

#### Normorphine:

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.46 (d,  $J$  = 8.0 Hz, H-2), 6.35 (d,  $J$  = 8.1 Hz, H-1), 5.55 (dp,  $J$  = 9.9, 1.5 Hz, H-7), 5.20 (dt,  $J$  = 9.8, 2.8 Hz, H-8), 4.67 (dd,  $J$  = 6.1, 1.3 Hz, H-5), 4.07 (dd,  $J$  = 6.1, 3.1 Hz, H-6), 3.72 (m, H-9), 2.88 (dd,  $J$  = 13.2, 4.7 Hz, H-16), 2.73 (m, H-10), 2.72 (m, H-16), 2.55 (p,  $J$  = 2.8 Hz, H-14), 1.92 (td,  $J$  = 13.0, 5.0 Hz, H-15), 1.68 (m, H-15), 1.20 (s, H-10)

$^{13}\text{C}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  146.7 (C4), 139.2 (C3), 134.5 (C7), 130.7 (C12), 127.6 (C8), 124.7 (C11), 119.1 (C1), 117.1 (C2), 92.1 (C5), 66.4 (C6), 51.4 (C9), 43.6 (C13), 39.6 (C14), 37.9 (C16), 35.0 (C15), 29.2 (C10)

#### Dihydronormorphine:

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.53 (d,  $J$  = 7.9 Hz, H-2), 6.42 (d,  $J$  = 8.0 Hz, H-1), 4.42 (d,  $J$  = 4.9 Hz, H-5), 3.81 (ddd,  $J$  = 8.6, 4.9, 3.5 Hz, H-6), 3.23 (dd,  $J$  = 6.2, 2.8 Hz, H-9), 2.79 (dd,  $J$  = 18.2, 6.3 Hz, H-10), 2.64 (m, H-16), 2.62 (m, H-10), 2.57 (m, H-16), 2.07 (ddd,  $J$  = 11.6, 6.7, 2.9 Hz, H-14), 1.69 (td,  $J$  = 12.5, 5.0 Hz, H-15), 1.48 (ddd,  $J$  = 12.5, 3.7, 1.5 Hz, H-15), 1.37 (m, H-8), 1.31 (m, H-7), 1.19 (m, H-7), 0.83 (tt,  $J$  = 12.2, 6.2 Hz, H-8)

$^{13}\text{C}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  146.4 (C4), 138.4 (C3), 130.3 (C12), 125.4 (C11), 118.4 (C1), 117.2 (C2), 90.5 (C5), 66.4 (C6), 52.3 (C9), 43.1 (C13), 38.6 (C14), 38.3 (C16), 37.7 (C15), 29.9 (C10), 26.3 (C7), 20.1 (C8)

#### Norcodeine:

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.60 (d,  $J$  = 8.2 Hz, H-2), 6.44 (d,  $J$  = 8.2 Hz, H-1), 5.52 (dp,  $J$  = 9.7, 1.5 Hz, H-7), 5.21 (dt,  $J$  = 9.8, 2.8 Hz, H-8), 4.64 (dd,  $J$  = 5.9, 1.4 Hz, H-5), 4.09 (dh,  $J$  = 5.4, 2.6 Hz, H-6), 3.72 (s, OCH<sub>3</sub>), 3.46 (dd,  $J$  = 5.9, 3.3 Hz, H-9), 2.71 (m, H-10), 2.67 (m, H-16), 2.65 (m, H-10), 2.46 (q,  $J$  = 2.8 Hz, H-14), 1.82 (td,  $J$  = 12.2, 5.5 Hz, H-15), 1.59 (dt,  $J$  = 12.3, 2.4 Hz, H-15)

$^{13}\text{C}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  147.7 (C4), 141.6 (C3), 133.7 (C7), 131.8 (C12), 129.1 (C8), 128.3 (C11), 118.7 (C1), 113.6 (C2), 93.1 (C5), 66.8 (C6), 56.5 (OCH<sub>3</sub>), 51.5 (C9), 44.3 (C13), 41.1 (C14), 38.4 (C16), 36.9 (C15), 31.3 (C10)

#### Dihydronorcodeine:

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.69 (d,  $J$  = 8.1 Hz, H-2), 6.53 (d,  $J$  = 8.1 Hz, H-1), 4.43 (d,  $J$  = 4.9 Hz, H-5), 3.81 (m, H-6), 3.76 (s, OCH<sub>3</sub>), 3.17 (s, H-9), 2.81 (dd,  $J$  = 18.1, 6.2 Hz, H-10), 2.61 (m, H-10), 2.59 (m, H-16), 2.54 (m, H-16), 2.06 (ddd,  $J$  = 11.8, 6.7, 2.8 Hz, H-14), 1.66 (td,  $J$  = 12.3, 5.2 Hz, H-15), 1.45 (m, H-15), 1.36 (m, H-8), 1.32 (m, H-7), 1.18 (m, H-7), 0.83 (tt,  $J$  = 11.9, 6.1 Hz, H-8)

$^{13}\text{C}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  147.5 (C4), 141.2 (C3), 130.9 (C12), 127.8 (C11), 118.5 (C1), 114.4 (C2), 91.1 (C5), 66.3 (C6), 56.7 (OCH<sub>3</sub>), 52.3 (C9), 43.0 (C13), 39.1 (C14), 38.4 (C16), 38.1 (C15), 30.5 (C10), 26.4 (C7), 20.2 (C8)

#### Noroxymorphine:

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.52 (d,  $J$  = 8.1 Hz, H-2), 6.49 (d,  $J$  = 8.1 Hz, H-1), 4.64 (s, H-5), 2.97 (m, H-9), 2.91 (m, H-10), 2.90 (m, H-7), 2.83 (m, H-10), 2.62 (dd,  $J$  = 13.1, 4.6 Hz, H-16), 2.37 (td,  $J$  = 12.8, 3.6 Hz, H-16), 2.29 (dd,  $J$  = 12.3, 4.8 Hz, H-15), 2.07 (dt,  $J$  = 14.2, 3.2 Hz, H-7), 1.74 (ddd,  $J$  = 13.6, 5.2, 2.9 Hz, H-8), 1.42 (td,  $J$  = 14.0, 3.5 Hz, H-8), 1.15 (dd,  $J$  = 12.1, 3.2 Hz, H-15)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 209.1 (C6), 143.9 (C4), 139.8 (C3), 130.0 (C12), 124.4 (C11), 119.4 (C1), 117.6 (C2), 89.9 (C5), 70.1 (C14), 57.3 (C9), 50.9 (C13), 37.8 (C16), 36.3 (C7), 31.83 (C10), 31.77 (C8), 30.0 (C15)

Noroxymorphone ethylene ketal:

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.53 (d, J = 8.0 Hz, H-2), 6.43 (d, J = 8.1 Hz, H-1), 4.28 (s, H-5), 4.04 (td, J = 6.9, 4.6 Hz) and 3.91 (q, J = 6.8 Hz) and 3.76 (q, J = 7.0 Hz) and 3.69 (td, J = 6.6, 4.7 Hz) (CH<sub>2</sub> ketal), 2.85 (dd, J = 17.7, 5.7 Hz, H-10), 2.80 (m, H-9), 2.79 (m, H-10), 2.52 (m, H-16), 2.39 (td, J = 12.7, 3.9 Hz, H-16), 2.09 (m, H-15), 2.05 (m, H-7), 1.36 (m, H-8), 1.23 (m, H-7), 1.05 (dd, J = 12.2, 3.5 Hz, H-15)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 145.1 (C4), 139.2 (C3), 131.1 (C12), 124.1 (C11), 118.0 (C1), 117.2 (C2), 108.6 (C6), 93.3 (C5), 69.8 (C14), 66.4 and 64.6 (ketal CH<sub>2</sub>), 57.7 (C9), 48.3 (C13), 37.9 (C16), 32.2 (C10), 31.0 (C15), 29.4 (C7), 29.2 (C8)

Noroxycodone:

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.70 (d, J = 8.2 Hz, H-2), 6.62 (d, J = 8.2 Hz, H-1), 4.70 (s, H-5), 3.78 (s, OCH<sub>3</sub>), 2.96 (m, H-10), 2.94 (m, H-9), 2.91 (m, H-7), 2.88 (m, H-10), 2.58 (dd, J = 13.3, 4.7 Hz, H-16), 2.34 (td, J = 12.6, 3.2 Hz, H-16), 2.30 (td, J = 12.0, 4.5 Hz, H-15), 2.08 (dt, J = 14.1, 3.2 Hz, H-7), 1.74 (ddd, J = 13.6, 5.1, 2.9 Hz, H-8), 1.40 (td, J = 14.1, 3.4 Hz, H-8), 1.14 (dd, J = 12.1, 3.0 Hz, H-15)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 208.9 (C6), 144.9 (C4), 142.3 (C3), 130.3 (C12), 126.8 (C11), 119.5 (C1), 115.1 (C2), 90.5 (C5), 70.1 (C14), 57.3 (C9), 56.8 (OCH<sub>3</sub>), 51.0 (C13), 37.9 (C16), 36.3 (C7), 32.2 (C10), 32.0 (C8), 30.2 (C15)

