

CHEMBIOCHEM

Supporting Information

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Supporting Information

for

In vitro Synthesis of New Cyclodepsipeptides of the PF1022-Type: Probing the α -D-Hydroxy Acid Tolerance of PF1022 Synthetase

Jane Müller, Sven C. Feifel, Timo Schmiederer,
Rainer Zocher, and Roderich D. Süssmuth*

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1. Experimental

1.1 General techniques

All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and Molybdat or Permanganate solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040 – 0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25, 0.5 or 1 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on a Bruker Advance-400 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; b, broad. Infrared spectra were recorded on a Nicolet Avat 360 FT-IR. High-resolution mass spectra (HRMS) were recorded on a Kratos MS 80 RFA mass spectrometer under electron impact ionization (EI) conditions.

1.2 Typical procedure for the enantioselective synthesis of α -D-hydroxy acids

1.2.1 α -D-amino acids; Typical Procedure

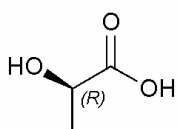
Boc- α -D-amino acid (1.0 mmol, 1.0 equiv) was dissolved in anhydrous CH_2Cl_2 (2 mL), and TFA (1 mL, 22.0 equiv) was added. After stirring for 3 h at room temperature, the reaction has completed, followed by TLC. When complete, the reaction mixture was treated with saturated aqueous Na_2CO_3 solution until pH 9 was achieved. Then, it was extracted with CH_2Cl_2 (2 x 30 mL), and the combined organic phase was dried over MgSO_4 followed by evaporation of the solvent, to obtain the unprotected amino acid (90-98%) as a white solid.

1.2.2 α -D-hydroxy carboxylic acids; Typical Procedure

α -D-amino acid (10.0 mmol, 1.0 equiv) was dissolved in 0.5 M H_2SO_4 (40 mL, 20.00 mmol, 2.0 equiv). This solution was cooled to 0 °C and a solution of sodium nitrite (4.14 g, 60.0 mmol, 6.0 equiv) in H_2O (13.5 mL) was added slowly while stirring, the temperature was maintained. The reaction was stirred at 0 °C for further 3 h, and then allowed to warm up to room temperature and stirred at this temperature for 24 h (followed by t.l.c. to completion). The reaction mixture was extracted with diethyl ether (3 x 50 mL), the organic phases were combined, washed with brine (50 mL) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the ether was evaporated in vacuo. The residual mass was recrystallized from hexane-ether to give, respectively, α -D-hydroxy carboxylic acid.

2. Analytical and spectral data of α -D-hydroxy acids

2.1 (R)-2-hydroxy-propionic acid (1)



Yield: 40%; yellow oil.

IR (film): 3206, 2990, 2943, 1729, 1277, 1203, 1124, 1096, 1043.

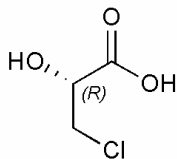
^1H NMR (400 MHz, DMSO): δ 1.21 (d, 1J = 6.85 Hz, 3H, CH_3), 2.95 (q, 1J = 6.90 Hz, 1H, CH).

^{13}C NMR (100 MHz, DMSO): δ 176.3, 65.7, 20.4.

MS: m/z (%) = 90 (35), 74 (15), 58 (28), 46 (100).

HRMS m/z calcd for $\text{C}_3\text{H}_6\text{O}_3$: 90.0316; found: 90.0329.

2.2 3-chloro-(*R*)-2-hydroxy-propionic acid (2).



Yield: 65%; yellowish solid.

IR (film): 3361, 3039, 2975, 1731, 1428, 1368, 1299, 1220, 1186, 1100, 675.

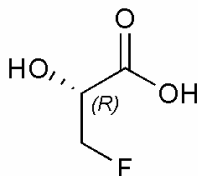
¹H NMR (400 MHz, DMSO): δ 3.75 (d, 1J = 4.43 Hz, 2H, CH₂), 4.29 (t, 1J = 4.43, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 172.5, 70.1, 47.2.

MS: m/z (%) = 125 (3), 108 (3), 92 (5), 81 (32), 79 (100), 75 (12), 63 (22), 48 (5).

HRMS m/z calcd for C₃H₆O₃Cl: [MH⁺] 125.0005; found: 125.0007.

2.3 3-fluoro-(*R*)-2-hydroxy-propionic acid (3).



Yield: 45%; yellowish oil.

IR (film): 3378, 3196, 2966, 2925, 2855, 1731, 1561, 1459, 1418, 1379, 1237, 1208, 1122.

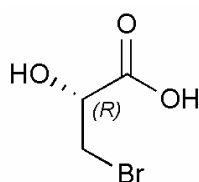
¹H NMR (400 MHz, DMSO): δ 4.19 (dd, 1J = 4.30 Hz, 2J = 2.96, 1H Hz, CH), 4.27 (dd, 1J = 4.30 Hz, 2J = 2.96 Hz, 1H, CH), 4.48 (dd, 1J = 5.44 Hz, 2J = 3.69 Hz, 1H, CH₂), 4.59 (dd, 1J = 4.90 Hz, 2J = 3.69 Hz, 1H, CH₂).

¹³C NMR (100 MHz, DMSO): δ 172.4, 85.9, 84.3, 69.8, 69.6.

