Supporting Information

# Transition-metal-free Decarbonylative Alkylation of N-Aryl α-Hydroxy Amides *via* Triple C-C Bond Cleavages and Their Selective Deuteration

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### **1. General Information**

Unless otherwise noted, all reagents were obtained commercially and used without further purification. Unless otherwise specified, all other reagents were purchased from Acros, Aldrich, Fisher, Adamas-beta Co. Ltd. or TCI and used without further purification. <sup>1</sup>H NMR spectra was recorded at 400 MHz and 600MHz, <sup>13</sup>C NMR spectra was recorded at 100 MHz and 150MHz. <sup>1</sup>H NMR spectra was recorded with tetramethylsilane ( $\delta$  0.00 ppm) as internal reference; <sup>13</sup>C NMR spectra was recorded with CDCl<sub>3</sub> ( $\delta$  77.00 ppm) as internal reference. Chemical shifts were reported in parts per million (ppm,  $\delta$ ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Chromatography was carried out with silica gel (200-300 mesh) using mixtures of petroleum ether (b.p. 60-80 °C) and ethyl acetate as eluents. Mass Spectra were obtained from the mass spectrometry facility of East China University of Science and Technology.

### 2. General procedure for the preparation of substrates

**2.1.** General procedure for the synthesis of  $\alpha$ -alkyl 1,3-dicarbonyl (3b as an example):



To a solution of 3-oxo-*N*-phenylbutanamide (885 mg, 5 mmol) in 20 mL of DMF, potassium carbonate (1.38 g, 10 mmol) and potassium iodide (1.66 g, 10 mmol) was added. After the solution was stirred for 5 min, bromocyclohexane (978 mg, 6 mmol) was added dropwise. The resulting solution was stirred at 80 °C for 12 h. After the completion of the reaction monitored by TLC. 50 mL CH<sub>2</sub>Cl<sub>2</sub> was added and the solution was extracted with water (50 mL × 3). The organic layer was washed with saturated brine, then dried over sodium sulfate. The solvent was removed under reduced pressure. The obtained residue was purified by column chromatography to give the compound as white soild (582 mg, 45%).



**2-Cyclohexyl-3-oxo-***N***-phenylbutanamide** (**3b**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 582 mg (45% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.38 (brs, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 1H), 3.37 (d, *J* = 10.2 Hz, 1H), 2.32 (s, 3H), 2.08-2.06 (m, 1H), 1.79-1.64 (m, 5H), 1.29-1.07 (m, 5H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.3, 165.8, 137.6, 129.0, 124.5, 120.0, 68.9, 41.3, 31.8, 31.4, 30.7, 25.9, 25.8, 25.7 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>21</sub>NNaO<sub>2</sub> 282.1470; Found 282.1469.



**2-Cyclopentyl-3-oxo-N-phenylbutanamide** (**3c**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 515 mg (42% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.32 (brs, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 1H), 3.36 (d, *J* = 10.2 Hz, 1H), 2.48-2.42 (m, 1H), 2.38 (s, 3H), 1.88-1.76 (m, 2H), 1.70-1.53 (m, 4H), 1.38-1.31 (m, 1H), 1.21-1.45 (m, 1H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.6, 166.3, 137.6, 129.0, 124.5, 120.0, 68.0, 42.9, 30.9, 30.8, 30.7, 24.8, 24.3 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>19</sub>NNaO<sub>2</sub> 268.1313; Found 268.1312.



**2-Cycloheptyl-3-oxo-***N***-phenylbutanamide (3d)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 532 mg (39% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.44 (brs, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 1H), 3.41 (d, *J* = 10.2 Hz, 1H), 2.31 (s, 3H), 1.94-1.78 (m, 2H), 1.64-1.42 (m, 9H), 1.34-1.24 (m, 2H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.8, 166.2, 137.7, 129.0, 124.5, 120.0, 69.4, 42.1, 32.5, 31.8, 30.8, 28.1, 28.0, 27.9, 26.1, 26.0 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>2</sub> 296.1626; Found 296.1628.



**2-Acetyl-N-phenylpent-4-enamide (3e)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 8/1), 575 mg (53% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.53 (brs, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.11 (d, *J* = 7.2 Hz, 1H), 5.79-5.72 (m, 1H), 5.15-5.08 (m, 2H), 3.59 (t, *J* = 7.2 Hz, 1H), 2.73-2.26 (m, 2H), 2.28 (s, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.0, 166.4, 137.5, 133.6, 129.0, 124.7, 120.2, 118.2, 64.2, 34.6, 29.7 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>13</sub>H<sub>15</sub>NNaO<sub>2</sub> 240.1000; Found 240.1002.



*N*-(4-Chlorophenyl)-2-cyclohexyl-3-oxobutanamide (3f) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 688 mg (47% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.46 (brs, 1H), 7.49-7.47 (m, 2H), 7.28-7.26 (m, 2H), 3.37 (d, *J* = 9.6 Hz, 1H), 2.32 (s, 3H), 2.07-2.01 (m, 1H), 1.78-1.73 (m, 2H), 1.66-1.65 (m, 2H), 1.30-1.06 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.5, 165.8, 136.2, 129.4, 129.0, 121.1, 68.6, 41.5, 32.0, 31.4, 30.6, 26.0, 25.9, 25.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>20</sub>ClNNaO<sub>2</sub> 316.1080; Found 316.1082.



**2-Cyclohexyl-***N***-(4-fluorophenyl)-3-oxobutanamide (3g)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 720 mg (52%

yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.45 (brs, 1H), 7.50-7.47 (m, 2H), 7.02-6.99 (m, 2H), 3.37 (d, *J* = 9.6 Hz, 1H), 2.32 (s, 3H), 2.07-2.05 (m, 2H), 1.77-1.65 (m, 4H), 1.30-1.07 (m, 5H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.4, 165.8, 159.4 (d, *J*<sub>C-F</sub> = 242.5 Hz), 133.6 (d, *J*<sub>C-F</sub> = 3.3 Hz), 121.7 (d, *J*<sub>C-F</sub> = 7.9 Hz), 115.6 (d, *J*<sub>C-F</sub> = 22.4 Hz), 68.6, 41.3, 31.8, 31.3, 30.6, 25.9, 25.8, 25.7 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>20</sub>FNNaO<sub>2</sub> 300.1376; Found 300.1375.



**2-Cyclohexyl-3-oxo**-*N*-(**p-tolyl**)**butanamide** (**3h**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 628 mg (46% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.13 (brs, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 3.28 (d, *J* = 10.2 Hz, 1H), 2.24-2.23 (m, 6H), 2.00-1.97 (m, 1H), 1.67-1.57 (m, 4H), 1.25-1.07 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.3, 165.6, 135.0, 134.1, 129.5, 120.0, 68.9, 41.3, 31.8, 31.4, 30.6, 26.0, 25.9, 25.8, 20.9 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>2</sub> 296.1626; Found 296.1625.



*N*-(4-(tert-Butyl)phenyl)-2-cyclohexyl-3-oxobutanamide (3i) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 677 mg (43% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.47 (brs, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 3.33 (d, J = 10.0 Hz, 1H), 2.30 (s, 3H), 2.11-2.03 (m, 1H), 1.80-1.64 (m, 4H), 1.29-1.02 (m, 15H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 209.1, 165.9, 147.5, 135.0, 125.8, 119.7, 69.0, 40.9, 34.4, 31.4, 31.3, 31.2, 30.6, 25.9, 25.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>29</sub>NNaO<sub>2</sub> 338.2096; Found 338.2094.



**2-Cyclohexyl-***N***-(4-methoxyphenyl)-3-oxobutanamide (3j)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 723 mg (50% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.35 (brs, 1H), 7.42 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 3.77 (s, 3H), 3.33 (d, *J* = 9.6 Hz, 1H), 2.31 (s, 3H), 2.11-2.07 (m, 1H), 1.81-1.63 (m, 4H), 128-1.04 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.1, 165.7, 156.5, 130.8, 121.7, 114.1, 68.9, 55.5, 40.9, 31.3, 30.7, 25.9, 25.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>3</sub> 312.1576; Found 312.1577.



**2-Cyclohexyl-***N***-(4-ethoxyphenyl)-3-oxobutanamide (3k)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 636 mg (42% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.15 (brs, 1H), 7.41-7.39 (m, 2H), 6.85-6.83 (m, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 3.34 (d, *J* = 9.6 Hz, 1H), 2.31 (s, 3H), 2.08-2.02 (m, 1H), 1.75-1.65 (m, 4H), 1.39 (t, *J* = 7.2 Hz, 3H), 1.34-1.05 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.4, 165.5, 155.9, 130.6, 121.6, 114.8, 68.8, 63.7, 41.3, 31.8, 31.4, 30.6, 26.0, 25.9, 25.8, 14.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>25</sub>NNaO<sub>3</sub> 326.1732; Found 326.1734.



*N*-(**3**-Chlorophenyl)-2-cyclohexyl-3-oxobutanamide (**3**l) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 702 mg (48% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.43 (brs, 1H), 7.67 (t, *J* = 1.8 Hz, 1H), 7.34 (dd, *J*<sub>1</sub> = 8.4 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.09-7.04 (m, 1H), 3.39 (d, *J* = 9.6 Hz, 1H), 2.33 (s, 3H), 2.05-2.00 (m, 1H), 1.75-1.64 (m, 4H), 1.30-1.07 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.6, 165.8, 138.7, 134.7, 130.0, 124.5, 120.0, 117.8, 68.5, 41.7, 32.3, 31.4, 30.6, 26.0, 25.9, 25.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>20</sub>ClNNaO<sub>2</sub> 316.1080; Found 316.1078.



