Supporting Information For:

A Highly Efficient Synthesis of the Hemibrevetoxin B Ring System

Jon D. Rainier*, Shawn P. Allwein, and Jason M. Cox

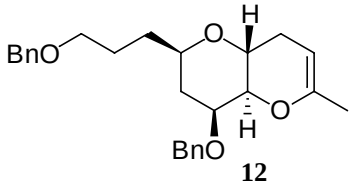
Department of Chemistry, The University of Arizona, Tucson, AZ 85721

Spectroscopic data for compounds **12-14**, **17**, **19**, and **21**.

Experimental

General Information.

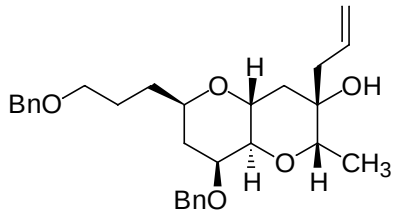
NMR spectra were recorded on a Bruker EM-600 spectrophotometer. Chemical shifts were reported in δ, parts per million (ppm), relative to chloroform (δ = 7.24 ppm) as an internal standard. Coupling constants, *J*, were reported in Hertz (Hz) and refer to apparent peak multiplicities and not true coupling constants. Mass spectra were recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Arizona on a Jeol HX-110A and are reported as % relative intensity to the molecular base peak. IR spectra were recorded on a Nicolet Impact 410.



12

Bicyclic enol ether **12**.

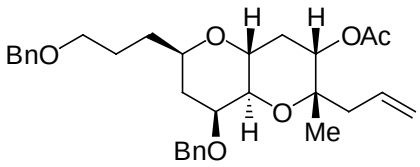
^{1}H NMR (600 MHz, $CDCl_3$) ∂ 7.35-7.28 (m, 8 H), 7.25-7.22 (m, 2 H), 4.75 (d, *J* = 12.5 Hz, 1 H), 4.64 (d, *J* = 12.4 Hz, 1 H), 4.46 (s, 2 H), 4.37 (d, *J* = 5.1 Hz, 1 H), 4.05 (ddd, *J* = 9.7, 9.7, 6.4 Hz, 1 H), 3.94 (dd, *J* = 6.0, 2.9 Hz, 1 H), 3.86-3.82 (m, 1 H), 3.55 (dd, *J* = 9.8, 3.0 Hz, 1 H), 3.50-3.42 (m, 2 H), 2.34-2.28 (m, 1 H), 2.16 (ddd, *J* = 15.9, 6.1, 6.1 Hz, 1 H), 1.97-1.92 (m, 3 H), 1.74-1.59 (m, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) ∂ 150.5, 139.3, 138.7, 128.3, 128.2, 127.6, 127.4, 127.2, 127.2, 93.0, 77.2, 72.9, 72.9, 72.7, 72.4, 70.2, 60.7, 32.6, 29.0, 27.6, 27.1, 19.6; IR (CCl_4) 1675, 1187, 1109 cm^{-1}; MS (FAB$^+$) 409 (MH^+), 91 m/z; HRMS calcd for $C_{26}H_{33}O_4$ (MH^+) 409.2379, found 409.2386.



13

Bicyclic tertiary alcohol **13**.

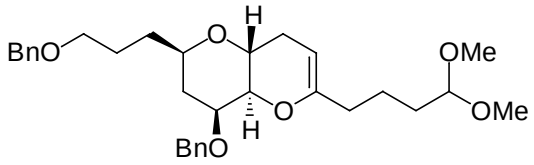
^{1}H NMR (600 MHz, $CDCl_3$) ∂ 7.31-7.20 (m, 10 H), 5.85 (ddt, *J* = 17.3, 9.9, 7.4 Hz, 1 H), 5.16 (d, *J* = 10.1, 1 H), 5.10 (d, *J* = 17.0, 1 H), 4.75 (d, *J* = 12.2 Hz, 1 H), 4.57 (d, *J* = 12.3 Hz, 1 H), 4.44 (s, 2 H), 3.88 (ddd, *J* = 10.9, 10.9, 4.9 Hz, 1 H), 3.83 (d, *J* = 2.7 Hz, 1 H), 3.81-3.75 (m, 2 H), 3.46-3.39 (m, 2 H), 3.36 (dd, *J* = 10.0, 2.4 Hz, 1 H), 2.52 (dd, *J* = 14.0, 7.9 Hz, 1 H), 2.38 (dd, *J* = 14.0, 7.3 Hz, 1 H), 2.23-2.18 (m, 1 H), 1.89-1.88 (m, 2 H), 1.82 (dd, *J* = 12.0, 5.0 Hz, 1 H), 1.65-1.53 (m, 5 H), 1.28 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) ∂ 139.5, 138.7, 132.9, 128.3, 128.2, 127.6, 127.5, 127.1, 126.8,119.9, 75.5, 74.3, 72.8, 72.7, 72.6, 72.5, 72.0, 70.1, 61.3, 43.5, 36.0, 33.2, 29.2, 27.0, 12.4; IR (CCl_4) 3446, 1118, 1031 cm^{-1}; MS (FAB^+) 467 (MH^+), 91 m/z; HRMS calcd for $C_{29}H_{39}O_5$ (MH^+) 467.2797, found 467.2816.



14-OAc

Bicyclic secondary alcohol **14** (acetate used to simplify characterization).

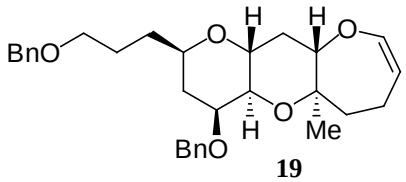
^{1}H NMR (600 MHz, $CDCl_3$) ∂ 7.32-7.21 (m, 10 H), 5.82-5.75 (m, 1 H), 5.12 (s, 1 H), 5.09 (d, *J* = 3.8, 1 H), 4.80 (dd, *J* = 12.0, 4.8 Hz, 1 H), 4.77 (d, *J* = 12.6 Hz, 1 H), 4.57 (d, *J* = 12.5 Hz, 1 H), 4.47 (s, 2 H), 3.90 (ddd, *J* = 10.7, 10.7, 4.8 Hz, 1 H), 3.82-3.79 (m, 2 H), 3.50-3.41 (m, 2H), 3.28 (dd, *J* = 9.9, 2.7 Hz, 1H), 2.79 (dd, *J* = 15.2, 6.2 Hz, 1 H), 2.25-2.20 (m, 1 H), 2.15 (ddd, *J* = 11.3, 4.8, 4.8 Hz), 2.12 (dd, *J* = 15.8, 7.8 Hz, 1 H), 2.05 (s, 3H), 1.89-1.87 (m, 2 H), 1.71- 1.56 (m, 4 H), 1.15 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ∂ 170.0, 139.5, 138.7, 132.7, 128.3, 128.2, 127.6, 127.4, 127.1, 127.0, 117.9, 75.3, 74.4, 73.7, 73.4, 72.9, 72.7, 72.5, 70.2, 62.5, 33.4, 33.1, 31.2, 29.2, 27.1, 24.5, 21.2; IR (CCl_4) 1750, 1239, 1109 cm^{-1}; MS (FAB^+) 509 (MH^+), 507, 467, 91 m/z; HRMS calcd for $C_{31}H_{41}O_6$ (MH^+) 509.2903, found 509.2916.



17

Bicyclic enol ether **17**.

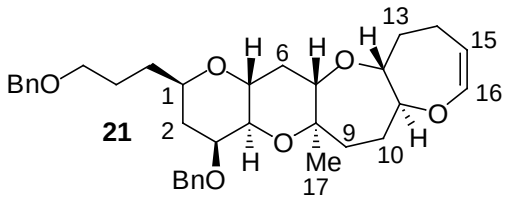
^{1}H NMR (600 MHz, $CDCl_3$) ∂ 7.36-7.22 (m, 10 H), 4.77 (d, *J* = 12.5 Hz, 1 H), 4.64 (d, *J* = 12.5 Hz, 1 H), 4.47 (s, 2 H), 4.41 (d, *J* = 4.5 Hz, 1 H), 4.32 (t, *J* = 5.5 Hz, 1 H), 4.06 (ddd, *J* = 9.6, 9.5, 6.5 Hz, 1 H), 3.95 (d, *J* = 2.9 Hz, 1 H), 3.86-3.84 (m, 1 H), 3.53 (dd, *J* = 9.7, 2.7 Hz, 1 H), 3.51- 3.43 (m, 2 H), 3.27 (s, 6 H), 2.34- 2.29 (m, 1 H), 2.18 (ddd, *J* = 15.8, 6.2, 6.0 Hz, 1 H), 2.04 (dd, *J* = 7.1, 7.1 Hz, 2 H), 1.96 (part. ob. dd, *J* = 15.0, 9.6 Hz, 1 H), 1.93 (dd, *J* = 3.3, 3.3 Hz, 2 H), 1.75-1.48 (m, 7 H); ^{13}C NMR (150 MHz, $CDCl_3$) ∂ 153.4, 139.3, 138.7, 128.3, 128.1, 127.6, 127.4, 127.1, 127.0, 104.3, 92.9, 77.2, 72.8, 72.8, 72.6, 72.4, 70.2, 60.8, 52.6, 52.5, 33.4, 32.7, 31.8, 29.0, 27.5, 27.1, 22.0; IR (CCl_4) 1678, 1229, 1166 cm^{-1}; MS (FAB$^+$) 511 (MH^+), 509, 479, 465, 91 m/z; HRMS calcd for $C_{31}H_{43}O_6$ (MH^+) 511.3060, found 511.3046.



