**Experimental Section**

**General**

(-)-*β*-Pinene was purchased from the spice company Jiangxi Jishui Hongda Natural Perfume Co., Limited, China, and other reagents were of reagent grade. Melting points were determined in WRS-2 melting point apparatus (Shanghai precision &scientific instrument Co., Ltd., China) and were uncorrected. IR spectra were recorded on a Nicolet IS10 FT-IR spectrometer (Nicolet, Madison, USA). 1H NMR and 13C NMR spectra were recorded on a Bruker DKX500 NMR spectrometer (Bruker, Karlsruhe, Germany) using CDCL3 or DMSO-*d*6 as solvent, and TMS as internal standard. ESI-MS were recorded on an Agilent-5973 mass spectrometer. Purity of compounds was detected by Agilent 1260 high performance liquid chromatography (Agilent, Santa Clara, USA) and Fuli GC-9750 gas chromatography (Zhejiang Fuli analysis instrument Co. Ltd., China). All reactions were traced by the thin layer chromatography (TLC). Madin-Darby canine kidney (MDCK) cells were obtained from the Institute of Biochemistry and Cell Biology, Shanghai Institute of Biological Science, Chinese Academy of Sciences, China. MDCK cells were propagated in Dulbecco's modified eagle medium (DMEM; GibcoTM, USA), supplemented with 10% fetal bovine serum (FBS; GibcoTM, USA) and 1% Penicillin-Streptomycin (PS; GibcoTM, USA) at 37℃ with 5% CO2 in a humidified atmosphere. The influenza virus A/Puerto Rico/8/34 was obtained from Southern Medical University. Experiments were performed with 100TCID50·ml-1. Ribavirin was purchased from Qianjiang Pharmaceutical Co., Ltd., Hubei, China. The forty-one tested compounds were dissolved in dimethyl sulfoxide (DMSO; Sigma-Aldrich, USA) at 0.1 M as stock solutions and kept at -80℃. The stock solutions were diluted serially in culture media prior to use. The final concentration of DMSO in testing solutions was always lower than 0.1%. Trypsin-EDTA Solution and 3-(4,5-dimetylthiazol-2-yl)-2,5- diphenyltetrazolium bromide (MTT) were purchased from Biosharp, China.

**Synthesis of** **(+)-nopinone (2)**

Potassium permanganate (23.705 g, 0.15 mol) was gradually added into a stirred solution of (-)-*β*-pinene (**1**)(6.951 g, 0.05 mol) and catalytic amount of sulfuric acid in solvent acetone (50 mL), the solution was stirred at room temperature for 8 h. Then, the resulting mixture was filtered, extracted by ethyl acetate, washed by water and concentrated under vacuum to give the (+)-nopinone (**2**). Characterization data for (+)-nopinone (**2**): Yield 82%, purity 90.35%, [α]D18 +33.9o (c 1.0 CHCl3), FT-IR *v* (cm-1): 2948, 2874 (C-H stretching vibration), 1705 (C=O stretching vibration), 1459, 1386 (C-H bending vibration). 1H NMR (500 MHz, CDCl3) δ: 2.56 (pd, J=12.4, 5.0 Hz, 3H, -CH- and -CH2-), 2.41-2.19 (m, 2H, -CH2-), 2.12-1.88 (m, 2H, -CH2-), 1.59 (d, J = 9.9 Hz, 1H, -CH-), 1.33 (s, 3H, -CH3), 0.86 (s, 3H, -CH3). ESI-MS: *m/z* 138.1 [M]+.

**General procedure for the synthesis of 3-cyanopyridine derivatives (4a~4m)**

To a mixture of (+)-nopinone (**2**) (4 mmol), ammonium acetate (6 mmol), ethyl cyanoacetate or malononitrile (4 mmol) and catalyst ytterbium triflate (0.2 mmol) in absolute ethanol (5 mL), aldehydes **3a~3m** (4 mmol) was added. The solution was stirred until the completion of reaction (according to the TLC analysis). Further purification was accomplished by silica gel chromatography to give pure products **4a~4m**.

**Compound 4a:**

2-amino-4-(3-bromophenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 79%, HPLC purity= 98.93%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 242-243 oC; IR *v* (cm-1): 3432, 3330 (N-H stretching vibration), 2978, 2929 (C-H stretching vibration), 2211 (C≡N stretching vibration), 1628, 1553, 1478, 1450 (aromatic ring framework vibration), 1368 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.68-7.66 (d, *J* = 8.0 Hz, 1H, phenyl), 7.60 (s, 1H, phenyl), 7.49-7.46 (t, *J* = 7.8 Hz, 1H, phenyl), 7.38-7.36 (d, *J* = 7.6 Hz, 1H, phenyl), 6.62 (s, 2H, -NH2), 2.73-2.71 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.63-2.59 (m, 1H, -CH-), 2.46-2.45 (d, *J* = 2.4 Hz, 1H), 2.36-2.32 (d, *J* = 16.3 Hz, 1H, -CH2-), 2.20 (s, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.25-1.23 (d, *J* = 9.4 Hz, 1H, -CH2-), 0.67 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.87, 158.55, 150.34, 138.30, 131.48, 130.83, 130.57, 127.35, 121.74, 116.71, 115.30, 50.11, 29.30, 28.85, 25.59, 21.13.

ESI-MS: *m/z* 369.3 [M+1]+; 390.3, 392.3 [M+23]+.

**Compound 4b:**

2-amino-4-(4-fluorophenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 71%, HPLC purity= 99.30%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 212-213 oC; IR *v* (cm-1): 3461, 3292, 3161 (N-H stretching vibration), 2963 (C-H stretching vibration), 2202 (C≡N stretching vibration), 1625, 1607, 1564, 1511, 1456 (aromatic ring framework vibration), 1379 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.43-7.41 (dd, J = 8.5, 5.6 Hz, 2H, phenyl), 7.35-7.32 (t, J = 8.9 Hz, 2H, phenyl), 6.58 (s, 2H, -NH2), 2.73-2.71 (t, J = 5.5 Hz, 1H, -CH2-), 2.63-2.59 (m, 1H, -CH-), 2.45-2.44 (d, J = 3.0 Hz, 1H, -CH2-), 2.38-2.34 (dd, J = 16.4, 2.2 Hz, 1H, -CH2-), 2.21-2.19 (m, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.23-1.21 (d, J = 9.5 Hz, 1H, -CH2-), 0.67 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.71, 163.69, 160.47, 158.58, 151.09, 132.31, 132.26, 130.50, 130.39, 133.41, 125.59, 118.04, 117.81, 117.69, 116.67, 115.47, 50.11, 29.29, 28.75, 25.58, 21.11.

ESI-MS: *m/z* 308.2 [M+1]+; 330.2 [M+23]+

**Compound 4c:**

2-amino-4-(4-bromophenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 74%, HPLC purity= 97.76%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 209-210 oC; IR *v* (cm-1): 3453, 3299, 3149 (N-H stretching vibration), 2954, 2925 (C-H stretching vibration), 2211 (C≡N stretching vibration), 1636, 1592, 1555, 1491, 1458 (aromatic ring framework vibration), 1370 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.72-7.70 (d, *J* = 8.4 Hz, 2H, phenyl), 7.35-7.33 (d, *J* = 8.3 Hz, 2H, phenyl), 6.70 (s, 2H, -NH2), 2.75-2.72 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.63-2.59 (dt, *J* = 22.3, 8.6 Hz, 1H, -CH2-), 2.45-2.44 (d, J = 2.9 Hz, 1H), 2.37-2.34 (d, *J* = 16.6 Hz, 1H, -CH2-), 2.20 (s, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.24-1.22 (d, *J* = 9.6 Hz, 1H, -CH2-), 0.67 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.82, 158.57, 150.80, 135.19, 133.17, 132.56, 131.62, 130.37, 122.08, 116.77, 115.24, 85.69, 55.17, 50.11, 30.30, 29.33, 28.88, 25.80, 21.08.

