Cofactor-dependent enzyme catalysis in functionalized ionic solvents

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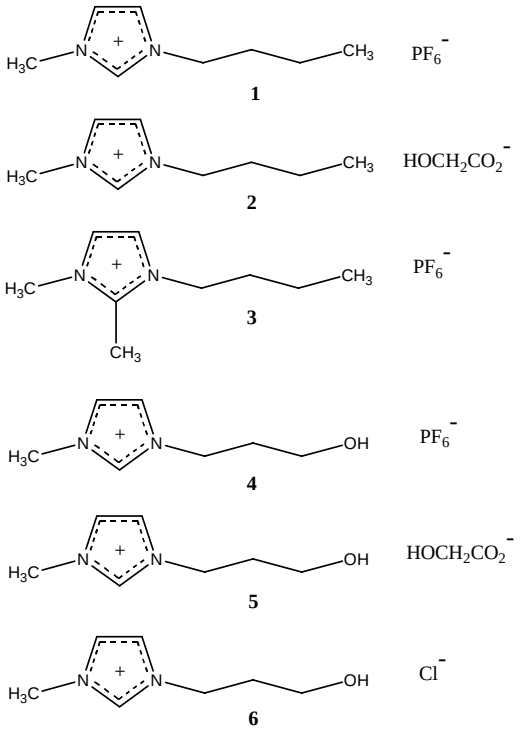
Electronic Supporting Information

i.) Structures and analytical data for novel ionic liquids (**2** and **4**-**6**)



2: NMR [^{1}H, 400 MHz, d_6-DMSO, δ(ppm)]: 0.88 (t, 3H, *J* = 10 Hz, δ-C<u>H</u>$_3$), 1.23 (h, 2H, *J* = 20 Hz, γ-C<u>H</u>$_2$), 1.75 (p, 2H, *J* = 12 Hz, β-C<u>H</u>$_2$), 3.46 (s, 2H, HOC<u>H</u>$_2$), 3.85 (s, 3H, *N*-C<u>H</u>$_3$), 4.17 (t, 2H, *J* = 6 Hz, α-C<u>H</u>$_2$), 4.35 (br. s, 1H, removed by D_2O shake, CH_2O<u>H</u>). 7.75 (d, 1H, *J* = 2 Hz, 4-<u>H</u>), 7.67 (d, 1H, *J* = 2 Hz, 5-<u>H</u>), 9.43 (br, 1H, reduced by D_2O shake, 2-<u>H</u>).
FT-IR [ATR, cm^{-1}]: 3373, 3063, 1169, 1568, 2960, 1464, 753, 1361.

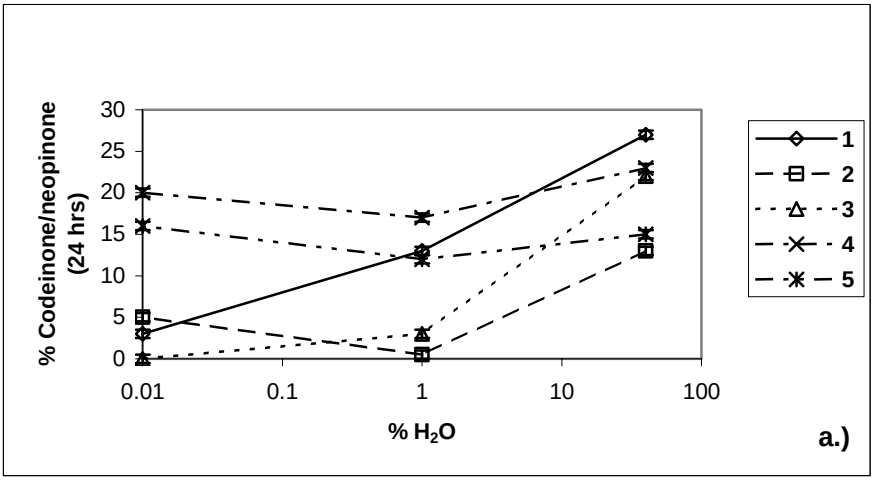
4: NMR [^{1}H, 400 MHz, d_6-DMSO, δ(ppm)]: 1.92 (p, 2H, *J* = 16 Hz, β-C<u>H</u>$_2$), 3.40 (t, 2H, *J* = 5 Hz, α-C<u>H</u>$_2$), 3.80 (s, 1H, removed by D_2O shake, CH_2O<u>H</u>), 3.83 (s, 3H, *N*-C<u>H</u>$_3$), 4.21 (t, 2H, *J* = 8 Hz, γ-C<u>H</u>$_2$), 7.65 (br. d, 1H, 4-<u>H</u>), 7.72 (br. d, 1H, 5-<u>H</u>), 9.13 (s, 1H, 2-<u>H</u>).
FT-IR [ATR, cm^{-1}]: 871, 3382, 1167, 1576, 2963, 559, 624, 1464, 742, 1340.

