Copper-catalyzed tandem reaction in ionic liquid: an efficient reusable catalyst and solvent media for the synthesis of fused poly hetero cyclic compounds

Shivaji Naidu and Sabbasani Rajasekhara Reddy*

Department of Chemistry, School of Advanced Sciences
VIT University, Vellore-632014, India
E-mail: sekharareddy@vit.ac.in or sekharareddyiitm@gmail.com; Mobile Number: +91-9884968303

Supporting Information

General Experimental Procedures: All the reactions were carried out in sealed tube. Commercially available starting materials and other chemicals are purchased from Sigma-Aldrich chemicals, SD-Fine chemicals (India). 4-pentynoic acid and 5-hexyenoic acid purchased from Sigma-Aldrich chemicals and used in reactions without further purification. Ionic liquid ([bmim]OTf) was prepared and purified as per reported method. Thin-layer chromatography (TLC) was performed using Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence lamp. Silica gel (particle size 100-200 mesh) purchased from Merck, was used for chromatography. 1H NMR spectra were recorded on a Bruker 400 MHz instrument. Spectra were reported relative to Me$_4$Si (δ 0.0 ppm) or CHCl$_3$ residual peak (δ 7.26 ppm). 13C 100 MHz NMR were reported relative to CDCl$_3$ (δ 77.16 ppm). All the products were characterized by their NMR, GC/MS LCMS ESI and HRMS spectra. The first-order peak patterns are indicated as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quadruplet). Complex non-first-order signals are indicated as m (multiplet). FTIR spectra were recorded on a Nicolet 6700 spectrometer and are reported in frequency of absorption (cm$^{-1}$). GCMS recorded on instrument Perkin Elmer mass spectrometer.

Experimental

General procedure for 3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one

A sealed tube was charged with1.25 mmol (123 mg) of 4-pentynoic acid, 0.5 mL of [bmim]OTf and Cu(OAc)$_2$.H$_2$O (5mol%,5 mg). After stirring the above solution for 15min at room temperature, o-amino benzyl alcohol 0.5mmol (62 mg) was added to the reaction vial and sealed. The reaction mixture was stirred in an oil bath maintained at 100 °C until the
completion of reaction. After the completion of reaction, 5mL of water and ethyl acetate were added to the reaction mixture and combined layers were filtered through celite bed and washed with minimum amount of ethyl acetate. The organic layers were separated and concentrated under reduced pressure and the deposit was purified by column chromatography with hexane and ethyl acetate as eluent in a ratio of 4:1 to afford compound 4a with 92% (94.2 mg) yield. Colourless solid, m.p. 68-72 °C; 1H NMR (400 MHz, CDCl3): δ 8.30 (d, J=8.24 Hz, 1H), 7.30 (t, J=7.6 Hz, 1H), 7.13 (t, J= 7.44 Hz, 1H), 7.05 (d, J=7.56 Hz, 1H), 5.03 (d, J=15.6 Hz, 1H), 4.88 (d, J=15.6 Hz, 1H), 2.69-2.54 (m, 2H), 2.29-2.08 (m, 2H), 1.51 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 171.5, 133.0, 127.7, 112.4, 124.2, 123.2, 120.7, 90.1, 62.9, 33.1, 30.3, 21.4. LC MS (m/z): [M + H+] calcd for C12H13NO2: 203.8; found: 204.9.

3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one\textsuperscript{4a}. Colourless solid, m.p. 68-72 °C; 1H NMR (400 MHz, CDCl3): δ 8.30 (d, J=8.24 Hz, 1H), 7.30 (t, J=7.6 Hz, 1H), 7.13 (t, J=7.44 Hz, 1H), 7.05 (d, J=7.56 Hz, 1H), 5.03 (d, J=15.6 Hz, 1H), 4.88 (d, J=15.6 Hz, 1H), 2.69-2.54 (m, 2H), 2.29-2.08 (m, 2H), 1.51 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 171.5, 133.0, 127.7, 112.4, 124.2, 123.2, 120.7, 90.1, 62.9, 33.1, 30.3, 21.4. LC MS (m/z): [M + H+] calcd for C12H13NO2: 203.8; found: 204.9.