**2-Cyclohexyl-3-oxo**-*N*-(**m-tolyl**)**butanamide** (**3m**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 628 mg (46% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.27 (brs, 1H), 7.38 (s, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 3.36 (d, *J* = 9.6 Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.07-2.05 (m, 1H), 1.75-1.65 (m, 4H), 1.28-1.07 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.3, 165.7, 139.0, 137.5, 128.8, 125.3, 120.5, 116.9, 69.0, 41.3, 31.8, 31.4, 30.6, 26.0, 25.9, 25.8, 21.5 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>2</sub> 296.1626; Found 296.1628.



*N*-(2-Chlorophenyl)-2-cyclohexyl-3-oxobutanamide (3n) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 731 mg (50% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.83 (brs, 1H), 8.29 (dd,  $J_1$  = 7.8 Hz,  $J_2$  = 1.2 Hz, 1H), 7.37 (dd,  $J_1$  = 7.8 Hz,  $J_2$  = 1.2 Hz, 1H), 7.26-7.24 (m, 1H), 7.06-7.04 (m, 1H), 3.43 (d, J = 9.6 Hz, 1H), 2.40 (s, 3H), 2.11-2.05 (m, 1H), 1.76-1.63 (m, 4H), 1.33-1.08 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.7, 165.9, 134.4, 129.1, 127.6, 124.9, 123.5, 121.7, 68.8, 41.7, 32.3, 31.4, 30.6, 26.0, 25.9, 25.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>20</sub>ClNNaO<sub>2</sub> 316.1080; Found 316.1079.



**2-Cyclohexyl-***N***-(2-fluorophenyl)-3-oxobutanamide (30)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 734 mg (53% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.56 (brs, 1H), 8.25-8.22 (m, 1H), 7.12-7.04 (m, 3H), 3.41 (d, *J* = 9.6 Hz, 1H), 2.33 (s, 3H), 2.10-2.05 (m, 1H), 1.80-1.65 (m, 5H), 1.30-1.08 (m, 5H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.7, 165.9, 152.8 (d, *J*<sub>*C*-*F*</sub> = 242.9 Hz), 126.0 (d, *J*<sub>*C*-*F*</sub> = 10.4 Hz), 125.0 (d, *J*<sub>*C*-*F*</sub> = 7.8 Hz), 124.5 (d, *J*<sub>*C*-*F*</sub> = 4.1 Hz), 121.8, 115.0 (d, *J*<sub>*C*-*F*</sub> = 19.2 Hz), 68.7, 41.5, 32.0, 31.4, 30.6, 25.9, 25.8, 25.7 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>20</sub>FNNaO<sub>2</sub> 300.1376; Found 300.1378.



**2-Cyclohexyl-3-oxo**-*N*-(**o-tolyl**)**butanamide** (**3p**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 682 mg (50% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.34 (brs, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.20-7.16 (m, 2H), 7.06-7.03 (m, 2H), 3.43 (d, *J* = 9.6 Hz, 1H), 2.33 (s, 3H), 2.28 (s, 3H), 2.08-2.01 (m, 1H), 1.83-1.70 (m, 4H), 1.29-1.08 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  209.9, 165.7, 135.6, 130.5, 128.5, 126.7, 124.9, 122.1, 68.5, 41.9, 32.4, 31.5, 30.6, 26.0, 25.9, 25.8, 17.7 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>2</sub> 296.1626; Found 296.1625.



**2-Cyclohexyl-***N***-(2-methoxyphenyl)-3-oxobutanamide (3q)** white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 665 mg (46% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.62 (brs, 1H), 8.33-8.31 (m, 1H), 7.04 (dd, *J*<sub>1</sub> = 7.8 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 6.95-6.93 (m, 1H), 6.88-6.87 (m, 1H), 3.90 (s, 3H), 3.32 (d, *J* = 9.6 Hz, 1H), 2.30 (s, 3H), 2.14-2.09 (m, 1H), 1.80-1.65 (m, 4H), 1.32-1.03 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.2, 165.6, 148.2, 127.4, 124.0, 120.9, 119.7, 110.1, 69.8, 55.9, 40.8, 31.3, 31.2, 30.7, 26.0, 25.9, 25.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>3</sub> 312.1576; Found 312.1577.



*N*-(4-Chloro-2-methylphenyl)-2-cyclohexyl-3-oxobutanamide (3r) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 660 mg (43% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.42 (brs, 1H), 7.85-7.84 (m, 1H), 7.15-7.14 (m, 2H), 3.44 (d, *J* = 9.0 Hz, 1H), 2.33 (s, 3H), 2.25 (s, 3H), 2.05-1.99 (m, 1H), 1.80-1.68 (m, 4H), 1.31-1.10 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  210.1, 165.8, 134.3, 130.3, 130.2, 130.0, 126.6, 123.2, 68.1, 42.1, 32.6, 31.5, 30.6, 26.0, 25.9, 25.8, 17.6 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>22</sub>ClNNaO<sub>3</sub> 330.1237; Found 330.1238.



**2-Cyclohexyl-3-oxo**-*N*-(**pyridin-2-yl**)**butanamide** (**3s**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 546 mg (42% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.67 (brs, 1H), 8.21-8.17 (m, 2H), 7.62-7.59 (m, 1H), 6.92-6.89 (m, 2H), 3.99-3.95 (m, 1H), 2.29 (s, 3H), 1.82-1.80 (m, 2H), 1.68-1.65 (m, 2H), 1.48-1.46 (m, 1H), 1.38-1.23 (m, 2H), 1.22-1.18 (m, 4H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  170.2, 166.3, 152.7, 147.5, 138.3, 118.8, 114.1, 93.7, 31.1, 25.4, 23.6, 19.6 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>NaO<sub>2</sub> 283.1422; Found 283.1423.



**2-Cyclohexyl-3-oxo**-*N*-(**quinolin-2-yl**)**butanamide** (**3t**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 635 mg (41% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  9.00 (brs, 1H), 8.29 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 9.0 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.63 (dd, *J*<sub>1</sub> = 7.8 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 7.57 (dd, *J*<sub>1</sub> = 7.2 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 7.37-7.34 (m, 1H), 3.31 (d, *J* = 9.6 Hz, 1H), 2.24 (s, 3H), 2.17-2.07 (m, 1H), 1.74-1.65 (m, 4H), 1.23-0.95 (m, 6H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.0, 166.9, 150.5, 146.6, 138.6, 130.0, 127.6, 127.5, 126.4, 125.3, 114.1, 69.5, 40.6, 31.4, 31.3, 30.7, 25.9, 25.8, 25.1 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>23</sub>N<sub>2</sub>O<sub>2</sub> 311.1760; Found 311.1761.



**2-Cyclohexyl-3-oxo-***N***-phenylpentanamide** (**3u**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 586 mg (43% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.41 (brs, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.10 (t, *J* = 7.8 Hz, 1H), 3.40 (d, *J* = 9.6 Hz, 1H), 2.70-2.56 (m, 2H), 2.06-2.00 (m, 1H), 1.80-1.62 (m, 4H), 1.28-1.06 (m, 9H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  212.2, 165.8, 137.6, 129.0, 124.4, 119.8, 68.1, 41.9, 38.8, 31.5, 30.7, 26.0, 25.9, 25.8, 7.2 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>23</sub>NNaO<sub>2</sub> 296.1626; Found 296.1627.



**2-Cyclohexyl-3-oxo-***N***-phenylhexanamide** (**3v**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 560 mg (39% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.31 (brs, 1H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.03 (t, *J* = 7.8 Hz, 1H), 3.32 (d, *J* = 10.2 Hz, 1H), 2.60-2.44 (m, 2H), 1.99-1.93 (m, 1H), 1.72-1.53 (m, 7H), 1.20-0.99 (m, 5H), 0.85 (t, *J* = 7.8 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  211.7, 165.8, 137.6, 129.0, 124.4, 120.0, 68.2, 47.3, 41.8, 31.5, 30.6, 26.0, 25.9, 25.8, 16.6, 13.6 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>25</sub>NNaO<sub>2</sub> 310.1783; Found 310.1782.

#### 2.2. General procedure for the synthesis of substrates

### 2.2.1 General procedure A (1b as an example):



To a solution of 2-cyclohexyl-3-oxo-*N*-phenylbutanamide (259 mg, 1.0 mmol) in DMSO (10 mL), KO*t*Bu (224 mg, 2.0 mmol) was added under oxygen atmosphere. The resulting solution was stirred at 85 °C for 30 min. After completion of the reaction, 30 mL water was added and the mixture was cooled gradually to room temperature. And the solution was extracted with dichloromethane. The organic layer was washed with saturated brine, then dried over sodium sulfate. The solvent was removed under reduced pressure. The obtained residue was purified by column chromatography to give the compound as white soild (138 mg, 50%).



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-phenylbutanamide (1b)** white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 138 mg (50% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.86 (brs, 1H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 4.84 (brs, 1H), 2.51 (s, 3H), 1.78-1.74 (m, 2H), 1.67-1.65 (m, 2H), 1.33-1.10 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.0, 167.4, 136.9, 129.1, 124.8, 119.7, 88.4, 44.2, 26.4, 26.2, 26.1, 26.0, 25.8, 25.0 ppm. HRMS (EI+) m/z: Calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub> 275.1521; Found 275.1519.



**2-Acetyl-2-hydroxy-***N***-phenylpentanamide (1a)** white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 141 mg (60% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.84 (brs, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 4.94 (brs, 1H), 2.52 (s, 3H), 2.22-2.15 (m, 1H), 1.97-1.89 (m, 1H), 1.46-1.35 (m, 2H), 0.95 (t, *J* = 7.6 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.5, 167.5, 136.9, 129.1, 124.8, 119.7, 85.3, 39.6, 24.8, 16.9, 14.0 ppm. HRMS (EI+) m/z: Calcd for C<sub>13</sub>H<sub>16</sub>NO<sub>3</sub> 235.1208; Found 235.1191.



