

SUPPLEMENTARY MATERIAL

SYNTHESIS OF BICYCLIC ORTHO ESTERS BY EPOXY ESTER REARRANGEMENTS AND STUDY OF THEIR RING OPENING REACTIONS

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Experimental protocols and spectral characterization for **11b**, **11c**, **12b**, **12c**, **29a**, **29b**, **31a**, and **31b**; ^1H and ^{13}C NMR spectra for all new compounds.

4-(1,2-Dimethyl-1-phenethyl-propoxy)-2-methyl-butane-1,2-diol (11b). According to the procedure described for **11a**, oily **11b** (0.21 g, 72%) was obtained as a 1:1 mixture of diastereomers from acetal **9** (0.25 g, 1.0 mmol) and i PrMgBr (2 M solution in Et₂O, 2.0 mL): IR (neat) 3468, 2933, 1718, 1069, 699 cm⁻¹; ¹H NMR δ 7.33-7.19 (m, 5 H), 3.88 (bs, 1 H), 3.69-3.61 (m, 1 H), 3.61-3.58 (m, 1 H), 3.55-3.40 (m, 2 H), 2.90 (b, 1 H), 2.65-2.59 (m, 2 H), 2.00-1.92 (m, 2 H), 1.83-1.76 (m, 2 H), 1.72-1.63 (m, 1 H), 1.24 (s, 3 H), 1.15 (s, 3 H), 0.96-0.90 (m, 6 H); ¹³C NMR δ 142.7, 128.6, 128.4, 125.9, 80.3, 72.8, 70.3, 57.4, 38.1, 38.0, 37.4, 33.7, 29.8, 24.5, 24.4, 19.0, 17.7, 17.2; HRMS (EI) calcd. for C₁₅H₂₃O₃ (M-C₃H₇) 251.1654, found 251.1647.

2-Methyl-4-(1-methyl-1,3-diphenyl-propoxy)-butane-1,2-diol (11c). According to the procedure described for **11a**, oily **11c** (0.21 g, 63%) was obtained from acetal **9** (0.25 g, 1.0 mmol) and C₆H₅MgBr (3 M solution in Et₂O, 1.3 mL): IR (neat) 3450, 2928, 1719, 1453 cm⁻¹; ¹H NMR δ 7.45-7.13 (m, 10 H), 3.96-3.73 (m, 2 H), 3.24-3.07 (m, 3 H), 2.93 (bs, 1 H), 2.57-2.50 (m, 2 H), 2.16 (t, J = 8.5 Hz, 2 H), 1.94-1.86 (m, 2 H), 1.71-1.66 (m, 1 H), 1.66 (s, 3 H), 1.28 (s, 3 H); ¹³C NMR δ 144.5, 142.2, 128.3, 128.2, 128.2, 127.0, 126.0, 125.7, 78.7, 73.0, 69.1, 59.3, 44.3, 39.8, 30.3, 24.7, 24.5, 23.5; HRMS (EI) calcd. for C₂₁H₂₉O₃ 329.2117, found 329.2122.

3,4-Dimethyl-1-phenyl-pentan-3-ol (12b). According to the procedure described for compound **12a**, oily **12b** (33 mg, 85%) was obtained from **11b** (59 mg, 0.20 mmol), pyridinium chlorochromate (0.34 g, 1.6 mmol, 8 eq.), 4Å molecular sieves (0.30 g) and 3.6 mL (9 eq.) of 0.5 M solution of piperidinium acetate in benzene: IR (neat) 3462, 2963, 1455, 1373 cm⁻¹; ¹H NMR δ 7.33-7.20 (m, 5 H), 2.75-2.68 (m, 2 H), 1.81-1.75 (m, 4 H), 1.19 (s, 3 H), 0.97 (d, J = 6.9 Hz, 3 H), 0.96 (d, J = 6.9 Hz, 3 H); ¹³C NMR δ 142.9, 128.4, 125.8, 74.8, 41.9, 37.1, 30.0, 23.1, 17.6, 17.0; HRMS (EI) calcd. for C₁₃H₁₈ (M-H₂O) 174.1409, found 174.1408.

2,4-Diphenyl-butan-2-ol (12c). According to the procedure described for compound **12a**, oily **12c** (36 mg, 80%) was obtained from **11c** (66 mg, 0.20 mmol), pyridinium chlorochromate (0.34 g, 1.6 mmol, 8 eq.), 4Å molecular sieves (0.30 g) and 3.6 mL (9 eq.) of 0.5 M solution of piperidinium acetate in benzene: IR (neat) 3448, 2930, 1495, 1446, 699 cm⁻¹; ¹H NMR δ 7.52-7.49 (m, 2 H), 7.40 (t, J = 7.7 Hz, 2 H), 7.31-7.25 (m, 3 H), 7.18-7.13 (m, 3 H), 2.74-2.56 (m, 1 H), 2.52-2.40 (m, 1 H), 2.19-2.12 (m, 2 H), 1.80 (bs, 1 H), 1.64 (s, 3 H); ¹³C NMR δ 147.6, 142.3, 128.5, 128.4, 126.8, 125.8, 124.9, 74.8, 46.0, 30.6, 30.5; HRMS (EI) calcd. for C₁₆H₁₈O 226.1358, found 226.1353.

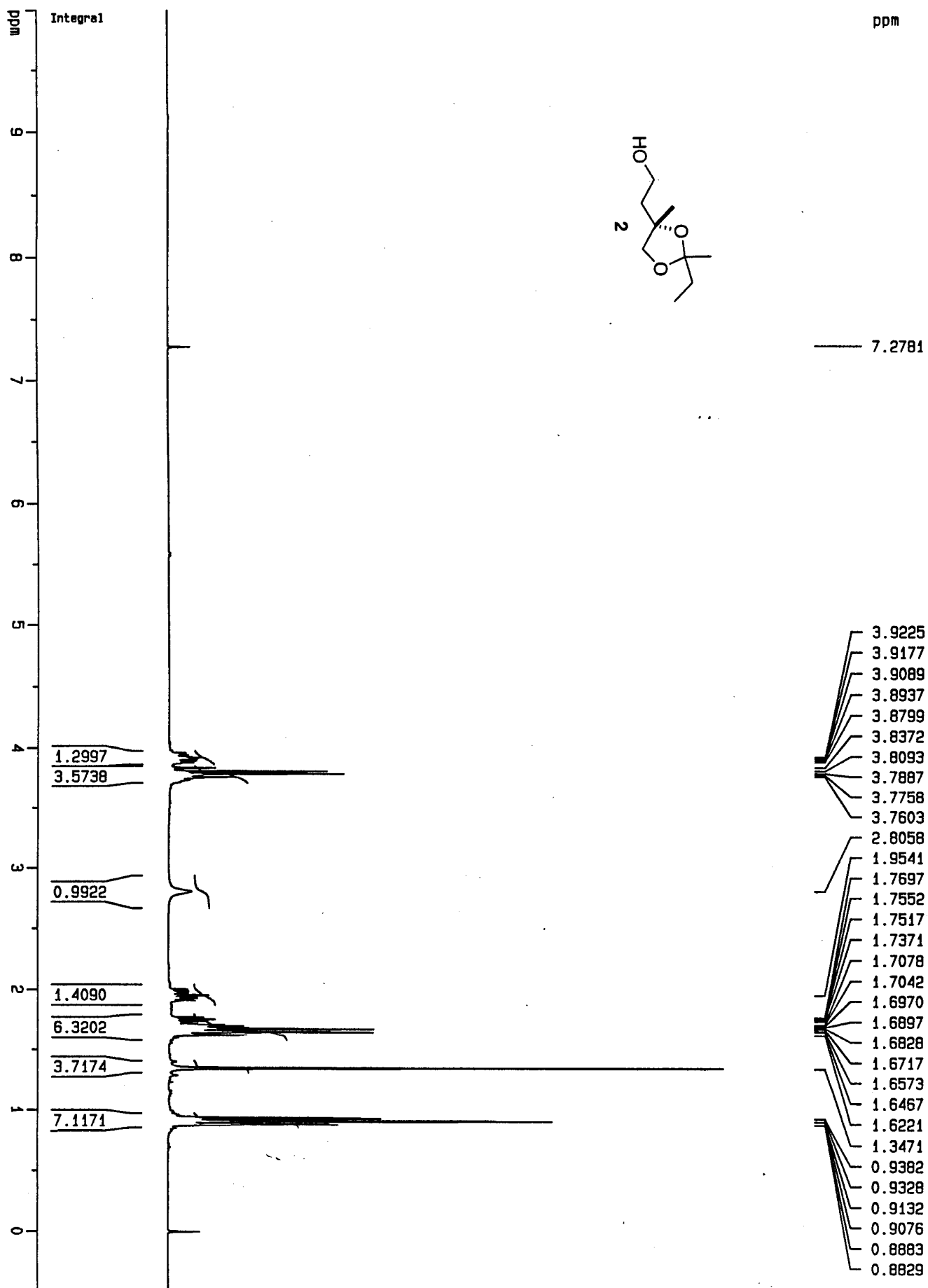
(2,5,5-Trimethyl-2-phenethyl-[1,3]dioxan-4-yl)-methanol (29a). According to the procedure described for **9**, oily **29a** (0.22 g, 84%) was obtained from ortho ester **15** (0.25 g, 1.0 mmol) and CH_3MgBr (3 M solution in Et_2O , 1.0 mL, 3.0 mmol, 3 eq.): IR (neat) 3440, 2958, 2871, 1378, 1251, 1131, 1036 cm^{-1} ; ^1H NMR δ 7.34-7.19 (m, 5 H), 3.76-3.58 (m, 4 H), 3.26 (d, J = 11.4 Hz, 1 H), 2.64 (t, J = 8.6 Hz, 2 H), 2.22-2.08 (m, 2 H), 1.98 (dd, J = 6.9, 10.7 Hz, 1 H), 1.48 (s, 3 H), 1.05 (s, 3 H), 0.80 (s, 3 H); ^{13}C NMR δ 141.9, 128.6, 128.3, 126.0, 100.3, 77.8, 71.7, 61.9, 32.9, 31.4, 30.7, 26.8, 21.7, 18.9; HRMS (EI) calcd. for $\text{C}_{16}\text{H}_{25}\text{O}_2$ 249.1855, found 249.1839.

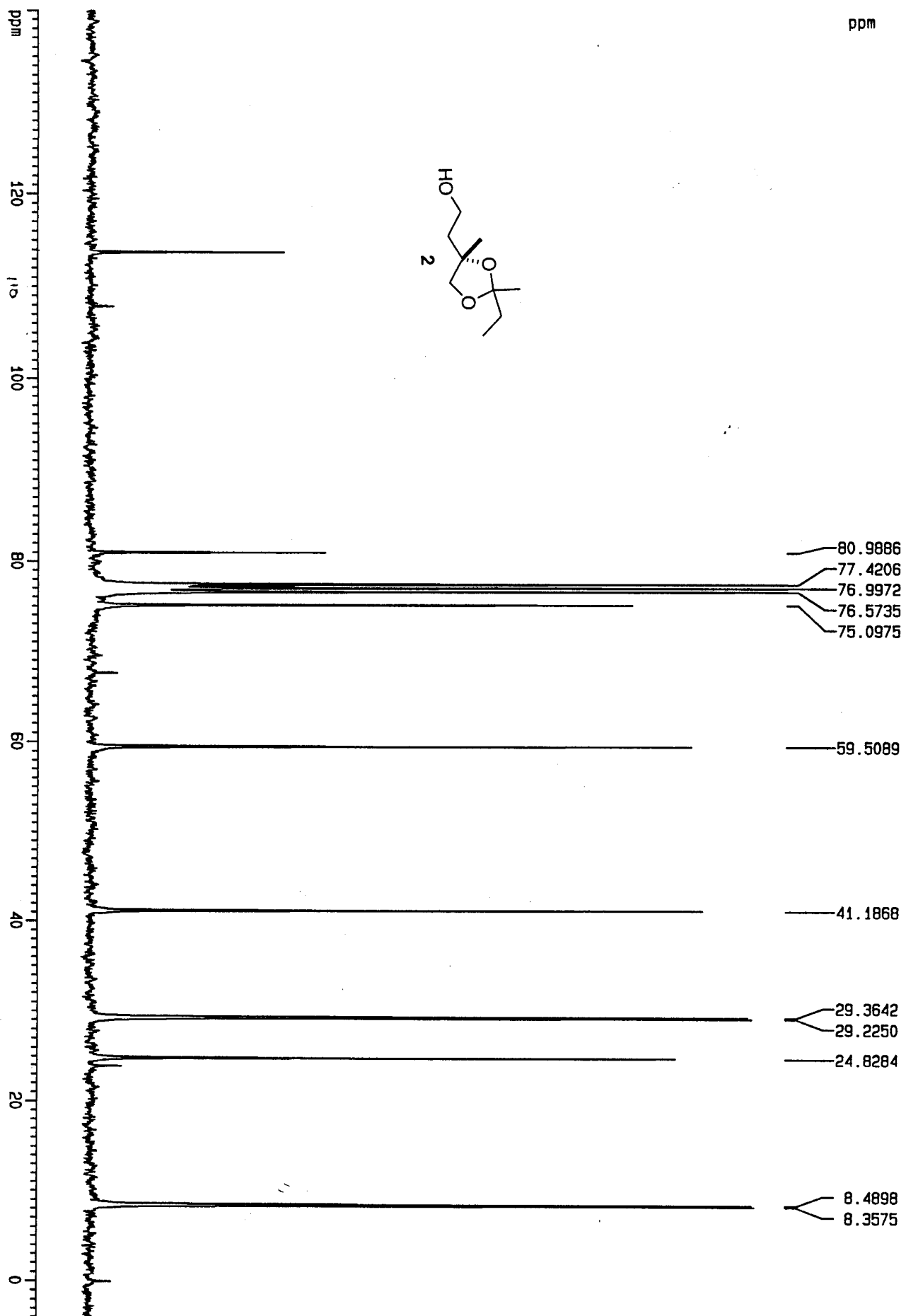
(5,5-Dimethyl-2-phenethyl-2-phenyl-[1,3]dioxan-4-yl)-methanol (29b). According to the procedure described for **9**, oily **29b** (0.26 g, 79%) was obtained as a 3:1 mixture of diastereomers from ortho ester **15** (0.25 g, 1.0 mmol) and $\text{C}_6\text{H}_5\text{MgBr}$ (3 M solution in Et_2O , 1.0 mL, 3.0 mmol, 3 eq.). Major isomer: IR (neat) 3426, 2958, 1149, 1124, 1027 cm^{-1} ; ^1H NMR δ 7.63 (d, J = 8.0 Hz, 2 H), 7.47-7.32 (m, 3 H), 7.28-7.24 (m, 3 H), 7.11 (d, J = 7.5 Hz, 2 H), 3.74-3.64 (m, 3 H), 3.37 (d, J = 11.0 Hz, 1 H), 2.85-2.78 (m, 1 H), 2.55-2.48 (m, 1 H), 2.44-2.35 (m, 2 H), 2.11-2.07 (m, 1 H), 1.99 (bs, 1 H), 0.97 (s, 3 H), 0.93 (s, 3 H); ^{13}C NMR δ 142.5, 141.3, 128.7, 128.4, 128.3, 128.1, 128.0, 127.3, 125.6, 101.3, 78.0, 71.8, 61.9, 34.9, 32.5, 30.1, 22.6, 19.2; HRMS (EI) calcd. for $\text{C}_{21}\text{H}_{26}\text{O}_3$ 326.1882, found 326.1875.

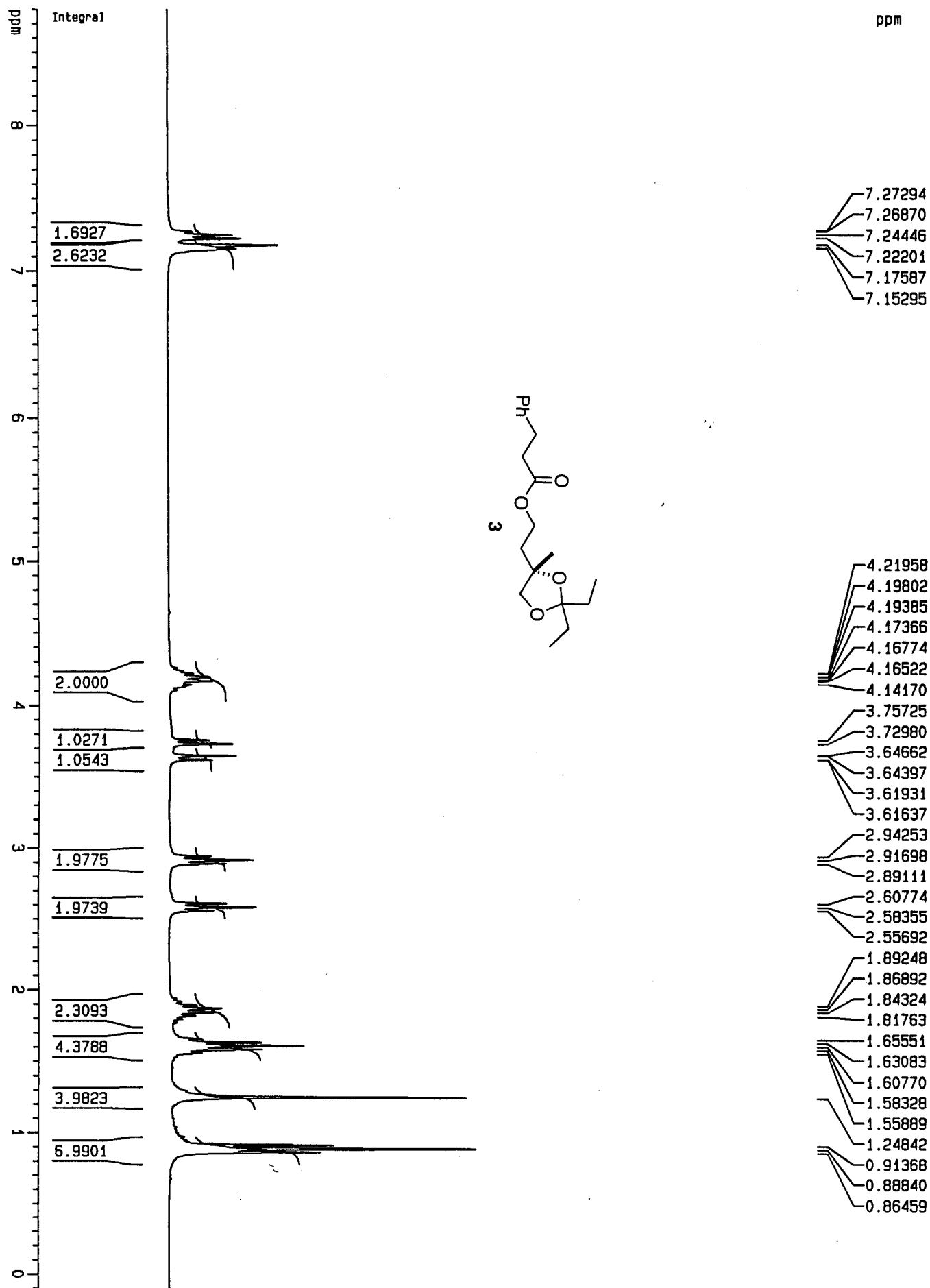
(2-Methyl-2-phenethyl-hexahydro-benzo[1,3]dioxin-8a-yl)-methanol (31a). According to the procedure described for **9**, oily **31a** (0.17 g, 57%) was obtained from ortho ester **16** (0.27 g, 1.0 mmol) and CH_3MgBr (3 M solution in Et_2O , 1.0 mL, 3.0 mmol, 3 eq.): IR (neat) 3399, 2933, 1040 cm^{-1} ; ^1H NMR δ 7.33-7.17 (m, 5 H), 4.02 (dd, J = 4.6, 11.6 Hz, 1 H), 3.89 (dd, J = 5.5, 12.0 Hz, 1 H), 3.74 (dd, J = 6.5, 11.7 Hz, 1 H), 3.41 (dd, J = 5.3, 6.2 Hz, 1 H), 2.81 (t, J = 8.6 Hz, 2 H), 2.06-1.31 (m, 12 H), 1.49 (s, 3 H); ^{13}C NMR δ 142.5, 128.4, 125.8, 99.2, 75.3, 67.4, 61.0, 43.8, 34.1, 32.3, 30.3, 26.1, 25.8, 22.8, 22.4; HRMS (EI) calcd. for $\text{C}_{18}\text{H}_{26}\text{O}_3$ 290.1882, found 290.1880.

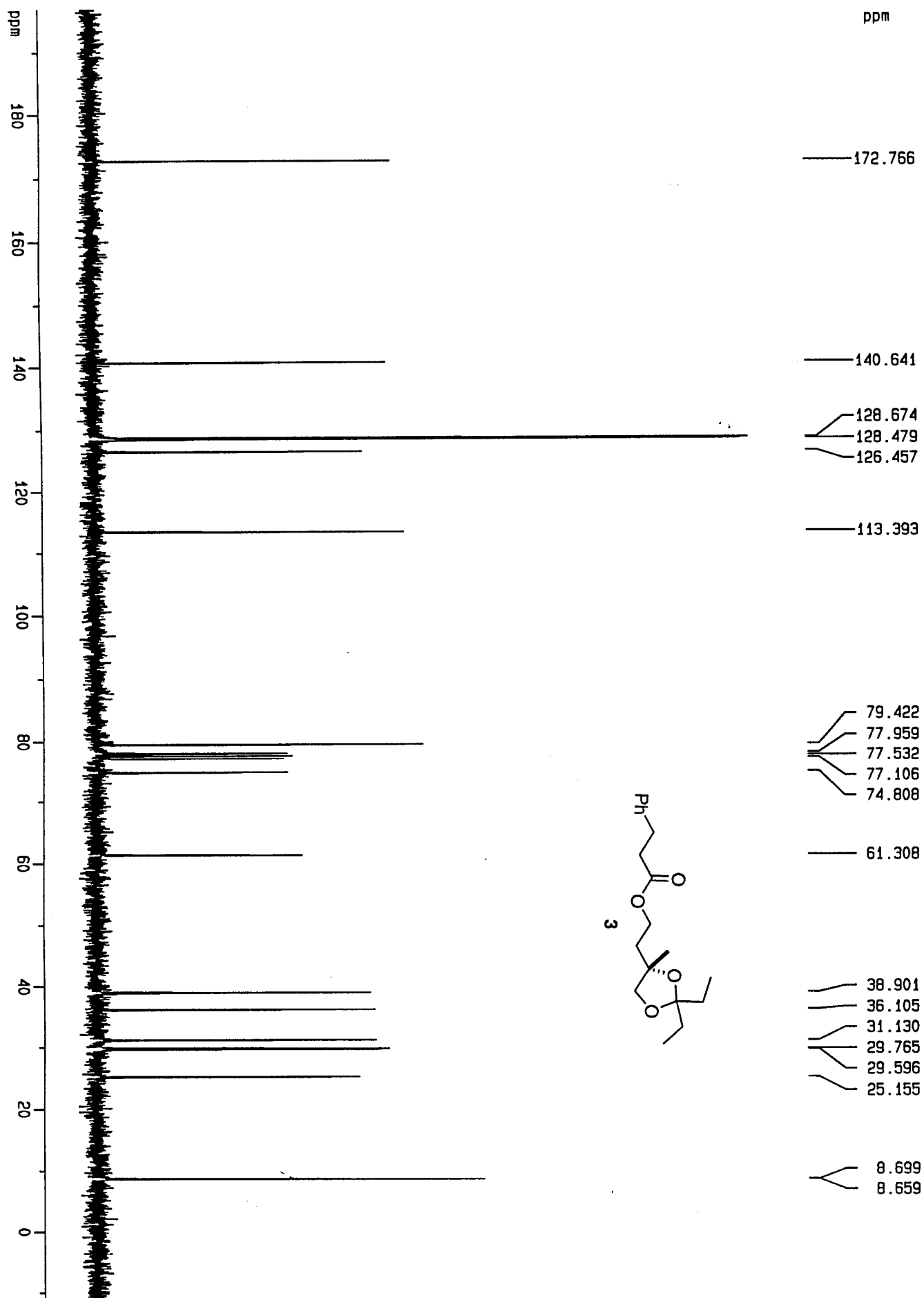
3-Phenyl-propionic acid 2-oxo-cyclohexylmethyl ester (31b). According to the procedure described for **9**, **31b** (0.24 g, 68%) was obtained from ortho ester **16** (0.27 g, 1.0 mmol) and $\text{C}_6\text{H}_5\text{MgBr}$ (3 M solution in Et_2O , 1.0 mL, 3.0 mmol, 3 eq.) as a colorless solid: Mp. 100-101 °C (hexanes); IR (neat) 3083, 2939, 1447, 1032 cm^{-1} ; ^1H NMR δ 7.53-7.50 (m, 2 H), 7.41-7.15 (m, 8 H), 4.19 (dd, J = 3.6, 7.8 Hz, 1 H), 3.66 (dd, J = 3.8, 8.1 Hz, 1 H), 3.31, 3.17 (AB of ABX, J_{AB} = 11.7 Hz, J_{AX} = 4.5 Hz, J_{BX} = 8.7 Hz, 2 H), 2.90 (dt, J = 4.8, 13.2 Hz, 1 H), 2.67 (dt, J = 4.5, 12.9 Hz, 1 H), 2.16-1.93 (m, 4 H),

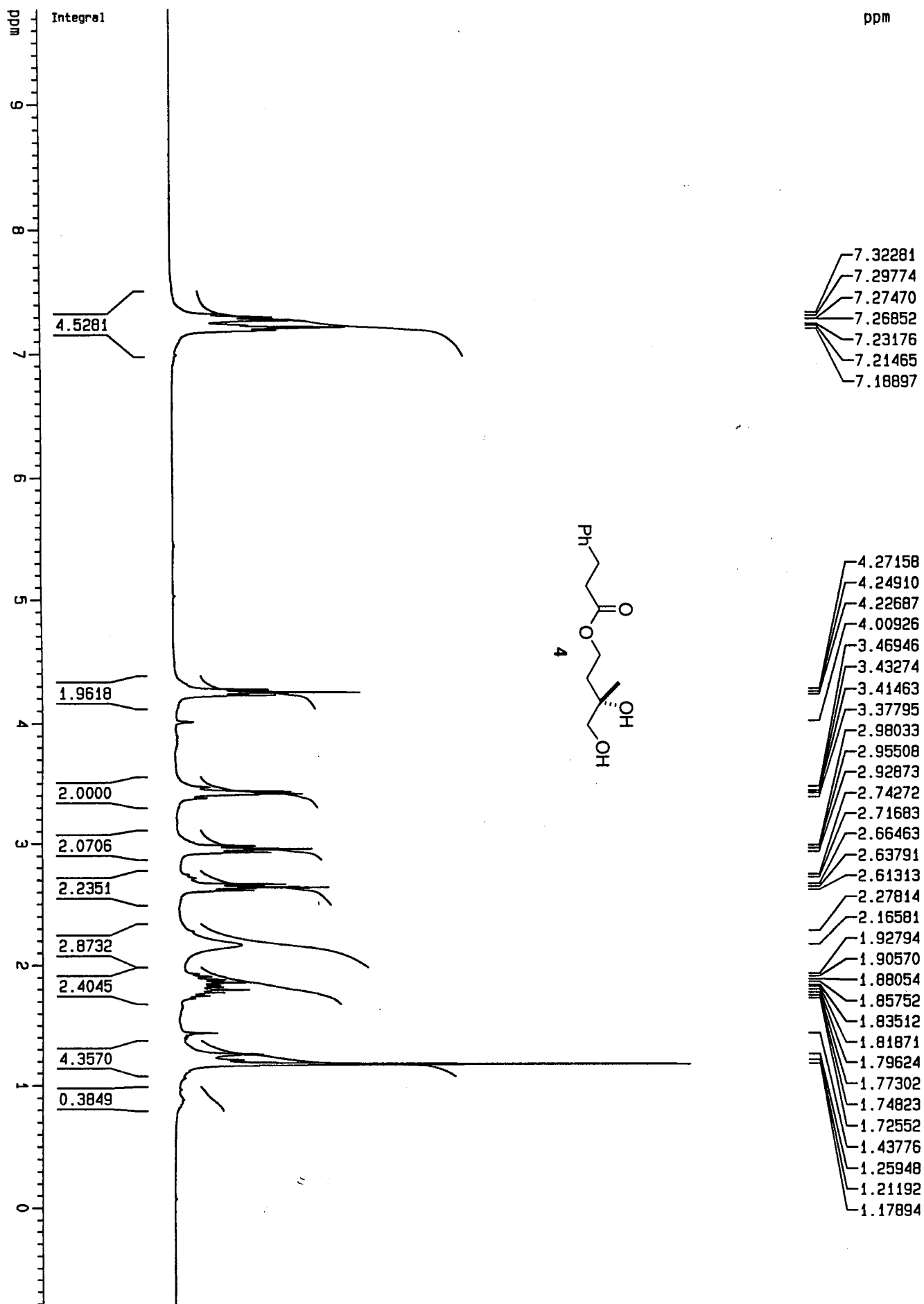
1.78-1.28 (m, 8 H); ^{13}C NMR δ 144.8, 142.4, 128.5, 128.3, 127.8, 125.6, 99.8, 75.3, 66.7, 65.9, 62.7, 48.2, 34.1, 32.6, 30.0, 25.8, 24.3, 21.5, 15.3; HRMS (EI) calcd. for $\text{C}_{23}\text{H}_{28}\text{O}_3$ 226.1358, found 226.1353.

