Efficient Enantio- and Diastereodivergent Synthesis of Poison-frog Alkaloids **251O** and **223B**

Naoki Toyooka,*[,1] Dejun Zhou,[1] Hideo Nemoto,[1] Yasuhiro Tezuka,[2] Shigetoshi Kadota,[2] Nirina R. Andriamaharavo,[3] H. Martin Garraffo,[3] Thomas F. Spande,[3] and John W. Daly[3]

1. Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Sugitani 2630, Toyama 930-0194, Japan
2 Institute of Natural Medicine, University of Toyama, Sugitani 2630, Toyama 930-0194, Japan
3 Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, DHHS, Bethesda, MD 20892, USA

Supporting Information

Table of Contents

General

All reactions were performed under argon atmosphere. All commercially available reagents were used without further purification unless otherwise noted. Column chromatography was performed with silica gel (0.063-0.2 mm). Solvents were evaporated under reduced pressure. All yields given refer to as isolated yields. Optical rotations were measured on a precision automated polarimeter. NMR spectra were recorded on a 300 or 500 MHz spectrometer. Chemical shifts (delta are reported in ppm downfield from tetramethylsilane. Coupling constants (J values) are reported in Hertz. IR spectra were recorded on a FT-IR spectrometer. MS and HRMS experiments were performed on a high/low resolution magnetic sector mass spectrometer. GCMS experiments were performed using a mass selective detector GC/MS system.

(2*S*,5*R*)-(+)-2-But-3-enyl-5-propylpyrrolidine-1-carboxylic acid *tert*-butyl ester (ent-4, R = *n*-Pr)

To a stirred solution of **9** (R = *n*-Pr, 1.22 g, 4.31 mmol) in CH_2Cl_2 (20 mL) was added a solution of $(C_6F_5)_3B$ (441 mg, 0.86 mmol) and Ph_3SiH (2.25, 8.62 mmol) in CH_2Cl_2 (25 mL) at -78 °C, and the reaction mixture was stirred at -78 °C for 30 min, and then at room temperature for 20 h. The reaction was quenched with Et_3N (4.0 mL), and the resulting mixture was stirred at room temperature for 20 min. The mixture was diluted with Et_2O, and the organic layer was washed successively with 10% AcOH (aq) solution and satd. $NaHCO_3$ (aq) solution, dried over $MgSO_4$, and evaporated to give a pale yellow oil, that was chromatographed on silica gel (60 g, hexane/acetone=200:1-150:1) to give ent-**4** (R = *n*-Pr, 839 mg, 73%) as a colorless oil.

The spectral data were identical with those of **4** (R = *n*-Pr). $[\alpha]_D^{26}$ +3.14 (*c* 1.07, $CHCl_3$).

(2*S*,5*R*)-(+)-2-But-3-enyl-5-heptylpyrrolidine-1-carboxylic acid *tert*-butyl ester (ent-4, R = *n*-C_7H_{15})

To a stirred solution of **9** (R = *n*-C_7H_{15}, 786 mg, 2.32 mmol) in CH_2Cl_2 (30 mL) was added a solution of $(C_6F_5)_3B$ (238 mg, 0.46 mmol) and Ph_3SiH (1.21 g, 4.64 mmol) in CH_2Cl_2 (5 mL) at -78 °C, and the reaction mixture was stirred at -78 °C for 30 min, and then at room temperature for 22 h. The reaction was quenched with Et_3N (2.5 mL), and the resulting mixture was stirred at room temperature for 20 min. The mixture was diluted with Et_2O, and the organic layer was washed successively with 10% AcOH (aq) solution and satd. $NaHCO_3$ (aq) solution, dried over $MgSO_4$, and evaporated to give a pale yellow oil, that was

chromatographed on silica gel (40 g, hexane/acetone=200:1-150:1) to give ent-**4** (R = *n*-C_7H_{15}, 644 mg, 86%) as a colorless oil.
The spectral data were identical with those of **4** (R = *n*-C_7H_{15}). $[\alpha]_D^{26}$ +0.92 (*c* 1.03, $CHCl_3$).

(2*S*,5*R*)-(+)-2-(4-Ethoxycarbonylbut-3-enyl)-5-propylpyrrolidine-1-carboxylic acid *tert*-butyl ester (ent-5, R = *n*-Pr)

To a stirred solution of ent-**4** (R = *n*-Pr, 637 mg, 2.38 mmol) in CH_2Cl_2 (25 mL) were added Grubbs 2nd catalyst (81 mg, 0.095 mmol) and ethyl acrylate (1.3 mL, 11.90 mmol), and the resulting mixture was refluxed for 6 h. After cooling, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (40 g, hexane/acetone=100:1-60:1) to give ent-**5** (R = *n*-Pr, 784 mg, 97%) as a pale yellow oil.
The spectral data were identical with those of **5** (R = *n*-Pr). $[\alpha]_D^{26}$ +6.42 (*c* 0.70, $CHCl_3$).

(2*S*,5*R*)-(+)-2-(4-Ethoxycarbonylbut-3-enyl)-5-heptylpyrrolidine-1-carboxylic acid *tert*-butyl ester (ent-5, R = *n*-C_7H_{15})

To a stirred solution of ent-**4** (R = *n*-C_7H_{15}, 644 mg, 1.99 mmol) in CH_2Cl_2 (25 mL) were added Grubbs 2nd catalyst (68 mg, 0.080 mmol) and ethyl acrylate (1.0 mL, 9.97 mmol), and the resulting mixture was refluxed for 5.5 h. After cooling, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (20 g, hexane/acetone=100:1-60:1) to give ent-**5** (R = *n*-C_7H_{15}, 748 mg, 95%) as a pale yellow oil.
The spectral data were identical with those of **5** (R = *n*-C_7H_{15}). $[\alpha]_D^{26}$ +1.59 (*c* 0.71, $CHCl_3$).

(3*R*,5*S*,8*S*)-(-)-(5-Propylhexahydropyrrolizin-3-yl)acetic acid ethyl ester (ent-6, R = *n*-Pr)

To a stirred solution of ent-**5** (R = *n*-Pr, 240 mg, 0.71 mmol) in CH_2Cl_2 (20 mL) was added $AlCl_3$ (206 mg, 1.56 mmol) at 0 °C, and the resulting suspension was stirred at room temperature for 24 h. The reaction was quenched with satd. $NaHCO_3$ (aq) solution, and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (15 mL x 5), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a residue. To a stirred solution of this residue in CH_2Cl_2 (20 mL) was added K_2CO_3 (200 mg, 1.42 mmol), and the resulting suspension was stirred at room temperature for 48 h. The insoluble material was filtered off, and washed with CH_2Cl_2. The filtrate was evaporated to afford the residue, that was chromatographed on silica gel (20 g, hexane/acetone=20:1-8:1) to give ent-**6** (R = *n*-Pr, 157 mg, 93%) as a pale yellow oil.

The spectral data were identical with those of **6** (R = Et). $[\alpha]_D^{26}$ -29.06 (*c* 0.53, $CHCl_3$).

(3*S*,5*R*,8*R*)-(-)-(5-Heptylhexahydropyrrolizin-3-yl)acetic acid ethyl ester (ent-6, R = *n*-C_7H_{15})

To a stirred solution of ent-**5** (R = *n*-C_7H_{15}, 120 mg, 0.30 mmol) in CH_2Cl_2 (10 mL) was added $AlCl_3$ (89 mg, 0.67 mmol) at 0 °C, and the resulting suspension was stirred at room temperature for 24 h. The reaction was quenched with satd. $NaHCO_3$ (aq) solution, and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (10 mL x 5), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a residue. To a stirred solution of this residue in CH_2Cl_2 (10 mL) was added K_2CO_3 (84 mg, 0.60 mmol), and the resulting suspension was stirred at room temperature for 48 h. The insoluble material was filtered off, and washed with CH_2Cl_2. The filtrate was evaporated to afford the residue, that was chromatographed on silica gel (20 g, hexane/acetone=20:1-8:1) to give ent-**6** (R = *n*-C_7H_{15}, 82 mg, 91%) as a pale yellow oil.

The spectral data were identical with those of **6** (R = *n*-C_6H_{13}). $[\alpha]_D^{26}$ -18.65 (*c* 1.00, $CHCl_3$).

(3*R*,5*R*,8*R*)-(-)-3-Heptyl-5-propylhexahydropyrrolizine (ent-7 R = *n*-Pr, R' = *n*-C_7H_{15})

To a stirred solution of ent-**6** (R = *n*-Pr, 81 mg, 0.33 mmol) in CH_2Cl_2 (7 mL) was added a solution of DIBAL (0.98 M in hexane, 0.37 mL, 0.36 mmol) at -50 °C, and the reaction mixture was stirred at -50 °C for 30 min. The reaction was quenched with MeOH, and satd. Rochelle (aq) solution, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 mL x 3), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a pale yellow oil, that was used directly in the next step.

To a stirred suspension of *n*-$C_5H_{11}P^+Ph_3Br^-$ (556 mg, 1.32 mmol) in THF (10 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 0.72 mL, 1.16 mmol) at 0 °C, and the resulting orange suspension was stirred at 0 °C for 10 min. To the suspension was added a solution of the above aldehyde in THF (3 mL) at 0 °C, and the resulting suspension was stirred at room temperature for 21 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (15 mL x 4). The organic extracts were combined, dried over K_2CO_3, and evaporated to give a residue, that was chromatographed on silica gel (20 g, hexane/acetone=25:1-10:1) to give the corresponding olefin (39 mg, 48%) as a mixture of *E*- and *Z*-isomers.

The ^1H NMR spectrum was identical with that of the enantiomer.

To a stirred solution of the above olefin (20 mg, 0.08 mmol) in EtOAc (3 mL) was added 10% Pd/C (10 mg), and the resulting suspension was stirred under a hydrogen atmosphere at 1 atm for 40 h. The catalyst was removed by filtration and the filtrate was evaporated to give ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}, 19 mg, 96%) as a pale yellow oil.

The spectral data were identical with those of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}). $[\alpha]_D^{26}$ +35.77 (*c* 0.37, $CHCl_3$).

(3*S*,5*R*,8*R*)-(-)-3-Allyl-5-heptylhexahydropyrrolizine

To a stirred solution of ent-**6** (R = *n*-C_6H_{13}, 95 mg, 0.32 mmol) in CH_2Cl_2 (7 mL) was added a solution of DIBAL (0.98 M in hexane, 0.36 mL, 0.35 mmol) at -50 °C, and the reaction mixture was stirred at -50 °C for 30 min. The reaction was quenched with MeOH, and then satd. Rochelle (aq) solution, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 mL x 3), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a pale yellow oil, that was used directly in the next step.

To a stirred suspension of $MeP^+Ph_3I^-$ (517 mg, 1.28 mmol) in THF (10 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 0.70 mL, 1.12 mmol) at 0 °C, and the resulting orange suspension was stirred at 0 °C for 10 min. To the suspension was added a solution of the above aldehyde in THF (3 mL) at 0 °C, and the resulting suspension was stirred at room temperature for 31 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (15 mL x 4). The organic extracts were combined, dried over K_2CO_3, and evaporated to give a residue, that was chromatographed on silica gel (20 g, hexane/acetone=20:1-10:1) to give the corresponding olefin (41 mg, 52%) as a pale yellow oil.

The spectral data were identical with those of the enantiomer. $[\alpha]_D^{26}$ -22.99 (*c* 0.10, $CHCl_3$).

(3*R*,5*R*,8*S*)-(-)-3-Heptyl-5-propylhexahydropyrrolizine (ent-7 R = *n*-C_7H_{15}, R' = *n*-Pr)

To a stirred solution of the above olefin (22 mg, 0.09mmol) in EtOAc (3 mL) was added 10% Pd/C (10 mg), and the resulting suspension was stirred under a hydrogen atmosphere at 1 atm for 48 h. The catalyst was removed by filtration and the filtrate was evaporated to give ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 22 mg, quant) as a pale yellow oil.

The spectral data were identical with those of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr). $[\alpha]_D^{26}$ -26.07 (*c* 0.25, $CHCl_3$).

(2*S*,5*R*)-(+)-2-But-3-enyl-5-butylpyrrolidine-1-carboxylic acid *tert*-butyl ester (ent-11)

To a stirred solution of **11** (155 mg, 0.52 mmol) in CH_2Cl_2 (5 mL) was added a solution of $(C_6F_5)_3B$ (54 mg, 0.10 mmol) and Ph_3SiH (260 mg, 1.04 mmol) in CH_2Cl_2 (10 mL) at -78 °C, and the reaction mixture was stirred at -78 °C for 30 min, and then at room temperature for 26 h. The reaction was quenched with Et_3N (1.0 mL), and the resulting mixture was stirred at room temperature for 20 min. The mixture was diluted with Et_2O, and the organic layer was washed successively with 10% AcOH (aq) solution and satd. $NaHCO_3$ (aq) solution, dried over $MgSO_4$, and evaporated to give a pale yellow oil, that was chromatographed on silica gel (20 g, hexane/acetone=200:1-150:1) to give ent-**11** (105 mg, 72%) as a colorless oil.

The spectral data were identical with those of **11**. $[\alpha]_D^{26}$ +3.10 (*c* 0.46, $CHCl_3$).

(2*S*,5*R*)-(+)-2-(4-Ethoxycarbonylbut-3-enyl)-5-butylpyrrolidine-1-carboxylic acid *tert*-butyl ester (ent-12)

To a stirred solution of ent-**11** (270 mg, 0.96 mmol) in CH_2Cl_2 (15 mL) were added Grubbs 2nd catalyst (33 mg, 0.04 mmol) and ethyl acrylate (0.52 mL, 4.80 mmol), and the resulting mixture was refluxed for 7 h. After cooling, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (20 g, hexane/acetone=100:1-60:1) to give ent-**12** (286 mg, 84%) as a pale yellow oil.

The spectral data were identical with those of **12**. $[\alpha]_D^{26}$ +2.81 (*c* 0.42, $CHCl_3$).

(3*S*,5*R*,8*R*)-(-)-(5-Butylhexahydropyrrolizin-3-yl)acetic acid ethyl ester (ent-13)

To a stirred solution of ent-**12** (276 mg, 0.78 mmol) in CH_2Cl_2 (15 mL) was added $AlCl_3$ (229 mg, 1.72 mmol) at 0 °C, and the resulting suspension was stirred at room temperature for 24 h. The reaction was quenched with satd. $NaHCO_3$ (aq) solution, and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (20 mL x 5), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a residue. To a stirred solution of this residue in CH_2Cl_2 (15 mL) was added K_2CO_3 (168 mg, 1.22 mmol), and the resulting suspension was stirred at room temperature for 58 h. The insoluble material was filtered off, and washed with CH_2Cl_2. The filtrate was evaporated to afford a residue, that was chromatographed on silica gel (30 g, hexane/acetone=20:1-8:1) to give ent-**13** (174 mg, 88%) as a pale yellow oil.

The spectral data were identical with those of **13**. $[\alpha]_D^{26}$ -24.01 (*c* 0.87, $CHCl_3$).

(3*R*,5*R*,8*R*)-(-)-3,5-Dibutylhexahydropyrrolizine (ent-14)

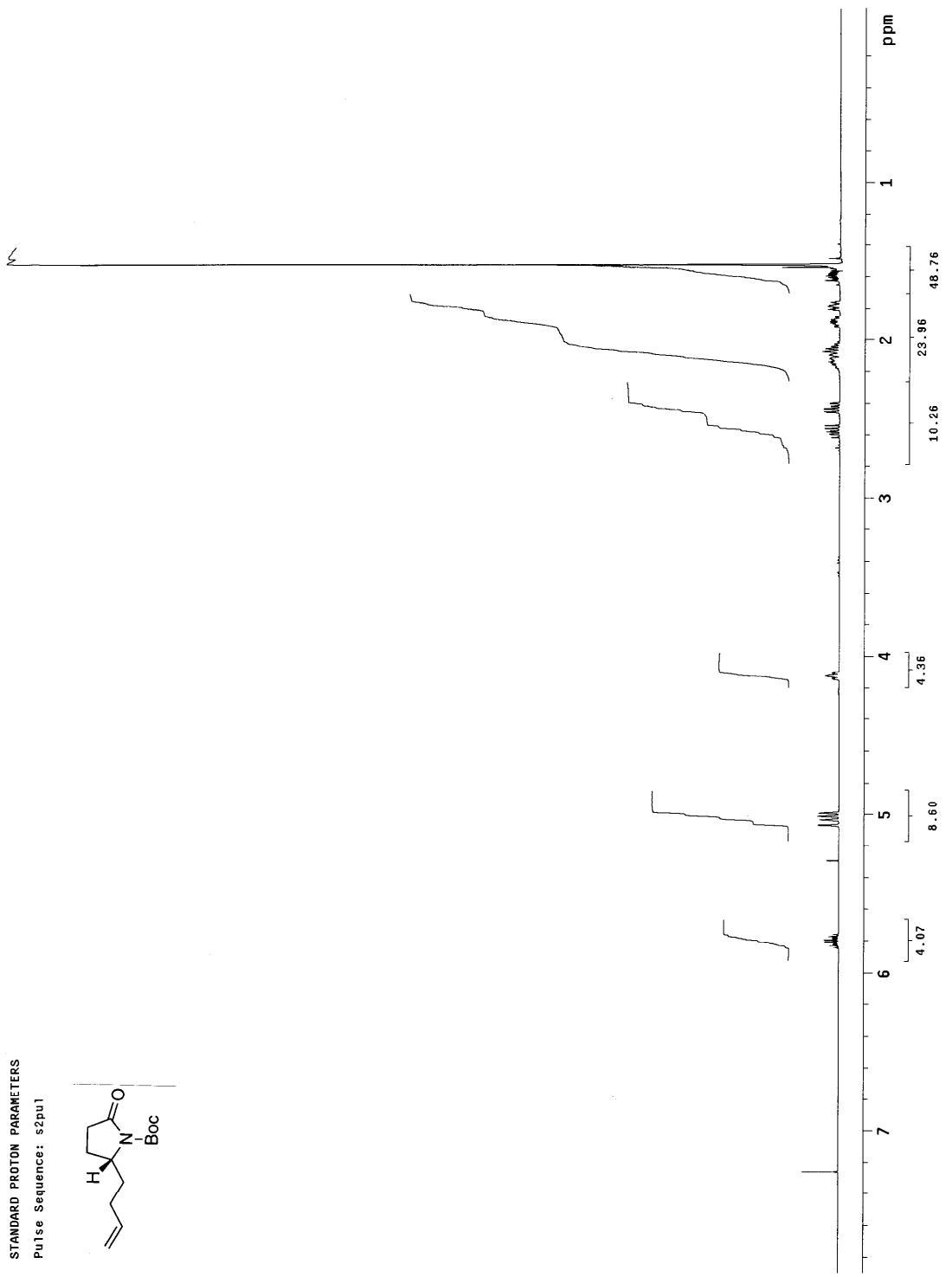
To a stirred solution of ent-**13** (75 mg, 0.30 mmol) in CH_2Cl_2 (7 mL) was added a solution of DIBAL (0.98 M in hexane, 0.34 mL, 0.33 mmol) at -50 °C, and the reaction mixture was stirred at -50 °C for 30 min. The reaction was quenched with MeOH, and satd. Rochelle (aq) solution, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 mL x 3), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a pale yellow oil, that was used directly in the next step.

To a stirred suspension of $EtP^+Ph_3Br^-$ (440 mg, 1.20 mmol) in THF (10 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 0.64 mL, 1.05 mmol) at 0 °C, and the resulting orange suspension was stirred at 0 °C for 10 min. To the suspension was added a solution of the above aldehyde in THF (3 mL) at 0 °C, and the resulting suspension was stirred at room temperature for 23 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (15 mL x 4). The organic extracts were combined, dried over K_2CO_3, and evaporated to give a residue, that was chromatographed on silica gel (20 g, hexane/acetone=25:1-10:1) to give the corresponding olefin (35 mg, 53%) as a mixture of *E*- and *Z*-isomers.

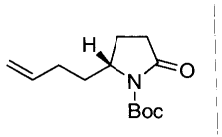
The ^{1}H NMR spectrum was identical with that of the enantiomer.

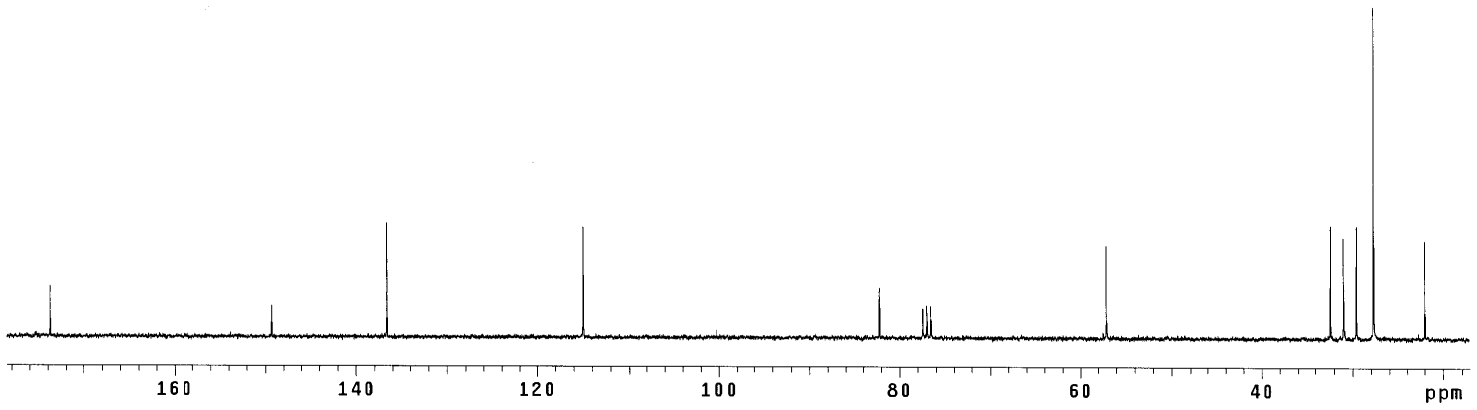
To a stirred solution of the above olefin (30 mg, 0.14 mmol) in EtOAc (5 mL) was added 10% Pd/C (20 mg), and the resulting suspension was stirred under a hydrogen atmosphere at 1 atm for 48 h. The catalyst was removed by filtration and the filtrate was evaporated to give ent-**14** (30 mg, quant) as a pale yellow oil.

