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# Design, synthesis, and solution behaviour of small polyamines as switchable water additives<sup>†</sup>

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The practice of adding salt to water to induce salting out of contaminants or to break emulsions and suspensions is generally avoided industrially because of the expense of the necessary treatment of the salty water afterwards. However, the use of switchable water, an aqueous solvent with switchable ionic strength, allows for reversible generation and elimination of salts in aqueous solution, through the introduction and removal of  $CO_2$ . In the effort to improve the efficiency of these switchable salts, a physical study modeling their reactivity and solution behaviour has been performed, resulting in a set of design principles for future switchable water additives. The resulting polyamines synthesized using this template show the highest efficiency recorded for a switchable water additive.

# Introduction

Addition of salt to water has many practical applications, from the breaking of emulsions, foams and suspensions to the removal of organic contaminants from water by "salting out". However, the addition of salt to water is generally avoided industrially because it is energetically costly to remove the salt from the water afterwards and the water can be neither recycled nor discarded while salty. We, in our previous communication, described an aqueous solution of switchable salinity. The solution, which we call "switchable water" or "SW", consists of an amine or polyamine dissolved in water. In the absence of  $CO_2$ , the ionic strength of the solution is very low (it would be zero but for the small dissociation of the amine in water as well as water itself). In the presence of CO<sub>2</sub>, however, the additive is converted to the bicarbonate salt, resulting in a dramatic and reversible rise in the ionic strength. If the amine or polyamine (B in eqn (1) and Fig. 1) is assumed to have n protonatable sites, and if the usual general equation for the ionic strength of an electrolyte solution is assumed (eqn (2)), then the ionic strength of the bicarbonate solution is governed by eqn (3) (where  $m_{\rm B}$  is the nominal molality of the SW additive and where we neglect the ionic strength due to the dissociation of water). While the chemistry is quite similar to that used in CO<sub>2</sub> capture, the utility of the solution is quite different; not surprisingly, then, we found in our

preliminary screening that the amines that are most effective for switchable water are different from those that are most effective for  $\rm CO_2$  capture.

$$\mathbf{B} + n\mathbf{H}_2\mathbf{O} + n\mathbf{CO}_2 \rightleftharpoons [\mathbf{BH}_n]^{n+} + n[\mathbf{HCO}_3]^-$$
(1)

$$I = \frac{1}{2} \Sigma m Z^2 \tag{2}$$

$$I = \frac{1}{2}m_{\rm B}(n^2 + n)$$
(3)

As evident from eqn (3), the ionic strength, I, of the solution is strongly dependent on the number of protonatable sites on the additive, but only if eqn (2) applies. Because ionic strength is not easily measured directly, we have used the salting out of THF from a SW solution as both an indirect measure of the ionic strength of the solution and a direct measure of the effectiveness of the SW additive for the salting out application. While salting out is certainly not the only application envisioned for



Fig. 1 Switchable water solutions are transformed from low ionic strength (left) to high ionic strength (right) by the addition of  $CO_2$ . The process is readily reversible.

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Table 1 The ability of several tertiary amine, amidine, and inorganic salt additives to separate THF from 1:1 w/w solutions of  $\rm H_2O$  and THF and the resulting retention of the additive in the aqueous phase when reacted with  $\rm CO_2$ 

Entry	Base or salt	Loading	% THF separated <sup>a</sup>	% Amine retained <sup>a</sup>
1	Dimethyl- ethanolamine	0.80 molal	$70\pm0.6\%^b$	$98.0 \pm 0.2\%^{b}$
2	$DBU^{c}$	0.80 molal	$59 \pm 0.7\%$	$96.5 \pm 1.7\%$
3	$1^{c}$	0.80 molal	$75 \pm 2.3\%$	$98.1 \pm 2.2\%$
4	2	0.80 molal	$82 \pm 0.6\%^{b}$	$99.2 \pm 0.4\%^{b}$
5	$3^d$	0.80 molal	$78\pm0.9\%^b$	$99.3 \pm 0.4\%^{b}$
6	NaCl	0.80 molal	$88 \pm 1.6\%$	n.a.
7	NaCl	varied <sup>e</sup>	$98 \pm 0.5\%$	n.a.
8	$(NH_4)_2SO_4$	0.80 molal	$92 \pm 1.2\%$	n.a.
9	$(NH_4)_2SO_4$	varied <sup>e</sup>	$99\pm0.6\%$	n.a.

