Highly Efficient Synthesis of Enantiomerically Pure 2-Hydroxymethylaziridines by Enzymatic Desymmetrization

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Supporting Information

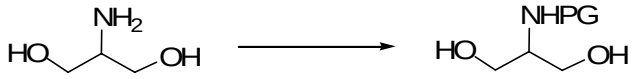
1. **Experimental Procedures**
2. **NMR spectra**
3. **Figure 1**

General Experimental

All reagents purchased were used as received. PPL (pig pancreatic lipase) was purchased from Sigma-Aldrich. Serinol was purchased from 3B Medical Systems. Tetrahydrofuran was distilled prior to use from sodium using benzophenone ketyl as indicator. Methylene chloride and triethylamine were distilled from calcium hydride prior to use.

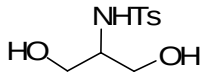
All NMR spectra were obtained on a 300-MHz Bruker NMR system using deuterochloroform with residual chloroform as the internal reference (δ 7.26 ppm, ^{1}H; δ 77.0 ppm, ^{13}C), dimethylsulfoxide-d6 with residual dimethylsulfoxide as the internal reference (δ 2.49 ppm, ^{1}H; δ 39.5 ppm, ^{13}C) or methanol-d4 with residual methanol as the internal reference (δ 3.30 ppm, ^{1}H; δ 49.0 ppm, ^{13}C). All chemical shifts are reported in ppm (δ), and multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet). All coupling constants (*J*) are reported in Hertz. Infrared spectra (IR) were obtained using a Magna-IR^{TM} 550 spectrometer. Mass spectral data were obtained from the Purdue University Mass Spectrometry Service, West Lafayette, IN. The low resolution EI and CI spectra were obtained using a Finnigan 4000 mass spectrometer with a Nova 4 data system with the molecular ion designated as "M". The high resolution mass spectra were obtained on a Kratos MS-50 instrument. Elemental analyses were conducted by Purdue University Microanalytical Laboratory. Optical purities of chiral compounds were analyzed by high performance liquid chromatography (HPLC) using a Beckman System Gold and Chiralcel OD column. Column chromatography was conducted using silica gel grade 60 (230-400 mesh) and alumina basic (150 mesh). Thin layer chromatography was performed using Analtech glass plates precoated with silica gel (250 microns). Visualization of the plates was accomplished using UV or ninhydrin solution. Melting points were obtained on a Mel-Temp II capillary melting point apparatus and are uncorrected.

General Procedure for the preparation of *N*-Protected Serinol 1a-f



To a solution of serinol (1.82 g, 20 mmol) in EtOH (60 mL) was added NEt_3 (3.1 mL, 22 mmol) followed by the corresponding electrophiles (TsCl, 2, 4, 6-MesitylSO_2Cl, FmocCl, CbzCl or TrCl, 20 mmol) at 0 ^{0}C. (Boc_2O was used without NEt_3 for the preparation of 1e) The reaction mixture was stirred for 2 h at room temperature. EtOH was removed under reduced pressure. Acetone (100 mL) was added to the residue, the resulting precipitate (triethyl amine hydrochride salt) was filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (5%-10% methanol in dichloromethane) to give the desired products 1a-1f.

2-(p-Toluenesulfonylamino)propane-1,3-diol 1a



Yield: 90%, white solid

Mp: 103-104 ^{0}C

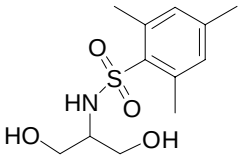
R_f: 0.25 (CH_2Cl_2/CH_3OH=10/1)

^{1}H NMR (300 MHz, DMSO-*d6*) δ 7.71 (2H, d, *J*=8.1 Hz), 7.34 (d and b, 2H and 1H, J=8.1 Hz), 4.54 (b, 2H), 3.30 (d, 4H, *J*=5.1 Hz), 3.03 (m, 1H), 2.36(S, 3H)

^{13}C NMR (75 MHz, DMSO-*d6*) δ 142.34, 139.07, 129.46, 126.57, 60.17, 56.83, 21.00

MS (EI): m/z 246 $(M + H + Na)^+$.

2-(2,4,6-Mesitylenesulfonylamino)propane-1,3-diol 1b



Yield: 84%, white solid

Mp: 107-108 ^{0}C

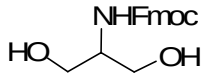
R_f: 0.27 (CH_2Cl_2/CH_3OH=10/1)

^{1}H NMR (300 MHz, DMSO-*d6*) δ 7.16 (d, 1H, *J*=8.1 Hz), 6.99 (s, 1H), 4.54 (t, 2H, *J*=5.1 Hz), 3.31 (t, 4H, *J*=5.1 Hz), 3.00 (m, 1H), 2.57 (s, 6H), 2.33 (s, 3H)

^{13}C NMR (75 MHz, DMSO-*d6*) δ 141.22, 138.37, 135.52, 131.59, 60.25, 56.32, 22.66, 20.44

MS (EI): m/z 274$(M + H + Na)^+$.

2-(9-Fluorenylmethoxycarbonylamino)propane-1,3-diol 1c



Yield: 89%, white solid

Mp: 144-145 ^{0}C

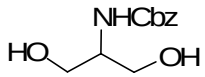
R_f: 0.30 (CH_2Cl_2/CH_3OH=10/1)

^{1}H NMR (300 MHz, DMSO-*d6*) δ 7.86 (d, 2H, *J*=7.9 Hz), 7.71 (d, 2H, *J*=7.9), 7.40 (t, 2H, *J*=7.5), 7.32 (t, 2H, *J*=7.5), 6.95 (d, 1H, *J*=4.2), 4.60 (b, 2H), 4.26 (m, 3H), 3.42 (m, 5H)

^{13}C NMR (75 MHz, DMSO-*d6*) δ 155.96, 143.95, 140.73, 127.62, 127.07, 125.28, 120.11, 65.35, 60.46, 54.99, 46.75

MS (EI): m/z 336(M + H +Na)$^+$.

2-(Benzyloxycarbonylamino)propane-1,3-diol 1d[1]



Yield: 83%, white solid

Mp: 107 ^{0}C

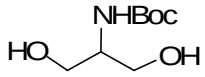
R_f: 0.30 (CH_2Cl_2/CH_3OH=10/1)

^{1}H NMR (300 MHz, DMSO-*d6*) δ 7.35 (b, 5H), 6.88 (d, 1H, *J*=6.6), 5.01 (s, 1H), 4.61 (b, 2H), 3.40 (b, 5H)

^{13}C NMR (75 MHz, DMSO-*d6*) δ 155.97, 137.25, 128.37, 127.78, 65.21, 60.50, 55.03

MS (EI): m/z 225(M^+).

2-(t-Butoxycarbonylamino)propane-1,3-diol 1e[2]



Yield: 75%, white solid

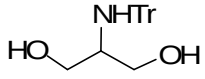
Mp: 84-85 ^{0}C

R_f: 0.35 (CH_2Cl_2/CH_3OH=10/1)

^{1}H NMR (300 MHz, DMSO-*d6*) δ 6.28 (d, 1H, *J*=5.7), 4.51 (t, 2H, *J*=4.9), 3.35 (b, 5H), 1.36 (s, 9H)

^{13}C NMR (75 MHz, DMSO-*d6*) δ 155.29, 77.53, 60.49, 54.30, 28.25

2-(Triphenylmethylamino)propane-1,3-diol 1f



Yield: 66%, white solid

Mp: 122-124 ^{0}C

R_f: 0.60 (CH_2Cl_2/CH_3OH=10/1)

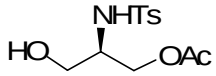
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, 6H, *J*=7.2), 7.30 (m, 9H), 3.41 (dd, 2H, *J*=3.3, 10.8), 3.02 (dd, 2H, *J*=6.6, 10.8), 2.76 (m, 1H), 2.17 (b, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 146.48, 128.60, 127.95, 127.74, 126.57, 64.66, 53.48

General Procedure for the Enzymatic Desymmetrization of N-protected-Serinols 1a-f

To a solution of N-protected serinol (1mmol) in vinyl acetate (10 or 20 mL) was added PPL (100 mg or 300 mg) at room temperature. When the starting material was consumed (as judged by TLC monitoring), the reaction was stopped by removing PPL via filtration. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (2/1= EtOAc/hexanes) to afford the corresponding monoacetates **2a-f**. (See Table 1 for chemical yield and enantiomeric ratios).

3-Acetoxy-2-(p-toluenesulfonylamino)propan-1-ol 2a



Mp: 90-92 ^{0}C

R_f: 0.50 (EtOAc/ Hexane= 2/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, 2H, *J*=8.4), 7.25 (d, 2H, *J*=8.4), 5.92 (d, 1H, *J*=7.8), 4.00 (m, 2H), 3.50 (m, 3H), 3.23 (b, 1H), 2.37 (s, 3H), 1.85 (s, 3H)

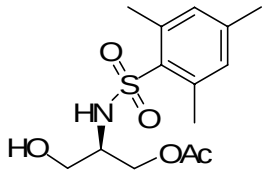
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.20, 143.43, 137.39, 129.59, 126.84, 62.81, 61.60, 53.67, 21.32, 20.44

MS (EI): m/z 310 $(M + H + Na)^+$.

$[\alpha]^{20}_D$= -0.9 (c=1.0, $CHCl_3$)

HPLC (Chiralcel OD column, 15% 2-propanol in hexanes, 0.8 mL/min, λ=254 nm): t_R= 21.7, 23.9(major)

3-Acetoxy-2-(2, 4, 6-mesitylenesulfonylamino)propan-1-ol 2b



Mp: 94-95 ^{0}C

R_f: 0.56 (EtOAc/ Hexane= 2/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (s, 2H), 5.72 (d, 2H, *J*=8.7), 4.01 (m, 2H), 3.57 (b, 2H), 3.43 (m, 1H), 2.60 (s, 6H), 2.26 (s, 3H), 1.87 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.13, 142.27, 138.90, 134.01, 131.89, 62.96, 61.59, 53.32, 22.74,

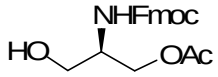
20.77, 20.42

MS (EI): m/z 338 $(M + H + Na)^+$.

$[\alpha]_D$= -6.0 (c=1.0, EtOAc)

HPLC (Chiralcel OD column, 10% 2-propanol in hexanes, 1.0mL/min, λ=254 nm): t_R= 18.3, 20.8 (major) min

3-Acetoxy-2-(9-fluorenylmethoxycarbonylamino)propan-1-ol 2c



Mp: 133-134 ^{0}C

R_f: 0.48 (EtOAc/ Hexane= 2/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, 2H, *J*=7.5), 7.58 (d, 2H, *J*=7.5), 7.40 (t, 2H, *J*=7.5), 7.32 (t, 2H, *J*=7.5), 5.28 (d, 1H, *J*=7.5), 4.42 (d, 2H, *J*=6.6), 4.21 (s, 3H), 3.94 (b, 1H), 3.66 (b, 2H), 2.56 (b, 1H), 2.01(s, 3H)

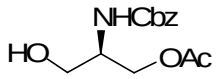
^{13}C NMR (75 MHz, $CDCl_3$) δ 171.47, 156.24, 143.73, 141.29, 127.71, 127.04, 124.95, 119.97, 66.83, 62.70, 61.59, 51.52, 47.15, 20.79

MS (EI): m/z 378 $(M + H + Na)^+$

$[\alpha]^{20}_D$= -6.7 (c=1.0, EtOAc)

HPLC (Chiralcell OD column, 20% 2-propanol in hexanes, 1.0 mL/min, λ=254 nm): t_R= 16.1 (major), 27.5

3-Acetoxy-2-(benzyloxycarbonylamino)propan-1-ol 2d



Mp: 55 ^{0}C

R_f: 0.40 (EtOAc/ Hexane= 2/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (b, 5H), 5.28 (b, 1H), 5.10 (s, 2H), 4.20 (m, 2H), 3.96 (m, 1H), 3.65 (m, 2H), 2.05 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.35, 156.24, 136.08, 128.46, 128.15, 128.03, 66.92, 62.87, 61.50, 51.48, 20.68

IR (NaCl) 3328 (m), 2923 (m), 1699 (s), 1531 (m), 1231 (s), 1039 (m)

MS (EI): m/z 267 (M^+).

Element Analysis: $C_{13}H_{17}NO_5$; Calculated: C, 58.42; H, 6.41; N, 5.24; Found: C, 58.57; H, 6.34; N, 5.05

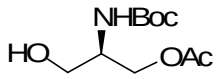
$[\alpha]^{20}_D$= -7.4 (c=1.0, EtOAc)

HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 0.8 mL/min, λ=215 nm): t_R= 55 min (no

separation)

HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 1.0 mL/min, λ=215 nm): t_R= 39.7 (major), 42.2 min for the corresponding (*R*)-MTPA ester of **2d**.

3-Acetoxy-2-(t-butoxycarbonylamino)propan-1-ol 2e[2]



R_f: 0.62 (EtOAc/ Hexane= 2/1)

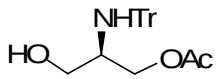
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.14 (d, 1H, *J*=8.4), 4.13 (d, 2H, *J*=5.7), 3.83 (b, 1H), 3.59 (m, 2H), 2.03 (s, 3H), 1.39 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.34, 155.78, 79.81, 63.07, 61.53, 50.92, 28.20, 25.07, 20.71

HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 1.0 mL/min, λ=215 nm): t_R= 11.9 min (no separation)

HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 1.0 mL/min, λ=215 nm): t_R= 11.1 (major), 13.7 for the corresponding (*R*)-MTPA ester of 2e

3-Acetoxy-2-(triphenylmethylamino)propan-1-ol 2f



R_f: 0.52 (EtOAc/ Hexane= 1/2)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (6H, *J*=7.2), 7.30 (t, 6H, *J*=7.2), 7.21 (t, 3H, *J*=7.2), 3.96 (dd, 1H, *J*=3.9, 11.4), 3.57 (dd, 2H, *J*=6.9, 11.1), 3.28 (dd, 1H, *J*=3.0, 11.1), 2.89 (m, 1H), 2.67 (dd, 1H, *J*=5.4, 11.4), 2.23 (b, 2H), 2.01 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.38, 146.47, 128.48, 127.94, 126.51, 70.81, 63.73, 61.05, 52.28, 20.82

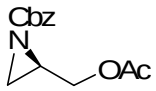
HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 1.0 mL/min, λ=215 nm): t_R= 7.5, 8.7 min (racemic)

(*R*)-N-benzyloxycarbonyl-2-acetoxymethylaziridine 3

To a solution of lipase product **2d** (1.07 g, 4 mmol) in CH_2Cl_2 (20 mL) was added NEt_3 (556 μL, 4 mmol) and MsCl (310 μL, 4 mmol) at 0 ^{0}C. The reaction mixture was stirred for 10 min and then concentrated under reduced pressure. EtOAc (100 mL) was added to the residue and the organic solution was washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated to afford the mesylate as a colorless oil, which used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) 7.35 (b, 5H), 5.96 (b, 1H), 5.11 (s, 2H), 4.20 (m, 4H), 3.00 (s, 3H), 2.07 (s, 3H).

The crude product was dissolved in THF (20 mL) and cooled at 0 ^{0}C. NaH (60% mineral dispersion in mineral oil, 240 mg, 6 mmol) was added to the solution at 0 ^{0}C. After stirring for 1h, the reaction mixture was added to saturated NH_4Cl and ice. The resulting solution was extracted with EtOAc (100 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated and purified by silica gel chromatography (EtOAc/ Hexane= 1/2) to afford (*R*)-Cbz-aziridine **3** as a colorless oil (897 mg, 90%).



R_f: 0.53 (EtOAc/ Hexane= 1/2)

^{1}H NMR (300M Hz, $CDCl_3$) δ 7.32 (b, 5H) 5.13 (s, 2H), 4.22 (dd, *J*=12.0, 6.0, 1H), 4.05 (dd, *J*=12.0, 4.5, 1H), 2.77 (m, 1H), 2.41 (d, *J*=4.2, 1H), 2.18 (d, *J*=2.4, 1H), 2.03 (s, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 100.55, 162.50, 135.40, 128.52, 128.35, 128.13, 68.32, 63.97, 35.22, 29.52, 20.62

IR (NaCl) 2983 (m), 1730 (s), 1234 (m), 1110 (m)

HRMS (EI) (M^+) calcd 249.1001, found 249.1000

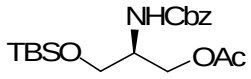
Element Analysis: $C_{13}H_{15}NO_4$; Calculated: C, 62.64; H, 6.07; N, 5.62; Found: C, 62.83; H, 6.22; N, 5.63

$[\alpha]^{20}_D$= +35.4 (c=1.0, EtOAc)

3-(t-Butyldimethylsilyloxy)-2-(benzyloxycarbonylamino)propan-1-ol 4

To a solution of lipase product **2d** (2.67g, 10 mmol) in CH_2Cl_2 (50 mL) was added imidazole (1.7 g, 25 mmol) and TBSCl (1.66g, 11 mmol) at 0 ^{0}C. The reaction mixture was stirred for 1 h at room temperature and diluted with CH_2Cl_2. The organic layer was washed with saturated NH_4Cl and brine, dried over $MgSO_4$, filtered and concentrated to give the fully protected TBS acetate, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (b, 5H) 5.10 (bs, 3H), 4.14 (m, 2H), 3.97 (b, 1H), 3.73 (m, 1H), 3.62 (m, 1H), 2.02 (s, 3H), 0.88 (s, 9H) 0.34 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.66, 155.81, 136.30, 128.45, 128.09, 66.76, 62.92, 61.71, 50.98

The crude product was dissolved in methanol (50 mL). K_2CO_3 powder (1.38g, 10 mmol) was added to the solution at 0 ^{0}C. After stirring for 1 h at 0 ^{0}C, the solution was diluted with EtOAc (100 mL). The organic layer was washed with saturated NH_4Cl and brine to give a colorless oil, which was purified by silica gel chromatography (EtOAc/Hexane= 1/3) to afford **4** as colorless oil (3.3 g, 97%).



R_f: 0.58 (EtOAc/ Hexane= 1/2)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (b, 5H), 5.43 (b, 1H), 5.09 (s, 2H), 3.72 (m, 5H), 2.92 (b, 1H, OH), 0.88 (s, 9H), 0.08 (s, 6H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 156.37, 136.31, 128.43, 128.02, 66.74, 63.42, 63.20, 53.07, 29.60, 25.73, 18.10, -5.66

IR (NaCl) 3442 (m), 2954 (m), 2858 (m), 1708 (s), 1529 (m), 1073 (s)

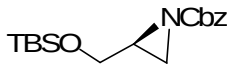
MS (ESI) m/z 362 $(M+ Na)^+$

Elemental Analysis: $C_{17}H_{29}NO_4Si$; Calculated C, 60.14; H, 8.61; N, 4.13; Found C, 59.99; H, 8.34; N, 3.78

$[\alpha]^{20}_D$= -13.5 (c=1.0, EtOAc)

(*S*)-N-benzyloxycarbonyl-2-(t-butyldimethylsilyloxymethyl)aziridine 5

To a solution of **4** (3.3g, 9.73 mmol) and PPh_3 (3.8g, 14.6 mmol) in THF (50 mL) was added DIAD (2.7 mL, 13.6 mmol) dropwise at 0 ^{0}C. The reaction mixture was stirred for 8 h at room temperature. The solution was concentrated under reduced pressure and the residue was purified by silica gel chromatography (EtOAc/Hexane= 1/10) to afford 5 as colorless oil (2.65g, 85%).



R_f: 0.35 (EtOAc/ Hexane= 1/10)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (b, 5H), 5.12 (s, 2H), 3.80 (dd, 2H), 2.64 (m, 1H), 2.30 (d, 2H, *J*=5.7), 2.23 (d, *J*=3.9), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.73, 135.82, 128.45, 128.16, 128.05, 67.96, 61.85, 38.47, 28.48, 25.76, 18.24, -5.41, -5.48

IR (NaCl) 2954(m), 2930 (m), 2857 (m), 1727 (s), 1296 (m), 1201 (m)

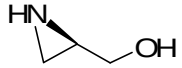
HRMS (EI) (M^+) calculated 321.1760, found 321.1763

Elementary Analysis: $C_{17}H_{27}NO_3Si$; Calculated C, 63.51; H, 8.47; N, 4.36; Found C, 63.21; H, 8.50; N 4.34

$[\alpha]^{20}_D$= -47.3 (c=2.5, EtOAc)

(*R*)-2-hydroxymethylaziridine 6[3]

To a solution of (*R*)-N-Cbz-aziridine **3** (250 mg, 1 mmol) in CH_3OH (5 mL) was added K_2CO_3 powder (138 mg, 1 mmol) at room temperature. The reaction mixture was stirred for 1 h, filtered and concentrated to give the crude oil, which was purified by chromatography on basic alumina (10% methanol in dichloromethane) and dried very carefully to give (*R*)-2-hydroxymethylaziridine **6** as colorless liquid (55 mg, 75%).



bp: 45-50 ^{0}C (1.5 mmHg, Kugelrohr bath temperature, partially decomposed)

R_f: 0.15 (CH_2Cl_2/CH_3OH = 10/1)

^{1}H NMR (CD_3OD, 300 MHz) δ 3.53 (dd, 1H, *J*=11.7, 4.8), 3.41 (dd, 1H, *J*=11.7, 4.8), 2.16 (m, 1H), 1.76 (d, *J*=6.0), 1.47 (d, *J*=3.6)

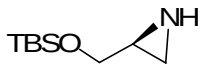
^{13}C NMR (CD_3OD, 75MHz) 64.77, 32.01, 22.82

HRMS (EI) (M^+-1) calculated 72.0449 found 72.0451

$[\alpha]^{20}_D$= -3.75 (c=0.4, CH_3OH)

(*S*)-2-(t-butyldimethylsilyloxymethyl)aziridine 7[4]

To a solution of **5** (580 mg, 1.8 mmol) in CH_3OH (9 mL) was added K_2CO_3 powder (250 mg, 1.8 mmol) at room temperature. The reaction mixture was stirred for 24 h, filtered and concentrated to give the crude oil, which was purified by silica gel chromatography to give the *N*-deprotected aziridine 7 as colorless liquid (282 mg, 84%).