**2-Cyclopentyl-2-hydroxy-3-oxo-***N***-phenylbutanamide** (1c) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 120 mg (46% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.78 (brs, 1H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.26 (t, J= 7.8 Hz, 2H), 7.06 (t, J= 7.2 Hz, 1H), 4.82 (brs, 1H), 2.96-2.90 (m, 1H), 2.46 (s, 3H), 1.70-1.64 (m, 1H), 1.58-1.54 (m, 2H), 1.50-1.42 (m, 3H), 1.39-1.34 (m, 1H), 1.13-1.06 (m, 1H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.3, 167.6, 137.0, 129.1, 124.8, 119.8, 86.4, 45.5, 26.8, 25.8, 25.5, 25.4, 24.9 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> C<sub>15</sub>H<sub>19</sub>NO<sub>3</sub>Na 284.1263; Found 284.1264.



**2-Cycloheptyl-2-hydroxy-3-oxo-***N***-phenylbutanamide (1d)** white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 118 mg (41% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.86 (brs, 1H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 4.88 (brs, 1H), 2.72-2.68 (m, 1H), 2.51 (s, 3H), 1.72-1.70 (m, 2H), 1.59-1.43 (m, 7H), 1.34-1.20 (m, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.9, 167.6, 136.9, 129.1, 124.8, 119.7, 89.7, 45.0, 28.6, 28.2, 28.1, 27.9, 26.9, 26.8, 24.9 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>17</sub>H<sub>24</sub>NO<sub>3</sub> 290.1756; Found 290.1752.



**2-Acetyl-2-hydroxy-***N***-phenylpent-4-enamide** (1e), yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 20/1), 142 mg (61% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.80 (brs, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 5.76-5.65 (m, 1H), 5.25-5.16 (m, 2H), 4.98 (brs, 1H), 2.94-2.81 (m, 2H), 2.52 (s, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  206.7, 166.9, 136.8, 130.5, 129.1, 124.9, 120.2, 119.8, 84.8, 41.7, 25.0 ppm. HRMS (ESI) m/z:

 $[M + H]^+ C_{13}H_{16}NO_3 234.1130$ ; Found 234.1120.



**2-Cyclohexyl-***N***-(4-fluorophenyl)-2-hydroxy-3-oxobutanamide** (1g) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 137 mg (46% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.85 (brs, 1H), 7.52-7.49 (m, 2H), 7.04-7.00 (m, 2H), 4.83 (brs, 1H), 2.51 (s, 3H), 1.78-1.75 (m, 2H), 1.68-1.62 (m, 2H), 1.33-1.12 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.8, 167.4, 160.0 (d, *J*<sub>*C-F*</sub> = 240.2 Hz), 133.0 (d, *J*<sub>*C-F*</sub> = 3.2 Hz), 121.5 (d, *J*<sub>*C-F*</sub> = 7.4 Hz), 115.7 (d, *J*<sub>*C-F*</sub> = 22.5 Hz), 83.3, 44.1, 26.4, 26.0, 26.0, 25.8, 25.0, 22.7 ppm. HRMS (EI+) m/z: Calcd for C<sub>16</sub>H<sub>20</sub>FNO<sub>3</sub> 293.1427; Found 293.1425.



*N*-(4-(tert-Butyl)phenyl)-2-cyclohexyl-2-hydroxy-3-oxobutanamide (1i) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 175 mg (53% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.74 (brs, 1H), 7.39 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 4.76 (brs, 1H), 2.43 (s, 3H), 1.69-1.67 (m, 2H), 1.60-1.56 (m, 2H), 1.22 (s, 9H), 1.18-1.02 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.2, 167.3 147.8, 134.3, 125.9, 119.5, 88.3, 44.2, 34.4, 31.3, 26.4, 26.2, 26.1, 26.0, 25.8, 25.1 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>20</sub>H<sub>30</sub>NO<sub>3</sub> 332.2226; Found 332.2216.



**2-Cyclohexyl-2-hydroxy-***N***-(4-methoxyphenyl)-3-oxobutanamide** (1j) yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 159 mg (52% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.68 (brs, 1H), 7.37 (d, *J* = 9.2 Hz, 2H), 6.78 (d, *J* = 9.2 Hz, 2H), 4.75 (brs, 1H), 3.71 (s, 3H), 2.43 (s, 3H), 1.70-1.67 (m, 2H), 1.58-1.57 (m, 2H), 1.25-1.02 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.2, 167.1, 156.7, 130.1, 121.4, 114.2, 88.3, 55.5, 44.1, 26.4, 26.1, 26.0, 25.8, 25.1 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>4</sub> 306.1705; Found 306.1709.



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-(m-tolyl)butanamide** (1m) yellow oil, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 159 mg (55% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.74 (brs, 1H), 7.35 (s, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 4.76 (brs, 1H), 2.44 (s, 3H), 2.27 (s, 3H), 1.70-1.67 (m, 2H), 1.60-1.57 (m, 2H), 1.27-1.03 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.0, 167.4, 139.1, 136.8, 128.9, 125.6, 120.3, 116.8, 88.3, 44.1, 26.4, 26.1, 25.9, 25.8, 25.0, 21.5 ppm. HRMS (ESI+) m/z: Calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>Na 312.1576; Found 312.1579.



**2-Cyclohexyl-***N***-(2-fluorophenyl)-2-hydroxy-3-oxobutanamide** (10) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc =

10/1), 137 mg (46% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.16 (brs, 1H), 8.31-8.27 (m, 1H), 7.15-7.06 (m, 3H), 4.85 (brs, 1H), 2.51 (s, 3H), 1.78-1.75 (m, 2H), 1.68-1.64 (m, 2H), 1.36-1.11 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.4, 167.8, 152.7 (d, *J*<sub>C-F</sub> = 243.3 Hz), 125.5 (d, *J*<sub>C-F</sub> = 10.4 Hz), 125.0 (d, *J*<sub>C-F</sub> = 7.8 Hz), 124.5 (d, *J*<sub>C-F</sub> = 4.1 Hz), 121.2, 115.1 (d, *J*<sub>C-F</sub> = 19.1 Hz), 88.6, 44.2, 26.4, 26.1, 26.0, 25.9, 25.8, 24.9 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>21</sub>FNO<sub>3</sub> 294.1515; Found 294.1513.



**2-Cyclohexyl-2-hydroxy-***N***-(2-methoxyphenyl)-3-oxobutanamide** (1q) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 159 mg (52% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.39 (brs, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.02-6.98 (m, 1H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 4.76 (brs, 1H), 3.81 (s, 1H), 2.44 (s, 3H), 1.70-1.67 (m, 2H), 1.60-1.57 (m, 2H), 1.25-1.08 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.1, 167.3, 148.5, 126.8, 124.4, 120.9, 119.3, 110.1, 88.6, 55.7, 44.2, 26.4, 26.2, 26.1, 26.0, 25.9, 25.0 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>4</sub> 306.1705; Found 306.1701.



*N*-(4-Chloro-2-methylphenyl)-2-cyclohexyl-2-hydroxy-3-oxobutanamide (1r) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 164 mg (50% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.83 (brs, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.19-7.17 (m, 2H), 4.86 (brs, 1H), 2.51 (s, 3H), 2.22 (s, 3H), 1.77-1.75 (m, 2H), 1.64-1.63 (m, 2H), 1.32-1.13 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.0, 167.4, 133.6, 130.3, 130.1, 130.0, 126.8, 122.6, 88.6, 44.2, 26.4,

26.0, 25.9, 25.8, 17.4 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>Cl 324.1366; Found 324.1357.



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-(pyridin-3-yl)butanamide** (1s) yellow solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 132 mg (48% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.44 (brs, 1H), 8.31 (d, *J* = 4.0 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.73-7.69 (m, 1H), 7.08-7.05 (m, 1H), 4.93 (brs, 1H), 2.50 (s, 3H), 1.75-1.63 (m, 4H), 1.37-1.13 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.1, 168.4, 150.4, 148.2, 138.3, 120.3, 113.7, 88.4, 44.2, 26.4, 26.1, 26.0, 25.9, 25.8, 24.9 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>15</sub>H<sub>21</sub>N<sub>2</sub>O<sub>3</sub> 277.1552; Found 277.1556.



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-(quinolin-2-yl)butanamide** (1t) yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 5/1), 146 mg (45% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.65 (brs, 1H), 8.40 (d, *J* = 8.8 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 4.92 (brs, 1H), 2.53 (s, 3H), 1.76-1.65 (m, 4H), 1.38-1.11 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.0, 168.8, 149.8, 146.7, 138.6, 130.1, 127.7, 127.5, 126.5, 125.5, 113.7, 88.5, 44.3, 26.5, 26.1, 26.0, 25.9, 25.8, 24.9 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>19</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub> 327.1709; Found 327.1693.



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-phenylpentanamide (1u)** white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 124 mg (43% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.87 (brs, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 4.90 (brs, 1H), 3.18-3.08 (m, 1H), 2.79-2.68 (m, 1H), 2.51-2.44 (m, 1H), 1.32-1.26 (m, 6H), 1.21-1.07 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  210.9, 167.7, 137.0, 129.1, 124.8, 119.7, 88.0, 26.5, 26.1, 26.0, 25.9, 25.8, 7.6 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>Na 312.1576; Found 312.1566.



