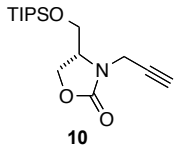
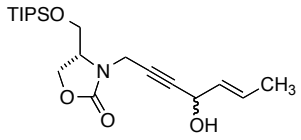


10

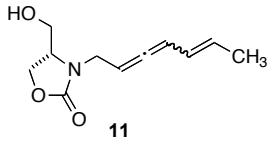
(*R*)-3-(prop-2-ynyl)-4-((triisopropylsilyloxy)methyl)oxazolidin-2-one (10).

To a CH_2Cl_2 solution of the alcohol precursor (74 mg, 0.48 mmol),[S1] a CH_2Cl_2 solution of imidazole (42 mg, 0.62 mmol) and DMAP (6.0 mg, 0.048 mmol) was added, and the reaction was stirred for 10 min at rt. Then triisopropylsilylmethanesulfonate (0.16 mL, 0.58 mmol) was added and the reaction was stirred at rt for 12 h, quenched with sat. NH_4Cl, extracted 3x with diethyl ether, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (3:1 hexane/ethyl acetate) to yield 126 mg (84%) of a thick yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.39 (dd, *J* = 17.8, 2.8 Hz, 1H), 4.35 (d, *J* = 8.5 Hz, 1H), 4.16 (dd, *J* = 8.5, 6.0 Hz, 1H), 4.01-4.06 (m, 1H), 3.82-3.89 (m, 3H), 2.27 (t, *J* = 2.3 Hz, 1H), 1.02-1.103 (m, 21H) ^{13}C-NMR (125 MHz, $CDCl_3$) 157.8, 77.2, 73.1, 64.8, 62.8, 55.7, 32.6, 17.9, 11.8 IR (KBr film, cm^{-1}) 3246, 2940, 2865, 1753, 1490, 1463, 1250, 880 HRMS (ESI) calcd. for $C_{16}H_{29}NO_3SiNa$ 334.1814, found 334.1811 $[M+Na]^+$



(*R*,*E*)-3-(4-hydroxyhept-5-en-2-ynyl)-4-((triisopropylsilyloxy)methyl)oxazolidin-2-one.

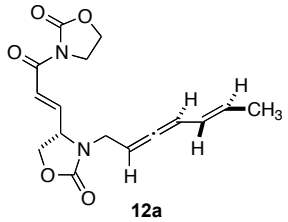
To a 9.0 mL THF solution of alkyne **10** (560 mg, 1.8 mmol) cooled at -50 °C, *n*-BuLi (1.56 mL, 2.34 mmol) was added dropwise and the reaction was stirred for 30 min. Then a 1.0 mL THF solution of crotonaldehyde (0.16 mL, 1.98 mmol) was added dropwise, and the reaction was stirred at -50 °C for 1.5 h, quenched with sat. NH_4Cl, extracted 3x with diethyl ether, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (2:1 hexane/ethyl acetate) to yield 450 mg (65%) of a thick yellow oil as two inseparable diastereomers with identical ^{1}H and and ^{13}C NMR data. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.82-5.90 (m, 1H), 5.59 (dd, ^{1}H, *J* = 15.2, 6.4, 1.6 Hz, 1H), 4.81 (br s, 1H), 4.47 (dd, *J* = 18.0, 1.6 Hz, 1H), 4.38 (t, *J* = 9.2 Hz, 1H), 4.17 (dd, *J* = 8.8, 5.6 Hz, 1H), 4.04 (sextet, *J* = 4.6 Hz, 1H), 3.91 (dd, J 18.0, 1.6 Hz, 1H), 3.84 (d, *J* = 4.8 Hz, 2H), 1.97 (t, *J* = 4.8 Hz, 1H), 1.73 (d, *J* = 6.8 Hz, 3H), 1.04-1.11 (m, 21H), ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.1, 130.1, 129.3, 84.6, 79.4, 65.1, 63.1, 55.9, 33.1, 31.8, 18.1, 17.7, 12.1 IR (KBr, cm^{-1}) HRMS 3401, 2942, 2865, 1739, 1463, 1436, 1249, 1106 (ESI) calcd. for $C_{20}H_{35}NO_4SiNa$ 404.2233, found 404.2228 $[M+Na]^+$



11

(4*S*)-3-(hepta-2,3,5-trienyl)-4-(hydroxymethyl)oxazolidin-2-one (11).

Tributyltin hydride (0.79 mL, 2.98 mmol), AIBN (61 mg, 0.37 mmol), and the proparyl alcohol above (708 mg, 1.86 mmol) were mixed and stirred neat at 90 °C for 5 h. The reaction was then cooled to 0 °C and diluted with 5.0 mL CH_2Cl_2. After stirring at 0 °C for 10 min, Et_3N (0.52 mL, 3.72 mmol) was added and the reaction was stirred at 0 °C for additional 10 min, after which MsCl (0.22 mL, 2.8 mmol) was added. The reaction was gradually warmed to rt, stirred for additional 30 min, quenched with 10% HCl, extracted 2x with diethyl ether, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (19:1, then 9:1 hexane/ethyl acetate) to yield a thick yellow oil. The oil was dissolved in 10.0 mL THF and treated with TBAF (2.6 mL, 2.6 mmol, 1.0 M in hexanes) for 1 h. The reaction was quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (4:1 ethyl acetate/hexane) to yield 177 mg (45% over three steps from alcohol precursor) of a thick yellow oil as two inseparable diastereomers. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.88-5.92 (m, 1H), 5.75-5.9 (m, 1H), 5.63-5.70 (m, 1H), 5.26-5.27 (m, 1H), 4.33 (dt, *J* = 17.0, 8.5 Hz, 1H) 4.24-4.28 (m, 1H), 4.04-4.10 (m, 1H), 3.86-3.94 (m, 1H), 3.76 (ddd, *J* = 16.5, 10.5, 6.0 Hz, 1H), 3.69 (ddt, *J* = 16.0, 7.0, 2.0 Hz, 1H), 3.60 (dd, *J* = 12.0, 3.0 Hz, 1H), 3.08 (br s, 1H), 1.73 (dd, *J* = 6.5, 1.5 Hz, 3H), ^{13}C-NMR (125 MHz, $CDCl_3$) δ 206.8, 206.5, 159.0, 158.9, 129.53, 129.46, 125.5, 125.4, 96.7, 96.5, 88.0, 87.9, 64.9, 60.6, 60.58, 56.4, 56.2, 41.8, 41.6, 18.4 IR (KBr, cm^{-1}) 3366, 2920, 2853, 1730, 1606, 1490, 1446, 1046 HRMS (EI) calcd. for $C_{11}H_{15}NO_3$ 209.1052, found 209.1041 $[M]^+$



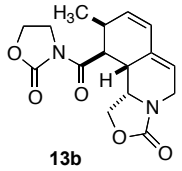
12a

(*S*)-3-((*S*,*E*)-hepta-2,3,5-trienyl)-4-((*E*)-3-oxo-3-(2-oxooxazolidin-3-yl)prop-1-enyl)oxazolidin-2-one (12a).

To a 4.0 mL -78 °C CH_2Cl_2 solution of oxalyl chloride (0.086 mL, 1.0 mmol), DMSO (0.14 mL, 2.0 mmol) was added, and the reaction was stirred for 10 min. Then a 1.0 mL CH_2Cl_2 solution of compound **11** (105 mg, 0.5 mmol) was added, and the reaction was stirred at -78 °C for 1.25 h. The reaction was quenched with triethylamine (0.42 mL, 3.0 mmol), and was allowed to warm to -20 °C. Then a 2.0 mL CH_2Cl_2 solution of the Wittig reagent (generated in situ form the phosphonium bromide salt: 470 mg, 1.0 mmol and

DMAP: 146 mg, 1.2 mmol at 0 °C, 20 min) was transferred to the reaction mixture via cannula. The reaction was stirred at -20 °C for 10 min, then was allowed to warm to rt while stirring for additional 3 h, quenched with a pH 8 buffer solution of NH_4Cl / NH_4OH, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (3:2 ethyl acetate /hexane) to yield 50 mg (31 %) of product **13b** as a thick yellow oil and 23 mg (14 %) of product **12a**. Compound **13b** was further purified by prep HPLC (HPLC parameters: *RAININ*, column: Varian Dynamax, 250 x 21.4 MM (L*1D) Flow, S/N 3007, Microsorb 60-8 Si R00083121C. Flow rate: 10 mL/min, 80% ethyl acetate/hexane, retention time: 24-26 min).

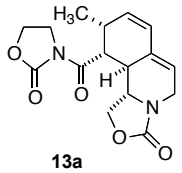
For compound **12a**: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 15.5 Hz, 1H), 6.88 (ddd, *J* = 15.5, 8.5 Hz, 1H), 5.92-5.94 (m, 1H), 5.78-5.83 (m, 1H), 3.65-3.72 (m, 1H), 5.21 (m, 1H) 4.53 (dd, *J* = 16.3, 7.8, 1H), 4.43-4.47 (m, 3H), 4.15 (dt, *J* = 16.0, 4.0 Hz, 1H), 4.08 (t, *J* = 8.3 Hz, 2H), 4.03 (t, *J* = 7.8 Hz, 1H), 3.51 (dd, *J* = 15.3, 6.8 Hz, 1H), 1.74 (d, *J* = 6.0 Hz, 3H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 206.9, 163.8, 157.7, 153.5, 143.9, 129.5, 125.5, 124.9, 96.8, 87.3, 66.5, 62.5, 56.6, 42.8, 41.7, 18.4 IR (KBr film, cm^{-1}) 2954, 2923, 2849, 1771, 1753, 1686, 1640, 1608, 1383, 1218, 1032, 823 HRMS (ESI) m/z calcd. for $C_{16}H_{18}N_2O_5$ 318.1216, found 318.1221 $[M]^+$



13b

(9*S*,10*S*,10a*R*,10b*S*)-9-methyl-10-(2-oxooxazolidine-3-carbonyl)-9,10,10a,10b-tetrahydro-1H-oxazolo[4,3-a]isoquinolin-3(5H)-one (13b).

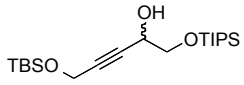
A thick yellow oil; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.06 (d, *J* = 9.5 Hz, 1H), 5.79 (dd, *J* = 9.5, 6.0 Hz, 1H), 5.66 (m, 1H), 4.44-4.48 (m, 2H), 4.33 (t, *J* = 9.5 Hz, 1H), 4.27 (dd, *J* = 9.5, 8.0 Hz, 1H), 4.15 (d, *J* = 19.0 Hz, 1H), 3.97-4.10 (m, 3H), 3.72 (d, *J* = 19.0 Hz, 1H), 3.54 (q, *J* = 8.83 Hz, 1H), 2.90-2.95 (m, 1H), 2.75 (sextet, *J* = 6.2 Hz, 1H), 0.95 (d, *J* = 7.0 Hz, 3H) ^{13}C-NMR (125 MHz, $CDCl_3$) 173.5, 157.4, 152.8, 132.0, 131.9, 126.6, 120.9, 70.4, 61.9, 55.9, 45.7, 42.8, 40.7, 35.6, 31.4, 16.3 IR (KBr film, cm^{-1}) 2918, 1751, 1684, 1653, 1559, 1387, 1206, 1093, 1024, 758 HRMS (ESI) calcd. for $C_{16}H_{18}N_2O_5Na$, 341.1113, found 341.1115 $[M+Na]^+$



13a

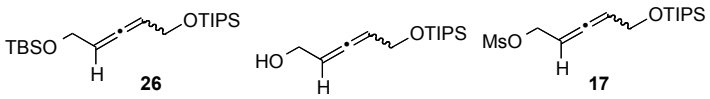
(9R,10R,10aS,10bS)-9-methyl-10-(2-oxooxazolidine-3-carbonyl)-9,10,10a,10b-tetrahydro-1H-oxazolo[4,3-a]isoquinolin-3(5H)-one (13a).