ESI-MS: *m/z* 369.1 [M+1]+; 390.1, 392.1, 393.1 [M+23]+

**Compound 4d:**

2-amino-4-(2-chlorophenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 60%, HPLC purity= 98.23%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 205-206 oC; IR *v* (cm-1): 3382, 3306, 3184 (N-H stretching vibration), 2950, 2917, 2840 (C-H stretching vibration), 2211 (C≡N stretching vibration), 1640, 1598, 1561, 1483, 1463 (aromatic ring framework vibration), 1378 (C-H bending vibration).

1H NMR (300 MHz, CDCl3) δ (ppm): 7.64-7.63 (dd, J = 6.3, 2.9 Hz, 1H, phenyl), 7.63-7.47 (m, 2H, phenyl), 7.38-7.36 (m, 1H, phenyl), 6.66 (s, 2H, -NH2), 2.73 (t, J = 5.5 Hz, 1H, -CH2-), 2.65-2.61 (m, 1H, -CH2-), 2.35-2.22 (m, 2H, -CH2-), 2.19 (d, J = 2.8 Hz, 1H, -CH-), 1.35 (s, 3H, -CH3), 1.25-1.23 (d, J = 9.6 Hz, 1H, -CH2-), 0.69-0.68 (d, J = 5.1 Hz, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.95, 158.21, 149.63, 130.53, 129.86, 129.52, 127.77, 127.73, 116.29, 115.90, 50.01, 29.60, 28.66, 25.70, 25.61, 21.10 20.83.

ESI-MS: *m/z* 324.8 [M+1]+; 346.8 [M+23]+

**Compound 4e:**

2-amino-4-(2-methoxyphenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 77%, HPLC purity= 99.12%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 207-208 oC; IR *v* (cm-1): 3388, 3304, 3173 (N-H stretching vibration), 2935, 2839 (C-H stretching vibration), 2208 (C≡N stretching vibration), 1640, 1605, 1561, 1498, 1459 (aromatic ring framework vibration), 1379 (C-H bending vibration).

1H NMR (300 MHz, CDCl3) δ (ppm): 7.45-7.42 (m, 1H, phenyl), 7.18-7.13 (m, 2H, phenyl), 7.08-7.05 (t, *J* = 7.4 Hz, 1H, phenyl), 6.46 (s, 2H, -NH2), 3.76-3.74 (m, 3H, -CH3), 2.71-2.69 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.63-2.58 (dt, *J* = 11.3, 5.5 Hz, 1H, -CH-), 2.35-2.27 (m, 1H, -CH2-), 2.17-2.16 (d, *J* = 2.8 Hz, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.21-1.16 (dd, *J* = 17.5, 9.5 Hz, 1H, -CH2-), 0.69-0.66 (d, *J* = 14.0 Hz, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.08, 158.37, 155.68, 149.70, 130.25, 129.27, 129.20, 124.60, 120.62, 116.84, 116.64, 111.58, 50.46, 49.94, 29.65, 29.56, 28.66, 25.67, 20.66.

ESI-MS: *m/z* 320.4 [M+1]+; 342.4 [M+23]+

**Compound 4f:**

2-amino-7,7-dimethyl-4-phenyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 75%, HPLC purity = 91.46%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 209-210 oC; IR *v* (cm-1): 3409, 3305, 3150 (N-H stretching vibration), 2949, 2925, 2842(C-H stretching vibration), 2203(C≡N stretching vibration), 1641, 1557, 1497, 1466 (aromatic ring framework vibration), 1376 (C-H bending vibration).

1H NMR (300 MHz, CDCl3) δ (ppm): 7.55-7.48 (m, 3H, phenyl), 7.35-7.32 (dd, J = 7.7, 1.7 Hz, 2H, phenyl), 5.40 (s, 2H, -NH2), 2.94-2.90 (t, J = 5.5 Hz, 1H, -CH-), 2.73-2.66 (dt, J = 9.9, 5.7 Hz, 1H, -CH2-), 2.58 (d, J = 2.9 Hz, 2H, -CH2-), 2.29-2.25 (m, 1H, -CH-), 1.41 (s, 3H, -CH3), 1.34-1.30 (d, J = 9.8 Hz, 1H, -CH2-), 0.76 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.62, 158.61, 152.50, 136.02, 128.58, 128.50, 128.10, 116.88, 115.33, 85.31, 55.11, 29.40, 29.00, 25.58, 21.07.

ESI-MS: *m/z* 290.4 [M+1]+; 312.4 [M+23]+.

**Compound 4g:**

2-amino-4-(3-methoxyphenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 87%, HPLC purity= 94.58%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 145-146 oC; IR *v* (cm-1): 3390, 3306, 3171 (N-H stretching vibration), 2933 (C-H stretching vibration), 2207 (C≡N stretching vibration), 1641, 1610, 1560, 1492, 1463 (aromatic ring framework vibration), 1370 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.44-7.40 (t, J = 8.0 Hz, 1H, phenyl), 7.03-7.01 (m, 1H, phenyl), 6.89 (s, 2H, phenyl), 6.55 (s, 2H, -NH2), 3.80 (s, 3H, -CH3), 2.73-2.71 (t, J = 5.5 Hz, 1H, -CH2-), 2.62-2.58 (m, 1H, -CH-), 2.48 (d, J = 2.8 Hz, 1H, -CH2-), 2.39-2.35 (dd, J = 16.5, 1.9 Hz, 1H, -CH2-), 2.20-2.18 (m, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.24-1.22 (d, J = 9.5 Hz, 1H, -CH2-), 0.67 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.60, 159.16, 158.55, 151.85, 137.35, 136.17, 129.85, 121.36, 120.15, 116.85, 115.33, 115.04, 113.84, 113.70, 113.16, 86.27, 55.16, 54.99, 50.11, 34.49, 29.39, 28.91, 25.59, 24.15, 22.43, 21.06.

ESI-MS: *m/z* 320.4 [M+1]+; 342.4 [M+23]+

**Compound 4h:**

2-amino-4-(3,4-dimethoxyphenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 52%, HPLC purity= 99.47%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 195-196 oC; IR *v* (cm-1): 3416, 3305, 3180 (N-H stretching vibration), 2952, 2935, 2835 (C-H stretching vibration), 2203 (C≡N stretching vibration), 1637, 1603, 1556, 1514, 1461 (aromatic ring framework vibration), 1370 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.07-7.06 (d, *J* = 8.2 Hz, 1H, phenyl), 6.94 (s, 1H, phenyl), 6.89-6.87 (d, *J* = 8.1 Hz, 1H, phenyl), 6.49 (s, 2H, -NH2), 3.78 (t, *J* = 17.4 Hz, 6H, -CH3), 2.71 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.66-2.57 (m, 1H, -CH-), 2.55 (d, J = 2.6 Hz, 1H, -CH2-), 2.41 (d, *J* = 16.5 Hz, 1H, -CH-), 2.21 (s, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.24 (d, *J* = 9.5 Hz, 1H, -CH2-), 0.66 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.45, 158.63, 151.98, 148.85, 148.47, 128.22,120. 64, 117.13, 115. 63, 111.86, 111.61, 86.68, 55.63, 55.41, 50.12, 30.65, 29.39, 29.03, 25.59, 21.07.

