Structural Elucidation and Characterization of *N*-Heterocyclic Salts with Various Anions

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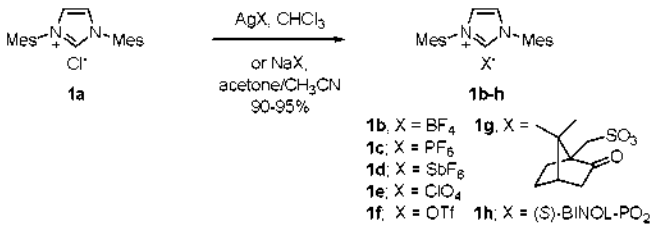
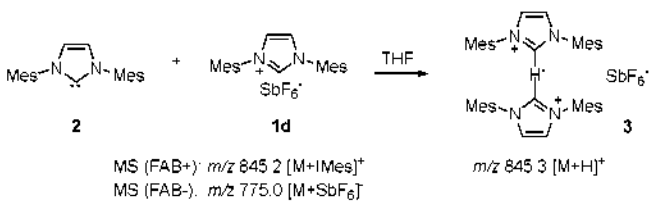
N-Heterocyclic carbenes (NHCs) have come to be heavily researched, for the role of nucleophilic carbenes as ancillary ligands for transition-metal catalysis and organocatalysts.[1] The remarkable success of NHCs is innately caused by their powerful capacity as two-electron donors.[2] Since the first stable carbene was reported in 1991 by Arduengo, the carbene scaffold has been extensively developed in preparations, such as diversifying azolium frameworks (imidazolium, imidazolinium, thiazolium, and triazolium), substituents, and chiral moieties.[3] The distinct difference in reactivities and mechanistic pathways of NHCs has brought about an increasing availability of *N*-heterocyclic salts.[4] Toward the goal of widening the scope of NHCs' use, we introduced various anions in *N*-heterocyclic salts and analyzed their structural features, which as yet have not been carefully studied. We envisioned that subtle anionic effects would have a dramatic impact on the chemistry of NHCs.

The general anions of *N*-heterocyclic salts, such as chloride and tetrafluoroborate, are introduced during either cyclization to azolium salt or *N*-alkylation of azole. These approaches are limited to halide (especially chloride) as anion and have the drawback of specific choice of *N*-substituent, sometimes needing the additional step of addition of catalytic HCl for clean salt formation. To the best of our knowledge, it can be difficult to introduce various anions in the early stage of NHC salt synthesis; thus, anion exchange reactions of azolium chlorides, which are the most easily obtained, seem an economic and efficient route of preparation.



Scheme 1. Synthesis of imidazolium salts by anion exchange.

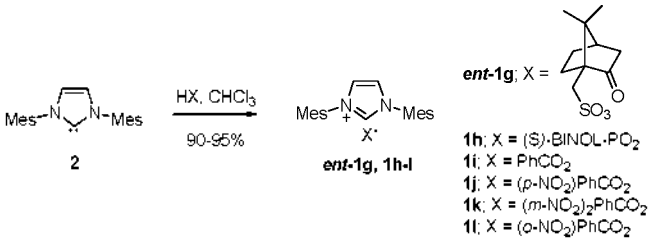


Scheme 2. Mass analysis of **1d** and **3** in FAB+ and FAB− mode.

Previous studies on ionic liquids (ILs) demonstrating the variation of the anion and investigating the subsequent change of their character, generally adopted the anion exchange method between imidazolium chloride and alkali or ammonium salts.[5] But all available data indicates that the organic soluble ion pair is not cleanly extracted. Thus, we have found that anion exchange with heavy metal salts is essential for the reproducible synthesis of NHC salts. The first results of anion exchange with metal salts are summarized in Scheme 1. Dimesityl imidazolium chloride **1a** was chosen as a versatile substrate and treated with commercially available silver salts in chloroform at room temperature. The use of heavy metal salts enables simpler isolation with efficient removal of the halide content, without any aqueous workup. BF_4^-, SbF_6^-, PF_6^-, ClO_4^-, and OTf^- were employed in this reaction taking 30 min; general filtration by a short pad of celite to remove AgCl and excess silver salts affords the corresponding imidazolium compounds. This approach is also used to synthesize chiral sulfonate and phosphate salts, which would be valuable in the application of a chiral counteranion strategy.