19

Tricyclic enol ether **19**.

^{1}H NMR (600 MHz, $CDCl_3$) ∂ 7.32-7.20 (m, 10 H), 6.25 (dd, *J* = 7.1, 2.4 Hz, 1 H) 4.77 (d, *J* = 12.6 Hz, 1 H), 4.71 (ddd, *J* = 7.1, 7.1, 3.6 Hz, 1 H), 4.57 (d, *J* = 12.6 Hz, 1 H), 4.46 (s, 2 H), 3.82-3.77 (m, 3 H), 3.49-3.42 (m, 3H) 3.31 (dd, *J* = 9.8, 2.6 Hz, 1 H), 2.27-2.22 (m, 1 H), 2.12-2.00 (m, 3 H), 1.90 (ddd, *J* = 14.6, 6.3, 3.1 Hz, 1 H), 1.88-1.81 (m, 2 H), 1.71-1.53 (m, 5 H), 1.18 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) ∂ 147.0, 139.6, 138.7, 128.3, 128.1, 127.6, 127.4, 127.0, 126.9, 109.0, 81.8, 78.2, 73.6, 73.4, 72.8, 72.6, 72.4, 70.2, 62.9, 40.6, 33.4, 33.0, 29.2, 27.0, 20.9, 13.7; IR (CCl_4) 1647, 1215, 1103 cm^{-1}; MS (FAB$^+$) 479 (MH^+), 460, 91 m/z; HRMS calcd for $C_{30}H_{39}O_5$ (MH^+) 479.2797, found 479.2809.



Tetracyclic enol ether **21**.

^{1}H NMR (600 MHz, $CDCl_3$) ∂ 7.34-7.21 (m, 10 H), 6.25 (d, *J* = 6.7 Hz, 1 H) 4.77 (d, *J* = 12.6 Hz, 1 H), 4.65 (ddd, *J* = 6.6, 6.6, 3.7 Hz, 1 H), 4.58 (d, *J* = 12.6 Hz, 1 H), 4.48 (s, 2 H), 3.93 (dd, *J* = 15.1, 7.0 Hz, 1 H), 3.82-3.78 (m, 3H), 3.63 (ddd, *J* = 8.8, 4.5, 4.5 Hz, 1 H), 3.50-3.44 (m, 2 H), 3.31 (dd, *J* = 9.9, 2.6 Hz, 1 H), 3.27 (dd, *J* = 12.2, 3.9 Hz, 1 H), 2.4-2.35 (m, 1 H), 2.30-2.23 (m, 1 H), 2.16-2.06 (m, 2 H), 3.99 (ddd, *J* = 11.6, 4.4, 4.4 Hz, 1 H), 1.93-1.81 (m, 5 H), 1.77-1.75 (m, 1 H), 1.74-1.66 (m, 1 H), 1.65-1.55 (m, 4 H), 1.19 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) ∂ 147.2, 139.7, 138.7, 128.3, 128.1, 127.6, 127.4, 127.0, 127.0, 108.5, 84.2, 83.7, 83.3, 73.9, 73.7, 72.8, 72.6, 72.4, 70.2, 63.6, 37.2, 33.8, 33.5, 33.1, 29.2, 28.7, 27.0, 20.8, 15.5; IR (CCl_4) 1542, 1221, 1110 cm^{-1}; MS (FAB$^+$) 549 (MH^+), 91 m/z; HRMS calcd for $C_{34}H_{45}O_6$ (MH^+) 549.3216, found 549.3219.

Summary of NOE Difference Experiments for **21**.

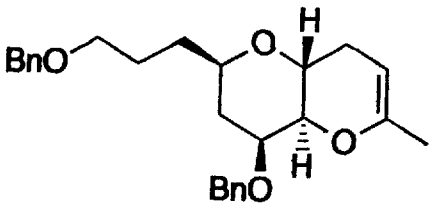
(1) Irradiation at 1.19 ppm (C17) resulted in enhancements at 3.93 (C11), 3.31 (C4), 2.09 (C10), and 1.61 (C6).

(2) Irradiation at 3.27 ppm (C7) resulted in enhancements at 3.81 (C5), and 3.63 (C12).

(3) Irradiation at 3.31 ppm (C4) resulted in enhancements at 3.80 (C1), 1.61 (C6), and 1.19 (C17).

(4) Irradiation at 3.63 ppm (C12) resulted in enhancements at 3.27 (C7), and 1.76 (C10).

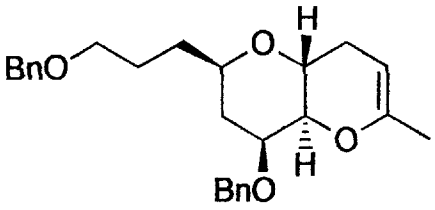
(5) Irradiation at 3.93 ppm (C11) resulted in enhancements at 6.25 (C16), 2.37 (C14), 2.13 (C13), and 1.19 (C17).