<sup>*a*</sup> Determined by <sup>1</sup>H NMR spectroscopy. <sup>*b*</sup> From Ref. 1. <sup>*c*</sup> This additive was able to salt out organics upon reaction with CO<sub>2</sub>, but CO<sub>2</sub> could not be released under working conditions to allow for recycling. <sup>*d*</sup> This additive, a tetramine, could only be protonated at two sites by carbonic acid, as determined by <sup>1</sup>H NMR spectroscopy. <sup>*e*</sup> Salt was added at various amounts until a consistent volume of THF separated from the aqueous solution was observed (see ESI<sup>†</sup>).

switchable water additives, it has the benefit of being easily and rapidly tested.

In general, the desired performance characteristics of a SW additive used for salting out are rapid switching, high level of THF expulsion from the aqueous phase, and high retention of the additive in the aqueous phase. Optimally, these additives should be commercially available or be easily synthesized from readily available and inexpensive starting materials. Our initial communication showed that several diamines have a greater ability to salt out THF from water than an equimolal amount of monoamines in the presence of  $CO_2$ . Here, we describe the results of our efforts to further delineate the structural design parameters that control the effectiveness of SW additives.

# **Results and discussion**

# a) Monoamines, diamines and amidines

Before attempting to find any more new amine additives, we sought to establish the amount of THF salted out by common inorganic salts (NaCl and  $(NH_4)_2SO_4$ ) at our standard test molality of 0.8 molal (Table 1, entries 6 and 8), as well as a ceiling amount of THF that could be removed from water by such inorganic salts at higher concentrations (Table 1, entries 7 and 9). The slightly larger amount of THF that is removed *via* these salts compared to the amine additives at equimolal loading (Table 1, compare entries 1–6 and 8) shows that improvement of switchable water additives is necessary to mimic the performance of typical non-switchable salts used in salting out processes.

We attempted to use amidine bases, such as DBU and compound 1 (Scheme 1), as switchable water additives but were not successful because the reversion from the amidinium bicarbonate species was too difficult at moderate temperatures. In addition, amidines are more expensive and suffer from hydrolytic instability at alkaline conditions.<sup>2</sup>

To mimic the salting out capabilities of the inorganic salts studied, diamines and larger polyamines, which when protonated



Scheme 1 Nitrogenous bases with multiple basic sites tested as switchable water additives.

generate bolaform electrolytes in solution, should be more effective than monoamines, according to eqn (3). A bolaform electrolyte is a polyvalent electrolyte species where the sites of charge are separated from each other by a series of atoms.<sup>3</sup> We have previously reported a diamine (compound **2**, Scheme 1) that was more effective than monoamines at salting out of THF from 1 : 1 w/w solutions of THF and H<sub>2</sub>O (Table 1). However, these salts are still not as capable of salting out organics as the inorganic salts shown in Table 1, so further improvement and development of larger polyamines is necessary.

For effective switching, the amine sites on an additive must be neither too basic nor insufficiently basic (similar to the findings for ionic liquids used for CO<sub>2</sub> capture);<sup>4</sup> in our experience, a  $pK_{aH}$  (the  $pK_a$  value of the protonated species) range of 8 to 10.5 is appropriate. If the amine is insufficiently basic, then CO<sub>2</sub> at 1 atm will be insufficient to protonate the amine with high conversion. If the amine is too basic, then the reversion will require severe conditions, take too long, or be impractical to achieve. Symmetry arguments predict that symmetric diprotic acids, a diprotonated diamine for example, with chemically equivalent functional groups will possess two dissociation constant values with a ratio of four  $(K_1/K_2 = 4)$  if the ionization events are completely independent of one another.<sup>5</sup> A deviation resulting in a ratio greater than four would represent some sort of dependence of the second ionization event upon the first ionization event. One possible intra-molecular based explanation of this deviation<sup>6</sup> is that when the two functional groups are too close, a single ionization event at one group affects the electron density and therefore acidity or basicity of the second functional group. Therefore, we must ensure that protonation events at one amine functional group on a polyamine chain do not greatly decrease the capacity of subsequent amine groups to be protonated (i.e.  $pK_{aH(1)} - pK_{aH(2)}$  should be close to 0.6).

