

## Supporting Information

### Reversal of selectivity in acetate aldol reactions of *N*-acetyl-(*S*)-4-isopropyl-1-[(*R*)-1-phenylethyl]imidazolidin-2-one

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## General Methods, Materials and Experimental

### 1. General Methods

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at 400 MHz and 100 MHz, respectively on a Bruker Avance DPX 400 (400 MHz) spectrometer in  $\text{CDCl}_3$  using TMS as an internal standard. The chemical shifts ( $\delta$ ) for  $^1\text{H}$  and  $^{13}\text{C}$  are given in ppm relative to residual signals of the solvent ( $\text{CHCl}_3$ ). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; brs, broad signal. Specific rotations were taken on Rudolph Autopol IV instrument and HRMS spectra were recorded on Bruker Maxis TOF spectrophotometer. The reactions were monitored by TLC (Merck). Evaporation of solvents was performed under reduced pressure using a Buchi rotary evaporator. Melting points are uncorrected.

### 2. Materials

Commercial grade reagents and solvents were used without further purification; L-valine, Boc-anhydride, ethylchloroformate, thionyl chloride, tosyl chloride, mesyl chloride, sodium hydride (60% suspension in mineral oil), 1,4-dioxane, aniline, diisopropyl ethylamine (DIPEA), benzaldehyde, 4-fluorobenzaldehyde, 4-chlorobenzaldehyde, 2-chlorobenzaldehyde, 4-bromobenzaldehyde, 4-methylbenzaldehyde, *N,N*-dimethylamine, (40% solution in  $\text{H}_2\text{O}$ ), *t*-butylamine, *N,N*-dimethylacetamide (DMA), *N,N*-dimethylaminopyridine (DMAP), acetyl chloride, triethylamine, THF, triphosgene (Spectrochem); (*R*)- $\alpha$ -methylbenzylamine, (*S*)- $\alpha$ -methylbenzylamine, lithium bis(trimethylsilyl)amide (LiHMDS), sodium bis(trimethylsilyl)amide (NaHMDS), potassium bis(trimethylsilyl)amide (KHMDS), lithium diisopropylamide (LDA), *n*-butyl lithium (*n*-BuLi), lithium aluminium hydride (LAH), titanium tetrachloride (1.0 M in DCM), 2-methoxybenzaldehyde, 2-furfurylaldehyde, thiophene-2-carboxaldehyde, 4-

fluorobenzotrifluoride (Aldrich); sodium hydrogen carbonate, toluene, sodium hydroxide, 1-naphthol, potassium carbonate, sodium borohydride, (CDH); benzylamine (Loba Chemie); DCM, methanol (Merck).

### 3. Experimental

**Synthesis of L-Boc-val-OH (1).** To a solution of L-valine (10.0 g, 85.1 mmol, 1.0 equiv) in THF (200 mL) was added aq solution of NaOH (10.2 g, 255.3 mmol, 3.0 equiv) followed by Boc-anhydride (20.4 g, 93.6 mmol, 1.1 equiv) and the reaction mixture was stirred for 12 h. It was then acidified with 1 N aq HCl and extracted with ethyl acetate (3X100 mL). The organic layer was dried over anhydrous sodium sulphate and evaporated under vacuum to give a gummy compound (yield 17.6 g, 95%)

Yield 95%;  $[\alpha]_D^{20}$  -9.7 (c 1, DMF);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.96 (d,  $J$  = 6.8 Hz, 3H), 1.00 (d,  $J$  = 6.8 Hz, 3H), 1.45 (s, 9H), 2.18–2.21 (m, 1H), 4.24–4.27 (m, 1H), 8.10 (brs, NH, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  17.42, 18.99, 28.27, 31.01, 58.39, 80.00, 155.85, 176.63; MS (APCI) = 218.34 (m/z).

**Synthesis of *tert*-butyl (*S*)-3-methyl-1-oxo-1-[(*R*)-1-phenylethylamino]butan-2-ylcarbamate (3a).** A solution of L-Boc-val-OH (16.0 g, 73.6 mmol, 1.0 equiv) in DCM (300 mL) was cooled to 0 °C and triethylamine (11.2 mL, 80.5 mmol, 1.1 equiv) was added under  $\text{N}_2$  environment. To this reaction mixture ethylchloroformate (7.9 mL, 80.5 mmol, 1.1 equiv) was introduced slowly and stirred for 1 h, followed by the addition of (*R*)- $\alpha$ -methylbenzylamine (9.5 mL, 73.6 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature for 2 h. The organic layer was washed with aq  $\text{NaHCO}_3$  and brine. It was then dried over anhydrous sodium sulphate and evaporated under vacuum to afford the product as a white solid (yield 21.6 g, 92%).

***tert*-Butyl (*S*)-3-methyl-1-oxo-1-[(*R*)-1-phenylethylamino]butan-2-ylcarbamate (3a).**

Yield 92%; white solid; mp 133–136 °C;  $[\alpha]_D^{20}$  +27.4 (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.91 (d,  $J$  = 6.6 Hz, 3H), 0.96 (d,  $J$  = 6.6 Hz, 3H), 1.42 (s, 9H), 1.48 (d,  $J$  = 6.8 Hz, 3H), 2.10–2.15 (m, 1H), 3.82–3.86 (m, 1H), 5.04–5.11 (m, 2H), 6.31 (d,  $J$  = 7.7 Hz, 1H), 7.22–7.33 (m, 5H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  17.95, 19.35, 21.89, 28.28, 30.53, 48.77, 60.23, 79.90, 125.76, 127.31, 128.64, 142.92, 155.93, 170.63; HRMS (ESI-TOF) calcd for  $\text{C}_{18}\text{H}_{29}\text{N}_2\text{O}_3[\text{M}+\text{H}]^+$ : 321.2178; found: 321.2178, and  $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 343.1998; found: 343.2075.

***tert*-Butyl (*S*)-3-methyl-1-oxo-1-[(*S*)-1-phenylethylamino]butan-2-ylcarbamate (3b).**

Yield 90%; white solid; mp 144–148 °C;  $[\alpha]_D^{20}$  +58.3 (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87–88 (m, 6H), 1.42 (s, 9H), 1.47 (d,  $J$  = 6.7 Hz, 3H), 2.01–2.05 (m, 1H), 3.85–3.89 (m, 1H), 5.11–5.18 (m, 2H), 6.47 (d,  $J$  = 6.7 Hz, 1H), 7.21–7.30 (m, 5H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  17.89, 19.34, 21.73, 28.29, 30.83, 48.71, 60.17, 79.82, 126.14, 127.29, 128.60, 143.06, 156.00, 170.82; HRMS (ESI-TOF) calcd for  $\text{C}_{18}\text{H}_{29}\text{N}_2\text{O}_3[\text{M}+\text{H}]^+$ : 321.2178; found: 321.2172, and  $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 343.1998; found: 343.2070.

***tert*-Butyl (*S*)-1-(benzylamino)-3-methyl-1-oxobutan-2-ylcarbamate (3c).**

Yield 90%; white solid; mp 124–127 °C;  $[\alpha]_D^{20}$  -10.1 (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.91 (d,  $J$  = 6.6 Hz, 3H), 0.96 (d,  $J$  = 6.6 Hz, 3H), 1.41 (s, 9H), 2.14–2.16 (m, 1H), 3.91–3.94 (m, 1H), 4.42–4.45 (m, 2H), 5.11–5.12 (m, 1H), 6.48 (brs, NH, 1H),

7.24–7.33 (m, 5H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  17.86, 19.39, 28.28, 30.68, 43.44, 60.20, 79.97, 127.50, 127.70, 128.69, 138.00, 155.95, 171.57; HRMS (ESI-TOF) calcd for  $\text{C}_{17}\text{H}_{27}\text{N}_2\text{O}_3[\text{M}+\text{H}]^+$ : 307.2022; found: 307.2022, and  $\text{C}_{17}\text{H}_{26}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 329.1841; found: 329.1914.

***tert*-Butyl (S)-3-methyl-1-oxo-1-(phenylamino)butan-2-ylcarbamate (3d).**

Yield 93%; white solid; mp 122–124 °C;  $[\alpha]_{\text{D}}^{20}$  –36.7 (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.99 (d,  $J$  = 6.8 Hz, 3H), 1.01 (d,  $J$  = 6.8 Hz, 3H), 1.45 (s, 9H), 2.23 (d,  $J$  = Hz, 1H), 3.98–4.02 (m, 1H), 5.14 (s, 1H), 7.08–7.12 (m, 1H), 7.28–7.35 (m, 2H), 7.50 (d,  $J$  = 7.7 Hz, 2H), 8.03 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  18.14, 19.42, 28.32, 30.70, 30.96, 80.26, 119.99, 124.34, 128.90, 137.58, 156.31, 170.31; HRMS (ESI-TOF) calcd for  $\text{C}_{16}\text{H}_{25}\text{N}_2\text{O}_3[\text{M}+\text{H}]^+$ : 293.1865; found: 293.1861, and  $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 315.1685; found: 315.1715.

**(S)-*tert*-butyl 1-(*tert*-butylamino)-3-methyl-1-oxobutan-2-ylcarbamate (3e).**

Yield 79%; white solid; mp 121–124 °C;  $[\alpha]_{\text{D}}^{20}$  –21.3 (c 1,  $\text{CH}_3\text{OH}$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.91 (d,  $J$  = 6.8 Hz, 3H), 0.94 (d,  $J$  = 6.8 Hz, 3H), 1.34 (s, 9H), 1.44 (s, 9H), 2.04–2.06 (m, 1H), 3.68–7.72 (m, 1H), 5.06 (brs, 1H, NH), 5.64 (brs, 1H, NH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  17.92, 19.26, 28.31, 28.72, 31.05, 51.40, 60.57, 79.79, 155.92, 170.68; HRMS (ESI-TOF) calcd for  $\text{C}_{14}\text{H}_{28}\text{N}_2\text{O}_3[\text{M}+\text{Na}]^+$ : 295.1998; found: 295.1992.