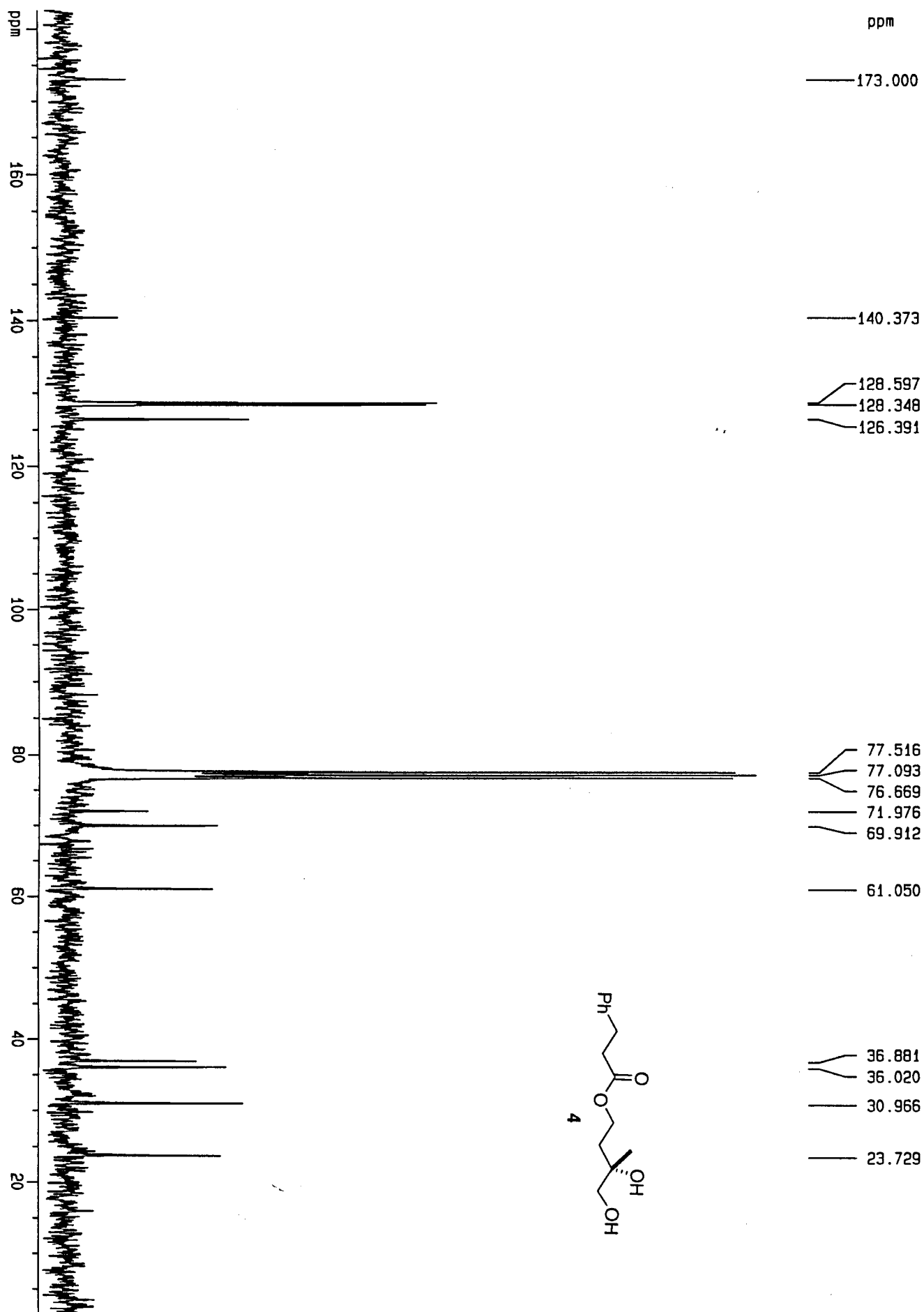


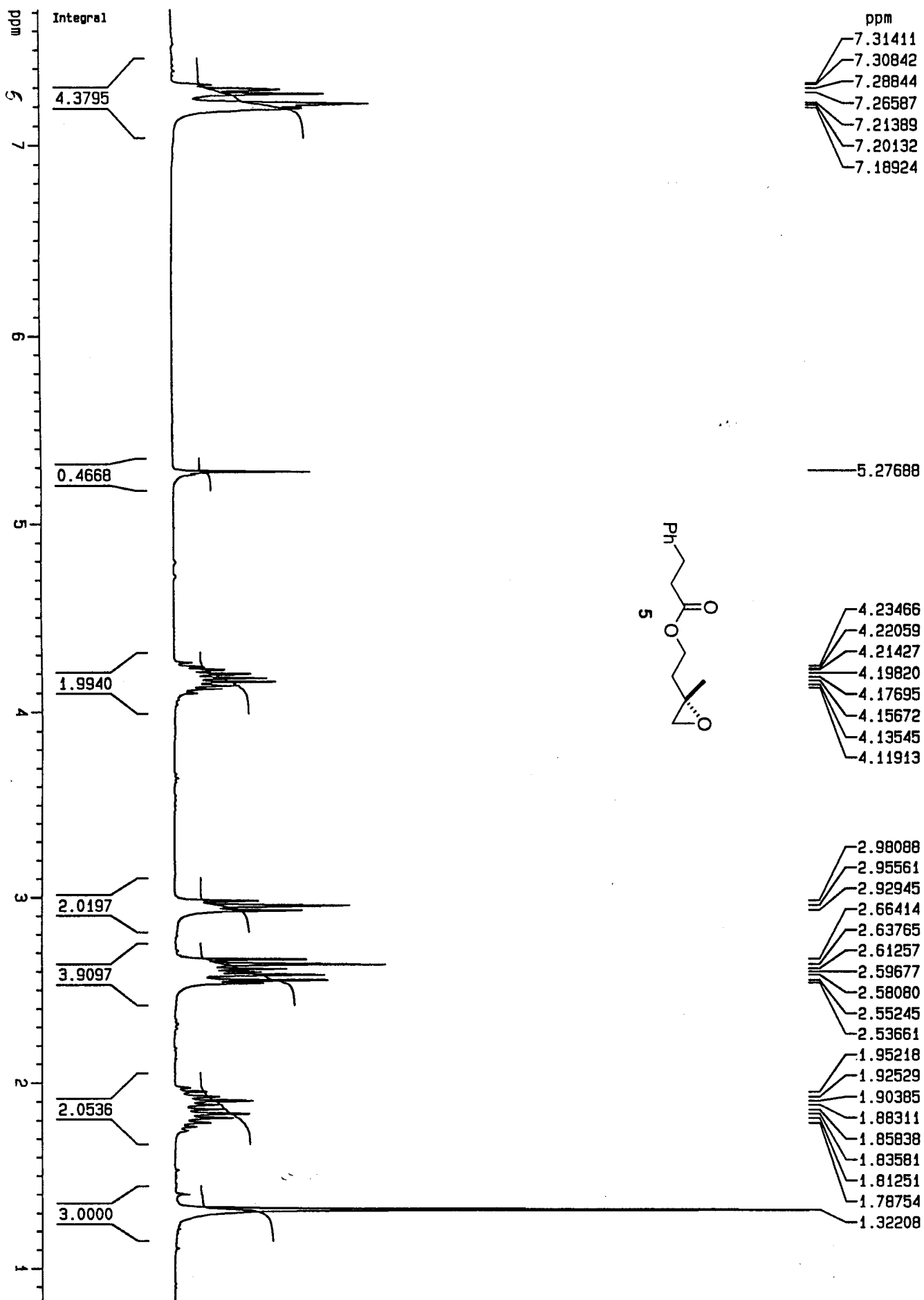




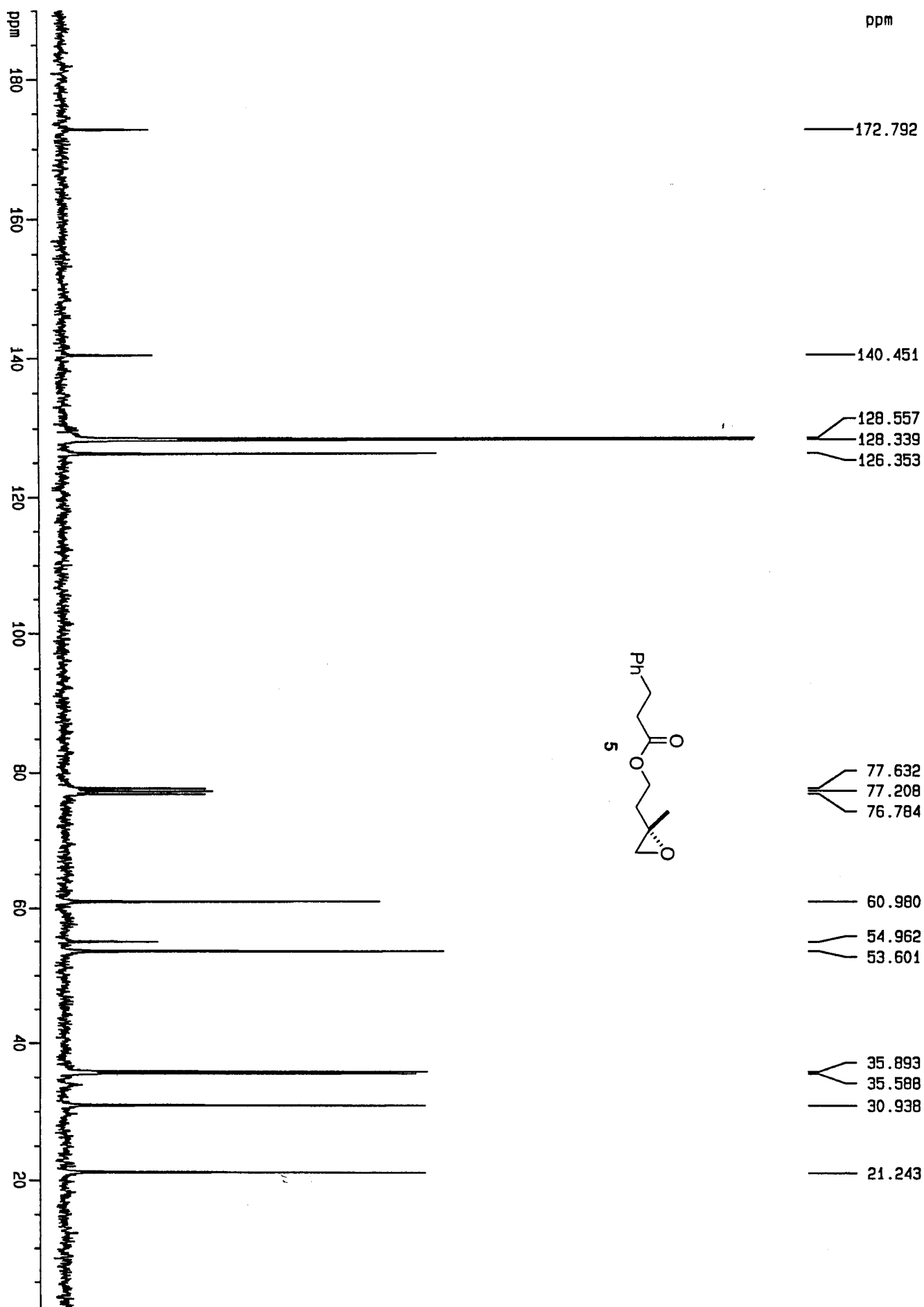


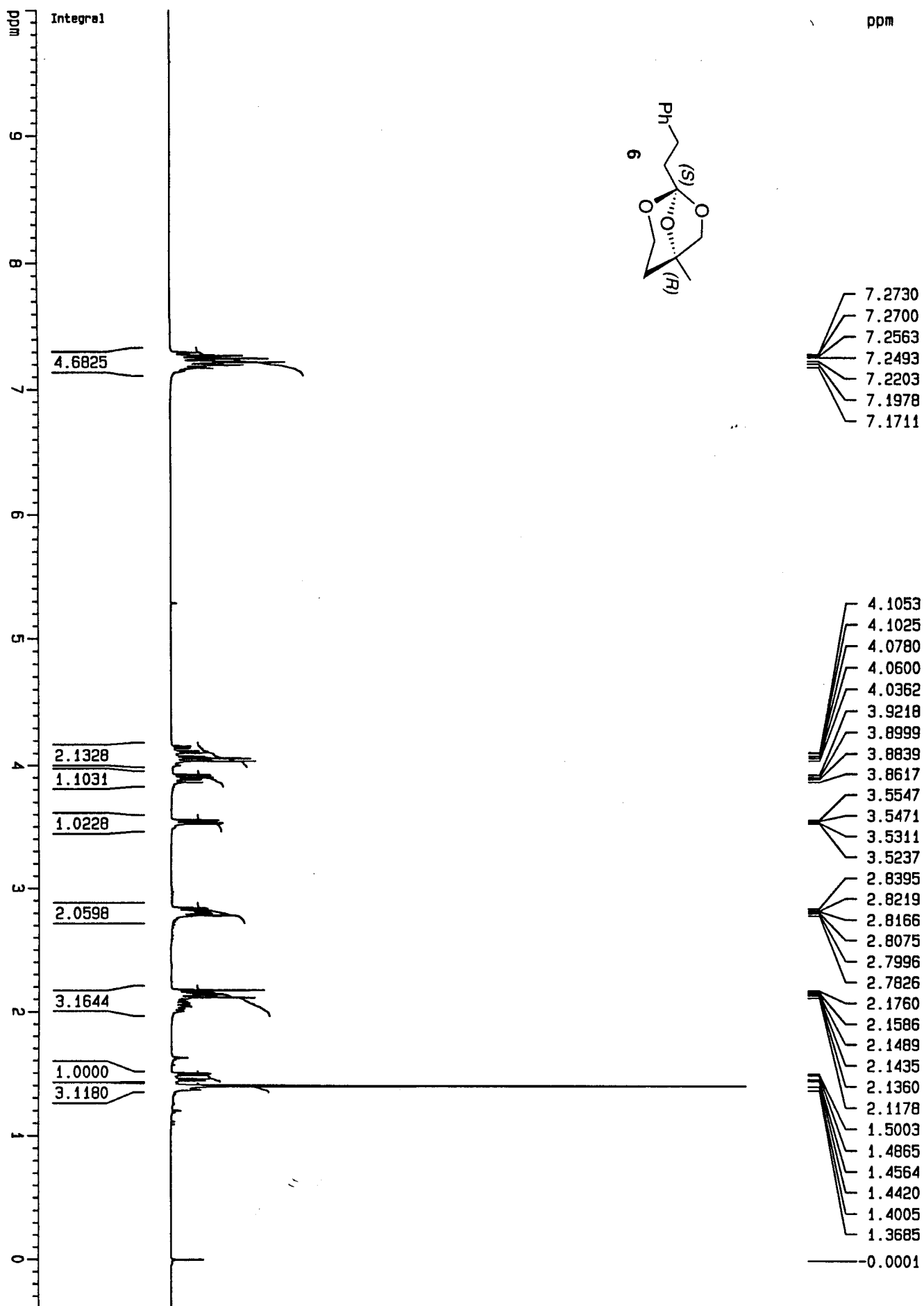


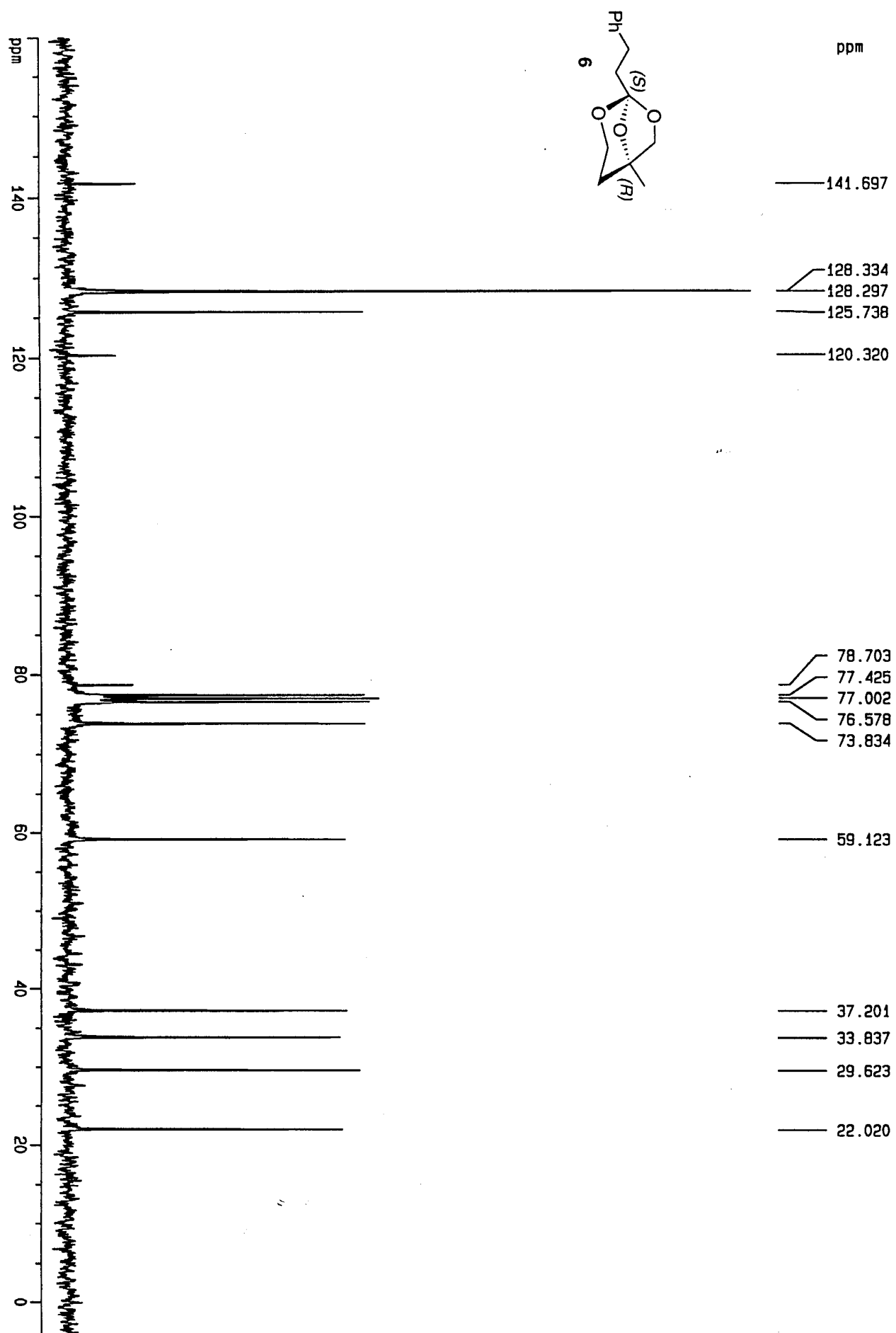


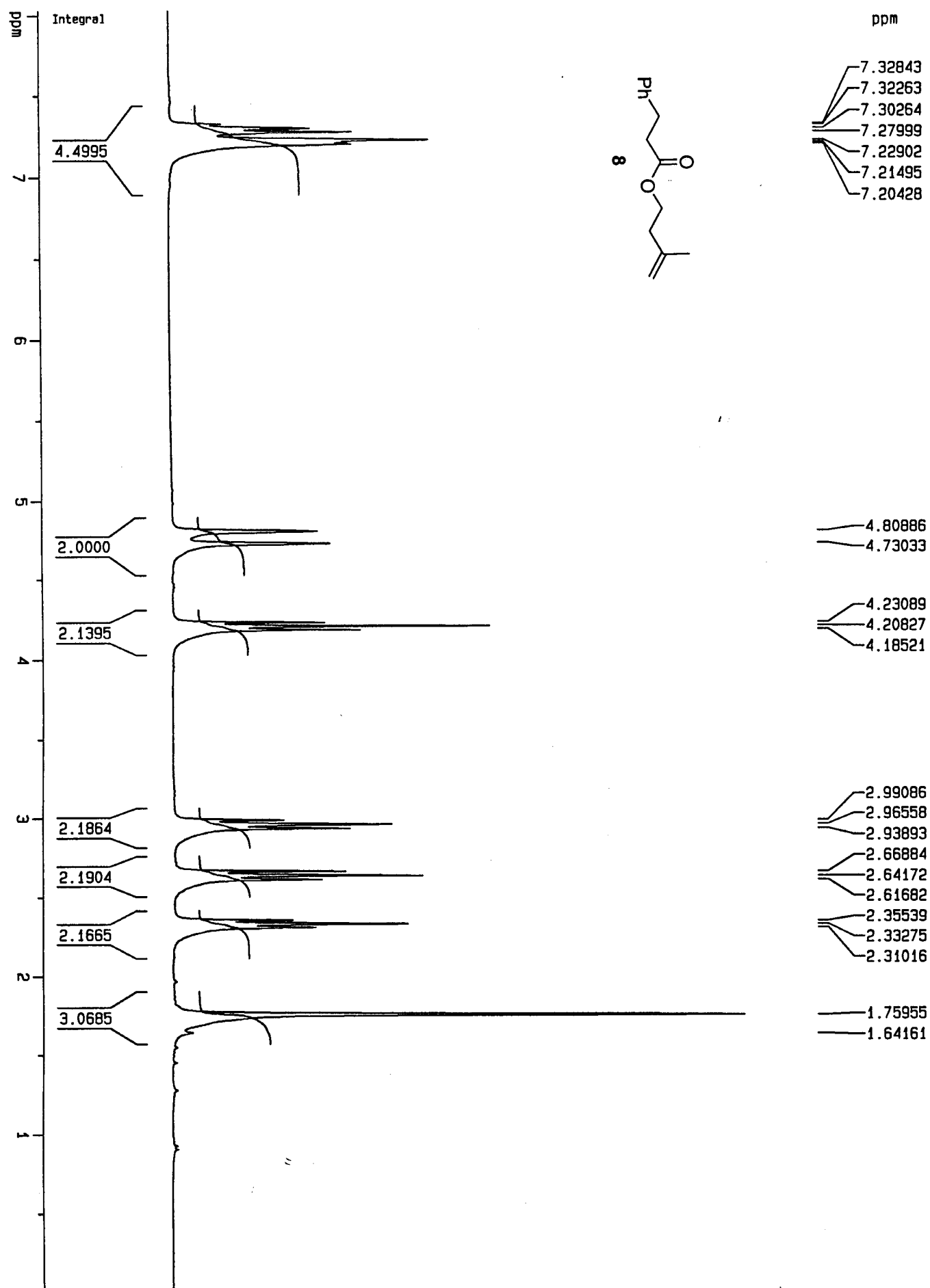


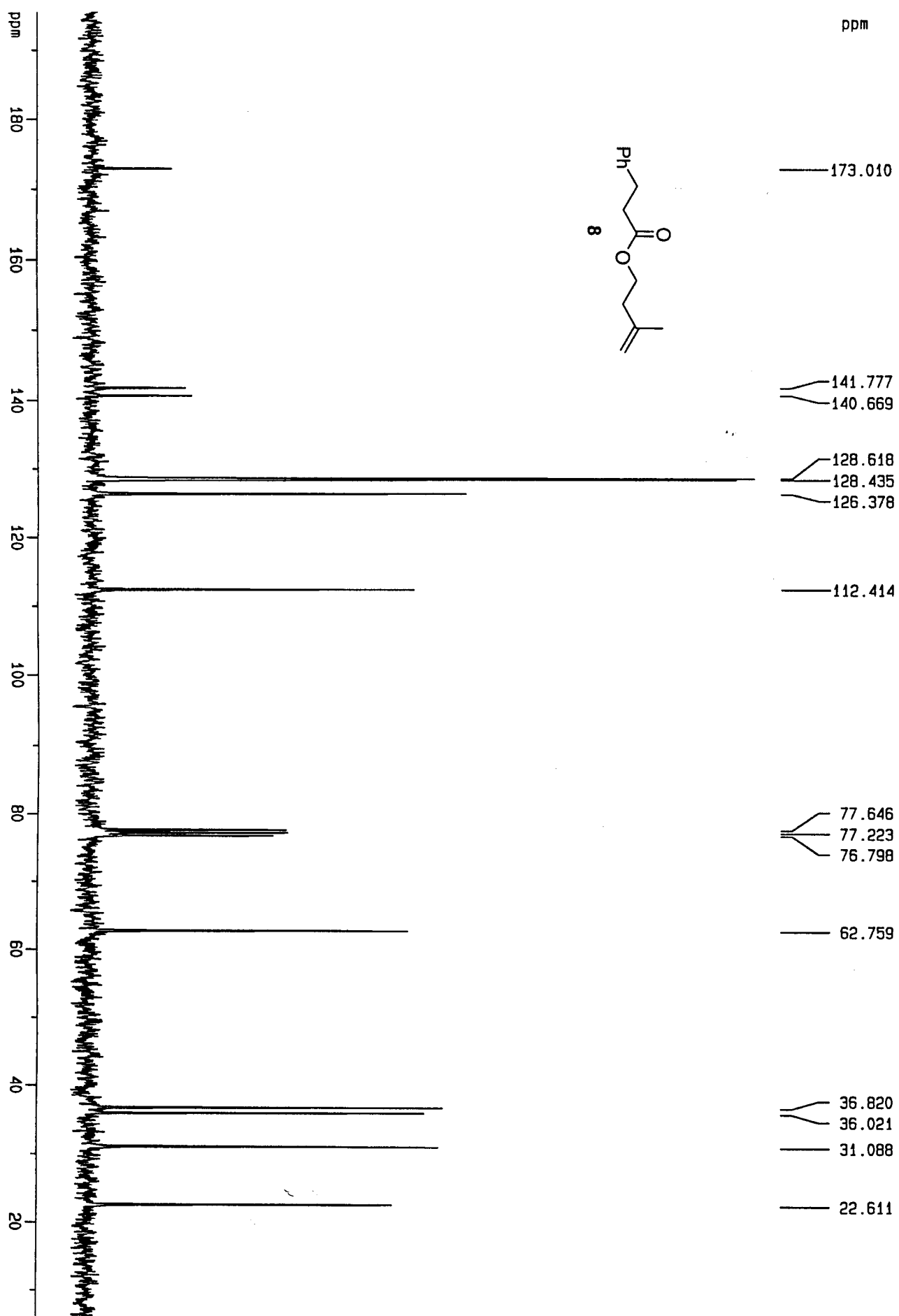
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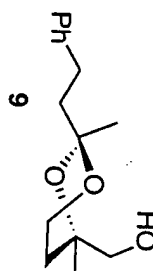