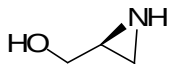
R_f: 0.40 (EtOAc/ Hexane= 2/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.71 (d, 2H, *J*=3.9), 2.12 (m, 1H), 1.66 (d, 1H, *J*=5.4), 1.55 (d, 1H, *J*=3.3), 0.89 (s, 9H), 0.06 (s, 6H)

$[\alpha]^{20}_D$= -4.2 (c=0.4, CH_3OH)

(*S*)-2-hydroxymethylaziridine 6

To a solution of **5** (321mg, 1mmol) in CH_3OH (5 mL) was added CsF powder (450 mg, 3 mmol) at room temperature. The reaction mixture was stirred under reflux for 8 h, filtered and concentrated to give the crude oil, which was purified by chromatography on basic alumina to give (*S*)-2-hydroxymethylaziridine **6** as a colorless liquid (54 mg, 74%).



^{1}H NMR (CD_3OD, 300 MHz) δ 3.53 (dd, 1H, *J*=11.7, 4.8), 3.41 (dd, 1H, *J*=11.7, 4.8), 2.16 (m, 1H), 1.76 (d, *J*=6.0), 1.47 (d, *J*=3.6)

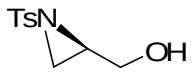
^{13}C NMR (CD_3OD, 75MHz) 64.77, 32.01, 22.82

$[\alpha]^{20}_D$= +3.94 (c=1.0, CH_3OH)

Determination of absolute configuration: (*R*)-*N*-(p-toluenesulfonyl)-2-hydroxymethylaziridine 8

To a solution of (*R*)-**6** in $CHCl_3$ (66 mg, 0.9 mmol) were added TsCl (172 mg, 0.9 mL) and NEt_3 (125

μL, 0.9 mmol) at 0 ^{0}C. The reaction mixture was stirred for 1 h at room temperature and diluted with CH_2Cl_2. The organic layer was washed with sat. NH_4Cl, brine, dried over $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography (EtOAc/Hexane= 1/1) to give **8** as white solid (174 mg, 85%), which was analyzed by Chiralcel OD HPLC.



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J*=8.4), 7.34 (d, *J*=8.4), 3.84 (dd, *J*=2.4, 12.3), 3.53 (dd, *J*=4.8, 12.3), 3.02 (m, 1H), 2.61 (d, 1H, *J*=6.9), 2.44 (s, 3H), 2.37 (d, 1H, *J*=8.7)

MS (ESI) m/z 250 $(M+ Na)^+$

$[\alpha]^{20}_D$ +31.6 (c=1.0, EtOAc) (the reported value[5] $[\alpha]_D$ +29.9 (c=9.9, EtOAc) for (*R*)-enantiomer.)

HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 1.0 mL/min, λ=225 nm): t_R= 35.7 and 38.0 min (authentic racemic compound)

HPLC (Chiralcel OD column, 5% 2-propanol in hexanes, 1.0 mL/min, λ=225 nm): t_R= 38.0 min (single peak for compound **8**)

REFERENCES

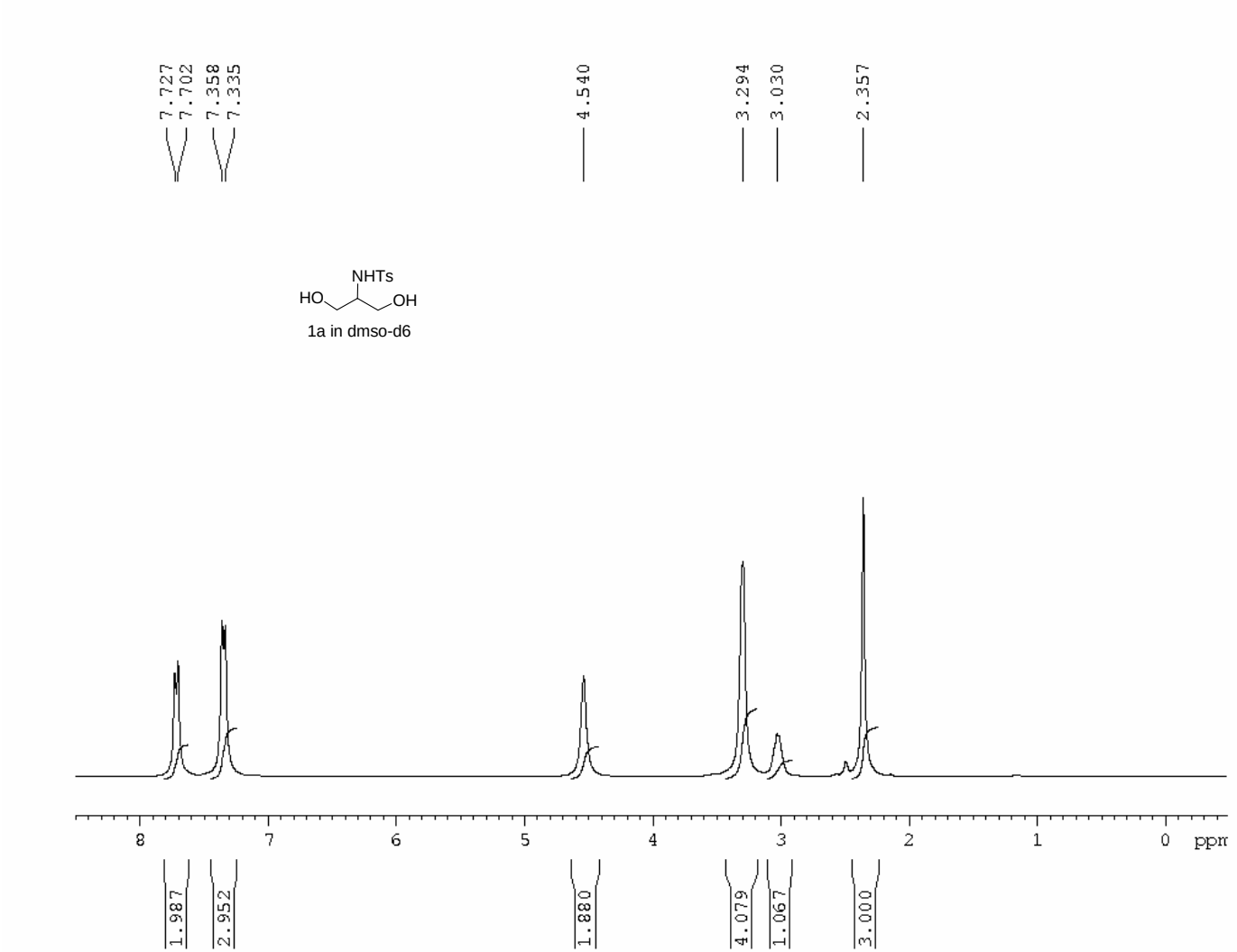
(1) Wang, Y.-F.; Lalonde, J. J.; Momongan, M.; Bergbreiter, D. E.; Wong, C.-H. *J. Am. Chem. Soc*. **1998**, *110*, 7200.
(2) Neri. C; Williams, J. M. J. *Adv. Synth. Catal*. **2003**, *345*, 835.
(3) Xu, J. *Tetrahedron: Asymmetry* **2002**, *13*, 1129.
(4) Bergmeier, S. C.; Seth P. P. *Tetrahedron Lett.* **1999**, *40*, 6181.
(5) Bergmeier, S. C.; Seth P. P. *J. Org. Chem.* **1997**, *62*, 2671.

Proton and Carbon NMR Spectra

Highly Efficient Synthesis of Enantiomerically Pure 2-Hydroxymethylaziridines by Enzymatic Desymmetrization

