Supporting Information

A Convenient and Efficient Synthesis of Dipeptidyl Benzoxaboroles and their Peptidomimetics

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Table of Contents:

Synthesis and Characteristic Data of 6………………………………………………………… SI-1
Synthesis and Characteristic Data of 9a…………………………………………………… SI-1
Synthesis and Characteristic Data of 9b…………………………………………………… SI-2
Synthesis and Characteristic Data of 9c…………………………………………………… SI-3
Synthesis and Characteristic Data of 9d…………………………………………………… SI-3
Synthesis and Characteristic Data of 9e…………………………………………………… SI-4
Synthesis and Characteristic Data of 9f…………………………………………………… SI-4
Synthesis and Characteristic Data of 9g…………………………………………………… SI-5
Synthesis and Characteristic Data of 9h…………………………………………………… SI-6
Synthesis and Characteristic Data of 9i…………………………………………………… SI-6
Synthesis and Characteristic Data of 10…………………………………………………… SI-7
Synthesis and Characteristic Data of 13a………………………………………………… SI-7
Synthesis and Characteristic Data of 13b………………………………………………… SI-8
Synthesis and Characteristic Data of 13c………………………………………………… SI-8
Synthesis and Characteristic Data of 13d………………………………………………… SI-9
Synthesis and Characteristic Data of 13e………………………………………………… SI-9
Synthesis and Characteristic Data of 13f………………………………………………… SI-9
Synthesis and Characteristic Data of 13g………………………………………………… SI-10
Synthesis and Characteristic Data of 13h……………………………………………… SI-10
Synthesis and Characteristic Data of 13i……………………………………………… SI-11
Synthesis and Characteristic Data of 14a……………………………………………… SI-11
Synthesis and Characteristic Data of 14b……………………………………………… SI-12
Synthesis and Characteristic Data of 14c……………………………………………… SI-12
Synthesis and Characteristic Data of 14d……………………………………………… SI-13
Synthesis and Characteristic Data of 14e……………………………………………… SI-13
Synthesis and Characteristic Data of 14f……………………………………………… SI-13
Synthesis and Characteristic Data of 14g……………………………………………… SI-14
Synthesis and Characteristic Data of 14h……………………………………………… SI-14
Synthesis and Characteristic Data of 14i .................................................. SI-15
Synthesis and Characteristic Data of 16a .................................................. SI-15
Synthesis and Characteristic Data of 16f .................................................. SI-16
Synthesis and Characteristic Data of 16g .................................................. SI-16
Synthesis and Characteristic Data of 16h .................................................. SI-17
Synthesis and Characteristic Data of 16i .................................................. SI-17
Synthesis and Characteristic Data of 17 .................................................. SI-18
Synthesis and Characteristic Data of 19 .................................................. SI-18
References .......................................................................................... SI-19
NMR spectra of 2a ................................................................................ SI-20
NMR spectra of 2b ................................................................................ SI-21
NMR spectra of 2c ................................................................................ SI-22
NMR spectra of 2d ................................................................................ SI-23
NMR spectra of 2e ................................................................................ SI-24
NMR spectra of 2f ................................................................................ SI-25
NMR spectra of 2g ................................................................................ SI-26
NMR spectra of 2h ................................................................................ SI-27
NMR spectra of 2i ................................................................................ SI-28
NMR spectra of 3a ................................................................................ SI-29
NMR spectra of 3b ................................................................................ SI-30
NMR spectra of 3c ................................................................................ SI-31
NMR spectra of 3d ................................................................................ SI-32
NMR spectra of 3e ................................................................................ SI-33
NMR spectra of 3f ................................................................................ SI-34
NMR spectra of 3g ................................................................................ SI-35
NMR spectra of 3h ................................................................................ SI-36
NMR spectra of 3i ................................................................................ SI-37
NMR spectra of 4a ................................................................................ SI-38
NMR spectra of 4b ................................................................................ SI-39
NMR spectra of 4c ................................................................................ SI-40
NMR spectra of 4h ................................................................................ SI-41
NMR spectra of 4i ................................................................................ SI-42
NMR spectra of 5 .................................................................................. SI-43
NMR spectra of 6 .................................................................................. SI-44
NMR spectra of 9a ................................................................................ SI-45
NMR spectra of 9b ................................................................................ SI-46
NMR spectra of 9c ................................................................................ SI-47
6-Aminobenzo[c][1,2]oxaborol-1(3H)-ol (6)

To a pre-cooled fuming HNO₃ (50 mL) were added benzo[c][1,2]oxaborol-1(3H)-ol (13.39 g, 99.97 mmol) as solid in portions with the aid of -30 °C cooler. After the completion of addition, the reaction mixture were stirred for 1 h to give yellow slurry, quenched by the addition of crushed ice at the same temperature, and warmed to r.t. slowly. The final yellow suspension was filtrated, washed to pH = 6-7 with water, dried to give 6-nitrobenzo[c][1,2]oxaborol-1(3H)-ol (13.21 g, 74%) as a light yellow solid; ¹H NMR (400 MHz, DMSO-d₆): δ 9.59 (br s, 1H), 8.57 (s, 1H), 8.32 (dd, J = 8.3, 1.9 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 5.12 (s, 2H); ¹³C NMR (101 MHz, DMSO-d₆): δ 160.5, 147.1, 125.5, 125.4, 122.9, 70.0; m/z (ESI) 223.03 (24), 224.02 (100, [M+HCOO]-), 225.02 (14), 237.02 (12), 238.02 (45, [M+CH₃COO]-), 239.02 (5).

To a yellow suspension of 6-nitrobenzo[c][1,2]oxaborol-1(3H)-ol (5.37 g, 30.01 mmol) in 10% (V/V) AcOH/THF (160 mL), which had been evacuated using nitrogen, were added 10% Pd/C (0.53 g) followed by stirring at r.t. with continuously bubbled hydrogen under atmospheric pressure for 24 h. After removing Pd/C by filtration through celite, the filtrate were concentrated to dryness in vacuo, resolved in EtOAc (50 mL), and treated with 1 M aq LiOH (150 mL) at r.t. for 30 min. The EtOAc layer were separated out, and washed with 1 M aq LiOH (3×10 mL). The alkaline water layer were combined, acidized to pH = 6-7 with 1M aq HCl, and extracted with EtOAc (5×10 mL). The extracts were combined, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (1:1 to 0:1 PE/EtOAc) to give the title compound 6[1] (3.18 g, 71%) as a white solid; ¹H NMR (400 MHz, acetone-d₆): δ 7.81 (br s, 1H), 7.08 (d, J = 8.1 Hz, 1H), 7.00 (s, 1H), 6.82 (dd, J = 8.1, 1.6 Hz, 1H), 4.87 (s, 2H), 4.55 (br s, 2H); ¹³C NMR (101 MHz, acetone-d₆): δ 148.4, 143.8, 122.4, 119.0, 115.8, 71.1; m/z (ESI⁺) 149.02 (21), 150.01 (100, [M+H]+), 151.02 (9), 163.03 (2), 164.02 (6), 165.01 (1).

(S)-3-phenyl-2-(pyrazine-2-carboxamido)propanoic acid (9a)

To a suspension of pyrazine-2-carboxylic acid (1.24 g, 9.99 mmol), Phe-OMe•HCl (2.16 g, 10.01 mmol) and TBTU (3.51 g, 10.93 mmol) in DCM (20 mL) were added i-Pr₂NEt (4.0 mL, 22.97 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (3:1 to 2:1 PE/EtOAc) to give 8a (2.53 g, 89%) as an off-white syrup; m/z (ESI⁺) 286.06 (82, [M+H]+), 287.08 (14), 308.04 (100, [M+Na]+), 309.05 (17), 593.10 (87, [2M+Na]+), 594.13 (28).
To a solution of 8a (1.44 g, 5.05 mmol) in THF (5 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 2-3 with 1 M aq HCl to give a white suspension, which were filtrated, washed to pH = 6-7 by water, and dried to give the title compound 9a (1.22 g, 89%) as a white solid; IR (KBr): 3388, 3035, 3010, 2918, 2850, 2764, 2499, 1715, 1686, 1592, 1519, 1359, 1281, 1183, 1149, 1055, 1023 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 13.06 (s, 1H), 9.14 (s, 1H), 8.93 – 8.82 (m, 2H), 8.74 (s, 1H), 7.29 – 7.14 (m, 5H), 4.79 – 4.70 (m, 1H), 3.28 – 3.16 (m, 2H); ¹³C NMR (101 MHz, DMSO-d₆) δ 172.4, 162.6, 147.9, 144.1, 143.5, 137.5, 129.1, 128.3, 126.5, 53.5, 36.1; m/z (ESI-) 269.98 (100, [M-H] -), 270.98 (17), 271.97 (2); HRMS-ESI: m/z [M-H] calcd for C₁₄H₁₂N₃O₃: 270.0879, found: 270.0880.

(S)-3-phenyl-2-(picolinamido)propanoic acid (9b)

To a suspension of picolinic acid (0.62 g, 5.04 mmol), Phe-OMe•HCl (1.08 g, 5.00 mmol) and TBTU (1.77 g, 5.51 mmol) in DCM (40 mL) were added i-Pr₂NEt (2.3 mL, 13.20 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (5:1 to 3:1 PE/EtOAc) to give 8b (1.67 g) as an off-white syrup.

