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Extending the range 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. All of the amine SHSs that we have reported previously lie within a particular basicity and hydrophilicity range (9.5 < pK_{aH} < 11 and 1.0 < log K_{uw} < 2.5, respectively). We report an extension of this range by altering the pressure of CO\textsubscript{2} as well as the water:SHS volume ratio used in the process. Increasing the pressure of CO\textsubscript{2} and/or the water:amine volume ratio allows some amines with pK_{aH} < 9.5 or log K_{uw} > 2.5 to function as SHSs.

1 Introduction

Separating organic products from solvents is a common step after organic syntheses and extraction processes. Industry regularly uses volatile organic solvents so that the solvent can be removed by distillation, but many of these solvents are flammable and smog-forming. In contrast, 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. Now that many SHSs are known,1,2 one can easily choose an SHS that is not volatile and that has little acute toxicity.1 The avoidance of distillation may also result in energy savings, but this depends upon the energy costs associated with switching the solvent. Their utility has been demonstrated for various separation processes - the isolation of bitumen from the oil sands,3 vegetable oil from soybeans,4,5 bio-oil from algae,5–7 polystyrene from waste polystyrene foam,8 and phenols from lignin.9 They can also be used as draw solutes for forward osmosis.10–12 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.

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 the transformation of the SHS occurs with the addition or removal of CO\textsubscript{2} (Figure 1). The resulting carbonated water reacts with the SHS, protonating it and forming a water-miscible bicarbonate salt (eqn. 1, where NR\textsubscript{3} is the hydrophobic form of the solvent and [HNR\textsuperscript{+3}][HCO\textsubscript{3}–] is the hydrophilic form). Reversion of the hydrophilic form to the hydrophobic form is achieved by removal of the CO\textsubscript{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 2. The formation of carbamate salts rather than bicarbonate salts is avoided by the use of tertiary or bulky secondary amine SHSs. Carbamate salts are not preferred because they require more energy input during the removal of CO\textsubscript{2} when restoring the amine solvent to its native hydrophobic state.13 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 is comparable to the acidity of the protonated amine (pK\textsubscript{a} ≈ 10).

\[ \text{NR}_3^{+} \text{aq} + \text{H}_2\text{O(l)} + \text{CO}_2(g) \rightleftharpoons \text{HNR}_3^{+} \text{aq} + \text{HCO}_3^{-} \text{aq} \] (1)

Many SHSs have been reported1,8,14,15 since our discovery of this kind of solvent in 2010.4 In a recent paper, we compared 23 different SHSs in terms of each amine’s effectiveness...
and environmental impact.\(^1\) It was shown that all successful tertiary and bulky secondary amine SHSs had acidities (\(pK_{\text{aH}}\)) and hydrophilicities (\(\log K_{\text{ow}}\)) within a particular range. The \(pK_{\text{aH}}\) ranged from 9.5 to 11, and the \(\log K_{\text{ow}}\) 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.\(^2\)

In the present study, these ranges are expanded to include solvents which are not miscible with water under our standard conditions (1 bar of \(\text{CO}_2\) 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,\(^2\) we can vary the extrinsic parameters such as the pressure of \(\text{CO}_2\) (\(P_{\text{CO}_2}\)) and the volume ratio of water to amine solvent (\(V_{\text{rat}}\)) and observe the effect on solvents which lay outside the originally identified range of required \(pK_{\text{aH}}\) and \(\log K_{\text{ow}}\) values. The effects of these parameters on SHS performance are described for the two-liquid system (SHS and water, Figure 1) and the three-liquid system (SHS/water/oil, as seen in the top right portion of Figure 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.

