Electronic Supplementary Material (ESI) for Green Chemistry.


# Good's buffers as a basis for developing self-buffering and biocompatible ionic liquids for biological research

Mohamed Taha, Francisca A. e Silva, Maria V. Quental, Sónia P. M. Ventura, Mara G. Freire, and João A. P. Coutinho*

**Corresponding Author**

* Tel.: +351 234 401 507; fax: +351 234 370 084.

E-mail address: jcoutinho@ua.pt (J.A.P. Coutinho)

**Table S1** Characterization of Good's buffer ionic liquids.

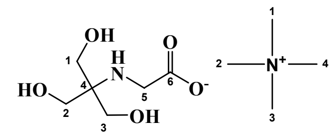
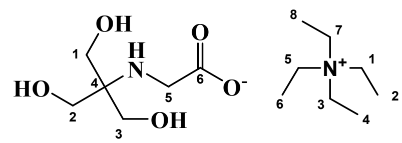
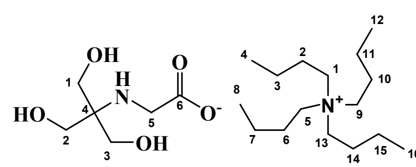
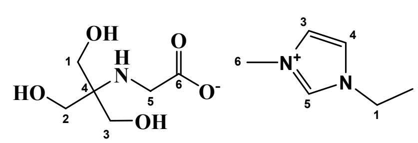
| | |
|---|---|
| **[$N_{1111}$][Tricine]:** [1]H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 3.11(12H, *s*, C1-C4's *H*); δ *[Tricine]*, 3.19 (6H, *s*, C1-C3's *H*), 2.87 (2H, *s*, C5's *H*). [13]C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 54.35 (*C1-C4*); δ *[Tricine]*, 60.55 (*C4*), 60.81 (*C1-C3*), 176.10 (*C6*), 46.14 (*C5*); melting point = 116 °C. |  [$N_{1111}$][Tricine]: |
| **[$N_{2222}$][Tricine]:** [1]H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 3.27(8H, *q*, C1C3C5C7's *H*), 1.26 (12H, *m*, C2C4C6C8's *H* ); δ *[Tricine]*, 3.52 (6H, *s*, C1-C3's *H*), 3.30 (2H, *s*, C5's *H*). [13]C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 54.71 (*C1C3C5C7*), 9.39 (*C2C4C6C8*); δ *[Tricine]*, 62.94 (*C4*), 63.14 (*C1-C3*), 182.80 (*C6*), 47.69 (*C5*); melting point = 168 °C. |  [$N_{2222}$][Tricine]: |
| **[$N_{4444}$][Tricine]:** [1]H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{4444}$]*, 0.93 (12H, *t*, C4C8C12C16's *H*), 1.37 (8H, *sext*, C3C7C11C15's *H*), 1.65 (8H, *quin*, C2C6C10C14's *H*), 3.21 (8H, *t*, C1C5C9C13's *H* ); δ *[Tricine]*, 3.53 (6H, *s*, C1-C3's *H*), 3.27 (2H, *s*, C5's *H*). [13]C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 15.71 (*C4C8C12C16*), 22.03 (*C3C7C11C15*), 26.00 (*C2C6C10C14*), 60.97 (*C1C5C9C13*); δ *[Tricine]*, 62.93 (*C4*), 63.15 (*C1-C3*), 182.83 (*C6*), 47.70 (*C5*); melting point = 101°C. |  [$N_{4444}$][Tricine]: |
| **[Emim][Tricine]:** [1]H NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 1.39 (3H, *t*, C2's *H*), 3.86 (3H, *s*, C6's *H* ), 4.20 (2H, *q*, C1's *H* ), 7.65 (1H, *s*, C4's *H* ), 7.85 (1H, *s*, C3's *H* ), 9.58 (1H, *s*, C5's *H*); δ *[Tricine]*, 3.18 (6H, *s*, C1-C3's *H*), 2.93 (2H, *s*, C5's *H*). [13]C NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 15.29 (*C2*), 35.61 (*C6*), 44.10 (*C1*), 122.10 (*C4*), 123.66 (*C3*), 136.94 (*C5*); δ *[Tricine]*, 60.41 (*C4*), 60.56 (*C1-C3*), 177.10 (*C6*), 46.16 (*C5*); viscous liquid. |  [Emim][Tricine]: |

