |       |                           |         | pK$_{aH3}$ = 6.4  
|       |       |                           |         | BH$^+$ = 100%  
|       |       |                           |         | BH$_2^{2+}$ = 99.7%  
|       |       |                           |         | BH$_3^{3+}$ = 32.7%  
<p>|       |       |                           |         | 0.41 |</p>
<table>
<thead>
<tr>
<th></th>
<th>Ionogen</th>
<th>pK&lt;sub&gt;aH1&lt;/sub&gt;</th>
<th>pK&lt;sub&gt;aH2&lt;/sub&gt;</th>
<th>pK&lt;sub&gt;aH3&lt;/sub&gt;</th>
<th>pK&lt;sub&gt;aH4&lt;/sub&gt;</th>
<th>BH&lt;sup&gt;+&lt;/sup&gt;</th>
<th>BH&lt;sup&gt;2+&lt;/sup&gt;</th>
<th>BH&lt;sup&gt;3+&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>HMTETA&lt;sub&gt;8&lt;/sub&gt;</td>
<td>7.9 ± 0.8</td>
<td>8.2</td>
<td>4.8</td>
<td>&lt; 2</td>
<td>100%</td>
<td>99.0%</td>
<td>3.7%</td>
</tr>
<tr>
<td>8</td>
<td>TEA&lt;sup&gt;93&lt;/sup&gt;</td>
<td>12.7 ± 0.3</td>
<td>7.6</td>
<td></td>
<td></td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>MDEA&lt;sup&gt;170&lt;/sup&gt;</td>
<td>6.2 ± 0.3</td>
<td>8.5</td>
<td></td>
<td></td>
<td>98.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>DMEA&lt;sup&gt;93&lt;/sup&gt;</td>
<td>4.9 ± 0.4</td>
<td>9.2</td>
<td></td>
<td></td>
<td>99.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>EDEA&lt;sup&gt;171&lt;/sup&gt;</td>
<td>5.1 ± 0.3</td>
<td>8.8</td>
<td></td>
<td></td>
<td>99.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>DEAE&lt;sup&gt;172&lt;/sup&gt;</td>
<td>8.9 ± 0.9</td>
<td>9.8</td>
<td></td>
<td></td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>3DMAP&lt;sup&gt;173&lt;/sup&gt;</td>
<td>3.1 ± 0.3</td>
<td>9.5</td>
<td></td>
<td></td>
<td>99.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>THEED&lt;sup&gt;174&lt;/sup&gt;</td>
<td>5.7 ± 0.1</td>
<td>8.4</td>
<td>4.3</td>
<td></td>
<td>98.2%</td>
<td>0.9%</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Imidazole&lt;sup&gt;175&lt;/sup&gt;</td>
<td>28.6 ± 0.3</td>
<td>6.9</td>
<td></td>
<td></td>
<td>91.9%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As mentioned in Chapter 3, all ionogens were submitted to a fixed pressure of 20 bar in a sight gauge and samples of the water-rich phase were obtained and analysed on a GC-FID. The amount of acetone remaining in the water-rich phase was calculated with the help of a calibration curve. The samples were initially prepared with approximately 10 g of acetone and 10 g of water (50:50 mass ratio). Table A2.2 presents the % protonation, the ionic strength at 20 bar, and the acetone mass remaining in the water-rich phase. The same equations were applied here to obtain the % protonation and the ionic strength.
Table A2.2 The amount of acetone remaining on the water-rich phase after phase separation at 20 bar (data obtained using the volume of phase and GC-FID composition). Additionally, the % protonation for each site of the ionogens and the ionic strength were estimated using mathematical calculations.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amine</th>
<th>Amine concentration/ molar</th>
<th>% protonation</th>
<th>Ionic strength/ molar</th>
<th>Mass of acetone left in aqueous phase/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TMEDA</td>
<td>0.351</td>
<td>BH$^+$ = 99.8% BH$_2^{2+}$ = 29.9%</td>
<td>0.56</td>
<td>5.66</td>
</tr>
<tr>
<td>2</td>
<td>TMPDA</td>
<td>0.352</td>
<td>BH$^+$ = 100% BH$_2^{2+}$ = 94.8%</td>
<td>1.02</td>
<td>4.51</td>
</tr>
<tr>
<td>3</td>
<td>TMBDA</td>
<td>0.354</td>
<td>BH$^+$ = 100% BH$_2^{2+}$ = 99.5%</td>
<td>1.06</td>
<td>3.19</td>
</tr>
<tr>
<td>4</td>
<td>PMDETA</td>
<td>0.234</td>
<td>BH$^+$ = 100% BH$_2^{2+}$ = 99.3% BH$_3^{3+}$ = 0%</td>
<td>0.70</td>
<td>5.22</td>
</tr>
<tr>
<td>5</td>
<td>TMTAD</td>
<td>0.233</td>
<td>BH$^+$ = 100% BH$_2^{2+}$ = 99.9% BH$_3^{3+}$ = 58.0%</td>
<td>1.10</td>
<td>3.50</td>
</tr>
<tr>
<td>6</td>
<td>HMTETA</td>
<td>0.176</td>
<td>BH$^+$ = 100% BH$_2^{2+}$ = 99.2% BH$_3^{3+}$ = 4.3%</td>
<td>0.55</td>
<td>5.68</td>
</tr>
<tr>
<td>7</td>
<td>TEA</td>
<td>0.704</td>
<td>BH$^+$ = 93.8%</td>
<td>0.66</td>
<td>4.22</td>
</tr>
<tr>
<td>8</td>
<td>MDEA</td>
<td>0.704</td>
<td>BH$^+$ = 99.2%</td>
<td>0.70</td>
<td>4.34</td>
</tr>
<tr>
<td>9</td>
<td>DMEA</td>
<td>0.704</td>
<td>BH$^+$ = 99.8%</td>
<td>0.70</td>
<td>4.32</td>
</tr>
<tr>
<td>10</td>
<td>EDEA</td>
<td>0.703</td>
<td>BH$^+$ = 99.5%</td>
<td>0.70</td>
<td>4.10</td>
</tr>
<tr>
<td>11</td>
<td>DEAE</td>
<td>0.706</td>
<td>BH$^+$ = 100%</td>
<td>0.71</td>
<td>4.74</td>
</tr>
</tbody>
</table>
A3. Additional plots of data obtained for ionogens

