

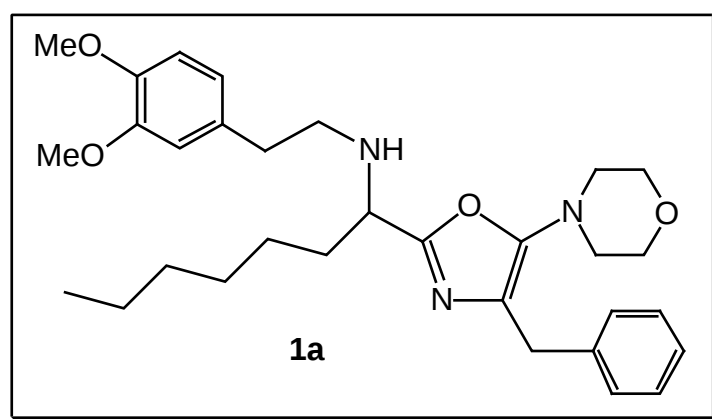
Supporting Information

A Novel Multicomponent Synthesis of Polysubstituted 5-Aminooxazole and Its New Scaffold-generating Reaction to Pyrrolo[3,4-b]pyridine

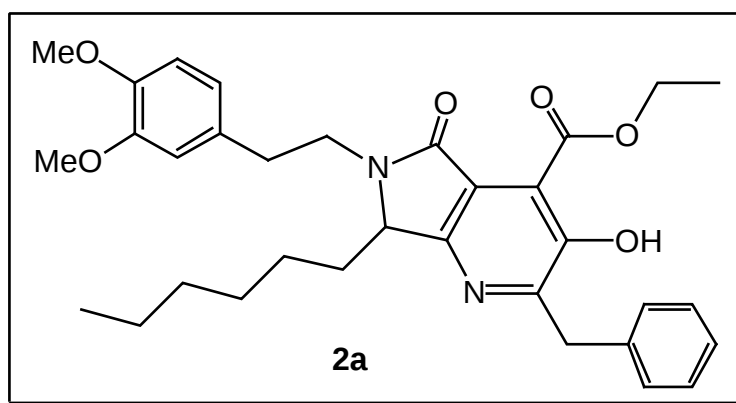
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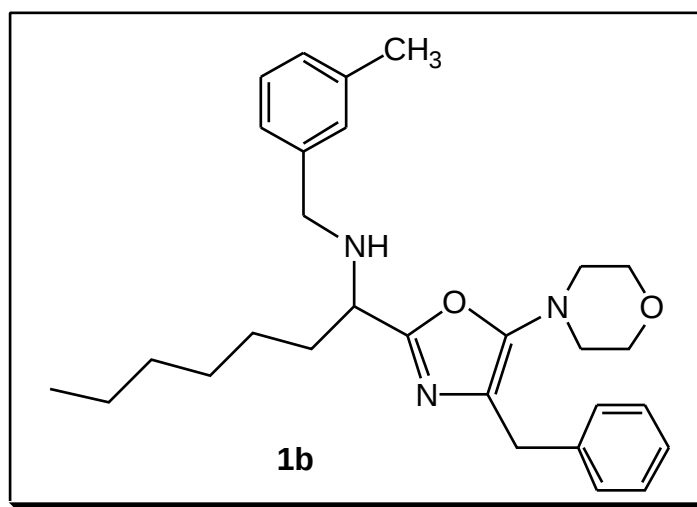
^b Rhône-Poulenc Industrialisation, 24 Av. Jean-Jaures, F-69153 Décines Cedex, France



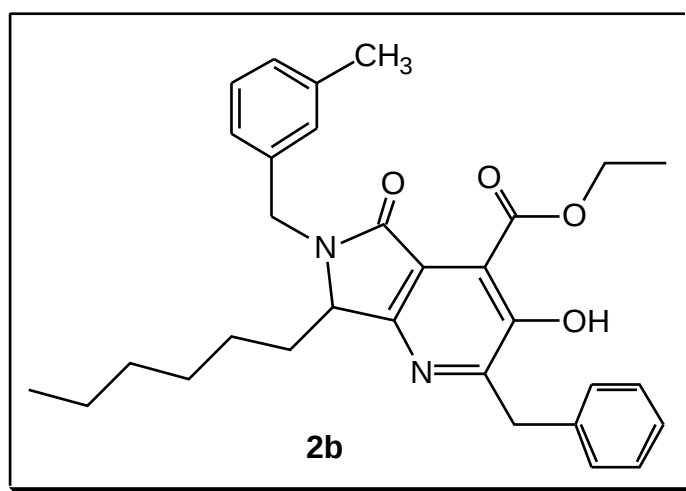
Pale yellow oil, yield: 68%; IR (CHCl₃) ν 3316, 2932, 2859, 1666, 1592, 1516, 1454, 1263, 1114 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 7.13-7.30 (m, 5H), 6.65-6.80 (m, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.81 (s, 2H), 3.71 (m, 5H), 2.93 (m, 4H), 2.60-2.82 (m, 4H), 1.74 (q, J = 7.0 Hz, 2H), 1.23(m, 8H), 0.85 (t, J = 6.5 Hz, 3H); ¹³C NMR (62.5MHz, CDCl₃) δ 160.8, 151.8, 149.0, 147.5, 139.7, 132.6, 128.4, 126.2, 124.4, 120.6, 112.1, 111.4, 67.0, 57.2, 56.0, 55.9, 51.1, 49.1, 36.0, 34.5, 31.9, 31.7, 29.0, 25.9, 22.6, 14.1; MS (EI): m/z 521 (M⁺, 29%).