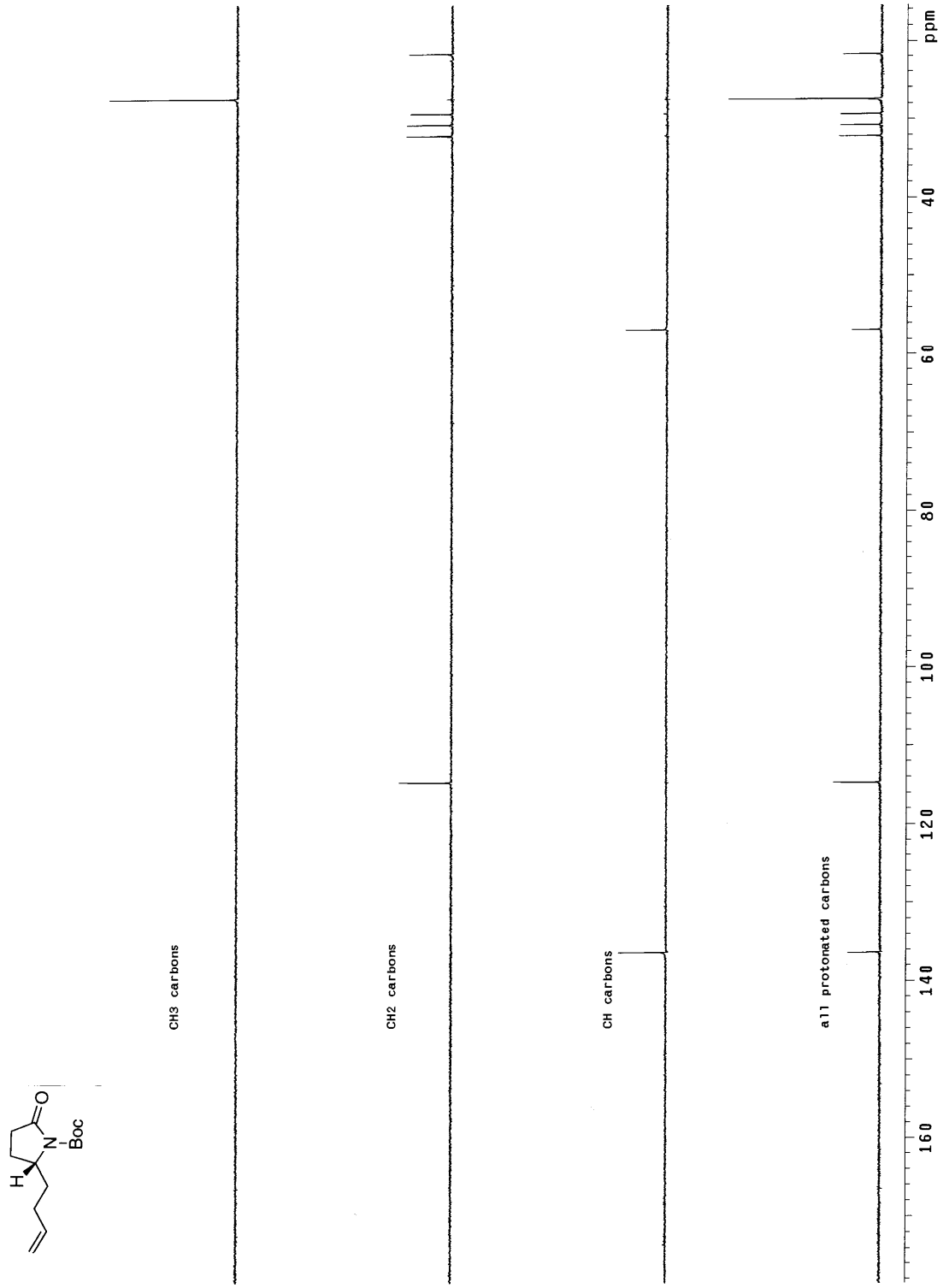
The spectral data were identical with those of **14**. $[\alpha]_D^{26}$ -29.94 (*c* 1.32, $CHCl_3$).

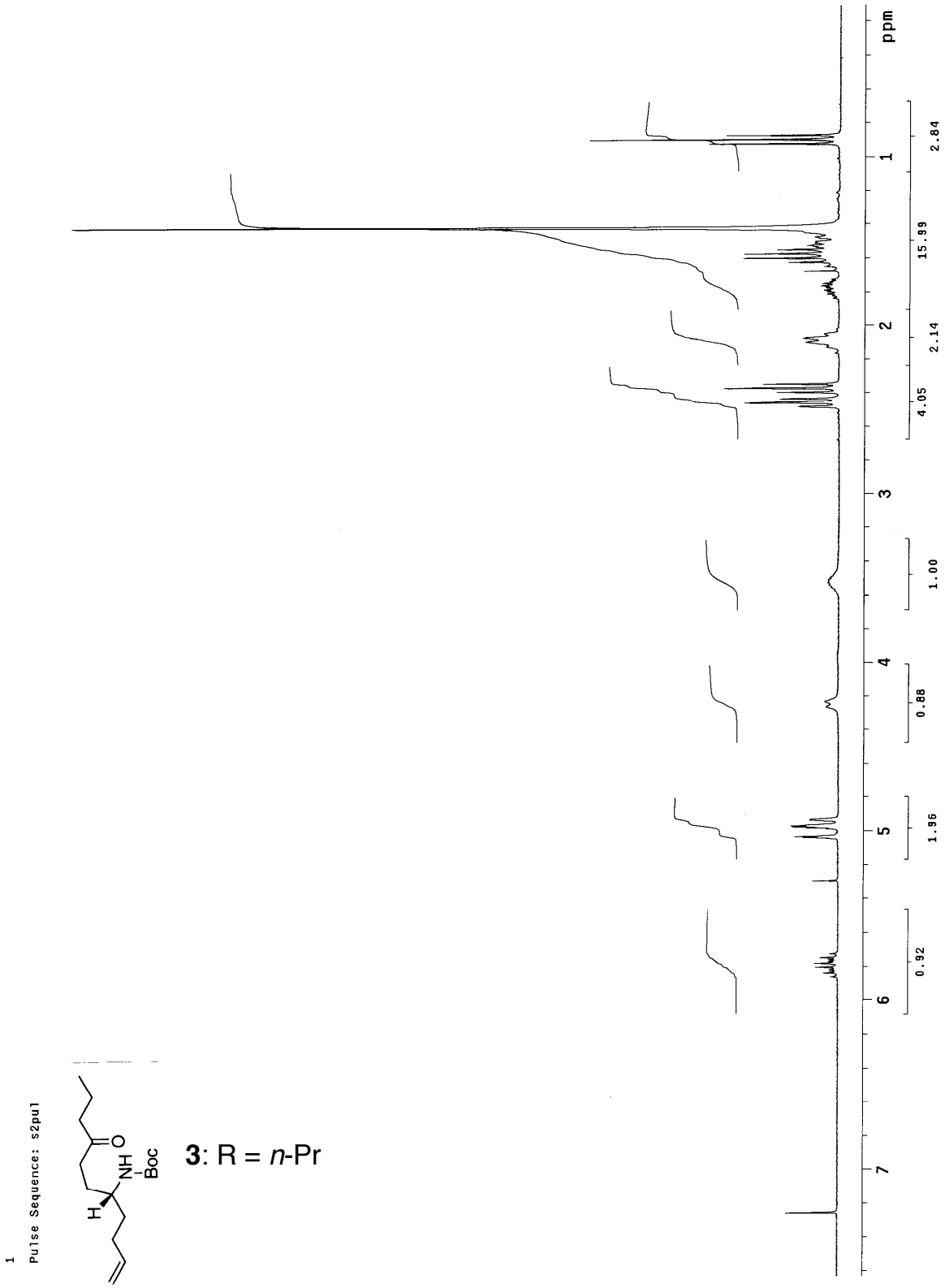

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
O
N
Boc
H
ppm
1
2
3
4
5
6
7
48.76
23.96
10.26
4.36
8.60
4.07

INDEX	FREQUENCY	PPM	HEIGHT
1	13108.832	173.737	8.5
2	11265.457	149.306	5.3
3	10310.809	136.654	19.3
4	8673.746	114.957	18.7
5	6202.893	82.210	8.4
6	5841.542	77.421	4.9
7	5808.581	76.984	5.4
8	5776.841	76.563	5.3
9	4307.025	57.083	15.7
10	2441.677	32.361	19.1
11	2335.469	30.953	17.1
12	2230.482	29.562	19.1
13	2090.093	27.701	56.6
14	1655.496	21.941	16.6



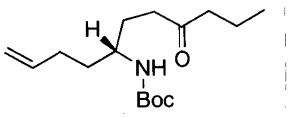



CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
160
140
120
100
80
60
40
O
N
Boc
H

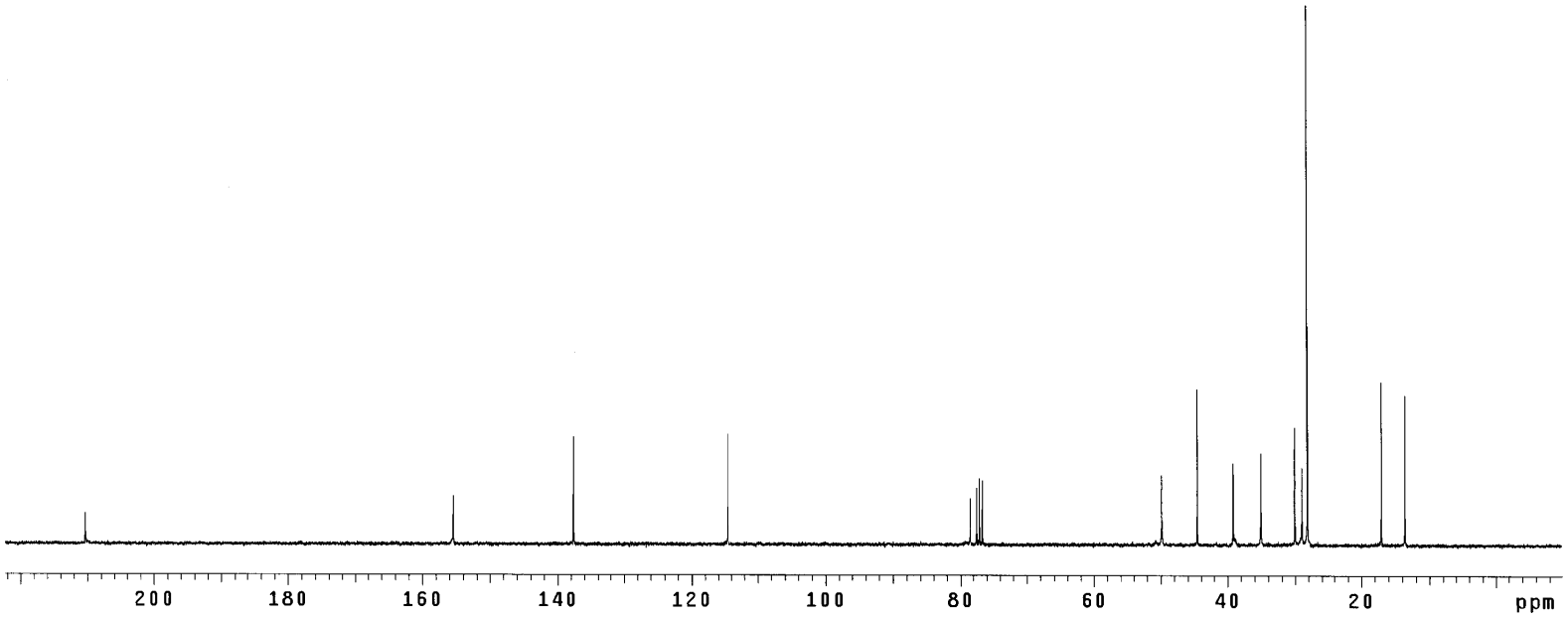

1
Pulse Sequence: s2pul
NH
Boc
O
H
ppm
1
2
3
4
5
6
7
2.84
15.99
2.14
4.05
1.00
0.88
1.96
0.92

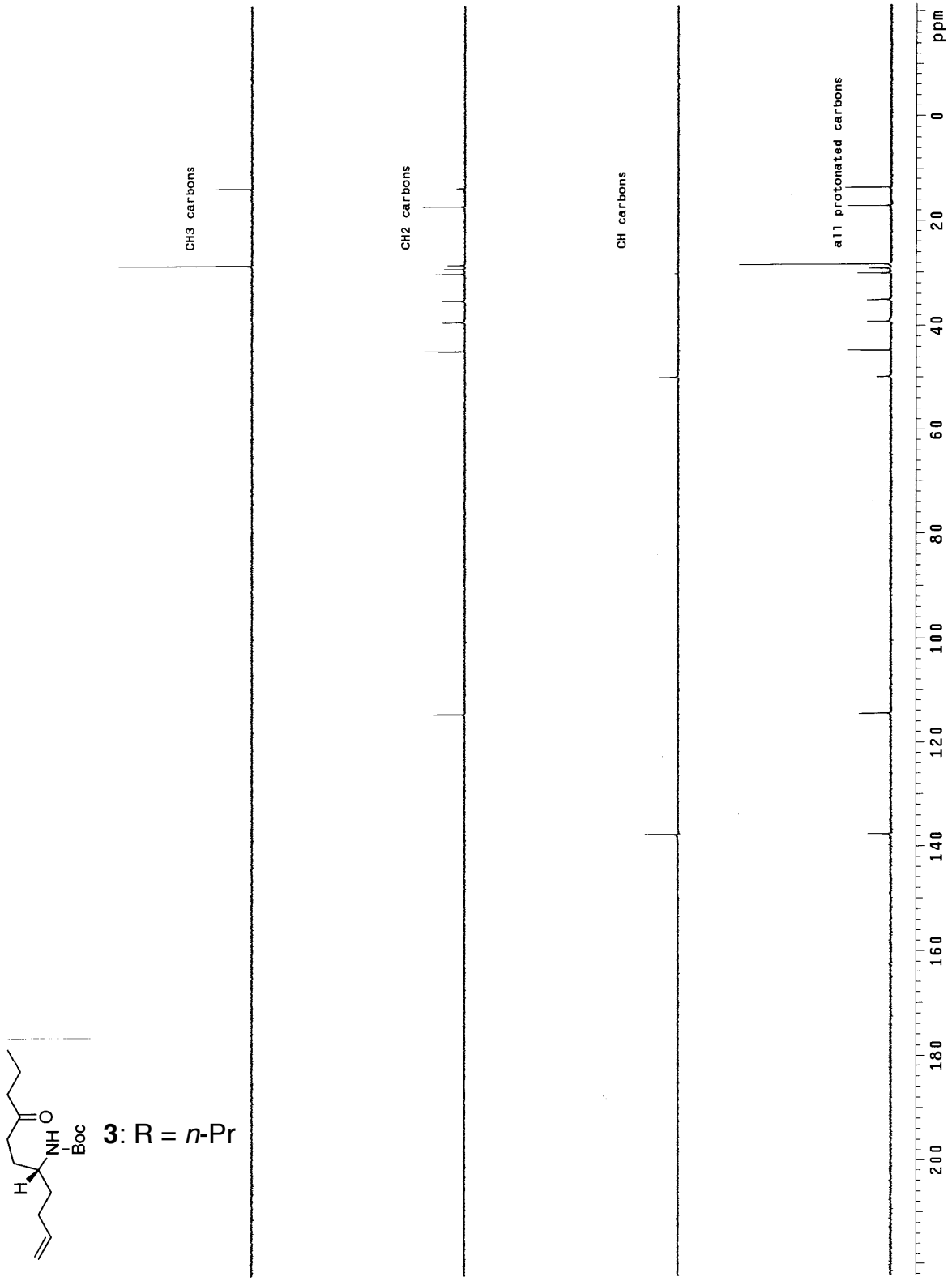
3: R = *n*-Pr

INDEX	FREQUENCY	PPM	HEIGHT
1	15867.788	210.303	4.9
2	11724.469	155.390	7.7
3	10381.614	137.592	17.4
4	8639.564	114.504	17.8
5	5922.113	78.489	7.4
6	5841.542	77.421	9.1
7	5809.801	77.000	10.7
8	5778.061	76.579	10.3
9	3761.336	49.851	11.3
10	3365.804	44.609	25.0
11	2951.961	39.124	13.1
12	2644.325	35.046	14.8
13	2267.105	30.047	18.9
14	2187.754	28.995	12.5
15	2126.715	28.186	86.5
16	1286.820	17.055	26.3
17	1023.132	13.560	24.1

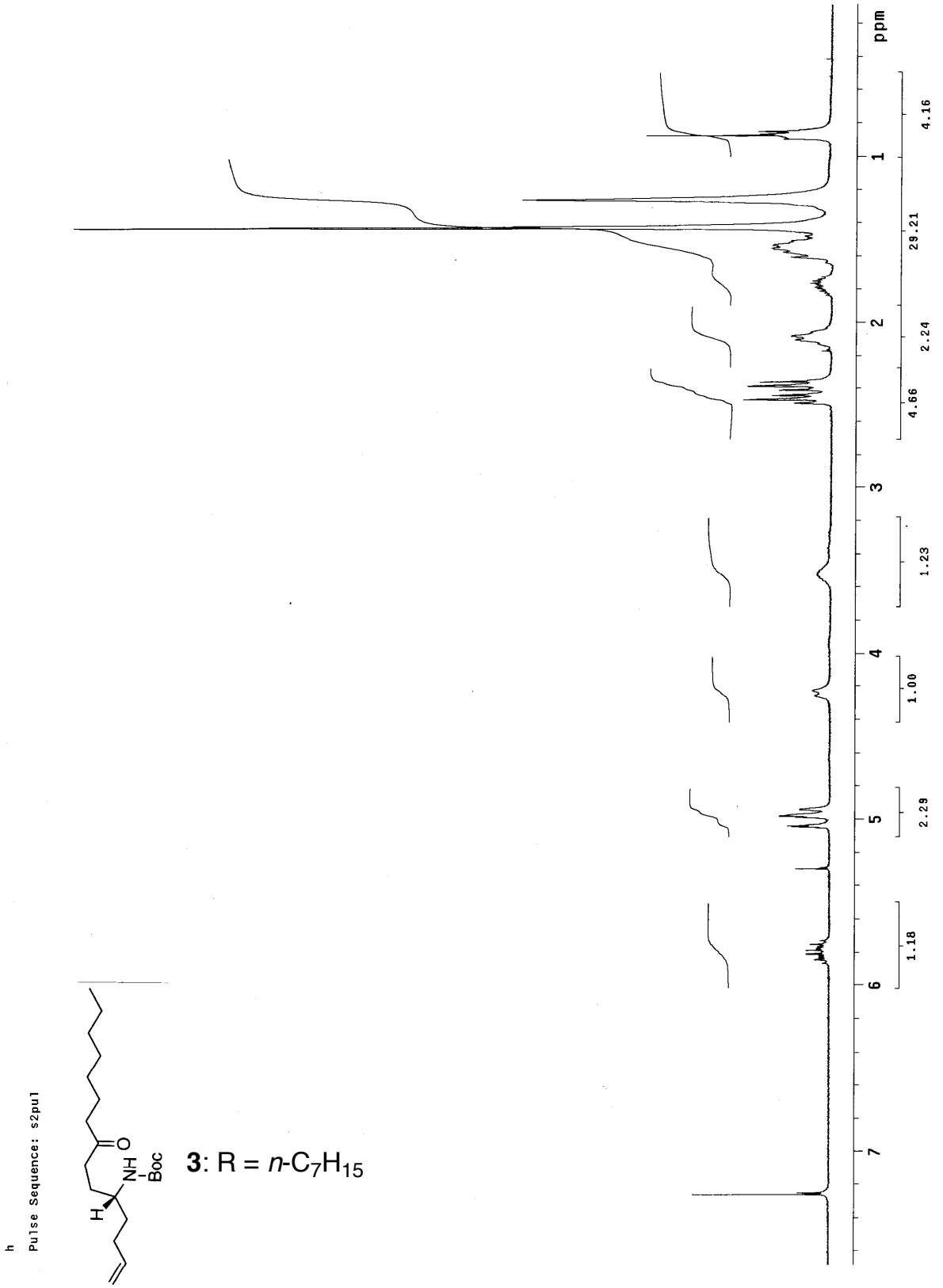


3: R = *n*-Pr

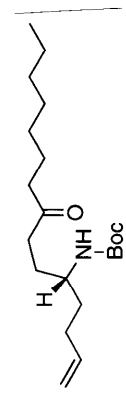



CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
0
20
40
60
80
100
120
140
160
180
200
NH
Boc
O
H

3: R = *n*-Pr


h
Pulse Sequence: s2pul
NH
Boc
O
H
ppm
1
2
3
4
5
6
7
4.16
29.21
2.24
4.66
1.23
1.00
2.29
1.18