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-phenylhexanamide** (**1v**) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 121 mg (40% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.86 (brs, 1H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 4.90 (brs, 1H), 3.15-3.07 (m, 1H), 2.71-2.62 (m, 1H), 2.51-2.49 (m, 1H), 1.67-1.61 (m, 5H), 1.37-1.21 (m, 6H), 0.94 (t, *J* = 7.2 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 210.2, 167.6, 137.0, 129.1, 124.7, 119.7, 88.1, 44.5, 38.9, 26.5, 26.2, 26.1, 26.0, 25.8, 16.8, 13.6 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> C<sub>18</sub>H<sub>25</sub>NO<sub>3</sub>Na 326.1732; Found 326.1732.

### 2.2.2 General procedure B (1n as an example)<sup>[1]</sup>:



To a solution of *N*-(2-chlorophenyl)-2-cyclohexyl-3-oxobutanamide (293 mg, 1.0 mmol) in 10 mL of DMF and 0.5 mL of water, sodium hydroxide (8 mg, 0.2 mmol) and cesium fluoride (15.2 mg, 0.1 mmol) was added slowly. After the completion of the reaction monitored by TLC. 30 mL CH<sub>2</sub>Cl<sub>2</sub> was added and the solution was extracted with water (30 mL×3). The organic layer was washed with saturated brine, then dried over sodium sulfate. The solvent was removed under reduced pressure. The obtained residue was purified by column chromatography to give the compound as white soild (170 mg, 53%).



*N*-(2-Chlorophenyl)-2-cyclohexyl-2-hydroxy-3-oxobutanamide (1n) yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 158 mg (51% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.52 (brs, 1H), 8.37 (dd, *J*<sub>1</sub> = 8.4 Hz, *J*<sub>2</sub> = 1.6 Hz, 1H), 7.38 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 7.27 (m, 1H), 7.06 (m, 1H), 4.89 (brs, 3H), 2.52 (s, 3H), 1.77-1.75 (m, 2H), 1.68-1.63 (m, 2H), 1.36-1.14 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.4, 167.8, 133.9, 129.2, 127.6, 125.1, 123.6, 121.0, 88.7, 44.2, 26.4, 26.1, 26.0, 25.9, 25.8, 24.9 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub>Cl 310.1210; Found 310.1200.



*N*-(4-Chlorophenyl)-2-cyclohexyl-2-hydroxy-3-oxobutanamide (1f) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 151 mg (49% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.89 (brs, 1H), 7.50 (d, *J* = 10/1), 151 mg (49% yield).

8.8 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H), 4.84 (brs, 1H), 2.50 (s, 3H), 1.78-1.74 (m, 2H), 1.64-1.60 (m, 2H), 1.31-1.10 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.6, 167.5, 135.5, 129.8, 129.1, 120.9, 88.4, 44.1, 26.4, 26.1, 26.0, 25.8, 24.9 ppm. HRMS (EI+) m/z: Calcd for C<sub>16</sub>H<sub>20</sub>CINO<sub>3</sub> 309.1132; Found 309.1131.



**2-Cyclohexyl-2-hydroxy-3-oxo-***N***-(p-tolyl)butanamide** (1h) yellow solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 141 mg (49% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.80 (brs, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.13 (t, *J* = 8.4 Hz, 2H), 4.83 (brs, 1H), 2.50 (s, 3H), 2.31 (s, 3H), 1.77-1.73 (m, 2H), 1.67-1.64 (m, 2H), 1.32-1.09 (m, 7H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  208.1, 167.2, 134.5, 134.4, 129.6, 119.7, 88.3, 44.2, 26.4, 24.0, 26.0, 26.0, 25.8, 25.1, 20.9 ppm. HRMS (EI+) m/z: Calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub> 289.1678; Found 289.1676.



**2-Cyclohexyl-***N***-(4-ethoxyphenyl)-2-hydroxy-3-oxobutanamide** (1k) white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 5/1), 147 mg (46% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.67 (brs, 1H), 7.36 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 4.74 (brs, 1H), 3.93 (q, *J* = 6.8 Hz, 2H), 2.43 (s, 3H), 1.70-1.68 (m, 2H), 1.59-1.57 (m, 2H), 1.32 (t, *J* = 6.8 Hz, 3H), 1.25-1.03 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  208.2, 167.1, 156.0, 130.0, 121.4, 114.8, 88.3, 63.7, 44.1, 26.4, 26.1, 26.0, 25.9, 25.8, 25.1, 14.8 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>18</sub>H<sub>26</sub>NO<sub>4</sub> 320.1862; Found 320.1857.



*N*-(**3**-Chlorophenyl)-2-cyclohexyl-2-hydroxy-3-oxobutanamide (11) colorless oil, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 169 mg (55% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.88 (brs, 1H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.36-7.33 (m, 1H), 7.26-7.23 (m, 1H), 7.12-7.10 (m, 1H), 4.84 (brs, 1H), 2.50 (s, 3H), 1.78-1.75 (m, 2H), 1.68-1.60 (m, 2H), 1.35-1.09 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  207.5, 167.7, 138.0, 134.8, 130.0, 124.8, 119.8, 117.7, 88.4, 44.2, 26.4, 26.1, 26.0, 25.9, 25.8, 24.9 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub>Cl 310.1210; Found 310.1201.



**2-Cyclohexyl-2-hydroxy-3-oxo**-*N*-(**o-tolyl**)**butanamide** (**1p**) white solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 168 mg (58% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.85 (brs, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.20 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 4.87 (brs, 1H), 2.51 (s, 3H), 2.25 (s, 3H), 1.77-1.75 (m, 2H), 1.68-1.66 (m, 2H), 1.32-1.11 (m, 7H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 208.4, 167.3, 135.0, 130.5, 128.3, 126.8, 125.1, 121.5, 88.6, 44.3, 26.4, 26.1, 26.0, 25.9, 25.8, 25.2, 17.6 ppm. HRMS (EI+) m/z: Calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub> 289.1678; Found 289.1676.

# 3. Optimization of multiple C-C bond cleavage conditions by employing 1a or 1b as substrates

Table S1. Optimization of multiple C-C bond cleavage conditions by employing **1a** as substrate<sup>a</sup>



<sup>*a*</sup> Reaction Conditions: **1a** (0.2 mmol) and base (0.4 mmol) in solvent (2 mL) was stirred at 85 °C under N<sub>2</sub> atmosphere. <sup>*b*</sup> Isolated yield. <sup>*c*</sup> 3 equiv of KOtBu was used. <sup>*d*</sup> The reaction was carried out at 100 °C with 1 equiv KOtBu. <sup>*e*</sup> The reaction was carried out at 70 °C. <sup>*f*</sup> 2 equiv 1,10-phenanthroline as the addictive.

Table S2. Optimization of multiple C-C bond cleavage conditions by employing **1b** as substrate<sup>a</sup>

	H 35 - OH Ph - N - 55 - 55 - 55 - 55 - 55 - 55 - 55	(X-ray structure of <b>1b</b> )	ОН
entry	base	solvent	yield (%) <sup>b</sup>
1 <sup>c</sup>	KOtBu	DMSO	65
2	<b>KOtBu</b>	DMSO	71
3 <sup>d</sup>	KOtBu	DMSO	33
4 <sup>e</sup>	KOtBu	DMSO	43
$5^{\rm f}$	KOtBu	DMSO	66
6 <sup>g</sup>	KOtBu	DMSO	45
$7^{\rm h}$	KOtBu	DMSO	61
8	KOtBu	toluene	<10
9	KOtBu	DCE	trace
10	KOtBu	t-BuOH	trace
11	KOtBu	DMSO: <i>t</i> -BuOH= 5:1	14
12	KOtBu	tetrahydrothiophene 1-oxide	42
13	TBD	DMSO	trace
14	DABCO	DMSO	trace
15	DBU	DMSO	trace
16	NaOtBu	DMSO	40
17	LiOtBu	DMSO	55
18 <sup><i>i</i></sup>	KOtBu	DMSO	29
19 <sup><i>i</i></sup>	KOtBu	DMSO	61

areaction Conditions: 1b (0.2 mmol) and base (0.4 mmol) in solvent (2 mL) was stirred at 85 °C under N2 atmosphere for 4 h. <sup>b</sup> Isolated yield. <sup>c</sup> 3 equiv of KOtBu was used. <sup>d</sup> 1 equiv of KOtBu was used. "The reaction was carried out for 2 h.<sup>f</sup> The reaction was carried out for 6 h.<sup>g</sup> The reaction was carried out at 70 °C. hThe reaction was carried out at 100 °C. i1,10-phenanthroline as the additive. j The reaction was carried out under air atmosphere.

# 4. Synthesis of α-hydroxy acylamide via C-C bond cleavages

4.1 Typical procedure for preparing products (2a as example):



Under N<sub>2</sub> atmosphere, KO*t*Bu (44.8 mg, 0.4 mmol) was dissolved in 2 mL DMSO. Substrate **1b** (55 mg, 0.2 mmol) was added into the solution. When the reaction finished in 4 h monitored by TLC, the reaction was quenched with 10 mL H<sub>2</sub>O. Then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL × 3), washed sequentially with saturated sodium chloride solution (50 mL). The combined organic phase was dried over MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (Petroleum ether/ EtOAc = 2:1) to give **2a** as a white solid (23 mg, 71% yield).



**2-Hydroxy-***N***-phenylpropanamide (2a)**,<sup>[2]</sup> white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 23 mg (70% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.66 (brs, 1H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.30 (m, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 4.29 (d, *J* = 5.2 Hz, 1H), 4.09 (brs, 1H), 1.47 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  173.3, 137.0, 129.1, 124.7, 120.0, 68.7, 21.1 ppm.