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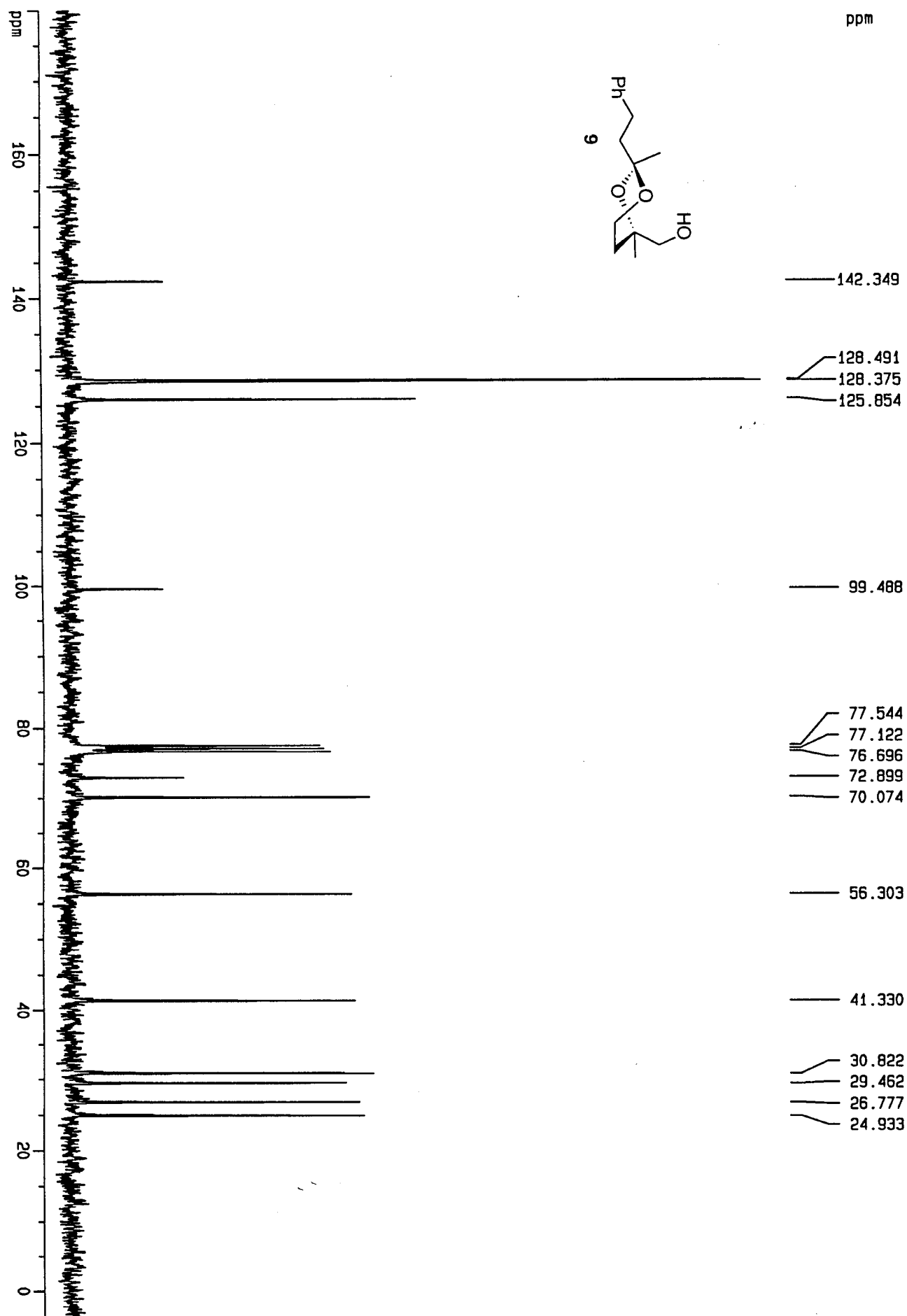
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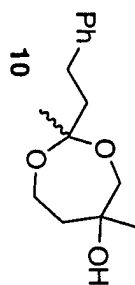
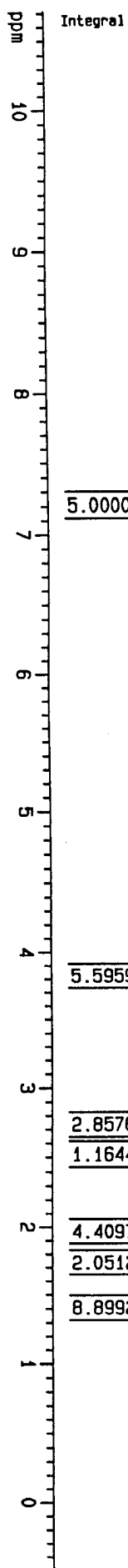
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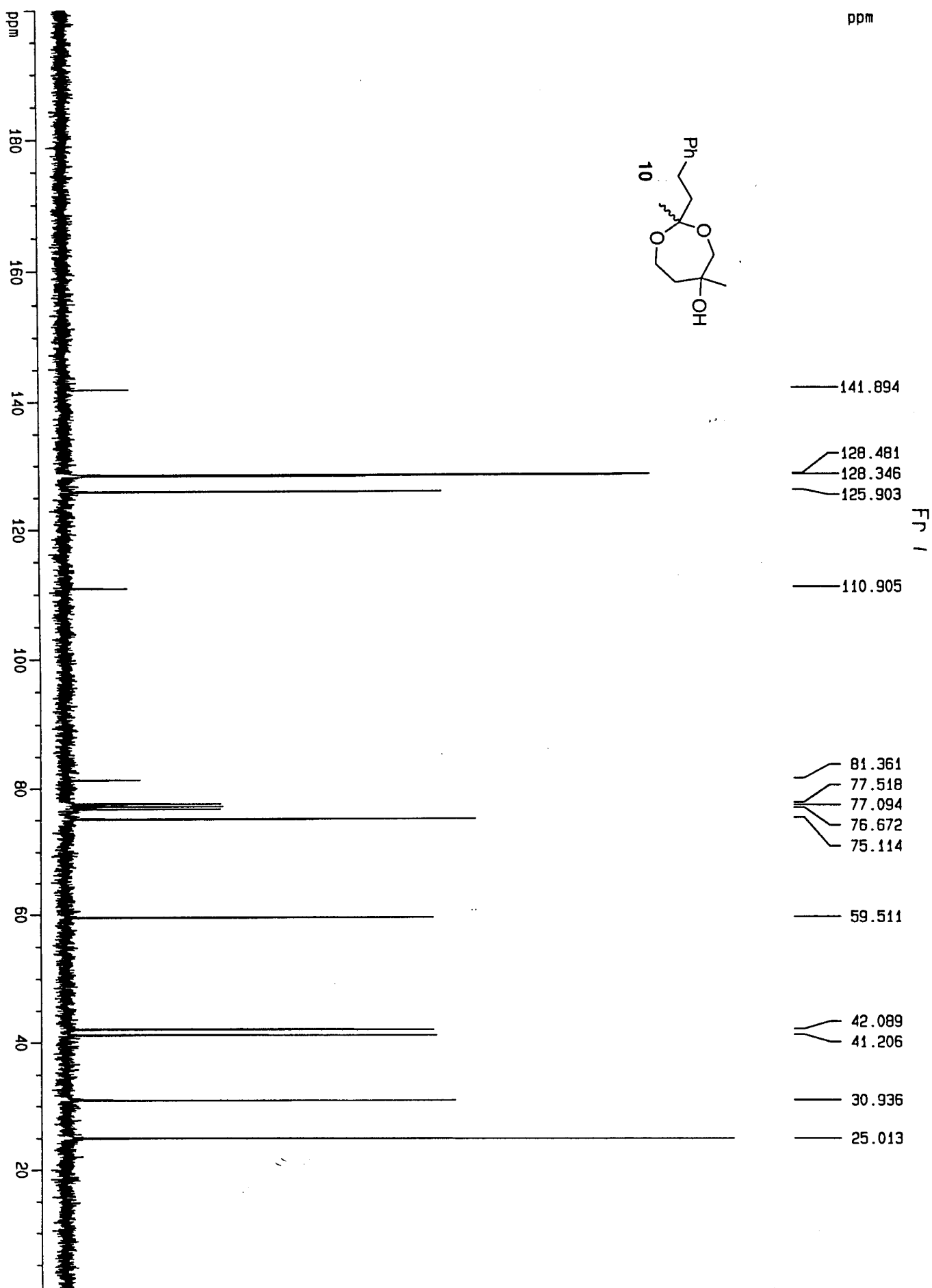
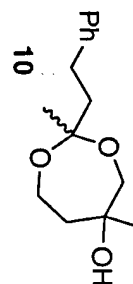
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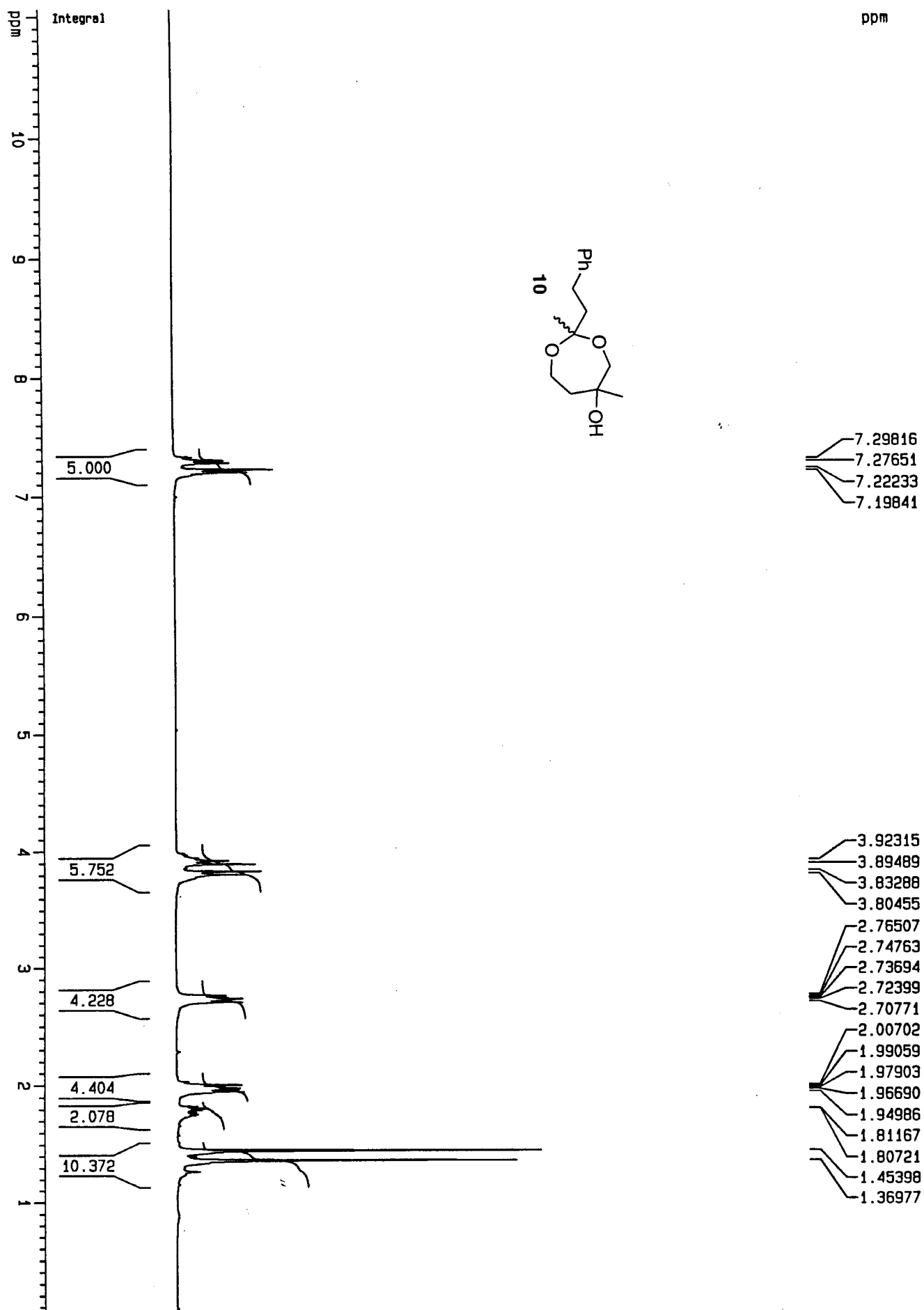
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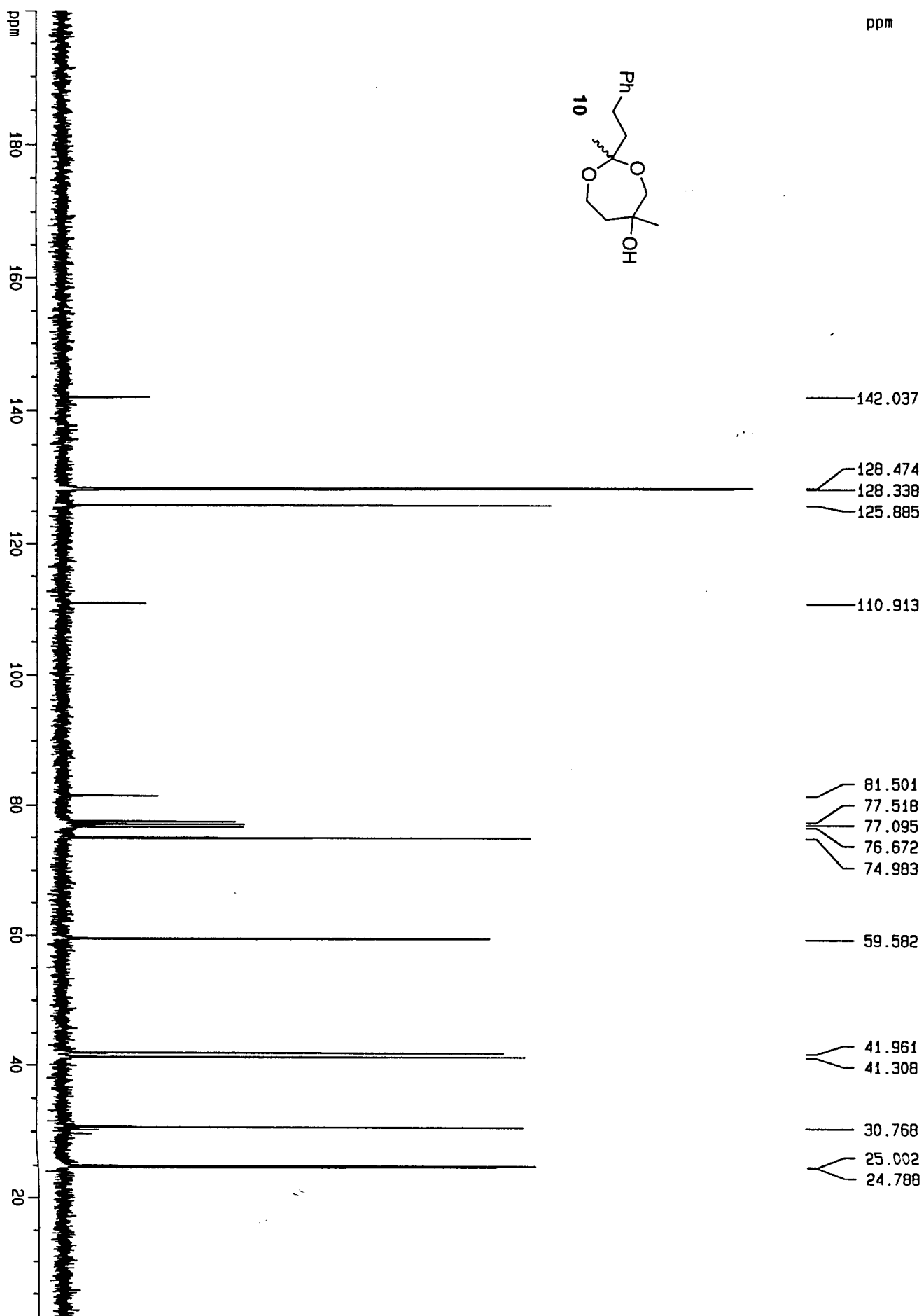
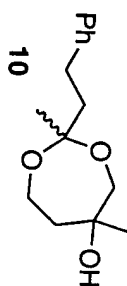
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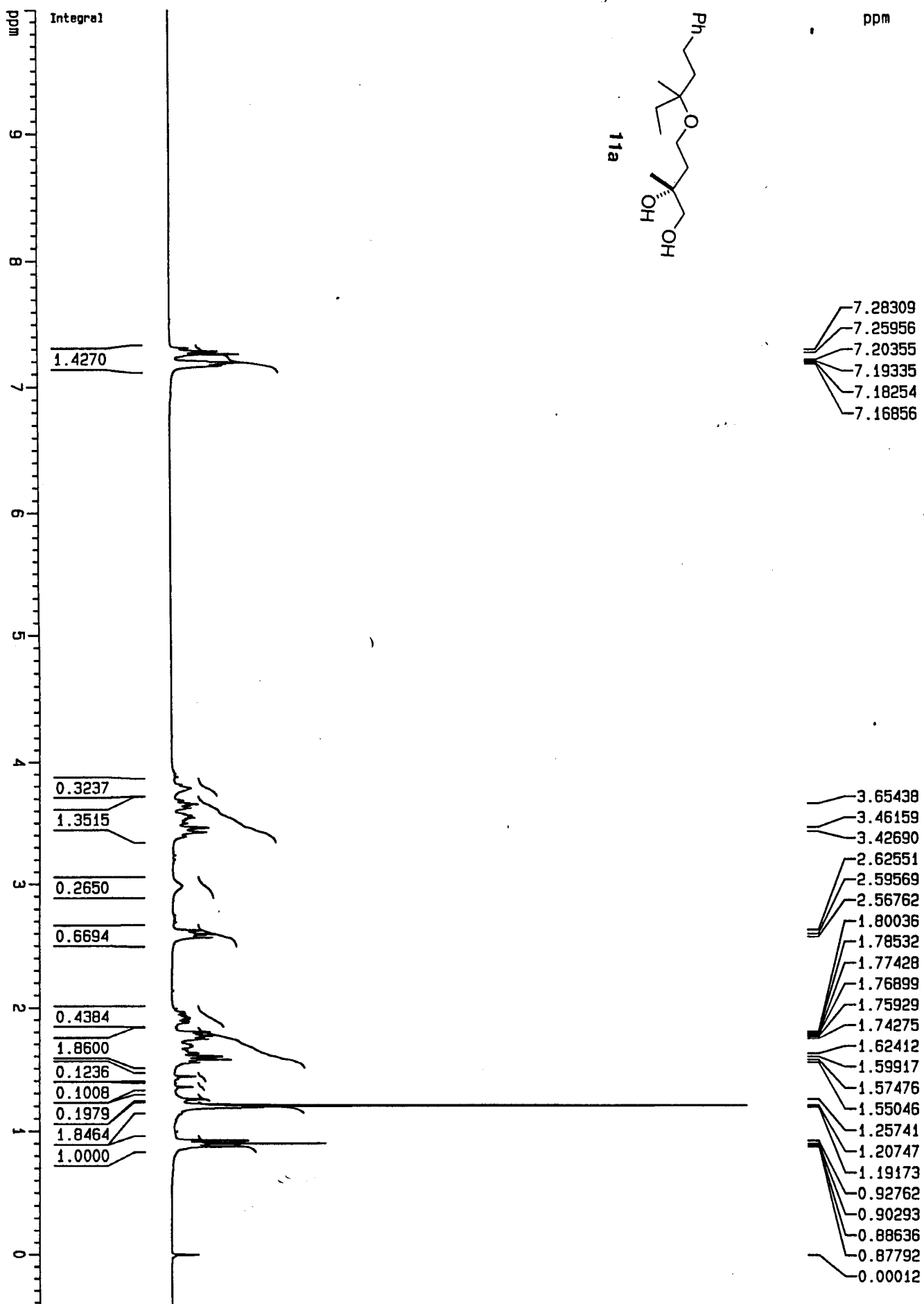
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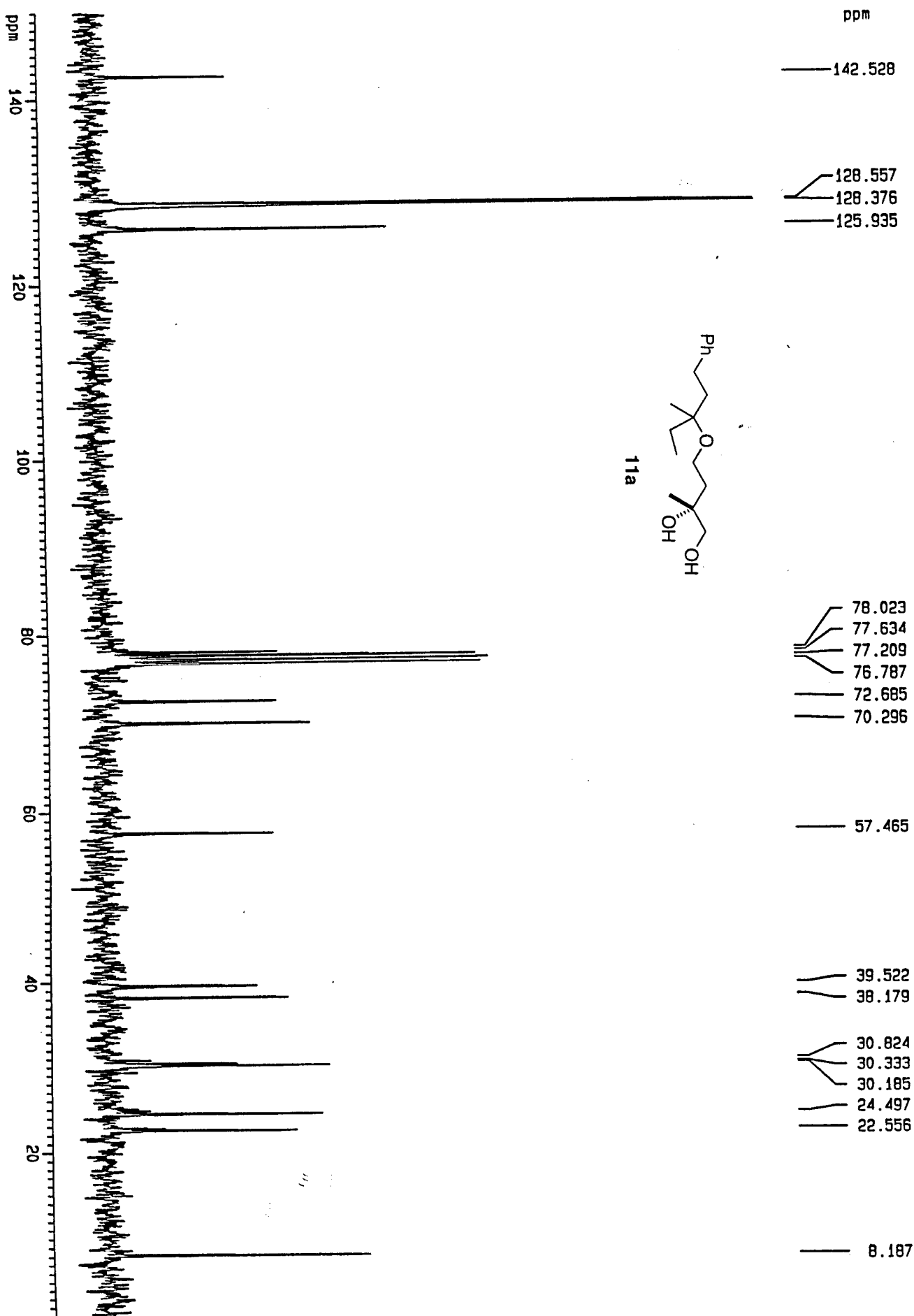


