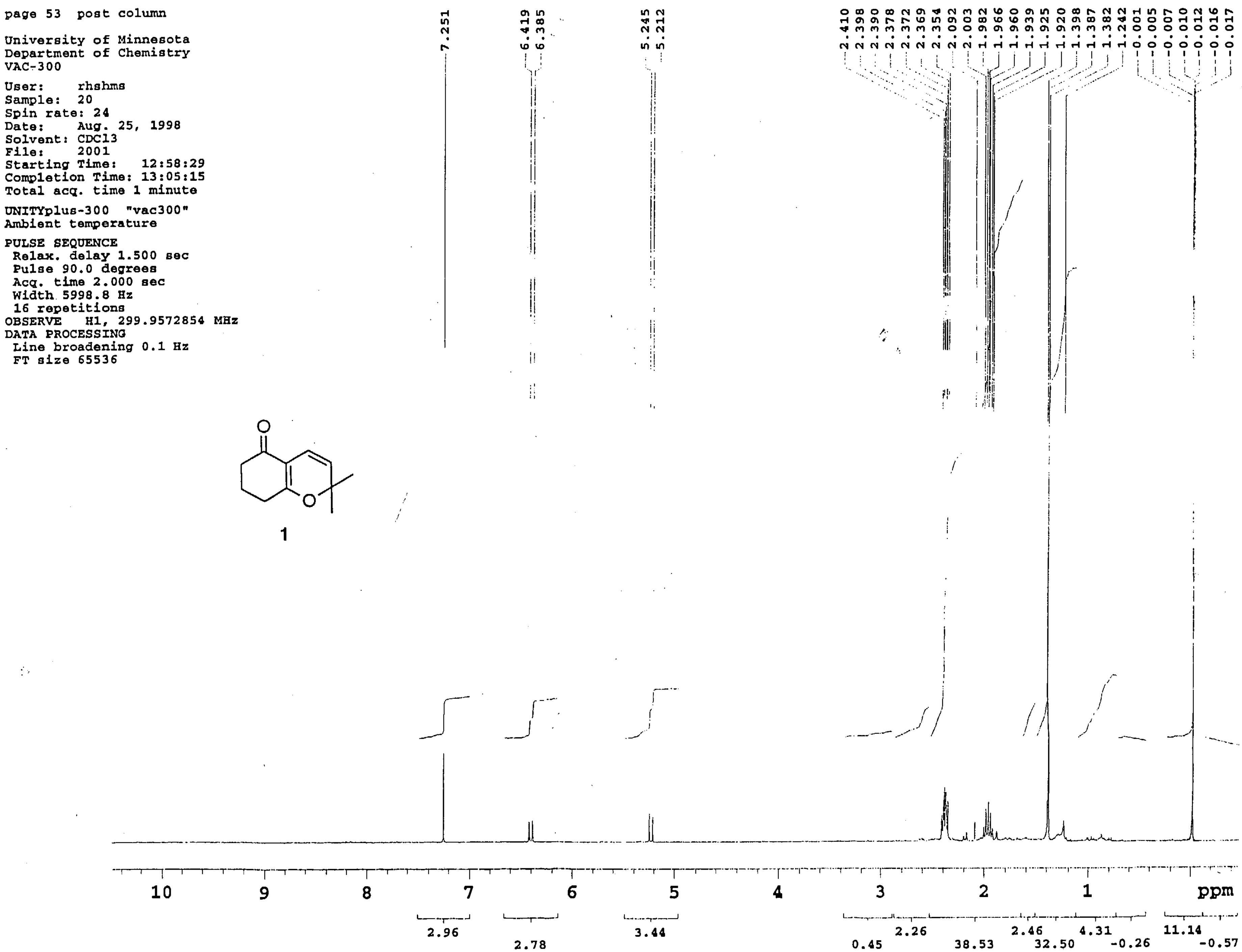


page 53 post column
University of Minnesota
Department of Chemistry
VAC-300
User: rhshms
Sample: 20
Spin rate: 24
Date: Aug. 25, 1998
Solvent: CDCl3
File: 2001
Starting Time: 12:58:29
Completion Time: 13:05:15
Total acq. time 1 minute
UNITYplus-300 "vac300"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 90.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9572854 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
O
O
1
7.251
6.419
6.385
5.245
5.212
2.410
2.398
2.390
2.378
2.372
2.369
2.354
2.092
2.003
1.982
1.966
1.960
1.939
1.925
1.920
1.398
1.387
1.382
1.242
-0.001
-0.005
-0.007
-0.010
-0.012
-0.016
-0.017
10
9
8
7
6
5
4
3
2
1
ppm
2.96
2.78
3.44
0.45
2.26
38.53
2.46
32.50
4.31
-0.26
11.14
-0.57

3

flashed

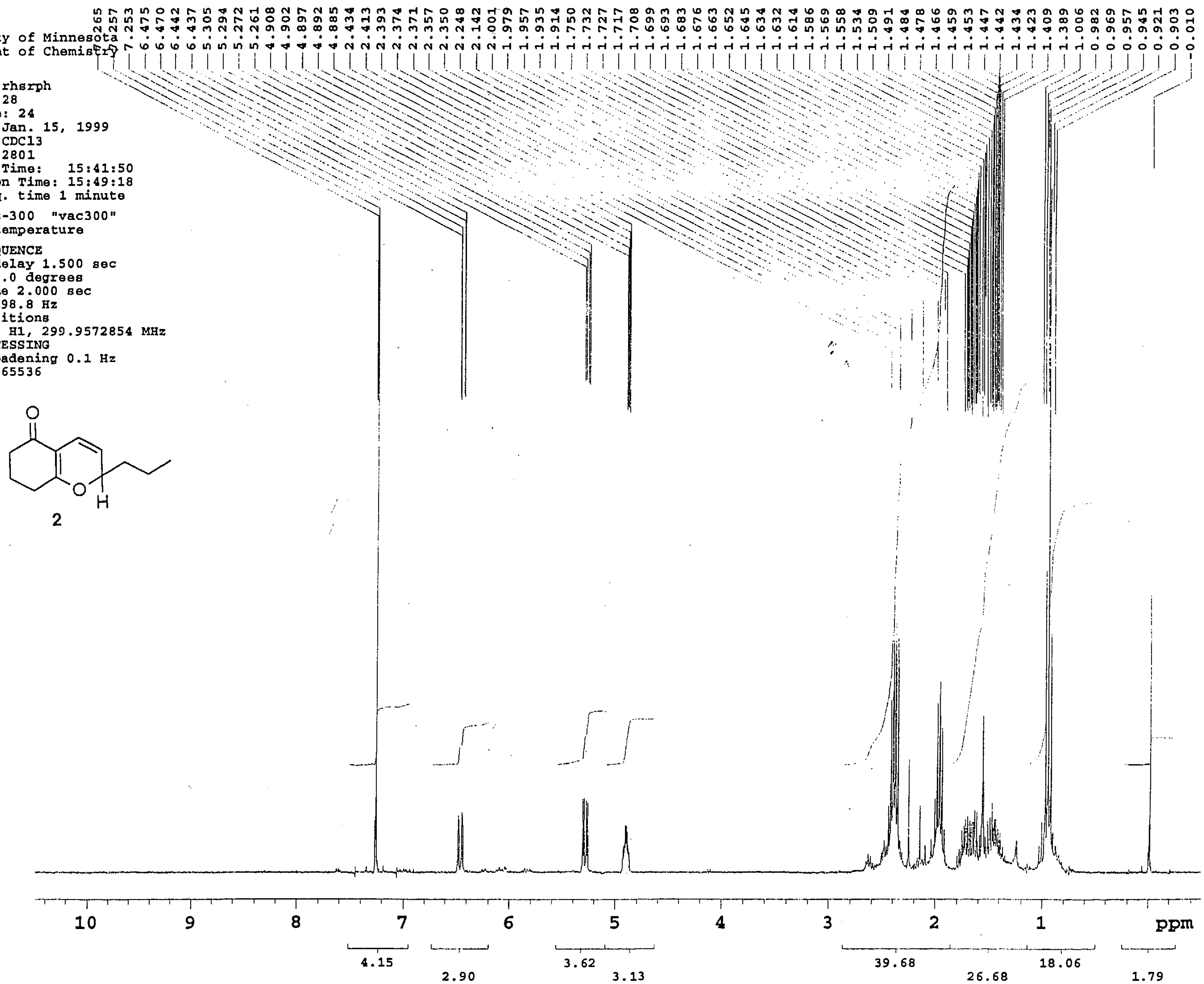
University of Minnesota
Department of Chemistry
VAC-300

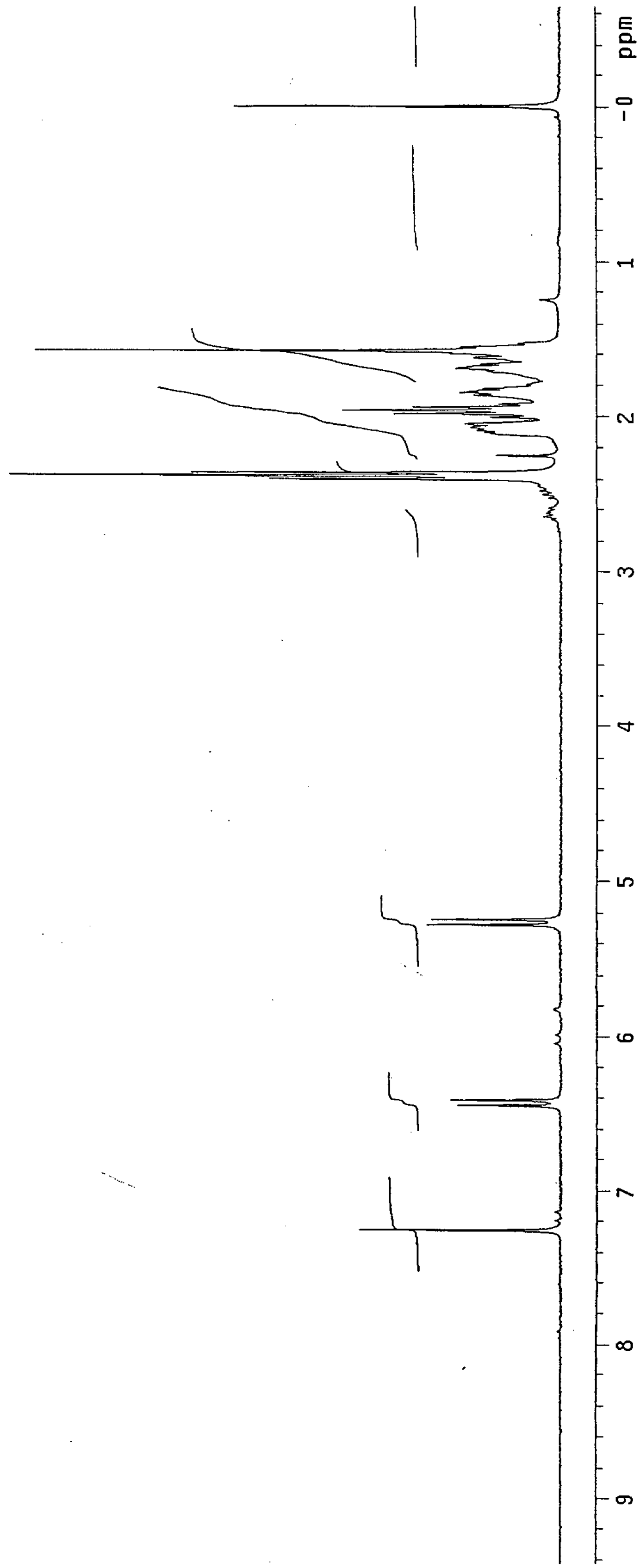
User: rhsrph
Sample: 28
Spin rate: 24
Date: Jan. 15, 1999
Solvent: CDCl3
File: 2801
Starting Time: 15:41:50
Completion Time: 15:49:18
Total acq. time 1 minute