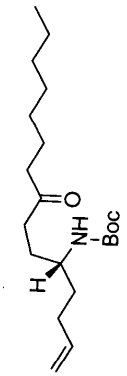
3: R = *n*-C_7H_{15}

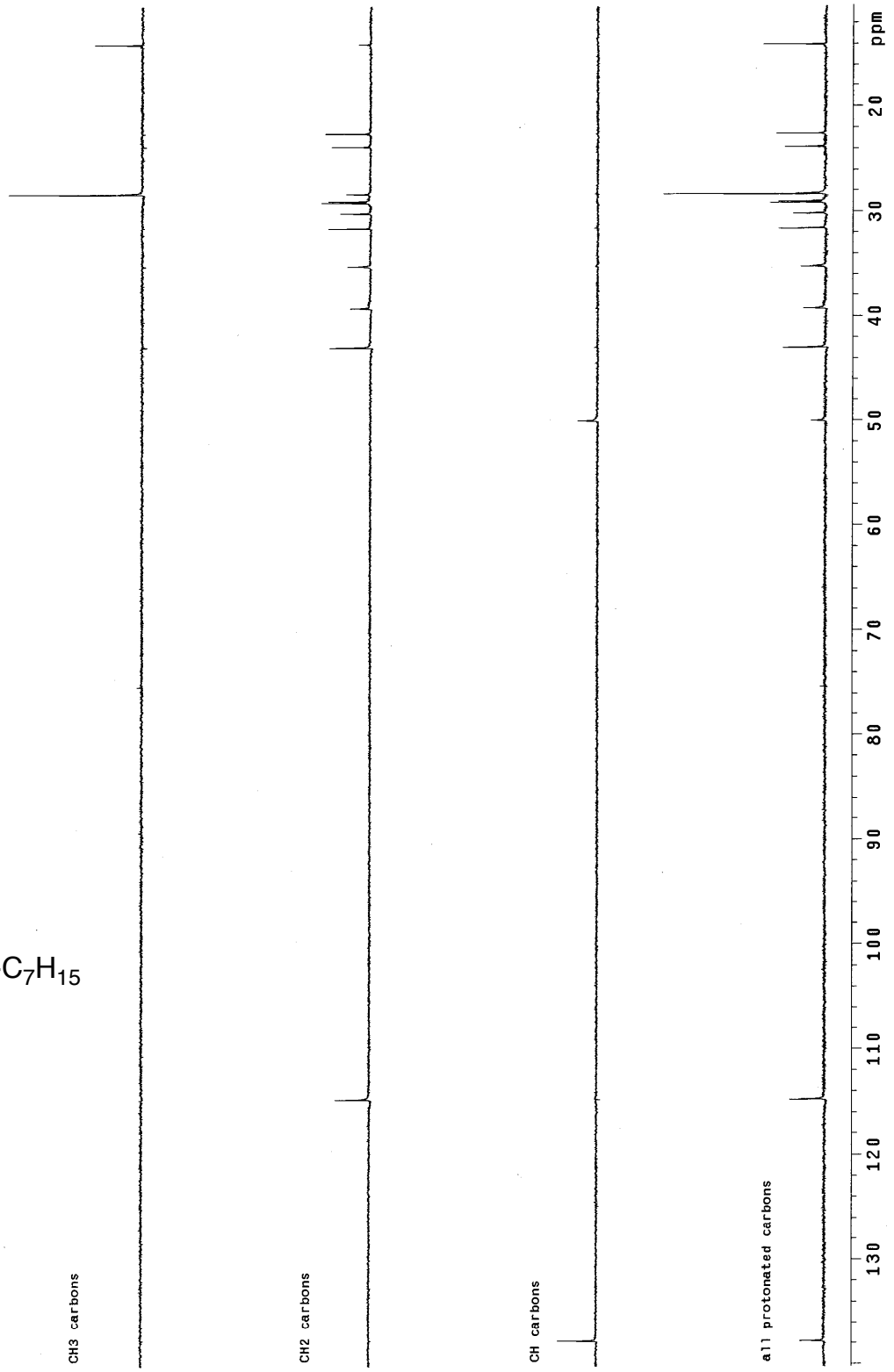


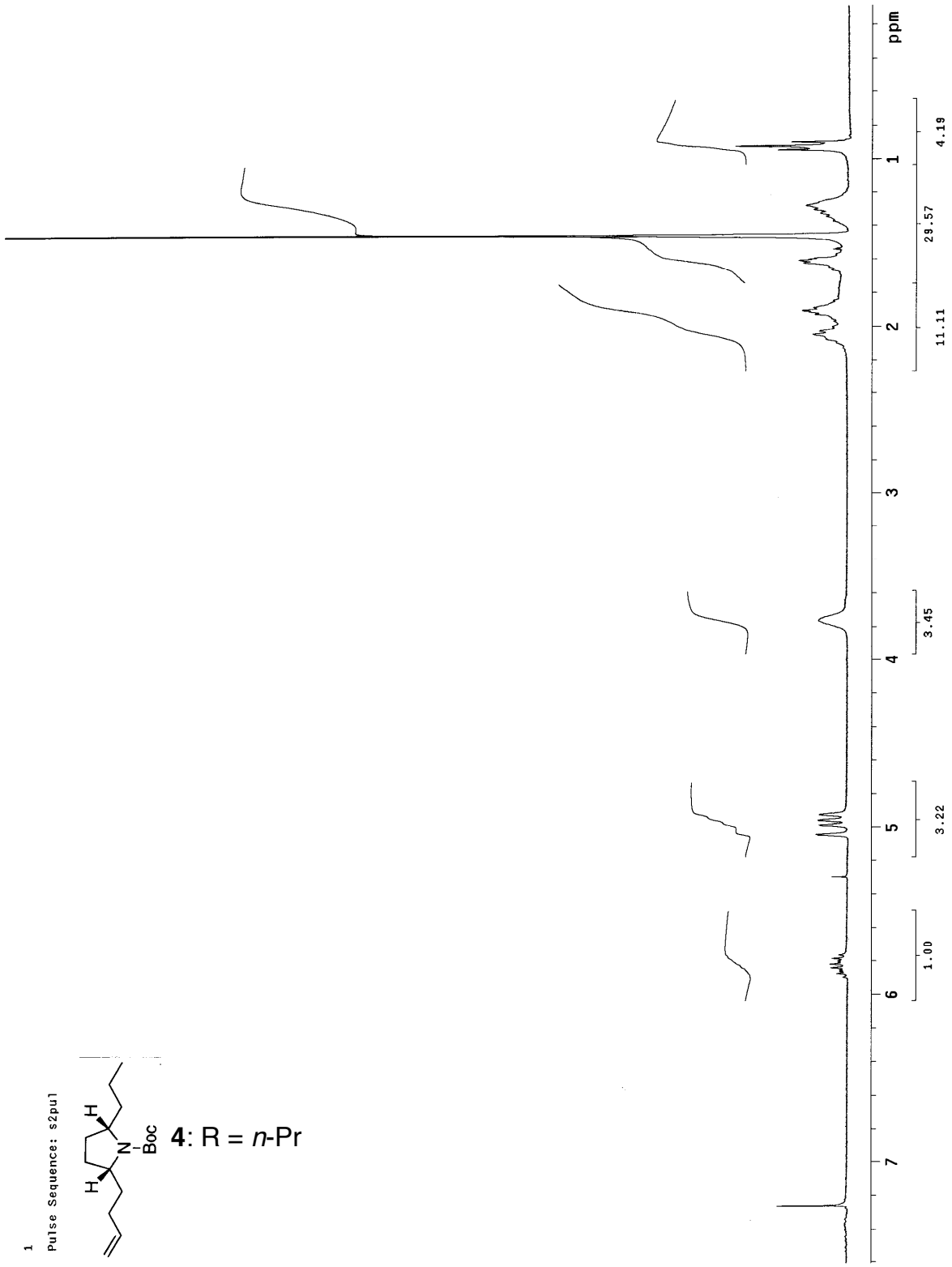
3: R = *n*-C_7H_{15}

INDEX	FREQUENCY	PPM	HEIGHT
1	15888.541	210.578	11.5
2	11728.131	155.438	12.7
3	10386.496	137.657	29.5
4	8873.953	117.611	-1.9
5	8648.109	114.617	34.0
6	5935.541	78.666	14.9
7	5841.541	77.421	24.3
8	5809.801	77.000	24.1
9	5776.840	76.563	22.3
10	3769.882	49.964	20.0
11	3235.181	42.877	49.4
12	2955.623	39.172	21.5
13	2652.870	35.160	26.1
14	2380.637	31.552	55.9
15	2323.260	30.791	-1.8
16	2273.208	30.128	34.8
17	2193.858	29.076	56.4
18	2185.312	28.963	58.2
19	2134.040	28.283	162.0
20	1791.001	23.737	54.1
21	1697.001	22.491	41.9
22	1054.872	13.981	56.2

3: R = *n*-C_7H_{15}


H
NH
Boc
O

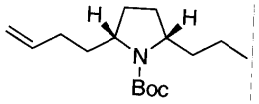

CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
130
120
110
100
90
80
70
60
50
40
30
20
ppm


1
Pulse Sequence: s2pul
ppm
1
2
3
4
5
6
7
4.19
29.57
11.11
3.45
3.22
1.00

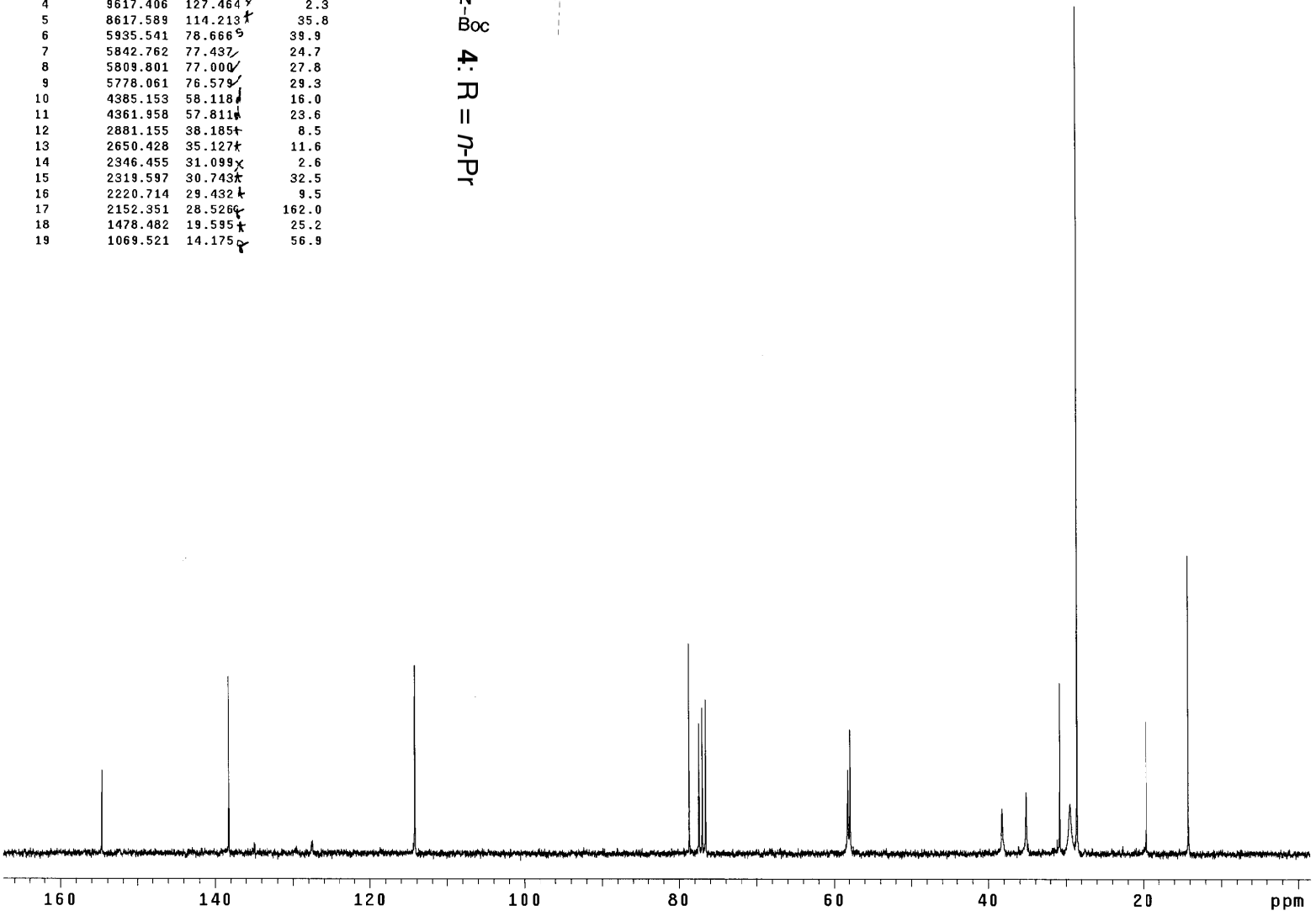
H
N
Boc
H

4: R = *n*-Pr

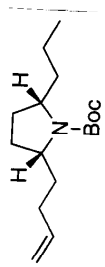
INDEX	FREQUENCY	PPM	HEIGHT
1	11669.533	154.662	15.8
2	10431.665	138.256	33.6
3	10181.405	134.939	1.9
4	9617.406	127.464	2.3
5	8617.589	114.213	35.8
6	5935.541	78.666	39.9
7	5842.762	77.437	24.7
8	5809.801	77.000	27.8
9	5778.061	76.579	29.3
10	4385.153	58.118	16.0
11	4361.958	57.811	23.6
12	2881.155	38.185	8.5
13	2650.428	35.127	11.6
14	2346.455	31.099	2.6
15	2319.597	30.743	32.5
16	2220.714	29.432	9.5
17	2152.351	28.526	162.0
18	1478.482	19.595	25.2
19	1069.521	14.175	56.9

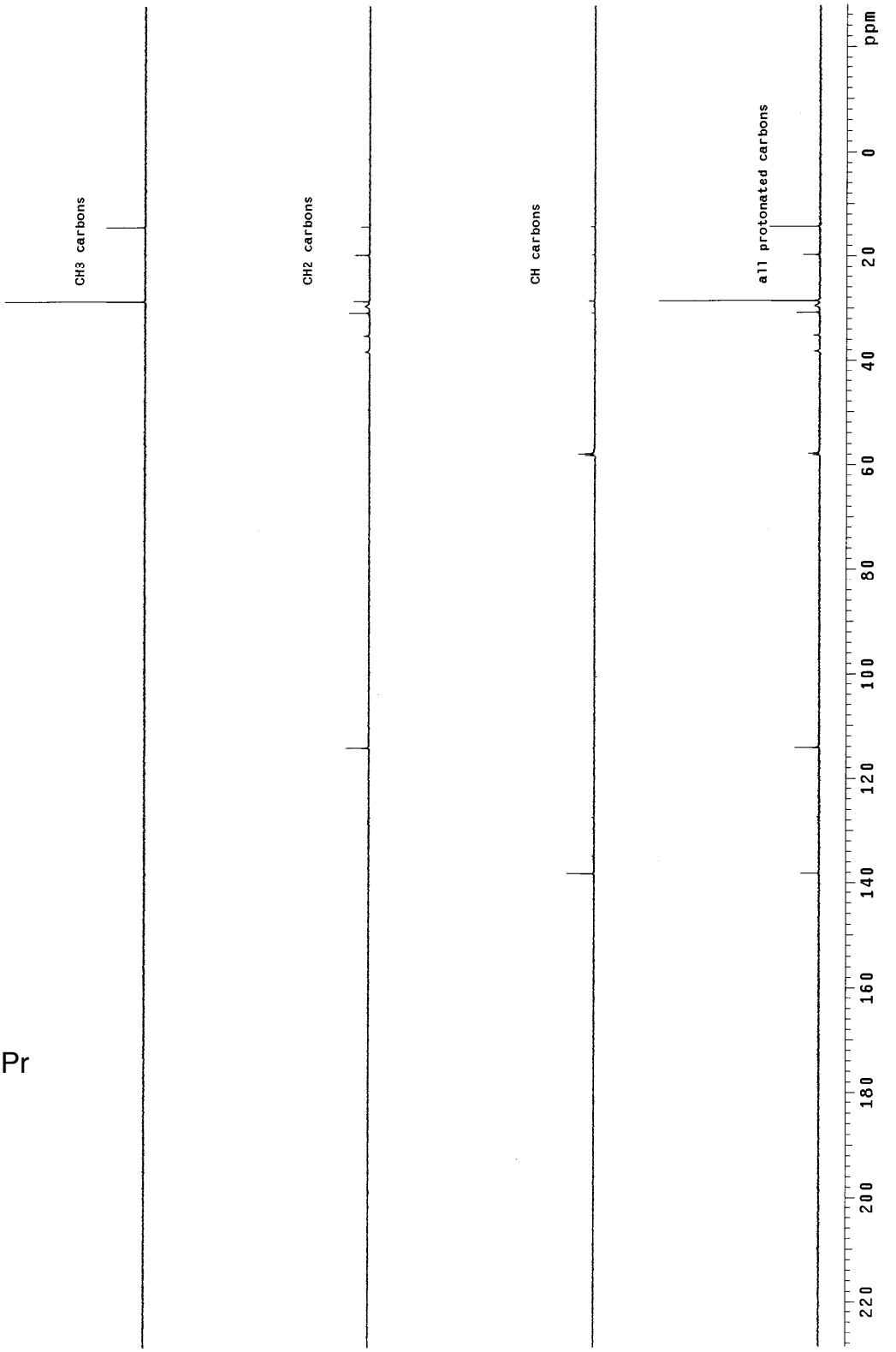


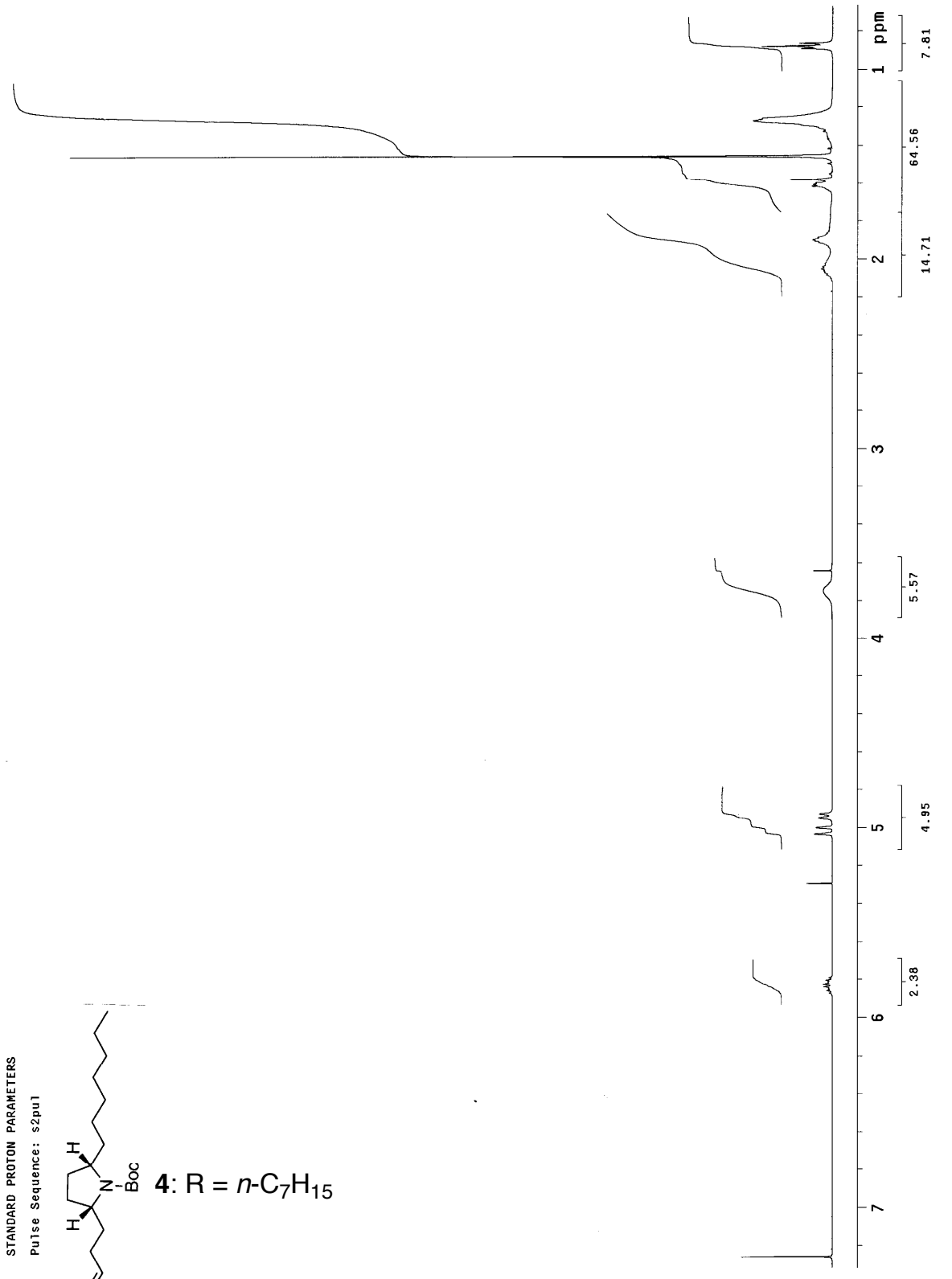
4: R = *n*-Pr



4: R = *n*-Pr

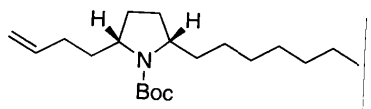

H
N
Boc
H


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
220
200
180
160
140
120
100
80
60
40
20
0

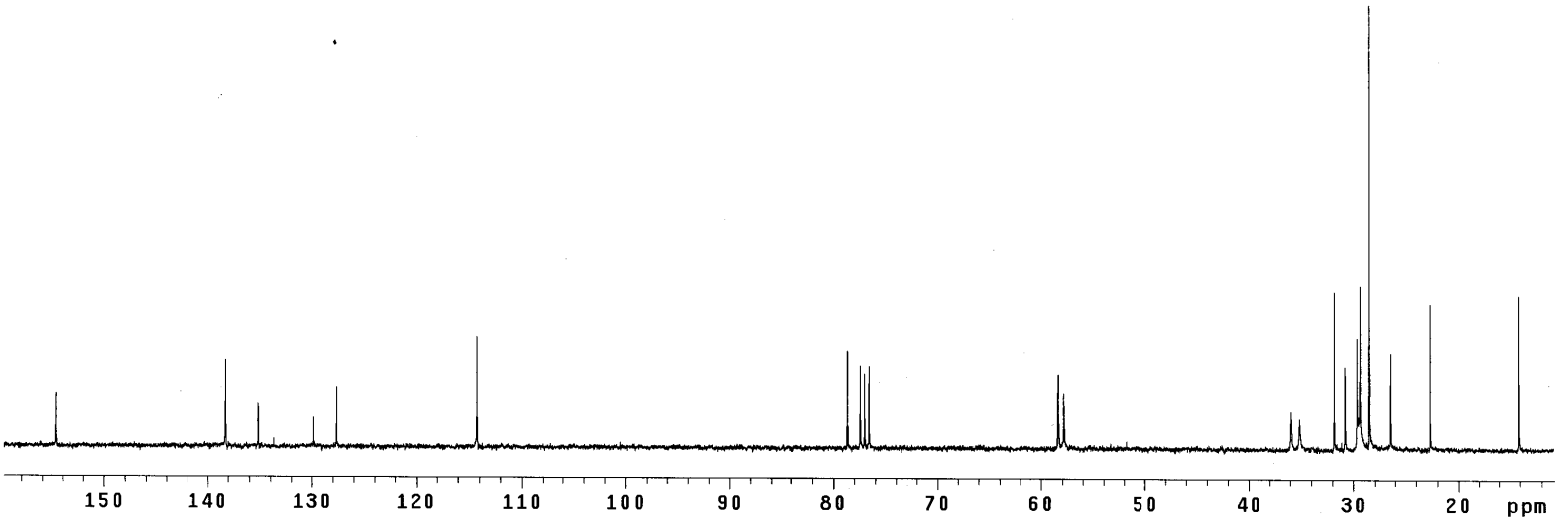

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
N-Boc
H
H
1 ppm
2
3
4
5
6
7
64.56
14.71
5.57
4.95
2.38
7.81