MS: m/z (%) = 109 (4), 92 (32), 72 (14), 63 (100), 46 (40).

HRMS m/z calcd for C₃H₆FO₃: [MH⁺] 109.0301; found: 109.0293.

2.4 3-bromo-(*R*)-2-hydroxy-propionic acid (4).



Yield: 63%; brownish solid.

IR (film): 3251, 3041, 2975, 2927, 2856, 1737, 1417, 1338, 1275, 1238, 1172, 1104, 976.

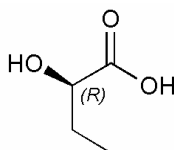
¹H NMR (400 MHz, DMSO): δ 3.52 (dd, $^1J = 10.68$ Hz, $^2J = 4.37$ Hz, 1H, CH₂), 3.56 (dd, $^1J = 10.61$ Hz, $^2J = 4.43$ Hz, 1H, CH₂), 4.31 (t, $^1J = 4.50$ Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 172.5, 69.7, 36.2.

MS: m/z (%) = 150 (20), 123 (100), 107 (5), 93 (7), 80 (6), 71 (25), 55 (5).

HRMS m/z calcd for C₃H₃O₂Br: [M-H₂O] 149.9316; found: 149.9312.

2.5 (R)-2-hydroxy-butyrac acid (5)



Yield: 69%; yellowish solid.

IR (film): 3449, 2971, 2939, 2883, 1718, 1460, 1381, 1360, 1333, 1238, 1214, 1128, 1059.

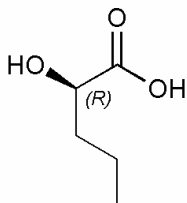
¹H NMR (400 MHz, DMSO): δ 0.86 (t, $^1J = 7.46$ Hz, 3H, CH₃), 1.48-1.65 (m, 2H, CH₂), 3.85-3.88 (m, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 175.7, 70.7, 27.0, 9.5.

MS: m/z (%) = 105 (73), 87 (4), 77 (13), 59 (100).

HRMS m/z calcd for C₄H₉O₃: [MH⁺] 105.0551; found: 105.0559.

2.6 (R)-2-hydroxy-pentanoic acid (6).



Yield: 90%; pale white solid.

IR (film): 3319, 2963, 2936, 2876, 1722, 1467, 1381, 1255, 1216, 1132, 1075.

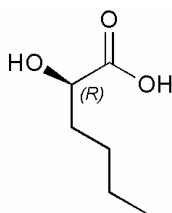
¹H NMR (400 MHz, DMSO): δ 0.85 (t, $^1J = 7.32$ Hz, 3H, CH₃), 1.29-1.38 (m, 2H, CH₂), 1.44-1.61 (m, 2H, CH₂), 3.91 (dd, $^1J = 7.79$ Hz, $^2J = 4.57$ Hz, 1H, CH)

¹³C NMR (100 MHz, DMSO): δ 175.9, 69.3, 36.0, 17.9, 13.7.

MS: m/z (%) = 119 (2), 100 (2), 73 (68), 55 (100).

HRMS m/z calcd for C₅H₁₁O₃: [MH⁺] 119.0708; found: 119.0712.

2.7 (R)-2-hydroxy-hexanoic acid (7)



Yield: 85%; white solid.

IR (film): 3459, 2957, 2930, 2874, 2862, 1731, 1467, 1460, 1380, 1367, 1338, 1271, 1242, 1208, 1134.

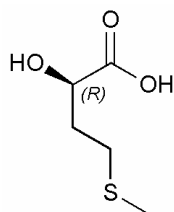
¹H NMR (400 MHz, DMSO): δ 0.84 (t, 1J = 7.19 Hz, 3H, CH₃), 1.21-1.32 (m, 4H, 2 x CH₂), 1.46-1.64 (m, 2H, CH₂), 3.89 (dd, 1J = 7.79 Hz, 2J = 4.57 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 175.9, 69.5, 33.6, 26.9, 21.9, 13.9.

MS: m/z (%) = 132 (2), 114 (2), 87 (43), 76 (15), 69 (100), 57 (10).

HRMS m/z calcd for C₆H₁₂O₃: 132.0786; found: 132.00782.

2.8 (R)-2-hydroxy-4-methylsulfanyl-butyrac acid (8)



Yield: 59%; yellow solid.

IR (film): 3324, 2969, 2919, 2848, 2635, 1722, 1429, 1366, 1265, 1221, 1171, 1092.

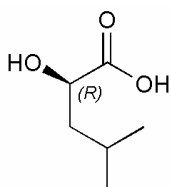
¹H NMR (400 MHz, DMSO): δ 1.69-1.78 (m, 1H, CH₂), 1.82-1.91 (m, 1H, CH₂), 2.02 (s, 3H, CH₃), 2.62 (t, 1J = 6.65 Hz, 2H, CH₂), 4.02 (dd, 1J = 8.53 Hz, 2J = 3.96 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 175.5, 68.4, 33.6, 29.3, 14.6.

MS: m/z (%) = 150 (68), 132 (6), 120 (13), 114 (5), 105 (8), 89 (7), 76 (35), 75 (47), 61 (100), 57 (18).

HRMS m/z calcd for C₅H₁₀O₃S: 150.0350; found: 150.0350.

2.9 (R)-2-hydroxy-4-methyl-pentanoic acid (9).



Yield: 88%; yellow solid.

