

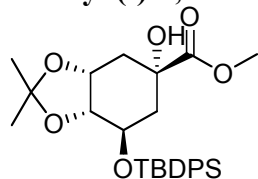
Progress Towards the Total Synthesis of Trichodermamide A and B: the Construction of the Oxazine Moiety

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Supporting Information

1

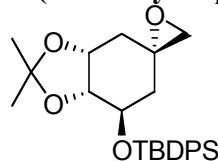
Methyl (-)-3, 4-*O*- isopropylidene-5-*O*-(*tert*-butyldiphenylsilyl)quinate



A mixture of Methyl (-)-3,4-*O*- Isopropylidenequininate (11.27 g, 45.8 mmol) and imidazole (9.36 g, 137.4 mmol) was dissolved in 100 ml dry CH₂Cl₂ and cooled down to 0°C. To this solution, was added dropwise 14.28 ml *tert*-butyldiphenylchlorosilane. The reaction mixture was allowed to gradually warm up to rt and stirred over night. The reaction was then quenched with saturated NH₄Cl aqueous solution and the organic layer was separated, washed with brine, dried with Na₂SO₄ and then concentrated under vacuum. The crude product was purified by column chromatography (50% EtOAc/50% Hexanes, *R_f* 0.77) to give a colorless oil **3** (22.20 g, 100%). ¹H NMR (CDCl₃): δ 7.76-7.73 (4 H, m), 7.67-7.64 (6 H, m), 4.48-4.44 (1 H, m), 4.20-4.15 (1 H, m), 4.10-4.07 (1 H, m), 3.72 (3 H, s), 3.18 (1 H, b), 2.31 (1 H, dd, *J* = 4.6, 15.4 Hz), 2.14 (1 H, dd, *J* = 2.0, 15.4 Hz), 1.95-1.84 (2 H, m), 1.28 (3 H, s), 1.18 (3 H, s), 1.10 (9 H, s); ¹³C NMR (CDCl₃): δ 174.7, 136.0, 135.7, 134.0, 133.3, 129.5, 127.4, 108.6, 79.6, 73.8, 73.5, 69.8, 52.6, 39.9, 34.1, 27.4, 26.8, 25.6, 19.1; HRMS (ESI): Calculated for C₂₇H₃₆O₆Si :484.2281, Found (*M* + Na⁺): 507.2178; IR(cm⁻¹): 3502 (b), 3071 (m), 3048 (m), 2983 (m), 2955 (s), 2932 (s), 2892 (m), 2857 (s), 1736 (s), 1589 (w), 1472 (m), 1428 (s), 1381 (m), 1368 (m), 1240 (s), 1218 (s), 1163 (m), 1112 (s), 1056 (s), 1011 (m), 966 (w), 940 (w), 922 (m), 862 (w), 831 (m), 802 (m); [α]_D²⁰ = -52.0°:

2

5-(*tert*-Butyl-diphenyl-silanyloxy)-6, 7-*O*-isopropylidene-1-Oxa-spiro[2.5]octane

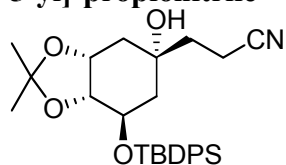


To a solution containing the corresponding mesylate (9.50 g, 17.8 mmol) in 200 ml dry THF which was cooled down to 0°C, was added dropwise LiHMDS (21.3 ml, 1 M solution in THF). The solution was allowed to warm up to rt and stirred for 0.5 h. The reaction was quenched with saturated NH₄Cl aqueous solution and the organic layer was separated. The aqueous layer was extracted with EtOAc twice and the organic layers were combined, washed

with brine, dried with Na₂SO₄ and concentrated under vacuum. The crude product was purified by column chromatography (30% EtOAc/70% Hexanes, *R_f* 0.53) to give white crystals **6** (6.62 g, 85%). ¹H NMR (CDCl₃): δ 7.68-7.61 (4 H, m), 7.47-7.33 (6 H, m), 4.52 (1 H, dt, *J* = 4.2, 6.2 Hz), 4.18-4.08 (2 H, m), 2.61 (1 H, d, *J* = 4.8 Hz), 2.48 (1 H, d, *J* = 4.8 Hz), 2.39 (1 H, dd, *J* = 4.2, 15.0 Hz), 1.94 (1 H, dd, *J* = 2.8, 14.2 Hz), 1.79 (1 H, dd, *J* = 4.2, 14.0 Hz), 1.53-1.46 (1 H, m), 1.40 (3 H, s), 1.29 (3 H, s), 1.08 (9 H, s); ¹³C NMR (CDCl₃): δ 135.7, 135.6, 133.7, 122.3, 129.9, 127.7, 108.6, 76.5, 72.7, 70.0, 53.8, 53.3, 33.8, 33.1, 27.2, 26.9, 24.8, 19.3; HRMS (ESI) calculated for C₂₆H₃₄O₄Si: 438.2226, Found: IR(cm⁻¹): [α]_D²⁰ = 0.10° (c = 2.02, CHCl₃); mp: 94-96°C

3

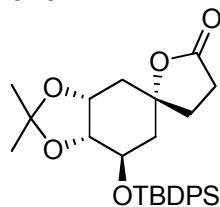
3-[7-(*tert*-Butyl-diphenyl-silanyloxy)-5-hydroxy-2,2-dimethyl-hexahydro-benzo[1,3]dioxol-5-yl]-propionitrile



The reaction was carried out in Ar atmosphere. To a solution containing *n*-BuLi (16.5 ml, 33.0 mmol, 2 M in cyclohexane) in 100 ml dry THF, was added dropwise diisopropylamine (4.66 ml, 33.0 mmol) at -78°C to make a fresh LDA/THF solution. Dry MeCN (1.6 ml, 30.0 mmol) was then added dropwise into the fresh LDA/THF solution and the solution was stirred for 1 h at -78°C until white slurry appeared. A THF solution containing the epoxide **2** (6.57 g, 15.0 mmol, in 20 ml THF) was cannulated into the slurry and the reaction mixture was allowed to warm up gradually from -78°C to rt. The reaction was then quenched with saturated NH₄Cl aqueous solution and the organic layer was separated. The aqueous layer was extracted with EtOAc twice and the organic layers were combined, washed with brine, dried with Na₂SO₄ and concentrated under vacuum. The crude product was purified by column chromatography (30% EtOAc/70% Hexanes, *R_f* 0.48) to give a colorless oil **7** (6.69 g, 93%). ¹H NMR (CDCl₃): δ 7.72-7.61 (4 H, m), 7.47-7.32 (6 H, m), 4.48 (1 H, penta, *J* = 3.0 Hz), 4.11-4.00 (2 H, m), 2.39-2.31 (1 H, m), 2.22-2.15 (1 H, m), 2.12-2.06 (1 H, m), 1.89 (1 H, dd, *J* = 6.8, 3.2 Hz), 1.82-1.74 (1 H, m), 1.70-1.63 (2 H, m), 1.43-1.37 (1 H, m), 1.29 (3 H, s), 1.23 (3 H, s), 1.08 (9 H, s); ¹³C NMR (CDCl₃): δ 136.0, 135.8, 134.0, 133.2, 129.9, 129.8, 127.7, 127.6, 127.5, 120.4, 108.7, 78.9, 73.9, 70.2, 69.9, 40.6, 38.4, 35.4, 27.4, 27.0, 25.9, 19.8, 10.8; HRMS (ESI) calculated for C₂₈H₃₇NO₄Si: Found (M + Na⁺): 502.2389 IR(cm⁻¹): 3500 (b), 3070 (m), 3044 (m), 2931 (s), 2857 (m), 2247 (w), 1472 (m), 1427 (s), 1382 (m), 1241 (m), 1218 (m), 1112 (s), 1045 (s), 1007 (w), 920 (m), 827 (m), 740 (m), 703 (s); [α]_D²⁰ = -124.5° (c = 1.43, CHCl₃)