**Table S1** continued

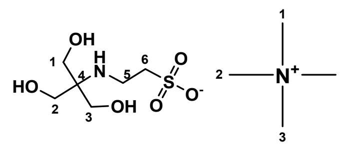
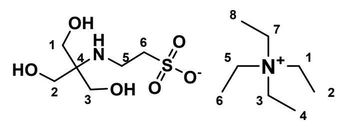
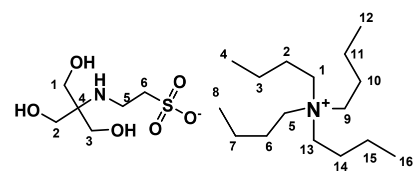
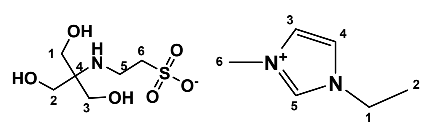
| | |
|---|---|
| **[$N_{1111}$][TES]:** $^1$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 3.11(12H, *s*, C1-C4's *H*); δ *[TES]*, 3.31 (6H, *s*, C1-C3's *H*), 2.86 (2H, *t*, C6's *H*), 2.62 (2H, *t*, C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 60.36 (*C1-C4*); δ *[TES]*, 60.73 (*C4*), 54.37 (*C1-C3*), 51.47 (*C6*), 37.73 (*C5*); melting point = 45 °C. |  [$N_{1111}$][TES] |
| **[$N_{2222}$][TES]:** $^1$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 3.27(8H, *q*, C1C3C5C7's *H*), 1.28 (12H, *m*, C2C4C6C8's *H* ); δ *[TES]*, 3.30 (6H, s, C1-C3's *H*), 2.85 (2H, t, C6's *H*), 2.61 (2H, t, C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 60.68 (*C1C3C5C7*), 7.46 (*C2C4C6C8*); δ *[TES]*, 60.94 (*C4*), 52.07 (*C1-C3*), 51.87 (*C6*), 37.98 (*C5*); viscous liquid. |  [$N_{2222}$][TES] |
| **[$N_{4444}$][TES]:** $^1$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{4444}$]*, 0.91 (12H, *t*, C4C8C12C16's *H*), 1.30 (8H, *sext*, C3C7C11C15's *H* ), 1.55 (8H, *quin*, C2C6C10C14's *H* ), 3.17 (8H, *t*, C1C5C9C13's *H* ); δ *[TES]*, 3.32 (6H, *s*, C1-C3's *H*), 2.86 (2H, *t*, C6's *H*), 2.60 (2H, *t*, C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 13.52 (*C4C8C12C16*), 19.25 (*C3C7C11C15*), 23.20 (*C2C6C10C14*), 60.49 (*C1C5C9C13*); δ *[TES]*, 60.55 (*C4*), 57.59 (*C1-C3*), 51.50 (*C6*), 37.65 (*C5*); melting point = 81 °C. |  [$N_{4444}$][TES]: |
| **[Emim][TES]:** $^1$H NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 1.39 (3H, *t*, C2's *H*), 3.85 (3H, *s*, C6's *H* ), 4.19 (2H, *q*, C1's *H* ), 7.70 (1H, *s*, C4's *H* ), 7.79 (1H, *s*, C3's *H* ), 9.20 (1H, *s*, C5's *H*); δ *[TES]*, 3.30 (6H, *s*, C1-C3's *H*), 2.88 (2H, *t*, C6's *H*), 2.65 (2H, *t*, C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 15.29 (*C2*), 35.76 (*C6*), 44.24 (*C1*), 122.10 (*C4*), 123.70 (*C3*), 136.55 (*C5*); δ *[TES]*, 60.65 (*C4*), 60.53 (*C1-C3*), 51.74 (*C6*), 37.75 (*C5*); viscous liquid. |  [Emim][TES]: |

**Table S1** continued

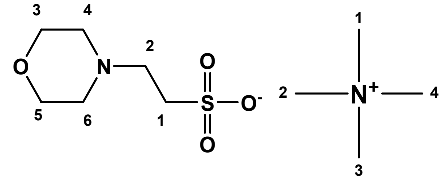
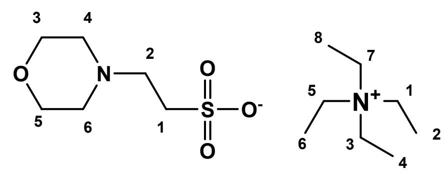
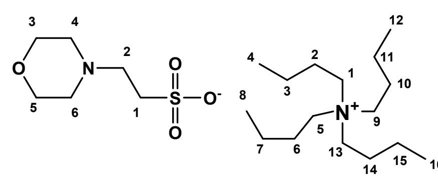
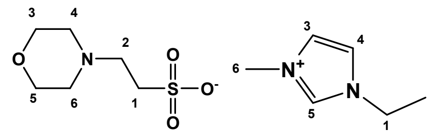
| | |
|---|---|
| **[$N_{1111}$][MES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 3.11(12H, *s*, C1-C4's *H*); δ *[MES]*, 2.47 (4H, *t*, C4C6's *H*), 2.71 (2H, *t*, C2's *H*), 2.98 (2H, *t*, C1's *H*), 3.63 (4H, *t*, C3C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 58.12 (*C1-C4*); δ *[MES]*, 50.15 (*C4C6*), 55.15 (*C2*), 55.48 (*C1*), 68.90 (*C3C5*); melting point = 127 °C. |  [$N_{1111}$][MES] |
| **[$N_{2222}$][MES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 3.21(8H, *q*, C1C3C5C7's *H*), 1.17 (12H, *m*, C2C4C6C8's *H* ); δ *[MES]*, 2.35 (4H, *t*, C4C6's *H*), 2.50 (2H, *t*, C2's *H*), 2.57 (2H, *t*, C1's *H*), 3.55 (4H, *t*, C3C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 54.81 (*C1C3C5C7*), 9.49 (*C2C4C6C8*); δ *[MES]*, 50.13 (*C4C6*), 54.72 (*C2*), 55.53 (*C1*), 68.87 (*C3C5*); melting point = 115 °C. |  [$N_{2222}$][MES] |
| **[$N_{4444}$][MES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{4444}$]*, 0.93 (12H, *t*, C4C8C12C16's *H*), 1.30 (8H, *sext*, C3C7C11C15's *H*), 1.55 (8H, *quin*, C2C6C10C14's *H*), 3.17 (8H, *t*, C1C5C9C13's *H*); δ *[MES]*, 2.32 (4H, *t*, C4C6's *H*), 2.49 (2H, *t*, C2's *H*), 2.51 (2H, *t*, C1's *H*), 3.53 (4H, *t*, C3C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 15.78 (*C4C8C12C16*), 22.07 (*C3C7C11C15*), 26.03 (*C2C6C10C14*), 61.00 (*C1C5C9C13*); δ *[MES]*, 50.19 (*C4C6*), 55.18 (*C2*), 55.53 (*C1*), 68.94 (*C3C5*); melting point = 92 °C. |  [$N_{4444}$][MES] |
| **[Emim][MES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 1.40 (3H, *t*, C2's *H*), 3.87 (3H, *s*, C6's *H* ), 4.20 (2H, *q*, C1's *H* ), 7.74 (1H, *s*, C4's *H* ), 7.83 (1H, *s*, C3's *H* ), 9.26 (1H, *s*, C5's *H*); δ *[MES]*, 2.40 (4H, *t*, C4C6's *H*), 2. 62 (2H, *t*, C2's *H*), 2.68 (2H, *t*, C1's *H*), 3.54 (42H, *t*, C3C5's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 15.22 (*C2*), 35.65 (*C6*), 44.10 (*C1*), 122.02 (*C4*), 123.59 (*C3*), 136.57 (*C5*); δ *[MES]*, 48.40 (*C4C6*), 53.06 (*C2*), 54.48 (*C1*), 65.91 (*C3C5*); viscous liquid. |  [Emim][MES] |