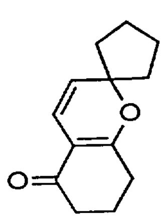
UNITYplus-300 "vac300"
Ambient temperature

PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 90.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9572854 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536

2







3

5

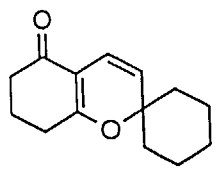
3+3 product

University of Minnesota
Department of Chemistry
VAC-300

User: rhscjd
Sample: 11
Spin rate: 24
Date: Feb. 25, 1999
Solvent: CDCl3
File: 1101
Starting Time: 13:24:24
Completion Time: 13:31:04
Total acq. time 1 minute

UNITYplus-300 "vac300"
Ambient temperature

PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 90.0 degrees
Acq. time 2.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 299.9572854 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536



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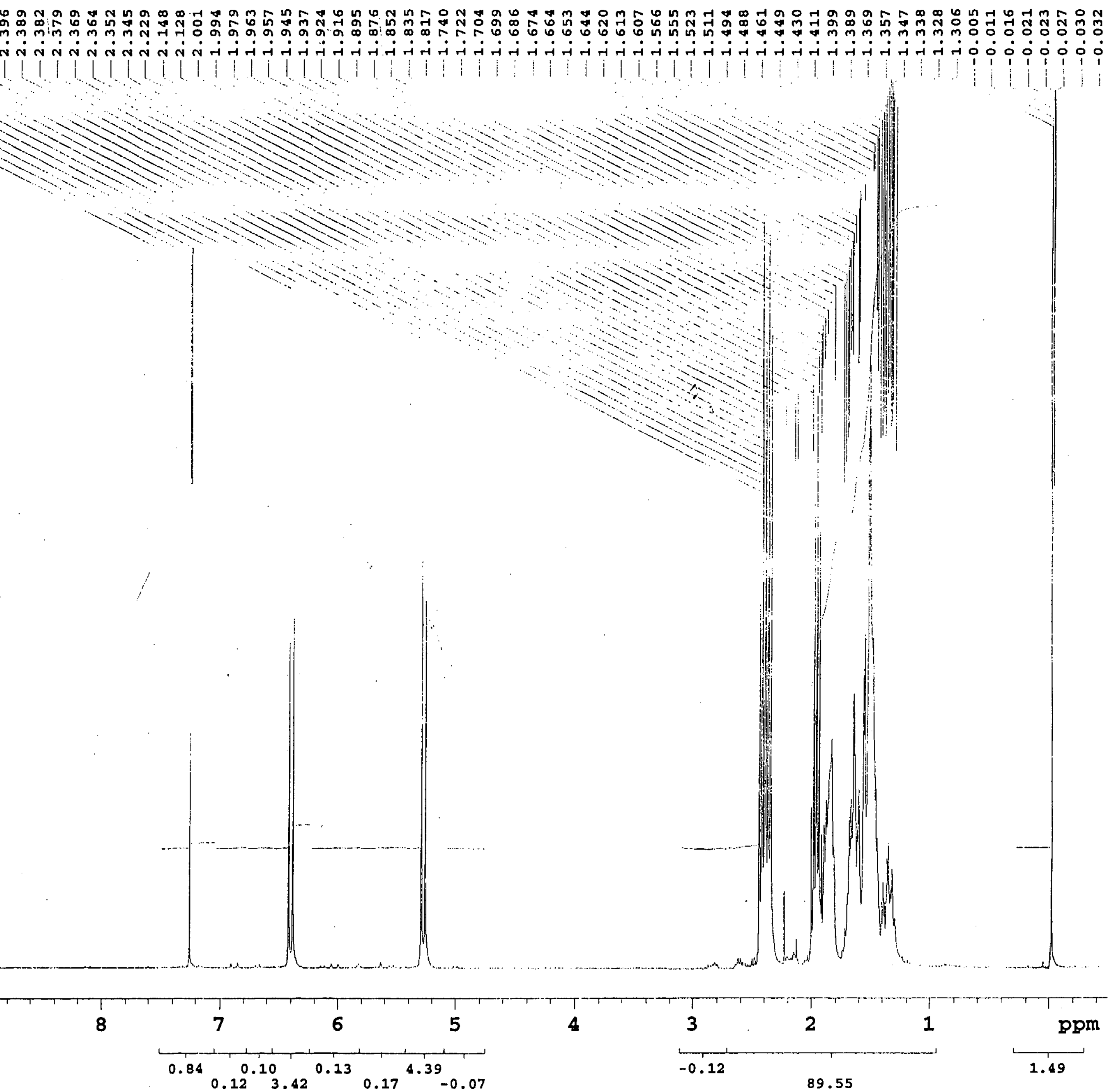
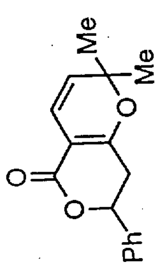
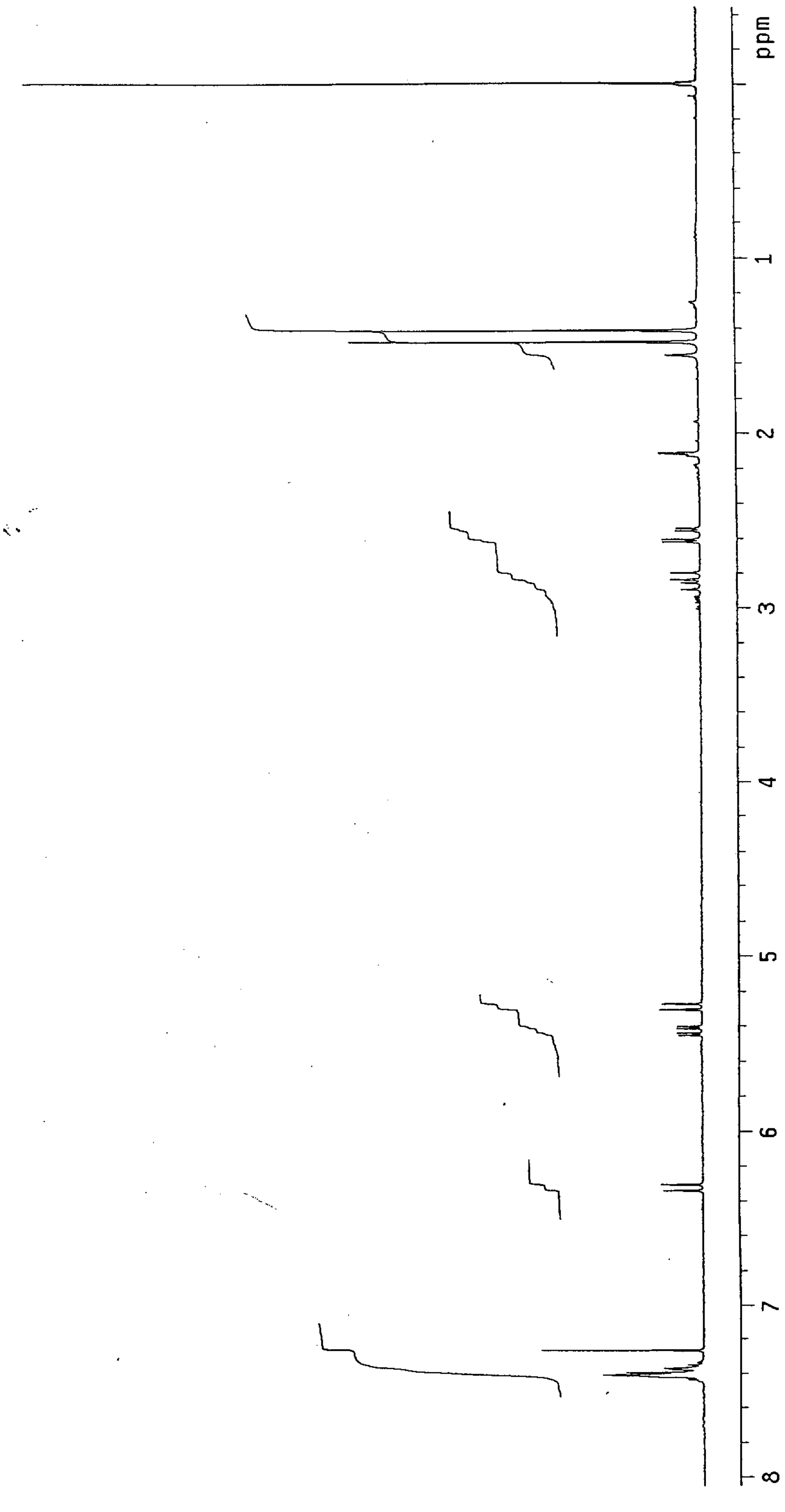
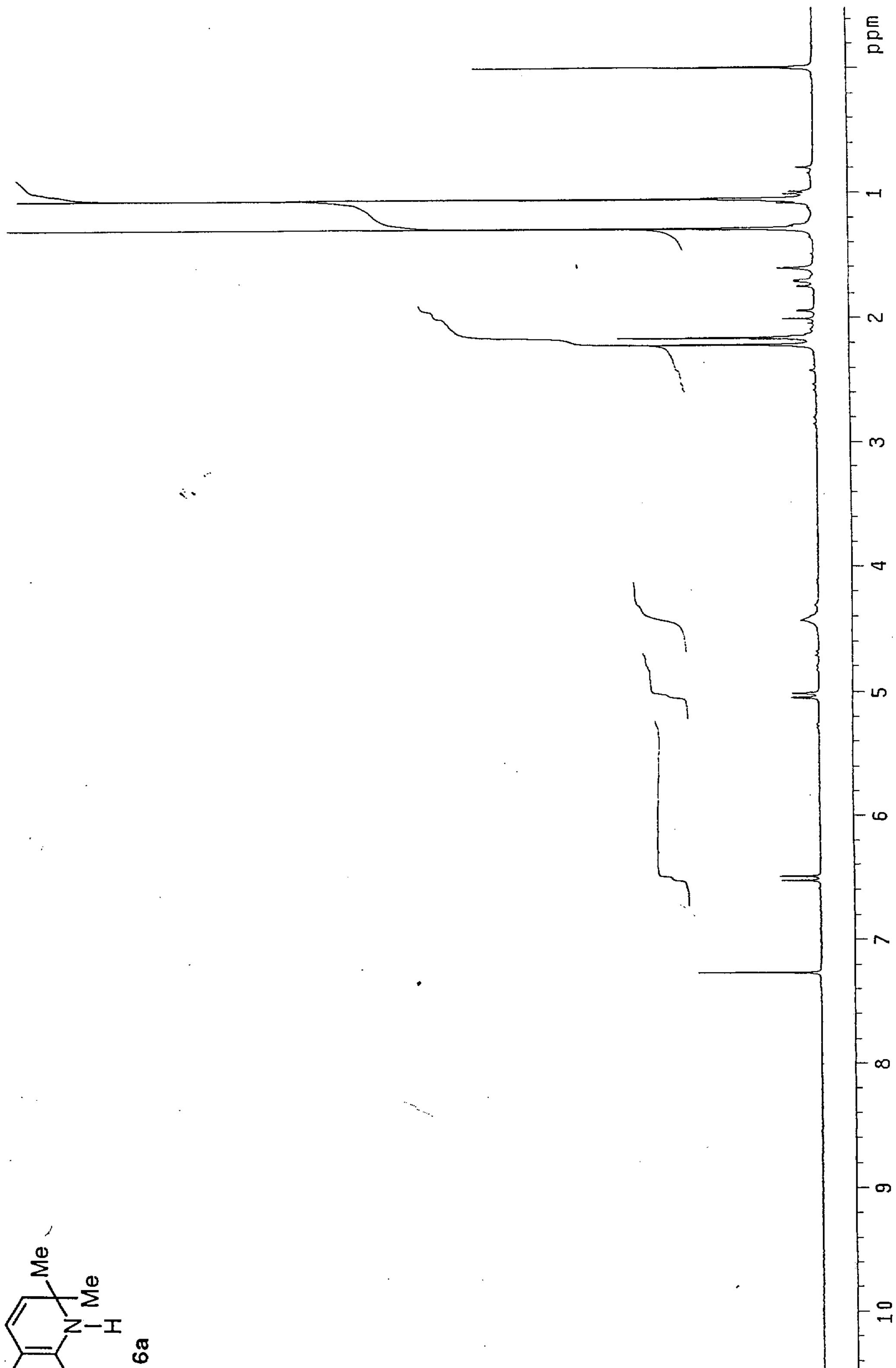
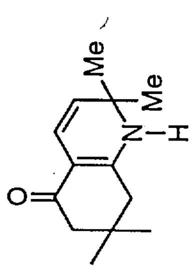