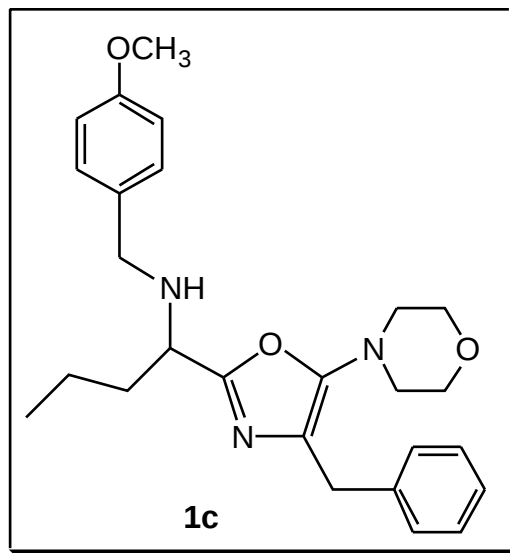
Pale yellow gum, yield: 65%; IR (CHCl₃) ν 3202, 3005, 2934, 1682, 1594, 1516, 1465, 1264, 1195 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 10.57 (s, 1H, OH), 7.15-7.41 (m, 5H), 6.77 (m, 3H), 4.55 (q, J = 7.1 Hz, 2H), 4.33 (d, J = 13.6 Hz, 1H), 4.24 (d, J = 13.6 Hz, 1H), 4.25 (m, 2H), 3.85 (s, 3H), 3.83 (s, 3H), 3.27 (m, 1H), 2.91 (m, 2H), 2.13 (m, 1H), 1.84 (m, 1H), 1.49 (t, J = 7.1 Hz, 3H), 1.15 (m, 6H), 1.06 (m, 1H), 0.83 (t, J = 6.7 Hz, 3H), 0.69 (m, 1H); ¹³C NMR (62.5MHz, CDCl₃): δ 168.8, 164.9, 156.4, 155.7, 153.2, 149.1, 147.8, 138.2, 131.4, 129.2, 128.4, 126.5, 121.2, 120.7, 115.8, 112.0, 111.5, 63.0, 59.4, 55.9, 42.1, 39.4, 34.2, 31.6, 29.5, 29.2, 22.5, 22.4, 14.2, 14.1; MS (EI): m/z 560 (M⁺, 19%).



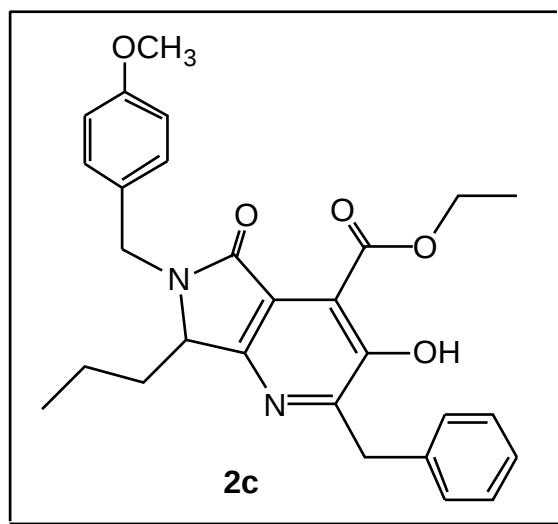
Pale yellow oil, yield: 65%; IR (CHCl₃) ν 3333, 2929, 2860, 1666, 1608, 1496, 1454, 1376, 1236, 1115 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 7.00-7.33 (m, 9H), 3.83 (s, 2H), 3.72 (m, 5H), 3.68 (d, J = 12.8 Hz, 1H), 3.60 (d, J = 12.8 Hz, 1H), 2.96 (m, 4H), 2.32 (s, 3H), 1.77 (q, J = 7.1 Hz, 2H), 1.23 (m, 8H), 0.85 (t, J = 6.4 Hz, 3H); ¹³C NMR (62.5MHz, CDCl₃) δ 161.0, 151.8, 140.0, 139.7, 138.0, 129.1, 128.5, 128.4, 128.3, 127.8, 126.2, 125.4, 124.6, 67.0, 56.6, 51.8, 51.2, 34.5, 31.9, 31.7, 29.0, 25.9, 22.6, 21.4, 14.1; MS (EI): m/z 461 (M⁺, 4%).



