

Supporting information

PIPECOLIC ACID DERIVATIVES AS SMALL-MOLECULE INHIBITORS OF THE *LEGIONELLA* MIP PROTEIN

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Experimental section

Synthesis of (S)-Ethyl piperidine-2-carboxylate (**S-1**)

(S)-Piperidine-2-carboxylic acid (1 eq) was dissolved in 40 mL anhydrous ethanol and thionyl chloride (3 eq) was added dropwise. The mixture was refluxed for 4 h under stirring. After the reaction had ceased (TLC control) the solvent was removed *in vacuo*. The residue was suspended in 20 mL NaHCO₃ and washed with 4 x 30 mL CHCl₃. The organic layers were dried over anhydrous Na₂SO₄ and the solvent was removed *in vacuo* to yield compound **S-1** as a yellow waxy substance (0.90 g, 90 %). ¹H-NMR (CDCl₃, δ [ppm], *J* [Hz]): 4.15 (q, 2H, ³*J* = 7.1); 3.52 (dd, 1H, ³*J* = 3.5, ³*J* = 9.8); 3.22 (m, 1H); 2.79-2.69 (m, 1H); 2.03-1.95 (m, 1H); 1.92 (s, 1H); 1.77-1.40 (m, 5H); 1.22 (t, 3H, ³*J* = 7.1). ¹³C-NMR (CDCl₃, δ [ppm], *J* [Hz]): 173.2; 60.3; 58.4; 45.5; 28.9; 25.6; 23.8; 13.9. IR [cm⁻¹]: 1046; 1205; 1370; 1456; 1740; 2695; 2906.

Ethyl 1-(3-methyl-2-oxopentanoyl)piperidine-2-carboxylate (**2a**)

After purification by column chromatography (silica gel, petroleum ether (40-60) : ethyl acetate = 70:30) **2a** was obtained as a yellow oil (0.28 g, 20 %). ¹H-NMR (CDCl₃, δ [ppm], *J* [Hz]): 5.41 (dd, 1H, ³*J* = 5.3, ³*J* = 11.8); 4.23-4.11 (m, 2H); 3.86 (d, 1H, ³*J* = 13.5); 3.26-3.17 (m, 1H); 2.73-2.59 (m, 1H); 2.30-2.20 (m, 1H); 1.84-1.52 (m, 4H); 1.50-1.29 (m, 3H); 1.24 (t, 3H, ³*J* = 7.1); 1.13-1.05 (m, 3H); 0.95-0.80 (m, 3H). ¹³C-NMR (CDCl₃, δ [ppm], *J* [Hz]): 216.4; 176.4; 171.5; 60.9; 51.8; 43.3; 36.8; 26.6; 25.5; 21.1; 17.2; 16.7; 14.2; 11.9. IR [cm⁻¹]: 1196; 1235; 1422; 1642; 1734, 2872; 2936. Anal. Calcd. for C₁₄H₂₃NO₄ (MW: 269.34 g/mol): C, 62.43; H, 8.61; N, 5.20. Found: C, 62.33; H, 8.37; N, 5.50.

Ethyl 1-(benzylsulfonyl)piperidine-2-carboxylate (**2b**)

2b was obtained as a yellow oil (1.25 g; 77 %). ¹H-NMR (CDCl₃, δ [ppm], *J* [Hz]): 7.49-7.33 (m, 5H); 4.55-4.47 (m, 1H); 4.27 (s, 2H); 4.24-4.13 (m, 2H); 3.49-3.41 (m, 1H); 3.15 (dt, 1H, ³*J* = 12.4, ³*J* = 3.1); 2.20-2.12 (m, 1H); 1.73-1.52 (m, 3H); 1.51-1.37 (m, 1H); 1.33-1.20 (m, 4H). ¹³C-NMR (CDCl₃, δ [ppm], *J* [Hz]): 171.6; 131.1; 129.5; 128.7; 128.6; 61.5; 58.9; 56.1; 43.6; 28.0; 25.2; 20.5; 14.4. IR [cm⁻¹]: 1148; 1200; 1335; 1455; 1732; 2860; 2940. Anal.

