# Supporting Information

# Synthesis and Antimicrobial Activity of a Novel Class of 15-membered Macrolide Antibiotics, "11a-Azalides"

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## 1. General Experimental

All reactions sensitive to air or moisture were carried out under nitrogen atmosphere with anhydrous solvents. All reagents and solvents were purchased commercially and used without purification unless otherwise noted. Column chromatography was performed on silica gel 60, particle size 40-50 μm. $^{1}H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ on a JEOL Alpha 500 or JEOL Lambda 500 spectrometer. Chemical shifts are reported in parts per million (ppm) with tetramethylsilane (TMS) as an internal standard. Coupling constants (*J*) are given in hertz (Hz). Multiplicities are indicated as br (broadened), s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet). All assignments were made based on $^{1}H$-$^{1}H$ correlation spectroscopy (COSY), heteronuclear multiple-quantum coherence (HMQC), and heteronuclear multiple-bond correlation (HMBC) methods. Mass spectra (MS) were obtained with a Micromass Platform LC or a Micromass Q-Tof 2. HRMS spectra were obtained with a Shimadzu LCMS-IT-TOF. IR spectra were recorded on a PerkinElmer Paragon 1000 spectrometer as KBr pellets and are reported as reciprocal centimeter ($cm^{-1}$). Elemental analyses were performed using a PerkinElmer 2400 CHN analyzer.

## 2. Experimental Procedures and Characterization Data

(9*S*)-9-dihydroerythromycin **4**[1]: $^{13}C$ NMR (125MHz, $CDCl_3$) δ 177.1, 103.5, 96.5, 84.6, 83.2, 79.3, 77.8, 75.1, 74.5, 72.7, 70.9, 70.8, 69.4, 66.2, 65.1, 49.4, 45.8, 41.8, 40.4, 37.1, 34.9, 34.2, 32.0, 28.9, 25.3, 21.8, 21.6, 21.2, 20.2, 18.2, 16.6, 15.2, 14.9, 11.2, 9.5; NMR data consistent with literature.[1]

Preparation of compound **5**: Chlorotriethylsilane (13.6 g, 90.0 mmol) and imidazole (18.4g, 270 mmol) were added to a solution of **4** (20.0 g, 25.7 mmol) in DMF (400 ml) at room temperature. After stirring at room temperature for 40 hours, the reaction mixture was diluted with ethylacetate (400 ml) and washed with distilled water (400 ml × 3). The organic layer was separated and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (hexane:acetone = 20:1) to yield compound **5** (26.5 g, 96%) as a colorless foam: $^{1}H$ NMR (500MHz, $CDCl_3$) δ 5.10 (d, *J* = 4.3 Hz, 1H), 4.88 (dd, *J* = 4.0, 8.2 Hz, 1H), 4.82 (d, *J* = 7.3 Hz, 1H), 4.13 (s, 1H), 4.04 - 4.12 (m, 1H), 3.81 - 3.92 (m, 3H), 3.65 (d, *J* = 4.3 Hz, 1H), 3.45 (d, *J* = 6.7 Hz, 1H), 3.34 (s, 3H), 3.25 (dd, *J* = 7.0, 10.1 Hz, 1H), 3.19 (d, *J* = 9.2 Hz, 1H), 2.83 (s, 1H), 2.59 - 2.67 (m, 1H), 2.50 - 2.56 (m, 1H), 2.37 (d, *J* = 15.3 Hz, 1H), 2.18 (s, 6H), 2.14 - 2.22 (m, 1H), 1.88 - 1.99 (m, 2H), 1.58 - 1.73 (m, 3H), 1.40 - 1.50 (m, 2H), 1.20 (d, *J* = 6.1 Hz, 3H), 1.07 - 1.19 (m, 23H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.90 - 1.00 (m, 30H), 0.54 - 0.73 (m, 18H); $^{13}C$ NMR (125MHz, $CDCl_3$) δ 177.1, 101.1, 94.6, 87.0, 81.7, 80.9, 76.9, 75.1, 74.2, 73.2, 70.1, 67.6, 65.4, 65.2, 48.9, 44.7, 44.4, 41.0, 39.0, 35.0, 32.6, 29.2, 23.3, 22.7, 22.5, 21.6, 19.3, 19.2, 16.2, 14.5, 12.9, 11.8, 9.9, 7.1, 7.0, 7.0, 6.6, 5.8, 5.4, 5.3, 5.1; IR (KBr) 3494, 2954, 1741, 1459, 742 $cm^{-1}$; Anal. calcd for

$C_{55}H_{111}NO_{13}Si_3$: C, 61.24; H, 10.37; N, 1.30. found: C, 61.13; H, 10.49; N, 1.18.

Preparation of compound **7**: Lead tetraacetate (90%, 2.40 g, 4.87 mmol) was added to a solution of compound **5** (5.00 g, 4.63 mmol) in $CH_2Cl_2$ (80 ml) at 0 °C. After stirring for 15 minutes at 0 °C, 2-aminoethanol (566 mg, 9.26 mmol) and sodium triacetoxyborohydride (1.47 g, 6.95 mmol) were added to the reaction mixture. After stirring for 4 hours at room temperature, 37% aqueous formaldehyde solution (2.38 g, 23.2 mmol) and sodium triacetoxyborohydride (1.47 g, 6.95 mmol) were added to the reaction mixture. After stirring at room temperature for 1 hour, the reaction was quenched by adding saturated $NaHCO_3$ (80 ml), and the aqueous layer was extracted with $CHCl_3$ (40 ml × 3). The combined organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH = 50:1) to yield compound **7** (4.06 g, 77%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 4.91 (dd, *J* = 4.8, 7.8 Hz, 1H), 4.72 (d, *J* = 4.9 Hz, 1H), 4.53 (d, *J* = 7.1 Hz, 1H), 4.23 - 4.31 (m, 1H), 4.06 (dd, *J* = 2.6, 7.0 Hz, 1H), 3.55 - 3.73 (m, 5 H), 3.30 (s, 3 H), 3.20 - 3.25 (m, 2H), 2.87 - 2.94 (m, 1H), 2.60 - 2.74 (m, 2H), 2.42 - 2.59 (m, 2H), 2.27 (s, 3H), 2.20 (s, 6H), 2.17 (s, 3H), 2.01 - 2.10 (m, 2H), 1.89 - 1.96 (m, 1H), 1.73 - 1.88 (m, 2H), 1.64 (dd, *J* = 4.5, 11.4 Hz, 1H), 1.53 (dd, *J* = 4.0, 14.1 Hz, 1H), 1.45 (dd, *J* = 4.9, 15.1 Hz, 1H), 1.26 (dd, *J* = 4.8, 14.1 Hz, 1H), 1.15 - 1.22 (m, 13H), 1.14 (d, *J* = 6.0 Hz, 3H), 1.11 (d, *J* = 7.4 Hz, 3H), 0.90 - 1.02 (m, 36H), 0.55 - 0.70 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 204.9, 175.5, 101.7, 96.0, 81.1, 80.7, 80.5, 79.7, 79.6, 75.3, 73.6, 72.7, 68.4, 65.9, 65.2, 60.9, 60.3, 58.2, 49.5, 41.8, 41.7, 41.0, 37.8, 36.2, 34.5, 30.6, 29.1, 26.5, 23.7, 23.6, 22.2, 21.4, 19.1, 18.4, 16.7, 11.9, 10.8, 9.8, 7.2, 7.1, 7.0, 5.5, 5.1; IR (KBr) 3452, 2955, 1729, 1458, 740 cm$^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1135.7984, calcd for $C_{58}H_{119}N_2O_{13}Si_3$ 1135.8015.

Preparation of compound **8**: Ethanol (10 ml), distilled water (10 ml), and lithium hydroxide monohydrate (55 mg, 1.31 mmol) were added to a solution of compound **7** (990 mg, 0.872 mmol) in THF (30 ml) at room temperature. After stirring at room temperature for 6 hours, the reaction was quenched by addition of saturated $NH_4Cl$ (20 ml). The organic solvent was removed *in vacuo* and the residual aqueous layer was extracted with $CHCl_3$ (20 ml × 3). The combined organic layers were dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH = 20:1) to yield compound **8** (600 mg, 65%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 4.74 (d, *J* = 4.7 Hz, 1H), 4.45 (d, *J* = 6.9 Hz, 1H), 4.19 - 4.27 (m, 2H), 3.83 - 3.95 (m, 2H), 3.49 - 3.62 (m, 3H), 3.32 - 3.40 (m, 1H), 3.31 (s, 3H), 3.14 - 3.24 (m, 3H), 2.78 (s, 3H), 2.76 - 2.84 (m, 1H), 2.60 - 2.68 (m, 1H), 2.43 - 2.60 (m, 3H), 2.33 (d, *J* = 14.8 Hz, 1H), 2.20 (s, 6H), 2.13 - 2.19 (m, 1H), 1.90 - 2.00 (m, 1H), 1.59 - 1.65 (m, 1H), 1.41 - 1.56 (m, 3H), 1.28 (s, 3H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.23 (d, *J* = 6.6 Hz, 3H), 1.19 (d, *J* = 7.4 Hz, 3H), 1.14 - 1.18 (m, 7H), 1.09 (d, *J* = 7.4 Hz, 3H), 0.89 - 1.02 (m, 30H), 0.54 - 0.72 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ

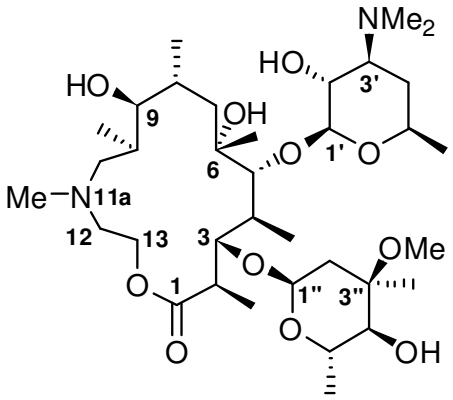
183.2, 103.1, 96.4, 83.0, 81.1, 80.8, 79.6, 76.0, 73.4, 73.1, 67.7, 65.4, 65.1, 62.3, 61.7, 56.4, 49.6, 46.1, 44.6, 41.0, 39.0, 36.2, 33.2, 30.8, 29.5, 25.6, 22.2, 21.7, 20.3, 19.1, 15.5, 10.0, 7.2, 7.1, 5.5, 5.4, 5.2; IR (KBr) 3436, 2958, 1723, 1575, 1459, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1051.7426, calcd for $C_{53}H_{111}N_2O_{12}Si_3$ 1051.7439.

Preparation of compound **9**: Triethylamine (48 mg, 0.478 mmol) and 2,4,6-trichlorobenzoyl chloride (111 mg, 0.456 mmol) were added to a solution of compound **8** (500 mg, 0.434 mmol) in THF (8.7 ml) at room temperature. After stirring at room temperature for 2 hours, the reaction mixture was added to a refluxed solution of DMAP (1.11 g, 10.9 mmol) in toluene (87 ml) for 0.5 hours. The reaction mixture was cooled and washed with saturated $NH_4Cl$ (50 ml). The organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (haxane:acetone = 20:1) to yield compound **9** (354 mg, 79%) as a colorless foam: $^1H$ NMR (500MHz, $CDCl_3$) δ 4.60 (d, *J* = 4.7 Hz, 1H), 4.56 (d, *J* = 6.9 Hz, 1H), 4.39 (br. s., 1H), 4.18 - 4.31 (m, 2H), 3.98 - 4.04 (m, 1H), 3.67 - 3.74 (m, 1H), 3.54 - 3.59 (m, 1H), 3.53 (d, *J* = 6.3 Hz, 1H), 3.31 (s, 3H), 3.18 - 3.24 (m, 2H), 2.75 - 2.82 (m, 1H), 2.68 - 2.74 (m, 1H), 2.61 - 2.67 (m, 1H), 2.43 - 2.55 (m, 2H), 2.31 (d, *J* = 14.8 Hz, 1H), 2.20 (s, 3H), 2.18 (s, 6H), 1.89 - 2.08 (m, 4H), 1.64 - 1.70 (m, 1H), 1.58 - 1.63 (m, 1H), 1.41 - 1.48 (m, 1H), 1.25 - 1.32 (m, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.12 - 1.21 (m, 13H), 1.07 (d, *J* = 7.4 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.90 - 1.00 (m, 30H), 0.55 - 0.72 (m, 18H); $^{13}C$ NMR (125MHz, $CDCl_3$) δ 176.8, 102.1, 95.1, 82.8, 80.8, 79.6, 75.0, 73.4, 73.0, 67.5, 65.6, 65.2, 61.9, 61.2, 56.1, 49.2, 44.0, 43.1, 42.0, 41.0, 40.2, 36.2, 35.6, 29.3, 24.6, 22.5, 21.7, 19.7, 18.7, 16.7, 12.1, 10.5, 7.1, 7.0, 7.0, 5.4, 5.3, 5.2; IR (KBr) 3511, 2957, 1736, 1459, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1033.7340, calcd for $C_{53}H_{109}N_2O_{11}Si_3$ 1033.7334.

Preparation of compound **10**: Hydrogen fluoride-pyridine (70%, 82 mg, 2.86 mmol) was added to a solution of compound **9** (296 mg, 0.286 mmol) in THF (2.0 ml) at room temperature. After stirring at room temperature for 18 hours, the reaction was neutralized with saturated $NaHCO_3$ (2.0 ml). The resulting mixture was diluted with ethylacetate (10 ml) and then separated. The organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 10:1:0.1) to yield compound **10** (177 mg, 90%) as a colorless foam: IR (KBr) 3455, 2973, 1732, 1460, 754 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 691.4759, calcd for $C_{35}H_{67}N_2O_{11}$ 691.4739.

$^{1}$H and $^{13}$C NMR assignment of **10**

| Site | Group | $^{1}$H NMR | | | $^{13}$C NMR |
|---|---|---|---|---|---|
| | | δ (ppm) | peak | *J* (Hz) | δ (ppm) |
| 1 | OC=O | | | | 175.8 |
| 2 | CH | 2.97 | m | | 44.0 |
| 2-Me | $CH_3$ | 1.18 | d | 6.9 | 12.9 |
| 3 | OCH | 4.4 | m | | 78.9 |
| 4 | CH | 2.15 | m | | 40.1 |
| 4-Me | $CH_3$ | 1.07 | d | 7.3 | 10.8 |
| 5 | OCH | 3.8 | d | 3.4 | 86.9 |
| 6 | OC | | | | 74.3 |
| 6-Me | $CH_3$ | 1.22 | s | | 27.3 |
| 7 | $CH_2$ | 1.96<br>1.27 | dd<br>m | 14.5, 7.3 | 39.0 |
| 8 | CH | 2.28 | m | | 31.5 |
| 8-Me | $CH_3$ | 0.96 | d | 7.3 | 17.2 |
| 9 | OCH | 3.50 | dd | 8.0, 3.1 | 80.4 |
| 10 | CH | 1.85 | m | | 32.0 |
| 10-Me | $CH_3$ | 0.81 | d | 6.9 | 15.5 |
| 11 | $NCH_2$ | 2.59<br>2.34 | m<br>m | | 65.6 |
| 11a-NMe | $NCH_3$ | 2.29 | s | | 41.7 |
| 12 | $NCH_2$ | 2.85<br>2.54 | m<br>m | | 56.7 |
| 13 | $OCH_2$ | 4.30<br>4.06 | m<br>m | | 60.7 |
| 1' | OCHO | 4.50 | d | 7.3 | 104.6 |
| 2' | OCH | 3.35 | dd | 9.9, 7.3 | 70.9 |
| 3' | NCH | 2.54 | m | | 64.9 |
| 3'-$NMe_2$ | $NCH_3$ | 2.33 | s | | 40.5 |
| 4' | $CH_2$ | 1.70 | m | | 29.6 |
| 5' | OCH | 3.59 | m | | 69.5 |
| 5'-Me | $CH_3$ | 1.25 | d | 6.1 | 21.2 |
| 1" | OCHO | 4.79 | dd | 4.8, 2.1 | 95.7 |
| 2" | $CH_2$ | 2.30<br>1.58 | m<br>dd | 14.9, 5.0 | 35.0 |
| 3" | OC | | | | 72.7 |
| 3"-Me | $CH_3$ | 1.22 | s | | 21.7 |
| 3"-OMe | $OCH_3$ | 3.29 | s | | 49.4 |
| 4" | OCH | 3.02 | m | | 77.7 |
| 5" | OCH | 4.08 | m | | 66.4 |
| 5"-Me | $CH_3$ | 1.29 | d | 6.1 | 18.0 |
| | OH | 4.60 | br s | | |
| | OH | 3.72 | br s | | |
| | OH | 2.40 | m | | |
| | $N^{+}H$ | 6.87 | br s | | |




**10**

Preparation of (*R*)-2-amino-3-(benzyloxy)propan-1-ol **11a**[2]: *O*-benzyl-L-serine (15.0 g, 76.8 mmol) was added to a suspension of lithium aluminum hydride (4.37 g, 115.3 mmol) in THF (150 ml) under reflux. After stirring at this temperature for 1.5 hours, the reaction mixture was cooled in an ice bath, and distilled water (4.4 ml), 10% aqueous NaOH (4.4 ml) and distilled water (4.4 ml) were added. After stirring at room temperature for 18 hours, the resulting mixture was filtrated and washed with THF. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 10:1:0.1) yield amino alcohol **11a** (6.43 g, 69%) as a colorless foam: $[\alpha]_D^{27}$ -5.0 (*c* 0.760, methanol); $^1$H NMR (200MHz, $CDCl_3$) δ 7.27 - 7.41 (m, 5H), 4.53 (s, 2H), 3.39 - 3.67 (m, 4H), 3.03 - 3.17 (m, 1H), 1.85 (br s, 3H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 137.9, 128.2, 127.55, 127.50, 73.1, 72.5, 63.7, 52.3; MS (ESI) m/z 182.2 $[M+H]^+$; NMR data consistent with literature.[3]

Preparation of (*S*)-2-amino-3-(benzyloxy)propan-1-ol **11b**[2]: *O*-benzyl-D-serine (10.0 g, 51.2 mmol) was added to a suspension of lithium aluminum hydride (2.92 g, 76.8 mmol) in THF (200 ml) under reflux. After stirring at this temperature for 2 hours, the reaction mixture was cooled in an ice bath, and distilled water (2.9 ml), 10% aqueous NaOH (2.9 ml) and distilled water (2.9 ml) were added. After stirring at room temperature for 18 hours, the resulting mixture was filtrated and washed with THF. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 10:1:0.1) yield amino alcohol **11b** (6.43 g, 69%) as a colorless foam: $[\alpha]_D^{27}$ +4.2 (*c* 1.062, methanol); $^1$H NMR (200MHz, $CDCl_3$) δ 7.27 - 7.41 (m, 5H), 4.53 (s, 2H), 3.39 - 3.67 (m, 4H), 3.03 - 3.17 (m, 1H), 1.87 (br s, 3H); MS (ESI) m/z 182.2 $[M+H]^+$.

Preparation of (*S*)-1-amino-3-(benzyloxy)propan-2-ol **11c**: (*S*)-Benzyl glycidyl ether (1.00 g, 6.09 mmol) was added to 25% aqueous ammonia (10 ml) at room temperature. After stirring at room temperature for 18 hours, the reaction mixture was extracted with $CHCl_3$ (20 ml × 3). The combined organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 10:1:0.1) to yield amino alcohol d **11c** (810 mg, 73%) as a colorless solid: $[\alpha]_D^{27}$ +5.3 (*c* 1.06, $CHCl_3$) (Lit.[4] $[\alpha]_D$ -5.1); $^1$H NMR (200MHz, $CDCl_3$) δ 7.27 - 7.38 (m, 5H), 4.55 (s, 2H), 3.68 - 3.83 (m, 1H), 3.39 - 3.56 (m, 2H), 2.66 - 2.89 (m, 2H), 1.80 (br s, 2H); MS (ESI) m/z 182.0 $[M+H]^+$; NMR data consistent with literature.[4]

Preparation of (*R*)-1-amino-3-(benzyloxy)propan-2-ol **11d**: (*R*)-Benzyl glycidyl ether (1.00 g, 6.09 mmol) was added to 25% aqueous ammonia (10 ml) at room temperature. After stirring at room temperature for 18 hours, the reaction mixture was extracted with $CHCl_3$ (20 ml × 3). The combined organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 10:1:0.1) to yield amino alcohol

**11d** (670 mg, 61%) as a colorless solid: $[\alpha]_D^{27}$ +5.6 (*c* 1.03, $CHCl_3$) (Lit.[5] $[\alpha]_D^{27}$ +6.25); $^1$H NMR (200MHz, $CDCl_3$) δ 7.27 - 7.42 (m, 5H), 4.55 (s, 2H), 3.67 - 3.82 (m, 1H), 3.39 - 3.55 (m, 2H), 2.65 - 2.87 (m, 2H), 1.99 (br s, 3H); MS (ESI) m/z 182.0 $[M+H]^+$; NMR data consistent with literature.[4]

Preparation of compound **12a**: Lead tetraacetate (90%, 959 mg, 1.95 mmol) was added to a solution of compound **5** (2.00 g, 1.85 mmol) in $CH_2Cl_2$ (30 ml) at 0 °C. After stirring for 15 min at 0 °C, amino alcohol **11a** (672 mg, 3.71 mmol) and sodium triacetoxyborohydride (589 mg, 2.78 mmol) were added to the reaction mixture. After stirring for 3 hours at room temperature, 37% aqueous formaldehyde solution (732 mg, 9.27 mmol) and sodium triacetoxyborohydride (589 mg, 2.78 mmol) were added to the reaction mixture. After stirring at room temperature for 20 minutes, the reaction was quenched by addition of saturated $NaHCO_3$ (20 ml); the aqueous layer was then extracted with $CHCl_3$ (20 ml × 2). The combined organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and used for the next reaction without further purification. Ethanol (10 ml), distilled water (10 ml), and lithium hydroxide monohydrate (117 mg, 2.78 mmol) were added to a solution of the product obtained above in THF (30 ml) at room temperature. After stirring at room temperature for 2 hours, the reaction was quenched by adding saturated $NH_4Cl$. The organic solvent was removed *in vacuo* and the residual aqueous layer was extracted with $CHCl_3$. The combined organic layers were then washed with brine. The organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH = 50:1 to 5:1) to yield seco-acid **12a** (974 mg, 45%, 2 steps) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.28 - 7.38 (m, 5H), 4.73 (d, *J* = 4.7 Hz, 1H), 4.49 - 4.54 (m, 2H), 4.48 (d, *J* = 6.9 Hz, 1H), 4.33 (d, *J* = 7.4 Hz, 1H), 4.18 - 4.26 (m, 1H), 4.08 (dd, *J* = 3.4, 13.3 Hz, 1H), 3.93 (dd, *J* = 8.8, 11.2 Hz, 1H), 3.68 (dd, *J* = 3.8, 11.2 Hz, 1H), 3.55 - 3.63 (m, 2H), 3.34 (d, *J* = 13.2 Hz, 1H), 3.30 (s, 3H), 3.25 - 3.30 (m, 2H), 3.16 - 3.21 (m, 2H), 2.98 (dd, *J* = 7.8, 13.6 Hz, 1H), 2.86 (s, 3H), 2.50 - 2.62 (m, 2H), 2.33 (d, *J* = 14.8 Hz, 1H), 2.24 - 2.30 (m, 1H), 2.20 (s, 6H), 2.08 - 2.17 (m, 1H), 1.96 - 2.03 (m, 1H), 1.60 - 1.65 (m, 1H), 1.56 (d, *J* = 14.5 Hz, 1H), 1.44 (dd, *J* = 4.8, 14.9 Hz, 1H), 1.33 - 1.39 (m, 1H), 1.31 (s, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.12 - 1.21 (m, 10H), 1.09 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.89 - 1.00 (m, 27H), 0.54 - 0.70 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 182.9, 136.9, 128.6, 128.2, 127.9, 102.9, 96.5, 83.6, 83.0, 81.1, 79.7, 75.2, 73.7, 73.4, 73.2, 67.8, 67.2, 66.8, 65.4, 65.0, 61.2, 59.6, 49.5, 46.0, 41.2, 41.0, 39.5, 38.9, 36.1, 33.2, 32.0, 29.5, 26.6, 22.2, 21.6, 20.6, 19.2, 19.0, 14.9, 10.2, 7.2, 7.1, 7.1, 5.5, 5.5, 5.2; IR (KBr) 3500, 2958, 1724, 1572, 1457, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1171.8019, calcd for $C_{61}H_{119}N_2O_{13}Si_3$ 1171.8015.

Preparation of compound **12b**: Compound **12b** was prepared from compound **5** (2.00 g, 1.85 mmol) and amino alcohol **11b** (672 mg, 3.71 mmol) according to the procedure used to prepare **12a**. Purification by silica gel chromatography ($CHCl_3$:MeOH = 50:1 to 5:1) to yield seco-acid **12b** (1.10

g, 51%, 2 steps) as a colorless foam: $^{1}$H NMR (500MHz, $CDCl_3$) δ 7.27 - 7.39 (m, 5H), 4.73 (d, *J* = 4.7 Hz, 1H), 4.51 (s, 2H), 4.44 (d, *J* = 7.1 Hz, 1H), 4.20 - 4.27 (m, 2H), 3.79 - 3.88 (m, 1H), 3.51 - 3.75 (m, 7H), 3.37 - 3.43 (m, 1H), 3.30 (s, 3H), 3.10 - 3.24 (m, 3H), 2.75 (s, 3H), 2.60 - 2.69 (m, 1H), 2.47 - 2.59 (m, 2H), 2.33 (d, *J* = 14.8 Hz, 1H), 2.20 (s, 6H), 1.89 - 1.98 (m, 1H), 1.58 - 1.65 (m, 1H), 1.39 - 1.53 (m, 3H), 1.27 (s, 3H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.12 - 1.20 (m, 13H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.88 - 1.02 (m, 27H), 0.54 - 0.71 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 183.0, 136.6, 128.7, 128.3, 127.9, 103.2, 96.4, 82.9, 81.1, 79.6, 76.2, 73.7, 73.4, 73.1, 67.7, 65.8, 65.4, 65.1, 61.8, 58.4, 49.6, 46.1, 41.0, 39.4, 36.2, 33.4, 32.0, 29.5, 25.6, 22.2, 21.8, 20.6, 19.1, 15.5, 9.9, 7.2, 7.1, 7.1, 5.5, 5.4, 5.2; IR (KBr) 3498, 2958, 1721, 1569, 1457, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1171.8001, calcd for $C_{61}H_{119}N_2O_{13}Si_3$ 1171.8015.

Preparation of compound **12c**: Compound **12c** was prepared from compound **5** (2.00 g, 1.85 mmol) and amino alcohol **11c** (672 mg, 3.71 mmol) according to the procedure used to prepare **12a**. Purification by silica gel chromatography ($CHCl_3$:MeOH = 50:1 to 5:1) to yield seco-acid **12c** (1.33 g, 61%, 2 steps) as a colorless foam: $^{1}$H NMR (500MHz, $CDCl_3$) δ 7.27 - 7.37 (m, 5H), 4.75 (d, *J* = 5.0 Hz, 1H), 4.48 - 4.56 (m, 2H), 4.42 (d, *J* = 6.9 Hz, 1H), 4.20 - 4.27 (m, 2H), 4.06 - 4.14 (m, 1H), 3.65 (dd, *J* = 4.6, 9.6 Hz, 1H), 3.52 - 3.59 (m, 2H), 3.48 (dd, *J* = 3.4, 13.4 Hz, 1H), 3.39 (dd, *J* = 8.6, 9.4 Hz, 1H), 3.31 - 3.33 (m, 1H), 3.30 (s, 3H), 3.14 - 3.22 (m, 3H), 2.96 (d, *J* = 12.6 Hz, 1H), 2.73 (s, 3H), 2.43 - 2.68 (m, 4H), 2.32 (d, *J* = 14.5 Hz, 1H), 2.20 (s, 6H), 2.15 - 2.20 (m, 1H), 1.87 - 1.98 (m, 1H), 1.57 - 1.68 (m, 1H), 1.36 - 1.54 (m, 3H), 1.29 (s, 3H), 1.27 (d, *J* = 6.1 Hz, 3H), 1.11 - 1.25 (m, 13H), 1.09 (d, *J* = 7.3 Hz, 3H), 0.89 - 1.01 (m, 30H), 0.54 - 0.71 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 183.0, 137.9, 128.5, 127.9, 127.8, 103.3, 96.6, 82.9, 81.1, 79.7, 76.1, 73.6, 73.4, 73.2, 72.2, 67.7, 65.4, 65.1, 64.1, 63.7, 62.4, 49.7, 46.4, 44.7, 41.0, 40.4, 39.4, 36.3, 33.7, 29.5, 26.0, 22.2, 21.8, 20.6, 19.1, 16.0, 10.0, 7.2, 7.1, 7.1, 5.5, 5.4, 5.2; IR (KBr) 3498, 2958, 1720, 1572, 1457, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1171.8026, calcd for $C_{61}H_{119}N_2O_{13}Si_3$ 1171.8015.