Kirkwood-Buff calculations were used in an earlier paper to explain why SW works. According to this theory, the solubility of the solute, in this case, acetone in SW, is strongly affected by the solute-ionogen intermolecular interaction. When CO$_2$ is absent, the solute-ionogen interaction is attractive, raising the solubility of the organic solute. However, when CO$_2$ is present and the ionogen becomes cationic, the solute-ionogen interaction becomes repulsive, significantly lowering the solubility of the solute.

While Kirkwood Buff calculations helped us understand why SW works, such calculations require too many measurements to be used as a general method for predicting the performance of yet-untested ionogens, so more easily calculated properties were used instead. For example, the ionic strength can be predicted using equations presented in section S1. A plot of the ionic strength of the ionogens versus the CP can be seen in Figure A3.1. Unfortunately, no clear correlation can be observed.
Figure A3.1 Comparison of the CP for the separation of acetone from acetone:water (50:50 mole ratio) solutions utilising tertiary diamines (TMBDA, TMPDA, TMEDA and THEED), tertiary polyamines (PMDETA, TMTAD and HMTETA), tertiary alkanolamines (TEA, MDEA, DMEA, EDEA, DEAE, 3DMAP and THEED) and imidazole as ionogens at 40 °C. The ionic strength (obtained using equations shown in Section A1) of the solutions at CP was used to compare the amines.
The pK_{aH1} and the partition coefficient (log P) obtained using the ALOGPS 2.1 tool were also compared graphically to the CP value (Figure A3.2). The amines with a green data point are the most efficient ones, while the red dots represent the amines with the lowest performances in terms of CP. No trend is apparent.
Figure A3.2 Partitioning coefficient (log P) vs pKₐ for ionogens tested. The data was arranged based on the CP obtained. ● Corresponds to CP below 3 bar, ■ corresponds to CP in between 3 and 5 bar; ◀ corresponds to CP in between 5 and 8 bar; ○ corresponds to CP in between 8 and 10 bar, and ● corresponds to CP above 10 bar.
An additional plot compares the pK_{a,H} and log P for the ionogens to the amount of acetone left in the aqueous phase after separations at 20 bar (Fig A3.3). The amount of acetone was obtained based on the water-rich phase volume and the GC-FID composition for acetone. The amines with a green data point are the most efficient ones, while the red dots represent the amines with the lowest performances in terms of acetone left in the water-rich phase after phase separation.
Figure A3.3 Partitioning coefficient (log P) vs pKₐH₁ (at 25 ºC) for ionogens tested. The data was arranged based on the amount of acetone left on the water-rich phase after phase separations at 20 bar of CO₂.

- ● corresponds toacetone mass below 4 g;
- ○ corresponds to acetone mass in between 4 and 4.5 g;
- ♦ corresponds to acetone mass in between 4.5 and 5 g, and
- ● corresponds to acetone mass above 5 g.
Similar to the plot obtained for the CP, no correlation was observed between the amines log P and the separation efficiency. However, the classification for some of the ionogens changed. Some cases worth noting are TEA which had a better performance at high pressures when considering its classification for the amount of acetone left compared to the CP. On the other hand, ionogens such as 3DMAP and DMAE did not improve with pressure increases. These are unoptimised results, so further analysis needs to be performed to see if there are ways to guarantee higher performances at higher pressures.