Calcd. for $C_{15}H_{21}NO_4S$ (MW: 311.40 g/mol): C, 57.86; H, 6.80; N, 4.50; S, 10.30. Found: C, 58.17; H, 6.54; N, 4.78; S, 10.36.

(S)-Ethyl 1-(benzylsulfonyl)piperidine-2-carboxylate (S-2b)

S-2b was obtained as a yellow oil (0.63 g; 70 %). 1H -NMR ($CDCl_3$, δ [ppm], J [Hz]): 7.49-7.33 (m, 5H); 4.55-4.47 (m, 1H); 4.27 (s, 2H); 4.24-4.13 (m, 2H); 3.49-3.41 (m, 1H); 3.15 (dt, 1H, $^3J = 12.4$, $^3J = 3.1$); 2.20-2.12 (m, 1H); 1.73-1.52 (m, 3H); 1.51-1.37 (m, 1H); 1.33-1.20 (m, 4H). ^{13}C -NMR ($CDCl_3$, δ [ppm], J [Hz]): 171.6; 131.1; 129.5; 128.7; 128.6; 61.5; 58.9; 56.1; 43.6; 28.0; 25.2; 20.5; 14.4. IR [cm^{-1}]: 1148; 1200; 1335; 1455; 1732; 2860; 2940. Anal. Calcd. for $C_{15}H_{21}NO_4S$ (MW: 311.40 g/mol): C, 57.86; H, 6.80; N, 4.50; S, 10.30. Found: C, 58.17; H, 6.54; N, 4.78; S, 10.36.

Ethyl 1-(phenylsulfonyl)piperidine-2-carboxylate (2c)

The synthesis of compound **2c** was previously described using a different pathway.¹ **2c** was obtained as a yellow oil (1.43 g; 92 %). 1H -NMR ($CDCl_3$, δ [ppm], J [Hz]): 7.82-7.77 (m, 2H); 7.58-7.43 (m, 3H); 4.73 (d, 1H, $^3J = 5.3$); 4.09-3.87 (m, 2H); 3.83-3.76 (m, 1H); 3.23 (dt, 1H, $^3J = 12.4$, $^3J = 3.0$); 2.17-2.08 (m, 1H); 1.82-1.57 (m, 3H); 1.56-1.41 (m, 1H); 1.37-1.20 (m, 1H); 1.13 (t, 3H, $^3J = 7.1$). ^{13}C -NMR ($CDCl_3$, δ [ppm], J [Hz]): 170.6; 140.1; 132.3; 128.8; 127.1; 61.0; 55.0; 42.6; 27.9; 24.7; 20.0; 14.0. IR [cm^{-1}]: 1155; 1181; 1337; 1446; 1733; 2862; 2943. Anal. Calcd. for $C_{14}H_{19}NO_4S$ (MW: 297.37 g/mol): C, 56.55; H, 6.44; N, 4.71; S, 10.78. Found: C, 56.24; H, 6.29; N, 4.65; S, 10.79.

Ethyl 1-((3-nitrophenyl)sulfonyl)piperidine-2-carboxylate (2d)

2d was obtained as a brown solid (1.52 g; 85 %). mp: 94.4 °C. 1H -NMR ($CDCl_3$, δ [ppm], J [Hz]): 8.63-8.59 (m, 1H); 8.43-8.38 (m, 1H); 8.12-8.09 (m, 1H); 7.70 (t, 1H, $^3J = 8.1$); 4.8 (d, 1H, $^3J = 5.4$); 4.09-3.92 (m, 2H); 3.88-3.80 (m, 1H); 3.18 (dt, 1H, $^3J = 12.6$, $^3J = 3.0$); 2.25-2.17 (m, 1H); 1.88-1.66 (m, 3H); 1.64-1.51 (m, 1H); 1.34-1.19 (m, 1H); 1.16 (t, 3H, $^3J = 7.1$). ^{13}C -NMR ($CDCl_3$, δ [ppm], J [Hz]): 170.2; 148.1; 142.1; 132.8; 130.0; 126.8; 122.5; 61.4; 55.5; 42.9; 28.0; 24.9; 20.0; 14.1; IR [cm^{-1}]: 1125; 1156; 1209; 1350; 1527; 1731; 2863;

2958. Anal. Calcd. for $C_{14}H_{18}N_2O_6S$ (MW: 342.37 g/mol): C, 49.11; H, 5.30; N, 8.18; S, 9.37. Found: C, 49.09; H, 5.24; N, 8.01; S, 9.29.

