Total Synthesis of Thaxtomin A and its Stereoisomers and Findings of their Biological Activities

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Supporting Information

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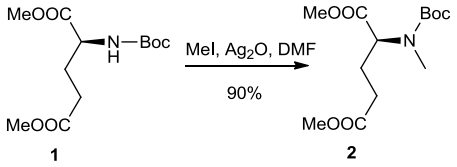
Part A

General procedures:

All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Reagents obtained from Alfa Aesar, Aldrich, and J&K were used without further purification. THF was dried by distillation over Na/benzophenone. CH_2Cl_2 was dried by distillation over CaH_2. TLC inspections were performed on silica gel GF254 plates. Column chromatography was performed on silica gel (200–300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE AV400 (400MHz and 100MHz). Signal positions were recorded in ppm with the abbreviations s, d, t, and m denoting singlet, doublet, triplet, and multiplet respectively. All NMR chemical shifts were referenced to residual solvent peaks or to $Si(CH_3)_4$ as an internal standard, spectra recorded in $CDCl_3$ were referenced to residual $CHCl_3$ at 7.26 ppm for ^{1}HNMR or 77.0 ppm for ^{13}CNMR, spectra recorded in CD_3OD were referenced to residual CD_2HOD at 3.31 ppm for ^{1}H or 49.15 ppm for ^{13}C, spectra recorded in $(CD_3)_2SO$ were referenced to residual $(CH_3)_2SO$ at 2.50 ppm for ^{1}H or 39.52 ppm for ^{13}C. All coupling constants *J* were quoted in Hz. HPLC analysis was performed on Shimadzu CTO-10AS by using a Chiralpak AD-H column purchased from Daicel Chemical Industries. High resolution mass spectra (HRMS) were obtained on a IonSpec QFT mass spectrometer with ESI ionization. Optical rotations were recorded on a Perkin–Elmer 341 polarimeter. Melting points were measured on X4 apparatus.

Part B

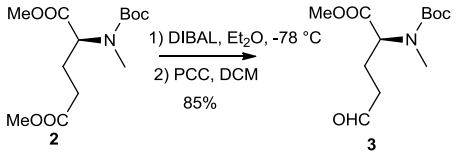
Preparation of compound 2:



Compound **1** (7.6 g, 27.7 mmol) was dissolved in anhydrous DMF (50 mL). To the resulting solution was added CH_3I (68.9 mL, 1108 mmol) and Ag_2O (19.25 g, 83.1 mmol). The mixture was stirred at room temperature for 24 h. The saturated Na_2SO_3 was added and the aqueous was extracted with EtOAc (200 mL × 3), the combined organic layer was washed with brine and dried over Na_2SO_4. Purification by silica gel column chromatography (PE/EtOAc 3:1) to afford the product **2** (7.2 g, 90% yield) as an oil.

2: TLC (PE:EtOAc, 75:25 v/v): R_f = 0.60; $[\alpha]^{25}_D$ = -35.0 °(c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) Mixture of rotamers δ 4.75 (m, 0.5H), 4.73 (m, 0.5H), 3.73 (s, 3H), 3.69 (s, 3H), 2.80 (d, *J* = 18.4 Hz, 3H), 2.33 (m, 1H), 2.04 (m, 1H), 1.45 (d, *J* = 14.4 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) Mixture of rotamers δ 173.1, 171.7, 171.6, 156.2, 155.3, 80.5, 80.2, 77.4, 76.8, 58.9, 57.4, 52.1, 51.6, 31.9, 30.9, 30.5, 30.2, 28.2, 24.4; HRMS (ESI) m/z calcd for $C_{13}H_{23}NO_6$ $(M + Na)^+$ 312.1418; found 312.1415.

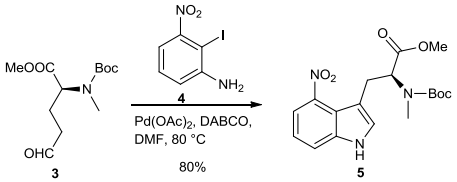
Preparation of compound 3:



To a stirred solution of **2** (7.2g, 24.9 mmol) in anhydrous ether (200 mL) was added DIBAL (27.5 mL, 1.0 M in hexane, 27.5 mmol) dropwise at -78 °C. The reaction mixture was stirred for 5 min, then quenched with H_2O (5 mL) and allowed to warm to room temperature. The mixture was stirred for 30 min, dried over $MgSO_4$ and filtered through a pad of Celite. The filtrate was evaporated and the residue was purified by silica gel column chromatography (PE/EtOAc 3:1) to yield **3** (5.5 g, 85% yield) as an oil.

3: TLC (PE:EtOAc, 75:25 v/v): R_f = 0.55; $[\alpha]^{25}_D$ = -18.4 °(c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) Mixture of rotamers δ 9.77 (d, *J* = 4.4 Hz, 1H), 4.69 (dd, *J* = 10.4 Hz, 4.8Hz, 0.5H), 4.37 (dd, *J* = 10.0 Hz, 5.2Hz, 0.5H), 3.72 (s, 3H), 2.81 (s, 1.5H), 2.76 (s, 1.5H), 2.51 (m, 2H), 2.30 (m, 1H), 2.03 (m, 1H), 1.46 (s, 4.5H), 1.42 (s, 4.5H); ^{13}C NMR R (100 MHz, $CDCl_3$) Mixture of rotamers δ 199.9, 199.8, 170.6, 155.3, 154.3, 79.7, 79.4, 57.8, 56.6, 51.2, 30.4, 30.2, 29.2, 28.7, 27.3, 20.8, 20.3; HRMS (ESI) m/z calcd for $C_{12}H_{21}NO_5$ $(M + Na)^+$ 282.1312; found 282.1313.

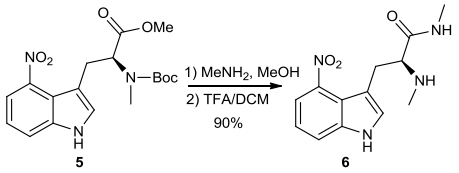
Preparation of compound 5:



A mixture of 3-nitro-2-iodo-aniline **4** (11.2 g, 42.4 mmol), aldehyde **3** (5.5 g, 21.2 mmol) and DABCO (14.0 g, 63.6 mmol) in DMF (100 mL) was degassed for 20min. $Pd(OAc)_2$ (476 mg, 2.12 mmol) was added, and the resulting reaction mixture was heated at 80°C under nitrogen atmosphere for 12h. The reaction mixture was then cooled to room temperature and diluted with water followed by extraction with EtOAc (3 × 100mL). The combined organic phases were washed with brine and dried over Na_2SO_4. After the purification by silica gel column chromatography (PE/EtOAc 5:1→PE/EtOAc 2:1), the starting aniline **4** (5.5 g) and the desired product **5** (6.4 g, 80% based on **3**) as yellowish powder was afforded.

5: mp 128-130°C; TLC (PE:EtOAc, 65:35 v/v): R_f = 0.30; $[\alpha]^{25}_D$ = -155.4 ° (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $(CD_3)_2SO$) Mixture of rotamers δ 11.82 (s, 0.6), 11.77 (s, 0.4), 7.82 (m, 2H), 7.53 (s, 1H), 7.24 (m, 1H), 4.81 (m, 1H), 4.64 (m, 1H), 3.70 (s, 1.8H), 3.68 (s, 1.2H), 3.51 (m, 1H), 3.11 (m, 1H), 2.63 (m, 1.8H), 2.59 (m, 1.2H), 1.10 (s, 3H), 0.91 (s, 6H); ^{13}C NMR R (100 MHz, $(CD_3)_2SO$) Mixture of rotamers δ 171.1, 154.1, 141.8, 139.4, 130.8, 119.9, 118.7, 118.3. 117.3, 109.1, 78.7, 60.0, 58.7, 52.1, 30.8, 27.6, 27.2, 26.7, 26.5; HRMS (ESI) m/z calcd for $C_{18}H_{23}N_3O_6$ $(M - H)^+$ 376.1513; found 376.1517.

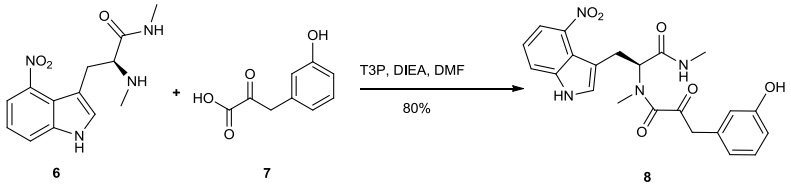
Preparation of compound 6:



A solution of **5** (6.4 g, 33.9 mmol) and the $MeNH_2$ (300 mmol) in anhydrous methanol (150 mL) was stirred at room temperature for 7 days. The reaction mixture was concentrated, follow by addition of a mixture of dichloromethane (80 mL) and trifluroacetic acid (20 mL), and stirring was continued at room temperature for another 30min. The reaction mixture was concentrated, the product **6** was obtained after recrystallization from methanol (4.2 g, 90% yield) as yellowish powder.

6: mp 134-136°C; TLC (CH_2Cl_2:CH_3OH, 75:25 v/v): R_f = 0.40; $[\alpha]^{25}_D$ = +124.0 ° (c = 1.0, CH_3OH); ^{1}H-NMR (CD_3OD, 400Mz) δ 7.87 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.36 (s, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 3.40 (m, 2H), 3.12 (m, 1H), 2.58 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 26.0, 31.6, 33.9, 66.5, 110.1, 118.7, 119.3, 120.1, 121.2, 131.3, 141.2, 143.7, 174.4; HRMS: Calcd for $C_{13}H_{16}N_4O_3$ $(M + H)^+$ 277.1295, found 277.1293.

Preparation of compound 8:

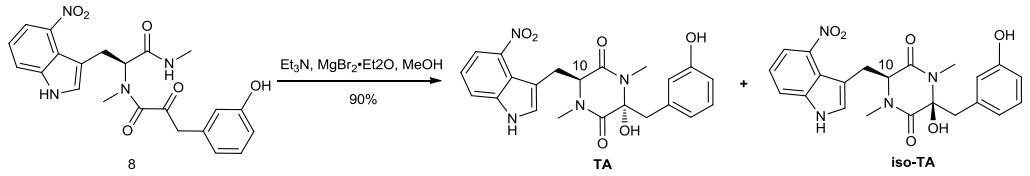


To a stirred solution of 4-nitrotryptophan derivative **6** (750 mg, 2.7 mmol), arylpyruvic acid **7** (730 mg, 4.1 mmol) and DIEA (1.45 mL, 8.1 mmol) in DMF (20 mL) was added propylphosphonic acid anhydride (cyclic trimer, T3P) (48% in DMF, 2.6 mL, 4.1 mmol) dropwise at room temperature. The reaction mixture was stirred at room temperature for 12h, concentrated, the residue was then purified by silica gel column chromatography (DCM/MeOH 10:1 →

DCM/MeOH 3:1) to yield **8** (1190 mg, 80% yield) as yellowish powder.

8: mp 181-182°C; TLC (CH_2Cl_2:CH_3OH, 75:25 v/v): R_f = 0.25; $[\alpha]^{25}_D$ = -92.4 °(c = 1.0, CH_3OH); ^{1}H-NMR (CD_3OD, 400Mz) δ 7.86 (d, *J* = 8.0 Hz, 0.5H), 7.73 (d, *J* = 8.0 Hz, 0.5H), 7.67 (m, 0.3H), 7.57 (m, 0.3H), 7.50 (d, *J* = 8.4 Hz, 0.5H), 7.42 (s, 0.5H), 7.35 (d, *J* = 8.0 Hz, 0.5H), 7.23 (s, 0.5), 7.20 (t, *J* = 8.0 Hz, 0.5H), 7.13 (s, 1H), 7.04 (t, *J* = 8.0 Hz, 0.5H), 6.65 (t, *J* = 8.0 Hz, 0.5H), 6.78 (m, 1H), 6.67 (s, 0.5H), 6.60 (d, *J* = 7.6 Hz, 0.5H), 6.52 (d, *J* = 7.6 Hz, 0.5H), 6.23 (d, *J* = 7.6 Hz, 0.5H), 4.80 (s, 0.5H), 4.55 (s, 0.5H), 3.65 (m, 0.5H), 3.73 (m, 0.5H), 3.24 (m, 1.0H), 2.95 (m, 0.8H), 2.87 (s, 1.5H), 2.85 (s, 1.5H), 2.81 (s, 1.5H), 2.74 (s, 1.5H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.6, 172.7, 171.1, 170.6, 158.3, 157.7, 144.1, 143.2, 141.2, 140.9, 136.0, 135.2, 132.3, 131.1, 130.8, 130.2, 129.8, 129.6, 122.2, 121.8, 121.2, 121.1, 120.6, 120.4, 119.8, 119.7, 119.1, 119.0, 118.8, 118.5, 116.7, 116.6, 115.9, 115.8, 111.6, 111.1, 66.6, 64.3, 31.7, 30.5, 27.1, 27.0, 26.6, 26.5; HRMS: Calcd for $C_{22}H_{22}N_4O_6$ $(M + Na)^+$ 461.1432; found.461.1441.