7-fluoro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one\textsuperscript{4b}. Colourless solid, m.p. 96-100 °C; 1H NMR (400 MHz, CDCl3): δ 8.29 (m, 1H), 7.02 (m, 1H), 6.79 (m, 1H), 5.01 (d, J=15.9 Hz, 2H), 4.86, (d, J=15.9 Hz, 1H), 2.69-2.59 (m, 2H), 2.31-2.16 (m, 2H), 1.50 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 171.4, 160.5 (d, J=250 Hz), 129.1, 126.6 (d, J=7 Hz), 122.6 (d, J=8 Hz) 114.8 (d, J=22 Hz), 111.0 (d, J=23 Hz) 90.8, 62.8, 33.03, 28.1, 21.3. GCMS: Calculated for C12H12FNO2: 221.0, found: 221.4.

8-fluoro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one\textsuperscript{4c}. Colourless solid, m.p. 78-81 °C; 1H NMR (400 MHz, CDCl3): δ 8.14 (m, 1H), 7.02 (m, 1H), 6.84, (m, 1H), 5.0 (d, J=15.3 Hz, 1H), 4.86, (d, J=15.3 Hz, 1H), 2.69-2.54 (m, 2H), 2.30-2.11 (m, 2H), 1.50 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 171.4, 163.1 (d, J=243 Hz), 134.1 (d, J=12 Hz), 125.5 (d, J=9 Hz), 118.5, 111.5 (d, J=22 Hz), 107.8 (d, J=27 Hz), 90.0, 62.6, 33.1, 30.3, 21.3. ESI-MS [M + H+] Calculated for C12H12FNO2: 221.0, found: 221.1.
6-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one \(^{4d}\). Colourless solid, m.p. 105-110°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.28 (d, J=8.2 Hz, 1H), 7.30 (t, J=8.0 Hz, 1H), 7.17 (d, J=7.9 Hz, 1H), 4.96 (d, J=16.5 Hz, 1H), 4.88 (d, J=16.8 Hz, 1H), 2.70-2.56 (m, 2H), 2.30-2.14 (m, 2H), 1.51 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 171.6, 134.5, 130.6, 128.2, 124.8, 121.4, 119.0, 89.9, 62.0, 32.9, 30.4, 21.3. LCMS Calculated for C\(_{12}\)H\(_{12}\)ClNO\(_2\): 237.6, found: 237.9.

7-chloro-3a-methyl-2,3,3a,4-tetrahydro-1H-benzo[b]pyrrolo[1,2-d][1,4]oxazin-1-one \(^{4e}\). Colourless solid, m.p. 80-85°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.28 (d, J=8.8 Hz, 1H), 7.24 (m, 1H), 7.05 (m, 1H), 5.0 (d, J=15.8 Hz, 1H), 4.80 (d, J=15.8 Hz, 1H), 2.58-2.64 (m, 2H), 2.29-2.13 (m, 2H), 1.49 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 171.4, 131.6, 129.5, 127.9, 124.9, 124.2, 122.0, 90.2, 62.6, 30.1, 30.3, 21.3. LCMS Calculated for C\(_{12}\)H\(_{12}\)ClNO\(_2\): 237.6, found: 237.8.

8-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one \(^{4f}\). Colourless solid, m.p. 127-130°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.38 (s, 1H), 7.10 (d, J=8.2 Hz, 1H), 6.99 (d, J=8.2 Hz, 1H), 4.99 (d, J=15.7 Hz, 1H), 4.85 (d, J=15.7 Hz, 1H), 2.64-2.59 (m, 2H), 2.29-2.12 (m, 2H), 1.49 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 171.4, 133.9, 133.3, 125.4, 124.4, 121.3, 120.5, 90.0, 62.6, 30.1, 30.3, 21.3. LCMS Calculated for C\(_{12}\)H\(_{12}\)ClNO\(_2\): 237.6, found: 237.9.