Noroxycodone ethylene ketal:

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.70 (d, J = 8.1 Hz, H-2), 6.54 (d, J = 8.2 Hz, H-1), 4.29 (s, H-5), 3.98 (td, J = 6.9, 4.6 Hz) and 3.77 (q, J = 6.8 Hz) and 3.74 (q, J = 7.0 Hz) and 3.65 (td, J = 6.6, 4.7 Hz) (CH<sub>2</sub> ketal), 2.85 (m, H-10), 2.79 (m, H-9), 2.49 (m, H-16), 2.32 (td, J = 12.7, 3.9 Hz, H-16), 2.07 (m, H-15), 2.01 (m, H-7), 1.34 (m, H-8), 1.29 (m, H-7), 1.03 (dd, J = 12.3, 3.6 Hz, H-15)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 146.2 (C4), 142.2 (C3), 131.3 (C12), 126.3 (C11), 118.2 (C1), 114.9 (C2), 108.9 (C6), 93.6 (C5), 69.9 (C14), 66.3 and 64.7 (ketal CH<sub>2</sub>), 57.5 (C9), 56.9 (OCH<sub>3</sub>), 48.3 (C13), 37.9 (C16), 32.0 (C10), 30.9 (C15), 29.3 (C7), 29.1 (C8)

N-carboxymethyl-normorphine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.40 (d, J = 8.0 Hz, H-2), 6.31 (d, J = 8.0 Hz, H-1), 5.49 (m, H-7), 5.19 (dt, J = 9.7, 2.8 Hz, H-8), 4.64 (dd, J = 6.1, 1.3 Hz, H-5), 4.09 (dd, J = 6.1, 3.1 Hz, H-6), 4.06 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.39 (s, CH<sub>2</sub> bridge), 3.35 (m, C-9), 3.23 (d, J = 16.5 Hz, CH<sub>2</sub> bridge), 2.77 (d, J = 18.5 Hz, H-10), 2.58 (m, H-16), 2.55 (m, H-14), 2.31 (td, J = 12.2, 3.4 Hz, H-16), 2.26 (dd, J = 18.5, 6.4 Hz, H-10), 1.98 (m, H-15), 1.58 (dt, J = 11.0, 2.2 Hz, H-15), 1.16 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 170.9 (ester C=O), 146.6 (C4), 138.9 (C3), 133.8 (C7), 131.3 (C12), 128.6 (C8), 125.7 (C11), 118.9 (C1), 116.7 (C2), 91.9 (C5), 66.7 (C6), 60.4 (ester CH<sub>2</sub>), 57.2 (C9), 56.5 (CH<sub>2</sub> bridge), 44.9 (C16), 43.5 (C13), 40.66 (C14), 35.6 (C15), 22.4 (C10), 14.5 (ester CH<sub>3</sub>)

N-carboxymethyl-dihydronormorphine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.49 (d, J = 8.0 Hz, H-2), 6.38 (d, J = 8.0 Hz, H-1), 4.41 (d, J = 4.8 Hz, H-5), 4.04 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.79 (dd, J = 9.1, 4.4 Hz, H-6), 3.31 (s, (CH<sub>2</sub> bridge), 3.15 (d, J = 16.4 Hz, (CH<sub>2</sub> bridge), 3.02 (dd, J = 6.0, 2.8 Hz, H-9), 2.71 (d, J = 18.3 Hz, H-10), 2.49 (m, H-16) 2.31 (dd, J = 18.4, 6.0 Hz, H-10), 2.18 – 2.09 (m, H-14, H-15), 1.78 (d, J = 5.1 Hz, H-15), 1.44 – 1.38 (m, H-15), 1.35 (dd, J = 13.4, 6.8 Hz, H-8), 1.28 (ddt, J = 12.8, 6.5, 3.9 Hz, H-7), 1.15 (t, J = 7.1 Hz, ester CH<sub>3</sub>), 1.11 (m, H-7), 0.83 (tt, J = 12.5, 6.4 Hz, H-8)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 171.0 (ester C=O), 146.4 (C<sub>4</sub>), 138.4 (C<sub>3</sub>), 130.4 (C<sub>12</sub>), 125.4 (C<sub>11</sub>), 118.4 (C<sub>1</sub>), 117.1 (C<sub>2</sub>), 90.3 (C<sub>5</sub>), 66.5 (C<sub>6</sub>), 60.4 (ester CH<sub>2</sub>), 58.3 (C<sub>9</sub>), 56.8 (CH<sub>2</sub> bridge), 44.9 (C<sub>16</sub>), 42.2 (C<sub>13</sub>), 38.2 (C<sub>14</sub>), 37.4 (C<sub>15</sub>), 26.0 (C<sub>7</sub>), 21.9 (C<sub>10</sub>), 19.9 (C<sub>8</sub>), 14.6 (ester CH<sub>3</sub>)

#### *N*-carboxymethyl-norcodeine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.58 (d, J = 8.2 Hz, H-2), 6.42 (d, J = 8.2 Hz, H-1), 5.49 (ddt, J = 9.8, 3.2, 1.5 Hz, H-7), 5.19 (dt, J = 9.8, 2.8 Hz, H-8), 4.66 (dd, J = 6.0, 1.3 Hz, H-5), 4.10 (tq, J = 5.7, 2.7 Hz, H-6), 4.05 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.70 (d, J = 2.2 Hz, CH<sub>2</sub> bridge), 3.69 (s, OCH<sub>3</sub>), 3.23 (d, J = 16.6 Hz, CH<sub>2</sub> bridge), 2.81 (d, J = 18.6 Hz, H-10), 2.57 (dp, J = 8.8, 3.3, 2.6 Hz, H-16), 2.56 (m, H-14), 2.34 – 2.25 (m, H-10, H-16), 1.98 (td, J = 12.6, 5.0 Hz, H-15), 1.62 – 1.53 (m, H-15), 1.16 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 170.6 (ester C=O), 147.2 (C<sub>4</sub>), 141.7 (C<sub>3</sub>), 133.9 (C<sub>7</sub>), 131.6 (C<sub>12</sub>), 128.7 (C<sub>8</sub>), 127.5 (C<sub>11</sub>), 118.9 (C<sub>1</sub>), 113.7 (C<sub>2</sub>), 92.5 (C<sub>5</sub>), 67.0 (C<sub>6</sub>), 60.5 (ester CH<sub>2</sub>), 57.3 (C<sub>9</sub>), 56.6 (CH<sub>2</sub> bridge), 56.5 (OCH<sub>3</sub>), 44.9 (C<sub>16</sub>), 43.5 (C<sub>13</sub>), 40.6 (C<sub>14</sub>), 35.6 (C<sub>15</sub>), 22.6 (C<sub>10</sub>), 14.6 (ester CH<sub>3</sub>)

#### *N*-carboxymethyl-dihydronorcodeine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.66 (d, J = 8.2 Hz, H-2), 6.50 (d, J = 8.1 Hz, H-1), 4.43 (dd, J = 7.8, 4.9 Hz, H-5), 4.04 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.79 (tt, J = 8.7, 4.1 Hz, H-6), 3.72 (s, OCH<sub>3</sub>), 3.32 (s, CH<sub>2</sub> bridge), 3.16 (d, J = 16.4 Hz, CH<sub>2</sub> bridge), 3.04 (dd, J = 5.9, 2.7 Hz, H-9), 2.75 (d, J = 18.4 Hz, H-10), 2.51 – 2.48 (m, H-16), 2.34 (dd, J = 18.4, 6.0 Hz, H-10), 2.17 – 2.09 (m, H-16, H-14), 1.79 (td, J = 12.4, 5.0 Hz, H-15), 1.40 (ddd, J = 12.5, 3.6, 1.7 Hz, H-15), 1.34 (dd, J = 13.3, 6.7 Hz, H-8), 1.29 (ddd, J = 13.4, 7.2, 4.2 Hz, H-7), 1.15 (t, J = 7.1 Hz, ester CH<sub>3</sub>), 1.13 – 1.08 (m, H-7), 0.84 (tt, J = 11.9, 6.1 Hz, H-8)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 170.9 (ester C=O), 147.4 (C<sub>4</sub>), 141.3 (C<sub>3</sub>), 130.7 (C<sub>12</sub>), 127.3 (C<sub>11</sub>), 118.4 (C<sub>1</sub>), 114.4 (C<sub>2</sub>), 90.7 (C<sub>5</sub>), 66.3 (C<sub>6</sub>), 60.3 (ester CH<sub>2</sub>), 58.2 (C<sub>9</sub>), 56.8 (CH<sub>2</sub> bridge), 56.7 (OCH<sub>3</sub>), 44.9 (C<sub>16</sub>), 42.4 (C<sub>13</sub>), 38.4 (C<sub>14</sub>), 37.3 (C<sub>15</sub>), 26.1 (C<sub>7</sub>), 22.0 (C<sub>10</sub>), 19.8 (C<sub>8</sub>), 14.5 (ester CH<sub>3</sub>)