Preparation of TA and iso-TA:



A solution of **8** (1190 mg, 2.7 mmol), $MgBr_2$ Ɛt_2O (7.0 g, 27 mmol) and Et_3N (100 mL) in MeOH (100 mL) was stirred at room temperature for 7 days, then concentrated. The residue was diluted with water followed by extraction with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated. Purification of the residue by silica gel column chromatography (DCM/MeOH 10:1), afforded the mixture of TA and iso-TA (904 mg, 90% based on **8**) as yellowish powder. The ratio of TA and iso-TA was determined to be 1:2.5 by ^{1}H NMR analysis (M-TA-1). Purification by preparative TLC (DCM-MeOH, 20:1), the mixture (7mg) afforded TA (2 mg) with 99% ee (TA-0) and iso-TA (5 mg). After recrystallization from MeOH, other mixture gave pure iso-TA (219mg). Treatment of mother liquid with Et_3N (1 mL) and anhydrous MeOH (50 mL) under reflux condition for 1h, then the reaction mixture was concentrated, the ratio of TA and iso-TA conversed to 2.6:1 (M-TA-MeOH). Recrystallization of the mixture from MeOH afforded the pure product TA (165 mg) with 99% C-10 *de* (TA-1).

TA: mp 227-229°C; TLC (CH_2Cl_2:CH_3OH, 95:5 v/v): R_f = 0.20; $[\alpha]^{33}_D$ = +15.2 ° (c = 0.5, CH_3OH); HRMS: Calcd for $C_{22}H_{22}N_4O_6$ $(M + H)^+$ 439.1612; found.439.1612. The ^{1}H NMR and ^{13}C NMR spectra of synthetic TA were in good agreement with those of authentic sample.

iso-TA: mp 225-226°C; TLC (CH_2Cl_2:CH_3OH, 95:5 v/v): R_f = 0.22; $[\alpha]^{33}_D$ = +49.8 ° (c = 0.5, CH_3OH); ^{1}H-NMR (CD_3OD, 400Mz) δ 7.75 (d, 1H, *J* = 7.6 Hz), 7.70 (d, 1H, *J* = 7.6 Hz), 7.18 (t, 2H, *J* = 7.2 Hz), 7.03 (t, 1H, *J* = 8.0 Hz), 6.66 (m, 1H), 6.43 (m, 2H), 3.55 (m, 1H), 3.29 (m, 2H), 3.13 (d, 1H, *J* = 13.2 Hz), 2.99 (d, 1H, *J* = 13.2 Hz), 2.79 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.5, 167.8, 158.6, 144.2, 140.8, 136.8, 130.4, 130.2, 121.7, 121.1, 120.2, 118.9, 118.4, 117.5, 115.5, 108.8, 87.6, 83.1, 45.0, 33.0, 30.5, 28.2; HRMS: Calcd for $C_{22}H_{22}N_4O_6$ $(M + H)^+$ 439.1612; found.439.1612.

Preparation of mirror-TA and mirror-iso-TA:

Mirror-TA and mirror-iso-TA were prepared from D-glutamic acid through the same synthetic rout

e as for TA and iso-TA.
mirror-TA: $[\alpha]^{33}_{D}$ = -15.2 °(c = 0.5, CH_3OH); The melting point, ^{1}H NMR, ^{13}C NMR spectra and HRMS data are all the same to TA.
Mirror-iso-TA: $[\alpha]^{33}_{D}$ = -49.8 °(c = 0.5, CH_3OH); The melting point, ^{1}H NMR, ^{13}C NMR spectra and HRMS data are all the same to iso-TA.

Herbicidal Activity Assay

Treatment. The emulsions of purified compounds were prepared by dissolving them in 100 μL of *N*,*N*-dimethylformamide with the addition of a little Tween 20 and proper water. There were three replicates for each treatment. The mixture of the same amount of water, *N*,*N*-dimethylformamide, and Tween 20 was used as the control.
Pre-emergence. Sandy clay (100 g) in a plastic box (11 cm × 7.5 cm × 6 cm) was wetted with water. Fifteen sprouting seeds of the weed under test were planted in fine earth (0.6 cm depth) in the glasshouse and sprayed with the test compound solution.
Postemergence. Seedlings (one leaf and one stem) of the weed were sprayed with the test compounds at the same rate as used for the pre-emergence test. For both methods, the fresh weights were determined 20 days later, and the percentage inhibition relative to the controls was calculated.

Fungicidal Activity Assay

The fungicidal activities of the compounds were tested *in vitro* against *Cercospora arachidicola*, and *Physalospora piricola*, and their relative inhibitory ratio (%) had been determined by using the mycelium growth rate method.[1] Phenazine-1-carboxylic acid was used as a control. After the mycelia grew completely, the diameters of the mycelia were measured and the inhibition rate was calculated according to the formula

$$I = (D1 - D2) / D1 \times 100\%$$

In the formula, *I* is the inhibition rate, D1 is the average diameter of mycelia in the blank test, and D2 is the average diameter of mycelia in the presence of those compounds. The inhibition ratio of those compounds at the dose of 50μgmL^{-1} is summarized. The EC50 of compounds and phenazine-1-carboxylic acid had been experimented and calculated by the Scatchard method.

Antiviral Biological Assay

Protective Effect of Compounds against TMV in Vivo. The compound solution was smeared on the left side, and the solvent served as a control on the right side of growing Nicotiana tabacum L. leaves of the same ages. The leaves were then inoculated with the virus after 12 h. A brush was dipped in TMV of 6 × 10^{-3} mg/mL to inoculate the leaves, which were previously scattered with silicon carbide. The leaves were then washed with water and rubbed softly along the nervature once or twice. The local lesion numbers appearing 3−4 days after inoculation were counted. There are three replicates for each compound.
Inactivation Effect of Compounds against TMV in Vivo. The virus was inhibited bymixing with the compound solution at the same volume for 30min. The mixture was then inoculated on the left side of the leaves of N. tabacum L., whereas the right side of the leaves was inoculated with the mixture of solvent and the virus for control. The local lesion numbers were recorded 3−4 days after inoculation. There are three replicates for each compound.

Curative Effect of Compounds against TMV in Vivo. Growing leaves of *Nicotiana tabacum* L. of the same ages were selected. TMV (concentration of 6.0×10^{-3} mg/mL) was dipped and inoculated on the whole leaves. Then, the leaves were washed with water and dried. The compound solution was smeared on the left side, and the solvent was smeared on the right side for control. The local lesion numbers were then counted and recorded 3−4 days after inoculation. There are three replicates for each compound.

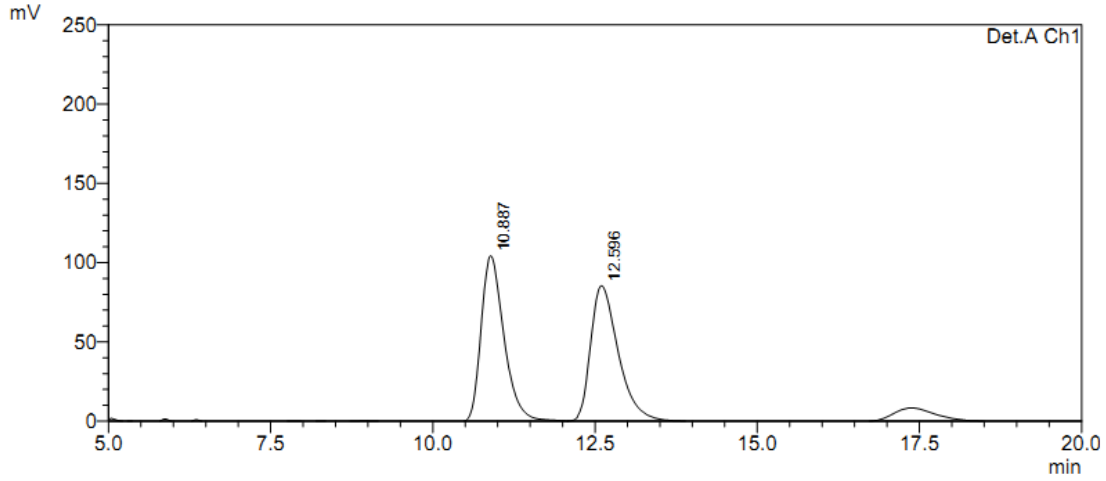
References

(1) Chen, N. C. *Bioassay of Pesticides*; Beijing Agriculture University Press: Beijing, China, 1991, pp 161-162.

Part C

HPLC methods

Racemic glutamic acid was used as starting material to establish the seperation method for analysis of TA and racemic TA.



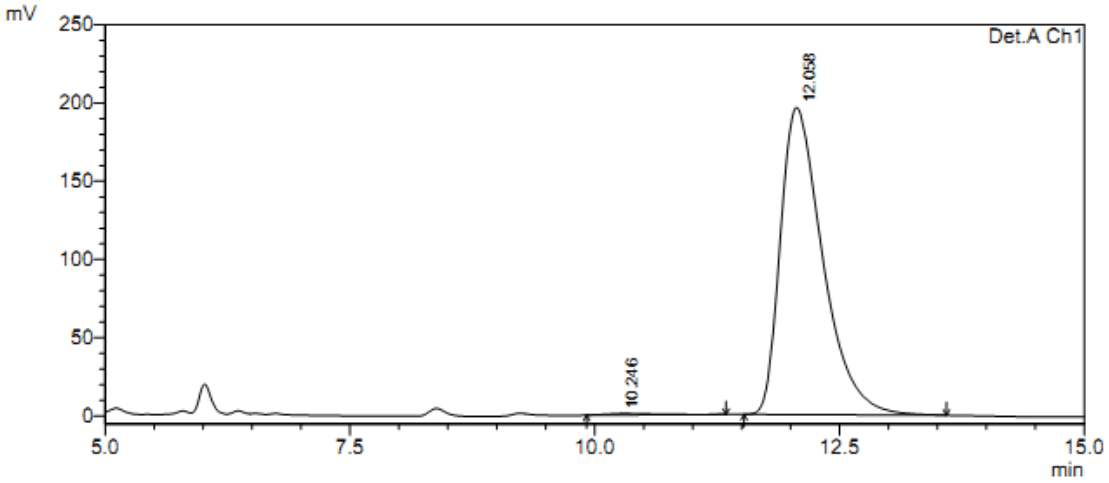
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.887	2611403	104924	50.040	54.921
2	12.596	2607237	86120	49.960	45.079
Total		5218640	191044	100.000	100.000

Racemic TA synthesised from racemic glutamic acid (AD-H, hexane/2-propanol = 85/15, 0.8 mL/min)



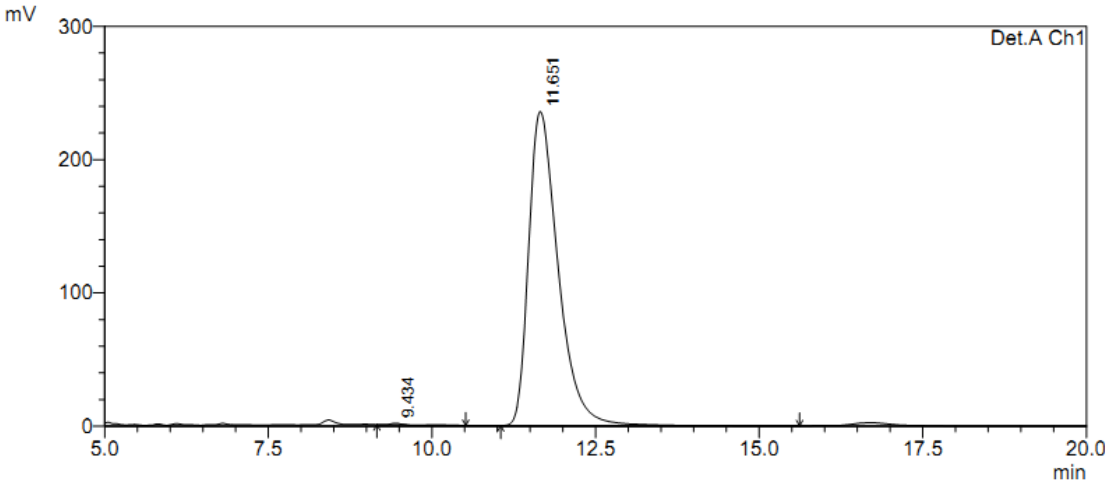
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.246	29602	972	0.498	0.493
2	12.058	5910746	196264	99.502	99.507
Total		5940348	197236	100.000	100.000

