Supplementary Information

The Design and Synthesis of Biodegradable Pyridinium Ionic Liquids

Jitendra R. Harjani, Robert D. Singer, M. Teresa Garcia and Peter J. Scammells

Medicinal Chemistry and Drug Action, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville 3052, Australia. Fax: +61 3 99039582; Tel: +61 3 9903 9542; E-mail: peter.scammells@vcp.monash.edu.au

Department of Chemistry, Saint Mary's University, Halifax, Nova Scotia, B3H 3C3 Canada

Department of Surfactant Technology, IIQAB-CSIC, Jordi Girona 18-26, 08034, Spain. Fax: +34 93 204 5904; Tel: +34 93 400 6100; E-mail: mtgbet@iiqab.csic.es

1-(2-Ethoxycarbonyl)methylpyridinium bromide (1a)

Ethyl bromoacetate (3.52 g, 40.0 mmol) was added to the solution of pyridine (2.63 g, 33.3 mmol) in toluene (20 mL) at 0 °C in an inert atmosphere. The reaction mixture was stirred at room temperature for 1 h and then heated at 70 °C for 24 h. A dense liquid layer separated from the reaction mixture. The quaternary salt was isolated by decanting the toluene layer to remove any unreacted starting material and solvent, and subsequently washing it with diethyl ether (2 × 20 mL), during which time the liquid solidified. The bromide salt was purified by dissolving it in acetonitrile (20 mL) and precipitation with diethyl ether (60–70 mL). It was separated by filtration and dried in a vacuum.
desiccator at reduced pressure to remove the volatile solvents. Yield 89%. $^1$H NMR (DMSO $d_6$): $\delta$
1.24–1.29 (t, $J = 7.2$ Hz, 3H), 4.21–4.28 (q, $J = 7.1$ Hz, 2H), 5.68 (s, 2H), 8.23–8.27 (m, 2H), 8.70–
8.75 (m, 1H), 9.05–9.07 (m, 2H). $^{13}$C NMR (DMSO $d_6$): $\delta$ 13.9, 60.2, 62.2, 127.7, 146.2, 146.7, 166.3.
MS (ESI, 20 eV): $m/z$, 166.1 [M–Br$^-$]$^+$; MS (ESI, 70 eV): $m/z$, 79 and 81 [Br$^-$].

3-(Butoxycarbonyl)-1-methylpyridinium iodide (2a)

A solution of butyl nicotinate (5.97 g, 33.3 mmol) in toluene (20 mL) was treated with iodomethane
(5.68 g, 40.0 mmol) under nitrogen atmosphere. The reaction mixture was heated at 45 °C for 24 h,
while being stirred in an inert atmosphere. A dense yellow liquid layer separated from the homogenous
solution of reactants. The toluene layer was decanted to separate the unreacted starting materials and
solvent from the product. The dense liquid solidified as it was washed with diethyl ether (2 × 20 mL).
The quaternary salt dissolved in acetonitrile (20 mL) and precipitated with diethyl ether (60–70 mL).
The purified iodide (a yellow solid) was collected by filtration and dried at low pressure in a vacuum
desiccator. Yield 98%. $^1$H NMR (DMSO $d_6$): $\delta$ 0.92–0.97 (t, $J = 7.4$ Hz, 3H), 1.39–1.52 (m, 2H),
1.70–1.79 (m, 2H), 4.39–4.45 (m, 5H), 8.24–8.29 (m, 1H), 8.95–8.98 (m, 1H), 9.19–9.21 (m, 1H), 9.52
(s, 1H). $^{13}$C NMR (DMSO $d_6$): $\delta$ 13.4, 18.4, 29.9, 48.4, 66.0, 127.8, 129.2, 144.6, 146.5, 148.7, 161.6.
MS (ESI, 20 eV): $m/z$ 194.0 (M–I$^-$)$^+$; MS (ESI, 70 eV): $m/z$, 126.8 [I$^-$].

General Procedure for the Preparation of Pyridinium octyl sulfates (1b, 2b, 2c, 3)

The quaternary halide salts are precursors to the syntheses of the corresponding octyl sulfate based ILs.
The method for the syntheses of quaternary alkylsulfates 1b, 2b, 2c and 3 was adapted from an earlier
report with minor modifications. Compound 1b was synthesized by using less than the stoichiometric
quantities of sodium octyl sulfate, which is recommended in the reported procedure. The synthesis of
2b, 2c and 3 was achieved by employing equimolar quantities of sodium octyl sulfate and alkyl halides. The general procedure is as follows; the quaternary halide (20 mmol) was dissolved in water (20 mL) and the resultant solution was treated with sodium octyl sulfate (15.4–20.0 mmol). The reaction mixture was stirred for 10 min to produce a clear solution. The quaternary octyl sulfate was obtained from the aqueous solution by extraction with dichloromethane (3 × 20 mL). The combined extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure to yield the corresponding octyl sulfate ionic liquid.

