Electronic Supplementary Information (ESI)

Designing Enzyme-Compatible Ionic Liquids That Can Dissolve Carbohydrates

Hua Zhao,[1*] Gary A. Baker,[2] Zhiyan Song,[1] Olarongbe Olubajo,[1]

Tanisha Crittle,[1] and Darkeysha Peters[1]

[1]*Chemistry Program, Savannah State University, Savannah, GA 31404, USA*

[2]*Chemical Sciences Division, Oak Ridge National Laboratory,*

Oak Ridge, TN 37831, USA

IL Preparations

All Tf_2N^- based ILs ([choline][Tf_2N] (**9**), [Amm110][Tf_2N] (**16**), [EMIM][Tf_2N] (**2**), [BMIM][Tf_2N] (**3**), and [HMIM][Tf_2N] (**4**)) were synthesized through a precipitation reaction:[13] an aqueous solution of halide-based IL (1 molar equiv.) was added drop wise into Li[Tf_2N] (1.1 molar equiv) solution. A turbid was formed immediately. The reaction mixture was stirred at room temperature for at least 2 h until the formation of two layers. After the phase separation, the IL layer was thoroughly washed with water three times. The silver nitrate test on the aqueous layer suggested the absence of halides. The resulting IL was collected and dried in an oven at 100 °C over 24 h. Acros® 3A molecular sieves were added into ILs to remove residual water. ^{1}H NMR, FT-IR and HPLC data confirmed that the prepared ILs are free of measurable impurities.

All dca^- or $HCOO^-$ based ILs ([choline][dca] (**10**), [Amm110][dca] (**17**), [Amm110][HCOO] (**18**), [BMIM][dca] (**12**), and [BMIM][HCOO] (**6**)) were prepared

* Corresponding authors. Email: zhaoh@savstate.edu (or huazhao98@gmail.com).

through an anion-exchange method. The procedures are briefly described as the following: about 100 mL of the resin (Amberlite® IRA-400 Cl, 1.4 meq/mL by wetted bed volume, 16-50 mesh) was packed in a glass chromatography column, and washed thoroughly with distilled water and methanol, until no yellow color was observed in the eluting water and no precipitate in the eluent could be detected by 0.1 M $AgNO_3$ solution. The Cl^- ions on the resin were exchanged by dca^- or $HCOO^-$ ions through slowly washing the column with an excess amount of sodium dicyanamide (> 20 g) or sodium formate (> 15 g) solution. The column was then washed with distilled water to remove the residue of salts in the column (as monitored by 0.1 M $AgNO_3$). 0.1 Mole of halide salts ([choline]Cl, [Amm110]Cl, or [BMIM]Br) in 200 mL water was further slowly dripping through the column, and the eluting solution was collected and decolorized with activated charcoal. Water was removed from the clear solution through a rotary evaporator under vacuum at 60 °C. The product was further dried in an oven at 100 ºC over 24 h, yielding a colorless liquid. ^{1}H NMR, FT-IR and HPLC data confirmed that the prepared ILs are free of measurable impurities. Dried Acros® 3A molecular sieves were added into ILs during storage.

Synthesis of glycol–substituted ILs

A solution of 2.5 equiv. sodium hydroxide in the same amount of distilled water was added into the mixture of 1.0 equiv. glycol monomethyl ether (ca. 40-50 g) in 100 mL toluene, and a catalytic amount (ca. 1 mL) of hexadecyltrimethylammonium hydroxide (as the Phase-Transfer Catalyst, or PTC). 1.1 Equiv. of benzenesulfonyl chloride was added dropwise (an ice-bath was used to keep the temperature below 70 ºC). The reaction mixture was maintained at 70 ºC with a constant stirring for 3 h. Precipitate

was rapidly formed in the solution. After filtering off the precipitate, toluene and water was removed from the filtrate through a vacuum evaporation. The residue was taken into dichloromethane and washed once with distilled water. After drying the organic layer with sodium sulfate, dichloromethane was evaporated through a rotary evaporator. The product was monomethyl glycol-benzenesulfonate.