To a 1.0 mL THF solution of $ZnCl_2$ (24 mg, 0.18 mmol) at 0 °C, 0.22 mL of MeLi (0.35 mmol, 1.6 M in diethyl ether) was added dropwise. The reaction was stirred at 0 °C for 10 min, then transferred via cannula to a 0.5 mL THF solution of $Ni(COD)_2$ (6.4 mg, 0.023 mmol) cooled at 0 °C. The reaction mixture was cooled to -20 °C and stirred at -20 °C for 10 min, then a 1.0 mL THF solution of compound **12a** (23 mg, 0.07 mmol) and titanium isopropoxide (0.021 mL, 0.07 mmol) was added dropwise. The reaction was slowly warmed to rt, and stirred at rt for 1 h, quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (2:1 ethyl acetate/hexane) to yield 14 mg (64%) of a thick yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.02 (d, *J* = 9.6 Hz, 1H), 5.85-5.88 (m, 1H), 5.71 (dd, *J* = 9.6 Hz, 1H), 4.39-4.51 (m, 4H), 4.03-4.16 (m, 4H), 3.93-4.00 (m, 1H), 3.74 (dd, *J* = 11.2, 8.4 Hz, 1H), 3.53 (d, *J* = 17.2 Hz, 1H), 3.22 (dd, *J* = 12.0, 8.8 Hz, 1H), 2.83 (sextet, *J* = 6.5 Hz, 1H), 0.84 (d, *J* = 7.2 Hz, 3H) ^{13}C-NMR (125 MHz, $CDCl_3$) 173.9, 157.8, 152.9, 133.4, 131.8, 127.2, 123.4, 66.5, 62.3, 53.1, 431, 42.9, 39.9, 31.4, 30.5, 16.5 IR (KBr film, cm^{-1}) 2958, 2919, 1758, 1687, 1388, 1217, 1038 HRMS (ESI) calcd. for $C_{16}H_{18}N_2O_5Na$, 341.1113 found 341.1109 $[M+Na]^+$

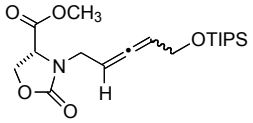


3,3-diisopropyl-2,11,11,12,12-pentamethyl-4,10-dioxa-3,11-disilatridec-7-yn-6-ol.

To a THF (60 mL) solution of TBS-protected propargyl alcohol (1.31 g, 7.7 mmol), *n*-BuLi (5.7 mL, 8.4 mmol, 1.48 M solution in hexanes) was added dropwise at -78 °C, and the reaction was stirred at -78 °C for 1h. Then a 10 mL THF solution of the aldehyde (1.51 g, 7.0 mmol) was added dropwise and the reaction was stirred at -78 °C for 1.5 h, then the temperature was brought up to -40 °C, and the reaction was stirred at -40 °C for additional 2 h. The reaction was quenched with sat. NH_4Cl, extracted 3x with diethyl ether, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified with silica gel column chromatography (10:1 pentane/diethyl ether) to yield 1.76 g (65 %) of a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.45 (m, 1H), 4.33 (d, *J* = 1.5 Hz, 2H), 3.84 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.72 (dd, *J* = 10.0, 7.5 Hz, 1H), 2.69 (br s, 1H), 1.06-1.12 (m, 21H), 0.89 (s, 9H), 0.10 (s, 6H) ^{13}C-NMR (125 MHz, $CDCl_3$) 84.1, 82.5, 67.1, 63.2, 51.7, 25.8, 18.3, 17.9, 17.8, 11.9, -5.2 IR (KBr, cm^{-1}) 3443, 2939, 2860, 2720, 2233, 1463, 1367, 1126, 1092, 836 HRMS (ES) m/z calcd. for $C_{20}H_{42}O_3Si_2$ 409.2570, found 409.2560 $[M+Na]^+$

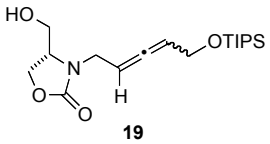


Prepared as described below for the **26a** to **17a** conversion.



(4*R*)-methyl 2-oxo-3-(5-(triisopropylsilyloxy)penta-2,3-dienyl)oxazolidine-4-carboxylate.

To a THF (4 mL) solution of the oxazolidinone methyl ester precursor cooled at 0 °C, (90 mg, 0.62 mmol), KHMDS (1.39 mL, 0.69 mmol, 0.5 M in toluene) was added dropwise and the reaction was stirred at 0 °C for 30 min. After that, a 2 mL solution of the allenyl mesylate **17** (314 mg, 0.94 mmol) was added dropwise and the reaction was allowed to stir at rt for 12 h. The reaction was quenched with a pH 8 buffer solution of NH_4Cl / NH_4OH, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (4:1 then 2:1 hexane /ethyl acetate) to yield 100 mg (41%) of a thick yellow oil as a 1:1 mixture of two inseparable diastereomers ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.37-5.41 (m, 2H), 5.17-5.21 (m, 2H), 4.56 (dd, *J* = 9.5, 4.5 Hz, 1H), 4.43-4.47 (m, 3H), 4.33-4.36 (m, 2H), 4.29-4.31 (m, 1H), 4.21-4.26 (m, 5H), 3.79 (s, 6H), 3.75 (ddd, *J* = 15.5, 7.5, 2.0 Hz, 1H), 3.70 (ddd, *J* = 15.8, 6.5, 1.5 Hz, 1H), 1.04-1.10 (m, 21H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 204.1, 203.6, 180.0, 170.1, 170.07, 157.3, 157.2, 94.9, 94.4, 87.9, 87.2, 64.3, 61.05, 60.8, 56.0, 55.7, 52.8, 52.7, 42.2, 41.7, 17.9, 17.8, 11.9, 11.87 IR (KBr, cm^{-1}) 2943, 2866, 1968, 1767, 1463, 1410, 1194, 1089, 1057, 882, 682 HRMS (ES) m/z calcd. for $C_{19}H_{33}NO_5SiNa$ 406.2026, found 406.2029 $[M+Na]^+$

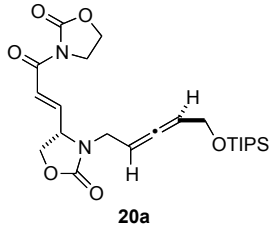


19

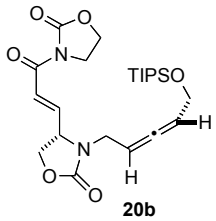
(4*S*)-4-(hydroxymethyl)-3-(5-(triisopropylsilyloxy)penta-2,3-dienyl)oxazolidin-2-one (19).

To a 95 % ethanol solution of oxazolidinone methyl ester identified above (137 mg, 0.36 mmol) cooled at 0 °C, sodium borohydride (35 mg, 0.86 mmol) was added portion-wise; the reaction was stirred at 0 °C for 1 h, then brought to rt and stirred for another 1 h. The reaction was quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, and dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (4:1 ethyl acetate/hexane) to yield 102 mg (80%) of a thick yellow oil. as a 1:1 mixture of two inseparable diastereomers ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.35-5.40 (m, 2H), 5.19-5.24 (m, 2H), 4.31 (t, *J* = 8.8 Hz, 2H), 4.19-4.25 (m, 6H), 4.10 (ddd, *J* = 15.5, 5.0, 3.1 Hz, 1H), 4.01 (ddd, *J* = 15.5, 5.5, 3.0 Hz, 1H), 3.90-

3.98 (m, 2H), 3.79 (dd, *J* = 7.0, 2.5 Hz, 1H), 3.74-3.78 (m, 2H), 3.67 (ddd, *J* = 15.5, 7.0, 2.0 Hz, 1H), 3.56-3.62 (m, 2H), 3.31 (t, *J* = 5.5 Hz, 1H), 3.25 (m, 1H), 1.02-1.10 (m, 42H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 203.9, 203.8, 158.7, 158.6, 94.5, 94.3, 88.5, 88.4, 64., 64.5, 61.1, 61.0, 60.9, 60.4, 56.4, 55.9 41.7, 41.2, 17.91, 17.90, 12.0, 11.9 IR (KBr, cm^{-1}) 3416, 2944, 2866, 1970, 1733, 1463, 1194, 1092, 882 HRMS (ES) m/z calcd. for $C_{18}H_{33}NO_4SiNa$ 378.2077, found 378.2068



20a



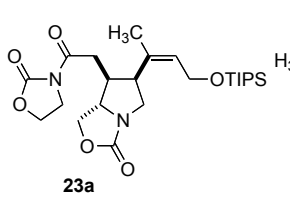
20b

(Diastereomeric mixture of **19** used here. Procedure with diastereomerically pure **19a** is provided below.)

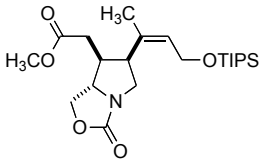
(*S*)-4-((E)-3-oxo-3-(2-oxooxazolidin-3-yl)prop-1-enyl)-3-((*S*)-5-(triisopropylsilyloxy)penta-2,3-dienyl)oxazolidin-2-one (20a) and (*S*)-4-((*E*)-3-oxo-3-(2-oxooxazolidin-3-yl)prop-1-enyl)-3-((*R*)-5-(triisopropylsilyloxy)penta-2,3-dienyl)oxazolidin-2-one (20b).

To a 3 mL CH_2Cl_2 solution of oxalyl chloride (0.048 mL, 0.56 mmol) cooled at -78 °C, DMSO (0.079 mL, 1.12 mmol) was added, and the reaction was stirred for 10 min. Then a 1.8 mL CH_2Cl_2 solution of compound **19** (100 mg, 0.28 mmol) was added, and the reaction was stirred at -78 °C for 1.25 h. The reaction was quenched with triethylamine (0.24 mL, 1.68 mmol), and was allowed to warm up to -20 °C. Then a 2.0 mL CH_2Cl_2 solution of the Wittig reagent (generated in situ form the phosphonium bromide salt: 263 mg, 0.56 mmol and DMAP: 82 mg, 0.67 mmol at 0 °C, 20 min) was transferred to the reaction mixture via cannula. The reaction was stirred at -20 °C for 10 min, then warmed up and stirred at rt for additional 3 h, quenched with a pH 8 buffer solution of NH_4Cl / NH_4OH, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (2:1 ethyl acetate /hexane) to yield 90 mg (69%) of a yellow oil as a 1:1 mixture of two diastereomers separable by prep HPLC. HPLC parameters (*Shimatzu*, Column specification: Altima Silica.5μ, Lot Number: 050700057, Part Number: 81118, Size: 250 mm, Flow Rate: 10 mL/min, 1:1 ethyl acetate/hexanes. Retention time for compound **20a** is 4.0 min, and for **20b** is 5.2 min. Compound **20a**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 15.6 Hz, 1H), 6.88 (dd, *J* = 15.2, 8.4 Hz, 1H), 5.34-5.39 (m, 1H), 5.15-5.21 (m, 1H), 5.47-5.64 (m, 1H), 4.45 (t, *J* = 8.0 Hz, 3H), 4.26 (d, *J* = 2.8 Hz, 1H), 4.25 (d, *J* = 2.4 Hz, 1H), 4.00-4.11 (m, 4H), 3.57 (ddd, *J* = 15.6, 6.8, 2.4 Hz, 1H), 1.04-1.07 (m, 21H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ 204.2, 163.6, 157.4, 153.2, 143.9, 124.4, 94.5, 87.3, 66.2, 62.2, 60.9, 56.3, 42.5, 41.4, 17.9, 11.9 IR (KBr, cm^{-1}) 2941, 2864, 1754, 1727, 1682, 1660, 1649, 1083 HRMS (ESI) m/z calcd. for $C_{23}H_{36}N_2O_6SiNa$ 487.2240, found 487.2236 $[M+Na]^+$

Compound **20b**: ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 15.0 Hz, 1H), 6.88 (dd, *J* = 15.3, 8.8 Hz, 1H), 5.41-5.46 (m, 1H), 5.12-5.16 (m, 1H), 4.59 (dd, *J* = 15.3, 8.8 Hz, 1H), 4.44-4.49(m, 3H), 4.24 (dd, *J* = 5.5, 3.0 Hz, 2H), 4.20 (dd, *J* = 4.8, 3.3 Hz, 1H), 4.07-4.13 (m, 2H), 4.04 (dd, *J* = 8.5, 7.0 Hz, 1H), 3.47 (ddd, *J* = 15.5, 8.0, 1.6 Hz, 1H), 1.03-1.10 (m, 21H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 204.1, 163.6, 157.4, 153.2, 143.7, 124.6, 94.7, 87.3, 66.2, 62.2, 61.0, 55.9, 42.6, 41.3, 17.9, 11.9 IR (KBr, cm^{-1}) 2941, 2864, 1967, 1756, 1684, 1645, 1382, 1363, 1221 HRMS (ESI) m/z calcd. for $C_{23}H_{36}N_2O_6SiNa$ 487.2240, found 487.2243.

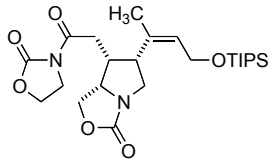


23a



24a

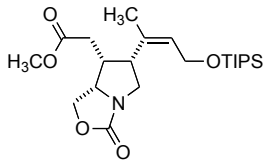
Prepared as described below for asymmetrically prepared **20a.**



23b

(6*R*,7*R*,7a*S*)-7-(2-oxo-2-(2-oxooxazolidin-3-yl)ethyl)-6-((*Z*)-4-(triisopropylsilyloxy)but-2-en-2-yl)tetrahydropyrrolo[1,2-c]oxazol-3(1H)-one (23b).