To a solution of above 8b (1.67 g) in THF (4 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 5-6 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL, washed with brine (3×5 mL), dried over anhydrous sodium sulfate, and concentrated in vacuo to give the title compound 9b (1.48 g) as a white syrup which was contaminated by 20 mol% TMU based on ¹H NMR analysis; IR (KBr): 3370, 3061, 3029, 2930, 1959, 1880, 1736, 1670, 1590, 1570, 1524, 1465, 1456, 1435, 1412, 1392, 1349, 1294, 1213, 1196, 1095, 998, 749, 701, 621, 555 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.87 (s, 1H), 8.61 – 8.38 (m, 2H), 8.16 (d, J = 7.8 Hz, 1H), 7.83 (dd, J = 7.7 Hz, 1H), 7.42 (dd, J = 6.8, 5.2 Hz, 1H), 7.35 – 7.15 (m, 4H), 5.09 (m, 1H), 3.35 (dd, J = 14.0, 5.5 Hz, 1H), 3.25 (dd, J = 14.0, 6.5 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 174.6, 164.5, 149.2, 148.4, 137.5, 136.1, 129.5, 128.7, 127.2, 126.6, 122.6, 53.6, 37.9; m/z (ESI) 269.16 (100, [M-H]), 270.16 (17), 271.97 (2); HRMS-ESI: m/z [M+H]⁺ calcd for C₁₅H₁₅N₂O₃: 271.1083, found: 271.1082.
(S)-2-(nicotinamido)-3-phenylpropanoic acid (9c)

To a suspension of nicotinic acid (0.63 g, 5.12 mmol), Phe-OMe•HCl (1.10 g, 5.10 mmol) and TBTU (1.80 g, 5.61 mmol) in DCM (40 mL) were added i-Pr₂NEt (2.3 mL, 13.20 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h to give a clear solution. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (1:1 PE/EtOAc) to give 8c (1.80 g) as a clear syrup.

To a solution of above 8c (1.80 g) in THF (10 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed to pH = 6-7 by water, and dried to give the title compound 9c (0.92 g, 67% two steps) as a white solid; IR (KBr): 3333, 3103, 3063, 3025, 2977, 2924, 2848, 2473, 1890, 1732, 1642, 1601, 1540, 1360, 1271, 1225, 1190, 1045, 708 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 12.88 (s, 1H), 8.97 (d, J = 8.1 Hz, 1H), 8.93 (s, 1H), 8.70 (d, J = 4.7 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 7.50 (dd, J = 7.8, 4.9 Hz, 1H), 7.33 (d, J = 7.5 Hz, 2H), 7.28 (dd, J = 7.4 Hz, 2H), 7.19 (dd, J = 7.1 Hz, 1H), 4.71 – 4.57 (m, 1H), 3.22 (dd, J = 13.8, 4.3 Hz, 1H), 3.06 (dd, J = 13.4, 11.1 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆) δ 172.9, 164.9, 152.0, 148.4, 138.0, 135.0, 129.4, 129.0, 128.2, 126.4, 123.4, 54.2, 36.3; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₅H₁₅N₂O₃: 271.1083, found: 271.1085.

(5S,5R)-2-(isonicotinamido)-3-phenylpropanoic acid (9d)

To a suspension of isonicotinic acid (0.61 g, 4.95 mmol), Phe-OMe•HCl (1.09 g, 5.05 mmol) and TBTU (1.78 g, 5.54 mmol) in DCM (20 mL) were added i-Pr₂NEt (2.0 mL, 11.48 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h to give a brown solution. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (2:1 to 1:1 PE/EtOAc) to give 8d (1.52 g) as a light yellow syrup.

To a solution of above 8d (1.52 g) in THF (5 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 5-6 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL, washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo, and recrystallized
from EtOAc to give the title compound 9d (0.76 g, 57% two steps) as a white solid; IR (KBr): 3312, 3083, 3058, 3031, 2943, 2924, 2856, 2515, 1889, 1729, 1650, 1542, 1497, 1411, 1349, 1269, 1222, 1185, 845, 761, 702 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 9.02 (d, J = 8.2 Hz, 1H), 8.71 (d, J = 5.0 Hz, 2H), 7.67 (d, J = 5.0 Hz, 2H), 7.31–7.16 (m, 4H), 7.18 (dd, J = 6.8 Hz, 1H), 4.68–4.58 (m, 1H), 3.21 (dd, J = 13.9, 4.4 Hz, 2H), 3.05 (dd, J = 13.5, 11.0 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆): δ 172.7, 164.8, 150.2, 129.0, 128.2, 126.4, 121.2, 54.2, 36.2; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₅H₁₅N₂O₃: 271.1083, found: 271.1082.

(S)-2-(furan-2-carboxamido)-3-phenylpropanoic acid (9e)

To a suspension of furan-2-carboxylic acid (0.56 g, 5.00 mmol), Phe-OMe•HCl (1.09 g, 5.05 mmol) and TBTU (1.78 g, 5.54 mmol) in DCM (40 mL) were added i-Pr₂NEt (2.3 mL, 13.20 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h to give a brown solution. The final reaction mixture was washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (5:1 PE/EtOAc) to give 8e (1.39 g) as colorless syrup.

To a solution of above 8e (1.39 g) in THF (5 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL, washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo to give the title compound 9e (1.25 g, 96% two steps) as a white foam; IR (KBr): 3407, 3315, 3131, 3061, 3030, 2929, 2607, 1958, 1883, 1735, 1594, 1569, 1524, 1224, 1192, 1142, 1080, 1015, 885, 759, 701 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.43 (d, J = 0.9 Hz, 1H), 7.35–7.26 (m, 3H), 7.23–7.18 (m, 2H), 7.14 (d, J = 3.5 Hz, 1H), 6.78 (d, J = 7.6 Hz, 1H), 6.49 (dd, J = 3.5, 1.7 Hz, 1H), 5.06 (m, 1H), 3.32 (dd, J = 14.1, 5.6 Hz, 1H), 3.24 (dd, J = 14.0, 6.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 174.7, 158.4, 147.2, 144.7, 135.6, 129.5, 128.9, 127.4, 115.5, 112.4, 53.0, 37.7; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₄H₁₁NO₄: 260.0923, found: 260.0925.

(S)-2-(1H-indole-2-carboxamido)-3-phenylpropanoic acid (9f)

To a brown solution of 1H-indole-2-carboxylic acid (1.62 g, 10.05 mmol), Phe-OMe•HCl (2.16 g, 10.01 mmol) and TBTU (3.51 g, 10.93 mmol) in DCM (20 mL) were added i-Pr₂NEt (4.0 mL, 22.97 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the title compound 9f (1.25 g, 65% two steps) as a white solid; IR (KBr): 3407, 3315, 3131, 3061, 3030, 2929, 2607, 1958, 1883, 1735, 1594, 1569, 1524, 1224, 1192, 1142, 1080, 1015, 885, 759, 701 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.43 (d, J = 0.9 Hz, 1H), 7.35–7.26 (m, 3H), 7.23–7.18 (m, 2H), 7.14 (d, J = 3.5 Hz, 1H), 6.78 (d, J = 7.6 Hz, 1H), 6.49 (dd, J = 3.5, 1.7 Hz, 1H), 5.06 (m, 1H), 3.32 (dd, J = 14.1, 5.6 Hz, 1H), 3.24 (dd, J = 14.0, 6.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 174.7, 158.4, 147.2, 144.7, 135.6, 129.5, 128.9, 127.4, 115.5, 112.4, 53.0, 37.7; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₄H₁₁NO₄: 260.0923, found: 260.0925.
the crude product, which was purified by flash chromatography (5:1 to 3:1 PE/EtOAc) to give 8f (2.63 g) as a brown syrup.

To a solution of above 8f (2.63 g) in THF (8 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed to pH = 6-7 by water, recrystallized from EtOAc, and dried to give the title compound 9f (1.85 g, 60% two steps) as a white solid; IR (KBr):3417, 3297, 3089, 3063, 3029, 2926, 1722, 1598, 1546, 1496, 1429, 1344, 1321, 1280, 1258, 1233, 766, 745, 699 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 12.81 (s, 1H), 11.51 (s, 1H), 8.69 (d, J = 8.3 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.33 (d, J = 7.2 Hz, 2H), 7.26 (t, J = 7.5 Hz, 2H), 7.21 – 7.13 (m, 3H), 7.03 (dd, J = 7.2 Hz, 1H), 4.67 (m, 1H), 3.21 (dd, J = 13.8, 4.4 Hz, 1H), 3.08 (dd, J = 13.8, 10.6 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆): δ 173.2, 161.0, 138.1, 136.4, 131.1, 129.1, 128.2, 127.0, 126.4, 123.4, 121.6, 119.7, 112.3, 103.2, 53.8, 36.4; HRMS-ESI: m/z [M-H]⁻ calcd for C₁₈H₁₅N₂O₃: 307.1083, found: 307.1082.

