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Extending the range of switchable-hydrophilicity solvents

Jeremy Durrelle, Jesse R. Vanderveen, Yi Quan, Courtney B. Chalifoux, Julia E. Kostin, and Philip G. Jessop*

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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 ($9.5 < \text{p}K_{\text{aH}} < 11$ and $1.0 < \log K_{\text{ow}} < 2.5$, 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 $\text{p}K_{\text{aH}} < 9.5$ or $\log K_{\text{ow}} > 2.5$ 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 is triggered by the addition of CO_2 (Figure 1). The resulting carbonated water reacts with the SHS, protonating it and forming a water-miscible bicarbonate salt (eqn. 1, where NR_3

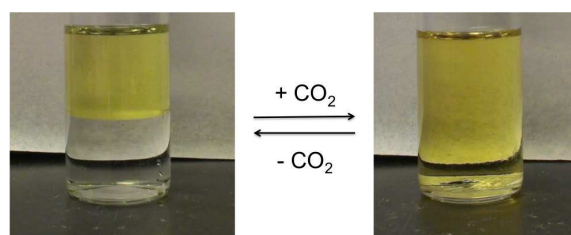
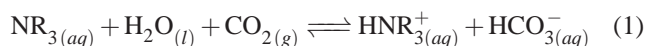


Fig. 1 A switchable-hydrophilicity solvent changes from hydrophobic to hydrophilic upon addition of CO_2 and then back to hydrophobic upon removal of CO_2 .

is the hydrophobic form of the solvent and $[\text{HNR}_3^+][\text{HCO}_3^-]$ 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 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_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 ($\text{p}K_{\text{a}} \approx 10$).



Many SHSs have been reported^{1,8,14,15} 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

Queen's University, Chermoff Hall, Kingston, Canada. E-mail: philip.jessop@chem.queensu.ca

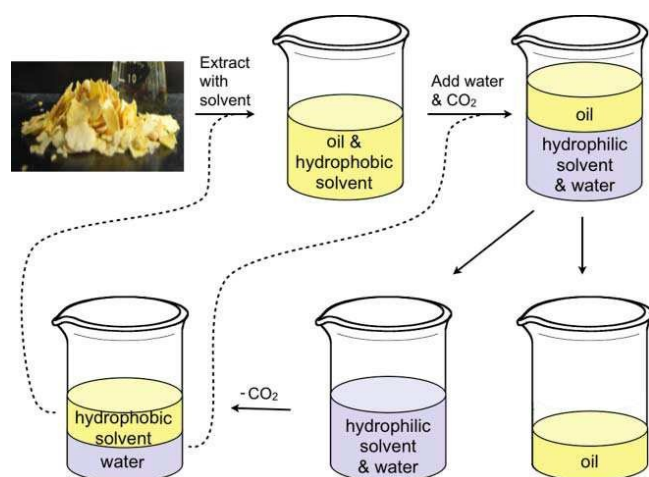


Fig. 2 The process by which an SHS can be used to extract soybean oil from soybean flakes without a distillation step. The dashed lines indicate the recycling of the solvent and the water. Reproduced from Ref. 1.

and environmental impact.¹ It was shown that all successful tertiary and bulky secondary amine SHSs had acidities ($\text{p}K_{\text{aH}}$) and hydrophilicities ($\log K_{\text{ow}}$) within a particular range. The $\text{p}K_{\text{aH}}$ 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 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 CO_2 (P_{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 $\text{p}K_{\text{aH}}$ 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_{CO_2} to be the partial pressure of CO_2 present when the SHS is supposed to be hydrophobic. We also define P'_{CO_2} to be the 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_{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

$$Z = \frac{n_B - n'_B}{n_{\text{tot}}} \quad (2)$$

where n_{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 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 (P_{CO_2}) and high (P'_{CO_2}), respectively. Eqn. 2 can be represented in a more convenient way,

$$Z = \frac{M}{\rho} V_{\text{rat}} (S' - S) \quad (3)$$

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

$$S = [\text{B}]_{\text{aq}} \left(1 + \frac{1}{K_{\text{aH}}} \sqrt{\frac{K_w + K_1 K_H P_{\text{CO}_2}}{1 + [\text{B}]_{\text{aq}} K_{\text{aH}}^{-1}}} \right) \quad (4)$$

and

$$S' = [\text{B}]_{\text{aq}} \left(1 + \frac{1}{K_{\text{aH}}} \sqrt{\frac{K_w + K_1 K_H P'_{\text{CO}_2}}{1 + [\text{B}]_{\text{aq}} K_{\text{aH}}^{-1}}} \right) \quad (5)$$

where $[\text{B}]_{\text{aq}}$ 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 $[\text{B}]_{\text{aq}} = S - [\text{HB}^+]_{\text{aq}}$. We assume that $[\text{B}]_{\text{aq}}$ remains unchanged after addition of CO_2 . K_1 is the apparent first acid dissociation constant of carbonic acid (4.6×10^{-7}),¹⁶ K_H is the Henry's law constant for CO_2 (0.034 M/bar),¹⁷ and K_w is the autoprotolysis constant of water (1×10^{-14}). Equation 3 can easily be rearranged for V_{rat} .