IR (film): 3186, 2959, 2938, 2872, 1723, 1470, 1456, 1435, 1388, 1369, 1266, 1271, 1141.

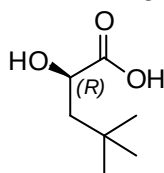
¹H NMR (400 MHz, DMSO): δ 0.86 (d, 1J = 6.31 Hz, 6H, (CH₃)₂), 1.35-1.47 (m, 2H, CH₂), 1.68-1.79 (m, 1H, CH), 3.92 (dd, 1J = 8.73 Hz, 2J = 4.48 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 176.4, 68.2, 42.9, 23.9, 23.2, 21.5.

MS: m/z (%) = 132 (4), 113 (4), 99 (9), 87 (73), 76 (31), 69 (100), 57 (20).

HRMS m/z calcd for C₆H₁₂O₃: 132.0786; found: 132.0788.

2.10 (R)-2-hydroxy-4,4-dimethylpentanoic acid (10).



Yield: 57%; white solid.

IR (film): 3411, 2964, 2954, 2922, 2870, 1729, 1710, 1464, 1447, 1394, 1370, 1366, 1255, 1242, 1189.

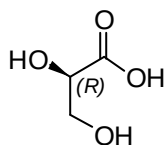
¹H NMR (400 MHz, DMSO): δ 0.92 (s, 9H, 3 x CH₃), 1.36-1.42 (m, 1H, CH₂), 1.53-1.57 (m, 1H, CH₂), 3.97 (dd, 1J = 8.93 Hz, 2J = 3.02 Hz, 1H, CH), 4.99 (s, 1H, OH).

¹³C NMR (100 MHz, DMSO): δ 176.7, 68.1, 47.2, 30.1, 29.8.

MS: m/z (%) = 147 (81), 119 (19), 113 (35), 101 (73), 95 (20), 83 (8), 69 (12), 57 (100).

HRMS m/z calcd for C₇H₁₅O₃: [MH⁺] 147.1021; found: 147.1027.

2.11 (R)-2,3-dihydroxypropanoic acid (11).



Yield: 81%; yellowish solid.

IR (film): 3380, 2924, 2870, 2607, 1734, 1649, 1496, 1454.

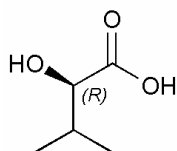
¹H NMR (400 MHz, DMSO): δ 3.51 (dd, 1J = 11.15 Hz, 2J = 5.24 Hz, 1H, CH₂), 3.54 (dd, 1J = 11.15 Hz, 2J = 5.24 Hz, 1H, CH₂), 3.94 (dd, 1J = 5.04 Hz, 2J = 4.10 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 174.3, 71.9, 63.7.

MS: m/z (%) = 107 (18), 90 (28), 76 (100), 61 (94), 58 (42).

HRMS m/z calcd for $C_3H_7O_4$: $[MH^+]$ 107.0344; found: 107.0344.

2.12 (*R*)-2-hydroxy-3-methyl-butyrlic acid (12)



Yield: 90%; pale white solid.

IR (film): 3423, 3171, 2967, 2936, 2878, 1720, 1468, 1390, 1371, 1254, 1215, 1178, 1137.

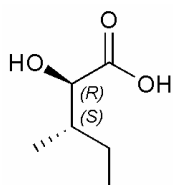
1H NMR (400 MHz, DMSO): δ 0.81 (d, 1J = 6.85 Hz, 3H, CH_3), 0.88 (d, 1J = 6.85 Hz, 3H, CH_3), 1.87-1.93 (m, 1H, CH), 3.72 (d, 1J = 4.57 Hz, 1H, CH).

^{13}C NMR (100 MHz, DMSO): δ 175.3, 74.5, 31.4, 18.9, 16.7.

MS: m/z (%) = 119 (2), 85 (3), 76 (100), 73 (87), 58 (23), 55 (31).

HRMS m/z calcd for $C_5H_{11}O_3$: $[MH^+]$ 119.0708; found: 119.0710.

2.13 (*allo*)-2-hydroxy-3-methyl-pentanonic acid (13)



Yield: 82%; white solid.

IR (film): 3314, 2966, 2937, 2879, 1718, 1463, 1381, 1363, 1273, 1242, 1216, 1135.

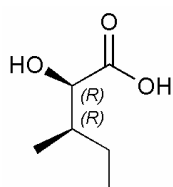
1H NMR (400 MHz, DMSO): δ 0.76 (d, 1J = 6.85, 3H, CH_3), 0.85 (t, 1J = 7.46, 3H, CH_3), 1.11-1.22 (m, 1H, CH_2), 1.34-1.45 (m, 1H, CH_2), 1.64-1.70 (m, 1H, CH), 3.89 (d, 1J = 3.63, 1H, CH).

^{13}C NMR (100 MHz, DMSO): δ 175.8, 72.1, 37.9, 25.6, 13.8, 11.7.

MS: m/z (%) = 133 (22), 115 (9), 105 (29), 97 (8), 87 (100), 76 (42), 69 (48), 57 (36).

HRMS m/z calcd for $C_6H_{13}O_3$: $[MH^+]$ 133.0864; found: 133.0863.

2.14 (*R*)-2-hydroxy-3-methyl-pentanonic acid (14).



Yield: 85%; white solid.