4: R = *n*-C_7H_{15}

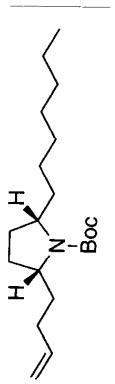
INDEX	FREQUENCY	PPM	HEIGHT
1	11669.533	154.662	8.4
2	10431.665	138.256	13.8
3	10196.055	135.133	6.9
4	9794.419	129.810	4.6
5	9632.056	127.658	9.4
6	8617.589	114.213	17.6
7	5934.320	78.650	15.5
8	5842.762	77.437	13.1
9	5809.801	77.000	11.8
10	5778.061	76.579	13.0
11	4403.465	58.361	11.9
12	4363.179	57.827	8.8
13	2711.467	35.936	6.0
14	2650.428	35.127	4.8
15	2400.169	31.811	25.2
16	2322.039	30.775	13.2
17	2235.364	29.626	17.7
18	2213.390	29.335	26.3
19	2152.351	28.526	71.8
20	1992.429	26.407	15.4
21	1709.209	22.653	23.3
22	1064.638	14.110	24.7

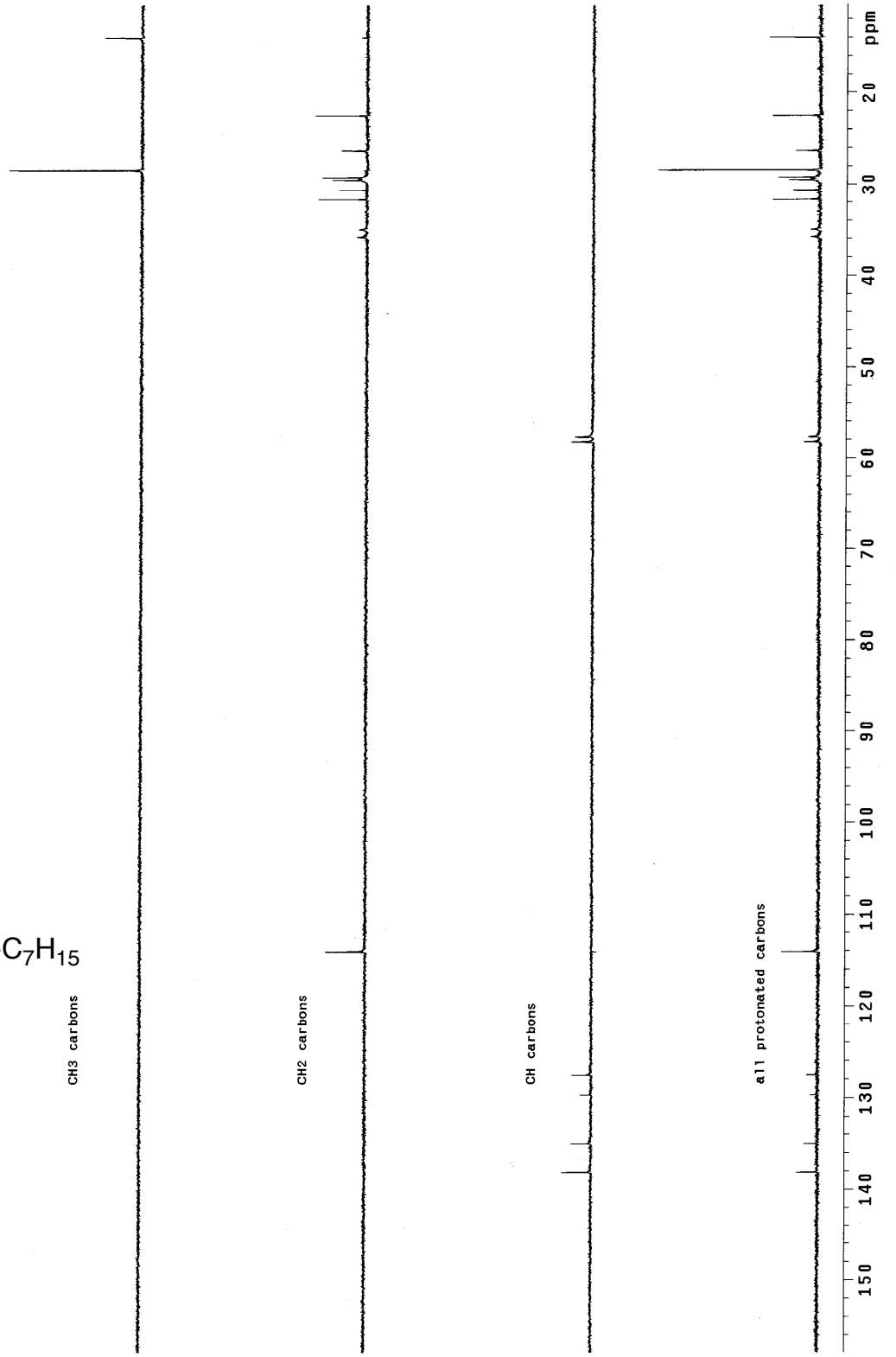


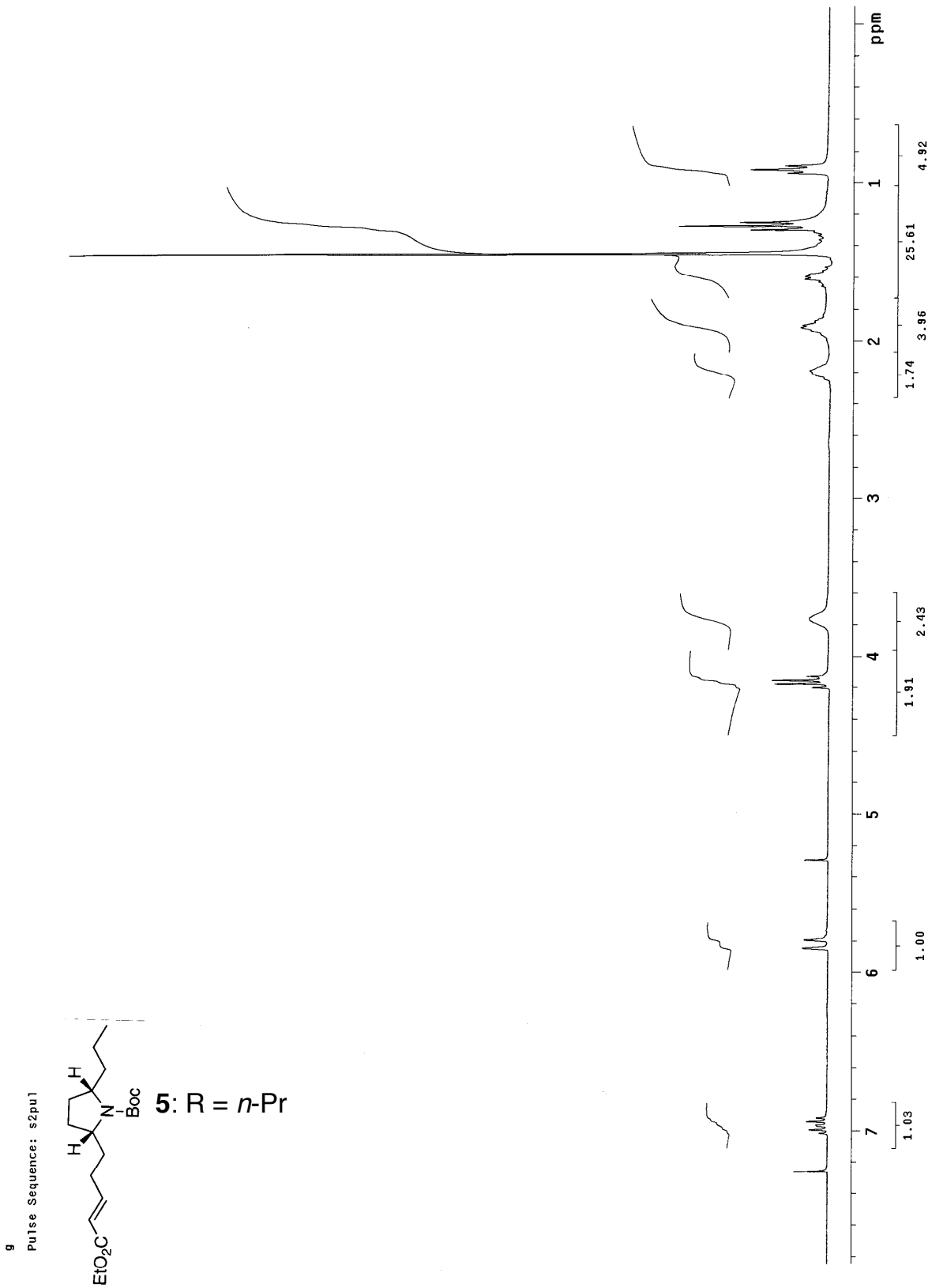
4: R = *n*-C_7H_{15}



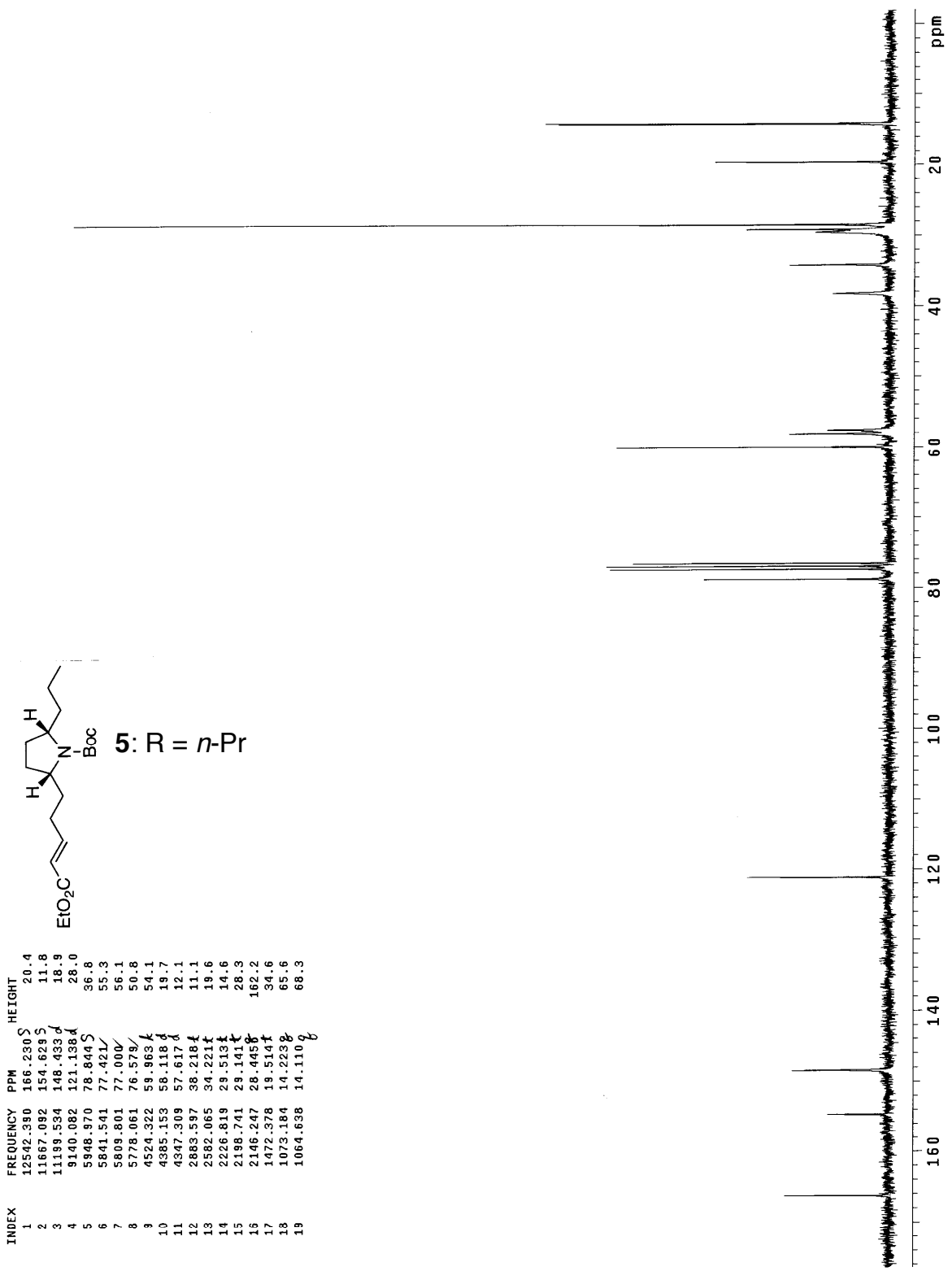
4: R = *n*-C_7H_{15}


H
N
Boc
H

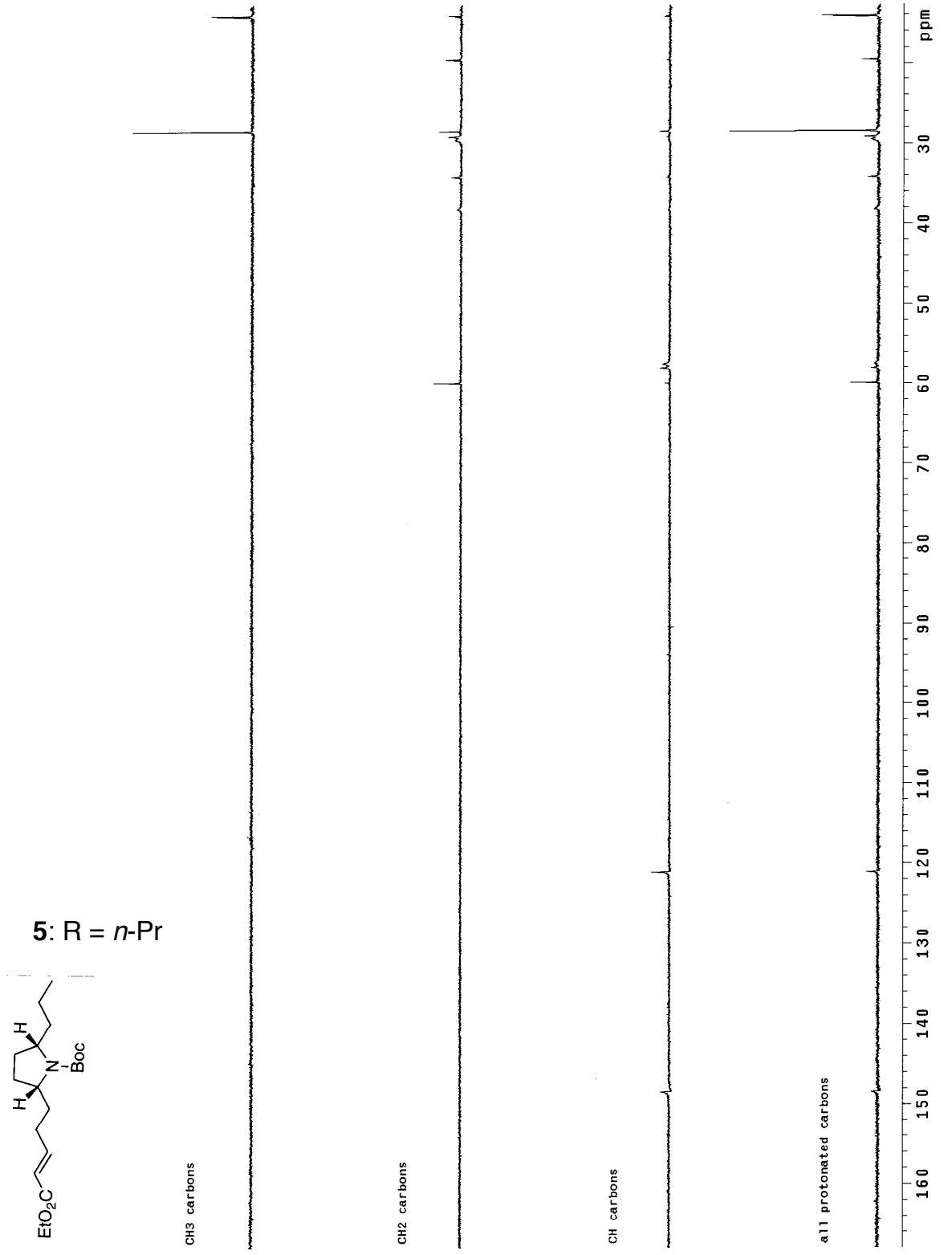

CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150

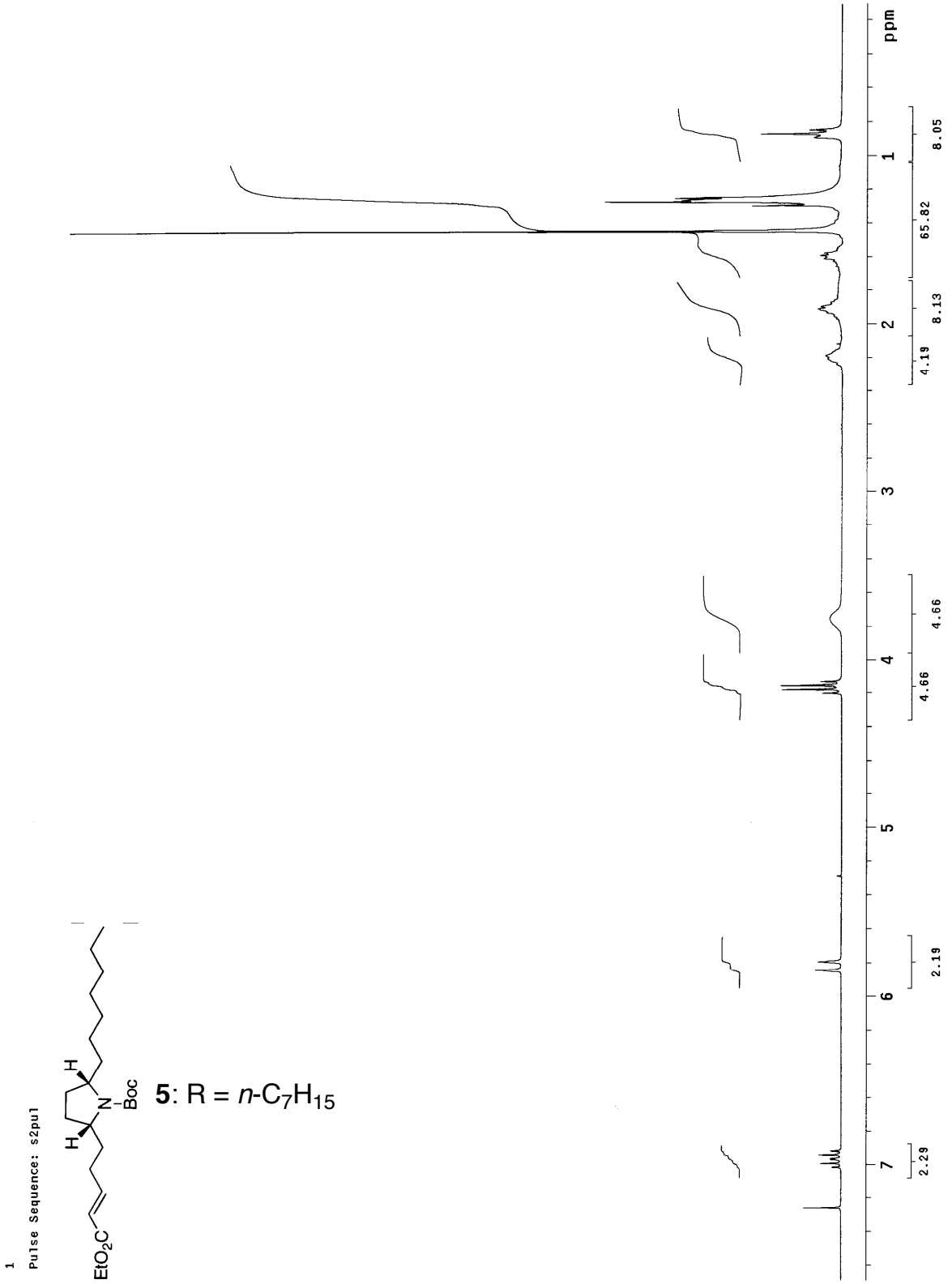

g
Pulse Sequence: s2pul
EtO2C
H
N
Boc
H
ppm
1
2
3
4
5
6
7
4.92
25.61
3.96
1.74
2.43
1.91
1.00
1.03

5: R = *n*-Pr



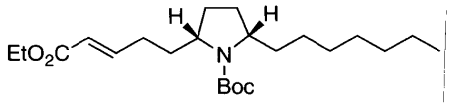
INDEX	FREQUENCY	PPM	HEIGHT
1	12542.390	166.230	20.4
2	11667.092	154.629	11.8
3	11199.534	148.433	18.9
4	9140.082	121.138	28.0
5	5948.970	78.844	36.8
6	5841.541	77.421	55.3
7	5809.801	77.000	56.1
8	5778.061	76.579	50.8
9	4524.322	59.963	54.1
10	4385.153	58.118	19.7
11	4347.309	57.617	12.1
12	2883.597	38.218	11.1
13	2582.065	34.221	19.6
14	2226.819	29.513	14.6
15	2198.741	29.141	28.3
16	2146.247	28.445	162.2
17	1472.378	19.514	34.6
18	1073.184	14.223	65.6
19	1064.638	14.110	68.3


5: R = n-Pr
EtO2C
H
N
Boc
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
160
150
140
130
120
110
100
90
80
70
60
50
40
30

