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Oxidative Desulfurization of Azole-2-thiones with Benzoyl Peroxide: Syntheses of Ionic Liquids and Other Azolium Salts

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1-Alkyl-3-methylimidazole-2-thiones were prepared from amino esters in one pot and converted to inherently halide-free 1-alkyl-3-methylimidazolium benzoates by oxidation with benzoyl peroxide followed by a novel anion exchange. Also reported are the outcomes of exchanges with other anions, acidifications of the imidazolium benzoates to other salts, and extension of the method to the syntheses of 1,3-diphenylimidazolium and 3-methyl- and -butylthiazolium salts.

Introduction

Ionic liquid (IL) literature[1–8] is dominated by 1-alkyl-3-methylimidazolium salts, of which 1-butyl-3-methylimidazolium ([bmim] or [C_4mim]) salts are the most recurrent (Figure 1). The preponderance of [C_4mim] ionic liquids in the literature, especially the tetrafluoroborate and hexafluorophosphate salts, probably derives from their synthetic accessibility.[9] A typical preparation of [$C_n$mim] ILs is the quaternization of methylimidazole followed by an anion exchange as idealized in Scheme 1. Recent directions in IL synthesis generally emphasize three points. First is the manufacture of ILs of higher purity, especially with no or low halide content. Inherently halide-free ILs have been furnished by syntheses in which the leaving group for the quaternization does not have to be exchanged (Table 1). A second area of ongoing research is manipulation of the alkyl substituents on the imidazolium cation. The substructure's hydrogen bonding and ligating abilities (as the N-heterocyclic carbene, NHC) feature prominently in reactions facilitated by ILs.[1,6,10–14] There is particular emphasis on new chiral structures,[15,16] and task-specific ILs (TSILs).[17–20]

The third theme is variation of the anion (and its method of introduction when necessary) from the ubiquitous tetrafluoroborate and hexafluorophosphate species. The direct path in Table 1 allows such modification, but the desired anion is not always available in a form that transfers the desired alkyl group. Acids remain the ideal source of the

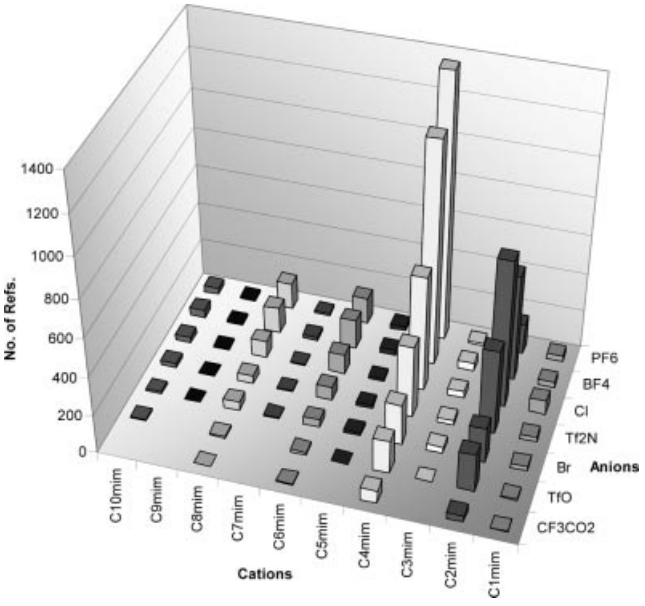
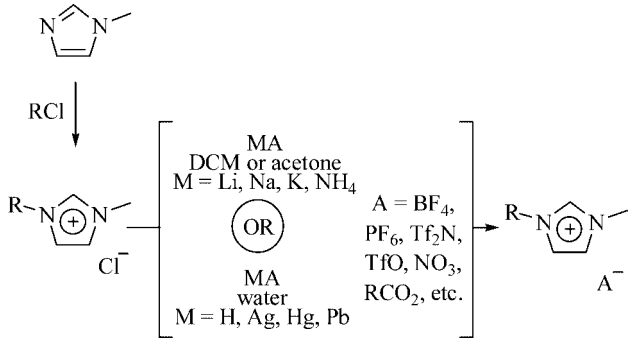


Figure 1. Abundance of $C_n$mim IL references as a function of ion pair.[21]



Scheme 1. Representative preparations of $C_n$mim ILs from chlorides.

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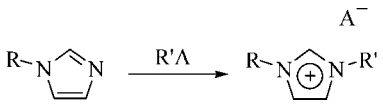
Table 1. Syntheses of halide-free ILs by direct alkylation of imidazoles to ILs.



R	R′	A	Ref.
Bu	$Me_2O{\cdot}Me$[a]	BF_4	[38]
Me, Et	Me	Tf_2N	[39]
Me	Et	CF_3CO_2	[40]
Me, Et, *n*Pr, *n*Bu	Me, Et	O_3SOR'	[41][b]

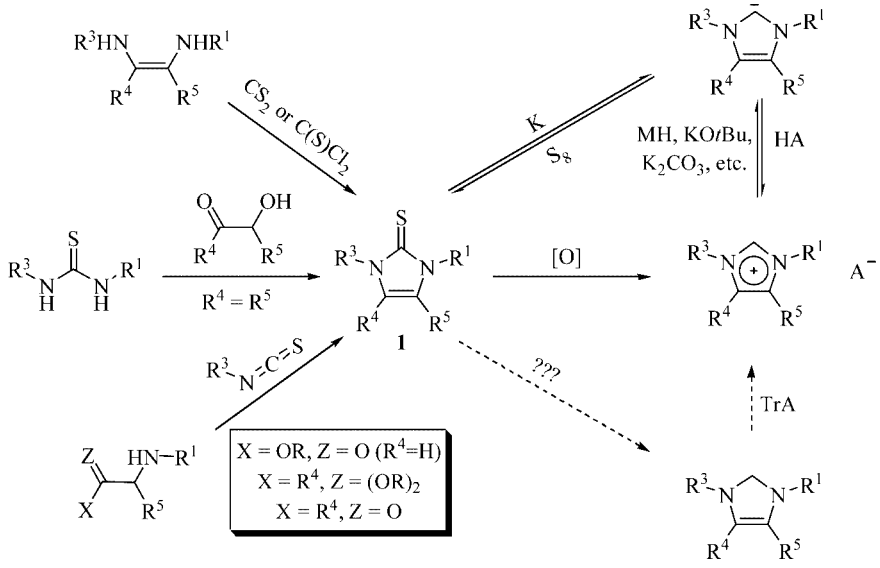
[a] The authors note the release of dimethyl ether as IL formed, and its removal under vacuum. [b] C(2)-Me ILs were also prepared.

desired anions to minimize inorganic contamination. Because an anion exchange cannot be efficiently done with the imidazolium halide and an acid weaker than a hydrohalic acid, routes to a wider range of conjugate bases must pass through a different intermediate. Towards this end (and that of higher purity ILs), Earle and Seddon transformed 1,3-dialkylimidazolium halides to NHCs (Scheme 2), which were distilled, and then reprotonated to ILs.[22] Because the carbenes are such potent bases,[23–26] this route could potentially incorporate a large number of anions. Maase and Massonne have reported a similar process.[27] Ohno and coworkers synthesized 1-ethyl-3-methylimidazolium ([emim] or [C_2mim]) ILs based on all 20 natural amino acids.[28] After using an anion exchange resin to convert [C_2mim][Br] to [C_2mim][OH], the imidazolium hydroxide was added to an amino acid to generate the IL and water, which was removed in vacuo. Several other electrophiles have been reacted with NHCs,[29–35] and a recent entry refers to ILs.[36]

We stipulated a conversion of imidazole-2-thiones (**1**) to ILs will unify these approaches (Scheme 2). Provided no halogenated reagents are used, the IL products will be inherently halide-free. Ideally, an all-organic reaction would lead to a product mixture with lipophilic impurities that could be washed from the IL product. Compounds **1** were all the more attractive for conversion to ILs because the method of assembly allows variation of the 1-, 3-, 4-, and 5-substituents,[37] and this adaptability has an obvious bearing on expanding the library of IL cations, including chiral entries.

A variety of anions could be introduced depending on the method for the desulfurization of **1**. A reductive desulfurization to the carbene[42] followed by treatment with acid, or an unprecedented route to the *gem*-diamine followed by oxidation should yield the desired IL. Regarding the latter, similar systems have been ionized with trityl tetrafluoroborate,[43] which releases triphenylmethane and would avoid the inorganic contamination possible by other conceivable routes. Oxidative desulfurizations of compounds **1** to imidazolium salts with hydrogen peroxide and an acid,[44–47] iron(III) chloride,[48] and nitric acid[49–51] are well known.[52] Some of Wanzlick's approaches to stable carbenes more than 30 years ago proceeded through oxidations of compounds of type **1**.[35] Dimethyldioxirane can be used,[53] and oxidation with *m*CPBA in the presence of perchloric acid yields an imidazolium perchlorate directly.[54] We were especially interested in preparing ILs based on carboxylates more basic than trifluoroacetate. Examples of these materials have been made by heavy metal anion exchange (to make [C_2mim][OBz]),[55] microwave promoted anion exchange of imidazolium chlorides and ammonium benzoate ([C_2mim], [C_4mim], and [C_6mim][OBz]),[56] anion exchange in acetone ([C_4mim][lactate]),[57] imidazole quaternization with dimethyl carbonate ([C_2mim][$MeOCO_2$]),[58] and by the protonations of NHCs[22,27] and [C_2mim][OH][28] described earlier.