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7-(*tert*-Butyl-diphenyl-silanyloxy)-8,9-*O*-isopropylidene-1-oxa-spiro[4.5]decan-one

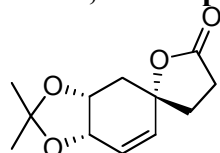


The nitrile **3** (14.78 g, 30.8 mmol) was dissolved in 200 ml dry MeOH and the solution was cooled down to 0°C. To this solution, was added all at once NaOMe (5.0 g, 92.4 mmol). The solution was allowed to warm up to rt, stirred for 3 h and neutralized with AcOH (5.29 ml, 92.4 mmol). The solution was then diluted with EtOAc and water, and the mixture was stirred for 4 h and monitored by TLC until the reaction completed. The organic layer was separated. The

aqueous layer was extracted with EtOAc twice and the organic layers were combined, washed with brine, dried with Na₂SO₄ and concentrated under vacuum. The crude product was purified by column chromatography (50% EtOAc/50% hexanes, *R_f* 0.55) to give a colorless oil **8** (10.60 g, 97% based the recovery of 3.90 g starting material). ¹H NMR (CDCl₃): δ 7.72-7.62 (4 H, m), 7.47-7.35 (6 H, m), 4.36 (1 H, dd, *J* = 5.8, 10.4 Hz), 4.22-4.15 (1 H, m), 3.98 (1 H, t, *J* = 10.4 Hz), 2.44-2.35 (1 H, m), 2.31-2.20 (1 H, m), 2.19-2.13 (1 H, m), 2.13-2.06 (1 H, m), 2.05-1.94 (2 H, m), 1.78 (1 H, dd, *J* = 2.9, 7.0 Hz), 1.54 (1 H, dd, *J* = 3.7, 7.0 Hz), 1.36 (3 H, s), 1.25 (3 H, s), 1.09 (9 H, s); ¹³C NMR (CDCl₃): δ 176.0, 135.9, 135.7, 133.8, 133.1, 130.0, 127.9, 127.7, 108.8, 84.1, 77.8, 72.2, 69.6, 38.1, 37.2, 34.7, 28.0, 27.7, 27.0, 25.4, 19.0 HRMS (ESI) calculated for C₂₈H₃₆O₅Si: Found (*M* + Na⁺): 503.2230; IR(cm⁻¹): 3075 (w), 3054 (w), 2931 (m), 2857 (m), 1773 (s), 1471 (m), 1427 (m), 130 (m), 1188 (m), 1110 (s), 1073 (m), 1048 (m), 914 (m), 823 (m), 738 (m), 702 (s); [α]_D²⁰ = -4.5° (c = 1.06, CHCl₃)

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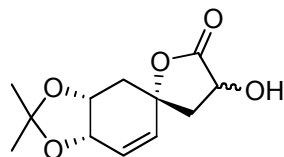
Δ^{6,7}-**8**, 9-*O*-isopropylidene-1-oxa-spiro[4.5]decan-2-one



The **7-Methanesulfonyloxy-8, 9-*O*-isopropylidene-1-oxa-spiro[4.5]decan-2-one** (1.55 g, 4.83 mmol) and DBU (7.22 ml, 48.3 mmol) was added to 42 ml toluene to form a suspension in microwave tube. The suspension was heated up to 150°C in about 15 min. in microwave and hold at this temperature for 20 min. The brown color solution was then cooled down to rt and diluted with toluene. Then solution was then washed with 5% HCl aqueous solution, saturated NaHCO₃ solution and brine in sequence, dried with Na₂SO₄ and concentrated under vacuum. The crude product was purified by column chromatography (50% EtOAc/50% hexanes, *R_f* 0.39) to give white crystals **11** (0.88 g, 81%). ¹H NMR (CDCl₃): δ 6.00-5.90 (2 H, m), 4.49 (1 H, dd, *J* = 2.6, 5.8 Hz), 4.39-4.31 (1 H, m), 2.65-2.60 (2 H, m), 2.18-2.04 (4 H, m), 1.48 (3 H, s), 1.38 (3 H, s); ¹³C NMR (CDCl₃): δ 175.9, 133.6, 126.3, 110.3, 82.7, 71.4, 70.0, 36.7, 33.0, 28.3, 28.0, 26.0; HRMS (ESI) calculated for C₁₂H₁₆O₄, Found (*M* + H⁺): 225.1120; IR(cm⁻¹): 3036 (w), 2985 (m), 2935 (m), 2874 (m), 1774 (m), 1457 (m), 1422 (m), 1400 (m), 1381 (m), 1372 (m), 1296 (m), 1240 (s), 1218 (s), 1189 (s), 1153 (s), 1066 (s), 1026 (s), 912 (m), 869 (m), 797 (m); [α]_D²⁰ = 44.6° (c = 0.84, CHCl₃); mp: 99-100°C

6

3-Hydroxyl-Δ^{6,7}-**8**, 9-*O*-isopropylidene-1-oxa-spiro[4.5]decan-2-one

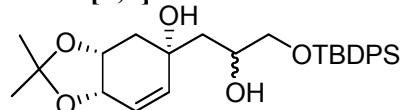


To a solution containing KHMDS (13.38 ml, 0.5 M solution in toluene) in 50 ml dry THF which was cooled down to -78°C, was added dropwise to a solution containing compound **5** (0.50 g, 2.2 mmol) while stirring, the solution turned dark blue gradually. The solution was allowed to stir at -78°C for 0.5 h, then Molybdenum pentaoxide · HMPA · Pyridine complex (MoOPH 1.94 g, 4.5 mmol) was added all at once. The reaction mixture was allowed to gradually warm up to rt and stirred for 2 h. The reaction was then quenched with Sat. Na₂SO₃ aqueous solution and the organic layer was separated. The aqueous layer was saturated with NaCl and extracted 4 times with EtOAc. The organic layers were combined, washed with brine, dried with Na₂SO₄ and concentrated under vacuum. The crude product was purified by column chromatography (50%

EtOAc/50% hexanes, R_f 0.17) to give a mixture of inseparable two diastereomers **12** (colorless oil, 0.36 g, 67%). ^1H NMR (CDCl_3): δ 6.00-5.83 (2 H, m), 4.68-4.60 (1 H, m), 4.52-4.48 (1 H, m), 4.43-4.34 (1 H, m), 3.60 (1 H, b), 2.56-2.44, 2.36-2.30 (1 H, m, diastereomeric), 2.23-2.00 (3 H, m), 1.48 (3 H, s), 1.38 (3 H, s) ^{13}C NMR (CDCl_3), (two sets): δ 177.0, 176.9, 134.0, 131.4, 128.1, 126.8, 110.5, 110.3, 80.5, 79.8, 71.4, 71.0, 69.9, 67.6, 67.5, 42.5, 40.5, 37.8, 36.5, 28.0, 27.9, 26.1, 26.0; HRMS (ESI) calculated for $\text{C}_{12}\text{H}_{16}\text{O}_5$: Found ($\text{M}-\text{Me}^+$): 225.0761; IR(cm^{-1}): 3418 (m, b), 2985 (m), 2926 (m), 2858 (m), 1773 (s), 1456 (m), 1383 (m), 1372 (m), 1240 (s), 1206 (s), 1123 (m), 1066 (m), 900 (w), 946 (m), 867(m), 762 (w)

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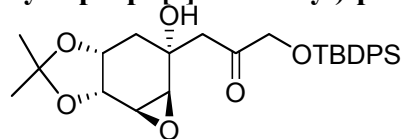
5-[3-(*tert*-Butyl-diphenyl-silanyloxy)-2-hydroxy-propyl]-2,2-dimethyl-3a,4,5,7a-tetrahydro-benzo[1,3]dioxol-5-ol



