Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Total synthesis of the marine toxin phorboxazole A using palladium(II)-mediated intramolecular alkoxycarbonylation for tetrahydropyran synthesis

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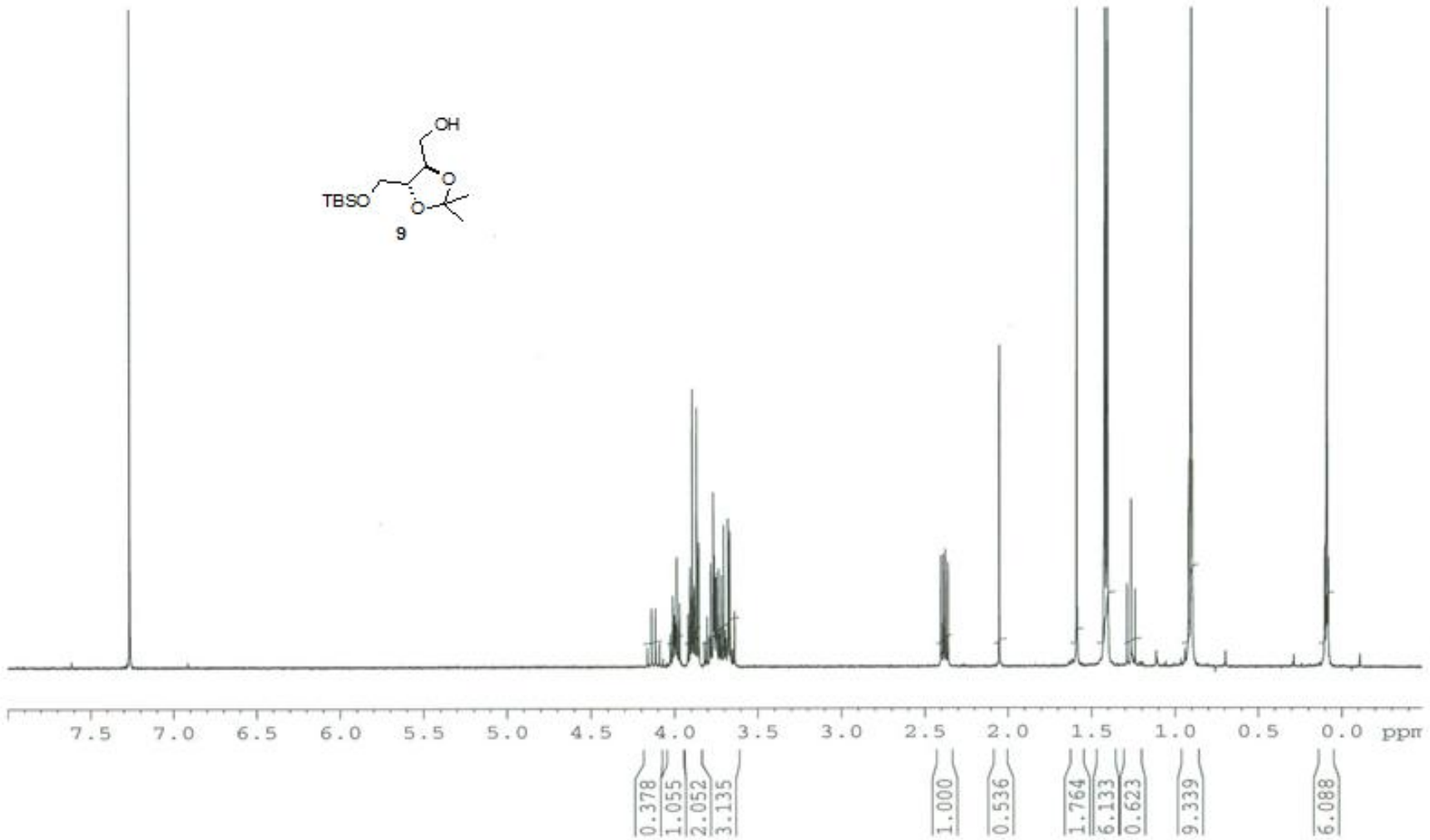
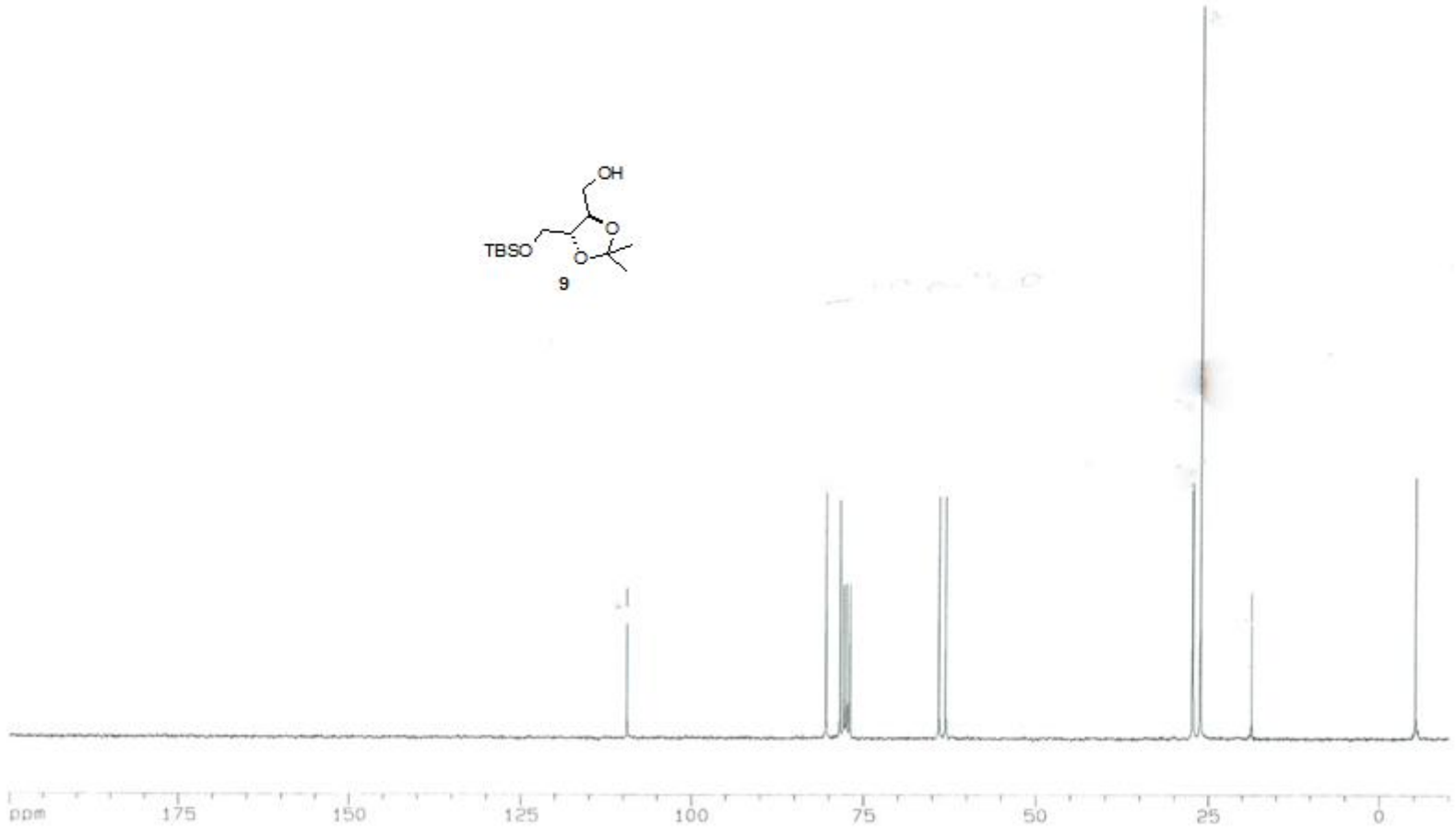
Content





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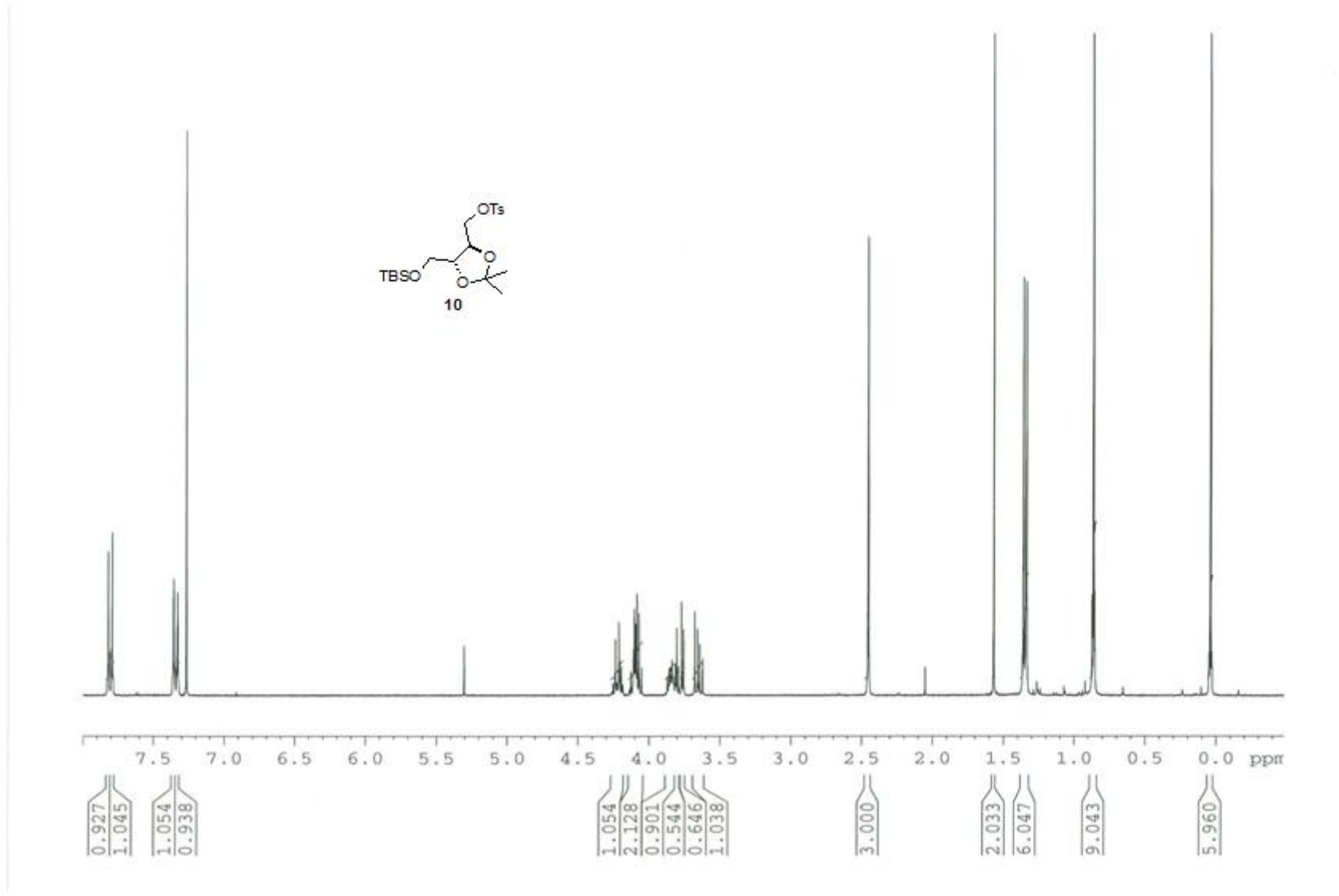

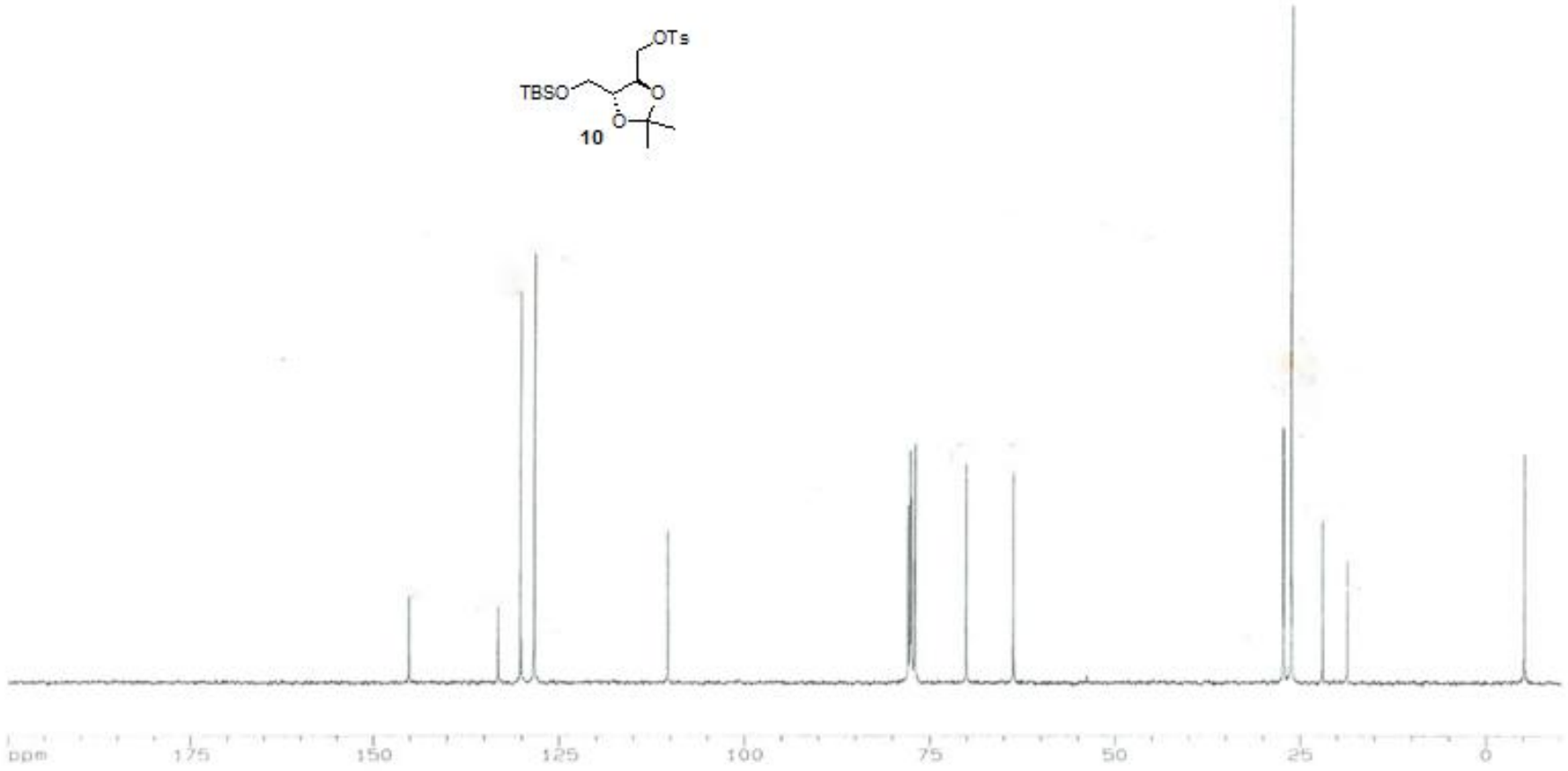

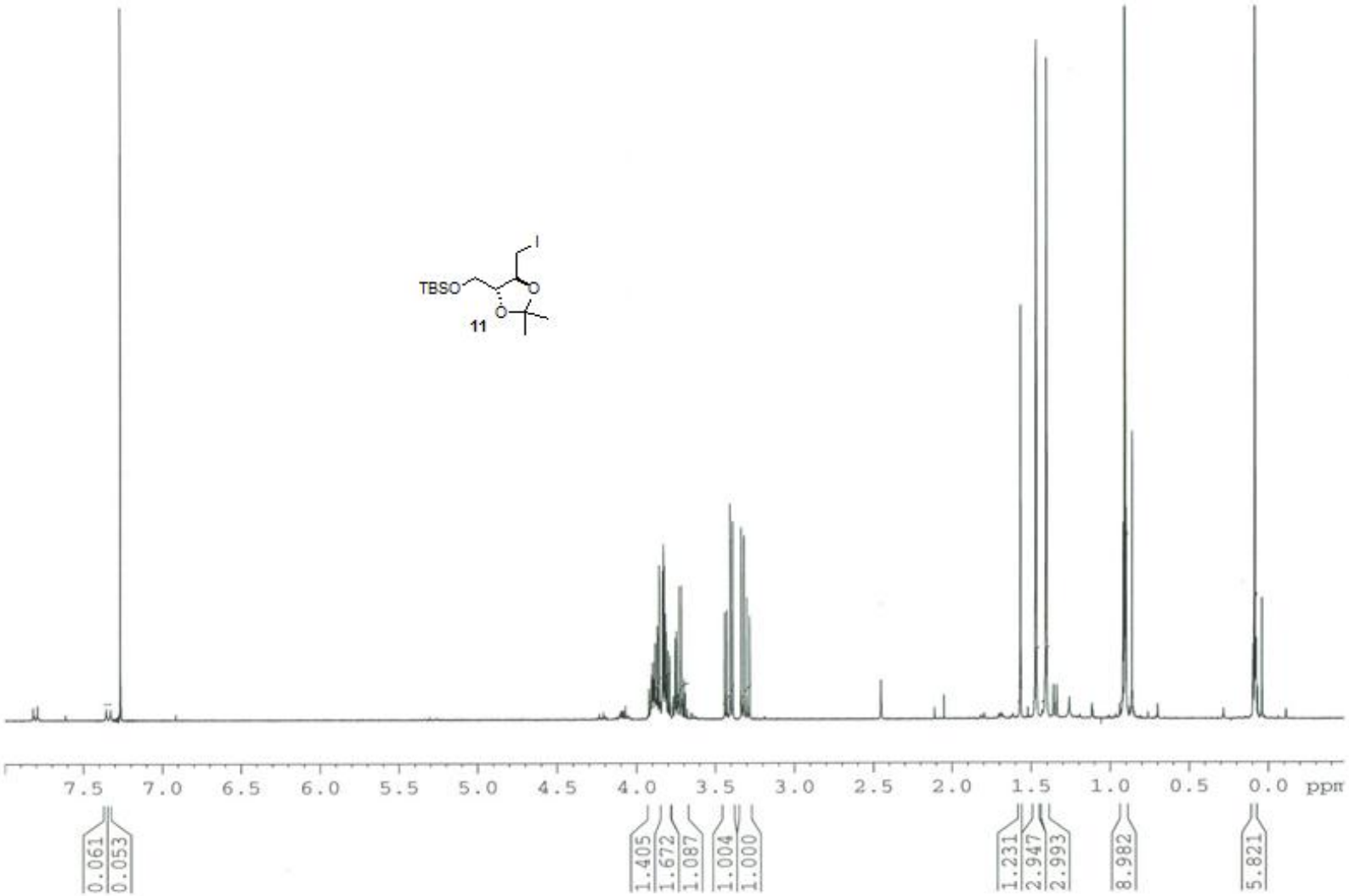

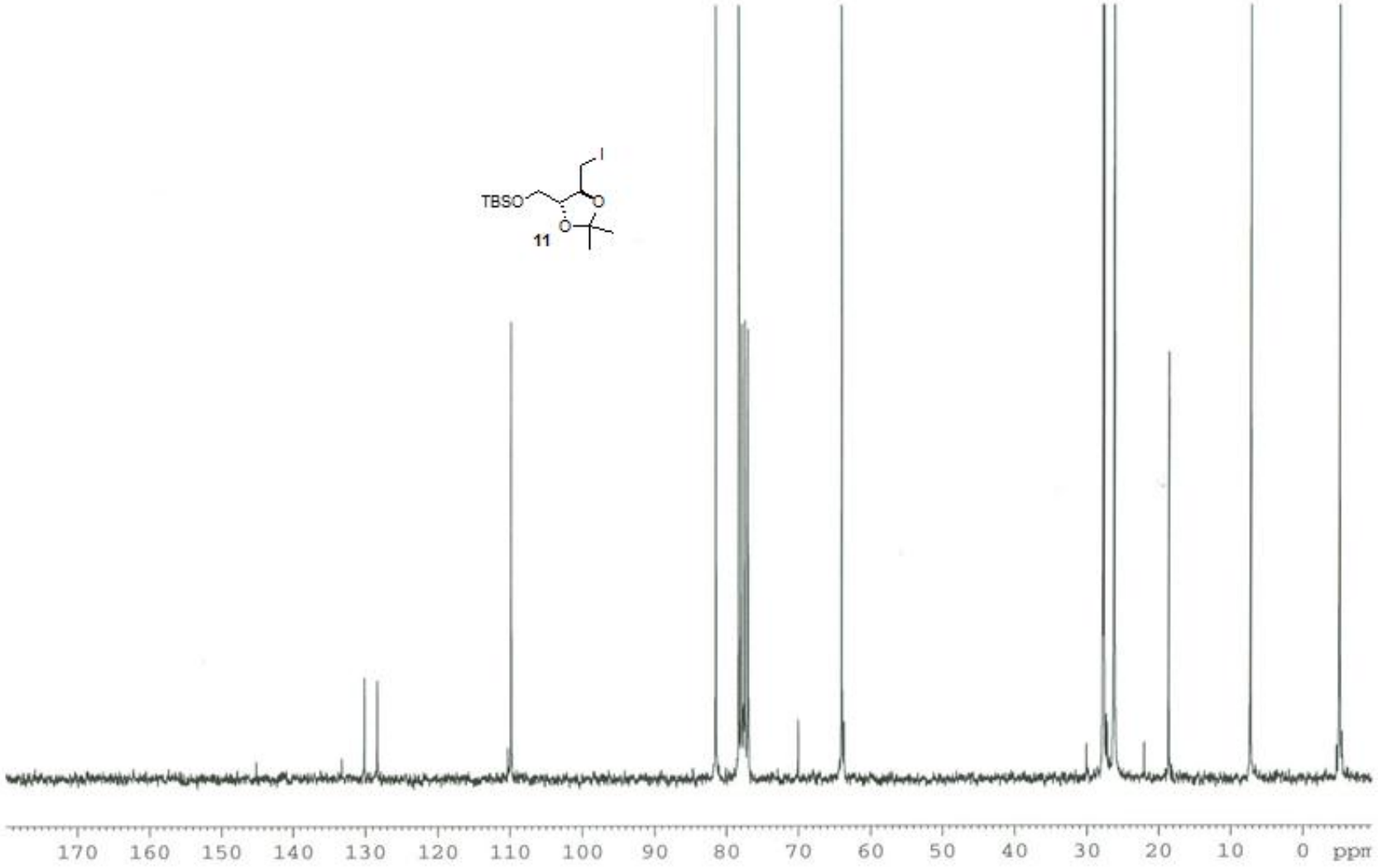

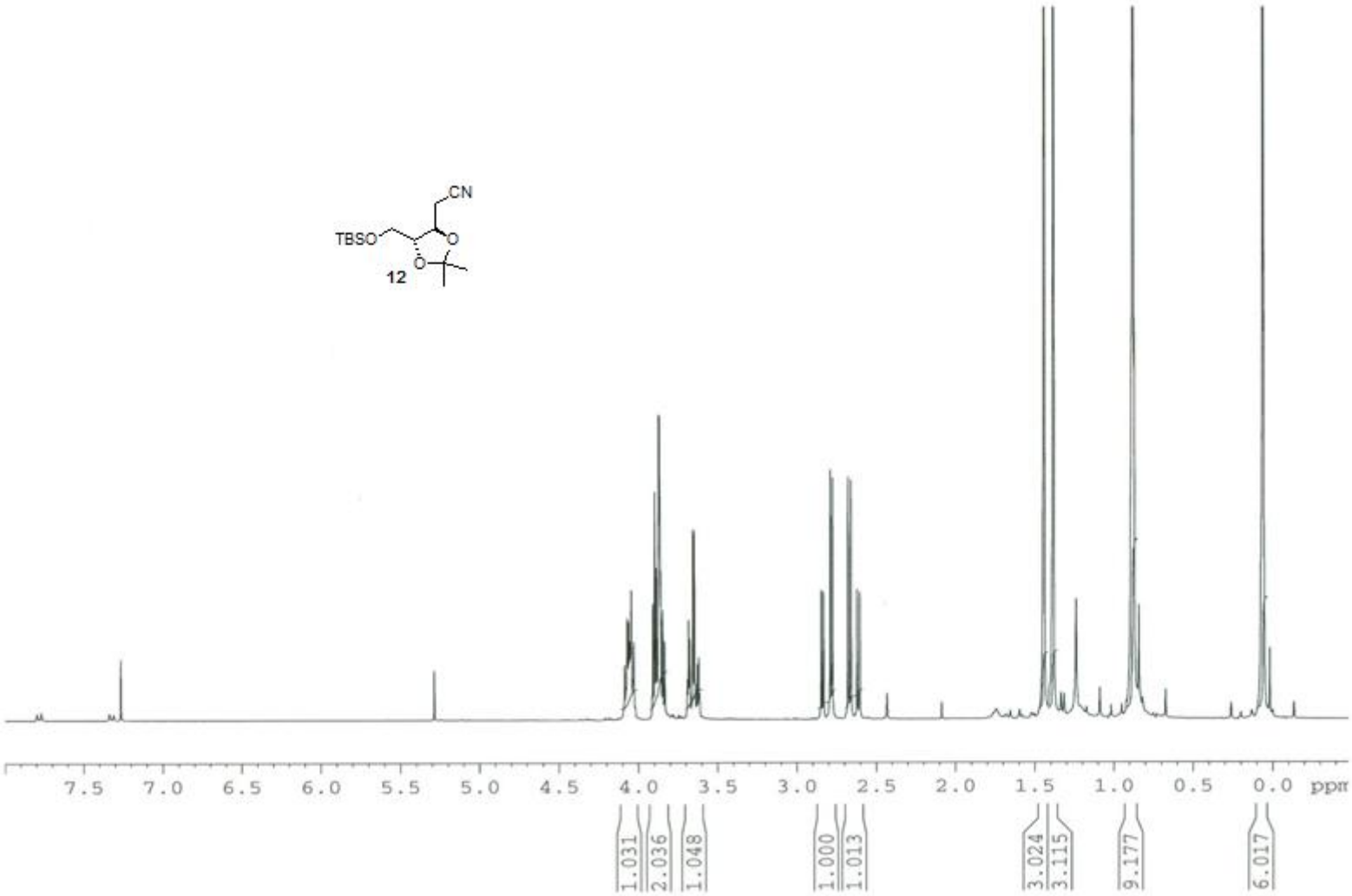

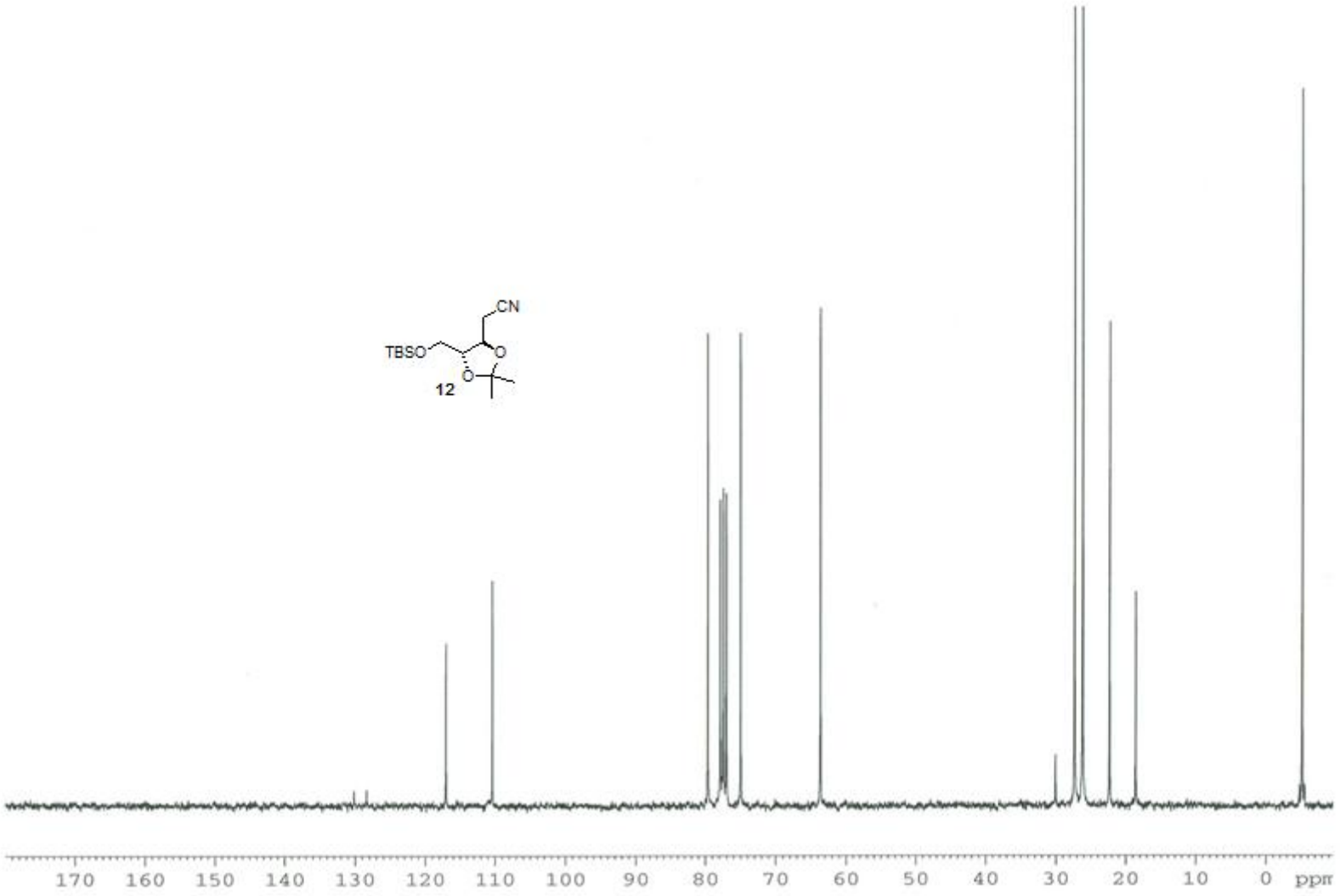

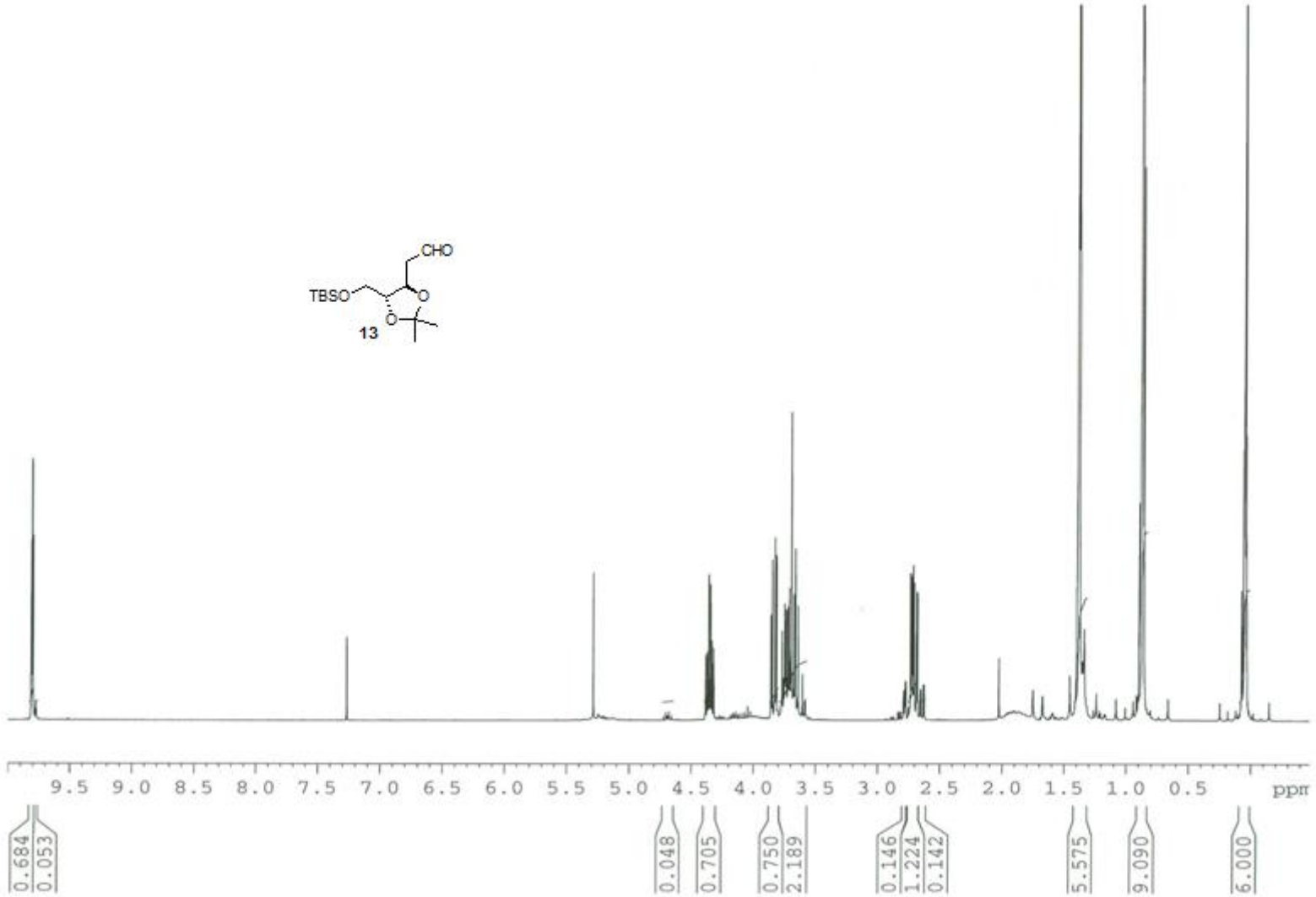

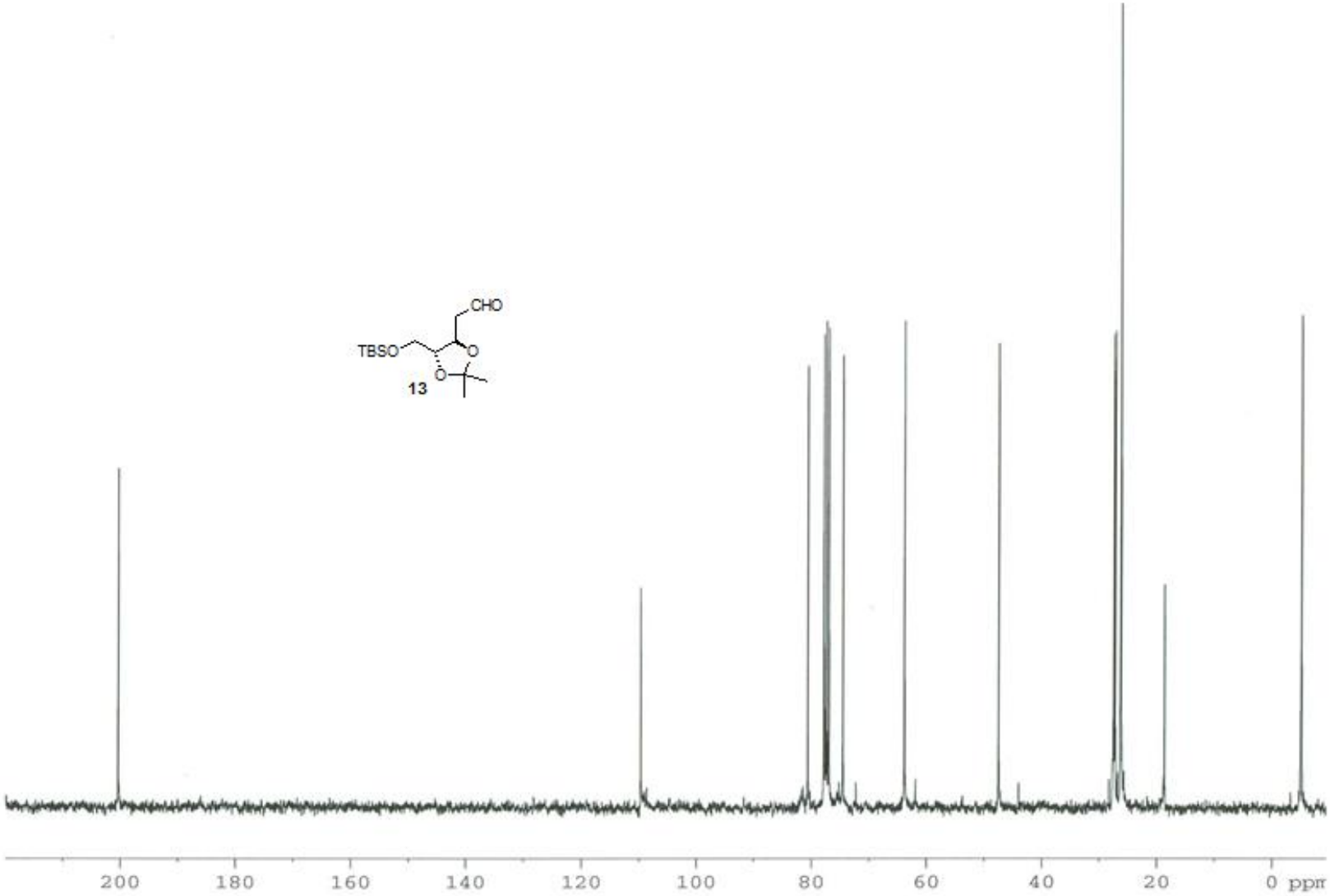

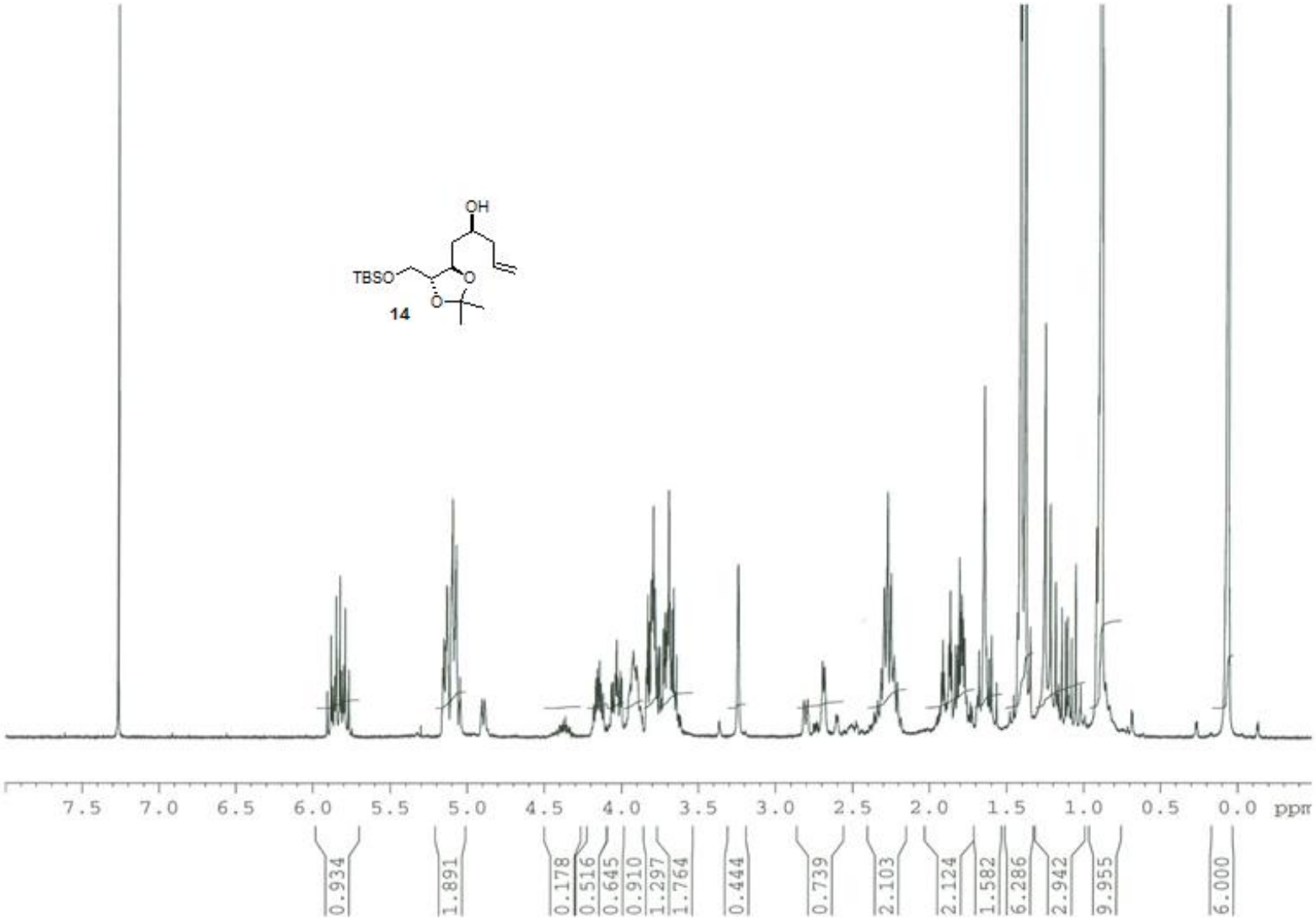

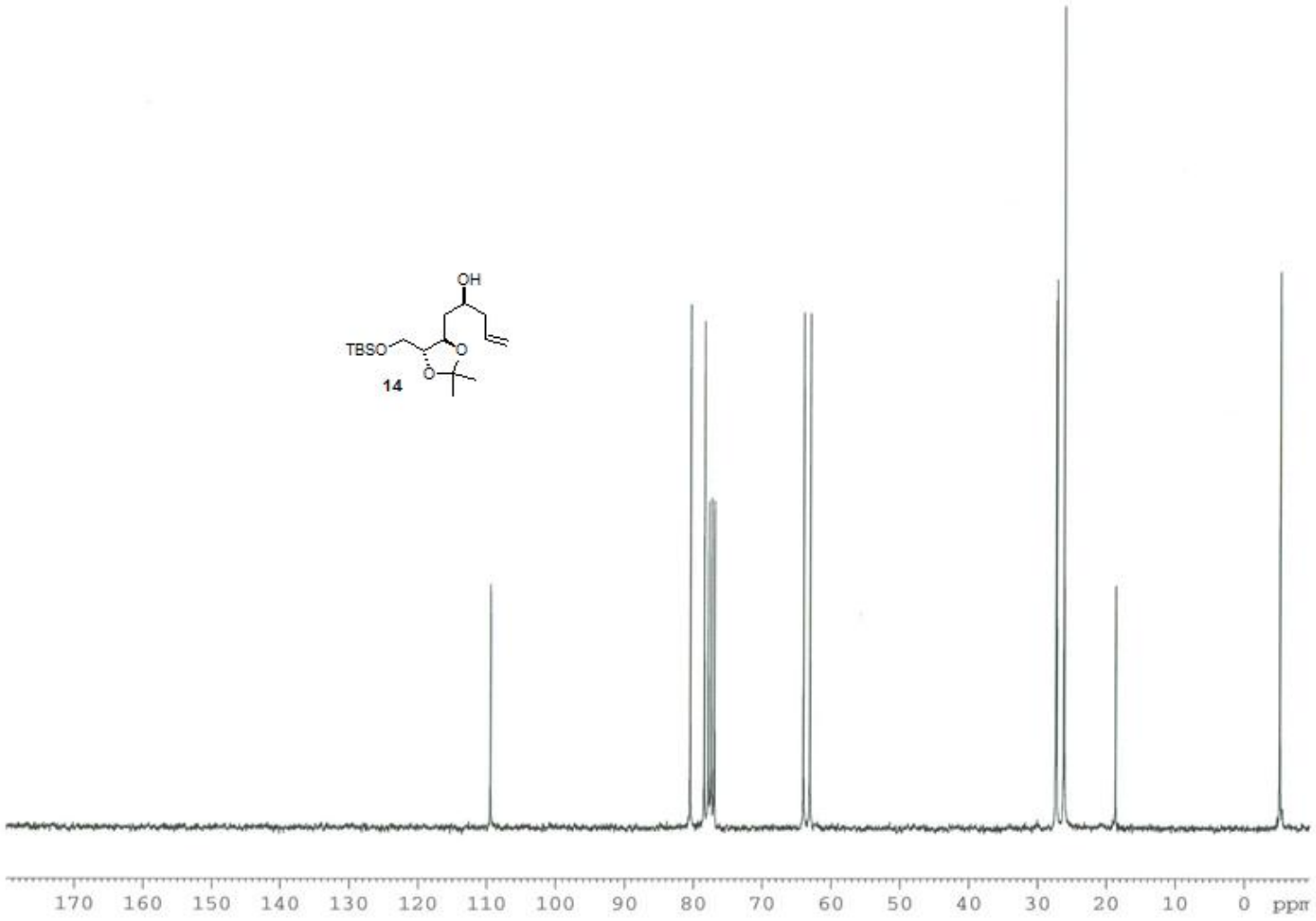

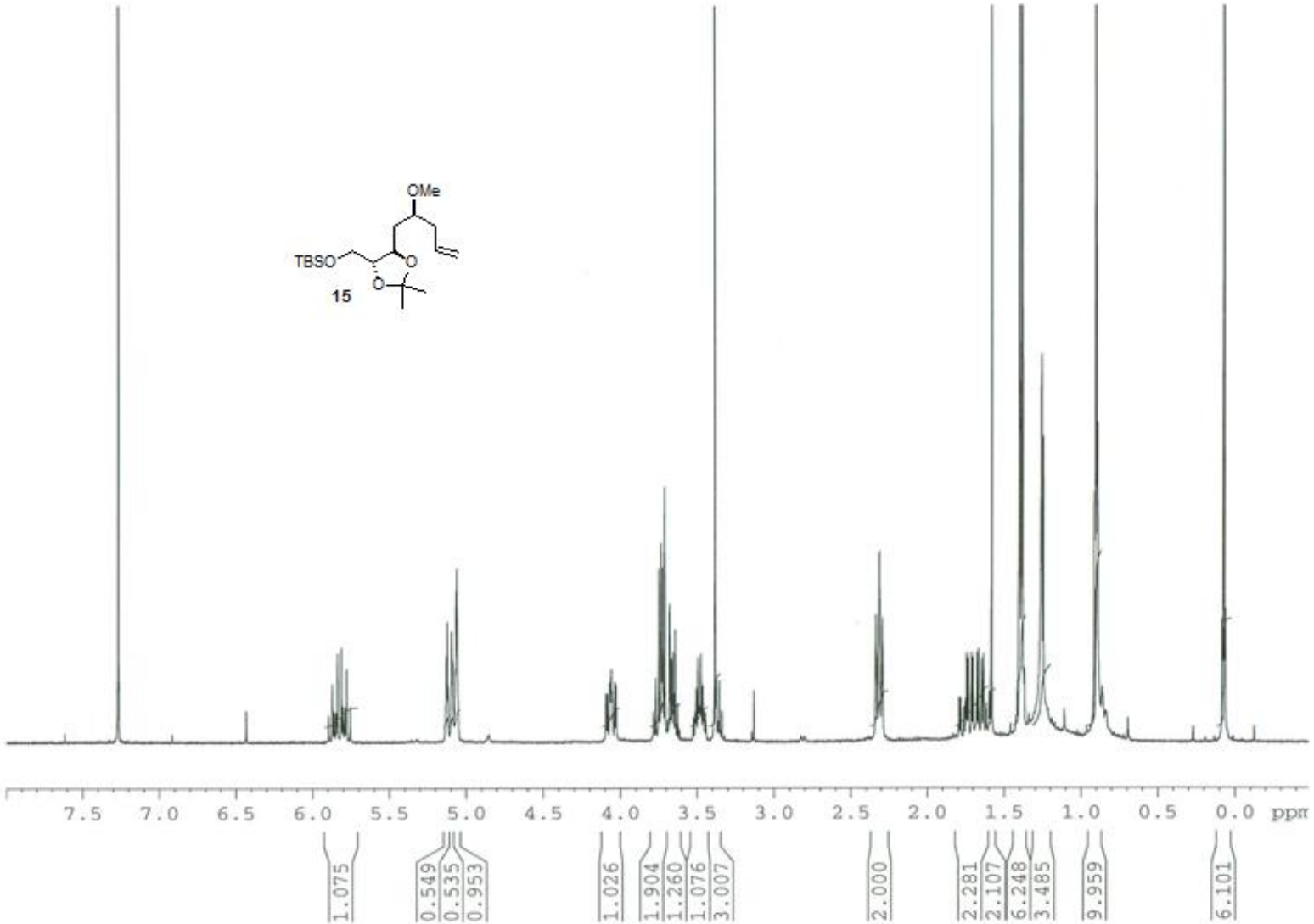

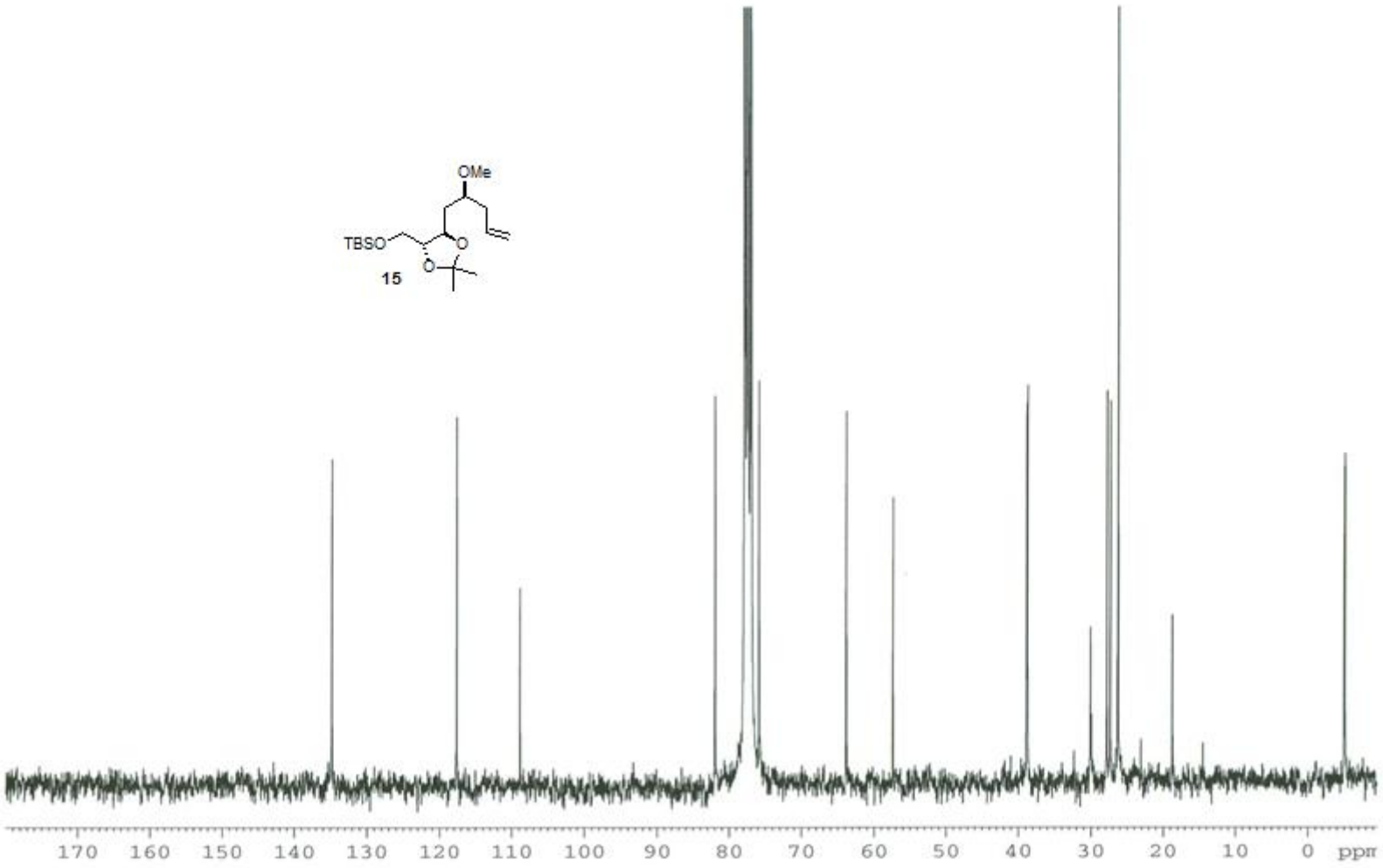

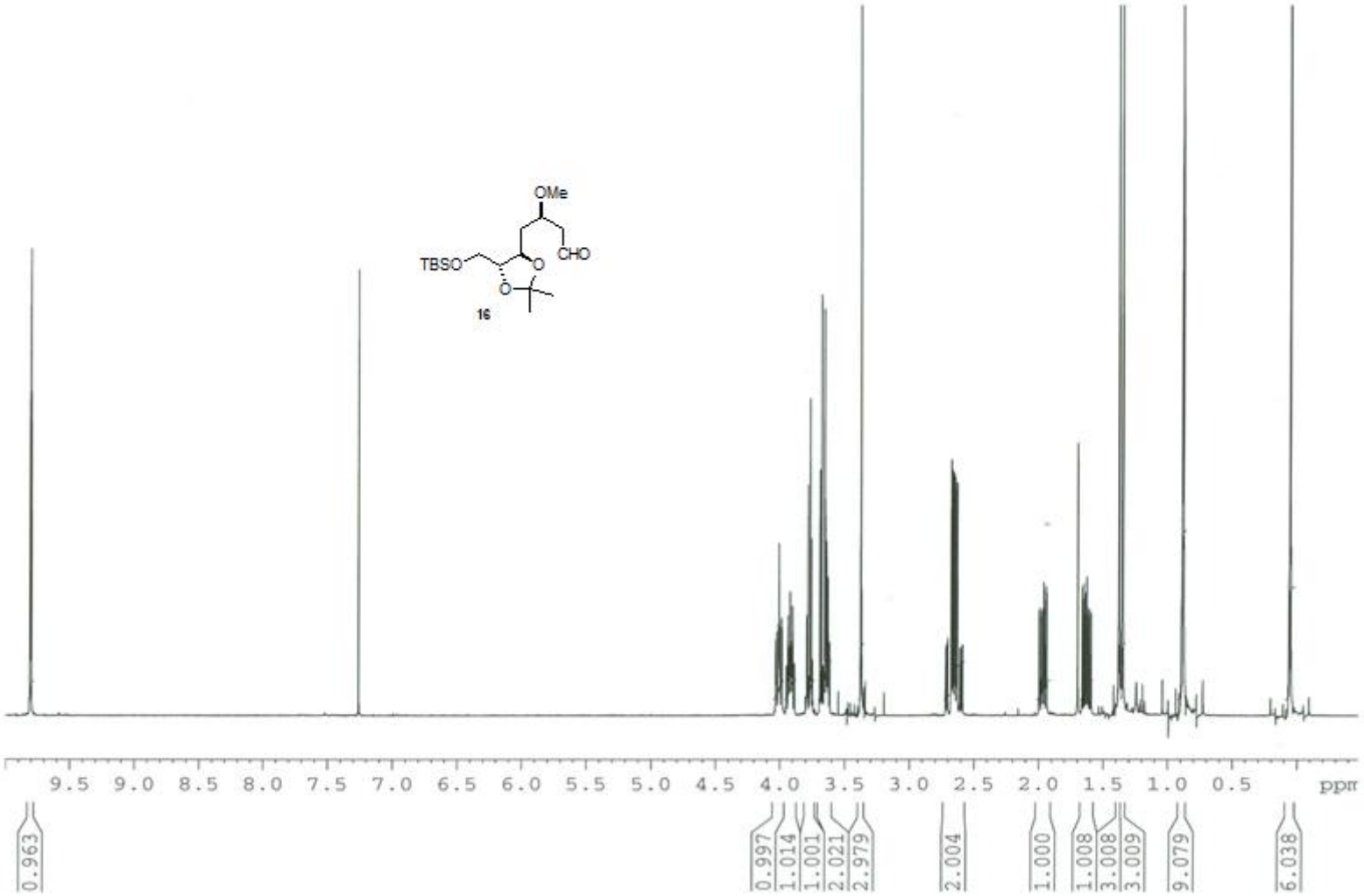

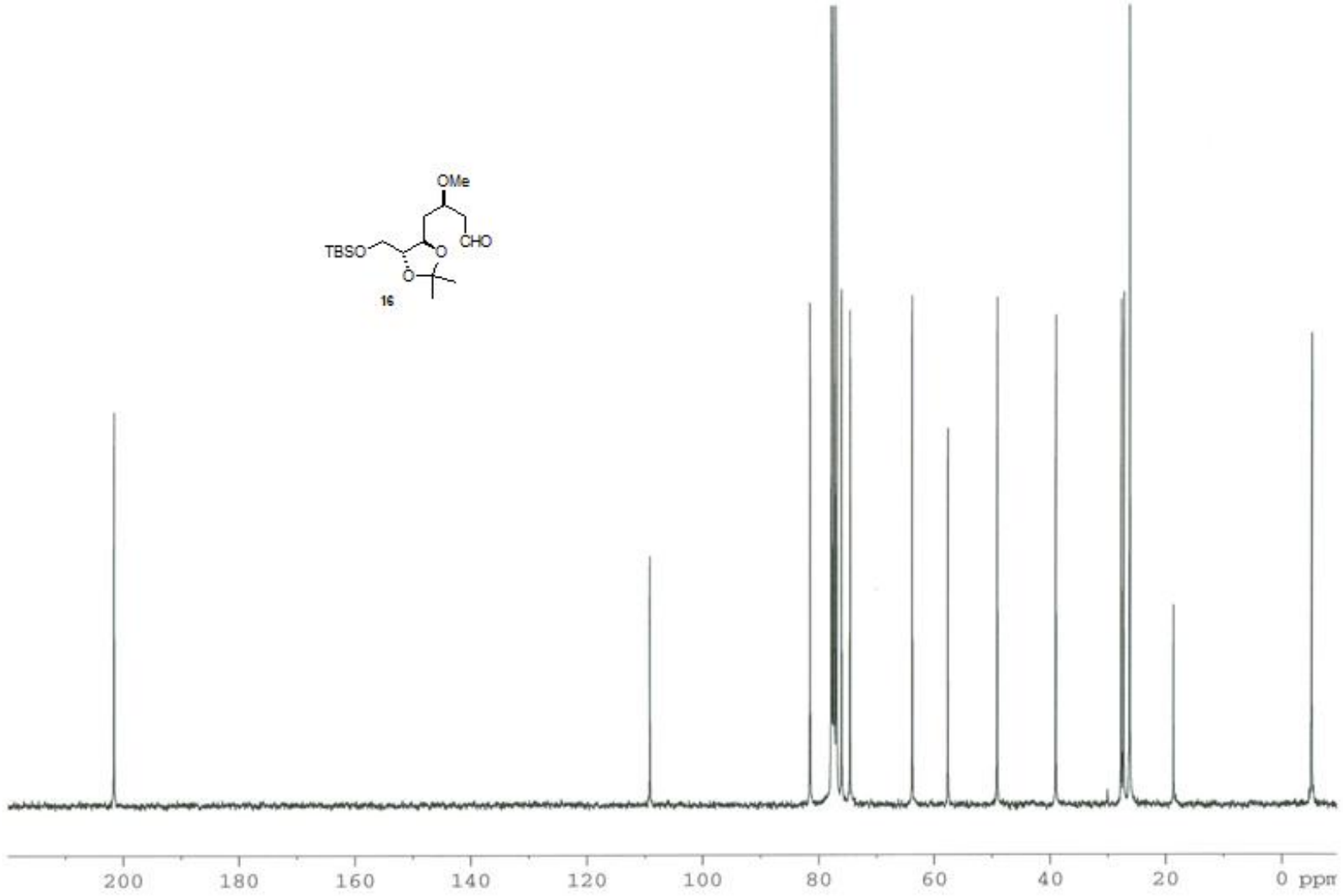

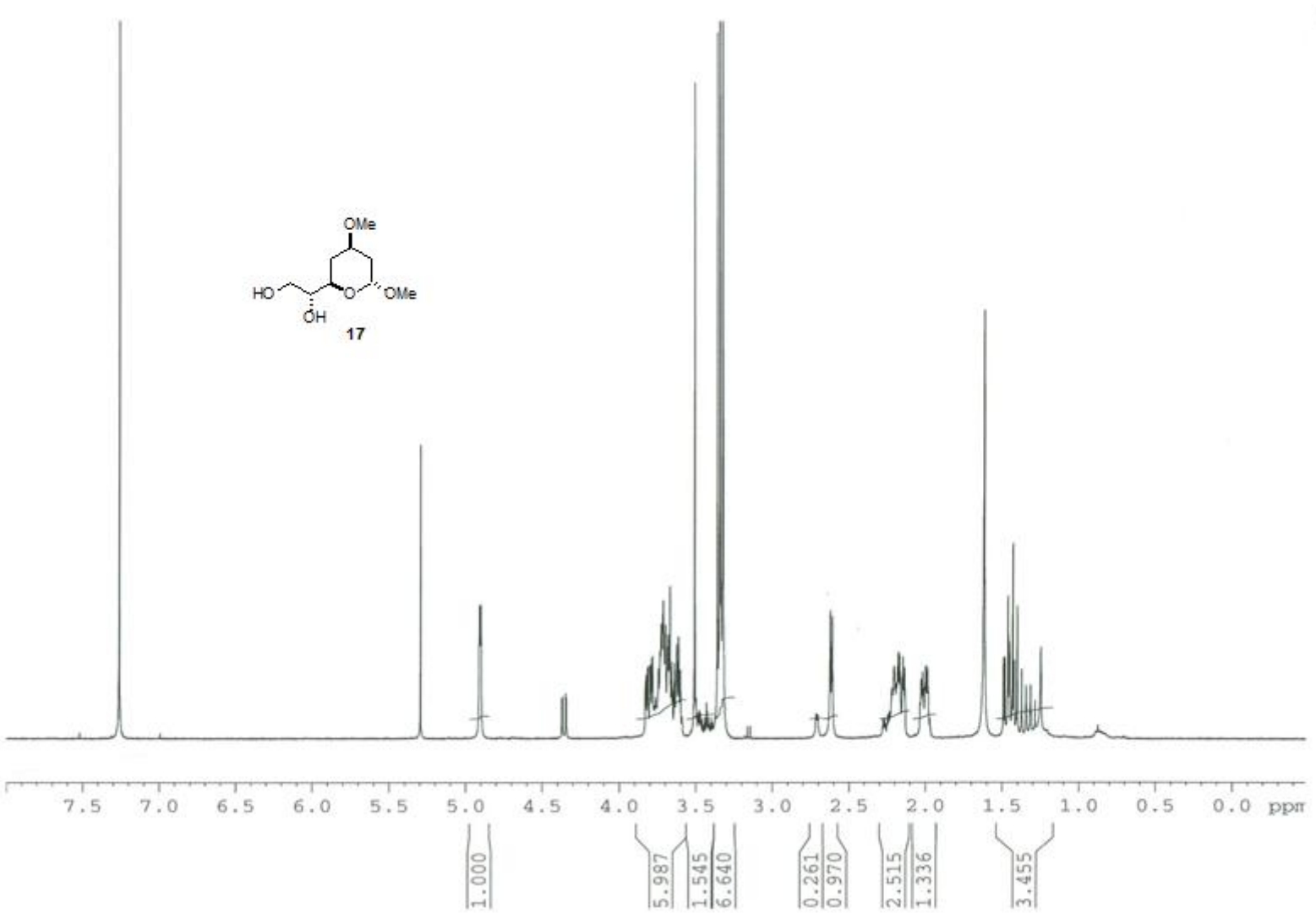

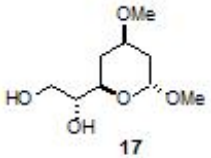

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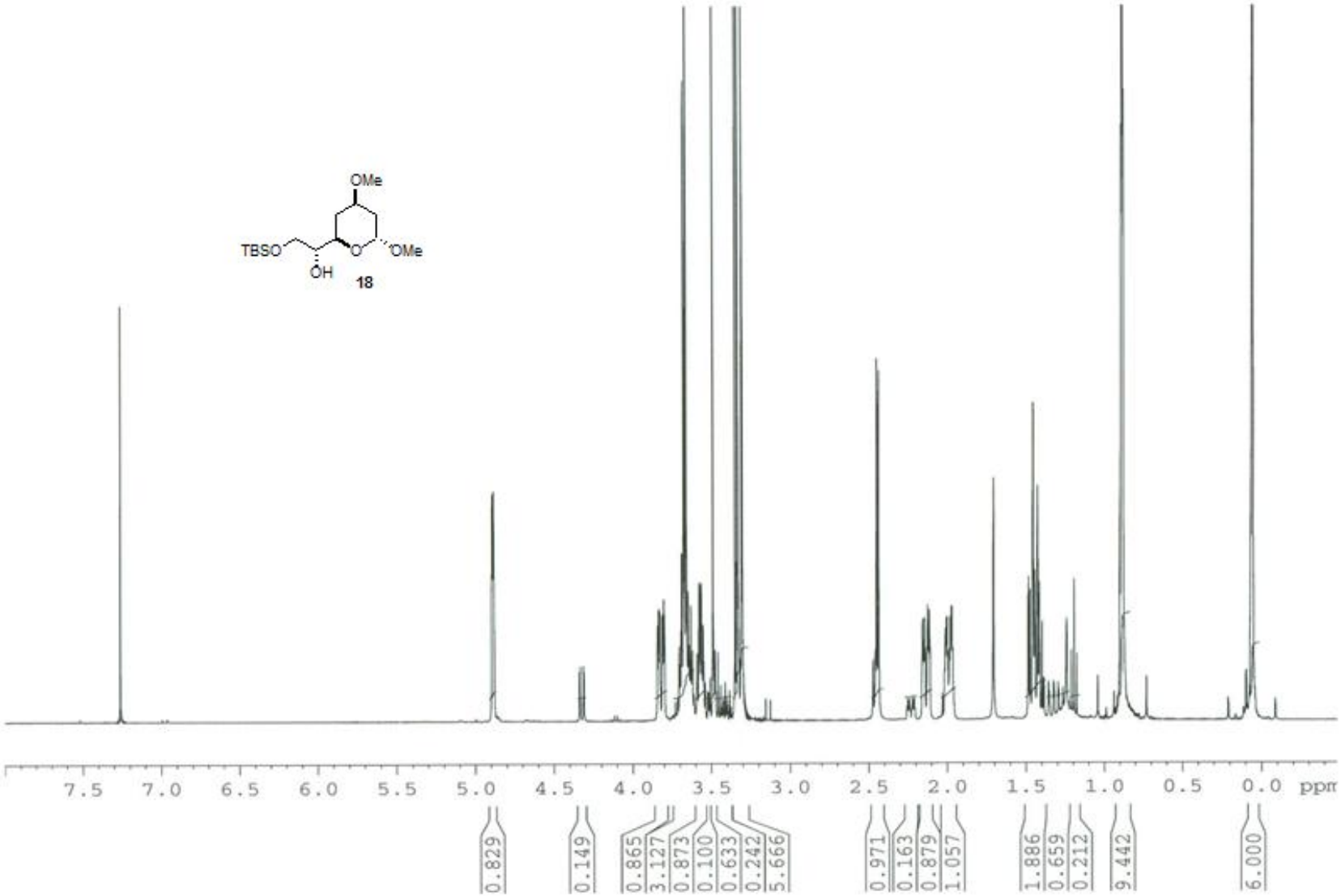

