SUPPORTING INFORMATION

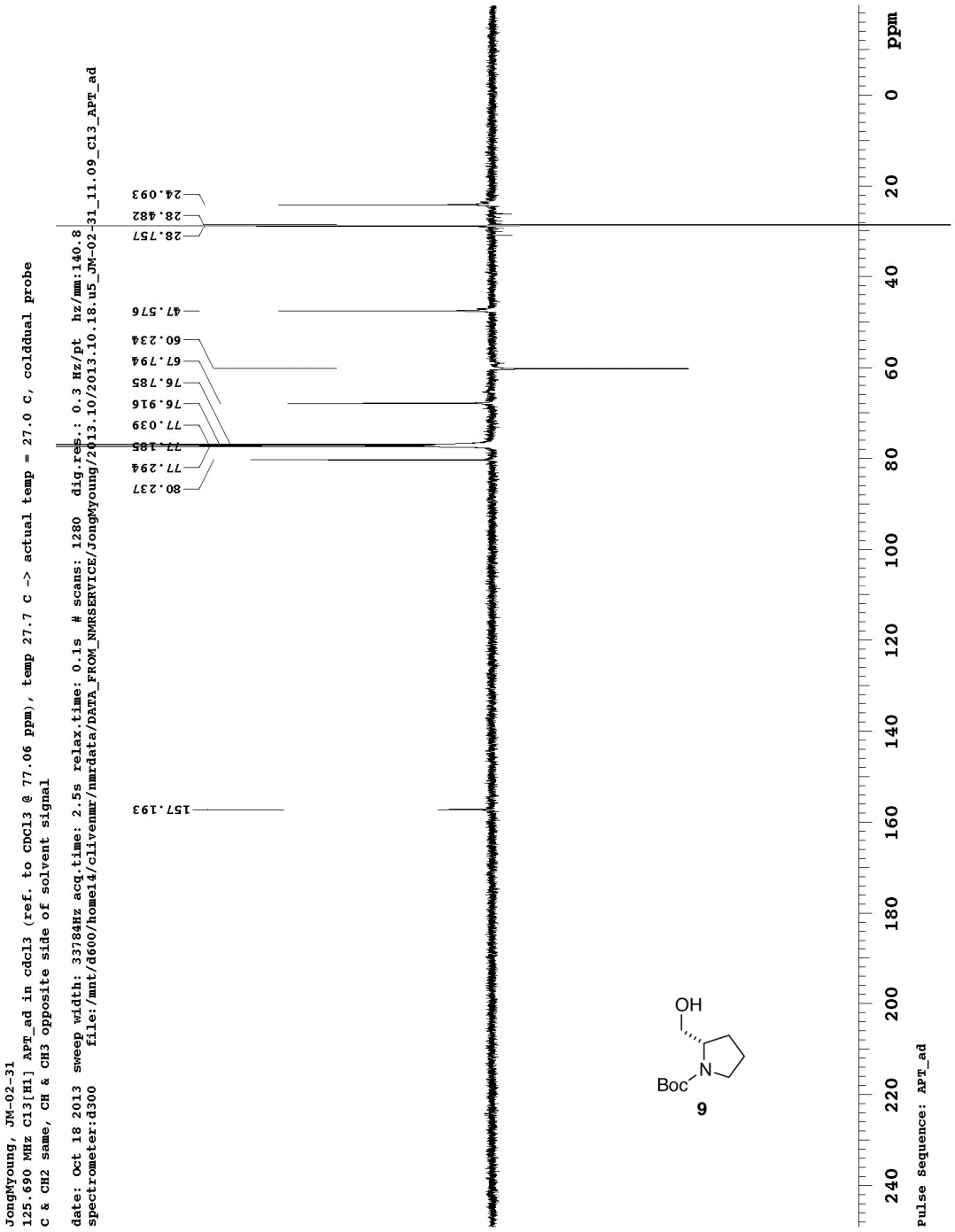
Synthesis of (+)-ipalbidine based on 6-*exo*-*trig* radical cyclization of a β-amino radical

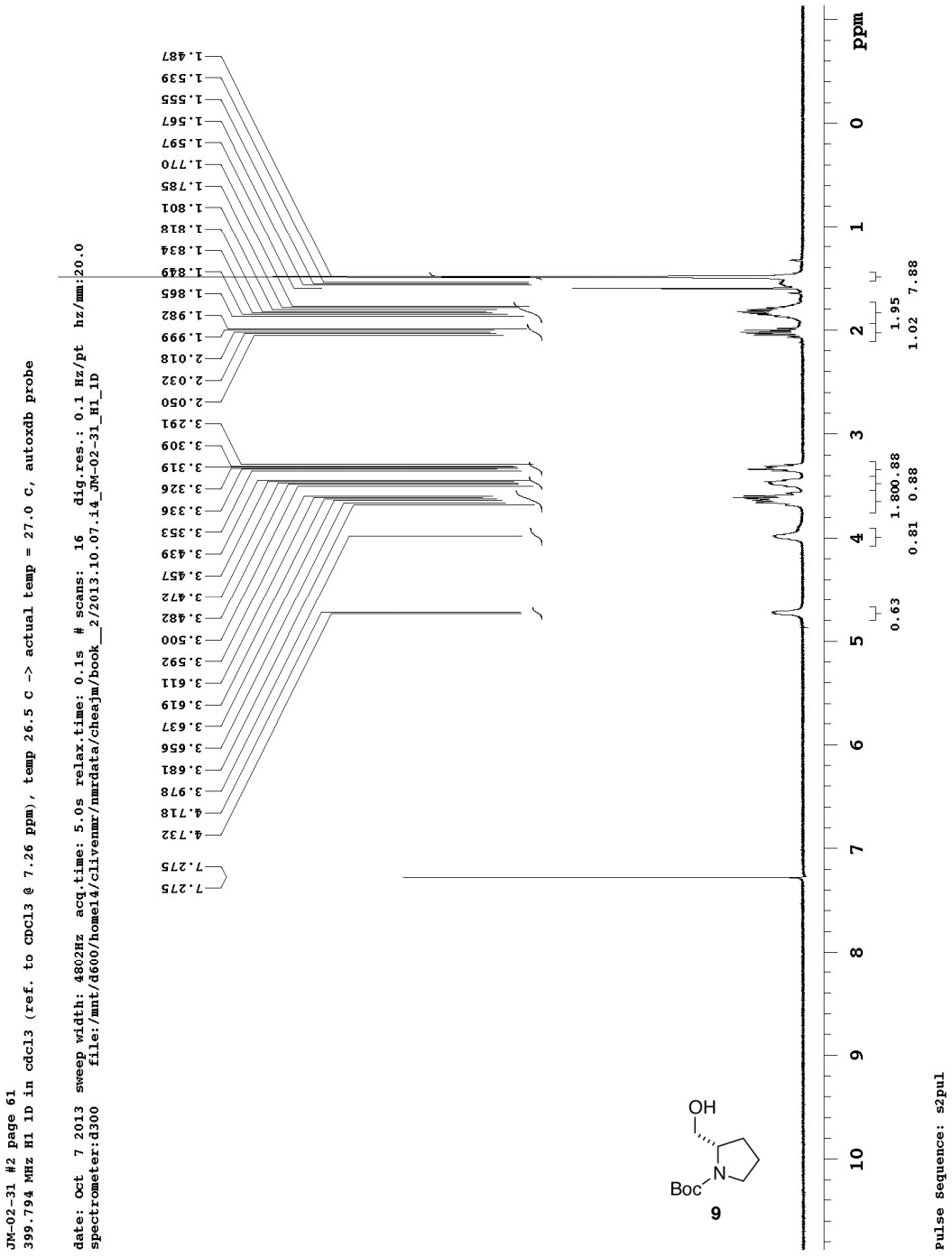
JongMyoung Chea and Derrick L. J. Clive*

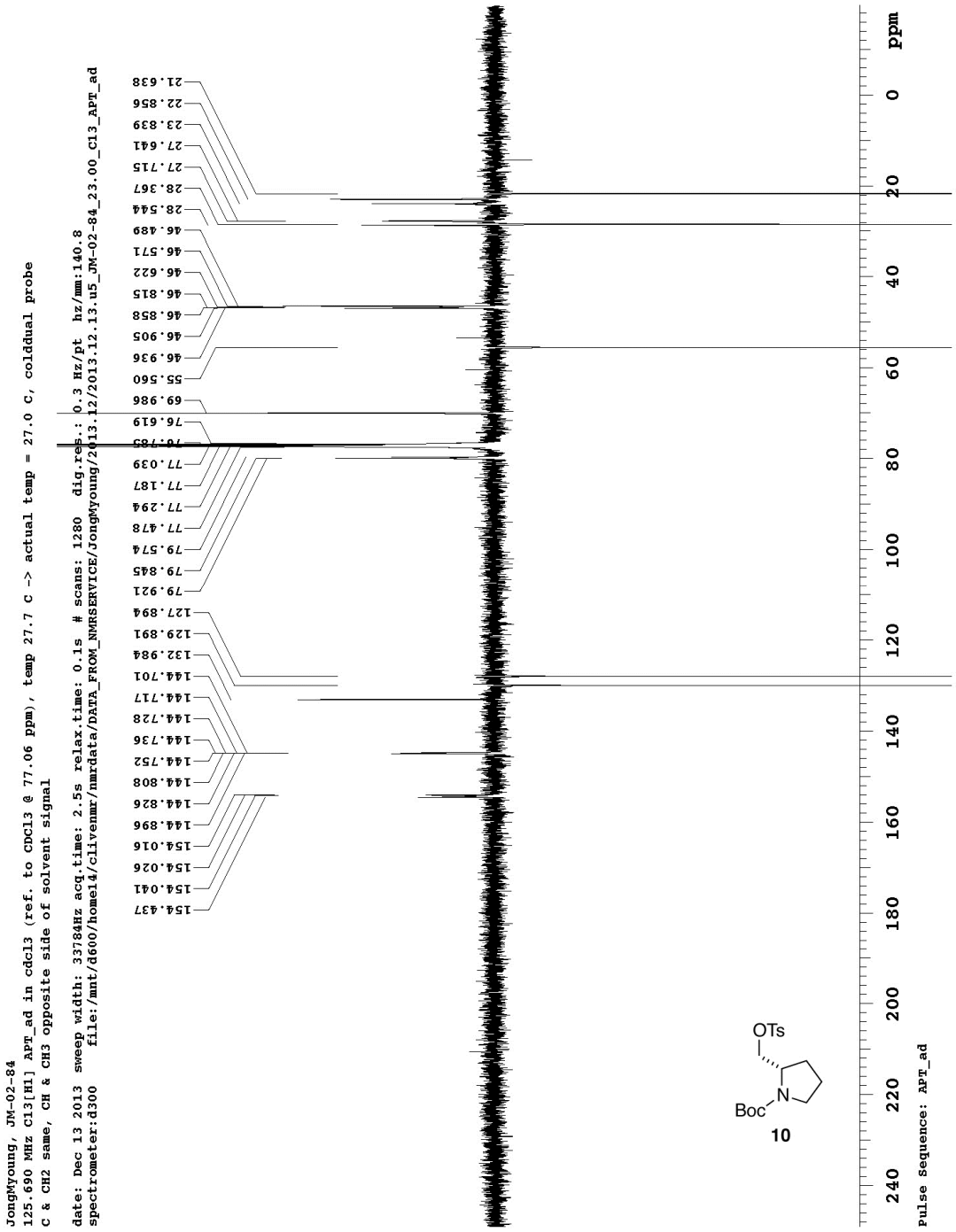
Chemistry Department, University of Alberta, Edmonton, Alberta T6G 2G2, Canada

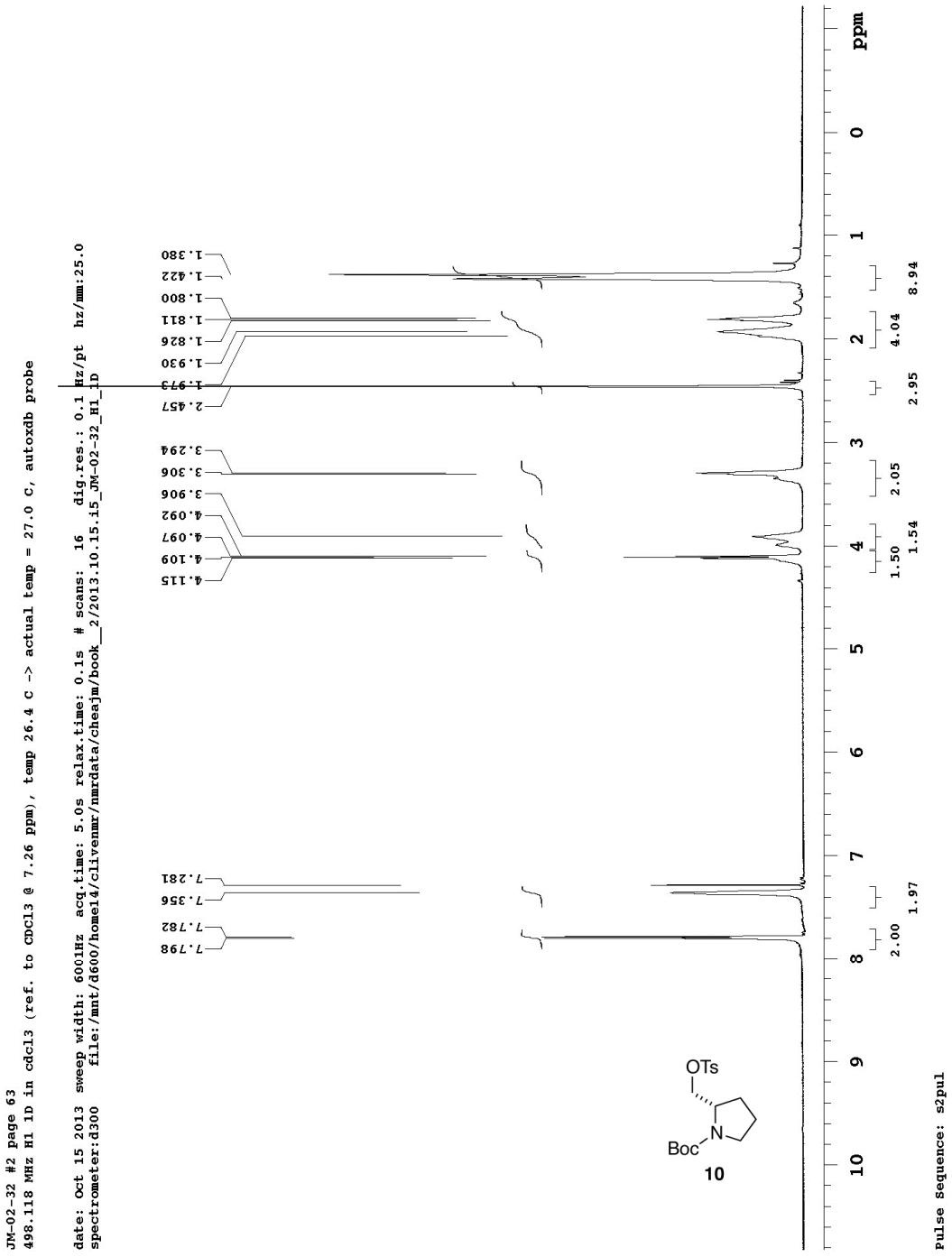
derrick.clive@ualberta.ca

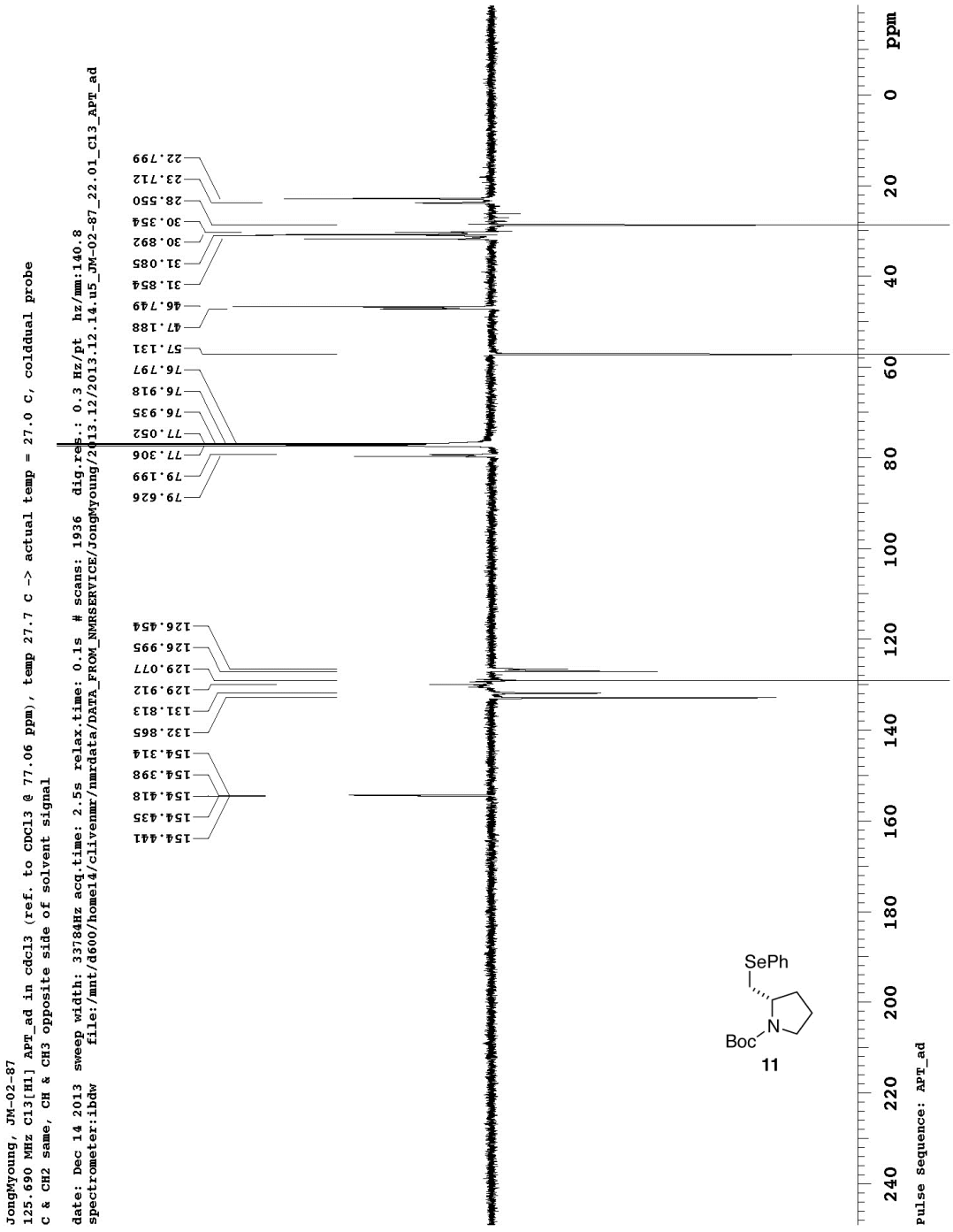
Syntheses of racemic ipalbidine, complete list of references: (a) Govindachari, T. R.; Sidhaye, A. R.; Viswanathan, N. *Tetrahedron* **1970**, *26*, 3829–3831. (b) Stevens, R. V.; Luh, Y. *Tetrahedron Lett.* **1977**, *18*, 979–982. (c) Hedges, S. H.; Herbert, R. B. *J. Chem. Research (S)* **1979**, 1. (d) Howard, A. S.; Gerrans, G. C.; Michael, J. P. *J. Org. Chem*. **1980**, *45*, 1713–1715. (e) Cragg, J. E.; Hedges, S. H.; Herbert, R. B. *Tetrahedron Lett.* **1981**, *22*, 2127–2130. (f) Iida, H.; Watanabe, Y.; Kibayashi, C. *J. Chem. Soc., Perkin Trans. 1* **1985**, 261–266; preliminary communication: Iida, H.; Watanabe, Y.; Kibayashi, C. *Chem. Lett*. **1983**, 1195–1196. (g) Danishefsky, S. J.; Vogel, C. *J. Org. Chem*. **1986**, *51*, 3915–3916. (h) Jefford, C. W.; Kubota, T.; Zaslona, A. *Helv. Chim. Acta* **1986**, *69*, 2048–2061. (i) Sheehan, S. M.; Padwa, A. *J. Org. Chem.* **1997**, *62*, 438–439. (j) Ikeda, M.; Shikaura, J.; Mackawa, N.; Daibuzono, K.; Teranishi, H.; Teraoka, Y.; Oda, N.; Ishibashi, H. *Heterocycles* **1999**, *50*, 31–34. (k) Padwa, A.; Sheehan, S. H.; Straub, C. S. *J. Org. Chem*. **1999**, *64*, 8648–8659.