Jun Young Choi and Richard F. Borch*

Department of Medicinal Chemistry and Molecular Phamacology, and the Cancer Center, Purdue University, West Lafayette, IN 47907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2.357
NHTs
HO
OH
1a in dmso-d6
8
7
6
5
4
3
2
1
0
ppm
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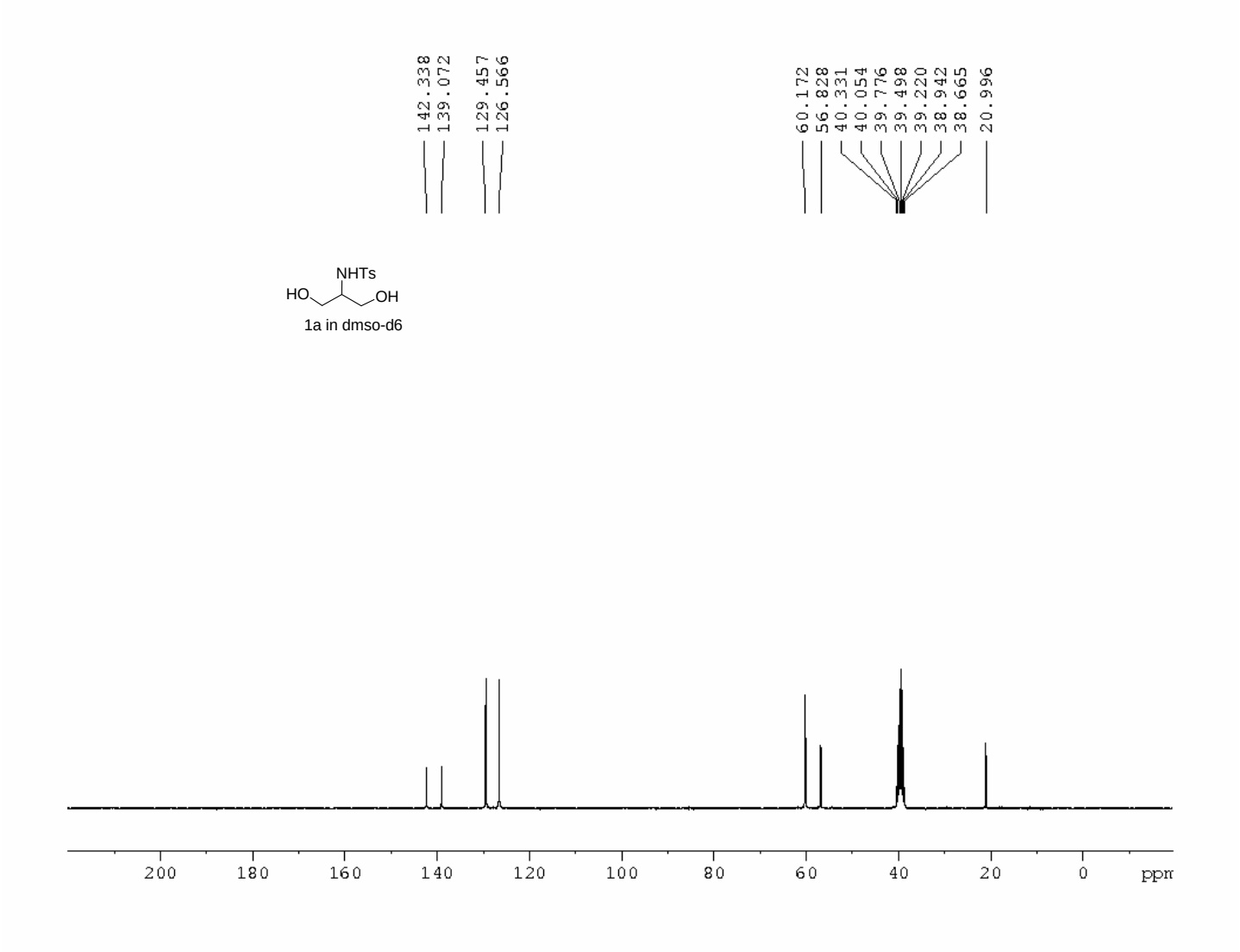
4.079
1.067
3.000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139.072
129.457
126.566
60.172
56.828
40.331
40.054
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39.498
39.220
38.942
38.665
20.996
NHTs
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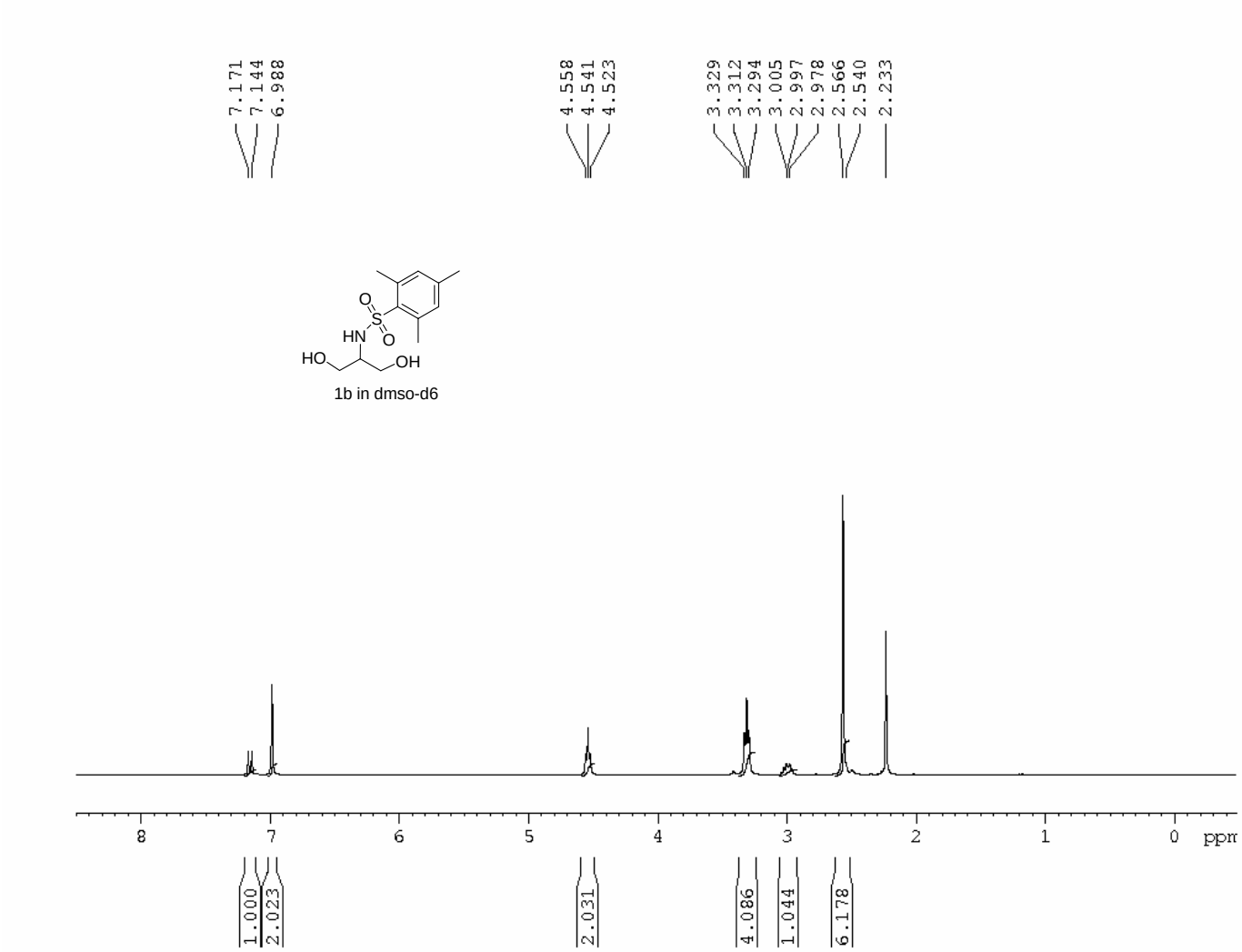
OH
1a in dmso-d6
200
180
160
140
120
100
80
60
40
20
0
ppm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7.144
6.988
4.558
4.541
4.523
3.329
3.312
3.294
3.005
2.997
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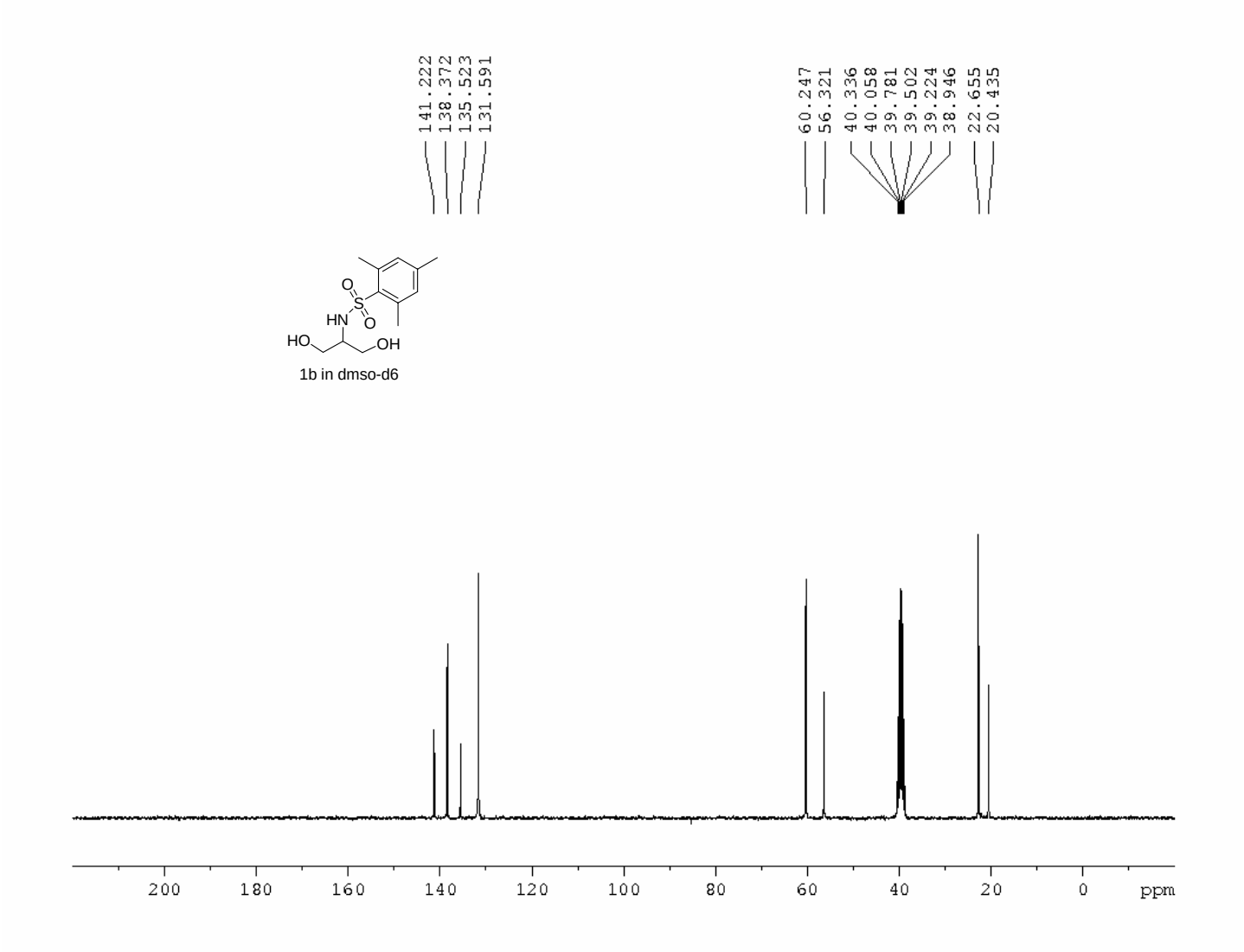
2.566
2.540
2.233
O
S
O
HN
HO
OH
1b in dmso-d6
8
7
6
5
4
3
2
1
0
ppm
1.000
2.023
2.031
4.086
1.044
6.178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138.372
135.523
131.591
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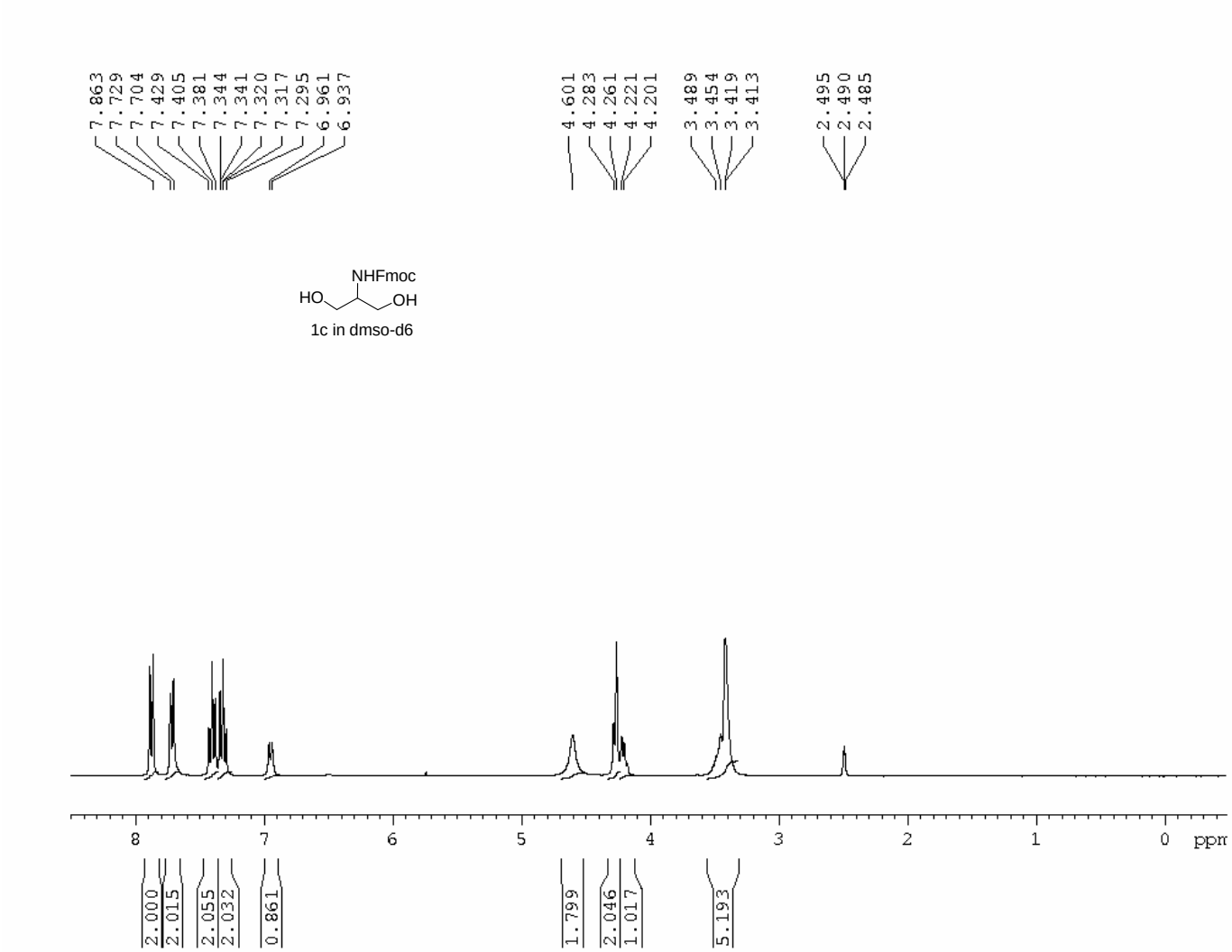
56.321
40.336
40.058
39.781
39.502
39.224
38.946
22.655
20.435
O
S
HN
O
HO
OH
1b in dmso-d6
200
180
160
140
120
100
80
60
40
20
0
ppm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7.405
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7.344
7.341
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7.317
7.295
6.961
6.937
4.601
4.283
4.261
4.221
4.201
3.489
3.454
3.419
3.413
2.495
2.490
2.485
NHFmoc
HO
OH
1c in dmso-d6
8
7
6
5
4
3
2
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ppm
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2.032
0.861
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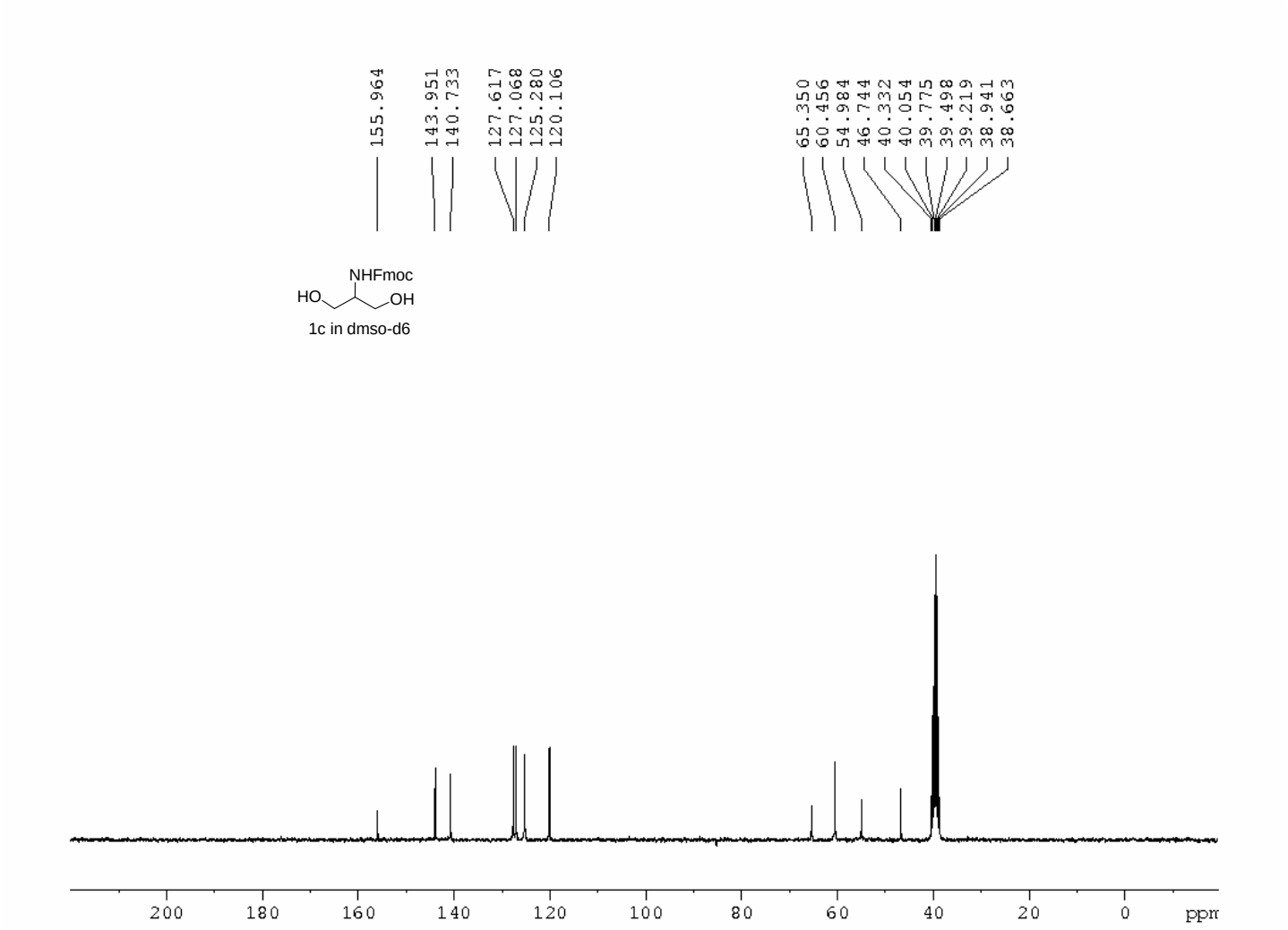
5.193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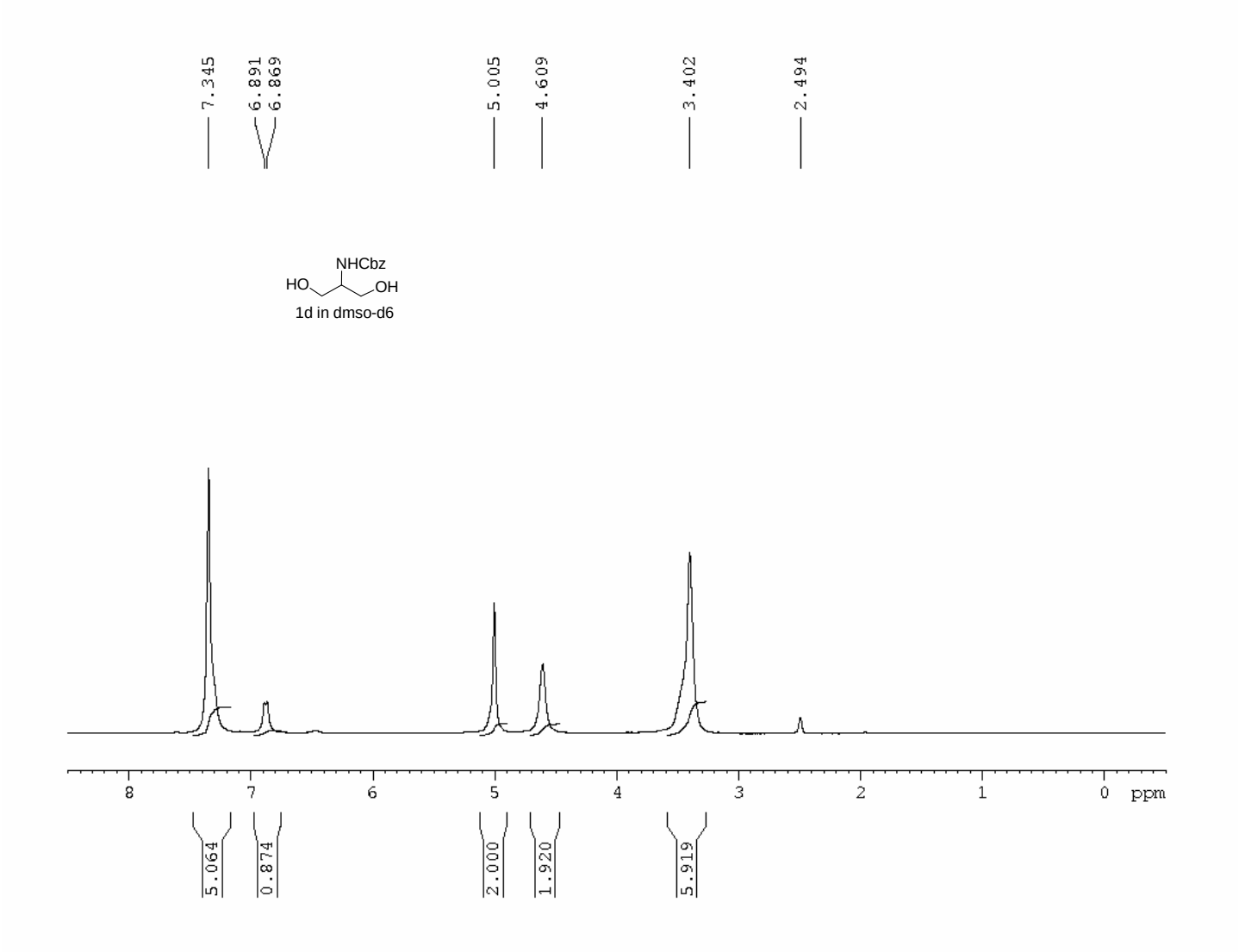