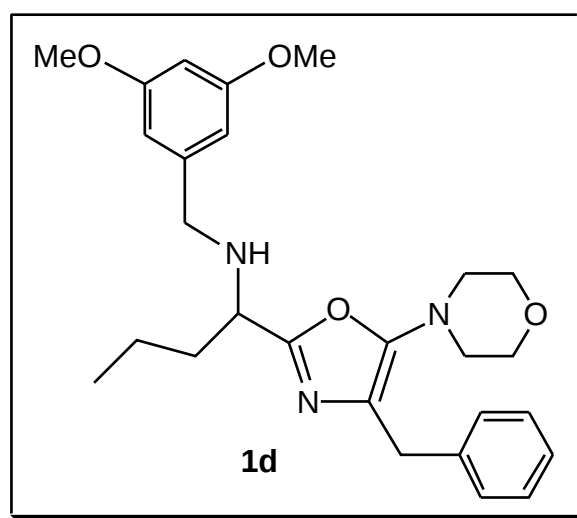
Pale yellow gum, yield: 58%; IR (CHCl₃) ν 3010, 2931, 2860, 1686, 1603, 1466, 1379, 1277, 1199 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 10.61 (s, 1H, OH), 7.00-7.38 (m, 9H), 5.35 (d, *J* = 15.0 Hz, 1H), 4.56 (q, *J* = 7.1 Hz, 2H), 4.28 (m, 3H), 4.08 (d, *J* = 15.0 Hz, 1H), 2.31 (s, 3H), 2.13 (m, 1H), 1.86 (m, 1H), 1.51 (t, *J* = 7.1 Hz, 3H), 1.15 (m, 6H), 1.05 (m, 1H), 0.84 (t, *J* = 6.7 Hz, 3H), 0.70 (m, 1H); ¹³C NMR (62.5MHz, CDCl₃) δ 169.0, 165.1, 156.6, 155.9, 153.3, 138.6, 138.3, 137.0, 129.3, 129.0, 128.7, 128.5, 128.4, 126.5, 125.4, 121.1, 115.9, 63.1, 58.5, 44.1, 39.4, 31.7, 29.2, 22.6, 22.3, 21.5, 14.2, 14.1; MS (ESI): *m/z* 501 (M+H⁺, 67%).



Pale yellow oil, yield: 60%; IR (CHCl₃) ν 3329, 2961, 2839, 1666, 1612, 1513, 1454, 1249, 1114 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 7.20-7.35 (m, 5H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.83 (s, 2H), 3.78 (s, 3H), 3.72 (m, 5H), 3.66 (d, *J* = 12.8 Hz, 1H), 3.57 (d, *J* = 12.8 Hz, 1H), 2.96 (m, 4H), 1.74 (q, *J* = 7.5 Hz, 2H), 1.32 (qt, *J* = 7.3, 7.5 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (62.5MHz, CDCl₃) δ 161.1, 158.7, 151.8, 139.8, 132.3, 129.5, 128.5, 128.5, 126.2, 124.6, 113.8, 67.0, 56.2, 55.3, 51.2, 36.8, 31.9, 19.3, 13.9; MS (ESI): *m/z* 436 (M+H⁺, 85%).

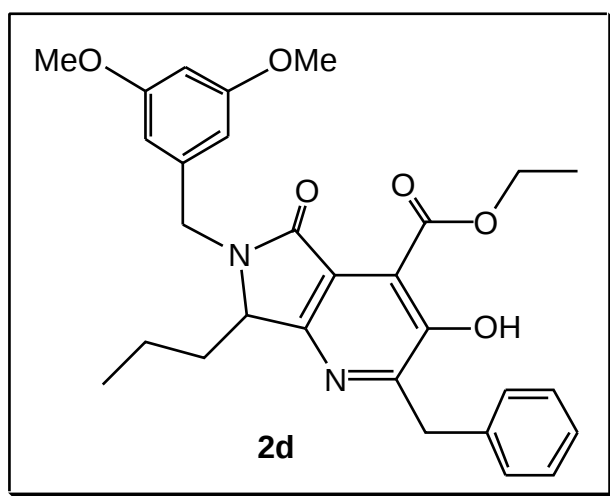


Pale yellow gum, yield: 57%; IR (CHCl₃) ν 3204, 2936, 2839, 1682, 1612, 1513, 1464, 1343, 1175 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 10.55 (br s, 1H, OH), 7.10-7.39 (m, 7H), 6.84 (d, J = 8.6 Hz, 2H), 5.34 (d, J = 14.9 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 4.27 (s, 2H), 4.26 (m, 1H), 4.06 (d, J = 14.9 Hz, 1H), 3.78 (s, 3H), 2.12 (m, 1H), 1.85 (m, 1H), 1.50 (t, J = 7.1 Hz, 3H), 1.14 (m, 1H), 0.82 (m, 4H); ¹³C NMR (62.5MHz, CDCl₃) δ 168.9, 165.0, 159.2, 156.7, 155.8, 153.3, 138.3, 129.6, 129.2, 128.4, 126.5, 121.1, 115.9, 114.2, 63.0, 58.3, 55.4, 43.6, 39.4, 31.5, 15.9, 14.2, 14.1; MS (ESI): m/z 475 (M+H⁺, 100%).