1-(3-Methyl-2-oxopentanoyl)piperidine-2-carboxylic acid (3a)

3a was obtained as a yellow oil (0.17 g, 67 %). $^1\text{H-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 5.45-5.36 (m, 1H); 3.86-3.78 (m, 1H); 3.22-3.12 (m, 1H); 2.72-2.60 (m, 1H); 2.27 (d, 1H, $^3J = 13.4$); 1.86-1.54 (m, 4H); 1.53-1.31 (m, 3H); 1.15-1.04 (m, 3H); 0.88 (t, 3H, $^3J = 7.4$). $^{13}\text{C-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 216.4; 177.6; 175.5; 51.9; 43.5; 37.0; 26.7; 25.4; 20.9; 17.2; 16.6; 11.9. IR [cm^{-1}]: 1091; 1154; 1415; 1654; 1718; 2885; 2941; 3285.

1-(Benzylsulfonyl)piperidine-2-carboxylic acid (3b)²

3b was obtained as a yellow oil (1.05 g, 92 %). $^1\text{H-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 7.49-7.33 (m, 5H); 4.60-4.55 (m, 1H); 4.27 (s, 2H); 3.49-3.41 (m, 1H); 3.15 (dt, 1H, $^3J = 12.4$, $^3J = 3.1$); 2.20-2.12 (m, 1H); 1.73-1.52 (m, 3H); 1.51-1.18 (m, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 176.6; 130.9; 129.1; 128.6; 128.5; 58.9; 55.7; 43.5; 27.5; 24.9; 20.3. IR [cm^{-1}]: 1060; 1118; 1317; 1455; 1728; 2854; 2952; 3192.

(S)-1-(Benzylsulfonyl)piperidine-2-carboxylic acid (S-3b)³

S-3b was obtained as a yellow oil (0.57 g, 90 %). $^1\text{H-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 7.49-7.33 (m, 5H); 4.60-4.55 (m, 1H); 4.27 (s, 2H); 3.49-3.41 (m, 1H); 3.15 (dt, 1H, $^3J = 12.4$, $^3J = 3.1$); 2.20-2.12 (m, 1H); 1.73-1.52 (m, 3H); 1.51-1.18 (m, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 176.6; 130.9; 129.1; 128.6; 128.5; 58.9; 55.7; 43.5; 27.5; 24.9; 20.3. IR [cm^{-1}]: 1060; 1118; 1317; 1455; 1728; 2854; 2952; 3192.

1-(Phenylsulfonyl)piperidine-2-carboxylic acid (3c)⁴

3c was obtained as a white oil (1.27 g, 98 %). $^1\text{H-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 7.83-7.78 (m, 2H); 7.59-7.45 (m, 3H); 4.78 (d, 1H, $^3J = 4.8$); 3.80-3.72 (m, 1H); 3.23 (dt, 1H, $^3J = 12.4$, $^3J = 3.0$); 2.20-2.12 (m, 1H); 1.80-1.60 (m, 3H); 1.51-1.23 (m, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 176.6; 139.9; 132.6; 128.9; 127.1; 54.8; 42.6; 27.5; 24.5; 20.0. IR [cm^{-1}]: 1075; 1100; 1325; 1445; 1724; 2878; 2960; 3205.