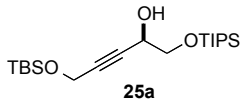
To a 0.5 mL THF solution of $ZnCl_2$ (15 mg, 0.11 mmol) at 0 °C, 0.19 mL of MeLi (0.21 mmol, 1.14 M in diethyl ether) was added dropwise. The reaction was stirred at 0 °C for 10 min, then transferred via cannula to a 0.5 mL THF solution of $Ni(COD)_2$ (2.4 mg, 0.0086 mmol) cooled to 0 °C. The reaction mixture was cooled down to -20 °C and stirred at -20 °C for 10 min, then a 0.8 mL THF solution of compound **20b** (20 mg, 0.043 mmol) and titanium isopropoxide (0.013 mL, 0.043 mmol) was added dropwise. The reaction was slowly warmed to rt, and stirred at rt for 2 h, quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (2:1 ethyl acetate/hexane) to yield 5 mg (24%) of a thick yellow oil ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.61 (t, *J* = 6.3 Hz, 1H), 4.40-4.48 (m, 3H), 4.24-4.33 (m, 2H), 4.13 (dd, *J* = 9.8, 4.8 Hz, 1H), 4.09 (t, *J* = 8.3 Hz, 1H), 3.97-4.00 (m, 1H), 3.64 (t, *J* = 10.0 Hz, 1H), 3.55-3.61 (m, 1H), 3.33 (dd, *J* = 10.3, 8.3 Hz, 1H) 3.00 (dd, *J* = 18.8, 2.3 Hz, 1H) 2.75-2.80 (m, 1H), 2.72 (d, *J* = 11.0 Hz, 1H), 2.68 (d, *J* = 11.0 Hz, 1H), 1.79 (d, *J* = 0.5 Hz, 3H), 1.04-1.09 (m, 21H), ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.3, 160.2, 153.2, 132.3, 131.1, 65.0, 62.1, 61.8, 59.5, 46.0, 45.3, 42.4, 39.7, 30.2, 23.3, 17.9, 11.9 IR (KBr, cm^{-1}) 2960, 2925, 2864, 1771, 1751 1734, 1697, 1653, 1393, 1094 HRMS (ESI) m/z calcd. for $C_{24}H_{40}N_2O_6SiNa$ 503.2553, found 503.2546 $[M+Na]^+$



24b

Methyl 2-((6R,7R,7aS)-3-oxo-6-((Z)-4-(triisopropylsilyloxy)but-2-en-2-yl)hexahydropyrrolo[1,2-c]oxazol-7-yl)acetate (24b).

To a 1.6 mL dry methanol stirred at 0 °C, MeMgBr (0.037 mL, 0.052 mmol, 1.4 M in 75:25 toluene/THF solution) was added dropwise and the reaction was stirred at 0 °C for 10 min, followed by dropwise addition of 1.0 mL methanol solution of compound **23b** (5 mg, 0.0104 mmol). The reaction was allowed to warm to room temperature and stir for 2 h, then it was cooled to 0 °C, quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (2:1 hexane/ethyl acetate) to yield 3.5 mg (79%) of a thick yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.61 (t, *J* = 6.0 Hz, 1H), 4.43 (d, *J* = 9.8, 8.3 Hz, 1H), 4.22-4.31 (m, 3H), 4.19 (dd, *J* = 10.0, 4.5 Hz, 1H), 3.67 (s, 3H), 3.61 (dd, *J* = 10.5, 10.0 Hz, 1H), 3.49-3.54 (m, 1H), 3.32 (dd, *J* = 11.0, 9.0 Hz, 1H), 2.69 (sextet, *J* = 5.2 Hz, 1H), 2.29 (d, *J* = 17.3, 4.3 Hz, 1H), 2.14 (dd, *J* = 17.0, 10.0 Hz, 1H), 1.73 (s, 3H), 1.04-1.10 (m, 21H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 172.9, 160.7, 131.6, 131.4, 64.4, 62.0, 59.6, 52.0, 46.2, 45.3, 40.6, 28.4, 23.5, 18.0, 12.0 IR (KBr, cm^{-1}) 2921, 2864, 1756, 1463, 1393, 1058, 882 HRMS (ESI) calcd. for $C_{22}H_{39}NO_5SiNa$ 448.2495, found 448.2493 $[M+Na]^+$.

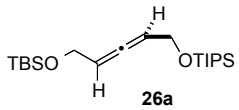


25a

(R)-3,3-diisopropyl-2,11,11,12,12-pentamethyl-4,10-dioxa-3,11-disilatridec-7-yn-6-ol (25a).

Following the Carreira procedure,[S2] zinc trifluoromethanesulfonate (2.032 g, 5.6 mmol) was added to a flame dried round bottom flask, and the solid was dried under vacuum at 130 °C for 12 h then allowed to cool to rt. (1*R*, 2*S*)-(-)-*N*-methylephedrine (1.074 g, 6.0 mmol) was then added as a solid, and the solid mixture was put under vacuum for 20 min. Toluene (25 mL) was added, followed by dropwise addition of freshly distilled triethylamine (835 μL, 6.0 mmol). After the white slurry was stirred for 2 h under nitrogen at rt, a 12 mL toluene solution of *t*-butyldimethylsilylpropargyl ether (1.020 g, 6.0 mmol) was added dropwise via syringe pump over 20 min at rt. The reaction was stirred for 30 min, then a 12 mL toluene solution of the aldehyde (864 mg, 4.0 mmol) was added dropwise over 22 h at rt. The reaction was quenched with sat. NH_4Cl, extracted 3x with diethyl ether, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified with silica gel column chromatography (10:1 pentane/diethyl ether) to yield 890 mg of **25a** as a colorless oil (58%, 94 % *ee*). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.45 (m, 1H), 4.33 (d, *J* = 1.5 Hz, 2H),

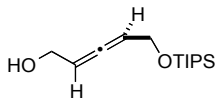
3.84 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.72 (dd, *J* = 10.0, 7.5 Hz, 1H), 2.69 (br s, 1H), 1.06-1.12 (m, 21H), 0.89 (s, 9H), 0.10 (s, 6H), ^{13}C-NMR (125 MHz, $CDCl_3$) 84.1, 82.5, 67.1, 63.2, 51.7, 25.8, 18.3, 17.9, 17.8, 11.9, -5.2 IR (KBr, cm^{-1}) 3443, 2939, 2860, 2720, 2233, 1463, 1367, 1126, 1092, 836 HRMS (ES) m/z calcd. for $C_{20}H_{42}O_3Si_2$ 409.2570, found 409.2560 $[M+Na]^+$ The *ee* of this reaction was determined by NMR analysis of the Mosher ester derivative of the (*R*)-propargyl alcohol and its racemate, comparing the signals at δ = 5.81 and δ = 5.74.



26a

(S)-11,11-diisopropyl-2,2,3,3,12-pentamethyl-4,10-dioxa-3,11-disilatrideca-6,7-diene (26a).

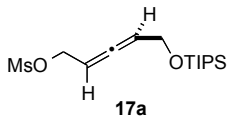
Following the Myers protocol for allene synthesis,[S3] triphenylphosphine (618 mg, 2.36 mmol) was loaded to a flame dried flask, and 10 mL of dry THF was added. The solution was cooled to -15 °C (materials crystallize out of solution when temperature falls below -20 °C) and DEAD (411 mg, 371 μL, 2.36 mmol) was added dropwise. The reaction was stirred at -15 °C for another 10 min, and 8 mL THF solution of alcohol **25a** (1.09 g, 2.82 mmol) was added over 5 min. After 10 min, a 10 mL THF solution of NBSH (518 mg, 2.36 mmol) was added dropwise. The reaction mixture was stirred at -15 °C for 2 h, then brought up to rt and stirred for 12 h, quenched with sat. NH_4Cl, and extracted 3x with diethyl ether. The ether solution was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by column chromatography (hexane/ethyl acetate, 50:1) to yield 400 mg (61%, 92% *ee*) of **26a** as a yellow oil. The *ee* of this reaction was determined by ^{1}H NMR analysis of the formed allene in presence of $Yb(hfc)_3$-Ag(FOD) as a chiral shift reagent according to the following ratio: allene:Ag:Yb = 1:2:1.5 (7.5 mg of allene, 17.0 mg of Ag(FOD), and 34.0 mg of $Yb(hfc)_3$ in 1.5 mL $CDCl_3$) and its racemate. The *ee* was determined by comparison of the ^{1}H NMR signals at δ = 5.61 and δ = 5.52. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.28-5.36 (m, 2H), 4.26 (ddd, *J* = 6.0, 4.5, 2.8 Hz, 2H), 4.19 (ddd, *J* = 5.5, 4.0, 2.8 Hz, 2H), 1.07-1.09 (m, 2H), 0.90 (s, 9H), 0.07 (s, 6H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 202.6, 93.3, 93.1, 61.6, 61.58, 25.9, 18.3, 17.97, 17.96, 12.0, -5.1 IR (KBr, cm^{-1}) 2940, 1864, 1963, 1493, 1255, 1090, 836 HRMS (ES) m/z calcd. for $C_{20}H_{42}O_2Si_2$ 393.2621, found 393.2616 $[M+Na]^+$



(S)-5-(triisopropylsilyloxy)penta-2,3-dien-1-ol).

To a 20 mL ethanol solution of **26a** (760 mg, 2.1 mmol) was added a catalytic amount of pyridine paratoluenesulfonate (160 mg, 0.62 mmol). The reaction was stirred at 55 °C for 2.5 h, quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, washed with sat. $NaHCO_3$, and brine, and dried over anh. $MgSO_4$. The solvent was removed in vacuo, and the crude product was purified by column chromatography (hexane/ethyl acetate, 10:1) to

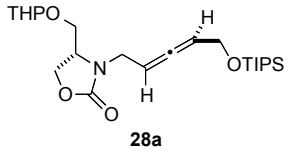
afford 440 mg (85%) of the corresponding alcohol as a light yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.38-5.44 (m, 2H), 4.24-4.26 (m, 2H), 4.10-4.12 (m, 2H), 2.13 (br s, 1H), 1.03-1.08 (m, 21H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ 202.5, 94.4, 93.4, 61.3, 60.3, 17.9, 11.9 IR (KBr, cm^{-1}) 3356, 2941, 2864, 2890, 1964, 1462, 1093, 881 HRMS (ESI) m/z calcd. for $C_{14}H_{28}O_2SiNa$ 279.1769, found 279.1743 $[M+Na]^+$



17a

(S)-5-(triisopropylsilyloxy)penta-2,3-dienyl methanesulfonate (17a).

Triethylamine was added to a CH_2Cl_2 solution of the alcohol precursor above (200 mg, 0.78 mmol) cooled to 0 °C, and the reaction was stirred for 10 min. Then the reaction was cooled to -25 °C and mesyl chloride (99 mg, 67 μL, 0.86 mmol) was added. The reaction mixture was allowed to gradually warm up to 0 °C, and then it was transferred to a separatory funnel, quickly and successively washed with ice cold solutions of 10% HCl, sat. $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, and the solvent was removed under vacuum to produce 258 mg of compound **17a** (98%) as a yellow oil that was used with no further purification.^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.47-5.51 (m, 1H), 5.40-5.45 (m, 1H), 4.72 (dd, J = 1.5, 1.0 Hz, 1H), 4.70 (dd, *J* = 2.0, 1.0 Hz, 1H), 4.29 (d, *J* = 3.0 Hz, 1H), 4.28 (d, *J* = 3.) Hz, 1H), 3.02 (s, 3H), 1.04-1.09 (m, 21H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ 205.4, 94.8, 87.6, 67.9, 60.6, 38.2, 17.9, 11.9 (KBr, cm^{-1}) 2926, 2853, 1963, 1606, 1493, 1190, 1050 HRMS (ESI) m/z calcd. for $C_{15}H_{30}O_4SSiNa$ 357.1532, found 357.1529 $[M+Na]^+$

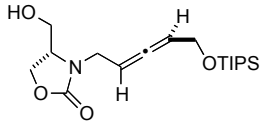


28a

(4S)-4-((tetrahydro-2H-pyran-2-yloxy)methyl)-3-((S)-5-(triisopropylsilyloxy)penta-2,3-dienyl)oxazolidin-2-one (28a).