12

^{1}H NMR, 600 MHz

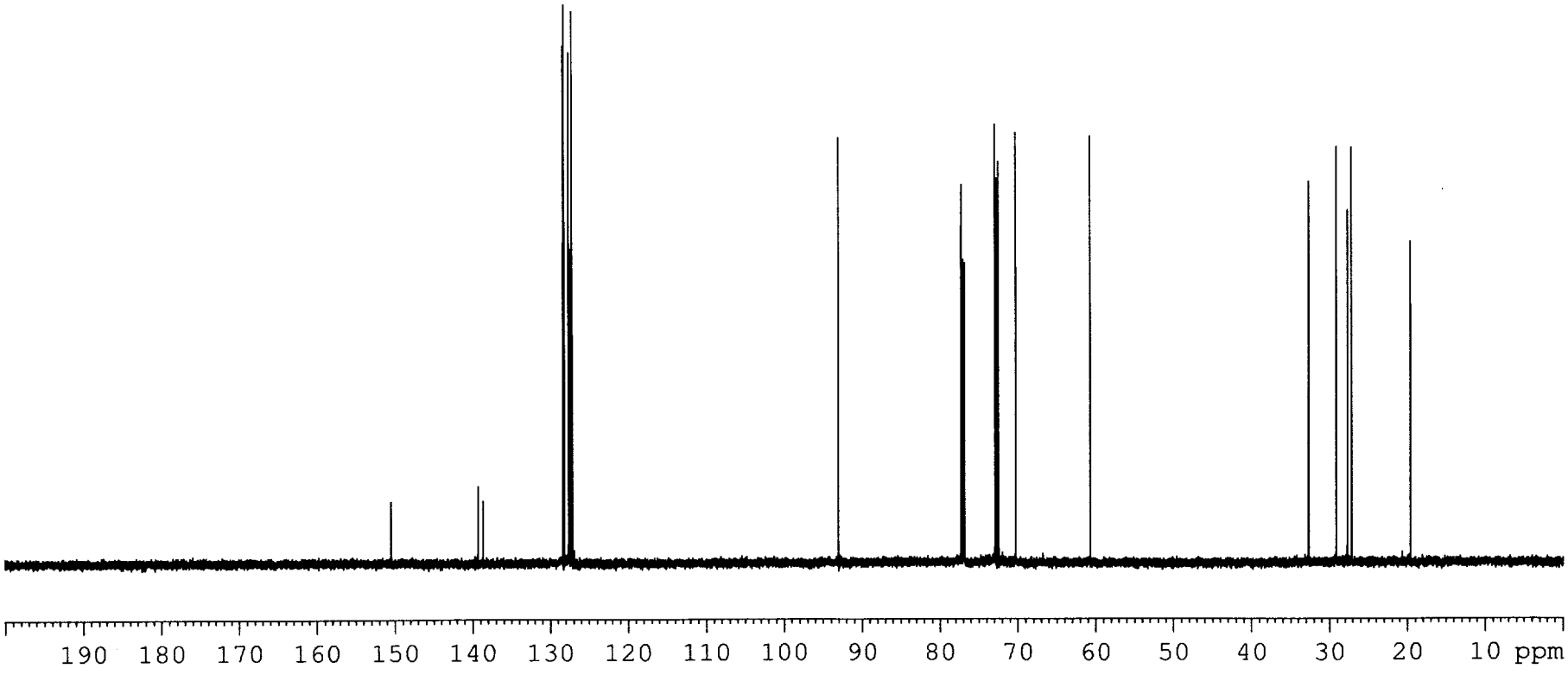
$CDCl_3$

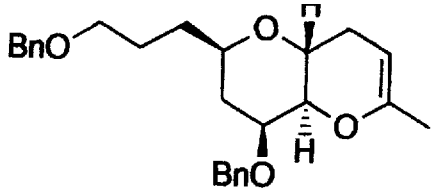


12

^{13}C NMR, 150 MHz

$CDCl_3$

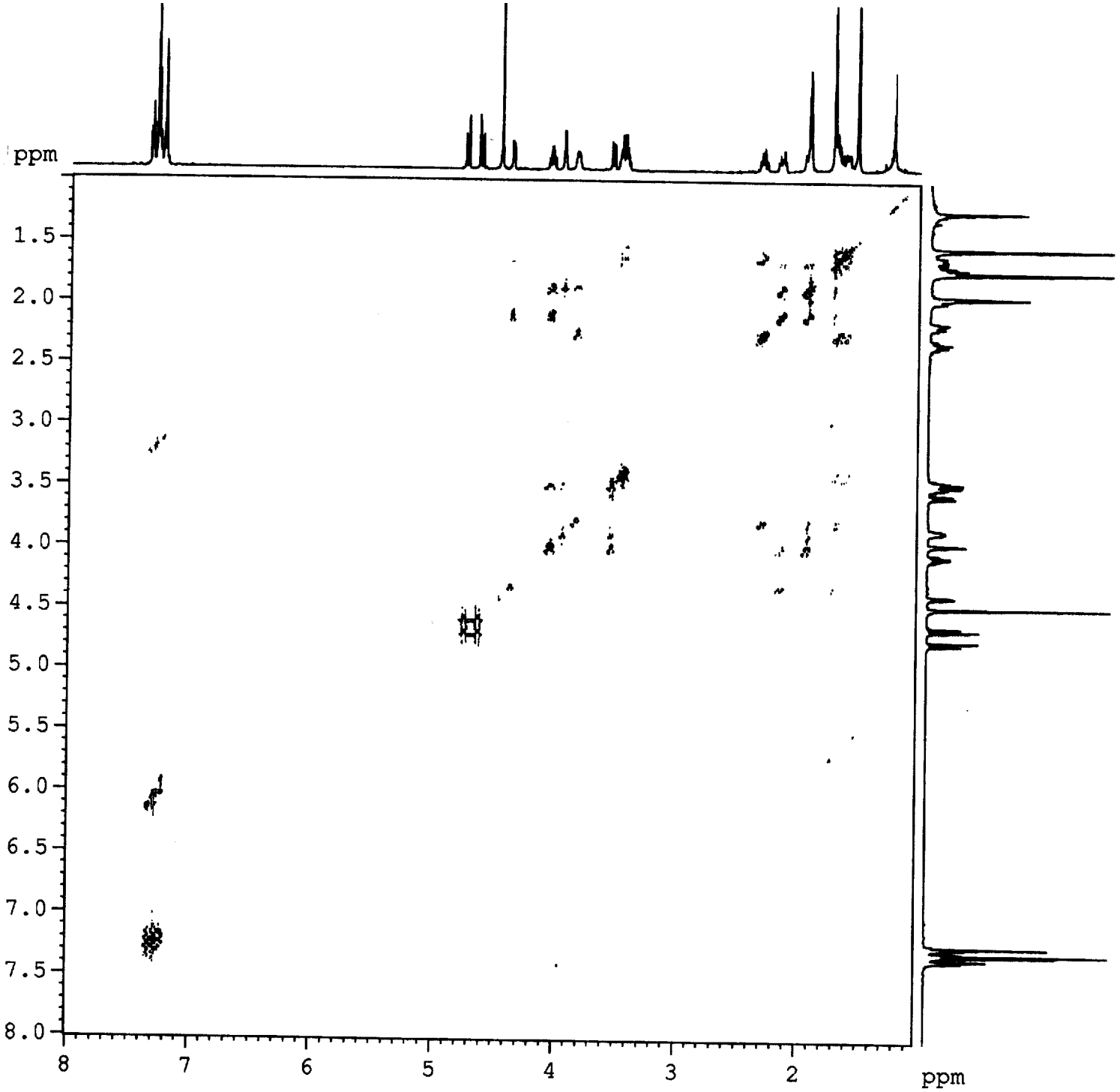


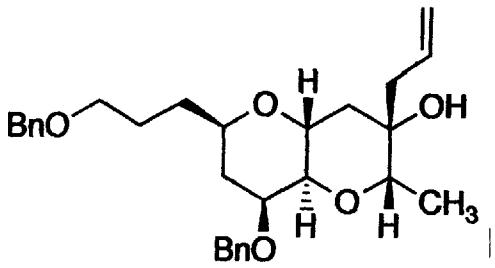


12

COSY, 500 MHz

$CDCl_3$

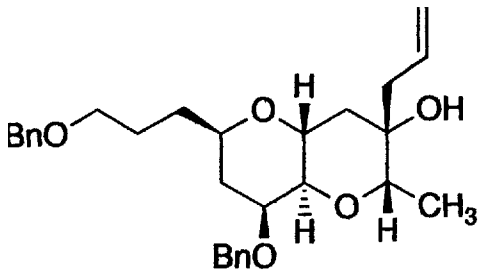




13

^{1}H NMR, 600 MHz