TA-0 (AD-H, hexane/2-propanol = 85/15, 0.8 mL/min)



1 Det.A Ch1/254nm

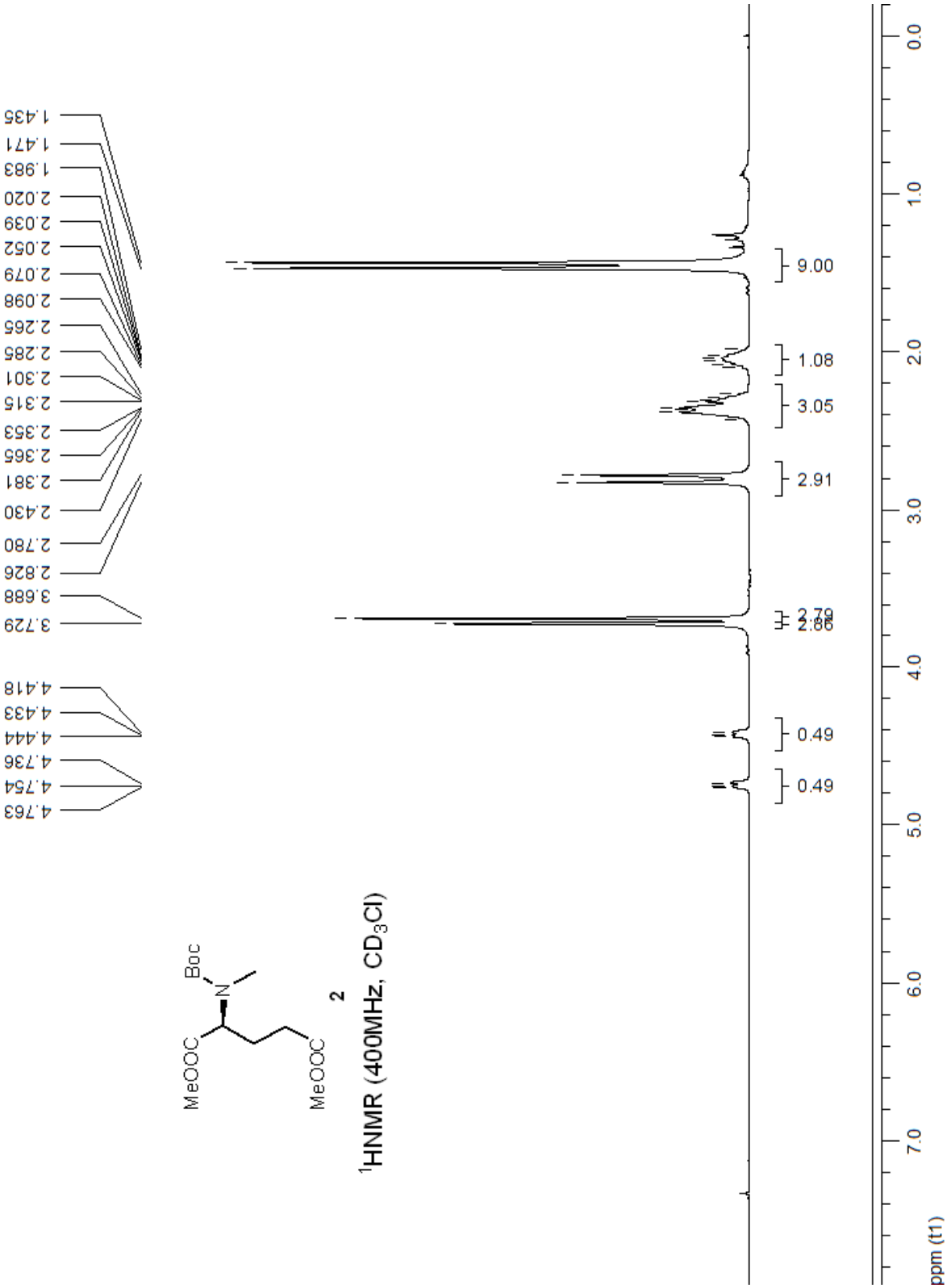
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.434	7187	1268	0.097	0.535
2	11.651	7393433	235781	99.903	99.465
Total		7400620	237049	100.000	100.000

TA-1 (AD-H, hexane/2-propanol = 85/15, 0.8 mL/min)