Using phase-transfer-catalyzed alkylation; a CH_2Cl_2 (5 mL) solution of the THP-protected hydroxymethyl oxazolidinone (201 mg, 1.0 mmol) was cooled to 5-10 °C. To this vigorously stirred solution benzyltriethylammonium bromide (136 mg, 0.5 mmol) as the phase-transfer catalyst, 50% aqueous NaOH (1.25 mL), and a 5 mL solution of the allenyl mesylate **17a** (334 mg, 1.0 mmol) were added dropwise and the reaction was allowed to slowly warm up to rt and further stirred for an additional 16 h at rt. The reaction was quenched with a buffer solution of NH_4Cl / NH_4OH, and the organic layer was separated and the aqueous layer was extracted 3x with CH_2Cl_2. The combined organic fractions were washed once with cold 1.0 M HCl solution and twice with cold water and finally with cold brine solution. The combined extracts were dried over anh. $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography (SiO_2; hexanes: ethyl acetate = 4:1 then 2:1) to yield 102

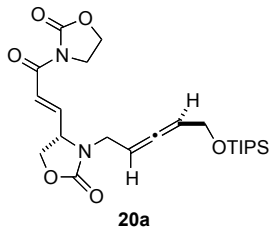
mg (50%) of **28a** as a thick yellow oil, together with (62 mg, 0.19 mmol) unreacted allenyl mesylate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.42-5.36 (m, 1H), 5.24-5.16(m, 1H), 4.59 (dt, *J* = 14.5, 3.0 Hz, 1H), 4.35 (td, *J* = 9.0, 3.5 Hz, 1H), 4.25-4.23 (m, 2H), 4.19-4.12 (m, 1H), 4.07-4.01 (m, 1H), 3.84-3.69(m, 2H), 3.53-3.44 (m, 2H), 1.80-1.49 (m, 8H), 1.08-1.03 (m, 21H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 203.9, 203.8, 158.11, 158.0, 99.2, 99.0, 94.2, 94.2, 87.99, 87.97, 66.7, 66.3, 65.02, 65.01, 62.4, 62.2, 61.3, 61.1, 54.3, 54.1, 41.9, 41.6, 30.4, 30.3, 25.3, 25.2, 19.2, 19.0, 17.93, 17.91, 11.9, 11.7; IR (film cm^{-1}) 2941, 2868, 2358, 2336, 1751, 1448, 1227, 1127, 1034; HRMS (ES$^+$) *m/z* calcd for $C_{23}H_{41}NO_5SiNa$ $[M+Na]^+$ 462.2652, found 462.2640.



19a

(S)-4-(hydroxymethyl)-3-((S)-5-(triisopropylsilyloxy)penta-2,3-dienyl)oxazolidin-2-one (19a).

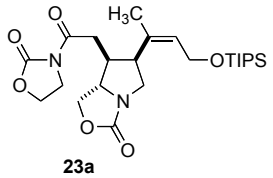
To a 5 mL ethanol solution of the THP-protected allenyl oxazolidinone **28a** (36 mg, 0.082 mmol) was added a catalytic amount of PPTS (pyridinium *p*-toluenesulfonate) (6 mg, 0.025 mmol). The reaction was stirred at 55 °C for 2.5 h. The reaction was then cooled to rt and the solution was concentrated under vacuum to *ca* 1 mL then ether was added to precipitate the PPTS. Sat. NH_4Cl was added and the product was extracted 3x with ethyl acetate, the combined organic layers were then washed with $NaHCO_3$ and brine, and dried over anh. $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (hexanes: ethyl acetate = 2:1 then 1:1) to produce 23 mg (76%, 91:9 *dr*) of **19a** as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.46-5.45 (m, 1H), 5.32-5.27 (m, 1H), 4.36 (t, *J* =9.0 Hz, 1H), 4.30-4.23 (ddq, *J* =13.3, 5.7, 3.3 Hz, 2H), 4.19 (dd, *J* = 8.7, 6.5 Hz, 1H), 4.02 (ddd, *J* =15.0, 5.5, 2.5 Hz, 1H), 3.97 (m, 1H), 3.91 (ddd, *J* = 8.0, 6.5, 3.0 Hz, H), 3.80 (dt, *J* = 12.0, 3.5 Hz, 1H), 3.67 (ddd, *J* = 11.5, 7.0, 4.0 Hz, 1H), 2.46 (dd, *J* = 7.5, 4.5 Hz, 1H), 1.12-1.11(m, 21H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ 204.1, 158.4, 94.3, 88.7, 64.3, 61.4, 61.0, 56.7, 17.9, 12.0 42.0, IR (KBr, cm^{-1}) 3419, 2942, 2865, 1967, 1733, 1445, 1365, 1247, 1090, 881, 681 HRMS (ES) m/z calcd. for $C_{18}H_{33}NO_4SiNa$ 378.2077, found 378.2064 $[M+Na]^+$



20a

***S*)-4-((E)-3-oxo-3-(2-oxooxazolidin-3-yl)prop-1-enyl)-3-((*S*)-5-(triisopropylsilyloxy)-penta-2,3-dienyl)oxazolidin-2-one (20a).**

To a 2 mL CH_2Cl_2 solution of oxalyl chloride (7.6 mg, 7 μL, 0.06 mmol) cooled to -78 °C, DMSO (9.5 mg, 7.7 μL, 0.12 mmol) was added, and the reaction was stirred for 10 min. Then a 1 mL CH_2Cl_2 solution of compound **19a** (11 mg, 0.03 mmol) was added, and the reaction was stirred at -78 °C for 1.3 h. The reaction was quenched with triethylamine (19 mg, 26 μL, 0.18 mmol), and was allowed to warm up to -20 °C. Then a 1 mL CH_2Cl_2 solution of the Wittig reagent (generated *in situ* form the corresponding phosphonium bromide salt (24 mg, 0.05 mmol) and DMAP (7 mg, 0.057 mmol) at 0 °C, 20 min) was transferred to the reaction mixture via cannula. The reaction was stirred at -20 °C for 10 min, then warmed up and stirred at rt for additional 3 h, quenched with a buffer solution of NH_4Cl/NH_4OH, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (ethyl acetate/hexane, 2:1 to 1:1) to afford 10.5 mg (74%) of **20a** as a thick yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 15.6 Hz, 1H), 6.88 (dd, *J* = 15.2, 8.4 Hz, 1H), 5.34-5.39 (m, 1H), 5.15-5.21 (m, 1H), 5.47-5.64 (m, 1H), 4.45 (t, *J* = 8.0 Hz, 3H), 4.26 (d, *J* = 2.8 Hz, 1H), 4.25 (d, *J* = 2.4 Hz, 1H), 4.00-4.11 (m, 4H), 3.57 (ddd, *J* = 15.6, 6.8, 2.4 Hz, 1H), 1.04-1.07 (m, 21H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ 204.2, 163.6, 157.4, 153.2, 143.9, 124.4, 94.5, 87.3, 66.2, 62.2, 60.9, 56.3, 42.5, 41.4, 17.9, 11.9 IR (KBr, cm^{-1}) 2941, 2864, 1754, 1727, 1682, 1660, 1649, 1083 HRMS (ESI) m/z calcd. for $C_{23}H_{36}N_2O_6SiNa$ 487.2240, found 487.2236 $[M+Na]^+$

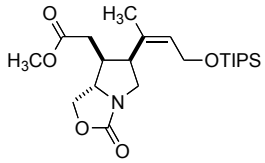


23a

(6*S*,7*S*,7a*S*)-7-(2-oxo-2-(2-oxooxazolidin-3-yl)ethyl)-6-((*Z*)-4(triisopropylsilyloxy)but-2-en-2-yl)tetrahydropyrrolo[1,2-c]oxazol-3(1H)-one (23a).

To a 0.5 mL 0 °C THF solution of anhydrous $ZnCl_2$ (68 mg, 0.5 mmol), 0.67 mL of MeLi (0.66 mL, 1.0 mmol, 1.5 M in diethyl ether) was added dropwise. After stirring for 10 min at 0 °C, the mixture was transferred by cannula to a 5 mL 0 °C THF solution of $Ni(COD)_2$ (12 mg, 0.04 mmol). The mixture was cooled to -20 °C, then an 8 mL THF solution of **20a** (100 mg, 0.2 mmol) and titanium isopropoxide (60 mg, 60 μL, 0.2 mmol) was added dropwise. The mixture was slowly warmed to rt, and stirred for 2 h, quenched with sat. NH_4Cl, extracted with ethyl acetate, and the combined extracts were washed with brine and dried over $MgSO_4$. After filtration, the solvent was removed under

vacuum, and the crude product was purified by flash column chromatography (hexane/ethyl acetate, 2:1 to 1:2) to yield 78 mg (77%, 94:6 *dr*) of **23a** as a thick oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.53 (td, *J* = 6.5, 1.0 Hz, 1H), 4.52 (dd, *J* = 9.0, 7.5 Hz, 1H), 4.41 (dd, *J* = 12.3, 7.8 Hz, 1H), 4.41 (dd, *J* = 7.3, 4.8 Hz, 1H), 4.24 (dd, *J* = 9.0, 4.0 Hz, 2H), 4.08 (ddd, *J* = 12.5, 5.0, 1.5 Hz, 1H), 3.97 (ddd, *J* = 16.5, 12.5, 8.0 Hz, 2H), 3.83 (dd, *J* = 12.0, 8.5, 1H), 3.79 (dd, *J* = 8.3, 3.8 Hz, 1H), 3.57 (ddd, *J* = 14.0, 8.5 Hz, 1H), 3.17 (dd, *J* = 12.0, 5.0 Hz, 1H), 3.15 (dd, *J* = 18.3, 7.3 Hz, 1H). 2.81 (dd, *J* = 18.0, 8.0 Hz, 1H), 2.46-2.53 (m, 1H), 1.73 (d, *J* = 1.5 Hz, 3H), 1.02-1.09 (m, 21H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.7, 161.2, 153.4, 132.9, 131.5, 68.3, 63.7, 62.2, 59.5,48.8, 43.3, 42.7, 42.3, 33.8, 2.5, 17.9, 11.9. IR (KBr, cm^{-1}) 2940, 2864, 1773, 1750, 1470, 1387 HRMS (ESI) m/z calcd. for $C_{24}H_{40}N_2O_6SiNa$ 503.2553, found 503.2541$[M+Na]^+$



24a

Methyl-2-((6*S*,7*S*,7a*S*)-3-oxo-6-((*Z*)-4-(triisopropylsilyloxy)but-2-en-2-yl)hexahydro-pyrrolo[1,2-c]oxazol-7-yl)acetate (24a).