IR (film): 3314, 2966, 2937, 2879, 1718, 1463, 1381, 1363, 1273, 1242, 1216, 1135.

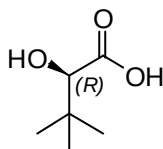
¹H NMR (400 MHz, DMSO): δ 0.82 (t, 1J = 7.80 Hz, 3H, CH₃), 0.85 (d, 1J = 6.98 Hz, 3H, CH₃), 1.10-1.17 (m, 1H, CH₂), 1.36-1.42 (m, 1H, CH₂), 1.62-1.69 (m, 1H, CH), 3.76 (d, 1J = 4.97 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 175.4, 74.0, 38.1, 23.7, 15.4, 11.5.

MS: m/z (%) = 133 (4), 115 (2), 87 (27), 76 (100), 69 (11), 57 (30).

HRMS m/z calcd for C₆H₁₃O₃: [MH⁺] 133.0864; found: 133.0861.

2.15 (R)-2-hydroxy-3,3-dimethylbutanoic acid (15).



Yield: 45%; yellowish solid.

IR (film): 3350, 2962, 2912, 2875, 1716, 1480, 1466, 1398, 1370, 1279, 1218, 1082.

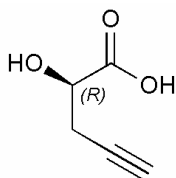
¹H NMR (400 MHz, DMSO): δ 1.03 (s, 9H, 3 x CH₃), 3.80 (t, 1J = 6.58 x 2 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 176.4, 67.6, 31.8, 26.1, 25.9.

MS: m/z (%) = 133 (2), 117 (3), 99 (8), 87 (23), 76 (20), 57 (100).

HRMS m/z calcd for C₆H₁₃O₃: [MH⁺] 133.0864; found: 133.0868.

2.16 (R)-2-hydroxy-pent-4-ynoic acid (16).



Yield: 73%; pale brown solid.

IR (film): 3340, 3290, 2926, 2122, 1726, 1422, 1361, 1329, 1283, 1205, 1093.

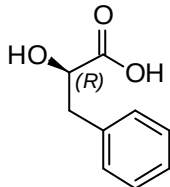
¹H NMR (400 MHz, DMSO): δ 2.32-2.45 (m, 2H, CH₂), 2.71 (t, 1J = 2.69 Hz, 1H, CH), 4.05 (dd, 1J = 6.45 Hz, 2J = 5.37 Hz, 1H, CH).

¹³C NMR (100 MHz, DMSO): δ 173.9, 80.8, 72.7, 68.7, 24.2.

MS: m/z (%) = 115 (100), 97 (30), 87 (19), 81 (9), 69 (21), 53 (5).

HRMS m/z calcd for $C_5H_7O_3$: $[MH^+]$ 115.0395; found: 115.0402.

2.17 (*R*)-2-hydroxy-3-phenylpropanoic acid (17)



Yield: 88%; white solid.

IR (film): 3396, 3087, 3064, 3030, 2930, 1723, 1604, 1585, 1521, 1497, 1455, 1260, 1221, 1190, 1091, 700.

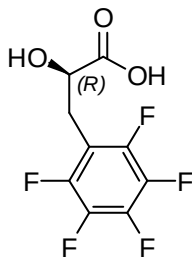
1H NMR (400 MHz, DMSO): δ 2.77 (dd, 1J = 13.70 Hz, 2J = 8.33 Hz, 1H, CH_2), 2.95 (dd, 1J = 13.70 Hz, 2J = 4.43 Hz, 1H, CH_2), 4.13 (dd, 1J = 3.83 Hz, 2J = 4.43 Hz, 1H, CH), 7.16-7.28 (m, 5H, Ph).

^{13}C NMR (100 MHz, DMSO): δ 175.1, 138.1, 129.4, 128.0, 126.1, 71.0, 40.0.

MS: m/z (%) = 166 (3), 148 (20), 131 (5), 121 (4), 103 (11), 91 (100), 77 (12), 65 (12), 51 (9).

HRMS m/z calcd for $C_9H_{10}O_3$: 166.0629; found: 166.0628.

2.18 (*R*)-2-hydroxy-3-(pentafluorophenyl)propanoic acid (18).



Yield: 51%; pale white solid.

IR (film): 3528, 3416, 2954, 2924, 2871, 2854, 1708, 1658, 1447, 1427, 1398, 1370, 1343, 1276, 1235, 1201, 1123, 1093, 1046, 980, 958, 927.

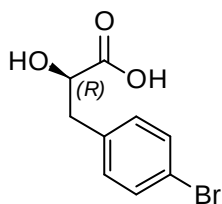
1H NMR (400 MHz, DMSO): δ 2.94 (dd, 1J = 13.70 Hz, 2J = 8.33 Hz, 1H, CH_2), 3.08 (dd, 1J = 13.70 Hz, 2J = 4.43 Hz, 1H, CH_2), 4.14 (dd, 1J = 8.26 Hz, 2J = 5.17 Hz, 1H, CH).

^{13}C NMR (100 MHz, DMSO): δ 174.1, 145.3, 145.2, 145.0, 144.9, 142.7, 142.4, 139.7, 138.3, 137.1, 137.0, 135.8, 111.0, 110.9, 110.7, 110.6, 110.4, 110.3, 67.8, 27.5.

