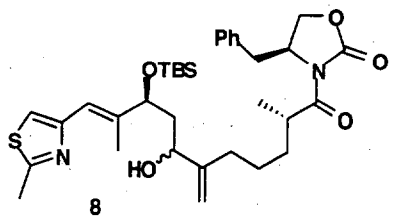
Supporting Information for

The Total Synthesis of Epothilone B and D.

Richard E. Taylor* and Chen Yue

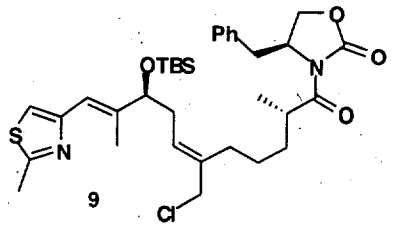
Department of Chemistry
University of Notre Dame
251 Nieuwland Science Hall
Notre Dame, IN 46556-5670



8

Allylic alcohol 8

To a suspension of $CrCl_2$ (3.86 g, 31.41 mmol) and $NiCl_2$ (204 mg, 1.57 mmol) in DMF (15 mL) was added the solution of the aldehyde **2** (2.55 g, 7.85 mmol) and vinyl iodide **4** (5.60 g, 13.1 mmol) in DMF (40 mL) under an atmosphere of nitrogen. The reaction mixture was stirred at room temperature for 40 min, diluted by Et_2O (300 mL) and quenched by H_2O (50 mL), then filtered through a bed of celite. The aqueous layer was extracted with Et_2O (3 × 50 mL), the combined organic layers were dried by anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography to obtain **8** (4.57 g, 93%) as a diastereomeric mixture (1:1). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.19 (m, 5H), 6.94, 6.91 (s, 1H), 6.54, 6.49 (s, 1H), 5.10, 5.09 (s, 1H), 4.84, 4.83 (s, 1H), 4.68-4.63 (m, 1H), 4.43 (m, 1H), 4.27-4.13 (m, 3H), 3.73-3.68 (m, 1H), 3.24 (dd, *J* = 13.0 Hz, 3.0 Hz, 1H), 2.76 (dd, *J* = 14.0 Hz, 9.0 Hz, 1H), 2.69 (s, 3H), 2.02, 2.01 (s, 3H), 2.09-1.95 (m, 2H), 1.90-1.67 (m, 3H), 1.52-1.40 (m, 3H), 1.21, 1.20 (d, *J* = 4.0 Hz, 3H), 0.92, 0.91 (s, 9H), 0.13, 0.10(s, 3H), 0.04, 0.03 (s, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz), δ 177.3,164.6, 164.6, 153.3, 153.2, 152.9, 151.6, 151.1, 141.8, 141.6,135.5, 129.6, 129.1, 127.5, 119.8, 118.9, 115.8, 115.6, 109.5, 109.4, 79.9, 76.1, 74.3, 71.8, 66.2, 55.5, 42.5, 41.7, 38.1, 37.8, 33.3, 33.2, 32.0, 31.8, 26.1, 26.0, 25.7, 25.6, 19.4, 19.3, 18.3, 18.2, 17.6, 17.5, 15.0, 13.9, -4.2, -4.4, -4.9, -5.1. IR (cm^{-1}) 3518, 2949, 2928, 2852, 1781, 1697, 1458, 1386, 1348, 1243, 1210, 1073. 836, 776. FAB HRMS *m/e* 627.3287, M + H^+ calcd for $C_{34}H_{50}N_2O_5SSi$ 627.3288.

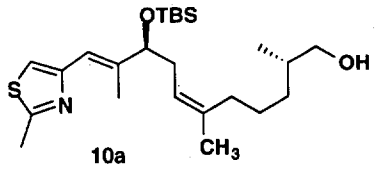


9

Chloride 9

At –78°C, to the solution of **8** (3.91 g, 6.23 mmol) in Et_2O/pentane (1 : 3, 300 mL) was added, the precooled solution of $SOCl_2$ (2.28 mL, 31.17 mmol) in Et_2O/pentane (1 : 3, 100 mL) in 1 min. The reaction mixture was kept at the same temperature for 2h, then warmed up to 0°C over 4.5 h. Et_3N (17.3 mL, 124.7 mmol) was added at –78°C, followed by saturated $NaHCO_3$ (150 mL). The organic