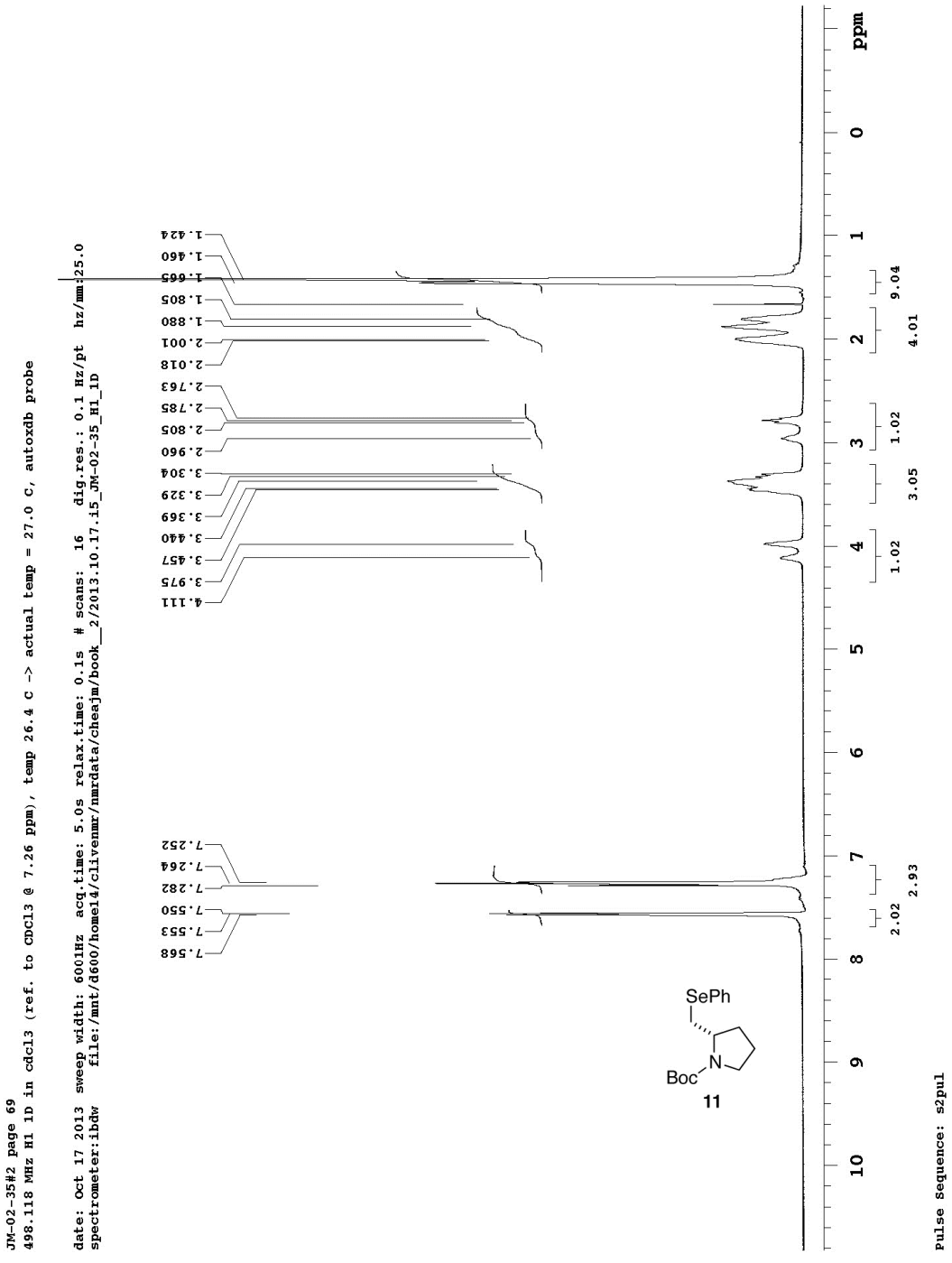

JongMyoung, JM-02-31
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Oct 18 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1280 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:d300 file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.10/2013.10.18.u5_JM-02-31_11.09_C13_APT_ad
157.193
80.237
77.294
77.185
77.039
76.916
76.785
67.794
60.234
47.576
28.757
28.482
24.093
OH
N
Boc
9
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad

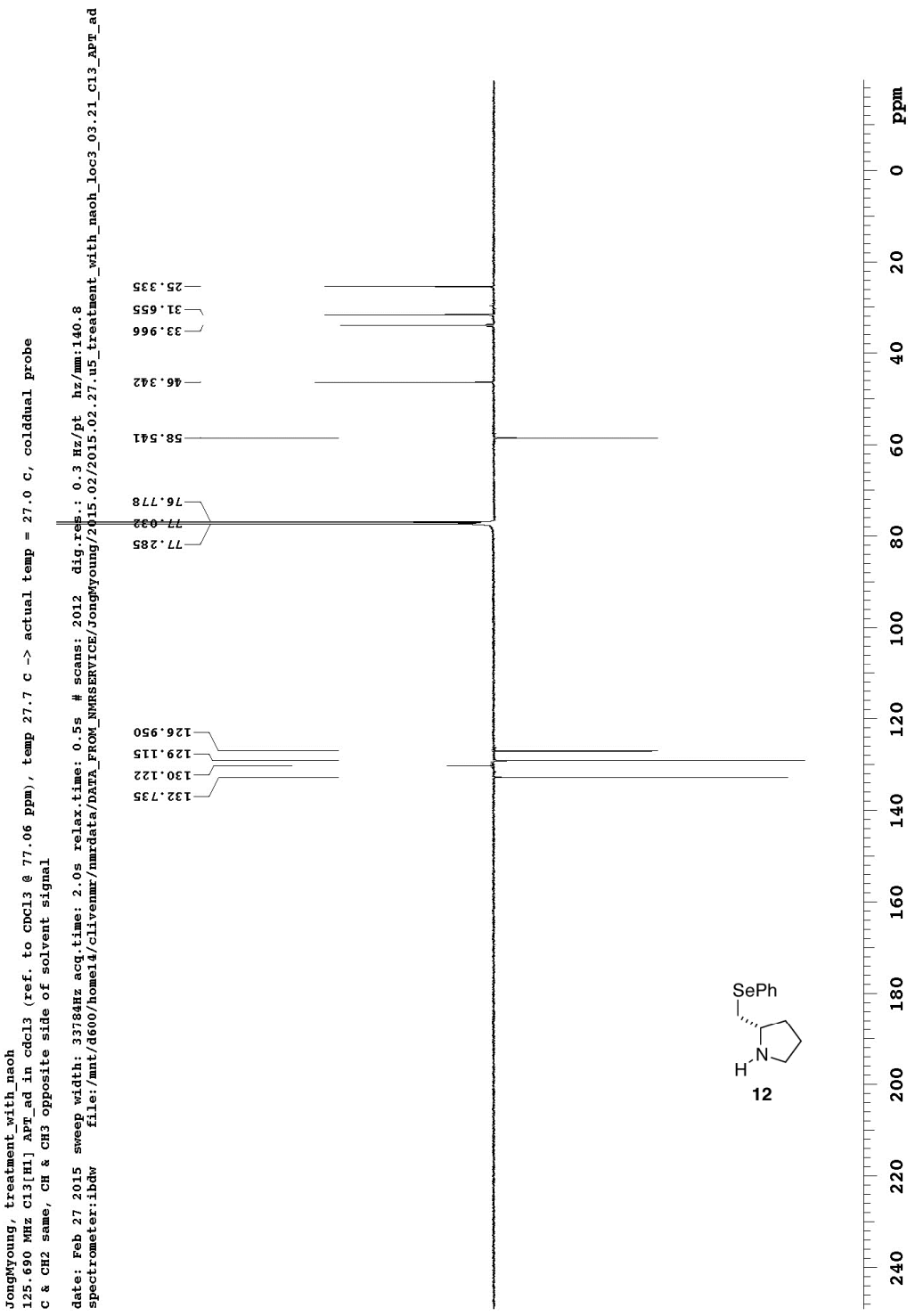

JM-02-31 #2 page 61
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Oct 7 2013 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0
spectrometer:d300 file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.10.07.i4_JM-02-31_H1_1D
7.275
7.275
4.732
4.718
3.978
3.681
3.656
3.637
3.619
3.611
3.592
3.500
3.482
3.472
3.457
3.439
3.353
3.336
3.326
3.319
3.309
3.291
2.050
2.032
2.018
1.999
1.982
1.865
1.849
1.834
1.818
1.801
1.785
1.770
1.597
1.567
1.555
1.539
1.487
0.63
1.800.88
0.81 0.88
1.95
1.02 7.88
ppm
OH
N
Boc
9
Pulse Sequence: s2pul

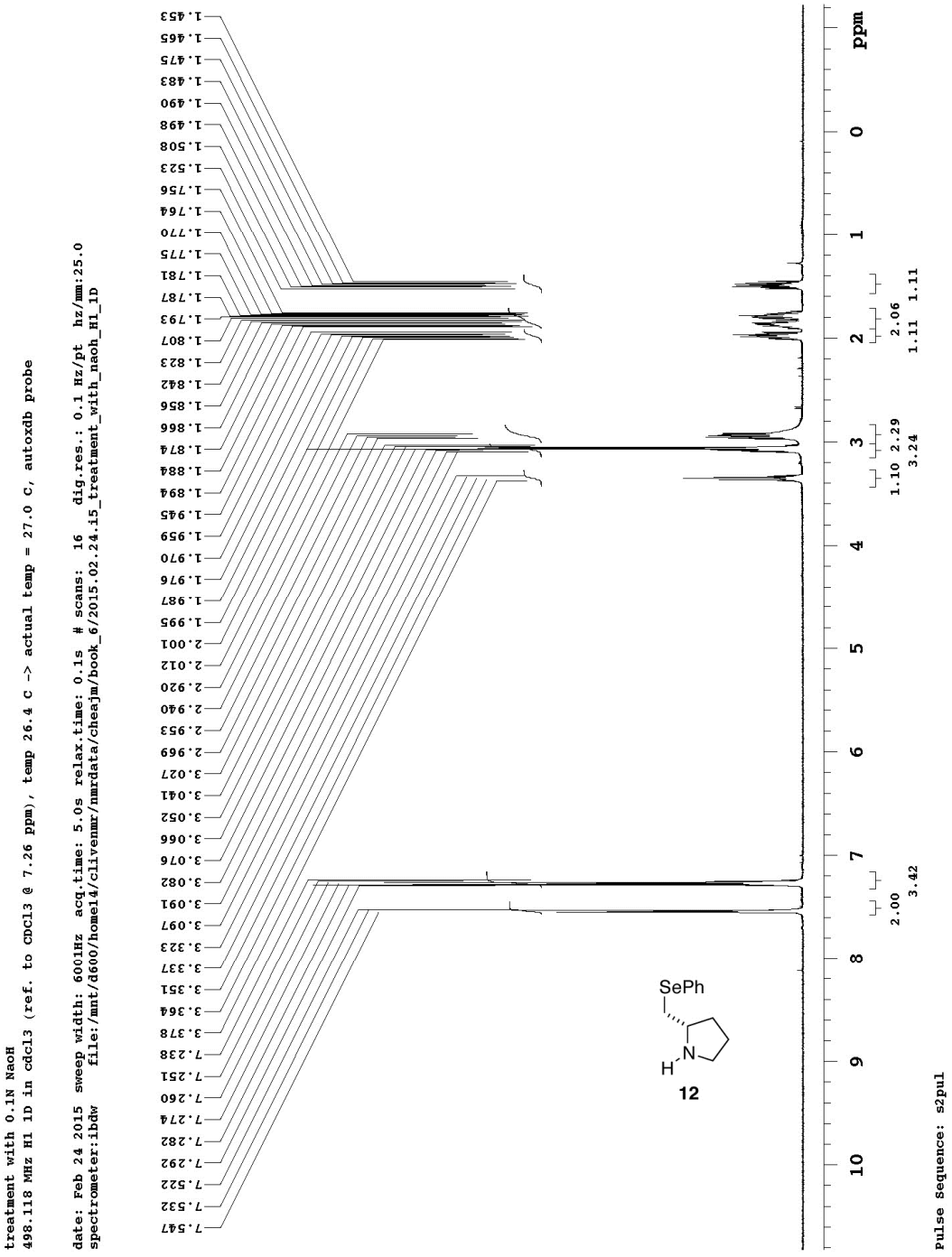

JongMyoung, JM-02-84
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Dec 13 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1280 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:d300 file:/mnt/d600/homel4/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.12/2013.12.13.u5_JM-02-84_23.00_C13_APT_ad
154.437
154.041
154.026
154.016
144.896
144.826
144.808
144.752
144.736
144.728
144.717
144.701
132.984
129.891
127.894
79.921
79.845
79.574
77.478
77.294
77.187
77.039
76.785
76.619
69.986
55.560
46.936
46.905
46.858
46.815
46.622
46.571
46.489
28.544
28.367
27.715
27.641
23.839
22.856
21.638
ppm
Pulse Sequence: APT_ad
OTs
N
Boc
10

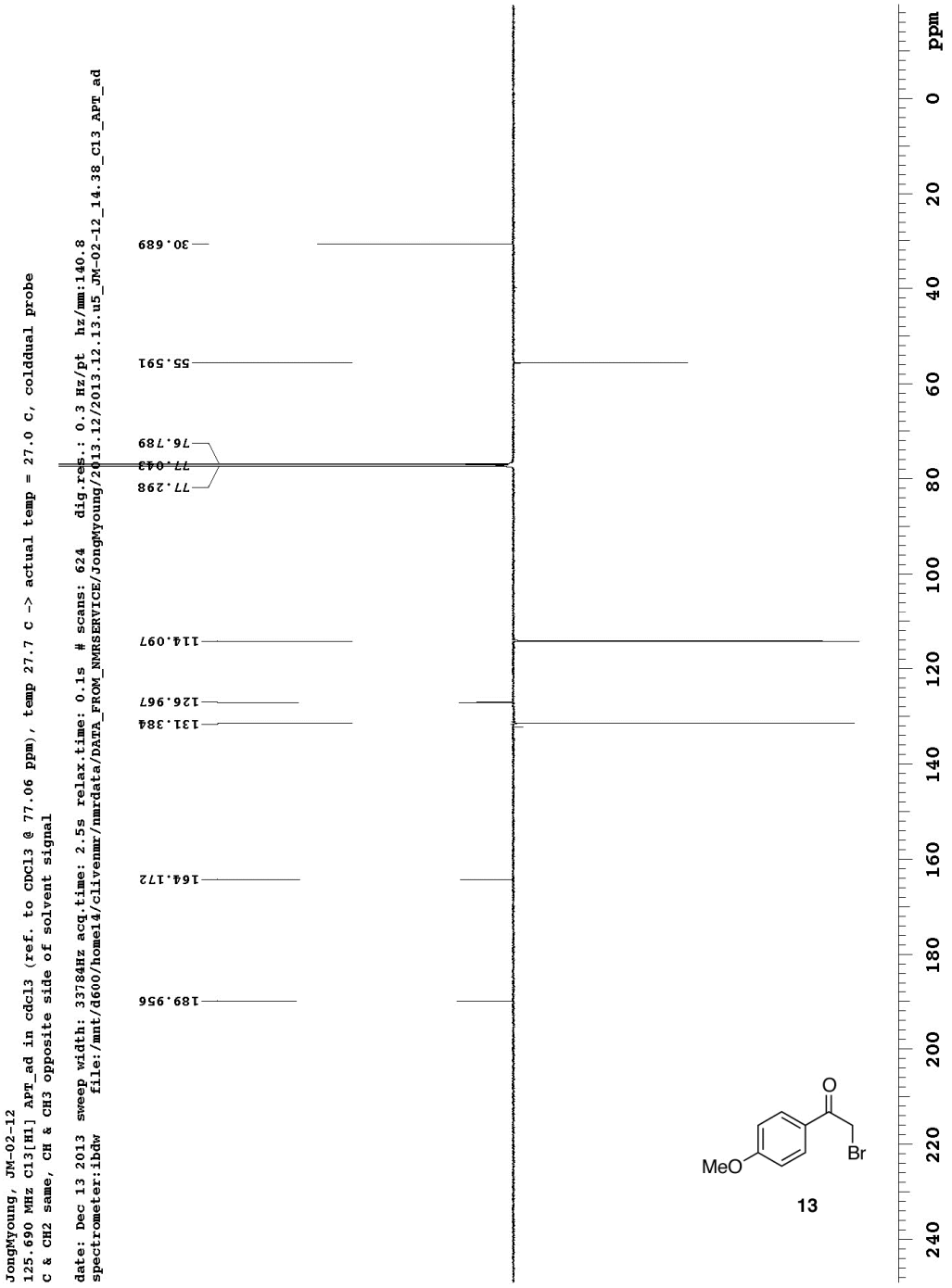

JM-02-32 #2 page 63
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Oct 15 2013 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:d300 file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.10.15.15_JM-02-32_H1_1D
7.798
7.782
7.356
7.281
4.115
4.109
4.097
4.092
3.906
3.306
3.294
2.457
1.973
1.930
1.826
1.811
1.800
1.422
1.380
ppm
OTs
N
Boc
10
Pulse Sequence: s2pul