For linear ditertiary diamines  $Me_2N(CH_2)_xNMe_2$ , the first and second  $pK_{aH}$  values show that four carbons are necessary to insulate the one basic site electronically from the other and thus to ensure that both  $pK_{aH}$  values fall within the range that is appropriate for facile switching (Fig. 2). N,N,N',N'-Tetramethyl-1,4-diaminobutane, **2**, is the smallest ditertiary diamine that has both  $pK_{aH}$  values within our working range. We conclude that polyamines should have a minimum of four carbons between each amine group to maintain appropriate basicity of each amine after the protonation of a neighbouring group.

How large an increase in the ionic strength could one expect when applying CO<sub>2</sub> to a solution of 0.1 molal of **2**? We can calculate an approximate answer by assuming solution ideality and by using molarity rather than molality. A 0.1 M solution of **2** would have a pH of 11.6 and the relevant ions would be  $[2 \cdot 2H^+]$ (0.006 mM),  $[2 \cdot H^+]$  (4 mM),  $[OH^-]$  (4 mM) and a negligible concentration of H<sup>+</sup>, giving a total ionic strength of ~4 mM. Adding CO<sub>2</sub> at 1 bar to that solution lowers the pH to 6.8, giving a solution containing  $[2 \cdot 2H^+]$  (99 mM),  $[2 \cdot H^+]$  (1 mM),



**Fig. 2**  $pK_{aH}$  values of Me<sub>2</sub>N(CH<sub>2</sub>)<sub>*x*</sub>NMe<sub>2</sub> ( $\bullet = pK_{aH(1)}$ ,  $\blacksquare = pK_{aH(2)}$ ) relative to the number of carbons found between the two amine groups.<sup>7–9</sup> The shaded region highlights the desired range of  $pK_{aH}$  values for a switchable water additive.



**Fig. 3** The amount of organic solvent salted out from 1:1 w/w mixtures of  $\bullet$ : THF/H<sub>2</sub>O or  $\blacksquare$ : acetonitrile/H<sub>2</sub>O with a 0.50 molal loading of  $\alpha, \omega$ -diaminoalkane dihydrochloride salts, [H<sub>3</sub>N(CH<sub>2</sub>)<sub>x</sub>NH<sub>3</sub>]Cl<sub>2</sub>, where *x* is the number of carbons between the ammonium groups.

[HCO<sub>3</sub><sup>-</sup>] (199 mM) and negligible concentrations of  $CO_3^{2-}$ , H<sup>+</sup> and OH<sup>-</sup>, giving a total ionic strength of ~300 mM. Therefore, in this idealized case, the ionic strength would jump two orders of magnitude upon addition of CO<sub>2</sub>.

#### b) Long-linker bolaform electrolytes

Once the minimum number of carbons between amine nitrogen atoms had been found to be four, we wondered whether there was either an optimum number or an upper limit beyond which salting out ability would be lost. We hypothesized that if the carbon spacer were excessively long, then the dication would begin to function more like a pair of singly charged cations and the Z term in eqn (2) would thus fall to 1 instead of 2.

To observe this threshold value of spacer length, we carried out a series of simple salting out experiments using 1:1 w/wsolutions of THF and H<sub>2</sub>O. Using a series of nonswitchable  $\alpha,\omega$ diaminoalkane dihydrochloride salts [H<sub>3</sub>N(CH<sub>2</sub>)<sub>x</sub>NH<sub>3</sub>]Cl<sub>2</sub> with a varying number of carbons between the ammonium groups, we observed the amount of THF expelled from each aqueous solution upon dissolution of the salts in the aqueous solution (Fig. 3).



**Fig. 4** Comparison of  $pK_{aH}$  values of linear  $\alpha, \omega$ -diaminoalkane hydrochlorides *versus* the number of carbons, *x*, separating the two amine groups.<sup>10–12</sup>  $\blacksquare pK_{aH(1)}$ ,  $\bigstar pK_{aH(2)}$ ,  $\bigoplus pK_{aH(1)} - pK_{aH(2)}$ .

As shown, the amount of THF salted out is nearly independent of x up to a value of 6, but the amount of THF salted out quickly decreases with the 1,7-diaminoheptane dihydrochloride salt and ultimately to zero salting out when the eight-, nine-, and 10-carbon spaced salts are used. A similar trend was observed with 1 : 1 w/w solutions of acetonitrile and water (Fig. 3). With either solvent, there appears to be a weak maximum at x = 4. On a practical level, it is clear that a four-carbon spacer is best, but the reason for the poor performance at x > 6 was not immediately clear. We then sought to elucidate the cause of the diminished salting out effect of diamine dihydrochloride salts with longer spacers.