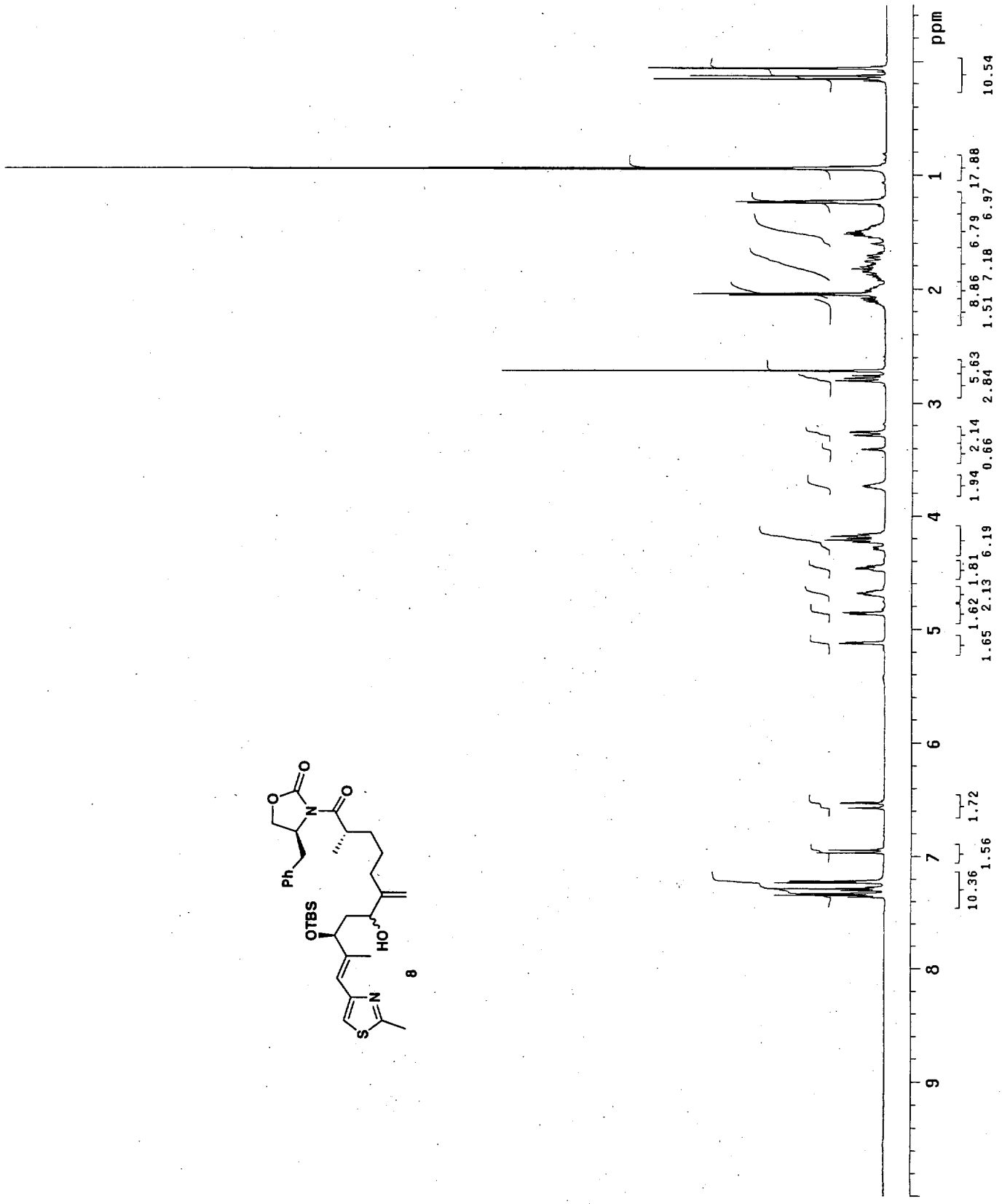
layer was separated and the aqueous layer was extracted by ethyl ether (2 × 200mL). The combined organic phase was washed by sat. NH_4Cl (2 × 100mL), dried by anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography to obtain 3.50 g (5.43 mmol, 87%) of **9** as colorless oil. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.23 (m, 5H), 6.93 (s, 1H), 6.46 (s, 1H), 5.58 (t, *J* = 7.0 Hz, H), 4.67 (m, 1H), 4.22-4.11 (m, 3H), 4.03 (d, J = 3.0 Hz, 2H), 3.71 (m, 1H), 3.24 (dd, *J* = 13.2 Hz, 3.0 Hz, 1H), 2.76 (dd, *J* = 13.2 Hz, 9.6 Hz, 1H), 2.69 (s, 3H), 2.38-2.26 (m, 2H), 2.22-2.15 (m, 2H), 2.00, (s, 3H), 1.80-1.66 (m, 2H), 1.48-1.39 (m, 2H), 1.21 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.00 (s, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz), δ 177.1,164.5, 153.3,153.2,142.1,136.8, 135.5, 129.7, 129.1, 128.6,127.5, 119.2,115.5, 78.4, 66.2, 55.5, 50.5, 38.1, 37.8, 35.5, 33.4, 28.2, 26.0, 25.8, 19.4,18.4, 17.7, 14.2, -4.5, -4.8. IR (cm^{-1}) 3029, 2933, 2929, 2856, 1781, 1698, 1499, 1471, 1455,1385, 1349, 1248, 1211, 1075. 837 776, 759. FAB HRMS *m/e* 645.2972, M + H^+ calcd for $C_{34}H_{50}ClN_2O_4SSi$ 645.2949.