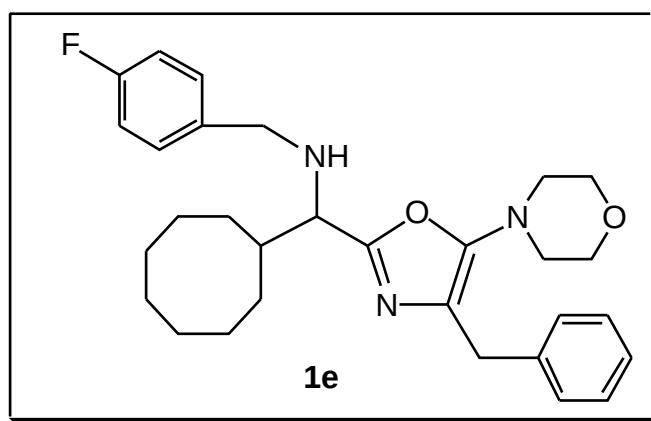


Pale yellow oil, yield: 75%; IR (CHCl₃) ν 3333, 2964, 2842, 1665, 1598, 1455, 1431, 1205, 1155, 1115 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 7.13-7.34 (m, 5H), 6.46 (d, J = 2.3 Hz, 2H), 6.34 (t, J = 2.3 Hz, 1H), 3.83 (s, 2H), 3.76 (s, 6H), 3.72 (m, 5H), 3.70 (d, J = 13.3 Hz, 1H), 3.59 (d, J = 13.3 Hz, 1H), 2.96 (m, 4H), 1.76 (q, J = 7.5 Hz, 2H), 1.35 (qt, J = 7.3, 7.5 Hz, 2H), 0.89 (t, J = 7.3

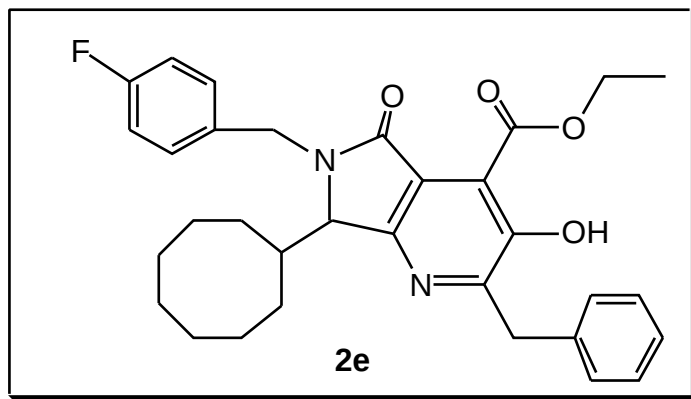
Hz, 3H); ^{13}C NMR (62.5MHz, CDCl_3) d 160.9, 160.8, 151.8, 142.6, 139.7, 128.4, 126.1, 124.4, 106.0, 99.1, 66.9, 56.1, 55.3, 51.8, 51.1, 36.7, 31.9, 19.3, 13.9; MS (EI): m/z 465 (M^+ , 16%).



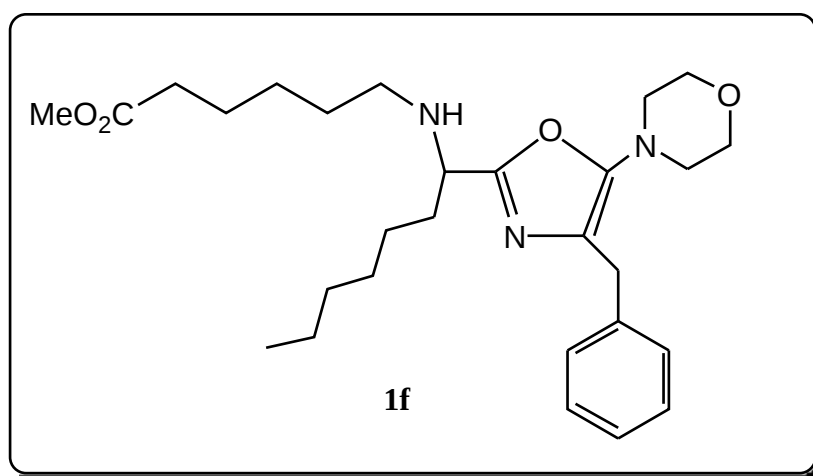
Pale yellow solid, mp 101-103°, yield: 68%; IR (CHCl_3) ν 3198, 2936, 2840, 1682, 1598, 1464, 1343, 1158 cm^{-1} ; ^1H NMR (250MHz, CDCl_3) d 10.57 (s, 1H, OH), 7.15-7.39 (m, 5H), 6.42 (d, J = 2.2 Hz, 2H), 6.36 (t, J = 2.2 Hz, 1H), 5.34 (d, J = 15.4 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 4.33 (dd, J = 3.3, 5.4 Hz, 1H), 4.28 (s, 2H), 4.04 (d, J = 15.4 Hz, 1H), 3.76 (s, 6H), 2.12 (m, 1H), 1.86 (m, 1H), 1.50 (t, J = 7.1 Hz, 3H), 1.15 (m, 1H), 0.82 (m, 4H); ^{13}C NMR (62.5MHz, CDCl_3) d 168.9, 165.0, 161.2, 156.6, 155.9, 153.2, 139.4, 138.2, 129.2, 128.4, 126.5, 120.9, 115.9, 106.3, 99.4, 63.0, 58.5, 55.4, 44.2, 39.4, 31.5, 15.9, 14.1, 14.1; MS (ESI): m/z 505 ($\text{M}+\text{H}^+$, 66%)



