ChemComm
www.rsc.org/chemcomm

Sweet success: ionic liquids derived from non-nutritive sweeteners†

Elke B. Carter,[a] Stephanie L. Culver,[a] Phillip A. Fox,[a] Russell D. Goode,[a] Ioanna Ntai,[a] Morgan D. Tickell,[a] Rachel K. Traylor,[a] Norris W. Hoffman*[a] and James H. Davis, Jr.‡*[ab]
[a] *Department of Chemistry, University of South Alabama, Mobile, Alabama 36688, USA.*
E-mail: jdavis@jaguar1.usouthal.edu; Fax: 251-460-7359; Tel: 251-460-7427
[b] *Center for Green Manufacturing, The University of Alabama, Tuscaloosa, Alabama 35487, USA*

Received (in Cambridge, UK) 17th October 2003, Accepted 27th January 2004
First published as an Advance Article on the web 10th February 2004

The anions of the sweeteners saccharin and acesulfame form ionic liquids when paired with a variety of organic cations.

Interest in the use of ionic liquids (IL) as solvents has reached a level sufficient to spur their commercialization.[1] One reason routinely cited to justify this interest is their "green" nature. However, it has been pointed out that the use of the term "green" to describe IL chemistry is something that should be done with care.[2] In a recent paper, Rogers and coworkers offered a superb commentary on this situation as it pertains to fluorous anions, which are the most widely used anion type in IL formulations.[3] While there are situations in which IL with fluorous anions will remain indispensible, there is much to be desired in identifying other (preferably innocuous) ions in formulating IL, especially for large-volume applications.[1,3] To this end, non-toxic organoanions such as acetate and lactate have been used.[3,4] However, carboxylates are basic, readily engage in hydrogen bonding, and are strongly coordinating towards transition-metal ions. Such attributes are *not* typical of the fluorous anions on which so many IL compositions are based. Mapped onto an IL, these properties are likely to be useful in some circumstances and detrimental in others.

Here, we report the use of saccharin and acesulfame in the formation of new ionic liquids. As alkali-metal salts, the anions of both are in widespread use in foodstuffs as non-nutritive sweeteners.[5] Significantly, when incorporated into IL these anions exhibit behaviors that in several regards more closely resemble those of certain *fluorous* anions than those of common carboxylates.

Both of the sweetener anions are *N*-acyl-*N*-sulfonyl imides [Fig. 1]. As such, they bear a similarity to the TSAC anion introduced by Matsumoto as a substitute for bis(trifluoromethyl)sulfonyl imide (Tf_2N^-) in IL chemistry.[6] Notably, the saccharinate (Sac) and acesulfamate (Ace) anions are—unlike TSAC and Tf_2N^-—non-fluorous and have well established toxicological profiles.[5]

When combined with *onium* cations, each anion gives rise to salts melting below 100 °C. Prototypes have been prepared in which each anion is paired with an array of cations, and select examples are presented here [Table 1]. All of the new ionic liquids are prepared *via* metathesis, combining the requisite onium halide salt with the sodium, potassium, or silver salt of the sweetener in acetone or acetone/water. The resulting IL are miscible with polar organic solvents—acetone, acetonitrile, methanol—and insoluble in less polar species such as ether, n-hexane and toluene. Conversely, the latter are generally soluble to a fair degree in the ionic liquids. Like IL incorporating small fluorous organoanions (*e.g.* $CF_3CO_2^-$, $CF_3SO_3^-$), the Sac and Ace salts are water miscible.

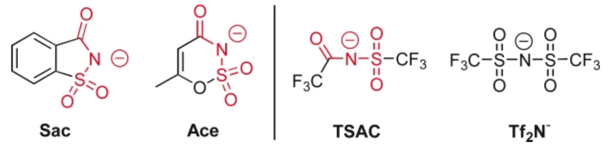

Fig. 1 Structures of the saccharinate (Sac), acesulfamate (Ace) and TSAC anions. Structurally homologous elements of the three are emphasized in red. The structure of the widely used bis(triflyl)imide (Tf_2N^-) anion is shown for comparison.

Several of the new IL are room-temperature liquids [Table 1]. Those that are are viscous, but become visibly less so with modest heating or when small quantities of water or organic solvents are added. The IL with melting points above room temperature readily form long-lived supercooled phases. In terms of melting points and viscosities, IL derived from the sweetner anions generally resemble those derived from other non-fluorous organoanions, as well as those of some larger perfluoro anions such as nonafluorobutanesulfonate, NfO^-.