Another solution was prepared by mixing 1.0 equiv. of imidazole (or diethylamine), 50 mL toluene, a catalytic amount (ca. 1 mL) of hexadecyltrimethylammonium hydroxide, and 3.0 equiv. sodium hydroxide dissolved in the same amount of distilled water. 1.1 Equiv. of monomethyl glycol-benzenesulfonate (ca. 20-30 g) was added dropwise into the above solution. The viscous mixture was stirred for 2 h at 70 ºC. After the vacuum evaporation of toluene, water was added into the mixture to dissolve most of the precipitate. The aqueous solution was extracted three times with dichloromethane. After drying the organic layers with sodium sulfate, the solvent was evaporated, yielding glycol-substituted imidazole (or amine).

Glycol-substituted imidazole or amine (ca. 20 g, 1 equiv) was dissolved in dried acetonitrile (or DMF) (200 mL), followed by the addition of an excess amount of bromoethane (or other alkyl halides) (2 equiv). The mixture was refluxed at 80 °C for 2 days. The product ([Glycol-Et-Im]Br or [Gycol-R_2-N]Br) was purified by washing with anhydrous diethylether.

The bromide anions in [Glycol-Et-Im]Br were replaced with acetate through an anion exchange using Amberlite® IRA-400 Cl resin (same procedures above). The aqueous solution of the final product was decolorized by activated charcoal, followed by an extensive drying in an oven at 100 ºC. The absence of halides in the product was

confirmed by the silver nitrate test. All final products were characterized by ^{1}H NMR and FT-IR spectra.

1-ethyl-3-(2-methoxyethoxy)ethyl)imidazolium acetate (**21**, [Me(OEt)$_2$-Et-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.37 (3H, t, C*H*$_3$CH$_2$N, J = 7.2 Hz), 1.91 (3H, s, C*H*$_3$COO$^-$), 3.36 (3H, s, NCH$_2$CH$_2$OCH$_2$CH$_2$OC*H*$_3$), 3.53 (2H, t, NCH$_2$CH$_2$OCH$_2$C*H*$_2$OCH$_3$, J = 2.8 Hz), 3.64 (2H, t, NCH$_2$CH$_2$OC*H*$_2$CH$_2$OCH$_3$, J = 2.4 Hz), 3.87 (2H, NCH$_2$C*H*$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.8 Hz), 4.36 (2H, q, CH$_3$C*H*$_2$N, J = 7.2 Hz), 4.59 (2H, t, NC*H*$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.8 Hz), 7.41 (1H, d, NC*H*CHN, J = 1.6 Hz), 7.58 (1H, d, NCHC*H*N, J = 1.6 Hz), 10.70 (1H, s, NC*H*N).

1-ethyl-3-(2-(2-methoxyethoxy)ethoxy)ethyl)imidazolium acetate (**22**, [Me(OEt)$_3$-Et-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.58 (3H, t, C*H*$_3$CH$_2$N, J = 7.2 Hz), 1.97 (3H, s, C*H*$_3$COO$^-$), 3.38 (3H, s, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OC*H*$_3$), 3.55 (2H, m, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$C*H*$_2$OCH$_3$), 3.64 (9H, m, NCH$_2$C*H*$_2$OC*H*$_2$C*H*$_2$OC*H*$_2$CH$_2$OCH$_3$ and CH$_3$COO$\cdots$(N)C*H*N), 4.36 (2H, q, CH$_3$C*H*$_2$N, J = 7.2 Hz), 4.61 (2H, t, NC*H*$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.4 Hz), 7.32 (1H, d, NC*H*CHN, J = 2.0), 7.64 (1H, d, NCHC*H*N, J = 1.6).

1-ethyl-3-(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)ethyl)imidazolium acetate (**23**, [Me(OEt)$_4$-Et-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.57 (3H, t, C*H*$_3$CH$_2$N, J = 7.2 Hz), 1.98 (3H, s, C*H*$_3$COO$^-$), 3.36 (3H, s, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OC*H*$_3$), 3.55 (2H, m, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$C*H*$_2$OCH$_3$), 3.64 (10H, m, NCH$_2$CH$_2$OC*H*$_2$C*H*$_2$OC*H*$_2$C*H*$_2$OC*H*$_2$CH$_2$OCH$_3$), 3.86 (2H, t, NCH$_2$C*H*$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.8 Hz), 4.36 (2H, q, CH$_3$C*H*$_2$N, J = 7.6 Hz), 4.60 (2H, t, NC*H*$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.0 Hz), 7.34 (1H, d, NC*H*CHN, J = 2.0 Hz), 7.65 (1H, d, NCHC*H*N, J = 1.6 Hz), 11.09 (1H, s, NC*H*N).