#### *N*-carboxymethyl-noroxymorphone ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.53 (d, J = 8.1 Hz, H-2), 6.50 (d, J = 8.1 Hz, H-1), 4.74 (s, H-5), 4.12 – 4.06 (m, ester CH<sub>2</sub>), 3.43 (d, J = 17.1 Hz, CH<sub>2</sub> bridge), 3.31 (d, J = 17.2 Hz, CH<sub>2</sub> bridge), 2.97 (d, J = 18.5 Hz, H-10), 2.90 (d, J = 5.9 Hz, H-9), 2.89 – 2.82 (m, H-7), 2.57 (d, J = 5.9 Hz, H-10), 2.49 (m, H-16), 2.38 – 2.29 (m, H-15), 2.18 (td, J = 12.0, 3.6 Hz, H-16), 2.06 (dt, J = 14.2, 3.2 Hz, H-7), 1.71 (ddd, J = 13.4, 5.0, 3.0 Hz, H-8), 1.40 (td, J = 14.1, 3.4 Hz, H-8), 1.28 – 1.22 (m, H-15), 1.18 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 209.0 (C<sub>6</sub>), 171.3 (ester C=O), 143.8 (C<sub>4</sub>), 139.8 (C<sub>3</sub>), 129.6 (C<sub>12</sub>), 123.6 (C<sub>11</sub>), 119.5 (C<sub>1</sub>), 117.6 (C<sub>2</sub>), 89.7 (C<sub>5</sub>), 70.4 (C<sub>14</sub>), 62.8 (C<sub>9</sub>), 60.7 (ester CH<sub>2</sub>), 55.6 (CH<sub>2</sub> bridge), 50.3 (C<sub>13</sub>), 43.9 (C<sub>16</sub>), 36.2 (C<sub>7</sub>), 31.5 (C<sub>8</sub>), 30.6 (C<sub>15</sub>), 24.3 (C<sub>10</sub>), 14.5 (ester CH<sub>3</sub>)

#### *N*-carboxymethyl-noroxycodone ethyl ester

$^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  6.72 (d,  $J$  = 8.2 Hz, H-2), 6.63 (d,  $J$  = 8.2 Hz, H-1), 4.81 (s, H-5), 4.15 – 4.03 (m, ester CH<sub>2</sub>), 3.75 (s, OCH<sub>3</sub>), 3.44 (d,  $J$  = 17.1 Hz, CH<sub>2</sub> bridge), 3.32 (d, CH<sub>2</sub> bridge), 3.01 (d,  $J$  = 18.6 Hz, H-10), 2.92 (d,  $J$  = 5.7 Hz, H-9), 2.87 (td,  $J$  = 14.4, 5.0 Hz, H-7), 2.59 (dd,  $J$  = 18.7, 5.8 Hz, H-10), 2.52 – 2.48 (m, H-16), 2.34 (td,  $J$  = 12.5, 5.3 Hz, H-15), 2.17 (td,  $J$  = 12.0, 3.6 Hz, H-16), 2.06 (dt,  $J$  = 14.1, 3.2 Hz, H-7), 1.72 (ddd,  $J$  = 13.5, 5.0, 3.0 Hz, H-8), 1.43 – 1.34 (m, H-8), 1.30 – 1.23 (m, H-15), 1.18 (t,  $J$  = 7.1 Hz, ester CH<sub>3</sub>)

$^{13}\text{C}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  208.8 (C<sub>6</sub>), 171.3 (ester C=O), 144.8 (C<sub>4</sub>), 142.4 (C<sub>3</sub>), 129.9 (C<sub>12</sub>), 125.8 (C<sub>11</sub>), 119.7 (C<sub>1</sub>), 115.2 (C<sub>2</sub>), 90.2 (C<sub>5</sub>), 70.3 (C<sub>14</sub>), 62.8 (C<sub>9</sub>), 60.7 (ester CH<sub>2</sub>), 56.8 (OCH<sub>3</sub>), 55.7 (CH<sub>2</sub> bridge), 50.2 (C<sub>13</sub>), 43.8 (C<sub>16</sub>), 36.3 (C<sub>7</sub>), 31.6 (C<sub>8</sub>), 30.5 (C<sub>15</sub>), 24.3 (C<sub>16</sub>), 14.5 (ester CH<sub>3</sub>)

#### *N*-carboxymethyl-normorphine

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.61 (d,  $J$  = 8.2 Hz, H-2), 6.53 (d,  $J$  = 8.2 Hz, H-1), 5.60 (m, H-7), 5.24 (d,  $J$  = 10.0 Hz, H-8), 4.92 (d,  $J$  = 6.5 Hz, H-5), 4.27 (m, H-9), 4.25 (m, H-6), 4.00 (m, CH<sub>2</sub> bridge) 3.48 (q,  $J$  = 7.1 Hz, H-16), 3.11 (d,  $J$  = 20.1 Hz, H-10), 2.99 (d,  $J$  = 18.1 Hz, H-14), 2.80 (dd,  $J$  = 20.0, 6.8 Hz, H-10), 2.39 – 2.19 (m, H-15), 2.02 (d,  $J$  = 14.6 Hz, H-13)

$^{13}\text{C}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  169.2 (ester C=O), 145.5 (C<sub>4</sub>), 137.8 (C<sub>3</sub>), 132.9 (C<sub>7</sub>), 129.0 (C<sub>12</sub>), 125.4 (C<sub>8</sub>), 123.0 (C<sub>11</sub>), 120.0 (C<sub>1</sub>), 117.6 (C<sub>2</sub>), 89.9 (C<sub>5</sub>), 65.5 (C<sub>6</sub>), 60.2 (C<sub>9</sub>), 54.9 (CH<sub>2</sub> bridge), 47.1 (C<sub>16</sub>), 41.8 (C<sub>13</sub>), 38.1 (C<sub>14</sub>), 32.2 (C<sub>15</sub>), 21.9 (C<sub>16</sub>)

#### *N*-carboxymethyl-dihydronormorphine

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.69 (d,  $J$  = 7.9 Hz, H-2), 6.62 (d,  $J$  = 8.2 Hz, H-1), 4.64 (m, H-5), 4.07 – 3.83 (m, H-6, H-9, CH<sub>2</sub> bridge), 3.34 (dd,  $J$  = 13.4, 4.4 Hz, H-16), 3.06 (d,  $J$  = 20.2 Hz, H-10), 2.91 (dd,  $J$  = 19.9, 6.0 Hz, H-10), 2.82 (ddd,  $J$  = 17.3, 13.9, 7.6 Hz, H-16), 2.47 (t,  $J$  = 19.4 Hz, H-14), 2.08 (td,  $J$  = 13.9, 5.0 Hz, H-15), 1.78 (dd,  $J$  = 14.7, 3.7 Hz, H-15), 1.44 (q,  $J$  = 6.2 Hz, H-7, H-8), 0.99 – 0.83 (m, H-8)

$^{13}\text{C}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  168.3 (carboxylic C=O), 145.2 (C<sub>4</sub>), 137.1 (C<sub>3</sub>), 128.4 (C<sub>12</sub>), 122.6 (C<sub>11</sub>), 119.8 (C<sub>1</sub>), 117.8 (C<sub>2</sub>), 89.0 (C<sub>5</sub>), 66.1 (C<sub>6</sub>), 61.5 (C<sub>9</sub>), 55.0 (CH<sub>2</sub> bridge), 47.5 (C<sub>16</sub>), 40.2 (C<sub>13</sub>), 38.3 (C<sub>14</sub>), 34.1 (C<sub>15</sub>), 26.0 (C<sub>7</sub>), 21.4 (C<sub>10</sub>), 17.7 (C<sub>8</sub>)

#### *N*-carboxymethyl-norcodeine

Under measurement.