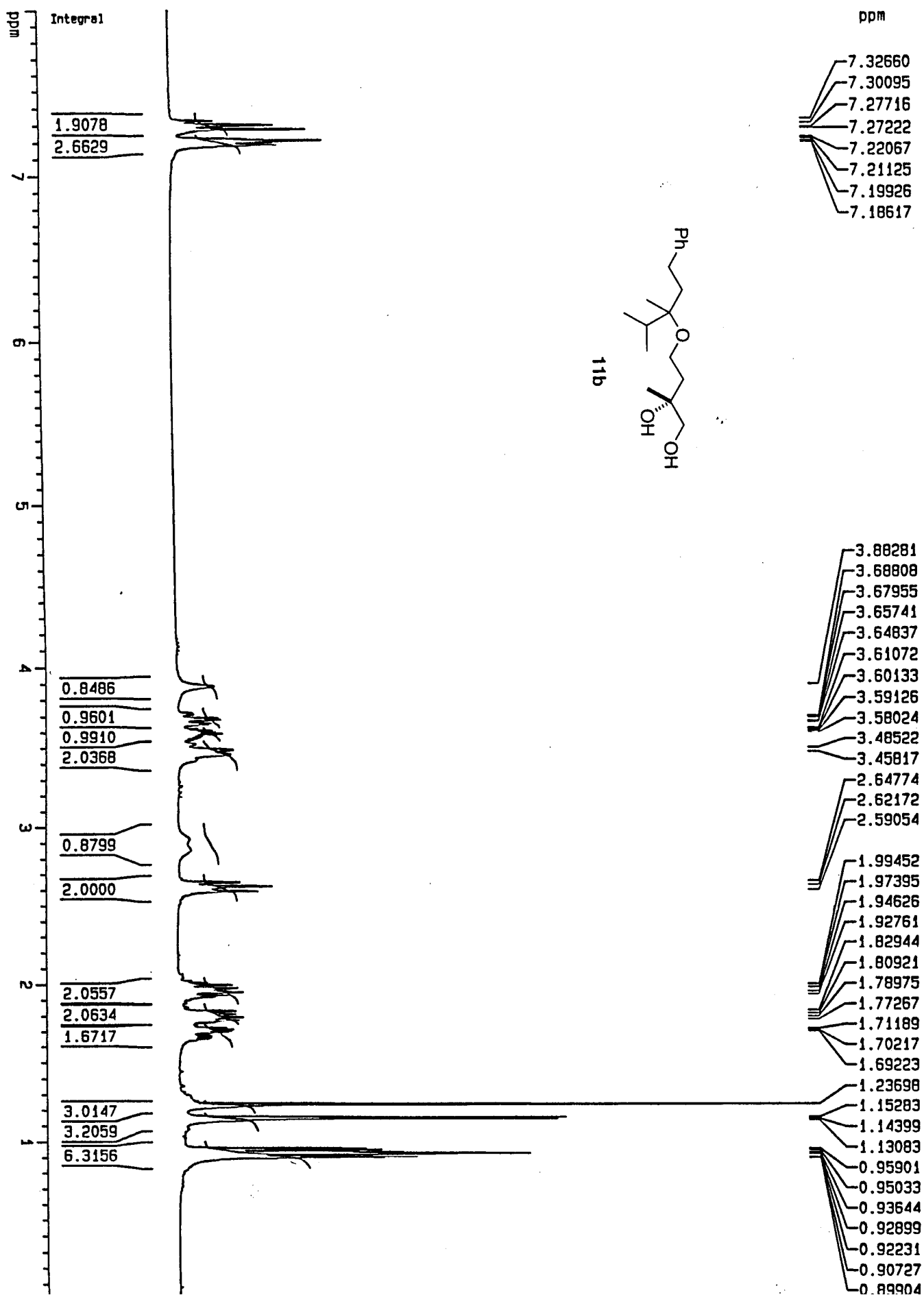
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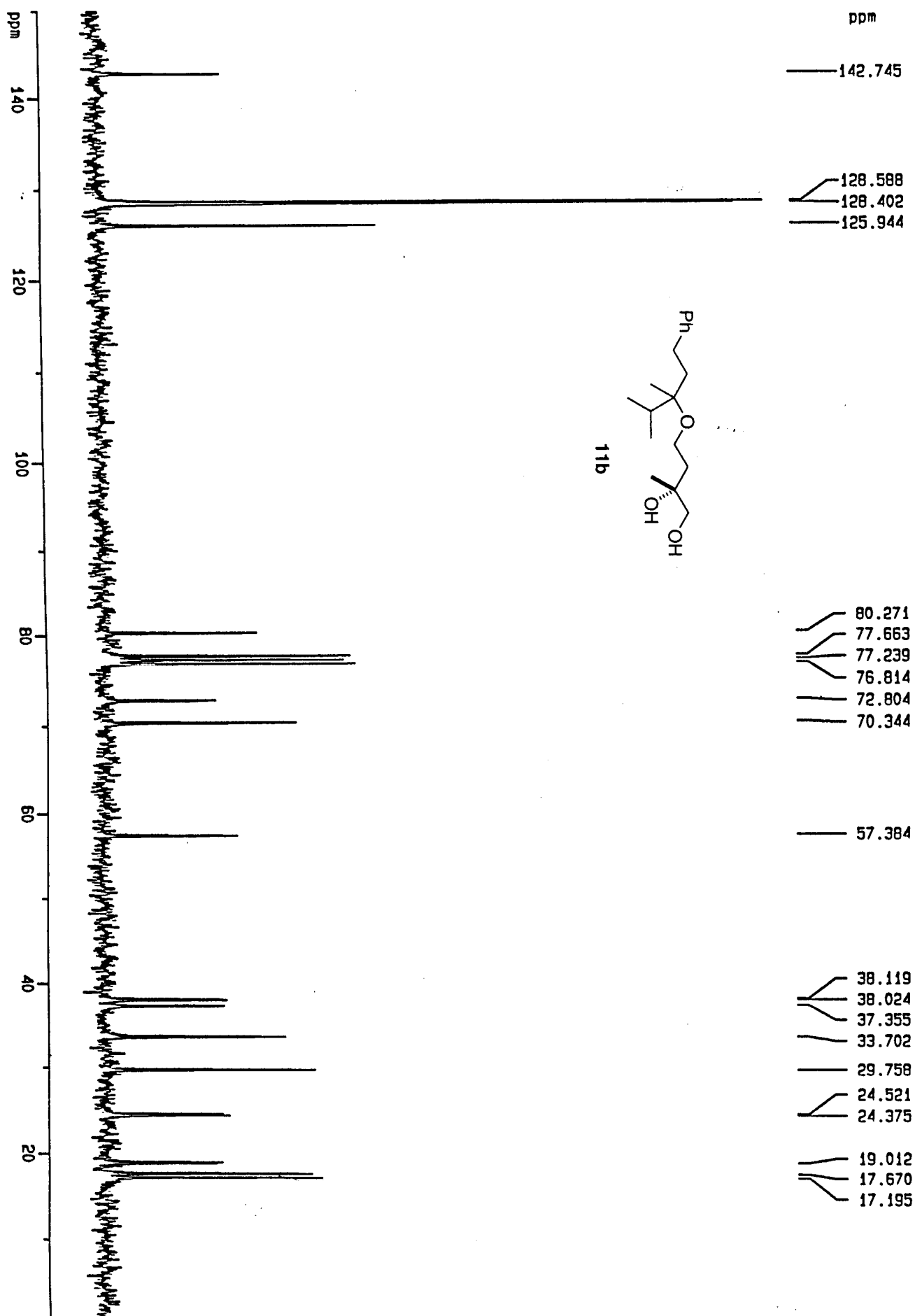
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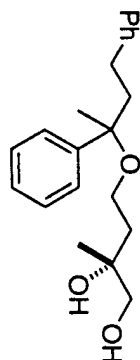


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11c



Integral

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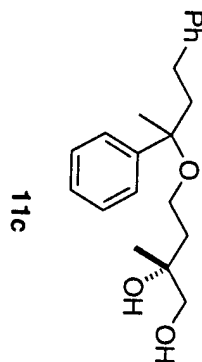
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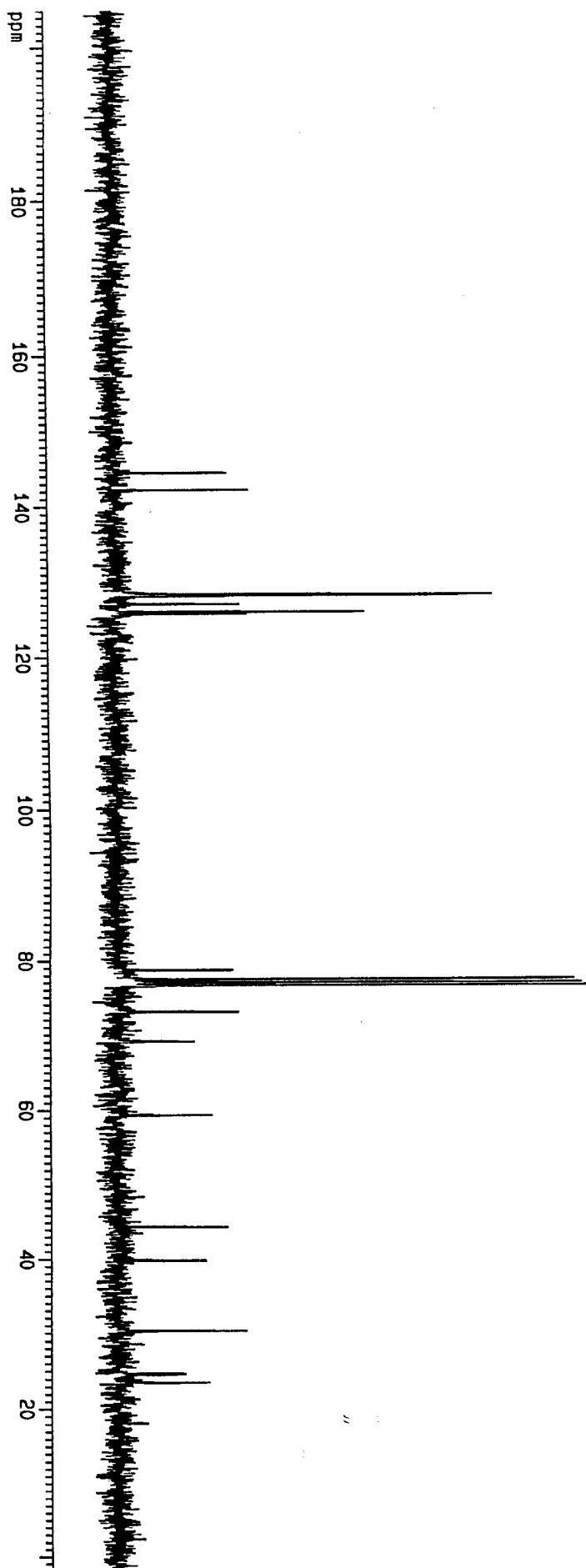
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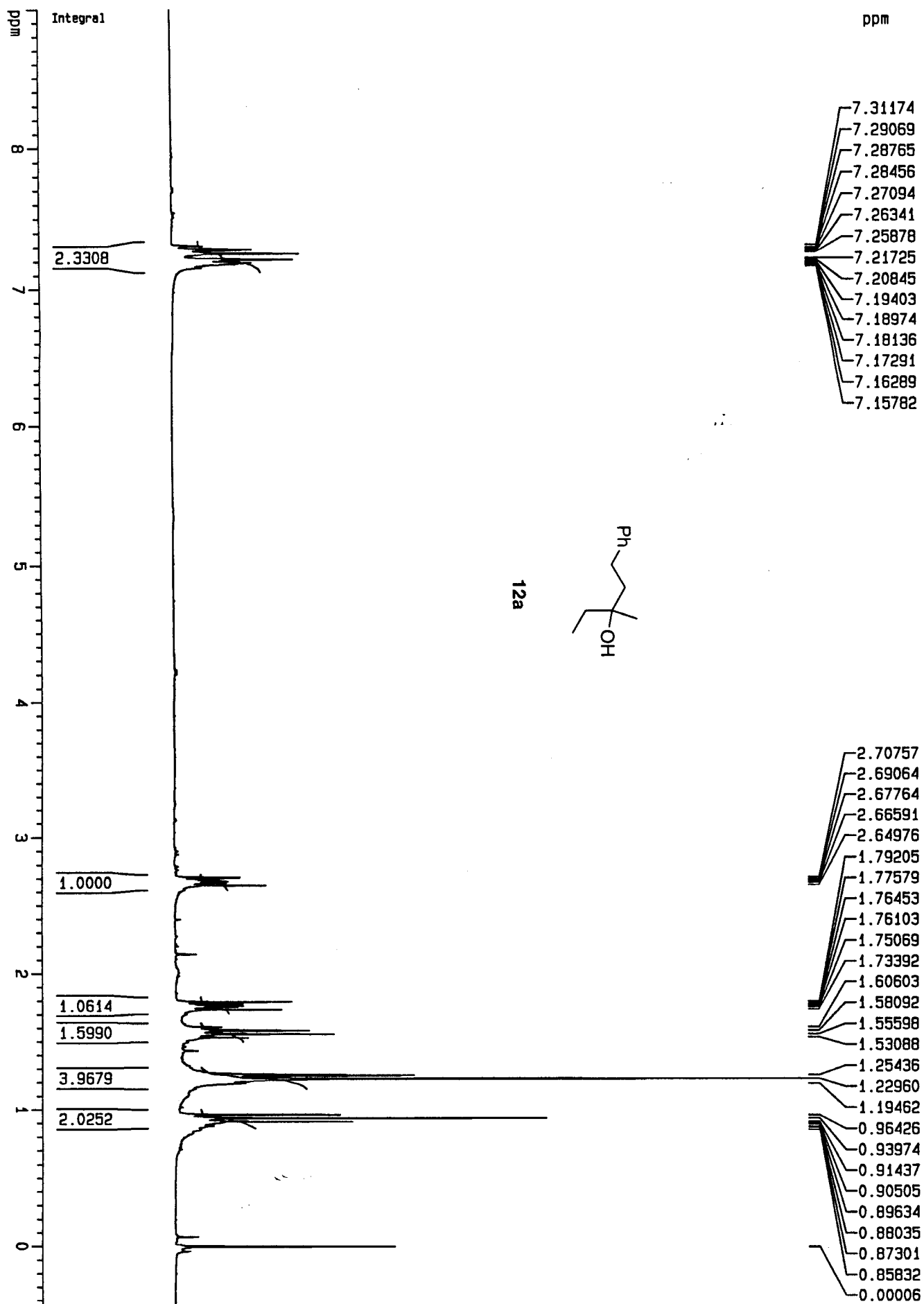
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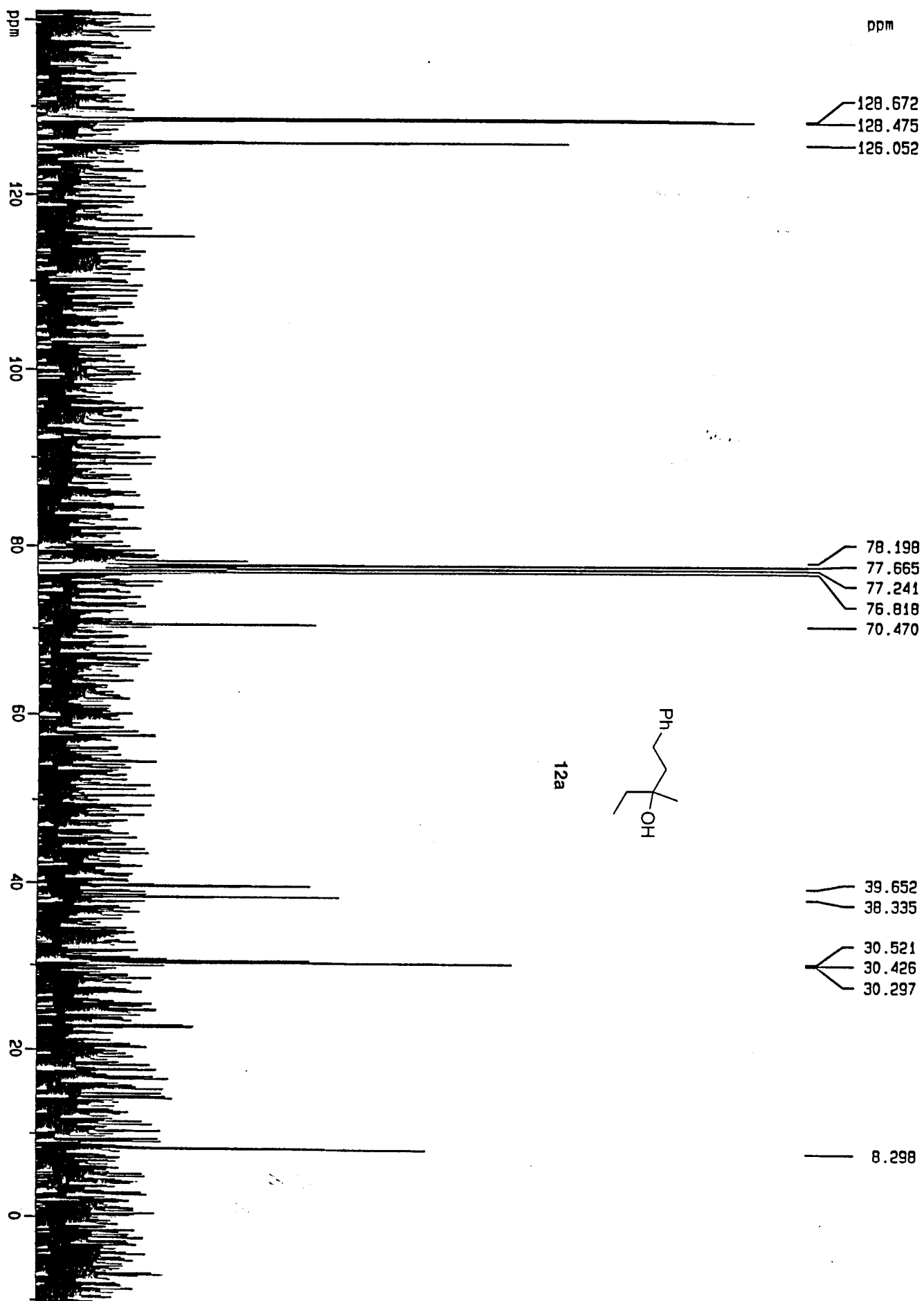
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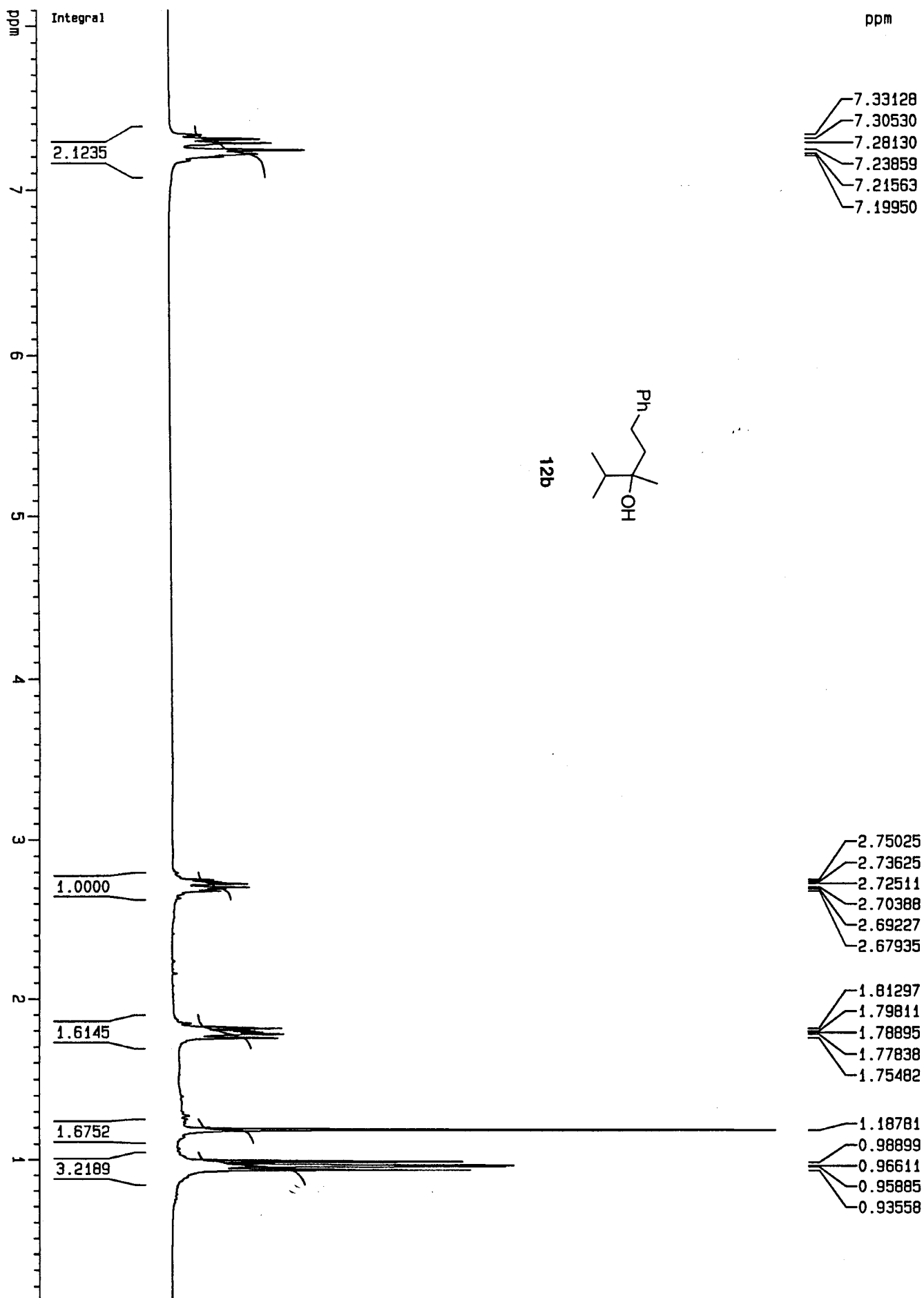
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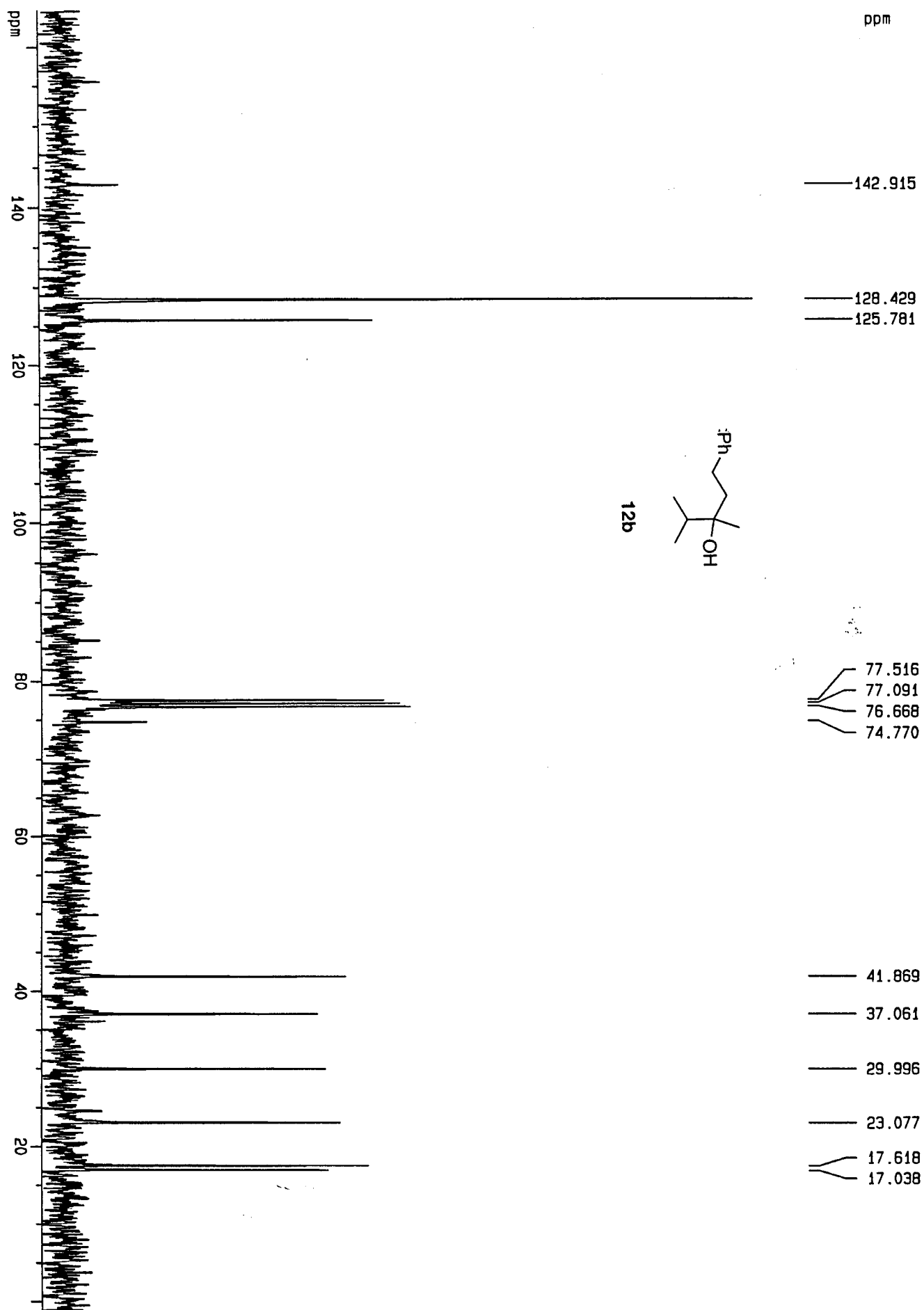
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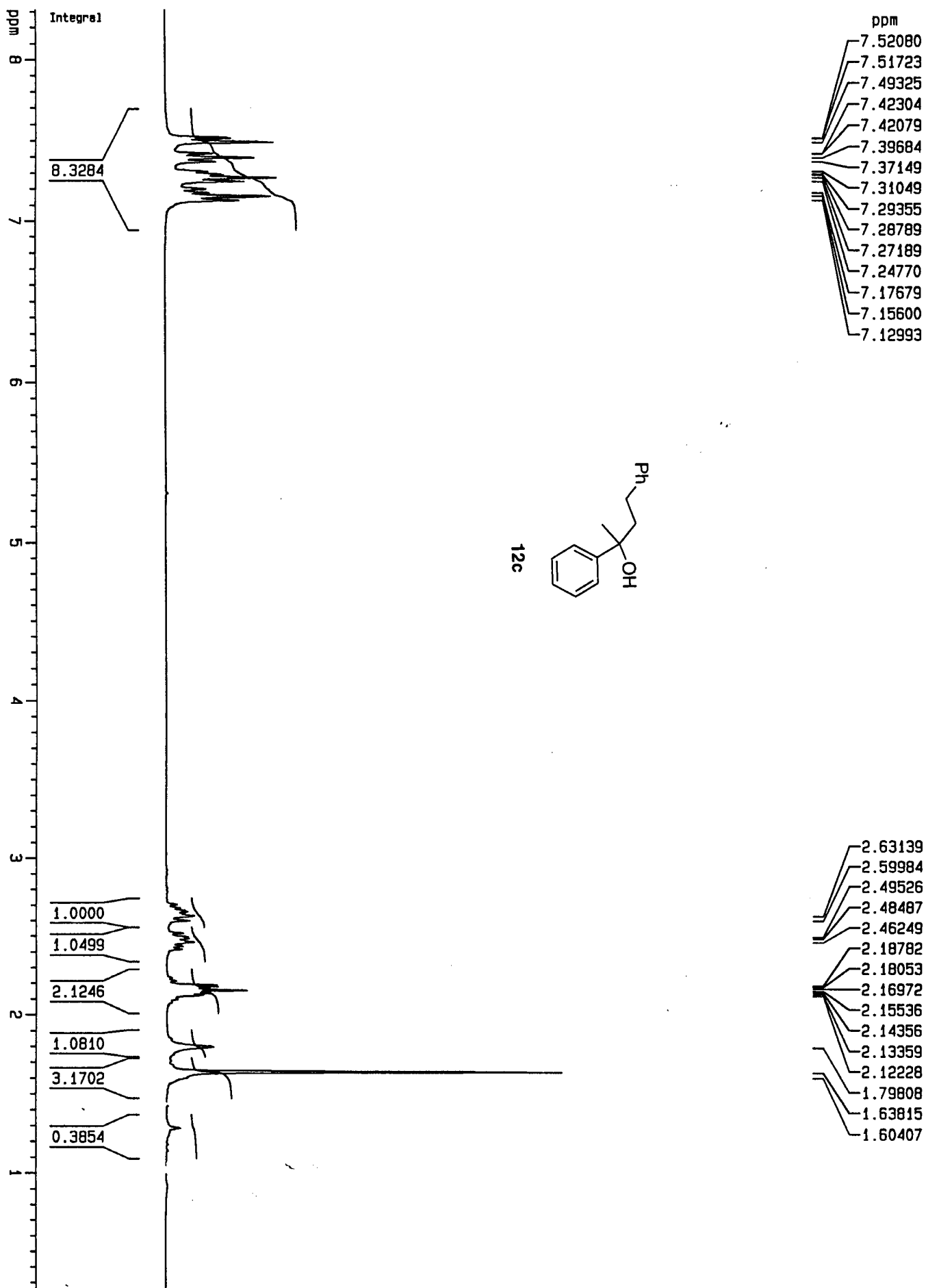