**Table S1** continued

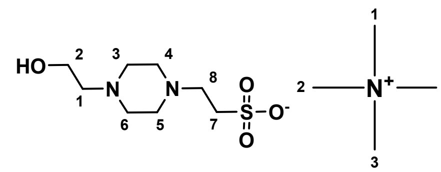
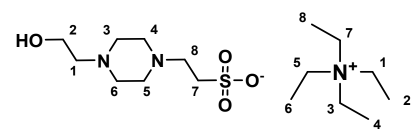
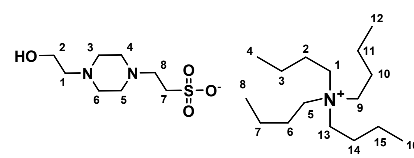
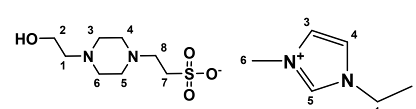
| | |
|---|---|
| **[$N_{1111}$][HEPES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 3.19(12H, *s*, C1-C4's *H*); δ *[HEPES]*, 2.35 (8H, *t*, C3C4C5C6's *H*), 2.50 (2H, *t*, C8's *H*), 2.55 (2H, *t*, C1's *H*), 2.61 (2H, *t*, C7's *H*), 3.46 (4H, *t*, C2's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 58.12 (*C1-C4*); δ *[HEPES]*, 50.45 (*C8*), 54.26 (*C4C5*), 54.83 (*C3C6*), 55.06 (*C1*), 60.97 (*C7*), 61.66 (*C2*); melting point = 156 °C. | <br>[$N_{1111}$][HEPES] |
| **[$N_{2222}$][HEPES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 3.22(8H, *q*, C1C3C5C7's *H*), 1.14(12H, *m*, C2C4C6C8's *H* ); *[HEPES]*, 2.33 (8H, *t*, C3C4C5C6's *H*), 2.50 (2H, *t*, C8's *H*), 2.54 (2H, *t*, C1's *H*), 2.60 (2H, *t*, C7's *H*), 3.45 (4H, *t*, C2's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 54.75 (*C1C3C5C7*), 9.48 (*C2C4C6C8*); δ *[HEPES]*, 50.46 (*C8*), 54.30 (*C4C5*), 54.71 (*C3C6*), 55.09 (*C1*), 61.00 (*C7*), 61.67 (*C2*); melting point = 70 °C. | <br>[$N_{2222}$][HEPES] |
| **[$N_{4444}$][HEPES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{4444}$]*, 0.93 (12H, *t*, C4C8C12C16's *H*), 1.33 (8H, *sext*, C3C7C11C15's *H*), 1.55 (8H, *quin*, C2C6C10C14's *H*), 3.17 (8H, *t*, C1C5C9C13's *H* ); *[HEPES]*, 2.34 (8H, *t*, C3C4C5C6's *H*), 2.50 (2H, *t*, C8's *H*), 2.54 (2H, *t*, C1's *H*), 2.61 (2H, *t*, C7's *H*), 3.46 (4H, *t*, C2's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 15.76 (*C4C8C12C16*), 22.06 (*C3C7C11C15*), 26.03 (*C2C6C10C14*), 60.97 (*C1C5C9C13*); δ *[HEPES]*, 50.45 (*C8*), 54.26 (*C4C5*), 54.83 (*C3C6*), 55.06 (*C1*), 60.97 (*C7*), 61.66 (*C2*); melting point = 102 °C. | <br>[$N_{4444}$][HEPES] |
| **[Emim][HEPES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 1.37 (3H, *t*, C2's *H*), 3.86 (3H, *s*, C6's *H* ), 4.20 (2H, *q*, C1's *H* ), 7.29 (1H, *s*, C4's *H* ), 7.80 (1H, *s*, C3's *H* ), 9.23 (1H, *s*, C5's *H*); *[HEPES]*, 2.33 (8H, *t*, C3C4C5C6's *H*), 2.50 (2H, *t*, C8's *H*), 2.55 (2H, *t*, C1's *H*), 2.63 (2H, *t*, C7's *H*), 3.45 (4H, *t*, C2's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 15.22 (*C2*), 35.66 (*C6*), 44.11 (*C1*), 122.01 (*C4*), 123.59 (*C3*), 136.51 (*C5*); δ *[HEPES]*, 48.98(*C8*), 52.65 (*C4C5*), 53.14 (*C3C6*), 54.18 (*C1*), 58.43 (*C7*), 60.25 (*C2*); viscous liquid. | <br>[Emim][HEPES] |