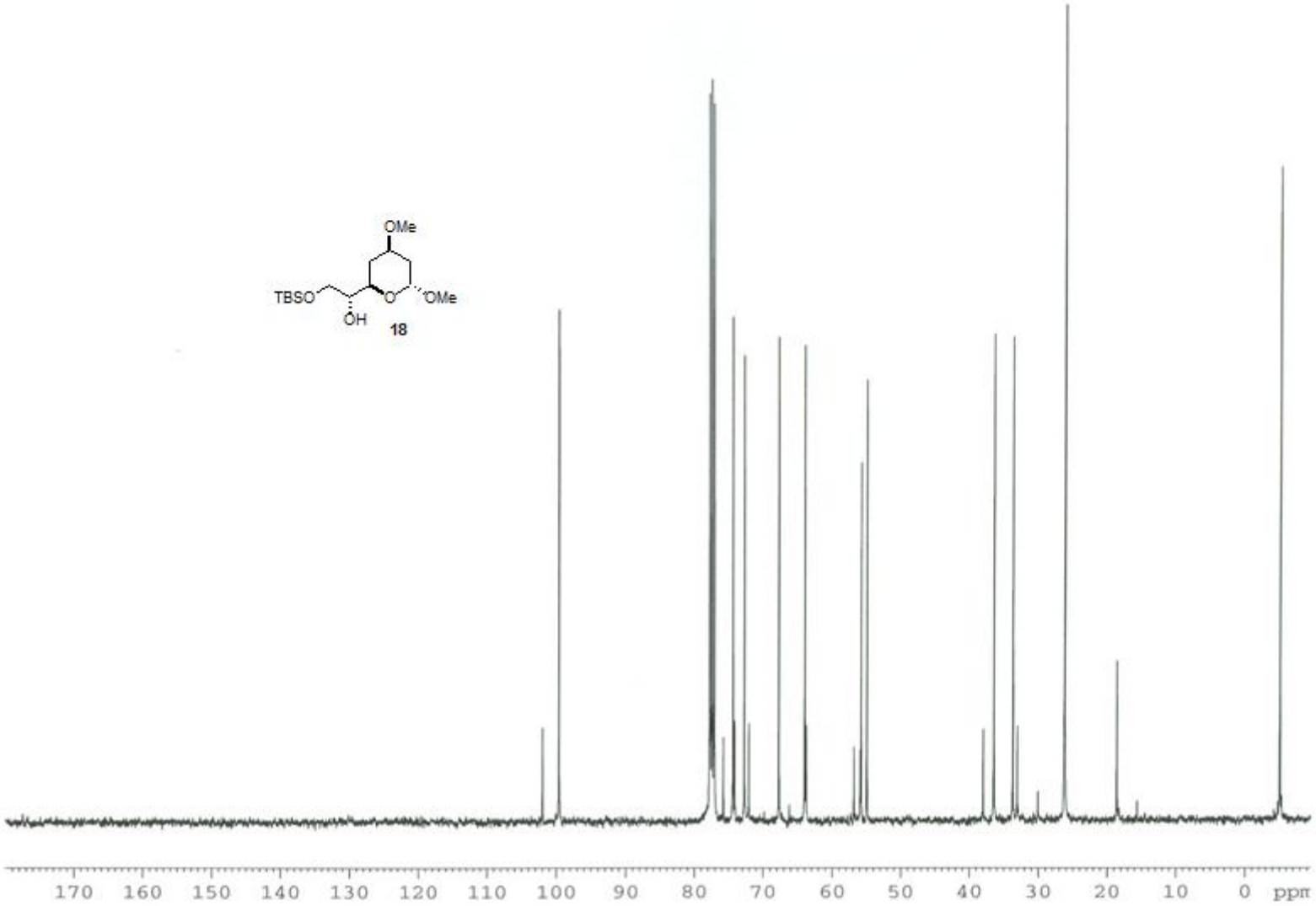

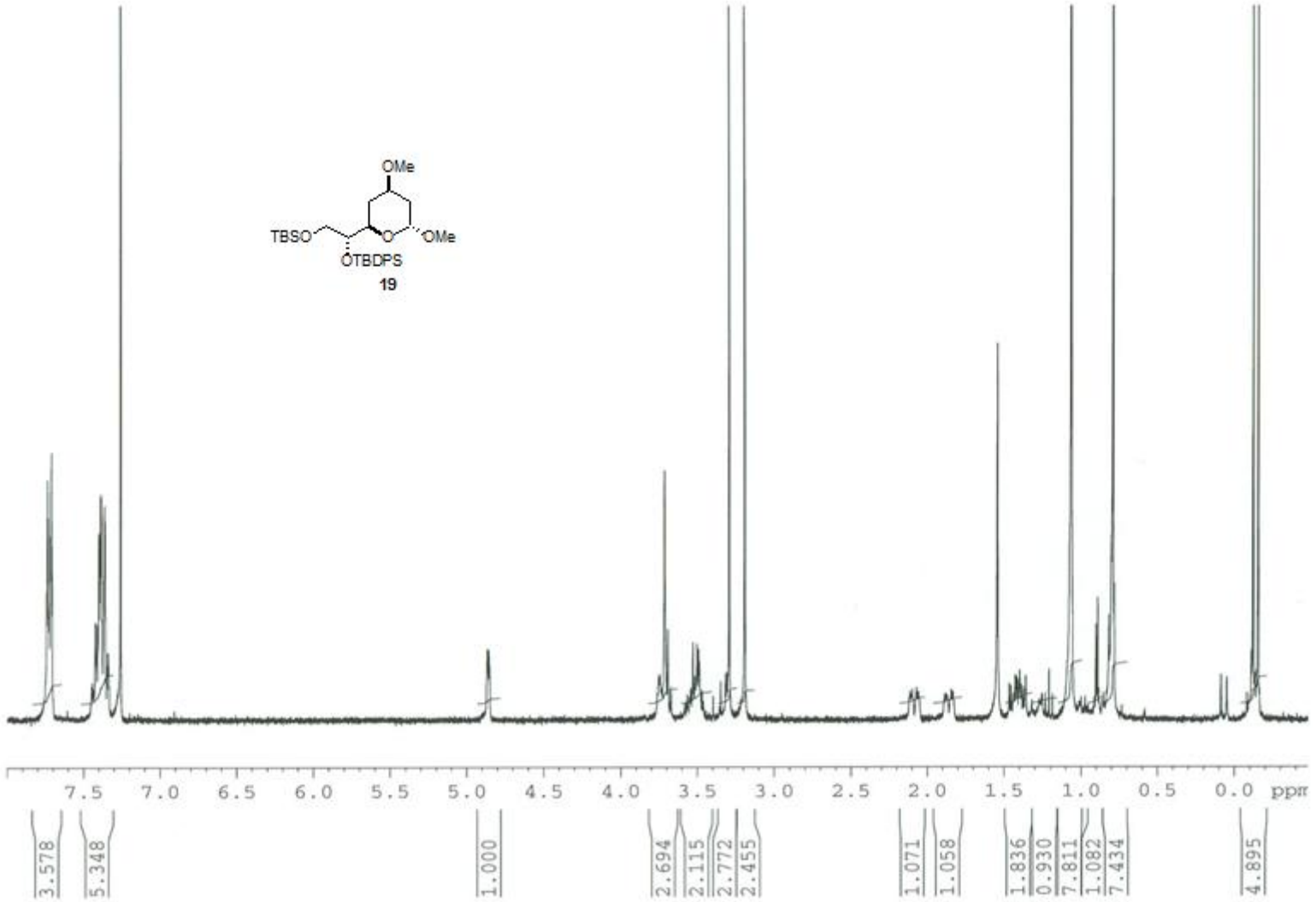

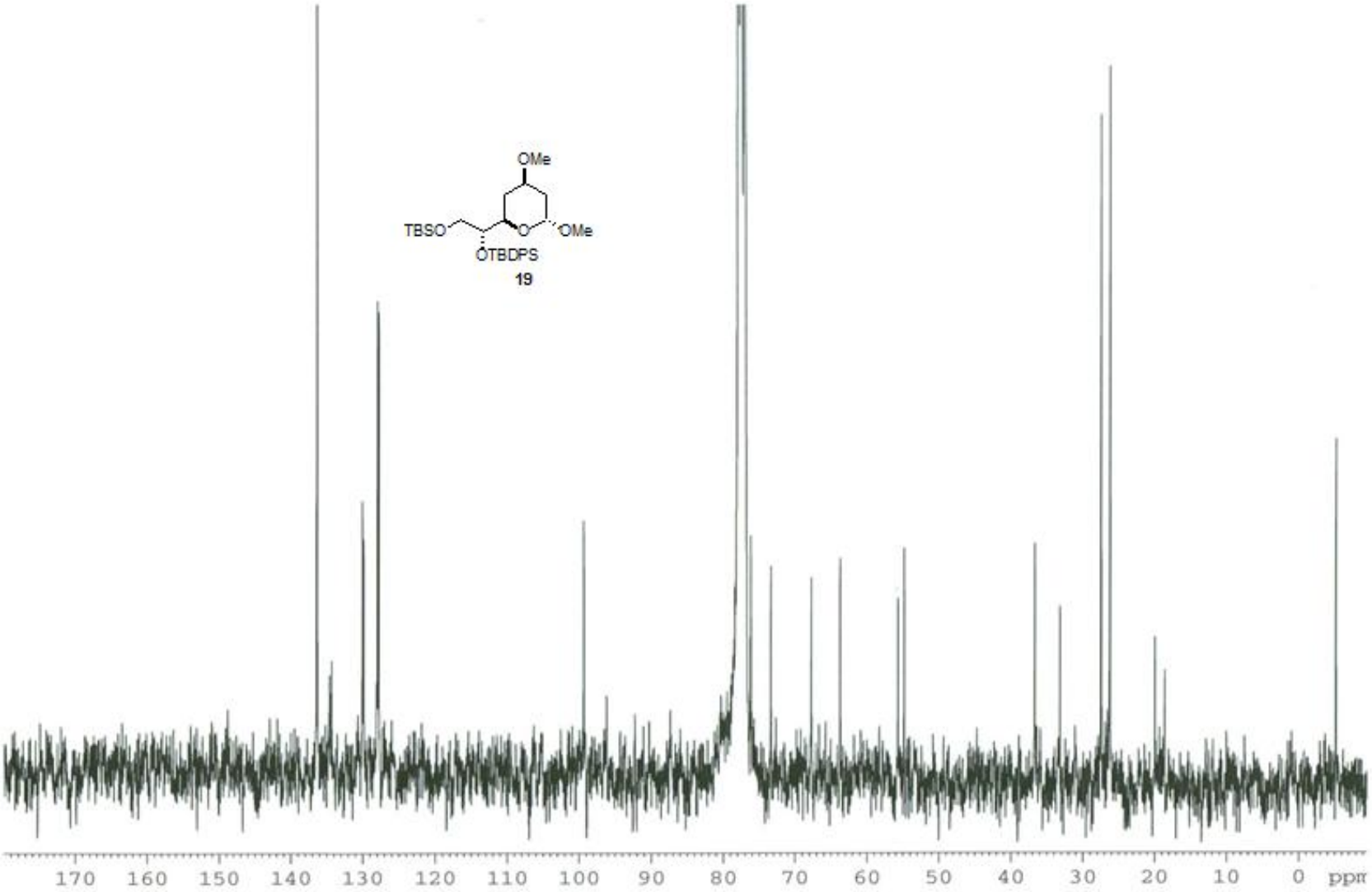

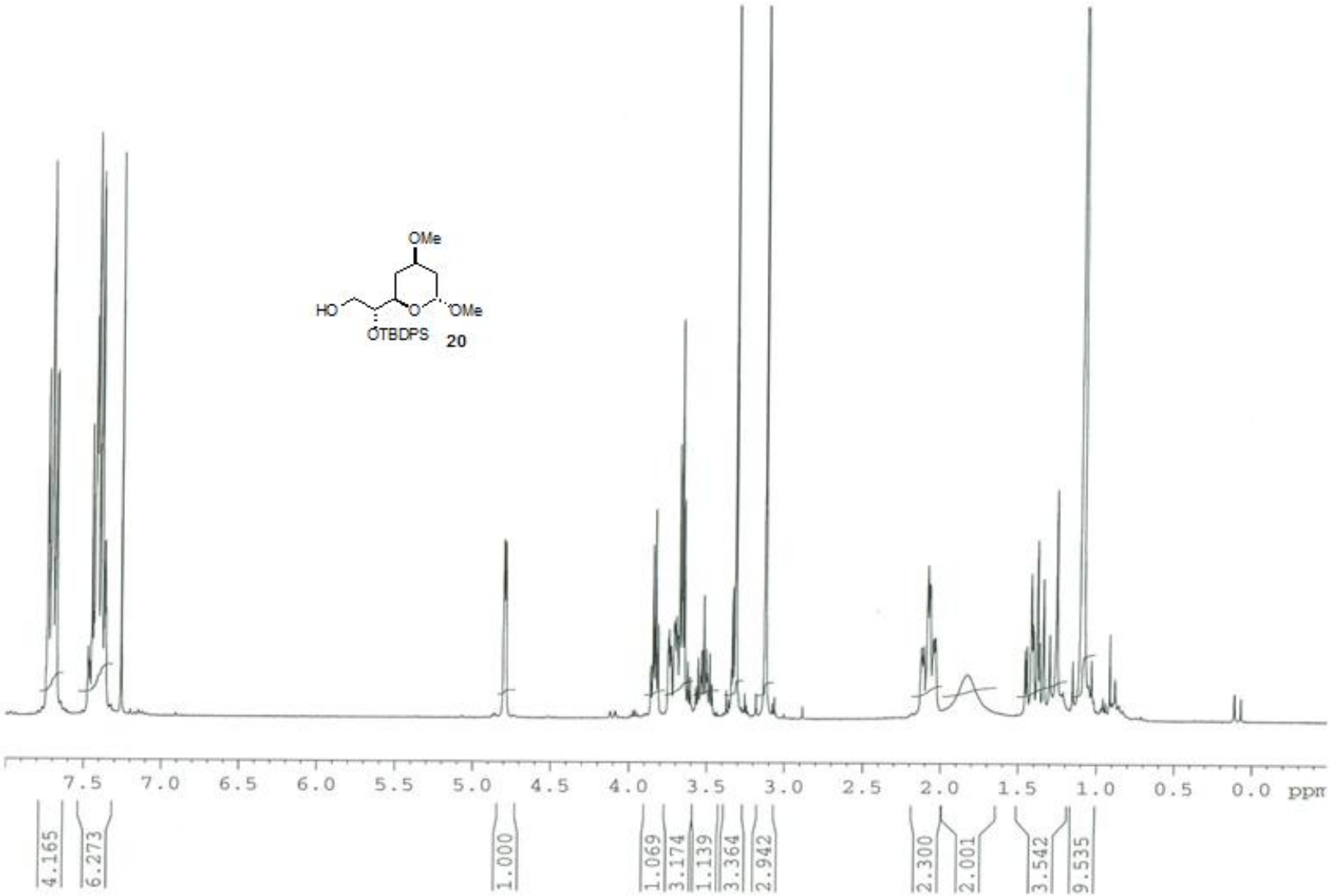

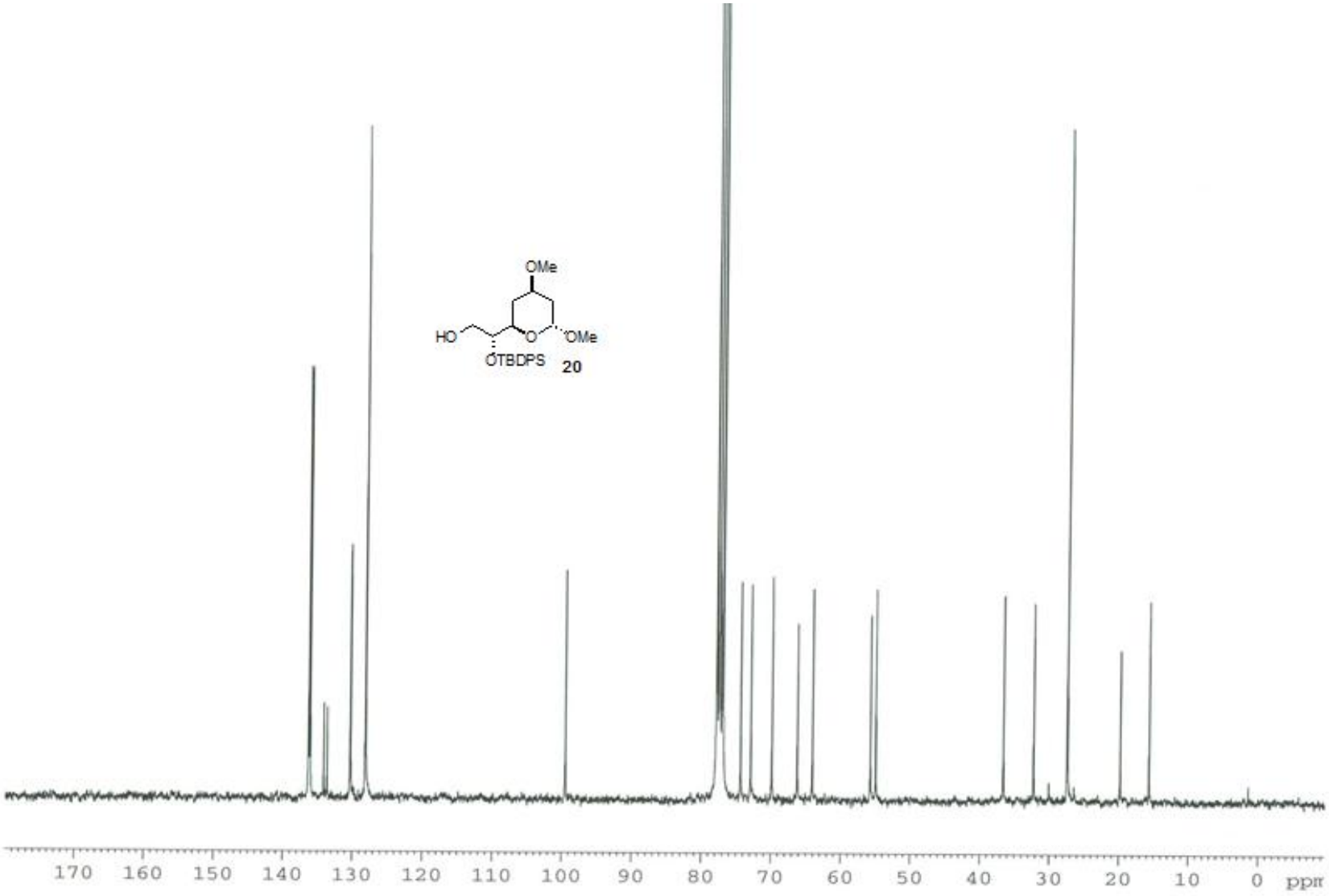

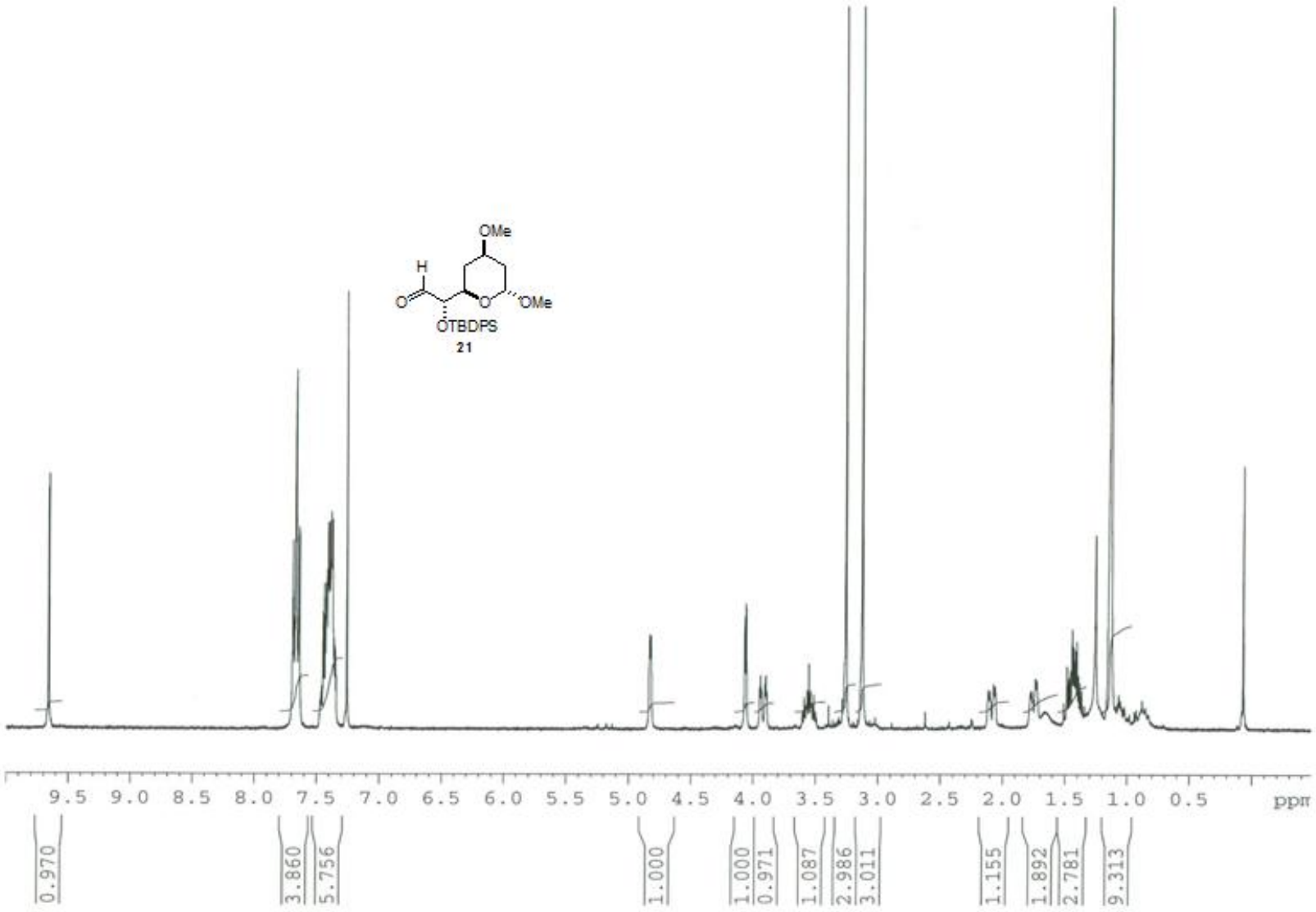

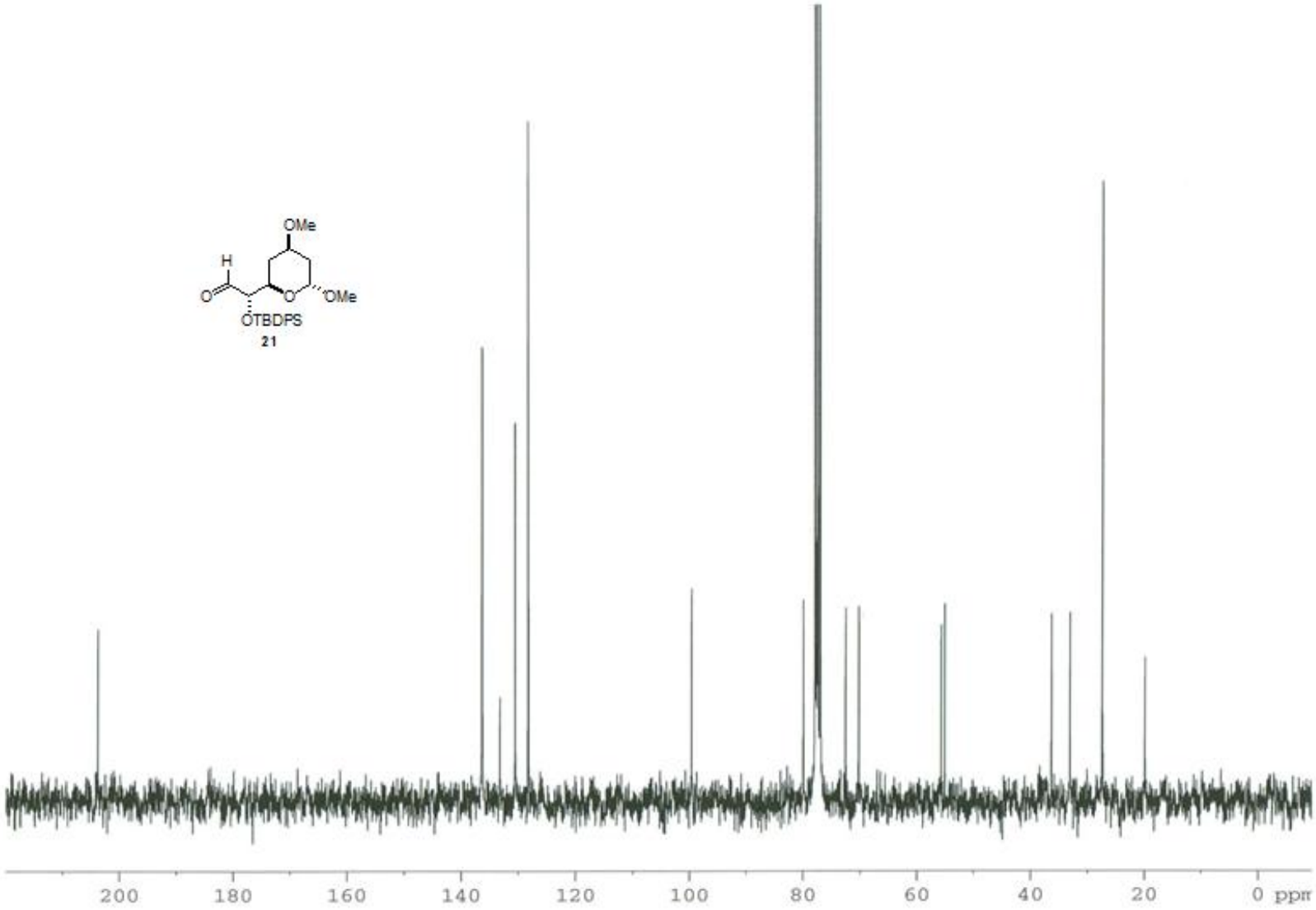

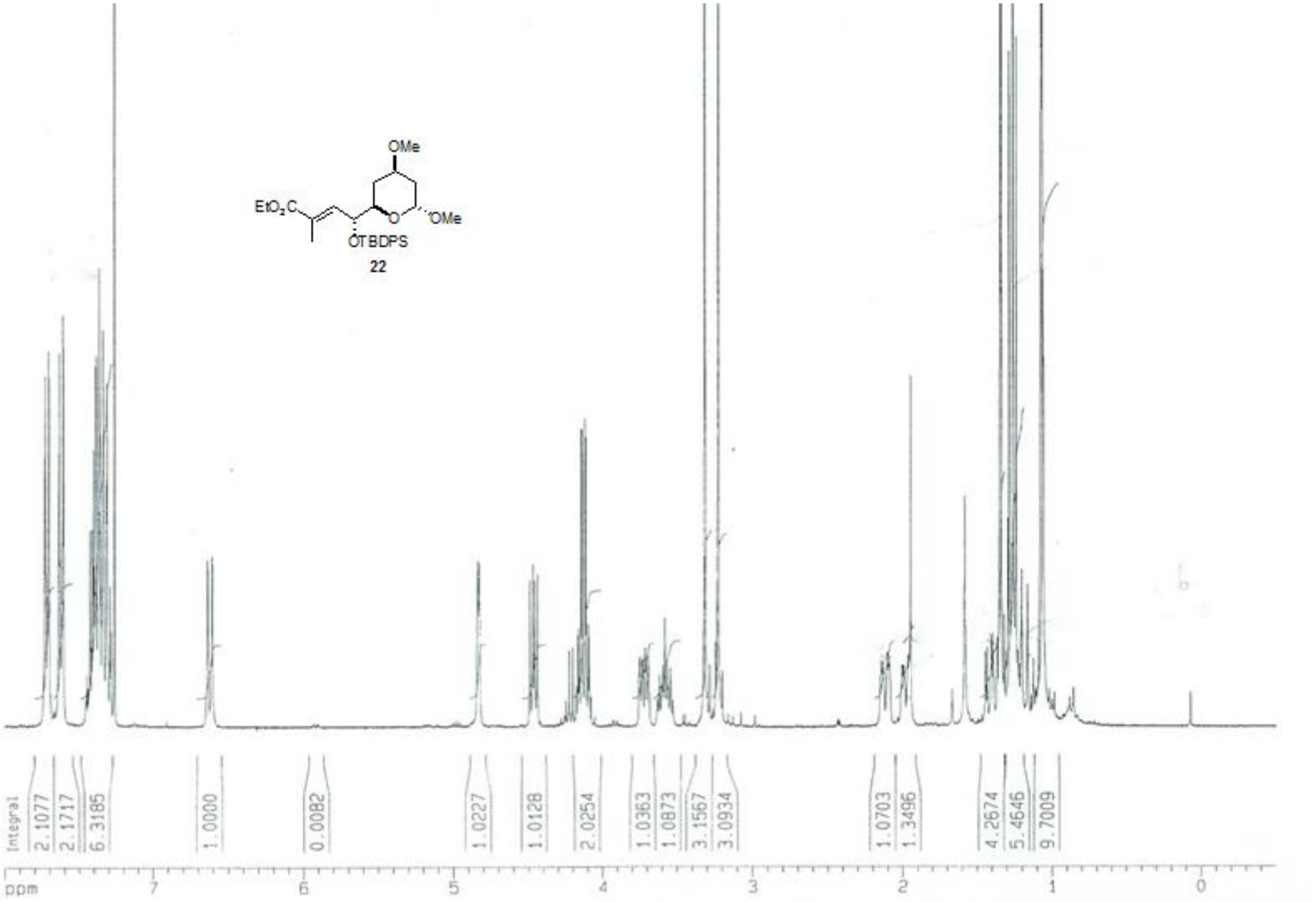

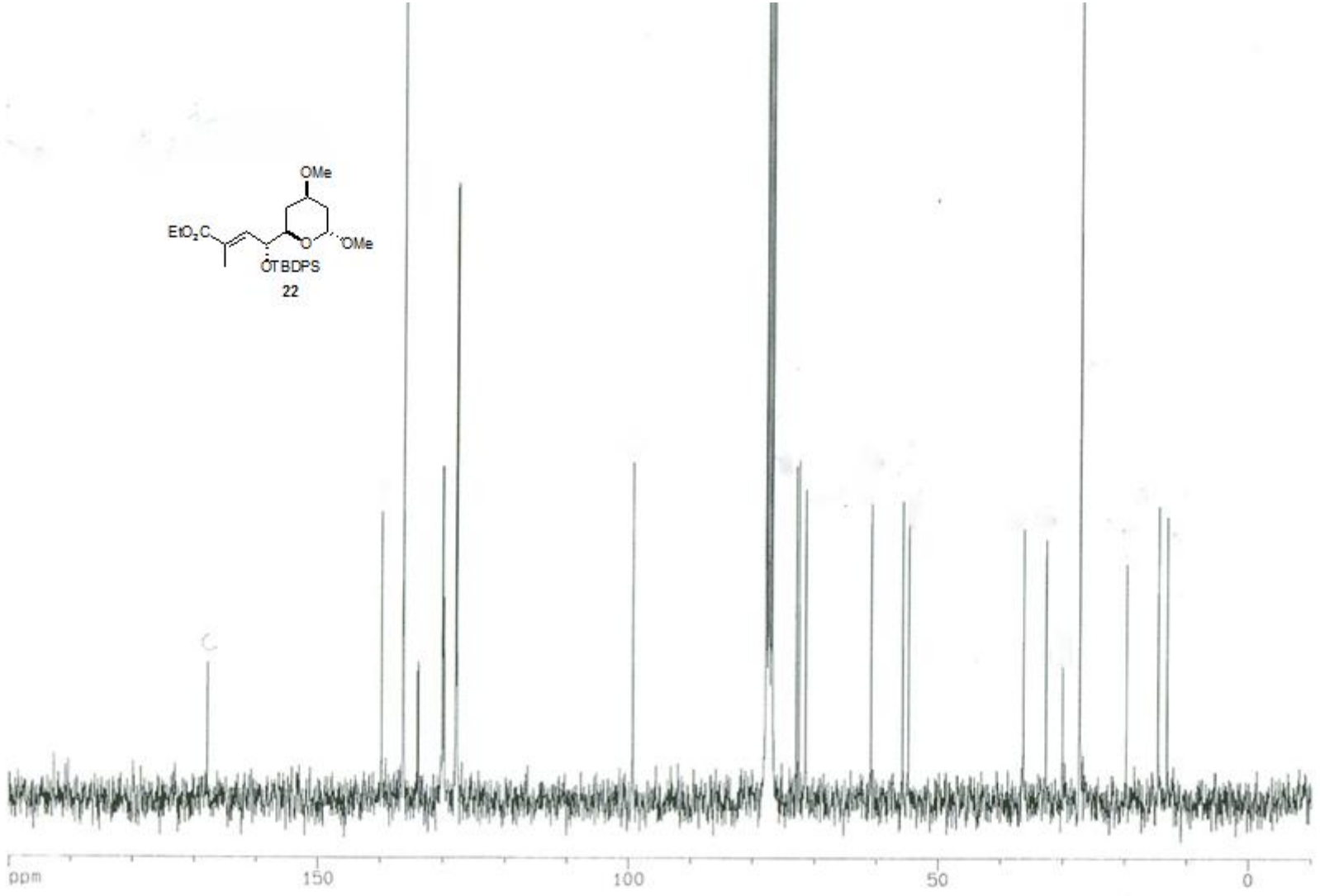

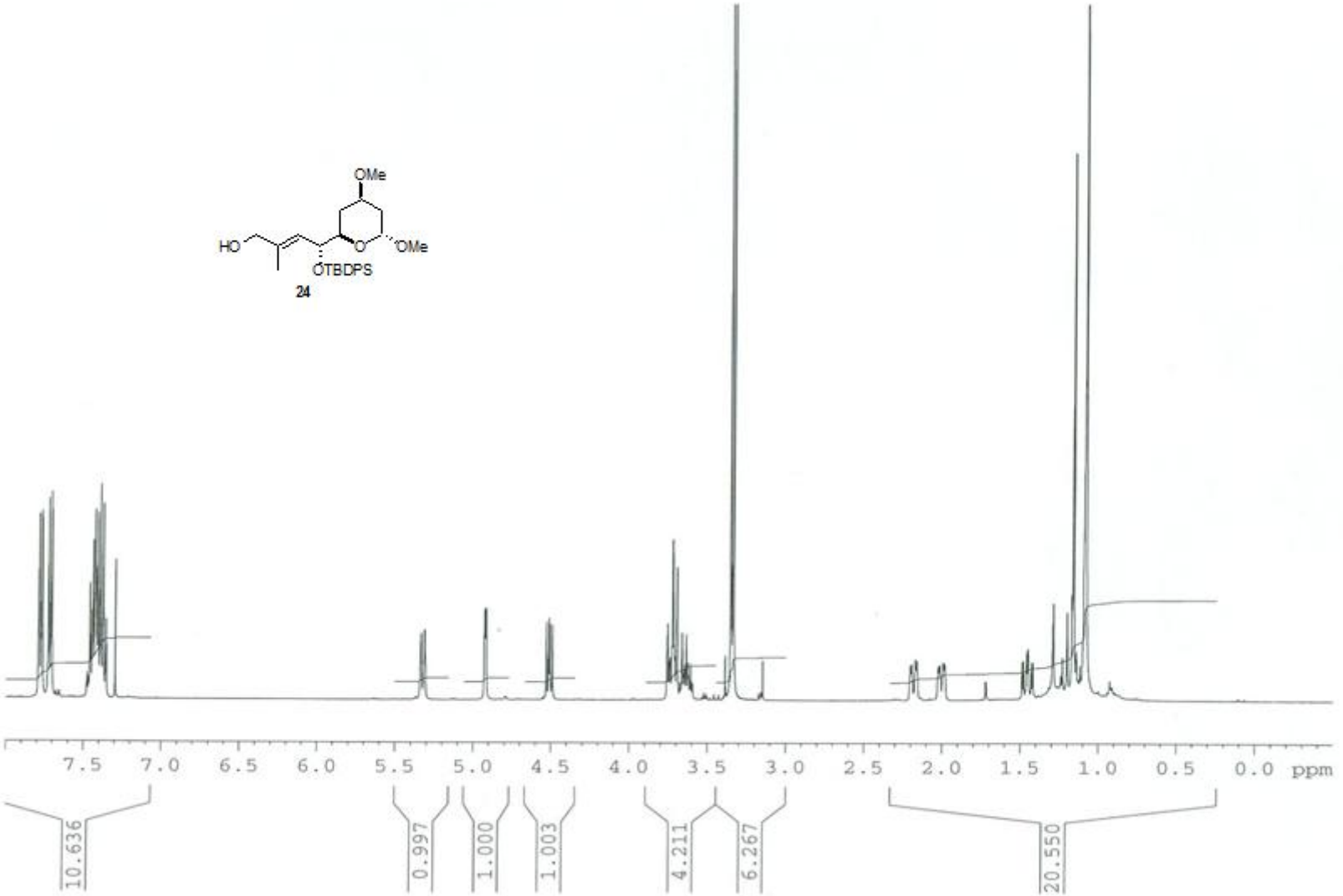

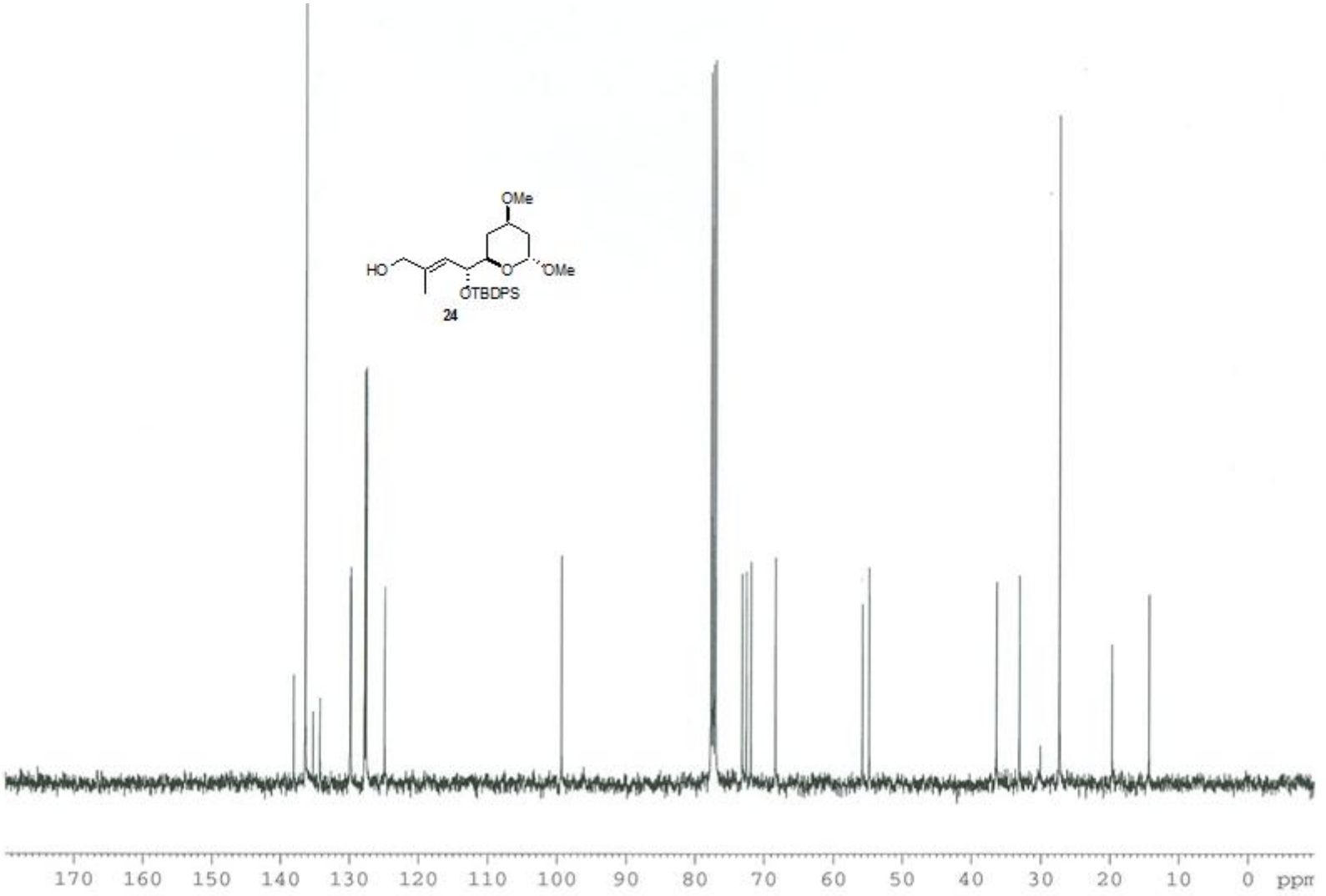

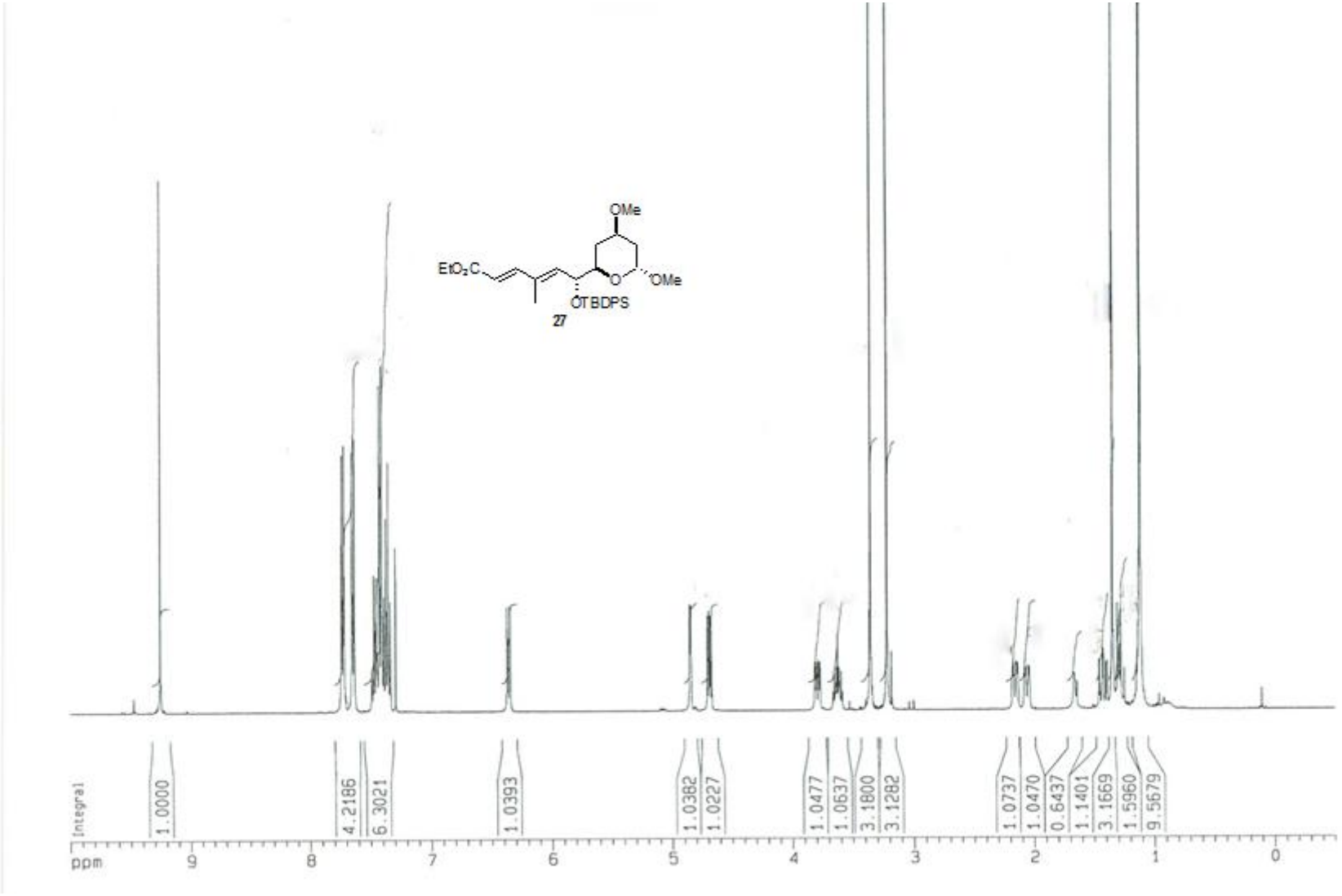

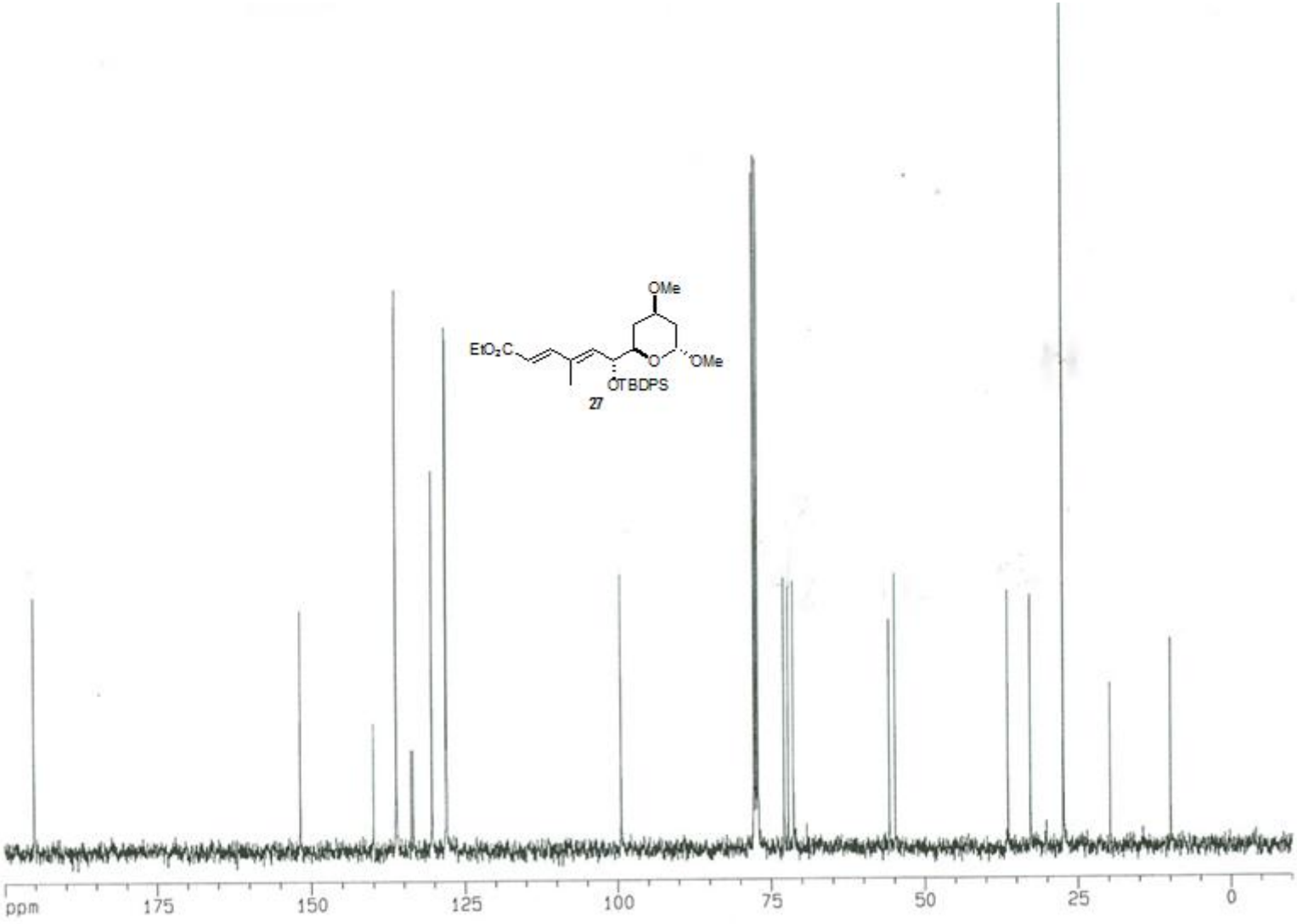

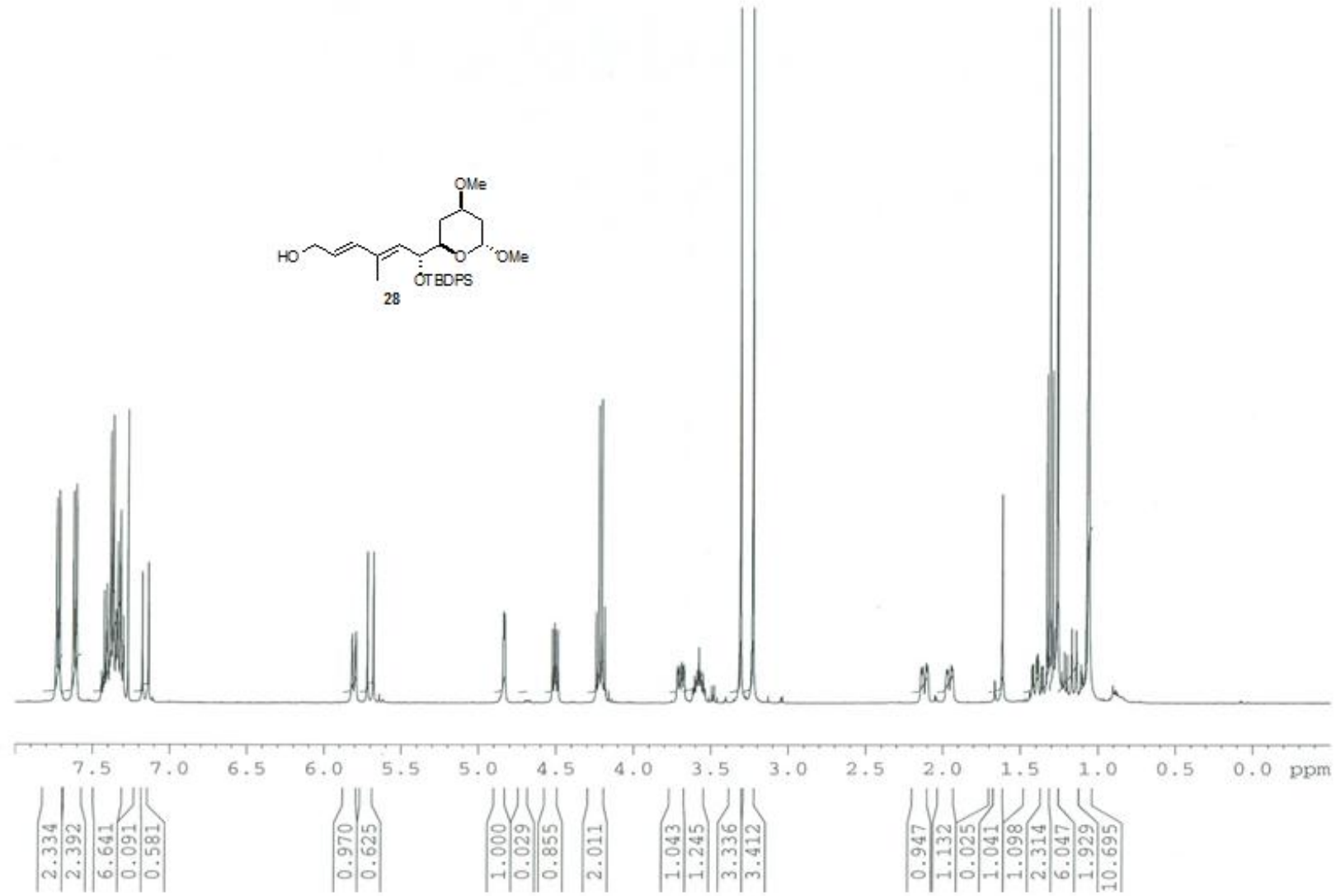

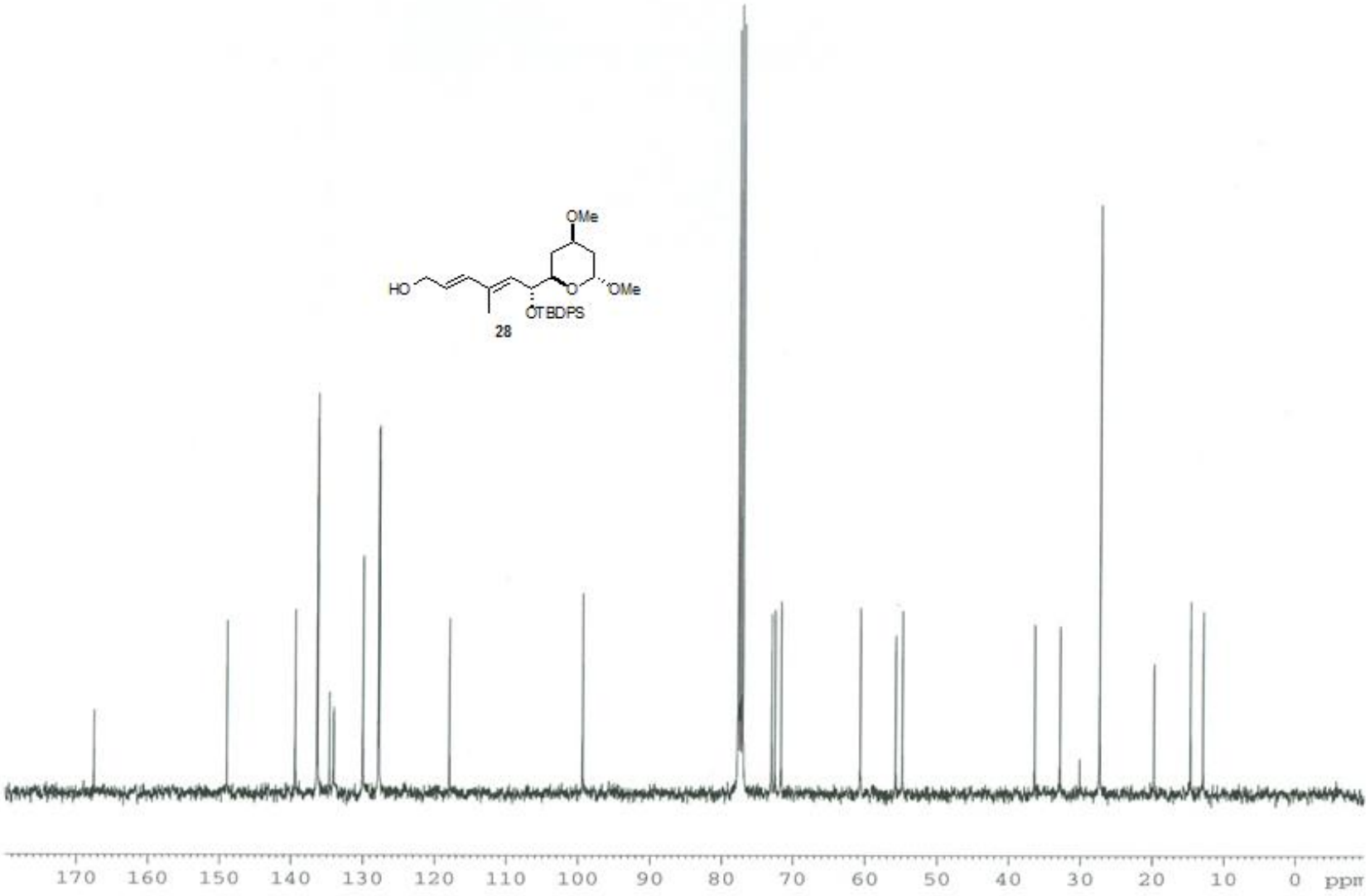

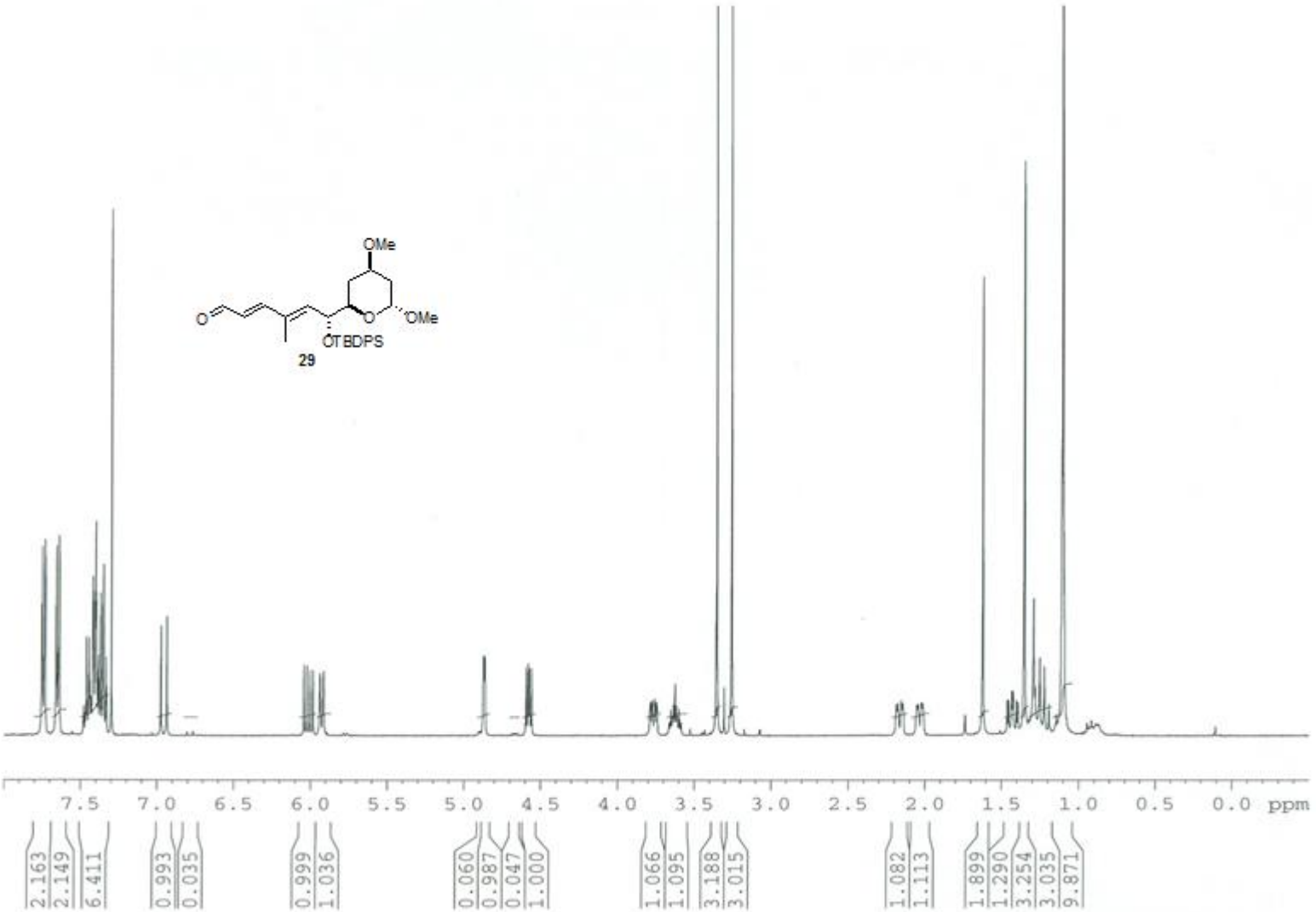

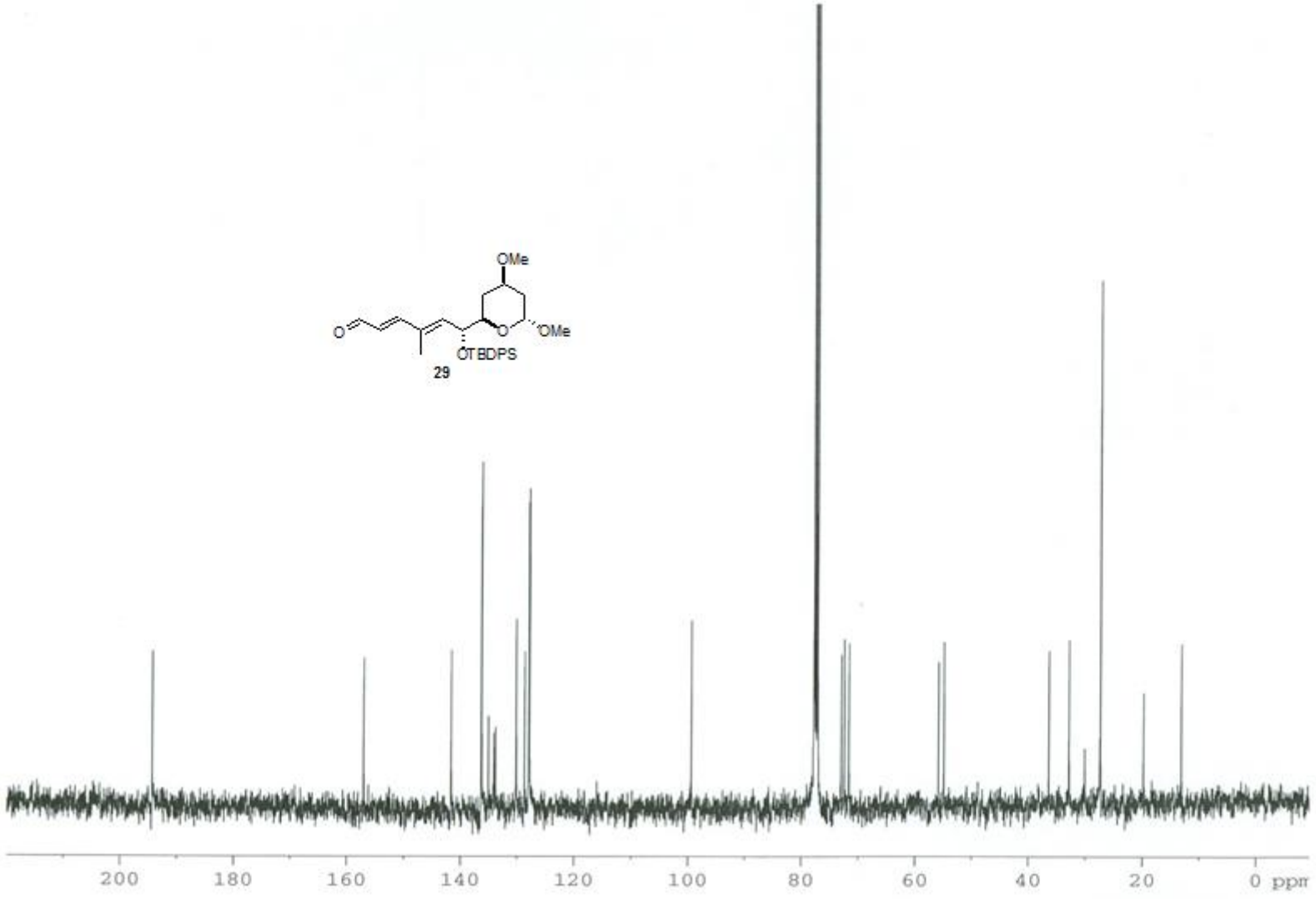

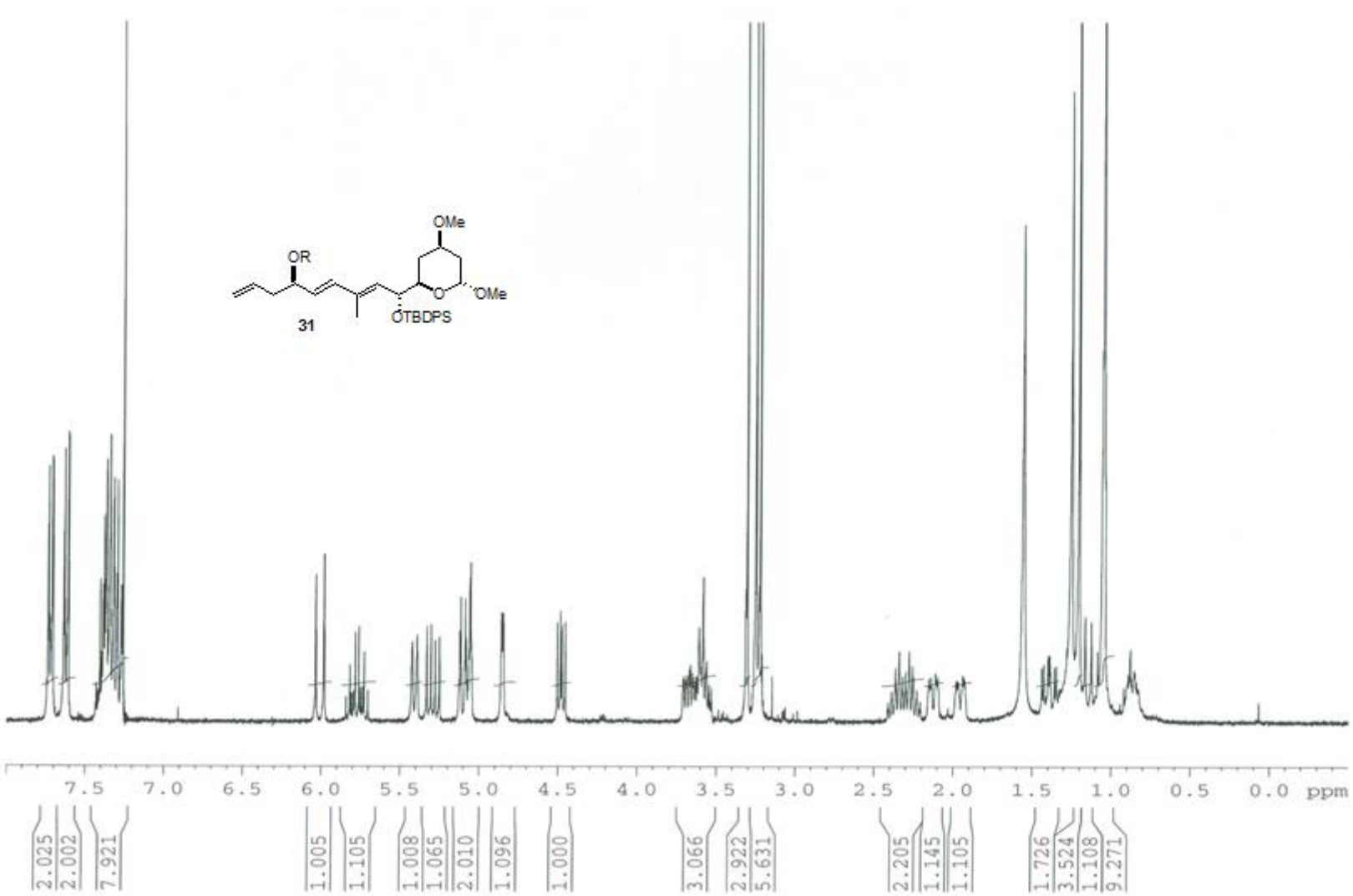

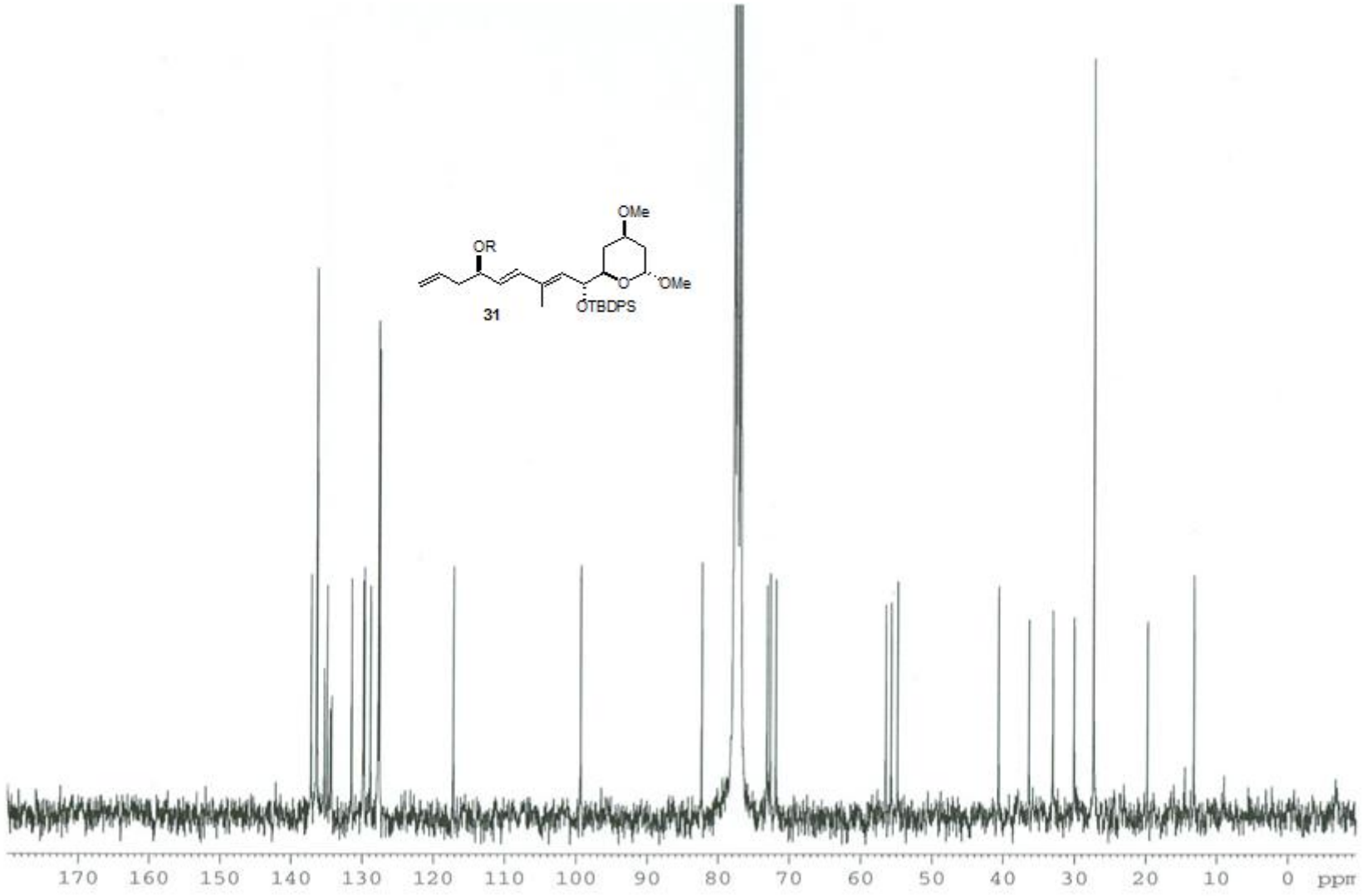

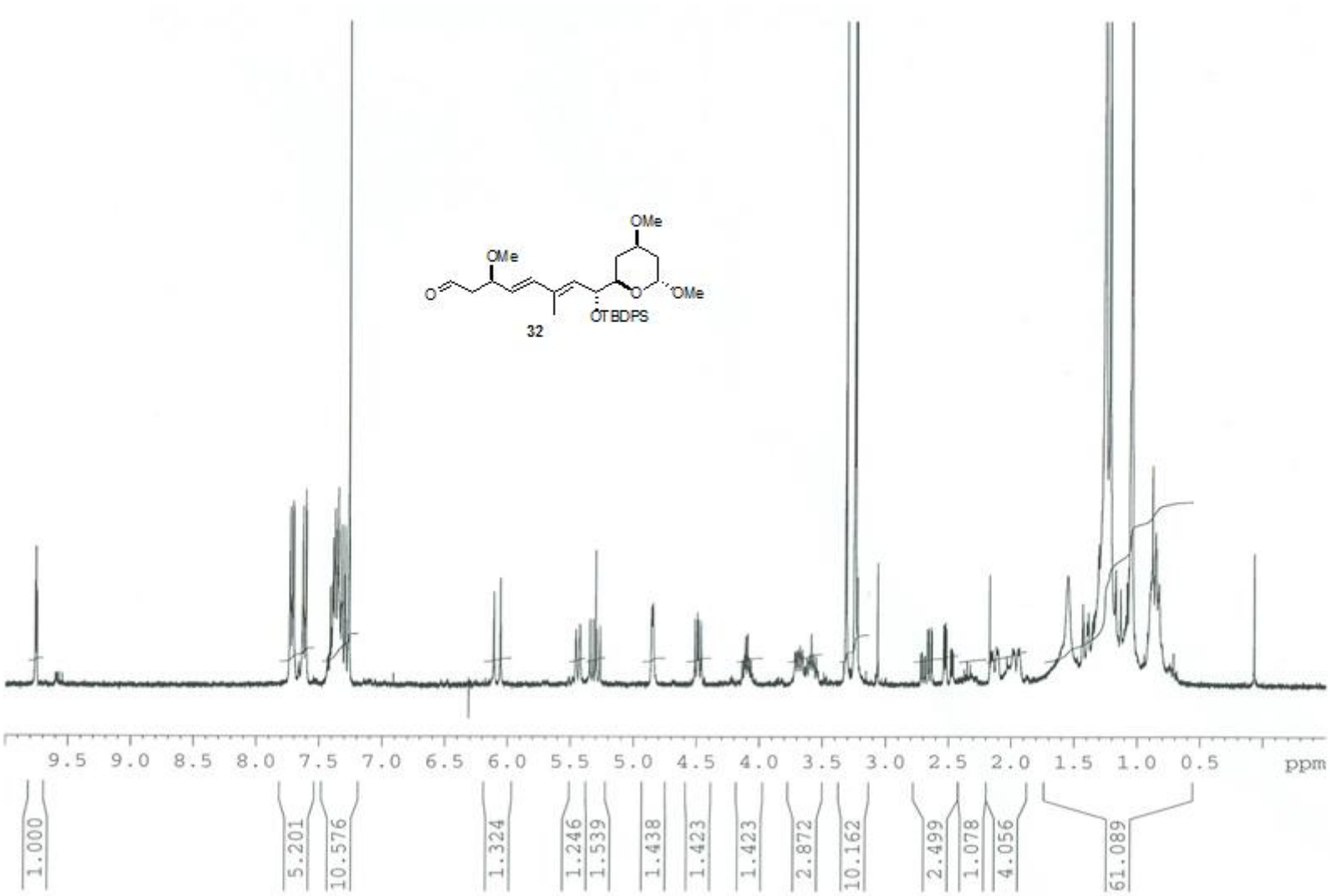

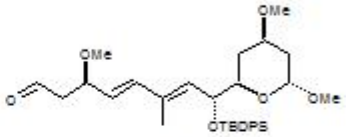

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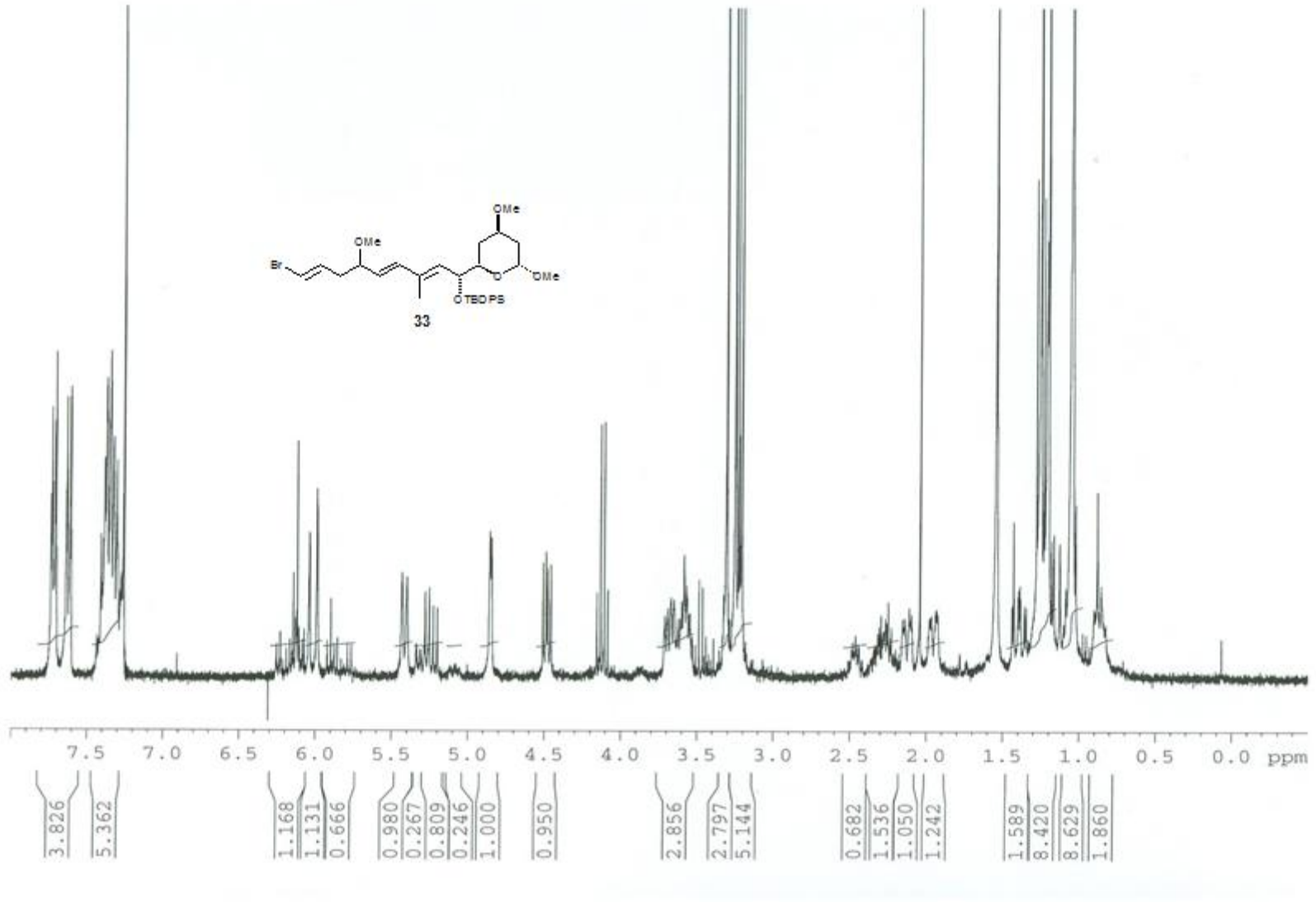

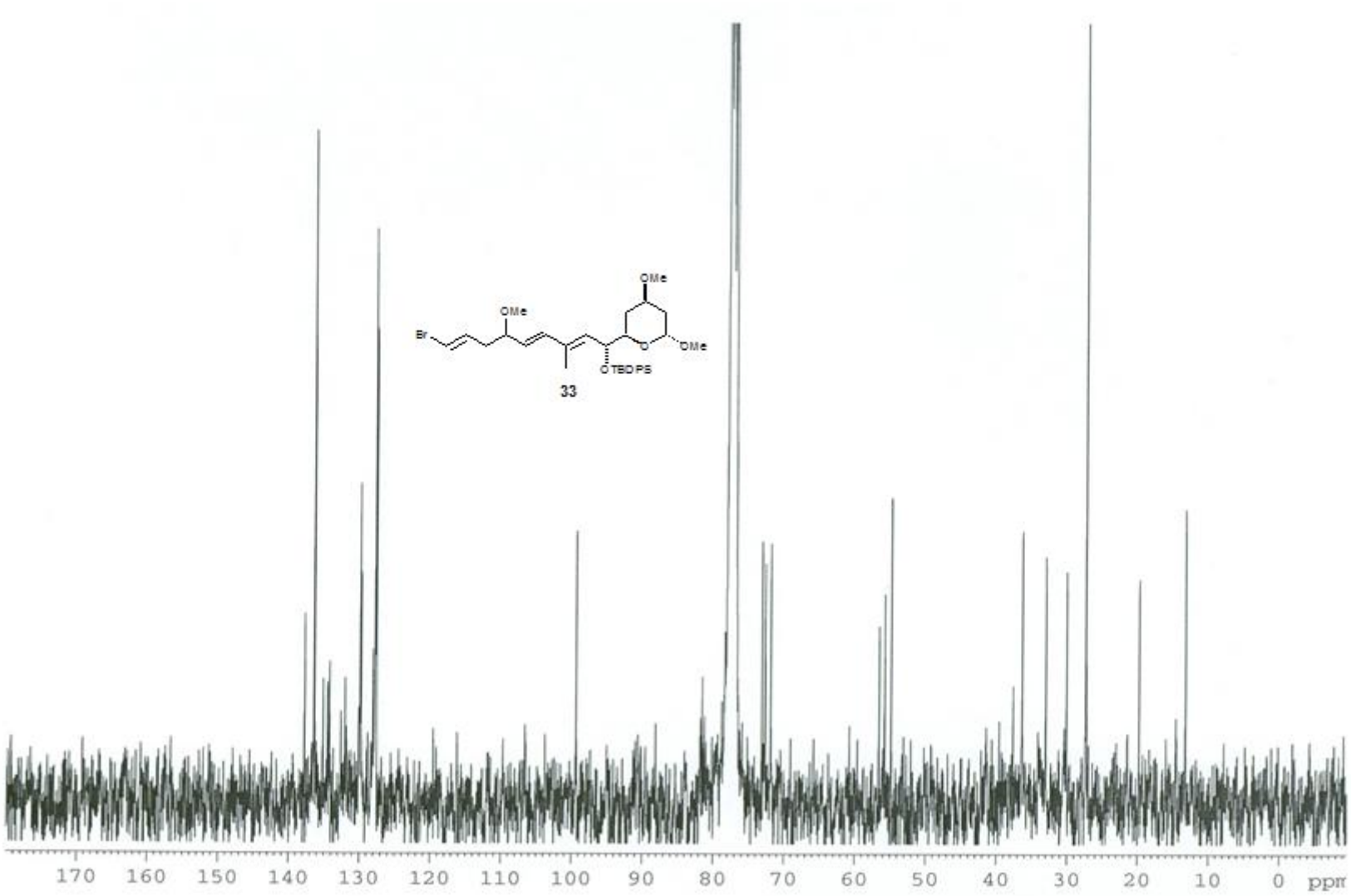

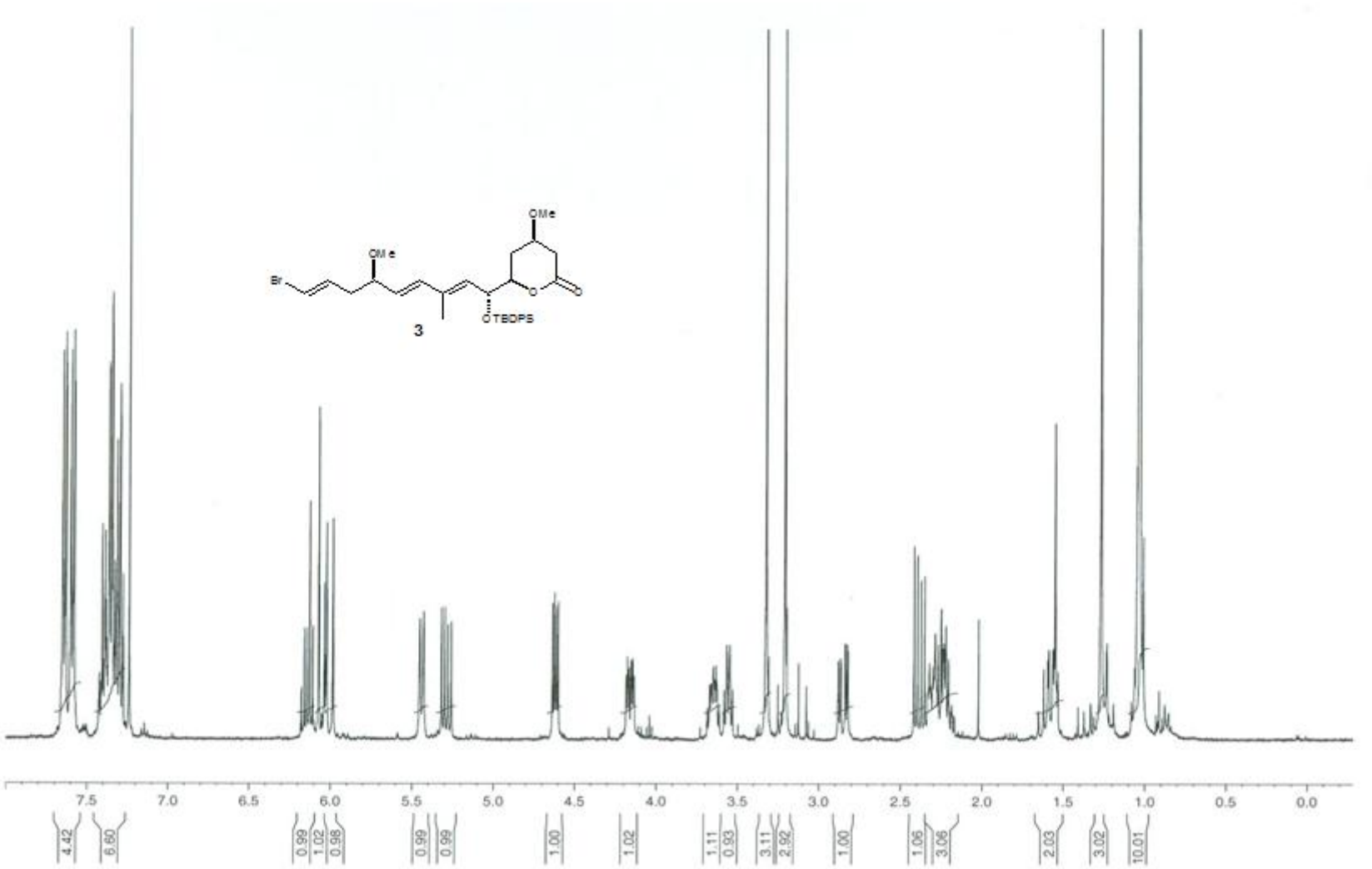

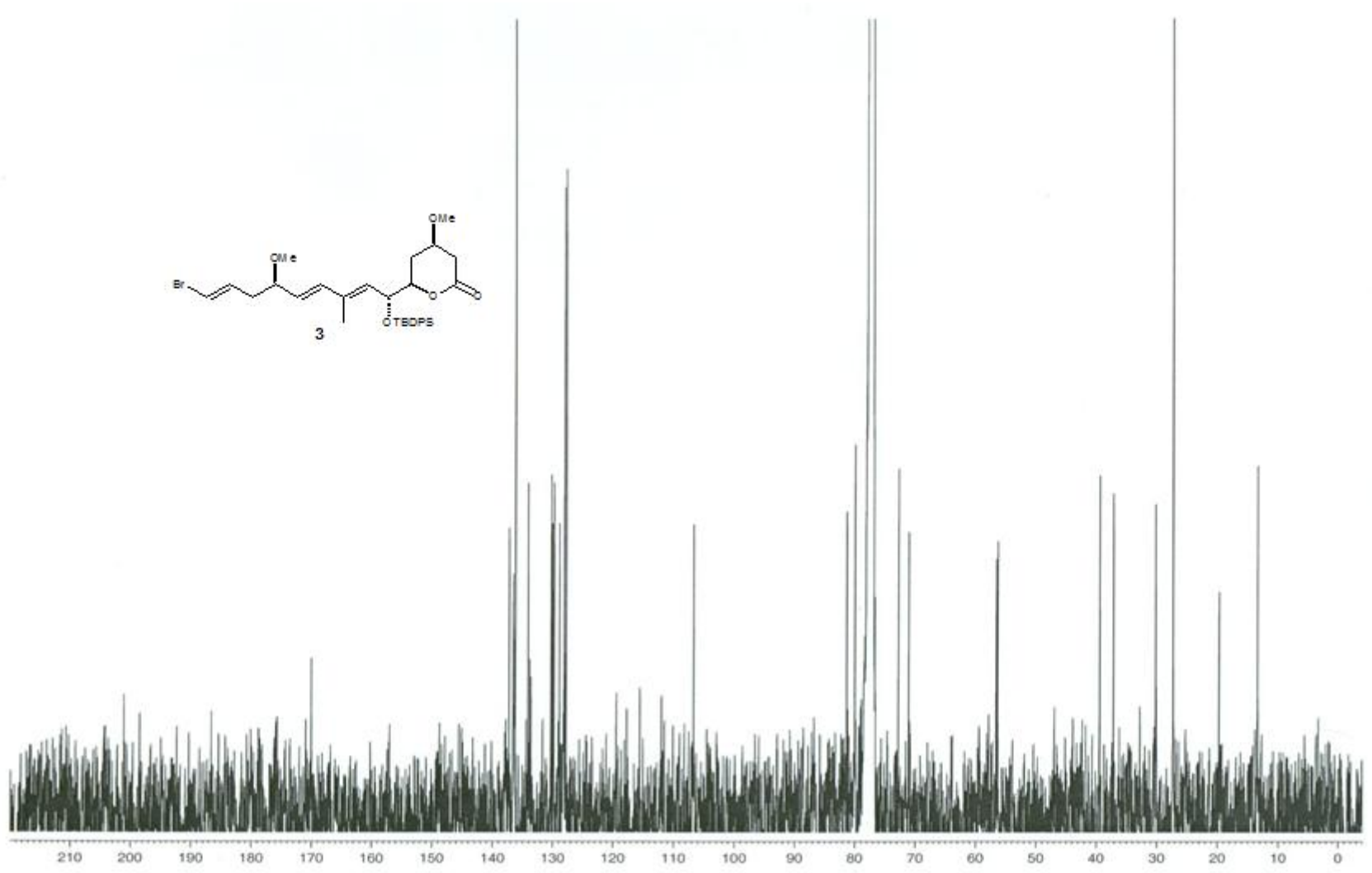

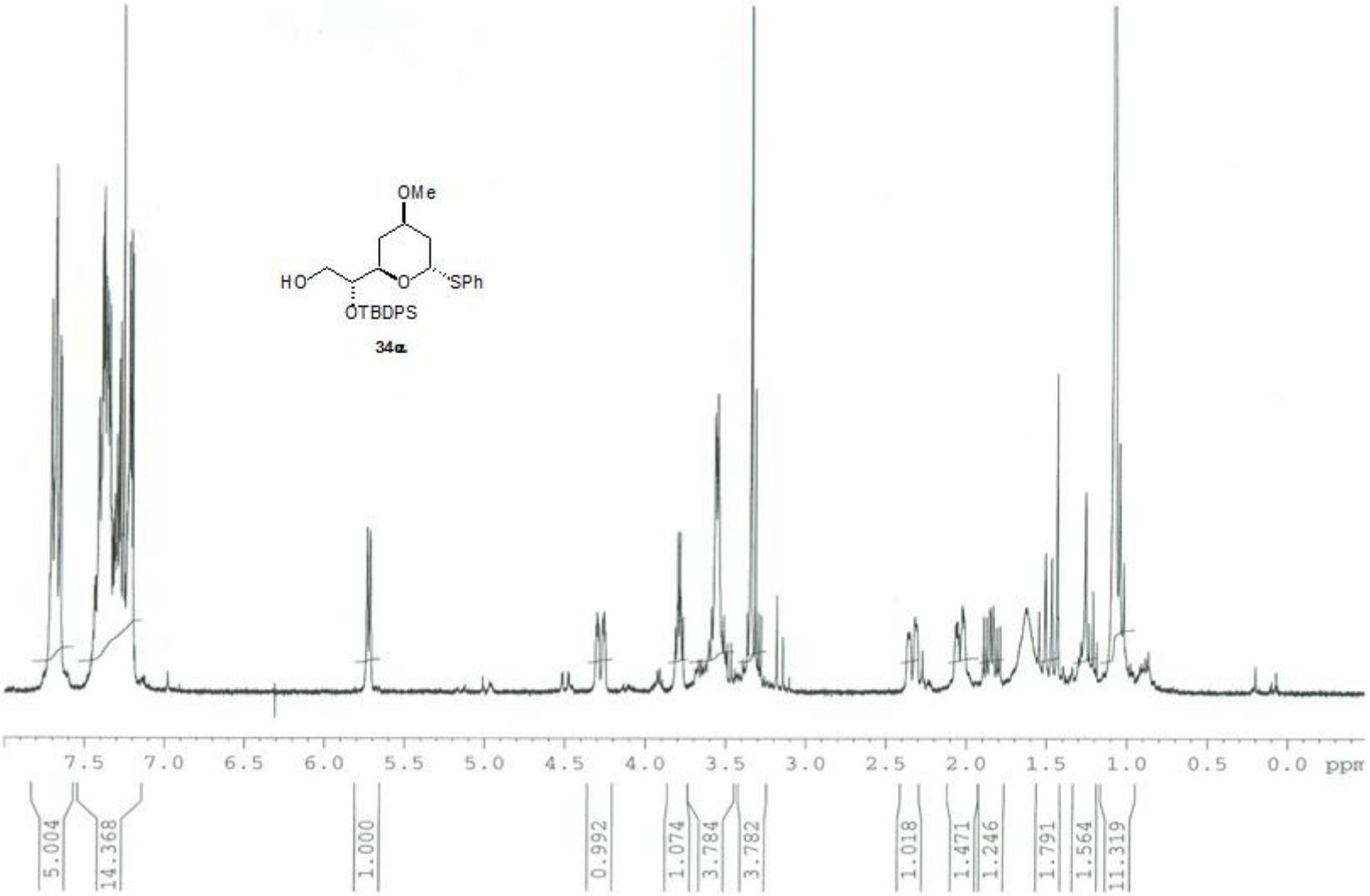

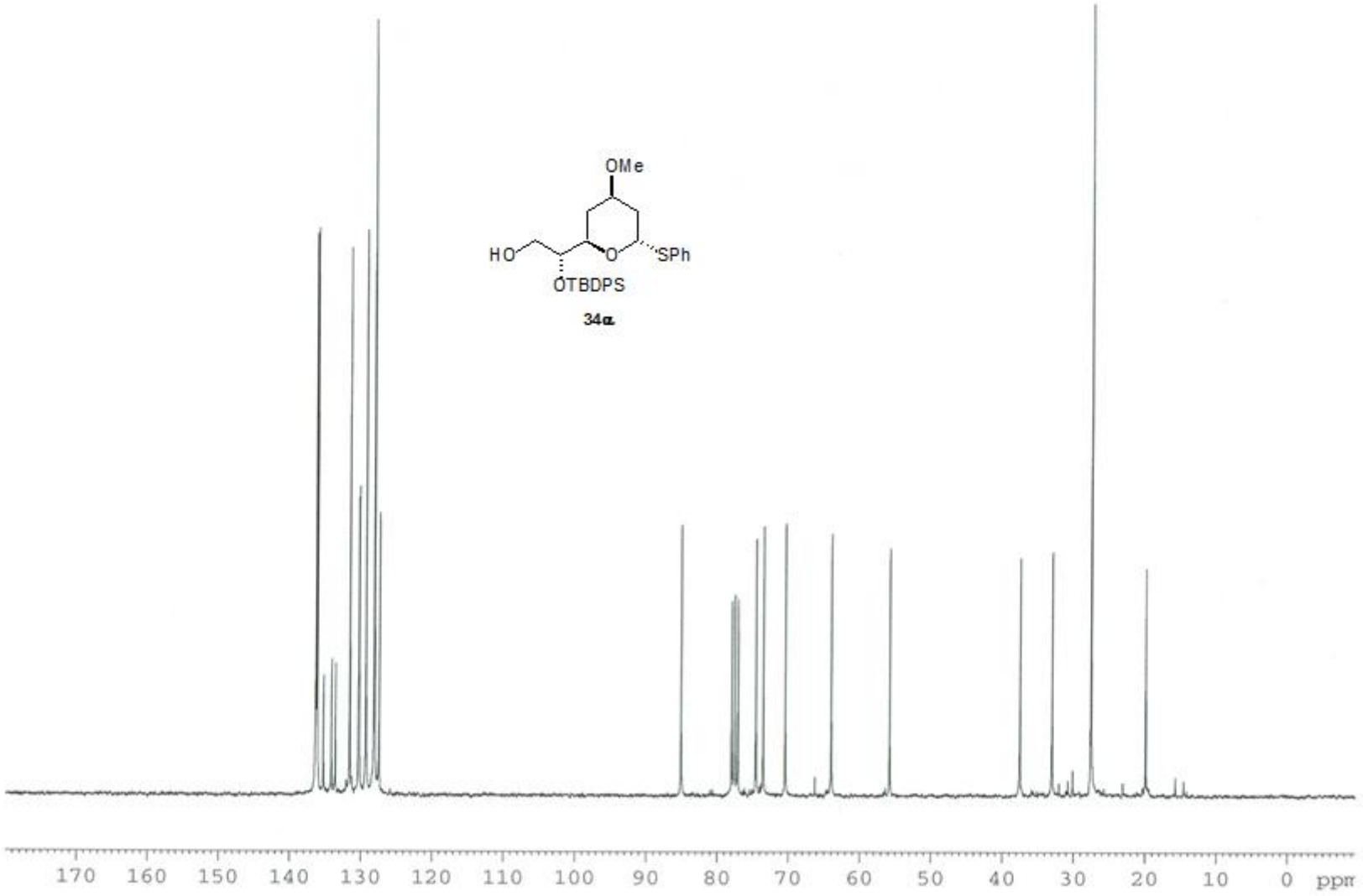

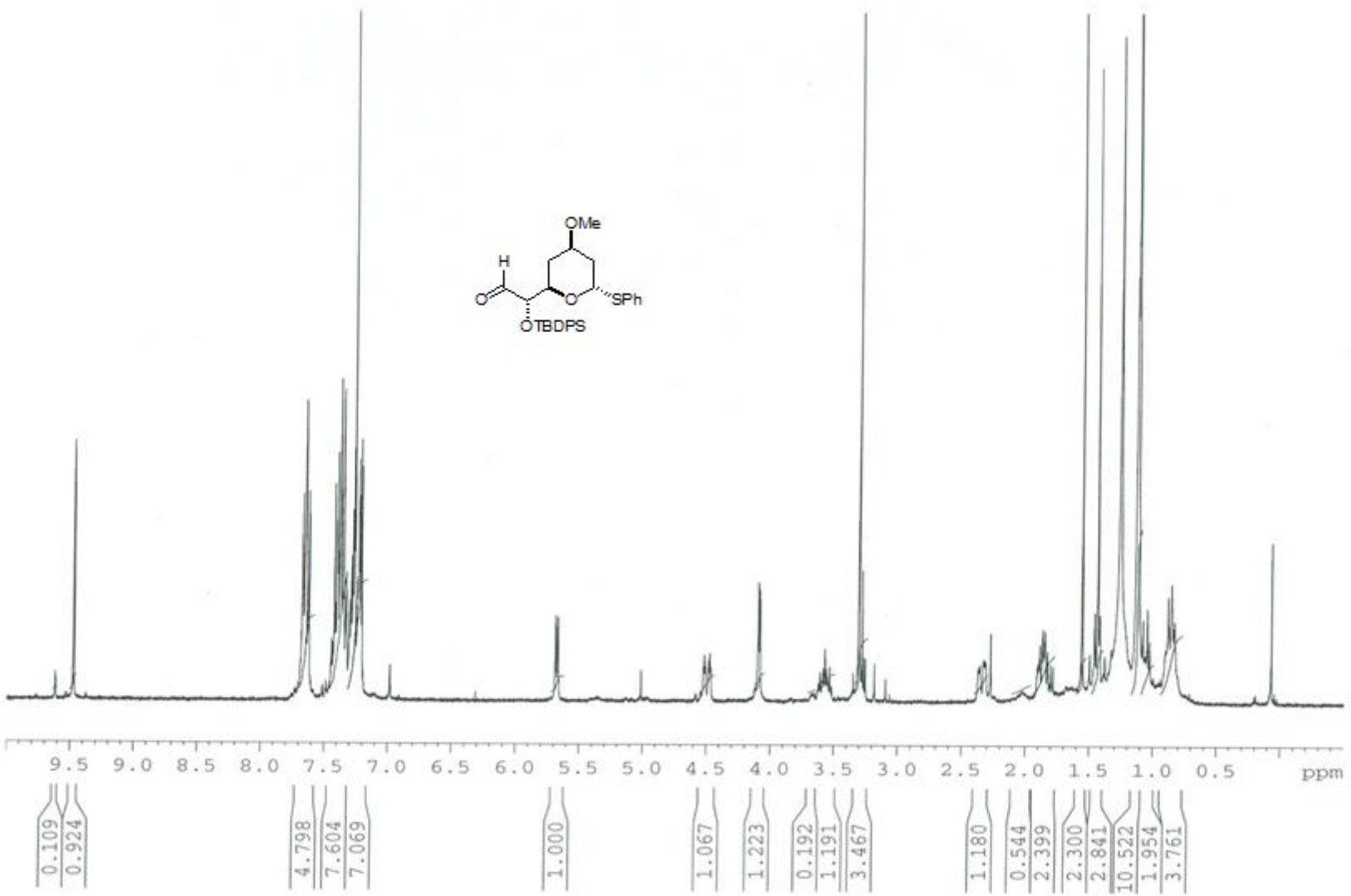

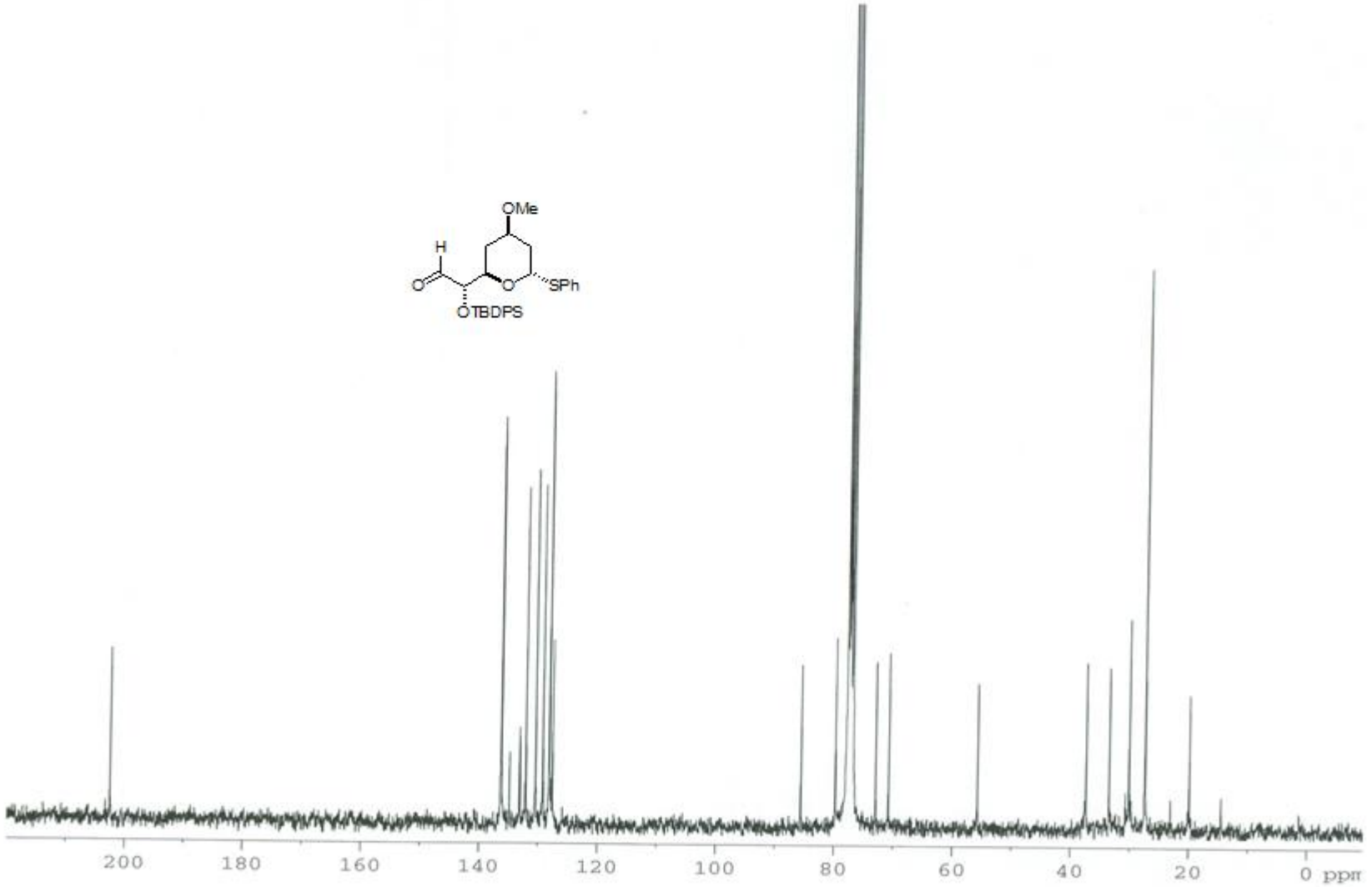

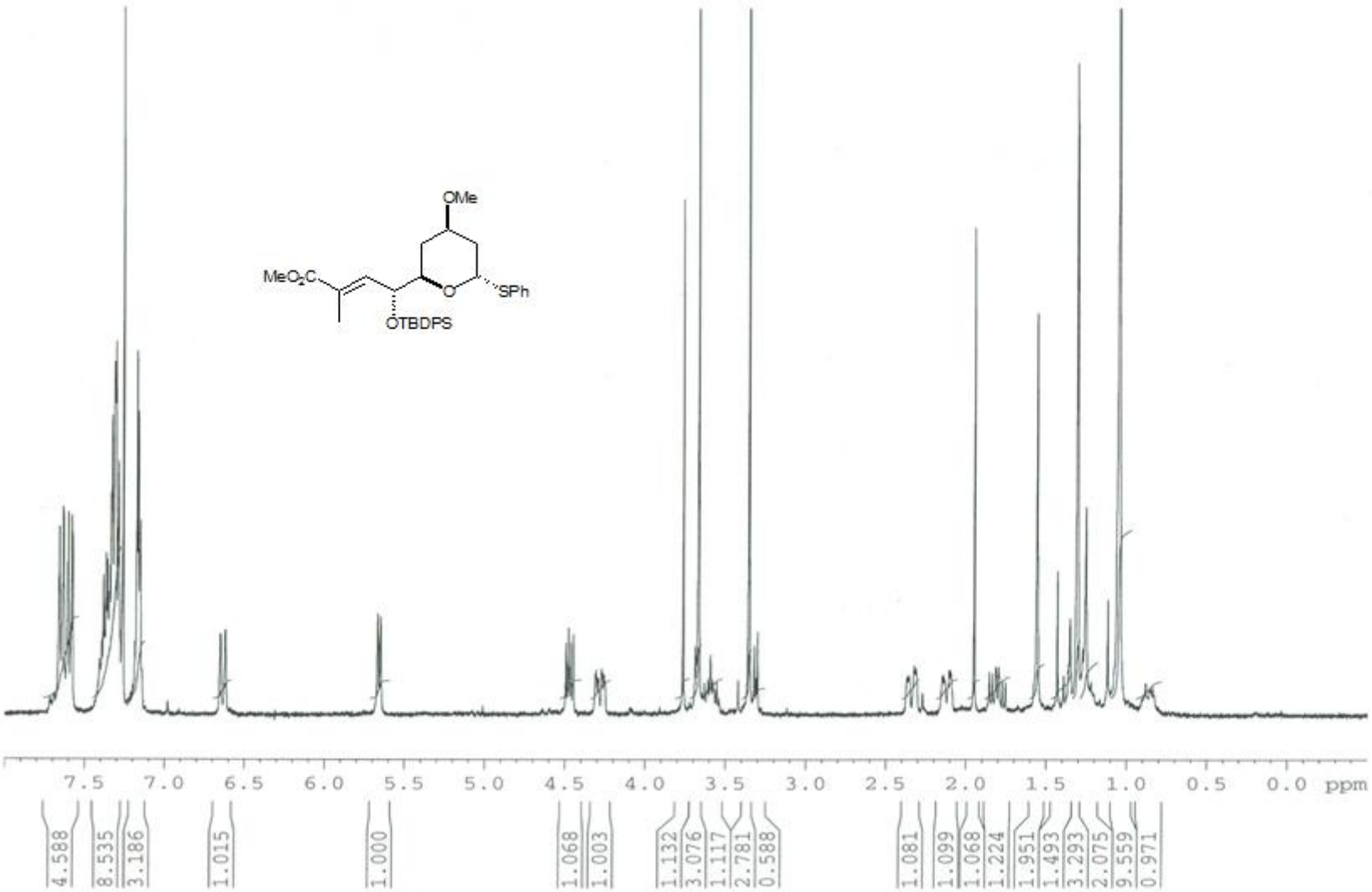

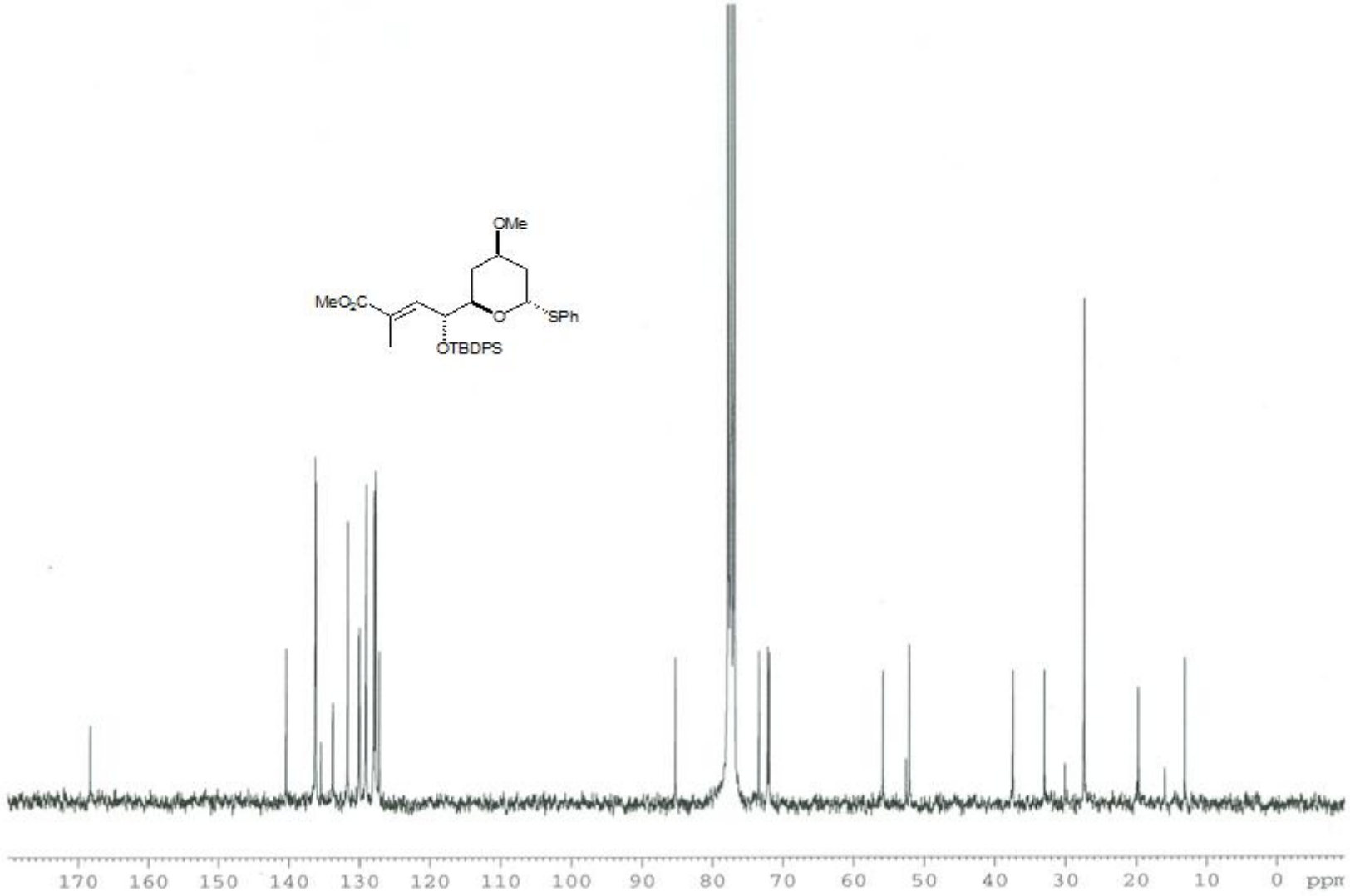

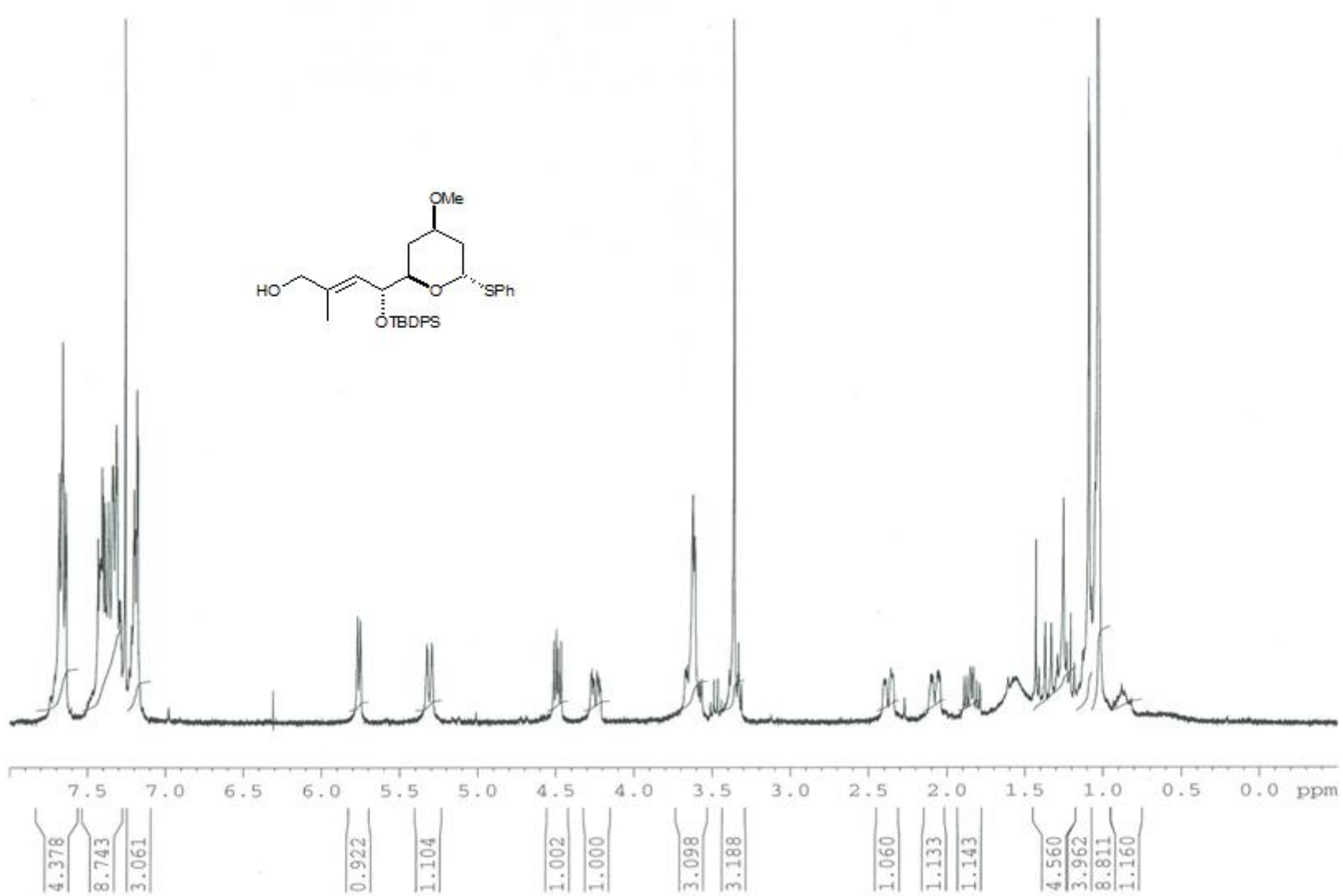

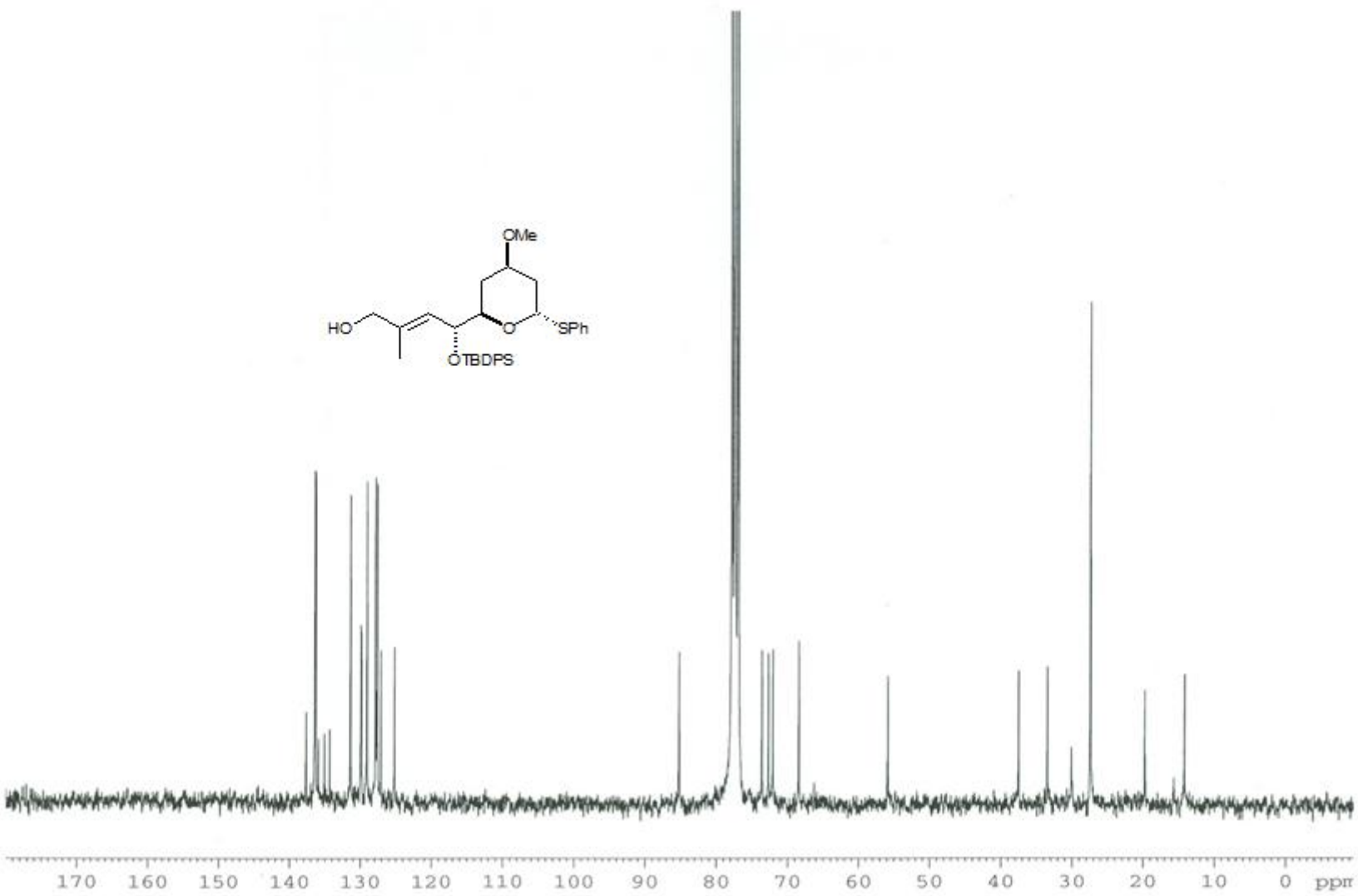

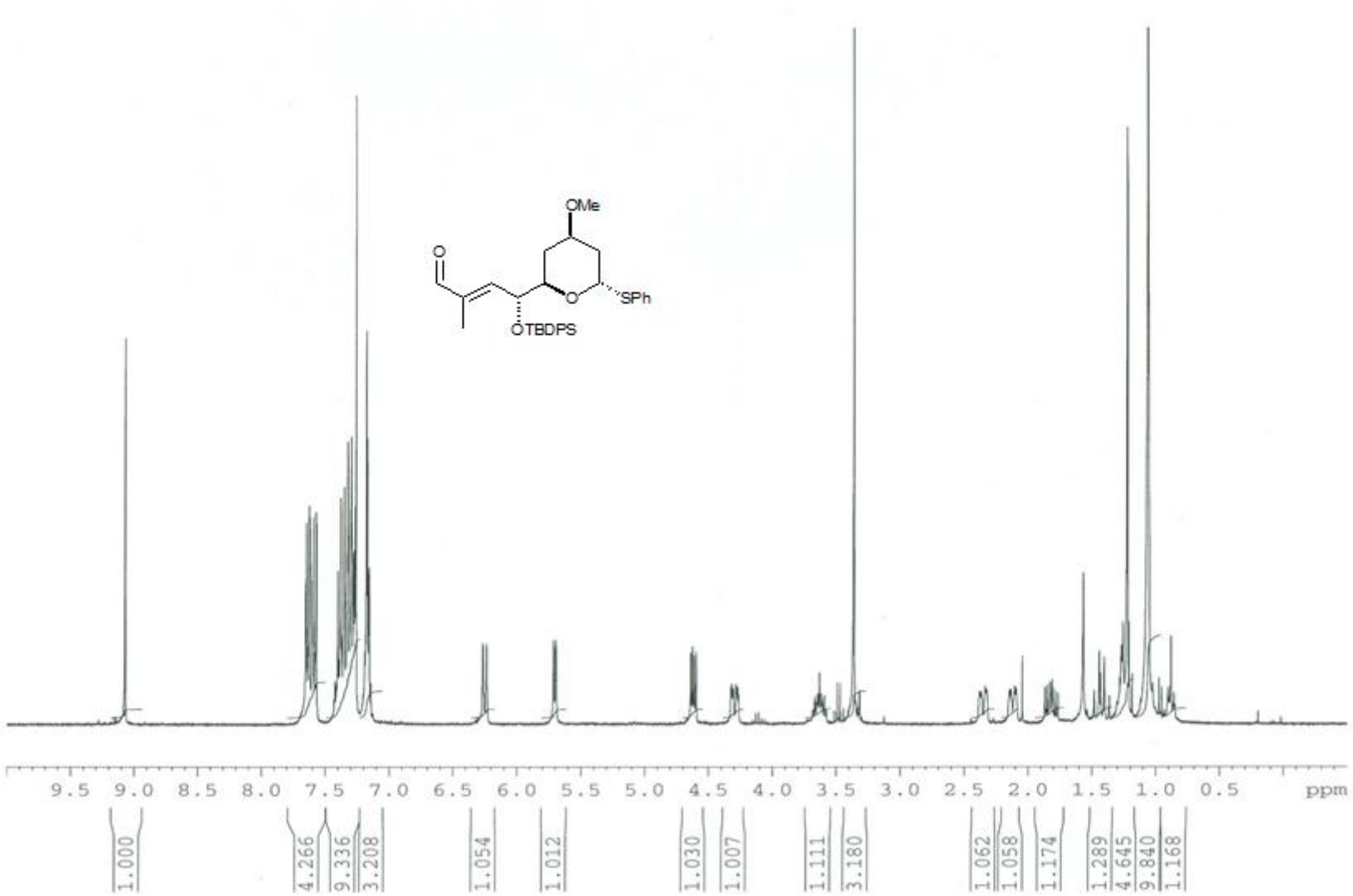

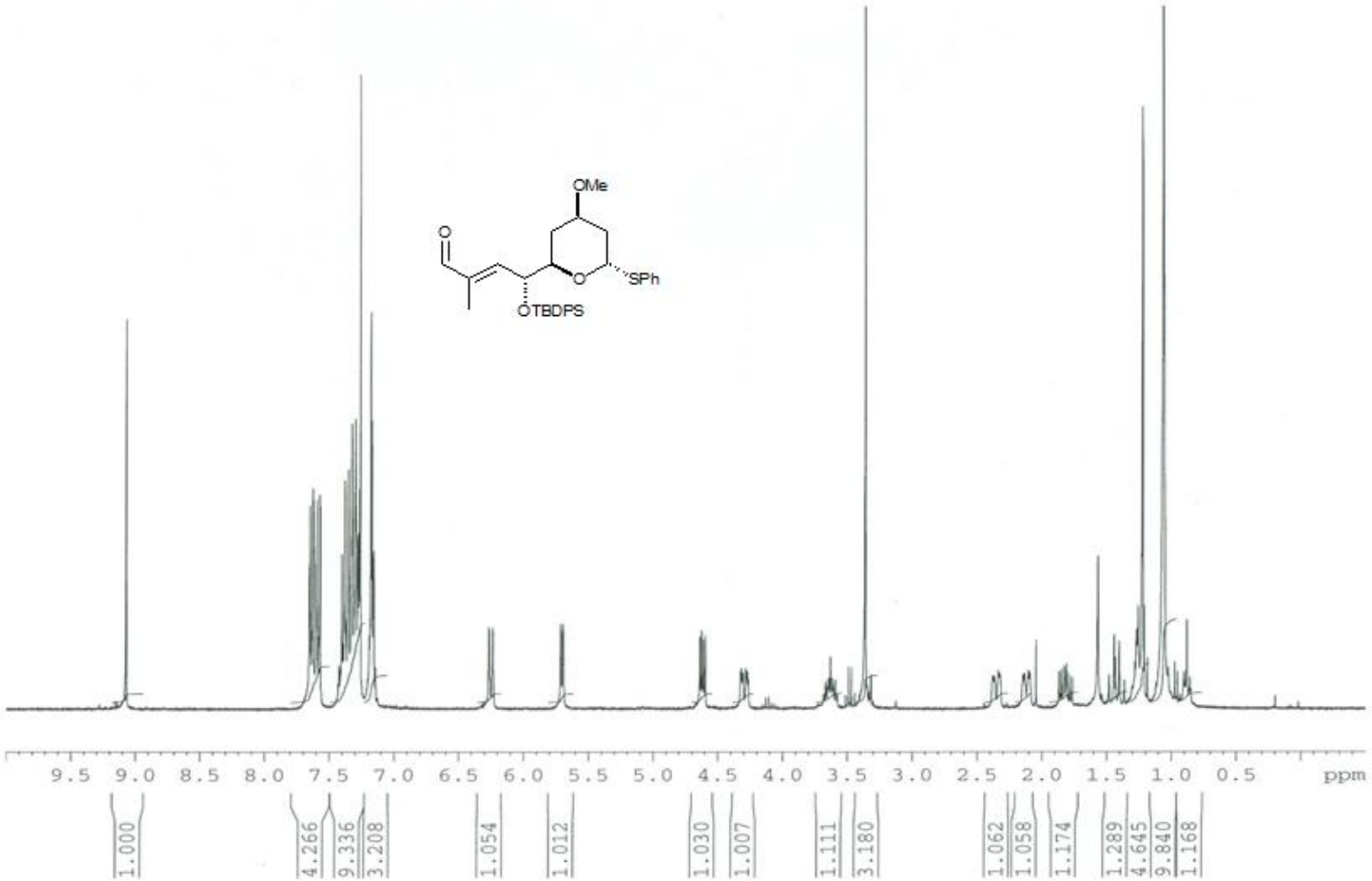

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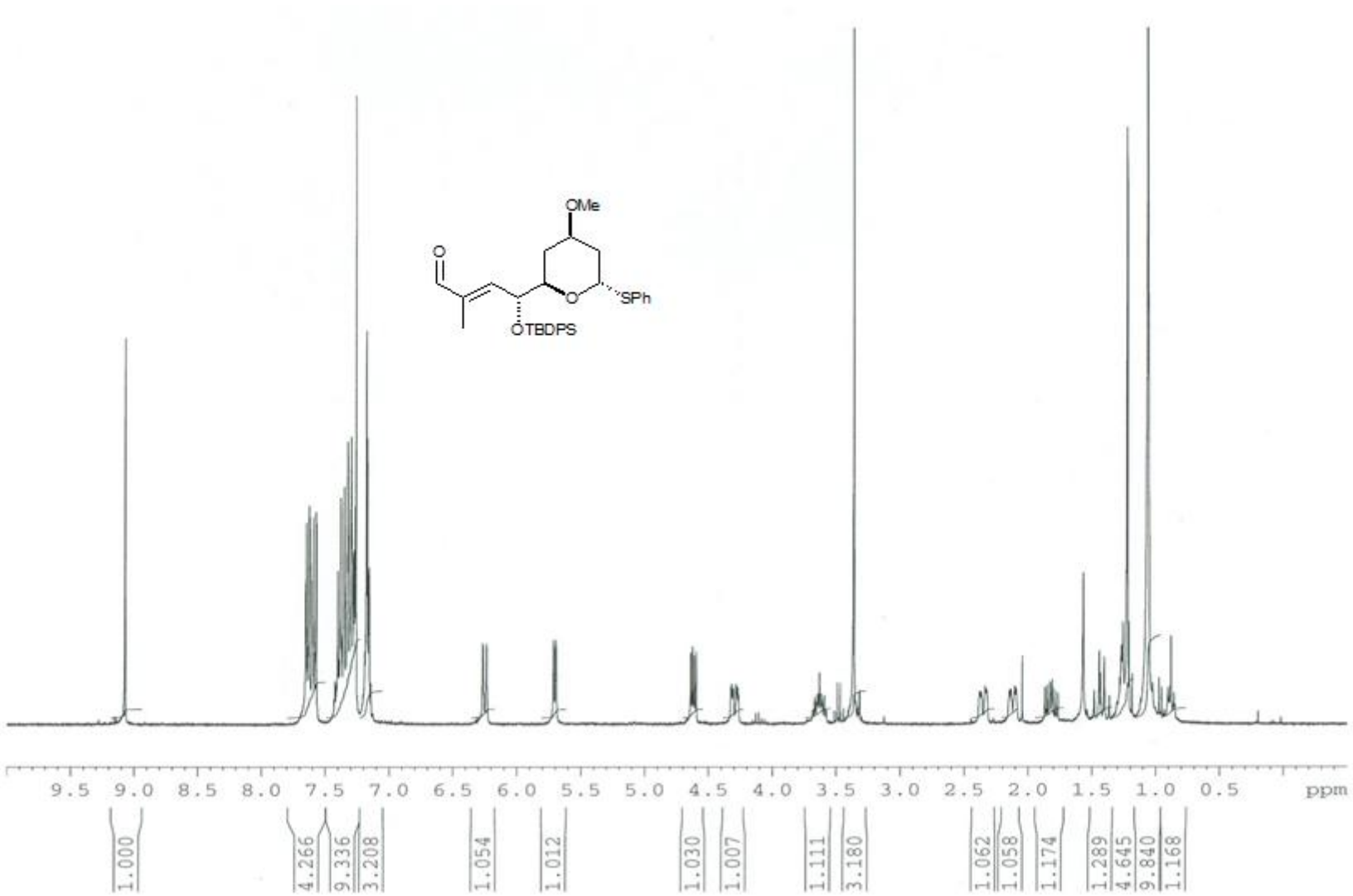

