Concise, Asymmetric Total Synthesis of Spirotryprostatin A

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Supporting Information

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^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : -0.22 (s, 9H), 1.49 (d, J = 10.2 Hz, 1H), 1.53 (d, J = 10.2 Hz, 1H), 2.65 (s, 1H), 3.79 (s, 3H), 6.45 (d, J = 1.8 Hz, 1H), 6.56 (dd, J = 1.8, 6.3 Hz, 1H), 7.23 (d, J = 6.3 Hz, 1H), 7.88 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : -1.1, 28.3, 55.5, 75.5, 97.5, 107.5, 123.4, 125.4, 141.1, 161.2, 180.6; IR (NaCl/neat) 3388, 1714, 1634, 1507, 1351, 1251, 1151, 1125, 840 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{13}\text{H}_{19}\text{O}_3\text{NSi}$ (m/z) 265.1134, found (m/z) 265.1132.

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$[\alpha]_{\text{D}}^{24} = -46.0$ (CHCl_3 , $c=1$); ^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : 1.02 (s, 3H), 1.09 (s, 3H), 1.36 (dd, J = 5.6, 15.6 Hz, 1H), 1.61 (dd, J = 2.1, 15.6 Hz, 1H), 2.44 (dd, J = 8.0, 12.6 Hz, 1H), 2.69 (dd, J = 10.4, 12.6 Hz, 1H), 3.04 (s, 3H), 3.81 (s, 3H), 4.01 (dd, J = 2.1, 5.6 Hz, 1H), 4.46 (dd, J = 8.0, 10.4 Hz, 1H), 4.85 (d, J = 2.6 Hz, 1H), 6.29 (d, J = 2.6 Hz, 1H), 6.55 (d, J = 2.1 Hz, 1H), 6.57 (dd, J = 2.1, 8.4 Hz, 1H), 6.99-7.05 (m, 2H), 7.13-7.33 (m, 9H), 8.35 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : 23.5, 25.0, 41.4, 44.5, 49.1, 55.5, 56.5, 56.7, 59.2, 64.6, 73.3, 76.4, 97.3, 107.4, 122.6, 125.5, 125.7, 127.2, 127.6, 128.0, 128.3, 128.8, 136.8, 136.8, 141.6, 160.2, 172.2, 179.2; IR (NaCl/neat) 1726, 1631, 1505, 1271, 1238, 1193, 1148, 755, 698 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{32}\text{H}_{35}\text{O}_5\text{N}_2$ (m/z) 527.2546, found (m/z) 527.2540.

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$[\alpha]_D^{24} = -36.4$ (CHCl_3 , $c=0.55$); ^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : 1.54 (s, 3H), 1.74 (s, 3H), 2.48 (dd, $J=8.4, 13.0$ Hz, 1H), 2.75 (dd, $J=9.6, 13.0$ Hz, 1H), 3.80 (s, 3H), 4.27 (d, $J=3.0$ Hz, 1H), 4.52 (d, $J=9.4$ Hz, 1H), 4.54 (dd, $J=8.4, 9.6$ Hz, 1H), 4.70 (d, $J=9.4$ Hz, 1H), 6.18 (d, $J=3.0$ Hz, 1H), 6.48 (d, $J=2.3$ Hz, 1H), 6.56 (dd, $J=2.3, 8.4$ Hz, 1H), 7.02-7.07 (m, 2H), 7.15-7.33 (m, 9H), 7.75 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : 18.6, 26.2, 40.0, 55.5, 56.3, 56.6, 60.2, 67.5, 97.2, 107.2, 120.8, 122.1, 125.6, 125.7, 127.4, 127.9, 128.0, 128.4, 128.9, 136.2, 136.4, 139.9, 141.2, 160.1, 168.5, 171.9, 178.3; IR (NaCl/neat) 3261, 1723, 1631, 1504, 1453, 1193, 1153, 755, 698 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{31}\text{H}_{31}\text{O}_4\text{N}_2$ (m/z) 495.2284, found (m/z) 495.2267.