127.068
125.280
120.106
65.350
60.456
54.984
46.744
40.332
40.054
39.775
39.498
39.219
38.941
38.663
NHFmoc
HO
OH
1c in dmso-d6
200
180
160
140
120
100
80
60
40
20
0
ppm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2.494
NHCbz
HO
OH
1d in dmso-d6
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6
5
4
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2
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ppm
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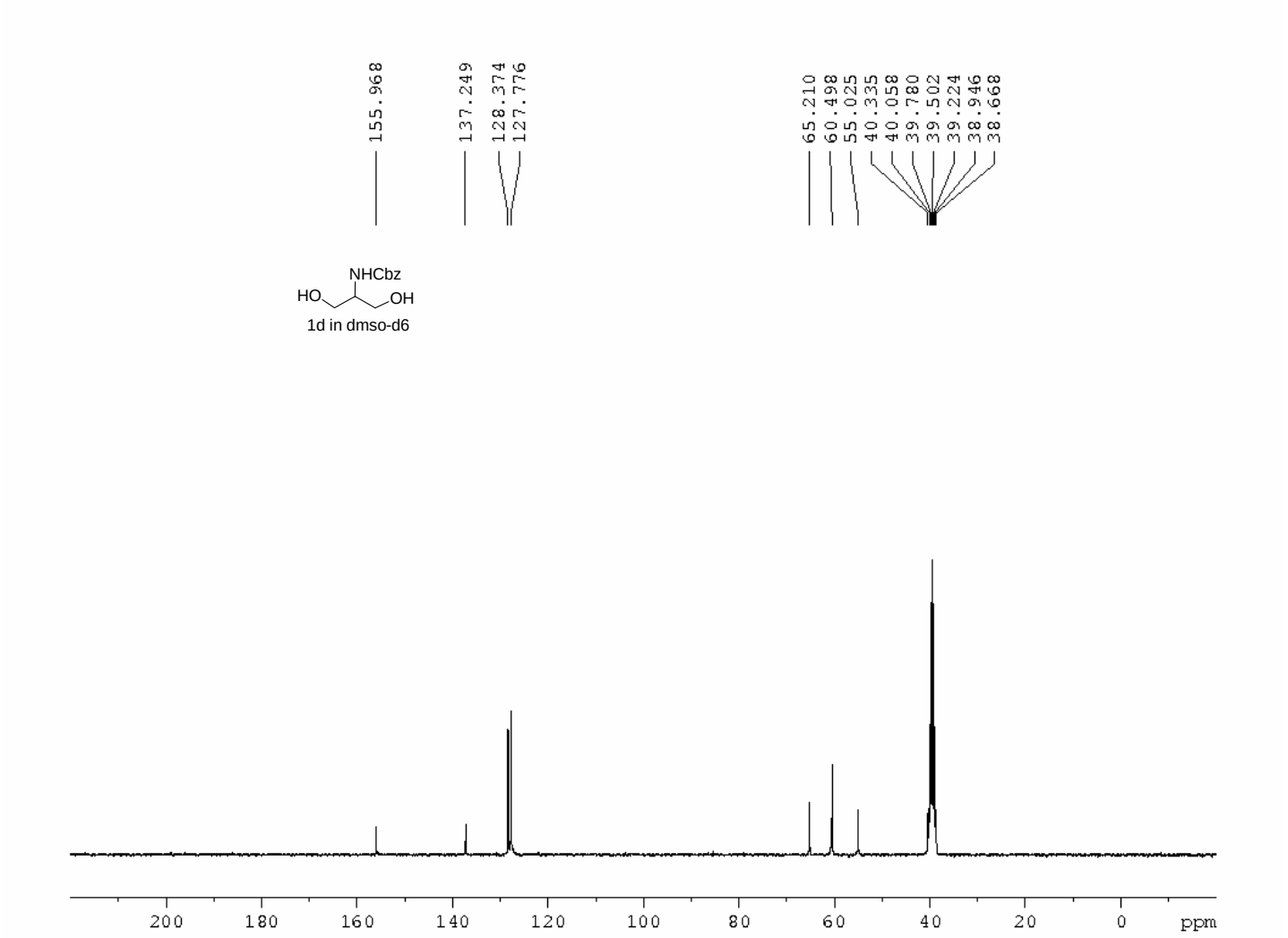
1.920
5.919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65.210
60.498
55.025
40.335
40.058
39.780
39.502
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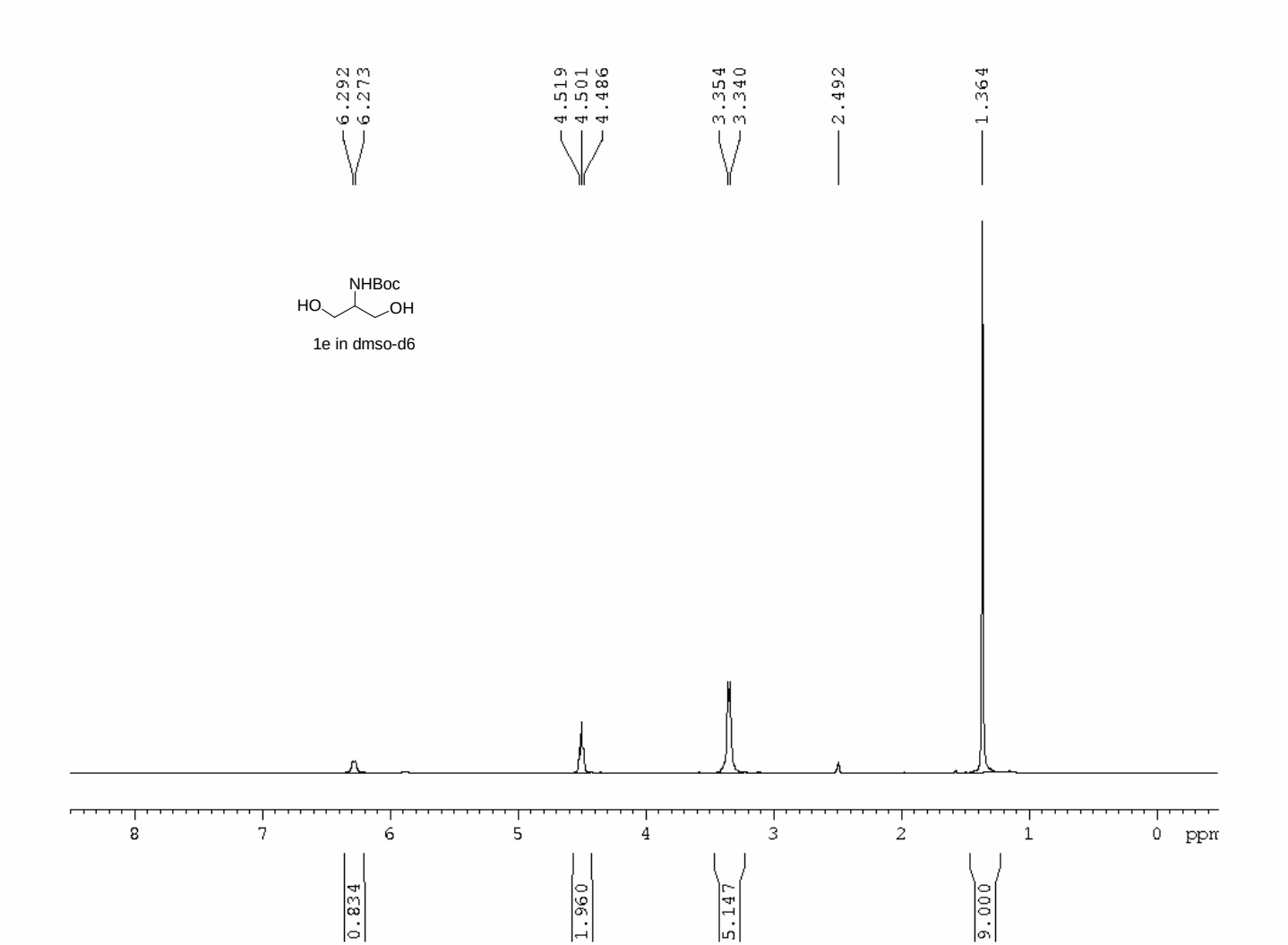
38.946
38.668
NHCbz
HO
OH
1d in dmso-d6
200
180
160
140
120
100
80
60
40
20
0
ppm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6.273
4.519
4.501
4.486
3.354
3.340
2.492
1.364
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HO
OH
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7
6
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4
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ppm
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1.960
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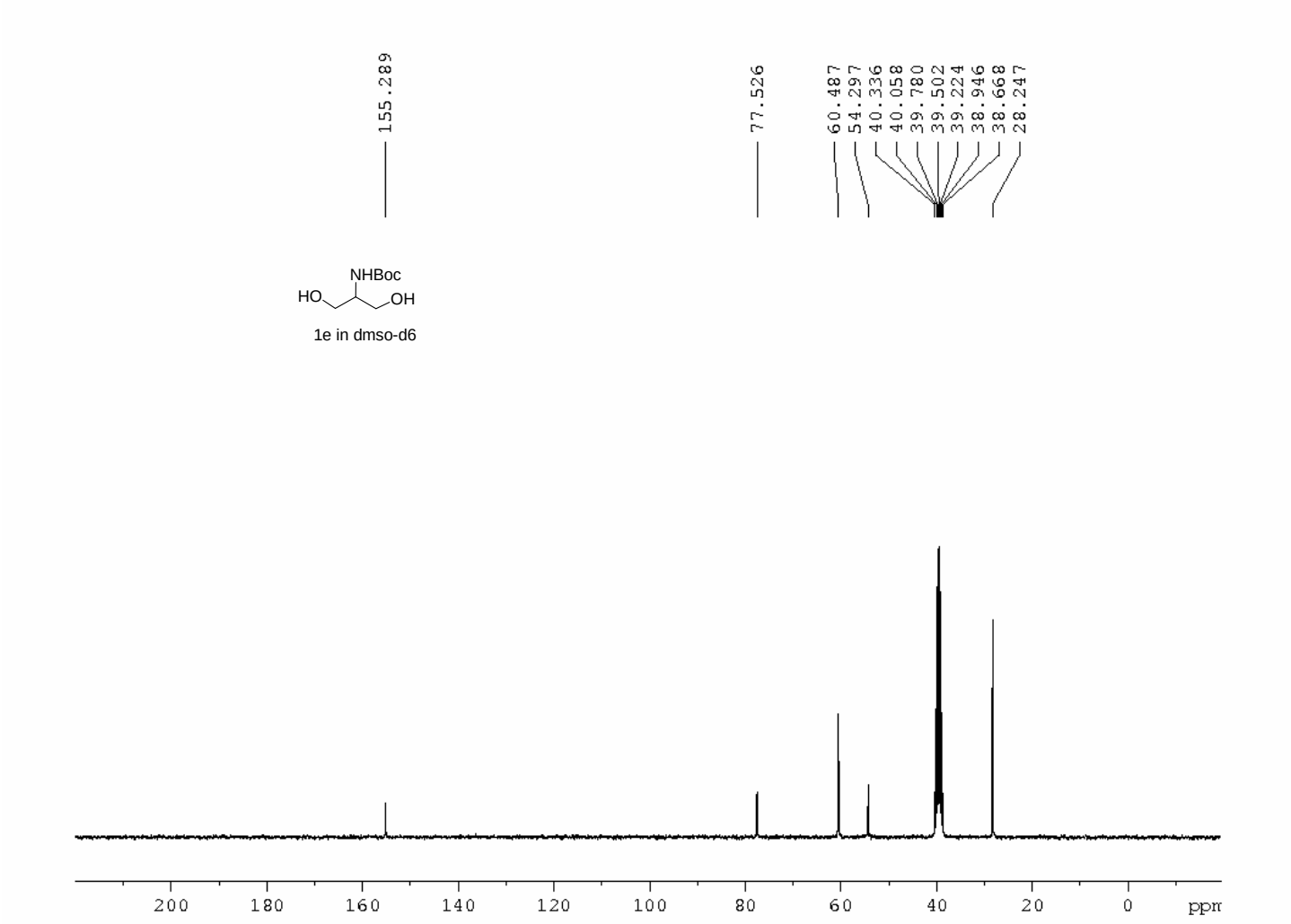
9.000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OH
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120
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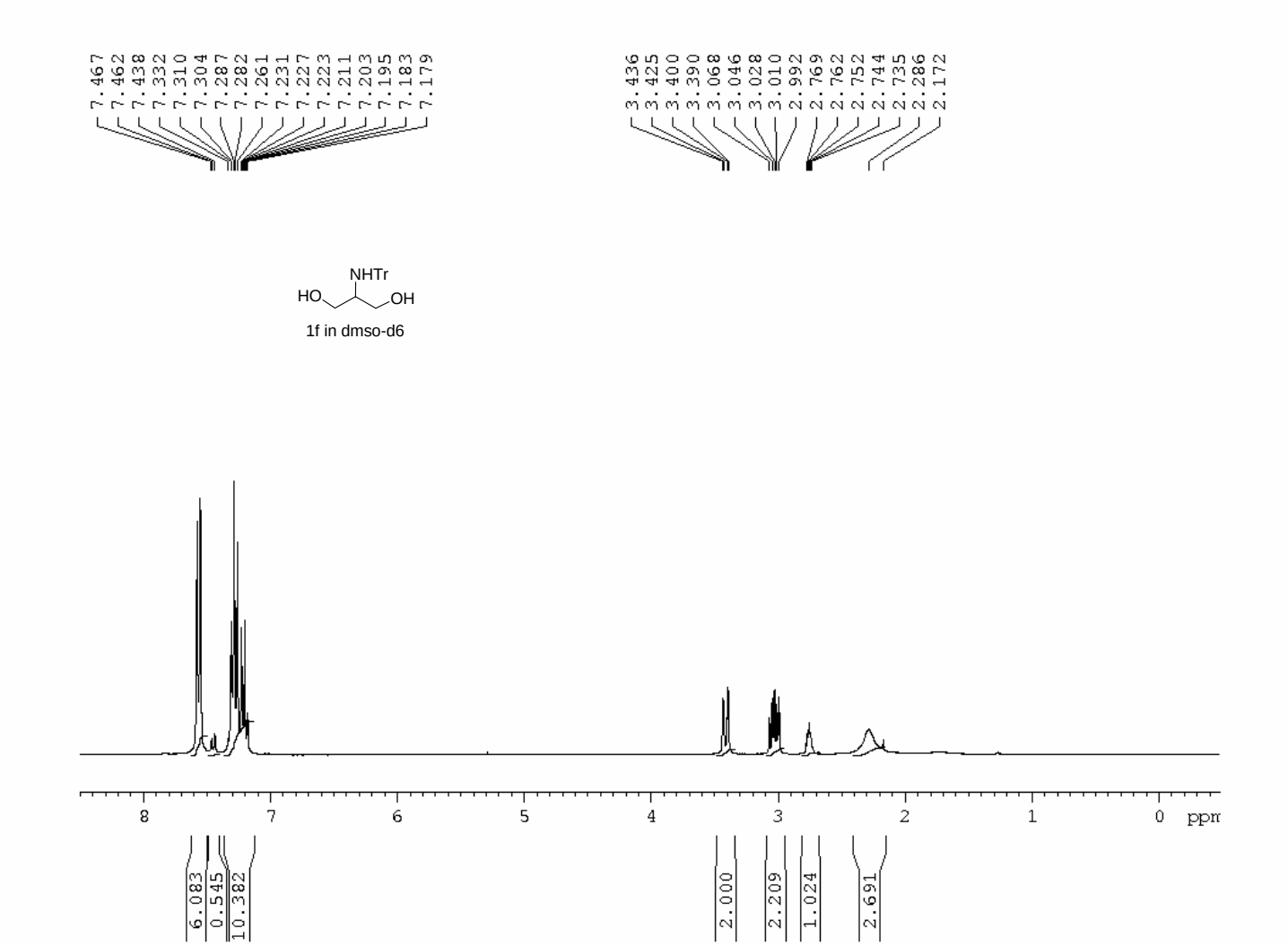
60
40
20
0
ppm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7.223
7.211
7.203
7.195
7.183
7.179
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3.425
3.400
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3.046
3.028
3.010
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2.769
2.762
2.752
2.744
2.735
2.286
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NHTr
HO
OH
1f in dmso-d6