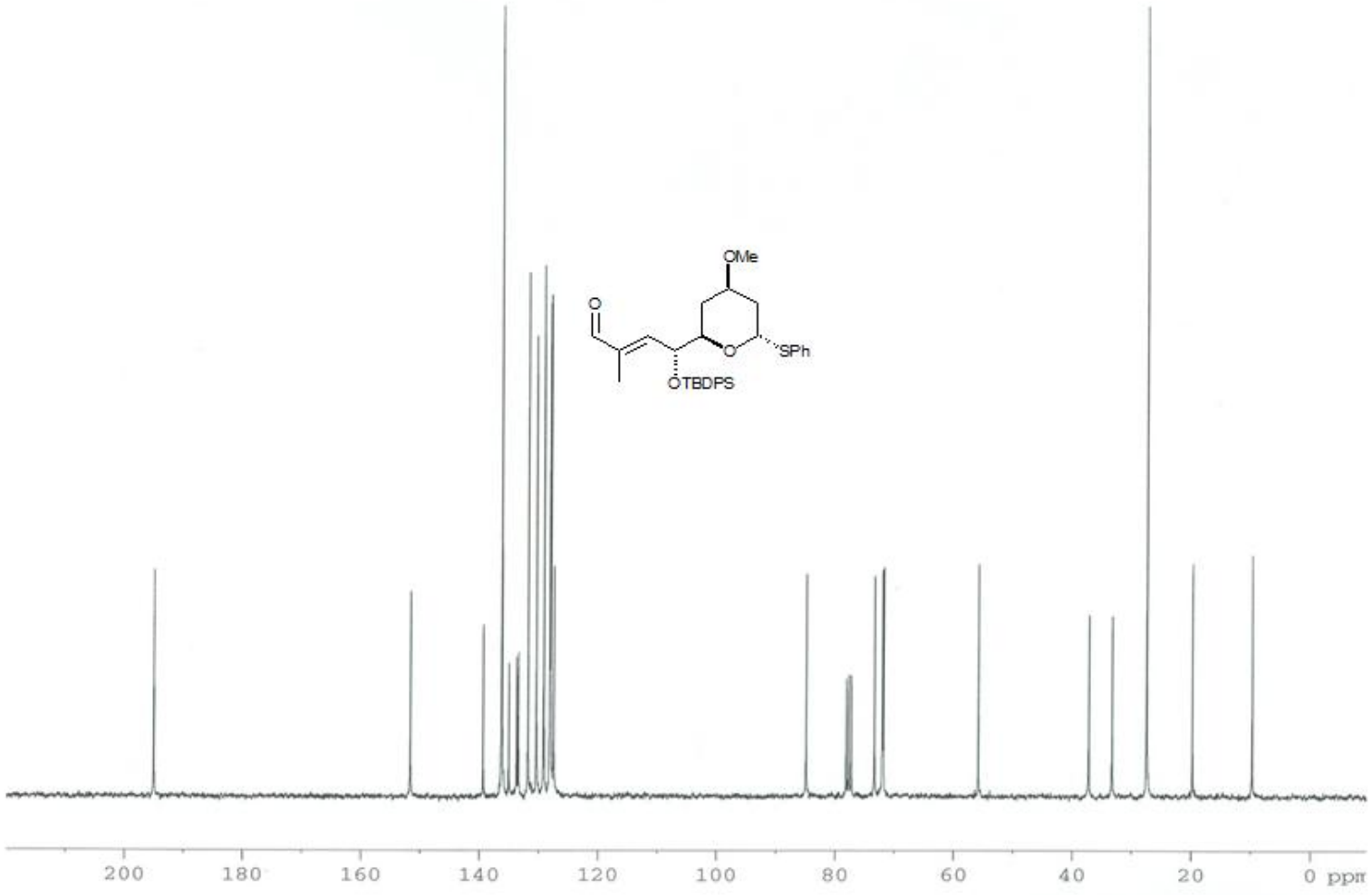

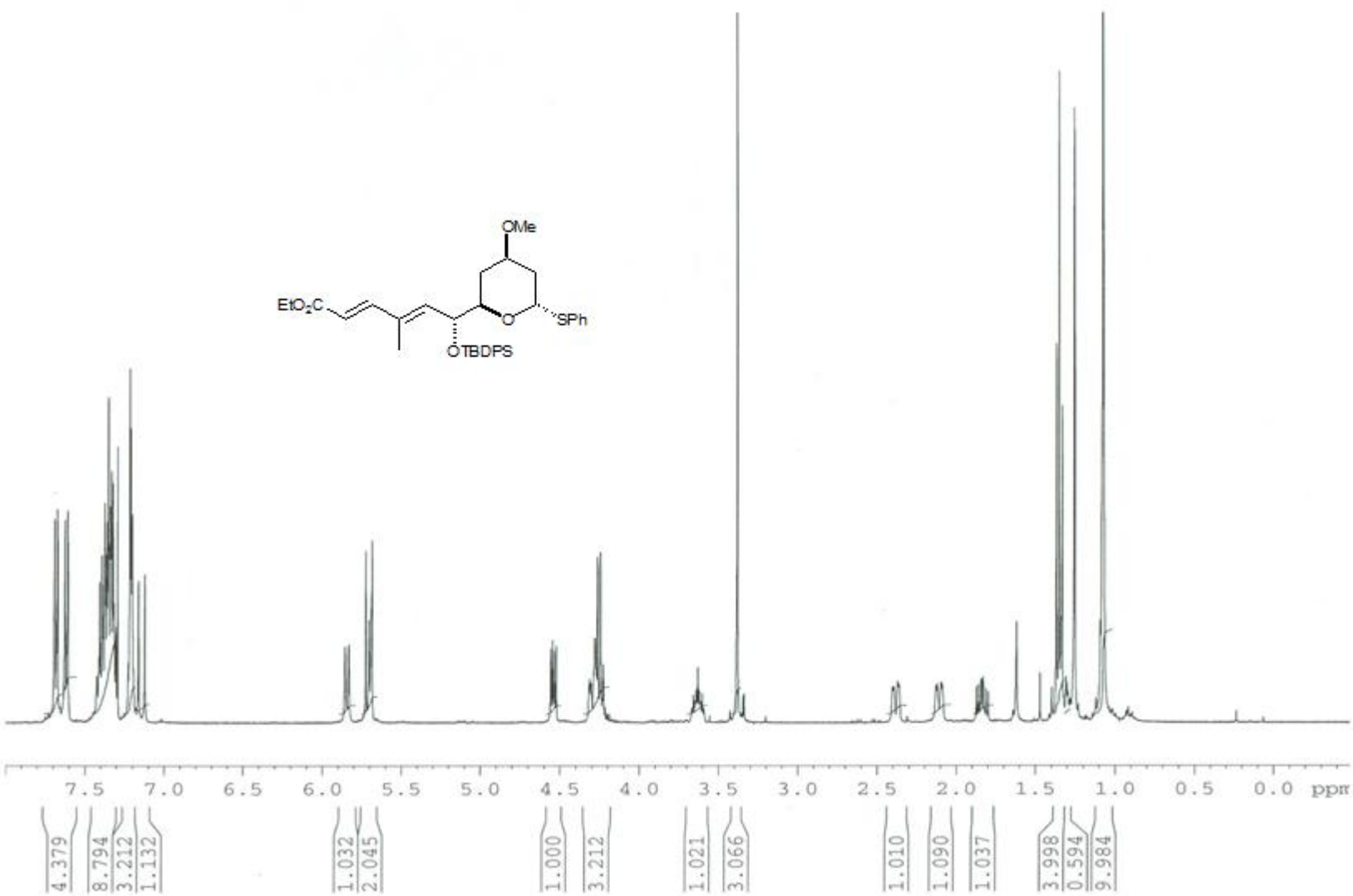

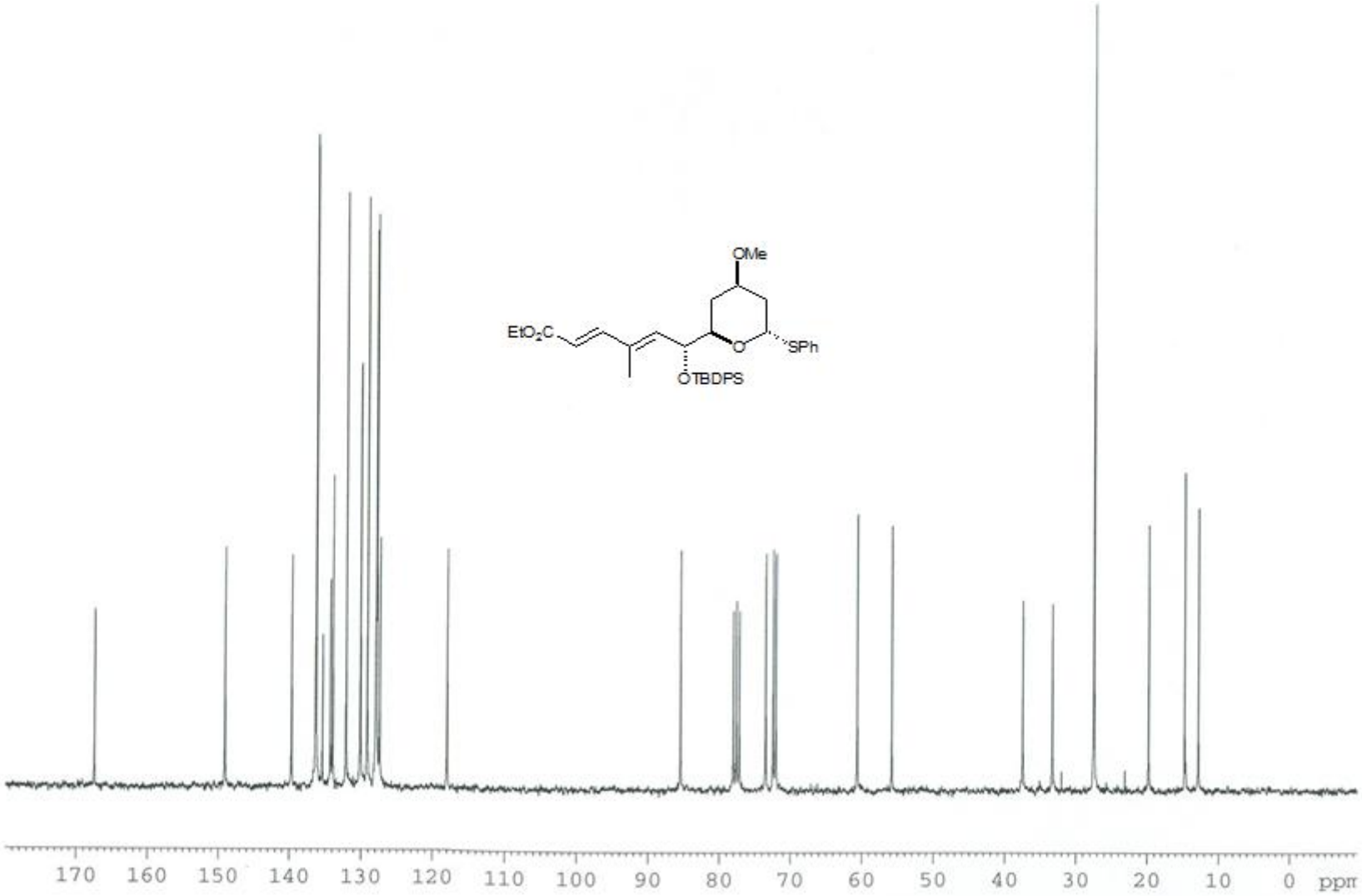

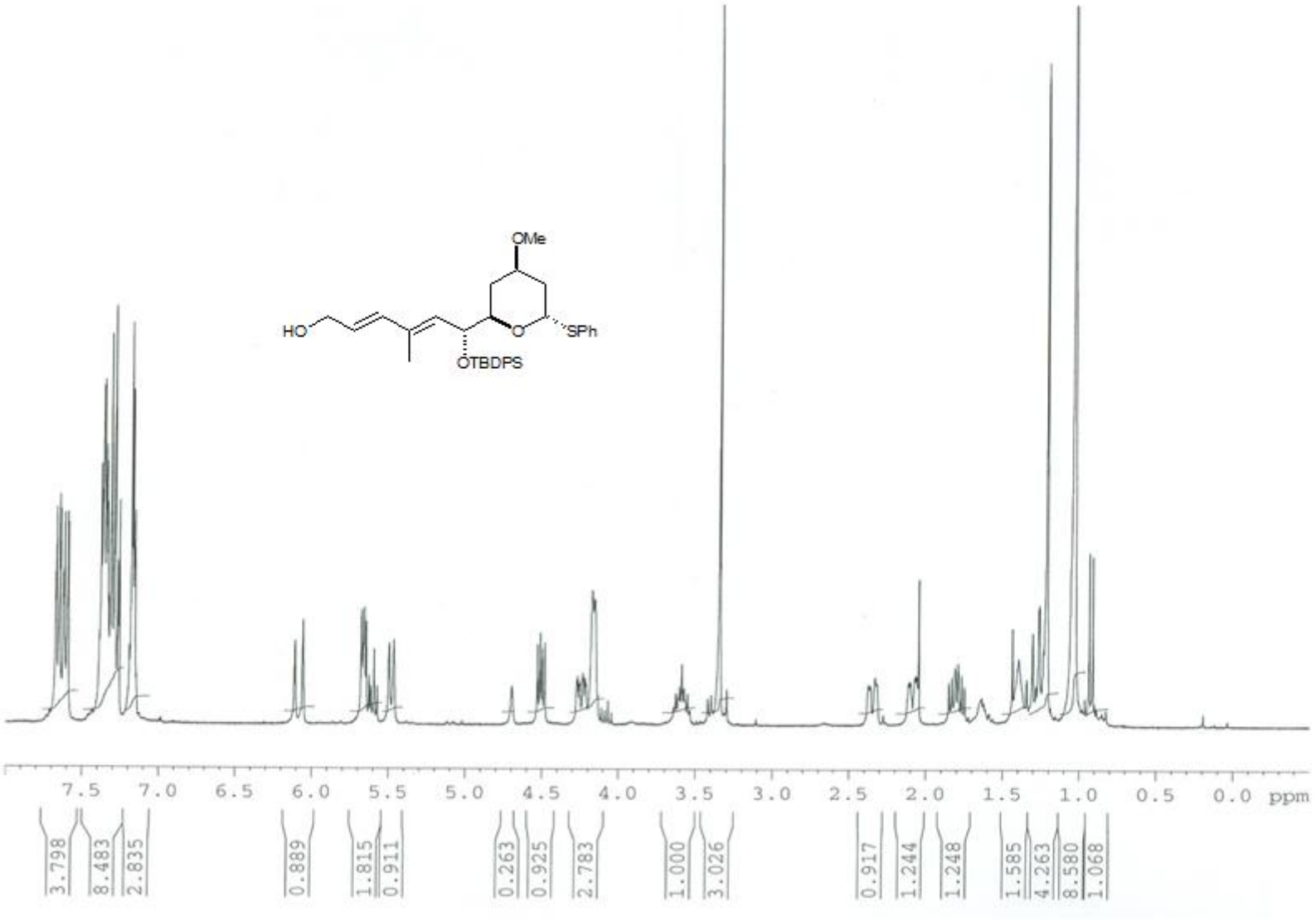

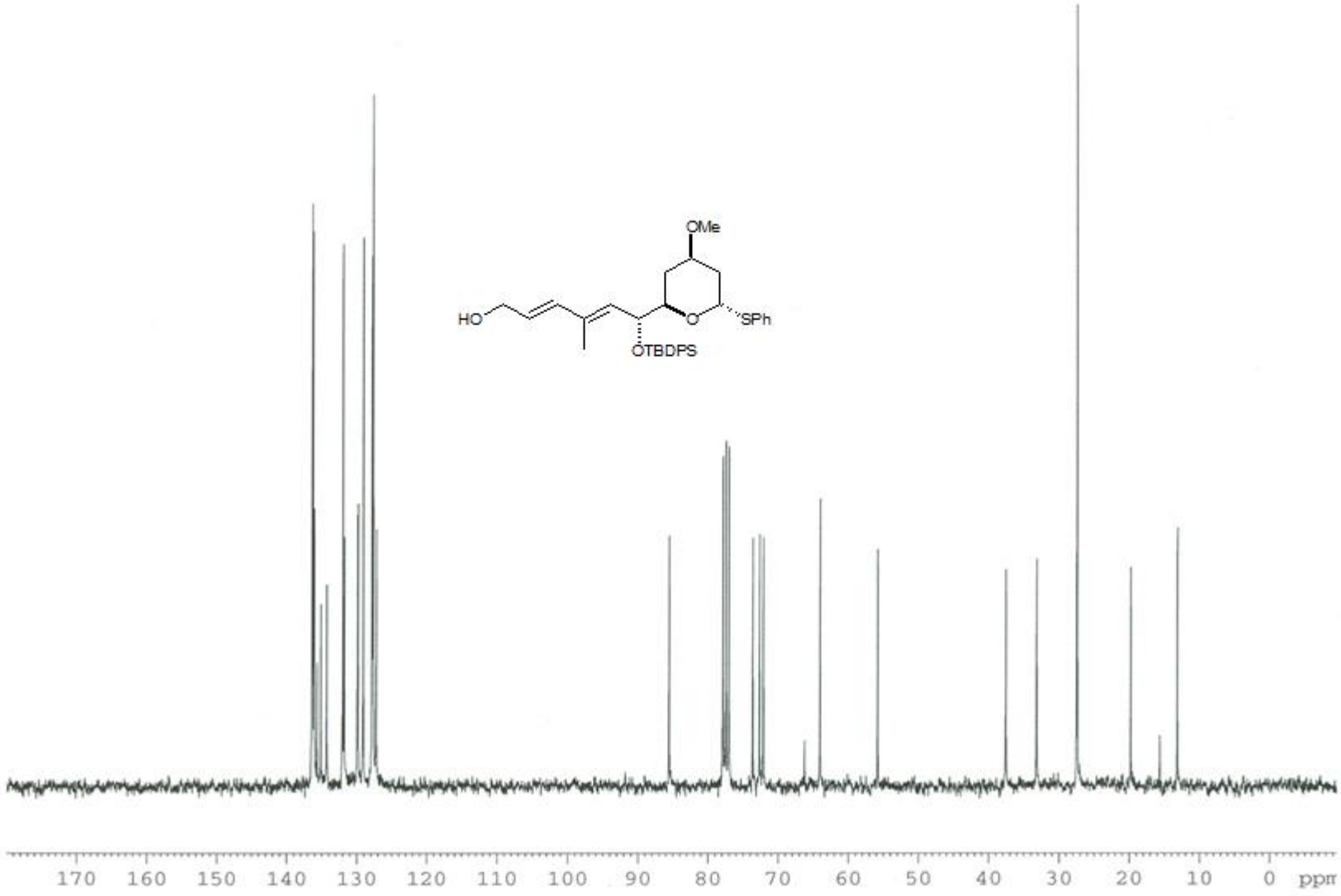

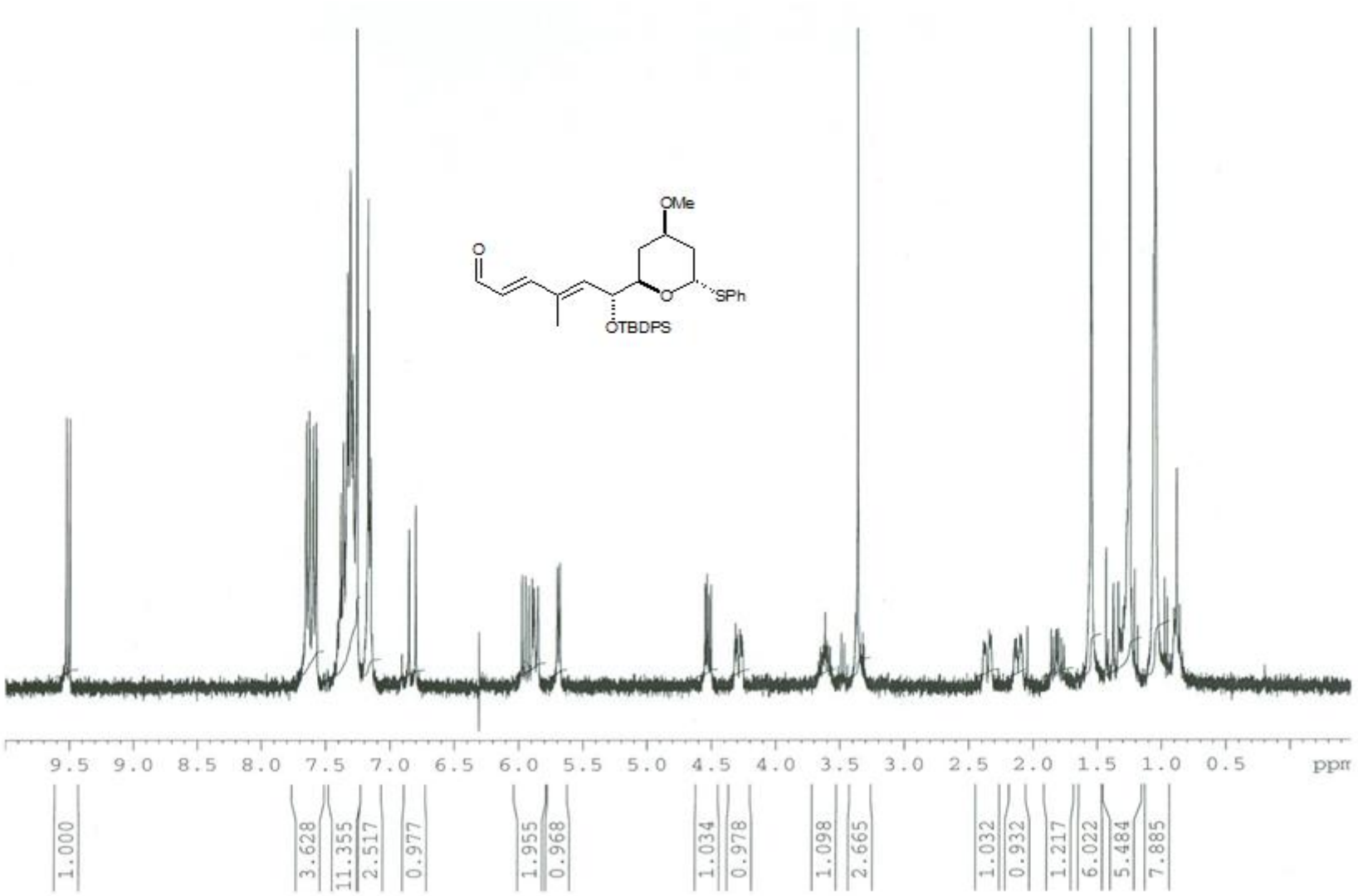

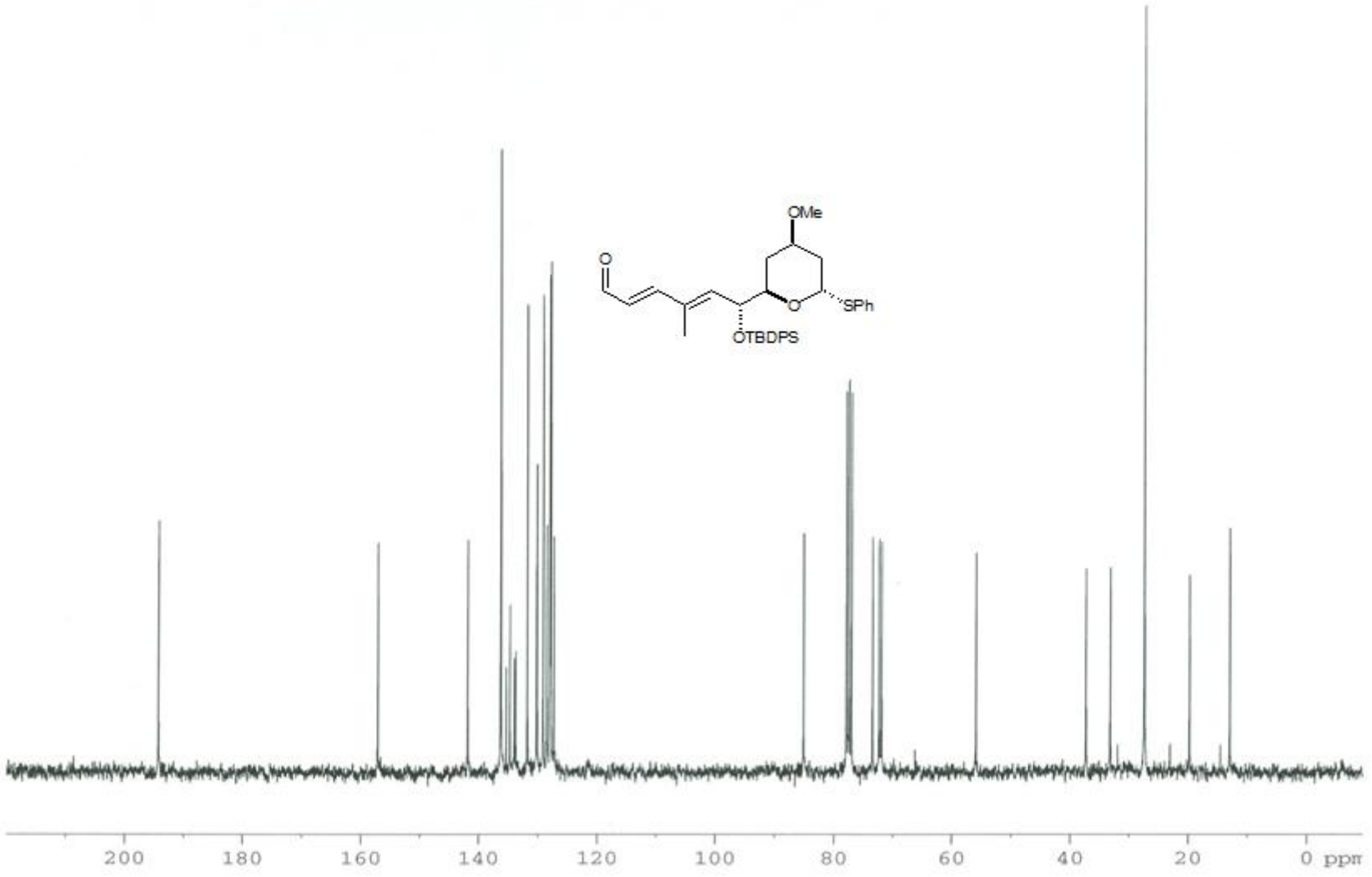

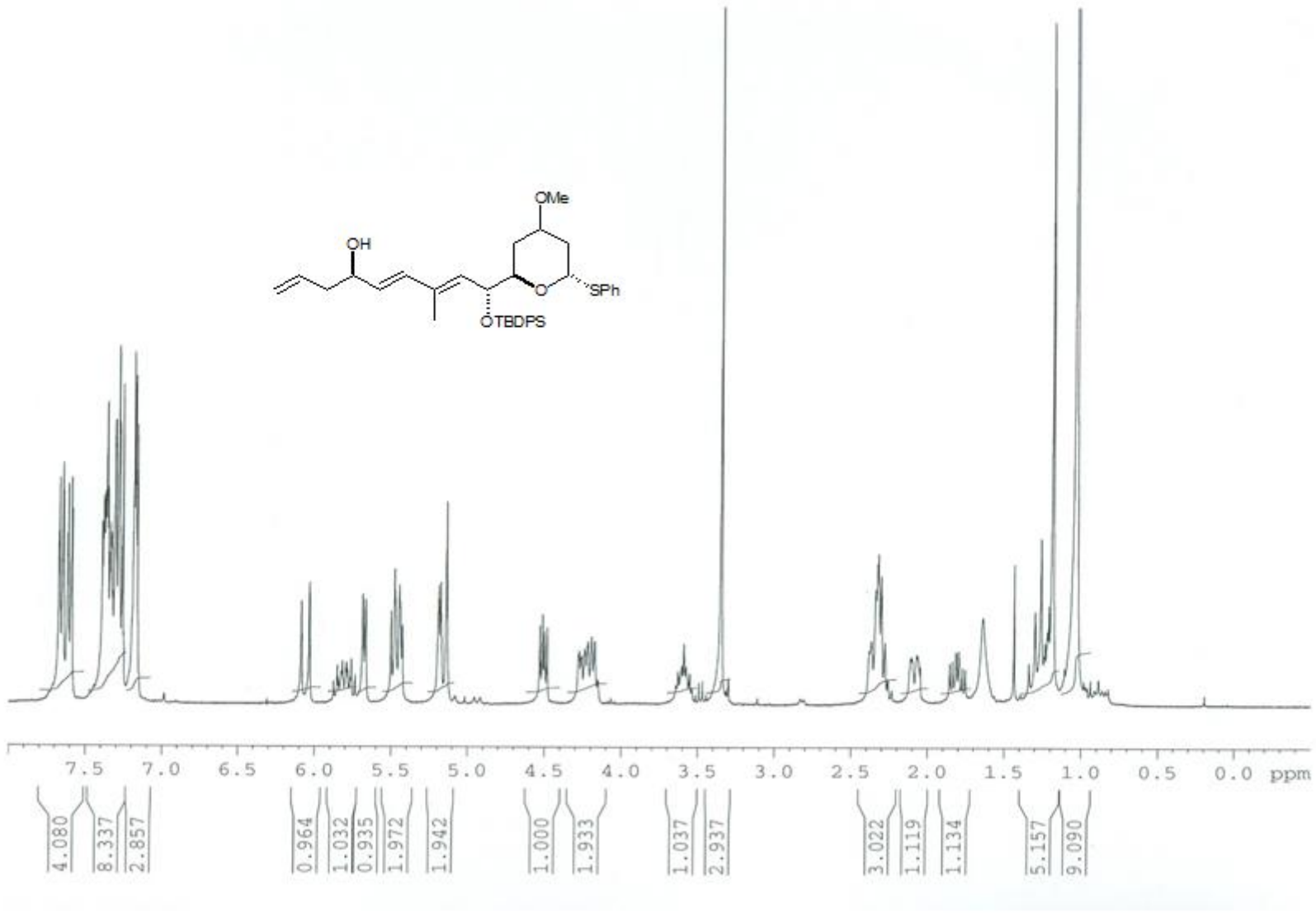

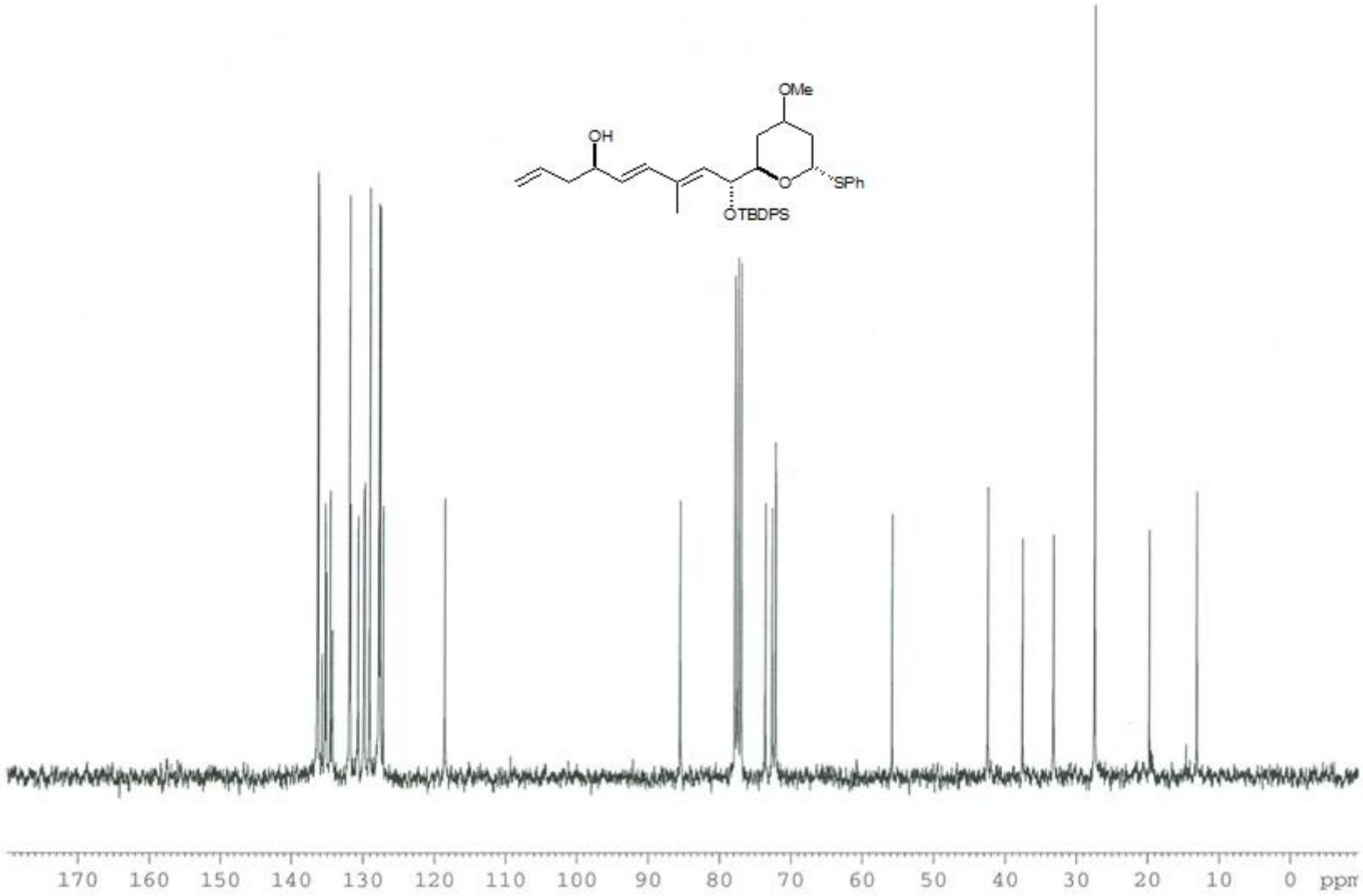

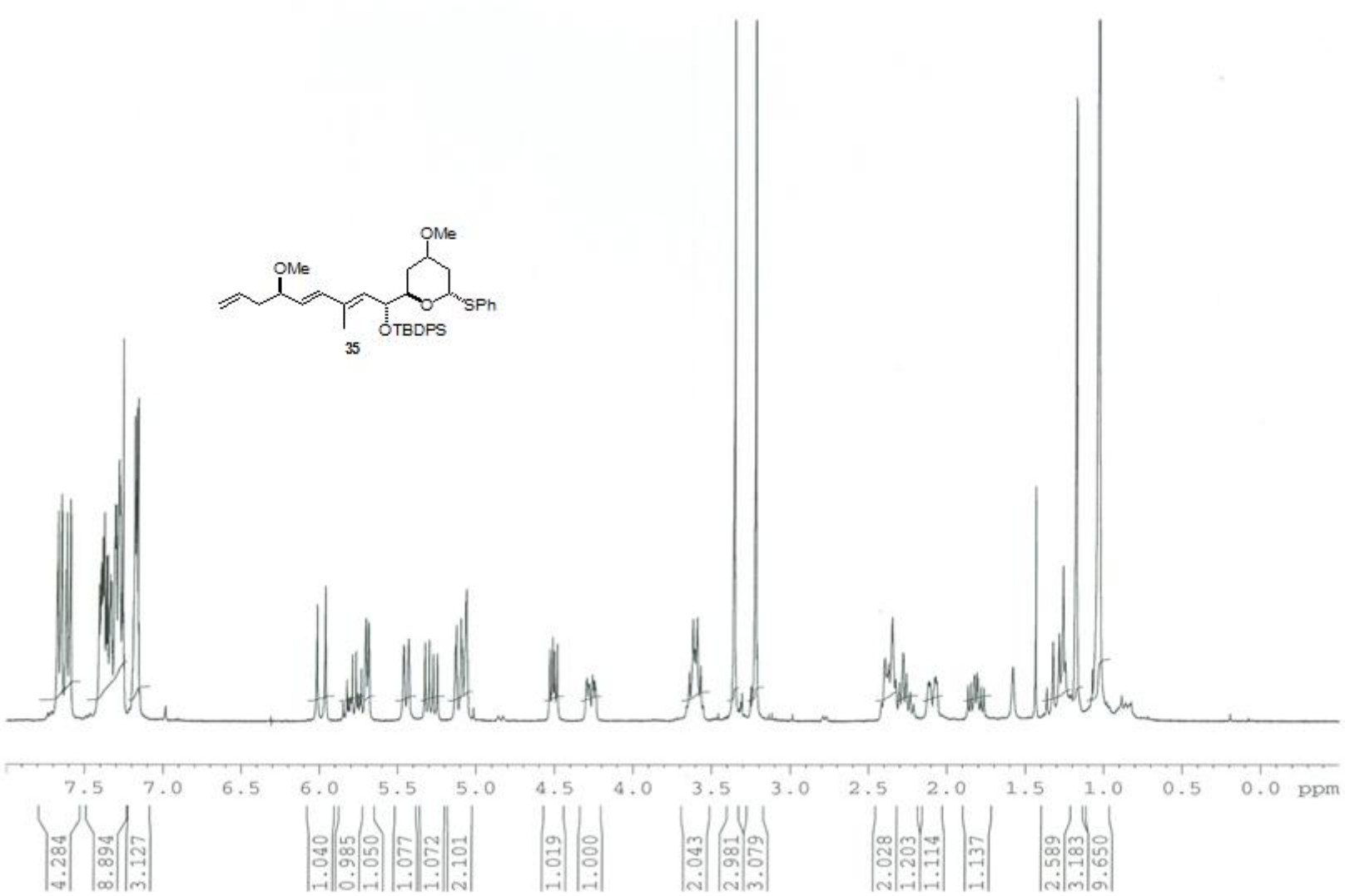

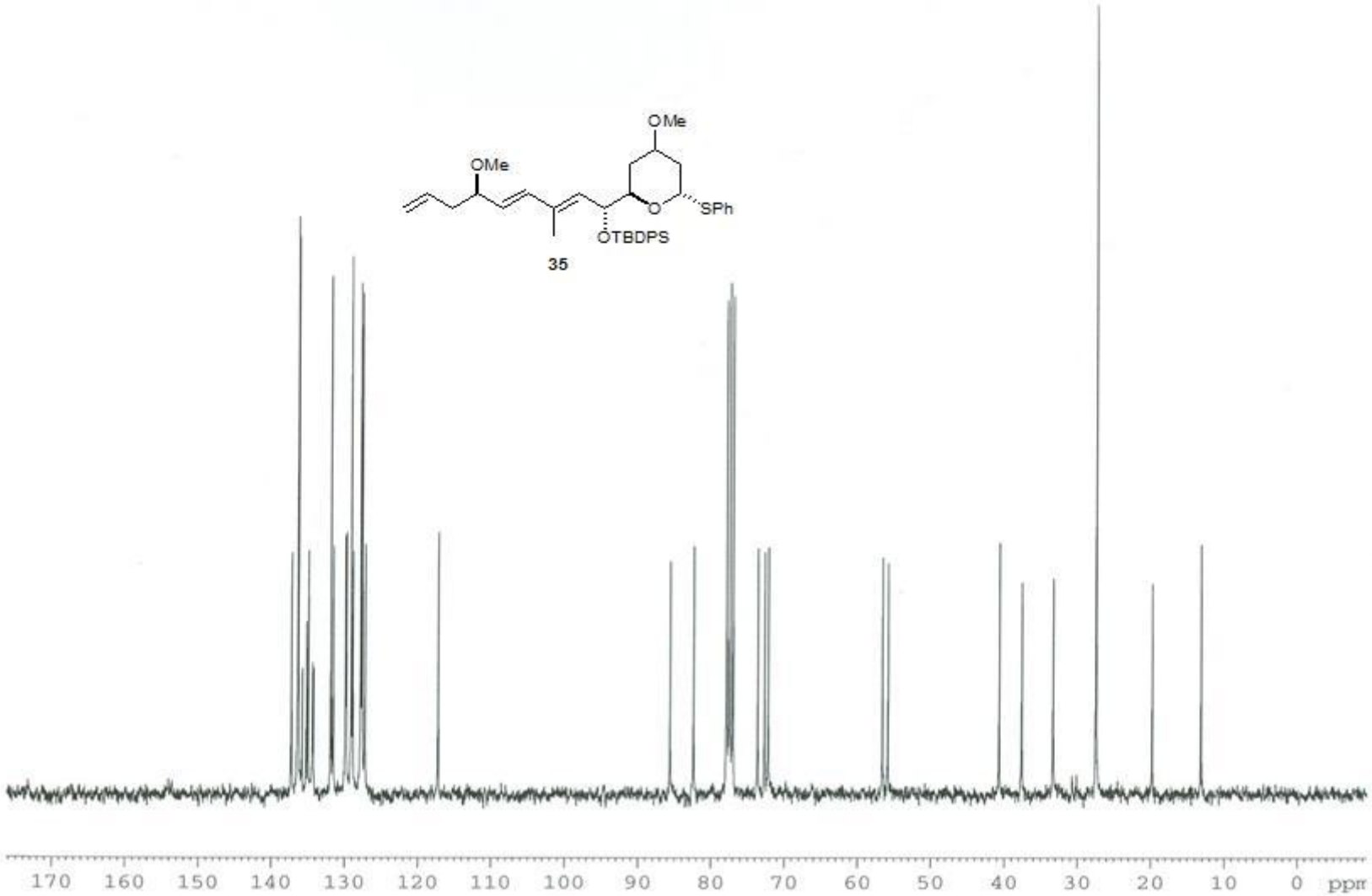

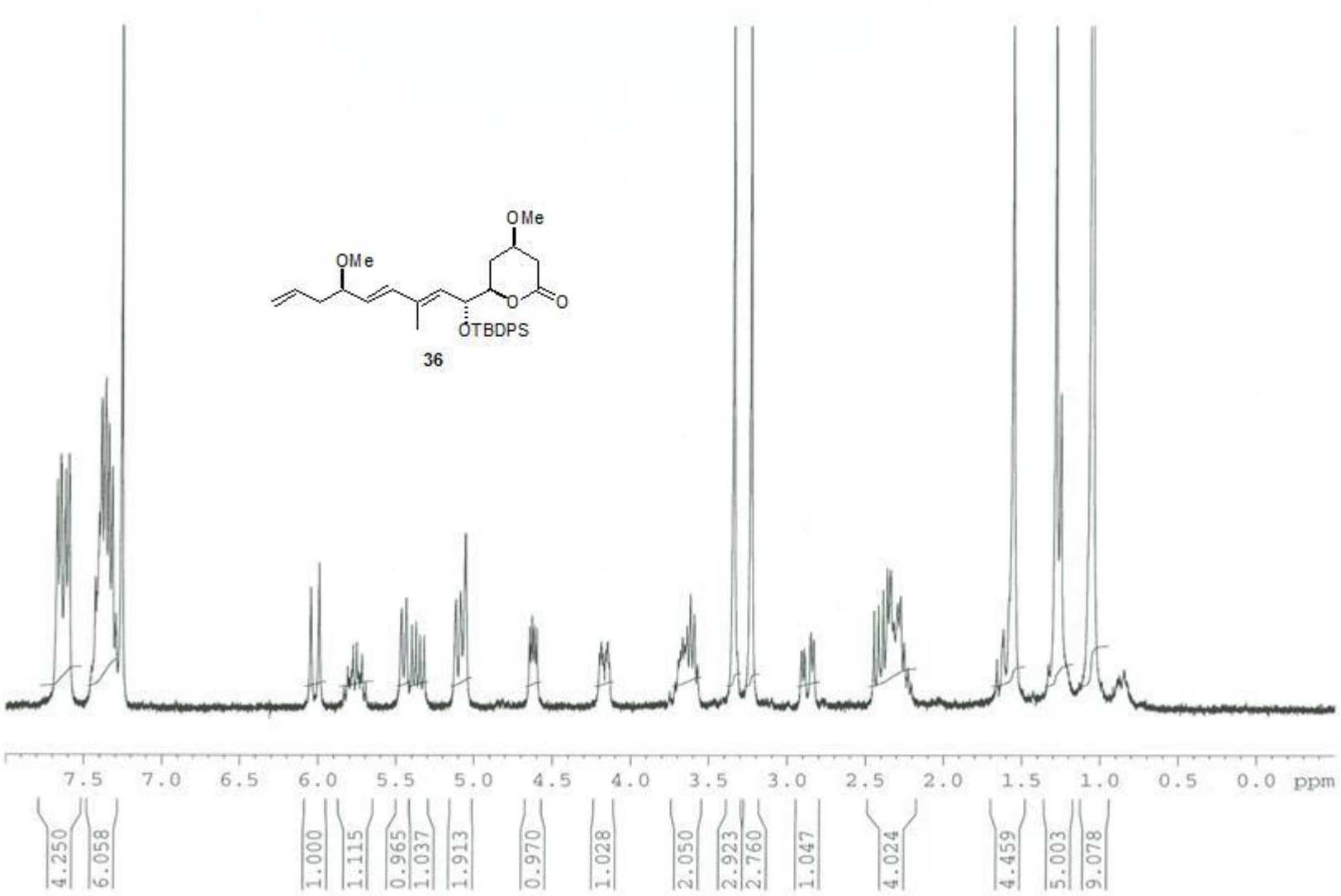

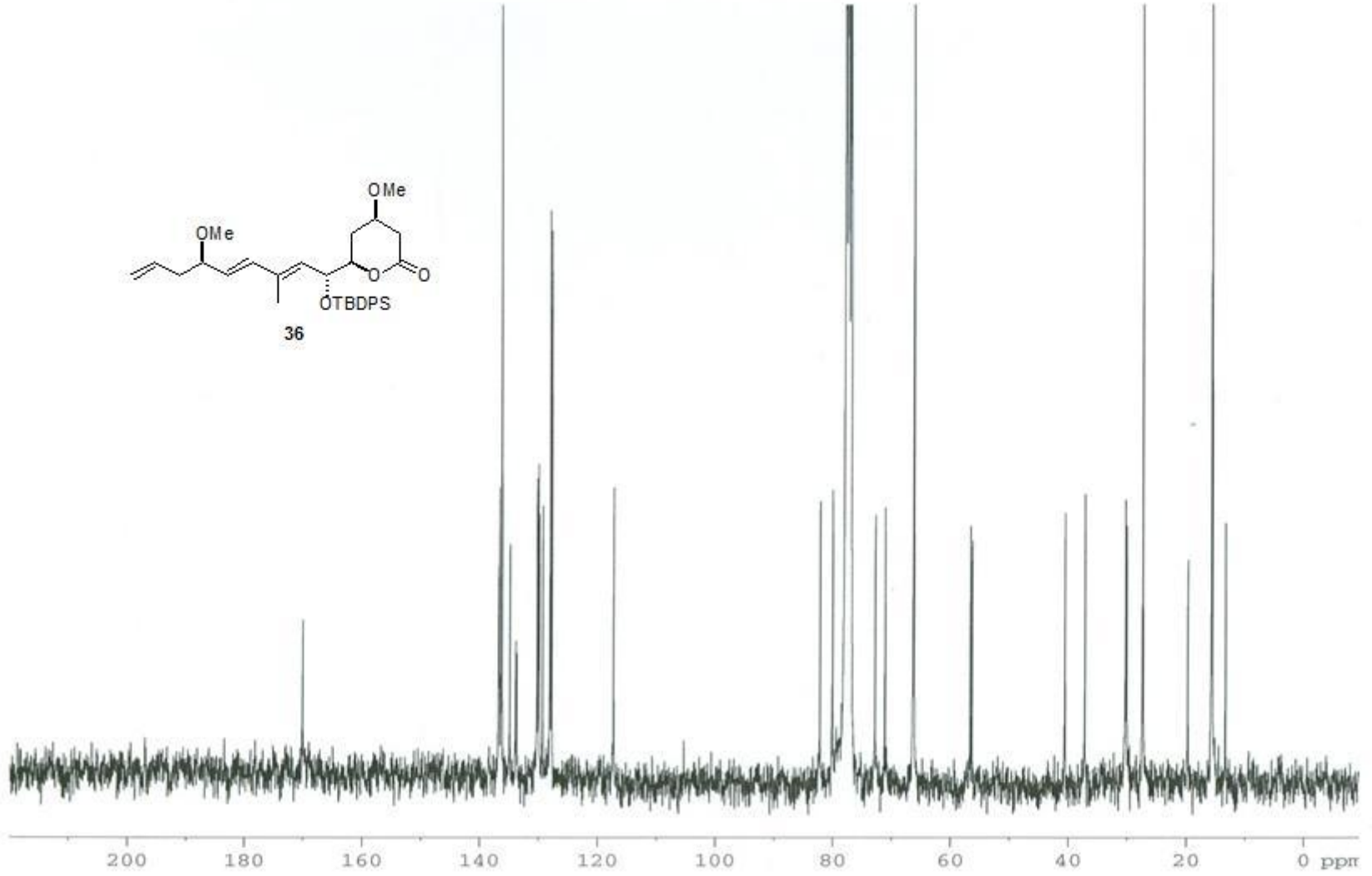

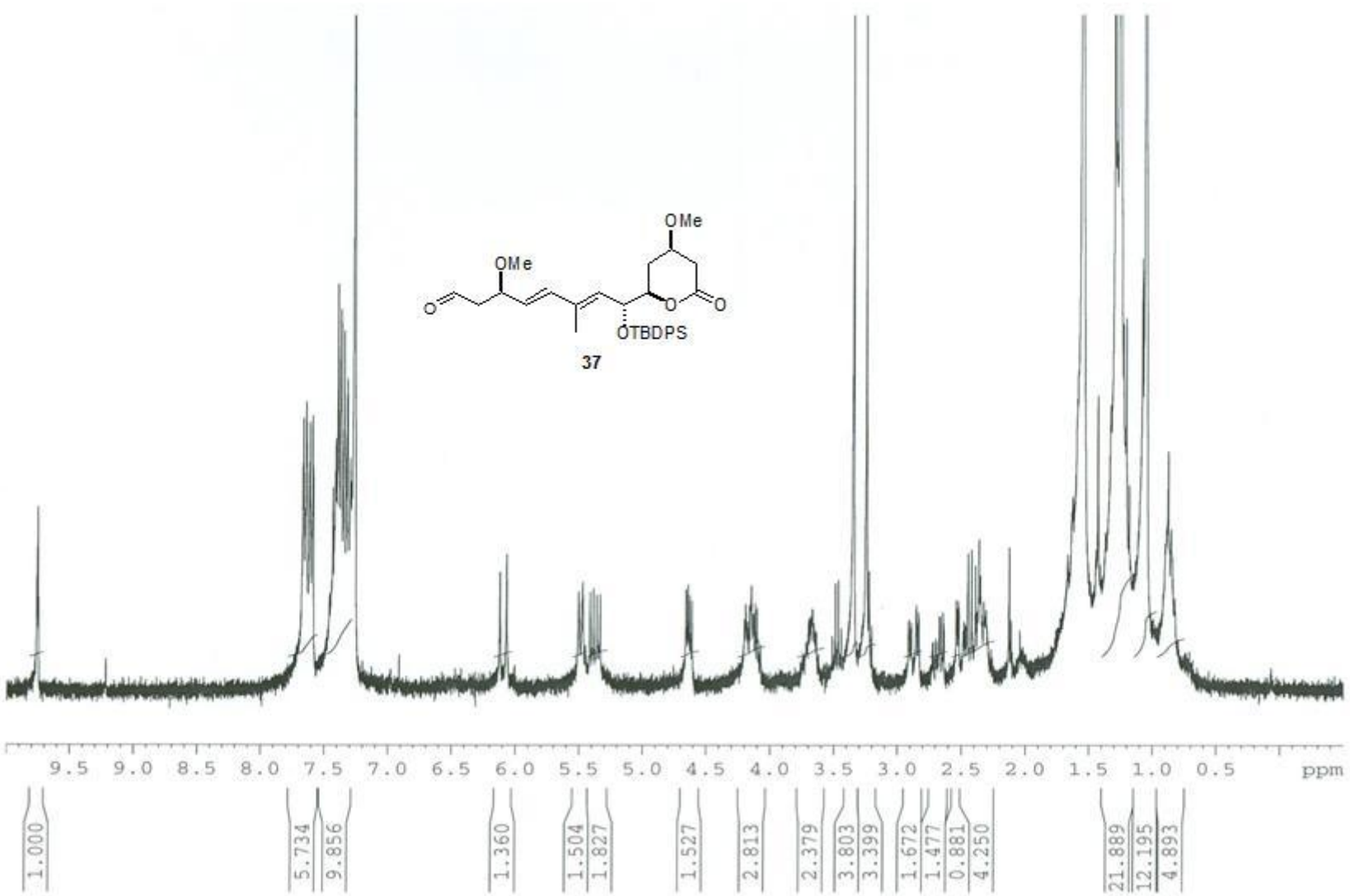

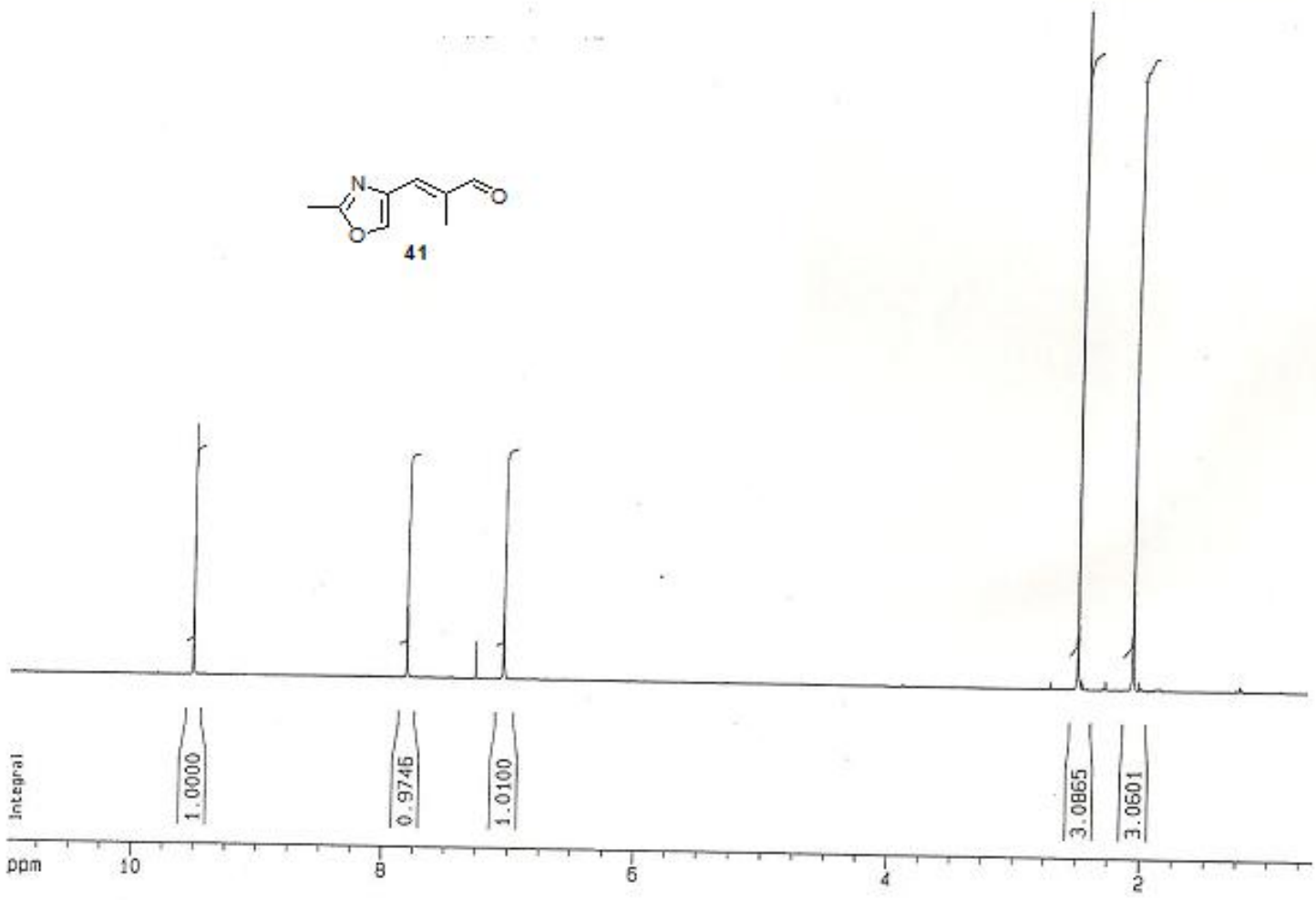

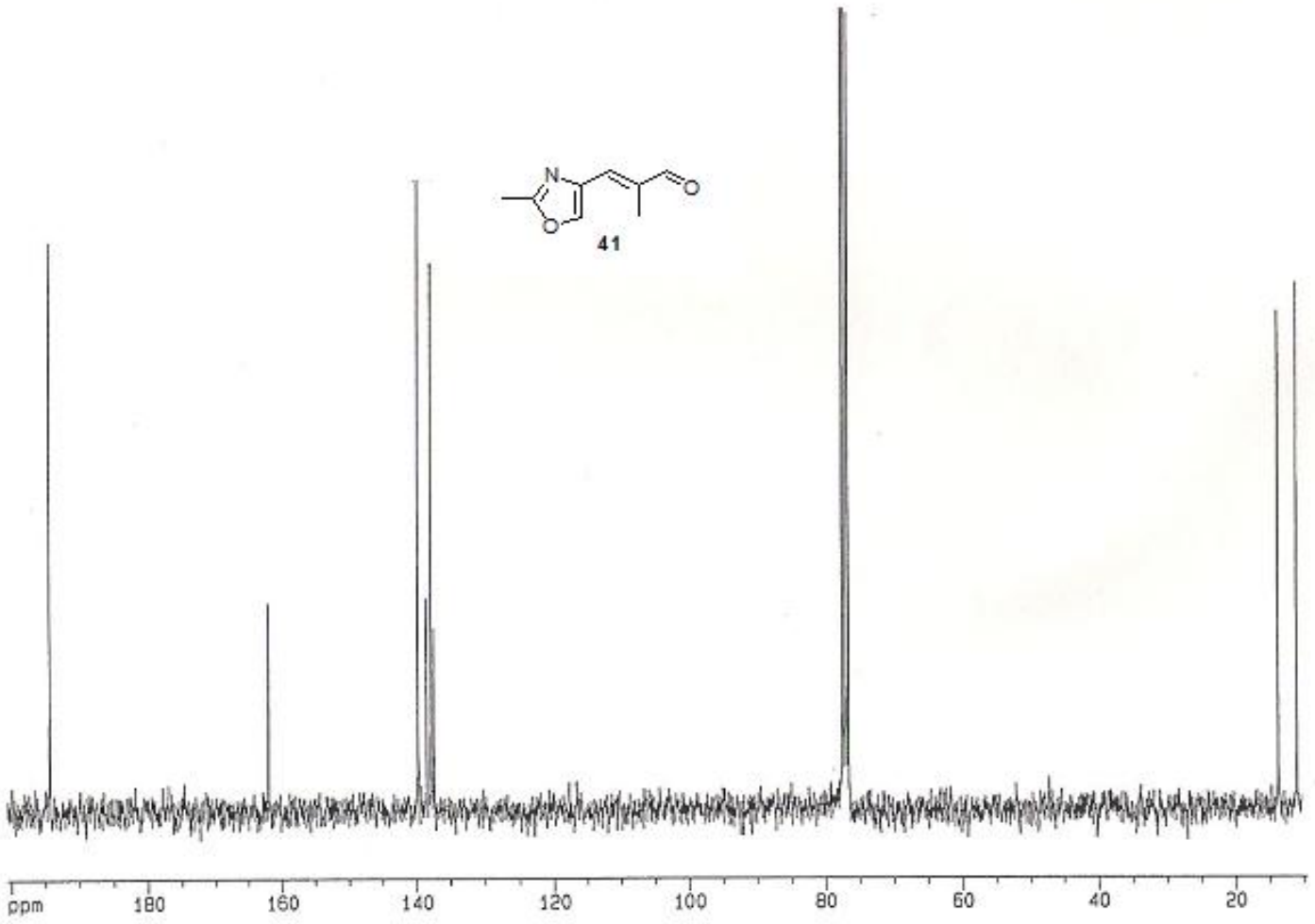

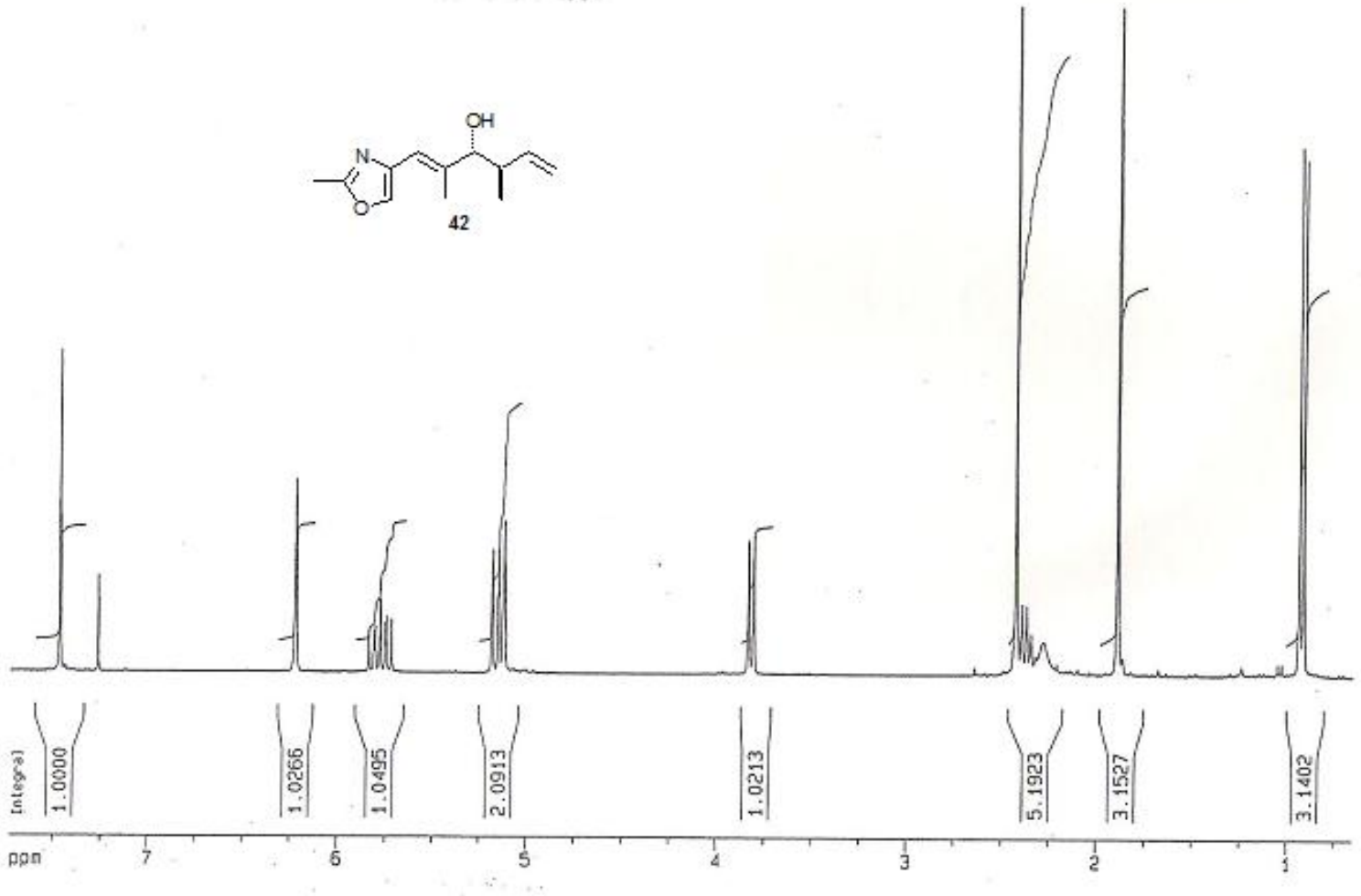

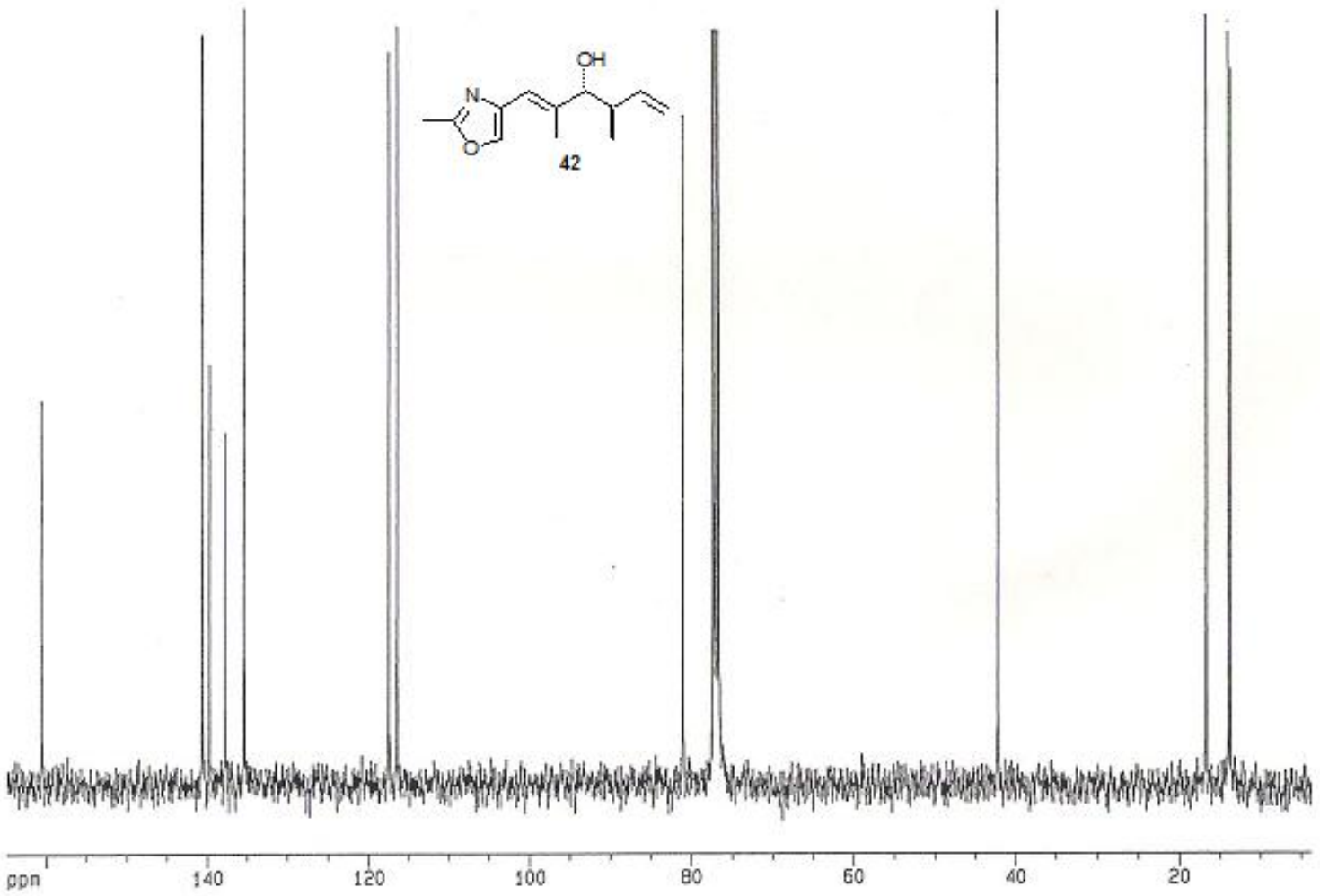

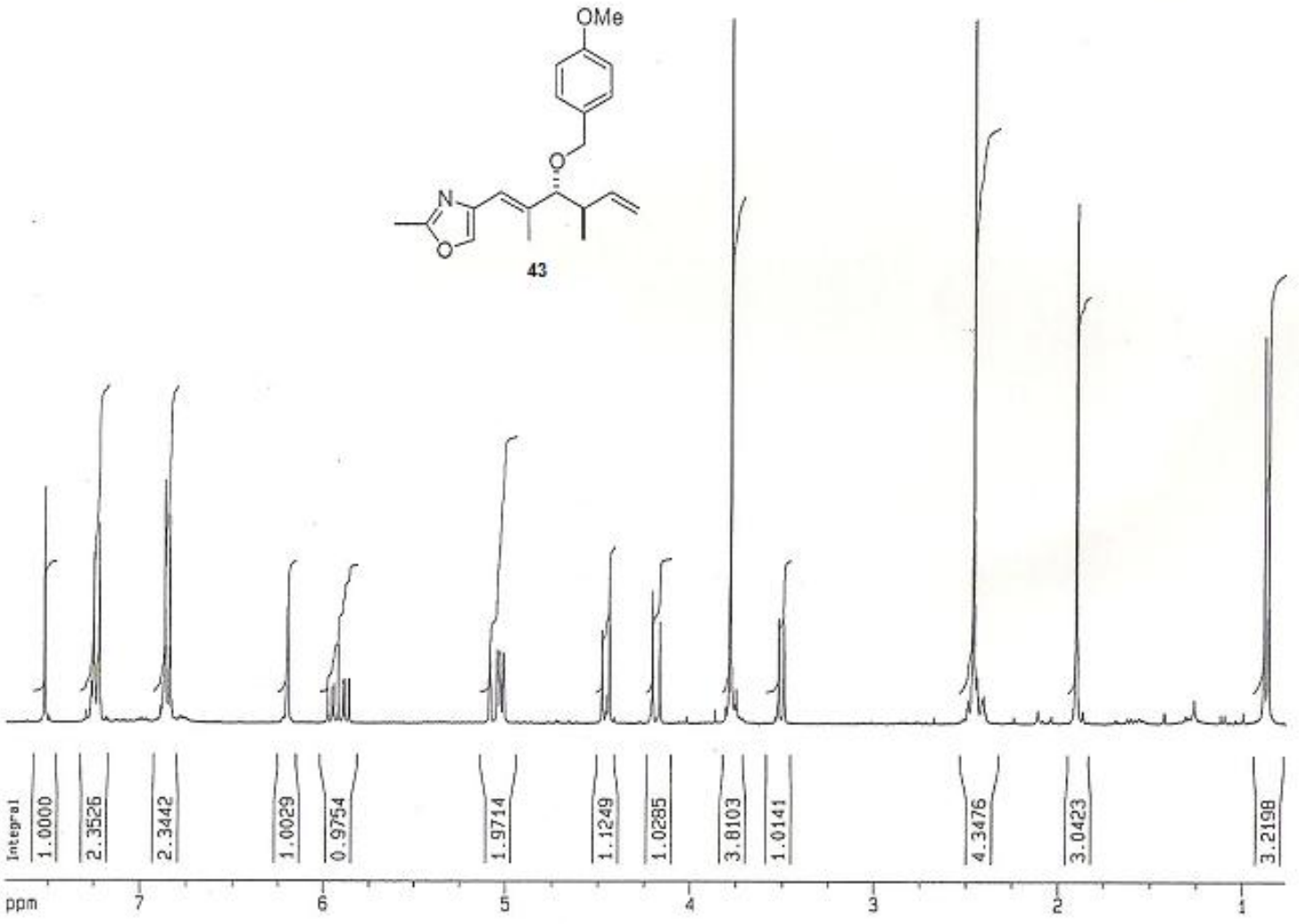

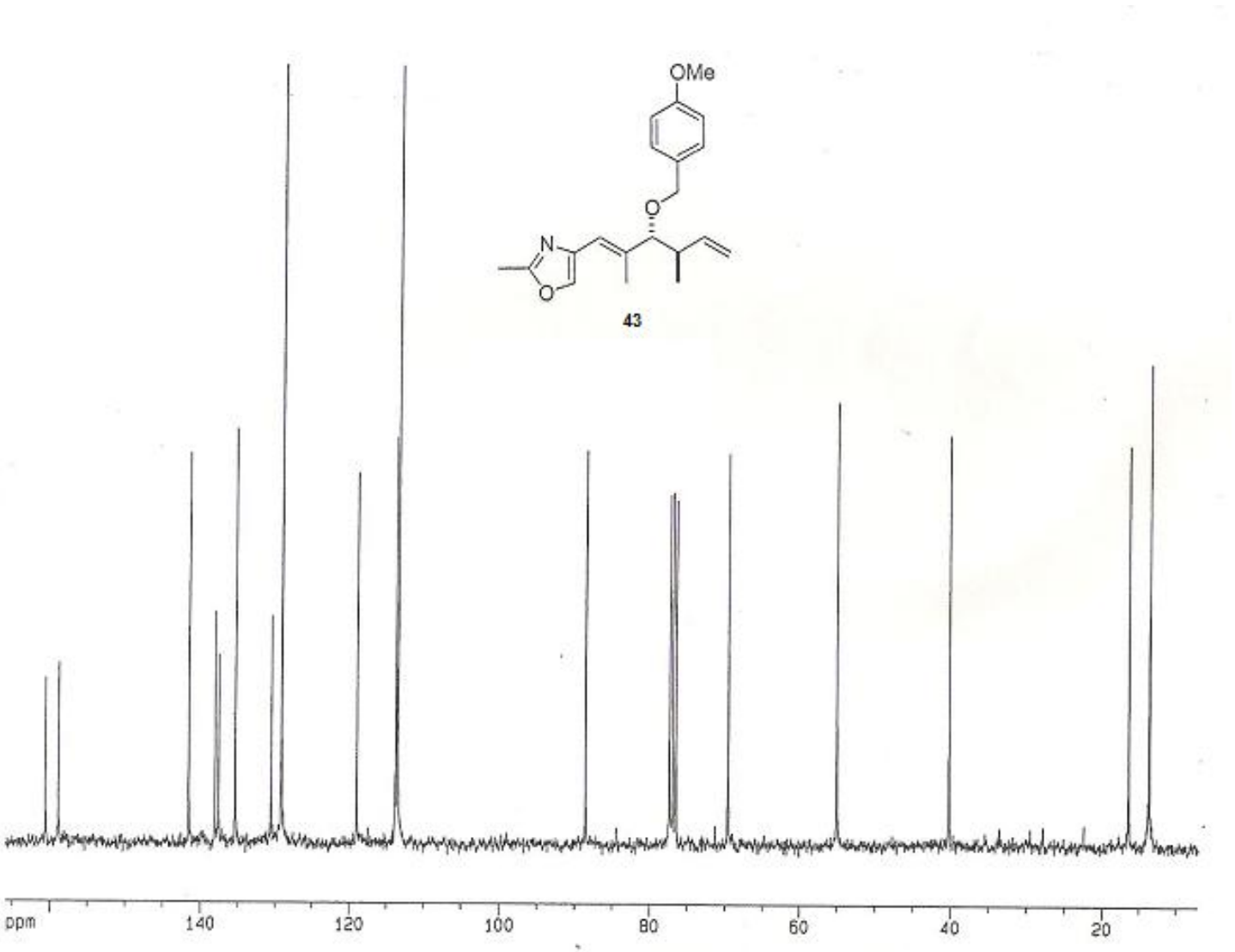

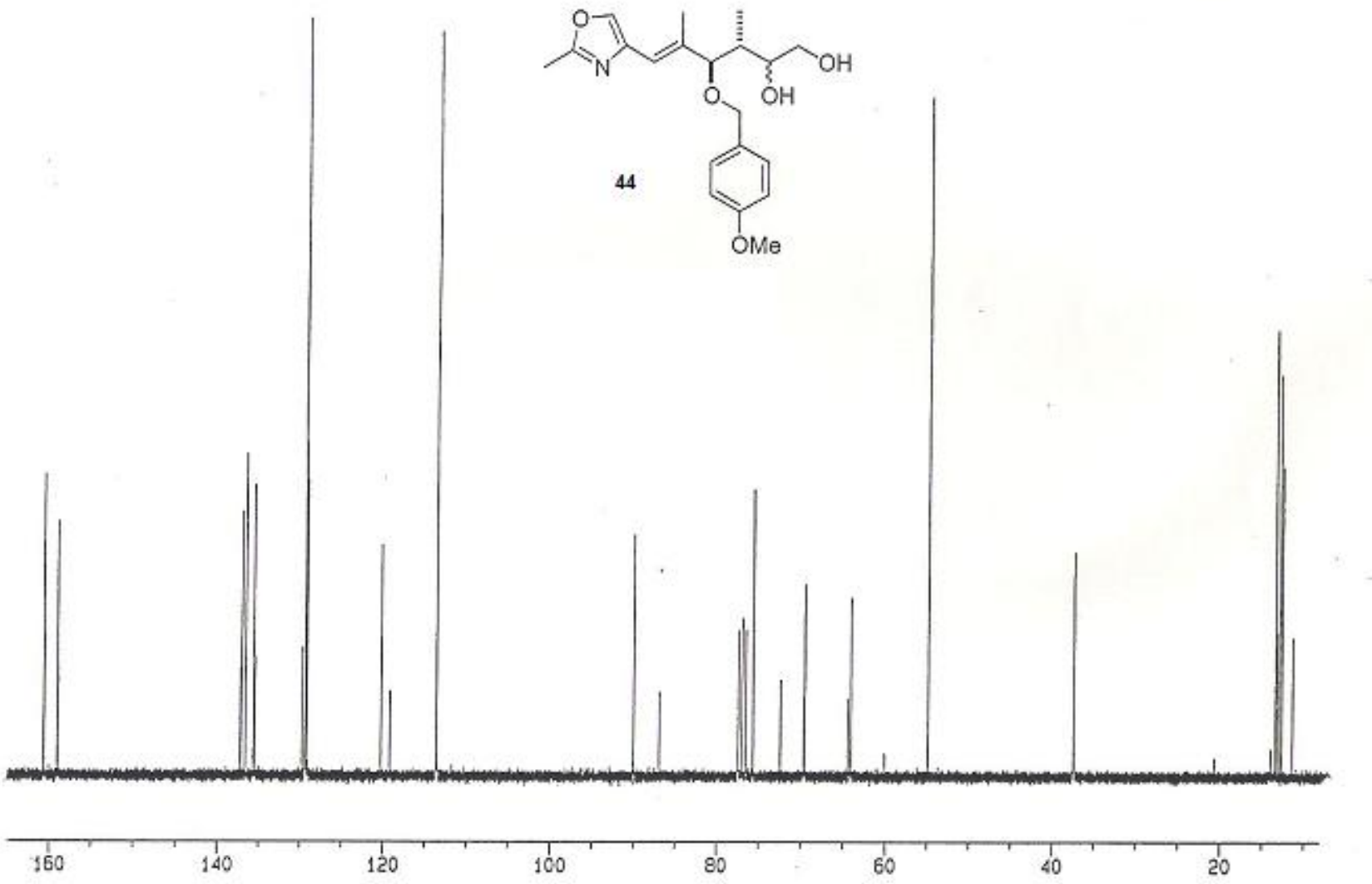

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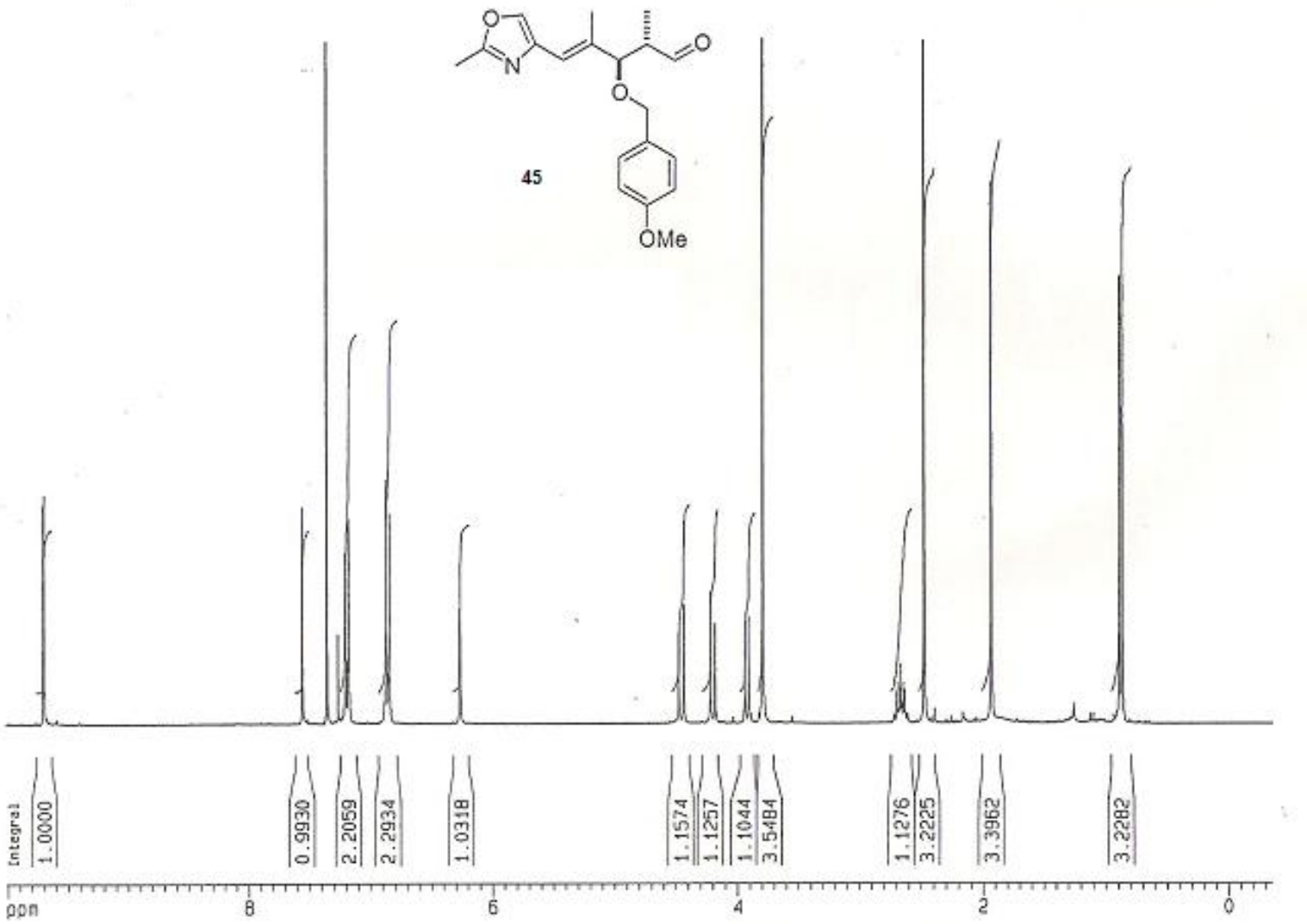
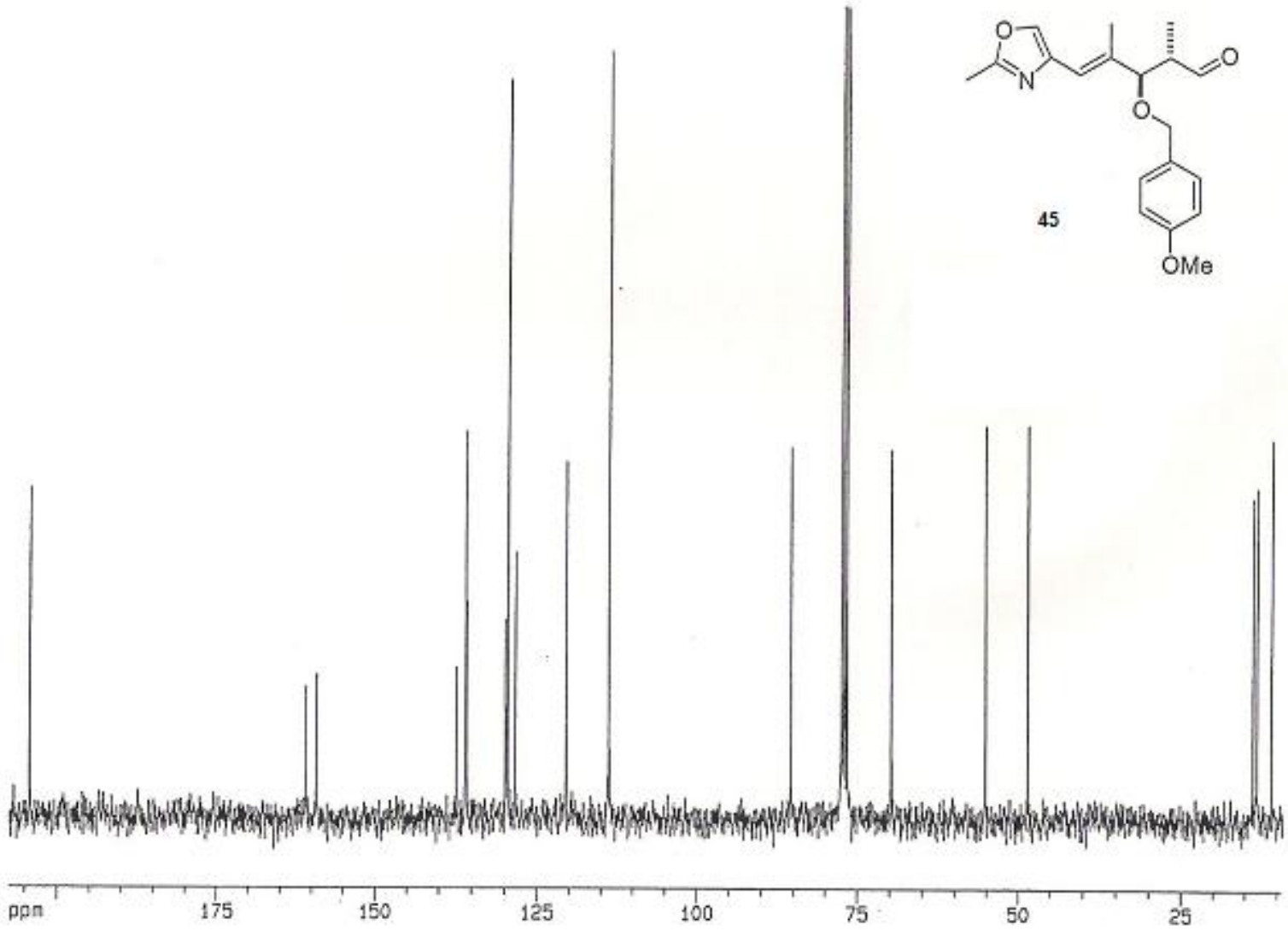
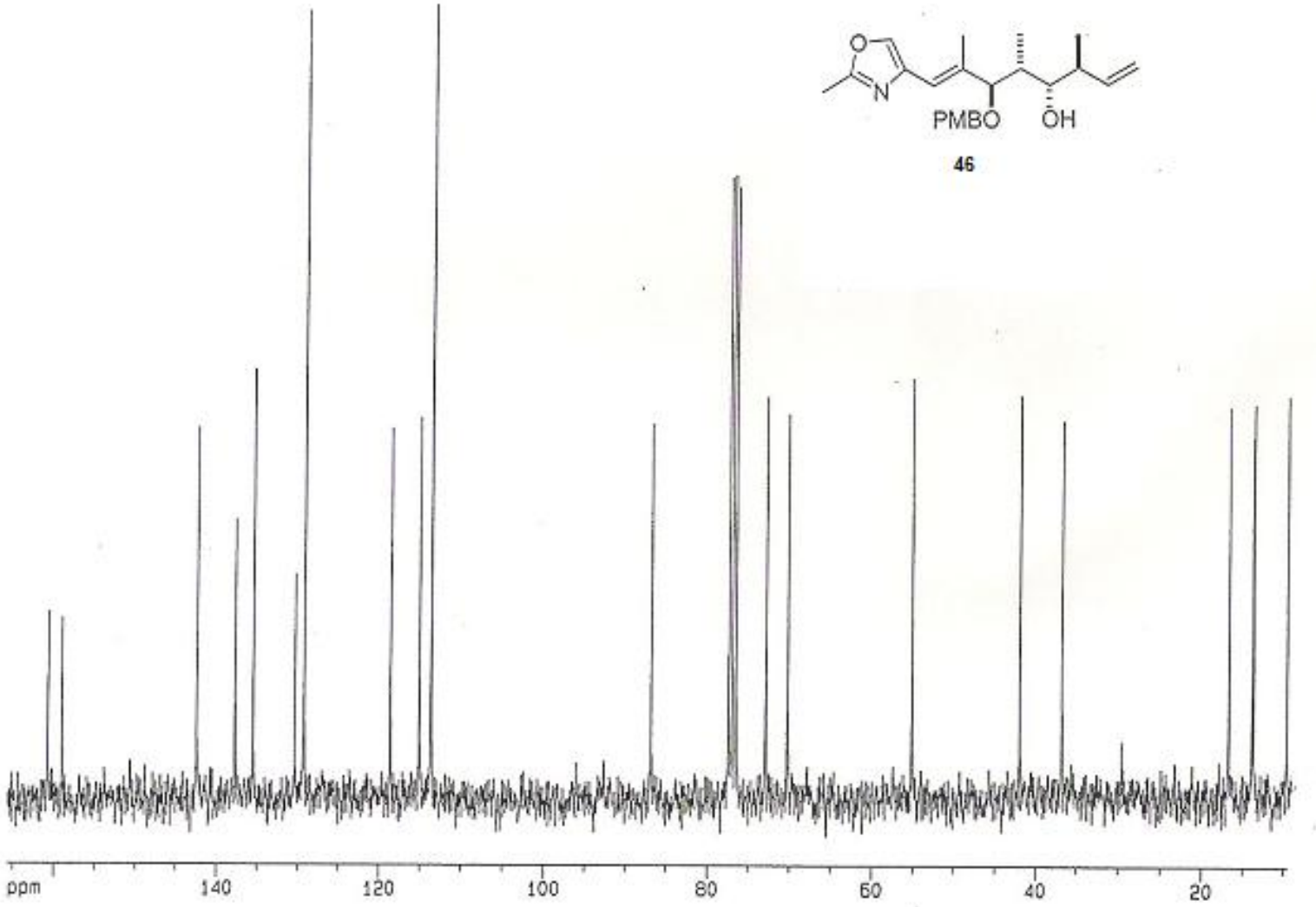
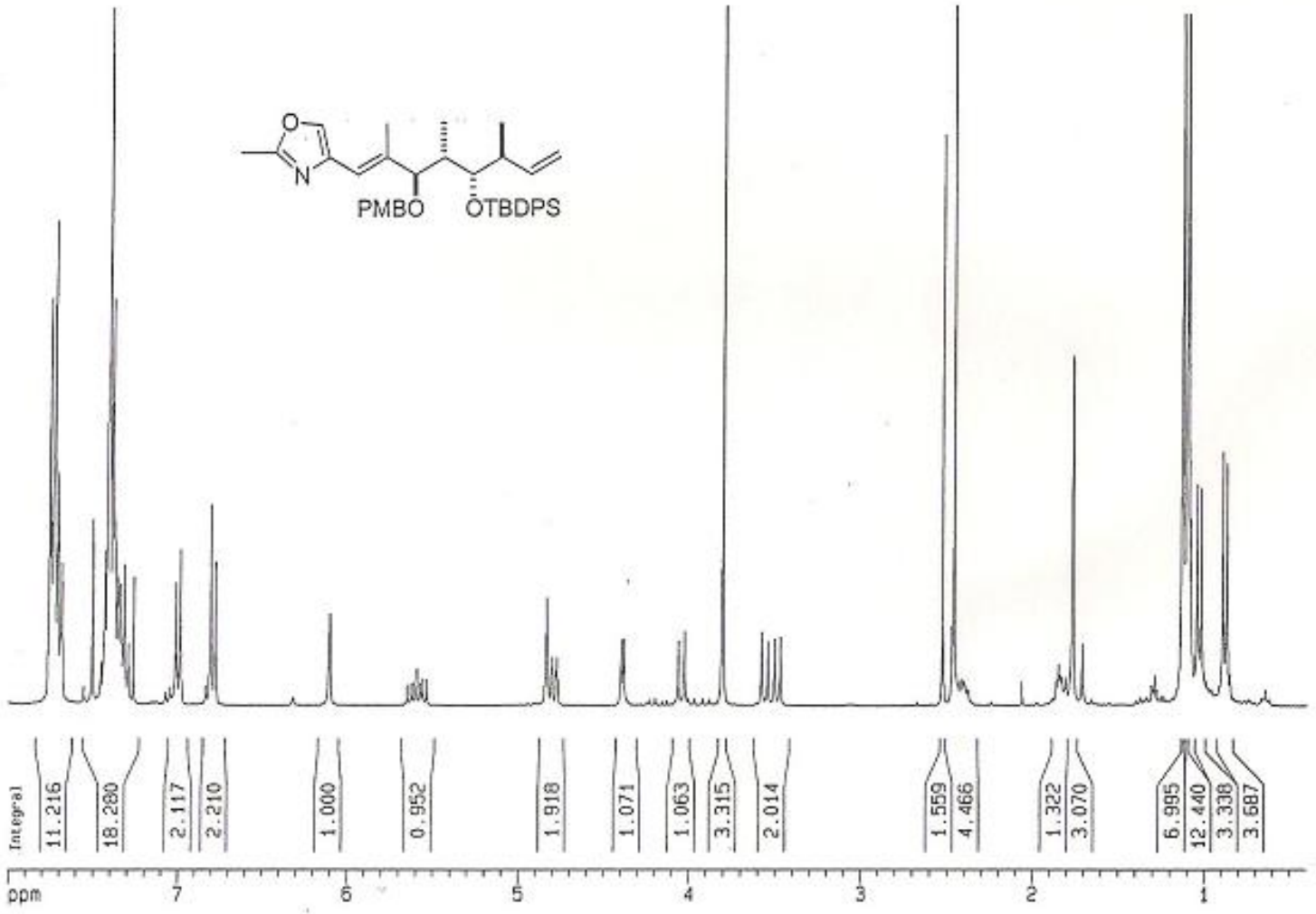
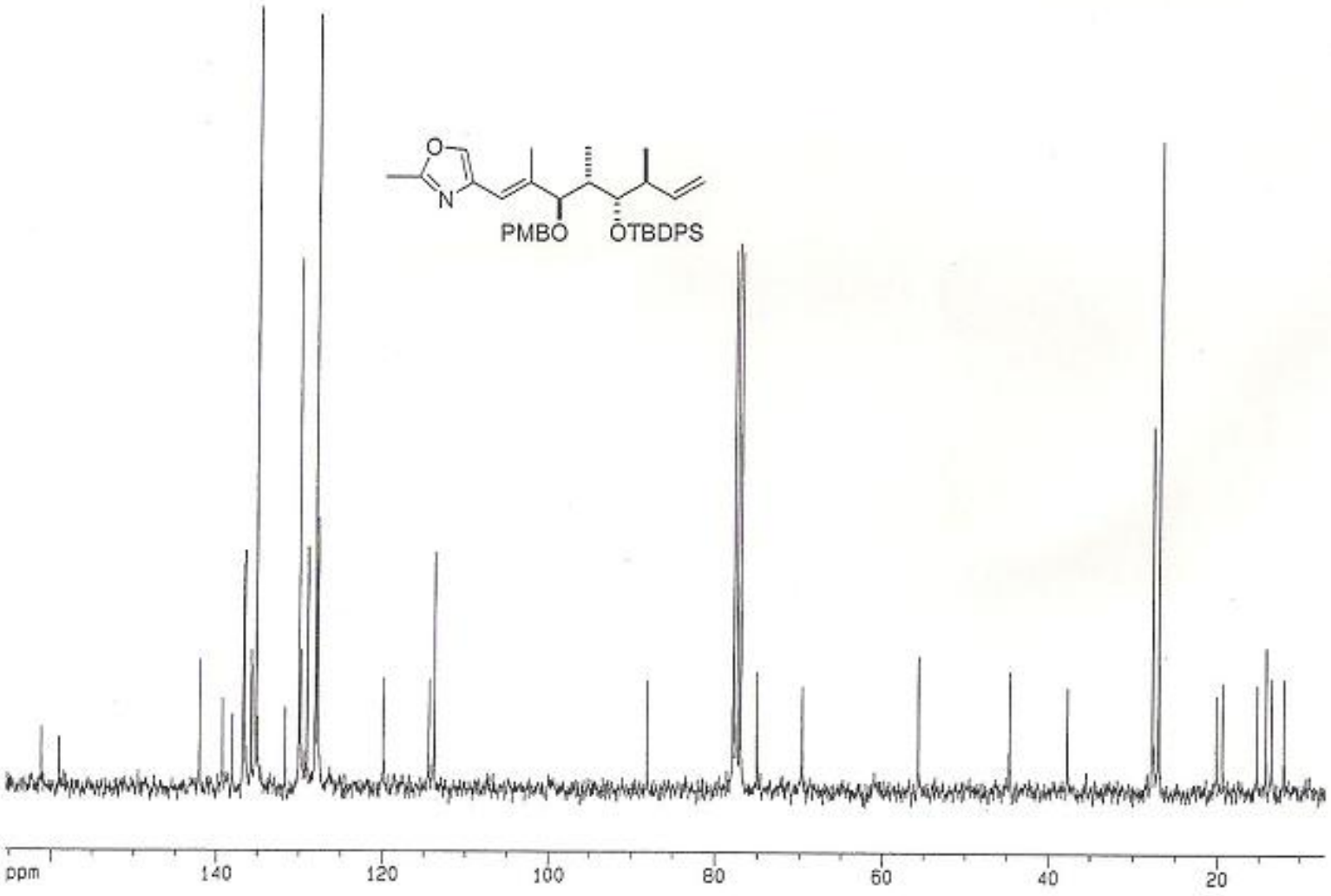
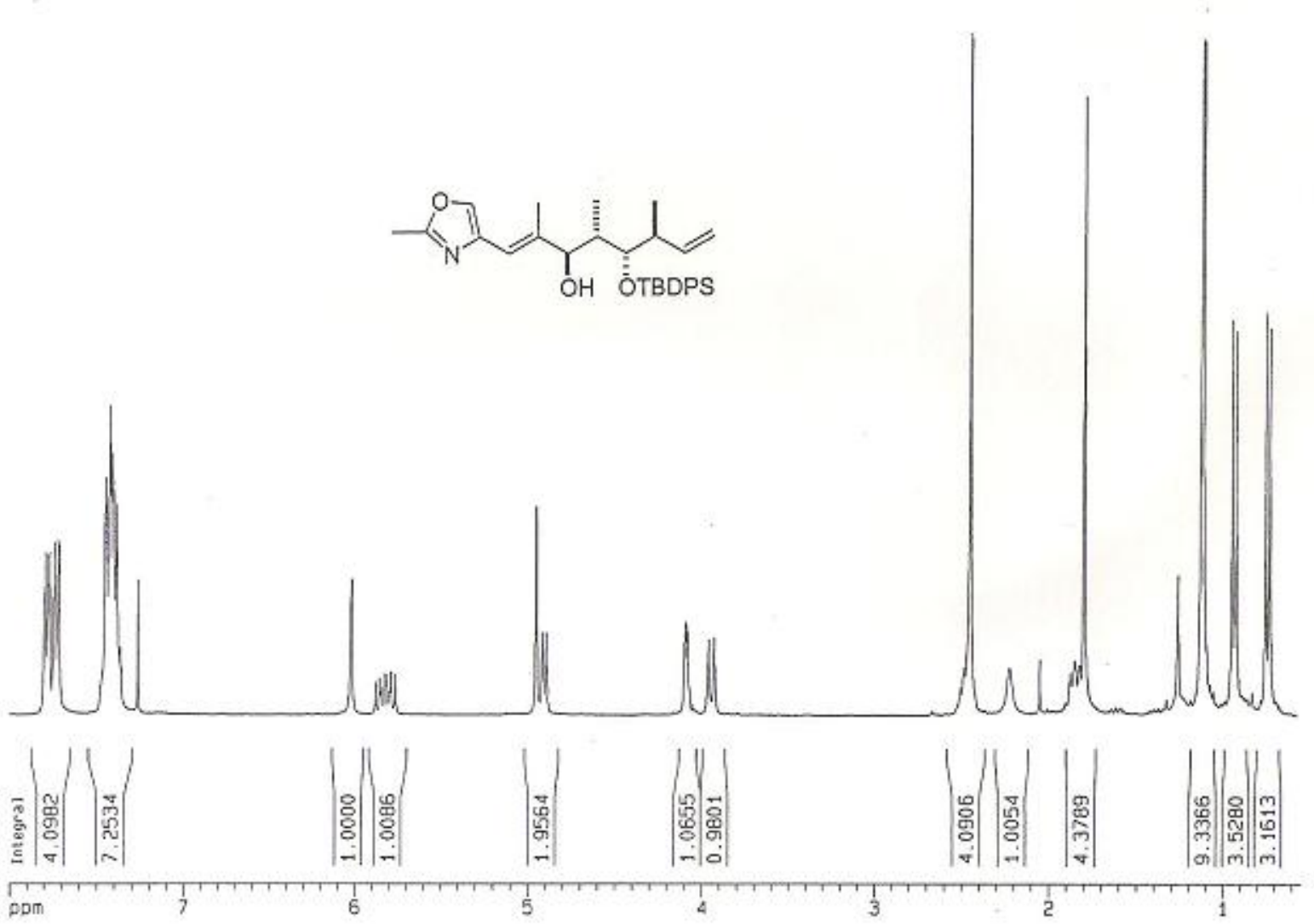


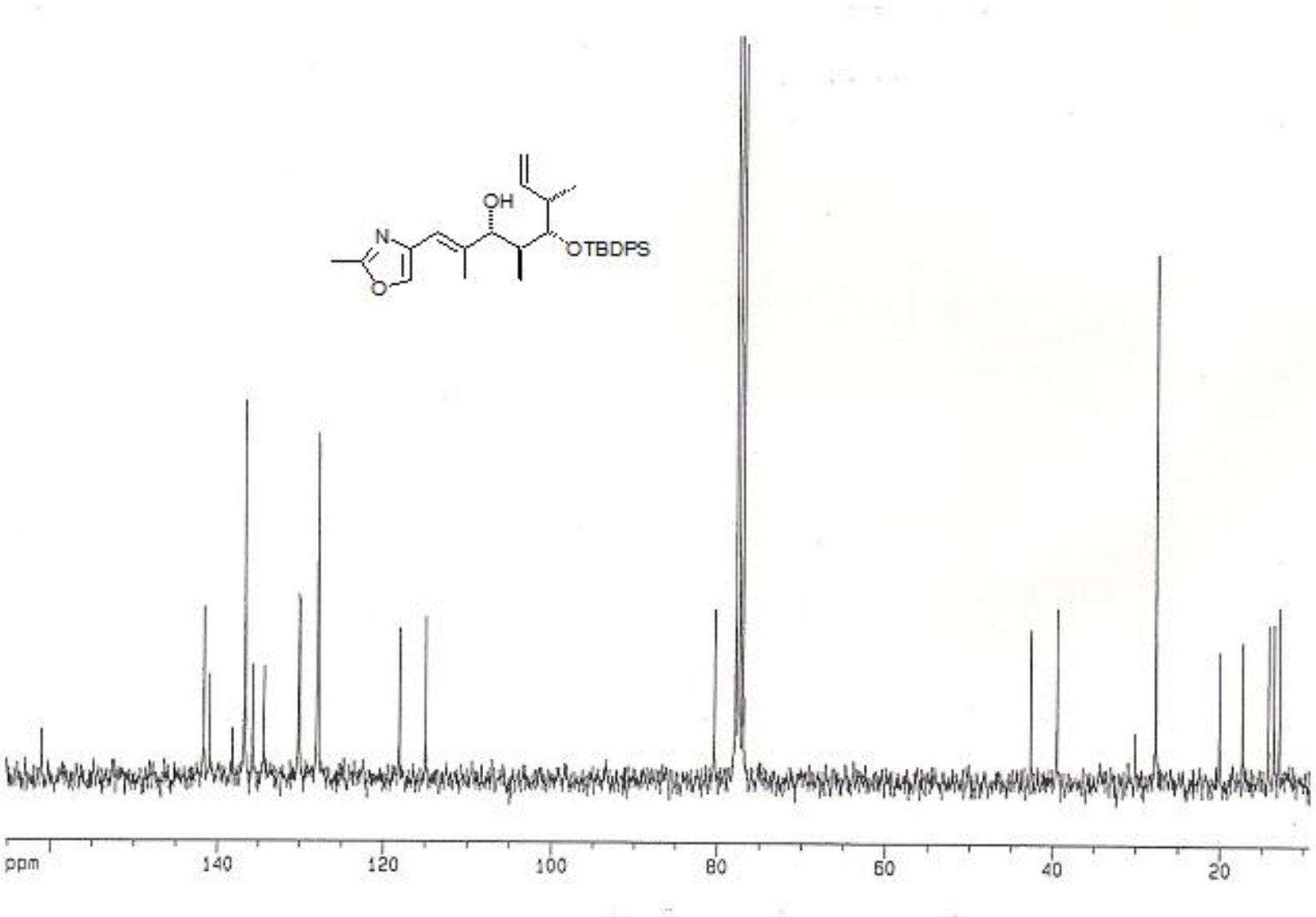


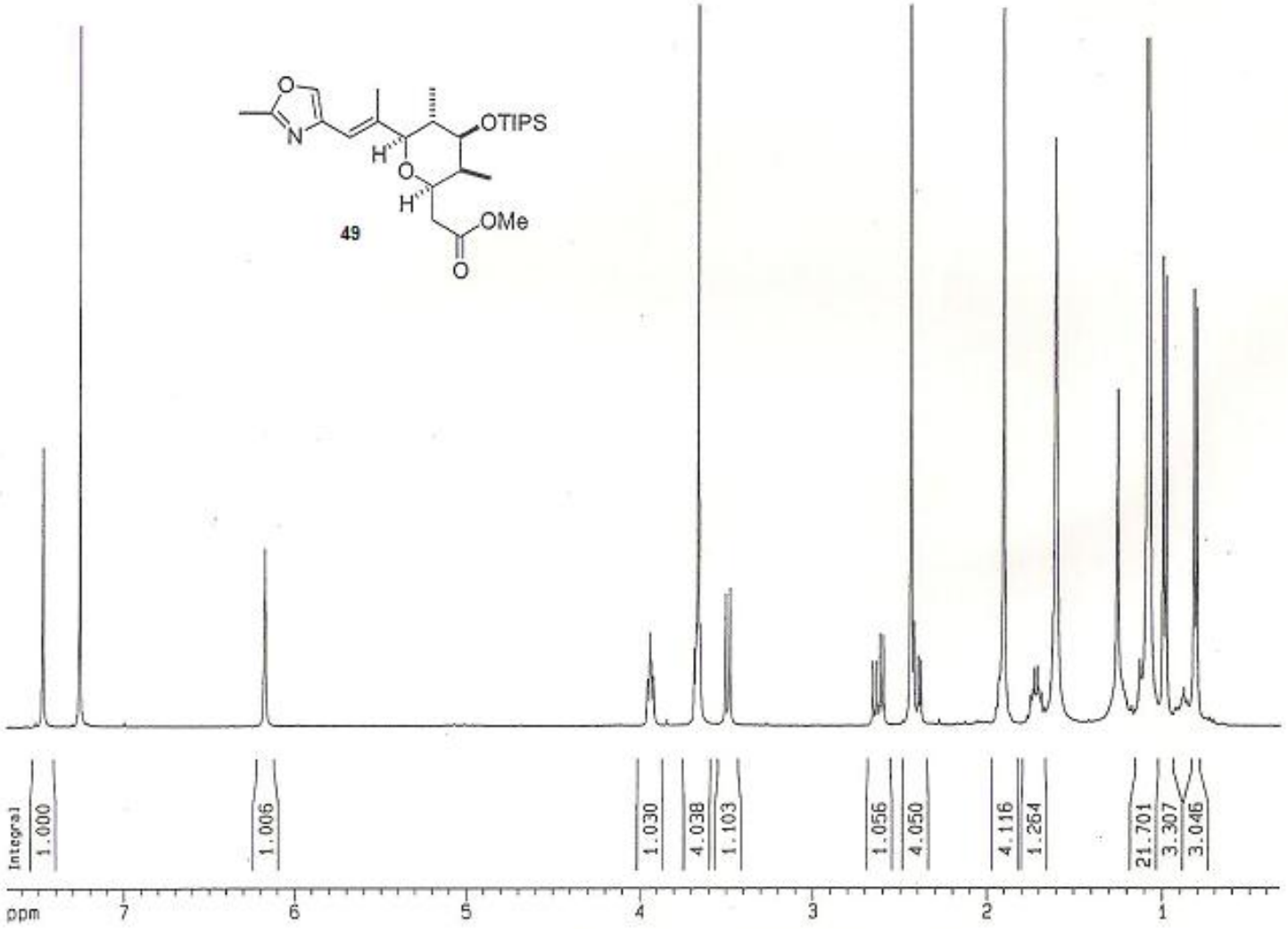


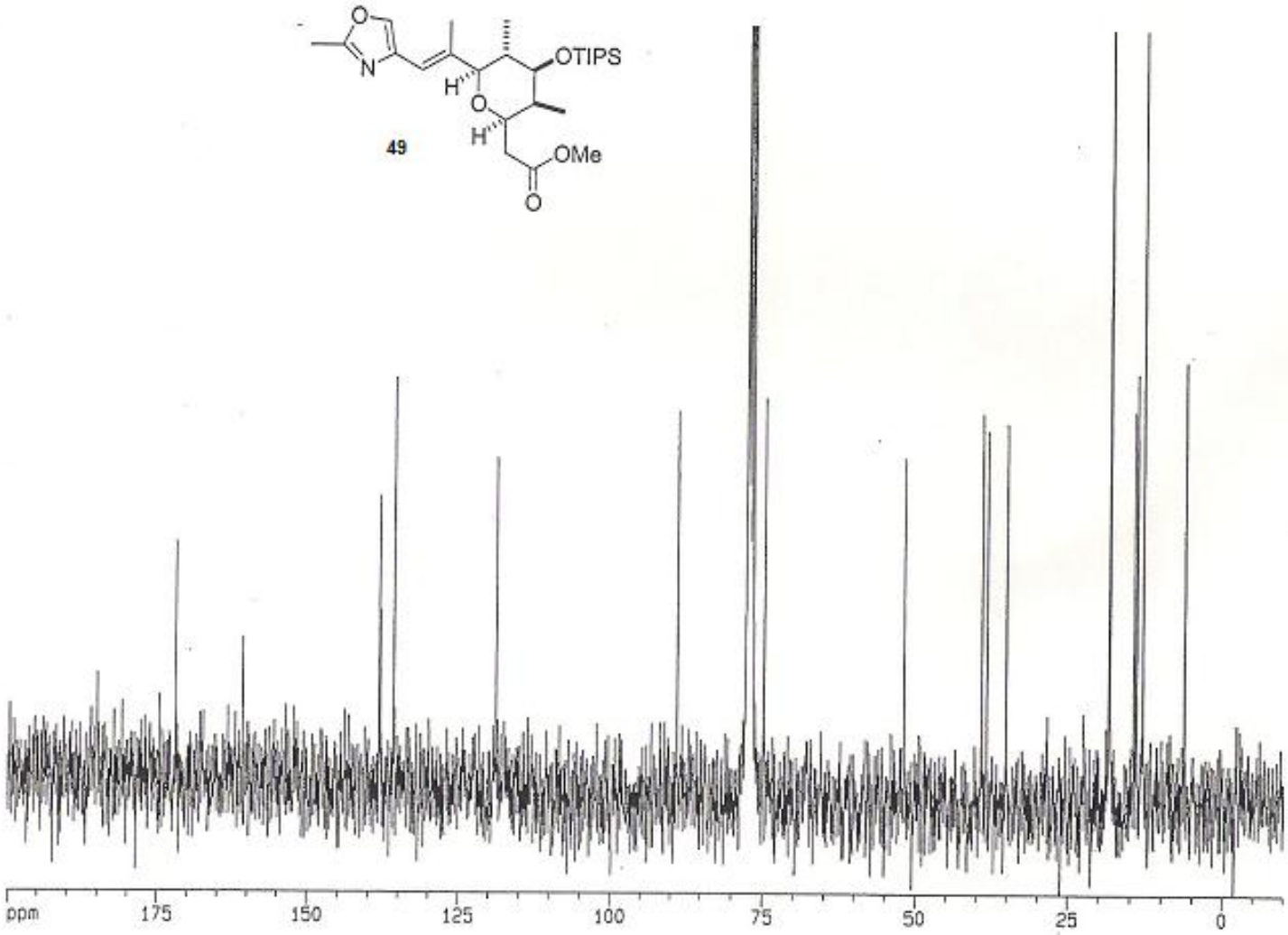


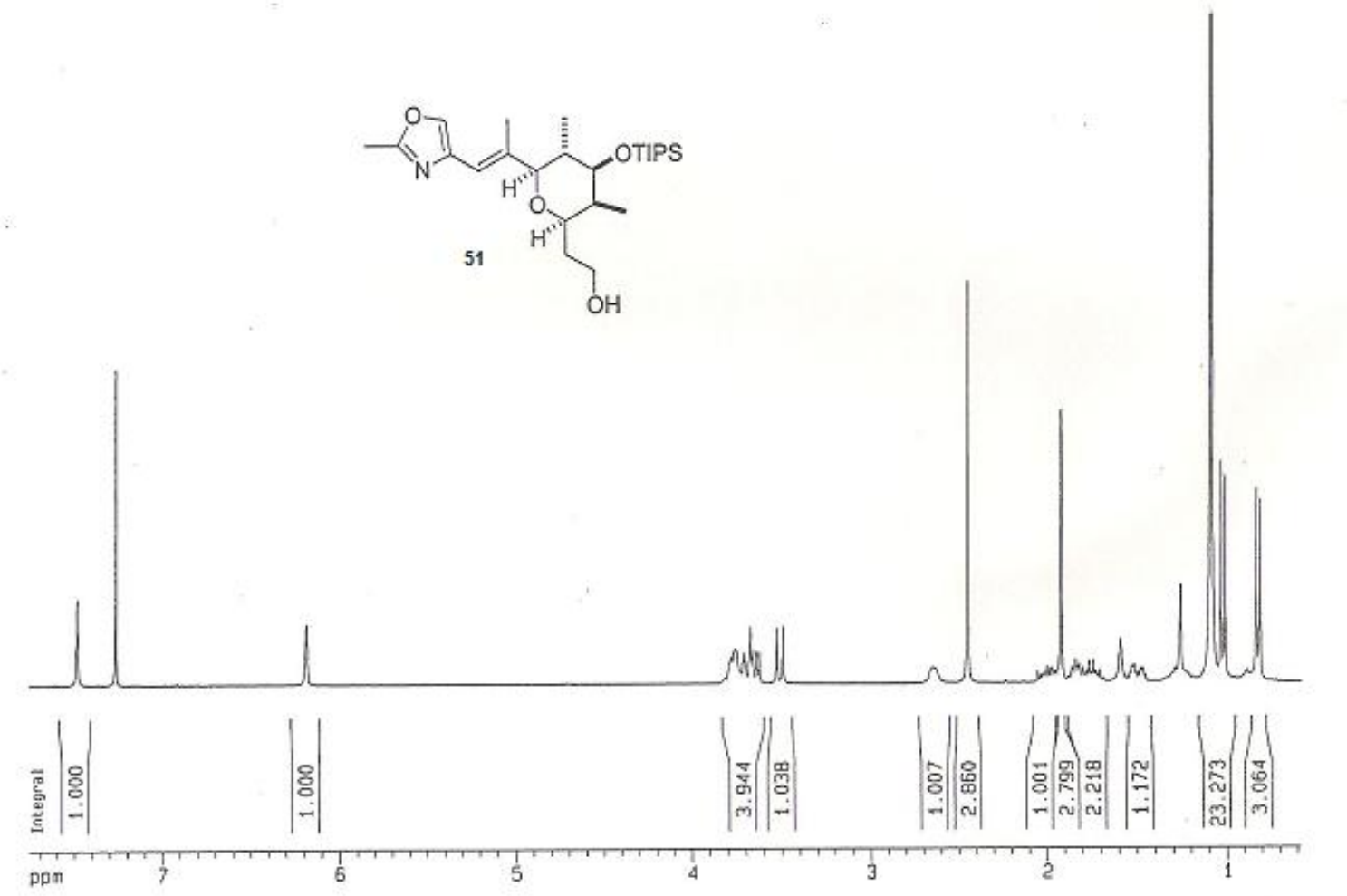


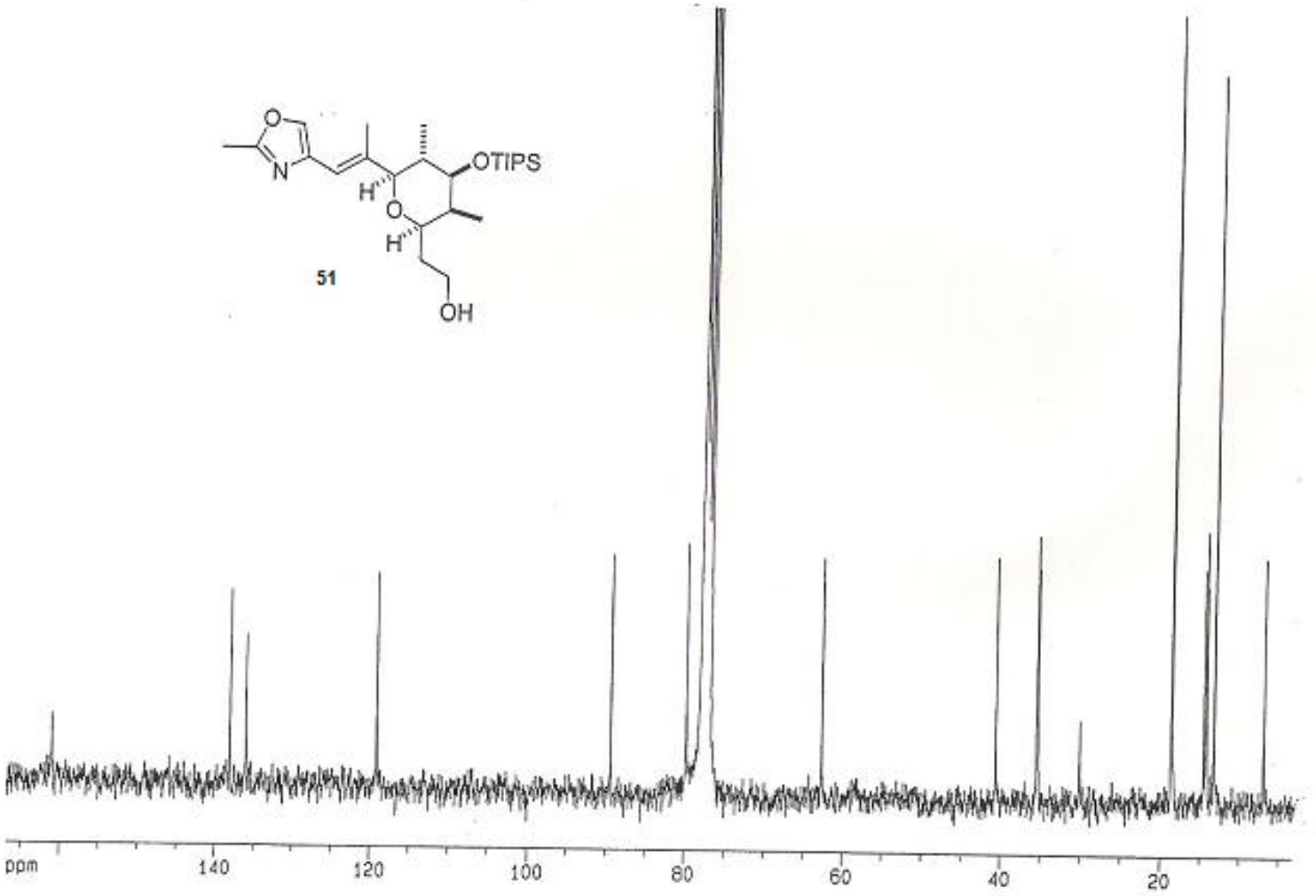


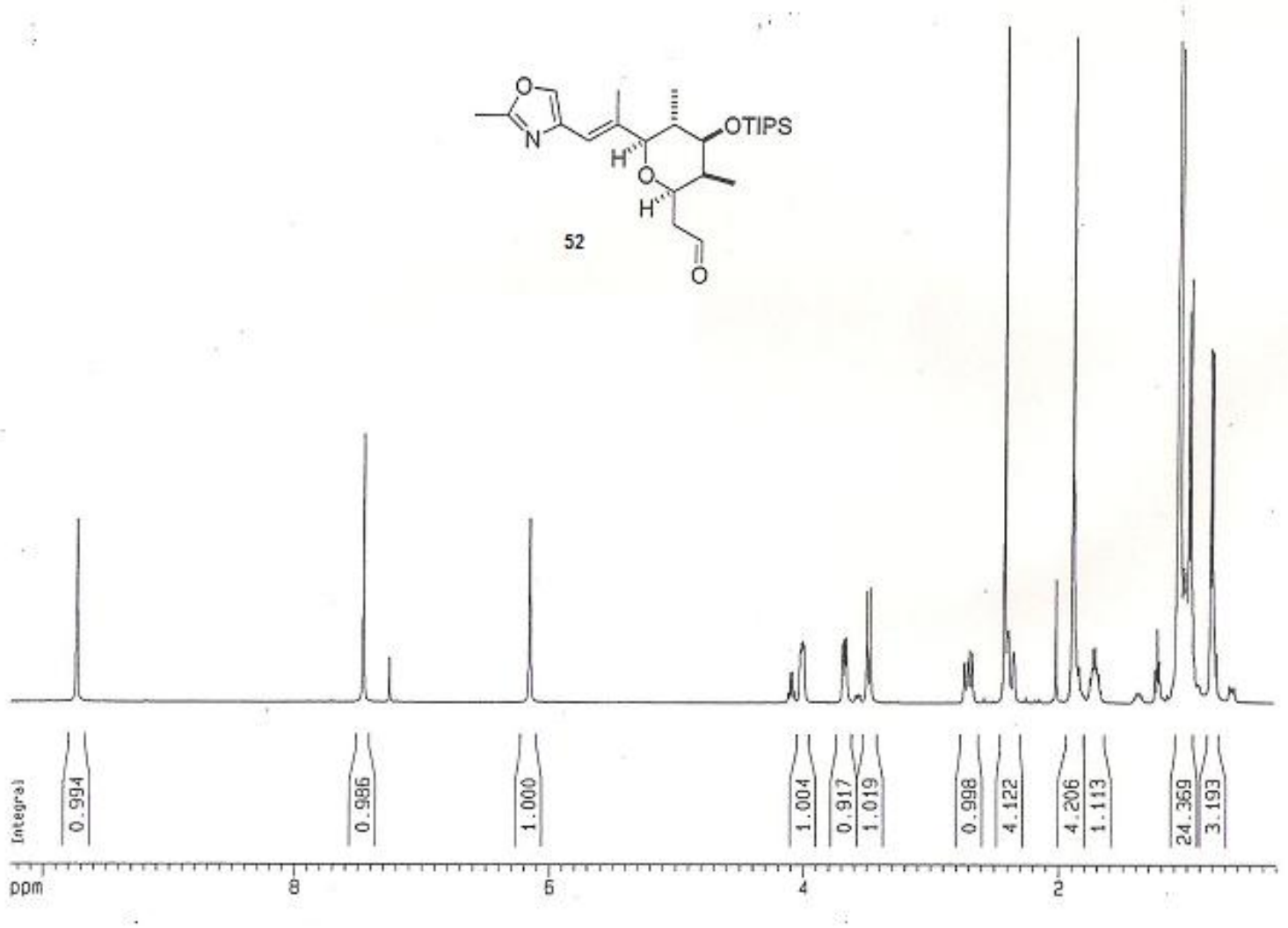


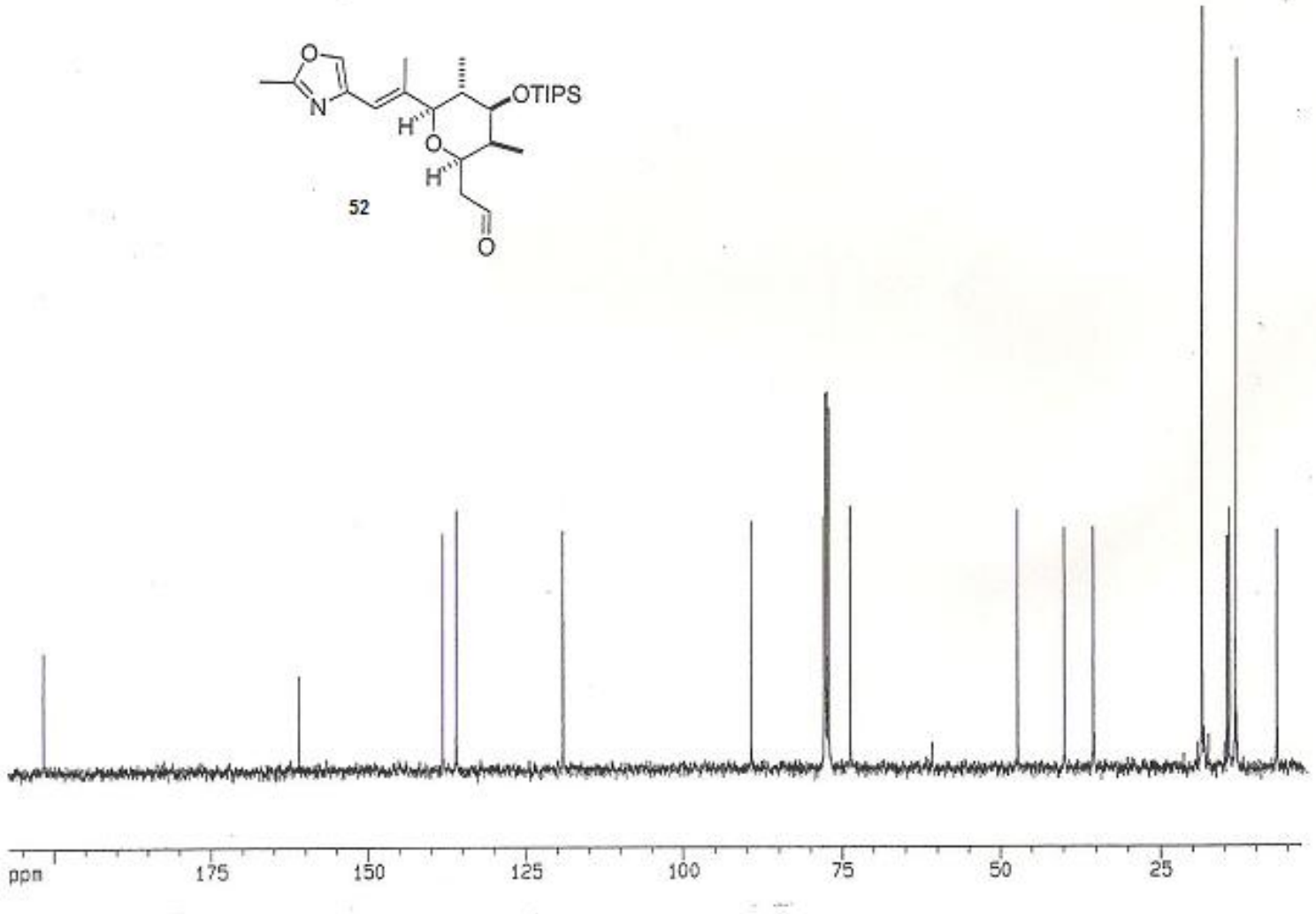


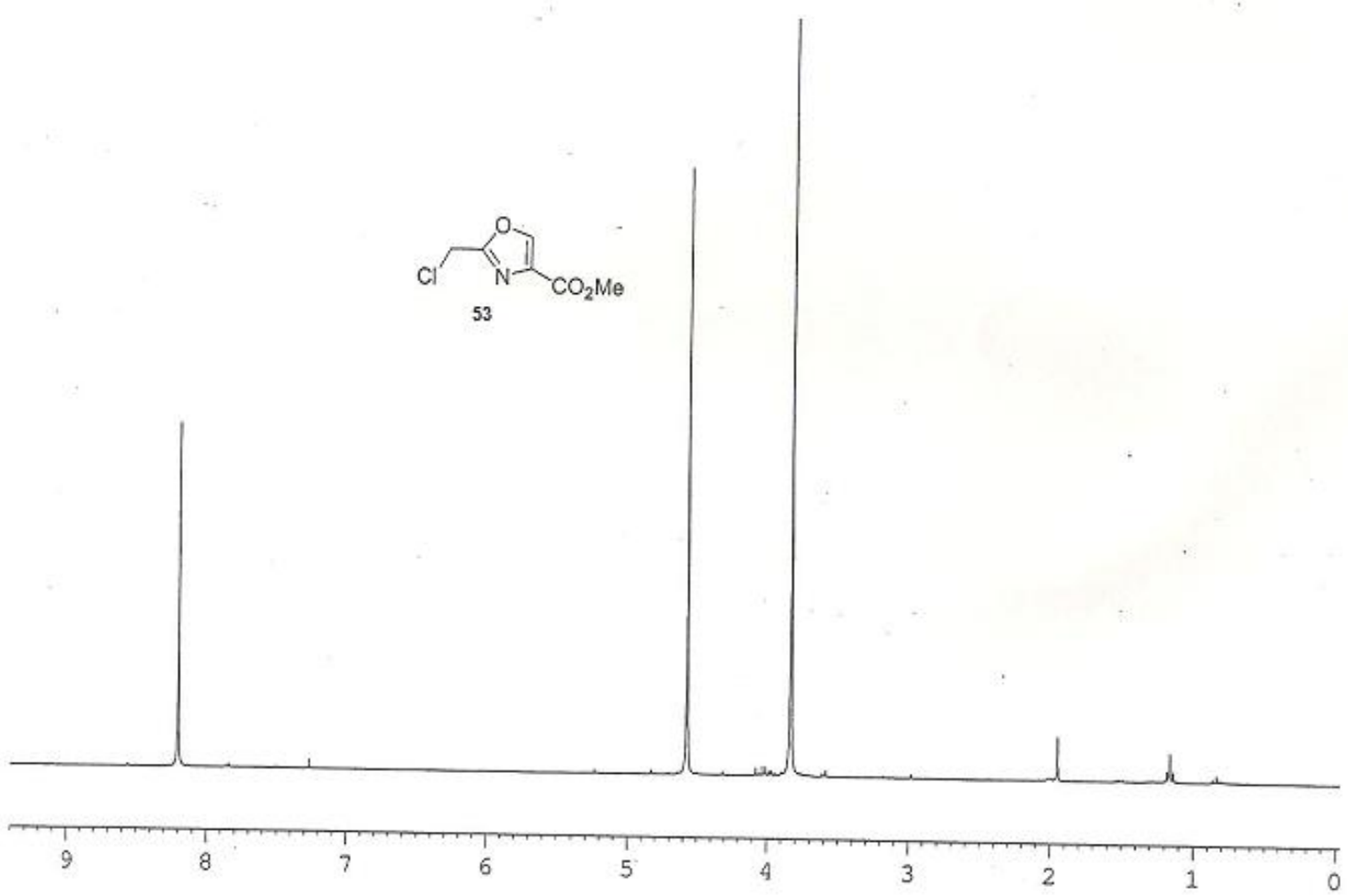


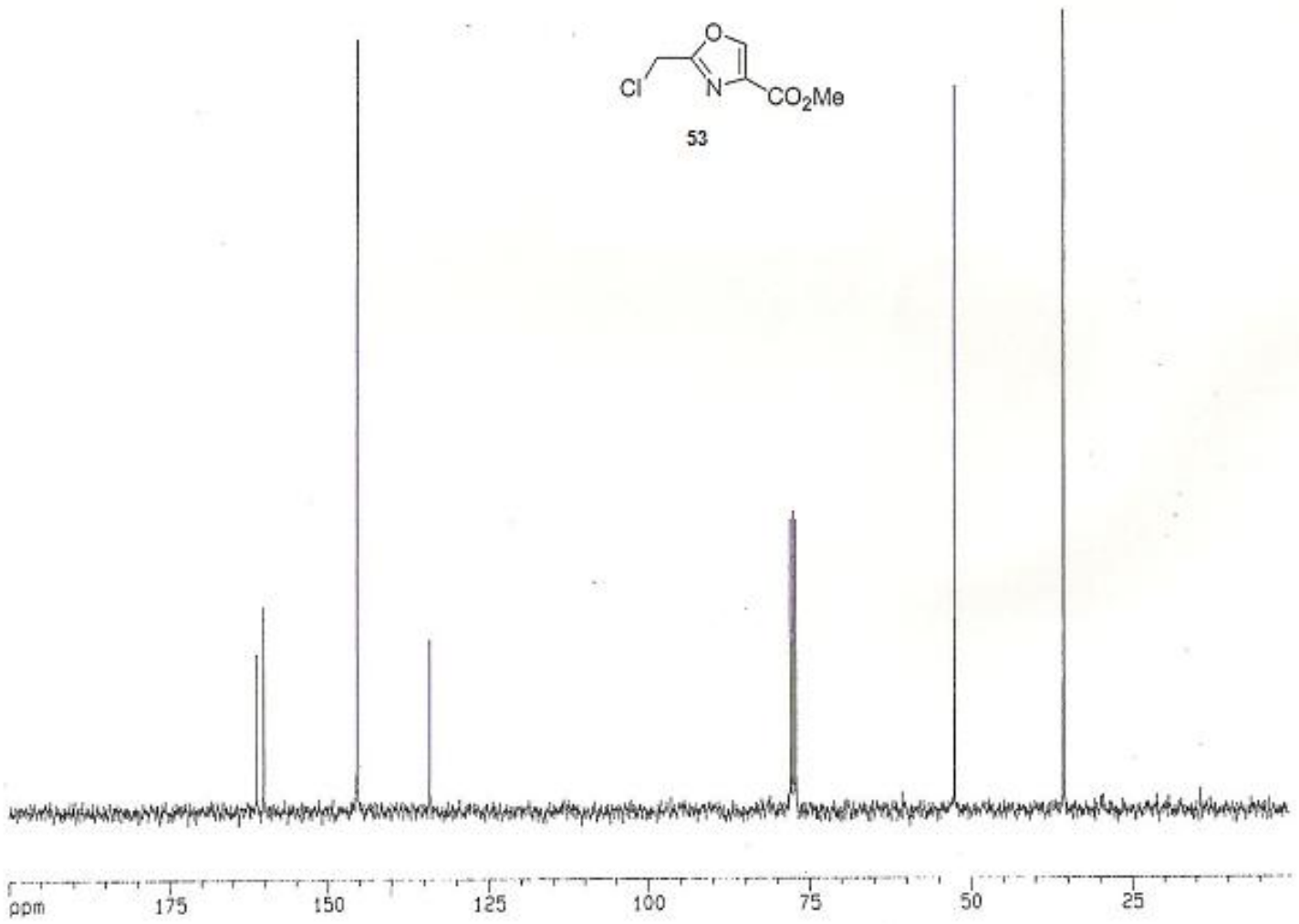


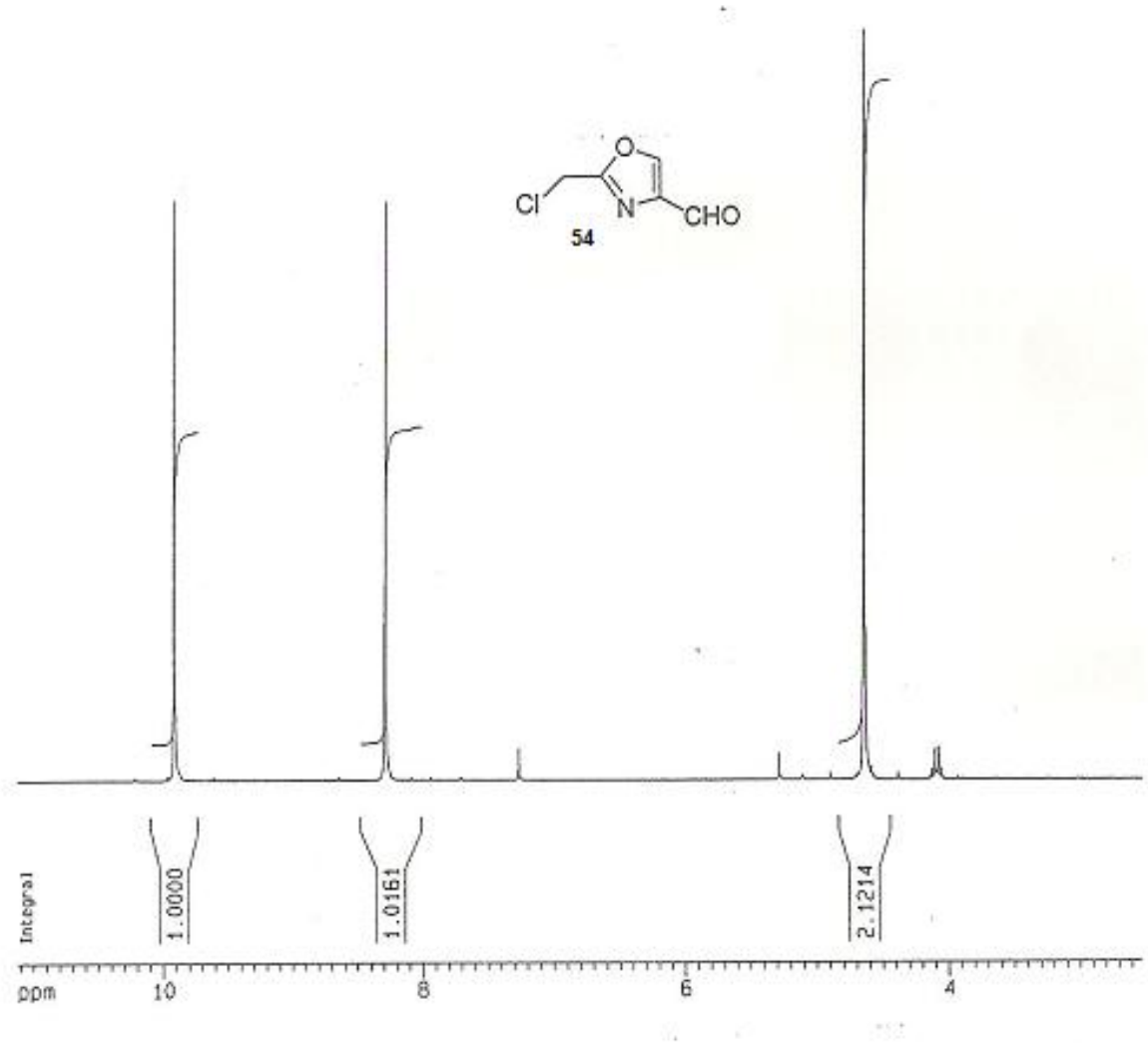


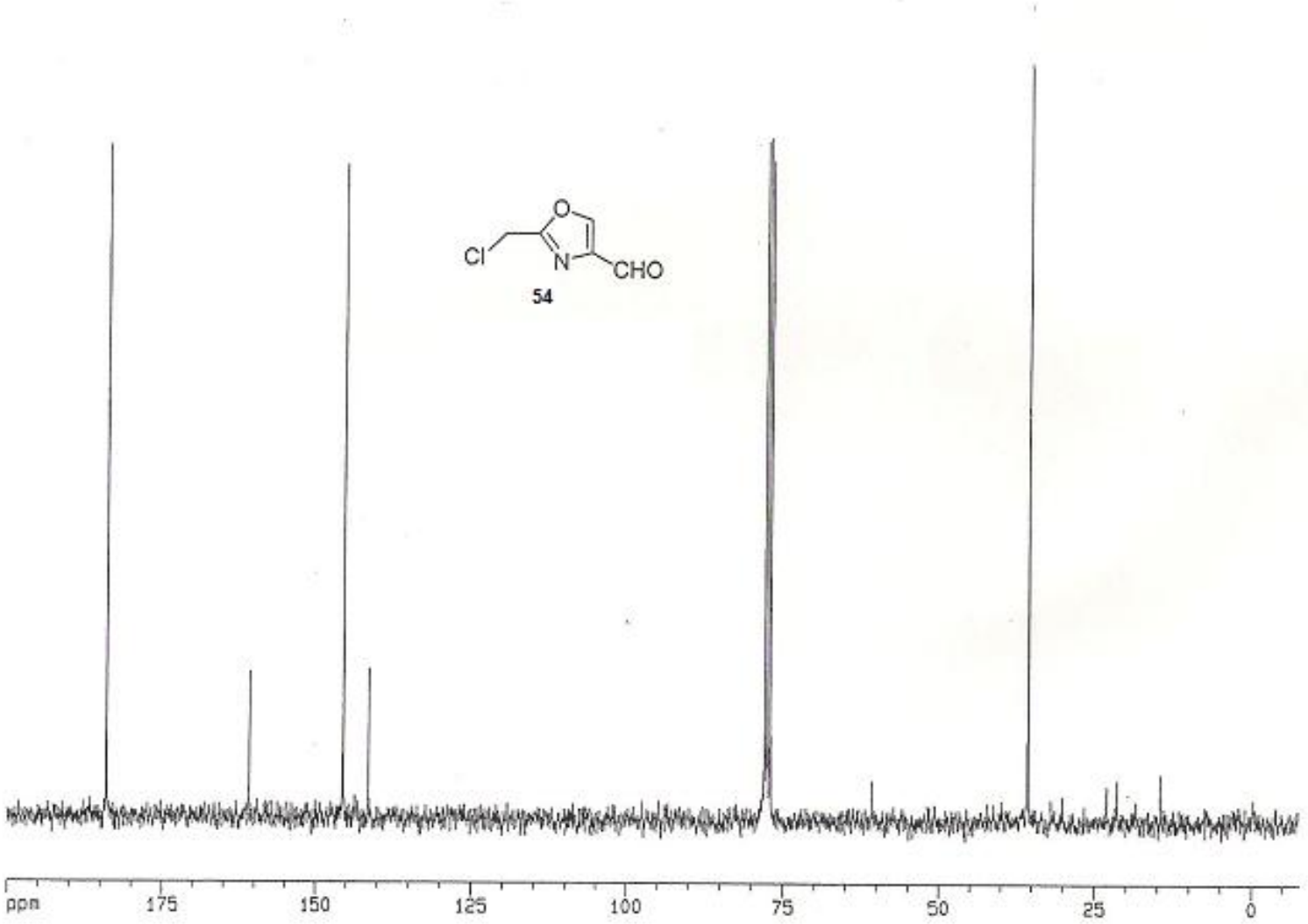


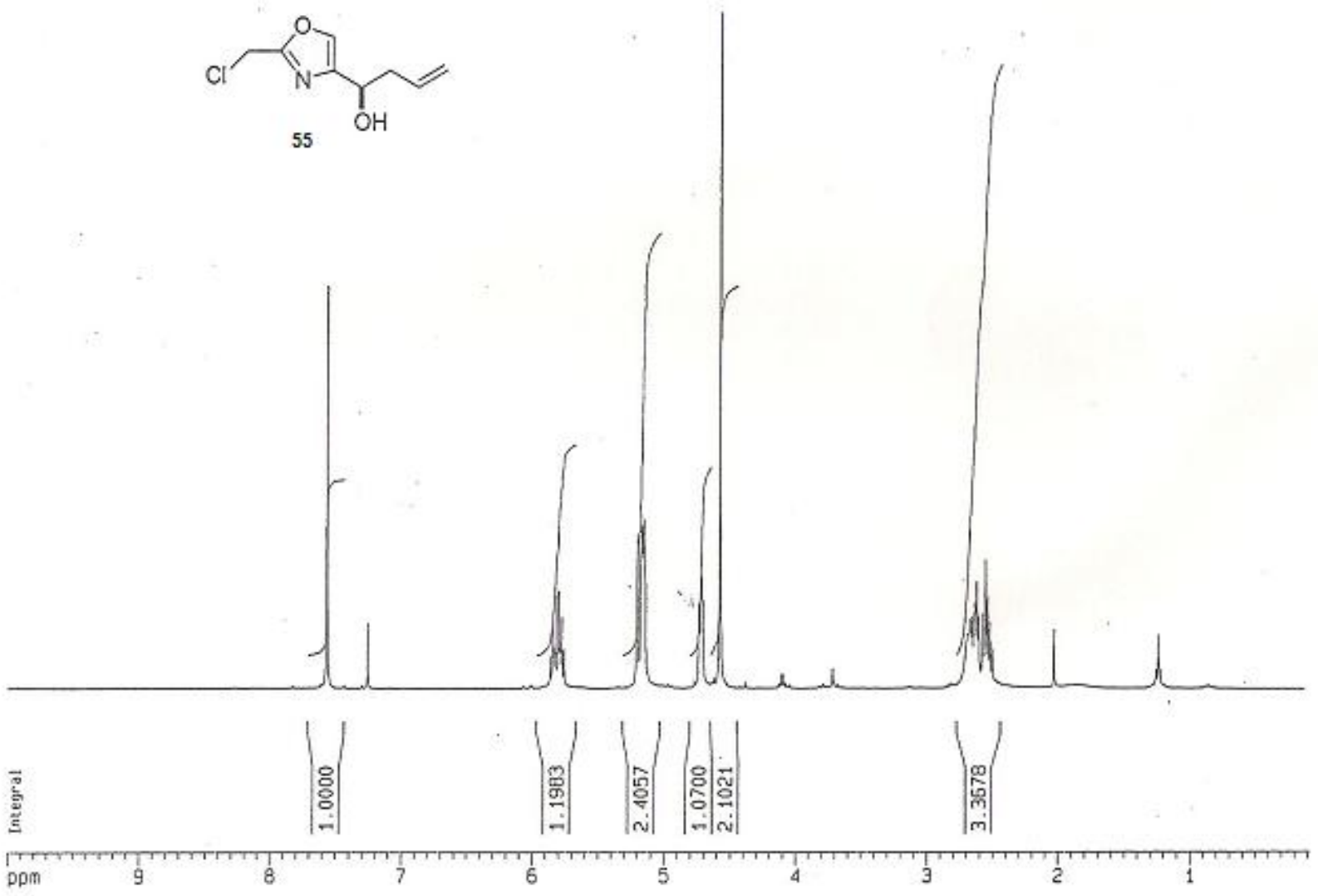


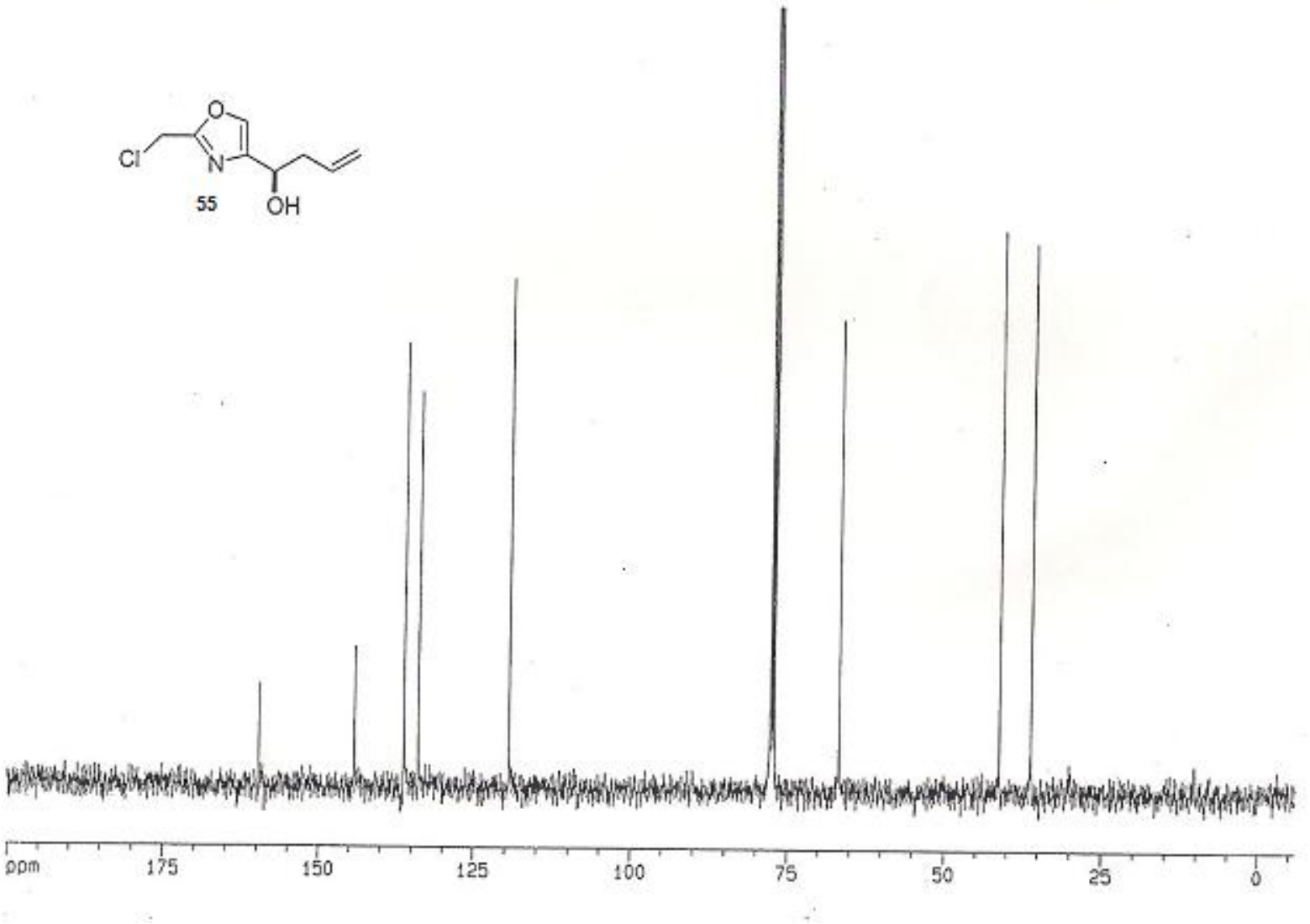


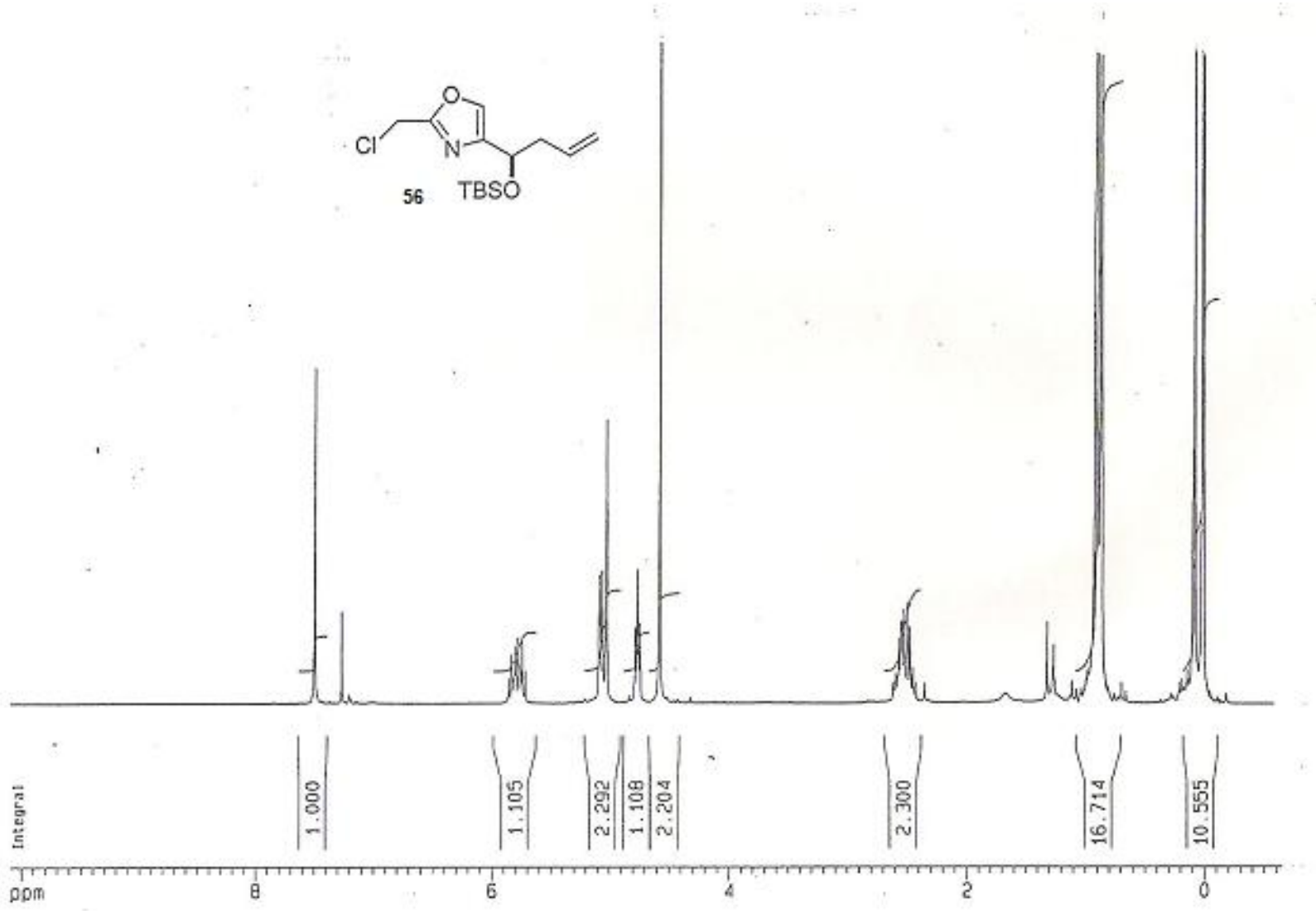


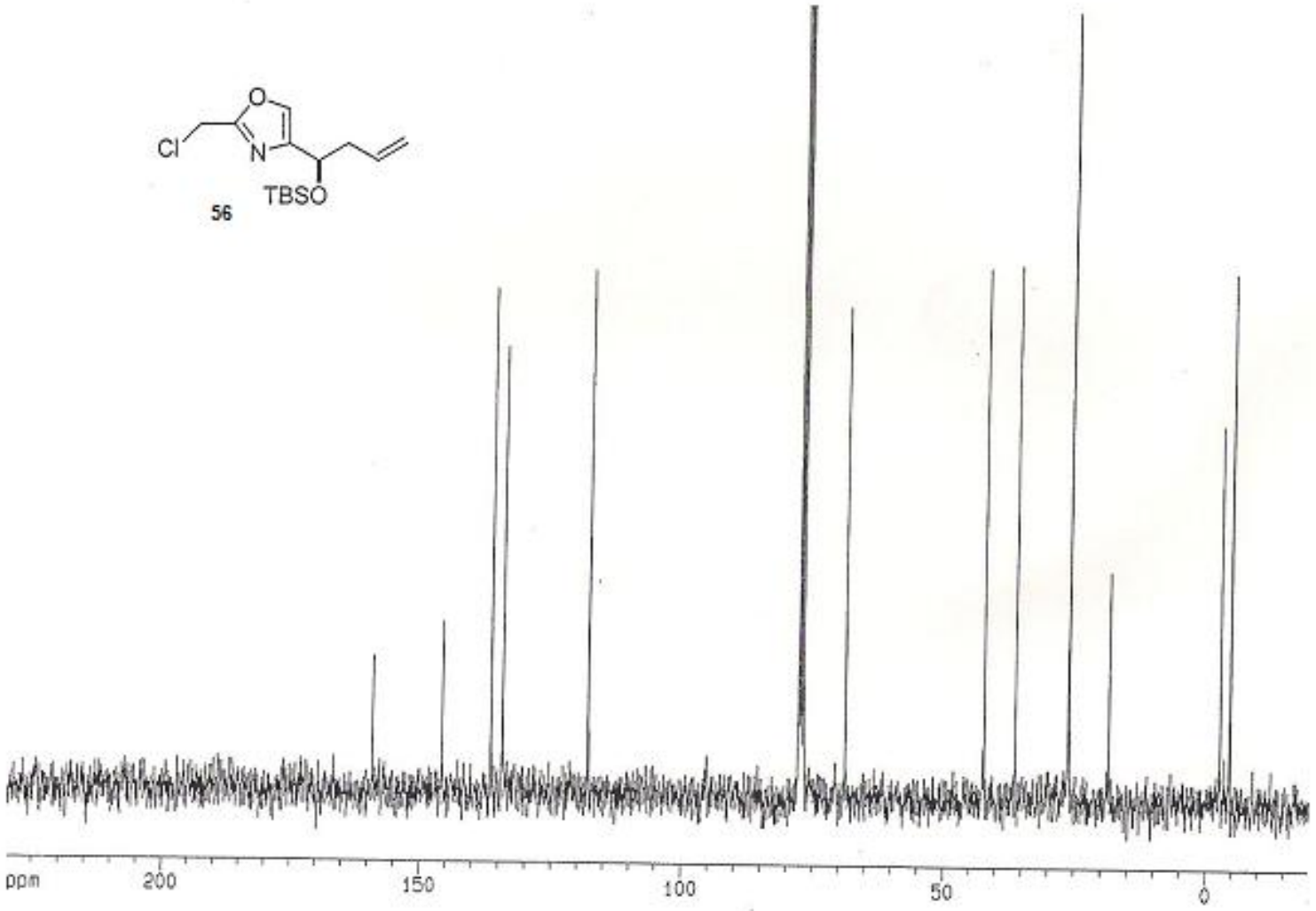


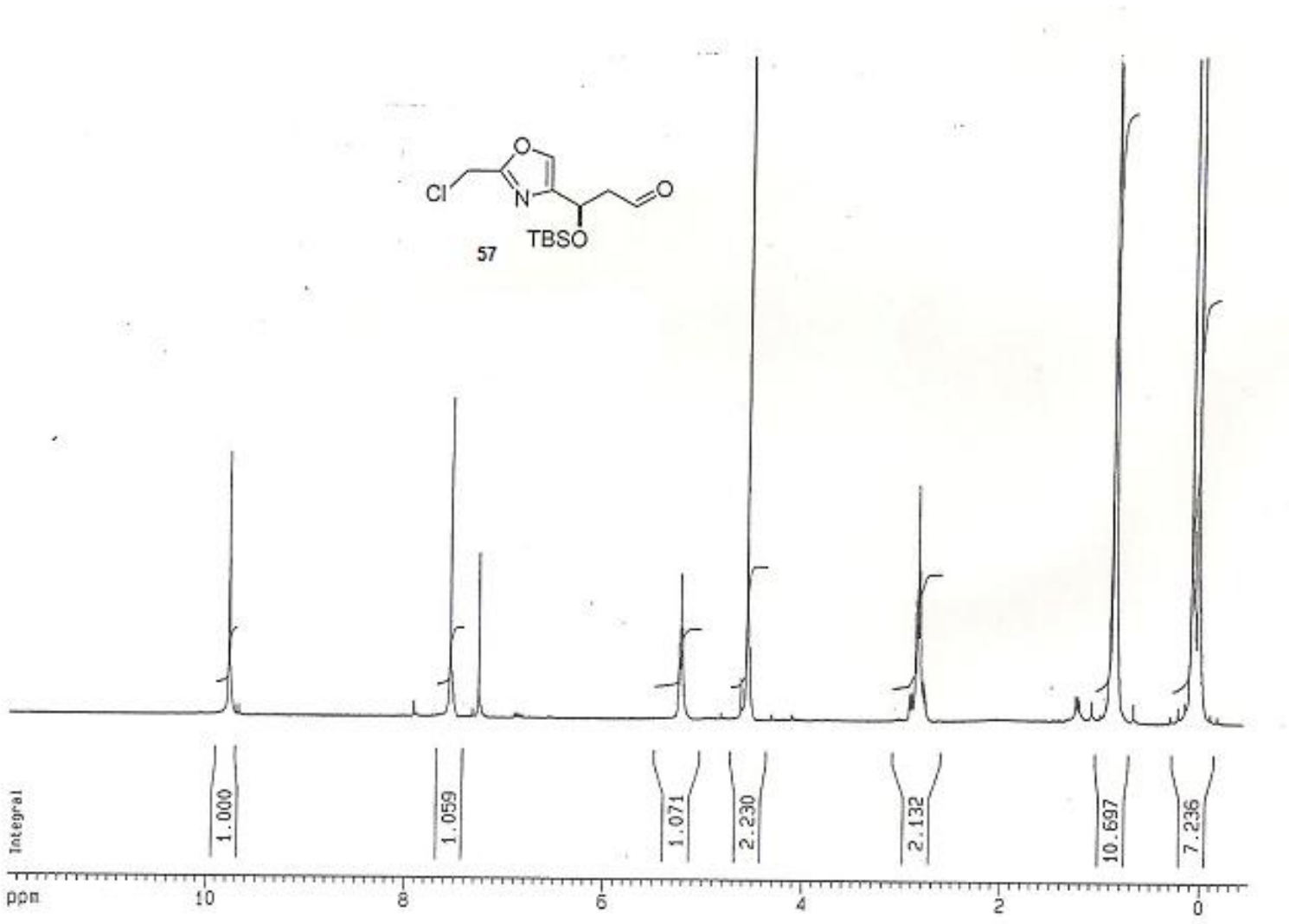




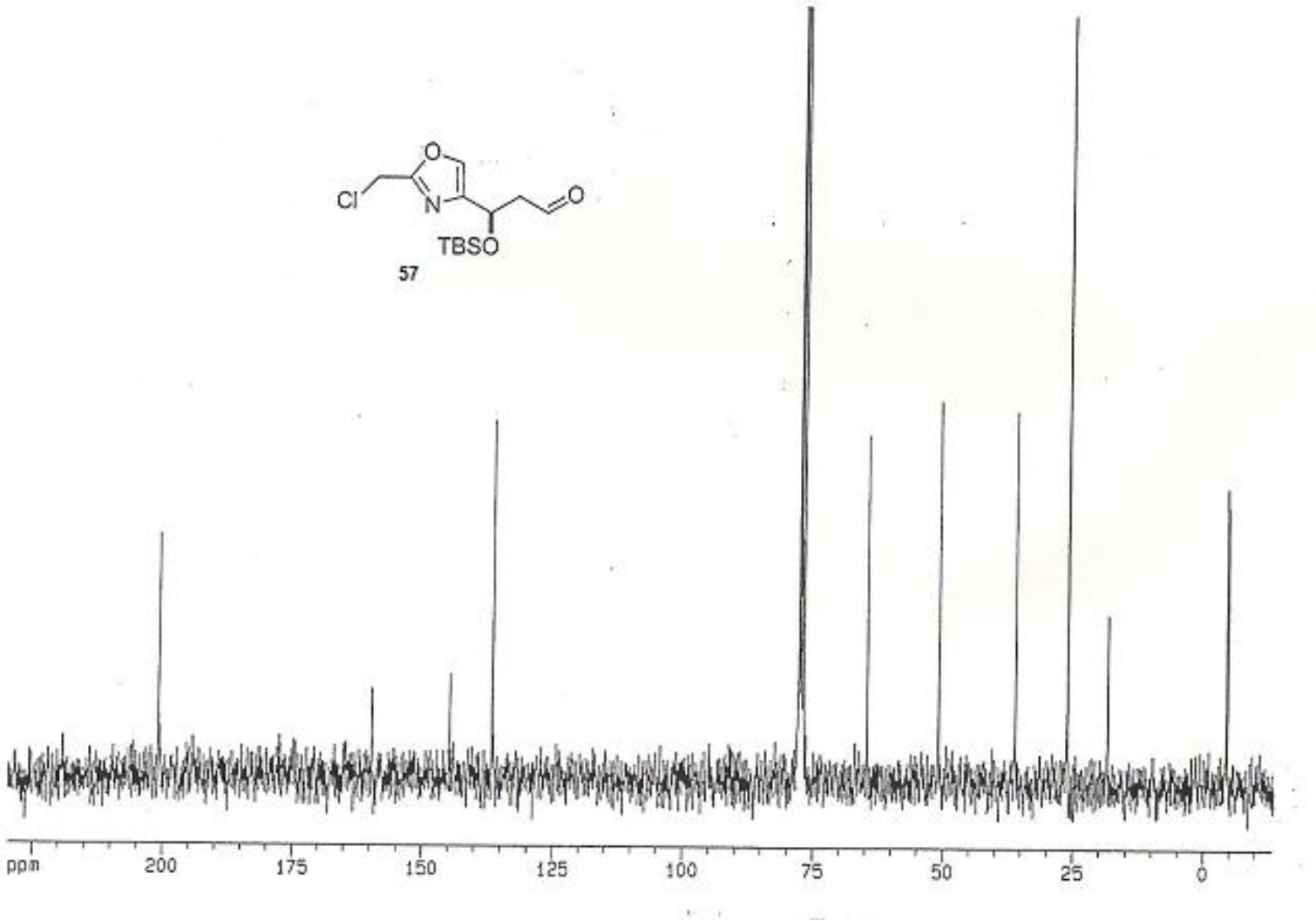


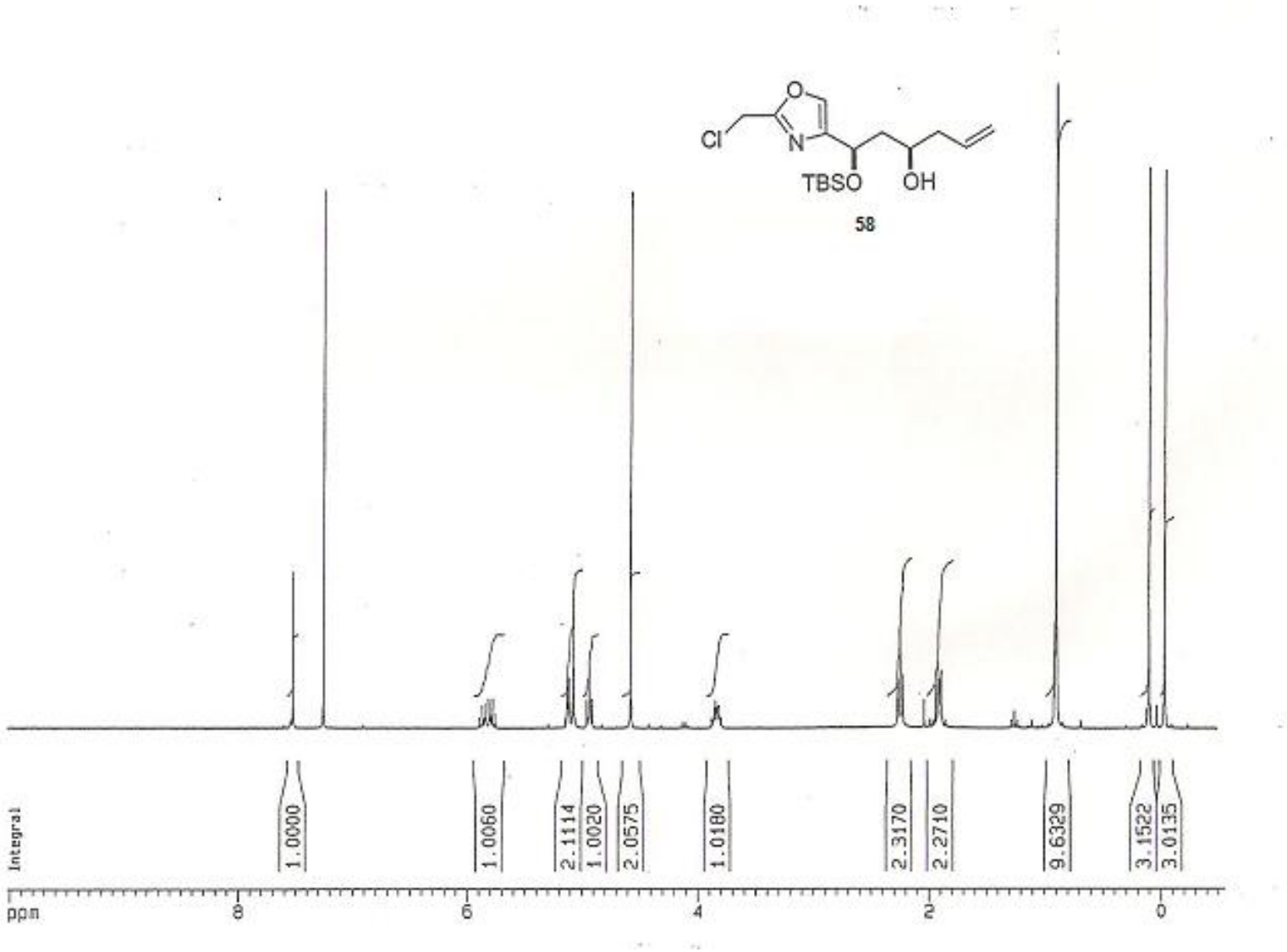


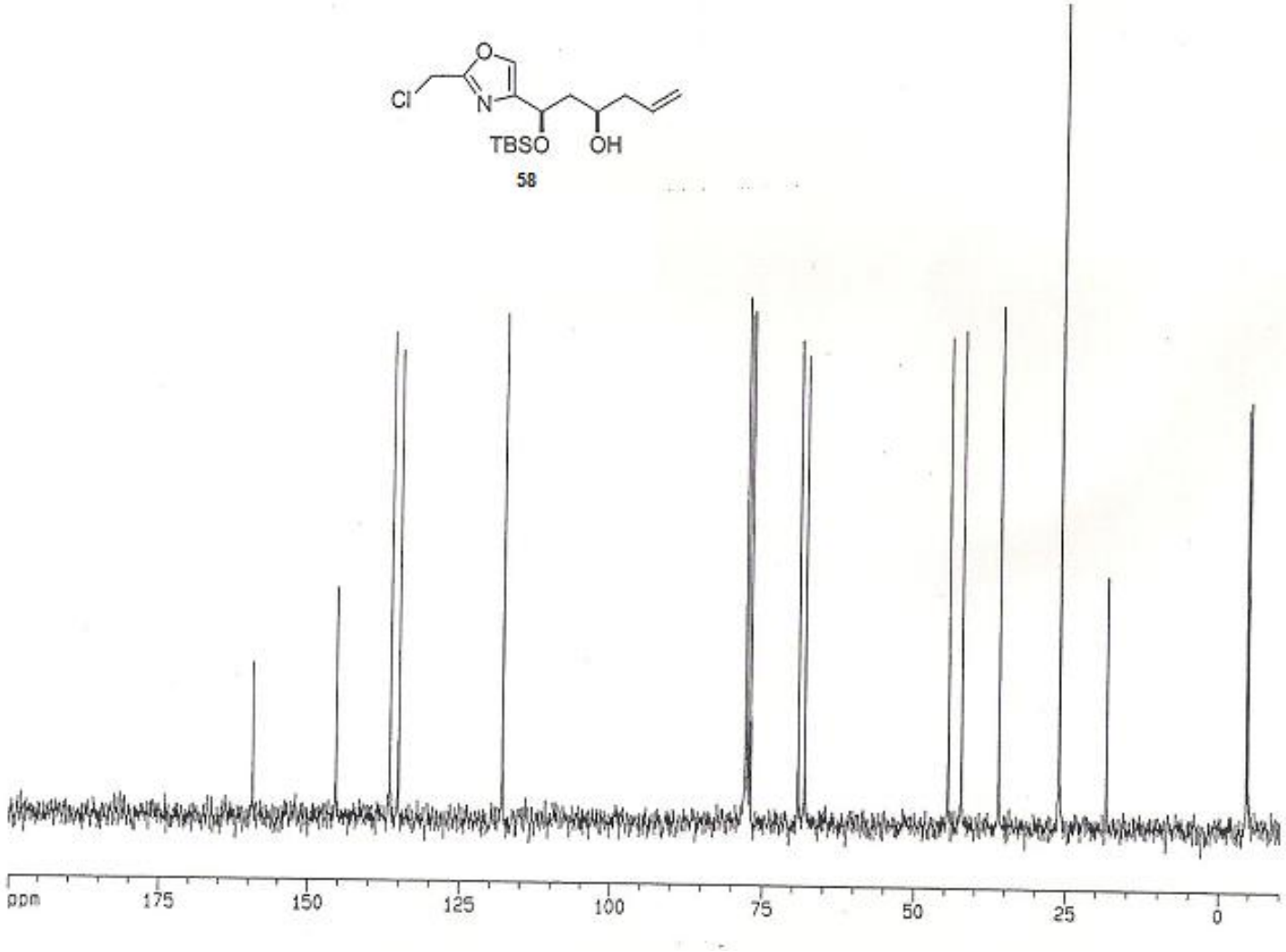


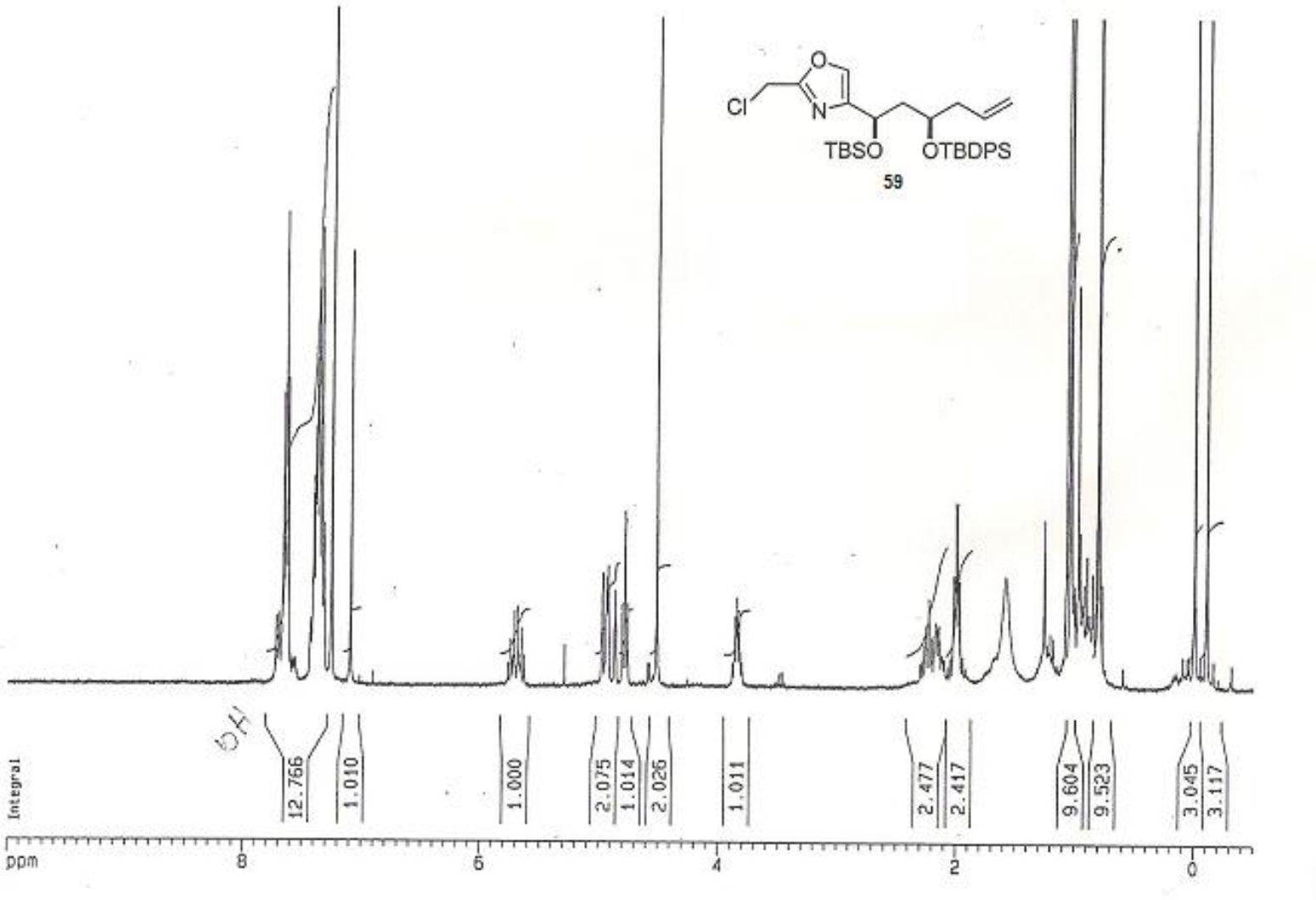


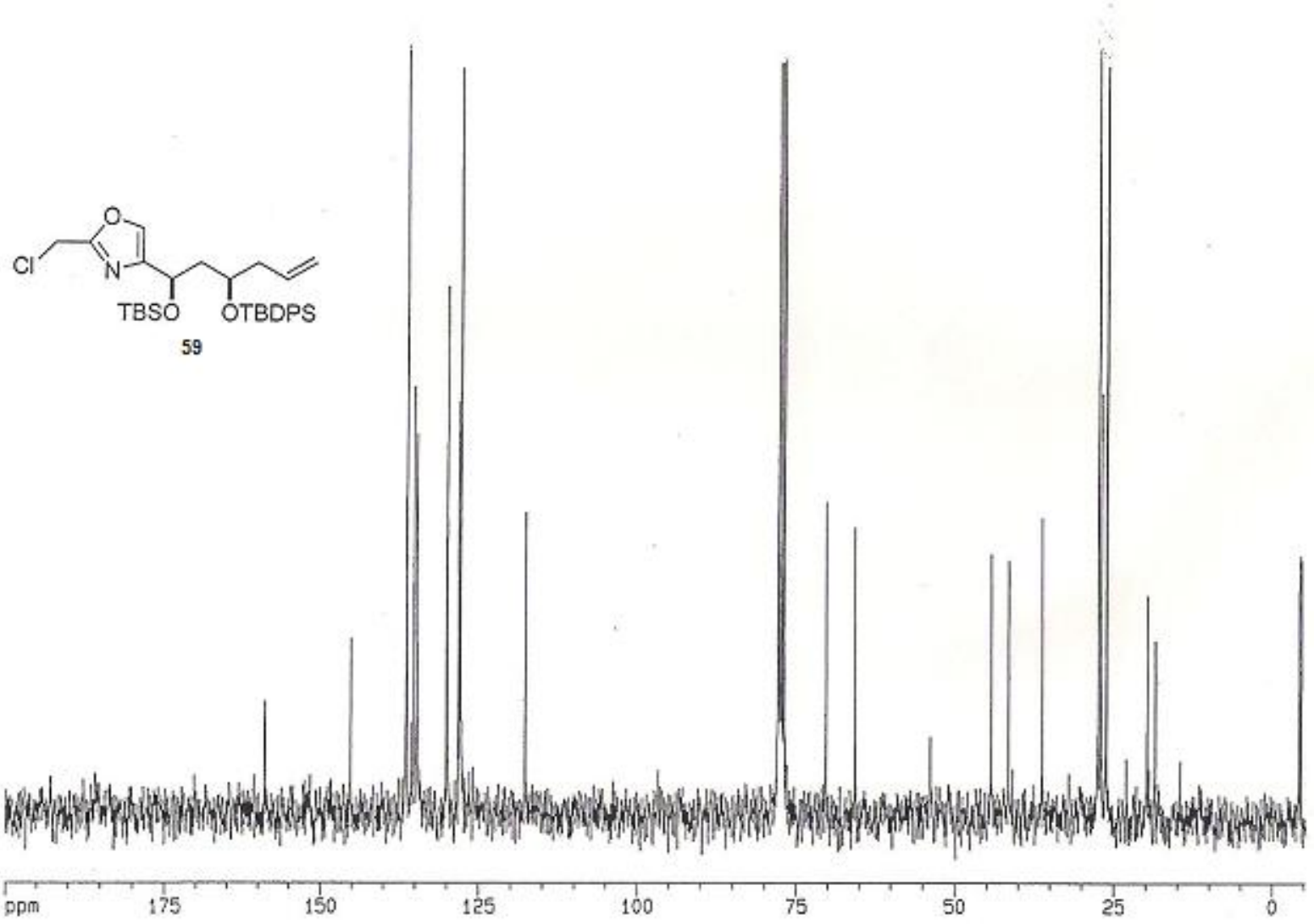
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