A4. Calibration curves obtained using the GC-FID traces and examples of GC-FID data for the phases obtained at 50 bar of CO$_2$ and the RO samples

In order to evaluate the composition of the water-rich phase for TMBDA or TMTAD systems after separation at 50 bar of CO$_2$, GC-FID traces were collected. For the acetone remaining in the water-rich phase, the peak area was compared to the calibration curve presented in Figure A4.1.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{calibration_curve.png}
\caption{Calibration curve obtained for acetone:water solutions with varying concentration. The samples were analysed on a GC-FID, and the data presented is based on multiple replicates.}
\end{figure}

\begin{equation}
y = 81716x + 317539 \\
R^2 = 0.9981
\end{equation}
In order to quantify the amount of TMBDA dissolved in the acetone-rich phase and the amount of TMBDA being lost during the RO separation, a calibration curve using acetonitrile as IS was prepared (Figure A4.2). The peak ratio between IS:TMBDA (based on the area under the peaks) was used to determine the mass ratio of these two components, and via calculations using the mass of the solution used to prepare the samples, the mass of TMBDA was determined, both in the sample and in the system.

![ Calibration curve using acetonitrile as IS and varying mass of TMBDA.](image)

Figure A4.2 Calibration curve using a fixed mass of acetonitrile as IS and varying mass of TMBDA, dissolved in acetone:water solutions.

Similar to TMBDA, a separate curve was obtained for the IS:TMTAD ratio based on GC-FID traces. Acetonitrile was also used as IS (Figure A4.3).
Figure A4.3 Calibration curve using a fixed mass of acetonitrile as IS and varying mass of TMTAD, dissolved in acetone:water solutions.

The same procedure described previously was used to obtain a calibration curve for 3DMAP (Figure A4.4).

Figure A4.4 Calibration curve using a fixed mass of acetonitrile as IS and varying mass of 3DMAP, dissolved in acetone:water solutions.
Regarding the amine remaining in the acetone-rich phase, the ratio between the internal standard (IS) and the amine peak (based on the area under each peak) was used and compared to the calibration curve shown in Figure A4.1. A GC-FID trace for the acetone-rich phase is presented in Figure A4.5. This is just an example; the final composition was obtained using the average of multiple GC-FID replicates for the same sample.
Figure A4.5 Example GC-FID trace obtained for a sample of the acetone-rich phase obtained after separation at 50 bar of CO₂ with a mixture containing TMBDA (0.80 molal). The IS peak appears at 3.32 min, the acetone peak appears at 3.47 min, and the TMBDA peak appears at around 7.02 min.
Similar to TMBDA, the phase composition for the acetone-rich phase was determined after separations using TMTAD, a polyamine that demonstrated great efficiency for phase separation were obtained. The GC-FID trace for the acetone-rich phase can be seen in Figure A4.6.

**Figure A4.6** Example GC-FID trace obtained for the acetone-rich phase obtained after separation at 50 bar of CO2 with a mixture containing TMTAD (0.53 molal). The IS peak appears at 3.17 min, the acetone peak appears at 3.31 min, and the TMTAD appears at 8.67 min.
The phase composition was also obtained after separations using 3DMAP, an alkanolamine system. Figure A4.7 presents an example of the GC-FID trace obtained for the acetone-rich phase.

**Figure A4.7** Example GC-FID trace obtained for the acetone-rich phase obtained after separation at 50 bar of CO₂ with a mixture containing 3DMAP (1.60 molal). The IS peak appears at 3.16 min, the acetone peak appears at 3.34 min, and the 3DMAP appears at 6.18 min.
Reverse osmosis (RO) was used as a way to recover the ionogens from solution simulating the water-rich phase obtained after separation with CO\textsubscript{2} at 20 bar. GC-FID was used to analyse the solution being added to the RO cell (70 bar of N\textsubscript{2} was used in the separations), the retentate and the solution being expelled from the cell. The IS:ionogen ratio was used as an indication of the quality of the separations for three ionogens, TMBDA, TMTAD and 3DMAP. Figure A4.8 presents an example of a GC-FID trace obtained for the mixture expelled from the RO cell for the TMBDA system.
Figure A4.8 Example GC-FID traces obtained for the solution being expelled from the RO cell for the TMBDA system. The IS peak appears at 3.17 min, the acetone peak appears at 3.33 min, and the TMBDA peak appears at 6.95 min.
A solution simulating the water-rich phase for the TMTAD system was also prepared and submitted to RO. One of the GC-FID traces obtained for the mixture being expelled from the RO cell can be seen in Figure A4.9.

**Figure A4.9** Example GC-FID traces obtained for the solution being expelled from the RO cell for the TMTAD system. The IS peak appears at 3.11 min, the acetone peak appears at 3.29 min, and the TMTAD peak appears at 8.67 min.
Attempts to recover 3DMAP were also made with RO. Figure A4.10 presents an example of a GC-FID trace obtained for the solution coming out of the RO cell.

