DESIGNING SWITCHABLE-HYDROPHILICITY SOLVENTS AND MODELLING THEIR BEHAVIOUR

by

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Abstract

Switchable-hydrophilicity solvents (SHSs) are solvents that in one state forms a biphasic mixture with water but can be reversibly switched to another state that is miscible with water. In theory, this switch can be triggered in a number of ways, however we focus on dissolved CO_2 as the switchable trigger. The most practical use of an SHS is for extraction of a water-immiscible liquid product from a solvent in which it is dissolved (as demonstrated by the extraction of bitumen from the oil sands, bio-oil from algae, etc). This technology provides a more environmentally-friendly means of extraction over current popular processes such as distillation. Since their discovery in 2010, more than 25 nitrogen-based SHSs have been reported in the literature. The SHS behaviour seems to be strongly correlated with hydrophilicity and basicity, not surprisingly. Indeed, amine solvents which demonstrate SHS behaviour are contained within a specific hydrophilicity and basicity range. This range can be predicted based on fundamental acid-dissociation and partitioning equations which, once developed, reveal other tuneable parameters. These parameters are intrinsic (molecular weight and density) as well as extrinsic (CO_2 pressure and water:SHS volume ratio). The extrinsic parameters enable the switchable range to expand - enabling less basic and more hydrophobic solvents to act as SHSs. This is of interest since one of the goals of SHS technology is to replace volatile, smog-forming and bio-accumulating solvents with environmentally benign ones. Having a greater range to choose SHSs from increases the chances of finding more environmentally benign solvents. The other goal of SHS technology is to be as effective, if not more, than conventional solvents for extractions. Equipped with a mathematical description of the SHS process, it is a simple matter of optimizing the resulting equations in terms of the extrinsic parameters. Increasing the pressure of CO_2 as well as the water:SHS volume ratio increases the amount of SHS that is extracted from the liquid product. This is true for the two-liquid system (composed of water and SHS) as well as the three-liquid system (composed of water, SHS, and a water-immisible organic liquid), though their mathematical descriptions are different.

Statement of Co-Authorship

The research presented in this thesis was done under the supervision of Philip Jessop at Queen's University. All the work presented here was done by the author (Jeremy Durelle) except where explicitly stated otherwise.

Chapter 2 contains a version of a paper published in Green Chemistry as: *Jesse R. Vanderveen, Jeremy Durelle and Philip G. Jessop, "Design and evaluation of switchable-hydrophilicity solvents", Green Chem., 2014,* ***16****, 1187.* Jesse Vanderveen is the lead author of this paper. I tested the tertiary amines for SHS behaviour and contributed data for Figure 2-1.

Chapter 3 contains a version of a paper published in Physical Chemistry Chemical Physics as: *Jeremy Durelle, Jesse R. Vanderveen and Philip G. Jessop, "Modelling the behaviour of switchable-hydrophilicity solvents", Phys. Chem. Chem. Phys., 2014,* ***16****, 5270.* I am the lead author of this paper. I wrote the manuscript, performed all the calculations and measurements and produced all the figures under the supervision of Philip Jessop. The Ω parameter originated from Jesse Vanderveen.

Chapter 4 contains a draft of a paper to be submitted to Physical Chemistry Chemical Physics as: *Jeremy Durelle, Jesse R. Vanderveen, Yi Quan, Courtney Chalifoux, Julia E. Kostin, and Philip G. Jessop, "Extending and optimizing the range of switchable-hydrophilicity solvents", Phys. Chem. Chem. Phys., 2014.* I am the lead author of this paper. I wrote the manuscript, performed all the calculations and produced all of the figures except for Figure 4-5 under the supervision of Philip Jessop. Yi Quan performed all of the experiments, collected all of the data with the help of Jesse Vanderveen and myself with the exception of the 1-dimethylamino-2-pentyne data which I had tested. Yi Quan produced Figure 4-5. Courtney Chalifoux and Julia Kostin helped with the optimization of the two and three-liquid system equations, respectively.

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Abbreviations and Variables

$[\mathrm{B}]_{\mathrm{aq}}$	- Molar concentration of base in the aqueous phase
$[\mathrm{B}]_{\mathrm{org}}$	- Molar concentration of base in the organic phase
$[\mathrm{CyNMe_3}]\mathrm{I}$	- Trimethylcyclohexylammonium iodide
D	- Distribution coefficient of the base (neutral and protonated) in a 1-octanol/water system
D_1	- Distribution coefficient of the base in the initial system (usually 0 bar)
D_2 or D'	- Distribution coefficient of the base in the final system
DECA	- N,N-diethylcyclohexylamine
DIISO	- N,N-diisopropylethylamine
DIPEA	- N,N-diisopropylethanol amine
DMAP	- 1-dimethylamino-2-pentyne
DMBA	- N,N-dimethylbenzylamine
DMCA or $\mathrm{CyNMe_2}$	- N,N-dimethylcyclohexylamine
EP	- Eutriphication potential
$[\mathrm{HB^+}]_{\mathrm{aq}}$	- Molar concentration of base in the aqueous phase
$[\mathrm{HB^+}]_{\mathrm{org}}$	- Molar concentration of base in the organic phase

K_1 - Acid dissociation constant of carbonic acid

K_H - Henry's law constant for CO_2

K_{ow} or K_{ow}^{neut} - Partition coefficient of the neutral base in a 1-octanol/water system

K'_{ow} or K_{ow}^{salt} - Partition coefficient of the protonated base in a 1-octanol/water system

K_w - Autoprotolysis constant for H_2O

LCA - Life-cycle assessment

M or MW - Molecular weight of the base

$n_{\text{B,aq}}$ - Moles of base in the aqueous phase

$n_{\text{B,org}}$ - Moles of base in the organic phase

$n_{\text{B},tot}$ or n_{tot} - Total moles of base in the system

$n_{\text{B,undiss}}$ or n_B - Moles of neutral base that failed to dissolve in the water

$n'_{\text{B,undiss}}$ or n'_B - Moles of protonated base that failed to dissolve in the water

$n_{\text{HB}^+\text{,aq}}$ - Moles of protonated base in the aqueous phase

$n_{\text{HB}^+\text{,org}}$ - Moles of protonated base in the organic phase

P - Mole fraction of protonated base to total amount of base in the system

P_{CO_2} - Pressure of CO_2 in initial system (usually 0 bar)

P'_{CO_2} - Pressure of CO_2 in final system

$\text{pK}_{a\text{H}}$ - Dissociation constant of the protonated base

S - Water solubility under initial CO_2 pressure (usually 0 bar)

S_0 - Water solubility of the neutral base (assumed constant)

S' - Water solubility under final CO_2 pressure

SHS	- Switchable hydrophilicity solvent
TEA	- Triethylamine
TEST	- Toxicity Estimation Software Tool
TPA	- Tripropylamine
V_{aq}	- Volume of the aqueous layer in the system
V_{B}	- Volume of base in the system
V_{org}	- Volume of the organic layer in the system
V_{rat}	- The volume ratio of the aqueous and organic layers
V_w	- Volume of water in the system
Z	- An SHS mapping parameter for the 2-liquid system
$\Delta \log K_{ow}$	- Difference in distribution coefficients of the neutral and protonated base
ν_{N}	- Number of nitrogen atoms
ν_{P}	- Number of phosphorus atoms
ν_{ThOD}	- Theoretical oxygen demand
ρ	- Density of the base
Ω	- An SHS mapping parameter for the 3-liquid system

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Chapter 1

Introduction

The alarming rate of carbon dioxide (CO_2) emission into the atmosphere is causing the average temperature of the oceans, and even the air, to steadily increase. This also affects the metabolism of plants we depend on [1]. Because humans have burned roughly 550 billion tons of carbon since the industrial revolution, the concentration of atmospheric CO_2 is 100 parts per million (ppm) higher than it was 200 years ago [2]. Despite this, energy demand is on the rise, which means we are burning more carbon faster. While CO_2 is not the only greenhouse gas produced when burning fossil fuels, it gets the most attention since it is responsible for 60% of the greenhouse gas effect [2]. Power plants produce a lot of waste CO_2. A strategy to ensure long-term sustainability is recycling the CO_2 emitted and captured from power generation and industrial processes into valuable products and uses. In fact, CO_2 can be used to make modern industrial and synthetic processes cheaper and more environmentally friendly. However, CO_2 utilization is not a solution to global warming. In most applications of CO_2, the CO_2 is only used temporarily and then it is released again. Furthermore, the amount of CO_2 used in these applications is small compared to the amount being emitted by human activities. Nevertheless, CO_2 utilization can make processes less environmentally damaging. For example, CO_2 is replacing hydrocarbon-based solvents for extractions (oil extraction and decaffeination of coffee and tea). Other CO_2 utilization technologies - including converting CO_2 into fuel, cement, minerals and plastics, enhanced fixation into fast-growing biomass, and using it as a feedstock for chemicals - are at various stages of development.

1.1 Green Chemistry

Green chemistry is a relatively new idea which focuses on reducing and improving the environmental impact of chemical processes [4]. It creates a new reality for chemistry and engineering by asking chemists and engineers to design chemicals, chemical processes and commercial products in a way that avoids, or at least minimizes, the creation of compounds which can significantly contribute to global warming, smog formation, ozone depletion, bioaccumulation among others [3]. There are 12 principles of green chemistry which provide a framework for chemists and engineers to bear in mind when designing or redesigning a particular process. They are presented below.

1. **Prevention:** It is better to prevent waste than to treat or clean up waste after it has been created.

2. **Atom Economy:** Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. **Less Hazardous Chemical Syntheses:** Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no

toxicity to human health and the environment.

4. **Designing Safer Chemicals:** Chemical products should be designed to affect their desired function while minimizing their toxicity.

5. **Safer Solvents and Auxiliaries:** The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.

6. **Design for Energy Efficiency:** Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.

7. **Use of Renewable Feedstocks:** A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.

8. **Reduce Derivatives:** Unnecessary derivatization (use of blocking groups, protection/ deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

9. **Catalysis:** Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. **Design for Degradation:** Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.

11. **Real-time analysis for Pollution Prevention:** Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

12. **Inherently Safer Chemistry for Accident Prevention:** Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

Metrics are used to determine how environmentally damaging a product or process is. It is imperative that these metrics accurately gauge environmental impact if they are to replace current products or processes. These are calculated estimations of the extent to which a process will contribute to smog formation, ozone depletion, eutrophication and other kinds of damage to health or the environment. Two very common but flawed metrics are atom economy [5] and environmental factor or "E-Factor" [6].

Atom economy represents the percentage of reagent atoms that are incorporated into a desired product. It is a measure of reaction efficiency. A high atom economy indicates an efficient chemical reaction.

$$\%Atom\ Economy = \frac{Molecular\ Weight\ of\ Desired\ Product}{Molecular\ Weight\ of\ All\ Reactants} \times 100 \tag{1.1}$$

The E-Factor represents the amount of side-products or waste products also produced in a reaction. It is the ratio of the amount of waste produced by a reaction and the mass of the desired product. A low E-Factor indicates minimal side reactions.

$$E\ Factor = \frac{Mass\ of\ Waste\ Generated}{Mass\ of\ Product\ Produced} \tag{1.2}$$

Though these two metrics are popular, they can be misleading when designing and evaluating a process. They do not take into account, for example, the nature of the generated waste. A small amount of an extremely toxic waste product is much more damaging than a large amount of an environmentally benign waste product. A multivariate evaluation is often employed instead of the simple atom economy and E-Factor metrics [7]. Life-cycle assessment (LCA) is a methodology to evaluate the environmental effects of a product or process by analyzing the whole life cycle of a particular product or process. This can include the energy costs of mining, extracting, and transporting the materials needed to synthesize a target product up until the product's release and interaction with the environment (cradle to grave, Figure 1.1). The environmental impact of each step of the target's life is assessed by multiple impact factors that depend not only on the nature of the reagents, reaction, and emission products, but also on the amount needed, used, and produced, respectively. Impact factors such as bioaccumulation potential, toxicity by ingestion (and inhalation) potential, global warming potential and eutrophication potential can be used to assess a target product or process. Eutrophication potential refers to the enrichment of nutrients in water. This causes accelerated algae growth which prevents sunlight from reaching the lower depths, leading to decrease in photosynthesis and oxygen production.

A full LCA is not always performed. For example, a company may be concerned with the environmental impact of the synthesis of a target via a particular synthetic route. Therefore, the company would assess the environmental impact of that synthetic route from the moment it receives the starting materials to the isolation of the target product just before it is distributed (gate to gate).

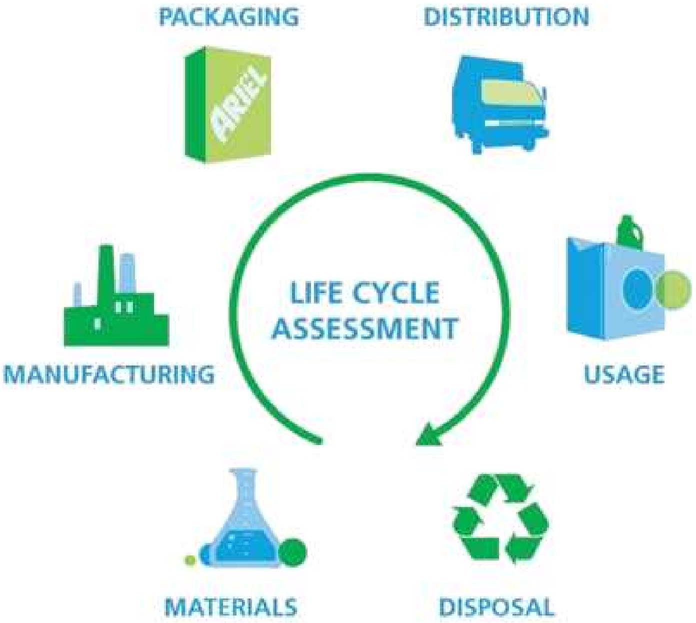

Figure 1.1: Life-cycle assessment (LCA) diagram.

1.2 CO_2

CO_2 plays an important role in our lives. A key by-product of the animal respiratory cycle necessary for plants to form sugar [8], it is also a greenhouse gas that greatly contributes to global warming. Therefore, the minimization of CO_2 emissions is important for industrial processes.

CO_2 has interesting properties. It is a colourless gas discovered in the 16th century as a by-product of combustion [9]. Composed of polar bonds (oxygen is more electronegative than carbon), its linear and symmetric nature results in a net-zero dipole moment. Though it is a gas under standard conditions, CO_2 can be used as a medium for chemical reactions as well as extractions at elevated pressures. The solubility of CO_2 in a solvent increases with pressure, thereby manipulating the solvent properties. At even higher pressures, beyond the critical point (72.9 bar, 304.2 K), CO_2 adopts a supercritical phase, having both gaseous and liquid properties. At extremely high pressures, however, CO_2 adopts a solid-phase even at elevated temperatures. Figure 1.2 shows the phases resulting from various pressures and temperatures.

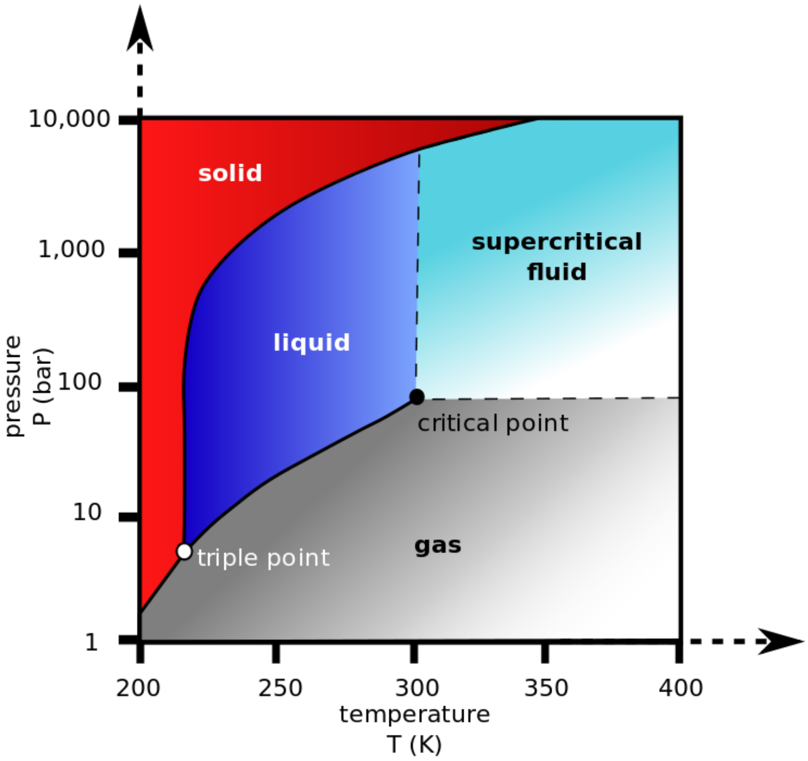

Figure 1.2: Phase diagram for CO_2. The triple point is the point at which all three phases (solid, liquid, and gas) are in equilibrium. The critical point is the point beyond which CO_2 is a supercritical fluid, having properties of a gas as well as a liquid [10].

When CO_2 is dissolved in water, hydrated CO_2 is formed. The solution becomes acidic, having a pH of about 4 under atmospheric pressure. Because it is a diprotic acid, H_2CO_3 has two pK_a values: 3.8 and 10.3 [11]. The apparent pK_a for carbonic acid, however, is 6.3. This is a result of the equilibrium governing the dissolution of gaseous CO_2 as shown in Equation 1.3.

$$\begin{aligned} CO_{2\,(g)} &\rightleftharpoons CO_{2\,(aq)} \\ CO_{2\,(aq)} + H_2O_{(l)} &\rightleftharpoons H_2CO_{3\,(aq)} \\ H_2CO_{3\,(aq)} &\rightleftharpoons HCO^-_{3(aq)} + H^+_{(aq)} \\ HCO^-_{3(aq)} &\rightleftharpoons CO^{2-}_{3(aq)} + H^+_{(aq)} \end{aligned} \tag{1.3}$$

The dissolved CO_2 differs from carbonic acid in that there is an equilibrium between the gaseous and dissolved CO_2 which is not the case in pure carbonic acid. The concentration of dissolved CO_2 is governed by Henry's Law (Equation 1.4) and depends on the pressure of CO_2 (P_{CO_2}), as well as Henry's law constant, K_H, which is a constant of proportionality equal to 0.034 mol L^{-1} bar^{-1} for CO_2 [11].

$$[CO_2]_{aq} = K_H \times P_{CO_2} \tag{1.4}$$

The relative amount of hydrated CO_2 ($CO_2 \cdot H_2O$), bicarbonate ion (HCO_3^-), and carbonate ion (CO_3^{2-}) present in solution is pH dependent (Figure 1.3).

Due to its ability to form an acidic solution when dissolved in water, CO_2 can be used to reversibly change a basic solvent from having poor water-miscibility to high water-miscibility, as presented in the next section. This has been demonstrated as an attractive alternative means of extraction and/or separation where current processes use distillation. As explained in the next section, this new means of extraction reduces energy costs as well as harmful emissions.

1.3 Switchable-Hydrophilicity Solvents

Adding a hydrophobic (water-hating) compound to water results in a mixture of two liquids, with the less dense compound forming the top layer. Usually, this liquid

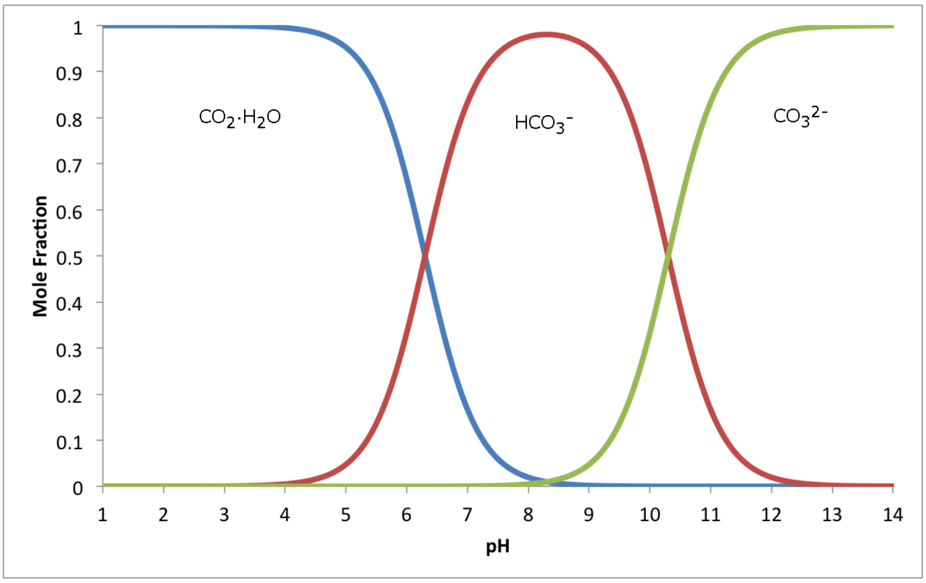

Figure 1.3: Hydrated CO_2 Speciation. The pH-dependent speciation of $CO_2 \cdot H_2O$. At low pH, the neutral form dominates. Between pH 6.3 and 10.3, the bicarbonate ion dominates. At pH higher than 10.3, the carbonate ion dominates.

separation is caused by the compound having hydrophobic groups, such as long alkyl chains. Even though the two components are poorly miscible, they will never be completely immiscible either; some of the hydrophobic compound will dissolve into the water according to its solubility. Upon adding CO_2 to this mixture, the gas is dissolved in the water forming hydrated CO_2. If the hydrophobic compound added to water is basic relative to water (amines, for example), then the hydrated CO_2 will protonate the base forming a bicarbonate salt. As the bicarbonate salts of amines are much more water miscible or soluble than the corresponding neutral amines, the two layers may become miscible (the amine becomes an ammonium bicarbonate salt which is hydrophilic or water-loving). The resulting solution typically has a pH around 8, indicating that the bicarbonate salt, rather than the carbonate salt, is dominant in the system (see Figure 1.3). The overall reaction is presented below. It should be noted that we avoid the formation of carbamate salts by using tertiary (or bulky secondary) amines.

$$H_2CO_{3\,(aq)} + NR_{3\,(aq)} \rightleftharpoons HNR^{+}_{3(aq)} + HCO^{-}_{3(aq)} \tag{1.5}$$

This process can be reversed by removing CO_2. Blowing a non-acidic gas (such as air, N_2 or Ar) through the system is usually sufficient to remove CO_2, but adding heat and stirring accelerates this process. If we remove the CO_2, the system is restored to its biphasic form. This is the reason we wish to avoid the formation of carbamate salts - they hinder this reversing process. Solvents that demonstrate this reversible phase behaviour when triggered with CO_2 are called switchable-hydrophilicity solvents (SHSs). In theory, switching a solvent's hydrophilicity can be triggered in a number of ways. However, CO_2 is an attractive trigger because it is abundant, cheap, and relatively safe to use and handle.