The draw of imidazolium carboxylates is their rarity (Figure 1) and the prospect of making other ILs simply by treatment with stronger acids.[58] The ability to vary four



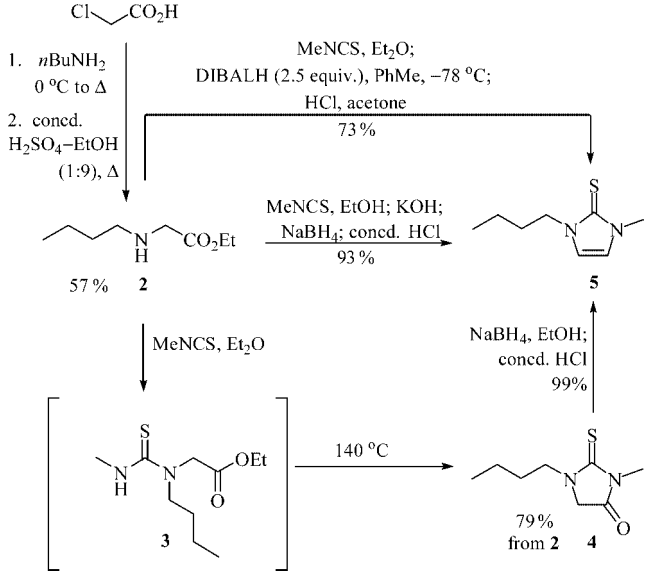
Scheme 2. Known and postulated routes to imidazolium salts through **1**.

alkyl groups is the reason to make them from compounds **1**. A path to ILs from compounds **1** would be complementary to the dominant paradigm, and could be one way to spur the development of new ILs.

Results and Discussion

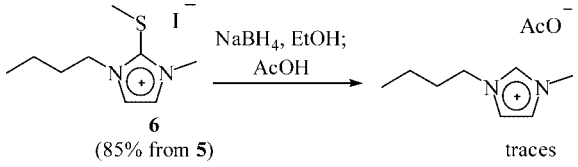
Synthesis of [C_4mim] ILs

The original synthetic plan was based on the monoreduction and cyclization of α-thioureido esters with DIBALH by Markwalder and co-workers.[59] Ethyl *N*-butylglycinate (**2**) has been reported to form in 71% yield by the butylamination of ethyl α-bromoacetate in benzene.[60] The reaction of *n*-butylamine with chloroacetic acid and esterification of the residue left after distillation of the amine gave the amino ester in 57% yield (Scheme 3). Following reaction of **2** with methyl isothiocyanate, two singlets consistent with α protons were found by ^{1}H NMR, suggesting that some 2-thiohydantoin (**4**) had spontaneously formed. It seemed preferable to accomplish the thioureidation, reduction, and cyclization in one pot with an excess of DIBALH to account for any that may be destroyed by ethanol released in the incidental cyclization of **3** to **4**. 1-Butyl-3-methylimidazole-2-thione (**5**) was isolated in good yield after chromatography. This plan was changed upon finding that **3** completely cyclized to **4** thermally, that **4** was sufficiently electrophilic to undergo sodium borohydride reduction,[61] and that crude **4** could be used. We later found the cyclization proceeded more easily with ethanolic potassium hydroxide, and accomplished a water-insensitive one-pot synthesis of **5** from **2**.



Scheme 3. Syntheses of **5**.

Three reductive desulfurizations of **5** were evaluated without success. Reduction with elemental potassium (Scheme 2) appeared to proceed as described by Kuhn,[42] but the isolate decomposed without releasing any product by distillation. Acidification of the residue with tetrafluoroboric acid left a brown solution unaffected by Celite, charcoal, silica gel, or aluminum oxide. Morel described several desulfurizations of azole-2-thiones, one of which was the reduction of a 2-methylthioimidazolium chloride to the imidazolium chloride with sodium borohydride.[62] After crystalline **6** was treated with sodium borohydride in ethanol and quenched with acetic acid (Scheme 4), all solvents were distilled and the ^{1}H NMR of the residue revealed the characteristic imidazolium protons at $\delta > 7$ ppm. However, [C_4mim][OAc] could not be adequately purified from the "ionic soup" of [C_4mim], sodium, iodide, and acetate. Although a proper IL was not secured by this approach, we note Morel's conversion of a 2-methylthioimidazolium salt to a crystalline imidazolium chloride could be useful to prepare more derivatives as IL precursors in the future. Reductive desulfurization of **5** with nickel(II) borohydride[63] could have left a *gem*-diamine, carbene, or [C_4mim] product, but there was no indication of any of these products and **5** was recovered in 28% yield.



Scheme 4. Attempted synthesis of [C_4mim][OAc] from **5**.

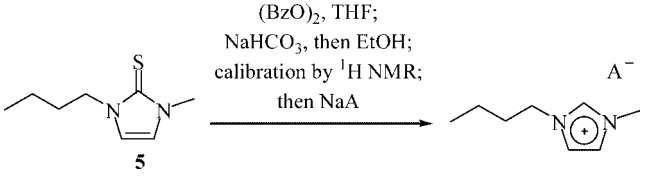
Oxidative desulfurizations were attempted next. To prepare [C_4mim] carboxylates, hydrogen peroxide and, alternately, acetic or benzoic acid were selected for the process, giving identical results. In a variety of organic solvents (toluene, glyme, *p*-dioxane, di-*n*-butyl ether), a solution of **5** and acid was unresponsive to 30% hydrogen peroxide up to 80 °C. Even at this temperature a surprisingly large amount of peroxide (ca. 15 equiv.) was required before the yellow color of **5** was consumed. An immiscible layer could be formed and washed to constant weight with tetrahydrofuran. However, this formulation was unacceptable for several reasons, primarily its stability. Upon standing at room temperature, the product, which was initially a very light yellow, darkened and released a precipitate. This decomposition was hastened when the sample was heated for drying, and prevented more thorough characterization.

Assuming residual hydrogen peroxide and acid were responsible for the decomposition, an oxidation of **1** with an organic peroxide that could be washed from the final sample was a logical adaptation. With no precedent using one, benzoyl peroxide seemed an appropriate selection. Compound **5** in toluene resisted oxidation by three equivalents of 75% benzoyl peroxide at 0 °C, room temperature, and reflux. After the gradual addition of two more equivalents of 75% benzoyl peroxide, however, the yellow color of the thione disappeared and **5** could no longer be detected by TLC. Conventional workup and removal of water left an acidic light gold oil which presented only [C_4mim] signals in ^{1}H NMR spectroscopy. The desulfurization likely proceeds via extrusion of sulfur dioxide from an intermediate imidazoliumsulfinic acid like the reaction with hydrogen

peroxide.[52] Direct isolation of [C_4mim] as the benzoate was most likely precluded by hydration of sulfur dioxide to sulfurous acid, which can be oxidized by benzoyl peroxide to sulfuric acid, and either of these acids would exchange with benzoate to leave the bisulfite or bisulfate. In this reaction, oxidation of sulfite to sulfate species must be nearly quantitative, because the isolate did not respond to bromine. Several isolates described later were randomly selected, and all passed this test. Further, Karkhanis and Field report the isolation of 1,3-dimethylimidazolium bi- and methylsulfates from the oxidation of 1,3-dimethylimidazole-2-thione in methanolic hydrogen peroxide, with no mention of sulfite species.[46] As we refined the process, we found addition of **5** to a slurry of benzoyl peroxide in tetrahydrofuran brought the reaction to spontaneous reflux, dissolving the benzoyl peroxide, obviating the need to supply heat, and requiring only 10 mL THF for the reaction of 10 g 75% benzoyl peroxide for each gram of **5**, but an anion exchange was necessary.

The first attempt at anion exchange was treatment with two equivalents sodium benzoate (based on the amount of **5** used) to simultaneously neutralize bisulfate and supply the desired anion. A solid was isolated. Although they did not capitalize on the phenomenon for isolation of the IL, Dupont and co-workers observed the separation of [C_4mim][BF_4] from sufficiently concentrated aqueous potassium chloride,[64] so we attempted to force a [C_4mim][OBz] layer from the aqueous wash with saturated sodium benzoate. Diethyl ether was added to wash out benzoic acid, and revealed two aqueous layers, one rich in IL and another denser layer containing primarily inorganic salts, but the IL solution still solidified after extraction with dichloromethane and concentration. It seemed likely these difficulties arose from the need to separate [C_4mim][OBz] from the excess sodium benzoate provided, and that careful application of a stoichiometric amount of sodium benzoate could lead to a more easily purified product.

We decided to solve the molar amount of [C_4mim] species per gram of solution by ^{1}H NMR prior to addition of sodium benzoate, and found sodium hydrogen carbonate and sulfate are insoluble in 2:1 ethanol/water. Hence, the acidic aqueous solution from the benzoyl peroxide oxidation was neutralized with sodium hydrogen carbonate (1 equiv. based on **5**), and addition of two volume equivalents ethanol precipitated the sodium salts. After filtration, an aliquot of the filtrate was concentrated, and spiked with dimethyl sulfoxide. Comparison of the integral of the [C_4mim] methyl proton resonance to the integral of the neatly resolved dimethyl sulfoxide singlet was used to solve for millimol [C_4mim] species per gram of filtrate. Note all three protons of a dialkylimidazolium ring can exchange with deuterium oxide (although the process requires supplied base[65,66] or a palladium catalyst[67] to be synthetically useful). After determination of [C_4mim] concentration with NMR, a stoichiometric amount of sodium benzoate was added to the remaining solution, precipitating a second crop of sodium salts (Scheme 5, A = OBz). The requirement for ethanol was surprisingly strict; the neutralized mother liquor was unaffected by tetrahydrofuran, *tert*-butyl alcohol, 2-propanol, or acetone. While methanol and acetonitrile forced out some sediment, the dry weight of the salt removed by suction filtration was less than that precipitated with ethanol. Note that Bach and co-workers reported a similar anion exchange with thiazolium salts using 2:1 methanol/water.[54] No additional solid was precipitated with more than two volume equivalents ethanol, and neither crop of precipitate gave any signals in the ^{1}H NMR spectroscopy. The calibration process also provided an estimate of the oxidation yield, which could vary from 60 to 80%, but was typically >70%. Concentration of the second filtrate left a suspension in need of further purification, which we address after making an observation on the relevance of this anion exchange to the larger body of IL preparation methodologies.



Scheme 5. General approach to the preparation of [C_4mim] ILs from **5**.