$$V_{\text{rat}} = \frac{Z\rho}{M(S' - S)} \quad (6)$$

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 $\log K_{\text{ow}}$ and $\text{p}K_{\text{aH}}$ (Figure 3a) shows the region where functional SHSs can be found. However, if one is willing to consider using a higher pressure of 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. P'_{CO_2} is contained within S' , but can be isolated algebraically.

$$P'_{\text{CO}_2} = \left(\frac{Z\rho K_{\text{aH}}}{M[\text{B}]_{\text{aq}} V_{\text{rat}}} \right)^2 \frac{(1 + [\text{B}]_{\text{aq}} K_{\text{aH}}^{-1})}{K_1 K_H} - \frac{K_w}{K_1 K_H} \quad (7)$$

The last term of eqn. 7 is very small and can be neglected. This suggests that amines with pK_{aH} s 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 $P'_{CO_2} = 10$ 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_{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/or to the left (lower pK_{aH}) of the area describing the switchable zone when $P'_{CO_2} = 1$ bar but within the area defined when $P'_{CO_2} = 10$ 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*-diisopropylethylamine (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'_{CO_2} , one can predict that DECA will become water-miscible at $P'_{CO_2} = 2.9$ bar (with $V_{rat} = 1.0$). 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'_{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 $P'_{CO_2} = 1$ bar. We predict that the DECA/water system will become monophasic under atmospheric pressure of CO_2 when $V_{rat} = 1.7$. 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'_{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 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

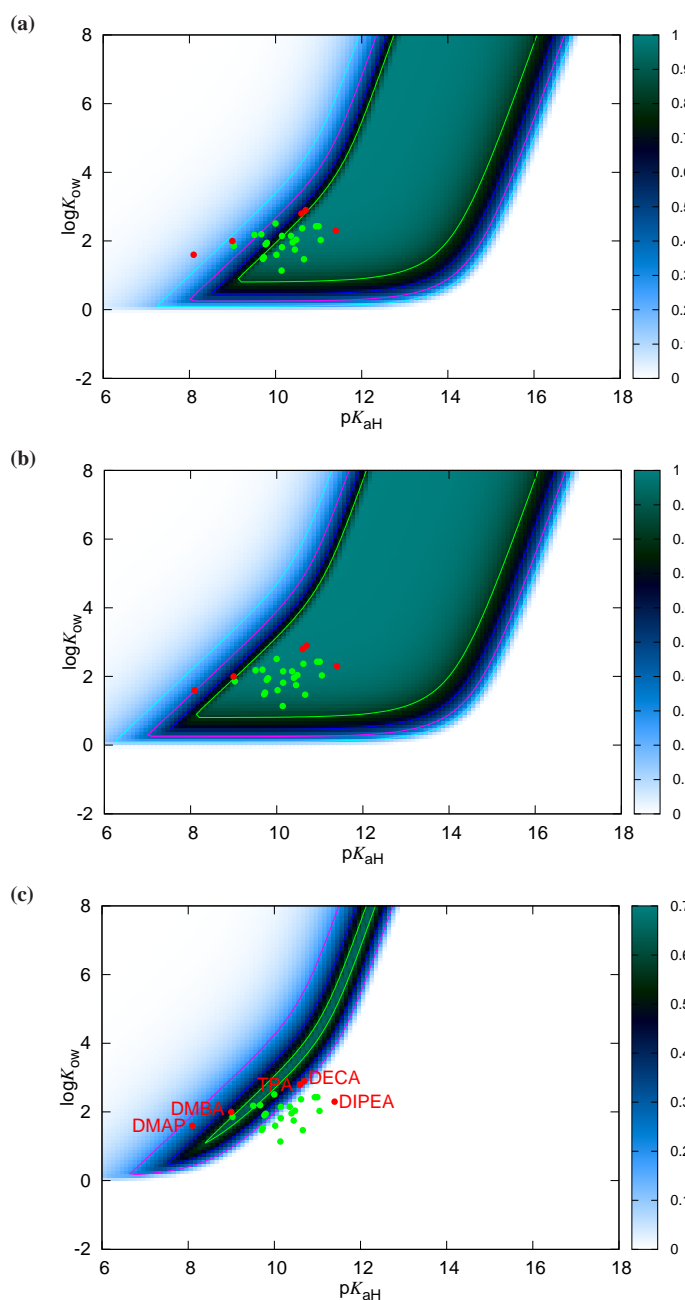


Fig. 3 Theoretical maps indicating the region of high SHS viability in a two-liquid system at (a) $P'_{CO_2} = 1$ bar and $P_{CO_2} = 0$ bar, or (b) $P'_{CO_2} = 10$ bar and $P_{CO_2} = 0$ bar. The region in (c) represents the high pressure SHSs which are water-miscible at $P'_{CO_2} = 10$ bar but biphasic at $P_{CO_2} = 1$ 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.