To determine the composition of the anion after the anion exchange experiment, mass spectrometry was performed with several imidazolium salts. All mass spectra provided a base peak at m/z = 305, which is responsible for the dimesitylimidazolium ion, $[IMes]^+$, without any molecular ion or M + 1 peak. Upon investigation of several modes of mass analysis, FAB+ and FAB− modes proved to be crucial for declaration of the anion in these imidazolium salts. The mass spectrum of antimonate **1d** obtained in FAB+ mode provided a small peak at m/z = 845 for $[M_{1d}+IMes]^-$, and a base peak at m/z = 305 for $[IMes]^+$. However, a small peak at m/z = 845 was duplicated in the FAB+ mass spectra of bis(carbene)-proton complex **3**, prepared from carbene **2** and dimesitylimidazolium antimonate **1d**.[6] With additional analysis in FAB− mode, we could confirm the composition of antimonate by a small peak at m/z = 775 for $[M_{1d}+SbF_6]^-$.

Because an anion exchange cannot be done efficiently with the imidazolium chloride and an acid weaker than a hydrochloric acid, routes to a wider range of counteranions must pass through a different intermediate. To this end, the *N*-heterocyclic carbene was treated with a large number of acids to incorporate with corresponding anions (Scheme 3). 1,3-Dimesitylimidazol-2-ylidene **2** was reprotonated by commercially available camphorsulfonic acid and BINOL hydrogenpho-



Scheme 3. Synthesis of imidazolium salts by reprotonation.

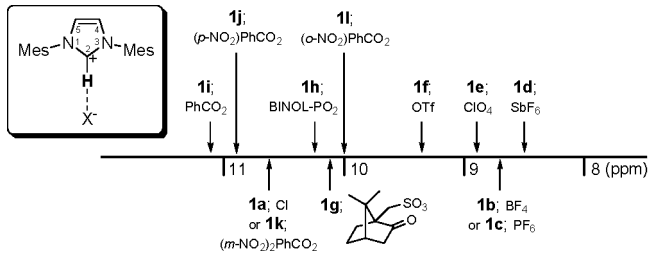
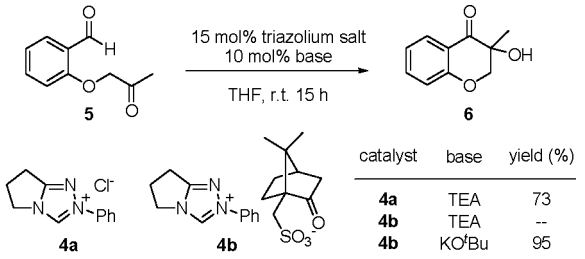


Figure 1. ^{1}H-NMR signals of C-2 protons in various NHC salts.

sphate, to give the chiral imidazolium sulfonate (**1g**) and phosphate (**1h**), resulting in data identical to that from the method used in Scheme 1. Benzoate (**1i**) and nitro-substituted derivatives (**1j-l**) were also introduced, showing different coordinating abilities of anions by nitro substituents. This method proved to generate a higher purity of NHC salts, without any other halide contents. The preparation, just removing solvents after reactions to afford imidazolium salts, was quite simpler.

The characteristic coordinating abilities of various anions in NHC salts were well reflected in ^{1}H-NMR spectra. In $CDCl_3$ solution at room temperature, imidazole ring protons at C-2 with weaker coordinating anions, such as BF_4^-, PF_6^-, or SbF_6^-, resonate at about δ 8.5, which is about 2.0 ppm upfield of imidazolium chloride. Those with stronger coordinating anions, such as Cl^- or $PhCO_2^-$, resonate at about δ 11.0, and the relative trend of nitro-substituted benzoate derivatives accorded with the acidities of corresponding benzoic acids. Based on the interesting correlation between ^{1}H-NMR signals and counteranions, the structures of NHC salts containing geometries and types of interaction could be inferred, as shown in Figure 1. The proton in the 2-position of the imidazolium cation serves as a site for hydrogen bonding, and the anion can function as a hydrogen bond acceptor. This interaction has been previously observed in the X-ray structures of several salts, in which anions are positioned in a near-linear C−H···X arrangement, with an angle of 172° in **1a**.[7] Thus, the ^{1}H-NMR signals of C-2 protons offer general insights into interactions with counteranions.