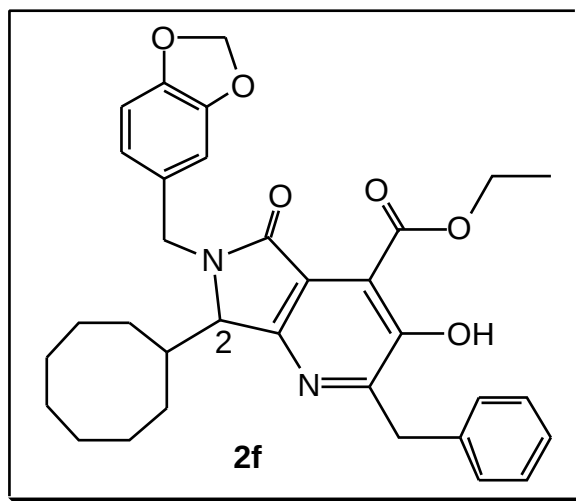
Pale yellow oil, yield: 60%; IR (CHCl_3) ν 3334, 2922, 2851, 1667, 1602, 1510, 1454, 1374, 1115 cm^{-1} ; ^1H NMR (250MHz, CDCl_3) d 7.13-7.32 (m, 5H), 7.08 (m, 2H), 6.93 (m, 2H), 3.82 (s, 2H), 3.73 (m, 4H), 3.47 (d, J = 7.2 Hz, 1H), 2.93 (m, 4H), 2.58-2.82 (m, 4H), 1.18-2.00 (m, 15H); ^{13}C NMR (62.5MHz, CDCl_3) d 161.5 (d, J = 242.3 Hz), 160.7, 151.8, 139.8, 135.8, 130.1 (d, J = 7.5 Hz), 128.4, 126.1, 124.4, 115.1 (d, J = 21.1 Hz), 67.0, 63.1, 51.2, 49.6, 41.8, 35.6, 31.8, 29.5, 29.4, 27.0, 26.8, 26.6, 26.0, 25.7; MS (ESI): m/z 506 ($\text{M}+\text{H}^+$, 85%).



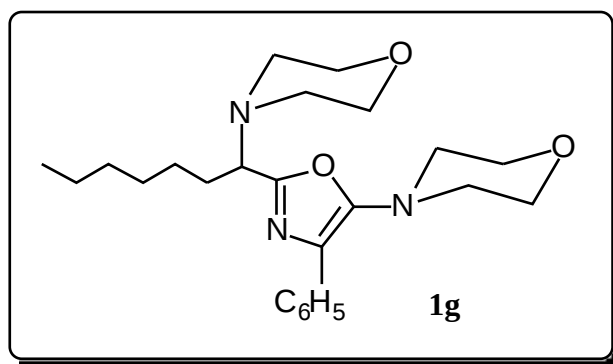
Pale yellow gum, yield: 66%; IR (CHCl₃) ν 3020, 2926, 1682, 1602, 1510, 1463, 1378, 1193 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 10.55 (s, 1H, OH), 7.12-7.40 (m, 7H), 6.98 (t, J = 8.6 Hz, 2H), 4.55 (q, J = 7.2 Hz, 2H), 4.38 (d, J = 13.4 Hz, 1H), 4.22 (m, 1H), 4.17 (d, J = 13.4 Hz, 1H), 4.15 (d, J = 3.1 Hz, 1H), 3.32 (m, 1H), 2.92 (m, 2H), 2.25 (m, 1H), 1.96 (m, 1H), 1.49 (t, J = 7.2 Hz, 3H), 1.07-1.80 (m, 11H), 0.84 (m, 2H); ¹³C NMR (62.5MHz, CDCl₃) δ 168.9, 165.3, 161.8 (d, J = 242.8 Hz), 156.0, 155.4, 153.1, 138.3, 134.6, 130.2 (d, J = 7.5 Hz), 129.4, 128.4, 126.5, 121.4, 115.7, 115.5 (d, J = 20.8 Hz), 65.5, 63.0, 42.4, 39.3, 38.9, 33.9, 30.1, 27.3, 26.65, 26.56, 26.50, 26.3, 26.1, 14.2; MS (ESI): m/z 545 (M+H⁺, 53%).