SHS's utility has been demonstrated for various separation processes - the isolation of bitumen from the oil sands [13], vegetable oil from soybeans [14], bio-oil from algae [12, 15, 16], polystyrene from waste polystyrene foam [17], and phenols from lignin [18]. They have also been used as draw solutes for forward osmosis [19]. Taking the oil sands example, the conventional method of bitumen extraction is to mix the oil sand with hot water to create a slurry that is separated into a bitumen fraction (which is the desired product), heavy solids (sand), and a middle fraction containing water, sand, clay, and oil ("tailings"). The production of the tailings slurry is a major disadvantage of the current process. The tailings are put into tailings ponds (about 77 km^2 of oil sands tailings ponds exist in Alberta presently (2014) [20]). The extraction process using switchable technology, however, generates clean, dry sand and therefore avoids the creation of tailing ponds.

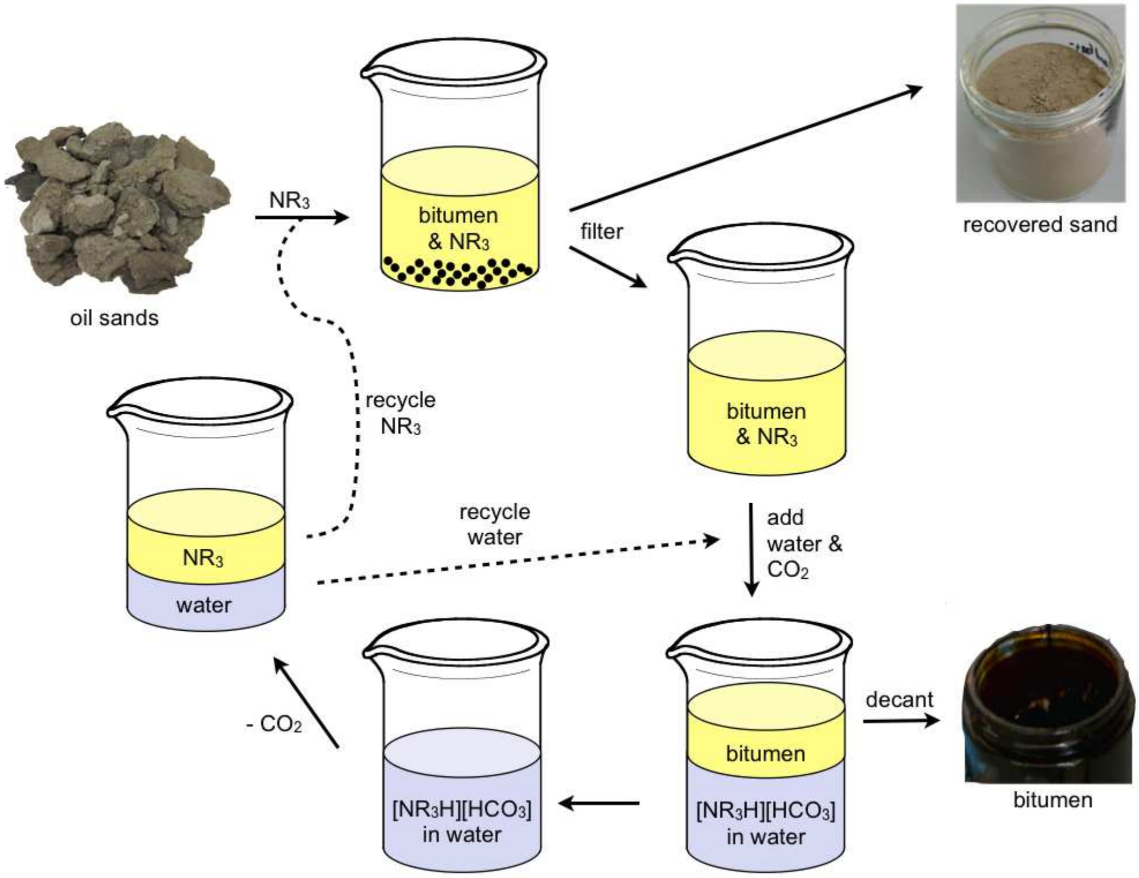

Figure 1.4: The extraction of bitumen from oil-sands using a tertiary amine SHS [13].

The oil can be extracted from the sand and the other solids using the switchable solvent. The solvent can then be extracted from the oil by carbonated water (the CO_2 in the water changes the solvent from hydrophobic to hydrophilic). Finally, to retrieve the solvent (which is dissolved in water), one can simply remove the CO_2 by heating and/or bubbling air through the solution. This switches the solvent back to its native hydrophobic state. Now that the solvent and water have been separated, they can both be reused in the next cycle. This process is illustrated in Figure 1.4.

Many SHSs have been reported [17, 21, 22, 23] since their discovery in 2010 [14].

It is important to remember that these solvents provide a method of solvent extraction that has much lower environmental impact than distillation which is commonly used. Most notably, the ease of its recycling gives an SHS a distinct advantage over conventional volatile and smog-forming solvents. The recycling of an SHS does not require temperatures high enough to boil the solvent, whereas this is necessary for distillation. Because of this, conventional solvents used for distillation have low boiling points and are therefore volatile. SHSs do not need to be volatile. Energy does need to be invested in order to break the solvent-solute interactions and release CO_2 from the water, but this is a small investment when compared to boiling a large sample of solvent. For example, the enthalpy of vaporization of triethylamine is 30 kJ/mol whereas the heat required to raise its temperature from 20°C to 60°C (the temperature used to switch the SHS back to its hydrophobic form) is only 8 kJ/mol. Using SHS-technology, one can recycle both the amine solvent and the water in the extraction process. It also uses a cheap, abundant and safe trigger to switch the hydrophilciity of the SHS.

The goal of this thesis is two-fold. First, we wish to discover as many environmentally benign SHSs as possible. It is known that some elements (such as sulfur and phosphorus) and even functional groups (such as phenols) cause significant environmental damage and should be avoided when designing SHSs. The second goal is to give insight into the major parameters governing SHS behaviour. Basicity and water-solubility of the SHS are obvious parameters, but there are others (both intrinsic and extrinsic) that can be used to optimize the SHS process. This aides not only in focussing the search field, but also allowing the user to modify the design of the SHS and the process itself to maximize the efficiency of an extraction.

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Chapter 2

Paper I: Design and Evaluation of Switchable-Hydrophilicity Solvents

Paper Title[1]: "Design and Evaluation of Switchable-Hydrophilicity Solvents"

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2.1 Abstract

Switchable-hydrophilicity solvents (SHSs) are solvents that can switch reversibly between one form that is miscible with water to another that forms a biphasic mixture with water. For these SHSs, we use CO_2 at 1 bar as a stimulus for triggering the transformation to the water-miscible form and removal of CO_2 to achieve the reverse. We now report the identification of 13 new SHSs, including the first secondary amine SHSs, and a comparison of all known SHSs in terms of safety and environmental impacts. Amines which include another functional group, especially oxygen-containing groups, are less hazardous than alkylamines. Secondary amines can have improved switching speeds relative to tertiary amines. The variety of SHSs identified suggests that amine SHSs can be designed to have ideal properties for a given application.

2.2 Introduction

The widespread use of volatile solvents contributes to a variety of health, safety, and environmental problems such as inhalation toxicity, flammability, and smog formation. It is well known that non-volatile organic solvents avoid all of the problems mentioned, but they are rarely used in industry because they cannot be distilled. Distillation is the standard method for removing solvent from product at the end of almost any chemical process that uses solvents. Industry's dependence on distillation is responsible for the continued widespread use of volatile organic solvents despite their known hazards. The use of switchable-hydrophilicity solvents (SHSs), in combination with water, has been proposed as an alternative to distillation for solvent removal that does not require the use of volatile compounds [1, 2, 3].

A SHS is a solvent which is poorly miscible with water in one form but completely miscible with water in another form and which can be switched between these two forms by a simple change in the system. Amidine and tertiary amine SHSs have been identified [1, 2] which can be switched between the two form by the addition or removal of CO_2 from the system. The change in miscibility is due to an acid-base reaction between either hydrated CO_2 or carbonic acid in the carbonated water and the SHS, resulting in the hydrophilic bicarbonate salt of the protonated SHS (Equation 2.1). This behaviour has been exploited as a method for removing solvent from products such as soybean oil [1], algae oil [4, 5], bitumen [6] and high density polystyrene powder [2].

$$NR_{3\,(aq)} + H_2O_{(l)} + CO_{2\,(g)} \rightleftharpoons HNR^{+}_{3(aq)} + HCO^{-}_{3(aq)} \tag{2.1}$$

The first known SHSs contained amidine functional groups, but were found to be impractical solvents because they are expensive to manufacture [1, 2]. Eight tertiary amine SHSs were then identified which overcame this limitation [2]. However, some of these SHSs have health and safety concerns associated with them, such as toxicity, volatility, or flammability, which would make them less desirable for use in an industrial setting. In this paper, we identify 13 new secondary and tertiary amine SHSs which are commercially available or easily prepared. The amines were selected in order to overcome one or more of the issues presented by previously confirmed SHSs. We compare all of the SHSs in terms of boiling point, flash point, eutrophication potential, toxicity, and effects on skin (where information is available) to identify the safest and most environmentally benign SHSs.

Before we could search for new SHSs, we needed to identify the properties of known SHSs and how they differ from compounds that are not SHS. Amines, amidines, and guanidines that have already been tested for SHS behaviour [1, 2] are listed in Table 2.1. If an organic liquid forms one phase when mixed with water before CO_2 is added, the system is considered monophasic and therefore not an SHS. If an organic liquid forms two phases when mixed with water both before and after CO_2 is added, the system is considered biphasic. If the mixture of organic compound and water forms two phases before CO_2 is added and forms one phase after CO_2 is added, it is an SHS. Some guanidines formed biphasic mixtures with water initially and became monophasic upon exposure to CO_2, but could not be reverted to biphasic mixtures, presumably because guanidines were far too basic. Compounds which displayed this behaviour are considered irreversible and were therefore rejected. The results of these tests are highly dependent on the proportions of water and organic solvent. The results shown in Table 2.1 were reported for 1:1 (v:v) mixtures of water to amine or 2:1 (v:v) mixtures of water to amidine or guanidines.

2.3 Results and Discussion

2.3.1 Selecting Amines for Switchable Behaviour

A variety of new amines were tested, but not all of them displayed SHS behaviour. Fig. 2.1 plots all the amines and amidines tested in this study and previous studies [1, 2] by the log of their octanol-water partition coefficient ($\log K_{ow}$) and the strength of their conjugate acids (pK_{aH}). A trend was observed for the amines tested. First, the amine must have a $\log K_{ow}$ between approximately 1.2 and 2.5 in order to be a SHS. Amines with lower $\log K_{ow}$ were too hydrophilic and formed monophasic mixtures with water in their neutral form. Amines with higher $\log K_{ow}$ were too hydrophobic

Table 2.1: Amines, amidines, and guanidines previously tested for their ability to serve as SHSs at room temperature [1, 2].

Behaviour	Compound	Ratio of Compound to Water (v:v)	log K_{ow} [a]	p$K_{a\mathrm{H}}$
Monophasic	triethanolamine	1:1	-1.51	7.85[7]
Monophasic	N,N,N′,N′-tetramethylethylenediamine	1:1	0.21	9.2[8]
Monophasic	N,N,N′,N′-tetramethylguanidine	2:1	0.3	13.6[9]
Monophasic	N-ethylmorpholine	1:1	0.3	7.70[10]
Monophasic	1,8-diazabicycloundec-7-ene	2:1	1.73	12[9]
Monophasic	N-hexyl-N′,N′-dimethylacetamide	2:1	2.94	12[b]
Irreversible	N″-hexyl-N,N,N′,N′-tetramethylguanidine	2:1	2.82	13.6[c]
Irreversible	N″-butyl-N,N,N′,N′-tetraethylguanidine	2:1	3.52	13.6[c]
Irreversible	N″-hexyl-N,N,N′,N′-tetraethylguanidine	2:1	4.43	13.6[c]
Switchable	triethylamine	1:1	1.47	10.68[11]
Switchable	N,N-dimethylbutylamine	1:1	1.60	10.02[12]
Switchable	N-ethylpiperidine	1:1	1.75	10.45[7]
Switchable	N-methyldipropylamine	1:1	1.96	10.4[13]
Switchable	N-dimethylcyclohexylamine	1:1	2.04	10.48[14]
Switchable	N-butylpyrrolidine	1:1	2.15	10.36[15]
Switchable	N,N-diethylbutylamine	1:1	2.37	10.51
Switchable	N,N-dimethylhexylamine	1:1	2.51	10.18
Switchable	N,N,N′-tripropylbutanamidine	2:1	4.20	12[b]
Switchable	N,N,N′-tributylpentanamidine	2:1	5.99	12[b]
Biphasic	N,N-dimethylaniline	1:1	2.11	5.06[14]
Biphasic	N,N-diisopropylethylamine	1:1	2.28	11.0[16]
Biphasic	tripropylamine	1:1	2.83	10.70[10]
Biphasic	N″-hexyl-N,N,N′,N′-tetrabutylguanidine	2:1	7.91	13.6[c]
Biphasic	trioctylamine	1:1	9.45	10.9[d]

[a] Predicted using ALOGPS software version 2.1 [17, 18, 19].
[b] Estimated to have a pK_{aH} similar to 1,8-diazabicycloundec-7-ene.
[c] Estimated to have a pK_{aH} similar to N,N,N′,N′-tetramethylguanidine.
[d] Estimated to have a pK_{aH} similar to tributylamine (pK_{aH} 10.89) [10].

and formed biphasic mixtures with water even after exposure to CO_2. This trend has been observed for previously identified tertiary amine SHSs [2]. Also, most amines that displayed switchable miscibility with water had pK_{aH} above 9.5. If an amine has insufficient basicity, it will not react with carbonated water enough for a switch from a biphasic to a monophasic mixture. Although SHSs met these criteria, some amines which were not SHSs met these criteria as well, suggesting that these are necessary but not sufficient requirements for switchable behaviour. The two amidine SHSs did not fit these criteria (see the upper right portion of Fig. 2.1), and yet behaved as SHSs for reasons which are unclear.

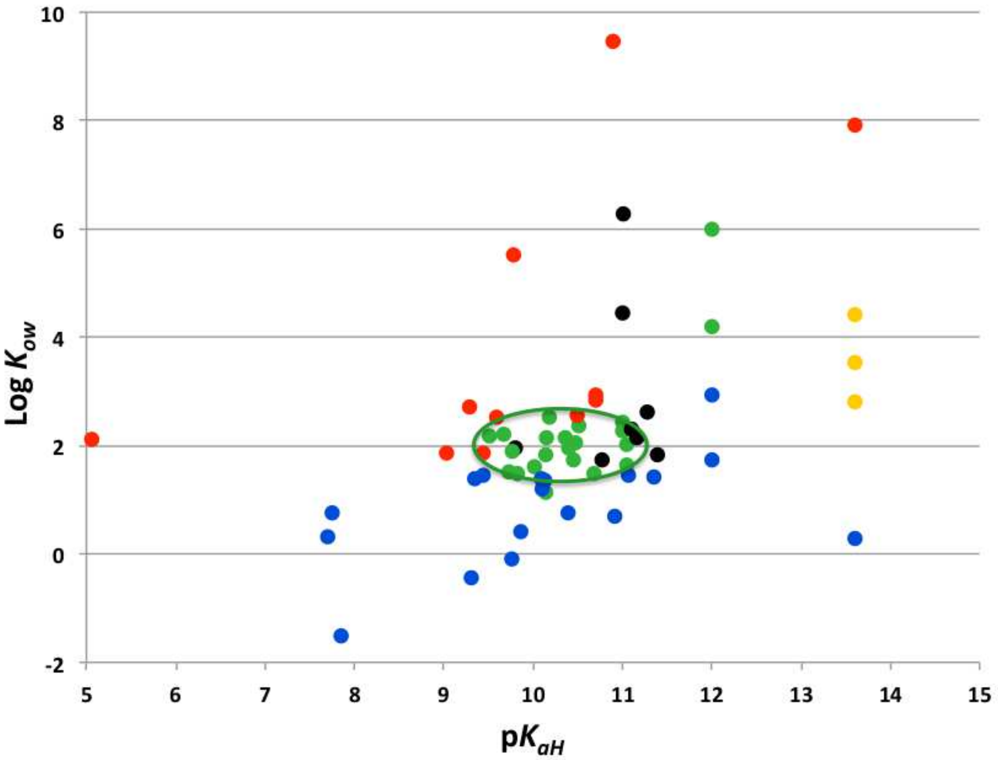

Figure 2.1: All compounds tested for switchable miscibility with water at room temperature and 1:1 or 2:1 volume ratio of water to amine, plotted by their logK_{ow} and pK_{aH} and coloured by their observed behaviour: monophasic (blue), irreversible (yellow), SHS (green), biphasic (red), and precipitation upon CO_2 addition (black). All amine SHSs fall within the green oval.

2.3.2 Amines with High Boiling and Flash Points

Non-volatile SHSs can be designed to capitalize on the previously described advantages of SHS separations. In order to reduce volatility, SHSs with large molecular weights are preffered, but increasing the molecular weights by simply extending the alkyl chains would increase the logK_{ow} excessively so that the bicarbonate salt of the amine would not be sufficiently soluble in carbonated water and the amine will therefore not be a SHS. By including hydrophilic functional groups in the structure of an amine while increasing the length of the alkyl chains, the solvent can be tailored to be less volatile and yet still fit within the logK_{ow} range required for SHS behaviour.

Hydrophilic functional groups also affect the basicity of the amine. The inductive effects of a functional group can decrease the pK_{aH} of the amine, depending on the proximity of the group to the N centre. When designing a SHS with these functional groups, the exact positions of the amine and the electron withdrawing group must be considered so that the amine will be a sufficiently strong base to act as a SHS. Of the tertiary amines tested which incorporated other functional groups, six formed monophasic mixtures with water, five formed biphasic mixtures with water, and six displayed switchable miscibility (Table 2.2). These six new SHSs all followed the logK_{ow} and pK_{aH} criteria suggested in Fig 2.1 except for N,N-dimethylbenzylamine. At a 1:1 volume ratio of water to amine, mixtures of water and N,N-dimethylbenzylamine remain biphasic even after prolonged bubbling of CO_2 through solution. This behaviour is expected because N,N-dimethylbenzylamine (pK_{aH} = 9.03) is a weaker base than most SHSs and will not be sufficiently protonated by carbonated water to form a monophasic mixture with water at a 1:1 volume ratio. At a 5:1 volume ratio of water to amine, the amine displays switchable miscibility. Adding more water to the mixture increases the amount of amine in the aqueous phase enough to form a monophasic mixture after addition of CO_2 without also resulting in a monophasic mixture when CO_2 is removed. Thus a liquid can be a SHS at one volume ratio, but not a SHS at another volume ratio.

The different functional groups investigated were alcohols, esters, ketones, acetals, and aromatic rings, each of which will affect the pK_{aH} of the amine differently. Alcohols placed two carbons away from a tertiary amine do not lower the amine's pK_{aH} enough to prevent an amino alcohol from displaying SHS behaviour. Aromatic rings must also be 2 carbons away from a tertiary amine for SHS behaviour to be observed at a 1:1 volume ratio of water to amine. N,N-Dimethylaniline (pK_{aH} 5.18) is not a strong enough base to have SHS behaviour, while N,N-dimethylbenzylamine (pK_{aH} 9.03) displays SHS behaviour in a 5:1 volume ratio of water to amine. Finally, N,N-dimethylphenethylamine (pK_{aH} 9.51) has SHS behaviour at a 1:1 volume ratio of water to amine. Ester groups must be 3 carbons away from a tertiary amine for an amino ester to display switchable miscibility, as evidenced by the glycine derivative and amino propanoates, which are not SHSs, and the amino butanoate, which is an SHS.

The SHSs identified in Table 2.2 are less volatile than trialkylamine SHSs. The SHSs with additional functional groups all have boiling points above 180°C and predicted flash points above 50°C (Table 2.4, discussed later). By comparison, the least volatile trialkylamine SHS, N,N-dimethylcyclohexylamine, has a boiling point of 162°C and a flash point of 41°C. The differences between the boiling and flash points of trialkylamine SHSs and SHSs with additional functional groups shows that

Table 2.2: Tertiary amines with other functional groups tested for switchable behaviour

Behaviour	Compound	$\log K_{ow}$ [a]	$\mathrm{p}K_{a\mathrm{H}}$
Monophasic	N,N-dimethylaminoethanol	-0.44	9.31[12]
Monophasic	N,N-dimethylaminopropanol	-0.08	9.76[20]
Monophasic	N,N-diethylaminoethanol	0.41	9.87[12]
Monophasic	N,N-diethylglycine methyl ester	0.76	7.75
Monophasic	N,N-diethylaminopropanol	0.77	10.39
Monophasic	5-(diethylamino)pentan-2-one	1.21	10.1[21]
Monophasic	ethyl 3-(diethylamino)propanoate	1.40	9.35
Switchable	diisopropylaminoethanol	1.16	10.14[22]
Switchable	4,4-diethoxy-N,N-dimethylbutanamine	1.48	9.83
Switchable	ethyl 4-(diethylamino)butanoate	1.82	10.15
Switchable[b]	N,N-dimethylbenzylamine	1.86	9.03[11]
Switchable[c]	5-(dipropylamino)pentan-2-one	2.15	10.15
Switchable	N,N-dimethylphenethylamine	2.18	9.51[23]
Switchable	dibutylaminoethanol	2.20	9.67[24]
Biphasic	propyl 3-(diethylamino)propanoate	1.85	9.45
Biphasic	N,N-dibutylaminopropanol	2.56	10.5
Biphasic	ethyl 2-(dipropylamino)propanoate	2.72	9.29
Biphasic	N,N-dibutylaminobutanol	2.93	10.7

[a] Predicted using ALOGPS software version 2.1 [17, 18, 19].
[b] At a 5:1 volume ratio of water to amine.
[c] At a 2:1 volume ratio of water to amine.

the design strategy for less-volatile SHSs is successful.