These methods also applied to the synthesis of triazolium salts, and the triazolium camphorsulfonate **4b** was obtained by anion exchange method with silver sulfonate. Next, we examined its catalytic capacity as a carbene precursor in the intramolecular crossed aldehyde-ketone benzoin reactions.[8] As summarized in Scheme 4, when triazolium chloride was used together with a weak base, Et_3N, to prevent the competing intramolecular aldol reactions, the desired acyloin **6** was synthesized in 73% yield. The use of catalyst **4b** and Et_3N



catalyst	base	yield (%)
4a	TEA	73
4b	TEA	--
4b	KO^{t}Bu	95

Scheme 4. Intramolecular crossed benzoin reactions with triazolium salts.

resulted in recovery of substrate **5**, without generation of carbene catalyst. When triazolium sulfonate **4b** was used with a stronger base, KO^{t}Bu, the reaction proceeded to completion smoothly, affording the desired product **6** in excellent yield (95%). It is worthy of note that there were no aldol byproduct and its dehydration product, benzofuran, which were obtained as major product in the experiments with triazolium chloride and DBU. The contrastive change in reactivity is understandable in view of the lower acidity of the proton in **4b**. The strong base was indispensible to make the generation of the key carbene species and accelerate the Breslow intermediate formation.

In conclusion, we prepared imidazolium salts with various anions (BF_4^-, PF_6^-, SbF_6^-, ClO_4^-, OTf^-, RSO_3^-, RPO_4^-, $PhCO_2^-$) from imidazolium chloride by anion exchange with silver salts or imidazolylidene by reprotonation. The FAB+ and FAB− modes for mass analysis proved to be crucial for determination of the anion's structure, and ^{1}H-NMR signals of C-2 proton provided general insights into interactions with counteranions. Most importantly, the triazolium sulfonate **4b** catalyzed the intramolecular aldehyde-ketone benzoin reaction in high yield, even with a strong base, KO^{t}Bu. The extension of the method to the syntheses of ionic liquids (ILs) and the development of new catalytic reactions and diastereoselective variants are subjects of ongoing investigations.

Experimental Section

General procedure for the anion exchange reaction. To a suspension of dimesityl imidazolium chloride **1a** (0.1 mmol) in $CHCl_3$ (1.0 mL) was added silver salt (0.1 mmol). After being stirred for 30 min, the reaction mixture was filtered through celite and the solvent was removed under reduced pressure. Recrystallization from Hex/CH_2Cl_2 gave the desired product (90 ~ 95%) as a white solid. **1b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.55 (s, 2H), 7.04 (s, 4H), 2.35 (s, 6H), 2.10 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.2, 137.0, 134.0, 130.5, 129.7, 125.2, 21.1, 17.1 ppm. **1c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.54 (s, 2H), 7.02 (s, 4H), 2.34 (s, 6H), 2.09 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 136.8, 133.9, 130.3, 129.9, 125.1, 21.1, 17.1 ppm. **1d**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.55 (s, 2H), 7.04 (s, 4H), 2.35 (s, 6H), 2.10 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 133.9, 130.1, 130.0, 125.2, 21.2, 17.1 ppm; MS (FAB+, relative intensity) 845.2 ([M+IMes]$^+$, 7), 305.2 ([M−SbF_6]$^+$, 100); HRMS (FAB+) calc'd for [$C_{42}H_{50}F_6N_4Sb$]$^+$: *m/z* 845.2978,