*N*-(4-Chlorophenyl)-2-hydroxypropanamide (2f),<sup>[3]</sup> yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 25 mg (62% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.51 (brs, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.20 (d,

*J* = 8.8 Hz, 2H), 4.27 (q, *J* = 6.8 Hz, 1H), 3.33 (brs, 1H), 1.43 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 172.9, 135.7, 129.7, 129.1, 121.1, 68.8, 21.1 ppm.



*N*-(4-Fluorophenyl)-2-hydroxypropanamide (2g),<sup>[2]</sup> white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 23 mg (61% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.56 (brs, 1H), 7.52-7.48 (m, 2H), 7.03-6.99 (m, 2H), 4.37-4.31 (m, 1H), 3.42 (brs, 1H), 1.50 (d, J = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 172.7, 159.5 (d,  $J_{C-F} = 242.4$  Hz), 133.2 (d,  $J_{C-F} = 3.3$  Hz), 121.6 (d,  $J_{C-F} = 8.1$  Hz), 115.8 (d,  $J_{C-F} = 22.5$  Hz), 68.8, 21.1 ppm.



**2-Hydroxy-***N***-(p-tolyl)propanamide** (2h),<sup>[2]</sup> yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 26 mg (72% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.54 (brs, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 4.30 (q, *J* = 6.8 Hz, 1H), 3.81 (brs, 1H), 2.30 (s, 3H), 1.47 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  173.1, 134.5, 134.3, 129.5, 120.0, 68.8, 21.1, 20.9 ppm.



*N*-(4-(tert-Butyl)phenyl)-2-hydroxypropanamide (2i), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 31 mg (69% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.61 (brs, 1H), 7.44 (d, *J* = 8.8 Hz, 2H), 4.30 (q, *J* = 6.8 Hz, 1H), 4.07 (brs, 1H), 1.47 (d, *J* = 6.8 Hz, 3H), 1.29 (s, 9H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  173.2, 147.7, 134.5, 125.9, 119.8, 68.7, 34.4, 31.4, 21.1 ppm.

HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>13</sub>H<sub>20</sub>NO<sub>2</sub> 222.1494; Found 222.1489.



**2-Hydroxy-***N***-(4-methoxyphenyl)propanamide (2j)**,<sup>[3]</sup> yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 25 mg (63% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.50 (brs, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.33-4.27 (m, 1H), 3.77-3.75 (m, 4H), 1.48 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  172.8, 156.6, 130.2, 121.7, 114.2, 68.7, 55.5, 21.1 ppm.



*N*-(4-Ethoxyphenyl)-2-hydroxypropanamide (2k),<sup>[4]</sup> white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 27 mg (65% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.53 (brs, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 4.28 (q, *J* = 6.8 Hz, 1H), 3.98 (q, *J* = 7.2 Hz, 2H), 1.46 (d, *J* = 6.8 Hz, 3H), 1.39 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  173.0, 156.0, 130.1, 121.7, 114.8, 68.7, 63.7, 21.1, 14.8 ppm.



*N*-(3-Chlorophenyl)-2-hydroxypropanamide (2l),<sup>[3]</sup> white oil, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 23 mg (58% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.63 (brs, 1H), 7.67 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 4.35 (q, *J* = 6.8 Hz, 1H), 3.45 (brs, 1H), 1.51 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  173.0, 138.3, 134.7, 130.1, 124.7, 120.0, 117.9, 68.8, 21.1 ppm.



**2-Hydroxy-***N***-(m-tolyl)propanamide (2m)**, white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 22 mg (62% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  8.43 (brs, 1H), 7.30 (s, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 1H), 3.39 (brs, 1H), 2.25 (s, 3H), 1.42 (d, *J* = 7.2 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.7, 139.0, 137.1, 128.9, 125.4, 120.5, 117.0, 68.8, 21.5, 21.2 ppm. HRMS (EI+) m/z: Calcd for C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub> 179.0946; Found 179.0945.



*N*-(2-Chlorophenyl)-2-hydroxypropanamide (2n),<sup>[3]</sup> yellow solid, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 27 mg (68% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 9.14 (brs, 1H), 8.39 (dd,  $J_1$  = 8.4 Hz,  $J_2$  = 1.2 Hz, 1H), 7.37 (dd,  $J_1$  = 8.0 Hz,  $J_2$  = 1.6 Hz, 1H), 7.29-7.25 (m, 1H), 7.07-7.03 (m, 1H), 4.42 (q, J = 2.8 Hz, 1H), 3.28 (brs, 1H), 1.55 (d, J = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 172.8, 134.1, 129.1, 127.7, 124.9, 123.3, 121.3, 69.2, 21.1 ppm.



*N*-(2-Fluorophenyl)-2-hydroxypropanamide (20), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 21 mg (58% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.77 (brs, 1H), 8.32 (t, *J* = 8.0 Hz, 1H), 7.15-7.05 (m, 3H), 4.40 (q, *J* = 6.8 Hz, 1H), 3.07 (brs, 1H), 1.55 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.7, 152.7 (d, *J*<sub>C-F</sub> = 242.4 Hz), 125.7 (d, *J*<sub>C-F</sub> = 10.4 Hz), 124.7 (d, *J*<sub>C-F</sub> = 7.8 Hz), 124.6 (d, *J*<sub>C-F</sub> = 4.1 Hz), 121.5, 114.9 (d, <sup>2</sup>*J*<sub>C-F</sub> = 19.2 Hz), 69.0, 21.1 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>9</sub>H<sub>10</sub>FNO<sub>2</sub> 184.0774; Found 184.0765.



**2-Hydroxy-***N***-(o-tolyl)propanamide** (**2p**), yellow oil, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 23 mg (65% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.44 (brs, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.23-7.17 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 4.37 (q, *J* = 3.2 Hz, 1H), 3.26 (brs, 1H), 2.26 (s, 3H), 1.53 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  172.7, 135.1, 130.5, 128.7, 126.8, 125.1, 122.2, 69.0, 21.3, 17.5 ppm. HRMS (EI+) m/z: Calcd for C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub> 179.0946; Found 179.0947.



**2-Hydroxy-***N***-(2-methoxyphenyl)propanamide** (**2q**), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 24 mg (61% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.96 (brs, 1H), 8.28 (dd,  $J_1$  = 8.0 Hz,  $J_2$  = 1.6 Hz, 1H), 6.99-6.96 (m, 1H), 6.89-6.85 (m, 1H), 6.80 (dd,  $J_1$  = 8.0 Hz,  $J_2$  = 0.8 Hz, 1H), 4.28 (q, J = 6.8 Hz, 1H), 3.78 (s, 3H), 3.44 (brs, 1H), 1.44 (d, J = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  172.8, 148.3, 126.9, 124.1, 120.9, 119.7, 110.0, 69.1, 55.7, 21.2 ppm. HRMS (EI+) m/z: Calcd for C<sub>10</sub>H<sub>13</sub>NO<sub>3</sub> 195.0895; Found 195.0896.



*N*-(4-Chloro-2-methylphenyl)-2-hydroxypropanamide (2r), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 25 mg (59% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.46 (s, 1H), 7.88 (s, *J* = 9.2 Hz, 1H), 7.17 (m, 2H), 4.37 (q, *J* = 6.8 Hz, 1H), 2.23 (s, 3H), 1.52 (d, *J* = 6.4 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 172.7, 133.7, 130.4, 130.2, 130.0, 126.8, 123.2, 69.0, 21.2, 17.4 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub>Cl 214.0635; Found 214.0631.



**2-Hydroxy-***N***-(pyridin-2-yl)propanamide** (**2s**), yellow oil, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 18 mg (52% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.68 (brs, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 8.24 (d, *J* = 4.8 Hz, 1H), 7.77-7.73 (m, 1H), 7.10-7.07 (m, 1H), 6.41 (brs, 1H), 4.46 (q, *J* = 6.8 Hz, 1H), 1.57 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  173.8, 150.9, 147.0, 139.1, 120.0, 114.3, 68.5, 21.1 ppm. HRMS (EI+) m/z: Calcd for C<sub>8</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub> 166.0742; Found 166.0741.



**2-Hydroxy-***N***-(quinolin-2-yl)propanamide (2t)**, white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 24 mg (56% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta$  9.66 (brs, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.84-7.80 (m, 2H), 7.72-7.69 (m, 1H), 7.50-7.47 (m, 1H), 5.10 (brs, 1H), 4.53 (q, *J* = 6.6 Hz, 1H), 1.63 (d, *J* = 6.6 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  173.7, 150.6, 146.1, 139.2, 130.4, 127.7, 126.9, 126.4, 125.5, 114.2, 68.7, 21.4 ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>12</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub> 217.0949; Found 217.0932.



2-Hydroxy-N-phenylbutanamide (2u),<sup>[5]</sup> white soild, purification by flash column

chromatography (eluent: Petroleum ether/EtOAc = 2/1), 18 mg (51% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.47 (brs, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 4.20 (q, *J* = 4.0 Hz, 1H), 2.98 (brs, 1H), 2.01-1.91 (m, 1H), 1.84-1.73 (m, 1H), 1.03 (t, *J* = 7.6 Hz, 3H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  172.0, 137.2, 129.1, 124.6, 119.8, 73.5, 27.8, 9.2 ppm.



**2-Hydroxy-N-phenylpentanamide** (**2v**), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 19 mg (48% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.45 (brs, 1H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 8.4 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H), 4.27-4.23 (m, 1H), 2.88 (brs, 1H), 1.95-1.87 (m, 1H), 1.78-1.70 (m, 1H), 1.55-1.47 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.6, 137.2, 129.0, 124.6, 119.9, 72.3, 36.8, 18.3, 13.8 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> C<sub>11</sub>H<sub>15</sub>NNaO<sub>2</sub> 216.1000; Found 216.0995.