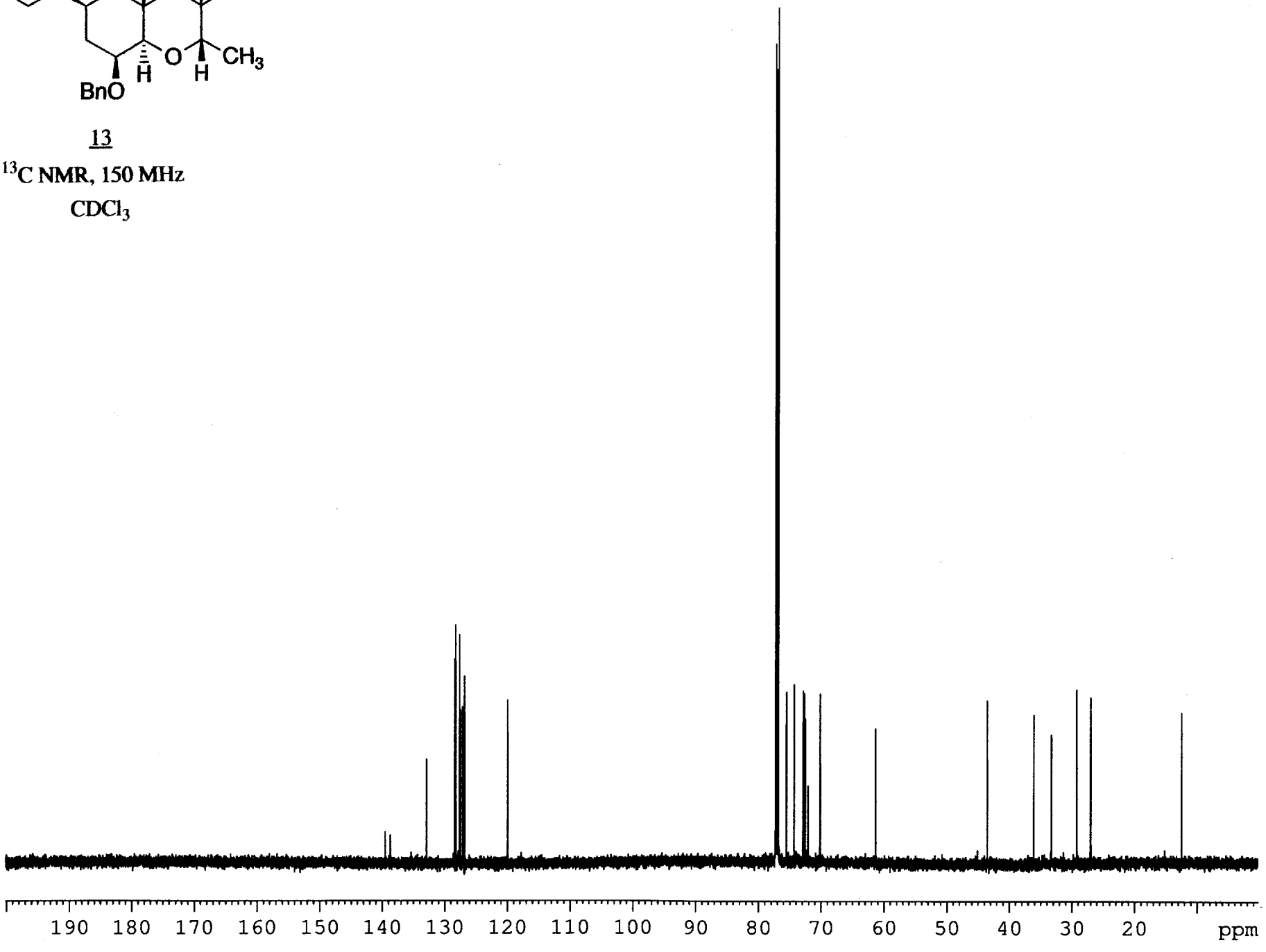
$CDCl_3$

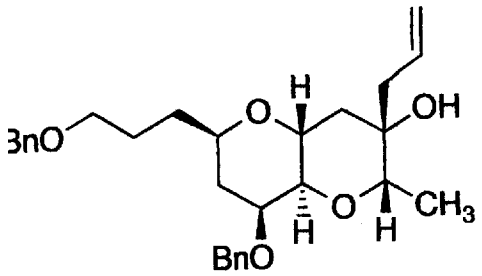


13

^{13}C NMR, 150 MHz

$CDCl_3$

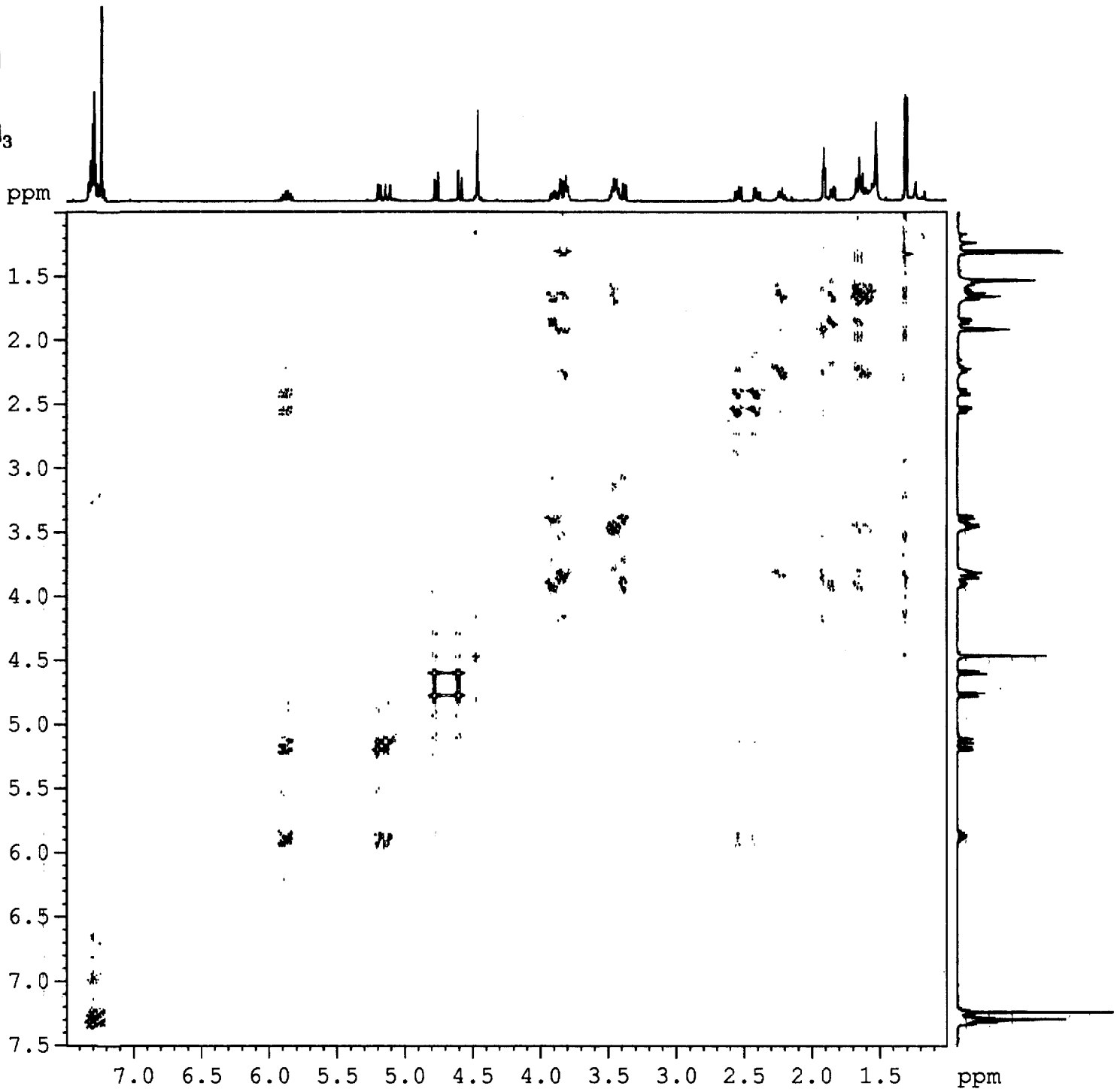


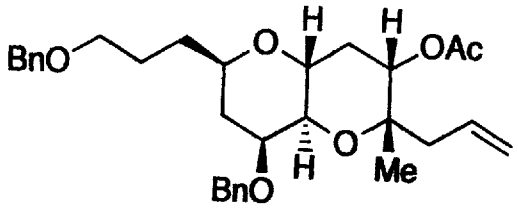


13

COSY, 500 MHz

$CDCl_3$

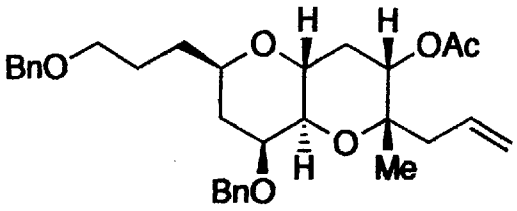




Acetate of <u>14</u>

^{1}H NMR, 600 MHz