MS: m/z (%) = 256 (3), 236 (24), 218 (13), 211 (26), 190 (12), 181 (100), 163 (49), 143 (12), 132 (4), 113 (3), 75 (8), 55 (5).

HRMS m/z calcd for $C_9H_5F_5O_3$: 256.0158; found: 256.0153.

2.19 3-(4-bromophenyl)-(R)-2-hydroxypropanoic acid (19)



Yield: 56%; brownish solid.

IR (film): 3444, 3061, 3028, 2960, 2932, 1724, 1592, 1488, 1437, 1406, 1367, 1235, 1186, 1106, 1072, 1012, 827, 811.

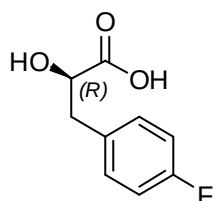
1H NMR (400 MHz, DMSO): δ 2.75 (dd, 1J = 13.70 Hz, 2J = 8.33 Hz, 1H, CH_2), 2.92 (dd, 1J = 13.70 Hz, 2J = 4.43 Hz, 1H, CH_2), 4.13 (dd, 1J = 8.19 Hz, 2J = 4.43 Hz, 1H, CH), 5.30 (s, 1H, OH), 7.17-7.25 (m, 2H, Ph), 7.43-7.50 (m, 2H, Ph).

^{13}C NMR (100 MHz, DMSO): δ 174.9, 137.6, 131.7, 131.2, 130.8, 119.3, 70.7, 57.8.

MS: m/z (%) = 244 (4), 228 (68), 209 (12), 183 (4), 171 (100), 138 (6), 102 (17), 90 (17), 77 (15), 51 (10).

HRMS m/z calcd for $C_9H_9O_3Br$: 243.9735; found: 243.9737.

2.20 3-(4-fluorophenyl)-(R)-2-hydroxypropanoic acid (20)



Yield: 68%; white-yellowish solid.

IR (film): 3299, 3074, 3046, 3007, 2933, 1725, 1651, 1603, 1510, 1438, 1418, 1365, 1279, 1223, 1159, 1101, 1084, 825.

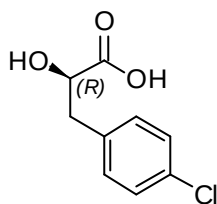
1H NMR (400 MHz, DMSO): δ 2.77 (dd, 1J = 13.70 Hz, 2J = 4.43 Hz, 1H, CH_2), 2.94 (dd, 1J = 13.70 Hz, 2J = 4.43 Hz, 1H, CH_2), 4.11 (dd, 1J = 8.26 Hz, 2J = 4.37 Hz, 1H, CH), 5.29 (s, 1H, OH), 7.04-7.10 (m, 2H, Ph), 7.24-7.27 (m, 2H, Ph).

^{13}C NMR (100 MHz, DMSO): δ 175.0, 162.1, 159.7, 134.3, 134.2, 131.2, 131.1, 114.7, 114.5, 70.9, 39.0.

MS: m/z (%) = 184 (4), 166 (12), 139 (4), 121 (6), 109 (100), 101 (4), 91 (2), 83 (8).

HRMS m/z calcd for $C_9H_9O_3F$: 184.0535; found: 184.0531.

2.21 3-(4-chlorophenyl)-(R)-2-hydroxypropanoic acid (21)



Yield: 66%; white solid.

IR (film): 3426, 3031, 2971, 2930, 2856, 1725, 1598, 1577, 1492, 1437, 1409, 1369, 1256, 1219, 1180, 1107, 1093, 1016, 813.

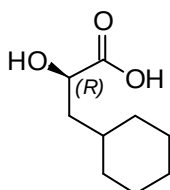
¹H NMR (400 MHz, DMSO): δ 2.78 (dd, 1J = 13.84 Hz, 2J = 4.30 Hz, 1H, CH₂), 2.93 (dd, 1J = 13.83 Hz, 2J = 4.30 Hz, 1H, CH₂), 4.14 (dd, 1J = 8.19 Hz, 2J = 4.43 Hz, 1H, CH), 7.23-7.25 (m, 2H, Ph), 7.35-7.37 (m, 2H, Ph).

¹³C NMR (100 MHz, DMSO): δ 174.9, 137.1, 135.5, 131.3, 128.2, 127.9, 70.7, 39.2.

MS: m/z (%) = 200 (6), 182 (24), 165 (8), 155 (3), 137 (8), 127 (28), 125 (100), 111 (3), 101 (10), 91 (10), 89 (12), 75 (8).

HRMS m/z calcd for C₉H₉O₃Cl: 200.0240; found: 200.0243.

2.22 3-cyclohexyl-(R)-2-hydroxypropanoic acid (22)



Yield: 89%; white solid.

IR (film): 3304, 2923, 2852, 1723, 1449, 1276, 1245, 1222, 1203, 1141, 1095, 1077.

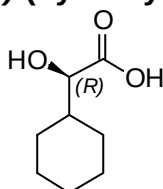
¹H NMR (400 MHz, DMSO): δ 1.02-1.18 (m, 6H, 3 x CH₂, Hex), 1.53-1.60 (m, 5H, 2 x CH₂, CH, Hex), 1.66-1.68 (m, 2H, CH₂), 3.71 (d, 1J = 4.43 Hz, 1H, CH), 4.95 (s, 1H, OH).