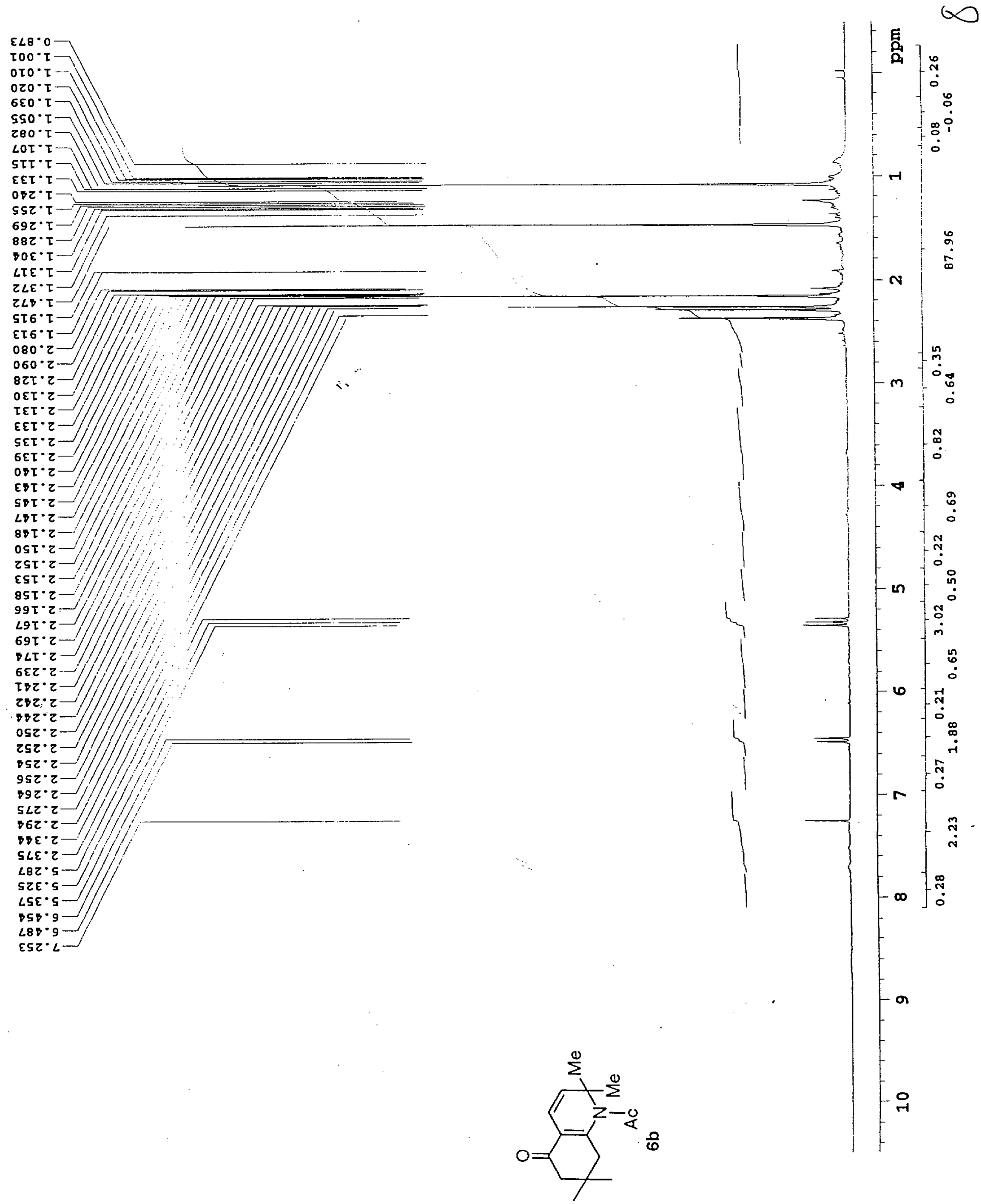
5

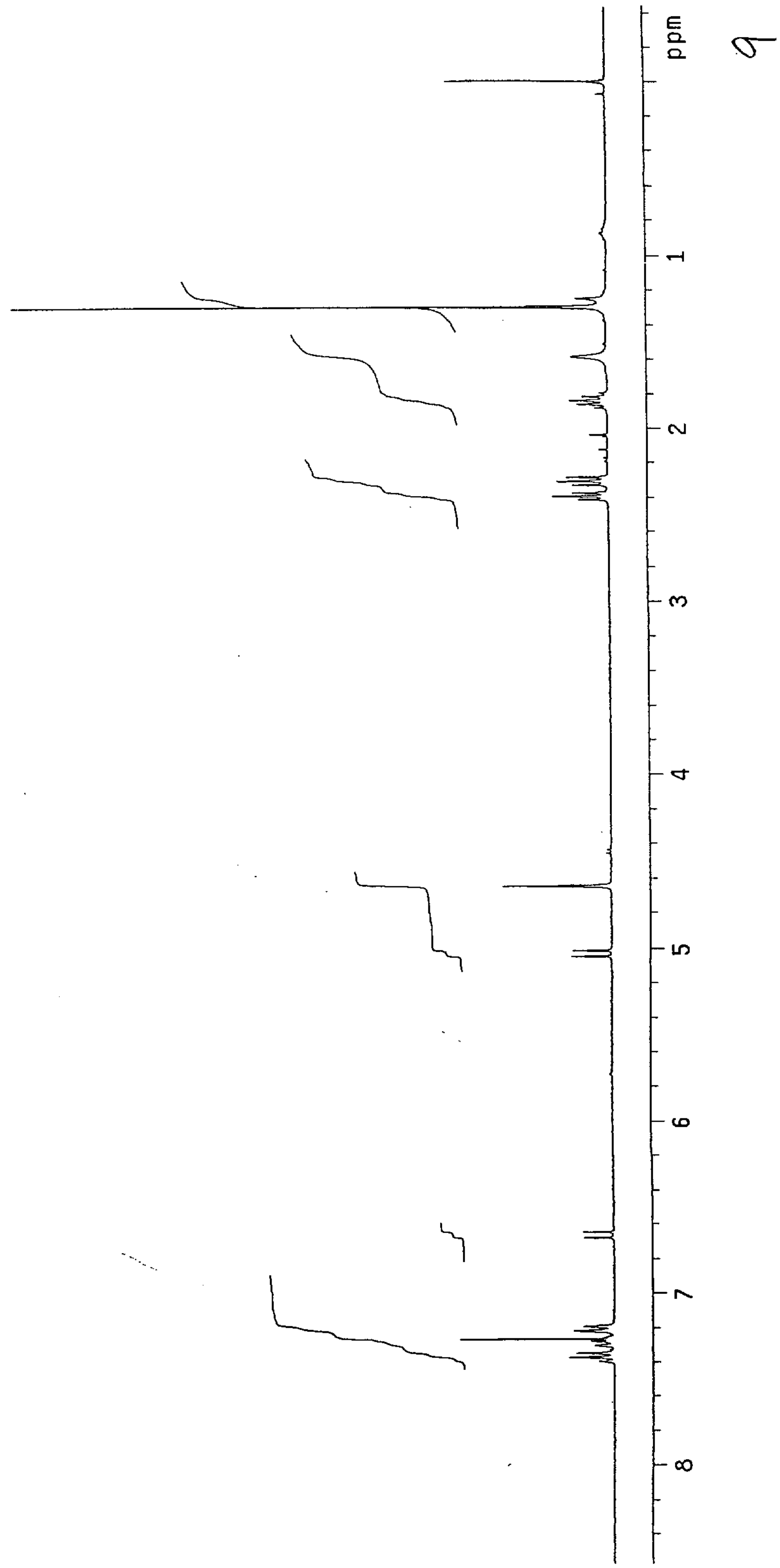


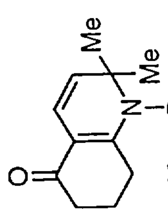




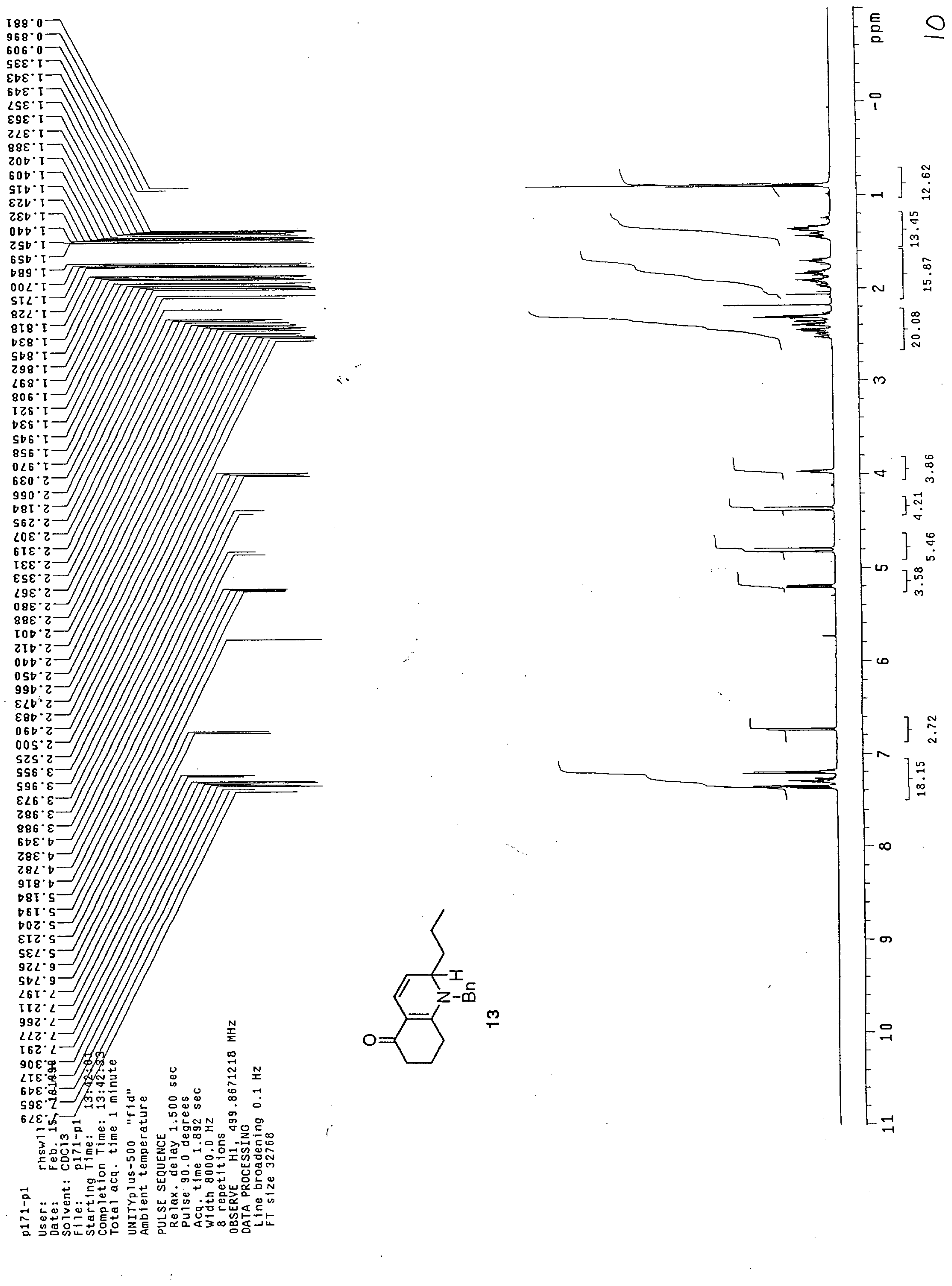
6a







12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1.363
1.372
1.388
1.402
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1.415
1.423
1.432
1.440
1.452
1.459
1.684
1.700
1.715
1.728
1.818
1.834
1.845
1.862
1.897
1.908
1.921
1.934
1.945
1.958
1.970
2.039
2.066
2.184
2.295
2.307
2.319
2.331
2.353
2.367
2.380
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3.965
3.973
3.982
3.988
4.349
4.382
4.782
4.818
5.184
5.194
5.204
5.213
5.235