(S)-3-phenyl-2-(quinoline-2-carboxamido)propanoic acid (9g)

To a suspension of quinoline-2-carboxylic acid (0.86 g, 5.00 mmol), Phe-OMe•HCl (1.08 g, 5.01 mmol) and TBTU (1.76 g, 5.48 mmol) in DCM (40 mL) were added i-Pr₂NEt (2.3 mL, 13.20 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO₃ (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (5:1 PE/EtOAc) to give 8g (1.64 g) as a colorless syrup.

To a solution of above 8g (1.64 g) in THF (5 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed to pH = 6-7 by water, and dried to give the title compound 9g (1.36 g, 85% two steps) as a white solid; IR (KBr):3357, 3342, 3028, 2954, 2921, 1754, 1643, 1561, 1532, 1500, 1454, 1427, 1381, 1343, 1328, 1272, 1226, 1210, 846, 823, 796, 778, 750, 735, 714, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.89 (d, J = 8.2 Hz, 1H), 8.58 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 2H), 8.09 (d, J = 8.2 Hz, 1H), 7.89 (dd, J = 7.6 Hz, 1H), 7.74 (dd, J = 7.5 Hz, 1H), 7.32 – 7.24 (m, 4H), 7.24 – 7.17 (m, 1H), 4.82 (m, 1H), 3.29 (d, J = 6.7 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃): δ 172.5, 163.6, 149.3, 145.9, 138.1, 137.3, 130.7, 129.2, 128.9,
128.3, 128.2, 128.1, 126.6, 118.4, 53.4, 36.4; HRMS-ESI: \( m/z \) \([M+H]^+ \) calcd for \( \text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_3 \): 321.1239, found: 321.1238.

**(S)-2-benzamido-3-phenylpropanoic acid (9h)**

To a white suspension of benzoic acid (0.62 g, 5.08 mmol), Phe-OMe•HCl (1.10 g, 5.10 mmol) and TBTU (1.79 g, 5.57 mmol) in DCM (40 mL) were added \( \text{t-Bu}_{2}\text{NEt} \) (2.3 mL, 13.20 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO\(_3\) (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated *in vacuo* to give \( \text{8h} \) (2.03 g) as a colorless syrup.

To a solution of above \( \text{8h} \) (2.03 g) in THF (5 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, and concentrated *in vacuo* to give the title compound \( \text{9h} \) (1.09 g, 80% two steps) as a white syrup which were solidified during handling at r.t.; IR (KBr): 3296, 3061, 3030, 2929, 1712, 1646, 1635, 1603, 1579, 1527, 1491, 1455, 1442, 1422, 1391, 1322, 1295, 1269, 1241, 753, 695, 652 cm\(^{-1}\); \( \text{1H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.59 (s, 1H), 7.69 (d, \( J = 7.6 \) Hz, 3H), 7.43 (m, 4H), 7.25 – 7.11 (m, 3H), 6.81 (d, \( J = 6.6 \) Hz, 1H), 5.20 – 5.02 (m, 1H), 3.36 (dd, \( J = 13.6, 5.3 \) Hz, 1H), 3.26 (dd, \( J = 13.8, 5.3 \) Hz, 1H); \( \text{13C} \) NMR (101 MHz, CDCl\(_3\)): \( \delta \) 174.4, 167.8, 136.0, 133.7, 132.0, 129.6, 128.7, 128.7, 127.2, 127.2, 53.8, 37.4; HRMS-ESI: \( m/z \) [M-H] calcd for \( \text{C}_{16}\text{H}_{14}\text{NO}_3 \): 268.0974, found: 268.0973.

**(S)-2-(benzo[d][1,3]dioxole-5-carboxamido)-3-phenylpropanoic acid (9i)**

To a suspension of benzo[d][1,3]dioxole-5-carboxylic acid (0.83 g, 5.00 mmol), Phe-OMe•HCl (1.08 g, 5.01 mmol) and TBTU (1.76 g, 5.48 mmol) in DCM (40 mL) were added \( \text{t-Bu}_{2}\text{NEt} \) (2.3 mL, 13.20 mmol) dropwise with the aid of -15 °C cooler, followed by stirring to r.t. gradually over 4 h. The final reaction mixture were washed with 1 M aq HCl (3×5 mL), sat. aq NaHCO\(_3\) (3×5 mL) and brine (3×5 mL) in turn, dried over anhydrous sodium sulfate, and the solvent evaporated *in vacuo* to give the crude product, which was purified by flash chromatography (5:1 PE/EtOAc) to give \( \text{8i} \) (1.29 g) as a white solid.

To a solution of above \( \text{8i} \) (1.29 g) in THF (5 mL) were added 1 M aq LiOH (6 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, and concentrated *in vacuo* to give \( \text{9i} \) (1.09 g, 80% two steps) as a white syrup which were solidified during handling at r.t.; IR (KBr): 3296, 3061, 3030, 2929, 1712, 1646, 1635, 1603, 1579, 1527, 1491, 1455, 1442, 1422, 1391, 1322, 1295, 1269, 1241, 753, 695, 652 cm\(^{-1}\); \( \text{1H} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.61 (s, 1H), 7.74 (d, \( J = 7.6 \) Hz, 3H), 7.43 (m, 4H), 7.25 – 7.11 (m, 3H), 6.81 (d, \( J = 6.6 \) Hz, 1H), 5.20 – 5.02 (m, 1H), 3.36 (dd, \( J = 13.6, 5.3 \) Hz, 1H), 3.26 (dd, \( J = 13.8, 5.3 \) Hz, 1H); \( \text{13C} \) NMR (101 MHz, CDCl\(_3\)): \( \delta \) 174.4, 167.8, 136.0, 133.7, 132.0, 129.6, 128.7, 128.7, 127.2, 127.2, 53.8, 37.4; HRMS-ESI: \( m/z \) [M-H] calcd for \( \text{C}_{16}\text{H}_{14}\text{NO}_3 \): 268.0974, found: 268.0973.
mL), dried over anhydrous sodium sulfate, concentrated in vacuo, and recrystallized from EtOAc to give the title compound 9i (0.87 g, 56% two steps) as a white solid; IR (KBr): 3369, 3202, 3062, 3027, 2954, 2937, 1950, 1739, 1684, 1651, 1605, 1568, 1533, 1506, 1486, 1447, 1399, 1353, 1252, 1218, 1184, 1128, 1111, 1035, 705, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.53 (d, ²J = 7.8 Hz, 1H), 7.32 (m, 6H), 7.18 (dd, ²J = 7.0 Hz, 1H), 6.97 (d, ²J = 8.1 Hz, 1H), 6.08 (d, ²J = 1.3 Hz, 2H), 4.71 – 4.51 (m, 1H), 3.24 – 3.13 (m, 1H), 3.13 – 2.98 (m, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 173.3, 165.4, 149.8, 147.2, 138.2, 129.0, 128.2, 127.8, 126.3, 122.4, 107.8, 107.4, 101.7, 54.3, 36.3; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₇H₁₆NO₅: 314.1028, found: 314.1029.

(S)-methyl 2-isothiocyanato-3-phenylpropanoate (10)

To a white suspension of Phe-OMe•HCl (11.15 g, 51.70 mmol) in DCM (100 mL) were added TEA (28.8 mL, 206.63 mmol) slowly and CS₂ (6.3 mL, 104.31 mmol) dropwise in turn with the aid of -5 °C cooler followed by stirring to r.t. gradually over 2 h to give a yellow suspension. Then, the reaction mixture was re-cooled by -5 °C and added TsCl (10.81 g, 56.70 mmol) in portions as solid followed by stirring to r.t. gradually over 10 h to give a brown suspension, which was diluted by THF (150 mL), removed the solid by filtration and concentrated in vacuo. The crude product was purified by flash chromatography (1:0 to 10:1 PE/EtOAc) to give 10[²] (9.32 g, 81%) as a light yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.27 (m, 3H), 7.22 (d, ²J = 7.1 Hz, 2H), 4.48 (dd, ²J = 8.3, 4.8 Hz, 1H), 3.79 (s, 3H), 3.25 (dd, ²J = 13.8, 8.4 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 168.4, 135.1, 129.3, 128.9, 127.9, 60.8, 53.2, 39.8.

(S)-methyl 3-phenyl-2-((5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13a)

To a suspension of pyrazine-2-carbohydrazide (0.28 g, 2.03 mmol) in THF (3 mL) were added 10 (0.46 g, 2.09 mmol) slowly at r.t. followed by stirring for 12 h to give a yellow clear solution, which were diluted by THF (25 mL) followed by the addition of TsCl (0.85 g, 4.46 mmol) and Py (0.63 mL, 7.79 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (20 mL), washed with brine (3 x 5 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (6:1 to 0:1 PE/EtOAc) to give 13a (0.44 g, 67%) as a white solid; IR (KBr): 3345, 3061, 3034, 2951, 2915, 2848, 1742, 1610, 1566, 1521, 1493, 1453, 1436, 1418, 1217, 1167, 1041, 1016, 737, 699 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.34 (s, 1H), 8.64 (d, ²J = 3.5 Hz, 2H), 7.33 – 7.22 (m, 3H), 7.14 (d, ²J = 7.2 Hz, 2H), 5.68 (br s, 1H), 4.86 (br d, ²J = 2.7 Hz, 1H), 3.79 (s, 3H), 3.37 (dd, ²J = 14.0, 5.4 Hz,
1H), 3.26 (dd, J = 14.0, 5.6 Hz, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.2, 163.0, 157.0, 145.4, 144.2, 143.4, 139.8, 135.0, 129.4, 128.8, 127.5, 56.8, 52.8, 37.6; HRMS-ESI: \(m/z\) [M+H]\(^{+}\) calcd for C\(_{16}\)H\(_{16}\)N\(_{5}\)O\(_{3}\): 326.1253, found: 326.1249.