The α -hydroxyl-lactone **6** (0.17 g, 0.69 mmol) was dissolved in 10 ml absolute EtOH and then NaBH_4 (52 mg, 1.38 mmol) and LiCl (58 mg, 1.38 mmol) were added all at once while stirring. After 1 h, the reaction was quenched with saturated NH_4Cl aqueous solution then diluted with EtOAc. The mixture was kept stirring until all the precipitate dissolved. The organic layer was separated and the aqueous layer was saturated with NaCl and extracted with EtOAc five times. The organic phase was dried with Na_2SO_4 and concentrated under vacuum to give foam-like solids. Without further purification, the crude product was then dissolved in dry 10 ml CH_2Cl_2 at 0°C . Imidazole (93.9 mg, 1.38 mmol) and TBDPSCI (0.18 ml, 0.69 mmol) was then added to the solution in sequence. The reaction mixture was allowed to warm up to rt and stirred over night. The reaction was then quenched with saturated NH_4Cl aqueous solution and the organic layer was separated. The aqueous layer was extracted twice with EtOAc. The organic layers were combined, washed with brine, dried with Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography (30% EtOAc/70% Hexanes, R_f 0.37) to give two inseparable diastereomers **16** (colorless oil, 0.28 g, 85% for two steps). ^1H NMR (CDCl_3): δ 7.68-7.62 (4 H, m), 7.45-7.34 (6 H, m), 5.93 and 5.80 (1 H, d, $J = 10.2$ Hz, diastereomeric), 5.68-5.60 (1 H, m, diastereomeric), 4.53-4.44 (2 H, m), 4.15-4.00 (1 H, m), 3.68-3.50 (2 H, m), 2.49-2.28 (1 H, m), 2.02-1.89 (1 H, m), 1.74-1.61 (2 H, m), 1.45 (3 H, s), 1.37 and 1.36 (3 H, s, diastereomeric), 1.06 (9 H, s); ^{13}C NMR (CDCl_3): (two sets) δ 135.5, 134.6, 134.0, 133.3, 133.2, 129.7, 127.8, 126.0, 125.7, 109.7, 109.6, 73.2, 73.1, 72.1, 71.9, 68.8, 68.6, 68.4, 68.0, 44.0, 43.9, 36.9, 35.0, 28.1, 26.8, 26.5, 26.4, 19.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{38}\text{O}_5\text{Si}$, Found ($\text{M} + \text{Na}^+$): 505.2395; IR(cm^{-1}): 3061 (w), 2982 (w), 2931 (m), 2856 (m), 1427 (m), 1380 (m), 1236 (m), 1223 (m), 1162 (m), 1112 (s), 1041 (m), 885 (w), 824 (m), 740 (m), 702 (s).

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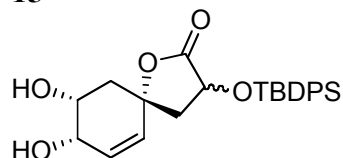
1-(*tert*-Butyl-diphenyl-silanyloxy)-3-(2-hydroxy-5,5-dimethyl-hexahydro-1,4,6-trioxacyclopropa[e]inden-2-yl)-propan-2-one



The diastereomeric epoxide **7** (23 mg, 0.046 mmol) was dissolved in 2 ml dry CH_2Cl_2 then NaHCO_3 (20 mg, 0.23 mmol) and Dess-Martin Reagent (39 mg, 0.092 mmol) were added in sequence. The reaction completed in 0.5 h. The reaction was then quenched with saturated Na_2SO_3 aqueous solution and the organic layer was separated. The aqueous layer was extracted twice with EtOAc. The organic layers were combined, washed with brine, dried with Na_2SO_4

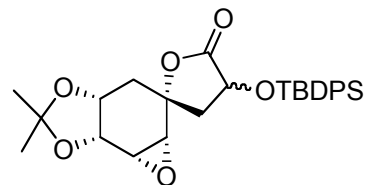
and concentrated under vacuum. The crude product was purified by column chromatography (30% EtOAc/70% Hexanes, R_f 0.44) to give a single diastereomer **20** (colorless oil, 20 mg, 87%). ^1H NMR (CDCl_3): δ 7.71-7.60 (4 H, m), 7.45-7.29 (4 H, m), 4.40-4.23 (4 H, m), 3.91 (1 H, s), 3.21 (1 H, d, J = 3.6 Hz), 3.10 (1 H, dd, J = 1.2, 3.6 Hz), 2.62 (1 H, d, J = 3.6 Hz), 2.59 (1 H, d, J = 3.6 Hz), 2.01-1.95 (1 H, m), 1.73 (1 H, dd, J = 2.0, 5.6 Hz), 1.47 (3 H, s), 1.35 (3 H, s), 1.11 (9 H, s); ^{13}C NMR (CDCl_3): δ 206.3, 135.7, 135.6, 132.9, 129.8, 127.7, 109.2, 72.5, 71.2, 70.2, 69.2, 56.9, 53.6, 47.0, 28.7, 27.8, 26.8, 25.3, 19.3; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{36}\text{O}_6\text{Si}$: 496.2281, Found: ; IR(cm^{-1}): 3490 (b), 3071 (w), 2985 (m), 2931 (s), 2857 (m), 1730 (s), 1588 (w), 1472 (m), 1428 (s), 1376 (s), 1322 (w), 1223 (m), 1152 (m), 1113 (s), 1083(m), 938 (w), 882 (m), 835 (m), 741 (m), 703 (s); $[\alpha]_D^{20}$ (need to be added)

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The corresponding acetone (0.563g, 1.18 mmol) was dissolved in a round-bottom flask containing 21 ml AcOH / THF / H_2O (3:2:2 volume ratio). The flask was then immersed into an oil bath which was pre-equilibrated at 45°C under the protection of Ar. The reaction mixture was heated at 45°C for 8 h. Then the reaction was cooled to rt, neutralized with NaHCO_3 , extracted with EtOAc, and washed with brine. The crude product was purified by column chromatography (50% EtOAc/hexanes, R_f 0.25) to give 0.42 g pure colorless oil as two inseparable diastereomers, while 0.11 g starting material was recovered. (Yield: 81%, but almost quantitative based on recovered starting material). ^1H NMR (CDCl_3): δ 7.79-7.77 (2 H, m), 7.68-7.66 (2 H, m), 7.48-7.37 (6 H, m), 5.93 (dd, J = 3.6, 10.2 Hz), 5.83 (d, J = 10.1 Hz), 5.79 (dd, J = 2.9, 10.1 Hz), 5.45 (d = 10.1 Hz) (from 5.93 to 5.45, totally 2 H), 4.51-4.46 (1 H, m), 4.11-4.03 (1 H, m), 3.92 (m), 3.75-3.71 (m) (from 53.92 to 3.71, totally 1 H), 2.63 (2 H, br), 2.41 (dd, J = 7.1, 14.3 Hz), 2.15-2.00 (m) (from 2.41 to 2.0, totally 3 H), 1.73 (1 H, dd, J = 2.8, 13.6 Hz), 1.10 (9 H, s); ^{13}C NMR (CDCl_3): δ 174.0, 173.9, 135.9, 135.6, 132.9, 132.2, 131.9, 131.8, 131.3, 130.2, 129.1, 127.9, 127.8, 79.5, 78.9, 68.8, 68.7, 66.5, 66.4, 66.3, 65.8, 43.5, 42.8, 39.4, 37.7, 26.6, 19.1; HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{30}\text{O}_5\text{Si}$: 438.1863, Found ($\text{M} + \text{Na}^+$): 461.1752; IR(cm^{-1}): 3395(m, b), 3072 (w), 3040 (w), 2932 (m), 2858 (m), 1784 (s), 1589 (w), 1472 (m), 1428 (s), 1255 (m), 1152 (s), 1112 (s), 1030 (m), 911 (m), 823 (m), 737 (m), 702 (s)