Preparation of compound **12d**: Compound **12d** was prepared from compound **5** (2.00 g, 1.85 mmol) and amino alcohol **11d** (672 mg, 3.71 mmol) according to the procedure used to prepare **12a**. Purification by silica gel chromatography ($CHCl_3$:MeOH = 50:1 to 5:1) to yield seco-acid **12d** (1.23 g, 57%, 2 steps) as a colorless foam: $^{1}$H NMR (500MHz, $CDCl_3$) δ 7.26 - 7.35 (m, 5H), 4.73 (d, *J* = 4.6 Hz, 1H), 4.52 (s, 2H), 4.48 (d, *J* = 6.9 Hz, 1H), 4.40 - 4.46 (m, 1H), 4.25 (d, *J* = 7.6 Hz, 1H), 4.19 - 4.24 (m, 1H), 3.57 - 3.65 (m, 2H), 3.54 (d, *J* = 8.4 Hz, 1H), 3.48 - 3.53 (m, 1H), 3.39 (dd, *J* = 8.0, 9.6 Hz, 1H), 3.32 - 3.37 (m, 1H), 3.31 (s, 3H), 3.23 - 3.29 (m, 1H), 3.15 - 3.22 (m, 2H), 2.88 - 2.93 (m, 1H), 2.87 (s, 3H), 2.41 - 2.64 (m, 4H), 2.33 (d, *J* = 14.9 Hz, 1H), 2.20 (s, 6H), 2.12 - 2.16 (m, 1H), 1.90 - 2.00 (m, 1H), 1.59 - 1.66 (m, 1H), 1.51 - 1.57 (m, 1H), 1.38 - 1.47 (m, 2H), 1.26 (s,

3H), 1.24 (d, *J* = 6.5 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.12 - 1.18 (m, 10H), 1.09 (d, *J* = 7.3 Hz, 3H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.89 - 0.99 (m, 27H), 0.55 - 0.72 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 183.2, 137.9, 128.4, 127.7, 127.6, 102.9, 96.1, 83.1, 81.1, 79.4, 75.8, 73.4, 73.4, 73.1, 72.2, 67.7, 65.5, 65.1, 62.8, 62.6, 49.5, 46.3, 46.0, 41.8, 41.0, 39.0, 36.1, 33.1, 31.4, 29.4, 25.5, 22.3, 21.7, 20.3, 20.1, 19.0, 14.7, 10.0, 7.1, 7.0, 5.5, 5.4, 5.2; IR (KBr) 3504, 2958, 1720, 1572, 1457, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1171.8021, calcd for $C_{61}H_{119}N_2O_{13}Si_3$ 1171.8015.

Preparation of compound **13a**: Triethylamine (47 mg, 0.469 mmol) and 2,4,6-trichlorobenzoyl chloride (109 mg, 0.448 mmol) were added to a solution of **12a** (500 mg, 0.427 mmol) in THF (8.5 ml) at room temperature. After stirring at room temperature for 2 hours, the reaction mixture was added to a refluxed solution of DMAP (1.01 g, 10.7 mmol) in toluene (85 ml) for 0.5 hours. After addition, the reaction mixture was cooled and washed with saturated $NH_4Cl$. The organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (haxane:acetone = 20:1) to yield compound **13a** (349 mg, 71%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.26 - 7.36 (m, 5H), 4.70 (d, *J* = 6.9 Hz, 1H), 4.52 - 4.56 (m, 1H), 4.50 (d, *J* = 3.8 Hz, 1H), 4.41 - 4.46 (m, 1H), 4.37 (s, 1H), 4.34 (dd, *J* = 2.3, 11.8 Hz, 1H), 4.11 - 4.19 (m, 2H), 3.89 (br. s., 1H), 3.76 - 3.83 (m, 1H), 3.57 (dd, *J* = 1.9, 5.0 Hz, 1H), 3.53 (dd, *J* = 5.2, 9.4 Hz, 1H), 3.46 (d, *J* = 5.4 Hz, 1H), 3.43 (dd, *J* = 8.0, 9.2 Hz, 1H), 3.31 (s, 3H), 3.25 (dd, *J* = 7.1, 9.7 Hz, 1H), 3.19 (d, *J* = 9.2 Hz, 1H), 3.07 - 3.14 (m, 1H), 2.84 - 2.90 (m, 1H), 2.46 - 2.55 (m, 2H), 2.35 (dd, *J* = 9.6, 12.2 Hz, 1H), 2.28 (d, *J* = 15.3 Hz, 1H), 2.12 - 2.21 (m, 7H), 1.79 - 1.88 (m, 2H), 1.74 (d, *J* = 13.4 Hz, 1H), 1.57 - 1.63 (m, 1H), 1.39 (dd, *J* = 5.0, 14.9 Hz, 1H), 1.33 - 1.34 (m, 1H), 1.19 - 1.24 (m, 6H), 1.16 (d, *J* = 6.1 Hz, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.06 - 1.17 (m, 2H), 1.07 (d, *J* = 7.3 Hz, 3H), 0.89 - 1.01 (m, 33H), 0.53 - 0.68 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 176.4, 138.3, 128.3, 127.7, 127.5, 101.3, 94.2, 84.0, 80.6, 79.6, 74.4, 73.3, 73.1, 73.0, 69.9, 67.5, 65.5, 65.1, 63.6, 62.6, 59.5, 48.9, 43.3, 42.9, 41.4, 40.9, 35.8, 35.5, 35.3, 33.3, 29.1, 22.6, 21.6, 19.9, 18.7, 15.9, 11.6, 11.3, 7.2, 7.0, 7.0, 5.3, 5.2, 5.1; IR (KBr) 3513, 2956, 1730, 1456, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1153.7908, calcd for $C_{61}H_{117}N_2O_{12}Si_3$ 1153.7909.

Preparation of compound **13b**: Compound **13b** was prepared from compound **12b** (500 mg, 0.427 mmol) according to the procedure used to prepare **13a**. Purification by silica gel chromatography (haxane:acetone = 20:1) to yield compound **13b** (353 mg, 72%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.27 - 7.35 (m, 5H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.50 (s, 2H), 4.45 - 4.49 (m, 2H), 4.37 (s, 1H), 4.12 - 4.20 (m, 2H), 4.07 (s, 1H), 3.79 - 3.88 (m, 1H), 3.45 - 3.55 (m, 4H), 3.31 (s, 3H), 3.26 (dd, *J* = 6.9, 9.9 Hz, 1H), 3.12 - 3.18 (m, 2H), 2.79 - 2.84 (m, 1H), 2.55 - 2.61 (m, 1H), 2.46 - 2.52 (m, 1H), 2.35 (dd, *J* = 11.3, 12.0 Hz, 1H), 2.28 (s, 3H), 2.25 - 2.28 (m, 1H), 2.17 (s, 6H), 2.13 - 2.19 (m, 1H), 1.87 - 1.94 (m, 1H), 1.80 - 1.85 (m, 1H), 1.76 (d, *J* = 12.6 Hz, 1H), 1.56 - 1.62 (m, 1H),

1.32 (dd, *J* = 5.0, 14.9 Hz, 1H), 1.23 (d, *J* = 6.1 Hz, 3H), 1.20 (d, *J* = 7.3 Hz, 3H), 1.16 (d, *J* = 6.1 Hz, 3H), 1.12 (s, 3H), 1.10 - 1.18 (m, 2H), 1.08 (s, 3H), 1.06 (d, *J* = 7.6 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.89 - 0.99 (m, 30H), 0.54 - 0.67 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 176.7, 138.4, 128.3, 127.5, 127.4, 101.3, 94.2, 83.9, 80.9, 80.7, 76.0, 74.0, 73.3, 73.1, 72.9, 70.3, 67.5, 65.5, 65.3, 63.3, 58.4, 55.9, 48.9, 43.7, 43.3, 41.3, 40.9, 39.6, 35.2, 34.0, 33.1, 29.0, 22.6, 21.6, 20.9, 19.9, 18.8, 17.5, 11.9, 10.9, 7.2, 7.0, 6.9, 5.3, 5.2, 5.1; IR (KBr) 3513, 2956, 1730, 1651, 1456, 740 cm$^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1153.7885, calcd for $C_{61}H_{117}N_2O_{12}Si_3$ 1153.7909.

Preparation of compound **13c**: Compound **13c** was prepared from compound **12c** (500 mg, 0.427 mmol) according to the procedure used to prepare **13a**. Purification by silica gel chromatography (haxane:acetone = 20:1) to yield compound **13c** (284 mg, 58%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.22 - 7.36 (m, 5H), 5.20 - 5.27 (m, 1H), 4.77 (d, *J* = 4.2 Hz, 1H), 4.47 - 4.59 (m, 2H), 4.30 (br. s., 1H), 4.17 - 4.25 (m, 1H), 3.59 - 3.70 (m, 2H), 3.47 - 3.57 (m, 3H), 3.31 (s, 3H), 3.15 - 3.24 (m, 2H), 3.02 (dd, *J* = 9.6, 13.0 Hz, 1H), 2.66 - 2.75 (m, 1H), 2.61 - 2.66 (m, 1H), 2.45 - 2.53 (m, 1H), 2.33 (d, *J* = 14.9 Hz, 1H), 2.19 (s, 6H), 2.16 (s, 3H), 2.09 - 2.15 (m, 1H), 1.87 - 1.99 (m, 4H), 1.56 - 1.64 (m, 2H), 1.45 (dd, *J* = 5.2, 15.1 Hz, 1H), 1.24 - 1.31 (m, 1H), 1.22 (d, *J* = 6.1 Hz, 3H), 1.19 (s, 3H), 1.10 - 1.23 (m, 10H), 1.07 (d, *J* = 7.3 Hz, 3H), 0.90 - 1.01 (m, 33H), 0.55 - 0.68 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 177.4, 138.1, 128.4, 127.7, 127.5, 102.3, 95.1, 82.7, 80.9, 79.1, 75.0, 73.4, 73.1, 73.0, 70.4, 69.7, 67.7, 65.6, 65.1, 61.8, 56.8, 49.3, 45.1, 43.8, 41.0, 36.7, 35.6, 29.3, 25.2, 22.4, 21.6, 19.1, 18.7, 12.8, 10.6, 7.1, 7.1, 7.0, 5.4, 5.4, 5.2; IR (KBr) 3509, 2958, 1733, 1649, 1457, 740 cm$^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1153.7873, calcd for $C_{61}H_{117}N_2O_{12}Si_3$ 1153.7909.

Preparation of compound **13d**: Compound **13d** was prepared from compound **12d** (300 mg, 0.256 mmol) according to the procedure used to prepare **13a**. Purification by silica gel chromatography (haxane:acetone = 20:1) to yield compound **13d** (63 mg, 21%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.25 - 7.36 (m, 5H), 5.23 - 5.30 (m, 1H), 4.79 (d, *J* = 4.7 Hz, 1H), 4.46 - 4.58 (m, 4H), 4.15 - 4.24 (m, 1H), 3.59 - 3.68 (m, 1H), 3.57 (d, *J* = 6.9 Hz, 1H), 3.48 - 3.53 (m, 1H), 3.43 - 3.48 (m, 1H), 3.35 - 3.40 (m, 1H), 3.27 (s, 3H), 3.19 (dd, *J* = 7.1, 9.9 Hz, 1H), 3.13 (d, *J* = 9.0 Hz, 1H), 2.88 (dd, *J* = 9.2, 13.8 Hz, 1H), 2.65 - 2.75 (m, 1H), 2.53 - 2.61 (m, 1H), 2.43 - 2.52 (m, 2H), 2.22 (s, 3H), 2.19 (s, 6H), 1.79 - 1.98 (m, 3H), 1.57 - 1.64 (m, 1H), 1.50 (d, *J* = 14.5 Hz, 1H), 1.34 (dd, *J* = 8.5, 14.3 Hz, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.20 (s, 3H), 1.18 (d, *J* = 7.1 Hz, 3H), 1.14 - 1.29 (m, 2H), 1.15 (d, *J* = 6.0 Hz, 3H), 1.10 (s, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.88 - 1.00 (m, 30H), 0.55 - 0.69 (m, 18H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 174.8, 138.1, 128.3, 127.5, 127.4, 102.3, 95.7, 82.3, 80.9, 80.5, 75.3, 73.2, 73.0, 70.7, 70.2, 67.7, 65.4, 65.2, 61.4, 60.5, 49.3, 46.1, 41.4, 41.0, 36.9, 35.6, 31.5, 29.3, 25.5, 22.3, 21.6, 19.8, 18.8, 13.7, 10.7, 7.1, 7.1, 7.0, 5.5,

5.4, 5.2; IR (KBr) 3520, 2957, 1731, 1654, 1456, 740 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 1153.7942, calcd for $C_{61}H_{117}N_2O_{12}Si_3$ 1153.7909.

Preparation of compound **14a**: Hydrogen fluoride-pyridine (70%, 6.2 mg, 0.217 mmol) was added to a solution of compound **13a** (25 mg, 0.0217 mmol) in THF (2 ml) at room temperature. After stirring at room temperature for 18 hours, the reaction was neutralized with saturated $NaHCO_3$ (2.0 ml). The resulting mixture was diluted with ethylacetate (10 ml) and then separated. The organic layer was dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 30:1:0.1) to yield compound **14a** (17 mg, 97%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.27 - 7.38 (m, 5H), 6.63 (br s, 1H), 4.71 (dd, *J* = 2.7, 4.7 Hz, 1H), 4.54 (s, 1H), 4.49 (s, 2H), 4.45 (d, *J* = 7.4 Hz, 1H), 4.36 (d, *J* = 5.5 Hz, 1H), 4.15 (dd, *J* = 3.0, 11.5 Hz, 1H), 3.99 - 4.12 (m, 2H), 3.86 (d, *J* = 1.4 Hz, 1H), 3.72 (br. s., 1H), 3.55 - 3.62 (m, 3H), 3.43 (dd, *J* = 5.9, 9.7 Hz, 1H), 3.38 (dd, *J* = 7.4, 10.1 Hz, 1H), 3.28 (s, 3H), 3.21 - 3.27 (m, 1H), 3.13 - 3.21 (m, 1H), 3.00 (t, *J* = 6.7 Hz, 1H), 2.85 (dd, *J* = 3.3, 12.9 Hz, 1H), 2.54 - 2.63 (m, 2H), 2.43 - 2.50 (m, 1H), 2.31 (s, 6H), 2.30 - 2.38 (m, 1H), 2.26 - 2.30 (m, 1H), 2.25 (s, 3H), 1.90 - 2.01 (m, 2H), 1.77 - 1.85 (m, 1H), 1.64 - 1.71 (m, 1H), 1.56 (dd, *J* = 4.7, 14.8 Hz, 1H), 1.28 (d, *J* = 6.3 Hz, 3H), 1.26 - 1.35 (m, 1H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.20 (s, 3H), 1.19 - 1.24 (m, 1H), 1.19 (s, 3H), 1.16 (d, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 7.1 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 176.0, 137.8, 128.4, 127.8, 127.5, 105.5, 95.8, 87.8, 79.0, 78.7, 77.6, 73.8, 73.4, 72.7, 70.9, 69.9, 67.6, 66.7, 66.4, 64.9, 64.8, 61.9, 49.4, 43.2, 40.5, 40.1, 39.7, 34.9, 33.7, 32.5, 31.0, 29.8, 27.7, 21.8, 21.2, 18.2, 15.6, 14.8, 11.2, 11.0; IR (KBr) 3456, 2973, 1731, 1457, 752 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 811.5333, calcd for $C_{43}H_{75}N_2O_{12}$ 811.5315.

Preparation of compound **14b**: Compound **14b** was prepared from compound **13b** (294 mg, 0.255 mmol) according to the procedure used to prepare **14a**. Purification by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 30:1:0.1) to yield compound **14b** (148 mg, 72%) as a colorless foam: $^1$H NMR (500MHz, $CDCl_3$) δ 7.27 - 7.38 (m, 5H), 6.36 (br. s., 1H), 4.74 (d, *J* = 4.6 Hz, 1H), 4.46 - 4.52 (m, 3H), 4.35 - 4.44 (m, 2H), 4.15 (dd, *J* = 4.0, 12.0 Hz, 1H), 4.07 - 4.12 (m, 1H), 3.93 (br. s., 1H), 3.75 (d, *J* = 3.4 Hz, 1H), 3.56 - 3.63 (m, 2H), 3.51 (dd, *J* = 6.3, 9.7 Hz, 1H), 3.47 (dd, *J* = 2.7, 8.0 Hz, 1H), 3.36 (dd, *J* = 7.5, 10.1 Hz, 1H), 3.28 (s, 3H), 3.19 - 3.26 (m, 1H), 2.93 - 3.02 (m, 2H), 2.56 - 2.68 (m, 2H), 2.43 - 2.46 (m, 1H), 2.42 (s, 3H), 2.32 (s, 6H), 2.25 - 2.37 (m, 3H), 2.07 - 2.15 (m, 1H), 2.01 (dd, *J* = 7.5, 14.7 Hz, 1H), 1.81 - 1.90 (m, 1H), 1.63 - 1.73 (m, 1H), 1.25 -1.34 (m, 1H), 1.17 – 1.26 (m, 1H), 1.47 (dd, *J* = 4.8, 15.1 Hz, 1H), 1.29 (d, *J* = 6.5 Hz, 3H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.21 (s, 3H), 1.20 (s, 3H), 1.18 (d, *J* = 7.3 Hz, 3H), 1.09 (d, *J* = 7.3 Hz, 3H), 0.93 (d, *J* = 7.3 Hz, 3H), 0.80 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (125MHz, $CDCl_3$) δ 176.0, 137.9, 128.5, 127.8, 127.5, 104.9, 96.4, 87.2, 79.8, 78.3, 77.8, 74.2, 73.4, 72.7, 70.7, 69.6, 66.0, 65.6, 64.7, 61.8, 61.0, 58.1, 49.4, 44.9, 41.4,

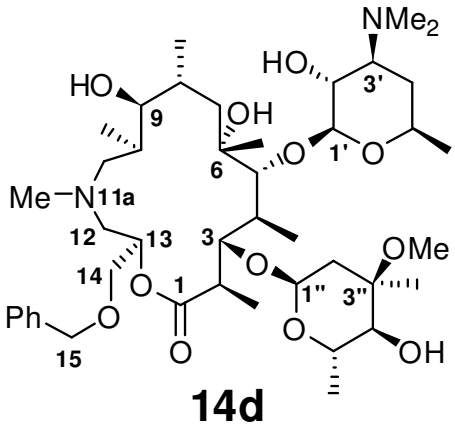
40.5, 40.2, 39.5, 35.0, 31.7, 31.1, 29.4, 27.3, 21.6, 21.1, 17.8, 16.6, 15.2, 12.9, 11.3; IR (KBr) 3455, 2973, 1731, 1645, 1456, 753 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 811.5313, calcd for $C_{43}H_{75}N_2O_{12}$ 811.5315.

Preparation of compound **14c**: Compound **14c** was prepared from compound **13c** (156 mg, 0.135 mmol) according to the procedure used to prepare **14a**. Purification by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 30:1:0.1) to yield compound **14c** (94 mg, 86%) as a colorless foam: $^1H$ NMR (500MHz, $CDCl_3$) δ 7.27 - 7.38 (m, 5H), 7.00 (br s, 1H), 5.34 - 5.41 (m, 1H), 4.82 (d, *J* = 4.7 Hz, 1H), 4.58 (d, *J* = 7.1 Hz, 1H), 4.45 - 4.56 (m, 3H), 4.10 - 4.18 (m, 1H), 3.92 (d, *J* = 3.6 Hz, 1H), 3.62 - 3.69 (m, 1H), 3.45 - 3.48 (m, 2H), 3.36 - 3.43 (m, 1H), 3.31 - 3.35 (m, 1H), 3.27 (s, 3H), 3.01 (t, *J* = 9.6 Hz, 1H), 2.87 (dd, *J* = 10.8, 13.3 Hz, 1H), 2.78 - 2.83 (m, 1H), 2.61 - 2.69 (m, 2H), 2.20 - 2.38 (m, 14H), 2.13 (dd, *J* = 2.5, 12.3 Hz, 1H), 1.96 (dd, *J* = 7.8, 14.7 Hz, 1H), 1.77 - 1.87 (m, 1H), 1.63 - 1.74 (m, 1H), 1.51 (dd, *J* = 4.9, 15.4 Hz, 1H), 1.34 (dd, *J* = 4.7, 14.8 Hz, 1H), 1.30 (d, *J* = 6.3 Hz, 1H), 1.22 - 1.28 (m, 7H), 1.21 (s, 3H), 1.18 (d, *J* = 7.4 Hz, 3H), 1.07 (d, *J* = 7.4 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.77 (d, *J* = 6.6 Hz, 3H); $^{13}C$ NMR (125MHz, $CDCl_3$) δ 175.7, 137.7, 128.5, 127.8, 127.7, 104.9, 96.9, 87.3, 80.6, 77.7, 74.2, 73.3, 72.8, 70.8, 70.4, 69.3, 68.6, 66.1, 64.5, 64.1, 58.2, 49.3, 46.1, 44.0, 42.2, 40.5, 39.8, 35.0, 31.7, 29.4, 28.4, 21.5, 21.1, 17.6, 15.2, 14.8, 11.0; IR (KBr) 3443, 2973, 1733, 1675, 1457, 752 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 811.5334, calcd for $C_{43}H_{75}N_2O_{12}$ 811.5315.

Preparation of compound **14d**: Compound **14d** was prepared from compound **13d** (33 mg, 0.0286 mmol) according to the procedure used to prepare **14a**. Purification by silica gel chromatography ($CHCl_3$:MeOH:$NH_4OH$ = 30:1:0.1) to yield compound **14d** (22 mg, 95%) as a colorless foam: $^1H$ NMR (500MHz, $CDCl_3$) δ 7.23 - 7.35 (m, 5H), 6.75 (br s, 1H), 5.04 - 5.10 (m, 1H), 4.77 - 4.84 (m, 1H), 4.40 - 4.58 (m, 3H), 4.30 (d, *J* = 5.2 Hz, 1H), 4.00 - 4.08 (m, 1H), 3.95 (s, 1H), 3.44 - 3.67 (m, 5H), 3.39 (dd, *J* = 7.4, 10.1 Hz, 1H), 3.25 (s, 3H), 2.96 (t, *J* = 8.8 Hz, 1H), 2.82 - 2.91 (m, 1H), 2.62 - 2.74 (m, 2H), 2.40 - 2.54 (m, 3H), 2.29 - 2.38 (m, 1H), 2.30 (s, 6H), 2.26 (s, 3H), 2.20 (dd, *J* = 2.3, 14.9 Hz, 1H), 1.83 - 1.95 (m, 2H), 1.60 - 1.81 (m, 2H), 1.38 (dd, *J* = 4.7, 14.8 Hz, 1H), 1.19 - 1.33 (m, 8H), 1.17 (s, 3H), 1.15 (s, 3H), 1.11 (d, *J* = 7.4 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 7.1 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H); $^{13}C$ NMR (125MHz, $CDCl_3$) δ 175.5, 138.0, 128.4, 127.7, 127.4, 105.7, 94.9, 87.3, 78.3, 78.1, 77.7, 73.6, 73.3, 72.5, 70.9, 70.2, 69.8, 66.2, 64.8, 62.2, 49.4, 43.2, 40.9, 40.7, 40.0, 39.8, 34.7, 33.4, 30.9, 30.3, 27.8, 21.8, 21.3, 18.5, 15.3, 14.5, 10.7; IR (KBr) 3464, 2974, 1731, 1651, 1456, 753 $cm^{-1}$; HRMS (ESI/APCI-dual, $[M+H]^+$) found 811.5313, calcd for $C_{43}H_{75}N_2O_{12}$ 811.5315.

$^{1}$H and $^{13}$C NMR assignment of **14d**

| Site | Group | $^{1}$H NMR | | | $^{13}$C NMR |
|---|---|---|---|---|---|
| | | δ (ppm) | peak | *J* (Hz) | δ (ppm) |
| 1 | OC=O | | | | 175.6 |
| 2 | CH | 3.49 | m | | 43.3 |
| 2-Me | $CH_3$ | 1.12 | d | 7.4 | 10.6 |
| 3 | OCH | 4.30 | d | 5.2 | 78.1 |
| 4 | CH | 1.92 | m | | 40.0 |
| 4-Me | $CH_3$ | 1.09 | d | 6.9 | 10.7 |
| 5 | OCH | 3.95 | s | | 87.3 |
| 6 | OC | | | | 73.6 |
| 6-Me | $CH_3$ | 1.17 | s | | 27.8 |
| 7 | $CH_2$ | 1.87<br>1.22 | m<br>m | | 39.8 |
| 8 | CH | 2.33 | m | | 30.9 |
| 8-Me | $CH_3$ | 0.86 | d | 7.1 | 15.3 |
| 9 | OCH | 3.63 | m | | 78.3 |
| 10 | CH | 1.75 | m | | 33.4 |
| 10-Me | $CH_3$ | 0.76 | d | 6.9 | 14.5 |
| 11 | $NCH_2$ | 2.65<br>2.44 | m<br>m | | 69.7 |
| 11a-NMe | $NCH_3$ | 2.26 | s | | 40.9 |
| 12 | $NCH_2$ | 2.87<br>2.72 | m<br>m | | 62.2 |
| 13 | OCH | 5.07 | m | | 69.88 |
| 14 | $OCH_2$ | 3.55<br>3.52 | m<br>m | | 70.2 |
| 15 | $OCH_2$ | 4.55<br>4.46 | d<br>d | 12.1<br>12.1 | 73.3 |
| Ph | CH | 7.23-7.35 | m | | 138.0, 128.4, 127.7, 127.4 |
| 1' | OCHO | 4.45 | d | 7.4 | 105.7 |
| 2' | OCH | 3.39 | dd | 10.2, 7.4 | 70.9 |
| 3' | NCH | 2.49 | m | | 64.9 |
| 3'-$NMe_2$ | $NCH_3$ | 2.30 | s | | 40.7 |
| 4' | $CH_2$ | 1.64<br>1.31 | m<br>m | | 30.3 |
| 5' | OCH | 3.59 | m | | 69.8 |
| 5'-Me | $CH_3$ | 1.27 | d | 6.3 | 21.3 |
| 1" | OCHO | 4.81 | m | | 94.9 |
| 2" | $CH_2$ | 2.20<br>1.38 | dd<br>dd | 14.9, 2.3<br>14.9, 4.7 | 34.7 |
| 3" | OC | | | | 72.5 |
| 3"-Me | $CH_3$ | 1.15 | s | | 21.9 |
| 3"-OMe | $OCH_3$ | 3.25 | s | | 49.4 |
| 4" | OCH | 2.96 | d | 8.8 | 77.8 |
| 5" | OCH | 4.05 | m | | 66.2 |
| 5"-Me | $CH_3$ | 1.25 | d | 6.3 | 18.5 |
| | OH | 2.44 | m | | |
| | OH | 3.61 | m | | |
| | OH | 4.48 | m | | |
| | $N^{+}H$ | 6.75 | br s | | |




**14d**

## 3. MIC measurements

The *in vitro* antibacterial activity is reported as the minimum inhibitory concentration (MIC) in μg/mL. MIC was determined by the broth microdilution method according to Clinical and Laboratory Standards Institute (formerly National Committee of Clinical Laboratory Standards) guidelines for *Streptococcus pneumoniae*.[6] *S. pneumoniae* ATCC49619 is erythromycin-susceptible strain. S. pneumoniae 205 is erythromycin-resistant strain encoded by *erm*(B) ribosomal methylase gene.

## 4. References

(1) Chen, W.-M.; Wong, H. N. C.; Chu, D. T. W.; Lin, X. *Tetrahedron* **2003**, *59*, 7033-7045.

(2) Keith, D. D.; De Bernardo, S.; Weigele, M. *Tetrahedron* **1975**, *31*, 2629-2632.

(3) Danklmaier, J. Hoenig, H. *Liebigs Ann. Chem.* **1988,** *9*, 851.

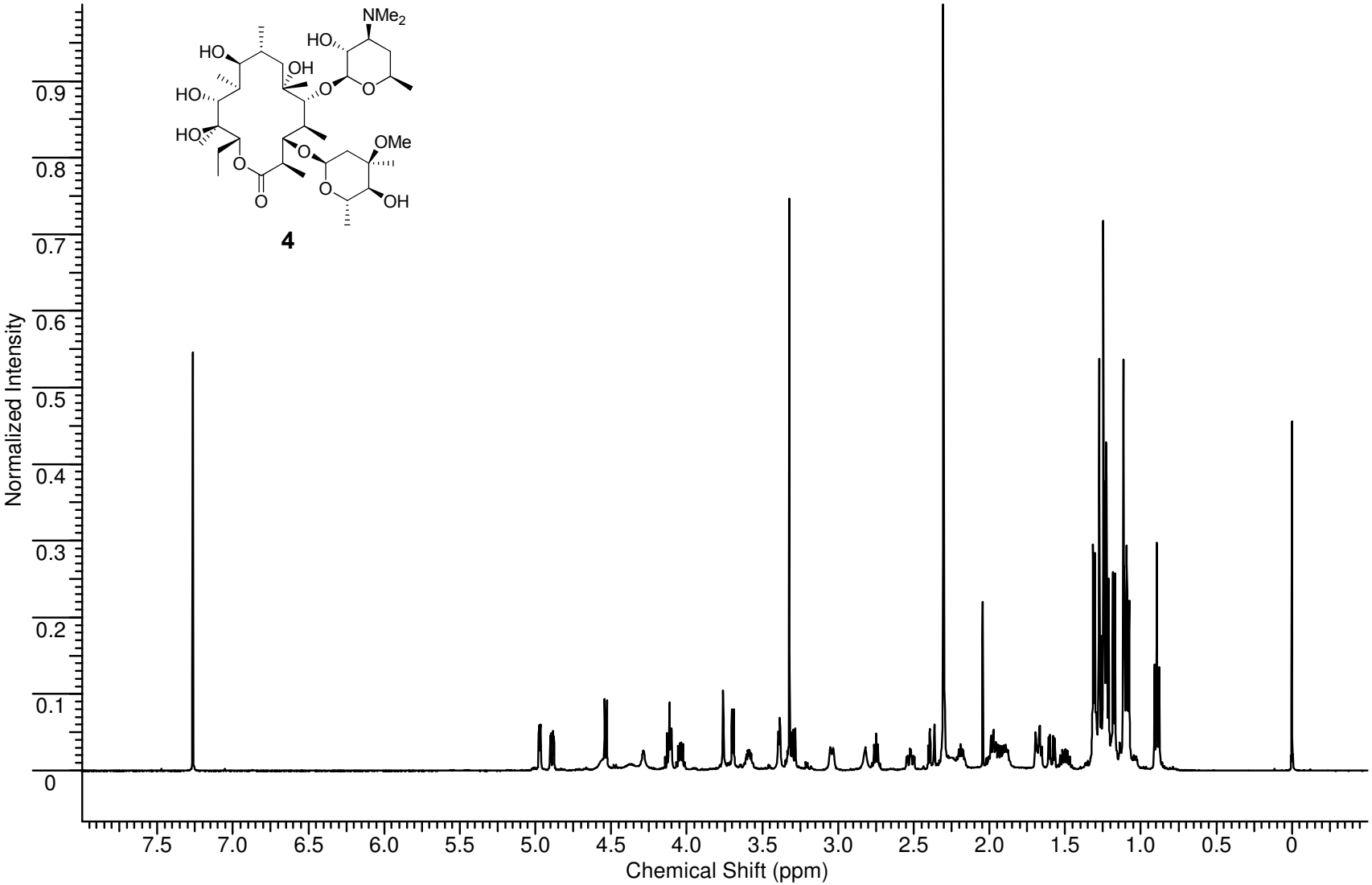
(4) Neimert-Andersson, K.; Blomberg, E.; Somfai, P. *J. Org. Chem.* **2004**, *69*, 3746-3752.