(S)-methyl 3-phenyl-2-((5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13b)

To a suspension of picolinohydrazide (0.69 g, 5.03 mmol) in THF (3 mL) were added 10 (1.32 g, 6.00 mmol) slowly at r.t. followed by stirring for 12 h to give a yellow clear solution, which were diluted by THF (25 mL) followed by the addition of TsCl (1.45 g, 7.61 mmol) and Py (1 mL, 12.36 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (5:1 to 0:1 PE/EtOAc) to give 13b (1.32 g, 81%) as a white solid; IR (KBr):3235, 3054, 3005, 2951, 1743, 1612, 1562, 1497, 1465, 1440, 789, 741, 699, 687 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.68 (d, \(J = 4.4\) Hz, 1H), 8.12 (d, \(J = 8.0\) Hz, 1H), 7.82 (dd, \(J = 7.8, 1.7\) Hz, 1H), 7.38 (ddd, \(J = 7.6, 4.9, 1.0\) Hz, 1H), 7.30 (dd, \(J = 11.3, 4.8\) Hz, 2H), 7.27–7.22 (m, 1H), 7.17–7.10 (m, 2H), 5.45 (d, \(J = 7.9\) Hz, 1H), 4.85 (m, 1H), 3.77 (s, 3H), 3.25 (dd, \(J = 14.0, 5.8\) Hz, 1H), 3.25 (dd, \(J = 14.0, 5.8\) Hz, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 171.2, 163.0, 157.0, 145.4, 144.2, 143.4, 139.8, 135.0, 129.4, 128.8, 127.5, 56.8, 52.8, 37.6; HRMS-ESI: \(m/z\) [M+H]\(^{+}\) calcd for C\(_{17}\)H\(_{17}\)N\(_{4}\)O\(_{3}\): 325.1301, found: 325.1301.

(S)-methyl 3-phenyl-2-((5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13c)

To a suspension of nicotinohydrazide (0.68 g, 4.96 mmol) in THF (3 mL) were added 10 (1.24 g, 5.60 mmol) slowly at r.t. followed by stirring for 12 h to give a yellow clear solution, which were diluted by THF (25 mL) followed by the addition of TsCl (1.43 g, 7.50 mmol) and Py (1 mL, 12.36 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (1:1 PE/EtOAc) to give 13c (1.08 g, 67%) as an off-white solid; IR (KBr):3446, 3222, 3064, 3027, 2951, 1748, 1632, 1604, 1576, 1557, 1541, 1497, 1455, 1210, 1177, 1150, 738, 702 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.12 (d, \(J = 1.6\) Hz, 1H), 8.64 (dd, \(J = 4.8, 1.3\) Hz, 1H), 8.24 (ddd, \(J = 8.0, 1.8\) Hz, 1H), 7.41 (dd, \(J = 8.0, 4.9\) Hz, 1H), 7.34–7.27 (m, 2H), 7.26–7.22 (m, 1H), 7.18–7.12 (m, 2H), 5.90 (br d, \(J = 6.3\) Hz, 1H), 4.83 (d, \(J = 5.3\) Hz, 1H), 3.80 (s, 3H), 3.37 (dd, \(J = 14.0, 5.5\) Hz, 1H), 3.25 (dd, \(J = 14.0, 5.8\) Hz, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.6,
162.6, 157.3, 151.2, 146.7, 135.4, 133.5, 129.5, 128.9, 127.5, 123.9, 121.0, 57.1, 52.8, 37.9; HRMS-ESI: m/z [M+H]^+ calcd for C\textsubscript{17}H\textsubscript{17}N\textsubscript{4}O\textsubscript{3}: 325.1301, found: 325.1299.

(S)-methyl 3-phenyl-2-((5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13d)

To a suspension of isonicotinohydrazide (0.77 g, 5.61 mmol) in THF (3 mL) were added 10 (1.32 g, 5.97 mmol) slowly at r.t. followed by stirring for 12 h to give a white slurry, which were diluted by THF (25 mL) followed by the addition of TsCl (1.43 g, 7.50 mmol) and Py (1 mL, 12.36 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (1:1 PE/EtOAc) to give 13d (1.34 g, 74%) as a yellow syrup; IR (KBr): 3214, 3030, 2957, 2925, 2854, 1747, 1618, 1573, 1543, 1496, 1455, 1416, 1376, 1347, 1261, 1218, 1128, 1080, 1059, 1031, 999, 961, 828, 801, 741, 701; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.72 (d, \(J= 2.8\) Hz, 2H), 7.72 (d, \(J= 4.8\) Hz, 2H), 7.36 – 7.21 (m, 3H), 7.16 (d, \(J= 7.2\) Hz, 2H), 5.86 (br s, 1H), 4.87 – 4.76 (m, 1H), 3.80 (s, 3H), 3.37 (dd, \(J= 14.1, 5.3\) Hz, 1H), 3.23 (dd, \(J= 14.0, 6.0\) Hz, 1H); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 171.5, 162.8, 157.5, 150.4, 135.2, 131.4, 129.3, 128.8, 127.4, 119.4, 57.0, 52.8, 37.8; m/z (ESI\textsuperscript{+}) 325.10 (100, [M+H]\(^+\)), 326.09 (35), 327.11 (5), 347.03 (36, [M+Na]\(^+\)), 348.08 (7); HRMS-ESI: m/z [M+H]\(^+\) calcd for C\textsubscript{17}H\textsubscript{17}N\textsubscript{4}O\textsubscript{3}: 325.1301, found: 325.1299.

(S)-methyl 2-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoate (13e)

To a clear solution of furan-2-carbohydrazide (0.76 g, 6.03 mmol) in THF (4 mL) were added 10 (1.46 g, 6.60 mmol) slowly at r.t. followed by stirring for 12 h to give a yellow clear solution, which were diluted by THF (25 mL) followed by the addition of TsCl (1.71 g, 8.97 mmol) and Py (1.2 mL, 14.84 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (3:1 to 2:3 PE/EtOAc) and recrystallized from EtOAc/i-Pr\textsubscript{2}O (1:2) to give 13e (1.12 g, 59%) as a white solid; IR (KBr): 3226, 3031, 2952, 2848, 1755, 1630, 1608, 1549, 1498, 1485, 1456, 1442, 1276, 1220, 1198, 1159, 1138, 1058, 755, 732, 698 cm\(^{-1}\); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.56 (d, \(J= 1.2\) Hz, 1H), 7.36 – 7.21 (m, 3H), 7.13 (d, \(J= 6.8\) Hz, 2H), 6.94 (d, \(J= 3.4\) Hz, 1H), 6.53 (dd, \(J= 3.2, 1.6\) Hz, 1H), 5.39 (br s, 1H), 4.79 (br s, 1H), 3.78 (s, 3H), 3.35 (dd, \(J= 14.0, 5.3\) Hz, 1H), 3.22 (dd, \(J= 14.0, 5.5\) Hz, 1H); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}): \(\delta\) 171.6, 161.6, 152.8, 144.9, 139.7, 135.3, 129.5, 128.9, 127.5, 112.2, 112.0, 57.0, 52.8, 37.8; HRMS-ESI: m/z [M+H]\(^+\) calcd for C\textsubscript{16}H\textsubscript{16}N\textsubscript{3}O\textsubscript{3}: 314.1141, found: 314.1140.
(S)-methyl 2-((5-(1H-indol-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoate (13f)

To a suspension of 1H-indole-2-carbohydrazide (0.87 g, 4.97 mmol) in THF (4 mL) were added 10 (1.22 g, 5.51 mmol) slowly at r.t. followed by stirring for 12 h, which were diluted by THF (25 mL) followed by the addition of TsCl (1.42 g, 7.45 mmol) and Py (1 mL, 12.36 mmol) in turn at r.t. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (4:1 to 2:1 PE/EtOAc) and recrystallized from EtOAc to give 13f (1.57 g, 87%) as a white solid; IR (KBr): 3284, 3169, 3060, 2954, 2921, 2845, 1730, 1644, 1604, 1574, 1539, 1489, 1434, 1400, 1346, 1303, 1269, 1195, 741, 701 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 10.44 (s, 1H), 7.68 (d, \(J = 8.3\) Hz, 1H), 7.64 (d, \(J = 8.0\) Hz, 1H), 7.35 – 7.24 (m, 4H), 7.22 – 7.16 (m, 2H), 7.13 (dd, \(J = 7.5\) Hz, 1H), 6.96 (d, \(J = 1.3\) Hz, 1H), 5.64 (d, \(J = 7.9\) Hz, 1H), 4.82 (m, 1H), 3.80 (s, 3H), 3.39 (dd, \(J = 14.0, 5.5\) Hz, 1H), 3.27 (dd, \(J = 14.0, 6.0\) Hz, 1H); \(^1\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 171.8, 161.9, 155.1, 137.8, 135.4, 129.5, 128.9, 127.8, 127.6, 124.5, 121.6, 121.6, 120.7, 112.4, 104.6, 57.3, 52.9, 37.9; HRMS-ESI: \(m/z\) [M+H]\(^+\) calcd for C\(_{20}\)H\(_{19}\)N\(_4\)O\(_3\): 363.1457, found: 363.1454.