**Table S1** continued**.**

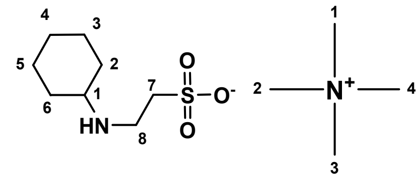
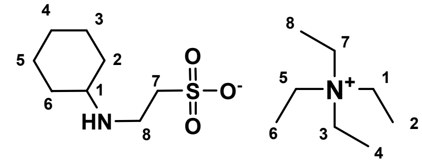
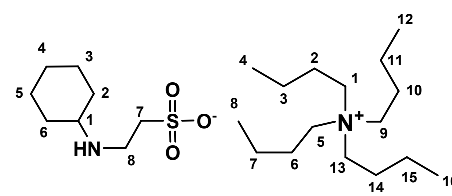
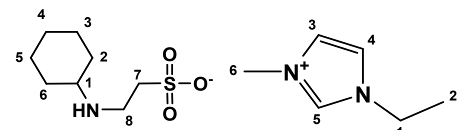
| | |
|---|---|
| **[$N_{1111}$][CHES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 3.10(12H, *s*, C1-C4's *H*); δ *[CHES]*, 0.95-1.79 (10H, *m*, C2-C6's *H*), 2.39-2.47 (H, *m*, C1's *H*), 2.57 (2H, *t*, C8's *H*), 2.82 (2H, *t*, C7's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{1111}$]*, 58.11 (*C1-C4*); δ *[CHES]*, 27.21 (*C3C5*), 28.26 (*C4*), 34.20 (*C2C6*), 43.28 (*C8*), 52.36 (*C7*), 58.60 (*C1*); melting point = 95 °C. |  [$N_{1111}$][CHES] |
| **[$N_{2222}$][CHES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 3.22(8H, *q*, C1C3C5C7's *H*), 1.16(12H, *m*, C2C4C6C8's *H* ); δ *[CHES]*, 0.97-1.78 (10H, *m*, C2-C6's *H*), 2.36-2.42 (H, *m*, C1's *H*), 2.54 (2H, *t*, C8's *H*), 2.80 (2H, *t*, C7's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 51.43 (*C1C3C5C7*), 7.12 (*C2C4C6C8*); δ *[CHES]*, 24.34 (*C3C5*), 25.81 (*C4*), 32.36 (*C2C6*), 42.58 (*C8*), 50.64 (*C7*), 55.86 (*C1*); melting point = 55 °C. |  [$N_{2222}$][CHES] |
| **[$N_{4444}$][CHES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[$N_{4444}$]*, 0.91 (12H, *t*, C4C8C12C16's *H*), 1.34 (8H, *sext*, C3C7C11C15's *H*), 1.57 (8H, *quin*, C2C6C10C14's *H*), 3.23 (8H, *t*, C1C5C9C13's *H*); δ *[CHES]*, 0.99-1.78 (10H, *m*, C2-C6's *H*), 2.39-2.44 (H, *m*, C1's *H*), 2.58 (2H, *t*, C8's *H*), 2.81 (2H, *t*, C7's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[$N_{2222}$]*, 13.30 (*C4C8C12C16*), 19.12 (*C3C7C11C15*), 23.12 (*C2C6C10C14*), 57.41 (*C1C5C9C13*); δ *[CHES]*, 24.23 (*C3C5*), 25.73 (*C4*), 32.22 (*C2C6*), 42.47 (*C8*), 50.43 (*C7*), 55.65 (*C1*); viscous liquid. |  [$N_{4444}$][CHES] |
| **[Emim][ CHES]:** $^{1}$H NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 1.39 (3H, *t*, C2's *H*), 3.87 (3H, *s*, C6's *H* ), 4.20 (2H, *q*, C1's *H* ), 7.77 (1H, *s*, C4's *H* ), 7.86 (1H, *s*, C3's *H* ), 9.30 (1H, *s*, C5's *H*); δ *[CHES]*, 0.95-1.79 (10H, *m*, C2-C6's *H*), 2.39-2.47 (H, *m*, C1's *H*), 2.57 (2H, *t*, C8's *H*), 2.82 (2H, *t*, C7's *H*). $^{13}$C NMR (300 MHz, $D_2O$/TSP); δ *[Emim]*, 15.24 (*C2*), 35.63 (*C6*), 44.11 (*C1*), 122.06 (*C4*), 123.61 (*C3*), 136.63 (*C5*); δ *[CHES]*, 24.34 (*C3C5*), 25.75 (*C4*), 32.02 (*C2C6*), 42.34 (*C8*), 50.47 (*C7*), 55.82 (*C1*); viscous liquid. |  [Emim][CHES] |

**Table S2** The mid-point pH, buffering pH range, and buffer capacity of the GB/GB-ILS in water.

| GB/GBILs | mid-point pH | buffering pH range[a] | buffer capacity[b] |
|---|---|---|---|
| Tricine | 8.3 | 6.8–9.42 | 0.040 |
| $[N_{1111}]$[Tricine] | 8.0 | 6.3–10.2 | 0.040 |
| $[N_{2222}]$[Tricine] | 8.2 | 6.3–10.2 | 0.036 |
| $[N_{4444}]$[Tricine] | 7.9 | 6.7–10.0 | 0.035 |
| [Emim][Tricine] | 8.0 | 6.3–10.3 | 0.018 |
| TES | 7.4 | 6.1–9.1 | 0.022 |
| $[N_{1111}]$[TES] | 7.8 | 6.2– 9.1 | 0.040 |
| $[N_{2222}]$[TES] | 7.2 | 5.6–9.3 | 0.023 |
| $[N_{4444}]$[TES] | 7.4 | 5.8–9.1 | 0.025 |
| [Emim][TES] | 7.4 | 5.7–9.2 | 0.021 |
| CHES | 9.3 | 7.5–10.7 | 0.019 |
| $[N_{1111}]$[CHES] | 9.4 | 7.5–10.9 | 0.024 |
| $[N_{2222}]$[CHES] | 9.4 | 7.7–10.9 | 0.024 |
| $[N_{4444}]$[CHES] | 9.4 | 7.7–10.9 | 0.026 |
| [Emim][CHES] | 9.3 | 7.7–10.9 | 0.026 |
| HEPES | 7.5 | 5.0–9.5 | 0.024 |
| $[N_{1111}]$[HEPES] | 7.4 | 5.7–9.8 | 0.035 |
| $[N_{2222}]$[HEPES] | 7.4 | 5.5–9.6 | 0.025 |
| $[N_{4444}]$[HEPES] | 7.3 | 5.5–9.7 | 0.026 |
| [Emim][HEPES] | 7.4 | 5.6–9.3 | 0.021 |
| MES | 6.0 | 3.6–7.9 | 0.016 |
| $[N_{1111}]$[ MES] | 6.0 | 4.4–8.3 | 0.036 |
| $[N_{2222}]$[MES] | 6.0 | 4.1–8.6 | 0.028 |
| $[N_{4444}]$[MES] | 6.0 | 4.1–8.7 | 0.026 |
| [Emim][MES] | 6.0 | 4.1–8.2 | 0.022 |