**Figure A4.10** Example GC-FID traces obtained for the solution being expelled from the RO cell for the 3DMAP system. The IS peak appears at 3.18 min, the acetone peak appears at 3.34 min, and the 3DMAP peak appears at 6.17 min.
A5. Calibration curves obtained using $^1$H NMR spectroscopy and spectra obtained for the acetone-rich phase for TMBDA, TMTAD or 3DMAP after phase separation

A calibration curve was obtained to determine the water:acetone ratio in the acetone-rich phase after phase separation at 50 bar of CO$_2$ (Figure A5.1). Samples with a fixed mass of acetone and varying mass of water were prepared. A known amount was dissolved in d6-DMSO and analysed using a 300 MHz NMR spectrometer (Bruker) using $^1$H NMR spectra. The singlet for the -CH$_3$ protons in the acetone were fixed as 1, and the singlet for H$_2$O was integrated relative to that value. The integration of H$_2$O and the water:acetone mass ratio was used to prepare the calibration curve shown in Figure A5.1.

$$y = 1.242x + 0.0148$$

$$R^2 = 0.9975$$

**Figure A5.1** Calibration curve obtained for solutions of water:acetone with varying ratios. The singlet for the H$_2$O peak was used to compare with the water:acetone ratio in each sample. The samples were dissolved in d6-DMSO, and $^1$H NMR was used. This calibration curve was used to determine the water:acetone ratio in samples obtained for the acetone-rich phase after separations at 50 bar.
Figure A5.2 presents the $^1$H NMR spectra obtained for the different acetone:water solutions. The integration for the H$_2$O singlet is presented, and the integration for the -CH$_3$ singlet for acetone was fixed at 1.

**Figure A5.2** $^1$H NMR spectra obtained for the solutions used to obtain a calibration curve to determine the water:acetone ratio in samples containing low amounts of H$_2$O.

The $^1$H NMR spectrum obtained for a sample of the acetone-rich phase collected after separation at 50 bar of CO$_2$ using TMBDA as the ionogen is presented in Figure A5.3.
Figure A5.3 $^1$H NMR spectrum obtained for the acetone-rich phase after separation at 50 bar of CO$_2$ using TMBDA.

The $^1$H NMR spectrum obtained for a sample of the acetone-rich phase collected after separation at 50 bar of CO$_2$ using TMTAD as the ionogen is presented in Figure A5.4.
Figure A5.4 $^1$H NMR spectrum obtained for the acetone-rich phase after separation at 50 bar of CO$_2$ using TMTAD.

The $^1$H NMR spectrum obtained for a sample of the acetone-rich phase collected after separation at 50 bar of CO$_2$ using 3DMAP as the ionogen is presented in Figure A5.5.
Figure A5.5 $^1$H NMR spectrum obtained for the acetone-rich phase after separation at 50 bar of CO$_2$ using 3DMAP.
Appendix B

HPSW and SA-HPSW separation of other biomass products

B1. Introduction

Biomass conversions of sugars and other substrates to value-added chemicals are growing at an accelerated pace. Considering this growth, technologies capable of supporting the field are also in high demand. The biomass products discussed in this section experience similar challenges to those seen in ethanol fermentation. The removal of water can be quite costly, and for some of the products discussed here, distillation might not be the most viable approach considering: (i) the low volatility and high boiling point (B.P.) of the products being obtained, and (ii) the composition of the final product mixture which can present multiple components which might not be efficiently separated using distillation. Therefore, HPSW and SA-HPSW were explored as alternative techniques to recover ethylene glycol (EG), propylene glycol (PG), 1,4-butanediol (1,4-BD), and ethyl lactate (EL) from aqueous mixtures. The surge in the development of biomass conversion presents an opportunity to explore new technologies that support the field.

B2. Materials and Methods

B2.1. Materials

Chemicals were used as received. The following amines were obtained from commercial sources (Sigma-Aldrich, TCI, Fisher): N,N,N′,N′-tetramethyl-1,4-butanediamine (TMBDA), 2,6,10-trimethyl-2,6,10-triazaundecane (TMTAD), 3-dimethylamino-1-propanol (3DMAP), methanol (anhydrous 99.8%), ethyl lactate (FCC, FG, ≥98%), ethylene glycol (anhydrous 99.8%), propylene glycol (FCC, FG, ≥99.5%), 1,4-butanediol (ReagentPlus®, 99%), 1,5-pentanediol (purum ≥97.0%) and isopropanol (anhydrous 99.5%). The water:organic mixtures were prepared using water with a conductivity of 18.2 MΩ obtained from a Milli-Q® purification system (Synergy UV). For the ¹H NMR spectroscopy, d4-CD3OD (Sigma-Aldrich) was used as the solvent. For the
quantifications via $^1$H NMR, 1,4-dioxane (anhydrous 99.8%, Sigma-Aldrich) was utilized as the internal standard. The Karl Fischer titrations were performed using Hydranal-Coulomat AK H (Fisher, Honeywell Fluka) as the titration media.

