## Constitutional dynamic systems of ionic and molecular liquids<sup>†</sup>‡

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The ionic liquids N-methylpyridinium-2-carboxaldehyde  $Tf_2N^$ and N-methylpyridinium-3-carboxaldehyde  $Tf_2N^-$  form readilyreversible covalent bonds with protic nucleophiles, creating all-liquid constitutionally dynamic materials.

Dynamism-as embodied in the equilibrium formation and scission of covalent bonds under mild conditions-is central to constitutional dynamic chemistry (CDC), dynamic combinatorial chemistry (DCC), and systems chemistry.<sup>1</sup> From these decidedly interconnected paradigms emerges a conceptual model<sup>1</sup> of stimulus-responsive soft materials, a prospective use of ionic liquids (ILs) that we believe is ripe for exploration.<sup>2</sup>

Demonstrating the viability of the concept of IL-based dynamic chemistry,<sup>3</sup> we describe here the reactions of protic nucleophiles with the new ILs N-methylpyridinium-2carboxaldehyde bis(trifluoromethanesulfonyl)amide, 1, and N-methylpyridinium-3-carboxaldehyde bis(trifluoromethanesulfonyl)amide, 2. The cations of these materials readily and reversibly react in a holo (self-contained)<sup>1d</sup> fashion with protic nucleophiles via their 'dynamism-disposed' aldehyde groups. In contrast to typical dynamic systems where the bulk of any liquid present is an inert solvent for relatively low concentrations of reactive components, here the liquids *are* the systems.

Both 1 and 2 are colorless liquids that react with  $H_2O$  to form gem diols and diastereomeric bis(hemialdal)s (Fig. 1). These derivatives are distinguishable in the <sup>1</sup>H-NMR by resonances between  $\delta$  6.7 and  $\delta$  7.3 arising from the unique gem diol and bis(hemialdal) C-H protons. The occurrence of these in a range devoid of other resonances is invaluable to the study of dynamic systems of 1 and 2 with H<sub>2</sub>O or alcohols.

To examine CD systems of 1 and H<sub>2</sub>O, freshly dried IL samples were charged with the latter in molar increments of 20%, 40%, 60%, 80%, 100% and 120% relative to 1. Each of these neat, homogeneous liquids was studied by <sup>1</sup>H- and <sup>13</sup>C-NMR at temperatures of 25, 35, 45, 55 and 85 °C (coaxial tube, external  $d_6$ -dmso lock and reference). In all cases, the 1-H<sub>2</sub>O combination quickly reaches equilibrium with the gem diol and bis(hemialdal) covalent conjugates. The extent of hydration is easily quantified by comparing the intensities of the unique diol and bis(hemialdal) C-H resonances to that of CHO in the unreacted cation (Fig. 2). In turn, the residual 'unbound' H<sub>2</sub>O is quantified by accounting for the amount of the added water bolus needed to form the gem diol and that

regenerated by the formation of bis(hemialdal). In some cases this net 'free' H<sub>2</sub>O can be independently quantified by direct NMR observation.

As expected, the proportion of aldehyde transformed in these systems increases steadily as the amount of H<sub>2</sub>O is increased (Fig. 3). For example, at 25 °C in the system 1-20 mol% H<sub>2</sub>O,  $\sim 20\%$  of the aldehyde reacts—the maximum possible if (within error/detection limits) all of the H<sub>2</sub>O is sequestered. At 25 °C and added H<sub>2</sub>O equivalent to 40 and 60 mol% of 1, virtually all is likewise bound. Even at 100 mol% added H<sub>2</sub>O, the conversion of ca. 70% of the aldehyde to hydrates means that  $\sim 50\%$  of this large H<sub>2</sub>O bolus is covalently sequestered.

The increasing hydrate contribution to the system constitution as a function of increasing added H2O is observed regardless of temperature. To illustrate, at 85 °C, the conversion of 1 to hydrates increases from 14% to 42% when progressing from 20 mol% added H<sub>2</sub>O to 100 mol%. However, in all cases the degree of hydration at equilibrium is less for any given system as the temperature is increased. For example, in the system 1 with 100 mol% added H<sub>2</sub>O, the amount of aldehyde hydrated at equilibrium is  $\sim 70\%$  at 25 °C, and about 43% at 85 °C. This is wholly consistent with the thermodynamic nature of aldehyde hydration in general.<sup>4</sup> It should be noted as well that as system temperatures are increased, their constitutions also change because the proportion of bis(hemialdal)s decreases relative to gem diol. Like the foregoing, this is reasonable since more 'free'  $H_2O$ becomes available at higher T, suppressing the condensation reaction in which the bis(hemialdal)s are formed and H<sub>2</sub>O is regenerated.

Constitutional Dynamic System Components relative proportions conditionally variable



Fig. 1 Ionic components of the ionic liquid-molecular liquid dynamic systems.

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Fig. 2 Left: NMR excerpt showing the unique aldehyde, gem diol and bis(hemialdal) C–H resonances in the dynamic system 1–40% H<sub>2</sub>O; right: NMR excerpt showing typical changes in the resonance of 'free' water in the system 2–20% H<sub>2</sub>O. It is independently verifiable that this is not adventitious water in the  $d_6$ -dmso lock/reference.