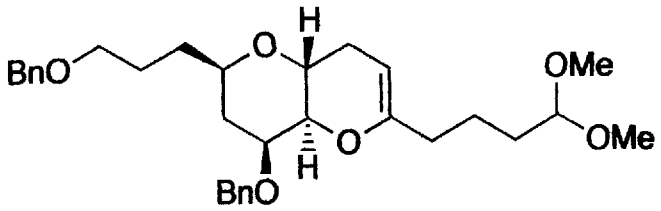
$CDCl_3$



Acetate of 14

^{13}C NMR, 150 MHz

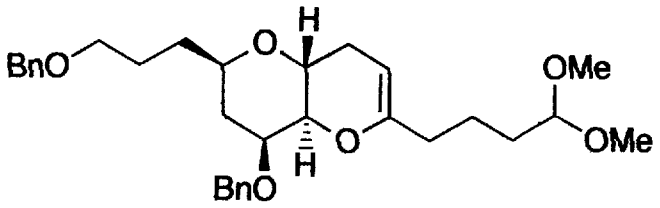
$CDCl_3$



17

^{1}H NMR, 600 MHz

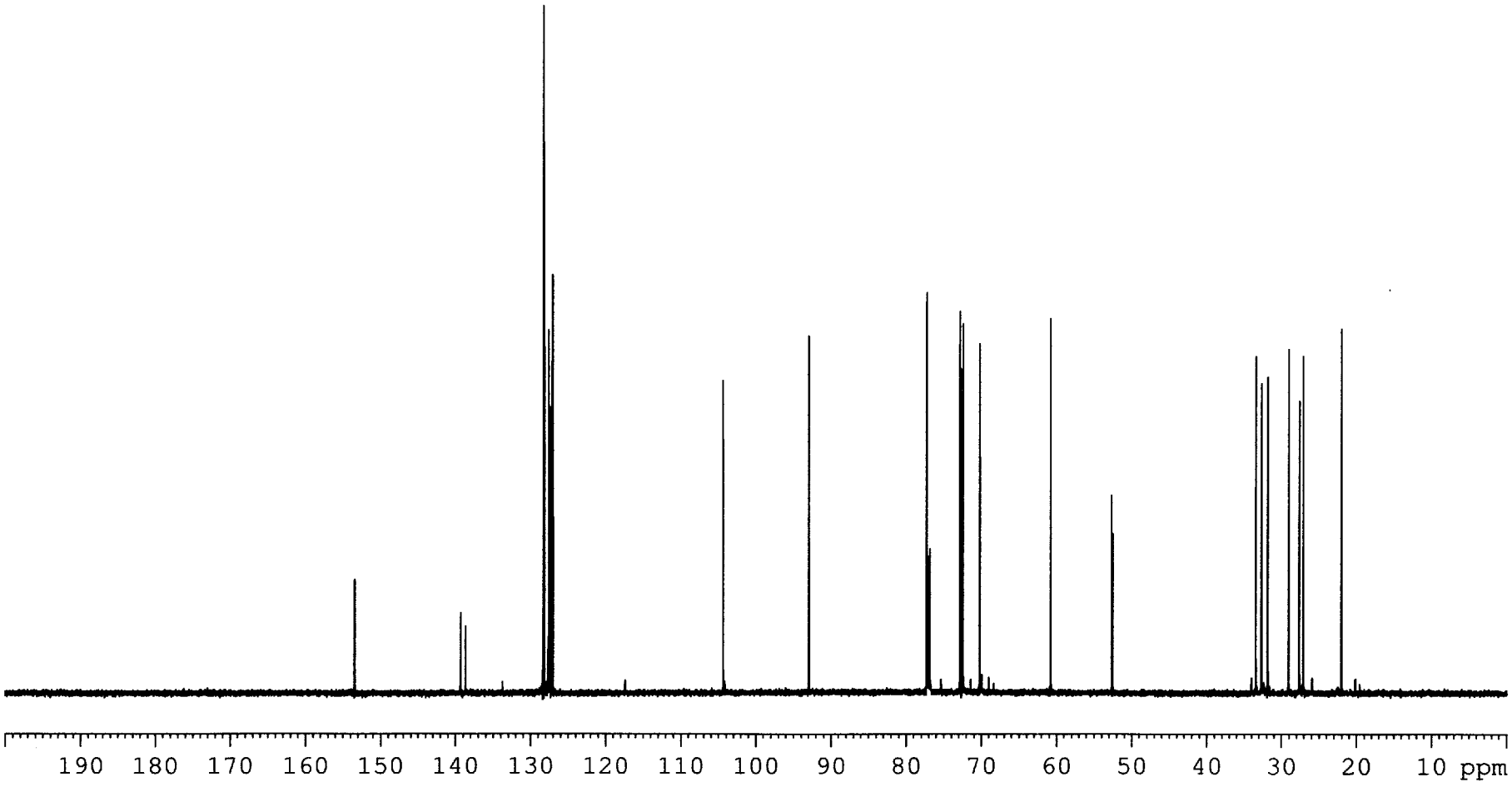
$CDCl_3$

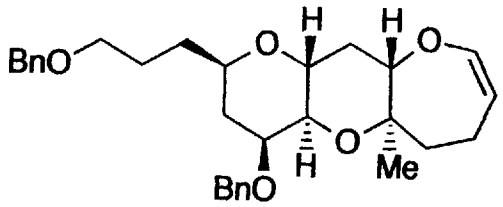


17

^{13}C NMR, 150 MHz

$CDCl_3$

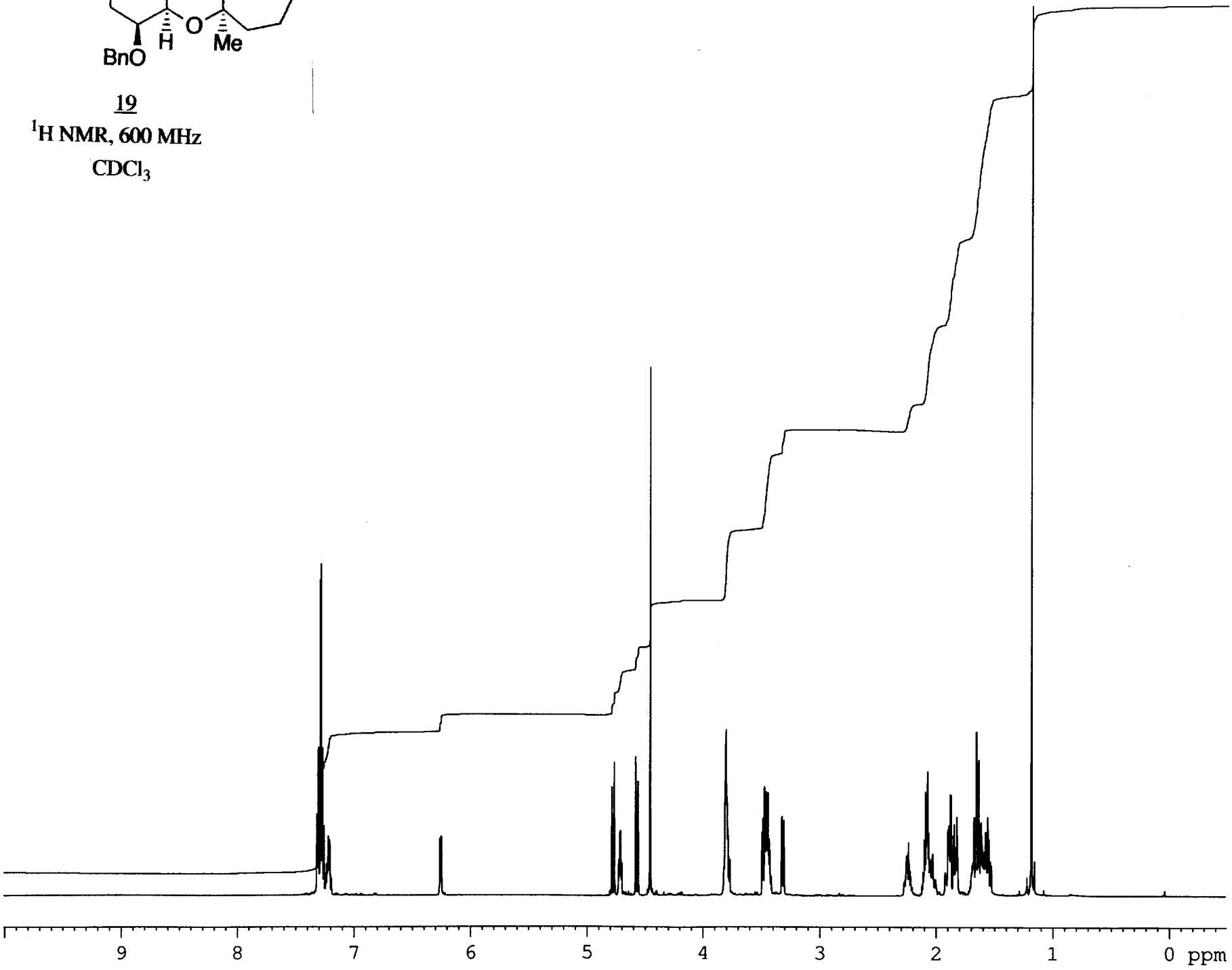


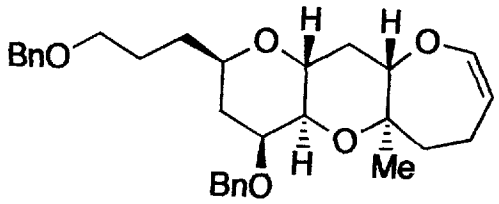