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$[\alpha]_D^{23} = -18.4$ (MeOH , $c=1$); ^1H NMR (400 MHz, CD_3OD) δ MeOH : 1.17 (s, 3H), 1.20 (s, 3H), 1.29 (dd, $J=2.0, 14.8$ Hz, 1H), 1.72 (dd, $J=9.9, 14.8$ Hz, 1H), 2.49 (dd, $J=9.0, 13.1$ Hz, 1H), 2.57 (dd, $J=9.0, 13.1$ Hz, 1H), 3.24 (s, 3H), 3.85 (s, 3H), 4.19 (dd, $J=2.0, 9.9$ Hz, 1H), 4.51 (t, $J=9.0$ Hz, 1H), 6.62 (d, $J=2.0$ Hz, 1H), 6.70 (dd, $J=2.0, 8.4$ Hz, 1H), 7.32 (d, $J=8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ MeOH : 22.2, 25.0, 40.8, 42.6, 49.6, 56.0, 59.1, 61.3, 63.7, 75.1, 98.9, 108.4, 121.3, 125.8, 144.2, 162.5, 172.3, 178.6; IR (NaCl/neat) 2968, 1716, 1633, 1600, 1507, 1456, 1346, 1193, 1156 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{18}\text{H}_{25}\text{O}_5\text{N}_2$ (m/z) 349.1764, found (m/z) 349.1778.

methyl ester of **10**

$[\alpha]_{\text{D}}^{25} = -32.0$ (CHCl_3 , $c=1$); ^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : 0.96 (dd, $J = 2.0, 14.3$ Hz, 1H), 1.05 (s, 3H), 1.13 (s, 3H), 1.28 (dd, $J = 9.7, 14.3$ Hz, 1H), 2.30 (dd, $J = 9.0, 13.1$ Hz, 1H), 2.50 (dd, $J = 6.8, 13.1$ Hz, 1H), 3.11 (s, 3H), 3.72 (dd, $J = 2.0, 9.7$ Hz, 1H), 3.77 (s, 3H), 3.80 (s, 3H), 4.12 (dd, $J = 6.8, 9.0$ Hz, 1H), 6.46 (d, $J = 2.1$ Hz, 1H), 6.54 (dd, $J = 2.1, 8.1$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 1H), 7.80 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : 24.3, 25.6, 39.8, 41.2, 49.2, 52.3, 55.5, 57.4, 57.7, 62.4, 74.3, 96.9, 107.0, 124.0, 125.7, 141.0, 159.8, 175.8, 179.7; IR (NaCl/neat) 2972, 2359, 1711, 1633, 1558, 1506, 1457, 1341, 1194, 1153, 1020, 771 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{19}\text{H}_{27}\text{O}_5\text{N}_2$ (m/z) 363.1920, found (m/z) 363.1923.

methyl ester of **10**; H/D exchange

$[\alpha]_{\text{D}}^{25} = -17.6$ (CHCl_3 , $c=0.25$); ^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : 0.96 (d, $J = 14.0$ Hz, 1H), 1.05 (s, 3H), 1.13 (s, 3H), 1.28 (dd, $J = 8.8, 14.0$ Hz, 1H), 2.31 (d, $J = 12.6$ Hz, 1H), 2.50 (d, $J = 12.6$ Hz, 1H), 3.12 (s, 3H), 3.73 (d, $J = 8.8$ Hz, 1H), 3.78 (s, 3H), 3.80 (s, 3H), 6.45 (d, $J = 2.3$ Hz, 1H), 6.55 (dd, $J = 2.3, 8.2$ Hz, 1H), 7.35 (d, $J = 8.2$ Hz, 1H), 7.54 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : 24.2, 25.6, 39.7, 41.2, 49.3, 52.4, 55.5, 57.3, 57.7, 62.4, 74.3, 97.0, 107.0, 123.9, 125.8, 140.9, 159.9, 175.7, 179.5; IR (NaCl/neat) 1710, 1630, 1505, 1461, 1270, 1244, 1193, 1153, 1122 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{19}\text{H}_{25}\text{DO}_5\text{N}_2$ (m/z) 363.1904, found (m/z) 363.1906.