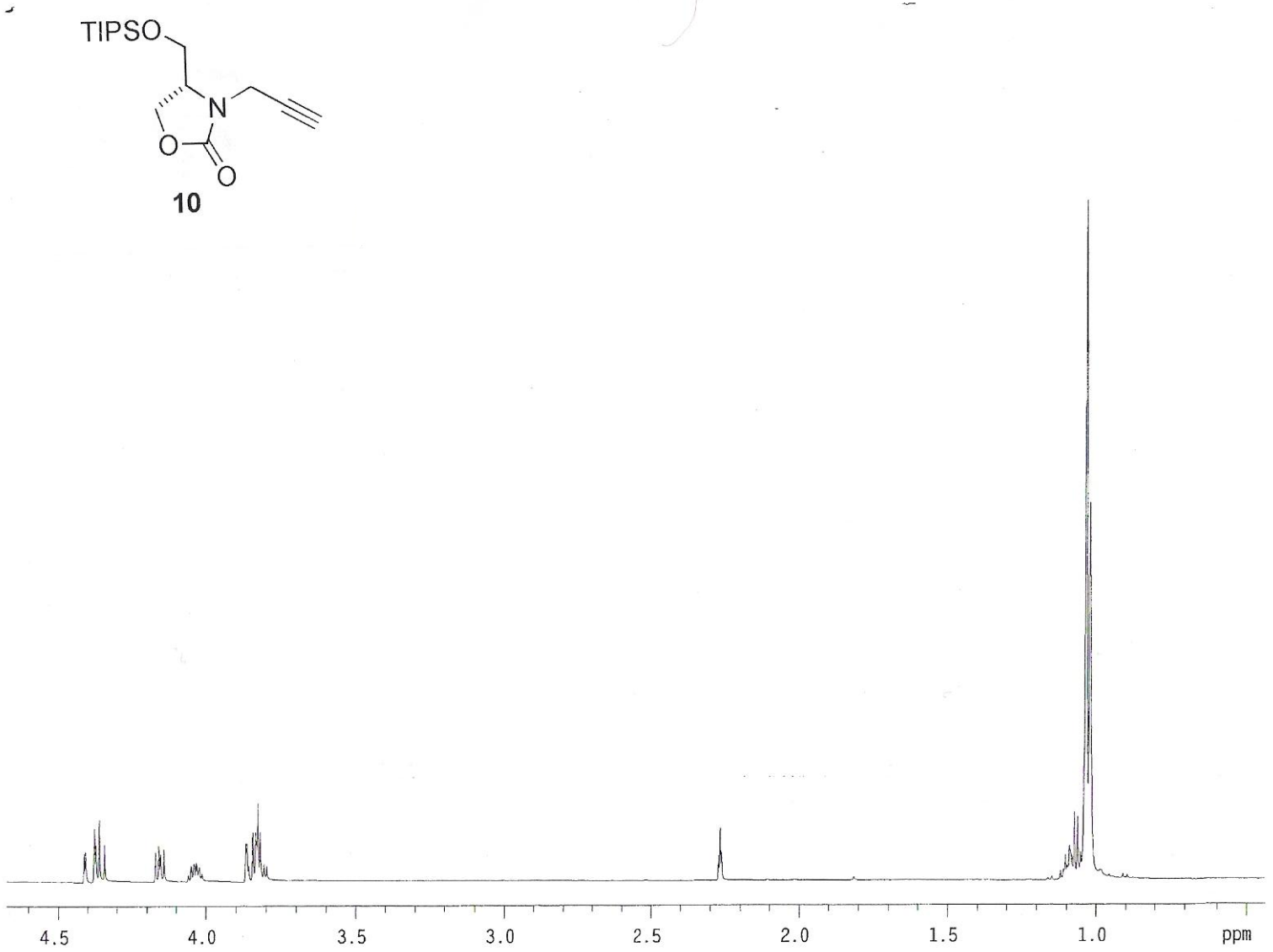
MeMgBr (104 μL, 0.125 mmol, 1.2 M) was added dropwise to a 2 mL dry methanol stirred at 0 °C. The mixture was stirred at 0 °C for 10 min and then 1.5 mL methanol solution of compound **23a** (12 mg, 0.025 mmol) were added drop wise. The reaction was allowed to warm to room temperature and stir for 2 h, and then it was cooled to 0 °C, quenched with sat. NH_4Cl, extracted 3x with ethyl acetate, and the extract was dried over $MgSO_4$. The solvent was removed under vacuum, and the crude product was purified by column chromatography (hexane/ethyl acetate, 4:1 to 2:1) to yield 7.8 mg (75%) of **24a** as a yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.56 (t, *J* = 6.0 Hz, 1H), 4.54 (dd, *J* = 9.0, 8.0, 1H), 4.27 (dd, *J* = 9.5, 4.0 Hz, 1H), 4.21 (dd, *J* = 12.5, 7.0 Hz, 1H), 4.11 (ddd, *J* = 13.0, 6.0, 1.0 Hz, 1H), 3.81 (dd, *J* = 12.0, 8.5, 1H), 3.66 (s, 3H), 3.57 (sextet, *J* = 4.5 Hz, 1H), 3.18 (dd, *J* = 12.0, 5.0 Hz, 1H), 2.42 (ddd, *J* = 18.5, 14.5, 9.5 Hz, 1H), 2.21 (dd, *J* = 16.8, 9.8, 1H), 1.71 (s, 3H), 1.03-1.08 (m, 21H) ^{13}C-NMR (125 MHz, $CDCl_3$) δ 172.7, 161.7, 133.5, 131.1, 68.7, 64.0, 59.3, 51.8, 48.6, 43.7, 43.1, 32.7, 21.6, 17.97, 11.9 IR (KBr, cm^{-1}) 2940, 2864, 1751, 1734, 1457, 1386, 1164, 1063, 881, 779, 681 HRMS (ESI) calcd. for $C_{22}H_{39}NO_5SiNa$ 448.2495, found 448.2496 $[M+Na]^+$

References

[S1] Y. Ni, R. M. Kassab, M. V. Chevliakov, J. Montgomery, *J. Am. Chem. Soc.* **2009**, *131*, 17714-17718.

[S2] E. El-Sayed, N. K. Anand, E. M. Carreira, *Org. Lett.* **2001**, *3*, 3017-3020.