2.3.3 Secondary Amines

Secondary amines have an alternate reactivity pathway which allows them to uptake CO_2 faster than tertiary amines. Like amidines and tertiary amines, secondary amines can be converted to bicarbonate salts upon exposure to carbon dioxide and water, but they can also undergo a direct reaction with carbon dioxide to form ammonium carbamate salts (Equation 2.2). This alternative reaction occurs faster than the bicarbonate salt formation, so secondary amine SHSs are likely to switch faster than tertiary amines [25]. However, the energy and temperature required to remove CO_2 from an aqueous ammonium carbamate solution is much larger than that required to remove CO_2 from an ammonium bicarbonate solution [25]. Therefore, using a secondary amine SHS can be more energy-intensive than using a tertiary amine SHS.

$$2\,R_2NH + CO_2 \rightleftharpoons R_2NH_2^+ + R_2NCOO^- \tag{2.2}$$

While the increased rate of reaction of secondary amines is appealing, the higher energy cost of regeneration is not, so it is important to prevent significant formation of carbamate salts of an SHS. Sterically hindered amines are known to either not form carbamates or form destabilized carbamates which are rapidly hydrolyzed to bicarbonates [25]. Carbamates may form as a kinetic product before being converted to bicarbonates, allowing for rapid uptake of CO_2 without the large energy requirements for removing CO_2 [25]. A sterically hindered secondary amine SHS may switch rapidly without increased energy requirements.

Of the secondary amines tested for switchable behaviour, three formed monophasic mixtures with water, five formed biphasic mixtures with non-carbonated water but formed a precipitate upon exposure to CO_2, and six displayed switchable miscibility (Table 2.3). X-ray crystallography of the precipitate formed from dibutylamine confirmed that it was the bicarbonate salt of the amine (Fig. 2.2). This result suggests that the bicarbonate salts of some secondary amines are not sufficiently soluble in water to make the amines useful as SHSs at a 1:1 volume ratio.

Increasing the temperature of the mixture or increasing the volume ratio of water to amine might result in complete dissolution of the bicarbonate salt in the water. A precipitate forms when CO_2 is bubbled through a 1:1 mixture of water and propyl-3-(sec-butylamino)propanoate at room temperature. If the volume ratio is adjusted to 2:1 water to amine and the mixture is heated to 50°C, bubbling CO_2 through the mixture forms a monophasic liquid which can be returned to a biphasic mixture if argon is bubbled through it while it is heated to 65°C. Other secondary amines which

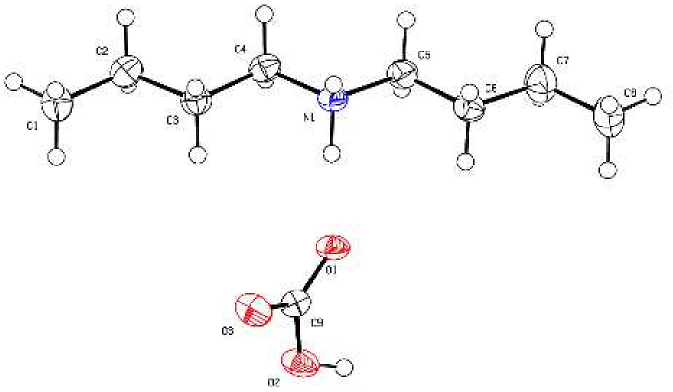

Figure 2.2: The structure of dibutylammonium bicarbonate, recrystallized from the solid formed after bubbling CO_2 through a dibutylamine/water mixture

form precipitates might display SHS behaviour under different conditions. Some secondary amines, such as N-propyl-sec-butylamine, form precipitates in carbonated water at room temperature but the heat released from the exothermic reaction of the amine and carbonated water can warm the solution enough to dissolve the bicarbonate salts completely.

Six secondary amines were confirmed to display SHS behaviour. With the exception of dipropylamine, each of these secondary amine SHSs contained sec-butyl or isopropyl groups to destabilize carbamate salts. The tert-butyl amine formed a precipitate upon bubbling CO_2 through the system which may be a consequence of the volume ratio of water to amine used. Converting bicarbonate salts of sterically hindered secondary amine SHSs to CO_2 and neutral amine was achieved at 65°C while passing N_2 through solution. Dipropylamine/water mixtures became biphasic upon heating to 65°C even without bubbling N_2 through solution, but the solution became monophasic again when cooled to room temperature. Dipropylamines temperature-dependent miscibility with carbonated water has been observed before [26], but is not the desired behaviour for a SHS. When the solution was heated to 90°C for 2 h without N_2 passing through it, it became biphasic and remained biphasic when cooled to room temperature. The increased temperature requirement to remove CO_2 from the solution is consistent with the formation of carbamate salts, as expected for sterically unhindered secondary amines such as dipropylamine. ^{13}C NMR analysis of carbonated water/dipropylamine solutions confirmed the presence of both bicarbonate salts and carbamate salts in solution, while no carbamates were observed for mixes of carbonated water with sterically-hindered secondary amine SHSs.

Every secondary amine SHS, except di-sec-butylamine, switched from a biphasic solution to a monophasic solution after less than 10 min of bubbling CO_2 through the solution, while tertiary amines switch after 20 to 120 min. Di-sec-butylamine switched at a pace comparable to tertiary amine SHSs. The two sec-butyl groups may be either decreasing the rate of carbamate formation substantially or preventing carbamate formation completely. Evidently, one branching group near the amine is enough to lower the energy requirements for removing CO_2 while still allowing for a rapid switch from biphasic to monophasic solutions.

2.3.4 Risk Evaluation of SHSs

In order for SHSs to be considered for use industrially, it is important to consider their effects on health and the environment, preferably in comparison to the solvents that they would replace. In order to identify the safety and environmental effects of SHSs, the LD_{50} (oral, rat), boiling point, flash point, eutrophication potential (EP), and skin effects of all SHSs identified in this study and previous studies [1, 2] are compared in Table 2.4. The reported safety and environmental data reveal trends in

Table 2.3: Secondary amines tested for switchable behaviour

Behaviour	Compound	$\log K_{ow}$ [a]	pK_{aH}
Monophasic	diethylamine	0.71	10.92[7]
Monophasic	ethyl 3-(tert-butylamino)propanoate	1.38	10.09
Monophasic	tert-butylethylamine	1.42	11.35
Monophasic	diisopropylamine	1.46	11.07[7]
Switchable	ethyl 3-(sec-butylamino)propanoate	1.53	9.73
Switchable	dipropylamine	1.64	11.05[11]
Switchable	butyl 3-(isopropylamino)propanoate	1.90	9.77
Switchable[b]	propyl 3-(sec-butylamino)propanoate	1.95	9.80
Switchable	N-propyl-sec-butylamine	2.03	11.05
Switchable	di-sec-butylamine	2.43	11.0[27]
Precipitates	ethyl 3-(isobutylamino)propanoate	1.46	9.45
Precipitates	ethyl 4-(tert-butylamino)butanoate	1.75	10.77
Precipitates	tert-butylisopropylamine	1.84	11.39
Precipitates	dibutylamine	2.61	11.28[7]
Precipitates	dihexylamine	4.46	11.0[28]

[a] Predicted using ALOGPS software version 2.1 [17, 18, 19].
[b] Requires a 2:1 volume ratio of water to amine and solution must be heated to 50°C.

the safety risks and environmental impacts of SHSs. We used hexane and toluene as representative conventional (non-switchable) solvents for comparison.

The toxicities of SHSs were compared using oral LD_{50} data (rat). Many SHSs do not have reported LD_{50} values. In these cases, the U.S. Environmental Protection Agency's Toxicity Estimation Software Tool (TEST) was used to predict oral LD_{50} values [29]. We find that the predicted toxicities of amines are within a factor of 3 of reported LD_{50} values 95% of the time. Despite the inherent inaccuracy of toxicity predictions, we expect that SHSs with predicted LD_{50} values above 2000 mg/kg are less toxic than SHSs with LD_{50} values of around 500 mg/kg or lower. Oxygen-containing SHSs have consistently higher LD_{50} values than dialkyl- and trialkylamine SHSs. Multiple different oral LD_{50} values have been reported for toluene. While toluene is less toxic than dialkyl- and trialkylamine SHSs, the varying reports of its LD_{50} and the uncertainty of the predicted LD_{50} values for other SHSs prevent us from drawing further conclusions. According to the LD_{50} data, hexane is much safer than every SHS. However, LD_{50} is a measure of acute toxicity, so solvents with chronic toxicity may appear safe even though they are not. For example, hexane is a known chronic neurotoxin, a serious problem that is not made evident by LD_{50} data [30, 31, 32].

The more volatile SHSs are not advantageous over toluene in terms of inhalation toxicity but the less volatile SHSs are probably much safer than toluene. There is little data regarding this form of toxicity for the SHSs. The inhalation LC_{50} values (rat, 4 h) for triethylamine and dipropylamine are 4.1 g/m^3 and 4.4 g/m^3, respectively [33], while the corresponding values for toluene and hexane are 30.1 g/m^3 and 169 g/m^3, respectively [78, 79]. Dimethylcyclohexane has a reported LC_{50} (rat, 2 h) of 1.9 g/m^3 [33]. The less-volatile SHSs may not pose an inhalation toxicity risk because their vapour pressures are much lower. For example the vapour pressure of propyl-3-(sec-butylamino)propanoate at 25°C was estimated to be 13 Pa using a nomograph. By comparison, the vapour pressures of triethylamine, toluene, and hexane at 25°C are 9670 Pa [80], 3804 Pa [81] and 20240 Pa [82], respectively. Propyl-3-(sec-butylamino)propanoate and other low-volatility amines are less likely to be inhaled because of their low vapour pressure, making them less of an inhalation toxicity risk than volatile solvents.

The boiling and flash points of SHSs give an indication of the volatility of the solvents. Flash points also show how flammable solvents are. If the boiling point at atmospheric pressure is not known, a value was estimated by extrapolating from a reduced-pressure boiling point. The TEST program can be used to predict flash points if the flash point of an SHS is not known. These predictions are accurate to within 8°C most of the time if the experimental flashpoint is above 20°C. Almost every SHS is safer than toluene and hexane in terms of volatility and flammability.

Table 2.4: Properties of known SHSs relating to safety hazards and environmental impacts of solvents

Substance	LD_{50} (oral, rat) (mg kg^{-1})	Boiling Point (°C)	Flash Point (°C)	Eutrophication Potential^{a}	Skin Effects	log K_{ow}^{b}
N,N,N′-Tributylpentanamidine	4000^{c}	367^{c}	176^{c}	0.17	n/a	5.92
N,N,N′-Tripropylbutanamidine	700^{c}	303^{c}	137^{c}	0.18	n/a	4.20
N,N-Dimethylcyclohexylamine	348[33]	159[34]	43[35]	0.17	Corrosive (1B)[36]	2.04
N-Ethylpiperidine	280[37]	128[38]	17[37]	0.17	Corrosive (1B)[37]	1.74
N-Butylpyrrolidine	51[39]^{d}	156[39]	35[39]	0.17	Irritant[40]	2.15
N,N-Dimethylhexylamine	500^{c}	148[41]	34[42]	0.17	Corrosive (1B)[42]	2.51
N,N-Dimethylbutylamine	188[43]	95[44]	5[43]	0.18	Corrosive (1A)[43]	1.60
N,N-Diethylbutylamine	300^{c}	136[45]	24[46]	0.17	Corrosive (1B)[46]	2.37
N-Methyldipropylamine	267^{c}	117[47]	3[48]	0.18	Corrosive (1B)[48]	1.96
Triethylamine	460[33]	89[34]	9[49]	0.18	Corrosive (1A)[50]	1.47
N,N-Diisopropylaminoethanol	940[51]	190[52]^{e}	64[53]	0.15	Corrosive (1B)[53]	1.16
N,N-Dibutylaminoethanol	1070[33]	230[54]^{e}	95[55]	0.15	Corrosive (1B)[55]	2.15
4,4-Diethoxy-N,N-dimethylbutanamine	2000^{c}	270[56]^{e}	70[57]	0.13	n/a	1.48
Ethyl 4-(diethylamino)butanoate	7000^{c}	220^{e}	77^{c}	0.13	n/a	1.82
N,N-Dimethylphenethylamine	300^{c}	210[58]	71[59]	0.16	Irritant[59]	2.18
Dipropylamine	460[33]	108[60]	17[49]	0.18	Corrosive (1A)[61]	1.64
Di-sec-butylamine	300^{c}	135[62]	21[63]	0.17	Corrosive (1A)[63]	2.46
5-Dipropylaminopentanone	3000^{c}	280^{e}	72^{c}	0.15	n/a	2.14
Ethyl 3-(sec-butylamino)propanoate	5000^{c}	210^{e}	93^{c}	0.13	n/a	1.53
Propyl 3-(sec-butylamino)propanoate	3000^{c}	220^{e}	89^{c}	0.13	n/a	1.94
Butyl 3-(isopropylamino)propanoate	3000^{c}	230^{e}	105^{c}	0.13	n/a	1.90
N-Propyl-sec-butylamine	300^{c}	124[64]	15^{c}	0.18	Corrosive (1B)[65]	2.03
N,N-Dimethylbenzylamine	265[33]	183[66]	53[67]	0.16	Corrosive (1B)[67]	1.86
Toluene	636 - 6400 [33, 68, 69, 70]^{f}	110[71]	4[49]	0.13	Irritant [72]	2.49
Hexane	28710[33]	69[73]	22[49]	0.15	Irritant[74]	3.55

[a] Calculated as mass equivalents of phosphate.

[b] Predicted using ALOGPS software version 2.1 [17, 18, 19].

[c] Predicted using TEST software version 4.1 [29].

[d] Oral LD_{50} value for mice.

[e] Boiling point at atmospheric pressure extrapolated from boiling point at reduced-pressure.

[f] Several LD_{50} values have been reported for toluene [33, 68, 69, 70]. The reported LD_{50} value of 636 mg kg^{-1} may be the result of a miscalculation [69, 70].

SHS containing another functional group in addition to an amine were designed to be less volatile and less flammable, and the data confirms that they are safer than other SHSs by these metrics. Under the UN globally-harmonized system of classification, these heavier SHSs would be classified as combustible rather than flammable liquids (flash points $> 60°C$).[83]

The eutrophication potential of the SHSs was calculated using a modified version of the equation described by Heijungs et al. [84], replacing chemical oxygen demand with theoretical oxygen demand, which was calculated using an equation described by Baker et al. [85]. The implications of these equations are that lower nitrogen content and higher oxygen content in a compound lowers its eutrophication potential. As a result, oxygen containing SHS have less eutrophication potential than other SHSs, with amino esters having the lowest potential. Indeed, amino ester SHSs have eutrophication potentials similar to toluene and lower than hexane, despite their nitrogen content.

Skin effects are another concern for SHSs; 13 of the SHSs are corrosive. In order to differentiate between different levels of corrosion, different classes of corrosion as defined by the Globally Harmonized System were used where information was available [83]. A class 1A corrosive substance shows effects after 3 minutes of exposure and less than 1 hour of observation. A class 1B corrosive substance shows effects after 1 hour of exposure and less than 14 days of observation. Class 1A corrosive SHSs should be avoided. By comparison, four of the SHSs and many conventional solvents like toluene and hexane are irritants, rather than corrosive liquids. For many of the SHSs, skin effect data is unavailable.

Bioaccumulation is not a concern for SHSs. Compounds with $\log K_{ow}$ values below

3.5 are considered to have low bioaccumulation potential [86]. All known amine SHSs have logK_{ow} between approximately 1.2 and 2.5. The amidine SHSs would not bioaccumulate, despite their high logK_{ow} values, because they are hydrolytically unstable and therefore would not likely persist in the environment long enough to pose a bioaccumulation risk. Some conventional solvents (e.g. hexane) have moderate bioaccumulation potential, while others have low potential (e.g. toluene).

The use of volatile solvents results in volatile organic compound emissions and contributes to smog formation [87]. With regards to this environmental concern, solvents are generally expected to be more benign if they are less volatile. SHSs with additional functional groups are much less volatile than conventional solvents like hexane and toluene. While volatile SHSs like triethylamine will have no advantages over conventional solvents, the low-volatility SHSs likely have less potential to contribute to smog formation than conventional solvents.

The persistence of a solvent when it is released into the environment is another concern when the solvent has a high toxicity. The persistence of non-toxic compounds are not as concerning. Compounds can degrade by a number of different pathways and it can be difficult to predict their persistence. However, some degradation trends in the atmosphere relating to chemical structures have been observed [88]. Quaternary carbon centres, extensive branching, heterocycles, and tertiary amines tend to decrease degradability. Features that increase degradability are oxygen atoms (particularly esters), unsubstituted alkyl chains of 4 or more, and unsubstituted phenyl rings.

When absorbed in aqueous solutions, secondary amine SHSs are expected to be more biodegradable than tertiary amine SHSs. Biodegradation is more likely in nutrient-rich environments such as water and soil. Howard et al. found that tertiary amines are poorly biodegradable [89]. Eide-Haugmo et al. suggest that secondary amines are more degradable than tertiary amines [90]. Although amine biodegradation data is sparse and many exceptions are apparent, the literature data does support the notion that secondary amines will biodegrade in water more readily than tertiary amines [89, 90, 91, 92, 93, 94]. For example, dipropylamine is biodegradable while triethylamine is not [94, 95]. Not all tertiary amines will persist however. The biodegradation of N,N-dimethylcyclohexylamine is not rapid, but it is considered to be biodegradable in an aqueous environment (Zahn-Wellens test) [96]. The available data also indicates that compounds with quaternary carbons are more resistant to biodegradation than straight chain compounds. A common opinion is that any branching will decrease biodegradability. However, Boethling et al. report that this is an oversimplification and only extensive branching and quaternary carbons show a trend of decreasing degradability in water and in soil [85]. Many secondary amine SHS contain a branching group to destabilize carbamate formation. An ideal secondary amine SHS would include one branching group to destabilize the carbamate product without significantly decreasing its biodegradability.

With regard to this information, secondary amino ester SHSs are expected to be the least persistent, particularly butyl 3-(isopropylamino)propanoate because it contains an n-butyl group. Tertiary amine SHSs containing other functional groups and dialkylamine SHSs are second choices, while trialklyamine SHSs will likely persist longer than the other SHSs. Toluene and hexane contain groups favourable to degradation and no groups resistant to degradation in the atmosphere. These conventional solvents are both biodegradable [97, 98]. Trialkylamine SHSs should be more persistent than conventional solvents, but we expect secondary amine SHSs and tertiary amine SHS with a second functional group to have biodegradability comparable to or better than conventional solvents.

From these trends, the most benign SHSs can be determined. The data available for oxygen-containing SHSs suggest that they are less toxic and less volatile than di- and tri-alkyl amine SHSs. They are also no more corrosive and have lower eutrophication potentials, making them the most benign SHSs identified according to the metrics listed in this study. The amidine SHSs also have favourable safety and environmental properties apart from a larger eutrophication potential and likely corrosivity, but they are unlikely ever to be used because of their high cost of synthesis. No differences between secondary and tertiary amine SHSs are apparent from the data in Table 2.4, but the secondary amines are likely to be more biodegradable. Not every risk is identified in Table 2.4. There is insufficient data to comment on chronic toxicity or carcinogenicity.

There are other considerations which can also be used to differentiate between SHSs. Some SHSs, such as the amino acetal and the amidines are prone to hydrolysis and are likely to degrade over time. Dipropylamine forms a stable carbamate salt and more energy must be put into the system to convert the salt back into CO_2 and neutral amine. Some SHSs also require different amounts of water to display switchability. Most SHSs work at a 1:1 volume ratio, but some require a 2:1 or even 5:1 water:amine volume ratio. The amount of energy required to heat the water when removing CO_2 increases as the amount of water increases. Some SHSs switch faster than others as well. In particular, secondary amines switch from biphasic to monophasic mixtures faster than tertiary amines. None of these factors are apparent from the information given in Table 2.4, but they can affect the overall viability of an SHS.

2.4 Conclusions

Several new SHSs have been identified, including secondary amines and amines incorporating an additional functional group. Amines which display SHS behaviour typically have $\log K_{ow}$ between 1.2 and 2.5 and $\mathrm{p}K_{aH}$ above 9.5. Dimethylbenzylamine is an exception ($\mathrm{p}K_{aH}$ 9.03), but is only switchable if the volume of water is much larger than the volume of amine. Secondary amines can also display switchable behaviour but can form carbamate salts and precipitate as bicarbonate salts. Secondary amine SHSs can be designed to avoid significant carbamate formation by making them sterically hindered. Amines incorporating other functional groups are more benign than other SHSs, commonly having lower toxicity, volatility, flammability, and eutrophication potential. Compared to toluene, the secondary amine ester SHSs are predicted to be safer for health and the environment in terms of flammability, smog formation, inhalation toxicity, and bioaccumulation (lower K_{ow}). They are comparable to toluene in terms of eutrophication and possibly biodegradation. The variety of compounds identified and their different properties show that SHSs can be designed to meet the requirements of an application.

2.5 Experimental

Chemicals were used as received. Amines were commercially available (Sigma-Aldrich, TCI, Fisher) except for amino propanoate/ butanoate esters and amino ketones, which were synthesized and characterized as described below. Argon (99.998%) and CO_2 (chromatographic grade) were purchased from Praxair.

2.5.1 Testing for Switchable Behaviour

To confirm the switchable miscibility, amines were mixed with water in a $1:1$ volume ratio. If two phases were observed, CO_2 was bubbled into the solution through a gas dispersion tube (Ace Glass, 2550 micron porosity) for 2 h. If the mixture became monophasic, N_2 was bubbled into the solution through a gas dispersion tube for 2 h while the solution was heated to 65°C. If the mixture became biphasic again, the amine was classified as a SHS. Other volume ratios were attempted for some amines.