¹³C NMR (100 MHz, DMSO): δ 175.3, 74.2, 41.2, 28.9, 25.8, 25.7, 25.6.

MS: m/z (%) = 172 (3), 154 (25), 127 (38), 109 (65), 97 (38), 83 (63), 76 (32), 67 (40), 55 (100).

HRMS m/z calcd for C₉H₁₆O₃: 172.1099; found: 172.1102.

2.23 Cyclohexyl-(R)-(hydroxyl)acetic acid (23)



Yield: 84%; white solid.

IR (film): 3304, 2929, 2854, 1716, 1451, 1279, 1262, 1256, 1227, 1095, 1077.

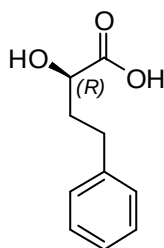
¹H NMR (400 MHz, DMSO): δ 1.00-1.24 (m, 6H, 3 x CH₂, Hex), 1.53-1.68 (m, 5H, 2 x CH₂, CH, Hex) 3.71 (d, ¹J = 4.43 Hz, 1H, CH), 4.95 (s, 1H, OH).

¹³C NMR (100 MHz, DMSO): δ 174.6, 77.7, 34.2, 29.8, 27.8, 26.4, 25.8.

MS: *m/z* (%) = 158 (3), 140 (3), 113 (10), 95 (41), 83 (78), 76 (79), 67 (24), 55 (100), 53 (20).

HRMS *m/z* calcd for C₈H₁₄O₃: 158.0942; found: 158.0944.

2.24 (*R*)-2-hydroxy-4-phenylbutanoic acid (24).



Yield: 62%; white solid.

IR (film): 3458, 3086, 3063, 3027, 3001, 2957, 2927, 2862, 2780, 1732, 1647, 1603, 1497, 1454, 1367, 1332, 1288, 1270, 1240, 1179, 1096, 696.

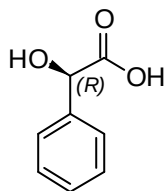
¹H NMR (400 MHz, DMSO): δ 1.73-1.82 (m, 1H, CH₂), 1.85-1.94 (m, 1H, CH₂), 2.64 (t, ¹J = 7.92 x 2 Hz, 2H, CH₂), 3.89 (dd, ¹J = 8.33 Hz, ²J = 4.16 Hz, 1H, CH), 7.17-7.31 (m, 5H, Ph).

¹³C NMR (100 MHz, DMSO): δ 175.8, 141.6, 128.5, 128.3, 125.8, 68.9, 35.8, 30.9.

MS: *m/z* (%) = 180 (10), 162 (5), 134 (3), 117 (15), 105 (77), 104 (32), 91 (100), 76 (19), 65 (17), 51 (11).

HRMS *m/z* calcd for C₁₀H₁₂O₃: 180.0786; found: 180.0784.

2.25 (*R*)-hydroxy(phenyl)acetic acid (25).



Yield: 91%; white solid.

IR (film): 3449, 3089, 3065, 3025, 2931, 1727, 1603, 1588, 1542, 1496, 1455, 1286, 1243, 1190, 1094, 693.

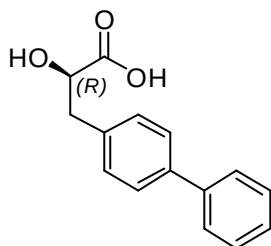
¹H NMR (400 MHz, DMSO): δ 1.73-1.82 (s, 1H, CH), 5.83 (s, 1H, OH), 7.27-7.41 (m, 5H, Ph).

¹³C NMR (100 MHz, DMSO): δ 174.1, 140.2, 128.1, 127.7, 126.6, 72.4.

MS: m/z (%) = 152 (12), 135 (3), 107 (100), 90 (5), 79 (58), 77 (49), 51 (14).

HRMS m/z calcd for C₈H₈O₃: 152.0473; found: 152.0477.

2.26 3-(1,1'-biphenyl-4-yl)-(R)-2-hydroxypropanoic acid (26)



Yield: 43%; white solid.

IR (film): 3418, 3079, 3059, 3030, 2975, 2928, 1709, 1599, 1586, 1578, 1558, 1496, 1452, 1276, 1217, 1200, 1180, 1072, 1032, 763, 759, 691.

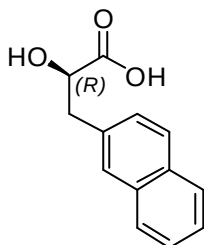
¹H NMR (400 MHz, DMSO): δ 2.81 (dd, 1J = 13.77 Hz, 2J = 4.50 Hz, 1H, CH₂), 3.04 (dd, 1J = 13.77 Hz, 2J = 4.50 Hz, 1H, CH₂), 4.18 (dd, 1J = 8.26 Hz, 2J = 4.50 Hz, 1H, CH), 5.39 (s, 1H, OH), 7.31-7.35 (m, 3H, Ph), 7.42-7.46 (m, 2H, Ph), 7.54-7.56 (m, 2H, Ph), 7.62-7.64 (m, 2H, Ph).

¹³C NMR (100 MHz, DMSO): δ 175.1, 140.1, 138.1, 137.4, 130.0, 128.9, 127.2, 126.5, 126.3, 71.0, 39.6.