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

Amine	pK_{aH}	$\log K_{ow}^a$	Predicted V_{rat}^b	Experimental V_{rat}^b	Predicted $P'_{CO_2}{}^c$ (bar)	Experimental $P'_{CO_2}{}^c$ (bar)
<i>N,N</i> -diisopropylethylamine (DIPEA)	11.4 ¹⁸	2.3	0.4	1.5-2.0	0.1	4.0-7.0
<i>N,N</i> -diethylcyclohexylamine (DECA)	10.7	2.9	1.7	1.5-2.0	2.9	3.0-3.5
tripropylamine (TPA)	10.6 ¹⁹	2.8	1.5	2.5-3.0	2.3	3.5-4.0
<i>N,N</i> -dimethylbenzylamine (DMBA)	9.0 ²⁰	2.0	3.6	4.5-5.0	14.9	4.0-7.0
1-dimethylamino-2-pentyne (DMAP)	7.98 ²¹	1.6	5.3	6.5-7.0	4.6 ^d	4.0-7.0 ^d

^a Predicted using VCCLAB software (ALOGPS)^{22,23}

^b The minimum water:amine ratio required to obtain miscibility under 1 bar of CO₂ at 25°C

^c The minimum CO₂ 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

monophasic. The sample with the lowest V_{rat} value that became monophasic after treatment with 1 bar of CO₂ 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_{aH} and low $\log K_{ow}$, one would expect DIPEA to be water-miscible under 1 bar of CO₂. We have assumed that steric bulk around the nitrogen has no effect on SHS performance, which may not be true.¹⁵ It could be that steric crowding 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 CO₂, whereas amines that act as SHSs under 1 bar CO₂ did not become biphasic unless heated and bubbled with N₂ or Ar. An amine that only becomes water-miscible under high pressures of CO₂ may require less energy and time to remove the CO₂ than amines that become water-miscible at 1 bar of CO₂ because incomplete CO₂ 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 CO₂ was removed over time. This was studied for DMCA/water and DIPEA/water mixtures. DMCA was water-miscible at 1 bar of CO₂ and DIPEA was water-miscible at 7 bar CO₂. 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

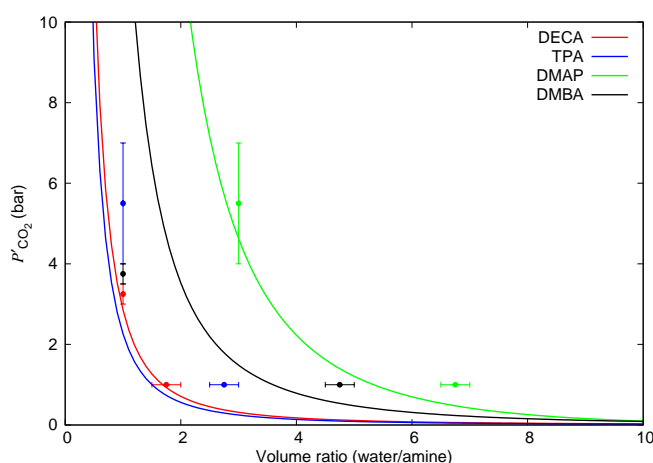


Fig. 4 The curves show the values of P'_{CO_2} which yield a maximum value of Z for DECA, TPA, DMAP and DMBA as a function of V_{rat} , calculated using eqn. 3. The data points indicate the experimentally determined range of pressures (within 0.5 bar) needed to achieve a monophasic system. Sudan III 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.

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 CO₂ 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 its biphasic state at a faster rate than the DMCA/water system.

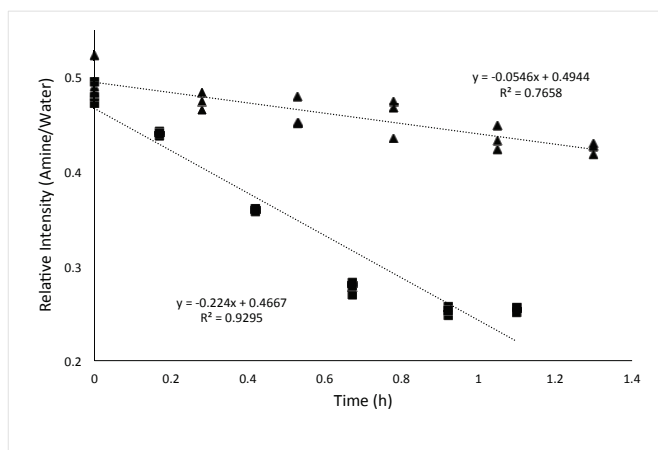


Fig. 5 The rate of amine removal from the aqueous phase as shown by relative intensities of amine to water signals by GC-TCD spectra. The system changing from 7 bar of CO_2 (DIPEA/water, square points) shows a steeper slope (-0.22 h^{-1}) than the system changing from 1 bar of CO_2 (DMCA/water, triangle points: -0.055 h^{-1}).