# 5. Synthesis of deuterated $\alpha$ -hydroxy acylamide via C-C bond cleavages

**Typical procedure for preparing deuterated products (2a'** as example):



Under N<sub>2</sub> atmosphere, KO*t*Bu (44.8 mg, 0.4 mmol) was dissolved in 1 mL DMSO-*d*<sub>6</sub>. Substrate **1b** (55 mg, 0.2 mmol) in 1 mL DMSO-*d*<sub>6</sub> was added into the solution. When the reaction finished in 4 h monitored by TLC, the reaction was quenched with 10 mL H<sub>2</sub>O. Then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL × 3), washed sequentially

with saturated sodium chloride solution (50 mL). The combined organic phase was dried over MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (Petroleum ether/ EtOAc = 2:1) to give **2a'** as a white solid (24 mg, 72% yield).



**2-Hydroxy-***N***-phenyl-2,3***-d***--propanamide (2a')**, white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 25 mg (72% yield). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): 8.45 (brs, 1H), 7.60-7.58 (m, 2H), 7.38-7.34 (m, 2H), 7.17-7.14 (m, 1H), 4.40 (m, 0.07H), 2.67 (brs, 1H), 1.53 (m, 0.07H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.2, 137.2, 129.1, 124.5, 119.8, 68.6 (m), 20.3 (m) ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>9</sub>H<sub>8</sub>D<sub>4</sub>NO<sub>2</sub> 170.1119; Found 170.1113.



*N*-(4-Chlorophenyl)-2-hydroxy-2,3-*d*<sub>4</sub>-propanamide (2f<sup>°</sup>), yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 25 mg (60% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.59 (brs, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 4.33 (m, 0.07H), 3.37 (brs, 1H), 1.46 (m, 0.08H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 172.9, 135.7, 129.6, 129.1. 121.1, 68.5 (m), 20.4 (m) ppm. HRMS (ESI) m/z:  $[M + H]^+ C_9 H_7 D_4 CINO_2 204.0729$ ; Found 204.0722.



**2-Hydroxy-***N***-(4-methoxyphenyl)** -2,3-*d*<sub>4</sub>**-propanamide** (2j'), yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1),

26 mg (64% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.43 (brs, 1H), 7.44 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 4.31 (m, 0.05H), 3.78 (s, 3H), 3.33 (brs, 1H), 1.46 (m, 0.1H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.6, 156.6, 130.3, 121.6, 114.1, 68.4 (m), 55.5, 20.3 (m) ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>10</sub>H<sub>10</sub>D<sub>4</sub>NO<sub>2</sub> 200.1225; Found 200.1229.



*N*-(**3**-Chlorophenyl)-2-hydroxy-2,3-*d*<sub>4</sub>-propanamide (2l'), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 23 mg (55% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.51 (brs, 1H), 7.71 (t, *J* = 1.2 Hz, 1H), 7.41 (d, *J* = 6.0 Hz, 1H), 7.25 (t, *J* = 6.8 Hz, 1H), 7.10 (d, *J* = 6.0 Hz, 1H), 4.38 (m, 0.09H), 2.73 (brs, 1H), 1.50 (m, 0.12H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>): δ 172.3, 138.3, 134.7, 130.0, 124.5, 119.8, 117.6, 68.6 (m), 20.2 (m) ppm. HRMS (ESI) m/z:  $[M + H]^+$ C<sub>9</sub>H<sub>7</sub>D<sub>4</sub>ClNO<sub>2</sub> 204.0729; Found 204.0719.



*N*-(2-Chlorophenyl)-2-hydroxy-2,3-*d*<sub>4</sub>-propanamide (2n'), yellow soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 28 mg (69% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.10 (s, 1H), 8.41 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 7.38 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 1.2 Hz, 1H), 7.30-7.26 (m, 1H), 7.08-7.03 (m, 1H), 4.42 (m, 0.09H), 2.85 (s, 1H), 1.56 (m, 0.04H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.5, 134.1, 129.1, 127.7, 124.9, 123.2, 121.2, 68.8 (m), 20.3 (m) ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>9</sub>H<sub>7</sub>D<sub>4</sub>ClNO<sub>2</sub> 204.0729; Found 204.0723.



**2-Hydroxy-***N***-(2-methoxyphenyl)-2,3-***d*<sub>4</sub>**-propanamide** (**2q**'), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 25 mg (62% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 9.04 (brs, 1H), 8.36-8.33 (m, 1H), 7.07-7.03 (m, 1H), 6.96-6.92 (m, 1H), 6.88-6.85 (m, 1H), 4.37 (m, 0.04H), 3.85 (s, 3H), 3.53 (brs, 1H), 1.47 (s, 0.05H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  172.9, 148.4, 126.9, 124.2, 121.0, 120.0, 110.0, 68.7 (m), 55.7, 20.4 (m) ppm. HRMS (ESI) m/z: [M + H]<sup>+</sup> C<sub>10</sub>H<sub>10</sub>D<sub>4</sub>NO<sub>2</sub> 200.1225; Found 200.1222.



**2-Hydroxy-N-phenyl-2,3-***d*<sub>3</sub>**-butanamide** (2v'), white soild, purification by flash column chromatography (eluent: Petroleum ether/EtOAc = 2/1), 18 mg (49% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 8.40 (brs, 1H), 7.57 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 8.0 Hz, 2H), 7.13 (t, J = 7.6 Hz, 1H), 4.22 (m, 0.07H), 2.64 (brs, 1H), 2.24-2.20 (m, 0.08H), 2.02-2.00 (m, 0.1H), 1.02 (s, 3H) ppm. <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>):  $\delta$  171.6, 137.2, 129.1, 124.5, 119.8, 73.1 (m), 27.1 (m), 8.9 ppm. HRMS (ESI) m/z: [M + Na]<sup>+</sup> C<sub>10</sub>H<sub>10</sub>D<sub>3</sub>NO<sub>2</sub>Na 205.1032; Found 205.1041.

# 6. Mechanistic Study

### 6.1 TEMPO as additive



Under N<sub>2</sub> atmosphere, KO*t*Bu (44.8 mg, 0.4 mmol) and TEMPO (62.5 mg, 0.4 mmol) were dissolved in 2 mL DMSO. Substrate **1b** (55 mg, 0.2 mmol) was added into the solution. When the reaction finished in 4 h, the reaction was quenched with 10 mL H<sub>2</sub>O. Then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL × 3), washed sequentially with saturated sodium chloride solution (50 mL). The combined organic phase was dried over MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (Petroleum ether/ EtOAc = 2:1) to give **2a** as a white solid (16.5 mg, 51% yield), and no 1-(cyclohexyloxy)-2,2,6,6-tetramethylpiperidine was found in the reaction system by EI-MS.<sup>[6]</sup>

### 6.2 Ethene-1,1-diyldibenzene as additive



Under N<sub>2</sub> atmosphere, KOtBu (44.8 mg, 0.4 mmol) and ethene-1,1-diyldibenzene (108 mg, 0.6 mmol) were dissolved in 2 mL DMSO. Substrate **1b** (55 mg, 0.2 mmol) was added into the solution. When the reaction finished in 4 h, the reaction was quenched with 10 mL H<sub>2</sub>O. Then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL × 3), washed sequentially with saturated sodium chloride solution (50 mL). The combined organic phase was dried over MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (Petroleum ether/ EtOAc = 2:1) to give **2a** as a white solid (20 mg, 61% yield). It showed no effect on the yield.
#### **6.3 EPR experiments**



The two oven-dried schlenk tubes equipped with a stir bar were loaded with DMSO (2 mL), and KOtBu (44.8 mg, 0.4 mmol) and substrate **1b** (55 mg, 0.2 mmol), respectively. The two mixtures were stirred under standard condition for 2 hours, followed by the addition of 5,5-dimethyl 1-pyridine *N*-oxide (DMPO) (45 mg, 0.4 mmol) to the sceond solution. Two solutions were stirred for another five minutes with sampling and analyzing by EPR respectively.





Figure S1. The EPR spectrum.

6.4 H<sub>2</sub><sup>18</sup>O as additive



Under N<sub>2</sub> atmosphere, KO*t*Bu (44.8 mg, 0.4 mmol) and H<sub>2</sub><sup>18</sup>O (12 mg, 0.6 mmol) were dissolved in 2 mL DMSO. Substrate **1b** (55 mg, 0.2 mmol) was added into the solution. When the reaction finished in 4 h monitored by TLC, the reaction was quenched with 10 mL H<sub>2</sub>O. Then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL × 3), washed sequentially with saturated sodium chloride solution (50 mL). The combined organic phase was dried over MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (Petroleum ether/ EtOAc = 2:1) to give **2a**" as a white solid.



Figure S2. ESI-MS spectrum of 2a".

#### 6.5 GC-MS study



Figure S3. (Methylsulfonyl)methane and leaving unit detected by GC-MS

#### **6.6 Crossover experiment**



Under N<sub>2</sub> atmosphere, KO*t*Bu (89 mg, 0.8 mmol), **1f** (62 mg, 0.2 mmol) and **1v** (61 mg, 0.2 mmol) were dissolved in 2 mL DMSO. The mixtures were stirred under standard condition for 4 h. After that, the reaction was quenched with 10 mL H<sub>2</sub>O. Then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL × 3), washed sequentially with saturated sodium chloride solution (50 mL). The combined organic phase was dried over MgSO<sub>4</sub>, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (Petroleum ether/ EtOAc = 2:1) to give the mixture of **2f** and **2v**. The yields of **2f** and **2v** were determined by <sup>1</sup>H NMR analysis.