ESI-MS: *m/z* 350.2 [M+1]+; 372.2 [M+23]+.

**Compound 4i:**

2-amino-4-(3,4-difluorophenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 52%, HPLC purity= 94.94%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 174-175 oC; IR *v* (cm-1): 3406, 3300, 3161 (N-H stretching vibration), 2924, 2837 (C-H stretching vibration), 2207 (C≡N stretching vibration), 1638, 1589, 1562, 1480, 1465 (aromatic ring framework vibration), 1385 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.60-7.55 (m, 2H, phenyl), 7.24-7.23 (d, *J* = 4.3 Hz, 1H, phenyl), 6.63 (s, 2H, -NH2), 2.73-2.71 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.63-2.59 (m, 1H, -CH-), 2.47 (s, 1H, -CH2-), 2.37-2.34 (d, *J* = 16.5 Hz, 1H, -CH2-), 2.21-2.19 (m, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.24-1.22 (d, *J* = 9.5 Hz, 1H, -CH2-), 0.67 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.90, 158.52, 149.83, 147.89, 147.72, 133.41, 125.59, 118.04, 117.81, 117.69, 116.67, 115.47, 86.11, 50.11, 29.29, 28.75, 25.58, 21.11.

ESI-MS: *m/z* 326.4 [M+1]+; 348.1 [M+23]+

**Compound 4j:**

2-amino-4-(4-chlorophenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 78%, HPLC purity= 96.37%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 167-168 oC; IR *v* (cm-1): 3379, 3311, 3189 (N-H stretching vibration), 2954, 2933 (C-H stretching vibration), 2205 (C≡N stretching vibration), 1639, 1603, 1574, 1556, 1494, 1462 (aromatic ring framework vibration), 1369 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.70-7.68 (d, J = 8.5 Hz, 1H), 7.58-7.56 (d, J = 8.4 Hz, 2H), 7.54-7.49 (m, 1H), 7.41-7.39 (d, J = 8.3 Hz, 2H), 6.61 (s, 2H, -NH2), 2.73-2.71 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.45-2.44 (d, J = 2.8 Hz, 1H, -CH2-), 2.37-2.34 (d, J = 16.7 Hz, 2H, -CH2-), 2.20 (s, 1H, -CH-), 1.34 (s, 3H, -CH3), 1.23-1.21 (d, *J* = 9.5 Hz, 1H, -CH2-), 0.67 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.80, 163.33, 158.59, 150.80, 134.83, 133.09, 132.35, 130.12, 128.72, 118.46, 116.77, 115.33, 55.19, 50.12, 30.32, 29.33, 28.88, 25.58, 21.09.

ESI-MS: *m/z* 325.1 [M+1]+; 346.1, 348.1 [M+23]+

**Compound 4k:**

2-amino-4-(3-hydroxyphenyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 55%, HPLC purity= 99.58%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 264-265 oC; IR *v* (cm-1): 3459(O-H stretching vibration), 3442, 3232 (N-H stretching vibration), 2922 (C-H stretching vibration), 2217 (C≡N stretching vibration), 1631, 1560, 1499, 1439 (aromatic ring framework vibration), 1370 (C-H bending vibration).

1H NMR (300 MHz, CDCl3) δ (ppm): 9.60 (s, 1H, -OH), 7.31-7.27 (t, *J* = 7.8 Hz, 1H, phenyl), 6.85-6.83 (dd, *J* = 8.1, 1.8 Hz, 1H, phenyl), 6.72-6.68 (d, *J* = 7.4 Hz, 2H, phenyl), 6.53 (s, 2H, -NH2), 2.72-2.70 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.62-2.58 (m, 1H, -CH-), 2.45-2.37 (dd, *J* = 29.5, 8.6 Hz, 2H, -CH2-), 2.20 (s, 1H-CH-), 1.34 (s, 3H, -CH3), 1.22-1.21 (d, *J* = 9.5 Hz, 1H, -CH-), 0.66 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.49, 158.66, 158.42, 152.00, 137.20, 129.78, 118.38, 115.20, 114.70, 50.10, 50.03, 29.38, 28.88, 28.84, 25.54, 20.99.

ESI-MS: *m/z* 306.4 [M+1]+; 328.4 [M+23]+.

**Compound 4l:**

2-amino-7,7-dimethyl-4-(p-tolyl)-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 73%, HPLC purity= 94.72%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 12 min; pale yellow crystals, m.p. 182-183 oC; IR *v* (cm-1): 3405, 3311, 3189 (N-H stretching vibration), 2931(C-H stretching vibration), 2204 (C≡N stretching vibration), 1687, 1637, 1599, 1556, 1515, 1461 (aromatic ring framework vibration), 1371 (C-H bending vibration).

1H NMR (300 MHz, DMSO-*d*6) δ (ppm): 7.32-7.30 (d, *J* = 7.9 Hz, 2H, phenyl), 7.24-7.22 (d, *J* = 7.9 Hz, 2H, phenyl), 6.52 (s, 2H, -NH2), 2.72-2.70 (t, *J* = 5.5 Hz, 1H, -CH2-), 2.62-2.58 (m, 1H), 2.45 (d, J = 2.9 Hz, 1H), 2.39-2.34 (m, 4H, -CH3 and -CH2-), 2.19 (s, 1H, -CH-), 1.34 (d, *J* = 3.4 Hz, 3H, -CH3), 1.22-1.20 (d, *J* = 9.5 Hz, 1H, -CH2-), 0.66 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.52, 158.62, 152.10, 137.90, 133.06, 130.74, 129.34, 129.13, 127.94, 116.96, 115.41, 85.43, 55.15, 50.09, 30.46, 29.39, 29.03, 26.89, 25.81,21.33, 21.04, 20.92, 20.82.

ESI-MS: *m/z* 304.2 [M+1]+; 326.2 [M+23]+

**Compound 4m:**

2-hydroxy-7,7-dimethyl-4-phenyl-5,6,7,8-tetrahydro-6,8-methanoquinoline-3-carbonitrile

Yield 31%, HPLC purity= 97.48%, (XDB-C-18 column; MeOH:H2O/80:20), tr = 6 min; pale yellow crystals, m.p. 252-253 oC; IR *v* (cm-1): 3131 (O-H), 2943, 2867 (C-H), 2214 (C≡N), 1627, 1585, 1537, 1468 (aromatic ring), 1435, 1370 (C-H), 758, 700 (C-H single substituted benzene).

1H NMR (300 MHz, CDCl3) δ (ppm): 7.57 (d, *J* = 6.8 Hz, 3H, phenyl), 7.39 (d, *J* = 6.1 Hz, 2H, phenyl), 3.07 (t, *J* = 5.3 Hz, 1H, -CH-), 2.79 (d, *J* = 10.2 Hz, 1H, -CH-), 2.53 (s, 2H, -CH2-), 2.33 (s, 1H, -CH2-), 1.49 (s, 3H, -CH3), 1.44 (d, *J* = 10.0 Hz, 1H, -CH2-), 0.88 (s, 3H, -CH3).

13C NMR (75 MHz, DMSO-*d*6) δ (ppm): 169.83, 163.91, 160.18, 156.59, 152.81, 136.12, 135.24, 129.08, 128.64, 127.48, 116.46, 112.92, 111.18, 109.50, 103.20, 45.04, 40.05, 29.03, 28.54, 25.16, 24.68, 20.86.

