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Modelling the behaviour of switchable-hydrophilicity solvents

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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.

1 Introduction

Industry regularly uses flammable and smog-forming volatile organic solvents in chemical processes, even though non-volatile 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 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 - 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 1). Figure 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.

$$NR_{3\,(aq)} + H_2O_{(l)} + CO_{2\,(g)} \rightleftharpoons HNR^+_{3(aq)} + HCO^-_{3(aq)} \quad (1)$$

The SHS reported so far by the Jessop group include 23 amines and amidines.[1–3] 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 or N_2) through the solution.

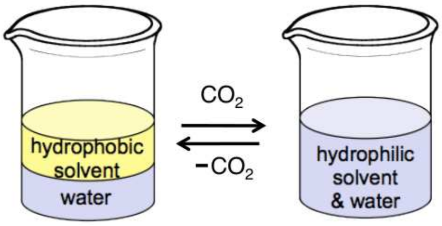

Fig. 1 A switchable-hydrophilicity solvent changes from hydrophobic to hydrophilic upon addition of CO_2 and then back to hydrophobic upon removal of CO_2.

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, 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 ($pK_a \approx 10$).

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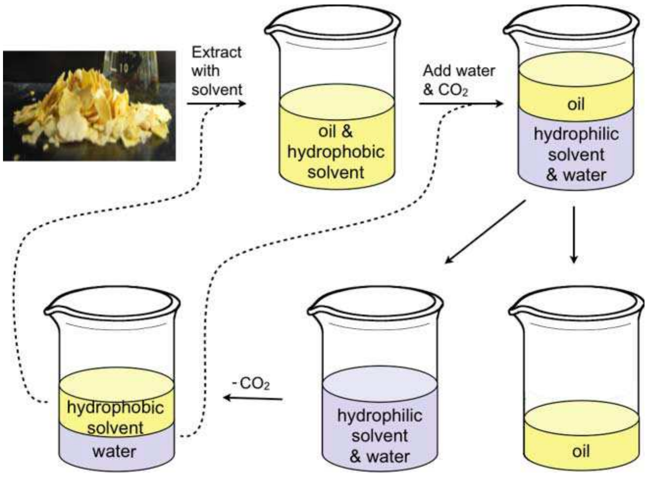

Fig. 2 The process by which an SHS can be used to extract soybean oil from soybean flakes without a distillation step. The dashed lines indicate the recycling of the solvent and the aqueous phase. Reproduced from Jessop *et al.* 2010 [1].

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.

2 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 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 2 to be practical. We can relate the solubility to the number of moles of amine that failed to dissolve in the water,

$$n_{B,\mathrm{undiss}} = \frac{\rho}{M} V_B - S V_w \tag{2}$$

$$n'_{B,\mathrm{undiss}} = \frac{\rho}{M} V_B - S' V_w \tag{3}$$

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 6 & 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:

$$S = [\mathrm{B}]_{aq} + [\mathrm{HB}^+]_{aq} \tag{4}$$

$$S' = [\mathrm{B}]_{aq} + [\mathrm{HB}^+]_{aq}{}' \tag{5}$$

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

$$K_{a\mathrm{H}} = \frac{[\mathrm{B}]_{aq}[\mathrm{H}^+]_{aq}}{[\mathrm{HB}^+]_{aq}} \tag{6}$$

$$K_1 = \frac{[\mathrm{H}^+][\mathrm{HCO}_3^-]}{K_H P_{\mathrm{CO}_2}} \tag{7}$$

where K_H is Henry's constant for CO_2 (0.034 M/atm). Substituting the above relations into the solubility equations leads to

$$S = [\mathrm{B}]_{aq}\left(1 + \frac{1}{K_{a\mathrm{H}}}\sqrt{\frac{K_w}{1+[\mathrm{B}]_{aq}K_{a\mathrm{H}}^{-1}}}\right) \tag{8}$$

and

$$S' = [\mathrm{B}]_{aq}\left(1 + \frac{1}{K_{a\mathrm{H}}}\sqrt{\frac{K_w + K_1 K_H P_{\mathrm{CO}_2}}{1+[\mathrm{B}]_{aq}K_{a\mathrm{H}}^{-1}}}\right) \tag{9}$$

where $[\mathrm{B}]_{aq}$ is evaluated from the equilibrium reaction with water, noting that equilibrium is reached when $[\mathrm{B}]_{aq} = S - [\mathrm{HB}^+]_{aq}$. We assume that $[\mathrm{B}]_{aq}$ remains unchanged after addition of CO_2.