On its face, anion exchange between [$C_n$mim][Cl] and alkali or ammonium salts (Scheme 1) seems ideal, but all available data indicate that the organic soluble ion pair is not cleanly extracted upon contact of two organic-insoluble salts. In this work alone, this point is borne out by our inability to recover [C_4mim][OBz] from excess sodium benzoate, or [C_4mim][OAc] from the reaction in Scheme 4. This anion exchange method generates an "ionic soup", and it is essential to wash a large concentrated solution of the IL product mixture in dichloromethane with several tiny portions of water (which is also necessary following an anion exchange with acid),[68] or to repetitively cool and filter[69] the mixture to remove inorganic contaminants by degrees. Anion exchange with heavy metal salts efficiently removes the halide, but the salts are expensive and toxic. Our observation is functionally similar to the clean precipitation of heavy metal halides, provided the imidazolium species is available as a sulfate, hydrogen carbonate, or mixture thereof. Like the precipitation of heavy metal halides, precipitation of sodium sulfate and hydrogen carbonate from the appropriate imidazolium and sodium salts in 2:1 ethanol/water follows the natural direction of precipitation, where two solutes release one precipitate, as opposed to the release of one solute from two precipitates. In a partial survey of sodium salts, we found the chlorate,[70] tetrafluoroborate, acetate, chloride, bromide, and trifluoroacetate were all soluble in 2:1 ethanol/water, so there was a great deal of latitude in the anion that could be introduced. Most significantly, anions not conveniently available as the acid, such as chlorate,[70] can be supplied. Unlike the nearly quantitative precipitation of heavy metal halides, where the mass of the precipitate relates the extent of halide removal, this anion exchange precipitates a mixture of sodium sulfate and hy-

drogen carbonate of unknown constitution, and the dry weight of the precipitate does not directly indicate the extent of anion exchange. However, the concentration of [C_4mim] species determined in the calibration step can be used to solve the theoretical yield of sodium sulfate and excess mass of sodium hydrogen carbonate. Numerous selected precipitates were dried to constant weight and returned at least 80% of the expected dry mass.

Final purification of ILs is typically effected with adsorbents – most commonly silica gel, aluminum oxide, charcoal, and Celite; spectroscopic grade ILs purified on one column layered with charcoal, silica gel, and Celite were recently described.[71] Silica gel chromatography (SGC) seemed particularly well-suited to this example because the concentrate from the reaction mixture at the stage of NMR calibration, which should contain only [C_4mim] and sodium cations paired with sulfate and hydrogen carbonate, was immobile on silica gel, even with ethanol as the eluent. The desired combinations of [C_4mim] and supplied anions were expected to be separable from other combinations of ions, although the effect of the desired ILs on the mobility of undesired ions could not be known. Assessments of IL purity beyond color, mobility, and appearance of ^{1}H and ^{13}C NMR spectra are rare,[1,4,71–73] but we required a quantitative handle for the purity of the isolates to compare several anion exchanges and purifications. Solving for total millimol [C_4mim] species per gram of sample with a dimethyl sulfoxide spike just as in the calibration step was straightforward. However, with no convenient way to confirm all [C_4mim] species were paired with the intended anion (except for [C_4mim][OBz]), this number could only be used to find the possible range of [C_4mim] content by mass, which is reported as % IL in Table 2.

These ranges necessarily start from the multiplicative product of the millimolecular weight of the lighter (or lightest) reasonable [C_4mim] product (on a per [C_4mim] basis) and millimol total [C_4mim] species, and run to the multiplicative product of the millimolecular weight of the effectively heavier (or heaviest) reasonable [C_4mim] product. In the reactions reported, *bis*-[C_4mim] sulfate (*MW* = 374.50, 187.25 on a per [C_4mim] basis) is the lightest combination of [C_4mim] and an available anion, except in the synthesis of [C_4mim][Cl] (*MW* = 174.67), where the low end of the range is actually the highest possible content of *desired* IL. In all cases, yields are reported on the basis of total *millimol* [C_4mim] species recovered, *not mass*, and are single numbers *inherently corrected for purity*. The anion exchanges proceeded almost quantitatively (see Exp. Sect.), so the reported numbers principally reflect the oxidation yield. This approximation was used to describe every IL formulation except [C_4mim][OBz], where the integrals of the anion resonances in the ^{1}H NMR spectrum leave little room for [C_4mim] paired with any other anion and IL content is reported as a single number. The maximum IL content of [C_4mim][ClO_3][70] isolated by Method F actually solves to 101%, which we ascribe to cumulative experimental error. Despite reference to "chromatography", note the amount of silica gel required was only 5 g silica gel (230–400 mesh) per 2 g crude IL in all cases. The products were recovered in bulk elutions of 30 to 50 mL per 2 g crude IL (except in Method C). Based on the dry masses of precipitates described earlier, we believe the content of undesired [C_4mim] species is low, and that the content of desired IL lies far to the high (low for [C_4mim][Cl]) end of the range.

Anion suitability and IL purification methods were ordered by this indicator of sample quality. Elution of the crude isolates over silica gel with ethanol returned [C_4mim][OBz], [BF_4], and [ClO_3][70] in roughly 40–60% yield and 60–80% IL content (Method A) as clear light gold, light brown, and brilliant yellow liquids, respectively. Dissolution of these in dichloromethane and treatment with Celite (Method B) gave mixed results. The tetrafluoroborate was purified, the chlorate[70] was essentially unchanged, and the benzoate was actually tainted, though this could be an effect of loss of IL to Celite, which was seen in all cases by decreased yields from **5**. To see if impurities more chromatographically mobile than the ILs could be removed, new isolates were subjected to SGC with a solvent gradient

Table 2. Approximate Purities of [C_4mim] ILs prepared according to Scheme 5.[a]

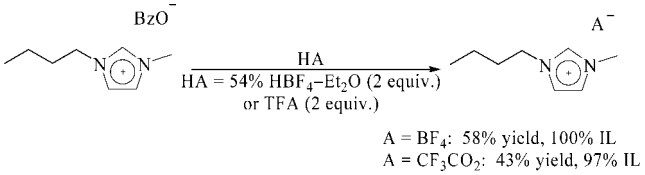
	Method of Purification A		B		C		D		E		F	
A	% IL[b]	Yield[c]	% IL[b]	Yield[c]	% IL[b]	Yield[c]	% IL[b]	Yield[c]	% IL[b]	Yield[c]	% IL[b]	Yield[c]
BzO	84	56	70	35	84	30	78	52	98	50	98 96[e]	61[d] 46[d,e]
ClO_3[70]	63–75	41	65–77	25	60–71	37	49–58	38	59–70	32	62–75 85–100[e]	59[d] 58[d,e]
BF_4	68–82	49	75–91	48	62–75	36	47–57	32	65–79	32	65–79	51[d]
AcO	58–61	32	–	–	–	–	48–51	46	53–56	46	–	–
Cl	65–70	37	–	–	–	–	52–56	49	63–68	49	–	–
Br	–	–	–	–	–	–	–	–	–	–	81–95	86[f]
CF_3CO_2	–	–	–	–	–	–	–	–	–	–	62–83	76[f]

[a] Key to methods: A = SGC in EtOH; B = A, then treatment with Celite in DCM; C = SGC with a solvent gradient from Et_2O to THF to EtOH; D = addition of 1:1 Et_2O/EtOH, refiltration; E = D then SGC in 1:1 Et_2O/EtOH; F = SGC in 1:1 Et_2O/EtOH. [b] IL content, as total grams [C_4mim] species per 100 g sample. [c] From **5** in every instance, *corrected for total IL content*. Salts in each column (method) were prepared by anion exchange from the same oxidation mother liquor, except Method F. [d] Yield from **5** following anion exchange from an oxidation proceeding in 62% yield. [e] Purity and yield after a second SGC step in 1:1 Et_2O/EtOH. [f] Yield from **5** following anion exchange from an oxidation proceeding in 98% yield.

(Method C). Fractions containing IL products were identified by TLC in ethanol, where the IL manifested as a streak from the origin after visualization with PMA (UV_{254} for [C_4mim][OBz]). Aside from the absence of IL product in fractions collected with less polar eluent, there were no discernible differences in any fractions by TLC or in selected fractions by NMR spectroscopy. When fractions containing IL product were combined, their IL content was no higher than those from Method A. Failure to detect an organic impurity by Method C and the similar IL contents from Methods A – C indicate the major contaminants are inorganic salts coeluting with IL in ethanol and/or dissolved silica gel. Fresh isolates were treated with 1:1 diethyl ether/ethanol and precipitates formed. When separated from the sediment simply by suction filtration, the dried formulations had lower IL contents than after Method A without exception (Method D, another testament to the difficulty of recouping IL from a mixture of insoluble salts). The ILs were usefully mobile for SGC in 1:1 diethyl ether/ethanol, and eluting the filtrates from Method D over silica gel with 1:1 diethyl ether/ethanol (Method E) gave IL contents rivaling those from Method A, except [C_4mim][OBz] which was significantly purer by this method. New isolates from the oxidation were suspended in 1:1 diethyl ether/ethanol, loaded on a short column with their associated precipitates, and recovered with the same solvent system (Method F). ILs of similar or better IL content than Method E were recovered, with [C_4mim][OBz] still the purest isolate. The lackluster chloride and acetate were replaced by the bromide and trifluoroacetate to see how softer anions behaved in the emerging method.

Table 2 demonstrates the success of the oxidation and anion exchange sequence depends strongly on the supplied anion, which makes acidifications of [C_4mim][OBz] to other ILs all the more desirable. Reaction with aqueous tetrafluoroboric acid followed by chromatography without first removing water was unsuccessful; distillation of water led to decomposition. Treatment with this acid in diethyl ether did not require distillation of water, and gave a solution that could be eluted with diethyl ether to two endpoints. First until the issue was not responsive to UV light when spotted on a silica gel plate (signifying the removal of benzoic acid), and second until the issue was not acidic (signifying the removal of excess tetrafluoroboric acid). Colorless [C_4mim][BF_4] was then washed off with 1:1 diethyl ether/ethanol; colorless [C_4mim][CF_3CO_2] was similarly obtained as a mobile liquid (Scheme 6). In both cases an excess of the acid was applied to destroy any residual hydrogen carbonate species. IL content is reported as a single number since these ILs derive from the benzoate, and solves to 101% for [C_4mim][BF_4], which we again believe is within experimental error for a very pure sample.