ESI-MS: *m/z* 291.0 [M+1]+; 313.0 [M+23]+

**Synthesis of myrtanol (5)**

To a solution of (-)-*β*-pinene (**1**)(0.4 mol) and sodium borohydride (0.15 mol) in dry tetrahydrofuran (200 mL), 47% boron trifluoride ether solution (0.2 mol) was added and the mixture was stirred at 0-5℃. After 6 h, ethanol (30 mL) was added to quench the hydroboration reaction. Then, a 3 mol/L sodium hydroxide aqueous solution (68 mL) and the 30% hydrogen peroxide (60 mL) were added in succession. The mixture was stirred at 40-45℃. After 3 h, saturated sodium thiosulfate solution (40 mL) was added to exhaust excessive amounts of hydrogen peroxide. The reaction mixture was evaporated under reduced pressure to remove the organic phase. The residues were extracted with ethyl acetate (3x, 100 mL). The resulting organic phase was washed by water (3×, 100 mL) and brine (100 mL), dried over sodium sulfate, filtered, and concentrated under vacuum to afford myrtanol (**5**). Characterization data for myrtanol (**5**): Yield 96.8%, purity 94.5%, FT-IR *v* (cm-1): 3313 (O–H), 1041 (C–O). 1H NMR (300 MHz, CDCl3) δ: 3.55 (dd, J = 7.6, 5.2 Hz, 2H), 2.44–2.31 (m, 1H), 2.31–2.14 (m, 1H), 2.05–1.97 (m, 2H), 1.98–1.78 (m, 4H), 1.54–1.35 (m, 1H), 1.19 (s, 3H), 0.97 (s, 3H), 0.93 (d, J = 9.6 Hz, 1H); 13C NMR (75 MHz, CDCl3) δ: 66.95, 43.77, 42.37, 40.93, 38.07, 32.63, 27.44, 25.48, 22.79, 18.29. GC-MS *m/z* = 154.1 [M]+.

**Synthesis of myrtanyl acid (6)**

Myrtanol (**5**)(0.2 mol) was dissolved in glacial acetic acid (200 mL), and the solution was slowly added to a solution of chromic anhydride (0.6 mol) in glacial acetic acid (250 mL) and water (50 mL). The mixture was stirred at room temperature. After 10 h, the mixture was poured into water, and precipitate was collected through filtration. The obtained precipitate was dissolved in saturated sodium hydroxide aqueous solution, extracted with EtOAc (2×, 50 mL). The resulting aqueous phase was neutralized by 10% hydrochloric acid, extracted with EtOAc (3×, 50 mL). The resulting organic phase was washed by water (3×, 50 mL) and brine (50 mL), dried over sodium sulfate, filtered, and concentrated under vacuum to afford myrtanyl acid **(6)**. Characterization data formyrtanyl acid **(6)**: Yield 24.5%, purity 98.7%, FT-IR *v* (cm-1): 3660, 3638, 3061 (O–H), 2990, 2950, 2920, 2903, 2869 (C–H), 1675 (C=O), 1478, 1458 (C–H), 1414 (O–H), 1386, 1364, 1338, 1320 (C–H), 1250 (C–O), 940 (O–H). 1H NMR (500 MHz, CDCl3) δ: 11.91 (s, 1H), 3.02 (dt, J = 10.3, 3.5 Hz, 1H), 2.54 (dd, J = 9.1, 5.5 Hz, 1H), 2.42–2.29 (m, 2H), 2.07–1.84 (m, 4H), 1.26 (s, 3H), 1.23 (d, J = 10.0 Hz, 1H), 0.91 (s, 3H); 13C NMR (126 MHz, CDCl3) δ: 183.04, 43.76, 42.98, 40.34, 38.74, 29.03, 26.88, 24.60, 21.51, 15.09. ESI-MS: *m/z* 191.1 [M+Na]+; 167.1 [M-H]-

**General procedure for the synthesis of myrtanyl acid acylthiourea derivatives (9a~9k)**

A solution of myrtanyl acid (**6**)(20 mmol) and oxalyl chloride (30 mmol) in dry dichloromethane (20 mL) was stirred at 50℃ for 4 h. Then, the reaction mixture was evaporated under reduced pressure to remove the organic phase and excessive amounts of oxalyl chloride. The resulting myrtanyl chloride (**7**) was redissolved in dry acetonitrile (10 mL), then slowly added into a solution of potassium thiocyanate (30 mmol) in dry acetonitrile (30 mL). The mixture then was stirred at room temperature. After 12 h, a solution of arylamine (30 mmol) or 4-arylthiazol-2-amine (20 mmol) in dry acetonitrile (30 mL) was added into the mixture. The mixture was stirred at 80 ◦C. After 8 h, the mixture was filtered, evaporated under reduced pressure to remove the organic phase and recrystallized from ethanol to afford compounds **9a~9k**.

**Compound 9a:**

(1S,2S,5S)-6,6-Dimethyl-N-(phenylcarbamothioyl)-Bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 82%; purity 96.4%, FT-IR *v* (cm-1): 3635, 3164, 3028, 2987, 2915, 2868, 1686, 1563, 1598, 1516, 1498, 1469, 1447, 1384, 1356, 1327, 1310, 1296, 1238, 1143, 1102, 756, 685. 1H NMR (300 MHz, CDCl3) δ: 12.47 (s, 1H), 8.55 (s, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.35-7.29 (m, 1H), 3.10-3.00 (m, 1H), 2.53-2.44 (m, 2H), 2.41 (ddd, J = 13.8, 6.9, 3.6 Hz, 1H), 2.13-1.93 (m, 4H), 1.32 (s, 3H), 1.25 (d, J = 9.7 Hz, 1H), 0.97 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 178.33, 176.81, 137.66, 129.25, 128.78, 126.69, 123.95, 46.22, 43.27, 40.36, 38.75, 30.00, 27.15, 24.61, 22.03, 14.81. ESI-MS: *m/z* 325.1 [M+Na]+; 301.2 [M-H]-.

**Compound 9b:**

(1S,2S,5S)-N-(benzyl(methyl)Carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 81%; purity 95.5%, FT-IR *v* (cm-1): 3634, 3197, 3174, 3073, 2983, 2926, 2868, 1713, 1541, 1643, 1587, 1494, 1467, 1391, 1365, 1327, 1313, 1269, 1224, 1175, 1163, 744, 722, 694. 1H NMR (300 MHz, CDCl3) δ: 8.06 (s, 1H), 7.48-7.29 (m, 5H), 5.26 (q, J = 14.5 Hz, 1H), 4.70 (s, 1H), 3.33-2.89 (m, 4H), 2.49-2.36 (m, 3H), 2.06-1.90 (m, 4H), 1.28 (s, 3H), 1.22 (d, J = 8.7 Hz, 1H), 0.95 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 181.85, 171.97, 134.88, 128.78, 127.75, 59.34, 46.19, 43.47, 40.38, 38.56, 29.98, 27.11, 24.70, 22.12, 15.03. ESI-MS: *m/z* 353.2 [M+Na]+; 329.1 [M-H]-.

