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 \([\H, 400 \text{ MHz, } d_6-\text{DMSO, } \delta(\text{ppm})]\): 0.88 (t, 3H, \(J = 10 \text{ Hz, } \delta-\text{CH}_3\)), 1.23 (h, 2H, \(J = 20 \text{ Hz, } \gamma-\text{CH}_2\)), 1.75 (p, 2H, \(J = 12 \text{ Hz, } \beta-\text{CH}_2\)), 3.46 (s, 2H, HOCH\(_2\)), 3.85 (s, 3H, N-CH\(_3\)), 4.17 (t, 2H, \(J = 6 \text{ Hz, } \alpha-\text{CH}_2\)), 4.35 (br. s, 1H, removed by D\(_2\)O shake, CH\(_2\)OH), 7.75 (d, 1H, \(J = 2 \text{ Hz, } 4-\text{H}\)), 7.67 (d, 1H, \(J = 2 \text{ Hz, } 5-\text{H}\)), 9.43 (br, 1H, reduced by D\(_2\)O shake, 2-H).

FT-IR [ATR, cm\(^{-1}\)]: 3373, 3063, 1169, 1568, 2960, 1464, 753, 1361.

4: NMR \([\H, 400 \text{ MHz, } d_6-\text{DMSO, } \delta(\text{ppm})]\): 1.92 (p, 2H, \(J = 16 \text{ Hz, } \beta-\text{CH}_2\)), 3.40 (t, 2H, \(J = 5 \text{ Hz, } \alpha-\text{CH}_2\)), 3.80 (s, 1H, removed by D\(_2\)O shake, CH\(_2\)OH), 3.83 (s, 3H, N-CH\(_3\)), 4.21 (t, 2H, \(J = 8 \text{ Hz, } \gamma-\text{CH}_2\)), 7.65 (br. d, 1H, 4-H), 7.72 (br. d, 1H, 5-H), 9.13 (s, 1H, 2-H).

FT-IR [ATR, cm\(^{-1}\)]: 871, 3382, 1167, 1576, 2963, 559, 624, 1464, 742, 1340.

5: NMR \([\H, 400 \text{ MHz, } d_6-\text{DMSO } \delta(\text{ppm})]\): 1.92 (p, 2H, \(J = 16 \text{ Hz, } \beta-\text{CH}_2\)), 3.40 (t, 2H, \(J = 5 \text{ Hz, } \alpha-\text{CH}_2\)), 3.80 (s, 1H, removed by D\(_2\)O shake, CH\(_2\)OH), 3.83 (s, 3H, N-CH\(_3\)), 4.21 (t, 2H, \(J = 8 \text{ Hz, } \gamma-\text{CH}_2\)), 7.65 (br. d, 1H, 4-H), 7.72 (br. d, 1H, 5-H), 9.13 (s, 1H, 2-H).

FT-IR [ATR, cm\(^{-1}\)]: 871, 3382, 1167, 1576, 2963, 559, 624, 1464, 742, 1340.
shake, CH$_2$OH), 3.83 (s, 3H, N-CH$_3$), 4.21 (t, 2H, $J$ = 8 Hz, $\gamma$-CH$_2$), 7.65 (br. d, 1H, 4-H), 7.72 (br. d, 1H, 5-H), 9.13 (s, 1H, 2-H).

FT-IR [ATR, cm$^{-1}$]: 1731, 1634, 1576, 3390, 1167, 871, 1061, 1088, 1228.

6: NMR [$^1$H, 400 MHz, $d_6$-DMSO, $\delta$(ppm)]: 1.85 (p, 2H, $J$ = 16 Hz, $\beta$-CH$_2$), 3.36 (t, 2H, $J$ = 5 Hz, $\alpha$-CH$_2$), 3.80 (s, 1H, removed by D$_2$O shake, CH$_2$OH), 3.83 (s, 3H, N-CH$_3$), 4.18 (t, 2H, $J$ = 8 Hz, $\gamma$-CH$_2$), 7.70 (br. d, 1H, 4-H), 7.78 (br. d, 1H, 5-H), 9.38 (s, 1H, reduced by D$_2$O shake, 2-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 [1H, 400 MHz, CDCl₃, 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-CH₂), 2.42 (s, 3H, N-CH₃), 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-CH₃), 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 [1H, 400 MHz, CDCl₃, 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-CH₂), 2.48 (s, 3H, N-CH₃), 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-CH₃), 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.