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 $\text{p}K_{aH}$ 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, they may be more difficult to remove from an organic liquid product (Figure 2).

The $\text{p}K_{aH}$ range can not be extended indefinitely. Carbonic acid is a weak acid ($\text{p}K_a$ 6.3) and will not protonate amine derivatives with $\text{p}K_{aH}$ values less than or equal to the pH of saturated carbonic acid (≈ 4). Figure 3b shows that the effective lower limit of the $\text{p}K_{aH}$ range is about 7 when $P'_{\text{CO}_2} = 10$ 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. However, as shown in Figure 3, high $\log K_{ow}$ values necessitate particularly strong bases, so that the 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.²⁴

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 Ω , a parameter designed to quantify the suitability of a compound as an SHS for a three-liquid system.²

$$\Omega = -\log D \times \log D' \quad (8)$$

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 ($[\text{HB}^+]_{aq}/[\text{B}]_{aq}$), which increases with the addition of CO_2 .

$$\log D = \log \left(\frac{K_{ow}^{\text{neut}}}{K_{ow}^{\text{salt}}} + \frac{[\text{HB}^+]_{aq}}{[\text{B}]_{aq}} \right) + \log K_{ow}^{\text{salt}} - \log \left(1 + \frac{[\text{HB}^+]_{aq}}{[\text{B}]_{aq}} \right) \quad (9)$$

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} .

$$P'_{\text{CO}_2} = \left(\frac{K_{aH}(K_{ow}^{\text{neut}} - D')}{D' - K_{ow}^{\text{salt}}} \right)^2 \frac{(1 + [\text{B}]_{aq}K_{aH}^{-1})}{K_1K_H} - \frac{K_w}{K_1K_H} \quad (10)$$

where D' can be isolated from eqn. 8. 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 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 $\log K_{ow}^{\text{salt}}$ (as $P'_{\text{CO}_2} \rightarrow \infty$, $\log D' \approx \log K_{ow}^{\text{salt}}$). 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.

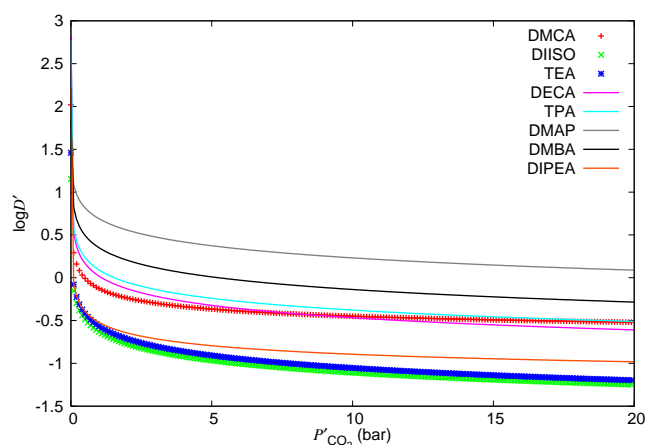


Fig. 6 Calculated distribution curves for low pressure SHSs (DMCA, DIISO, TEA, points) and high pressure SHSs (DECA, TPA, DIPEA, DMAP, lines) as a function of P'_{CO_2} . As expected, amines which function as SHSs under atmospheric pressure of CO_2 are easier to separate from a liquid product than amines 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.

The bicarbonate salts of DMBA and DMAP are assumed to partition very favorably into the aqueous layer due to their low $\log K_{ow}^{\text{salt}}$ values. However, due to their low $\text{p}K_{aH}$ values ($\text{p}K_{aH} = 9.0$ 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 $\text{p}K_{aH}$ and $\log K_{ow}$ 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 $\text{p}K_{aH} < 8.5$ require considerable CO_2 pressure before they can become water-miscible (if they can at all). We predict that DMBA, having a relatively low $\text{p}K_{aH}$ (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 simultaneously allows for a significant extension of the original SHS range. Of course, amines with $\text{p}K_{aH}$ values nearing the pH of carbonic acid (≈ 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 $\text{p}K_{aH}$ and $\log K_{ow}$ values for amines that become water-miscible at 1 bar of CO_2 . We suspect that steric factors may be at play.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_{ow} values would not be recommended for practical use.

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