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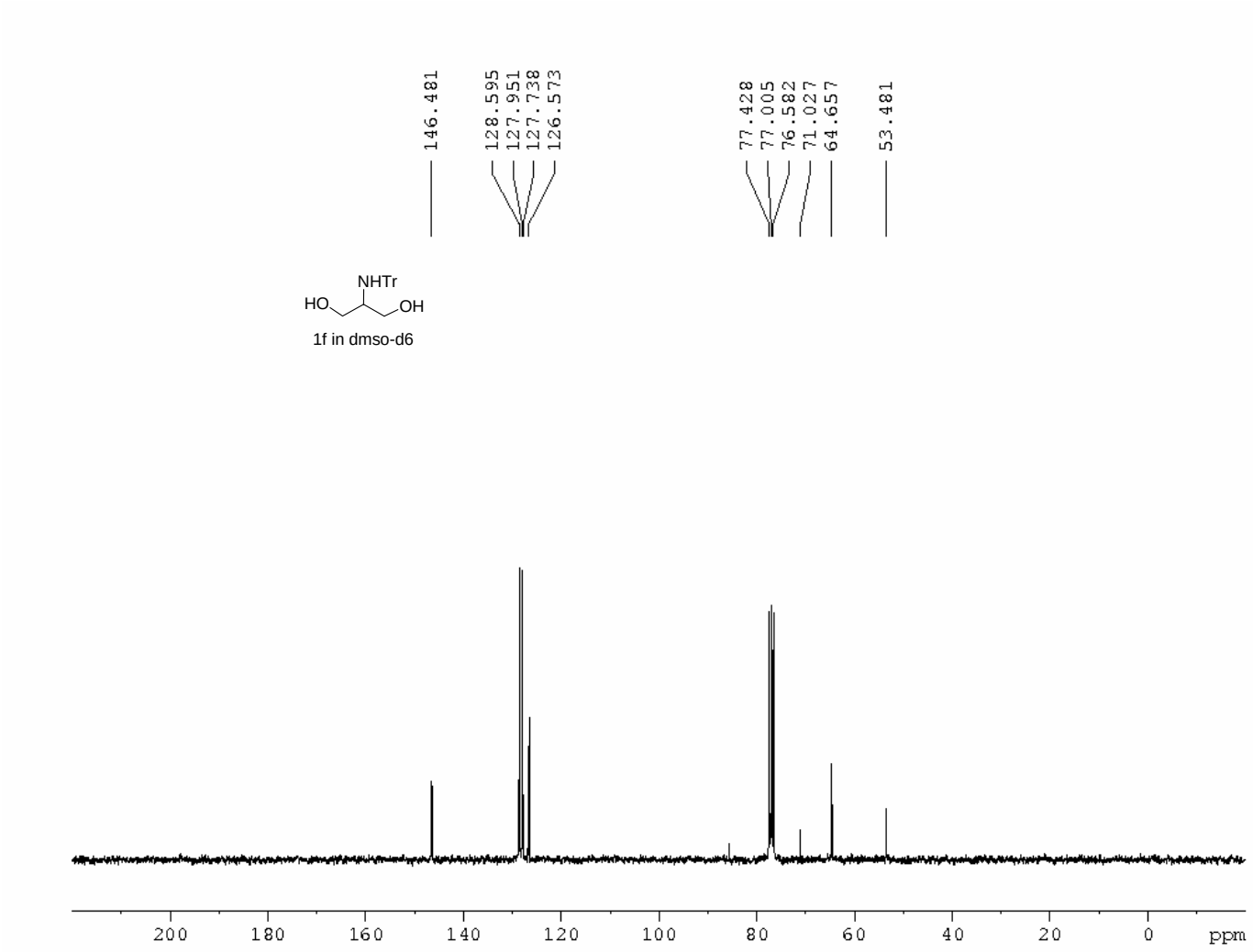
2.691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76.582
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64.657
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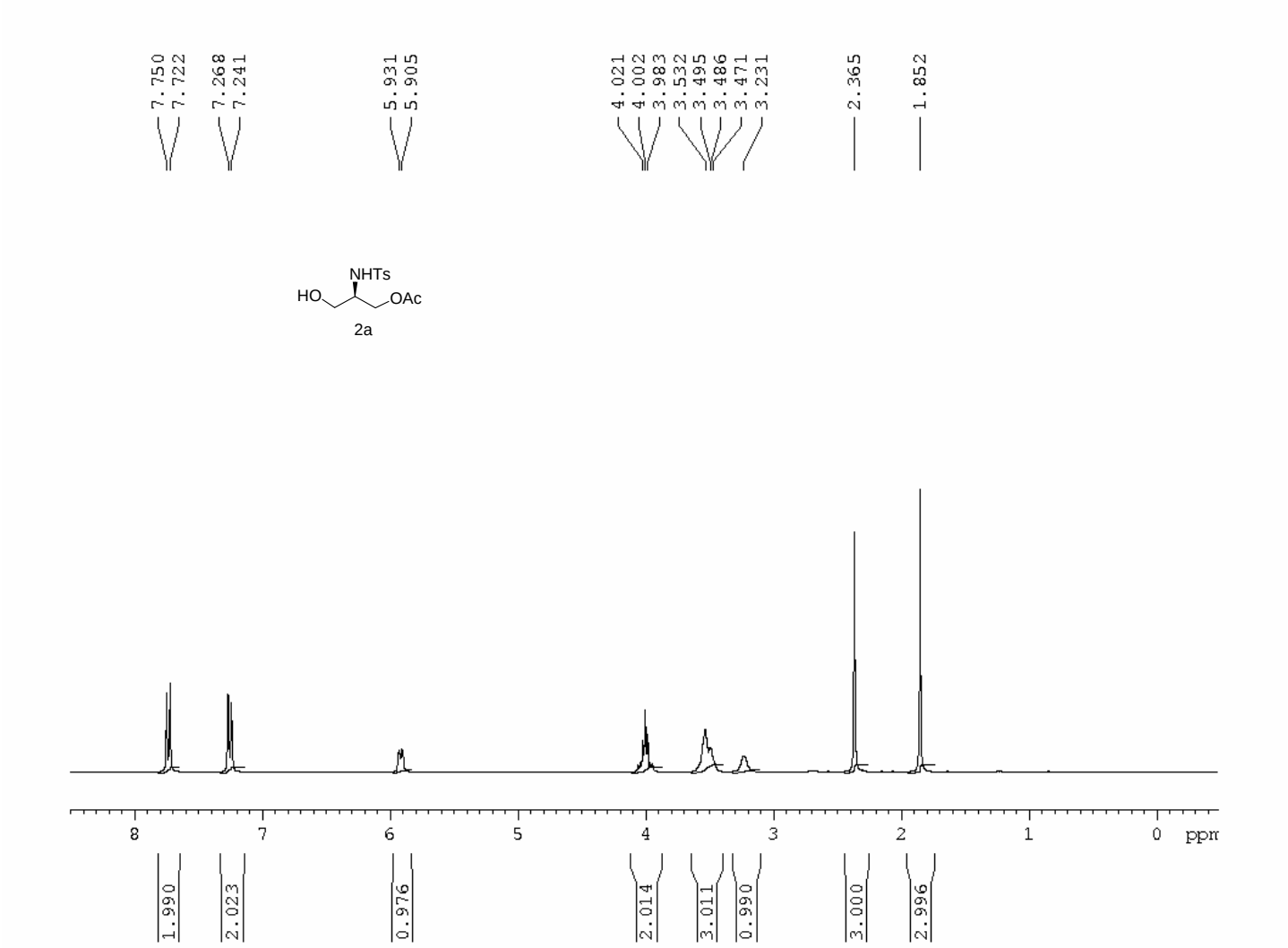
NHTr
HO
OH
1f in dmso-d6
200
180
160
140
120
100
80
60
40
20
0
ppm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3.231
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NHTs
HO
OAc
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6
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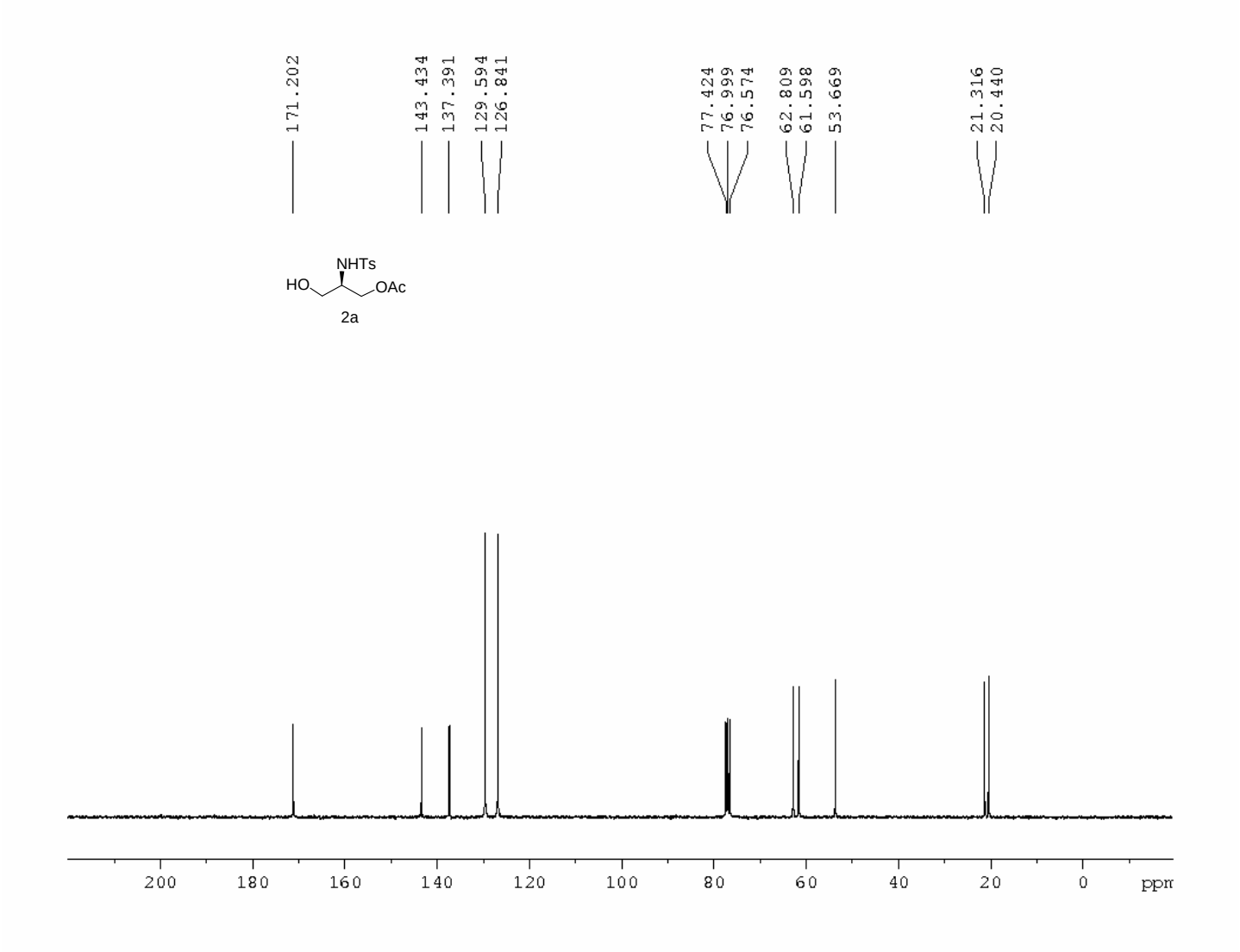
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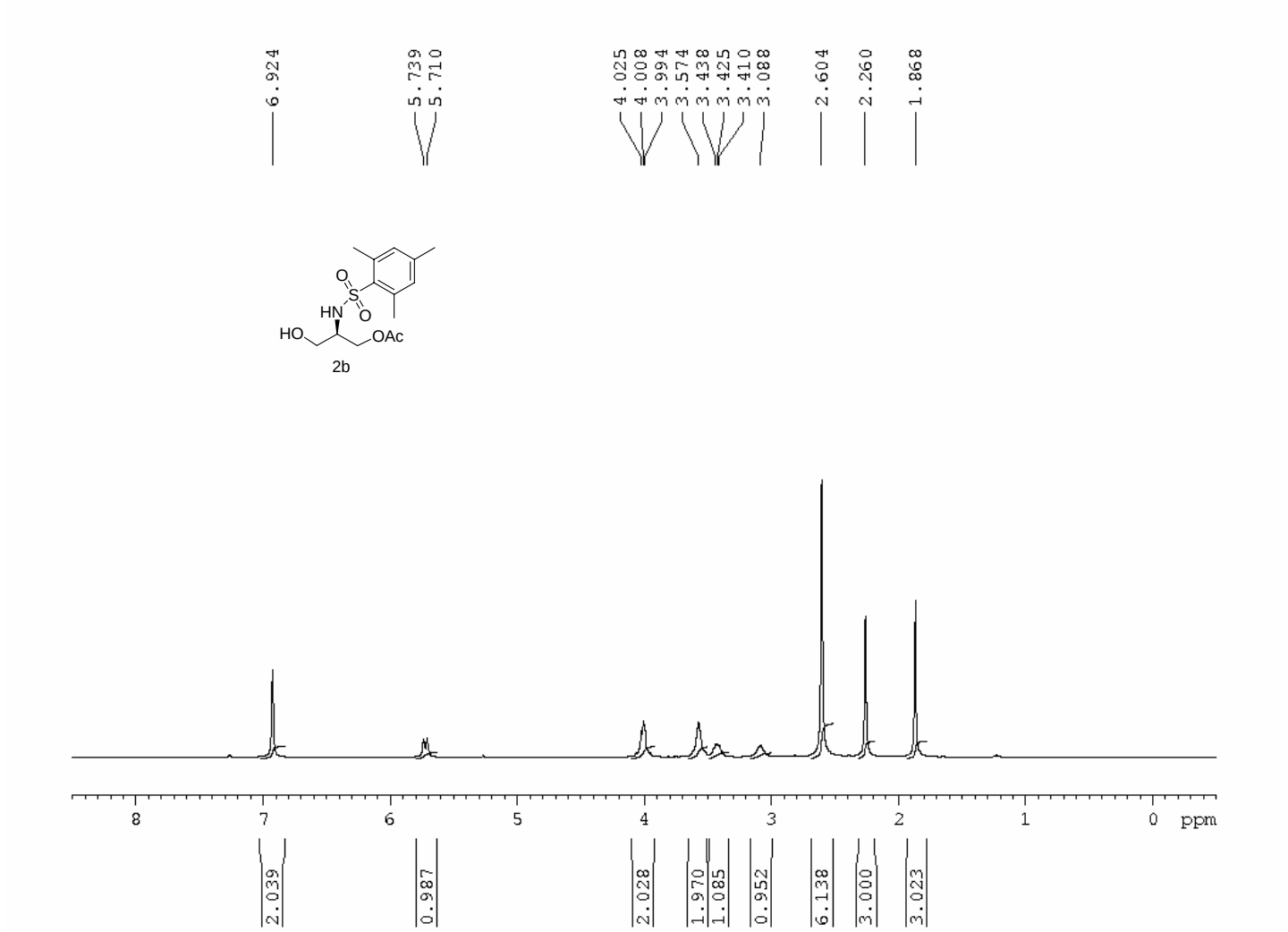
40
20
0
ppm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5
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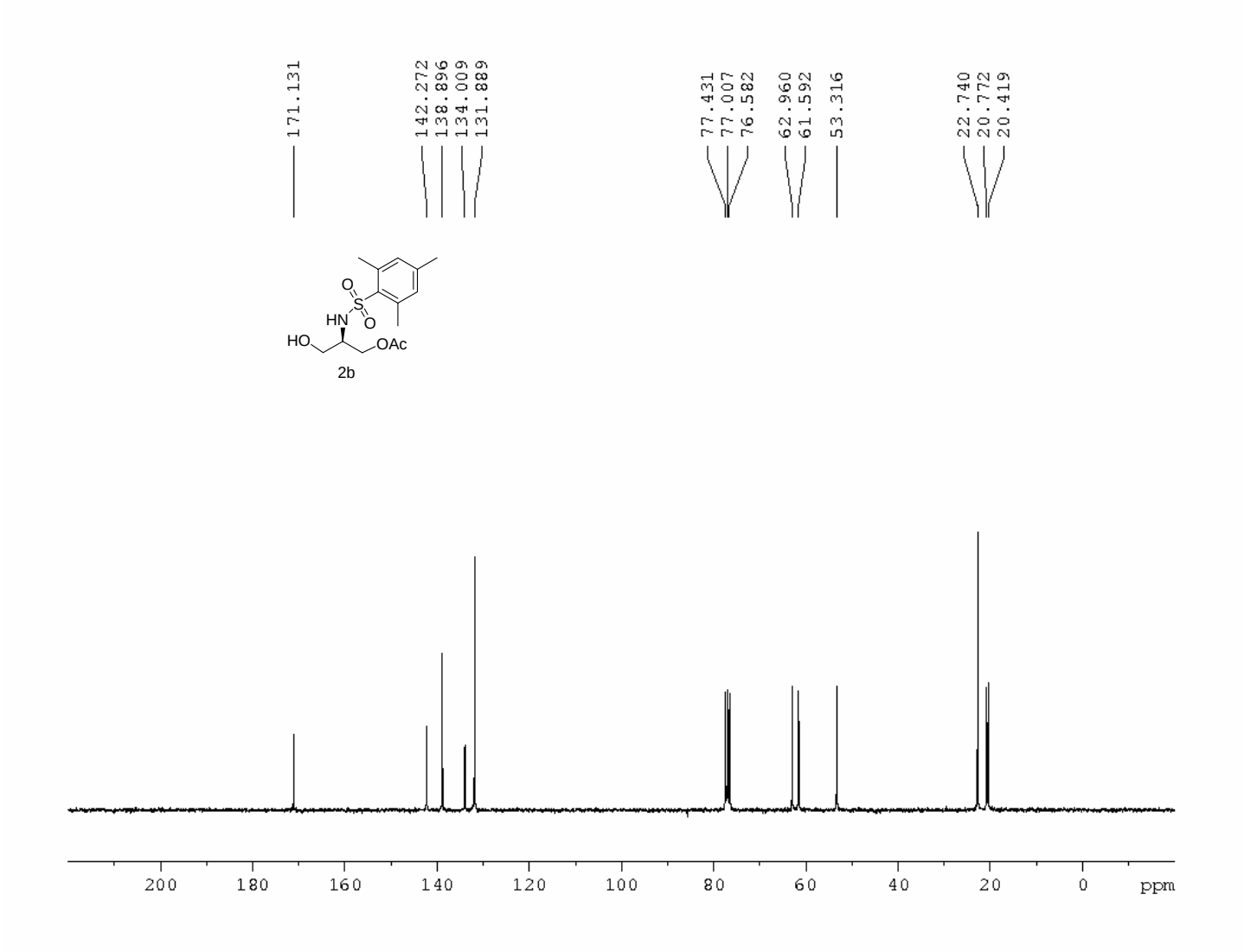
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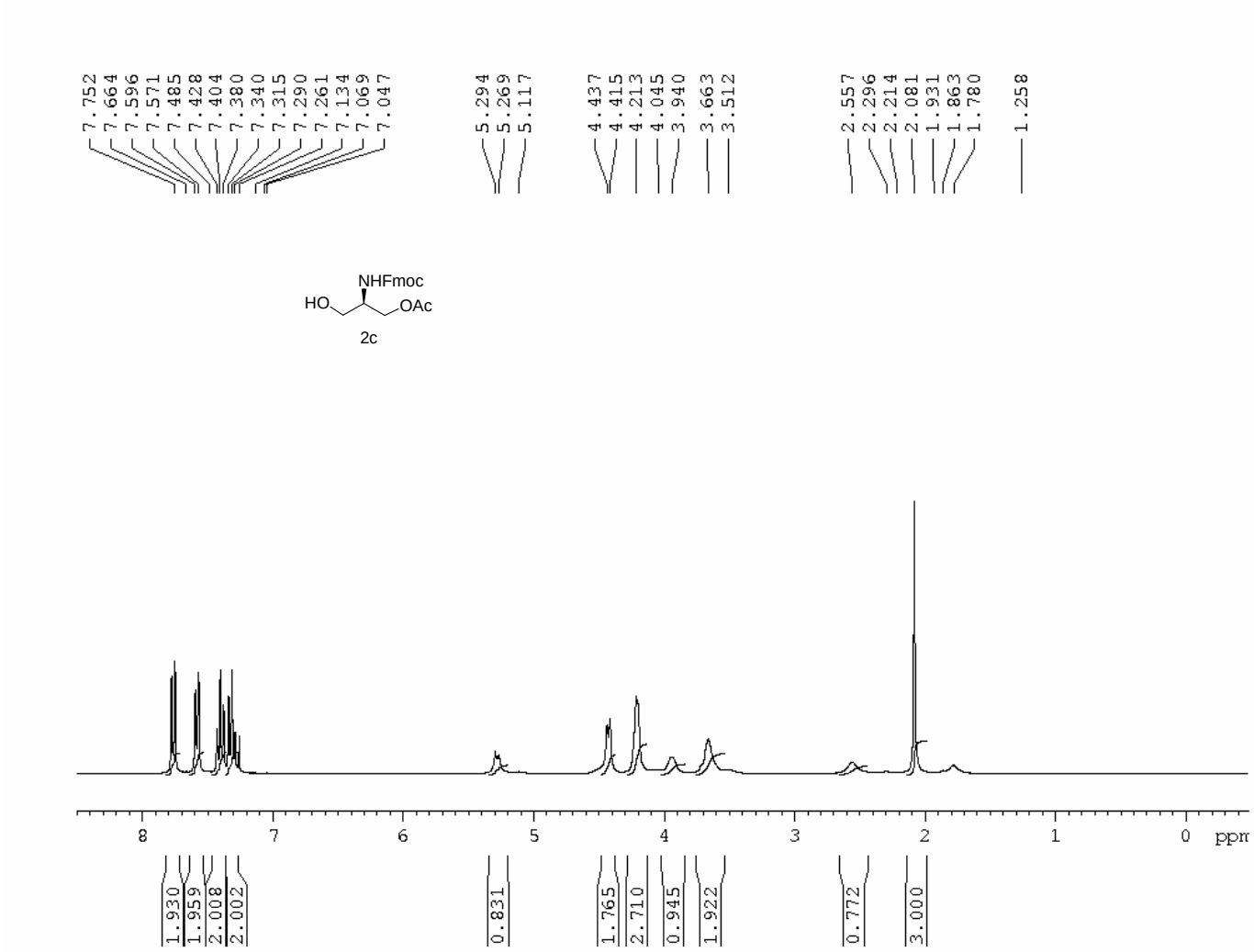
ppm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5.117
4.437
4.415
4.213
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1.863
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HO
OAc
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7
6
5
4
3
2
1
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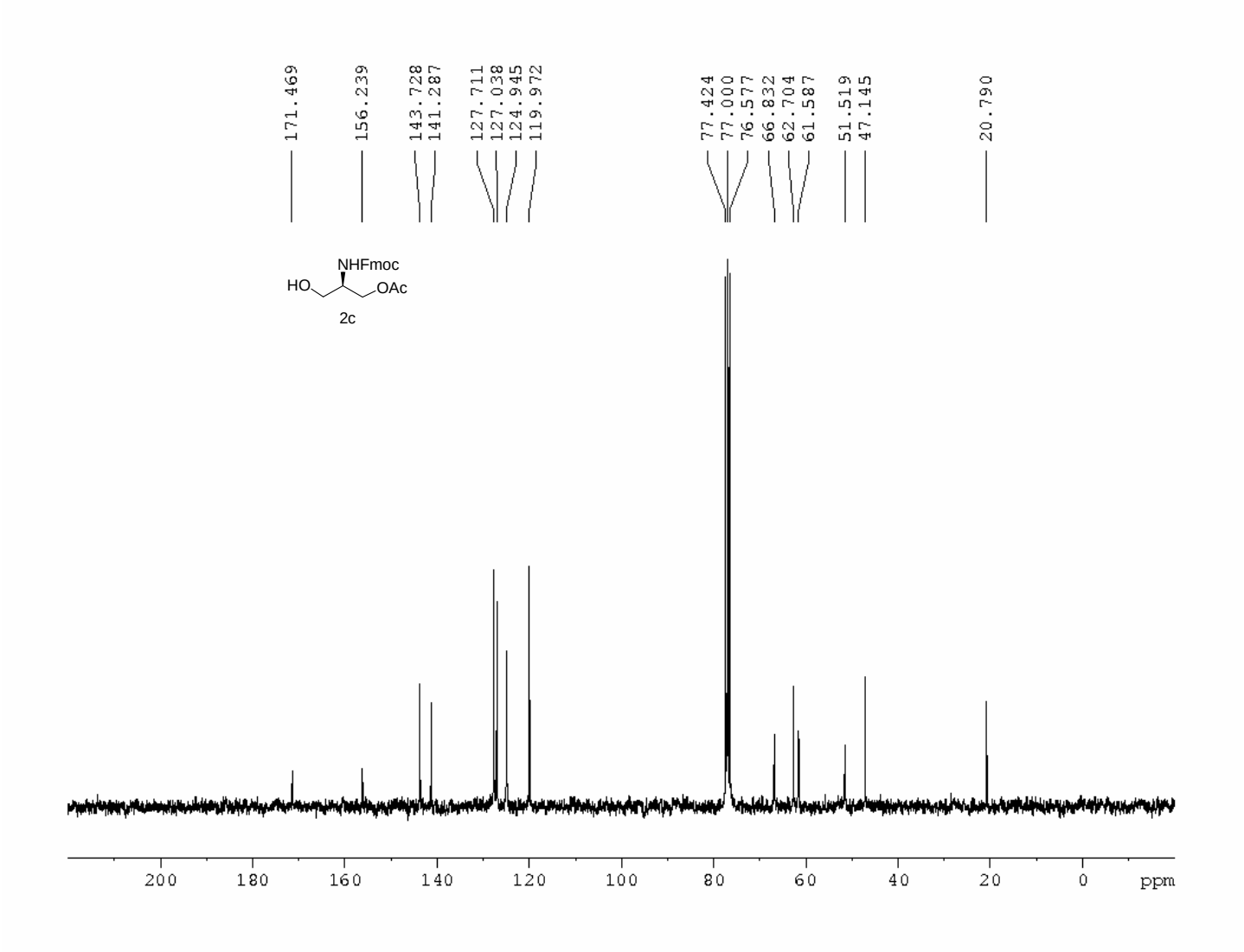
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77.000
76.577
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51.519
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120
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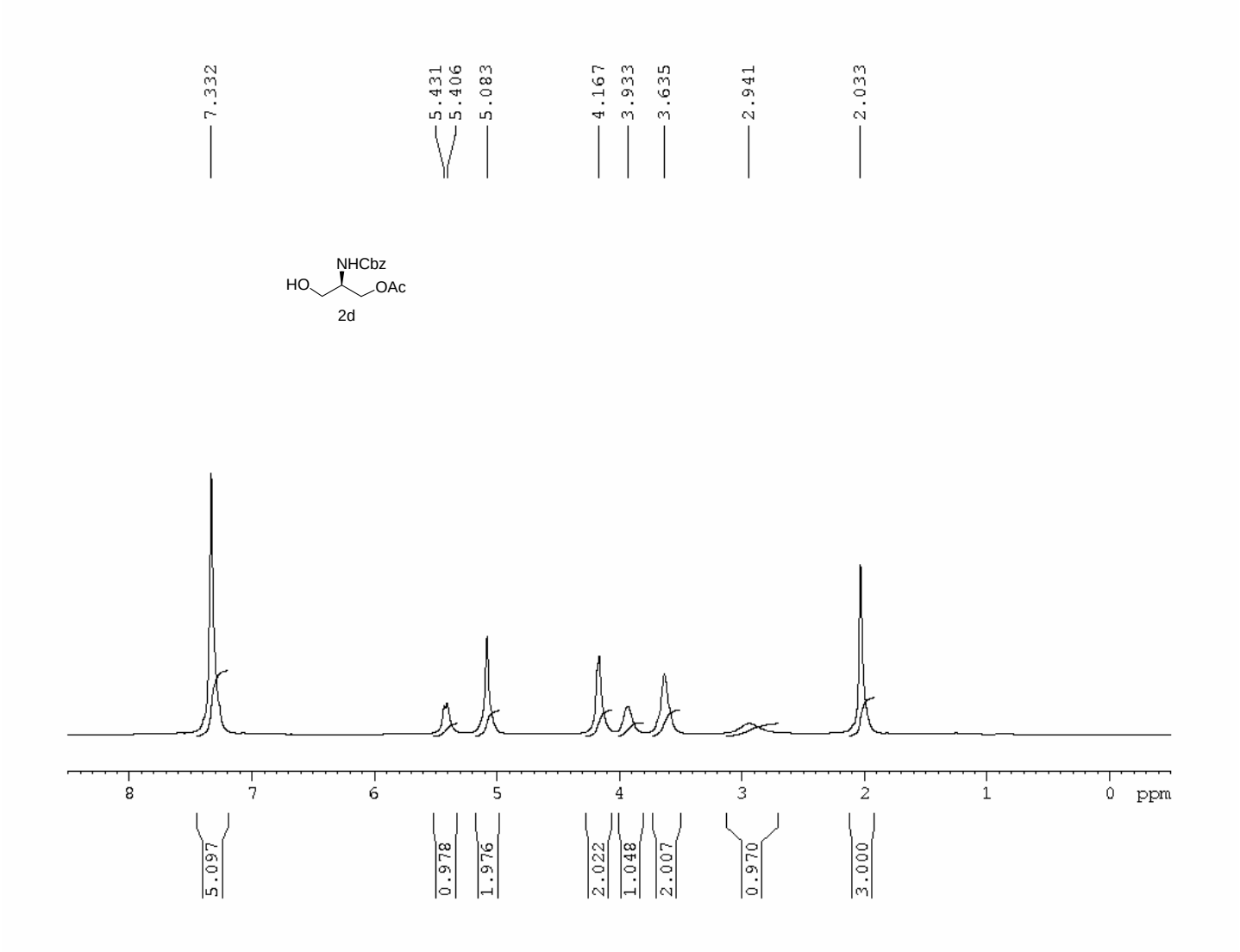
60
40
20
0
ppm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8
7
6
5
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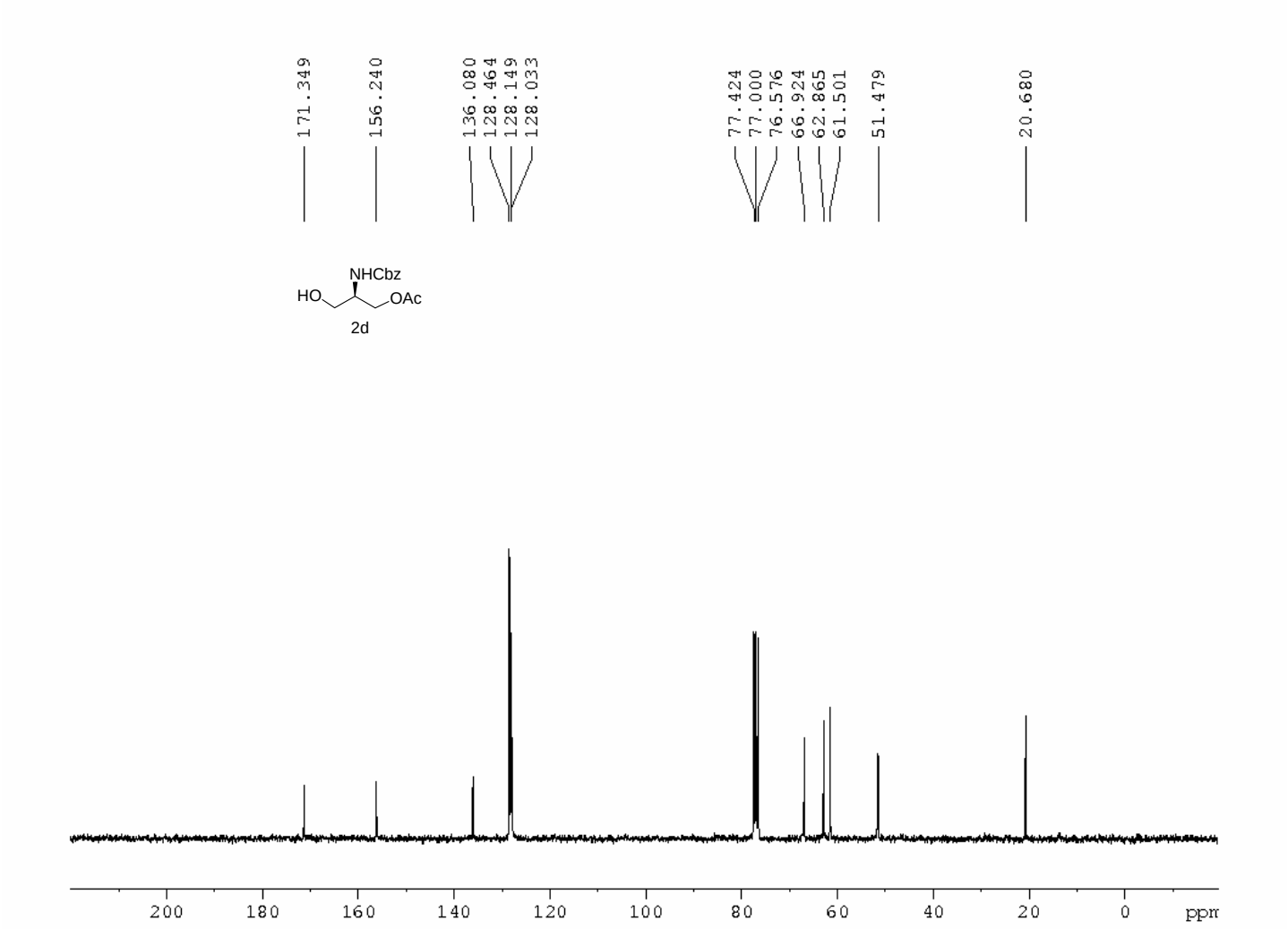
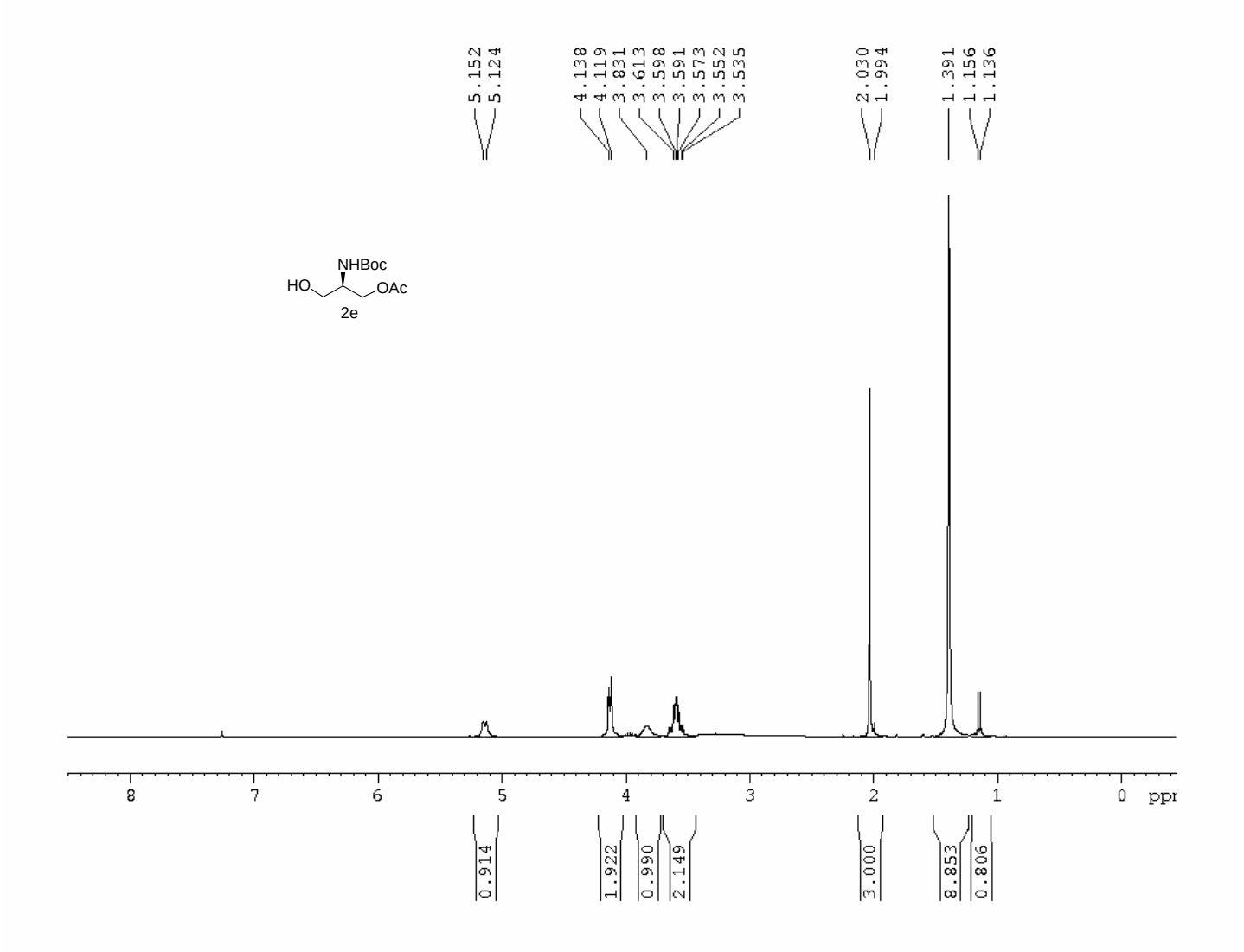
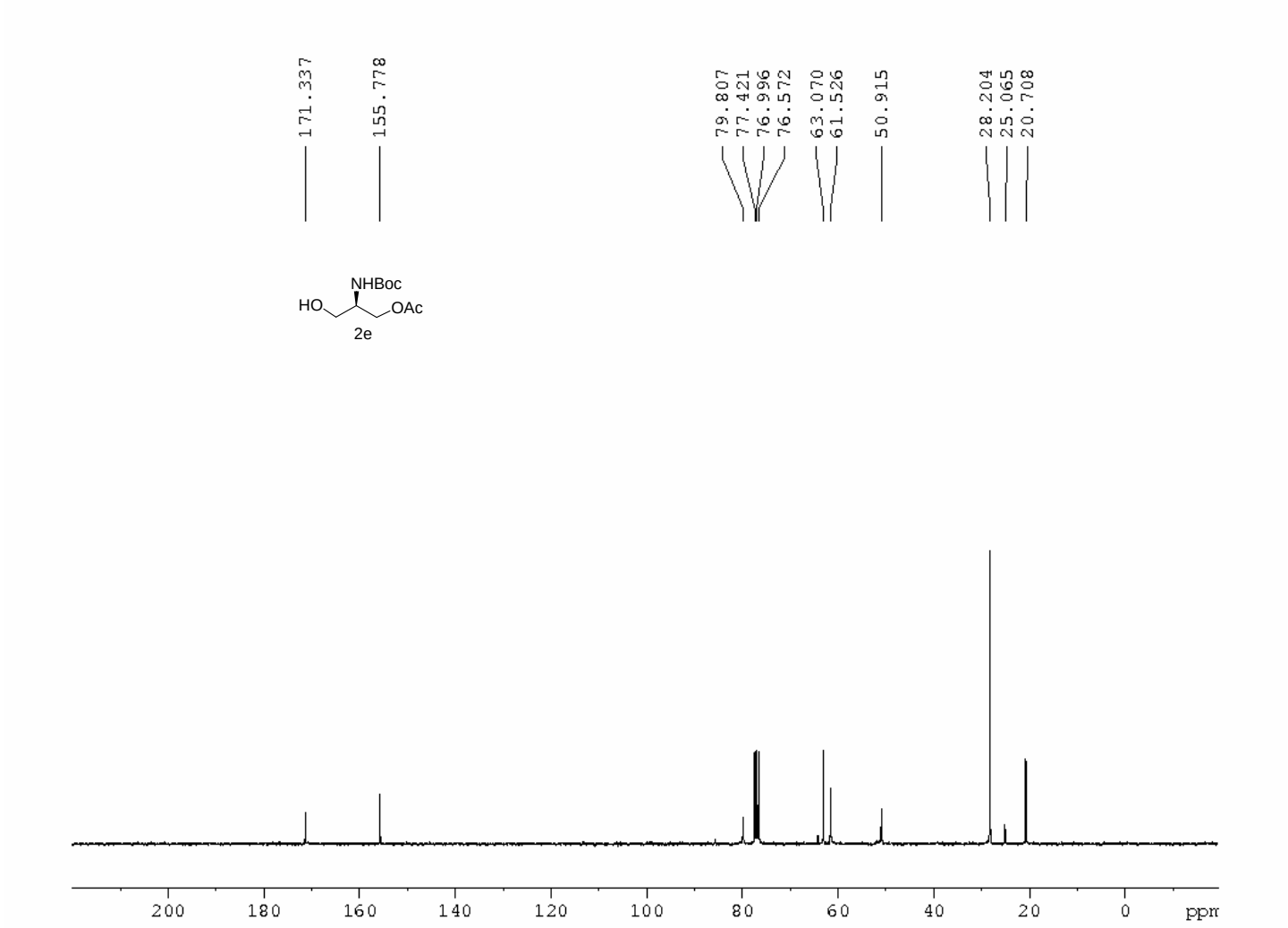
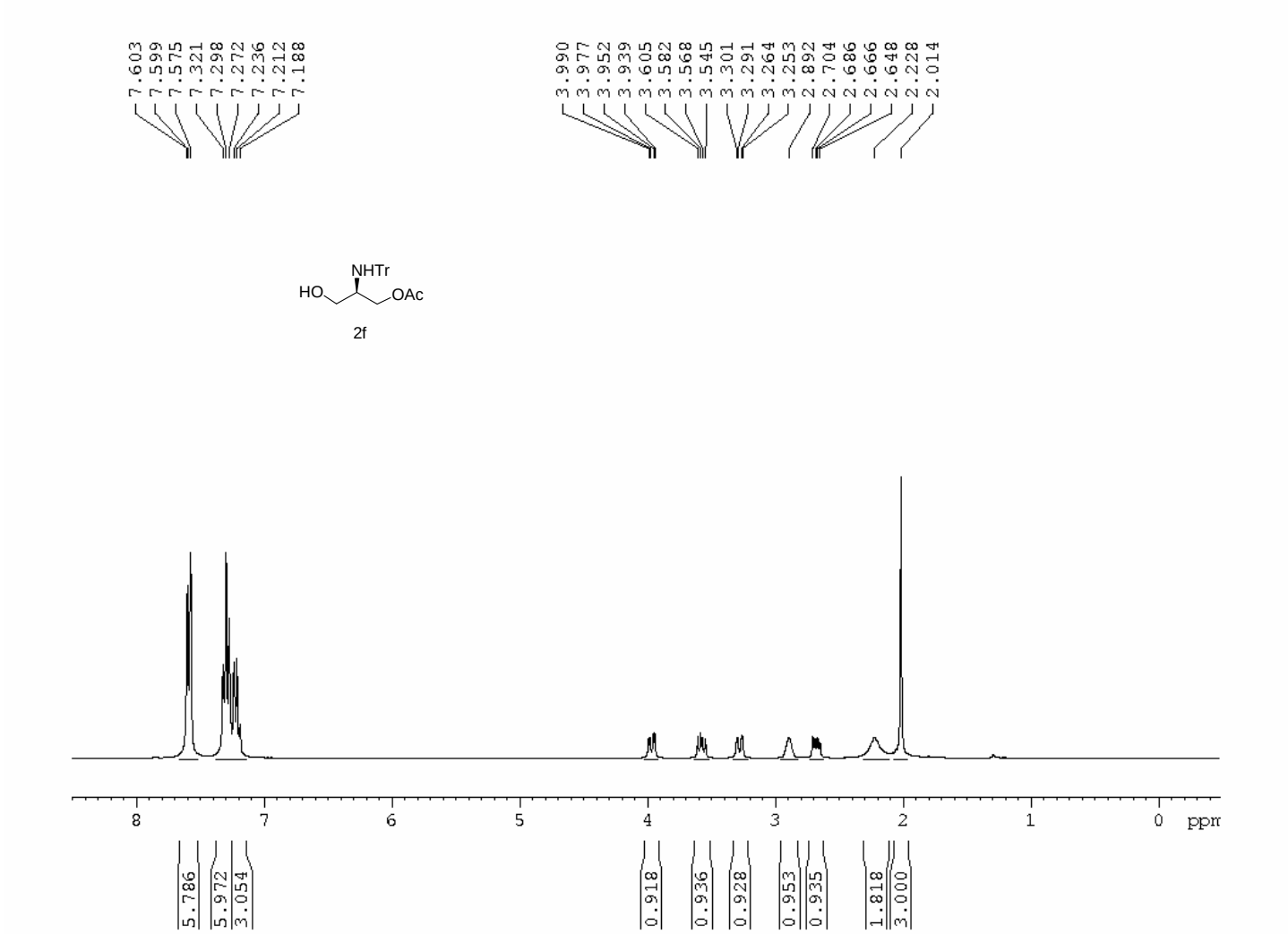
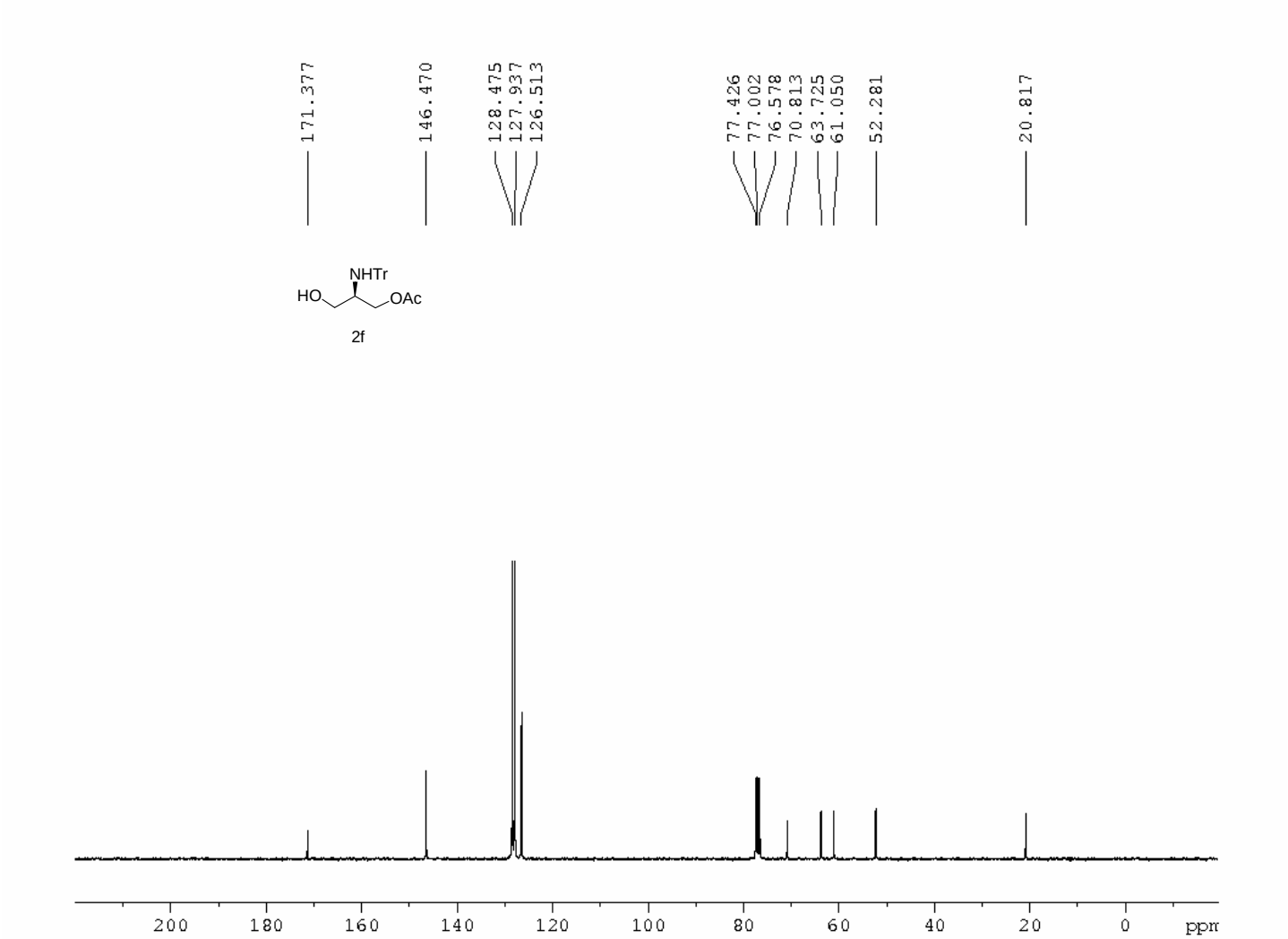
0.970
3.000