7-bromo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one \(^{4g}\). Colourless solid, m.p. 116-120°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.23 (d, J=8.8 Hz, 1H), 7.41 (m, 1H), 7.21 (m, 1H), 5.0 (d, J=15.8 Hz, 1H), 4.8 (d, J=15.8 Hz, 1H), 2.64-2.58 (m, 2H), 2.30-2.15 (m, 2H), 1.50 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 171.4, 132.1, 130.8, 127.2, 125.2, 122.3, 117.2, 90.1, 62.4, 30.1, 30.3, 21.3. LCMS Calculated for C\(_{12}\)H\(_{12}\)BrNO\(_2\): 281.0, found: 281.8.
7-iodo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one$^\text{4h}\text{.}$ Colorless liquid, $^1\text{H}$ NMR (400 MHz, CDCl$_3$): $\delta$ 8.30 (m, 1H), 7.39 (m, 1H), 7.13 (m, 1H), 5.04 (dd, 1H), 4.88 (dd, $J=15.6$ Hz, 1H), 2.64-2.57 (m, 2H), 2.32-1.92 (m, 2H), 1.51-1.49 (d, $J=8.1$ Hz, 3H); $^{13}\text{C}$ NMR (100 MHz, CDCl$_3$): $\delta$ 171.4 (d, $J=7.5$ Hz), 136.5, 132.9 (d, $J=9.6$ Hz), 127.6, 124.1 (d, $J=3.9$ Hz), 122.3, 120.5, 90.0 (d, $J=5.9$ Hz), 62.9, 33.0, 30.2, 21.2. ESI-MS (m/z): [M + H$^+$]; Calculated for C$_{12}$H$_{12}$INO$_2$: 328.9, found: 329.9.

3a,7-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one$^\text{5f}\text{.}$ Colourless solid, m.p. 89-94 $^\circ$C; $^1\text{H}$ NMR (400 MHz, CDCl$_3$): $\delta$ 8.18 (d, $J=8.36$ Hz, 1H), 7.10 (d, $J=7.76$ Hz, 1H), 6.85 (s, 1H), 4.99-4.79 (dd, 2H), 2.67-2.52 (m, 2H), 2.30 (s, 3H), 2.28-2.11 (m, 2H), 1.49 (s, 3H); $^{13}\text{C}$ NMR (100 MHz, CDCl$_3$): $\delta$ 171.2, 133.8, 130.5, 128.3, 124.5, 123.0, 120.5, 90.1, 62.9, 33.1, 30.3, 21.3, 21.0. LCMS Calculated for C$_{13}$H$_{15}$NO$_2$: 217.1, found: 217.9.

3a,6-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one $^\text{4j}\text{.}$ Semisolid, $^1\text{H}$ NMR (400 MHz, CDCl$_3$): $\delta$ 8.14 (d, $J=8.28$ Hz, 1H), 7.22 (t, $J=7.48$ Hz, 1H), 6.95 (d, $J=7.48$ Hz, 1H), 4.84 (d, $J=7$ Hz, 1H), 2.67-2.54 (m, 2H), 2.28-2.18 (m, 2H), 1.49 (s, 3H); $^{13}\text{C}$ NMR (100 MHz, CDCl$_3$): $\delta$ 171.6, 133.5, 132.9, 127.4, 125.9, 121.8, 118.5, 89.7, 62.1, 33.0, 30.3, 21.3, 18.1. ESI-MS (m/z): [M + H$^+$]; Calculated for C$_{13}$H$_{15}$NO$_2$: 217.1, found: 217.8. HRMS: [M + H$^+$]; Calculated for C$_{13}$H$_{16}$NO$_2$: 218.1176, found: 218.1176.

7,8-dimethoxy-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one $^\text{4k}\text{.}$ Semisolid, $^1\text{H}$ NMR (400 MHz, CDCl$_3$): $\delta$ 7.96 (s, 1H), 6.51 (s, 1H), 4.96 (d, $J=15.2$ Hz, 1H), 4.80 (d, $J=15.2$ Hz, 1H), 3.90 (s, 3H), 3.83 (s, 3H), 2.63-2.55 (m, 2H), 2.27-2.13 (m, 2H), 1.49 (s, 3H); $^{13}\text{C}$ NMR (100 MHz, CDCl$_3$): $\delta$ 171.1, 148.3, 146.1, 126.5, 114.9, 106.8, 104.4, 90.1, 62.8, 56.2, 56.2, 33.1, 30.4. ESI-MS (m/z): [M + H$^+$]; Calculated for C$_{14}$H$_{17}$NO$_3$: 263.1, found: 264.2. HRMS: [M + H$^+$]; Calculated for C$_{14}$H$_{18}$NO$_4$: 264.12303, found: 264.12403.
4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless oil; 
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78 (d, J=8.2 Hz, 1H), 7.25 (m, 1H), 7.14 (d, J=7.56 Hz, 1H), 7.01 (d, J=7.0 Hz, 1H), 4.91 (s, 2H), 2.69-2.49 (m, 2H), 2.15-1.91 (m, 3H), 1.83-1.72 (m, 1H), 1.47 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.7, 134.7, 127.4, 126.6, 126.4, 125.0, 123.9, 86.7, 62.8, 37.1, 34.3, 23.8, 16.9. ESI-MS (m/z): [M + H$^+$]; Calculated for C$_{13}$H$_{15}$NO$_2$: 217.3, found: 218.1.