(5) Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. *Chem. Eur. J.* **2004**, *10*, 1752-1764.

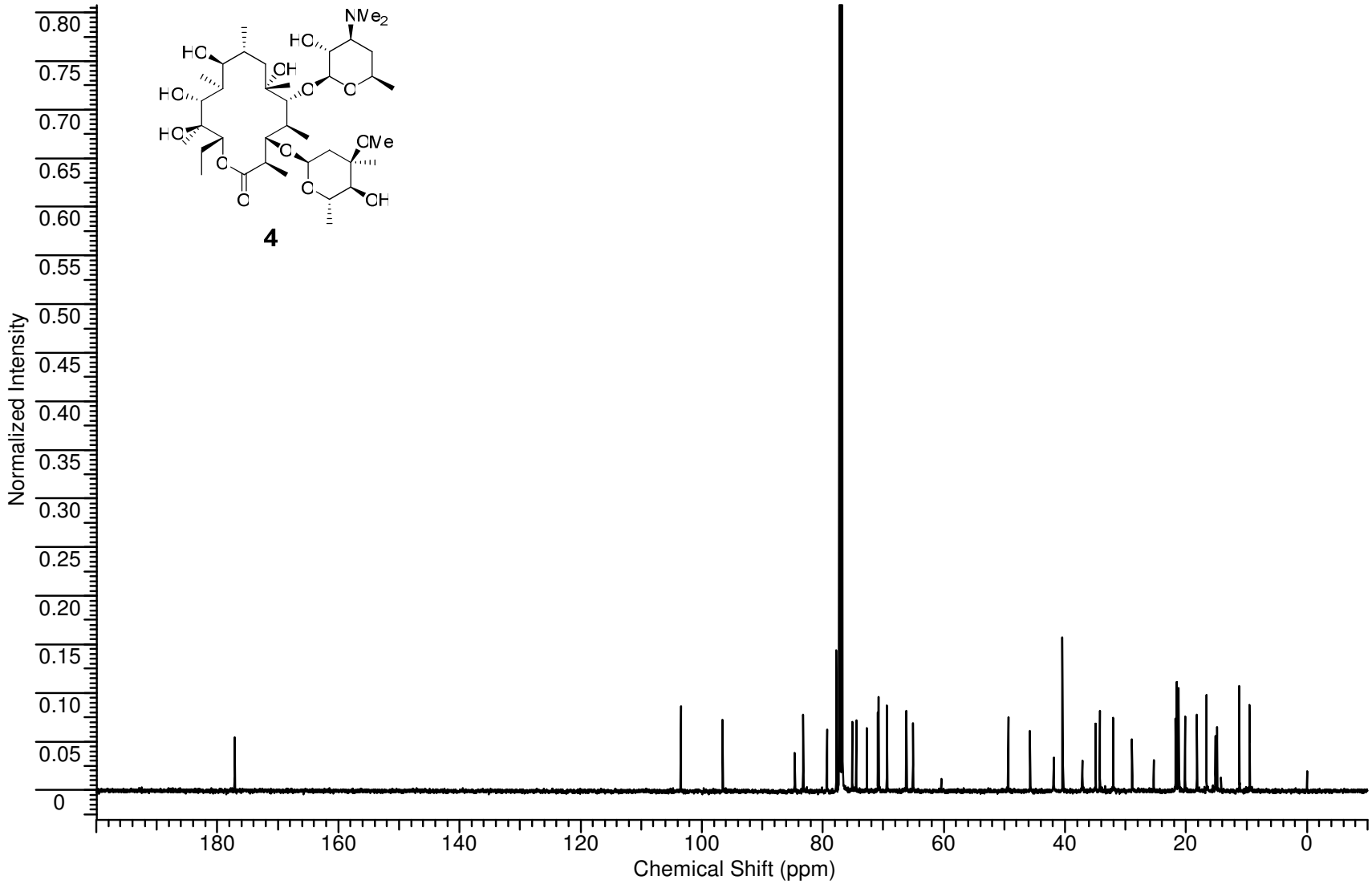
(6) Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard, 6th ed.; NCCLS document M7-A6; NCCLS: Wayne, PA, 2003.