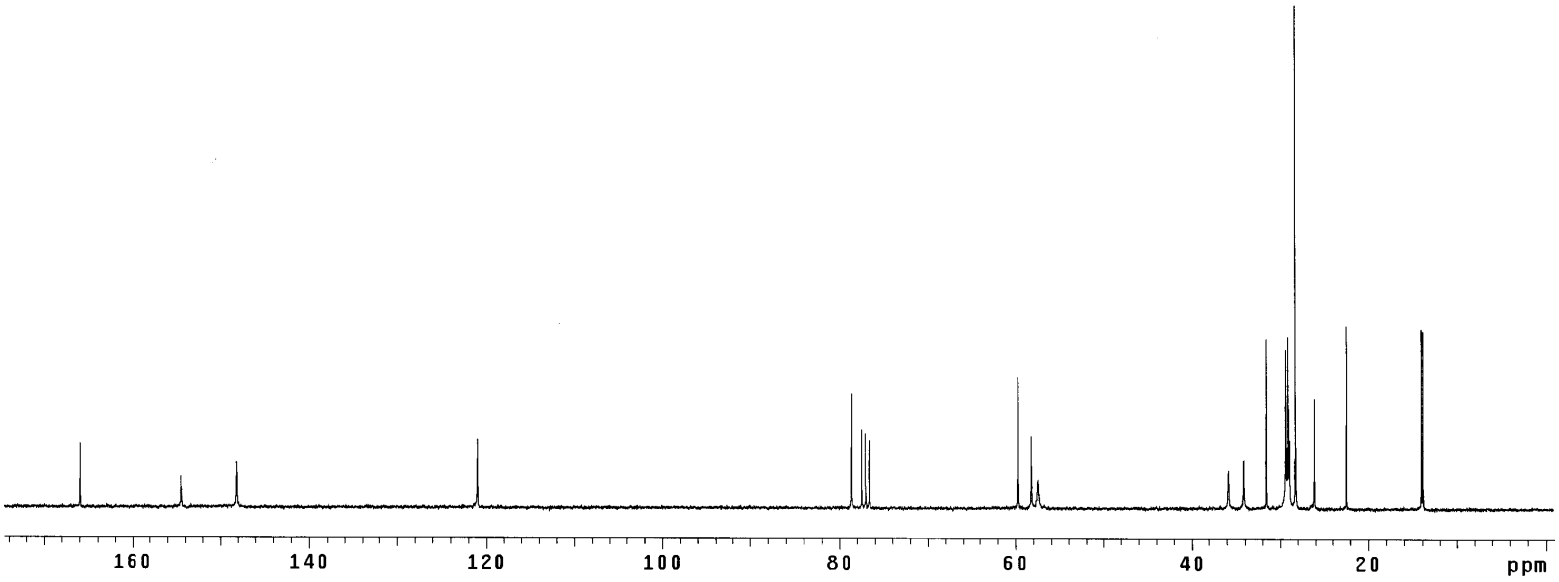

1
Pulse Sequence: s2pul
EtO2C
H
N
Boc
H
ppm
1
2
3
4
5
6
7
8.05
65.82
8.13
4.19
4.66
4.66
2.19
2.29

5: R = *n*-C_7H_{15}

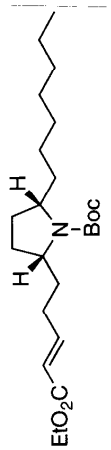
INDEX	FREQUENCY	PPM	HEIGHT
1	12519.195	165.923	10.1
2	11651.222	154.419	4.9
3	11180.002	148.174	7.2
4	9130.317	121.008	10.9
5	5929.438	78.586	18.4
6	5841.542	77.421	12.5
7	5809.801	77.000	12.0
8	5776.840	76.563	10.9
9	4504.790	59.704	21.0
10	4391.258	58.199	11.5
11	4333.881	57.439	4.5
12	2700.481	35.791	6.0
13	2571.078	34.076	7.7
14	2381.858	31.568	27.3
15	2215.832	29.367	25.6
16	2195.079	29.092	27.6
17	2186.533	28.979	11.0
18	2132.819	28.267	81.2
19	1972.897	26.148	17.6
20	1690.898	22.410	29.4
21	1059.756	14.045	28.8
22	1047.548	13.884	28.5

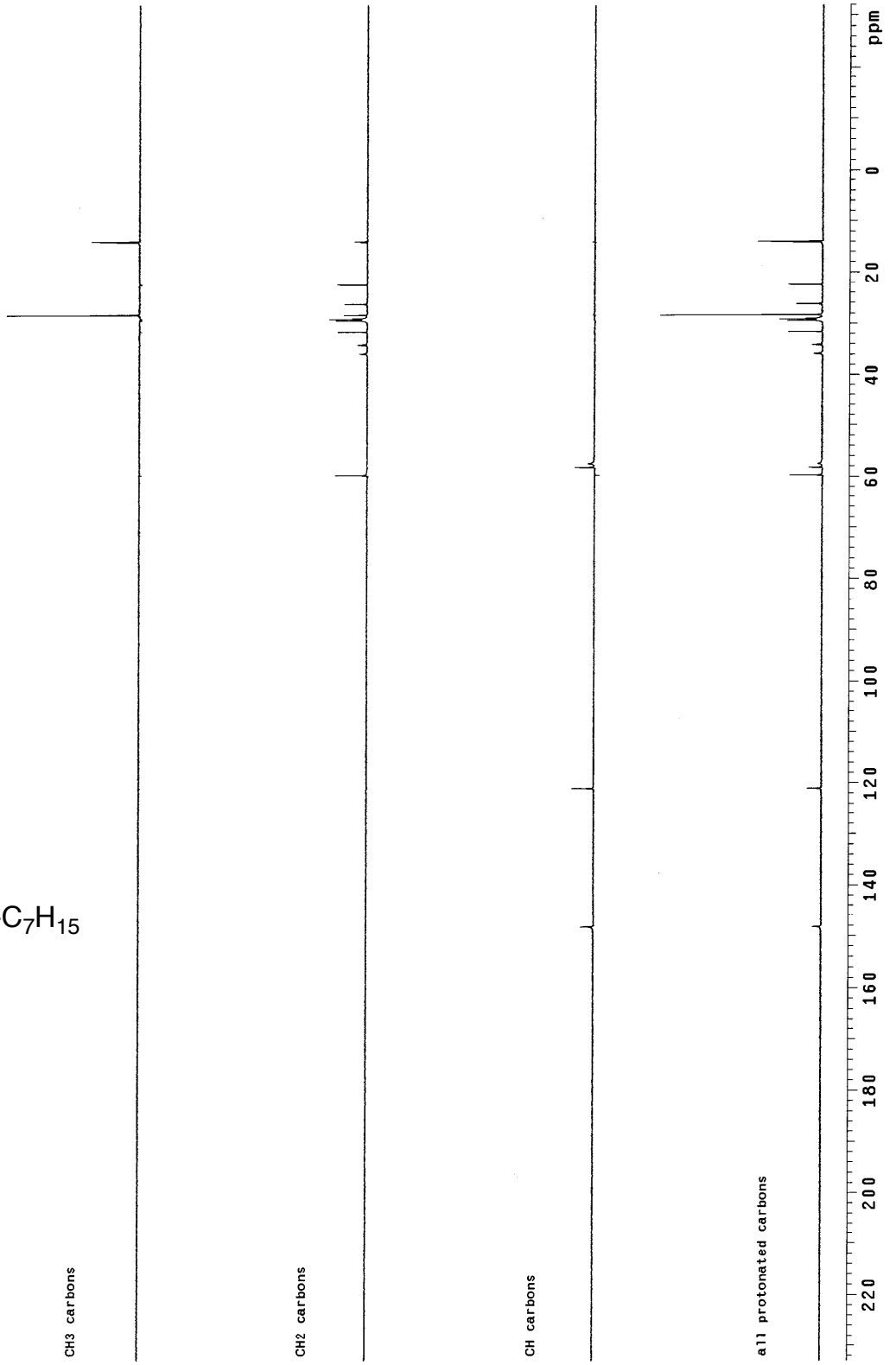


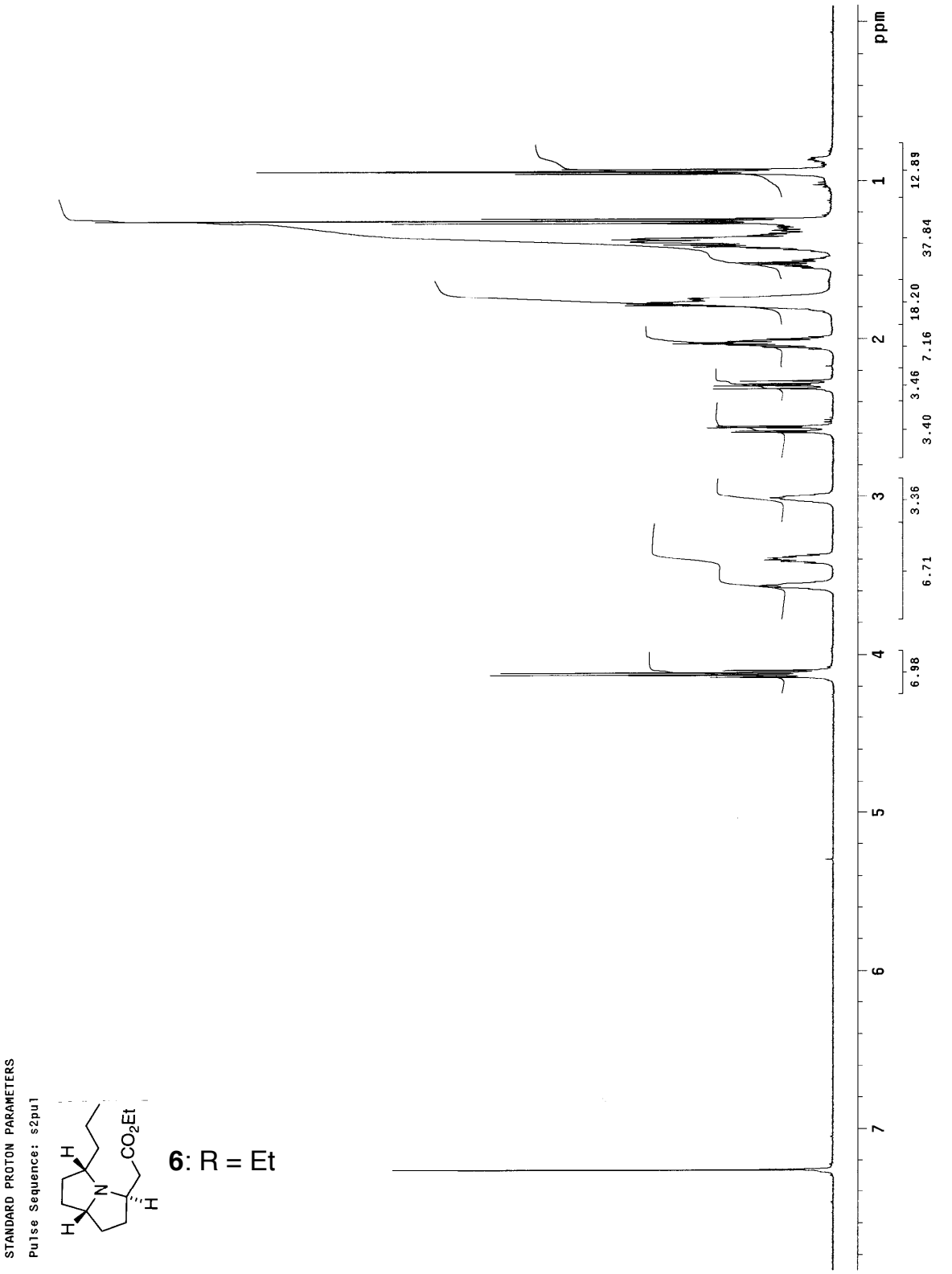
5: R = *n*-C_7H_{15}



5: R = *n*-C_7H_{15}

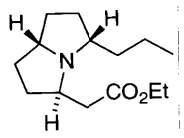

H
N
Boc
H
EtO2C


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
0
20
40
60
80
100
120
140
160
180
200
220

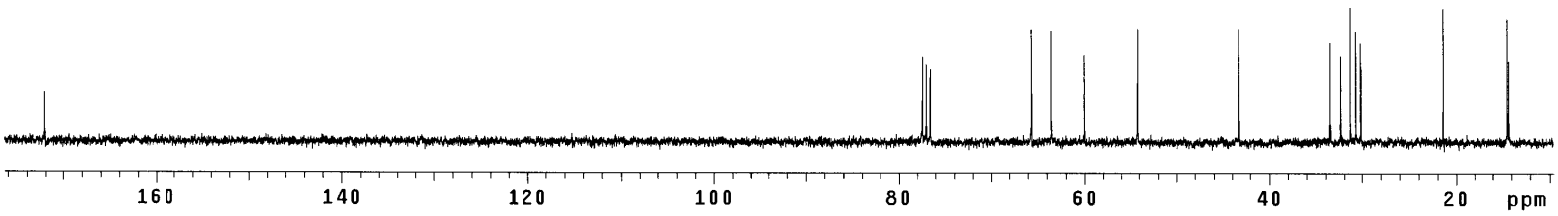

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
ppm
1
2
3
4
5
6
7
12.89
37.84
18.20
7.16
3.46
3.40
3.36
6.71
6.98

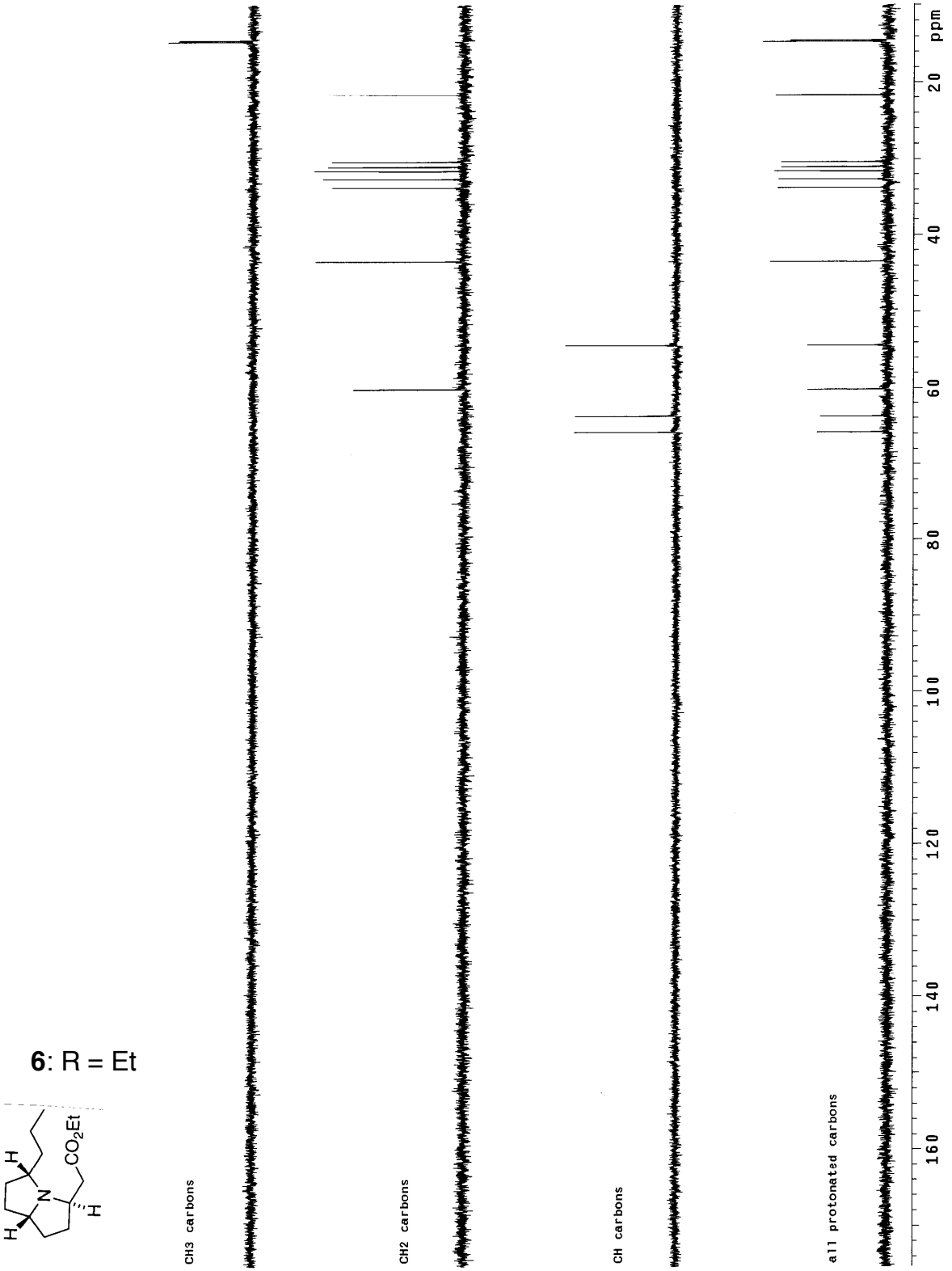
6: R = Et

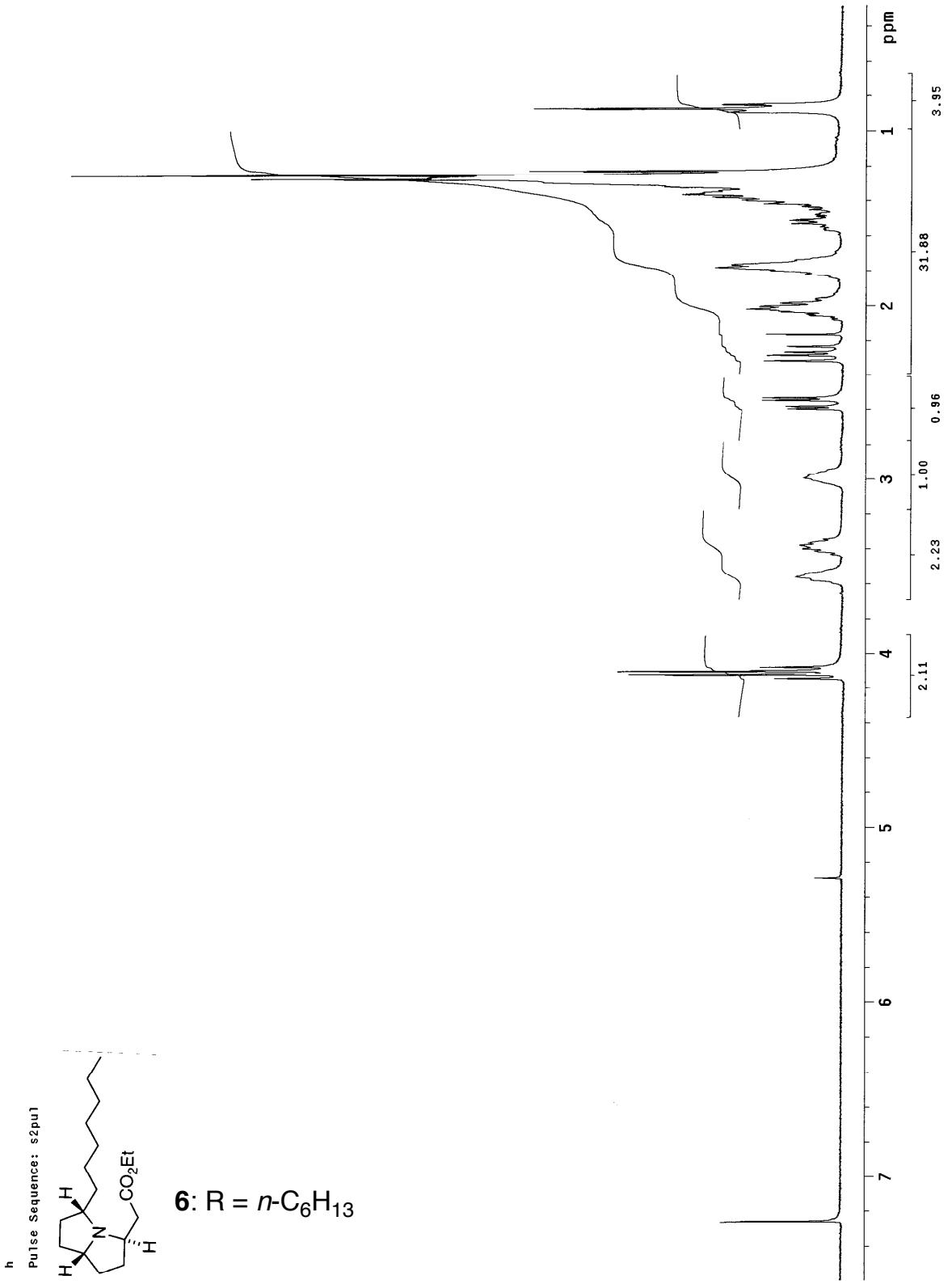
INDEX	FREQUENCY	PPM	HEIGHT
1	12983.090	172.071	7.8
2	5841.541	77.421	13.7
3	5809.801	77.000	12.4
4	5776.840	76.563	11.7
5	4950.373	65.610	18.0
6	4791.672	63.506	17.9
7	4529.205	60.028	13.9
8	4086.063	54.154	18.2
9	3259.596	43.201	18.1
10	2527.130	33.493	16.0
11	2441.675	32.361	13.8
12	2363.545	31.325	21.6
13	2320.818	30.759	17.8
14	2273.208	30.128	15.9
15	1613.988	21.391	21.5
16	1085.391	14.385	19.9
17	1073.184	14.223	13.0



6: R = Et

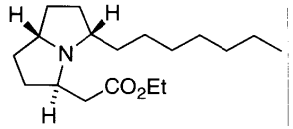



6: R = Et
CO2Et
H
N
H
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
140
120
100
80
60
40
20
ppm