**Synthesis of (S)-2-amino-3-methyl-*N*-[(*R*)-1-phenylethyl]butanamide (4a).** A solution of *tert*-butyl (S)-3-methyl-1-oxo-1-[(*R*)-1-phenylethylamino]butan-2-ylcarbamate (20.0 g, 62.4 mmol, 1.0 equiv) in methanol (100 mL) was cooled to 0 °C. Conc'd HCl (10.0 mL, 93.6 mmol, 1.5 equiv, 10 N) was added to it dropwise and stirred for 4 h at room temperature. The reaction mixture was evaporated under vacuum, neutralized with aq  $\text{NaHCO}_3$  and extracted with ethyl acetate. The ethyl acetate layer was dried over anhydrous sodium sulphate and concentrated to give the desired product (yield 13.3 g, 97%).

**(S)-2-Amino-3-methyl-*N*-[(*R*)-1-phenylethyl]butanamide (4a).**

Yield 97%; gummy;  $[\alpha]_{\text{D}}^{20}$  +59.3 (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.75 (d,  $J$  = 6.8 Hz, 3H), 0.95 (d,  $J$  = 6.8 Hz, 3H), 1.48 (d,  $J$  = 6.6 Hz, 3H), 2.23–2.31 (m, 1H), 3.21 (d,  $J$  = 3.9 Hz, 1H), 5.07–5.15 (m, 1H), 7.21–7.24 (m, 1H), 7.28–7.34 (m, 4H), 7.69 (d,  $J$  = 7.6 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  16.08, 19.74, 22.06, 30.91, 48.21, 60.04, 126.11, 127.12, 128.55, 143.65, 173.42; HRMS (ESI-TOF) calcd for  $\text{C}_{13}\text{H}_{21}\text{N}_2\text{O}[\text{M}+\text{H}]^+$ : 221.1654; found: 221.1694, and  $\text{C}_{13}\text{H}_{20}\text{N}_2\text{ONa}[\text{M}+\text{Na}]^+$ : 243.1473; found: 243.1529.

**(S)-2-Amino-3-methyl-*N*-[(*S*)-1-phenylethyl]butanamide (4b).**

Yield 85%; gummy;  $[\alpha]_{\text{D}}^{20}$  –115.4 (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.84 (d,  $J$  = 6.9 Hz, 3H), 0.96 (d,  $J$  = 6.9 Hz, 3H), 1.47 (d,  $J$  = 6.7 Hz, 3H), 2.25–2.31 (m, 1H), 3.18–3.19 (m, 1H), 5.08–5.15 (m, 1H), 7.31–7.34 (m, 5H), 7.65 (brs, NH, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  16.04, 19.67, 22.10, 30.93, 48.19, 60.02, 125.91, 127.17, 128.33, 143.49, 173.38; HRMS (ESI-TOF) calcd for  $\text{C}_{13}\text{H}_{21}\text{N}_2\text{O}[\text{M}+\text{H}]^+$ : 221.1654; found: 221.1692, and  $\text{C}_{13}\text{H}_{20}\text{N}_2\text{ONa}[\text{M}+\text{Na}]^+$ : 243.1473; found: 243.11523.

**(S)-2-Amino-*N*-benzyl-3-methylbutanamide (4c).**

Yield 94%; gummy;  $[\alpha]_D^{20} +24.7$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.87–0.90 (m, 6H), 2.13–2.16 (m, 1H), 3.68–3.69 (m, 1H), 4.22–4.26 (m, 1H), 4.34–4.38 (m, 1H), 7.16–7.24 (m, 5H), 8.12 (brs, NH, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  17.26, 18.49, 30.42, 43.34, 59.26, 127.38, 127.55, 128.56, 137.71, 170.44; HRMS (ESI-TOF) calcd for C<sub>12</sub>H<sub>19</sub>N<sub>2</sub>O[M+H]<sup>+</sup>: 207.1497; found: 207.1535, and C<sub>12</sub>H<sub>18</sub>N<sub>2</sub>ONa[M+Na]<sup>+</sup>: 229.1317; found: 229.1316.

**(S)-2-Amino-3-methyl-N-phenylbutanamide (4d).**

Yield 95%; gummy;  $[\alpha]_D^{20} +239.1$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.87 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 2.43–2.48 (m, 1H), 3.38 (d, *J* = 3.6 Hz, 1H), 7.07–7.12 (m, 1H), 7.29–7.35 (m, 2H), 7.59–7.61 (m, 2H), 9.05 (brs, 1H, NH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  16.24, 19.60, 30.76, 60.30, 119.61, 124.17, 128.96, 137.64, 172.01; HRMS (ESI-TOF) calcd for C<sub>11</sub>H<sub>17</sub>N<sub>2</sub>O[M+H]<sup>+</sup>: 193.1341; found: 193.1359, and C<sub>11</sub>H<sub>16</sub>N<sub>2</sub>ONa[M+Na]<sup>+</sup>: 215.1160; found: 215.1164.

**(S)-2-amino-N-tert-butyl-3-methylbutanamide (4e).**

Yield 81%; gummy;  $[\alpha]_D^{20} -57.1$  (c 1, CH<sub>3</sub>OH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.87 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 1.35 (s, 9H), 1.45 (brs, 2H, NH), 2.15–2.29 (m, 1H), 3.07 (d, *J* = 3.9 Hz, 1H), 7.16 (brs, 1H, NH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  15.92, 19.65, 28.65, 30.78, 50.30, 60.40, 173.55; HRMS (ESI-TOF) calcd for C<sub>9</sub>H<sub>20</sub>N<sub>2</sub>ONa[M+Na]<sup>+</sup>: 195.1473; found: 195.1471.

**Synthesis of (S)-3-methyl-N1-phenylbutane-1,2-diamine (5a).** To a stirred solution of (S)-2-amino-3-methyl-N-[(S)-1-phenylethyl]butanamide (12 g, 54.5 mmol, 1.0 equiv) in dry THF and under N<sub>2</sub> environment was added lithium aluminium hydride (8.3 g, 217.8 mmol, 4.0 equiv) in portion-wise at 0 °C. The reaction mixture was then refluxed for 12 h. Thereafter it was cooled and slowly quenched with water, aq NaOH and again washed with water to form a slurry which was filtered through celite bed. The filtrate was taken in ethyl acetate, washed with brine, and dried over anhydrous sodium sulphate. It was evaporated under vacuum to afford the desired product (yield 10.0 g, 89%).

**(S)-3-Methyl-N1-[(R)-1-phenylethyl]butane-1,2-diamine (5a).**

Yield 89%; gummy;  $[\alpha]_D^{20} +37.9$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.83–0.85 (m, 6H), 1.37 (d, *J* = 6.5 Hz, 3H), 2.12–2.18 (m, 1H), 2.53–2.61 (m, 2H), 3.72–3.76 (m, 1H), 7.21–7.23 (m, 1H), 7.29–7.34 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  17.99, 19.34, 24.64, 32.47, 51.76, 56.84, 58.24, 126.10, 126.78, 128.48, 145.83; HRMS (ESI-TOF) calcd for C<sub>13</sub>H<sub>23</sub>N<sub>2</sub>[M+H]<sup>+</sup>: 207.1861; found: 207.1861.

**(S)-3-Methyl-N1-[(S)-1-phenylethyl]butane-1,2-diamine (5b).**

Yield 91%; gummy;  $[\alpha]_D^{20} -38.4$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.84 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 1.34 (d, *J* = 6.5 Hz, 3H), 2.24–2.29 (m, 1H), 2.46–2.51 (m, 2H), 3.69–3.74 (m, 1H), 7.19–7.20 (m, 1H), 7.27–7.29 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  17.44, 19.45, 24.44, 32.14, 52.25, 56.87, 58.81, 126.12, 126.52, 128.34, 146.07; HRMS (ESI-TOF) calcd for C<sub>13</sub>H<sub>23</sub>N<sub>2</sub>[M+H]<sup>+</sup>: 207.1861; found: 207.1869.

**(S)-N1-Benzyl-3-methylbutane-1,2-diamine (5c).**

Yield 90%; gummy;  $[\alpha]_D^{20} +34.2$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.84–0.88 (m, 6H), 2.36–2.45 (m, 2H), 2.68–2.62 (m, 1H), 2.69–2.73 (m, 1H), 3.77–3.83 (m, 2H), 7.28–7.33 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  17.82, 19.39, 36.02, 53.57, 54.11, 56.72, 126.79, 128.08, 128.36, 140.58; HRMS (ESI-TOF) calcd for C<sub>12</sub>H<sub>20</sub>N<sub>2</sub>Na[M+Na]<sup>+</sup>: 215.1524; found: 215.1543.

**(S)-3-Methyl-N1-phenylbutane-1,2-diamine (5d).**

Yield 90%; white solid;  $[\alpha]_D^{20} +16.3$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.96 (d, *J* = 6.4 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 1.81–1.86 (m, 1H), 3.72–3.76 (m, 1H), 3.82–3.86 (m, 1H), 4.19 (t, *J* = 9.7 Hz, 1H), 7.22–7.24 (m, 1H), 7.37–7.42 (m, 2H), 7.55–7.58 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  17.94, 18.10, 32.76, 55.65, 59.55, 124.40, 126.35, 128.78, 139.92; HRMS (ESI-TOF) calcd for C<sub>11</sub>H<sub>19</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 179.1548; found: 179.1548, and C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>Na[M+Na]<sup>+</sup>: 201.1368; found: 201.1375.

**(S)-N1-tert-butyl-3-methylbutane-1,2-diamine (5e).**

Yield 51%; liquid;  $[\alpha]_D^{20} +7.3$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.92 (d, *J* = 6.8 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.25 (brs, 3H, NH), 1.35 (s, 9H), 2.25–2.31 (m, 2H), 2.46–2.50 (m, 1H), 2.64 (dd, *J* = 3.3, 11.0 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  17.75, 19.72, 29.08, 32.52, 46.54, 57.39, 60.49; HRMS (ESI-TOF) calcd for C<sub>11</sub>H<sub>19</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 179.1548; found: 179.1548, and C<sub>9</sub>H<sub>22</sub>N<sub>2</sub>Na[M+Na]<sup>+</sup>: 181.1681; found: 181.1680.