The concentration of neutral amine in the aqueous phase $[\mathrm{B}]_{aq}$ 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 ($CyNMe_2$) was measured in increasingly salty aqueous phases. Trimethylcyclohexylammonium iodide ($[CyNMe_3]I$) was added to the mixture to best simulate the system as the protonated amine is drawn into the aqueous phase. Figure 3 shows that the solubility of $CyNMe_2$ increases in aqueous solutions of $[CyNMe_3]I$. A biphasic system could not be attained after the salt concentration reached about 1.0 mol L^{-1} indicating that $CyNMe_2$ 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 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.

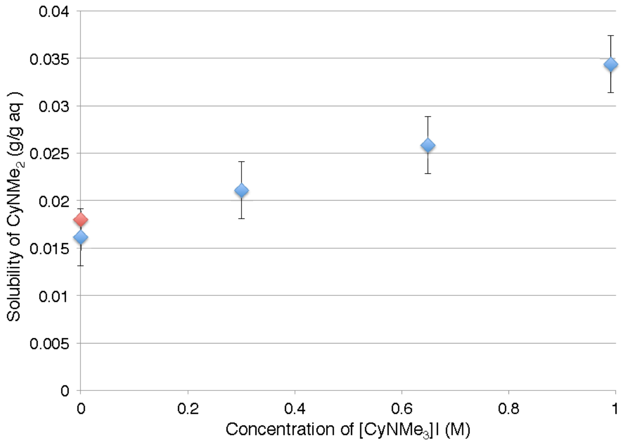

Fig. 3 Solubility of $CyNMe_2$ in aqueous solutions of organic salt $[CyNMe_3]I$. The red point corresponds to the reported water solubility of $CyNMe_2$ in the literature.[2]

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

$$Z = \frac{n_B - n'_B}{n_{tot}} \tag{10}$$

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, respectively, 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 an amine with $Z \approx 0$ will not. S_0 was converted to $\log K_{ow}$ using Equation 11 from Meylan *et al*[4] which accounts for the molecular weight and the effect of an aliphatic liquid amine.

$$\log S = 0.796 - 0.854 \log K_{ow} - 0.00728(M) + \Sigma f_i \tag{11}$$

where $f_i = 1.008$ for aliphatic amines.

The map shown in Figure 4 outlines the ranges of $\log K_{ow}$ and pK_{aH} 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 pK_{aH}. 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 $V_w > V_B$.

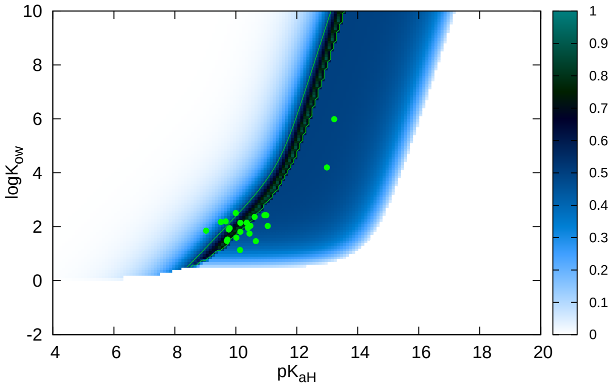

Fig. 4 Theoretical map indicating the region of high SHS viability in a two-liquid system. The z-axis represents Z from Equation 10 and the green dots represent confirmed SHS tertiary and bulky secondary amines and the two SHS amidines at the upper right.