19

^{1}H NMR, 600 MHz

$CDCl_3$

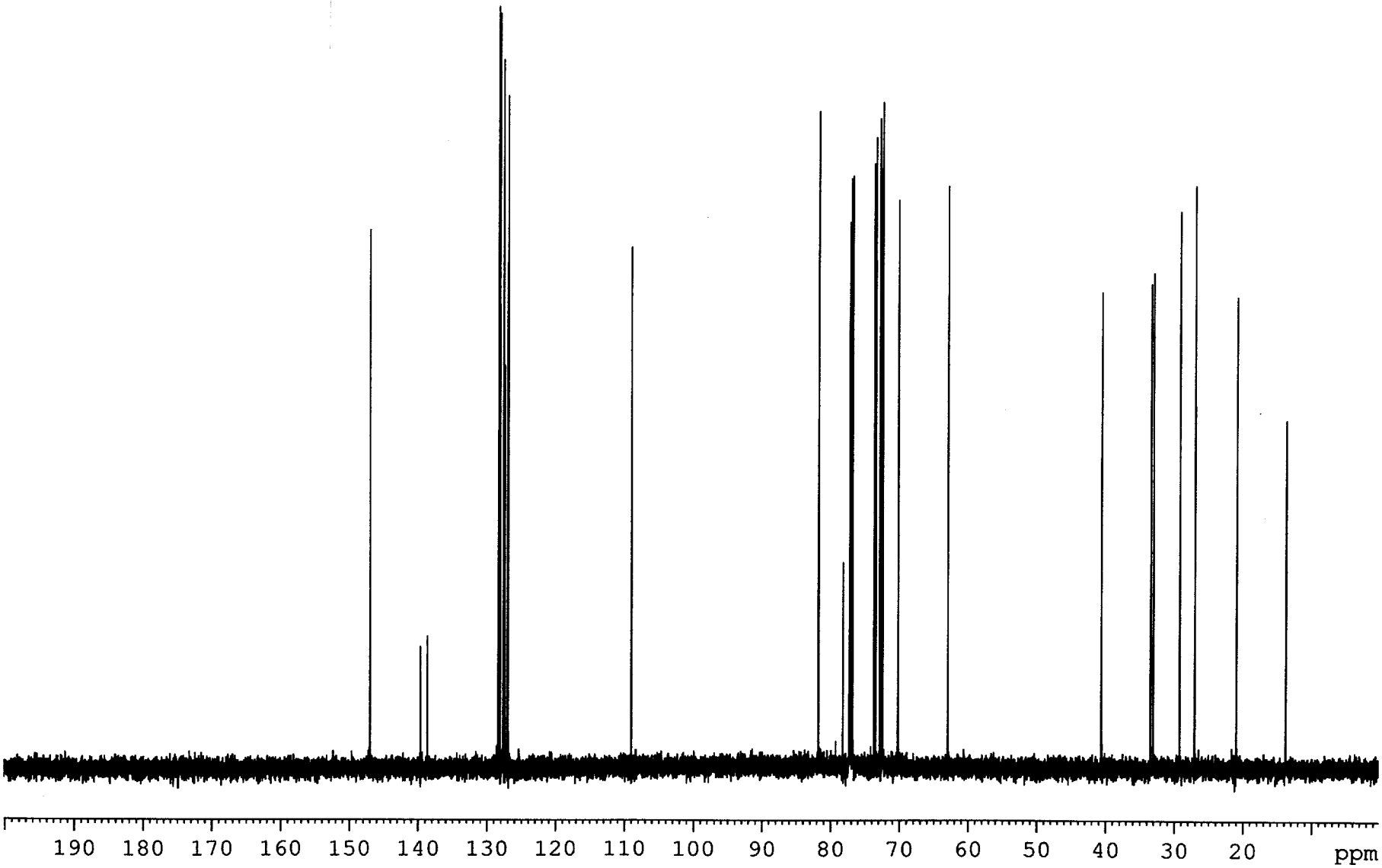


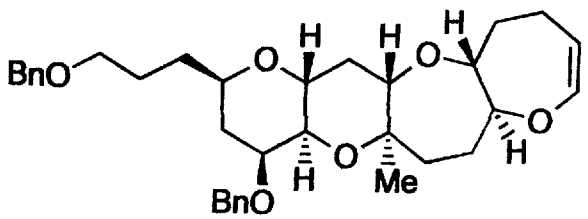


19

^{13}C NMR, 150 MHz

$CDCl_3$

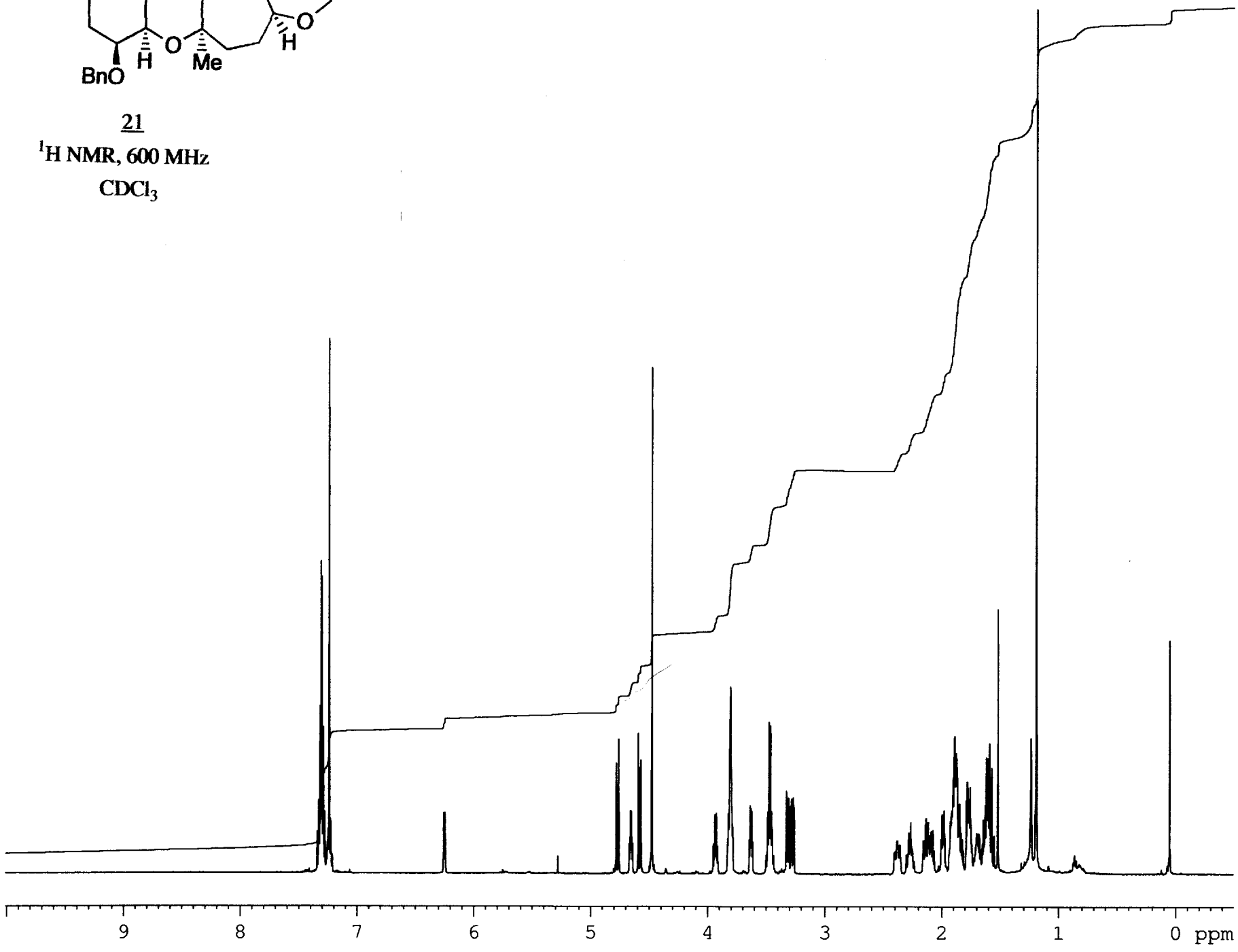


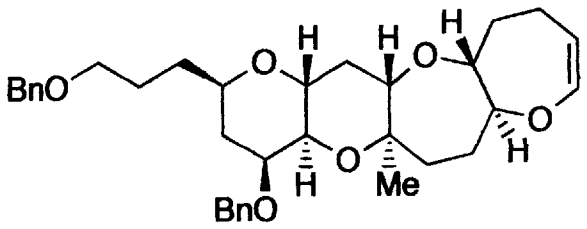


21

^{1}H NMR, 600 MHz

$CDCl_3$

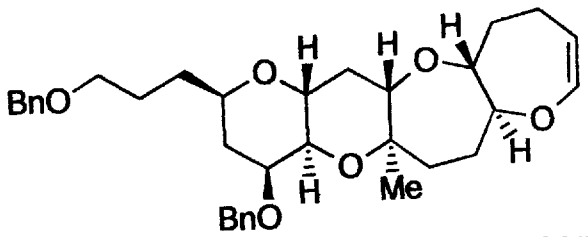




21