1-((3-Nitrophenyl)sulfonyl)piperidine-2-carboxylic acid (3d)

3d was obtained as a white-yellow solid (1.28 g, 92 %). $^1\text{H-NMR}$ (DMSO, δ [ppm], J [Hz]): 12.97 (br, 1H); 8.53-8.41 (m, 2H); 8.25-8.21 (m, 1H); 7.89 (t, 1H, $^3J = 8.0$); 4.65 (d, 1H, $^3J = 4.2$); 3.76-3.68 (m, 1H); 3.10 (dt, 1H, $^3J = 12.8$, $^3J = 2.7$); 2.10-2.02 (m, 1H); 1.68-1.53 (m, 3H); 1.38-1.09 (m, 2H). $^{13}\text{C-NMR}$ (DMSO, δ [ppm], J [Hz]): 171.3; 147.5; 141.3; 132.7; 131.0; 127.0; 121.3; 54.8; 42.3; 27.1; 24.0; 19.4. IR [cm^{-1}]: 1044; 1085; 1353; 1536; 1714; 2894; 2974; 3325.

1,3 Diphenylpropyl 1-(3-methyl-2-oxopentanoyl)piperidine-2-carboxylate (4a)

After purification by column chromatography (silica gel; petroleum ether (40-60) : ethyl acetate = 70:30) **4a** was obtained as a cheerless oil (0.11 g, 37 %). $^1\text{H-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 7.39-7.10 (m, 10H); 5.87-5.63 (m, 1H); 5.55-5.42 (m, 1H); 4.68-4.55 (m, 1H); 3.90-3.80 (m, 1H); 3.26-3.04 (m, 1H); 2.80-2.49 (m, 2H); 2.42-2.00 (m, 4H); 1.80-1.54 (m, 3H); 1.50-1.20 (m, 3H); 1.15-1.11 (m, 3H); 0.95-0.86 (m, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 216.4; 176.8; 170.8; 144.6; 141.8; 128.5; 127.6; 125.9; 73.8; 55.7; 51.8; 43.3; 40.5; 32.0; 26.9; 26.7; 25.6; 21.1; 16.6; 11.9. IR [cm^{-1}]: 1192; 1236; 1453; 1643; 1737; 2860; 2934; Anal. Calcd. for $\text{C}_{27}\text{H}_{33}\text{NO}_4$ (MW: 435.56 g/mol): C, 74.45; H, 7.64; N, 3.22. Found: H, 7.62; N, 2.82.

3-(3,4,5-Trimethoxyphenyl)propyl 1-(3-methyl-2-oxopentanoyl)piperidine-2-carboxylate (4b)

After purification by column chromatography (silica gel; cyclohexane : ethyl acetate = 1:1) **4b** was obtained as a cheerless oil (0.10 g, 30 %). $^1\text{H-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 6.38 (s, 2H); 5.49-5.42 (m, 1H); 4.15 (t, 2H, $^3J = 6.5$); 3.85 (s, 6H); 3.82 (s, 3H); 3.30-3.20 (m, 1H); 2.75-2.57 (m, 3H); 2.35-2.25 (m, 1H); 2.00-1.91 (m, 2H); 1.78-1.62 (m, 4H); 1.51-1.30 (m, 4H); 1.15-1.09 (m, 3H); 0.97-0.85 (m, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , δ [ppm], J [Hz]): 216.4; 176.7; 171.8; 153.4; 136.9; 105.5; 64.5; 61.0; 56.5; 52.0; 43.5; 37.3; 32.7; 30.5; 26.9; 26.8; 25.3; 21.3; 17.4; 11.9. IR [cm^{-1}]: 1125; 1235; 1420; 1640; 1734; 2872; 2936; Anal. Calcd. for $\text{C}_{24}\text{H}_{35}\text{NO}_7$ (MW: 449.57 g/mol): C, 64.12; H, 7.85; N, 3.12. Found: C, 63.90; H, 7.78; N, 3.36.