(**24**, [Me(OEt)$_7$-Et-Im][OAc] where 7 is the averaged number; the data below suggested a mixture). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.58 (3H, t, C*H*$_3$CH$_2$N, J = 7.2 Hz), 1.98 (3H, s, C*H*$_3$COO$^-$), 3.37 (6H, m, NCH$_2$CH$_2$O(CH$_2$CH$_2$O)$_6$C*H*$_3$), 3.65 (48H, m, NCH$_2$CH$_2$O(C*H*$_2$C*H*$_2$O)$_6$CH$_3$), 3.87 (2H, t, NCH$_2$C*H*$_2$O(CH$_2$CH$_2$O)$_6$CH$_3$, J = 4.0 Hz), 4.36 (2H, q, CH$_3$C*H*$_2$N, J = 7.6 Hz), 4.60 (2H, m, NC*H*$_2$CH$_2$O(CH$_2$CH$_2$O)$_6$CH$_3$), 7.42 (1H, m, NC*H*CHN), 7.66 (1H, m, NCHC*H*N), 11.14 (1H, m, NC*H*N).

1-((2-methoxyethoxy)methyl)-3-(2-(2-methoxyethoxy)ethoxy)ethyl)imidazolium acetate (**25**, [Me(OEt)$_3$-MeOEtOMe-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.96 (3H, s, C*H*$_3$COO$^-$), 3.37 (6H, m, NCH$_2$OCH$_2$CH$_2$OC*H*$_3$ and NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OC*H*$_3$), 3.59 (12H, m, NCH$_2$OC*H*$_2$C*H*$_2$OCH$_3$ and NCH$_2$CH$_2$OC*H*$_2$C*H*$_2$OC*H*$_2$C*H*$_2$OCH$_3$), 4.20 (2H, m, NCH$_2$C*H*$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$), 4.55 (2H , t, NC*H*$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.8 Hz), 5.78 (2H, t, NC*H*$_2$OCH$_2$CH$_2$OCH$_3$, J = 19.2 Hz), 7.02 (2H, m, NC*H*CHN), 7.56 (2H, m, NCHC*H*N), 7.91 (1H, s, NC*H*N).

1-(2-(2-hydroxylethoxy)ethyl)-3-methylimidazolium acetate (**26**, [H(OEt)$_2$-Me-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.93 (3H, s, CH_3COO$^-$), 3.57 (2H, t, NCH$_2$CH$_2$OCH$_2$CH_2OH, J = 4.8 Hz), 3.68 (2H, t, NCH$_2$CH$_2$OCH_2CH$_2$OH), 3.82 (2H, t, NCH$_2$CH_2OCH$_2$CH$_2$OH, J = 4.4 Hz), 4.01 (3H, s, H_3CN), 4.49 (2H, t, NCH_2CH$_2$OCH$_2$CH$_2$OH, J = 4.0 Hz), 7.42 (1H, d, NC*H*CHN, J = 1.6 Hz), 7.71 (1H, d, NCHC*H*N, J = 1.2 Hz), 10.46 (1H, s, NC*H*N).

1-(2-(2-(2-hydroxylethoxy)ethoxy)ethyl)-3-methylimidazolium acetate (**27**, [H(OEt)$_3$-Me-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.92 (3H, s, CH_3COO$^-$), 3.58 (4H, m, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH_2CH_2OH), 3.65 (2H, m, NCH$_2$CH$_2$OCH$_2$CH_2OCH$_2$CH$_2$OH), 3.70 (2H, t, NCH$_2$CH$_2$OCH_2CH$_2$OCH$_2$CH$_2$OH, J = 4.4 Hz), 3.86 (2H, t, NCH$_2$CH_2OCH$_2$CH$_2$OCH$_2$CH$_2$OH, J = 4.8 Hz), 4.00 (3H, s, H_3CN), 4.50 (2H, t, NCH_2CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OH, J = 4.4 Hz), 7.51 (1H, d, NC*H*CHN, J = 2.0 Hz), 7.71 (1H, d, NCHC*H*N, J = 1.6 Hz), 10.27 (1H, s, NC*H*N).