#### *N*-carboxymethyl-dihydronorcodeine

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.85 (d,  $J$  = 7.9 Hz, H-2), 6.72 (d,  $J$  = 8.2 Hz, H-1), 4.69 (d,  $J$  = 5.4 Hz, H-5), 4.16 – 3.79 (m, H-6, H-9, CH<sub>2</sub> bridge), 3.80 – 3.70 (s, OCH<sub>3</sub>), 3.38 – 3.29 (m, H-16), 3.09 (d,  $J$  = 20.2 Hz, H-10), 2.99 – 2.87 (m, H-10), 2.80 (t,  $J$  = 12.6 Hz, H-16), 2.46 (d,  $J$  = 11.6 Hz, H-14), 2.08 (dd,  $J$  = 14.7, 10.0 Hz, H-15), 1.78 (d,  $J$  = 14.0 Hz, H-15), 1.45 (d,  $J$  = 8.7 Hz, H-7, H-8), 0.98 – 0.87 (m, H-8)

$^{13}\text{C}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  168.5 (carboxylic C=O), 145.8 (C<sub>4</sub>), 141.3 (C<sub>3</sub>), 127.8 (C<sub>12</sub>), 123.4 (C<sub>11</sub>), 119.9 (C<sub>1</sub>), 115.0 (C<sub>2</sub>), 89.2 (C<sub>5</sub>), 66.0 (C<sub>6</sub>), 61.5 (C<sub>9</sub>), 56.7 (OCH<sub>3</sub>), 55.1 (CH<sub>2</sub> bridge), 47.4 (C<sub>16</sub>), 40.1 (C<sub>13</sub>), 38.2 (C<sub>14</sub>), 34.1 (C<sub>15</sub>), 26.0 (C<sub>7</sub>), 21.4 (C<sub>10</sub>), 17.6 (8)

#### *N*-carboxymethyl-noroxymorphine

$^1\text{H}$  NMR (600 MHz,  $\text{D}_2\text{O}$ )  $\delta$  6.70 (d,  $J = 8.2$  Hz, H-2), 6.68 (d,  $J = 8.3$  Hz, H-1), 4.92 (s, H-5), 3.93 (d,  $J = 16.7$  Hz, CH2 bridge), 3.88 (d,  $J = 6.2$  Hz, H-9), 3.69 (d,  $J = 16.7$  Hz, CH2 bridge), 3.29 (d,  $J = 20.0$  Hz, H-10), 3.18 (dd,  $J = 13.1, 4.9$  Hz, H-16), 3.06 (dd,  $J = 20.1, 6.4$  Hz, H-10), 2.89 (td,  $J = 14.8, 5.1$  Hz, H-7), 2.81 (td,  $J = 13.0, 4.1$  Hz, H-16), 2.65 (td,  $J = 13.5, 5.0$  Hz, H-15), 2.20 (dt,  $J = 14.9, 3.2$  Hz, H-7), 1.96 (ddd,  $J = 14.6, 5.2, 2.9$  Hz, H-8), 1.65 (dd,  $J = 12.9, 3.7$  Hz, H-15), 1.60 (dd,  $J = 14.6, 3.6$  Hz, H-8)

$^{13}\text{C}$  NMR (600 MHz,  $\text{D}_2\text{O}$ )  $\delta$  209.3 (C6), 168.8 (carboxylic C=O), 143.0 (C4), 138.5 (C3), 127.2 (C12), 121.7 (C11), 121.1 (C1), 118.7 (C2), 89.2 (C5), 70.7 (C14), 64.9 (C9), 54.7 (CH2 bridge), 48.6 (C13), 46.7 (C16), 34.6 (C7), 30.5 (C8), 27.5 (C15), 23.9 (C10)

#### *N*-carboxymethyl-noroxycodone

$^1\text{H}$  NMR (600 MHz,  $\text{D}_2\text{O}$ )  $\delta$  6.86 (d,  $J = 8.4$  Hz, H-2), 6.78 (d,  $J = 8.4$  Hz, H-1), 4.95 (s, H-5), 3.94 – 3.79 (m, H-9, CH2 bridge), 3.74 (s, OCH3), 3.63 (d,  $J = 16.4$  Hz, CH2 bridge), 3.31 (d,  $J = 20.0$  Hz, H-10), 3.17 (ddt,  $J = 13.1, 5.0, 1.4$  Hz, H-16), 3.12 – 3.05 (m, H-10), 2.90 (td,  $J = 14.8, 5.1$  Hz, H-7), 2.80 (td,  $J = 13.0, 4.1$  Hz, H-16), 2.65 (td,  $J = 13.5, 5.0$  Hz, H-15), 2.21 (dt,  $J = 14.9, 3.2$  Hz, H-7), 1.96 (ddd,  $J = 14.5, 5.1, 2.9$  Hz, H-8), 1.65 (dd,  $J = 14.2, 3.8$  Hz, H-15), 1.60 (dd,  $J = 14.6, 3.5$  Hz, H-8)

$^{13}\text{C}$  NMR (600 MHz,  $\text{D}_2\text{O}$ )  $\delta$  210.3 (C6), 169.2 (carboxylic C=O), 143.9 (C4), 142.4 (C3), 127.1 (C12), 122.5 (C11), 121.1 (C1), 115.6 (C2), 89.4 (C5), 70.4 (C14), 64.9 (C9), 56.7 (OCH3), 55.2 (CH2 bridge), 48.7 (C13), 46.6 (C16), 34.5 (C7), 30.5 (C8), 27.6 (C15), 23.9 (C10)

#### *N*-carboxyethyl-normorphine ethyl ester

$^1\text{H}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  6.44 (d,  $J = 8.0$  Hz, H-2), 6.34 (d,  $J = 8.1$  Hz, H-1), 5.52 (dp,  $J = 9.7, 1.5$  Hz, H-7), 5.22 (dt,  $J = 9.8, 2.8$  Hz, H-8), 4.66 (dd,  $J = 6.1, 1.3$  Hz, H-5), 4.15 – 4.00 (m, H-6, ester CH2), 3.35 (m, H-9), 2.78 (dt,  $J = 14.3, 5.9$  Hz, H-10, ethylene bridge CH2), 2.64 (dt,  $J = 12.9, 6.6$  Hz, ethylene bridge CH2), 2.60 – 2.53 (m, H-16), 2.48 – 2.39 (m, H-14, ethylene bridge CH2), 2.33 – 2.21 (m, H-16, H-10), 1.92 (td,  $J = 12.5, 5.0$  Hz, H-15), 1.61 (ddd,  $J = 12.5, 3.4, 1.7$  Hz, H-15), 1.19 (t,  $J = 7.1$  Hz, ester CH3)

$^{13}\text{C}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  172.3 (ester C=O), 146.8 (C4), 138.7 (C3), 133.9 (C7), 131.2 (C12), 128.8 (C8), 125.7 (C11), 118.9 (C1), 116.8 (C2), 92.0 (C5), 66.8 (C6), 60.3 (ester CH2), 57.1 (C9), 50.8 (ethylene bridge CH2), 44.6 (C16), 43.8 (C13), 41.6 (C14), 36.0 (C15), 33.7 (ethylene bridge CH2), 22.2 (C10), 14.7 (ester CH3)

#### *N*-carboxyethyl-dihydronormorphine ethyl ester

$^1\text{H}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  6.53 (d,  $J = 8.0$  Hz, H-2), 6.41 (d,  $J = 8.0$  Hz, H-1), 4.44 (d,  $J = 4.8$  Hz, H-5), 4.06 (q,  $J = 7.1$  Hz, ester CH2), 3.80 (dq,  $J = 8.7, 4.2$  Hz, H-6), 3.16 – 2.99 (m, H-9), 2.77 (d,  $J = 18.5$  Hz, H-10), 2.46 (d,  $J = 6.9$  Hz, ethylene bridge CH2), 2.12 (d,  $J = 39.2$  Hz, H-16), 1.82 – 1.72 (m, H-15), 1.46 (d,  $J = 12.4$  Hz, H-15), 1.38 (dq,  $J = 13.5, 6.9$  Hz, H-8), 1.30 (dtd,  $J = 13.2, 6.5, 3.4$  Hz, H-7), 1.18 (td,  $J = 7.2, 4.2$  Hz, H-7, ester CH3), 0.87 (tt,  $J = 12.6, 6.4$  Hz, H-8)

$^{13}\text{C}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  172.2 (ester C=O), 146.5 (C4), 138.3 (C3), 130.1 (C12), 125.2 (C11), 117.8 (C1), 116.6 (C2), 89.6 (C5), 65.8 (C6), 59.6 (ester CH2), 57.4 (C9), 49.9 (ethylene bridge), 44.0 (C16), 42.7 (C13), 37.6 (C14), 36.7 (C15), 32.6 (ethylene bridge CH2), 25.4 (C7), 20.9 (C10), 19.3 (C8), 14.2 (ester CH3)

#### *N*-carboxyethyl-norcodeine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.61 (d, J = 8.2 Hz, H-2), 6.45 (d, J = 8.2 Hz, H-1), 5.53 (dp, J = 9.8, 1.5 Hz, H-7), 5.23 (dt, J = 9.8, 2.8 Hz, H-8), 4.67 (dd, J = 5.9, 1.3 Hz, H-5), 4.11 (dt, J = 5.7, 2.9 Hz, H-6), 4.07 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.71 (s, OCH<sub>3</sub>), 3.36 (s, H-9), 2.86 – 2.74 (m, H-10, ethylene bridge), 2.64 (dt, J = 12.9, 6.7 Hz, ethylene bridge), 2.61 – 2.53 (m, H-16), 2.49 – 2.42 (m, H-14, ethylene bridge), 2.31 (dd, J = 18.6, 6.3 Hz, H-10), 2.24 (td, J = 12.2, 3.4 Hz, H-16), 1.92 (td, J = 12.5, 5.0 Hz, H-15), 1.61 (ddd, J = 12.6, 3.4, 1.7 Hz, H-15), 1.18 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 171.7 (ester C=O), 145.0 (C<sub>4</sub>), 141.2 (C<sub>3</sub>), 133.1 (C<sub>7</sub>), 130.7 (C<sub>12</sub>), 128.0 (C<sub>8</sub>), 127.0 (C<sub>11</sub>), 118.1 (C<sub>1</sub>), 113.0 (C<sub>2</sub>), 91.7 (C<sub>5</sub>), 66.2 (C<sub>6</sub>), 59.5 (ester CH<sub>2</sub>), 56.2 (C<sub>9</sub>), 55.8 (OCH<sub>3</sub>), 49.9 (ethylene bridge CH<sub>2</sub>), 43.7 (C<sub>16</sub>), 43.4 (C<sub>13</sub>), 40.2 (C<sub>14</sub>), 35.2 (C<sub>15</sub>), 32.9 (ethylene bridge CH<sub>2</sub>), 21.5 (C<sub>10</sub>), 14.0 (ester CH<sub>3</sub>)