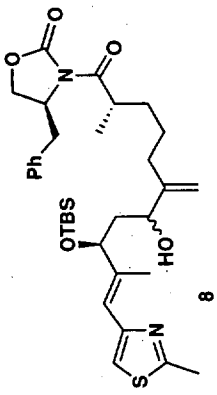


10a

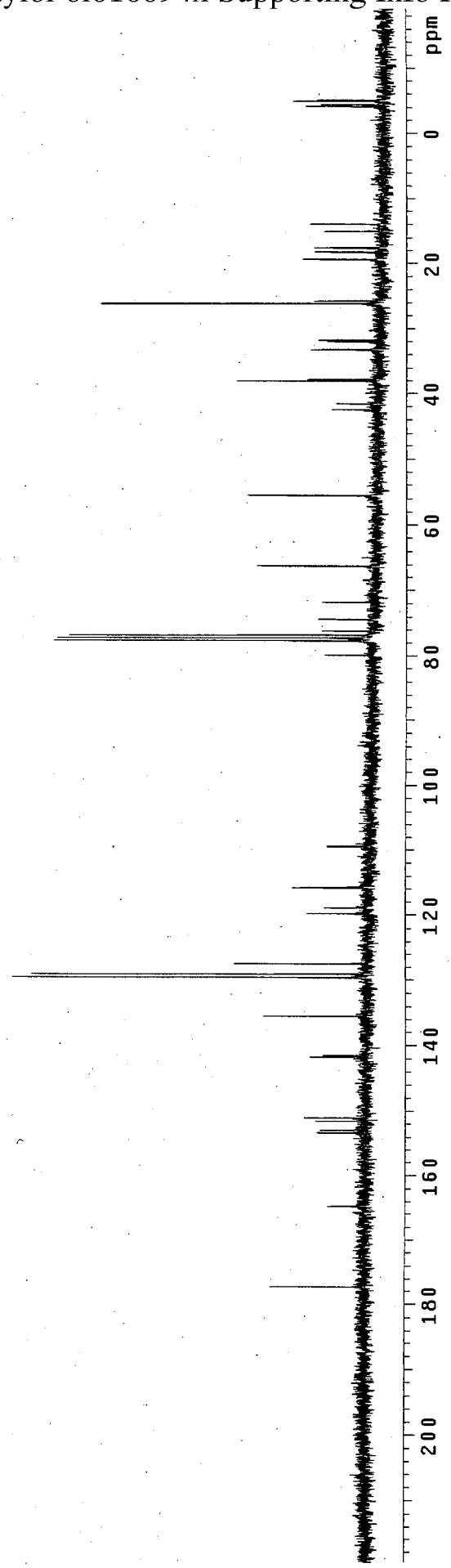
Alcohol 10a

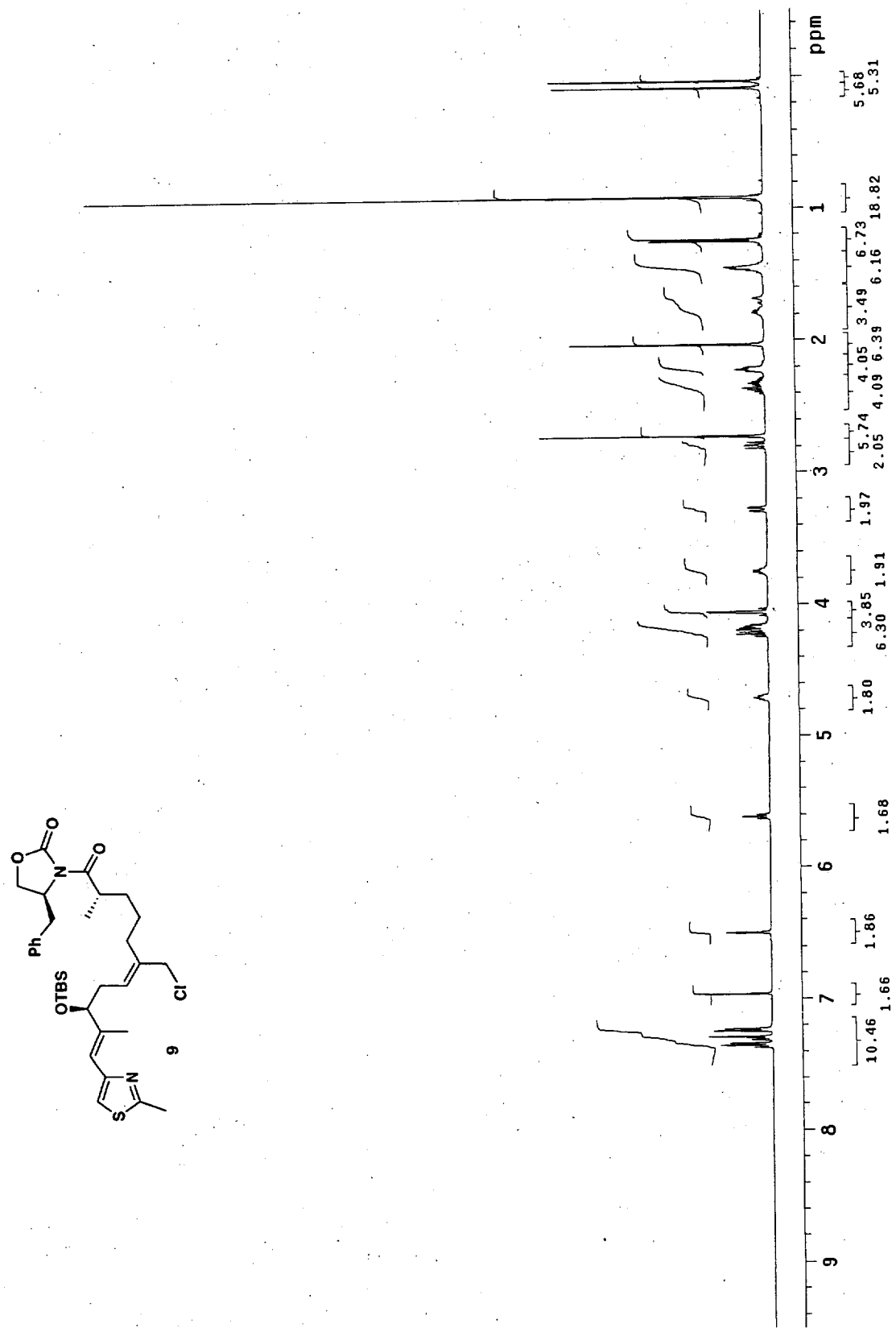
To a solution of **9** (3.42 g, 5.300 mmol) in THF (70 mL) was added a solution of $LiEt_3BH$ (53 mL, 53 mmol, 1.0 M in THF) dropwise at -78°C, which was stirred at the same temperature for 1h. The reaction was then allowed to warm to room temperature and stirred for 1h. The solution was diluted with Et_2O (300 mL), followed by 2N NaOH (50 mL). The organic layer was separated and the aqueous layer was extracted by Et_2O (3 × 100 mL). The combined organic phase was washed by sat. NH_4Cl (100 mL), dried by anhydrous $MgSO_4$, filtered, and concentrated. Purification by flash column