Figure S4. <sup>1</sup>H NMR analysis of the mixture of 2f and

# 7. X-ray structure of 1b.





Table 1.Crystal data and structure refinement for d8v20635.

Identification code	d8v20635	
Empirical formula	C16 H21 N O3	
Formula weight	275.34	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 17.3280(6)  Å	$\alpha = 90^{\circ}$ .
	b = 5.5386(2) Å	$\beta = 115.7840(10)^{\circ}.$
	c = 17.0245(6) Å	$\gamma = 90^{\circ}$ .
Volume	1471.22(9) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.243 Mg/m <sup>3</sup>	
Absorption coefficient	0.085 mm <sup>-1</sup>	
F(000)	592	
Crystal size	0.200 x 0.140 x 0.120 m	m <sup>3</sup>
Theta range for data collection	2.801 to 25.998°.	
Index ranges	-21<=h<=16, -6<=k<=6,	-17<=1<=20
Reflections collected	6846	
Independent reflections	2873 [R(int) = 0.0220]	
Completeness to theta = $25.242^{\circ}$	98.8 %	
	S42	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6747
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	2873 / 0 / 184
Goodness-of-fit on F <sup>2</sup>	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0371, wR2 = 0.0891
R indices (all data)	R1 = 0.0443, wR2 = 0.0952
Extinction coefficient	0.034(6)
Largest diff. peak and hole	0.241 and -0.175 e.Å <sup>-3</sup>

Table 2. Atomic coordinates (  $x \ 10^4$ ) and equivalent isotropic displacement parameters (Å<sup>2</sup>x 10<sup>3</sup>)

	х	у	Z	U(eq)
O(1)	2485(1)	10165(2)	1690(1)	33(1)
O(2)	2409(1)	4451(2)	2619(1)	29(1)
O(3)	988(1)	4023(2)	1228(1)	39(1)
N(1)	3231(1)	6654(2)	1867(1)	25(1)
C(1)	4515(1)	5641(2)	1752(1)	31(1)
C(2)	5155(1)	6128(3)	1497(1)	41(1)
C(3)	5145(1)	8250(3)	1065(1)	43(1)
C(4)	4478(1)	9858(3)	877(1)	39(1)
C(5)	3828(1)	9402(2)	1127(1)	31(1)
C(6)	3854(1)	7286(2)	1575(1)	25(1)
C(7)	2608(1)	8039(2)	1904(1)	24(1)
C(8)	2025(1)	6657(2)	2231(1)	24(1)
C(9)	1172(1)	6114(2)	1420(1)	27(1)
C(10)	614(1)	8137(3)	907(1)	37(1)
C(11)	1872(1)	8228(2)	2899(1)	24(1)
C(12)	1203(1)	7141(3)	3158(1)	33(1)
C(13)	1055(1)	8802(3)	3794(1)	42(1)
C(14)	1885(1)	9280(3)	4606(1)	44(1)
C(15)	2571(1)	10288(3)	4369(1)	38(1)
C(16)	2711(1)	8674(3)	3716(1)	32(1)

for d8v20635. U(eq) is defined as one third of the trace of the orthogonalized  $U^{ij}$  tensor.

Table 3. Bond lengths [Å] and angles  $[\circ]$  for d8v20635.

O(1)-C(7)	1.2233(15)
O(2)-C(8)	1.4112(14)
O(2)-H(2)	0.8400
O(3)-C(9)	1.2078(15)
N(1)-C(7)	1.3475(15)
N(1)-C(6)	1.4156(15)
N(1)-H(1)	0.8800
C(1)-C(2)	1.3825(19)
C(1)-C(6)	1.3892(17)
C(1)-H(1A)	0.9500
C(2)-C(3)	1.382(2)
C(2)-H(2A)	0.9500
C(3)-C(4)	1.381(2)
C(3)-H(3)	0.9500
C(4)-C(5)	1.3891(19)
C(4)-H(4)	0.9500
C(5)-C(6)	1.3886(18)
C(5)-H(5)	0.9500
C(7)-C(8)	1.5516(16)
C(8)-C(11)	1.5426(16)
C(8)-C(9)	1.5505(17)
C(9)-C(10)	1.4895(18)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-C(12)	1.5329(16)
C(11)-C(16)	1.5330(17)
C(11)-H(11)	1.0000
C(12)-C(13)	1.5252(19)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.523(2)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-C(15)	1.518(2)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900

C(15)-C(16)	1.5251(19)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(8)-O(2)-H(2)	109.5
C(7)-N(1)-C(6)	128.69(10)
C(7)-N(1)-H(1)	115.7
C(6)-N(1)-H(1)	115.7
C(2)-C(1)-C(6)	120.11(13)
C(2)-C(1)-H(1A)	119.9
C(6)-C(1)-H(1A)	119.9
C(3)-C(2)-C(1)	120.44(13)
C(3)-C(2)-H(2A)	119.8
C(1)-C(2)-H(2A)	119.8
C(4)-C(3)-C(2)	119.21(13)
C(4)-C(3)-H(3)	120.4
C(2)-C(3)-H(3)	120.4
C(3)-C(4)-C(5)	121.24(13)
C(3)-C(4)-H(4)	119.4
C(5)-C(4)-H(4)	119.4
C(6)-C(5)-C(4)	119.03(12)
C(6)-C(5)-H(5)	120.5
C(4)-C(5)-H(5)	120.5
C(5)-C(6)-C(1)	119.95(11)
C(5)-C(6)-N(1)	123.66(11)
C(1)-C(6)-N(1)	116.39(11)
O(1)-C(7)-N(1)	124.96(11)
O(1)-C(7)-C(8)	121.69(10)
N(1)-C(7)-C(8)	113.34(10)
O(2)-C(8)-C(11)	109.91(9)
O(2)-C(8)-C(9)	108.80(9)
C(11)-C(8)-C(9)	111.31(9)
O(2)-C(8)-C(7)	110.26(9)
C(11)-C(8)-C(7)	109.45(9)
C(9)-C(8)-C(7)	107.08(9)
O(3)-C(9)-C(10)	122.36(12)

O(3)-C(9)-C(8)	117.63(11)
C(10)-C(9)-C(8)	120.01(10)
C(9)-C(10)-H(10A)	109.5
C(9)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(9)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(12)-C(11)-C(16)	109.81(10)
C(12)-C(11)-C(8)	112.58(10)
C(16)-C(11)-C(8)	111.19(10)
C(12)-C(11)-H(11)	107.7
C(16)-C(11)-H(11)	107.7
C(8)-C(11)-H(11)	107.7
C(13)-C(12)-C(11)	110.46(11)
C(13)-C(12)-H(12A)	109.6
C(11)-C(12)-H(12A)	109.6
C(13)-C(12)-H(12B)	109.6
C(11)-C(12)-H(12B)	109.6
H(12A)-C(12)-H(12B)	108.1
C(14)-C(13)-C(12)	111.40(11)
C(14)-C(13)-H(13A)	109.3
C(12)-C(13)-H(13A)	109.3
C(14)-C(13)-H(13B)	109.3
C(12)-C(13)-H(13B)	109.3
H(13A)-C(13)-H(13B)	108.0
C(15)-C(14)-C(13)	111.21(11)
C(15)-C(14)-H(14A)	109.4
C(13)-C(14)-H(14A)	109.4
C(15)-C(14)-H(14B)	109.4
C(13)-C(14)-H(14B)	109.4
H(14A)-C(14)-H(14B)	108.0
C(14)-C(15)-C(16)	111.69(12)
C(14)-C(15)-H(15A)	109.3
C(16)-C(15)-H(15A)	109.3
C(14)-C(15)-H(15B)	109.3
C(16)-C(15)-H(15B)	109.3
H(15A)-C(15)-H(15B)	107.9

C(15)-C(16)-C(11)	111.54(10)
C(15)-C(16)-H(16A)	109.3
C(11)-C(16)-H(16A)	109.3
C(15)-C(16)-H(16B)	109.3
C(11)-C(16)-H(16B)	109.3
H(16A)-C(16)-H(16B)	108.0

Symmetry transformations used to generate equivalent atoms:

Table 4.Anisotropic displacement parameters $(Å^2x \ 10^3)$  for d8v20635.The anisotropicdisplacement factor exponent takes the form: $-2\pi^2$ [  $h^2 \ a^{*2}U^{11} + ... + 2 \ h \ k \ a^* \ b^* \ U^{12}$  ]

	U <sup>11</sup>	U <sup>22</sup>	U <sup>33</sup>	U <sup>23</sup>	U <sup>13</sup>	U <sup>12</sup>
O(1)	39(1)	22(1)	46(1)	4(1)	26(1)	5(1)
O(2)	31(1)	21(1)	35(1)	4(1)	14(1)	4(1)
O(3)	32(1)	27(1)	51(1)	-8(1)	11(1)	-3(1)
N(1)	25(1)	22(1)	30(1)	3(1)	14(1)	2(1)
C(1)	30(1)	35(1)	30(1)	1(1)	14(1)	4(1)
C(2)	32(1)	55(1)	41(1)	0(1)	19(1)	8(1)
C(3)	38(1)	61(1)	40(1)	-2(1)	26(1)	-4(1)
C(4)	47(1)	42(1)	34(1)	2(1)	24(1)	-5(1)
C(5)	34(1)	33(1)	29(1)	1(1)	15(1)	1(1)
C(6)	23(1)	30(1)	22(1)	-4(1)	10(1)	-1(1)
C(7)	24(1)	24(1)	22(1)	-2(1)	9(1)	0(1)
C(8)	24(1)	20(1)	28(1)	2(1)	11(1)	2(1)
C(9)	26(1)	26(1)	30(1)	-3(1)	14(1)	-1(1)
C(10)	32(1)	33(1)	33(1)	1(1)	4(1)	2(1)
C(11)	24(1)	25(1)	26(1)	1(1)	11(1)	1(1)
C(12)	26(1)	40(1)	34(1)	2(1)	15(1)	-1(1)
C(13)	34(1)	60(1)	38(1)	3(1)	22(1)	8(1)
C(14)	47(1)	60(1)	31(1)	0(1)	21(1)	8(1)
C(15)	40(1)	44(1)	27(1)	-3(1)	11(1)	0(1)
C(16)	25(1)	40(1)	29(1)	-2(1)	11(1)	-2(1)

Table 5. Hydrogen coordinates (  $x \ 10^4$ ) and isotropic displacement parameters (Å<sup>2</sup>x 10<sup>3</sup>) for d8v20635.