A mixture of *1-ethyl-3-(2-(2-methoxypropyloxy)propyloxy)propyl)imidazolium acetate* and *1-ethyl-3-(2-(2-methoxyisopropyloxy)isopropyloxy)isopropyl)imidazolium acetate* (**29**, [Me(OPr)$_3$-Et-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.12 (9H, m, CH_3CH$_2$N and partial NCH$_2$(CH_3)CHOCH$_2$(CH_3)CHOCH$_2$(CH_3)CHOCH$_3$), 1.58 (6H, m, NCH$_2$CH_2CH$_2$OCH$_2$CH_2CH$_2$OCH$_2$CH_2CH$_2$OCH$_3$), 1.96 (3H, s, CH_3COO$^-$), 3.36 (10H, m), 3.60 (2H, m), 3.80 (2H, m), 4.39 (2H, m), 7.34 (1H, m, NC*H*CHN), 7.67 (1H, m, NCHC*H*N), 10.70 (1H, m, NC*H*N).

1-butyl-3-(2-(2-methoxyethoxy)ethoxy)ethyl)imidazolium acetate (**30**, [Me(OEt)$_3$-Bu-Im][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 0.93 (3H, t, CH_3CH$_2$CH$_2$CH$_2$N, J = 7.6 Hz), 1.34 (2H, sextet, CH$_3$CH_2CH$_2$CH$_2$N, J = 8.0 Hz), 1.84 (5H, m, CH_3COO$^-$ and CH$_3$CH$_2$CH_2CH$_2$N), 3.36 (1H, s, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH_3), 3.54 (2H, m, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH_2OCH$_3$), 3.60 (4H, m, NCH$_2$CH$_2$OCH$_2$CH_2OCH_2CH$_2$OCH$_3$), 3.65 (4H, m, NCH$_2$CH_2OCH_2CH$_2$OCH$_2$CH$_2$OCH$_3$), 3.85 (2H, t, CH$_3$CH$_2$CH$_2$CH_2N, J = 4.4 Hz), 4.26 (2H, t, NCH_2CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 7.6 Hz), 7.42 (1H, t, NC*H*CHN, J = 1.6 Hz), 7.68 (1H, t, NCHC*H*N, J = 2.0 Hz), 9.57 (1H, s, NC*H*N).

Triethyl (2-(2-methoxyethoxy)ethoxy)ethylammonium acetate (**31**, [Me(OEt)$_3$-Et$_3$N][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.37 (9H, t, (CH_3CH$_2$)$_3$N, J = 7.2 Hz), 1.91 (3H, s, CH_3COO$^-$), 3.37 (3H, s, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH_3), 3.52 (6H, m, (CH$_3$CH_2)$_3$N), 3.61 (4H, m, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH_2CH_2OCH$_3$), 3.66 (6H, m, NCH$_2$CH_2OCH_2CH_2OCH$_2$CH$_2$OCH$_3$), 3.75 (2H, t, NCH_2CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.4 Hz).

Triethyl (2-methoxyethoxy)ethylammonium acetate (**32**, [Me(OEt)$_2$-Et$_3$N][OAc]). ^{1}H-NMR (400 MHz, $CDCl_3$, [ppm]) δ = 1.37 (9H, t, (CH_3CH$_2$)$_3$N, J = 7.2 Hz), 1.91 (3H, s, CH_3COO$^-$), 3.35 (3H, s, NCH$_2$CH$_2$OCH$_2$CH$_2$OCH_3), 3.53 (8H, m, (CH$_3$CH_2)$_3$N and NCH$_2$CH$_2$OCH$_2$CH_2OCH$_3$), 3.65 (4H, m, NCH$_2$CH_2OCH_2CH$_2$OCH$_3$), 3.77 (2H, t, NCH_2CH$_2$OCH$_2$CH$_2$OCH$_3$, J = 4.4 Hz).