2.5.2 Evaluation

LogK_{ow} values were predicted using ALOGPS 2.1 [17, 18, 19]. pK_{aH} values were found from literature or determined titrimetrically. Flash points, skin effects, and LD_{50} values were found from literature or MSDS. If flash point or LD_{50} values were unavailable, they were calculated using the TEST program [29]. Eutrophication potentials (EP) were calculated using a variation of the method proposed by Heijungs et al., which calculates the eutrophication potential of a compound based on its molecular weight (MW), the number of phosphorus and nitrogen atoms it contains (ν_{P} and ν_{N}), and its theoretical oxygen demand (ν_{ThOD}) (eqn (2.3) and (2.4)) [81]. Theoretical oxygen demands were calculated using the method described by Baker, Milke, and Mihelcic (eqn (2.5) and (2.6)) [82], which assumes that nitrogen atoms are converted to NH_3 and that all carbon atoms are completely oxidized. The reference compound for eutrophication potential is PO_4^{3-}.

$$\nu_{\mathrm{tot},i} = \nu_{\mathrm{P},i} + \nu_{\mathrm{N},i}/16 + \nu_{\mathrm{ThOD},i}/138 \tag{2.3}$$

$$\mathrm{EP}_i = \frac{\nu_{\mathrm{tot},i}/\mathrm{MW}_i}{\nu_{\mathrm{tot,ref}}/\mathrm{MW}_{\mathrm{ref}}} \tag{2.4}$$

$$\mathrm{C_aH_bN_cO_d} + \mathrm{nO_2} \longrightarrow \mathrm{aCO_2} + \frac{b-3c}{2}\mathrm{H_2O} + \mathrm{cNH_3} \tag{2.5}$$

$$\nu_{\mathrm{ThOD}} = 2n = 2a + \frac{b-3c}{2} - d \tag{2.6}$$

2.5.3 Dibutylammonium Bicarbonate Crystal Formation

Dibutylamine (5 mL) and water (5 mL) were combined in a vial. CO_2 was bubbled through the mixture until a large quantity of precipitate formed. The mixture was heated to 40°C, resulting in a biphasic mixture with no solids. Upon cooling to room temperature, needle-like crystals formed at the interface between the liquid phases.

2.5.4 Observation of Secondary Amine Speciation in Carbonated Water

Amine (dipropylamine, di-sec-butylamine, or sec-butylisopropylamine, 1 mL) was mixed with 1 mL H_2O in a vial and CO_2 was bubbled through the solution until it became monophasic. CH_3CN (0.2 mL) was added to solution as a reference compound and the solution was characterized by ^{13}C $\{^1$H$\}$ NMR spectroscopy.

2.5.5 Measuring the pK_{aH} of Amines

For most amines, a ∼20 mL solution containing ∼0.02 g amine in distilled water was titrated with ∼0.1 M HCl. The pH of the solution was recorded after each addition of titrant (Orion 4 Star pH meter, Thermo Scientific). The equivalence point was determined using a derivative plot and the pH at the half equivalence point was taken as the pK_{aH} of the amine. Titrations were performed at least twice.

Dibutylaminobutanol and dibutylaminopropanol were not sufficiently soluble in water to measure their aqueous pK_{aH} directly. The pK_{aH} of these compounds were measured in ethanol-water solutions and extrapolated to a completely aqueous solution using the method described by Gowland and Schmid [96].

2.5.6 Synthesis

Amino esters and ketones were synthesized using procedures adapted from literature for similar compounds [97, 98]. NMR spectra were collected on a Bruker Avance-500 or a Bruker Avance-300 NMR spectrometer. IR spectra were collected with a Varian 640 FT-IR spectrometer. Mass Spectra were collected with a Perkin Elmer Clarus 600 T mass spectrometer connected to a Perkin Elmer Clarus 680 gas chromatograph.

Ethyl 3-(diethylamino)propanoate

Ethyl acrylate (9.2 g, 0.092 mol) and diethylamine (6.7 g, 0.092 mol) were added to a round bottom flask and stirred for 24 h. Distillation under vacuum afforded the pure product (14.9 g, 94% yield); bp 57-59°C (4 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J = 7.2 Hz, 6H), 1.18 (t, J = 7.2 Hz, 3H), 2.36 (t, J = 7.4, 2H), 2.44 (q, J = 7.2 Hz, 4H), 2.71 (t, J = 7.4 Hz, 2H), 4.05 (q, J = 7.2 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 12.12, 14.18, 32.49, 46.93, 48.22, 60.34, 172.75; $\nu_{\max}$ (ATR) cm^{-1} 2972, 2935, 2874, 2806, 1735 (C=O), 1448, 1371, 1298, 1251, 1198, 1118, 1094, 1048, 984, 856, 787; *m/z* (EI) 173 (6), 158 (15), 144 (3), 130 (3), 116 (1), 99 (1), 86 (100), 73 (6), 72 (6), 58 (15), 56 (10), 55 (15); Anal. Calcd for $C_9H_{19}NO_2$: C 62.39, H 11.05, N 8.09; found C 62.15, H 11.05, N 8.07. The ^{1}H NMR data match literature values [97].

Ethyl 3-(dipropylamino)propanoate

Using the same procedure as for ethyl 3-(diethylamino)propanoate, 4.0 g (0.040 mol) of ethyl acrylate yielded 6.2 g product (77% yield); bp 76-77°C (4 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80 (t, J = 7.4 Hz, 6H), 1.19 (t, J = 7.1 Hz, 3H), 1.38 (apparent sextet, J = 7.4 Hz, 4H), 2.30 (t, J = 7.4 Hz, 4H), 2.36 (t, J = 7.4 Hz, 2H), 2.71 (t, J = 7.4 Hz, 2H), 4.06 (q, J = 7.1 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 11.65, 14.08, 20.31, 32.50, 49.56, 56.06, 60.12, 172.78; $\nu_{\max}$ (ATR) cm^{-1} 2959, 2937, 2873, 2805, 1736 (C=O), 1463, 1371, 1341, 1301, 1250, 1192, 1078, 1053, 855, 791; *m/z* (EI) 201 (9), 172 (100), 156 (2), 144 (12), 130 (4), 114 (59), 101 (6), 86 (13), 84 (27), 72 (26), 70 (12), 56 (10), 55 (26); Anal. Calcd for $C_{11}H_{23}NO_2$: C 65.62, H 11.52, N 6.96; found C 65.63, H 11.60, N 6.97. The ^{1}H NMR data matches literature values [97].

Ethyl 4-(diethylamino)butanoate

Ethyl 4-bromobutanoate (5.0 g, 0.026 mol) and diethylamine (8.8 g, 0.12 mol) were added to a round bottom flask containing 20 ml acetonitrile. The mixture was stirred at 65°C for 24 h. The resulting solution was concentrated by distillation, added to 25 ml 1 M NaOH, and extracted with 3 × 25 ml hexanes. Distillation under vacuum afforded the pure product (3.20 g, 66% yield); bp 65°C (4 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 7.1 Hz, 6H), 1.19 (t, J = 7.1 Hz, 3H), 1.70 (p, J = 7.3 Hz, 2H), 2.26 (t, J = 7.3 Hz, 2H), 2.37 (t, J = 7.3 Hz, 2H), 2.4 (q, J = 7.1 Hz, 4H) 4.07 (q, J =

7.1 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 11.81, 14.17, 22.39, 32.20, 46.81, 52.08, 60.01, 173.61; $\nu_{\max}$ (ATR) cm^{-1} 2969, 1735 (C=O), 1184; *m/z* (EI) 187 (6), 172 (3), 158 (1), 142 (12), 115 (5), 114 (6), 98 (2), 86 (100), 58 (9), 56 (5); Anal. Calcd for $C_{10}H_{21}NO_2$: C 64.12, H 11.31, N 7.48; found C 64.12, H 11.44, N 7.48.

Ethyl 3-(*sec*-butylamino)propanoate

Ethyl acrylate (4.5 g, 0.045 mol) and sec-butylamine (6.6 g, 0.9 mol) were added to a round bottom flask and stirred for 24 h. Distillation afforded the pure product (7.0 g, 89% yield); bp: 65°C (4 torr): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.77 (t, J = 7.4 Hz, 3H), 0.91 (d, J = 6.2 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H), 1.20 (m, 1H), 1.35 (m, 1H), 2.37 (t, J = 6.6 Hz, 2H), 2.44 (apparent sextet, J = 6.2 Hz, 1H), 2.75 (m, 2H), 4.02 (q, J = 7.2 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 10.1, 14.1, 19.7, 29.4, 34.8, 42.2, 54.1, 60.1, 172.7; $\nu_{\max}$ (ATR) cm^{-1} 3331 (N−H), 2963, 2932, 2875, 1731 (C=O), 1463, 1372, 1255, 1186, 1096, 1056, 1028, 788, 734; *m/z* (EI) 172, 158 (7), 144 (94), 130, (5), 112 (7), 98 (65), 86 (56), 84 (7), 70 (37), 56 (100); Anal. Calcd for $C_9H_{19}NO_2$: C 62.39, H 11.05, N 8.09; found C 62.29, H 11.29, N 8.04.

Ethyl 3-(*tert*-butylamino)propanoate

Using the same procedure as for ethyl 3-(sec-butylamino)propanoate, 1.9 g (0.019 mol) ethyl acrylate and 2.9 g (0.040 mol) tert-butylamine yielded 1.7 g product (51% yield); bp 62°C (4 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.21 (t, J = 7.1 Hz, 2H), 2.43 (t, J = 6.6 Hz, 2H), 2.77 (t, J = 6.6 Hz, 2H), 4.09 (q, J = 7.1 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 14.1, 28.9, 35.5, 38.0, 50.3, 60.2, 172.9; $\nu_{\max}$ (ATR) cm^{-1} 3319 (N−H), 2964, 2868, 1731 (C=O), 1362, 1230, 1174, 1099, 102; *m/z* (EI), 173 (1), 158 (94), 144 (3), 130 (4), 116 (5), 112 (31), 86 (50), 70 (100), 58 (20), 57 (21), 56 (11), 55 (19); Anal. Calcd for $C_9H_{19}NO_2$: C 62.39, H 11.05, N 8.09; found C 62.28, H 11.13, N 8.07.

Ethyl 3-(isobutylamino)propanoate

Using the same procedure as for ethyl 3-(sec-butylamino)propanoate, 1.9 g (0.019 mol) ethyl acrylate and 3.1 g (0.042 mol) isobutylamine yielded 2.4 g product (73% yield); bp: 68°C (4 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (d, J = 6.6 Hz, 6H), 1.24 (t, J = 7.1 Hz, 3H), 1.36 (broad, 1H) 1.71 (apparent nonet, J = 6.7 Hz, 1H), 2.40 (d, J = 6.8 Hz, 2H), 2.48 (t, J = 6.5 Hz, 2H), 2.84 (t, J = 6.5 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 14.1, 20.6, 28.3, 34.8, 45.1, 57.7, 60.2, 173.1; $\nu_{\max}$ (ATR) cm^{-1} 3338 (N−H), 2954, 2871, 2821, 1731 (C=O), 1467, 1372, 1254, 1186, 1121, 1061, 1029, 750; *m/z* (EI) 173 (3), 130 (70), 116 (7), 86 (38), 84 (100), 70 (7), 57 (13), 56 (9), 55 (9); Anal. Calcd for $C_9H_{19}NO_2$: C 62.39, H 11.05, N 8.09; found C 62.26, H 11.23, N 8.04.

5-(diethylamino)pentan-2-one

Using the same procedure as for ethyl 4-(diethylamino)butanoate, 6.35 g (0.0526 mol) 5-chloropentan-2-one and 19.2 g (0.263 mol) diethylamine yielded 0.3488 g of 5-(diethylamino)pentan-2-one (20% yield); bp 66°C (4 torr): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, J = 7.1 Hz, 6H), 1.67 (p, 7.2 Hz, 2H), 2.10 (s, 3H), 2.34 (t, J = 7.2 Hz, 2H), 2.41 (t, J = 7.2 Hz, 2H), 2.45 (q, J = 7.1 Hz, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 11.67, 21.24, 29.93, 41.48, 46.71, 51.94, 208.83; $\nu_{\max}$ (ATR) cm^{-1} 2968, 2934, 2874, 2800, 1714 (C=O), 1410, 1361, 1294, 1202, 1175, 1121, 1069, 961, 764, 714; *m/z* (EI) 157 (4), 142 (1), 99 (4), 86 (100), 72 (2), 71 (2), 70 (2), 58 (12), 56 (5); HRMS (EI): C9H19NO for M^+ calculated 157.1467, found 157.1462.

5-(dipropylamino)pentan-2-one

Using the same procedure as for ethyl 4-(diethylamino)butanoate, 3.95 g (0.0328 mol) 5- chloro-pentan-2-one and 11.09 g (0.110 mol) dipropylamine yielded 1.2204 g of 5-(dipropylamino)-pentan-2-one (20% yield); bp 96°C (4 torr): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (t, J = 7.4 Hz, 6H), 1.41 (apparent sextet, J = 7.4 Hz, 4H), 1.68 (p, J = 7.1 Hz, 2H), 2.12 (s, 3H), 2.32 (multiplet, 6H), 2.37 (t, J = 7.2 Hz, 2H), 2.45 (t, 2H, J = 7.2 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 11.85, 20.23, 21.36, 29.88, 41.31, 53.14, 56.02, 208.86; $\nu_{\max}$ (ATR) cm^{-1} 2957, 2872, 2800, 1715 (C=O), 1462, 1362, 1174, 1078, 1020, 960, 746; *m/z* (EI) 185 (8), 156 (37), 154 (1), 140 (1), 127 (2), 114 (64), 98 (3), 85 (100), 72 (22), 70 (6), 56 (5); HRMS (EI): $C_{11}H_{23}NO$ for M^+ calculated 185.1780, found 185.1775.

Ethyl 4-(*tert*-butylamino)butanoate

Ethyl 4-bromobutanoate (6.8 g, 0.035 mol) and tert-butylamine (5.1 g, 0.070 mol) were added to a round bottom flask containing 20 ml acetonitrile. The mixture was stirred at 70°C under a nitrogen atmosphere for 48 h. The resulting solution was concentrated by distillation, added to 20 ml 4 M NaOH, and extracted with 3 × 20 ml pentane. Distillation afforded the pure product (3.9 g, 60% yield); bp 72°C (4 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.51 (broad, 1H), 0.96 (s, 9H), 1.13 (t, J = 7.1 Hz, 3H), 1.64 (p, J = 7.2 Hz, 2H), 2.24 (t, J = 7.3 Hz, 2H), 2.45 (t, J = 7.1 Hz, 2H), 4.00 (q, J = 7.1 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 14.10, 26.36, 28.93, 32.20, 41.69, 50.01, 59.99, 173.40; $\nu_{\max}$ (ATR) 3452 (N–H), 2963, 1732 (C=O), 1447, 1366, 1229, 1159, 1102, 1030, 768, 708; *m/z* (EI) 187 (1), 172 (100), 158 (1), 142 (3), 126 (31), 115 (25), 98 (5), 86 (82), 84 (17), 69 (17), 57 (33); Anal. Calcd for $C_{10}H_{21}NO_2$: C 64.12, H 11.31, N 7.48; found C 63.94, H 11.54, N 7.47.

Propyl 3-(*sec*-butylamino)propanoate

Using the same procedure as for ethyl 3-(sec-butylamino)propanoate, 2.1 g (0.021 mol) of propyl acrylate and 2.7 g (0.037 mol) of sec-butylamine yielded 3.2 g of product (92.7% yield); bp 74°C (4 torr): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, J = 7.4 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H), 1.01 (d, J = 6.3 Hz, 3H), 1.30 (m, 1H), 1.46 (m, 1H), 1.64 (apparent sextet, J = 7.1 Hz, 3H), 2.49 (t, J = 6.5 Hz, 2H), 2.54 (m, 1H), 2.86 (m, 2H), 4.03 (t, J = 6.7 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 10.15, 10.37, 19.75, 21.94, 29.43, 34.96, 42.39, 54.25, 66.02, 172.95; $\nu_{\max}$ (ATR) cm^{-1} 3323 (N–H), 2964, 2934, 2878, 1731 (C=O), 1463, 1377, 1356, 1259, 1186, 1099, 1063, 1002, 736; *m/z* (EI) 187 (1), 186 (1), 172 (8), 158 (100), 144 (1), 130 (8), 128 (6), 116 (9), 112 (8), 98 (65), 86 (60), 84 (8), 72 (15), 70 (36), 56 (98); Anal. Calcd for $C_{10}H_{21}NO_2$: C 64.12, H 11.31, N 7.48; found C 64.01, H 11.54, N 7.46.

Butyl 3-(isopropylamino)propanoate

Using the same procedure as for ethyl 3-(sec-butylamino)propanoate, 4.7 g (0.037 mol) of propyl acrylate and 7.2 g (0.1.221 mol) of secbutylamine yielded 6.5 g of product (94.3% yield); bp 83°C (4 torr): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, J = 7.4 Hz, 3H), 0.98 (d, J = 6.3 Hz, 6H), 1.31 (apparent sextet, J = 7.5 Hz, 2H) 1.54 (p, J = 7.1, 2H), 2.43 (t, J = 6.6 Hz, 2H), 2.74 (septet, J = 6.3 Hz, 1H), 2.80 (t, J =

6.6 Hz, 2H), 4.02 (t, J = 6.7 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 13.54, 19.10, 22.85, 30.60, 34.87, 42.49, 48.31, 64.20, 172.76; ν_{max} (ATR) cm^{-1} 3331 (N–H), 2960, 2873, 1731 (C=O), 1467, 1379, 1337, 1262, 1173, 1148, 1064, 1021, 840, 739; *m/z* (EI) 187 (2), 186 (2), 172 (70), 144 (14), 130 (4), 116 (13), 114 (17), 98 (64), 88 (10), 72 (100), 70 (22), 56 (89); Anal. Calcd for $C_{10}H_{21}NO_2$: C 64.12, H 11.31, N 7.48; found C 64.08, H 11.45, N 7.49.

Propyl 3-(diethylamino)propanoate

Using the same procedure as for ethyl 3-(diethylamino)propanoate, 1.2 g (0.011 mol) propyl acrylate and 1.4 g (0.019 mol) of diethylamine yielded 1.6 g of product (85% yield); bp 67°C (4 torr): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, J = 7.4 Hz, 3H), 1.02 (t, J = 7.2 Hz, 6H), 1.64 (apparent sextet, J = 7.1 Hz, 2H), 2.44 (t, J = 7.5 Hz, 2H), 2.51 (q, J = 7.2 Hz, 4H), 2.79 (t, J = 7.5 Hz, 2H), 4.03 (t, J = 6.7 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 10.36, 11.85, 21.96, 32.30, 46.80, 48.12, 65.94, 172.96; ν_{max} (ATR) cm^{-1} 2968, 2937, 2878, 2805, 1735 (C=O), 1465, 1382, 1266, 1198, 1178, 1062, 996, 909; *m/z* (EI) 187 (6), 172 (17), 158 (2), 144 (1), 130 (6), 128 (3), 100 (1), 99 (1), 98 (1), 86 (100), 73 (17), 70 (2), 58 (17), 55 (2); Anal. Calcd for $C_{10}H_{21}NO_2$: C 64.12, H 11.31, N 7.48; found C 63.94, H 11.46, N 7.46.

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Chapter 3

Paper II: Modelling the Behaviour of Switchable-Hydrophilicity Solvents

Paper Title[1]: “Modelling the behaviour of switchable-hydrophilicity solvents”

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[1] This chapter contains a version of a paper published in Physical Chemistry Chemical Physics as: Jeremy Durelle, Jesse R. Vanderveen and Philip G. Jessop, *Phys. Chem. Chem. Phys.*, 2014, **16**, 5270

3.1 Abstract

A switchable-hydrophilicity solvent (SHS) is a solvent that in one state forms a biphasic mixture with water but can be reversibly switched to another state that is miscible with water. We describe a mathematical model of the behaviour of CO_2-triggered SHS that narrows the search field for these solvents in terms of their acidity and hydrophilicity. By its predictive power, the mathematical model can assist in the optimization of processes using SHSs in terms of extrinsic parameters such as pressure and the relative volumes of solvent and water used. Models are presented for both a two-liquid system (consisting of the amine solvent and water) and a three-liquid system (consisting of the amine solvent, water, and 1-octanol). Partitioning data with toluene as the third component is also shown for comparison with 1-octanol.

3.2 Introduction

Industry regularly uses flammable and smog-forming volatile organic solvents in chemical processes, even though nonvolatile organic solvents would be safer, because distillation is the standard method for removing solvent from product. Removal of solvent by distillation requires that the solvent be volatile. We earlier proposed an alternative method for removing solvent which does not require distillation: the use of a switchable-hydrophilicity solvent (an SHS) [1, 2]. A SHS is a hydrophobic solvent that can become hydrophilic upon the application of a trigger such as the bubbling of carbon dioxide through a water/solvent mixture (Figure 3.1). Thus, if an SHS has been used as the solvent in a process, then the solvent can be separated from the product by the addition of water and CO_2. Adding water forms a biphasic mixture -

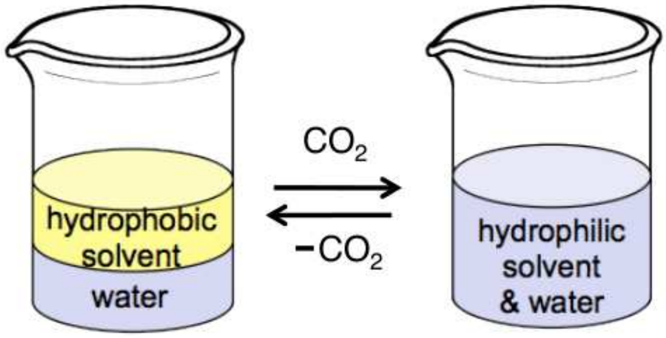

Figure 3.1: A switchable-hydrophilicity solvent changes from hydrophobic to hydrophilic upon addition of CO_2 and then back to hydrophobic upon removal of CO_2.

one layer is the solvent with product dissolved in it, and the other is water. If CO_2 is bubbled through the system, the solvent becomes protonated and partitions into the water layer as a bicarbonate salt (Equation 3.1). Figure 3.2 demonstrates the extraction of soybean oil using SHS technology. Because an SHS can be removed without distillation, it is not necessary for the solvent to be volatile and therefore it will be neither flammable or smog-forming.

$$NR_{3\,(aq)} + H_2O_{(l)} + CO_{2\,(g)} \rightleftharpoons HNR^+_{3(aq)} + HCO^-_{3(aq)} \tag{3.1}$$

The SHS reported so far by the Jessop group include 23 amines and amidines [1, 2, 3]. For each of these compounds, bubbling CO_2 through water/SHS mixtures resulted in an increase in the water miscibility of the amine. This could be reversed upon removing the CO_2 by heating and/or bubbling of an inert gas (such as Ar, air, or N_2) through the solution.