3-(3,4,5-Trimethoxyphenyl)propyl 1-(benzylsulfonyl)piperidine-2-carboxylate (4c)

Compound **4c** was described without any synthesis and spectroscopy information.⁵ After purification by column chromatography (aluminum oxide; chloroform : ethyl acetate = 1:1) **4c** was obtained as a yellow waxy substance (0.87 g, 48 %). ¹H-NMR (CDCl₃, δ [ppm], *J* [Hz]): 7.49-7.33 (m, 5H); 6.41 (s, 2H); 4.55-4.50 (m, 1H); 4.27 (s, 2H); 4.24-4.15 (m, 2H); 3.84 (s, 6H); 3.82 (s, 3H); 3.46-3.40 (m, 1H); 3.17 (dt, 1H, ³*J* = 12.4, ³*J* = 3.1); 2.68-2.62 (m, 2H); 2.20-2.12 (m, 1H); 2.03-1.95 (m, 2H); 1.75-1.50 (m, 3H); 1.51-1.18 (m, 2H). ¹³C-NMR (CDCl₃, δ [ppm], *J* [Hz]): 171.5; 153.2; 137.9; 136.7; 131.0; 129.3; 128.6; 128.5; 105.4; 64.6; 60.9; 58.9; 56.1; 56.1; 43.5; 32.5; 30.3; 27.8; 25.0; 20.4. IR [cm⁻¹]: 1124; 1335; 1455; 1589; 1733; 2857; 2938. Anal. Calcd. for C₂₅H₃₃NO₇S (MW: 491.60 g/mol): C, 61.08; H, 6.77; N, 2.85; S, 6.52. Found: C, 60.86; H, 6.87; N, 3.06; S, 6.13.

(S)-3-(3,4,5-Trimethoxyphenyl)propyl 1-(benzylsulfonyl)piperidine-2-carboxylate (S-4c)

After purification by column chromatography (aluminum oxide; chloroform : ethyl acetate = 1:1) **S-4c** was obtained as a yellow waxy substance (0.12 g, 21 %). ¹H-NMR (CDCl₃, δ [ppm], *J* [Hz]): 7.49-7.33 (m, 5H); 6.41 (s, 2H); 4.55-4.50 (m, 1H); 4.27 (s, 2H); 4.24-4.15 (m, 2H); 3.84 (s, 6H); 3.82 (s, 3H); 3.46-3.40 (m, 1H); 3.17 (dt, 1H, ³*J* = 12.4, ³*J* = 3.1); 2.68-2.62 (m, 2H); 2.20-2.12 (m, 1H); 2.03-1.95 (m, 2H); 1.75-1.50 (m, 3H); 1.51-1.18 (m, 2H). ¹³C-NMR (CDCl₃, δ [ppm], *J* [Hz]): 171.5; 153.2; 137.9; 136.7; 131.0; 129.3; 128.6; 128.5; 105.4; 64.6; 60.9; 58.9; 56.1; 56.1; 43.5; 32.5; 30.3; 27.8; 25.0; 20.4. IR [cm⁻¹]: 1124; 1335; 1455; 1589; 1733; 2857; 2938. Anal. Calcd. for C₂₅H₃₃NO₇S (MW: 491.60 g/mol): C, 61.08; H, 6.77; N, 2.85; S, 6.52. Found: C, 60.86; H, 6.87; N, 3.06; S, 6.13.

3-(3,4,5-Trimethoxyphenyl)propyl 1-(phenylsulfonyl)piperidine-2-carboxylate (4d)

After purification by column chromatography (aluminium oxide; cyclohexane : ethyl acetate = 80:20) **4d** was obtained as a yellow solid (0.64 g, 28 %). mp: 82.3 °C. ¹H-NMR (CDCl₃, δ [ppm], *J* [Hz]): 7.82-7.78 (m, 2H); 7.58-7.41 (m, 3H) 6.38 (s, 2H); 4.80-4.75 (m, 1H); 4.08-3.93 (m, 2H); 3.84 (s, 6H); 3.82 (s, 3H); 3.80-3.73 (m, 1H); 3.25 (dt, 1H, ³*J* = 12.7, ³*J* = 2.9);