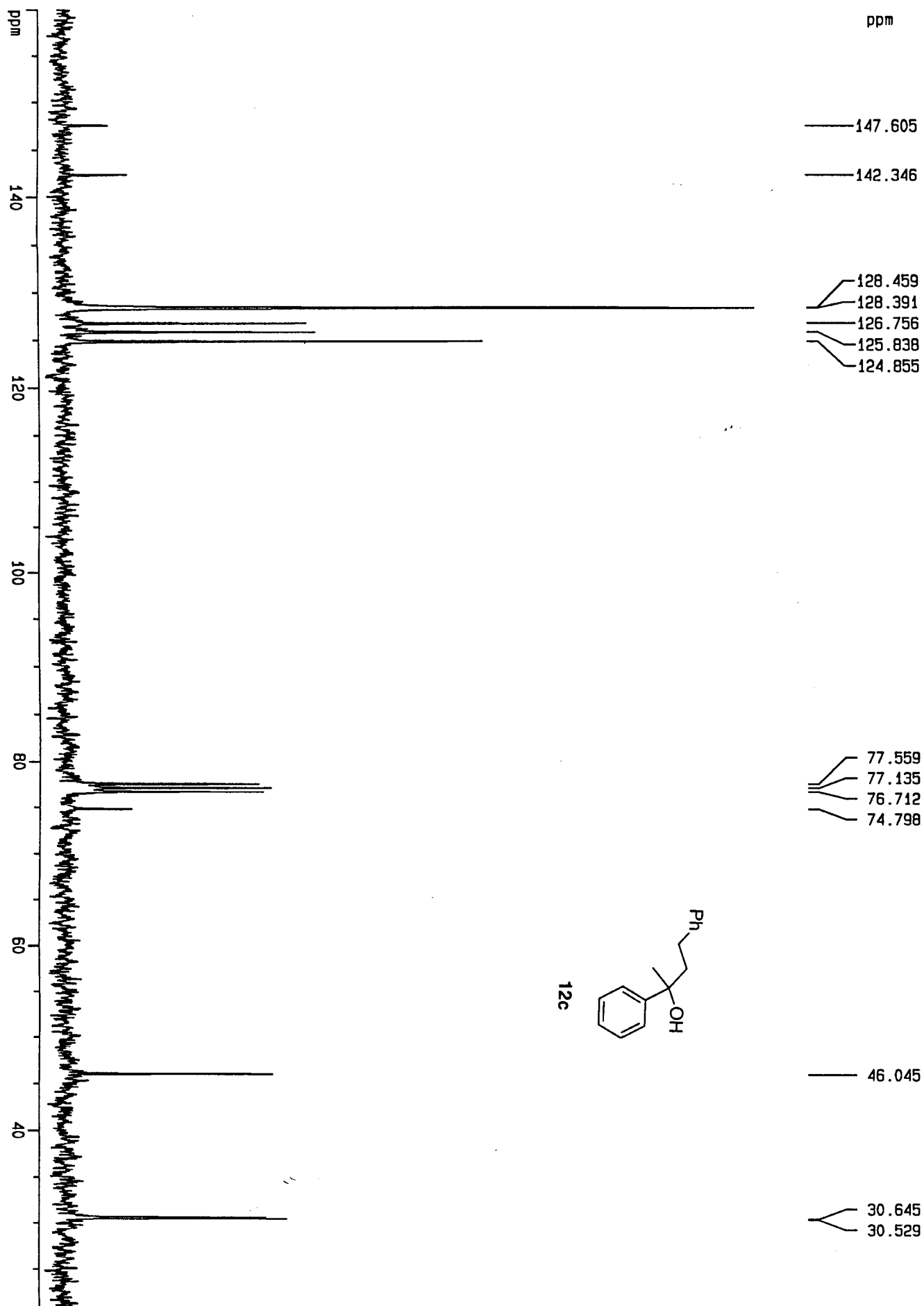


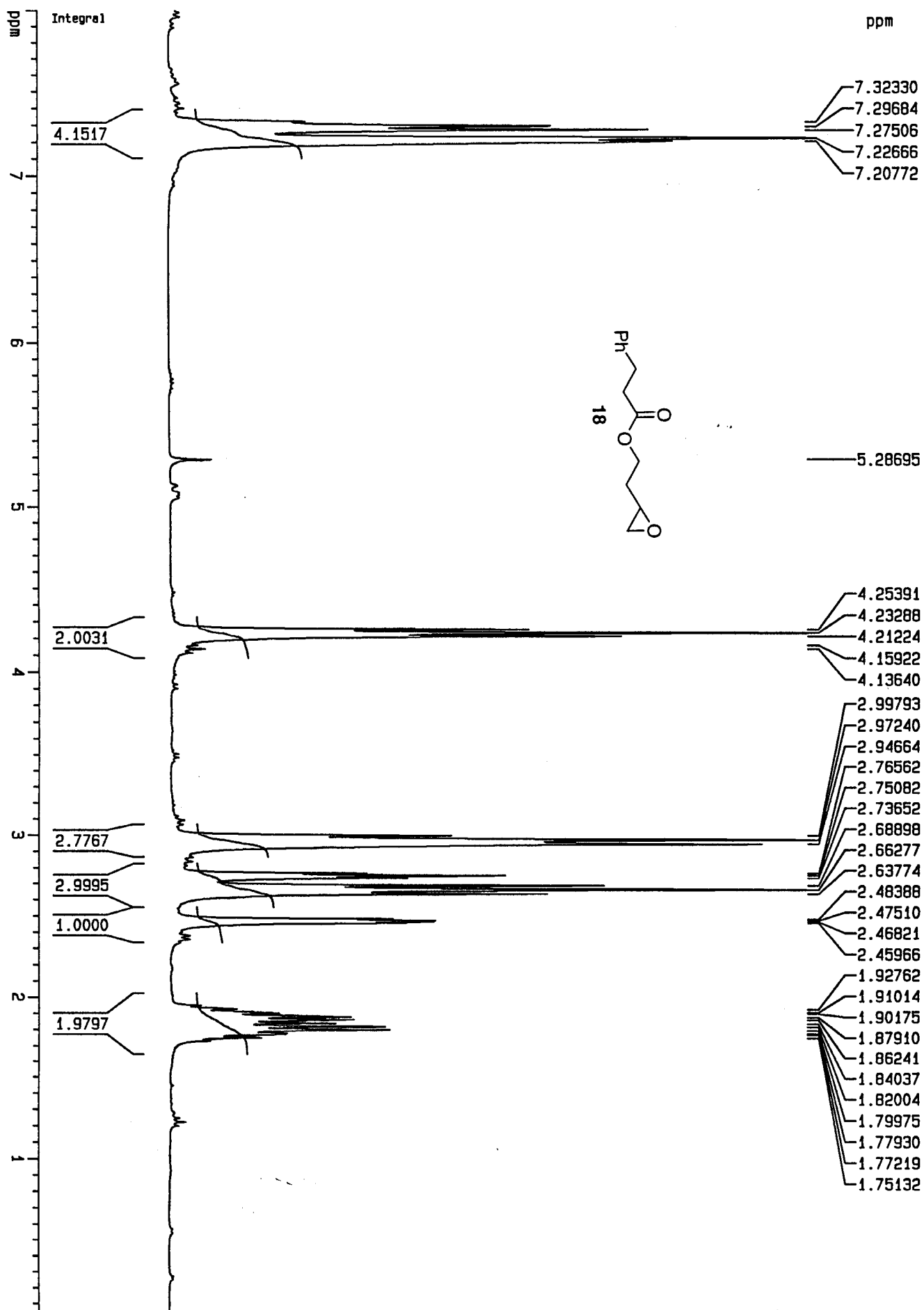


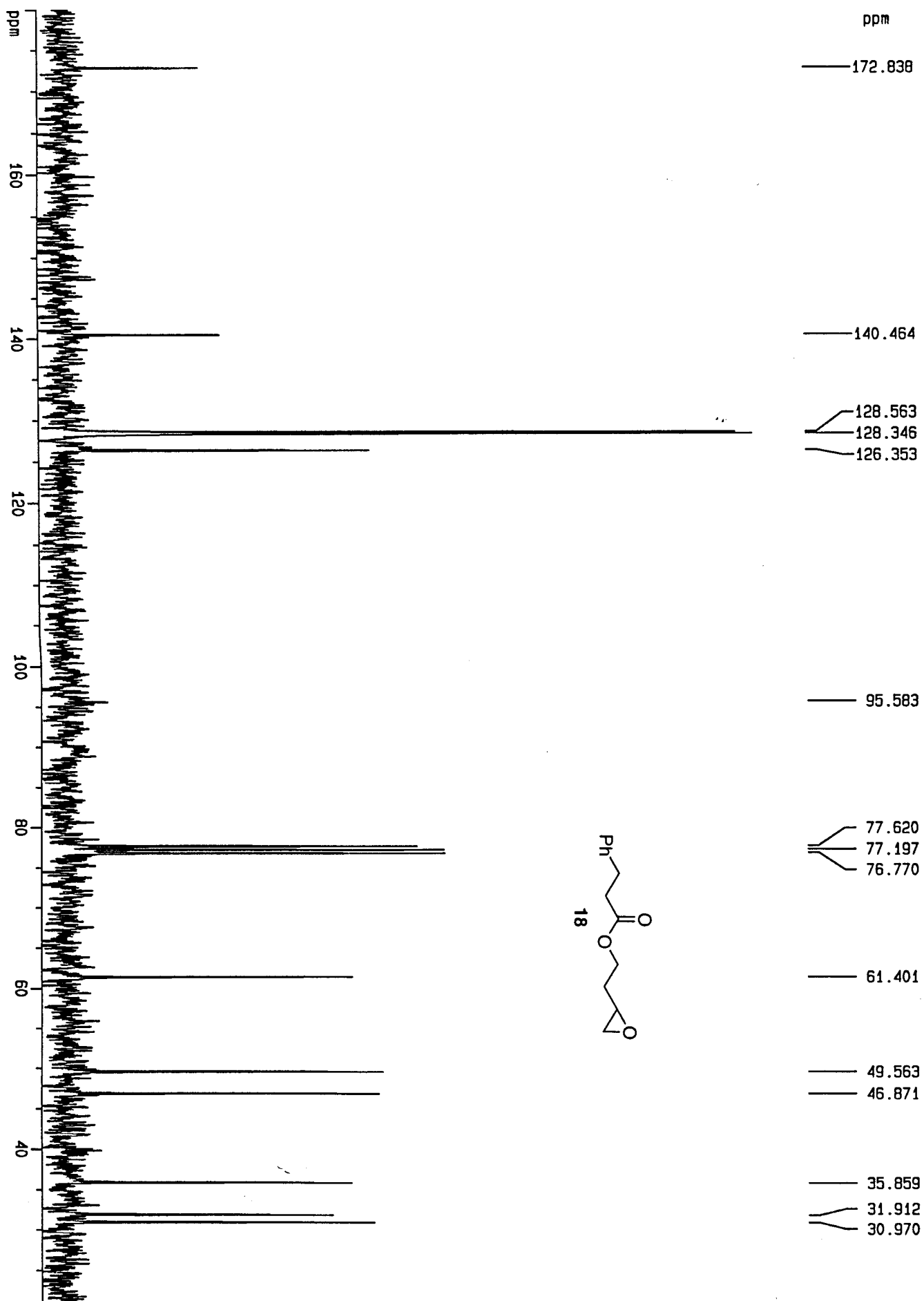


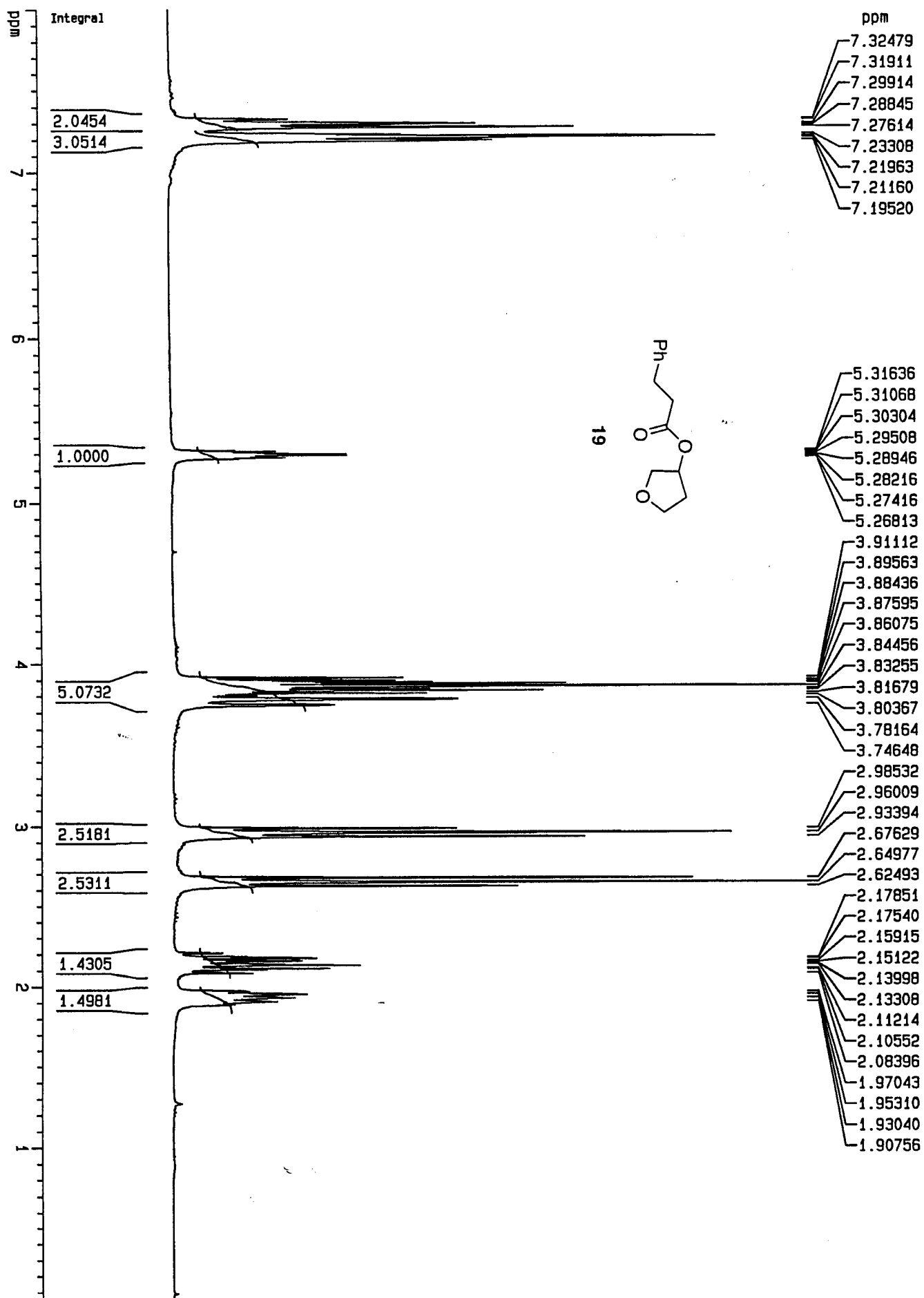


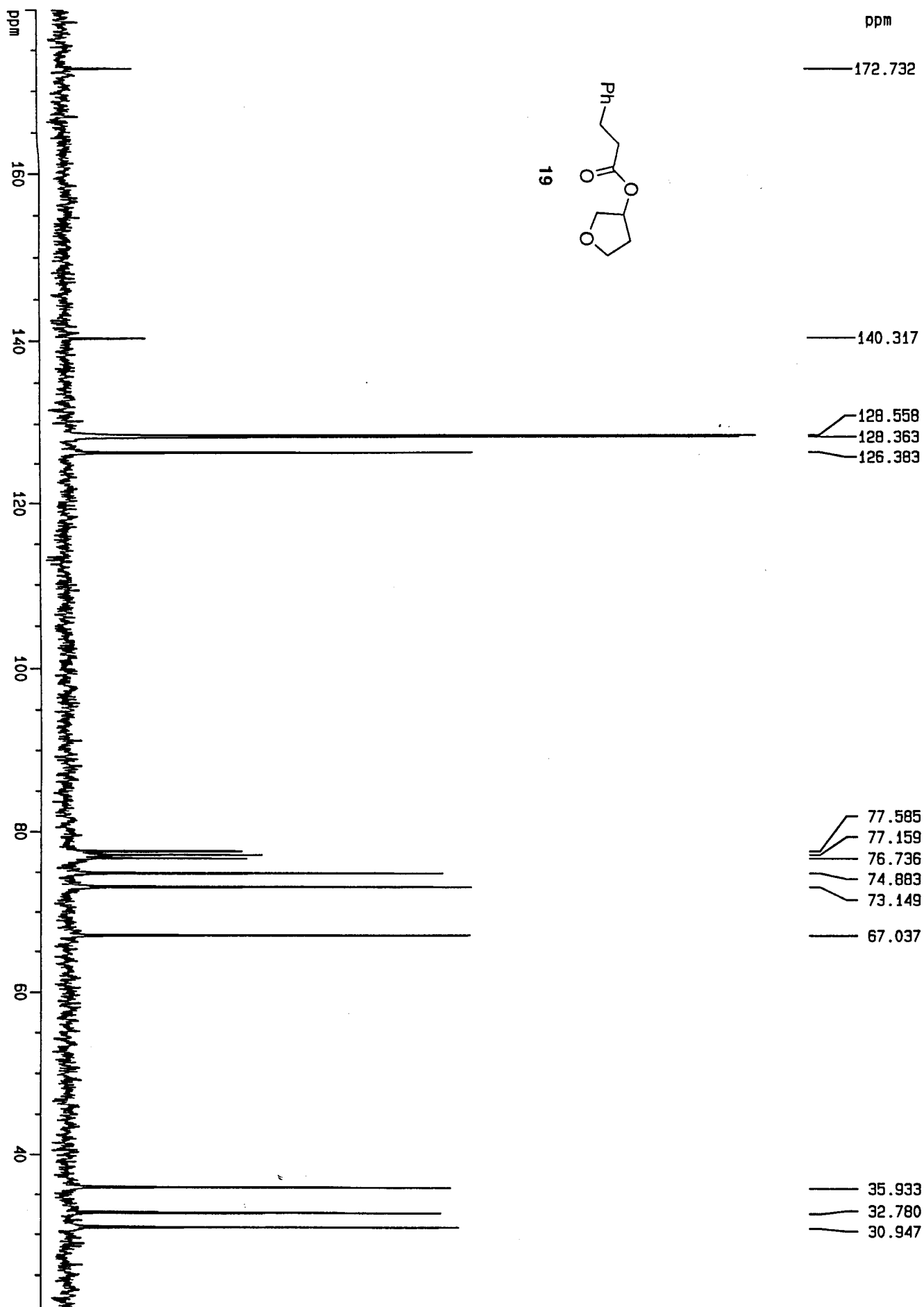


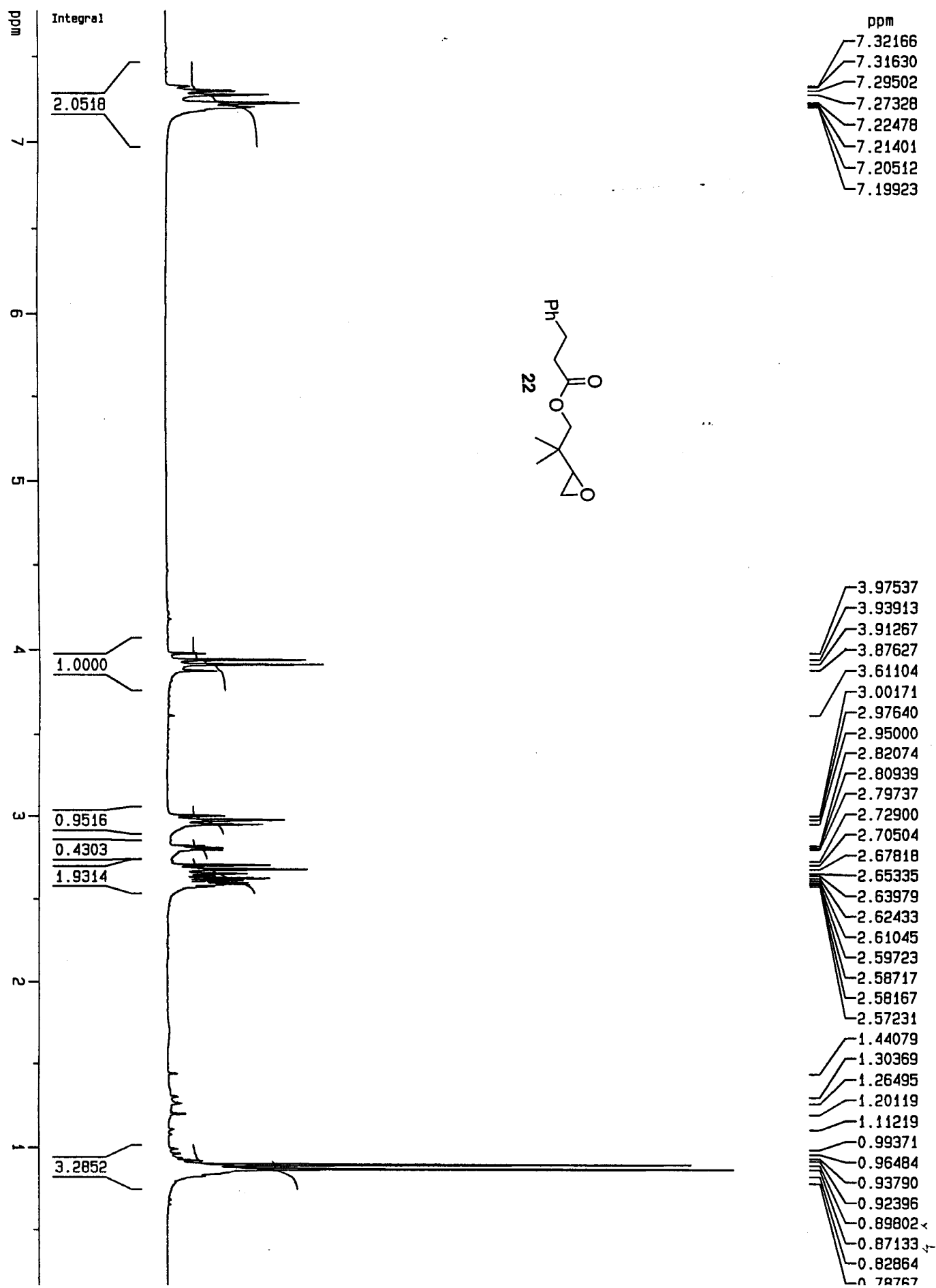


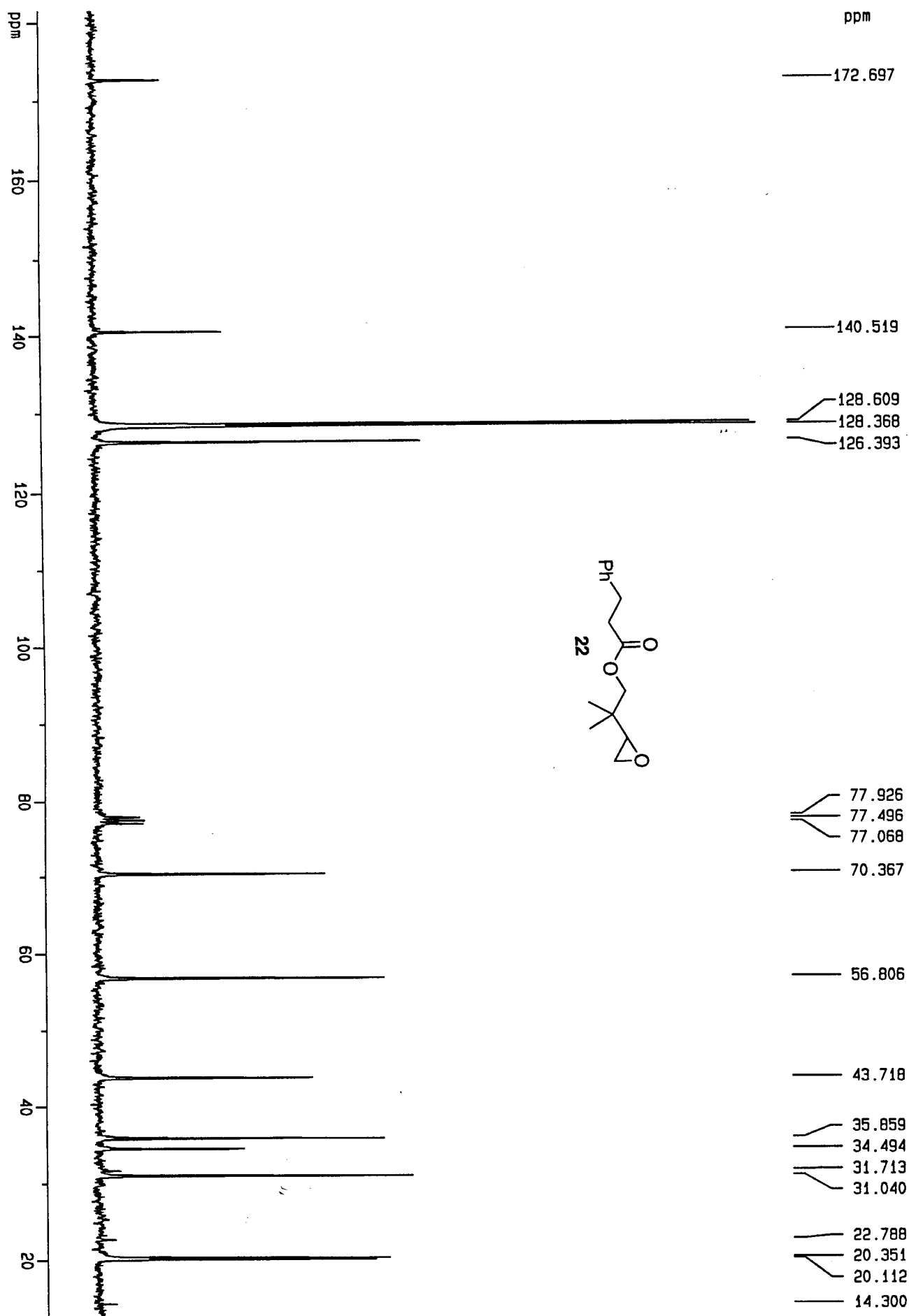












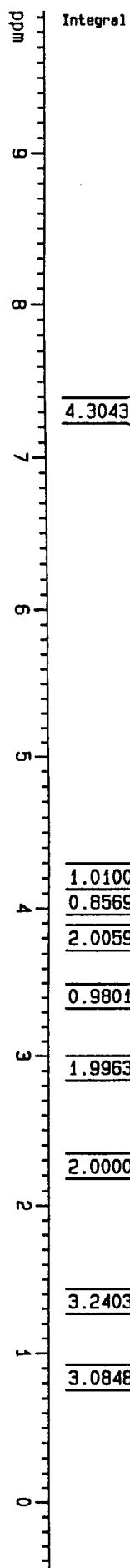
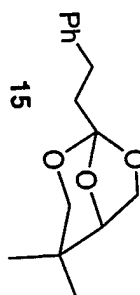