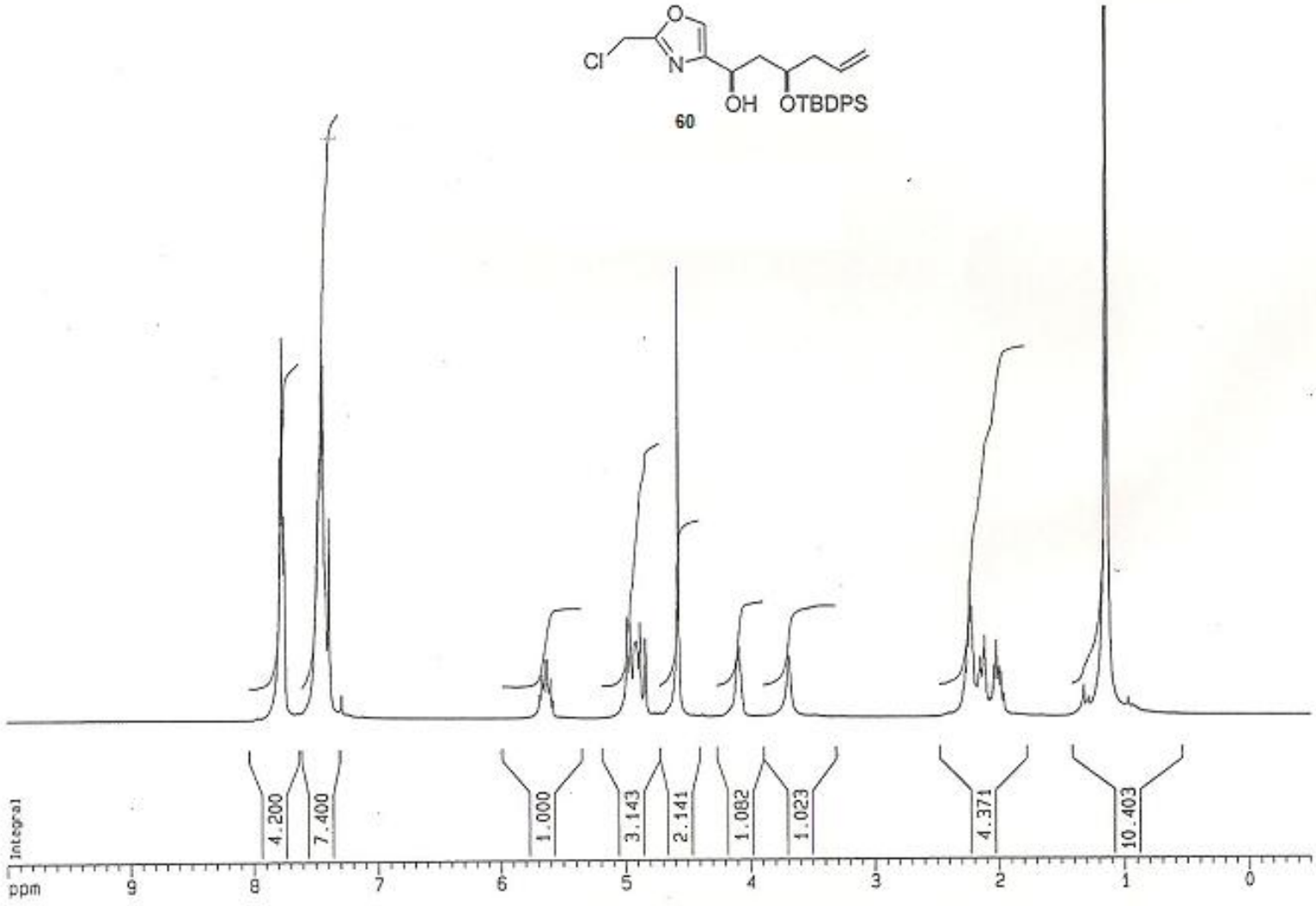


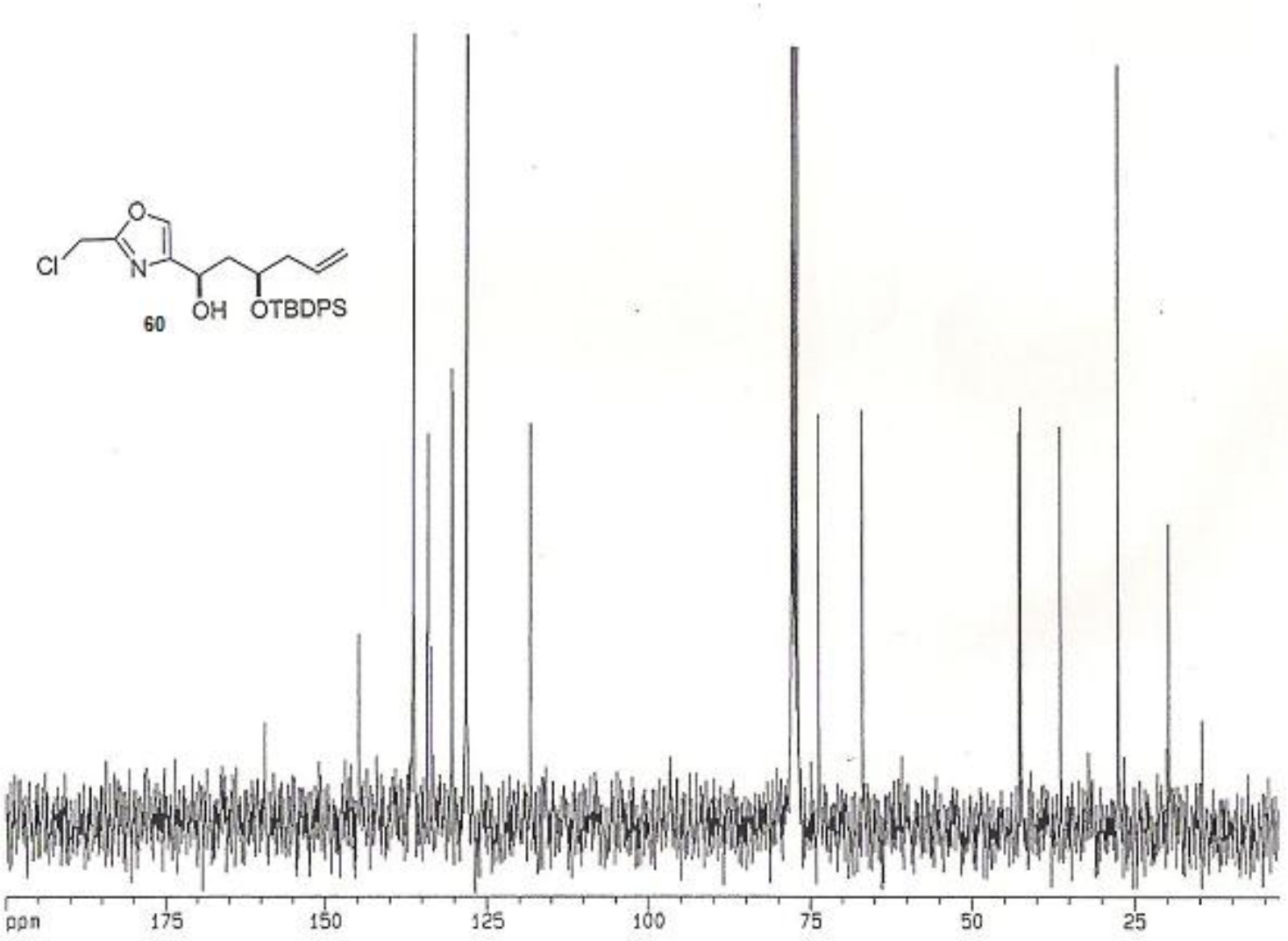


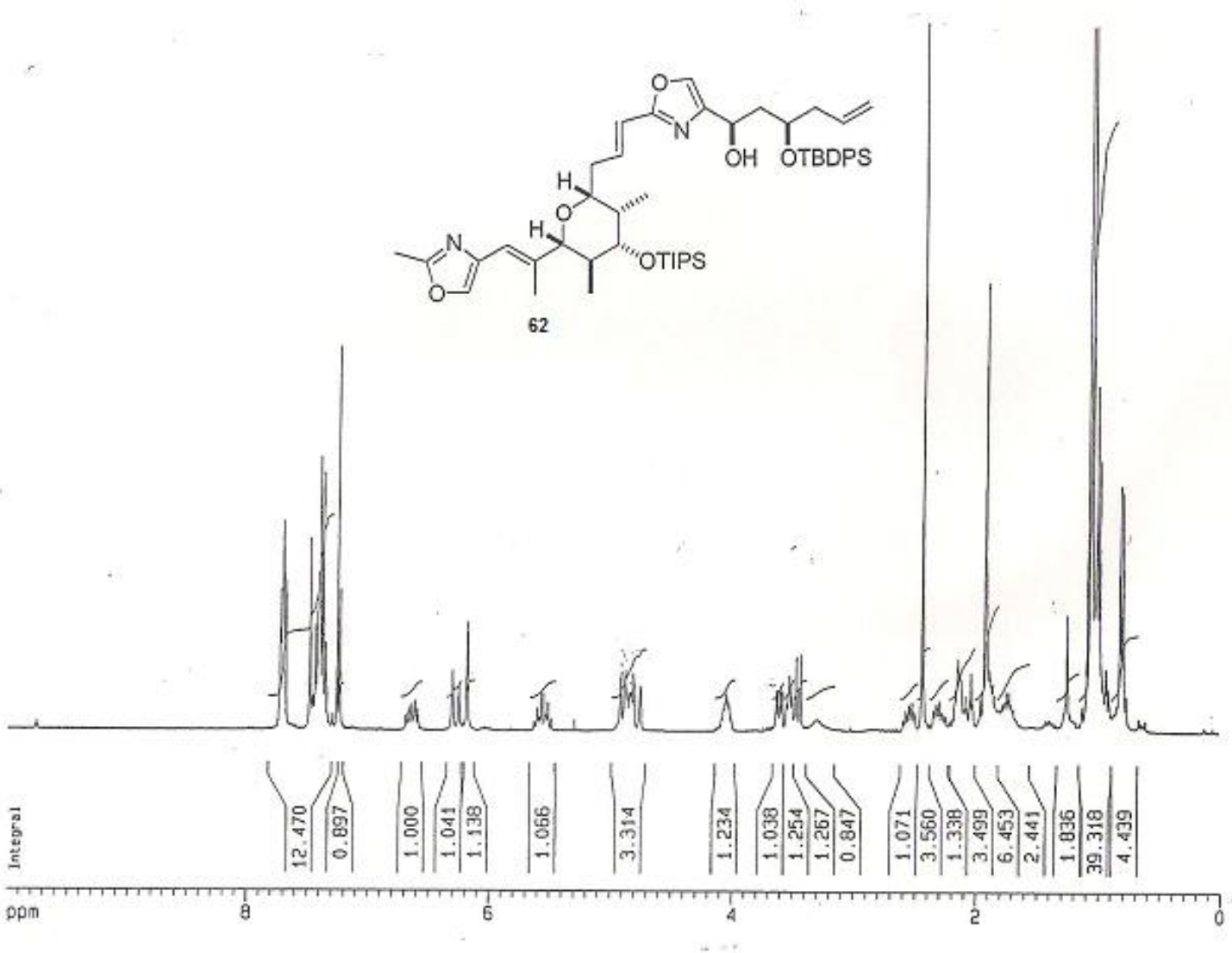


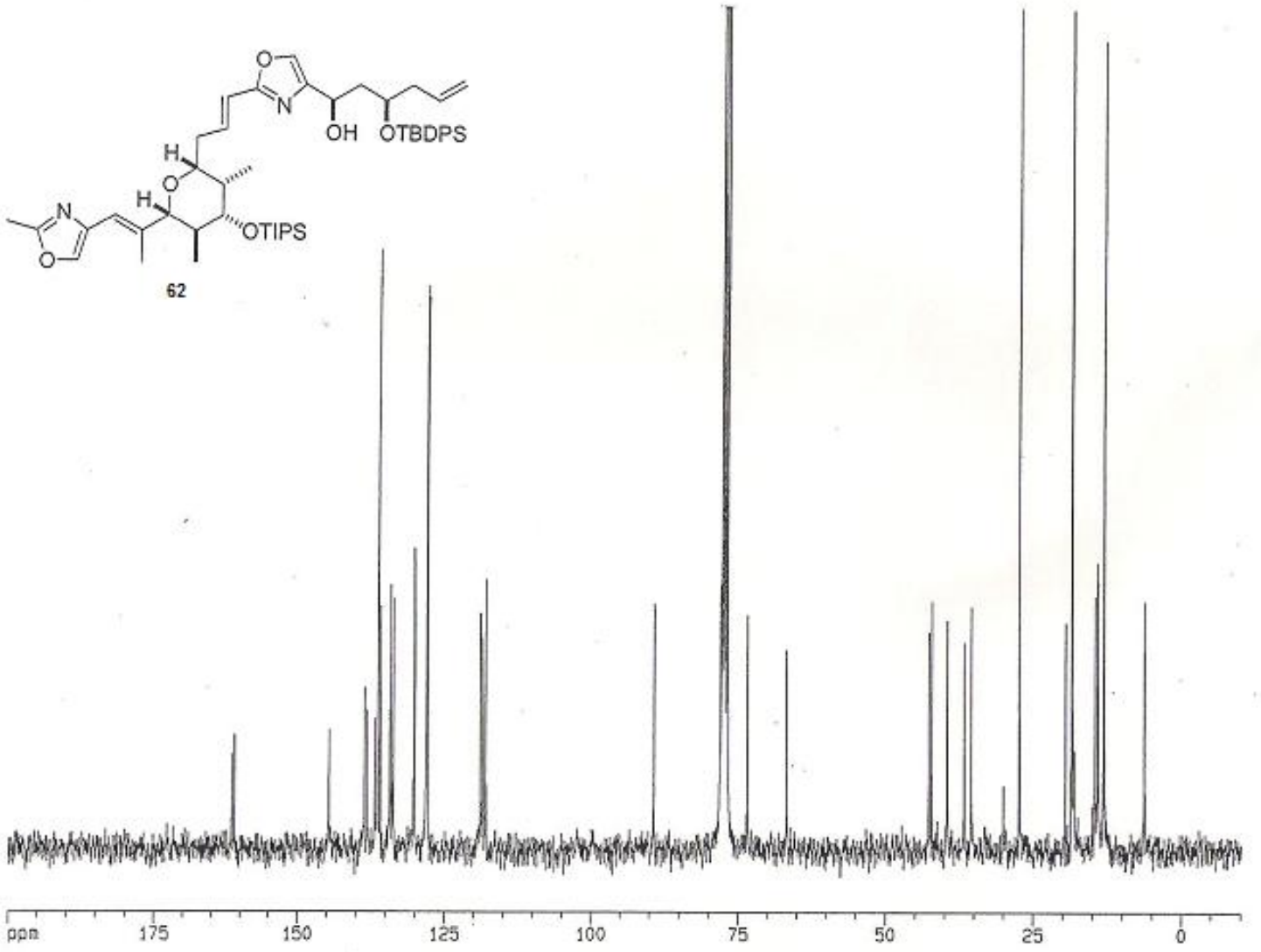


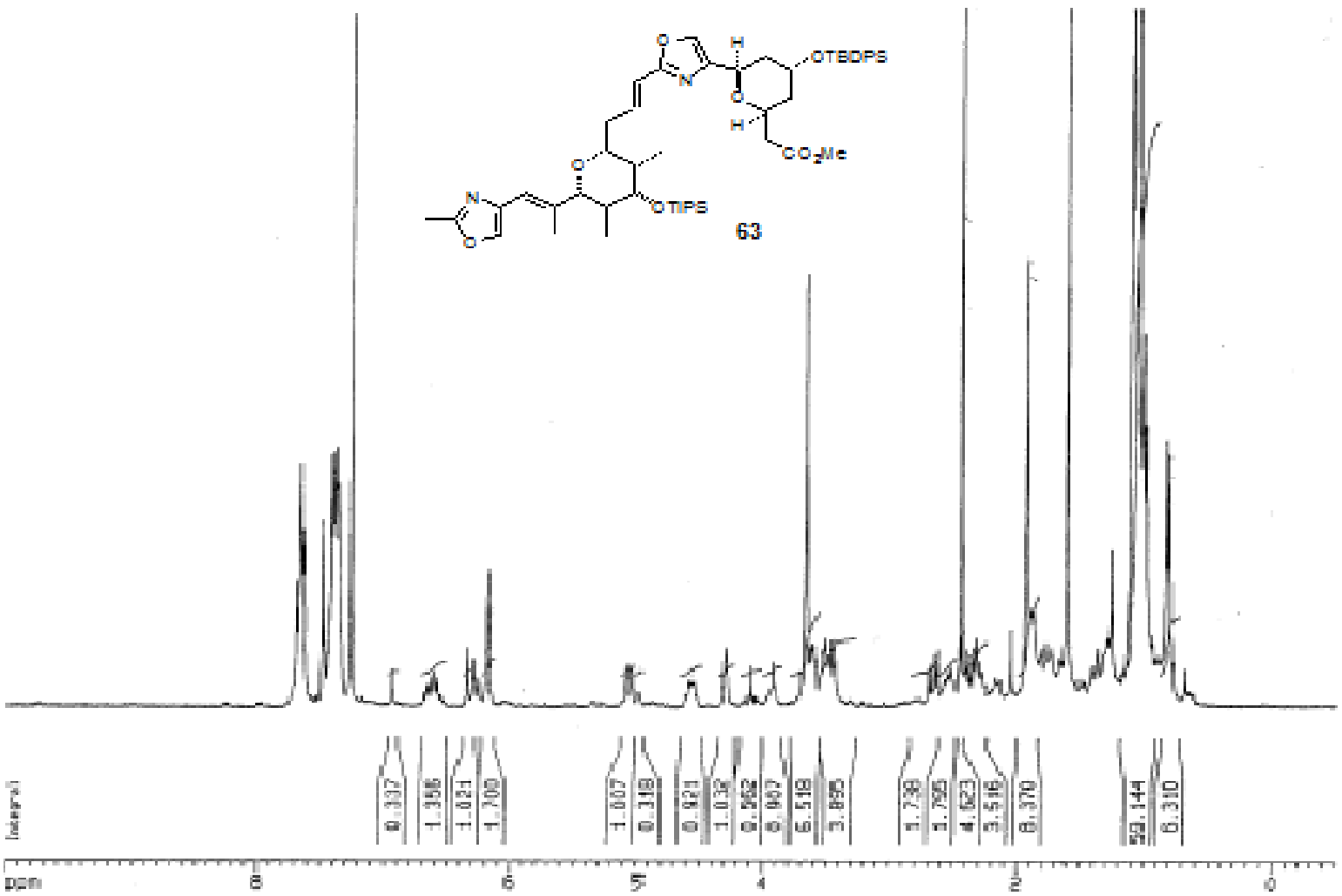


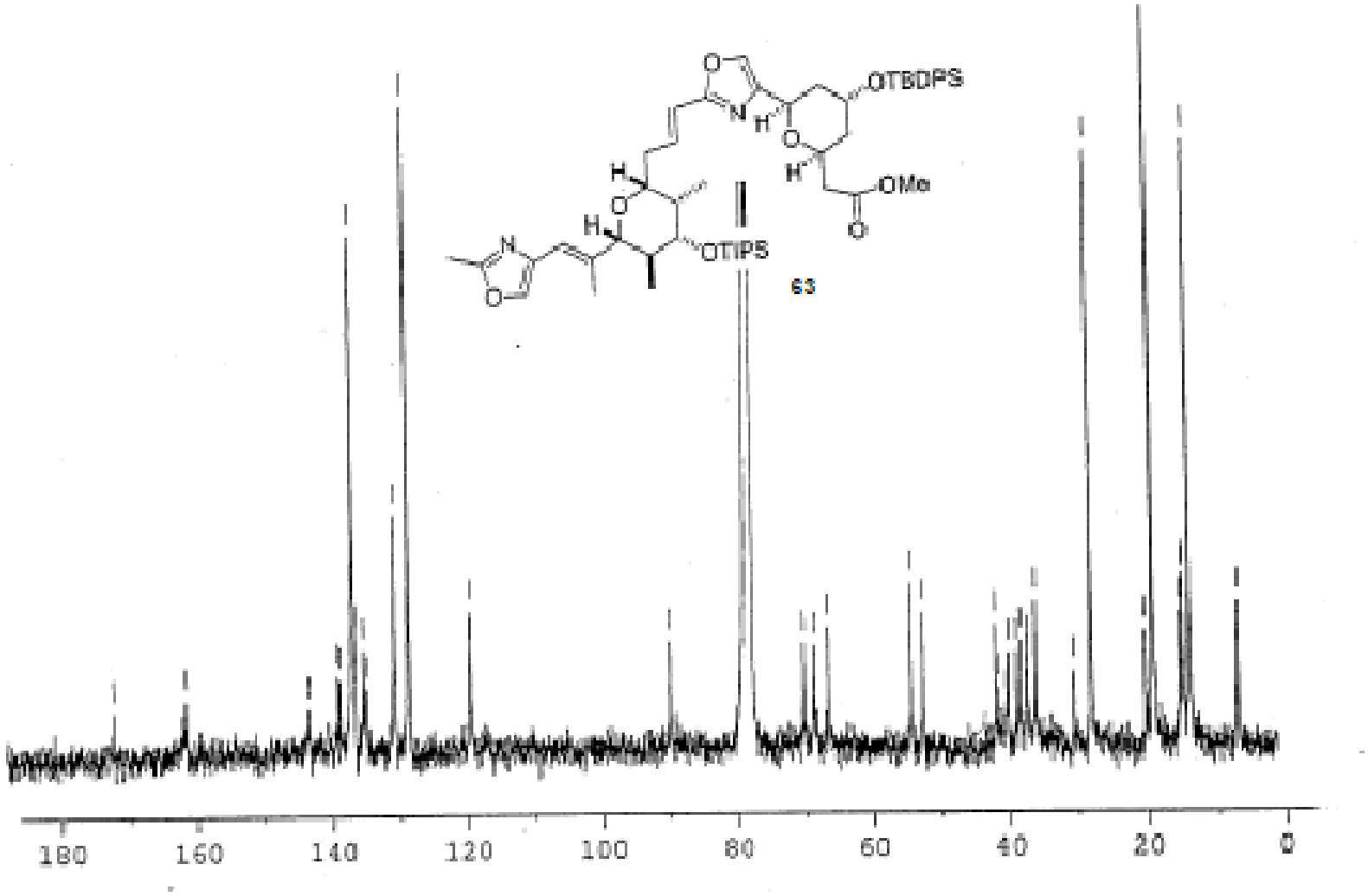


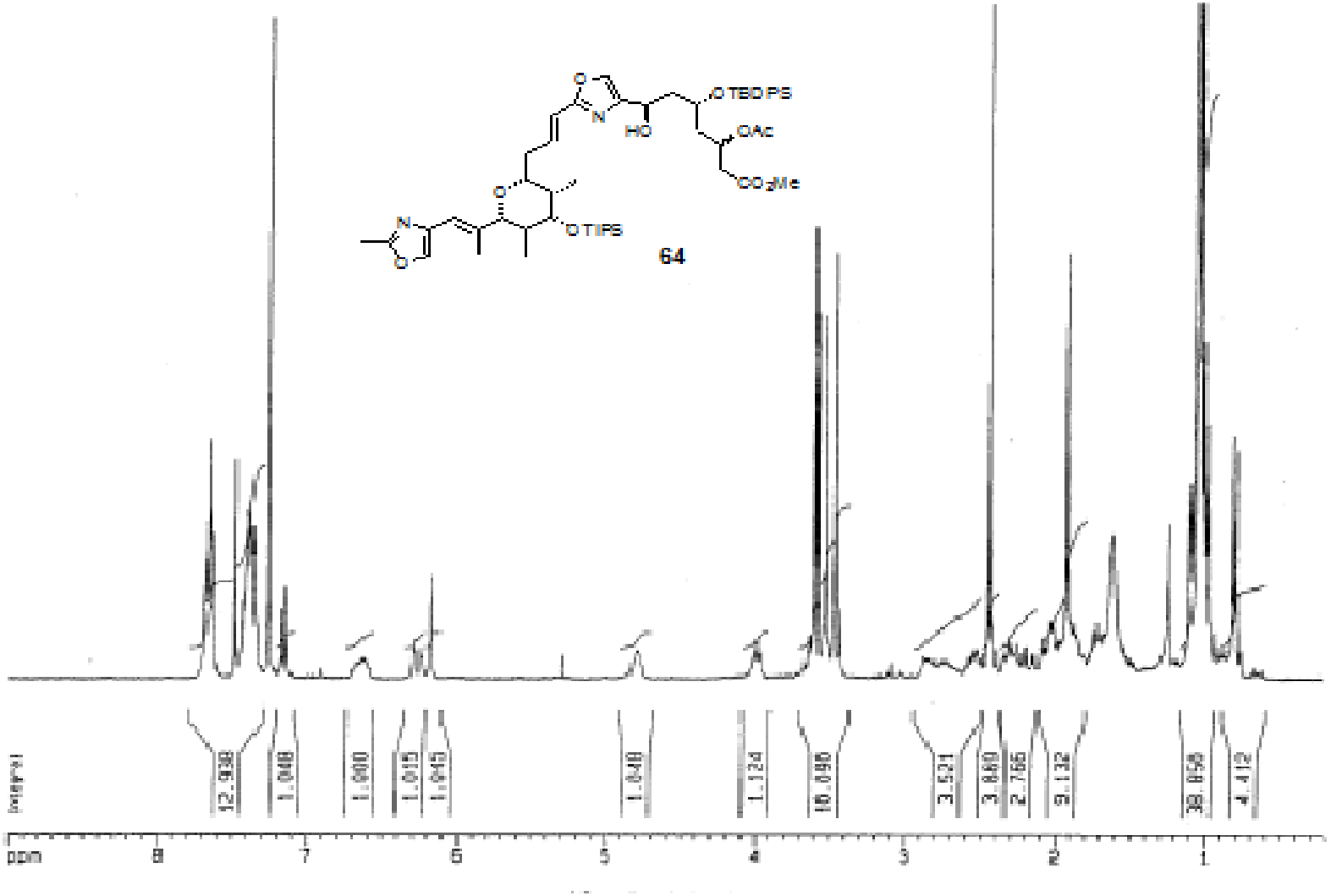


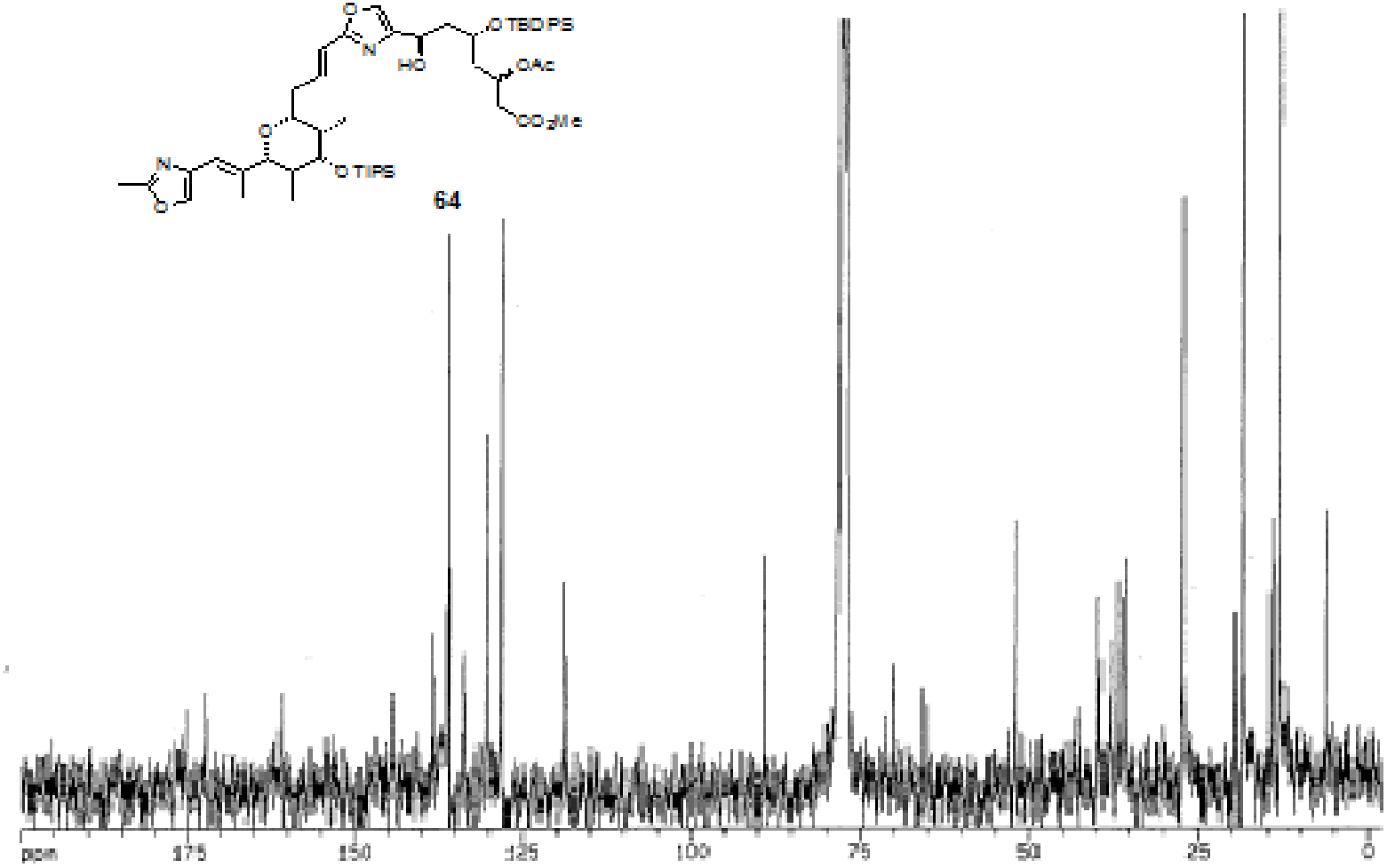


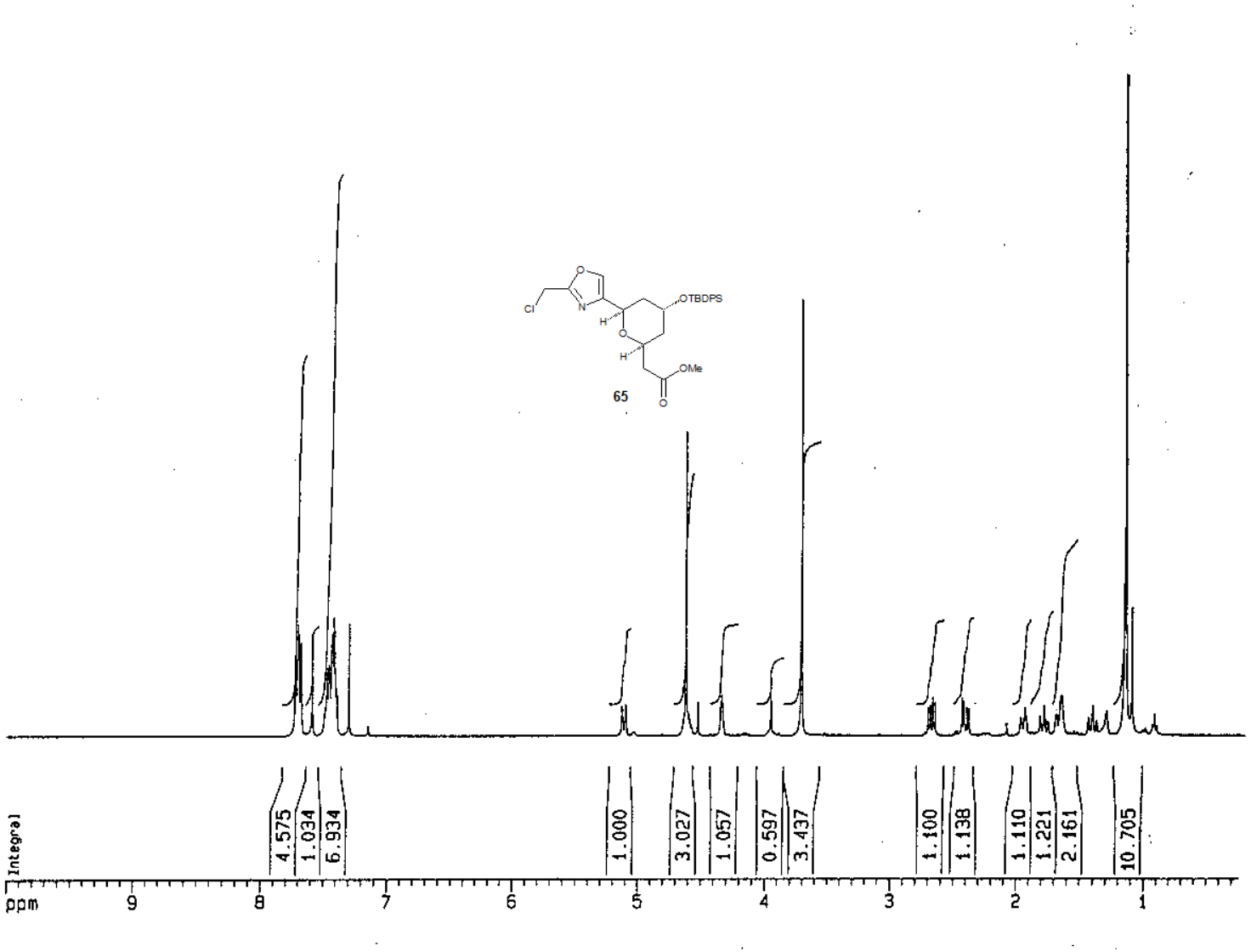


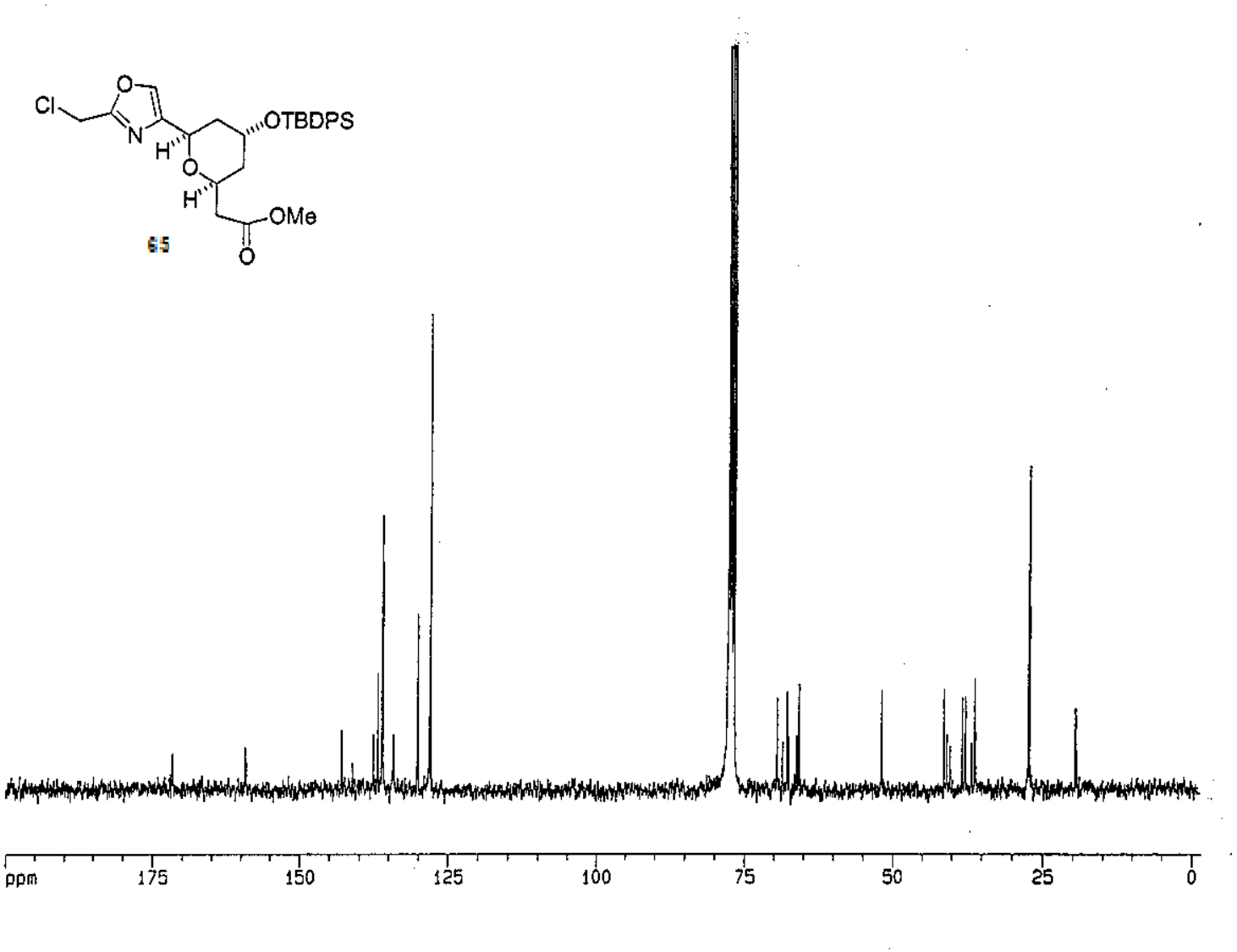


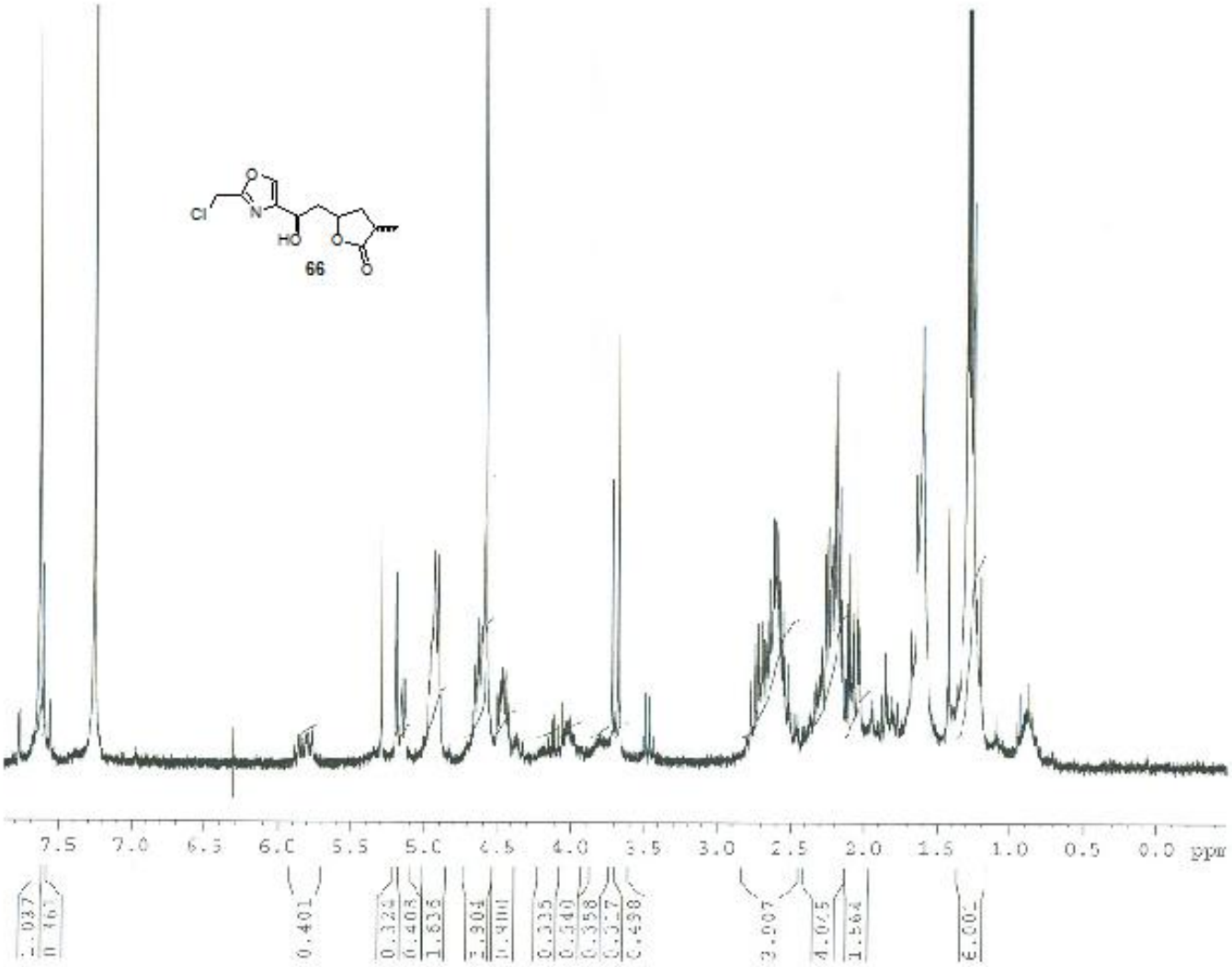


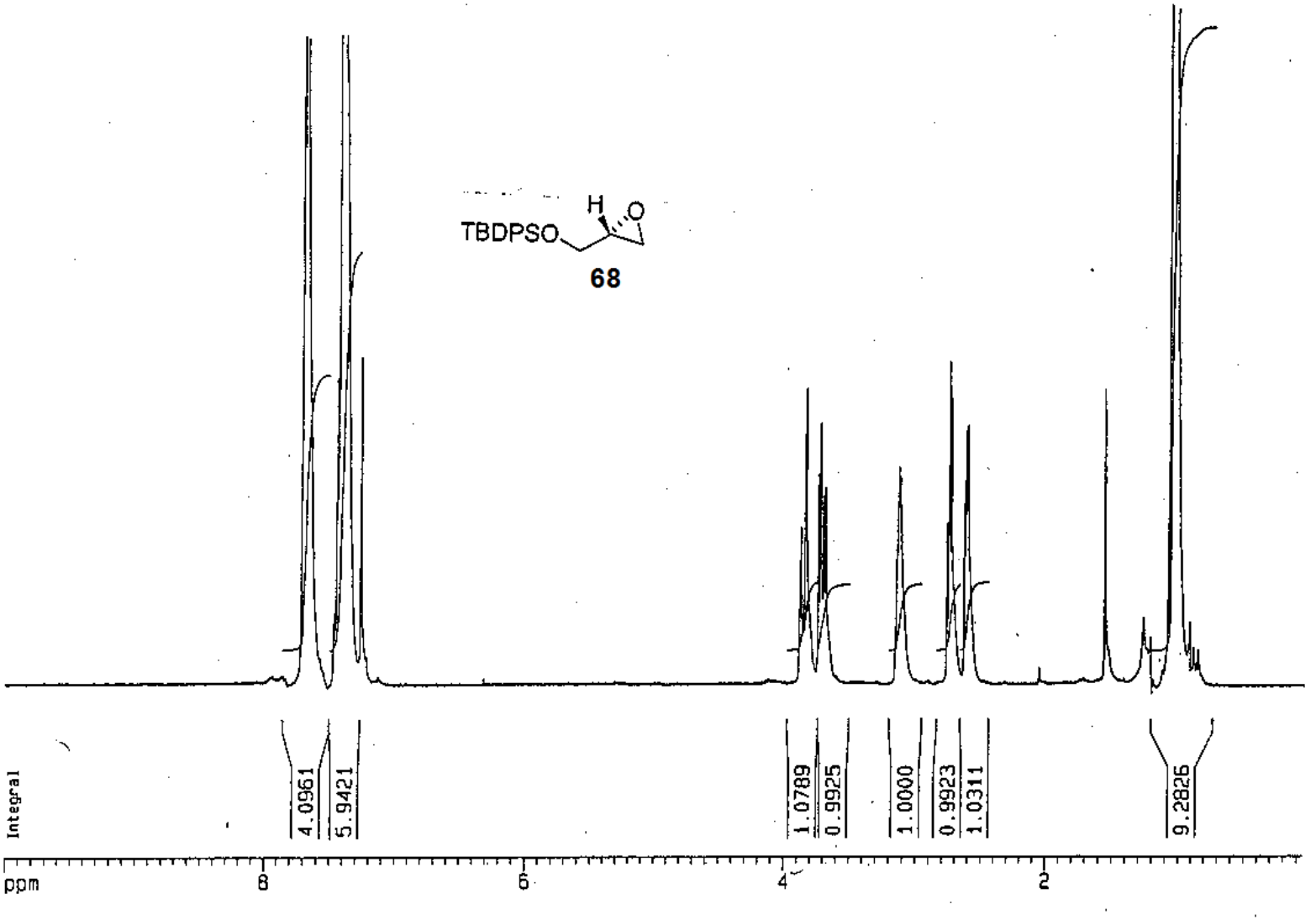


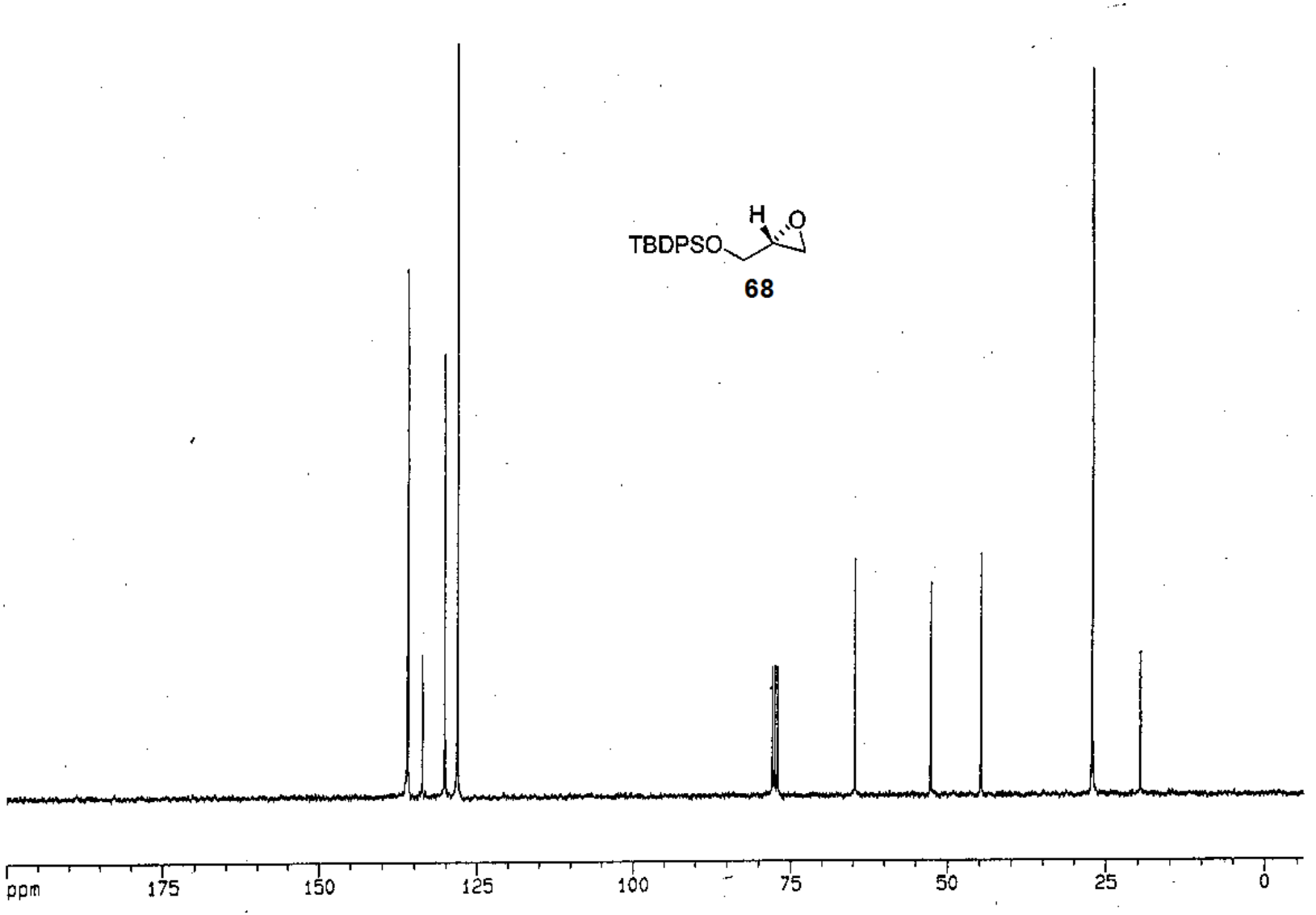


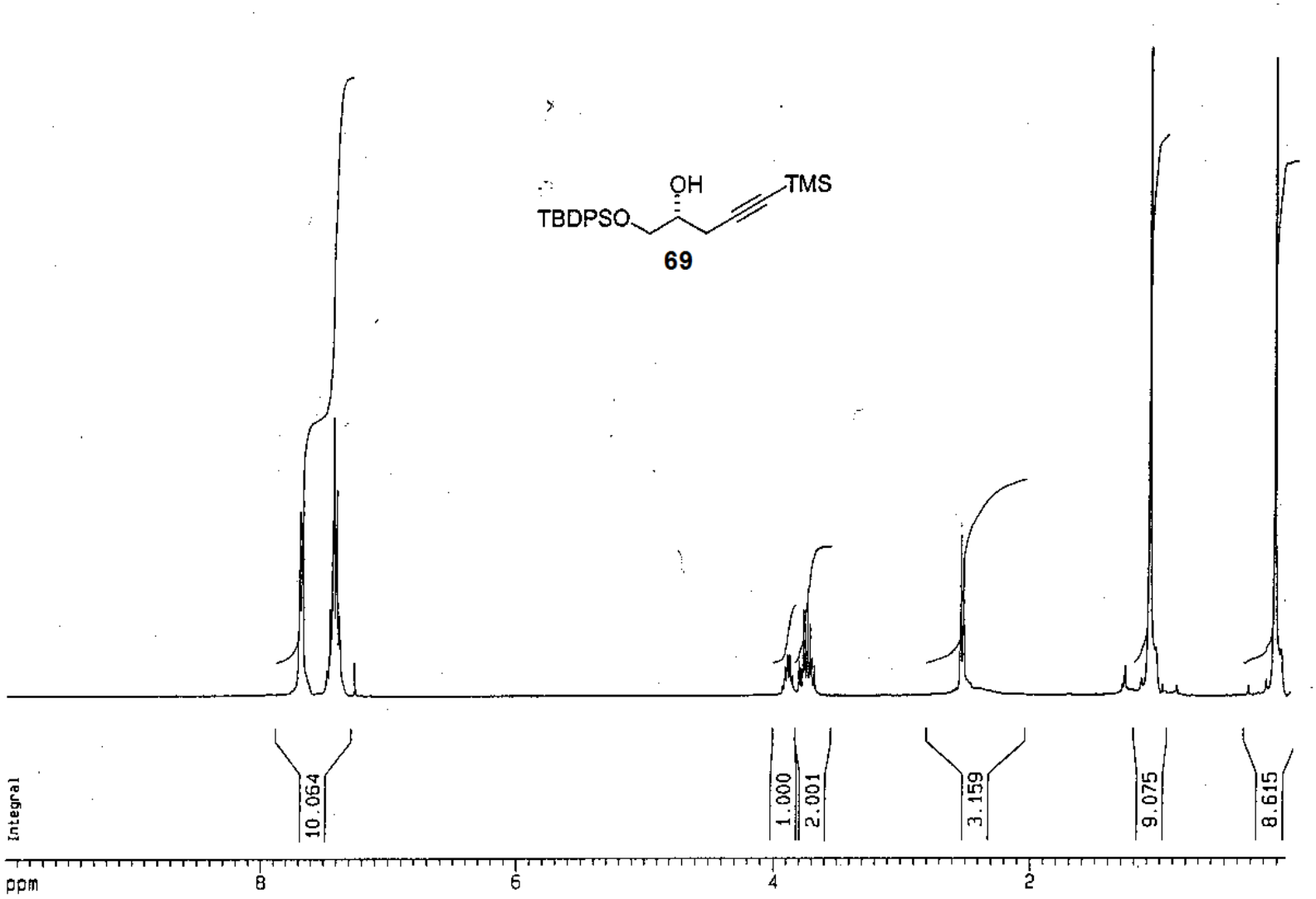


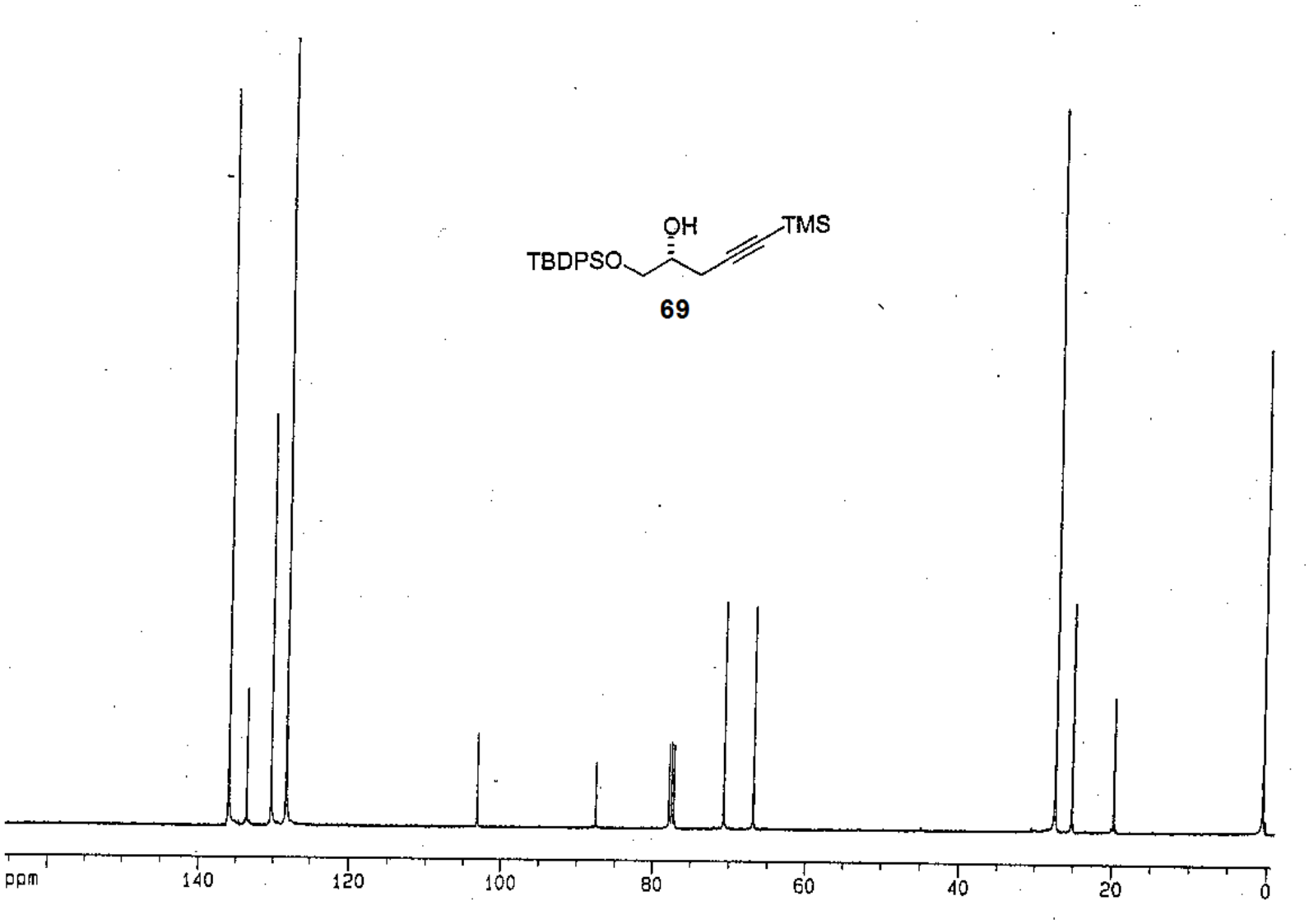


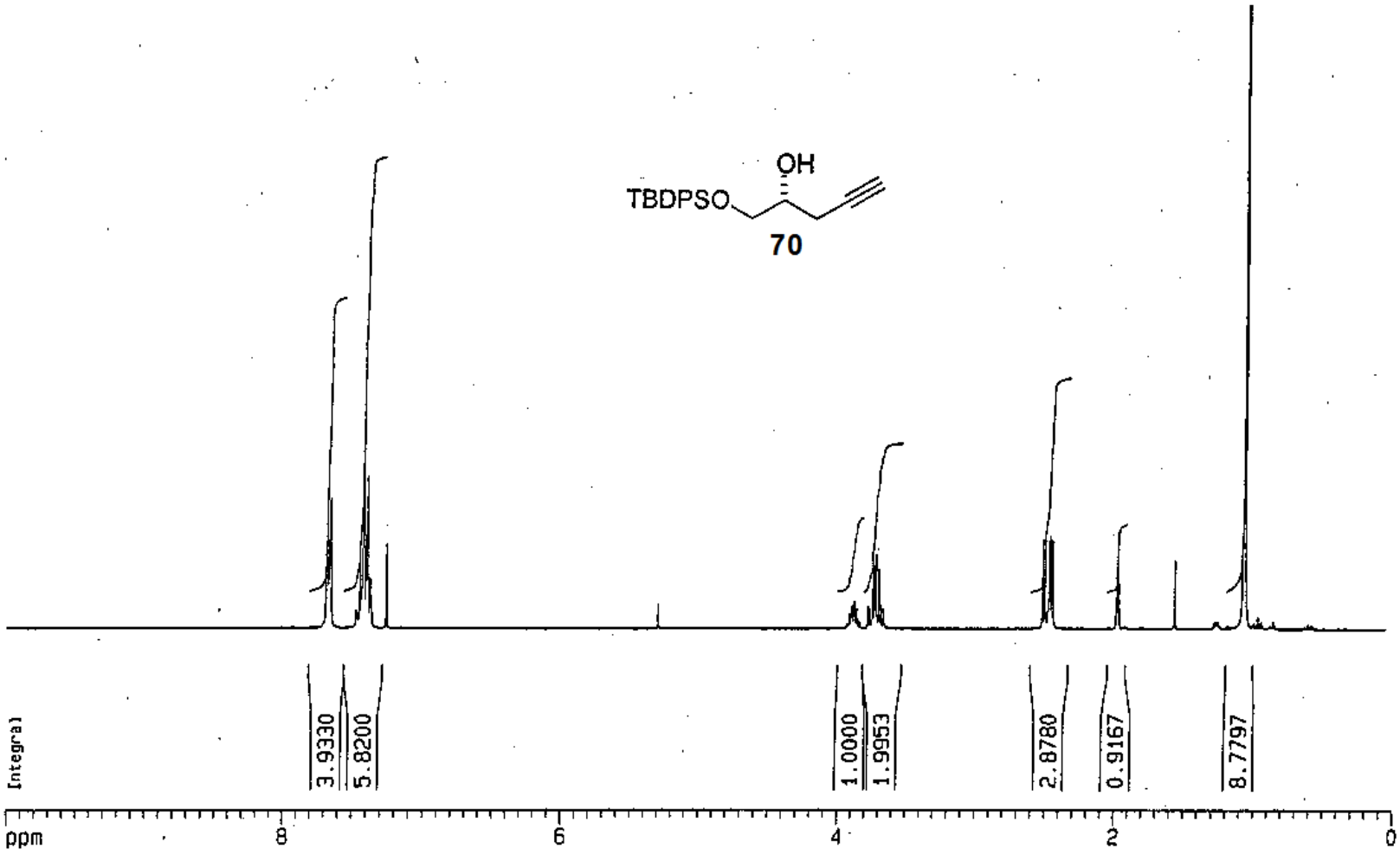


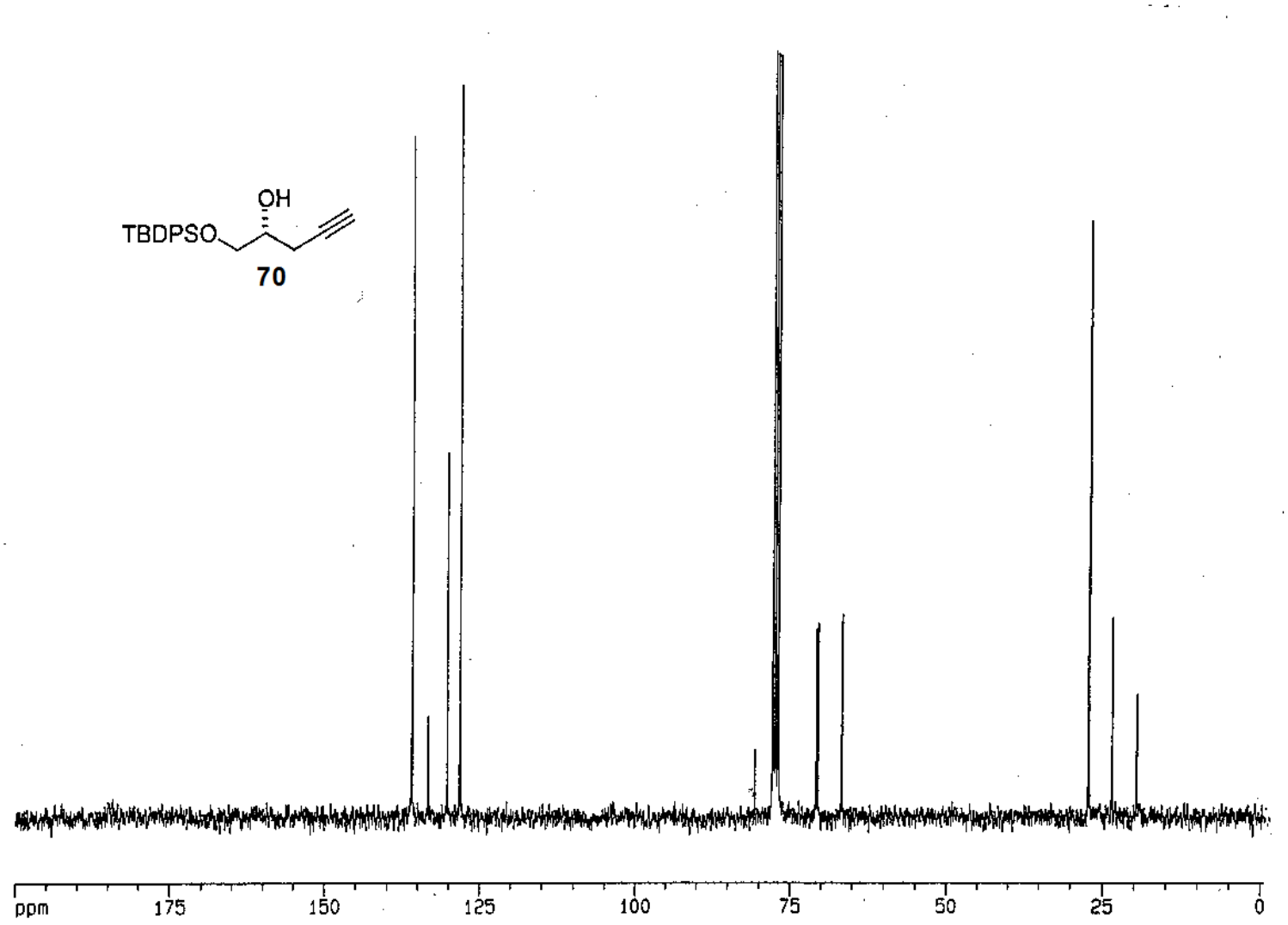


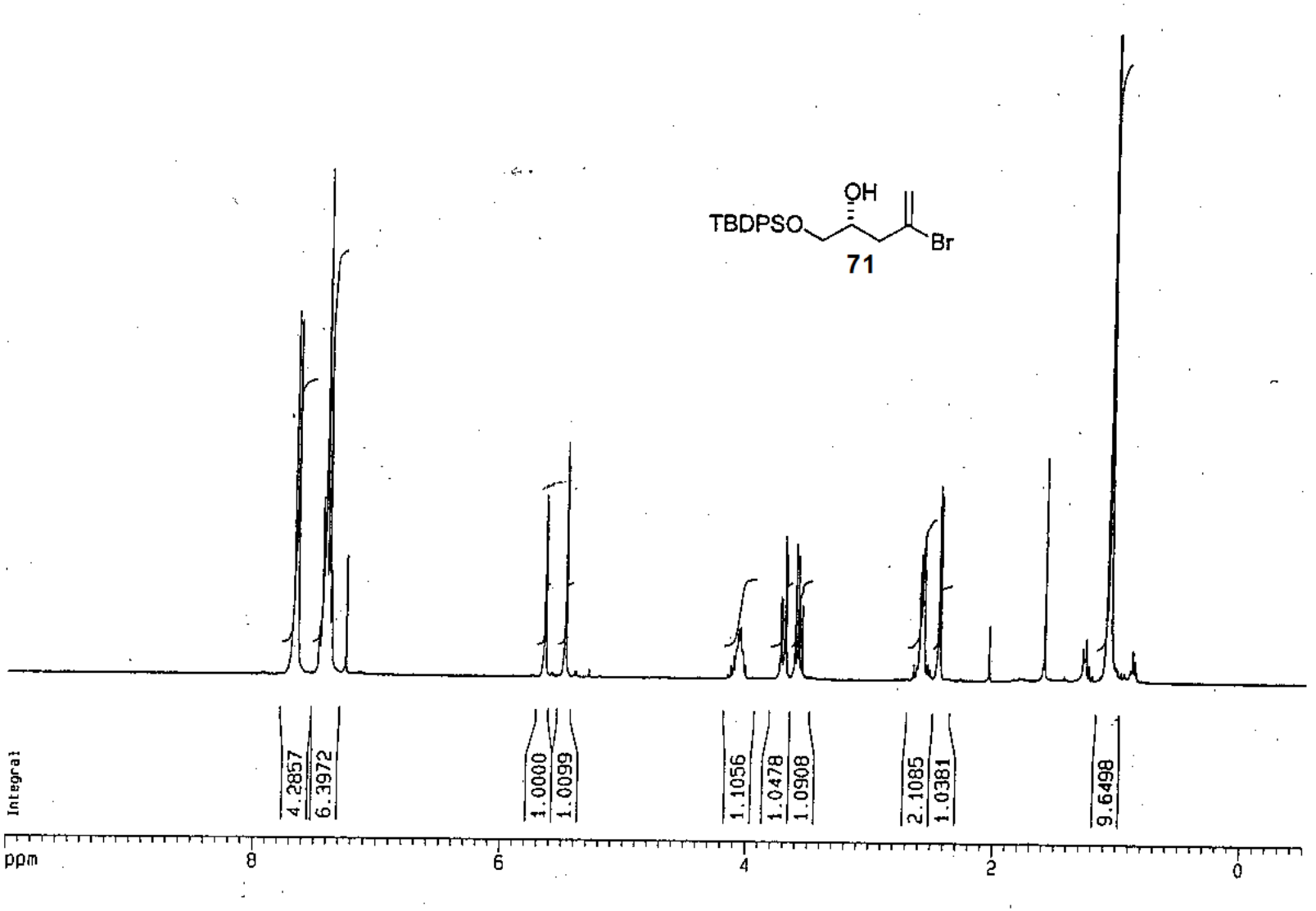


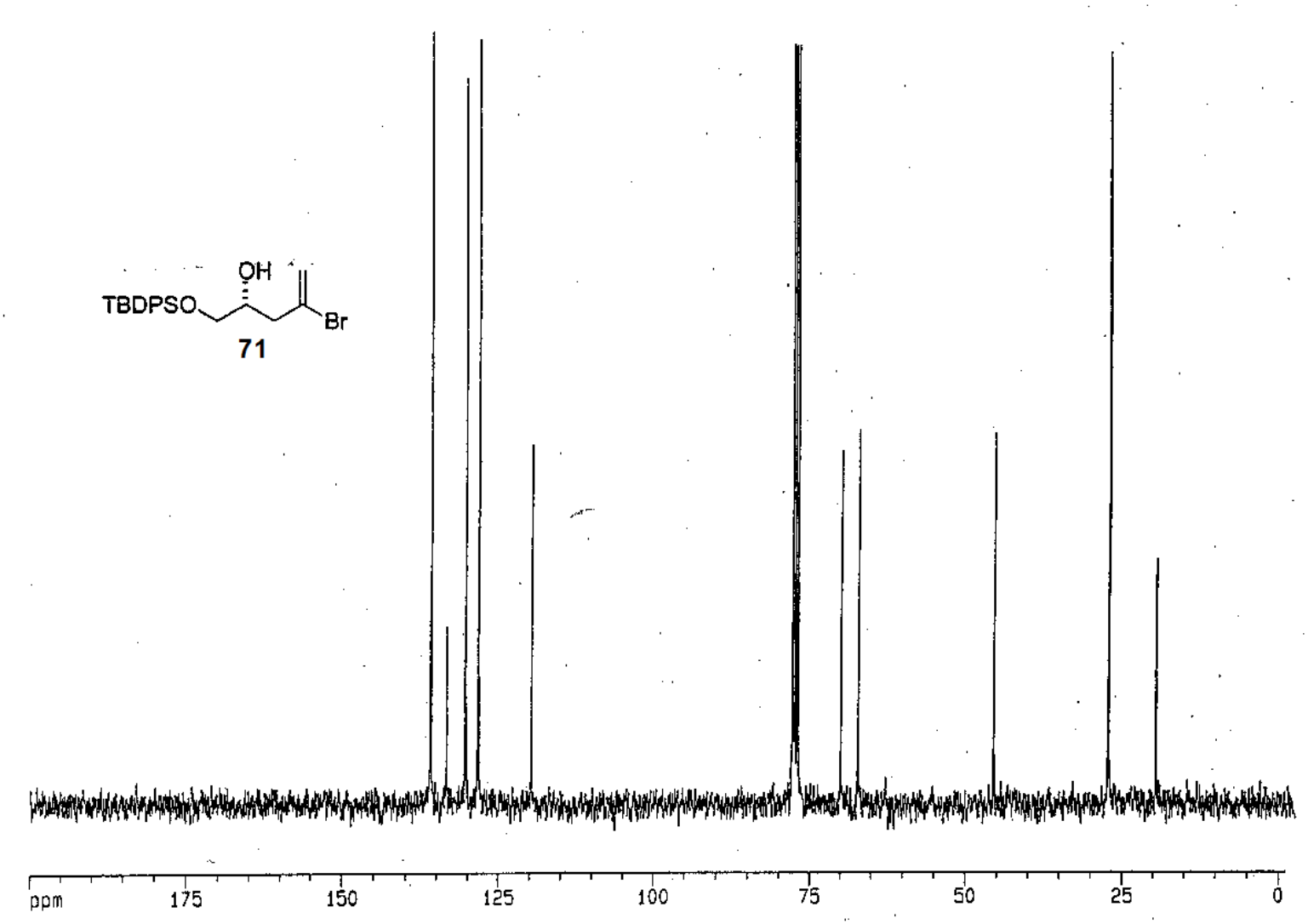


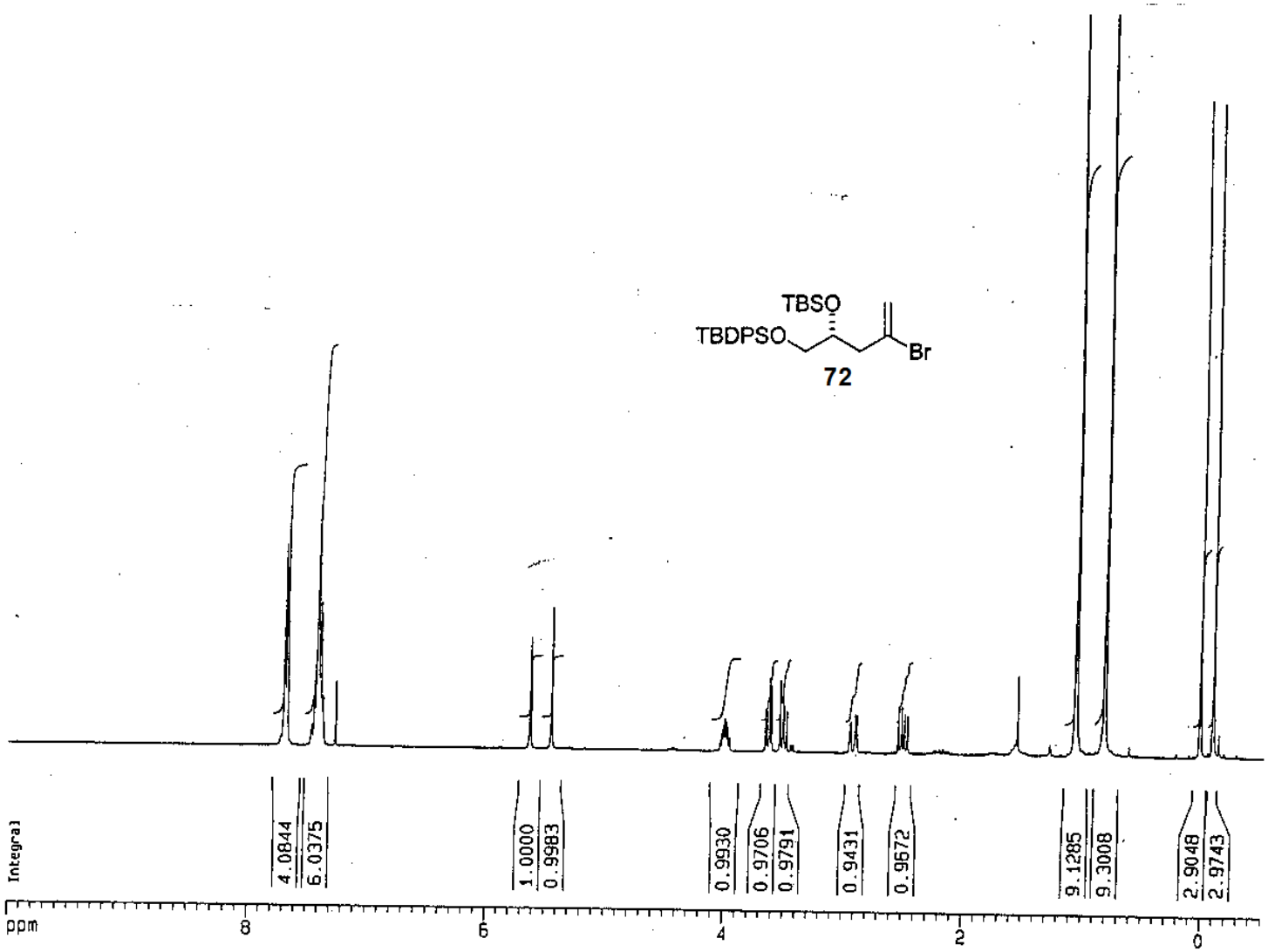


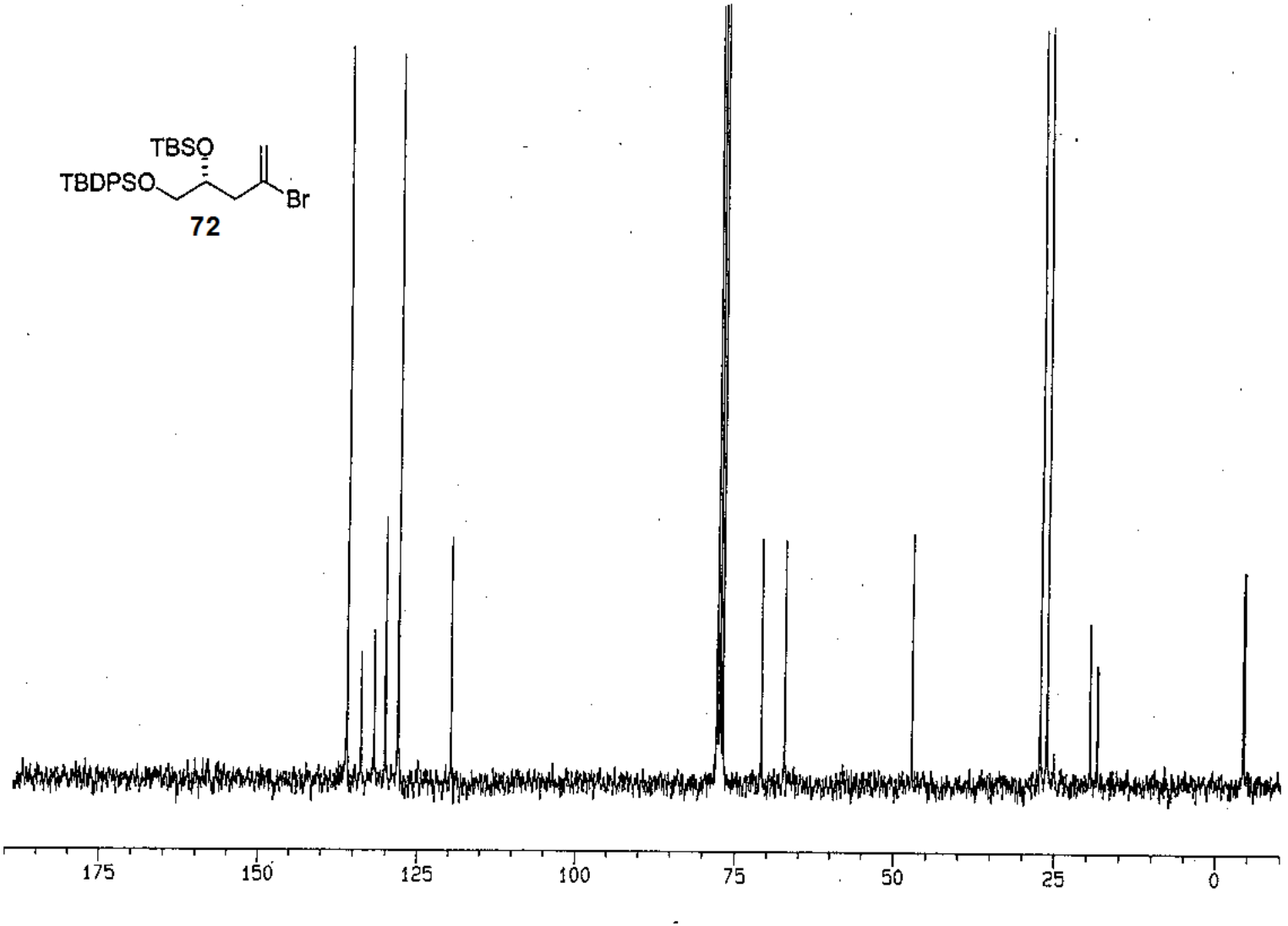


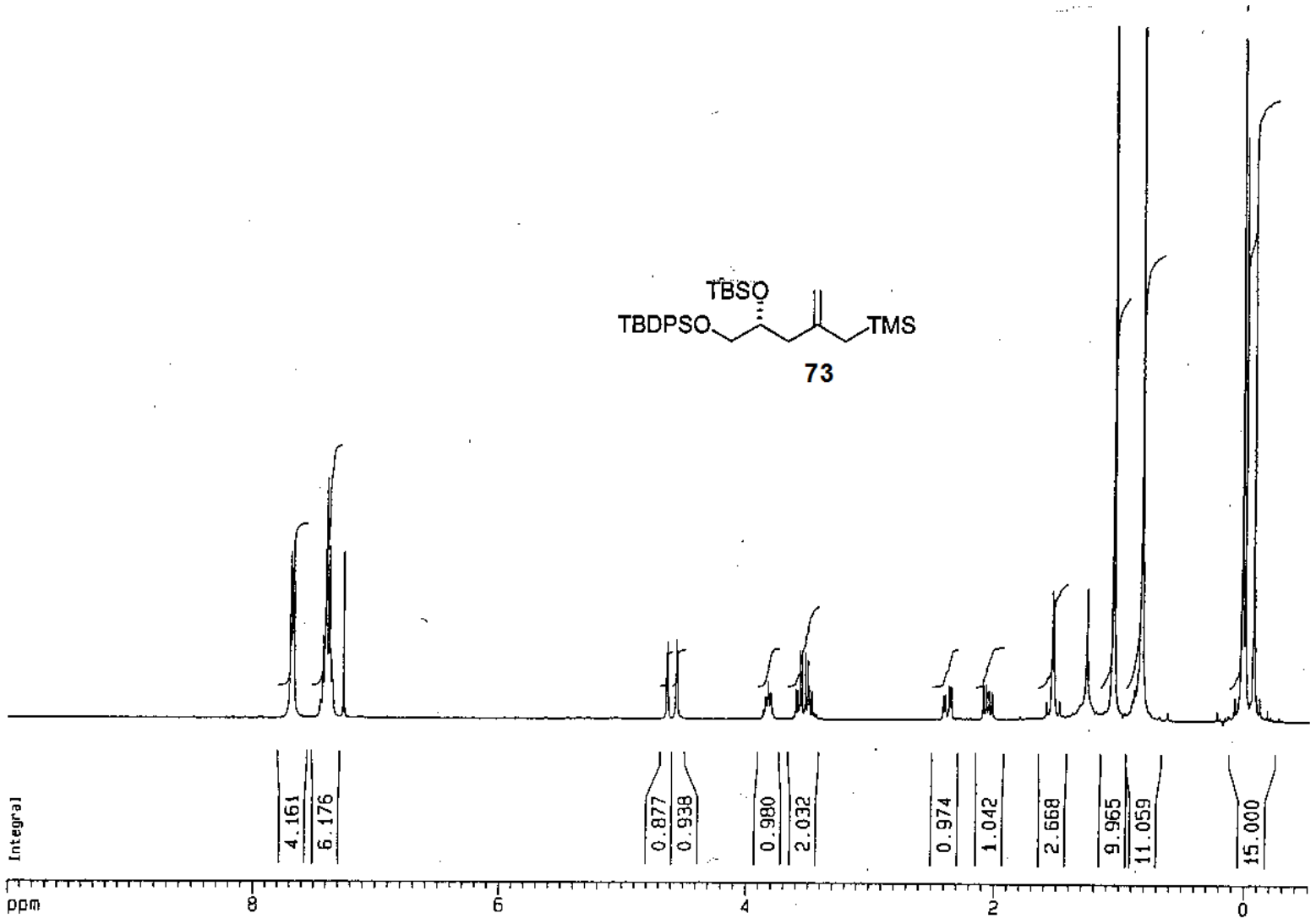


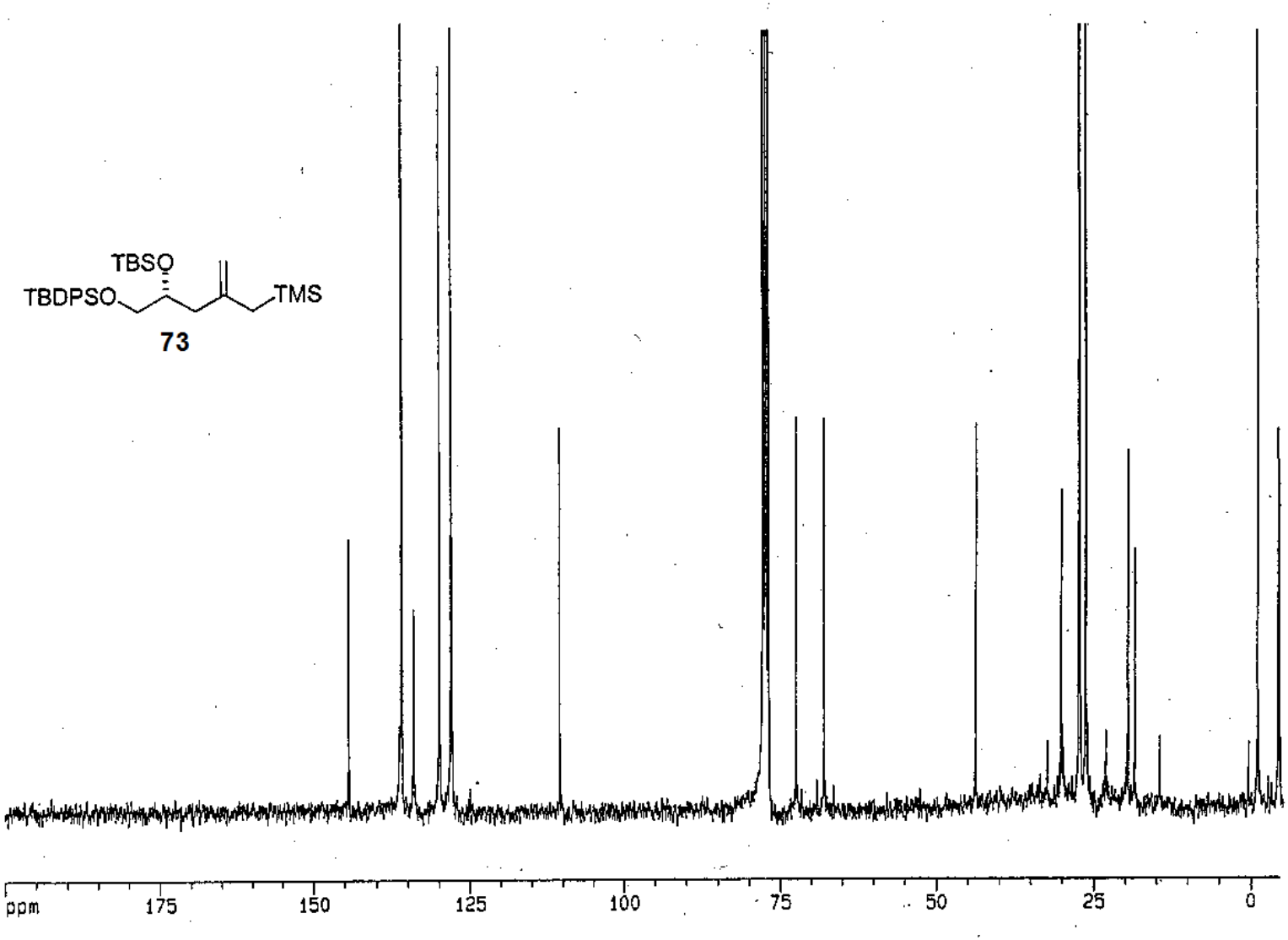


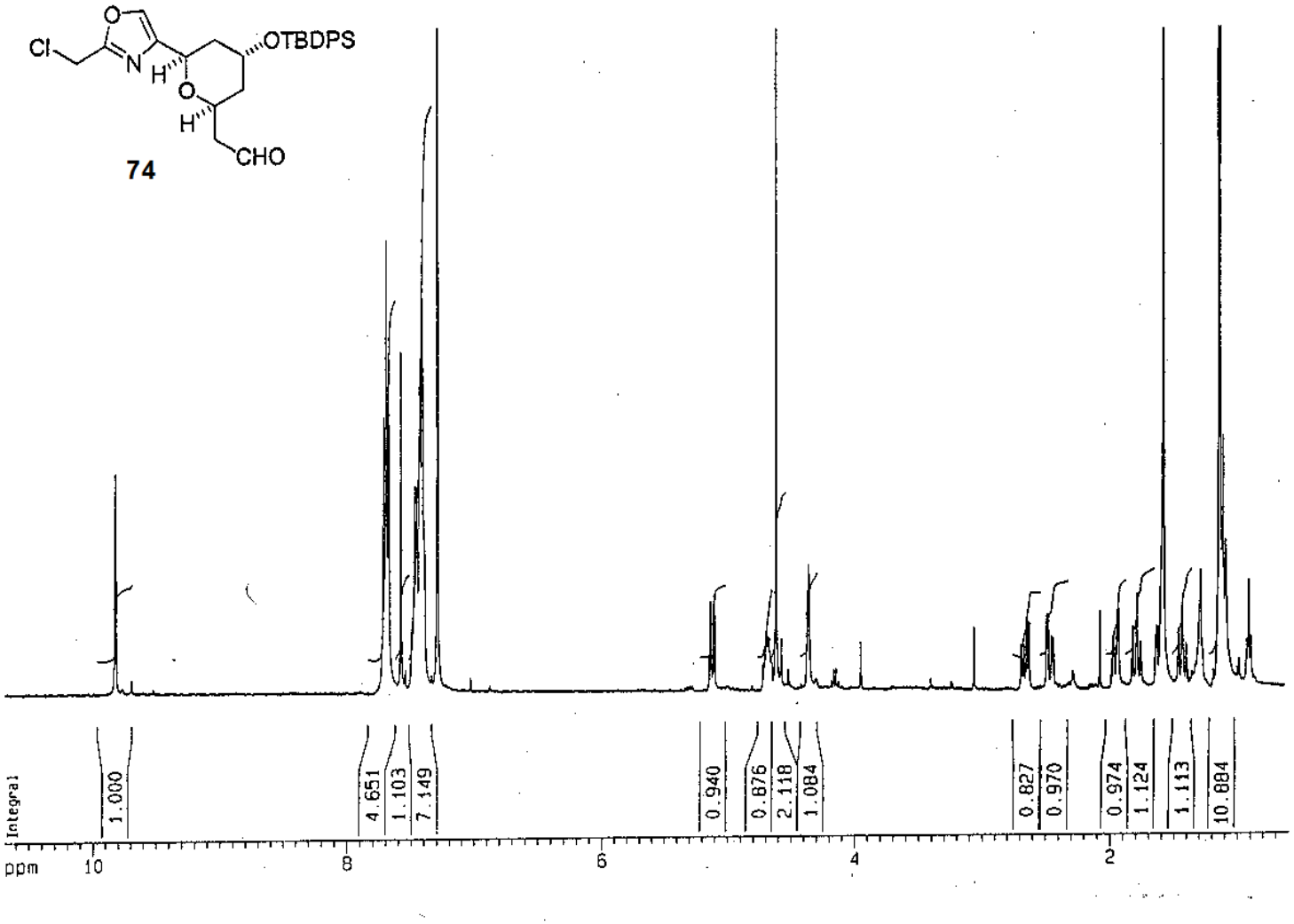


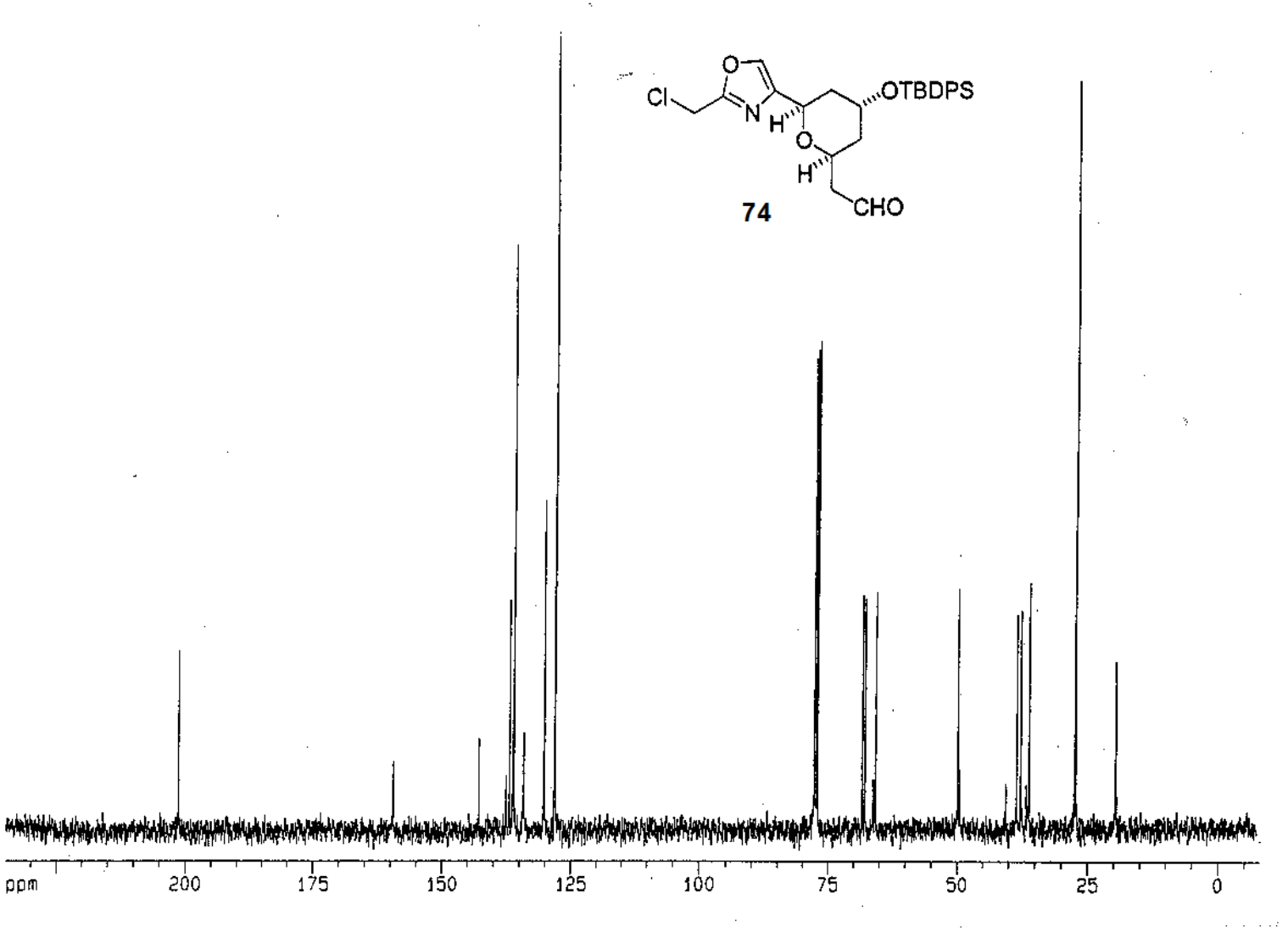


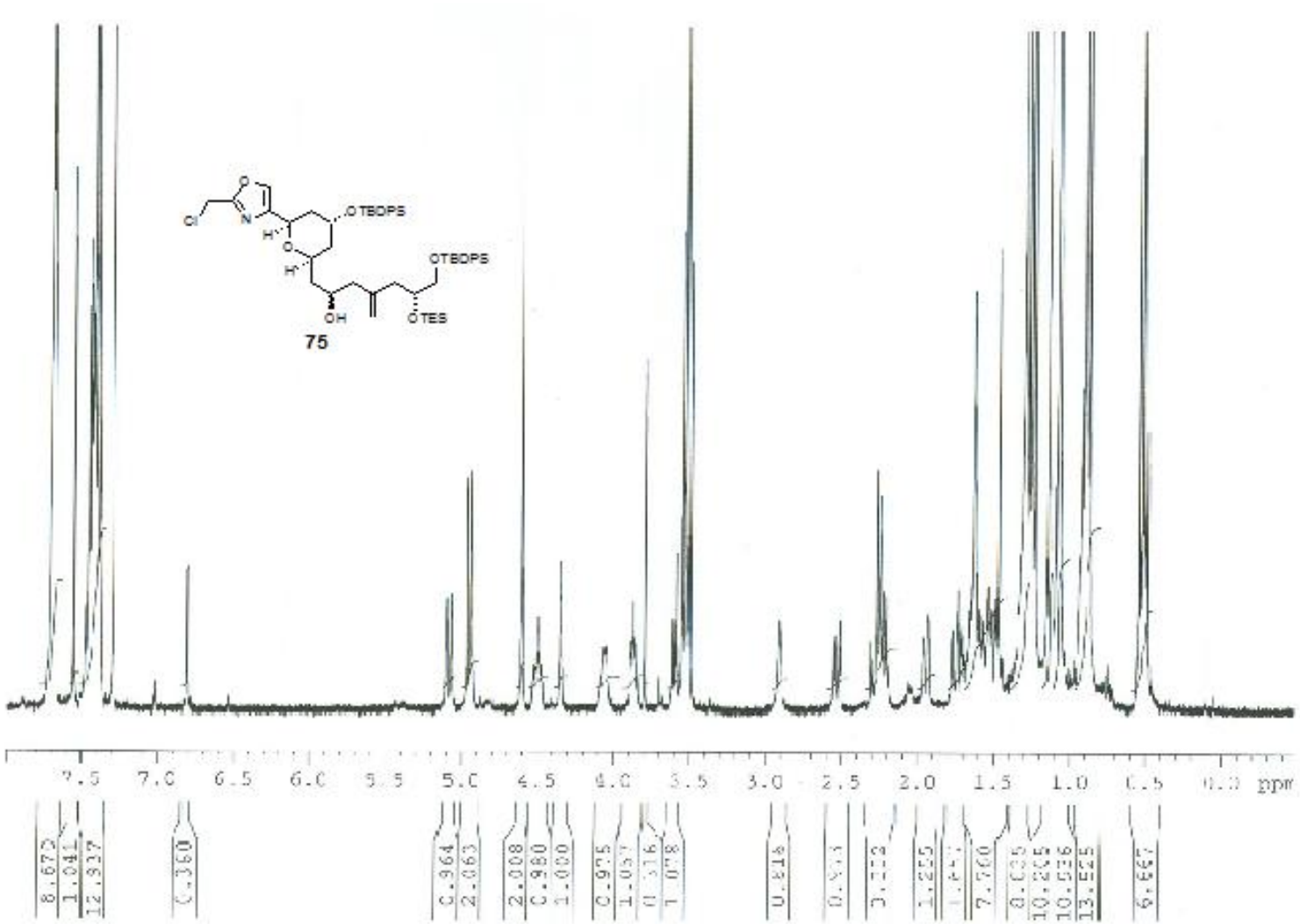


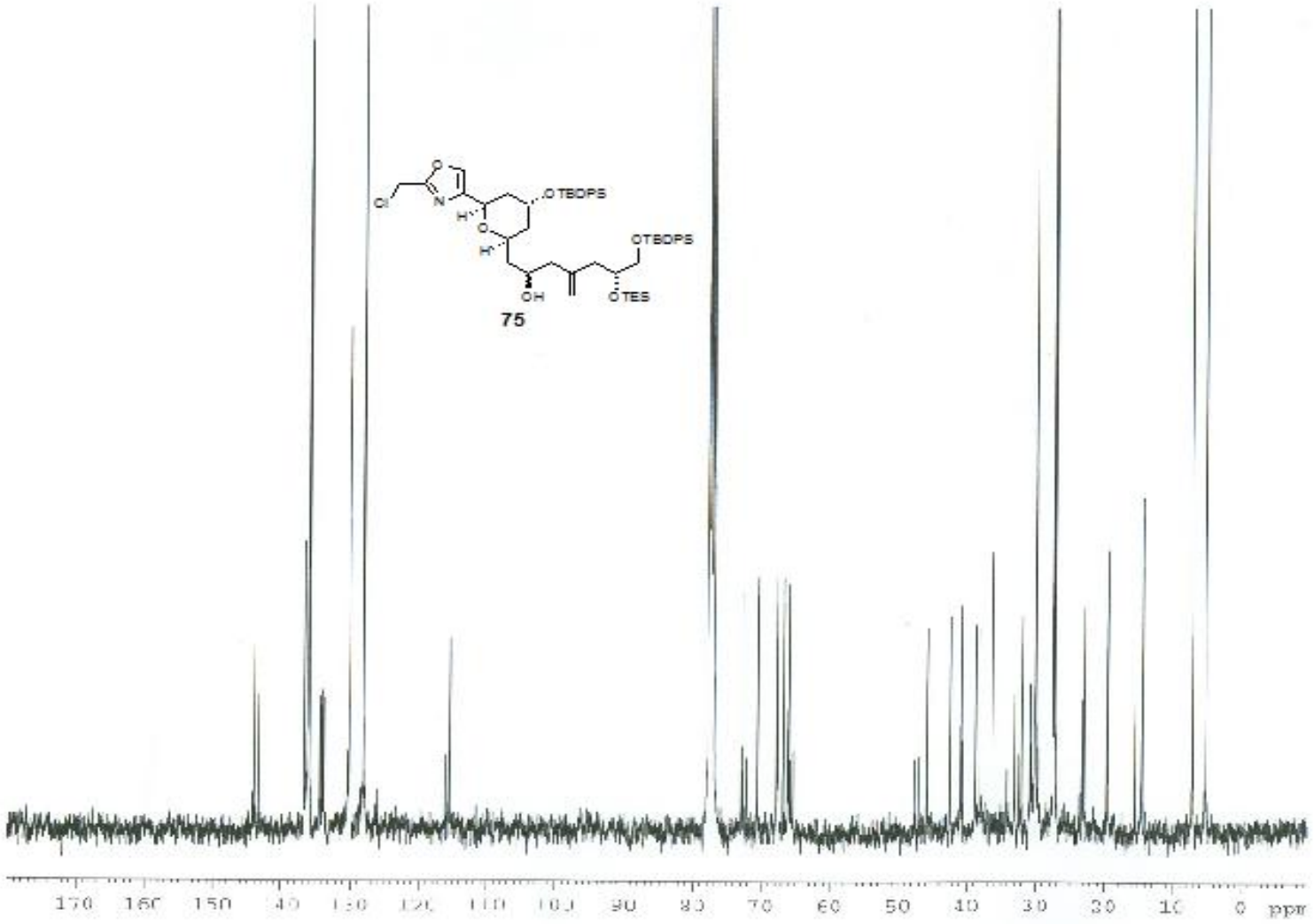


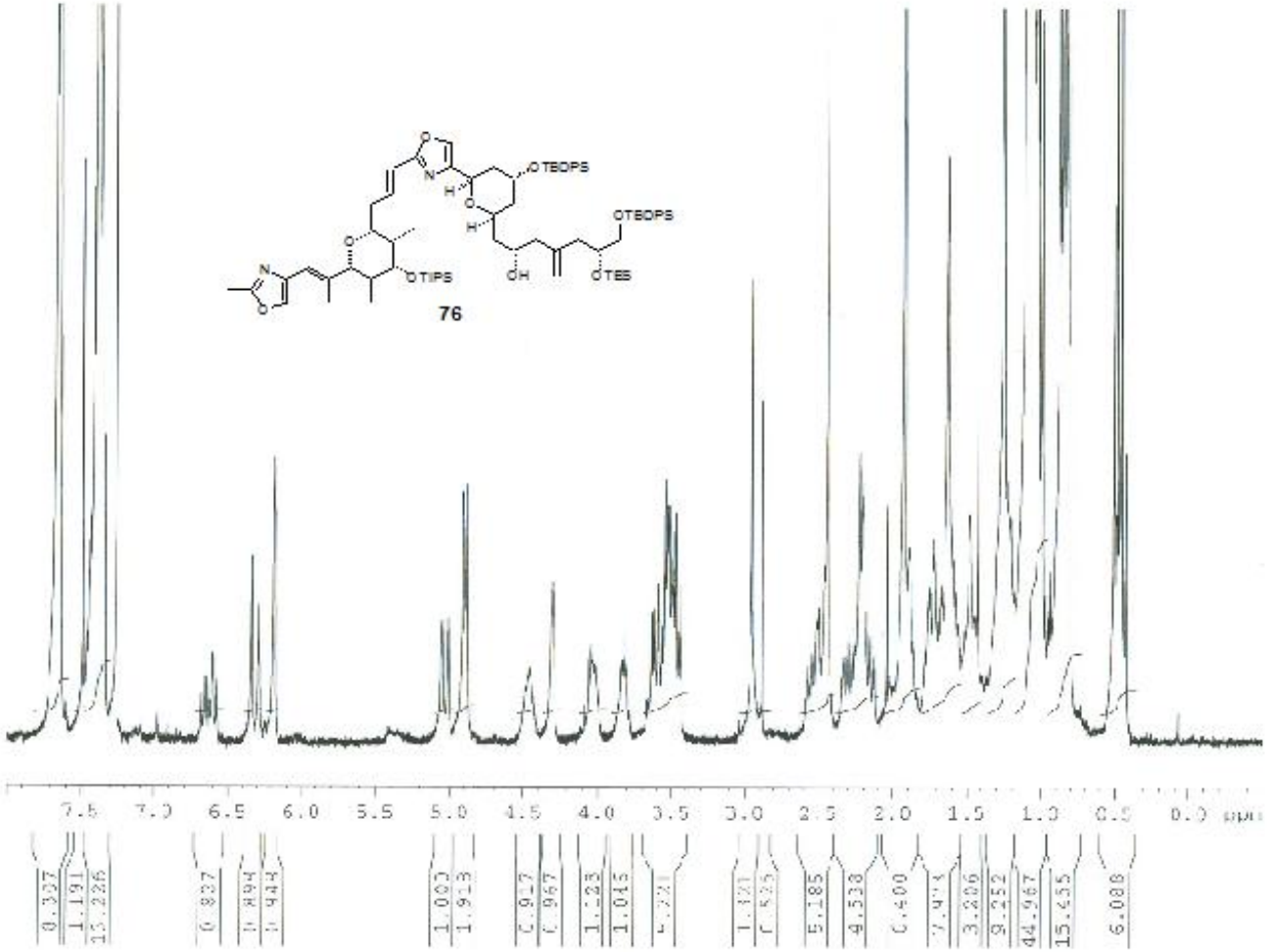


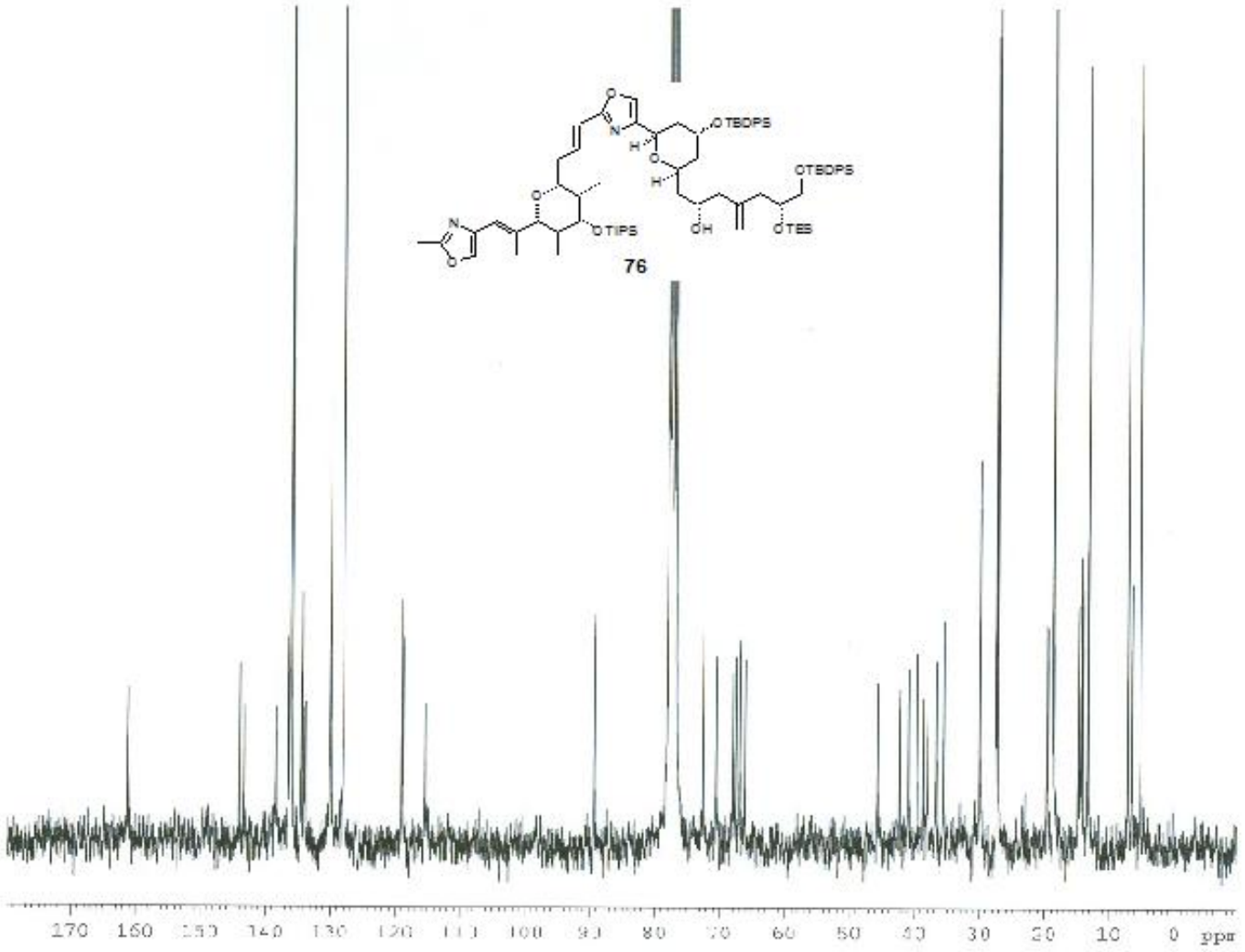


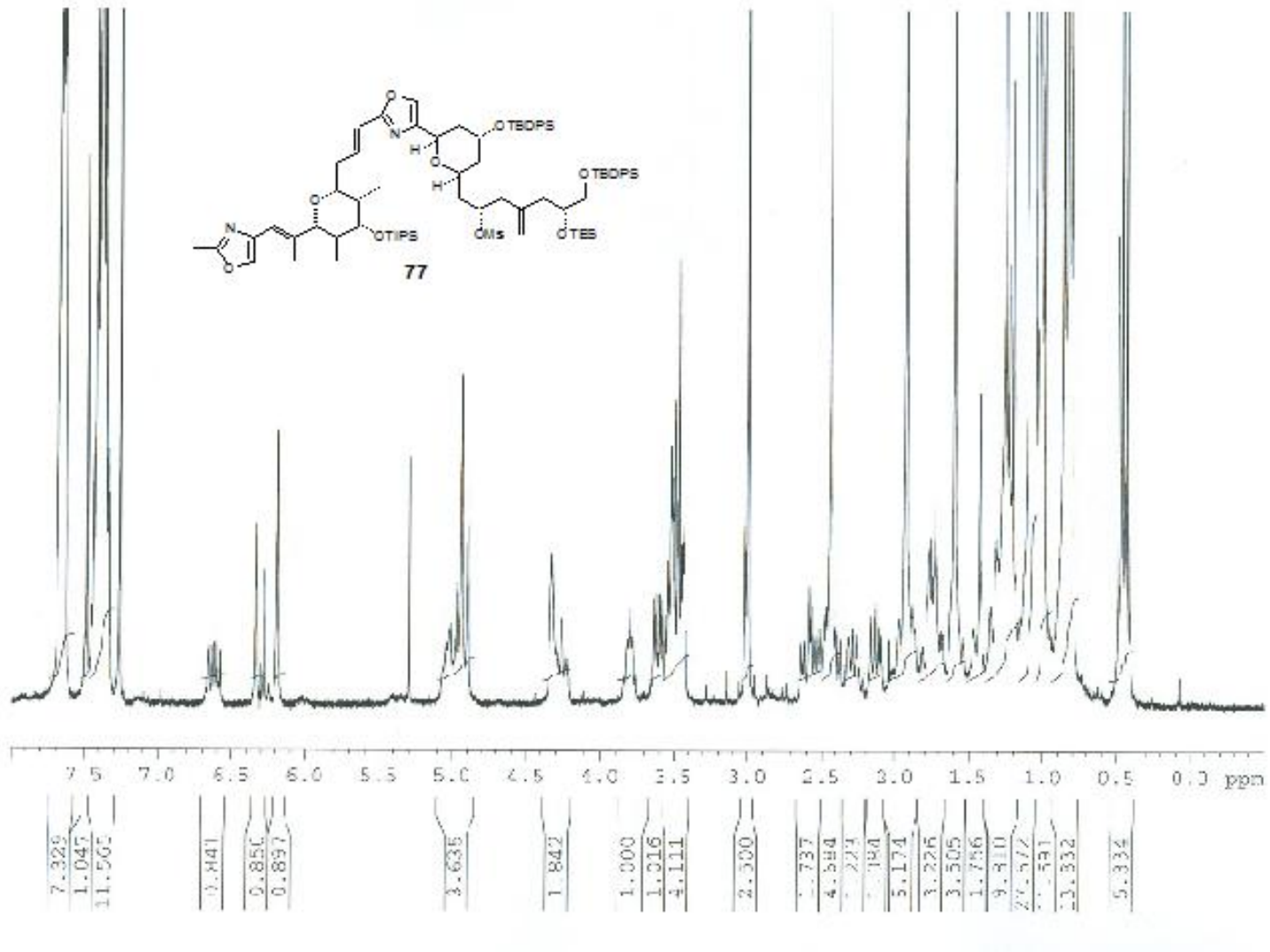


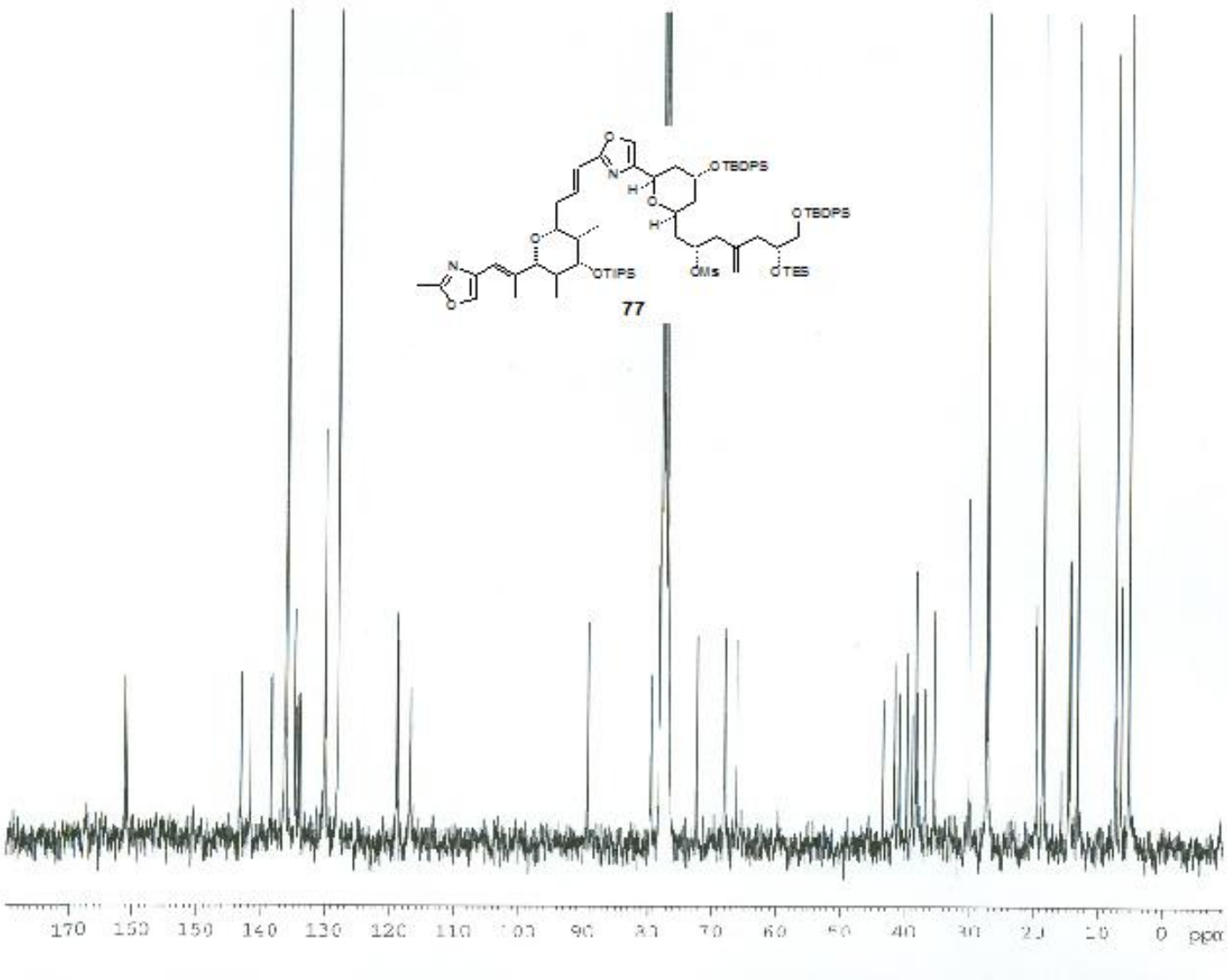


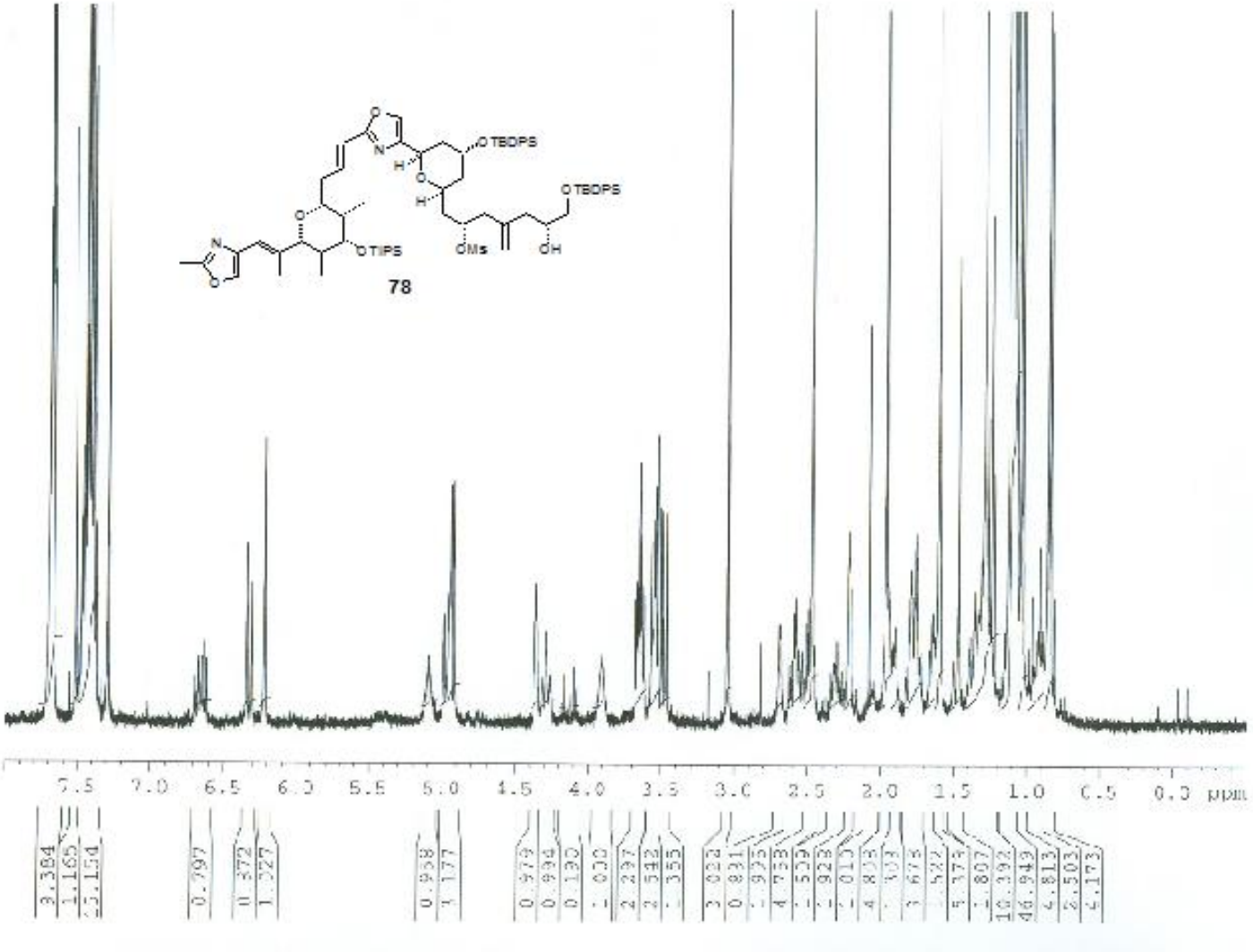


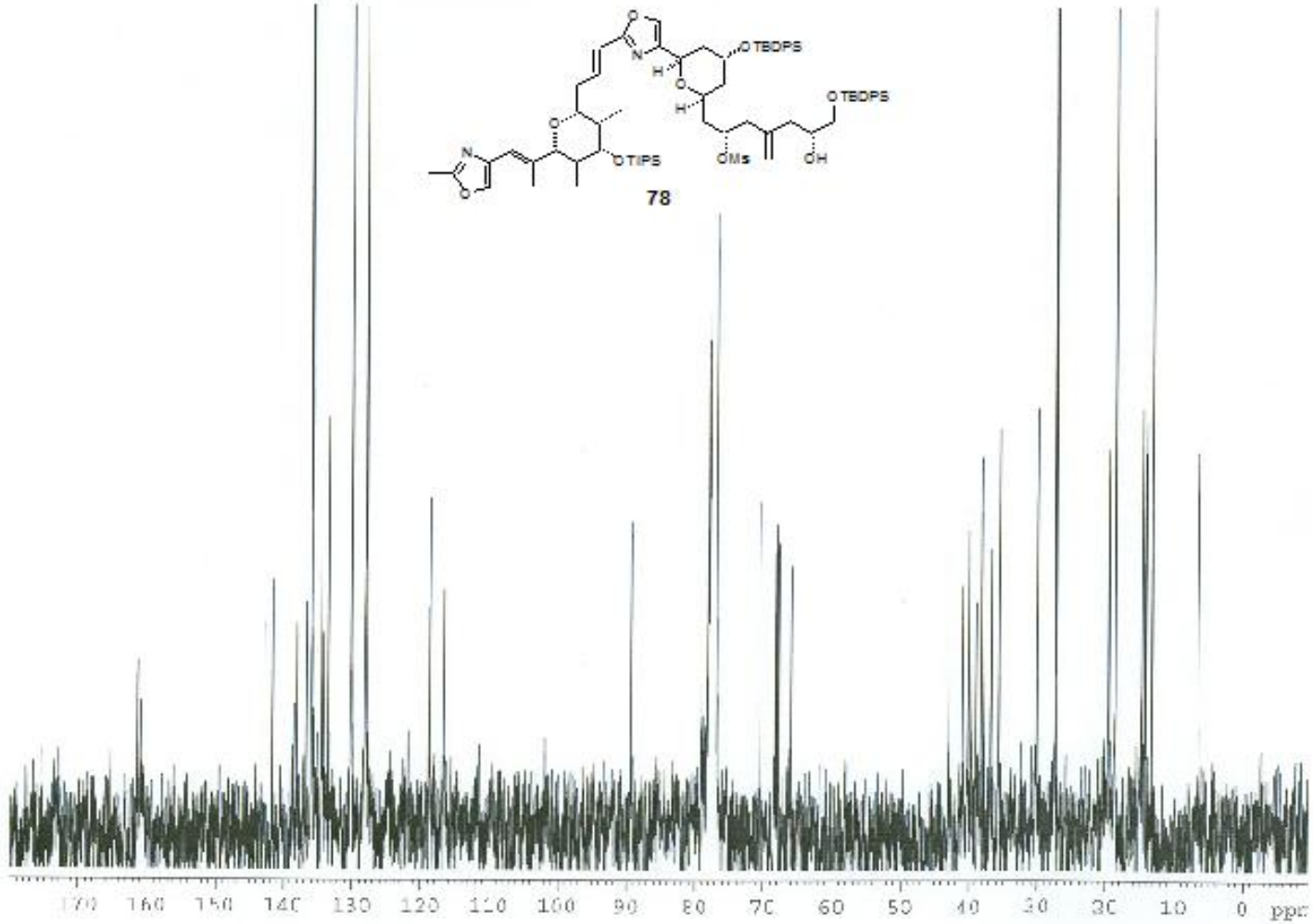