## 4. Reproductions of $^{1}H$, $^{13}C$ NMR Spectra

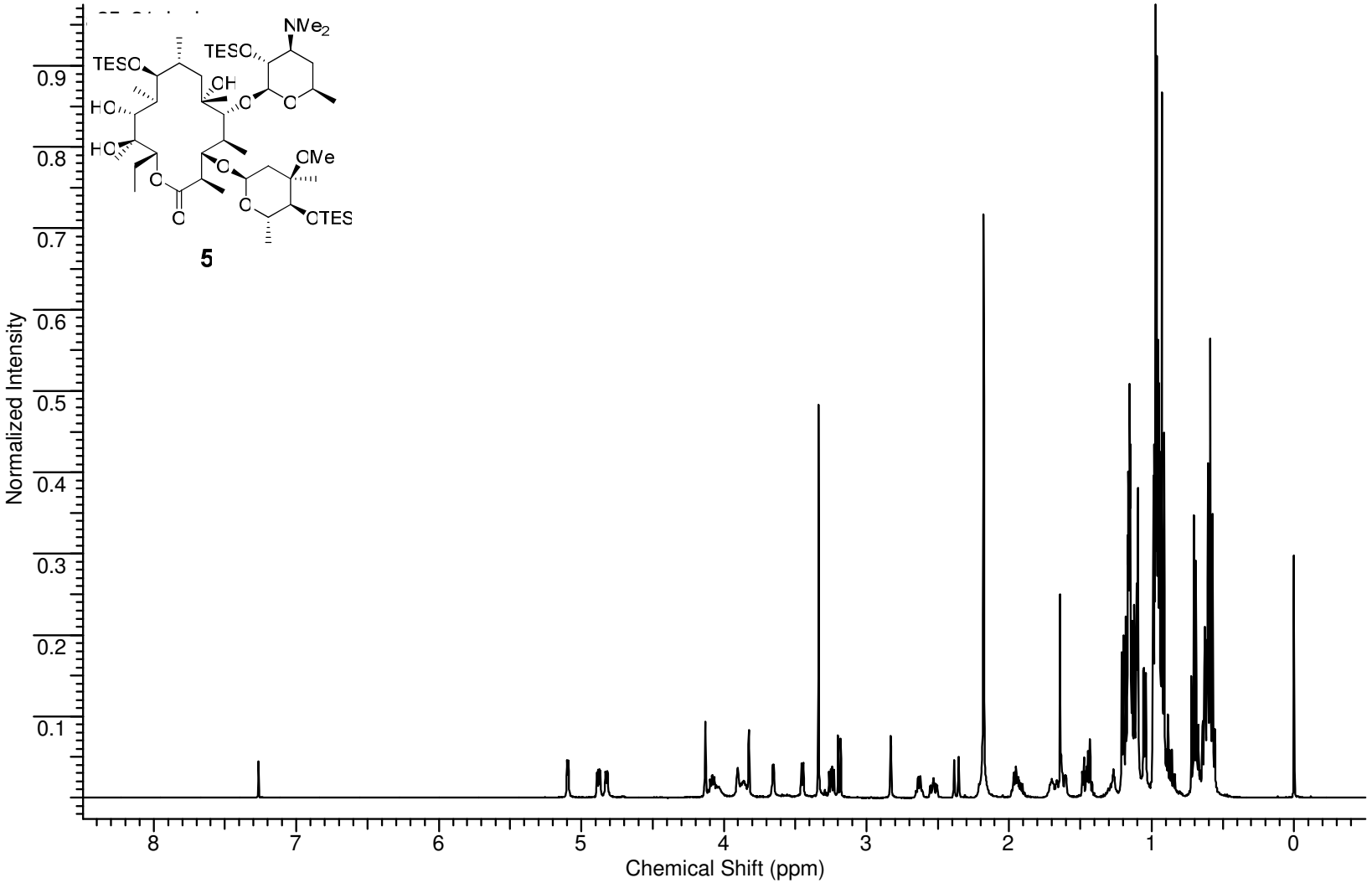
$^{1}H$ NMR Spectrum of **4**



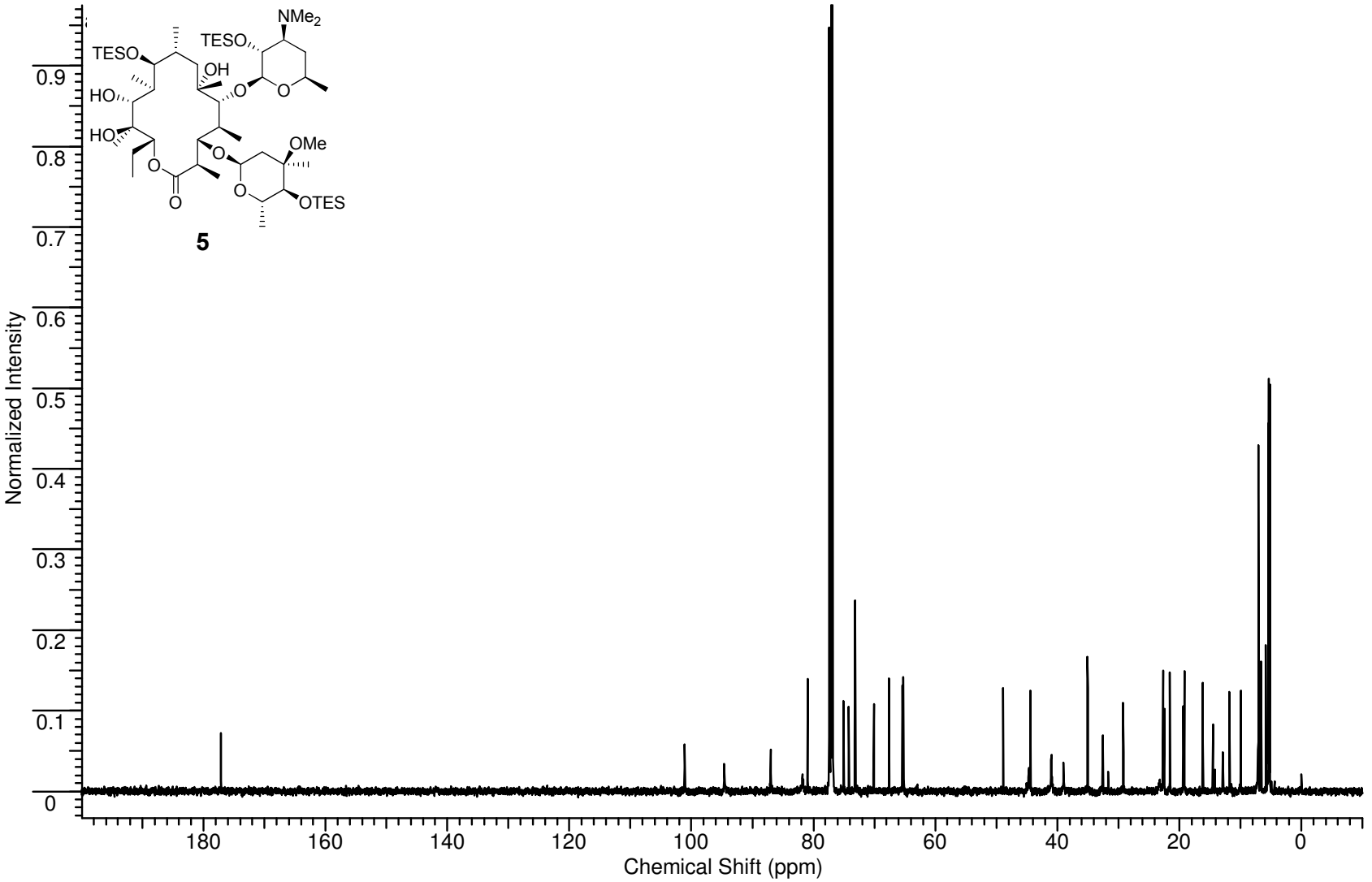
$^{13}$C NMR Spectrum of **4**



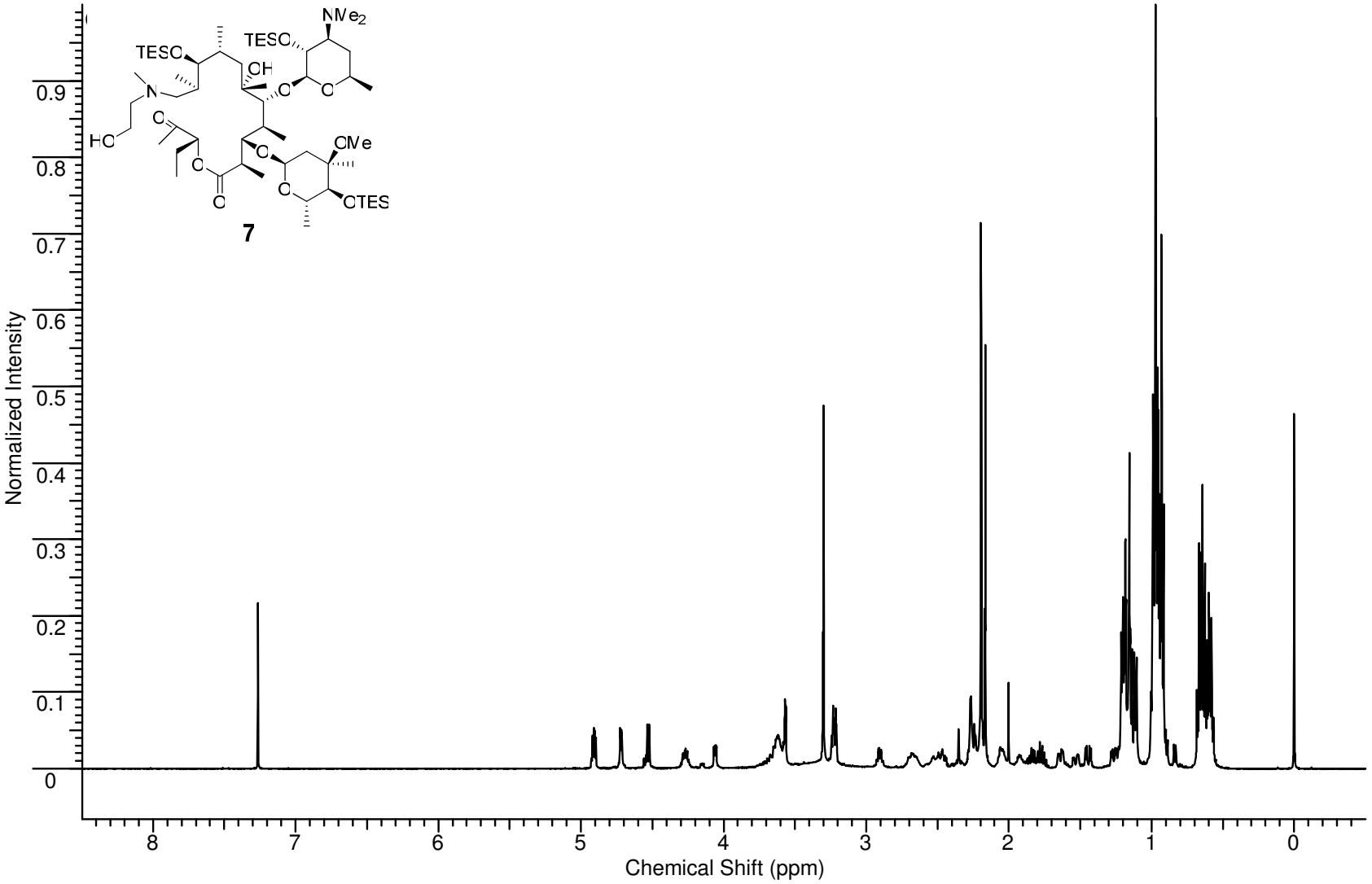
$^{1}$H NMR Spectrum of **5**



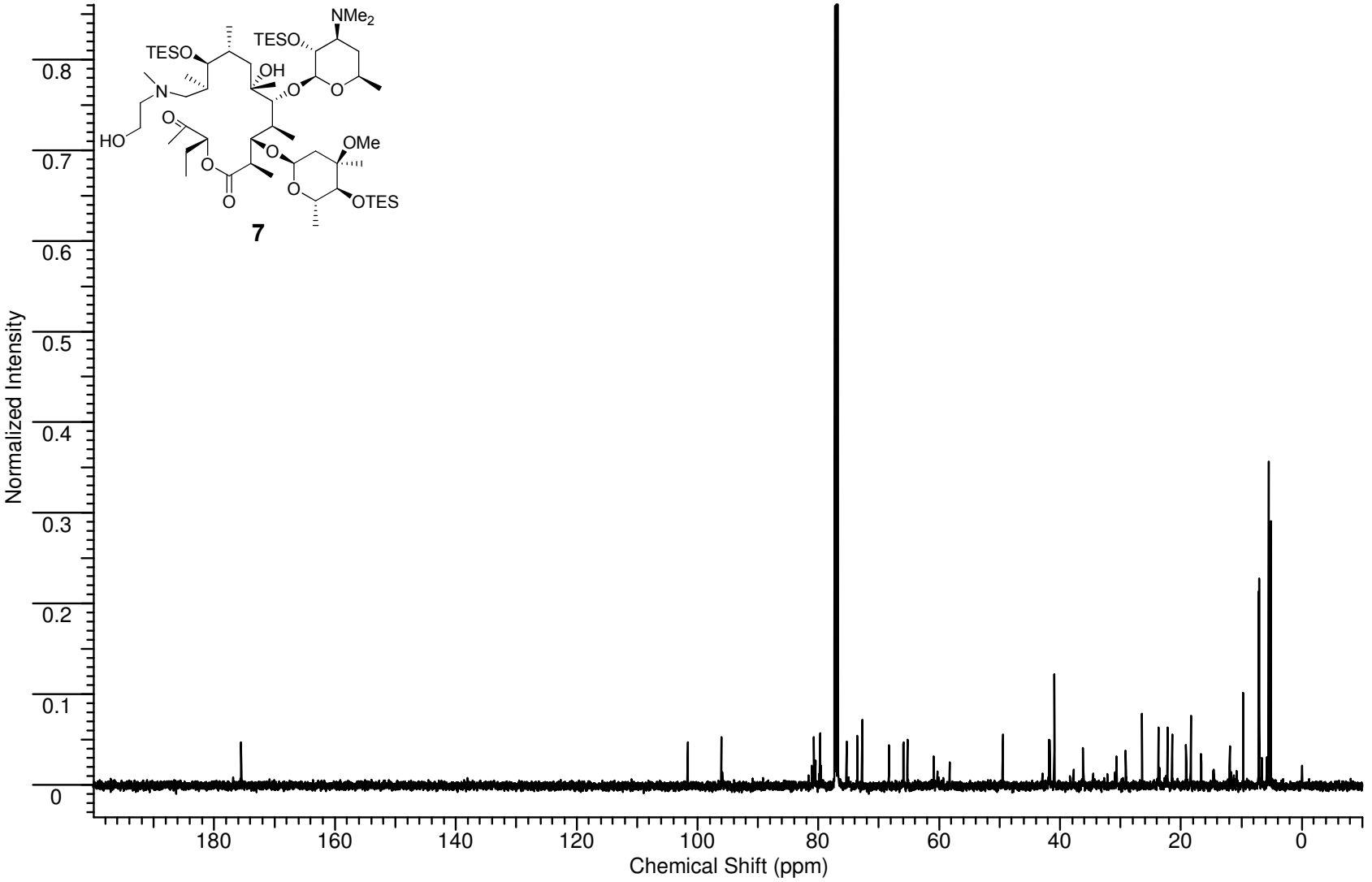
$^{13}$C NMR Spectrum of **5**



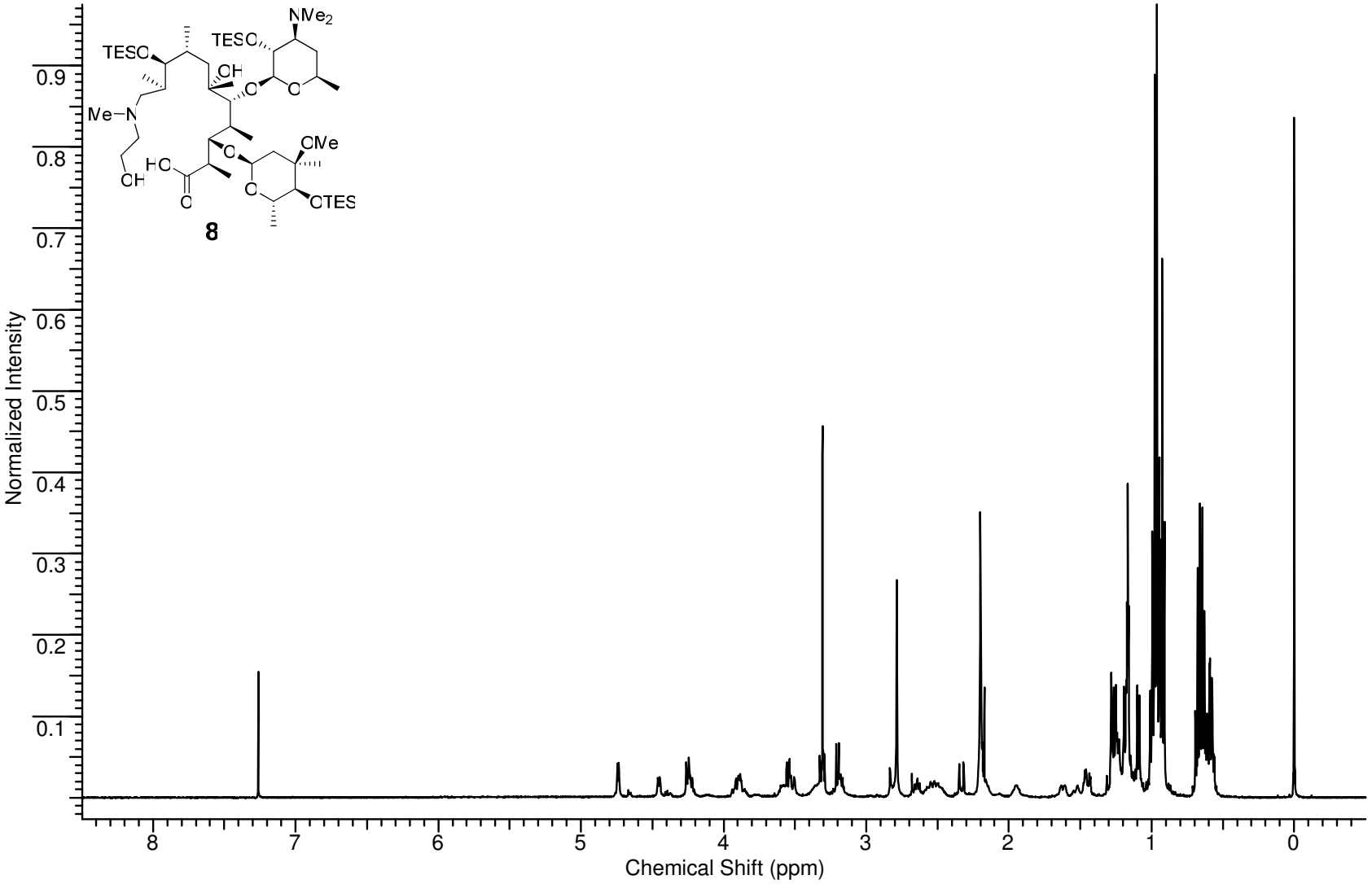
$^{1}$H NMR Spectrum of **7**



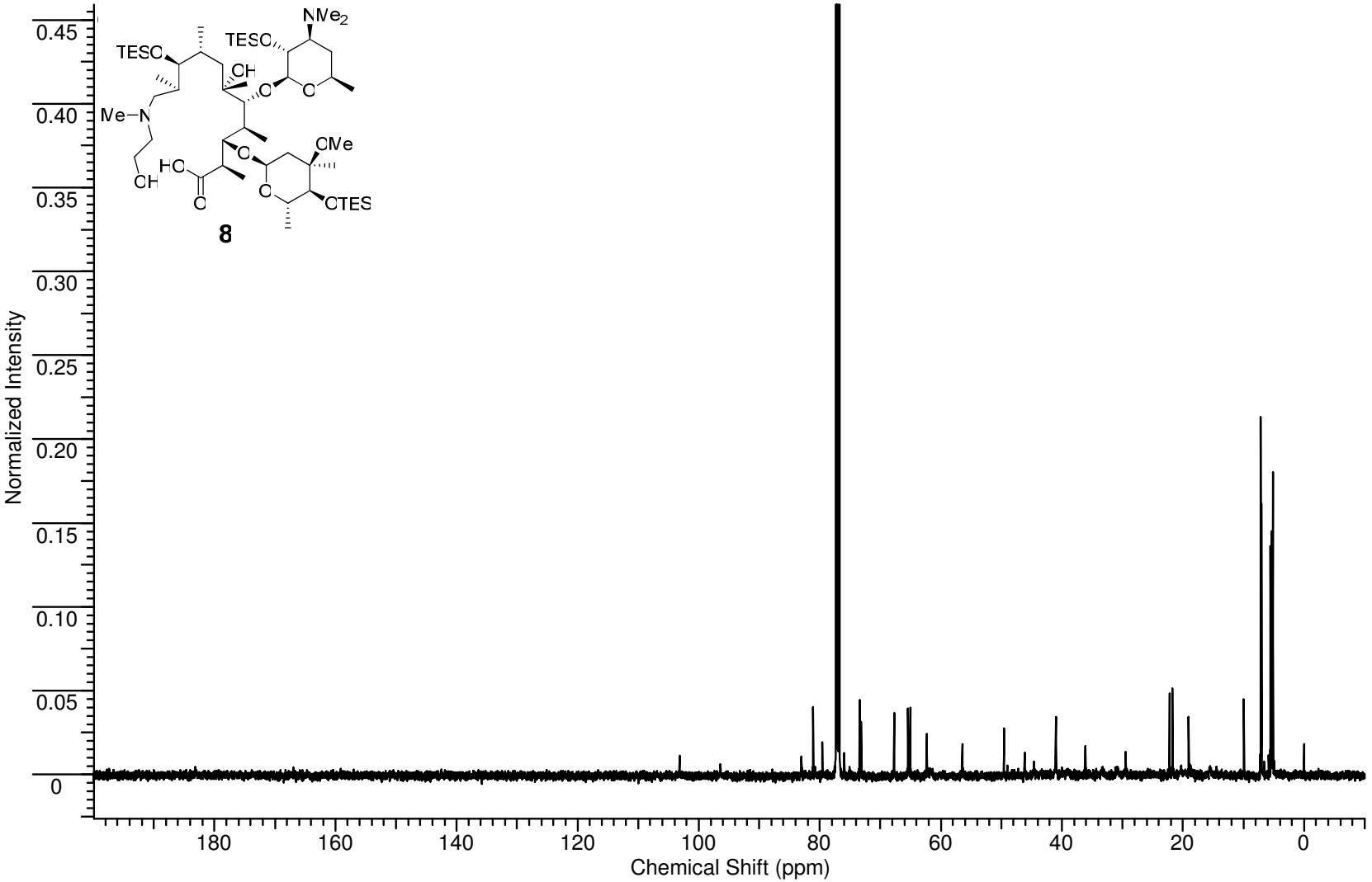
$^{13}$C NMR Spectrum of **7**



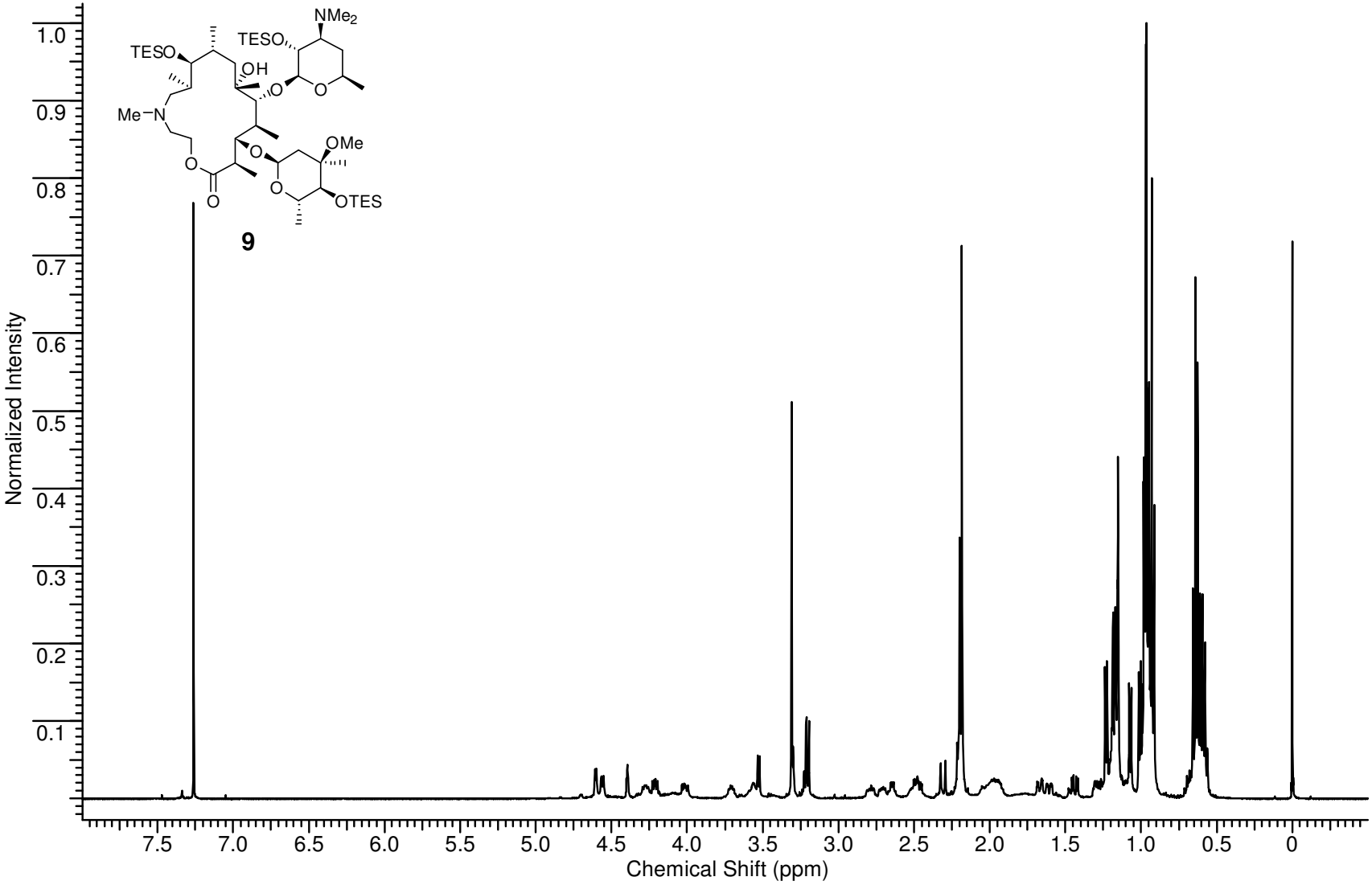
$^{1}$H NMR Spectrum of **8**



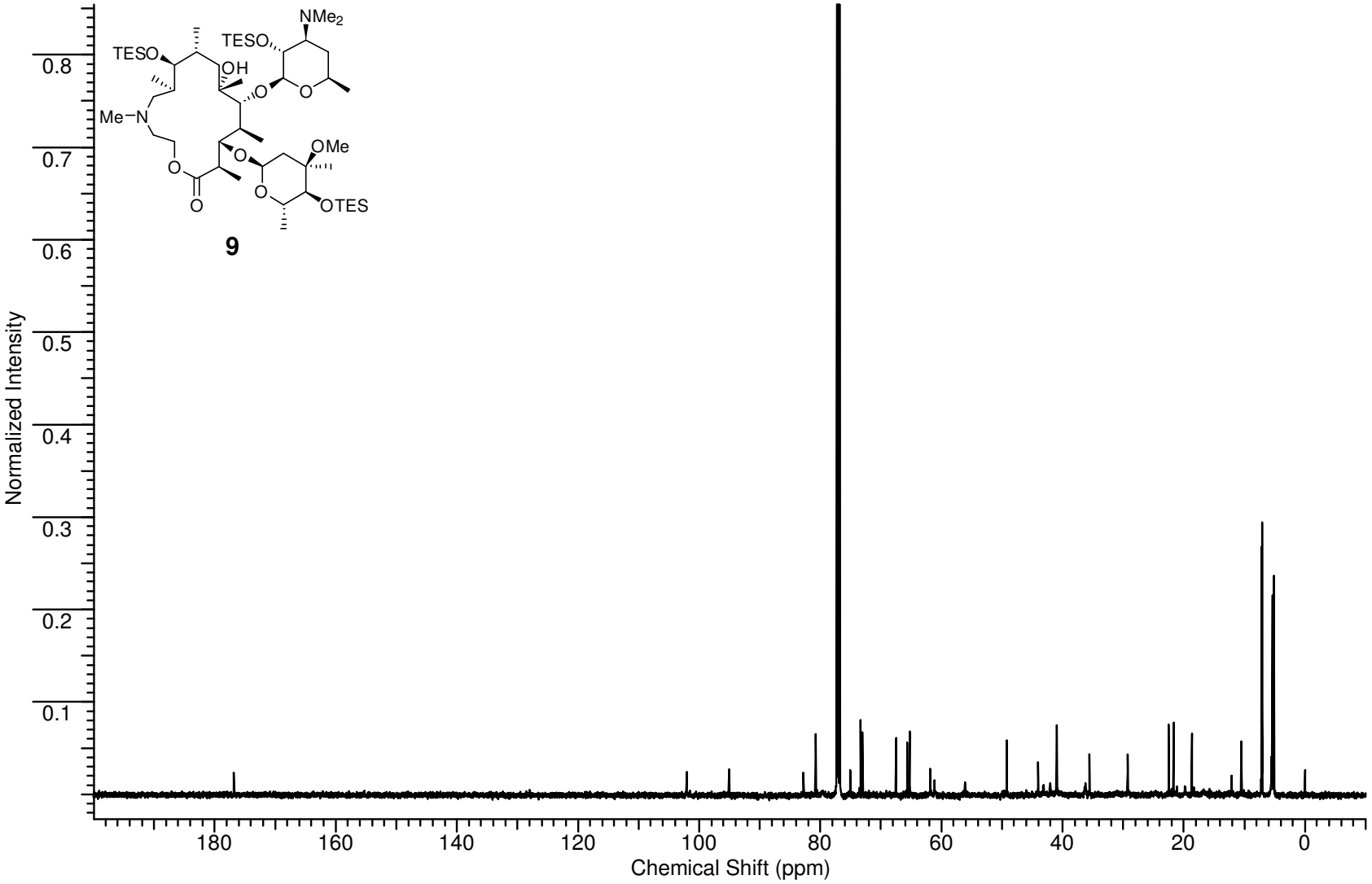
$^{13}$C NMR Spectrum of **8**



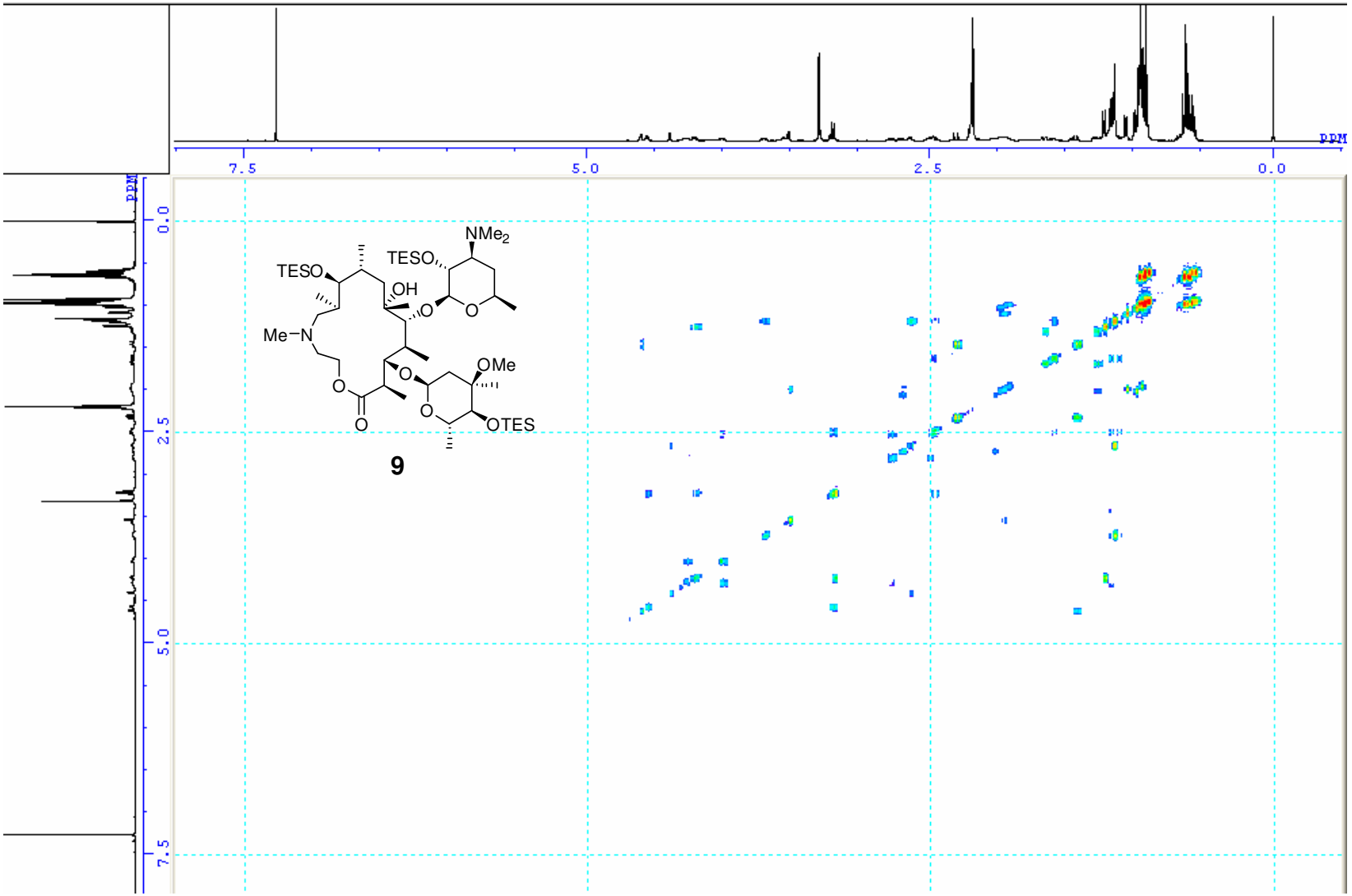
$^{1}$H NMR Spectrum of **9**