#### *N*-carboxyethyl-dihydronorcodeine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.69 (d, J = 8.2 Hz, H-2), 6.53 (d, J = 8.1 Hz, H-1), 4.45 (dd, J = 6.7, 4.9 Hz, H-5), 4.06 (qd, J = 7.1, 1.2 Hz, ester CH<sub>2</sub>), 3.84 – 3.77 (m, H-6), 3.76 (s, OCH<sub>3</sub>), 3.04 (dd, J = 5.9, 2.8 Hz, H-9), 2.81 – 2.70 (m, H-10, ethylene bridge CH<sub>2</sub>), 2.59 (dq, J = 12.8, 6.6, 5.9 Hz, ethylene bridge CH<sub>2</sub>), 2.46 – 2.38 (m, ethylene bridge CH<sub>2</sub>), 2.36 (dd, J = 18.4, 6.0 Hz, H-10), 2.12 – 2.02 (m, H-14, H-16), 1.74 (ddd, J = 14.3, 11.2, 4.9 Hz, H-15), 1.44 (ddd, J = 12.4, 3.6, 1.7 Hz, H-15), 1.37 (dt, J = 13.4, 6.8 Hz, H-8), 1.31 (dq, J = 10.0, 3.5 Hz, H-7), 1.18 (t, J = 7.1 Hz, ester CH<sub>3</sub>), 1.16 – 1.11 (m, H-8), 0.94 – 0.82 (m, H-7)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 172.4 (ester C=O), 147.4 (C<sub>4</sub>), 140.9 (C<sub>3</sub>), 130.7 (C<sub>12</sub>), 127.2 (C<sub>11</sub>), 118.4 (C<sub>1</sub>), 114.4 (C<sub>2</sub>), 90.7 (C<sub>5</sub>), 66.3 (C<sub>6</sub>), 60.1 (ester CH<sub>2</sub>), 57.9 (C<sub>9</sub>), 56.7 (OCH<sub>3</sub>), 50.6 (ethylene bridge CH<sub>2</sub>), 44.5 (C<sub>16</sub>), 42.6 (C<sub>13</sub>), 38.6 (C<sub>14</sub>), 37.5 (C<sub>15</sub>), 33.6 (ethylene bridge CH<sub>2</sub>), 26.1 (C<sub>7</sub>), 21.6 (C<sub>10</sub>), 19.8 (C<sub>8</sub>), 14.6 (ester CH<sub>3</sub>)

#### *N*-carboxyethyl-noroxymorphone ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.56 (d, J = 8.1 Hz, H-2), 6.52 (d, J = 8.1 Hz, H-1), 4.75 (s, H-5), 4.08 (qd, J = 7.1, 2.8 Hz, ester CH<sub>2</sub>), 2.97 (d, J = 18.5 Hz, H-10), 2.91 (d, J = 5.9 Hz, H-9), 2.90 – 2.84 (m, H-7), 2.75 (dt, J = 12.7, 7.2 Hz, ethylene bridge CH<sub>2</sub>), 2.67 (dt, J = 12.6, 6.2 Hz, ethylene bridge CH<sub>2</sub>), 2.60 – 2.53 (m, H-10), 2.53 – 2.51 (m, H-16), 2.27 (td, J = 12.6, 5.1 Hz, H-15), 2.08 (dt, J = 14.1, 3.2 Hz, H-7), 2.02 (td, J = 12.1, 3.7 Hz, H-16), 1.74 (ddd, J = 13.3, 5.0, 2.9 Hz, H-8), 1.43 (td, J = 14.0, 3.4 Hz, H-8), 1.32 – 1.25 (m, H-15), 1.21 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 208.7 (C<sub>6</sub>), 172.0 (ester C=O), 143.4 (C<sub>4</sub>), 139.4 (C<sub>3</sub>), 129.4 (C<sub>12</sub>), 123.3 (C<sub>11</sub>), 119.0 (C<sub>1</sub>), 117.2 (C<sub>2</sub>), 89.3 (C<sub>5</sub>), 69.8 (C<sub>14</sub>), 62.60 (C<sub>9</sub>), 59.9 (ester CH<sub>2</sub>), 50.1 (C<sub>13</sub>), 49.7 (ethylene bridge CH<sub>2</sub>), 42.7 (C<sub>16</sub>), 35.8 (C<sub>7</sub>), 32.9 (ethylene bridge CH<sub>2</sub>), 31.1 (C<sub>8</sub>), 30.2 (C<sub>15</sub>), 23.1 (C<sub>10</sub>), 14.2 (ester CH<sub>3</sub>)

#### *N*-carboxyethyl-noroxycodone ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.74 (d, J = 8.3 Hz, H-2), 6.66 (d, J = 8.2 Hz, H-1), 4.83 (d, J = 7.8 Hz, H-5), 4.09 (qd, J = 7.1, 2.8 Hz, ester CH<sub>2</sub>), 3.78 (s, OCH<sub>3</sub>), 3.02 (d, J = 18.6 Hz, H-10), 2.94 (d, J = 5.7 Hz, H-9), 2.89 (d, J = 5.0 Hz, H-7), 2.81 – 2.72 (m, ethylene bridge CH<sub>2</sub>), 2.68 (dt, J = 12.6, 6.2 Hz, ethylene bridge CH<sub>2</sub>), 2.59 (dd, J = 18.7, 5.8 Hz, H-10), 2.57 – 2.52 (m, ethylene bridge CH<sub>2</sub>), 2.28 (td, J = 12.6, 5.2 Hz, H-15), 2.08 (dt, J = 14.1, 3.2 Hz, H-7), 2.00 (td, J = 12.2, 3.7 Hz, H-16), 1.75 (ddd, J = 13.4, 5.0, 3.0 Hz, H-8), 1.46 – 1.37 (m, H-8), 1.33 – 1.26 (m, H-15), 1.21 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

<sup>13</sup>C NMR (151 MHz, DMSO-d<sub>6</sub>) δ 208.7 (C<sub>6</sub>), 172.2 (ester C=O), 144.6 (C<sub>4</sub>), 142.2 (C<sub>3</sub>), 129.8 (C<sub>12</sub>), 125.7 (C<sub>11</sub>), 119.4 (C<sub>1</sub>), 114.9 (C<sub>2</sub>), 89.9 (C<sub>5</sub>), 69.9 (C<sub>14</sub>), 62.7 (C<sub>9</sub>), 60.0 (ester CH<sub>2</sub>), 56.5 (OCH<sub>3</sub>), 50.2

(C13), 49.8 (ethylene bridge CH2), 42.8 (C16), 35.9 (C7), 33.0 (ethylene bridge CH2), 31.3 (C8), 30.3 (C15), 23.3 (C10), 14.4 (ester CH3)

#### *N*-carboxyethyl-normorphine

<sup>1</sup>H NMR (600 MHz, D2O) δ 6.64 (d, J = 8.2 Hz, H-2), 6.56 (d, J = 8.2 Hz, H-1), 5.62 (d, J = 9.7 Hz, H-7), 5.27 (d, J = 10.1 Hz, H-8), 4.94 (dd, J = 6.4, 1.3 Hz, H-5), 4.29 – 4.18 (m, H-6, H-9), 3.48 – 3.33 (m, H-16, ethylene bridge CH2), 3.13 (d, J = 20.1 Hz, H-10), 2.96 (t, J = 13.2 Hz, H-16), 2.89 – 2.78 (m, H-14, H-10), 2.71 (td, J = 7.0, 2.7 Hz, ethylene bridge CH2), 2.22 (t, J = 13.8 Hz, H-15), 2.04 (d, J = 14.3 Hz, H-15)

<sup>13</sup>C NMR (600 MHz, D2O) δ 175.3 (carboxylic C=O), 145.1 (C4), 137.8 (C3), 129.3 (C12), 133.1 (C7), 125.5 (C8), 123.2 (C11), 120.3 (C1), 117.6 (C2), 90.3 (C5), 65.6 (C6), 58.8 (C9), 50.7 (ethylene bridge CH2), 46.0 (C16), 41.8 (C13), 38.1 (C14), 32.5 (C15), 29.6 (ethylene bridge CH2), 21.2 (C10)