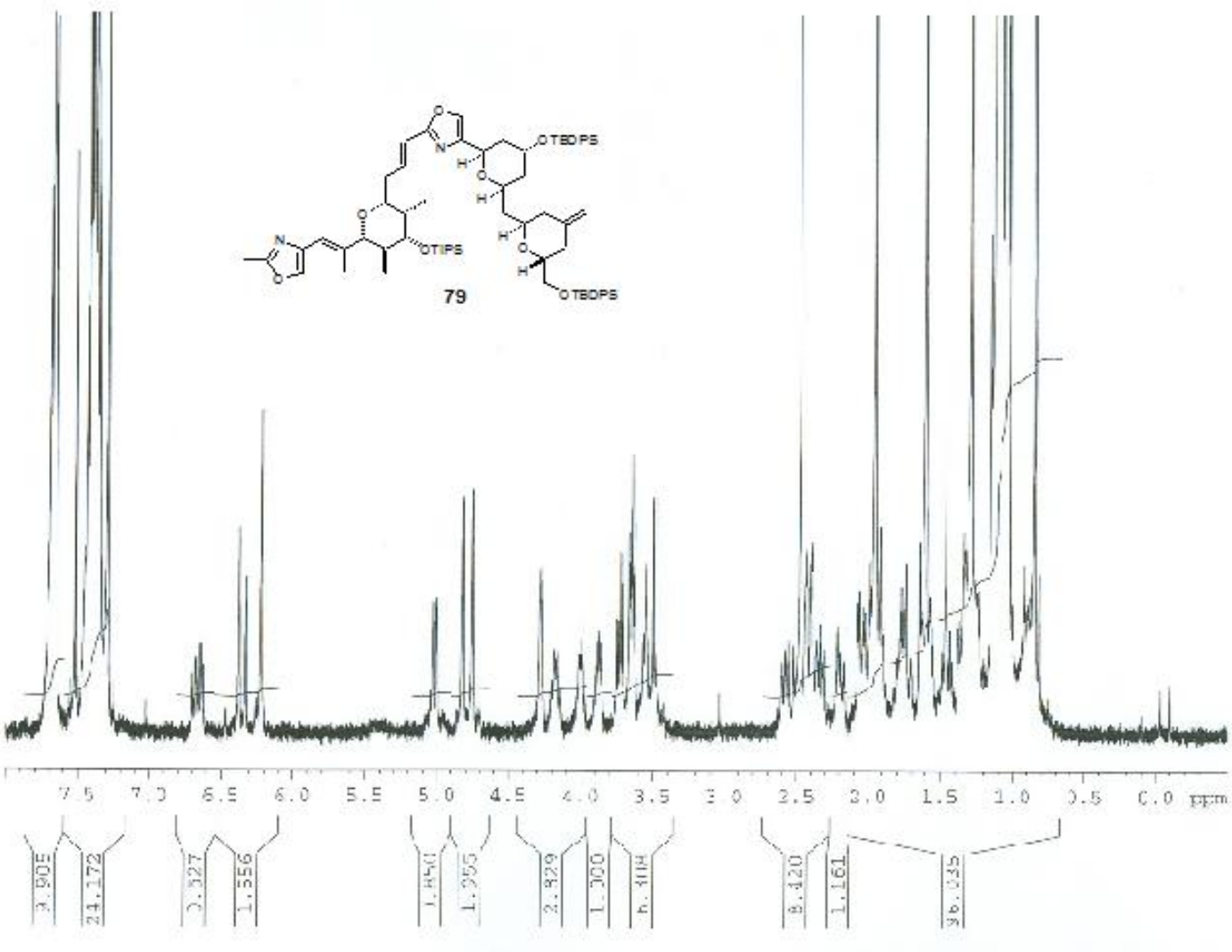


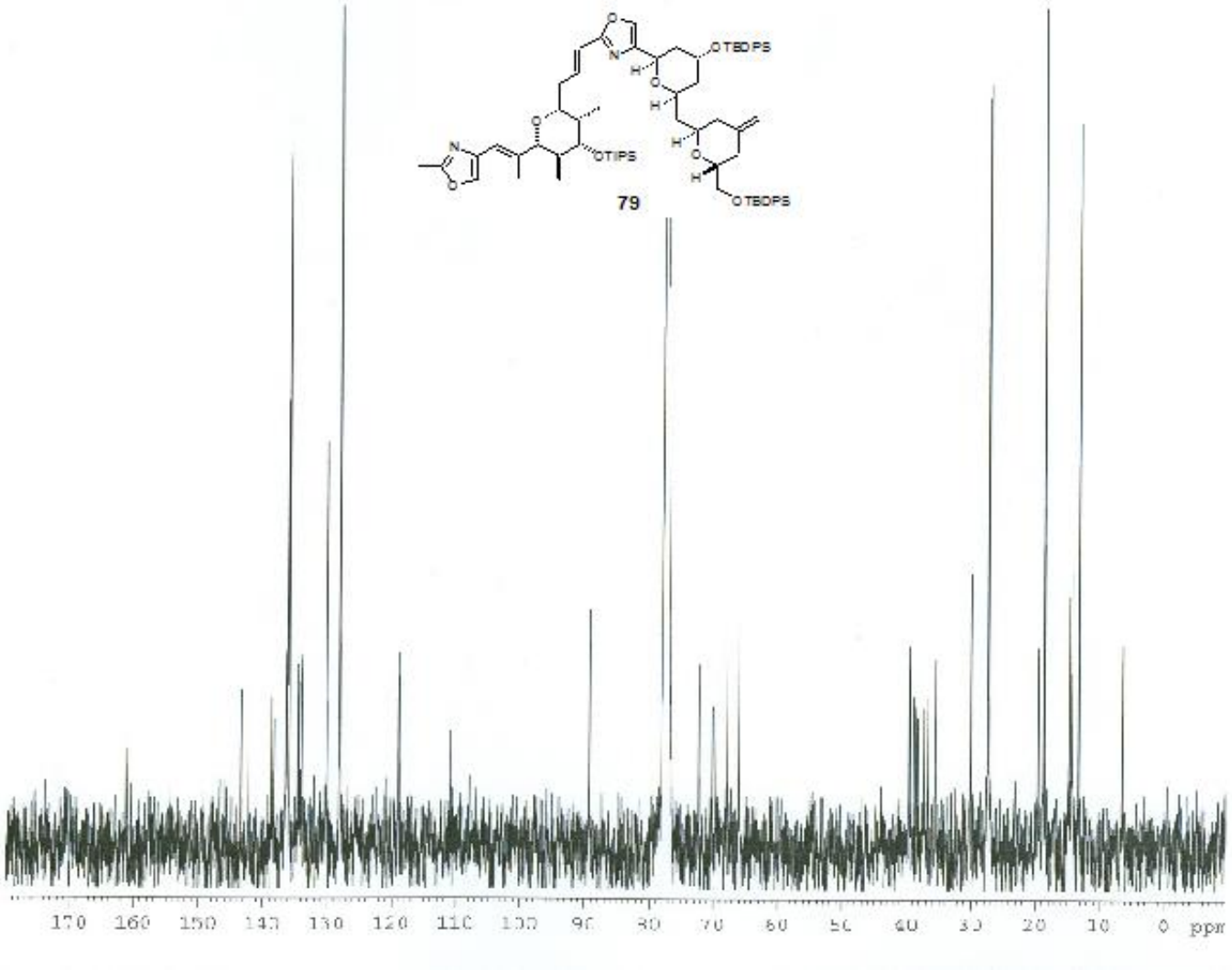


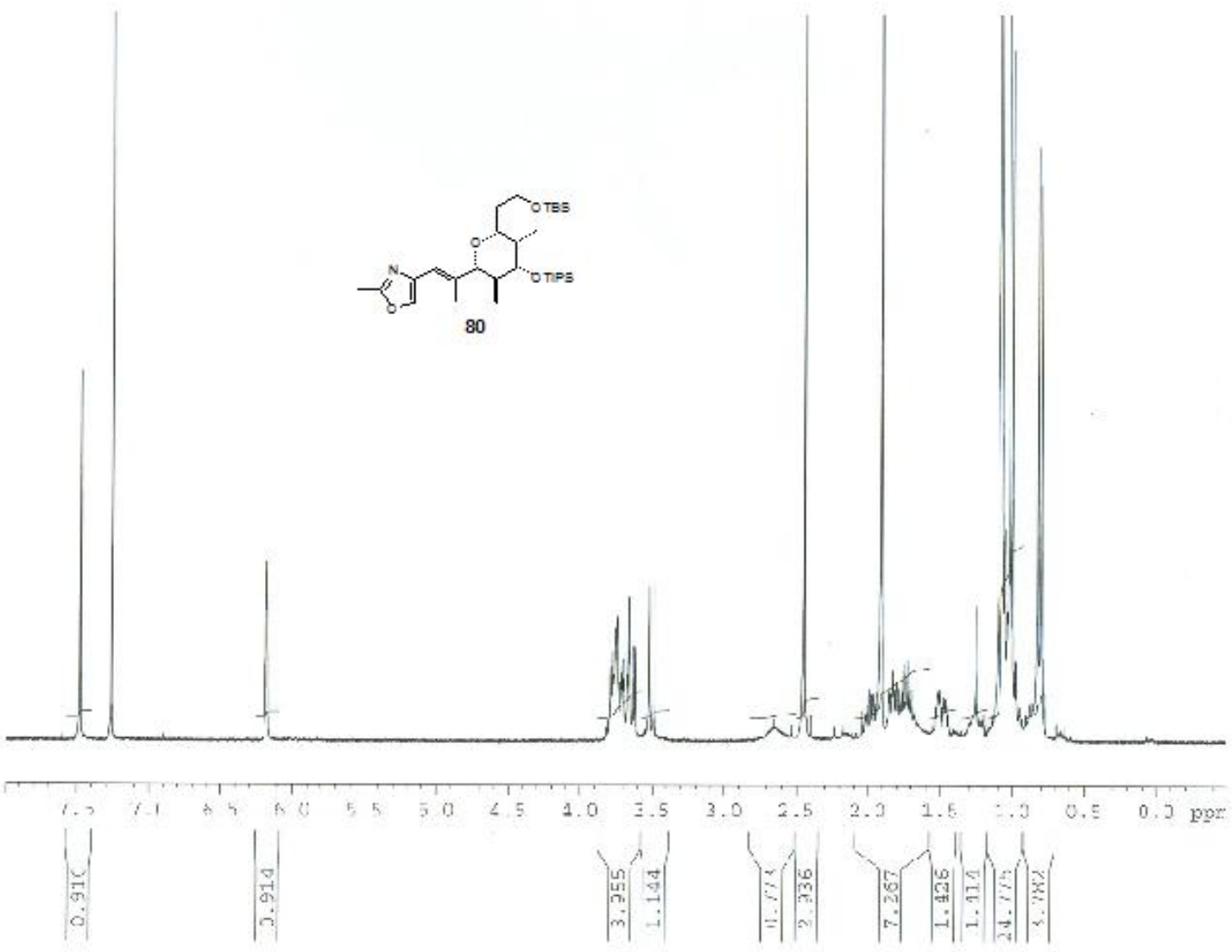


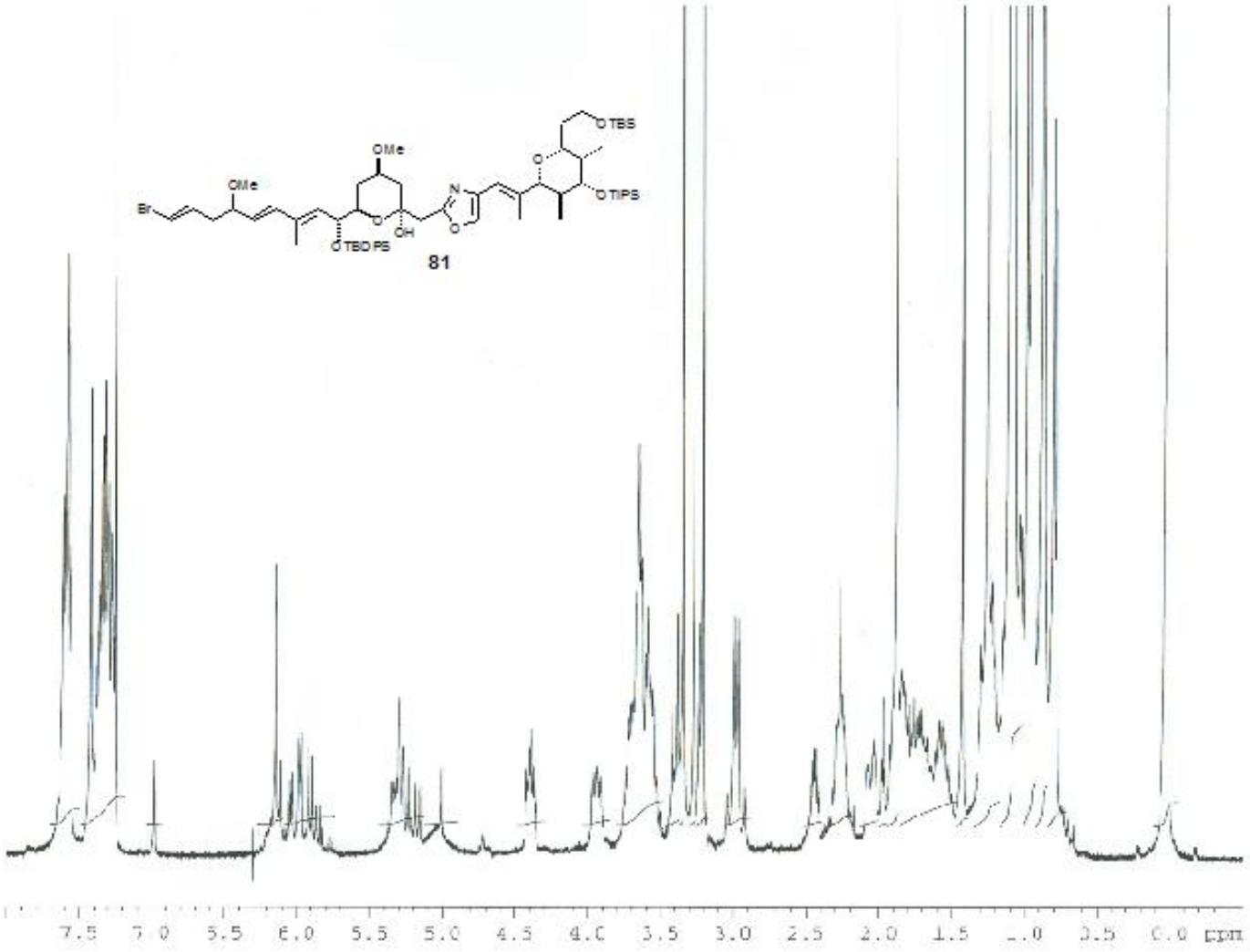


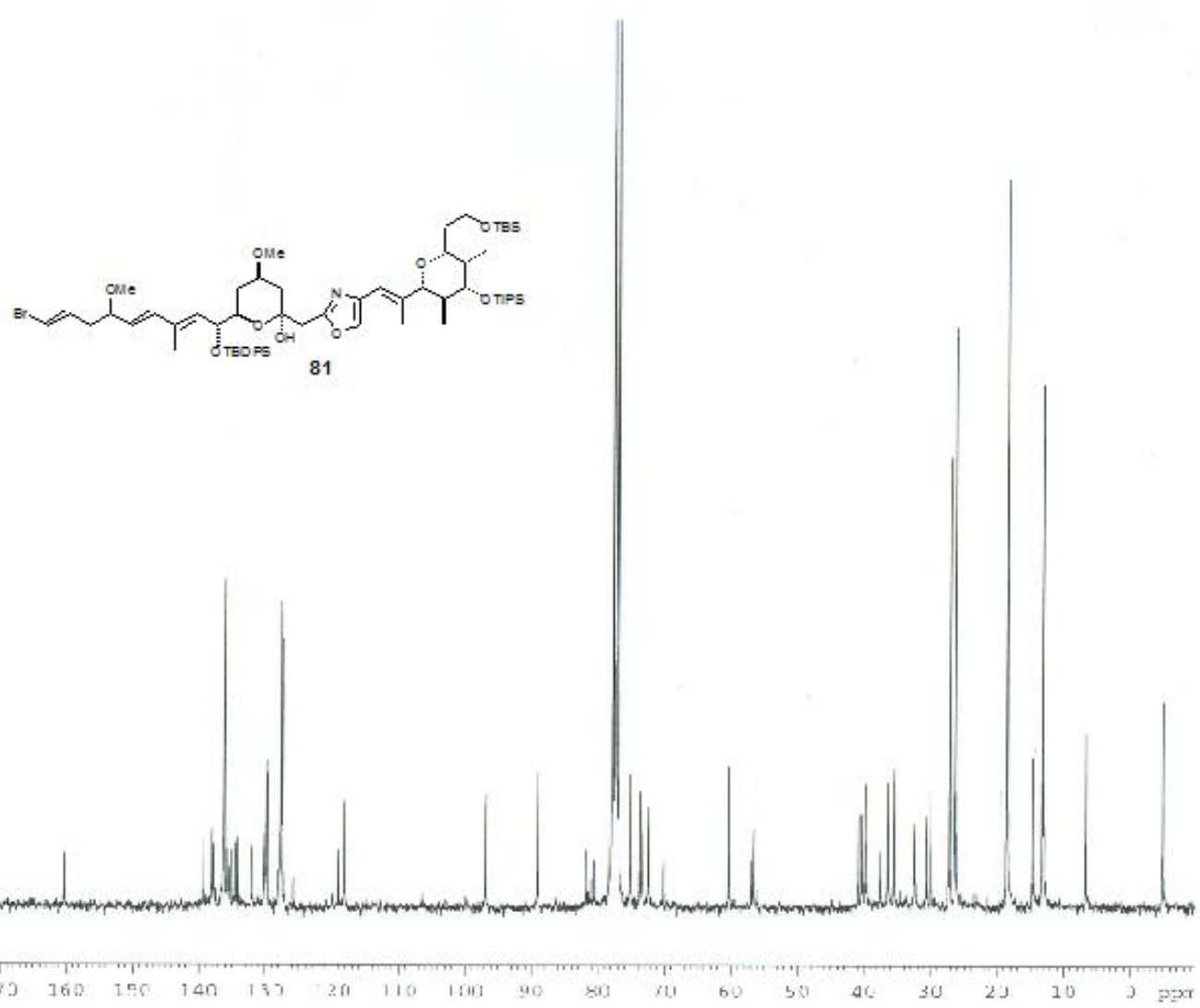


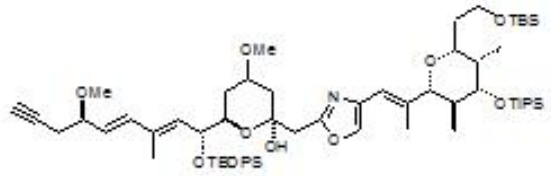












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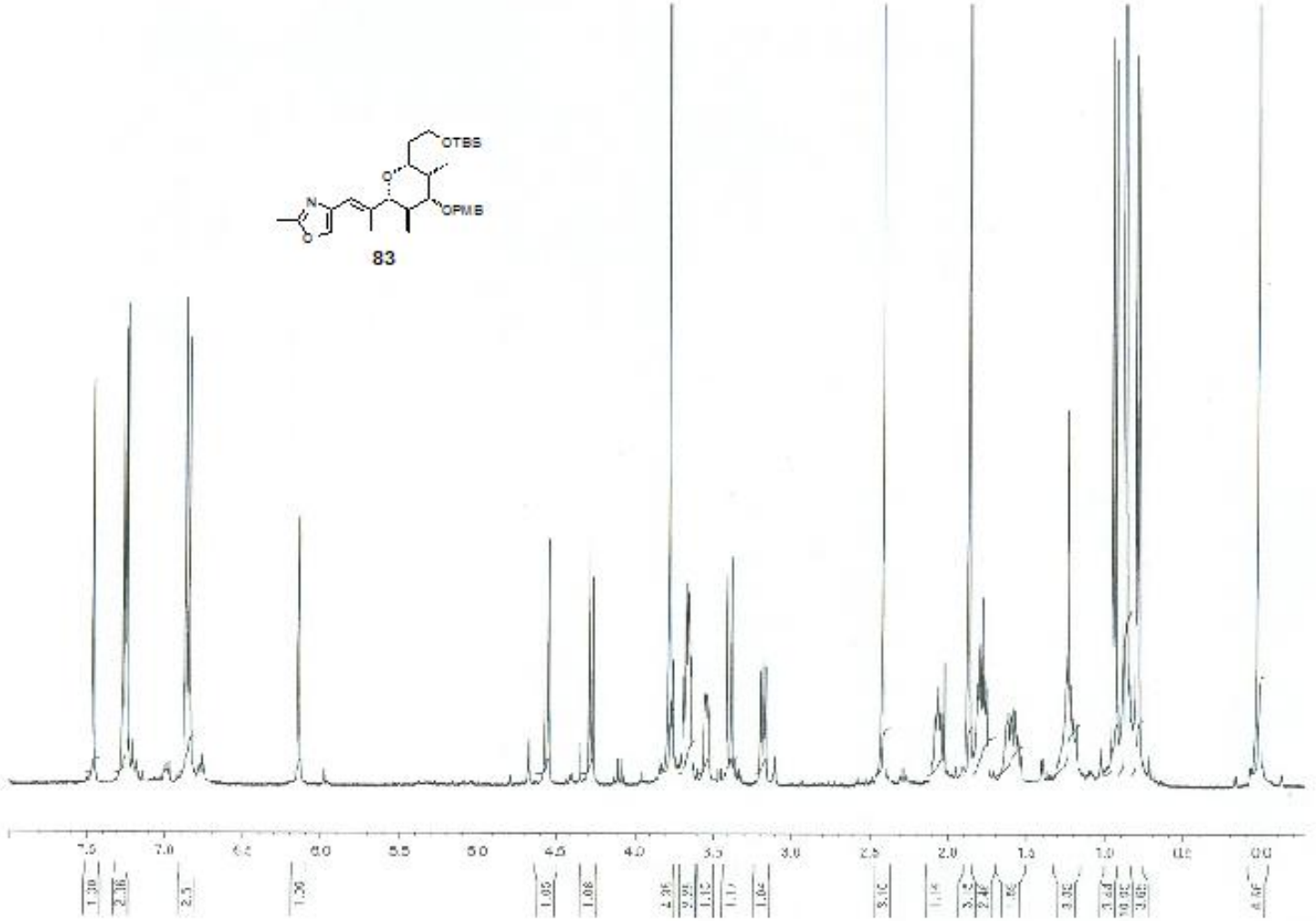

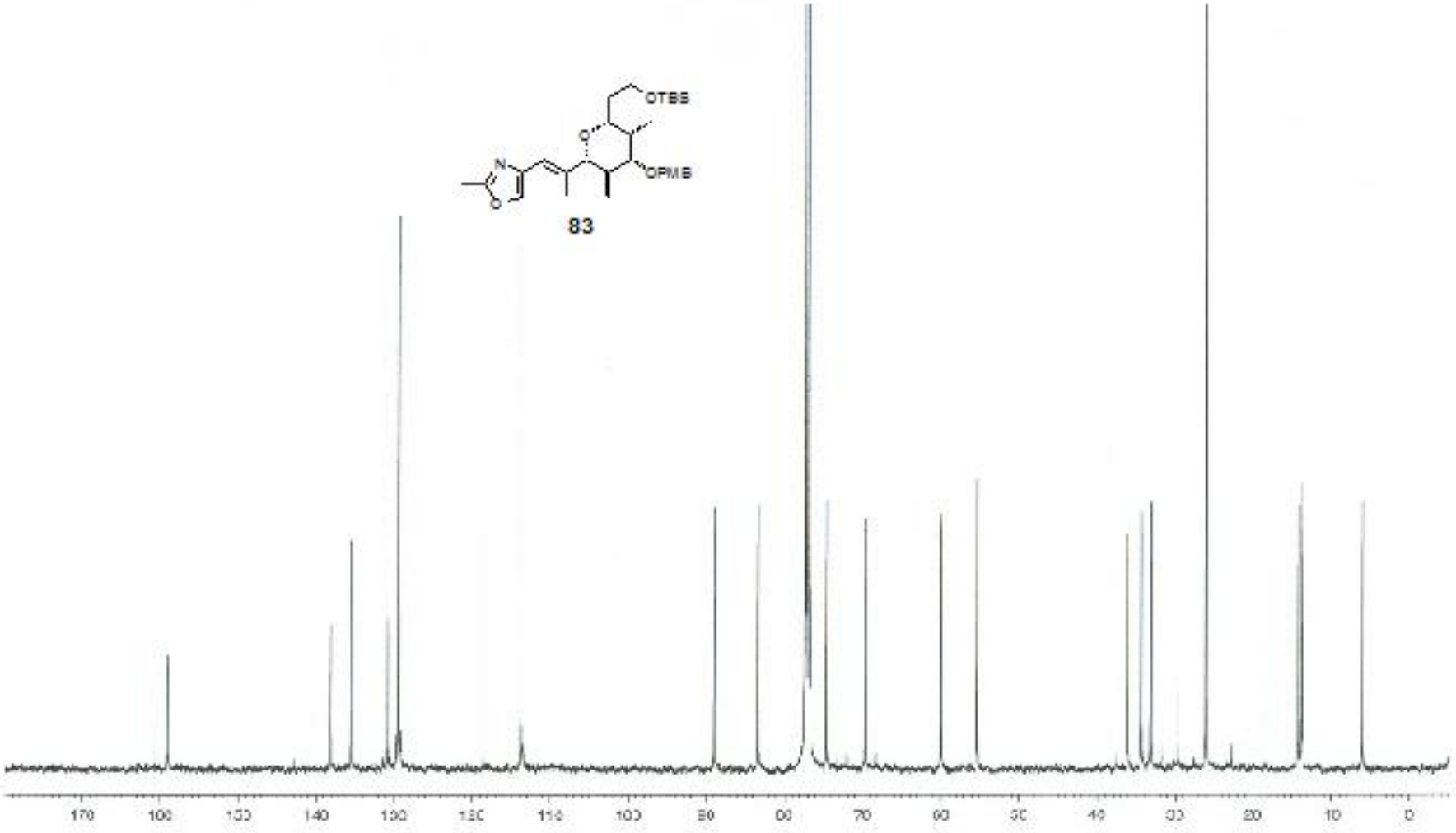

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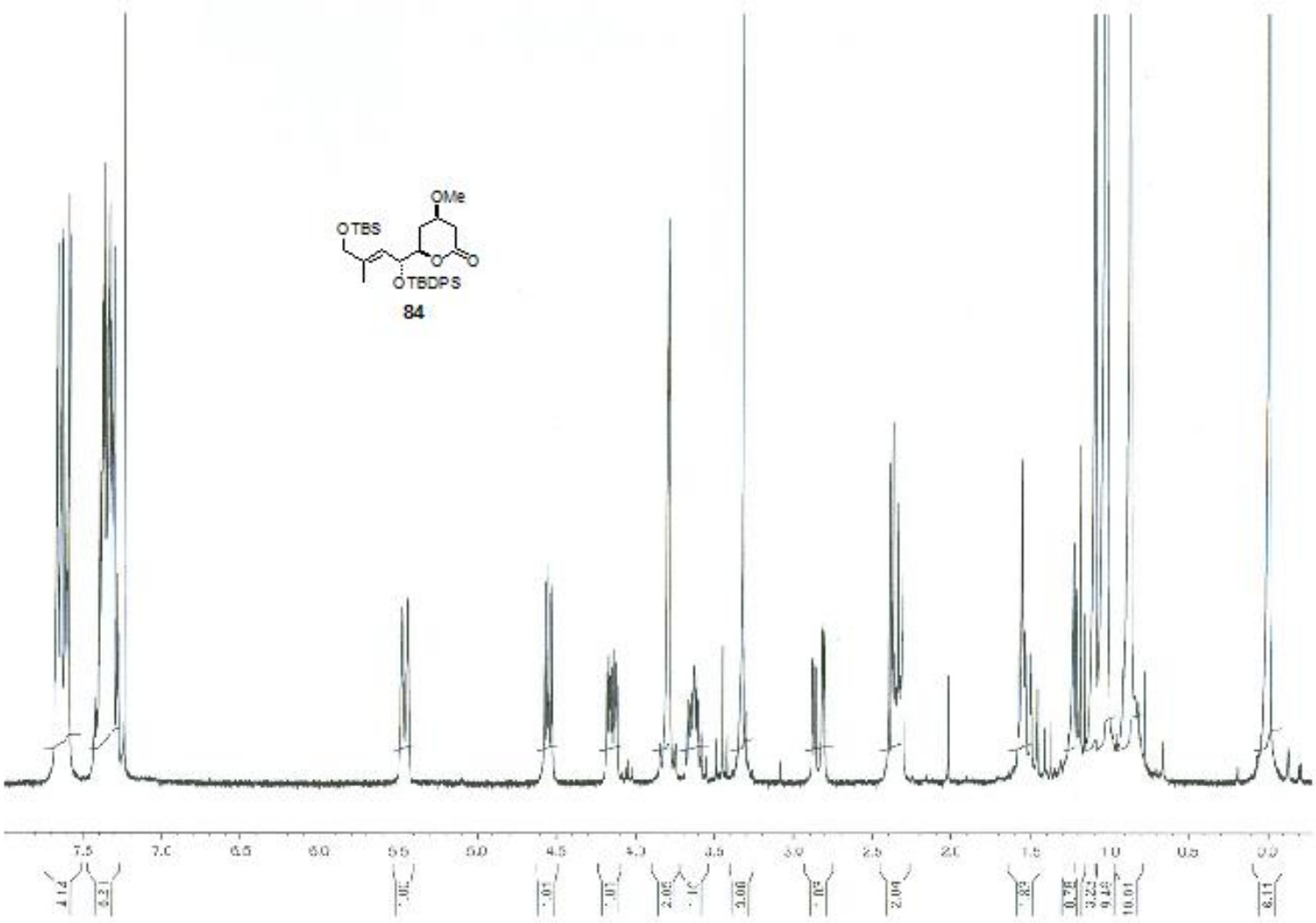
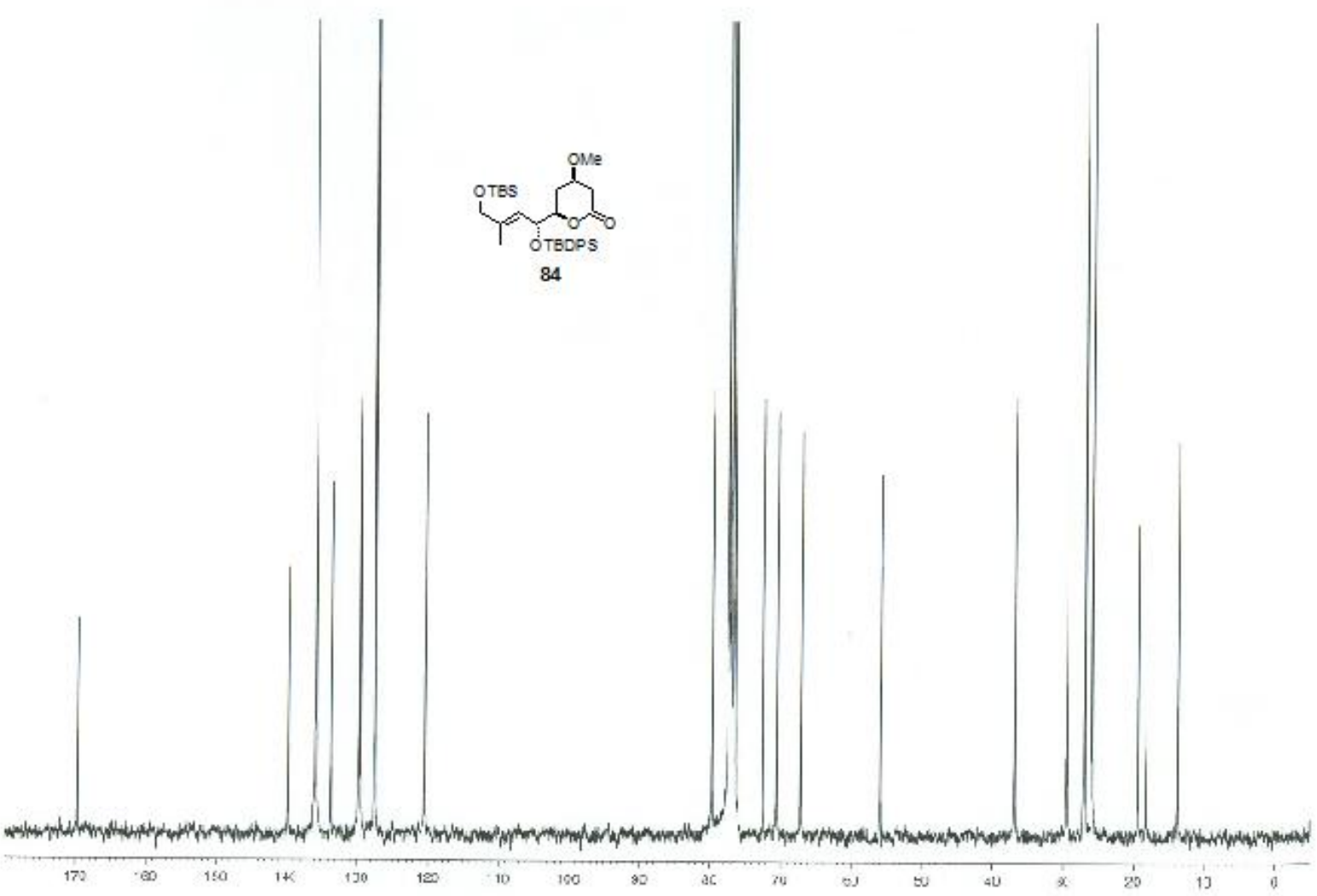
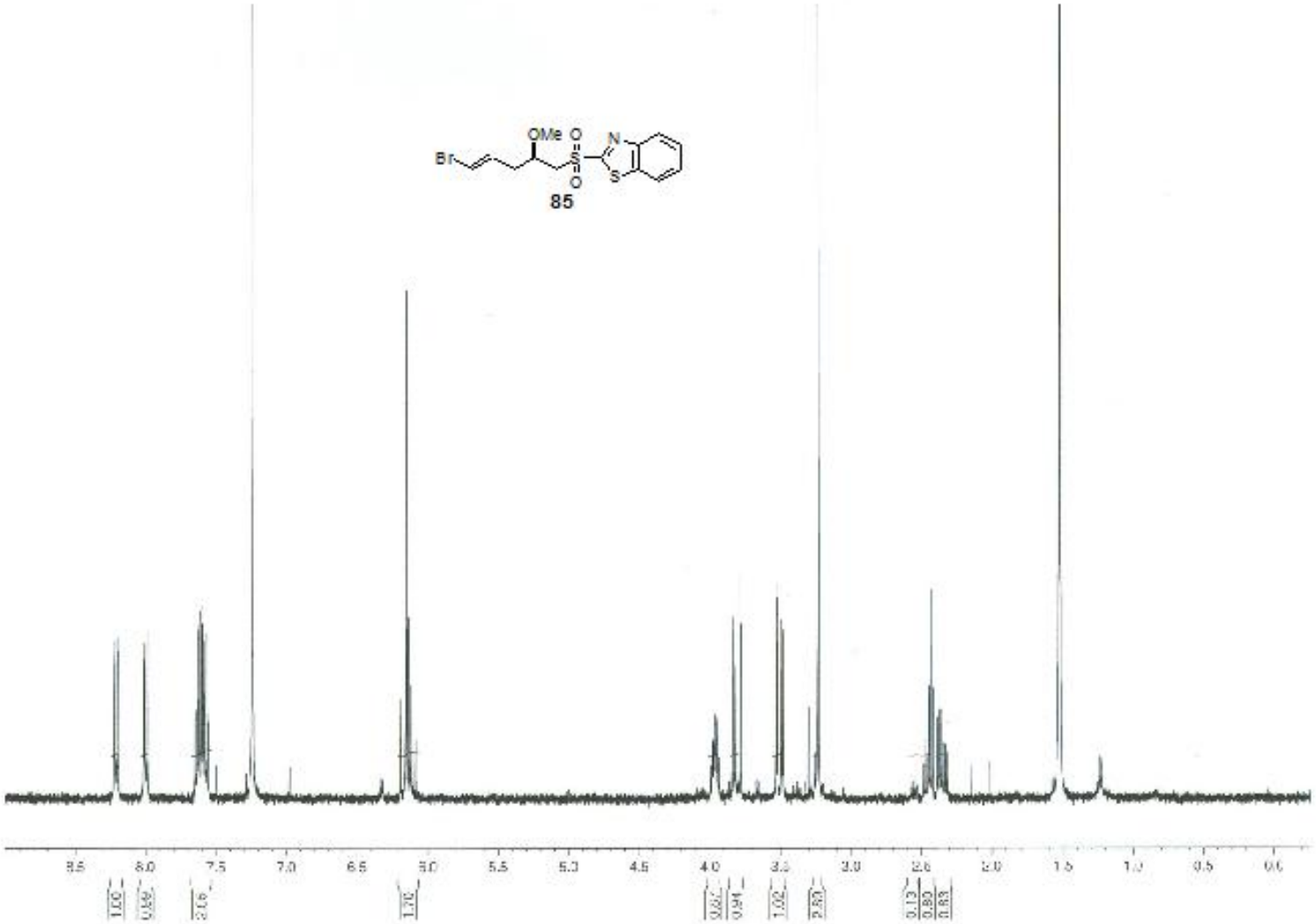
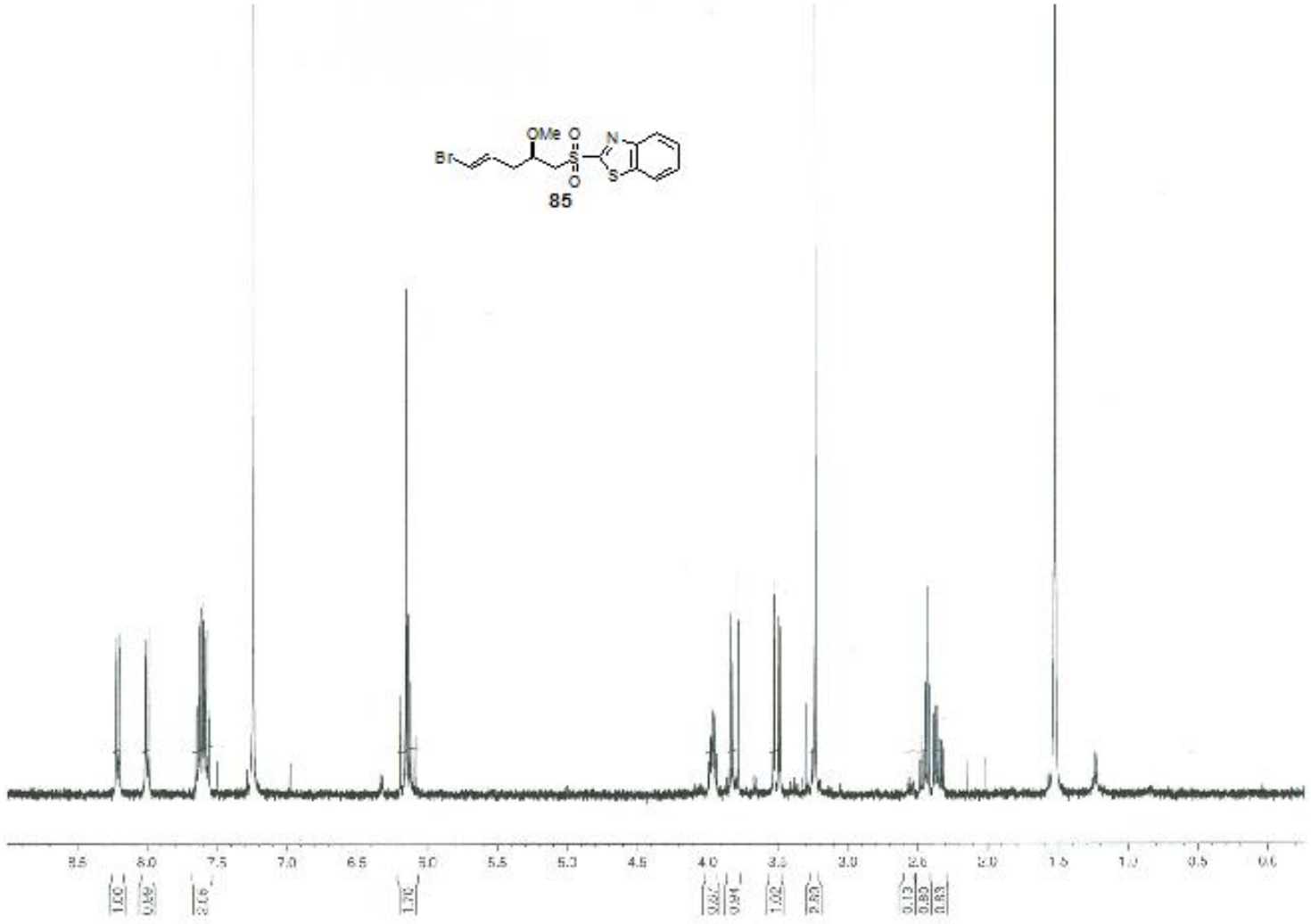
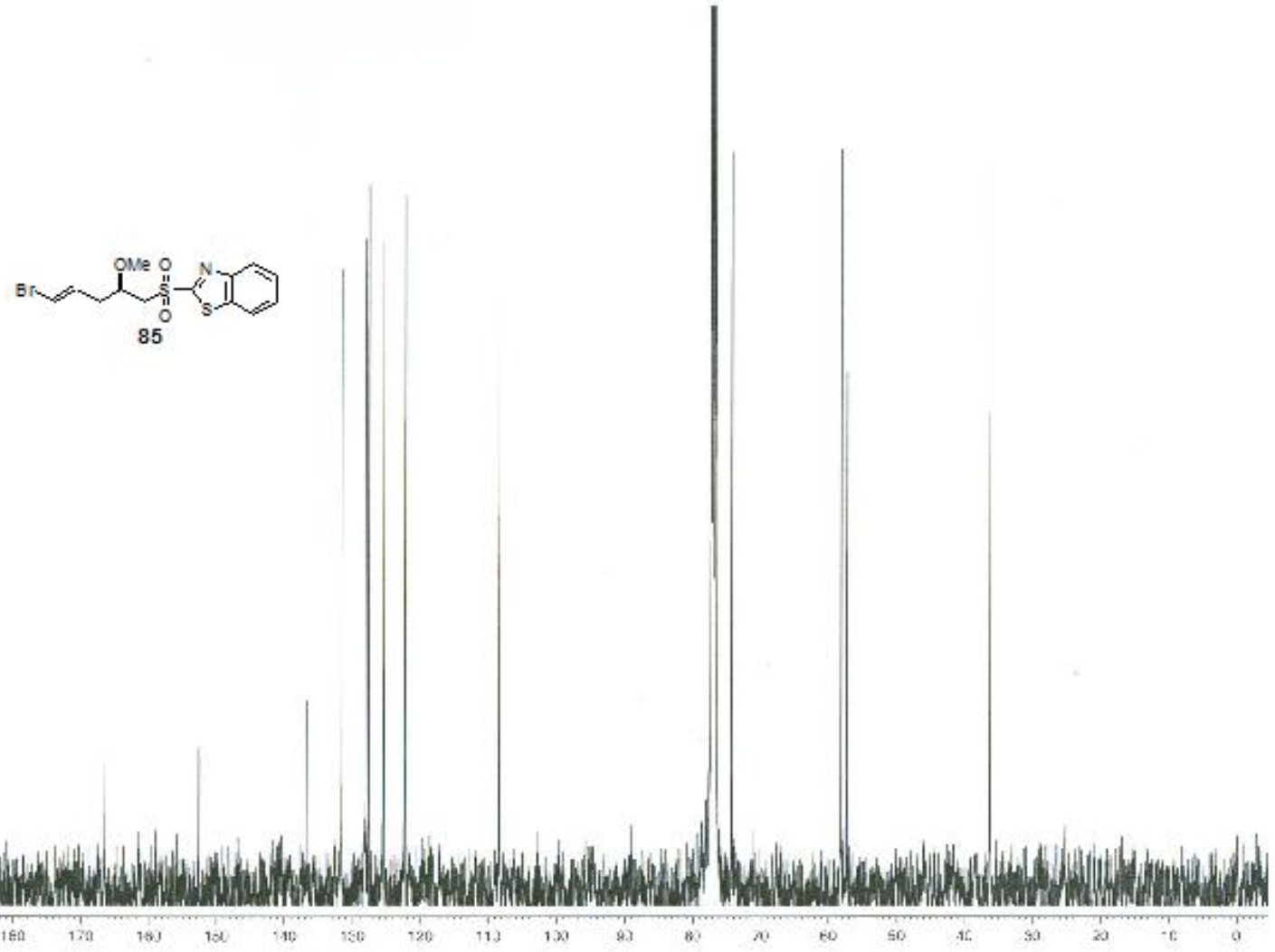


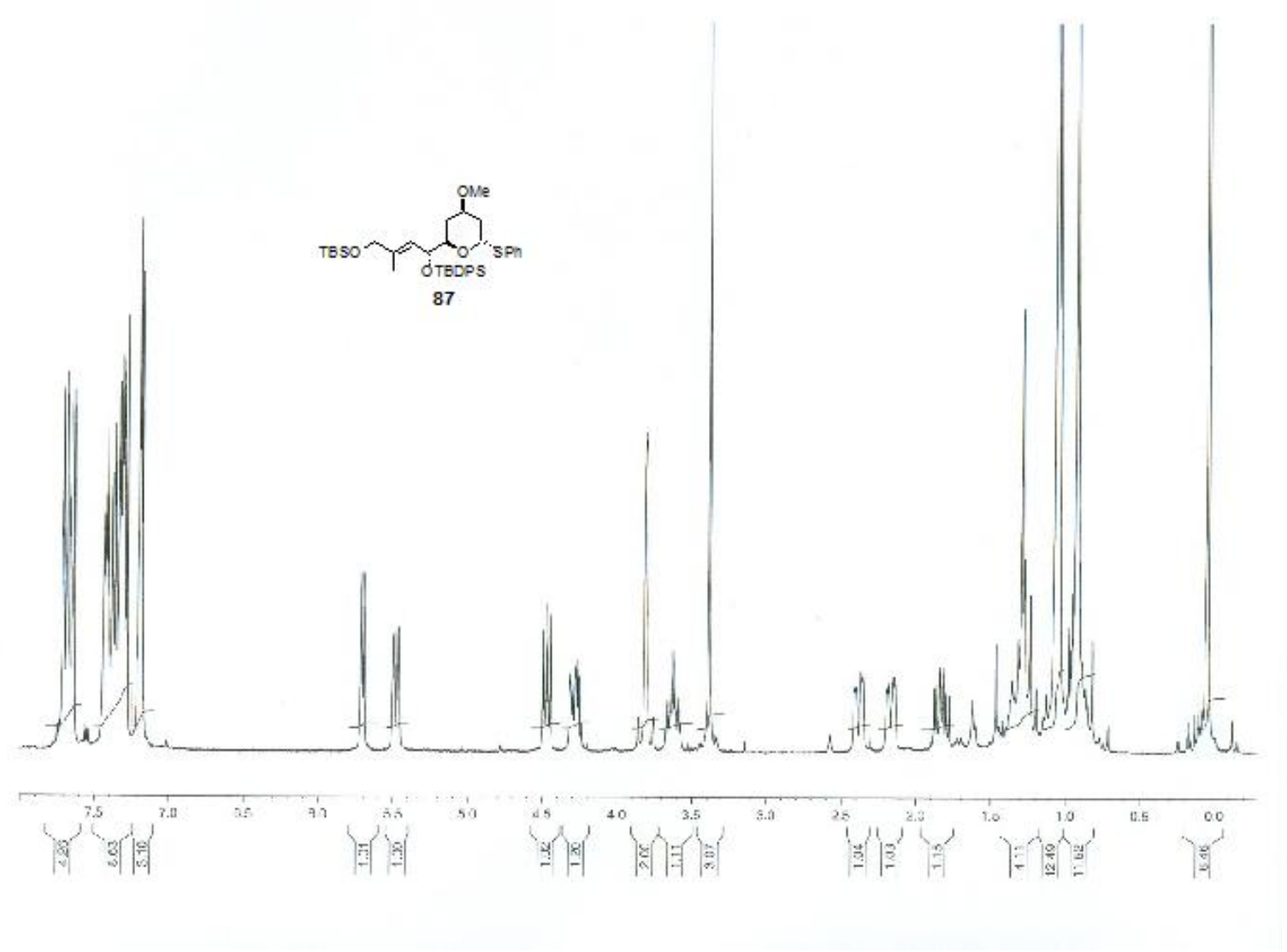


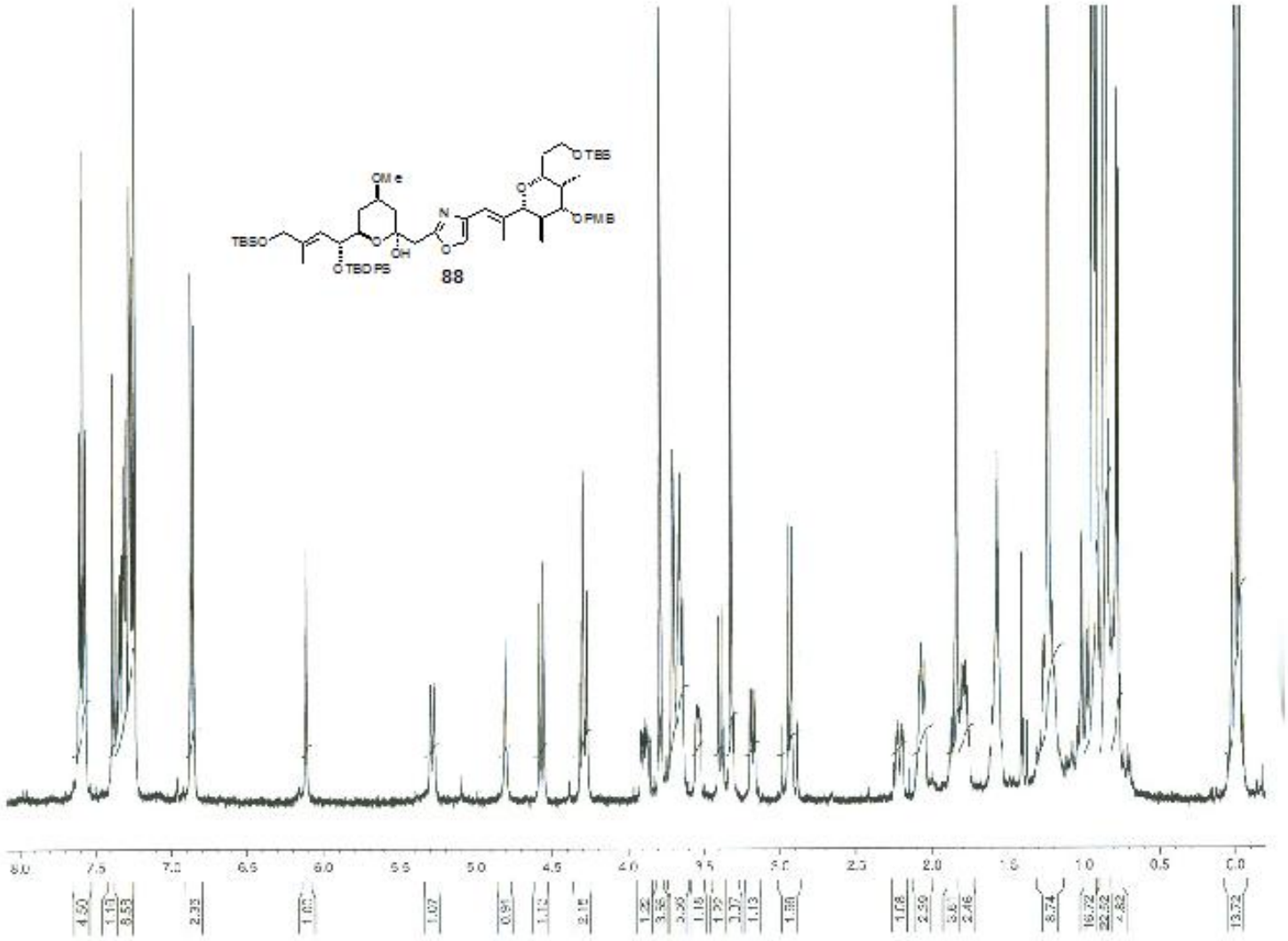


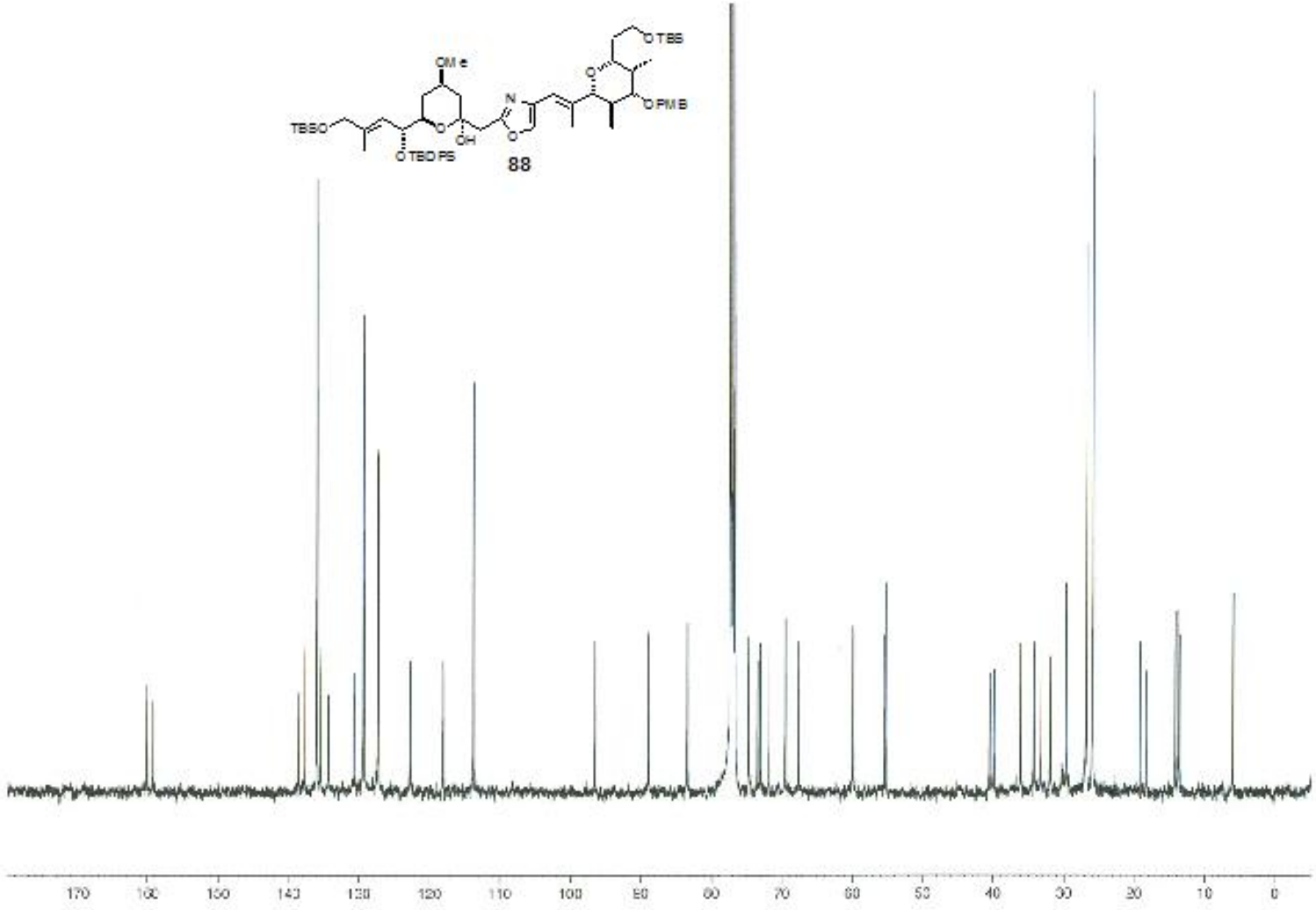
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

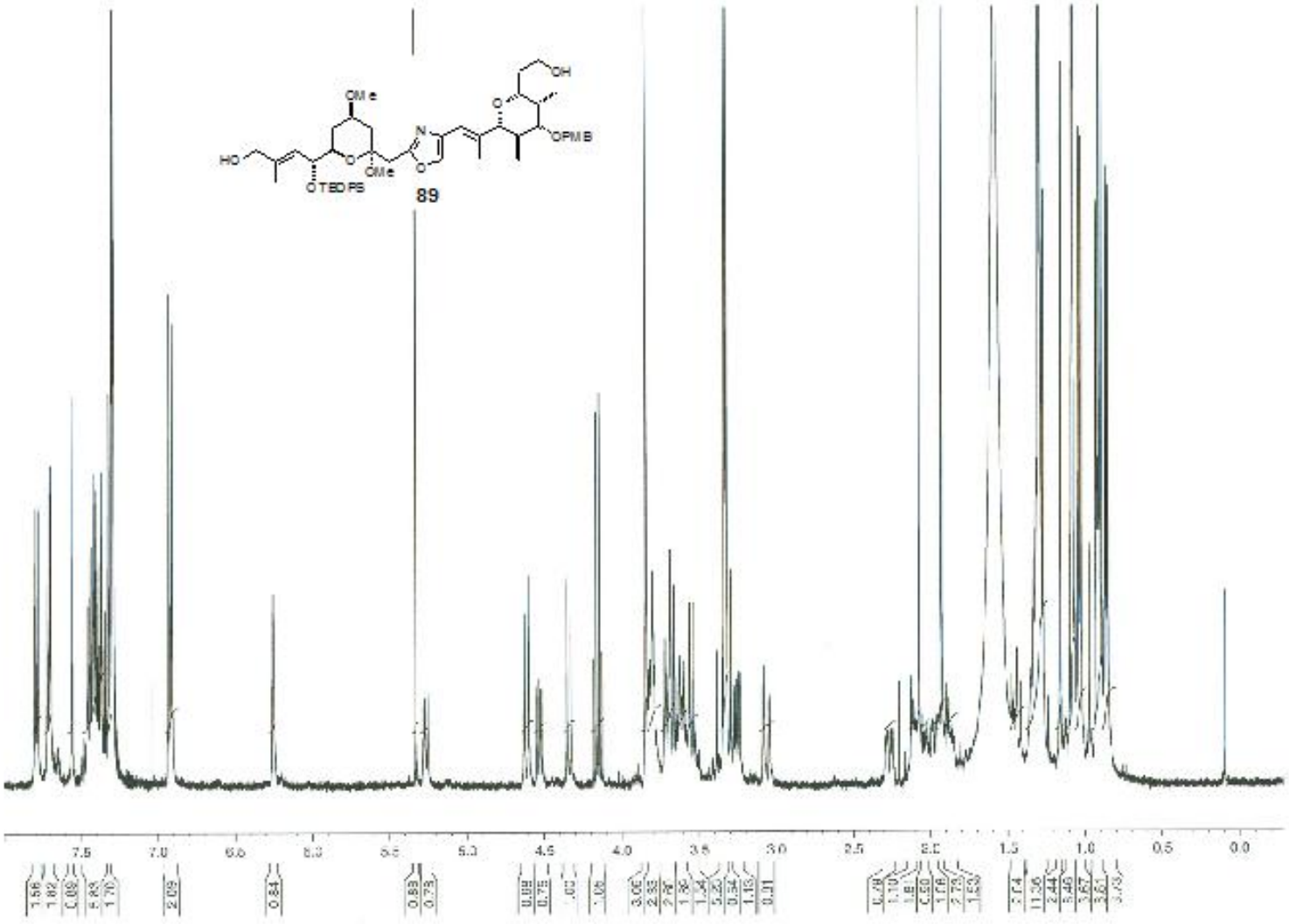


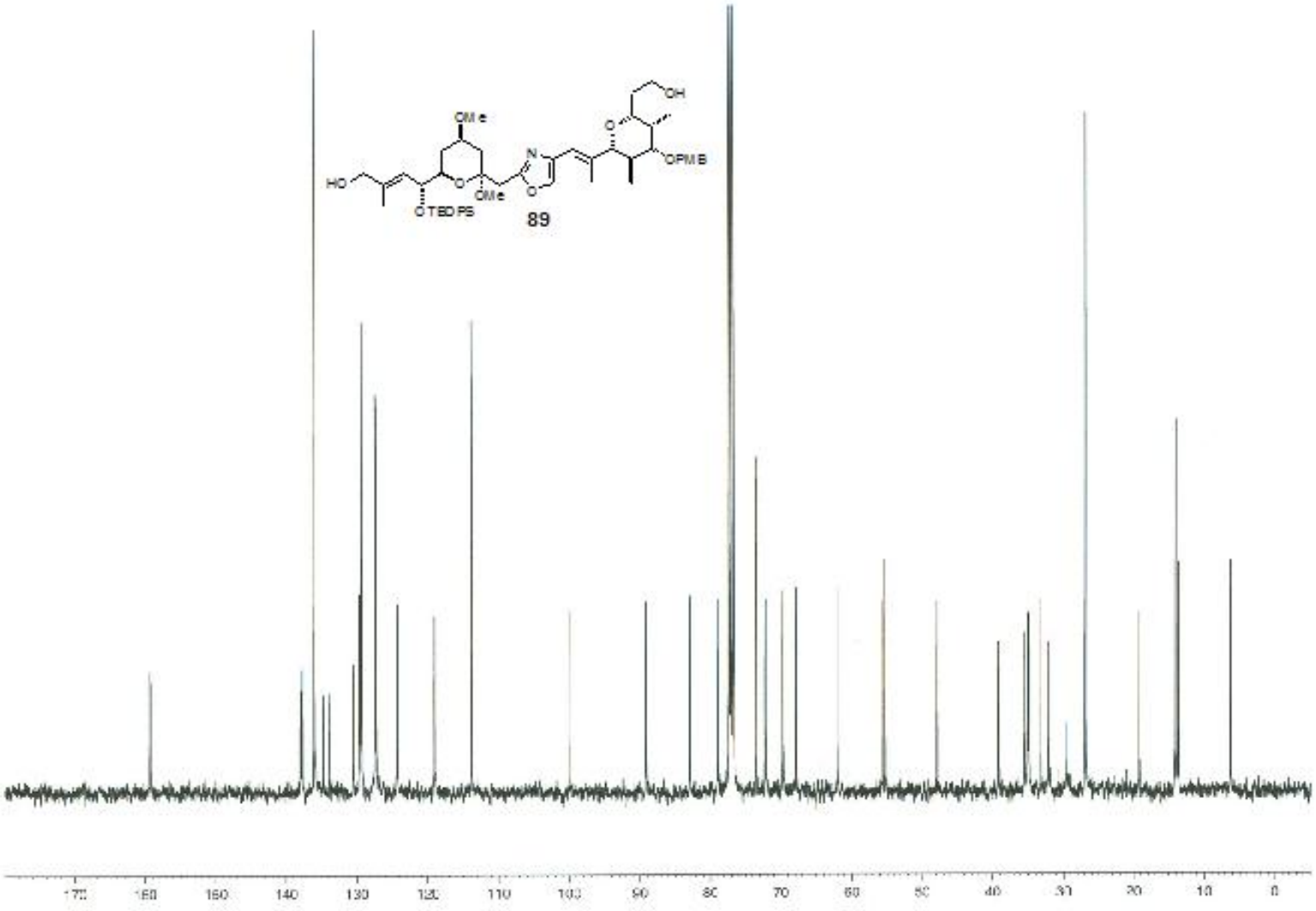


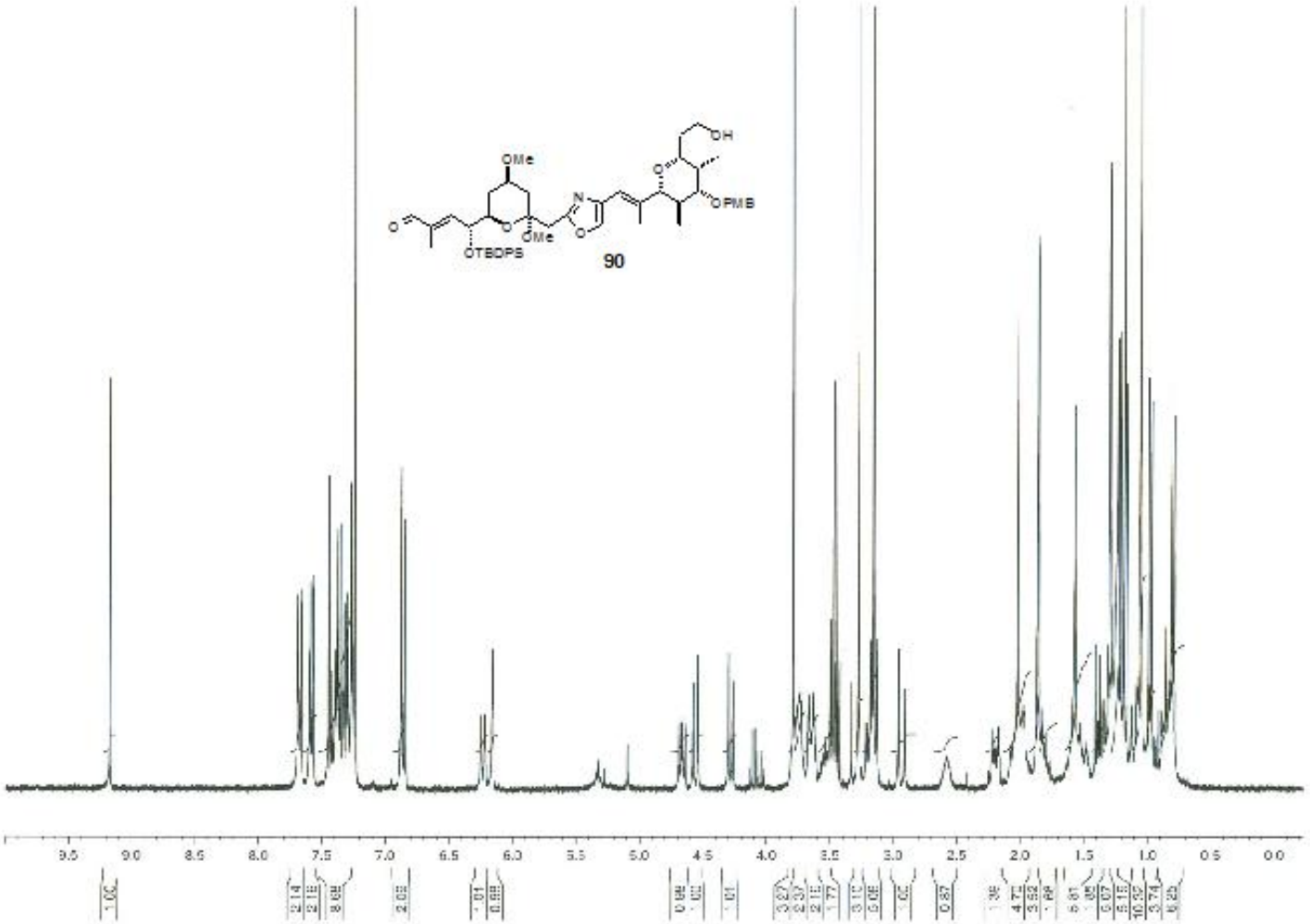


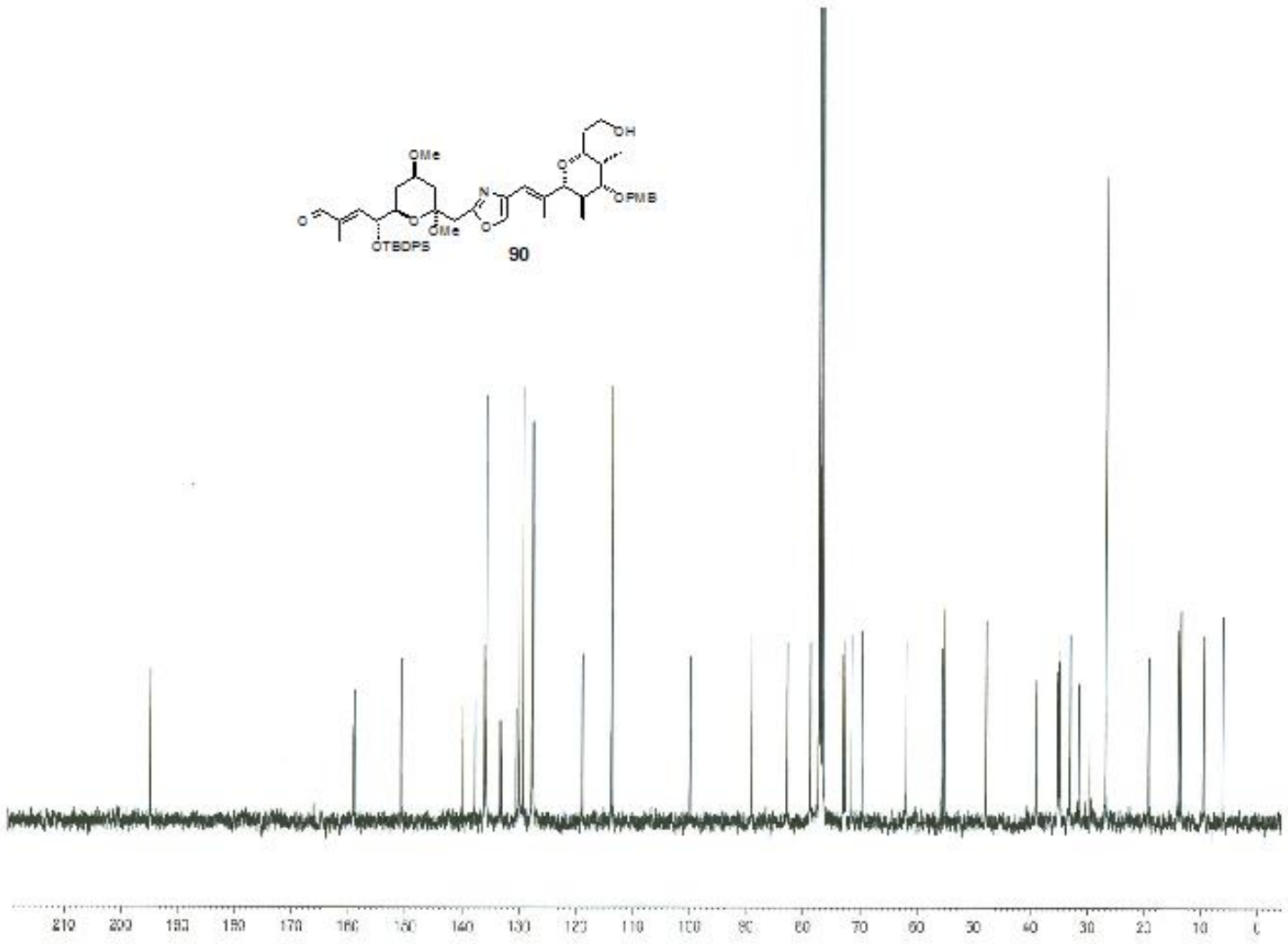


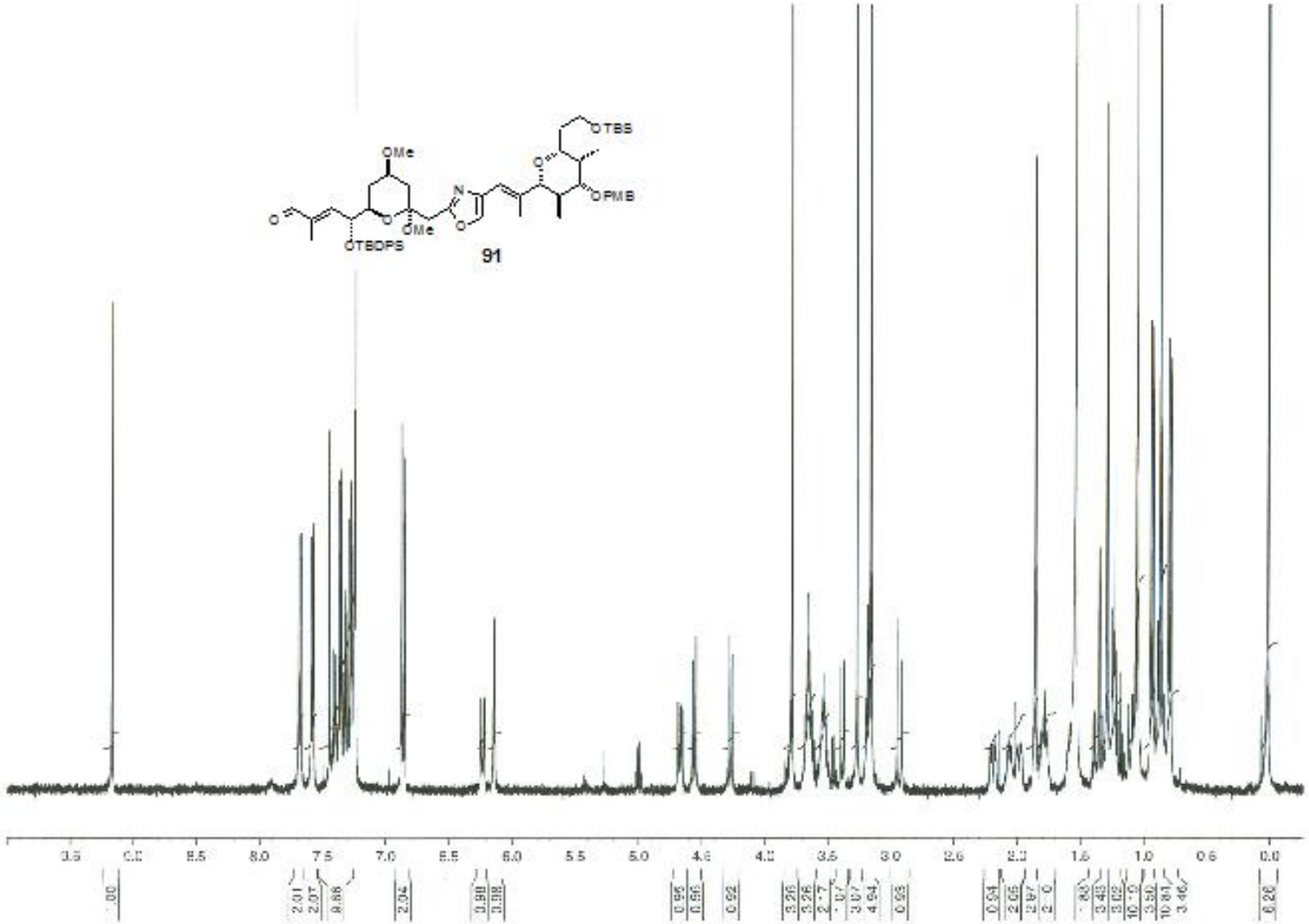


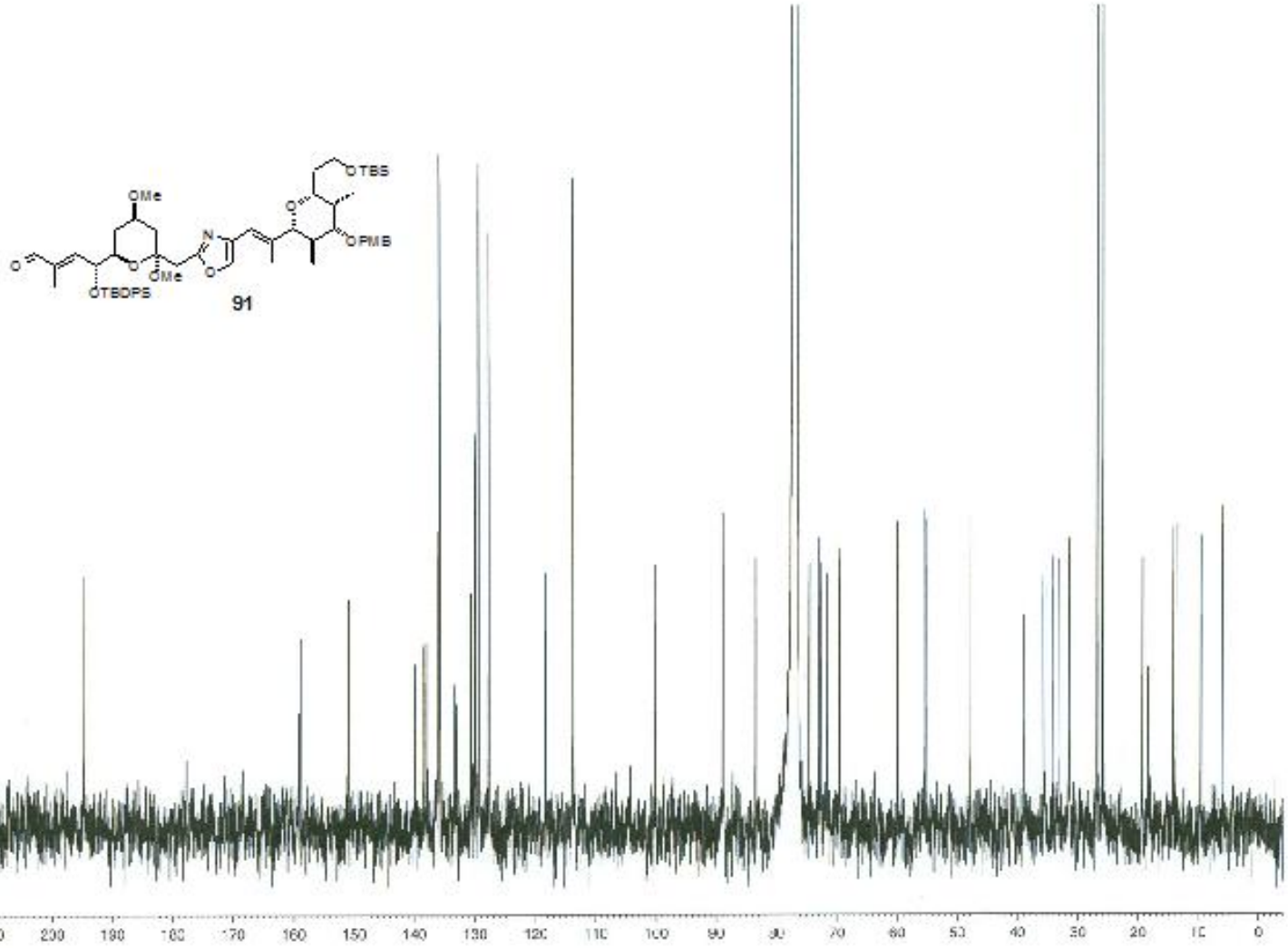


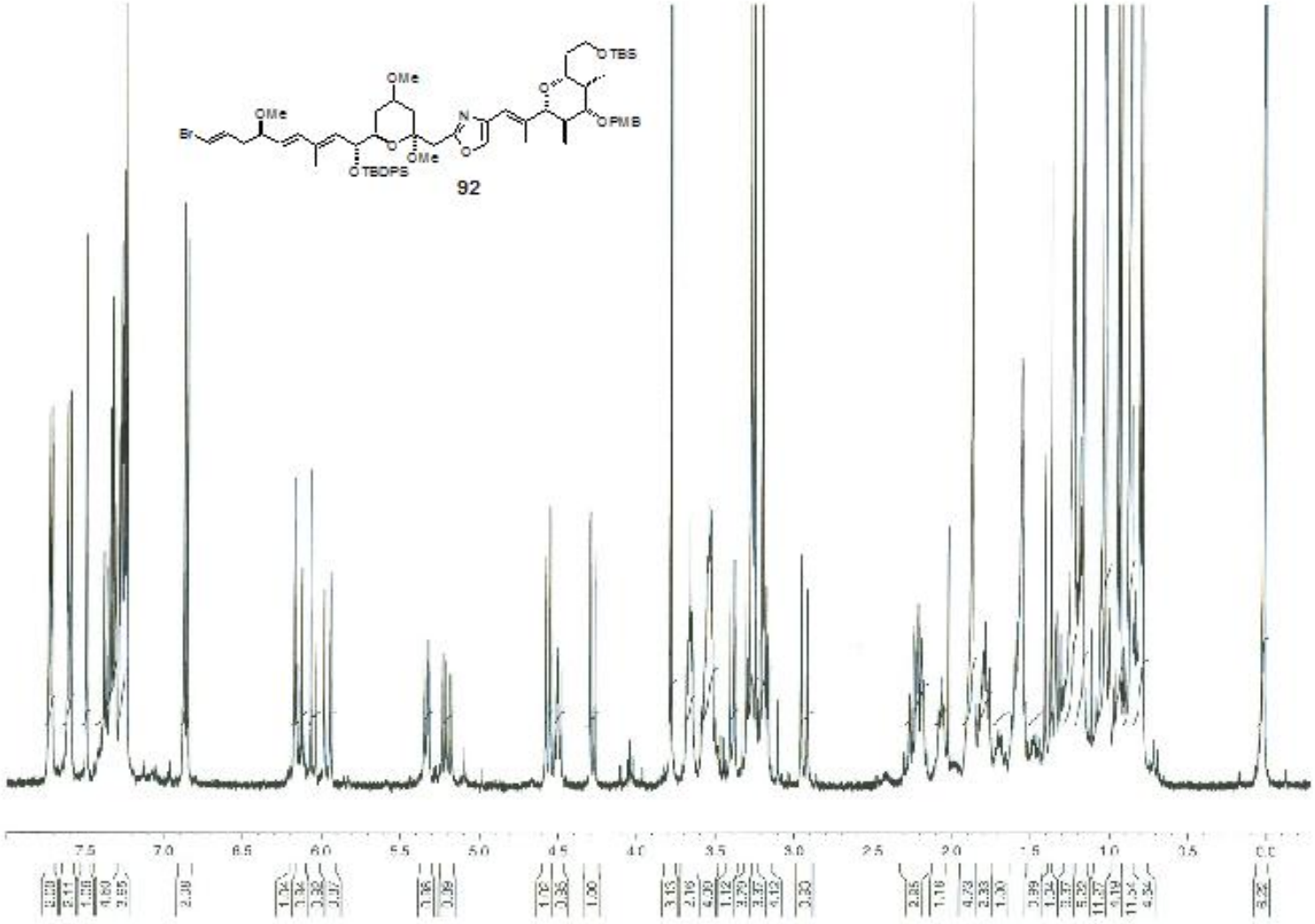


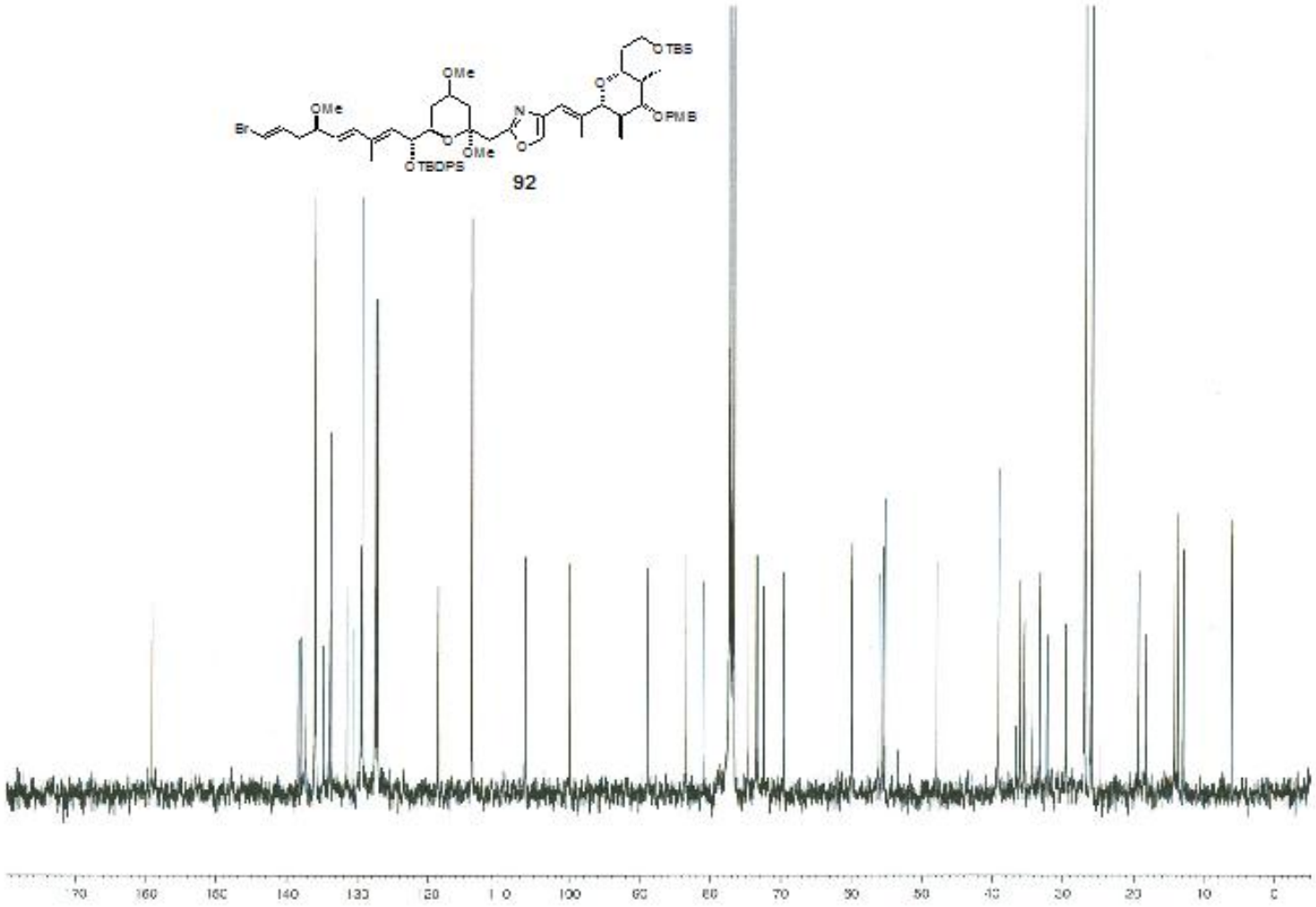


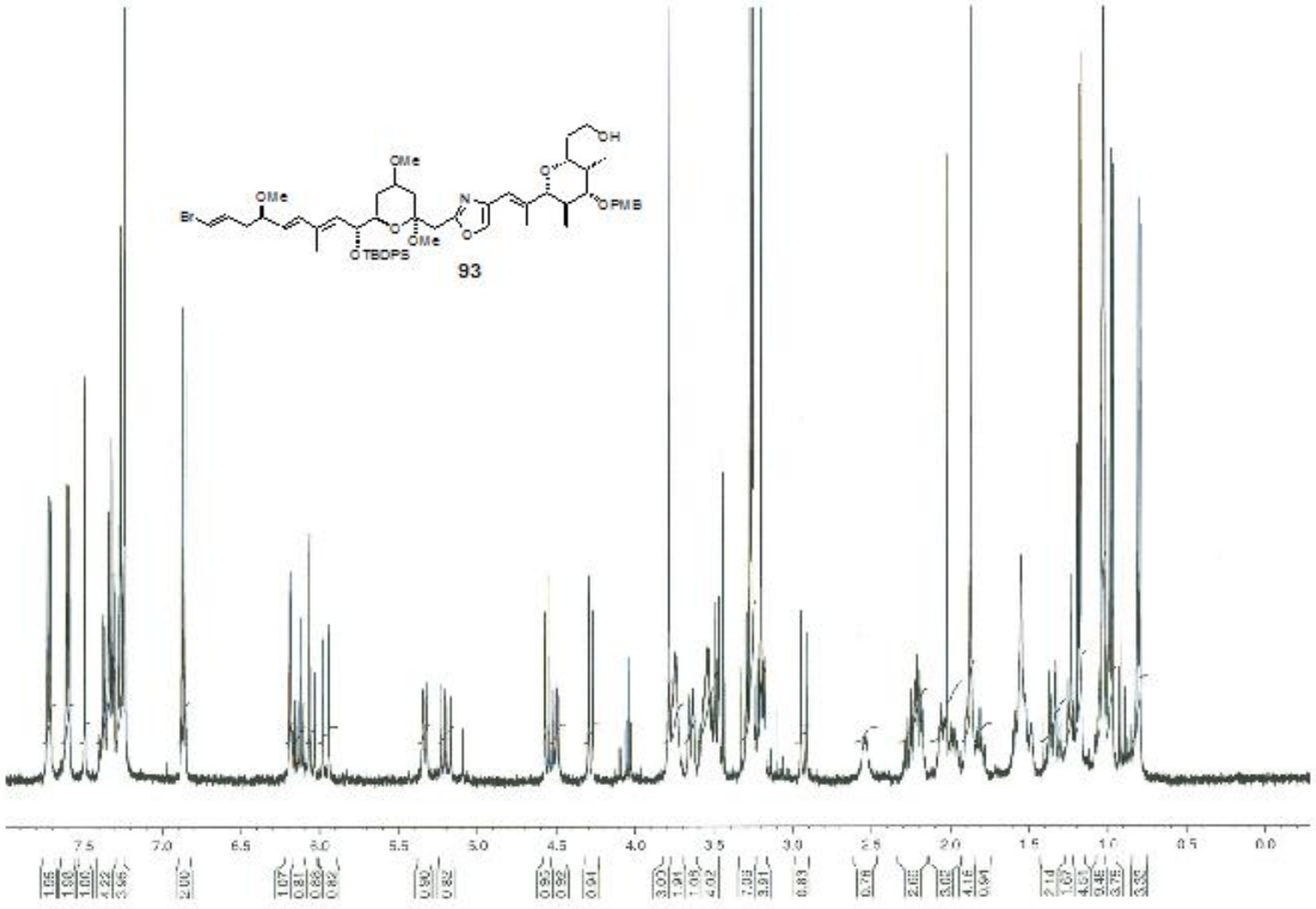


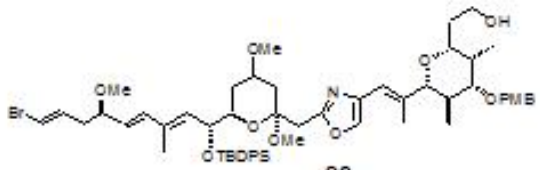












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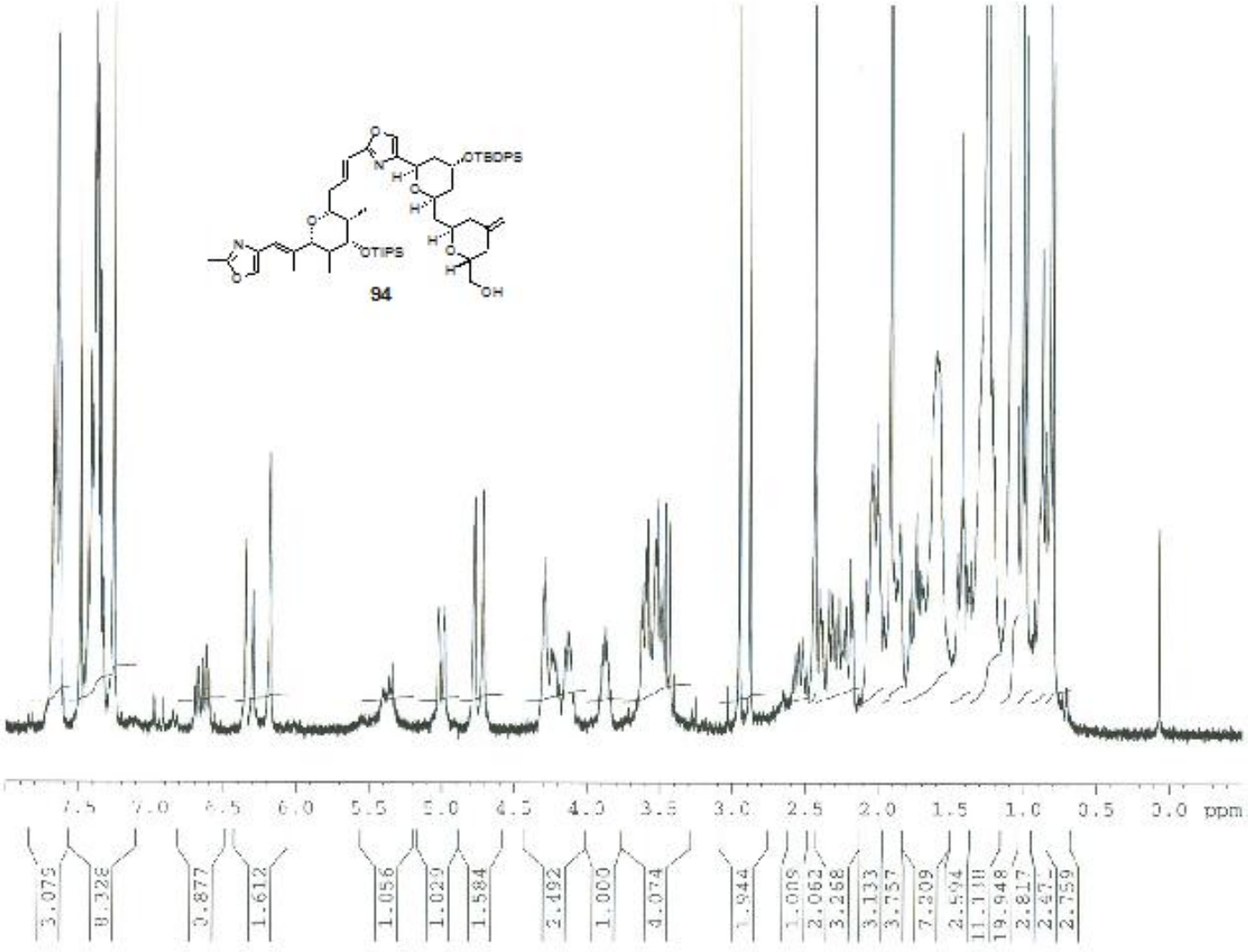