methyl ester of *epi*-**10**; H/D exchange

$[\alpha]_D^{25} = -18.6$ (CHCl₃, c=0.167); ¹H NMR (400 MHz, CDCl₃) δ CHCl₃: 1.02 (d, J= 14.4 Hz, 1H), 1.08 (s, 3H), 1.10 (s, 3H), 1.31 (dd, J= 9.2, 14.4 Hz, 1H), 2.13 (d, J= 13.8 Hz, 1H), 2.76 (d, J= 13.8 Hz, 1H), 3.09 (s, 3H), 3.54 (d, J= 9.2 Hz, 1H), 3.77 (s, 3H), 3.79 (s, 3H), 6.44 (d, J= 2.4 Hz, 1H), 6.54 (dd, J= 2.4, 8.0 Hz, 1H), 7.24 (bs, 1H), 7.41 (d, J= 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ CHCl₃: 24.3, 25.4, 38.0, 40.6, 41.2, 49.2, 52.3, 55.5, 57.4, 65.0, 74.1, 97.0, 107.1, 123.4, 125.7, 140.9, 159.8, 175.7, 180.1; IR (NaCl/neat) 1722, 1630, 1506, 1463, 1275, 1194, 1155, 1123, 1077 cm⁻¹; HRMS (FAB+) calcd for C₁₉H₂₅DO₅N₂ (*m/z*) 363.1904, found (*m/z*) 363.1910.

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$[\alpha]_D^{25} = -60.0$ (CHCl₃, c=0.33); ¹H NMR (400 MHz, CDCl₃) δ CHCl₃: 0.93 (s, 6H), 1.86-2.24 (m, 5H), 2.30-2.66 (m, 3H), 2.83 (s, 3H), 3.57 (dd, J= 5.4, 8.2 Hz, 2H), 3.79 (s, 3H), 4.20-4.27 (m, 2H), 4.77 (t, J= 8.8 Hz, 1H), 6.43 (s, 1H), 6.54 (d, J= 8.4 Hz, 1H), 7.04 (d, J= 8.4 Hz, 1H), 7.64 (bs, 1H); ¹³C NMR (100 MHz, CDCl₃) δ CHCl₃: 23.3, 23.6, 24.9, 27.9, 30.0, 34.9, 40.8, 45.0, 48.7, 55.5, 58.4, 59.8, 61.4, 74.0, 97.1, 106.5, 121.4, 126.3, 142.0, 160.2, 166.7, 168.1, 181.4; IR (NaCl/neat) 1716, 1665, 1633, 1506, 1461, 1343, 1193, 1157, 732 cm⁻¹; HRMS (FAB+) calcd for C₂₃H₃₀O₅N₃ (*m/z*) 428.2185, found (*m/z*) 428.2193.

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$[\alpha]_D^{25} = -77.0$ (CHCl_3 , $c=0.2$); ^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : 1.02 (s, 3H), 1.19 (s, 3H), 1.76-1.86 (m, 2H), 1.87-2.08 (m, 3H), 2.41-2.53 (m, 3H), 2.93 (s, 3H), 3.40 (ddd, $J=3.6, 9.4, 12.4$ Hz, 1H), 3.80 (s, 3H), 3.94 (dt, $J=12.4, 8.3$ Hz, 1H), 4.22 (dd, $J=5.4, 11.4$ Hz, 1H), 4.61 (t, $J=8.8$ Hz, 1H), 4.81 (t, $J=6.8$ Hz, 1H), 6.47 (s, 1H), 6.54 (d, $J=8.2$ Hz, 1H), 7.09 (d, $J=8.2$ Hz, 1H), 7.58 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : 21.7, 23.2, 24.7, 30.0, 40.6, 40.7, 44.7, 48.5, 54.8, 55.5, 58.8, 60.7, 61.0, 74.4, 97.5, 106.7, 121.3, 125.9, 142.0, 160.3, 163.6, 165.8, 181.0; IR (NaCl/neat) 2927, 1718, 1653, 1506, 1456, 1343, 1303, 1194, 1157 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{23}\text{H}_{30}\text{O}_5\text{N}_3$ (m/z) 428.2185, found (m/z) 428.2193.