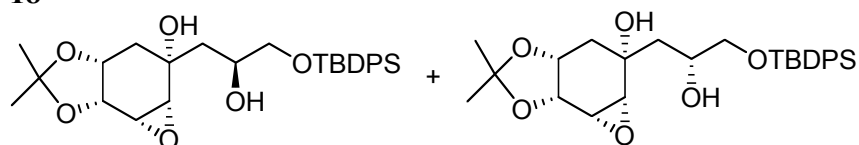
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Compound **16** (0.118 g, 0.26 mmol) was dissolved in 5 ml acetone then 1ml 2,2-dimethoxypropane and 5.2 mg $\text{TsOH} \cdot \text{H}_2\text{O}$ (0.026 mmol) were added in sequence. The mixture was stirred at rt and monitored by TLC until the reaction completed. The reaction was quenched with saturated NaHCO_3 solution, extracted with EtOAc. The organic layer was separated, washed with brine and dried with Na_2SO_4 . The crude product was concentrated and purified by column chromatography (30% EtOAc / Hexanes, R_f 0.39 and 0.385) to give a mixture of two diastereomers that were not separated. ^1H NMR (CDCl_3): δ 7.80-7.76 (2 H, m), 7.70-7.66 (2 H, m), 7.50-7.39 (6 H, m), 4.52-4.43 (1 H, m), 4.34-4.30 (1 H, m), 4.12-4.07 (m), 3.95-3.89 (m) (these two sets of peaks added up to 1 H), 3.49 (dd, J = 3.2, 3.9 Hz), 3.40-3.39 (m), 3.00 (d, J = 3.2 Hz), 2.27 (0.5 H dd, J = 11.3, 11.7 Hz), 2.12-1.90 (3H, m), 1.60 (0.5 H, dd, J = 12.3, 12.7

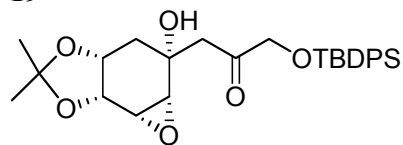
Hz), 1.52 and 1.48 (3 H, s), 1.33 and 1.30 (3 H, s), 1.102 and 1.100 (9 H, s); ^{13}C NMR (CDCl_3) (theoretically two sets): δ 173.5, 135.9, 135.8, 135.6, 132.9, 131.5, 130.3, 127.9, 127.8, 109.8, 81.7, 81.2, 71.4, 71.3, 69.0, 68.6, 56.9, 56.4, 56.1, 52.1, 52.0, 39.1, 38.0, 35.6, 34.1, 27.1, 27.0, 25.2, 24.9, 24.8, 19.1; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{34}\text{O}_6\text{Si}$: 494.2125, Found ($\text{M} + \text{Na}^+$): 617.2003; IR (cm^{-1}): 3072 (w), 2933 (m), 2858 (m), 1787 (s), 1588 (w), 1472 (m), 1427 (s), 1381 (m), 1370 (m), 1259 (m), 1211 (m), 1145 (s), 1112 (s), 1068 (m), 1009 (m), 914 (m), 856 (m), 822 (m), 743 (m), 702 (s)

18



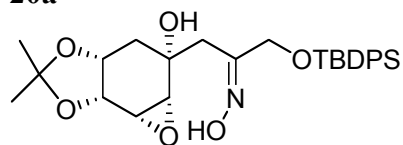
Compound **24** (0.196 g, 0.40 mmol) was dissolved in 10 ml EtOH and the solution was cooled to -15°C . CeCl_3 (0.391 g, 1.59 mmol) was added all at once to the solution and stirred for 10 min. NaBH_4 (60 mg, 1.59 mmol) was then added and the mixture was stirred around -15°C for 30 min. The reaction was then quenched with saturated NH_4Cl solution and extracted with EtOAc. The organic phase was washed with brine and dried over Na_2SO_4 . The four diastereomeric lactols obtained (0.156 g) were concentrated and dried under vacuum without further separation. The crude product was dissolved in 10 ml EtOH at 0°C and excess NaBH_4 was added. The reaction was monitored by TLC until all the starting materials were consumed. The reaction was then quenched with saturated NH_4Cl solution and extracted with EtOAc. The organic phase was washed with brine and dried over Na_2SO_4 . The two diastereomers (0.150 g, 0.30 mmol) were separated by column chromatography (30% EtOAc / hexanes, R_f = 0.15 (**25a**), 0.13 (**25b**)). (75% yield for two steps). **25a**: ^1H NMR (CDCl_3): δ 7.67-7.63 (4 H, m), 7.47-7.37 (6 H, m), 4.34 (1 H, dd, J = 3.0, 7.4 Hz), 4.24-4.18 (1 H, m), 4.17-4.12 (1 H, m), 3.63-3.55 (2 H, m), 3.43 (1 H, dd (looked like t), J = 3.6, 3.9 Hz), 3.30 (1 H, d, J = 4.0 Hz), 3.16 (1 H, b), 1.98-1.88 (2 H, m), 1.60 (2 H, d, J = 6.2 Hz), 1.53 (3 H, s), 1.33 (3 H, s), 1.07 (9 H, s); ^{13}C NMR (CDCl_3): δ 135.5, 133.0, 132.9, 129.9, 127.8, 109.3, 71.9, 71.5, 71.2, 68.5, 68.0, 59.0, 53.5, 40.0, 37.3, 26.9, 26.8, 24.8, 19.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{38}\text{O}_6\text{Si}$: 498.2438, Found ($\text{M} + \text{Na}^+$): 521.2279; IR (cm^{-1}): 3440 (m, b), 3070 (w), 3048 (w), 2931 (m), 2858 (m), 1589 (w), 1472 (m), 1462 (m), 1428 (s), 1381 (m), 1258 (m), 1209 (m), 1112 (s), 1055 (s), 966 (w), 912 (m), 834 (m), 740 (m), 703 (s), $[\alpha]_D^{23}$ = 18.2° (c = 1.84, CHCl_3); **25b**: ^1H NMR (CDCl_3): δ 7.66-7.63 (4 H, m), 7.47-7.37 (6 H, m), 4.32 (1 H, dd, J = 3.0, 7.3 Hz), 4.16-4.11 (1 H, m), 4.06 (1 H, dd, J = 7.5, 15.8 Hz), 3.63-3.55 (1 H, m), 3.43 (1 H, dd (looked like t), J = 3.3, 4.0 Hz), 3.31 (1 H, d, J = 4.1 Hz), 3.21 (1 H, b), 1.98-1.95 (2 H, m), 1.69 (1 H, dd, J = 10.2, 15.6 Hz), 1.53 (3 H, s), 1.49 (1 H, dd, J = 1.9, 14.6 Hz), 1.31 (3 H, s), 1.07 (9 H, s); ^{13}C NMR (CDCl_3): δ 135.5, 133.0, 129.91, 129.90, 127.8, 109.3, 71.8, 71.4, 68.8, 67.8, 59.5, 53.0, 38.7, 35.8, 26.9, 26.8, 24.7, 19.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{38}\text{O}_6\text{Si}$: 498.2438, Found ($\text{M} + \text{Na}^+$): 521.2326 IR (cm^{-1}): 3441 (m, b), 3070 (w), 3048 (w), 2931 (m), 2858 (m), 1588 (w), 1472 (m), 1462 (m), 1428 (s), 1381 (m), 1258 (m), 1209 (m), 1112 (s), 1055 (s), 966 (w), 912 (m), 834 (m), 740 (m), 703 (s), $[\alpha]_D^{23}$ = 17.4 (c = 1.65 CHCl_3)