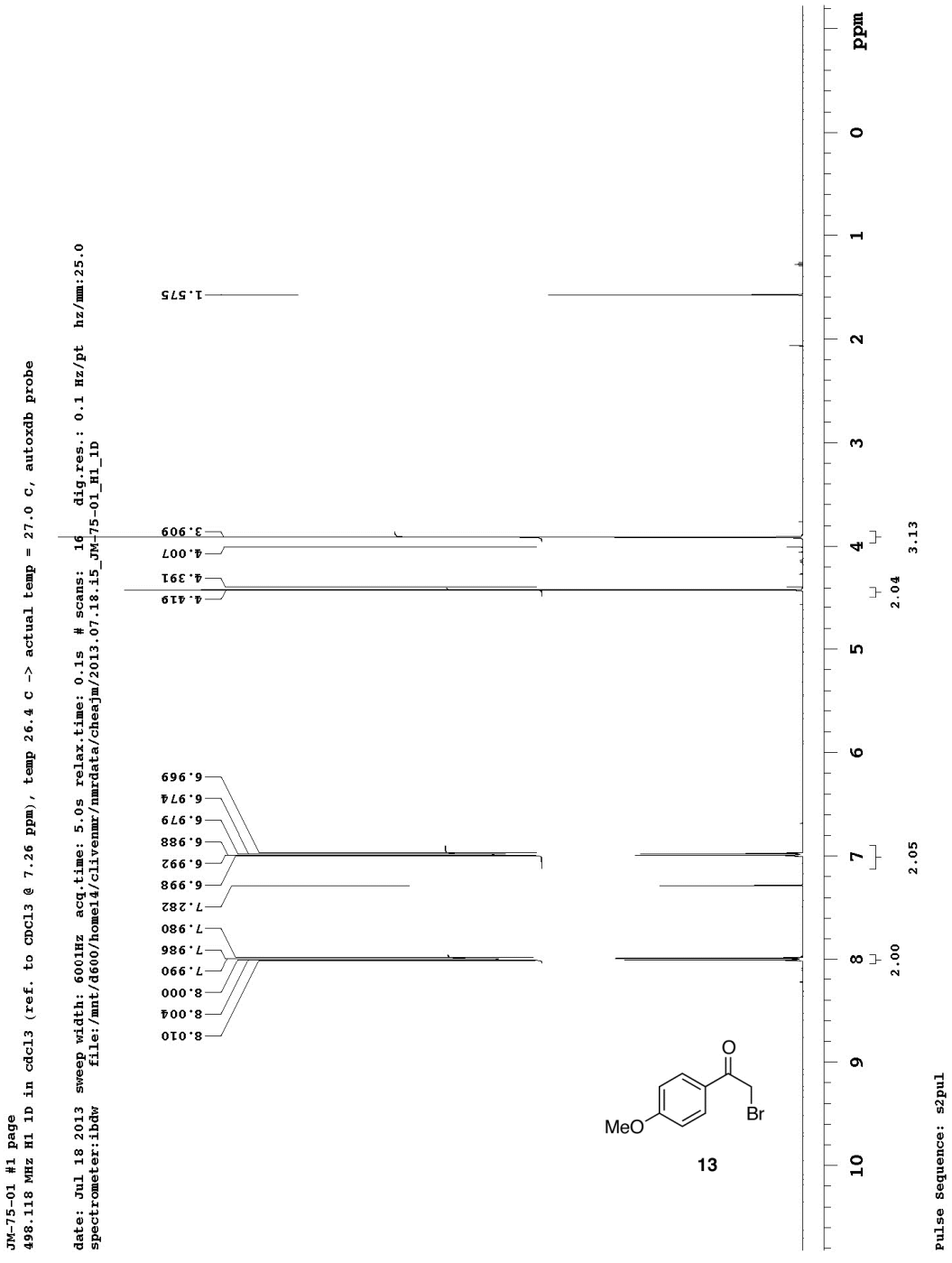

JongMyoung, JM-02-87
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Dec 14 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1936 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.12/2013.12.14.u5_JM-02-87_22.01_C13_APT_ad
22.799
23.712
28.550
30.354
30.892
31.085
31.854
46.749
47.188
57.131
76.797
76.918
76.935
77.052
77.306
79.199
79.626
126.454
126.995
129.077
129.912
131.813
132.865
154.314
154.398
154.418
154.435
154.441
SePh
N
Boc
11
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad

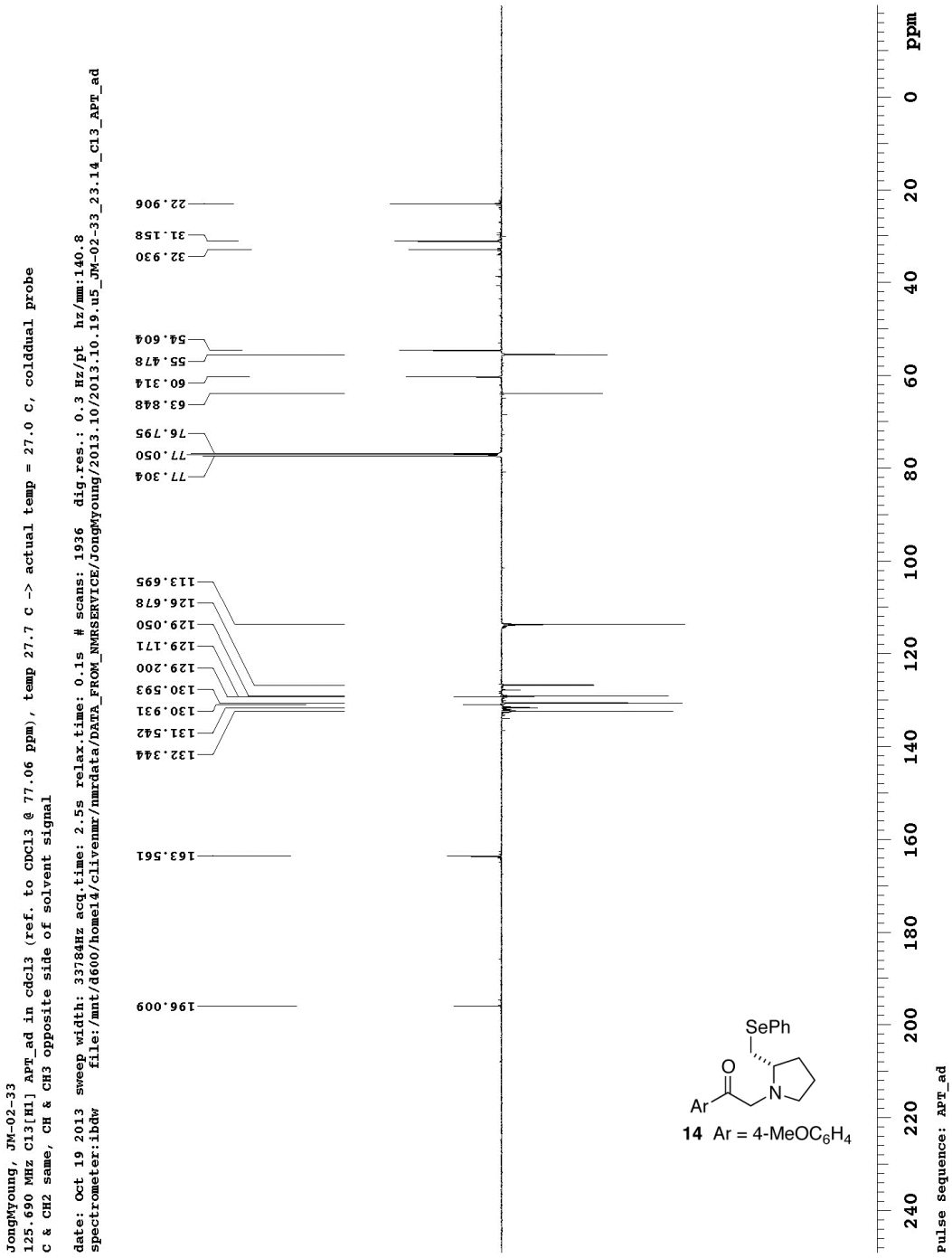

JM-02-35#2 page 69
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Oct 17 2013 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.10.17.15_JM-02-35_H1_1D
7.568
7.553
7.550
7.282
7.264
7.252
4.111
3.975
3.457
3.440
3.369
3.329
3.304
2.960
2.805
2.785
2.763
2.018
2.001
1.880
1.805
1.665
1.460
1.424
SePh
N
Boc
11
ppm
2.02
2.93
1.02
3.05
1.02
4.01
9.04
Pulse Sequence: s2pul

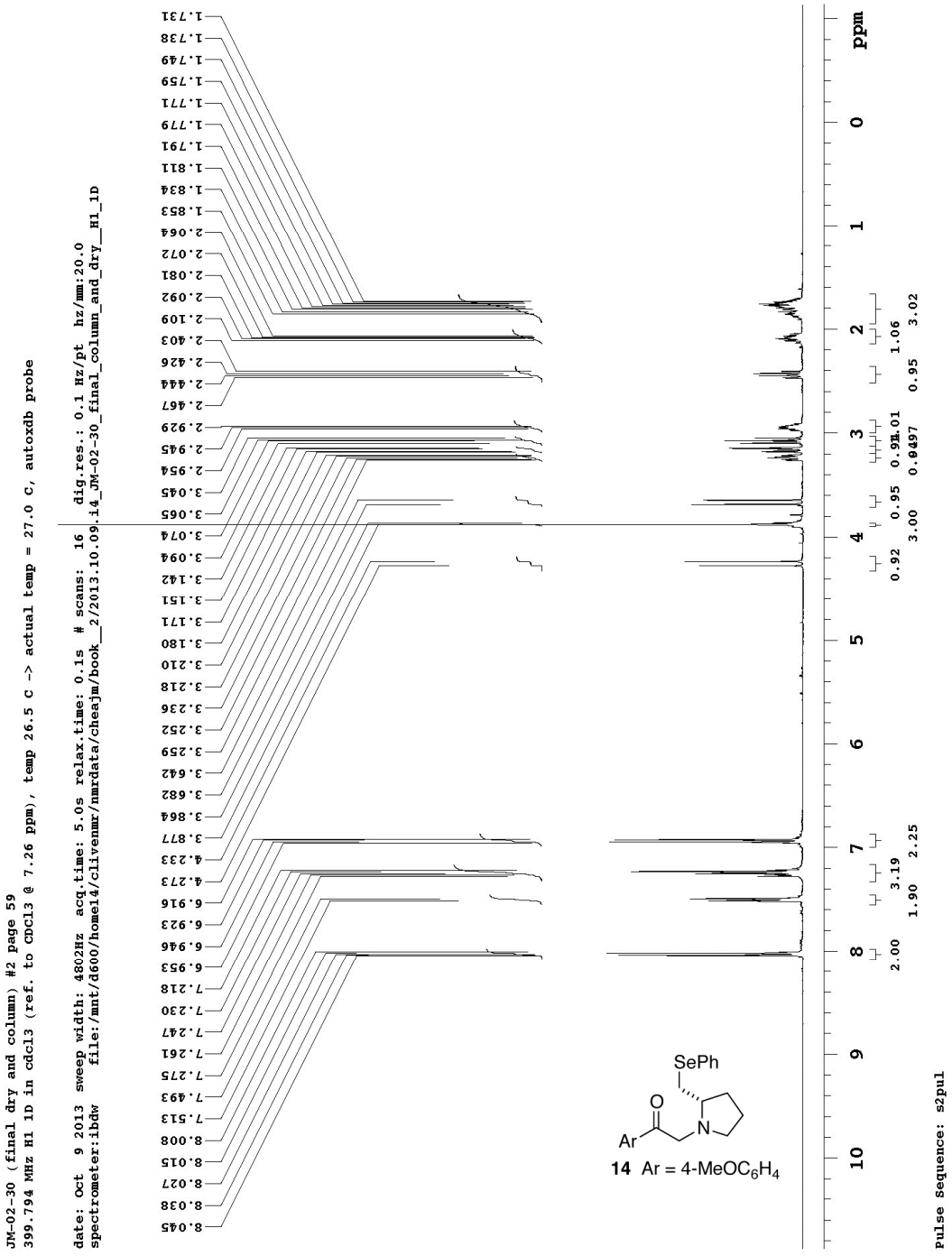

JongMyoung, treatment_with_naoh
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Feb 27 2015 sweep width: 33784Hz acq.time: 2.0s relax.time: 0.5s # scans: 2012 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2015.02/2015.02.27.u5_treatment_with_naoh_loc3_03.21_C13_APT_ad
25.335
31.655
33.966
46.342
58.541
76.778
77.032
77.285
126.950
129.115
130.122
132.735
SePh
N
H
12
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm
Pulse Sequence: APT_ad

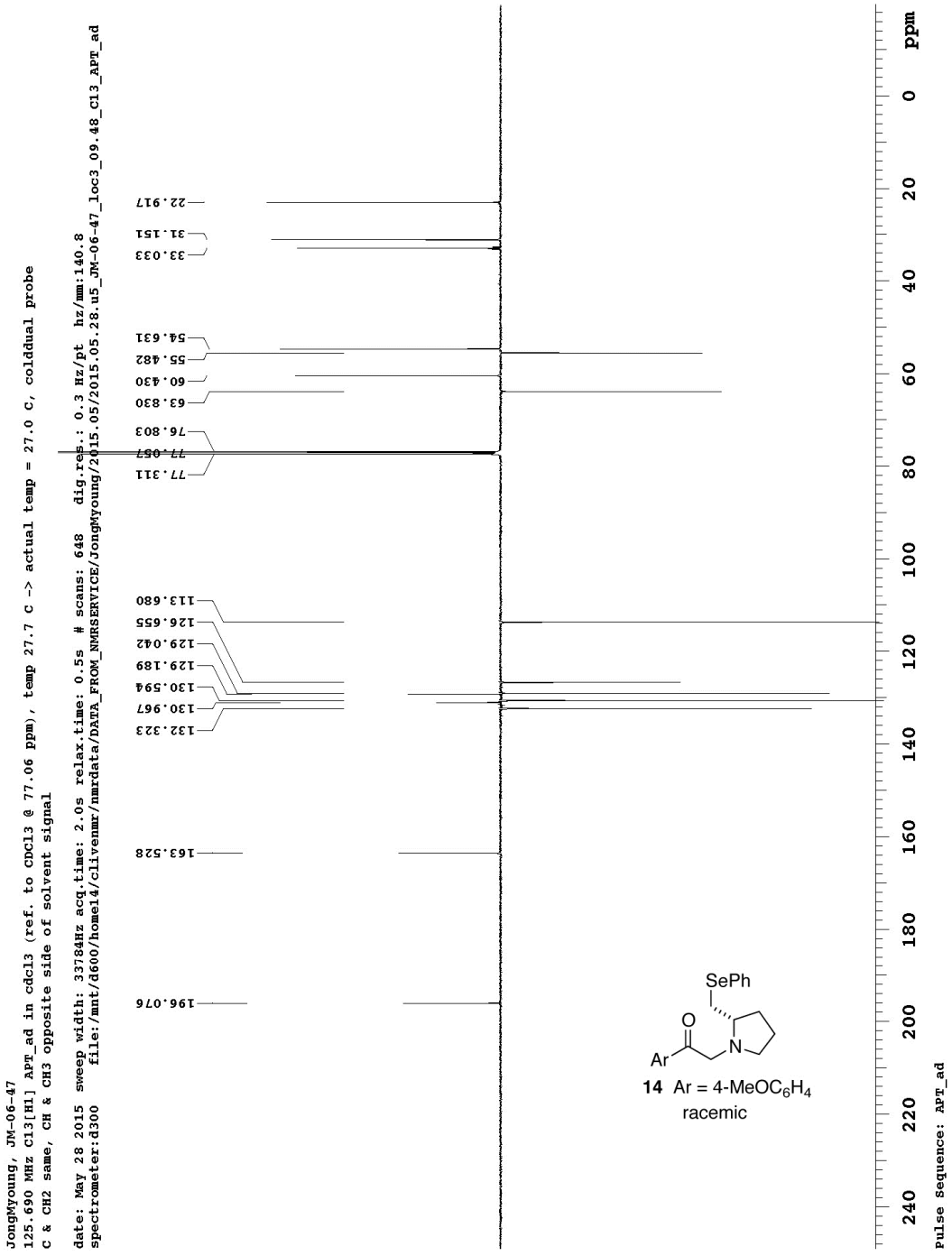

treatment with 0.1N NaoH
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Feb 24 2015 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book_6/2015.02.24.i5_treatment_with_naoh_H1_1D
SePh
H
N
12
ppm
2.00
3.42
1.10 2.29
3.24
2.06
1.11 1.11
Pulse Sequence: s2pul