**Compound 9c:**

(1S,2S,5S)-6,6-Dimethyl-N-((4-(trifluoromethyl)-phenyl)Carbamothioyl)Bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 83%; purity 95.4%, FT-IR *v* (cm-1): 3247, 3200, 3017, 2999, 2921, 2870, 1700, 1524, 1612, 1596, 1466, 1409, 1387, 1369, 1319, 1256, 1160, 1122, 1103, 1063, 1015, 841. 1H NMR (300 MHz, CDCl3) δ: 12.73 (s, 1H), 8.71 (s, 1H), 7.92 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 3.07 (dd, J = 6.0, 3.1 Hz, 1H), 2.55-2.43 (m, 2H), 2.39 (t, J = 10.2 Hz, 1H), 2.12-1.93 (m, 4H), 1.32 (s, 3H), 1.25 (d, J = 9.9 Hz, 1H), 0.97 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 178.50, 177.19, 140.71, 128.43, 128.17, 125.97, 124.92, 123.56, 122.75, 46.29, 43.52, 43.33, 40.34, 38.74, 30.11, 27.16, 24.60, 22.07, 14.83. ESI-MS: *m/z* 371.1 [M+H]+; 369.1 [M-H]-.

**Compound 9d:**

(1S,2S,5S)-N-((4-fluorophenyl)Carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 82%; purity 96%, FT-IR *v* (cm-1): 3638, 3132, 3028, 2986, 2920, 2866, 1687, 1524, 1607, 1505, 1465, 1411, 1385, 1367, 1331, 1253, 1215, 1151, 1010, 837. 1H NMR (300 MHz, CDCl3) δ: 12.39 (s, 1H), 8.57 (s, 1H), 7.66 (dd, J = 8.7, 4.7 Hz, 2H), 7.12 (t, J = 8.5 Hz, 2H), 3.05 (dd, J = 6.3, 3.4 Hz, 1H), 2.48 (dd, J = 16.8, 7.2 Hz, 2H), 2.43-2.36 (m, 1H), 2.11-1.97 (m, 4H), 1.32 (s, 3H), 1.25 (d, J = 9.9 Hz, 1H), 0.97 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 179.16, 178.87, 176.92, 161.87, 159.91, 133.67, 126.05, 115.74, 115.56, 46.24, 43.92, 43.28, 40.35, 39.92, 38.76, 30.02, 27.15, 26.27, 24.61, 23.91, 23.56, 22.05, 20.17, 16.16, 14.83. ESI-MS: *m/z* 343.1 [M+Na]+; 319.1 [M-H]-.

**Compound 9e:**

(1S,2S,5S)-N-((4-ethylphenyl)Carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 81%; purity 97.2%, FT-IR *v* (cm-1): 3295, 3161, 3004, 2965, 2922, 2862, 1687, 1657, 1518, 1588, 1462, 1412, 1384, 1327, 1249, 1155, 1136, 835. 1H NMR (300 MHz, CDCl3) δ: 12.37 (s, 1H), 8.47 (s, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.31 (s, 1H), 7.26 (s, 1H), 3.05 (s, 1H), 2.70 (q, J = 7.5 Hz, 2H), 2.48 (dd, J = 14.1, 6.9 Hz, 2H), 2.39 (d, J = 9.8 Hz, 1H), 2.02 (dd, J = 33.3, 21.1 Hz, 5H), 1.32 (s, 3H), 1.30 (d, J = 7.5 Hz, 3H), 1.28 (s, 1H), 0.97 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 178.26, 176.70, 142.94, 135.27, 128.19, 123.99, 46.21, 43.24, 40.37, 38.77, 29.96, 28.41, 27.14, 24.61, 22.02, 15.33, 14.81. ESI-MS: *m/z* 331.2 [M+H]+; 329.1 [M-H]-.

**Compound 9f:**

(1S,2S,5S)-N-((2,6-difluorophenyl)Carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 82%; purity 95.8%, FT-IR *v* (cm-1): 3406, 3152, 3001, 2981, 2921, 2862, 1685, 1519, 1628, 1595, 1469, 1376, 1345, 1304, 1253, 1238, 1164, 1138, 995, 740. 1H NMR (300 MHz, CDCl3) δ: 11.68 (s, 1H), 8.78 (s, 1H), 7.41-7.33 (m, 1H), 7.04 (t, J = 8.5 Hz, 2H), 3.07 (d, J = 10.4 Hz, 1H), 2.48 (dt, J = 11.7, 8.0 Hz, 2H), 2.44-2.39 (m, 1H), 2.12-1.94 (m, 4H), 1.32 (s, 3H), 1.26 (d, J = 9.6 Hz, 1H), 0.98 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 181.73, 176.87, 159.24, 157.22, 129.32, 115.22, 111.88, 111.77, 111.59, 46.19, 43.30, 40.38, 38.81, 29.94, 27.14, 24.59, 21.92, 14.76. ESI-MS: *m/z* 361.1 [M+Na]+; 337.1 [M-H]-.

**Compound 9g:**

(1S,2S,5S)-N-((2-bromophenyl)Carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 81%; purity 96.9%, FT-IR *v* (cm-1): 3300, 3141, 3002, 2943, 2918, 2865, 1681, 1516, 1576, 1467, 1442, 1382, 1366, 1332, 1309, 1285, 1238, 1159, 1122, 744. 1H NMR (300 MHz, CDCl3) δ: 12.45 (s, 1H), 8.68 (s, 1H), 8.22 (d, J = 8.1 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 7.7 Hz, 1H), 7.19 (t, J = 7.7 Hz, 1H), 3.07 (d, J = 7.6 Hz, 1H), 2.52-2.41 (m, 3H), 2.13-1.92 (m, 4H), 1.32 (s, 3H), 1.27 (d, J = 7.7 Hz, 1H), 0.98 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 179.20, 176.60, 136.52, 132.86, 128.13, 127.37, 118.66, 46.11, 43.37, 40.38, 38.84, 29.84, 27.18, 24.56, 21.93, 14.65. ESI-MS: *m/z* 403.0 [M+Na]+; 379.1 [M-H]-.

**Compound 9h:**

(1S,2S,5S)-N-((4-(4-fluorophenyl)Thiazol-2-yl)carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 10%; purity 90.9%, FT-IR *v* (cm-1): 3603, 3245, 3187, 3007, 2942, 2917, 2870, 1697, 1531, 1546, 1484, 1449, 1412, 1386, 1309, 1293, 1277, 1226, 1209, 1158, 1126, 1062, 1012,

837. 1H NMR (300 MHz, CDCl3) δ: 13.75 (s, 1H), 8.49 (s, 1H), 7.87 (dd, J = 8.5, 5.4 Hz, 2H), 7.11 (dd, J = 14.3, 5.6 Hz, 3H), 3.05 (dd, J = 6.6, 3.6 Hz, 1H), 2.44 (ddd, J = 20.7, 15.9, 9.3 Hz, 3H), 2.10-1.92 (m, 4H), 1.29 (s, 3H), 1.25 (d, J = 9.8 Hz, 1H), 0.93 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 176.57, 174.90, 158.50, 149.69, 127.86, 115.66, 115.49, 107.60, 46.24, 43.25, 40.33, 38.86, 29.86, 27.13, 24.55, 22.02, 14.73. ESI-MS: *m/z* 404.1 [M+H]+; 402.1 [M-H]-.

**Compound 9i:**

(1S,2S,5S)-N-((4-(4-methoxyphenyl)Thiazol-2-yl)Carbamothioyl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 11%; purity 92.8%, FT-IR *v* (cm-1): 3598, 3423, 3248, 3194, 2995, 2918, 2834, 1698, 1530, 1611, 1546, 1487, 1451, 1416, 1388, 1301, 1249, 1209, 1167, 1131, 1109, 1065, 1033, 836. 1H NMR (300 MHz, CDCl3) δ: 13.73 (s, 1H), 8.53 (s, 1H), 7.83 (d, J = 8.6 Hz, 2H), 7.07 (s, 1H), 6.95 (d, J = 8.6 Hz, 2H), 3.85 (s, 3H), 3.04 (dd, J = 6.4, 3.5 Hz, 1H), 2.51-2.37 (m, 3H), 2.02 (ddd, J = 35.9, 21.6, 11.8 Hz, 4H), 1.28 (s, 3H), 1.23 (d, J = 9.8 Hz, 1H), 0.93 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 176.51, 174.74, 159.66, 158.23, 150.46, 127.41, 127.12, 114.06, 106.42, 55.31, 46.22, 43.27, 40.33, 38.83, 29.90, 27.13, 24.56, 22.02, 14.72. ESI-MS: *m/z* 416.1 [M+H]+; 414.1 [M-H]-.