The focus of this paper is the development of a mathematical description of two processes: one where the system consists of 2 liquids (water and SHS), and another where the system consists of 3 liquids (water, SHS, and product). With an accurate description, these processes could be optimized in terms of both intrinsic (basicity,

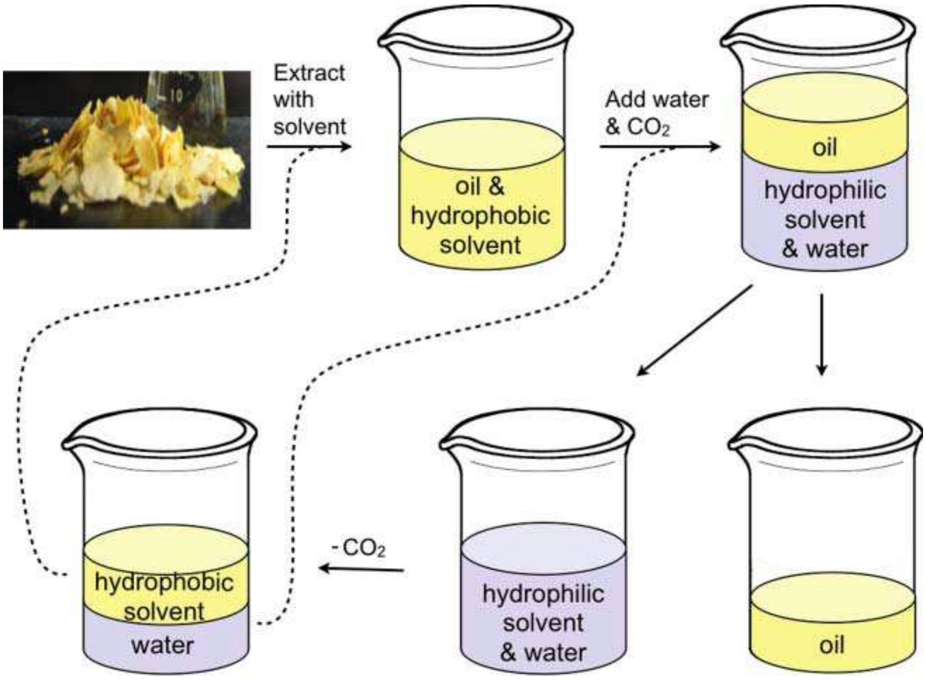

Figure 3.2: The process by which an SHS can be used to extract soybean oil from soybean flakes without a distillation step. The dashed lines indicate the recycling of the solvent and the aqueous phase. Reproduced from Jessop *et al.* 2010 [1].

hydrophilicity, molecular weight, density) and extrinsic (volume, pressure) parameters.

In the search for new examples of SHS, we have been careful to avoid amines that might produce carbamates. Upon bubbling of CO_2 through a mixture of water and either a primary or a non-bulky secondary amine, both bicarbonate and carbamate salts of the amine are produced. Tertiary and bulky secondary amines are unable to produce carbamates. Furthermore, carbonates are not observed due to the instability of the carbonate salt at the pH ranges observed when comparable volumes of water and amine are carbonated. The acidity of the second proton of carbonic acid is close to the acidity of the protonated amine ($\mathrm{pK}_a \approx 10$).

In what follows, we describe and optimize the switchable behaviour in a two-liquid system (water and amine) and then in a three-liquid system (water, amine, and an unreactive organic liquid such as an oil or 1-octanol). The results will be summarized in the conclusion section.

3.3 Two-liquid system

The two-liquid system consists of water and an amine solvent which is being tested for suitability as an SHS (see Figure 3.1). To qualify as an SHS, the amine must have a low water solubility in the absence of CO_2 (S, in moles per litre) and a high solubility upon carbonation of the system (S'). Here we use the term “solubility” to include “miscibility” so that we can include both solid and liquid species. A low S and a high S' are also required for the process in Figure 3.2 to be practical. We can relate the solubility to the number of moles of amine that failed to dissolve in the water,

$$n_{B,\mathrm{undiss}} = \frac{\rho}{M} V_B - S V_w \tag{3.2}$$

$$n'_{B,\mathrm{undiss}} = \frac{\rho}{M} V_B - S' V_w \tag{3.3}$$

where ρ and M represent the amine's density and molecular weight, respectively. V_B and V_w represent the volumes of amine and water added to the system. S and S' are derived from Equations 3.6 & 3.7 and from the charge balance equations (before and after addition of CO_2). We also consider that water itself may contribute to the amine protonation, producing a hydroxide salt. Assuming that the aqueous phase is always saturated with B, which is true when there is a separate amine phase and when there is just enough water to make that separate phase merge with the aqueous phase, we can write:

$$S = [\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{aq}} \tag{3.4}$$

$$S' = [\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{aq}}{}' \tag{3.5}$$

To complete the solubility equations, we consider the charge balance of the system before and after CO_2 addition as well as the absorption of CO_2 by water

$$K_{a\mathrm{H}} = \frac{[\mathrm{B}]_{\mathrm{aq}}[\mathrm{H}^+]_{\mathrm{aq}}}{[\mathrm{HB}^+]_{\mathrm{aq}}} \tag{3.6}$$

$$K_1 = \frac{[\mathrm{H}^+][\mathrm{HCO}_3-]}{K_H P_{\mathrm{CO}_2}} \tag{3.7}$$

where K_H is Henry's constant for CO_2 (0.034 M/atm) and K_1 is the first acid-dissociation constant for hydrated CO_2. Substituting the above relations into the solubility equations leads to

$$S = [\mathrm{B}]_{\mathrm{aq}} \left(1 + \frac{1}{K_{a\mathrm{H}}} \sqrt{\frac{K_w}{1 + [\mathrm{B}]_{\mathrm{aq}} K_{a\mathrm{H}}^{-1}}} \right) \tag{3.8}$$

and

$$S' = [\mathrm{B}]_{\mathrm{aq}} \left(1 + \frac{1}{K_{a\mathrm{H}}} \sqrt{\frac{K_w + K_1 K_H P_{\mathrm{CO}_2}}{1 + [\mathrm{B}]_{\mathrm{aq}} K_{a\mathrm{H}}^{-1}}}\right) \tag{3.9}$$

where $[\mathrm{B}]_{\mathrm{aq}}$ is evaluated from the equilibrium reaction with water, noting that equilibrium is reached when $[\mathrm{B}]_{\mathrm{aq}} = S - [\mathrm{HB}^+]_{\mathrm{aq}}$. We assume that $[\mathrm{B}]_{\mathrm{aq}}$ remains unchanged after addition of CO_2 to simplify the model. Even though $[\mathrm{B}]_{\mathrm{aq}}$ increases with ionic strength, this increase is negligible when compared to the solubility of the bicarbonate salt.

The concentration of neutral amine in the aqueous phase $[\mathrm{B}]_{\mathrm{aq}}$ is assumed to be equal to the water solubility of the neutral amine at saturation, S_0, and is assumed to remain constant throughout the process. To determine whether S_0 is a constant throughout the process or whether it is affected by the increasing concentration of HB^+ as CO_2 is added, the solubility of N,N-dimethylcyclohexylamine ($\mathrm{CyNMe_2}$) was measured in increasingly salty aqueous phases. Trimethylcyclohexylammonium iodide ($[\mathrm{CyNMe_3}]\mathrm{I}$) was added to the mixture to best simulate the system as the protonated amine is drawn into the aqueous phase. Figure 3.3 shows that the solubility of $\mathrm{CyNMe_2}$ increases in aqueous solutions of $[\mathrm{CyNMe_3}]\mathrm{I}$. A biphasic system could not be attained after the salt concentration reached about 1.0 mol L^{-1} indicating that $\mathrm{CyNMe_2}$ is completely miscible with the aqueous phase at such high salt concentrations. This higher solubility is likely due to favourable interactions between neutral amine and the organic cation, which are both relatively hydrophobic species in a hydrophilic environment. Therefore, the solubility of the neutral amine in the aqueous phase would increase as CO_2 is bubbled into the mixture, due to the hydrotropic effect of the ammonium cation. As CO_2 is removed from the system, the ammonium salt returns to its neutral form, decreasing the salt concentration in solution and thereby

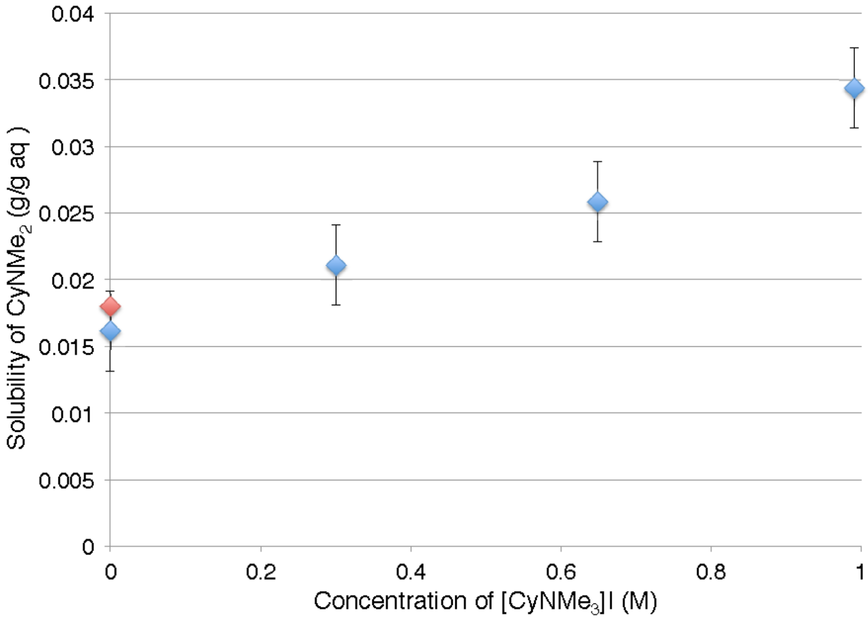

Figure 3.3: Solubility of $CyNMe_2$ in aqueous solutions of organic salt $[CyNMe_3]I$. The red point corresponds to the reported water solubility of $CyNMe_2$ in the literature [2].

negating the hydrotropic effect. The increase in solubility of the neutral amine has minimal effect on the model, allowing for switchable behaviour with more hydrophobic amines having slightly lower pK_{aH} values than predicted without this correction.

We now introduce a mapping parameter Z which is at a maximum when $n_B \gg n'_B$, and zero when $n_B = n'_B$,

$$Z = \frac{n_B - n'_B}{n_{tot}} \tag{3.10}$$

where n_{tot} is the total number of moles of amine added to the system ($n_{tot} = \rho V_B/M$). We restrain the system by assuming a density and molecular weight typical of SHSs, $\rho = 0.85$ g/mL and $M = 130$ g/mol, and that $V_w = V_B$. Z is used to gauge SHS viability. An amine which has a Z value close to 1 will be an effective SHS whereas

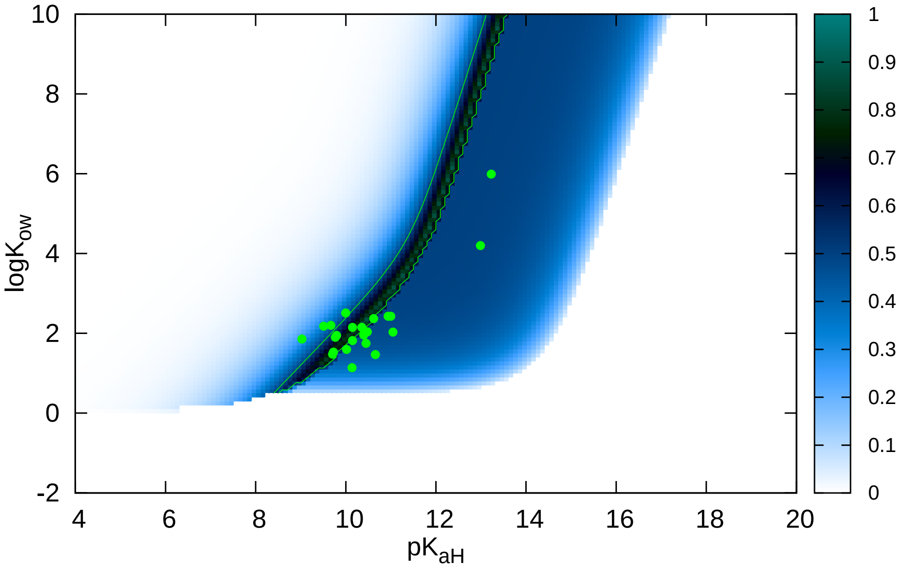

Figure 3.4: Theoretical map indicating the region of high SHS viability in a two-liquid system. The z-axis represents Z from Equation 3.10 and the green dots represent confirmed SHS tertiary and bulky secondary amines and the two SHS amidines at the upper right.

an amine with $Z \approx 0$ will not. S_0 was converted to $\log K_{ow}$ using Equation 3.11 from Meylan *et al* [4] which accounts for the molecular weight and the effect of an aliphatic liquid amine.

$$\log S = 0.796 - 0.854 \log K_{ow} - 0.00728(M) + \Sigma f_i \tag{3.11}$$

where f_i is a correction factor dependent on the functional group added to the molecule and is equal to 1.008 for aliphatic amines.

The map shown in Figure 3.4 outlines the ranges of $\log K_{ow}$ and $\mathrm{pK}_{a\mathrm{H}}$ which are optimal for switchable behaviour. A very basic solvent must be quite hydrophobic in order to not be miscible with water (as a hydroxide salt) before the addition of CO_2.

As a result, there is a steep increase in the required K_{ow} at high $\mathrm{pK}_{a\mathrm{H}}$. This map is in good agreement with the confirmed tertiary and bulky secondary amines. The two amidine SHSs deviate from the optimal Z range, however they follow the general trend. Better agreement with these SHSs is attained when $V_w > V_B$.

3.4 Three-liquid system

In practice, this technology is used to separate a product from a solvent, such as the separation of a water-immiscible organic oil from the amine solvent that it is dissolved in. The need to separate organic liquid and solid products from solvents is common in organic synthesis and in extraction processes. The products which have been isolated using switchable technology include bitumen from oil sands [5], vegetable oil from soybeans [1], bio-oil from algae [6] and polystyrene from waste polystyrene foam [2]. For this paper, we consider the case of a liquid organic product. The product must be immiscible with water to separate it from the SHS using this process (top right part of Figure 3.2).

The product oil layer complicates the SHS phase behaviour by adding a third component to the mixture. Now there is partitioning of neutral amine (K_{ow}) and charged ammonium bicarbonate (K'_{ow}) species between the aqueous and organic layers. Strictly speaking, K_{ow} refers to the partitioning of the amine between 1-octanol and water, however these values may be adjusted appropriately for a given liquid product with the equations remaining the same. We use 1-octanol as a model compound to represent a generic hydrophobic liquid product.

$$\mathrm{NR}_{3\,(\mathrm{aq})} \xrightleftharpoons{K_{ow}} \mathrm{NR}_{3\,(\mathrm{org})}$$

$$[\mathrm{HNR}_3^+\ \mathrm{HCO}_3^-]_{(\mathrm{aq})} \xrightleftharpoons{K'_{ow}} [\mathrm{HNR}_3^+\ \mathrm{HCO}_3^-]_{(\mathrm{org})}$$

where

$$K_{ow} = \frac{[\mathrm{B}]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}}} \tag{3.12}$$

$$K'_{ow} = \frac{[\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{HB}^+]_{\mathrm{aq}}} \tag{3.13}$$

To simplify matters, we assume that the load of amine present in the water/organic solvent system will not affect the properties of either phase and thus the partition coefficients remain constant, although in the future it would be desirable to develop a model that does not make this assumption.

The pH-dependent distribution of neutral and charged species between two immiscible liquid phases is described by the distribution coefficient, D, which is defined as the ratio of concentration of species contained in the organic layer to the concentration of species in the aqueous layer [7].

$$D = \frac{[\mathrm{B}]_{\mathrm{org}} + [\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{aq}}}$$

It follows that

$$\begin{aligned} \log D = \log K_{ow} + \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}} - \mathrm{pH} - \Delta \log K_{ow}}\right) \\ - \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}} - \mathrm{pH}}\right) \end{aligned} \tag{3.14}$$

given that $\Delta \log K_{ow} = \log K_{ow} - \log K'_{ow}$ [8].

The term $\Delta \log K_{ow}$ represents the difference in distribution coefficients of the neutral and charged amine and is assumed to be a constant for species belonging to the same family [9, 10]. However, this is likely dependent on the counter-ion (bicarbonate in this case). As such, there is a higher error associated to K'_{ow} than there is to K_{ow}. In essence, this affects how large $\Delta \log K_{ow}$ is and therefore how effective the SHS will perform. At high pH levels, most of the amine is unprotonated and $\log D \approx \log K_{ow}$, whereas at low pH levels, most of the amine is protonated and thus $\log D \approx \log K'_{ow}$. Indeed, Equation 3.14 follows these approximates at extreme pH levels. $\Delta \log K_{ow}$ was calculated for N,N-dimethylcyclohexylamine (CyNMe$_2$) in 1-octanol and toluene by measuring the partition coefficients at varying pH levels (Figure 3.5). The results are consistent with Equation 3.14 and also show that $\Delta \log K_{ow} \approx 2.8$ when the organic phase is 1-octanol and nearly the same when the organic phase is toluene.

A more convenient way to represent Equation 3.14 is by substituting the pH variable with a ratio of charged to neutral species. One arrives at the following relationship

$$\begin{aligned}\log D = \log &\left(\frac{K_{ow}}{K'_{ow}} + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}\right) \\ - \log &\left(\frac{1}{K'_{ow}} + \frac{1}{K'_{ow}}\frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}\right)\end{aligned} \tag{3.15}$$

which has the fraction $[\mathrm{HB}^+]_{\mathrm{aq}}/[\mathrm{B}]_{\mathrm{aq}}$ being the only term that changes after bubbling CO$_2$ through the system. The charge balance equation of this system leads to

$$\frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}} = \frac{1}{K_{a\mathrm{H}}}\left(\frac{K_w}{1 + [\mathrm{B}]_{\mathrm{aq}}K_{a\mathrm{H}}^{-1}}\right)^{1/2}$$

before the addition of CO$_2$ and

$$\frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}} = \frac{1}{K_{a\mathrm{H}}}\left(\frac{K_w + K_1 K_H P_{\mathrm{CO}_2}}{1 + [\mathrm{B}]_{\mathrm{aq}}K_{a\mathrm{H}}^{-1}}\right)^{1/2}$$

after the addition of CO$_2$.

We now define the mapping parameter Ω based upon the product of $\log D_1$ and $\log D_2$, where D_1 and D_2 represent the distribution coefficients of the amine before and after addition of CO$_2$, respectively. An effective SHS will have a positive number for $\log D_1$ as a requirement that the solvent be hydrophobic enough to make a biphasic mixture with water. The amine solvent should partition preferentially into

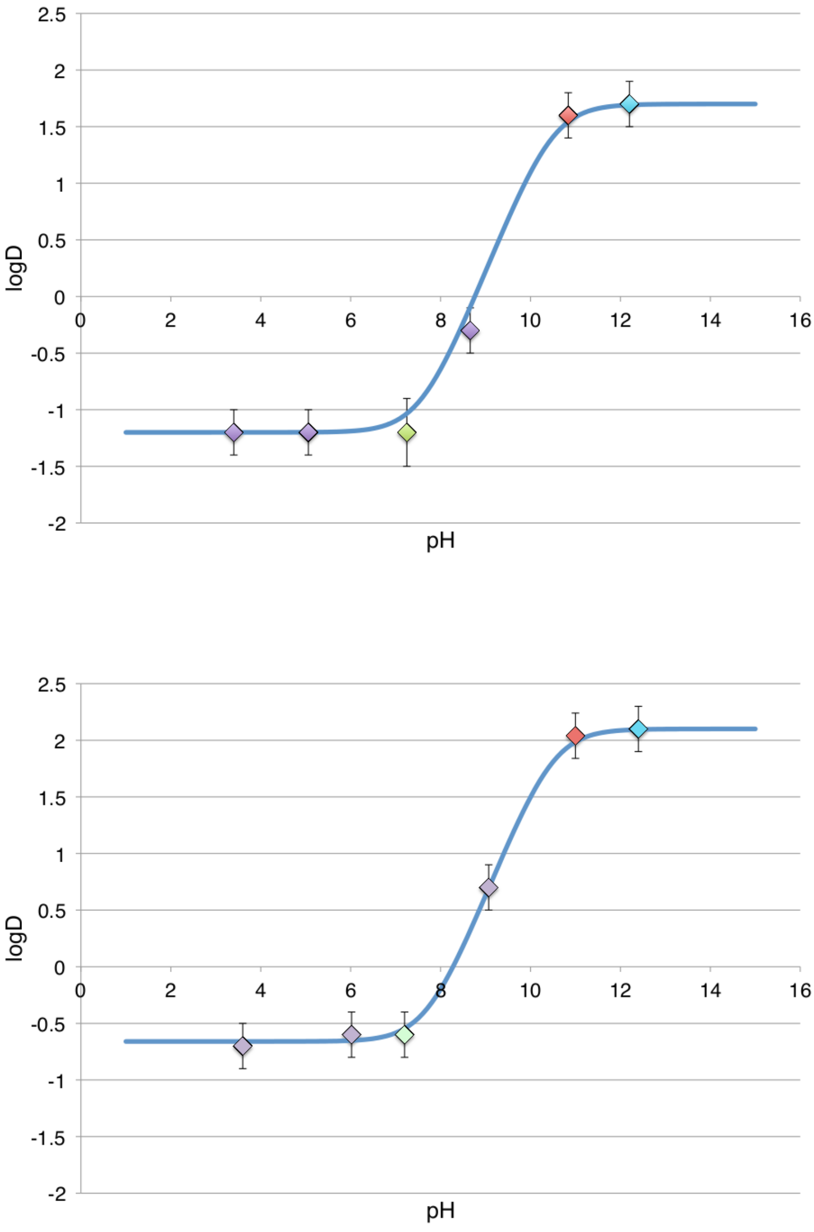

Figure 3.5: Distribution coefficient of $CyNMe_2$ between toluene and water (top) and between 1-octanol and water (bottom). The distribution of 3.3 mmol of amine between the organic solvent and water (5 mL each) at ambient temperature is represented by the red point. The distribution after saturation of the mixture with CO_2 at 1.0 atm is represented by the green point. To adjust the pH, 0.5, 1.0, and 2.0 mole equivalents of glycolic acid (purple points) or 1.0 equivalent of NaOH (blue point) were used. The curve predicted by Equation 3.14 is overlaid to show agreement with the data.

the aqueous phase rather than the organic product phase after CO_2 has been bubbled through the system, as represented by a negative value for $\log D_2$. Thus the product of $\log D_1$ and $\log D_2$ will be negative for effective SHS. To create a positive map, we multiply the product by (-1):

$$\Omega = -\log D_1 \times \log D_2 \tag{3.16}$$

Figure 3.6 shows the map produced by Equation 3.16 as well as the dataset of confirmed tertiary and bulky secondary amine SHS.