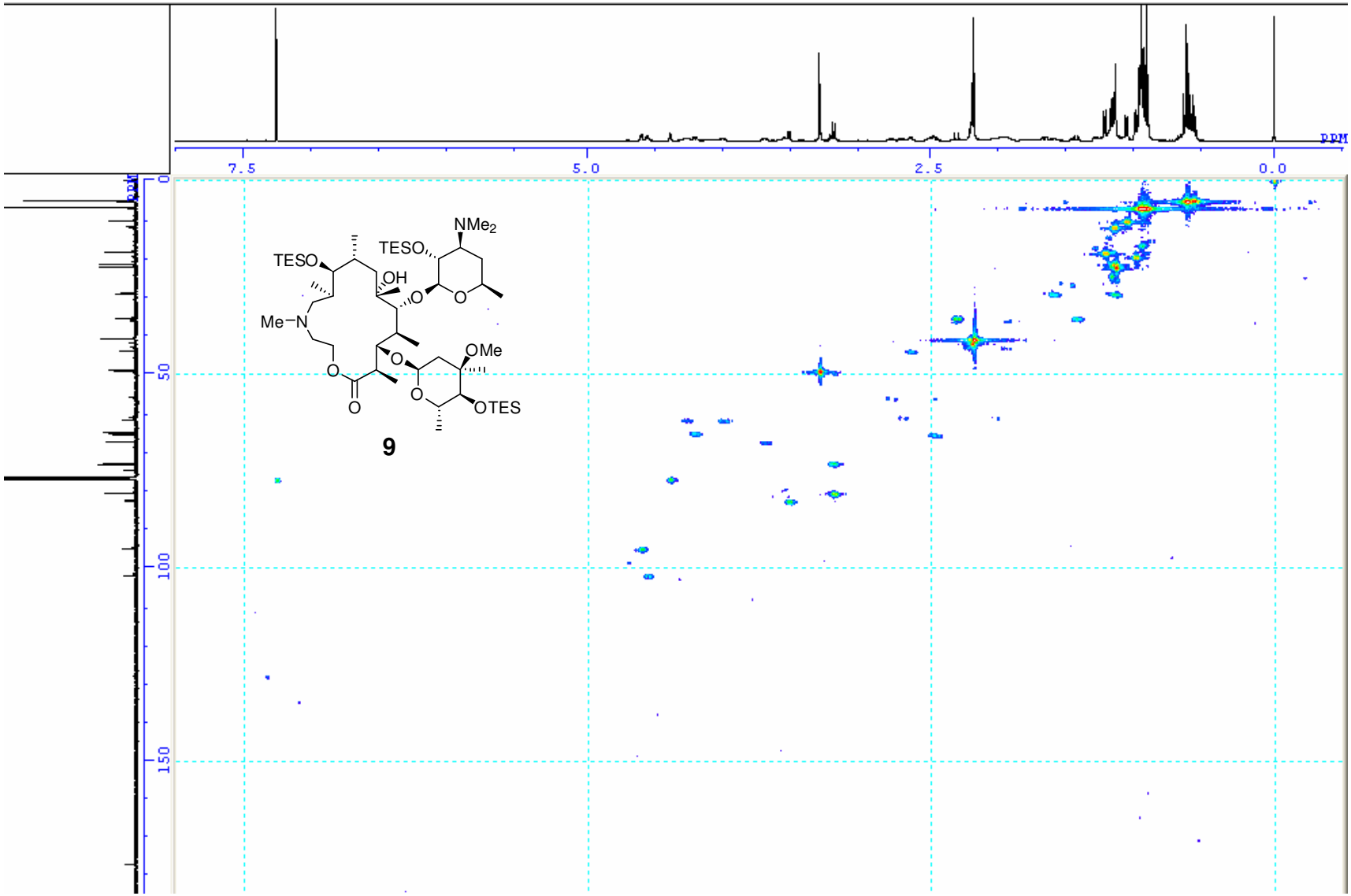
$^{13}$C NMR Spectrum of **9**



COSY Spectrum of **9**

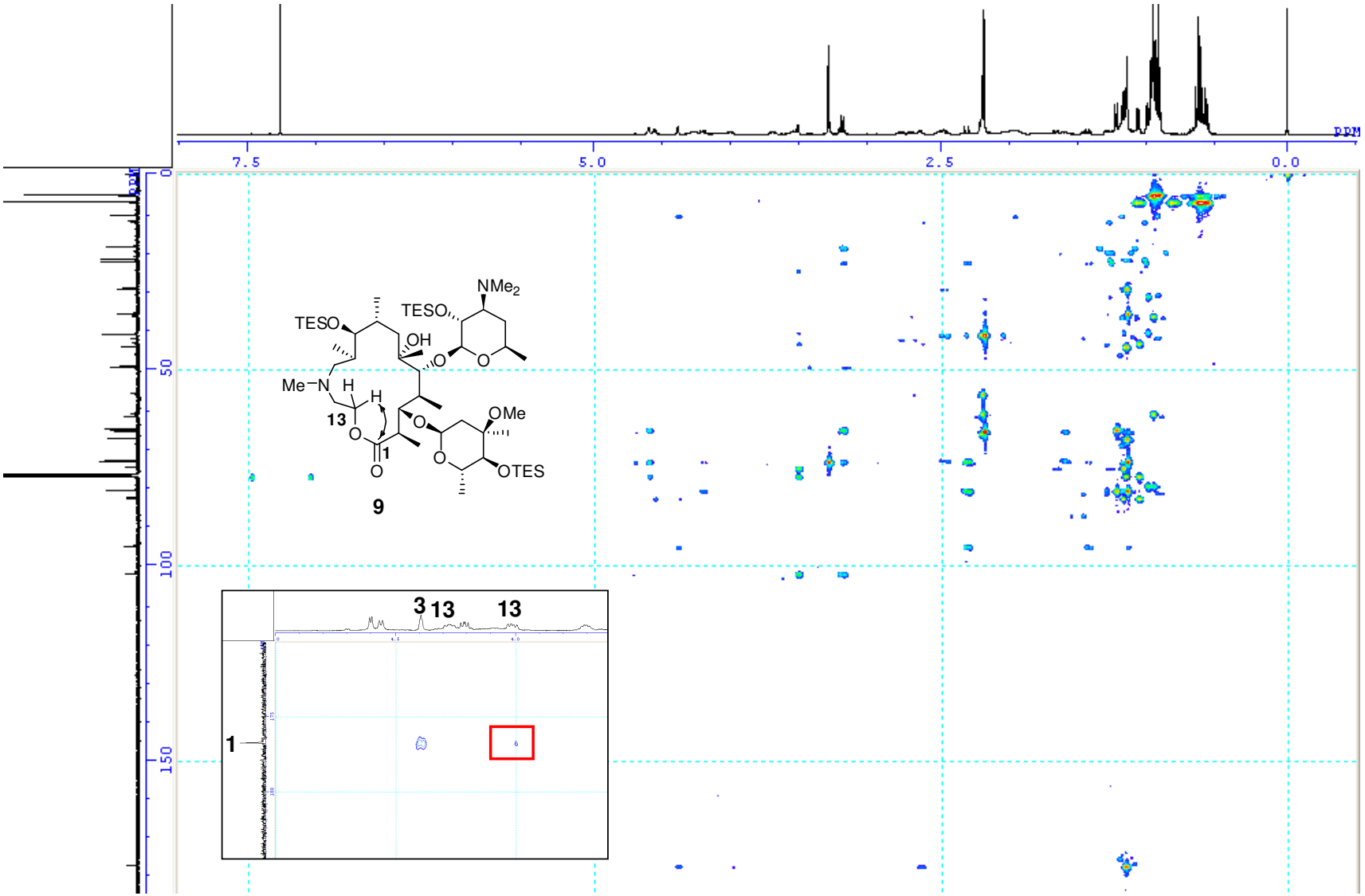


HMQC Spectrum of **9**

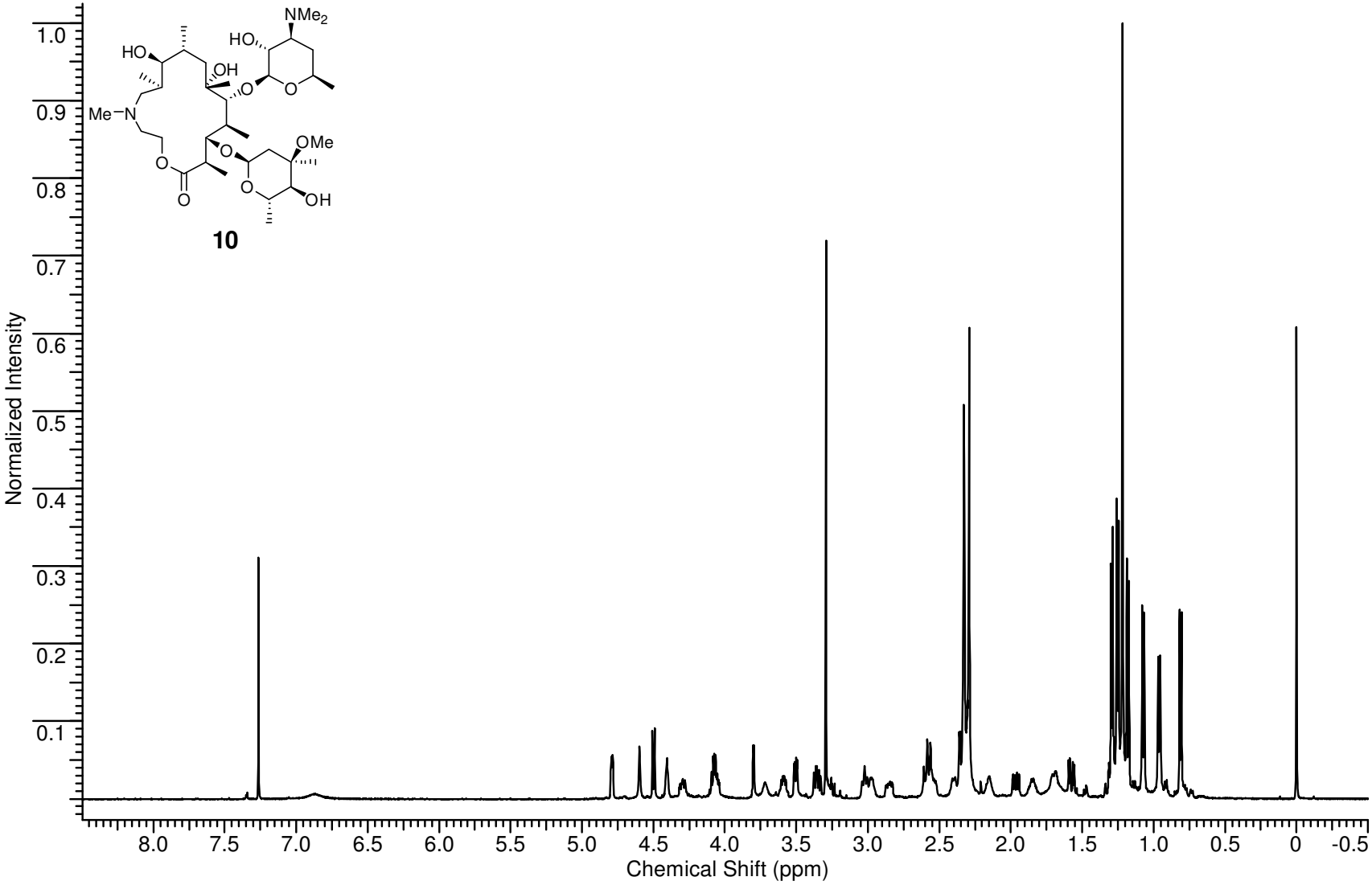



**9**

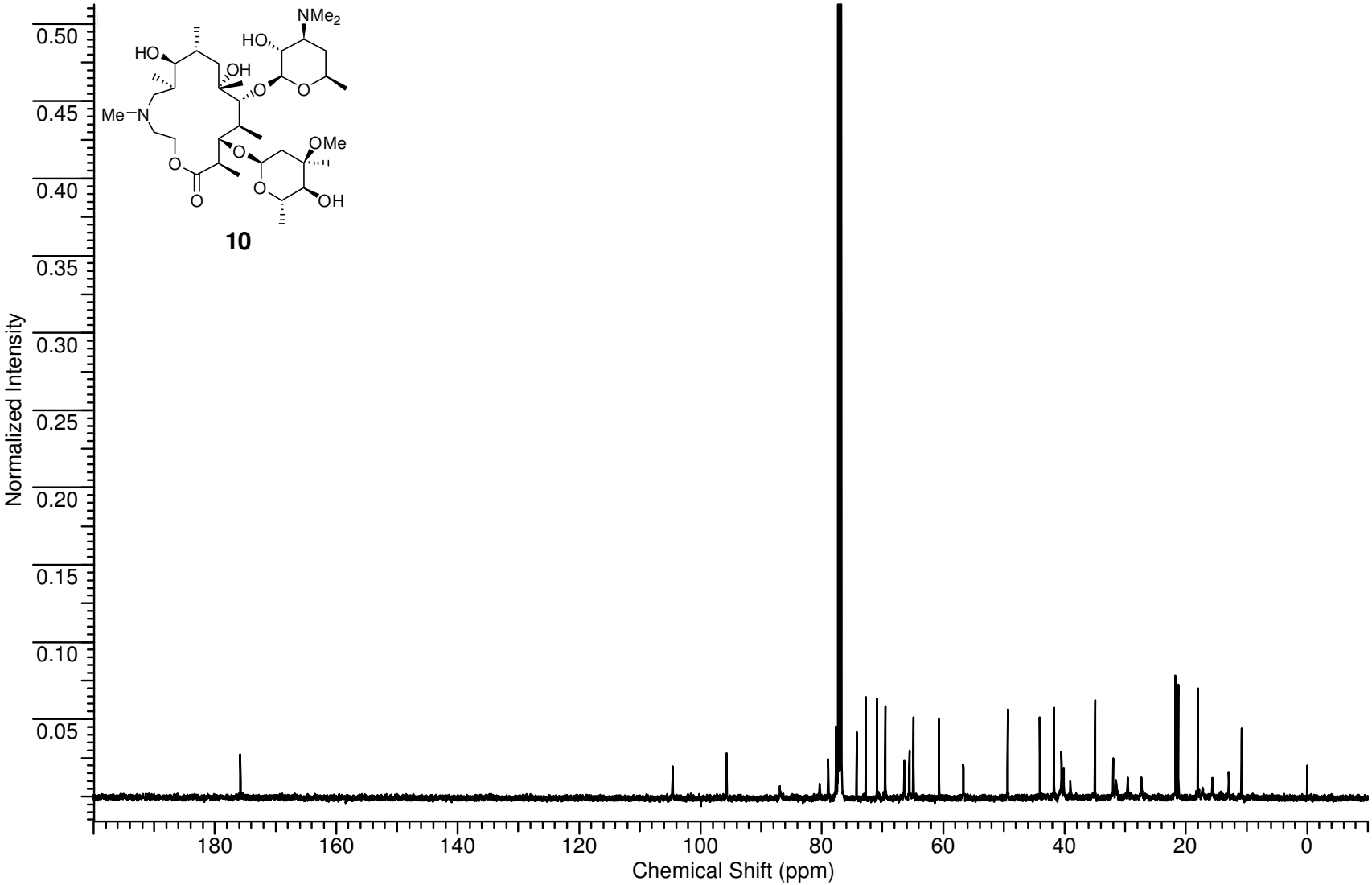
HMBC Spectrum of **9**



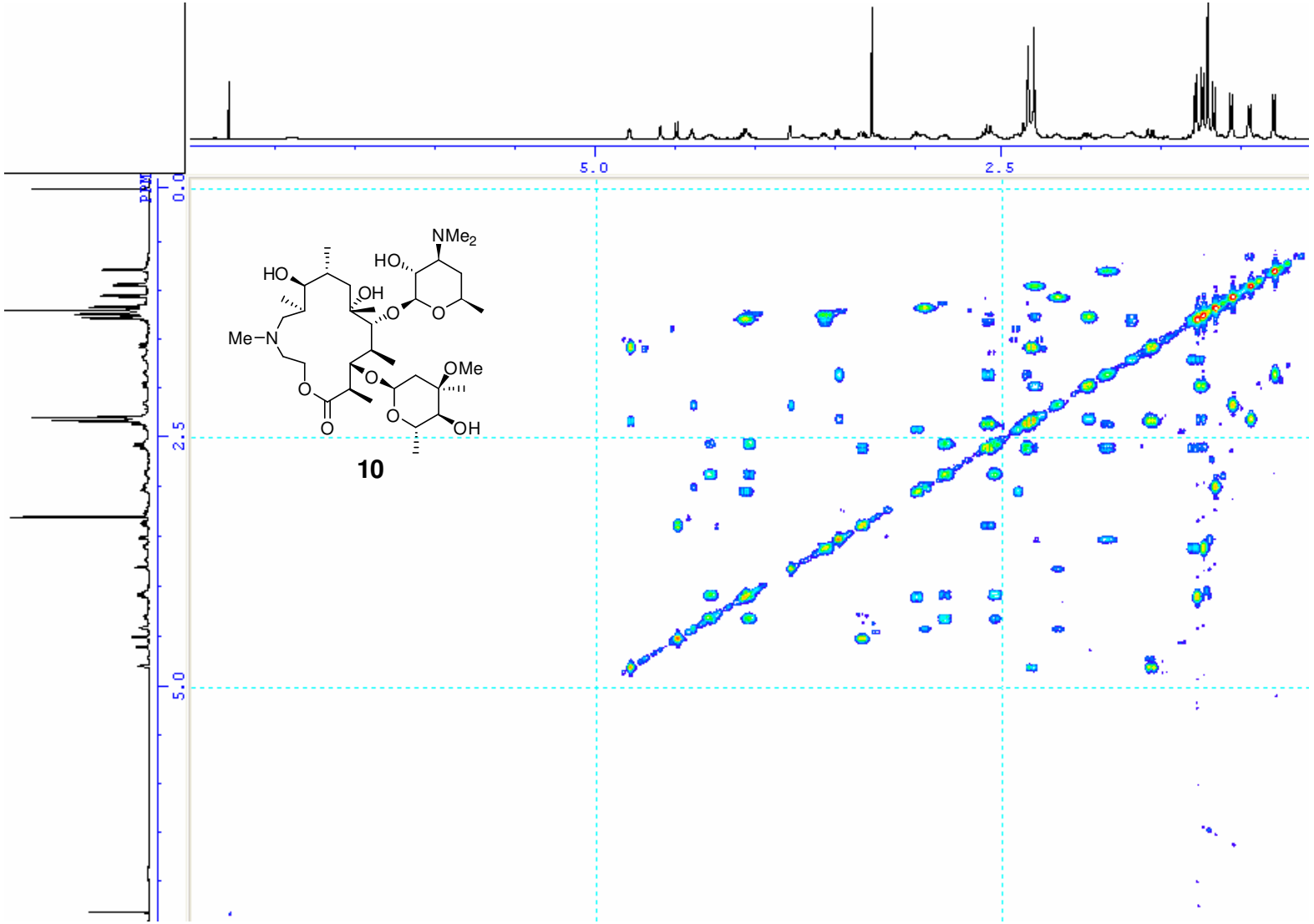
$^{1}$H NMR Spectrum of **10**



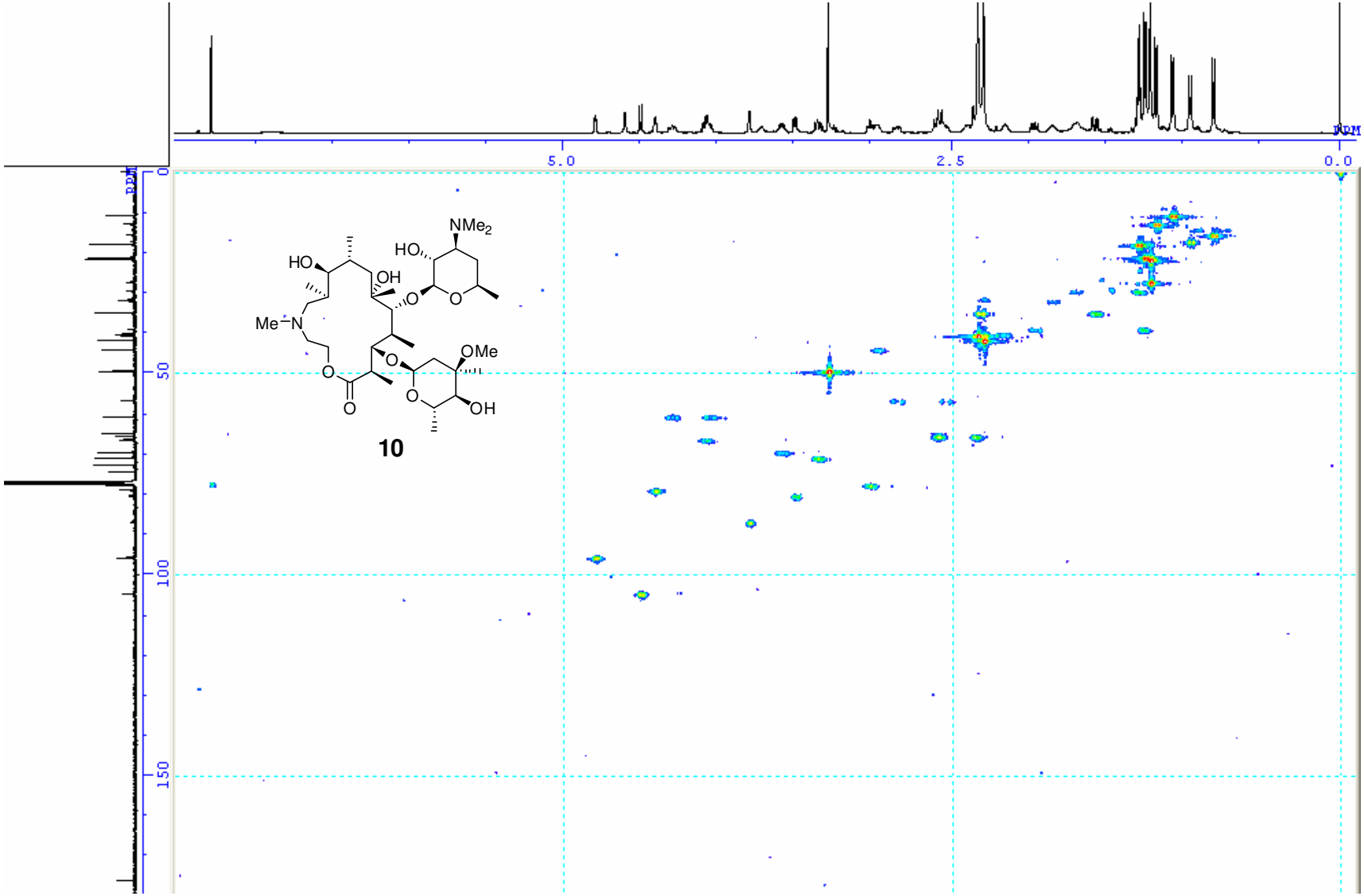
$^{13}$C NMR Spectrum of **10**



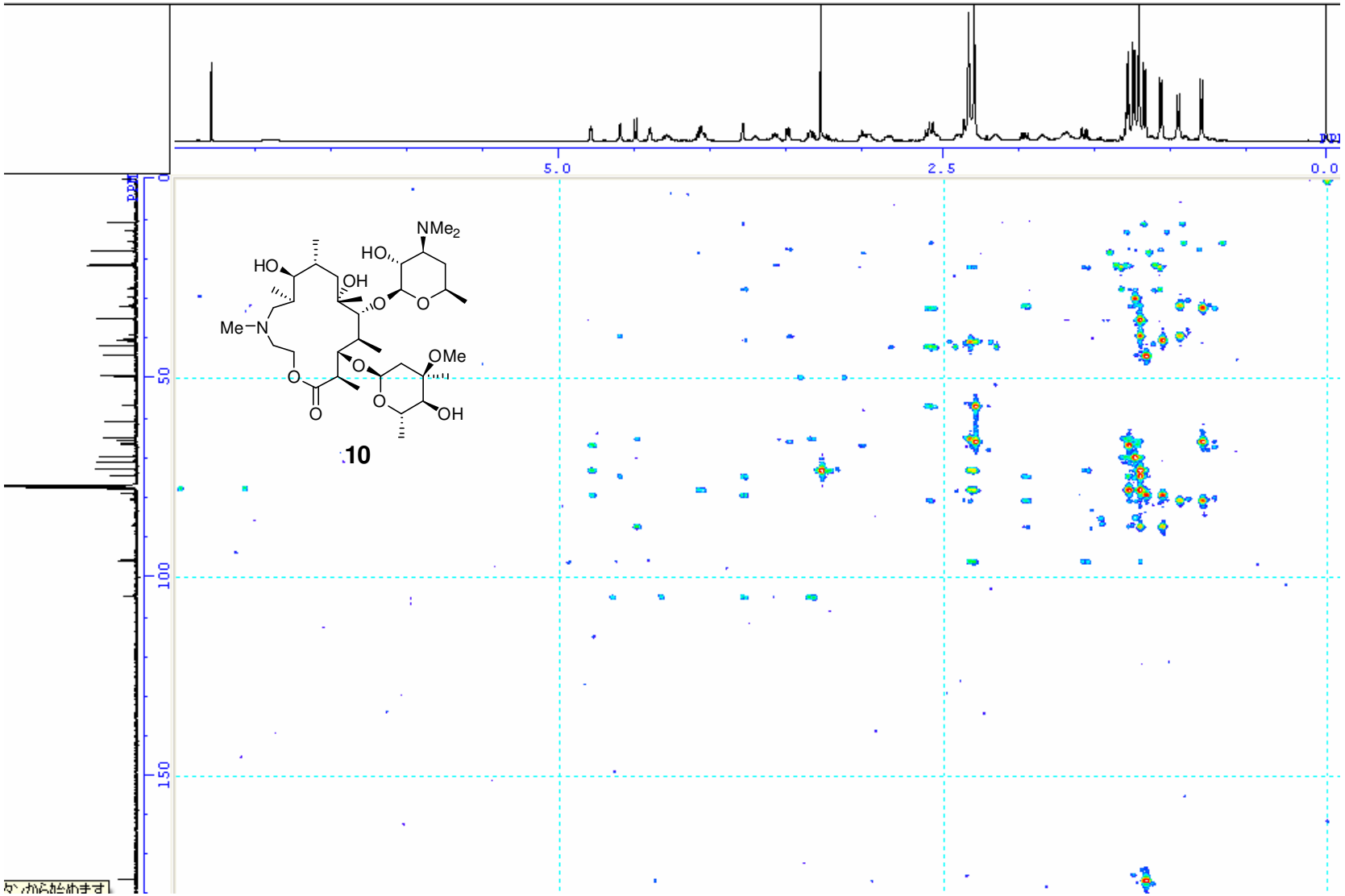
COSY Spectrum of **10**



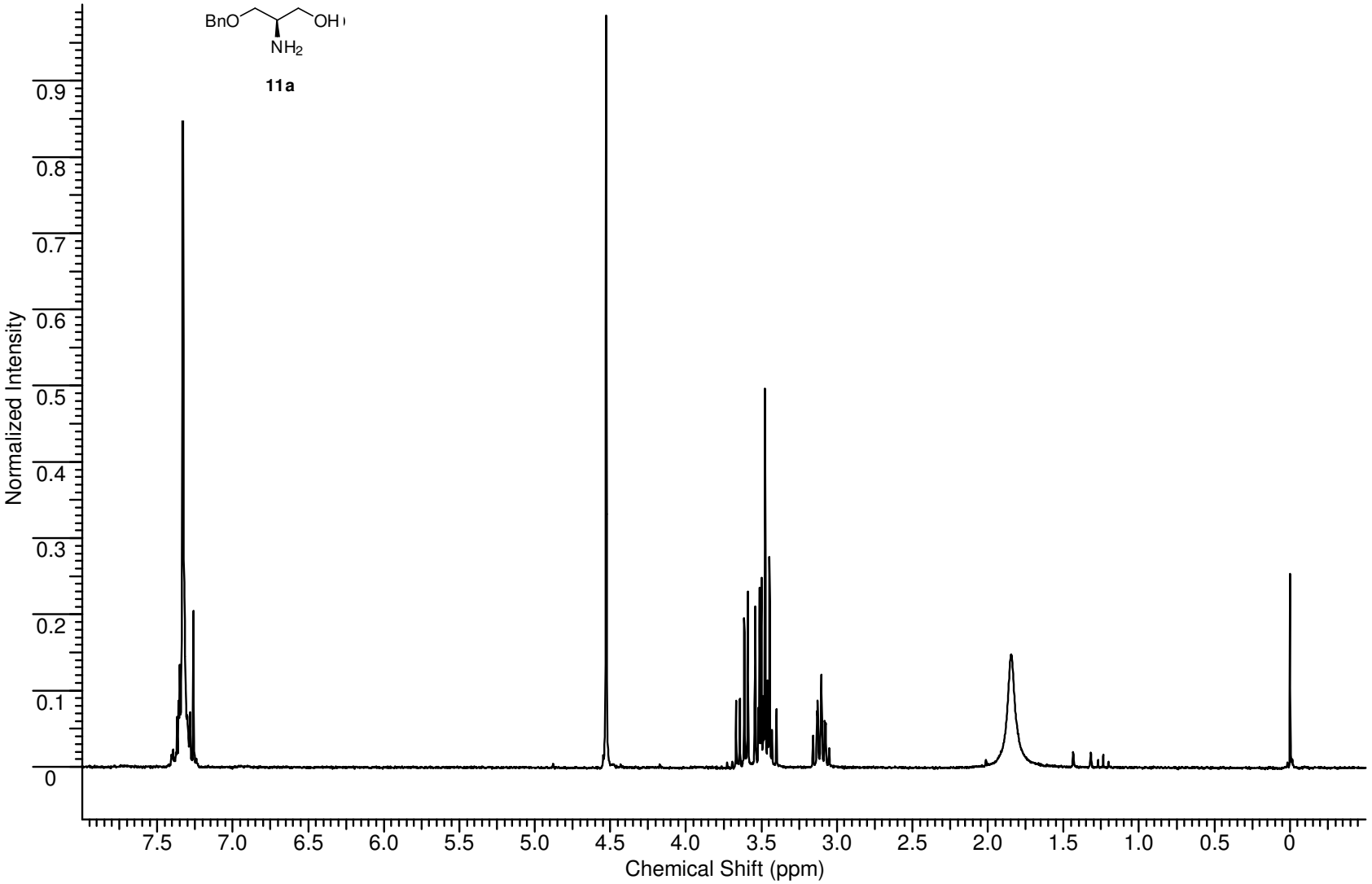
HMQC Spectrum of **10**



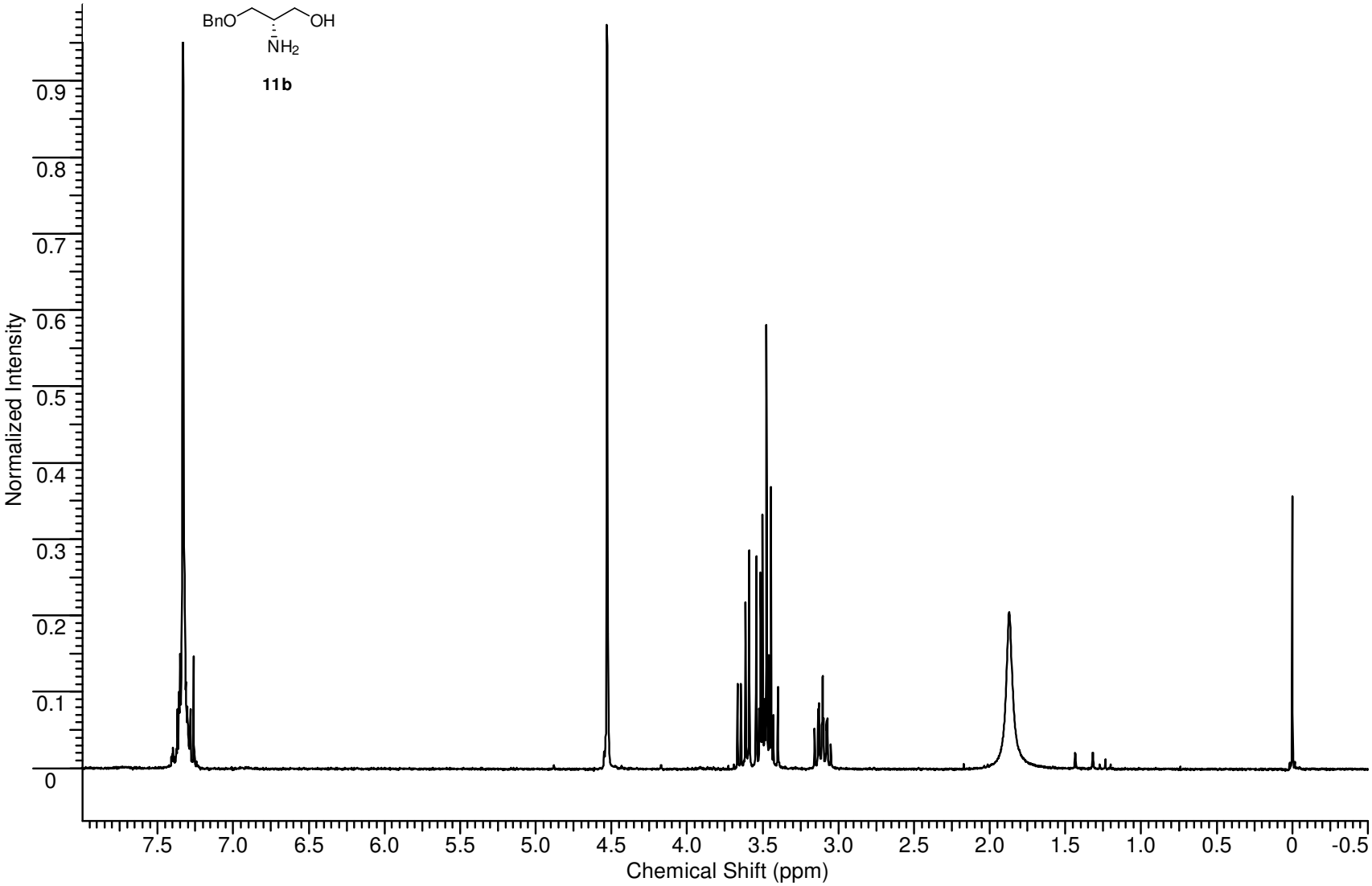
HMBC Spectrum of **10**



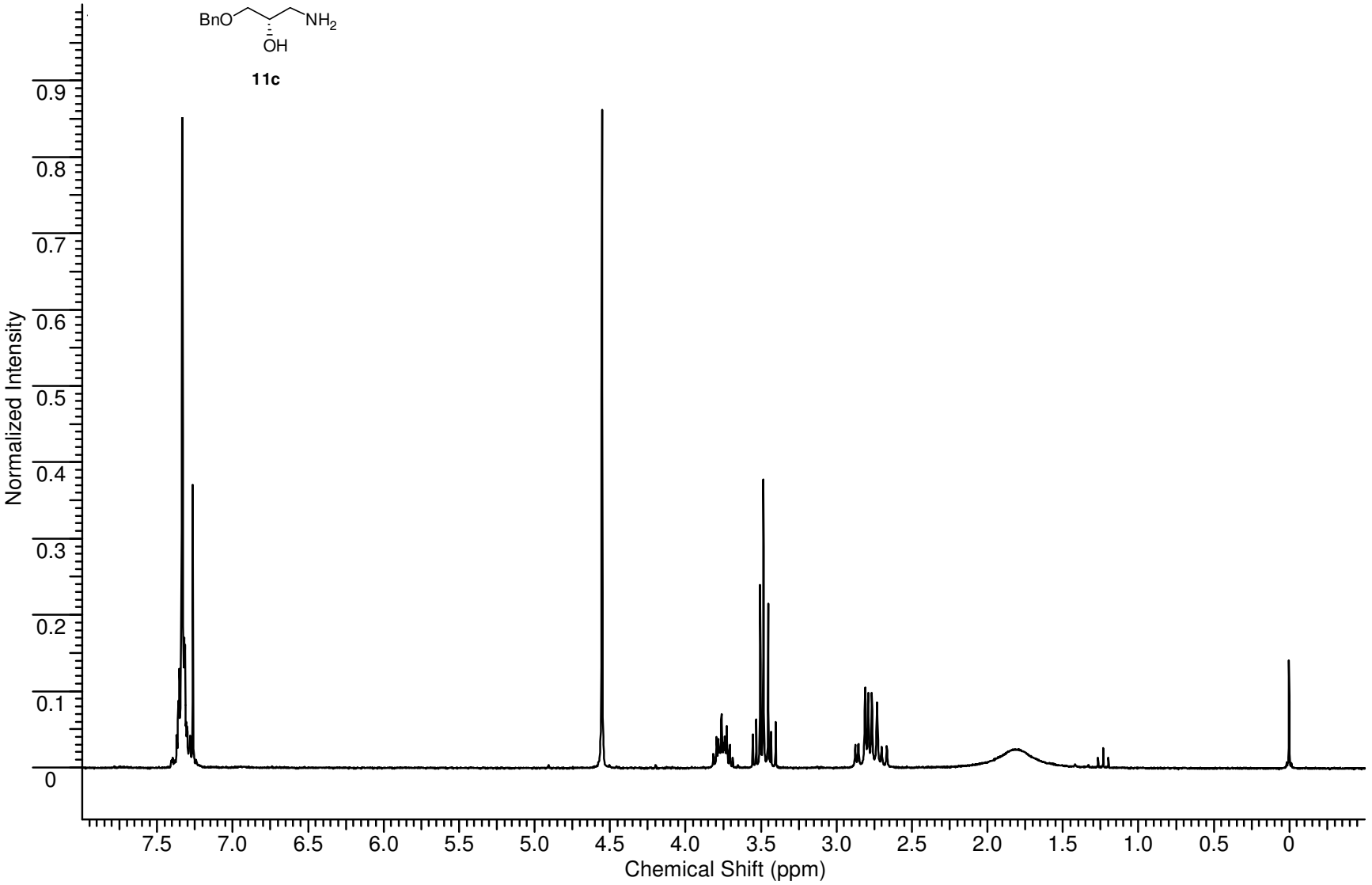
$^{1}$H NMR Spectrum of **11a**