(S)-methyl 3-phenyl-2-((5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13g)

To a white suspension of quinoline-2-carbohydrazide (0.94 g, 5.02 mmol) in THF (6 mL) were added 10 (1.21 g, 5.47 mmol) slowly at r.t. followed by stirring for 12 h to give a clear brown solution, which were diluted by THF (25 mL) followed by the addition of TsCl (1.41 g, 7.40 mmol) and Py (1 mL, 12.36 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (5:1 to 2:3 PE/EtOAc) and recrystallized from EtOAc to give 13g (1.64 g, 87%) as a white solid; IR (KBr): 3230, 3031, 2951, 2845, 1730, 1644, 1604, 1574, 1379, 1217, 1139, 1126, 1070, 833, 765, 698 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.30 – 8.23 (m, 2H), 7.61 (t, \(J = 7.9\) Hz, 1H), 7.34 – 7.27 (m, 3H), 7.18 – 7.12 (m, 2H), 5.57 (d, \(J = 7.8\) Hz, 1H), 4.90 (m, 1H), 3.79 (s, 3H), 3.39 (dd, \(J = 14.0, 5.5\) Hz, 1H), 3.28 (dd, \(J = 14.0, 5.4\) Hz, 1H); \(^1\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 171.5, 163.2, 159.4, 147.8, 143.8, 137.5, 135.2, 130.7, 129.9, 129.6, 129.0, 128.6, 128.1, 128.0, 127.7, 119.3, 57.0, 52.9, 37.8; HRMS-ESI: \(m/z\) [M+H]\(^+\) calcd for C\(_{21}\)H\(_{19}\)N\(_4\)O\(_3\): 375.1457, found: 375.1456.

(S)-methyl 3-phenyl-2-((5-(phenyl-1,3,4-oxadiazol-2-yl)amino)propanoate (13h)
To a brown suspension of benzoylhydrazide (0.86 g, 6.32 mmol) in THF (4 mL) were added 10 (1.54 g, 6.96 mmol) slowly at r.t. followed by stirring for 12 h to give a clear brown solution, which were diluted by THF (25 mL) followed by the addition of TsCl (1.81 g, 9.49 mmol) and Py (1.3 mL, 16.07 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (3:1 to 1:1 PE/EtOAc) and recrystallized from EtOAc/i-Pr2O (1:1) to give 13h (0.95 g, 46%) as a white solid; IR (KBr): 3245, 3056, 2950, 2915, 2848, 1755, 1620, 1588, 1560, 1538, 1499, 1487, 1449, 775, 746, 732, 694 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.92–7.84 (m, 2H), 7.49–7.40 (m, 3H), 7.34–7.27 (m, 2H), 7.26–7.22 (m, 1H), 7.19–7.12 (m, 2H), 5.44 (br s, 1H), 4.80 (dd, J = 5.4 Hz, 1H), 3.78 (s, 3H), 3.37 (dd, J = 14.0, 5.5 Hz, 1H), 3.23 (dd, J = 14.0, 5.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 171.8, 162.2, 159.7, 135.4, 130.9, 129.5, 129.0, 128.8, 127.5, 126.1, 124.3, 57.0, 52.8, 37.9; HRMS-ESI: m/z [M+H]+ calcd for C₁₈H₁₈N₃O₃: 324.1348, found: 324.1349.

(S)-methyl 2-((5-(benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenyl propanoate (13i)

To a white suspension of benzo[d][1,3]dioxole-5-carbohydrazide (0.90 g, 5.00 mmol) in THF (4 mL) were added 10 (1.22 g, 5.51 mmol) slowly at r.t. followed by stirring for 12 h to give a clear brown solution, which were diluted by THF (25 mL) followed by the addition of TsCl (1.40 g, 7.34 mmol) and Py (1 mL, 12.36 mmol) in turn at r.t.. After being stirred for 24 h at r.t., the final reaction mixture were diluted with EtOAc (50 mL), washed with brine (3×10 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was recrystallized from EtOAc to give 13i (1.18 g, 64%) as a white solid; IR (KBr): 3446, 3210, 3034, 2948, 2903, 2859, 2786, 1753, 1740, 1633, 1606, 1576, 1504, 1488, 1455, 1435, 1278, 1264, 1230, 1034, 741, 703, 683 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.42–7.21 (m, 5H), 7.18–7.13 (m, 2H), 6.85 (d, J = 8.1 Hz, 1H), 6.02 (s, 2H), 5.41 (br s, 1H), 4.77 (dd, J = 5.5 Hz, 1H), 3.78 (s, 3H), 3.35 (dd, J = 14.0, 5.5 Hz, 1H), 3.22 (dd, J = 14.0, 5.8 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 171.8, 161.9, 159.5, 150.0, 148.3, 135.4, 129.5, 128.8, 127.5, 126.1, 124.3, 57.0, 52.8, 37.9; HRMS-ESI: m/z [M+H]+ calcd for C₁₉H₁₈N₃O₅: 368.1246, found: 368.1247.

(S)-3-phenyl-2-((5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14a)

To a suspension of 13a (0.44 g, 1.35 mmol) in THF (4 mL) were added 1 M aq LiOH (2 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h to give a red brown solution. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH =
6-7 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water, and dried to give the title compound 14a (0.38 g, 90%) as a white solid; IR (KBr): 3194, 3082, 3028, 2971, 2933, 2848, 2751, 1734, 1635, 1580, 1514, 1493, 1453, 1423, 1341, 1262, 1245, 1219, 755, 742, 701 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 13.08 (s, 1H), 9.15 (d, \(J = 1.0\) Hz, 1H), 8.78 – 8.69 (m, 2H), 8.63 (d, \(J = 8.8\) Hz, 1H), 7.38 – 7.15 (m, 5H), 4.38 (m, 1H), 3.23 (dd, \(J = 13.9, 4.2\) Hz, 1H), 2.99 (dd, \(J = 13.9, 10.5\) Hz, 1H); \(^{13}\)C NMR (101 MHz, DMSO-d\(_6\)): \(\delta\) 172.7, 164.0, 156.0, 145.6, 144.6, 142.4, 139.4, 137.5, 129.2, 128.3, 126.6, 57.5, 36.7; HRMS-ESI: m/z [M+H\(^+\)] calcd for C\(_{15}\)H\(_{14}\)N\(_5\)O\(_3\): 312.1097, found: 312.1094.

\((S)-3\)-phenyl-2-((5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14b)

To a suspension of 13b (0.33 g, 1.02 mmol) in THF (3 mL) were added 1 M aq LiOH (1.2 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo, and triturated in \(i\)-Pr\(_2\)O to give the title compound 14b (0.29 g, 92%) as a white solid; IR (KBr): 3294, 3212, 3062, 3027, 2926, 2522, 1895, 1727, 1660, 1627, 1605, 1599, 1575, 1497, 1464, 1364, 1340, 1274, 1229, 1198, 788, 742, 701 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 13.02 (br s, 1H), 8.67 (d, \(J = 4.7\) Hz, 1H), 8.46 (d, \(J = 8.8\) Hz, 1H), 8.04 – 7.90 (m, 2H), 7.56 – 7.45 (m, 1H), 7.38 – 7.16 (m, 5H), 4.36 (m, 1H), 3.23 (dd, \(J = 13.9, 4.2\) Hz, 1H), 2.99 (dd, \(J = 13.9, 10.5\) Hz, 1H); \(^{13}\)C NMR (101 MHz, DMSO-d\(_6\)): \(\delta\) 172.8, 163.7, 149.9, 143.3, 137.6, 137.5, 129.1, 128.2, 126.5, 125.1, 121.4, 57.4, 36.7; HRMS-ESI: m/z [M+H\(^+\)] calcd for C\(_{16}\)H\(_{15}\)N\(_4\)O\(_3\): 311.1144, found: 311.1146.