6.726
6.745
7.197
7.211
7.266
7.277
7.291
7.306
7.317
7.349
7.365
7.379
p171-p1
User: rhswl11
Date: Feb. 15 1999
Solvent: CDCl3
File: p171-p1
Starting Time: 13:42:01
Completion Time: 13:42:33
Total acq. time 1 minute
UNITYplus-500 "fid"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 90.0 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.8671218 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
O
N
H
Bn
13
12.62
13.45
15.87
20.08
3.86
4.21
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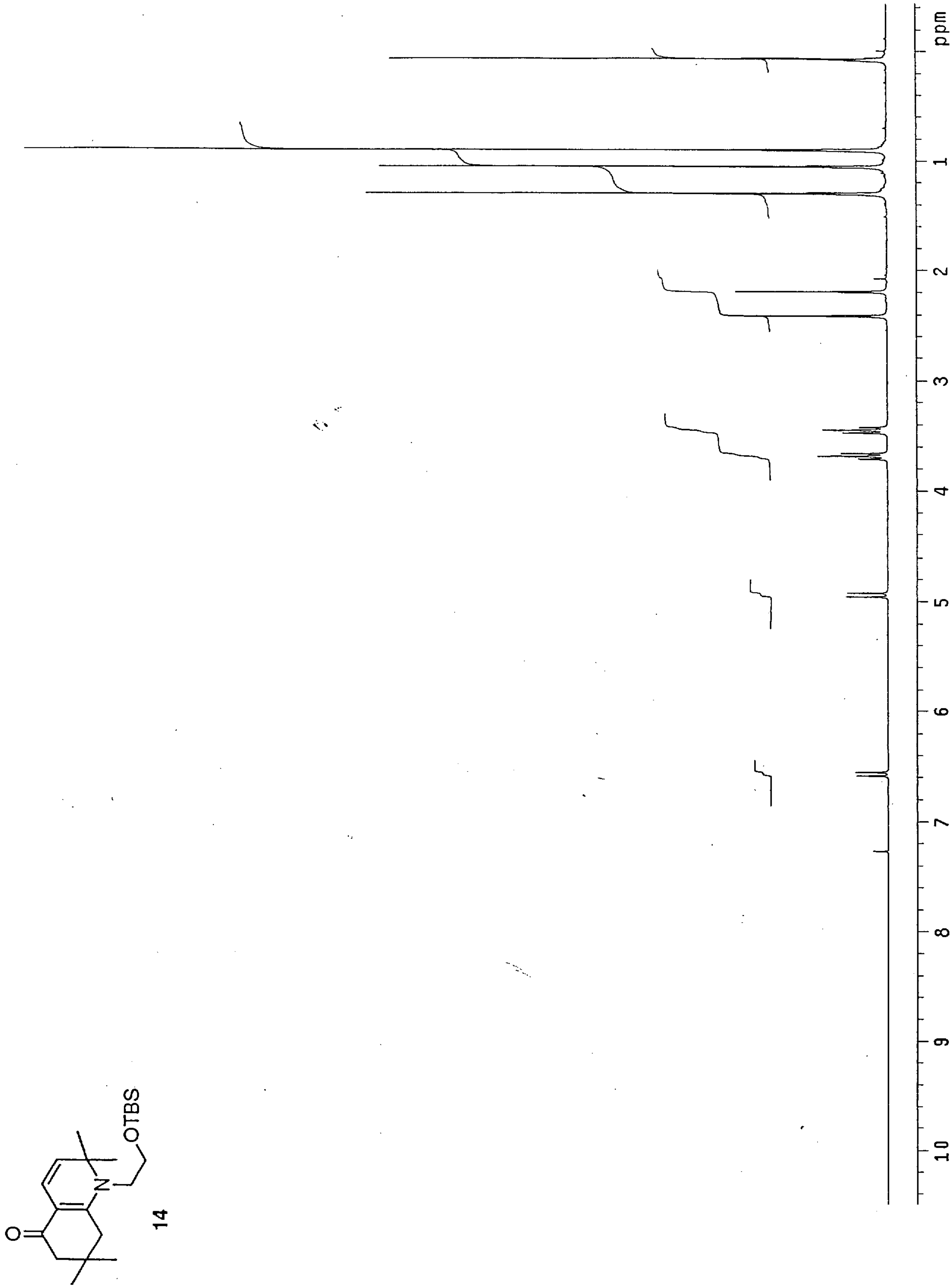
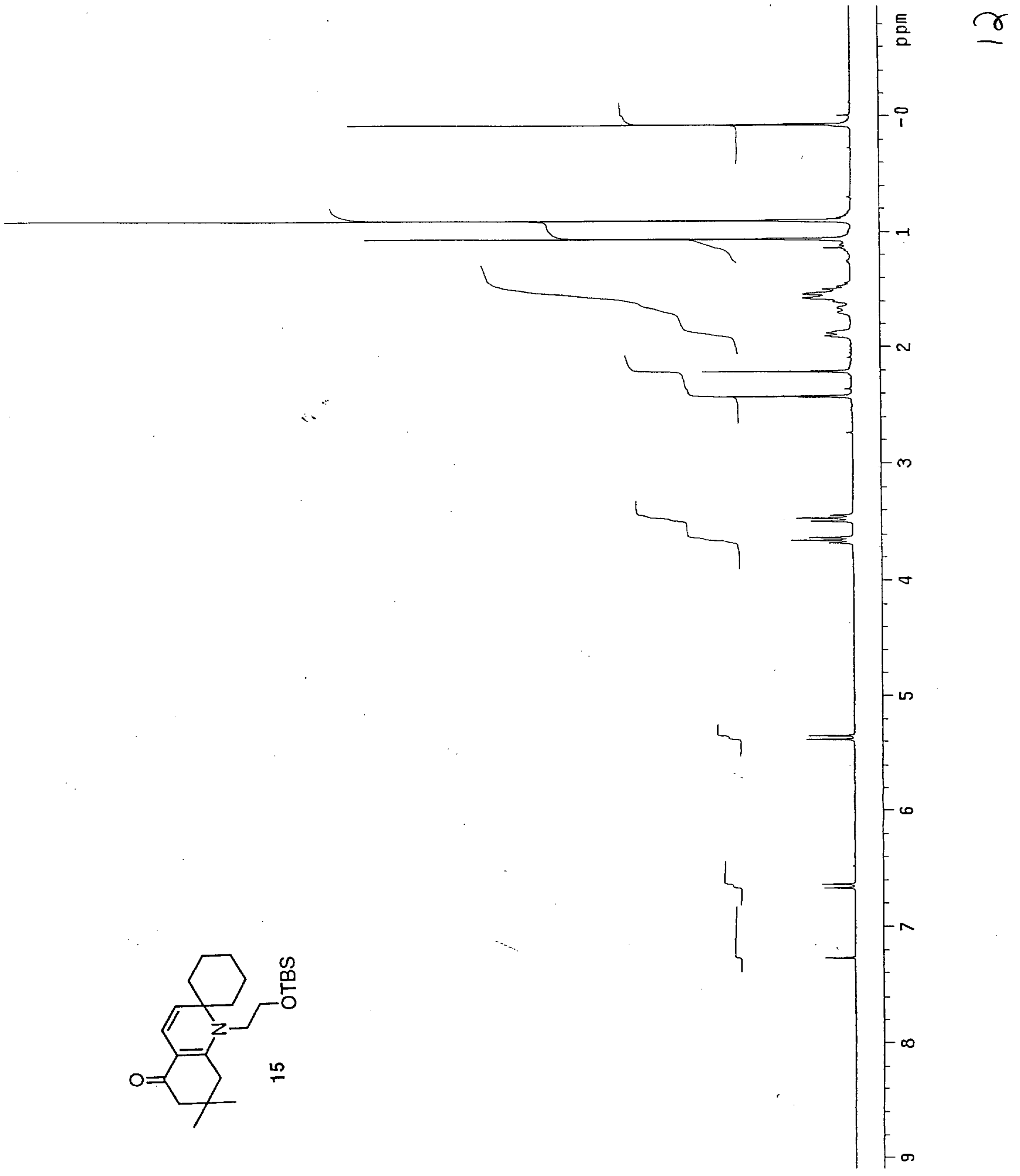
18.15
ppm
0
1
2
3
4
5
6
7
8
9
10
11
10