[S3] A. G. Myers, B. Zheng, *J. Am. Chem. Soc.* **1996**, *118*, 4492-4493.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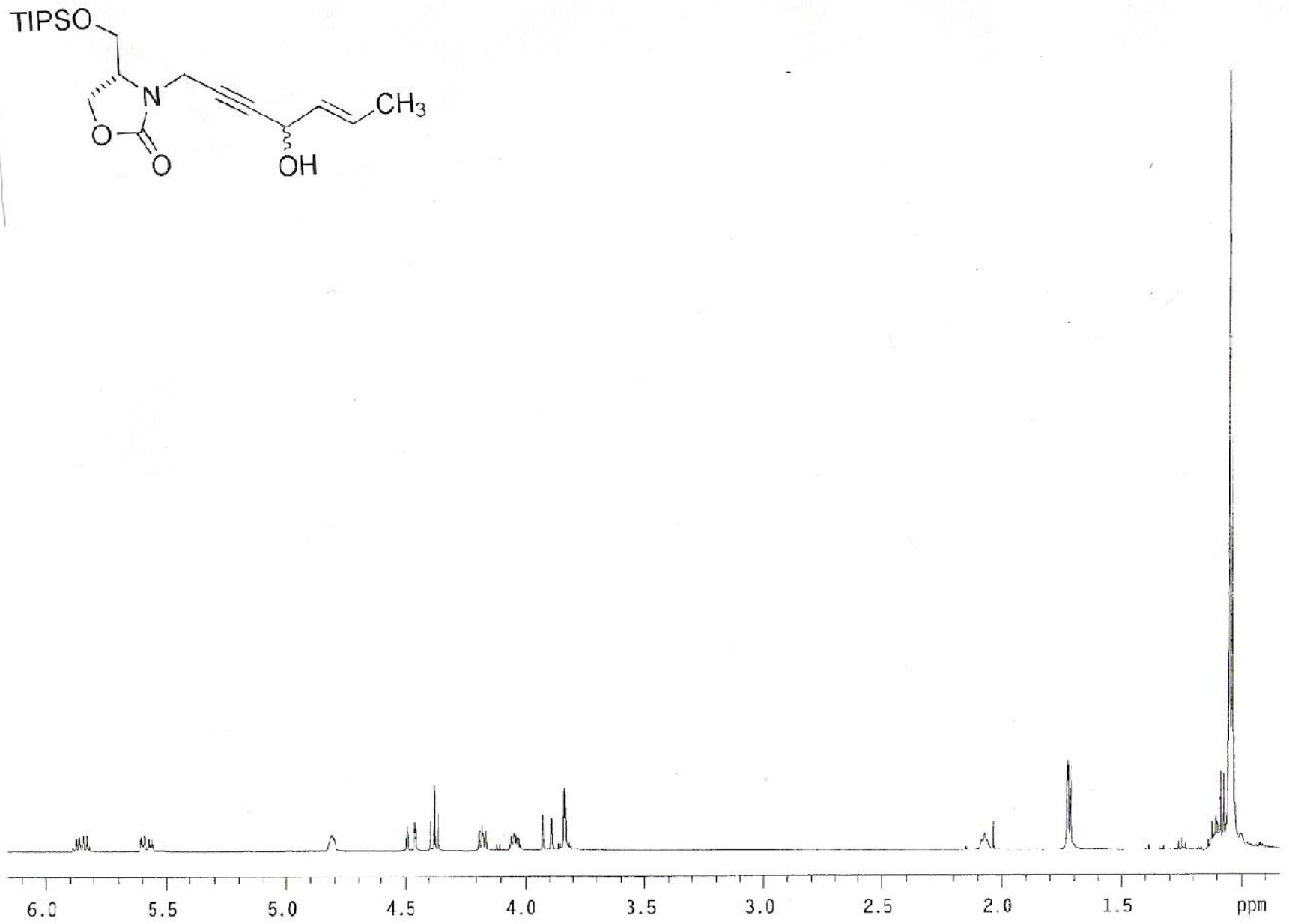
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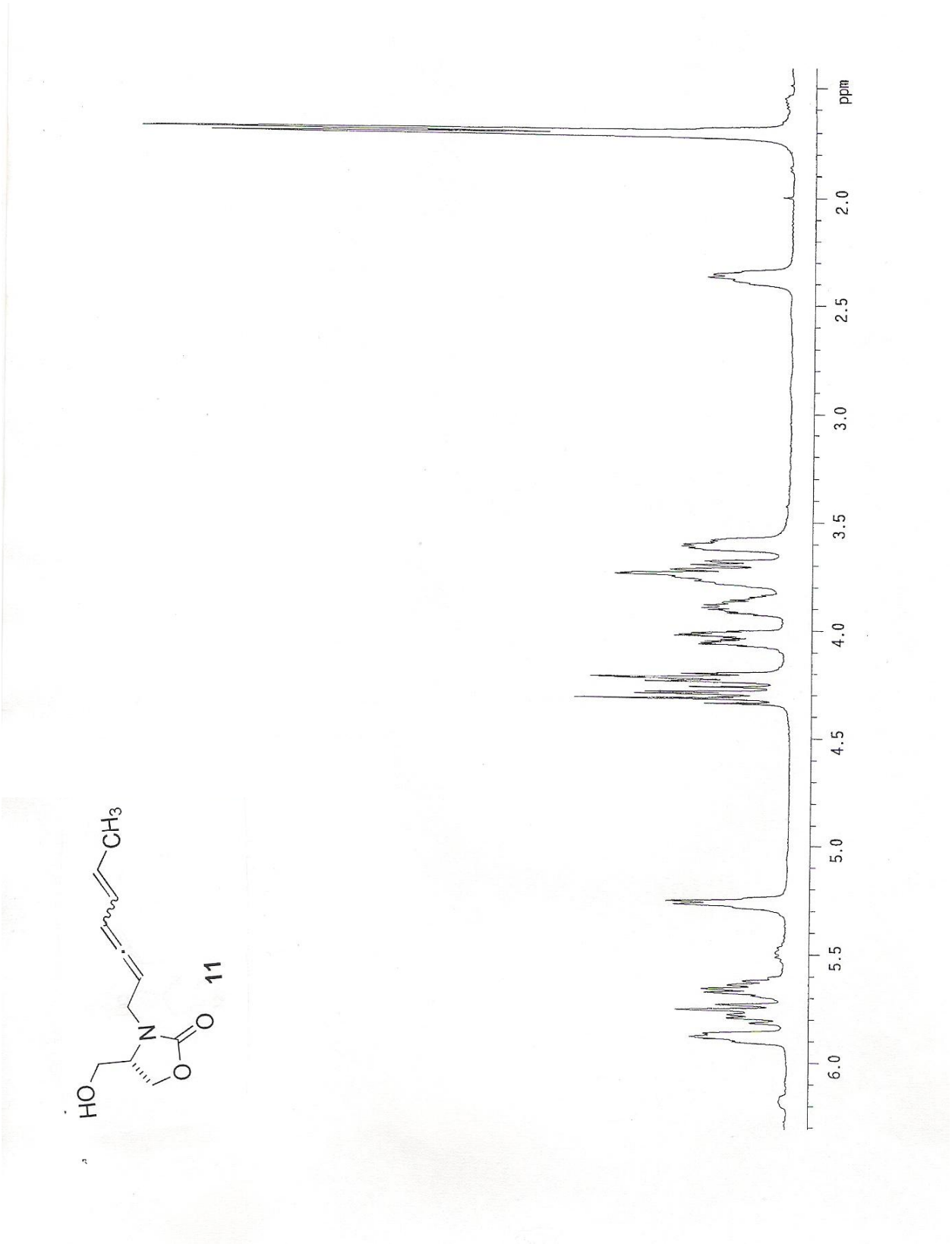
1.5
ppm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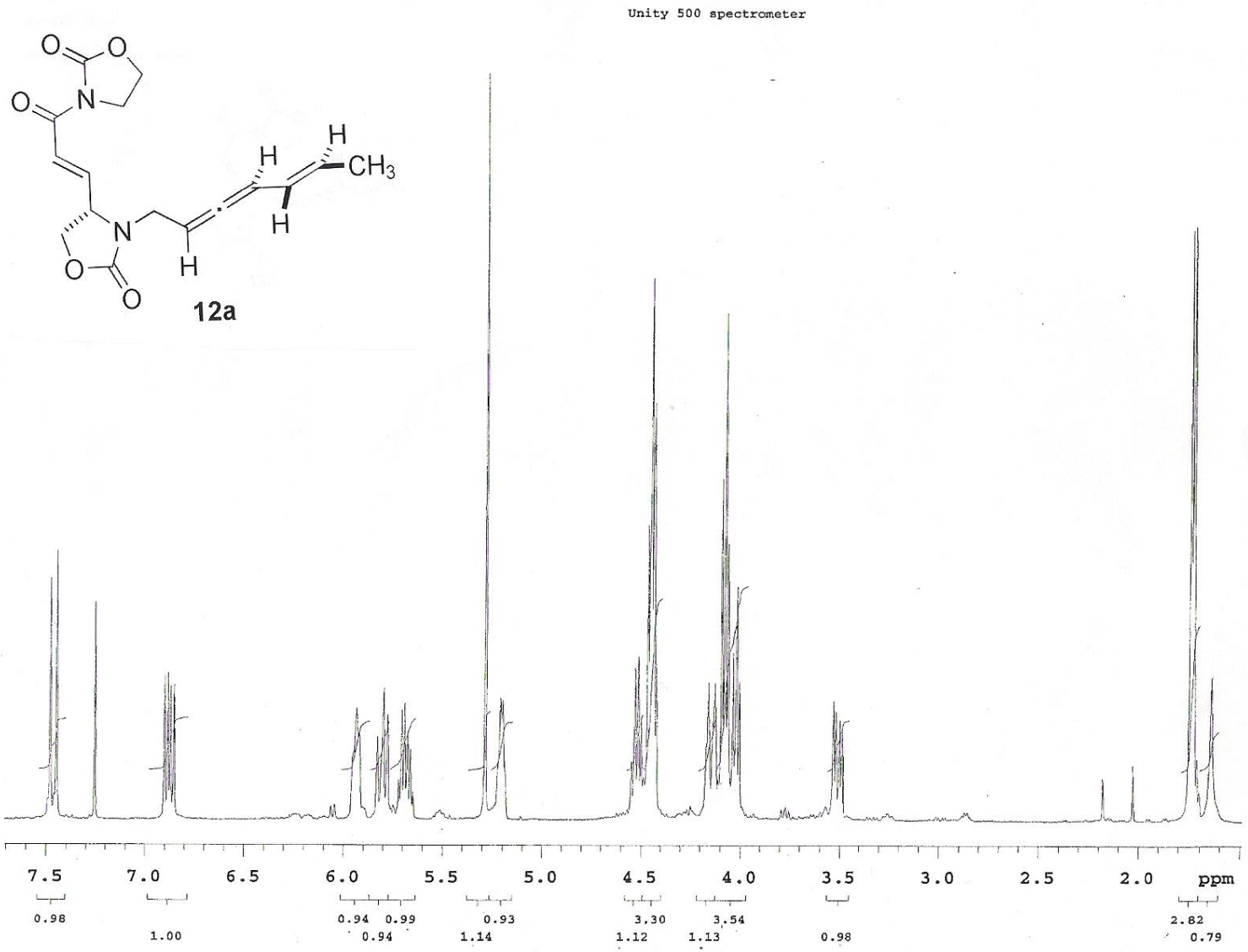
2.0
ppm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2.0
ppm
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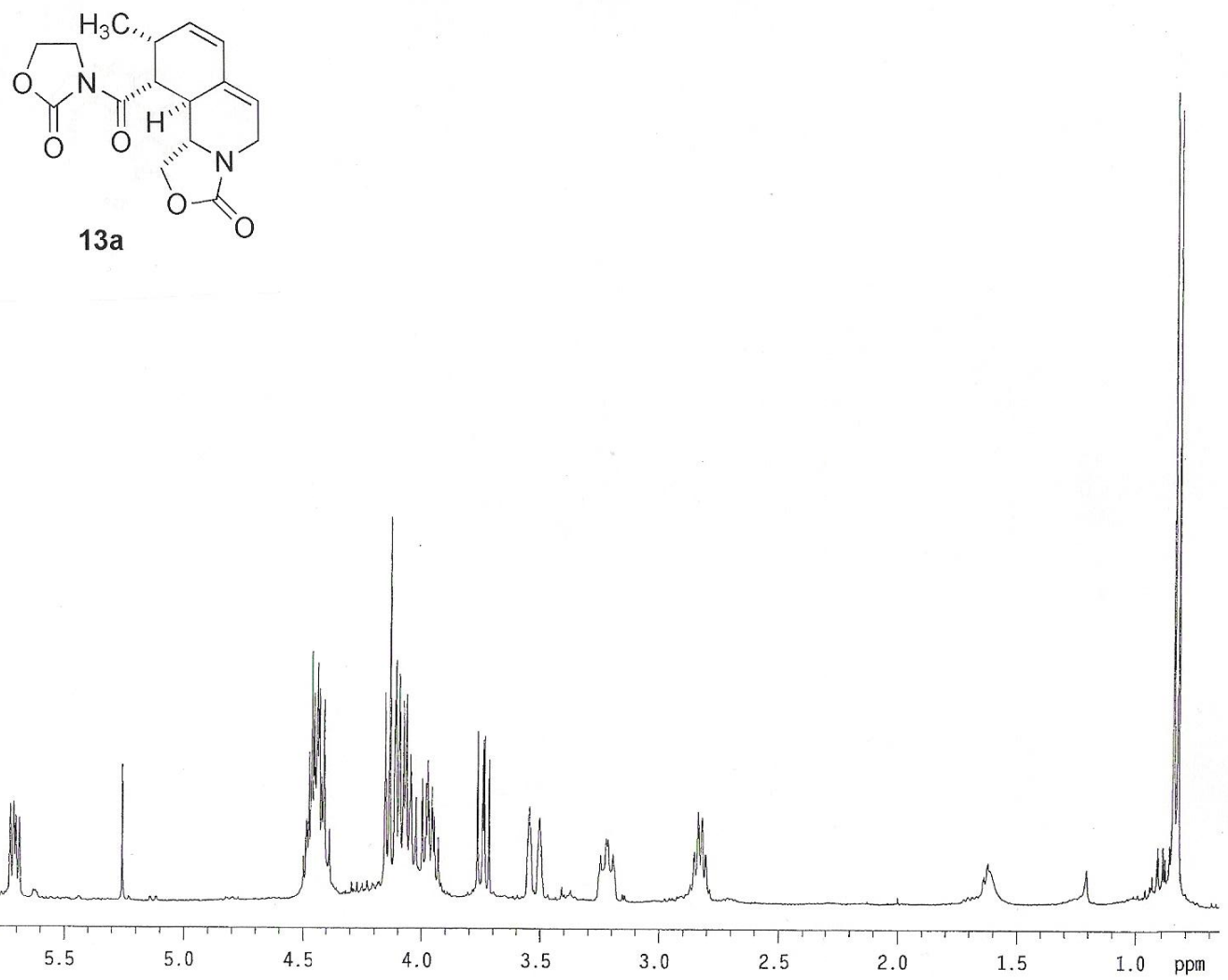
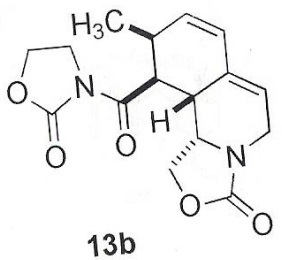
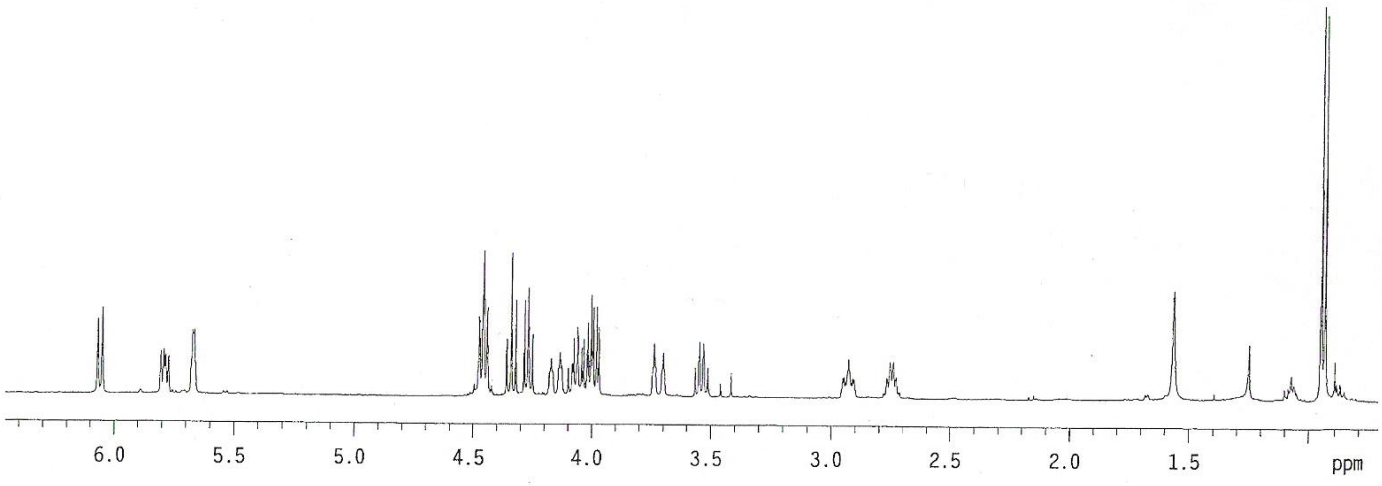
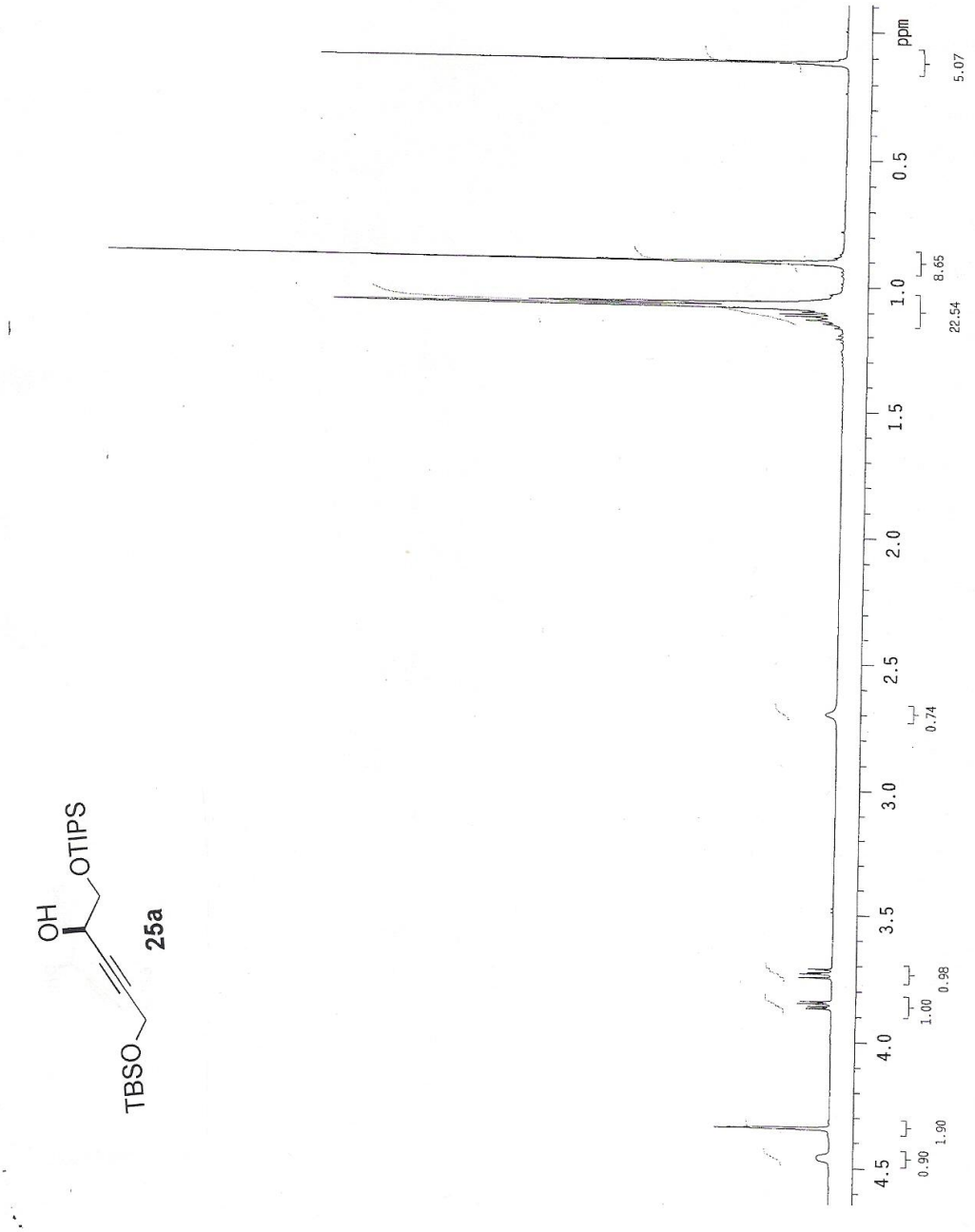