**Synthesis of (S)-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one (6a).** To a stirred solution of (S)-3-methyl-N1-[(R)-1-phenylethyl]butane-1,2-diamine (8 g, 38.8 mmol, 1.0 equiv) in toluene (100 mL) was added a solution of K<sub>2</sub>CO<sub>3</sub> (10.7 g, 77.6 mmol, 2 equiv) in water (100 mL) and cooled to 0 °C. A solution of triphosgene (5.7 g, 19.4 mmol, 0.5 equiv) in toluene (20 mL) was added dropwise to the reaction mixture and stirred at room temperature for 2 h. The reaction mixture was washed with brine, dried over anhydrous sodium sulphate and evaporated under vacuum to afford a gummy compound which solidified on cooling to afford the product (yield 8.8 g, 98%).

**(S)-4-Isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one (6a).**

Yield 98%; white solid; mp 81–84 °C;  $[\alpha]_D^{20} +42.8$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.84 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H), 1.50 (d, *J* = 6.8 Hz, 3H), 1.58–1.69 (m, 1H), 3.01–3.09 (m, 2H), 3.26–3.32 (m, 1H), 4.68 (brs, NH, 1H), 5.23–5.28 (m, 1H), 7.24–7.29 (m, 1H), 7.32–7.36 (m, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  15.86, 17.83, 18.30, 33.15, 43.84, 49.54, 55.81, 127.11, 127.28, 128.46, 140.82, 161.36; HRMS (ESI-TOF) calcd for C<sub>14</sub>H<sub>21</sub>N<sub>2</sub>O [M+H]<sup>+</sup>: 233.1654; found: 233.1647, and C<sub>14</sub>H<sub>20</sub>N<sub>2</sub>ONa[M+Na]<sup>+</sup>: 255.1473; found: 255.1519.

**(S)-4-Isopropyl-1-[(S)-1-phenylethyl]imidazolidin-2-one (6b).**

Yield 94%; white solid; mp 67–70 °C;  $[\alpha]_D^{20} -85.2$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.75 (d, *J* = 6.4 Hz, 3H), 0.84 (d, *J* = 6.4 Hz, 3H), 1.51 (d, *J* = 6.8 Hz, 3H), 2.64–2.70 (m, 1H), 3.32–3.41 (m, 2H), 4.91–4.93 (m, 1H), 5.25–5.30 (m, 1H), 7.26–7.33 (m, 5H), 7.41 (brs, NH, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  16.19, 16.35, 17.68, 32.99, 43.64, 49.44, 55.89, 127.16, 127.32, 128.43, 140.46, 161.46; HRMS (ESI-TOF) calcd for

$C_{14}H_{21}N_2O$   $[M+H]^+$ : 233.1654; found: 233.1650, and  $C_{14}H_{20}N_2ONa[M+Na]^+$ : 255.1473; found: 255.1520.

**(S)-1-Benzyl-4-isopropylimidazolidin-2-one (6c).**

Yield 95%; white solid; mp 41–43 °C;  $[\alpha]_D^{20}$  –16.9 (c 1,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.82 (d,  $J$  = 6.7 Hz, 3H), 0.89 (d,  $J$  = 6.7 Hz, 3H), 1.60–1.65 (m, 1H), 2.92–2.96 (m, 1H), 3.30–3.38 (m, 2H), 4.35 (m, 2H), 5.04 (brs, NH, 1H), 7.25–7.28 (m, 3H), 7.31–7.35 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  17.79, 18.29, 35.05, 47.50, 48.31, 55.75, 127.39, 128.01, 128.57, 137.18, 161.95; HRMS (ESI-TOF) calcd for  $C_{13}H_{19}N_2O$   $[M+H]^+$ : 219.1497; found: 219.1497, and  $C_{13}H_{18}N_2ONa[M+Na]^+$ : 241.1317; found: 241.1350.

**(S)-4-Isopropyl-1-phenylimidazolidine-2-one (6d).**

Yield 96%; white solid; mp 109–111 °C;  $[\alpha]_D^{20}$  –15.3 (c 1,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.94 (d,  $J$  = 6.4 Hz, 3H), 0.98 (d,  $J$  = 6.4 Hz, 3H), 1.71–1.77 (m, 1H), 3.50–3.59 (m, 2H), 3.88–3.95 (m, 1H), 6.07 (brs, NH, 1H), 7.01–7.05 (m, 1H), 7.29–7.35 (m, 2H), 7.51–7.53 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  17.74, 18.09, 33.12, 49.01, 54.87, 117.77, 123.62, 129.03, 140.01, 159.47; HRMS (ESI-TOF) calcd for  $C_{12}H_{17}N_2O$   $[M+H]^+$ : 205.1341; found: 205.1341, and  $C_{12}H_{16}N_2ONa[M+Na]^+$ : 227.1160; found: 227.1168.

**(S)-1-tert-butyl-4-isopropylimidazolidin-2-one (6e).**

Yield 80%; white solid; mp 75–80 °C;  $[\alpha]_D^{20}$  +220.7 (c 1,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.87 (d,  $J$  = 6.7 Hz, 3H), 0.91 (d,  $J$  = 6.7 Hz, 3H), 1.35 (s, 9H), 1.58–1.66 (m, 1H), 3.08 (t,  $J$  = 8.1 Hz, 1H), 3.19–3.26 (m, 1H), 3.49 (t,  $J$  = 8.4 Hz, 1H), 4.62 (brs, 1H, NH);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  17.97, 18.48, 27.61, 32.99, 47.47, 52.79, 55.33, 162.24; HRMS (ESI-TOF) calcd for  $C_{10}H_{20}N_2ONa[M+Na]^+$ : 207.1473; found: 207.1470.

**Synthesis of *N*-acetyl or propionyl-(S)-4-isopropyl-1-phenylimidazolidine-2-one (7a).** To a stirred solution of (S)-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one (8 g, 34.4 mmol, 1.0 equiv) in dry THF (100 mL) and under  $N_2$  environment was added sodium hydride (60% suspension in paraffin oil, 1.7 g, 41.3 mmol, 1.2 equiv) in portion-wise at 0 °C. After 1h, acetyl chloride (3.2 mL, 41.3 mmol, 1.2 equiv) was added drop-wise and stirring was continued for another hour. The reaction mixture was quenched with aq  $NH_4Cl$ , washed with aq  $NaHCO_3$  and dried over anhydrous sodium sulphate. It was evaporated under vacuum to give a gummy compound (yield 9.0 g, 95%).

**(S)-3-Acetyl-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one (7a).**

Yield 95%; gummy;  $[\alpha]_D^{20}$  +170.1 (c 1,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.80 (d,  $J$  = 6.4 Hz, 3H), 0.85 (d,  $J$  = 6.4 Hz, 3H), 1.57 (d,  $J$  = 6.8 Hz, 3H), 2.38–2.43 (m, 1H), 2.55 (s, 3H), 2.89–2.94 (m, 1H), 3.06–3.08 (m, 1H), 4.18–4.20 (m, 1H), 5.33–5.39 (m, 1H), 7.31–7.39 (m, 5H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.40, 16.08, 18.06, 24.13, 28.60, 37.02, 50.29, 55.06, 127.17, 127.90, 128.55, 139.05, 154.67, 170.74; HRMS (ESI-TOF) calcd for  $C_{16}H_{23}N_2O_2$   $[M+H]^+$ : 275.1760; found: 275.1767, and  $C_{16}H_{22}N_2O_2Na[M+Na]^+$ : 297.1579; found: 297.1658.

**(S)-3-Acetyl-4-isopropyl-1-[(S)-1-phenylethyl]imidazolidin-2-one (7b).**

Yield 96%; gummy;  $[\alpha]_D^{20}$   $-36.2$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.43 (d,  $J$  = 6.4 Hz, 3H), 0.80 (d,  $J$  = 6.4 Hz, 3H), 1.55 (d,  $J$  = 6.8 Hz, 3H), 2.25–2.30 (m, 1H), 2.55 (s, 3H), 2.71–2.74 (m, 1H), 3.28–3.33 (m, 1H), 4.22–4.25 (m, 1H), 5.33–5.35 (m, 1H), 7.27–7.34 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.09, 15.28, 17.88, 24.08, 28.45, 36.98, 50.32, 55.14, 127.17, 127.95, 128.58, 139.21, 154.62, 170.75; HRMS (ESI-TOF) calcd for C<sub>16</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 275.1760; found: 275.1755, and C<sub>16</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>Na[M+Na]<sup>+</sup>: 297.1579; found: 297.1645.

**(S)-3-Acetyl-1-benzyl-4-isopropylimidazolidin-2-one (7c).**

Yield 94%; gummy;  $[\alpha]_D^{20}$   $+37.9$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.67 (d,  $J$  = 6.4 Hz, 3H), 0.84 (d,  $J$  = 6.4 Hz, 3H), 2.34–2.39 (m, 1H), 2.56 (s, 3H), 2.96–2.99 (m, 1H), 3.20–2.50 (m, 1H), 4.23–4.25 (m, 1H), 4.30 (d,  $J$  = 14.7 Hz, 1H), 4.49 (d,  $J$  = 14.7 Hz, 1H), 7.31–7.35 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.30, 17.93, 24.05, 29.70, 41.27, 47.71, 55.23, 128.02, 128.35, 128.60, 135.61, 155.22, 170.76; HRMS (ESI-TOF) calcd for C<sub>15</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 261.1603; found: 261.1608, and C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>Na[M+Na]<sup>+</sup>: 283.1422; found: 283.1428.

**N-Acetyl-(S)-4-isopropyl-1-phenylimidazolidine-2-one (7d).**

Yield 92%; gummy;  $[\alpha]_D^{20}$   $+40.1$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.84 (d,  $J$  = 6.4 Hz, 3H), 0.96 (d,  $J$  = 6.4 Hz, 3H), 2.41–2.47 (m, 1H), 2.57 (s, 3H), 3.53–3.56 (m, 1H), 3.87–3.89 (m, 1H), 4.40–4.45 (m, 1H), 7.13–7.17 (m, 1H), 7.36–7.42 (m, 2H), 7.53–7.55 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.58, 18.09, 24.28, 28.89, 43.14, 54.73, 119.22, 124.47, 129.05, 138.66, 153.22, 170.74; HRMS (ESI-TOF) calcd for C<sub>14</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 247.1447; found: 247.1447, and C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>Na[M+Na]<sup>+</sup>: 269.1266; found: 269.1347.