Treatment of [C_4mim][OBz] with concentrated aqueous hexafluorophosphoric acid did not generate a separate [C_4mim][PF_6] layer, even upon standing for several days. A small amount of very low quality IL separated from saturated aqueous potassium hexafluorophosphate; washing the sample with fresh water left only an impure specimen from

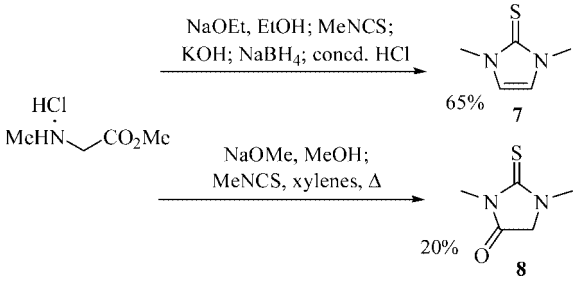


Scheme 6. Preparation of [C_4mim][BF_4] and [CF_3CO_2] from [OBz].

which no IL was recovered after SGC. The last experiment in the [C_4mim] series was an attempt to convert the benzoate to acetate. Percolation of an aqueous solution of [C_4mim][OBz] and an excess of acetic acid with diethyl ether slowly removed benzoic acid; it was necessary to periodically refresh the supply of acetic acid until the wash no longer contained benzoic acid. Unfortunately, the IL recovered after removal of water had decomposed and tenaciously retained a large amount of acetic acid.

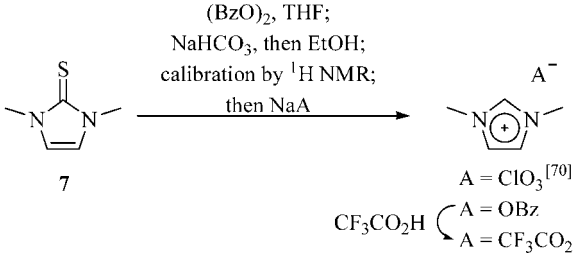
Synthesis of [C_1mim] ILs

Arduengo and co-workers described the preparation of 1,3-dimethylimidazole-2-thione (**7**) from the imidazolium iodide via the carbene as exemplified in Scheme 2.[74] On the basis of the synthesis of **5**, **7** was made in one pot from methyl sarcosinate hydrochloride after neutralization with fresh sodium ethoxide (Scheme 7). The intermediate hydantoin (**8**) was isolable in poor yield.



Scheme 7. Syntheses of **7** and **8**.

Table 3. Preparation of [C_1mim] ILs from **7**.



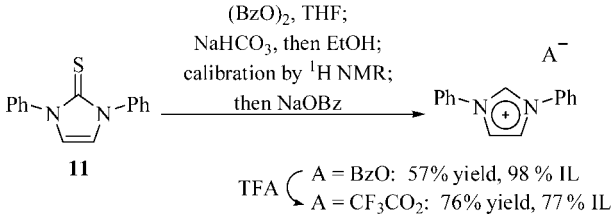
A	% IL[a]	Yield[b]
OBz	77	58
	73[c]	37[c]
ClO_3[70]	68–85	60
	70–88[c]	41[c]
CF_3CO_2	85[d]	75[d]

[a] IL content, as total grams [C_1mim] species per 100 g sample. [b] From an oxidation of **7** proceeding in 85% yield, *corrected for total IL content*. [c] Yield and % IL after a second chromatographic step. [d] Yield and % IL from once chromatographed [C_1mim][OBz].

Compound **7** was much more sensitive to the conditions of oxidation than **5**. Calibration of the imidazolium concentration revealed yields on the order of 30–40% unless the temperature was carefully controlled with an ice bath, in which case the yield exceeded 80%. The rest of the process for [C_4mim] IL synthesis (Scheme 5) was extended to [C_1mim] ILs without alteration (Table 3).

Synthesis of 1,3-Diphenylimidazolium ([dpim]) Salts

1,3-Diarylimidazolium salts are usually accessed by condensation of two equivalents aromatic amine with a 1,2-dicarbonyl compound, and condensation of the diimine with formaldehyde, orthoformates, or alkyl chloromethyl ethers.[31,75] Wanzlick and Schönherr alkylated aniline with chloroacetaldehyde dimethyl acetal under the influence of sodium amide in diethyl ether, treated the product acetal **9** with phenyl isothiocyanate, and cyclized the intermediate α-thioureido acetal with acid to make 1,3-diphenylimidazole-2-thione (**11**) in 17% yield over three steps (Scheme 8).[35] We succeeded in preparing **9**, although we preferred sodium hydride in dimethyl sulfoxide, but were unable to secure **11** from it. Note that Wanzlick and Schönherr also alkylated aniline with chloroacetaldehyde diethyl acetal, and carried it through to **11** in 45% total yield. Although that result demonstrates that **9** is not an ideal precursor to **11**, we were unable to recover *any* **11** from **9**. We undertook syntheses of **11** from commercial *N*-phenylglycine, which comes in 95% purity as a brown powder with visible heterogeneities. First, *N*-phenylglycine was subjected to a Fischer esterification, and the crude product reacted to **10** with phenyl isothiocyante. Second, based on Johnson and Buchanan's synthesis of 1-methyl-2-thiohydantoin,[76] *N*-phenylglycine was dissolved in aqueous ethanolic potassium hydroxide and acylated with phenyl isothiocyanate. The putative intermediate α-thioureido acid was precipitated, then cyclized in low yield, likely the result of competitive *S*-alkylation in the acylium intermediate.[77,78] The specimens were indistinguishable by TLC, IR, and ^{1}H and ^{13}C NMR spectroscopy. The melting point of **10** after Fischer esterification was only a few degrees lower and broader than **10** accessed by the α-thioureido acid. These similarities carried over to **11** following sodium borohydride reduction. However, [dpim][OBz] prepared from **11** following Fischer esterification contained an impurity that was not sufficiently removed by SGC and four crystallizations, all of which required hot gravity filtrations. On the other hand, **11** prepared via the α-thioureido acid delivered [dpim][OBz] freed from heterogeneities after silica gel filtration and three crystallizations, only the first of which required a hot gravity filtration (Scheme 9).

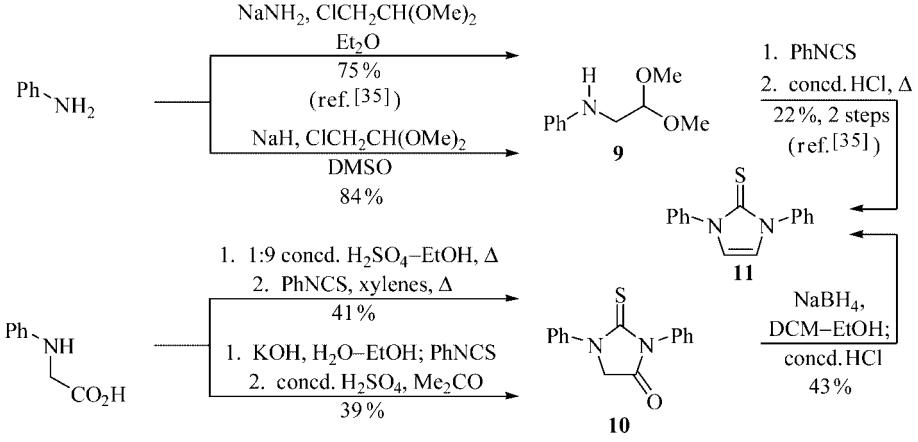


Scheme 9. Syntheses of [dpim] salts.

Synthesis of 1-Methyl- ([C_1tz]) and 1-Butylthiazolium ([C_4tz]) Salts

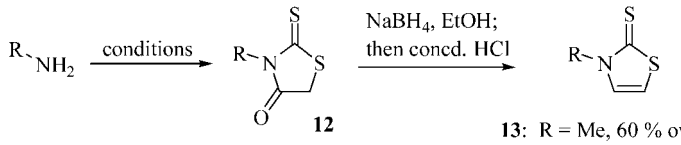
Virtually all work on thiazolium salts has been on derivatives of 5-(2-hydroxyethyl)-4-methylthiazole, a subunit of vitamin B_1 (thiamin) and popular catalysts for the benzoin and Stetter reactions.[79–81] In the context of IL chemistry, Pizzo, Vaccaro and co-workers recently prepared a pair of thiazolopyridinium ILs,[82] Davis and Forrester prepared *N*-butyl-4- and -5-methylthiazolium tetrafluoroborates,[83] Deetlefs and Seddon prepared *N*-butyl, -hexyl-, and -octyl-4-methylthiazolium bromides and iodides,[84] and Gaumont and co-workers have prepared thiazolinium salts derived from the chiral pool.[85] In their paper, Deetlefs and Seddon call their *N*-alkyl-4-methylthiazolium cations "[$C_n$mtz]", and it follows the 4-unsubstituted compounds should be termed "[$C_n$tz]".

Thiazole-2-thiones are classically prepared by alkylating an *N*-alkylthiocarbamate (formed in situ from an amine and carbon disulfide) with an α-halocarbonyl compound, and cyclizing the substitution product with acid.[86–89] We



Scheme 8. Syntheses of **11**.

Table 4. Syntheses of **13** and **14**.