#### *N*-carboxyethyl-dihydronormorphine

<sup>1</sup>H NMR (600 MHz, D2O) δ 6.70 (dd, J = 8.2, 0.9 Hz, H-2), 6.63 (d, J = 8.1 Hz, H-1), 4.65 (d, J = 5.5 Hz, H-5), 4.02 (td, J = 5.9, 2.8 Hz, H-6), 3.91 (dd, J = 6.4, 2.6 Hz, H-9), 3.48 – 3.32 (m, ethylene bridge CH2), 3.26 (dd, J = 13.1, 5.3 Hz, H-16), 3.08 (d, J = 19.7 Hz, H-10), 2.90 (dd, J = 19.9, 6.1 Hz, H-10), 2.83 – 2.72 (m, H-16, ethylene bridge CH2), 2.33 (ddd, J = 11.7, 5.3, 2.8 Hz, H-14), 2.01 (td, J = 13.6, 4.8 Hz, H-15), 1.83 – 1.76 (m, H-15), 1.51 – 1.38 (m, H-7, H-8), 1.00 – 0.86 (m, H-8)

<sup>13</sup>C NMR (600 MHz, D2O) δ 174.2 (carboxylic C=O), 145.1 (C4), 137.3 (C3), 128.1 (C12), 122.4 (C11), 119.8 (C1), 117.9 (C2), 88.9 (C5), 66.0 (C6), 60.0 (C9), 50.0 (ethylene bridge CH2), 46.9 (C16), 40.6 (C13), 38.3 (C14), 34.0 (C15), 29.0 (ethylene bridge CH2), 25.9 (C7), 20.5 (C10), 17.6 (C8)

#### *N*-carboxyethyl-norcodeine

<sup>1</sup>H NMR (600 MHz, D2O) δ 6.78 (d, J = 8.3 Hz, H-2), 6.65 (d, J = 8.3 Hz, H-1), 5.61 (d, J = 9.8 Hz, H-7), 5.26 (d, J = 9.9 Hz, H-8), 4.94 (dd, J = 6.4, 1.3 Hz, H-5), 4.32 – 4.15 (m, H-6, H-9), 3.71 (s, OCH3), 3.51 (q, J = 7.1 Hz, ethylene bridge CH2), 3.48 – 3.34 (m, H-16), 3.17 (d, J = 20.3 Hz, H-10), 3.00 – 2.78 (m, H-16, H-14, H-10), 2.75 (td, J = 7.0, 2.5 Hz, ethylene bridge CH2), 2.22 (d, J = 13.9 Hz, H-15), 2.03 (d, J = 14.4 Hz, H-15)

<sup>13</sup>C NMR (600 MHz, D2O) δ 175.1 (carboxylic C=O), 146.3 (C4), 142.0 (C3), 133.1 (C7), 129.00 (C12), 125.6 (C8), 124.0 (C11), 120.3 (C1), 114.4 (C2), 90.5 (C5), 65.7 (C6), 58.9 (C9), 56.4 (OCH3), 50.6 (ethylene bridge CH2), 46.1 (C16), 41.9 (C13), 38.3 (C14), 32.5 (C15), 29.4 (ethylene bridge CH2), 21.2 (C10)

#### *N*-carboxyethyl-dihydronorcodeine

<sup>1</sup>H NMR (600 MHz, D2O) δ 6.82 (d, J = 8.2 Hz, H-2), 6.70 (d, J = 8.2 Hz, H-1), 4.64 (m, H-5), 3.99 (q, J = 4.9 Hz, H-6), 3.92 (dd, J = 6.3, 2.6 Hz, H-9), 3.73 (s, OCH3), 3.43 (dt, J = 14.1, 7.2 Hz, ethylene bridge CH2), 3.37 (dt, J = 13.7, 7.0 Hz, ethylene bridge CH2), 3.25 (dd, J = 13.2, 4.7 Hz, H-16), 3.10 (d, J = 19.8 Hz, H-10), 2.90 (dd, J = 19.9, 6.2 Hz, H-10), 2.79 (td, J = 7.1, 4.4 Hz, ethylene bridge CH2), 2.71 (td, J = 13.3, 4.1 Hz, H-16), 2.35 (ddd, J = 12.0, 5.4, 2.7 Hz, H-14), 2.03 (td, J = 13.7, 4.8 Hz, H-15), 1.77 – 1.68 (m, H-15), 1.48 – 1.34 (m, H-8, H-7), 0.90 (tt, J = 11.3, 6.0 Hz, H-8)

<sup>13</sup>C NMR (151 MHz, D2O) δ 173.8 (carboxylic C=O), 146.0 (C4), 141.5 (C3), 128.1 (C12), 123.5 (C11), 119.9 (C1), 114.9 (C2), 89.2 (C5), 66.0 (C6), 60.1 (C9), 56.6 (OCH3), 49.9 (ethylene bridge CH2), 46.9 (C16), 40.5 (C13), 38.1 (C14), 34.1 (C15), 28.9 (ethylene bridge CH2), 25.8 (C7), 20.6 (C10), 17.6 (C8)

### *N*-carboxyethyl-noroxymorphone

<sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O) δ 6.72 (d, J = 8.2 Hz, H-2), 6.69 (d, J = 8.3 Hz, H-1), 4.93 (s, H-5), 3.74 (d, J = 6.1 Hz, H-9), 3.41 (hept, J = 6.8, 5.9 Hz, ethylene bridge CH<sub>2</sub>), 3.34 – 3.25 (m, H-16, H-10), 3.05 (dd, J = 19.9, 6.3 Hz, H-10), 2.89 (td, J = 14.8, 5.1 Hz, H-7), 2.85 – 2.66 (m, H-16, ethylene bridge CH<sub>2</sub>), 2.60 (td, J = 13.4, 4.8 Hz, H-15), 2.21 (dt, J = 14.8, 3.2 Hz, H-7), 1.95 (ddd, J = 14.5, 5.2, 3.0 Hz, H-8), 1.64 (ddd, J = 17.9, 13.7, 3.5 Hz, H-8, H-15)

<sup>13</sup>C NMR (151 MHz, D<sub>2</sub>O) δ 211.5 (C6), 175.0 (carboxylic C=O), 143.2 (C4), 138.7 (C3), 127.2 (C12), 121.7 (C11), 120.9 (C1), 118.7 (C2), 89.5 (C5), 70.6 (C14), 64.0 (C9), 49.7 (ethylene bridge CH<sub>2</sub>), 49.1 (C13), 45.8 (C16), 34.4 (C7), 30.5 (C8), 28.2 (ethylene bridge CH<sub>2</sub>), 27.1 (C15), 23.1 (C10)

### *N*-carboxyethyl-noroxycodone

<sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O) δ 6.87 (d, J = 8.3 Hz, H-2), 6.78 (d, J = 8.4 Hz, H-1), 4.95 (s, H-5), 3.75 (d, J = 4.5 Hz, H-9, OCH<sub>3</sub>), 3.42 (t, J = 6.6 Hz, ethylene bridge CH<sub>2</sub>), 3.32 (d, J = 20.1 Hz, H-10, H-16), 3.08 (dd, J = 20.0, 6.3 Hz, H-10), 2.89 (td, J = 14.8, 5.1 Hz, H-7), 2.82 (dt, J = 18.2, 6.6 Hz, ethylene bridge CH<sub>2</sub>), 2.70 (td, J = 13.5, 12.9, 4.5 Hz, H-16), 2.60 (td, J = 13.4, 4.8 Hz, H-15), 2.20 (dt, J = 14.9, 3.2 Hz, H-7), 1.95 (ddd, J = 14.6, 5.2, 3.0 Hz, H-8), 1.68 – 1.59 (m, H-8, H-15)

<sup>13</sup>C NMR (151 MHz, D<sub>2</sub>O) δ 211.0 (C6), 174.9 (carboxylic C=O), 144.3 (C4), 142.6 (C3), 127.1 (C12), 122.4 (C11), 121.1 (C1), 115.6 (C2), 89.4 (C5), 70.2 (C14), 64.0 (C9), 56.7 (OCH<sub>3</sub>), 49.7 (ethylene bridge CH<sub>2</sub>), 48.4 (C13), 45.9 (C16), 34.4 (C7), 30.5 (C8), 28.2 (ethylene bridge CH<sub>2</sub>), 27.2 (C15), 23.1 (C10)

### *N*-acetyl-glycine-normorphine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 6.42 (d, J = 8.0 Hz, H-2), 6.32 (d, J = 8.1 Hz, H-1), 5.53 (dp, J = 9.9, 1.6 Hz, H-7), 5.20 (dt, J = 9.8, 2.8 Hz, H-8), 4.67 (dd, J = 6.1, 1.3 Hz, H-5), 4.06 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.85 (qd, J = 17.4, 6.2 Hz, glycine CH<sub>2</sub>), 3.35 (dd, J = 6.1, 3.0 Hz, H-9), 3.20 (d, J = 16.1 Hz, CH<sub>2</sub> bridge), 2.98 (d, J = 16.1 Hz, CH<sub>2</sub> bridge), 2.76 (d, J = 18.4 Hz, H-10), 2.71 (dd, J = 4.7, 2.5 Hz, H-14), 2.55 (dd, J = 12.1, 4.6 Hz, H-16), 2.41 – 2.29 (m, H-10, H-16), 2.05 (td, J = 12.5, 4.9 Hz, H-15), 1.61 (d, J = 12.7 Hz, H-15), 1.16 (t, J = 7.1 Hz, ester CH<sub>3</sub>).