\((S)-3\)-phenyl-2-((5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14c)

To a white suspension of 13c (0.69 g, 2.13 mmol) in THF (3 mL) were added 1 M aq LiOH (3 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water to pH = 6-7, and dried to give the title compound 14c (0.56 g, 85%) as a white solid; IR (KBr): 3420, 3024, 2965, 2925, 2850, 1738, 1633, 1605, 1563, 1526, 1495, 1455, 1334, 1317, 1243, 1218, 1199, 1124, 1066, 1026, 736, 721, 700 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \(\delta\) 13.04 (br s, 1H), 8.96 (d, \(J = 1.8\) Hz, 1H), 8.69 (dd, \(J = 4.8, 1.4\) Hz, 1H), 8.43 (d, \(J = 8.8\) Hz, 1H), 8.14 (ddd, \(J = 8.0, 1.8\) Hz, 1H), 7.56 (dd, \(J = 8.9, 4.9\) Hz, 1H), 7.36 – 7.25 (m, 4H), 7.20 (dd, \(J = 7.0\) Hz, 1H), 4.37 (m, 1H), 3.22 (dd, \(J = 14.0, 4.2\) Hz, 1H), 2.98 (dd, \(J = 13.9, 10.5\) Hz, 1H); \(^{13}\)C NMR (101 MHz, DMSO-d\(_6\)): \(\delta\) 172.9, 163.5, 155.9, 151.2, 146.0, 137.6, 132.7, 129.2, 128.3, 126.6, 124.3, 120.5,
(S)-3-phenyl-2-((5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14d)

To a white suspension of 13d (0.78 g, 2.40 mmol) in THF (2 mL) were added 1 M aq LiOH (3.5 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo, and triturated in i-Pr2O/EtOAc to give the title compound 14d (0.41 g, 55%) as a off-white solid; IR (KBr): 3374, 3086, 3062, 3026, 2945, 2453, 1717, 1616, 1574, 1496, 1455, 1419, 1339, 1320, 1291, 1218, 1188, 1131, 1080, 1019, 887, 836, 815, 740, 703, 686 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 13.08 (s, 1H), 8.73 (d, J = 4.9 Hz, 2H), 8.57 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 4.9 Hz, 2H), 7.36 – 7.25 (m, 4H), 7.20 (dd, J = 6.8 Hz, 1H), 4.39 (m, 1H), 3.23 (dd, J = 13.9, 3.9 Hz, 1H), 2.99 (dd, J = 13.5, 10.9 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆): δ 172.7, 163.7, 156.2, 150.7, 137.5, 130.9, 129.1, 128.3, 126.6, 118.9, 57.4, 36.7; m/z (ESI-) 309.00 (100, [M-H]⁻), 310.00 (16), 311.07 (2); HRMS-ESI: m/z [M+H]⁺ calcd for C₁₆H₁₅N₄O₃: 311.1144, found: 311.1148.

(S)-2-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (14e)

To a clear light brown solution of 13e (0.32 g, 1.02 mmol) in THF (4 mL) were added 1 M aq LiOH (1.5 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water to pH = 6-7, and dried to give the title compound 14e (0.27 g, 88%) as a white solid; IR (KBr): 3230, 3029, 2920, 2848, 1739, 1652, 1631, 1606, 1548, 1497, 1456, 1443, 1386, 754, 698 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 7.88 (s, 1H), 7.39 – 7.05 (m, 6H), 6.95 (s, 1H), 6.68 (s, 1H), 3.99 – 3.89 (m, 1H), 3.29 – 3.21 (m, 1H), 2.95 (dd, J = 13.4, 7.9 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆): δ 172.2, 162.8, 150.4, 145.2, 139.6, 139.4, 129.4, 127.8, 125.7, 112.1, 111.1, 59.5, 37.4; m/z (ESI) 297.85 (100, [M-H⁻]), 298.89 (13), 299.93 (2); HRMS-ESI: m/z [M+H]⁺ calcd for C₁₅H₁₄N₃O₄: 300.0984, found: 300.0981.

(S)-2-((5-(1H-indol-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (14f)

To a clear solution of 13f (0.54 g, 1.49 mmol) in THF (4 mL) were added 1 M aq LiOH (1.5 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with...
EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water to pH = 6-7, and dried to give the title compound 14f (0.47 g, 91%) as a white solid; IR (KBr): 3212, 3128, 3083, 3062, 3029, 2928, 2495, 1697, 1649, 1608, 1577, 1532, 1497, 1455, 1434, 1407, 1345, 1305, 1278, 1259, 1200, 1072, 806, 740, 699 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 13.05 (s, 1H), 11.97 (s, 1H), 8.36 (d, J = 8.9 Hz, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.2 Hz, 1H), 7.37 – 7.16 (m, 6H), 7.06 (dd, J = 7.5 Hz, 1H), 6.90 (s, 1H), 4.35 (m, 1H), 3.23 (dd, J = 13.9, 3.9 Hz, 1H), 3.00 (dd, J = 13.7, 10.7 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆): δ 173.0, 162.7, 153.4, 137.7, 137.4, 129.1, 128.3, 127.3, 126.5, 123.5, 121.9, 121.0, 120.0, 112.0, 102.5, 57.6, 36.7; HRMS-ESI: m/z [M+H]^+ calcd for C₁₉H₁₇N₄O₃: 349.1301, found: 349.1298.

**((S)-3-phenyl-2-((5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14g))**

To a clear solution of 13g (0.57 g, 1.52 mmol) in THF (2 mL) were added 1 M aq LiOH (2.0 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water to pH = 6-7, and dried to give the title compound 14g (0.43 g, 79%) as a white solid; IR (KBr): 3446, 3243, 3057, 2929, 1725, 1611, 1570, 1555, 1505, 1456, 1433, 1377, 137.4, 129.1, 128.3, 127.3, 126.5, 123.5, 121.9, 121.0, 120.0, 112.0, 102.5, 57.6, 36.7; HRMS-ESI: m/z [M+H]^+ calcd for C₂₀H₁₇N₄O₃: 361.1301, found: 361.1298.

**((S)-3-phenyl-2-((5-phenyl-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14h))**

To a clear solution of 13h (0.32 g, 0.99 mmol) in THF (2 mL) were added 1 M aq LiOH (1.2 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water to pH = 6-7, and dried to give the title compound 14h (0.29 g, 95%) as an
off-white solid; IR (KBr): 3394, 3224, 3060, 3030, 2965, 2934, 1766, 1725, 1667, 1634, 1607, 1588, 1563, 1496, 1449, 1269, 1242, 1216, 1201, 1058, 1025, 772, 758, 735, 703, 691 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.44 (s, 1H), 7.63 (d, J = 6.9 Hz, 2H), 7.51 – 7.37 (m, 3H), 7.29 (d, J = 7.4 Hz, 2H), 7.21 (dd, J = 7.6 Hz, 2H), 7.04 (dd, J = 7.3 Hz, 1H), 4.65 (dd, J = 8.0, 3.2 Hz, 1H), 3.52 (dd, J = 13.8, 3.9 Hz, 1H), 3.14 (dd, J = 13.7, 8.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 174.8, 162.2, 157.7, 136.9, 131.1, 129.7, 128.9, 127.2, 126.0, 123.4, 58.3, 40.8; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₇H₁₆N₃O₃: 310.1192, found: 310.1188.

(S)-2-((5-(benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (14i)

To a yellow suspension of 13i (0.37 g, 1.00 mmol) in THF (2 mL) were added 1 M aq LiOH (1.2 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white suspension, which were filtrated, washed by water to pH = 6-7, and recrystallized from DCM/i-Pr₂O to give the title compound 14i (0.30 g, 85%) as a white solid; IR (KBr): 3342, 3080, 3026, 2999, 2965, 2845, 2513, 1867, 1722, 1634, 1606, 1580, 1502, 1485, 1455, 1432, 1359, 1348, 1307, 1259, 1249, 1229, 1202, 1031, 741, 700 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ 13.06 (br s, 1H), 8.19 (d, J = 8.8 Hz, 1H), 7.36 – 7.24 (m, 6H), 7.20 (dd, J = 6.8 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 6.12 (s, 2H), 4.33 (m, 1H), 3.21 (dd, J = 13.9, 4.0 Hz, 1H), 2.98 (dd, J = 13.7, 10.6 Hz, 1H); ¹³C NMR (101 MHz, DMSO-d₆): δ 173.0, 162.8, 157.6, 149.3, 148.0, 137.7, 129.1, 128.2, 126.5, 120.0, 117.9, 109.0, 105.1, 101.8, 57.4), 36.8; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₈H₁₆N₃O₅: 354.1090, found: 354.1087.

(S)-2-(methyl(5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (16a)

To a clear solution of 13a (0.16 g, 0.49 mmol) in THF (5mL) were added K₂CO₃ (0.35 g, 2.53 mmol) and dimethyl sulfate (100 μL, 1.05 mmol) in turn at r.t. followed by stirring for 48 h. The inorganic solid were removed by filtration and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (2:1 to 1:1 PE/EtOAc) to give 15a (0.16 g, 96%) as a white syrup.