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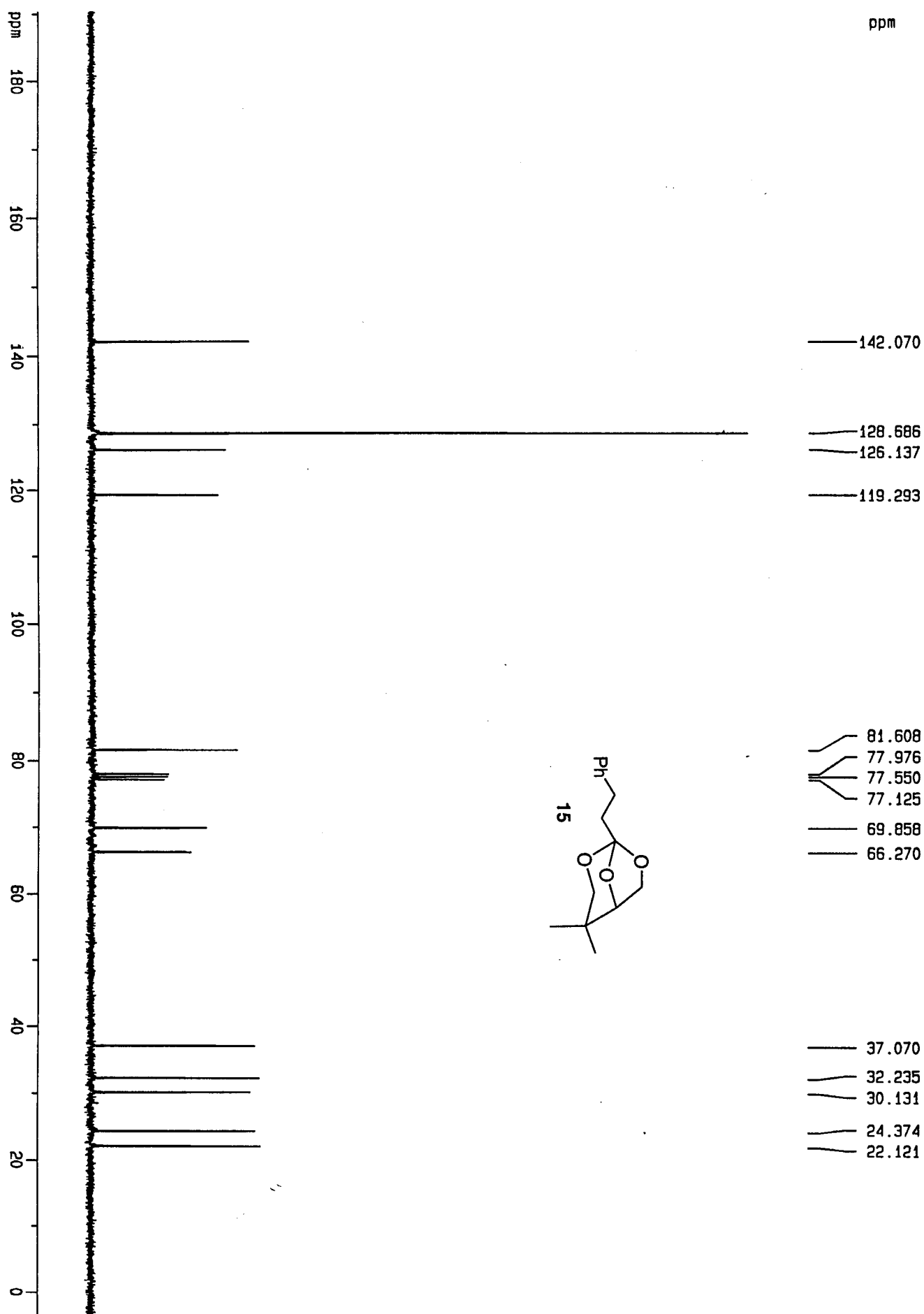
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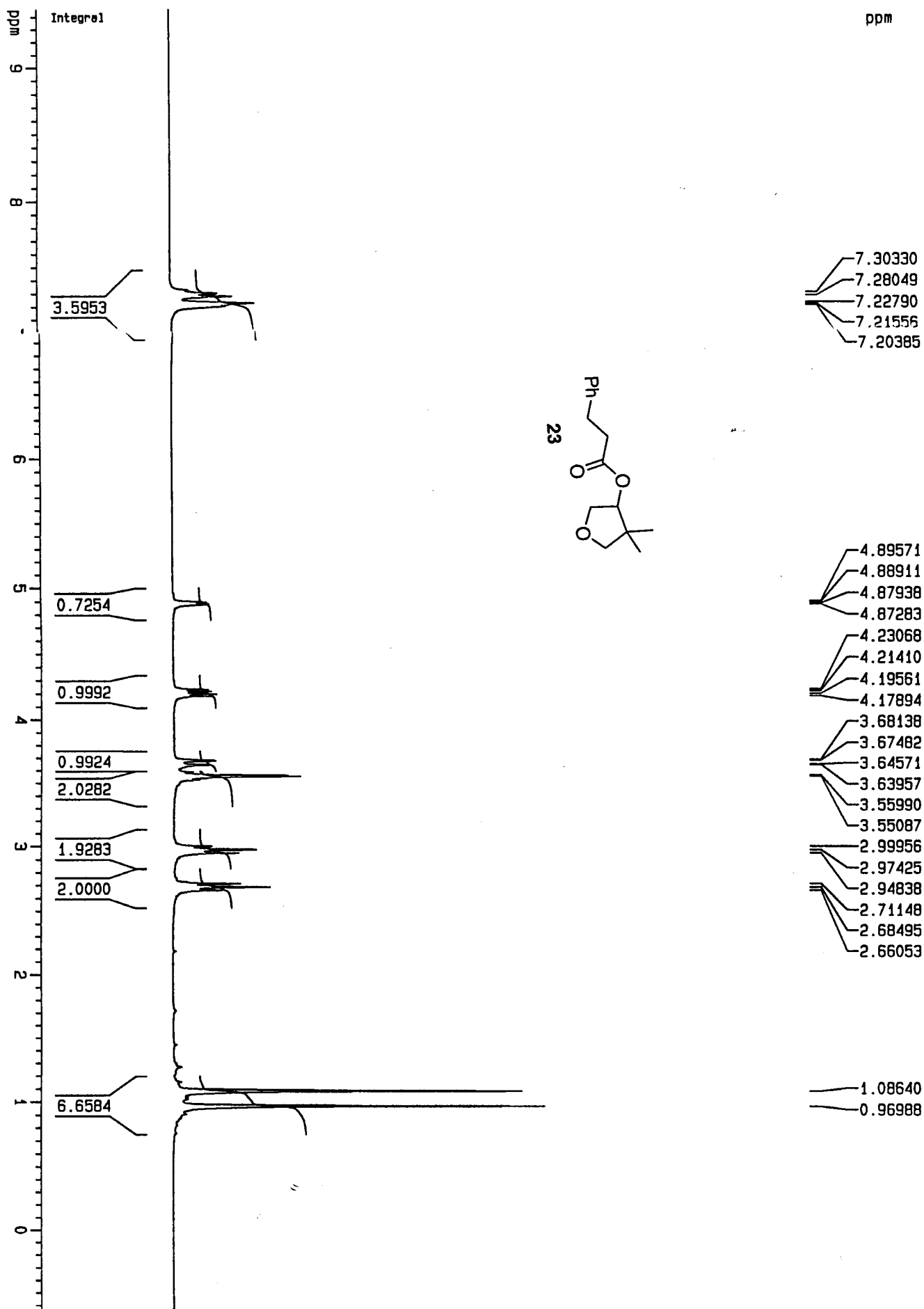
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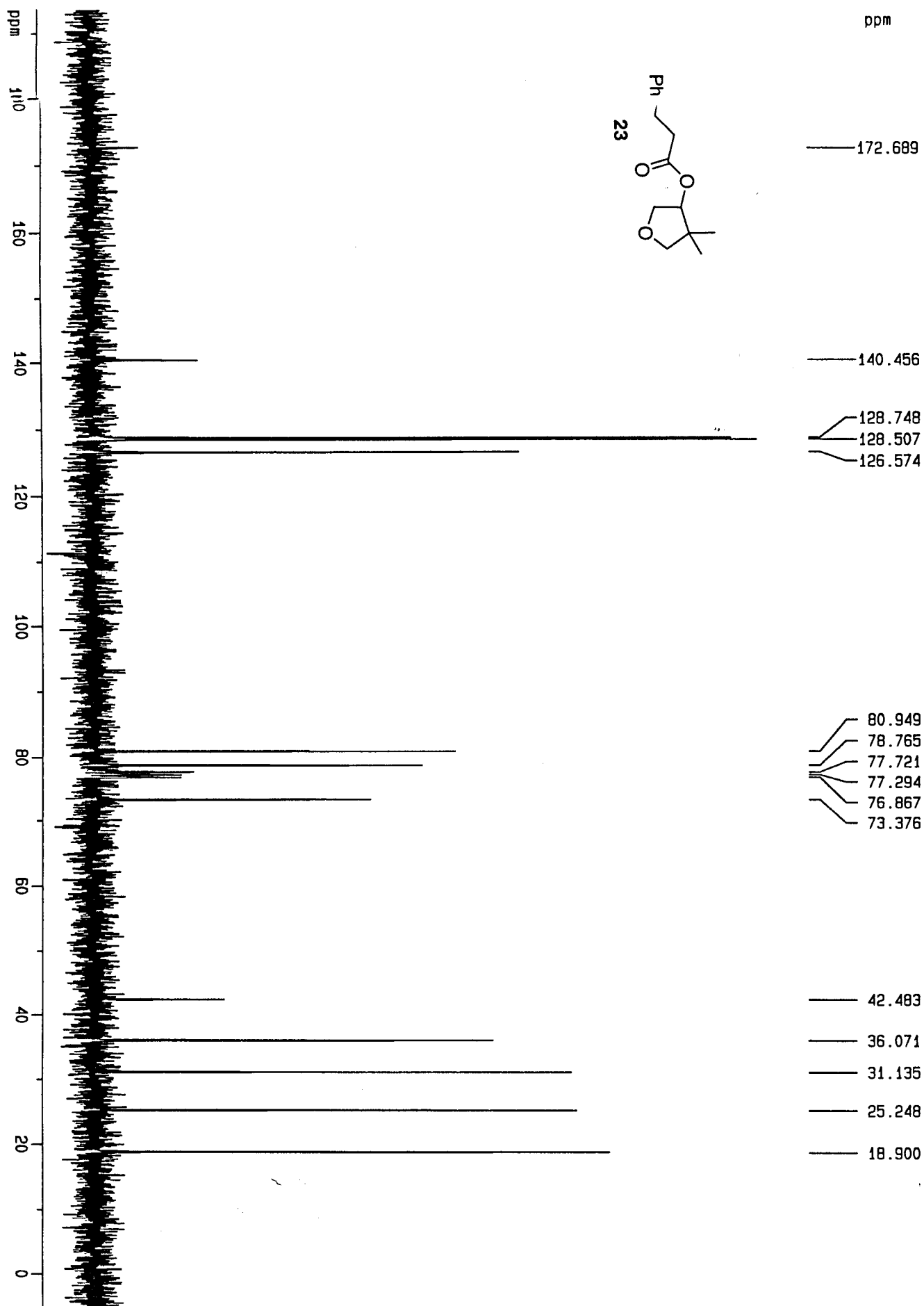
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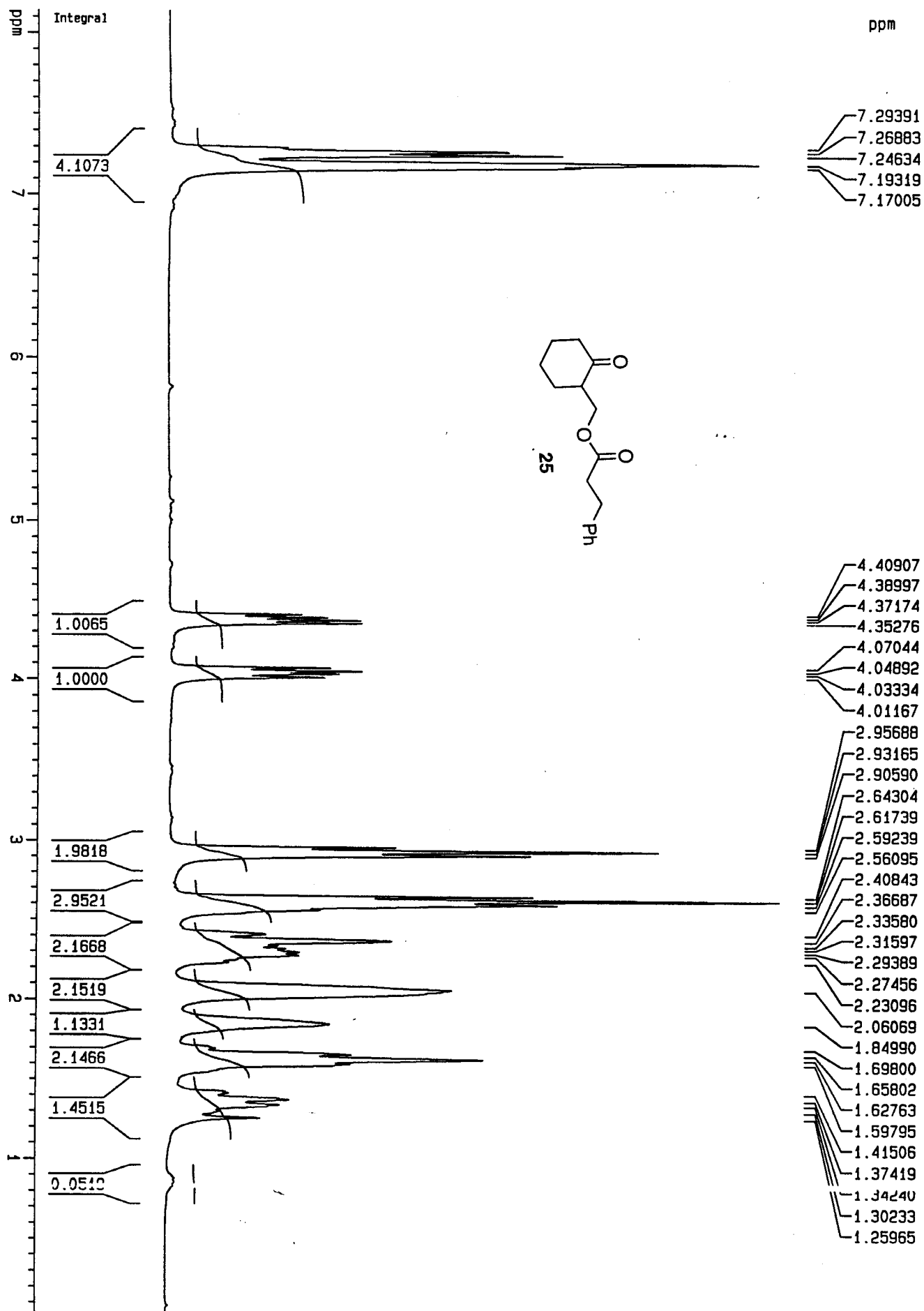