Part D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2.430
2.780
2.826
3.688
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4.433
4.444
4.736
4.754
4.763
9.00
1.08
3.05
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2.79
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0.49
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1.0
2.0
3.0
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MeOOC
MeOOC
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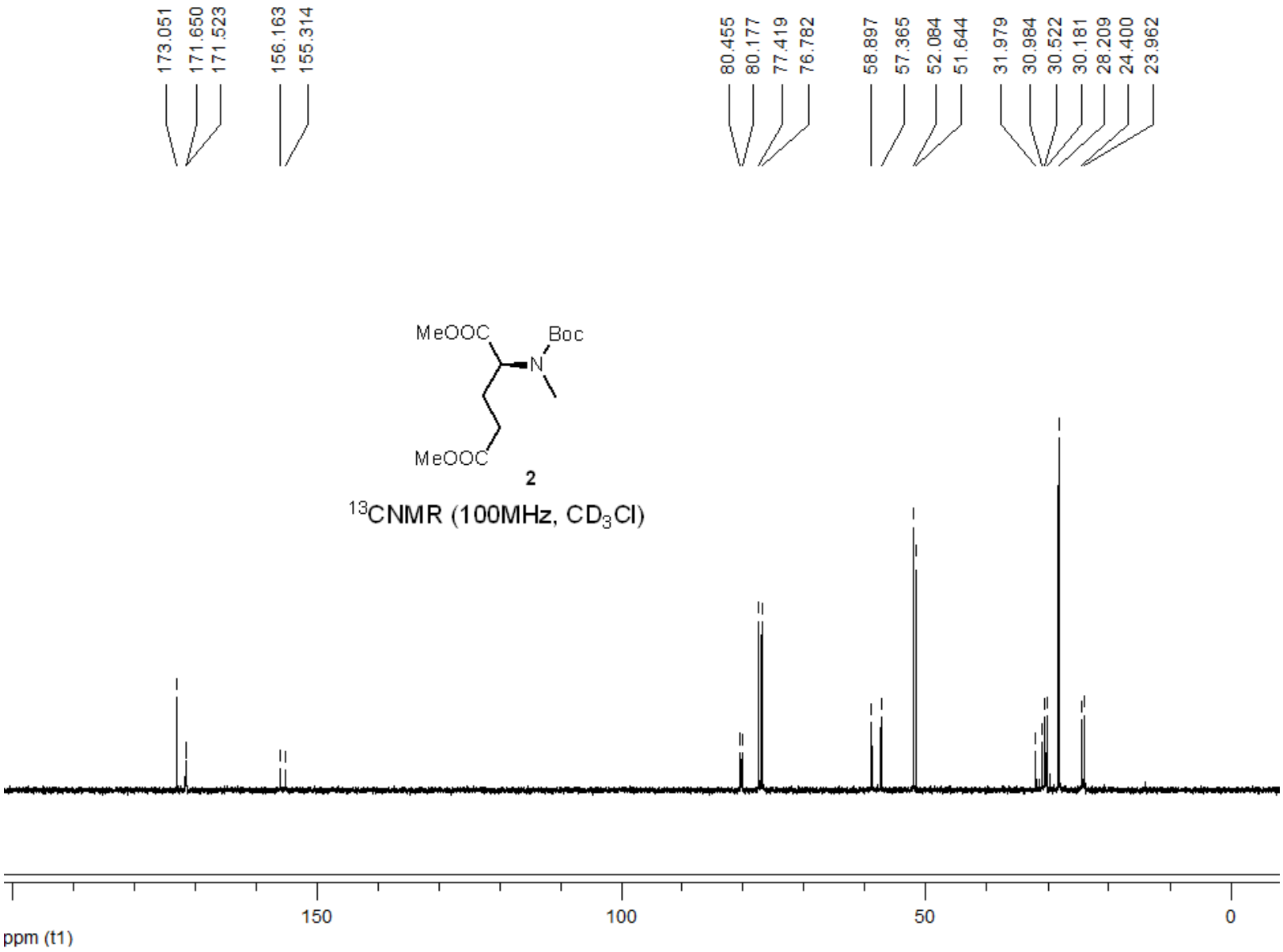
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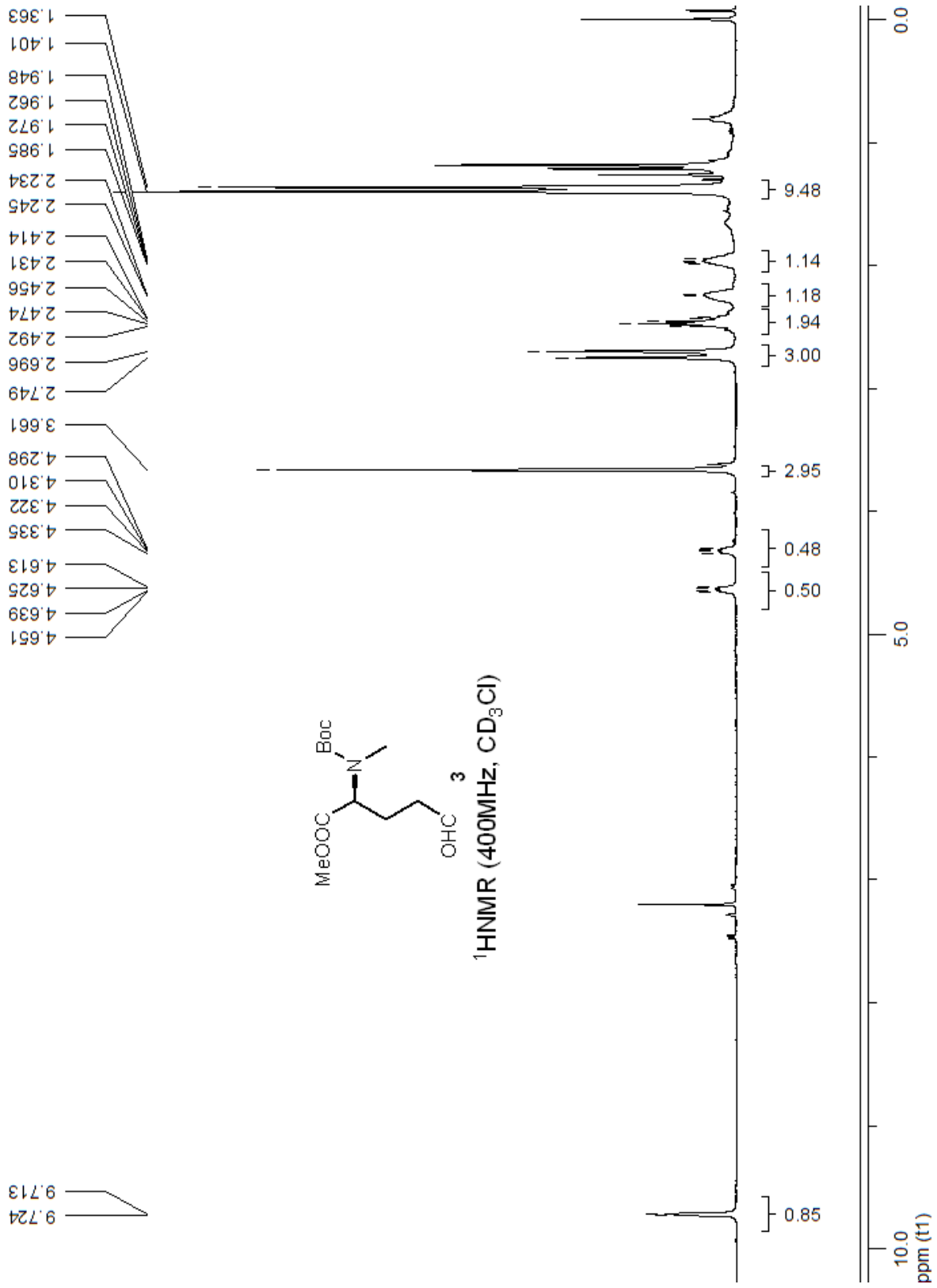
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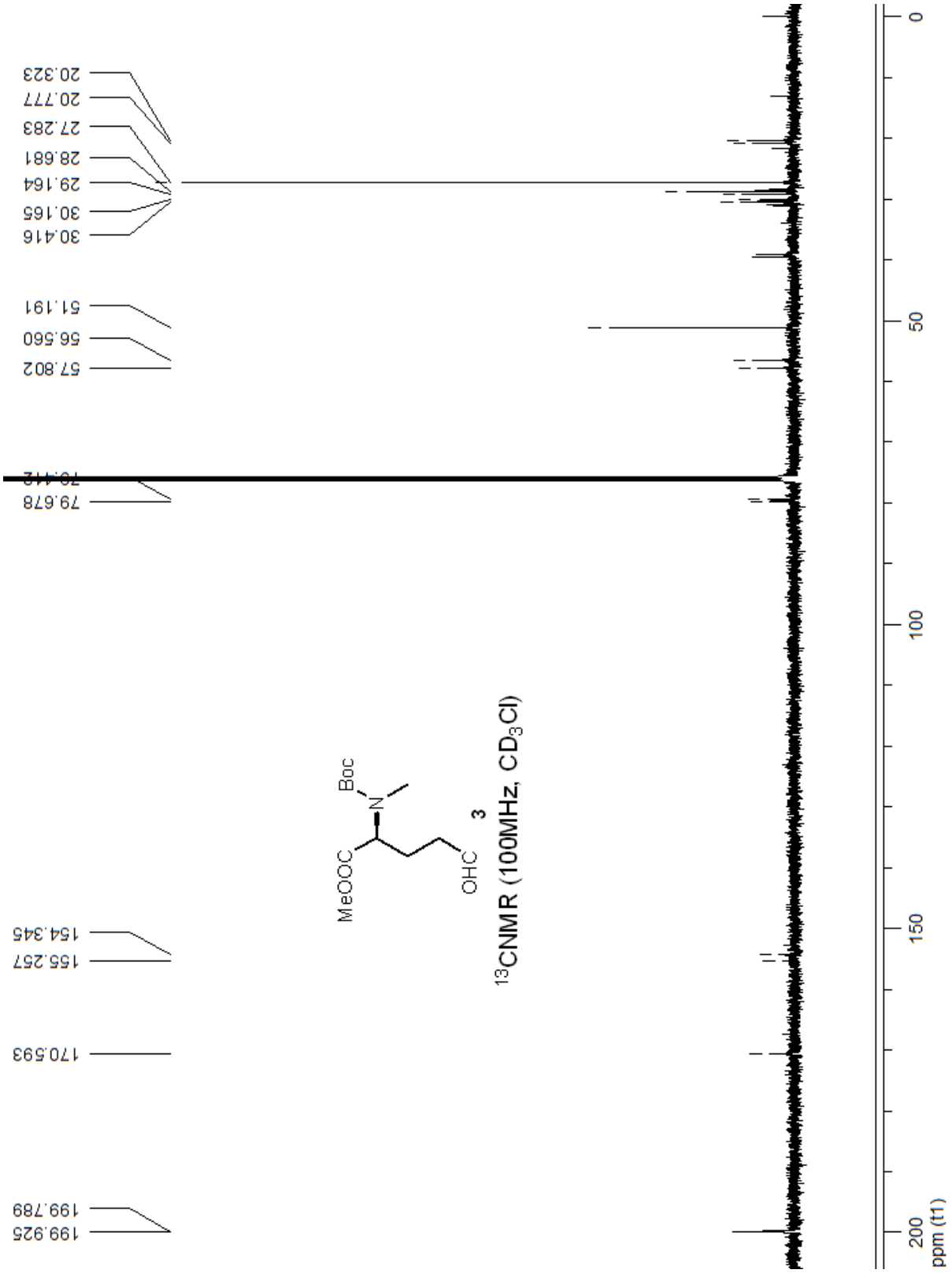
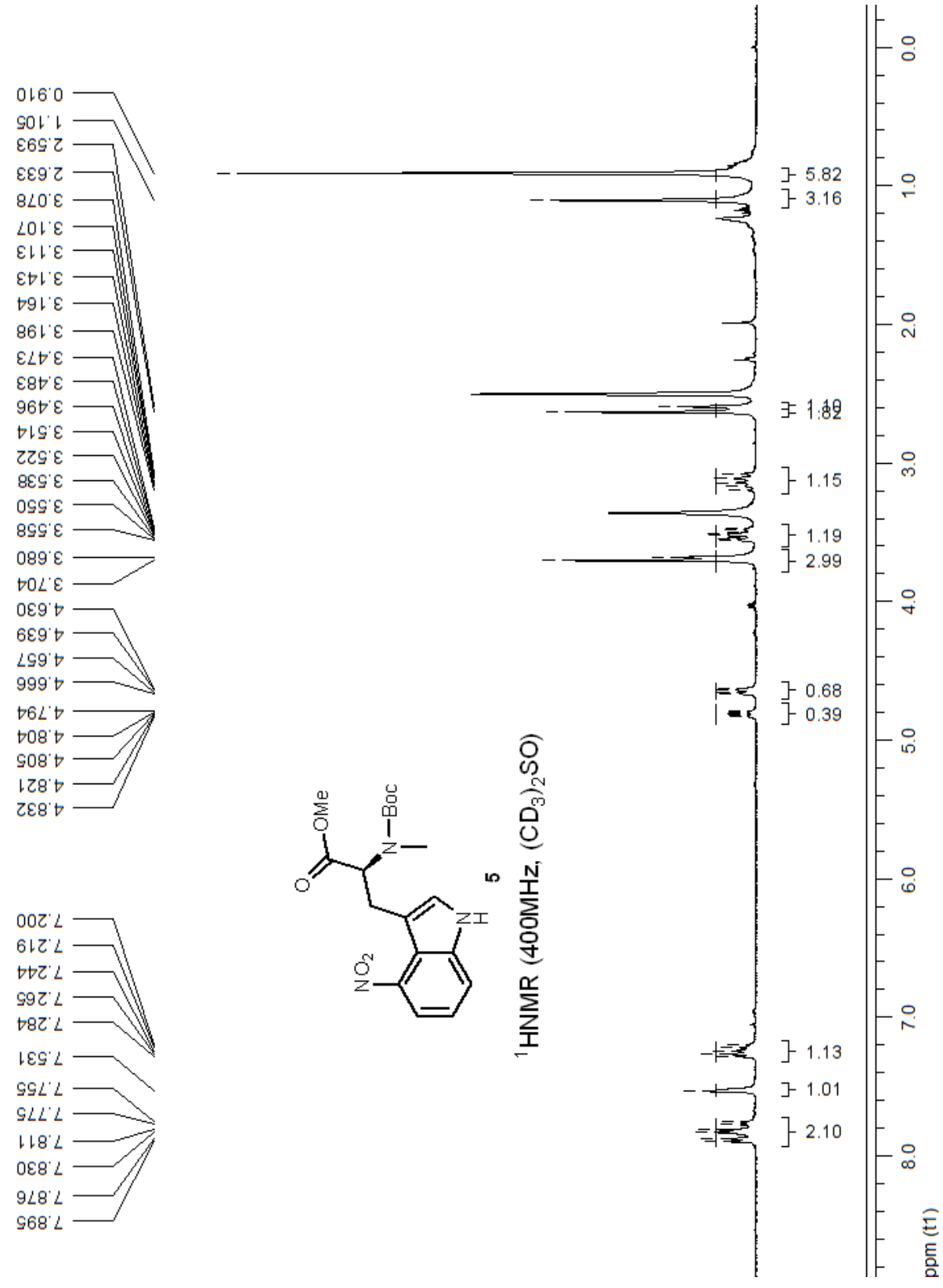
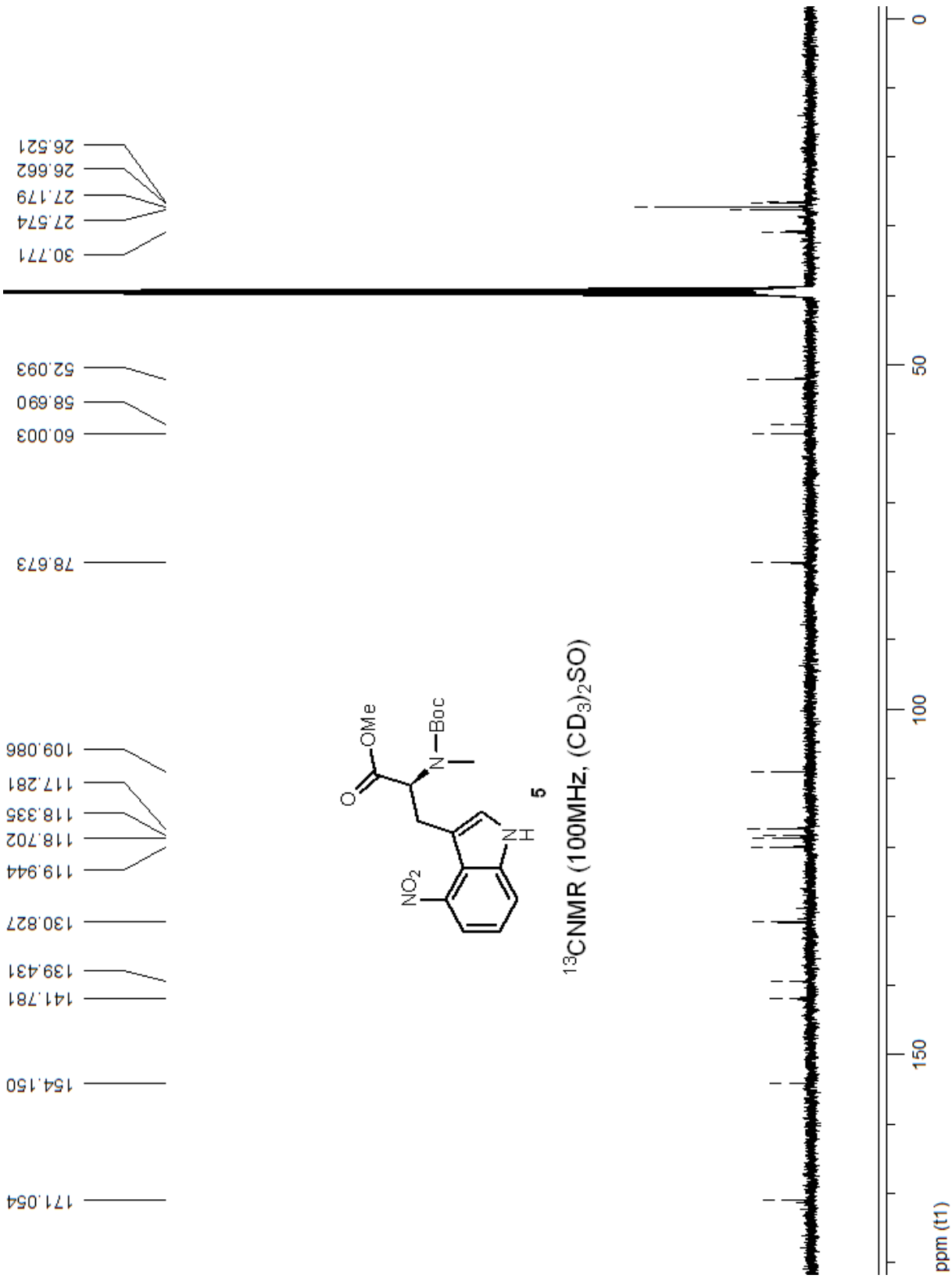
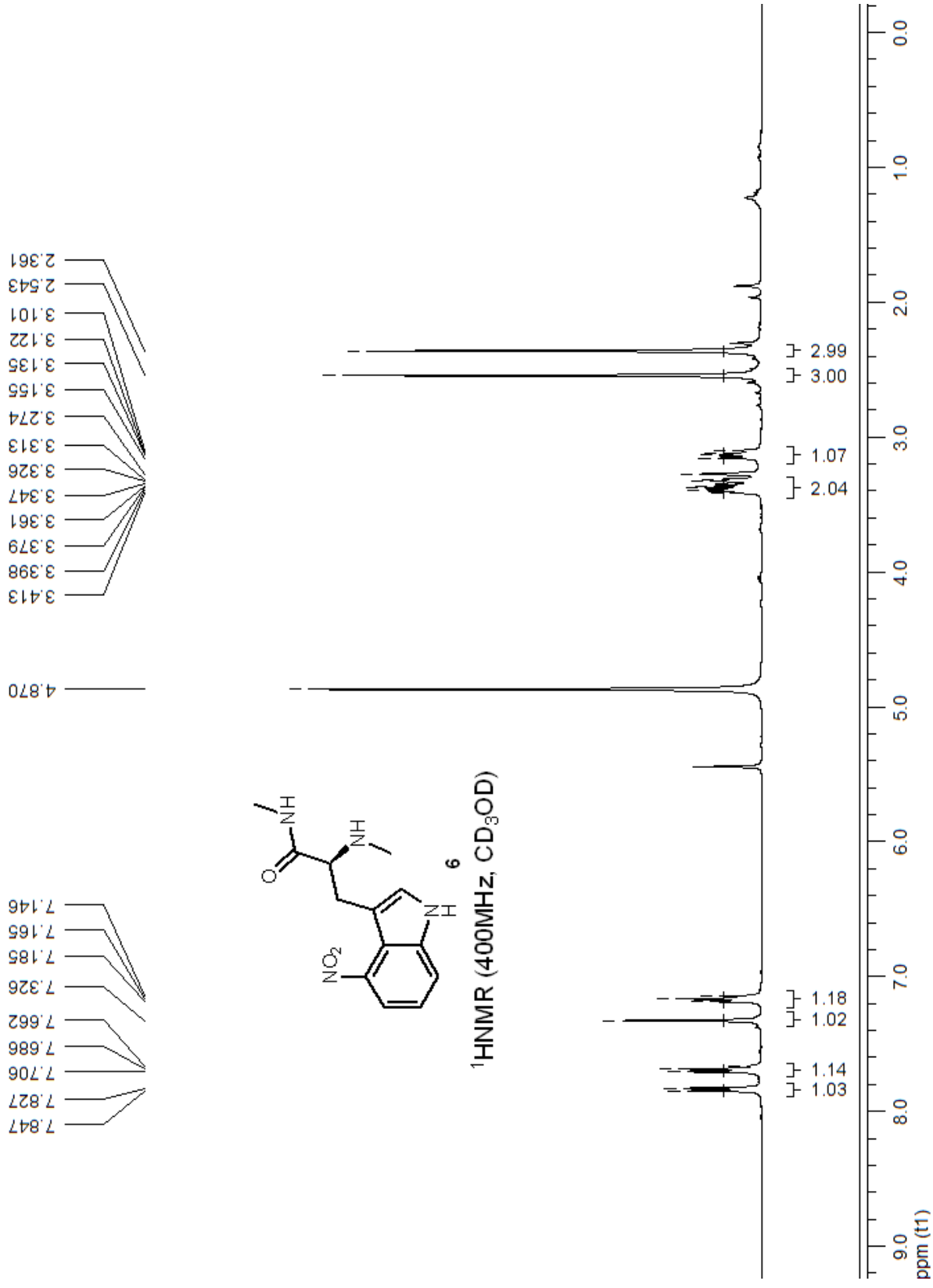
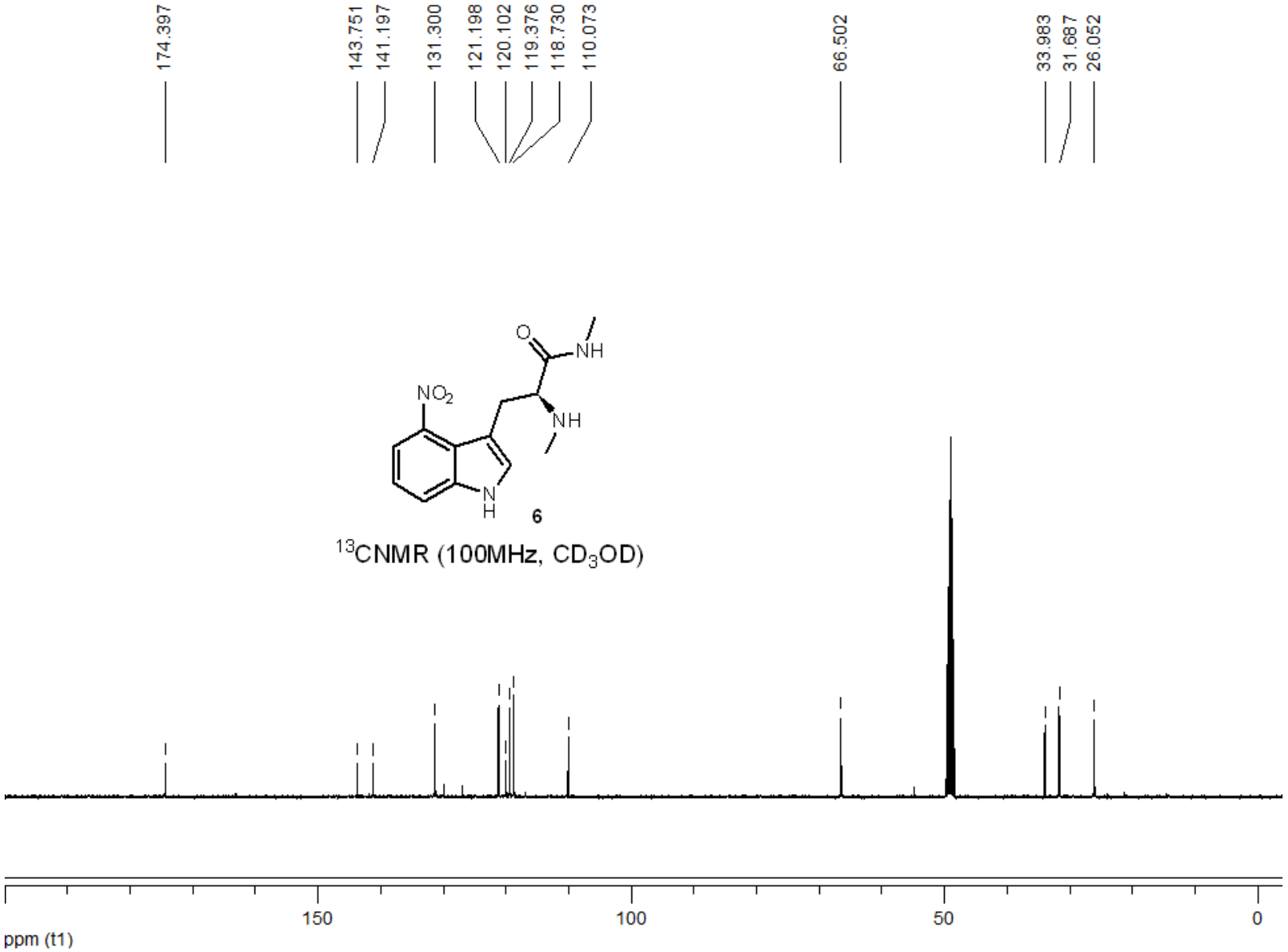
3
1HNMR (400MHz, CD3Cl)