**B2.2. Evaluation of the efficiency of HPSW for the separation of biomass products from aqueous mixtures**

Phase behaviour was observed using a phase monitor from Supercritical Fluid Technologies Inc (see Section 2.2.2 for diagram and picture of setup). Solutions with the desired organic:water, and amine were prepared prior to being added to the phase monitor. The phase monitor consisted of a stainless-steel vessel (100 mL of internal volume) attached to a thermocouple and a pressure gauge. The vessel was also equipped with two zirconia windows. A microscope CMOS camera (Veho, Discovery VMS-004 Deluxe) connected to a computer was placed facing one of the windows allowing real-time observations of the phase behaviour in the sealed vessel. A needle valve regulated the CO$_2$ addition, and the pressure was adjusted by a piston that was able to change the internal volume of the vessel. The vessel temperature (40 °C) was controlled with a heating mantle. The solutions remained under agitation thanks to a magnetic stir bar. Experiments were performed in triplicate, and the cloud pressures (CP) are presented as averages. The CP was obtained by adding the solutions to the phase monitor and slowly increasing the CO$_2$ pressure until cloudiness, or if the formation of a separate liquid phase could be visually identified. To ensure that the pressure being recorded was correct, the pressure was slightly raised and decreased for a few cycles. The visual behaviour of the system was used to confirm the pressure being recorded for CP.

The samples were prepared with either 25 or 50 wt% of organic in water. Tests were performed using TMBDA and TMTAD as ionogen for both ratios, and with 3DMAP as the ionogen
for the 50 wt% samples. The concentration of ionogen used was 0.80 molal (ionogen concentrations are reported relative to the mass of water).

**B2.3. Solvent-assisted high pressure switchable water (SA-HPSW) phase separation setup**

The same setup used for the recovery of ethanol (Section 3.2.2) from aqueous mixtures was used for methanol, ethylene glycol, propylene glycol, 1,4-butandiol and 1,5-pentanediol as the organic being recovered from water instead of ethanol. The aqueous solutions prepared had a 25 wt% concentration of the organic being recovered to water. The extraction solvent used was isopropanol, and the extraction solvent:water was 1:1 in terms of the mass of water present. The phase separations were performed in the same sight gauge used for ethanol, and the mixtures were pressurized to 50 bar of CO₂.

**B2.3.1. Measurements of the composition of the water- and isopropanol-rich phases**

The amount of organic and TMTAD dissolved in the water- and isopropanol-rich phases were determined via ¹H NMR. After the samples were collected from the sight gauge, they were mixed with a fixed amount of dioxane (used as IS) and CD₃CD and analyzed in a Bruker Avance 300.13 MHz NMR spectrometer using a ¹H NMR probe. The samples were prepared using approximately 0.20 g of either the water- or isopropanol-rich phase sample collected, approximately 0.10 g of dioxane, and 0.70 g of CD₃OD. In order to quantify the amount of each component, the singlet for dioxane (-CH₂, 8H) at 3.66 ppm was used as a reference. Considering the integration for peaks specific to each component, the amount of that component in the sample analysed was determined. Finally, the total amount of each component was approximately determined using the height vs volume relationship of the sight gauge (used to obtain the approximate mass of each phase).
In order to determine the amount of water dissolved in the isopropanol-rich phase, Karl-Fischer titrations were performed. The titrations were performed using a Coulometric KF Titrator without a diaphragm (Mettler Toledo, C20S). The titration solution used was the Hydranal-Coulomat AK H (Fisher, Honeywell Fluka), which is suitable for titrating ketones and aldehydes. For this analysis, approximately 0.1 mL samples of the isopropanol-rich phase were obtained with a syringe, the mass of the syringe and sample was measured, and after injection in the KF titrator, the mass of the “empty” syringe was measured, and the weight of the sample injected was obtained by difference. The amount of water was automatically determined by the KF titrator. Considering the mass of water obtained, and using the height vs volume relationship of the sight gauge (used to obtain the approximate mass of each phase), the approximate amount of water carried over to the isopropanol-rich phase was obtained.

For the experiments using methanol as the organic being recovered, GC-FID traces were collected for both the water- and isopropanol-rich phases. The procedure and GC configuration followed the protocol presented in Section 3.2.3.

B3. Results and Discussion

B3.1. Evaluation of the behaviour of the organics when HPSW is attempted

Phase behaviour experiments were performed with different hydrophilic organics, which can be obtained by means of biomass conversion. Cloud pressures (CP) were obtained for these organics at different organic:water concentrations (Table B3.1). The ionogens selected in this study were TMBDA, TMTAD and 3DMAP due to their proven efficiency in the HPSW separations of acetone. A comparison using the partition coefficient (log P) for the organics tested was also performed for all three ionogens with organic:water solutions with a 50:50 mass ratio (Figure B3.1).
Table B3.1 The CP (absolute pressure at 40 ºC) of several hydrophilic organics was obtained with organic:water mixtures of 25:75 and 50:50 mass ratios.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Organic</th>
<th>Amine</th>
<th>Concentration of organic / wt%</th>
<th>CP pressure / bar</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-propanol</td>
<td>TMBDA</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
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<td>44</td>
<td>PG</td>
<td>3DMAP</td>
<td>50</td>
<td>N/Aa</td>
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</table>

Experiments were performed at 40 °C. Amine concentration was maintained at 0.80 molal (relative to the mass of water initially added to prepare the mixture).