#### c) Accounting for the diminishing salting out effect

In the attempt to rationalize these observations we explored four possible hypotheses.

**Hypothesis #1.** Our first hypothesis was that intra-molecular (through-bond) communication between the two ammonium groups diminishes or is lost when the carbon spacer is larger than six carbons, so that the two charge centres are functioning essentially as two monocations as far as eqn (2) is concerned. To determine the spacer length at which electronic communication is lost, we first looked into the dependence of basicity on spacer length. A survey of  $pK_{aH}$  values of primary  $\alpha$ , $\omega$ -diaminoalkane dihydrochlorides from literature<sup>10-12</sup> (Fig. 4) shows that the ratio of the first and second  $K_{aH}$  dissociation constants levels off at a value of roughly 4 (or  $pK_{aH(1)} - pK_{aH(2)} \sim 0.6$ ) as the number of carbons between the two functional groups exceeds six. This suggests that simple diamines with carbon spacers of greater than six, when protonated, have two ammonium groups that are electronically independent of each other.

To determine whether a lack of electronic communication is the deciding factor in disallowing salting out by diammonium salts with large carbon spacers, we performed another set of THF salting out experiments using benzidine dihydrochloride, 7,

Compound	Structure	Loading	% THF separated
4	H <sub>2</sub> NNH <sub>2</sub> · 2HCl	0.50 molal	0%
5	H <sub>2</sub> NNH <sub>2</sub> · 2HCl	0.50 molal	51%
5	H <sub>2</sub> NNH <sub>2</sub> · 2HCl	0.30 molal	46%
6	H <sub>2</sub> NNH <sub>2</sub> · 2HCl	0.50 molal	58%
<b>7</b> <sup><i>a</i></sup>	H <sub>2</sub> N	0.30 molal	0%
<b>8</b> <sup><i>a</i></sup>	H <sub>2</sub> NNH <sub>2</sub> · 2HCl	0.30 molal	0%
9	H <sub>2</sub> N_0 NH <sub>2</sub> ·2HC	0.50 molal	53%
10	N N N 2HCI	0.50 molal	68%
11	N N Y HCI	0.50 molal	73%

 $^a$  0.30 molal was used rather than the typical 0.50 molal loading due to low solubility of the salt in water.

a biphenyl analogue (Table 2). This species has  $pK_{aH}$  values of 3.85 and 4.95<sup>13</sup> resulting in  $K_{aH(1)}/K_{aH(2)}$  ratio much greater than 4, showing that electronic communication still exists between the N atoms. One may then expect this salt to act similarly to the simple diamines of six carbons or fewer. However, this salt did not cause salting out of THF at 0.30 molal loading. The same experiment was performed using the slightly less rigid diamine 1,4-benzenediethanamine dihydrochloride, 8, at 0.30 molal loading, however, we obtained a similar result to the benzidine salt in our experiments. These two diamines, despite having electronic communication between the N atoms, do not salt out THF. In contrast, a very long chain diamine with ether linkages (compound 9 in Table 2) did indeed salt out THF. We conclude that the presence or absence of electronic communication throughout the backbone linking the ammonium groups is not the deciding factor that determines the salting out abilities of these diammonium species.

Hypothesis #2. In our second hypothesis, we proposed that intra-molecular communication (through-space) is diminishing or lost past a separation of six carbons, again giving an ion containing two monocations rather than a single dication. As a model, we consulted photoelectron spectroscopy literature on lone-pair interactions of diamines to see if a potential through space communication effect could be leading to the enhanced salting out ability of the diamine salts with  $\leq 6$  carbon spacers. However, such a through space effect is not likely leading to this effect as it has been suggested that radical cation species with terminal nitrogens will have little chance of interacting intramolecularly through space when the number of carbons between the amine groups are greater than four. This has been attributed to the great number of possible orientations of the nitrogen groups in space which are unfavorable towards lone-pair interaction.<sup>14</sup> As the diminishing salting out effect is not noticeably prevalent until the seven-carbon spaced species, rather than the

four-carbon spaced species, we concluded this was not the cause of our observations.