3 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 the 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 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.

$$NR_{3\,(aq)} \xrightleftharpoons{K_{ow}} NR_{3\,(org)}$$
$$[HNR_3^+\ HCO_3^-]_{(aq)} \xrightleftharpoons{K'_{ow}} [HNR_3^+\ HCO_3^-]_{(org)}$$

where

$$K_{ow} = \frac{[B]_{org}}{[B]_{aq}} \tag{12}$$

$$K'_{ow} = \frac{[\mathrm{HB}^+]_{org}}{[\mathrm{HB}^+]_{aq}} \tag{13}$$

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]

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

It follows that

$$\begin{aligned} \log D = \log K_{ow} + \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}} - \mathrm{pH} - \Delta \log K_{ow}}\right) \\ - \log\left(1 + 10^{\mathrm{p}K_{a\mathrm{H}} - \mathrm{pH}}\right) \end{aligned} \tag{14}$$

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] 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 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 5). The results are consistent with Equation 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 14 is by substituting the pH variable with a ratio of charged to neutral species. One arrives at the following relationship

$$\begin{aligned} \log D = \log\left(\frac{K_{ow}}{K'_{ow}} + \frac{[\mathrm{HB}^+]_{aq}}{[\mathrm{B}]_{aq}}\right) \\ - \log\left(\frac{1}{K'_{ow}} + \frac{1}{K'_{ow}}\frac{[\mathrm{HB}^+]_{aq}}{[\mathrm{B}]_{aq}}\right) \end{aligned} \tag{15}$$

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

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

before the addition of CO$_2$ and

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

after the addition of CO$_2$.

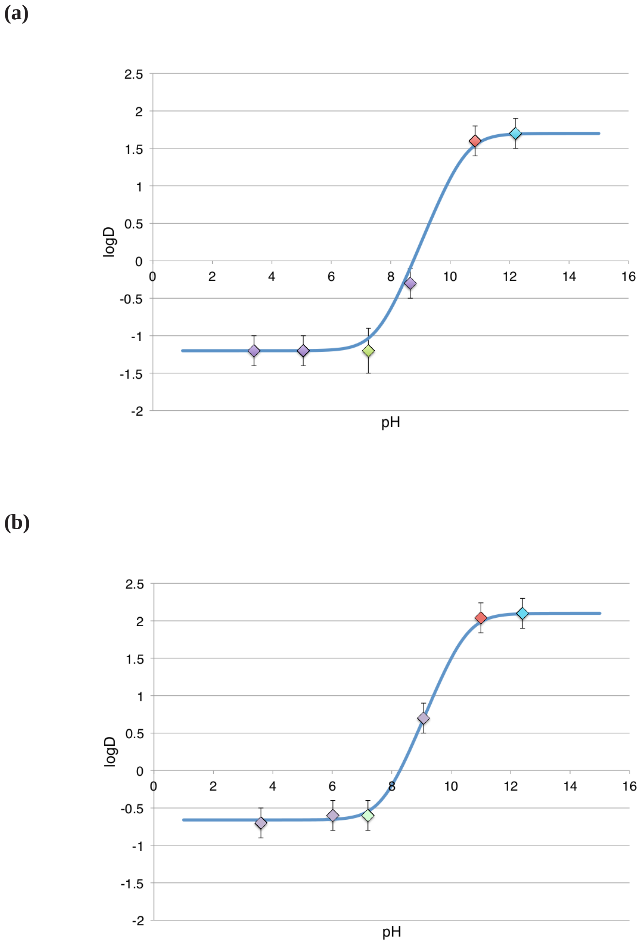

Fig. 5 Distribution coefficient of CyNMe$_2$ a) between toluene and water and b) between 1-octanol and water. The distribution of 3.3 mmol of amine between the organic solvent and water (5 mL each) at ambient temperature is represented by the red point. The distribution after saturation of the mixture 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 14 is overlaid to show agreement with the data.

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 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):

$$\Omega = -\log D_1 \times \log D_2 \tag{16}$$

Figure 6 shows the map produced by Equation 16 as well as the dataset of confirmed tertiary and bulky secondary amine SHS.