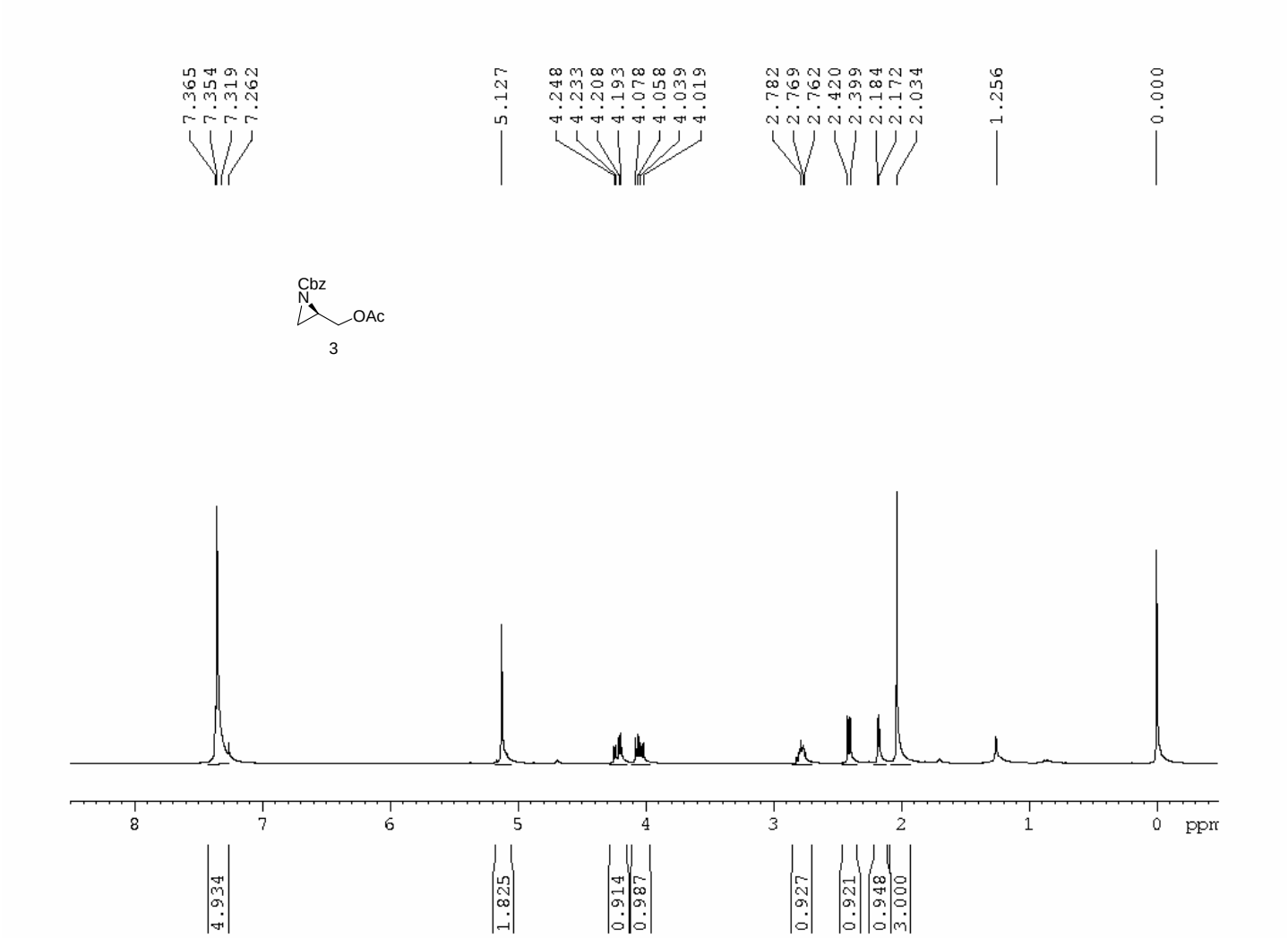

171.349
156.240
136.080
128.464
128.149
128.033
77.424
77.000
76.576
66.924
62.865
61.501
51.479
20.680
NHCbz
HO
OAc
2d
200
180
160
140
120
100
80
60
40
20
0
ppm

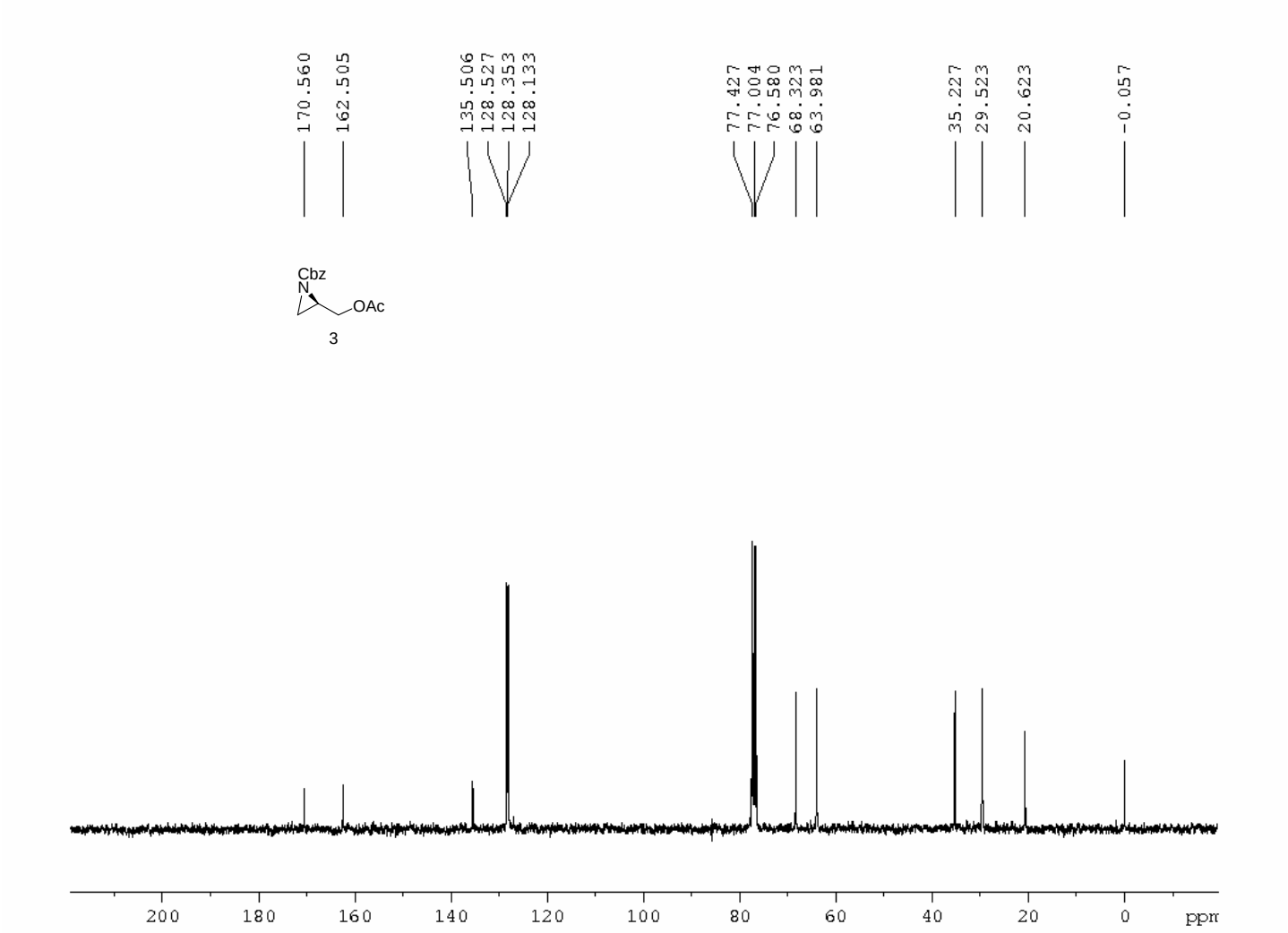

5.152
5.124
4.138
4.119
3.831
3.613
3.598
3.591
3.573
3.552
3.535
2.030
1.994
1.391
1.156
1.136
NHBoc
HO
OAc
2e
8
7
6
5
4
3
2
1
0
ppm
0.914
1.922
0.990
2.149
3.000
8.853
0.806

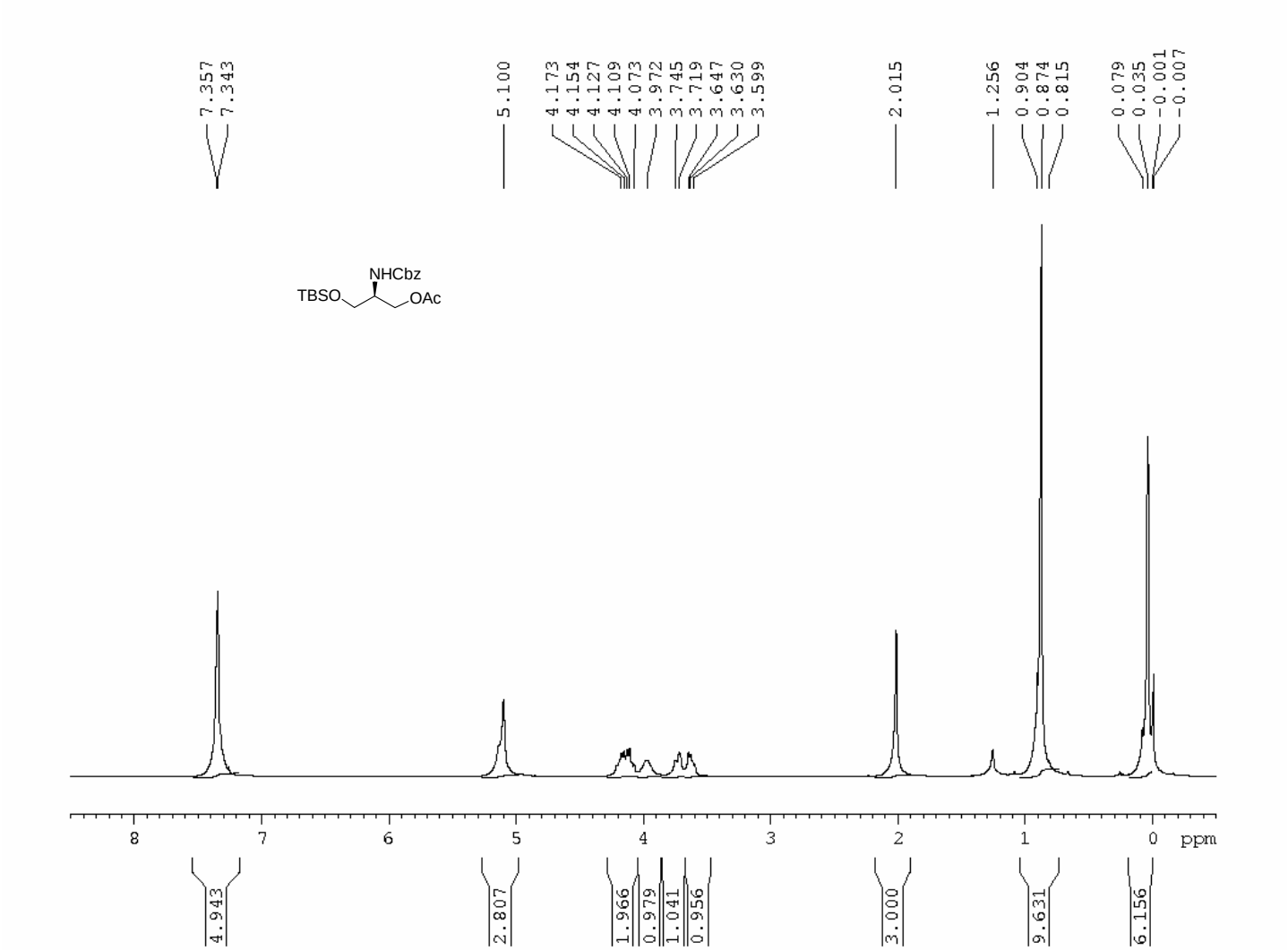

171.337
155.778
79.807
77.421
76.996
76.572
63.070
61.526
50.915
28.204
25.065
20.708
NHBoc
HO
OAc
2e
200
180
160
140
120
100
80
60
40
20
0
ppm

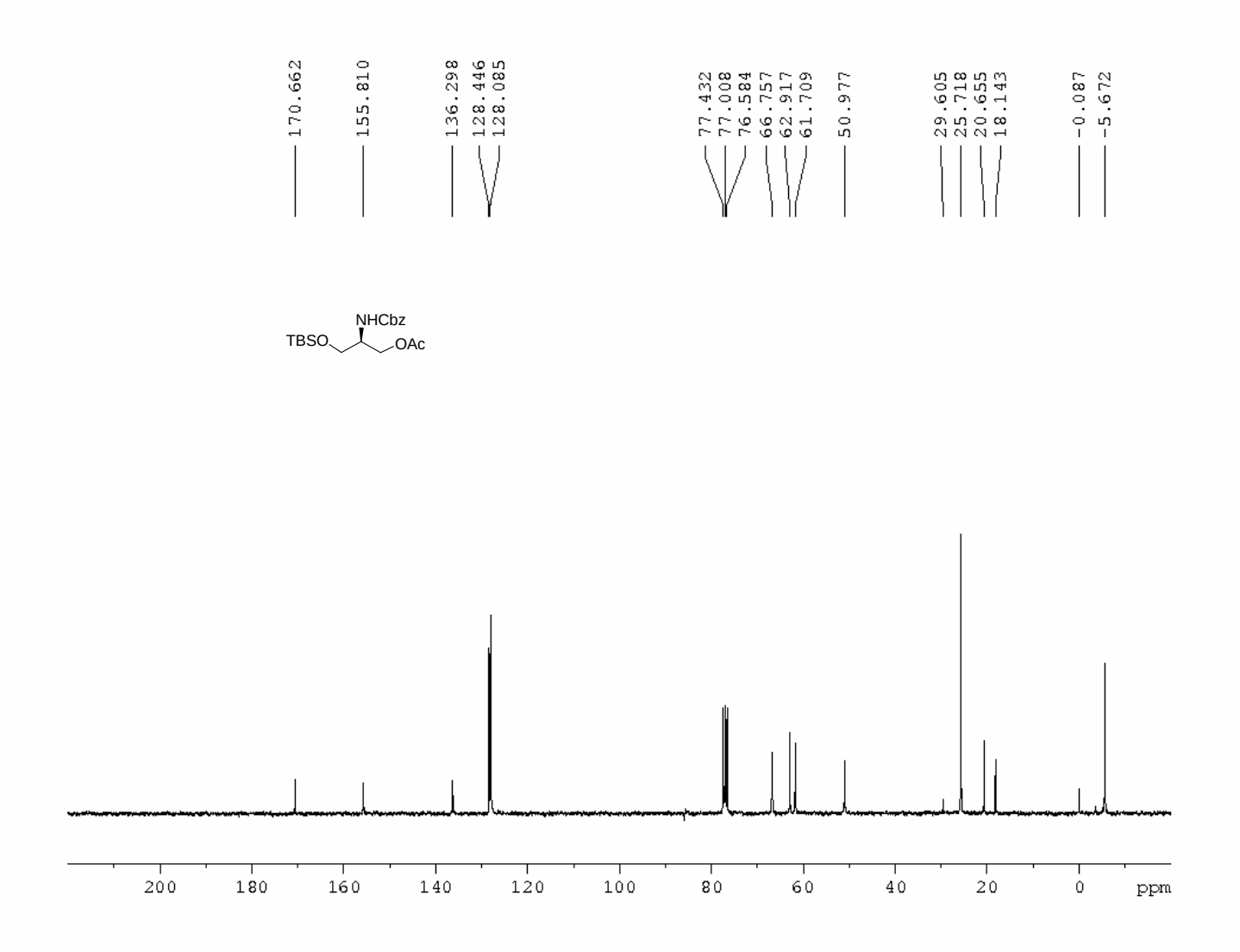

7.603
7.599
7.575
7.321
7.298
7.272
7.236
7.212
7.188
3.990
3.977
3.952
3.939
3.605
3.582
3.568
3.545
3.301
3.291
3.264
3.253
2.892
2.704
2.686
2.666
2.648
2.228
2.014
NHTr
HO
OAc
2f
8
7
6
5
4
3
2
1
0
ppm
5.786
5.972
3.054
0.918
0.936
0.928
0.953
0.935
1.818
3.000