^{13}C NMR, 150 MHz

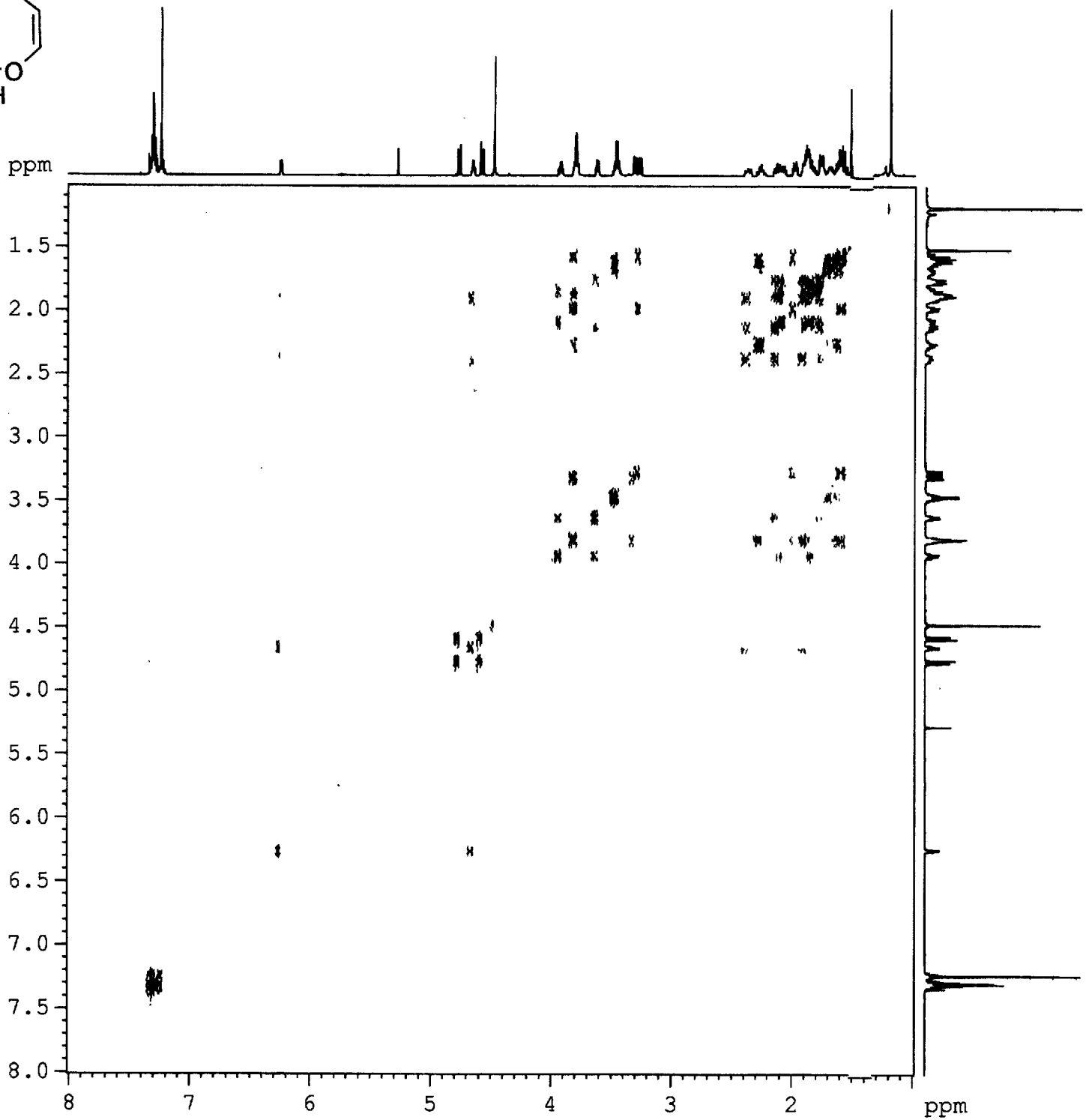
$CDCl_3$

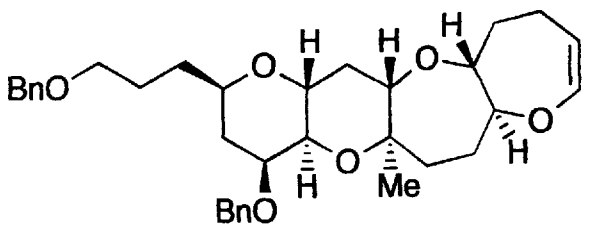


21

COSY, 600 MHz

$CDCl_3$

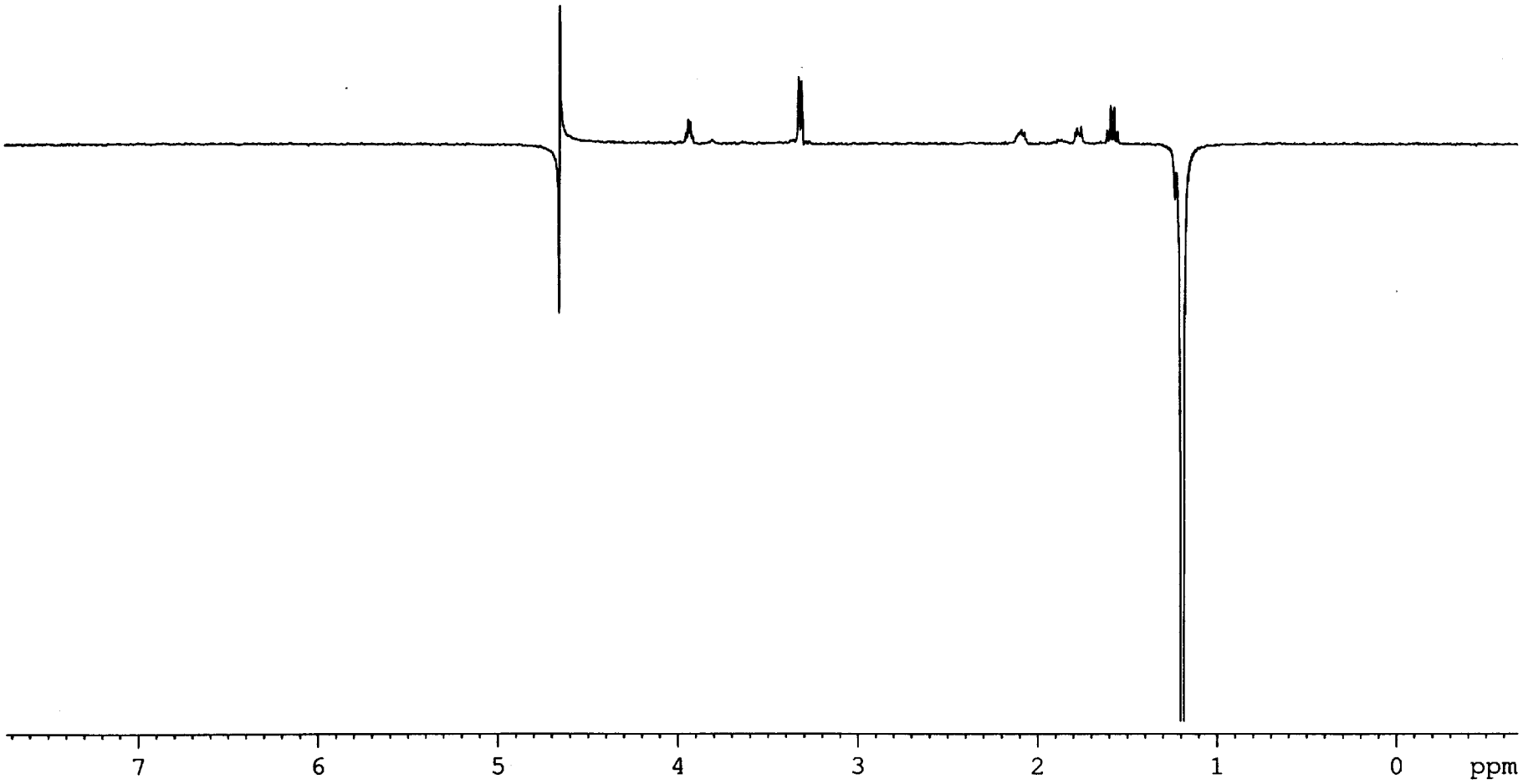


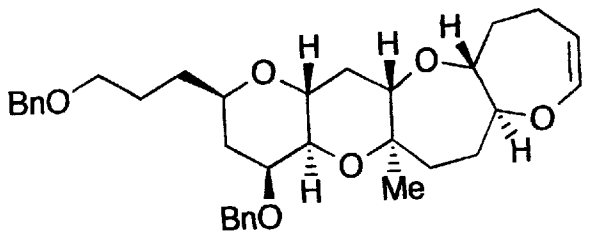


21

NOE Difference, 600 MHz

$CDCl_3$

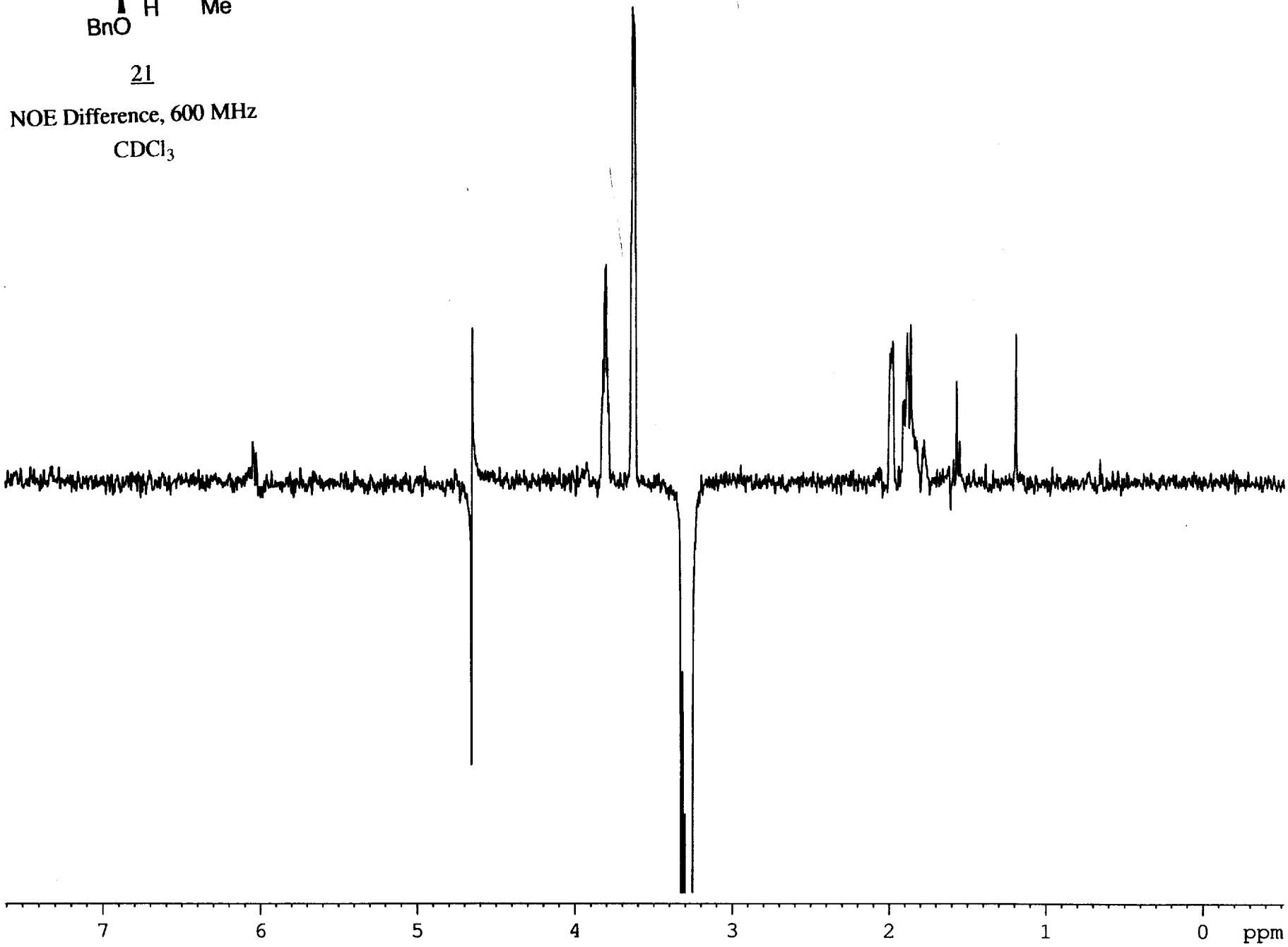


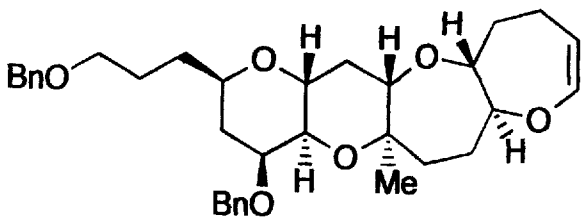