**(S)-3-acetyl-1-tert-butyl-4-isopropylimidazolidin-2-one (7e).**

Yield 93%; gummy;  $[\alpha]_D^{20}$   $+64.7$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.82 (d,  $J$  = 6.9 Hz, 3H), 0.91 (d,  $J$  = 6.9 Hz, 3H), 1.41 (s, 9H), 2.33–2.40 (m, 1H), 2.47 (s, 3H), 3.24 (dd,  $J$  = 2.6, 9.5 Hz, 1H), 3.40 (t,  $J$  = 9.3 Hz, 1H), 4.16–4.19 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.54, 18.01, 23.92, 27.14, 28.71, 40.12, 54.06, 55.83, 154.51, 170.41; HRMS (ESI-TOF) calcd for C<sub>12</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub>Na[M+Na]<sup>+</sup>: 249.1579; found: 249.1579.

**General procedure for the acetate aldol reaction with LiHMDS.**

To a solution of (S)-3-acetyl-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one (0.6 g, 2.2 mmol, 1.0 equiv) in anhydrous THF (5 mL) under N<sub>2</sub> environment was added LiHMDS solution (2.4 mL, 2.4 mmol, 1.1 equiv; 1 M in THF) at  $-78$  °C, and stirred for 1 h. Benzaldehyde (0.25 mL, 2.4 mmol, 1.1 equiv) was then introduced into the reaction mixture and stirred for another 30 min. The reaction was quenched with saturated aq NH<sub>4</sub>Cl solution, extracted with EtOAc and further washed with brine. It was dried over anhydrous sodium sulphate, concentrated and purified by column chromatography [silica gel (60-120 mesh), eluent petroleum ether:EtOAc = 6:4] to afford the desired product (yield 0.77 g, 92%).

**(S)-3-[(S)-3-Hydroxy-3-phenylpropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(i)].**

Yield 92%; gummy;  $[\alpha]_D^{20}$   $+211.2$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.71 (d,  $J$  = 6.4 Hz, 3H), 0.80 (d,  $J$  = 6.4 Hz, 3H), 1.50 (d,  $J$  = 6.4 Hz, 3H), 2.30–2.32 (m, 1H),

2.85 (t,  $J = 9.4$  Hz, 1H), 3.00 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.20 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.47 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.05 (brs, 1H, OH), 4.12–4.15 (m, 1H), 5.05–5.07 (m, 1H), 5.22–5.27 (m, 1H), 7.11–7.17 (m, 4H), 7.20–7.29 (m, 4H), 7.34–7.39 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.46, 16.08, 18.06, 28.73, 37.27, 44.40, 50.48, 55.35, 70.83, 125.80, 127.17, 127.44, 128.03, 128.40, 128.79, 138.80, 143.18, 154.56, 172.55; HRMS (ESI-TOF) calcd for  $\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}_3$   $[\text{M}+\text{H}]^+$ : 381.2178; found: 381.2176, and  $\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 403.1998; found: 403.2016.

**(S)-3-[(S)-3-Hydroxy-3-phenylpropanoyl]-4-isopropyl-1-[(S)-1-phenylethyl]imidazolidin-2-one [8b(i)].**  
Yield 90%; gummy;  $[\alpha]_{\text{D}}^{20} -102.1$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.55 (d,  $J = 6.4$  Hz, 3H), 0.87 (d,  $J = 6.4$  Hz, 3H), 1.70 (d,  $J = 6.4$  Hz, 3H), 2.40–2.45 (m, 1H), 2.88 (dd,  $J = 2.8, 9.7$  Hz, 1H), 3.42–3.52 (m, 2H), 3.69 (dd,  $J = 9.7, 16.5$  Hz, 1H), 4.33 (brs, 1H, OH), 4.40–4.44 (m, 1H), 5.30 (dd,  $J = 2.4, 9.7$  Hz, 1H), 5.44–5.49 (m, 1H), 7.45–7.51 (m, 8H), 7.58–7.60 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.12, 15.30, 17.87, 28.56, 37.21, 44.45, 50.48, 55.43, 70.81, 125.79, 127.33, 127.43, 128.12, 128.40, 128.66, 138.86, 143.23, 154.53, 172.54; HRMS (ESI-TOF) calcd for  $\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 403.1998; found: 403.2007.

**(S)-1-Benzyl-3-[(S)-3-hydroxy-3-phenylpropanoyl]-4-isopropylimidazolidin-2-one [8c(i)].**  
Yield 76%; gummy;  $[\alpha]_{\text{D}}^{20} +38.9$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.66 (d,  $J = 6.4$  Hz, 3H), 0.82 (d,  $J = 6.4$  Hz, 3H), 2.35–2.38 (m, 1H), 3.00 (dd,  $J = 2.8, 9.6$  Hz, 1H), 3.25 (t,  $J = 9.6$  Hz, 1H), 3.37 (dd,  $J = 3.0, 16.3$  Hz, 1H), 3.57 (dd,  $J = 9.6, 16.4$  Hz, 1H), 4.13 (brs, 1H, OH), 4.24–4.29 (m, 1H), 4.32 (d,  $J = 14.7$  Hz, 1H), 4.47 (d,  $J = 14.7$  Hz, 1H), 5.18–5.23 (m, 1H), 7.25–7.28 (m, 2H), 7.30–7.37 (m, 6H), 7.44–7.45 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.35, 17.90, 28.56, 41.45, 44.35, 47.72, 55.51, 70.79, 125.80, 127.39, 127.43, 128.12, 128.39, 128.86, 135.32, 143.24, 155.08, 172.52; HRMS (ESI-TOF) calcd for  $\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 389.1841; found: 389.1843.

**(S)-3-[(S)-3-Hydroxy-3-phenylpropanoyl]-4-isopropyl-1-phenylimidazolidin-2-one [8d(i)].**  
Yield 71%; gummy;  $[\alpha]_{\text{D}}^{20} +20.3$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.81 (d,  $J = 6.4$  Hz, 3H), 0.95 (d,  $J = 6.4$  Hz, 3H), 2.39–2.43 (m, 1H), 3.33 (dd,  $J = 2.8, 9.6$  Hz, 1H), 3.52–3.59 (m, 2H), 3.86 (t,  $J = 9.4$  Hz, 1H), 4.41–4.45 (m, 1H), 4.50 (brs, 1H, OH), 5.16–5.19 (m, 1H), 7.17–7.17 (m, 1H), 7.22–7.26 (m, 1H), 7.30–7.33 (m, 2H), 7.34–7.38 (m, 2H), 7.40–7.42 (m, 2H), 7.49–7.51 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.67, 18.07, 29.03, 43.40, 44.66, 54.99, 70.72, 119.42, 124.79, 125.80, 127.49, 128.41, 129.10, 138.34, 143.09, 153.14, 172.61; HRMS (ESI-TOF) calcd for  $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 375.1685; found: 375.1687.

**(S)-1-tert-butyl-3-[(R)-3-hydroxy-3-phenylpropanoyl]-4-isopropylimidazolidin-2-one [8e(i)].**  
Yield 67%; gummy;  $[\alpha]_{\text{D}}^{20} +26.1$  (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.81 (d,  $J = 6.8$  Hz, 3H), 0.91 (d,  $J = 6.8$  Hz, 3H), 1.38 (s, 9H), 2.33–2.37 (m, 1H), 3.23 (t,  $J = 2.8$  Hz, 1H), 3.27 (dd,  $J = 2.8, 10.4$  Hz, 2H), 3.37–3.48 (m, 2H), 4.19–4.23 (m, 2H), 5.11–5.13 (m, 1H), 7.22–7.24 (m, 1H), 7.30–7.34 (m, 2H), 7.42 (d,  $J = 7.7$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.74, 18.14, 27.48, 28.98, 40.50, 44.48, 54.26, 54.45, 70.83,



125.83, 127.36, 128.34, 143.27, 154.54, 172.60; HRMS (ESI-TOF) calcd for  $C_{19}H_{28}N_2O_3Na[M+Na]^+$ : 355.1998; found: 355.1997.

**(S)-3-[(S)-3-(4-Fluorophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(ii)].**

Yield 90%; gummy;  $[\alpha]_D^{20} +150.7$  (c 0.25,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.79 (d,  $J = 6.4$  Hz, 3H), 0.88 (d,  $J = 6.4$  Hz, 3H), 1.57 (d,  $J = 6.4$  Hz, 3H), 2.35–2.41 (m, 1H), 2.95 (t,  $J = 9.4$  Hz, 1H), 3.09 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.28 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.51 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.15 (d,  $J = 4.4$  Hz, 1H), 4.19–4.23 (m, 1H), 5.10–5.13 (m, 1H), 5.29–5.34 (m, 1H), 6.99–7.05 (m, 2H), 7.28–7.34 (m, 4H), 7.37–7.41 (m, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.44, 16.08, 18.02, 28.73, 37.32, 44.35, 50.54, 55.34, 70.19, 115.27, 127.14, 127.44, 127.52, 128.04, 128.72, 138.96, 154.52, 163.35, 172.40; HRMS (ESI-TOF) calcd for  $C_{23}H_{27}FN_2O_3Na[M+Na]^+$ : 421.1903; found: 421.1904.

**(S)-3-[(S)-3-(4-Chlorophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(iii)].**

Yield 86%; gummy;  $[\alpha]_D^{20} +211.6$  (c 0.25,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.78 (d,  $J = 6.4$  Hz, 3H), 0.87 (d,  $J = 6.4$  Hz, 3H), 1.56 (d,  $J = 6.4$  Hz, 3H), 2.32–2.40 (m, 1H), 2.94 (t,  $J = 9.4$  Hz, 1H), 3.08 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.29 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.53 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.18–4.23 (m, 2H), 5.09–5.12 (m, 1H), 5.28–5.34 (m, 1H), 7.27–7.31 (m, 4H), 7.34–7.39 (m, 5H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.42, 16.09, 18.02, 28.73, 37.30, 44.21, 50.54, 55.35, 70.17, 127.15, 127.24, 128.06, 128.48, 128.80, 133.03, 138.75, 149.79, 154.50, 172.24; HRMS (ESI-TOF) calcd for  $C_{23}H_{27}ClN_2O_3Na[M+Na]^+$ : 437.1608; found: 437.1613.