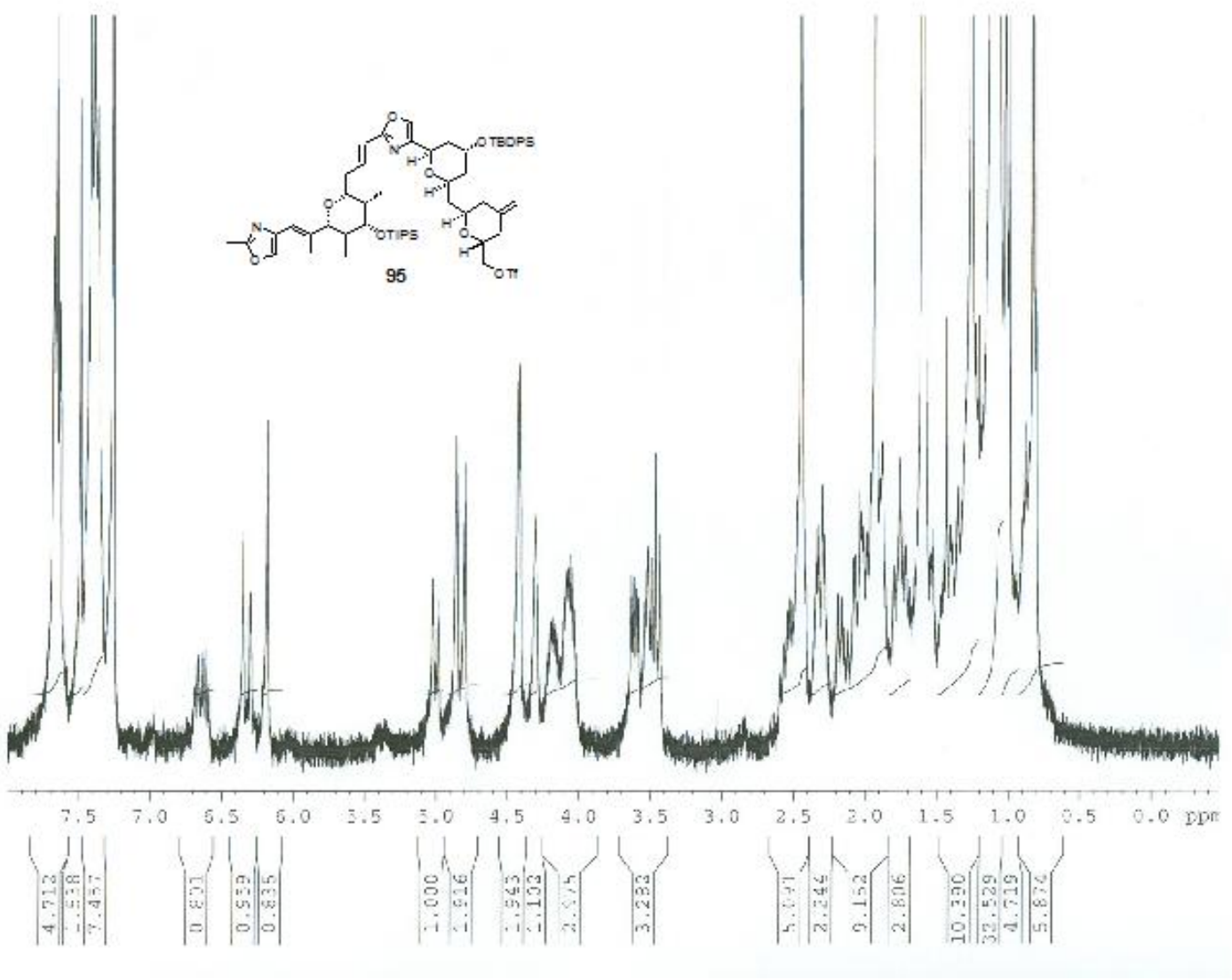

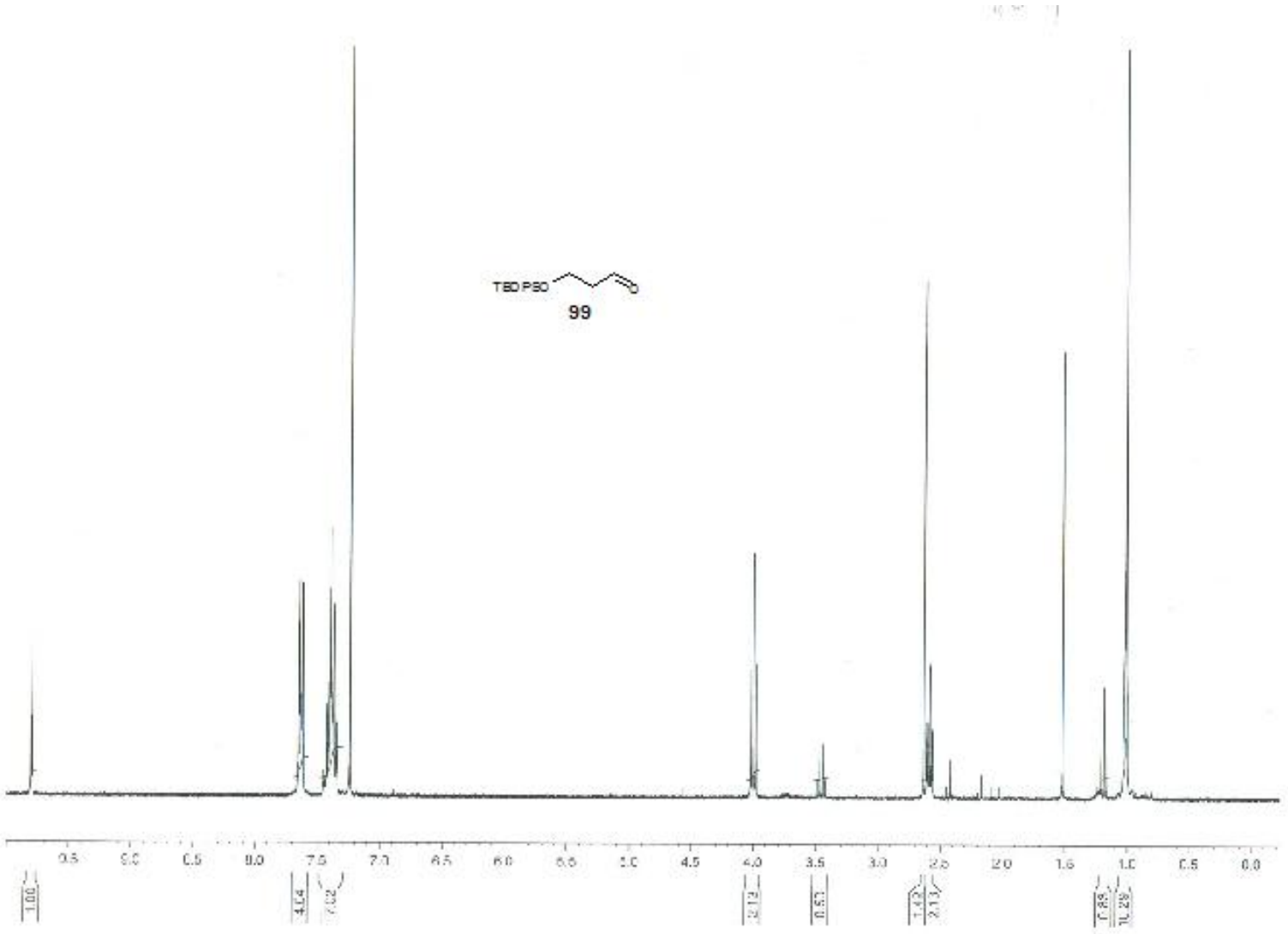

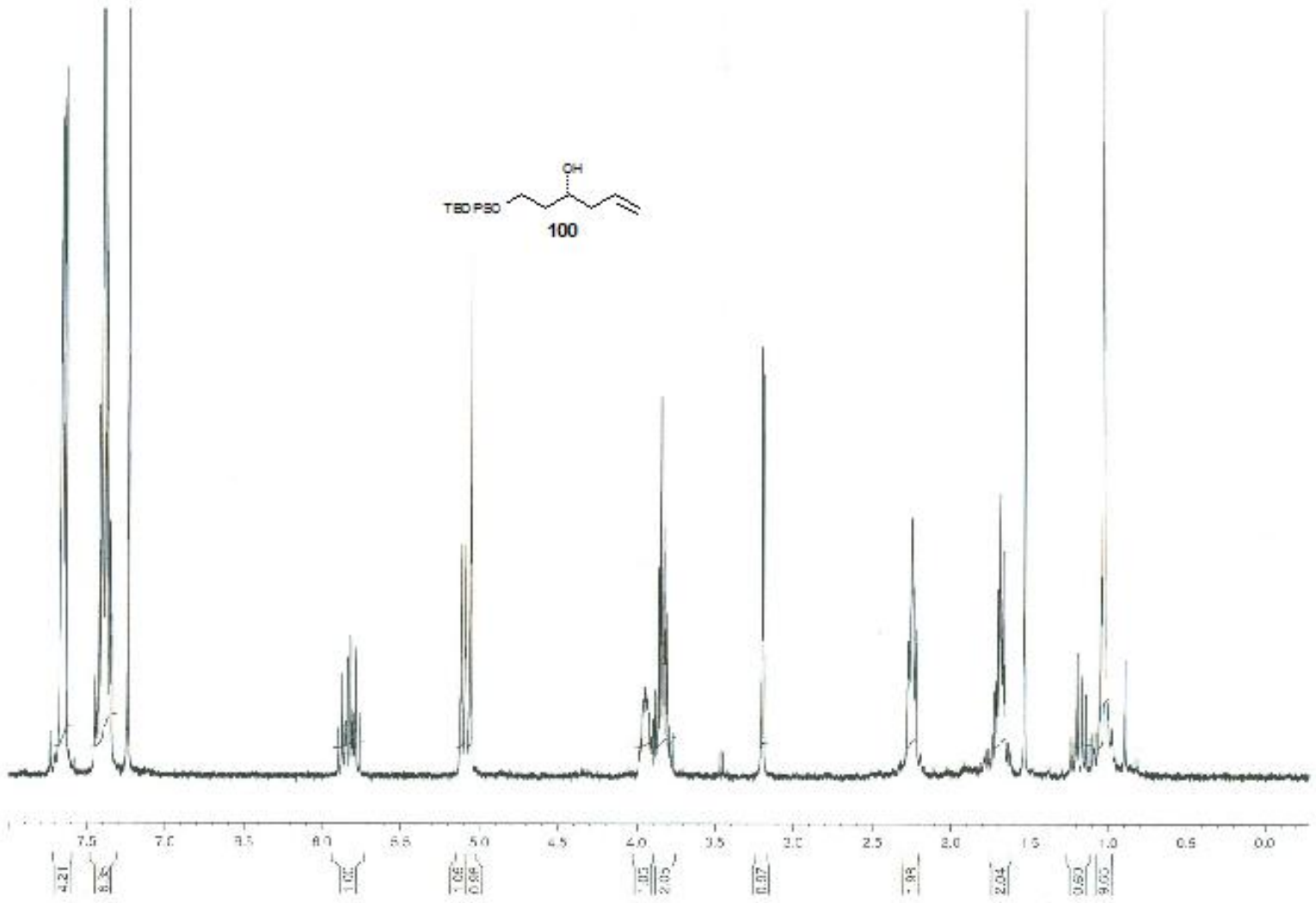

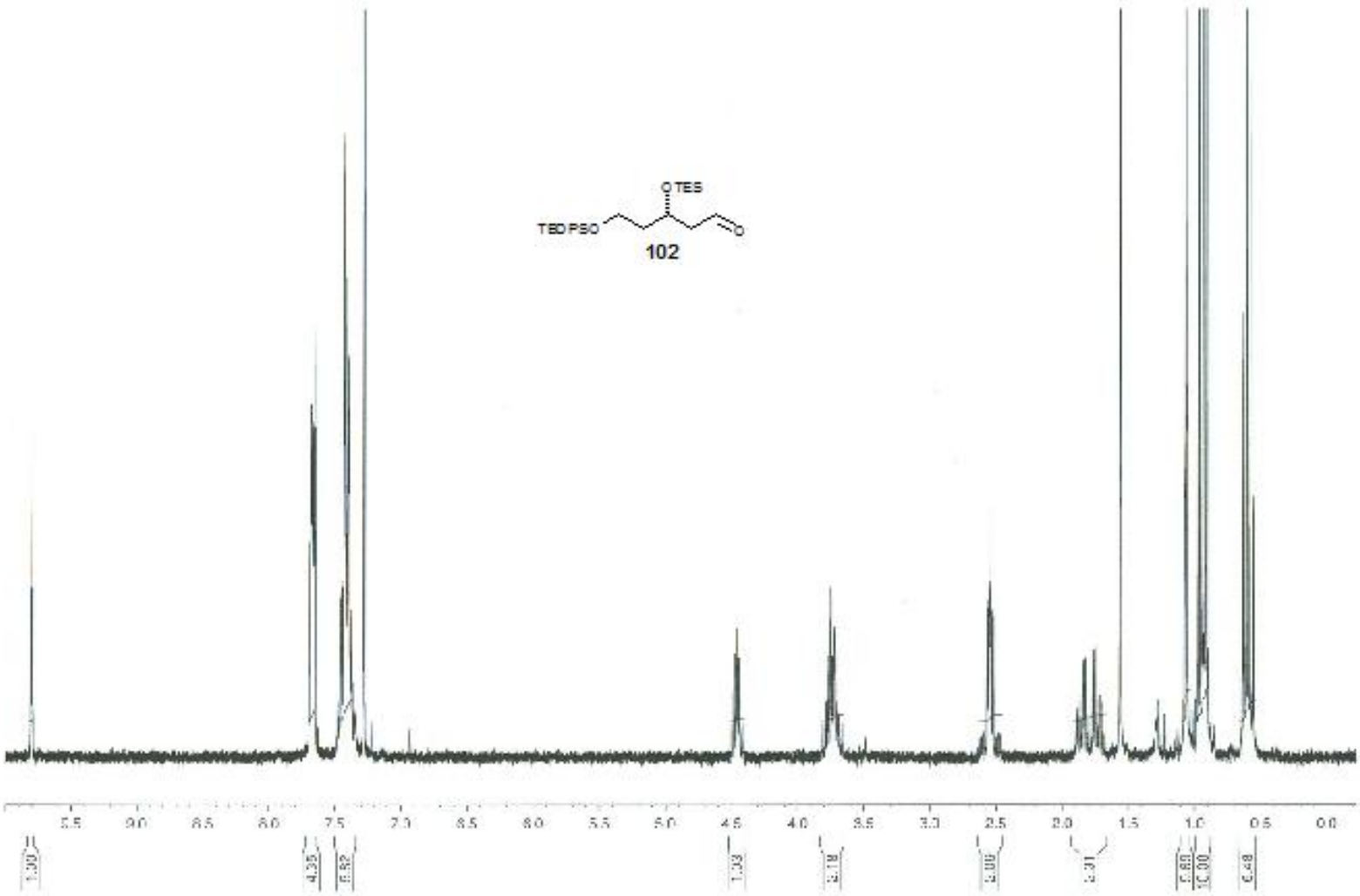

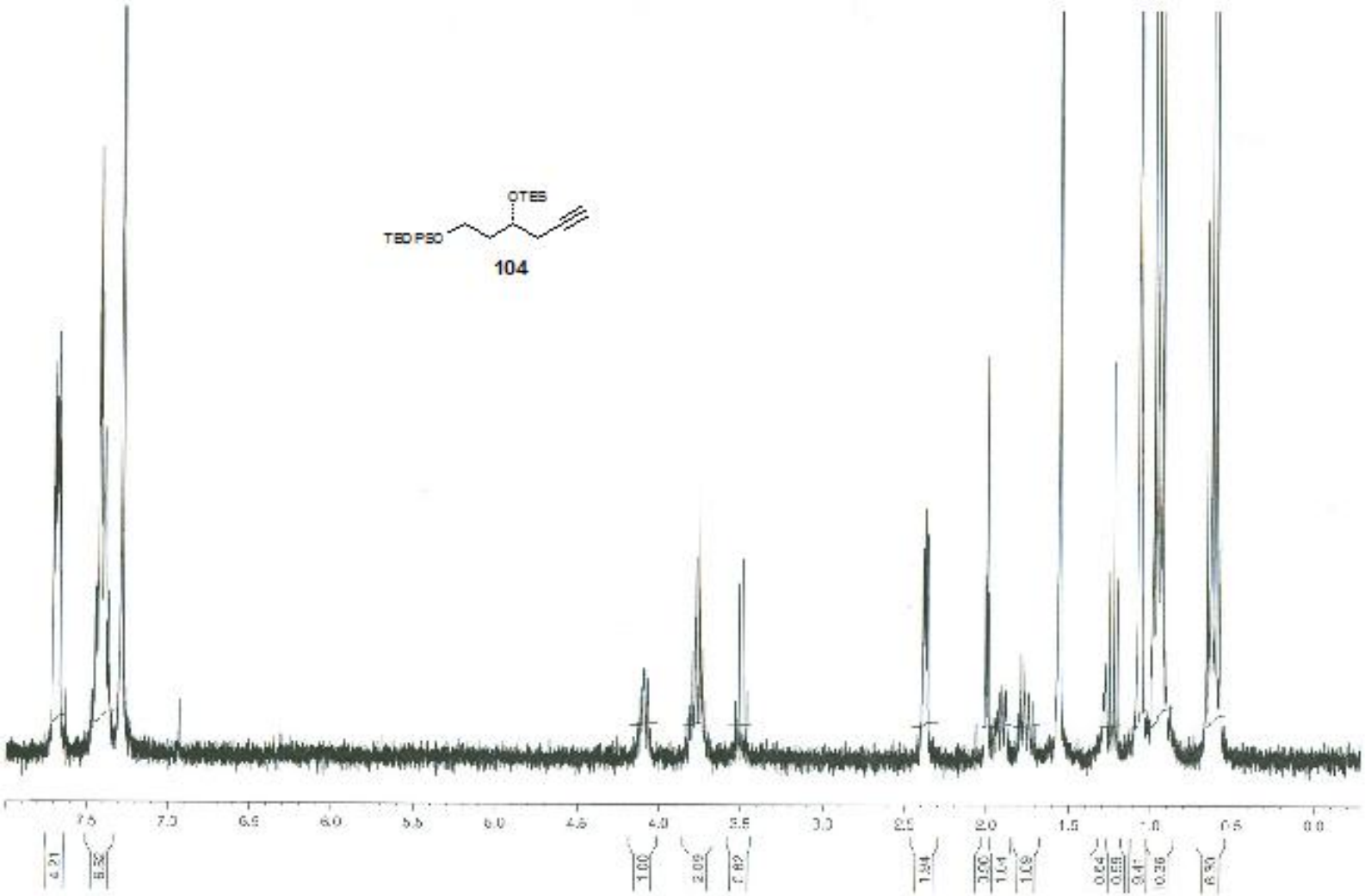

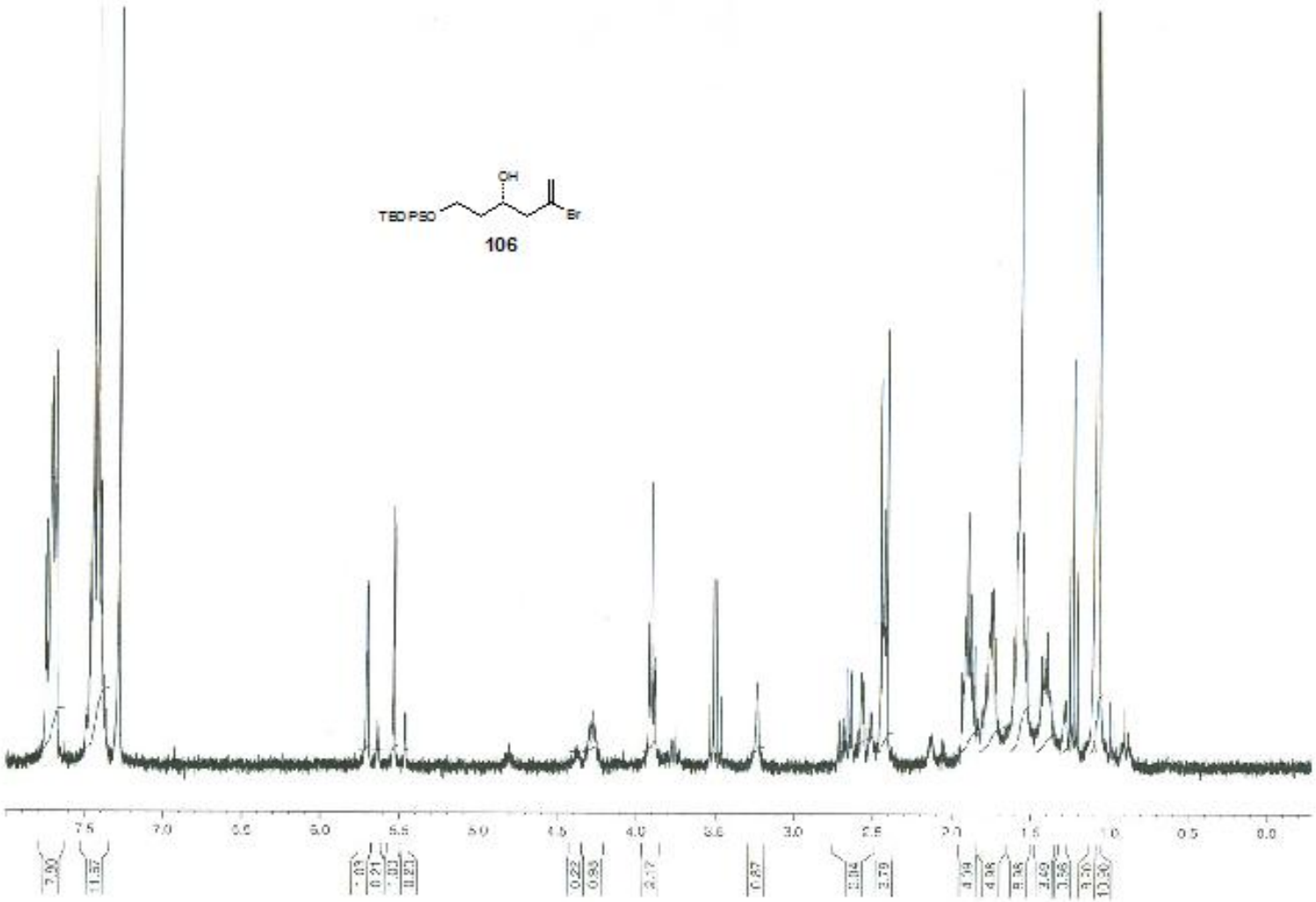

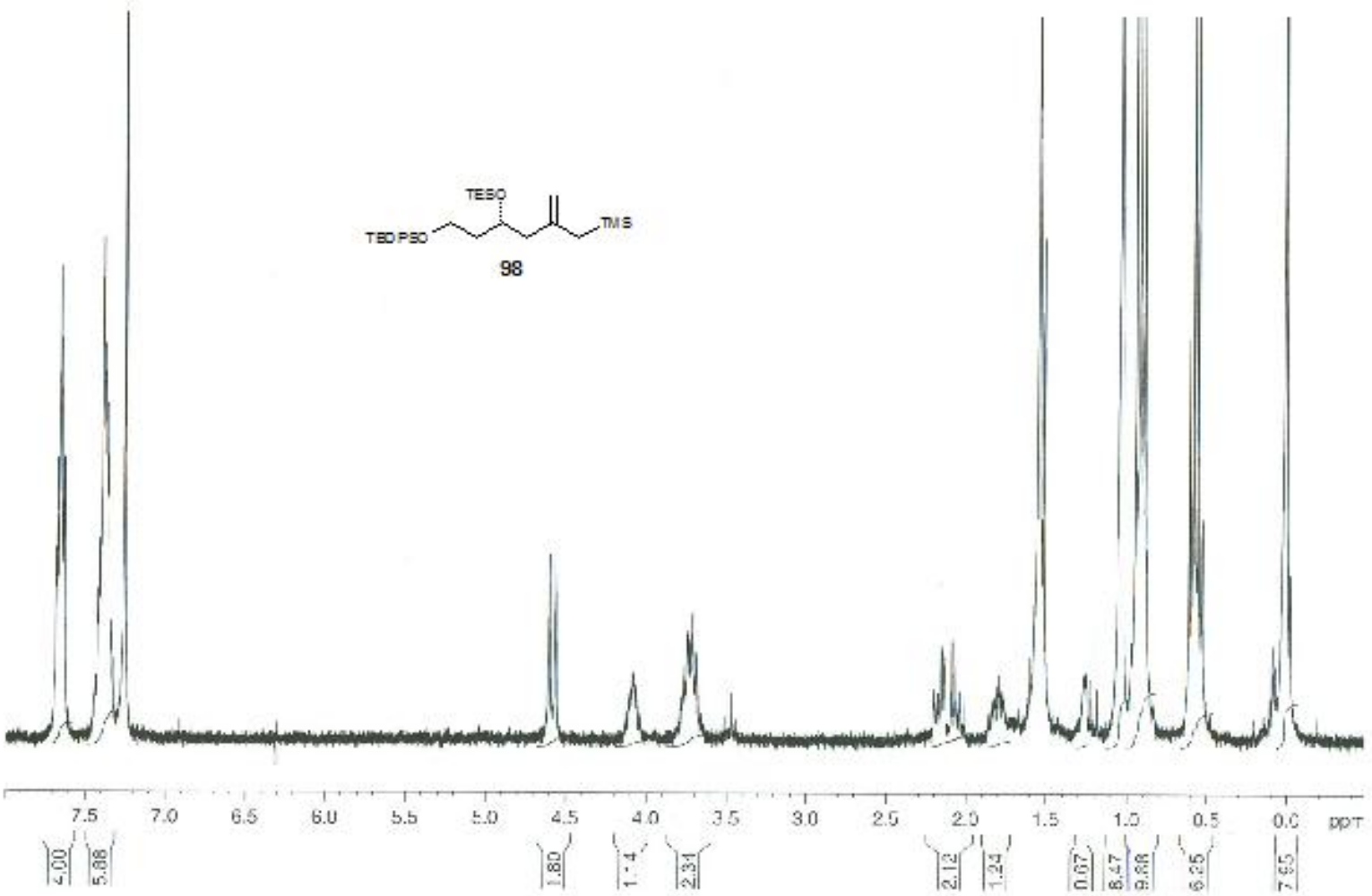

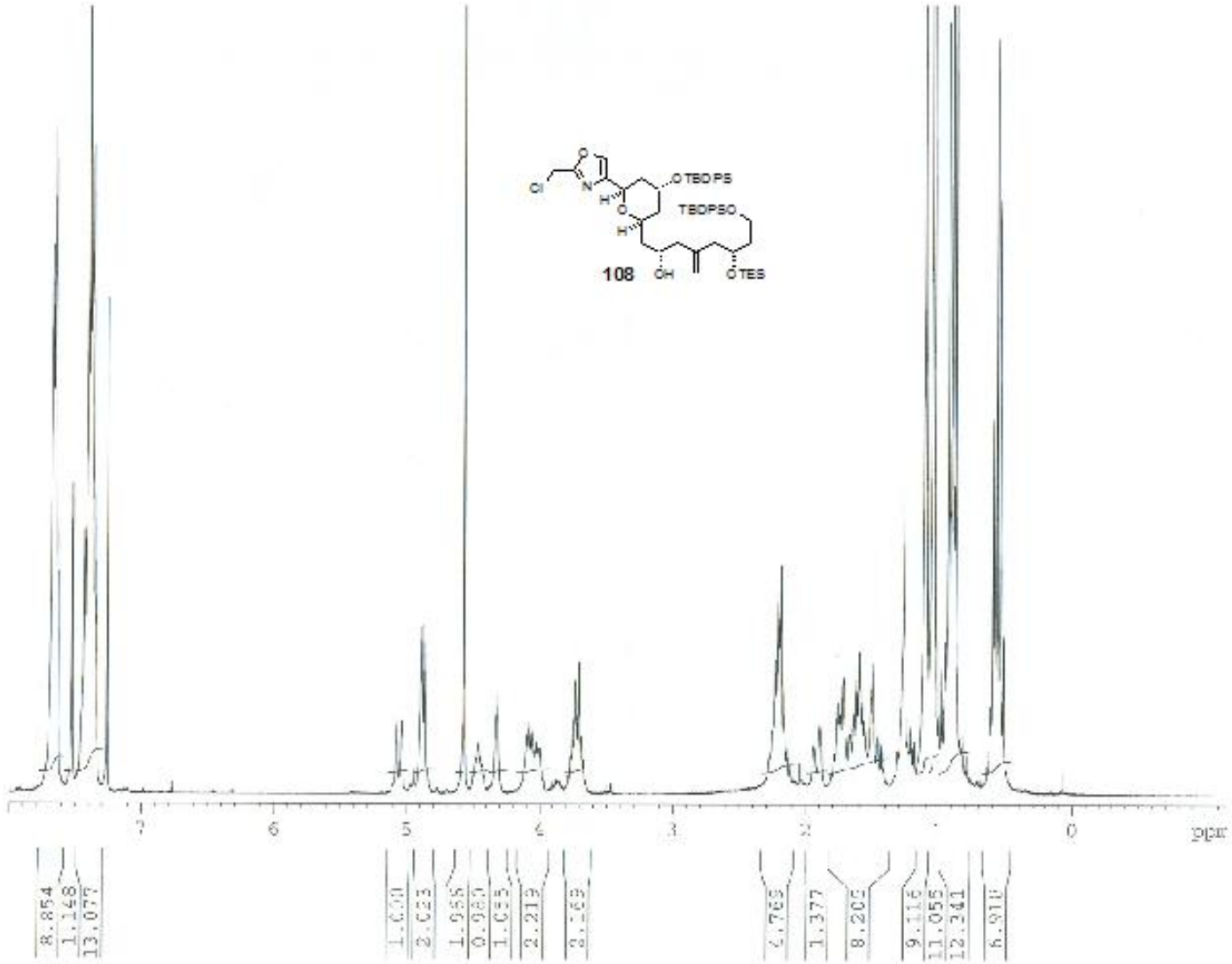

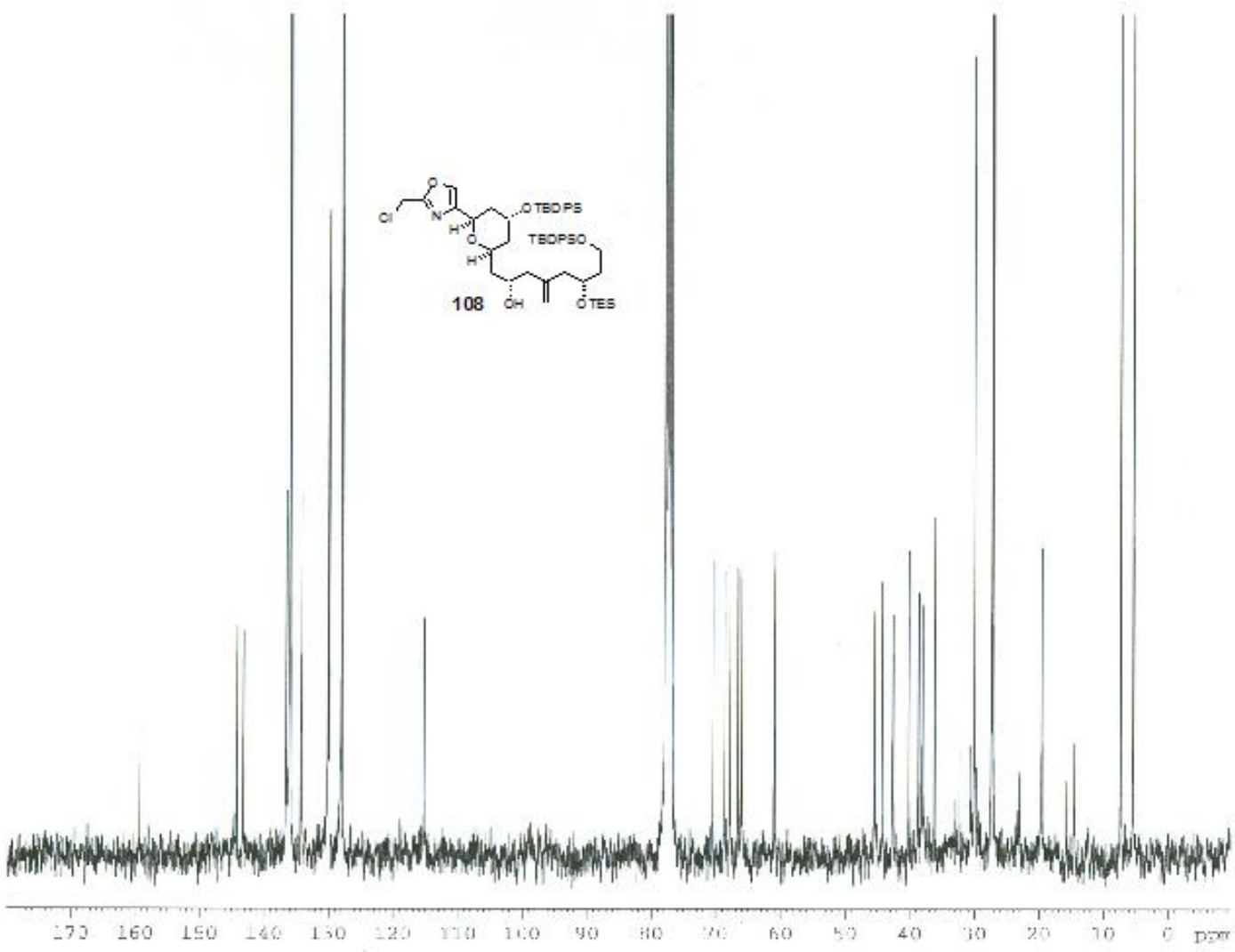

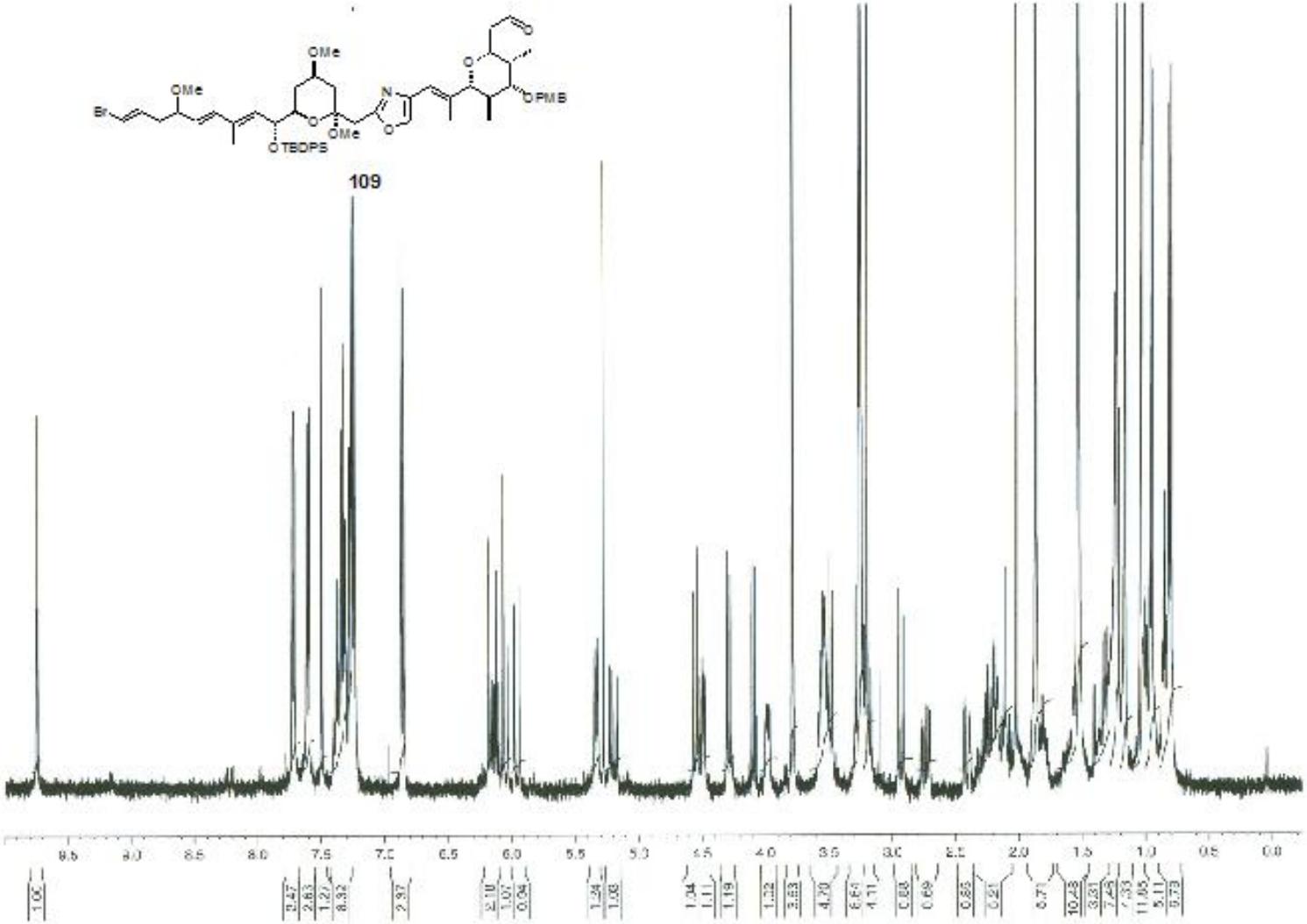

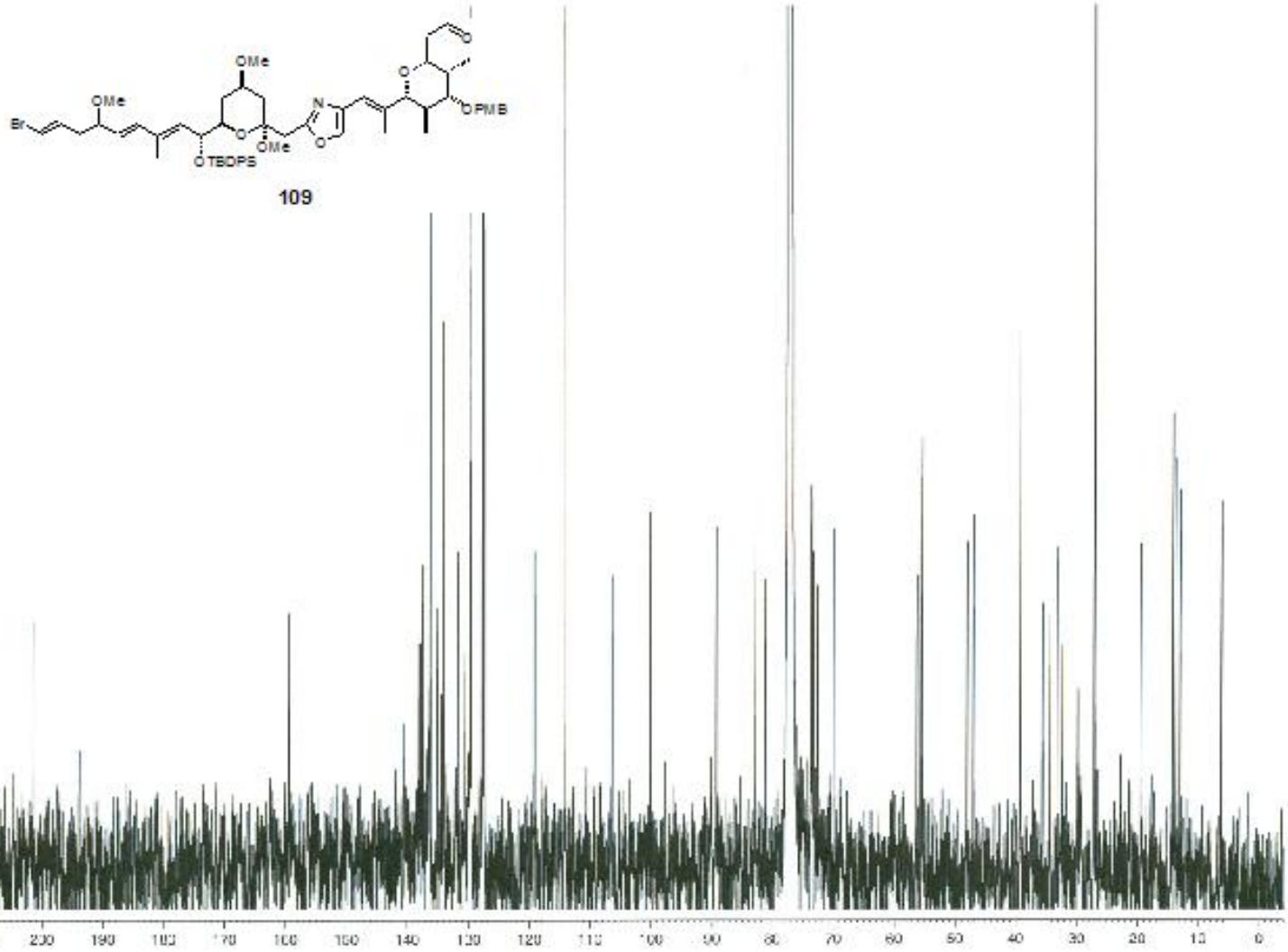

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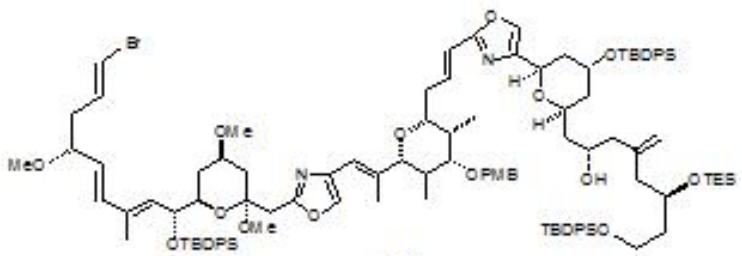

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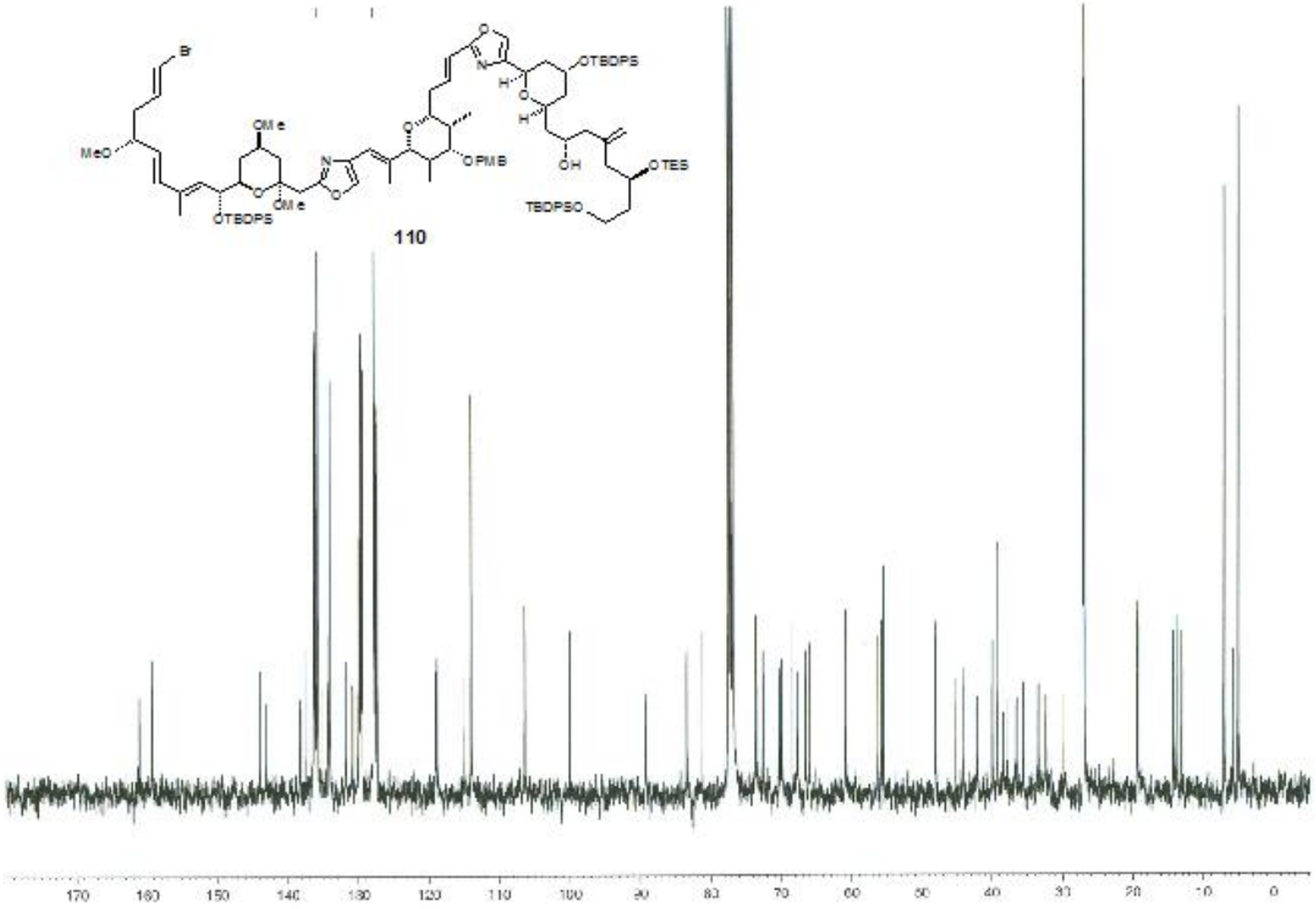
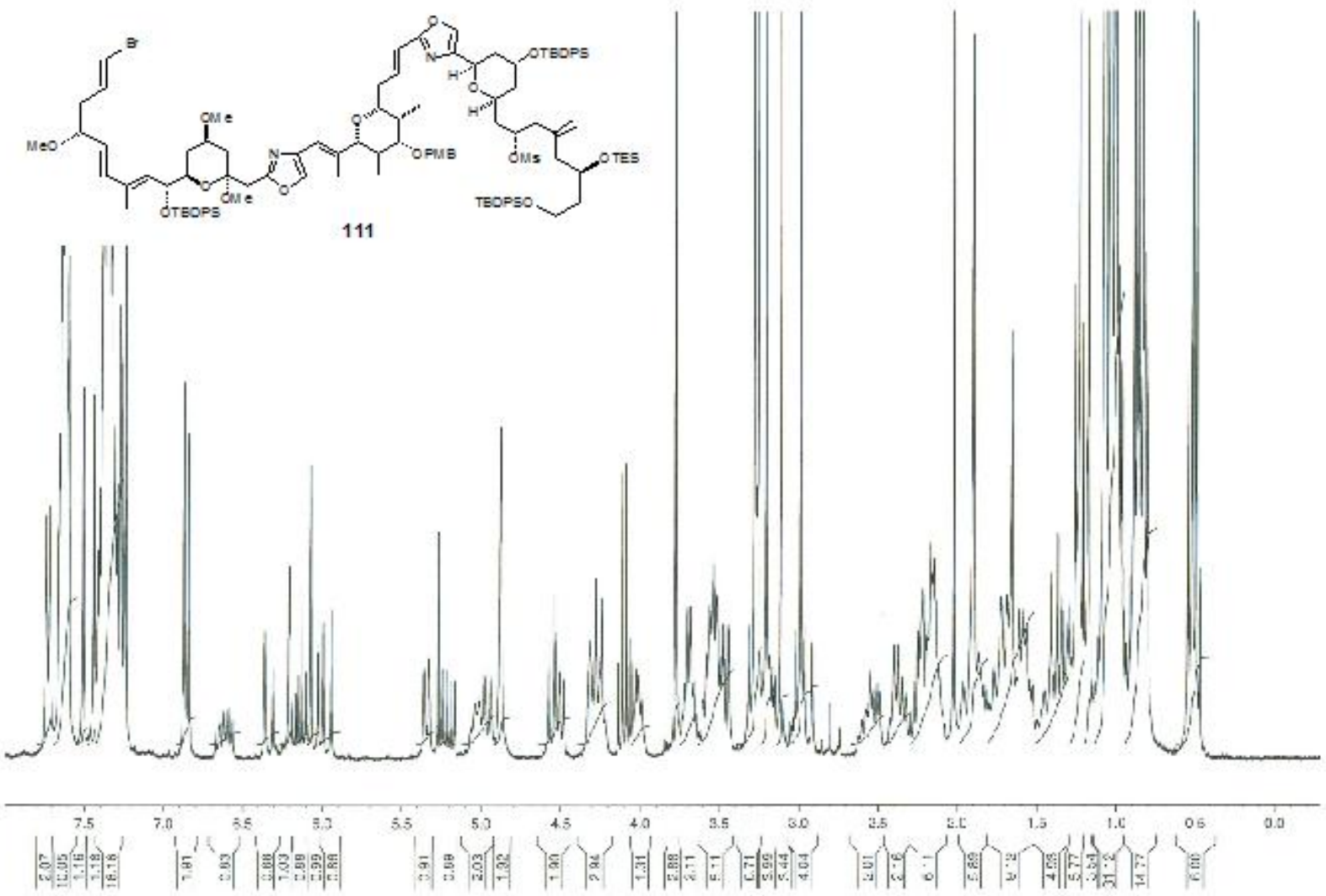
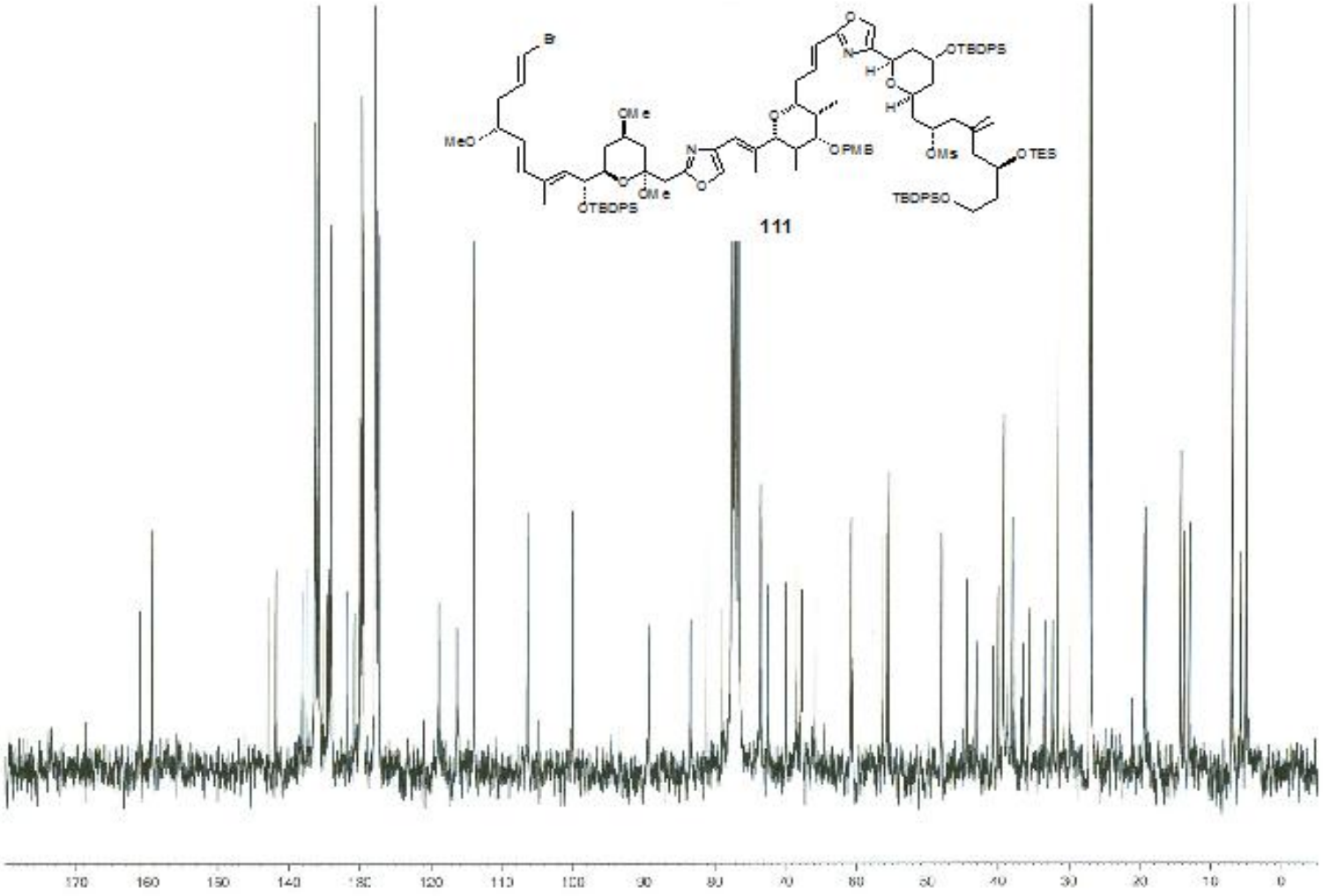
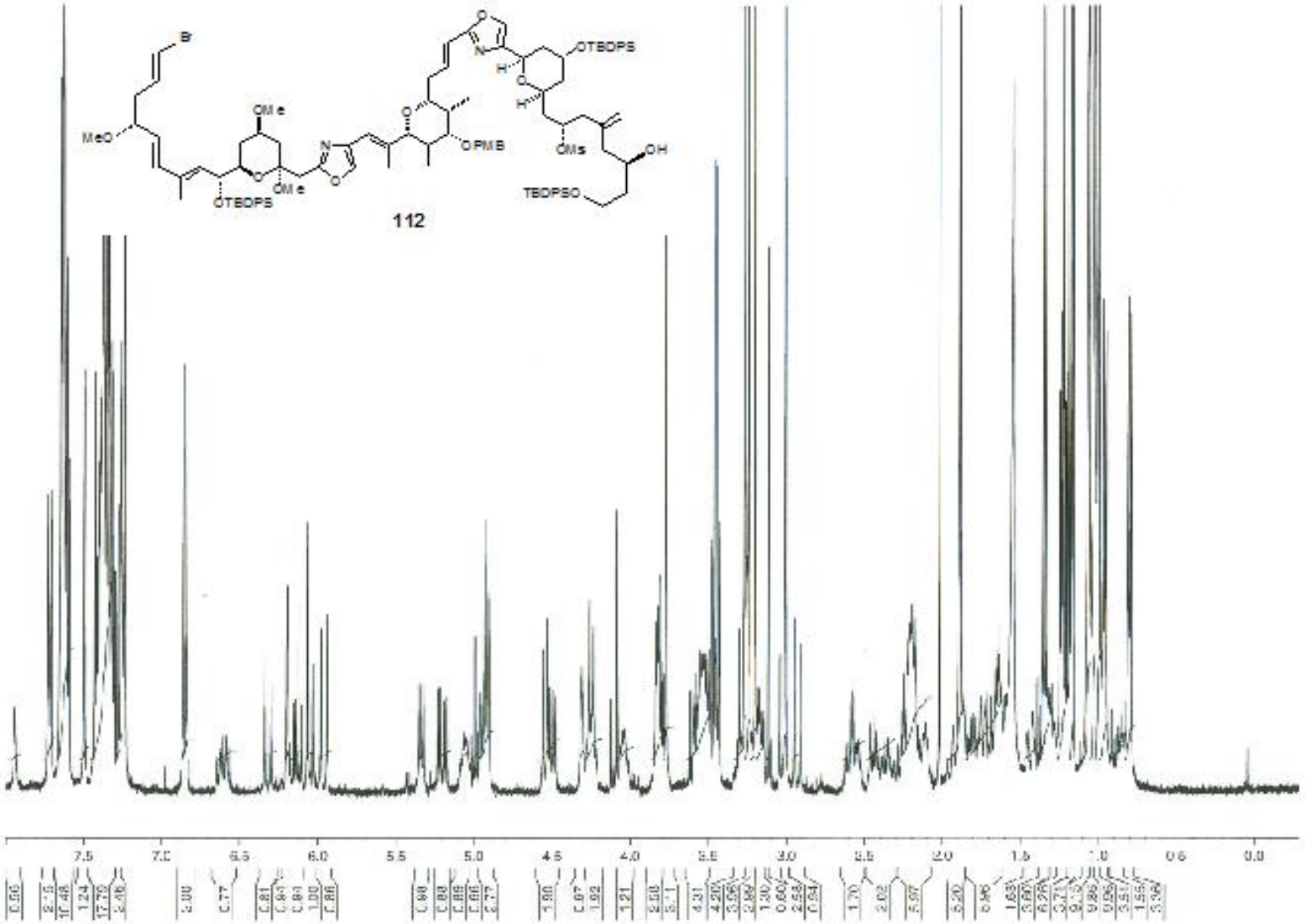
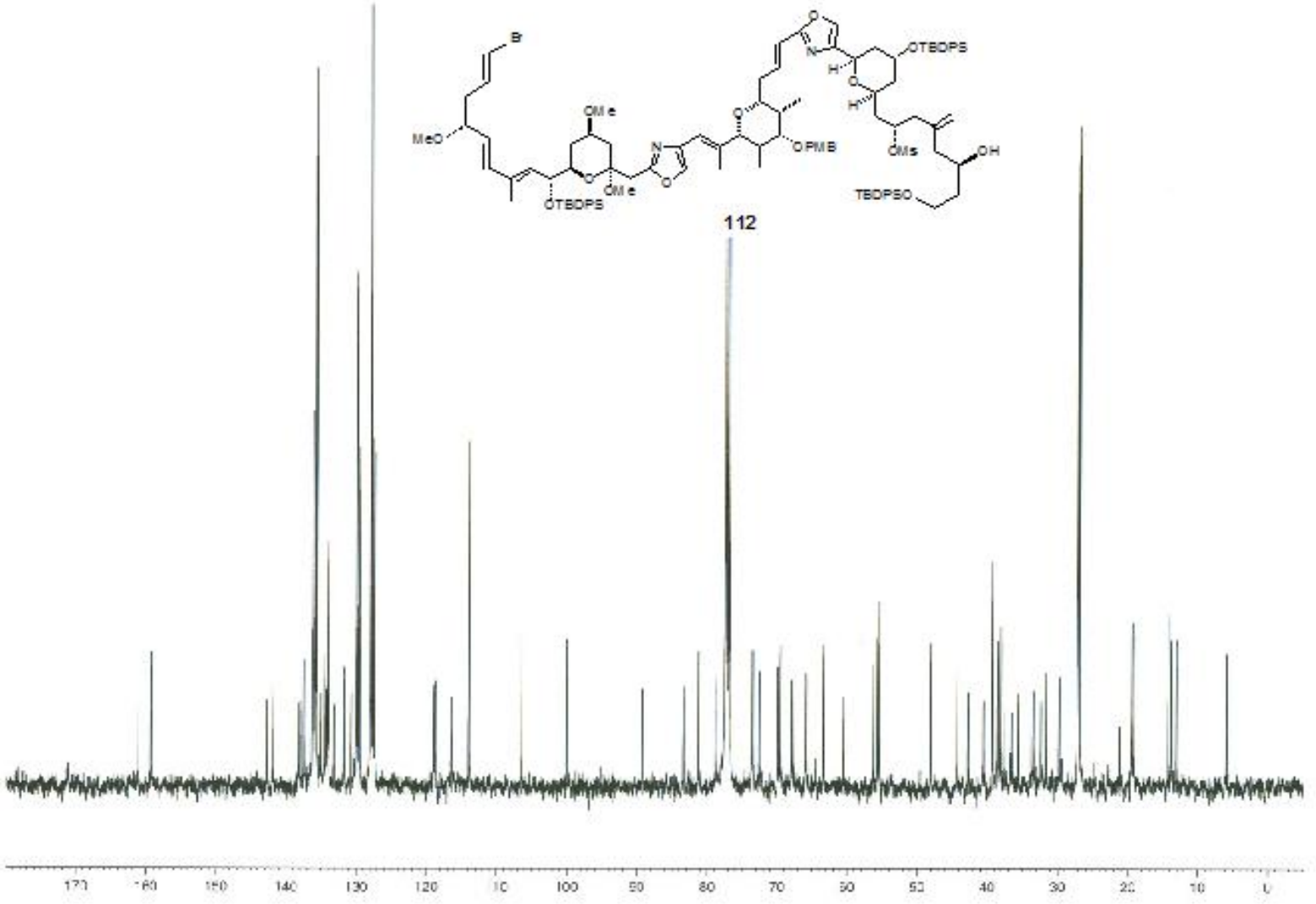
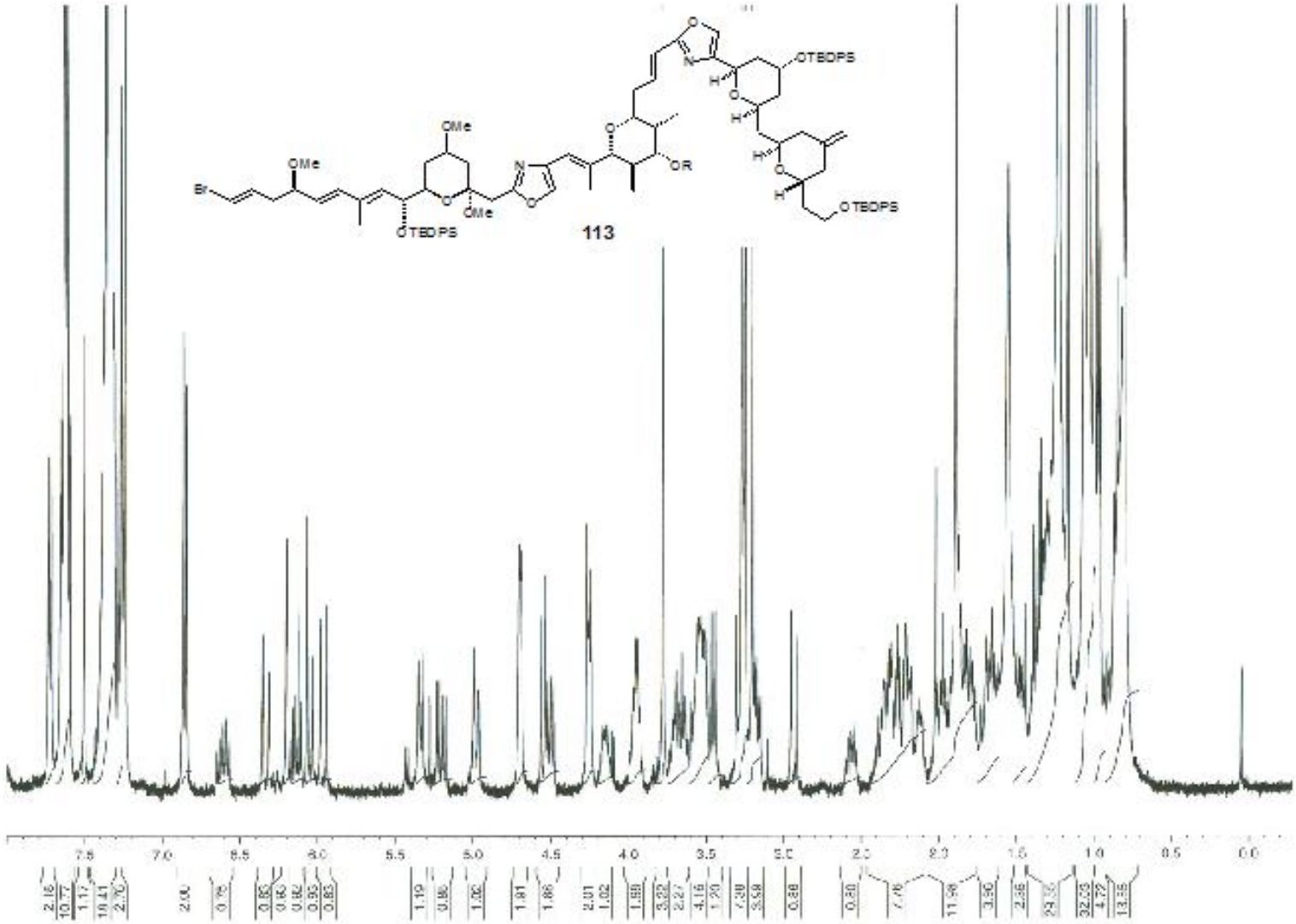


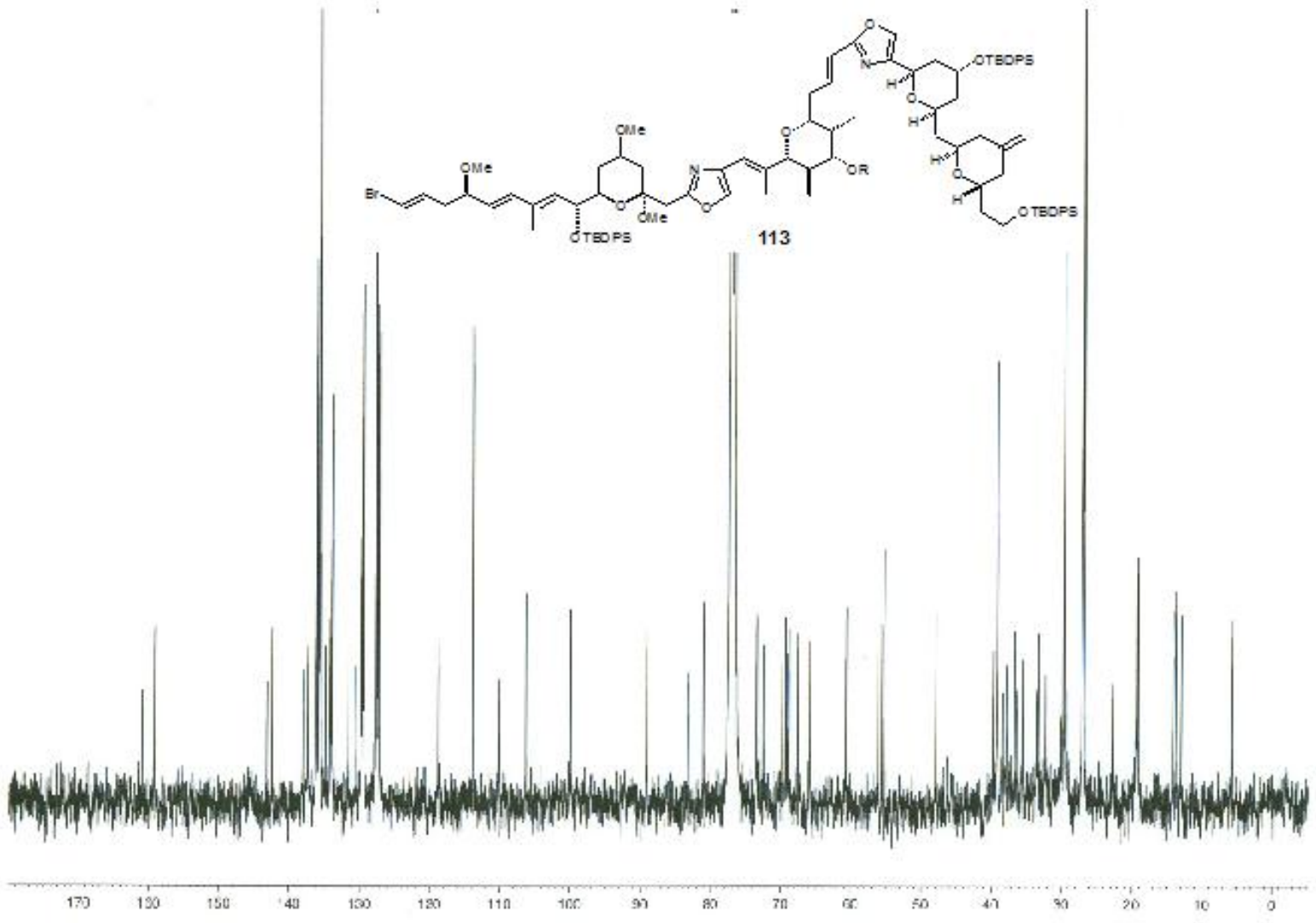


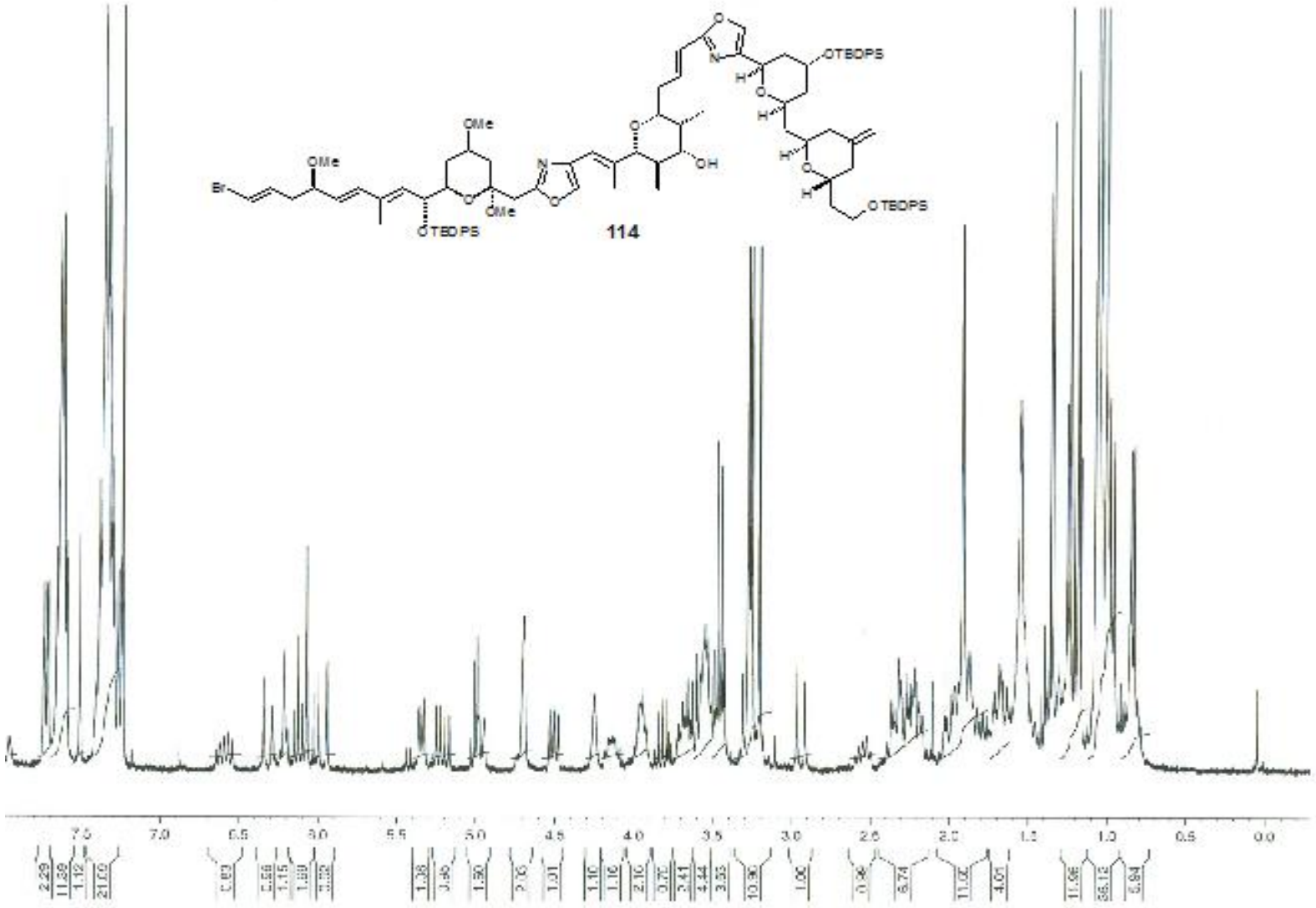


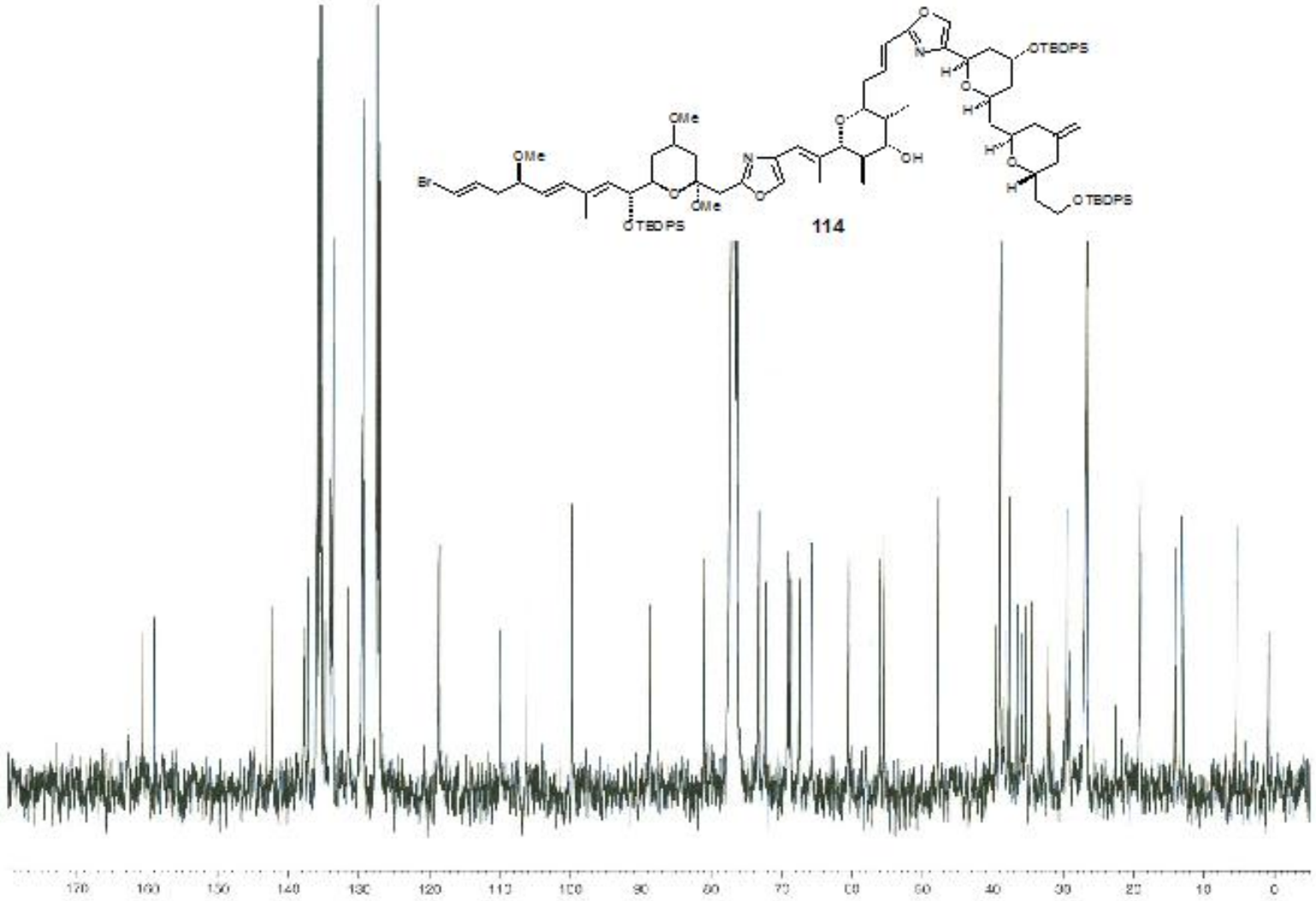


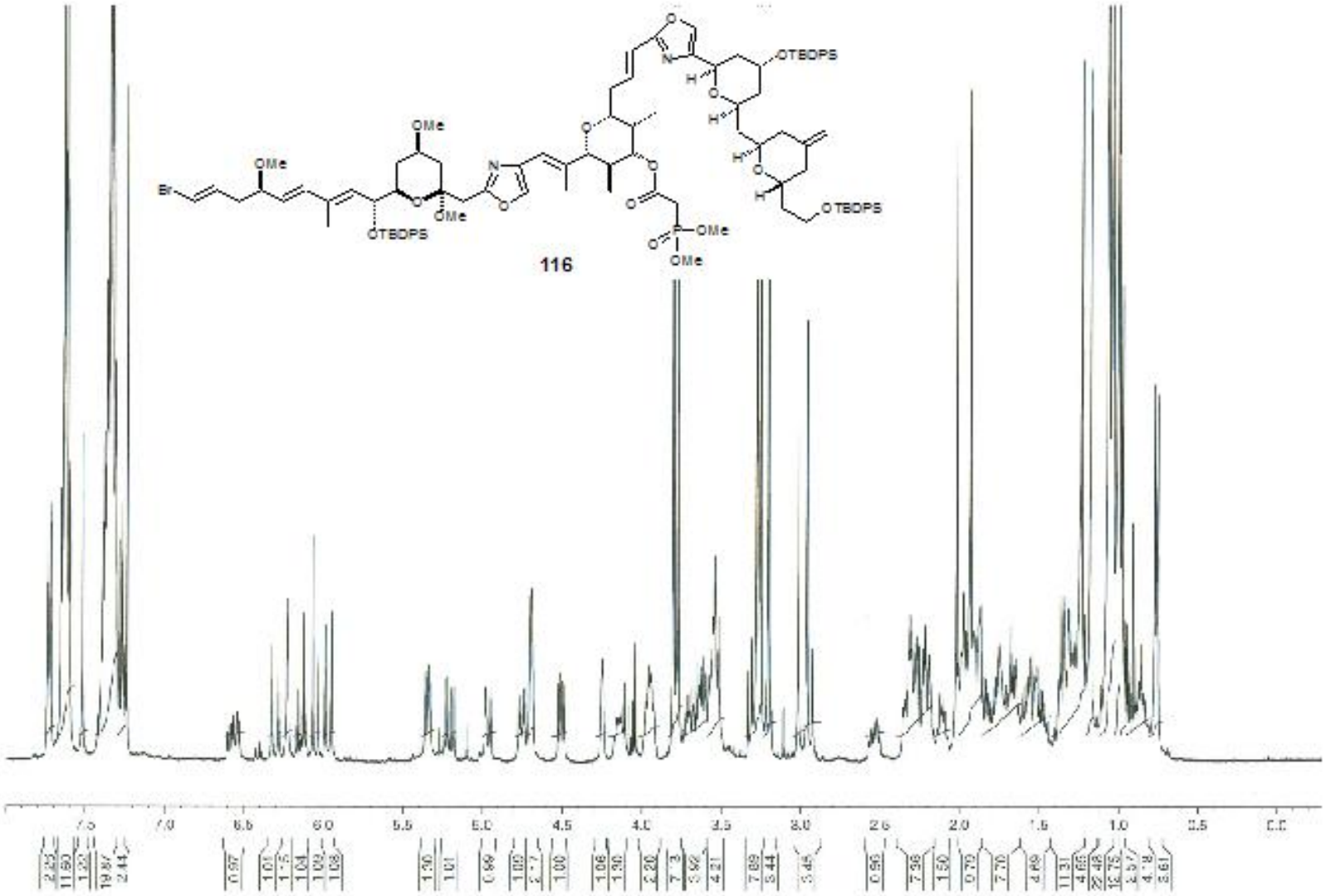


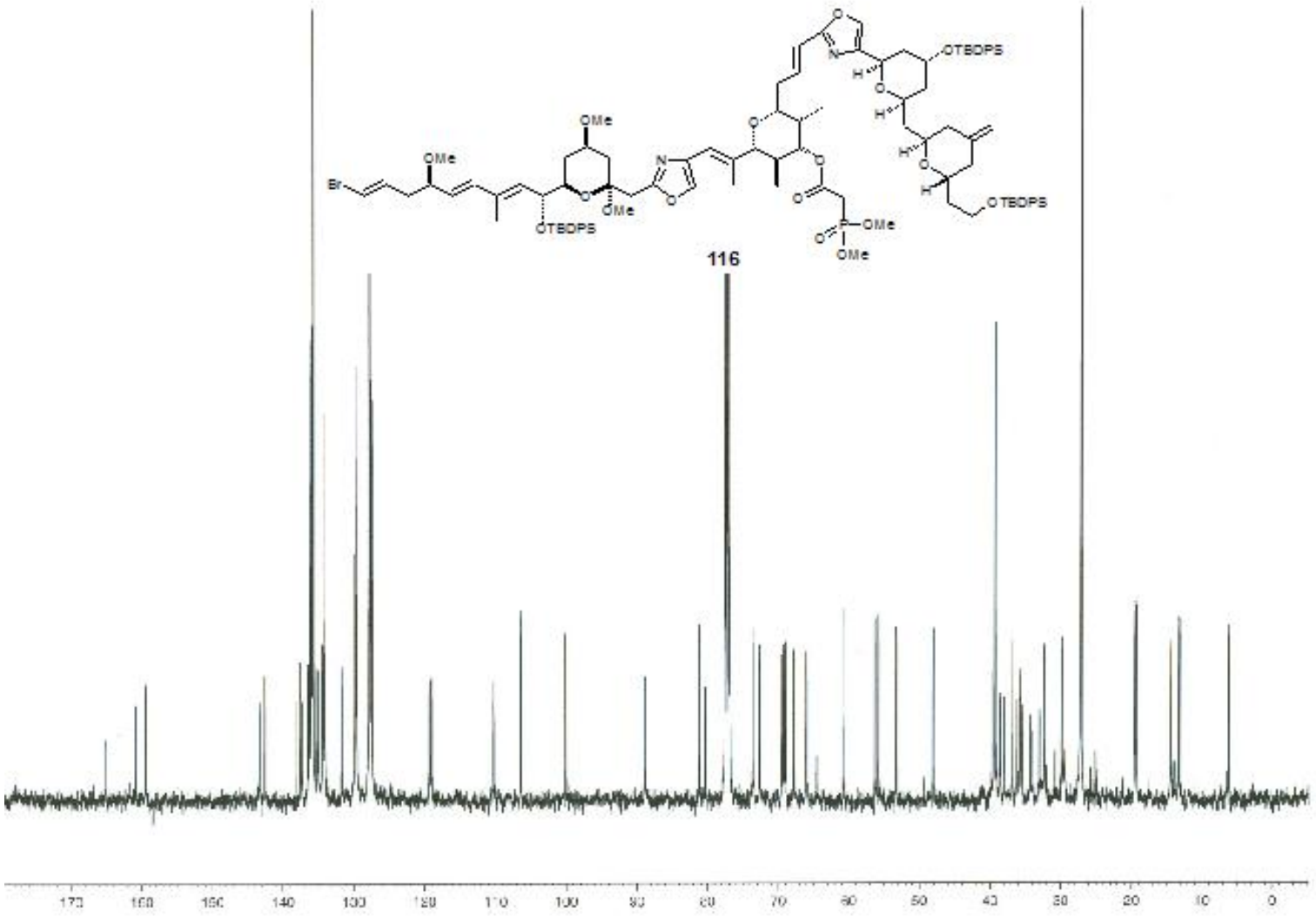


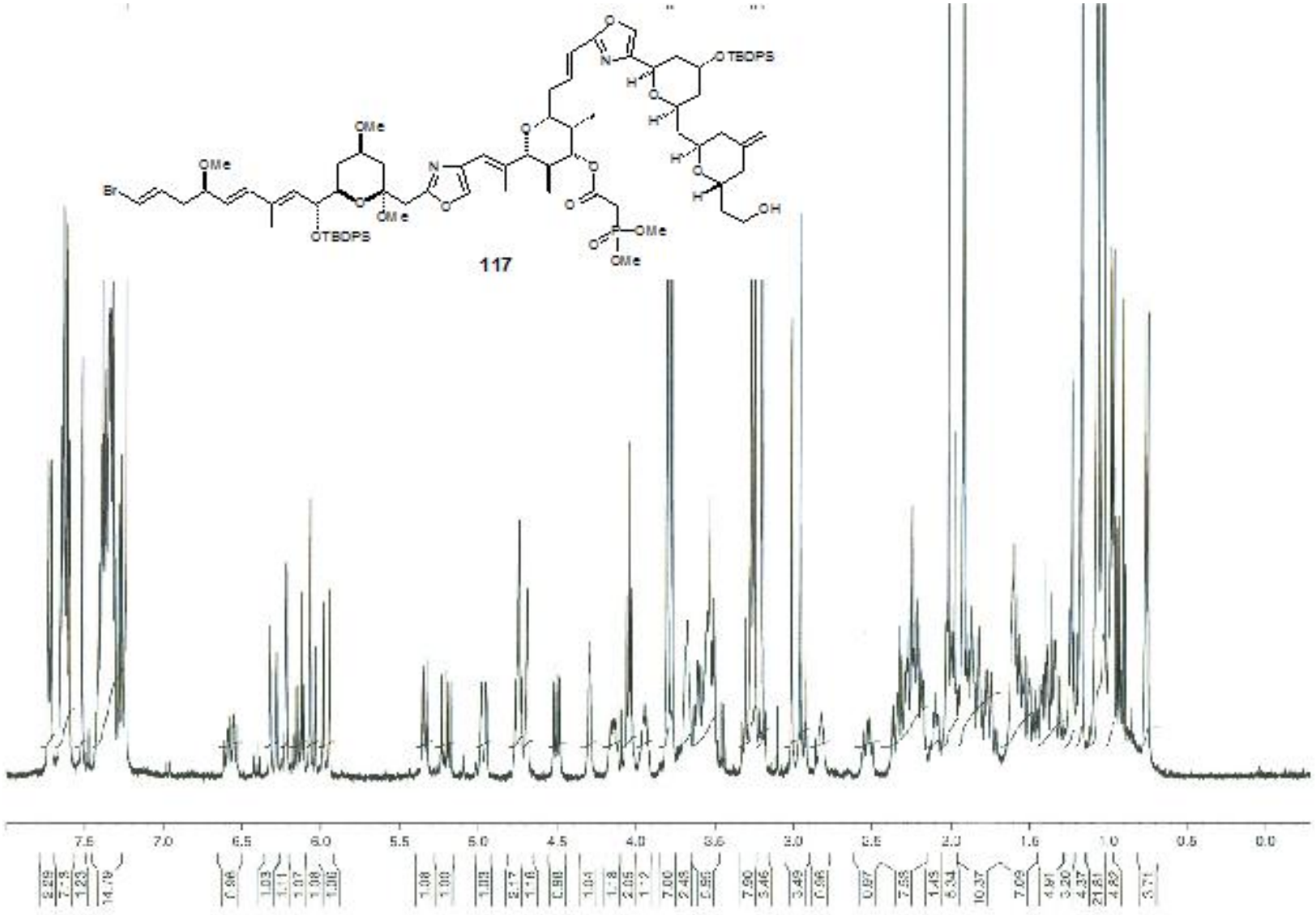


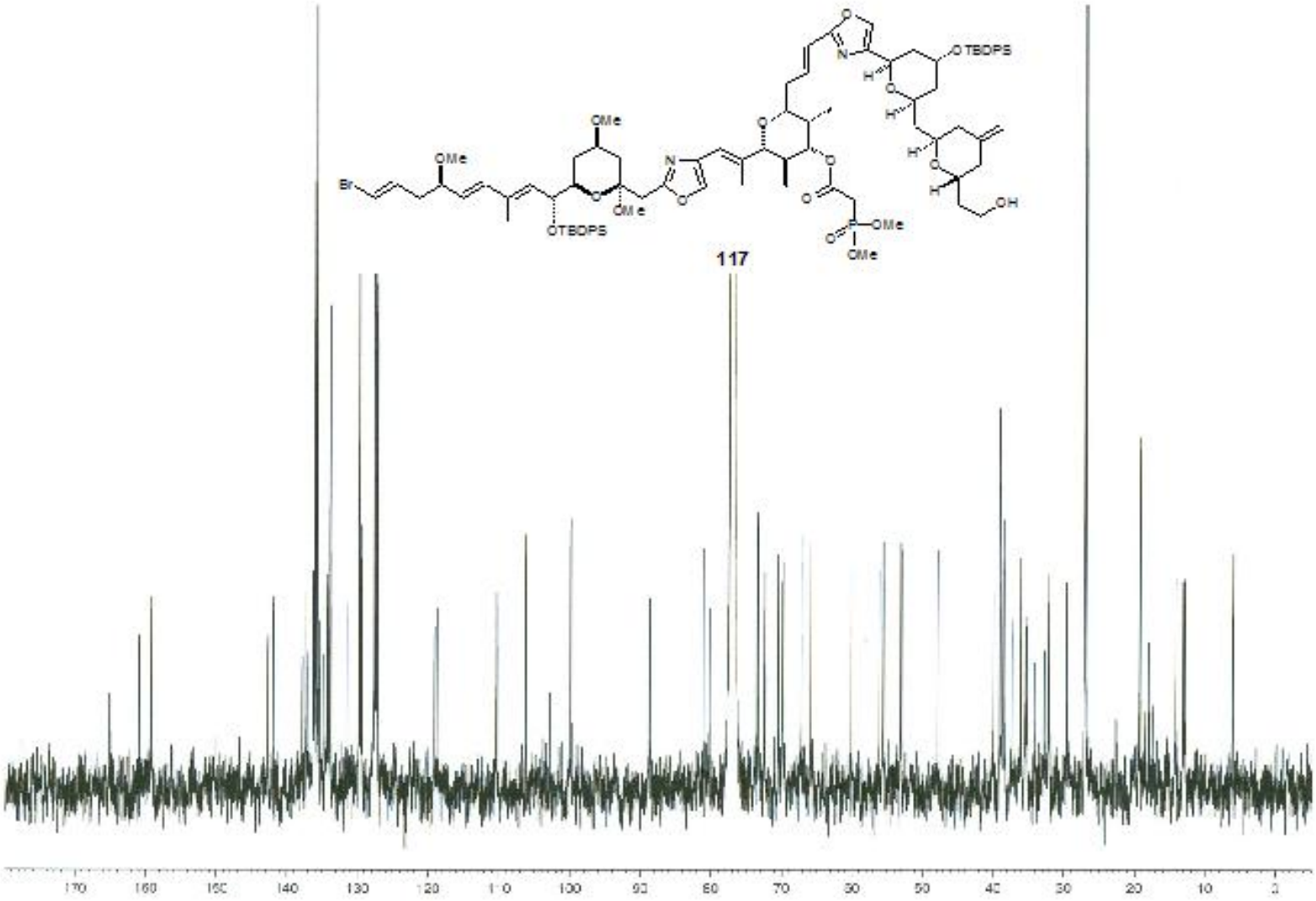


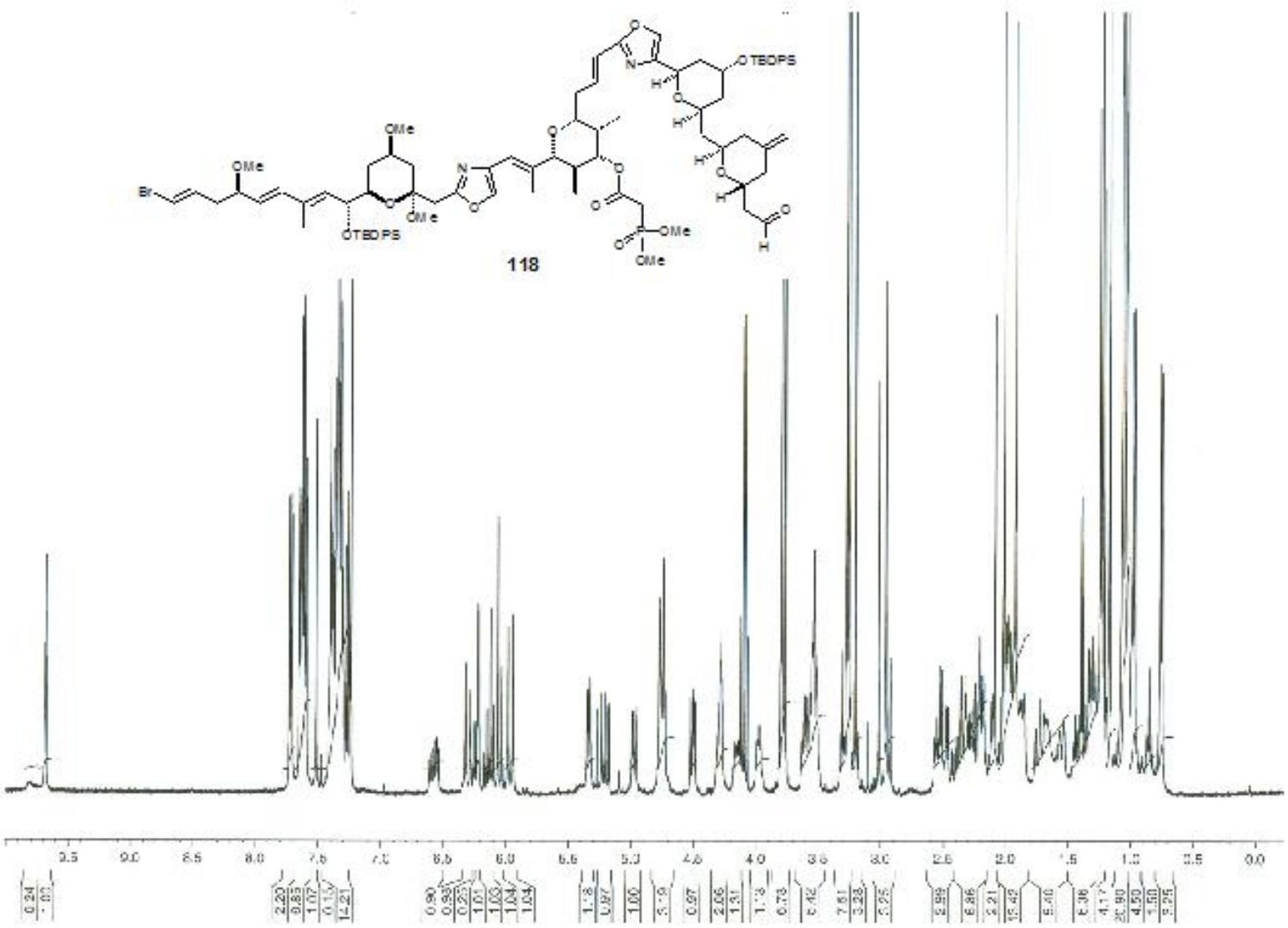


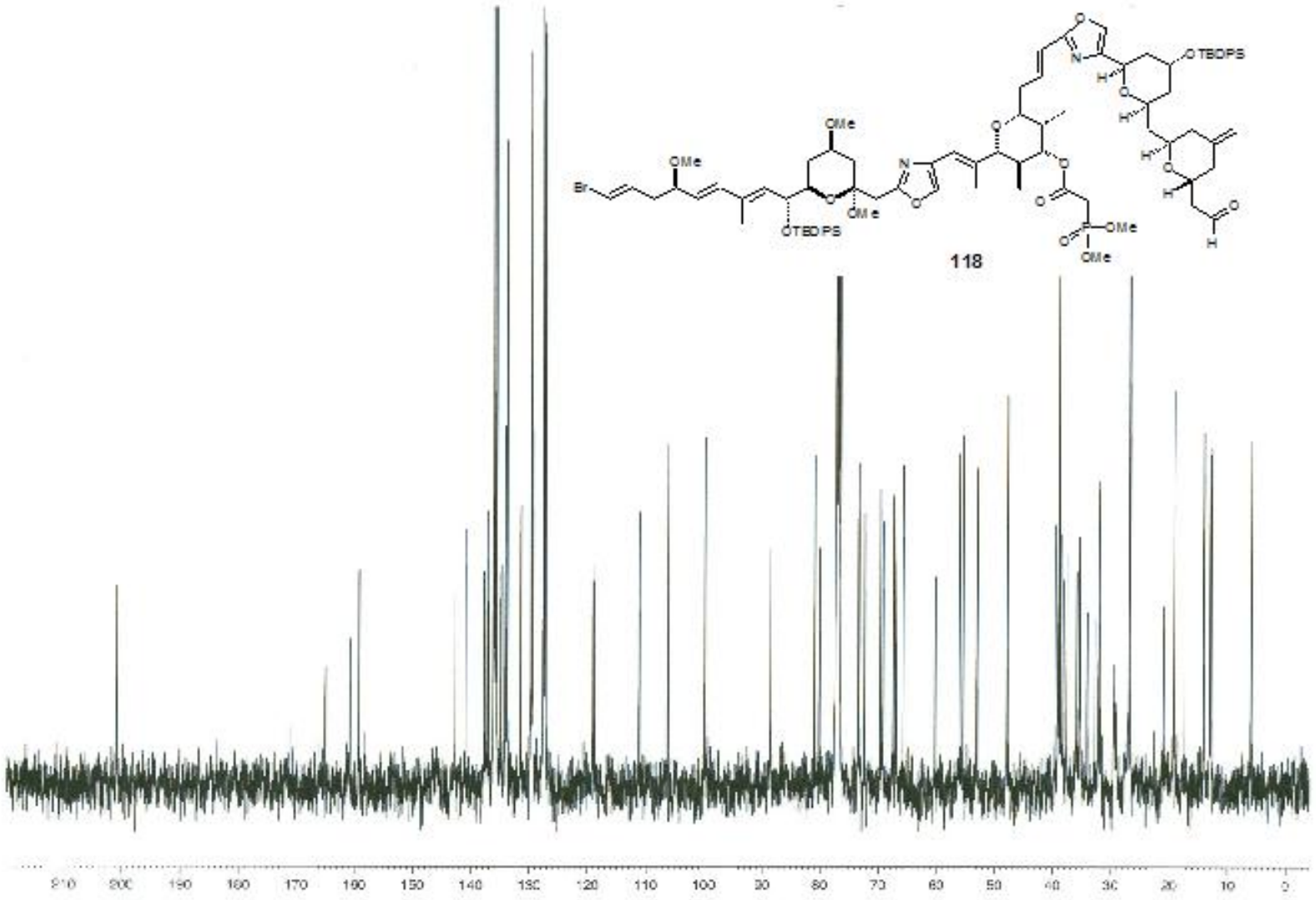


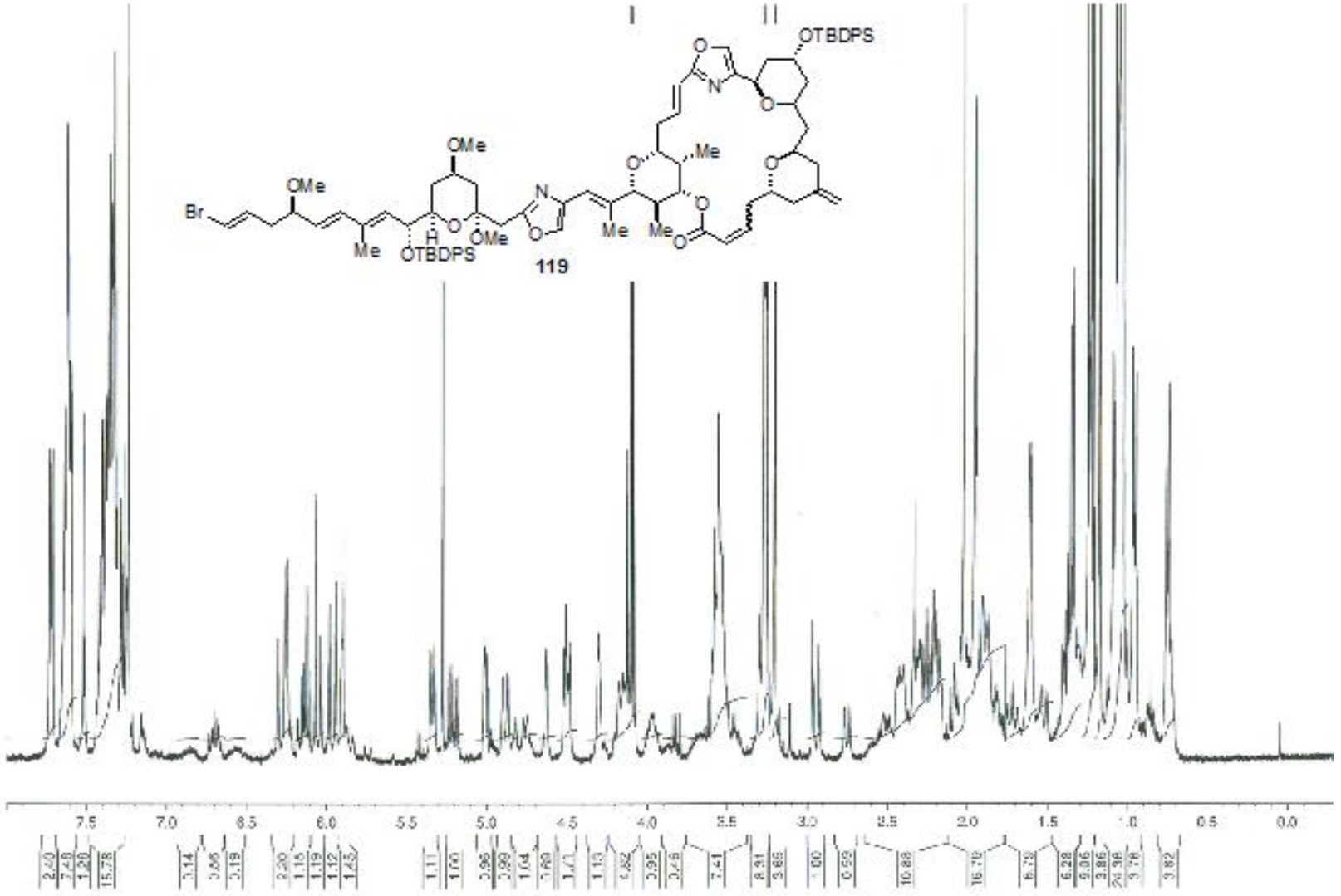


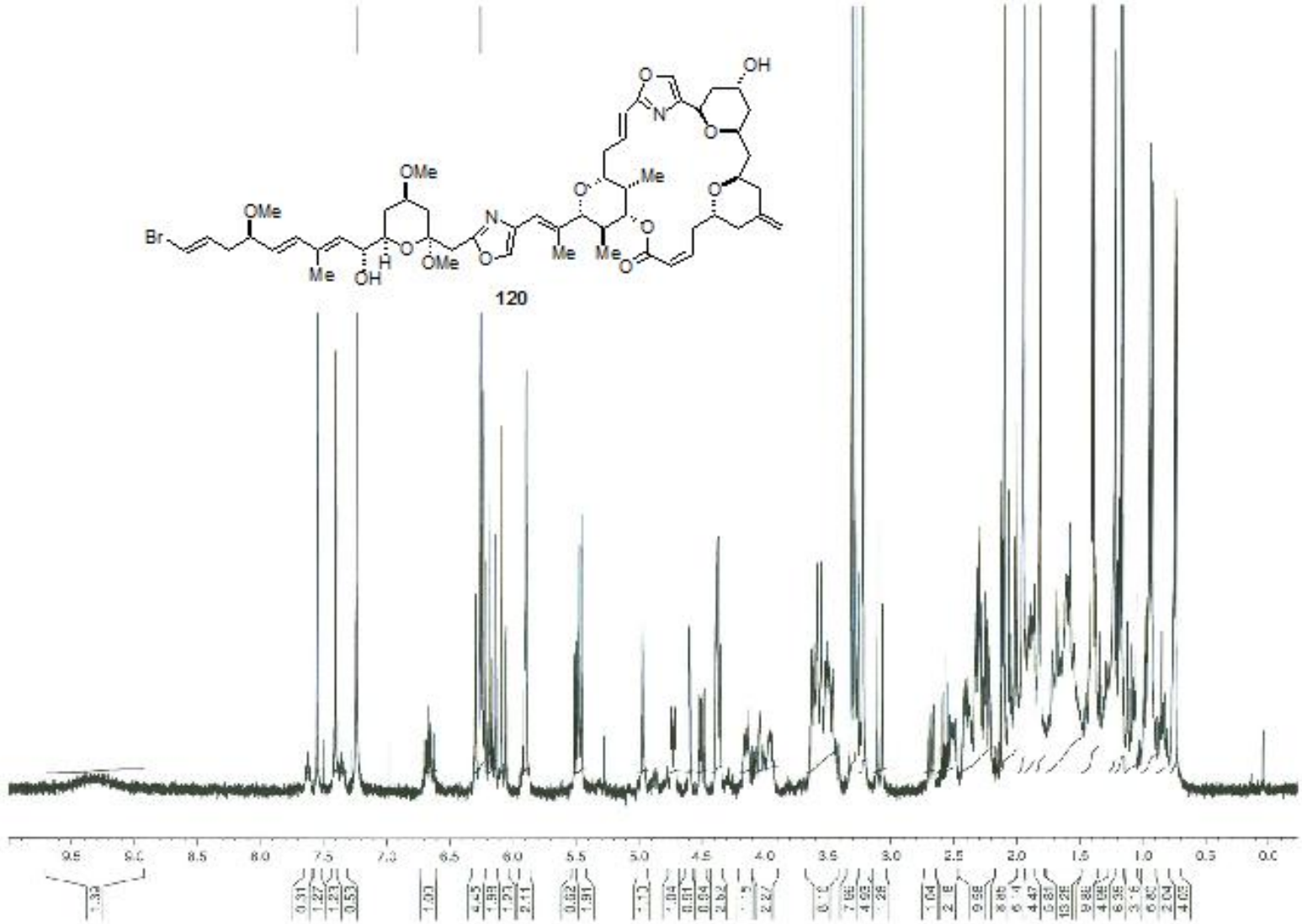


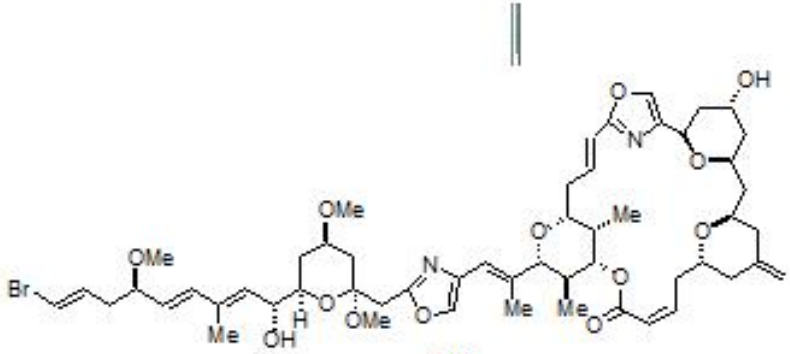




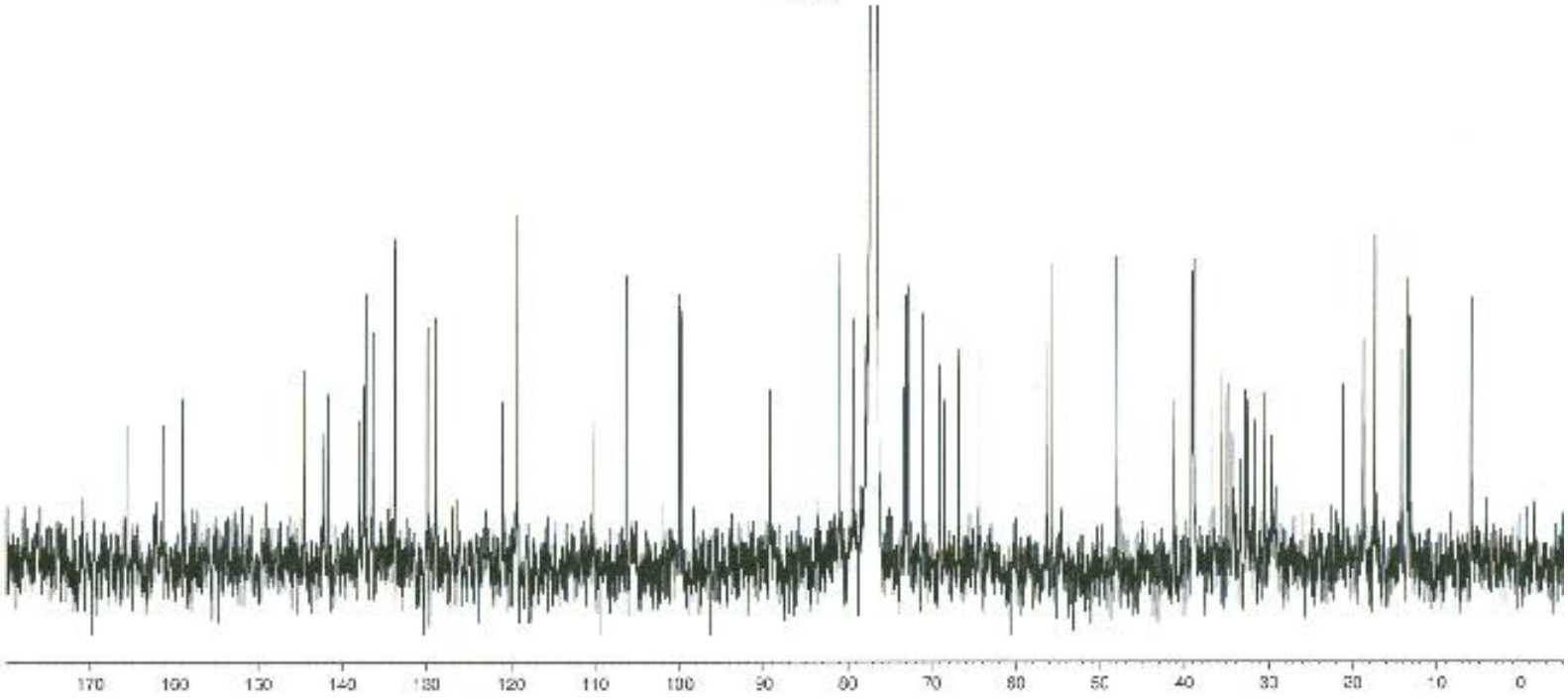


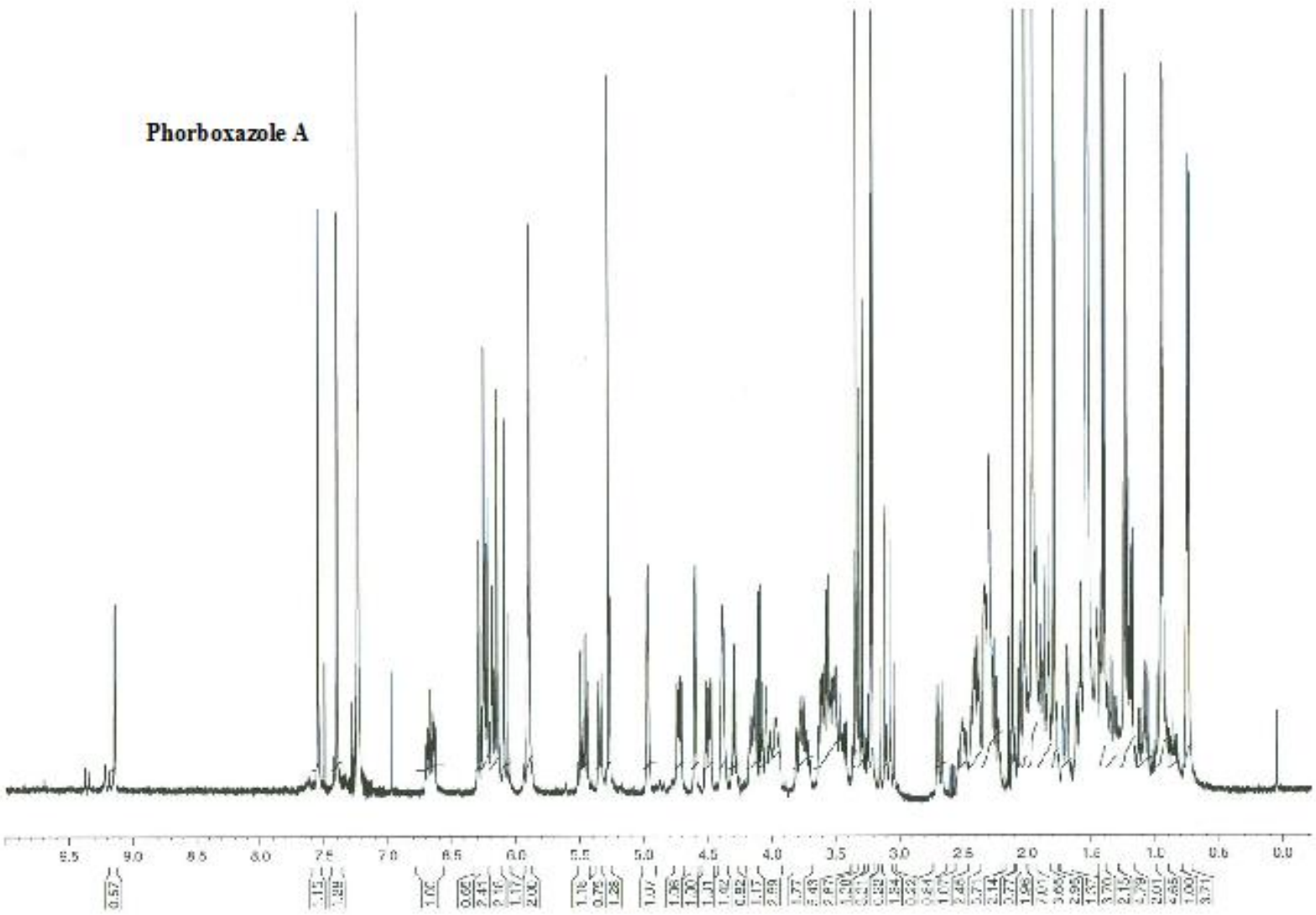






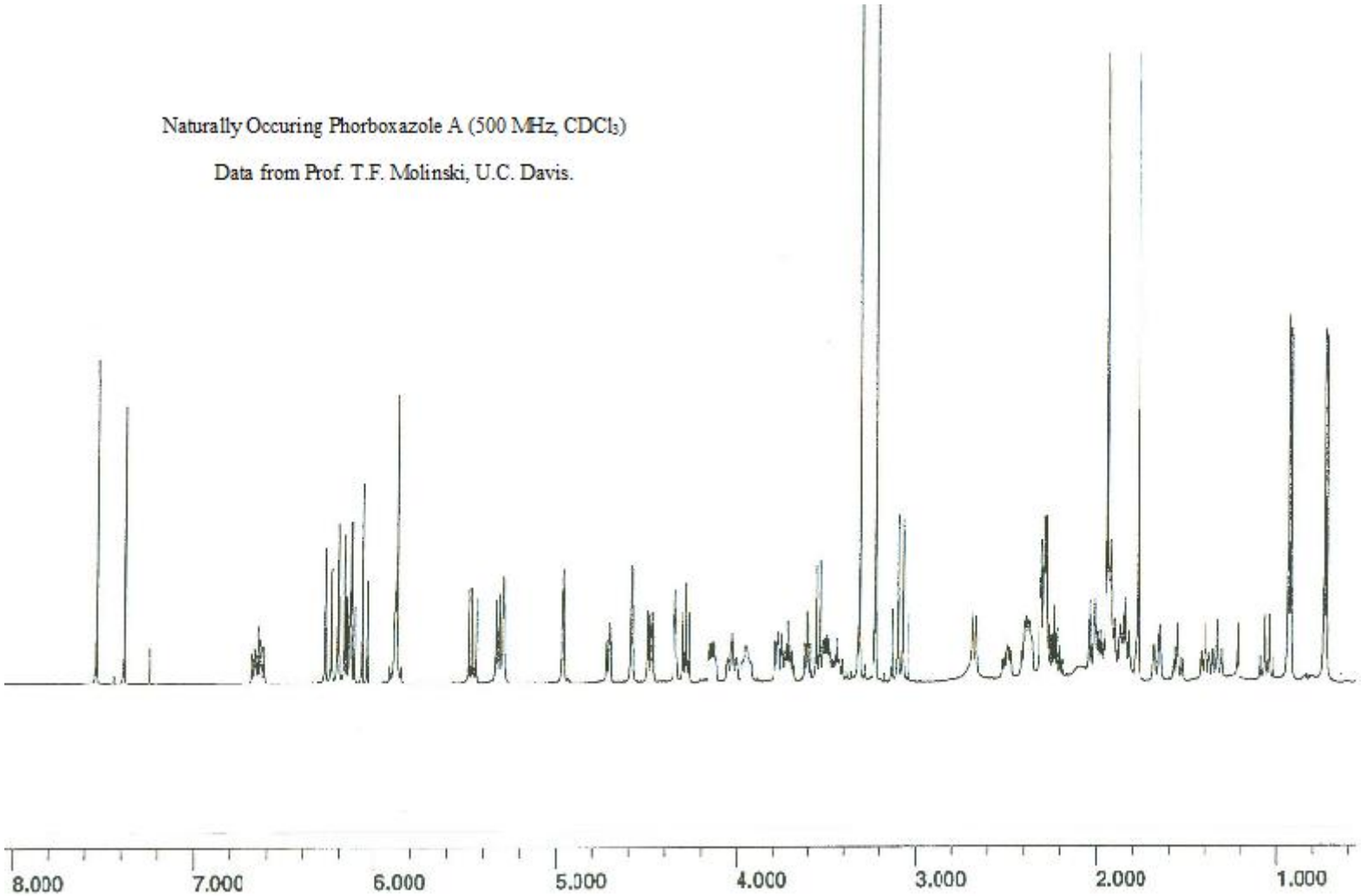
120



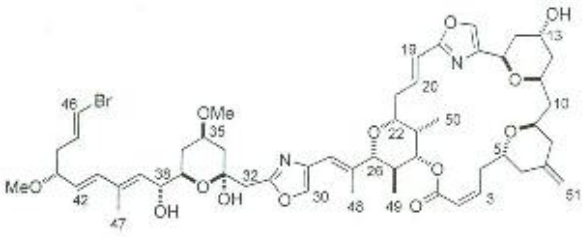


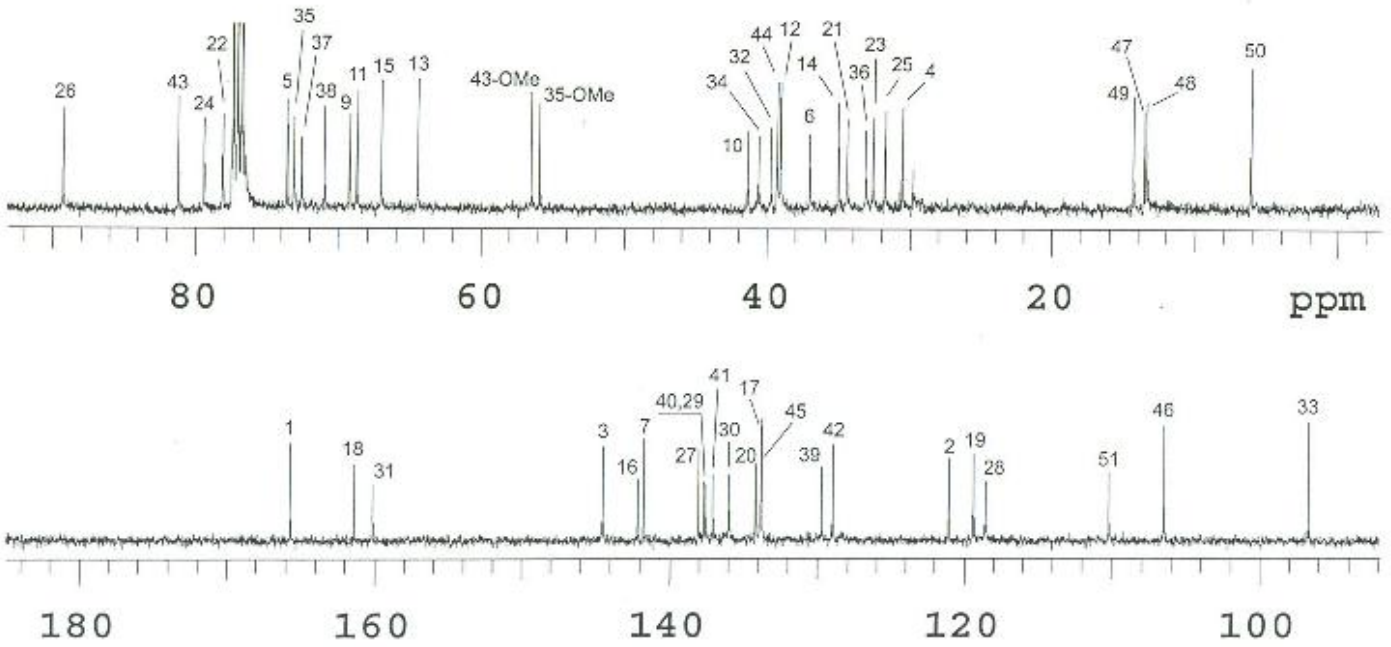
Naturally Occuring Phorboxazole A (500 MHz, $CDCl_3$)

Data from Prof. T.F. Molinski, U.C. Davis.



^{13}C NMR (100 MHz) spectrum of synthetic phorboxazole A



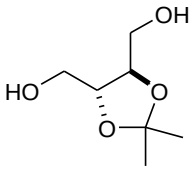


Position	Natural* (δ, ppm)	Synthetic** (δ, ppm)	Δδ	Position	Natural * (δ, ppm)	Synthetic** (δ, ppm)	Δδ	Position	Natural * (δ, ppm)	Synthetic** (δ, ppm)	Δδ
1	165.6	165.7	+0.1	28	118.5	118.5	0.0	10	41.2	41.3	+0.1
18	161.3	161.4	+0.1	51	110.1	110.2	+0.1	34	40.4	40.5	+0.1
31	160.0	160.1	+0.1	46	106.4	106.4	0.0	32	39.7	39.7	0.0
3	144.4	144.5	+0.1	33	96.6	96.7	+0.1	44	39.2	39.3	+0.1
16	142.1	142.0	-0.1	26	89.2	89.2	0.0	12	39.0	39.0	0.0
7	141.7	141.7	0.0	43	81.1	81.1	0.0	8	38.9	39.0	+0.1
27	137.9	138.0	+0.1	24	79.3	79.3	0.0	6	36.9	37.0	+0.1
40	137.5	137.7	+0.2	22	78.0	78.0	0.0	14	34.9	35.0	+0.1
29	137.5	137.5	0.0	35	73.0	73.0	0.0	21	34.3	34.4	+0.1
41	137.0	137.4	+0.4	37	72.5	72.5	0.0	36	33.0	33.1	+0.1
30	135.9	136.0	+0.1	38	70.9	71.0	+0.1	23	32.5	32.6	+0.1
20	134.1	134.2	+0.1	9	69.1	69.1	0.0	25	31.7	31.7	0.0
17	133.7	133.8	+0.1	11	68.6	68.6	0.0	4	30.4	30.5	+0.1
45	133.7	133.8	+0.1	15	66.9	66.9	0.0	48	14.2	14.2	0.0
39	129.9	129.7	-0.2	13	64.3	64.4	+0.1	47	13.4	13.5	+0.1
42	128.9	128.8	-0.1	43-OMe	56.3	56.3	0.0	49	13.3	13.4	+0.1
2	121.0	121.0	0.0	35-OMe	55.7	55.8	+0.1	50	6.0	6.0	0.0
19	119.3	119.3	0.0								
5	73.5	73.5	0.0								

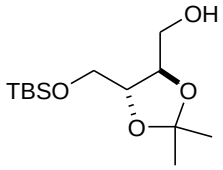
* Recorded in CDCl3 at 100MHz, reported by Molinski *et al*.

** Recorded in CDCl3 at 150MHz

^{13}C NMR Data for Natural and Synthetic Phorboxazole A

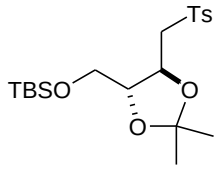


((4*R*,5*R*)-2,2-Dimethyl-1,3-dioxolane-4,5-diyl)dimethanol (8). To a solution of lithium aluminium hydride (4.16 g, 0.109 mol) in ether (80 mL) was added a solution of (4*S*,5*S*)-diethyl 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (15.75 g, 65.24 mmol) in ether (40 mL) dropwise over 40 min. The mixture was refluxed for 24 h, then was cooled to 0~5 ^{o}C and cautiously treated with water (4.2 mL), 4N aqueous sodium hydroxide solution (4.2 mL), and water (12.6 mL). The mixture was stirred at room temperature until the unreacted lithium aluminium hydride had completely decomposed, then was filtered through a Büchner funnel and the collected solid was extracted with tetrahydrofuran. The combined extract was dried (Na_2SO_4), and concentrated under reduced pressure, and the residual oil was purified by flash chromatography to give **8 (**7.78 g, 73%) as a colourless oil. The spectral data matched those reported for **8**.[46]



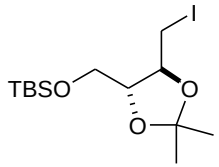
((4*R*,5*R*)-5-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (9). To a suspension of hexane-washed sodium hydride (1.36 g, 33.9 mmol) in tetrahydrofuran (50 mL) was added **8** (5.50 g, 33.9 mmol) and the mixture was stirred for 45 min, at which time a white precipitate had

formed. *tert*-Butyldimethylsilyl chloride was added and vigorous stirring was continued for 10 h. The mixture was poured into ethyl acetate (250 mL), washed with 10% aqueous potassium carbonate (50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The resulting oil was purified by flash chromatography on silica gel to give **9** (7.60 g, 81%) as a colourless oil: $[\alpha]_D^{23}$ -16.3 (c 7.5, $CHCl_3$); IR (neat) 3471, 2986, 2930, 2858, 1472, 1463, 1370, 1254, 1217, 1167, 1082, 1004, 837, 778, 675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.00 (dd, *J* = 5, 8 Hz, 1H), 3.92 – 3.89 (m, 2H), 3.82 – 3.64 (m, 3H), 2.38 (dd, *J* = 5, 8 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.5, 80.5, 78.4, 64.1, 63.1, 27.4, 27.3, 26.2, 18.7, -5.1; MS (CI) *m/z* 277 $(M+H)^+$, 261, 245, 220, 219, 187, 161, 143, 131, 117, 89; HRMS (CI) *m/z* 277.1833 (calcd for $C_{13}H_{29}O_4Si$: 277.1835).

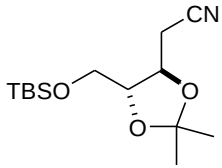


((4R,5R)-5-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl 4-methylbenzenesulfonate (10). A solution of **9** (1.323 g, 4.79 mmol) and *p*-toluenesulfonyl chloride (1.37 g, 7.17 mmol) in pyridine (5 mL) was stirred for 16 h at 0 °C and then was diluted with water and extracted with ethyl acetate (20 mL x 3). The combined extract was washed with aqueous sodium bicarbonate solution (30 mL) and brine (20 mL), and dried (Na_2SO_4). The solvents were removed under reduced pressure and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to give **10** (1.88 g, 91%) as a colourless oil: $[\alpha]_D^{23}$ +6.6 (c 5, $CHCl_3$); IR (neat) 2986, 2930, 2857, 1598, 1471, 1462, 1369, 1253, 1178, 1095, 983, 838, 780, 665, 555 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8 Hz, 2H), 7.34 (d, J = 8 Hz, 2H), 4.26 – 4.18 (m, 1H), 4.14 – 4.05 (m, 2H), 3.87 – 3.81 (m, 1H), 3.78 (dd, J = 4, 10 Hz, 1H), 3.64 (dd, J = 6, 10 Hz, 1H), 2.45 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H), 0.86 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 133.2,

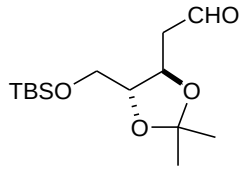
130.2, 128.4, 110.4, 77.6, 76.9, 70.1, 63.7, 27.3, 27.2, 26.2, 22.0, 18.6, -5.1; MS (CI) *m/z* 431 $(M+H)^+$, 415, 373, 355, 315, 271, 259, 229, 201, 173, 143; HRMS (CI) *m/z* 431.1916 (calcd for $C_{20}H_{35}O_6SSi$: 431.1924).



***tert*-Butyl(((4*R*,5*S*)-5-(iodomethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane (11).** A solution of **10** (8.07 g, 18.7 mmol) and sodium iodide (8.43 g, 56.2 mmol) in acetone (50 mL) was heated under reflux for 30 h. The solvent was evaporated, water (50 mL) was added, and the resulting solution was extracted with ether (50 mL x 3). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 12:1) to give **11** (7.00 g, 96%) as a colourless oil: $[\alpha]_D^{23}$ +2.8 (c 5.0, $CHCl_3$); IR (neat) 2986, 2954, 2929, 2857, 1471, 1370, 1253, 1137, 1091, 1005, 938, 838, 778, 675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.92 – 3.78 (m, 3H), 3.76 – 3.68 (m, 1H), 3.42 (dd, *J* = 5, 10, 1H), 3.31 (dd, *J* = 5, 10, 1H), 1.56 (s, 3H), 1.47 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.9, 81.5, 78.3, 64.1, 27.9, 27.7, 26.3, 18.7, 7.3, -5.0; MS (CI) *m/z* 387 $(M+H)^+$, 371, 313, 285, 271, 241, 184, 143, 117, 75; HRMS (CI) *m/z* 387.0855 (calcd for $C_{13}H_{28}IO_3Si$: 387.0853).

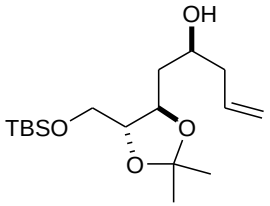


2-((4*R*,5*R*)-5-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)acetonitrile (12). A solution of **11** (0.118 g, 0.199 mmol) and potassium cyanide (0.032 g, 0.49 mmol) in dimethyl sulfoxide (0.7 mL) was stirred for 3 d at room temperature. Water (15 mL) was added to the mixture and the resulting solution was extracted with ethyl acetate (10 mL x 3). The combined extract was washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel to give **12** (0.056 g, 99%) as a colourless oil: $[\alpha]_D^{23}$ +7.1 (c 1.1, $CHCl_3$); IR (neat) 2988, 2955, 2930, 2858, 2253, 1472, 1372, 1253, 1143, 1088, 1006, 972, 837, 779, 671 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.09 – 4.03 (m, 1H), 3.91 – 3.84 (m, 2H), 3.65 (ddd, *J* = 2, 5, 10 Hz, 1H), 2.81 (dd, *J* =4, 17 Hz, 1H), 2.64 (dd, *J* =4, 17 Hz, 1H), 1.44 (s, 3H), 1.38 (s, 3H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 117.1, 110.4, 79.7, 75.0, 63.7, 27.4, 26.2, 22.4, 18.6, -5.1,; MS (CI) *m/z* 286 $(M+H)^+$, 267, 228, 170, 156, 140, 117, 97, 73; HRMS (CI) *m/z* 286.1835 (calcd for $C_{14}H_{28}NO_3Si$: 286.1839).



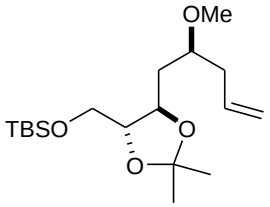
2-((4*R*,5*R*)-5-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)acetaldehyde (13). To a solution of **12** (0.287g, 1.00 mmol) in ether (3 mL) at –78 °C was added slowly neat diisobutylaluminium hydride (0.197 mL, 1.1 mmol). The mixture was stirred at -78 °C for 2 h, after which it was transferred to a pre-cooled (0 °C) saturted solution of potassium sodium tartrate. The mixture was stirred, the layers were separated and the aqueous layer was extracted with ether (10 mL x 3). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 10:1) to yield **13** (202 mg, 69%) as a colourless oil: $[\alpha]_D^{23}$ +2.2 (c 5, $CHCl_3$); IR (neat) 2987, 2955, 2930, 2858, 1730, 1472, 1380, 1254, 1086, 837, 778 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (dd, *J* = 2, 2 Hz, 1H), 4.35 (ddd, *J* = 4, 8, 8 Hz, 1H), 3.83 (dd, *J*

= 4, 10 Hz, 1H), 3.73 (ddd, *J* = 4, 6, 8 Hz, 1H), 3.66 (dd, *J* = 6, 10 Hz, 1H), 2.75 (ddd, *J* = 2, 4, 17 Hz, 1H), 2.66 (ddd, *J* = 2, 8, 17 Hz, 1H), 1.39 (s, 3H), 1.38 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 190.7, 80.7, 74.6, 63.8, 47.5, 27.5, 27.2, 26.2, 18.7, -5.1; MS (CI) *m/z* 287 $(M-H)^+$, 273, 245, 231, 213, 173, 155, 145, 115; HRMS (CI) *m/z* 287.1676 (calcd for $C_{14}H_{27}O_4Si$: 287.1679).

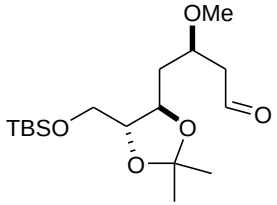


(*S*)-1-((4*R*,5*R*)-5-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-en-2-ol (14). To a solution of (-)-*B*-methoxydiisopinocampheyl -borane (1.98 g, 6.26 mmol) in ether (7 mL) at 0 °C was added allylmagnesium bromide (1.0M solution in hexane, 5.36 mL) and the solution was allowed to warm to room temperature. After 1 h, the solution was cooled to –100 °C and a solution of **13** (0.967 g, 3.35 mmol) in ether (10 mL) was added slowly. The solution was allowed to warm to –78 °C over 1 h and then to 0 °C. After 1 h, 30% hydrogen peroxide (1.37 mL) and 4N aqueous sodium hydroxide (0.68 mL) were added and the mixture was stirred for 8 h. The mixture was diluted with water (10 mL) and extracted with ether (20 mL x 3), and the combined extract was dried (Na_2SO_4) and concentrated. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 20:1) to yield a mixture of **14** and isopinylcampheol (1.53 g) as a colourless oil. This mixture was used in the next step without further purification. Data for **14**: IR (neat) 3482, 3073, 2929, 2858, 1469, 1372, 1253, 1216, 1084, 913, 836, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 (ddd, *J* = 7, 10, 17 Hz, 1H), 5.17 – 5.07 (m, 2H), 4.15 – 4.01 (m, 1H), 3.98 – 3.87 (m, 1H), 3.87 – 3.64 (m, 3H), 2.36 – 2.20 (m, 2H), 1.94 – 1.77 (m, 2H), 1.41 (s, 3H), 1.38 (s, 3H), 0.89 (s,

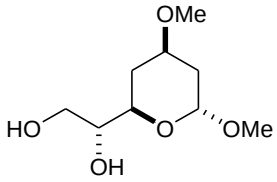
9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.1, 118.2, 117.9, 109.0, 81.6, 80.9, 79.7, 77.6, 77.2, 70.9, 68.6, 64.1, 63.9, 42.4, 40.1, 39.5, 27.7, 27.3, 26.3, 18.7, -5.0, -5.1; MS (CI) *m/z* 331 $(M+H)^+$, 316, 315, 273, 255, 215, 197, 145, 123, 89, 75; HRMS (CI) *m/z* 331.2300 (calcd for $C_{17}H_{35}O_4Si$: 331.2305).



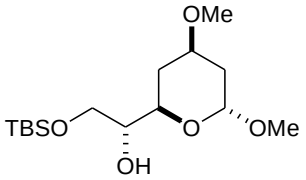
***tert*-Butyl(((4*R*,5*R*)-5-((*S*)-2-methoxypent-4-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane (15)**. To a stirred solution of **14** containing isopinylcampheol (32 mg, 0.097 mmol) in tetrahydrofuran (1.2 mL) was added hexane-washed sodium hydride (12 mg, 0.30 mmol) and the mixture was heated under reflux for 1 h. The mixture was cooled to room temperature and methyl iodide was added dropwise. The resulting solution was heated at reflux for 1.5 h, cooled to 0 ^{o}C, diluted with water (1 mL) and extracted with ether (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by column chromatography on silica gel to yield **15** (26 mg, 79% from **13**) as a colourless oil: $[\alpha]_D^{23}$ +2.5 (c 6.6, $CHCl_3$); IR (neat) 3077, 2984, 2930, 2858, 1472, 1378, 1369, 1253, 1216, 1137, 1095, 913, 837, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 7, 10, 17 Hz, 1H), 5.13 – 5.06 (m, 2H), 4.06 (ddd, *J* = 3, 8, 9 Hz, 1H), 3.78 – 3.71 (m, 2H), 3.70 – 3.61 (m, 1H), 3.52 – 3.44 (m, 1H), 3.38 (s, 3H), 2.33 – 2.29 (m, 2H), 1.74 (ddd, *J* = 3, 9, 14 Hz, 1H), 1.63 (ddd, *J* = 4, 9, 14 Hz, 1H), 1.40 (s, 3H), 1.38 (s, 3H), 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.8, 117.6, 108.9, 82.0, 77.6, 75.9, 63.9, 57.4, 38.9, 38.8, 27.8, 27.4, 26.3, 18.8, -4.9; MS (CI) *m/z* 345 $(M+H)^+$, 331, 289, 257, 231, 199, 171, 169, 125, 113, 75; HRMS (CI) *m/z* 345.2459 (calcd for $C_{18}H_{37}O_4Si$: 345.2461).



(*R*)-4-((4*R*,5*R*)-5-((*tert*-Butyldimethylsilanyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-3-methoxybutanal (16). Ozone was passed into a solution of **15** (0.362 g, 1.05 mmol) in dichloromethane (12 mL) at -78 ^{o}C until a light blue color persisted. Triphenylphosphine (1.38 g, 5.26 mmol) was added and the solution was warmed to room temperature and stirred for 30 min. The mixture was concentrated and the residual oil was purified by flash chromatography on silica gel to give **16** (0.346 g, 95%) as a colourless oil: $[\alpha]_D^{23}$ +9.0 (c 2.6, $CHCl_3$); IR (neat) 2985, 2954, 2930, 2858, 1727, 1472, 1463, 1379, 1253, 1216, 1087, 1005, 837, 778 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (dd, *J* = 2, 2 Hz, 1H), 4.00 (ddd, *J* = 2, 8, 10 Hz, 1H), 3.92 (dddd, *J* = 5, 5, 7, 8 Hz, 1H), 3.80 – 3.74 (m, 1H), 3.69 – 3.61 (m, 2H), 3.38 (s, 3H), 2.69 (ddd, *J* = 2, 5, 16 Hz, 1H), 2.62 (ddd, *J* = 2, 7, 16 Hz, 1H), 1.96 (ddd, *J* = 2, 8, 14 Hz, 1H), 1.62 (ddd, *J* = 5, 10, 14 Hz, 1H), 1.37 (s, 3H), 1.35 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.7, 109.2, 81.5, 76.1, 74.7, 63.8, 57.7, 49.2, 39.1, 27.7, 27.3, 26.3, 18.7, -5.0, -5.1; MS (CI) *m/z* 347 $(M+H)^+$, 329, 303, 287, 255, 245, 213, 197, 173, 143, 129, 85, 73; HRMS (CI) *m/z* 347.2249 (calcd for $C_{17}H_{35}O_5Si$: 347.2254).