8-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless solid, m.p. 76-79 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.7 (m, 1H), 6.96 (m, 1H), 6.72 (m, 1H), 4.87 (s, 2H), 2.71-2.48 (m, 2H), 2.15-1.91 (m, 3H), 1.81-1.73 (m, 1H), 1.45 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.8, 158.5 (d, J=243 Hz), 130.6 (d, J=3 Hz), 129.3 (d, J=7 Hz), 128.4 (d, J=8 Hz), 113.9 (d, J=22 Hz), 110.3 (d, J=23 Hz), 86.7, 62.6, 37.0, 34.2, 23.7, 16.8. GCMS: Calculated for C$_{13}$H$_{14}$FNO$_2$: 235.1, found: 235.1.

9-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colorless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.65-7.62 (m, 1H), 6.97-6.93 (m, 1H), 6.87-6.82 (m, 1H), 4.87 (s, 2H), 2.68-2.50 (m, 2H), 2.15-1.91 (m, 3H), 1.86-1.73 (m, 1H), 1.42 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.7, 159.8 (d, J=240 Hz), 135.7 (d, J=10 Hz), 124.8 (d, J=10 Hz), 122.8 (d, J=10 Hz), 113.2 (d, J=30 Hz), 112.3 (d, J=30 Hz), 86.8, 62.3, 37.0, 34.3, 23.5, 16.8. ESI-MS (m/z): [M + H$^+$]; Calculated for C$_{13}$H$_{14}$FNO$_2$: 236.2.

7-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless solid, m.p. 116-121 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.22 (d, J=8.08 Hz, 1H), 7.21 (m, 2H), 4.88 (d, J=16.52 Hz, 2H), 2.68-2.49 (m, 2H), 2.15-1.91 (m, 3H), 1.82-1.72 (m, 1H), 1.47 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.9, 136.2, 130.1, 127.2, 125.5, 125.1, 124.9, 86.5, 61.7, 37.1, 34.4, 23.3, 16.7. ESI-MS (m/z): [M + H$^+$]; [M + 2]; Calculated for C$_{13}$H$_{14}$ClNO$_2$: 251.0, found: 252.2, 254.2. HRMS (m/z): [M + H$^+$]; Calculated for C$_{13}$H$_{15}$ClNO$_2$: 252.07953, found: 252.07858.
8-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless oil; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.76 (d, J=8.8 Hz, 1H), 7.20 (m, 1H), 7.0 (m, 1H), 4.86 (s, 2H), 2.71-2.49 (m, 2H), 2.16-1.90 (m, 3H), 1.81-1.73 (m, 1H), 1.46 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 169.8, 133.2, 130.3, 129.0, 127.8, 126.8, 123.8, 86.8, 62.3, 37.0, 34.2, 23.5, 16.9. ESI-MS (m/z): [M + H\(^+\)], [M + 2]; Calculated for C\(_{13}\)H\(_{14}\)ClNO\(_2\): 251.7, found: 252.2, 254.2.

9-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless oil; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.87 (d, J=2.04 Hz, 1H), 7.11 (dd, J=6.2 Hz, 1H), 6.94 (d, J=8.32 Hz, 1H), 4.87 (s, 2H), 2.68-2.46 (m, 2H), 2.11-1.91 (m, 3H), 1.80-1.70 (m, 1H), 1.46 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 169.7, 135.6, 132.1, 126.3, 125.6, 125.3, 124.9, 86.8, 62.4, 36.9, 34.3, 23.6, 16.7. ESI-MS (m/z): [M + H\(^+\)], [M + 2]; Calculated for C\(_{13}\)H\(_{14}\)ClNO\(_2\): 251.7, found: 252.2, 254.1.

8-bromo-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless oil; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.71 (d, J=8.8 Hz, 1H), 7.35 (d, J=8.8 Hz, 1H), 7.15 (s, 1H), 4.86 (s, 2H), 2.66-2.48 (m, 2H), 2.12-1.92 (m, 3H), 1.81-1.72 (m, 1H), 1.46 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 169.7, 135.6, 134.6, 132.8, 129.6, 129.3, 118.1, 86.8, 62.2, 36.9, 34.3, 23.6, 16.9. ESI-MS (m/z): [M + H\(^+\)], [M + 2]; Calculated for C\(_{13}\)H\(_{14}\)BrNO\(_2\): 295.0, found: 296.1, 298.0.