20.323
20.777
27.283
28.681
29.164
30.165
30.416
51.191
56.560
57.802
79.412
79.678
154.345
155.257
170.593
199.789
199.925
Boc
N
MeOOC
OHC
3
^{13}CNMR (100MHz, CD_3Cl)
0
50
100
150
200
ppm (t1)


0.910
1.105
2.593
2.633
3.078
3.107
3.113
3.143
3.164
3.198
3.473
3.483
3.496
3.514
3.522
3.538
3.550
3.558
3.680
3.704
4.630
4.639
4.657
4.666
4.794
4.804
4.805
4.821
4.832
7.200
7.219
7.244
7.265
7.284
7.531
7.755
7.775
7.811
7.830
7.876
7.895
OMe
N—Boc
NO2
H
N
5
1HNMR (400MHz, (CD3)2SO)
5.82
3.16
1.19
1.15
1.19
2.99
0.68
0.39
1.13
1.01
2.10
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (t1)

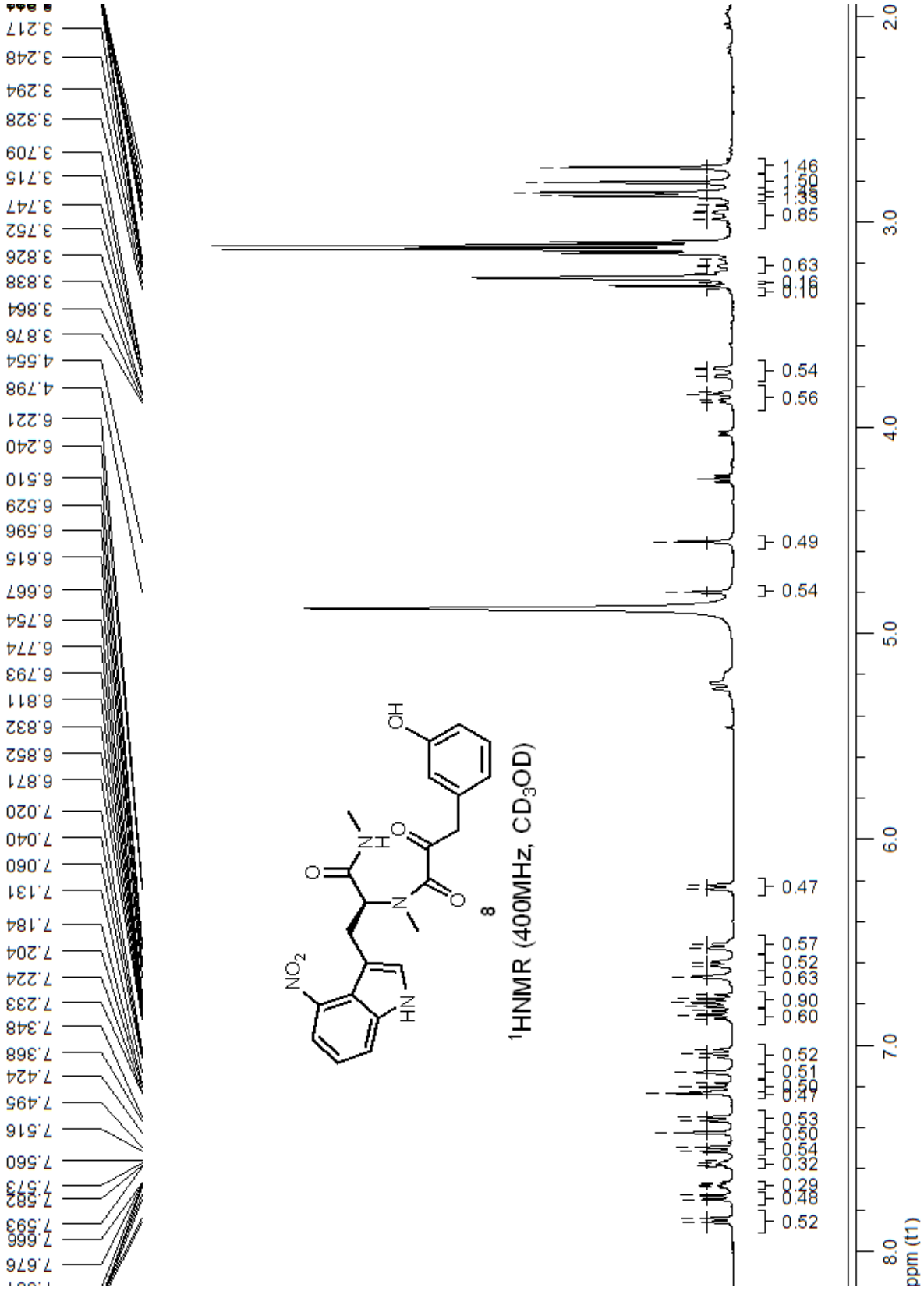

26.521
26.662
27.179
27.574
30.771
52.093
58.690
60.003
78.673
109.086
117.281
118.335
118.702
119.944
130.827
139.431
141.781
154.150
171.054
OMe
N—Boc
NO2
H
N
5
13CNMR (100MHz, (CD3)2SO)
0
50
100
150
ppm (t1)