13: R = Me, 60 % overall
14: R = Bu, 57 % overall

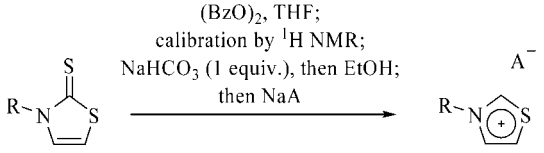
R	Conditions	Crude yield for **12**
Me, HCl	NaOH (2 equiv.), water; then CS_2 (1 equiv.); then aq. KO_2CCH_2Cl (1 equiv.); then H_2SO_4	77%
Bu	K_2CO_3 (0.5 equiv.), CS_2 (1 equiv.), MeOH; then KO_2CCH_2Cl (1 equiv.), MeOH; then H_2SO_4	94%

attempted syntheses of **13** and **14** from the appropriate amine, carbon disulfide, and chloroacetaldehyde, but recovered mixtures that did not suitably carry through the oxidation. No reaction took place between the *N*-alkylthiocarbamates and chloroacetaldehyde dimethyl acetal, even in refluxing acetonitrile. Chloroacetic acid readily accepted the *N*-alkylthiocarbamate nucleophiles, and the rhodanine intermediates[90,91] were accessed by a one-pot synthesis. Whereas these intermediates resisted bulk purification, we found **13** and **14** easily sublimed and distilled, respectively, and deferred purification until the crude isolates were reduced and dehydrated (Table 4).

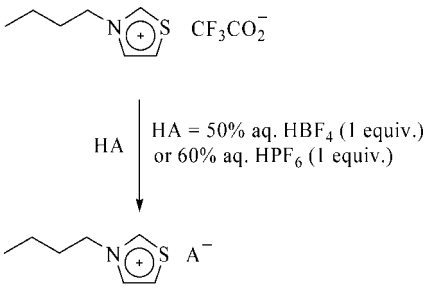
Oxidation of **13** and **14** to thiazolium salts required some operationally trivial but chemically significant modifications to the existing process (Table 5). When the aqueous oxidation mother liquor was treated with sodium hydrogen carbonate, then ethanol, and an aliquot of the filtrate was concentrated for ^{1}H NMR calibration, the specimens turned pink and no thiazolium species were visible in the spectra. The pK_a values of thiazolium C(2) protons have been reported as 17–19 in deuterium oxide[92,93] and as 12.9 (for vitamin B_1) in methanol.[94] Although these values are several orders of magnitude higher than the pK_a of carbonic acid in water (3.6), the decomposition is likely the result of carbene dimerization, which does not require quantitative conversion of salt to carbene.[95] For comparison, the pK_a values of imidazolium salts in water are >20[26] (a data point that can be considered alongside other reports of NHC basicity[23–25]), which explains why decomposition was not observed in the synthesis of imidazolium salts, and why catalysis with NHCs is ordinarily accomplished by addition of discrete carbene or treatment of an imidazolium with a powerful base.[80,81,96–98]

After seeing how easily these salts could be destroyed, we used the calibration step to limit hydrogen carbonate to one equivalent against putative [C$_n$tz][HSO_4]. We did not expect successful isolations of azolium benzoates (or other simple carboxylates) since the pK_a of benzoic acid is 4.2 in water, but for completeness these exchanges were attempted; total [C$_n$tz] species decreased at each measurement from the calibration to each concentration following two SGC steps. We focused instead on poorly basic anions that proved adequate for direct exchange in the [C_4mim] series – [Br], [BF_4], and [CF_3CO_2]. Additional to inorganic contaminants, these crude isolates contained highly colored, comparatively mobile impurities that could be removed by SGC in tetrahydrofuran to a visible endpoint. Thiazolium salts were then collected with 1:1 Et_2O/EtOH. Skipping the first chromatographic step returned [C$_n$tz] formulations with roughly 50% IL content. Note that the same three sodium salts were deployed across both thiazole-2-thiones, but [C_1tz][CF_3CO_2] decomposed upon isolation, and [BF_4] was lost to the initial tetrahydrofuran eluent. Having seen hot aqueous acid was well tolerated by the thiazolium salts during concentration for calibration, aqueous acids were used to convert [C_4tz][CF_3CO_2] to [BF_4] and [PF_6] (Scheme 10). A second approximation is used to report the IL content of [C_4tz][Br], [CF_3CO_2], and [PF_6], which had upper bounds of 115, 110, and 112 g IL per 100 g sample, respectively, by the first approximation. This simple adaptation is fully

Table 5. Synthesis of [C_1tz] and [C_4tz] salts via anion exchange.



R	X	% IL	Yield
Me	Br	73–89	12
Bu	Br	99–100, not more than 9.6% as [C_4tz][Br]	26
Bu	BF_4	77–92	10
Bu	CF_3CO_2	82–100, not more than 72% as [C_4tz][CF_3CO_2]	41



A = BF_4: 72% yield, 82 — 99% IL content
A = PF_6: 45% yield, 75 — 100% IL content,
not more than 75% as [C_4tz][PF_6]

Scheme 10. Acidification of [C_4tz][CF_3CO_2] to [BF_4] and [PF_6].

described in Supporting Information. Interested parties will note it could also be used in descriptions of ILs prepared by quarternization and anion exchange.

Conclusions

A new oxidative desulfurization of compounds **1** with benzoyl peroxide followed by a carefully regulated anion exchange is best suited to the preparation of inherently halide-free 1,3-dialkylimidazolium benzoate ILs, which can be converted to other ILs with acid. Preparations of [C_4mim][BF_4] and [CF_3CO_2], and of [C_1mim] and [dpim][CF_3CO_2] demonstrate the viability of this oxidation–anion exchange–acidification protocol. The sequence furnishes ILs with varied imidazolium ring substitutents, as seen in the synthesis of [dpim] salts. The sodium borohydride reductions of hydantoins[61] with or without their isolation and the one-pot preparation of **7** are striking, as is the two-step synthesis of [C_1mim][OBz] from commercially available sarcosine methyl ester hydrochloride. This protocol also provides a hitherto unknown route to [$C_n$tz] ILs.

Experimental Section

General: Methyl isothiocyanate (97%) was distilled prior to use. All other reagents were used as received from commercial sources. NMR spectra of compounds in the [C_4mim], [dpim], and [$C_n$tz] series were recorded with a Varian Mercury 400; compounds in the [C_1mim] series were analyzed with a Bruker AV400WB. Mass spectra were collected with a Hewlett–Packard 5970 (EI). IR spectra were taken in ATR mode with a BioRad Excalibur Series FTS 4000 (Harrick Split Pea or Specac Golden Gate Diamond accessory) or a Bruker Optics IFS 48 (Specac Golden Gate Diamond accessory). HRMS analyses were performed with a Finnigan MAT 95 (EI). M.p. values were recorded with a MelTemp apparatus or a Büchi SMP-20 and are uncorrected. All chromatographic purifications were performed with 230–400 mesh silica gel. This section contains protocols for syntheses of **2**, **4**, **5** from **4**, **7**, **10** from α-thioureido acid cyclization, **13**, **14**, oxidations of all azole-2-thiones, anion exchanges (AEs) and purifications leading to [C_4mim][OBz] and [C_4tz][CF_3CO_2], and acidifications of these salts to [C_4mim][CF_3CO_2] and [C_4tz][BF_4], respectively. These AE and acidification methods are representative of all imidazolium and [$C_n$tz] syntheses, respectively. Specific quantities of reagents used for AEs and acidifications leading to all other salts are included in Supporting Information (SI, for supporting information see also the footnote on the first page of this paper), as are synthetic protocols for all other neutral compounds; these salts and neutrals are enumerated at the end of this section. In both sections, yields from both the oxidation and the AE are included for each salt.

The observed ^{1}H NMR coupling constants between C(4) and C(5) protons from azole-2-thiones with C_s symmetry (**5**, **13**, **14**) are small (J = 3–4 Hz). This fine structure is obscured by line broadening in at least one ^{1}H NMR signal of most salt formulations derived from these thiones; only [C_1tz] and [C_4tz][Br], and [C_4tz][BF_4] are unaffected. This effect has been discussed in terms of the magnetic properties of nitrogen and sulfur and of H–D exchange in nitrogen heterocycles;[99–102] because this broadening is observed for the salts but not the thiones, we suspect the latter case is the dominant factor here. When this distortion is observed, it is designated in the line assignment of the affected peak with an "LB" before the apparent multiplicity of the affected peak. Three salts ([C_4tz][BF_4] and [Br], and [dpim][OBz]) underwent C(2) H–D exchange too rapidly to see the C(2) proton in ^{1}H NMR; the associated C(2) triplets in ^{13}C NMR spectra were observed. Copies of spectra are included in SI for inspection.

Ethyl *N*-Butylglycinate (2): Over the course of 30 min, chloroacetic acid (100.05 g, 1.06 mol) was cautiously added portionwise to nBuNH$_2$ (1.0 L, 740 g, 10.0 mol) cooled with an ice bath. After addition, the ice bath was removed and the mixture was refluxed 4 h, whereupon nBuNH$_2$ was removed by distillation. Residual nBuNH$_2$ was released by three additions and distillations of EtOH (100 mL each). The mixture was cautiously acidified with 1:9 (v/v) concd. H_2SO_4/EtOH (1.0 L), then refluxed 48 h. EtOH (ca. 500 mL) was removed by rotary evaporation, and the remaining solution was poured into Na_2CO_3 (175 g) in water (1.1 L). The mixture was extracted with DCM (3 × 200 mL), and the combined organic layers were washed with water, then brine (1 × 100 mL each), dried ($MgSO_4$), filtered, and concentrated. Amino ester **2** (96.15 g, 604 mmol, 57%) was distilled from the crude mixture (b.p.$_{0.23}$ 42 °C, ref.[60] b.p.$_{1.1}$ 52 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.14 (q, J = 7.1 Hz, 2 H), 3.33 (s, 2 H), 2.54 (t, J = 7 Hz, 2 H), 1.50 (br. s, 1 H), 1.44 (quint, J = 7 Hz, 2 H), 1.34 (sext, J = 7 Hz, 2 H), 1.22 (t, J = 7 Hz, 3 H), 0.85 (t, J = 7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 60.5, 50.9, 49.1, 32.0, 20.2, 14.0, 13.8 ppm.