8-iodo-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless oil; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.59 (m, 2H), 7.35 (s, 1H), 4.85 (s, 2H), 2.66-2.48 (m, 2H), 2.30 (s, 3H), 2.14-1.90 (m, 3H), 1.81-1.71 (m, 1H), 1.46 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 169.6, 135.6, 134.6, 132.8, 129.6, 129.3, 118.1, 86.8, 61.9, 37.0, 34.3, 23.6, 16.8. ESI-MS (m/z): [M + H\(^+\)]; Calculated for C\(_{13}\)H\(_{14}\)INO\(_2\): 343.0, found: 344.1.

4a,8-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one. Colourless oil; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.67 (d, J=8.4 Hz, 1H), 7.05 (d, J=8.3 Hz, 1H), 6.80 (s, 1H), 4.86 (s, 2H), 2.66-2.48 (m, 2H), 2.30 (s, 3H), 2.14-1.90 (m, 3H), 1.81-1.71 (m, 1H), 1.46 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \( \delta \) 169.7, 134.7, 132.1, 127.4, 127.0, 126.1, 124.2, 86.7, 62.8, 37.1, 34.3, 23.7, 21.1, 16.9. ESI-MS (m/z): [M + H\(^+\)]; Calculated for C\(_{14}\)H\(_{17}\)NO\(_2\): 231.1, found 232.3.
4a,7-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4u. Colourless oil; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.59 (d, J=8.24 Hz, 1H), 7.17 (t, J=7.8 Hz, 1H), 6.95 (d, J=7.44 Hz, 1H), 4.81 (d, J=3.24 Hz, 2H), 2.67-2.48 (m, 2H), 2.14 (s, 3H), 2.12-1.91 (m, 3H), 1.82-1.72 (m, 1H), 1.46 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.9, 134.5, 133.0, 126.9, 126.2, 125.6, 124.2, 86.1, 61.8, 37.2, 34.4, 23.5, 17.8, 16.8. ESI-MS (m/z): [M + H$^+$]: Calculated for C$_{14}$H$_{17}$NO$_2$: 231.1, found: 232.3. HRMS: [M + H$^+$]: Calculated for C$_{14}$H$_{18}$NO$_2$: 232.13394, found: 232.13321.

$^1$HNMR spectrum of 3a-methyl-2,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4a
$^{13}$C NMR spectrum of 3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4a
LCMS of 3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4a
$^{1}$HNMR spectrum of 7-fluoro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4b

$^{13}$C NMR spectrum of 7-fluoro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4b
GCMS of 7-fluoro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4b
$^{1}$HNMR spectrum of 8-fluoro-3α-methyl-2,3,3α,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4c

$^{13}$C NMR spectrum of 8-fluoro-3α-methyl-2,3,3α,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4c
ESI-MS of 8-fluoro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4c

\[
\text{SRM} - 913
\]

\[
\text{HNMR spectrum of 6-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4d}
\]
\[^{13}\text{C} \text{ NMR} \text{ spectrum of 6-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4d}\]
LCMS of 6-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4d
\(^1\)HNMR spectrum of 7-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one\textsuperscript{4e}

\(^13\)C NMR spectrum of 7-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one\textsuperscript{4e}
LCMS of 7-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4e
$^1$HNMR spectrum of 8-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4f
$^{13}$C NMR spectrum of 8-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4f
LCMS of 8-chloro-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4f
\(^1\)HNMR spectrum of 7-bromo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzopyrrolo[2,1-b][1,3]oxazin-1-one (4g)
$^{13}$C NMR spectrum of 7-bromo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one $^4g$
## Sample Information

- **Sample Name**: SKV-MA1414-52LS
- **Date Acquired**: 4/18/2014 8:28:23 PM
- **Data File**: 160414M 54.lcd
- **Method File**: Test Method - LCMS.icm
- **Tuning File**: D:/Shimadzu MS DataTuning Files/ESI 060314----4.lct
- **Vial**: 28
- **Column**: X-Select CSH C18 (50x3.0mm, 3.5µm)
- **M.P.**: A-0.05% Aq TFA, B-ACN
- **T%**: 0.01/0.5/0.5/0.5/1/0.8/0.8/0.8
- **Flow**: 0.8mL/min (Gradient)