**Hypothesis #3.** We then hypothesized that an increase in ionpairing of the alkylammonium and chloride ions occurs at greater spacer lengths, reducing the effective ionic strength generated by the  $\alpha, \omega$ -diaminoalkane dihydrochloride salts. Past literature has noted that bolaform electrolytes are prone to extensive ion-pairing in aqueous solution.<sup>3</sup> If this phenomenon is dependent on the carbon spacer length between the diammonium ions, this could account for the lack of salting out ability of the longer salts due to a diminished effective concentration of charged species and resulting ionic strength in solution. However, a recent study of ion-pair association constants of similar diamine dihydrohalide species has shown that the association constant values,  $K_A$ , of the diamine dihydrohalide ion pairs decrease as the number of carbon spacers between ammonium groups is increased.<sup>15</sup>

Hypothesis #4. Our attention then focused upon the increasing organic content of the salts. We proposed that the increase of organic content in the longer bolaform electrolytes is helping to solubilize the organic substrates in aqueous solution, thus preventing a salting out effect despite the high ionic strength. Previous modeling studies by Wang and co-workers have shown that a dicarboxylate dianion, when adequately solvated, will fold in, bringing its two charged termini closer than expected. Remarkably, the aqueous solvation stabilization overcomes electrostatic repulsions of the two charged ends leaving the organic backbone sticking out in the aqueous solution.<sup>16</sup> We hypothesized that a similar folding of the diammonium species may be occurring, which could give increasingly large pockets of organic content as the carbon spacers of the diammonium salts are increased. An increasing size of local organic environments in aqueous solution might stabilize the THF or MeCN in aqueous solution via a hydrophobic effect, despite the higher ionic strength environment in the bulk solution.

To support this hypothesis, salting out experiments were performed using 1,8-diamino-3,6-dioxaoctane dihydrochloride, 9, a 1,8-diaminooctane dihydrochloride analogue with two oxygen atoms in the backbone  $(pK_{aH(1)} = 8.74, pK_{aH(2)} = 9.68)$ .<sup>17</sup> This salt provided considerable salting out of THF from aqueous solution despite having a linker length of eight atoms between the ammonium groups. The presence of a more hydrophilic backbone and an observed salting out effect suggests that the carbon content of the bolaform electrolyte must be taken into account when assessing salting out capability. Additional diammonium dihydrochloride salts shown in Table 2 (entries 10 and 11) demonstrate that it is hydrophobic organic content far from the centres of charge (in these cases in the chain between the ammonium groups) which affects the salting out effect; additional methyl groups on the N atom seem to make little difference. Compound 10, despite having eight carbon atoms, is closer in performance to compound 5 than compound 4.

We also observed that shorter chain salts at low ionic strength can still expel organics from aqueous solution, while longer chain salts at a supposed greater ionic strength are still unable to salt out these organics, further suggesting that the organic content of the salt may play a role in its salting out ability. For

Salt	Loading	Ionic strength assuming single dication	Ionic strength assuming two monocations	% THF separated
4 5	0.50 molal	1.5 molal	1.0 molal	0%
	0.30 molal	0.9 molal	0.6 molal	46%



**Fig. 5** •: Amount of THF salted out and  $\blacksquare$ : amount of acetonitrile salted out from a 1 : 1 w/w solution of THF or acetonitrile and H<sub>2</sub>O with a 1.00 molal loading of alkylammonium chloride salts, [H(CH<sub>2</sub>)<sub>*x*</sub>NH<sub>3</sub>] Cl, where *x* is the number of carbons on the alkyl chain.

example (Table 3), a 0.50 molal solution of the 1,8-diaminooctane dihydrochloride salt, **4**, provides no salting out of THF despite an ionic strength of 1.5 molal (if the salt acts as a Z = 2dication) or an ionic strength of 1.0 molal if it is assumed that the two ammonium sites are independent of one another (resulting in two singly charged cations). However, a 0.30 molal solution of 1,6-diaminohexane dihydrochloride, **5**, provides a lower ionic strength of 0.90 molal (if the ammonium sites are considered to be giving a doubly charged cation) and still salts out roughly 46% of THF in conditions similar to those presented in Fig. 3. While these calculations can not be considered accurate because they assume ideality, this result cannot be purely explained by the lack of electronic communication between the ammonium groups, but can be explained by the greater organic content of salt **4**.

The notion of increasing the organic character of a salt, resulting in a lower salting out ability is not only limited to the bolaform electrolytes studied. A similar set of salting out studies using monoamine hydrochloride salts,  $[H(CH_2)_xNH_3]Cl$ , (Fig. 5) again shows a decrease in the salting out efficiency of the alkylammonium salts as the carbon chain is lengthened.