14


ppm
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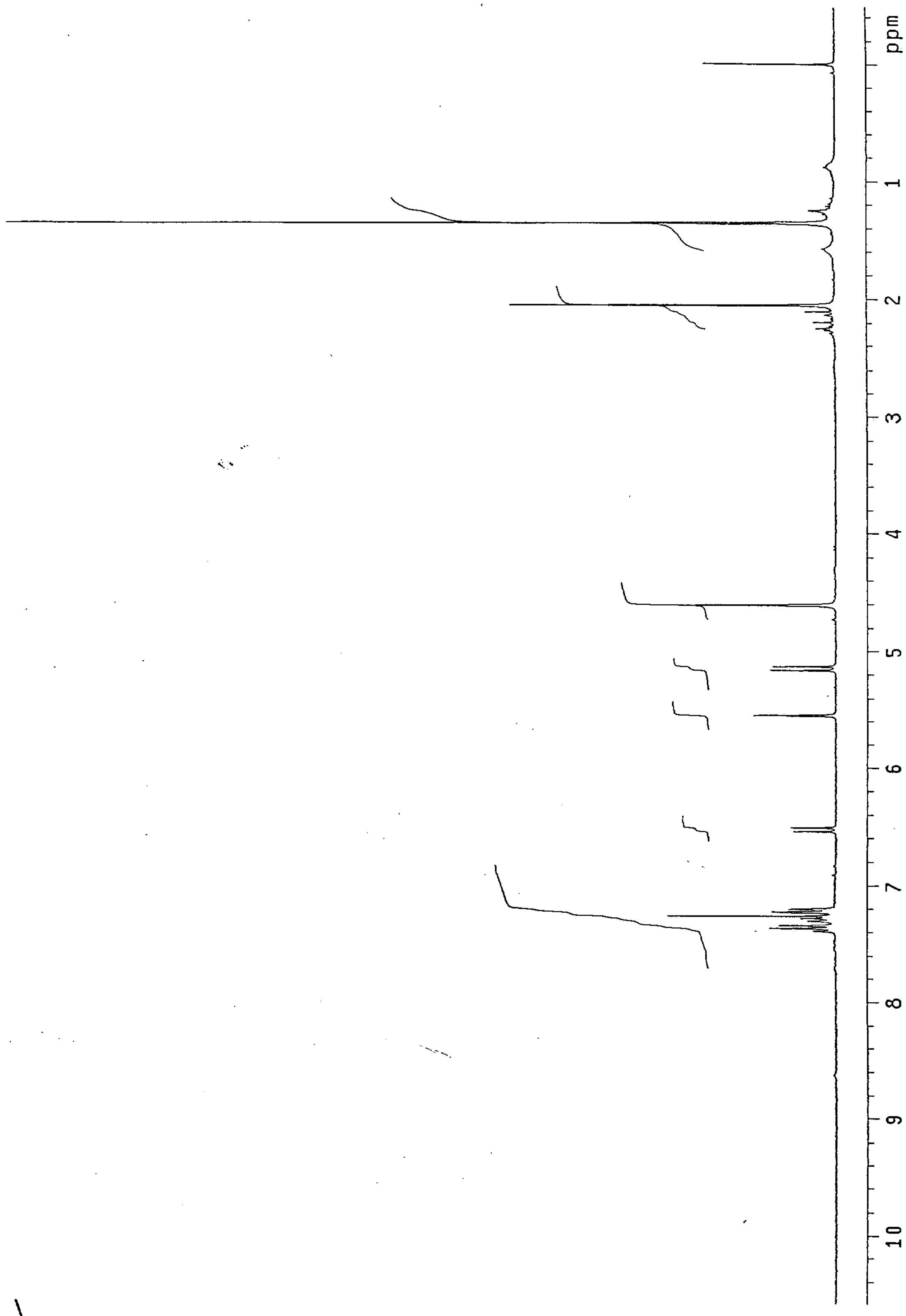
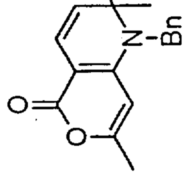
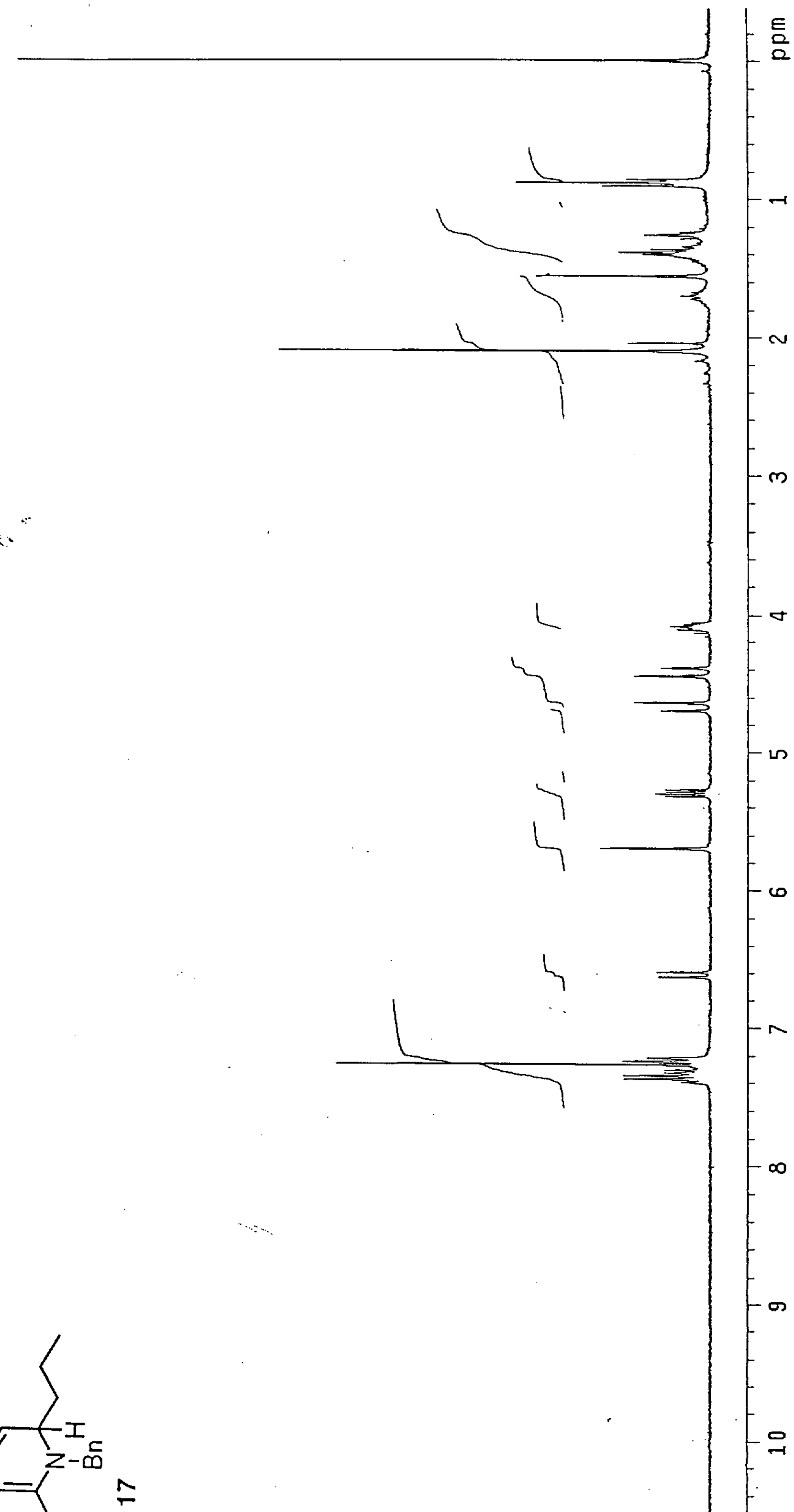
2
3
4
5
6
7
8
9
O
N
OTBS
15
12