### Chromatogram

![Chromatogram](image)

1. **PDA Multi 1**: 212nm-400nm

### MS Chromatogram

![MS Chromatogram](image)

- **Ret Time**: 2.850-2.950
- **Polarity**: Pos.
- **Base Peak**: 203.95

### MS Spectrum

![MS Spectrum](image)

- **m/z**: 129.8, 245.9, 304.8
LCMS of 7-bromo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4g
$^{1}$HNMR spectrum of 7-iodo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4h
$^{13}$C NMR spectrum of 7-iodo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one$^{4h}$
ESI-MS of 7-iodo-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4h
\[ \text{HNMR spectrum of 3a,7-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4i} \]
$^{13}$C NMR spectrum of 3a,7-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4i
LCMS of 3a,7-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4i
$^{1}$HNMR spectrum of 3a,6-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one-4j

$^{13}$C NMR spectrum of 3a,6-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one4j
ESI-MS of 73a,6-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4j
HRMS of 73a,6-dimethyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4j
$^{1}$HNMR spectrum of 7,8-dimethoxy-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4k

$^{13}$C NMR spectrum of 7,8-dimethoxy-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4k
ESI-MS of 7,8-dimethoxy-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4k
HRMS of 7,8-dimethoxy-3a-methyl-2,3,3a,5-tetrahydro-1H-benzo[d]pyrrolo[2,1-b][1,3]oxazin-1-one 4k
$^1$HNMR spectrum of 4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4l

$^{13}$C NMR spectrum of 4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4l
ESI-MS of 4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one

\[4l\]

Signature SIF VIT VELLORE
SRSM-207

\[8\]-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one

\[4m\]

\[1^1\]HNMR spectrum of 8-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one

\[4m\]
$^{13}$C NMR spectrum of 8-fluoro-4a-methyl-2,3,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one\textbf{4m}
GCMS of 8-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4m
$^{1}$HNMR spectrum of 9-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4n

$^{13}$C NMR spectrum of 9-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4n
ESI-MS of 9-fluoro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4n
$^1$HNMR spectrum of 7-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4o

$^{13}$CNMR spectrum of 7-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4o
ESI-MS of 7-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 40

HRMS of 7-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 40
$^1$HNMR spectrum of 8-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one $\text{4p}$
$^{13}$C NMR spectrum of 8-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one
ESI-MS of 8-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one4p
1H NMR spectrum of 9-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4q

13C spectrum of 9-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4q
ESI-MS of 9-chloro-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4q
1\textsuperscript{H}NMR spectrum of 8-bromo-4\textalpha-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4r

1\textsuperscript{3}C NMR spectrum of 8-bromo-4\textalpha-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4r
ESI-MS of 8-bromo-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4r
$^1$H NMR spectrum  8-iodo-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4s

$^{13}$C NMR spectrum  8-iodo-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4s
ESI-MS of 8-iodo-4a-methyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4s
$^{1}$HNMR spectrum of 4a,8-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4t

$^{13}$C NMR spectrum of 4a,8-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4t
ESI-MS of 4a,8-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4t
1H NMR spectrum of 4a,7-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4u

13C NMR spectrum of 4a,7-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4u
ESI-MS of 4a,7-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4u
HRMS of 4a,7-dimethyl-2,3,4,4a-tetrahydrobenzo[d]pyrido[2,1-b][1,3]oxazin-1(6H)-one 4u
$^{1}$HNMR spectrum of 5-methylenedihydrofuran-2(3H)-one II

$^{13}$C NMR spectrum 5-methylenedihydrofuran-2(3H)-one II
$[{\text{bmim}}]^{\text{OTf}}$
$^{13}$C NMR spectrum of [bmim]OTf
19F-NMR spectrum of [bmim]OTf

1-Butyl-3-methylimidazolium trifluoromethanesulfonate

Colourless liquid; 1H NMR (400 MHz, CDCl3): δ 9.11 (s, 1H), 7.35 (s, 1H), 7.31 (s, 1H), 4.21 (t, J= 7 Hz, 2H), 3.96(s , 3H), 1.87-1.83 (m,2H), 1.38-1.33 (m, 2H), 0.96 (s, J= 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ 137.0, 123.7, 122.2, 119.2, 50.0, 36.5, 32.0, 19.5, 13.4. 19F-NMR (376.5 MHz, CDCl3 ): δ -78.6.

References