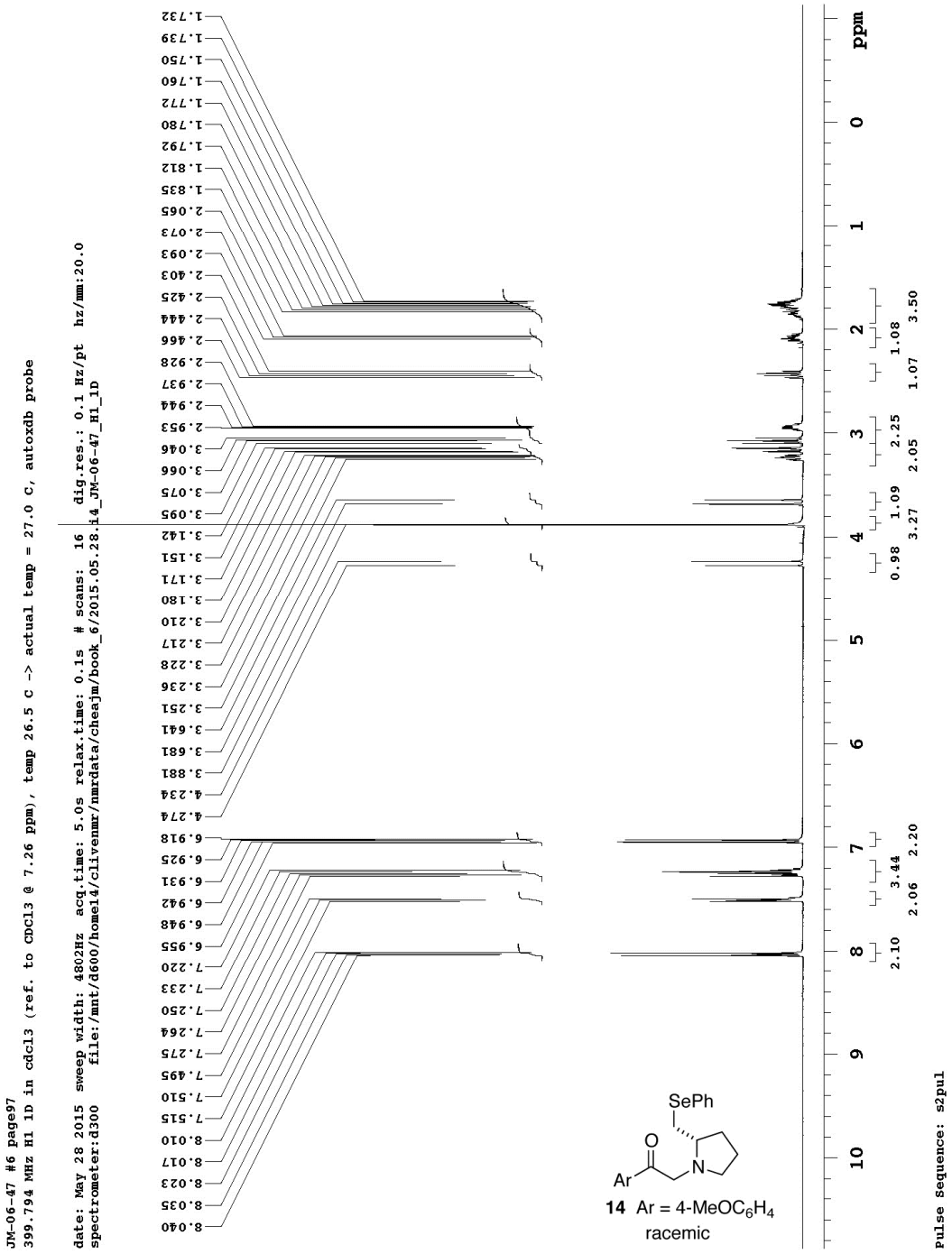

JongMyoung, JM-02-12
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Dec 13 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 624 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.12/2013.12.13.u5_JM-02-12_14.38_C13_APT_ad
30.689
55.591
76.789
77.043
77.298
114.097
126.967
131.384
164.172
189.956
MeO
Br
O
13
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad

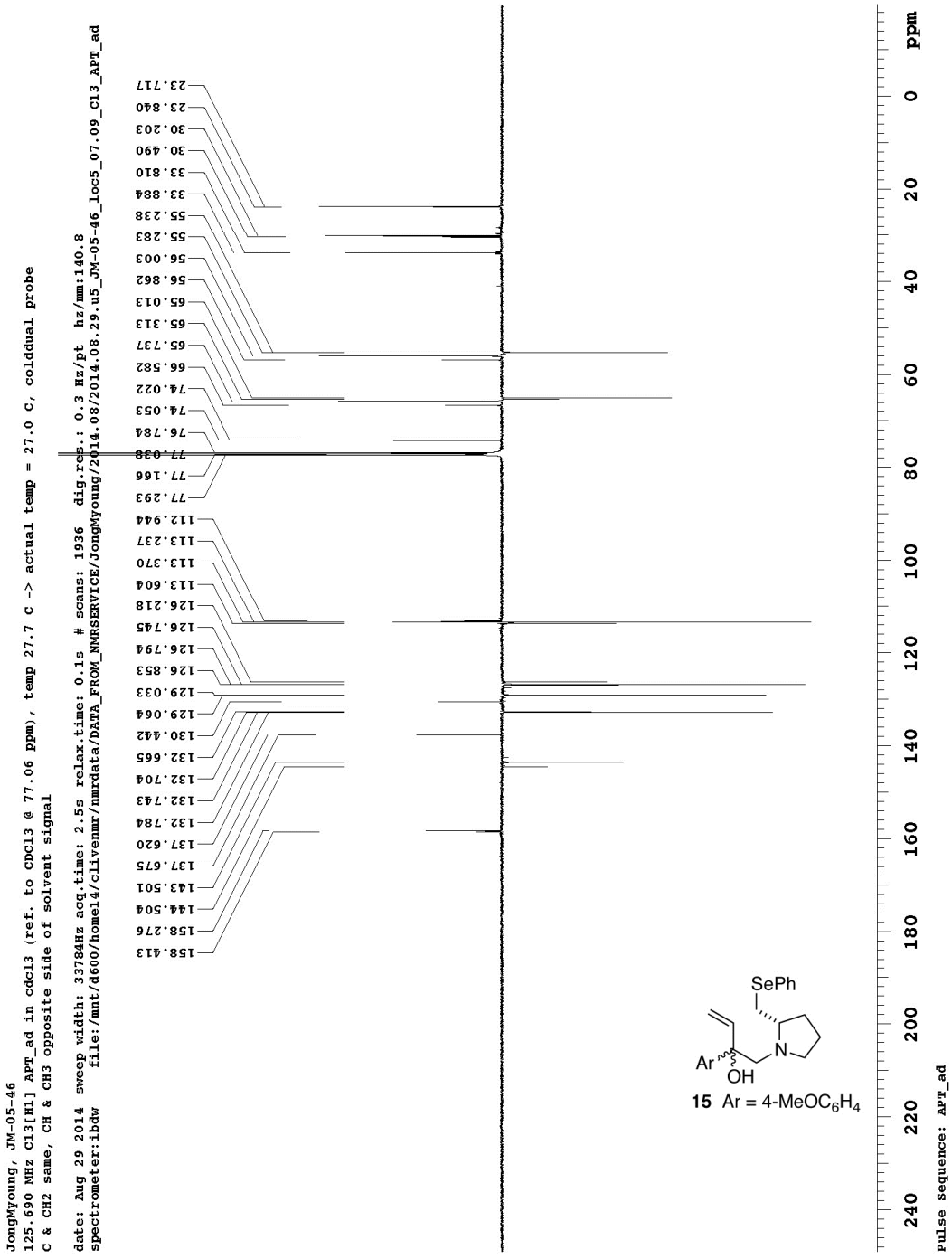

JM-75-01 #1 page
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Jul 18 2013 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/2013.07.18.i5_JM-75-01_H1_1D
1.575
3.909
4.007
4.391
4.419
6.969
6.974
6.979
6.988
6.992
6.998
7.282
7.980
7.986
7.990
8.000
8.004
8.010
2.00
2.05
2.04
3.13
MeO
Br
O
13
ppm
Pulse Sequence: s2pul

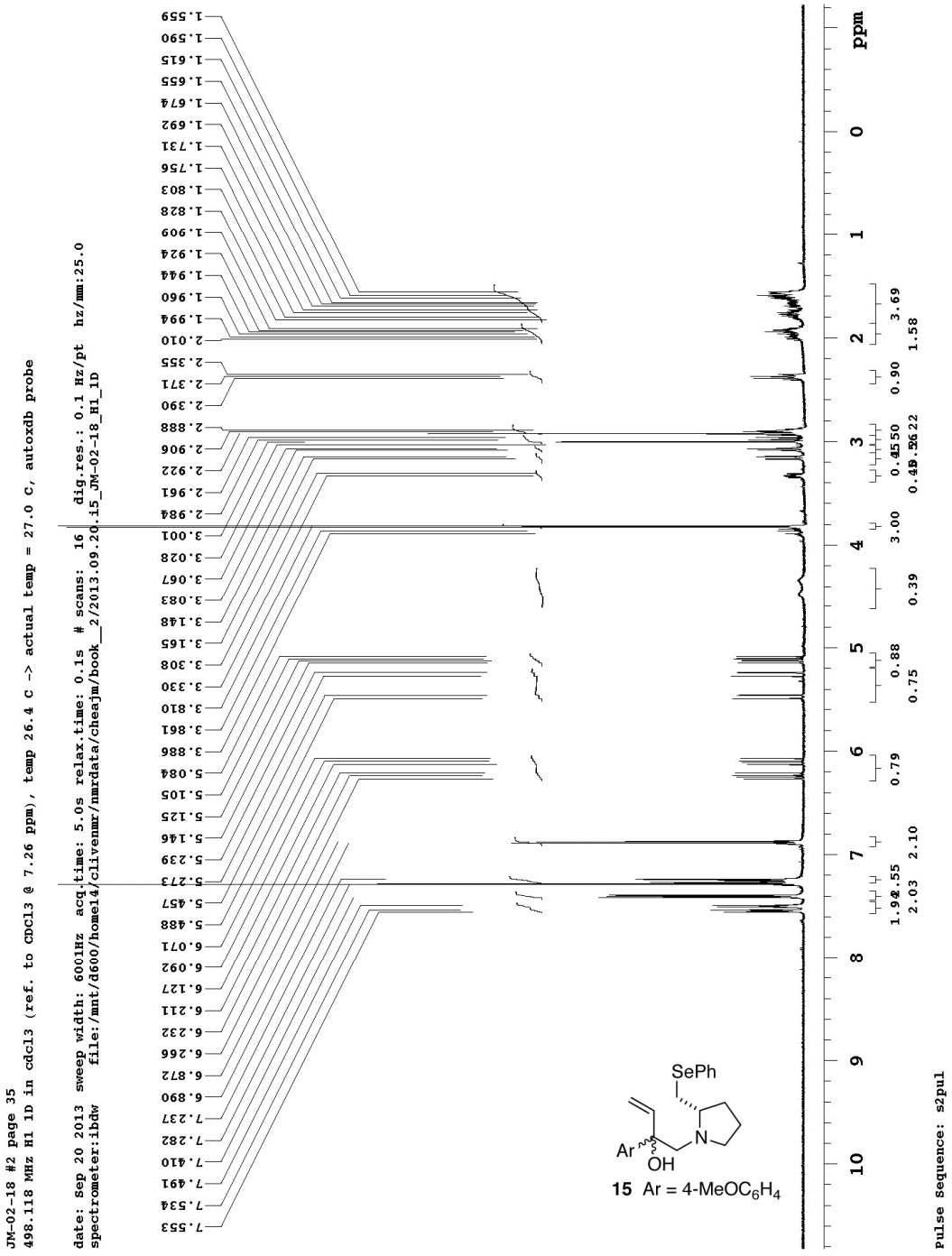

JongMyoung, JM-02-33
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Oct 19 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1936 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.10/2013.10.19.u5_JM-02-33_23.14_C13_APT_ad
22.906
31.158
32.930
54.604
55.478
60.314
63.848
76.795
77.050
77.304
113.695
126.678
129.050
129.171
129.200
130.593
130.931
131.542
132.344
163.561
196.009
SePh
O
Ar
N
14 Ar = 4-MeOC6H4
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm
Pulse Sequence: APT_ad

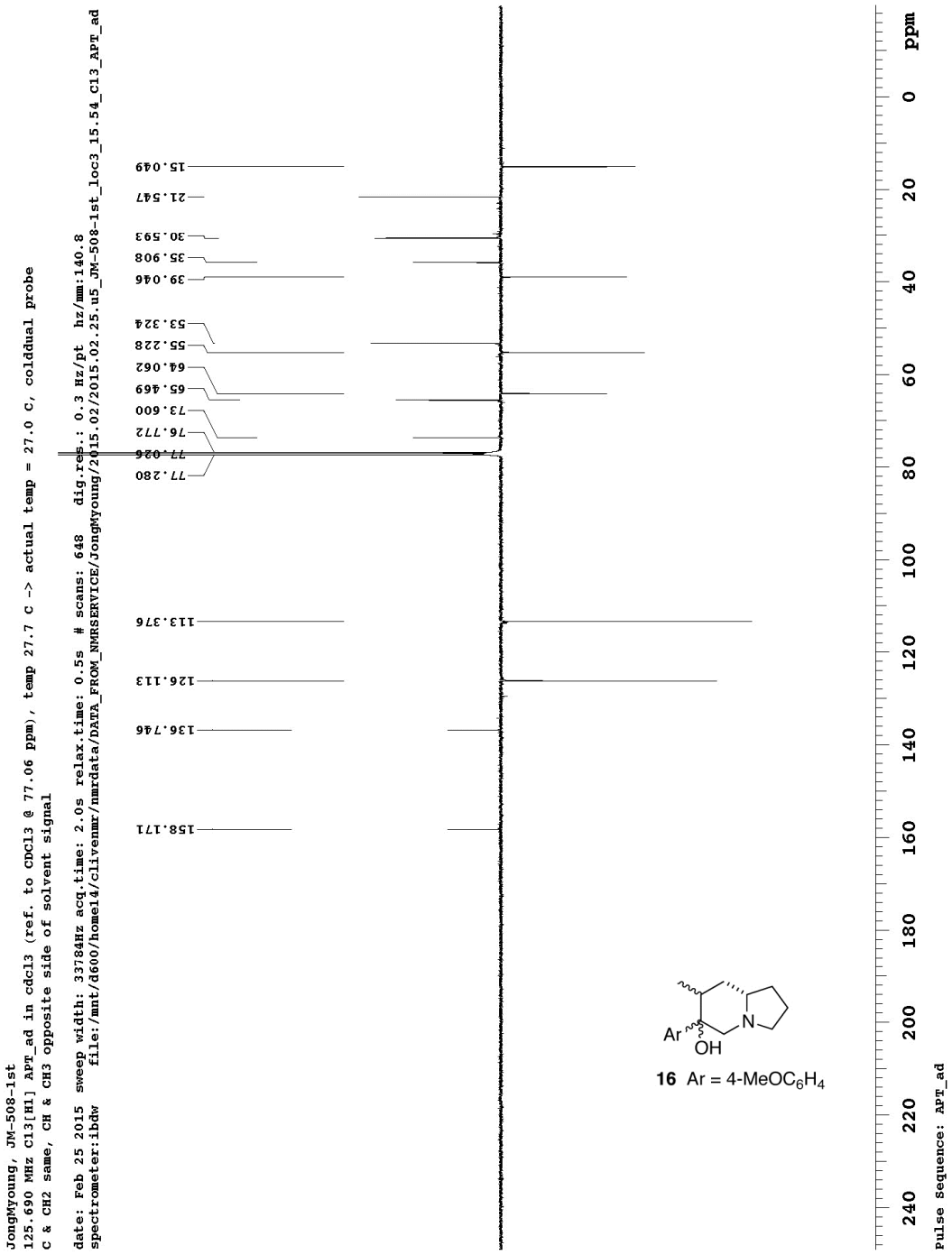

JM-02-30 (final dry and column) #2 page 59
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Oct 9 2013 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.10.09.14_JM-02-30_final_column_and_dry__H1_1D
8.045
8.038
8.027
8.015
8.008
7.513
7.493
7.275
7.261
7.247
7.230
7.218
6.953
6.946
6.923
6.916
4.273
4.233
3.877
3.864
3.682
3.642
3.259
3.252
3.236
3.218
3.210
3.180
3.171
3.151
3.142
3.094
3.074
3.065
3.045
2.954
2.945
2.929
2.467
2.444
2.426
2.403
2.109
2.092
2.081
2.072
2.064
1.853
1.834
1.811
1.791
1.779
1.771
1.759
1.749
1.738
1.731
SePh
O
Ar
N
14 Ar = 4-MeOC6H4
ppm
10
9
8
7
6
5
4
3
2
1
0
2.00
3.19
1.90
2.25
0.92
0.95
3.00
1.01
0.97
0.95
1.06
3.02
Pulse Sequence: s2pul

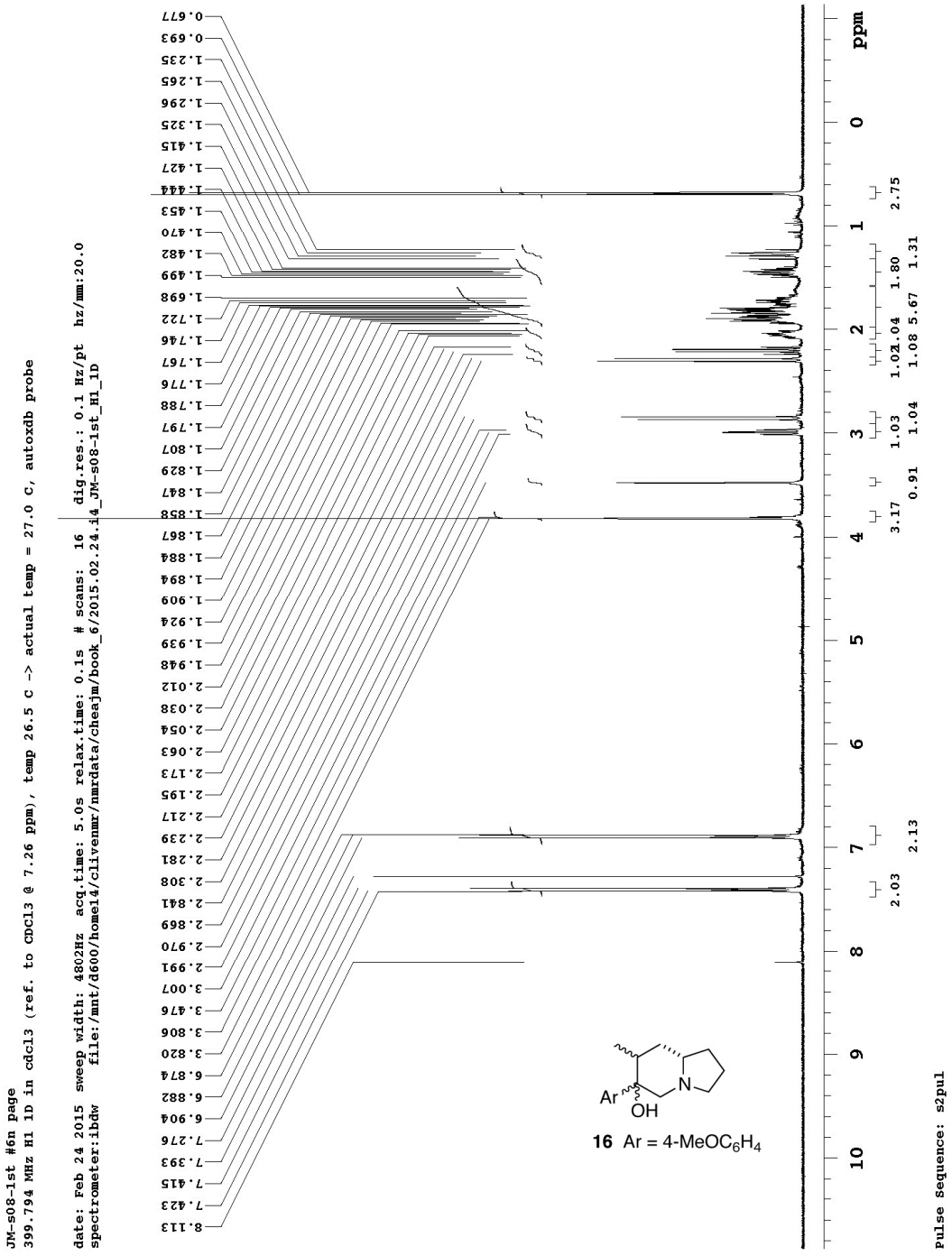

JongMyoung, JM-06-47
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: May 28 2015 sweep width: 33784Hz acq.time: 2.0s relax.time: 0.5s # scans: 648 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:d300 file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2015.05/2015.05.28.u5_JM-06-47_loc3_09.48_C13_APT_ad
22.917
31.151
33.033
54.631
55.482
60.430
63.830
76.803
77.057
77.311
113.680
126.655
129.042
129.189
130.594
130.967
132.323
163.528
196.076
SePh
O
N
Ar
14 Ar = 4-MeOC6H4
racemic
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad

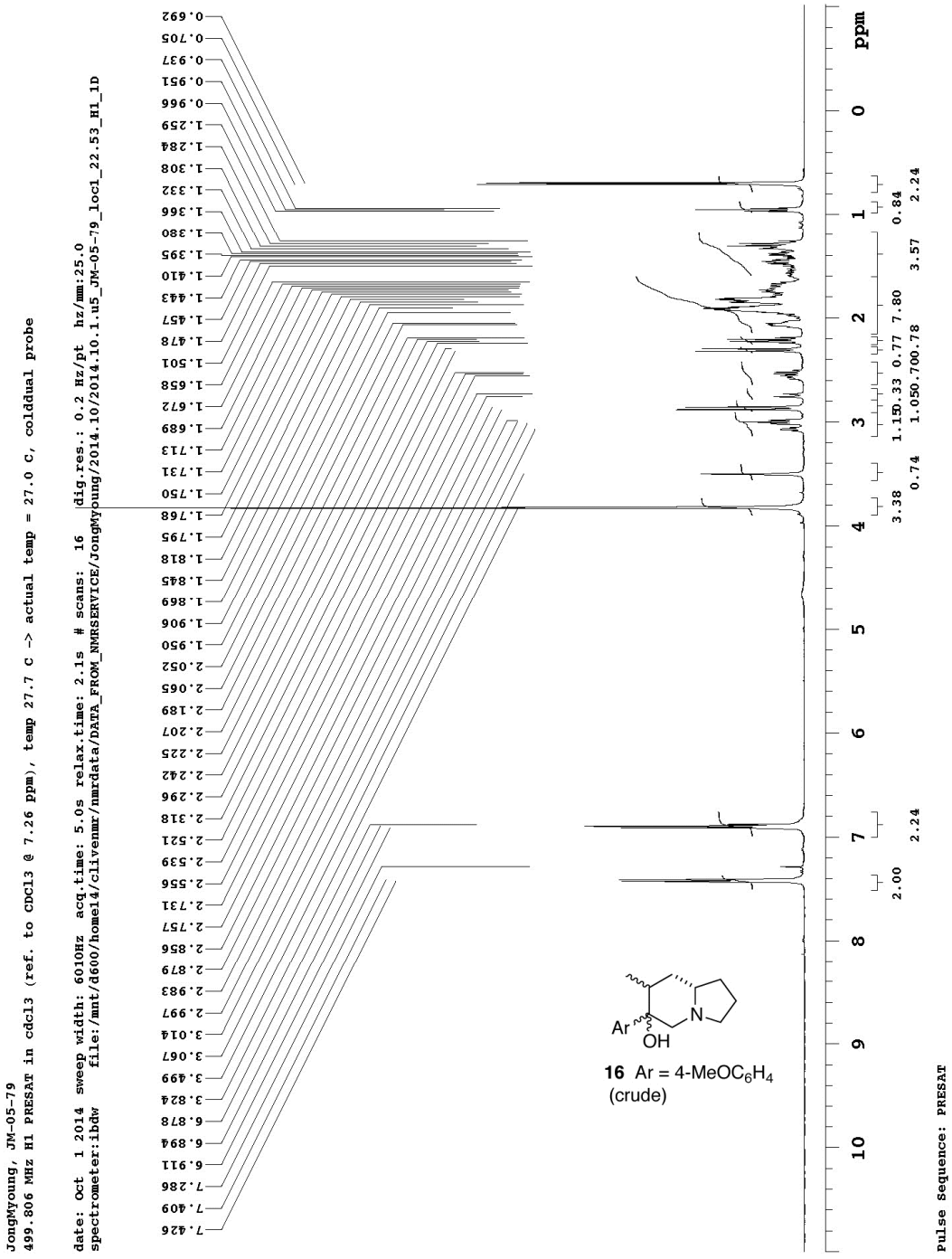

JM-06-47 #6 page97
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: May 28 2015 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0
spectrometer:d300 file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book_6/2015.05.28.i4_JM-06-47_H1_1D
SePh
O
Ar
N
14 Ar = 4-MeOC6H4
racemic
ppm
Pulse Sequence: s2pul

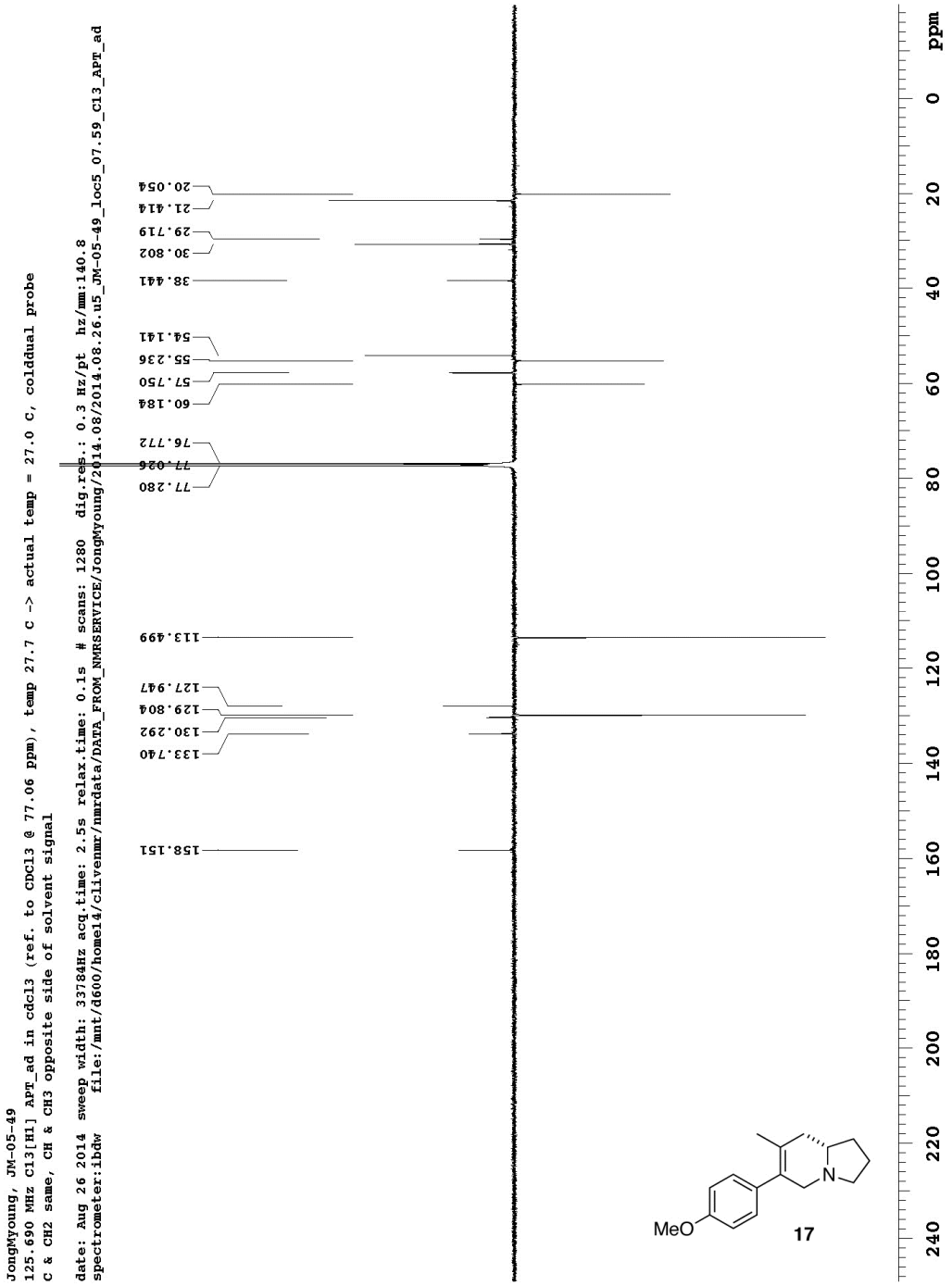

JongMyoung, JM-05-46
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Aug 29 2014 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1936 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2014.08/2014.08.29.u5_JM-05-46_loc5_07.09_C13_APT_ad
158.413
158.276
144.504
143.501
137.675
137.620
132.784
132.743
132.704
132.665
130.442
129.064
129.033
126.853
126.794
126.745
126.218
113.604
113.370
113.237
112.944
77.293
77.166
77.038
76.784
74.053
74.022
66.582
65.737
65.313
65.013
56.862
56.003
55.283
55.238
33.884
33.810
30.490
30.203
23.840
23.717
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm
Pulse Sequence: APT_ad
SePh
N
Ar
OH
15 Ar = 4-MeOC6H4

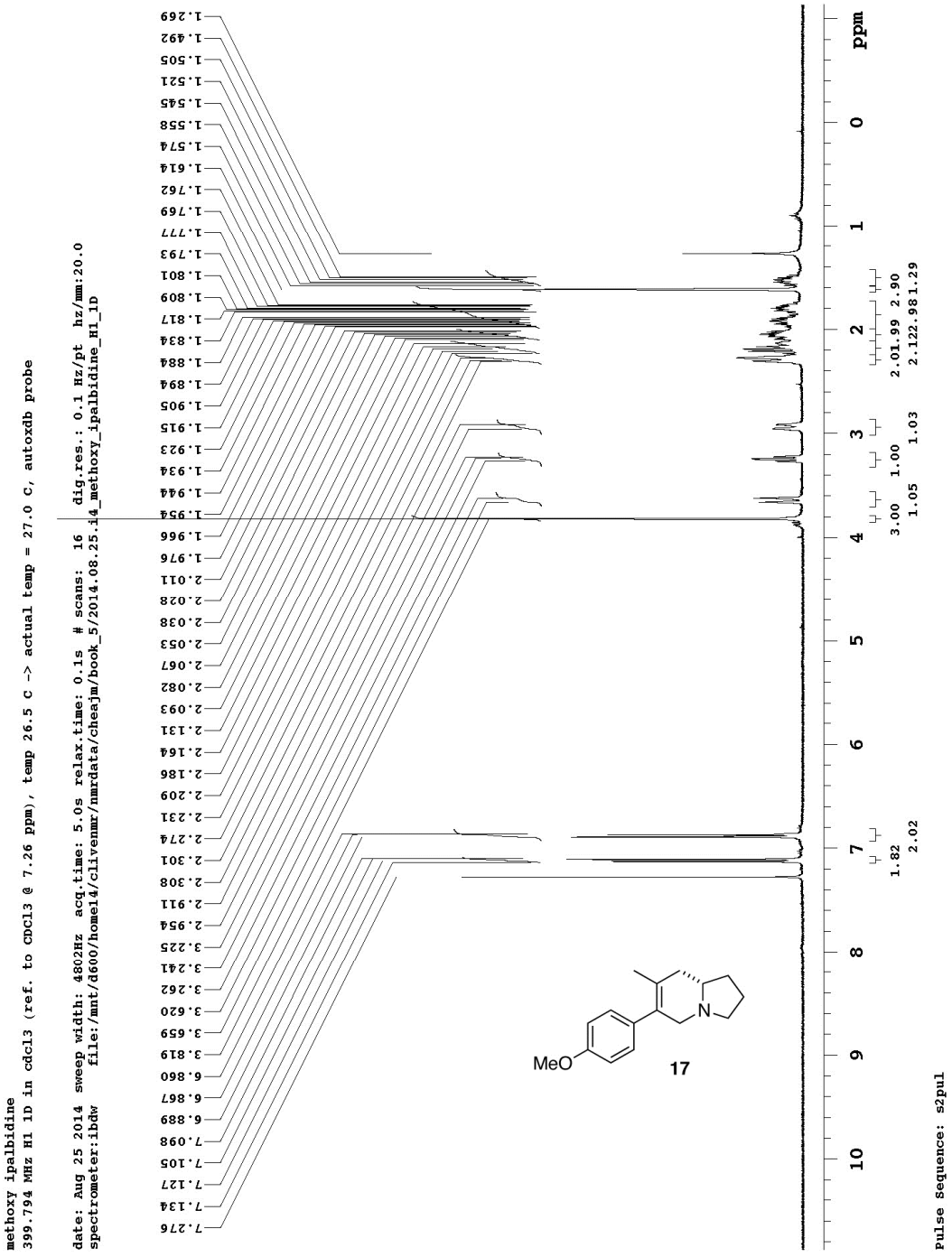

JM-02-18 #2 page 35
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Sep 20 2013 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.09.20.15_JM-02-18_H1_1D
7.553
7.534
7.491
7.410
7.282
7.237
6.890
6.872
6.266
6.232
6.211
6.127
6.092
6.071
5.488
5.457
5.273
5.239
5.146
5.125
5.105
5.084
3.886
3.861
3.810
3.330
3.308
3.165
3.148
3.083
3.067
3.028
3.001
2.984
2.961
2.922
2.906
2.888
2.390
2.371
2.355
2.010
1.994
1.960
1.944
1.924
1.909
1.828
1.803
1.756
1.731
1.692
1.674
1.655
1.615
1.590
1.559
SePh
Ar
OH
N
15 Ar = 4-MeOC6H4
ppm
1.94 2.55
2.03 2.10
0.79
0.75 0.88
0.39
3.00
0.45 0.50
0.49 0.62
0.90
1.58
3.69
Pulse Sequence: s2pul

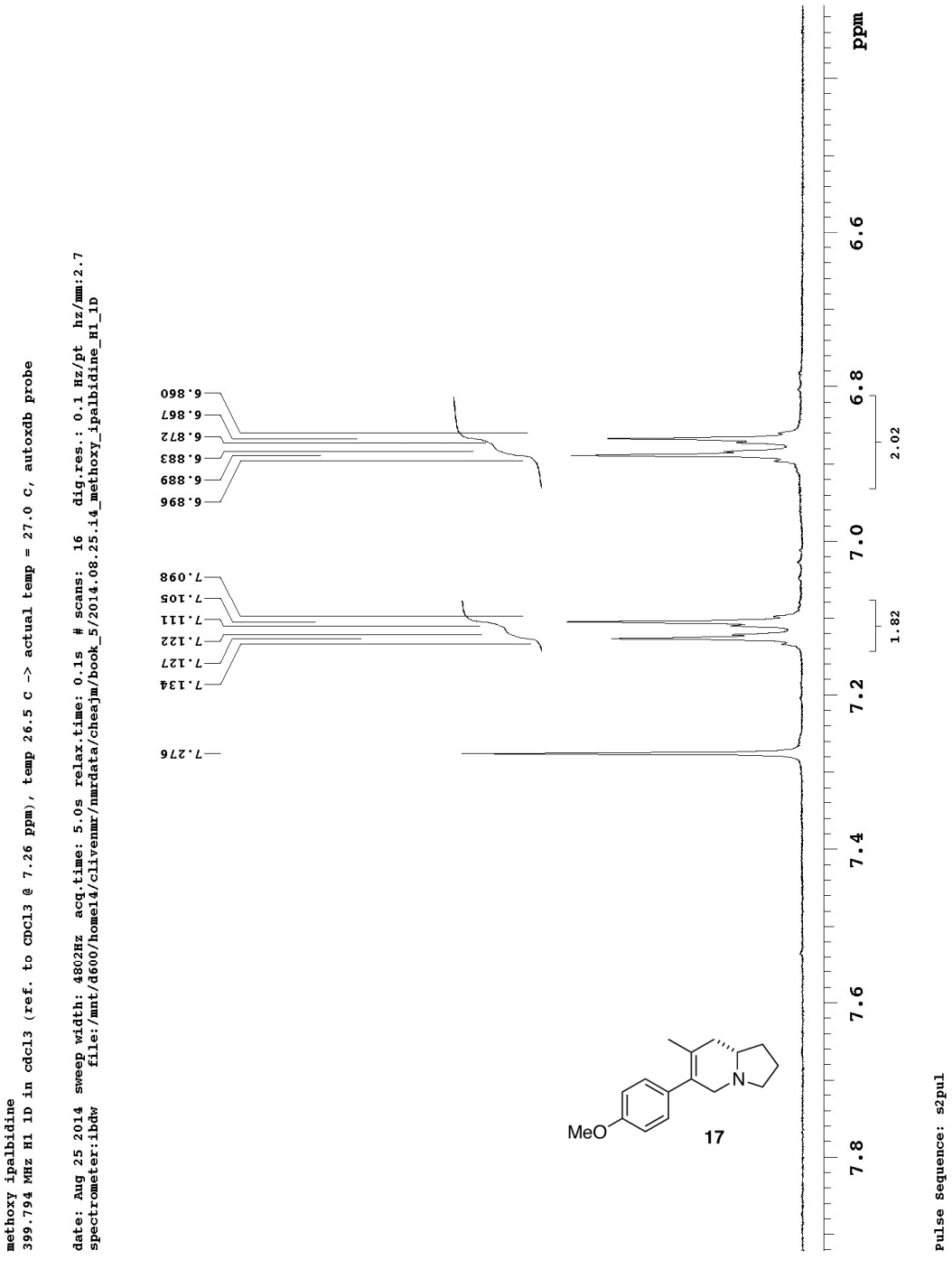

JongMyoung, JM-508-1st
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Feb 25 2015 sweep width: 33784Hz acq.time: 2.0s relax.time: 0.5s # scans: 648 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2015.02/2015.02.25.u5_JM-508-1st_loc3_15.54_C13_APT_ad
15.049
21.547
30.593
35.908
39.046
53.324
55.228
64.062
65.469
73.600
76.772
77.026
77.280
113.376
126.113
136.746
158.171
Ar
OH
N
16 Ar = 4-MeOC6H4
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad

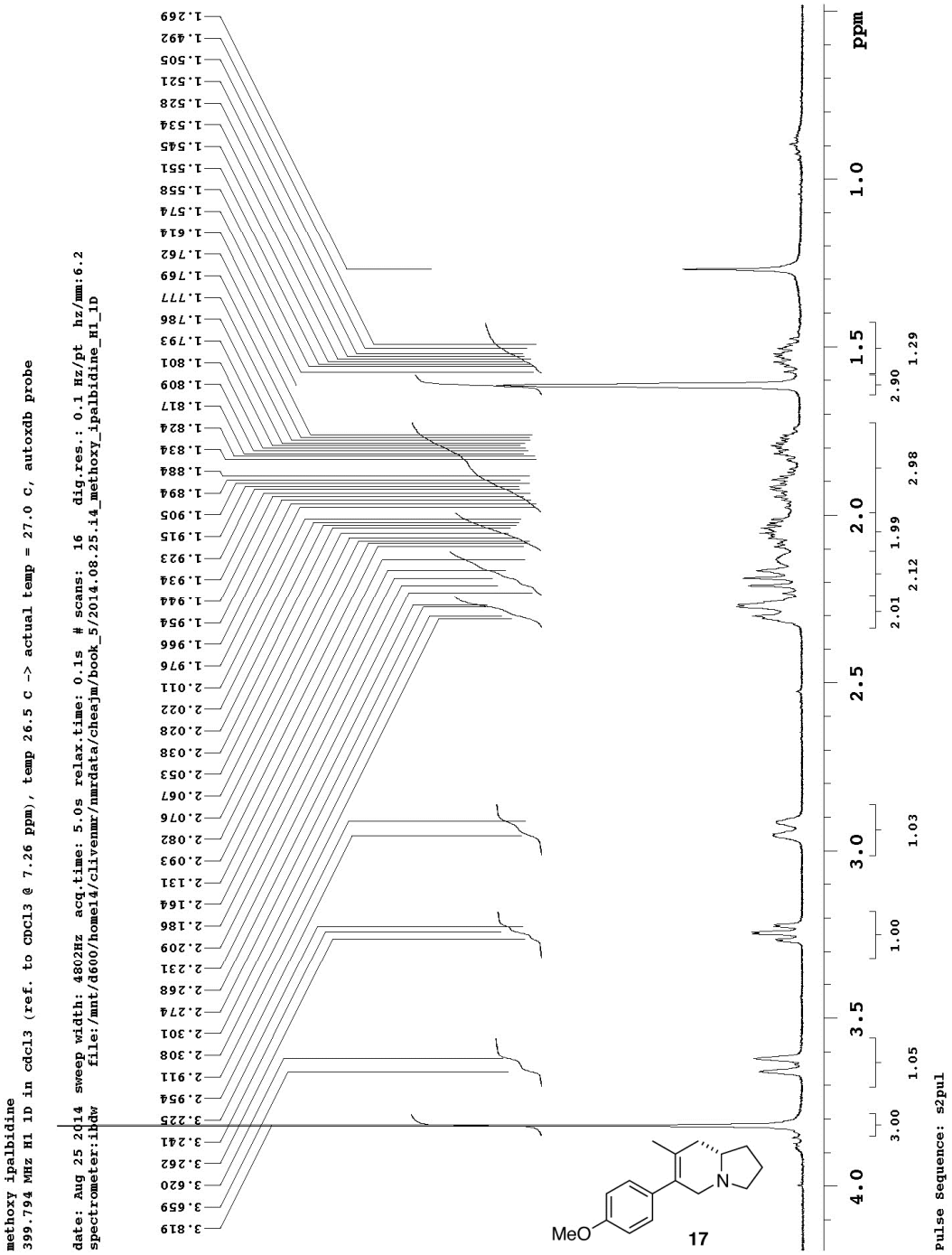

JM-s08-1st #6n page
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Feb 24 2015 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0
spectrometer:ibdw file:/mnt/d600/homel4/clivenmr/nmrdata/cheajm/book_6/2015.02.24.i4_JM-s08-1st_H1_1D
8.113
7.423
7.415
7.393
7.276
6.904
6.882
6.874
3.820
3.806
3.476
3.007
2.991
2.970
2.869
2.841
2.308
2.281
2.239
2.217
2.195
2.173
2.063
2.054
2.038
2.012
1.948
1.939
1.924
1.909
1.894
1.884
1.867
1.858
1.847
1.829
1.807
1.797
1.788
1.776
1.767
1.746
1.722
1.698
1.499
1.482
1.470
1.453
1.444
1.427
1.415
1.325
1.296
1.265
1.235
0.693
0.677
10
9
8
7
6
5
4
3
2
1
0
ppm
2.03
2.13
3.17
1.03
1.04
0.91
1.02
1.04
1.08
5.67
1.80
1.31
2.75
Ar
OH
N
16 Ar = 4-MeOC6H4
Pulse Sequence: s2pul

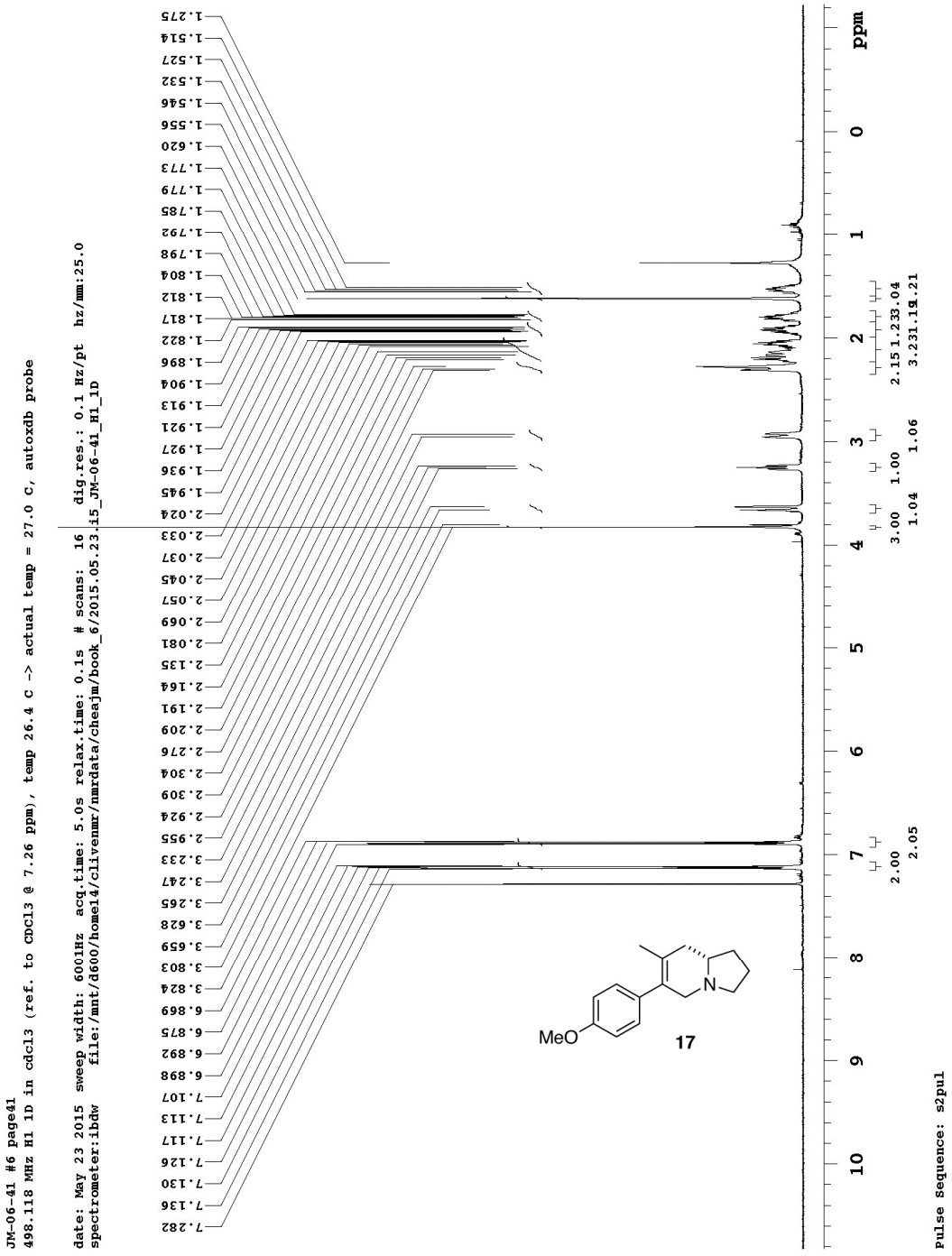

JongMyoung, JM-05-79
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Oct 1 2014 sweep width: 6010Hz acq.time: 5.0s relax.time: 2.1s # scans: 16 dig.res.: 0.2 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2014.10/2014.10.1.u5_JM-05-79_locl_22.53_H1_1D
7.426
7.409
7.286
6.911
6.894
6.878
3.824
3.499
3.067
3.014
2.997
2.983
2.879
2.856
2.757
2.731
2.556
2.539
2.521
2.318
2.296
2.242
2.225
2.207
2.189
2.065
2.052
1.950
1.906
1.869
1.845
1.818
1.795
1.768
1.750
1.731
1.713
1.689
1.672
1.658
1.501
1.478
1.457
1.443
1.410
1.395
1.380
1.366
1.332
1.308
1.284
1.259
0.966
0.951
0.937
0.705
0.692
Ar
OH
N
16 Ar = 4-MeOC6H4
(crude)
ppm
10
9
8
7
6
5
4
3
2
1
0
2.00
2.24
3.38
0.74
1.15
1.05
0.33
0.70
0.77
0.78
7.80
3.57
0.84
2.24
Pulse Sequence: PRESAT

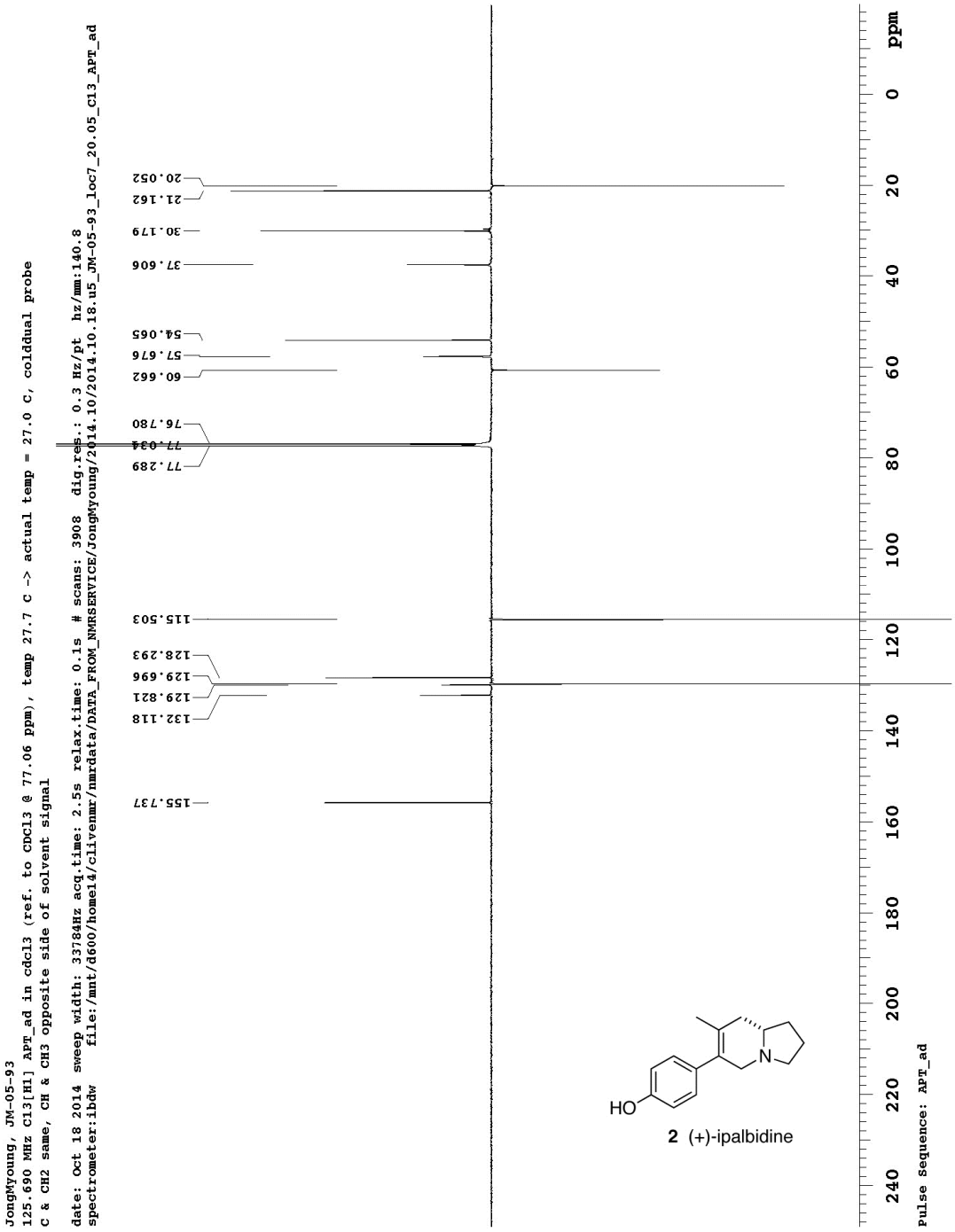

JongMyoung, JM-05-49
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Aug 26 2014 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1280 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2014.08/2014.08.26.u5_JM-05-49_loc5_07.59_C13_APT_ad
20.054
21.414
29.719
30.802
38.441
54.141
55.236
57.750
60.184
76.772
77.026
77.280
113.499
127.947
129.804
130.292
133.740
158.151
MeO
N
17
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad

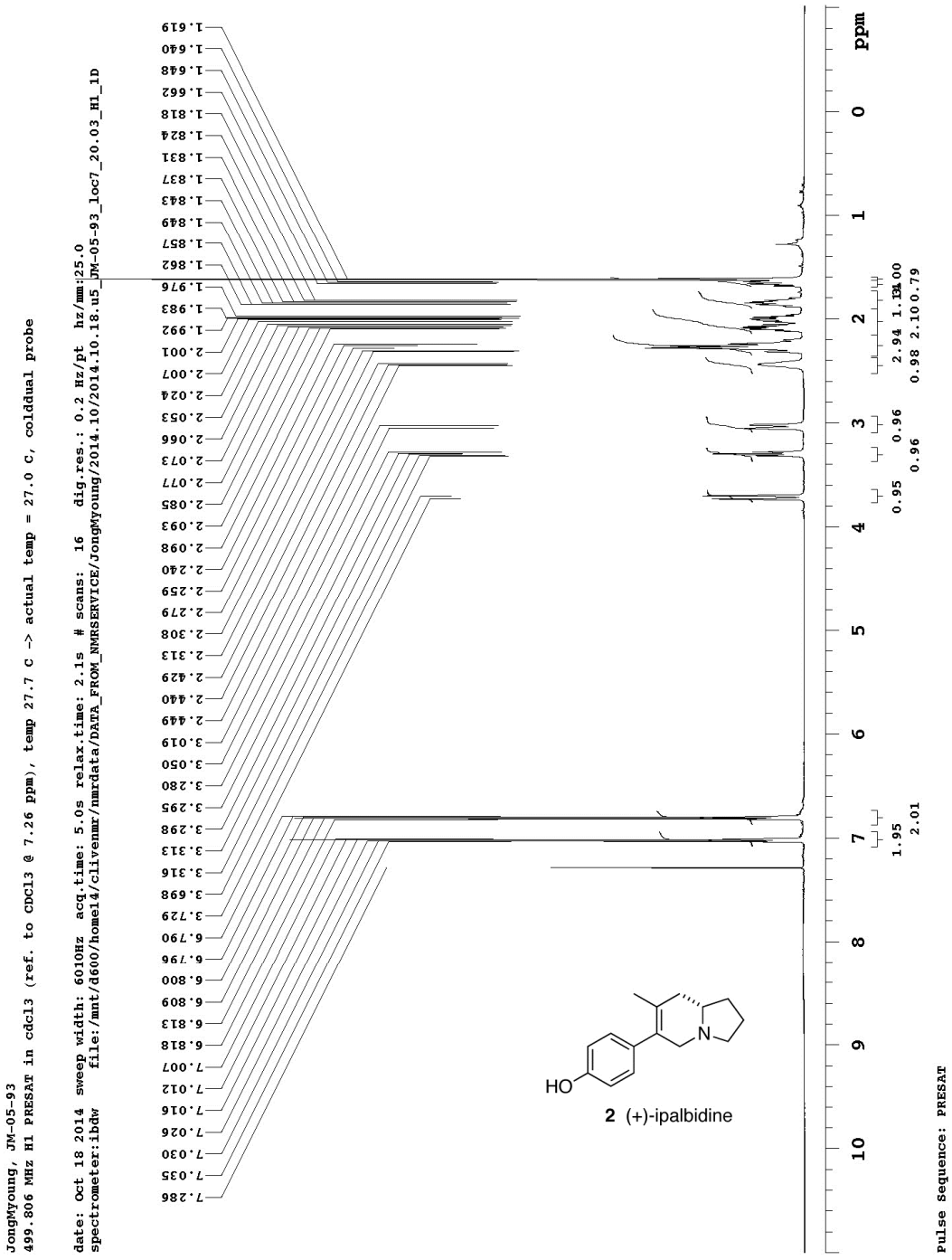

methoxy ipalbidine
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Aug 25 2014 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book_5/2014.08.25.i4_methoxy_ipalbidine_H1_1D
7.276
7.134
7.127
7.105
7.098
6.889
6.867
6.860
3.819
3.659
3.620
3.262
3.241
3.225
2.954
2.911
2.308
2.301
2.274
2.231
2.209
2.186
2.164
2.131
2.093
2.082
2.067
2.053
2.038
2.028
2.011
1.976
1.966
1.954
1.944
1.934
1.923
1.915
1.905
1.894
1.884
1.834
1.817
1.809
1.801
1.793
1.777
1.769
1.762
1.614
1.574
1.558
1.545
1.521
1.505
1.492
1.269
10
9
8
7
6
5
4
3
2
1
0
ppm
1.82
2.02
3.00
1.00
1.05
1.03
2.01.99
2.90
2.122.98
1.29
MeO
17
Pulse Sequence: s2pul