[a] The buffer offers significant buffering capacity when the solution pH is within ~ 1 unit of the mid-point pH ($pKa_2$).

[b] Buffer capacity is a measure of a buffer's ability to resist change in pH upon the addition of acid or base; and mathematically, buffer capacity (β) is defined as $\beta = {dC_b}/{d(pH)} = -{dC_a}/{d(pH)}$ , where $C_b$ and $C_b$, are the number of moles of strong base or acid added *per* liter.

**Table S3** Experimental mass fraction data for the binodal curve of the system composed of $[N_{4444}][GB]$ (1) + $C_6H_5K_3O_7$ (2) at (25 ± 1) °C.

| $[N_{4444}][TES]$ | | $[N_{4444}][MES]$ | | $[N_{4444}][HEPES]$ | | $[N_{4444}][CHES]$ | | $[N_{4444}][Tricine]$ | |
|---|---|---|---|---|---|---|---|---|---|
| 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ |
| 60.62 | 3.52 | 61.41 | 2.80 | 55.73 | 3.41 | 57.57 | 4.36 | 48.25 | 8.58 |
| 56.12 | 4.11 | 56.72 | 3.59 | 49.48 | 4.86 | 49.80 | 5.49 | 44.65 | 10.77 |
| 54.16 | 4.89 | 52.42 | 4.03 | 46.29 | 6.39 | 45.08 | 6.43 | 43.34 | 11.58 |
| 47.72 | 7.15 | 49.63 | 5.01 | 43.76 | 7.68 | 42.48 | 7.36 | 42.13 | 12.25 |
| 44.94 | 8.47 | 47.38 | 5.82 | 42.00 | 8.25 | 40.44 | 8.24 | 41.06 | 12.75 |
| 40.14 | 11.29 | 44.34 | 6.60 | 39.30 | 9.61 | 37.89 | 8.72 | 39.84 | 13.55 |
| 35.20 | 14.39 | 41.60 | 7.29 | 37.17 | 10.65 | 35.73 | 9.35 | 38.19 | 14.61 |
| 29.83 | 18.17 | 40.54 | 7.87 | 34.78 | 12.08 | 34.68 | 9.91 | 36.27 | 15.77 |
| 27.20 | 20.03 | 37.77 | 8.34 | 33.39 | 12.92 | 32.72 | 10.85 | 34.61 | 16.77 |
| 23.30 | 23.02 | 34.77 | 9.99 | 31.37 | 14.11 | 29.99 | 11.62 | 33.14 | 17.79 |
| 21.97 | 24.03 | 33.04 | 10.90 | 29.21 | 15.53 | 27.23 | 13.33 | 32.16 | 18.18 |
| 20.38 | 26.10 | 29.86 | 12.80 | 28.41 | 15.96 | 25.60 | 13.51 | 31.75 | 18.34 |
| 18.06 | 27.81 | 28.50 | 13.72 | 26.25 | 17.69 | 24.14 | 13.97 | 31.01 | 18.84 |
| 15.67 | 38.63 | 27.12 | 14.52 | 24.96 | 18.43 | 23.17 | 14.39 | 29.98 | 19.63 |
| | | 25.69 | 15.49 | 24.17 | 18.97 | 22.09 | 15.10 | 28.11 | 21.00 |
| | | 24.66 | 16.11 | 22.59 | 20.27 | 21.36 | 15.54 | 26.48 | 22.20 |
| | | 23.42 | 17.22 | 20.90 | 21.42 | 20.35 | 15.54 | 25.92 | 22.54 |
| | | 22.47 | 17.81 | 19.64 | 22.13 | 19.41 | 16.13 | 25.21 | 23.03 |
| | | 21.80 | 18.56 | 18.45 | 23.13 | 18.05 | 17.05 | 24.42 | 23.66 |
| | | 21.06 | 19.11 | 17.07 | 24.15 | 17.35 | 16.85 | 23.48 | 24.34 |
| | | | | 16.34 | 24.77 | 16.02 | 17.82 | 22.94 | 24.70 |
| | | | | 15.23 | 25.75 | 15.06 | 18.08 | 22.34 | 25.18 |
| | | | | 14.43 | 26.20 | 14.39 | 18.39 | 21.89 | 25.45 |
| | | | | 14.24 | 26.26 | 13.95 | 18.40 | 21.31 | 25.90 |
| | | | | 13.03 | 27.32 | 13.43 | 18.83 | 20.79 | 26.30 |
| | | | | 12.22 | 28.06 | 12.74 | 19.24 | 19.89 | 26.92 |
| | | | | 11.56 | 28.59 | 12.04 | 19.63 | 18.97 | 27.64 |
| | | | | 11.00 | 29.07 | 11.55 | 19.88 | 18.51 | 28.06 |
| | | | | 10.58 | 29.50 | 10.94 | 20.06 | 18.34 | 28.15 |
| | | | | 10.03 | 29.82 | 10.23 | 20.36 | 17.79 | 28.59 |
| | | | | 9.77 | 30.11 | 9.72 | 21.06 | 17.05 | 29.15 |
| | | | | 9.37 | 30.61 | 9.05 | 22.12 | 16.31 | 29.74 |
| | | | | | | 8.29 | 21.34 | 15.76 | 30.14 |
| | | | | | | 8.14 | 21.37 | 15.25 | 30.54 |
| | | | | | | 8.08 | 21.54 | 14.62 | 31.07 |
| | | | | | | 7.63 | 21.75 | 14.10 | 31.48 |
| | | | | | | 7.48 | 21.91 | 13.52 | 31.96 |
| | | | | | | 7.14 | 22.76 | 12.86 | 32.52 |
| | | | | | | 6.92 | 23.05 | 12.23 | 33.02 |
| | | | | | | 6.70 | 23.16 | 12.01 | 33.18 |
| | | | | | | 6.37 | 23.66 | 11.65 | 33.49 |
| | | | | | | 6.07 | 23.64 | 11.50 | 33.63 |
| | | | | | | 5.88 | 24.08 | 11.16 | 33.90 |
| | | | | | | | | 10.50 | 34.50 |
| | | | | | | | | 9.94 | 35.01 |
| | | | | | | | | 9.50 | 35.38 |
| | | | | | | | | 9.13 | 35.75 |
| | | | | | | | | 8.61 | 36.24 |
| | | | | | | | | 8.09 | 36.70 |
| | | | | | | | | 7.76 | 36.99 |
| | | | | | | | | 7.35 | 37.39 |
| | | | | | | | | 7.14 | 37.63 |
| | | | | | | | | 6.78 | 37.96 |
| | | | | | | | | 6.50 | 38.21 |