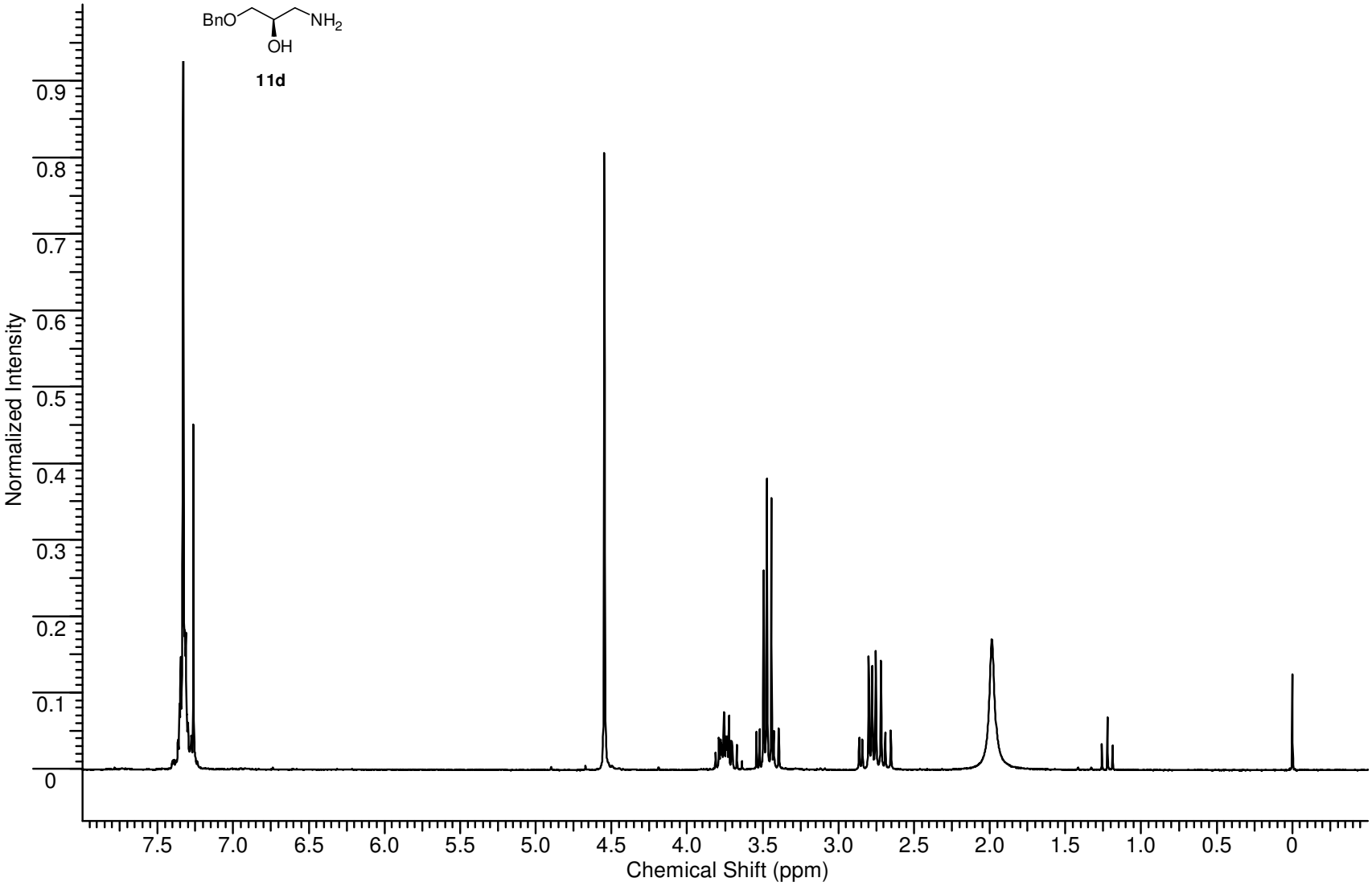
$^{1}$H NMR Spectrum of **11b**



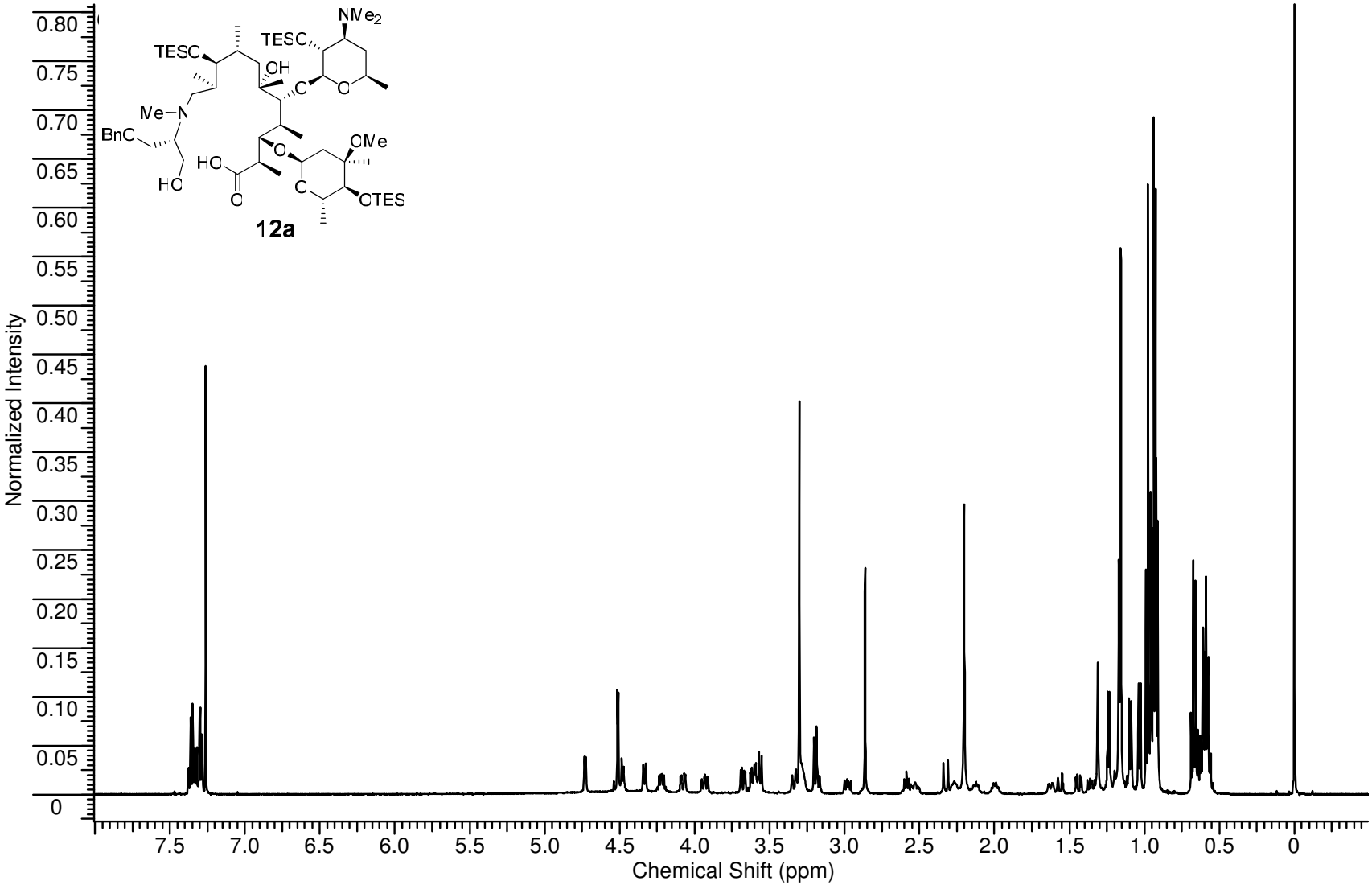
$^{1}$H NMR Spectrum of **11c**



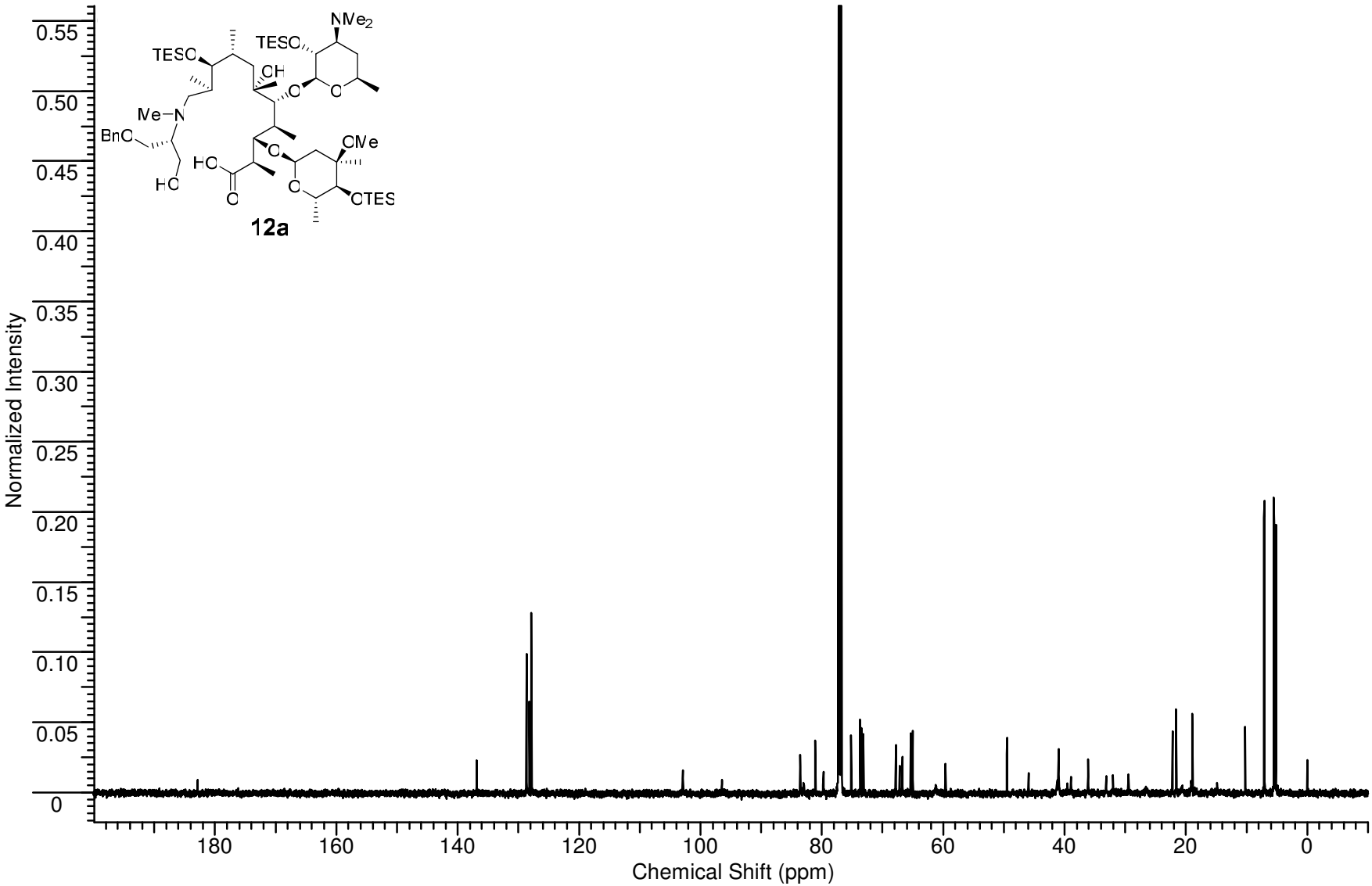
$^{1}$H NMR Spectrum of **11d**



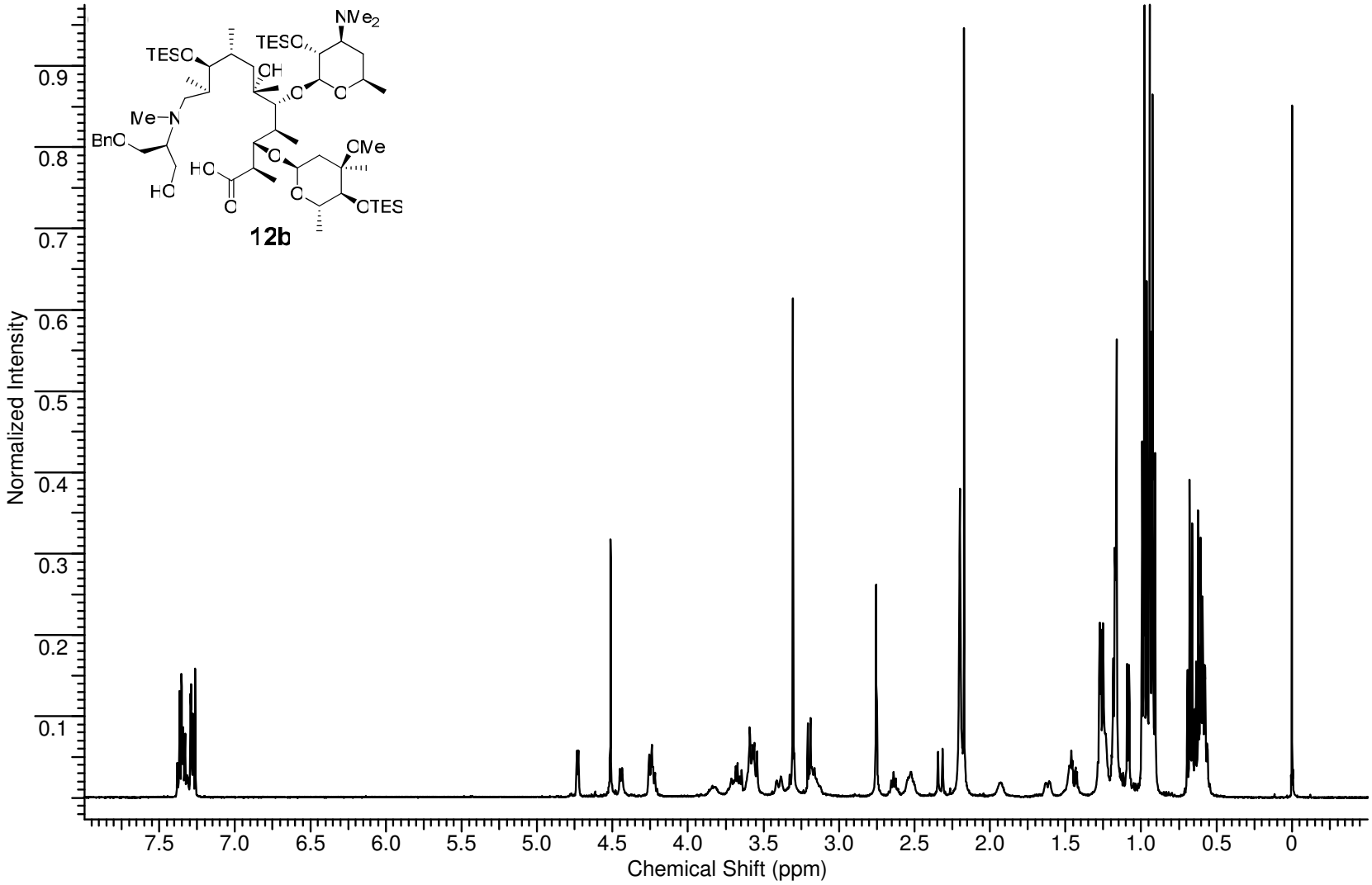
$^{1}$H NMR Spectrum of **12a**



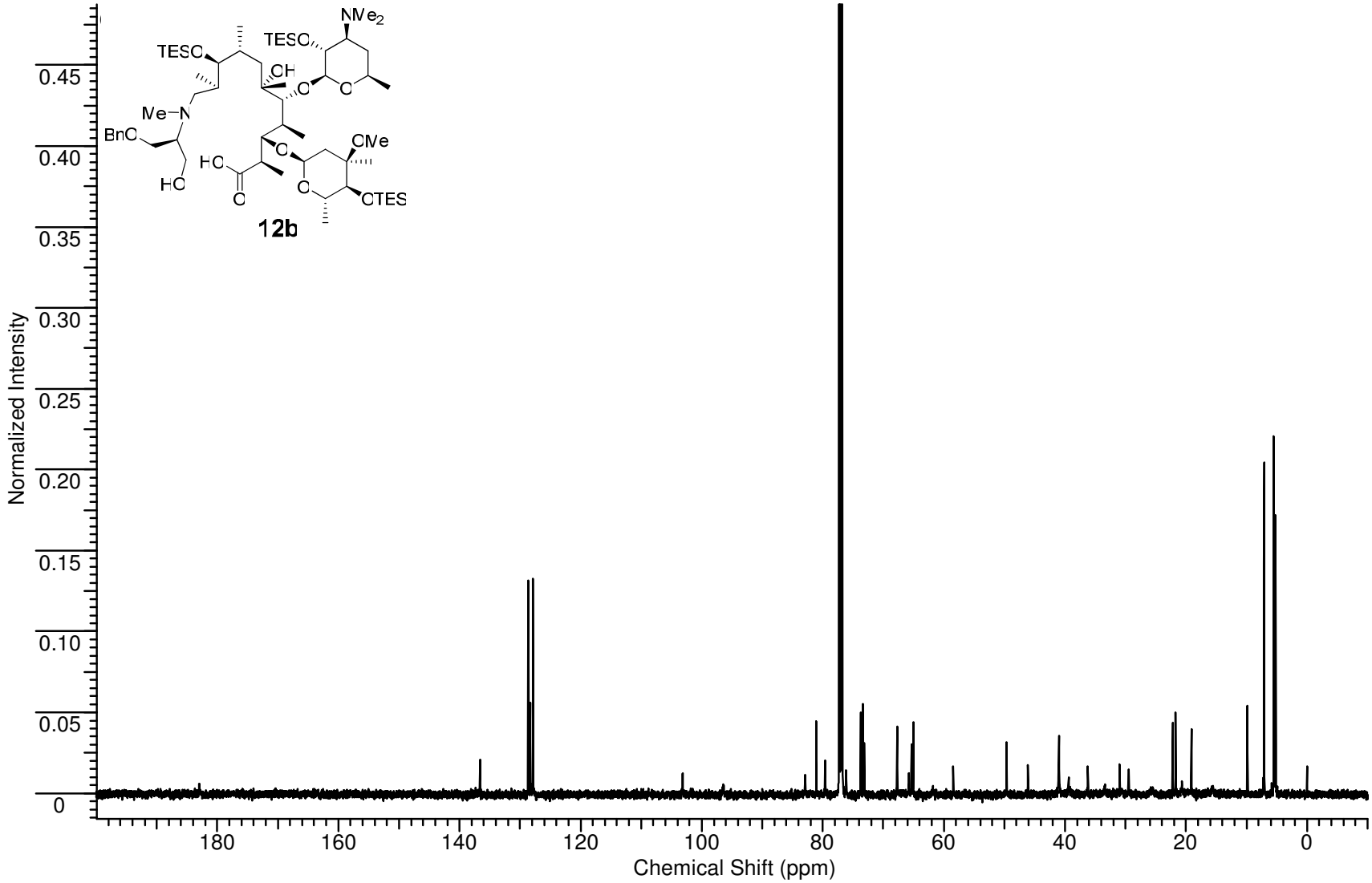
$^{13}$C NMR Spectrum of **12a**



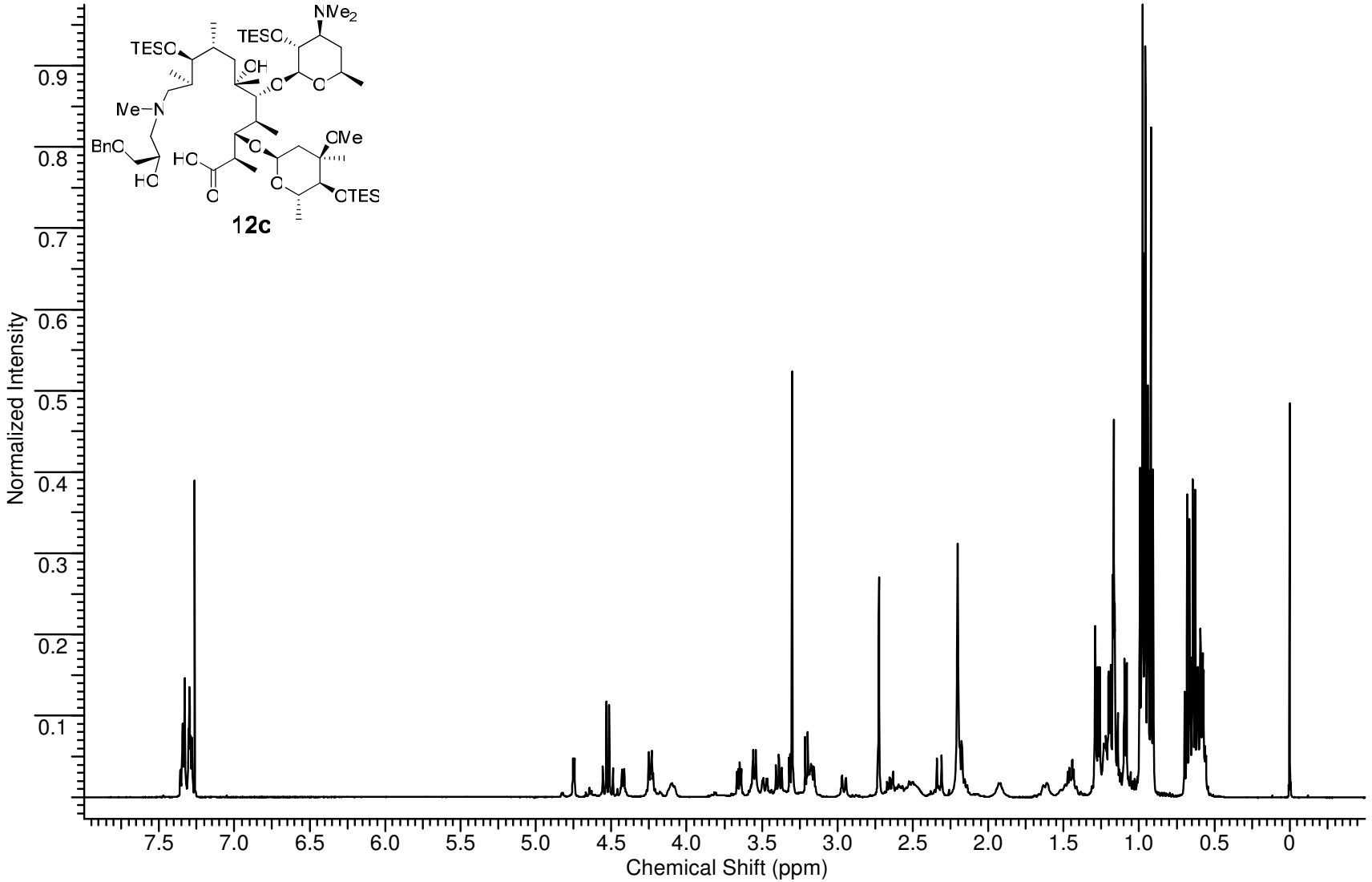
$^{1}$H NMR Spectrum of **12b**



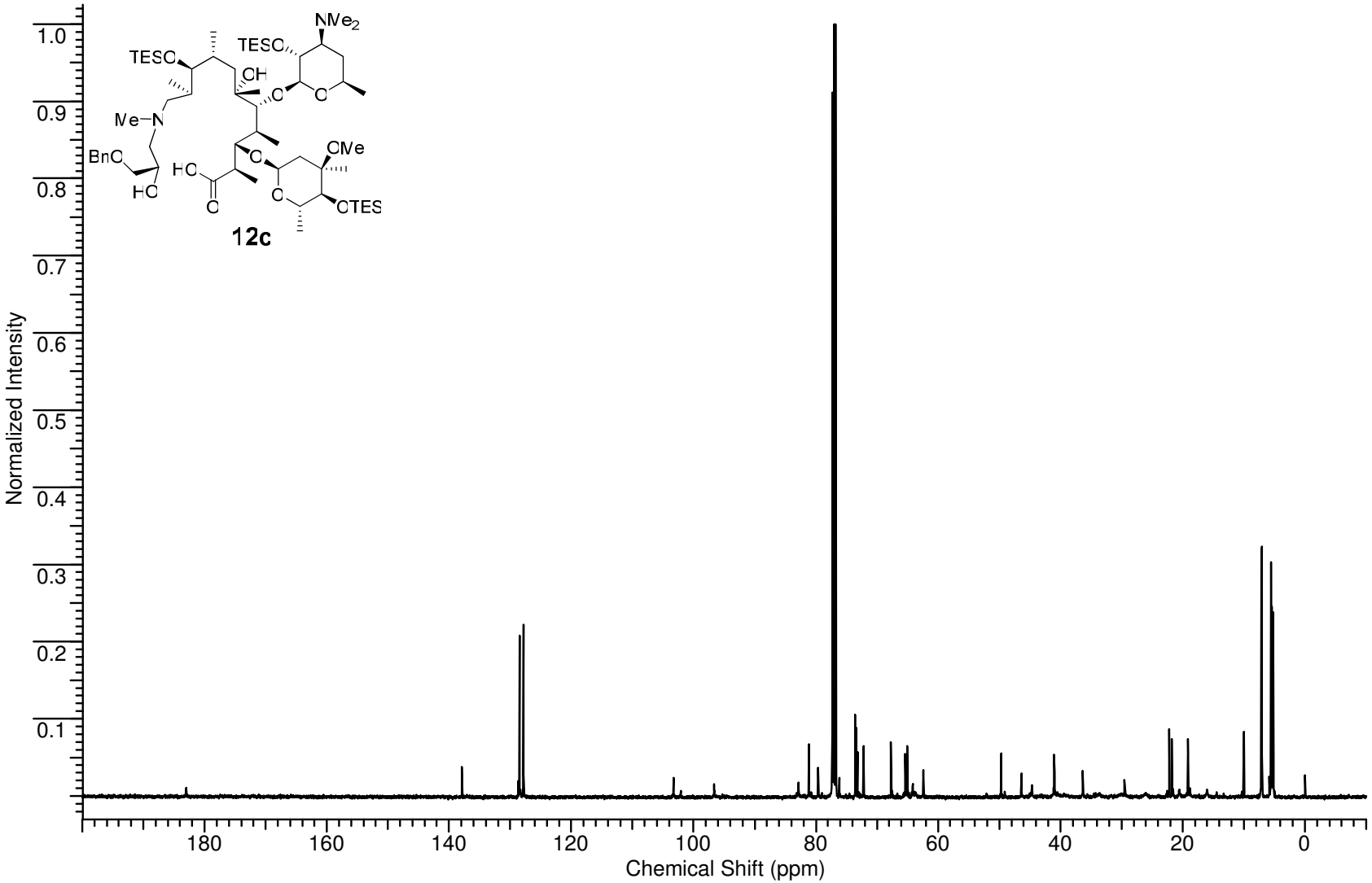
$^{13}$C NMR Spectrum of **12b**



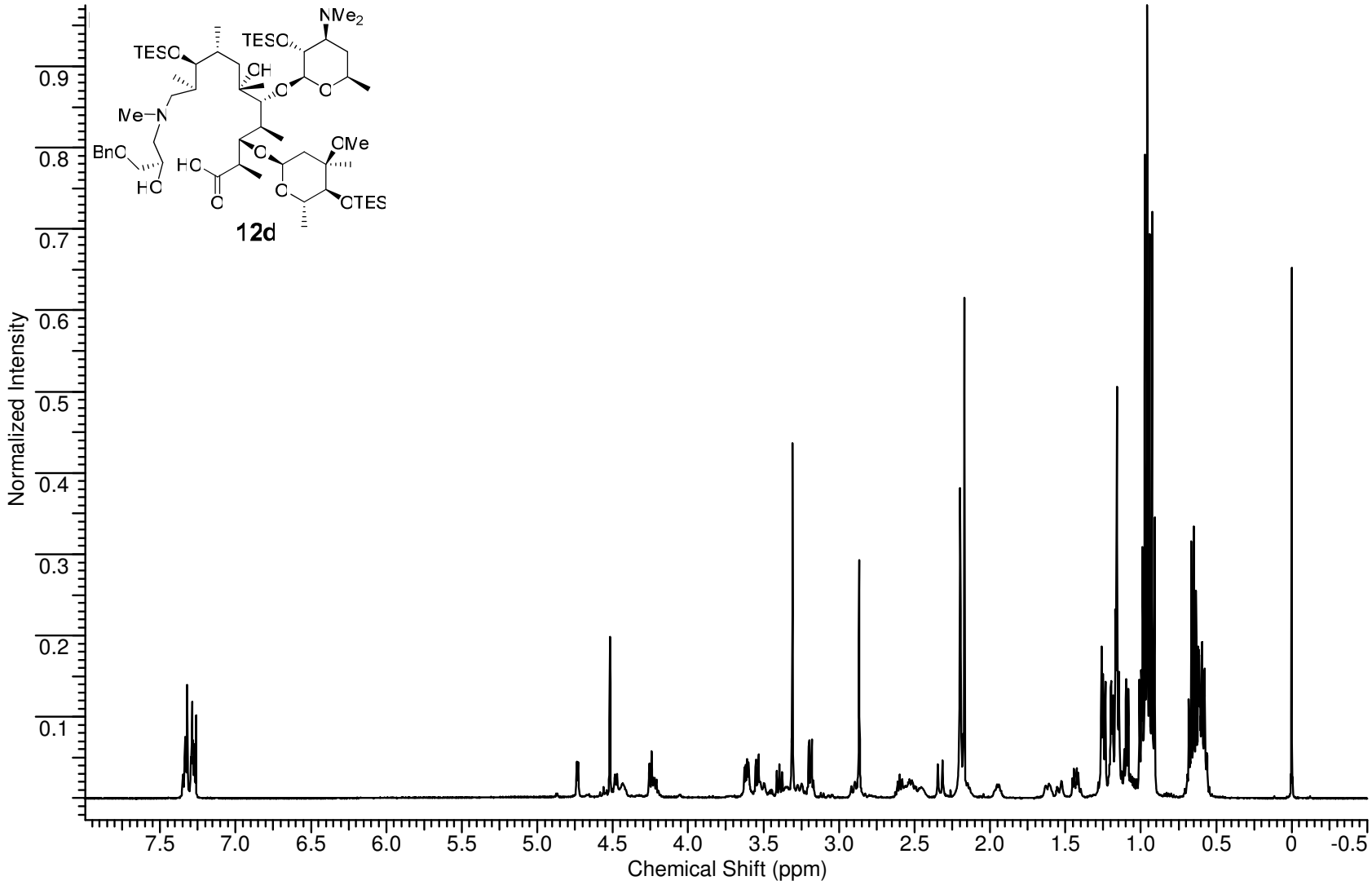
$^{1}$H NMR Spectrum of **12c**



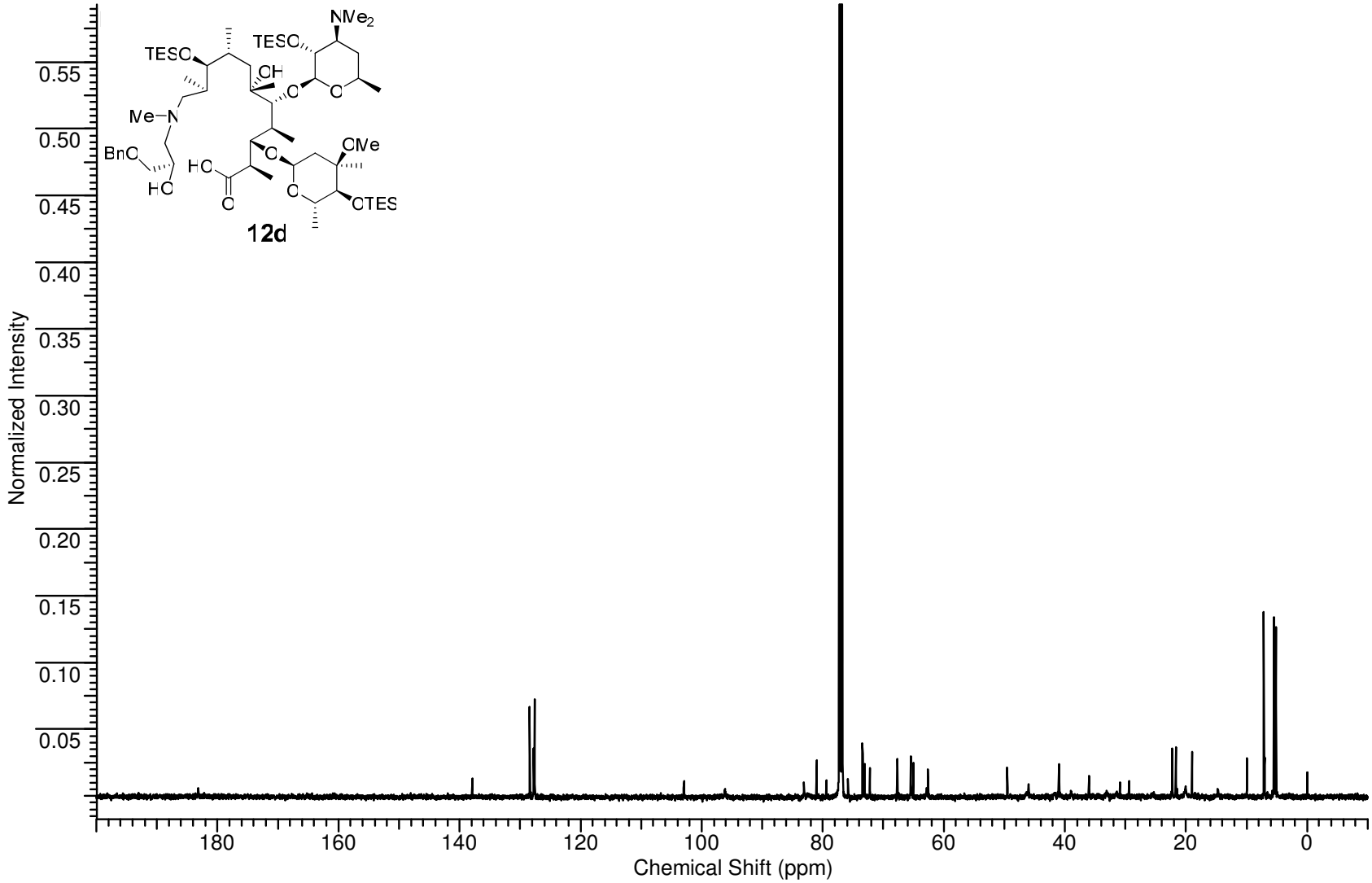
$^{13}$C NMR Spectrum of **12c**



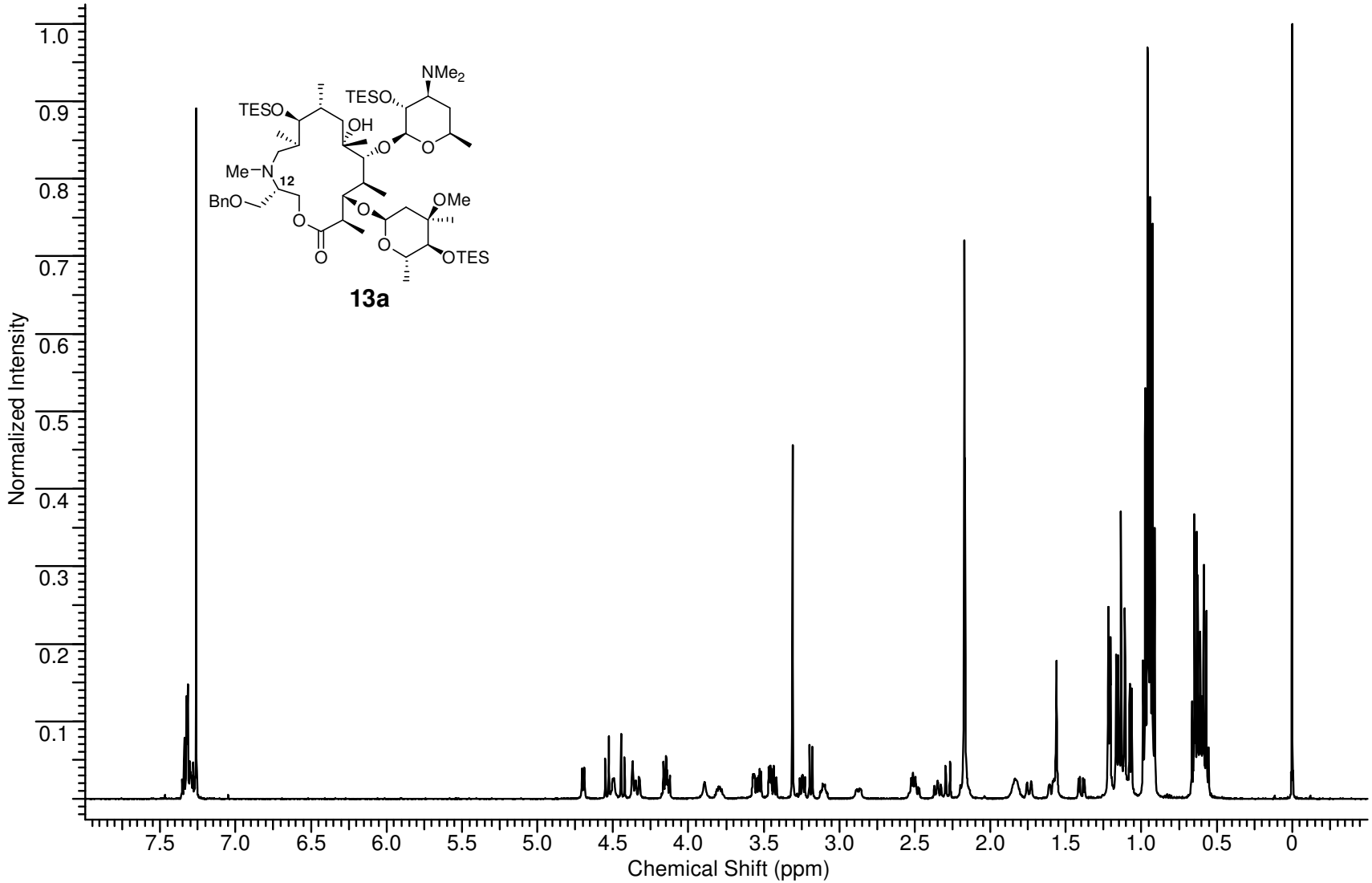