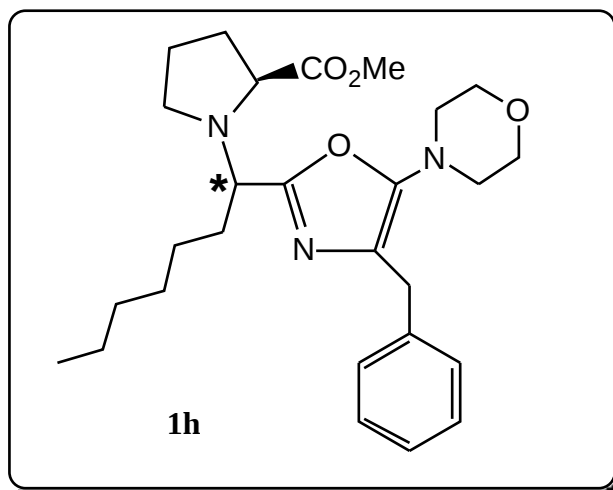
Yield: 65%; IR (CHCl₃) ν 3019, 2954, 2931, 2860, 1731, 1661, 1643, 1586, 1495, 1454, 1438, 1375, 1302, 1264, 1222, 1212, 1160, 1114, 1000, 909 cm⁻¹; ¹H NMR (250 MHz, CDCl₃) δ 7.26 (m, 5H), 3.86 (s, 2H), 3.76 (m, 4H), 3.72 (t, J = 4.9 Hz, 1H), 3.69 (s, 3H), 3.01 (m, 4H), 2.54 (t, J = 7.4 Hz, 2H), 2.33 (t, J = 7.4 Hz, 2H), 1.80 (q, J = 6.9 Hz, 2H), 1.64 (qt, J = 7.4 Hz, 2H), 1.20-1.50 (m, 12 H), 0.90 (t, J = 6.5 Hz, 3H); ¹³C NMR (62.5 MHz, CDCl₃) δ 174.1, 160.0, 152.0, 139.5, 128.3, 126.1, 124.3, 66.8, 57.1, 53.4, 51.4, 51.0, 47.2, 34.0, 33.9, 31.7, 31.6, 92.4, 14.1; MS (ES⁺): m/z 486 (M+H)⁺



Pale yellow solid, mp 109-111°, yield: 58%; IR (CHCl₃) ν 3009, 2925, 1690, 1601, 1490, 1377, 1246, 1197 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 10.57 (s, 1H, OH), 7.12-7.40 (m, 5H), 6.75 (m, 3H), 5.92 (d, *J* = 1.8 Hz, 2H), 5.28 (d, *J* = 15.0 Hz, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 4.34 (d, *J* = 14.1 Hz, 1H), 4.17 (d, *J* = 14.1 Hz, 1H), 4.14 (d, *J* = 2.8 Hz, 1H), 4.08 (d, *J* = 15.0 Hz, 1H), 2.28 (m, 1H), 1.97 (m, 1H), 1.50 (t, *J* = 7.1 Hz, 3H), 1.05-1.80 (m, 12H), 0.83 (m, 1H); ¹³C NMR (62.5MHz, CDCl₃) δ 169.0, 165.5, 156.3, 155.5, 153.1, 148.2, 147.1, 138.3, 131.1, 129.4, 128.4, 126.5, 121.5, 121.2, 115.7, 108.7, 108.4, 101.2, 64.5, 63.0, 44.2, 39.3, 38.4, 30.3, 27.0, 26.6, 26.4, 26.3, 26.1, 14.2; MS (ESI): *m/z* 557 (M+H⁺, 100%).

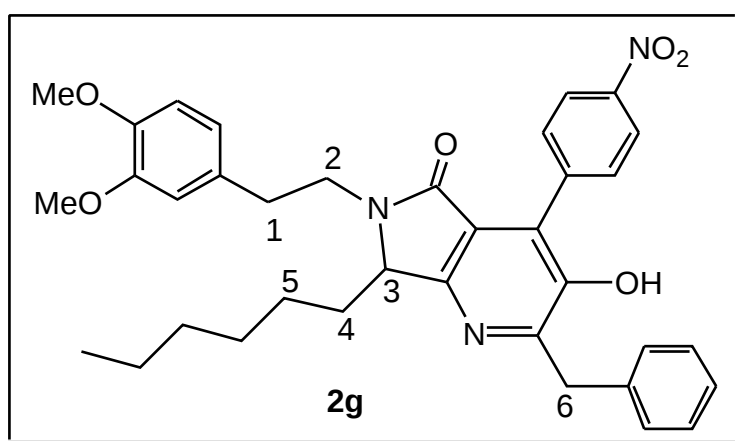


Yield 90%; IR (CHCl₃) ν 2961, 2860, 1637, 1497, 1453, 1374, 1263, 1194, 1115, 1070, 985, 911, 862 cm⁻¹; ¹H NMR (250 MHz, CDCl₃) δ 7.93 (m, 2H), 7.39 (m, 2H), 7.25 (m, 1H), 3.86 (m, 4H), 3.61 - 3.73 (m, 5H), 3.11 (m, 4H), 2.52 - 2.61 (m, 4H), 1.90 (m, 2H), 1.26 - 1.31 (m, 8H), 0.87 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (62.5 MHz, CDCl₃) δ 157.8, 150.7, 131.8, 128.3, 126.8, 125.9, 123.5, 67.2, 66.8, 63.1, 50.3, 50.0, 31.5, 29.7, 28.9, 26.1, 22.5, 13.9; MS (EI), *m/z* 413 (M⁺, 3%), 328 (15), 184 (100), 126 (7).