1, spirotryprostatin A

$[\alpha]_D^{25} = -30.5$ (CHCl_3 , $c=0.2$); ^1H NMR (400 MHz, CDCl_3) δ CHCl_3 : 1.17 (s, 3H), 1.64 (s, 3H), 1.86-2.08 (m, 2H), 2.20-2.39 (m, 2H), 2.38 (dd, $J=7.2, 13.5$ Hz, 1H), 2.60 (dd, $J=10.7, 13.5$ Hz, 1H), 3.50-3.68 (m, 2H), 3.79 (s, 3H), 4.27 (t, 8.4 Hz, 1H), 4.77 (d, $J=9.0$ Hz, 1H), 4.99 (dd, $J=7.2, 10.7$ Hz, 1H), 5.02 (d, $J=9.0$ Hz, 1H), 6.41 (d, $J=2.4$ Hz, 1H), 6.49 (dd, $J=2.4, 8.5$ Hz, 1H), 6.92 (d, $J=8.5$ Hz, 1H), 7.48 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ CHCl_3 : 18.0, 23.7, 25.5, 27.4, 34.4, 45.2, 55.5, 58.5, 60.2, 60.2, 61.0, 96.6, 106.7, 118.7, 121.4, 127.3, 138.4, 141.6, 160.4, 167.1, 168.2, 180.5; IR (NaCl/neat) 2924, 1716, 1669, 1653, 1635, 1507, 1457, 1419, 1340, 1157 cm^{-1} ; HRMS (FAB+) calcd for $\text{C}_{22}\text{H}_{26}\text{O}_4\text{N}_3$ (m/z) 396.1923, found (m/z) 396.1909.

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$[\alpha]_D^{25} = -25.0$ (CHCl₃, c=0.1); ¹H NMR (400 MHz, CDCl₃) δ CHCl₃: 0.62 (s, 3H), 1.11 (s, 3H), 1.79 (dd, J= 4.3, 15.4 Hz, 1H), 1.92 (dd, J= 4.3, 15.4 Hz, 1H), 1.89-2.10 (m, 2H), 2.16-2.40 (m, 2H), 2.46 (dd, J= 8.7, 13.6 Hz, 1H), 2.65 (dd, J= 8.7, 13.6 Hz, 1H), 3.60 (dd, J= 5.4, 8.2 Hz, 2H), 3.79 (s, 3H), 4.29 (t, J= 8.2 Hz, 1H), 4.36 (t, J= 4.3 Hz, 1H), 4.45 (bs, 1H), 4.87 (t, J= 8.7 Hz, 1H), 6.46 (d, J= 2.4 Hz, 1H), 6.56 (dd, J= 2.4, 8.4 Hz, 1H), 6.97 (d, J= 8.4 Hz, 1H), 7.40 (bs, 1H); ¹³C NMR (100 MHz, CDCl₃) δ CHCl₃: 23.6, 27.0, 27.7, 31.5, 33.9, 43.3, 45.2, 55.5, 59.0, 59.4, 61.0, 68.7, 77.2, 97.5, 107.1, 120.4, 126.3, 142.0, 160.7, 168.1, 168.3, 181.4; IR (NaCl/neat) 2923, 2850, 1717, 1683, 1652, 1636, 1507, 1456, 1433, 1158 cm⁻¹; HRMS (FAB+) calcd for C₂₂H₂₈O₅N₃ (*m/z*) 414.2029, found (*m/z*) 414.2020.

9-*epi*-spiroytryprostatin A (14)

$[\alpha]_D^{25} = +30.0$ (CHCl₃, c=0.4); ¹H NMR (400 MHz, CDCl₃) δ CHCl₃: 1.42 (s, 3H), 1.67 (s, 3H), 1.85-2.10 (m, 2H), 2.30 (dt, J= 5.5, 8.2 Hz, 2H), 2.51 (dd, J= 9.0, 13.4 Hz, 1H), 2.94 (dd, J= 5.2, 13.4 Hz, 1H), 3.57 (ddd, J= 3.5, 8.2, 11.6 Hz, 1H), 3.68 (dt, J= 11.6, 8.2 Hz, 1H), 3.79 (s, 3H), 4.24 (t, J= 8.2 Hz, 1H), 4.62 (dd, J= 5.2, 9.0 Hz, 1H), 5.11 (s, 2H), 6.46 (d, J= 2.3 Hz, 1H), 6.51 (dd, J= 2.3, 8.3 Hz, 1H), 7.01 (d, J= 8.3 Hz, 1H), 7.88 (bs, 1H); ¹³C NMR (100 MHz, CDCl₃) δ CHCl₃: 18.1, 23.3, 25.7, 27.8, 35.9, 45.7, 54.2, 55.5, 58.9, 60.0, 61.6, 97.0, 106.9, 119.1, 119.6, 125.7, 138.4, 142.1, 160.3, 165.6, 166.1, 179.7; IR (NaCl/neat) 1720, 1662, 1598, 1506, 1426, 1342, 1310, 1278, 1193, 1156 cm⁻¹; HRMS (FAB+) calcd for C₂₂H₂₆O₄N₃ (*m/z*) 396.1923, found (*m/z*) 396.1915.