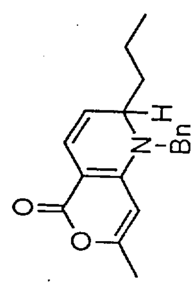




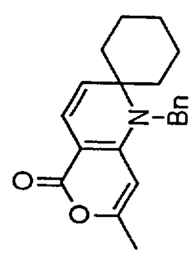
16

14

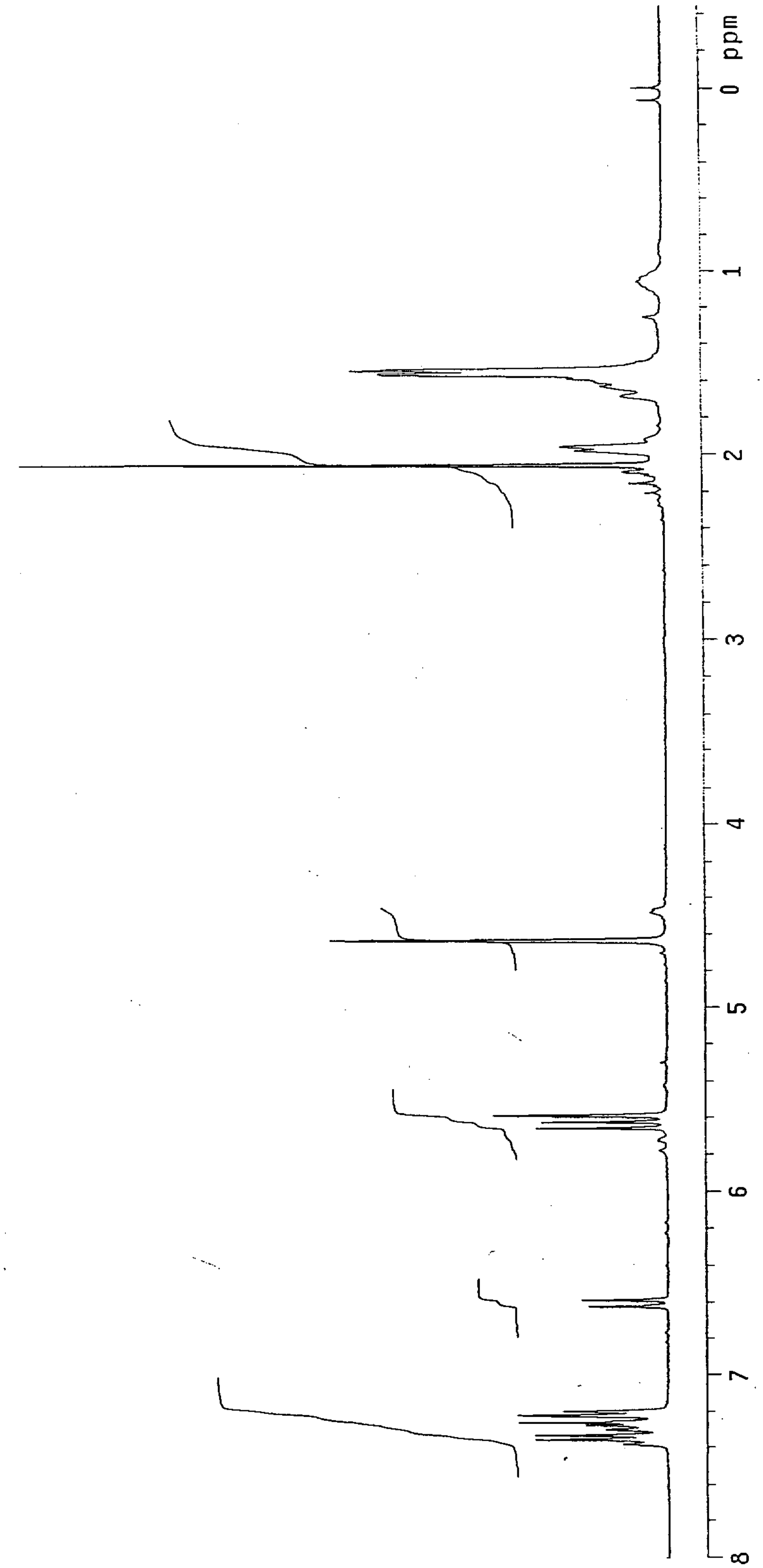


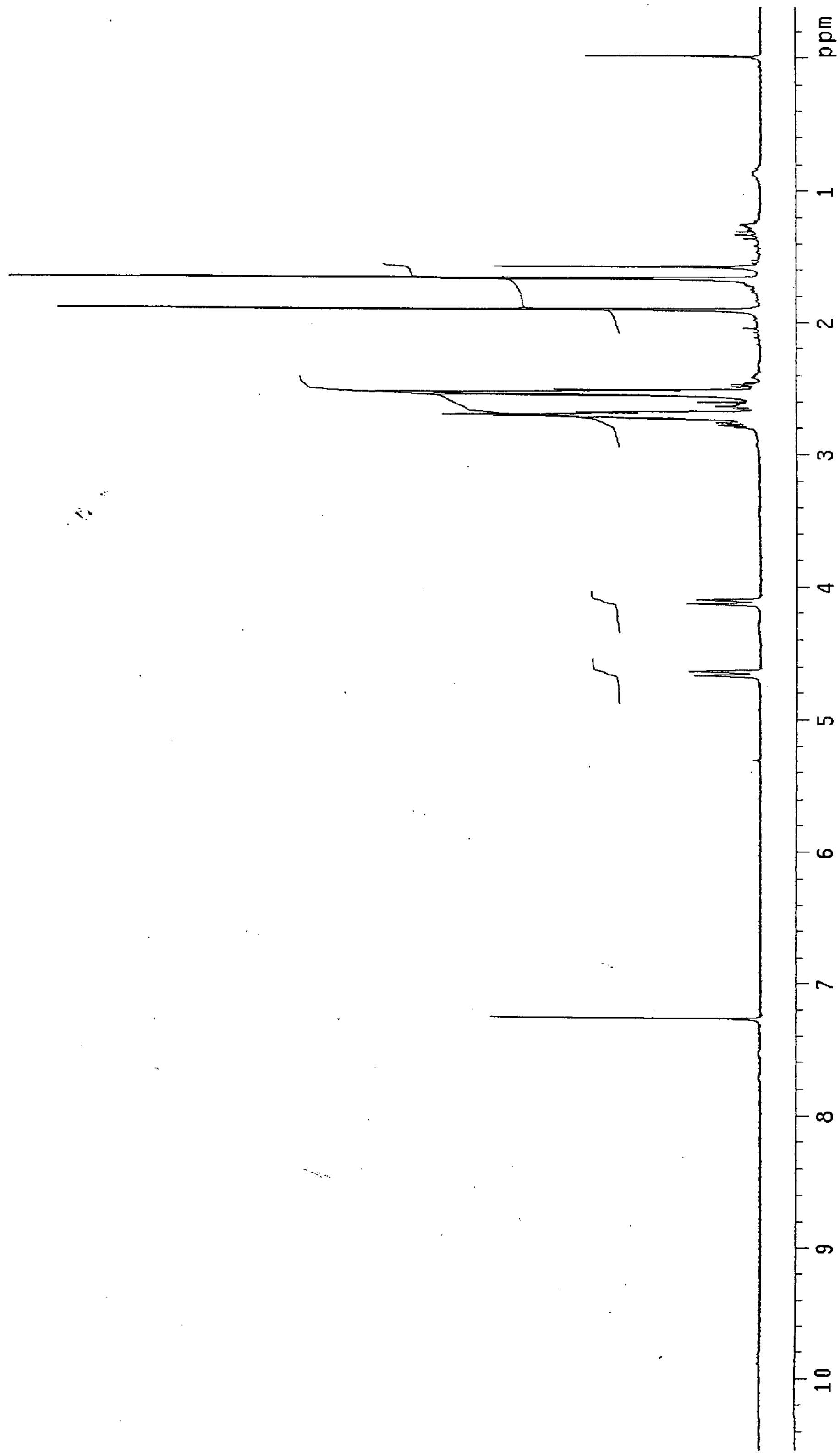


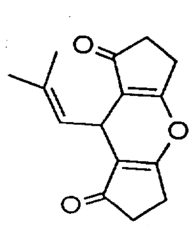
17



18

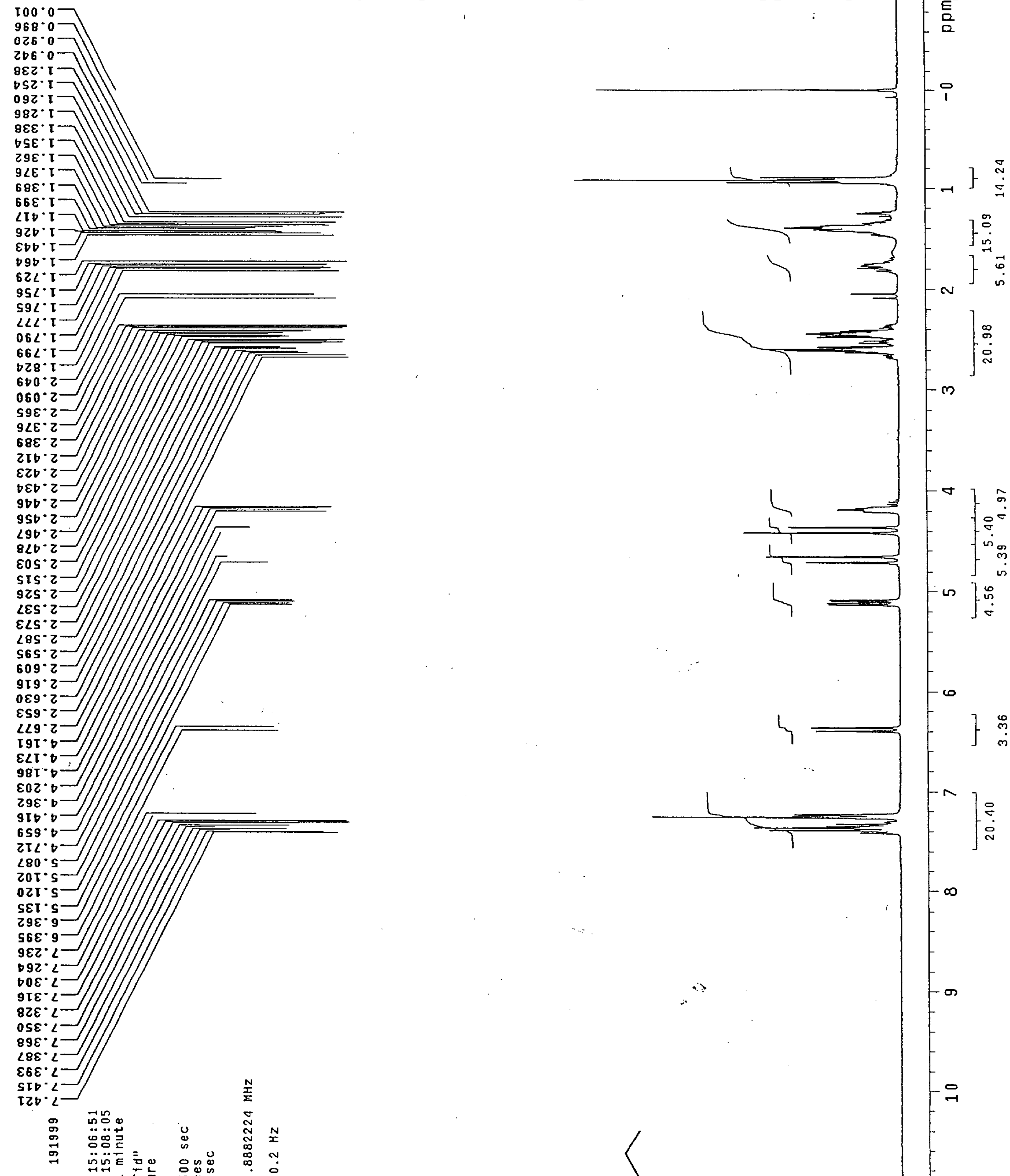






22

17


p175-2p
User: rhswll
Date: Feb. 19, 191999
Solvent: CDCl3
File: p175-2p
Starting Time: 15:06:51
Completion Time: 15:08:05
Total acq. time 1 minute
UNITYplus-500 "fid"
Ambient temperature
PULSE SEQUENCE
Relax. delay 1.500 sec
Pulse 90.0 degrees
Acq. time 2.001 sec
Width 5997.9 Hz
16 repetitions
OBSERVE H1, 299.8882224 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
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0.920
0.942
1.238
1.254
1.260
1.286
1.338
1.354
1.362
1.376
1.389
1.399
1.417
1.426
1.443
1.464
1.729
1.756
1.765
1.777
1.790
1.799
1.824
2.049
2.090
2.365
2.376
2.389
2.412
2.423
2.434
2.446
2.456
2.467
2.478
2.503
2.515
2.526
2.537
2.573
2.587
2.595
2.609
2.618
2.630
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2.677
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4.173
4.186
4.203
4.362
4.416
4.659
4.712
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5.102
5.120
5.135
6.362
6.395
7.236
7.264
7.304
7.316
7.328
7.350
7.368
7.387
7.393
7.415
7.421
14.24
15.09
5.61
20.98
4.97
5.40
5.39
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3
4
5
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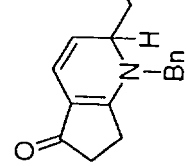
7
8
9
10
11


H
N
Bn
O

28

SUPPLEMENTARY MATERIAL FOR

the
communication
entitled

Formal Cycloaddition Reactions of Vinylogous Amides with α,β-Unsaturated Iminiums. A Strategy for Constructing Piperidinyl Heterocycles.

Richard P. Hsung*, Lin-Li Wei, Heather M. Sklenicka, Christopher J. Douglas,[1] Michael J. McLaughlin, Jason A. Mulder, and Letitia J. Yao[2]

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

General Procedure for the Reactions of 1,3-Diketones or Vinylogous Amides with α,β-Unstaurated Iminiums.

The appropriate starting enal (1-2 mmol) (filtered through silica gel if it is from commercial sources) was dissolved in anhydrous EtOAc (dried over CaH_2 quickly, filtered through celite, and stored over molecular seives), and 2.0 eq piperidine was added dropwise via syringe. The solution was cooled to -10 °C (ice in acetone), and 2.0 eq of acetic anhydride was added carefully dropwise. After stirring for an additional 5 minutes at -10 °C, the iminium mixture was sealed under a blanket of anhydrous nitrogen and heated at 85 °C (sand bath) for 1 h. The warm iminium solution was then transferred quickly via a cannula to a solution of appropriate starting diketones or vinylogous amides (0.4 to 0.5 mole% to the starting enal) in anhydrous toluene (the ratio of EtOAc to toluene was usually 2:3). The reaction mixture was again sealed under a blanket of nitrogen and heated at 150 °C in a sand bath for 18-96 h. The reaction progress was monitored by using TLC analysis (mostly 50% ethyl acetate in hexane or pure EtOAc. When the reaction was completed, the mixture was concentrated under reduced pressure, and the desired cyclized product was isolated using silica gel column chromatography (gradient eluent: ethyl acetate in hexane, 5-100%).

Characterizations for Isolated Products:

For Compound **1**.