1-(2-Ethoxycarbonyl)methylpyridinium octyl sulfate (1b)

Yield 83%. $^1$H NMR (DMSO $d_6$): $\delta$ 0.84–0.88 (t, $J = 5.7$ Hz, 3H), 1.25–1.29 (m, 12H), 1.45–1.47 (m, 2H), 3.65–3.69 (t, $J = 6.8$ Hz, 3H), 4.21–4.28 (q, $J = 7.1$ Hz, 2H), 5.65 (s, 2H), 8.22–8.27 (m, 2H), 8.69–8.74 (m, 1H), 9.02–9.05 (m, 2H). $^{13}$C NMR (DMSO $d_6$): $\delta$ 13.9, 22.0, 25.5, 28.6, 28.7, 29.0, 31.2, 60.3, 62.3, 65.4, 127.8, 146.3, 146.7, 166.3. MS (ESI, 20 eV): $m/z$, 166.1 [M–C$_8$H$_{17}$OSO$_3$]$^+$; MS (ESI, 20 eV): $m/z$, 209.1 [C$_8$H$_{17}$OSO$_3$]$^+$. 
3-(Butoxycarbonyl)-1-methylpyridinium octyl sulfate (2b)

Yield 100%. $^1$H NMR (CDCl$_3$): $\delta$ 0.85–0.90 (t, $J = 6.5$ Hz, 3H), 0.97–1.02 (t, $J = 7.4$ Hz, 3H), 1.26–1.35 (m, 10H), 1.42–1.66 (m, 4H), 1.76–1.86 (m, 2H), 3.91–3.96 (t, $J = 6.9$ Hz, 2H), 4.43–4.48 (t, $J = 6.8$ Hz, 2H), 4.72 (s, 3H), 8.24–8.29 (m, 1H), 8.88–8.91 (m, 1H), 9.26 (s, 1H), 9.59–9.61 (m, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$ 13.8, 19.2, 22.8, 25.5, 28.6, 28.7, 29.0, 30.0, 31.2, 32.7, 60.9, 65.4, 66.1, 128.4, 130.7, 144.8, 146.5, 150.0, 161.5. MS (ESI, 20 eV): $m/z$ 194.0 [M–C$_8$H$_{17}$OSO$_3$]$^+$; MS (ESI, 20 eV): $m/z$, 209.0 [C$_8$H$_{17}$OSO$_3$]$^+$. 

3-(Butoxycarbonyl)-1-butylpyridinium octyl sulfate (2c)

Yield 93%. $^1$H NMR (DMSO $d_6$): $\delta$ 0.84–0.97 (m, 9H), 1.25–1.52 (m, 16H), 1.70–1.80 (m, 2H), 1.87–1.97 (m, 2H), 3.64–3.69 (t, $J = 6.6$ Hz, 2H), 4.39–4.43 (t, $J = 6.6$ Hz, 2H), 4.69–4.74 (t, $J = 7.5$ Hz, 2H), 8.26–8.30 (m, 1H), 8.97–9.00 (m, 1H), 9.27–9.29 (m, 1H), 9.59 (s, 1H). $^{13}$C NMR (DMSO $d_6$): $\delta$ 13.2, 13.5, 13.8, 18.5, 18.7, 22.0, 25.5, 28.6, 28.7, 29.0, 30.0, 31.2, 32.7, 60.9, 65.4, 66.1, 128.4, 130.0, 145.0, 145.8, 147.9, 161.7. MS (ESI, 20 eV): $m/z$ 236.2 [M–C$_8$H$_{17}$OSO$_3$]$^+$; MS (ESI, 20 eV): $m/z$, 209.1 [C$_8$H$_{17}$OSO$_3$]$^+$. 

3-(Butylcarbamoyl)-1-butylpyridinium octyl sulfate (3)

Yield 87%. $^1$H NMR (DMSO $d_6$): $\delta$ 0.82–0.95 (m, 9H), 1.25–1.60 (m, 18H), 1.88–1.98 (m, 2H), 3.30–3.37 (m, 2H), 3.65–3.69 (t, $J = 6.6$ Hz, 2H), 4.63–4.68 (t, $J = 7.5$ Hz, 2H), 8.23–8.28 (m, 1H), 8.89–8.91 (m, 1H), 8.98–9.02 (m, 1H), 9.18–9.20 (s, 1H), 9.43 (s, 1H). $^{13}$C NMR (CDCl$_3$): $\delta$ 13.5, 13.9, 14.2, 19.5, 20.4, 22.8, 26.0, 29.3, 29.4, 29.7, 31.2, 31.9, 33.8, 40.7, 62.4, 68.2, 128.4, 135.8, 143.7, 144.9, 146.5, 161.0. MS (ESI, 20 eV): $m/z$ 235.1 [M–C$_8$H$_{17}$OSO$_3$]$^+$; MS (ESI, 20 eV): $m/z$, 209.1 [C$_8$H$_{17}$OSO$_3$]$^+$. 
3-(Butoxycarbonyl)-1-methylpyridinium triflimide (2d)

3-(Butoxycarbonyl)-1-methylpyridinium iodide (2a) (3.21 g, 10 mmol) was dissolved in water (20 mL). This solution was treated with the aqueous lithium triflimide (3.16 g, 11 mmol) and the resultant mixture was stirred at room temperature for 10 min. The water immiscible triflimide based IL that separated from the aqueous solution was extracted with dichloromethane (3 × 20 mL). The combined extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure to yield the corresponding triflimide based IL. Yield 92%. ¹H NMR (CDCl₃): δ 0.96–1.01 (t, J = 7.4 Hz, 3H), 1.41–1.53 (m, 2H), 1.75–1.85 (m, 2H), 4.43–4.48 (t, J = 6.8 Hz, 2H), 4.52 (s, 3H), 8.12–8.16 (m, 1H), 8.93–8.95 (m, 2H), 9.14 (s, 1H). ¹³C NMR (DMSO d₆): δ 13.4, 18.5, 30.0, 48.3, 66.1, 119.5 (CF₃), 127.9, 129.5, 144.7, 146.7, 148.8, 161.7. MS (ESI, 20 eV): m/z, 194.1 [M–[N(SO₂CF₃)₂]⁺]; MS (ESI, 20 eV): m/z, 280.0 [N(SO₂CF₃)₂].