**Table S4** Experimental mass fraction data for the binodal curve of the system composed of $[N_{4444}][GB]$ (1) $+Na_2SO_4$ (2) at (25 ± 1) °C.

| $[N_{4444}]$[Tricine] | | | | $[N_{4444}]$[MES] | | | |
|---|---|---|---|---|---|---|---|
| 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ | 100 $w_1$ | 100 $w_2$ |
| 30.37 | 7.33 | 11.50 | 17.20 | 46.84 | 1.41 | 18.61 | 9.70 |
| 28.87 | 7.86 | 10.99 | 17.53 | 44.39 | 2.07 | 18.04 | 10.01 |
| 28.12 | 8.15 | 10.53 | 17.83 | 41.18 | 2.50 | 17.54 | 10.29 |
| 26.86 | 8.74 | 10.07 | 18.14 | 36.53 | 3.43 | 17.04 | 10.55 |
| 25.79 | 9.21 | 9.59 | 18.46 | 34.35 | 3.78 | 16.55 | 10.81 |
| 24.54 | 9.79 | 9.15 | 18.77 | 32.33 | 4.06 | 15.96 | 11.19 |
| 23.37 | 10.32 | 8.79 | 19.00 | 31.13 | 4.41 | | |
| 22.15 | 10.95 | 8.46 | 19.24 | 30.03 | 4.78 | | |
| 20.91 | 11.58 | 8.05 | 19.54 | 28.99 | 5.13 | | |
| 19.68 | 12.30 | 7.72 | 19.78 | 26.80 | 6.07 | | |
| 18.58 | 12.90 | 7.38 | 20.03 | 25.26 | 6.52 | | |
| 17.42 | 13.58 | 7.14 | 20.21 | 24.23 | 7.04 | | |
| 16.65 | 14.02 | 6.85 | 20.43 | 23.58 | 7.23 | | |
| 15.69 | 14.62 | 6.43 | 20.74 | 22.65 | 7.72 | | |
| 14.85 | 15.11 | 6.06 | 21.03 | 22.10 | 7.88 | | |
| 14.12 | 15.50 | 5.49 | 21.52 | 21.27 | 8.29 | | |
| 13.27 | 16.07 | 5.05 | 21.92 | 20.53 | 8.68 | | |
| 12.62 | 16.50 | 4.26 | 22.68 | 19.86 | 9.03 | | |
| 12.13 | 16.80 | | | 19.20 | 9.38 | | |

**Table S5.** Correlation parameters used to describe the experimental binodal data by Eq. 1[a] and respective standard deviations ($\sigma$) and correlation coefficients

| IL | $A \pm \sigma$ | $B \pm \sigma$ | $10^5 (C \pm \sigma)$ | $R^2$ |
|---|---|---|---|---|
| $[N_{4444}]$[TES] | 96.0 ± 2.0 | -0.256 ± 0.008 | 1.47 ± 0.18 | 0.99863 |
| $[N_{4444}]$[Tricine] | 83.3 ± 1.1 | -0.185 ± 0.004 | 2.41 ± 0.01 | 0.99262 |
| $[N_{4444}]$[HEPES] | 87.7 ± 0.7 | -0.250 ± 0.003 | 2.92 ± 0.05 | 0.99964 |

[a] $[IL] = A \times \exp\left(B[salt]^{0.5} - [salt]^{3}\right)$ (1); where [IL] and [salt] are the IL and salt weight percentages, respectively. The coefficients $A$, $B$, and $C$ are adjustable parameters obtained by the regression.