$^{1}$H NMR Spectrum of **12d**



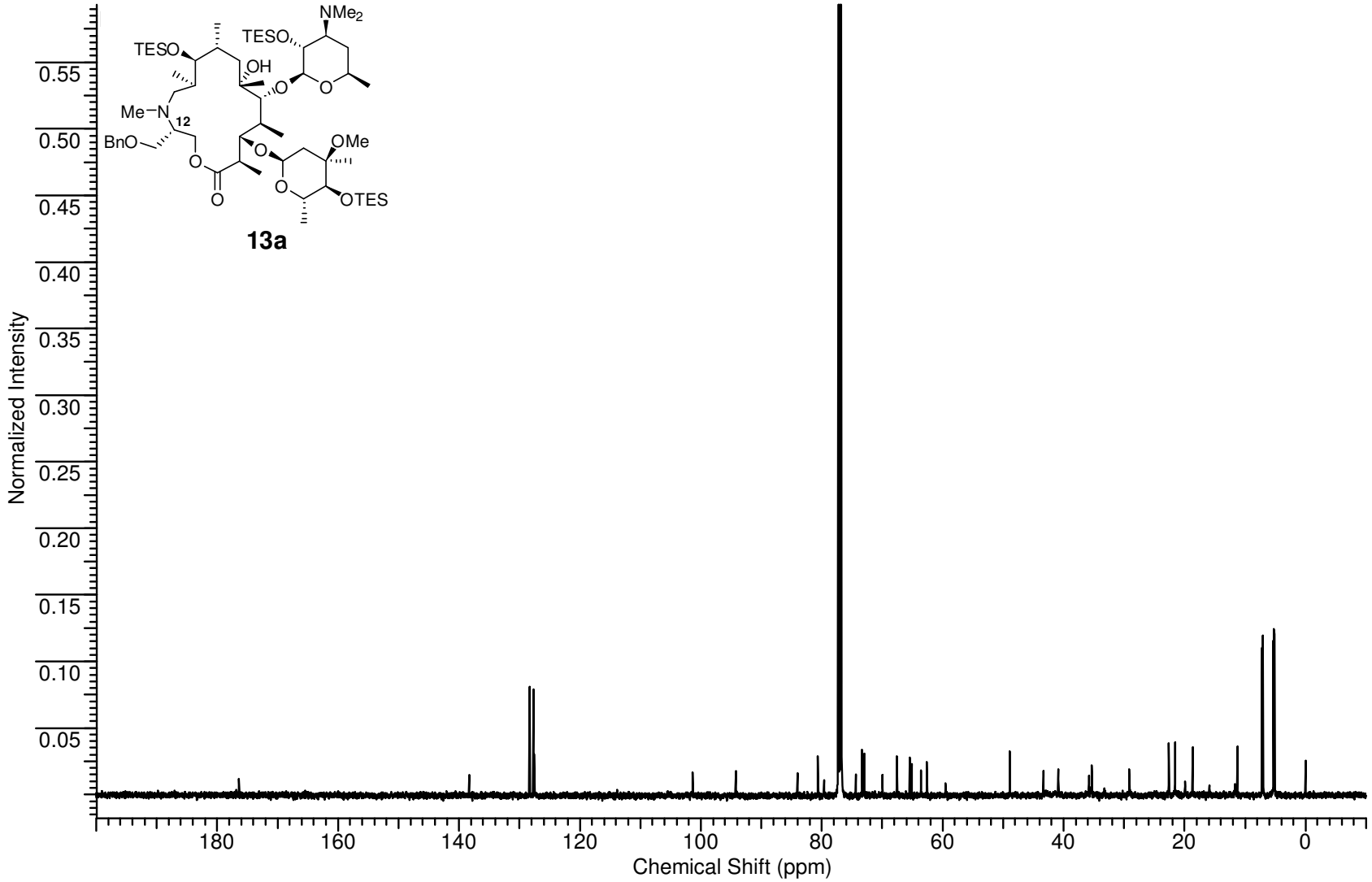
$^{13}$C NMR Spectrum of **12d**



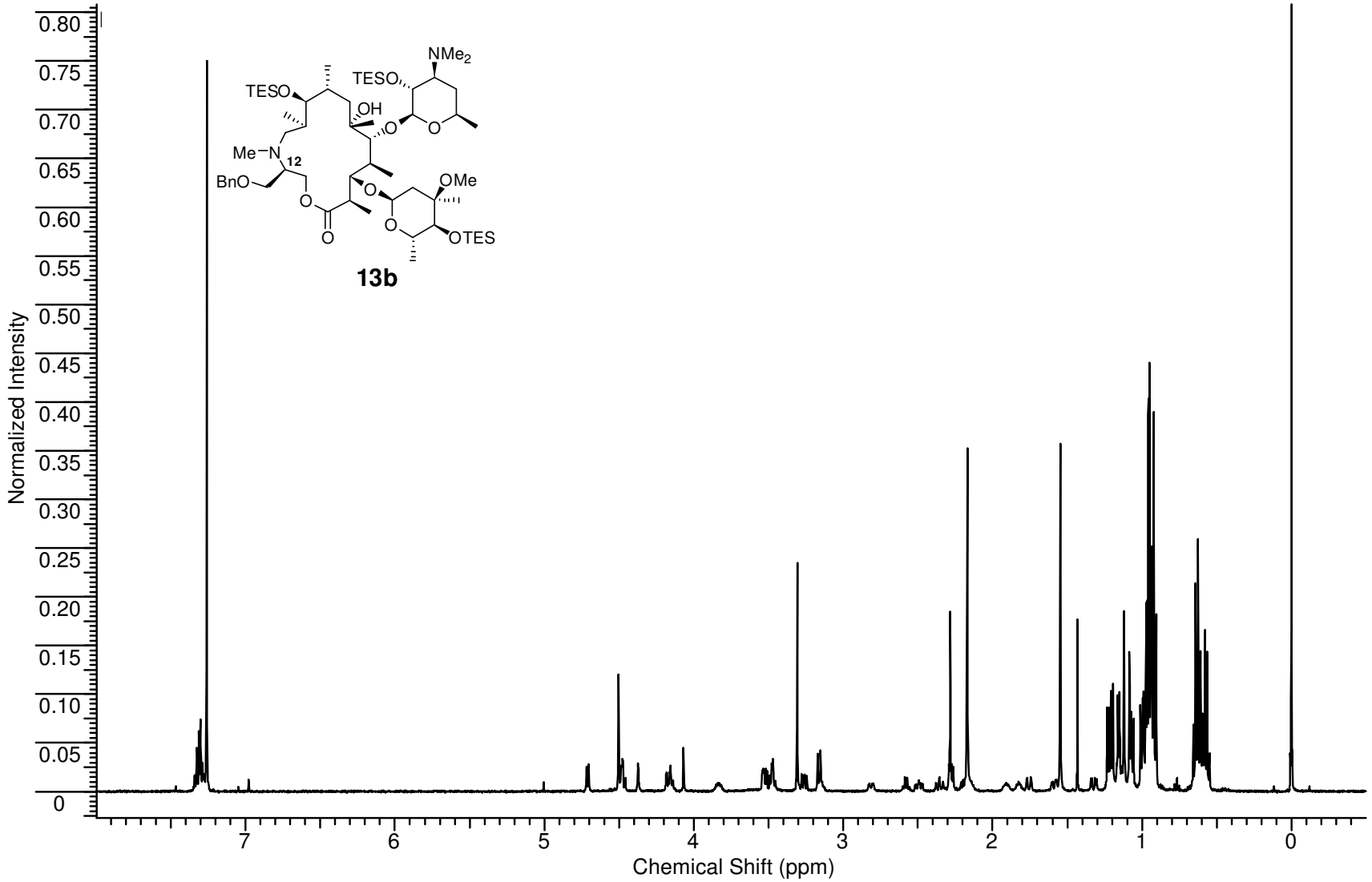
$^{1}$H NMR Spectrum of **13a**



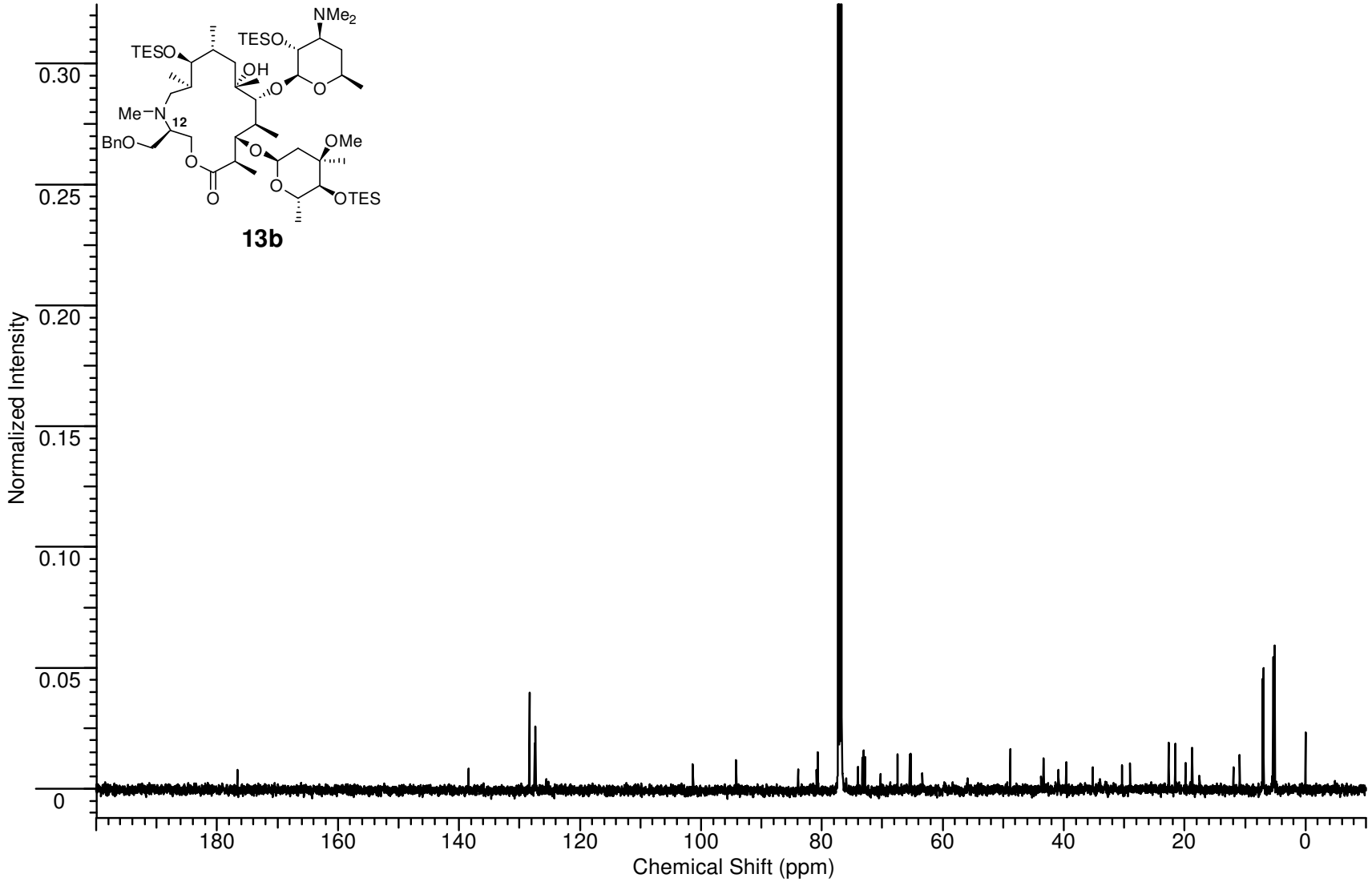
$^{13}$C NMR Spectrum of **13a**



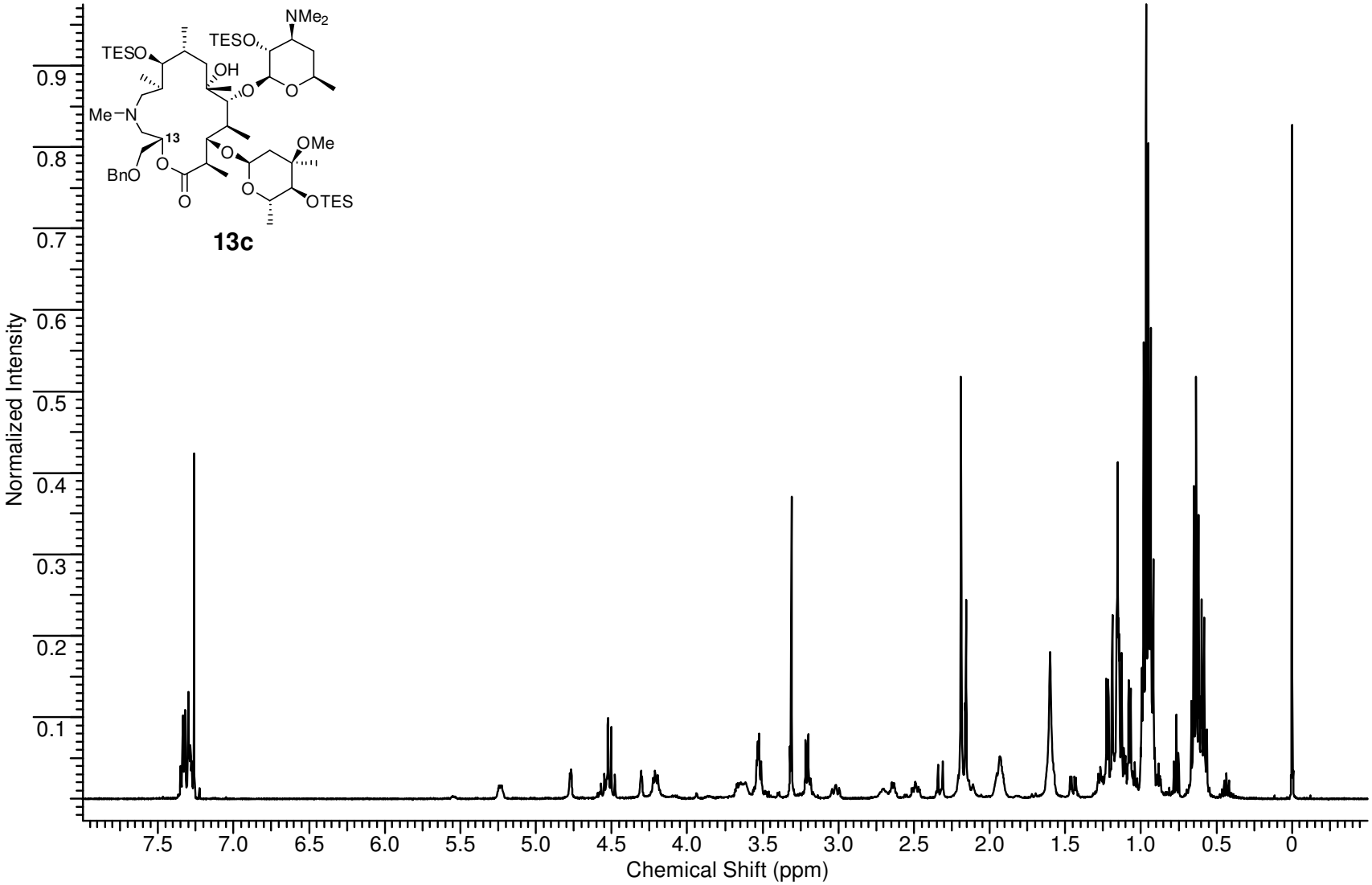
$^{1}$H NMR Spectrum of **13b**



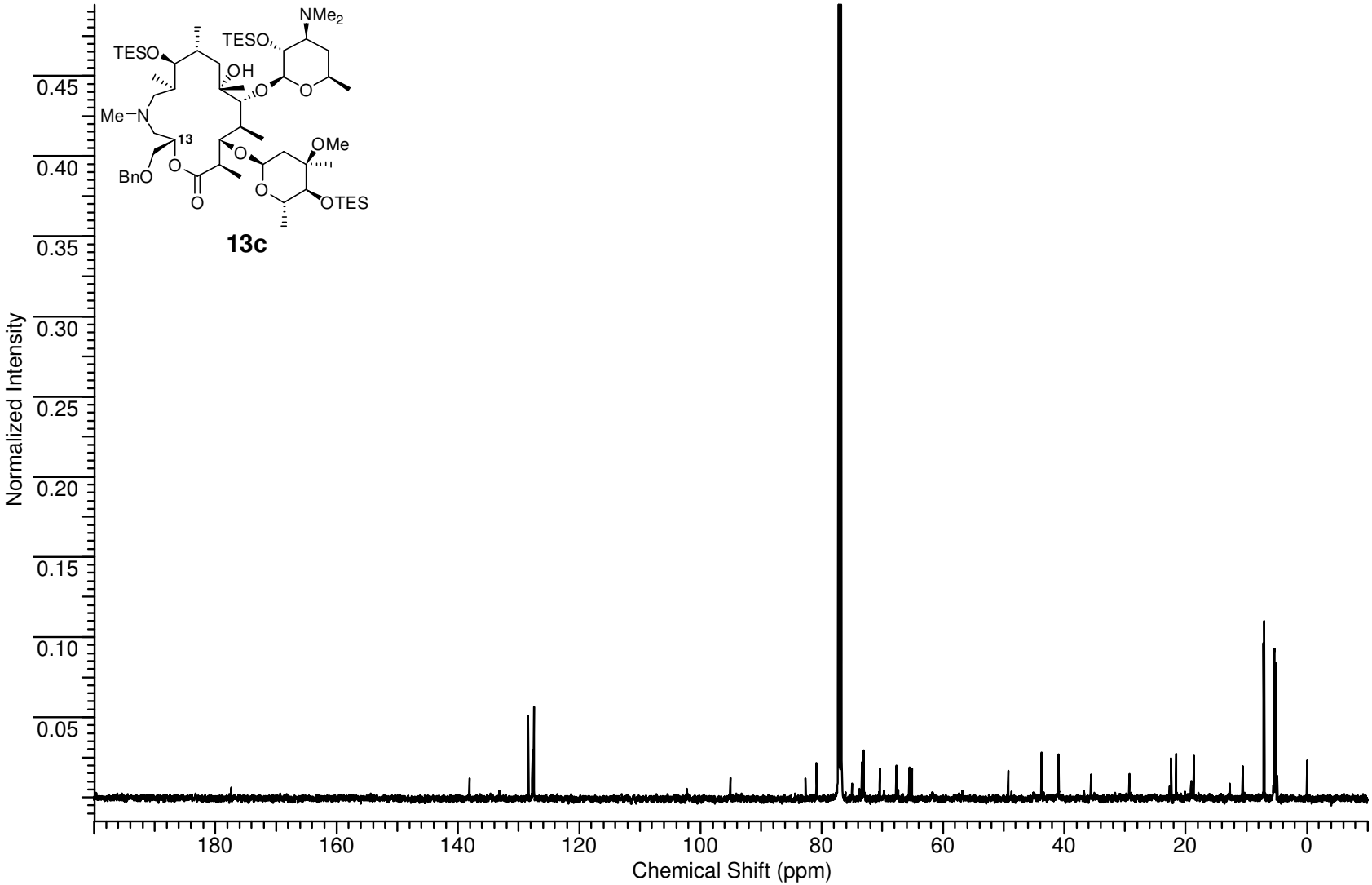
$^{13}$C NMR Spectrum of **13b**



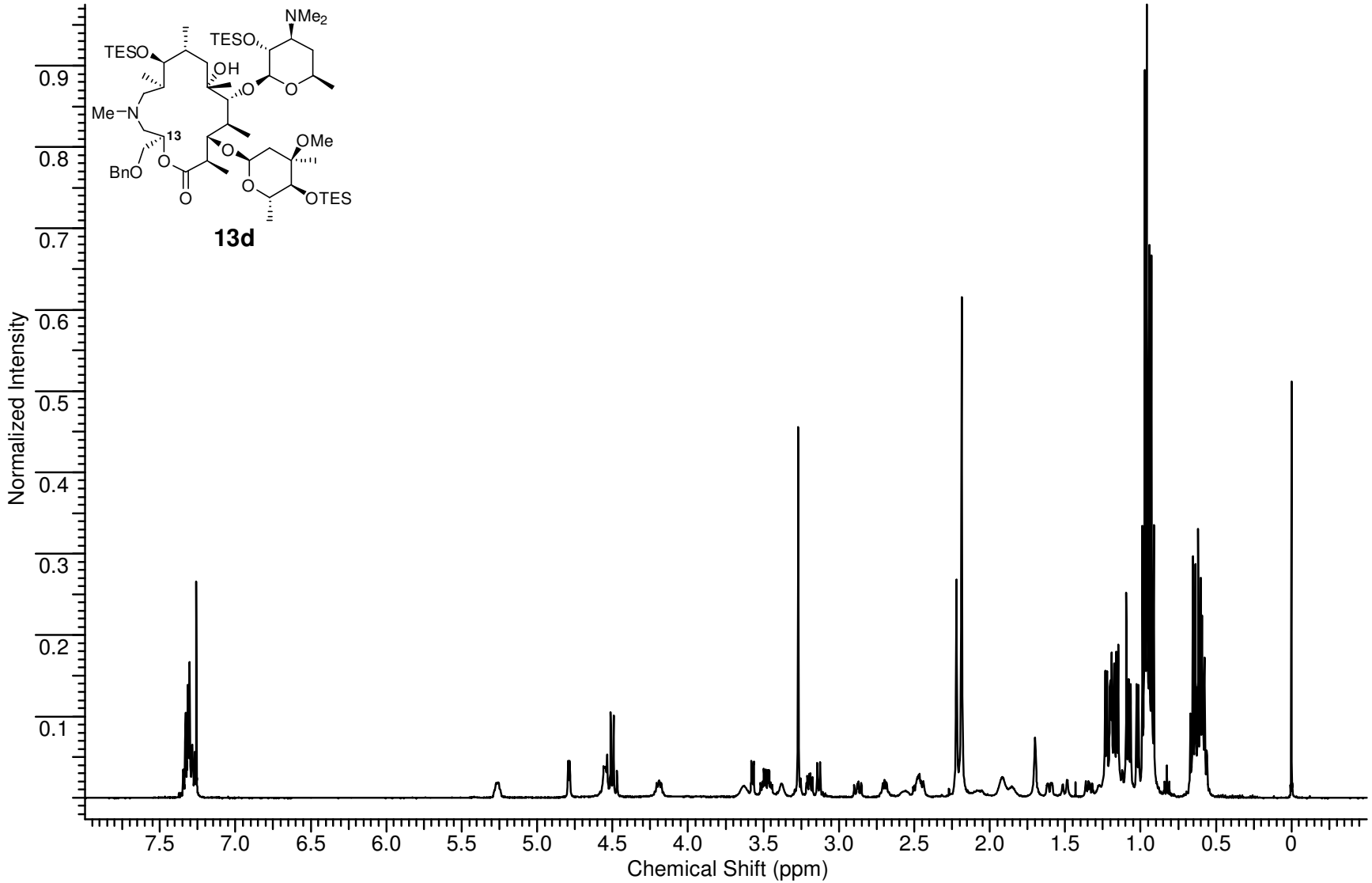
$^{1}$H NMR Spectrum of **13c**



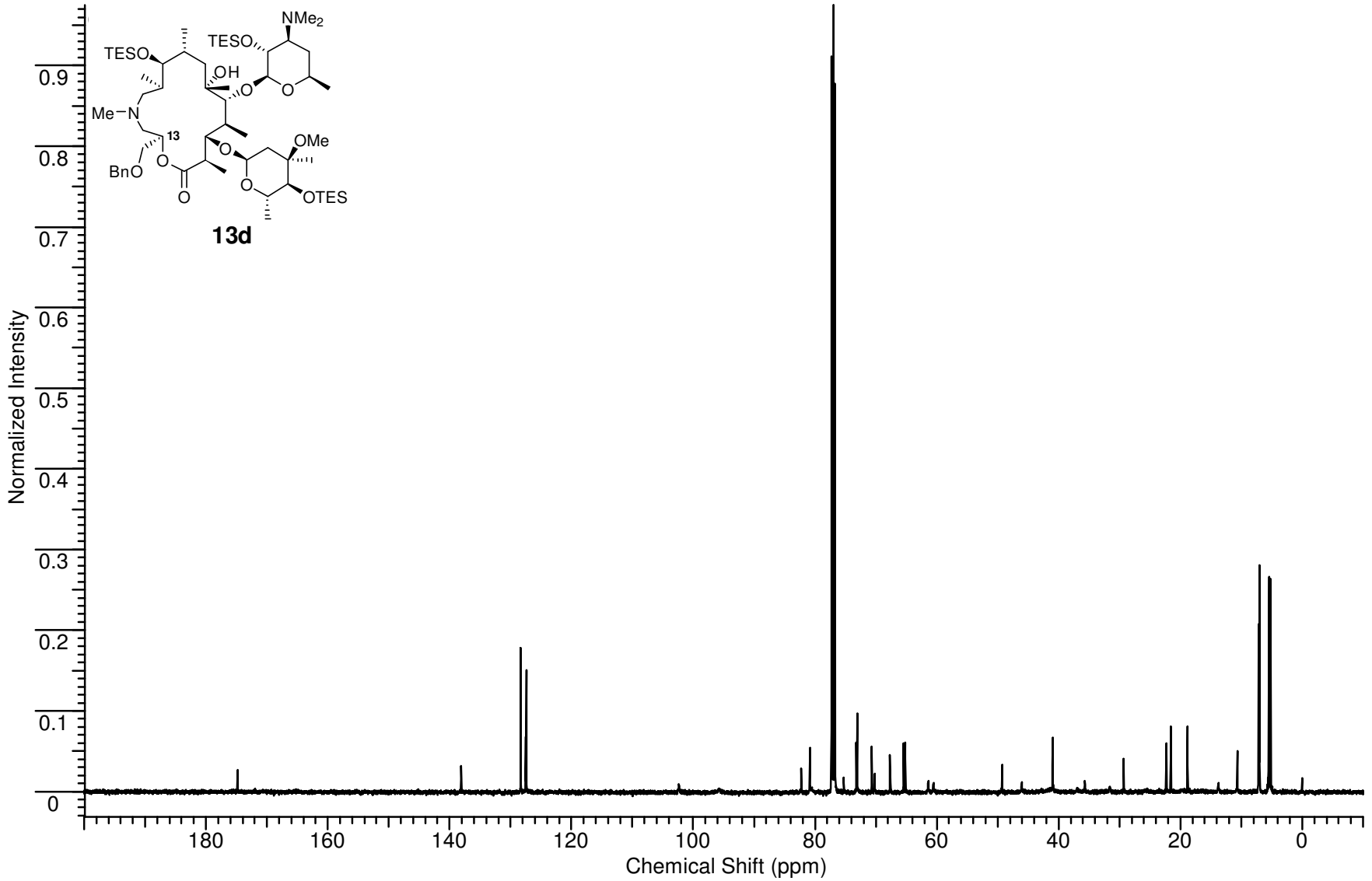
$^{13}$C NMR Spectrum of **13c**



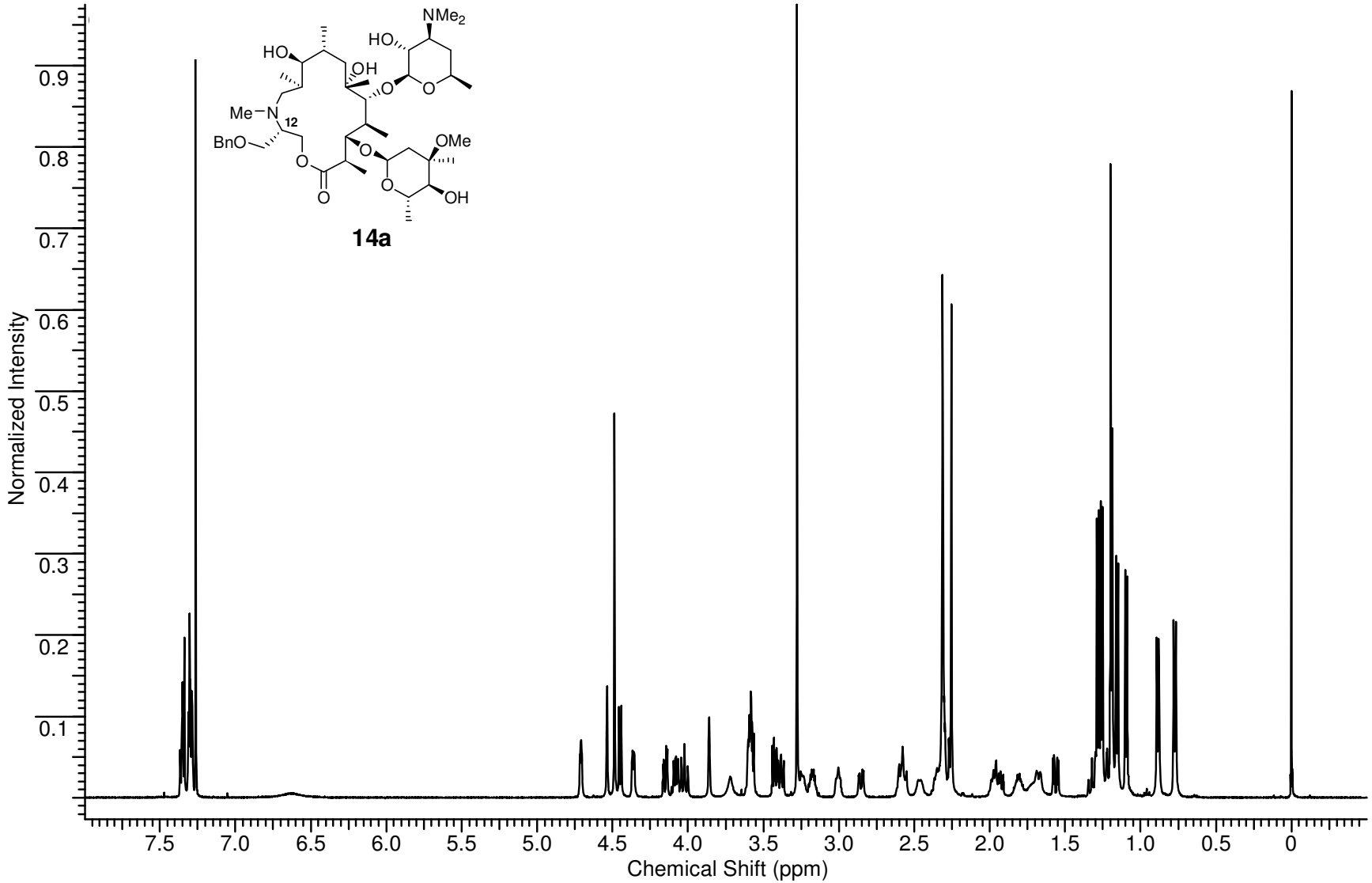
$^{1}$H NMR Spectrum of **13d**



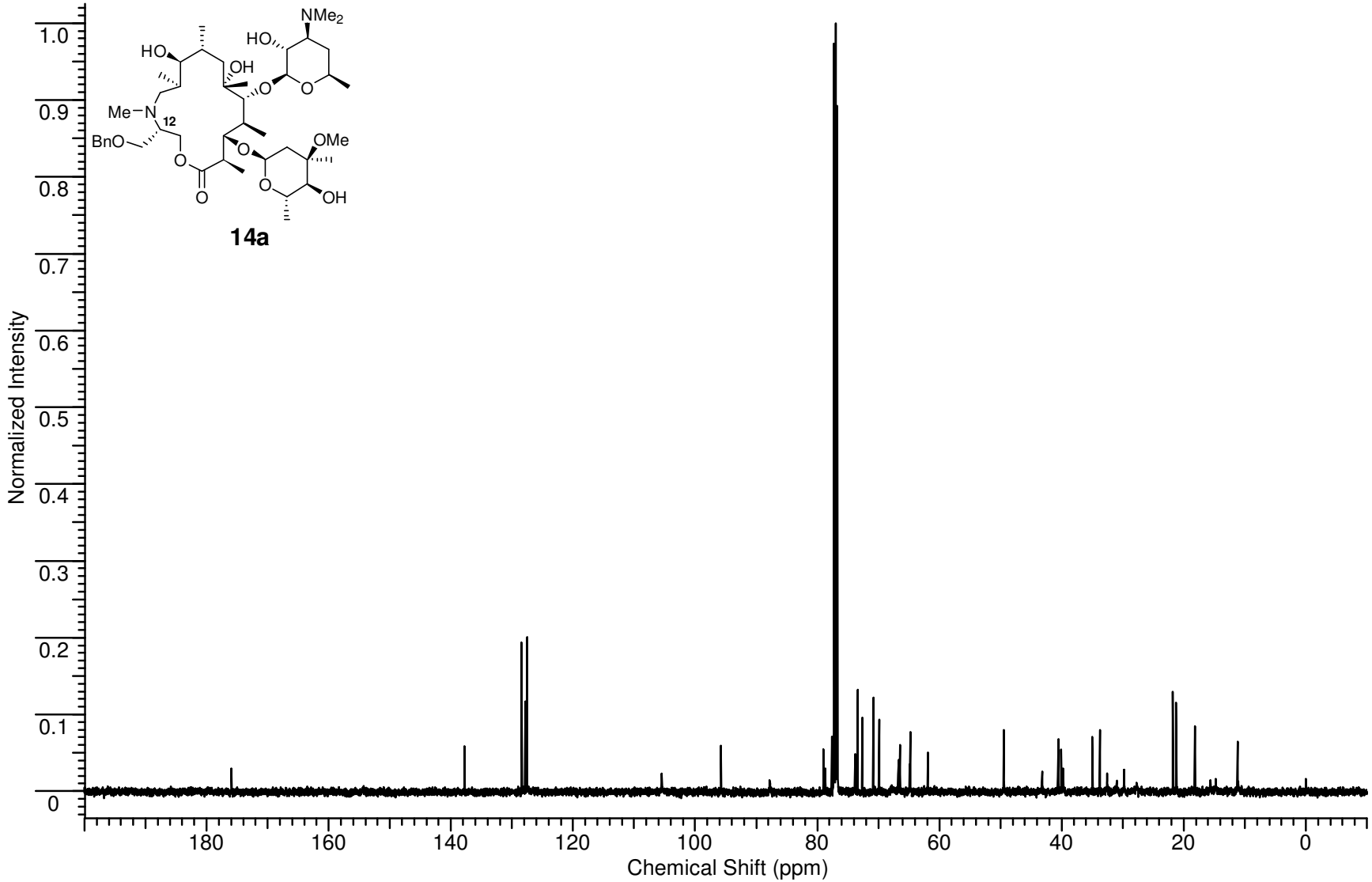