**(S)-3-[(S)-3-(2-Chlorophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(iv)].**

Yield 86%; gummy;  $[\alpha]_D^{20} +188.6$  (c 0.5,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.79 (d,  $J = 6.4$  Hz, 3H), 0.88 (d,  $J = 6.4$  Hz, 3H), 1.55 (d,  $J = 6.4$  Hz, 3H), 2.36–2.44 (m, 1H), 2.92–2.97 (m, 1H), 3.06–3.10 (m, 1H), 3.37–3.41 (m, 2H), 4.18–4.24 (m, 1H), 4.32 (d,  $J = 3.7$  Hz, 1H), 5.28–5.33 (m, 1H), 5.51–5.58 (m, 1H), 7.15–7.20 (m, 1H), 7.28–7.35 (m, 7H), 7.63–7.67 (m, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.52, 16.07, 18.07, 28.78, 37.38, 42.79, 50.51, 55.39, 67.43, 127.10, 127.18, 127.37, 128.03, 128.46, 128.78, 129.26, 131.47, 138.79, 140.51, 154.50, 172.42; HRMS (ESI-TOF) calcd for  $C_{23}H_{27}ClN_2O_3Na[M+Na]^+$ : 437.1608; found: 437.1608.

**(S)-3-[(S)-3-(4-Bromophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(v)].**

Yield 89%; gummy;  $[\alpha]_D^{20} +132.6$  (c 1,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.77 (d,  $J = 6.4$  Hz, 3H), 0.86 (d,  $J = 6.4$  Hz, 3H), 1.56 (d,  $J = 6.4$  Hz, 3H), 2.35–2.37 (m, 1H), 2.96 (t,  $J = 9.4$  Hz, 1H), 3.07 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.28 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.52 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.18–4.22 (m, 2H), 5.07–5.10 (m, 1H), 5.28–5.33 (m, 1H), 7.27–7.37 (m, 7H), 7.43–7.46 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.44, 16.10, 18.02, 28.75, 37.35, 44.16, 50.56, 55.36, 70.21, 121.16, 127.15, 127.60, 128.05, 128.79,

131.42, 138.77, 124.37, 154.50, 172.18; HRMS (ESI-TOF) calcd for  $C_{23}H_{27}BrN_2O_3Na[M+Na]^+$ : 481.1103; found: 481.1100.

**(S)-3-[(S)-3-(4-Methylphenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(vi)].**

Yield 86%; gummy;  $[\alpha]_D^{20} +223.8$  (c 0.5,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.78 (d,  $J = 6.4$  Hz, 3H), 0.84 (d,  $J = 6.4$  Hz, 3H), 1.56 (d,  $J = 6.4$  Hz, 3H), 2.32 (s, 3H), 2.35–2.41 (m, 1H), 2.92 (t,  $J = 9.4$  Hz, 1H), 3.06 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.26 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.56 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.05 (brs, 1H, OH), 4.18–4.22 (m, 1H), 5.09–5.11 (m, 1H), 5.29–5.34 (m, 1H), 7.13 (d,  $J = 7.8$  Hz, 2H), 7.29–7.36 (m, 7H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.46, 16.08, 18.07, 21.14, 28.75, 37.26, 44.42, 50.47, 55.34, 70.71, 125.77, 127.18, 128.02, 128.78, 129.05, 136.99, 138.84, 140.32, 154.59, 172.54; HRMS (ESI-TOF) calcd for  $C_{24}H_{30}N_2O_3Na[M+Na]^+$ : 417.2154; found: 417.2154.

**(S)-3-[(S)-3-(2-Methoxyphenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(vii)].**

Yield 91%; gummy;  $[\alpha]_D^{20} +135.5$  (c 1,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.79 (d,  $J = 6.4$  Hz, 3H), 0.88 (d,  $J = 6.4$  Hz, 3H), 1.56 (d,  $J = 6.6$  Hz, 3H), 2.37–2.43 (m, 1H), 2.93 (t,  $J = 9.4$  Hz, 1H), 3.07 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.33 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.48 (dd,  $J = 9.8, 16.4$  Hz, 1H), 3.84 (s, 3H), 4.11 (d,  $J = 4.4$  Hz, 1H), 4.20–4.24 (m, 1H), 5.31 (q,  $J = 7.1$  Hz, 1H), 5.40–5.45 (m, 1H), 6.84 (d,  $J = 8.2$  Hz, 1H), 6.94–6.98 (m, 1H), 7.20–7.24 (m, 1H), 7.28–7.31 (m, 3H), 7.33–7.37 (m, 2H), 7.48–7.50 (m, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.50, 16.10, 18.10, 28.76, 37.20, 42.99, 50.33, 55.28, 55.32, 66.39, 110.20, 120.69, 126.69, 127.19, 127.98, 128.24, 128.75, 131.23, 138.96, 154.57, 155.99, 172.91; HRMS (ESI-TOF) calcd for  $C_{24}H_{30}N_2O_4Na[M+Na]^+$ : 433.2103; found: 433.2103.

**(S)-3-[(S)-3-(Furan-2-yl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(viii)].**

Yield 80%; gummy;  $[\alpha]_D^{20} +198.4$  (c 0.5,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.82 (d,  $J = 6.4$  Hz, 3H), 0.88 (d,  $J = 6.4$  Hz, 3H), 1.58 (d,  $J = 6.4$  Hz, 3H), 2.37–2.42 (m, 1H), 2.95 (t,  $J = 9.4$  Hz, 1H), 3.09 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.37 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.74 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.05 (d,  $J = 4.3$  Hz, 1H), 4.20–4.24 (m, 1H), 5.14–5.17 (m, 1H), 5.31–5.37 (m, 1H), 6.30–6.32 (m, 2H), 7.27–7.31 (m, 3H), 7.34–7.38 (m, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  14.45, 16.08, 18.10, 28.69, 37.29, 41.05, 50.48, 55.28, 64.69, 106.07, 110.15, 127.16, 128.01, 128.77, 138.82, 141.97, 154.48, 155.47, 172.06; HRMS (ESI-TOF) calcd for  $C_{21}H_{26}N_2O_4Na[M+Na]^+$ : 393.1790; found: 393.1790.

**(S)-3-[(S)-3-Hydroxy-3-(thiophen-2-yl)propanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(ix)].**

Yield 78%; gummy;  $[\alpha]_D^{20} +191.5$  (c 0.5,  $CHCl_3$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.79 (d,  $J = 6.5$  Hz, 3H), 0.86 (d,  $J = 6.6$  Hz, 3H), 1.56 (d,  $J = 6.6$  Hz, 3H), 2.36–2.38 (m, 1H), 2.93 (t,  $J = 9.4$  Hz, 1H), 3.08 (dd,  $J = 2.9, 9.7$  Hz, 1H), 3.38 (dd,  $J = 3.0, 16.4$  Hz, 1H), 3.70 (dd,  $J = 9.8, 16.4$  Hz, 1H), 4.19–4.21 (m, 1H), 4.28 (d,  $J = 4.3$  Hz, 1H), 5.30–5.35 (m, 2H), 6.94–7.00 (m, 2H), 7.19–7.22 (m, 1H), 7.25–7.30 (m, 3H), 7.36 (d,  $J = 6.6$  Hz,

2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.47, 16.10, 18.03, 28.73, 37.31, 41.11, 50.52, 55.31, 67.15, 123.34, 124.46, 126.64, 127.18, 128.04, 128.79, 138.81, 147.32, 154.45, 172.05; HRMS (ESI-TOF) calcd for  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_3\text{SNa}[\text{M}+\text{Na}]^+$ : 409.1562; found: 409.1562.

**(S)-3-[(S,E)-3-hydroxy-5-phenylpent-4-enoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(x)].**

Yield 95%; gummy;  $[\alpha]_{\text{D}}^{20} +189.5$  (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.79 (d,  $J$  = 7.0 Hz, 3H), 0.87 (d,  $J$  = 7.0 Hz, 3H), 1.57 (d,  $J$  = 7.1 Hz, 3H), 2.35–2.43 (m, 1H), 2.91–2.96 (m, 1H), 3.08 (dd,  $J$  = 2.7, 9.7 Hz, 1H), 3.25 (dd,  $J$  = 3.5, 16.3 Hz, 1H), 3.44 (dd,  $J$  = 7.3, 9.8, 1H), 3.90 (brs, 1H, OH), 4.19–4.23 (m, 1H), 4.74–4.80 (m, 1H), 5.35 (q,  $J$  = 7.0 Hz, 1H), 6.30 (dd,  $J$  = 5.7, 16.9 Hz, 1H), 6.65 (dd,  $J$  = 0.9, 15.9 Hz, 1H), 7.19–7.23 (m, 1H), 7.27–7.33 (m, 5H), 7.35–7.37 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.47, 16.11, 18.05, 28.75, 37.30, 42.60, 50.51, 55.33, 69.25, 126.54, 127.67, 127.51, 128.03, 128.50, 128.79, 130.01, 130.87, 136.81, 138.85, 154.56, 172.37; HRMS (ESI-TOF) calcd for  $\text{C}_{25}\text{H}_{30}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 429.2154; found: 429.2154.

**(S)-3-[(S)-3-hydroxy-4-methylpentanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(xi)].**

Yield 82%; gummy;  $[\alpha]_{\text{D}}^{20} +191.4$  (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (d,  $J$  = 6.9 Hz, 3H), 0.88 (d,  $J$  = 6.9 Hz, 3H), 0.96–1.00 (m, 6H), 1.57 (d,  $J$  = 6.9 Hz, 3H), 1.72–1.82 (m, 1H), 2.36–2.43 (m, 1H), 2.89–2.96 (m, 1H), 3.02–3.09 (m, 2H), 3.20–3.36 (m, 1H), 3.58 (d,  $J$  = 4.4 Hz, 1H), 3.77–3.85 (m, 1H), 4.17–4.23 (m, 1H), 5.34 (q,  $J$  = 7.1 Hz, 1H), 7.28–7.31 (m, 3H), 7.34–7.38 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.43, 14.46, 16.05, 17.71, 18.02, 28.69, 33.69, 37.21, 39.84, 50.43, 55.30, 73.45, 127.14, 127.98, 128.76, 138.80, 154.77, 173.60; HRMS (ESI-TOF) calcd for  $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 369.2154; found: 369.2154.