* For the samples without a CP value, no phase separation was observed when CO$_2$ pressures of up to 70 bar were applied.
Figure B3.1 Comparison of the cloud pressure (CP) for the separation of different hydrophilic organics (with varying log P, calculated using ) from organic:water (50:50 wt%) solutions using TMBDA (red circles, ●), TMTAD (blue diamonds, ♦) and 3DMAP (green triangles, ▲) as the ionogen.

The CP observations were made in the phase monitor, and the temperature was maintained at 40 °C. The systems labelled “fail” did not present a CP at pressures up to 70 bar CO₂.
Considering the data obtained for the organic:water systems, the log P can be used to identify binary (organic:water) systems that might separate once HPSW is performed. With the exception of 1,5-PD, the organic molecules that present moderate to low miscibility in water (log P above -0.4) could be separated from the aqueous phase when HPSW was performed. For the systems that do separate when HPSW is applied, a correlation between log P and CP was observed. Although acetone and isopropanol have very similar chemical structures, the Kamlet-Taft solvatochromic parameters for these solvents differ quite a lot. In terms of H-bonding donating ability (\(\alpha\)), acetone presents a 0.08 value, while for isopropanol, the value is 0.76.\(^\text{106}\) This difference is also observed for H-bonding accepting ability (\(\beta\)), 0.48 for acetone and 0.88 average for isopropanol.\(^\text{106}\) The polarizability (\(\pi^*\)) of these molecules also differs, acetone presents a 0.71 value while isopropanol is 0.48.\(^\text{106}\) These differences in the Kamlet-Taft parameters are also observed when the solvents are expanded with CO\(_2\).\(^\text{106}\) As a result, the CP pressure might result from a combination of the extent of the miscibility of an organic molecule in water, but also its intrinsic properties to promote H-bond, and its polarity. Efforts to identify the correlation between CP values, log P and Kamlet-Taft parameters are an essential avenue to be explored in the future.

Although log P gave an indication of what system would undergo phase separation via HPSW, not all organic:water combinations followed that trend. 1,5-PD presents a log P value of around -0.1, based on log P alone, this molecule should phase separate. But log P is not the only aspect determining phase separation. In the case of 1,5-PD, an important visual observation was made when performing the experiments. Such observation might explain the inability of this molecule to separate from water during HPSW. No considerable volumetric expansion of the 1,5-PD:water mixtures was observed. As discussed, volumetric expansion is directly related to the mass% of CO\(_2\) dissolved in the organic liquid. Considering that 1,5-PD did not expand (in terms of volume), it could be inferred that the mass% of CO\(_2\) dissolved is low, although measurements for the amount of CO\(_2\) dissolved were not performed. This would place 1,5-PD in Class I of CXL.
organic liquids, which also includes water and glycerol, an organic molecule with a structure very similar to 1,5-PD. HPSW relies on the synergistic effect between SW and CXL. If the organic liquid cannot expand with the addition of CO₂, SW is the predominant force promoting phase separation. As discussed, SW cannot promote phase separation of hydrophilic organics, which would justify the result observed. Based on the limited data collected, predicting the expected CP value based on log P is not possible, but the log P values might be used to identify if HPSW will take place if volumetric expansion is also observed.

The log P values might also be used to identify organic:water mixtures that a phase separation would not be expected via HPSW. Although the precise reasons as to why molecules with a log P value below -0.4 did not undergo phase separation are known, some experimental observations might provide some insight. During the experiments performed in the phase monitor, visual evidence of volumetric expansion were not observed for the diols testes (1,4-BD, EG and PG). These molecules presented a similar behaviour to 1,5-PD. Based only on visual observations, these diols would probably be placed in Class I in the CXL classification. As such, without the occurrence of expansion upon the addition of CO₂, these systems exclusively rely on SW to separate from the aqueous phase. Effectively, HPSW is not taking place, instead of it, SW is the force behind any separation, and SW is not capable of promoting phase separation of hydrophilic organics. On the other hand, volumetric expansion was observed for ethanol and methanol, but phase separation did not occur. These organic liquids would both be considered Class II liquids in the CXL classification, but still, the lower critical solution pressure (LCSP) for a methanol:water mixture only occurs when 80 bar of CO₂ is applied (when CXL is applied by itself). For ethanol:water solutions CXL is not able to promote liquid-liquid phase separation. The results observed with CXL and HPSW demonstrate that having the ability to dissolve large amounts of CO₂ and undergo volumetric expansion is not enough to promote phase separation from water. Although the reasons why phase separation was not observed are not completely clear, it could be hypothesized that the
interactions between the species in the mixture might be the reason as to why this behaviour is observed. In order to probe such an assumption, Kirkwood-Buff integrals (KBI) would need to be obtained for these systems. KBI are very useful to quantify the associations between components of a mixture. Online tools are available to calculate KBIs, but the extent to which these tools could be applied to high-pressure systems was not evaluated. Although log P can be used to identify systems that might not undergo phase separation under specific conditions (concentrations, ionogen used, pressures) via HPSW, there is still much to be explored as to why this behaviour is present even in systems that undergo volumetric expansion with CO₂.