2.62-2.56 (m, 2H); 2.19-2.10 (m, 1H); 1.93-1.82 (m, 2H); 1.80-1.60 (m, 3H); 1.53-1.39 (m, 1H); 1.37-1.20 (m, 1H). ^{13}C -NMR (CDCl_3 , δ [ppm], J [Hz]): 170.8; 153.2; 140.2; 136.6; 136.4; 132.4; 128.8; 127.1; 105.4; 64.4; 60.8; 56.1; 55.1; 42.7; 32.4; 30.2; 27.8; 24.6; 20.1. IR [cm^{-1}]: 1115; 1334; 1450; 1591; 1739; 2860; 2947; Anal. Calcd. for $\text{C}_{24}\text{H}_{31}\text{NO}_7\text{S}$ (MW: 477.57 g/mol): C, 60.36; H, 6.54; N, 2.93; S, 6.71. Found: C, 60.00; H, 6.31; N, 2.72; S, 6.38.

3-(Pyridine-3-yl)propyl 1-((3-nitrophenyl)sulfonyl)piperidine-2-carboxylate (4e)

After purification by column chromatography (silica gel; ethyl acetate) **4e** was obtained as a yellow waxy substance (1.43 g, 81 %). ^1H -NMR (CDCl_3 , δ [ppm], J [Hz]): 8.62-8.59 (m, 1H); 8.50-8.44 (m, 2H); 8.41-8.37 (m, 1H); 8.13-8.09 (m, 1H); 7.69 (t, 1H, $^3J = 8.0$); 7.59-7.55 (m, 1H); 7.32-7.27 (m, 1H); 4.81 (d, 1H, $^3J = 4.9$); 4.08-3.99 (m, 2H); 3.83-3.76 (m, 1H); 3.18 (dt, 1H, $^3J = 12.7$, $^3J = 2.9$); 2.71-2.66 (m, 2H); 2.24-2.16 (m, 1H); 1.96-1.87 (m, 2H); 1.87-1.67 (m, 3H); 1.61-1.47 (m, 1H); 1.32-1.10 (m, 1H). ^{13}C -NMR (CDCl_3 , δ [ppm], J [Hz]): 170.3; 148.9; 148.1; 146.9; 142.1; 136.7; 136.5; 132.7; 130.1; 126.9; 123.8; 122.4; 64.3; 55.5; 43.0; 29.7; 29.2; 27.9; 24.7; 20.1. IR [cm^{-1}]: 1125; 1161; 1300; 1350; 1530; 1736; 2861; 2947; Anal. Calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_6\text{S}$ (MW: 433.48 g/mol): C, 55.42; H, 5.35; N, 9.69; S, 7.40. Found: C, 55.28; H, 5.45; N, 9.57; S, 7.21.

3-(3,4,5-Trimethoxyphenyl)propyl 1-((3-nitrophenyl)sulfonyl)piperidine-2-carboxylate (4f)

After purification by column chromatography (silica gel; cyclohexane : ethyl acetate = 1:1) **4f** was obtained as a yellow waxy substance (0.86 g, 40 %). ^1H -NMR (CDCl_3 , δ [ppm], J [Hz]): 8.62-8.60 (m, 1H); 8.41-8.37 (m, 1H); 8.12-8.08 (m, 1H); 7.68 (t, 1H, $^3J = 8.0$); 6.37 (s, 2H); 4.82 (d, 1H, $^3J = 4.9$); 4.07-3.96 (m, 2H); 3.85 (s, 6H); 3.83 (s, 3H); 3.75-3.69 (m, 1H); 3.20 (dt, 1H, $^3J = 12.7$, $^3J = 3.0$); 2.60-2.54 (m, 2H); 2.24-2.17 (m, 1H); 1.94-1.83 (m, 2H); 1.94-1.66 (m, 3H); 1.62-1.47 (m, 1H); 1.35-1.12 (m, 1H). ^{13}C -NMR (CDCl_3 , δ [ppm], J [Hz]): 170.3; 153.3; 148.1; 142.1; 136.5; 135.5; 132.7; 130.1; 126.8; 122.5; 105.3; 64.7; 60.8; 56.1; 55.5; 42.9; 32.4; 30.1; 28.0; 24.8; 20.0. IR [cm^{-1}]: 1123; 1238; 1350; 1531; 1589; 1736; 2860;

2940. Anal. Calcd. for $C_{24}H_{30}N_2O_9S$ (MW: 522.57 g/mol): C, 55.16; H, 5.79; N, 5.36; S, 6.14. Found: C, 55.54; H, 6.01; N, 5.13; S, 5.84.