2.361
2.543
3.101
3.122
3.135
3.155
3.274
3.313
3.326
3.347
3.361
3.379
3.398
3.413
4.870
7.146
7.165
7.185
7.326
7.662
7.686
7.706
7.827
7.847
2.99
3.00
1.07
2.04
1.18
1.02
1.14
1.03
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (f1)
NH
O
NH
NH
NO2
6
1HNMR (400MHz, CD3OD)

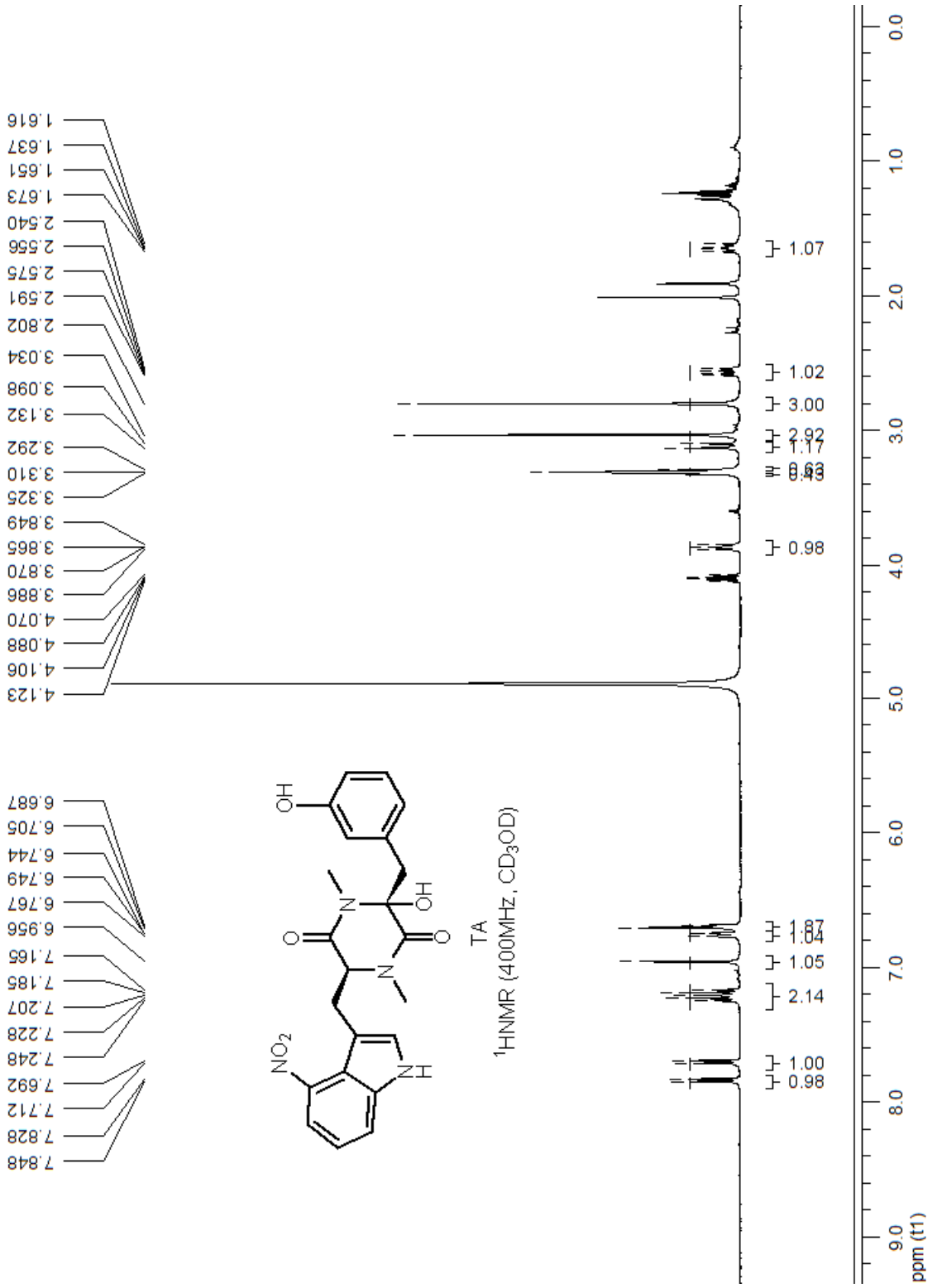


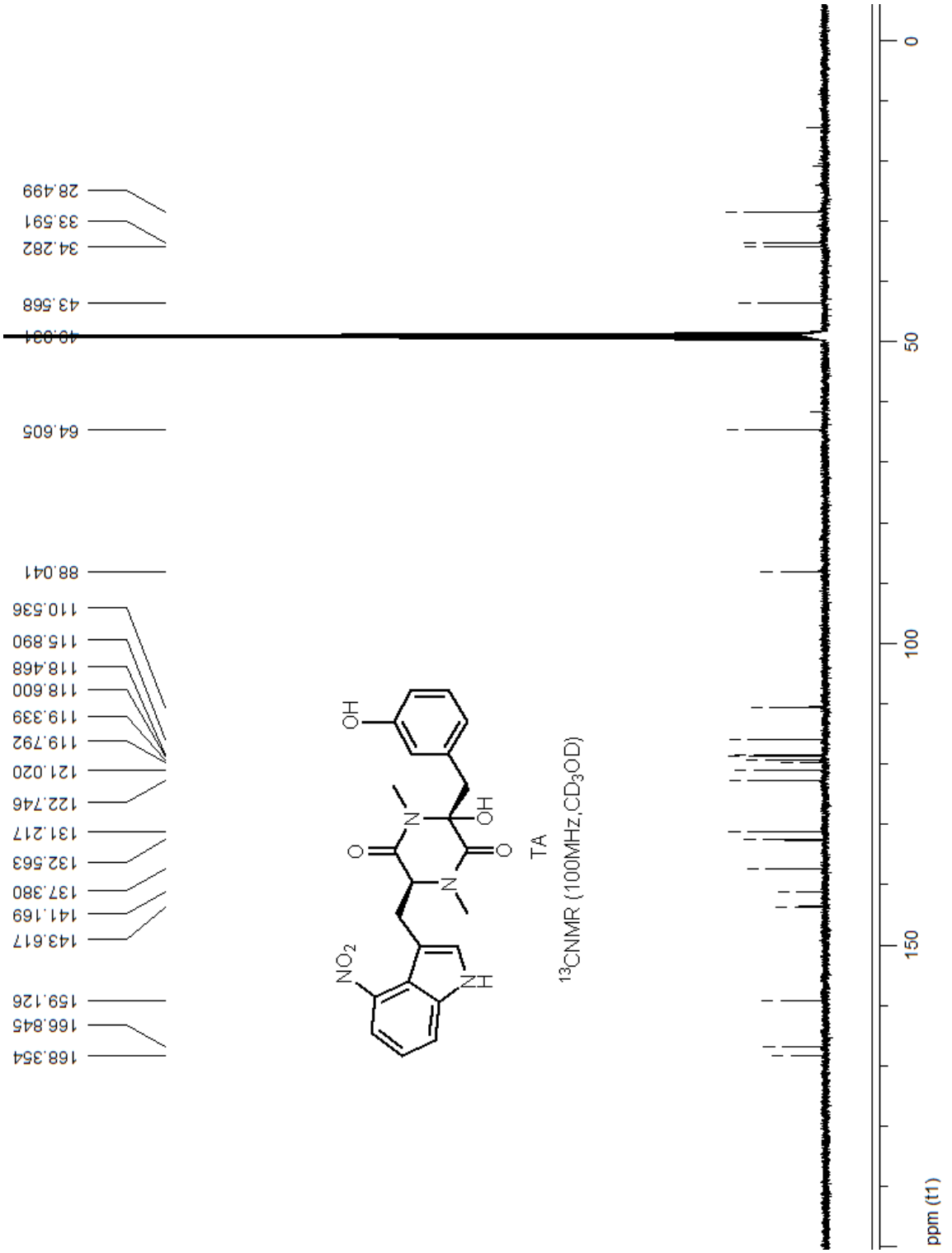
6

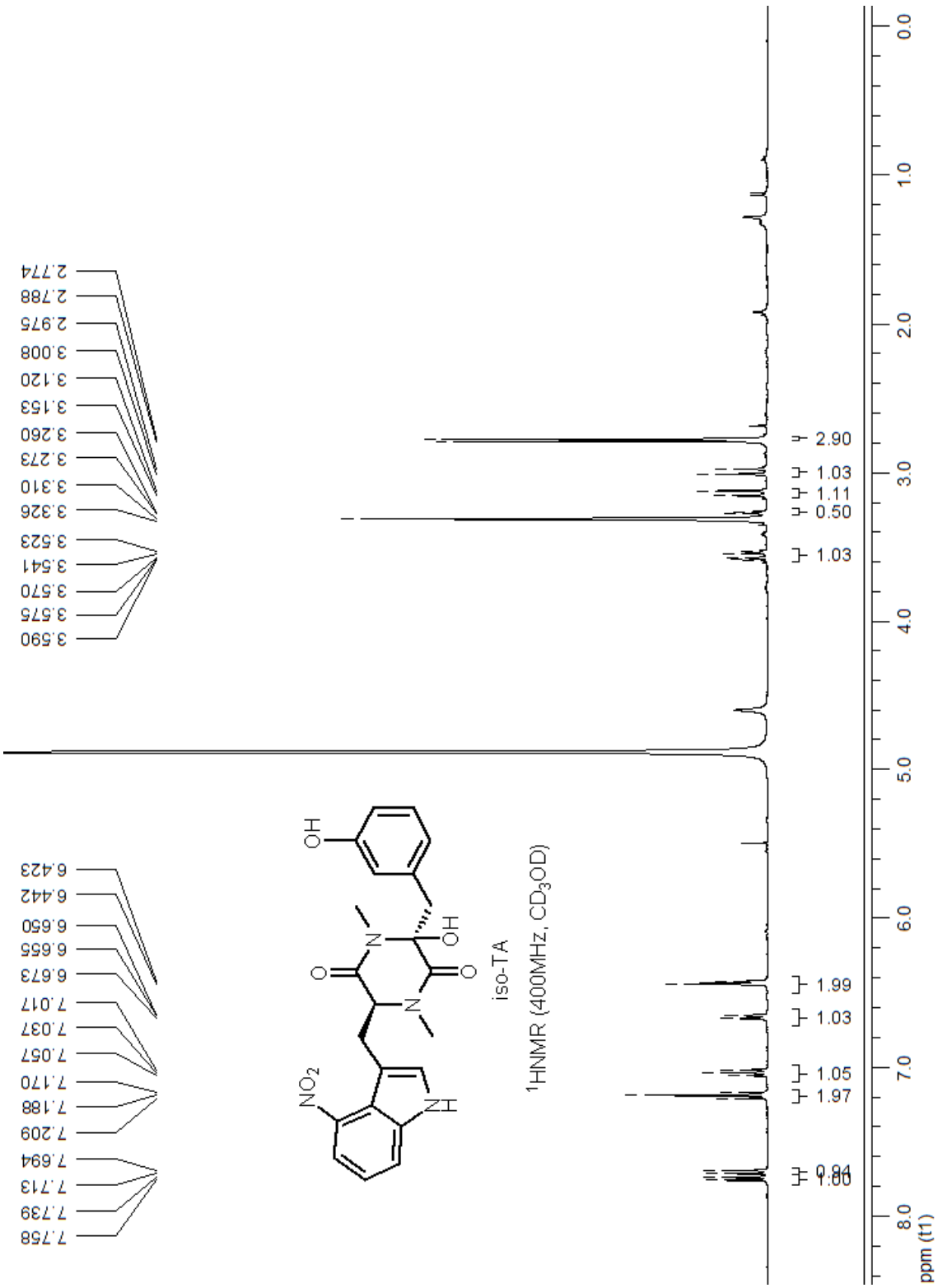
^{13}CNMR (100MHz, CD_3OD)