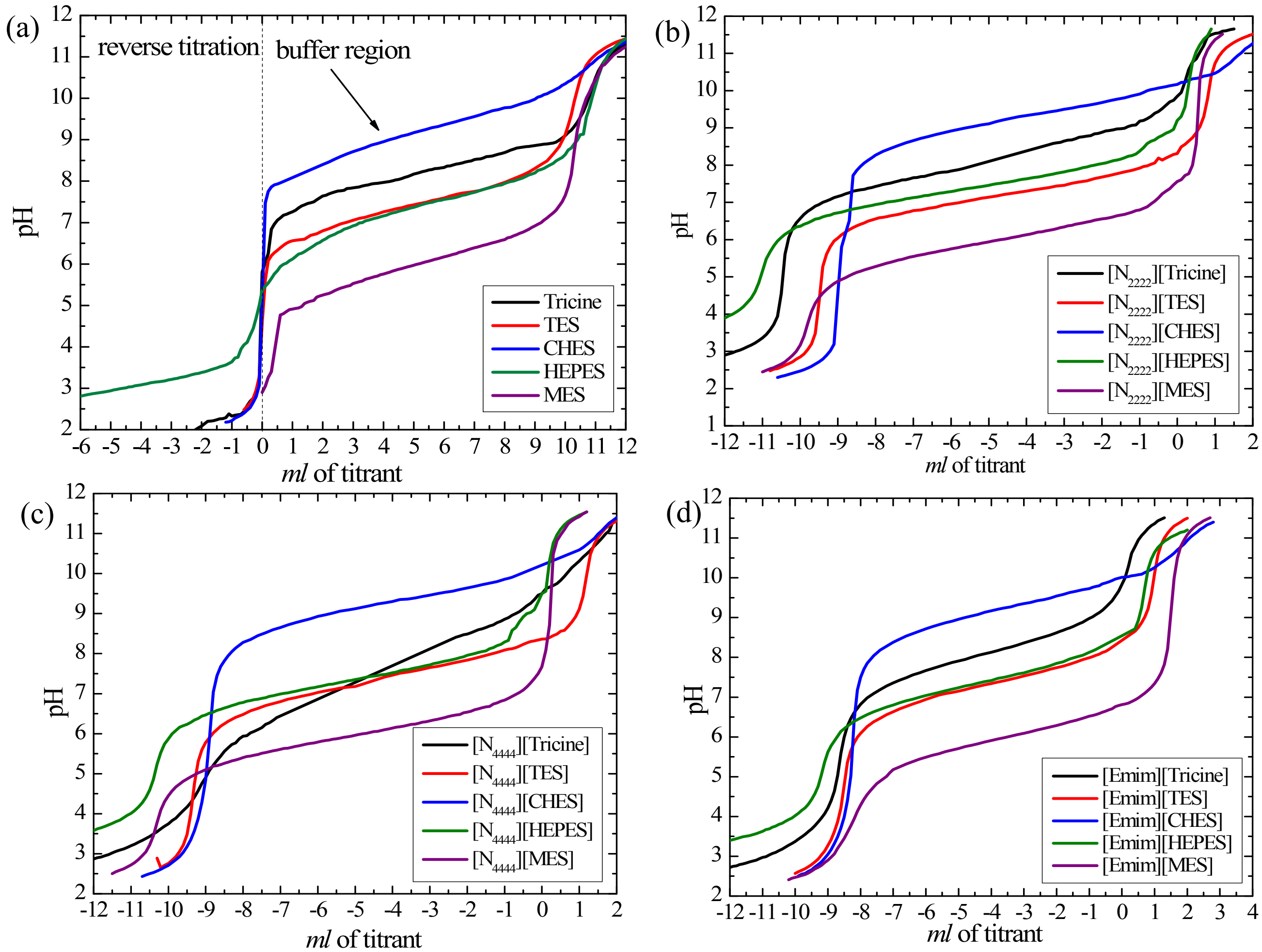



**Figure S1.** The pH profiles of the investigated GB/GB-ILs in water at 20 °C. 10 ml of 0.05 M GB/GB-ILs titrated with 0.05 M HCl/NaOH; (a) GB, (b) $[N_{2222}]$[GB], (c) $[N_{4444}]$[GB], and (d) [Emim][GB] . The (-1 mL) entries correspond to the volumes of 0.05 M HCl that needed to lower the pH, and we call the addition of acid a reverse titration.