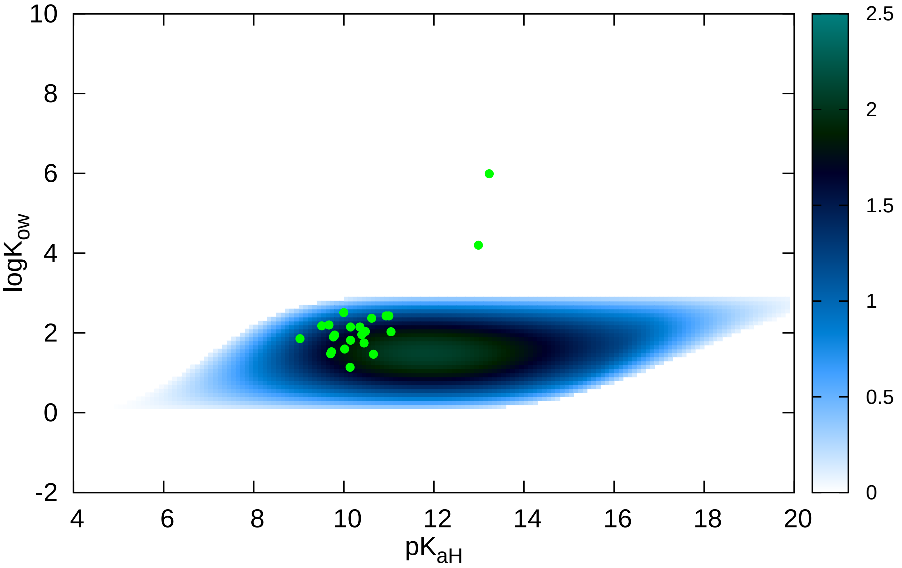

Figure 3.6: A map of Ω, indicating the region of high SHS viability in a three-liquid system, assuming that $\Delta \log K_{ow} = 2.8$. The green dots represent the confirmed SHS amines and the two SHS amidines at the upper right.

It is important that $\log D_1$ and $\log D_2$ be centred around zero. The most effective SHSs will be very hydrophobic before the addition of CO_2 (a large positive $\log D_1$

value) and very hydrophilic upon addition of CO_2 (a large negative $\log D_2$ value). A large $\Delta \log K_{ow}$ value does not insure this. For example, a solvent with $\Delta \log K_{ow} = 5$ where $\log D_1 = 4$ and $\log D_2 = -1$ would not be an efficient SHS since the bicarbonate salt does not partition very well into the aqueous phase (10% would still remain in the organic layer). Figure 3.6 is in good agreement with all but two confirmed SHSs - the amidines. The figure suggests that for a 3 liquid system where the liquid product is 1-octanol, amines with a $\log K_{ow} > 3$ will not function as SHSs. It should be noted, however, that this parameter map assumed a value for $\Delta \log K_{ow}$ of 2.8. This holds true for the family of tertiary amines but is likely a different value for amidine derivatives.

Finally, we may also predict what percentage of the amine is protonated by CO_2. Because unprotonated amine molecules are likely to be left behind in the organic liquid product, the percent protonation governs the ability of the SHS to be separated from the liquid product. In order to have effective switching of the SHS into its hydrophilic form, and therefore efficient removal of the SHS from the organic product layer, the CO_2 addition must be sufficient to bring the pH down well below the system midpoint (i.e. the pH at which $P = 0.5$). In the absence of an organic layer, the fraction of protonated amine (P) is dependent on the pH of the solution as well as the acid dissociation constant of the protonated amine ($K_{a\mathrm{H}}$),

$$P = \frac{[\mathrm{H}^+]}{[\mathrm{H}^+] + K_{a\mathrm{H}}} \tag{3.17}$$

and the system midpoint is at pH = $\mathrm{p}K_{a\mathrm{H}}$. However, with an organic layer present, one must account for the partitioning between the layers. Fundamentally, P is the ratio of protonated amine in both the aqueous and organic layers to the total amount of amine (neutral and protonated) in the system

$$P = \frac{n_{\mathrm{HB^+,org}} + n_{\mathrm{HB^+,aq}}}{n_{\mathrm{B},tot}} \tag{3.18}$$

Recalling that $n_{\mathrm{B},tot} = n_{\mathrm{B},org} + n_{\mathrm{B},aq} + n_{\mathrm{HB^+},org} + n_{\mathrm{HB^+},aq}$, one readily attains the expression for P in a biphasic system.

$$P = \frac{[\mathrm{H^+}]}{[\mathrm{H^+}] + K_{a\mathrm{H}}\left(\frac{1+V_{\mathrm{rat}}K_{ow}}{1+V_{\mathrm{rat}}K'_{ow}}\right)} \tag{3.19}$$

where $V_{\mathrm{rat}} = V_{\mathrm{org}}/V_{\mathrm{aq}}$. With only an aqueous phase, the equation reduces to Equation 3.17. The exchange between aqueous and organic layers results in a decrease of protonated species at a particular pH. Figure 3.7 shows that the presence of an organic layer makes it necessary to have a much more acidic environment in order to substantially protonate the base. Given that the acid being used to protonate the solvent is carbonic acid (p$K_{a1} = 6.4$)[3], it is wise to use a low V_{rat} in order to ensure a greater percentage of amine protonation.

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[3] This is the apparent acidity of dissolved CO_2 rather than the pK_a of H_2CO_3 itself.

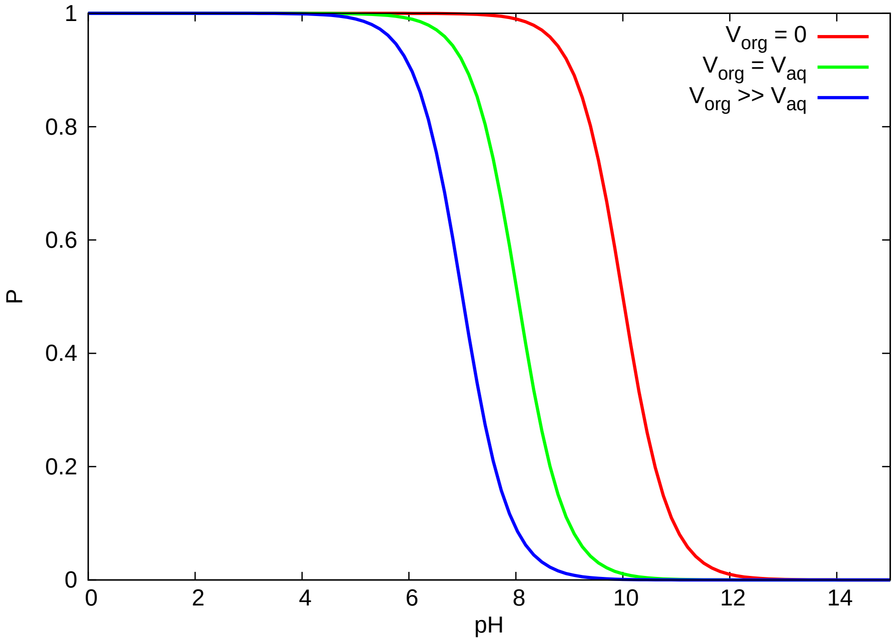

Figure 3.7: The effect of the organic layer volume on the fraction of protonated base. If V_{rat} is nearly zero, then the system midpoint is essentially the p$K_{a\mathrm{H}}$ of the amine, while if V_{rat} is much larger than 1, then the system midpoint is shifted down by about 3 pH units. K_{ow} and the acid dissociation constant are assumed to be 10^2 and 10^{-10}, respectively.

3.5 Conclusions

We have mathematically described the switching process for tertiary and bulky secondary amine SHS for the two- and three-liquid systems. The acidity and hydrophilicity ranges are correlated and can be optimized by maximizing the mapping parameters Z and Ω. Plots of these two mapping functions indicate a narrow range of acceptable $\log K_{ow}$ and p$\mathrm{K}_{a\mathrm{H}}$ values, which matches the values of known amine SHS. One of these mapping functions indicates values expected for amines that will switch readily between water-miscible and forming a biphasic mixture with water. The other mapping function indicates those amines that will switch from partitioning into an oil layer to partitioning in an aqueous layer. The two mapping functions indicate similar but not identical ranges of $\mathrm{pK}_{a\mathrm{H}}$ and $\log K_{ow}$. An ideal amine SHS would perform well by both criteria and would therefore fit within the ranges predicted by both mapping functions. Hence the confirmed SHS examples fall in the left half of the optimum area in Figure 3.6 because that allows them to also fall in or close to the optimum area in Figure 3.4. Amidine SHS fall outside of the prescribed range of Figure 3.6, suggesting that while they may technically be SHS, they are less likely to be ideal for extraction processes like that illustrated in Figure 3.2.

We have also discovered that the water solubility of the neutral amine increases as more protonated amine enters the aqueous phase as a bicarbonate salt. This is likely due to favourable hydrophobic-hydrophobic attractions between the neutral amine and the organic cations. In the three-liquid system, both $\log K_{ow}$ and $\log K'_{ow}$ change if the organic layer is changed from 1-octanol to toluene. The difference between these two partition coefficients $\Delta \log K_{ow}$, however, is not significantly affected.

3.6 Appendix

3.6.1 Reaction equations

$$
\begin{array}{ccc r}
\mathrm{B} + \mathrm{H_2O} & \rightleftharpoons & \mathrm{HB^+} + \mathrm{OH^-} & K_w/K_{a\mathrm{H}} \\
\mathrm{H_2CO_3} + \mathrm{H_2O} & \rightleftharpoons & \mathrm{H_3O^+} + \mathrm{HCO_3^-} & K_1 \\
\mathrm{B} + \mathrm{H_2CO_3}\ ^2 & \rightleftharpoons & \mathrm{HB^+} + \mathrm{HCO_3^-} & K_1/K_{a\mathrm{H}} \\
\mathrm{HB^+} + \mathrm{H_2O} & \rightleftharpoons & \mathrm{B} + \mathrm{H_3O^+} & K_{a\mathrm{H}} \\
\mathrm{CO_2(g)} & \rightleftharpoons & \mathrm{CO_2(aq)} & K_H \\
\mathrm{B(aq)} & \rightleftharpoons & \mathrm{B(org)} & K_{ow} \\
\mathrm{HB^+(aq)} & \rightleftharpoons & \mathrm{HB^+(org)} & K'_{ow}
\end{array}
$$

* The concentration of H_2CO_3 includes both carbonic acid and hydrated dissolved CO_2.

3.6.2 Derivations

Concentration of protonated base before addition of CO_2

$$[\mathrm{H_3O^+}] + [\mathrm{HB^+}] = [\mathrm{OH^-}]$$

$$[\mathrm{H_3O^+}] + [\mathrm{HB^+}] = K_w/[\mathrm{H_3O^+}]$$

$$[\mathrm{H_3O^+}]^2 + [\mathrm{HB^+}][\mathrm{H_3O^+}] = K_w$$

Because $K_{a\mathrm{H}} = [\mathrm{H_3O^+}][\mathrm{B}]/[\mathrm{HB^+}]$ then

$$\left(\frac{[\mathrm{HB^+}]}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}}\right)^2 + \frac{[\mathrm{HB^+}]^2}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}} = K_w$$

$$[\mathrm{HB^+}]^2\left(\frac{1}{([\mathrm{B}]K_{a\mathrm{H}}^{-1})^2} + \frac{1}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}}\right) = K_w$$

$$\frac{[\mathrm{HB^+}]^2}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}}\left(\frac{1}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}} + 1\right) = K_w$$

$$\frac{[\mathrm{HB^+}]^2}{([\mathrm{B}]K_{a\mathrm{H}}^{-1})^2}(1 + [\mathrm{B}]K_{a\mathrm{H}}^{-1}) = K_w$$

$$\therefore [\mathrm{HB^+}] = [\mathrm{B}]K_{a\mathrm{H}}^{-1}\sqrt{\frac{K_w}{1 + [\mathrm{B}]K_{a\mathrm{H}}^{-1}}}$$

Concentration of protonated base after addition of CO_2

$$\begin{aligned}
[\mathrm{H_3O^+}] + [\mathrm{HB^+}] &= [\mathrm{OH^-}] + [\mathrm{HCO_3^-}] \\
[\mathrm{H_3O^+}] + [\mathrm{HB^+}] &= \frac{K_w}{[\mathrm{H_3O^+}]} + \frac{K_1[\mathrm{H_2CO_3}]}{[\mathrm{H_3O^+}]} \\
[\mathrm{H_3O^+}] + [\mathrm{HB^+}] &= \frac{1}{[\mathrm{H_3O^+}]}(K_w + K_1 K_H P_{\mathrm{CO_2}}) \\
[\mathrm{H_3O^+}]^2 + [\mathrm{HB^+}][\mathrm{H_3O^+}] &= K_w + K_1 K_H P_{\mathrm{CO_2}} \\
\left(\frac{[\mathrm{HB^+}]}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}}\right)^2 + \frac{[\mathrm{HB^+}]^2}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}} &= K_w + K_1 K_H P_{\mathrm{CO_2}} \\
[\mathrm{HB^+}]^2\left(\frac{1}{([\mathrm{B}]K_{a\mathrm{H}}^{-1})^2} + \frac{1}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}}\right) &= K_w + K_1 K_H P_{\mathrm{CO_2}} \\
\frac{[\mathrm{HB^+}]^2}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}}\left(\frac{1}{[\mathrm{B}]K_{a\mathrm{H}}^{-1}} + 1\right) &= K_w + K_1 K_H P_{\mathrm{CO_2}} \\
\frac{[\mathrm{HB^+}]^2}{([\mathrm{B}]K_{a\mathrm{H}}^{-1})^2}(1 + [\mathrm{B}]K_{a\mathrm{H}}^{-1}) &= K_w + K_1 K_H P_{\mathrm{CO_2}}
\end{aligned}$$

$$\therefore [\mathrm{HB^+}] = [\mathrm{B}]K_{a\mathrm{H}}^{-1}\sqrt{\frac{K_w + K_1 K_H P_{\mathrm{CO_2}}}{1 + [\mathrm{B}]K_{a\mathrm{H}}^{-1}}}$$

Solubility

$$S = [\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB^+}]_{\mathrm{aq}}$$

$$S' = [\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB^+}]_{\mathrm{aq}}{}'$$

Substituting $[\mathrm{HB^+}]_{\mathrm{aq}}$ from the charge balance equation,

$$S = [\mathrm{B}]_{\mathrm{aq}}\left(1 + \frac{1}{K_{a\mathrm{H}}}\sqrt{\frac{K_w}{1 + [\mathrm{B}]_{\mathrm{aq}}K_{a\mathrm{H}}^{-1}}}\right)$$

Similarly, the solubility after the introduction of CO_2 is given by

$$S' = [\mathrm{B}]_{\mathrm{aq}}\left(1 + \frac{1}{K_{a\mathrm{H}}}\sqrt{\frac{K_w + K_1 K_H P_{\mathrm{CO_2}}}{1 + [\mathrm{B}]_{\mathrm{aq}}K_{a\mathrm{H}}^{-1}}}\right)$$

Distribution coefficient

$$
\begin{aligned}
D &= \frac{[\mathrm{B}]_{\mathrm{org}} + [\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{aq}}} \\
&= \frac{\frac{[\mathrm{B}]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}}} + \frac{[\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}}}}{1 + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}} \\
&= \frac{K_{ow} + \frac{[\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}}}}{1 + \frac{[\mathrm{H_3O}^+]}{K_{a\mathrm{H}}}} \\
&= \frac{K_{ow}K_{a\mathrm{H}} + \frac{[\mathrm{H_3O}^+][\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{HB}^+]_{\mathrm{aq}}}}{K_{a\mathrm{H}} + [\mathrm{H_3O}^+]} \\
&= \frac{K_{a\mathrm{H}}K_{ow} + [\mathrm{H_3O}^+]K'_{ow}}{K_{a\mathrm{H}} + [\mathrm{H_3O}^+]} \\
&= \frac{10^{-\mathrm{p}K_{a\mathrm{H}}}K_{ow} + 10^{-\mathrm{pH}}K'_{ow}}{10^{-\mathrm{p}K_{a\mathrm{H}}} + 10^{-\mathrm{pH}}} \\
&= \frac{K_{ow} + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}K'_{ow}}{1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}} \\
&= K_{ow}\left(\frac{1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}\ K'_{ow}/K_{ow}}{1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}}\right)
\end{aligned}
$$

$$\therefore \log D = \log K_{ow} + \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}\ K'_{ow}/K_{ow}\right) - \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}\right)$$

Now,

$$\frac{K'_{ow}}{K_{ow}} = 10^{\log K'_{ow} - \log K_{ow}}.$$

So if we let $\Delta \log K_{ow} = \log K_{ow} - \log K'_{ow}$, then

$$\log D = \log K_{ow} + \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}-\Delta\log K_{ow}}\right) - \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}}-\mathrm{pH}}\right)$$

To eliminate the pH variable, we begin in a similar way

$$\begin{aligned}
D &= \frac{[\mathrm{B}]_{\mathrm{org}} + [\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{aq}}} \\
&= \frac{\frac{[\mathrm{B}]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}}} + \frac{[\mathrm{HB}^+]_{\mathrm{org}}}{[\mathrm{B}]_{\mathrm{aq}}}}{1 + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}} \\
&= \frac{K_{ow} + K'_{ow}\frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}}{1 + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}} \\
&= \frac{(K_{ow}/K'_{ow}) + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}}{\frac{1}{K'_{ow}}\left(1 + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}\right)}
\end{aligned}$$

$$\therefore \log D = \log\left(\frac{K_{ow}}{K'_{ow}} + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}\right) + \log(K'_{ow}) - \log\left(1 + \frac{[\mathrm{HB}^+]_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{aq}}}\right)$$

Fraction of protonation

$$\begin{aligned}
P &= \frac{n_{\mathrm{HB}^+,\mathrm{org}} + n_{\mathrm{HB}^+,\mathrm{aq}}}{n_{\mathrm{B},tot}} \\
&= \frac{[\mathrm{HB}^+]_{\mathrm{org}}V_{\mathrm{org}} + [\mathrm{HB}^+]_{\mathrm{aq}}V_{\mathrm{aq}}}{[\mathrm{B}]_{\mathrm{org}}V_{\mathrm{org}} + [\mathrm{B}]_{\mathrm{aq}}V_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{org}}V_{\mathrm{org}} + [\mathrm{HB}^+]_{\mathrm{aq}}V_{\mathrm{aq}}} \\
\frac{1}{P} &= 1 + \frac{[\mathrm{B}]_{\mathrm{aq}}V_{\mathrm{aq}} + [\mathrm{B}]_{\mathrm{org}}V_{\mathrm{org}}}{[\mathrm{HB}^+]_{\mathrm{aq}}V_{\mathrm{aq}} + [\mathrm{HB}^+]_{\mathrm{org}}V_{\mathrm{org}}} \\
&= 1 + \frac{V_{\mathrm{aq}} + V_{\mathrm{org}}([\mathrm{B}]_{\mathrm{org}}/[\mathrm{B}]_{\mathrm{aq}})}{V_{\mathrm{aq}}([\mathrm{HB}^+]_{\mathrm{aq}}/[\mathrm{B}]_{\mathrm{aq}}) + V_{\mathrm{org}}([\mathrm{HB}^+]_{\mathrm{org}}/[\mathrm{B}]_{\mathrm{aq}})} \\
&= 1 + \frac{1 + V_{\mathrm{rat}}K_{ow}}{([\mathrm{HB}^+]_{\mathrm{aq}}/[\mathrm{B}]_{\mathrm{aq}}) + V_{\mathrm{rat}}K'_{ow}([\mathrm{HB}^+]_{\mathrm{aq}}/[\mathrm{B}]_{\mathrm{aq}})} \\
&= 1 + \frac{1 + V_{\mathrm{rat}}K_{ow}}{[\mathrm{H_3O^+}]K_{a\mathrm{H}}^{-1}(1 + V_{\mathrm{rat}}K'_{ow})}
\end{aligned}$$

$$\begin{aligned}\therefore P &= \frac{[\mathrm{H_3O^+}]K_{a\mathrm{H}}^{-1}(1+V_{\mathrm{rat}}K'_{ow})}{[\mathrm{H_3O^+}]K_{a\mathrm{H}}^{-1}(1+V_{\mathrm{rat}}K'_{ow})+(1+V_{\mathrm{rat}}K_{ow})}\\ &= \frac{[\mathrm{H_3O^+}](1+V_{\mathrm{rat}}K'_{ow})}{[\mathrm{H_3O^+}](1+V_{\mathrm{rat}}K'_{ow})+K_{a\mathrm{H}}(1+V_{\mathrm{rat}}K_{ow})}\\ &= \frac{[\mathrm{H_3O^+}]}{[\mathrm{H_3O^+}]+K_{a\mathrm{H}}\left(\frac{1+V_{\mathrm{rat}}K_{ow}}{1+V_{\mathrm{rat}}K'_{ow}}\right)}\end{aligned}$$

3.6.3 Measuring the solubility of $\mathrm{CyNMe_2}$ in aqueous solutions of $[\mathrm{CyNMe_3}]\mathrm{I}$

Four samples of distilled water (average of 5 g accurate to 0.1 mg) were placed in 20 mL vials. To each vial, an average of 0.0, 450.0 , 900.0, and 1350.0 mg of N,N,N-trimethylcyclohexylammonium iodide salt ($[\mathrm{CyNMe_3}]\mathrm{I}$, a white powder) was added to make 0.0000, 0.3343, 0.6686 and 1.0030 M aqueous solutions, respectively. N,N-dimethylcyclohexylamine ($\mathrm{CyNMe_2}$) was then added to each solution until a biphasic mixture was observed. It should be noted that this biphasic mixture could not be attained for salt solutions with concentrations greater than 1.0 M. The mixtures were stirred for 30 min and allowed to settle for 3 h at which point it was assumed that equilibrium had been established. A sample from each aqueous layer was taken (450.0 mg average) and placed in a 50 mL volumetric flask. Acetophenone (20.0 μL) was added to each flask as an internal standard and then each flask was filled with HPLC-grade methanol to the 50 mL mark. These samples were then analyzed by gas chromatography with flame-ionization detection (GC-FID). The weight of $\mathrm{CyNMe_2}$ was calculated by a calibration curve of weight ratio (of acetophenone to $\mathrm{CyNMe_2}$) to peak area ratio (of acetophenone to $\mathrm{CyNMe_2}$). This was repeated in triplicate.