$^{13}$C NMR Spectrum of **13d**



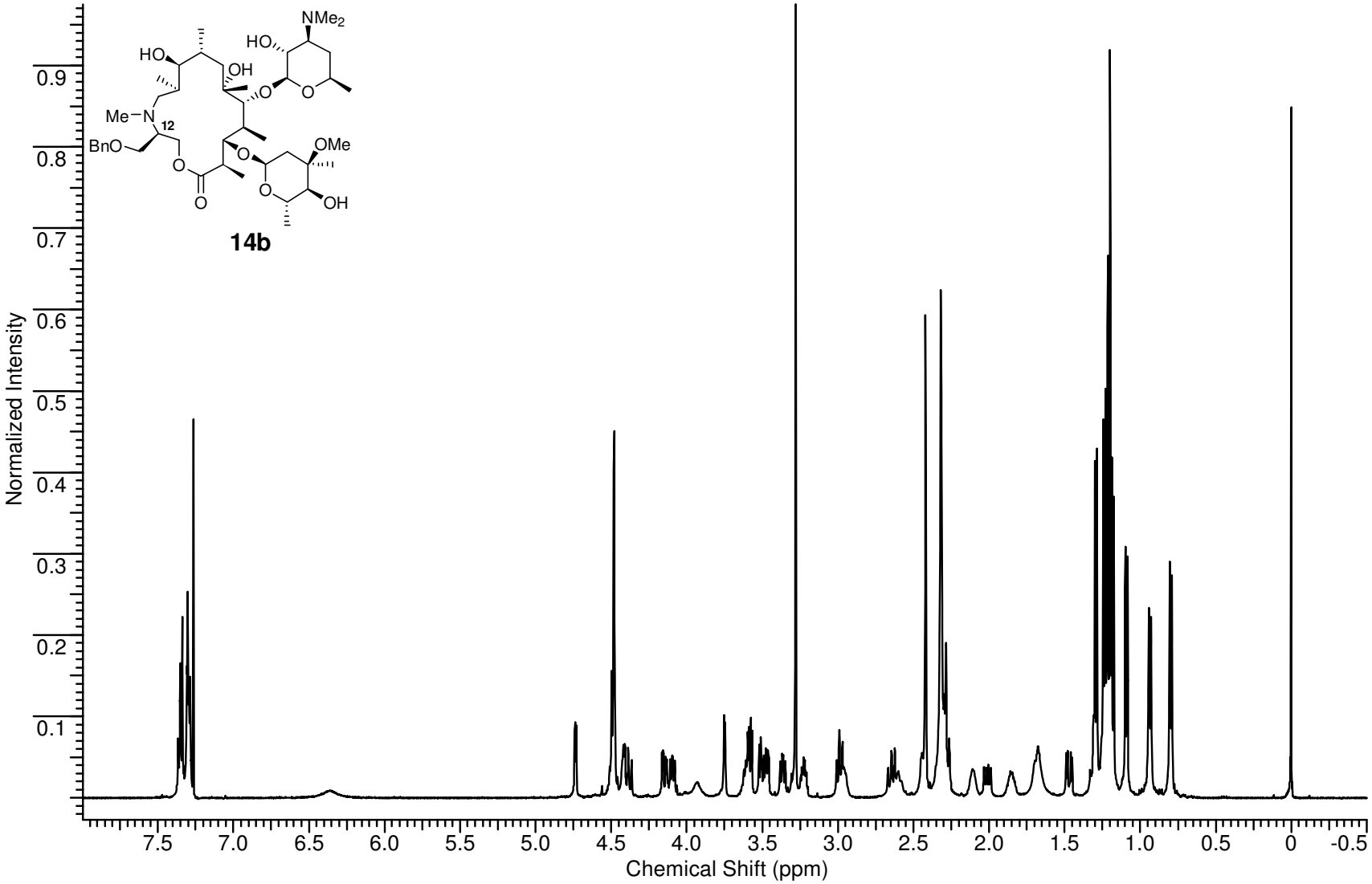
$^{1}$H NMR Spectrum of **14a**



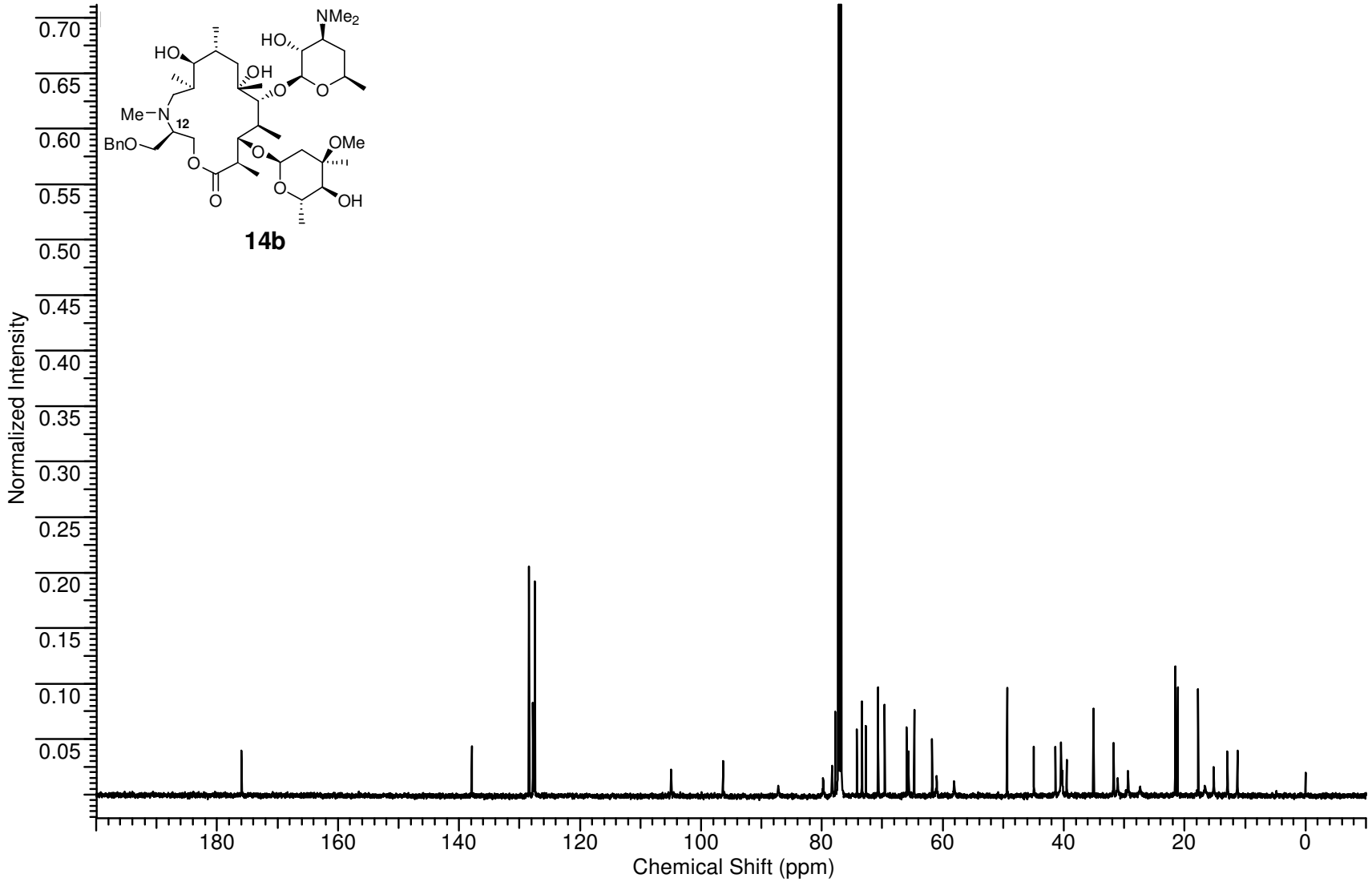
$^{13}$C NMR Spectrum of **14a**



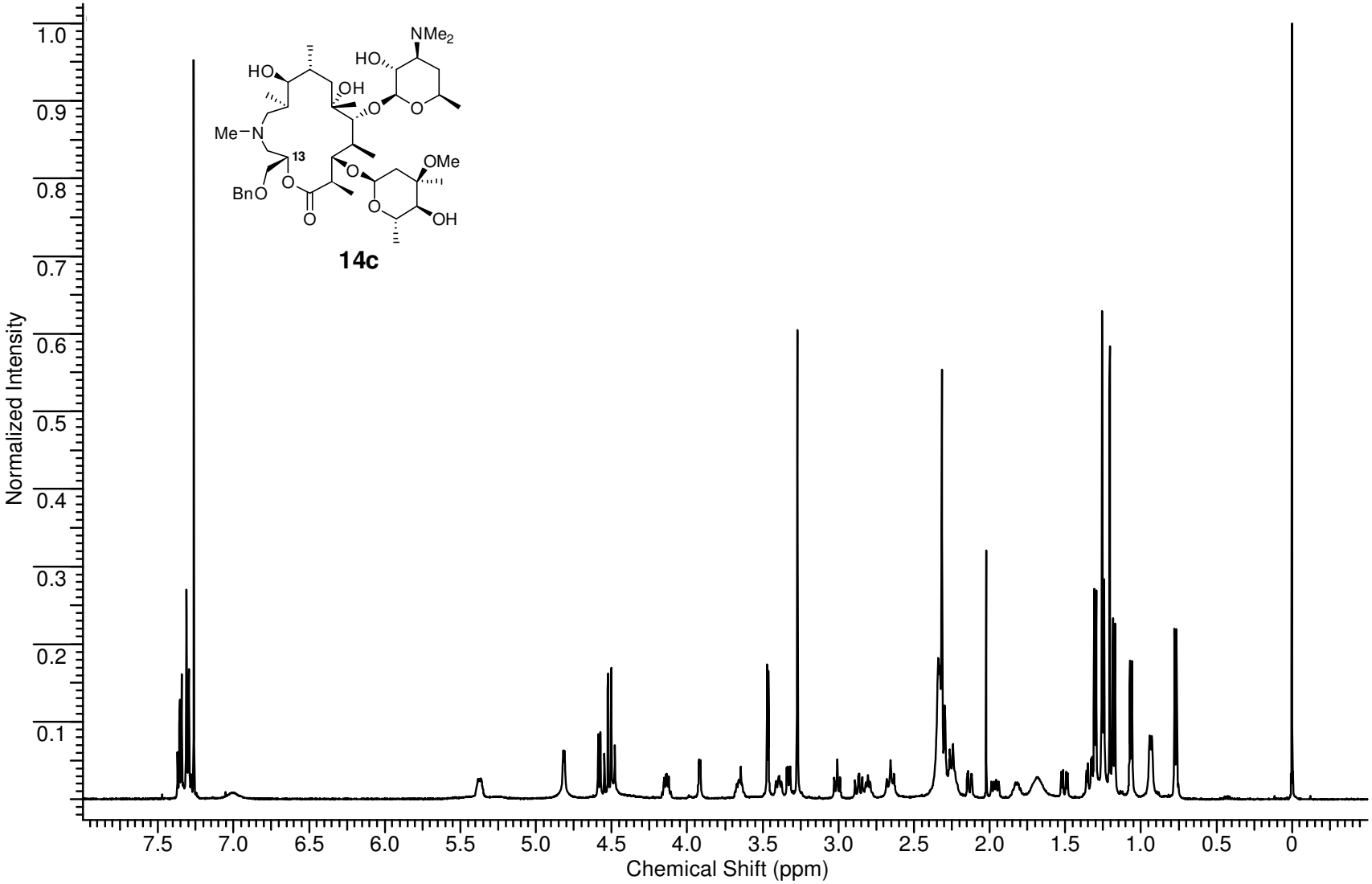
$^{1}$H NMR Spectrum of **14b**



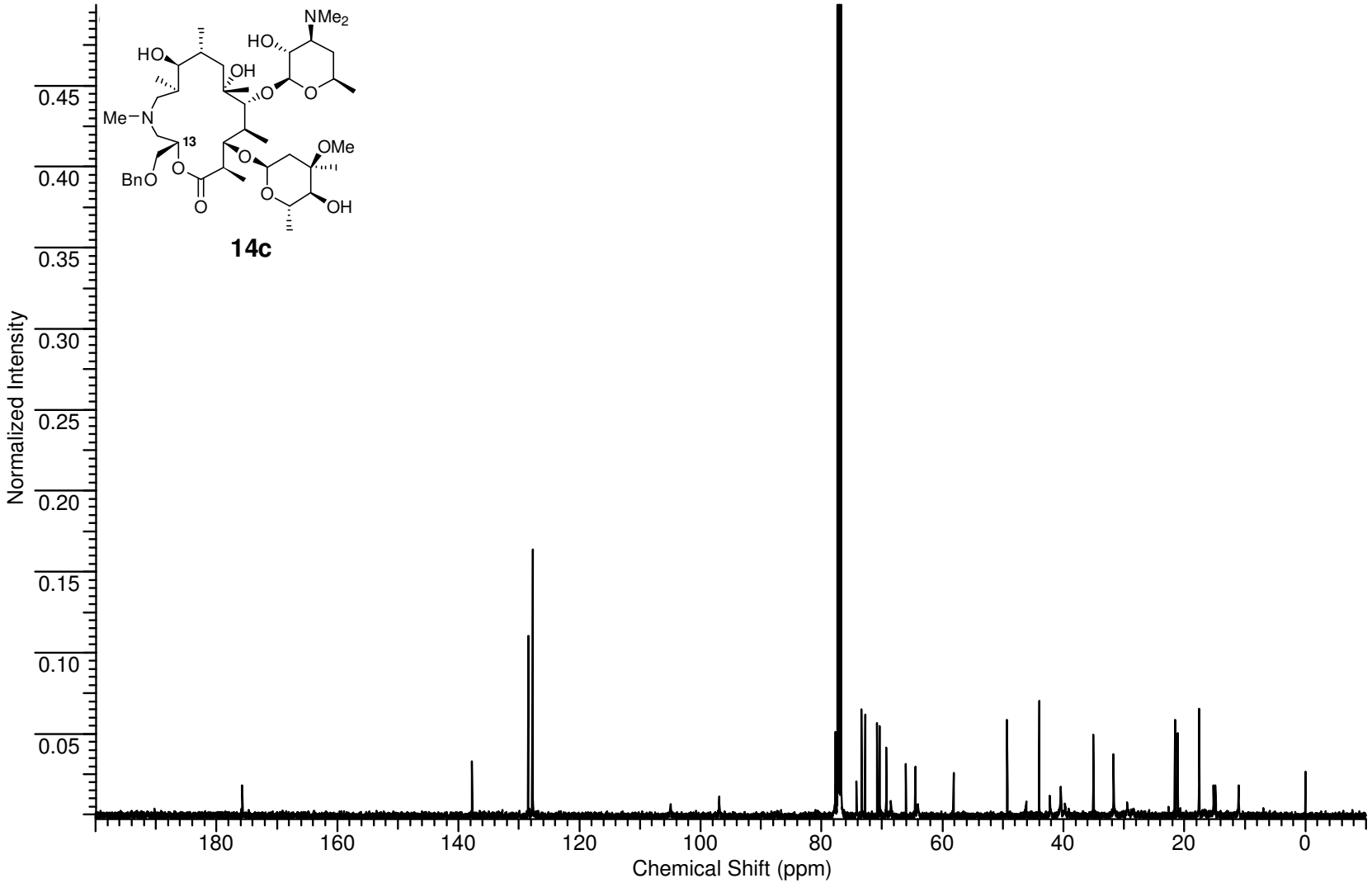
$^{13}$C NMR Spectrum of **14b**



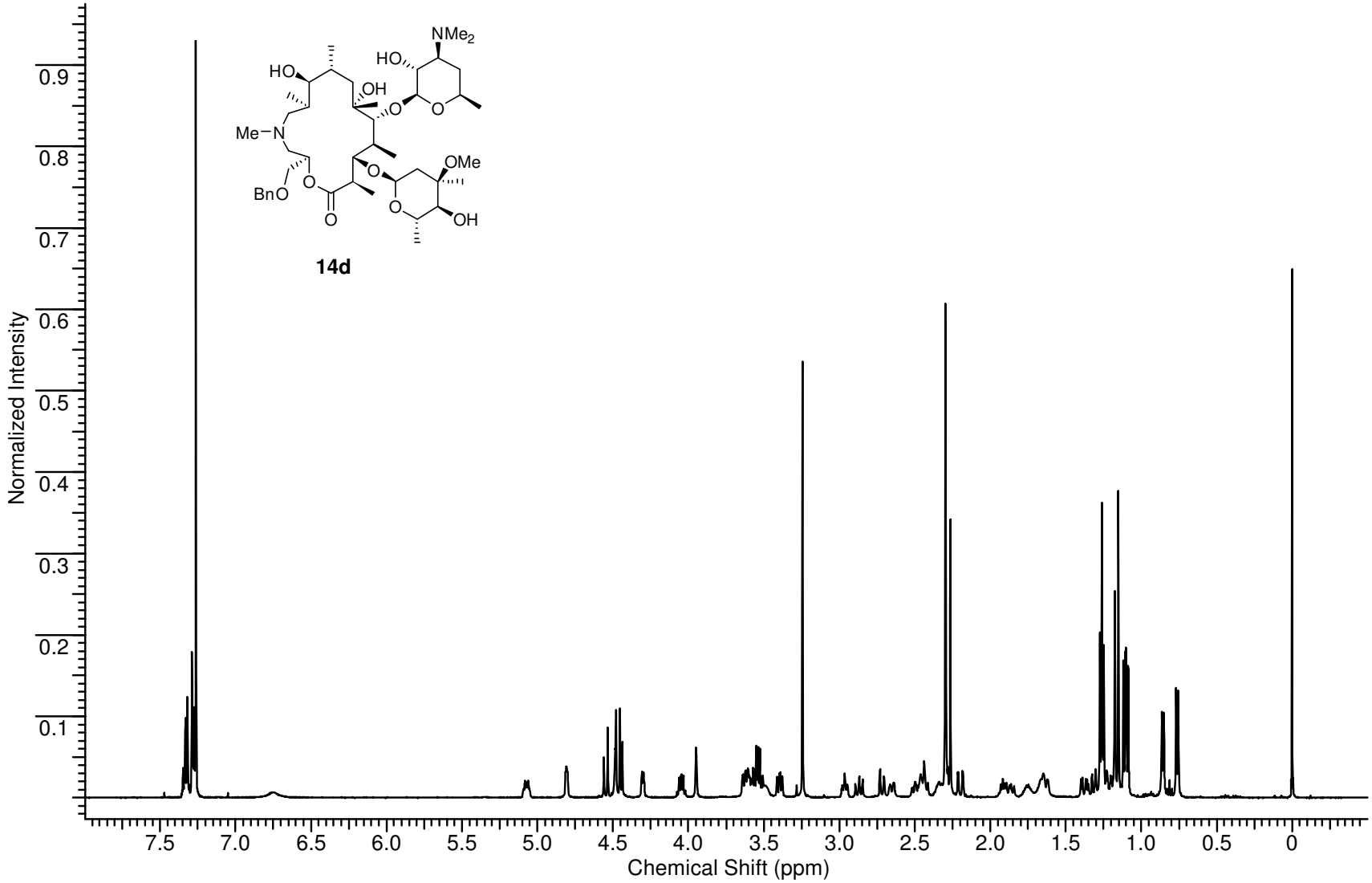
$^{1}$H NMR Spectrum of **14c**



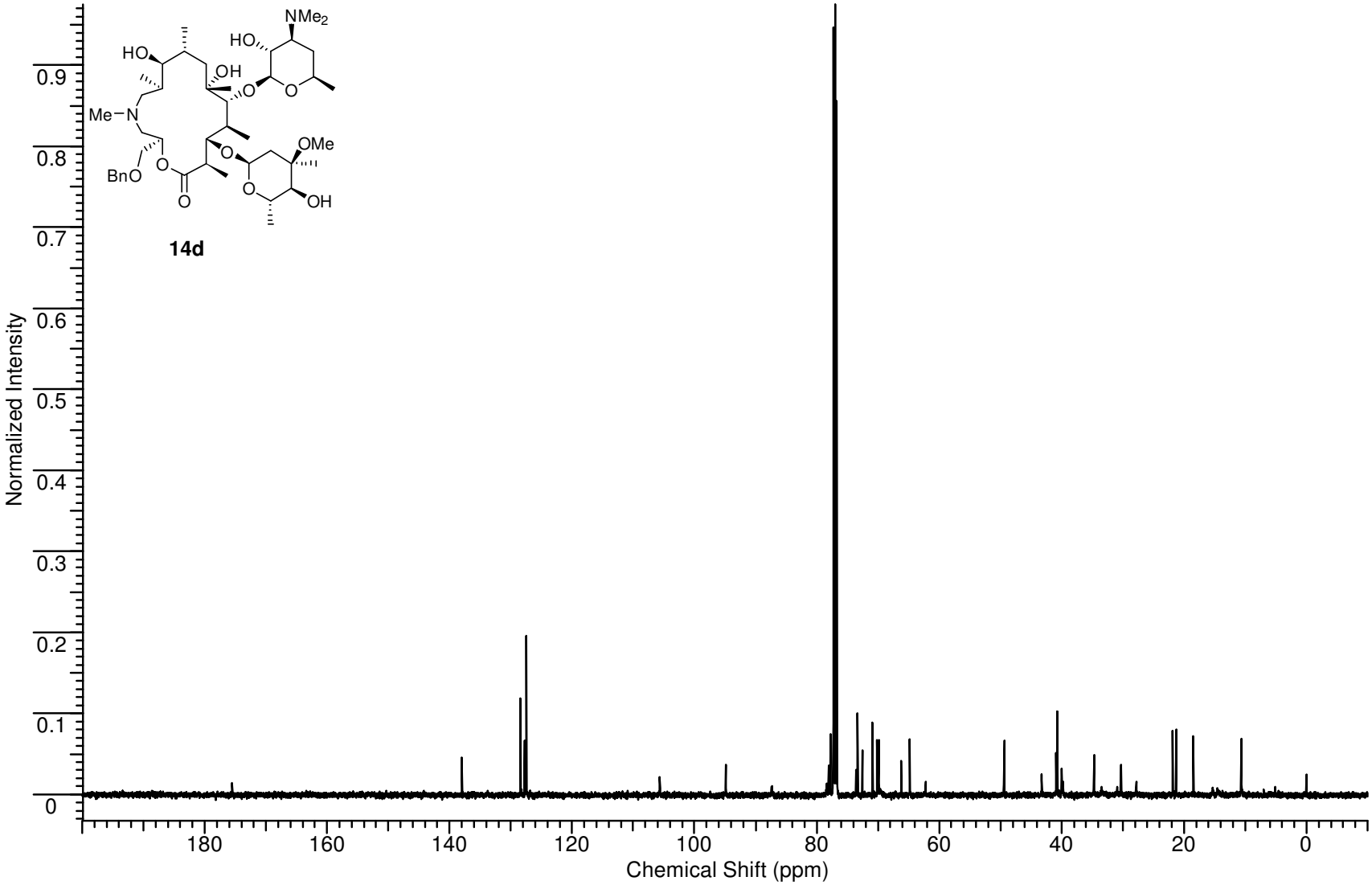
$^{13}$C NMR Spectrum of **14c**



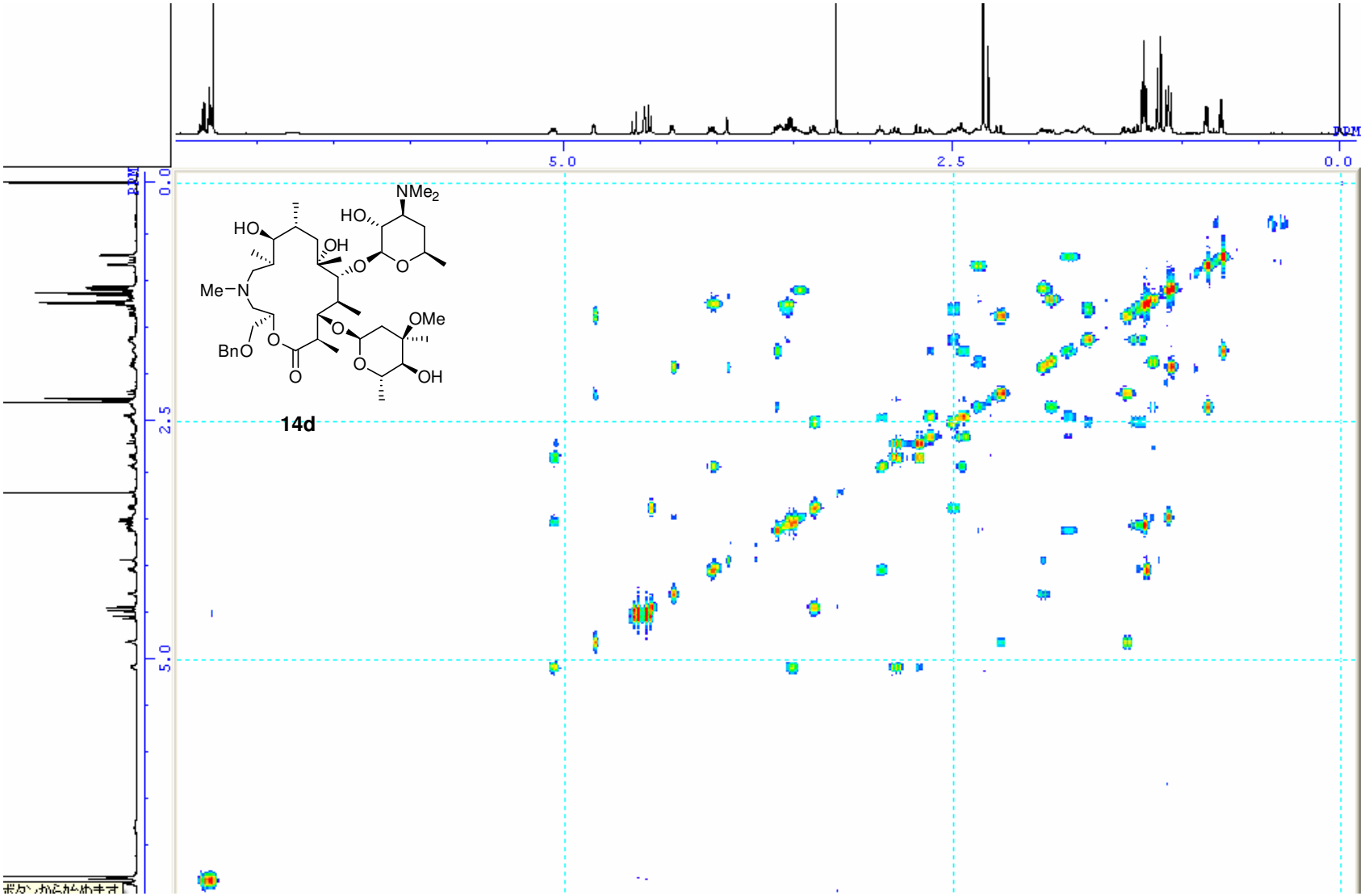
$^{1}$H NMR Spectrum of **14d**



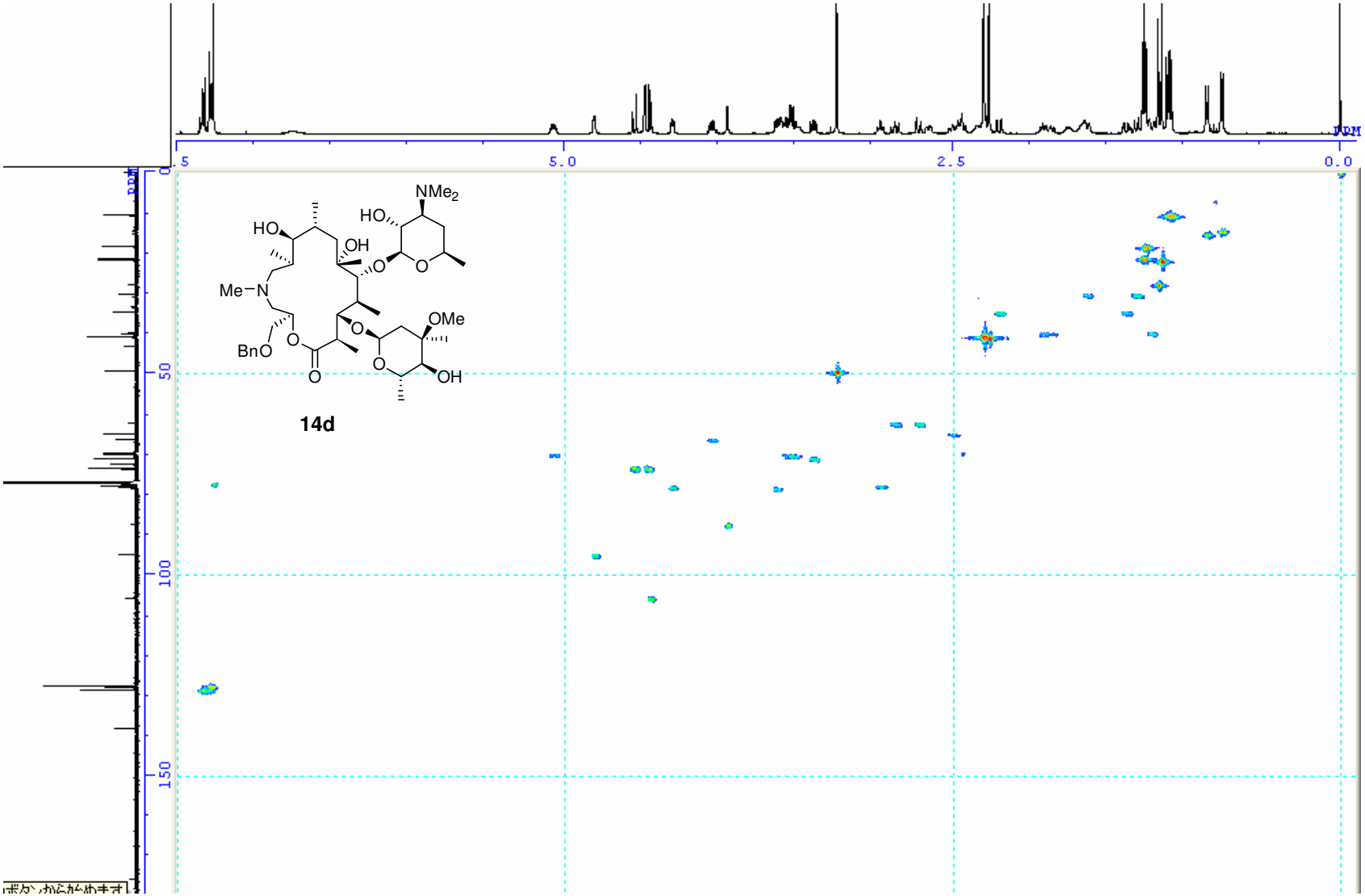
$^{13}$C NMR Spectrum of **14d**



COSY Spectrum of **14d**



HMQC Spectrum of **14d**



HMBC Spectrum of **14d**