2 Optimizing the two-liquid system

First, we define \(P_{\text{CO}_2}\) to be the partial pressure of \(\text{CO}_2\) present when the SHS is supposed to be hydrophobic. We also define \(P'_{\text{CO}_2}\) to be the \(\text{CO}_2\) partial pressure when the SHS is supposed to be hydrophilic. Under our standard conditions, \(P_{\text{CO}_2} = 0\) bar and \(P'_{\text{CO}_2} = 1\) bar. In this paper, \(P_{\text{CO}_2}\) is assumed to be zero except where otherwise specified. All pressures are absolute rather than gauge pressures. In our earlier study, a parameter \(Z\) was introduced where \(0 < Z < 1.2\) Solvents with \(Z\) close to 1 were predicted to be successful SHS. \(Z\) is defined as

\[
Z = \frac{n_B - n'_B}{n_{\text{tot}}}
\]  

(2)

where \(n_{\text{tot}}\) is the total number of moles of amine present in 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 \(\text{CO}_2\), 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 \(\text{CO}_2\) is low (\(P_{\text{CO}_2}\)) and high (\(P'_{\text{CO}_2}\)), respectively. Eqn. 2 can be represented in a more convenient way,

\[
Z = \frac{M}{\rho} V_{\text{rat}} (S' - S)
\]  

(3)

where \(M\) is the molar mass of the solvent and \(\rho\) is the density. \(S\) and \(S'\) represent the water solubility of the solvent under different pressures of \(\text{CO}_2\) (\(P_{\text{CO}_2}\) and \(P'_{\text{CO}_2}\), respectively). They are described by

\[
S = [B]_{\text{aq}} \left(1 + \frac{1}{K_{\text{aH}}} \frac{K_{\text{H}} P_{\text{CO}_2}}{1 + [B]_{\text{aq}} K_{\text{aH}}} \right)
\]  

(4)

and

\[
S' = [B]_{\text{aq}} \left(1 + \frac{1}{K_{\text{aH}}} \frac{K_{\text{H}} P'_{\text{CO}_2}}{1 + [B]_{\text{aq}} K_{\text{aH}}} \right)
\]  

(5)

where \([B]_{\text{aq}}\) 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 \([B]_{\text{aq}} = S - [HB^+]_{\text{aq}}\). We assume that \([B]_{\text{aq}}\) remains unchanged after addition of \(\text{CO}_2\). \(K_{\text{H}}\) is the apparent first acid dissociation constant of carbonic acid (\(4.6 \times 10^{-7}\)).\(^16\) \(K_{\text{H}}\) is the Henry’s law constant for \(\text{CO}_2\) (0.034 M/bar),\(^17\) and \(K_{\text{ow}}\) is the autoprotolysis constant of water (\(1 \times 10^{-14}\)). Equation 3 can easily be rearranged for \(V_{\text{rat}}\).

\[
V_{\text{rat}} = \frac{Z \rho}{M (S' - S)}
\]  

(6)

At first we assumed that \(P'_{\text{CO}_2}\), the pressure used to switch the amine to the hydrophilic form, was 1 bar. A plot of \(Z\) as a function of \(\log K_{\text{ow}}\) and \(pK_{\text{aH}}\) (Figure 3a) shows the region where functional SHSs can be found. However, if one is willing to consider using a higher pressure of \(\text{CO}_2\) to trigger the change to hydrophilicity, then these equations can be used with \(P'_{\text{CO}_2}\) as a variable and \(P_{\text{CO}_2}\) is assumed to be zero. \(P'_{\text{CO}_2}\) is contained within \(S'\), but can be isolated algebraically.

\[
P'_{\text{CO}_2} = \left(\frac{Z \rho K_{\text{aH}}}{M [B]_{\text{aq}} V_{\text{rat}}}\right)^2 \left(1 + \frac{[B]_{\text{aq}} K_{\text{aH}}^{-1}}{K_{\text{H}}} \right) - \frac{K_{\text{H}}}{K_{\text{H}}}
\]  

(7)
The last term of eqn. 7 is very small and can be neglected. This suggests that amines with $pK_{\text{ah}}$ lower than 9.5 can still serve as SHSs if a higher pressure of CO$_2$ is used during the switching process. Indeed, a map of $Z$ assuming $P_{\text{CO}_2}' = 10$ bar of CO$_2$ produces a larger range of SHSs than when assuming 1 bar of CO$_2$ (Figure 3b). A high pressure SHS will switch back to its native hydrophobic state when the system is depressurized.