**Fig. 3** Conversion of 1 to H<sub>2</sub>O and *t*-BuOH addition products as a function of both temperature and quantity of protic nucleophile. The system 1–*t*-BuOH was not studied at 85 °C because of the bp of the alcohol (83 °C).<sup>12</sup>

Building on these results, we initiated a parallel study using 2,2-dimethylpropan-1-ol (tert-butanol, t-BuOH). While H<sub>2</sub>O is the least sterically demanding protic nucleophile reversibly reactive with 1 or 2, this alcohol provides an opportunity to probe the dynamic nature of systems with a participant at the opposite steric extreme. Despite its bulky nature, alcoholysis was observed at all proportions of t-BuOH and 1. At 25 °C and 20 mol% of added alcohol, the degree of addition was the same (within error) as that in the system 1-20 mol% added H<sub>2</sub>O. However, all of the systems with larger alcohol proportions relative to 1 evidenced measurably lower magnitudes of addition than the analogous aqueous systems. Since aldehyde alcoholysis is preferred over hydration,<sup>5</sup> we conclude that sterics play a meaningful role in modulating these dynamic systems. Accordingly, we see hinted at in this result the possibility of designing dynamism-disposed ILs useful in molecular recognition and sorting.

Having established the dynamic parameters of systems of **1** and  $H_2O/alcohols$ , we turned to the study of systems based on **2**, the cation of which features the aldehyde group at the pyridinium ring 3-position. Since iodide salts of the latter cation do not, as solids, tend to form hydrates<sup>6</sup> (unlike their 2-analogs), we speculated that the corresponding ILs would form systems with  $H_2O$  with different *constitutions* (proportion of aldehyde plus  $H_2O$  vs. hydrates) under identical conditions. This proved to be the case. On a same-temperature basis, at all molar proportions of **2**–H<sub>2</sub>O, we observed the formation of CD systems which invariably manifested lower hydrate proportions than those in the same-condition systems of **1**.

As a case in point, at 25 °C the system  $1-80 \text{ mol}\% \text{ H}_2\text{O}$  sees approximately 64% of 1 being hydrated. Under identical conditions in the system containing 2, only 20% is converted to hydration products. The superficially minor difference in cation structure in 2 *versus* 1 clearly leads to substantial differences in the constitutions of the dynamic systems they form, emphasizing the ease with which tuning can be achieved. But, this is not the only way in which the systems of 1 and 2 differ.

In many of the 1/2-H<sub>2</sub>O systems a portion of H<sub>2</sub>O is plainly not sequestered at equilibrium. As mentioned, this 'free' H<sub>2</sub>O can sometimes be observed in the <sup>1</sup>H-NMR (Fig. 2), its identity as such supported by the disappearance of its resonance on D<sub>2</sub>O doping. In a representative system where free water is observed, that of 2-20 mol% added  $H_2O$ , the unsequestered H<sub>2</sub>O appears as a broad peak at ca.  $\delta$  4.2 (25 °C), which simultaneously shifts and sharpens as T is increased to 55 °C ( $\delta$  4.0), then 85 °C ( $\delta$  3.6). In a 1-based system where the resonance of 'free' H<sub>2</sub>O is cleanly observed, 1-80 mol% H<sub>2</sub>O, the same progression is seen though the chemical shift values are quite different:  $\delta$  5.6 (25 °C);  $\delta$  5.2 (55 °C); and  $\delta$  4.6 (85 °C). Significantly, when H<sub>2</sub>O is observed in any of the 1-based systems it is always in this general chemical shift range, as is likewise true for any system of 2 and the range specified for the 2-20 mol% added H<sub>2</sub>O example. This non-correspondence may indicate that the residual H<sub>2</sub>O is in appreciably different environments in systems derived from the two different cations.<sup>7</sup> Indeed, since 1 and 2 have the same anion, and since gem diols are known to have "a higher requirement for solvation by water than does water itself,"<sup>8</sup> our data might suggest that the cations of **1** and **2** exert a significant effect on the structure of the ostensibly free H<sub>2</sub>O, albeit to observably different degrees. It is important to note, however, that in the absence of additional data the basis of this behavior does remain an open issue; for example, we cannot presently exclude the possibility that the observed water signal in these spectra is not the product of signal averaging with that of (the unobserved) *gem* diol OH protons.

Having established the feasibility of designing dynamic IL systems, we set out to determine if we could exploit one in a model application, the slow release of an odorant. As a proofof-concept, a system was prepared from 1 and 20 mol% added menthol,<sup>9</sup> a volatile alcohol used as a palliative in conjunction with nasal and chest congestion. A control of menthol in the non-functionalized IL [BMIM]Tf<sub>2</sub>N was likewise prepared. Samples of each system were placed in a vacuum desiccator and their masses checked periodically over four days, the materials being maintained under active vacuum in the interim. Over this period the control mass diminished essentially to that of the base IL, the menthol loss being verified by <sup>1</sup>H-NMR. In contrast,  $\sim 40\%$  of the initial menthol charge remained in the system based on 1. This is consistent with dynamic covalent bonding between the non-volatile IL and the highly volatile menthol resulting in the dampening of the evaporation of the latter. These results further cement findings by Lehn et al. concerning the utility of dynamic systems for slow-release applications.<sup>10</sup> However, unlike the systems in the foregoing work, the IL-based system contains only one volatile component, the fragrance compound.

In summary, we have shown that constitutionally dynamic systems can be easily created using simply functionalized ionic liquids as reactive components. The constitutions of these systems are tunable and thermally responsive. They require no solvent *per se* but instead comprise stimulus-responsive liquid materials. In the case of the IL–H<sub>2</sub>O systems, the IL component can be regarded as 'self-drying' (and as such merits investigation as an additive to other ILs expressly for the purpose of water sequestration). In conjunction with volatile alcohols of interest, effective materials for the slow release of the latter can be prepared. Among obvious extensions of this work are the creation of systems in which all dynamic

components are ionic, systems based on dynamic reactions beyond those of aldehydes with protic nucleophiles, and applications of dynamic IL systems in separations and in absorptive cooling.<sup>11</sup>

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## Notes and references

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