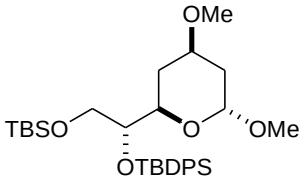


(*R*)-1-((2*R*,4*R*,6*R*)-4,6-Dimethoxytetrahydro-2*H*-pyran-2-yl)ethane-1,2-diol (17). A solution of **16** (52 mg, 0.15 mmol) and pyridinium *p*-toluenesulfonate (2 mg) in methanol (2 mL) was heated under reflux for 12 h and was concentrated. The residual oil was purified by flash chromatography on silica gel (dichloromethane:methanol 95:5) to yield **17** (27 mg, 87%) as a colourless oil: $[\alpha]_D^{23}$ -87.5 (c 1.19, $CHCl_3$); IR (neat) 3420, 2930, 2829, 1456, 1374, 1205, 1121, 1046, 1005, 966, 888 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.90 (d, *J* = 3 Hz, 1H), 3.84 – 3.61 (m, 5H), 3.34 (s, 3H), 3.32 (s, 3H), 2.61 (d, *J* = 5 Hz, 1H), 2.23 – 2.13 (m, 2H), 2.03 – 1.98 (m, 1H), 1.49 – 1.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 99.7, 74.2, 72.3, 69.2, 64.2, 55.9, 55.1, 36.3, 33.7; MS (CI) *m/z* 207 $(M+H)^+$, 197, 175, 156, 143, 117, 113, 87, 71; HRMS (CI) *m/z* 207.1230 (calcd for $C_9H_{19}O_5$: 207.1233).



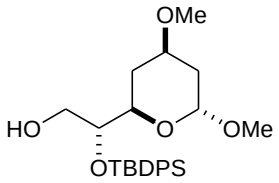
(*R*)-2-(*tert*-Butyldimethylsilanyloxy)-1-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)ethanol (18). Imidazole (18.8 mg, 0.276 mmol), *tert*-butyldimethylsilyl chloride (41 mg, 0.28 mmol) and 4-*N*,*N*-dimethylaminopyridine (2 mg) were added sequentially to a solution of **17** (26 mg, 0.13 mmol) in dimethylformamide (1 mL). After 12 h, the solution was poured into saturated aqueous sodium bicarbonate (5 mL) and extracted with ether (5mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to yield **18** (31.0 mg, 78%) as a colourless oil: $[\alpha]_D^{23}$ - 39.6 (c 0.66, $CHCl_3$); IR (neat) 3473, 2955, 2930, 2858, 2362, 1472, 1362, 1254, 1123, 1053, 1003, 967, 837, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.89 (d, *J* = 3 Hz, 1H), 3.82 (ddd, *J* = 2, 4, 12 Hz, 1H), 3.70 – 3.55 (m, 4H), 3.32 (s, 3H), 3.30 (s, 3H), 2.44 (d, *J* = 5 Hz, 1H), 2.13 (dddd, *J* = 2, 3, 4, 13 Hz, 1H), 2.01 – 1.96 (m, 1H), 1.48 – 1.38 (m, 2H), 0.89

(s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.6, 74.3, 72.7, 67.7, 64.0, 55.8, 55.0, 36.4, 33.7, 26.2, 18.6, -5.0; MS (CI) *m/z* 321 $(M+H)^+$, 313, 289.1, 257.1, 239.1, 213, 199, 173, 145, 117, 89, 75; HRMS (CI) *m/z* 319.19409 (M^+ – H) (calcd for $C_{15}H_{31}O_5Si$: 319.19408).

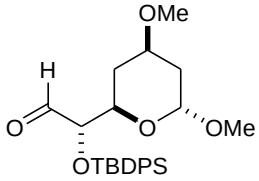


(*R*)-5-((2*R*,4*R*,6*R*)-4,6-Dimethoxytetrahydro-2*H*-pyran-2-yl)-2,2,8,8,9,9-hexamethyl-3,3-diphenyl-4,7-dioxa-3,8-disiladecane (19). A solution of **18** (282 mg, 0.879 mmol) in dichloromethane (7.5 mL) at 0 °C was treated with 2,6-lutidine (0.32 mL, 2.6 mmol) and *tert*-butyldiphenylsilyl trifluoromethanesulfonate (529 mg, 1.32 mmol). The solution was stirred at 0 °C for 30 min and at room temperature for 5 h, and the reaction was quenched with saturated sodium bicarbonate solution. After addition of dichloromethane (25 mL), the pH of the aqueous phase was adjusted to *ca*. 7.0 with 1M hydrochloric acid. The aqueous phase was extracted with dichloromethane (20 mL x 3), and the combined extract was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 15:1) to yield **19** (471 mg, 96%) as a colourless oil: $[\alpha]_D^{23}$ –50.3 (c 0.95, $CHCl_3$); IR (neat) 3069, 3045, 2955, 2930, 2894, 2857, 2826, 1472, 1427, 1389, 1361, 1303, 1256, 1204, 1191, 1123, 1111, 1050, 1006, 972, 939, 927, 898, 836, 776, 739, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.70 (m, 4H), 7.44 – 7.33 (m, 6H), 4.86 (d, *J* = 3 Hz, 1H), 3.77 – 3.67 (m, 3H), 3.59 – 3.45 (m, 2H), 3.29 (s, 3H), 3.19 (s, 3H), 2.12 – 2.04 (m, 1H), 1.90 – 1.82 (m, 1H), 1.46 – 1.18 (m, 2H), 1.06 (s, 9H), 0.79 (s, 9H), -0.11 (s, 3H), -0.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 134.6, 134.3, 130.1, 129.9, 128.0, 127.8, 99.3, 76.2, 73.4, 67.7, 63.7, 55.7, 54.8,

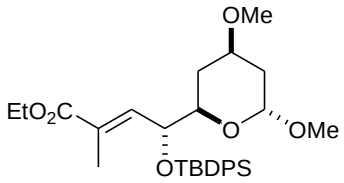
36.7, 33.2, 27.5, 26.3, 20.0, 18.6, -1.0, -5.2; MS (CI) *m/z* 501 $(M - t\text{-}Bu)^+$, 469, 437, 385, 345, 313, 261, 199, 147, 113, 89; HRMS (CI) *m/z* 501.2490 (calcd for $C_{27}H_{41}O_5Si_2$: 501.2493, M – t-Bu).



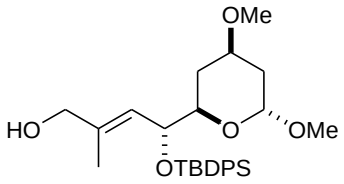
(*R*)-2-(*tert*-Butyldiphenylsilanyloxy)-2-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)ethanol (20). A solution of **19** (57 mg, 0.096 mmol) and pyridinium *p*-toluenesulfonate (1.2 mg, 4.8 μmol) in methanol (5 mL) was heated at reflux for 3 h. The solution was poured into a saturated sodium bicarbonate solution and extracted with ether (5 mL x 3), and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 3:1) to give **20** (34 mg, 75%) as a colourless oil: $[\alpha]_D^{23}$ –35.8 (c 0.75, $CHCl_3$); IR (neat) 3462, 2930, 2856, 1472, 1427, 1362, 1261, 1112, 1049, 822, 776, 740, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 4H), 7.47 – 7.35 (m, 6H), 4.79 (d, *J* = 3 Hz, 1H), 3.84 (dt, *J* = 5, 5 Hz, 1H), 3.72 (ddd, *J* = 2, 4, 12 Hz, 1H), 3.71 – 3.60 (m, 2H), 3.57 – 3.46 (m, 1H), 3.31 (s, 3H), 3.12 (s, 3H), 2.13 – 2.03 (m, 2H), 1.80 (bs, 1H), 1.45 – 1.25 (m, 2H), 1.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 136.1, 134.2, 133.7, 130.4, 130.3, 128.2, 99.5, 74.4, 72.9, 69.9, 64.1, 55.8, 55.0, 36.6, 32.3, 27.5, 19.8; MS (CI) *m/z* 413 $(M - OMe)^+$, 355, 323, 303, 271, 245, 213, 199, 163, 135, 113, 91; HRMS (CI) *m/z* 413.2138 (calcd for $C_{24}H_{33}O_4Si$: 413.2148, M – OMe).



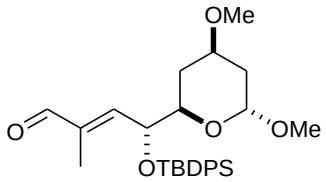
(*S*)-2-(*tert*-Butyldiphenylsilanyloxy)-2-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)acetaldehyde (21). A solution of dimethyl sulfoxide (47 μL, 0.66 mmol) in dichloromethane (2 mL) at –78 °C was treated with oxalyl chloride (29 μL, 0.33 mmol) and after 15 min a solution of **20** (98 mg, 0.22 mmol) in dichloromethane (1 mL) was added. After a further 15 min, triethylamine (92 μL, 0.66 mmol) was added and the solution was warmed to –10 °C over1 h, then warmed to room temperature for 30 min. The solution was poured into a mixture of ether (5 mL) and saturated ammonium chloride solution (5 mL), and the aqueous layer was separated and extracted with ether (5 mL x 3). The combined extract was washed with saturated sodium bicarbonate solution (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 6:1) to give **21** (97 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ –93.9 (c 0.59, $CHCl_3$); IR (neat) 2957, 2932, 2896, 2858, 2830, 1736, 1472, 1428, 1376, 1258, 1114, 1047, 969, 921, 890, 822, 741, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.65 (d, *J* = 1 Hz, 1H), 7.69 – 7.63 (m, 4H), 7.44 – 7.26 (m, 6H), 4.82 (d, *J* = 3 Hz, 1H), 4.06 (d, *J* = 1, 3 Hz, 1H), 3.91 (dt, *J* = 12, 3 Hz, 1H), 3.59 – 3.49 (m, 1H), 3.25 (s, 3H), 3.12 (s, 3H), 2.11 – 2.05 (m, 1H), 1.78 – 1.72 (m, 1H), 1.48 – 1.36 (m, 2H), 1.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 136.3, 133.2, 130.5, 128.2, 99.6, 79.9, 72.5, 70.2, 55.7, 55.1, 36.4, 33.1, 27.4, 19.9; MS (CI) *m/z* 441 $(M - H)^+$; HRMS (CI) *m/z* 441.2099 (calcd for $C_{25}H_{33}O_5Si$: 441.2097, M - H).



(*R*,*E*)-Ethyl 4-(*tert*-butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*R*)-4,6-dimethoxytetra hydro-2*H*-pyran-2-yl)-2-methylbut-2-enoate (22). To a solution of **21** (10.2 mg, 23 μmol) in toluene (1.5 mL) was added **23** (25 mg, 69 μmol) and the solution was heated at 100 ^{o}C for 12 h under argon. The solution was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 12:1) to give **22** (11.7 mg, 96%) as a colourless oil: $[\alpha]_D^{23}$ –71.1 (c 0.52, $CHCl_3$); IR (neat) 2957, 2931, 2894, 2857, 2829, 1714, 1472, 1428, 1237, 1112, 1049, 970, 822, 740, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 – 7.60 (m, 4H), 7.42 – 7.25 (m, 6H), 6.62 (dq, *J* = 1, 9 Hz, 1H), 4.83 (d, *J* = 3 Hz, 1H), 4.46 (dd, *J* = 6, 9 Hz, 1H), 4.17 – 4.07 (m, 2H), 3.72 (ddd, *J* = 2, 6, 12 Hz, 1H), 3.63 – 3.52 (m, 1H), 3.31 (s, 3H), 3.22 (s, 3H), 2.14 – 2.08 (m, 1H), 2.00 – 1.94 (m, 1H), 1.34 (d, *J* = 1 Hz, 3H), 1.26 (t, *J* = 7 Hz, 3H), 1.44 – 1.16 (m, 2H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 139.8, 136.4, 134.1, 133.9, 130.1, 130.0, 129.9, 128.0, 127.8, 99.4, 73.0, 72.6, 71.5, 60.9, 55.8, 54.9, 36.4, 32.8, 27.8, 19.8, 14.6, 13.2; MS (CI) *m/z* 495 $(M - OMe)^+$, 437, 377, 353, 279, 239, 199, 113, 87; HRMS (CI) *m/z* 495.2564 (calcd for $C_{29}H_{39}O_5Si$: 495.2567, M^+-OMe).

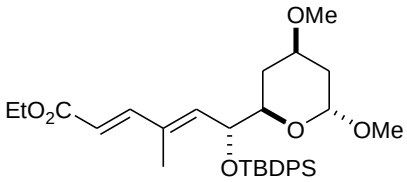


(*R*,*E*)-4-(*tert*-Butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-2-methylbut-2-en-1-ol (24). To a solution of **22** (92 mg, 0.18 mmol) in toluene (0.5 mL) at -78 ^{o}C was added diisobutylaluminium hydride (75 μL, 0.44 mmol, 0.25M solution in toluene) and the mixture was stirred for 1 h at –78 ^{o}C. Saturated Rochelle salt solution (1 mL) and ethyl acetate (2 mL) were added, and the mixture was allowed to warm to room temperature and was stirred for 2 h. The organic layer was separated, the aqueous layer was extracted with ethyl acetate (5 mL x 3) and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 4:1) to give **24** (81.8 mg, 96%) as a colourless oil: $[\alpha]_D^{23}$ -46.4 (c 2.56, $CHCl_3$); IR (neat) 3448, 3071, 3048, 2957, 2931, 2895, 2857, 2822, 1472, 1427, 1370, 1303, 1260, 1204, 1157, 1112, 1066, 1049, 969, 908, 823, 740, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.70 (m, 4H), 7.47 – 7.35 (m, 6H), 5.32 (dq, *J* = 9, 1 Hz, 1H), 4.92 (d, *J* = 3 Hz, 1H), 4.51 (dd, *J* = 6, 9 Hz, 1H), 3.73 (d, *J* = 13 Hz, 1H), 3.68 (d, *J* = 13 Hz, 1H), 3.75 – 3.59 (m, 2H), 3.35 (s, 3H), 3.33 (s, 3H), 2.20 – 2.16 (m, 1H), 2.02 – 1.98 (m, 1H), 1.49 – 1.42 (m, 1H), 1.25 – 1.10 (m, 1H), 1.16 (d, *J* = 1 Hz, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 136.5, 135.3, 134.3, 130.0, 129.9, 127.9, 127.7, 125.0, 99.4, 73.2, 72.6, 72.0, 68.4, 55.9, 54.9, 36.4, 33.1, 30.1, 27.4, 19.8, 14.4; MS (CI) *m/z* 453 (M - OMe)$^{+}$, 409, 395, 363, 339, 311, 253, 199, 165, 135, 113, 87; HRMS (CI) *m/z* 453.2457 (calcd for $C_{27}H_{37}O_4Si$: 453.2461, M^{+} - OMe).



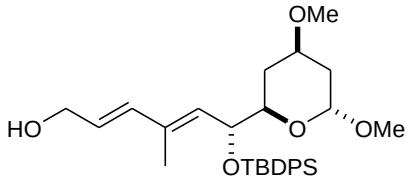
(*R*,*E*)-4-(*tert*-Butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-2-methylbut-2-enal (25). A solution of dimethyl sulfoxide (8.3 μL, 0.12 mmol) in dichloromethane (1 mL) at –78 ^{o}C was treated with oxalyl chloride (5.1 μL, 0.059 mmol), and after 15 min a solution of **24**

(19 mg, 0.039 mmol) in dichloromethane (1.5 mL) was added. After a further 15 min, triethylamine (16 μL, 0.12 mmol) was added and the solution was warmed to –10 °C over 1 h, then warmed to room temperature for 0.5 h. The solution was poured into a mixture of ether (5 mL) and saturated ammonium chloride solution (5 mL) and the aqueous layer was separated and extracted with ether (5 mL x 3). The combined extract was washed with saturated sodium bicarbonate solution (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 6:1) to yield **25** (17.6 mg, 93%) as a colourless oil: $[\alpha]_D^{23}$ –63.6 (c 2.4, $CHCl_3$); IR (neat) 3071, 3045, 2954, 2931, 2895, 2857, 2828, 1693, 1472, 1427, 1377, 1260, 1203, 1112, 1071, 1048, 999, 972, 910, 822, 803, 740, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.47 (s, 1H), 7.74 – 7.62 (m, 4H), 7.49 – 7.33 (m, 6H), 6.36 (dq, *J* = 9, 1 Hz, 1H), 4.85 (d, *J* = 3 Hz, 1H), 4.68 (dd, *J* = 5, 9 Hz, 1H), 3.79 (ddd, *J* = 2, 5, 12 Hz, 1H), 3.66 – 3.58 (m, 1H), 3.34 (s, 3H), 3.21 (s, 3H), 2.18 – 2.13 (m, 1H), 2.08 – 2.04 (m, 1H), 1.46 – 1.24 (m, 2H), 1.34 (d, *J* = 1 Hz, 3H), 1.12 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 151.8, 140.0, 136.3, 133.9, 133.5, 130.4, 128.1, 128.0, 99.5, 72.9, 72.2, 71.4, 55.9, 54.9, 36.4, 32.7, 27.4, 19.8, 9.9; MS (CI) *m/z* 451 $(M - OMe)^+$, 425, 393, 361, 338, 309, 281, 263, 231, 199, 163, 145, 113, 87; HRMS (CI) *m/z* 451.2308 (calcd for $C_{27}H_{35}O_4Si$: 451.2305, M^+ - OMe).



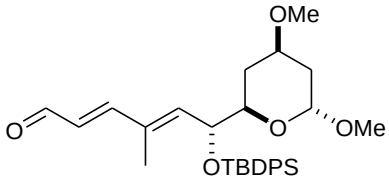
(*R*,2*E*,4*E*)-Ethyl 6-(*tert*-butyldiphenylsilanyloxy)-6-((2*R*,4*R*,6*R*)-4,6-dimethoxy tetrahydro-2*H*-pyran-2-yl)-4-methylhexa-2,4-dienoate (26). To a slurry of hexane-washed sodium hydride (8 mg, 0.197 mmol) in tetrahydrofuran (1.5 mL) at 0 °C was added **27** (39.2 μL, 0.197 mmol) and the mixture was stirred for 0.5 h. A solution of **25** (47.7 mg, 0.0988 mmol) in tetrahydrofuran (1 mL) was added and the mixture was allowed to warm to room temperature and was

stirred for 1 h. The reaction was quenched with water (1 mL) and the mixture was extracted with ether (3 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1) to afford **26** (52.4 mg, 96%) as a colourless oil: $[\alpha]_D^{23}$ -148.5 (c 0.57, $CHCl_3$); IR (neat) 2958, 2930, 2890, 2857, 2824, 1714, 1622, 1472, 1427, 1366, 1305, 1269, 1173, 1111, 1068, 1048, 976, 822, 740 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.60 (m, 4H), 7.40 – 7.31 (m, 6H), 7.15 (dd, *J* = 1, 16 Hz, 1H), 5.80 (d, *J* = 9 Hz, 1H), 5.70 (d, *J* = 16 Hz, 1H), 4.83 (d, *J* = 3 Hz, 1H), 4.50 (dd, *J* = 6, 9 Hz, 1H), 4.21 (q, *J* = 7 Hz, 2H), 3.69 (ddd, *J* = 2, 6, 12 Hz, 1H), 3.60 – 3.55 (m, 1H), 3.30 (s, 3H), 3.23 (s, 3H), 2.14 – 2.09 (m, 1H), 1.97 – 1.93 (m, 1H), 1.31 (t, *J* = 7 Hz, 3H), 1.26 (d, *J* = 1 Hz, 3H), 1.42 – 1.09 (m, 2H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 149.0, 139.5, 136.4, 134.7, 134.2, 134.1, 130.1, 127.9, 127.8, 118.0, 99.4, 73.0, 72.6, 71.7, 60.7, 55.9, 54.9, 36.4, 32.9, 27.4, 19.8, 14.7, 13.0; MS (CI) *m/z* 552 $(M)^+$ 520, 495, 463, 437, 403, 379, 349, 321, 305, 265, 227, 199, 145, 113, 87; HRMS (FAB) *m/z* 552.2897 (calcd for $C_{32}H_{44}O_6Si$: 552.2907).



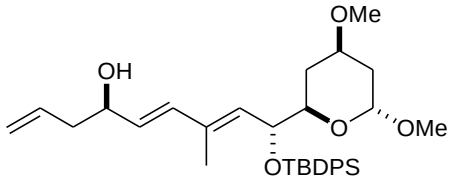
(*R*,2*E*,4*E*)-6-(*tert*-Butyldiphenylsilanyloxy)-6-((2*R*,4*R*,6*R*)-4,6-dimethoxytetra hydro-2*H*-pyran-2-yl)-4-methylhexa-2,4-dienol (28). To a solution of **26** (52.4 mg, 0.0947 mmol) in toluene (2 mL) at -78 °C was added diisobutylaluminium hydride (1.5 mL, 0.280 mmol, 0.187M solution in toluene) and the solution was stirred for 1 h at –78 °C. Saturated Rochelle salt solution (1 mL) and ethyl acetate (2 mL) were added, and the mixture was allowed to warm to room temperature and was stirred for 2 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (5 mL x 3). The combined

extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 4:1) to yield **28** (45.4 mg, 94%) as a colourless oil: $[\alpha]_D^{23}$ –111.4 (c 0.42 , $CHCl_3$); IR (neat) 3435, 2954, 2929, 2890, 2856, 2822, 1472, 1427, 1260, 1203, 1157, 1112, 1066, 1048, 967, 909, 822, 739, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.60 (m, 4H), 7.43 – 7.28 (m, 6H), 6.10 (dd, *J* = 1, 16 Hz, 1H), 5.63 (dt, *J* = 16, 6 Hz, 1H), 5.44 (d, *J* = 9 Hz, 1H), 4.83 (d, *J* = 3 Hz, 1H), 4.47 (dd, *J* = 6, 9 Hz, 1H), 4.16 (d, *J* = 6 Hz, 2H), 3.69 (ddd, *J* = 2, 6, 12 Hz, 1H), 3.60 – 3.52 (m, 1H), 3.30 (s, 3H), 3.22 (s, 3H), 2.13 – 2.07 (m, 1H), 1.97 – 1.91 (m, 1H), 1.24 (d, *J* = 1 Hz, 3H), 1.42 – 1.08 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 136.4, 136.2, 135.3, 134.5, 134.4, 131.8, 129.9, 129.8, 127.8, 127.7, 99.4, 73.2, 72.7, 71.9, 66.3, 64.2, 55.8, 54.9, 36.4, 33.0, 30.1, 27.4, 19.8, 13.3; MS (CI) *m/z* 510 $(M)^+$, 453, 421, 365, 348, 289, 229, 199, 145, 113, 87; HRMS (CI) *m/z* 510.2796 (calcd for $C_{30}H_{42}O_5Si$: 510.2802, M^+).



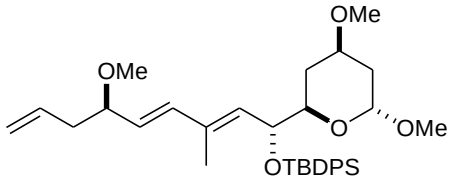
(*R*,2*E*,4*E*)-6-(*tert*-Butyldiphenylsilanyloxy)-6-((2*R*,4*R*,6*R*)-4,6-dimethoxytetra hydro-2*H*-pyran-2-yl)-4-methylhexa-2,4-dienal (29). A solution of dimethyl sulfoxide (19 μL, 0.27 mmol) in dichloromethane (2 mL) at –78 °C was treated with oxalyl chloride (11.7 μL, 0.133 mmol) and after 15 min a solution of **28** (45.4 mg, 0.089 mmol) in dichloromethane (1 mL) was added. After a further 15 min, triethylamine (37 μL, 0.27 mmol) was added and the solution was warmed to –10 °C for 1 h, then was warmed to room temperature for 0.5 h. The solution was poured into a mixture of ether (5 mL) and saturated ammonium chloride solution (5 mL), and the aqueous layer was separated and extracted with ether (5 mL x 3). The combined extract was washed with

saturated sodium bicarbonate solution (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 6:1) to give **29** (41.5 mg, 92%) as a colourless oil: $[\alpha]_D^{23}$ –163.8 (c 0.32, $CHCl_3$); IR (neat) 3065, 3045, 2954, 2930, 2894, 2856, 2822, 1682, 1631, 1605, 1427, 1374, 1260, 1203, 1112, 1068, 969, 910, 822, 803, 740, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.56 (d, *J* = 8 Hz, 1H), 7.75 – 7.63 (m, 4H), 7.46 – 7.33 (m, 6H), 6.95 (d, *J* = 16 Hz, 1H), 6.01 (dd, *J* = 8, 16 Hz, 1H), 5.92 (d, *J* = 9 Hz, 1H), 4.86 (d, *J* = 3 Hz, 1H), 4.57 (dd, *J* = 5, 9 Hz, 1H), 3.76 (ddd, *J* = 2, 5, 12 Hz, 1H), 3.65 – 3.59 (m, 1H), 3.35 (s, 3H), 3.25 (s, 3H), 2.18 – 2.14 (m, 1H), 2.05 – 2.01 (m, 1H), 1.35 (d, *J* = 1 Hz, 3H), 1.46 – 1.19 (m, 2H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 157.1, 141.7, 136.4, 136.3, 135.1, 134.1, 133.8, 130.2, 128.7, 128.0, 127.9, 99.5, 73.0, 72.4, 71.6, 55.9, 54.9, 36.4, 32.9, 27.4, 19.8, 13.1; MS (CI) *m/z* 509 $(M+H)^+$, 491, 452, 419, 387, 364, 335, 305, 277, 229, 199, 161, 145, 113; HRMS (CI) *m/z* 509.2720 (calcd for $C_{30}H_{41}O_5Si$: 509.2723, M+H).



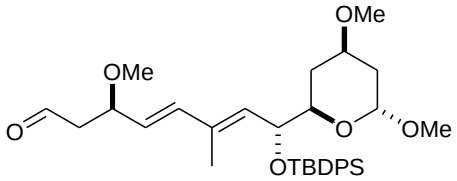
***tert*-Butyl((1*R*,2*E*,4*E*,6*R*)-1-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-6-hydroxy-3-methylnona-2,4,8-trienyloxy)diphenylsilane (30)**. To a solution of (+)-*B*-methoxydiisopinocampheylborane (152 mg, 0.480 mmol) in ether (1.5 mL) at 0 °C was added via syringe allylmagnesium bromide (0.285 mL, 0.285 mmol, 1.0M solution in ether) and the solution was allowed to warm to room temperature. After 1 h, the solution was cooled to –78 °C and a solution of **29** (41.5 mg, 81 μmol) in ether (1 mL) was added slowly. The solution was allowed to warm to –15 °C and after 1 h 30% hydrogen peroxide (130 μL) and 4N aqueous sodium hydroxide (65 μL) were added. The mixture was stirred overnight, diluted with water (1 mL) and extracted with ether (2 mL x

3). The combined extract was dried (Na_2SO_4) and concentrated, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1) to give **30** (32.8 mg, 73%) as a colourless oil: $[\alpha]_D^{23}$ –107.6 (c 0.23, $CHCl_3$); IR (neat) 3441, 3071, 2958, 2929, 2894, 2856, 2822, 1427, 1374, 1299, 1260, 1203, 1111, 1066, 1048, 967, 910, 822, 803, 739, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.59 (m, 4H), 7.43 – 7.27 (m, 6H), 6.08 (d, *J* = 16 Hz, 1H), 5.86 – 5.73 (m, 1H), 5.47 (dd, *J* = 7, 16 Hz, 1H), 5.42 (d, *J* = 10 Hz, 1H), 5.19 – 5.12 (m, 2H), 4.83 (d, *J* = 3 Hz, 1H), 4.48 (dd, *J* = 6, 9 Hz, 1H), 4.18 (q, *J* = 6 Hz, 1H), 3.66 (ddd, *J* = 2, 6, 12 Hz, 1H), 3.60 – 3.51 (m, 1H), 3.30 (s, 3H), 3.24 (s, 3H), 2.37 – 2.23 (m, 2H), 2.14 – 2.08 (m, 1H), 1.97 – 1.92 (m, 1H), 1.63 (bs, 1H), 1.21 (d, *J* = 1 Hz, 3H), 1.46 – 1.08 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 136.4, 135.4, 134.6, 134.4, 131.7, 130.8, 129.9, 129.8, 127.8, 127.7, 118.7, 99.4, 73.2, 72.8, 72.2, 71.9, 55.8, 54.9, 42.5, 36.4, 33.0, 27.4, 19.8, 13.3; MS (CI) *m/z* 519 $(M - OMe)^+$ 493, 461, 443, 405, 388, 336, 322, 289, 239, 213, 199, 145, 113, 87; HRMS (CI) *m/z* 519.2939 (calcd for $C_{32}H_{43}O_4Si$: 519.2931, M – OMe).



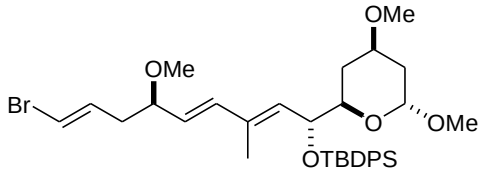
***tert*-Butyl((1*R*.2*E*,4*E*,6*R*)-1-(2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-6-methoxy-3-methylnona-2,4,8-trienyloxy)diphenylsilane (31).** To a stirred solution of **30** (32.8 mg, 59 μmol) in tetrahydrofuran (2.5 mL) was added hexane-washed sodium hydride (15 mg, 0.37 mmol) and the suspension was heated under reflux for 1 h. The solution was cooled to room temperature and methyl iodide (37 μL, 0.59 mmol) was added. The solution was heated under reflux for 1.5 h, cooled to 0 °C, diluted with water (1 mL) and extracted with ether (3 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 19:1) to

give **31** (30 mg, 89%) as a colourless oil: $[\alpha]_D^{23}$ –99.1 (c 0.15, $CHCl_3$); IR (neat) 3071, 2954, 2929, 2894, 2855, 2822, 1463, 1427, 1374, 1260, 1203, 1111, 1066, 1049, 967, 911, 822, 803, 739, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.60 (m, 4H), 7.43 – 7.26 (m, 6H), 6.00 (d, *J* = 16 Hz, 1H), 5.77 (ddt, *J* = 17, 10, 7 Hz, 1H), 5.40 (d, *J* = 9 Hz, 1H), 5.29 (dd, *J* = 8, 16 Hz, 1H), 5.12 – 5.04 (m, 2H), 4.85 (d, *J* = 3 Hz, 1H), 4.48 (dd, *J* = 6, 9 Hz, 1H), 3.71 – 3.53 (m, 3H), 3.30 (s, 3H), 3.25 (s, 3H), 3.22 (s, 3H), 2.42 – 2.20 (m, 2H), 2.17 – 2.09 (m, 1H), 2.00 – 1.90 (m, 1H), 1.20 (d, *J* = 1 Hz, 3H), 1.42 – 1.08 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 136.5, 136.4, 135.4, 135.0, 134.6, 134.3, 131.5, 129.9, 129.8, 128.9, 127.8, 127.6, 117.2, 99.4, 82.4, 73.2, 72.7, 71.9, 56.6, 55.8, 54.9, 40.7, 36.4, 33.1, 27.4, 19.8, 13.3; MS (CI) *m/z* 533 $(M - OMe)^+$ 507, 475, 419, 388, 335, 299, 239, 199, 145, 113, 85; HRMS (CI) *m/z* 533.3073 (calcd for $C_{33}H_{45}O_4Si$: 533.3087, M – OMe).



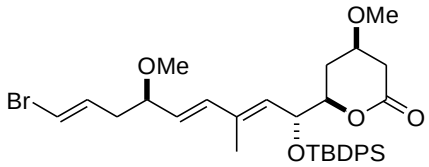
(3*R*,4*E*,6*E*,8*R*)-8-(*tert*-Butyldiphenylsilanyloxy)-8-((2*R*,4*R*,6*R*)-4,6-dimethoxytetra hydro-2*H*-pyran-2-yl)-3-methoxy-6-methylocta-4,6-dienal (32). To a solution of **31** (34.1 mg, 60.4 μmol) in tetrahydrofuran-water (1:1, 6 mL) were added osmium tetraoxide (0.04M in H_2O, 75.4 μL, 5 mol %) and sodium periodate (26 mg, 121 μmol) and the mixture was stirred at room temperature for 20 h under argon. The mixture was diluted with water (5 mL) and extracted with ether (5 mL x 3), and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 7:1) to furnish **32** (18.3 mg, 54%) as a colourless oil: $[\alpha]_D^{23}$ -65.3 (c 0.19, $CHCl_3$); IR (neat) 2954, 2920, 2850, 1727, 1463, 1427, 1375, 1111, 1067, 1048, 968, 822, 804, 740, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 1, 3 Hz, 1H),

7.73 – 7.60 (m, 4H), 7.43 – 7.29 (m, 6H), 6.08 (d, *J* = 16 Hz, 1H), 5.44 (d, *J* = 9 Hz, 1H), 5.30 (dd, *J* = 8, 16 Hz, 1H), 4.85 (d, *J* = 3 Hz, 1H), 4.49 (dd, *J* = 6, 9 Hz, 1H), 4.10 (dt, *J* = 8, 4 Hz, 1H), 3.69 (ddd, *J* = 2, 6, 12 Hz, 1H), 3.64 – 3.53 (m, 1H), 3.31 (s, 3H), 3.24 (s, 3H), 3.22 (s, 3H), 2.68 (ddd, *J* = 3, 8, 16 Hz, 1H), 2.50 (ddd, *J* = 2, 5, 16 Hz, 1H), 2.17 – 2.09 (m, 1H), 2.00 – 1.92 (m, 1H), 1.22 (d, *J* = 1 Hz, 3H), 1.45 – 1.20 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.2, 137.9, 136.4, 135.0, 134.5, 132.6, 130.0, 129.8, 127.8, 127.7, 127.2, 99.4, 73.1, 72.6, 71.9, 56.7, 55.8, 54.9, 49.9, 36.3, 33.0, 30.1, 27.4, 19.8, 13.3; MS (CI) *m/z* 534 (M^+ – MeOH) 476, 421, 390, 360, 336, 289, 252, 199, 183, 135, 113; HRMS (CI) *m/z* 534.2795 (calcd for $C_{32}H_{42}O_5Si$: 534.2802, M – MeOH).



((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-((2*R*,4*R*,6*R*)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-6-methoxy-3-methylnona-2,4,8-trienyloxy)(*tert*-butyl)diphenylsilane (33). To a suspension of chromium(II) chloride (304 mg, 2.47 mmol) in tetrahydrofuran (17 mL) at 0 °C was added a solution of **32** (80.9 mg, 0.143 mmol) and bromoform (75 μL, 0.86 mmol) in tetrahydrofuran (1 mL). The suspension was allowed to warm to room temperature and was stirred for 12 h, then was diluted with water (10 mL) and extracted with ether (10 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the resulting oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 15:1) to yield **33** (59.8 mg, 65%) as a colourless oil: $[\alpha]_D^{23}$ -61.0 (c 0.15, $CHCl_3$); IR (neat) 2950, 2928, 2855, 2818, 1623, 1472, 1427, 1363, 1261, 1111, 1066, 1048, 968, 937, 909, 822, 803, 739, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.60 (m, 4H), 7.43 – 7.30 (m, 6H), 6.25 – 6.10 (m, 0.5H), 6.13 (d, *J* = 8 Hz, 1H), 6.01 (d, *J* = 16 Hz, 1H), 5.92 – 5.76 (m, 0.5H), 5.42 (d, *J* = 9 Hz, 1H), 5.24 (dd, *J* = 8, 16 Hz, 1H), 4.86 (d, *J* = 3 Hz, 1H), 4.49 (dd, *J* = 6, 9 Hz, 1H),

3.72 – 3.40 (m, 3H), 3.31 (s, 3H), 3.25 (s, 3H), 3.21 (s, 3H), 2.50 – 2.20 (m, 2H), 2.17 – 2.09 (m, 1H), 1.99 – 1.92 (m, 1H), 1.42 – 1.32 (m, 1H), 1.21 (d, *J* = 1 Hz, 3H), 1.20 – 1.10 (m, 1H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8, 136.5, 135.2, 134.6, 134.3, 132.1, 129.9, 129.8, 128.2, 127.8, 127.7, 99.4, 81.6, 73.2, 72.7, 71.9, 56.6, 55.8, 54.9, 36.4, 33.1, 30.1, 27.4, 19.8, 13.3; MS (CI) *m/z* 610 (M^+ – MeOH) 541, 499, 453, 422, 336, 299, 213, 199, 113, 87; HRMS (CI) *m/z* 610.2109 (calcd for $C_{33}H_{43}O_4{}^{79}BrSi$: 610.2114, M – MeOH).

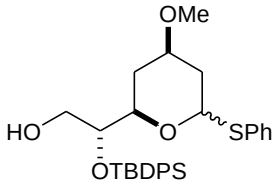


(4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-4-methoxytetrahydropyran-2-one (3).

From 33. To a solution of **33** (29 mg, 46 μmol) in tetrahydrofuran (14 mL) was added 10% hydrochloric acid (5.7 mL) and the mixture was heated for 13 h at 61-65 ^{o}C. The mixture was cooled to room temperature, diluted with ether (10 mL) and washed with saturated sodium bicarbonate solution (10 mL x 3). The separated organic layer was dried and concentrated under reduced pressure and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to give a hemiacetal that was used immediately for the next reaction.

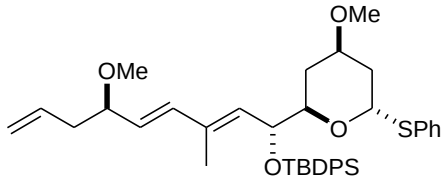
To a solution of the hemiacetal obtained above in dichloromethane (3 mL) was added pyridinium chlorochromate (100 mg, 0.46 mmol), sodium acetate (30 mg, 0.37 mmol) and 4A molecular sieves, and the mixture was stirred for 2 h at room temperature. The mixture was filtered through a short column of silica gel to give **3** (4.5 mg, 16%) as a colourless oil: $[\alpha]_D^{23}$ -23.4 (c 0.22, $CHCl_3$); IR (neat) 3065, 2954, 2926, 2854, 1743, 1625, 1462, 1427, 1360, 1235, 1110, 998, 968, 937, 822, 800, 741, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.58 (m, 4H), 7.42 – 7.27 (m, 6H), 6.17 – 6.11 (m, 1H), 6.05 (d, *J* = 14 Hz,

1H), 6.00 (d, *J* = 16 Hz, 1H), 5.44 (d, *J* = 9 Hz, 1H), 5.29 (dd, *J* = 8, 16 Hz, 1H), 4.62 (dd, *J* = 5, 9 Hz, 1H), 4.16 (ddd, *J* = 3, 5, 12 Hz, 1H), 3.68 – 3.61 (m, 1H), 3.56 (dt, *J* = 13, 6 Hz, 1H), 3.32 (s, 3H), 3.21 (s, 3H), 2.85 (ddd, *J* = 1, 6, 17 Hz, 1H), 2.39 (dd, *J* = 8, 17 Hz, 1H), 2.37 – 2.17 (m, 3H), 1.40 – 1.32 (m, 1H), 1.27 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 136.9, 136.3, 135.9, 133.8, 129.9, 129.7, 129.5, 128.6, 127.7, 127.5, 106.4, 81.0, 79.7, 72.4, 70.7, 56.3, 56.0, 39.1, 36.8, 29.9, 27.0, 19.4, 13.0; MS (CI) *m/z* 569 (M^+ – *t*-Bu), 537, 497, 453, 407, 375, 319, 283, 239, 199, 187, 135; HRMS (CI) *m/z* 569.1368 (calcd for $C_{29}H_{34}O_5{}^{79}BrSi$: 569.1359, M – *t*-Bu).



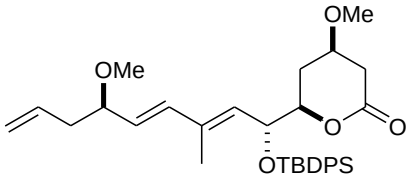
(*R*)-2-(*tert*-Butyldiphenylsilanyloxy)-2-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio) tetrahydro-2*H*-pyran-2-yl)ethanol (34α). To a solution of **20** (207 mg, 0.466 mmol) in 1,2-dichloroethane (6 mL) at 0 °C were added zinc iodide (287 mg, 0.899 mmol) and trimethyl(phenylthio)silane (264 μL, 1.39 mmol). The mixture was allowed to warm to room temperature and was stirred for 5 h, then was diluted with ether (20 mL) and washed with 10% hydrochloric acid (10 mL). The organic layer was separated, washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 10 : 1) to give **34**□ (113 mg, 47%) as a colourless oil: $[\alpha]_D^{23}$ -167.2 (c 0.75, $CHCl_3$); IR (neat) 3470, 3070, 3049, 2956, 2930, 2890, 2856, 1584, 1472, 1427, 1362, 1260, 1111, 1067, 997, 950, 853, 822, 740, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 5H), 7.47 – 7.35 (m, 10H), 5.73 (d, *J* = 5 Hz, 1H), 4.28 (ddd, *J* = 2, 3, 12 Hz, 1H), 3.79 (dt, *J* = 5, 4 Hz, 1H), 3.67 – 3.46 (m, 3H), 3.34 (s, 3H), 2.37 – 2.31 (m, 1H), 2.07 – 2.01 (m, 1H), 1.84 (ddd, *J* = 6, 12, 13 Hz, 1H), 1.55 – 1.40 (m, 1H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 136.2, 136.1,

135.3, 134.2, 133.6, 131.6, 130.4, 130.3, 129.4, 128.2, 127.5, 85.1, 74.6, 73.6, 70.5, 64.0, 55.8, 37.5, 33.0, 27.6, 19.9; MS (CI) *m/z* 413 $(M - SPh)^+$ 381, 323, 303, 257, 225, 179, 111, 79; HRMS (CI) *m/z* 413.2135 (calcd for $C_{24}H_{33}O_4Si$: 413.2148, M – SPh). There was also obtained **34β** (52 mg, 21%) as a colourless oil.



***tert*-Butyl((1*R*,2*E*,4*E*,6*R*)-6-methoxy-1-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio) tetrahydro-2H-pyran-2-yl)-3-methylnona-2,4,8-trienyloxy)diphenylsilane (35)**. To a solution of (4*R*,5*E*,7*E*,9*R*)-9-(*tert*-butyldiphenylsilanyloxy)-9-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-7-methylnona-1,5,7-trien-4-ol obtained from **34α** (21.0 mg, 33 μmol) in tetrahydrofuran (2.5 mL) was added hexane-washed sodium hydride (13 mg, 0.33 mmol) and the mixture was heated at reflux for 1 h. The solution was cooled to room temperature, methyl iodide (21 μL, 0.33 mmol) was added and the solution was heated at reflux for 1.5 h. The mixture was cooled to 0 ^oC, diluted with water (1 mL) and extracted with ether (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 19:1) to give **35** (21.4 mg, 89%) as a colourless oil: $[\alpha]_D^{23}$ –174.4 (c 2.2, $CHCl_3$); IR (neat) 3071, 2956, 2924, 2854, 1463, 1428, 1361, 1260, 1111, 966, 911, 821, 804, 740, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.60 (m, 4H), 7.40 – 7.15 (m, 11H), 5.99 (d, *J* = 16 Hz, 1H), 5.85 – 5.72 (m, 1H), 5.70 (d, *J* = 5 Hz, 1H), 5.45 (d, *J* = 9 Hz, 1H), 5.29 (dd, *J* = 8, 16 Hz, 1H), 5.14 – 5.05 (m, 2H), 4.51 (dd, *J* = 5, 9 Hz, 1H), 4.27 (ddd, *J* = 2, 5, 12 Hz, 1H), 3.66 – 3.55 (m, 2H), 3.36 (s, 3H), 3.22 (s, 3H), 2.42 – 2.21 (m, 3H), 2.14 – 2.05 (m, 1H), 1.82 (ddd, *J* = 6, 12, 17 Hz, 1H), 1.40 – 1.20 (m,

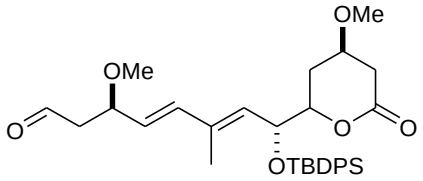
1H), 1.18 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 136.4, 136.4, 135.8, 135.3, 135.0, 134.5, 134.3, 131.9, 131.6, 130.0, 129.8, 129.1, 128.9, 127.9, 127.7, 127.3, 117.3, 85.6, 82.4, 73.6, 72.7, 72.2, 56.6, 55.9, 40.7, 37.6, 33.4, 27.5, 19.8, 13.2; MS (CI) *m/z* 643 $(M + H)^+$, 611, 579, 533, 501, 469, 419, 355, 323, 277, 245, 199, 179, 111, 75; HRMS (CI) *m/z* 643.3280 (calcd for $C_{39}H_{51}O_4SiS$: 643.3277, M + H).



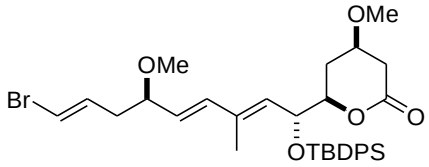
(4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*)-1-(*tert*-Butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-4-methoxytetrahydropyran-2-one (36). To a solution of **35** (42.5 mg, 66 μmol) in tetrahydrofuran-water (5:1, 6 mL) was added silver nitrate (231 mg, 1.36 mmol) and 2,6-lutidine (268 μL, 0.230 mmol) and the solution was stirred for 3 h at room temperature. The solution was diluted with water (5 mL) and the aqueous layer was separated and extracted with ethyl acetate (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was passed through a column of silica gel (hexane:ethyl acetate 4:1) to give the pure hemiacetal as a colourless oil. This material was used immediately in the next reaction.

To a solution of the hemiacetal obtained above in dichloromethane (5 mL) was added tetra-*n*-propylammonium perruthenate (3.8 mg, 11 μmol), 4-methylmorpholine *N*-oxide (45 mg, 0.38 mmol) and 4□ molecular sieves and the mixture was stirred for 3 h at room temperature. The mixture was filtered through silica gel (hexane:ethyl acetate 4:1) to give pure **36** (30.4 mg, 84%) as a colourless oil: $[\alpha]_D^{23}$ –55.3 (c 0.55, $CHCl_3$); IR (neat) 3071, 2928, 2855, 2814, 1748, 1472, 1427, 1360, 1234, 1110, 998, 967, 914, 822, 741, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.60 (m, 4H), 7.43 – 7.26 (m, 6H), 6.02

(d, *J* = 16 Hz, 1H), 5.77 (ddt, *J* = 17, 11, 7 Hz, 1H), 5.45 (d, *J* = 9 Hz, 1H), 5.36 (dd, *J* = 8, 16 Hz, 1H), 5.12 – 5.05 (m, 2H), 4.62 (dd, *J* = 5, 9 Hz, 1H), 4.20 – 4.14 (m, 1H), 3.72 – 3.57 (m, 2H), 3.34 (s, 3H), 3.23 (s, 3H), 2.87 (ddd, *J* = 1, 5, 17 Hz, 1H), 2.41 (dd, *J* = 8, 17 Hz, 1H), 2.34 – 2.21 (m, 3H), 1.60 – 1.50 (m, 1H), 1.28 (d, *J* = 1 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 136.8, 136.7, 136.3, 134.9, 133.9, 133.7, 130.3, 130.0, 129.9, 129.4, 128.1, 127.8, 117.3, 82.2, 80.1, 72.8, 71.2, 56.7, 56.4, 40.6, 37.2, 30.3, 30.1, 27.4, 19.8, 15.7, 13.4; MS (CI) *m/z* 549 $(M + H)^+$ 517, 485, 459, 419, 363, 321, 289, 239, 199, 179, 137, 79; HRMS (CI) *m/z* 549.3019 (calcd for $C_{33}H_{45}O_5Si$: 549.3036, M + H).

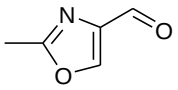


(3*R*,4*E*,6*E*,8*R*)-8-(*tert*-Butyldiphenylsilanyloxy)-3-methoxy-8-((4R)-4-methoxy-6-oxotetrahydro-2*H*-pyran-2-yl)-6-methylocta-4,6-dienal (37). To a solution of **36** (24.1 mg, 44 μmol) in tetrahydrofuran-water (1:1, 4.39 mL, 0.01M) was added osmium tetraoxide (0.001M in *tert*-butanol, 176 μL, 0.4 mol %) and sodium periodate (28.2 mg, 132 μmol) and the mixture was stirred at room temperature for 20 h under argon. The mixture was diluted with water (5 mL) and extracted with ether (5 mL x 3), and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane: EtOAc 5:1) to give **37** (13.7 mg, 57%) as a colourless oil: IR (neat) 3069, 2925, 2854, 1734, 1463, 1427, 1361, 1235, 1156, 1110, 998, 969, 822, 800, 741, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (t, *J* = 2 Hz, 1H), 7.74 – 7.60 (m, 4H), 7.43 – 7.26 (m, 6H), 6.09 (d, *J* = 16 Hz, 1H), 5.49 (d, *J* = 8 Hz, 1H), 5.37 (dd, *J* = 8, 16 Hz, 1H), 4.64 (dd, *J* = 5, 9 Hz, 1H), 4.21 – 4.09 (m, 2H), 3.72 – 3.63 (m, 1H), 3.35 (s, 3H), 3.25 (s, 3H), 2.88 (dd, *J* = 5, 17 Hz, 1H), 2.53 (dd, *J* = 2, 5 Hz, 1H), 2.50 – 2.28 (m, 4H), 1.60 – 1.50 (m, 1H), 1.28 (d, *J* = 1 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ; MS (ES) *m/z* 568 $(M^+ + NH_4)$; HRMS (ES) *m/z* 568.3049 (calcd for $C_{32}H_{46}NO_6Si$: 568.3094, M + NH_4).



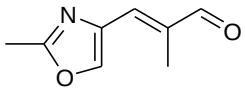
(4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-4-methoxytetrahydropyran-2-one (3).

From 37. Chromium(III) bromide monohydrate was placed in a flame-dried flask which was heated at 130 °C for 24 h. During this period, the colour of the chromium(III) bromide hydrate changed from black to the dark green colour of anhydrous chromium(III) bromide. To this anhydrous chromium(III) bromide (467 mg, 1.60 mmol) at 0 °C was added tetrahydrofuran (7 mL) which caused a change in colour from green to dark brown. A solution of lithium aluminium hydride (0.80 mL, 0.8 mmol, 1M solution in tetrahydrofuran) was added dropwise, during which the colour of the solution changed from brown to bright green. To this solution were added **37** (57 mg, 93 μmol) and bromoform (70 μL, 0.801 mmol) and the mixture was stirred for 12 h at 50 °C. The mixture was diluted with water (10 mL) and extracted with ether (10 mL x 3), and the combined extract was washed with brine (5 mL), dried and concentrated under reduced pressure. The resulting oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 8:1) to furnish **3** (23.4 mg, 40%), identical with material obtained from **33**.

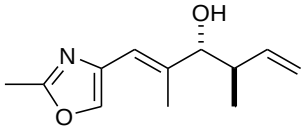


2-Methyloxazole-4-carboxaldehyde (39). To a solution of **38** (756 mg, 5.40 mmol) in ether (100mL) at –78 °C under argon was added diisobutylaluminium hydride (1.0M, 10.8 mL, 10.8 mmol) in one portion. The mixture was allowed to warm to room temperature and stirred for 3 h. Methanol (2.0 mL) was added and the mixture was diluted with dichloromethane (100 mL) and washed with saturated aqueous sodium potassium tartrate

solution (100 mL). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to give **39** (332 mg, 61%) as a colourless oil: IR (film) 2959, 2931, 1701, 1458, 1260, 1016, 797 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □□2.53□(s,3H)□□, 8.16 □s□□1H□, 9.89 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □□13.74, 140.9, 144.5, 163.0, 183.8; MS (CI) *m/z* 112 $(M+H)^+$, 95, 84, 69; HRMS (CI) *m/z* 112.0401, calcd for $C_5H_6NO_2$ *m/z* 112.0399.

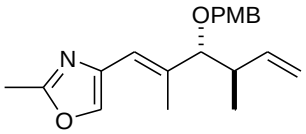


(1*E*)-2-Methyl-3-(2-methyloxazol-4-yl)prop-2-enal (41). A solution of **39** (2.23 g, 20.1 mmol) and **40** (7.025 g, 22.1 mmol) in benzene (300 mL) was heated at 80 °C for 18 h. Benzene was removed under reduced pressure and ether (200 mL) was added to the residue. The mixture was filtered, the filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 2:1) to give **41** (2.82 g, 93%) as a colourless oil: IR (film) 3128, 3058, 2974, 2931, 2838, 2728, 1701, 1686, 1663, 1637, 1630, 1597, 1414, 1380, 1360, 1327, 1286, 1218, 1172, 1109, 1030, 975, 904, 844, 791 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 2.07 (s, 3H), 2.50 (s, 3H), 7.05 (s, 1H), 7.81 (s, 1H), 9.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 11.0, 13.8, 137.4, 137.8, 138.5, 139.7, 161.7, 194.3.



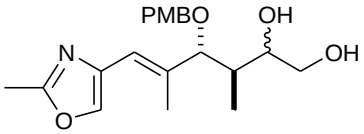
(3*R*,4*R*,1*E*)-2,4-Dimethyl-1-(2-methyloxazol-4-yl)hexa-1,5-dien-3-ol (42). To a solution of potassium *tert*-butoxide (2.98 g, 26.4 mmol) in dry tetrahydrofuran (27 mL) at -78 ˚C was added *trans*-2-butene (5 mL) followed dropwise by *n*-butyllithium (2.6M solution in hexanes, 10.2 mL, 26.4 mmol). The mixture was stirred for 15 min at -45 ˚C and was cooled to -78 ˚C, after which a solution of (+)-*B*-methoxydiisopinylcampheylborane (8.29 g, 26.4

mmol) in dry tetrahydrofuran (30 mL) was added dropwise. The mixture was stirred for 30 min and boron trifluoride etherate (4.1 mL, 35.1 mmol) was added, followed by a solution of **41** (2.67 g, 17.7 mmol) in tetrahydrofuran (25 mL). The mixture was stirred for 6 h at -78 ˚C and a saturated aqueous solution of sodium bicarbonate (52 mL) and 30% hydrogen peroxide (10.7 mL) were added. The resulting mixture was allowed to warm to room temperature and was stirred for 16 h. The phases were separated and the organic phase was washed with water (25 mL). The aqueous phase was extracted with ether (3 x 25 mL), and the combined extract was washed with brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (ethyl acetate:hexanes:triethylamine 100:200:3) to yield **42** (2.44 g, 67%) as a pale yellow oil: $[\alpha]_D^{23}$ +14.3 (c 0.78, $CHCl_3$); IR (film) 3359, 3174, 3077, 2970, 2929, 2870, 1668, 1638, 1584, 1452, 1383, 1318, 1222, 1107, 1010 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 0.93 (d, *J* = 7 Hz, 3H), 1.89 (s, 3H), 2.28 (bs, 1H), 2.36 (m, 1H), 2.43 (s, 3H), 3.82 (d, *J* = 8 Hz, 1H), 5.13 (ddd, *J* = 1, 2, 10 Hz, 1H), 5.15 (ddd, *J* = 1, 2, 17 Hz, 1H), 5.78 (ddd, *J* = 8, 10, 17 Hz, 1H), 6.22 (m, 1H), 7.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 13.7, 14.0, 16.7, 42.2, 81.0, 116.5, 117.5, 135.4, 137.7, 139.7, 140.6, 160.6; MS (EI) *m/z* 208 $(M+H)^+$, 190, 174, 152, 124, 110, 84; HRMS (CI) *m/z* 207.1257, calcd for $C_{12}H_{17}NO_2$ *m/z* 207.1259.



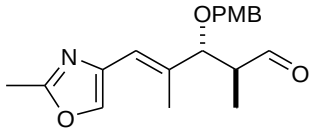
4-[(3*R*,4*R*,1*E*)-3-(4-Methoxybenzyloxy)-2,4-dimethylhexa-1,5-dienyl]-2-methyloxazole (43). To a solution of **42** (400 mg, 1.93 mmol) in dry tetrahydrofuran (15 mL) was added sodium hydride (60% suspension in mineral oil, 175 mg, 4.29 mmol), and the suspension was stirred for 40 min at reflux. After the mixture had cooled to room temperature, *p*-methoxybenzyl chloride (0.45 mL, 3.25 mmol) and tetra-*n*-butylammonium iodide (25 mg) were added. The mixture was stirred under argon at reflux for 6 h and at room temperature for 10 h. A saturated aqueous solution of ammonium chloride (2.5 mL) and

water (10 mL) were added and the mixture was extracted with dichloromethane (3 x 25 mL). The combined extract was washed with brine (5 mL), dried (Na_2SO_4), and concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate:hexanes 1:4 with 1% triethylamine) to yield **43** (565 mg, 89 %) as a colourless oil: $[\alpha]_D^{23}$ +42.5 (c 3.67, $CHCl_3$); IR (film) 3071, 2961, 2932, 2860, 2836, 1613, 1586, 1513, 1457, 1302, 1248, 1108, 1072, 1036, 917, 821, 635 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 0.87 (d, *J* = 7 Hz, 3H), 1.90 (d, *J* = 1 Hz, 3H), 2.46 (s, 3H), 2.46 (m, 1H), 3.50 (d, *J* = 9 Hz, 1H), 3.78 (s, 3H), 4.19 (d, *J* = 12 Hz, 1H), 4.45 (d, *J* = 12 Hz, 1H), 5.02 (ddd, *J* = 1, 2, 10 Hz, 1H), 5.07 (ddd, *J* = 1, 2, 17 Hz, 1H), 5.92 (ddd, *J* = 7, 10, 17 Hz, 1H), 6.20 (m, 1H), 6.85 (m, 2H), 7.23 (m, 2H), 7.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 13.7, 13.7, 16.5, 40.2, 55.0, 69.7, 88.6, 113.5, 113.8, 119.0, 129.2, 130.6, 135.4, 137.6, 138.1, 141.6, 158.9, 160.6; MS (CI) *m/z* 328 $(M+H)^+$, 281, 273, 137, 121, 84; HRMS (CI) *m/z* 328.1908, calcd for $C_{20}H_{26}NO_3$ *m/z* 328.1913.

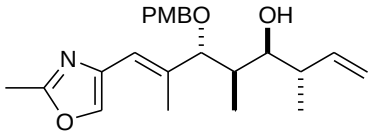


(3*R*,4*R*,5*E*)-4-(4-Methoxybenzyloxy)-3,5-dimethyl-6-(2-methyloxazol-4-yl)hex-5-ene-1,2-diol (44). To a solution of **43** (5.21 g, 15.9 mmol) in tetrahydrofuran (125 mL) and water (4.7 mL) at 0 °C was added osmium tetraoxide (0.2M solution in *tert*-butanol, 3.04 mL, 0.63 mmol) followed by an aqueous solution of *N*-methylmorpholine-*N*-oxide (60 %, 2.45 g, 19.3 mmol). The mixture was stirred for 10 h at room temperature, ether (300 mL) was added, and the organic phase was separated and washed with water (100 mL) and brine (90 mL). The aqueous phase was extracted with dichloromethane (2 x 100 mL) and the combined organic extract was dried (Na_2SO_4) and concentrated. The residual oil was purified by flash chromatography on silica gel (ethyl acetate:ethanol:triethylamine 95:5:1) to give **44** (4.80 g, 84 %) as a colourless oil (1:1 mixture of diastereomers): IR (film) 3419, 2962, 2933, 2870, 1613,

1585, 1514, 1457, 1385, 1302, 1248, 1175, 1108, 1061, 1035 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) □ 0.67 (two d, *J* = 7 Hz, 3H), 1.83 (two s, 3H), 1.96 (m, 1H), 2.39 (s, 3H), 3.06 (s, 1H), 3.48-3.59 (m, 3H), 3.68 (s, 3H), 3.71 (m, 1H), 4.13 (d, *J* = 11 Hz, 1H), 4.38 (two d, *J* = 11 Hz, 1H), 4.68 (s, 1H), 6.18 (two s, 1H), 6.78 (two d, *J* = 9 Hz, 2H), 7.17 (d, *J* = 9 Hz, 2H), 7.49 (two s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 11.4, 12.7, 12.9, 13.2, 13.4, 37.4, 37.5, 54.9, 64.1, 64.5, 69.6, 69.8, 72.5, 75.7, 86.9, 90.0, 113.6, 113.7, 119.2, 120.3, 129.2, 129.3, 129.4, 129.8, 135.5, 135.6, 136.6, 137.1, 137.2, 137.3, 158.9, 159.1, 160.6, 160.7; MS (FAB) *m/z* 362 $(M+H)^+$, 307, 224, 164, 154, 121, 107, 89; HRMS (FAB) *m/z* 362.1971, calcd for $C_{20}H_{28}NO_5$ *m/z* 362.1968.

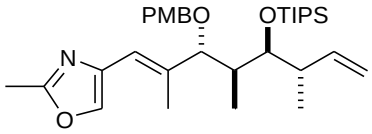


(2*S*,3*R*,4*E*)-3-(4-Methoxybenzyloxy)-2,4-dimethyl-5-(2-methyloxazol-4-yl)pent-4-enal (45). To a solution of **44** (1.88 g, 5.20 mmol) in tetrahydrofuran (20 mL) and water (50 mL) was added sodium metaperiodate (1.35 g, 6.40 mmol) and the solution was stirred for 30 min at room temperature. The mixture was extracted with dichloromethane (3 x 40 mL) and the combined extract was dried (Na_2SO_4) and concentrated to give pure **45** (1.67 g, 98%) as a colourless oil: $[\alpha]_D^{23}$ +62.4 (c 1.05, $CHCl_3$); IR (film) 2965, 2933, 2855, 2837, 1726, 1613, 1586, 1514, 1457, 1284, 1174, 1109, 1064, 1034, 820 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) □ 0.80 (d, *J* = 7 Hz, 3H), 1.93 (d, *J* = 1 Hz, 3H), 2.48 (s, 3H), 2.67 (ddt, *J* = 3, 7, 10 Hz, 1H), 3.80 (s, 3H), 3.93 (d, *J* = 10, 1H), 4.20 (d, *J* = 11 Hz, 1H), 4.46 (d, *J* = 11 Hz, 1H), 6.27 (m, 1H), 6.86 (d, *J* = 8 Hz, 2H), 7.19 (d, *J* = 8 Hz, 2H), 7.56 (s, 1H), 9.70 (d, *J* = 3, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 10.9, 13.1, 13.8, 48.6, 55.2, 69.7, 85.3, 113.8, 120.5, 129.5, 129.8, 135.8, 136.0, 137.3, 159.2, 161.0, 204.2; MS (EI) *m/z* 330 $(M+H)^+$, 311, 272, 255, 231, 208, 193, 164, 121, 91, 78; HRMS (EI) *m/z* 330.17002, calcd for $C_{19}H_{24}NO_4$ *m/z* 330.17053.

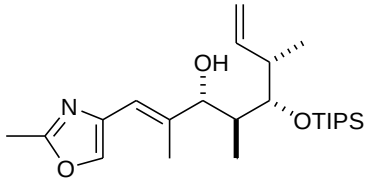


(3*S*,4*S*,5*R*,6*R*,7*E*)-6-(4-Methoxybenzyloxy)-3,5,7-trimethyl-8-(2-methyloxazol-4-yl)octa-1,7-dien-4-ol (46). To a solution of potassium *tert*-butoxide (2.62 g, 23.2 mmol) in dry tetrahydrofuran (21 mL) at -78 ˚C was added *trans*-2-butene (ca. 8 mL, excess) followed dropwise by *n*-butullithium (1.6M solution in hexanes, 14.2 mL, 23.2 mmol). The mixture was stirred for 15 min at -45 ˚C and was cooled to –78 ˚C. A solution of (–)-*B*-methoxydiisopinylcampheylborane (7.32 g, 23.2 mmol) in dry tetrahydrofuran (32 mL) was added dropwise, and after 30 min boron trifluoride etherate (3.61 mL, 31.1 mmol) was added followed by a solution of **45** (4.15 g, 12.6 mmol) in tetrahydrofuran (21 mL). The mixture was stirred for 19 h at -78 ˚C and the reaction was quenched with methanol (12 mL) and 2-aminoethanol (36 mL). The mixture was allowed to warm to room temperature and was stirred for 3 h, after which dichloromethane (200 mL) and water (80 mL) were added. The phases were separated, the organic phase was washed with water (50 mL) and brine (50 mL), and the aqueous phase was extracted with dichloromethane (2 x 50 ml). The combined extract was dried (Na_2SO_4) and concentrated to give a crude product containing a 6.1:1 mixture of diastereomers (determined by ^{13}C NMR). Flash chromatography of the mixture on silica gel (ethyl acetate:hexanes:triethylamine 33:66:1) gave pure **46 (**2.55 mg, 53 %) as a pale yellow oil: $[\alpha]_D^{23}$ +37.6 (c 3.73, $CDCl_3$); IR (film) 3385, 2970, 2932, 2872, 1652, 1615, 1586, 1559, 1514, 1457, 1381, 1302, 1248, 1173, 1108, 1068, 1036, 918, 821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 0.78 (d, *J* = 7 Hz, 3H), 0.93 (d, *J* = 7 Hz, 3H), 1.90 (d, *J* = 1 Hz, 3H), 1.93 (m, 1H), 2.16 (s, 1H), 2.23 (m, 1H), 2.46 (s, 3H), 3.71 (d, *J* = 9 Hz, 1H), 3.78 (s, 3H), 3.86 (d, *J* = 8 Hz, 1H), 4.20 (d, *J* = 11 Hz, 1H), 4.45 (d, *J* = 11 Hz, 1H), 5.04 (dd, *J* = 2, 10 Hz, 1H), 5.09 (dd, *J* = 2, 17 Hz, 1H), 5.80 (ddd, *J* = 9, 10, 17 Hz, 1H), 6.28 (s, 1H), 6.85 (d, *J* = 9 Hz, 2H), 7.23 (d, *J* = 9 Hz, 2H), 7.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 9.7, 13.7, 13.9, 16.7, 36.7, 42.0, 55.1, 70.2, 72.9, 86.8, 113.7, 115.1,

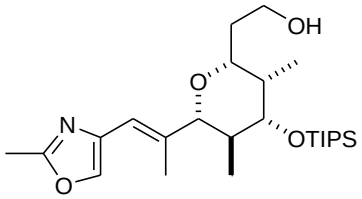
118.6, 129.3, 130.4, 135.5, 137.7, 137.8, 142.4, 159.0, 160.7; MS (EI) *m/z* 385 (M^+), 368, 330, 284, 272, 264, 249, 193, 172, 164, 148, 140, 121, 77; HRMS (EI) *m/z* 385.2257, calcd for $C_{23}H_{31}NO_4$ *m/z* 385.2253.



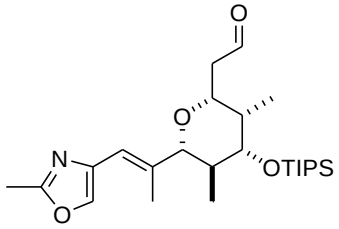
4-[(3*R*),(4*S*),(5*S*),(6*S*),(1*E*)-3-(4-Methoxybenzyloxy)-2,4,6-triisopropylsilanyl oxyocta-1,7-dienyl]-2-methyloxazole (47). To a solution of **46** (130 mg, 338 μmol) in dry dichloromethane (9 mL) at 0 ˚C was added 2,6-lutidine (94 μL, 810 μmol), followed by triisopropylsilyl triflate (110 μL, 407 μmol). The solution was stirred for 2 h at room temperature and dichloromethane (10 mL) was added. The solution was washed with brine (15 mL), dried (Na_2SO_4) and concentrated and the residue was purified by flash chromatography on silica gel (ethyl acetate:hexanes:triethylamine 25:75:1) to give **47** (142 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ –12.6 (c 4.20, $CHCl_3$); IR (film) 2962, 2942, 2891, 2866, 1653, 1616, 1586, 1514, 1463, 1457, 1383, 1248, 1108, 1041, 1012, 992, 917, 883, 820, 677 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 0.81 (d, *J* = 7 Hz, 3H), 0,99 (d, *J* = 7 Hz, 3H), 1.10 (m, 21H), 1.71 (m, 1H), 1.91 (d, *J* = 1Hz, 3H), 1.93 (m, 1H), 2.40 (dd, *J* = 16,6 Hz, 1H), 2.45 (s, 3H), 2.63 (dd, *J* = 16,8 Hz, 1H), 3.49 (d, *J* = 10 Hz, 1H), 3.67 (s, 3H), 3.68 (m, 1H), 3.94 (ddd, *J* = 2, 17 Hz, 1H), 6.18 (s, 1H), 5.59 (ddd, *J* = 8, 6, 2 Hz, 1H), 6.11 (s, 1H), 6.80 (d, *J* = 9 Hz, 2H), 7.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 6.3, 13.0, 14.0, 14.1, 14.5, 18.4 (x 2), 35.1, 38.3, 39.2, 51.9, 74.8, 77.7, 89.0, 118.8, 135.8, 138.0, 138.1, 160.8, 172.0; MS (CI) *m/z* 479 (M^+), 448, 436, 404, 378, 355, 305, 285, 273, 243, 164, 131, 121; HRMS (CI) *m/z* 479.3072, calcd for $C_{25}H_{45}NO_5Si$ *m/z* 479.3067.



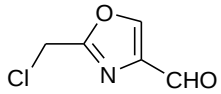
4-[(3*R*,4*S*,5*S*,6*S*,1*E*)-3-Hydroxy-2,4,6-trimethyl-5-triisopropylsilanyloxyocta-1,7-dienyl]-2-methyloxazole (48). To a solution of **47** (255 mg, 481 µmol) in dry dichloromethane (4 mL) was added ethanethiol (140 µL, 1.88 mmol) and the mixture was cooled to –20 ˚C under argon. A solution of anhydrous aluminium trichloride (52.7 mg, 383 µmol) in dichloromethane (8 mL) was added dropwise, and the mixture was stirred for 30 min at -5 ˚C. Additional quantities of anhydrous aluminum trichloride (19.8 mg, 144 µmol) were added after 1 h and 2 h, and the mixture was stirred at –5 °C for 2h. A saturated aqueous solution of sodium bicarbonate (7 mL), aqueous sodium potassium tartrate solution (2M, 7 mL), and water (3 mL) were added, and the mixture was stirred for an additional 20 min at room temperature. The phases were separated, the aqueous layer was extracted with dichloromethane (3 x 20 mL), and the combined extract was washed with brine (10 mL), dried (Na_2SO_4), and concentrated. The residual oil was purified by flash chromatography on silica gel (ethyl acetate:hexanes:triethylamine 20:80:1) to give **48** (101 mg, 90%) as a pale yellow oil: $[\alpha]_D^{23}$ –51.2 (c 4.40, $CHCl_3$); IR (film) 3327, 3080, 3049, 2926, 2865, 2721, 1638, 1585, 1462, 1453, 1385, 1319, 1237, 1217, 1103, 1043, 933, 913, 883, 736, 635 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) □ 0.72 (d, *J* = 7 Hz, 3H), 1.06 (m, 24H), 1.82 (s, 3H), 1.92 (m, 1H), 2.42 (s, 3H), 2.56 (m, 1H), 3.01 (s, 3H), 4.15 (m, 2H), 5.01 (d, *J* = 11 Hz, 1H), 5.08 (d, *J* = 17 Hz, 1H), 5.98 (ddd, *J* = 7, 11, 17 Hz, 1H), 6.18 (s, 1H), 7.48 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 12.9, 13.1, 13.2, 13.7, 17.2, 18.2, 18.3, 39.6, 42.2, 77.4, 80.4, 114.2, 117.8, 135.3, 137.8, 140.7, 141.3, 160.6; MS (FAB) *m/z* 504 (M^+), 404, 378, 306, 241, 230, 215, 190, 157, 152, 131, 115, 103, 87; HRMS (FAB) *m/z* 422.3092, calcd for $C_{24}H_{44}NO_3Si$ *m/z* 422.3091.



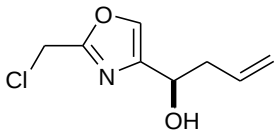
(2*R*,3*S*,4*R*,5*S*,6*R*)-3,5-Dimethyl-6-[(1*E*)-1-methyl-2-(2-methyloxazol-5-yl)vinyl]-4-triisopropylsilanyloxytetrahydropyran-2-ylethanol (52). To a suspension of lithium aluminium hydride (100 mg, 2.67 mmol) in ether (20 mL) at 0 °C was added dropwise a solution of **49** (1.28 g, 2.67 mmol) in ether (10 mL), and the mixture was stirred for 3 h at 10 °C. The reaction was quenched by careful addition of water (0.6 mL) and aqueous sodium hydroxide (15 %, 0.16 mL) and the mixture was stirred at room temperature for 30 min. The suspension was filtered through Celite, the collected solid was washed with tetrahydrofuran (400 mL), and the filtrate was dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (ethyl acetate:hexanes 1:1) to give **51** (947 mg (79 %) as a colourless oil: $[\alpha]_D^{23}$ +24.5 (c 0.55, $CDCl_3$); IR (film) 3384, 2944, 2927, 2891, 2867, 1653, 1586, 1462, 1457, 1387, 1362, 1312, 1159, 1109, 1084, 1065, 1030, 920, 882, 808, 676 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.82 (d, *J* = 7 Hz, 3H), 1.02 (d, *J* = 7 Hz, 3H), 1.09 (m, 21H), 1.48 (m, 1H), 1.68-1.86 (m, 2H), 1.92 (d, *J* = 1 Hz, 3H), 1.98 (m, 1H), 2.45 (s, 3H), 2.66 (s, 1H), 3.51 (d, *J* = 10 Hz, 1H), 3.63-3.78 (m, 4H), 6.19 (s, 1H), 7.49 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.9, 13.3, 14.2, 14.3, 14.6, 18.6, 18.7, 35.3, 35.5, 40.6, 62.7, 77.6, 78.0, 79.8, 89.4, 119.2, 136.1, 138.1, 161.1; MS (FAB) *m/z* 452 $(M+H)^+$, 408, 390, 350, 306, 277, 245, 215, 187, 164, 157, 152, 136, 115, 87, 75, 59; HRMS (FAB) *m/z* 452.3195, calcd for $C_{25}H_{46}NO_4Si$ *m/z* 452.3196.



(2*R*,3*S*,4*R*,5*S*,6*R*)-3,5-Dimethyl-6-[(1*E*)-1-methyl-2-(2-methyloxazol-5-yl)vinyl]-4-triisopropylsilanyloxytetrahydropyran-2-ylacetaldehyde (4). To a solution of **52** (95 mg, 214 μmol) in dichloromethane (8 mL) at 0 ^{o}C was added a solution of Dess-Martin periodinane (120 mg, 282 μmol) in dichloromethane (17 mL) and the solution was stirred for 3 h at room temperature. The solution was poured into a saturated aqueous solution of sodium bicarbonate (40 mL) containing sodium thiosulfate (10 g) and the mixture was stirred for 15 min. The phases were separated and the organic phase was washed with saturated aqueous sodium bicarbonate (30 mL), water (35 ml) and brine (35 ml), then was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (ethyl acetate:hexanes 1:1) to give **4** (82 mg, 85 %) as a colourless oil: $[\alpha]_D^{23}$ +28.8 (c 2.73, $CHCl_3$); IR (film) 3149, 2962, 2891, 2724, 1728, 1586, 1462, 1383, 1312, 1240, 1112, 1031, 997, 807, 678, 636 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (d, *J* = 7 Hz, 3H), 0.98 (d, *J* = 7 Hz, 3H), 1.07 (s, 21H), 1.74 (m, 1H), 1.84 (m, 1H), 1.90 (s, 3H), 2.37 (dd, *J* = 3, 17 Hz, 1H), 2.42 (s, 3H), 2.70 (ddd, *J* = 1, 7, 17 Hz, 1H), 3.48 (d, *J* = 10 Hz, 1H), 3.69 (dd, *J* = 5, 10 Hz, 1H), 4.00 (dd, *J* = 3, 9 Hz, 1H), 6.16 (s, 1H), 7.47 (s, 1H), 9.74 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.8, 13.3, 14.2, 14.3, 14.7, 18.6, 18.7, 35.4, 39.9, 47.3, 73.7, 77.9, 89.4, 119.1, 136.0, 138.1, 161.0, 201.7; MS (FAB) *m/z* 450 $(M+H)^+$, 350, 306, 269, 243, 215, 199, 157, 115, 87, 59; HRMS (FAB) *m/z* 450.3034, calcd for $C_{25}H_{44}NO_4Si$ *m/z* 450.3040.

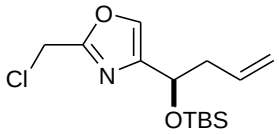


2-Chloromethyloxazole-4-carboxaldehyde (54). To a solution of **53** (840 mg, 4.78 mmol) in dichloromethane (50 mL) at –78 °C was added dropwise diisobutylaluminium hydride (1.0M in dichloromethane, 9.56 mL, 9.56 mmol) and the mixture was stirred for 3 h at –78 °C. The reaction was quenched with methanol (20 mL), and the mixture was allowed to warm to room temperature and diluted with dichloromethane (100 mL). The solution was washed with saturated aqueous sodium potassium tartrate solution (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **54** (680 mg, 98%) as a colourless oil: IR (film) 3145, 2846, 1700, 1559, 1117, 997, 793 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.65 (s, 2H), 8.30 (s, 1H), 9.92 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 35.6, 141.4, 145.6, 160.8, 184.0; MS (CI) *m/z* 145 $(M+H)^+$, 125, 110, 97, 84, 70; HRMS (CI) *m/z* 144.9932, calcd for $C_5H_4NO_2{}^{35}Cl$ *m/z* 144.9900.



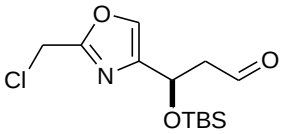
(3*R*)-3-(2-Chloromethyloxazol-4-yl)-3-hydroxybut-1-ene (55). To a solution of (+)-*B*-methoxydiisopinylcampheylborane (1.26 g, 3.87 mmol) in dry ether (15 mL) under argon at 0°C was added allylmagnesium bromide (1.0M solution in ether, 3.30 mL, 3.30 mmol) dropwise. The mixture was allowed to warm to room temperature and was stirred for 1 h. The solvent was removed under vacuum and the residue was extracted with *n*-pentane (4 x 30 mL). The resulting suspension was filtered under argon through a Schlenk tube and the filtrate was concentrated under vacuum. The residue was dissolved in ether (20 mL), the solution was cooled to –100°C and a solution of **54** (280 mg, 1.93 mmol) in ether (20 mL) at -78 °C was added. The mixture was stirred at –100°C for 1h and

the reaction was quenched with methanol (0.1 mL). The mixture was allowed to warm to room temperature, after which aqueous sodium hydroxide (2N, 1.5 mL) and 30% hydrogen peroxide (3.0 mL) were added and the mixture was stirred for 10 h. The mixture was washed with brine (40 mL), the organic layer was separated and dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **55** (306 mg, 84%) as a colourless oil in which the enantiomeric ratio was determined to be >20:1 from the ^{13}C NMR spectrum of its Mosher ester: $[\alpha]_D^{23}$ +9.0 (c 1.44, $CHCl_3$); IR (film) 3431, 2909, 1642, 1569, 1432, 924, 798 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (ddd, *J* = 5, 8, 14 Hz, 1H), 2.64 (ddd, *J* = 1, 5, 7 Hz, 1H) 2.69 (bs, 1 H) 4.58 (s, 2H), 4.72 (dd, *J* = 6, 9 Hz, 1H), 5.16 (dd, *J* = 1, 9 Hz, 1H), 5.19 (d, *J* = 17 Hz, 1H), 5.81 (m, 1H), 7.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.1, 41.1, 66.7, 119.4, 133.9, 136.3, 144.2, 159.7; MS (CI) *m/z* 187 $(M+H)^+$, 170, 161, 148, 146, 110, 84; HRMS (CI) *m/z* 187.0398, calcd for $C_8H_{10}NO_2{}^{35}Cl$ *m/z* 187.0400.

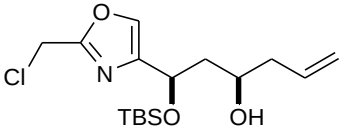


(4*R*)-4-(Chloromethyloxazol-4-yl)-4-*tert*-butyldimethylsilanyl-oxybut-1-ene (56). To an ice-cold solution of **55** (295 mg, 1.57 mmol) and 2,6-lutidine (0.37 mL, 3.1 mmol) in dichloromethane (3 mL) under argon was added *tert*-butyldimethylsilyl triflate (0.54 mL, 2.4 mmol) and the solution was allowed to warm to room temperature during 1 h. The solution was poured into an ice-cold saturated aqueous solution of sodium bicarbonate (10 mL) and the mixture was extracted with hexanes (5 x 10 mL). The combined extract was dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was purified by chromatography on silica gel (ethyl acetate:hexanes 2:1) to give **56** (469 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ +6.3 (c 2.23, $CHCl_3$); IR (film) 2955, 2930, 2857, 1569, 1258, 1100, 914, 836, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 2.51 (ddd, *J* = 1, 5, 7 Hz, 2H), 4.58 (s,

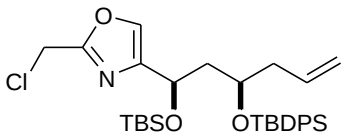
2H), 4.76 (dd, *J* = 5, 5 Hz, 1H), 5.05 (d, *J* = 11 Hz, 1H), 5.06 (d, *J* = 17 Hz, 1H), 5.79 (dddd, *J* = 7, 7, 11, 17 Hz, 1H), 7.49 (d, *J* = 1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.4, -2.6, 18.6, 26.1, 26.2, 36.3, 42.4, 68.9, 118.0, 134.4, 136.6, 145.8, 159.1; MS (CI) *m/z* 302$(M+H)^+$, 286, 244, 189, 147, 117, 75; HRMS (CI) *m/z* 302.1336, calcd for $C_{14}H_{25}NO_2{}^{35}ClSi$ *m/z* 302.1343.



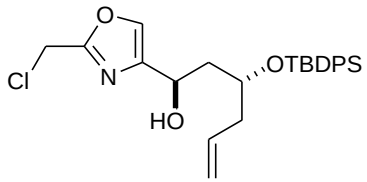
(3*R*)-3-(2-Chloromethyloxazol-4-yl)-3-*tert*-butyldimethylsilanyl-oxypropanal (57). To a solution of **56** (468 mg, 1.55 mmol) in tetrahydrofuran (40 mL) and water (40 mL) was added osmium tetraoxide (2.5% solution in *tert*-butanol, 2.04 mL, 0.16 mmol) followed by sodium periodate (1.33 g, 6.20 mmol). After 3 h, the reaction was quenched with a saturated aqueous solution of sodium thiosulfate (350 mL), and after a further 30 min brine (500 mL) was added. The mixture was extracted with ether (5 x 100 mL) and the combined extract was dried ($MgSO_4$) and concentrated under reduced pressure to give **57** (330 mg, 70%) as a colourless oil: $[\alpha]_D^{23}$ +27.3 (c 1.24, $CHCl_3$); IR (film) 2930, 2858, 1727, 1259, 1106, 838, 779 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (d, *J* = 20 Hz, 6H), 0.89 (s, 9H), 2.86 (dddd, *J* = 2, 6, 16, 20 Hz, 2H), 4.58 (s, 2H), 5.24 (ddd, *J* = 1, 6, 6 Hz, 1H), 7.56 (d, *J* = 1 Hz, 1 H), 9.79 (t, *J* = 2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.7, -4.4, 18.4, 26.1, 36.1, 50.9, 64.7, 136.7, 144.7, 159.7, 200.9; MS (CI) *m/z* 304 $(M+H)^+$, 288, 246, 172, 143, 108, 84, 75; HRMS (CI) *m/z* 304.1140, calcd for $C_{13}H_{23}NO_3Si^{35}Cl$ *m/z* 304.1136.



(4*R*,6*R*)-6-(2-Chloromethyloxazol-4-yl)-6-*tert*-butyldimethyl-silanyloxy-4-hydroxyhex-1-ene (58). To a solution of (+)-*B*-methoxydiisopinylcampheylborane (726 mg, 2.29 mmol) in ether (10 mL) at 0 °C was added allylmagnesium bromide (2.0 mL, 2.0 mmol) and the mixture was stirred at room temperature for 1 h. The solvent was removed under vacuum and the residue was extracted with *n*-pentane (4 x 10 mL), The resulting suspension was filtered under argon through a Schlenk tube and pentane was removed from the filtrate under vacuum. The residue was dissolved in ether (20 mL), the solution was cooled to –100°C and a solution of **57** (346 mg, 1.14 mmol) in ether (20 mL) at –78 °C was added via cannula. The mixture was stirred at –100 °C for 1 h and the reaction was quenched with methanol (1.0 mL). The mixture was allowed to warm to room temperature and was treated with aqueous sodium hydroxide (2N, 1.0 mL) and 30% hydrogen peroxide (2.0 mL). The mixture was stirred for 10 h and was extracted with ether (4 x 10 mL), and the extract was washed with brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give crude **58** as a 12:1 mixture of diastereomers. The crude material was purified by flash column chromatography on silica gel (ethyl acetate:hexanes 1:2) to give **58** (249 mg, 66%) as a colourless oil: $[\alpha]_D^{23}$ +31.2 (c 1.39, $CHCl_3$); IR (film) 3420, 2929, 2359, 1258, 1096, 837, 778 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ -0.05 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.89 (m, 2H), 2.23 (t, *J* = 6 Hz, 2H), 3.03 (b, 1H), 3.82 (dddd, *J* = 1, 6, 7, 9 Hz, 1H), 4.56 (d, *J* = 1 Hz, 2H), 4.92 (t, *J* = 6 Hz, 1H), 5.07 (dd, *J* = 1, 9 Hz, 1H), 5.08 (dd, *J* = 1, 17 Hz, 1H), 5.81 (dddd, *J* = 7, 7, 9, 17 Hz, 1H), 7.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.6, -4.3, 18.4, 26.1, 36.1, 42.3, 44.5, 68.1, 69.2, 118.0, 135.1, 136.5, 145.5, 159.3; MS (CI) *m/z* 346 $(M+H)^+$, 310, 288, 196, 145, 110; HRMS (CI) *m/z* 346.1599, calcd for $C_{16}H_{29}NO_3{}^{35}ClSi$ *m/z* 346.1605.

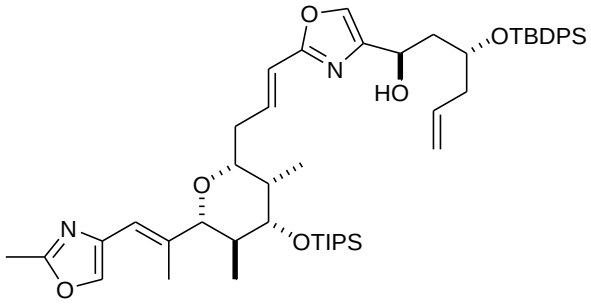


(4*R*,6*R*)-6-(2-Chloromethyloxazol-4-yl)-6-*tert*-butydimethyl-silanyloxy-4-*tert*-butyldiphenylsilanyloxyhex-1-ene (59). To an ice-cold solution of **58** (30 mg, 0.09 mmol) and 2,6-lutidine (20 μL, 0.18 mmol) in dichloromethane (1 mL) under argon was added *tert*-butyldiphenylsilyl triflate (52 mg, 0.14 mmol) and the mixture was stirred at room temperature for 6 h. The mixture was poured into an ice-cold saturated aqueous solution of sodium bicarbonate (10 mL) and was extracted with hexanes (5 x 10 mL). The combined extract was dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was purified by chromatography on silica gel (ethyl acetate:hexanes 1:3) to give **59** (45.0 mg, 89%) as a colourless oil: $[\alpha]_D^{23}$ +14.1 (c 1.82, $CHCl_3$); IR (film) 3073, 2955, 2893, 2857, 1427, 1257, 1111, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ -0.10 (s, 3H), 0.00 (s, 3H), 0.81 (s, 9H), 1.04 (s, 9H), 2.00 (td, *J* = 4, 8 Hz, 2H), 2.20 (m, 2H), 3.85 (td, *J* = 6, 12 Hz, 1H), 4.52 (s, 2H), 4.78 (t, *J* = 7 Hz, 1H), 4.90 (dd, *J* = 2, 17 Hz, 1H), 4.96 (dt, *J* = 1, 12 Hz, 1H), 5.71 (dddd, *J* = 7, 7, 10, 17 Hz, 1H), 7.10 (s, 1H), 7.55 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.5, -4.2, 18.5, 19.8, 26.2, 27.0, 36.3, 41.6, 44.3, 53.8, 65.7, 70.3, 117.7, 127.9, 128.1, 129.9, 130.1, 134.6, 134.7, 135.2, 135.6, 136.4, 136.5, 145.2, 158.9; MS (CI) *m/z* 584 $(M+H)^+$,568, 526, 492, 260, 199, 135; HRMS (CI) *m/z* 584.2780, calcd for $C_{32}H_{47}NO_3{}^{35}ClSi_2$ *m/z* 584.2783.



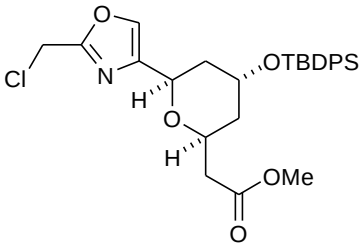
(4*R*,6*R*)-6-(2-Chloromethyloxazol-4-yl)-6-hydroxy-4-*tert*-butyldiphenylsilanyloxy hex-1-ene (60). To a solution of **59** (40 mg, 0.07 mmol) in tetrahydrofuran (15 mL) was added hydrochloric acid (3N, 3 mL) and the mixture was stirred for 10 h at room temperature. The mixture was cooled to 0 °C and solid sodium bicarbonate was added in small portions until gas evolution had subsided. The aqueous layer was extracted with ether (4 x 10 mL) and the

combined extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **60** (31 mg, 95%) as a colourless oil: $[\alpha]_D^{23}$ +12.7 (c 1.00, $CHCl_3$); IR (film) 3389, 2930, 2857, 1427, 1111, 702, 610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.07 (s, 9H), 2.10 (m, 4H), 4.05 (ddd, *J* = 4, 7, 12 Hz, 1H), 4.55 (s, 2H), 4.79 (dd, *J* = 2, 17 Hz, 1H), 4.87 (dd, *J* = 4, 9 Hz, 1H), 4.92 (dd, *J* = 2, 12 Hz, 1H), 5.56 (dddd, *J* = 7, 7, 12, 17 Hz, 1H), 7.55 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 19.7, 27.4, 42.3, 42.7, 66.7, 73.6, 118.1, 128.0, 128.2, 130.2, 130.3, 134.2, 136.3, 144.7, 159.4; MS (CI) *m/z* 470 $(M+H)^+$, 452, 412, 334, 269, 199, 139, 78; HRMS (CI) *m/z* 470.1914, calcd for $C_{26}H_{33}NO_3{}^{35}ClSi$ *m/z* 470.1918.



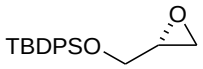
(1*R*,3*R*)-3-(*tert*-butyldiphenylsilanyloxy)-1-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-ylprop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)hex-5-en-1-ol (62). To a solution of **60** (86 mg, 0.18 mmol) in dimethylformamide (5 mL) under argon at room temperature was added tri-*n*-butylphosphine (0.23 mL, 0.90 mmol) and the mixture was stirred at room temperature for 3 h, then was cooled to 0 °C. A solution of **52** (164 mg, 0.36 mmol) in dimethylformamide (5 mL) was added via followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (3.6 mL, 0.18 mmol), and the solution was stirred at 0 °C for 30 min. The mixture was diluted with ethyl acetate (25 mL), and the reaction was quenched with saturated aqueous ammonium chloride (10 mL). The phases were separated, the aqueous phase was extracted with ethyl

acetate (3 x 10 mL) and the combined extract was washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexanes-ethyl acetate 3:1) to afford **62** (152 mg, 96%) as a colourless oil: $[\alpha]_D^{23}$ +23.8 (c 1.26, $CHCl_3$); IR (film) 3331, 2930, 2865, 1735, 1587, 1463, 1428, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (d, *J* = 7 Hz, 3H), 1.05 (m, 33H), 1.75 (m, 1H), 1.90 (m, 2H), 1.94 (s, 3H), 2.10 (m, 4H), 2.33 (ddd, *J* = 3, 6, 7 Hz, 1H), 2.44 (s, 3H), 2.55 (ddd, *J* = 3, 6, 7 Hz, 1H), 3.31 (b, 1H), 3.46 (d, *J* = 10 Hz, 1H), 3.54 (t, *J* = 1 Hz, 1H), 3.62 (dd, *J* = 4, 10 Hz, 1H), 4.05 (ddd, *J* =3, 4, 7 Hz, 1H), 4.79 (dd, *J* = 2, 17 Hz, 1H), 4.85 (dd, *J* = 3, 9 Hz, 1H), 4.90 (dd, *J* = 2, 10 Hz, 1H), 5.56 (dddd, *J* = 7, 7, 10, 17 Hz, 1H), 6.19 (s, 1H), 6.29 (d, *J* = 16 Hz, 1H), 6.65 (ddd, *J* = 6, 8, 16 Hz, 1H), 7.24 (s, 1H), 7.50 (s, 1H), 7.54 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.5, 13.3, 13.5, 14.2, 14.4, 15.1, 18.2, 18.6, 18.7, 19.7, 27.4, 30.1, 35.6, 3.8, 39.7, 42.3, 42.8, 66.8, 73.5, 78.2, 89.3, 118.1, 118.6, 118.9, 128.0, 128.2, 130.2, 130.3, 133.8, 134.4, 136.0, 136.3, 136.8, 138.2, 138.6, 144.6, 161.0, 161.5; MS (FAB) *m/z* 867 (M^+), 809, 731, 611, 541, 472, 350, 309, 239, 199, 135, 87; HRMS (FAB) *m/z* 867.5206, calcd for $C_{51}H_{75}N_2O_6Si_2$ *m/z* 867.5164.



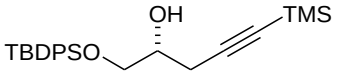
Methyl 2-((2*S*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(2-(chloromethyl)oxazol-4-yl)tetrahydro-2H-pyran-2-yl)acetate (65). To a mixture of **60** (112 mg , 0.238 mmol), dichlorobis(acetonitrile)palladium(II) (6.2 mg, 24 μmol, 10 mol%) and sublimed *p*-benzoquinone (12.9 mg, 0.119 mmol) under carbon monoxide at room temperature were added methanol (6 mL) and acetonitrile (6 mL), and the mixture was stirred at room temperature for 2 h. Over the next

10 h, further additions of *p*-benzoquinone (13 mg, 0.12 mmol, 0.5 equivalent) in methanol-acetonitrile (1:1, 2 mL) were made to the mixture at regular intervals until the reaction was complete (total of 5.5 equivalents of *p*-benzoquinone). After 11 h, the solution was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 12:1) to produce **65** (72 mg, 58%) as a colourless oil: $[\alpha]_D^{23}$ +13.4 (c 2.10, $CHCl_3$); IR (film) 2930, 2857, 1740, 1428, 1112, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.54 (m, 10 H), 4.58 (s, 2H), 4.56 (m, 1H), 4.30 (s, 1H), 3.67 (s, 3H), 2.64 (dd, *J* = 15, 7 Hz, 1H), 2.37 (dd, *J* = 16, 6 Hz, 1H), 1.80 (m, 4H), 1.11 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 159.4, 159.2, 143.0, 141.2, 137.7, 136.9, 136.2, 136.1, 134.3, 134.2, 130.2, 128.1, 69.6, 68.7, 67.9, 67.7, 66.2, 65.9, 52.0, 41.5, 41.0, 40.4, 38.4, 37.8, 36.8, 36.3, 36.1, 27.3, 19.7, 19.5; MS (CI) *m/z* 528 (M^+), 492, 470, 436, 367, 327, 307, 254, 225, 199, 183, 153; HRMS (CI) *m/z* 528.1977 (calcd for $C_{28}H_{35}NO_5Si^{35}Cl$: 528.1973). There was also recovered **60** (19 mg, 17%).

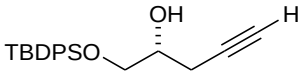


(*R*)-*tert*-Butyldiphenylsilanylglycidol (68). To a solution containing (*S*)-(-)-glycidol (0.1 mL, 1.51 mmol), imidazole (205 mg, 3.02 mmol) and 4-*N*,*N*-dimethylaminopyridine (18 mg, 0.15 mmol) in dry dimethylformamide (10 mL) at room temperature was added *tert*-butyldimethylsilyl triflate (0.39 mL, 1.51 mmol) and the mixture was stirred for 3 h. To the solution was added *n*-pentane (40 mL) and water (30 mL), and the aqueous layer was separated and extracted with pentane (2 x 20 mL). The combined extract was dried $(MgSO)_4$ and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **68** (436 mg, 93%) as a colourless oil: $[\alpha]_D^{23}$ +8.7 (c 1.90, $CHCl_3$), lit[47] $[\alpha]_D^{25}$ +2.40 (c 9.07 $CHCl_3$); IR (film) 3071, 3050, 2930, 2858, 1472, 1428, 1113, 918, 824, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (s, 9H), 2.62 (dd, *J* = 7, 12 Hz, 1H),

2.75 (dd, *J* = 4, 7 Hz, 1H), 3.13 (m, 1H), 3.72 (dd, *J* = 5, 12 Hz, 1H), 3.86 (dd, *J* = 3, 12 Hz, 1H), 7.40 (m, 6H), 7.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 27.2, 44.9, 52.7, 64.8, 128.2, 130.2, 133.7, 136.0, 136.1.

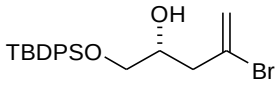


(4*R*)-5-*tert*-Butyldiphenylsilanyloxy-4-hydroxy-1-trimethylsilyl -pentyne (69). To a solution of trimethylsilylacetylene (0.16 mL, 1.1 mmol) in tetrahydrofuran (10 mL) at –78 °C under argon was added *tert*-butyllithium (1.23M in hexane, 0.89 mL, 1.1 mmol). After 10 min, boron trifluoride etherate (0.15 mL, 1.2 mmol) was added followed by a solution of **68** (230 mg, 0.74 mmol) in tetrahydrofuran (2 mL). The mixture was stirred at -78 °C for 1 h and at 0 °C for 20 min. A saturated aqueous solution of ammonium chloride (1 mL) was added and the mixture was extracted with ethyl acetate (3 x 5 mL). The combined extract was washed with brine (10 mL), dried ($MgSO_4$), and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **69** (291 mg, 96%) as a colourless oil: $[\alpha]_D^{23}$ + 11.4 (c 1.30, $CHCl_3$); IR (film) 3565, 3445, 3306, 3071, 2931, 2858, 2176, 1472, 1427, 1113, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 9H), 1.08 (s, 9H), 2.55 (d, *J* = 2 Hz, 2H), 3.74 (m, 2H), 3.89 (m, 1H), 7.45 (m, 6H), 7.73 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.3, 0.5, 0.8, 19.4, 19.8, 20.1, 25.2, 27.4, 28.5, 30.5, 66.9, 70.7, 87.5, 103.2, 127.9, 128.3, 128.5, 130.2, 130.6, 133.2, 136.0; HRMS (CI) *m/z* 410.2105, calcd for $C_{24}H_{34}O_2Si_2$ *m/z* 410.2097.

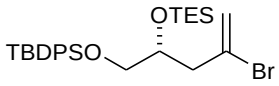


(4*R*)-5-*tert*-Butyldiphenylsilanyloxy-4-hydroxypentyne (70). To a solution of **69** (89 mg, 0.22 mmol) in methanol (10 mL) was added solid potassium carbonate and the mixture was stirred at room temperature for 3 h. Ether (20 mL) and water (20 mL) were added, the phases were separated and the aqueous

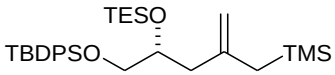
phase was extracted with ethyl acetate (3x10 mL). The combined extract was washed with brine (10 mL), dried ($MgSO_4$), and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **70** (74 mg, 98%) as a colourless oil: $[\alpha]_D^{23}$ +6.2 (c 1.50, $CHCl_3$); IR (film) 3565, 3445, 3306, 3071, 2931, 2858, 1472, 1427, 1113, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.97 (t, *J* = 2 Hz, 1H), 2.47 (dd, *J* = 7, 3 Hz, 1H), 2.52 (d, *J* = 6 Hz, 1H), 3.74 (m, 2H), 3.89 (m, 1H), 7.45 (m, 6H), 7.73 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 23.6, 27.2, 66.7, 70.6, 70.9, 128.2, 130.3, 133.4, 136.0; HRMS (CI) *m/z* 398.1696, calcd for $C_{26}H_{26}O_2Si$ *m/z* 398.1702.



(4*R*)-2-Bromo-4-hydroxy-5-*tert*-butyldiphenylsilanyloxypentene (71). To a solution of **70** (27 mg, 0.08 mmol) in dichloromethane (5 mL) at 0 °C under argon was added 9-bromo-9-borabicyclo[3.3.1]nonane (1.0M solution in dichloromethane, 0.40 mL, 0.40 mmol) and the mixture was allowed to warm to room temperature overnight. The solution was cooled to 0 °C, ethanolamine (0.1 mL) and methanol (1 mL) were added, and the mixture was diluted with ether (5 mL). The solution was washed with a saturated aqueous solution of sodium potassium tartrate (5 mL) and the phases were separated. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 5:1) to give **71** (28 mg, 80%) as a colourless oil: $[\alpha]_D^{23}$ +4.7 (c 1.0, $CHCl_3$); IR (film) 3583, 3445, 3071, 2929, 2857, 1428, 1112, 701, 608, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 9H), 2.50 (d, *J* = 2 Hz, 1H), 2.65 (m, 2H), 3.62 (dd, *J* = 7, 10 Hz, 1H), 3.77 (dd, *J* = 7, 12 Hz, 1H), 5.55 (s, 1H), 5.73 (s, 1H), 7.45 (m, 6H), 7.73 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 27.0, 27.3, 45.5, 67.1, 70.0, 119.7, 128.1, 128.3, 130.1, 130.5, 133.4, 135.2, 136.0; MS (CI) *m/z* 419 $(M+H)^+$, 389, 349, 347, 311, 309, 241, 199, 181, 163, 135, 117, 91; HRMS (CI) *m/z* 390.1008, calcd for $C_{20}H_{32}Osi^{79}Br$ *m/z* 390.1015.

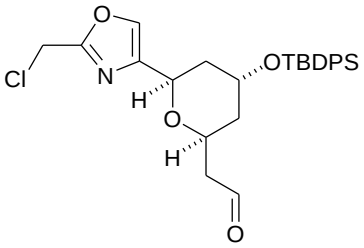


(4*R*)-2-Bromo-4-triethylsilanyloxy-5-*tert*-butyldiphenylsilanyloxy-1-pentene (72). To a solution of **71** (14 mg, 0.03 mmol) in dichloromethane (5 mL) at 0 °C was added 2,6-lutidine (11 μL, 0.10 mmol) and triethylsilyl triflate (15 μL, 0.07 mmol). The mixture was allowed to warm to room temperature and stirred for 1h, then was poured into an ice-cold saturated aqueous solution of sodium bicarbonate (5 mL). The phases were separated, the aqueous layer was extracted with *n*-pentane (4 x 10 mL), and the combined organic extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **72** (16 mg, 100%) as a colourless oil: $[\alpha]_D^{23}$ +12.7 (c 1.44, $CHCl_3$); IR (film) 2955, 2875, 1427, 1112, 1075, 739, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.60 (m, 6H), 1.05 (m, 9H), 1.17 (s, 9H), 2.55 (dd, *J* = 15, 7 Hz, 1H), 3.01 (dd, *J* = 12, 7 Hz, 1H), 3.67 (m, 2H) ,4.05 (m, 1H), 5.45 (s, 1H), 5.67 (s, 1H), 7.45 (m, 6H), 7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 5.2, 6.8, 7.2, 19.6, 27.2, 30.1, 47.2, 67.4, 71.0, 119.6, 127.8, 128.1, 129.7, 130.0, 131.6, 133.9, 135.5, 136.0; HRMS (CI) *m/z* 532.1834, calcd for $C_{27}H_{41}BrO_2Si_2$ *m/z* 532.1828.



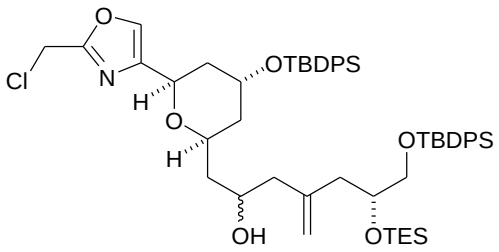
(4*R*)-4-Triethylsilanyloxy-5-*tert*-butyldiphenylsilanyloxy-2-trimethylsilylmethyl-1-pentene (73). To a solution of trimethylsilylmethyl-magnesium chloride (1.0M solution in ether, 50 μL, 0.1 mmol) in tetrahydrofuran (3 mL) was added a solution of **72** (16 mg, 33 μmol) in tetrahydrofuran (2 mL) followed by 1,3-bis(diphenylphos phino)propanenickel(II) chloride (4 mg, 7 μmol) and the mixture was heated at reflux for 3 h. After cooling to room temperature, the reaction was quenched with a saturated aqueous solution of ammonium chloride (1 mL). Ether (5 mL) was added, the layers were separated

and the organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 10:1) to give **73** (6.4 mg, 40%) as a colourless oil: $[\alpha]_D^{23}$ +12.3 (c 1.2, $CHCl_3$); IR (film) 3071, 2955, 2876, 1427, 1113, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 9H), 0.55 (m, 6H), 0.10 (s, 9H), 0.91 (m, 9H), 1.15 (s, 9H), 1.56 (m, 2H), 2.05 (dd, *J* = 14, 7 Hz, 1H), 2.38 (dd, *J* = 14, 5 Hz, 1H), 3.60 (m, 2H), 3.88 (m, 1H), 4.57 (s, 1H), 4.65 (s, 1H), 7.45 (m, 6H), 7.73 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -2.7, -1.0, 1.4, 5.3, 7.3, 19.6, 27.3, 27.5, 29.6, 30.1, 43.7, 68.0, 72.5, 110.4, 128.0, 130,0, 134.0, 134.2, 136.0, 144.5; HRMS (CI) *m/z* 572.3498, calcd for $C_{36}H_{52}O_2Si_3$ *m/z* 572.3506.



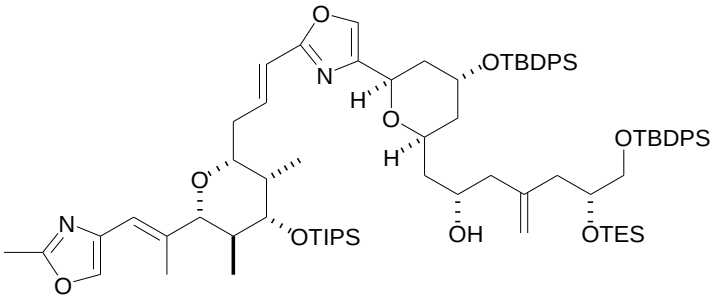
2-((2*S*,4*R*,6*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-6-(2-(chloromethyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)acetaldehyde (74). To a solution of **65** (58 mg, 0.11 mmol) in dichloromethane (10 mL) under argon at –78 °C was added dropwise diisobutylaluminium hydride (1.0M in dichloromethane, 0.22 mL, 0.22 mmol) and the mixture was stirred for 3 h at –78 °C. The reaction was quenched with methanol (5 mL), and the mixture was allowed to warm to room temperature and was diluted with dichloromethane (20 mL). The solution was washed with saturated aqueous potassium sodium tartrate solution (20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexanes:ethyl acetate 3:1) to give **74** (50 mg, 92%) as a colourless oil: $[\alpha]_D^{23}$ +32.4 (c 1.02, $CHCl_3$); IR (film) 3095, 2930, 2857, 1710, 1428, 1112, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.81 (t, *J* = 2 Hz, 1H), 7.72 – 7.66 (m, 4H), 7.57 (s, 1H), 7.47 – 7.28 (m, 6 H), 5.12 (dd, *J* = 2, 12 Hz, 1H), 4.72 – 4.62 (m, 1H), 4.60 (s, 2H), 4.36 (t, *J* = 3 Hz,

1H), 2.67 (dd, *J* = 2, 8 Hz, 0.5H), 2.62 (dd, *J* = 2, 8 Hz, 0.5H), 2.48 (dd, *J* = 2, 5 Hz, 0.5H), 2.42 (dd, *J* = 2, 5 Hz, 0.5H), 2.00 – 1.90 (m, 1H), 1.84 – 1.73 (m, 1H), 1.66 – 1.56 (m, 1H), 1.50 – 1.36 (m, 1H), 1.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 159.5, 142.8, 137.6, 136.9, 136.3, 136.2, 136.1, 134.3, 134.1, 130.3, 128.2, 77.8, 77.5, 77.2, 68.4, 68.3, 67.9, 66.3, 66.1, 65.8, 49.9, 49.6, 40.6, 38.6, 37.8, 36.7, 36.3, 36.1, 27.5, 27.4, 19.7; MS (FAB) *m/z* 498 (M^+ + H), 484, 410, 392, 337, 297, 239, 197, 154, 135, 89; HRMS (FAB) *m/z* 498.1859 (calcd for $C_{27}H_{33}O_4N^{35}ClSi$: 498.1867, M^+ + H).



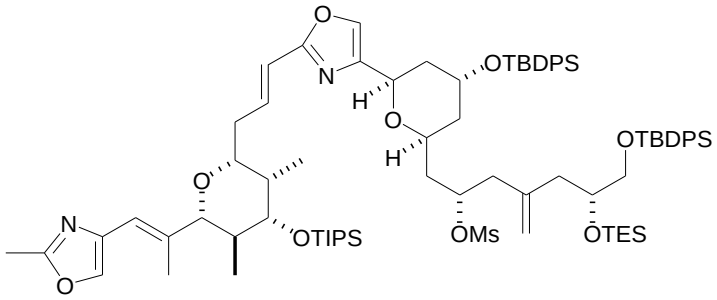
(2*S*,6*R*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(2-(chloromethyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)-4-methylene-6-(triethylsilanyloxy)heptan-2-ol (75). To a solution of **73** (37 mg, 68 μmol) in dichloromethane (2 mL) at –78 °C was added tin tetrachloride (1.0M solution in dichloromethane, 55 μL, 55 μmol) and the solution was stirred at –78 °C for 30 min. A solution of **74** (13.6 mg, 27.3 μmol) in dichloromethane (0.5 mL) was added and the mixture was stirred for 1 h at –78 °C. The reaction was quenched with saturated sodium bicarbonate solution (2 mL) and the mixture was extracted with dichloromethane (10 mL x 3). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure and the resulting oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 20:1 to 10:1) to give **72** (20.4 mg, 77%) as a colourless oil: IR (neat) 3507, 3071, 3049, 2954, 2931, 2875, 2858, 1471, 1427, 1361, 1265, 1237, 1185, 1112, 1007, 896, 822, 739, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.67 (m, 8H), 7.55 (s, 1H), 7.48 – 7.38 (m, 12H), 5.09 (d, *J* = 10 Hz, 1H), 4.95 (d, *J* = 10 Hz, 2H), 4.60 (s, 2H), 4.52 – 4.48 (m, 1H), 4.34 (m, 1H), 4.10 – 4.02 (m, 1H), 3.87 – 3.84 (m, 1H), 3.59 (dd, *J* = 5, 10 Hz, 1H), 2.90 (brs, 1H), 2.52 (dd, *J* = 5, 14 Hz, 1H), 2.27 – 2.18 (m, 3H), 1.94 (d, *J* = 10 Hz, 1H),

1.77 – 1.42 (m, 6H), 1.13 (s, 9H), 1.07 (s, 9H), 0.89 (t, *J* = 8 Hz, 9H), 0.51 (q, *J* = 8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 144.1, 143.3, 136.6, 136.2, 136.1, 136.0, 136.0, 134.4, 134.3, 134.0, 133.9, 130.4, 130.2, 130.1, 128.1, 128.1, 115.6, 115.5, 72.8, 70.5, 67.9, 67.7, 66.9, 66.3, 66.2, 45.9, 42.4, 40.8, 38.8, 38.2, 36.3, 34.1, 33.2, 32.0, 30.7, 30.1, 27.5, 27.3, 23.3, 23.1, 19.7, 19.6, 15.7, 14.6, 7.3, 5.3; MS (ES) *m/z* 988 $(M + Na)^+$; HRMS (ES) *m/z* 988.4522 (calcd for $C_{55}H_{76}NO_6Si_3ClNa$: 988.4567, M + Na).



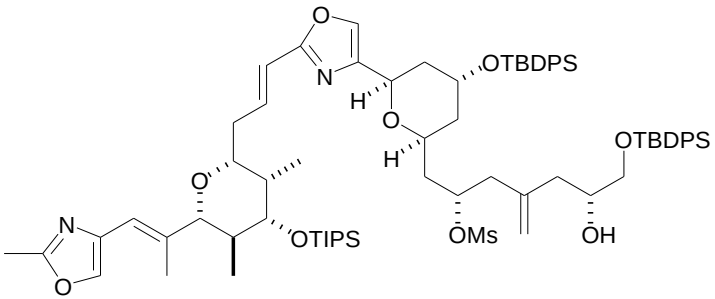
(2*S*,6*R*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-yl)prop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)-4-methylene-6-(triethylsilanyloxy)heptan-2-ol (76). To a solution of **75** (8.2 mg, 8.5 μmol) in dimethylformamide (1.5 mL) under argon at room temperature was added tri-*n*-butylphosphine (13 μL, 0.052 mmol) and the solution was stirred for 4 h. A solution of **52** (8.8 mg, 20 μmol) in dimethylformamide (1 mL) containing 1,8-diazabicyclo[5.4.0]undec-7-ene (1.7 μL, 11 μmol) was added and the mixture was stirred at room temperature for 1 h, then was diluted with ethyl acetate (5 mL). Saturated aqueous ammonium chloride (5 mL) was added, the phases were separated and the aqueous phase was extracted with ethyl acetate (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 15:1) to give **76** (9.1 mg, 78%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 –

7.63 (m, 8H), 7.48 (s, 1H), 7.44 – 7.29 (m, 13H), 6.62 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.32 (d, *J* = 16 Hz, 1H), 6.19 (s, 1H), 5.03 (d, *J* = 11 Hz, 1H), 4.90 (d, *J* = 6 Hz, 2H), 4.46 (brs, 1H), 4.30 (brs, 1H), 4.05 – 4.00 (m, 1H), 3.85 – 3.80 (m, 1H), 3.66 – 3.43 (m, 5H), 2.60 – 2.45 (m, 2H), 2.44 (s, 3H), 2.38 – 2.10 (m, 5H), 2.05 – 1.85 (m, 3H), 1.92 (d, *J* = 1 Hz, 3H), 1.80 – 1.45 (m, 5H), 1.09 – 0.97 (m, 45H), 0.85 (t, *J* = 8 Hz, 9H), 0.47 (q, *J* = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 161.0, 144.1, 143.3, 138.6, 138.2, 136.5, 136.2, 136.0, 134.4, 134.4, 134.0, 133.9, 130.1, 130.0, 128.1, 119.0, 118.8, 115.4, 89.3, 78.2, 72.7, 70.5, 68.1, 67.7, 66.9, 66.2, 45.7, 42.3, 40.9, 39.6, 38.7, 38.1, 36.8, 35.6, 30.1, 27.5, 27.3, 19.7, 19.6, 18.7, 18.6, 14.8, 14.4, 14.2, 13.3, 7.3, 6.5, 5.2.



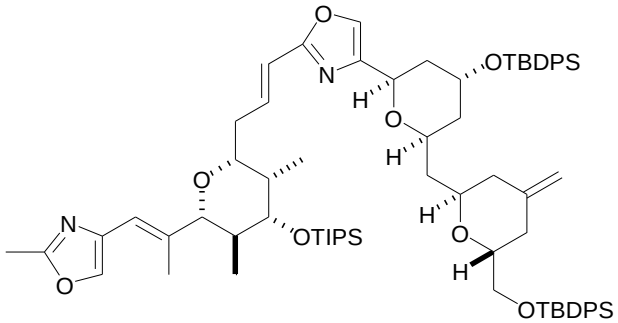
(2*S*,6*R*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-((2*S*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-yl)prop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)-4-methylene-6-(triethylsilanyloxy)heptan-2-yl methanesulfonate (77). To a solution of **76** (9.0 mg, 6.6 μmol) and triethylamine (11 μL, 79 μmol) in dichloromethane (1.5 mL) under argon at 0 ^{o}C was added methanesulfonyl chloride (3 μL, 39 μmol) and the solution was stirred at room temperature for 3 h. Saturated sodium bicarbonate solution (3 mL) was added and the phases were separated. The aqueous phase was extracted with dichloromethane (5 mL x 3) and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 7:1) to give **77** (7.3 mg, 77%) as a colourless oil: $[\alpha]_D^{23}$ +34.8 (c 0.70, $CHCl_3$); IR (neat) 2929, 2865, 1361,

1174, 1111, 911, 740, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 8H), 7.48 (s, 1H), 7.43 – 7.33 (m, 13H), 6.62 (ddd, *J* = 6, 8, 15 Hz, 1H), 6.31 (d, *J* = 16 Hz, 1H), 6.19 (s, 1H), 5.04 – 4.89 (m, 4H), 4.32 – 4.22 (m, 2H), 3.84 – 3.76 (m, 1H), 3.61 (dd, *J* = 4, 10 Hz, 1H), 3.55 – 3.41 (m, 5H), 3.00 (s, 3H), 2.65 – 2.20 (m, 5H), 2.44 (s, 3H), 2.13 (dd, *J* = 7, 14 Hz, 1H), 2.00 – 1.40 (m, 7H), 1.92 (d, *J* = 1 Hz, 3H), 1.09 – 0.97 (m, 45H), 0.84 (t, *J* = 8 Hz, 9H), 0.45 (q, *J* = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 161.0, 143.1, 141.8, 138.5, 138.2, 136.6, 136.1, 136.0, 134.7, 134.5, 134.2, 134.0, 133.9, 130.2, 130.0, 128.1, 128.1, 119.0, 118.8, 116.9, 89.3, 79.4, 78.2, 77.6, 72.3, 68.1, 68.0, 67.8, 66.3, 66.1, 43.3, 41.6, 40.9, 39.7, 39.0, 38.3, 38.1, 36.8, 35.6, 30.1, 27.5, 27.2, 19.7, 19.6, 18.7, 18.6, 14.8, 14.4, 14.2, 13.3, 7.3, 6.5, 5.2; MS (ES) *m/z* 1463 (M^+ + Na); HRMS (ES) *m/z* 1463.7571 (calcd for $C_{81}H_{120}N_2O_{11}SSi_4Na$: 1463.7588, M + Na).



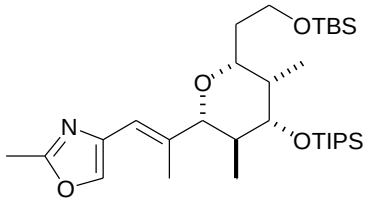
(2*S*,6*R*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-((2*S*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-yl)prop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)-6-hydroxy-4-methyleneheptan-2-yl methanesulfonate (78). To a solution of **77** (7.0 mg, 4.9 μmol) in methanol (1 mL) was added pyridinium *p*-toluenesulfonate (4.3 mg, 17 μmol) and the solution was stirred at room temperature for 1 h. Saturated sodium bicarbonate (3 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and

concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 3:1) to yield **78** (6.1 mg, 95%) as a colourless oil: $[\alpha]_D^{23}$ +39.8 (c 0.69, $CHCl_3$); IR (neat) 3371, 2927, 2858, 1360, 1173, 1111, 911, 740, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.67 (m, 8H), 7.52 (s, 1H), 7.45 – 7.37 (m, 13H), 6.65 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.32 (d, *J* = 16 Hz, 1H), 6.21 (s, 1H), 5.09 – 5.04 (m, 1H), 4.97 (d, *J* = 10 Hz, 1H), 4.93 (d, *J* = 10 Hz, 2H), 4.35 (brs, 1H), 4.29 (t, *J* = 11 Hz, 1H), 3.91 (brs, 1H), 3.67 – 3.62 (m, 2H), 3.57 – 3.47 (m, 3H), 3.04 (s, 3H), 2.70 – 2.48 (m, 4H), 2.48 (s, 3H), 2.30 – 2.20 (m, 3H), 2.08 – 1.24 (m, 8H), 1.96 (d, *J* = 1 Hz, 3H), 1.12 (s, 9H), 1.11 (m, 21H), 1.08 (s, 9H), 1.04 (d, *J* = 7 Hz, 3H), 0.85 (d, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 161.0, 142.9, 141.8, 138.5, 138.2, 136.8, 136.1, 136.0, 134.6, 134.5, 134.2, 133.6, 130.2, 128.2, 128.2, 119.0, 118.7, 116.7, 89.3, 79.1, 78.2, 70.6, 68.3, 68.1, 67.9, 66.1, 43.1, 40.9, 40.1, 39.7, 38.9, 38.3, 37.9, 36.8, 35.6, 30.1, 27.5, 27.3, 19.7, 19.7, 18.7, 18.6, 14.8, 14.4, 14.3, 13.3, 6.5; MS (ES) *m/z* 1327 (M^+ + H); HRMS (ES) *m/z* 1327.6895 (calcd for $C_{75}H_{107}N_2O_{11}SSi_3$: 1327.6903, M + H).