**B3.2. Recovery of organics using SA-HPSW**

SA-HPSW was performed using isopropanol as the extraction solvent for the organics that did not present a CP when HPSW was performed. Experiments were performed using methanol, EG, PG, 1,4-BD and 1,5-PD aqueous mixtures with an organic concentration of 25 wt%. TMTAD was selected as the ionogen, and the concentration used was 0.80 molal (relative to the mass of water). The isopropanol:water mass ratio used was 1:1. The composition of both the water- and isopropanol-rich was determined (Table B3.2). For the experiments with methanol, GC-FID was used to determine the methanol, isopropanol and TMTAD contents, and the water amount in the isopropanol-rich phase was determined via Karl-Fischer titration. While for EG, PG, 1,4-BD and 1,5-PD phase composition was obtained via 1H NMR (dioxane as IS and CD3OD as solvent), and the water content in the isopropanol-rich phase was determined via Karl-Fischer titration.
Table B3.2 Composition of the water- and isopropanol-rich phases obtained after SA-HPSW separation performed at 50 bar of CO$_2$ (at 40 °C).

<table>
<thead>
<tr>
<th>Organic</th>
<th>Water-rich phase</th>
<th>Isopropanol-rich phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mass of organic / g (wt% from initial)$^a$</td>
<td>Isopropanol mass / g (wt% from initial)$^a$</td>
</tr>
<tr>
<td>MeOH$^b$</td>
<td>0.6 (21)</td>
<td>1.3 (14)</td>
</tr>
<tr>
<td>EG$^c$</td>
<td>1.5 (50)</td>
<td>2.2 (24)</td>
</tr>
<tr>
<td>PG$^c$</td>
<td>0.8 (25)</td>
<td>1.1 (12)</td>
</tr>
<tr>
<td>1,4-BD$^c$</td>
<td>0.8 (27)</td>
<td>1.3 (14)</td>
</tr>
<tr>
<td>1,5-PD$^c$</td>
<td>0.5 (18)</td>
<td>0.9 (10)</td>
</tr>
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</table>

The initial aqueous mixtures were prepared with the organic concentration in water of 25 wt% (approximately 3 g of organic in 9 g of water). TMTAD was used as the ionogen at a 0.80 molal (relative to the mass of water) concentration (approximately 1.45 g of TMTAD). The isopropanol:water mass ratio was 1:1 (approximately 9 g of isopropanol).

$^a$ The number in brackets refers to the wt% relative to the amount of the component initially added to prepare the mixture. As such, the number in the water-rich phase combined with the number in the isopropanol-rich phase for each component adds up to 100%.

$^b$ Composition of MeOH, isopropanol and TMTAD obtained via GC-FID using dioxane as IS. Amount of water obtained via Karl-Fischer titration.

$^c$ Composition of organic, isopropanol and TMTAD obtained via $^1$H NMR using dioxane as IS. Amount of water obtained via Karl-Fischer titration.
SA-HPSW was able to recover, to a certain degree of satisfaction, all the hydrophilic organics tested, but the hydrophilicity of isopropanol impacted the amount of water being transferred to this isopropanol-rich phase. Recoveries above 70% (considering the initial mass of organic added) were observed for all the hydrophilic organics, with the exception of EG. These results are encouraging, considering that concentrating the organics in a solvent with better thermal properties than water might favourably impact the energy requirements to obtain purified organics. However, the results demonstrated that the isopropanol-rich phase presented a substantial amount of water still dissolved. With the exception of the EG system, in all the other mixtures, the amount of water transferred to the isopropanol-rich phase was above 50% based on the initial amount of water used to prepare the aqueous mixtures. Isopropanol is not only a miscible solvent in water but also can promote H-bonding with water. As a result, this extracting solvent has favourable interactions with both components (organic and water) of the aqueous mixture. These interactions, in combination with the creation of a still hydrophilic isopropanol-rich phase, might be the reasons as to why so much water is being transferred. Considering the goal of improving the distillation step required for purification of the organics by replacing water with a more volatile solvent (i.e. isopropanol) via SA-HPSW. The presence of such large amounts of water in the isopropanol-rich phase might compromise the energy required to purify the organic molecules. Although energy calculations were not performed for these systems, considering the better thermal properties of isopropanol (lower boiling point and higher volatility), it is envisioned that the energy required in the purification step via distillation will be lower than if distillation was performed to the organic:water solution. This assumption needs to be probed via calculations performed using ASPEN. In addition, the presence of ionogen in the isopropanol-rich phase cannot be neglected, considering that TMTAD also presents a high boiling point, and the separation of this amine from the organics might not be simple. Therefore, SA-HPSW was shown to promote the recovery of hydrophilic organics to the extracting solvent, but the same properties that made the extracting
solvent efficient at recovering the organics were also promoting an undesirable transfer of water to
the isopropanol-rich phase.