To a solution of 15a (0.16 g, 0.47 mmol) in THF (2 mL) were added 1 M aq LiOH (2 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo to give the title compound 16a (0.11 g, 72%) as an off-white foam; IR (KBr): 3628, 3506, 3380, 3264, 3224, 3060, 3030, 2965, 2934, 1766, 1725, 1667, 1634, 1607, 1588, 1563, 1496, 1449, 1269, 1242, 1216, 1201, 1058, 1025, 772, 758, 735, 703, 691 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.44 (s, 1H), 7.63 (d, J = 6.9 Hz, 2H), 7.51 – 7.37 (m, 3H), 7.29 (d, J = 7.4 Hz, 2H), 7.21 (dd, J = 7.6 Hz, 2H), 7.04 (dd, J = 7.3 Hz, 1H), 4.65 (dd, J = 8.0, 3.2 Hz, 1H), 3.52 (dd, J = 13.8, 3.9 Hz, 1H), 3.14 (dd, J = 13.7, 8.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 174.8, 162.2, 157.7, 136.9, 131.1, 129.7, 128.9, 127.2, 126.0, 123.4, 58.3, 40.8; HRMS-ESI: m/z [M+H]⁺ calcd for C₁₈H₁₆N₃O₅: 354.1090, found: 354.1087.
2925, 2854, 1793, 1732, 1697, 1621, 1579, 1495, 1452, 1423, 1398, 1277, 1206, 1176, 1137, 1078, 1020, 979, 916, 889, 871, 770, 747, 701 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.43 (s, 1H), 9.33 (s, 1H), 8.79 (s, 1H), 8.53 (s, 1H), 7.38 – 7.16 (m, 5H), 4.35 (dd, J = 5.0 Hz, 1H), 3.32 (dd, J = 14.5, 4.5 Hz, 1H), 3.23 (dd, J = 14.5, 5.5 Hz, 1H), 2.94 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 169.4, 161.5, 153.6, 148.5, 144.9, 143.0, 142.6, 134.4, 129.5, 129.0, 127.7, 61.9, 35.7, 29.4; m/z (ESI -) 324.08 (100, [M-H]-), 325.08 (20), 326.07 (2), 342.08 (38, [M+H₂O-H]-), 343.07 (7), 344.08 (1), 356.09 (17, [M+CH₃OH-H]-), 357.09 (3); HRMS-ESI: m/z [M+H]⁺ calcd for C₁₆H₁₆N₅O₃: 326.1253, found: 326.1250.

(S)-2-(methyl(5-(1-methyl-1H-indol-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (16f)

To a mixture of 13f (0.18 g, 0.50 mmol) in THF (5 mL) were added K₂CO₃ (0.35 g, 2.53 mmol) and dimethyl sulfate (100 μL, 1.05 mmol) in turn at r.t. followed by stirring for 48 h. The inorganic solid were removed by filtration and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (3:1 PE/EtOAc) to give 15f (0.19 g, 98%) as a yellow syrup.

To a solution of 15f (0.19 g, 0.49 mmol) in THF (4 mL) were added 1 M aq LiOH (1 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo to give the title compound 16f (0.17 mg, 92%) as a gray foam. ¹H NMR analysis indicated 16f were contaminated by some inseparable impurities which could be purified in the next step. HRMS-ESI: m/z [M+H]⁺ calcd for C₂₁H₁₉N₄O₃: 375.1457, found: 375.1456.

(S)-2-(methyl(5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (16g)

To a suspension of 13g (0.19 g, 0.51 mmol) in THF (5 mL) were added K₂CO₃ (0.34 g, 2.46 mmol) and dimethyl sulfate (48 μL, 0.51 mmol) in turn at r.t. followed by stirring for 48 h. The inorganic solid were removed by filtration and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (3:1 to 2:1 PE/EtOAc) to give 15g (0.17 g, 86%) as an off-white syrup.

To a solution of 15g (0.17 g, 0.44 mmol) in THF (4 mL) were added 1 M aq LiOH (2 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a yellow suspension, which were filtrated, washed by water to pH = 6-7 to give the title
compound **16g** (0.14 g, 85%) as a yellow solid; IR (KBr): 3338, 3061, 3027, 2960, 2929, 2870, 1791, 1739, 1704, 1622, 1513, 1482, 1455, 1420, 1394, 1256, 1209, 1185, 1139, 778, 750, 702 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.72 (s, 1H), 8.32 (d, \(J = 8.4\) Hz, 1H), 8.21 (d, \(J = 8.4\) Hz, 1H), 8.10 (d, \(J = 8.4\) Hz, 1H), 7.88 (d, \(J = 8.1\) Hz, 1H), 7.78 (dd, \(J = 7.6\) Hz, 1H), 7.65 (dd, \(J = 7.5\) Hz, 1H), 7.39 – 7.21 (m, 5H), 4.37 (dd, \(J = 4.7\) Hz, 1H), 3.35 (dd, \(J = 14.5\), 4.0 Hz, 1H), 3.26 (dd, \(J = 14.4\), 5.5 Hz, 1H), 2.96 (s, 3H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.6, 162.8, 153.8, 147.2, 146.4, 137.7, 134.6, 130.5, 129.9, 129.7, 129.4, 128.9, 128.6, 127.8, 127.6, 119.0, 61.8, 35.8, 29.3; \(m/z\) (ESI) 372.97 (100, [M-H]) –, 373.98 (26), 374.97 (4), 390.98 (49, [M+H\(_2\)O-H]) –, 391.98 (12), 392.98 (2); HRMS-ESI: \(m/z\) [M+H]\(^+\) calcd for C\(_{21}\)H\(_{19}\)N\(_4\)O\(_3\): 375.1457, found: 375.1458.

**((S)-2-(methyl(5-phenyl-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (16h)**

To a mixture of **12h** (0.20 g, 0.62 mmol) in THF (5mL) were added K\(_2\)CO\(_3\) (0.43 g, 3.11 mmol) and dimethyl sulfate (70 \(\mu\)L, 0.74 mmol) in turn at r.t. followed by stirring for 48 h. The inorganic solid were removed by filtration and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (5:1 PE/EtOAc) to give **15h** (0.15 g, 72%) as an off-white syrup.

To a solution of **15h** (0.15 g, 0.44 mmol) in THF (2 mL) were added 1 M aq LiOH (1 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo to give the title compound **16h** (0.11 g, 77%) as a white solid; IR (KBr): 3420, 3255, 3021, 2921, 2533, 1829, 1727, 1629, 1588, 1562, 1494, 1450, 1419, 1364, 1317, 1299, 1273, 1245, 1224, 1197, 1142, 1088, 1061, 1027, 962, 931, 878, 810, 761, 732, 698, 695 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta\) 13.23 (br s, 1H), 7.86 – 7.78 (m, 2H), 7.55 – 7.49 (m, 3H), 7.32 (d, \(J = 7.4\) Hz, 2H), 7.25 (dd, \(J = 7.3\) Hz, 2H), 7.15 (dd, \(J = 7.1\) Hz, 1H), 4.98 (dd, \(J = 11.1\), 4.1 Hz, 1H), 3.40 – 3.33 (m, 1H), 3.27 – 3.19 (m, 1H), 2.99 (s, 3H); \(^13\)C NMR (101 MHz, DMSO-d\(_6\)) \(\delta\) 171.4, 164.1, 158.0, 137.6, 130.6, 129.2, 128.8, 128.3, 126.5, 125.2, 123.9, 62.0, 33.8, 33.1; HRMS-ESI: \(m/z\) [M+H]\(^+\) calcd for C\(_{18}\)H\(_{18}\)N\(_3\)O\(_3\): 324.1348, found: 324.1348.

**((S)-2-((5-(benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)(methyl)amino)-3-phenylpropanoic acid (16i)**

To a mixture of **13i** (0.18 g, 0.49 mmol) in THF (5mL) were added K\(_2\)CO\(_3\) (0.37 g, 2.68 mmol) and dimethyl sulfate (50 \(\mu\)L, 0.53 mmol) in turn at r.t. followed by stirring for 48 h. The inorganic solid were removed by filtration and the solvent
evaporated in vacuo to give the crude product, which was purified by flash chromatography (3:1 PE/EtOAc) to give 15i (0.10 g, 54%) as a colorless syrup.

To a solution of 15i (0.10 g, 0.26 mmol) in THF (2 mL) were added 1 M aq LiOH (1 mL) dropwise with the aid of ice-water bath followed by stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated in vacuo to give the title compound 16i (67.3 mg, 70%) as a white foam; IR (KBr): 3431, 3254, 3028, 2926, 1727, 1674, 1603, 1485, 1442, 1360, 1303, 1260, 1202, 1104, 1037, 1005, 930, 826, 809, 757, 703 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) δ 12.61 (br s, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.43 (s, 1H), 7.23 – 7.08 (m, 5H), 7.05 (d, J = 8.1 Hz, 1H), 6.13 (s, 2H), 4.32 – 4.24 (m, 1H), 2.99 (s, 3H), 2.98 – 2.91 (m, 2H); ¹³C NMR (101 MHz, DMSO-d₆) δ 173.4, 164.8, 157.3, 150.3, 147.3, 137.6, 129.2, 128.0, 126.3, 126.2, 123.0, 108.0, 107.7, 101.8, 54.5, 36.8, 35.4; m/z (ESI⁻) 366.13 (100, [M-H]⁻), 367.13 (21), 368.17 (4); HRMS-ESI: m/z [M+Na⁺] calcd for C₁₉H₁₈N₃O₆: 384.1196, found: 384.1198.