5: NMR [^{1}H, 400 MHz, d_6-DMSO, δ (ppm)]: 1.92 (p, 2H, *J* = 16 Hz, β-C<u>H</u>$_2$), 2.0 (br. s, 1H <u>H</u>OC$H_2CO_2^-$), 3.40 (t, 2H, J = 5 Hz, α-C<u>H</u>$_2$), 3.52 (s, 2H, C<u>H</u>$_2$CO_2^-), 3.75 (br. s, 1H, removed by D_2O

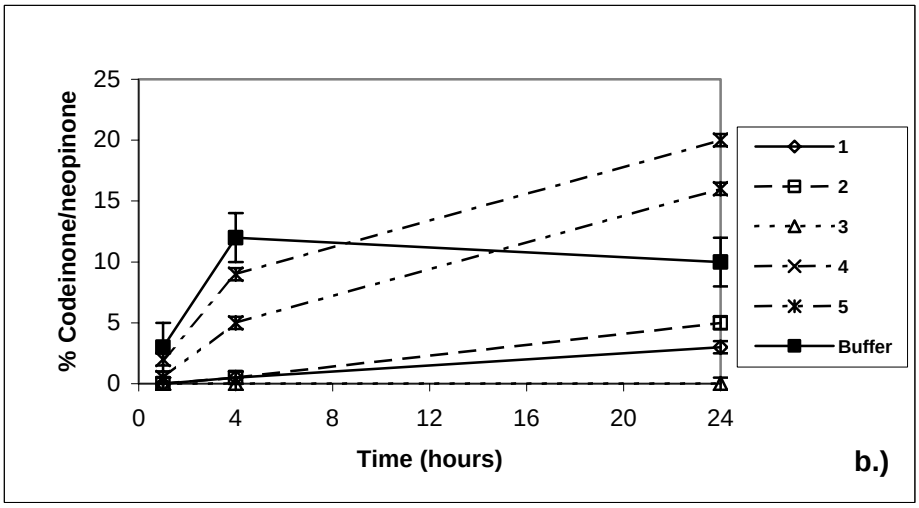
shake, $CH_2O\underline{H}$), 3.83 (s, 3H, *N*-$C\underline{H_3}$), 4.21 (t, 2H, *J* = 8 Hz, γ-$C\underline{H_2}$), 7.65 (br. d, 1H, 4-$\underline{H}$), 7.72 (br. d, 1H, 5-H), 9.13 (s, 1H, 2-$\underline{H}$).
FT-IR [ATR, cm^{-1}]: 1731, 1634, 1576, 3390, 1167, 871, 1061, 1088, 1228

6: NMR [^1H, 400 MHz, d_6-DMSO, δ(ppm)]: 1.85 (p, 2H, *J* = 16 Hz, β-$C\underline{H_2}$), 3.36 (t, 2H, *J* = 5 Hz, α-$C\underline{H_2}$), 3.80 (s, 1H, removed by D_2O shake, $CH_2O\underline{H}$), 3.83 (s, 3H, *N*-$C\underline{H_3}$), 4.18 (t, 2H, *J* = 8 Hz, γ-$C\underline{H_2}$), 7.70 (br. d, 1H, 4-$\underline{H}$), 7.78 (br. d, 1H, 5-$\underline{H}$), 9.38 (s, 1H, reduced by D_2O shake, 2-$\underline{H}$).