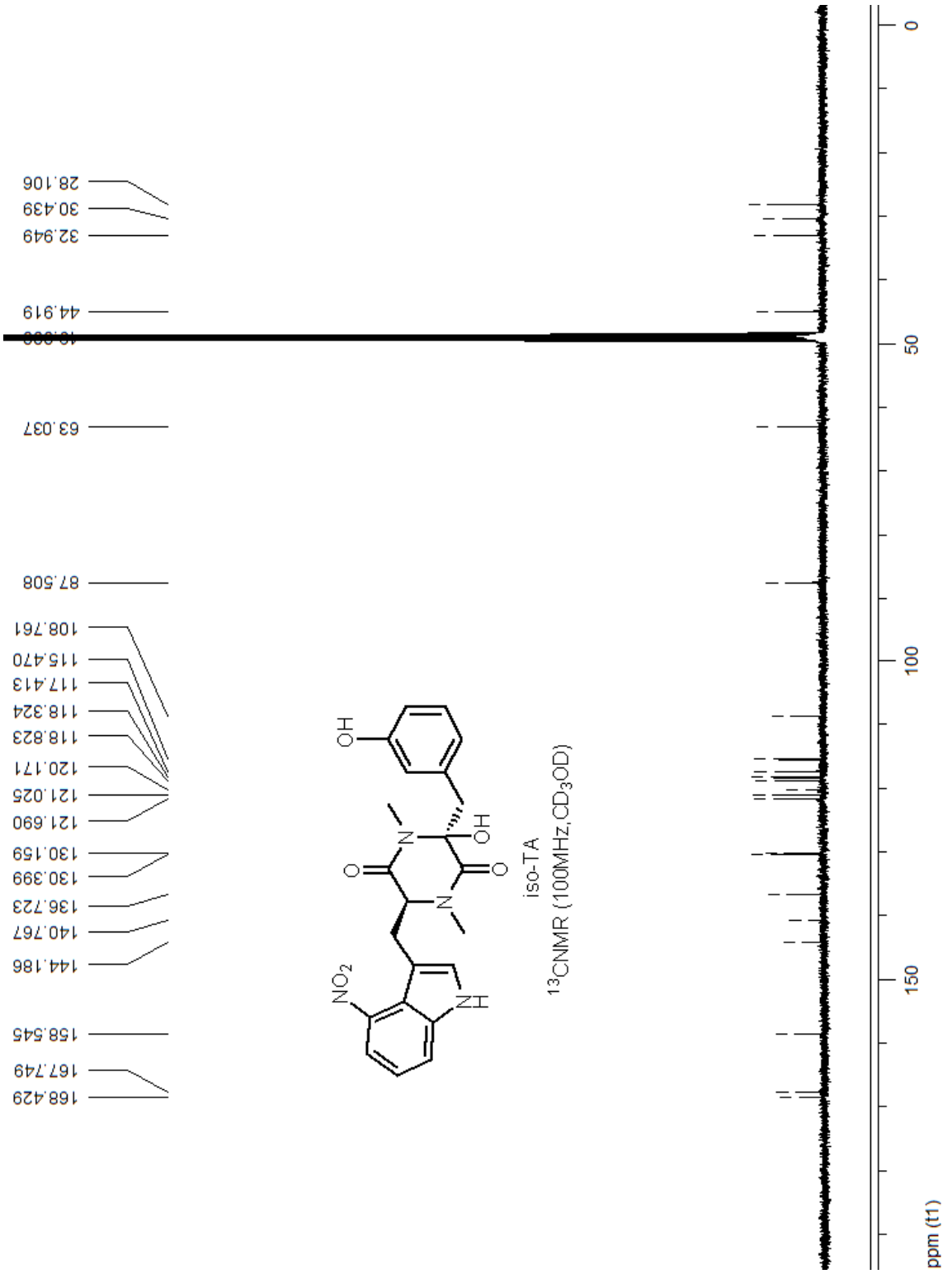

3.217
3.248
3.294
3.328
3.709
3.715
3.747
3.752
3.826
3.838
3.864
3.876
4.554
4.798
6.221
6.240
6.510
6.529
6.596
6.615
6.667
6.754
6.774
6.793
6.811
6.832
6.852
6.871
7.020
7.040
7.060
7.131
7.184
7.204
7.224
7.233
7.348
7.368
7.424
7.495
7.516
7.560
7.573
7.582
7.593
7.666
7.676
1.46
1.50
1.33
0.85
0.63
0.16
0.10
0.54
0.56
0.49
0.54
0.47
0.57
0.52
0.63
0.90
0.60
0.52
0.51
0.47
0.53
0.50
0.54
0.32
0.29
0.48
0.52
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (f1)
OH
O
N
H
O
O
N
O
NO2
HN
8
1HNMR (400MHz, CD3OD)

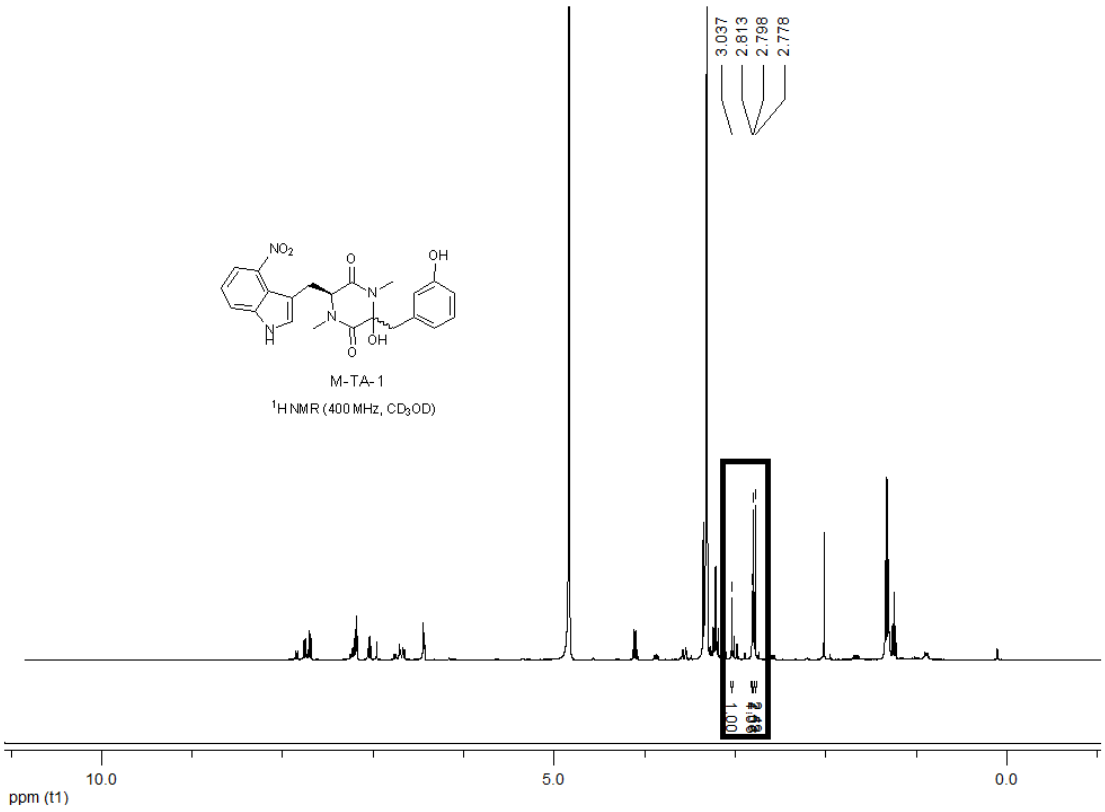
27.030
27.128
30.508
31.737
64.323
66.672
111.121
111.616
115.808
115.935
116.603
116.757
118.519
118.847
119.081
119.186
119.721
119.779
120.417
120.674
121.134
121.167
121.876
122.224
129.616
129.890
130.223
130.817
131.183
132.378
135.256
136.071
140.969
141.252
143.266
144.170
157.781
158.387
170.635
171.140
172.752
OH
O
N
H
O
N
O
NO2
HN
8
13CNMR (100MHz, CD3OD)
50
100
150
ppm (t1)

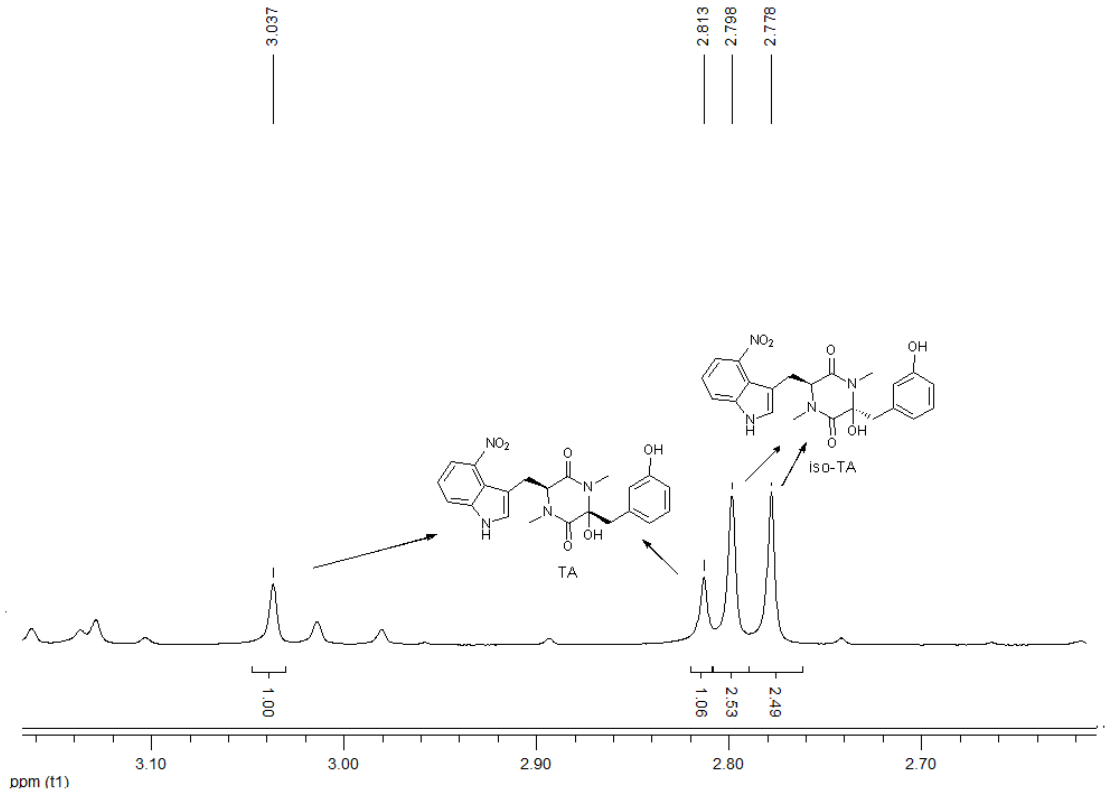

TA
^{1}HNMR (400MHz, CD_3OD)
1.616
1.637
1.651
1.673
2.540
2.556
2.575
2.591
2.802
3.034
3.098
3.132
3.292
3.310
3.325
3.849
3.865
3.870
3.886
4.070
4.088
4.106
4.123
6.687
6.705
6.744
6.749
6.767
6.956
7.165
7.185
7.207
7.228
7.248
7.692
7.712
7.828
7.848
1.07
1.02
3.00
2.92
1.17
0.98
1.87
1.04
1.05
2.14
1.00
0.98
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (f1)