The new ionic liquids have been characterized by ^1H- and ^{13}C-NMR as well as FAB-MS. The ^1H-NMR spectra of the imidazolium-Sac and Ace IL are particularly informative when viewed in the context of same-cation salts of other anions. It has been shown that for solutions of like concentration, a correlation exists between the chemical shift of the ring protons (especially that on C^2) and the hydrogen-bonding capacity of the anion.[9] Generally, the H–C^2 resonance is observed at higher δ values with more strongly H-bonding species (halides, carboxylates, *etc.*) and at lower values when more poorly H-bonding anions (PF_6^-, Tf_2N^-, *etc.*) are used. Comparatively, the sweetner anions of our new IL produce H–C^2 shifts [Table 1] falling between those observed for IL with perfluorocarboxylate and perfluorosulfonate anions.[9] For example, the H–C^2 proton in $[C_4MIM]Sac$ appears at 9.53 ppm and that in

Table 1 Select properties of representative saccharin and acesulfame-derived ionic liquids

Ionic liquid[a]	H–C^2 δ[b]	mp/°C[c]
$[C_4MIM]Sac$	9.53	RT
$[C_5MIM]Sac$	9.60	64
$[C_6MIM]Sac$	9.80	RT
$[C_9MIM]Sac$	9.64	RT
[BDMIM]Sac[d]	—	70
$[C_4MIM]Ace$	9.51	RT
$[C_6MIM]Ace$	9.62	RT
$[C_9MIM]Ace$	9.59	RT
$[Me_3N(CH_2)_2OC(O)(CH_2)_2CH_3]Sac$	—	89
$[P1(CH_2)_2OCH_2CH_3]Sac$[e]	—	RT
$[n\text{-}Pr_4N]Sac$	—	96
$[MeEt_3N]Sac$	—	26[f]
$[Me_3N(CH_2)_2OC(O)(CH_2)_2CH_3]Ace$	—	49
$[n\text{-}Pr_4N]Ace$	—	73
$[MeEt_3N]Ace$	—	39[f]

[a] $[C_4MIM]$ = 1-methyl-3-(n-butyl)imidazolium; $[C_6MIM]$ = 1-methyl-3-(n-hexyl)imidazolium; $[C_9MIM]$ = 1-methyl-3-(n-nonyl)imidazolium. [b] Imidazolium ring C^2 proton, 300 MHz, 0.50 M, acetone-d^6, δ. [c] RT = liquid at or below room temperature.[7] [d] 1-Butyl-2,3-dimethylimidazolium. [e] P1 = *N*-methylpyrrolidinyl.[8] [f] These materials are waxy semi-solids at room temperature. The reported mp is the temperature at which the sample fully liquified.

---

† Electronic supplementary information (ESI) available: experimental details; IR spectra. See http://www.rsc.org/suppdata/cc/b3/b313068a/

‡ Address correspondence to this author at the University of South Alabama address.

DOI: 10.1039/b313068a

$[C_4MIM]$Ace at 9.51 ppm. The trifluoroacetate salt of the same cation exhibits the H–C^2 signal at δ 9.88. When paired with either NfO$^-$ or TfO$^-$, the same resonance is observed at δ 9.11. In the only reported imidazolium TSAC salt ($[C_2MIM]$; acetone-d^6), the signal is observed at δ 9.06.[6] In striking contrast to these values, the H–C^2 signal of $[C_4MIM]Cl$ is observed at δ 10.79 and that for $[C_4MIM]$acetate at 11.02.[9a] The chemical shifts of the H–C^2 resonances of the Sac and Ace salts acquired at 0.50 M concentration in $CDCl_3$ give peaks 0.15–0.20 ppm downfield relative to their positions in acetone. This is likely indicative of the formation in this solvent of "quasi-molecular" species that pi-stack, shielding the C^2 protons.[9c] In either solvent, the chemical shifts of the C^2-protons in both the Sac$^-$ and Ace$^-$ salts exhibit only a small change as a function of concentration. Like the C^2–H chemical shift values, this phenomenon is strongly indicative of a weak capacity on the part of Sac$^-$ and Ace$^-$ to engage in hydrogen bonds in solution with the imidazolium cations.[9]