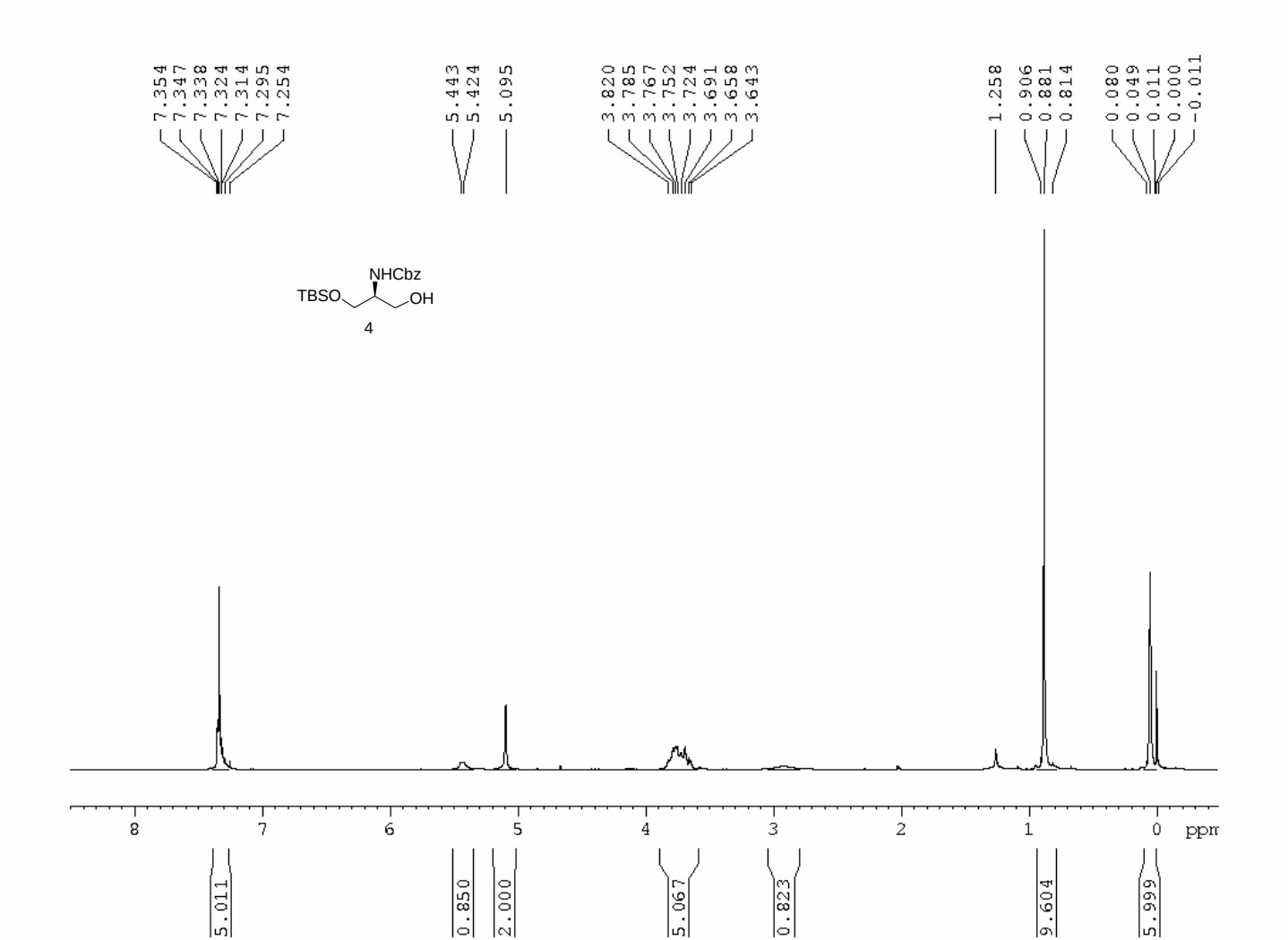

171.377
146.470
128.475
127.937
126.513
77.426
77.002
76.578
70.813
63.725
61.050
52.281
20.817
NHTr
HO
OAc
2f
200
180
160
140
120
100
80
60
40
20
0
ppm

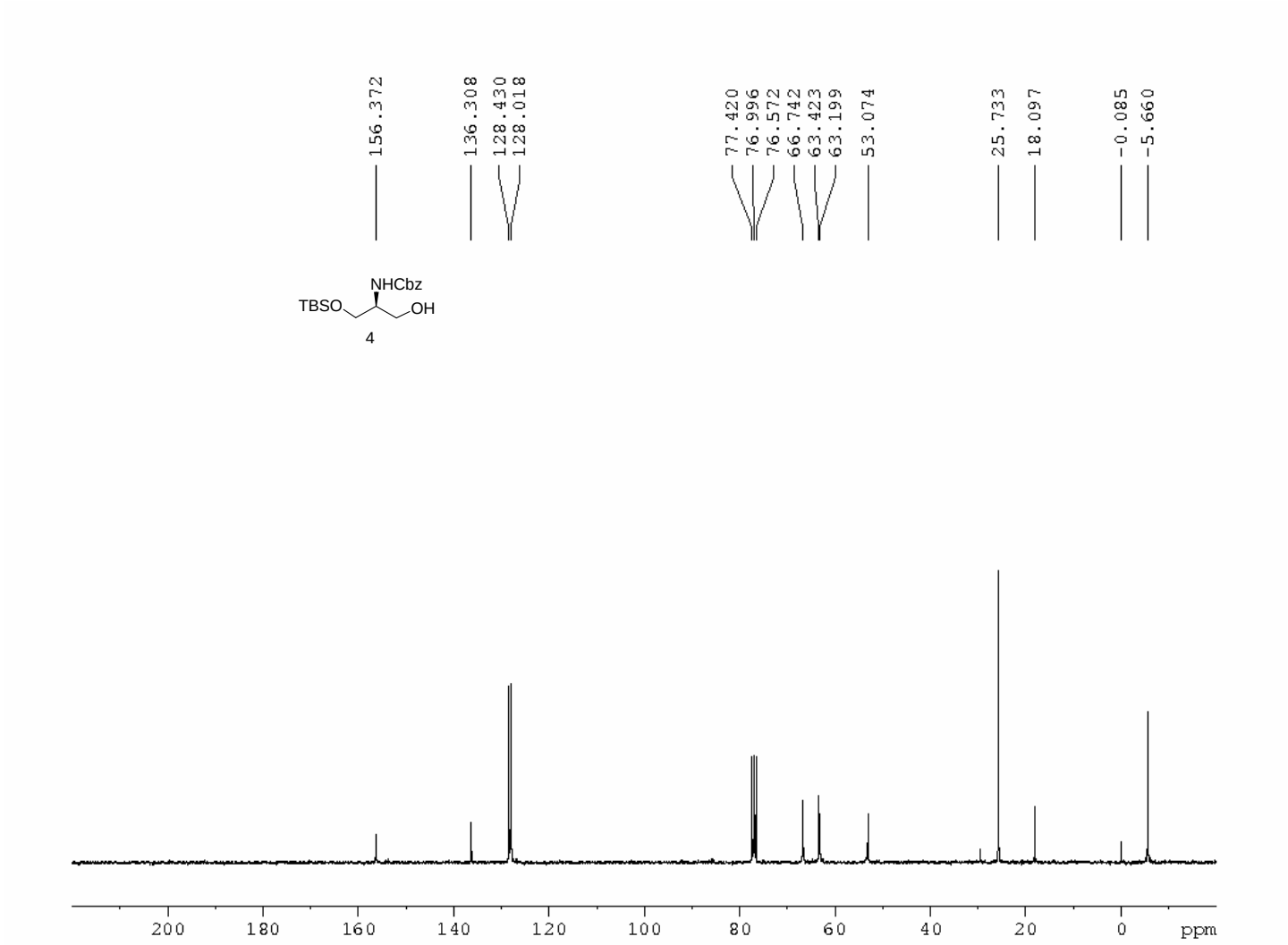

7.365
7.354
7.319
7.262
5.127
4.248
4.233
4.208
4.193
4.078
4.058
4.039
4.019
2.782
2.769
2.762
2.420
2.399
2.184
2.172
2.034
1.256
0.000
Cbz
N
OAc
3
8
7
6
5
4
3
2
1
0
ppm
4.934
1.825
0.914
0.987
0.927
0.921
0.948
3.000

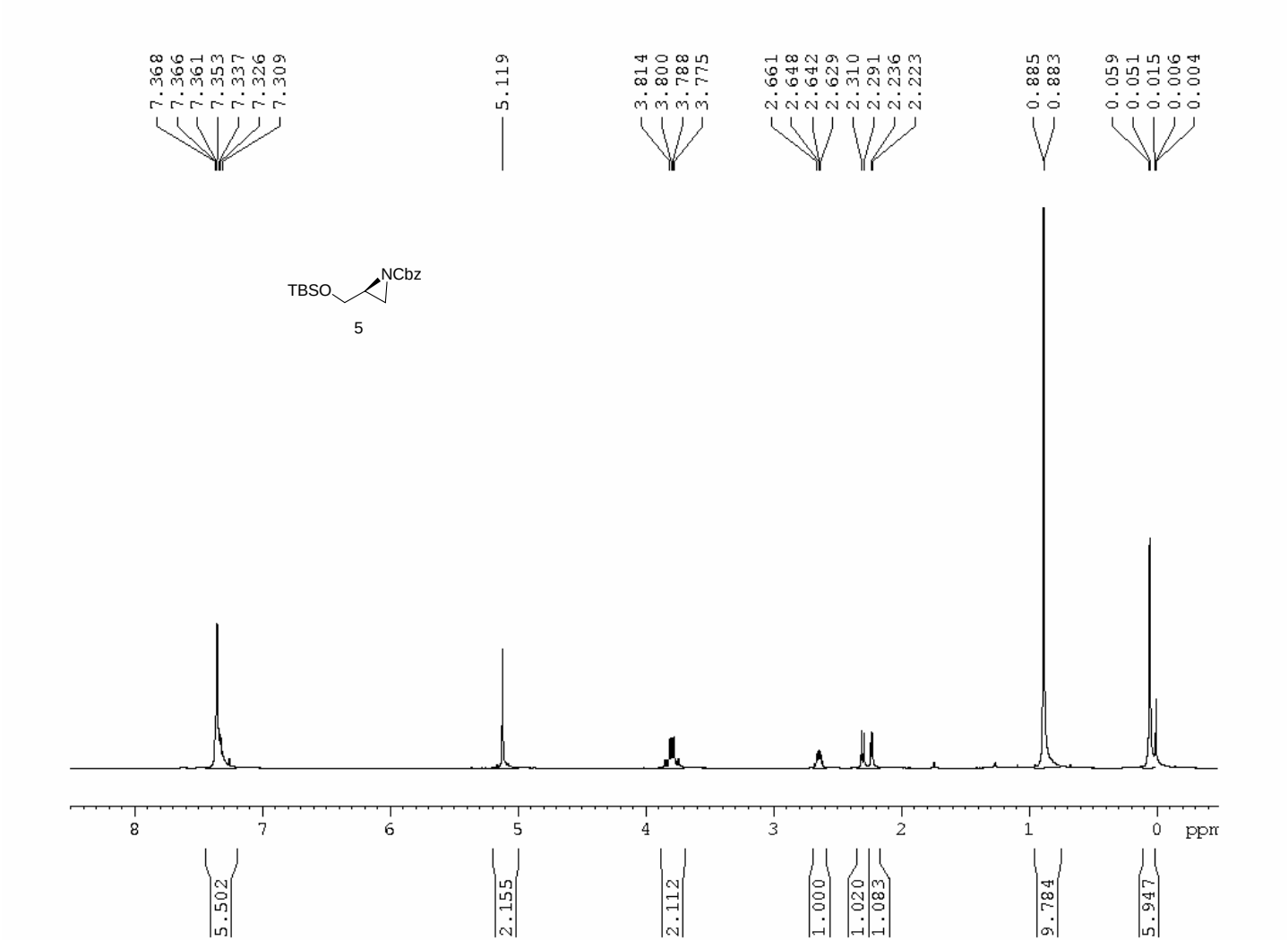

170.560
162.505
135.506
128.527
128.353
128.133
77.427
77.004
76.580
68.323
63.981
35.227
29.523
20.623
-0.057
Cbz
N
OAc
3
200
180
160
140
120
100
80
60
40
20
0
ppm

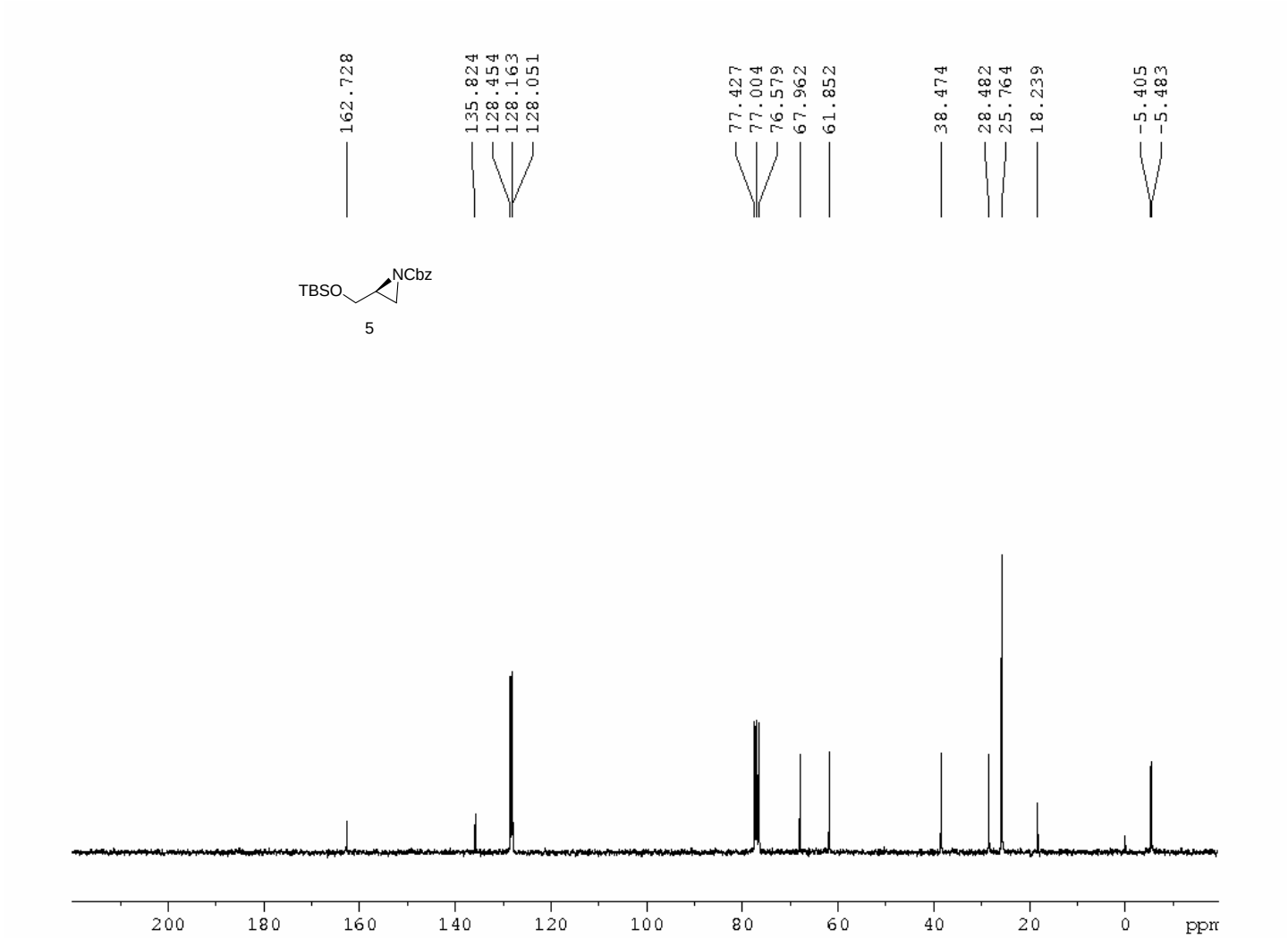

7.357
7.343
5.100
4.173
4.154
4.127
4.109
4.073
3.972
3.745
3.719
3.647
3.630
3.599
2.015
1.256
0.904
0.874
0.815
0.079
0.035
-0.001
-0.007
NHCbz
TBSO
OAc
8
7
6
5
4
3
2
1
0
ppm
4.943
2.807
1.966
0.979
1.041
0.956
3.000
9.631
6.156

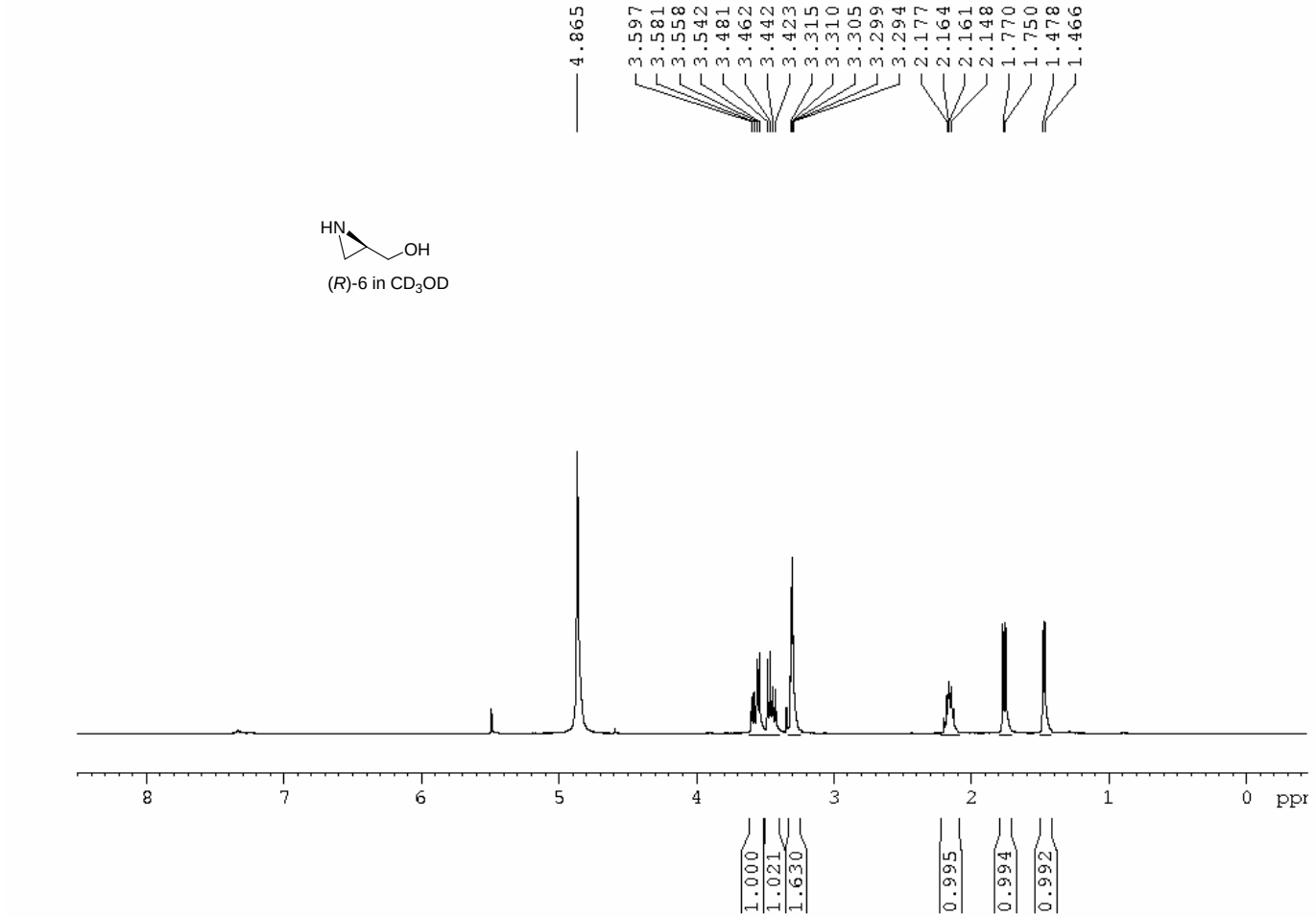

170.662
155.810
136.298
128.446
128.085
77.432
77.008
76.584
66.757
62.917
61.709
50.977
29.605
25.718
20.655
18.143
-0.087
-5.672
NHCbz
TBSO
OAc
200
180
160
140
120
100
80
60
40
20
0
ppm