1-Butyl-3-methyl-2-thiohydantoin (4): Methyl isothiocyanate (44.15 g, 604 mmol) was dissolved in dry Et_2O (50 mL) and added dropwise to freshly distilled **2** (96.15 g, 604 mmol) cooled with an ice bath. The reaction was continued at 0 °C for 10 min after complete addition, then fitted with a simple distillation apparatus for the removal of Et_2O. The thick orange residue was stirred neat and heated 3 d at 140–150 °C. The product at this stage was used for the synthesis of **5** described below, but can be distilled (b.p.$_{0.55}$ 126 °C, 79% yield). After one distillation each, compound **4** was the same red hue as **5** made from it. The distillates had similar b.p. values, which probably reflect a common codistilling impurity. Their appearance and b.p. values could be resolved by further purification, but their respective spectroscopic and chromatographic characteristics were unchanged. In this case, distilled **4** (4.63 g) was chromatographed (100 g silica gel, eluent: 2:1 Et_2O/petroleum ether, R_f = 0.6) and redistilled (b.p.$_{0.15}$ 86 °C), returning **4** (3.25 g) as a dull yellow oil (70% recovery, 55% yield from **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.01 (s, 2 H), 3.81 (t, J = 8 Hz, 2 H), 3.24 (s, 3 H), 1.65 (quint, J = 8 Hz, 2 H), 1.40 (sext, J = 8 Hz, 2 H), 0.97 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 183.0, 170.6, 51.7, 46.5, 29.0, 28.1, 19.7, 13.6 ppm. MS: m/z (%) = 186 (100) [M^+], 157 (18) [M^+ – Et], 153 (25) [M^+ – SH], 144 (46) [M^+ – propene], 130 (20) [M^+ – butene]. IR (film): $\tilde{\nu}$ = 3597, 3480, 2958, 2932, 2872, 1744, 1496, 1334 cm^{-1}. HRMS (EI) calcd. for $C_8H_{14}N_2OS$: 186.0827, found 186.0822.

1-Butyl-3-methylimidazole-2-thione (5). From 4: Crude **4** prepared as described above was diluted with EtOH (200 mL) and cautiously treated with $NaBH_4$ (22.84 g, 604 mmol) in EtOH (600 mL). The mixture turned from the deep red color of crude **4** to a bright purple while stirring 7 h, and was then slowly treated with concd. aq. HCl (200 mL, 2.40 mol), turning an intense yellow while stirring 30 min. The slurry was poured into water (750 mL) containing NaCl (100 g), and shaken with DCM (500 mL). The mixture slowly separated into two layers, and the organic layer was collected. The aq. layer was extracted with more DCM (3 × 100 mL), the combined organic layers were washed with water (1 × 100 mL) and re-

petitively with brine (100 mL) until the recovered volume was approximately equal to the volume invested (requiring at least 3 ×), then dried ($MgSO_4$), filtered and concentrated to leave crude **5** (98.97 g) as an oil that was distilled ($b.p._{0.4}$ 132 °C) (81.15 g, 477 mmol, 79% from **2**, 99% from **4**). After one distillation each, compound **5** was the same red hue as **4** used to make it. The distillates had similar b.p. values, which probably reflect a common codistilling impurity. Their appearance and b.p. values could be resolved by further purification, but their respective spectroscopic and chromatographic characteristics were unchanged. In this case, distilled **5** (4.38 g) was chromatographed (105 g silica gel, eluent: 2:1 Et_2O/petroleum ether, R_f = 0.4) and redistilled ($b.p._{0.15}$ 77 °C), returning **5** as a brilliant yellow oil (1.68 g, 38% recovery, 30% from **2**). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.84 (d, J = 4 Hz, 1 H), 6.83 (d, J = 4 Hz, 1 H), 4.03 (t, J = 8 Hz, 2 H), 3.60 (s, 3 H), 1.75 (quint, J = 8 Hz, 2 H), 1.37 (sext, J = 8 Hz, 2 H), 0.96 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 117.1, 116.0, 46.8, 34.2, 30.1, 18.9, 12.9 ppm. MS: m/z (%) = 170 (100) [M^+], 141 (33) [M^+ – Et], 137 (77) [M^+ – SH], 128 (43) [M^+ – propene], 114 (72) [M^+ – butene]. IR (film): $\tilde{\nu}$ = 3449, 3095, 2957, 2932, 2872, 1569, 1461, 1413, 1401 cm^{-1}. HRMS (EI) calcd. for $C_8H_{14}N_2S$: 170.0878, found 170.0878.

Oxidation of 5 with $(BzO)_2$: A two-necked flask containing a magnetically stirred slurry of 75% $(BzO)_2$ (190.10 g, MW_{eff} = 322.97, 589 mmol) in THF (200 mL) was cooled in an ice bath, and fitted with an addition funnel containing neat **5** (20.04 g, 118 mmol) and a condenser. The reaction first bubbled and fumed locally as **5** was introduced dropwise, then achieved reflux, dissolving $(BzO)_2$. The persistent yellow color of **5** disappeared as the oxidation continued. The reaction stood at room temp. until excess $(BzO)_2$ precipitated. The mixture was filtered, and the filter cake was washed with water (100 mL). The filtrate was diluted with Et_2O (200 mL) and shaken, the aq. layer was recovered, washed with DCM (5 × 20 mL), drained onto $NaHCO_3$ (9.86 g, 117 mmol), stirred 15 min, then treated with EtOH (300 mL) and stirred 30 min. The supernatant was recovered by suction filtration into a tared flask, and the filter cake was washed with EtOH (2 × 20 mL). An aliquot (4.5803 g) was removed from the aq. EtOH solution (407.67 g), concentrated, spiked with DMSO (0.1018 g, 1.30 mmol), and the entire mixture was taken up in D_2O. When the integral of the neatly resolved C(3) methyl singlet at ca. 4 ppm was set to 3.0, the integral of the neatly resolved DMSO singlet at ca. 2.8 ppm integrated to 9.48 H, corresponding to a [C_4mim] species concentration of 0.8247 mmol/4.5803 g solution, or 0.1800 mmol [C_4mim] species/g solution (73.4 mmol, 62%).

AE to [C_4mim][OBz]: A portion of the calibrated solution from the oxidation of **5** (367.67 g, 66.2 mmol, representing 106 mmol **5**) was treated with NaOBz (9.54 g, 66.2 mmol), stirred 2.5 h, suction filtered, and concentrated. The product and associated sediment were taken up in 1:1 Et_2O/EtOH (100 mL) and loaded on silica gel (50 g) packed in 1:1 Et_2O/EtOH. The column was drained to level the loaded volume with the top of the column below the insoluble matter. The vessel originally containing the sample was rinsed with fresh 1:1 Et_2O/EtOH (100 mL), which was loaded on the column and similarly leveled. The column was washed with fresh 1:1 Et_2O/EtOH (400 mL). All column issue was collected in one vessel, concentrated, then dried at 0.2 Torr to leave a light gold liquid (17.18 g, 3.78 mmol [C_4mim][OBz] per g; 64.9 mmol, 16.90 g [C_4mim][OBz] total, 98% from AE, 61% from **5**). A portion of this formulation (2.45 g, 9.26 mmol [C_4mim][OBz]) was rechromatographed (5 g silica gel, 10 mL loading and rinsing vol, 40 mL wash vol), returning a light gold liquid (1.88 g, 3.69 mmol [C_4mim][OBz] per g; 6.94 mmol, 1.81 g [C_4mim][OBz] total, 75% recovery, 46% from **5**) after drying in vacuo. ^1H NMR (400 MHz, D_2O): δ = 8.36 (s, 1 H), 7.71 (d, J = 8 Hz, 2 H), 7.33 (t, J = 8 Hz, 1 H), 7.26 (t, J = 8 Hz, 2 H), 7.15 (LB s, 1 H), 7.13 (LB s, 1 H), 3.85 (t, J = 8 Hz, 2 H), 3.62 (s, 3 H), 1.54 (quint, J = 8 Hz, 2 H), 1.06 (sext, J = 8 Hz, 2 H), 0.74 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 179.1, 140.9, 140.3, 136.1, 133.8, 133.1, 128.2, 126.9, 54.0, 43.7, 36.0, 23.6, 17.6 ppm. IR (film): $\tilde{\nu}$ = 3153, 3061, 2963, 2859, 1597, 1556, 1364 cm^{-1}.

Acidification of [C_4mim][OBz] to [C_4mim][CF_3CO_2]: Once-chromatographed [C_4mim][OBz] (2.0 g, 7.56 mmol) was treated with neat TFA (1.2 mL, 1.84 g, 16.2 mmol). Before the mixture could cool, it was loaded on silica gel (5 g) packed in Et_2O. The column was washed with Et_2O until the collected wash did not respond to UV light when spotted on a TLC plate and was not acidic (requiring ca. 30 mL). The column was then washed with 1:1 Et_2O/EtOH (50 mL), the collected issue was concentrated and dried in vacuo to isolate [C_4mim][CF_3CO_2] (0.82 g, 3.88 mmol [C_4mim][CF_3CO_2] per g; 3.18 mmol, 0.80 g [C_4mim][CF_3CO_2] total, 43%). ^1H NMR (400 MHz, D_2O): δ = 8.75 (s, 1 H), 7.48 (LB s, 1 H), 7.44 (LB s, 1 H), 4.17 (t, J = 7.2 Hz, 2 H), 3.89 (s, 3 H), 1.81 (quint, J = 7.2 Hz, 2 H), 1.29 (sext, J = 7.2 Hz, 2 H), 0.89 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 166.8 [q, $^2J(^{13}C\text{-}^{19}F)$ = 35 Hz], 140.5, 128.3, 127.0, 119.8 [q, $^1J(^{13}C\text{-}^{19}F)$ = 291 Hz], 54.0, 43.6, 36.0, 23.5, 17.4 ppm. IR (film): $\tilde{\nu}$ = 3157, 3092, 2966, 2865, 1683, 1576, 1197, 1164, 1110 cm^{-1}.