**(S)-3-[(R)-3-hydroxy-5-methylhexanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(xii)].**

Yield 89%; gummy;  $[\alpha]_{\text{D}}^{20} +99.7$  (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (d,  $J$  = 7.0 Hz, 3H), 0.88 (d,  $J$  = 7.1 Hz, 3H), 0.91–0.93 (m, 6H), 1.23–1.30 (m, 1H), 1.48–1.55 (m, 1H), 1.57 (d,  $J$  = 7.0 Hz, 3H), 1.82–1.89 (m, 1H), 2.36–2.43 (m, 1H), 2.95–2.99 (m, 1H), 3.07–3.12 (m, 2H), 3.47 (d,  $J$  = 4.6 Hz, 1H), 4.08–4.14 (m, 1H), 4.18–4.23 (m, 1H), 5.33 (q,  $J$  = 7.0 Hz, 1H), 7.28–7.31 (m, 3H), 7.35–7.38 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.46, 16.08, 18.04, 22.16, 23.32, 24.42, 28.82, 37.23, 43.04, 46.10, 50.43, 55.21, 66.68, 127.15, 127.98, 128.75, 138.87, 154.60, 173.23; HRMS (ESI-TOF) calcd for  $\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 383.2311; found: 383.2311.

**(S)-3-[(S)-3-hydroxy-4,4-dimethylpentanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(xiii)].**

Yield 90%; gummy;  $[\alpha]_{\text{D}}^{20} +273.8$  (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.81 (d,  $J$  = 7.1 Hz, 3H), 0.88 (d,  $J$  = 7.1 Hz, 3H), 0.97 (s, 9H), 1.57 (d,  $J$  = 6.9 Hz, 3H), 2.38–2.42 (m, 1H), 2.89–2.94 (m, 1H), 3.00–3.08 (m, 2H), 3.18–3.32 (m, 1H), 3.58 (d,  $J$  = 4.6 Hz, 1H), 3.72–3.75 (m, 1H), 4.19–4.23 (m, 1H), 5.33 (q,  $J$  = 6.5 Hz, 1H), 7.29–7.32 (m, 3H), 7.34–7.38 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.43, 16.04, 18.06, 25.76, 28.73, 34.92, 37.08, 49.75, 50.43, 55.45, 76.07, 127.17, 128.00, 128.79, 138.72, 154.71, 174.07; HRMS (ESI-TOF) calcd for  $\text{C}_{21}\text{H}_{32}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 383.2311; found: 383.2310.

**(S)-3-[(R)-3-hydroxy-4-phenylbutanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [8a(xiv)].**  
Yield 79%; gummy;  $[\alpha]_D^{20} +70.6$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.79 (d,  $J$  = 7.1 Hz, 3H), 0.85 (d,  $J$  = 7.1 Hz, 3H), 1.55 (d,  $J$  = 7.0 Hz, 3H), 2.31–2.41 (m, 1H), 2.78–2.84 (m, 1H), 2.86–2.91 (m, 2H), 3.01–3.08 (m, 1H), 3.15–3.18 (m, 1H), 3.58 (brs, 1H, OH), 4.14–4.18 (m, 1H), 4.28–4.35 (m, 1H), 5.29–5.35 (m, 1H), 7.19–7.23 (m, 1H), 7.25–7.30 (m, 7H), 7.32–7.38 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.50, 16.11, 18.07, 28.70, 37.24, 42.15, 43.40, 50.46, 55.25, 69.71, 126.39, 127.21, 128.04, 128.43, 128.80, 129.59, 138.34, 138.84, 154.61, 172.79; HRMS (ESI-TOF) calcd for C<sub>24</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 417.2154; found: 417.2153.

**General procedure for the aldol reaction with aryl aldehydes using TiCl<sub>4</sub>-DIPEA.**

To a solution of (S)-3-acetyl-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one (0.6 g, 2.2 mmol, 1.0 equiv) in anhydrous DCM (10 mL, dried over calcium hydride) and under N<sub>2</sub> environment, was added TiCl<sub>4</sub> solution (4.4 mL, 4.4 mmol, 2.0 equiv, 1 M in DCM) at –78 °C. The reaction mixture was warmed to 0 °C, stirred for 10 min and again cooled to –78 °C. To this reaction mixture, DIPEA (0.39 mL, 2.2 mmol, 1.0 equiv) was added and stirred for 1 h. Further benzaldehyde (0.25 mL, 2.4 mmol, 1.1 equiv) was introduced into it and stirred for 30 min. The reaction was quenched with saturated aq NH<sub>4</sub>Cl solution, and the DCM layer was washed with brine, dried over anhydrous sodium sulphate and concentrated to afford crude product. It was purified by column chromatography [silica gel (60–120 mesh), eluent petroleum ether:EtOAc = 7:3] to afford the desired product (yield 0.75 g, 90%).

**(S)-3-[(R)-3-Hydroxy-3-phenylpropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(i)].**  
Yield 90%; gummy;  $[\alpha]_D^{20} +24.1$  (c 0.5, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.81 (d,  $J$  = 6.8 Hz, 3H), 0.87 (d,  $J$  = 6.8 Hz, 3H), 1.55 (d,  $J$  = 7.1 Hz, 3H), 2.34–2.41 (m, 1H), 2.90 (t,  $J$  = 9.4 Hz, 1H), 3.06 (dd,  $J$  = 2.8, 7.7 Hz, 1H), 3.31 (dd,  $J$  = 9.4, 16.6 Hz, 1H), 3.51 (dd,  $J$  = 2.9, 16.6 Hz, 1H), 3.82 (brs, 1H, OH), 4.18–4.21 (m, 1H), 5.18–5.21 (m, 1H), 5.28–5.33 (m, 1H), 7.24–7.7.30 (m, 4H), 7.31–7.7.37 (m, 4H), 7.34–7.39 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.49, 16.08, 18.04, 28.81, 37.27, 44.53, 50.45, 55.24, 70.61, 127.15, 127.40, 127.63, 127.99, 128.35, 128.77, 138.82, 143.05, 154.45, 172.51; HRMS (ESI-TOF) calcd for C<sub>23</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 403.1998; found: 403.2006.

**(S)-3-[(R)-3-(4-Fluorophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(ii)].**

Yield 84%; gummy;  $[\alpha]_D^{20} +218.2$  (c 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.80 (d,  $J$  = 6.8 Hz, 3H), 0.87 (d,  $J$  = 6.8 Hz, 3H), 1.56 (d,  $J$  = 7.1 Hz, 3H), 2.36–2.38 (m, 1H), 2.92 (t,  $J$  = 9.4 Hz, 1H), 3.07 (dd,  $J$  = 2.8, 7.7 Hz, 1H), 3.29 (dd,  $J$  = 9.4, 16.6 Hz, 1H), 3.52 (dd,  $J$  = 2.9, 16.6 Hz, 1H), 3.92 (brs, 1H, OH), 4.19–4.21 (m, 1H), 5.10–5.19 (m, 1H), 5.30–5.32 (m, 1H), 6.98–7.02 (m, 2H), 7.28–7.29 (m, 3H), 7.33–7.38 (m, 4H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.44, 16.08, 18.03, 28.73, 37.31, 44.51, 50.54, 55.23, 70.18, 127.14, 127.45, 127.53, 128.04, 128.79, 138.77, 154.41, 160.90, 163.34, 172.36; HRMS (ESI-TOF) calcd for C<sub>23</sub>H<sub>27</sub>FN<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 421.1903; found: 421.1903.

**(S)-3-[(R)-3-(4-Chlorophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(iii)].**

Yield 86%; gummy;  $[\alpha]_D^{20} +257.8$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (d,  $J = 6.8$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H), 1.58 (d,  $J = 7.2$  Hz, 3H), 2.34–2.43 (m, 1H), 2.93 (t,  $J = 9.4$  Hz, 1H), 3.07 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.28 (dd,  $J = 9.4, 16.6$  Hz, 1H), 3.52 (dd,  $J = 2.9, 16.6$  Hz, 1H), 3.90 (brs, 1H, OH), 4.58–4.23 (m, 1H), 5.16–5.19 (m, 1H), 5.29–5.36 (m, 1H), 7.29–7.32 (m, 5H), 7.34–7.38 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.41, 16.08, 18.04, 28.78, 37.31, 44.32, 50.54, 55.35, 69.97, 127.13, 128.05, 128.48, 128.69, 128.72, 133.06, 138.70, 141.47, 154.39, 172.29; HRMS (ESI-TOF) calcd for  $\text{C}_{23}\text{H}_{27}\text{ClN}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 437.1608; found: 437.1608.

**(S)-3-[(R)-3-(2-Chlorophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(iv)].**

Yield 83%; gummy;  $[\alpha]_D^{20} +329.1$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.84 (d,  $J = 6.8$  Hz, 3H), 0.89 (d,  $J = 6.8$  Hz, 3H), 1.57 (d,  $J = 7.2$  Hz, 3H), 2.40–2.42 (m, 1H), 2.92 (t,  $J = 9.4$  Hz, 1H), 3.07 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.24 (dd,  $J = 9.4, 16.6$  Hz, 1H), 3.57 (dd,  $J = 2.9, 16.6$  Hz, 1H), 4.14–4.19 (m, 2H), 5.29–5.31 (m, 1H), 5.56–5.58 (m, 1H), 7.16–7.19 (m, 1H), 7.28–7.29 (m, 5H), 7.33–7.35 (m, 2H), 7.63–7.67 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.52, 16.08, 18.07, 28.79, 37.28, 42.79, 50.50, 55.39, 67.23, 127.04, 127.17, 127.36, 128.01, 128.46, 128.78, 129.25, 131.49, 138.79, 140.26, 154.50, 172.42; HRMS (ESI-TOF) calcd for  $\text{C}_{23}\text{H}_{27}\text{ClN}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 437.1608; found: 437.1608.

**(S)-3-[(R)-3-(4-Bromophenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(v)].**

Yield 88%; gummy;  $[\alpha]_D^{20} +250.6$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (d,  $J = 6.8$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H), 1.57 (d,  $J = 7.2$  Hz, 3H), 2.35–2.41 (m, 1H), 2.94 (t,  $J = 9.4$  Hz, 1H), 3.08 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.28 (dd,  $J = 9.4, 16.6$  Hz, 1H), 3.53 (dd,  $J = 2.9, 16.6$  Hz, 1H), 3.90 (d,  $J = 3.9$  Hz, 1H), 4.17–4.22 (m, 1H), 5.14–5.17 (m, 1H), 5.28–5.34 (m, 1H), 7.28–7.36 (m, 7H), 7.43–7.47 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.45, 16.08, 18.04, 28.73, 37.25, 44.28, 50.55, 55.36, 70.01, 121.19, 127.19, 127.86, 128.81, 129.88, 131.21, 138.75, 142.04, 154.39, 172.23; HRMS (ESI-TOF) calcd for  $\text{C}_{23}\text{H}_{27}\text{BrN}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 481.1103; found: 481.1100.