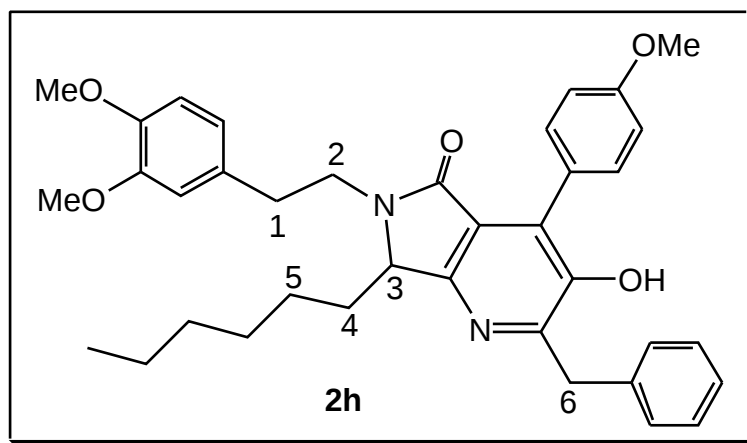
Diastereomer A: yield 68%; $[\alpha]_D = -44.8^\circ$; IR (CHCl₃) ν 3025, 3019, 2956, 2929, 2860, 1736, 1665, 1635, 1495, 1454, 1437, 1375, 1262, 1221, 1204, 1177, 1114, 1030, 920 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.23 (m, 5H), 3.95 (t, $J = 7.3$ Hz 1H), 3.81 (s, 2H), 3.71 (m, 4H), 3.69 (s, 3H), 3.44 (dd, $J = 8.1$ Hz, 6.4 Hz, 1H) 3.08 (m, 1H), 2.94 (m, 4H), 2.66 (m, 1H), 1.95-1.60 (m, 8H), 1.37-1.21 (m, 6H), 0.86 (m, 3H); ¹³C NMR (62 MHz, CDCl₃) δ 174.7, 158.7, 151.9, 139.8, 128.5, 128.4, 126.2, 124.2, 66.9, 62.8, 58.3, 51.8, 51.1, 47.4, 31.8, 29.4, 29.1, 23.6, 22.7, 14.2; MS (ES⁺): m/z (M+Na)⁺ 492.

Diastereomer B: yield 28%; $[\alpha]_D = -25.7^\circ$; IR (CHCl₃) ν 3026, 3016, 2957, 2929, 2859, 1736, 1664, 1635, 1495, 1454, 1436, 1375, 1262, 1228, 1205, 1174, 1114, 1030, 928 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.23 (m, 5H), 3.83-3.77 (m, 4H), 3.72 (m, 4H), 3.69 (s, 3H), 3.20 (m, 1H), 2.96 (m, 4H), 2.63 (m, 1H), 1.95-1.60 (m, 8H), 1.33-1.15 (m, 6H), 0.84 (m, 3H); ¹³C NMR (62 MHz, CDCl₃) δ 175.5, 158.7, 151.7, 139.5, 128.2, 125.9, 124.0, 66.7, 60.9, 60.6, 52.2, 51.5, 50.9, 32.1, 31.6, 31.4, 30.4, 29.5, 28.8, 26.0, 23.9, 22.3, 13.9; MS (ES⁺): m/z (M+Na)⁺ 492.