<sup>13</sup>C NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 171.0 (amide C=O), 170.3 (ester C=O), 146.7 (C4), 139.1 (C3), 133.8 (C7), 131.2 (C12), 128.7 (C8), 125.4 (C11), 119.0 (C1), 116.7 (C2), 91.8 (C6), 66.9 (C6), 60.8 (ester CH<sub>2</sub>), 58.9 (CH<sub>2</sub> bridge), 57.6 (C9), 45.0 (C16), 43.5 (C13), 40.9 (glycine CH<sub>2</sub>), 40.7 (C14), 35.7 (C15), 23.3 (C10), 14.5 (ester CH<sub>3</sub>)

### *N*-acetyl-glycine-dihydronormorphine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 6.53 (d, J = 8.0 Hz, H-2), 6.42 (d, J = 8.0 Hz, H-1), 4.47 (d, J = 4.8 Hz, H-5), 4.09 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.88 (d, J = 6.4 Hz, glycine CH<sub>2</sub>), 3.85 (d, J = 6.0 Hz, glycine CH<sub>2</sub>), 3.83 – 3.78 (m, H-6), 3.19 (d, J = 16.1 Hz, CH<sub>2</sub> bridge), 3.07 (d, J = 3.2 Hz, H-9), 2.93 (d, J = 16.0 Hz, CH<sub>2</sub> bridge), 2.73 (d, J = 18.3 Hz, H-10), 2.48 (m, H-16), 2.38 (t, J = 1.8 Hz, H-10), 2.29 (s, H-14), 2.26 – 2.18 (m, H-16), 1.90 (td, J = 12.3, 4.9 Hz, H-15), 1.46 (dt, J = 10.8, 2.3 Hz, H-15), 1.40 (dq, J = 13.8, 7.1 Hz, H-8), 1.32 (td, J = 6.7, 3.6 Hz, H-7), 1.18 (m, ester CH<sub>3</sub>, H-7), 0.86 (d, J = 18.8 Hz, H-8).

<sup>13</sup>C NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ 171.0 (amide C=O), 170.6 (ester C=O), 146.5 (C4), 138.5 (C3), 130.4 (C12), 125.3 (C11), 118.5 (C1), 117.2 (C2), 90.4 (C5), 66.7 (C6), 61.0 (ester CH<sub>2</sub>), 59.2 (CH<sub>2</sub> bridge), 58.8 (C9), 45.1 (C16), 42.5 (C13), 41.0 (glycine CH<sub>2</sub>), 38.2 (C14), 37.5 (C15), 26.0 (C7), 23.0 (C10), 20.0 (C8), 14.6 (ester CH<sub>3</sub>)



*N*- acetyl-glycine -norcodeine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.59 (d, J = 8.2, H-2), 6.44 (d, J = 8.3, H-1), 5.53 (d, J = 9.8 Hz, H-7), 5.21 (dt, J = 7.4, 3.4 Hz, H-8), 4.69 (d, J = 5.4 Hz, H-5), 4.10 (m, H-6), 4.06 (tdd, J = 7.2, 4.7, 2.6 Hz, ester CH<sub>2</sub>), 3.86 (m, glycine CH<sub>2</sub>), 3.69 (d, J = 3.2 Hz, OCH<sub>3</sub>), 3.37 (dt, J = 7.6, 3.8 Hz, H-9), 3.20 (dd, J = 16.3, 4.2 Hz, CH<sub>2</sub> bridge), 2.98 (dd, J = 15.7, 3.8 Hz, CH<sub>2</sub> bridge), 2.80 (dd, J = 18.5, 4.1 Hz, H-10), 2.75 – 2.69 (m, H-14), 2.58 (m, H-16), 2.41 – 2.31 (m, H-10, H-16), 2.11 – 1.99 (m, H-15), 1.61 (d, J = 12.9 Hz, H-15), 1.16 (ddd, J = 7.1, 4.7, 2.3 Hz, ester CH<sub>3</sub>).

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 170.9 (amide C=O), 170.5 (ester C=O), 147.7 (C<sub>4</sub>), 141.8 (C<sub>3</sub>), 133.7 (C<sub>7</sub>), 131.5 (C<sub>12</sub>), 128.7 (C<sub>8</sub>), 127.5 (C<sub>11</sub>), 118.8 (C<sub>1</sub>), 113.8 (C<sub>2</sub>), 92.4 (C<sub>5</sub>), 67.0 (C<sub>6</sub>), 60.9 (ester CH<sub>2</sub>), 58.9 (CH<sub>2</sub> bridge), 57.7 (C<sub>9</sub>), 44.9 (C<sub>16</sub>), 43.6 (C<sub>13</sub>), 40.9 (glycine CH<sub>2</sub>), 40.6 (C<sub>14</sub>), 35.7 (C<sub>15</sub>), 23.4 (C<sub>10</sub>), 14.5 (ester CH<sub>3</sub>)

*N*- acetyl-glycine -dihydronorcodeine ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.70 (d, J = 8.2 Hz, H-2), 6.54 (d, J = 8.2 Hz, H-1), 4.49 (dd, J = 4.9, 3.6 Hz, H-5), 4.08 (q, J = 7.1 Hz, ester CH<sub>2</sub>), 3.88 (d, J = 6.3 Hz, glycine CH<sub>2</sub>), 3.84 (d, J = 5.9 Hz, glycine CH<sub>2</sub>), 3.82 (q, J = 3.9 Hz, H-6), 3.20 (d, J = 16.1 Hz, CH<sub>2</sub> bridge), 3.09 (dd, J = 6.1, 2.7 Hz, H-9), 2.93 (d, J = 16.1 Hz, CH<sub>2</sub> bridge), 2.77 (d, J = 18.4 Hz, H-10), 2.48 – 2.40 (m, H-10), 2.30 (ddd, J = 11.5, 6.7, 2.7 Hz, H-14), 2.20 (td, J = 12.2, 3.4 Hz, H-16), 1.90 (td, J = 12.4, 4.9 Hz, H-15), 1.45 (dd, J = 11.6, 3.1 Hz, H-15), 1.39 (dt, J = 13.4, 6.8 Hz, H-8), 1.32 (qd, J = 6.8, 4.7 Hz, H-7), 1.18 (t, J = 7.1 Hz, ester CH<sub>3</sub>), 0.89 (tt, J = 12.7, 6.4 Hz, H-8)

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 171.0 (amide C=O), 170.4 (ester C=O), 147.4 (C<sub>4</sub>), 141.3 (C<sub>3</sub>), 130.6 (C<sub>12</sub>), 127.2 (C<sub>11</sub>), 118.5 (C<sub>1</sub>), 114.5 (C<sub>2</sub>), 90.7 (C<sub>5</sub>), 66.4 (C<sub>6</sub>), 60.8 (ester CH<sub>2</sub>), 59.1 (CH<sub>2</sub> bridge), 58.6 (C<sub>9</sub>), 45.0 (C<sub>16</sub>), 42.3 (C<sub>13</sub>), 40.9 (glycine CH<sub>2</sub>), 38.3 (C<sub>14</sub>), 37.3 (C<sub>15</sub>), 26.1 (C<sub>7</sub>), 22.9 (C<sub>10</sub>), 19.8 (C<sub>8</sub>), 14.5 (ester CH<sub>3</sub>)

*N*- acetyl-glycine -noroxymorphone ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.56 (d, J = 8.1 Hz, H-2), 6.53 (d, J = 8.1 Hz, H-1), 4.77 (s, H-5), 4.09 (qd, J = 7.1, 1.2 Hz, ester CH<sub>2</sub>), 3.95 (d, J = 6.7 Hz, glycine CH<sub>2</sub>), 3.80 (d, J = 5.7 Hz, glycine CH<sub>2</sub>), 3.23 (d, J = 16.0 Hz, CH<sub>2</sub> bridge), 3.02 – 2.89 (m, CH<sub>2</sub> bridge, H-9, H-7), 2.59 – 2.53 (m, H-16), 2.53 – 2.51 (m, H-10), 2.43 (td, J = 12.6, 5.0 Hz, H-15), 2.08 (dt, J = 14.3, 3.2 Hz, H-7), 1.99 (td, J = 12.0, 3.7 Hz, H-16), 1.73 (ddd, J = 13.3, 5.2, 3.0 Hz, H-8), 1.29 (dt, J = 11.9, 2.7 Hz, H-15), 1.18 (t, J = 7.1 Hz, ester CH<sub>3</sub>).