chromatography provided **10a** (2.04 g, 88%), a colorless oil, as a 9:1 mixture of inseparable diastereomers. ^1H NMR ($CDCl_3$, 500 MHz) δ 6.91 (s, 1H), 6.44 (s, 1H), 5.14 (t, *J* = 7.0 Hz, 1H), 4.08 (t, *J* = 6.5 Hz, 1H), 3.44 (dd, J = 7.5 Hz, 6.0 Hz, 1H) 3.39 (dd, J = 7.5 Hz, 6.5 Hz, 1H), 2.69 (s, 3H), 2.28-2.19(m, 3H), 2.00 (m, 1H), 1.98 (s, 3H), 1.66 (s, 1H), 1.62 (m, 1H), 1.43-1.36 (m, 3H), 1.08 (m, 1H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 3H), -0.01 (s, 3H). ^{13}C NMR ($CDCl_3$, 300 MHz), δ 164.6, 153.3, 142.9, 136.9, 121.8, 118.8, 115.0, 79.4, 68.2, 35.9, 35.6, 33.3, 32.3, 26.0, 25.5, 23.6, 19.2, 18.4, 16.8, 14.1, -4.50, -4.78. FAB HRMS *m/e* 438.2848, M + H^+ calcd for $C_{24}H_{44}NO_2SSi$ 438.2862.