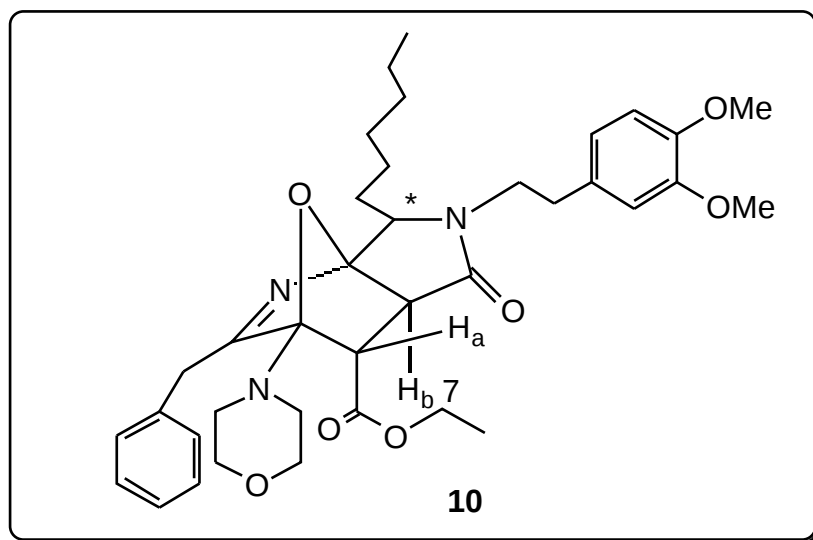


Yellow solid, mp 161-163°, yield: 63%; IR (CHCl₃) ν 3553, 3022, 2935, 2860, 1678, 1604, 1518, 1465, 1350, 1263, 1157 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 8.33 (d, $J = 8.8$ Hz, 2H), 7.62

(d, $J = 8.8$ Hz, 2H), 7.18-7.39 (m, 5H), 6.75 (m, 3H), 5.19 (s, 1H, OH), 4.42 (dd, $J = 3.3, 5.3$ Hz, 1H), 4.36 (d, $J = 14.2$ Hz, 1H), 4.29 (d, $J = 14.2$ Hz, 1H), 4.10 (m, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.28 (m, 1H), 2.86 (m, 2H), 2.20 (m, 1H), 1.90 (m, 1H), 1.22 (m, 7H), 0.90 (m, 1H), 0.86 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (62.5MHz, CDCl_3) d 166.1, 157.6, 153.2, 149.1, 148.2, 147.8, 146.7, 138.0, 136.8, 131.4, 131.1, 130.3, 129.0, 128.7, 126.9, 123.6, 121.3, 120.7, 112.0, 111.5, 59.9, 56.0, 41.9, 40.1, 34.3, 31.7, 29.6, 29.2, 22.64, 22.6, 14.1; MS (ESI): m/z 610 ($\text{M}+\text{H}^+$, 100%).



Pale yellow gum, yield: 55%; IR (CHCl_3) ν 3529, 3022, 2935, 2859, 1678, 1610, 1516, 1464, 1258, 1150 cm^{-1} ; ^1H NMR (250MHz, CDCl_3) d 7.16-7.40 (m, 7H), 7.04 (d, $J = 8.8$ Hz, 2H), 6.75 (m, 3H), 5.50 (s, 1H, OH), 4.38 (dd, $J = 3.3, 5.1$ Hz, 1H), 4.33 (d, $J = 13.7$ Hz, 1H), 4.25 (d, $J = 13.7$ Hz, 1H), 4.11 (m, 1H), 3.85 (s, 6H), 3.80 (s, 3H), 3.26 (m, 1H), 2.86 (m, 2H), 2.19 (m, 1H), 1.88 (m, 1H), 1.19 (m, 7H), 0.85 (m + t $J = 6.6$ Hz, 4H); ^{13}C NMR (62.5MHz, CDCl_3): d 166.7, 160.6, 157.3, 152.0, 149.1, 147.8, 147.1, 138.9, 131.9, 131.4, 131.2, 129.1, 128.4, 126.4, 121.5, 121.1, 120.7, 114.7, 112.0, 111.5, 59.8, 56.0, 55.4, 42.0, 39.9, 34.4, 31.7, 29.7, 29.3, 22.6, 14.1; MS (ESI): m/z 695 ($\text{M}+\text{H}^+$, 100%).



Two diastereomeres were produced and one of them was isolated in pure form (relative stereochemistry unknown): pale yellow gum, yield: 45%; IR (CHCl₃) ν 3011, 2934, 2859, 1732, 1681, 1594, 1516, 1455, 1263, 1119 cm⁻¹; ¹H NMR (250MHz, CDCl₃) δ 7.10-7.35 (m, 5H), 6.75 (m, 3H), 4.27 (dq, J = 7.1, 10.9 Hz, 1H), 4.11 (dq, J = 7.1, 10.9 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.83 (m, 1H), 3.60-3.78 (m, 5H), 3.68 (d, J = 16.4 Hz, 1H), 3.54 (d, J = 16.4 Hz, 1H), 3.37 (d, J = 4.1 Hz, 1H, Ha), 3.21 (m, 1H), 3.01 (m, 2H), 2.98 (d, J = 4.1 Hz, 1H, Hb), 2.82 (m, 2H), 2.57 (m, 2H), 1.82 (m, 2H), 1.57 (m, 1H), 1.20-1.48 (m, 10H), 0.89 (t, J = 6.6 Hz, 3H); ¹³C NMR (62.5MHz, CDCl₃) δ 178.3, 171.4, 169.3, 149.0, 147.8, 135.5, 131.3, 129.4, 128.4, 126.9, 121.0, 112.1, 111.3, 108.1, 101.3, 67.0, 61.7, 60.8, 56.03, 55.98, 53.0, 48.8, 43.3, 35.5, 33.5, 31.7, 29.6, 29.4, 25.3, 22.6, 14.3, 14.2; MS (IC): m/z 648 (M+H⁺, 100%).