3.6.4 Measuring Δ log K_{ow}

$CyNMe_2$ (averaging 450.0 mg) was added to a mixture of water (averaging 5.0000 g) and 1-octanol (averaging 4.5000 g) at room temperature. The mixture was stirred for 30 min and was left to settle for 3 h. The pH of the aqueous layer was then measured. A sample of the aqueous layer (500.0 mg average) was drawn from the mixture and placed in a 50 mL volumetric flask. Acetophenone (20.0 μL) was added as an internal standard. The solution was diluted to the mark with HPLC-grade methanol and analyzed by GC-FID. The weight of $CyNMe_2$ was calculated by a calibration curve of weight ratio (of acetophenone to $CyNMe_2$) to peak area ratio (of acetophenone to $CyNMe_2$).

Another mixture of $CyNMe_2$, water, and 1-octanol was prepared and the pH was measured after CO_2 was bubbled through the system for 1 h under 101.3 kPa. Again, a sample from the aqueous layer (100.0 mg average) was taken and treated with excess base (to deprotonate the ammonium salt). Acetophenone (20 μL) was added and the sample was diluted with methanol to the 50 mL mark. A smaller sample size was used to avoid saturating the GC column with the amine analyte.

Three more mixtures were prepared as described above. Glycolic acid was added to each mixture in 0.500, 1.00, and 2.00 mol equivalents to $CyNMe_2$, respectively. Glycolic acid was chosen because its conjugate base is more stable than the bicarbonate anion and yet similar in size and hydrogen-bonding ability. The pH of each aqueous layer was measured. A 100.0 mg sample from each aqueous layer was taken and acetophenone (20.0 μL) was added. The sample was treated with base, diluted with methanol to the 50 mL mark, and analyzed by GC-FID.

Finally, another mixture was prepared and treated with NaOH (1.00 mol equivalent to $CyNMe_2$). The pH of the aqueous layer was measured and 500.0 mg of the aqueous layer was analyzed by GC-FID as described above.

Each sample was prepared in triplicate. This procedure was repeated with toluene in place of 1-octanol.

Acknowledgements

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Chapter 4

Paper III: Extending and Optimizing the Range of Switchable-Hydrophilicity Solvents

Paper Title[1]: "Extending and optimizing the range of switchable-hydrophilicity solvents"

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[1] This chapter contains a draft of a paper to be submitted to Physical Chemistry Chemical Physics as: Jeremy Durelle, Jesse R. Vanderveen, Yi Quan, Courtney Chalifoux, Julia E. Kostin, and Philip G. Jessop, *Phys. Chem. Chem. Phys.*, 2014

4.1 Abstract

Switchable-hydrophilicity solvents (SHSs) are solvents that in one state forms a biphasic mixture with water but can be reversibly switched to another state that is miscible with water. All of the amine SHSs that we have reported previously lie within a particular basicity and hydrophilicity range ($9.5 < \mathrm{pK}_{a\mathrm{H}} < 11$ and $1.0 < \log K_{ow} < 2.5$, respectively). We report an extension of this range by altering the pressure of CO_2 as well as the water:SHS volume ratio used in the process. Increasing the pressure of CO_2 and/or the water:amine volume ratio allows some amines with $\mathrm{pK}_{a\mathrm{H}} < 9.5$ or $\log K_{ow} > 2.5$ to function as SHSs.

4.2 Introduction

Separating organic products from solvents is common in organic synthesis and in extraction processes. Industry regularly uses flammable and smog-forming volatile organic solvents so that the solvent can be removed by distillation. Switchable hydrophilicity solvents (SHSs), because they can be removed from product and recycled without distillation, do not need to be volatile; they therefore offer a potentially safer alternative. Their utility has been demonstrated for various separation processes - the isolation of bitumen from the oil sands [1], vegetable oil from soybeans [2], bio-oil from algae [3, 4, 5], polystyrene from waste polystyrene foam [6] and phenols from lignin [7]. They have also been used as draw solutes for forward osmosis [8]. While other nonvolatile solvents, such as ionic liquids and liquid polymers, have been suggested in the literature, the removal of product from such solvents often requires the assistance of a volatile organic solvent, which negates the safety advantages.

Table 4.1: Tertiary amines exhibiting switchable behaviour under non-standard conditions

Amine	pK$_{a\mathrm{H}}$	$\log K_{ow}$[a]	V_{rat}[b] (pred.)	V_{rat}[b] (exp.)	P'_{CO_2}[c] (pred., bar)	P'_{CO_2}[c] (exp., bar)
N,N-diisopropylethylamine	11.4[9]	2.3	0.4	1.5-2.0	0.1	4.0-7.0
N,N-diethylcyclohexylamine	10.7	2.9	1.7	1.5-2.0	2.9	3.0-3.5
tripropylamine	10.6[10]	2.8	1.5	2.5-3.0	2.3	3.5-4.0
N,N-dimethylbenzylamine	9.0[11]	2.0	3.6	4.5-5.0	14.9	4.0-7.0
1-dimethylamino-2-pentyne	8.1[12]	1.6	5.3	6.5-7.0	4.6[d]	4.0-7.0[d]

[a] Predicted using VCCLAB software (ALOGPS) [13, 14]

[b] The minimum water:amine ratio required to obtain miscibility under 1 bar of CO_2 at 25°C

[c] The minimum CO_2 pressure required to trigger miscibility in a 1:1 water:amine (v/v) mixture at 25°C

[d] At a 3:1 volume ratio of water to amine

An SHS is a solvent that exists in two forms, one of which is hydrophobic and has low miscibility with water while the other is hydrophilic and has high miscibility with water. The transformation of the one form to the other could in theory be triggered in a number of ways, but in published examples is triggered by the addition of CO_2 (Figure 4.1). The resulting carbonated water reacts with the SHS, protonating it and forming a water-miscible bicarbonate salt (eqn 4.1, where NR_3 is the hydrophobic form of the solvent and $[HNR_3^+][HCO_3^-]$ is the hydrophilic form). Reversion of the hydrophilic form to the hydrophobic form is achieved by removal of the CO_2 by heating and/or sparging the mixture with air. The method by which an SHS can be used and recovered without distillation is illustrated by the extraction process shown in Figure 4.2. The formation of carbamate salts rather than bicarbonate salts is avoided by the use of tertiary and bulky secondary amine SHSs. Carbamate salts are not preferred because they require more energy input during the removal of CO_2 when restoring the amine solvent to its native hydrophobic state [15]. The predominant anion is bicarbonate rather than carbonate due to the instability of the carbonate anion over the observed pH ranges. The acidity of the second proton of carbonic acid

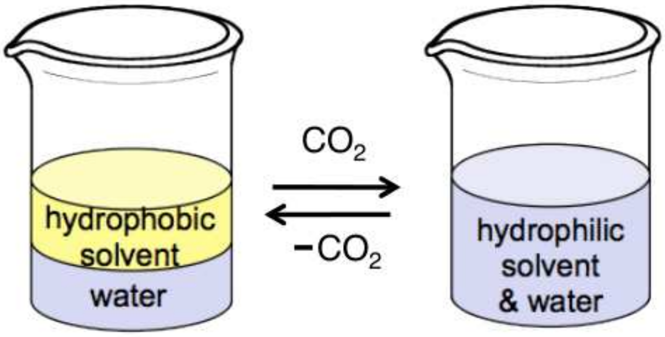

Figure 4.1: A switchable-hydrophilicity solvent changes from hydrophobic to hydrophilic upon addition of CO_2 and then back to hydrophobic upon removal of CO_2.

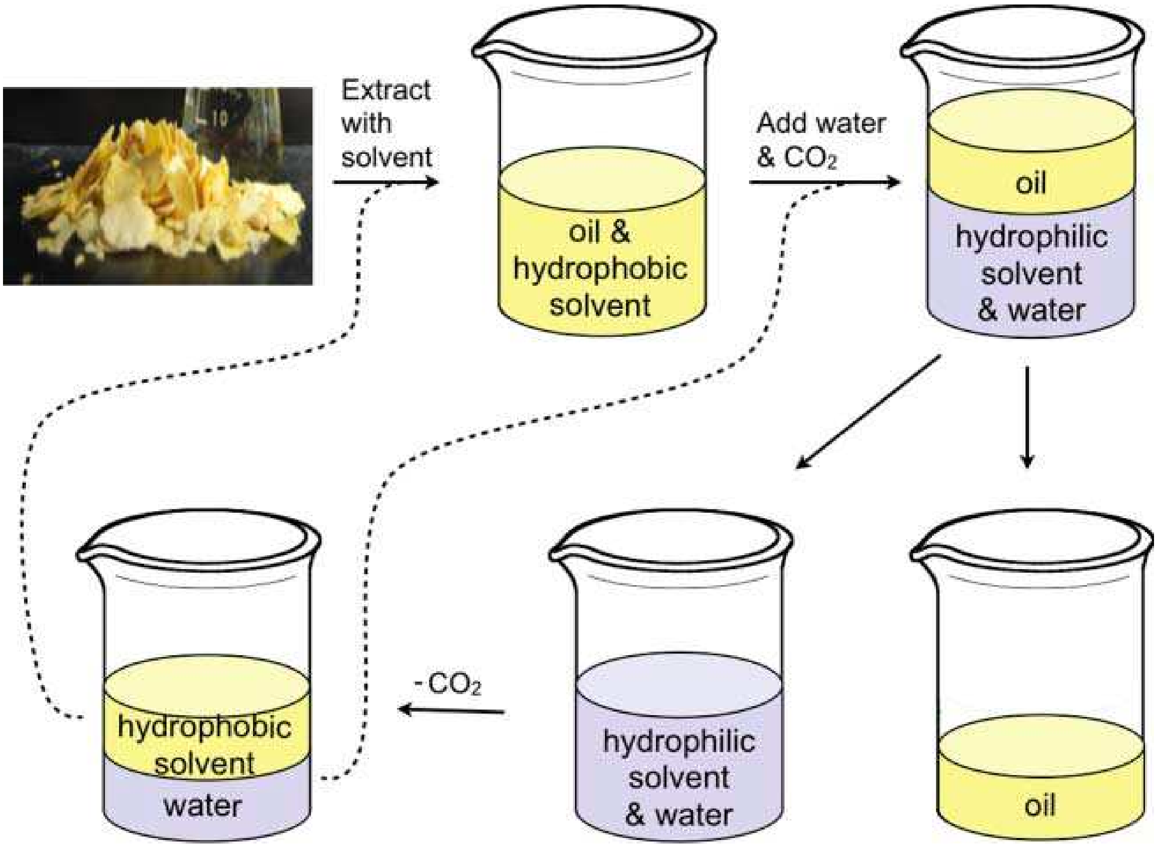

Figure 4.2: The process by which an SHS can be used to extract soybean oil from soybean flakes without a distillation step. The dashed lines indicate the recycling of the solvent and the water. Reproduced from Jessop *et al.* 2010 [1].

is comparable to the acidity of the protonated amine ($\mathrm{pK}_a \approx 10$).

$$\mathrm{NR_{3\,(aq)}} + \mathrm{H_2O_{(l)}} + \mathrm{CO_{2\,(g)}} \rightleftharpoons \mathrm{HNR^+_{3(aq)}} + \mathrm{HCO^-_{3(aq)}} \tag{4.1}$$

Many SHSs have now been reported [6, 16, 17, 18] since our discovery of SHSs in 2010 [2]. In a recent paper, we compared 23 different SHSs in terms of each amine's effectiveness and environmental impact [16]. It was shown that all successful tertiary and bulky secondary amine SHSs had acidities ($\mathrm{pK}_{a\mathrm{H}}$) and hydrophilicities ($\log K_{ow}$) within a particular range. The $\mathrm{pK}_{a\mathrm{H}}$ ranged from 9.5 to 11, and the $\log K_{ow}$ ranged from 1.0 to 2.5. These ranges were predicted from a mathematical model which could be used to narrow the search for SHS candidates [19].

In the present study, these ranges are expanded to include solvents which are not miscible with water under our standard conditions (1 bar of CO_2 and a 1:1 volume ratio of water to amine solvent) but which become water-miscible under other conditions. By using the mathematical model we recently published [19], we can vary the extrinsic parameters such as the pressure of CO_2 ($P_{\mathrm{CO_2}}$) and the volume ratio of water to amine solvent (V_{rat}) and observe the effect on solvents which lay outside the originally identified range of required $\mathrm{pK}_{a\mathrm{H}}$ and $\log K_{ow}$ values. The effects of these parameters on SHS performance are described for the two-liquid system (SHS and water, Figure 4.1) and the three-liquid system (SHS/water/oil, as seen in the top right portion of Figure 4.2). While the nature of the oil phase could vary greatly depending on the application, we have used 1-octanol in this study as a representative oil phase.

4.3 Optimizing the two-liquid system

First, we define $\mathrm{P}_{\mathrm{CO}_2}$ to be the partial pressure of CO_2 present when the SHS is supposed to be hydrophobic. We also define $\mathrm{P}'_{\mathrm{CO}_2}$ to be the CO_2 partial pressure when the SHS is supposed to be hydrophilic. Under our standard conditions, $\mathrm{P}_{\mathrm{CO}_2} = 0$ bar and $\mathrm{P}'_{\mathrm{CO}_2} = 1$ bar. In this paper, $\mathrm{P}_{\mathrm{CO}_2}$ is assumed to be zero except where otherwise specified. In our earlier study, a parameter Z was introduced where $0 < Z < 1$ [19]. Solvents with Z close to 1 were predicted to be succesful SHSs. Z is defined as

$$Z = \frac{n_B - n'_B}{n_{tot}} \tag{4.2}$$

where n_{tot} is the total number of moles of amine added to the system. We originally defined n_B and n'_B as the number of moles of amine dissolved in the water before and after addition of CO_2, but we now modify the definitions of n_B and n'_B to mean the number of moles of amine dissolved in the water when the partial pressure of CO_2 is low ($\mathrm{P}_{\mathrm{CO}_2}$) and high ($\mathrm{P}'_{\mathrm{CO}_2}$), respectively. Eqn 4.2 can be represented in a more convenient way,

$$Z = \frac{M}{\rho} V_{\mathrm{rat}}(S' - S) \tag{4.3}$$

where M is the molar mass of the solvent and ρ is the density. S and S' represent the water solubility of the solvent under different pressures of CO_2 (P_{CO_2} and P'_{CO_2}, respectively). They are described by

$$S = [\mathrm{B}]_{\mathrm{aq}} \left(1 + \frac{1}{K_{a\mathrm{H}}} \sqrt{\frac{K_w + K_1 K_H P_{\mathrm{CO}_2}}{1 + [\mathrm{B}]_{\mathrm{aq}} K_{a\mathrm{H}}^{-1}}} \right) \tag{4.4}$$

and

$$S' = [\mathrm{B}]_{\mathrm{aq}} \left(1 + \frac{1}{K_{a\mathrm{H}}} \sqrt{\frac{K_w + K_1 K_H P'_{\mathrm{CO}_2}}{1 + [\mathrm{B}]_{\mathrm{aq}} K_{a\mathrm{H}}^{-1}}} \right) \tag{4.5}$$

where $[\mathrm{B}]_{\mathrm{aq}}$ represents the concentration of neutral amine dissolved in the aqueous layer and is evaluated from the equilibrium reaction with water, noting that equilibrium is reached when $[\mathrm{B}]_{\mathrm{aq}} = S - [\mathrm{HB}^{+}]_{\mathrm{aq}}$. We assume that $[\mathrm{B}]_{\mathrm{aq}}$ remains unchanged after addition of CO_2. K_1 is the apparent first acid dissociation constant of carbonic acid (4.6×10^{-7}) [20], K_H is Henry's law constant for CO_2 (0.034 M/bar) [21] and K_w is the autoprotolysis constant of water (10^{-14}).

At first we assumed that P'_{CO_2}, the pressure used to switch the amine to the hydrophilic form, was 1 bar. A plot of Z as a function of $\log K_{ow}$ and $\mathrm{pK}_{a\mathrm{H}}$ (Figure 4.3a) shows the region where functional SHSs can be found. However, if one is willing to consider using a higher pressure of CO_2 to trigger the change to hydrophilicity, then these equations can be used with P'_{CO_2} as a variable and P_{CO_2} is assumed to be zero. This suggests that amines with $\mathrm{pK}_{a\mathrm{H}}$s lower than 9 can still serve as SHSs if a higher pressure of CO_2 is used during the switching process. Indeed, a map of Z assuming $P'_{\mathrm{CO}_2} = 10$ bar of CO_2 produces a larger range of SHSs than when assuming 1 bar of CO_2 (Figure 4.3b). A high pressure SHS will switch back to its native hydrophobic state upon depressurizing the system.

We can further modify the system by supposing that P_{CO_2}, the partial pressure of CO_2 present when the amine is supposed to be hydrophobic, is not zero but rather some positive pressure such as 1 bar. By this method, we can predict which of these SHSs will switch off very easily when the 10 bar of CO_2 is released. We predict that these SHSs will be above (higher $\log K_{ow}$) and to the left (lower $\mathrm{pK}_{a\mathrm{H}}$) of the area describing the switchable zone when $P'_{\mathrm{CO}_2} = 1$ bar but within the area defined when $P'_{\mathrm{CO}_2} = 10$ bar (Figure 4.3c). N,N-diethylcyclohexylamine (DECA), tripropylamine (TPA), N,N-dimethylbenzylamine (DMBA), and 1-dimethylamino-2-pentyne

(DMAP) fall within the predicted region but N,N-diisopropylethylamine (DIISO) does not and will be discussed later.

We can predict what pressure of CO_2 is needed in order to cause the system to be monophasic by setting n'_B equal to zero. DECA (properties listed in Table 4.1) does not switch to a hydrophilic form when using an equal volume of water and 1 bar of CO_2, but N,N-dimethylcyclohexylamine (DMCA) does. By setting $n'_B = 0$ and solving for $P'_{\mathrm{CO_2}}$, one can predict that DECA will become water-miscible at $P'_{\mathrm{CO_2}} = 2.9$ bar (with $V_{\mathrm{rat}} = 1.0$). In practice, the DECA/water mixture was biphasic at 3.0 bar and monophasic at 3.5 bar, showing that the predictions of the minimum $P'_{\mathrm{CO_2}}$ by the equations are not particularly accurate. However, with the exception of sterically bulky DIISO and TPA, the equations predict the correct trends. The same procedure can be used to determine the water:SHS volume ratio needed to switch when $P'_{\mathrm{CO_2}} =$ 1 bar. We predict that the DECA/water system will become monophasic under atmospheric pressure of CO_2 when $V_{\mathrm{rat}} = 1.7$. Table 4.1 summarizes these results for four other amine solvents and compares the predicted values to experimental observations. As noted above, DIISO is qualitatively different from the other four and therefore will be discussed separately.

It should be noted that the $P'_{\mathrm{CO_2}}$ required to trigger miscibility is a function of V_{rat}. Therefore, it is possible to predict the effect of changing both variables simultaneously. Figure 4.4 shows that as V_{rat} for 4 amines (DECA, TPA, DMAP and DMBA) is increased, less pressure is needed to trigger miscibility. The data points at 1 bar of CO_2 were measured by preparing water/amine mixtures with increasing V_{rat} values in intervals of 0.5. CO_2 was bubbled through each amine/water system, starting with the lowest V_{rat}, until the system became monophasic. The sample with

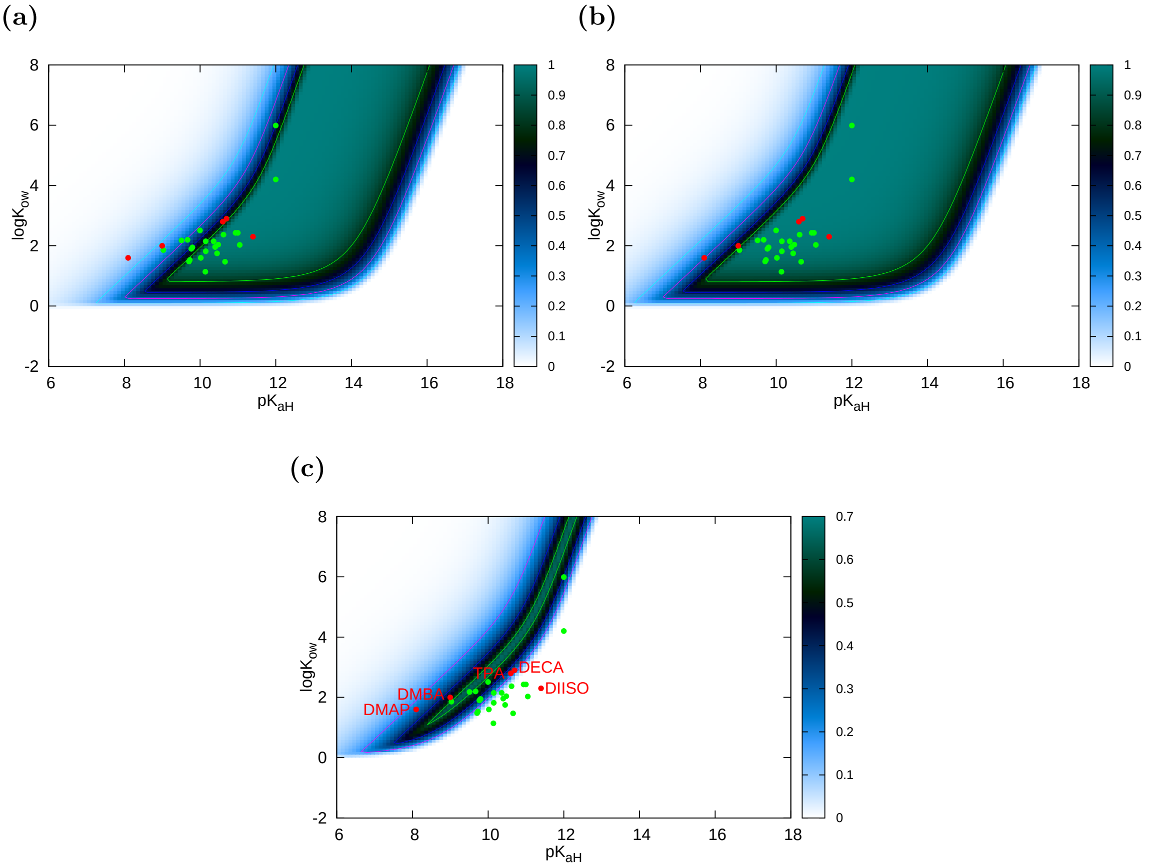

Figure 4.3: Theoretical maps indicating the region of high SHS viability in a two-liquid system at (a) $P'_{\mathrm{CO}_2} = 1$ bar and $P_{\mathrm{CO}_2} = 0$ bar, or (b) $P'_{\mathrm{CO}_2} = 10$ bar and $P_{\mathrm{CO}_2} = 0$ bar. The region in (c) represents the high pressure SHSs which are water-miscible at $P'_{\mathrm{CO}_2} = 10$ bar but biphasic at $P_{\mathrm{CO}_2} = 1$ bar. These SHSs should switch off very easily. Map (c) is the difference between maps (a) and (b). The green dots represent confirmed SHS amines and the two SHS amidines at the upper right. The red dots represent the new SHSs presented in this study.

the lowest V_{rat} value that became monophasic after treatment with 1 bar of CO_2 is reported as the high value in Table 4.1.