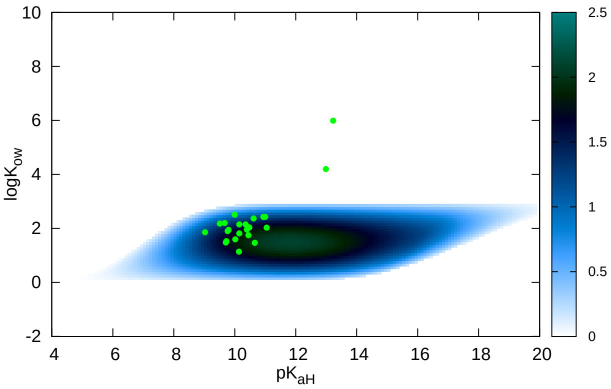

Fig. 6 A map of Ω, indicating the region of high SHS viability in a three-liquid system, assuming that $\Delta\log K_{ow} = 2.8$. The green dots represent the confirmed SHS amines and the two SHS amidines at the upper right.

Figure 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 ($K_{a\mathrm{H}}$),

$$P = \frac{[\mathrm{H}^+]}{[\mathrm{H}^+] + K_{a\mathrm{H}}} \tag{17}$$

and the system midpoint is at pH = 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

$$P = \frac{n_{\mathrm{HB}^+,\mathrm{org}} + n_{\mathrm{HB}^+,\mathrm{aq}}}{n_{\mathrm{B},tot}} \tag{18}$$

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.

$$P = \frac{[\mathrm{H}^+]}{[\mathrm{H}^+] + K_{a\mathrm{H}}\left(\frac{1+V_{\mathrm{rat}}K_{ow}}{1+V_{\mathrm{rat}}K'_{ow}}\right)}, \tag{19}$$

where $V_{\mathrm{rat}} = V_{\mathrm{org}}/V_{\mathrm{aq}}$. With only an aqueous phase, the equation reduces to Equation 17. The exchange between aqueous and organic layers results in a decrease of protonated species at a particular pH. Figure 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$K_{a1} = 6.4$)‡, it is wise to use a low V_{rat} in order to ensure a greater percentage of amine protonation.

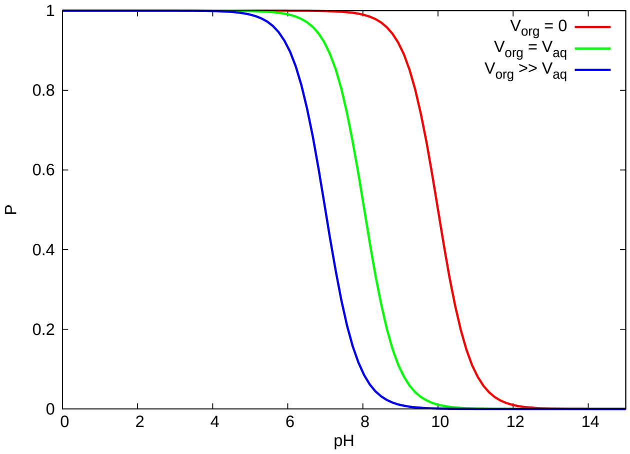

Fig. 7 The effect of the organic layer volume on the fraction of protonated base. If V_{rat} is nearly zero, then the system midpoint is essentially the p$K_{a\mathrm{H}}$ of the amine, while if V_{rat} is much larger than 1, then the system midpoint is shifted down by about 3 pH units. K_{ow} and the acid dissociation constant are assumed to be 10^2 and 10^{-10}, respectively.

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‡ This is the apparent acidity of dissolved CO_2 rather than the pKa of H_2CO_3 itself.

4 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 $\mathrm{p}K_{a\mathrm{H}}$ 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 $\mathrm{p}K_{a\mathrm{H}}$ 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 6 because that allows them to also fall in or close to the optimum area in Figure 4. Amidine SHS fall outside of the prescribed range of Figure 6, suggesting that while they may technically be SHS, they are less likely to be ideal for extraction processes like that illustrated in Figure 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.

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