<sup>13</sup>C NMR (600 MHz, DMSO-d<sub>6</sub>) δ 209.3 (C<sub>6</sub>), 170.5 (amide C=O), 170.4 (ester C=O), 143.8 (C<sub>4</sub>), 139.8 (C<sub>3</sub>), 130.1 (C<sub>12</sub>), 123.9 (C<sub>11</sub>), 119.5 (C<sub>1</sub>), 117.6 (C<sub>2</sub>), 89.7 (C<sub>5</sub>), 70.7 (C<sub>14</sub>), 64.0 (C<sub>9</sub>), 60.9 (ester CH<sub>2</sub>), 59.5 (CH<sub>2</sub> bridge), 50.1 (C<sub>13</sub>), 44.2 (C<sub>16</sub>), 40.9 (glycine CH<sub>2</sub>), 36.2 (C<sub>7</sub>), 31.6 (C<sub>8</sub>), 29.8 (C<sub>15</sub>), 24.5 (C<sub>10</sub>), 14.5 (ester CH<sub>3</sub>)

*N*- acetyl-glycine -noroxycodone ethyl ester

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>) δ 6.75 (d, J = 8.2 Hz, H-2), 6.67 (d, J = 8.2 Hz, H-1), 4.85 (s, H-5), 4.09 (qd, J = 7.1, 1.4 Hz, ester CH<sub>2</sub>), 3.94 (dd, J = 17.3, 6.7 Hz, glycine CH<sub>2</sub>), 3.79 (s, glycine CH<sub>2</sub>), 3.24 (d, J = 16.0 Hz, CH<sub>2</sub> bridge), 3.08 – 2.92 (m, CH<sub>2</sub> bridge, H-7, H-10), 2.65 – 2.54 (m, H-10, H-16), 2.40 – 2.37 (m, H-15), 2.08 (dt, J = 14.1, 3.1 Hz, H-7), 1.97 (td, J = 12.0, 3.7 Hz, H-16), 1.75 (ddd, J = 13.3, 5.1, 2.9 Hz, H-8), 1.51 – 1.37 (m, H-8), 1.32 – 1.27 (m, H-15), 1.19 (t, J = 7.1 Hz, ester CH<sub>3</sub>)

$^{13}\text{C}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  209.0 (amide C=O), 170.4 (ester C=O), 170.3 (C6), 142.5 (C3), 144.8 (C4), 130.3 (C12), 126.1 (C11), 119.8 (C1), 115.3 (C2), 90.1 (C5), 70.6 (C14), 60.9 (ester CH<sub>2</sub>), 59.4 (CH<sub>2</sub> bridge), 56.8 (OCH<sub>3</sub>), 50.2 (C13), 44.1 (C16), 40.7 (glycine CH<sub>2</sub>), 36.0 (C7), 31.8 (C8), 63.9 (C9), 29.4 (C15), 24.6 (C10), 14.5 (ester CH<sub>3</sub>)

#### *N*-acetyl-glycine-normorphine

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.65 (d,  $J$  = 8.1 Hz, H-2), 6.57 (d,  $J$  = 8.2 Hz, H-1), 5.63 (dd,  $J$  = 9.8, 2.8 Hz, H-7), 5.25 (d,  $J$  = 10.0 Hz, H-8), 4.96 (dd,  $J$  = 6.4, 1.2 Hz, H-5), 4.33 – 4.00 (m, H-6, H-9), 3.94 (s, glycine CH<sub>2</sub>), 3.51 (d,  $J$  = 7.1 Hz, CH<sub>2</sub> bridge), 3.38 (s, H-16), 3.15 (d,  $J$  = 20.1 Hz, H-10), 3.02 (s, H-14), 2.42 – 2.23 (m, H-15), 2.05 (d,  $J$  = 14.4 Hz, H-15)

$^{13}\text{C}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  173.1 (carboxylic C=O), 165.3 (amide C=O), 145.5 (C4), 138.0 (C3), 133.1 (C7), 129.2 (C12), 125.5 (C8), 123.0 (C11), 120.3 (C1), 117.7 (C2), 90.3 (C5), 65.2 (C6), 60.4 (C9), 57.6 (CH<sub>2</sub> bridge), 47.1 (C16), 41.7 (C13), 41.2 (glycine CH<sub>2</sub>), 38.0 (C14), 32.2 (C15), 22.0 (C10)

#### *N*-acetyl-glycine-dihydronormorphine

Under measurement.

#### *N*-acetyl-glycine-norcodeine

Under measurement.

#### *N*-acetyl-glycine-dihydronorcodeine

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.87 (d,  $J$  = 8.3 Hz, H-2), 6.74 (d,  $J$  = 8.4 Hz, H-1), 4.70 (d,  $J$  = 5.4 Hz, H-5), 4.03 (d,  $J$  = 4.7 Hz, H-6), 3.94 (s, H-9, glycine CH<sub>2</sub>), 3.76 (s, OCH<sub>3</sub>), 3.30 (d,  $J$  = 13.0 Hz, H-16), 3.12 (d,  $J$  = 19.4 Hz, H-10), 2.80 – 2.74 (m, CH<sub>2</sub> bridge), 2.49 (s, H-14), 2.11 (s, H-15), 1.79 (d,  $J$  = 14.0 Hz, H-15), 1.48 – 1.43 (m, H-8), 0.96 – 0.91 (m, H-8)

$^{13}\text{C}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  172.8 (carboxylic C=O), 165.6 (amide C=O), 145.8 (C4), 141.7 (C3), 127.9 (C12), 123.3 (C11), 120.0 (C1), 115.1 (C2), 89.2 (C5), 66.0 (C6), 61.5 (C9), 57.0 (OCH<sub>3</sub>), 54.4 (CH<sub>2</sub> bridge), 47.9 (C16), 41.4 (glycine CH<sub>2</sub>), 40.6 (C13), 38.2 (C14), 33.9 (C15), 26.0 (C7), 21.4 (C10), 17.6 (C8)

#### *N*-acetyl-glycine-noroxymorphone

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.73 (d,  $J$  = 8.2 Hz, H-2), 6.70 (d,  $J$  = 8.3 Hz, H-1), 4.95 (s, H-5), 4.19 (d,  $J$  = 16.1 Hz, CH<sub>2</sub> bridge), 3.99 – 3.88 (m, CH<sub>2</sub> bridge, glycine CH<sub>2</sub>), 3.83 (d,  $J$  = 6.1 Hz, H-9), 3.33 (s, H-10), 3.20 (dd,  $J$  = 13.2, 4.9 Hz, H-16), 3.08 (dd,  $J$  = 20.1, 6.3 Hz, H-10), 2.90 (td,  $J$  = 14.8, 4.8 Hz, H-7), 2.68 (td,  $J$  = 13.5, 5.0 Hz, H-15), 2.22 (dt,  $J$  = 14.8, 3.2 Hz, H-7), 1.99 – 1.92 (m, H-8), 1.72 – 1.59 (m, H-8, H-15)

$^{13}\text{C}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  211.5 (C6), 172.4 (carboxylic C=O), 165.2 (amide C=O), 143.2 (C4), 138.8 (C3), 127.1 (C12), 121.5 (C11), 121.1 (C1), 118.7 (C2), 89.3 (C5), 70.7 (C14), 65.0 (C9), 53.6 (CH<sub>2</sub> bridge), 48.7 (C13), 47.0 (C16), 41.6 (glycine CH<sub>2</sub>), 34.5 (C7), 30.4 (C8), 27.4 (C15), 23.8 (C10),

#### *N*-acetyl-glycine-noroxycodone

$^1\text{H}$  NMR (600 MHz, D<sub>2</sub>O)  $\delta$  6.89 (d,  $J$  = 8.3 Hz, H-2), 6.81 (d,  $J$  = 8.4 Hz, H-1), 4.98 (s, H-5), 4.18 (d,  $J$  = 16.1 Hz, CH<sub>2</sub> bridge), 3.95 (d,  $J$  = 16.2 Hz, CH<sub>2</sub> bridge), 3.86 (d,  $J$  = 6.2 Hz, H-9), 3.79 (d,  $J$  = 3.6 Hz, glycine CH<sub>2</sub>), 3.77 (s, OCH<sub>3</sub>), 3.35 (d,  $J$  = 20.1 Hz, H-10), 3.22 (dd,  $J$  = 13.0, 4.8 Hz, H-16), 3.11 (dd,  $J$  =

20.1, 6.3 Hz, H-10), 2.97 – 2.83 (m, H-7), 2.69 (td, J = 13.5, 5.0 Hz, H-15), 2.22 (dt, J = 14.9, 3.3 Hz, H-7), 1.98 (ddd, J = 14.5, 5.3, 3.1 Hz, H-8), 1.73 – 1.66 (m, H-15), 1.63 (td, J = 14.6, 3.4 Hz, H-8)

<sup>13</sup>C NMR (600 MHz, D<sub>2</sub>O) δ 211.3, 175.1 (carboxylic C=O), 165.2 (amide C=O), (C6), 144.0 (C4), 142.8 (C3), 127.1 (C12), 122.5 (C11), 121.0 (C1), 115.6 (C2), 89.4 (C5), 70.8 (C14), 65.0 (C9), 53.8 (CH<sub>2</sub> bridge), 48.8 (C13), 47.0 (C16), 42.8 (glycine CH<sub>2</sub>), 34.4 (C7), 30.4 (C8), 27.3 (C15), 23.8 (C10)