Given the low H-bonding capacity suggested by the NMR data for these non-fluorous anions, we next assessed their relative transition-metal coordinating ability. Previous work has shown that ν_{Rh-CO} in *trans*-$Rh(PPh_3)_2(CO)X$ (Vaska complexes; {Rh}X hereafter) is sensitive to the donor nature of ligand X$^-$, increasing as bonding power decreases.[10] The values for ν_{Rh-CO} for a range of weakly binding X$^-$ and relative affinities thereof for {Rh}$^+$ have been determined.[11] Both AgSac and AgAce cleanly abstracted Cl$^-$ from {Rh}Cl in benzene or $CDCl_3$ and transferred the respective sweetener anion to {Rh}$^+$; yellow microcrystals of the new species were isolated in over 90% yield.[12] However, the ν_{Rh-CO} of 1987 cm^{-1} for {Rh}Sac and 1980 cm^{-1} for {Rh}Ace did not match their respective affinities for {Rh}$^+$ as determined in $CDCl_3$ by ^{19}F and/or ^{31}P NMR for (*below*) eqn. (1) (Z = TFA, K = 0.091; Z = 3-$FC_6H_4CO_2$, K = 31; Z = CH_3CO_2, K = 99;) and eqn. (2) (Z = TFA, K = 1.1).[13]

$$\{Rh\}Sac + [N(PPh_3)_2]Z = \{Rh\}Z + [N(PPh_3)_2]Sac \qquad (1)$$

$$\{Rh\}Ace + [N(PPh_3)_2]Z = \{Rh\}Z + [N(PPh_3)_2]Ace \qquad (2)$$

The actual order of relative affinities for {Rh}$^+$ of Sac$^-$ > TFA$^-$ > Ace$^-$ > ONO_2^- is displayed in Fig. 2 by their increasing tendency to be displaced from their complexes by 4-picoline. Thus Sac$^-$ behaves not like the quite weakly binding $OPOF_2^-$ (same values for ν_{Rh-CO}) but more akin to the mid-range 3-$FC_6H_4CO_2^-$, and Ace$^-$ (same ν_{Rh-CO} as for Cl$^-$) just slightly weaker than the moderately weakly binding TFA$^-$. While the anion affinities for {Rh}$^+$ fail to closely correlate with ^{31}P and ^{13}C NMR parameters of {Rh}X, it is clear from the competition reactions that the sweetener anions complex {Rh}$^+$ much more weakly than does acetate. As no ready explanation exists for the apparent similarities of both Sac$^-$ and Ace$^-$ to fluorous anions in H-bonding capacity but not for Sac$^-$ in metal-coordinating ability, further study of the latter is in progress.

A final relationship which bears commenting upon is the relative basicity of the anions. In this regard, the properties of the sweetener anions are not bounded by fluorous sulfonates and carboxylates, but rather by fluorous and non-fluorous carboxylates. For example, the pK_b of the trifluoroacetate anion (TFA) is 13.7 and that of acetate is 9.0. In turn, the pK_b values of Sac and Ace are 11.8 and 11.6 respectively—making them roughly one thousand times less basic than acetate, but around one hundred times more basic than TFA.

Like other non-fluorous anions evaluated to date, Sac and Ace are not viable replacements for fluorous species such as PF_6^- and Tf_2N^- for giving rise to poorly coordinating *hydrophobic* ionic liquids.[14] However, in other regards they compare quite favorably as IL anions to widely used fluorous sulfonates and fluorous carboxylates. Further, the successful creation of IL by pairing these non-toxic anions with cations also known to be non-toxic such as butyryl choline [Table 1] further underscores the possibilities which exist for creating new ionic liquids that may prove to be wholly benign both environmentally and toxicologically.