13a



13b

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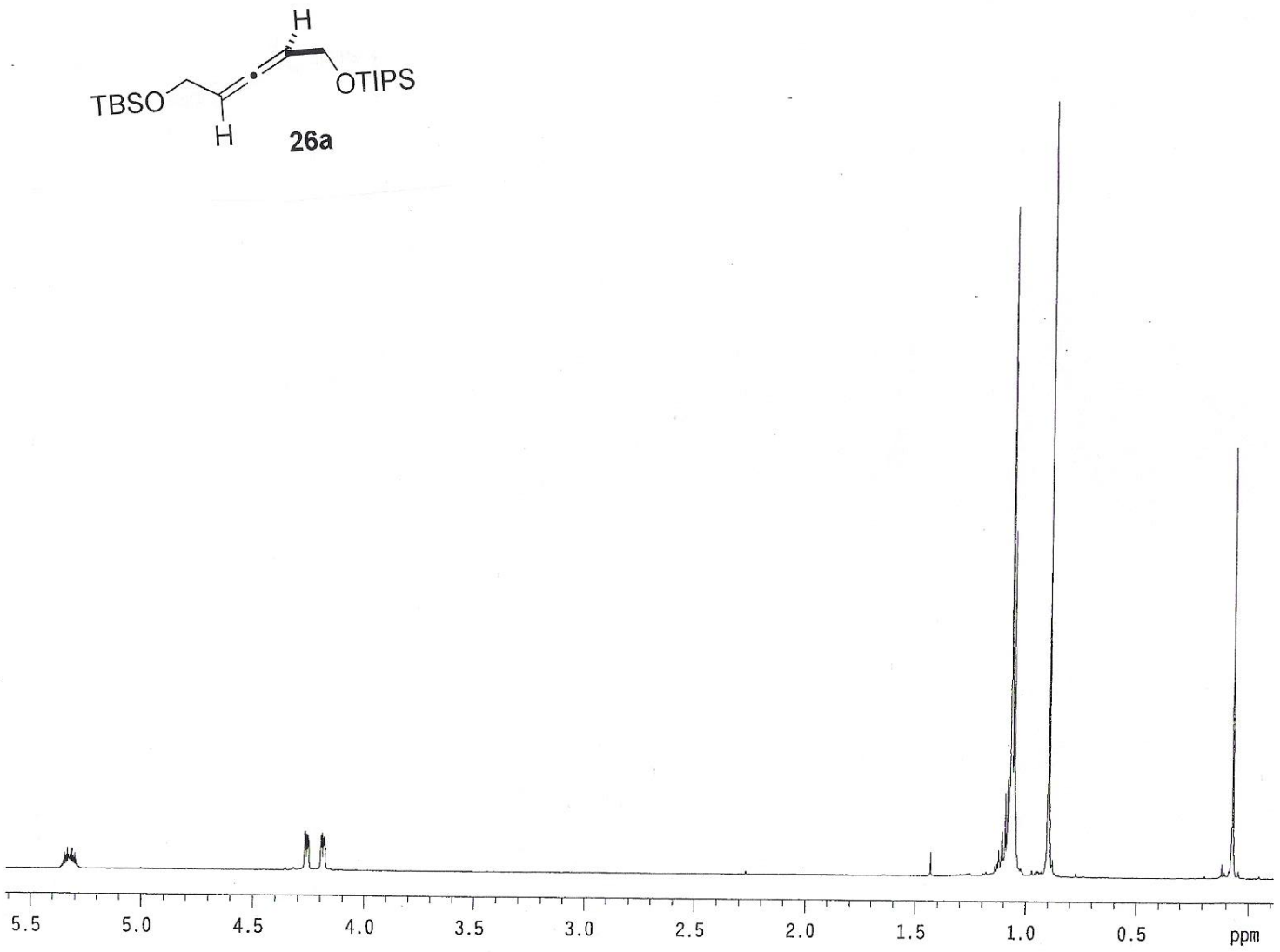
1.90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H
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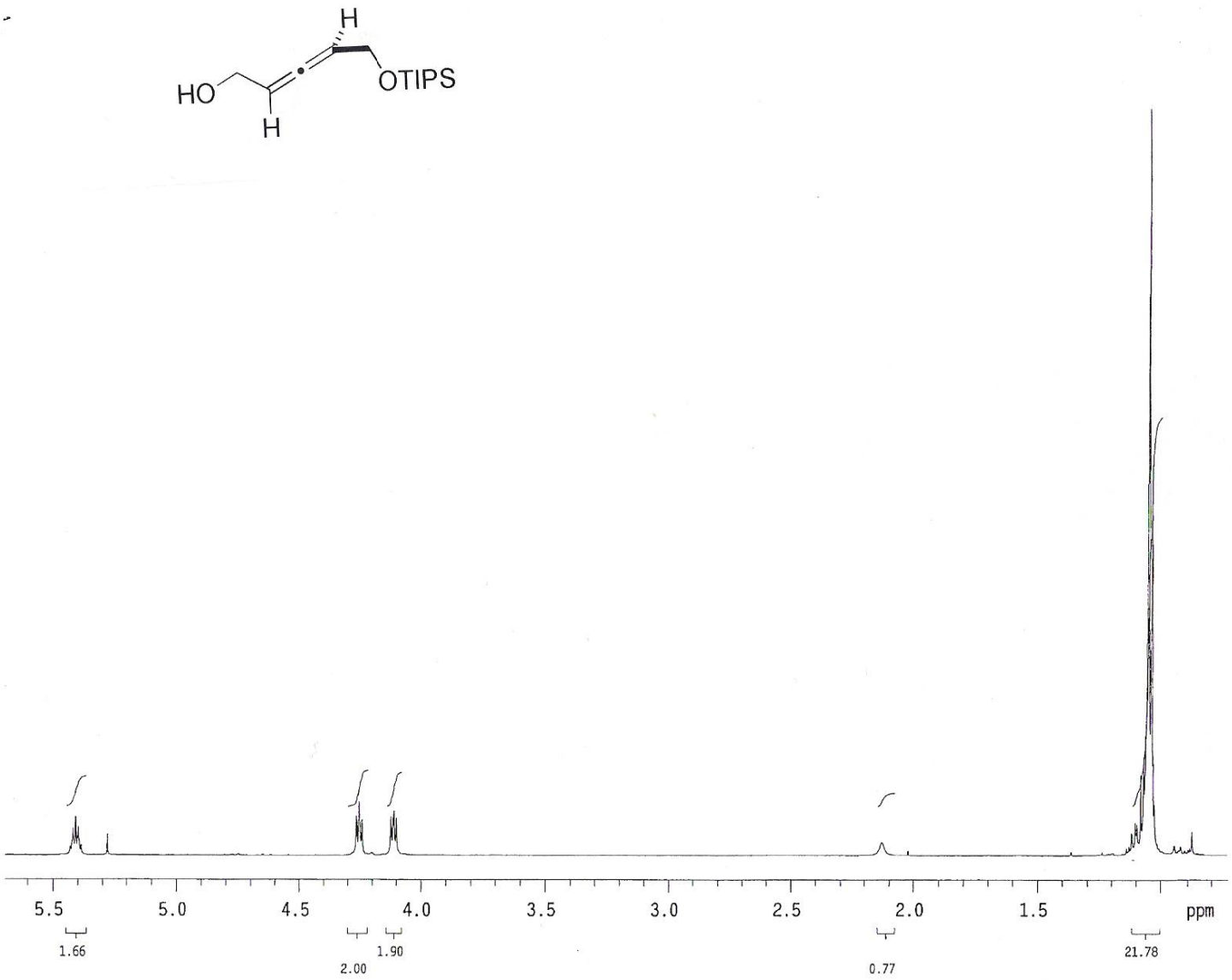
H
HO
OTIPS
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3.0
2.5
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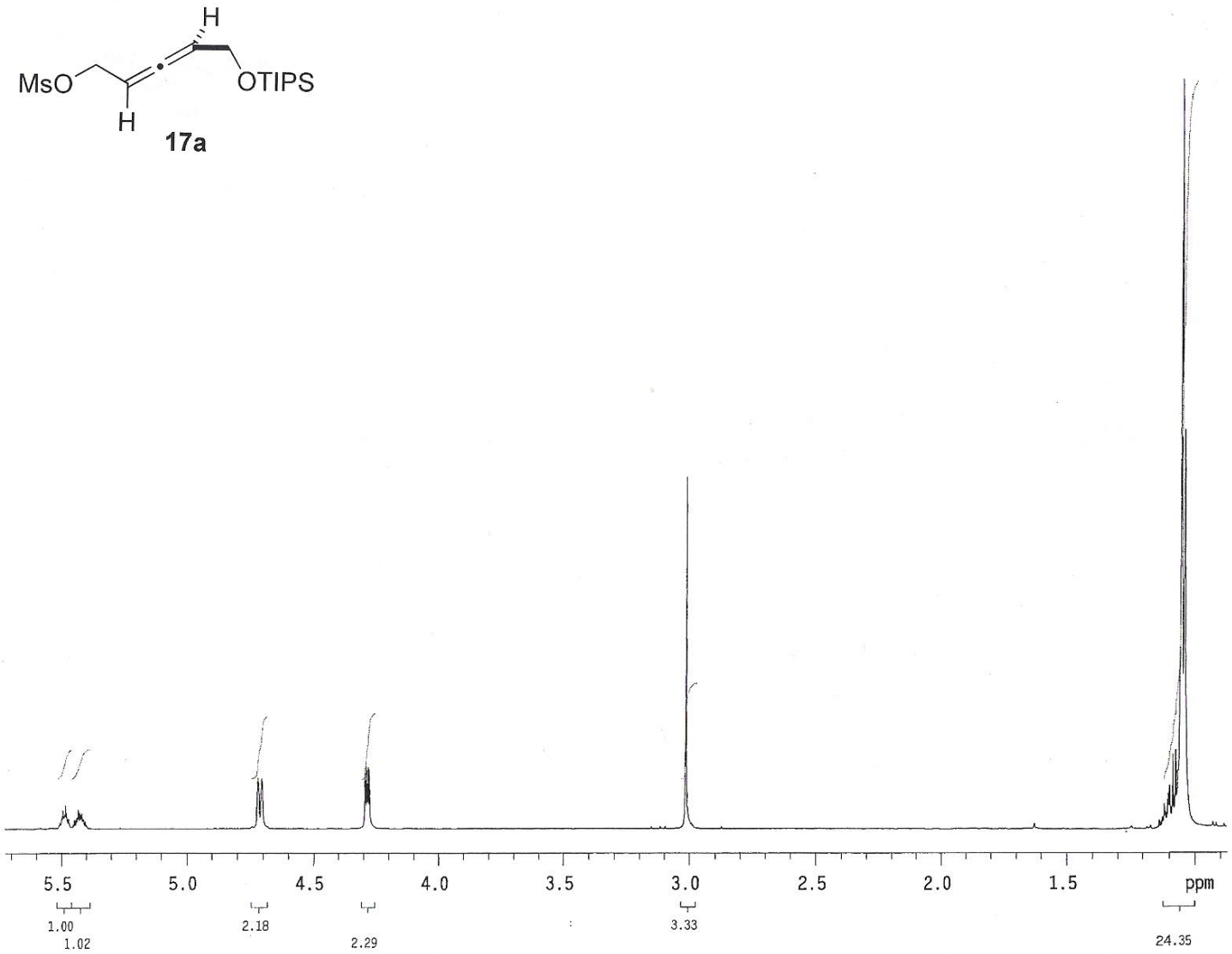
0.77
21.78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OTIPS
H
H
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1.5
ppm
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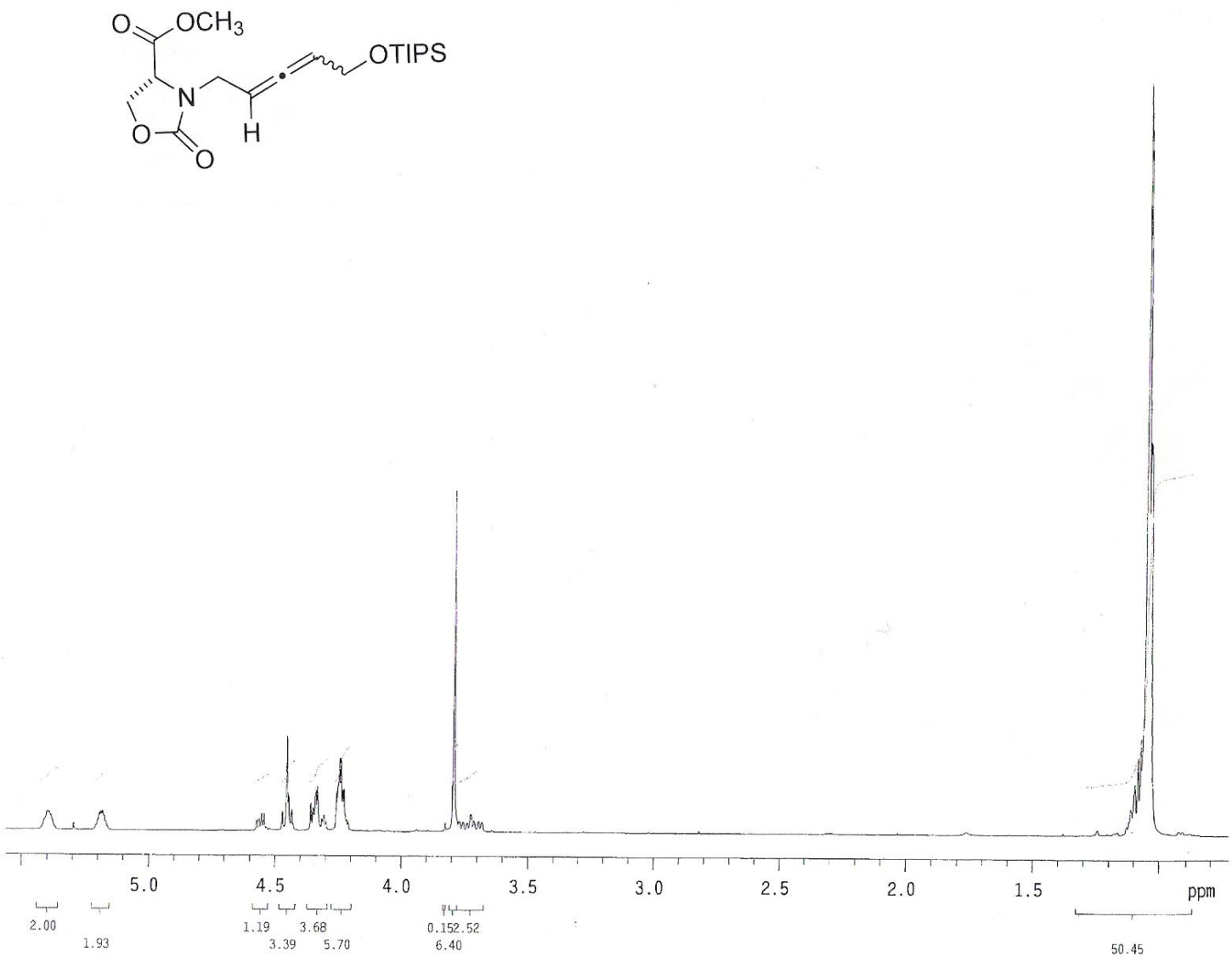
2.29
3.33
24.35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OTIPS
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O
H
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1.5
ppm
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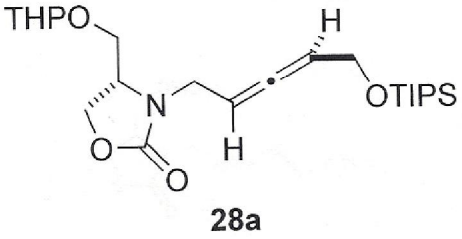
50.45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OTIPS
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H
O