19



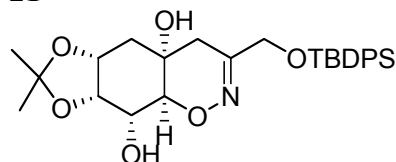
Compound **18** (47.7 mg, 0.096 mmol) was dissolved in 2 ml dry CH_2Cl_2 then NaHCO_3 (40 mg, 0.48 mmol) and Dess-Martin reagent (162 mg, 0.38 mmol) were added in sequence. The mixture was stirred at rt and monitored by TLC until the reaction completed. The mixture was quenched with saturated Na_2SO_3 solution, extracted with EtOAc. The organic layers were combined, washed with brine and dried with Na_2SO_4 . The crude product was concentrated and purified by column chromatography (30% EtOAc / Hexanes, R_f 0.27) to give a colorless oil (43.3 mg, 0.087 mmol, 90%). ^1H NMR (CDCl_3): δ 7.66-7.63 (4 H, m), 7.48-7.37 (6 H, m), 4.34 (1 H, dd, J = 3.0, 7.2 Hz), 4.25 (2 H, s), 4.11 (1 H, m), 3.40 (1 H, dd (looked like t), J = 3.2, 4.0 Hz), 3.30 (1 H, s), 3.25 (1 H, d, J = 4.0 Hz), 2.74 and 2.68 (2 H, d, J = 16.4 Hz), 1.93-1.84 (2 H, m), 1.53 (3 H, s), 1.32 (3 H, s), 1.11 (9 H, s); ^{13}C NMR (CDCl_3): δ 208.6, 135.53, 135.51, 132.4, 132.3, 130.1, 127.9, 109.4, 71.8, 71.5, 70.5, 70.0, 58.7, 53.2, 45.1, 36.3, 26.9, 26.7, 24.9, 19.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{36}\text{O}_6\text{Si}$: 496.2281, Found ($\text{M} + \text{Na}^+$): 519.2185; IR (cm^{-1}): 3446 (m, b), 3071 (w), 2932 (m), 2858 (m), 1726 (s), 1589 (w), 1473 (m), 1428 (s), 1382 (m), 1259 (m), 1210 (M), 1164 (m), 1113 (s), 1056 (s), 909 (m), 824 (m), 740 (m), 704 (s); $[\alpha]_D^{23}$ = 14.1 (c = 1.71 CHCl_3)

20a



Compound **19** (43.3 mg, 0.087 mmol) was dissolved in 1 ml EtOH at rt. To this stirred solution, was added dropwise 0.5 ml aqueous solution containing $\text{NH}_2\text{OH}\cdot\text{HCl}$ (18.2 mg, 0.261 mmol) and NaOAc (21.4 mg, 0.261 mmol). The reaction mixture was stirred at rt and monitored by TLC until all the starting material was consumed. The mixture was then diluted with 10 ml EtOAc and washed with brine. The organic layer was separated and dried with Na_2SO_4 . The crude product was purified by column chromatography (30% EtOAc / Hexanes) to give two separable oximes as colorless oil **27a** (29.0 mg, 0.057 mmol R_f 0.27) and **27b** (14.0 mg, 0.027 mmol, R_f 0.13) Yield: 96%. **27b** could be isomerized back to **27a** at a ratio of 1:2 when heated at 45°C in EtOH/ H_2O solution. Compound **27a**: ^1H NMR (CDCl_3): 7.69-7.63 (4 H, m), 7.46-7.38 (6 H, m), 4.40 (1 H, dd, J = 2.9, 7.3 Hz), 4.36-4.31 (1 H, m), 4.30 (2 H, s), 3.61 (1 H, b), 3.42 (1 H, dd, looked like t, J = 3.4, 3.7 Hz), 3.20 (1H, d, J = 4.1 Hz), 2.82 (1 H, d, J = 13.2 Hz), 2.68 (1 H, d, J = 13.2 Hz), 1.92-1.88 (2 H, m); 1.53 (3 H, s), 1.32 (3 H, s), 1.07 (9 H, s); $\delta^{13}\text{C}$ NMR (CDCl_3): δ 155.9, 135.6, 135.2, 132.3, 132.2, 130.0, 129.9, 127.9, 109.2, 72.0, 71.52, 71.49, 66.0, 59.4, 53.6, 37.1, 33.4, 27.0, 26.7, 24.9, 19.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{37}\text{NO}_6\text{Si}$: 511.2390, Found ($\text{M} + \text{Na}^+$): 534.2309; IR (cm^{-1}): 3406 (b, m), 3072 (w), 3050 (w), 2933 (m), 2858 (m), 1589 (w), 1472 (m), 1462 (m), 1428 (s), 1381 (m), 1370 (m), 1258 (m), 1211 (m), 1166 (m), 1112 (s), 1051 (s), 1007 (m), 940 (m), 911 (m), 856 (w), 823 (m), 737 (s), 703 (s); $[\alpha]_D^{23}$ = 10.9 (c = 1.00 CHCl_3)

21



A THF solution (1 ml) of the oxime **20a** (20 mg, 0.039 mmol) was added dropwise into a freshly prepared LDA/THF solution (containing 0.086 mmol LDA) at -78°C . The solution was warmed up to rt and stirred for around 5 h until all the starting material was consumed (monitored by TLC). The reaction was quenched with saturated NH_4Cl solution and the aqueous phase was extracted with EtOAc. The organic layers were combined, washed with brine and dried with Na_2SO_4 . The crude product was concentrated and purified by column chromatography (50% EtOAc / Hexanes, R_f 0.22) to give a colorless oil (16.5 mg, 0.032 mmol, 83%). ^1H NMR (CDCl_3): δ 7.66-7.64 (4 H, m), 7.47-7.38 (6 H, m), 4.50-4.47 (1 H, m), 4.43 (1 H, dd, $J = 4.2, 7.2$ Hz), 4.34 (1H, d, $J = 12.6$ Hz), 4.28 (1H, d, $J = 12.6$ Hz), 4.09 (1 H, d, $J = 7.6$ Hz, overlapped with a weak broad $-\text{OH}$ peak), 3.69 (1 H, dd, $J = 4.2, 7.6$ Hz), 2.47 (1 H, d, $J = 15.8$ Hz), 2.33 (1 H, d, $J = 15.8$ Hz), 2.12 (1 H, dd, $J = 2.5, 15.5$ Hz), 1.71 (1 H, dd, $J = 3.6, 15.5$ Hz); 1.56 (3 H, s), 1.37 (3 H, s), 1.07 (9 H, s); ^{13}C NMR (CDCl_3): δ 165.5, 135.6, 135.5, 132.6, 132.5, 130.0, 127.9, 109.0, 81.9, 73.2, 72.8, 70.4, 67.2, 64.4, 34.8, 34.4, 26.8, 26.0, 23.5, 19.2; HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{37}\text{NO}_6\text{Si}$: 511.2390, Found ($\text{M} + \text{Na}^+$): 534.2039; IR (cm^{-1}): 3483 (b, s), 3071 (m), 2931 (s), 2857 (s), 2249 (m), 1627 (m), 1589 (m), 1472 (m), 1383 (m), 1259 (m), 1213 (m), 1161 (m), 1113 (s), 1017 (m), 913 (m), 738 (m), 703 (s); $[\alpha]_D^{24} = -20.0$ (c = 2.02 CHCl_3)