While the ability of the organic chain in  $\alpha$ , $\omega$ -diaminoalkane salts to solubilize organic molecules such as THF is believed to be the reason for the poor salting out ability, a further hypothesis might be that the salts, when folded in half, can act as surfactants. A plot of conductivity as a function of salt concentration in water was found not to have a sharp break, which would have been indicative of a critical micelle concentration (see Fig. S2 in the ESI†). Therefore the solubilizing effect of the long-chain salts is merely by molecular association and not likely to be by micelle formation.



Scheme 2 Newly developed switchable water additives.

**Table 4** Comparison of the ability, at 0.80 molal loading, of switchable water polyamine additives to separate THF from 1:1 w/w solutions of H<sub>2</sub>O and THF, the resulting retention of the additive in the aqueous phase when reacted with CO<sub>2</sub> and the average number of amine groups protonated during the treatment

Compound	% THF separated <sup>a</sup>	% Amine retained <sup><i>a</i></sup>	Average N atoms protonated <sup><i>a</i></sup>
12	$85 \pm 1.2\%$	$99.8 \pm 0.1\%$	3.7
$12^b$	$84 \pm 3.5\%$	$94.9 \pm 2.2\%$	3.7
13	$76 \pm 0.9\%$	$94.7 \pm 0.3\%$	2.8
14	$86\pm1.3\%$	$99.1\pm0.6\%$	3.0
<sup>a</sup> Determine	1 by <sup>1</sup> H NMR s	pectroscopy $^{b}$ 1.2	molal loading of additive

A rigorous molecular dynamics study of H<sub>2</sub>O:THF:diammo-

nium dichloride salt interactions in aqueous solution will be presented in a future publication to further elucidate the role of carbon content in the salting out ability of the bolaform electrolytes. Ultimately, it would seem that even when studying very similar salts, a slight difference in carbon content results in a changed ability of the salt to induce organic substrates to salt out of aqueous solution. This finding is not only important to the design of switchable water additives but is likely to find use in other chemical separation technologies.

#### d) Triamines and tetramines

was used.

With a reasonable set of principles for the design of polyamine additives, we prepared linear and cyclic polyamines from readily available precursors. A modified N-methylated spermine analogue, 12, was envisioned (Scheme 2). We initially had some reservations about the presence of only three carbon positions between N1 and N2 and between N3 and N4, but all four  $pK_{aH}$ values of spermine  $(pK_{aH(0.1 \text{ N KCl})} = 7.95, 8.82, 10.05, 10.86)^{18}$ fell close to or within the acceptable working range of 8-10.5 and thus synthesis and testing for function as a switchable water additive was performed. Compound 12 was synthesized using a modified method developed by Bieber and co-workers<sup>19</sup> in a 49% yield. Compound 12 showed the ability to salt out approximately 85% of THF from our system, the highest we have observed (Table 4), even though <sup>1</sup>H NMR spectroscopy showed that incomplete protonation of all the amine sites on compound 12 had occurred, as shown in the table. This suggests that a minimum of four carbon positions between the amine groups is necessary to allow for full protonation by carbonic acid. Increasing the amount of compound 12 in solution did not yield a greater THF salting out (Table 4). This was likely due to the now greater organic content solution helping to solubilize the THF.

In an attempt to force the utilization all amine functional groups available on a carbon scaffold, we then prepared compound 13, a triamine analogue of N,N-dimethylbenzylamine  $(pK_{aH} = 9.03)$ <sup>20</sup> where the amine groups are separated by 5 carbons. This molecular design should minimize the impact of neighbouring ionization events while maintaining an enhanced ionic strength effect and avoiding the presence of excess organic content in the scaffolding. Compound 13 was synthesized using a modification of the method of Hirsch and co-workers<sup>21</sup> in an 84% yield. Compound 13 showed the capacity to salt out roughly 76% THF from a 1:1 w/w solution of THF and H<sub>2</sub>O. <sup>1</sup>H NMR spectroscopy again showed, however, that incomplete protonation of compound 13 had occurred when it was reacted with carbonic acid, which likely contributed to the lower than expected salting out ability. We then moved to the synthesis of a saturated analogue of compound 13 to eliminate the conjugation in the carbon backbone. Novel compound 14 was synthesized in a 54% yield using a modified preparation from Shirai and coworkers<sup>22</sup> followed by a LiAlH<sub>4</sub> reduction from the triamide to triamine. Compound 14 showed an improved ability to salt out THF from 1:1 w/w solutions of H<sub>2</sub>O and THF, comparable to compound 12, as shown in Table 4. We were unable to definitively conclude what resulted in the similar salting out effect between the tetramine 12 and the triamine 14, but we hypothesize that the less conformationally rigid compound 12 may shield some charge by folding onto itself when solvated, comparable to the conclusions in the modeling of Yang and coworkers,<sup>16</sup> while compound 14 cannot undergo conformational shifts to such an extent. Nonetheless, both compounds 12 and 14 show a greater salting out ability than any amine additive previously tested and are comparable in effectiveness to a equimolal loading of NaCl (88% THF removed). Additionally, compounds 12 and 14 at 0.8 molal are as good at salting out THF as a 2.3 molal solution<sup>1</sup> of compound 2 but with 65 mol% less additive. Higher loadings of compound 14 in THF/water systems were not possible due to insufficient solubility.