	Х	У	Z	U(eq)
H(2)	2183	3317	2266	44
H(1)	3252	5157	2048	31
H(1A)	4526	4179	2049	38
H(2A)	5605	4997	1620	50
H(3)	5591	8597	900	52
H(4)	4464	11304	571	47
H(5)	3373	10520	993	38
H(10A)	150	7499	374	55
H(10B)	955	9288	753	55
H(10C)	369	8956	1257	55
H(11)	1652	9830	2620	29
H(12A)	657	6903	2630	40
H(12B)	1403	5545	3434	40
H(13A)	813	10354	3501	50
H(13B)	633	8052	3966	50
H(14A)	1774	10444	4987	53
H(14B)	2091	7757	4935	53
H(15A)	3116	10441	4904	46
H(15B)	2399	11920	4115	46
H(16A)	2952	7108	3996	38
H(16B)	3131	9445	3546	38

	Table 6.	Torsion	angles [	°] for	d8v20635
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C(6)-C(1)-C(2)-C(3)	0.0(2)
C(1)-C(2)-C(3)-C(4)	-1.2(2)
C(2)-C(3)-C(4)-C(5)	1.1(2)
C(3)-C(4)-C(5)-C(6)	0.1(2)
C(4)-C(5)-C(6)-C(1)	-1.28(18)
C(4)-C(5)-C(6)-N(1)	179.40(11)
C(2)-C(1)-C(6)-C(5)	1.23(18)
C(2)-C(1)-C(6)-N(1)	-179.40(12)
C(7)-N(1)-C(6)-C(5)	-11.86(19)

C(7)-N(1)-C(6)-C(1)	168.79(11)
C(6)-N(1)-C(7)-O(1)	-0.80(19)
C(6)-N(1)-C(7)-C(8)	177.73(10)
O(1)-C(7)-C(8)-O(2)	-166.60(11)
N(1)-C(7)-C(8)-O(2)	14.81(13)
O(1)-C(7)-C(8)-C(11)	-45.59(15)
N(1)-C(7)-C(8)-C(11)	135.82(10)
O(1)-C(7)-C(8)-C(9)	75.19(13)
N(1)-C(7)-C(8)-C(9)	-103.40(11)
O(2)-C(8)-C(9)-O(3)	-2.80(15)
C(11)-C(8)-C(9)-O(3)	-124.06(12)
C(7)-C(8)-C(9)-O(3)	116.36(12)
O(2)-C(8)-C(9)-C(10)	177.43(11)
C(11)-C(8)-C(9)-C(10)	56.17(15)
C(7)-C(8)-C(9)-C(10)	-63.42(14)
O(2)-C(8)-C(11)-C(12)	-66.70(12)
C(9)-C(8)-C(11)-C(12)	53.90(13)
C(7)-C(8)-C(11)-C(12)	172.08(9)
O(2)-C(8)-C(11)-C(16)	57.01(13)
C(9)-C(8)-C(11)-C(16)	177.62(10)
C(7)-C(8)-C(11)-C(16)	-64.21(12)
C(16)-C(11)-C(12)-C(13)	57.46(14)
C(8)-C(11)-C(12)-C(13)	-178.07(10)
C(11)-C(12)-C(13)-C(14)	-57.51(16)
C(12)-C(13)-C(14)-C(15)	55.45(17)
C(13)-C(14)-C(15)-C(16)	-53.94(17)
C(14)-C(15)-C(16)-C(11)	55.00(15)
C(12)-C(11)-C(16)-C(15)	-56.41(14)
C(8)-C(11)-C(16)-C(15)	178.31(11)

Symmetry transformations used to generate equivalent atoms:

Table 7.	Hydrogen bonds for d8v20635	[Å and °].		
 D-HA	d(D-H)	d(HA)	d(DA)	<(DHA)

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## 9. <sup>1</sup>H and <sup>13</sup>C-NMR Spectra Data

2-Cyclohexyl-3-oxo-N-phenylbutanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]







# 2-Cycloheptyl-3-oxo-*N*-phenylbutanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



### $N\-(4-Chlorophenyl)\-2\-cyclohexyl\-3\-oxobutanamide$



#### **2-Cyclohexyl-***N***-(4-fluorophenyl)-3-oxobutanamide** [<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]





#### N-(4-(tert-Butyl)phenyl)-2-cyclohexyl-3-oxobutanamide



#### 2-Cyclohexyl-N-(4-methoxyphenyl)-3-oxobutanamide





#### N-(3-Chlorophenyl)-2-cyclohexyl-3-oxobutanamide





2-Cyclohexyl-3-oxo-*N*-(m-tolyl)butanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]

#### N-(2-Chlorophenyl)-2-cyclohexyl-3-oxobutanamide



#### 2-Cyclohexyl-N-(2-fluorophenyl)-3-oxobutanamide





#### 2-Cyclohexyl-3-oxo-*N*-(o-tolyl)butanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]

#### 2-Cyclohexyl-N-(2-methoxyphenyl)-3-oxobutanamide

#### [<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]

### 



#### N-(4-Chloro-2-methylphenyl)-2-cyclohexyl-3-oxobutanamide



2-Cyclohexyl-3-oxo-N-(pyridin-2-yl)butanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26

ppm)]



### $\label{eq:cyclohexyl-3-oxo-N-(quinolin-2-yl)} but an amide$



**2-Cyclohexyl-3-oxo-***N***-phenylpentanamide**[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]





2-Cyclohexyl-3-oxo-N-phenylhexanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



 130 120 110

210 200
# 2-Cyclohexyl-2-hydroxy-3-oxo-*N*phenylbutanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



## 2-Cyclopentyl-2-hydroxy-3-oxo-*N*phenylbutanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



 <sup>2
 240
 220
 220
 10
 200
 180
 170
 160
 130
 120
 110
 100
 90
 80
 70
 60
 50
 40
 30
 20
 10
 0
 -10
 -20
 -30
 -4</sup>

#### 2-Cycloheptyl-2-hydroxy-3-oxo-N-phenylbutanamide

[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



**2-Acetyl-2-hydroxy-***N***-phenylpent-4-enamide**[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



### *N*-(4-Chlorophenyl)-2-cyclohexyl-2-hydroxy-3oxobutanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]







### 2-Cyclohexyl-2-hydroxy-3-oxo-*N*-(ptolyl)butanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]





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### *N*-(3-Chlorophenyl)-2-cyclohexyl-2-hydroxy-3oxobutanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



## 2-Cyclohexyl-2-hydroxy-3-oxo-*N*-(mtolyl)butanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]







#### 2-Cyclohexyl-*N*-(2-fluorophenyl)-2-hydroxy-3oxobutanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



## 2-Cyclohexyl-2-hydroxy-3-oxo-*N*-(otolyl)butanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]







*N*-(4-Chloro-2-methylphenyl)-2-cyclohexyl-2-hydroxy-3oxobutanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



2-Cyclohexyl-2-hydroxy-3-oxo-*N*-(pyridin-3yl)butanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



# 2-Cyclohexyl-2-hydroxy-3-oxo-*N*-(quinolin-2yl)butanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]









2-Cyclohexyl-2-hydroxy-3-oxo-*N*phenylhexanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



2-Hydroxy-N-phenylpropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



*N*-(4-Chlorophenyl)-2-hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]











*N*-(4-(tert-Butyl)phenyl)-2-hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



**2-Hydroxy-***N***-(4-methoxyphenyl)propanamide**[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



*N*-(4-Ethoxyphenyl)-2-hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



*N*-(3-Chlorophenyl)-2-hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]





*N*-(2-Chlorophenyl)-2-hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



*N*-(2-Fluorophenyl)-2-hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



2-Hydroxy-N-(o-tolyl)propanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



**2-Hydroxy-***N***-(2-methoxyphenyl)propanamide**[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



## *N*-(4-Chloro-2-methylphenyl)-2hydroxypropanamide[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]








655 512 2225 512 2210 8837 719 711 717 717 717 717 719 719 882 882 882 881 5 801 498 691 498 691 475 693 477 693 477 693 4788 691 4788 691 4788 693 770 571 770 571 770 770 771 770 770	.097 550 527 527 515	635
0 8 8 8 8 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 4444	<del></del>
		$\vee$









2-Hydroxy-*N*-phenyl l-2,3-*d*<sub>4</sub>-propanamide[<sup>1</sup>H\_NMR\_600MHz\_(CDCl<sub>3</sub>:7.26 ppm)]





## $N\-(3-Chlorophenyl)\-2\-hydroxy\-2,3\-d_4\-propanamide$

[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]



## N-(2-Chlorophenyl)-2-hydroxy-2,3-d4-propanamide

[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]





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**2-Hydroxy-***N***-phenyl-2,3***-d*<sub>3</sub>**-butanamide**[<sup>1</sup>H\_NMR\_400MHz\_(CDCl<sub>3</sub>:7.26 ppm)]