**(S)-3-[(R)-3-(4-Methylphenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(vi)].**

Yield 80%; gummy;  $[\alpha]_D^{20} +182.4$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.81 (d,  $J = 6.8$  Hz, 3H), 0.89 (d,  $J = 6.8$  Hz, 3H), 1.56 (d,  $J = 7.2$  Hz, 3H), 2.32 (s, 3H), 2.36–2.42 (m, 1H), 2.91 (t,  $J = 9.4$  Hz, 1H), 3.06 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.34 (dd,  $J = 9.4, 16.6$  Hz, 1H), 3.48 (dd,  $J = 2.9, 16.6$  Hz, 1H), 3.74 (brs, 1H, OH), 4.18–4.22 (m, 1H), 5.15–5.19 (m, 1H), 5.30–5.35 (m, 1H), 7.14 (d,  $J = 7.9$  Hz, 2H), 7.29–7.36 (m, 7H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.46, 16.06, 18.07, 21.14, 28.77, 37.19, 44.47, 50.38, 55.21, 70.48, 125.72, 127.16, 128.01, 128.78, 129.04, 137.00, 138.78, 139.99, 154.46, 172.61; HRMS (ESI-TOF) calcd for  $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 417.2154; found: 417.2154.

**(S)-3-[(R)-3-(2-Methoxyphenyl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(vii)].**

Yield 70%; gummy;  $[\alpha]_D^{20} +154.6$  (c 0.25,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (d,  $J = 6.8$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H), 1.56 (d,  $J = 7.2$  Hz, 3H), 2.38–2.42 (m, 1H), 2.91 (t,  $J = 9.4$  Hz, 1H), 3.07 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.37 (dd,  $J = 9.4, 16.6$  Hz, 1H), 3.47 (dd,  $J = 2.9, 16.6$  Hz, 1H), 3.84 (s, 3H), 3.98 (d,  $J = \text{Hz}$ , 1H), 4.19–4.23 (m, 1H), 5.29–5.34 (m, 1H), 5.44–5.49 (m, 1H), 6.84–6.86 (m, 1H), 6.94–6.98 (m, 1H), 7.21–7.23 (m, 1H), 7.28–7.38 (m, 5H), 7.46–7.50 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.47, 16.06, 18.09, 28.73, 37.17, 42.91, 50.30, 55.25, 55.27, 66.36, 110.18, 120.66, 126.64, 126.68, 127.17, 127.96, 128.75, 130.94, 138.86, 154.51, 156.00, 172.85; HRMS (ESI-TOF) calcd for  $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_4\text{Na}[\text{M}+\text{Na}]^+$ : 433.2103; found: 433.2101.

**(S)-3-[(R)-3-(Furan-2-yl)-3-hydroxypropanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(viii)].**

Yield 78%; gummy;  $[\alpha]_D^{20} +229.4$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.82 (d,  $J = 6.8$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H), 1.57 (d,  $J = 7.2$  Hz, 3H), 2.38–2.49 (m, 1H), 2.93 (t,  $J = 9.4$  Hz, 1H), 3.08 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.50–3.62 (m, 2H), 3.69–3.75 (m, 1H), 4.20–4.22 (m, 1H), 5.16–5.22 (m, 1H), 5.33–5.35 (m, 1H), 6.31–6.33 (m, 2H), 7.31–7.35 (m, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.45, 16.06, 18.03, 28.69, 37.26, 41.46, 50.49, 55.29, 64.56, 106.09, 110.15, 127.15, 128.02, 128.78, 138.81, 142.00, 154.43, 155.28, 172.00; HRMS (ESI-TOF) calcd for  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_4\text{Na}[\text{M}+\text{Na}]^+$ : 393.1790; found: 393.1793.

**(S)-3-[(R)-3-Hydroxy-3-(thiophen-2-yl)propanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(ix)].**

Yield 69%; gummy;  $[\alpha]_D^{20} +301.1$  (c 0.5,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.81 (d,  $J = 6.8$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H), 1.57 (d,  $J = 7.2$  Hz, 3H), 2.36–2.39 (m, 1H), 2.90 (t,  $J = 9.4$  Hz, 1H), 3.08 (dd,  $J = 2.9, 7.7$  Hz, 1H), 3.49–3.59 (m, 2H), 4.03 (brs, 1H, OH), 4.18–4.28 (m, 1H), 5.30–5.36 (m, 1H), 5.42–5.44 (m, 1H), 6.93–6.95 (m, 1H), 7.00 (m, 1H), 7.20–7.21 (m, 1H), 7.28–7.38 (m, 5H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.48, 16.07, 18.04, 28.78, 37.26, 44.25, 50.51, 55.31, 67.01, 123.34, 124.44, 126.63, 127.16, 128.03, 128.79, 138.76, 146.98, 154.38, 172.06; HRMS (ESI-TOF) calcd for  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_3\text{SNa}[\text{M}+\text{Na}]^+$ : 409.1562; found: 409.1563.

**(S)-3-[(R,E)-3-hydroxy-5-phenylpent-4-enoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(x)].**

Yield 86%; gummy;  $[\alpha]_D^{20} +220.5$  (c 1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.80 (d,  $J = 7.1$  Hz, 3H), 0.89 (d,  $J = 7.0$  Hz, 3H), 1.57 (d,  $J = 7.1$  Hz, 3H), 2.35–2.43 (m, 1H), 2.90–2.96 (m, 1H), 3.06–3.10 (m, 1H), 3.19–3.27 (m, 1H), 3.38–3.48 (m, 1H), 3.85 (brs, 1H, OH), 4.19–4.23 (m, 1H), 4.75–4.80 (m, 1H), 5.34 (q,  $J = 7.1$  Hz, 1H), 6.30 (dd,  $J = 5.8, 16.8$  Hz, 1H), 6.60 (dd,  $J = 0.9, 15.9$  Hz, 1H), 7.21–7.27 (m, 1H), 7.29–7.35 (m, 5H), 7.37–7.40 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.46, 16.10, 18.05, 28.79, 37.28, 42.58, 50.44, 55.24, 69.24, 126.53, 127.16, 127.51, 128.03, 128.50, 128.80, 130.64, 130.83, 136.80, 138.79, 154.55, 172.39; HRMS (ESI-TOF) calcd for  $\text{C}_{25}\text{H}_{30}\text{N}_2\text{O}_3\text{Na}[\text{M}+\text{Na}]^+$ : 429.2154; found: 429.2154.

**(S)-3-[(R)-3-hydroxy-4-methylpentanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(xi)].**

Yield 78%; gummy;  $[\alpha]_D^{20} +171.5$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.82 (d,  $J$  = 7.1 Hz, 3H), 0.88 (d,  $J$  = 7.0 Hz, 3H), 0.96–1.00 (m, 6H), 1.58 (d,  $J$  = 7.0 Hz, 3H), 1.72–1.78 (m, 1H), 2.38–2.43 (m, 1H), 2.90–2.95 (m, 1H), 3.02–3.08 (m, 2H), 3.17–3.21 (m, 1H), 3.55 (brs, 1H, OH), 3.77–3.80 (m, 1H), 4.19–4.23 (m, 1H), 5.34 (q,  $J$  = 7.0 Hz, 1H), 7.28–7.31 (m, 3H), 7.35–7.38 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.48, 16.06, 17.71, 18.03, 18.56, 28.75, 33.71, 37.26, 39.86, 50.46, 55.33, 73.50, 127.17, 127.99, 128.76, 138.84, 154.80, 173.53; HRMS (ESI-TOF) calcd for C<sub>20</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 369.2154; found: 369.2151.

**(S)-3-[(S)-3-hydroxy-5-methylhexanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(xii)].**  
Yield 91%; gummy;  $[\alpha]_D^{20} +113.4$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.83 (d,  $J$  = 6.9 Hz, 3H), 0.89 (d,  $J$  = 6.9 Hz, 3H), 0.91–0.93 (m, 6H), 1.22–1.30 (m, 1H), 1.49–1.54 (m, 1H), 1.57 (d,  $J$  = 6.9 Hz, 3H), 1.82–1.89 (m, 1H), 2.36–2.43 (m, 1H), 2.91–2.95 (m, 1H), 3.06–3.12 (m, 3H), 3.51 (brs, 1H, OH), 4.07–4.14 (m, 1H), 4.16–4.22 (m, 1H), 5.33 (q,  $J$  = 7.0 Hz, 1H), 7.28–7.31 (m, 3H), 7.35–7.38 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.46, 16.08, 18.04, 22.16, 23.32, 24.41, 28.82, 37.23, 43.04, 46.09, 50.43, 55.21, 66.68, 127.14, 127.98, 128.75, 138.87, 154.60, 173.23; HRMS (ESI-TOF) calcd for C<sub>21</sub>H<sub>32</sub>N<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 383.2311; found: 383.2311.

**(S)-3-[(R)-3-hydroxy-4,4-dimethylpentanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(xiii)].**

Yield 85%; gummy;  $[\alpha]_D^{20} +168.9$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.82 (d,  $J$  = 6.9 Hz, 3H), 0.88 (d,  $J$  = 6.9 Hz, 3H), 0.97 (s, 9H), 1.57 (d,  $J$  = 6.9 Hz, 3H), 2.37–2.42 (m, 1H), 2.89–2.92 (m, 1H), 3.00–3.08 (m, 2H), 3.19–3.32 (m, 1H), 3.61–3.63 (m, 1H), 4.19–4.22 (m, 1H), 5.35 (q,  $J$  = 7.1 Hz, 1H), 7.28–7.31 (m, 3H), 7.34–7.38 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.43, 16.03, 18.03, 25.76, 28.73, 34.91, 37.07, 37.91, 50.42, 55.43, 75.95, 127.19, 128.55, 128.70, 138.76, 154.97, 173.69; HRMS (ESI-TOF) calcd for C<sub>21</sub>H<sub>32</sub>N<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 383.2311; found: 383.2311.