Rf = 0.46 (50% EtOAc in hexane);

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 6H) 1.96 (m, 2H) 2.38 (m, 4H) 5.23 (d, 1H, J = 9.9 Hz) 6.40 (d, 1H, J = 10.2 Hz) ;

^{13}C NMR (300 MHz, $CDCl_3$) δ 20.7, 28.4, 28.7, 29.7, 36.5, 79.8, 110.61, 115.9, 122.9, 171.7, 195.0;

IR (neat) cm^{-1} 3054 (m), 2974 (s), 1724 (m), 1651 (s), 1588 (s), 1411 (s), 1267 (m);

mass spectrum (EI): m/e (%relative intensity) 178 (13) M^+, 163 (100), 135 (5), 121 (6), 107 (5), 79 (10);

For Compound **2**.

Rf = 0.47 (50% EtOAc in hexane);

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, 3H, J = 3.6 Hz), 1.44 (m, 2H), 1.53 (m, 2H), 1.66 (m, 2H), 1.97 (m, 2H), 2.37 (m, 2H), 4.90 (m, 1H), 5.28 (dd, 1H, J = 3.3, 9.9 Hz), 6.45 (dd, 1H, J = 1.5, 9.9);

^{13}C NMR (300 MHz, $CDCl_3$) δ 13.9, 17.6, 20.6, 28.3, 36.4, 37.9, 77.5, 111.4, 117.5, 117.9, 172.7, 195.0;

IR (neat) cm^{-1} 3078(w), 2959 (s), 2935 (s), 2873 (m), 1650 (s), 1594 (m), 1221 (m);

mass spectrum (EI): m/e (%relative intensity) 192 (7) M^+, 150 (12) 149 (100), 107 (7), 77 (5);

$C_{12}H_{16}O_2$ (192)

For Compound **3**.

Rf = 0.53 (50% EtOAc in hexane);

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (m, 2H), 1.82 (m, 2H), 1.99 (sext, 4H, J = 6.6 Hz), 2.09 (m, 2H), 2.37 (t, 4H, J = 6.6 Hz), 5.26 (d, 1H, J = 9.9 Hz), 6.43 (d, 1H, J = 9.9 Hz);

^{13}C NMR (50 MHz, $CDCl_3$) δ 20.7, 23.5, 28.8, 36.5, 40.7, 83.4, 90.5, 116.5, 121.7, 172.4, 194.9;

IR (neat) cm^{-1} 2959 (s), 1641 (s), 1607 (s), 1588 (s);

mass spectrum (EI): m/e (%relative intensity) 204 (20) M^+, 175 (100), 148 (9), 91 (9), 55 (8);

For Compound **4**.

Rf = 0.50 (50% EtOAc in hexane);

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (m, 2H), 1.53 (m, 4H), 1.61 (m, 2H), 1.84 (m, 2H), 1.95 (sext, 2H, J = 6.6 Hz), 2.37 (t, 2H, J = 4.8 Hz), 2.42 (d, 2H, J = 4.8 Hz), 5.27 (d, 1H, J = 10.2 Hz), 6.72 (d, 1H, J = 10.2);

^{13}C NMR (50 MHz, $CDCl_3$) δ 20.7, 20.9, 21.0, 25.1, 28.6, 36.5, 80.7, 111.3, 116.4, 122.3, 171.8, 195.0;

IR (neat) cm^{-1} 2930 (s), 1651 (s), 1611 (s);

mass spectrum (EI): m/e (%relative intensity) 218 (35) M^+, 175 (100), 162 (10), 91 (10), 41 (9);

For Compound **5**.

Rf = 0.47 (50% EtOAc in hexane);

^{1}H NMR (200 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.48 (s, 3H), 2.57 (dd, 1H, J = 4.6, 17.6 Hz), 2.87 (dd, 1H, J = 5.8, 17.6 Hz), 5.27 (d, 1H, J = 10 Hz) 5.42 (dd, 1H, J = 4.2, 1.88 Hz), 6.32 (d, 1H, J = 10 Hz), 7.40 (m, 5H);

^{13}C NMR (300 MHz, $CDCl_3$) δ 28.5, 28.6, 34.6, 80.9, 100.4, 116.5, 123.2, 126.0, 128.6, 128.7, 138.3, 165.1, 165.2;

IR (neat) cm^{-1} 3063 (s), 3035 (s), 2976 (s), 2929 (s), 1709 (s), 1644 (m), 1423 (m), 1147 (m);

mass spectrum (EI): m/e (%relative intensity) 256 (13) M^+, 241 (88), 152 (7), 135 (100), 104 (35), 77 (30), 51 (13);

For Compound **6a**.

Rf = 0.15 (50% EtOAc in hexane);

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (s, 6H), 1.27 (s, 6H), 2.18 (s, 2H), 2.22 (s, 2H), 4.4.1 (brs, 1H), 5.00 (dd, 1H, J = 1.8, 9.9 Hz), 6.51 (d, 1H, J = 9.9 Hz);

^{13}C NMR (75 MHz, $CDCl_3$) δ 26.4, 28.3, 31.7, 42.5, 50.3, 53.7, 110.4, 117.6, 120.4, 157.9, 190.5;

IR (neat) cm^{-1} 3241s, 3196w, 2939s, 2870w, 1634s, 1585s, 1526s, 1457s, 1364m, 1246w, 1142w;

mass spectrum (EI): m/e (%relative intensity) 205 (10) M^+, 190 (100), 134 (15), 106 (10);

For Compound **6b**.