(S)-methyl 2-((3-(1-methoxy-1-oxo-3-phenylpropan-2-yl)thiourea)benzoate (17)

To a colorless clear solution of 16 (0.75 g, 4.96 mmol) in DMF (4 mL) were added 10 (1.22 g, 5.51 mmol) slowly at r.t. followed by stirring for 12 h. The final reaction mixture were diluted with EtOAc (20 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, and the solvent evaporated in vacuo to give the crude product, which was purified by flash chromatography (10:1 to 2:1 PE/EtOAc) and recrystallized from PE/EtOAc (5:1) to give the title compound 17 (1.51 g, 82%) as a white solid; IR (KBr): 3311, 3125, 3032, 3002, 2952, 2855, 1719, 1686, 1606, 1530, 1471, 1454, 1444, 1435, 1340, 1319, 1257, 1217, 1189, 1165, 1151, 1089, 763, 752, 738, 710 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 10.39 (br s, 1H), 8.00 (dd, J = 7.9, 1.5 Hz, 1H), 7.72 (br s, 1H), 7.45 – 7.36 (m, 1H), 7.33 – 7.20 (m, 3H), 7.12 (dd, J = 10.7, 4.4 Hz, 3H), 6.68 (d, J = 7.1 Hz, 1H), 5.44 (d, J = 5.1 Hz, 1H), 3.93 (s, 3H), 3.76 (s, 3H), 3.42 (dd, J = 13.9, 6.1 Hz, 1H), 3.23 (dd, J = 13.9, 5.1 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 179.8, 172.1, 167.7, 139.8, 135.8, 133.9, 131.8, 129.5, 128.8, 127.4, 124.0, 122.3, 119.0, 58.3, 52.7, 52.6, 37.5; HRMS-ESI: m/z [M+Na⁺] calced for C₁₉H₂₀N₂NaO₄S: 395.1041, found: 395.1048.

(S)-2-((4-oxo-4H-benzo[d][1,3]thiazin-2-yl)amino)-3-phenylpropanoic acid (19)

A suspension of 17 (0.56 g, 1.50 mmol) in PPA (17.9 g) were stirred at 80 °C for 12 h. After cooling to r.t., the reaction mixture were quenched by crushed ice carefully, and extracted by EtOAc (3×10 mL). The extracts were combined, washed
by sat. aq NaHCO\textsubscript{3} to pH = 7, dried over anhydrous sodium sulfate, and the solvent evaporated \textit{in vacuo} to give a light brown syrupy mixture of 18 and 19. The above mixture were resolved in THF (4 mL) followed by the addition of 1 M aq LiOH (1.8 mL) dropwise with the aid of ice-water bath and stirring to r.t. over 2 h. The reaction mixture were diluted with water (20 mL) and extracted with EtOAc (3×5 mL). The alkaline water layer were acidized to pH = 3-4 with 1 M aq HCl to give a white emulsion, which were extracted with DCM (3×10 mL), washed with brine (3×5 mL), dried over anhydrous sodium sulfate, concentrated \textit{in vacuo} and recrystallized from EtOAc to give the title compound 19 (0.21 mg, 43%) as a white solid; IR (KBr): 3446, 3269, 3147, 3051, 3024, 2979, 2921, 2899, 2850, 1716, 1662, 1624, 1538, 1487, 1405, 1265, 1254, 1195, 1154, 955, 796, 759, 745, 722, 700, 693 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, DMSO-d\textsubscript{6}): \(\delta\) 12.95 (s, 1H), 12.83 (s, 1H), 7.98 (d, \(J = 7.6 \) Hz, 1H), 7.76 (dd, \(J = 7.5 \) Hz, 1H), 7.43 – 7.27 (m, 2H), 7.26 – 7.02 (m, 5H), 6.81 (dd, \(J = 7.0 \) Hz, 1H), 3.57 (dd, \(J = 13.9, 6.5 \) Hz, 1H), 3.28 (dd, \(J = 14.0, 8.0 \) Hz, 1H); \textsuperscript{13}C NMR (101 MHz, DMSO-d\textsubscript{6}): \(\delta\) 175.9, 170.0, 158.9, 138.8, 137.7, 135.9, 129.3, 128.0, 127.2, 126.3, 124.9, 115.6, 115.5, 60.6, 34.4; HRMS-ESI: \(m/z\) [M+Na]\textsuperscript{+} calcd for C\textsubscript{17}H\textsubscript{14}N\textsubscript{2}NaO\textsubscript{3}S: 349.0623, found: 349.0626.

References


(S)-N-(1-((1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino)-1-oxo-3-phenylpropan-2-yl)pyrazine-2-carboxamide (2a)
(S)-N-(1-((1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino)-1-oxo-3-phenylpropan-2-yl)picolinamide (2b)
$(S)-N-(1-((1\text{-hydroxy}-1,3\text{-dihydrobenzo}[c][1,2]oxaborol-6-y1)amino)-1\text{-oxo-3-phenylpropan-2-yl})\text{nicotinamide}$ (2c)
(S)-N-((1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino)-1-oxo-3-phenylpropan-2-yl)isonicotinamide (2d)
(S)-N-1-((1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino)-1-oxo-3-phenylpropan-2-yl)furan-2-carboxamide (2e)
(S)-N-1-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-ylamino)-1H-indole-2-carboxamide (2f)
(S)-N-[(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino]-1-oxo-3-phenylpropan-2-yl)quinoline-2-carboxamide (2g)
(S)-N-(1-((1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino)-1-oxo-3-phenylpropan-2-yl)benzamide (2h)
(S)-N-(1-((1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)amino)-1-oxo-3-phenylpropan-2-yl)benzo[d][1,3]dioxole-5-carboxamide (2i)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenyl-2-((5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanamide (3a)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenyl-2-((5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanamide (3b)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenyl-2-((5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)amino)propanamide (3c)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenyl-2-((5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)amino)propanamide (3d)
(S)-2-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)amino)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenylpropanamide (3e)
(S)-2-((5-(1H-indol-2-yl)-1,3,4-oxadiazol-2-yl)amino)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenylpropanamide (3f)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenyl-2-((5-phenyl-1,3,4-oxadiazol-2-yl)amino)propanamide (3h)
(S)-2-((5-(benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)amino)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenylpropanamide (3i)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-2-(methyl(5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanamide

(4a)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborolo[6,5-g]-1-methyl-1H-indol-2-yl)-3,4-oxadiazol-2-yl)amino)-3-phenylpropamide (4f)
(S)-N-(1-methoxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-2-(methyl(5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanamide
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-2-(methyl(5-phenyl-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanamide (4h)
(S)-2-((5-(benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)(methyl)amino)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-3-phenyl-propanamide (4i)
(S)-N-(1-hydroxy-1,3-dihydrobenzo[c][1,2]oxaborol-6-yl)-2-((4-oxo-4H-benzo[d][1,3]thiazin-2-yl)amino)-3-phenylpropanamide (5)
6-Aminobenzo[c][1,2]oxaborol-1(3H)-ol (6)
(S)-3-phenyl-2-(pyrazine-2-carboxamido)propanoic acid (9a)
(S)-3-phenyl-2-(picolinamido)propanoic acid (9b)
(S)-2-(nicotinamido)-3-phenylpropanoic acid (9c)
(S)-2-((furan-2-carboxamido))-3-phenylproanoic acid (9e)
(S)-2-(1H-indole-2-carboxamido)-3-phenylpropanoic acid (9f)
(S)-3-phenyl-2-(quinoline-2-carboxamido)propanoic acid (9g)
(S)-2-benzamido-3-phenylproanoic acid (9h)
(S)-2-(benzo[d][1,3]dioxole-5-carboxamido)-3-phenylpropanoic acid (9i)
(S)-methyl 2-isothiocyanato-3-phenylpropanoate (10)
(S)-methyl 3-phenyl-2-((5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13a)
(S)-methyl
3-phenyl-2-((5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate
(13b)
(S)-methyl 3-phenyl-2-((5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13c)
(S)-methyl
3-phenyl-2-((5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate
(13d)
(S)-methyl 2-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoate (13e)
(S)-methyl

2-((5-(1H-indol-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoate (13f)
(S)-methyl 3-phenyl-2-((5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoate (13g)
(S)-methyl 3-phenyl-2-((5-phenyl-1,3,4-oxadiazol-2-yl)amino)propanoate (13h)
(S)-methyl

2-((5-(benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenyl propanoate (13i)
(S)-3-phenyl-2-((5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14a)
(S)-3-phenyl-2-((5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14b)
(S)-3-phenyl-2-((5-(pyridin-3-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14c)
(S)-3-phenyl-2-((5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14d)
(S)-2-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (14e)
(S)-2-(((1H-indol-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (14f)
(S)-3-phenyl-2-((5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl)amino)propanoic acid (14g)
(S)-3-phenyl-2-((5-phenyl-1,3,4-oxadiazol-2-yl)amino)propanoic acid

(14h)
(S)-2-((5-(benzo[\text{d}][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (14i)
(S)-2-(methyl(5-(pyrazin-2-yl)-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropionic acid (16a)
(S)-2-(methyl(5-phenyl-1,3,4-oxadiazol-2-yl)amino)-3-phenylpropanoic acid (16h)
(S)-2-((5-(benzo[\textit{d}][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2-yl)(methyl)amino)-3-phenylpropanoic acid (16i)
(S)-methyl

2-(3-(1-methoxy-1-oxo-3-phenylpropan-2-yl)thioureido)benzoate (17)
(S)-2-((4-oxo-4H-benzo[d][1,3]thiazin-2-yl)amino)-3-phenylpropanoic acid (19)