Modifications must be made to the SA-HPSW separations to address the issues observed. Using a less hydrophilic organic than isopropanol might be an avenue to explore. However, this organic still needs to have favourable interactions with the diols and alcohols. H-bonding solvents might still be considered, but determining the extent of water being transferred cannot be predicted at this moment. In order to address the issues regarding the amine contamination in the isopropanol-rich phase, one alternative could be using ionogens that, during the distillation step after SA-HPSW, would precipitate as solids and separate from the diols. The Jessop group has extensively developed polymers and solid particles containing CO₂-switchable groups. Some switchable materials present low solubility in water in the absence of CO₂. This behaviour in the presence and absence of CO₂ could be explored to facilitate the removal of the polymers from the still hydrophilic isopropanol phase after SA-HPSW. Alternatives to address the issues faced by SA-HPSW are available and could be explored to maximize the efficiency of this new separation technique.

B4.1. ¹H NMR spectra obtained for the water- and organic-rich phases

¹H NMR spectra obtained for the phases after SA-HPSW separation (at 50 bar of CO₂ and with isopropanol as extracting solvent) were analysed using dioxane as IS and CD₃OD as the solvent. The dioxane peak (and integration) was used to quantify the amount of the other components present in the mixtures. Arrows are used in the spectra to identify the peaks used in the quantification of each component.
Figure B4.1 $^1$H NMR spectra obtained for the water- and isopropanol-rich phases in the recovery of EG.
Figure B4.2 $^1$H NMR spectra obtained for the water- and isopropanol-rich phases in the recovery of PG.
Figure B4.3: $^1$H NMR spectra obtained for the water- and isopropanol-rich phases in the recovery of 1,4-BD.
Figure B4.4 $^1$H NMR spectra obtained for the water- and isopropanol-rich phases in the recovery of 1,5-PD.
B5.1. Calibration curve obtained using GC-FID traces for MeOH:water mixtures

In order to evaluate the composition of the water-rich phase, GC-FID traces were collected. This section will present the calibration curve obtained using dioxane as IS. Figure B5.1 shows the calibration curve of methanol in water.

\[
y = 0.9947x + 0.0549 \\
R^2 = 1.0000
\]

**Figure B5.1** Calibration curve obtained for methanol:water solutions with varying concentrations. The samples were analysed on a GC-FID using dioxane as IS, and the data presented is based on multiple replicates.
Appendix C
Additional data for Chapter 3

C1. Calibration curves obtained using GC-FID traces

In order to evaluate the composition of the water-rich phase, GC-FID traces were collected. This appendix will present the calibration curves obtained using dioxane as IS. Figure C1.1 presents the calibration curve of ethanol in water.

![Graph showing calibration curve with equation y = 0.8448x - 0.1596 and R² = 0.9998]

**Figure C1.1** Calibration curve obtained for ethanol:water solutions with varying concentrations. The samples were analysed on a GC-FID using dioxane as IS, and the data presented is based on multiple replicates.

In order to quantify the amount of extraction solvent remaining in the water-rich phase, calibration curves were obtained for isopropanol (Figure C1.2), acetone (Figure C1.3) and 1-butanol (Figure C1.4). The GC-FID traces obtained with dioxane as IS were used for these calibration curves.
Figure C1.2 Calibration curve obtained for isopropanol:water solutions with varying concentrations. The samples were analysed on a GC-FID using dioxane as IS, and the data presented is based on multiple replicates.

\[ y = 0.6979x + 0.0094 \quad R^2 = 1.0000 \]

Figure C1.3 Calibration curve obtained for acetone:water solutions with varying concentrations. The samples were analysed on a GC-FID using dioxane as IS, and the data presented is based on multiple replicates.

\[ y = 0.6805x - 0.0239 \quad R^2 = 1.0000 \]
Figure C1.4 Calibration curve obtained for 1-butanol:water solutions with varying concentrations. The samples were analysed on a GC-FID using dioxane as IS, and the data presented is based on multiple replicates.

In order to quantify the amount of TMTAD dissolved in the organic-rich phase and the amount of TMTAD being lost during the RO separation, a calibration curve using dioxane as IS was prepared (Figure C1.5). The peak ratio between IS:TMTAD (based on the area under the peaks) was used to determine the mass ratio of these two components, and via calculations using the mass of the solution used to prepare the samples, the mass of TMTAD was determined, both in the sample and in the system.
**Figure C1.5** Calibration curve obtained for TMTAD:water solutions with varying concentrations. The samples were analysed on a GC-FID using dioxane as IS, and the data presented is based on multiple replicates.