28a

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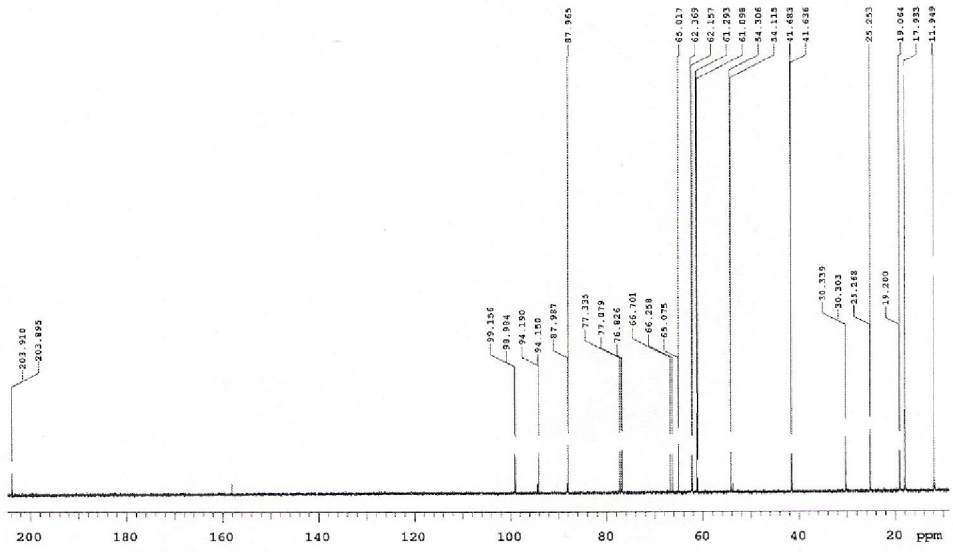
ppm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54.115
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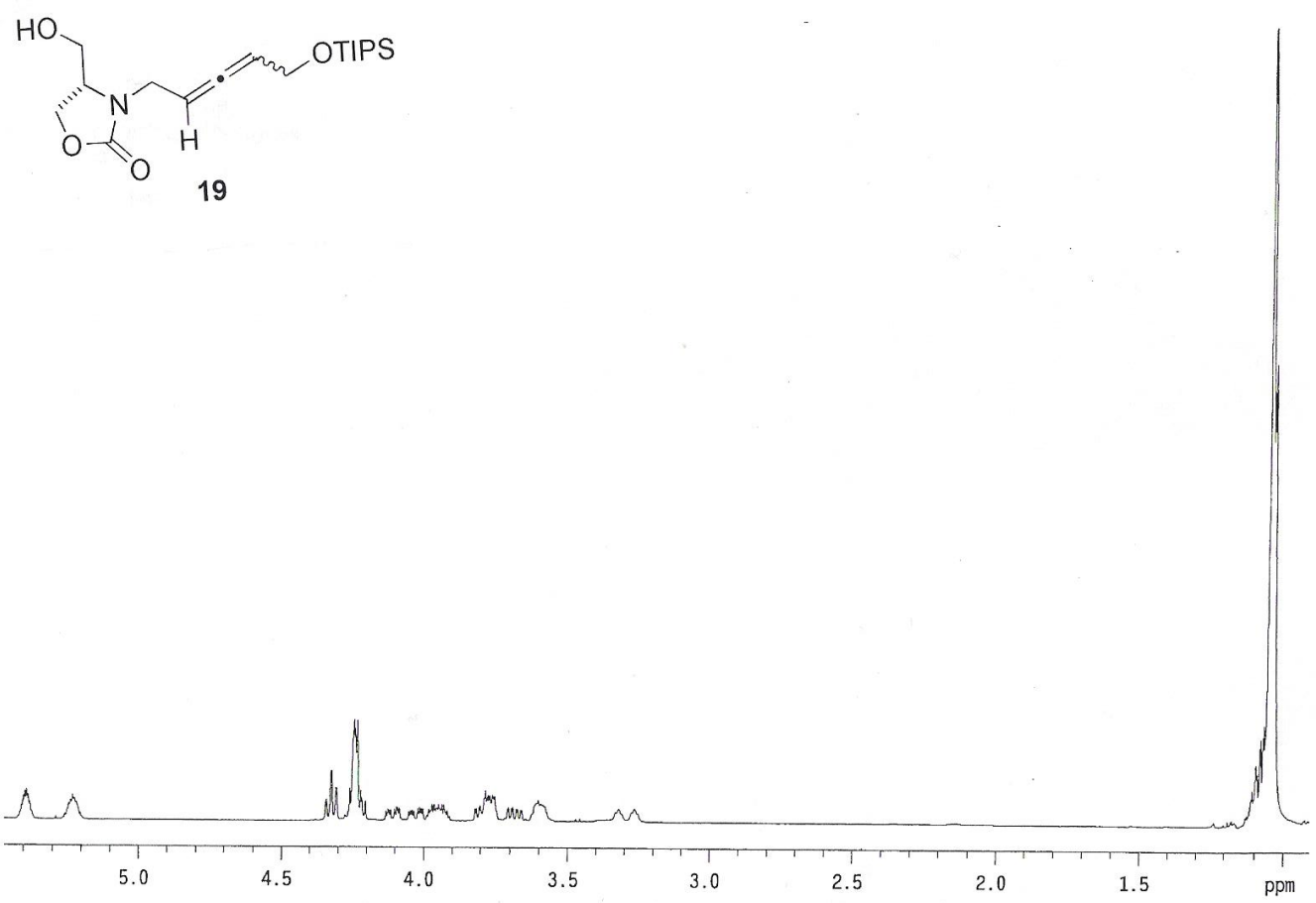
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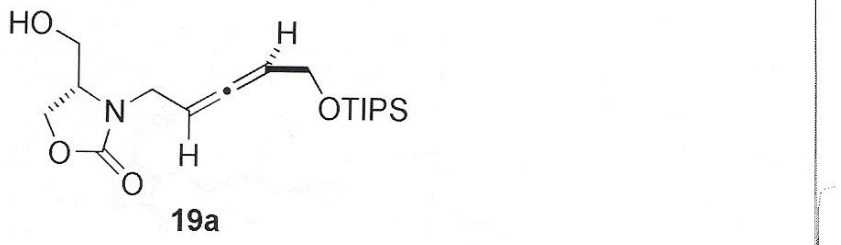
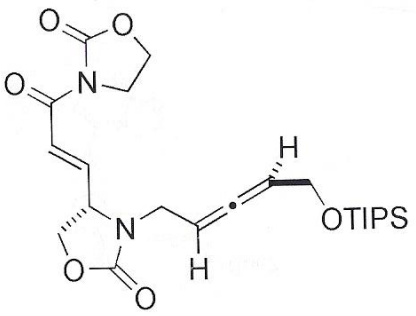
ppm



19a



20a

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H
20b
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O
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N
O
O
ppm
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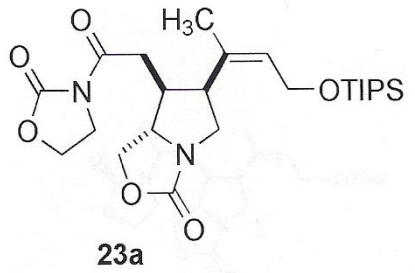
4
5
6
7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23a

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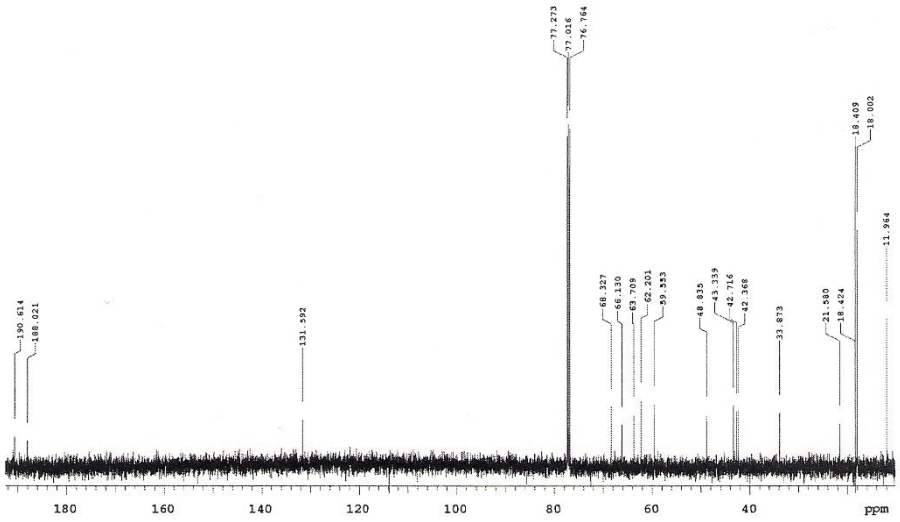
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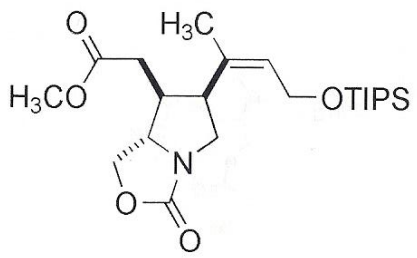
O
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H3CO
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O
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24a

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2.0
1.5
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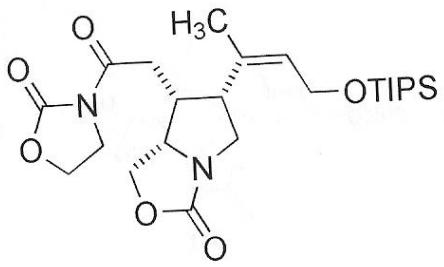
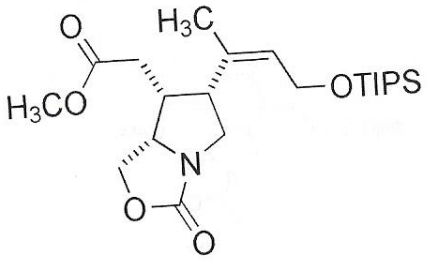


23b



24b