MS: m/z (%) = 242 (15), 224 (5), 179 (5), 167 (100), 152 (12), 115 (3), 91 (2), 69 (7).

HRMS m/z calcd for C₁₅H₁₄O₃: 242.0942; found: 242.0943.

2.27 (R)-2-hydroxy-3-(2-naphthyl)propanoic acid (27).



Yield: 50%; orange solid.

IR (film): 3341, 3061, 3048, 3010, 2958, 2935, 1723, 1598, 1511, 1434, 1397, 1356, 1278, 1257, 1212, 1190, 1094, 799, 792, 777.

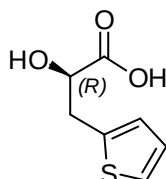
¹H NMR (400 MHz, DMSO): δ 3.15 (dd, 1J = 14.57 Hz, 2J = 8.66 Hz, 1H, CH₂), 3.36 (dd, 1J = 14.04 Hz, 2J = 8.66 Hz, 1H, CH₂), 4.26 (dd, 1J = 8.66 Hz, 2J = 4.37 Hz, 1H, CH), 7.39-7.53 (m, 4H, Naph), 7.90-8.11 (m, 3H, Naph).

^{13}C NMR (100 MHz, DMSO): δ 175.3, 134.2, 133.4, 128.7, 128.6, 127.9, 127.7, 126.9, 126.4, 125.8, 125.4, 123.7, 70.7, 37.3.

MS: m/z (%) = 216 (6), 198 (5), 186 (4), 166 (3), 153 (22), 141 (100), 127 (7), 115 (17), 89 (3), 63 (4).

HRMS m/z calcd for $\text{C}_{13}\text{H}_{12}\text{O}_3$: 216.0786; found: 216.0786.

2.28 (R)-2-hydroxy-3-thien-2-yl-propanoic acid (28)



Yield: 73%; orange solid.

IR (film): 3477, 3105, 3072, 2929, 2576, 1726, 1650, 1558, 1534, 1437, 1426, 1361, 1342, 1266, 1236, 1141, 1086, 1078, 1070, 701, 694.

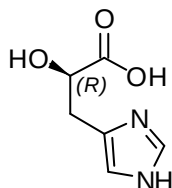
^1H NMR (400 MHz, DMSO): δ 3.01 (dd, 1J = 14.50 Hz, 2J = 8.66 Hz, 1H, CH_2), 3.16 (dd, 1J = 14.50 Hz, 2J = 8.66 Hz, 1H, CH_2), 4.12 (dd, 1J = 7.66 Hz, 2J = 4.30 Hz, 1H, CH), 5.45 (s, 1H, OH), 6.88 (dd, 1J = 3.06 Hz, 2J = 1.21 Hz, 1H, CH, Thien), 6.92 (dd, 1J = 3.08 Hz, 2J = 1.26 Hz, 1H, CH, Thien), 7.31 (dd, 1J = 5.10 Hz, 2J = 1.34 Hz, 1H, CH, Thien).

^{13}C NMR (100 MHz, DMSO): δ 174.6, 139.7, 126.5, 126.1, 124.5, 70.7, 34.3.

MS: m/z (%) = 172 (8), 154 (4), 142 (3), 127 (2), 97 (100), 85 (3), 65 (4), 53 (3).

HRMS m/z calcd for $\text{C}_7\text{H}_8\text{O}_3\text{S}$: 172.0194; found: 172.0194.

2.29 (R)-2-hydroxy-3-(1H-imidazol-4-yl)-propanoic acid (29).



Yield: 35%; white solid.

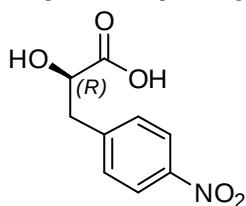
IR (film): 3271, 3136, 2958, 2925, 1740, 1598, 1521, 1505, 1437, 1423, 1382, 1260, 1221, 1120, 1068, 1050, 857, 864.

^1H NMR (400 MHz, DMSO): δ 2.96 (dd, 1J = 8.06 Hz, 2J = 4.33 Hz, 1H, CH_2), 3.01 (dd, 1J = 8.06 Hz, 2J = 4.33 Hz, 1H, CH_2), 4.33 (dd, 1J = 8.06 Hz, 2J = 4.57 Hz, 1H, CH), 6.81 (s, 1H, NH), 7.12 (d, 1J = 1.48 Hz, 1H, CH, ImI), 8.01 (d, 1J = 1.53 Hz, 1H, CH, ImI).

^{13}C NMR (100 MHz, DMSO): δ 173.0, 135.2, 130.5, 119.7, 68.7, 29.2.

MS: m/z (%) = 157 (4), 139 (24), 137 (7), 111 (54), 95 (21), 81 (100), 89 (12), 75 (8).

2.30 (*R*)-2-hydroxy-3-(4-nitro-phenyl)-propionic acid (30).



Yield: 45%; white solid.

IR (film): 3452, 3112, 3080, 2977, 2942, 2856, 1727, 1606, 1518, 1494, 1437, 1347, 1264, 1183, 1109, 1089, 859.