**Compound 9j:**

(1S,2S,5S)-6,6-Dimethyl-N-((4-(4-nitrophenyl)thiazol-2-yl)Carbamothioyl)bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 8%; purity 93.2%, FT-IR *v* (cm-1): 3418, 3252, 3197, 2942, 2921, 2870, 1699, 1527, 1600, 1545, 1515, 1477, 1446, 1412, 1385, 1342, 1316, 1300, 1283, 1209, 1166, 1127, 1107, 1061, 856, 730. 1H NMR (300 MHz, CDCl3) δ: 13.81 (s, 1H), 8.57 (s, 1H), 8.27 (d, J = 8.7 Hz, 2H), 8.04 (d, J = 8.7 Hz, 2H), 7.38 (s, 1H), 3.12-3.03 (m, 1H), 2.52-2.37 (m, 3H), 2.02 (ddd, J = 27.5, 21.0, 14.2 Hz, 4H), 1.29 (s, 3H), 1.25 (d, J = 9.8 Hz, 1H), 0.94 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 176.81, 175.24, 159.03, 148.21, 147.28, 139.96, 126.62, 124.11, 111.28, 46.27, 43.24, 40.29, 38.83, 29.89, 27.12, 24.53, 22.03, 14.73. ESI-MS: *m/z* 453.2 [M+Na]+; 429.1 [M-H]-.

**Compound 9k:**

(1S,2S,5S)-6,6-Dimethyl-N-((4-phenylthiazol-2-yl)Carbamothioyl)Bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 10%; purity 94.2%, FT-IR *v* (cm-1): 3487, 3234, 3195, 3026, 2979, 2918, 2867, 1690, 1527, 1585, 1482, 1446, 1381, 1365, 1295, 1280, 1224, 1208, 1168, 1129, 1061, 775, 712. 1H NMR (300 MHz, CDCl3) δ: 13.79 (s, 1H), 8.60 (s, 1H), 7.94 (d, J = 7.5 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 7.24 (s, 1H), 3.09 (d, J = 7.0 Hz, 1H), 2.56-2.41 (m, 3H), 2.05 (dt, J = 27.2, 12.2 Hz, 4H), 1.32 (s, 3H), 1.27 (d, J = 9.5 Hz, 1H), 0.97 (s, 3H). 13C NMR (126 MHz, CDCl3) δ: 176.55, 174.89, 158.35, 150.64, 134.12, 128.66, 128.09, 126.11, 108.06, 46.23, 43.98, 43.27, 40.32, 38.83, 29.91, 27.13, 24.55, 22.02, 14.72. ESI-MS: *m/z* 386.1 [M+H]+; 408.1 [M+Na]+; 384.2 [M-H]-.

**General procedure for the synthesis of myrtanyl acid amide derivatives (10a~10o)**

A solution of myrtanyl acid (**6**)(20 mmol) and oxalyl chloride (30 mmol) in dry dichloromethane (20 mL) was stirred at 50℃ for 4 h. Then, the reaction mixture was evaporated under reduced pressure to remove the organic phase and excessive amounts of oxalyl chloride. The resulting myrtanyl chloride (**7**) was redissolved in dry dichloromethane (10 mL), and then slowly added into a solution of arylamine (30 mmol) or 4-arylthiazol-2-amine (20 mmol) and triethylamine (20 mmol) in dry dichloromethane (20 mL). The mixture was stirred at room temperature. After 12 h, the mixture was washed by 10% hydrochloric acid (3×, 10 mL), water (3×,10 mL), and brine (10 mL), dried over sodium sulfate, filtered, and concentrated under vacuum to afford crude products. The crude products were recrystallized from ethanol to afford compound **10a~10o**.

**Compound 10a:**

(1S,2S,5S)-N-(2,6-difluorophenyl)-6,6-Dimethyl-bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 88.2%; purity 95.4%, FT-IR *v* (cm-1): 3328, 3310 (N–H), 2987, 2948, 2917, 2867 (C–H), 1677, 1659 (C=O), 1622, 1597, 1510, 1465 (C=C), 1385, 1366 (C–H), 1288 (C–N), 1006 (C–F), 776, 702. 1H NMR (300 MHz, CDCl3) δ: 7.14 (s, 1H), 6.96–6.79 (m, 3H), 3.05 (s, 1H), 2.42 (d, J = 20.8 Hz, 3H), 1.95 (dd, J = 45.4, 21.0 Hz, 4H), 1.24 (s, 4H), 0.94 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 174.16, 172.21, 158.88, 156.89, 127.13, 114.41, 111.52, 111.37, 45.27, 44.03, 42.91, 40.52, 40.30, 38.81, 29.94, 29.11, 27.26, 26.87, 24.83, 24.49, 21.71, 15.05. ESI-MS: *m/z* 280.1 [M+H]+; 278.1 [M-H]-.

**Compound 10b:**

(1S,2S,5S)-N-(2-bromophenyl)-6,6-Dimethyl-bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 91%; purity 96.7%, FT-IR *v* (cm-1): 3406, 3310, 3066, 2949, 2927, 2902, 2869, 1655, 1621, 1588, 1502, 1472, 1436, 1383, 1293, 753, 579. 1H NMR (300 MHz, CDCl3) δ: 8.40 (dd, J = 8.3, 1.5 Hz, 1H), 7.84 (s, 1H), 7.53 (dd, J = 8.0, 1.4 Hz, 1H), 7.35-7.28 (m, 1H), 6.96 (td, J = 7.9, 1.6 Hz, 1H), 3.14 -3.02 (m, 1H), 2.58-2.38 (m, 3H), 2.10-1.87 (m, 4H), 1.32 (s, 1H), 1.29 (s, 3H), 0.90 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.58, 135.37, 131.62, 127.93, 124.22, 121.13, 112.73, 45.65, 43.17, 40.00, 38.44, 29.03, 26.71, 24.26, 21.39, 14.53. ESI-MS: *m/z* 322.1 [M+H]+; 344.1 [M+Na]+; 320.1 [M-H]-.

**Compound 10c:**

(1S,2S,5S)-N-Benzyl-6,6-Dimethylbicyclo[3.1.1]-Heptane-2-carboxamide

Yield 87%; purity 96.5%, FT-IR *v* (cm-1): 3321, 3281, 3090, 3063, 3025, 2995, 2973, 2917, 2875, 1641, 1606, 1537, 1496, 1465, 1453, 1384, 1363, 1259, 1234, 722, 694. 1H NMR (300 MHz, CDCl3) δ: 7.31 (dd, J=13.6, 7.8 Hz, 5H), 5.76 (s, 1H), 4.52-4.37 (m, 2H), 2.86 (dd, J=5.8, 3.3 Hz, 1H), 2.50-2.26 (m, 3H), 2.04-1.83 (m, 4H), 1.21 (d, J=7.7 Hz, 3H), 1.16 (d, J=9.3 Hz, 1H), 0.87 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 175.44, 138.70, 128.60, 127.97, 127.35, 45.09, 43.78, 40.65, 38.71, 30.12, 27.38, 24.96, 22.03, 15.44. ESI-MS: *m/z* 280.1 [M+Na]+; 256.1 [M-H]-.