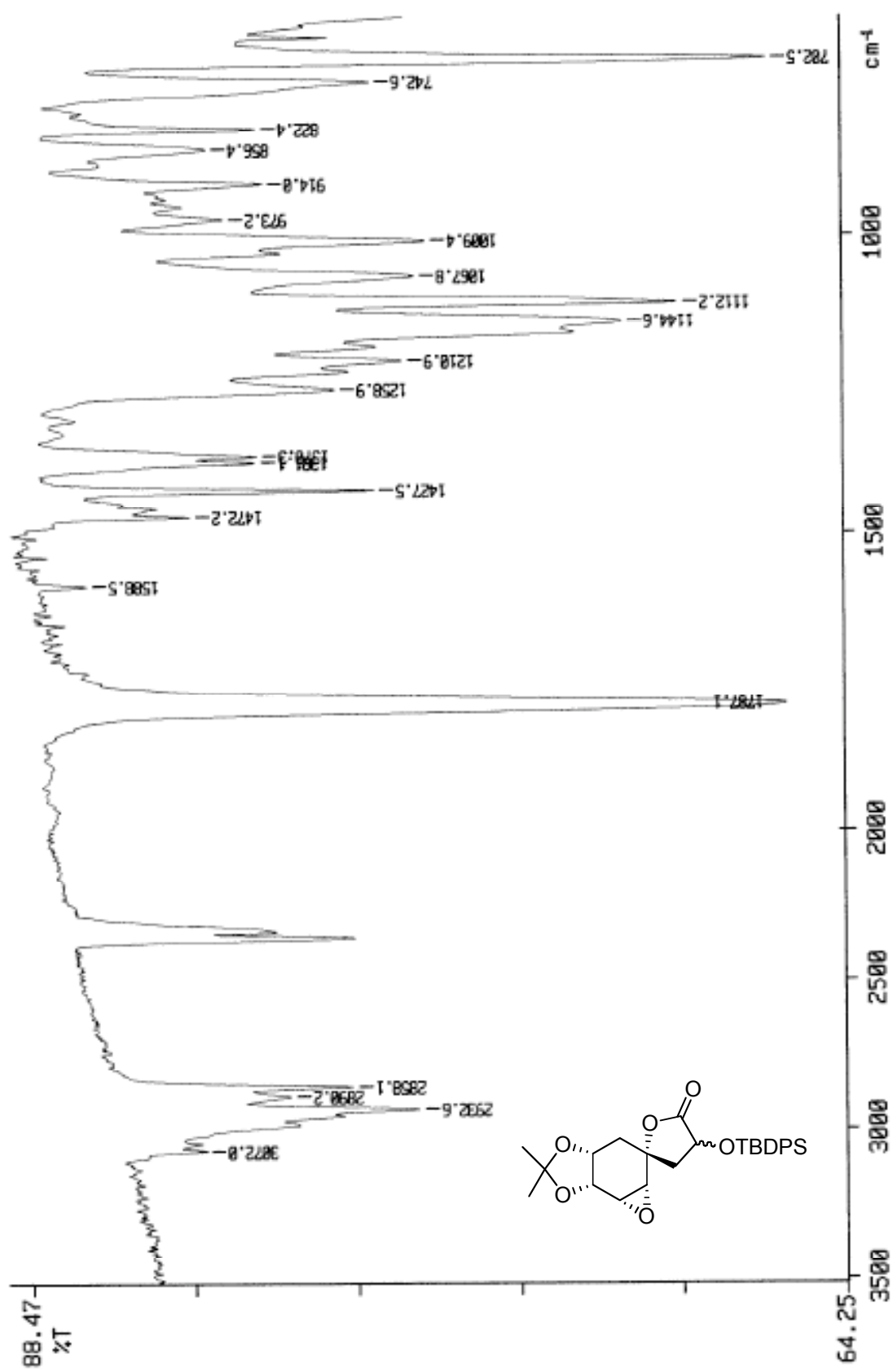


Figure 3: IR spectrum of compound 17.

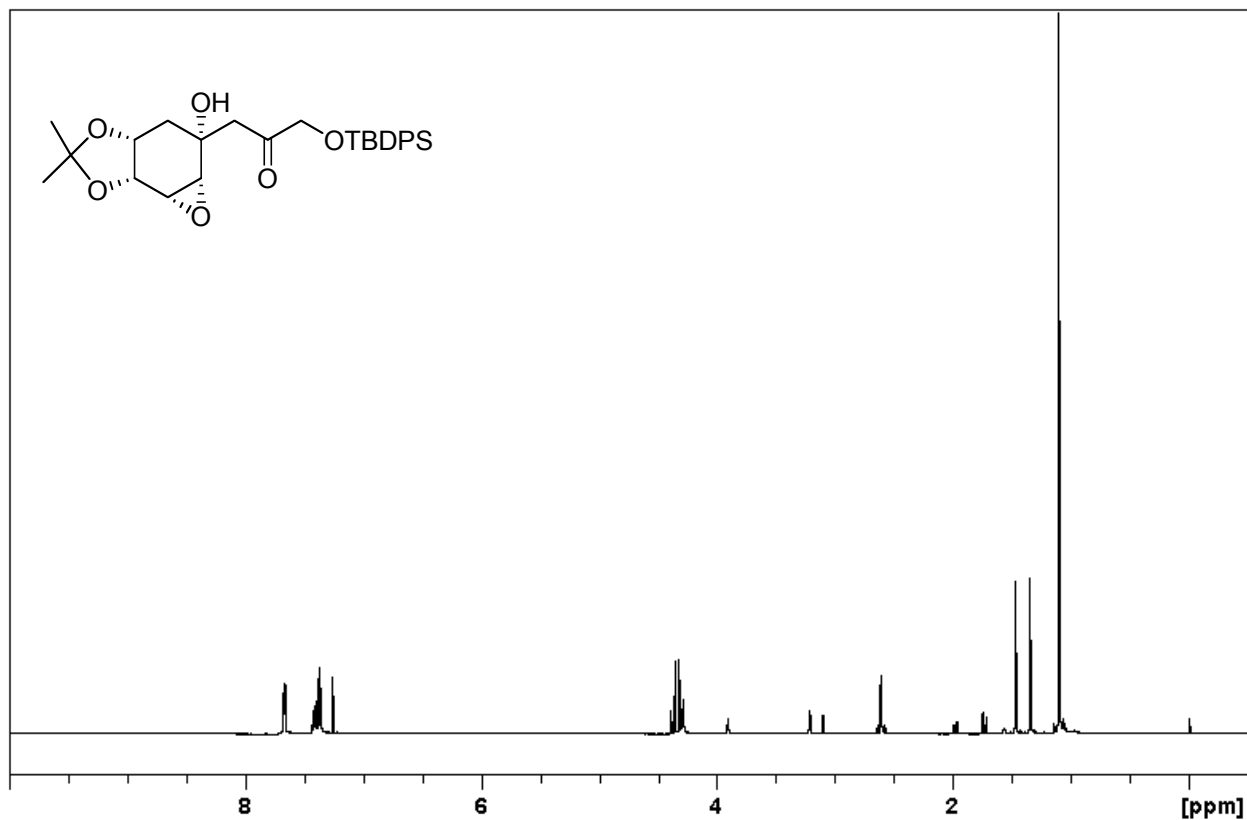


Figure 4: ^1H NMR spectrum of compound **19**.