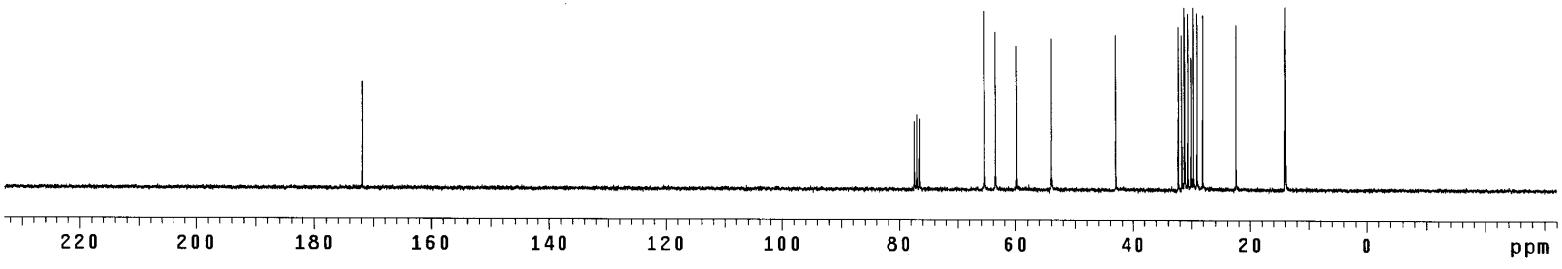


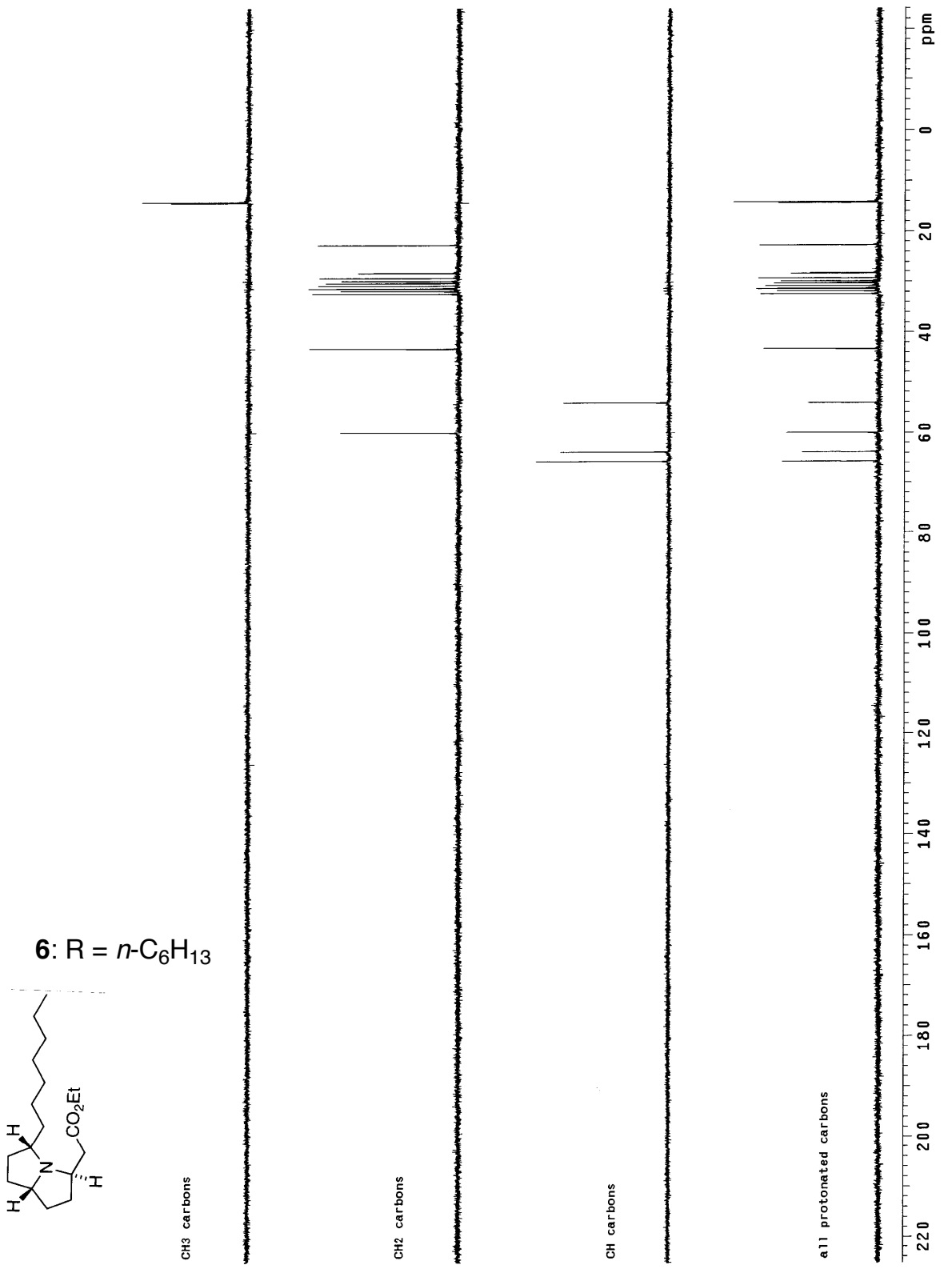
6: R = *n*-C_6H_{13}

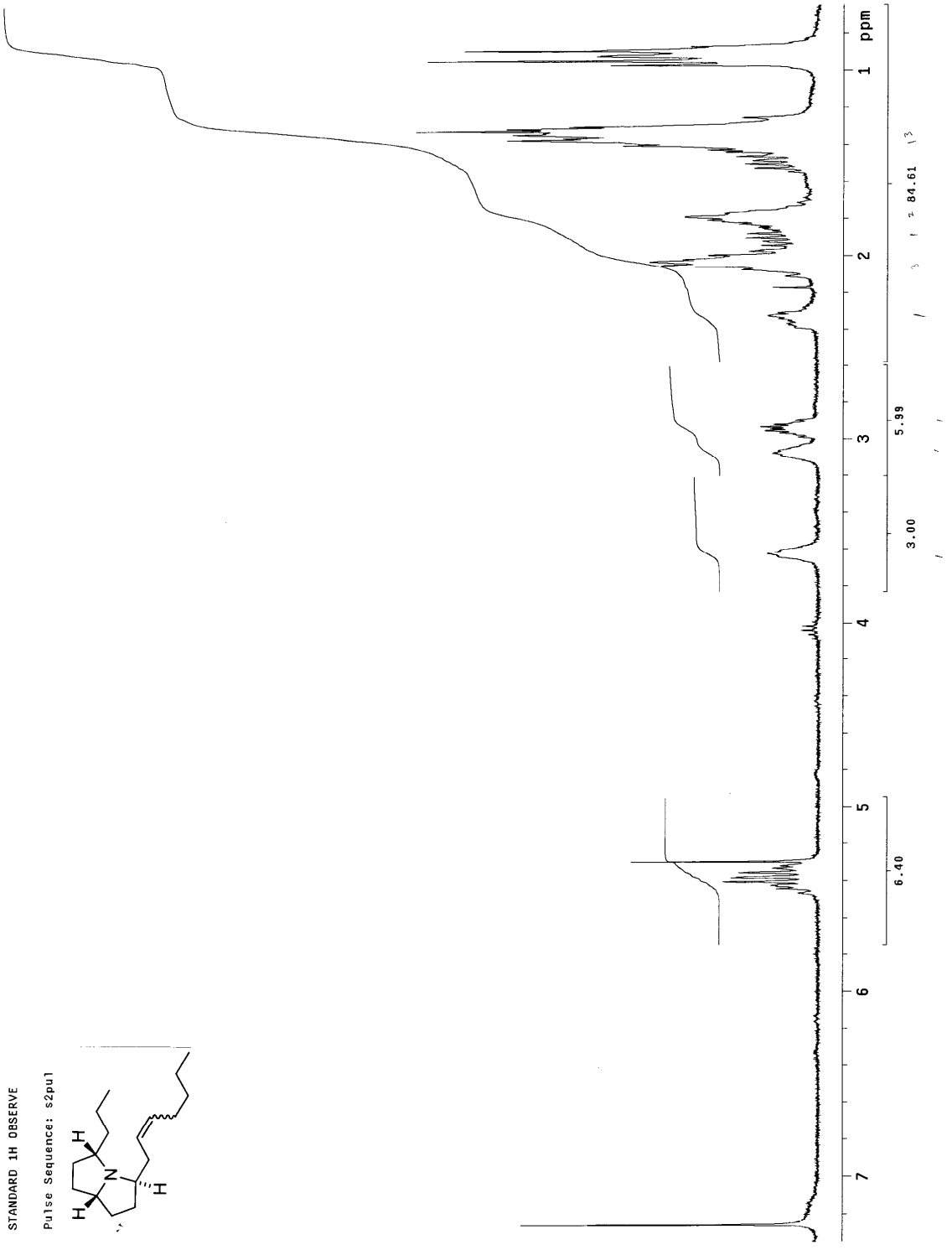
INDEX	FREQUENCY	PPM		HEIGHT
1	12964.948	171.830	s	17.0
2	5839.269	77.391	✓	10.9
3	5807.529	76.970	✓	12.0
4	5775.788	76.549	✓	11.3
5	4939.556	65.466	d	28.7
6	4797.945	63.589	d	25.3
7	4512.283	59.803	t	23.0
8	4072.804	53.979	d	24.2
9	3249.999	43.074	t	24.8
10	2432.078	32.233	t	26.2
11	2386.910	31.635	t	24.8
12	2353.949	31.198	t	29.3
13	2347.845	31.117	t	27.7
14	2310.001	30.616	t	28.3
15	2269.715	30.082	t	21.1
16	2240.416	29.693	t	29.3
17	2195.248	29.095	t	28.4
18	2120.780	28.108	t	28.1
19	1695.949	22.477	t	26.5
20	1062.366	14.080	q	25.7
21	1051.379	13.934	q	29.4

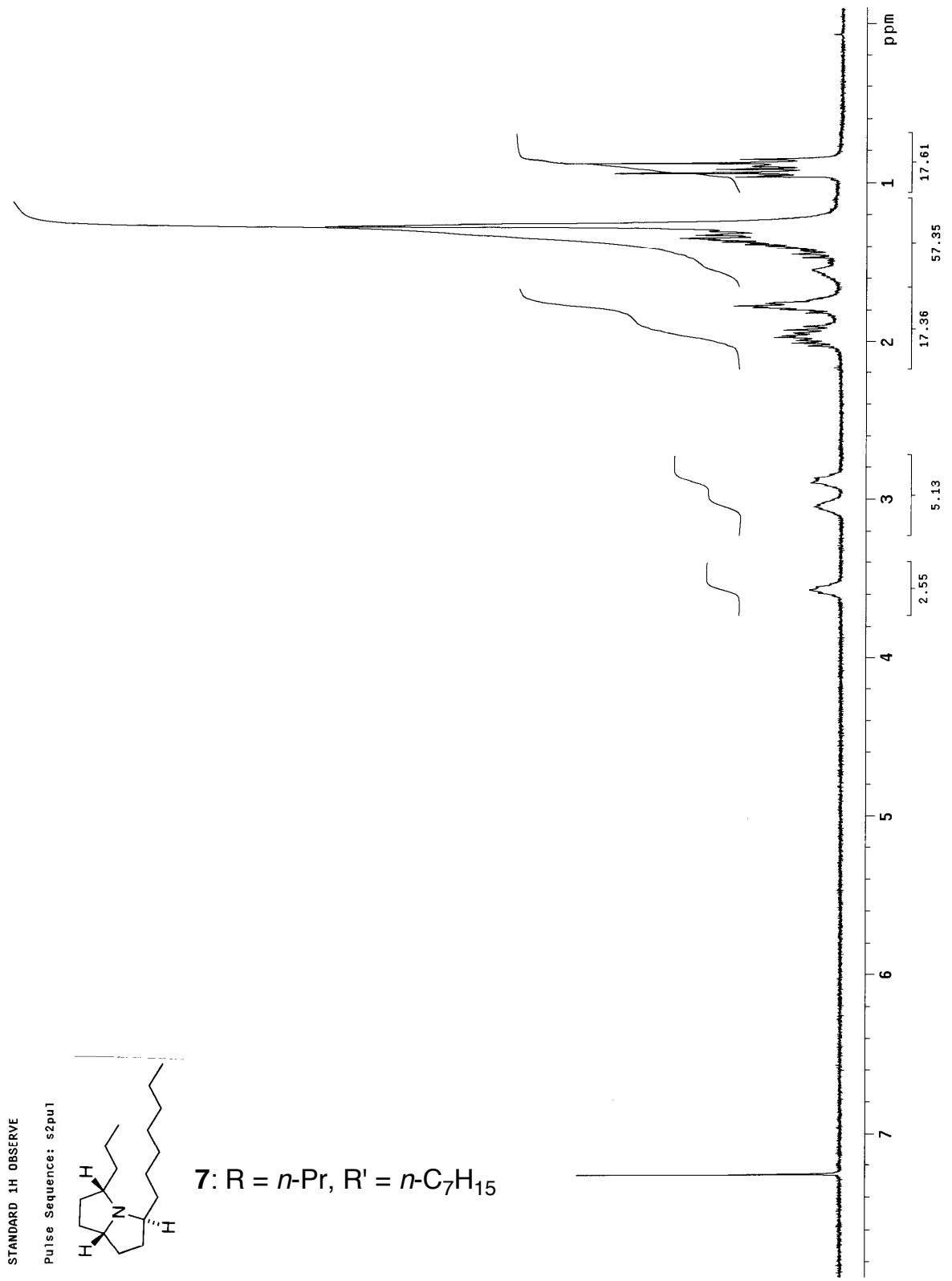


6: R = *n*-C_6H_{13}

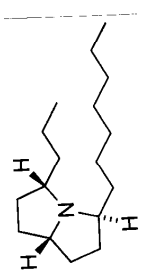



6: R = n-C6H13
CO2Et
H
N
H
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
220
200
180
160
140
120
100
80
60
40
20
0


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
H
N
H
H
7
6
5
4
3
2
1
ppm
6.40
3.00
5.99
84.61



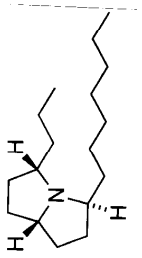
7: R = *n*-Pr, R' = *n*-C_7H_{15}

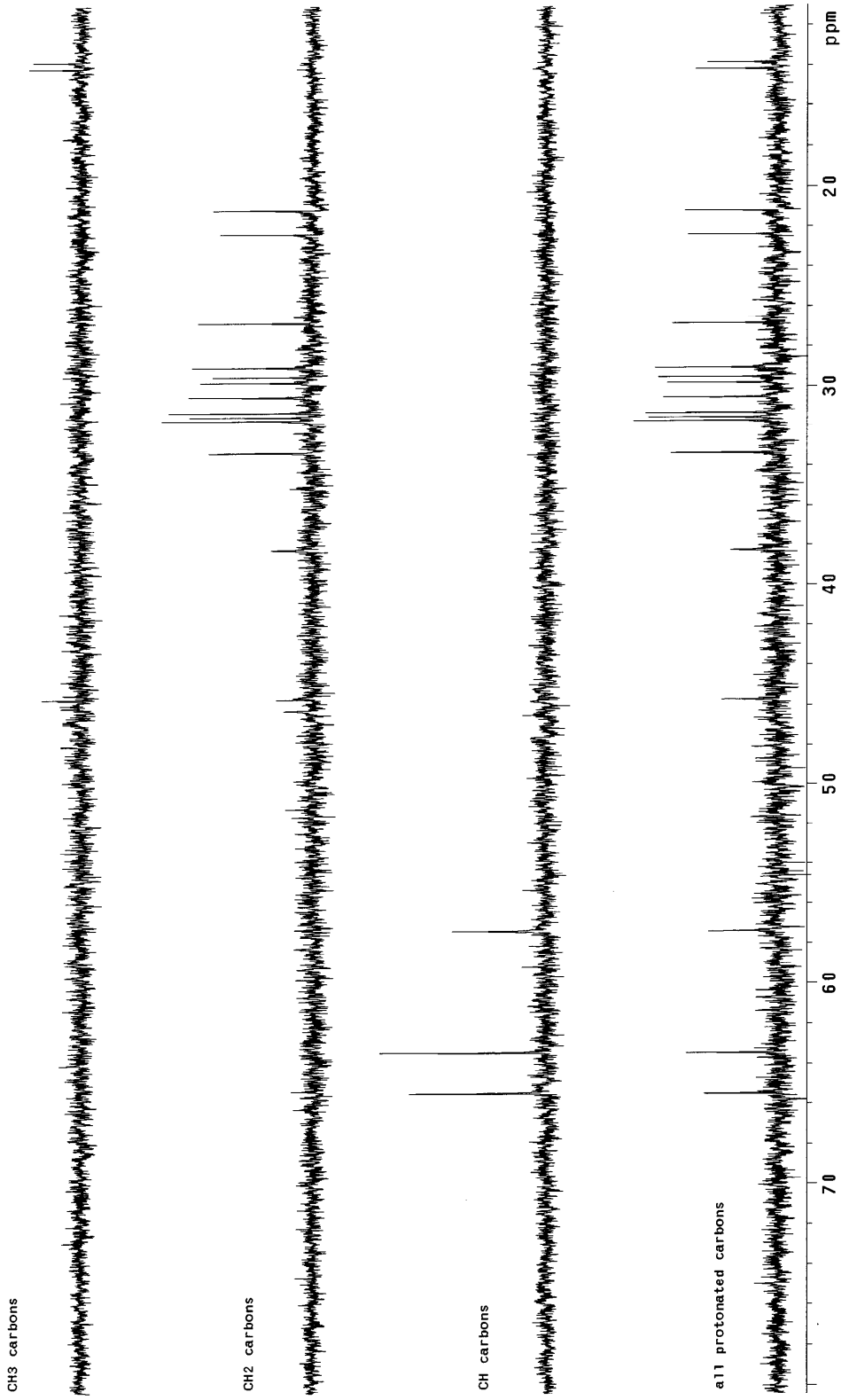


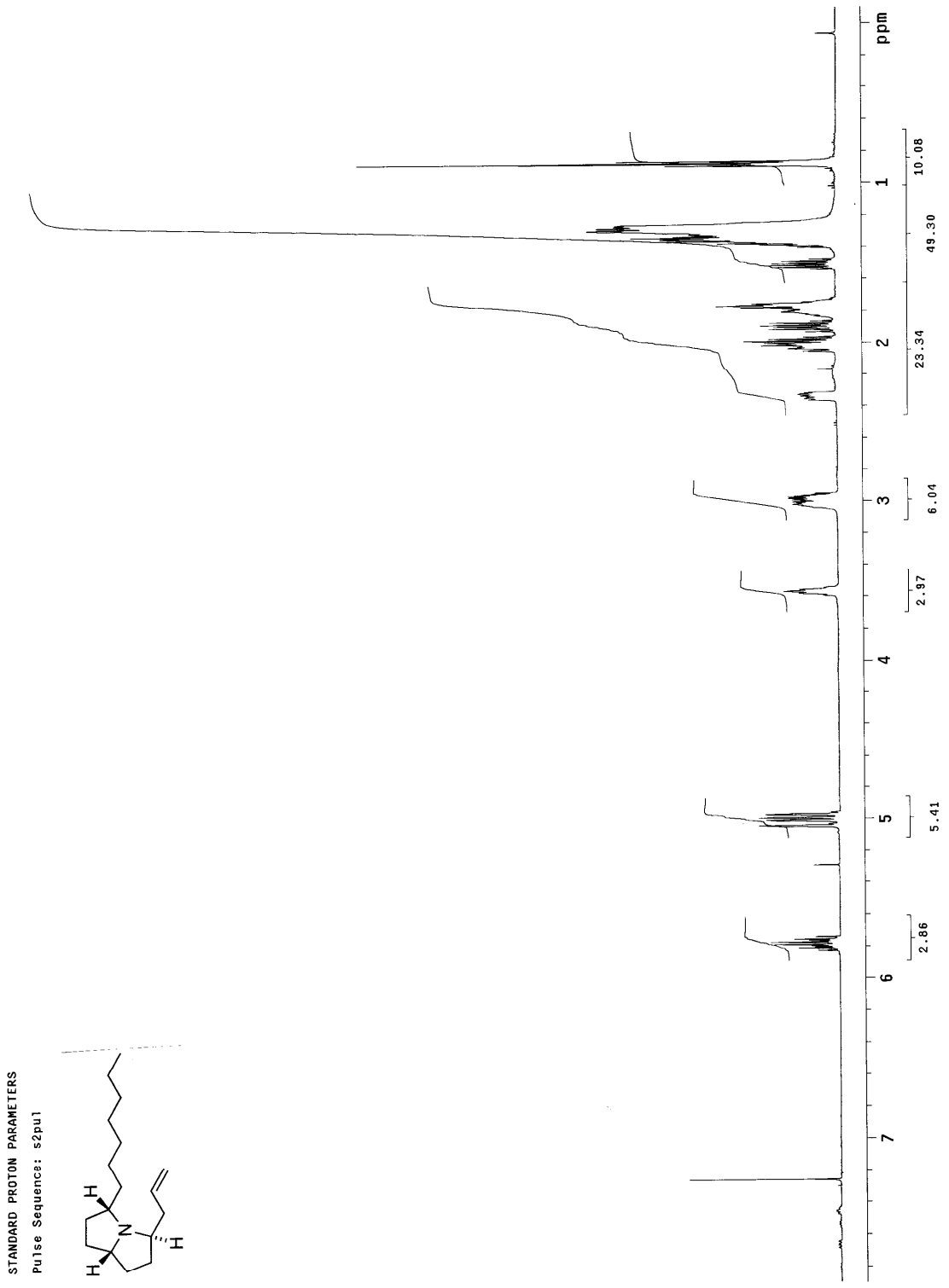
7: R = *n*-Pr, R' = *n*-C_7H_{15}

INDEX	FREQUENCY	PPM	HEIGHT
1	5841.541	77.421	161.8
2	5809.800	77.000	158.6
3	5778.060	76.579	149.2
4	4967.464	65.836	15.0
5	4811.204	63.765	14.7
6	4354.633	57.714	9.0
7	2915.337	38.638	6.3
8	2546.662	33.752	14.3
9	2422.142	32.102	12.3
10	2409.935	31.940	12.5
11	2392.844	31.713	13.5
12	2333.026	30.921	17.1
13	2278.091	30.193	14.9
14	2256.117	29.901	16.1
15	2220.714	29.432	15.3
16	2053.468	27.216	17.8
17	1717.754	22.766	15.9
18	1627.416	21.568	16.9
19	1097.599	14.547	16.9
20	1071.962	14.207	17.0