1,3-Dimethylimidazole-2-thione (7): Fresh ethanolic NaOEt was prepared by the dissolution of Na (8.90 g, 387 mmol) in EtOH (250 mL). Solid methyl sarcosinate hydrochloride (50 g, 358 mmol) was cautiously added to the solution through a powder funnel, and any residue was washed in with EtOH (ca. 100 mL). The solution was stirred 30 min, cooled to 0 °C, then methyl isothiocyanate (26.2 g, 358 mmol) in EtOH (300 mL) was added, the ice bath was removed, and the reaction was stirred 1 h before the addition of 85% KOH (2.25 g, 34.1 mmol). Solid $NaBH_4$ (13.6 g, 360 mmol) was added 2 h later. Stirring was continued overnight, then concd. HCl (150 mL, 1.80 mol) was added. After 30 min, the bright yellow slurry was diluted with water (400 mL) and extracted with DCM (2 × 400 mL, 1 × 200 mL). The combined organic layers were washed with water, then brine (1 × 200 mL each), dried ($MgSO_4$), filtered and evaporated to leave crude **7** (33.3 g) as a yellow solid which was crystallized twice from EtOH (350 mL) to leave colorless **7** (29.89 g, 233 mmol, 65%). M.p. 177–179.5 °C (ref.[74] = 182–184 °C). The ^1H and ^{13}C NMR spectra match the reference.[74]

Oxidation of 7 with $(BzO)_2$: To oxidize **7** (32.72 g, 255 mmol), a magnetically stirred slurry of 75% $(BzO)_2$ (412.0 g, MW_{eff} = 322.97, 1.28 mol) in THF (250 mL) was first treated with small (ca. 150 mg) portions of **7**, which turned orange and fumed, until the stiff slurry stirred freely, and the flask was warm to the touch, but not hot enough to completely dissolve $(BzO)_2$. Then an ice bath was added, and small portions of **7** were added at a faster rate, stopping for ca. 1 min every time vigorous gas evolution was observed. Complete addition required 30 min, after which time the ice bath was removed and the solution was stirred for 1 h. Unlike the analogous reaction with **5**, excess $(BzO)_2$ did not precipitate, so the stock solution was thinned with Et_2O (400 mL) and water (100 mL). The aq. layer was recovered, and the organic layer was washed with water (1 × 50 mL). The combined aq. layers were washed with DCM (5 × 40 mL), then drained onto solid $NaHCO_3$ (21.5 g, 256 mmol), stirred 15 min, treated with EtOH (600 mL), stirred 30 min, suction filtered into a tared flask, and the filter cake washed with EtOH (2 × 50 mL). An aliquot (6.095 g) was removed from the solution (803.395 g), concentrated, spiked with DMSO

(0.080 g), and the ^{1}H NMR revealed a concentration of 0.2708 mmol [C_1mim] species/g solution (218 mmol, 85%).

1,3-Diphenyl-2-thiohydantoin (10). Through α-Thioureido Acid Cyclization: *N*-Phenylglycine (95%, 8.45 g, 53.1 mmol) was added to a mixture of 50% aq. KOH (6.27 g, 55.9 mmol), EtOH (18 mL) and water (10 mL). After dissolution, EtOH (8 mL) was added, the mixture cooled to 0 °C, then phenylisothiocyanate (7.56 g, 55.9 mmol) in EtOH (6 mL) was added dropwise via addition funnel. The funnel was rinsed with EtOH (5 mL), then the ice bath was removed and the reaction stirred 3 h. Following addition of 1 M HCl (200 mL), the mixture was stirred 30 min, cooled to 0 °C, and the intermediate acid was collected by suction filtration. The filter cake was taken up in acetone (400 mL), dried ($MgSO_4$), and filtered. At this point TLC analysis (eluent: diethyl ether) showed a mixture of two compounds, one of which (R_f = 0.9, Et_2O) proved to be **10** and another (R_f = 0.0 to 0.3), which was presumed to be the intermediate acid. The solution was treated with 98% H_2SO_4 (5 mL), and the slower spot disappeared while stirring 3 d at room temp. Acetone was removed by rotary evaporation, and the residue was treated with satd. aq. $NaHCO_3$ (250 mL), stirred 30 min, and filtered. The filter cake was reprecipitated twice from 1.5:1 DCE/*i*PrOH to deliver **10** (5.61 g, 20.9 mmol, 39%); the first reprecipitation required a hot gravity filtration. M.p. 218–220 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, J = 8 Hz, 2 H), 7.54–7.46 (m, 5 H), 7.37 (m, 3 H), 4.59 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.1, 169.1, 138.0, 133.2, 129.4, 129.3, 129.2, 128.5, 128.0, 125.4, 55.1 ppm. MS: *m*/*z* (%) = 268 (100) [M^+], 239 (21), 105 (39), 77 (23) [Ph^+]. IR (ATR): $\tilde{\nu}$ = 3056, 2939, 1756, 1592, 1453 cm^{-1}.

1,3-Diphenylimidazole-2-thione (11): A solution of **10** (15.22 g, 56.7 mmol) prepared by α-thioureido acid cyclization was brought to vigorous reflux in DCM (200 mL) prior to treatment with $NaBH_4$ (2.36 g, 62.4 mmol) in EtOH (75 mL). Monitoring the reaction by TLC was difficult because **10** and **11** had identical R_f values in a variety of solvent systems; however, **10** was dark purple when viewed at 254 nm while **11** was a brilliant blue. After 2.5 h at reflux, the solution was cooled to room temp., cautiously treated with concd. aq. HCl (40 mL, 480 mmol), stirred 30 min at room temp., then diluted with water (200 mL). The released DCM was collected, and the water washed with DCM (2 × 100 mL). The combined organic extracts were washed with water, then brine (1 × 100 mL each), dried ($MgSO_4$), filtered, and concentrated. Crystallization of the residue from EtOH returned **11** (6.21 g, 24.6 mmol, 43%). M.p. 156–158.5 °C (ref.[35] m.p. 161 °C). Wanzlick and Schönherr's ^{1}H NMR was reported on the τ scale and only resolved aromatic from α protons at 100 MHz.[35] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, J = 8 Hz, 4 H), 7.51 (t, J = 8 Hz, 4 H), 7.42 (t, J = 8 Hz, 2 H), 6.97 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 138.0, 128.9, 128.3, 126.1, 118.6 ppm. MS: *m*/*z* (%) = 252 (76) [M^+], 251 (100) [M^+ – H], 77 (12) [Ph^+]. IR (ATR): $\tilde{\nu}$ = 3175, 3141, 1594, 1493 cm^{-1}.

Oxidation of 11 with $(BzO)_2$: A magnetically stirred slurry of 75% $(BzO)_2$ (31.99 g, MW_{eff} = 322.97, 99.0 mmol) in THF (40 mL) was slowly treated with **11** (5.0 g, 19.8 mmol) in THF (30 mL). Addition of solid instead of dissolved **11** resulted in violent gas evolution. The reaction cycled through reflux, dissolving $(BzO)_2$, and cooled back to room temp., precipitating $(BzO)_2$, within 1 h, after which the mixture was diluted with water (25 mL), filtered, and the filter cake was washed with water (25 mL). The first addition of water was necessary because the solid salt product was not freely soluble in the wet THF mother liquor, as evidenced by an obvious dissolution of some of the filter cake in wash water if the first addition of water was neglected. The filtrate was shaken with Et_2O (100 mL), the aq. layer was recovered and washed with DCM (5 × 5 mL), and then drained onto solid $NaHCO_3$ (1.66 g, 19.8 mmol) and stirred 15 min. Additional water (ca. 25 mL) was needed for solubility, and brought the total volume of water to ca. 83 mL [ca. 8 mL from 75% $(BzO)_2$, and 75 mL wash water]. Sufficient EtOH (175 mL) was added to precipitate putative Na_2SO_4, and the mixture was suction filtered into a tared flask. An aliquot (2.7861 g) was removed from the solution (212.49 g), concentrated, spiked with DMSO (0.0257 g, 0.329 mmol), and the ^{1}H NMR revealed a concentration of 0.0894 mmol [dpim] species/g solution (19.0 mmol, 96%).

3-Methylthiazole-2-thione (13): To a solution of NaOH (26.58 g, 665 mmol) in water (200 mL) was added methylamine hydrochloride (22.51 g, 333 mmol), which was dissolved before the addition of CS_2 (20 mL, 25.32 g, 333 mmol). Over the course of 2 h, a clear red solution resulted, which was stirred a further 3 h before the addition of a prepared solution of chloroacetic acid (31.43 g, 333 mmol) and K_2CO_3 (23.22 g, 168 mmol) in water (150 mL). The mixture was stirred 5 h, then cautiously treated with concd. H_2SO_4 (10 mL, 180 mmol) and stirred overnight. The formed precipitate (50.86 g) was collected by suction filtration, dissolved in DCM (300 mL), washed with water (1 × 50 mL), satd. aq. $NaHCO_3$ (1 × 100 mL), water (1 × 50 mL), brine (1 × 100 mL), dried ($MgSO_4$), filtered and concentrated to give orange crystals (37.74 g, 256 mmol putative rhodanine intermediate). These crystals were dissolved in EtOH (800 mL), cooled to 0 °C, treated with $NaBH_4$ (9.70 g, 256 mmol), stirred 20 min at 0 °C before the ice bath was removed, then allowed 40 min to achieve room temp. The mixture had turned brown. After the slow addition of concd. HCl (125 mL, 1.50 mol), the bright yellow mixture was stirred 30 min, then concentrated by rotary evaporation at 100 mbar in a 60 °C water bath until most EtOH had been removed. The mixture was diluted with water (500 mL) and washed with DCM (3 × 100 mL). The combined organic extracts were washed successively with water and brine (1 × 100 mL each), dried ($MgSO_4$), filtered and concentrated to leave crude, brown **13** (27.64 g) which was sublimed twice at 0.15 Torr from a 95–100 °C oil bath to yield **13** (26.36 g, 201 mmol, 60%) as sticky orange crystals. M.p. 45–47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12 (d, J = 4 Hz, 1 H), 6.65 (d, J = 4 Hz, 1 H), 3.71 (s, 3 H) ppm. ^{13}C (100 MHz, $CDCl_3$): 187.4, 132.3, 110.9, 37.5 ppm. MS: *m*/*z* (%) = 131 (100) [M^+], 72 (20) [H_2CNCS^+], 58 (21) [$HCCSH^+$]. IR (ATR): $\tilde{\nu}$ = 3124, 3090, 3050, 1556 cm^{-1}.