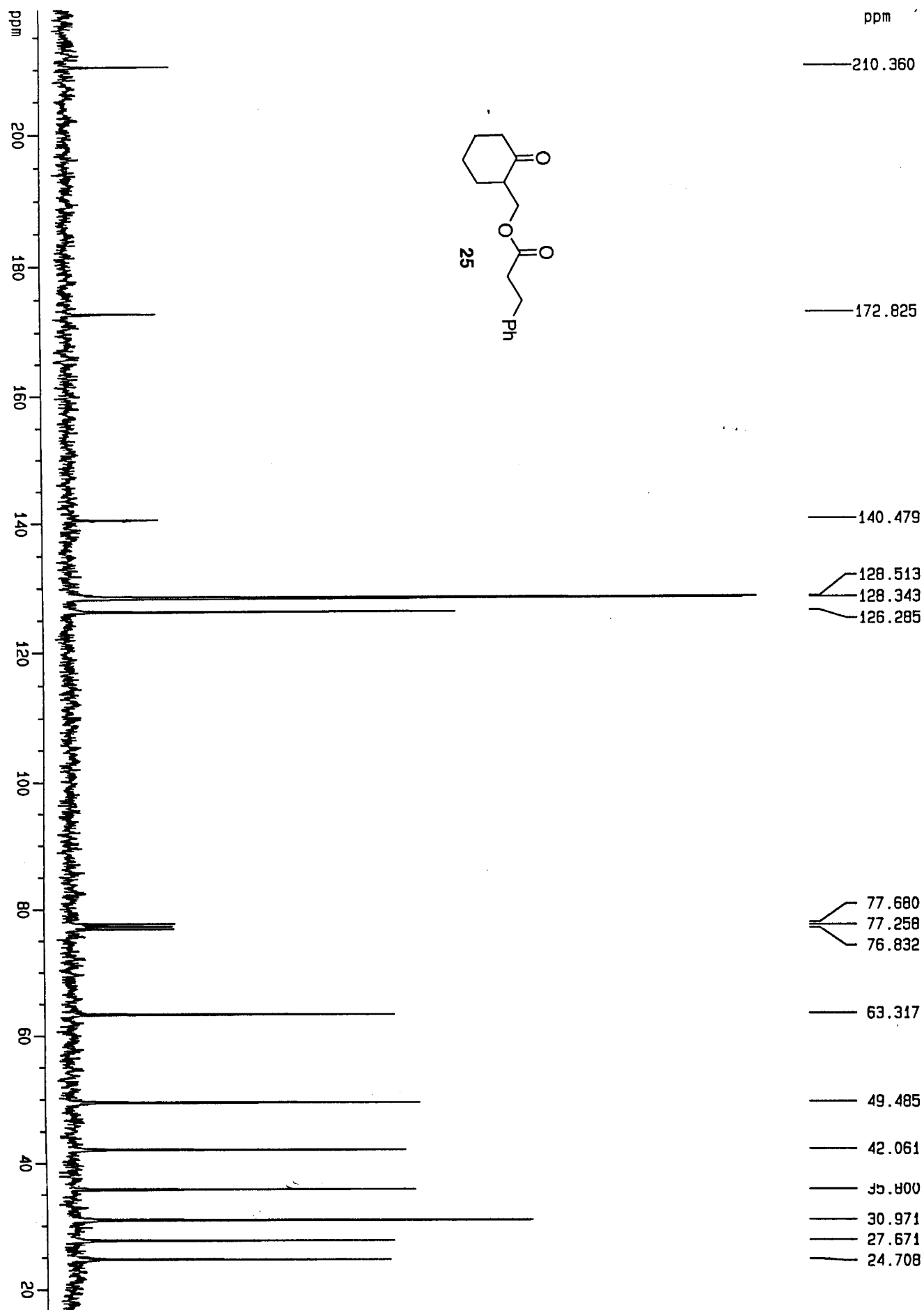
ppm

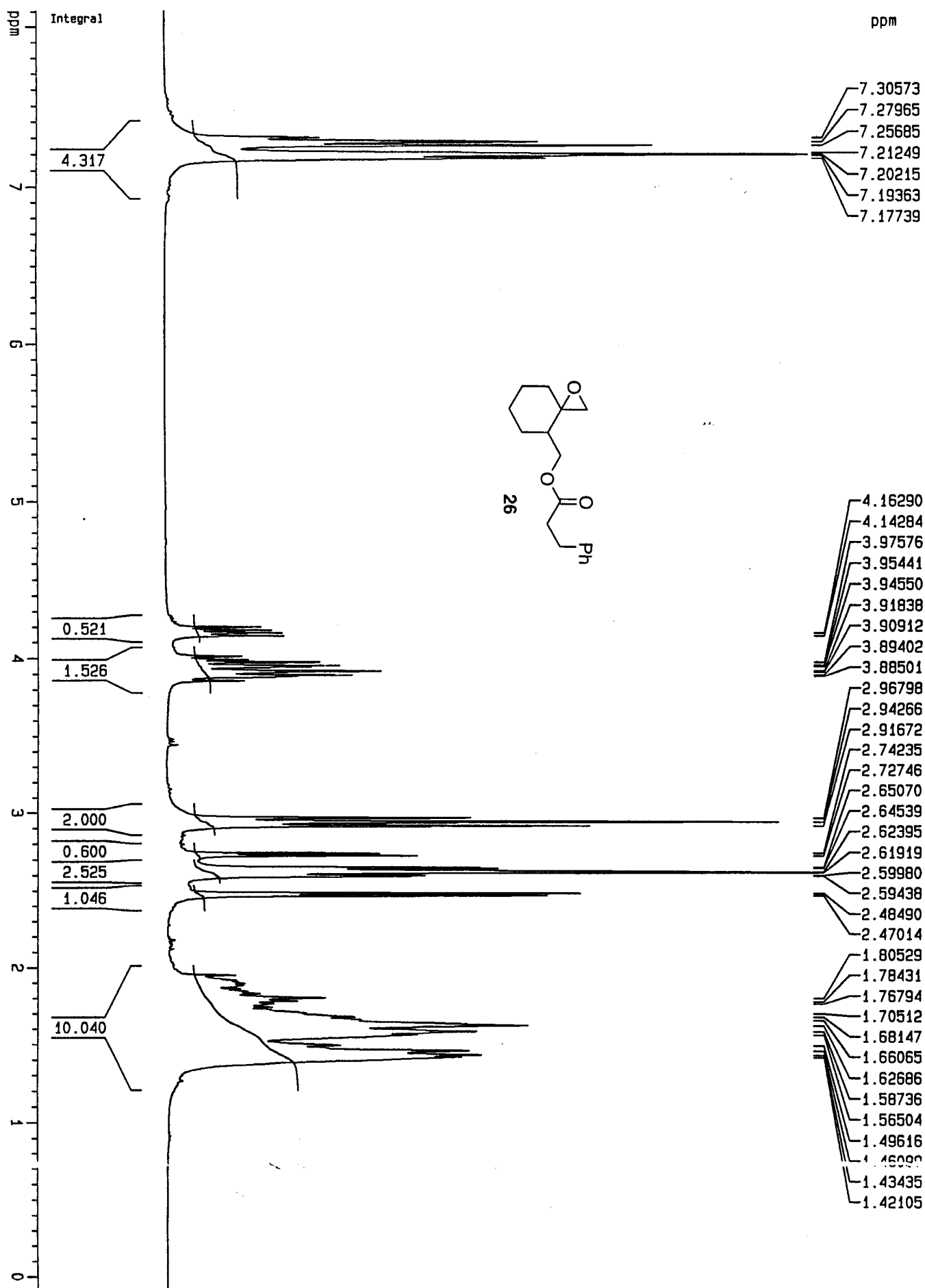


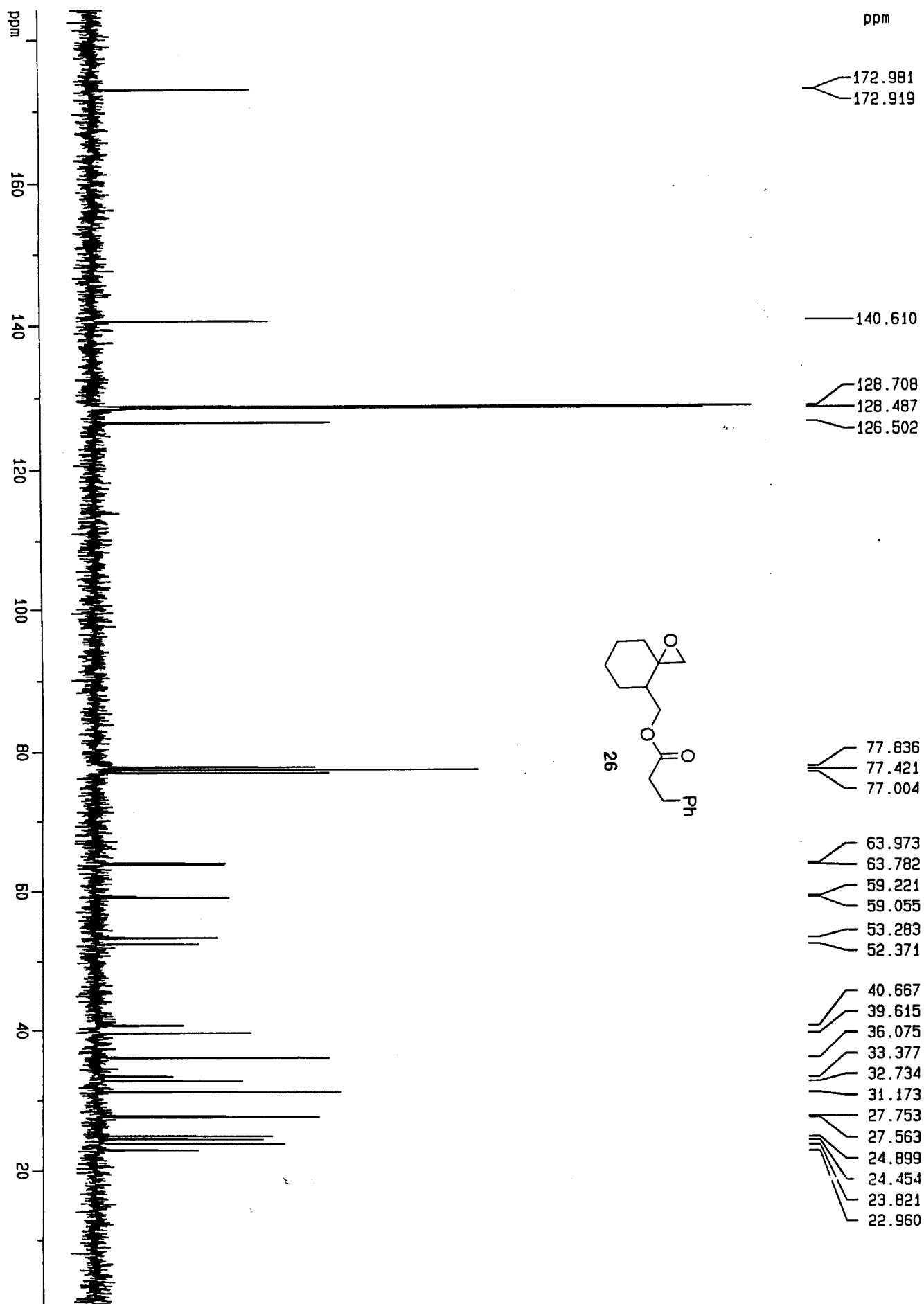


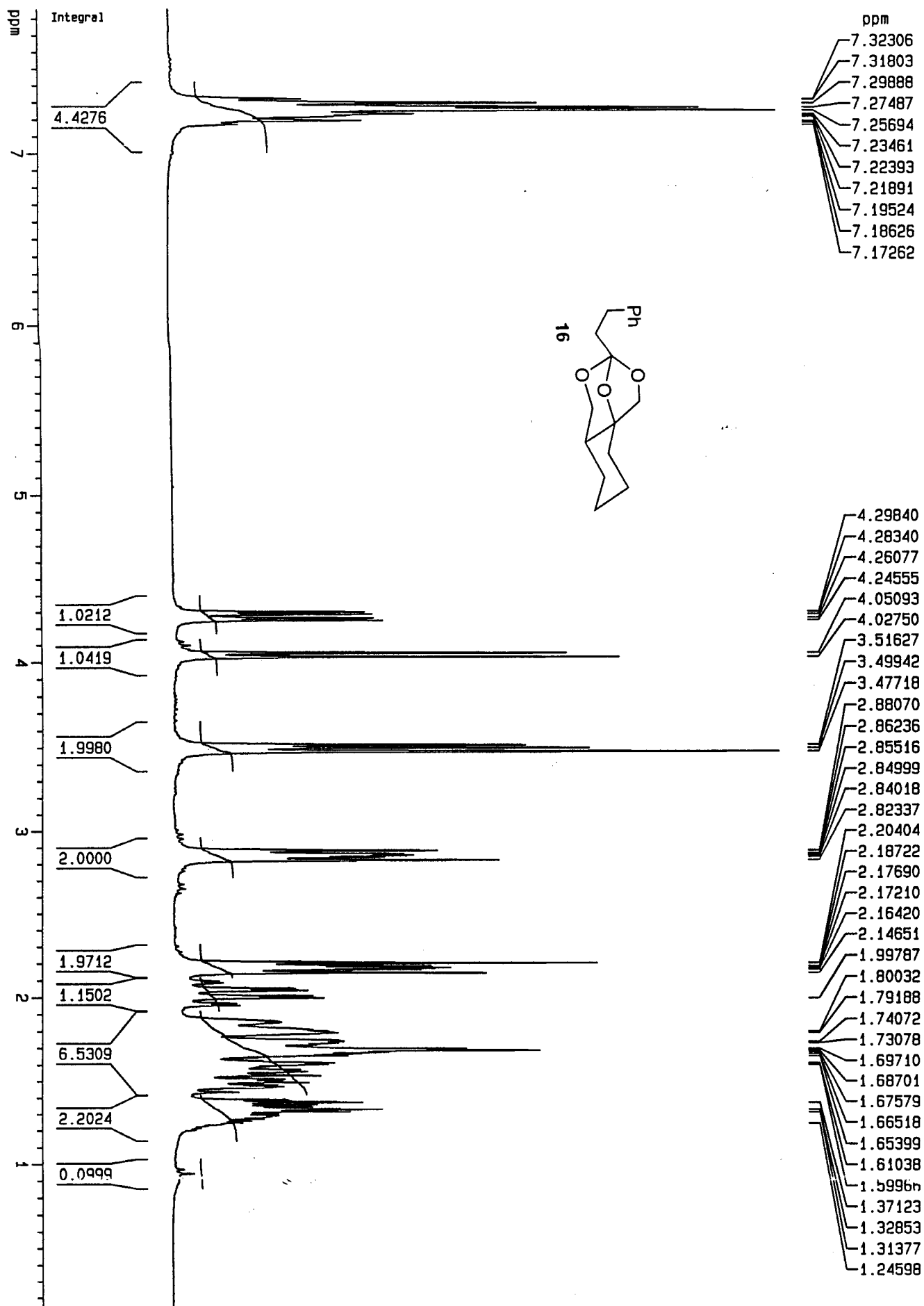




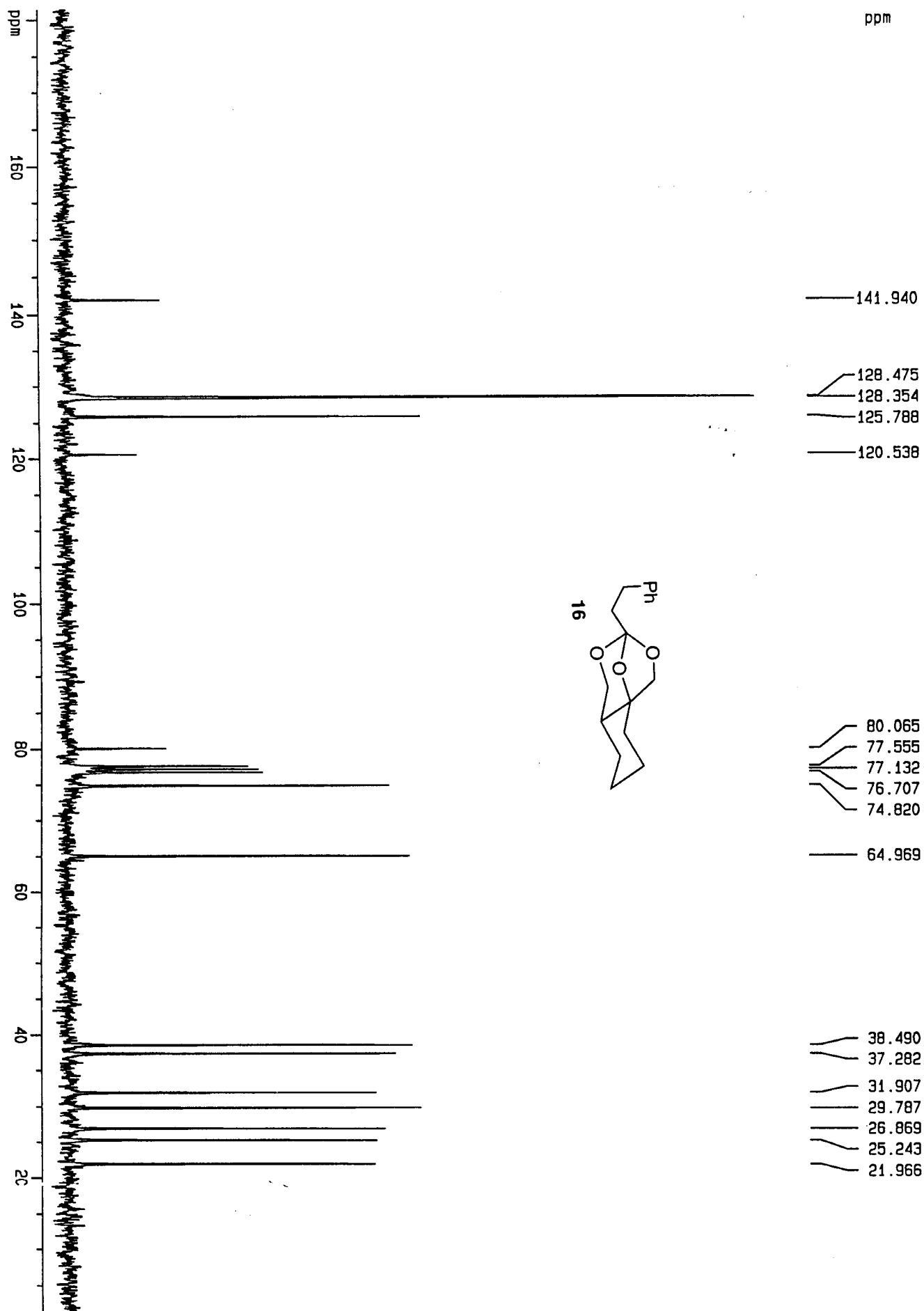


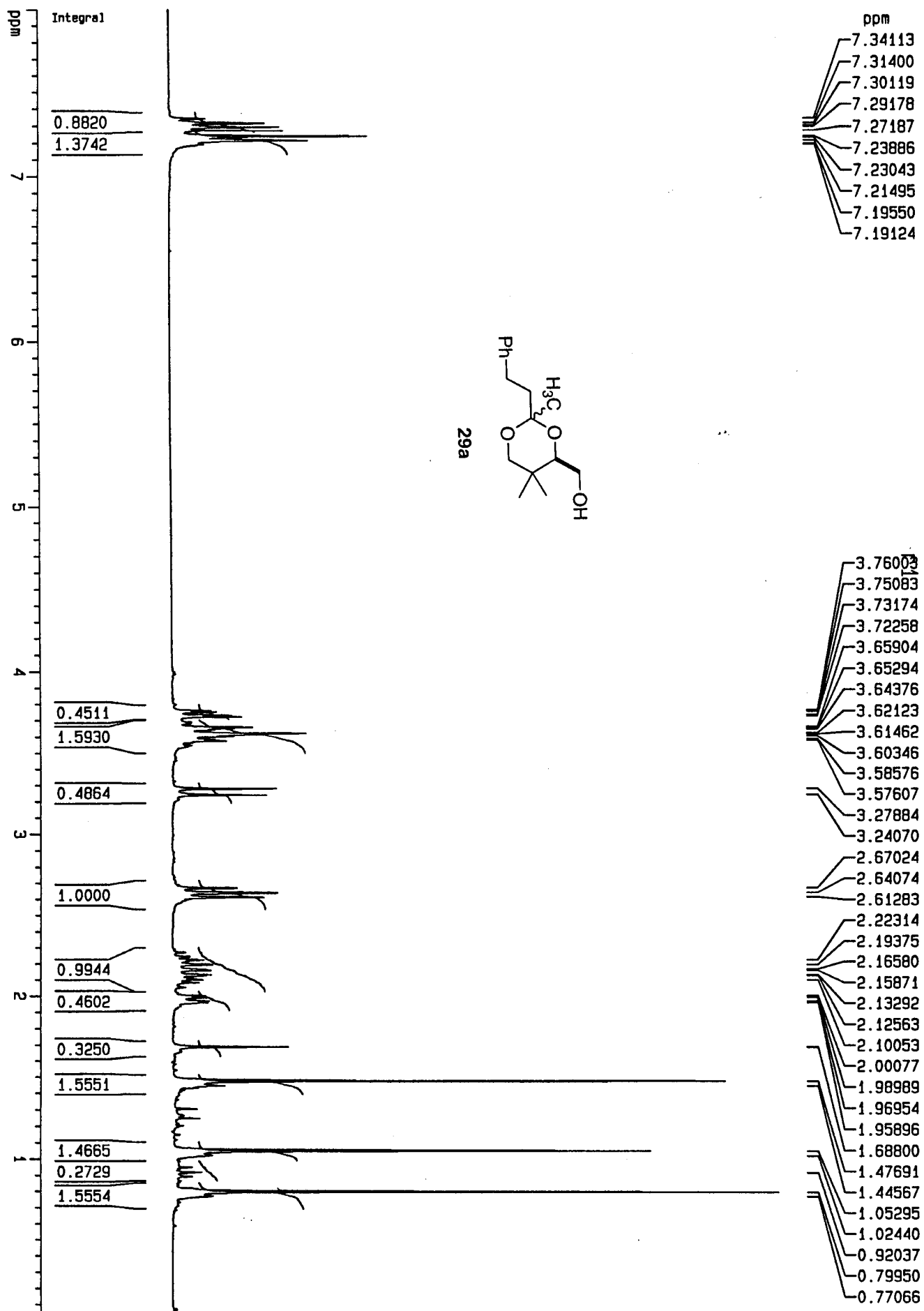


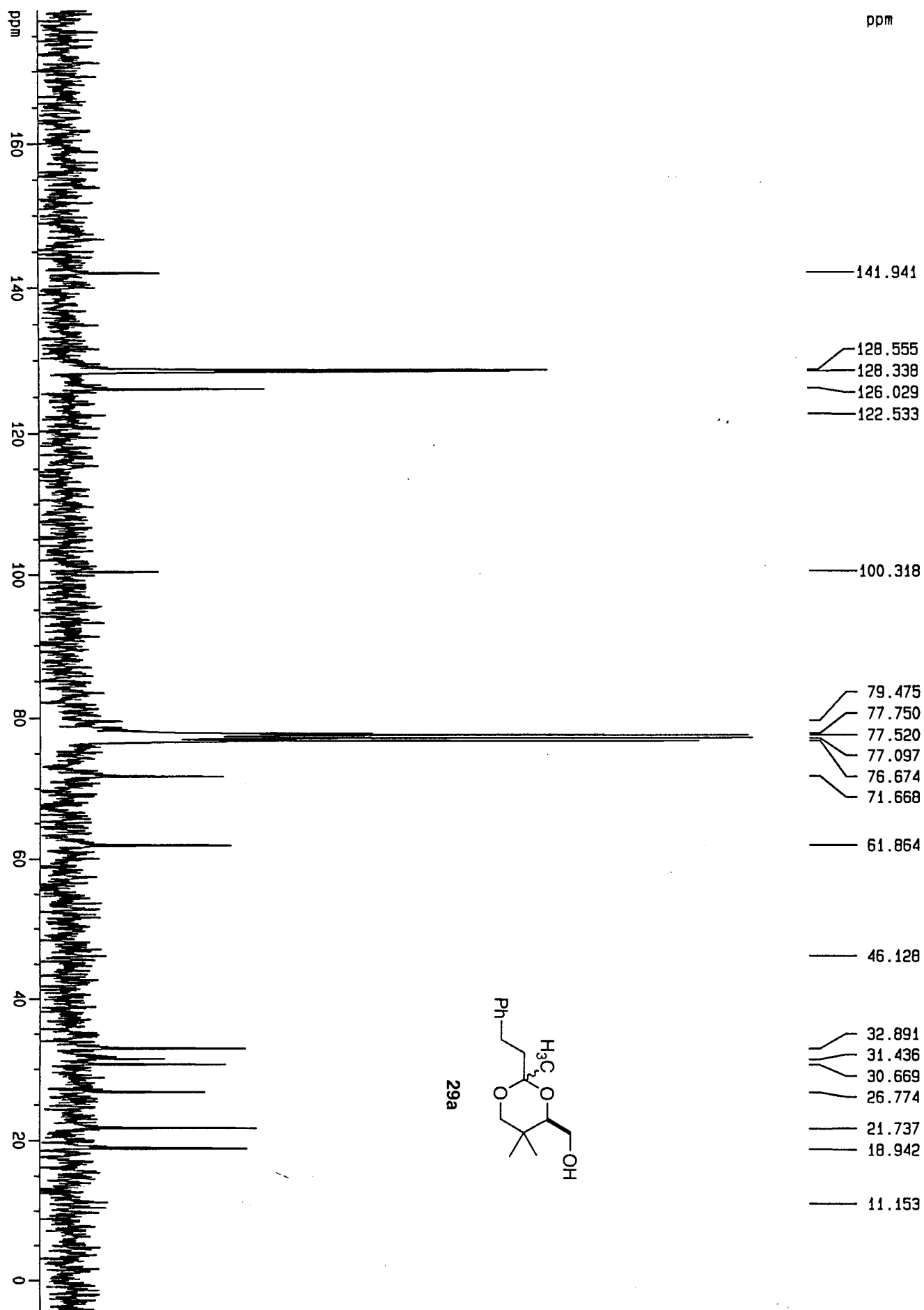


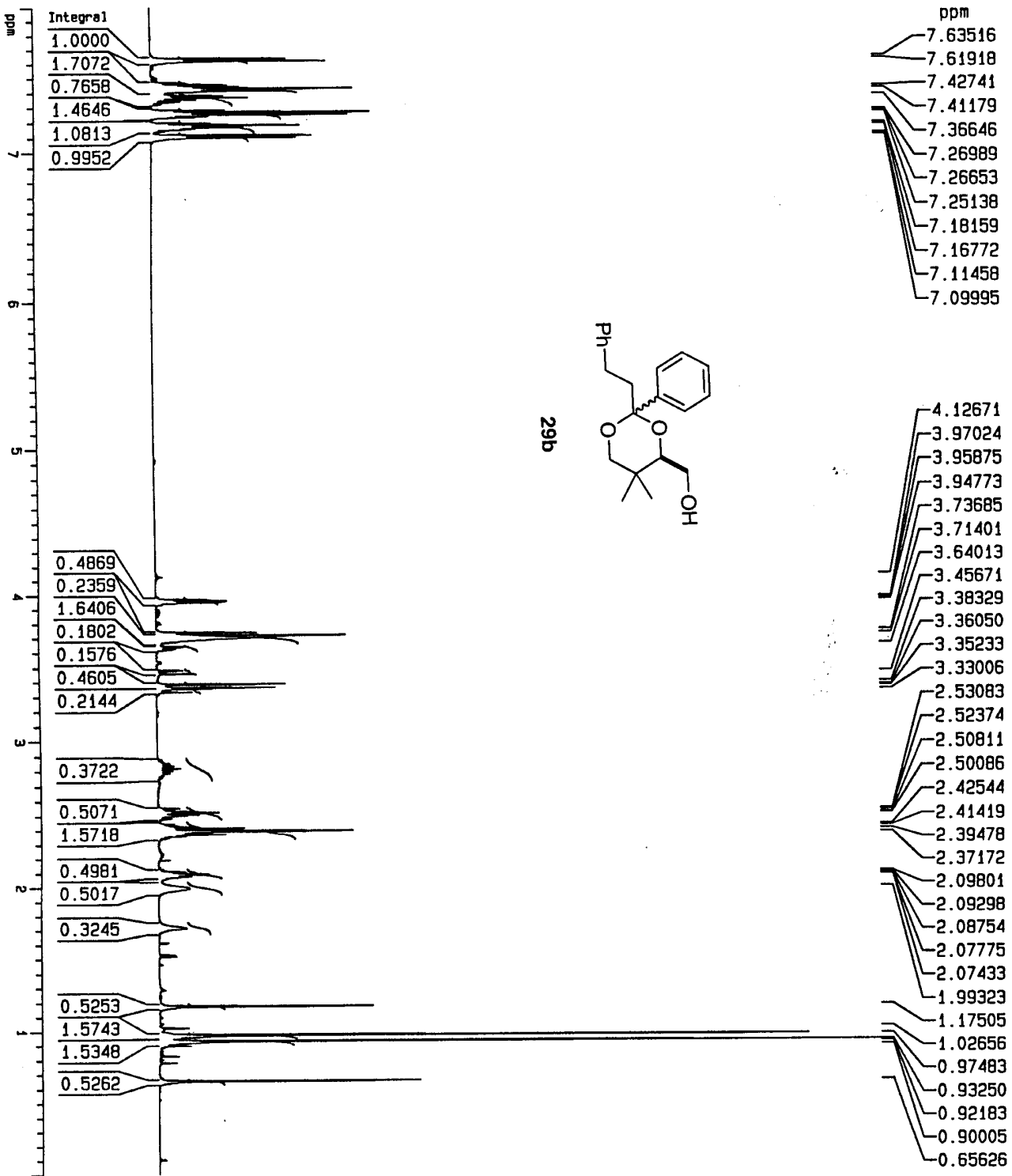


ppm









Current Data Parameters

NAME da-p11-x4

EXPNO 1

PROCNO 1

F2 - Acquisition Parameters

Date_ 500000

Time 12.48

INSTRUM spect

PROBHD 5 mm TXI 13C

PULPROG zg

TD 32768

SOLVENT CDCl3

NS 8

DS 0

SMH 7507.507 Hz

FIDRES 0.229114 Hz

AQ 2.1823988 sec

RG 35.9

DW 66.600 usec

DE 6.00 usec

TE 290.0 K

D1 12.0000000 sec

P1 19.20 usec

DE 6.00 usec

SFO1 500.133008 MHz

NUC1 1H

PL1 -1.00 dB

F2 - Processing parameters

SI 16384

SF 500.1300077 MHz

WDW EM

SSB 0

LB 0.40 Hz

GB 0

PC 1.00

1D NMR plot parameters

CX 20.00 cm

F1P 8.000 ppm

F1 4001.04 Hz

F2P 0.000 ppm

F2 0.00 Hz

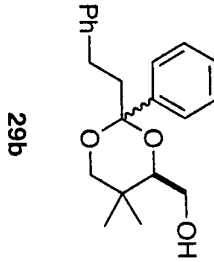
PPMCM 0.40000 ppm/ci

HZCM 200.05200 Hz/cm

ppm

Integral

142.47
142.24
141.82
139.99
128.67
128.41
128.28
128.06
127.98
127.85
127.27
125.90
125.59
102.34
101.26
78.74
78.04
77.34
77.09
76.84
71.83
61.98
61.87
34.87
32.46
31.53
30.14
22.62
21.42
19.20

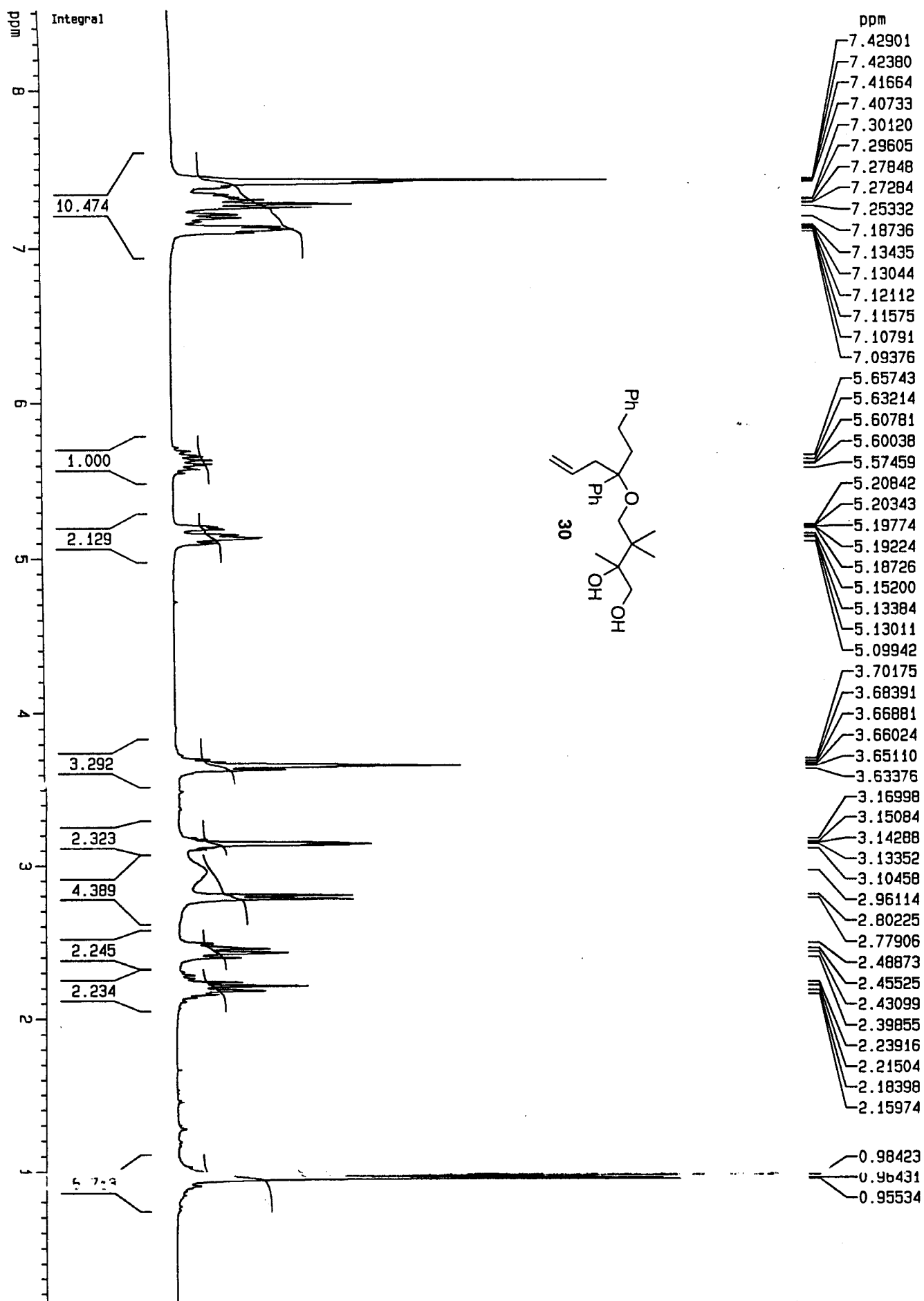


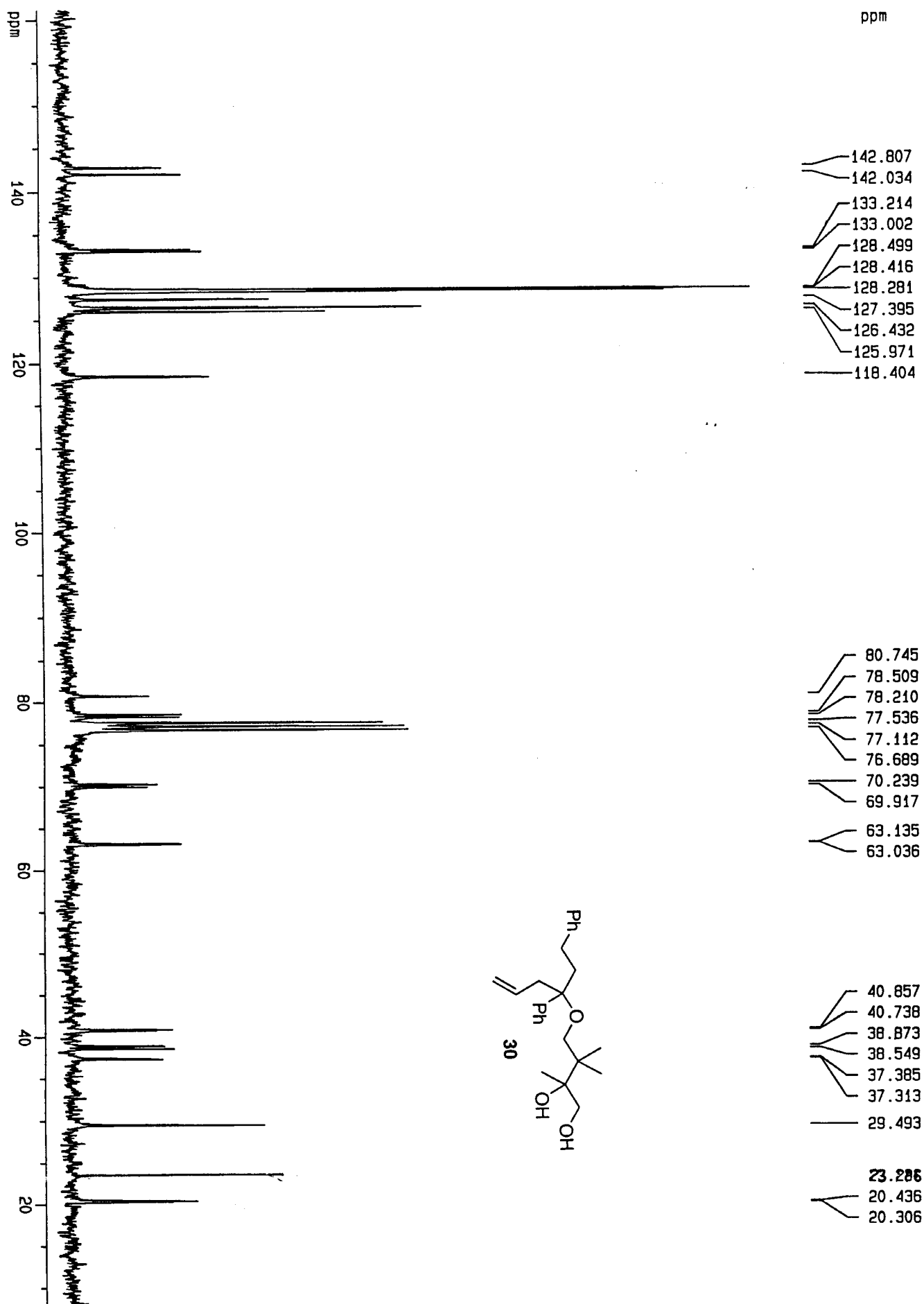
Current Data Parameters
NAME da-p11-x4
EXPNO 2
PROCNO 1