ii.) Reaction plots

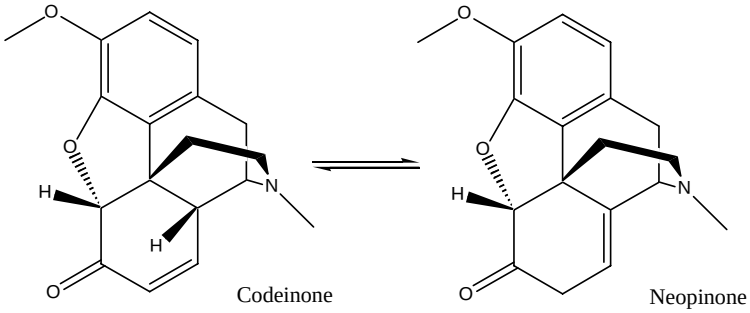


a.) Effect of varying water content on level of accumulated codeinone/neopinone produced from codeine by morphine dehydrogenase after 24 hours in ionic liquids **1**-**5**. Cofactor recycling was elicited using alcohol dehydrogenase in **1**-**3**, glucose dehydrogenase in **4** & **5**.



b.) Accumulation of codeinone/neopinone produced from codeine by morphine dehydrogenase in ionic liquids **1**-**5** and phosphate buffer. RTIL water content < 100 ppm. Cofactor recycling as above.

iii.) Product analytical data



Codeinone: NMR [^{1}H, 400 MHz, $CDCl_3$, δ(ppm)]: 1.81 (d, 1H, *J* = 13 Hz, 15α-H), 2.03 (t, 1H, *J* = 10 Hz, 15β-H), 2.28 (m, 2H, 16-H_2), 2.42 (s, 3H, *N*-CH_3), 2.57 (d, 1H, *J* = 16 Hz, 10α-H), 3.08 (d, 1H, *J* = 26 Hz, 10β-H), 3.16 (s, 1H, 9-H), 3.38 (s, 1H, 14-H), 3.81 (s, 3H, 3-*O*-CH_3), 4.67 (s, 1H, 5-H), 6.05 (d, 1H, *J* = 14 Hz, 7-H), 6.59 (d, 1H, *J* = 17 Hz, 2-H), 6.63 (m, 2H, 1-H + 8-H).
FT-IR [KBr, cm^{-1}]: 1670 (C=O stretch), 1271, 1501, 1057, 800, 1238, 936, 1436, 1028.

Neopinone: NMR [^{1}H, 400 MHz, $CDCl_3$, δ(ppm)]: 1.88 (t, 1H, *J* = 15 Hz, 15α-H), 1.92 (tt, 1H, *J* = 10 Hz, 15β-H), 2.31 (m, 2H, 16-H_2), 2.48 (s, 3H, *N*-CH_3), 2.77 (d, 1H, *J* = 6 Hz, 10α-H), 3.27 (d, 1H, *J* = 10 Hz, 10β-H), 3.33 (br. s, 1H, 7α-H), 3.64 (d, 1H, *J* = 6 Hz, 9-H), 3.91 (s, 3H, 3-*O*-CH_3), 3.95 (d, 1H, *J* = 15 Hz, 7β-H), 5.00 (s, 1H, 5-H), 5.50 (d, 1H, *J* = 5 Hz, 8-H), 6.69 (d, 1H, *J* = 8 Hz, 2-H), 6.72 (d, 1H, *J* = 8 Hz, 1-H).
FT-IR [ATR, cm^{-1}]: 1051, 1256, 750, 1440, 1504, 1155, 1730 (C=O stretch), 1607.