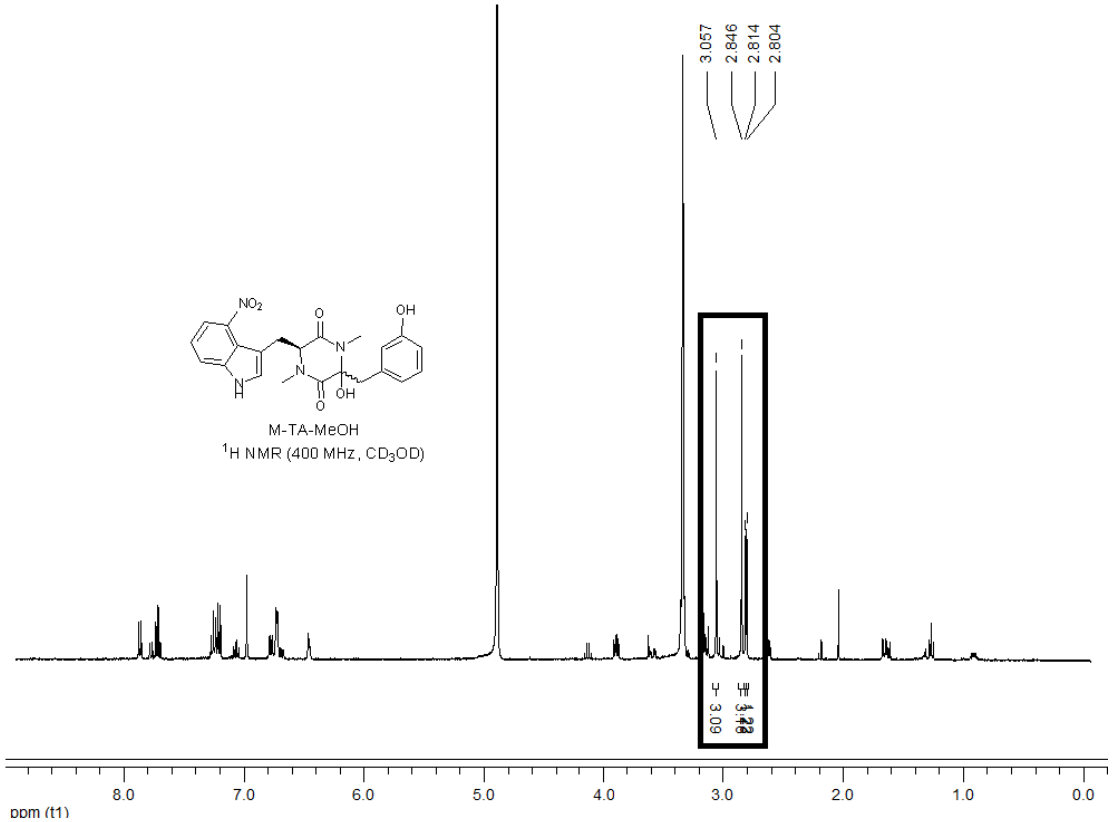

28.499
33.591
34.282
43.568
49.031
64.605
88.041
110.536
115.890
118.468
118.600
119.339
119.792
121.020
122.746
131.217
132.563
137.380
141.169
143.617
159.126
166.845
168.354
OH
OH
O
O
N
N
NO2
NH
TA
13CNMR (100MHz,CD3OD)
0
50
100
150
ppm (t1)

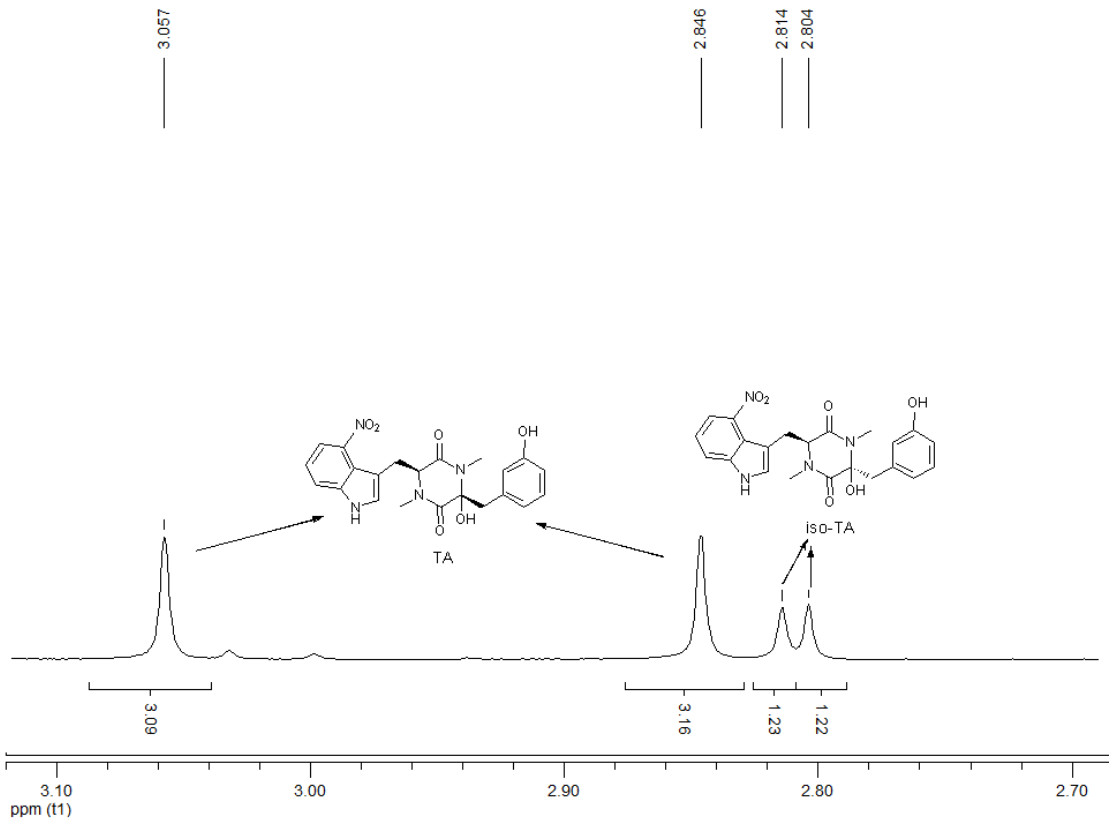

2.774
2.788
2.975
3.008
3.120
3.153
3.260
3.273
3.310
3.326
3.523
3.541
3.570
3.575
3.590
6.423
6.442
6.650
6.655
6.673
7.017
7.037
7.057
7.170
7.188
7.209
7.694
7.713
7.739
7.758
2.90
1.03
1.11
0.50
1.03
1.99
1.03
1.05
1.97
0.84
1.00
OH
N
OH
O
O
N
NO2
NH
iso-TA
1HNMR (400MHz, CD3OD)
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (t1)


28.106
30.439
32.949
44.919
63.037
87.508
108.761
115.470
117.413
118.324
118.823
120.171
121.025
121.690
130.159
130.399
136.723
140.767
144.186
158.545
167.749
168.429
OH
O
N
OH
O
N
NO2
NH
iso-TA
13CNMR (100MHz,CD3OD)
0
50
100
150
ppm (t1)


3.037
2.813
2.798
2.778
M-TA-1
^{1}H NMR (400 MHz, CD_3OD)
10.0
5.0
0.0
ppm (t1)


3.037
2.813
2.798
2.778
TA
iso-TA
1.00
1.06
2.53
2.49
3.10
3.00
2.90
2.80
2.70
ppm (t1)

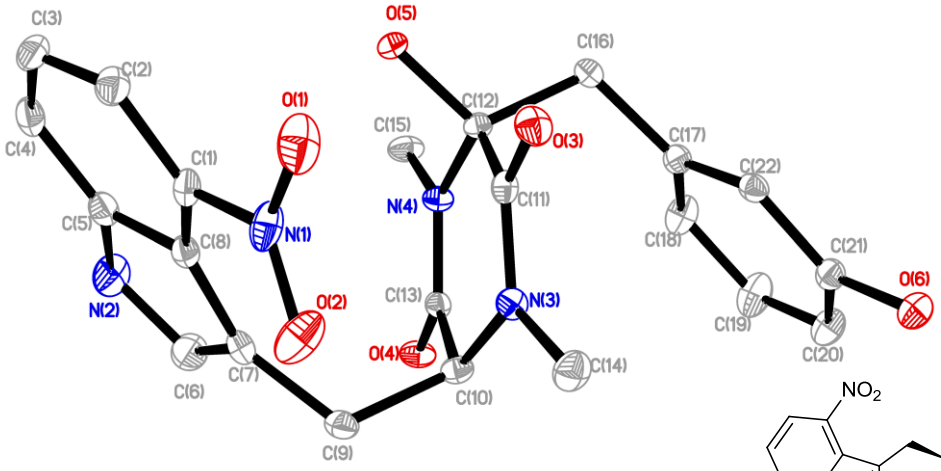

3.057
2.846
2.814
2.804
NO2
OH
M-TA-MeOH
1H NMR (400 MHz, CD3OD)
3.09
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

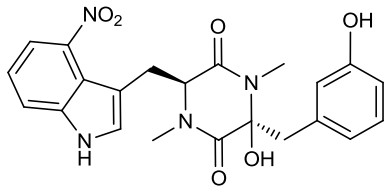

3.057
2.846
2.814
2.804
NO2
OH
TA
iso-TA
3.09
3.16
1.23
1.22
3.10
3.00
2.90
2.80
2.70
ppm (t1)

Part E

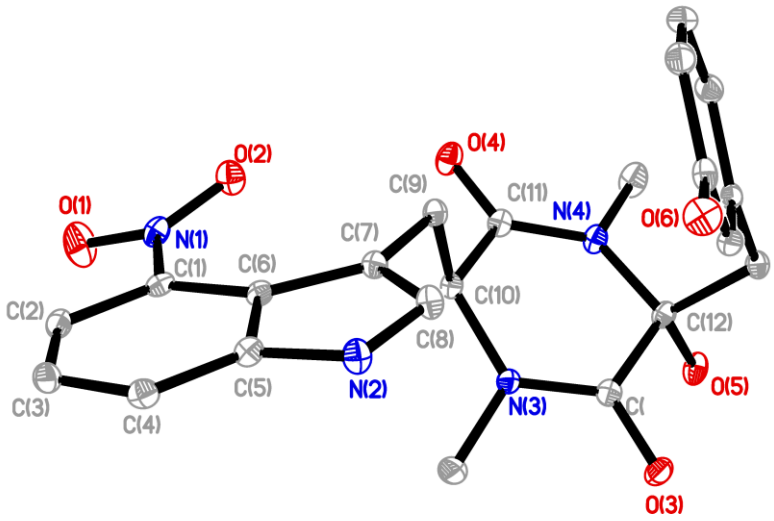
X-Ray Crystallographic Data

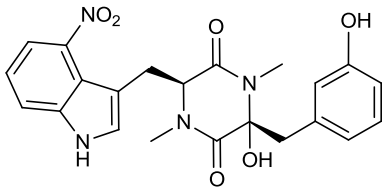
Prism-like specimens of TA and iso-TA were prepared from mixture of methanol and diethyl ether. The X-ray intensity data were measured on a Rigaku 007 saturn 70.





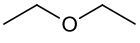
iso-TA

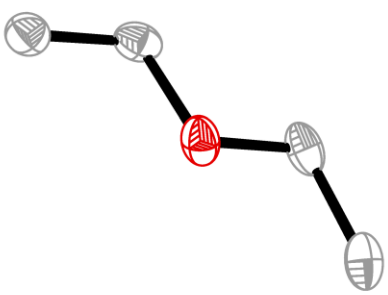




TA

\+





Items	**iso-TA**	**TA**
CCDC deposition number	943364	943363
Empirical formula	$C_{22}H_{22}N_4O_6$	$C_{26}H_{21}N_4O_7$
Formula weight	438.44	511.55
Temperature [K]	113(2)	113(2)
Wavelength [Å]	0.71073	0.71073
Crystal system, Space group	Monoclinic, C2	Triclinic, P-1
a [Å]	14.897(3)	8.057(3)
b [Å]	6.8317(14)	9.258(3)
c [Å]	20.380(4)	17.387(5)
α [°]	90	80.687(10)
β [°]	102.13(3)	79.096(11)
γ [°]	90	87.104(13)
V [Å^3]	2027.8(7)	1256.5(7)
Z	4	2
Calculated density [g/cm^{-3}]	1.436	1.352
Absorption coefficient [mm^{-1}]	0.107	0.099
Crystal size [mm]	0.20 x 0.18 x 0.12	0.20 x 0.18 x 0.12
θ range [°]	2.77 to 26.01	2.23 to 27.95
Limiting indices	$-18 \le h \le 17$	$-10 \le h \le 10$
	$-8 \le k \le 8$	$-12 \le k \le 12$
	$-24 \le l \le 25$	$-22 \le l \le 22$
Reflections collected / unique	8786 / 3887	15845 / 5974
Max. and min. transmission	0.9873 and 0.9790	0.9882 and 0.9804
Refinement method	on F^2	on F^2
Parameters	297	340
Goodness of fit	0.975	1.050
*R*1 indices (obsd data)	0.0483	0.0436
w*R*2 indices (obsd data)	0.1041	0.1183
Largest diff peak/hole [e Å^{-3}]	0.203/-0.297	0.637 /-0.375