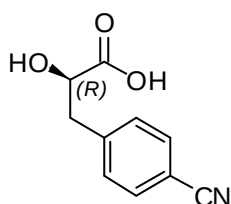
^1H NMR (400 MHz, DMSO): δ 2.93 (dd, 1J = 13.77 Hz, 2J = 8.40 Hz, 1H, CH_2), 3.09 (dd, 1J = 13.70 Hz, 2J = 4.30 Hz, 1H, CH_2), 4.22 (dd, 1J = 8.40 Hz, 2J = 4.23 Hz, 1H, CH), 5.44 (s, 1H, OH), 7.52 (d, 1J = 8.73 Hz, 1H, Ph), 7.60 (d, 1J = 8.60 Hz, 1H, Ph), 8.12-8.18 (m, 2H, Ph).

^{13}C NMR (100 MHz, DMSO): δ 174.7, 146.6, 146.2, 130.7, 123.0, 70.3, 39.6.

MS: m/z (%) = 211 (2), 194 (100), 176 (21), 166 (11), 147 (9), 136 (37), 120 (8), 106 (16), 91 (43), 78 (30), 63 (12), 51 (17).

HRMS m/z calcd for $\text{C}_9\text{H}_9\text{O}_5\text{N}$: 211.0481; found: 211.0491.

2.31 3-(4-cyanophenyl)-(*R*)-2-hydroxypropanoic acid (31).



Yield: 54%; white solid.

IR (film): 3404, 3095, 3071, 2974, 2229, 1726, 1641, 1609, 1544, 1506, 1415, 1262, 1217, 1179, 1114, 1091, 824.

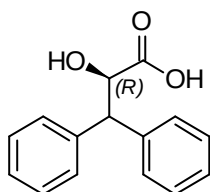
^1H NMR (400 MHz, DMSO): δ 2.86 (dd, 1J = 13.84 Hz, 2J = 8.46 Hz, 1H, CH_2), 3.05 (dd, 1J = 13.84 Hz, 2J = 4.30 Hz, 1H, CH_2), 4.19 (dd, 1J = 8.40 Hz, 2J = 4.23 Hz, 1H, CH), 5.41 (s, 1H, OH), 7.44 (d, 1J = 8.33 Hz, 2H, Ph), 7.71-7.74 (m, 2H, Ph).

^{13}C NMR (100 MHz, DMSO): δ 174.8, 144.3, 131.8, 130.6, 119.0, 109.0, 70.4, 39.8.

MS: m/z (%) = 191 (6), 173 (64), 172 (16), 146 (18), 128 (13), 116 (100), 102 (6), 89 (22), 57 (16).

HRMS m/z calcd for $\text{C}_{10}\text{H}_9\text{O}_3\text{N}$: 191.0582; found: 191.0582.

2.32 (R)-2-hydroxy-3,3-diphenylpropanoic acid (32)



Yield: 41%; white solid.

IR (film): 3525, 3450, 3079, 3056, 3031, 2953, 2925, 1947, 1915, 1880, 1723, 1600, 1582, 1564, 1521, 1487, 1451, 1432, 1407, 1346, 1300, 1242, 1188, 1120, 1089, 1078, 757.

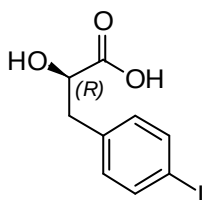
¹H NMR (400 MHz, DMSO): δ 3.71 (d, 1J = 10.34 Hz, 1H, CH), 5.04 (d, 1J = 10.34 Hz, 1H, CH), 7.08-7.13 (m, 3H, Ph), 7.25-7.28 (m, 2H, Ph), 7.35-7.39 (m, 3H, Ph), 7.59-7.61 (m, 2H, Ph).

¹³C NMR (100 MHz, DMSO): δ 173.8, 142.8, 137.0, 128.7, 127.4, 126.5, 75.2, 60.1.

MS: m/z (%) = 243 (3), 225 (21), 207 (3), 180 (49), 167 (100), 152 (19), 136 (52), 118 (36), 107 (23), 91 (26), 77 (27), 51 (17).

HRMS m/z calcd for $C_{15}H_{15}O_3$: $[MH^+]$ 243.1021; found: 243.1027.

2.33 (R)-2-hydroxy-3-(4-iodophenyl)propanoic acid (33)



Yield: 67%; yellowish solid.

IR (film): 3440, 3057, 3022, 2976, 2956, 2928, 1724, 1606, 1588, 1565, 1519, 1485, 1436, 1401, 1346, 1256, 1197, 1187, 1105, 1061, 1007, 823, 808.

¹H NMR (400 MHz, DMSO): δ 2.73 (dd, 1J = 13.84 Hz, 2J = 4.43 Hz, 1H, CH₂), 2.90 (dd, 1J = 13.77 Hz, 2J = 8.26 Hz, 1H, CH₂), 4.11 (dd, 1J = 8.19 Hz, 2J = 4.43 Hz, 1H, CH), 7.02-7.11 (m, 2H, Ph), 7.59-7.67 (m, 2H, Ph).

¹³C NMR (100 MHz, DMSO): δ 174.9, 137.0, 136.7, 131.9, 91.9, 70.7, 59.7.

MS: m/z (%) = 292 (11), 274 (56), 257 (8), 230 (4), 217 (100), 203 (2), 138 (7), 127 (28), 103 (32), 91 (61), 77 (38), 63 (30), 51 (35).

HRMS m/z calcd for $C_9H_9IO_3$: 291.9596; found: 291.9595.