We can further modify the system by supposing that $P_{\text{CO}_2}$, 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 $K_{\text{ow}}$) and/or to the left (lower $pK_{\text{ah}}$) of the area describing the switchable zone when $P_{\text{CO}_2}' = 1$ bar but within the area defined when $P_{\text{CO}_2}' = 10$ bar (Figure 3c). Four amines that we will discuss, $N,N$-diethylcyclohexylamine (DECA), tripropylamine (TPA), $N,N$-dimethylbenzylamine (DMBA), and 1-dimethylamino-2-pentyne (DMAP), fall within the predicted region but a fifth, $N,N$-disopropylethylamine (DIPEA), does not.

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 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 $P_{\text{CO}_2}'$, one can predict that DECA will become water-miscible at $P_{\text{CO}_2}' = 2.9$ bar (with $V_{\text{rat}} = 1.0$). 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 $P_{\text{CO}_2}'$ by the equations are not particularly accurate. However, with the exception of sterically bulky DIPEA 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 $P_{\text{CO}_2}' = 1$ bar. We predict that the DECA/water system will become monophasic under atmospheric pressure of CO$_2$ when $V_{\text{rat}} = 1.7$. Table 1 summarizes these results for four other amine solvents and compares the predicted values to experimental observations. As noted above, DIPEA is qualitatively different from the other four and therefore will be discussed separately.

It should be noted that the $P_{\text{CO}_2}'$ required to trigger miscibility is a function of $V_{\text{rat}}$. Therefore, it is possible to predict the effect of changing both variables simultaneously. Figure 4 shows that as $V_{\text{rat}}$ 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 $V_{\text{rat}}$ values in intervals of 0.5. CO$_2$ was bubbled through each amine/water system, starting with the lowest $V_{\text{rat}}$, until the system became

![Fig. 3 Theoretical maps indicating the region of high SHS viability in a two-liquid system at (a) $P_{\text{CO}_2}' = 1$ bar and $P_{\text{CO}_2} = 0$ bar, or (b) $P_{\text{CO}_2}' = 10$ bar and $P_{\text{CO}_2} = 0$ bar. The region in (c) represents the high pressure SHSs which are water-miscible at $P_{\text{CO}_2}' = 10$ bar but biphasic at $P_{\text{CO}_2}' = 1$ bar. These SHSs should switch off very easily. Map (c) is the difference between maps (a) and (b). The green dots represent confirmed amine SHSs. The red dots represent the new SHSs presented in this study.]
monophasic. The sample with the lowest $V_{rat}$ value that became monophasic after treatment with 1 bar of CO$_2$ is reported as the high value in Table 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.

DIPEA differs from the other four new SHSs in that it does not fall into the region predicted in Figure 3c. It is not included in Figure 4 because eqn. 3 predicts that it should switch under normal conditions. Indeed, given its relatively high $pK_{a}$ and low log $K_{w}$, one would expect DIPEA to be water-miscible under 1 bar of CO$_2$. We have assumed that steric bulk around the nitrogen may destabilize a SHS:bicarbonate counter-ion network in the aqueous phase, thus requiring a higher energy investment to promote a switch to a hydrophilic form. Further development of the equations may be necessary to include steric effects.

It was observed that the DIPEA/water system became biphasic once it was depressurized from 7.0 bar of CO$_2$, whereas amines that act as SHSs 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. This was studied for DMCA/water and DIPEA/water mixtures. DMCA was water-miscible at 1 bar of CO$_2$ and DIPEA 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 20.0 mL tubular glass vial with a magnetic stir bar. At room temperature with 200 rpm of stirring, 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 DIPEA/water monophasic system. 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 DIPEA and DMCA (Figure 5). The results show that the DIPEA/water system switches back to it biphasic state at a faster rate then the DMCA/water system.