found 845.3002; MS (FAB−, relative intensity) 775.0 ([M+ SbF_6]$^-$, 8), 234.9 ([SbF_6]$^-$, 100); HRMS (FAB−) calc'd for [$C_{21}H_{25}F_{12}N_2Sb_2$]$^+$: *m/z* 774.9903, found 774.9918; Anal calc'd for $C_{21}H_{25}F_6N_2Sb$: C, 46.61; H, 4.66; N, 5.18; found: C, 45.49; H, 4.38; N, 5.32. **1e**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (d, 1H, *J* = 1.5 Hz), 7.56 (t, 2H, *J* = 2.7 Hz), 6.99 (s, 4H), 2.31 (s, 6H), 2.08 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 137.4, 133.9, 130.0, 129.8, 125.0, 21.1, 17.3 ppm. **1f**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.57 (s, 2H), 7.01 (s, 4H), 2.34 (s, 6H), 2.09 (s, 12H) ppm. **1g**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.59 (s, 2H), 7.04 (s, 4H), 2.84 (d, 1H, *J* = 14.6 Hz), 2.62-2.55 (m, 1H), 2.35 (s, 6H), 2.18 (s, 12H), 1.90-1.89 (m, 3H), 1.71 (d, 1H, *J* = 17.9 Hz), 1.34-1.17 (m, 3H), 0.99 (s, 3H), 0.69 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.9, 141.2, 140.1, 134.3, 13.07, 129.8, 124.4, 58.4, 47.5, 46.5, 42.8, 42.6, 27.0, 24.2, 21.1, 20.1, 19.7, 17.6 ppm. **1h**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.36 (s, 1H), 7.83 (d, 2H, *J* = 8.0 Hz), 7.75 (d, 2H, *J* = 8.8 Hz), 7.35 (t, 8H, *J* = 7.5 Hz), 7.19 (t, 2H, *J* = 7.5 Hz), 6.93 (s, 4H), 2.30 (s, 6H), 2.05 (s, 6H), 1.94 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.0, 140.2, 134.1, 132.5, 130.9, 130.6, 129.7, 129.6, 128.1, 127.1, 125.5, 124.2, 124.0, 122.3, 122.1, 31.6, 21.1, 17.3, 17.1, 14.1 ppm. **4b**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.39 (s, 1H), 7.99-7.95 (m, 2H), 7.54-7.50 (m, 3H), 4.85-4.81 (m, 2H), 3.30-3.25 (m, 4H), 2.92-2.79 (m, 3H) 2.80 (d, 1H, *J* = 13.2 Hz), 2.63-2.60 (m, 2H), 2.30-2.24 (m, 1H), 2.00-1.98 (m, 3H), 1.81 (d, 1H, *J* = 18.5 Hz), 1.71-1.67 (m, 2H), 1.31-1.25 (m, 1H), 1.04 (s, 3H), 0.78 (s, 3H) ppm.

General procedure for the reprotonation reaction. A solution of carbene **2** (0.1 mmol) in $CHCl_3$ (1.0 mL) was treated with HX (0.1 mmol) at room temperature. After being stirred for 30 min, the reaction mixture was concentrated under reduced pressure. Recrystallization from Hex/CH_2Cl_2 gave the corresponding product (90 ~ 95%) as a white solid. **1i**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.2 (s, 1H), 7.63 (d, 2H, *J* = 6.9 Hz), 7.46 (s, 2H), 7.23-7.19 (m, 1H), 7.09 (t, 2H, *J* = 7.3 Hz), 6.82 (s, 4H), 2.18 (s, 6H), 2.07 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 140.9, 140.7, 137.7, 134.0, 130.7, 129.7, 129.2, 129.1, 126.8, 124.1, 21.0, 17.4 ppm. **1j**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.52 (s, 1H), 8.04 (d, 2H, *J* = 7.1 Hz), 7.89 (d, 2H, *J* = 8.8 Hz), 7.48 (s, 2H), 6.89 (s, 4H), 2.22 (s, 6H), 2.12 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 147.9, 144.8, 141.1, 139.9, 133.9, 130.5, 129.8, 129.7, 129.5, 124.3, 124.2, 122.1, 20.9, 17.3 ppm. **1k**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.86-8.82 (m, 3H), 7.49 (s, 2H), 6.88 (s, 4H), 2.18 (s, 6H), 2.16 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 147.6, 141.3, 134.1, 130.6, 129.8, 129.6, 129.0, 124.0, 118.6, 20.9, 17.4 ppm. **1l**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.53(s, 1H), 7.57 (s, 2H), 7.52 (d, 1H, *J* = 8.2 Hz), 7.29 (t, 2H, *J* = 2.7 Hz), 7.18-7.14 (m, 1H), 6.94 (s, 4H), 2.28 (s, 6H), 2.11 (s, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 140.8, 134.1, 130.7, 129.8, 129.8, 129.5, 124.6, 122.5, 21.1, 17.4 ppm.

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