The time to remove  $CO_2$  from the additives (to return the solution to the original ionic strength) varied between additives (Fig. S1 in the ESI<sup>†</sup>). The conversion of the bicarbonate salts to neutral amines was not 100% even after several hours, but the conversion of all the additives was sufficient after N<sub>2</sub> sparging at 50 °C for 30–60 min to restore the miscibility of the THF/water mixture.

## e) Primary and secondary amines

In our first publication on switchable water, we hypothesized that only tertiary amine additives would work well as switchable additives because they react with  $CO_2$  in water to exclusively form bicarbonate salts rather than carbamate salts. Carbamate salt formation is not preferred because it is more difficult to reverse<sup>23</sup> and because it creates fewer ions in solution per mole of amine additive (compare eqn (4) and (5)). In the case of non-tertiary polyamines, there is also the risk that zwitterionic carbamate species can form<sup>24</sup> which would further decrease the ionic strength.

 $2 \text{ NHR}_2 + \text{CO}_2 \ \rightleftharpoons \ \left[\text{NH}_2\text{R}_2\right]^+ + \left[\text{NR}_2\text{C}(\text{O})\text{O}\right]^- \qquad (4)$ 

$$NR_3 + H_2O + CO_2 \rightleftharpoons [NR_3H]^+ + [HCO_3]^-$$
(5)

Table 5 The ability of several sterically-hindered secondary amines to separate THF from 1:1 w/w solutions of H<sub>2</sub>O and THF and the resulting retention of the additive in the aqueous phase when reacted with  $CO_2$ 

Base	Loading	% THF separated <sup>a</sup>	% Amine retained <sup>a</sup>
<sup>t</sup> BuNHCH <sub>2</sub> CH <sub>2</sub> OH <sup>t</sup> BuNHMe	1.60 molal 1.60 molal	$\begin{array}{c} 69 \pm 0.4\% \\ 68 \pm 0.8\% \end{array}$	$\begin{array}{c} 99.8 \pm 0.1\% \\ 99.8 \pm 0.1\% \end{array}$

However, the  $CO_2$ -capture literature has shown that carbamate formation from secondary amines can be prevented by sterically bulky groups near or attached to the nitrogen.<sup>25</sup> This potentially allows for the development of a secondary amine SW additive. This would be attractive because secondary amines generally have faster kinetics for  $CO_2$  uptake than tertiary amines<sup>26</sup> and still may afford the desired reverse reaction at moderate conditions.

Two sterically-hindered secondary amines, *N-tert*-butylethanolamine (<sup>*I*</sup>BuNHCH<sub>2</sub>CH<sub>2</sub>OH) and *N-tert*-butyl-methylamine (<sup>*I*</sup>BuNHMe), were found to reversibly salt out THF from 1 : 1 w/w THF/H<sub>2</sub>O solutions *via* the introduction and removal of CO<sub>2</sub> and thus could function as switchable water additives (Table 5). Although these secondary amines are not as effective in salting out THF as the tertiary amine additives previously studied, they offer a proof that further exploration of secondary amines as switchable water additives is not necessarily a fruitless endeavor. Additionally, the secondary amine additives have excellent retention in the aqueous phase, which would decrease losses of amine to the separated organic phase.