**Table 1** Tertiary amines exhibiting switchable behaviour under non-standard conditions

<table>
<thead>
<tr>
<th>Amine</th>
<th>$pK_{a}$</th>
<th>log $K_{w}$</th>
<th>Predicted $V_{rat}$</th>
<th>Experimental $V_{rat}$</th>
<th>Predicted $P_{CO_2}$ (bar)</th>
<th>Experimental $P_{CO_2}$ (bar)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N,N$-diisopropylethylamine (DIPEA)</td>
<td>11.4$^{18}$</td>
<td>2.3</td>
<td>0.4</td>
<td>1.5-2.0</td>
<td>0.1</td>
<td>4.0-7.0</td>
</tr>
<tr>
<td>$N,N$-diethylethylamine (DECA)</td>
<td>10.7</td>
<td>2.9</td>
<td>1.7</td>
<td>1.5-2.0</td>
<td>2.9</td>
<td>3.0-3.5</td>
</tr>
<tr>
<td>trisopropylamine (TPA)</td>
<td>10.6$^{19}$</td>
<td>2.8</td>
<td>1.5</td>
<td>2.5-3.0</td>
<td>2.3</td>
<td>3.5-4.0</td>
</tr>
<tr>
<td>$N,N$-dimethylethylamine (DMBA)</td>
<td>9.0$^{20}$</td>
<td>2.0</td>
<td>3.6</td>
<td>4.5-5.0</td>
<td>14.9</td>
<td>4.0-7.0</td>
</tr>
<tr>
<td>1-dimethylamino-2-pentyne (DMAP)</td>
<td>7.98$^{21}$</td>
<td>1.6</td>
<td>5.3</td>
<td>6.5-7.0</td>
<td>4.6$^{d}$</td>
<td>4.0-7.0$^{d}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{a}$ Predicted using VCCLAB software (ALOGPS)$^{22,23}$</td>
</tr>
<tr>
<td>$^{b}$ The minimum water:amine ratio required to obtain miscibility under 1 bar of CO$_2$ at 25°C</td>
</tr>
<tr>
<td>$^{c}$ The minimum CO$_2$ pressure required to trigger miscibility in a 1:1 water:amine (v/v) mixture at 25°C</td>
</tr>
<tr>
<td>$^{d}$ At a 3:1 volume ratio of water to amine</td>
</tr>
</tbody>
</table>

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**Fig. 4** The curves show the values of $P_{CO_2}$ which yield a maximum value of $Z$ for DECA, TPA, DMAP and DMBA as a function of $V_{rat}$, calculated using eqn. 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.
3 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 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 2, the amine must partition strongly into the carbonated water phase rather than the organic oil phase. We recently introduced $\Omega$, a parameter designed to quantify the suitability of a compound as an SHS for a three-liquid system.

$$\Omega = -\log D \times \log D'$$  \hspace{1cm} (8)

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 $\Omega < 0$ are undesirable because they would either have high water-miscibility in the absence of $CO_2$ (too hydrophilic; both $\log D$ and $\log D'$ are negative) or low water-miscibility even in the presence of $CO_2$ (too hydrophobic; both $\log D$ and $\log D'$ are positive). Thus, only amines with 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 $\log K_{ow}^{\text{neut}} - \log K_{ow}^{\text{salt}} = 2.8$.\(^2\) The values of $\log K_{ow}^{\text{salt}}$ were measured by GC-FID using glycolic salts instead of bicarbonate salts. The distribution coefficient (eqn. 9) is related to the partition coefficients and the ratio of protonated and neutral species in the aqueous layer ($[HB^+]_{aq}/[B]_{aq}$), which increases with the addition of $CO_2$.

$$\log D = \log \left( \frac{K_{ow}^{\text{neut}}}{K_{ow}^{\text{salt}}} \right) + \log K_{ow}^{\text{salt}}$$  \hspace{1cm} (9)

where $D'$ can be isolated from eqn. 8. Again, the last term is very small and can be neglected. The biggest difference