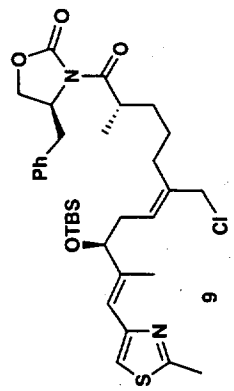

ppm
1
2
3
4
5
6
7
8
9
10.54
17.88
6.97
6.79
7.18
8.86
1.51
5.63
2.84
2.14
0.66
1.94
1.81
6.19
1.62
2.13
1.65
1.72
10.36
1.56
Ph
OTBS
HO
N
S
8



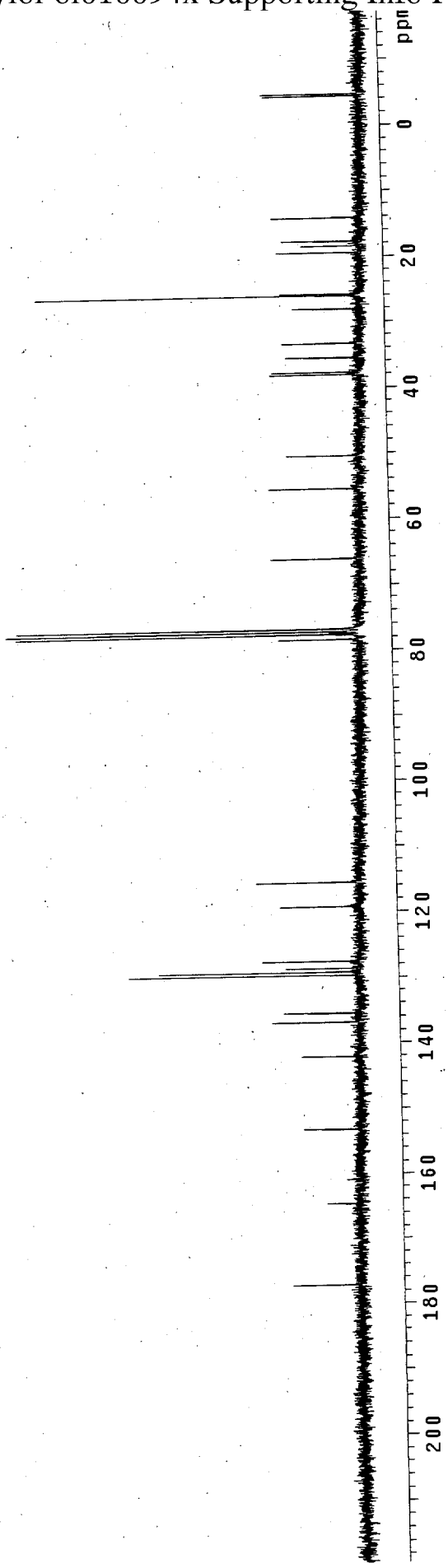
8

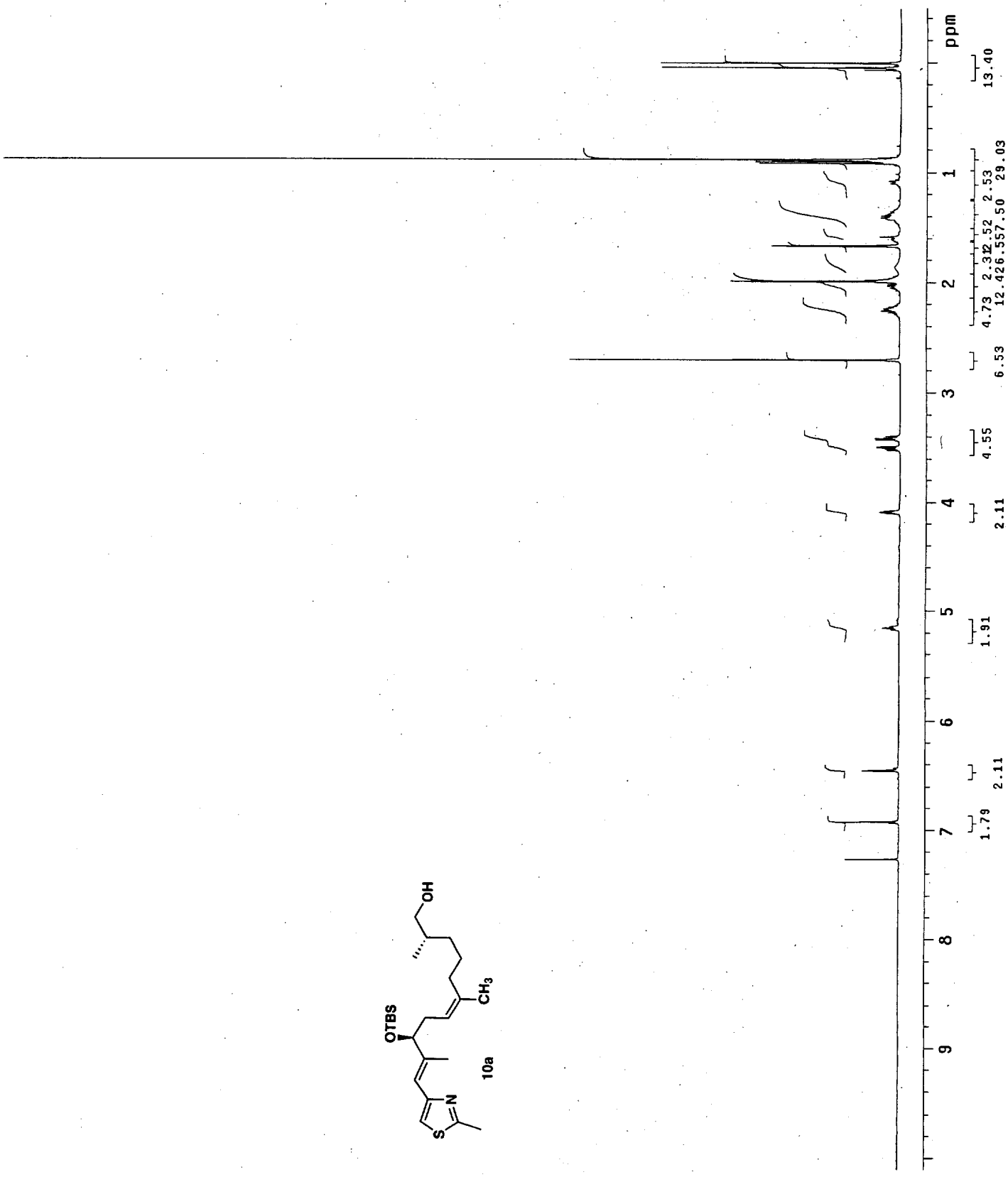