**(S)-3-[(S)-3-hydroxy-4-phenylbutanoyl]-4-isopropyl-1-[(R)-1-phenylethyl]imidazolidin-2-one [9a(xiv)].**

Yield 82%; gummy;  $[\alpha]_D^{20} +170.1$  (c 1, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  0.81 (d,  $J$  = 6.9 Hz, 3H), 0.87 (d,  $J$  = 6.9 Hz, 3H), 1.56 (d,  $J$  = 7.0 Hz, 3H), 2.38–2.39 (m, 1H), 2.80–2.85 (m, 1H), 2.88–2.93 (m, 2H), 3.06 (dd,  $J$  = 2.7, 9.7 Hz, 1H), 3.16–3.18 (m, 1H), 3.58 (d,  $J$  = 4.4 Hz, 1H), 4.16–4.20 (m, 1H), 4.25–4.32 (m, 1H), 5.34 (q,  $J$  = 7.1 Hz, 1H), 7.19–7.23 (m, 1H), 7.27–7.38 (m, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.46, 16.08, 18.05, 28.66, 37.23, 42.12, 43.37, 50.43, 55.23, 69.69, 126.38, 127.18, 128.01, 128.41, 128.78, 129.54, 138.33, 138.84, 154.60, 172.82; HRMS (ESI-TOF) calcd for C<sub>24</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub>Na[M+Na]<sup>+</sup>: 417.2154; found: 417.2154.

**Synthesis of (S)/(R)-3-hydroxy-3-phenylpropanoic acid (10/11).**

To a solution of **8a(i)** or **9a(i)** (3.0 g, 7.88 mmol, 1.0 equiv.) in THF (50 mL, 1:1, v/v) was added aq NaOH (0.63 g, 15.7 mmol, 2.0 equiv, 10 mL H<sub>2</sub>O) and refluxed for 2 h. The reaction mixture was extracted with DCM, dried over anhydrous sodium sulphate and concentrated under vacuum to recover the chiral auxiliary **6a** (1.61 g, 90%). The aqueous layer was acidified, extracted with ethyl acetate, dried and concentrated to afford the corresponding hydroxy acid (**10**, yield 1.2 g, 95% or **11**, yield 1.3 g, 97%).

**(S)-3-Hydroxy-3-phenylpropanoic acid (10).**

White solid; Mp 116–118 °C; yield 95%;  $[\alpha]_{\text{D}}^{20}$  –17.9 (c 1, EtOH),  $[\alpha]_{\text{D}}^{20}$  –57.5 (c 1, CHCl<sub>3</sub>); for its antipode: **11** lit<sup>1a</sup>  $[\alpha]_{\text{D}}^{20}$  +15.5 (c 0.9, EtOH), lit<sup>1b</sup>  $[\alpha]_{\text{D}}^{20}$  +54.8 (c 1.00, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.72–2.85 (m, 2H), 5.15 (dd, *J* = 9.29, 3.76 Hz, 1H), 7.28–7.37 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  43.04, 70.24, 125.69, 128.00, 128.66, 142.18, 176.55; HRMS (ESI-TOF) calcd for C<sub>9</sub>H<sub>10</sub>O<sub>3</sub> [M]<sup>+</sup>: 166.0630; found: 166.1227; and C<sub>9</sub>H<sub>10</sub>O<sub>3</sub>Na [M+Na]<sup>+</sup>: 189.0528; found: 189.1081.

**(R)-3-Hydroxy-3-phenylpropanoic acid (11).**

White solid; Mp 115–119 °C; yield 97%;  $[\alpha]_{\text{D}}^{20}$  +18.2 (c 1.00, EtOH),  $[\alpha]_{\text{D}}^{20}$  +55.9 (c 1.00, CHCl<sub>3</sub>); lit<sup>1a</sup>  $[\alpha]_{\text{D}}^{20}$  +15.5 (c 0.9, EtOH), lit<sup>1b</sup>  $[\alpha]_{\text{D}}^{20}$  +54.8 (c 1.00, CHCl<sub>3</sub>). All the other analytical data were found to be identical with its isomer **10**.

**Synthesis of (S)/(R)-3-hydroxy-N-methyl-3-phenylpropanamide (12/15).**

To a solution of **8a(i)** or **9a(i)** (3.0 g, 7.88 mmol, 1.0 equiv) in methanol (50 mL) was added aq methylamine (1.8 mL, 23.6 mmol, 3.0 equiv; 40% in H<sub>2</sub>O), and refluxed for 5 h. After completion of the reaction the solvent was removed under vacuum, and the reaction mixture was extracted with ethyl acetate, dried, concentrated and purified by column chromatography [silica gel (60–120 mesh), eluent EtOAc:hexanes = 3:7] to afford the chiral auxiliary (1.7 g, 94%) and the corresponding hydroxy amide (eluent EtOAc:hexanes = 4:6; **12**, yield 1.24 g, 88% or **15**, yield 1.26 g, 90%).

**(S)-3-Hydroxy-N-methyl-3-phenylpropanamide (12).**

White solid; Mp 133–136 °C;  $[\alpha]_{\text{D}}^{20}$  –76.3 (c 0.5, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.49–2.59 (m, 2H), 2.82 (s, 3H), 5.07–5.10 (m, 1H), 5.91 (brs, NH, 1H), 7.28–7.36 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  26.20, 44.57, 70.91, 125.57, 127.69, 128.52, 143.05, 172.47; HRMS (ESI-TOF) calcd for C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub>Na [M+Na]<sup>+</sup>: 202.0844; found: 202.0847.

**(R)-3-Hydroxy-N-methyl-3-phenylpropanamide (15).**

White solid; Mp 133–137 °C;  $[\alpha]_{\text{D}}^{20}$  +75.8 (c 0.5, CHCl<sub>3</sub>). All the other analytical data were found to be identical with its isomer **12**.

**Synthesis of (S)/(R)-3-(methylamino)-1-phenylpropan-1-ol (13/16).**

To a solution of **12** or **15** (1.5 g, 8.38 mmol, 1.0 equiv.) in dry THF (15 mL) was added lithium aluminium hydride (1.27 g, 33.5 mmol, 4.0 equiv), and refluxed for 6 h. The reaction mixture was slowly quenched with aq NaOH (1.5 mL, 1 M solution), and the thick slurry was filtered through celite bed. The filtrate was dried over anhydrous sodium sulphate and concentrated to afford the desired product (**13**, yield 1.23 g, 89% or **16**, yield 1.19 g, 86%).

**(S)-3-(Methylamino)-1-phenylpropan-1-ol (13).**



Liquid;  $[\alpha]_D^{20} -35.3$  (c 1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.75–1.91 (m, 2H), 2.45 (s, 3H), 2.83–2.94 (m, 2H), 4.94 (dd,  $J = 8.7, 3.7$  Hz, 1H), 7.23–7.26 (m, 1H) 7.32–7.39 (m, 4H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  36.03, 36.85, 50.43, 75.63, 125.60, 126.95, 128.22, 145.04; HRMS (ESI-TOF) calcd for  $\text{C}_{10}\text{H}_{16}\text{NO}[\text{M}+\text{H}]^+$ : 166.1232; found: 166.1231 and  $\text{C}_{10}\text{H}_{15}\text{NONa}[\text{M}+\text{Na}]^+$ : 188.1051; found: 188.1051.

**(R)-3-(Methylamino)-1-phenylpropan-1-ol (16).**

Liquid;  $[\alpha]_D^{20} +34.8$  (c 1.00,  $\text{CHCl}_3$ ), lit<sup>2</sup>  $[\alpha]_D^{20} +35.1$  (c 0.75,  $\text{CHCl}_3$ ), lit<sup>3</sup>  $[\alpha]_D^{20} +37.1$  (c 1.0,  $\text{CHCl}_3$ ). All the other analytical data were found to be identical with its isomer **13**.

**Synthesis of (S)/(R)-fluoxetine (14/17).**

To a solution of **13/16** (0.3 g, 1.81 mmol, 1.0 equiv.) in dry *N,N*-dimethylacetamide (10 mL) was added sodium hydride (60% suspension in paraffin oil, 0.08 g, 1.99 mmol, 1.1 equiv), and heated at 90 °C for 30 min under  $\text{N}_2$  atmosphere. The reaction mixture was cooled and then 4-fluorobenzotrifluoride (0.33 g, 1.99 mmol, 1.1 equiv) was added to it. Heating was continued at 100 °C for 5 h. The reaction mixture was cooled and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulphate and concentrated to afford the crude product which was purified by column chromatography [neutral alumina, eluent DCM:MeOH = 9:1] to afford the desired compound (**14**, yield 0.51 g 91, or **17**, yield 0.49 g, 88%).

**(S)-Fluoxetine (14).**

Liquid;  $[\alpha]_D^{20} -3.9$  (c 1.00,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.88 (brs, NH, 1H), 2.00–2.07 (m, 1H), 2.17–2.26 (m, 1H), 2.44 (s, 3H), 2.74–2.75 (m, 2H), 5.31 (dd,  $J = 4.7, 8.2$  Hz, 1H), 6.91 (d,  $J = 8.6$  Hz, 2H), 7.24–7.28 (m, 1H), 7.30–7.37 (m, 4H), 7.43 (d,  $J = 8.6$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  29.70, 36.42, 38.65, 48.21, 78.63, 115.75, 125.77, 126.76, 126.80, 127.84, 128.79, 141.00, 160.53; HRMS (ESI-TOF) calcd for  $\text{C}_{17}\text{H}_{19}\text{F}_3\text{NO}[\text{M}+\text{H}]^+$ : 310.1419; found: 310.1419.

**(R)-Fluoxetine (17).**

Liquid;  $[\alpha]_D^{20} +4.3$  (c 1.00,  $\text{CHCl}_3$ ), lit<sup>2</sup>  $[\alpha]_D^{20} +3.8$  (c 0.9,  $\text{CHCl}_3$ ), lit<sup>3</sup>  $[\alpha]_D^{20} +4.1$  (c 1.0,  $\text{CHCl}_3$ ). All the other analytical data were found to be identical with its isomer **14**.

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