Rf = 0.50 (50% EtOAc in hexane);

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 6H), 1.47 (s, 6H), 2.26 (s, 3H), 2.29 (s, 2H), 2.38 (s, 2H), 5.34 (d, 1H, J = 9.8 Hz), 6.47 (d, 1H, J = 9.8 Hz);

^{13}C NMR (75 MHz, $CDCl_3$) δ 27.4, 28.0, 29.4, 34.6, 45.1, 50.4, 59.1, 116.2, 116.8, 131.1, 150.7, 174.9, 193.8;

IR (neat) cm^{-1} 2958s, 2929m, 2870w, 1697s, 1643s, 1575s, 1467m, 1413m, 1364m, 1265s, 1216s, 1172m, 1142w;

mass spectrum (EI): m/e (%relative intensity) 247 (5) M^+, 232 (15), 190 (100), 174 (4), 134 (5);

For Compound **12**.

Rf = 0.70 (EtOAc);

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 6H), 1.84 (quint, 2H, J = 6.3 Hz), 2.31 (t, 2H, J = 6.5 Hz), 2.39 (t, 2H, J = 6.1 Hz), 4.64 (s, 2H), 5.02 (d, 1H, J = 9.8 Hz), 6.67 (d, 1H, J = 9.8 Hz), 7.20 (d, 2H, J = 7.2 Hz), 7.28 (t, 1H, J = 7.8 Hz), 7.35 (t, 2H, J = 7.5 Hz);

^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 28.9, 35.5, 42.5, 47.8, 59.5, 118.4, 121.1, 125.2, 127.2, 128.9, 138.5, 160.7, 169.0, 191.9;

IR (neat) cm^{-1} 3056w, 2948m, 2919m, 2870w, 1604s, 1530s, 1432s, 1349m, 1167w, 1093w;
mass spectrum (EI): m/e (%relative intensity) 267 (12) M^+, 252 (100), 190 (5), 133 (5);

For Compound **13**.
Rf = 0.45 (10% MeOH in EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, 3H, J = 7.2 Hz), 1.40 (m, 3H), 1.68-1.97 (m, 3H), 2.42 (m, 4H), 3.98 (m, 1H), 4.37 (d, 1H, J = 17.0 Hz), 4.80 (d, 1H, J = 17.0 Hz), 5.21 (dd, 1H, J = 4.9, 9.8 Hz), 6.73 (d, 1H, J = 9.8 Hz), 7.29 (m, 5H);
^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 17.0, 21.3, 26.6, 35.5, 37.4, 52.8, 60.1, 108.5, 113.7, 120.9, 125.9, 127.7, 129.1, 136.7, 160.4, 191.8;
IR (neat) cm^{-1} 2955m, 2932m, 2871w, 1711w, 1659w, 1611s, 1529s, 1496w, 1477w, 1449m, 1421m, 1342m, 1319m, 1177m,;
mass spectrum (EI): m/e (%relative intensity) 281 (9) M^+, 238 (35), 190 (12), 161 (4), 119 (4), 91 (100);

For Compound **14**.
Rf = 0.47 (EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 1.07 (s, 6H), 1.31 (s, 6H), 2.21 (s, 2H), 2.41 (s, 2H), 3.45 (t, 2H, J = 6.6 Hz), 3.69 (t, 2H, J = 6.6 Hz), 4.95 (d, 1H, J = 9.6 Hz), 6.58 (d, 1H, J = 9.6 Hz);
^{13}C NMR (75 MHz, $CDCl_3$) δ -5.5, 18.3, 26.0, 26.1, 28.4, 32.3, 40.8, 46.3, 49.6, 59.1, 63.4, 106.7, 118.3, 121.1, 159.9, 191.5 ;
IR (neat) cm^{-1} 2958s, 2929m, 2860w, 1590s, 1521s, 1432s, 1359w, 1334w, 1147w, 1088w, 840w;
mass spectrum (EI): m/e (%relative intensity) 363 (18) M^+, 348 (100), 234 (35), 216 (20), 91 (20);

For Compound **15**.
Rf = 0.52 (EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.91 (s, 9H), 1.06 (s, 6H), 1.57 (m, 6H), 1.68 (m, 2H), 1.89 (m, 2H), 2.22 (s, 2H), 2.43 (s, 2H), 3.47 (t, 2H, J = 6.6 Hz), 3.64 (t, 2H, J = 6.6 Hz), 5.37 (d, 1H, J = 9.6 Hz), 6.65 (d, 1H, J = 9.6 Hz);
^{13}C NMR (75 MHz, $CDCl_3$) δ -5.4, 18.3, 21.6, 25.3, 25.8, 28.6, 32.4, 35.2, 41.4, 45.8, 49.0, 61.1, 63.4, 107.9, 115.9, 115.9, 119.4, 159.7, 191.6;
IR (neat) cm^{-1} 2929s, 2860m, 1614s, 1526m, 1467w, 1427s, 1329w, 1250w, 1237w, 1103m, 1049w, 837s;
mass spectrum (EI): m/e (%relative intensity) 403 (10) M^+, 375 (5), 344 (100), 288 (9), 258 (24), 189 (10), 133 (9);

For Compound **16**.
R_f = 0.65 (EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 6H), 2.04 (s, 3H), 4.60 (s, 2H), 5.13 (d, 1H, J = 9.9 Hz), 5.54 (s, 1H), 6.50 (d, 1H, J = 9.9 Hz), 7.20 (d, 2H, J = 7.2 Hz), 7.28 (t, 1H, J = 7.8 Hz), 7.35 (t, 2H, J = 7.5 Hz);
^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 29.2, 47.5, 58.8, 92.8, 96.3, 118.2, 123.7, 125.6, 127.3, 128.9, 137.5, 153.2, 161.0, 162.1;
IR (neat) cm^{-1} 3047w, 3027w, 2958m, 2919m, 2870w, 1682s, 1526s, 1486s, 1452s, 1344m, 1157w, 1049w;
mass spectrum (EI): m/e (%relative intensity) 281 (10) M^+, 266 (100), 194 (5), 175 (5), 128 (5);

For Compound **17**.
R_f = 0.68 (EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3H, J = 7.2 Hz), 1.22 (m, 1H), 1.39 (m, 2H), 1.66 (m, 1H), 2.09 (s, 3H), 4.10 (m, 1H), 4.41 (d, 1H, J = 17.4 Hz), 4.66 (d, 1H, J = 17.4 Hz), 5.28 (dd, 1H, J = 5.4, 9.9 Hz), 5.69 (s, 1H), 6.60 (d, 1H, J = 9.9 hz), 7.21 (d, 2H, J = 7.3 Hz), 7.29 (t, 1H, J = 7.9 Hz), 7.36 (t, 2H, J = 7.7 Hz);
^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 16.8, 20.5, 37.7, 52.5, 59.4, 93.6, 95.8, 116.5, 120.7, 126.2, 127.7, 129.0, 136.2, 153.2, 161.3, 162.2;
IR (neat) cm^{-1} 2958m, 2929m, 2870w, 1684s, 1643m, 1521s, 1491m, 1452m, 1329w, 1260w;
mass spectrum (EI): m/e (%relative intensity) 295 (11) M^+, 252 (100), 204 (30), 175 (30), 146 (5), 121 (5);

For Compound **18**.
R_f = 0.61 (EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58 (m, 6H), 1.64 (m, 2H), 1.98 (m, 2H), 2.07 (s, 3H), 4.64 (s, 2H), 5.59 (s, 1H), 5.65 (d, 1H, J = 10.0 Hz), 6.61 (d, 1H, J = 10.0 Hz), 7.21 (d, 2H, J = 8.1 Hz), 7.30 (t, 1H, J = 8.7 Hz), 7.36 (t, 2H, J = 8.1 Hz);
^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5, 21.2, 25.0, 35.8, 47.1, 61.2, 93.5, 96.6, 118.9, 125.7, 127.2, 128.6, 128.8, 137.7, 153.7, 160.9, 162.2;
IR (neat) cm^{-1} 2929m, 2850w, 1682s, 1644m, 1521s, 1481m, 1452m, 1339w, 1246w, 1019w, 955w;
mass spectrum (EI): m/e (%relative intensity) 321 (4) M^+, 319 (89), 318 (100), 290 (9), 262 (100), 250 (11), 191 (21), 165 (10), 115 (35);

For Compound **22**.
Rf = 0.53 (50% EtOAc in hexane);
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.67 (d, 3H, J = 1.2 Hz), 1.91 (d, 3H, J = 1.2 Hz), 2.46 (m, 4H), 2.65 (m, 4H), 4.11 (d, 1H, J = 9.6 Hz), 4.34 (brd, 1H, J = 9.6 Hz);
^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 24.9, 25.9, 26.7, 34.2, 120.7, 122.8, 135.1, 177.7, 201.9;
IR (neat) cm^{-1} 2918 (s), 1693 (s), 1668 (s), 1614 (s), 1339 (s);
mass spectrum (EI): m/e (%relative intensity) 229 (25) M^+, 189 (100);

For Compound **28**.
Rf = 0.32 (10% MeOH in EtOAc);
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, 3H, J = 7.3 Hz), 1.35-1.80 (m, 4H), 2.43 (m, 2H), 2.59 (m, 2H), 4.18 (m, 1H), 4.38 (d, 1H, J = 16.1 Hz), 4.67 (d, 1H, J = 16.1 Hz), 5.10 (dd, 1H, J = 4.4, 9.8 Hz), 6.37 (d, 1H, J = 9.8 Hz), 7.24-7.40 (m, 5H);
^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 16.7, 25.2, 33.9, 36.8, 51.2, 59.3, 110.1, 116.2, 118.5, 126.7, 128.0, 129.1, 135.4, 173.5, 196.8;
IR (neat) cm^{-1} 2956w, 2929s, 2870m, 1710w, 1656m, 1625s, 1586m, 1561s, 1495s, 1452m, 1408w, 1364m, 1311m, 1257w, 1234w, 1030w;
mass spectrum (EI): m/e (%relative intensity) 267 (5) M^+, 266 (15), 224 (100), 247 (9), 133 (3);