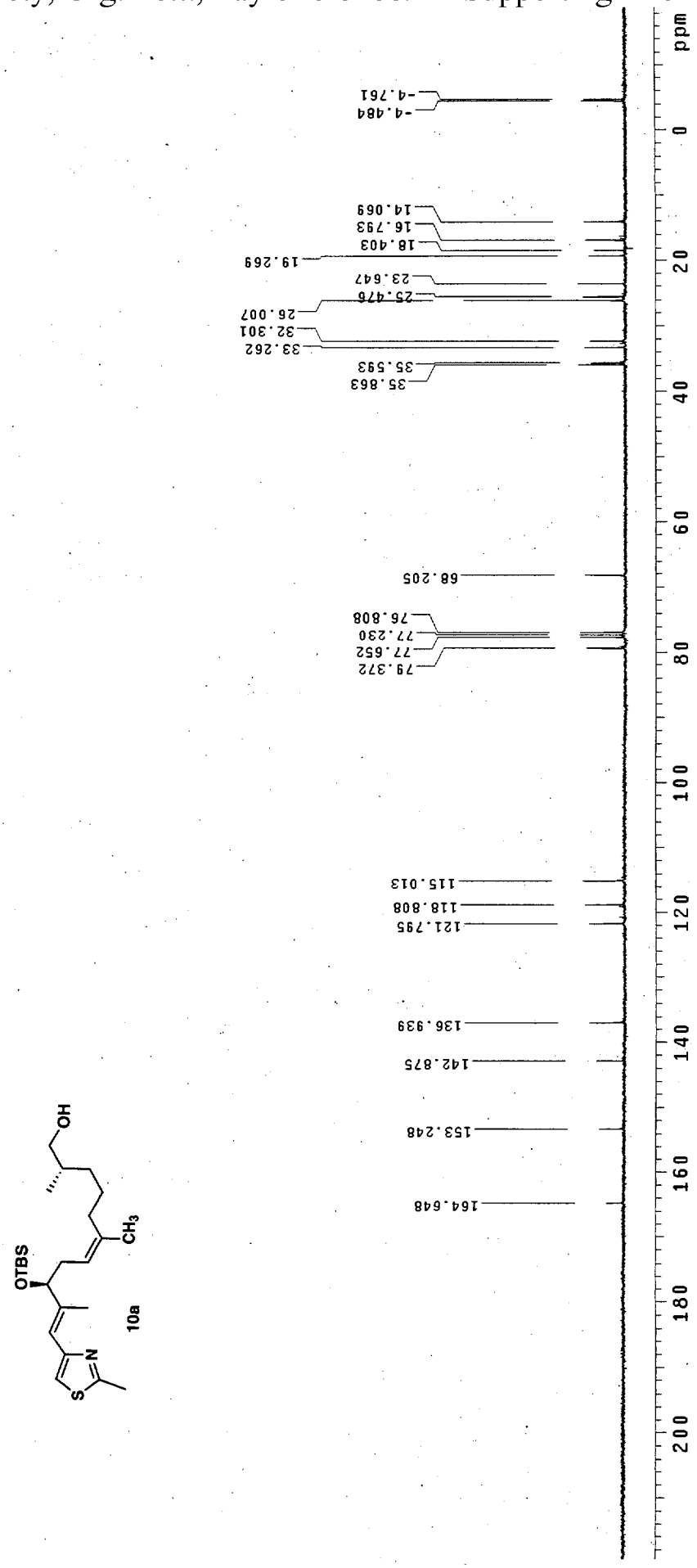

O
O
N
O
Ph
OTBS
Cl
9
N
S
ppm
1
2
3
4
5
6
7
8
9
5.68
5.31
18.82
6.73
6.16
3.49
6.39
4.05
4.09
5.74
2.05
1.97
1.91
3.85
6.30
1.80
1.68
1.86
1.66
10.46



9




ppm
13.40
29.03
2.53
12.50
7.55
6.52
2.31
4.73
12.42
6.53
4.55
2.11
1.91
2.11
1.79
OH
CH3
OTBS
N
S
10a


-4.761
-4.484
14.069
16.793
18.403
19.269
23.647
25.476
26.007
32.301
33.262
35.593
35.863
68.205
76.808
77.230
77.652
79.372
115.013
118.808
121.795
136.939
142.875
153.248
164.648
ppm
0
20
40
60
80
100
120
140
160
180
200
OH
CH3
OTBS
N
S
10a