3-(Pyridine-3-yl)propyl 1-((3-aminophenyl)sulfonyl)piperidine-2-carboxylate (5a)

After purification by column chromatography (silica gel; triethylamine : ethylacetate = 5:95) **5a** was obtained as a yellow waxy substance (0.71 g, 54 %). 1H -NMR (DMSO, δ [ppm], J [Hz]): 8.43-8.39 (m, 2H); 7.64-7.60 (m, 1H); 7.34-7.29 (m, 1H); 7.16 (t, 1H, $^3J = 7.9$); 6.97-6.94 (m, 1H); 6.86-6.82 (m, 1H); 6.77-6.73 (m, 1H); 5.57 (s, 2H); 4.56 (d, 1H, $^3J = 5.1$); 4.05-3.85 (m, 2H); 3.63-3.55 (m, 1H); 3.21-3.11 (m, 1H); 2.64-2.58 (m, 2H); 2.00-1.92 (m, 1H); 1.86-1.77 (m, 2H); 1.65-1.53 (m, 3H); 1.31-1.10 (m, 2H). ^{13}C -NMR (DMSO, δ [ppm], J [Hz]): 169.9; 149.1; 149.0; 146.8; 139.7; 135.9; 135.3; 129.1; 123.0; 117.0; 112.7; 110.5; 63.4; 54.1; 41.8; 28.7; 27.9; 26.5; 23.3; 18.9. IR [cm^{-1}]: 1150; 1176; 1313; 1481; 1598; 1731; 2860; 2945; 3376; 3453. Anal. Calcd. for $C_{20}H_{25}N_3O_4S$ (MW: 403.50 g/mol): C, 59.53; H, 6.25; N, 10.4; S, 7.95. Found: C, 59.14; H, 6.39; N, 10.02; S, 7.56.

3-(3,4,5-Trimethoxyphenyl)propyl 1-((3-aminophenyl)sulfonyl)piperidine-2-carboxylate (5b)

After purification by column chromatography (silica gel; triethylamine : ethyl acetate = 5:95) **5b** was obtained as a yellow waxy substance (0.66 g, 82 %). 1H -NMR (DMSO, δ [ppm], J [Hz]): 7.13 (t, 1H, $^3J = 7.9$); 6.93-6.90 (m, 1H); 6.82-6.79 (m, 1H); 6.75-6.71 (m, 1H); 6.45 (s, 2H); 5.54 (s, 2H); 4.55-4.50 (m, 1H); 4.03-3.84 (m, 2H); 3.72 (s, 6H); 3.60-3.52 (m, 4H); 3.19-3.09 (m, 1H); 2.53-2.45 (m, 2H); 1.96-1.91 (m, 1H); 1.82-1.74 (m, 2H); 1.61-1.50 (m, 3H); 1.29-1.11 (m, 2H). ^{13}C -NMR (DMSO, δ [ppm], J [Hz]): 170.1; 152.4; 149.2; 139.9; 136.4; 135.3; 129.3; 117.2; 113.0; 110.7; 105.2; 63.7; 59.6; 55.5; 54.3; 41.9; 31.4; 29.3; 26.7; 23.5; 19.2. IR [cm^{-1}]: 1122; 1238; 1315; 1453; 1589; 1732; 2859; 2940; 3371; 3464. Anal. Calcd. for $C_{24}H_{32}N_2O_7S$ (MW: 492.59 g/mol): C, 58.52; H, 6.55; N, 5.69; S, 6.51. Found: C, 58.35; H, 6.65; N, 5.31; S, 6.12.

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