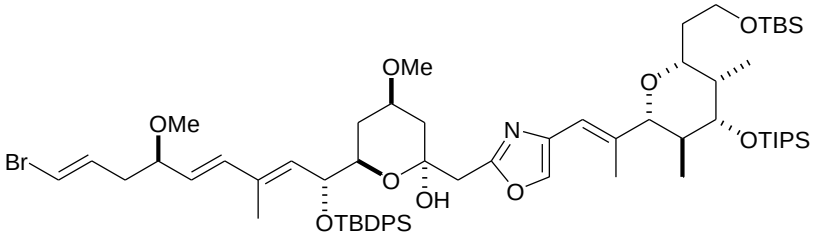
4-((2*R*,4*R*,6*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-6-(((2*R*,6*R*)-6-((*tert*-butyldiphenylsilanyloxy)methyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methyl)tetrahydro-2*H*-pyran-2-yl)-2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-yl)prop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)-2-methyloxazole (79). To a solution of **78** (22.1 mg, 16.6 μmol) in acetonitrile (6.5 mL)

was added triethylamine (232 μL, 1.66 mmol) and the solution was heated at reflux for 20 h, then was concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1) to give **79** (18.8 mg, 92%) as a colourless oil: $[\alpha]_D^{23}$ +29.4 (c 0.60, $CHCl_3$); IR (neat) 3070, 2928, 2857, 1463, 1427, 1387, 1107, 1031, 883, 822, 740, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.65 (m, 8H), 7.52 (s, 1H), 7.45 – 7.34 (m, 13H), 6.66 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.36 (d, *J* = 16 Hz, 1H), 6.22 (s, 1H), 5.02 (d, *J* = 11 Hz, 1H), 4.82 (s, 1H), 4.75 (s, 1H), 4.23 (brs, 1H), 4.20 – 4.16 (m, 1H), 4.01 – 3.99 (m, 1H), 3.90 – 3.86 (m, 1H), 3.73 (dd, *J* = 5, 10 Hz, 1H), 3.67 – 3.62 (m, 2H), 3.55 (t, *J* = 6 Hz, 1H), 3.49 (d, *J* = 10 Hz, 1H), 2.57 – 2.18 (m, 5H), 2.48 (s, 3H), 2.05 (dd, *J* = 5, 13 Hz, 1H), 2.00 – 1.24 (m, 8H), 1.96 (d, *J* = 1 Hz, 3H), 1.10 (m, 21H), 1.08 (s, 9H), 1.05 (s, 9H), 1.04 (d, *J* = 7 Hz, 3H), 0.85 (d, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 161.0, 143.4, 142.3, 138.6, 138.3, 136.4, 136.2, 136.1, 136.0, 134.6, 134.4, 134.2, 134.0, 130.1, 130.0, 128.1, 128.1, 119.0, 118.9, 110.8, 89.3, 78.2, 72.2, 70.2, 69.7, 68.0, 66.2, 66.0, 39.6, 39.5, 39.0, 38.7, 38.2, 37.3, 36.8, 35.6, 30.1, 27.4, 27.3, 19.7, 19.7, 18.7, 18.6, 14.8, 14.4, 14.3, 13.3, 6.5; MS (ES) *m/z* 1253 (M^+ + Na); HRMS (ES) *m/z* 1231.7048 (calcd for $C_{74}H_{103}N_2O_8Si_3$: 1231.7022, M + H).



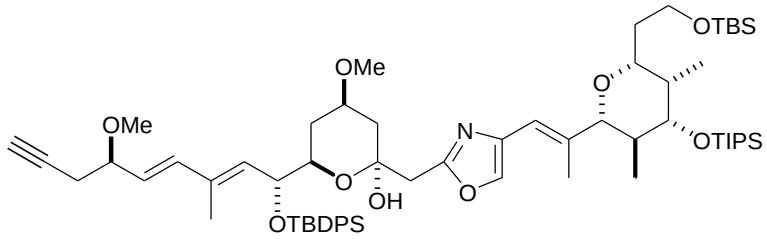
4-((*E*)-2-((2*R*,3*S*,4*S*,5*S*,6*R*)-6-(2-(*tert*-Butyldimethylsilanyloxy)ethyl)-3,5-dimethyl-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)-2-methyloxazole (80). To a solution of **51** (12 mg, 27 μmol) in dichloromethane (2 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (9 μL, 39 μmol) and 2,6-lutidine (6 μL, 51 μmol) and the solution was stirred at room temperature for 1 h. The solution was poured into saturated aqueous sodium

bicarbonate (5 mL) and extracted with ether (5 mL x 3), and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 5 : 1) to yield **80** (14 mg, 93%) as a colourless oil: $[\alpha]_D^{23}$ -26.6 (c 0.24 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 6.20 (s, 1H), 3.70 – 3.63 (m, 4H), 3.44 (d, *J* = 10 Hz, 1H), 2.48 (s, 3H), 1.94 (d, *J* = 1 Hz, 3H), 1.90 – 1.70 (m, 3H), 1.60 – 1.50 (m, 1H), 1.15 – 1.05 (m, 21H), 1.00 (d, *J* = 7 Hz, 3H), 0.92 (s, 9H), 0.84 (d, *J* = 7 Hz, 3H), 0.07 (d, *J* = 4 Hz, 6H); HRMS (EI) *m/z* 349.3977, calcd for $C_{31}H_{59}NO_4Si_2$ 349.3983.



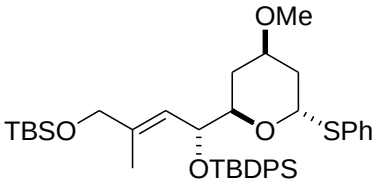
(2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2-((4-((*E*)-2-((2*R*,3*S*,4*S*,5*S*,6*R*)-6-(2-(*tert*-butyldimethylsilanyloxy)ethyl)-3,5-dimethyl-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-2-yl)methyl)-4-methoxytetrahydro-2*H*-pyran-2-ol (81). A flask containing a solution of **50** (24.2 mg, 43 μmol) and diethylamine (27 μL, 261 μmol) in tetrahydrofuran (400 μL) was cooled to –78 °C and *n*-butyllithium (2.30M solution in hexane, 24 μL, 56 μmol) was added dropwise via syringe. The colour of the solution, which turned bright yellow, was stirred for 20 min at –78 °C and a solution of **3** (15.9 mg, 25 μmol) in tetrahydrofuran (250 μL) at –78 °C was added dropwise via syringe. The solution turned dark yellow, and after 1 h the reaction was quenched with water (1 mL) and the mixture was extracted with ether (5 mL x 3). The combined extract was washed with brine (5 mL), dried and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 20:1 to 15:1) to produce **81** (18.2 mg, 45%) as a colourless oil: $[\alpha]_D^{23}$ +20.2 (c 0.82, $CHCl_3$); IR (neat)

3381, 2928, 2894, 2864, 1463, 1428, 1388, 1361, 1252, 1084, 1028, 833, 808, 775, 740, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 4H), 7.40 – 7.27 (m, 6H), 7.42 (s, 1H), 6.18 (s, 1H), 6.20 – 5.80 (m, 2H), 5.40 – 5.15 (m, 3H), 5.15 – 4.95 (brs, 1H), 4.45 – 4.35 (m, 1H), 4.00 – 3.90 (m, 1H), 3.70 – 3.50 (m, 7H), 3.45 – 3.25 (m, 1H), 3.34 (s, 3H), 3.22 (s, 3H), 3.02 (d, *J* = 15 Hz, 1H), 2.95 (d, *J* = 15 Hz, 1H), 2.50 – 2.40 (m, 1H), 2.35 – 2.15 (m, 2H), 2.10 – 2.00 (m, 1H), 1.88 (s, 3H), 1.90 – 1.50 (m, 5H), 1.43 (s, 3H), 1.15 – 1.05 (m, 21H), 0.98 (d, *J* = 7 Hz, 3H), 0.95 (s, 9H), 0.87 (s, 9H), 0.80 (d, *J* = 6 Hz, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 139.4, 138.2, 138.0, 136.4, 136.3, 135.8, 135.3, 135.2, 134.6, 134.3, 132.1, 130.1, 129.9, 129.8, 127.8, 127.6, 127.2, 125.9, 119.2, 118.2, 96.9, 89.2, 81.9, 81.1, 80.8, 78.5, 77.6, 75.3, 73.8, 73.4, 72.4, 70.3, 60.3, 56.9, 56.6, 56.0, 40.9, 40.2, 39.8, 37.6, 36.5, 35.7, 32.5, 30.7, 30.1, 27.3, 26.3, 26.2, 19.6, 18.7, 18.6, 14.9, 14.5, 13.3, 13.2, 6.7, -5.0; MS (ES) *m/z* 1192 $(M + H)^+$; HRMS (ES) *m/z* 1192.5850 (calcd for $C_{64}H_{103}{}^{79}BrNO_9Si_3$: 1192.6124, M + H).

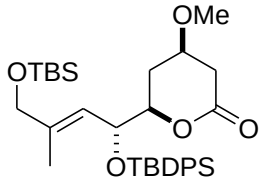


There was also obtained (2*S*,4*R*,6*R*)-2-((4-((*E*)-2-((2*R*,3*S*,4*S*,5*S*,6*R*)-6-(2-(*tert*-butyldimethylsilanyloxy)ethyl)-3,5-dimethyl-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-2-yl)methyl)-6-((1*R*,2*E*,4*E*,6*R*)-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4-dien-8-ynyl)-4-methoxytetrahydro-2*H*-pyran-2-ol **(82**, 13.3 mg, 33%) as a colourless oil: IR (neat) 3381, 3312, 2928, 2865, 2123, 1575, 1463, 1427, 1388, 1361, 1253, 1093, 1028, 969, 882, 834, 776, 740, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 – 7.57 (m, 4H), 7.45 (s, 1H), 7.43 – 7.27 (m, 6H), 6.17 (s, 1H), 6.04 (d, *J* = 16 Hz, 1H), 5.39 – 5.31 (m, 2H), 4.41 (dd, *J* = 6, 9 Hz, 1H), 3.99 – 3.94 (m, 1H), 3.76 – 3.57 (m, 7H), 3.44 – 3.41 (m, 1H),

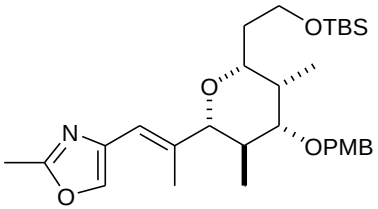
3.36 (s, 3H), 3.29 (s, 3H), 3.05 (d, *J* = 15 Hz, 1H), 2.97 (d, *J* = 15 Hz, 1H), 2.46 – 2.43 (m, 2H), 2.28 (dd, *J* = 4, 12 Hz, 1H), 2.19 (s, 1H), 2.13 – 2.05 (m, 1H), 2.00 (t, *J* = 3 Hz, 1H), 1.95 – 1.68 (m, 5H), 1.90 (s, 3H), 1.65 – 1.52 (m, 2H), 1.15 – 1.05 (m, 21H), 1.00 (d, *J* = 7 Hz, 3H), 0.97 (s, 9H), 0.89 (s, 9H), 0.82 (d, *J* = 6 Hz, 3H), 0.04 (s, 3H), 0.01 (s, 3H); HRMS (ES) *m/z* 1112.6754 (calcd for $C_{64}H_{102}NO_9Si_3$: 1112.6862, M + H).



(*R*,*E*)-5-((2*R*,4*R*)-4-Methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-2,2,7,10,10,11,11-heptamethyl-3,3-diphenyl-4,9-dioxa-3,10-disiladodec-6-ene (87). To a solution of **86** (20 mg, 36 □mol) in dichloromethane (2.7 mL) at room temperature was added a *tert*-butyldimethylsilyl chloride (25.4 mg, 0.169 mmol), *N*,*N*-diisopropylethylamine (50 μL, 0.287 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (0.4 mg). After 12 h, the solution was poured into saturated aqueous. sodium bicarbonate (5 mL) and extracted with ether (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 10 : 1) to yield **87** (24 mg, 98%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 4H), 7.25 – 7.13 (m, 8H), 7.12 – 7.08 (m, 3H), 5.71 (d, *J* = 5 Hz, 1H), 5.48 (dd, *J* = 1, 9 Hz, 1H), 4.47 (dd, *J* = 6, 9 Hz, 1H), 4.31 – 4.25 (m, 1H), 3.83 (d, *J* = 15 Hz, 1H), 3.79 (d, *J* = 15 Hz, 1H), 3.66 – 3.56 (m, 1H), 3.38 (s, 3H), 2.41 – 2.35 (m, 1H), 2.19 – 2.14 (m, 1H), 1.83 (ddd, *J* = 6, 12, 17 Hz, 1H), 1.40 – 1.20 (m, 1H), 1.06 (s, 9H), 1.04 (d, *J* = 1 Hz, 3H), 0.92 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); HRMS (ES) *m/z* 676.3431, calcd for $C_{39}H_{56}O_4SSi_2$ 676.3438.

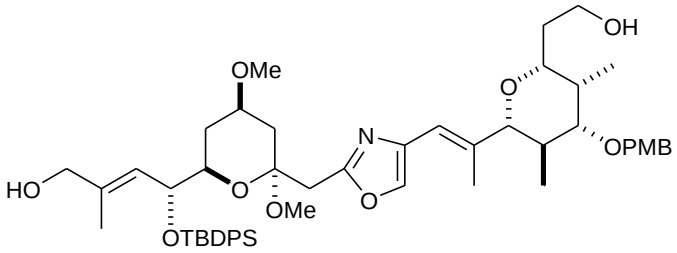


(4*R*,6*R*)-6-((*R*,*E*)-2,2,7,10,10,11,11-Heptamethyl-3,3-diphenyl-4,9-dioxa-3,10-disiladodec-6-en-5-yl)-4-methoxytetrahydropyran-2-one (84). To a solution of **87** (24 mg, 35 μmol) in tetrahydrofuran-water (5:1, 3 mL) was added silver nitrate (90 mg, 0.53 mmol) and 2,6-lutidine (124 μL, 1.07 mmol), and the mixture was stirred for 18 h at room temperature. The solution was diluted with water (5 mL) and extracted with ethyl acetate (5 mL x 3), and the combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 10:1) to give a hemiacetal. To a solution of the hemiacetal in dichloromethane (3 mL) was added tetra-*n*-propylammonium perruthenate (2.5 mg, 7.1 μmol), 4-methylmorpholine *N*-oxide (258 mg, 2.20 mmol) and 4□ molecular sieves, and the mixture was stirred for 1 h at room temperature. The solution was filtered through a column of silica gel (hexane:ethyl acetate 4:1 as eluent) to produce **84** (15.6 mg, 75%) as a colourless oil: $[\alpha]_D^{23}$ -9.8 (c 0.55, $CHCl_3$); IR (neat) 2954, 2929, 2891, 2856, 1747, 1471, 1427, 1361, 1250, 1192, 1111, 1006, 837, 777, 740, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 – 7.59 (m, 4H), 7.42 – 7.28 (m, 6H), 5.47 (dd, *J* = 1, 9 Hz, 1H), 4.55 (dd, *J* = 5, 9 Hz, 1H), 4.15 (ddd, *J* = 3, 5, 12 Hz, 1H), 3.79 (t, *J* = 15 Hz, 2H), 3.66 – 3.58 (m, 1H), 3.32 (s, 3H), 2.87 (dd, *J* = 2, 6 Hz, 0.5H), 2.82 (dd, *J* = 2, 6 Hz, 0.5H), 2.40 – 2.31 (m, 2H), 1.55 – 1.41 (m, 1H), 1.10 (s, 3H), 1.03 (s, 9H), 0.87 (s, 9H), 0.00 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 139.7, 135.9, 133.6, 129.8, 129.6, 127.6, 127.4, 120.5, 79.8, 77.2, 72.5, 70.5, 67.2, 56.0, 36.9, 29.7, 29.6, 27.0, 25.9, 19.3, 18.3, 13.8, -5.3, -5.4; MS (ES) *m/z* 605 $(M + Na)^+$; HRMS (ES) *m/z* 605.3054 (calcd for $C_{33}H_{50}O_5Si_2{}^{23}Na$: 605.3095, M + Na).



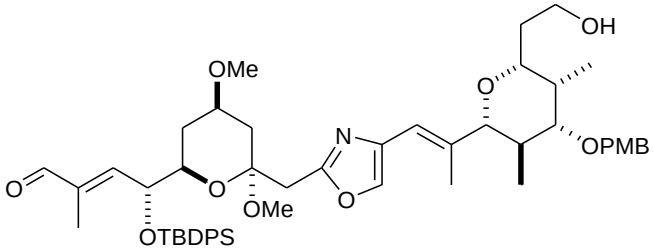
4-((*E*)-2-((2*R*,3*R*,4*S*,5*S*,6*R*)-6-(2-(*tert*-Butyldimethylsilanyloxy)ethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2H-pyran-2-yl)prop-1-enyl)-2-methyloxazole (83). To a solution of **87** (174 mg, 0.424 mmol) in tetrahydrofuran (9 mL) was added sodium hydride (62 mg, 1.55 mmol, 60% suspension in mineral oil) and the mixture was heated at reflux for 1.5 h. After the mixture had cooled to room temperature, *p*-methoxybenzyl chloride (98 μL, 0.72 mmol) and tetra-*n*-butylammonium iodide (78 mg, 0.21 mmol) were added, and the mixture was heated at reflux for 4.5 h. After the mixture had cooled to room temperature, the reaction was quenched with saturated ammonium chloride solution (5 mL) and the mixture was extracted with ether (10 mL x 3). The combined extract was washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 15:1) to give **83** (215 mg, 95%) as a colourless oil: $[\alpha]_D^{23}$ +40.2 (c 0.70, $CHCl_3$); IR (neat) 2954, 2927, 2854, 1612, 1585, 1513, 1462, 1386, 1302, 1248, 1172, 1093, 1035, 971, 834, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.32 (d, *J* = 9 Hz, 2H), 6.92 (d, *J* = 9 Hz, 2H), 6.20 (s, 1H), 4.62 (d, *J* = 11 Hz, 1H), 4.33 (d, *J* = 11 Hz, 1H), 3.84 (s, 3H), 3.73 –3.70 (m, 2H), 3.62 – 3.58 (m, 1H), 3.46 (d, *J* = 10 Hz, 1H), 3.24 (dd, *J* = 5, 10 Hz, 1H), 2.48 (s, 3H), 2.15 – 2.10 (m, 1H), 1.92 (s, 3H), 1.90 – 1.80 (m, 2H), 1.70 – 1.60 (m, 1H), 1.00 (d, *J* = 7 Hz, 3H), 0.93 (s, 9H), 0.85 (d, *J* = 6 Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 159.2, 138.3, 137.9, 135.5, 130.7, 129.4, 118.6, 113.8, 89.0,

83.5, 74.6, 69.6, 59.9, 55.3, 36.1, 34.3, 33.3, 29.7, 26.0, 18.4, 15.3, 14.2, 14.1, 13.8, 13.8, 6.1, -5.3; MS (ES) *m/z* 530 $(M + H)^+$; HRMS (ES) *m/z* 530.3313 (calcd for $C_{30}H_{48}NO_5Si$: 530.3302, M + H).



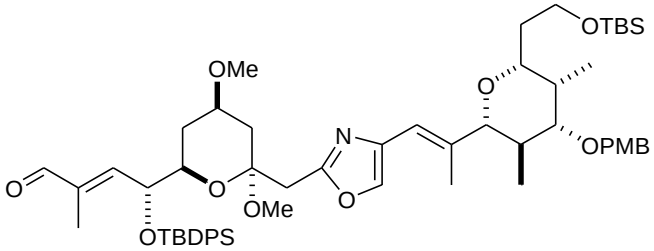
(2*S*,4*R*,6*R*)-6-((*R*,*E*)-1-(*tert*-Butyldiphenylsilanyloxy)-4-hydroxy-3-methylbut-2-enyl)-2-((4-((*E*)-2-((2*R*,3*R*,4*S*,5*S*,6*R*)-6-(2-hydroxyethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-2-yl)methyl)-4-methoxytetrahydro-2*H*-pyran-2-ol (89). To a solution of **88** (34.3 mg, 30.8 □mol) in methanol (5 mL) was added *p*-toluenesulfonic acid monohydrate (5.9 mg, 30.8 □mol) and the solution was stirred for 1 h. A saturated solution of sodium bicarbonate (3 mL) was added, most of the methanol was evaporated under reduced pressure and the remaining liquid was extracted with ethyl acetate (10 mL x 3). The combined extract was washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the resulting oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:3) to give **89** (28.0 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ +14.6 (c 0.50, $CHCl_3$); IR (neat) 3377, 2959, 2930, 2856, 1576, 1513, 1457, 1428, 1361, 1247, 1110, 1090, 1035, 823, 756, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8 Hz, 2H), 7.71 (d, *J* = 8 Hz, 2H), 7.56 (s, 1H), 7.46 – 7.27 (m, 8H), 6.92 (d, *J* = 9 Hz, 2H), 6.26 (s, 1H), 5.27 (dd, *J* = 1, 9 Hz, 1H), 4.62 (d, *J* = 11 Hz, 1H), 4.53 (dd, *J* = 6, 9 Hz, 1H), 4.34 (d, *J* = 11 Hz, 1H), 3.85 (s, 3H), 3.83 – 3.79 (m, 2H), 3.72 – 3.54 (m, 5H), 3.55 (d, *J* = 10 Hz, 1H), 3.34 (s, 3H), 3.33 (s, 3H), 3.26 (dd, *J* = 5, 10 Hz, 1H), 3.07 (d, *J* = 15 Hz, 1H), 2.30 – 2.28 (m, 1H), 2.20 – 1.87 (m, 5H), 1.94 (d, *J* = 1 Hz, 3H), 1.62 – 1.31 (m, 3H), 1.17

(d, *J* = 1 Hz, 3H), 1.09 (s, 9H), 1.04 (d, *J* = 7 Hz, 3H), 0.87 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 159.2, 138.0, 137.8, 137.7, 136.1, 136.1, 134.8, 133.9, 130.6, 129.6, 129.5, 129.4, 127.5, 127.3, 124.4, 119.1, 113.8, 99.9, 89.2, 82.9, 78.9, 77.3, 73.5, 72.2, 69.7, 67.9, 64.4, 62.1, 55.7, 55.3, 47.9, 39.2, 35.6, 35.1, 35.0, 33.2, 32.1, 30.7, 29.7, 27.0, 19.3, 19.1, 14.1, 13.7, 6.3; MS (ES) *m/z* (M^+ + H), 898; HRMS (ES) *m/z* 920.4745 (calcd for $C_{52}H_{71}NO_{10}Si$: 920.4770, M^+ + Na).



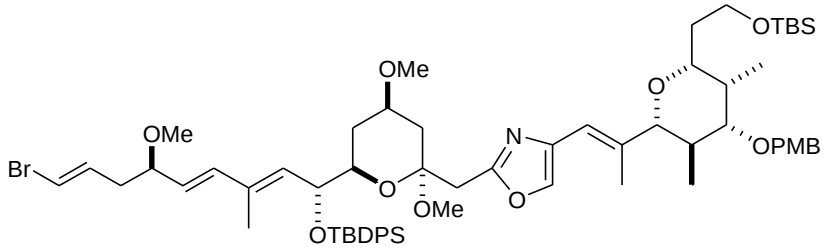
(*R*,*E*)-4-(*tert*-Butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*S*)-6-((4-((*E*)-2-((2*R*,3*R*,4*S*,5*S*,6*R*)-6-(2-hydroxyethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-2-yl)methyl)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-2-methylbut-2-enal (90). To a solution of **89** (28.0 mg, 30.8 □mol) in dichloromethane (6.5 mL) was added freshly prepared manganese dioxide (75 mg, 0.86 mmol) and the suspension was stirred vigorously for 2 h. The suspension was loaded on to a column of silica gel which was flushed with hexane:ethyl acetate (1:1) to yield **90** (23.6 mg, 84%) as a colourless oil: $[\alpha]_D^{23}$ +4.4 (c 0.50, $CHCl_3$); IR (neat) 3456, 2959, 2930, 2857, 1692, 1613, 1577, 1513, 1462, 1428, 1385, 1361, 1247, 1107, 1091, 1034, 822, 755, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.68 (d, *J* = 8 Hz, 2H), 7.58 (d, *J* = 8 Hz, 2H), 7.45 (s, 1H), 7.42 – 7.30 (m, 8H), 6.86 (d, *J* = 9 Hz, 2H), 6.23 (dd, *J* = 1, 9 Hz, 1H), 6.16 (s, 1H), 4.67 (dd, *J* = 6, 9 Hz, 1H), 4.56 (d, *J* = 11 Hz, 1H), 4.28 (d, *J* = 11 Hz, 1H), 3.79 (s, 3H), 3.77 – 3.73 (m, 2H), 3.67 – 3.42 (m, 3H), 3.27 (s, 3H), 3.15 (s, 3H), 3.27 – 3.13 (m, 2H), 2.94 (d, *J* = 15 Hz, 1H), 2.58 (brs, 1H), 2.25 – 2.15 (m, 1H), 2.10 – 1.80 (m, 5H), 1.86 (d,

J = 1 Hz, 3H), 1.57 – 1.30 (m, 3H), 1.30 (d, *J* = 1 Hz, 3H), 1.06 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.81 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 159.2, 158.9, 150.8, 139.9, 137.9, 137.8, 136.2, 135.9, 135.8, 133.4, 133.1, 130.6, 130.1, 129.4, 127.8, 127.6, 118.9, 113.8, 100.0, 89.2, 82.9, 78.9, 77.3, 73.1, 72.8, 71.6, 69.7, 62.0, 55.7, 55.3, 47.9, 39.1, 35.4, 35.1, 35.0, 33.2, 31.6, 29.7, 26.9, 19.3, 14.1, 13.7, 9.7, 6.3; MS (ES) *m/z* (M^+ + H) 896; HRMS (ES) *m/z* 896.4769 (calcd for $C_{52}H_{70}NO_{10}Si$: 896.4820, M^+ + H).



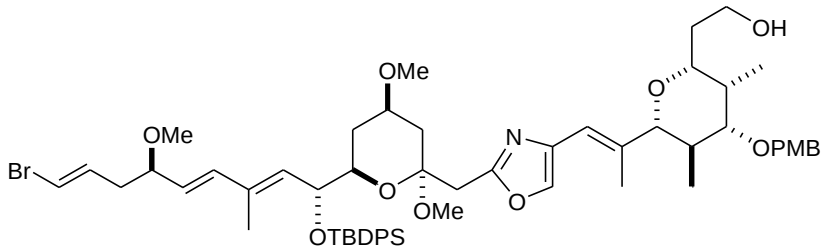
(*R*,*E*)-4-((2*R*,4*R*,6*S*)-6-((4-((*E*)-2-((2*R*,3*R*,4*S*,5*S*,6*R*)-6-(2-(*tert*-Butyldimethylsilanyloxy)ethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-2-yl)methyl)-4,6-dimethoxytetrahydro-2*H*-pyran-2-yl)-4-(*tert*-butyldiphenylsilanyloxy)-2-methylbut-2-enal (91). To a solution of **90** (23.6 mg, 26.3 μmol) in dichloromethane (5 mL) was added *tert*-butyldimethylsilyl chloride (15.3 mg, 0.102 mmol) and imidazole (9.3 mg, 0.137 mmol) and the solution was stirred at room temperaure for 12 h, after which it was poured into saturated aqueous sodium bicarbonate (10 mL) and extracted with ether (10 mL x 3). The combined extract was washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to yield **91** (22.8 mg, 86%) as a colourless oil: $[\alpha]_D^{23}$ +9.0 (c 0.42, $CHCl_3$); IR (neat) 2954, 2929, 2856, 1694, 1613, 1577, 1513, 1462, 1428, 1387, 1248, 1092, 1036, 835, 777, 741, 703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.68 (d, *J* = 8 Hz, 2H), 7.57 (d, *J* = 8 Hz, 2H), 7.45 (s, 1H), 7.42 – 7.25 (m, 8H), 6.83 (d, *J* = 9 Hz, 2H), 6.23 (dd, *J* = 1, 9 Hz, 1H), 6.14 (s, 1H),

4.67 (dd, *J* = 6, 9 Hz, 1H), 4.56 (d, *J* = 11 Hz, 1H), 4.28 (d, *J* = 11 Hz, 1H), 3.79 (s, 3H), 3.68 – 3.62 (m, 3H), 3.55 – 3.52 (m, 2H), 3.39 (d, *J* = 10 Hz, 1H), 3.27 (s, 3H), 3.16 (s, 3H), 3.20 – 3.16 (m, 2H), 2.94 (d, *J* = 15 Hz, 1H), 2.23 – 2.17 (m, 1H), 2.10 – 1.95 (m, 2H), 1.86 (d, *J* = 1 Hz, 3H), 1.81 – 1.76 (m, 2H), 1.40 – 1.12 (m, 3H), 1.29 (d, *J* = 1 Hz, 3H), 1.06 (s, 9H), 0.94 (d, *J* = 7 Hz, 3H), 0.87 (s, 9H), 0.80 (d, *J* = 6 Hz, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 159.2, 158.9, 150.8, 139.9, 138.5, 138.1, 136.1, 135.9, 135.8, 133.4, 133.1, 130.8, 130.1, 130.1, 129.4, 127.8, 127.7, 118.4, 113.8, 100.1, 89.0, 83.5, 74.7, 73.1, 72.8, 71.7, 69.6, 60.0, 55.6, 55.3, 47.9, 39.1, 36.1, 35.4, 34.3, 33.3, 31.6, 26.9, 26.0, 19.3, 18.4, 14.3, 13.8, 9.7, 6.1, -5.3; MS (ES) *m/z* (M^+ + H) 1171; HRMS (ES) *m/z* 1010.5634 (calcd for $C_{58}H_{84}NO_{10}Si_2$: 1010.5601, M^+ + H).



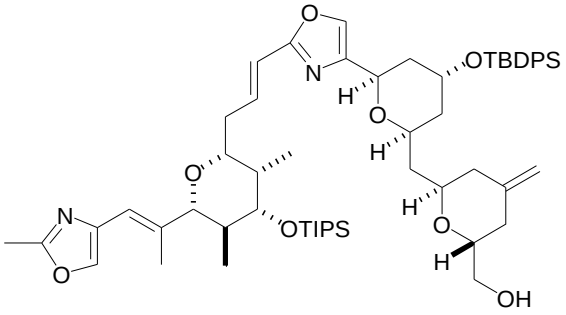
2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)-4-((*E*)-2-((2*R*,3*R*,4*S*,5*S*,6*R*)-6-(2-(*tert*-butyldimethylsilanyloxy)ethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazole (92). To a solution of **91** (23.0 mg, 22.8 μmol) and **85** (21.4 mg, 56.9 μmol) in tetrahydrofuran (1 mL) at –78 °C was added dropwise sodium bis(trimethylsilyl)amide (1M soluton in tetrahydrofuran, 55 μL, 55 μmol,) over 3 min. The mixture was stirred at –78°C for 0.5 h, then warmed to 0 °C for 15 min, and finally stirred at room temperature for 0.5 h. The reaction was quenched with pH 7 buffer solution (10 mL) and the mixture was extracted with ether (10 mL x 3). The combined extract was washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and

the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 7:1) to give **92** (26.9 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ -21.3 (c 0.28, $CHCl_3$); IR (neat) 2928, 2855, 1614, 1578, 1513, 1462, 1427, 1387, 1361, 1248, 1103, 1035, 834, 777, 741, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 1, 8 Hz, 2H), 7.61 (dd, *J* = 1, 8 Hz, 2H), 7.50 (s, 1H), 7.38 – 7.25 (m, 8H), 6.86 (d, *J* = 9 Hz, 2H), 6.17 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.96 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.20 (dd, *J* = 8, 16 Hz, 1H), 4.56 (d, *J* = 11 Hz, 1H), 4.50 (dd, *J* = 7, 9 Hz, 1H), 4.28 (d, *J* = 11 Hz, 1H), 3.79 (s, 3H), 3.68 – 3.65 (m, 2H), 3.59 – 3.52 (m, 4H), 3.40 (d, *J* = 10 Hz, 1H), 3.28 (s, 3H), 3.26 (s, 3H), 3.20 (s, 3H), 3.33 – 3.17 (m, 2H), 2.94 (d, *J* = 15 Hz, 1H), 2.27 – 2.18 (m, 3H), 2.07 – 2.02 (m, 1H), 1.88 (d, *J* = 1 Hz, 3H), 1.83 – 1.62 (m, 3H), 1.60 – 1.11 (m, 4H), 1.17 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H), 0.94 (d, *J* = 7 Hz, 3H), 0.88 (s, 9H), 0.81 (d, *J* = 6 Hz, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 138.4, 138.0, 137.3, 136.1, 136.0, 136.0, 134.9, 134.2, 133.9, 131.6, 130.8, 129.6, 129.4, 129.4, 127.7, 127.4, 127.2, 118.6, 113.8, 106.3, 99.9, 89.0, 83.5, 81.1, 74.7, 73.5, 73.5, 72.5, 69.6, 60.0, 56.2, 55.7, 55.3, 48.0, 39.2, 36.7, 36.1, 35.5, 34.4, 33.3, 32.3, 29.7, 27.0, 26.0, 19.4, 18.4, 14.3, 13.8, 13.0, 6.1, -5.3; MS (ES) *m/z* (M^+ + H) 1171; HRMS (ES) *m/z* 1071.5600 (calcd for $C_{64}H_{94}{}^{79}BrNO_{10}Si_2$: 1071.5507, M^+ + H).

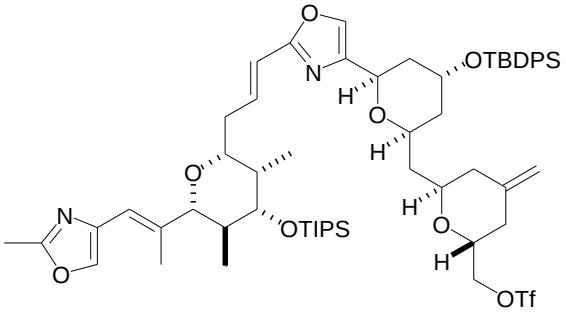


2-((2*R*,3*S*,4*S*,5*R*,6*R*)-6-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)ethanol

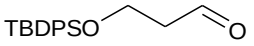
(93). To a solution of **92** (27.3 mg, 23.3 μmol) in methanol (5 mL) was added *p*-toluenesulfonic acid monohydrate (4.4 mg, 23 μmol) and the solution was stirred for 45 min. A saturated solution of sodium bicarbonate (3 mL) was added, methanol was partially evaporated under reduced pressure and the remaining liquid was extracted with ethyl acetate (10 mL x 3). The combined organic extract was washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:1) to afford **93** (22.6 mg, 92%) as a colourless oil: $[\alpha]_D^{23}$ -27.1 (c 0.24, $CHCl_3$); IR (neat) 3109, 2928, 2855, 1614, 1585, 1513, 1461, 1427, 1362, 1247, 1106, 1035, 822, 742, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 1, 8 Hz, 2H), 7.60 (dd, *J* = 1, 8 Hz, 2H), 7.49 (s, 1H), 7.40 – 7.25 (m, 8H), 6.86 (d, *J* = 9 Hz, 2H), 6.19 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.96 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.20 (dd, *J* = 8, 16 Hz, 1H), 4.56 (d, *J* = 11 Hz, 1H), 4.50 (dd, *J* = 7, 9 Hz, 1H), 4.29 (d, *J* = 11 Hz, 1H), 3.79 (s, 3H), 3.79 – 3.74 (m, 2H), 3.65 (d, *J* = 10 Hz, 1H), 3.59 – 3.51 (m, 4H), 3.27 (s, 3H), 3.26 (s, 3H), 3.20 (s, 3H), 3.33 – 3.17 (m, 2H), 2.93 (d, *J* = 15 Hz, 1H), 2.54 (brs, 1H), 2.29 – 2.18 (m, 3H), 2.06 – 1.80 (m, 5H), 1.88 (d, *J* = 1 Hz, 3H), 1.60 – 1.20 (m, 2H), 1.17 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.81 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 137.8, 137.7, 137.4, 136.2, 136.1, 136.0, 135.9, 135.8, 134.9, 134.3, 133.9, 131.6, 130.6, 129.6, 129.4, 129.4, 127.7, 127.4, 127.2, 119.0, 113.8, 106.3, 99.9, 89.2, 82.9, 81.1, 79.0, 73.5, 73.4, 72.5, 69.7, 62.1, 56.2, 55.7, 55.3, 48.0, 39.2, 35.5, 35.1, 35.0, 33.2, 32.3, 29.7, 27.0, 19.4, 14.1, 13.7, 13.0, 6.3; MS (ES) *m/z* (M^+ + H) 1056; HRMS (ES) *m/z* 1056.4657 (calcd for $C_{58}H_{79}{}^{79}BrNO_{10}Si$: 1056.4594, M^+ + H).



((2*R*,6*R*)-6-(((2*R*,4*R*,6*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-yl)prop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)methyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methanol (94). To a solution of **79** (10.9 mg, 8.9 μmol) in dimethylformamide (6 mL) at 0 °C was added tris(dimethylamino)sulfur (trimethylsilyl)difluoride (34.0 mg, 123 μmol) and the solution was stirred for 48 h at 0 °C. Phosphate buffer (pH 7.2, 1 mL) was added and the mixture was extracted with ether (1 mL x 3). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:1 to ethyl acetate only) to give **94** (5.1 mg, 74%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) □ 7.69 – 7.63 (m, 4H), 7.49 (s, 1H), 7.44 – 7.35 (m, 7H), 6.65 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.32 (d, *J* = 16 Hz, 1H), 6.18 (s, 1H), 5.00 (d, *J* = 10 Hz, 1H), 4.78 (s, 1H), 4.72 (s, 1H), 4.30 (brs, 1H), 4.25 – 4.09 (m, 2H), 3.92 – 3.83 (m, 1H), 3.72 – 3.40 (m, 5H), 2.60 – 1.35 (m, 14H), 2.44 (s, 3H), 1.92 (d, *J* = 1 Hz, 3H), 1.08 (m, 30H), 1.00 (d, *J* = 7 Hz, 3H), 0.81 (d, *J* = 7 Hz, 3H); HRMS (ES) *m/z* 980.5797, calcd for $C_{57}H_{84}N_2O_8Si_2$ 980.5766.



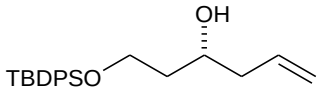
((2*R*,6*R*)-6-(((2*R*,4*R*,6*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*S*,6*R*)-3,5-dimethyl-6-((*E*)-1-(2-methyloxazol-4-yl)prop-1-en-2-yl)-4-(triisopropylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)methyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methyl trifluoromethanesulfonate (95). To a solution of **94** (4.9 mg, 4.9 μmol) in dichloromethane (2 mL) at –78 °C was added pyridine (2 μL, 12 μmol) and trifluoromethanesulfonic anhydride (2.5 μL, 15 μmol). The solution was stirred for 1 h at –78 °C, a saturated solution of sodium bicarbonate (1 mL) was added and the mixture was warmed to room temperature. The mixture was extracted with ether (1 mL x 3) and the combined extract was dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to give **95** (5.6 mg, 64%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.74 – 7.64 (m, 4H), 7.49 (s, 1H), 7.43 – 7.37 (m, 7H), 6.64 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.32 (d, *J* = 16 Hz, 1H), 6.18 (s, 1H), 5.01 (d, *J* = 11 Hz, 1H), 4.86 (s, 1H), 4.80 (s, 1H), 4.42 (d, *J* = 5 Hz, 2H), 4.30 (brs, 1H), 4.22 – 4.02 (m, 2H), 3.63 – 3.43 (m, 4H), 2.59 – 1.35 (m, 14H), 2.44 (s, 3H), 1.92 (d, *J* = 1 Hz, 3H), 1.08 (m, 30H), 1.00 (d, *J* = 7 Hz, 3H), 0.81 (d, *J* = 7 Hz, 3H).



3-(*tert*-Butyldiphenylsilanyloxy)propanal (99). To a solution of 1,3-propanediol (4.18 g, 55 mmol) in dichloromethane (50 mL) was added *tert*-butyldiphenylsilyl chloride (5 mL, 19.5 mmol) and *N*,*N*-diisopropylethylamine (10 mL, 71.7 mmol) and the solution was stirred for 12 h, after which it was

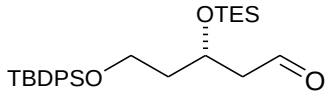
diluted with water (50 mL). The mixture was extracted with ethyl acetate (50 mL x 3) and the combined extract was washed with brine (25 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 2:1) to give 3-(*tert*-butyldiphenylsilanyloxy)propanol (6.14 g, 99%) which was used immediately for the next reaction.

To a solution of dimethyl sulfoxide (0.913 mL, 12.9 mmol) in dichloromethane (22 mL) at –78 °C was added oxalyl chloride (0.56 mL, 6.45 mmol), and after 25 min a solution of the alcohol obtained above (1.35 g, 4.29 mmol) in dichloromethane (8 mL) was added. After a further 25 min, triethylamine (1.79 mL, 12.9 mmol) was added and the solution was allowed to warm slowly to –10 °C over 1 h, then was warmed to room temperature for 0.5 h. The solution was poured into a mixture of ether (25 mL) and saturated ammonium chloride solution (25 mL) and the aqueous layer was separated and extracted with ether (25 mL x 3). The combined extract was washed with saturated sodium bicarbonate solution (25 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 15 : 1) to yield **99** (1.34 g, 99%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (t, *J* = 2 Hz, 1H), 7.65 – 7.61 (m, 4H), 7.42 – 7.34 (m, 6H), 4.00 (t, *J* = 6 Hz, 1H), 2.59 (dt, *J* = 6, 2 Hz, 1H), 1.01 (s, 9H). This aldehyde is unstable and was used immediately for the next reaction.



(*R*)-1-(*tert*-Butyldiphenylsilanyloxy)hex-5-en-3-ol (100). To a solution of (+)-*B*-methoxydiisopinocampheylborane (3.21 g, 10.15 mmol) in ether (25 mL) at 0 °C was added allylmagnesium bromide (1.0M solution in hexane, 8.6 mL) and the mixture was allowed to warm to room temperature. The solvent was removed under vacuum, the residue was extracted with pentane (10 mL x 4) and the resulting suspension was filtered under argon through a Schlenk tube. Pentane was removed from the filtrate under vacuum, the residue was dissolved in ether (25 mL) and the solution was cooled to –100°C. To this solution was added a solution of **99** (1.34 g, 4.29 mmol) in ether (25 mL) at –78 °C and the mixture was stirred at –100 °C for 1 h, after which the reaction was

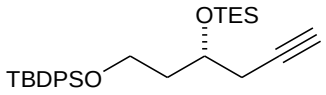
quenched with methanol (1.0 mL). The mixture was allowed to warm to room temperature, then was treated with saturated sodium bicarbonate solution (10 mL) and 30% hydrogen peroxide (5 mL) and was stirred for 10 h. The mixture was extracted with ether (25 mL x 3), and the combined extract was washed with brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 25:1) to yield **100** (1.52 g, 88%) as a colourless oil with enantiomeric ratio >96:4 by Mosher ester analysis of its ^{19}F NMR spectrum: ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 4H), 7.42 – 7.34 (m, 6H), 5.83 (ddt, *J* = 7, 10, 17 Hz, 1H), 5.12 – 5.05 (m, 2H), 3.95 – 3.90 (m, 1H), 3.88 – 3.80 (m, 2H), 3.20 (d, *J* = 3 Hz, 1H), 2.27 – 2.22 (m, 2H), 1.73 – 1.68 (m, 2H), 1.03 (s, 9H); HRMS (EI) *m/z* 354.2003, calcd for $C_{22}H_{30}O_2Si$ 354.2015.



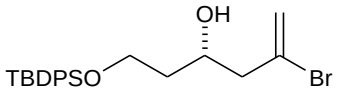
(*S*)-5-(*tert*-Butyldiphenylsilanyloxy)-3-(triethylsilanyloxy)pentanal (102). To a solution of **100** (99 mg, 0.28 mmol) in dichloromethane (9 mL) at 0 °C were added 2,6-lutidine (0.097 mL, 0.837 mmol) and triethylsilyl trifluoromethanesulfonate (95 μL, 0.42 mmol), and the solution was stirred at 0 °C for 30 min and at room temperature for 5 h. The reaction was quenched with saturated sodium bicarbonate solution, dichloromethane (10 mL) was added and the pH of the aqueous phase was adjusted to *ca*. 7.0 with 1M hydrochloric acid. The aqueous phase was extracted with dichloromethane (10 mL x 3), and the combined extract was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 40:1) to give **101** (117 mg, 90%) as a colourless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (m, 4H), 7.39 (m, 6H), 5.78 (ddt, *J* = 17, 10, 7 Hz, 1H), 4.99 (m, 2H), 3.94 (m, 1H), 3.69 (m, 2H), 2.20 (m, 2H), 1.66 (m, 2H), 1.02 (s, 9H), 0.91 (t, *J* = 8 Hz, 9H), 0.55 (q, *J* = 8 Hz, 6H).

Ozone was passed through a solution of **101** (50.1 mg, 0.107 mmol) in dichloromethane (5 mL) at 0 °C until a light blue color persisted. Triphenylphosphine (140 mg, 0.534 mmol) was added and the mixture was warmed to room temperature and was stirred for 30 min. The mixture was concentrated and the residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 10:1) to yield **102** (39.9 mg, 80%) as a colourless oil:

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (t, *J* = 2 Hz, 1H), 7.68 – 7.64 (m, 4H), 7.45 – 7.28 (m, 6H), 4.46 (tt, *J* = 6, 6 Hz, 1H), 3.81 – 3.66 (m, 2H), 2.63 – 2.47 (m, 2H), 1.91 – 1.68 (m, 2H), 1.07 (s, 9H), 0.94 (t, *J* = 8 Hz, 9H), 0.60 (q, *J* = 8 Hz, 6H). This aldehyde was unstable and was used immediately for the next reaction.



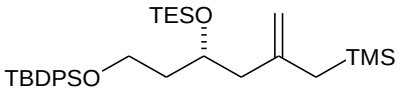
(*R*)-9,9-Diethyl-2,2-dimethyl-3,3-diphenyl-7-(prop-2-ynyl)-4,8-dioxa-3,9-disilaundecane (104). A freshly prepared solution of sodium methoxide (75 mL, 1M solution in methanol) was added to a solution of **103** (178 mg, 0.924 mmol) in tetrahydrofuran (10 mL) at –78 °C, and after 5 min neat **102** (174 mg, 0.370 mmol) was added. The solution was stirred for 10 min at –78 °C, then was warmed to room temperature. After 30 min, the reaction was quenched with saturated ammonium chloride solution (5 mL) and the aqueous phase was separated and extracted with ether (10 mL x 3). The combined extract was dried ($MgSO_4$), filtered, and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 20:1) to yield **104** (154 mg, 90%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (m, 4H), 7.36 (m, 6H), 4.09 (m, 1H), 3.76 (m, 2H), 2.37 (m, 2H), 2.00 (t, *J* = 3 Hz, 1H), 1.89 (m, 1H), 1.75 (m, 1H), 1.06 (s, 9H), 0.96 (t, *J* = 8 Hz, 9H), 0.62 (q, *J* = 8 Hz, 6H); HRMS (EI) *m/z* 466.2739, calcd for $C_{28}H_{42}O_2Si_2$ 466.2723.



(*S*)-5-Bromo-1-(*tert*-butyldiphenylsilanyloxy)hex-5-en-3-ol (106). To a solution of **104** (196 mg, 0.42 mmol) in methanol (5 mL) was added pyridinium *p*-toluenesulfonate (5 mg) and the solution was stirred for 2 h, then was concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 15:1) to give **105** (148 mg, 99%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (m, 4H), 7.42 –

7.25 (m, 6H), 4.08 (m, 1H), 3.87 (m, 2H), 3.41 (d, *J* = 3 Hz, 1H), 2.42 (m, 2H), 2.02 (t, *J* = 3 Hz, 1H), 1.80 (m, 2H), 1.05 (s, 9H). This material was used immediately for the next reaction.

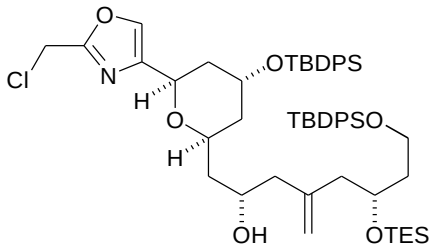
To a solution of **105** (148 mg, 0.42 mmol) in dichloromethane (5 mL) at 0 °C under argon was added 9-bromo-9-borabicyclo[3.3.1]nonane (1.0M solution in dichloromethane, 2 mL, 2 mmol). The mixture was allowed to warm to room temperature and was stirred overnight, then was cooled to 0 °C and ethanolamine (0.5 mL) and methanol (2 mL) were added. The mixture was diluted with ether (10 mL) and was washed with a saturated aqueous solution of sodium potassium tartrate (10 mL). The phases were separated and the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 30:1) to yield **106** (153 mg, 84%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (m, 4H), 7.46 – 7.28 (m, 6H), 5.70 (d, *J* = 1 Hz, 1H), 5.53 (d, *J* = 1 Hz, 1H), 4.28 (m, 1H), 3.91 (m, 2H), 3.23 (brs, 1H), 2.71 – 2.50 (m, 2H), 1.81 (m, 2H), 1.07 (s, 9H).



(*R*)-9,9-Diethyl-2,2-dimethyl-3,3-diphenyl-7-(2-((trimethylsilyl)methyl)allyl)-4,8-dioxa-3,9-disilaundecane (98). To a solution of **106** (153 mg, 0.353 mmol) in dichloromethane (7 mL) at 0 °C were added 2,6-lutidine (0.21 mL, 1.81 mmol) and triethylsilyl trifluoromethanesulfonate (0.21 mL, 0.93 mmol). The solution was stirred at 0 °C for 30 min and at room temperature for 5 h, and the reaction was quenched with saturated sodium bicarbonate solution. The aqueous phase was separated and was extracted with dichloromethane (10 mL x 3), and the combined extract was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 40:1) to yield **107** (161 mg, 83%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 4H), 7.33 – 7.25 (m, 6H), 5.57 (s, 1H), 5.41 (d, *J* = 1 Hz, 1H), 4.23 (m, 1H), 3.71 (m, 2H), 2.53 (m,

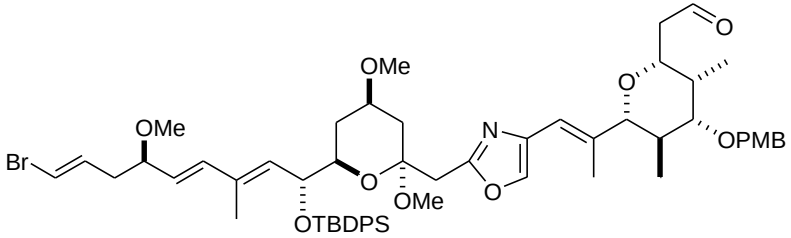
2H), 1.82 (m, 1H), 1.64 (m, 1H), 1.03 (s, 9H), 0.91 (t, *J* = 8 Hz, 9H), 0.58 (q, *J* = 8 Hz, 6H). This material was carried forward immediately to the next reaction.

To a solution of (trimethylsilyl)methylmagnesium chloride (1.0M solution in ether, 0.69 mL, 0.69 mmol) in tetrahydrofuran (12 mL) was added a solution of **107** (252 mg, 0.46 mmol) in tetrahydrofuran (2 mL) followed by [1,3-bis(diphenylphosphino)propane]nickel(II) chloride (25 mg, 46 μmol) and the mixture was heated at reflux for 12 h. After cooling to room temperature, the reaction was quenched with saturated ammonium chloride solution (15 mL) and ether (15 mL) was added. The phases were separated and the organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 200:1) to give **98** (220 mg, 86%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (m, 4H), 7.37 (m, 6H), 4.58 (d, *J* = 10 Hz, 2H), 4.10 (m, 1H), 3.73 (m, 2H), 2.17 (dd, *J* = 6, 13 Hz, 1H), 2.05 (dd, *J* = 7, 13 Hz, 1H), 1.78 (m, 1H), 1.59 (m, 1H), 1.52 (s, 2H), 1.04 (s, 9H), 0.92 (t, *J* = 8 Hz, 9H), 0.57 (q, *J* = 8 Hz, 6H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 136.0, 134.5, 134.4, 129.9, 128.0, 110.3, 68.5, 61.2, 47.2, 40.3, 27.5, 27.3, 19.6, 7.4, 5.5, -1.0; HRMS (ES) *m/z* 596.3888, calcd for $C_{35}H_{60}O_2Si_3$ 598.3901.



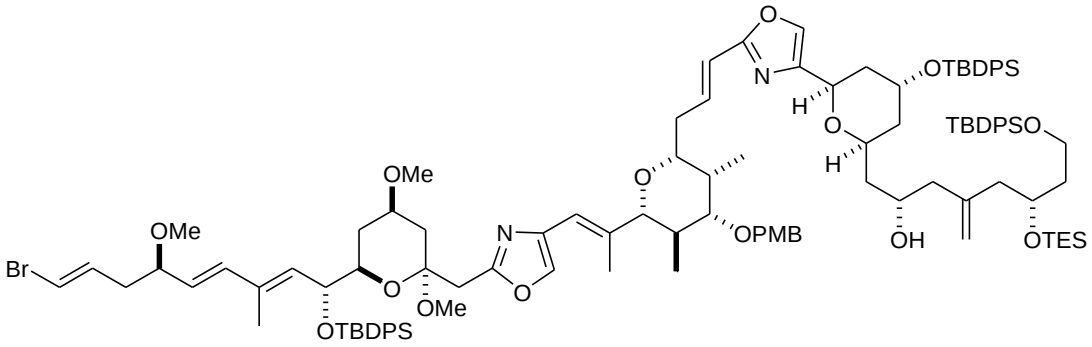
(*R*)-8-(*tert*-Butyldiphenylsilanyloxy)-1-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(2-(chloromethyl)oxazol-4-yl)tetrahydro-2*H*-pyran-2-yl)-4-methylene-6-(triethylsilanyloxy)octan-2-ol (108). To a solution of **98** (117 mg, 0.211 mmol) in dichloromethane (7 mL) at –78 °C was added tin tetrachloride (1.0M solution in dichloromethane, 188 μL, 188 μmol) and the solution was stirred at –78 °C for 30 min. A solution of **74** (45.8 mg, 92 μmol) in

dichloromethane (2.5 mL) was added and the mixture was stirred for 1 h at –78 °C. The reaction was quenched with saturated sodium bicarbonate solution (2 mL) and the mixture was extracted with dichloromethane (10 mL x 3). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 20:1 to 10:1) to give **108** (56.8 mg, 63%) as a colourless oil: $[\alpha]_D^{23}$ +10.1 (c 0.98, $CHCl_3$); IR (neat) 3477, 3070, 2953, 2927, 2855, 1471, 1427, 1238, 1110, 894, 822, 739, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 7.67 – 7.65 (m, 8H), 7.52 (s, 1H), 7.43 – 7.36 (m, 12H), 5.05 (d, *J* = 10 Hz, 1H), 4.88 (d, *J* = 5 Hz, 2H), 4.57 (s, 2H), 4.48 – 4.40 (m, 1H), 4.32 (s, 1H), 4.09 – 4.02 (m, 2H), 3.76 – 3.67 (m, 2H), 2.77 (brs, 1H), 2.22 – 2.16 (m, 4H), 2.00 – 1.85 (m, 2H), 1.80 – 1.35 (m, 6H), 1.10 (s, 9H), 1.04 (s, 9H), 0.90 (t, *J* = 8 Hz, 9H), 0.55 (q, *J* = 8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) □ 159.3, 144.3, 143.3, 136.6, 136.1, 136.0, 134.4, 134.3, 130.2, 130.0, 128.1, 128.0, 115.3, 77.6, 70.5, 68.7, 67.9, 66.7, 66.1, 61.1, 45.5, 44.3, 42.6, 40.2, 38.7, 38.1, 36.2, 32.3, 30.7, 30.1, 29.8, 27.5, 27.3, 23.1, 19.7, 19.6, 15.7, 14.5, 7.3, 5.4; MS (ES) *m/z* (M + Na)$^+$ 1002; HRMS (ES) *m/z* 1002.4739 (calcd for $C_{56}H_{78}ClNO_6Si_3Na$: 1002.4723, M + Na).



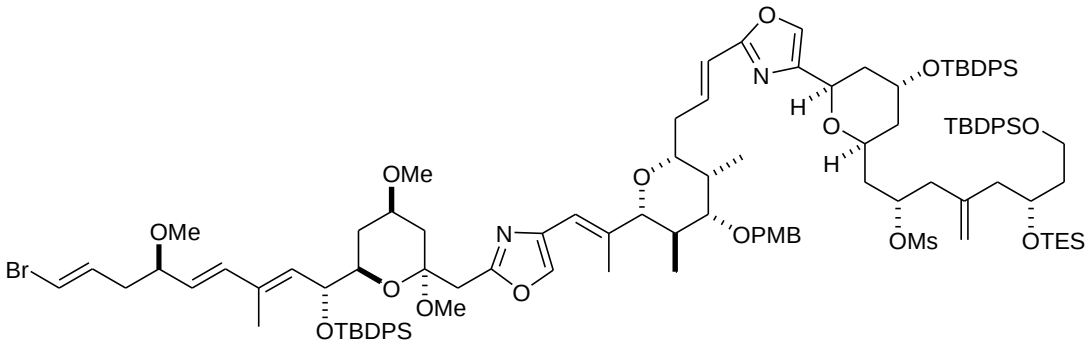
2-((2*R*,3*S*,4*S*,5*R*,6*R*)-6-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)acetaldehyde (109). To a solution of **93** (6.0 mg, 5.5 μmol) in dichloromethane (1.6 mL) under argon at room temperature was added Dess-Martin periodinane (4.9 mg, 12 μmol) and the solution was stirred at room temperature for 1 h. The solution was poured into an ice-cold mixture of saturated

aqueous sodium bicarbonate (1 mL) containing sodium thiosulfate (0.5 g) and was extracted with ethyl acetate (2 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1) to give **109** (5.7 mg, 95%) as a colourless oil: $[\alpha]_D^{23}$ -21.3 (c 0.18, $CHCl_3$); IR (neat) 2929, 2855, 1727, 1615, 1513, 1457, 1428, 1361, 1247, 1106, 1034, 822, 741, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.75 (t, *J* = 2 Hz, 1H), 7.72 (dd, *J* = 1, 8 Hz, 2H), 7.60 (dd, *J* = 1, 8 Hz, 2H), 7.40 (s, 1H), 7.40 – 7.27 (m, 8H), 6.87 (d, *J* = 9 Hz, 2H), 6.18 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.96 (d, *J* = 16 Hz, 1H), 5.33 (d, *J* = 9 Hz, 1H), 5.20 (dd, *J* = 8, 16 Hz, 1H), 4.56 (d, *J* = 11 Hz, 1H), 4.50 (dd, *J* = 7, 9 Hz, 1H), 4.30 (d, *J* = 11 Hz, 1H), 4.01 – 3.97 (m, 1H), 3.79 (s, 3H), 3.79 – 3.74 (m, 2H), 3.59–3.50 (m, 3H), 3.27 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 3.29 – 3.17 (m, 1H), 2.94 (d, *J* = 15 Hz, 1H), 2.74 (ddd, *J* = 2, 9, 17 Hz, 1H), 2.41 (ddd, *J* = 2, 5, 17 Hz, 1H), 2.29 – 2.10 (m, 4H), 1.89 – 1.78 (m, 2H), 1.87 (d, *J* = 1 Hz, 3H), 1.37 –1.19 (m, 2H), 1.17 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H), 0.97 (d, *J* = 7 Hz, 3H), 0.80 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 159.3, 140.5, 137.9, 137.7, 137.4, 136.3, 136.2, 136.1, 136.0, 136.0, 134.9, 134.3, 133.9, 131.6, 130.4, 129.6, 129.4, 129.4, 127.7, 127.4, 127.2, 119.0, 113.9, 113.9, 106.3, 99.9, 89.2, 82.7, 81.1, 73.5, 73.2, 72.5, 69.8, 56.2, 55.6, 55.3, 48.0, 47.0, 39.2, 35.5, 34.3, 33.1, 32.3, 27.0, 19.4, 14.1, 13.7, 13.0, 6.2; MS (ES) *m/z* (M^+ + H) 1054; HRMS (ES) *m/z* 1054.4500 (calcd for $C_{58}H_{77}{}^{81}BrNO_{10}Si$: 1054.4490, M^+ + H).



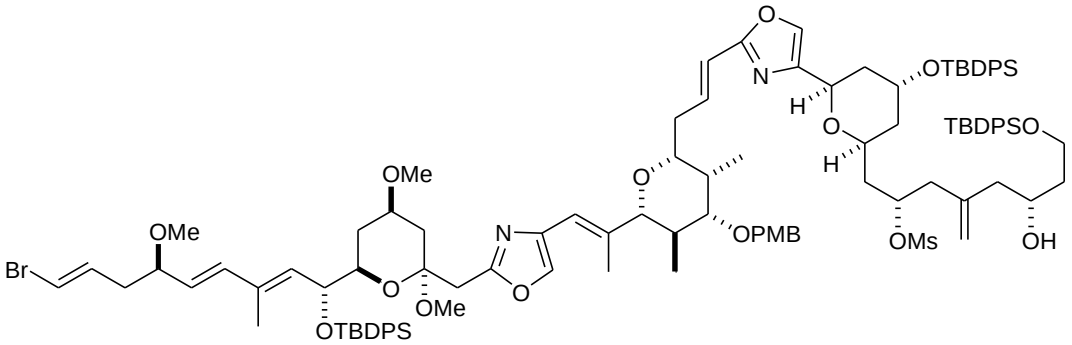
(2*S*,6*R*)-1-((2*R*,4*R*,6*R*)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*R*,6*R*)-6-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)-4-(*tert*-butyldiphenylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)-8-(*tert*-butyldiphenylsilanyloxy)-4-methylene-6-(triethylsilanyloxy)octan-2-ol (110). To a solution of **108** (55.0 mg, 56 μmol) in dimethylformamide (2 mL) under argon at room temperature was added tri-*n*-butylphosphine (98 μL, 392 μmol) and the mixture was stirred at room temperature for 3 h. A solution of **109** (21.7 mg, 20.6 μmol) in dimethylformamide (0.5 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (3.7 μL, 24.7 μmol) were added and the mixture was stirred at room temperature for 1 h, then was diluted with ethyl acetate (5 mL). Saturated aqueous ammonium chloride (5 mL) was added, the phases were separated and the aqueous phase was extracted with ethyl acetate (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 15:1 to 4:1) to afford **110** (34.5 mg, 85%) as a colourless oil: $[\alpha]_D^{23}$ +3.8 (c 0.32, $CHCl_3$); IR (neat) 3519, 2929, 2856, 1513, 1457, 1428, 1361, 1247, 1106, 1035, 969, 822, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 1, 8 Hz, 2H), 7.66 – 7.60 (m, 10H), 7.51 (s, 1H), 7.40 – 7.25 (m, 21H), 6.86 (d, *J* = 9 Hz, 2H), 6.63 (ddd, *J* = 6, 8, 15 Hz, 1H), 6.34 (d, *J* = 16 Hz, 1H), 6.21 (s, 1H), 6.14 (dd, *J* = 7, 14 Hz, 1H), 6.06 (d, *J* = 14 Hz, 1H), 5.97 (d, *J* = 16 Hz, 1H), 5.35 (d, *J* = 9 Hz, 1H), 5.21 (dd, *J* = 8, 16 Hz, 1H), 5.03 (d, *J* = 11 Hz, 1H), 4.85 (d, *J* = 9 Hz, 2H), 4.56 (d, *J* = 11 Hz, 1H), 4.51 (dd, *J* = 7, 9 Hz, 1H), 4.45 (m, 1H), 4.31 (s, 1H), 4.27 (d, *J* = 11 Hz, 1H), 4.10 –3.95 (m, 2H), 3.78 (s, 3H), 3.71 (m, 2H), 3.59 – 3.48 (m, 4H), 3.47 (d, *J* = 10 Hz, 1H), 3.28 (s, 3H), 3.26 (s, 3H), 3.21 (s, 3H), 3.31 – 3.16 (m, 2H), 2.95 (d, *J* = 15 Hz, 1H), 2.89 (brs, 1H), 2.56 (m, 1H), 2.38 (m, 1H), 2.31 – 2.12 (m, 9H), 1.91 (d, *J* = 1 Hz, 3H), 1.90 – 1.20 (m, 11H), 1.18 (d, *J* = 1 Hz, 3H), 1.08 (s, 9H), 1.05 (s, 9H), 1.02 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.88 (t, *J* = 8 Hz, 9H), 0.82 (d, *J* = 6 Hz, 3H), 0.54 (q, *J* = 8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 159.4, 144.0, 143.1, 138.2, 138.1, 137.5, 136.3, 136.2, 135.9, 135.8, 135.8, 135.1, 134.4, 134.3, 134.3, 134.1, 134.1,

134.1, 131.8, 130.8, 130.0, 130.0, 129.8, 129.6, 129.5, 127.9, 127.9, 127.8, 127.6, 127.4, 119.0, 118.9, 115.0, 114.0, 106.5, 100.1, 89.3, 83.4, 81.3, 77.5, 73.7, 73.6, 72.7, 70.3, 70.0, 68.4, 67.8, 66.6, 66.0, 60.9, 56.4, 55.8, 55.5, 48.2, 45.2, 44.2, 42.2, 40.0, 39.4, 38.5, 37.8, 36.6, 35.7, 33.8, 33.5, 32.5, 29.9, 27.3, 27.2, 27.1, 19.6, 19.5, 19.3, 14.4, 14.0, 13.2, 7.1, 5.2; HRMS (MALDI) calcd for $C_{108}H_{139}N_2O_{15}Si_3{}^{79}BrNa$ (M – TES + H + Na, $^{79}Br)^+$ 1889.8617, found 1889.8559.

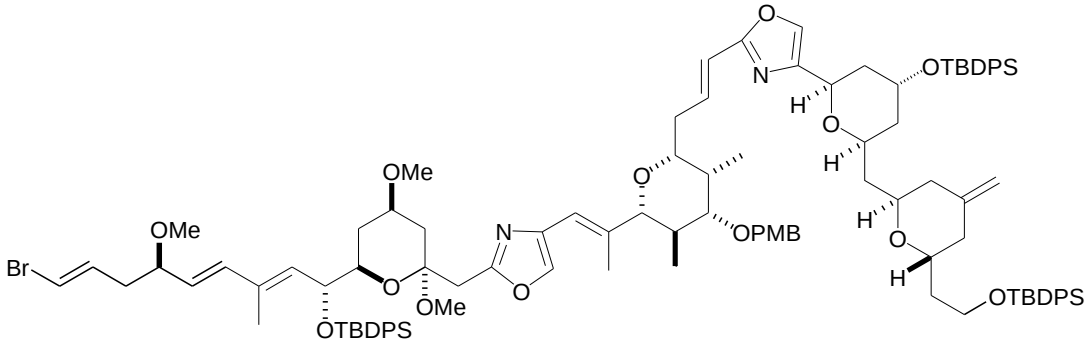


(2*S*,6*R*)-1-((2*S*,4*R*,6*R*)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*R*,6*R*)-6-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)-4-(*tert*-butyldiphenylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)-8-(*tert*-butyldiphenylsilanyloxy)-4-methylene-6-(triethylsilanyloxy)octan-2-yl methanesulfonate (111). To a solution of **110** (31.1 mg, 15.6 μmol) in dichloromethane (5 mL) at 0 °C were added triethylamine (48 μL, 344 μmol) and methanesulfonyl chloride (8 μL, 103 μmol) and the solution was allowed to warm to room temperature. After 1.5 h, a saturated aqueous solution of sodium bicarbonate (3 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1 to 3:1) to give **111** (32.2 mg, 99%) as a colourless

oil: $[\alpha]_D^{23}$ +5.0 (c 0.40, $CHCl_3$); IR (neat) 2929, 2856, 1513, 1462, 1427, 1360, 1247, 1173, 1105, 1035, 970, 910, 822, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 1, 8 Hz, 2H), 7.66 – 7.60 (m, 10H), 7.51 (s, 1H), 7.44 (s, 1H), 7.41 – 7.29 (m, 18H), 7.26 (d, *J* = 9 Hz, 2H), 6.86 (d, *J* = 9 Hz, 2H), 6.62 (ddd, *J* = 6, 8, 15 Hz, 1H), 6.33 (d, *J* = 16 Hz, 1H), 6.21 (s, 1H), 6.14 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.97 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.21 (dd, *J* = 8, 16 Hz, 1H), 5.03 (m, 1H), 4.96 (d, *J* = 11 Hz, 1H), 4.88 (s, 2H), 4.56 (d, *J* = 11 Hz, 1H), 4.51 (dd, *J* = 6, 9 Hz, 1H), 4.25 (m, 3H), 4.01 (m, 1H), 3.78 (s, 3H), 3.68 (m, 2H), 3.58 – 3.44 (m, 5H), 3.28 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 3.31 – 3.15 (m, 2H), 2.99 (s, 3H), 2.94 (d, *J* = 15 Hz, 1H), 2.60 – 2.10 (m, 10H), 1.90 (d, *J* = 1 Hz, 3H), 2.00 – 1.20 (m, 12H), 1.18 (d, *J* = 1 Hz, 3H), 1.08 (s, 9H), 1.04 (s, 9H), 1.01 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.87 (t, *J* = 8 Hz, 9H), 0.82 (d, *J* = 6 Hz, 3H), 0.51 (q, *J* = 8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 159.3, 142.9, 141.8, 138.2, 138.1, 137.5, 136.3, 136.2, 135.9, 135.8, 135.8, 135.1, 134.6, 134.4, 134.3, 134.1, 134.1, 134.0, 131.8, 130.8, 130.0, 130.0, 129.8, 129.6, 129.5, 127.9, 127.8, 127.8, 127.6, 127.4, 119.0, 118.9, 116.3, 114.0, 106.5, 100.1, 89.3, 83.4, 81.3, 79.0, 77.4, 73.6, 72.7, 70.0, 68.5, 67.9, 67.7, 65.9, 60.9, 60.6, 56.4, 55.8, 55.5, 48.2, 44.6, 43.2, 40.8, 40.1, 39.4, 38.7, 38.2, 37.8, 36.8, 36.6, 35.7, 33.8, 33.5, 32.5, 31.7, 29.9, 27.3, 27.2, 27.1, 21.2, 19.6, 19.5, 19.3, 14.4, 14.0, 13.2, 7.1, 5.2; MS (ES) *m/z* 2059 (M^+ + H); HRMS (ES) *m/z* 2058.9288 (calcd for $C_{115}H_{155}N_2O_{17}SSi_4Br$: 2058.9307, M^+).

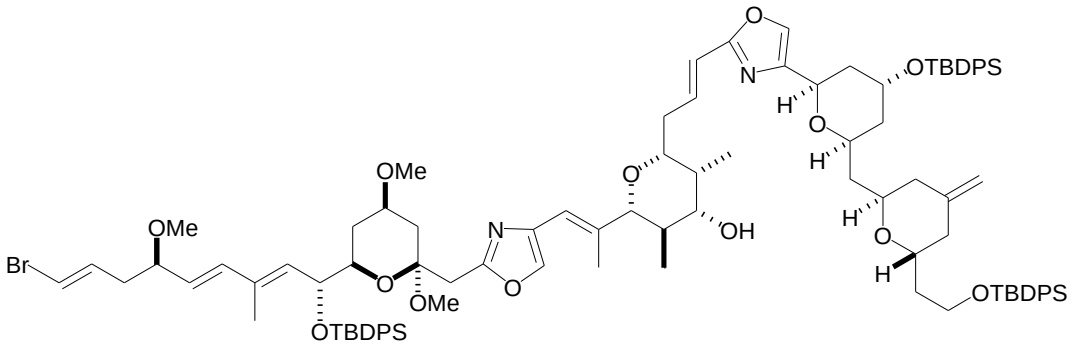


(2*S*,6*R*)-1-((2*S*,4*R*,6*R*)-6-(2-((*E*)-3-((2*R*,3*S*,4*S*,5*R*,6*R*)-6-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazol-4-yl)-4-(*tert*-butyldiphenylsilanyloxy)tetrahydro-2*H*-pyran-2-yl)-8-(*tert*-butyldiphenylsilanyloxy)-6-hydroxy-4-methyleneoctan-2-yl methanesulfonate (112). To a solution of **111** (32.0 mg, 15.6 μmol) in methanol (5 mL) was added pyridinium *p*-toluenesulfonate (2.2 mg, 8.8 μmol) and the solution was stirred at room temperature for 1.5 h. The solution was concentrated under reduced pressure and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1 to 1:1) to give **112** (29.7 mg, 98%) as a colourless oil: $[\alpha]_D^{23}$ +8.3 (c 0.30, $CHCl_3$); IR (neat) 3504, 2959, 2856, 1513, 1462, 1427, 1360, 1248, 1173, 1105, 1035, 970, 910, 822, 756, 742, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 1, 8 Hz, 2H), 7.64 – 7.59 (m, 10H), 7.50 (s, 1H), 7.43 (s, 1H), 7.42 – 7.30 (m, 18H), 7.27 (d, *J* = 9 Hz, 2H), 6.85 (d, *J* = 9 Hz, 2H), 6.60 (ddd, *J* = 6, 8, 15 Hz, 1H), 6.32 (d, *J* = 16 Hz, 1H), 6.20 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.96 (d, *J* = 16 Hz, 1H), 5.33 (d, *J* = 9 Hz, 1H), 5.20 (dd, *J* = 8, 16 Hz, 1H), 5.07 (m, 1H), 4.93 (m, 3H), 4.55 (d, *J* = 11 Hz, 1H), 4.50 (dd, *J* = 6, 9 Hz, 1H), 4.35 – 4.22 (m, 3H), 4.12 – 4.00 (m, 1H), 3.85 – 3.79 (m, 3H), 3.77 (s, 3H), 3.59 – 3.43 (m, 4H), 3.27 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 3.32 – 3.15 (m, 2H), 3.01 (s, 3H), 2.93 (d, *J* = 15 Hz, 1H), 2.62 – 2.10 (m, 10H), 1.89 (d, *J* = 1 Hz, 3H), 2.00 – 1.20 (m, 12H), 1.17 (d, *J* = 1 Hz, 3H), 1.07 (s, 9H), 1.04 (s, 9H), 1.01 (s, 9H), 0.97 (d, *J* = 7 Hz, 3H), 0.81 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 159.3, 142.8, 141.8, 138.2, 138.1, 137.5, 136.3, 136.3, 136.2, 135.9, 135.7, 135.0, 134.5, 134.3, 134.2, 134.0, 134.0, 133.3, 133.2, 131.8, 130.8, 129.8, 129.6, 129.5, 128.0, 128.0, 127.8, 127.6, 127.4, 119.0, 118.8, 116.5, 114.0, 106.5, 100.1, 89.3, 83.4, 81.2, 78.9, 77.4, 73.7, 72.7, 70.0, 69.6, 68.0, 67.6, 65.9, 63.4, 60.6, 56.3, 55.8, 55.5, 48.1, 44.4, 42.8, 40.6, 39.3, 38.7, 38.5, 38.2, 37.8, 36.8, 36.6, 35.7, 33.8, 33.5, 32.4, 31.7, 29.9, 27.2, 27.1, 27.0, 21.2, 19.6, 19.5, 19.2, 14.4, 14.0, 13.2, 5.9; HRMS (ES) *m/z* 1945.8572 (calcd for $C_{109}H_{142}N_2O_{17}SSi_3Br$: 1945.8520, M + H).



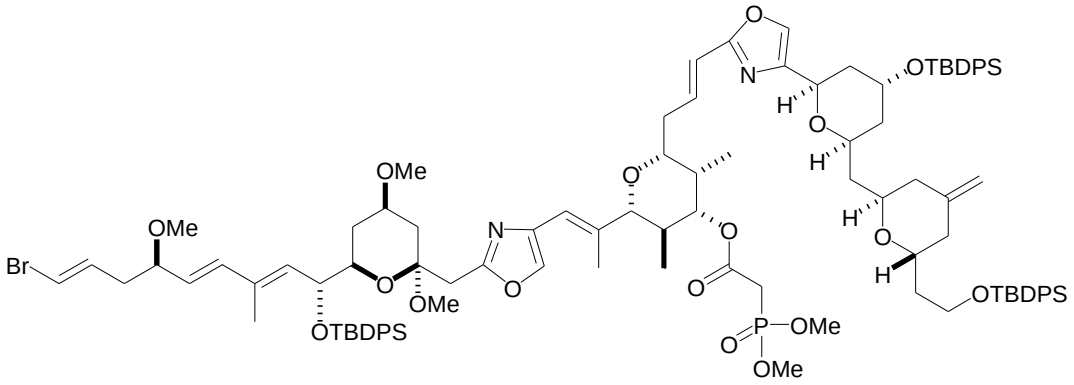
2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)-4-((*E*)-2-((2*R*,3*R*,4*S*,5*S*,6*R*)-6-((*E*)-3-(4-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(((2*R*,6*R*)-6-(2-(*tert*-butyldiphenylsilanyloxy)ethyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methyl)tetrahydro-2*H*-pyran-2-yl)oxazol-2-yl)allyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2*H*-pyran-2-yl)prop-1-enyl)oxazole (113). To a solution of **112** (29.7 mg, 15.3 μmol) in acetonitrile (7 mL) was added triethylamine (0.85 mL, 6.1 mmol) and the solution was heated at reflux for 24 h. The solution was concentrated under reduced pressure and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 10:1 to 5:1) to give **113** (24.2 mg, 86%) as a colourless oil: $[\alpha]_D^{23}$ -3.4 (c 0.41, $CHCl_3$); IR (neat) 2930, 2856, 1513, 1471, 1427, 1360, 1248, 1106, 1035, 969, 822, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 1, 8 Hz, 2H), 7.66 – 7.60 (m, 10H), 7.51 (s, 1H), 7.42 – 7.31 (m, 19H), 7.26 (d, *J* = 9 Hz, 2H), 6.86 (d, *J* = 9 Hz, 2H), 6.61 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.34 (d, *J* = 16 Hz, 1H), 6.21 (s, 1H), 6.14 (dd, *J* = 7, 14 Hz, 1H), 6.06 (d, *J* = 14 Hz, 1H), 5.97 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.21 (dd, *J* = 8, 16 Hz, 1H), 4.99 (d, *J* = 12 Hz, 1H), 4.70 (d, *J* = 3 Hz, 2H), 4.56 (d, *J* = 11 Hz, 1H), 4.51 (dd, *J* = 6, 9 Hz, 1H), 4.25 (m, 2H), 4.14 (m, 1H), 3.96 (m, 2H), 3.78 (s, 3H), 3.75 – 3.50 (m, 5H), 3.46 (d, *J* = 10 Hz, 1H), 3.28 (s, 3H), 3.26 (s, 3H), 3.21 (s, 3H), 3.29 (m, 2H), 3.16 (m, 1H), 2.94 (d, *J* = 15 Hz, 1H), 2.56 (m, 1H), 2.40 – 2.10 (m, 8H), 1.88 (d, *J* = 1 Hz, 3H), 2.00 – 1.20 (m, 13H), 1.18 (d, *J* = 1 Hz, 3H), 1.08 (s, 9H), 1.05 (s, 9H), 1.01 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.83 (d, *J* = 6 Hz,

3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 159.2, 143.1, 142.4, 138.0, 137.9, 137.4, 136.1, 136.0, 135.8, 135.7, 135.6, 135.6, 134.9, 134.2, 134.2, 134.1, 134.0, 134.0, 133.9, 131.6, 130.6, 129.8, 129.7, 129.6, 129.4, 129.4, 127.6, 127.6, 127.4, 127.2, 118.8, 118.8, 113.8, 110.1, 106.3, 99.9, 89.1, 83.3, 81.1, 73.5, 73.4, 72.5, 69.8, 69.3, 69.1, 68.9, 67.6, 65.9, 60.7, 56.2, 55.6, 55.3, 48.0, 39.7, 39.2, 38.5, 37.8, 36.7, 36.4, 35.5, 33.6, 33.3, 32.3, 32.0, 30.1, 29.7, 29.4, 27.1, 27.0, 26.9, 22.7, 19.4, 19.3, 19.2, 14.2, 14.2, 13.8, 13.0, 5.8; HRMS (ES) *m/z* 1849.8639 (calcd for $C_{108}H_{138}N_2O_{14}Si_3Br$: 1849.8582, M + H).

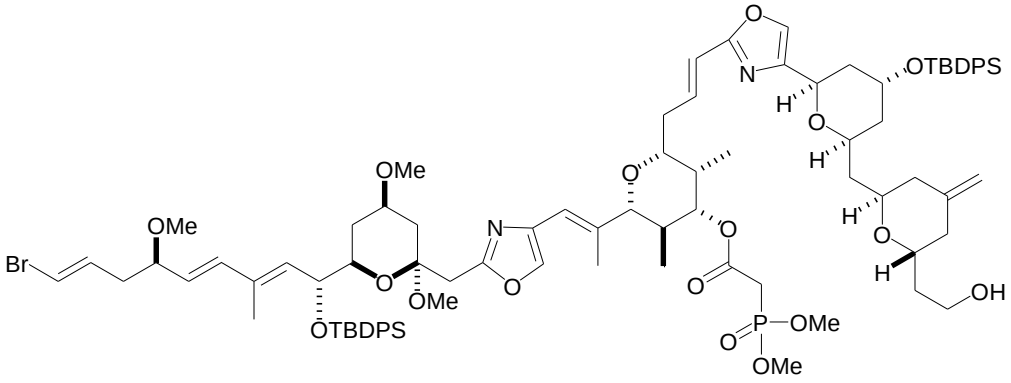


(2*R*,3*R*,4*S*,5*R*,6*R*)-2-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-6-((*E*)-3-(4-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(((2*R*,6*R*)-6-(2-(*tert*-butyldiphenylsilanyloxy)ethyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methyl)tetrahydro-2*H*-pyran-2-yl)oxazol-2-yl)allyl)-3,5-dimethyltetrahydro-2*H*-pyran-4-ol (114). 2,3-Dichloro-5,6-dicyanobenzoquinone (15.0 mg, 66 μmol) was added to a solution of **113** (24.7 mg, 13.3 μmol) in dichloromethane (5 mL) containing pH 7 buffer (0.5 mL) at room temperature and the mixture was stirred vigorously for 2 h. The reaction was quenched with saturated aqueous sodium bicarbonate (3 mL) and the mixture was diluted with dichloromethane and poured into a saturated aqueous sodium bicarbonate–brine solution (6 mL). The aqueous phase was separated and was extracted with dichloromethane (10 mL x 3), and the combined extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1 to 1:1)

to give **114** (19.5 mg, 84%) as a colourless oil: $[\alpha]_D^{23}$ -6.4 (c 0.32, $CHCl_3$); IR (neat) 3444, 2930, 2856, 1472, 1428, 1257, 1106, 1052, 822, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 1, 8 Hz, 2H), 7.66 – 7.59 (m, 10H), 7.51 (s, 1H), 7.42 – 7.26 (m, 19H), 6.59 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.32 (d, *J* = 16 Hz, 1H), 6.21 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.97 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.21 (dd, *J* = 8, 16 Hz, 1H), 4.97 (d, *J* = 13 Hz, 1H), 4.70 (s, 2H), 4.51 (dd, *J* = 7, 9 Hz, 1H), 4.25 (s, 1H), 4.15 (m, 1H), 3.95 (m, 2H), 3.71 – 3.43 (m, 8H), 3.32 – 3.18 (m, 2H), 3.28 (s, 3H), 3.26 (s, 3H), 3.21 (s, 3H), 2.94 (d, *J* = 15 Hz, 1H), 2.55 (m, 1H), 2.40 – 2.15 (m, 7H), 1.82 (d, *J* = 1 Hz, 3H), 2.02 – 1.20 (m, 14H), 1.18 (d, *J* = 1 Hz, 3H), 1.07 (s, 9H), 1.04 (s, 9H), 1.01 (s, 9H), 0.97 (d, *J* = 7 Hz, 3H), 0.84 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 159.2, 143.1, 142.4, 137.9, 137.8, 137.3, 136.1, 136.0, 135.8, 135.7, 135.6, 135.6, 134.9, 134.2, 134.1, 134.0, 134.0, 133.9, 133.9, 131.6, 129.7, 129.7, 129.5, 129.4, 127.6, 127.6, 127.4, 127.2, 118.7, 110.1, 106.3, 99.9, 88.8, 81.1, 77.2, 73.5, 72.5, 69.3, 69.1, 68.8, 67.6, 65.9, 60.7, 56.2, 55.6, 48.0, 39.7, 39.2, 39.2, 38.5, 37.9, 36.6, 36.1, 35.5, 34.6, 32.3, 29.7, 29.3, 27.1, 27.0, 26.9, 19.4, 19.3, 19.2, 14.3, 13.4, 13.0, 5.5; HRMS (MALDI) calcd for $C_{100}H_{129}N_2O_{13}Si_3{}^{79}BrNa$ (M + Na, $^{79}Br)^+$ 1751.7907, found 1751.7878.

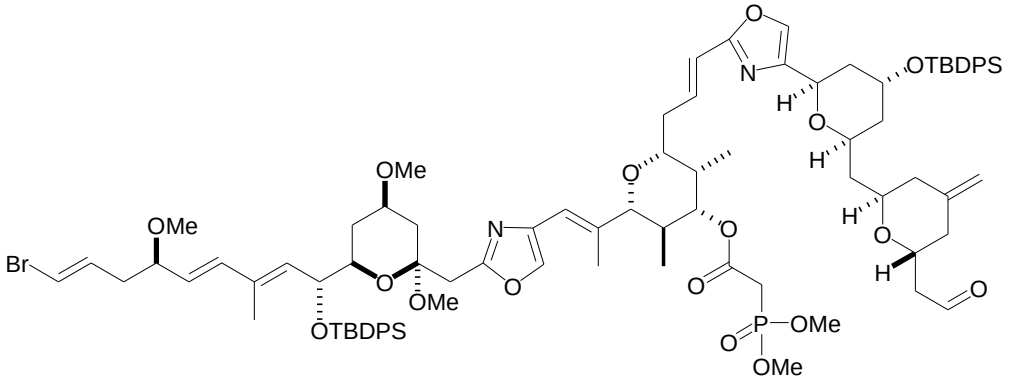


(2*R*,3*R*,4*S*,5*S*,6*R*)-2-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-6-((*E*)-3-(4-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(((2*R*,6*R*)-6-(2-(*tert*-butyldiphenylsilanyloxy)ethyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methyl)tetrahydro-2*H*-pyran-2-yl)oxazol-2-yl)allyl)-3,5-dimethyltetrahydro-2*H*-pyran-4-yl 2-(dimethoxyphosphoryl)acetate (116). To a solution of **114** (19.5 mg, 11.3 μmol) and dimethylphosphonoacetic acid (**115**, 6.8 mg, 40 μmol) in dichloromethane (4.5 mL) was added dicyclohexylcarbodiimide (6.5 mg, 32 μmol) and the mixture was stirred at room temperature for 20 h. The mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 2:1 to 1:1 to ethyl acetate only) to yield **116** (21.2 mg, 91%): $[\alpha]_D^{23}$ -9.7 (c 0.30, $CHCl_3$); IR (neat) 2922, 2856, 1734, 1463, 1428, 1361, 1264, 1105, 1035, 886, 822, 805, 755, 742, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 1, 8 Hz, 2H), 7.66 – 7.60 (m, 10H), 7.52 (s, 1H), 7.42 – 7.27 (m, 19H), 6.56 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.30 (d, *J* = 16 Hz, 1H), 6.22 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.97 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.21 (dd, *J* = 8, 16 Hz, 1H), 4.96 (d, *J* = 11 Hz, 1H), 4.75 (dd, *J* = 5, 11 Hz, 1H), 4.70 (d, *J* = 3 Hz, 2H), 4.51 (dd, *J* = 7, 9 Hz, 1H), 4.25 (s, 1H), 4.17 – 4.11 (m, 1H), 3.96 (m, 2H), 3.80 (d, *J* = 2 Hz, 3H), 3.77 (d, *J* = 2 Hz, 3H), 3.73 – 3.42 (m, 8H), 3.28 (s, 3H), 3.25 (s, 3H), 3.21 (s, 3H), 2.99 (d, *J* = 22 Hz, 2H), 2.94 (d, *J* = 16 Hz, 1H), 2.55 (m, 1H), 2.35 – 2.16 (m, 7H), 1.93 (d, *J* = 1 Hz, 3H), 2.11 – 1.20 (m, 14H), 1.18 (d, *J* = 1 Hz, 3H), 1.07 (s, 9H), 1.04 (s, 9H), 1.00 (s, 9H), 0.99 (d, *J* = 7 Hz, 3H), 0.76 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 165.2, 160.9, 159.4, 143.3, 142.6, 138.0, 137.5, 137.3, 136.5, 136.3, 136.2, 136.0, 135.9, 135.7, 135.7, 135.2, 135.0, 134.4, 134.3, 134.3, 134.1, 134.1, 134.0, 134.0, 131.8, 129.9, 129.9, 129.7, 129.6, 127.8, 127.8, 127.6, 127.4, 119.3, 119.1, 110.3, 106.4, 100.1, 88.9, 81.2, 80.4, 73.7, 73.7, 72.6, 69.5, 69.2, 69.0, 67.8, 66.0, 64.5, 60.8, 56.3, 55.8, 53.3, 53.3, 48.1, 39.8, 39.3, 39.3, 38.6, 38.0, 36.8, 36.2, 35.7, 35.5, 34.3, 34.1, 33.0, 32.4, 32.3, 27.2, 27.1, 27.0, 19.6, 19.5, 19.4, 14.4, 13.4, 13.2, 6.3; HRMS (MALDI) calcd for $C_{104}H_{136}N_2O_{17}PSi_3{}^{79}BrNa$ (M + Na, $^{79}Br)^+$ 1901.7976, found 1901.7960.



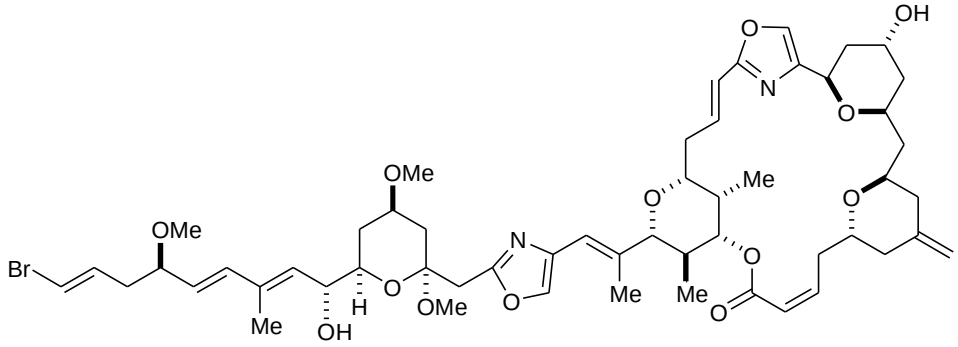
(2*R*,3*R*,4*S*,5*S*,6*R*)-2-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-6-((*E*)-3-(4-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(((2*R*,6*R*)-6-(2-hydroxyethyl)-4-methylenetetrahydro-2*H*-pyran-2-yl)methyl)tetrahydro-2*H*-pyran-2-yl)oxazol-2-yl)allyl)-3,5-dimethyltetrahydro-2*H*-pyran-4-yl 2-(dimethoxyphosphoryl)acetate (117). Ammonium fluoride (127 mg, 3.43 mmol) was added to a solution of **116** (18.9 mg, 10.0 μmol) in methanol (3 mL) and the solution was stirred at 50 ^{o}C for 5 h. The reaction was quenched with saturated ammonium chloride solution and the mixture was extracted with ethyl acetate (20 mL x 3). The extract was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:2 to ethyl acetate only) to give **117** (12.2 mg, 73%) as a colourless oil: $[\alpha]_D^{23}$ -11.9 (c 0.57, $CHCl_3$); IR (neat) 3456, 2927, 2855, 1734, 1463, 1428, 1362, 1270, 1105, 1035, 883, 805, 755, 703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 1, 8 Hz, 2H), 7.66 – 7.60 (m, 7H), 7.52 (s, 1H), 7.43 – 7.26 (m, 12H), 6.57 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.30 (d, *J* = 16 Hz, 1H), 6.22 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.96 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.21 (dd, *J* = 8, 16 Hz, 1H), 4.97 (d, *J* = 11 Hz, 1H), 4.77 – 4.69 (m, 3H), 4.51 (dd, *J* = 7, 9 Hz, 1H), 4.29 (s, 1H), 4.14 (m, 1H), 3.94 (m, 1H), 3.80 (d, *J* = 2 Hz, 3H), 3.77 (d, *J* = 2 Hz, 3H), 3.67 – 3.51 (m, 7H), 3.33 – 3.18 (m, 2H), 3.28 (s, 3H), 3.25 (s,

3H), 3.21 (s, 3H), 2.99 (d, *J* = 22 Hz, 2H), 2.94 (d, *J* = 16 Hz, 1H), 2.82 (brs, 1H), 2.53 (m, 1H), 2.38 – 2.16 (m, 7H), 1.93 (d, *J* = 1 Hz, 3H), 2.13 – 1.30 (m, 14H), 1.18 (d, *J* = 1 Hz, 3H), 1.08 (s, 9H), 1.04 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.76 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 161.0, 159.3, 142.6, 141.9, 137.8, 137.3, 137.2, 136.3, 136.1, 136.0, 135.8, 135.8, 135.4, 134.9, 134.4, 134.2, 133.9, 133.9, 131.6, 129.8, 129.8, 129.6, 129.4, 127.7, 127.7, 127.4, 127.2, 119.1, 118.7, 110.4, 106.3, 99.9, 88.7, 81.1, 80.2, 77.0, 73.5, 73.5, 72.5, 70.5, 70.0, 69.8, 67.3, 65.9, 60.2, 56.2, 55.6, 53.2, 53.1, 48.0, 40.0, 39.2, 39.2, 38.7, 37.5, 36.2, 36.0, 35.5, 35.4, 34.2, 32.9, 32.2, 32.2, 27.1, 27.0, 19.4, 19.4, 14.3, 13.2, 13.0, 6.1; HRMS (MALDI) calcd for $C_{88}H_{118}N_2O_{17}PSi_2{}^{79}BrNa$ (M + Na, ^{79}Br)$^+$ 1663.6769, found 1663.6782.

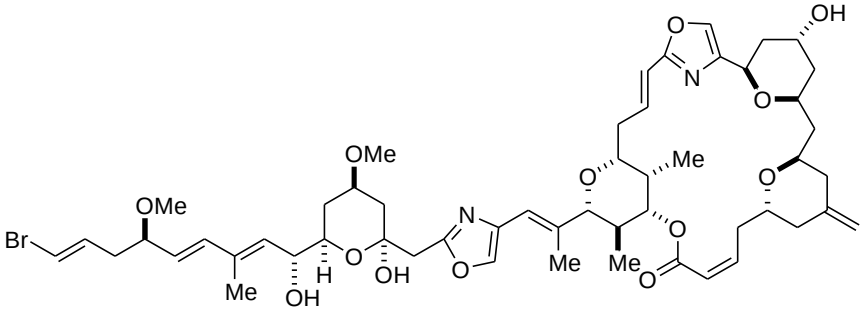


(2*R*,3*R*,4*S*,5*S*,6*R*)-2-((*E*)-1-(2-(((2*S*,4*R*,6*R*)-6-((1*R*,2*E*,4*E*,6*R*,8*E*)-9-Bromo-1-(*tert*-butyldiphenylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl)-2,4-dimethoxytetrahydro-2*H*-pyran-2-yl)methyl)oxazol-4-yl)prop-1-en-2-yl)-6-((*E*)-3-(4-((2*R*,4*R*,6*R*)-4-(*tert*-butyldiphenylsilanyloxy)-6-(((2*R*,6*R*)-4-methylene-6-(2-oxoethyl)tetrahydro-2*H*-pyran-2-yl)methyl)tetrahydro-2*H*-pyran-2-yl)oxazol-2-yl)allyl)-3,5-dimethyltetrahydro-2*H*-pyran-4-yl 2-(dimethoxyphosphoryl)acetate (118). To a solution of **117** (12.2 mg, 7.4 μmol) in dichloromethane (4 mL) at 0 °C was added Dess-Martin periodinane (12.3 mg, 29 μmol) and the solution was allowed to warm to room temperature and was stirred for 1 h. The mixture was poured into an ice-cold solution of

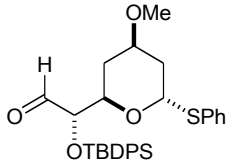
saturated sodium bicarbonate (1 mL) containing sodium thiosulfate (0.5 g) and was extracted with ethyl acetate (2 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:2) to give **118** (11.6 mg, 95%) as a colourless oil: $[\alpha]_D^{23}$ -12.1 (c 0.43, $CHCl_3$); IR (neat) 2955, 2929, 2856, 1732, 1463, 1428, 1266, 1104, 1035, 755, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (t, *J* = 2 Hz, 1H), 7.72 (dd, *J* = 1, 8 Hz, 2H), 7.65 – 7.59 (m, 7H), 7.52 (s, 1H), 7.42 – 7.26 (m, 12H), 6.57 (ddd, *J* = 6, 8, 16 Hz, 1H), 6.30 (d, *J* = 16 Hz, 1H), 6.22 (s, 1H), 6.13 (dd, *J* = 7, 14 Hz, 1H), 6.05 (d, *J* = 14 Hz, 1H), 5.96 (d, *J* = 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.20 (dd, *J* = 8, 16 Hz, 1H), 4.98 (d, *J* = 11 Hz, 1H), 4.77 – 4.73 (m, 3H), 4.50 (dd, *J* = 6, 9 Hz, 1H), 4.32 – 4.26 (bs, 2H), 4.15 (m, 1H), 3.97 (m, 1H), 3.80 (d, *J* = 2 Hz, 3H), 3.77 (d, *J* = 2 Hz, 3H), 3.63 – 3.49 (m, 5H), 3.28 (m, 1H), 3.27 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 2.99 (d, *J* = 22 Hz, 2H), 2.94 (d, *J* = 16 Hz, 1H), 2.58 – 2. 16 (m, 10H), 1.93 (d, *J* = 1 Hz, 3H), 2.14 – 1.20 (m, 12H), 1.18 (d, *J* = 1 Hz, 3H), 1.07 (s, 9H), 1.04 (s, 9H), 0.98 (d, *J* = 7 Hz, 3H), 0.76 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 165.0, 160.8, 159.2, 142.8, 141.4, 140.9, 137.8, 137.3, 137.1, 136.3, 136.0, 136.0, 135.7, 135.7, 135.2, 134.8, 134.3, 134.1, 133.8, 133.8, 131.6, 129.7, 129.7, 129.5, 129.4, 127.6, 127.6, 127.4, 127.2, 119.1, 118.8, 111.2, 106.2, 99.8, 88.7, 81.0, 80.2, 77.0, 73.5, 72.4, 69.7, 69.3, 67.4, 67.0, 65.8, 60.4, 56.1, 55.6, 53.1, 53.1, 47.9, 39.7, 39.1, 39.1, 38.9, 38.7, 38.3, 37.7, 36.0, 35.5, 35.3, 34.2, 32.8, 32.2, 32.2, 27.0, 26.9, 19.3, 19.3, 14.2, 14.2, 13.2, 13.0, 6.1; HRMS (MALDI) calcd for $C_{88}H_{116}N_2O_{17}PSi_2{}^{79}BrNa$ (M + Na, $^{79}Br)^+$ 1661.6620, found 1661.6626.



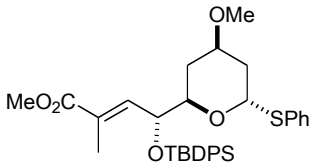
33-*O*-Methylphorboxazole A (120). To a solution of **119** (5.6 mg, 3.7 μmol) in tetrahydrofuran (0.6 mL) at 0 °C was added tetra-*n*-butylammonium fluoride (1M solution in tetrahydrofuran, 74 μL, 74 μmol) and the solution was stirred at room temperature for 20 h. The mixture was filtered through a short pad of silica gel, using ethyl acetate-methanol (15:1) as eluent, and the filtrate was concentrated under vacuum. The crude residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:1 to 1:3 to ethyl acetate only) to afford pure **120** (1.9 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.40 (s, 1H), 6.67 (ddd, *J* = 6, 10, 16 Hz, 1H), 6.30 – 6.13 (m, 4H), 6.07 (d, *J* = 14 Hz, 1H), 5.91 (m, 2H), 5.49 (m, 2H), 4.97 (s, 1H), 4.73 (dd, *J* = 4, 10 Hz, 1H), 4.60 (s, 1H), 4.50 (dd, *J* = 4, 11 Hz, 1H), 4.38 (m, 2H), 4.17 – 3.94 (m, 3H), 3.65 – 3.41 (m, 8H), 3.32 (s, 3H), 3.29 (s, 3H), 3.26 (m, 1H), 3.23 (s, 3H), 3.09 (d, *J* = 15 Hz, 1H), 2.69 (d, *J* = 12 Hz, 1H), 2.46 – 0.80 (m, 20H), 1.83 (d, *J* = 1 Hz, 3H), 1.17 (d, *J* = 1 Hz, 3H), 0.95 (d, *J* = 7 Hz, 3H), 0.76 (d, *J* = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 161.4, 159.0, 144.4, 142.1, 141.7, 137.9, 137.4, 137.3, 137.2, 136.3, 134.2, 133.8, 130.0, 129.0, 121.0, 119.3, 110.2, 106.4, 100.1, 89.2, 81.1, 79.4, 78.0, 73.5, 73.1, 72.9, 71.1, 69.1, 68.6, 66.9, 64.5, 56.3, 55.7, 52.9, 48.2, 41.3, 39.2, 39.2, 39.0, 39.0, 37.0, 35.6, 35.0, 34.4, 32.9, 32.6, 31.8, 30.5, 21.2, 14.3, 13.5, 13.3; HRMS (MALDI) calcd for $C_{54}H_{73}N_2O_{13}{}^{79}BrK$ (M + K, ^{79}Br)$^+$ 1075.3903, found 1075.3928.



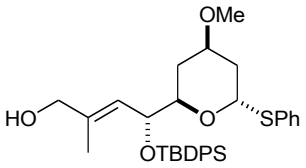
Phorboxazole A (1). To a solution of **120** (1.9 mg, 1.8 μmol) in tetrahydrofuran (1 mL) at 0 ^{o}C was added dropwise hydrochloric acid (6%, 0.4 mL), and after 10 min the mixture was warmed to room temperature and was stirred for 4 d. The mixture was cooled to 0°C, treated dropwise with saturated sodium bicarbonate solution (1 mL) and was extracted with ether (1 mL x 3). The combined extract was dried (Na2SO4), filtered and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane:ethyl acetate 1:3 to ethyl acetate only, then methanol:dichlorormethane 1:19) to give **1** (0.7 mg, 37%) as an off-white solid: $[\alpha]_D^{23}$ +43.7 (c 0.12 MeOH), lit[1] $[\alpha]_D$ +44.8 (c 1.0 MeOH); ^{1}H NMR (400 MHz, CDCl3) δ 7.55 (s, 1H), 7.40 (s, 1H), 6.67 (ddd, *J* = 6, 10, 16 Hz, 1H), 6.29 – 6.14 (m, 4H), 6.08 (d, *J* = 14 Hz, 1H), 5.91 (m, 2H), 5.47 (dd, *J* = 8, 16 Hz, 1H), 5.34 (d, *J* = 9 Hz, 1H), 5.27 (d, *J* = 2 Hz, 1H), 4.97 (s, 1H), 4.72 (dd, *J* = 4, 10 Hz, 1H), 4.60 (s, 1H), 4.50 (dd, *J* = 4, 11 Hz, 1H), 4.38 (s, 1H), 4.30 (t, *J* = 8 Hz, 1H), 4.17 – 3.95 (m, 3H), 3.81 – 3.70 (m, 2H), 3.65 – 3.42 (m, 4H), 3.34 (s, 3H), 3.22 (s, 3H), 3.14 (d, *J* = 16 Hz, 1H), 3.06 (d, *J* = 16 Hz, 1H), 2.69 (d, *J* = 12 Hz, 1H), 2.55 – 2.20 (m, 9H), 2.08 – 1.78 (m, 8H), 1.96 (d, *J* = 1 Hz, 3H), 1.79 (d, *J* = 1 Hz, 3H), 1.74 – 1.57 (m, 2H), 1.47 – 1.11 (m, 3H), 0.95 (d, *J* = 7 Hz, 3H), 0.75 (d, *J* = 6 Hz, 3H); ^{13}C NMR (150 MHz, CDCl3) δ 165.7, 161.4, 160.1, 144.5, 142.0, 141.7, 138.0, 137.7, 137.5, 137.4, 136.0, 134.2, 133.8, 133.8, 129.7, 128.8, 121.0, 119.3, 118.5, 110.2, 106.4, 96.7, 89.2, 81.1, 79.3, 78.0, 73.5, 73.0, 72.5, 71.0, 69.1, 68.6, 66.9, 64.4, 56.3, 55.8, 41.3, 40.5, 39.7, 39.3, 39.0, 39., 94220, 37.0, 35.0, 34.4, 33.1, 32.6, 31.7, 30.5, 14.2, 13.5, 13.4, 6.0; HRMS (MALDI) calcd for $C_{53}H_{71}N_2O_{13}{}^{79}BrNa$ (M + Na, ^{79}Br)$^{+}$ 1045.3984, found 1045.4032.



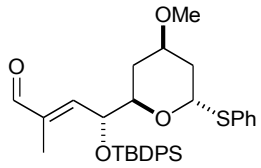
(*S*)-2-(*tert*-Butyldiphenylsilanyloxy)-2-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2H-pyran-2-yl)acetaldehyde. A solution of dimethyl sulfoxide (92 μL, 1.3 mmol) in dichloromethane (5 mL) at –78 °C was treated with oxalyl chloride (57 μL, 0.65 mmol) and after 15 min a solution of **34α** (113 mg, 0.216 mmol) in dichloromethane (4 mL) was added. After a further 15 min, triethylamine (181 μL, 1.30 mmol) was added and the solution was warmed to –10 °C for 1 h, then warmed to room temperature for 0.5 h. The solution was poured into a mixture of ether (10 mL) and saturated ammonium chloride solution (10 mL) and the aqueous layer was separated and extracted with ether (10 mL x 2). The combined extract was washed with saturated sodium bicarbonate solution (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 15 : 1) to give the title compound (110 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ –164.9 (c 0.93, $CHCl_3$); IR (neat) 3071, 3048, 2956, 2930, 2890, 2857, 2824, 1736, 1585, 1472, 1427, 1375, 1233, 1113, 1063, 1006, 923, 851, 741, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.47 (d, *J* = 1 Hz, 1H), 7.66 – 7.61 (m, 5H), 7.41 – 7.21 (m, 10H), 5.68 (d, *J* = 5 Hz, 1H), 4.50 (dt, *J* = 12, 3 Hz, 1H), 4.09 (dd, *J* = 1, 3 Hz, 1H), 3.62 – 3.52 (m, 1H), 3.30 (s, 3H), 2.37 – 2.31 (m, 1H), 1.91 – 1.78 (m, 2H), 1.15 – 1.05 (m, 1H), 1.12 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 136.3, 134.9, 133.2, 133.1, 132.1, 130.5, 129.3, 128.2, 128.2, 127.6, 85.6, 79.8, 77.6, 73.0, 70.8, 55.8, 37.4, 33.5, 27.4, 19.9; MS (CI) *m/z* 411 $(M\text{-}SPh)^+$ 379, 351, 301, 257, 199, 179, 111, 79; HRMS (CI) *m/z* 411.1988 (calcd for $C_{24}H_{31}O_4Si$: 411.1992, M-SPh).



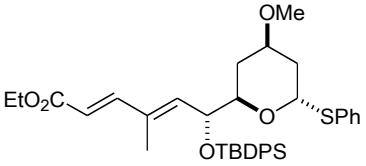
(*R*,*E*)-Methyl 4-(*tert*-butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-2-methylbut-226-enoate. To a solution of the aldehyde obtained above (110 mg, 0.211 mmol) in toluene (11 mL) was added **23** (226 mg, 0.649 mmol) and the solution was heated at 100 ^{o}C for 12 h under argon. The solution was concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 12:1) to give the title compound (117 mg, 92%) as a colourless oil: $[\alpha]_D^{23}$ –151.0 (c 0.98, $CHCl_3$); IR (neat) 3070, 3045, 2950, 2930, 2886, 2857, 1717, 1653, 1472, 1428, 1361, 1240, 1192, 1112, 1057, 998, 949, 909, 822, 741, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 – 7.58 (m, 5H), 7.40 – 7.28 (m, 10H), 6.64 (dd, *J* = 1, 9 Hz, 1H), 5.66 (d, *J* = 5 Hz, 1H), 4.47 (dd, *J* = 5, 9 Hz, 1H), 4.28 (ddd, *J* = 2, 5, 12 Hz, 1H), 3.67 (s, 3H), 3.64 – 3.54 (m, 1H), 3.36 (s, 3H), 2.38 – 2.30 (m, 1H), 2.16 – 2.08 (m, 1H), 1.84 (ddd, *J* = 6, 12, 13 Hz, 1H), 1.31 (d, *J* = 1 Hz, 3H), 1.39 – 1.22 (m, 1H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 140.4, 136.4, 136.3, 135.5, 133.9, 131.8, 130.2, 130.1, 129.2, 129.1, 128.0, 127.8, 127.3, 85.3, 77.6, 73.5, 72.2, 72.0, 55.9, 52.6, 52.1, 37.5, 33.0, 27.4, 19.7, 16.0, 13.1; MS (CI) *m/z* 591 $(M + H)^+$ 481, 449, 411, 371, 335, 303, 239, 199, 179, 111, 79; HRMS (CI) *m/z* 591.2603 (calcd for $C_{34}H_{43}O_5SiS$: 591.2600, $M^+ + H$).



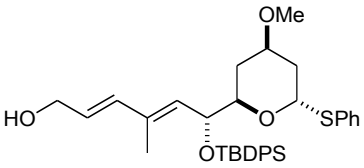
(*R*,*E*)-4-(*tert*-Butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-2-methylbut-2-en-1-ol. To a solution of the ester obtained above (37 mg, 63 μmol) in toluene (2 mL) at -78 °C was added diisobutylaluminium hydride (45 μL, 0.25 mmol) and the solution was stirred for 1 h at –78 °C. Saturated Rochelle salt solution (5 mL) and ethyl acetate (10 mL) were added, and the mixture was allowed to warm to room temperature and was stirred for 2 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 5:1) to yield the title compound (32 mg, 91%) as a colourless oil: $[\alpha]_D^{23}$ -156.4 (c 1.66, $CHCl_3$); IR (neat) 3441, 3070, 3049, 2953, 2929, 2890, 2856, 2821, 1472, 1427, 1361, 1158, 1111, 1056, 949, 822, 740, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 – 7.58 (m, 5H), 7.40 – 7.28 (m, 10H), 5.76 (d, *J* = 5 Hz, 1H), 5.31 (dd, *J* = 1, 9 Hz, 1H), 4.49 (dd, *J* = 5, 9 Hz, 1H), 4.28 – 4.22 (m, 1H), 3.67 – 3.57 (m, 3H), 3.36 (s, 3H), 2.41 – 2.34 (m, 1H), 2.11 – 2.05 (m, 1H), 1.84 (ddd, *J* = 6, 12, 13 Hz, 1H), 1.09 (d, *J* = 1 Hz, 3H), 1.39 – 1.15 (m, 1H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 136.5, 136.3, 135.6, 135.1, 134.4, 131.4, 130.0, 129.9, 129.1, 127.9, 127.7, 127.1, 125.2, 85.2, 73.7, 72.7, 72.1, 68.5, 55.9, 37.5, 33.5, 30.1, 27.4, 19.8, 14.2; MS (CI) *m/z* 453 $(M - SPh)^+$ 421, 375, 343, 275, 239, 199, 179, 111, 79; HRMS (CI) *m/z* 453.2454 (calcd for $C_{27}H_{37}O_4Si$: 453.2461, M^+ - SPh).



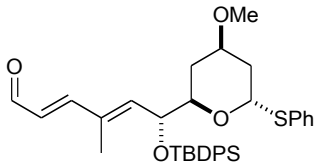
(*R*,*E*)-4-(*tert*-Butyldiphenylsilanyloxy)-4-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-2-methylbut-2-enal. A solution of dimethyl sulfoxide (25 μL, 0.35 mmol) in dichloromethane (2 mL) at –78 °C was treated with oxalyl chloride (15 μL, 0.17 mmol) and after 15 min a solution of the alcohol obtained above (32 mg, 57 μmol) in dichloromethane (2 mL) was added. After a further 15 min, triethylamine (49 μL, 0.35 mmol) was added and the solution was warmed to –10 °C for 1 h, then warmed to room temperature for 0.5 h. The solution was poured into a mixture of ether (5 mL) and saturated ammonium chloride solution (5 mL) and the the aqueous layer was separated and extracted with ether (5 mL x 3). The combined extract was washed with saturated sodium bicarbonate solution (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 10:1) to furnish the title compound (27.8 mg, 87%) as a colourless oil: $[\alpha]_D^{23}$ –133.7 (c 0.22, $CHCl_3$); IR (neat) 3073, 2958, 2928, 2856, 1695, 1470, 1387, 1112, 1005, 949, 908, 822, 804, 741, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.65 – 7.57 (m, 4H), 7.40 – 7.29 (m, 11H), 6.25 (dd, *J* = 1, 9 Hz, 1H), 5.70 (d, *J* = 5 Hz, 1H), 4.62 (dd, *J* = 4, 9 Hz, 1H), 4.30 (ddd, *J* = 2, 4, 12 Hz, 1H), 3.69 – 3.58 (m, 1H), 3.36 (s, 3H), 2.39 – 2.33 (m, 1H), 2.16 – 2.08 (m, 1H), 1.82 (ddd, *J* = 6, 11, 17 Hz, 1H), 1.46 (d, *J* = 12 Hz, 0.5H), 1.39 (d, *J* = 12 Hz, 0.5H), 1.23 (d, *J* = 1 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.1, 151.7, 139.4, 136.3, 135.1, 133.8, 133.5, 131.9, 130.5, 129.2, 128.2, 128.1, 127.6, 84.9, 73.4, 72.1, 71.9, 55.9, 37.2, 33.3, 27.5, 19.8, 9.8; MS (CI) *m/z* 561 $(M + H)^+$ 529, 451, 419, 373, 341, 305, 273, 239, 195, 163, 111, 75; HRMS (CI) *m/z* 561.2502 (calcd for $C_{33}H_{41}O_4SiS$: 561.2495, M^+ + H).



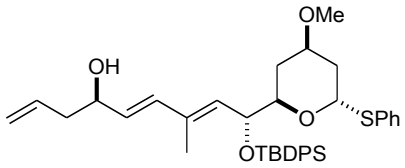
(*R*,2*E*,4*E*)-Ethyl 6-(*tert*-Butyldiphenylsilanyloxy)-6-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-4-methylhexa-2,4-dienoate. To a slurry of hexane-washed sodium hydride (6.8 mg, 0.17 mmol) in tetrahydrofuran (1.5 mL) at 0 ^{o}C was added **27** (34 μL, 0.17 mmol) and the mixture was stirred for 30 min at 0 ^{o}C. A solution of the aldehyde obtained above (31.8 mg, 57 μmol) in tetrahydrofuran (2 mL) was added and the solution was allowed to warm to room temperature and was stirred for 1 h. The reaction was quenched by adding water (1 mL) and the mixture was extracted with ether (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1) to yield the title compound (29.7 mg, 83%) as a colourless oil: $[\alpha]_D^{23}$ -161.0 (c 0.28 , $CHCl_3$); IR (neat) 3071, 3048, 2953, 2928, 2856, 2824, 1716, 1623, 1472, 1363, 1306, 1270, 1203, 1173, 1111, 1055, 823, 740, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.67 (m, 4H), 7.43 – 7.30 (m, 11H), 7.15 (d, *J* = 16 Hz, 1H), 5.85 (d, *J* = 9 Hz, 1H), 5.71 (d, *J* = 16 Hz, 1H), 5.70 (d, *J* = 6 Hz, 1H), 4.54 (dd, *J* = 5, 9 Hz, 1H), 4.32 – 4.22 (m, 3H), 3.68 – 3.58 (m, 1H), 3.38 (s, 3H), 2.41 – 2.35 (m, 1H), 2.14 – 2.08 (m, 1H), 1.84 (ddd, *J* = 6, 12, 18 Hz, 1H), 1.35 (t, *J* = 7 Hz, 3H), 1.40 – 1.20 (m, 1H), 1.25 (d, *J* = 1 Hz, 3H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 149.1, 139.8, 136.4, 136.3, 135.4, 134.4, 134.0, 132.2, 130.2, 129.2, 128.0, 127.9, 127.5, 118.0, 85.5, 73.5, 72.5, 72.1, 60.7, 55.8, 37.5, 33.3, 27.5, 19.8, 14.8, 12.9; MS (CI) *m/z* 630 (M^+), 553, 521, 489, 443, 411, 375, 343, 297, 265, 233, 179, 139, 111, 75; HRMS (CI) *m/z* 630.2823 (calcd for $C_{37}H_{46}O_5SiS$: 630.2835, M^+).



(*R*,2*E*,4*E*)-6-(*tert*-Butyldiphenylsilanyloxy)-6-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-4-methylhexa-2,4-dien-1-ol. To a solution of the ester obtained above (29.7 mg, 0.0947 mmol) in toluene (2 mL) at -78 °C was added diisobutylaluminium hydride (0.07 mL, 0.393 mmol) and the solution was stirred for 1 h at –78 °C. Saturated Rochelle salt solution (1 mL) and ethyl acetate (2 mL) were added, and the mixture was allowed to warm to room temperature and was stirred stirred for 2 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (5 mL x 3). The combined extract was washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 4:1) to give the title compound (27 mg, 99%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.60 (m, 4H), 7.40 – 7.15 (m, 11H), 6.09 (d, *J* = 16 Hz, 1H), 5.68 – 5.58 (m, 2H), 5.48 (d, *J* = 9 Hz, 1H), 4.51 (dd, *J* = 5, 9 Hz, 1H), 4.28 – 4.14 (m, 3H), 3.65 – 3.53 (m, 1H), 3.35 (s, 3H), 2.39 – 2.31 (m, 1H), 2.12 – 2.06 (m, 1H), 1.80 (ddd, *J* = 6, 11, 17 Hz, 1H), 1.40 – 1.20 (m, 1H), 1.21 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H), 0.90 (d, *J* = 7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 136.3, 136.1, 135.7, 135.2, 134.4, 132.0, 131.8, 130.0, 129.9, 129.2, 127.9, 127.8, 127.3, 85.6, 73.7, 72.7, 72.2, 64.1, 55.8, 37.6, 33.2, 27.5, 19.8, 13.2; MS (ES) *m/z* 606 $(M + NH_4)^+$ 520, 476, 432, 388, 344, 300, 239, 195; HRMS (ES) *m/z* 606.3052 (calcd for $C_{35}H_{48}NO_4SiS$: 606.3073, $M + NH_4^+$).



(*R*,2*E*,4*E*)-6-(*tert*-Butyldiphenylsilanyloxy)-6-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-4-methylhexa-2,4-dienal. A solution of dimethyl sulfoxide (20 μL, 0.29 mmol) in dichloromethane (2 mL) at –78 °C was treated with oxalyl chloride (13 μL, 0.14 μmol) and after 15 min a solution of the alcohol obtained above (27 mg, 46 μmol) in dichloromethane (2 mL) was added. After a further 15 min, triethylamine (40 μL, 0.29 mmol) was added and the solution was warmed to –10 °C for 1 h, then was warmed to room temperature for 0.5 h. The solution was poured into a mixture of ether (5 mL) and saturated ammonium chloride solution (5 mL) and the aqueous layer was extracted with ether (5 mL x 3). The combined extract was washed with saturated sodium bicarbonate solution (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel (hexane:ethyl acetate 10:1) to give the title compound (24.7 mg, 90%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (d, *J* = 8 Hz, 1H), 7.70 – 7.60 (m, 4H), 7.40 – 7.15 (m, 11H), 6.83 (d, *J* = 16 Hz, 1H), 5.94 (dd, *J* = 8, 16 Hz, 1H), 5.87 (d, *J* = 9 Hz, 1H), 5.69 (d, *J* = 6 Hz, 1H), 4.53 (dd, *J* = 5, 9 Hz, 1H), 4.34 – 4.22 (m, 1H), 3.67 – 3.56 (m, 1H), 3.36 (s, 3H), 2.39 – 2.32 (m, 1H), 2.16 – 2.08 (m, 1H), 1.81 (ddd, *J* = 6, 11, 17 Hz, 1H), 1.40 – 1.20 (m, 1H), 1.24 (d, *J* = 1 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.3, 157.2, 141.9, 136.3, 136.3, 135.4, 134.7, 134.0, 133.8, 131.8, 130.3, 130.2, 129.2, 128.6, 128.1, 127.9, 127.4, 85.1, 73.5, 72.4, 71.9, 55.9, 37.3, 33.2, 27.4, 19.8, 13.0; MS (CI) *m/z* 587 $(M+H)^+$ 477, 445, 367, 331, 239, 179, 139, 111, 79; HRMS (CI) *m/z* 587.2636 (calcd for $C_{35}H_{43}O_4SSi$: 587.2651, M+H).



(4*R*,5*E*,7*E*,9*R*)-9-(*tert*-Butyldiphenylsilanyloxy)-9-((2*R*,4*R*,6*S*)-4-methoxy-6-(phenylthio)tetrahydro-2*H*-pyran-2-yl)-7-methylnona-1,5,7-trien-4-ol. To a solution of (+)-*B*-methoxydiisopinocampheylborane (65 mg, 0.205 mmol) in ether (1.5 mL) at 0 ^{o}C was added allylmagnesium bromide (0.175 mL, 0.175 mmol, 1.0M solution in ether) *via* syringe and the solution was allowed to warm to room temperature. After 1 h, the solution was cooled to –78 ^{o}C and a solution of the aldehyde obtained above (24.7 mg, 42 μmol) in ether (1 mL) was added slowly. After 3 h, 30% hydrogen peroxide (0.4 mL) and saturated sodium bicarbonate (0.8 mL) were added and the mixture was stirred for 10 h. The mixture was diluted with water (1 mL), the layers were separated and the aqueous layer was extracted with ether (5 mL x 3). The combined extract was dried (Na_2SO_4) and concentrated under reduced pressure and the residual oil was purified by flash chromatography on silica gel (hexane:ethyl acetate 9:1) to give the title compound (21 mg, 79%) as a colourless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.60 (m, 4H), 7.40 – 7.15 (m, 11H), 6.03 (d, *J* = 16 Hz, 1H), 5.88 – 5.74 (m, 1H), 5.68 (d, *J* = 5 Hz, 1H), 5.50 – 5.43 (m, 2H), 5.21 – 5.12 (m, 2H), 4.51 (dd, *J* = 5, 9 Hz, 1H), 4.30 – 4.15 (m, 2H), 3.66 – 3.53 (m, 1H), 3.35 (s, 3H), 2.40 – 2.23 (m, 3H), 2.13 – 2.04 (m, 1H), 1.81 (ddd, *J* = 6, 12, 17 Hz, 1H), 1.40 – 1.20 (m, 1H), 1.18 (d, *J* = 1 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 136.4, 135.8, 135.4, 135.2, 134.7, 134.4, 134.3, 132.0, 131.8, 130.8, 130.0, 129.8, 129.2, 127.9, 127.7, 127.2, 118.6, 85.6, 73.7, 72.7, 72.3, 72.2, 55.9, 42.5, 37.6, 33.3, 27.5, 19.8, 13.2; MS (CI) *m/z* 519 (M – SPh)$^{+}$ 469, 445, 409, 239, 179, 111; HRMS (CI) *m/z* 519.2920 (calcd for C_{32} $H_{43}O_4Si$: 519.2931, M – SPh).