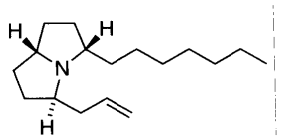
7: R = *n*-Pr,
R' = *n*-C_7H_{15}

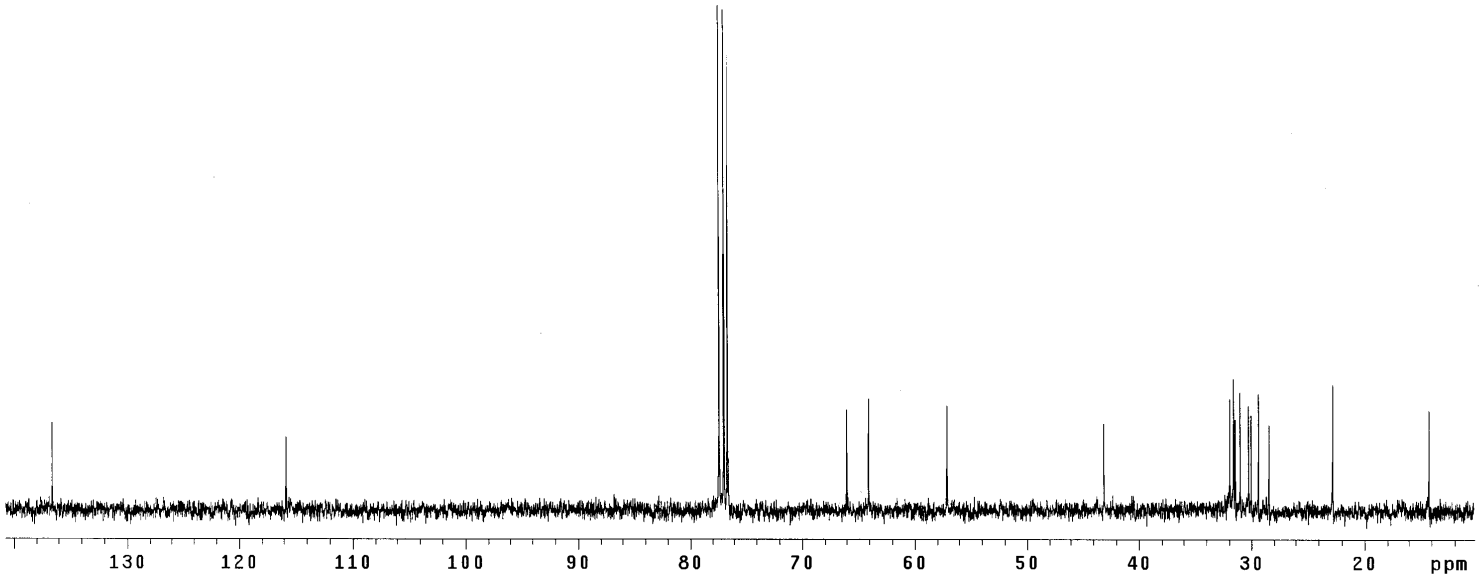


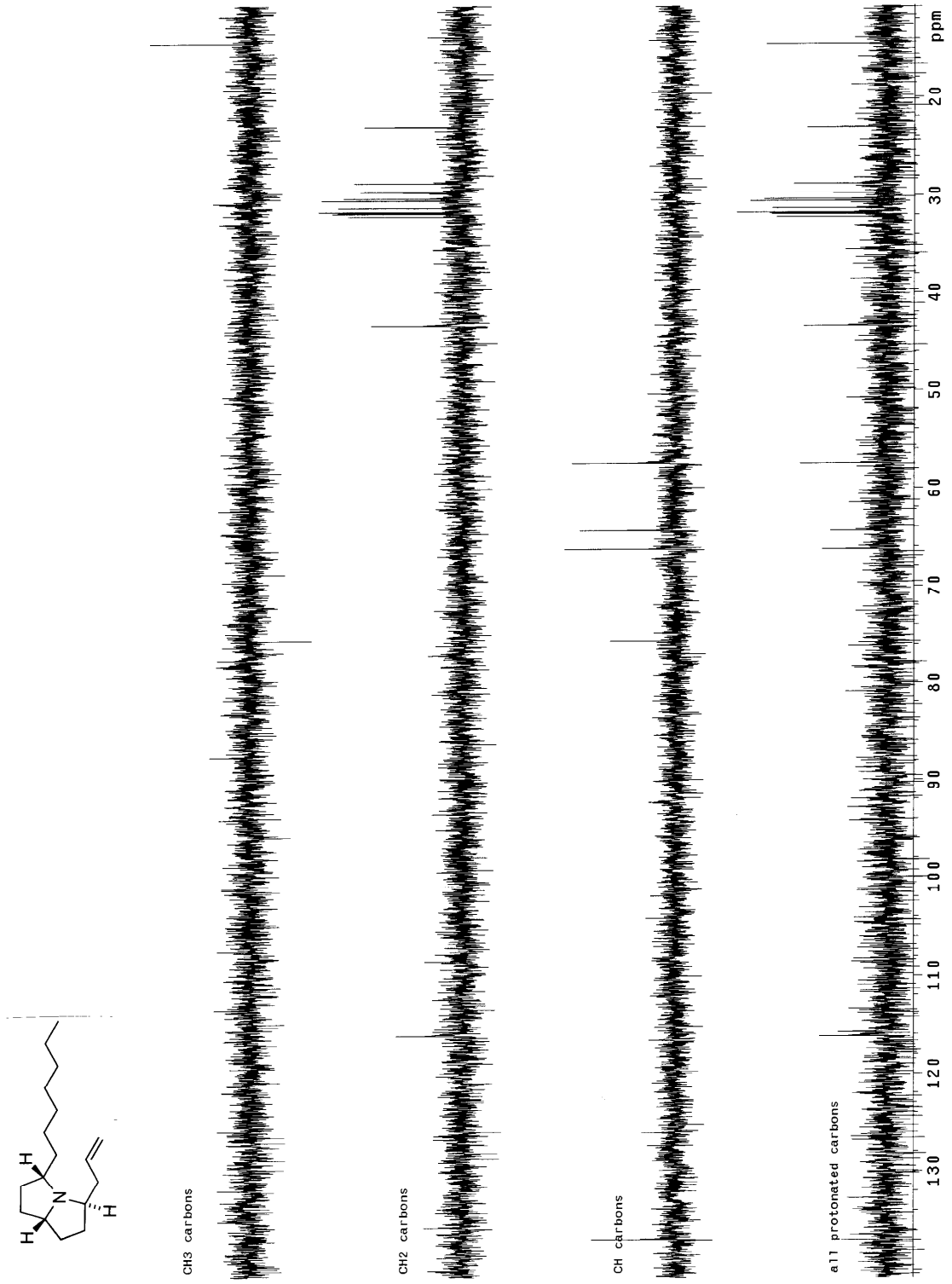


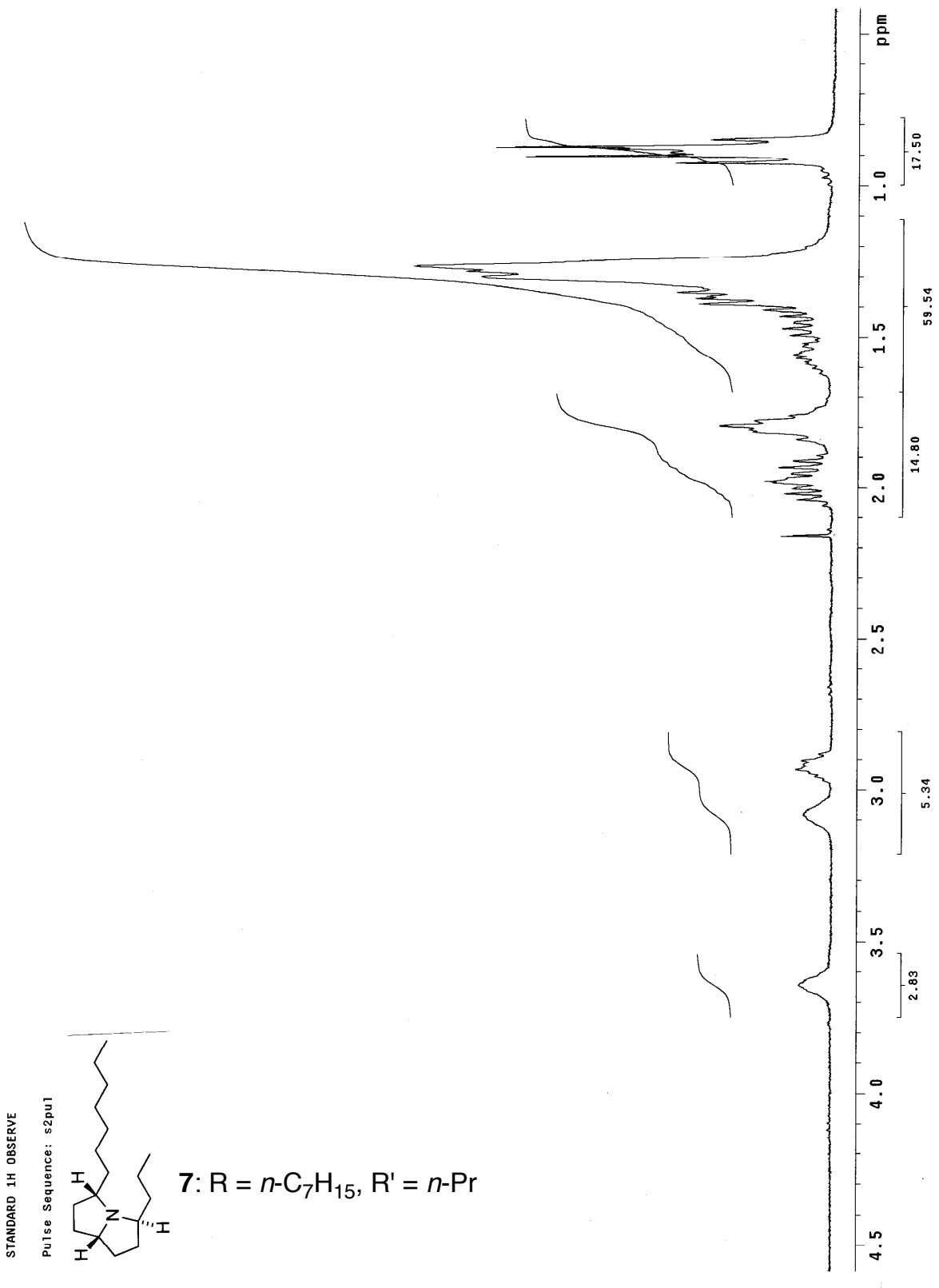

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
ppm
1
2
3
4
5
6
7
10.08
49.30
23.34
6.04
2.97
5.41
2.86

INDEX	FREQUENCY	PPM	HEIGHT
1	10303.483	136.557	14.6
2	8737.225	115.799	12.2
3	5841.541	77.421	85.8
4	5809.800	77.000	85.2
5	5778.060	76.579	80.8
6	4977.230	65.966	16.9
7	4831.958	64.040	18.8
8	4310.686	57.132	17.6
9	3247.388	43.039	14.6
10	2407.493	31.908	18.8
11	2381.857	31.568	22.1
12	2379.415	31.536	20.4
13	2370.870	31.422	15.3
14	2336.688	30.969	19.9
15	2279.312	30.209	17.6
16	2262.221	29.982	16.0
17	2214.610	29.351	19.7
18	2145.026	28.429	14.4
19	1716.533	22.750	21.2
20	1071.962	14.207	16.8

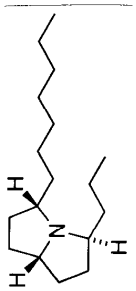





CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
20
30
40
50
60
70
80
90
100
110
120
130

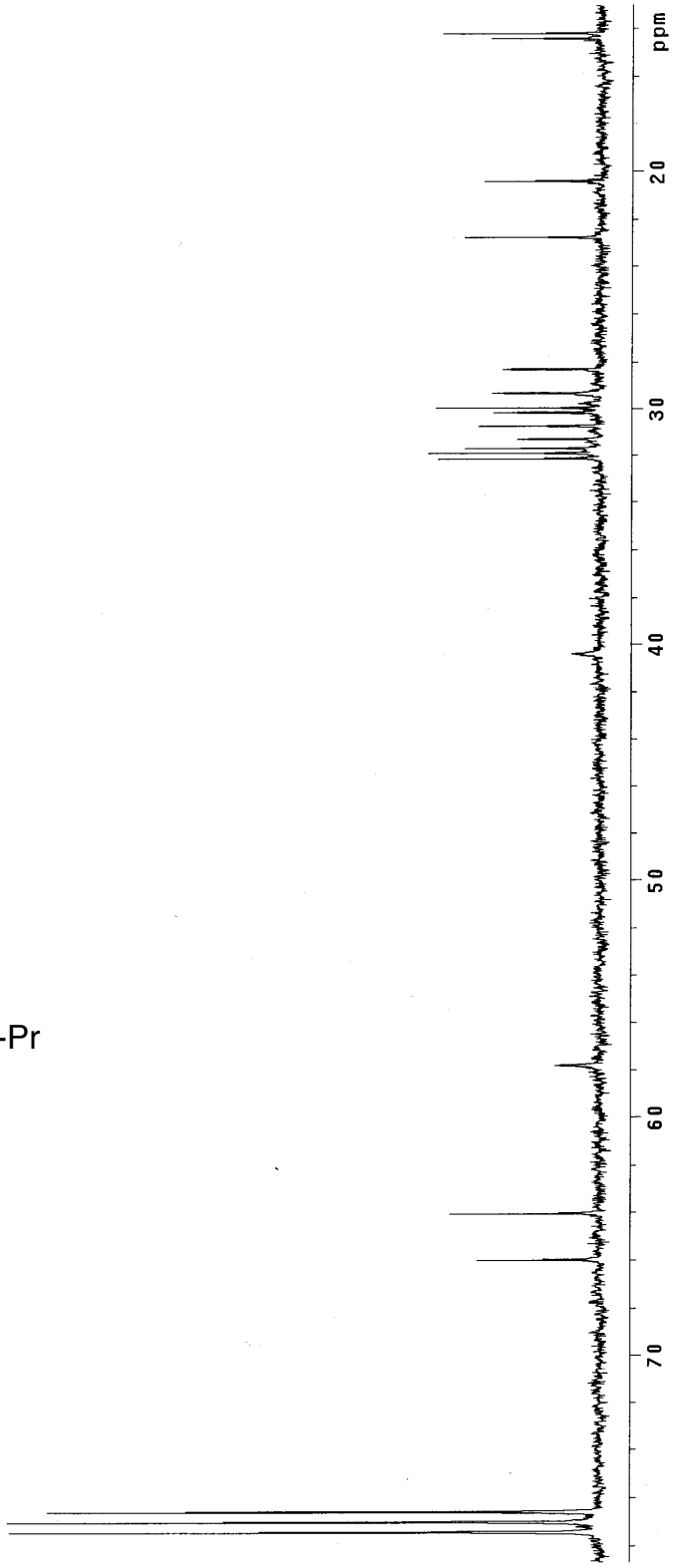


7: R = *n*-C_7H_{15}, R' = *n*-Pr

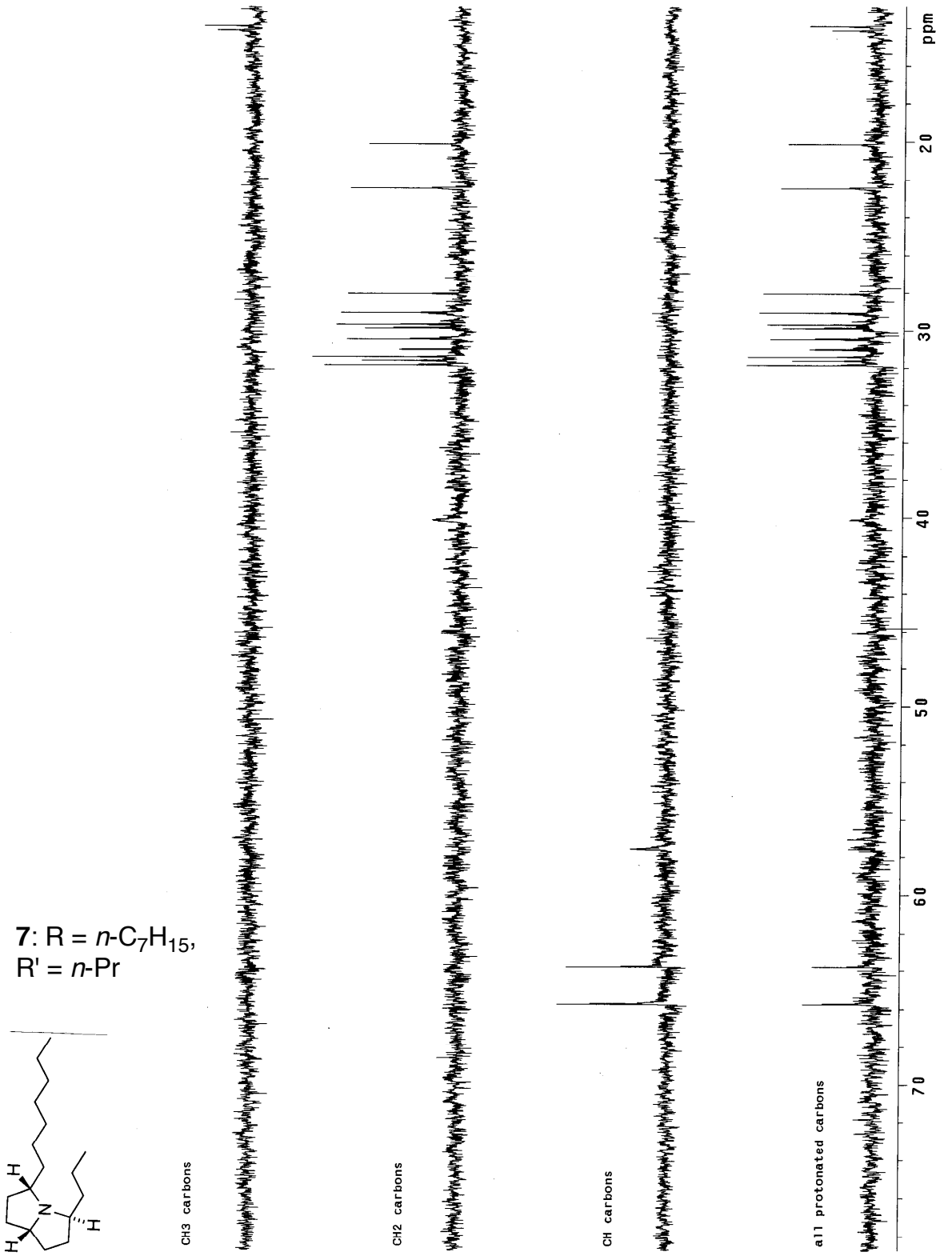


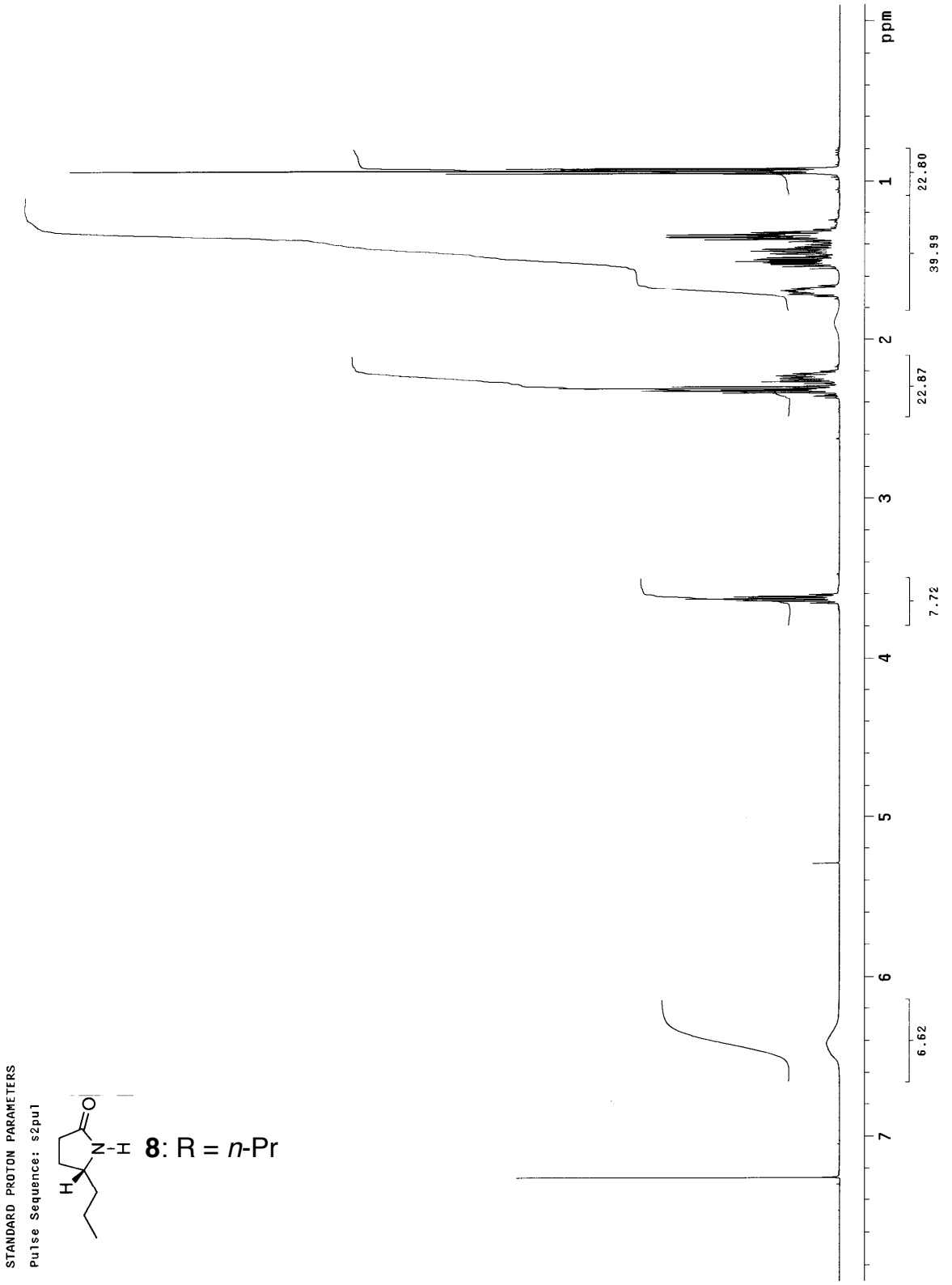
7: R = *n*-C_7H_{15}, R' = *n*-Pr

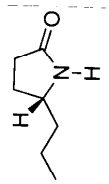
INDEX	FREQUENCY	PPM	HEIGHT
1	5841.541	77.421	94.8
2	5809.800	77.000	95.0
3	5778.060	76.579	88.6
4	4978.451	65.982	19.5
5	4831.958	64.040	23.9
6	4360.737	57.795	7.1
7	3047.181	40.386	4.5
8	2423.363	32.118	26.1
9	2405.052	31.875	27.7
10	2390.402	31.681	21.8
11	2359.883	31.277	13.4
12	2318.376	30.727	19.7
13	2274.428	30.144	17.2
14	2259.779	29.950	26.5
15	2212.169	29.319	17.4
16	2136.481	28.316	15.8
17	1715.312	22.734	21.8
18	1538.300	20.388	18.7
19	1086.612	14.401	17.7
20	1070.742	14.191	25.5