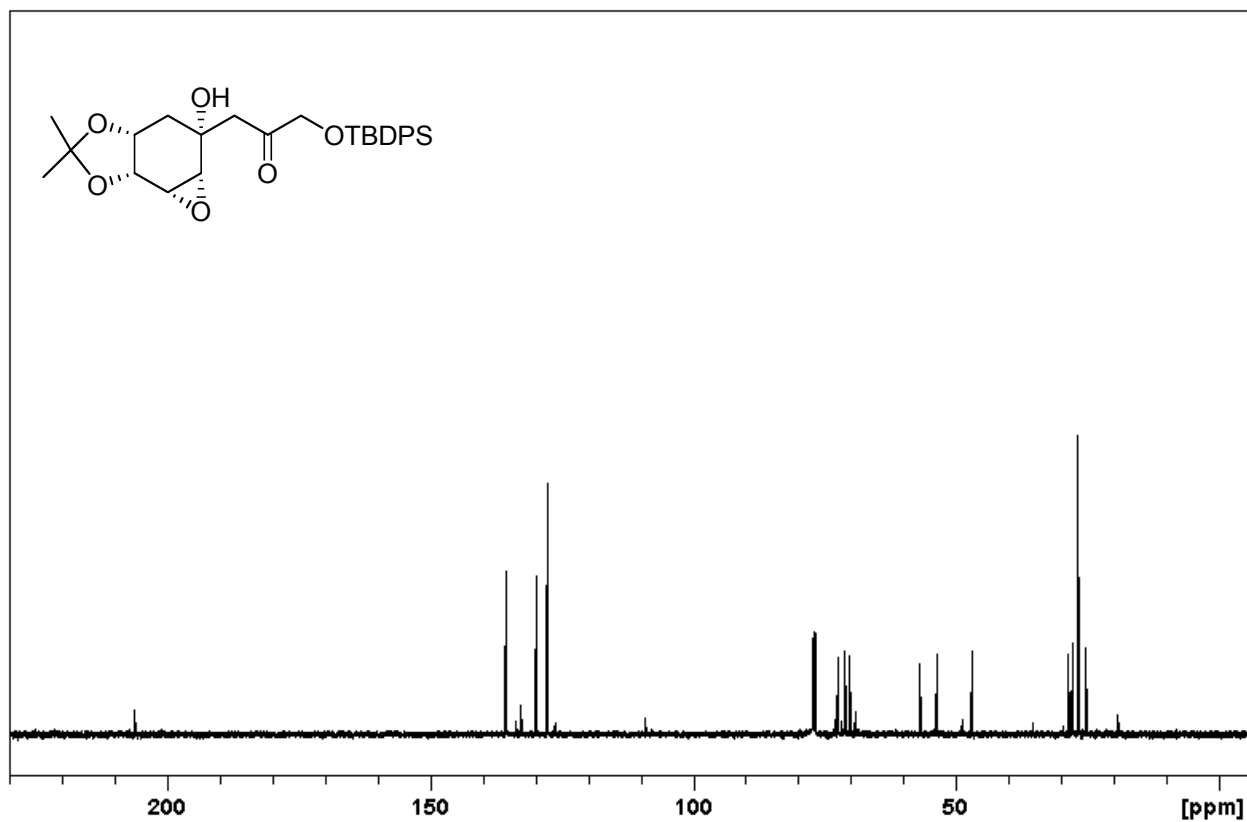


Figure 5: ^{13}C NMR spectrum of compound **19**.

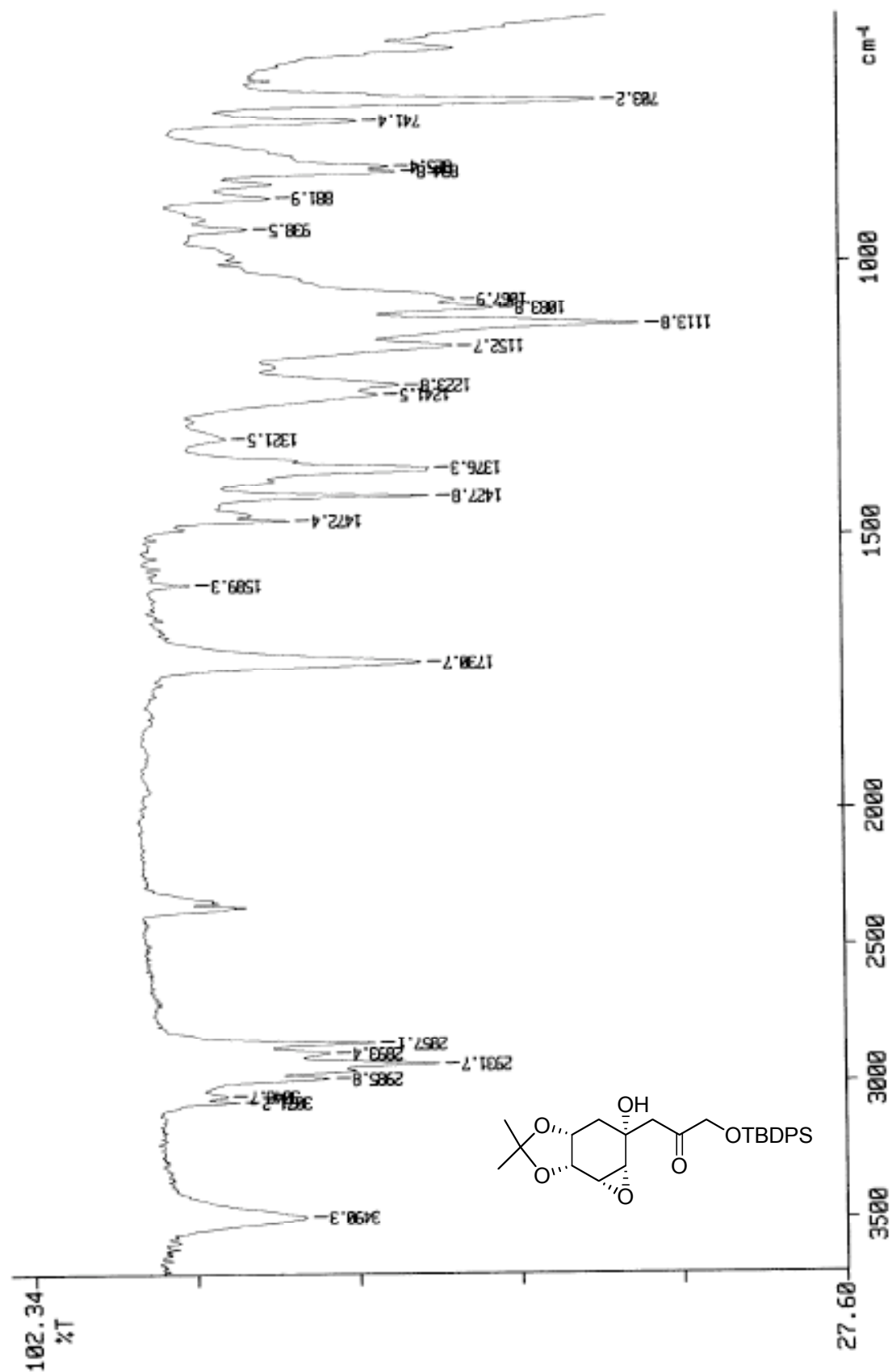
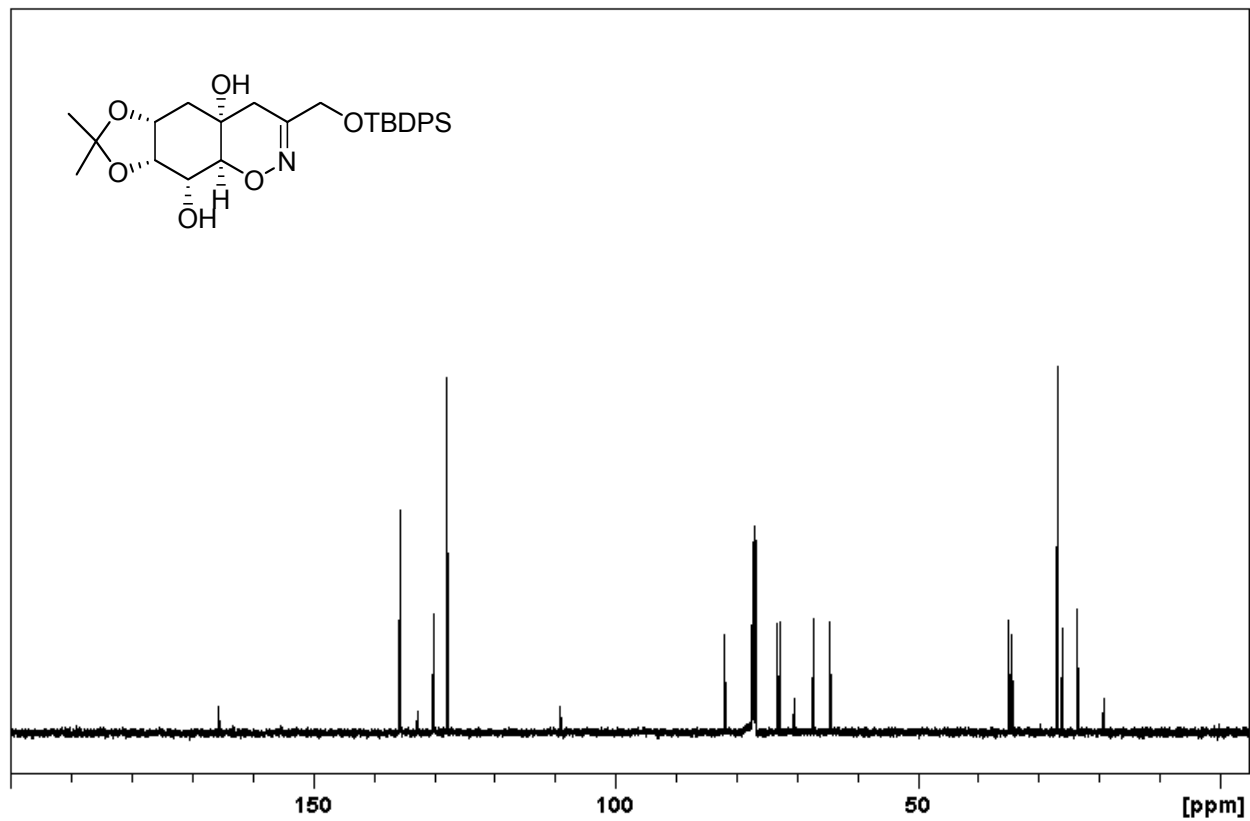
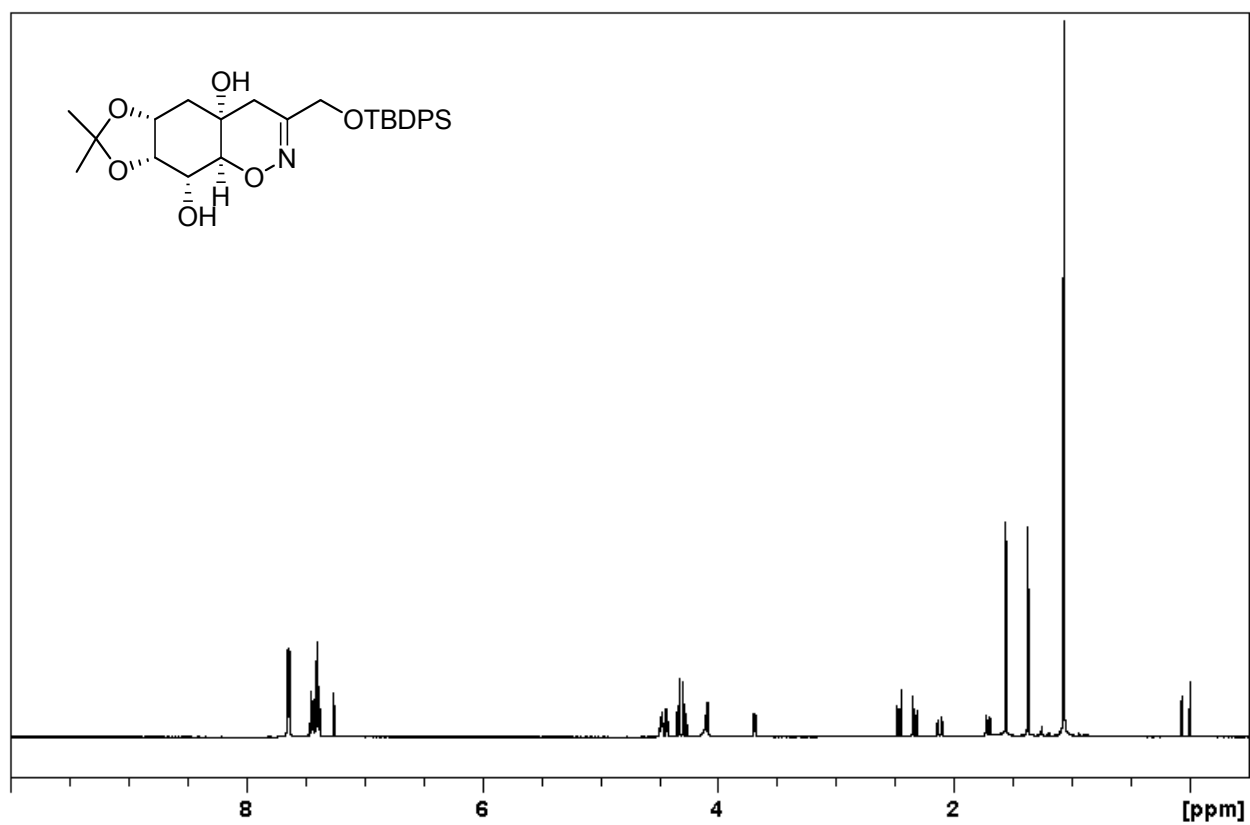