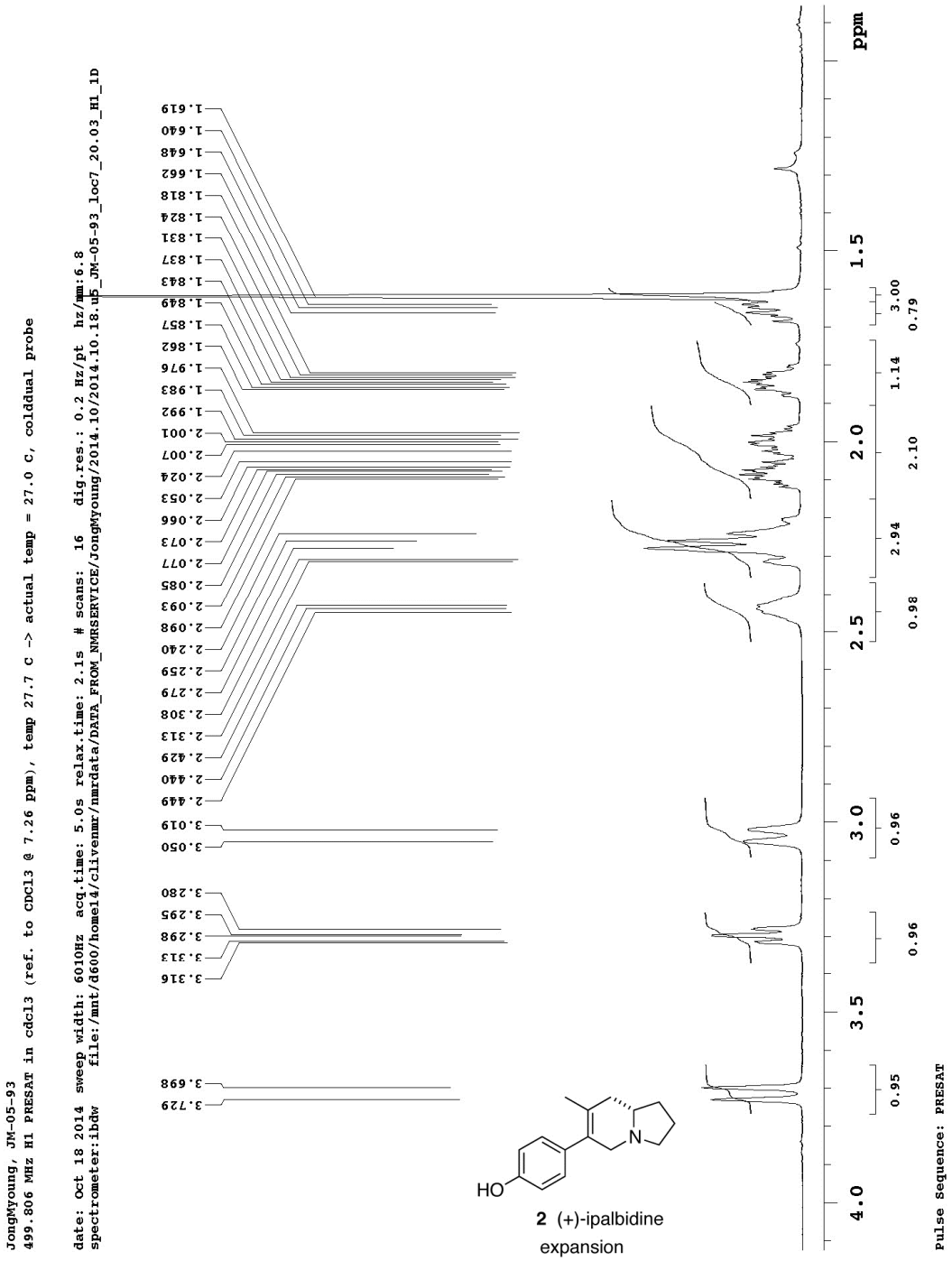

methoxy ipalbidine
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Aug 25 2014 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:2.7
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book_5/2014.08.25.i4_methoxy_ipalbidine_H1_1D
7.276
7.134
7.127
7.122
7.111
7.105
7.098
6.896
6.889
6.883
6.872
6.867
6.860
1.82
2.02
MeO
17
7.8
7.6
7.4
7.2
7.0
6.8
6.6
ppm
Pulse Sequence: s2pul

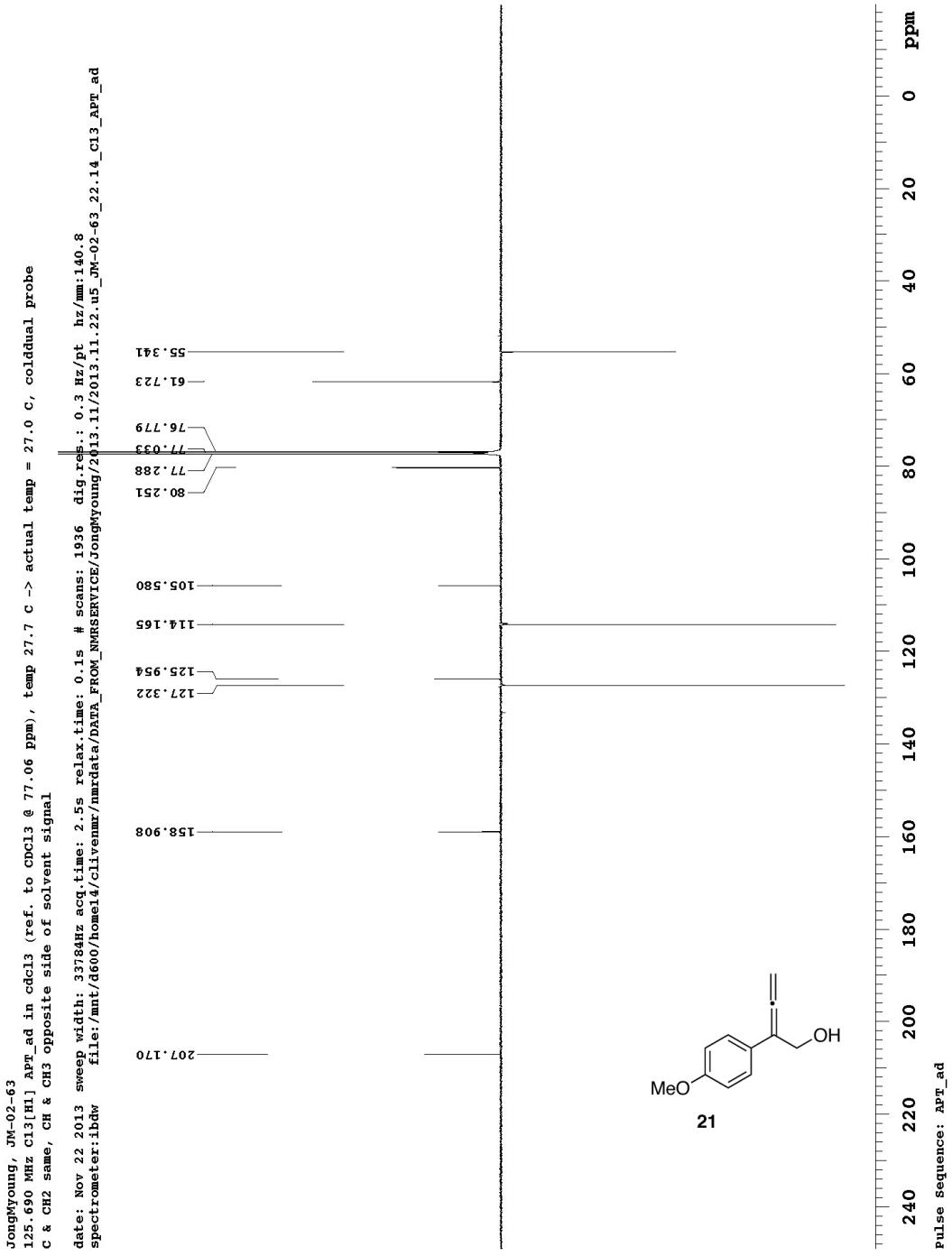

methoxy ipalbidine
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.5 C -> actual temp = 27.0 C, autoxdb probe
date: Aug 25 2014 sweep width: 4802Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:6.2
spectrometer:ihdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book_5/2014.08.25.i4_methoxy_ipalbidine_H1_1D
MeO
17
ppm
Pulse Sequence: s2pul

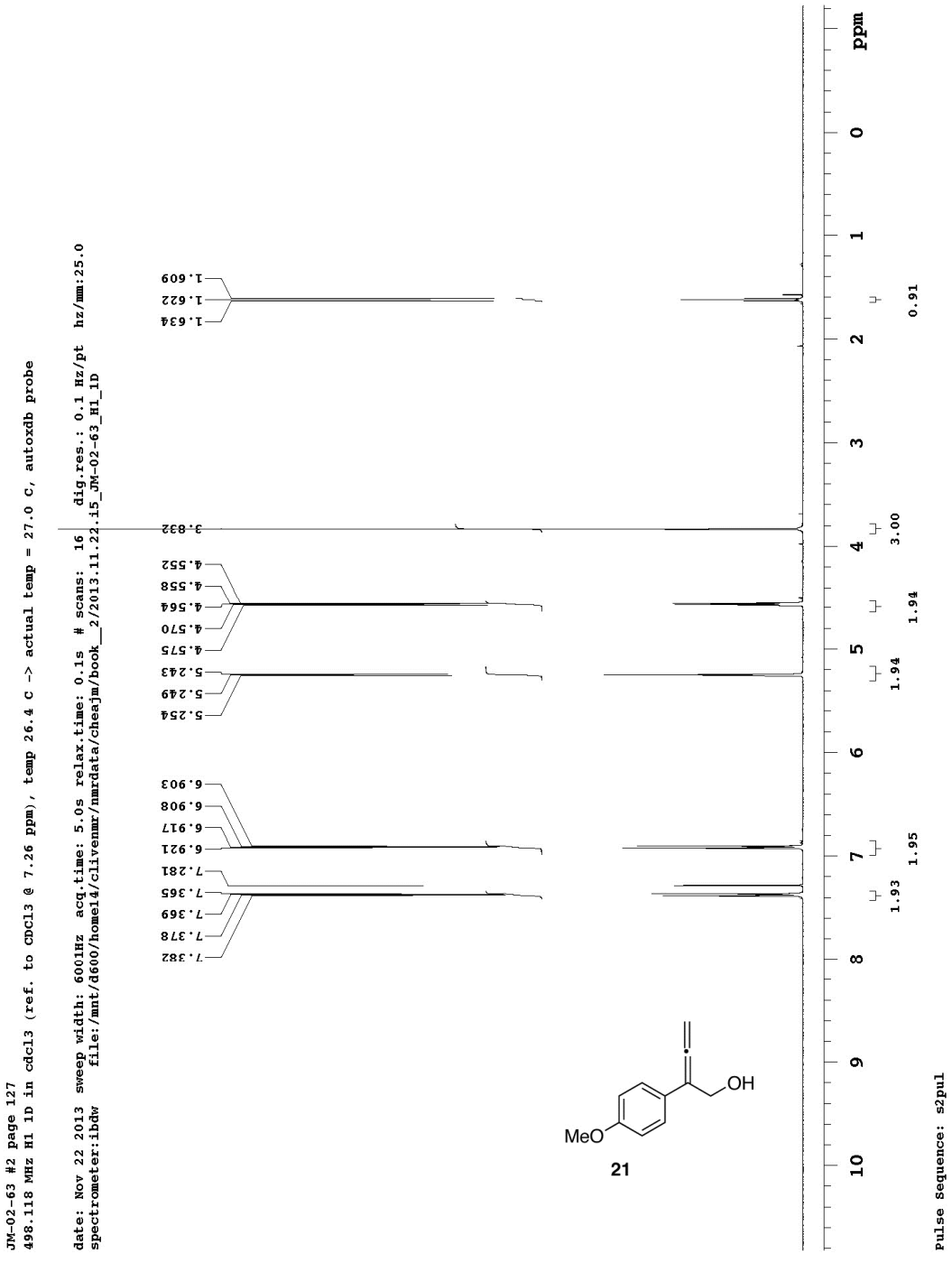

JM-06-41 #6 page41
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: May 23 2015 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book_6/2015.05.23.i5_JM-06-41_H1_1D
MeO
17
ppm
Pulse Sequence: s2pul

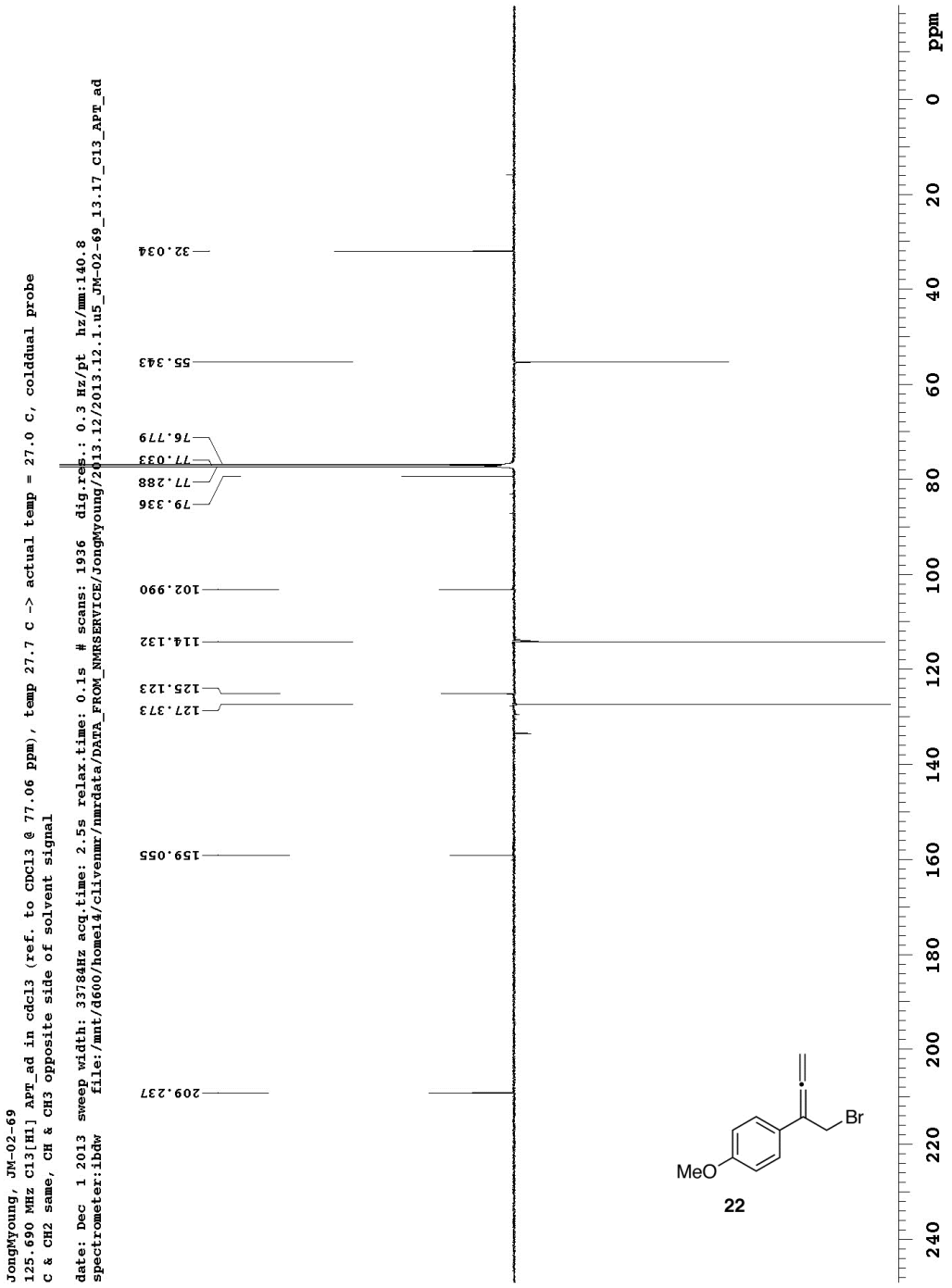

JongMyoung, JM-05-93
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Oct 18 2014 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 3908 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2014.10/2014.10.18.u5_JM-05-93_loc7_20.05_C13_APT_ad
20.052
21.162
30.179
37.606
54.065
57.676
60.662
76.780
77.034
77.289
115.503
128.293
129.696
129.821
132.118
155.737
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm
Pulse Sequence: APT_ad
HO
N
2 (+)-ipalbidine

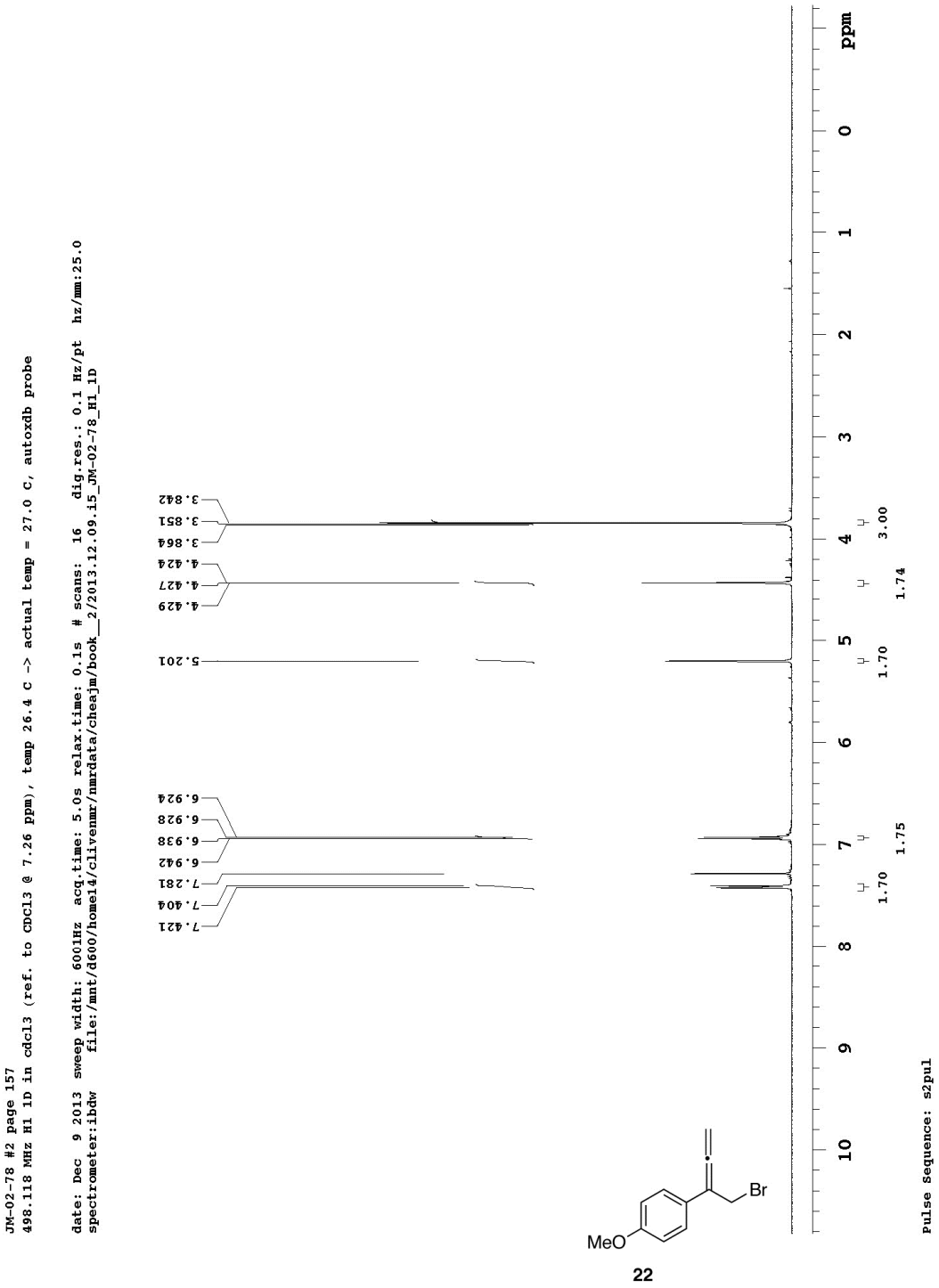

JongMyoung, JM-05-93
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Oct 18 2014 sweep width: 6010Hz acq.time: 5.0s relax.time: 2.1s # scans: 16 dig.res.: 0.2 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2014.10/2014.10.18.u5_JM-05-93_loc7_20.03_H1_1D
7.286
7.035
7.030
7.026
7.016
7.012
7.007
6.818
6.813
6.809
6.800
6.796
6.790
3.729
3.698
3.316
3.313
3.298
3.295
3.280
3.050
3.019
2.449
2.440
2.429
2.313
2.308
2.279
2.259
2.240
2.098
2.093
2.085
2.077
2.073
2.066
2.053
2.024
2.007
2.001
1.992
1.983
1.976
1.862
1.857
1.849
1.843
1.837
1.831
1.824
1.818
1.662
1.648
1.640
1.619
ppm
10
9
8
7
6
5
4
3
2
1
0
1.95
2.01
0.95
0.96
0.96
2.94
1.13
1.00
0.98
2.10
0.79
HO
N
2 (+)-ipalbidine
Pulse Sequence: PRESAT