**Compound 10d:**

(1S,2S,5S)-N-(4-fluorophenyl)-6,6-dimethylbicyclo-[3.1.1]Heptane-2-Carboxamide

Yield 90%; purity 97.7%, FT-IR *v* (cm-1): 3286, 3256, 3209, 3145, 3067, 2986, 2929, 2866, 1669, 1641, 1610, 1506, 1462, 1406, 1383, 1366, 1296, 1012, 993, 832. 1H NMR (300 MHz, CDCl3) δ: 7.48-7.38 (m, 2H), 7.11 (s, 1H), 7.05-6.94 (m, 2H), 3.04-2.93 (m, 1H), 2.55-2.35 (m, 3H), 2.08-1.85 (m, 4H), 1.25 (s, 3H), 1.21 (d, J=3.8 Hz, 1H), 0.93 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.95, 160.21, 158.28, 134.10, 121.83, 115.57, 115.39, 45.87, 44.00, 40.60, 38.81, 30.04, 27.39, 24.84, 21.95, 15.23. ESI-MS: *m/z* 284.1 [M+Na]+; 260.1 [M-H]-.

**Compound 10e:**

(1S,2S,5S)-6,6-Dimethyl-N-(4-(trifluoromethyl)-phenyl)Bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 94%; purity 97.3%, FT-IR *v* (cm-1): 3301, 3198, 3128, 2984, 2953, 2912, 2866, 1670, 1601, 1524, 1464, 1407, 1384, 1367, 1320, 837. 1H NMR (300 MHz, CDCl3) δ: 7.62 (d, J=8.7 Hz, 2H), 7.55 (d, J=8.7 Hz, 2H), 7.32 (s, 1H), 3.01 (dd, J=6.3, 2.6 Hz, 1H), 2.55-2.37 (m, 3H), 2.08-1.88 (m, 4H), 1.25 (s, 3H), 1.21 (d, J=2.1 Hz, 1H), 0.92 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 175.16, 142.15, 127.18, 120.29, 47.16, 44.98, 41.53, 39.82, 31.00, 28.35, 25.77, 22.90, 16.13. ESI-MS: *m/z* 334.1 [M+Na]+; 310.1 [M-H]-.

**Compound 10f:**

(1S,2S,5S)-N-Benzyl-N,6,6-Trimethylbicyclo-[3.1.1] Heptane-2-Carboxamide

Yield 89%; purity 94.9%, FT-IR *v* (cm-1): 3090, 3061, 3028, 2981, 2937, 2912, 2864, 1640, 1494, 1468, 1451, 1397, 1353, 1255, 1203, 731, 698. 1H NMR (300 MHz, CDCl3) δ: 7.30 (dd, J=6.5, 2.9 Hz, 3H), 7.21 (s, 2H), 4.75-4.33 (m, 2H), 3.14 (d, J=8.2 Hz, 1H), 2.89 (t, J=8.6 Hz, 3H), 2.33 (d, J=33.1 Hz, 3H), 2.15-1.74 (m, 4H), 1.23 (s, 3H), 1.03 (d, J=18.3 Hz, 4H). 13C NMR (75 MHz, CDCl3) δ: 130.47, 127.83, 127.37, 53.96, 52.18, 50.51, 45.62, 44.42, 44.42, 44.24, 41.91, 39.37, 35.84, 33.62, 28.95, 26.87, 24.16, 18.63. ESI-MS: *m/z* 294.1 [M+Na]+; 270.1 [M-H]-.

**Compound 10g:**

(1S,2S,5S)-6,6-Dimethyl-N-(4-nitrophenyl)Bicyclo-[3.1.1]Heptane-2-Carboxamide

Yield 84%; purity 96.2%, FT-IR *v* (cm-1): 3359, 3117, 3084, 2987, 2916, 2868, 1703, 1609, 1594, 1540, 1495, 1463, 1405, 1384, 1368, 1327, 1296, 1249, 854. 1H NMR (300 MHz, CDCl3) δ: 8.17 (d, J=9.1 Hz, 2H), 7.69 (d, J=9.2 Hz, 2H), 7.66 (d, J=3.2 Hz, 1H), 3.03 (dd, J=5.9, 2.6 Hz, 1H), 2.43 (dt, J=12.4, 6.3 Hz, 3H), 2.07-1.87 (m, 4H), 1.23 (s, 3H), 1.20 (d, J=4.0 Hz, 1H), 0.95-0.82 (m, 3H). 13C NMR (75 MHz, CDCl3) δ: 175.50, 145.16, 144.19, 125.99, 120.01, 47.42, 46.32, 44.93, 43.90, 41.38, 39.79, 31.13, 30.06, 28.33, 27.85, 25.75, 25.46, 22.86, 16.05. ESI-MS: *m/z* 311.1 [M+Na]+; 287.1 [M-H]-.

**Compound 10h:**

(1S,2S,5S)-6,6-Dimethyl-N-phenylbicyclo[3.1.1]-Heptane-2-Carboxamide

Yield 97%; purity 98.3%, FT-IR *v* (cm-1): 3292, 3267, 3195, 3134, 2992, 2912, 2866, 1674, 1657, 1595, 1532, 1491, 1465, 1438, 1367, 1332, 1300, 753, 694. 1H NMR (300 MHz, CDCl3) δ: 7.49 (d, J=7.9 Hz, 2H), 7.31 (t, J=7.9 Hz, 2H), 7.09 (t, J=7.4 Hz, 2H), 3.00 (dd, J=6.4, 2.7 Hz, 1H), 2.46 (ddd, J=17.9, 10.5, 5.8 Hz, 3H), 2.10-1.84 (m, 4H), 1.25 (s, 3H), 1.22 (s, 1H), 0.94 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.92, 138.18, 128.92, 123.97, 119.95, 46.03, 44.06, 40.63, 38.83, 30.10, 27.43, 24.90, 21.97, 15.24. ESI-MS: *m/z* 266.1 [M+Na]+; 242.1 [M-H]-.

**Compound 10i:**

(1S,2S,5S)-6,6-Dimethyl-N-(pyridin-2-yl)bicycle-[3.1.1]Heptane-2-Carboxamide

Yield 86%; purity 96.1%, FT-IR *v* (cm-1): 2990, 2948, 2914, 2867, 1695, 1638, 1577, 1508, 1463, 1429, 1383, 1367, 1295, 871, 776. 1H NMR (300 MHz, CDCl3) δ: 8.57 (s, 1H), 8.34-8.18 (m, 1H), 7.73 (s, 1H), 7.04 (s, 1H), 3.08 (s, 1H), 2.50 (dd, J=51.2, 27.8 Hz, 3H), 1.97 (s, 4H), 1.27 (s, 4H), 0.95 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 181.14, 179.43, 174.63, 172.17, 151.77, 149.37, 146.99, 138.65, 124.36, 119.26, 114.18, 46.92, 46.32, 45.30, 43.98, 43.73, 43.19, 42.90, 40.73, 38.72, 38.39, 31.52, 30.20, 29.35, 29.11, 27.30, 26.94, 25.85, 25.48, 24.51, 22.02, 16.84, 15.31, 15.04. ESI-MS: *m/z* 267.1 [M+Na]+; 243.1 [M-H]-.