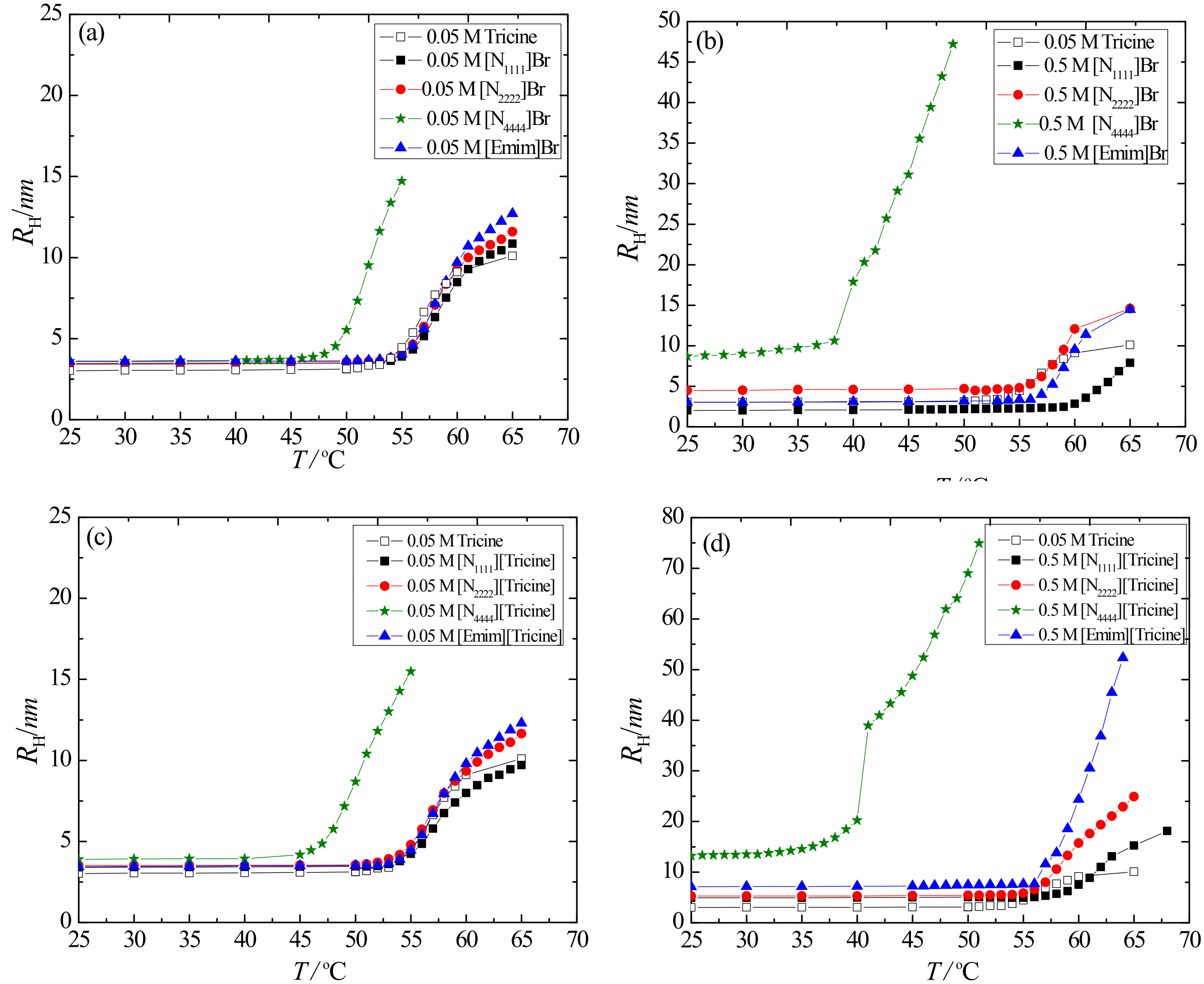



**Figure S2.** The hydrodynamic radius of BSA in 0.05 tetralkylammonium/Emim bromide (a), 0.5 M tetralkylammonium/ Emim bromide (b), 0.05 M GB-ILs (c), and 0.5 M GB-ILs (d), as a function of temperature at pH 7.4.

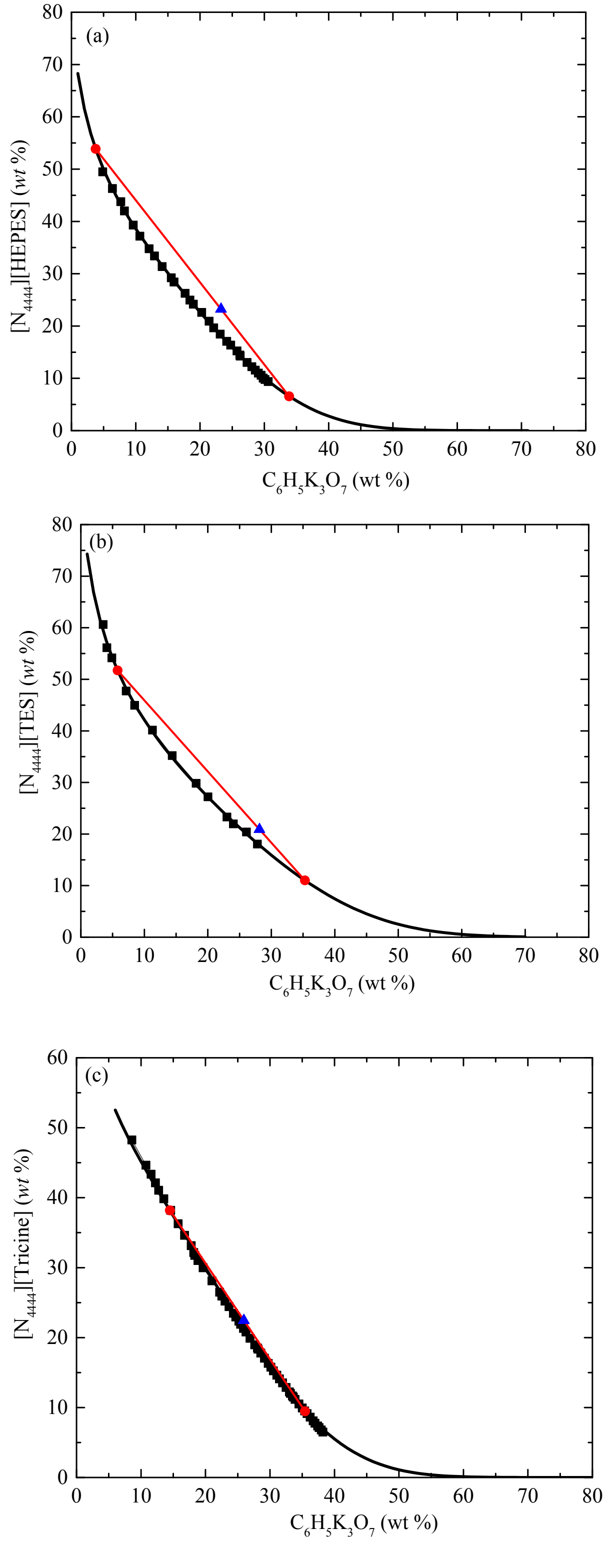



**Fig. S3.** Phase diagrams for the ternary systems composed of (a) $[N_{4444}]$[TES] + $C_6H_5K_3O_7$, (b) $[N_{4444}]$[HEPES] + $C_6H_5K_3O_7$, and (c) $[N_{4444}]$[Tricine] + $C_6H_5K_3O_7$, at 25 ± 1 °C; (◷) weight fraction compositions (wt.%), (◘) initial mixture composition, and (⬲) TL data, (—) binodal adjusted data through Eq.(1), $[IL] = A \times \exp\left(B[salt]^{0.5} - [salt]^{3}\right)$.