Non-sterically hindered primary and secondary amines such as monoethanolamine are readily switched to ionic species (bicarbonate salts and carbamate salts) but are less easily converted back to the neutral species. However, non-bulky secondary and primary amines are more hydrophilic than tertiary amines and bulky secondary amines. This additional hydrophilicity could be advantageous in switchable water systems because a) the amines could be soluble at higher loadings and b) because the ability of the salts of these amines to solvate THF may be lessened, compared to tertiary amines, by the greater hydrophilicity. We therefore evaluated the use of primary amines as switchable water additives for the salting out of THF. MEA, a monoamine, does salt out THF but not to a great extent. Among the primary diamines  $(H_2N(CH_2)_rNH_2)$ , the chain length affects their ability to salt out THF when exposed to CO<sub>2</sub> (Fig. 6). As was found with the diamine dihydrochloride salts (Fig. 3), the four carbon-spaced diamine (1,4-diaminobutane) performed the best. While those tests were performed at 0.8 molal loading, we found that increasing the amount of 1,4-diaminobutane in the THF/water mixture to 1.2 molal increases the amount of THF expelled from the aqueous phase but increasing the loading of diamine further does not help. This suggests that there is a balance between additive concentration to generate sufficient ionic strength and the resulting organic content being built up in the aqueous solution working against the ionic strength effects. In a similar salting out test, spermine (the non-methylated analogue of compound 12) also demonstrated an impressive removal of THF at 0.80 or 1.2 molal loading (Table 6). This was



 
 Table 6
 The ability of several primary amines to separate THF from
1:1 w/w solutions of H<sub>2</sub>O and THF at various loadings when reacted with CO2 for 30 min

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7

8

Base	Loading	% THF separated <sup>a</sup>
MEA	0.80 molal	$65 \pm 0.8\%$
1,4-Diaminobutane	0.80 molal	$79\pm0.8\%$
1,4-Diaminobutane	1.20 molal	$89\pm0.4\%$
1,4-Diaminobutane	1.60 molal	$86 \pm 1.2\%$
Spermine	0.80 molal	$91 \pm 3.3\%$
Spermine	1.20 molal	$92 \pm 1.9\%$
<sup>a</sup> Determined by <sup>1</sup> H NMI	R spectroscopy.	

likely due to all the nitrogens in the backbone participating in salt formation (whether as bicarbonates or carbamates). Spermine, in the presence of CO<sub>2</sub>, is more effective than NaCl at equal molality. A future design principle will be to synthesize additives with greater hydrophilicity so that they may counteract the effect of increasing organic content in aqueous solution.

While these primary and secondary amines, especially spermine, are impressive in their ability to salt out THF (spermine is the best so far, at 92% expulsion), they are not easily switched back to the neutral form. Although MEA, upon treatment with  $CO_2$ , does salt out organics, the reverse reaction, removing  $CO_2$ , does not occur under our mild conditions of heating to 50 °C while bubbling an inert gas (N<sub>2</sub> or air) through the solution. Primary amines can be switched back to neutral at higher temperatures, as has already been demonstrated in the literature,<sup>27</sup> but often temperatures over 100 °C are required.

## Conclusions

The ability to salt out organic compounds from water and then easily recycle the water without desalination should be an asset to industry both from environmental and cost perspectives. Use of "switchable water", a switchable ionic strength aqueous solvent, offers a means of salting out water-miscible organic compounds from aqueous solutions through the use of  $CO_2$ . These solvent systems can also easily be recycled by removal of CO2. To make these systems more attractive, alkylammonium bicarbonate salts derived from polyamines are required. These bicarbonate salts can provide solutions of greater ionic strength at lower loadings in water.

Before the synthesis of a new generation of additives could take place, we developed a set of principles for future additive design. These principles evolved from a study of the dependence of diamine  $pK_{aH}$  on the chain length between the functional groups. We have provided evidence suggesting that the organic content in the backbone of a bolaform electrolyte plays a large role in its salting out capabilities, potentially due to enhanced interactions of the carbon backbone with organic substrates in aqueous solution. A detailed modeling study of the molecular interactions of similar aqueous systems will be presented in a future publication.

We found that polyamines should have a minimum of four atom carbons between the amine groups (to allow for appropriate basicity) but otherwise a minimum of hydrophobic organic content (to allow for maximum salting out capacity). We have synthesized and tested several new polyamines which showed improved salting out capabilities compared to our original set of amine additives. Primary and secondary polyamines are more effective at salting out than tertiary polyamines, but the reversion of the primary and secondary polyamines to the neutral form requires significantly more energy. Further development of larger, more efficient polyamine additives as well as studies of new applications of the switchable water solvent systems are currently being pursued in our lab.

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