21

NOE Difference, 600 MHz

$CDCl_3$

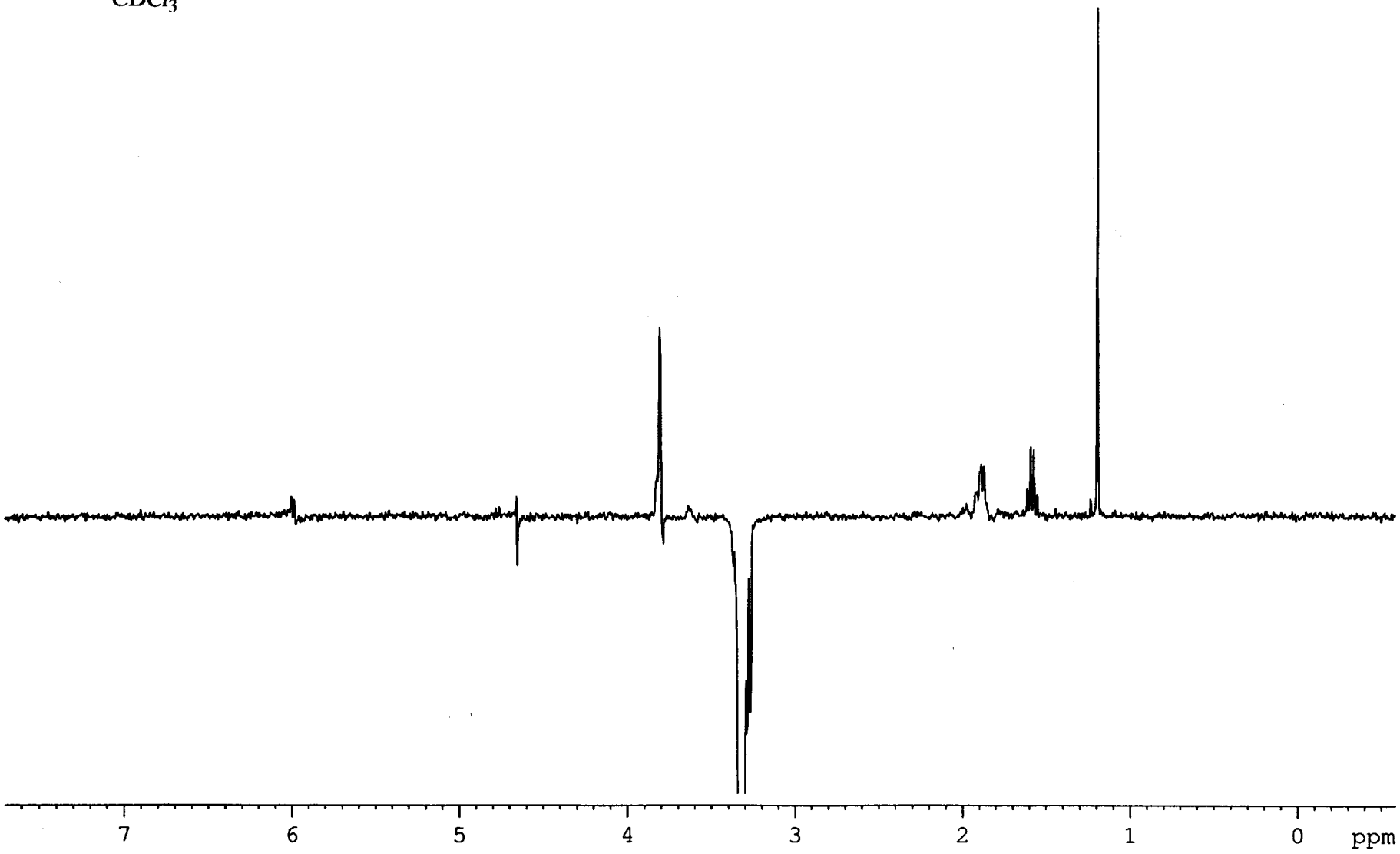


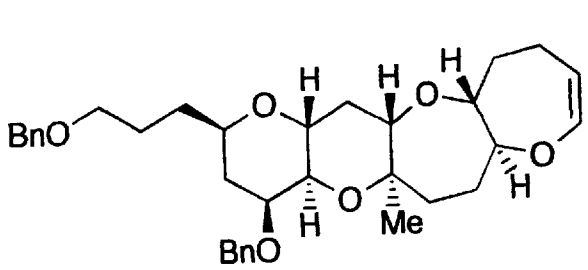


21

NOE Difference, 600 MHz

$CDCl_3$

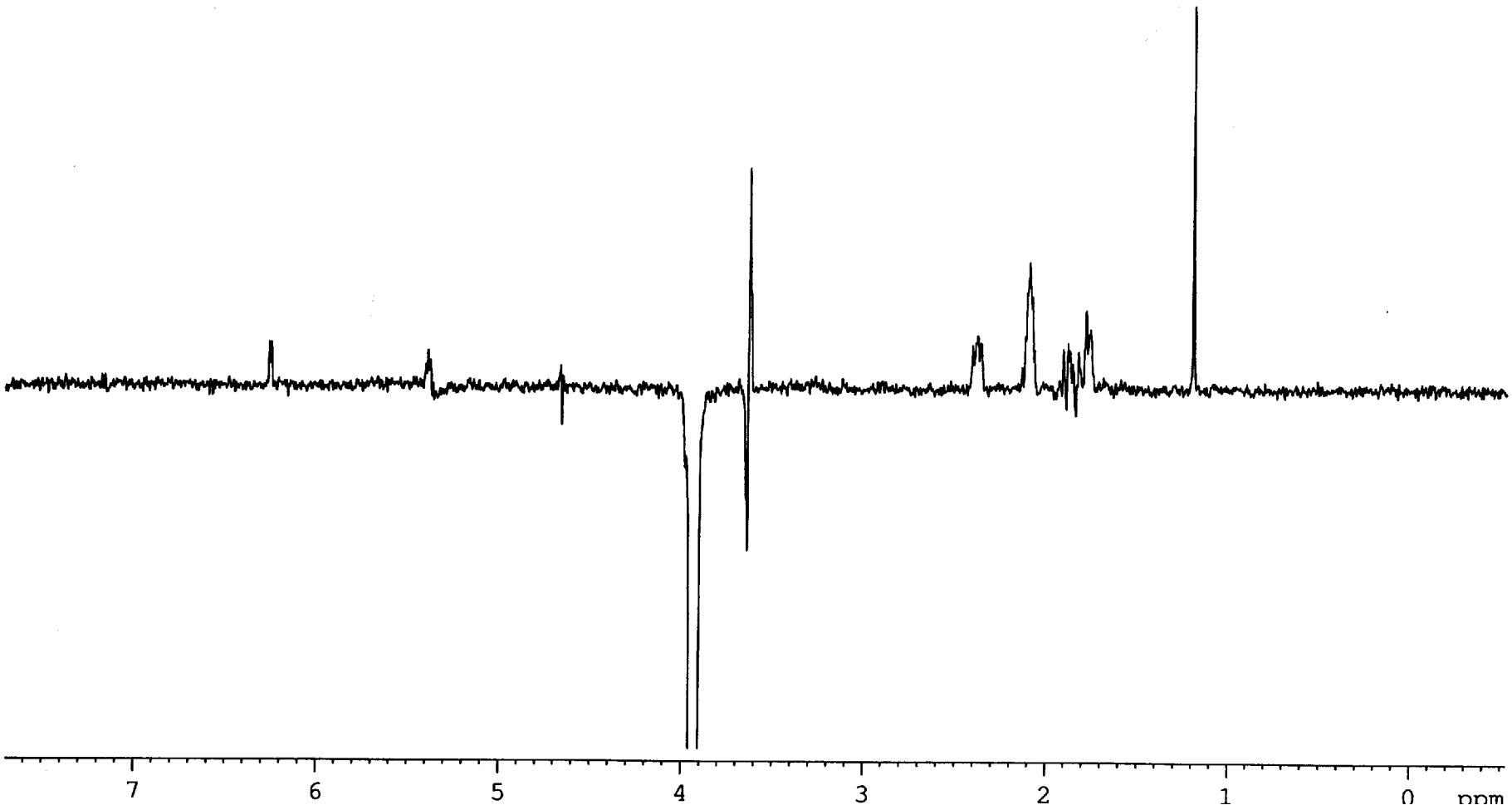


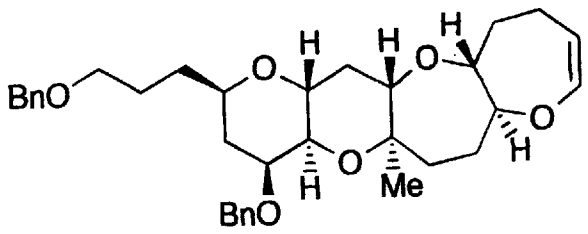


21

NOE Difference, 600 MHz

$CDCl_3$





21

NOE Difference, 600 MHz

$CDCl_3$