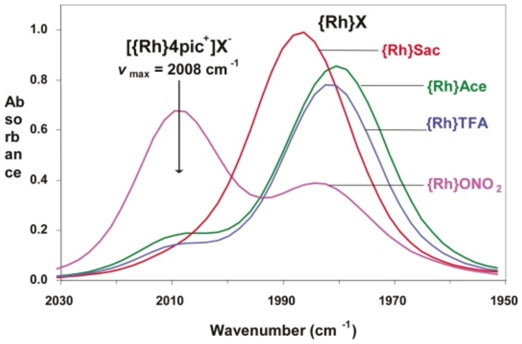

Fig. 2 IR spectra of CH_2Cl_2 solutions initially 1.60 mM in {Rh}X and 3.20 mM in 4-picoline, showing the relative anion affinity of X$^-$ for {Rh}$^+$ *via* partitioning into {Rh}X and [{Rh}4pic$^+$]X$^-$.

Notes and references

1 J. H. Davis, Jr. and P. A. Fox, *Chem. Commun.*, 2003, 1209.

2 J. D. Holbrey, M. B. Turner and R. D. Rogers, in *Ionic Liquids as Green Solvents-Progress and Prospects*, ed. R. D. Rogers and K. R. Seddon, ACS Symp. Ser. 856, ACS, Washington DC, 2003, p. 2.

3 (*a*) R. P. Swatlowski, J. D. Holbrey and R. D. Rogers, *Green Chem.*, 2003, **5**, 361; (*b*) We thank L. Crowhurst, N. L. Lancaster, J. M. Perez-Arlandis and T. Welton for an advance copy of a manuscript dealing with ion effects in IL, submitted by them for publication in an ACS Symposium Series monograph on ionic liquids.

4 (*a*) M. J. Earle, P. B. McCormac and K. R. Seddon, *Green Chem.*, 1999, **1**, 23.

5 G.-R. von Rymon Lipinski, *Ullman's Encyclopedia of Industrial Chemistry*, 6th edn., Wiley-VCH, Weinheim, 2003, vol. 35, p. 407.

6 H. Matsumoto, H. Kageyama and Y. Miyazaki, *Chem. Commun.*, 2002, 1726.

7 These compounds have remained liquids despite repeated attempts to crystallize them.

8 D. R. MacFarlane, P. Meakin, J. Sun, N. Amini and M. Forsyth, *J. Phys. Chem.*, 1999, **103**, 4164.

9 (*a*) P. Bonhote, A.-P. Dias, N. Papageorgiou, K. Kalyanasundaram and M. Gratzel, *Inorg. Chem.*, 1996, **35**, 1168; (*b*) A. Elaiwi, P. B. Hitchcock, K. R. Seddon, N. Srinivasan, Y. M. Tan, T. Welton and J. A. Zora, *J. Chem. Soc., Dalton Trans.*, 1995, 3467; (*c*) A. G. Avent, P. A. Chalconer, M. P. Day, K. R. Seddon and T. Welton, *J. Chem. Soc., Dalton Trans.*, 1994, 3405.

10 F. Araghizadeh, D. M. Branan, N. W. Hoffman, J. H. Jones, E. A. McElroy, N. C. Miller, D. L. Ramage, A. B. Salazar and S. H. Young, *Inorg. Chem.*, 1988, **27**, 3752. PM3(tm) structures computed for {Rh}NCO and {Rh}NCS show the two previous exceptions to this trend to have the CO stretching vibration coupled strongly to *trans* NCO and NCS stretching, respectively.

11 (*a*) D. M. Branan, N. W. Hoffman, E. A. McElroy, N. Prokopuk, A. B. Salazar, M. J. Robbins, W. E. Hill and T. R. Webb, *Inorg. Chem.*, 1991, **30**, 1200; (*b*) A. Svetlana-Larsen and J. L. Hubbard, *Inorg. Chem.*, 1996, **35**, 3073; (*c*) A. Svetlana-Larsen, C. R. Zoch and J. L. Hubbard, *Organometallics*, 1996, **15**, 3076.

12 Like the new ILs, these complexes have been fully characterized by spectroscopic means, and satisfactory elemental analyses have been obtained as well. Note that numerous transition-metal complexes of sweetener anions have been previously documented: M. N. Hughes, *Coordination Compounds in Biology*, in *Comprehensive Coordination Chemistry*, ed. G. Wilkinson, Pergamon, Oxford, 1987, vol. 6, ch. 62.1, p. 541.

13 Greater detail on using fluorinated carboxylates as ^{19}F NMR reporter ligands will be published separately.

14 We have also prepared IL from another sweetner, sodium *N*-cyclohexyl sulfamate. These IL are different in several respects to those of Ace and Sac, and will be described in a separate report.