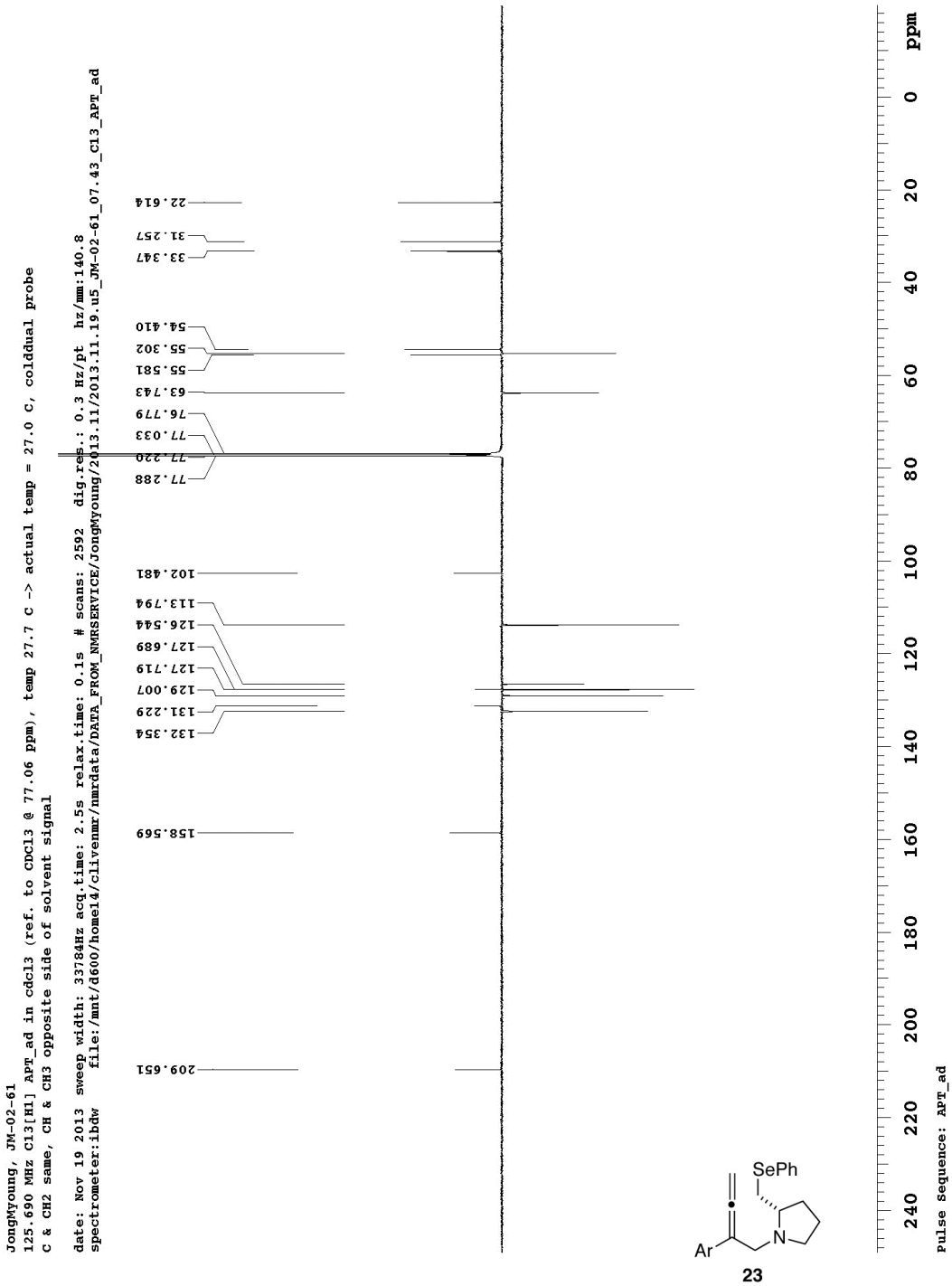

JongMyoung, JM-05-93
499.806 MHz H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
date: Oct 18 2014 sweep width: 6010Hz acq.time: 5.0s relax.time: 2.1s # scans: 16 dig.res.: 0.2 Hz/pt hz/mm:6.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2014.10/2014.10.18.u5_JM-05-93_loc7_20.03_H1_1D
3.729
3.698
3.316
3.313
3.298
3.295
3.280
3.050
3.019
2.449
2.440
2.429
2.313
2.308
2.279
2.259
2.240
2.098
2.093
2.085
2.077
2.073
2.066
2.053
2.024
2.007
2.001
1.992
1.983
1.976
1.862
1.857
1.849
1.843
1.837
1.831
1.824
1.818
1.662
1.648
1.640
1.619
HO
2 (+)-ipalbidine
expansion
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.95
0.96
0.96
0.98
2.94
2.10
1.14
3.00
0.79
Pulse Sequence: PRESAT

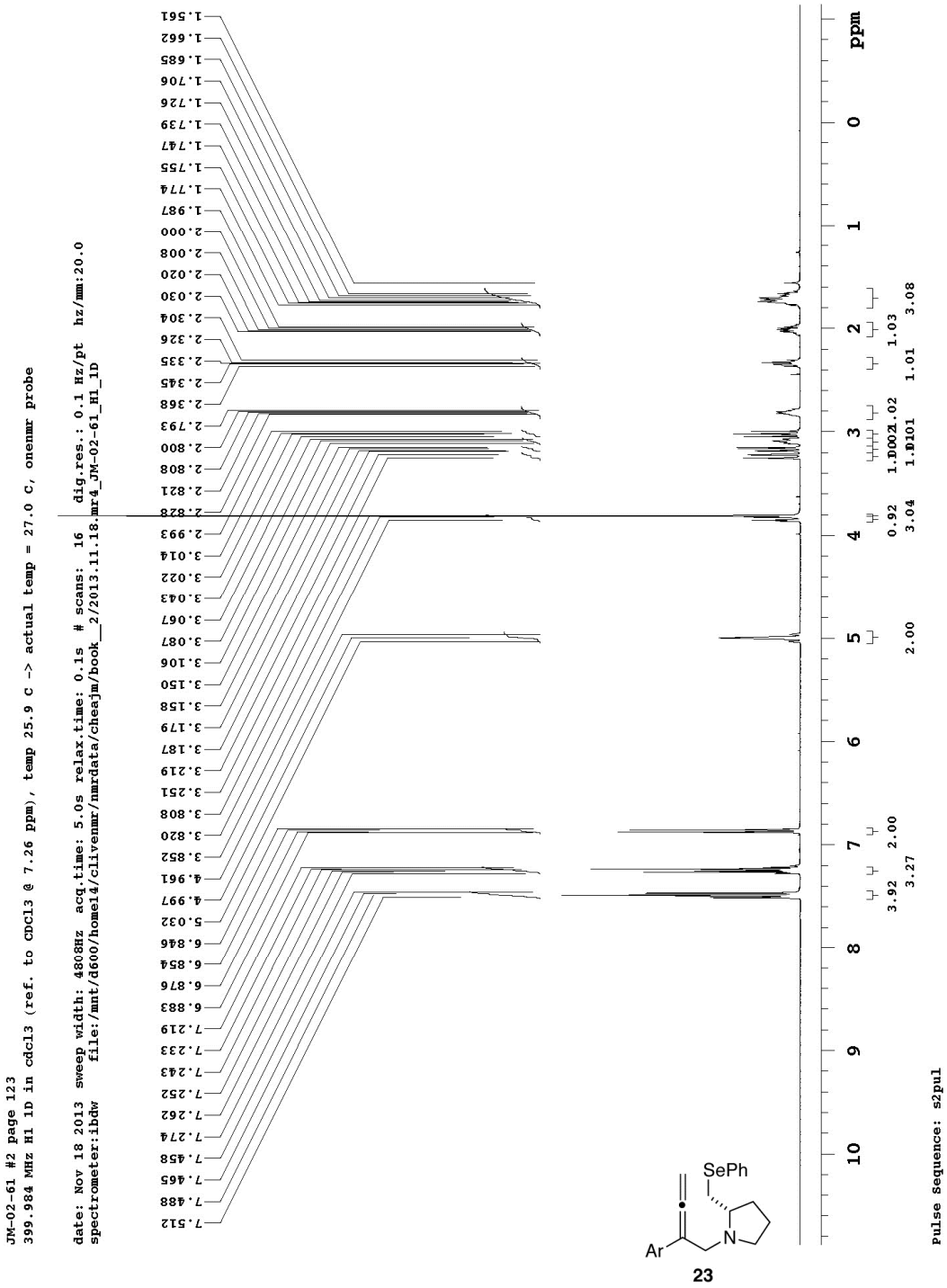

JongMyoung, JM-02-63
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Nov 22 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1936 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.11/2013.11.22.u5_JM-02-63_22.14_C13_APT_ad
207.170
158.908
127.322
125.954
114.165
105.580
80.251
77.288
77.033
76.779
61.723
55.341
MeO
OH
21
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad


JM-02-63 #2 page 127
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Nov 22 2013 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.11.22.15_JM-02-63_H1_1D
1.634
1.622
1.609
3.832
4.552
4.558
4.564
4.570
4.575
5.243
5.249
5.254
6.903
6.908
6.917
6.921
7.281
7.365
7.369
7.378
7.382
MeO
OH
21
ppm
1.93
1.95
1.94
1.94
3.00
0.91
Pulse Sequence: s2pul


JongMyoung, JM-02-69
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Dec 1 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 1936 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.12/2013.12.1.u5_JM-02-69_13.17_C13_APT_ad
32.034
55.343
76.779
77.033
77.288
79.336
102.990
114.132
125.123
127.373
159.055
209.237
MeO
Br
22
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad


JM-02-78 #2 page 157
498.118 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 26.4 C -> actual temp = 27.0 C, autoxdb probe
date: Dec 9 2013 sweep width: 6001Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:25.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.12.09.15_JM-02-78_H1_1D
7.421
7.404
7.281
6.942
6.938
6.928
6.924
5.201
4.429
4.427
4.424
3.864
3.851
3.842
1.70
1.75
1.70
1.74
3.00
ppm
MeO
Br
22
Pulse Sequence: s2pul

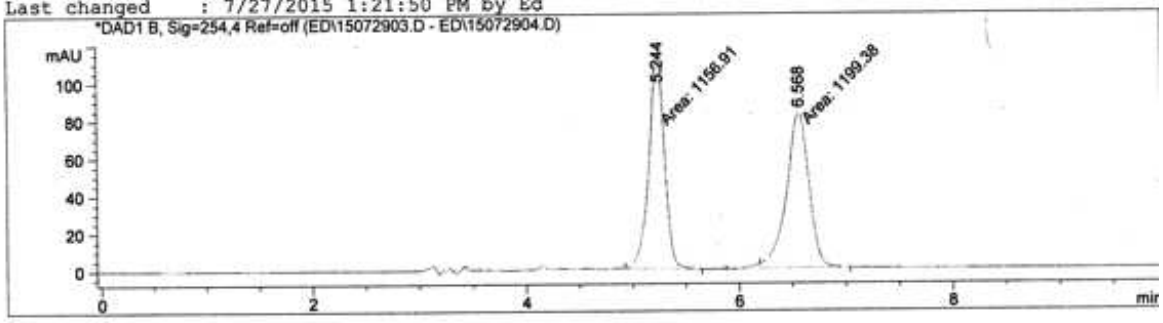

JongMyoung, JM-02-61
125.690 MHz C13[H1] APT_ad in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, colddual probe
C & CH2 same, CH & CH3 opposite side of solvent signal
date: Nov 19 2013 sweep width: 33784Hz acq.time: 2.5s relax.time: 0.1s # scans: 2592 dig.res.: 0.3 Hz/pt hz/mm:140.8
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/DATA_FROM_NMRSERVICE/JongMyoung/2013.11/2013.11.19.u5_JM-02-61_07.43_C13_APT_ad
22.614
31.257
33.347
54.410
55.302
55.581
63.743
76.779
77.033
77.229
77.288
102.481
113.794
126.544
127.689
127.719
129.007
131.229
132.354
158.569
209.651
SePh
N
Ar
23
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm
Pulse Sequence: APT_ad


JM-02-61 #2 page 123
399.984 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 25.9 C -> actual temp = 27.0 C, onenmr probe
date: Nov 18 2013 sweep width: 4808Hz acq.time: 5.0s relax.time: 0.1s # scans: 16 dig.res.: 0.1 Hz/pt hz/mm:20.0
spectrometer:ibdw file:/mnt/d600/home14/clivenmr/nmrdata/cheajm/book__2/2013.11.18.mr4_JM-02-61_H1_1D
7.512
7.488
7.465
7.458
7.274
7.262
7.252
7.243
7.233
7.219
6.883
6.876
6.854
6.846
5.032
4.997
4.961
3.852
3.820
3.808
3.251
3.219
3.187
3.179
3.158
3.150
3.106
3.087
3.067
3.043
3.022
3.014
2.993
2.828
2.821
2.808
2.800
2.793
2.368
2.345
2.335
2.326
2.304
2.030
2.020
2.008
2.000
1.987
1.774
1.755
1.747
1.739
1.726
1.706
1.685
1.662
1.561
ppm
0.92
3.04
1.00
1.01
1.03
3.08
3.92
2.00
3.27
2.00
SePh
Ar
N
23
Pulse Sequence: s2pul

ata File C:\HPCHEM\1\DATA\ED\15072903.D Sample Name: IPALBIDINE race

CLA column HEX/Ethanol=90:10 0.1% DEA 20C 1 ml/min

Injection Date : 7/29/2015 9:06:23 AM Seq. Line : 3
Sample Name : IPALBIDINE race Location : Vial 82
Acq. Operator : Ed Inj : 1
Acq. Instrument : Instrument 1 Inj Volume : 3 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 1 µl
Acq. Method : C:\HPCHEM\1\METHODS\CLA-2.M
Last changed : 7/29/2015 8:42:06 AM by Ed
Analysis Method : C:\HPCHEM\1\METHODS\CLA-3.M
Last changed : 7/27/2015 1:21:50 PM by Ed



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=254,4 Ref=off
Signal has been modified after loading from rawdata file!

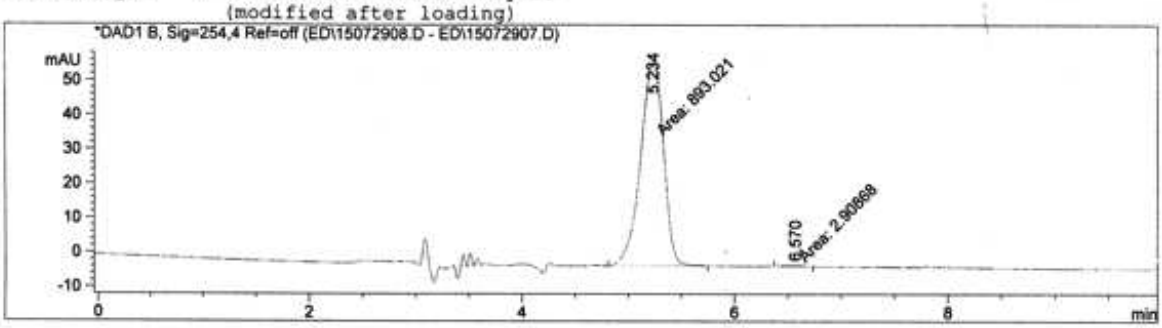
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.244	MM	0.1678	1156.90637	114.91517	49.0987
2	6.568	FM	0.2417	1199.37939	82.69852	50.9013
Totals :				2356.28577	197.61369	

*** End of Report ***

[redacted] C:\HPCHEM\1\DATA\ED\15072908.D Sample Name: IPALBIDINE (+)

[redacted]A column HEX/Ethanol=90:10 0.1% DEA 20C 1 ml/min

```
Injection Date  : 7/29/2015 10:30:09 AM        Seq. Line :   8
Sample Name     : IPALBIDINE (+)                Location : Vial 84
Acq. Operator   : Ed                               Inj :   1
Acq. Instrument : Instrument 1                 Inj Volume : 3 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 2 µl
Acq. Method     : C:\HPCHEM\1\METHODS\CLA-2.M
Last changed    : 7/29/2015 8:42:06 AM by Ed
Analysis Method : C:\HPCHEM\1\METHODS\CLA-3.M
Last changed    : 7/29/2015 12:28:40 PM by Ed
                  (modified after loading)
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=254,4 Ref=off
 Signal has been modified after loading from rawdata file!

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.234 MM    0.2525  893.02130   58.93895  99.6753
   2   6.570 MM    0.2293    2.90868 2.11378e-1   0.3247

Totals :                   895.92998   59.15033

                          *** End of Report ***
```