**Compound 10j:**

(1S,2S,5S)-N-(3-bromophenyl)-6,6-Dimethyl-bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 91%; purity 95.4%, FT-IR *v* (cm-1): 3435, 3321, 3189, 3120, 2984, 2950, 2915, 2868, 1670, 1592, 1524, 1476, 1417, 1368, 1331, 1302, 774, 681, 569. 1H NMR (300 MHz, CDCl3) δ: 7.77 (d, J = 1.9 Hz, 1H), 7.39 (d, J = 7.7 Hz, 1H), 7.20 (ddd, J = 18.8, 11.1, 4.7 Hz, 3H), 2.99 (dd, J = 6.2, 3.3 Hz, 1H), 2.54-2.34 (m, 3H), 2.07-2.01 (m, 1H), 2.00-1.86 (m, 3H), 1.25 (s, 3H), 1.21 (d, J = 4.3 Hz, 1H), 0.91 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.82, 138.93, 129.70, 126.46, 122.42, 122.07, 117.96, 45.54, 43.43, 40.04, 38.33, 29.57, 26.90, 24.35, 21.54, 14.70. ESI-MS: *m/z* 322.1 [M+Na]+; 320.1 [M-H]-.

**Compound 10k:**

(1S,2S,5S)-N-(4-ethylphenyl)-6,6-Dimethylbicyclo-[3.1.1]Heptane-2-Carboxamide

Yield 96%; purity 98.7%, FT-IR *v* (cm-1): 3288, 3253, 3184, 3114, 3037, 2987, 2962, 2914, 2865, 1656, 1595, 1514, 1462, 1410, 1382, 1367, 1329, 1298, 826. 1H NMR (300 MHz, CDCl3) δ: 7.40 (d, J=8.4 Hz, 2H), 7.27 (t, J=9.6 Hz, 1H), 7.13 (d, J=8.3 Hz, 2H), 3.04-2.90 (m, 1H), 2.61 (q, J=7.6 Hz, 2H), 2.46 (ddd, J=23.4, 11.7, 5.9 Hz, 3H), 2.08-1.81 (m, 4H), 1.27-1.18 (m, 7H), 0.94 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.84, 140.00, 135.83, 128.19, 120.13, 45.92, 44.08, 40.64, 38.82, 30.10, 28.25, 27.44, 24.92, 21.97, 15.63, 15.25. ESI-MS: *m/z* 294.1 [M+Na]+; 270.1 [M-H]-.

**Compound 10l:**

(1S,2S,5S)-6,6-Dimµethyl-N-(4-phenylthiazol-2-yl)-Bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 28%; purity 95.8%, FT-IR *v* (cm-1): 3362, 3248, 3187, 3145, 3109, 2983, 2949, 2919, 2868, 1702, 1687, 1596, 1549, 1464, 1445, 1384, 1366, 1327, 1278, 1246, 1184, 1134, 1111, 1061, 746, 695. 1H NMR (300 MHz, CDCl3) δ: 11.82 (s, 1H), 7.80-7.72 (m, 2H), 7.51-7.36 (m, 3H), 7.09 (s, 1H), 3.24-3.13 (m, 1H), 2.38-2.25 (m, 3H), 2.00-1.92 (m, 4H), 1.21 (s, 3H), 1.16 (d, J = 6.1 Hz, 1H), 0.88 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 174.43, 160.96, 128.91, 128.72, 125.69, 106.41, 59.73, 45.06, 43.37, 42.43, 39.86, 38.27, 30.44, 29.25, 28.58, 26.51, 24.21, 21.52, 20.98, 14.78, 14.37, 13.71. ESI-MS: *m/z* 327.1 [M+H]+; 325.1 [M-H]-.

**Compound 10m:**

(1S,2S,5S)-6,6-Dimethyl-N-(4-(4-nitrophenyl)-thiazol-2-yl)bicyclo[3.1.1]Heptane-2-Carboxamide

Yield 16%; purity 97.3%, FT-IR *v* (cm-1): 3430, 3351, 3100, 2973, 2950, 2920, 2870, 1670, 1598, 1538, 1511, 1464, 1444, 1411, 1385, 1368, 1341, 1318, 1269, 1180, 1107, 1078, 1063, 856, 844. 1H NMR (300 MHz, CDCl3) δ: 9.42 (s, 1H), 8.33-8.24 (m, 2H), 8.03-7.92 (m, 2H), 7.34 (s, 1H), 3.13 (dd, J = 10.5, 3.4 Hz, 1H), 2.49 (dt, J = 9.8, 7.6 Hz, 3H), 2.09-1.90 (m, 4H), 1.29 (d, J = 4.1 Hz, 1H), 1.27 (s, 3H), 0.86 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.46, 168.89, 153.93, 146.67, 126.05, 123.73, 120.89, 110.80, 44.71, 42.84, 39.93, 38.35, 29.22, 26.63, 24.12, 21.32, 14.26. ESI-MS: *m/z* 372.1 [M+H]+; 370.1 [M-H]-.

**Compound 10n:**

(1S,2S,5S)-N-(4-(4-methoxyphenyl)thiazol-2-yl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 21%; purity 96.6%, FT-IR *v* (cm-1): 3434, 3117, 3045, 2945, 2916, 2870, 2837, 1687, 1612, 1540, 1492, 1463, 1440, 1419, 1385, 1367, 1326, 1285, 1249, 1173, 1110, 1062, 834. 1H NMR (300 MHz, CDCl3) δ: 11.04 (s, 1H), 7.72 (dq, J = 4.5, 1.8 Hz, 2H), 7.03-6.89 (m, 3H), 3.85 (s, 3H), 3.19-3.11 (m, 1H), 2.60-2.53 (m, 1H), 2.49-2.38 (m, 2H), 2.09-1.89 (m, 4H), 1.25 (s, 3H), 1.23 (s, 1H), 0.85 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 174.68, 165.59, 164.21, 131.99, 126.84, 113.68 (s), 112.44, 105.36, 54.86, 44.63, 42.88, 39.95, 29.24, 26.60, 25.82, 24.13, 21.29, 14.15. ESI-MS: *m/z* 357.1 [M+H]+; 355.1 [M-H]-.

**Compound 10o:**

(1S,2S,5S)-N-(4-(4-fluorophenyl)Thiazol-2-yl)-6,6-Dimethylbicyclo[3.1.1]Heptane-2-Carboxamide

Yield 19%; purity 95.5%, FT-IR *v* (cm-1): 3432, 3192, 3117, 3056, 2919, 2869, 1687, 1654, 1597, 1539, 1491, 1465, 1410, 1385, 1368, 1321, 1270, 1174, 1156, 1061, 839. 1H NMR (300 MHz, CDCl3) δ: 11.91 (s, 1H), 7.74 (dd, J = 8.8, 5.2 Hz, 1H), 7.64-7.30 (m, 2H), 7.14 (t, J = 8.7 Hz, 1H), 7.02 (s, 1H), 3.24-3.12 (m, 1H), 2.54 (s, 1H), 2.48-2.36 (m, 1H), 2.31 (s, 1H),

2.10-1.83 (m, 4H), 1.27 (s, 1H), 1.23 (s, 3H), 0.85 (s, 3H). 13C NMR (75 MHz, CDCl3) δ: 173.66, 163.81, 160.52, 158.91, 148.09, 130.05, 127.36, 115.40, 115.12, 106.80, 44.60, 42.94, 39.90, 38.09, 31.44, 30.98, 29.69, 29.24, 28.78, 26.58, 24.08, 22.21, 21.27, 13.78. ESI-MS: *m/z* 345.1 [M+H]+; 343.1 [M-H]-.