All data points at higher pressures were determined using a high pressure vessel. A mixture of water and amine was placed in a pressure vessel. Sudan III dye, which dissolved in the amine layer, was added to help improve the visual contrast between the phases. The pressure was increased in 0.5 bar intervals until a red solution was observed. At each interval, the system was allowed 60 minutes to equilibrate.

DIISO differs from the other four new SHS in that it does not fall into the region predicted in Figure 4.3c. It is not included in Figure 4.4 because eqn 4.3 predicts that it should switch under normal conditions. Indeed, given its relatively high $\text{pK}_{a\text{H}}$ and low $\log K_{ow}$, one would expect DIISO to be water-miscible under 1 bar of CO_2. We have assumed that steric bulk around the nitrogen has no effect on SHS performance, which may not be true [18]. Further development of the equations may be necessary to include steric effects.

It was observed that DIISO/water system became biphasic once it was depressurized from 7.0 bar of CO_2, whereas amines that act as SHS under 1 bar CO_2 did not become biphasic unless heated and bubbled with N_2 or Ar. An amine that only becomes water-miscible under high pressures of CO_2 may require less energy and time to remove the CO_2 than amines that become water-miscible at 1 bar of CO_2 because incomplete CO_2 removal would not inhibit separation of the amine from the water. To investigate the possibility further, the amount of amine in a carbonated aqueous phase was monitored by GC-TCD as CO_2 was removed over time. DMCA was water-miscible at 1 bar of CO_2 and DIISO was water-miscible at 7 bar CO_2. A 4.0 mL sample of the DMCA/water monophasic solution was taken and placed in a

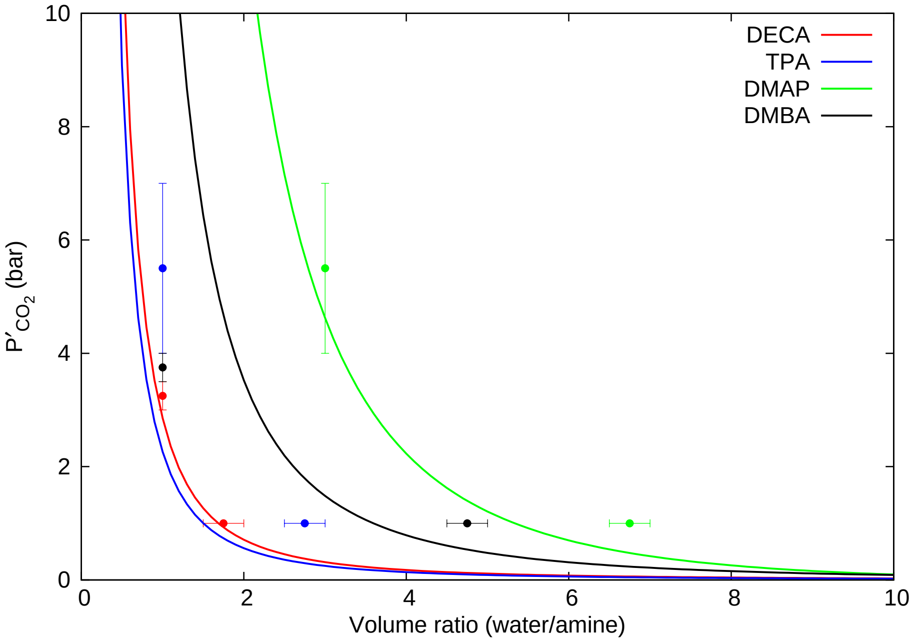

Figure 4.4: The curves show the values of $P'_{\mathrm{CO_2}}$ which yield a maximum value of Z for DECA, TPA, DMAP and DMBA as a function of V_{rat}, calculated using eqn 4.3. The data points indicate the experimentally determined range of pressures (within 0.5 bar) needed to achieve a monophasic system. Sudan III dye was used to monitor the phase switch in the pressure vessel. Each amine/water mix is monophasic at conditions above and to the right of the shown curve, and biphasic below and to the left of the curve.

20.0 mL tubular glass vial with a magnetic stir bar. At 60°C with 200 rpm of stirring and nitrogen bubbling through the system, the phases began to separate. A 0.10 mL GC-TCD sample of the aqueous layer was taken every 15 minutes for 6 consecutive trials. This was repeated for the DIISO/water monophasic system, however no heat or nitrogen was applied to the system; it was simply depressurized from 7.0 bar CO_2. This was to determine the effect of a high pressure gradient on the rate of CO_2 removal. The 0.10 ml samples were diluted with DriSolv Methanol. An amine to water intensity plot as a function of time was plotted for DIISO and DMCA (Figure 4.5).

These SHSs which require higher CO_2 pressures and/or higher water to amine

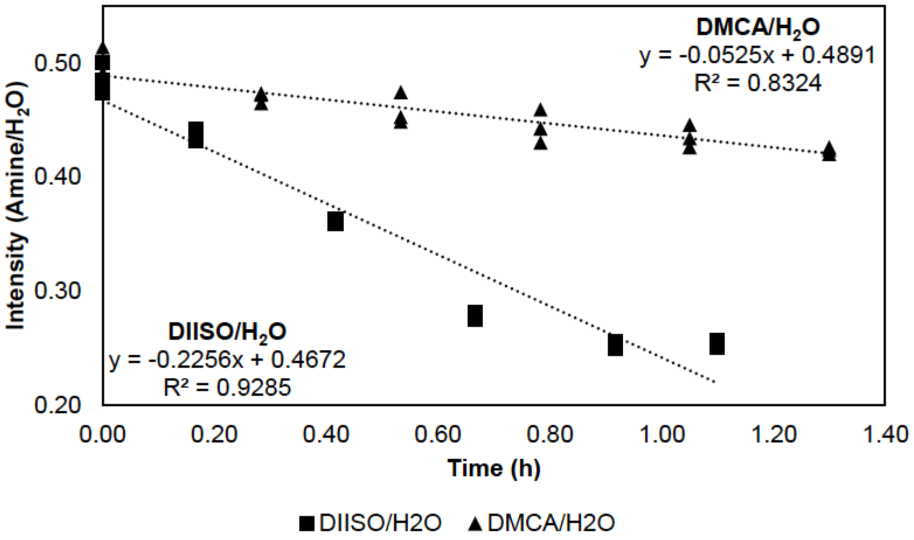

Figure 4.5: The rate of CO_2 removal as shown by relative intensities of amine to water signals in the aqueous layer by GC-TCD spectra. The system changing from 7 bar of CO_2 (DIISO/water) shows a steeper slope (-0.23 h^{-1}) than the system changing from 1 bar of CO_2 (DMCA/water: -0.05 h^{-1}).

volume ratios are of interest because they are able to revert back to their water-immisible state quickly and easily. While high $\log K_{ow}$ SHSs are not particularly desirable due to their high bio-accumulation, low pK_{aH} SHSs are desirable. The amines presented in this paper do not require CO_2 pressures over 10 bar (with the exception of 1-dimethylamino-2-pentyne which is estimated to require 60 - 70 bar at a 1:1 water to amine volume ratio). This amount of pressure is not very taxing to industrial processes. Though these amines are not necessarily less water-soluble than regular SHSs, it is likely that they are more difficult to remove from an organic liquid product (Figure 4.2).

The pK_{aH} range can not be extended indefinitely. Because carbonic acid is a weak acid (pK_a 6.3) whose pH is around 4. Therefore, it will not protonate amine derivatives with pK_{aH} values less than or equal to 4. Figure 4.3b shows that the effective lower limit of the pKa range is about 7 when $P'_{\mathrm{CO}_2} = 10$ bar. In theory, there is no limit to the $\log K_{ow}$ range provided it is above zero and carbonic acid is strong enough to protonate the nitrogen. For practical environmental purposes, however, one should avoid SHSs with high $\log K_{ow}$ values due to the greater toxicity, bioaccumulation potential, and the likely difficulty in recovering them from organic liquid products. Only compounds with $\log K_{ow}$ values less than 3.5 are considered to have low bioaccumulation potential [22].

4.4 Optimizing the three-liquid system

Switchable technology can be readily applied to a three-component system composed of water, amine solvent, and a water-immiscible organic liquid that represents an oily product (top right part of Figure 4.2). Separations of this nature would be required if SHSs were to be used in organic synthesis or in extraction processes. For a separation process such as that shown in Figure 4.2, the amine must partition strongly into the carbonated water phase rather than the organic oil phase. We recently introduced Ω, a parameter designed to quantify the suitability of a compound as an SHS for a three-liquid system [19].

$$\Omega = -\log D \times \log D' \tag{4.6}$$

where $\log D$ and $\log D'$ represent the distribution coefficients of the amine (both neutral and protonated) between the organic and aqueous layers at P_{CO_2} and P'_{CO_2}, respectively. Amines with $\Omega < 0$ would either have high water-miscibility in the absence of CO_2 or low water-miscibility even in the presence of CO_2. Thus, only values of $\Omega > 0$ qualify as SHSs. The distribution of the amine in its neutral form is represented by $\log K_{ow}^{\text{neut}}$ while its salt form is represented by $\log K_{ow}^{\text{salt}}$. As these terms only consider one species (either neutral or charged), they are called partition coefficients. It is assumed that the hydroxide and bicarbonate salts have similar partition coefficients. The partition coefficient of DMCA in its neutral form is related to the partition coefficient of its bicarbonate salt by $\log K_{ow}^{\text{DMCA}} - \log K_{ow}^{\text{salt}} = 2.8$ [19]. It has been shown that $\Delta \log K_{ow}$ is relatively constant for compounds belonging to the same family (and have the same counter-ion) [23, 24]. For the simulations, we assume that this value of $\Delta \log K_{ow}$ is representative for all tertiary alkyl amines and their bicarbonate salts. This assumption likely fails when other functional groups are present or the molar mass is significantly different. The distribution coefficient (eqn 4.7) is related to the partition coefficients and the ratio of protonated and neutral species in the aqueous layer ($[\text{HB}^+]_{\text{aq}}/[\text{B}]_{\text{aq}}$), which increases with the addition of CO_2.

$$\begin{aligned} \log D = \log\left(\frac{K_{ow}^{\text{NR}_3}}{K_{ow}^{\text{salt}}} + \frac{[\text{HB}^+]_{\text{aq}}}{[\text{B}]_{\text{aq}}}\right) + \log K_{ow}^{\text{salt}} \\ - \log\left(1 + \frac{[\text{HB}^+]_{\text{aq}}}{[\text{B}]_{\text{aq}}}\right) \end{aligned} \tag{4.7}$$

Following the same optimization procedure as the two-liquid system, one can predict the amount of CO_2 pressure needed to quantitatively protonate an amine so that it can partition according to K_{ow}^{salt} (again here we are assuming that P_{CO_2} is zero).

$$\begin{aligned} P'_{\text{CO}_2} = \left(\frac{\text{K}_{a\text{H}}(K_{ow}^{\text{NR}_3} - D')}{D' - K_{ow}^{\text{salt}}}\right)^2 \frac{(1 + [B]_{aq}\text{K}_{a\text{H}}^{-1})}{K_1 K_H} \\ - \frac{K_w}{K_1 K_H} \end{aligned} \tag{4.8}$$

where D' can be isolated from eqn 4.6. Again, the last term is very small and can be neglected. The biggest difference between Z and Ω is that Ω does not range between 0 and 1. Therefore, we cannot assign an arbitrary value for Ω that is representative of all amines. Figure 4.6 shows how $\log D'$ is affected by the pressure of CO_2 for 3 SHSs which become water-miscible at $P'_{CO_2} = 1$ bar (DMCA, N,N-diisopropylethanol amine (DIPEA), and triethylamine (TEA)) and 4 SHSs which only become water-miscible at $P'_{CO_2} > 1$ bar (DECA, TPA, DMAP, and N,N-dimethylbenzylamine (DMBA)). The immiscible organic layer is represented by 1-octanol. In order for an SHS to be easily removable from a liquid organic product, $\log D'$ must be less than zero. The $\log D'$ of DMCA, DIPEA, and TEA become negative with CO_2 pressures lower than 1 bar. DECA, TPA, DMAP, and DMBA on the other hand, require pressures greater than 10 bar before they prefer the aqueous layer. It should be noted that each curve levels off according to $\log K_{ow}^{\text{salt}}$ (as $P'_{CO_2} \to \infty$, $\log D' \approx \log K_{ow}^{\text{salt}}$). It is possible that some amines would not be effective as SHSs in a 3-liquid system if $\log K_{ow}^{\text{salt}} > 0$. However, more SHS can be extracted from the oil layer by using a greater volume of water.

The bicarbonate salts of DMBA and DMAP are assumed to partition very favorably into the aqueous layer due to their predicted low $\log K_{ow}^{\text{salt}}$ values. However, due to their low $\text{pK}_{a\text{H}}$ values ($\text{pK}_{a\text{H}} = 9.0$ and 8.1, respectively), a high CO_2 pressure is needed to quantitatively protonate these compounds.

4.5 Conclusions

The SHS amines that we have reported previously are, when mixed 1:1 by volume with water, biphasic at 0 bar of CO_2 and monophasic at 1 bar. These amine SHSs are found in a narrow range of $\text{pK}_{a\text{H}}$ and $\log K_{ow}$ values. However, the range of SHSs can be

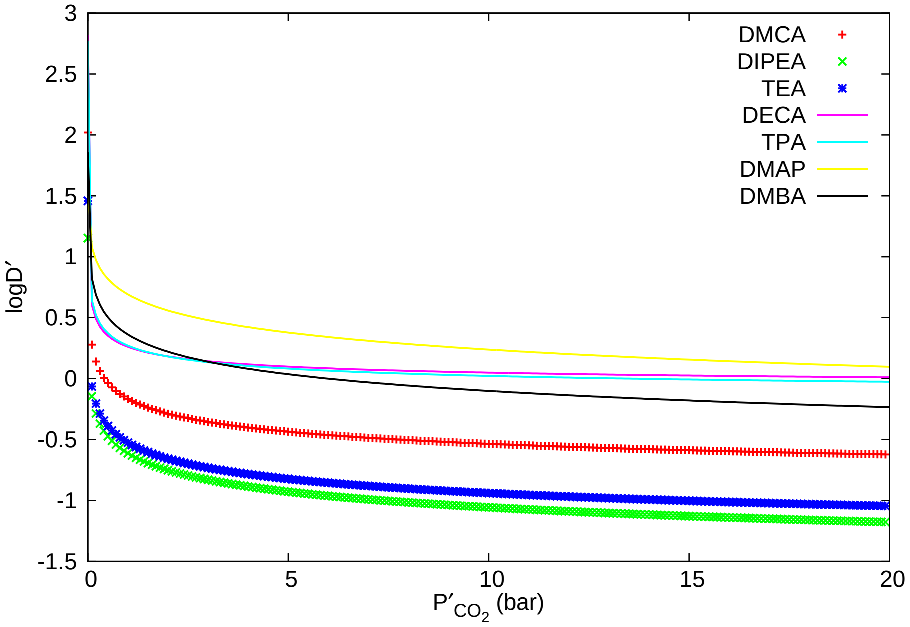

Figure 4.6: Calculated distribution curves for low pressure SHSs (DMCA, DIPEA, TEA, points) and high pressure SHSs (DECA, TPA, DMAP, lines) as a function of P'_{CO_2} assuming $\Delta \log K_{ow} = 2.8$. As expected, amines which function as SHSs under atmospheric pressure of CO_2 are easier to separate from a liquid product than amines which require pressures higher than 1 bar. The effectiveness of the SHS (given an infinite amount of pressure) is governed by the partition coefficient of its bicarbonate salt.

extended by increasing the water to amine volume ratio or the pressure of CO_2 used to trigger miscibility. Amines with high octanol-water partition coefficients and/or low basicities can become water-miscible by varying either of these extrinsic parameters. Amines with $\mathrm{pK}_{a\mathrm{H}} < 8.5$ require considerable CO_2 pressure before they can become water-miscible (if they can at all). Increasing the water to amine volume ratio relaxes the required CO_2 pressure and thus using both parameters simultaneously allows for a significant extension of the original SHS range. Of course, amines with $\mathrm{pK}_{a\mathrm{H}}$ values nearing the pK_a of carbonic acid (6.3) are unlikely to ever serve as SHSs.

It is curious that DIISO does not readily switch to its hydrophilic form when treated with 1 bar of CO_2. This amine fits neither our mathematical models nor our prior observations of the range of $\mathrm{pK}_{a\mathrm{H}}$ and $\log K_{ow}$ values for amines that become water-miscible at 1 bar of CO_2. We conclude that steric factors are likely at play.

A simulated 3-liquid system revealed that the SHSs already reported in the literature are easier to separate from a liquid product (represented by 1-octanol) than the new SHSs which require higher CO_2 pressures or water to amine volume ratios before they become water-miscible. The effectiveness of the separation is governed by the partitioning of the bicarbonate salt and therefore amines with high K_{ow} values would not be recommended for practical use.

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Chapter 5

Conclusion

5.1 Summary

We have searched for and designed amine compounds that can switch from having low to high water-miscibility by the addition of CO_2. Tertiary and secondary amines (and their derivatives) were screened for SHS behaviour. Though secondary amines are less toxic in general, more energy is required to remove the CO_2 due to carbamate salt formation. This can be avoided by having steric bulk around the nitrogen of a secondary amine. Tertiary amines do not form carbamate salts. Care was taken to consider environmentally benign SHSs. Boiling point, flash point, bioaccumulation and toxicity are among the top factors to consider when using SHSs. In general, a high boiling point can be attained by increasing the molecular weight of the compound. Simply adding longer alkyl chains to tertiary or secondary amines will achieve this, but this practice will also increase the hydrophobicity which will push the compound outside of the switchable zone and add to bioaccumulation. Therefore, other functional groups can be added to increase the molecular weight without drastically affecting the hydrophilicity. Some functional groups considered were alcohols, amides, esters, as well as other amine groups. These functional groups can be used to design a solvent which can act as an SHS and have low environmental impact factors.

We have also described the switchable process mathematically, both for the two-liquid system (composed of water and SHS) and the three-liquid system (composed of water, SHS, and a water-immiscible organic liquid). This revealed other important variables such as density, molecular weight, CO_2 pressure and water:SHS volume ratio. The latter two are extrinsic variables that can be tuned to optimize the SHS process. Further, the mathematical model accurately predicts which amine solvents will demonstrate SHS behaviour, although there are a few unexplained exceptions. Some amine compounds (such as N,N-diisoethylpropylamine) are not SHSs at a 1:1 volume ratio with water and under 1 bar of CO_2 even though the model would suggest that they should be SHSs. This discrepency may be due to kinetic and/or steric factors, which the model does not take into account. Amines with $\mathrm{pK}_{a\mathrm{H}}$ and $\log K_{ow}$ values outside of the usual range can still function as SHSs given a higher CO_2 pressure and/or water:amine volume ratio. Increasing the CO_2 pressure increases the concentration of carbonic acid in solution, thereby lowering the pH. This facilitates the protonation of amines with $\mathrm{pK}_{a\mathrm{H}} < 9$. Though this also allows SHS behaviour for amines with high $\log K_{ow}$ values, these compounds will likely be avoided in practice due to the difficulty of extracting them from the oil.

5.2 Future Work

5.2.1 Other Variables

The mathematical model falsely predicts that N,N-diisopropylethylamine will behave as an SHS. We believe this discrepancy is due to steric factors which the model does not take into account. Because the SHS mechanism is largely based on acid-base chemistry, it is curious that sterics would hinder proton transfer. Including steric effects in an analytic description is not a simple matter. It may be possible to introduce cone-angles of substrates surrounding the nitrogen center, but how this affects SHS behaviour is still unclear.

Another tunable parameter to include in the mathematical model is temperature. This could easily be incorporated into the model. The only change would be having the equilibrium constants as functions of temperature (the Van't Hoff equation). Thermodynamic data would also need to be available to predict how these equilibrium constants would change with temperature.

5.2.2 Kinetics

The mathematical model says nothing about kinetics. Currently, the switching process takes a few hours one average, to switch on and then back off again. The time required for this process can likely be reduced by manipulating the system from a kinetics standpoint, rather than an equilibrium one. However, the relationship between the kinetics and the steric bulk of secondary and tertiary amines is an interesting problem which was not addressed in this thesis but its effects were noted (bulky amines do not necessarily follow the derived mathematical description). Optimizing this process with time could involve modelling the rate at which a bubble of CO_2 gas is dissolved in an aqueous sample.

5.2.3 Diamines as SHSs

Diamines are attractive as SHSs because there are two sites which can be protonated, though only one may be required to become water-miscible. Not only would they be easier to switch on, they would also be easier to switch off. This is mostly due to the higher density of protonatable sites. Having two protonatable sites, diamines are statistically more likely to be protonated by hydrated CO_2. Further, if both sites become protonated, then the diamine bicarbonate salt will be much better stabilized in a polar solvent like water. The switch off would be facilitated by the fact that di-cationic species are unstable. Once one site is deprotonated, the species will become amphiphilic, having a hydrophic end and a hydrophilic end. The hydrophobic end will migrate towards the oil layer and facilitate the release of the second acidic proton. Despite this attractive theory, we could not find any diamine SHSs with $\log K_{ow} < 4$. As previously discussed, compounds with $\log K_{ow} > 3.5$ contribute to bioaccumulation and are difficult to extract from the oil layer. Diamine SHSs may be designed to include other functional groups to lower their $\log K_{ow}$ but none have been discovered yet. The reason for diamines having a different switchable zone than secondary and tertiary monoamines is unclear. The mathematical model may only need minor modifications to adopt diamine behaviour - perhaps letting n_B represent the number of protonatable sites and allowing $\mathrm{pK}_{a\mathrm{H}}$ to be recycled (assuming similar $\mathrm{pK}_{a\mathrm{H}}$ values) is sufficient. It is worth investigating diamines as potential SHSs both experimentally and mathematically.