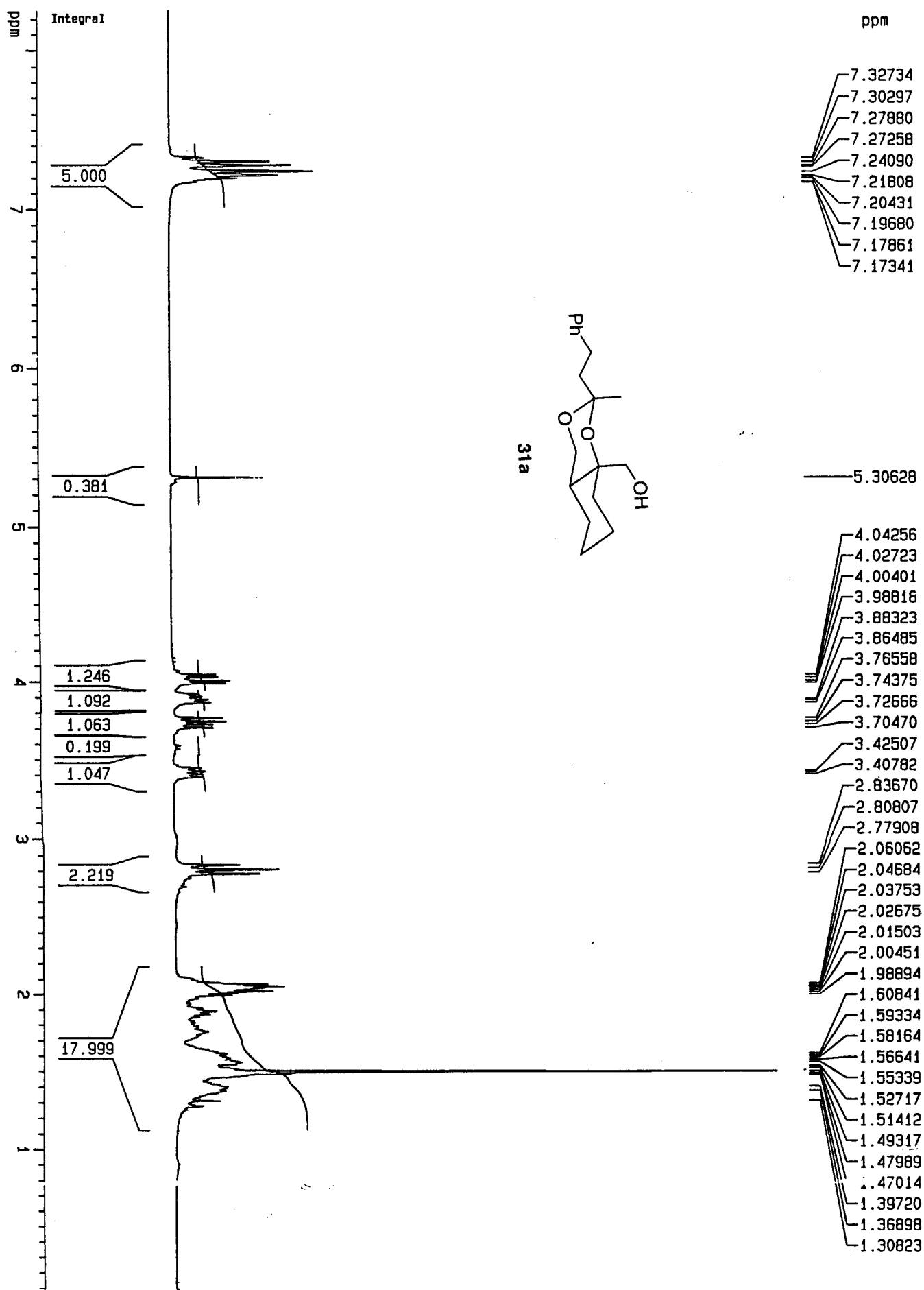
F2 - Acquisition Parameters
Date_ 500000
Time 10.46
INSTRUM spect
PROBHD 5 mm TXI 13C
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 611
DS 2
SWH 32679.738 Hz
FIDRES 0.597306 Hz
AQ 0.5014004 sec
RG 32768
DM 15.300 usec
DE 6.00 usec
TE 290.0 K
D3 0.00100000 sec
PL12 12.00 dB
D1 12.00000000 sec
CPDPRG2 waltz16
PCPD2 100.00 usec
SF02 500.1325006 MHz
NUC2 1H
PL2 120.00 dB
P1 8.50 usec
DE 6.00 usec
SF04 125.7715724 MHz
NUC4 13C
PL4 3.00 dB

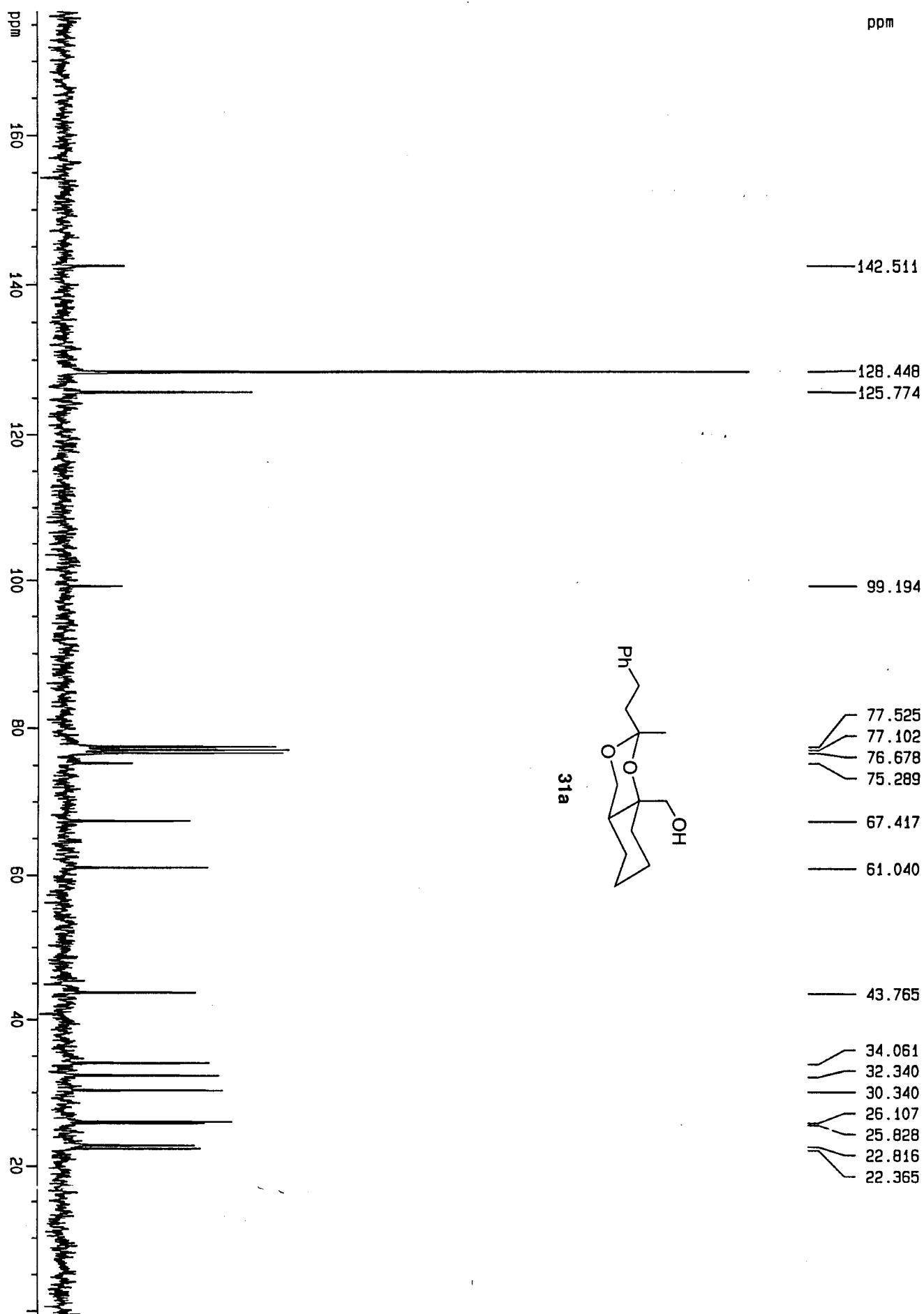
F2 - Processing parameters
SI 8192
SF 125.757887 MHz
WDW EM
SSB 0
LB 4.00 Hz
GB 0
PC 1.00

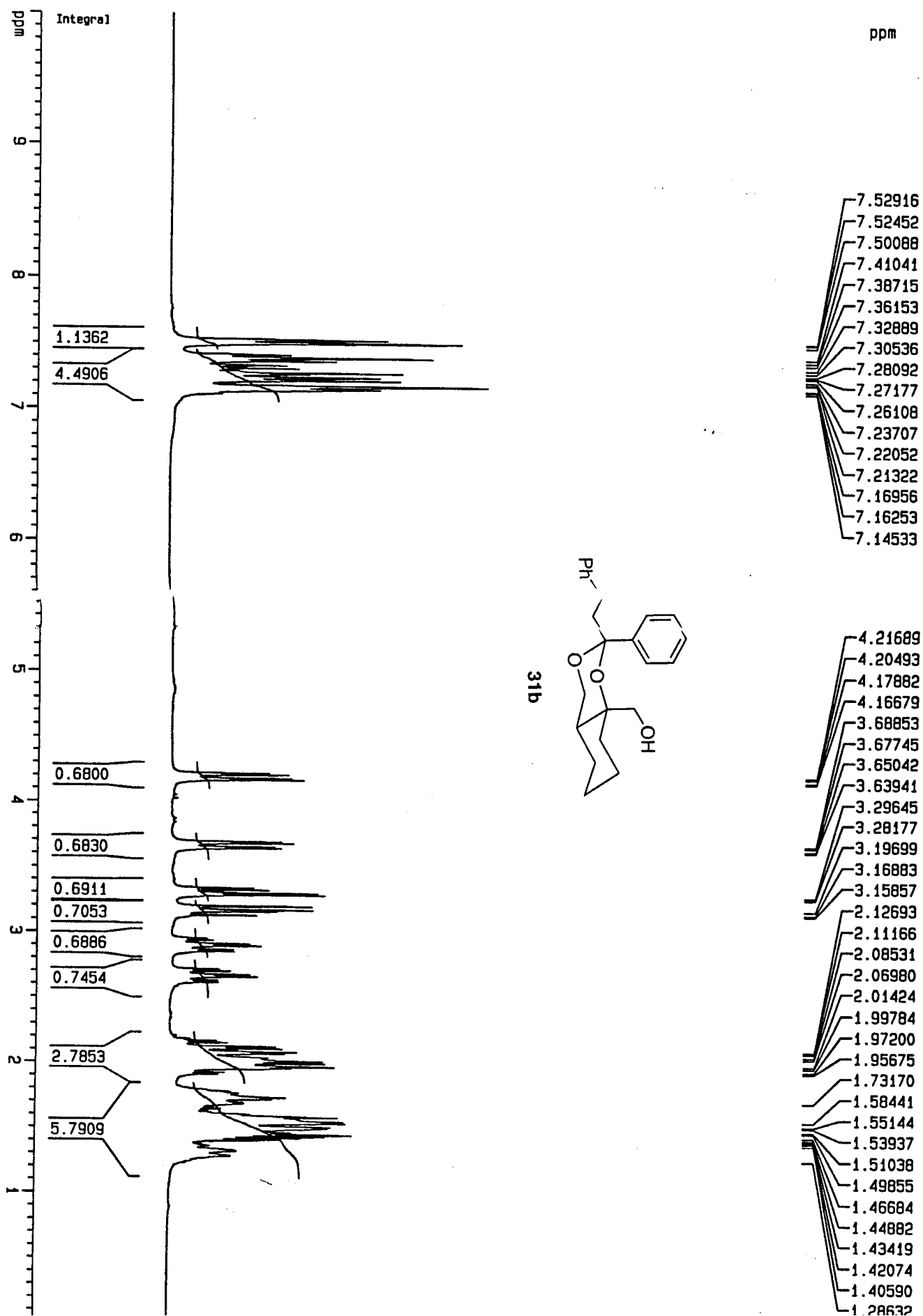
1D NMR plot parameters
CX 20.00 cm
F1P 200.000 ppm
F1 25151.56 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 10.00000 ppm/cm
HZCM 1257.57788 Hz/cm

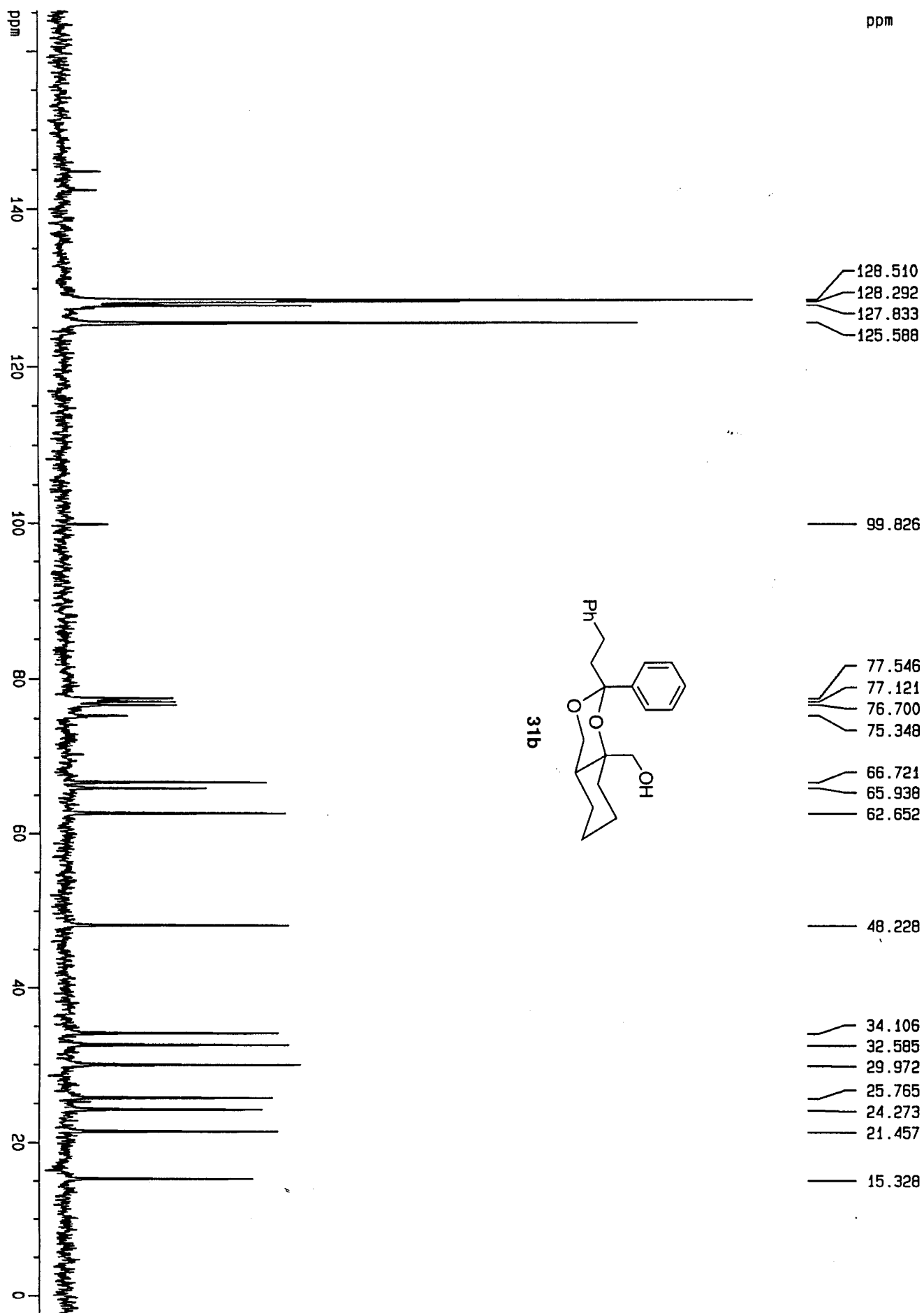


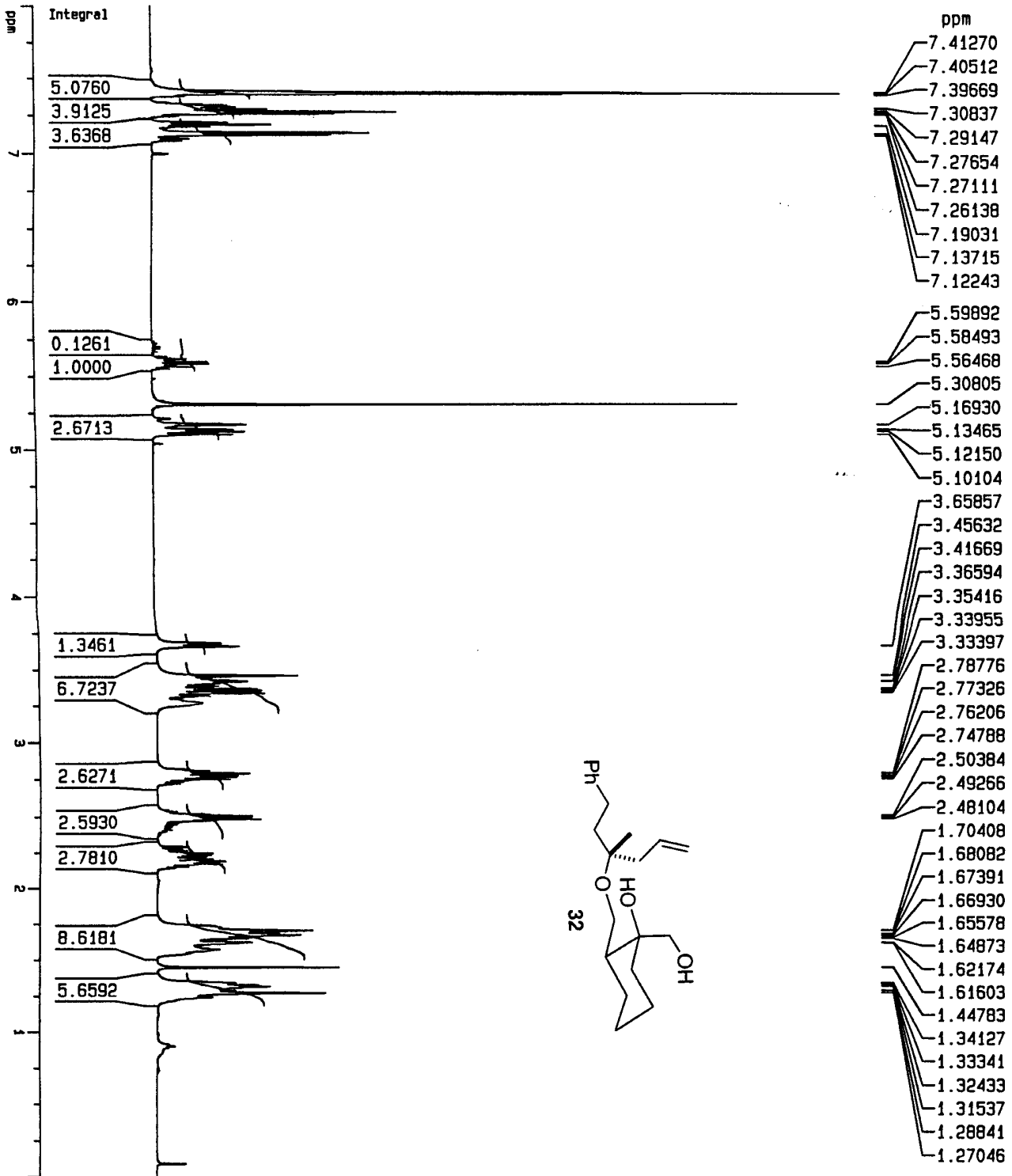












Current Data Parameters

NAME p-142-4m

EXPNO 1

PROCNO 1

F2 - Acquisition Parameters

Date_ 500000

Time 14.59

INSTRUM spect

PROBHD 5 mm TXI 13C

PULPROG zg

TD 32768

SOLVENT CDCl3

NS 8

DS 0

SWH 7507.507 Hz

FIDRES 0.229111 Hz

AQ 2.1823988 sec

RG 20.2

DW 66.600 usec

DE 6.00 usec

TE 290.0 K

D1 12.0000000 sec

P1 9.00 usec

DE 6.00 usec

SFO1 500.1330008 MHz

NUC1 1H

PL1 0.00 dB

F2 - Processing parameters

SI 16384

SF 500.1300073 MHz

WDW EM

SSB 0

LB 0.40 Hz

GB 0

PC 1.00

1D NMR plot parameters

CX 20.00 cm

F1P 8.000 ppm

F1 4001.04 Hz

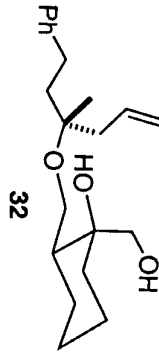
F2P 0.000 ppm

F2 0.00 Hz

PPMKM 0.40000 ppm/ci

HZCM 200.05200 Hz/cm

ppm



142.66
141.97
132.92
128.51
128.42
128.32
127.49
126.43
125.99
118.50

81.53
77.35
77.09
76.84
72.64
70.11
63.77

53.50
42.74
41.28
38.23
35.09
29.57
26.30
25.73
21.42

Current Data Parameters
NAME d-142-4m
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters

Date_ 500000
Time 16.16
INSTRUM spect
PROBHD 5 mm TXI 13C
PULPROG c13monoc
TD 32768
SOLVENT CDCl3
NS 159
DS 2
SWH 32679.738 Hz
FIDRES 0.997306 Hz
AQ 0.5014004 sec
RG 32768
DM 15.300 usec
DE 6.00 usec
TE 290.0 K
D3 0.00100000 sec
PL12 6.00 dB
D1 12.00000000 sec
CPDPRG2 waltz16
PCPD2 100.00 usec
SF02 500.1325006 MHz
NUC2 1H
PL2 120.00 dB
P1 12.50 usec
DE 6.00 usec
SF01 125.7715724 MHz
NUC1 13C
PL1 -6.00 dB

F2 - Processing parameters

SI 8192
SF 125.7577847 MHz
MDM EM
SSB 0
LB 4.00 Hz
GB 0
PC 1.00

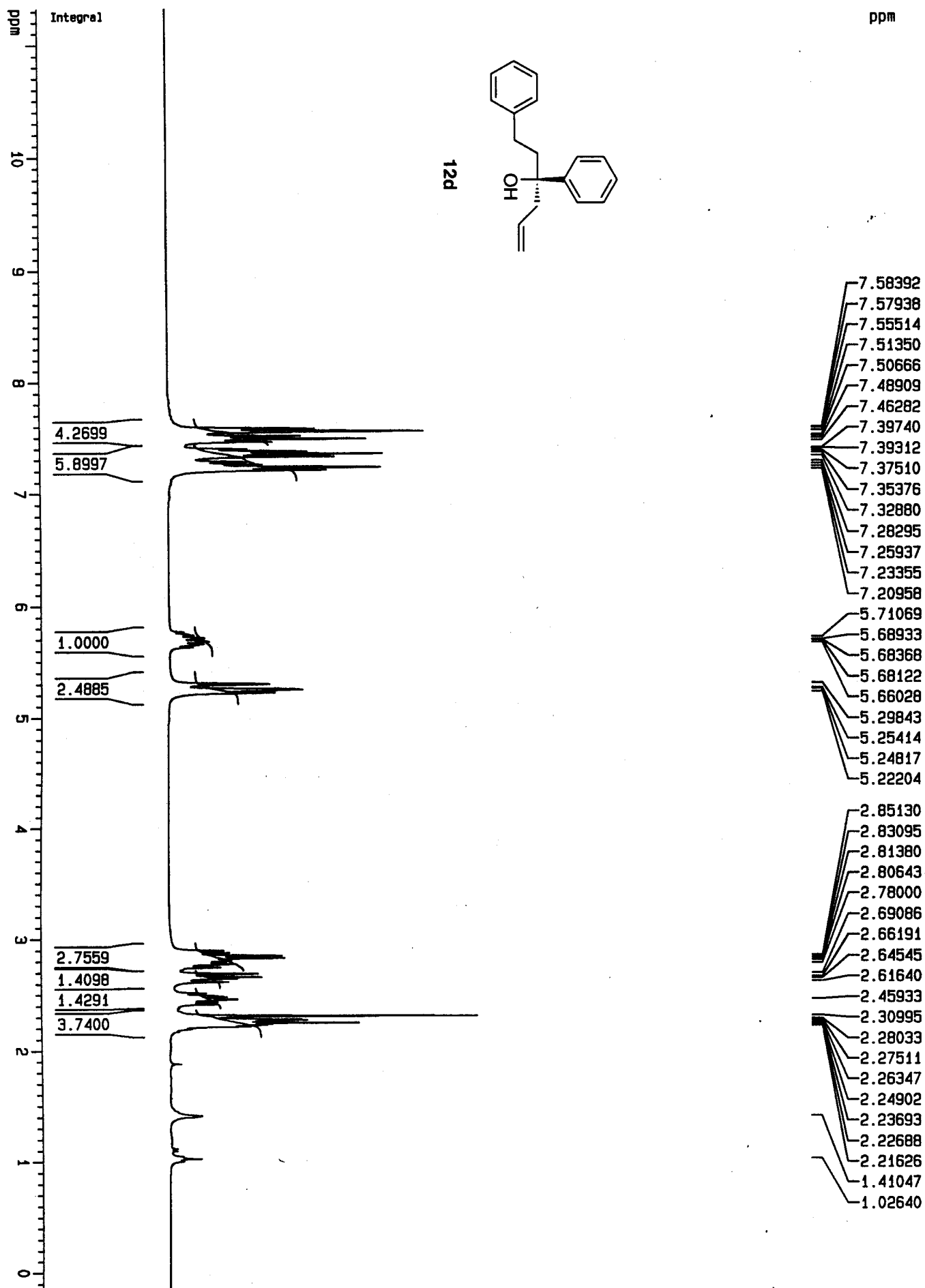
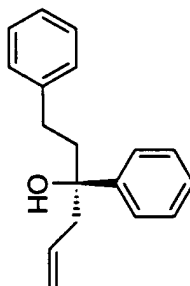
1D NMR plot parameters

CX 20.00 cm
F1P 200.000 ppm
F1 25151.56 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCH 10.00000 ppm/cm
HZCM 1257.57788 Hz/cm

ppm
180
160
140
120
100
80
60
40
20

ppm

12d



ppm