Oxidation of 13 with $(BzO)_2$: A stirred slurry of $(BzO)_2$ (184.58 g, MW_{eff} = 322.97, 572 mmol) in THF (250 mL) was treated with solid **13** (15.0 g, 114 mmol) in one portion. After the reaction refluxed under its own power and cooled back to room temp., an ice bath was added to force the precipitation of excess $(BzO)_2$, which was removed by suction filtration. The filter cake was washed with water (75 mL), and the filtrate was shaken with Et_2O (250 mL). The aqueous layer was separated and washed with DCM (5 × 15 mL), then recovered in a tared flask. An aliquot (4.1421 g) was removed from the isolated solution (102.75 g), concentrated, spiked with DMSO (0.0483 g), and the ^{1}H NMR in D_2O revealed a concentration of 0.9138 mmol [C_1tz] species/g solution (ca. 94 mmol, 82%).

3-Butylthiazole-2-thione (14): A mixture of *n*$BuNH_2$ (25 mL, 18.5 g, 253 mmol), K_2CO_3 (17.24 g, 125 mmol), and CS_2 (15 mL, 18.99 g, 249 mmol) in MeOH (300 mL) required ca. 3 h to cleanly dissolve, whereupon a prepared solution of chloroacetic acid (23.90 g, 253 mmol) and K_2CO_3 (17.45 g, 126 mmol) in MeOH (400 mL) was added. The KCl precipitated during the reaction was removed by suction filtration every 1.5 h to allow easy stirring of the mix-

ture. After 4.5 h at room temp., and three suction filtrations, no more KCl precipitate formed, and the mixture was cautiously acidified with concd. H_2SO_4 (30 mL, 540 mmol). The solution was stirred overnight, then most EtOH was removed by rotary evaporation. The mixture was diluted with water (200 mL) and washed with DCM (3 × 100 mL). The combined organic layers were washed with satd. aq. $NaHCO_3$, then water, then brine (1 × 100 mL each), dried ($MgSO_4$), filtered and concentrated to leave a yellow oil (44.14 g, 233 mmol putative rhodanine intermediate), which was dissolved in EtOH (200 mL) and cooled to 0 °C. The solution was treated with $NaBH_4$ (8.81 g, 233 mmol), stirred 20 min at 0 °C before the ice bath was removed, then allowed 40 min. to achieve room temp. The mixture had turned brown, but during the slow addition of concd. HCl (100 mL, 1200 mmol), turned yellow again. The acidified mixture stirred 30 min at room temp. before it was diluted with water (750 mL) and washed with DCM (3 × 150 mL). The combined organic layers were washed successively with water and brine (1 × 100 mL each), dried ($MgSO_4$), filtered and concentrated to leave crude **14** (27.69 g), which was distilled (b.p.$_{0.20}$ 118–130 °C) to deliver **14** (24.41 g, 141 mmol, 57%) as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12 (d, J = 4 Hz, 1 H), 6.65 (d, J = 4 Hz, 1 H), 4.17 (t, J = 8 Hz, 2 H), 1.79 (quint, J = 8 Hz, 2 H), 1.41 (sext, J = 8 Hz, 2 H), 0.96 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.0, 131.4, 111.1, 49.6, 30.4, 19.7, 13.6 ppm. MS: m/z (%) = 173 (90) [M^+], 144 (17) [M^+ – Et], 140 (62) [M^+ – SH], 131 (26) [M^+ – propene], 117 (100) [M^+ – butene]. IR (film): $\tilde{\nu}$ = 3099, 3049, 2956, 2930, 2870, 1548 cm^{-1}.

Oxidation of 14 with $(BzO)_2$: A stirred slurry of 75% $(BzO)_2$ (130.90 g, MW_{eff} = 322.97, 405 mmol) in THF (110 mL) was treated with neat **14** (14.02 g, 80.9 mmol), added through a funnel in one portion. The holding vessel and funnel were rinsed with THF (2 × 10 mL). The reaction cycled from room temp. to reflux, dissolving $(BzO)_2$, and back to room temp., precipitating $(BzO)_2$, in less than 1 h. The precipitate was removed by suction filtration, and the filter cake was washed with water (70 mL). The filtrate was shaken with Et_2O (130 mL), the aq. layer was recovered and washed with DCM (5 × 14 mL), then drained into a tared flask. An aliquot (3.1377 g) was removed from the isolated solution (92.31 g), concentrated, and spiked with DMSO (0.0634 g), and the ^{1}H NMR in D_2O revealed a concentration of 0.4062 mmol [C_4tz] species/g solution (37.5 mmol, 46%).

AE to $[C_4tz][CF_3CO_2]$: A portion of the calibrated solution from the oxidation of **14** (44.05 g, 17.9 mmol, representing 38.6 mmol **14**) was treated with $NaHCO_3$ (3.01 g, 35.8 mmol), then TFA (2.04 g, 17.9 mmol), and stirred 30 min before the addition of EtOH (100 mL). The mixture was stirred 2 h, suction filtered, and concentrated by rotary evaporation. The crude isolate was slurried in THF (20 mL), loaded on a column of silica gel (20 g) packed in THF, and the loading volume was forced down to the top of the column. The reaction vessel was rinsed with THF (20 mL), which was similarly loaded and forced down. The column was then washed with fresh THF until the issue was nearly colorless (requiring ca. 90 mL). The column was washed with 1:1 EtOH/Et_2O (300 mL), the collected issue was concentrated and the residue was dried in vacuo to isolate $[C_4tz][CF_3CO_2]$ (3.68 g, 4.30 mmol [C_4tz] salts per g; 15.8 mmol [C_4tz] salts total, 88% from AE, 41% from **14**). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.03 (s, 1 H), 8.56 (d, J = 3.2 Hz, 1 H), 8.36 (LB t, 1 H), 4.68 (t, J = 7.4 Hz, 2 H), 1.96 (quint, J = 7.4 Hz, 2 H), 1.35 (sext, J = 7.4 Hz, 2 H), 0.93 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2 [q, $^2J(^{13}C\text{-}^{19}F)$ = 33 Hz], 159.7, 137.2, 126.5, 117.3 [q, $^1J(^{13}C\text{-}^{19}F)$ = 294 Hz], 55.5, 32.4, 19.3, 13.2 ppm. IR (film): $\tilde{\nu}$ = 3397, 3056, 2964, 2939, 2878, 1666, 1197, 1164, 1117 cm^{-1}.

Acidification of $[C_4tz][CF_3CO_2]$ to $[C_4tz][BF_4]$: A solution of $[C_4tz][CF_3CO_2]$ (1.5 g, 6.45 mmol) in water (5 mL) was treated with 50% aq. (8.029 M) HBF_4 (0.81 mL, 6.50 mmol), and concentrated by distillation at atmospheric pressure. After distillation, the sample was put under the light vacuum provided by a water aspirator for 1 h, then taken up in DCM (5 mL), loaded on silica gel (4 g) packed in Et_2O, and the column was eluted with Et_2O until the issue was neutral when spotted on pH paper, requiring ca. 80 mL. The column was then eluted with 1:1 EtOH/Et_2O (70 mL), the collected issue was concentrated and the residue was dried in vacuo to isolate $[C_4tz][BF_4]$ (1.17 g, 3.99 mmol [C_4tz] salts per g; 4.67 mmol [C_4tz] salts total, 72%). The C(2) proton was invisible by ^{1}H NMR (400 MHz, $CDCl_3$/CD_3OD): δ = 8.43 (d, J = 3.5 Hz, 1 H), 8.26 (d, J = 3.5 Hz, 1 H), 4.60 (t, J = 8 Hz, 2 H), 1.99 (quint, J = 8 Hz, 2 H), 1.39 (sext, J = 8 Hz, 2 H), 0.98 (t, J = 8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$/CD_3OD): δ = 157.9 [t, $^1J(^{13}C\text{-}D)$ = 75 Hz], 137.4, 126.5, 55.8, 32.4, 19.5, 13.2 ppm. IR (film): $\tilde{\nu}$ = 3116, 2964, 2937, 2877, 1025 cm^{-1}.

Supporting Information (see also the footnote on the first page of this article): Quantities for AEs leading to $[C_4mim][ClO_3]$,[70] $[C_1mim][OBz]$ and $[ClO_3]$,[70] [dpim][OBz], $[C_1tz]$ and $[C_4tz][Br]$, and $[C_4tz][BF_4]$. Acidification protocols leading to $[C_4mim][BF_4]$, $[C_1mim]$ and $[dpim][CF_3CO_2]$, and $[C_4tz][PF_6]$. Protocols for syntheses of **5** from a DIBALH reduction, **5** from a one-pot reaction, **6**, **8**, **9**, **10** from Fischer esterification, and $[C_4mim][BF_4]$ from a quaternization and AE approach. Copies of all spectral characterizations.

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[70] ***CAUTION:*** Although [C_1mim][ClO_3] was formed, chromatographed, concentrated at 60 °C, and seemingly unremarkable, there was a detonation in an unoccupied laboratory several weeks later which we have every reason to believe was caused by a 5-g sample of the once chromatographed chlorate. A 1-g sample from the same batch and a 1-g sample of twice chromatographed material were unchanged, and a 1-g sample of [C_4mim][ClO_3] was stable for several months, but we must insist no one else attempt the synthesis of these materials.
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