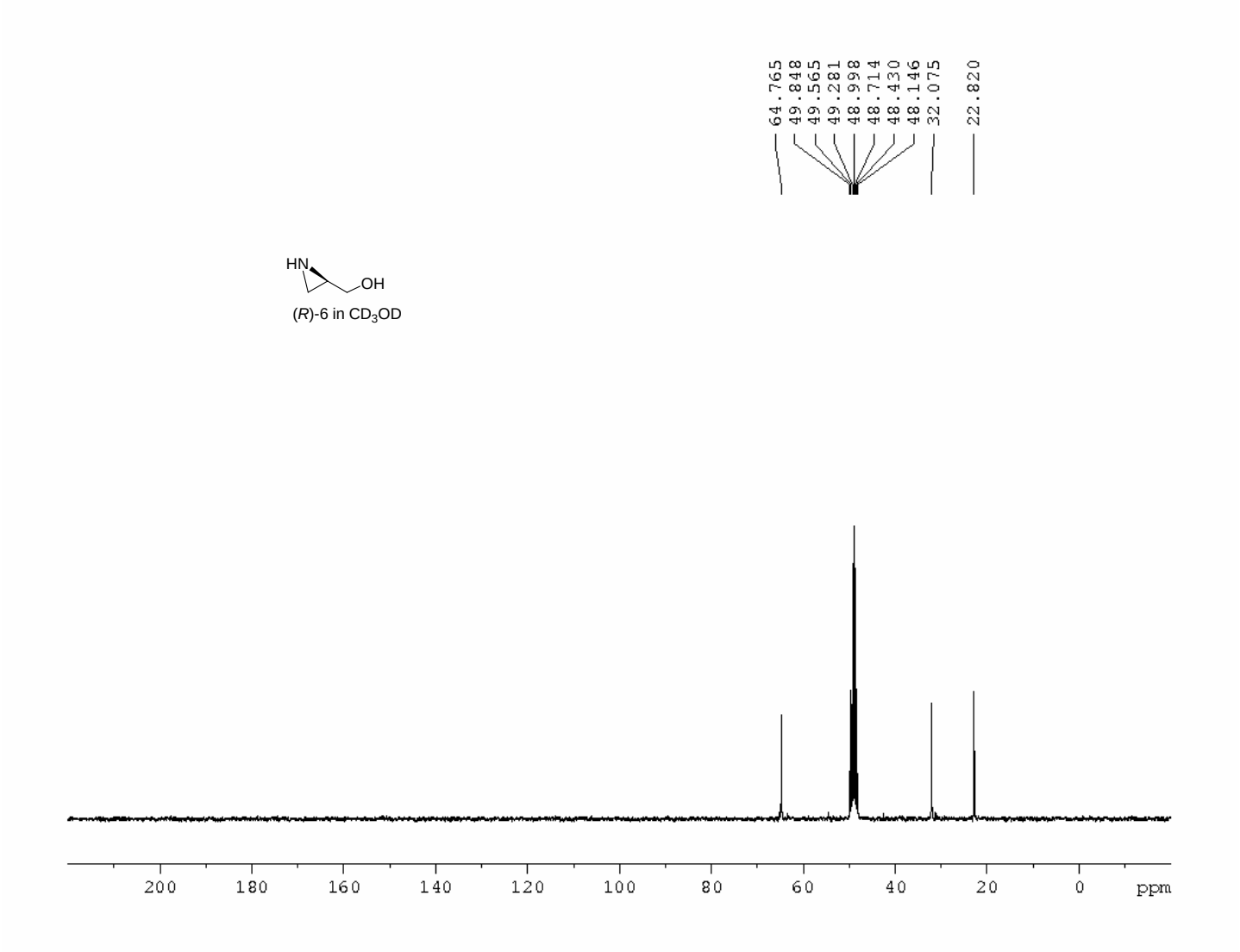

7.354
7.347
7.338
7.324
7.314
7.295
7.254
5.443
5.424
5.095
3.820
3.785
3.767
3.752
3.724
3.691
3.658
3.643
1.258
0.906
0.881
0.814
0.080
0.049
0.011
0.000
-0.011
NHCbz
TBSO
OH
4
8
7
6
5
4
3
2
1
0
ppm
5.011
0.850
2.000
5.067
0.823
9.604
5.999

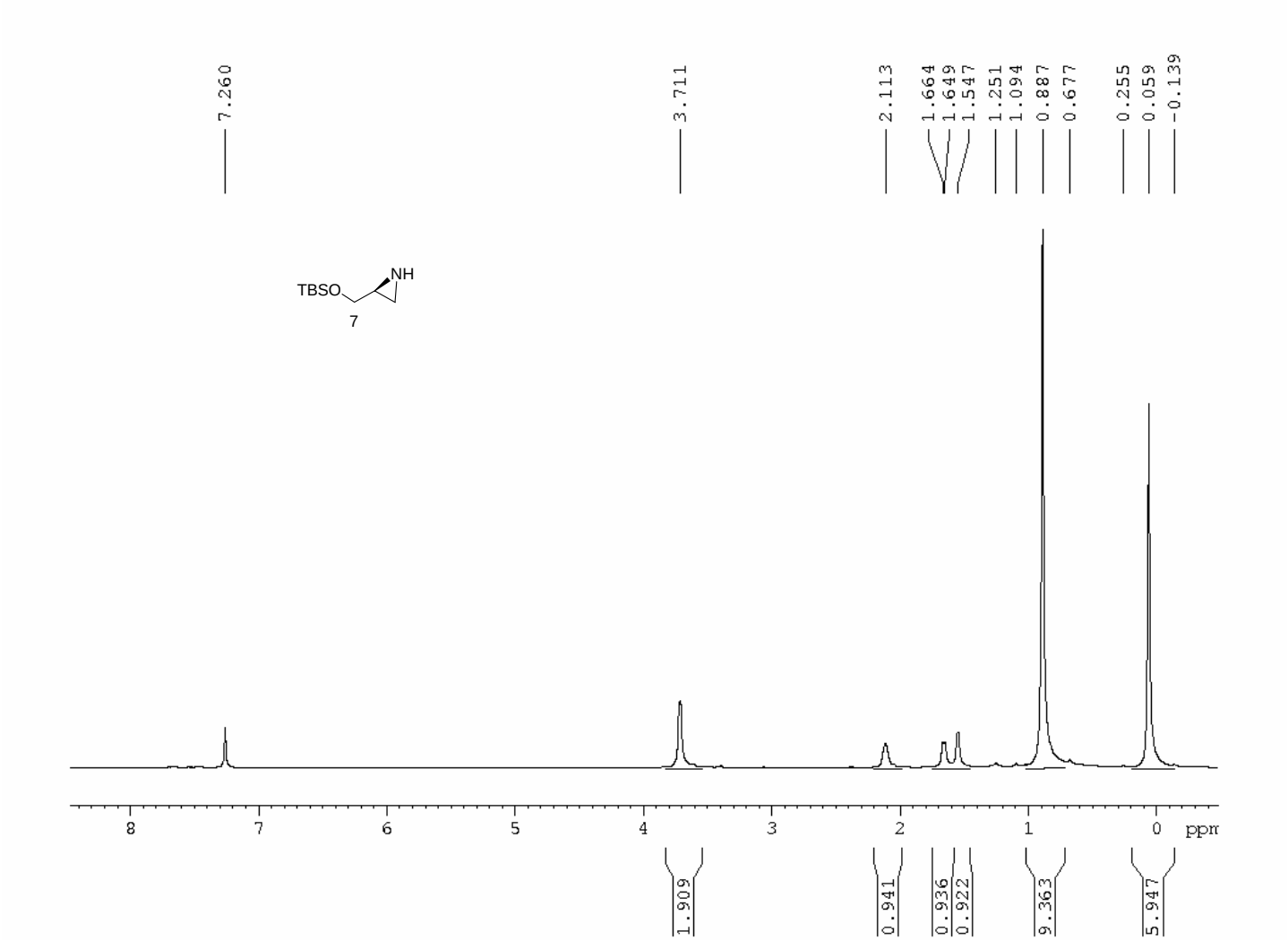

156.372
136.308
128.430
128.018
77.420
76.996
76.572
66.742
63.423
63.199
53.074
25.733
18.097
-0.085
-5.660
NHCbz
TBSO
OH
4
200
180
160
140
120
100
80
60
40
20
0
ppm


7.368
7.366
7.361
7.353
7.337
7.326
7.309
5.119
3.814
3.800
3.788
3.775
2.661
2.648
2.642
2.629
2.310
2.291
2.236
2.223
0.885
0.883
0.059
0.051
0.015
0.006
0.004
TBSO
NCbz
5
8
7
6
5
4
3
2
1
0
ppm
5.502
2.155
2.112
1.000
1.020
1.083
9.784
5.947


162.728
135.824
128.454
128.163
128.051
77.427
77.004
76.579
67.962
61.852
38.474
28.482
25.764
18.239
-5.405
-5.483
TBSO
NCbz
5
200
180
160
140
120
100
80
60
40
20
0
ppm


4.865
3.597
3.581
3.558
3.542
3.481
3.462
3.442
3.423
3.315
3.310
3.305
3.299
3.294
2.177
2.164
2.161
2.148
1.770
1.750
1.478
1.466
HN
OH
(R)-6 in CD3OD
8
7
6
5
4
3
2
1
0
ppm
1.000
1.021
1.630
0.995
0.994
0.992


64.765
49.848
49.565
49.281
48.998
48.714
48.430
48.146
32.075
22.820
HN
OH
(R)-6 in CD3OD
200
180
160
140
120
100
80
60
40
20
0
ppm


7.260
3.711
2.113
1.664
1.649
1.547
1.251
1.094
0.887
0.677
0.255
0.059
-0.139
TBSO
NH
7
8
7
6
5
4
3
2
1
0
ppm
1.909
0.941
0.936
0.922
9.363
5.947

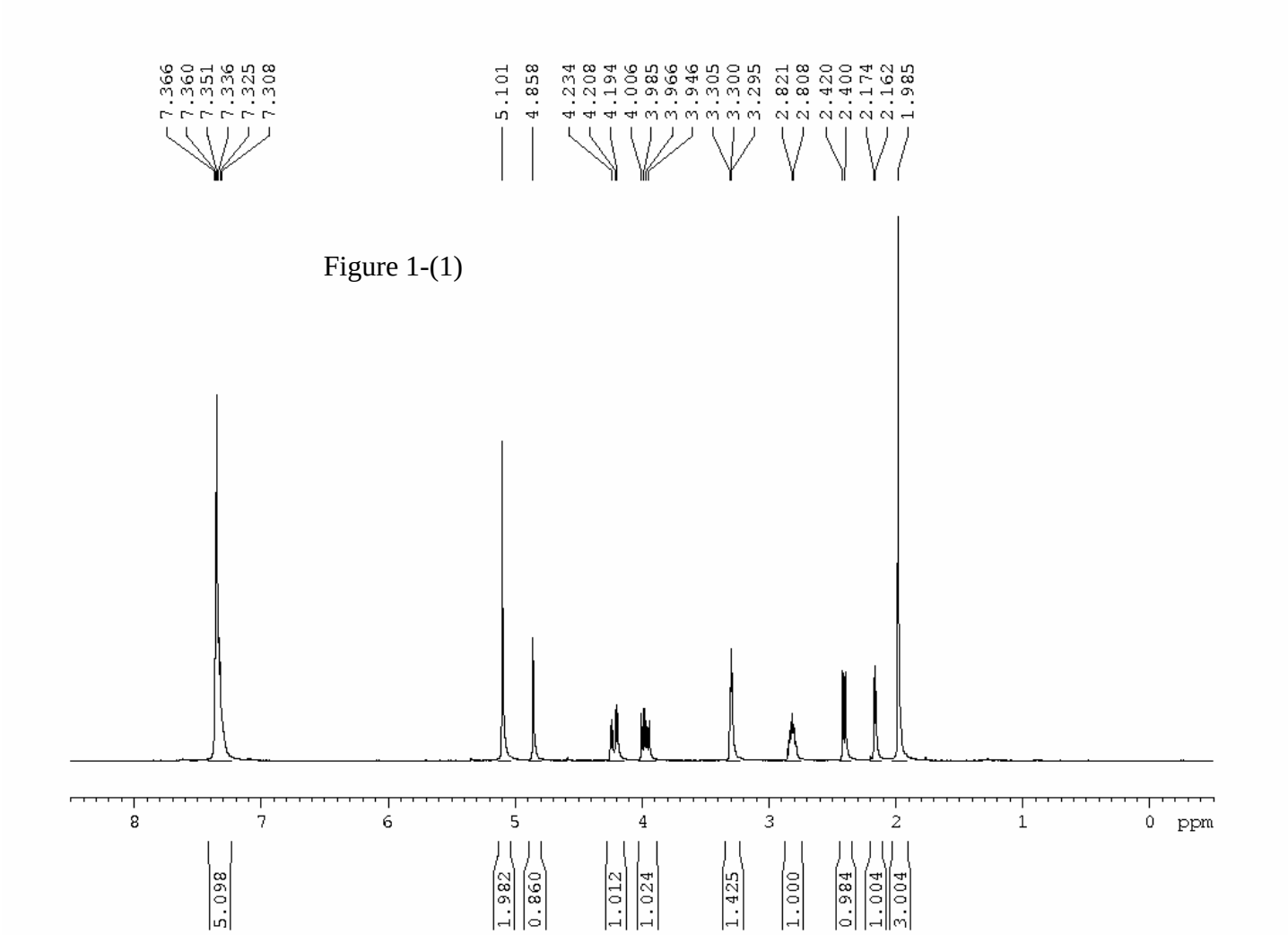

7.366
7.360
7.351
7.336
7.325
7.308
5.101
4.858
4.234
4.208
4.194
4.006
3.985
3.966
3.946
3.305
3.300
3.295
2.821
2.808
2.420
2.400
2.174
2.162
1.985
8
7
6
5
4
3
2
1
0
ppm
5.098
1.982
0.860
1.012
1.024
1.425
1.000
0.984
1.004
3.004

Figure 1-(1)

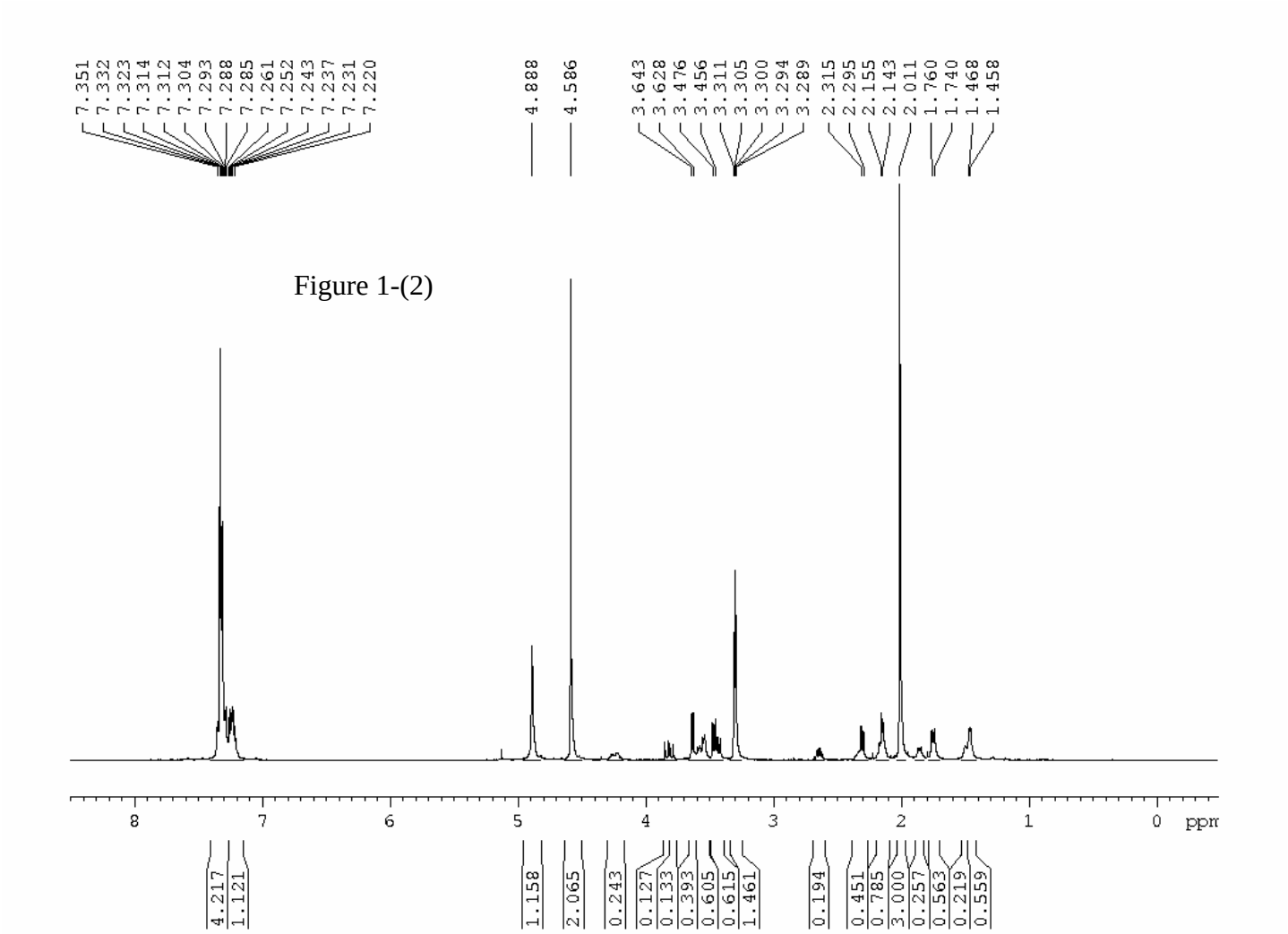

7.351
7.332
7.323
7.314
7.312
7.304
7.293
7.288
7.285
7.261
7.252
7.243
7.237
7.231
7.220
4.888
4.586
3.643
3.628
3.476
3.456
3.311
3.305
3.300
3.294
3.289
2.315
2.295
2.155
2.143
2.011
1.760
1.740
1.468
1.458
8
7
6
5
4
3
2
1
0
ppm
4.217
1.121
1.158
2.065
0.243
0.127
0.133
0.393
0.605
0.615
1.461
0.194
0.451
0.785
3.000
0.257
0.563
0.219
0.559

Figure 1-(2)

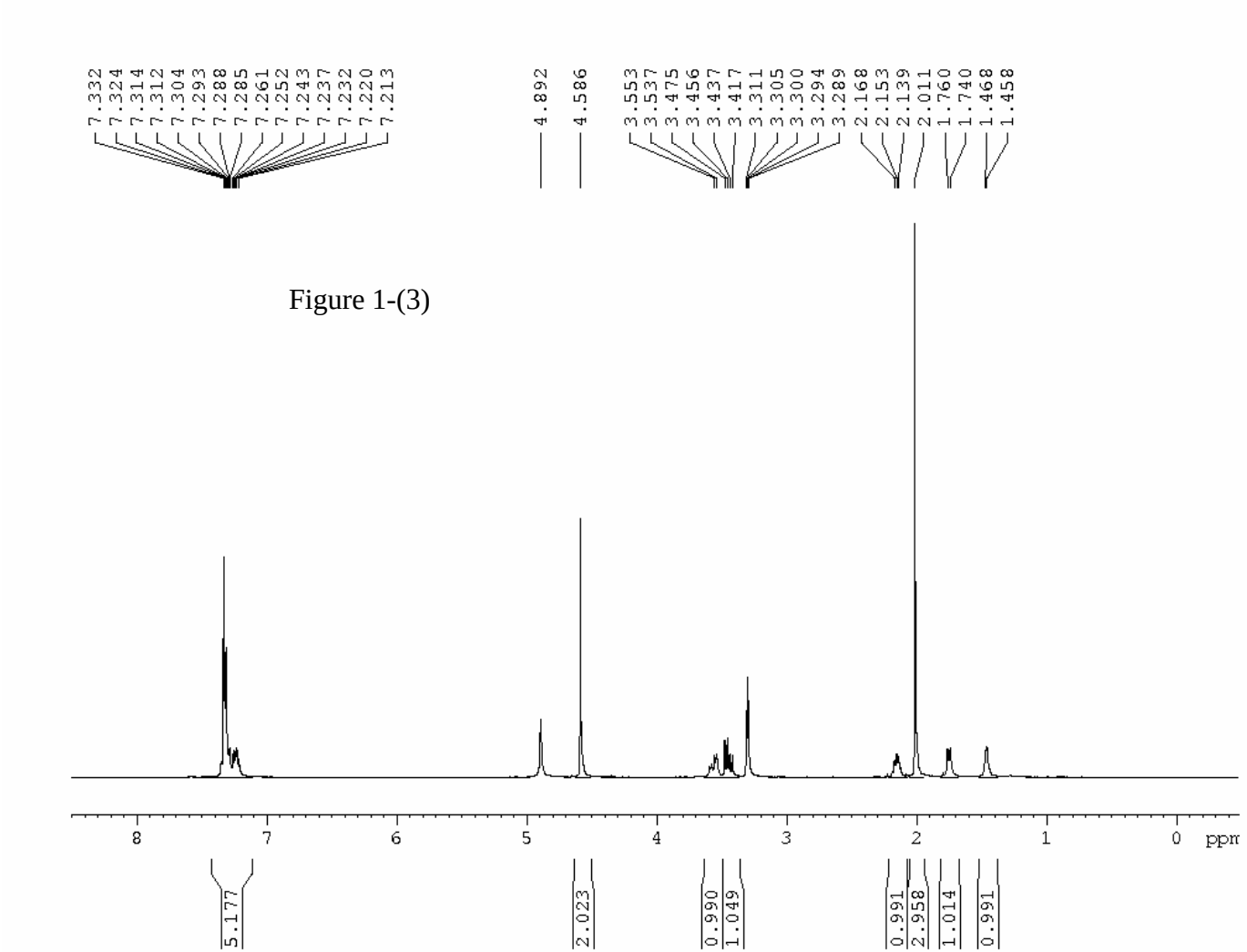

7.332
7.324
7.314
7.312
7.304
7.293
7.288
7.285
7.261
7.252
7.243
7.237
7.232
7.220
7.213
4.892
4.586
3.553
3.537
3.475
3.456
3.437
3.417
3.311
3.305
3.300
3.294
3.289
2.168
2.153
2.139
2.011
1.760
1.740
1.468
1.458
8
7
6
5
4
3
2
1
0
ppm
5.177
2.023
0.990
1.049
0.991
2.958
1.014
0.991

Figure 1-(3)