The SHSs which require higher $CO_2$ pressures and/or higher water to amine volume ratios are of interest because they are able to revert back to their water-immiscible state quickly and easily. While high $\log K_{ow}$ SHSs are not particularly desirable due to their high bio-accumulation, low $pK_{a}$ SHSs are desirable. The amines presented in this paper do not require $CO_2$ pressures over 10 bar (with the exception of $DMCA$ in its neutral form is related to the partition coefficients and the ratio of protonation and deprotonation of the amine, when $CO_2$ is removed, will be energetically costly. For environmental purposes, one should avoid SHSs with high $\log K_{ow}$ values due to the greater 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.\(^2\)

\[ p_{CO_2}' = \left( \frac{K_{a} (K_{ow}^{\text{neut}} - D')}{D' - K_{ow}^{\text{salt}}} \right)^2 \left( 1 + \frac{[B]_{aq}}{[HB^+]_{aq}} K_{H}^{-1} \right) \]

$$\frac{K_{ow}^{\text{salt}}}{K_{ow}^{\text{neut}} \cdot K_{H}}$$  \hspace{1cm} (10)
between $Z$ and $\Omega$ is that $\Omega$ does not range between 0 and 1. Therefore, we do not have a single value for omega that represents an ideal SHS. Figure 6 shows how $\log D'$ is affected by the pressure of CO$_2$ for 3 SHSs which become water-miscible at $P'_\text{CO}_2 = 1$ bar (DMCA, $N,N$-diisopropylethanol amine (DIISO), and triethylamine (TEA)) and 5 SHSs which only become water-miscible at $P'_\text{CO}_2 > 1$ bar (DECA, TPA, DMAP, DIPEA, 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, DIISO, 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 1 bar before they partition primarily into the aqueous layer. DIPEA requires high CO$_2$ pressures before it becomes water-miscible, despite what the model predicts. We believe this is a consequence of its bulky nature which is not accounted for in the model. It should be noted that each curve levels off according to $\log K^\text{salt}_{\text{ow}}$ (as $P'_\text{CO}_2 \to \infty$, $\log D' \approx \log K^\text{salt}_{\text{ow}}$). It is possible that some amines would not be effective as SHSs in a 3-liquid system if $\log K^\text{salt}_{\text{ow}} > 0$. However, more SHS can be extracted from the oil layer by using a greater volume of water.

![Figure 6 Calculated distribution curves for low pressure SHSs (DMCA, DIISO, TEA, points) and high pressure SHSs (DECA, TPA, DIPEA, DMAP, lines) as a function of $P'_\text{CO}_2$. 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.](image)

The bicarbonate salts of DMBA and DMAP are assumed to partition very favorably into the aqueous layer due to their low $\log K^\text{salt}_{\text{ow}}$ values. However, due to their low $pK_{\text{diss}}$ values ($pK_{\text{diss}} = 9.0$ and 8.1, respectively), a high CO$_2$ pressure is needed to quantitatively protonate these compounds.

4 Conclusions

The amine SHSs 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 $pK_{\text{diss}}$ and $\log K^\text{salt}_{\text{ow}}$ values. However, the range of SHSs can be 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 $pK_{\text{diss}} < 8.5$ require considerable CO$_2$ pressure before they can become water-miscible (if they can at all). We predict that DMBA, having a relatively low $pK_{\text{diss}}$ (9.0), will give a negative $\log D'$ value with just over 15 bar of CO$_2$. Increasing the water to amine volume ratio relaxes the required CO$_2$ pressure and thus using both parameters simulataneously allows for a significant extension of the original SHS range. Of course, amines with $pK_{\text{diss}}$ values nearing the pH of carbonic acid ($\approx 4$) are unlikely to ever serve as SHSs.

It is curious that DIPEA 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 $pK_{\text{diss}}$ and $\log K^\text{salt}_{\text{ow}}$ values for amines that become water-miscible at 1 bar of CO$_2$. We suspect that steric factors may be at play.\textsuperscript{15}

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 $K^\text{ow}$ values would not be recommended for practical use.

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