Figure 6: IR spectrum of compound 19.



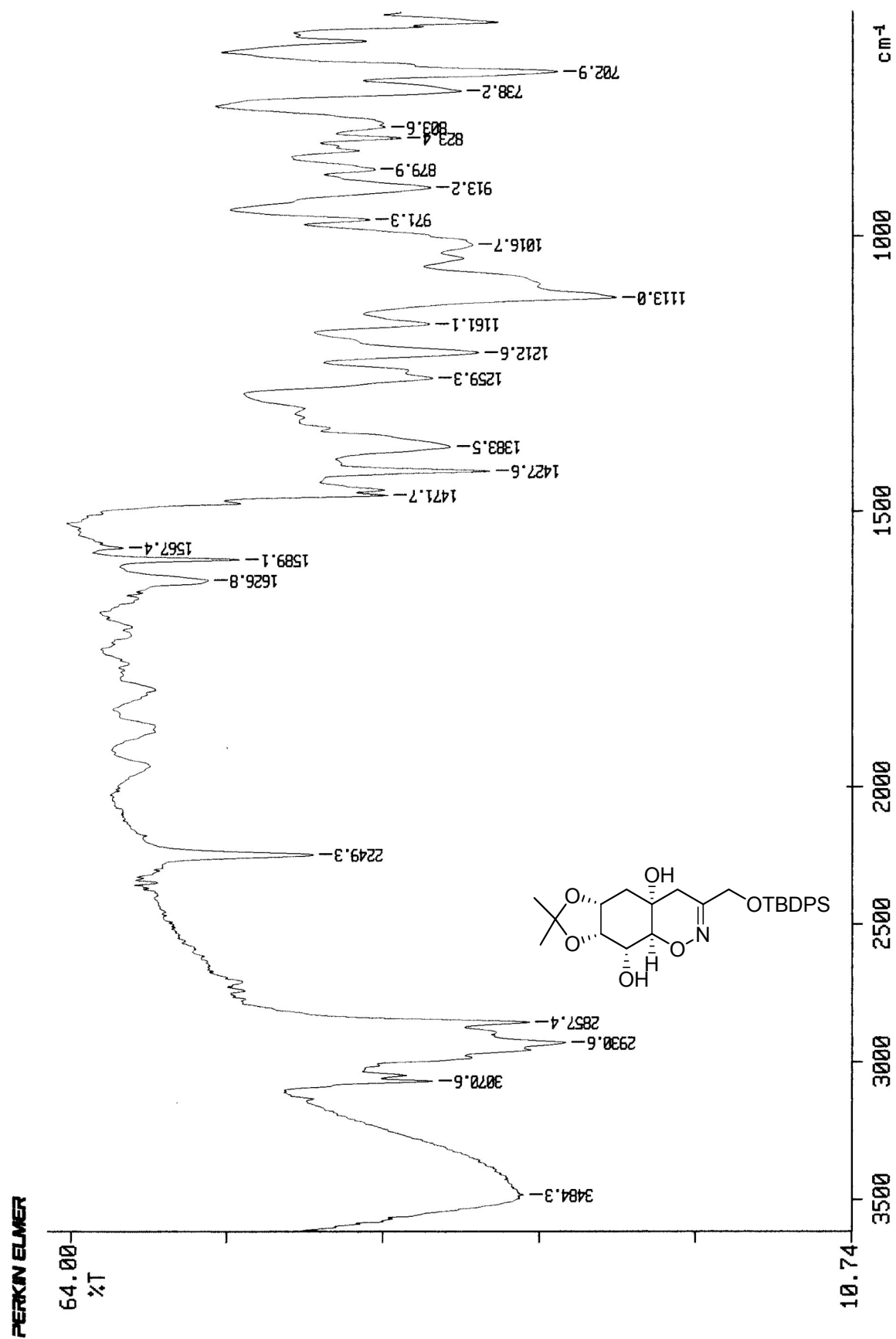


Figure 9: IR spectrum of compound 21

06/09/22 15:30
X: 16 scans, 4.0cm-1