7: R = *n*-C_7H_{15},
R' = *n*-Pr

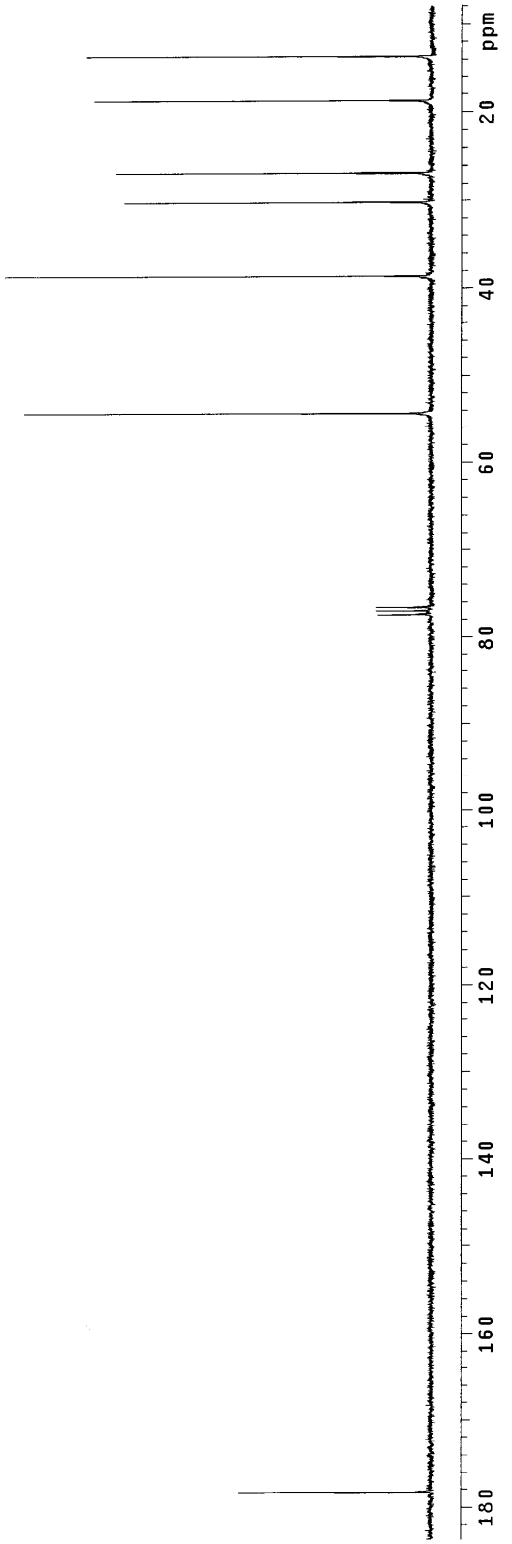



STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
H
N-H
O
8: R = n-Pr
ppm
1
2
3
4
5
6
7
22.80
39.99
22.87
7.72
6.62

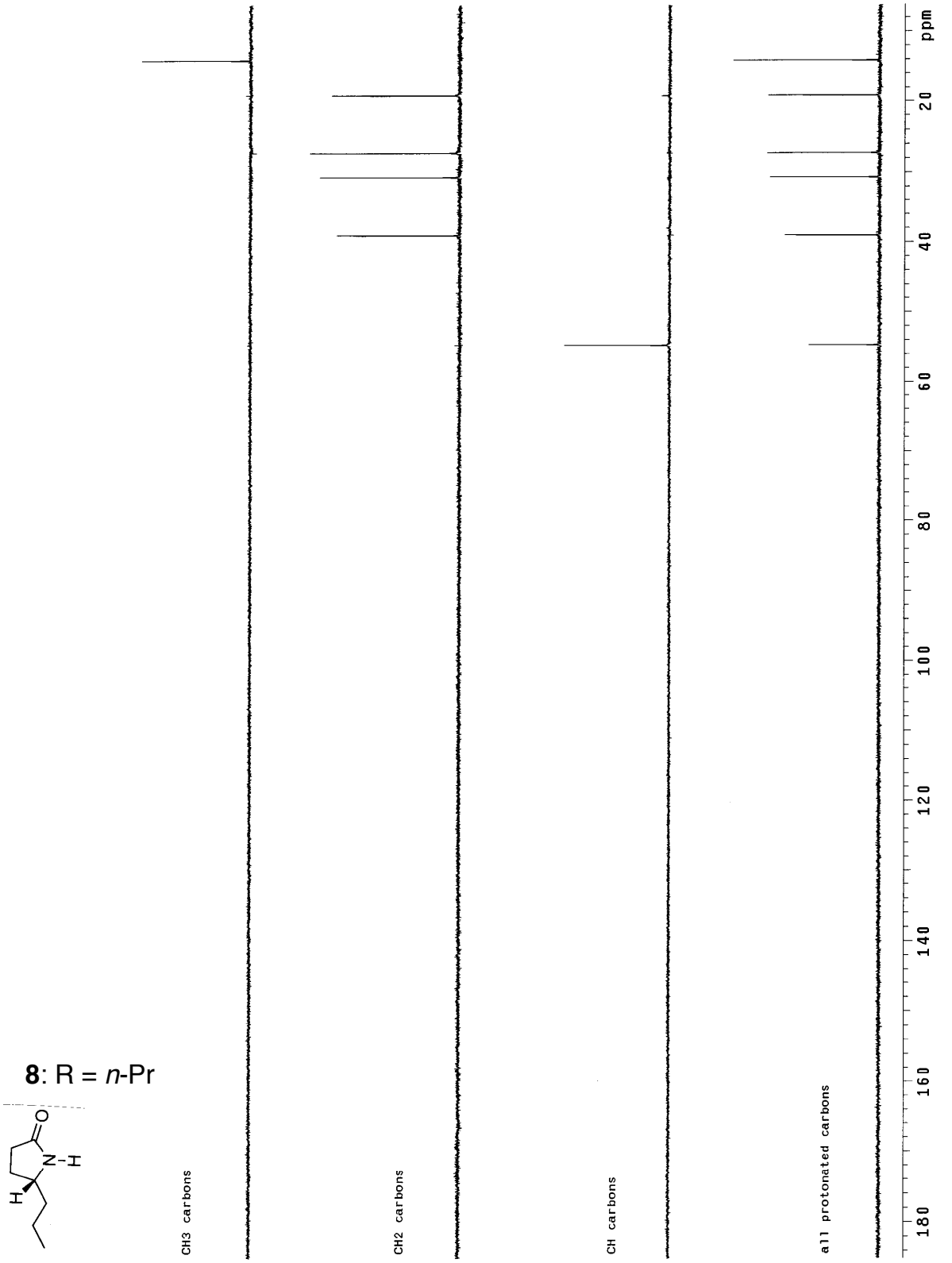


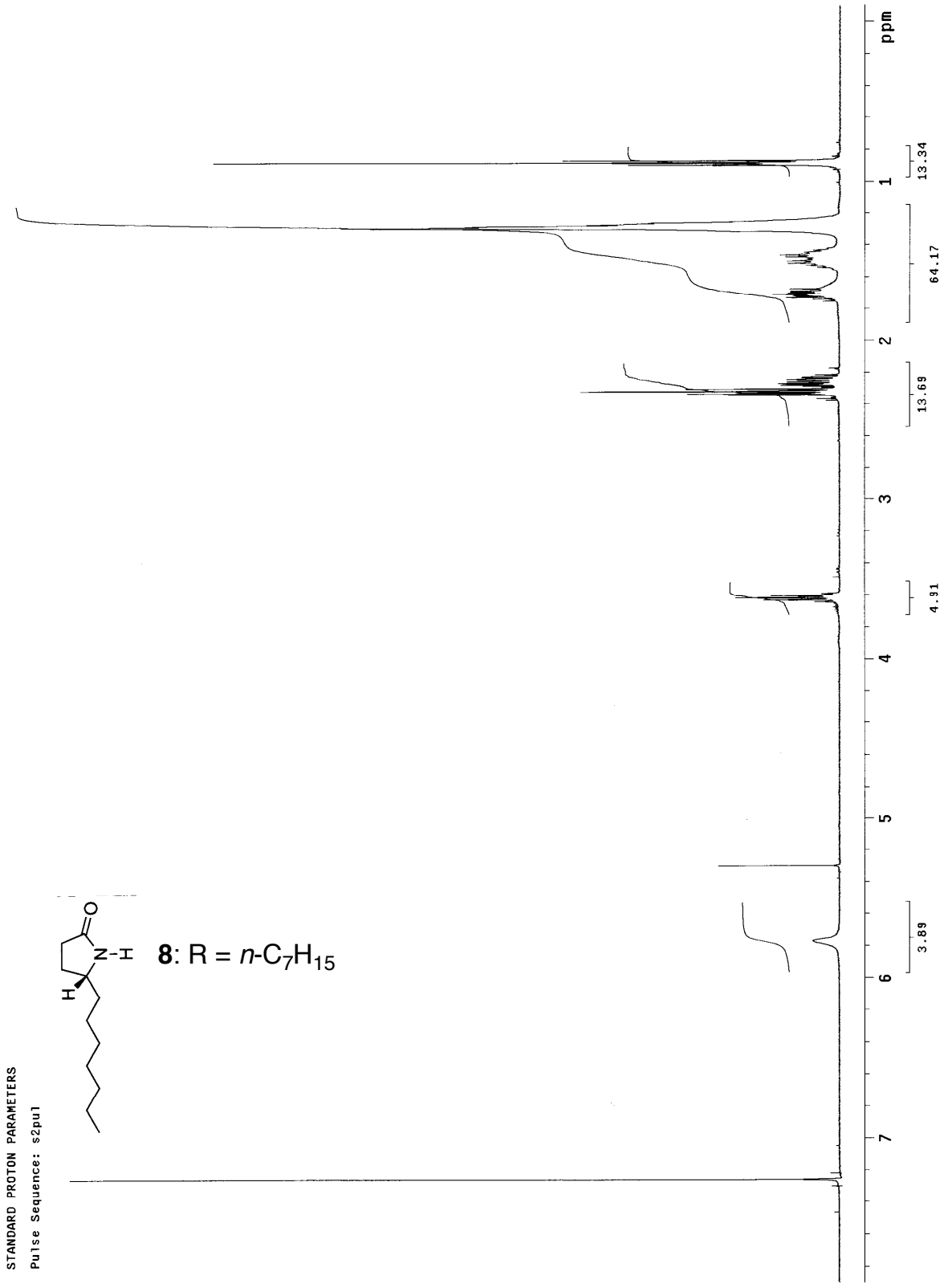
8: R = *n*-Pr

INDEX	FREQUENCY	PPM	HEIGHT
1	13451.870	178.284	31.4
2	5841.543	77.421	8.7
3	5809.802	77.000	9.0
4	5776.841	76.563	9.0
5	4095.831	54.284	66.5
6	2911.676	38.530	69.7
7	2275.651	30.160	49.9
8	2020.509	26.779	51.4
9	1413.782	18.738	54.9
10	1028.016	13.625	56.3



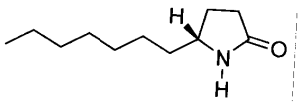
8: R = *n*-Pr


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
20
40
60
80
100
120
140
160
180

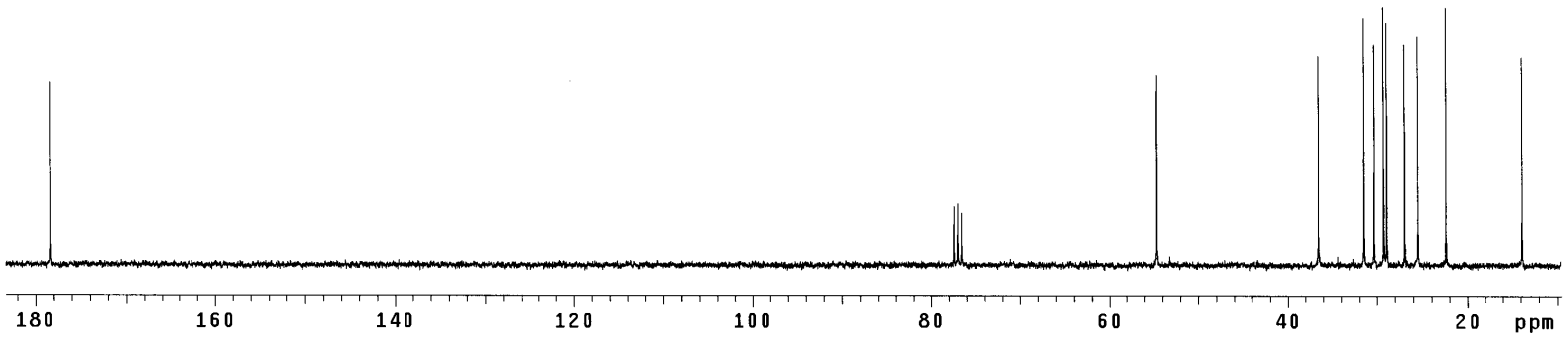

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
ppm
1
2
3
4
5
6
7
13.34
64.17
13.69
4.91
3.89

8: R = *n*-C_7H_{15}

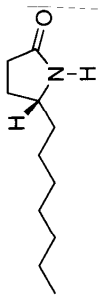
INDEX	FREQUENCY	PPM	HEIGHT
1	13454.311	178.316	29.4
2	5841.542	77.421	9.5
3	5809.802	77.000	10.0
4	5778.061	76.579	8.4
5	4121.466	54.624	30.6
6	2754.195	36.503	33.7
7	2378.196	31.519	39.8
8	2285.417	30.290	35.6
9	2206.066	29.238	41.6
10	2179.209	28.882	39.0
11	2032.716	26.941	35.5
12	1924.066	25.501	37.0
13	1688.456	22.378	41.5
14	1043.886	13.835	33.6

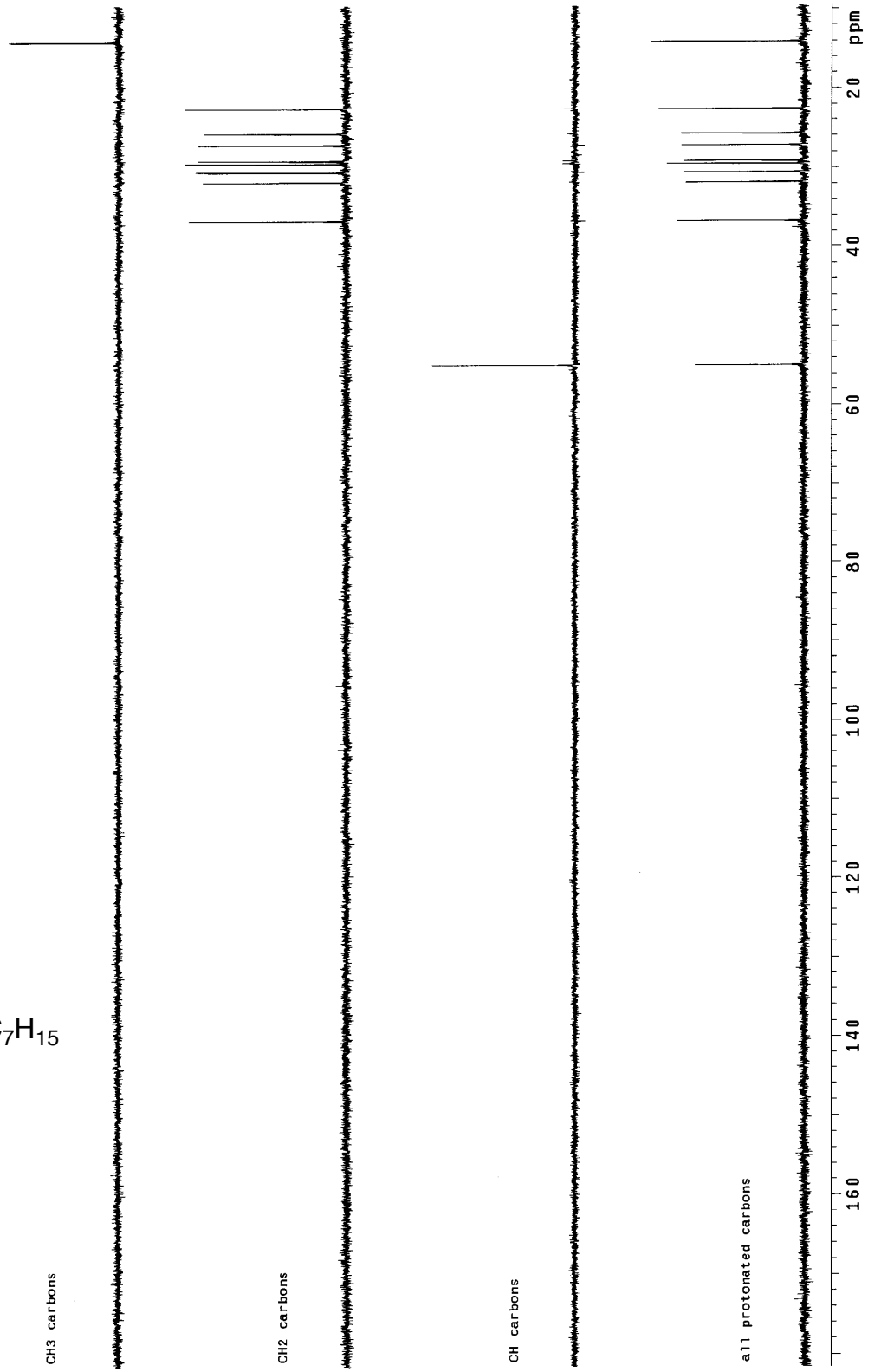


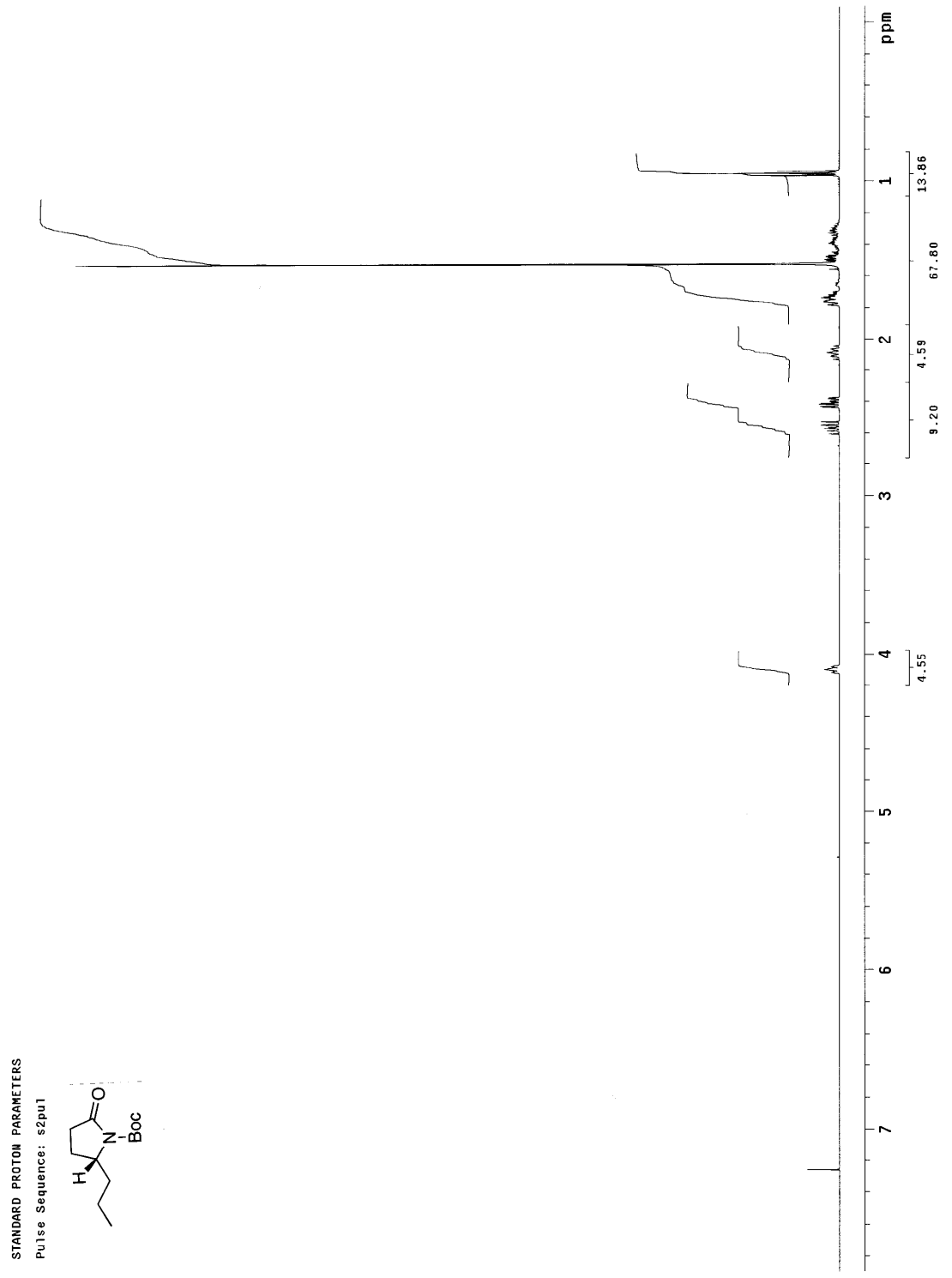
8: R = *n*-C_7H_{15}



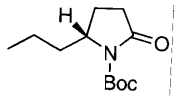
8: R = *n*-C_7H_{15}

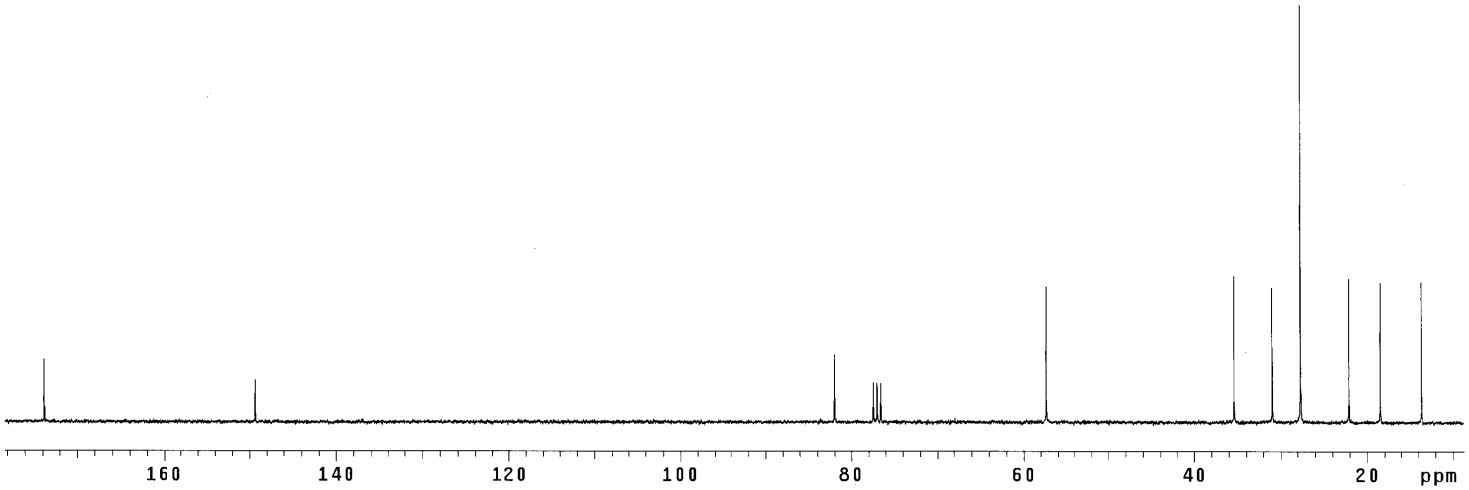

O
N-H
H

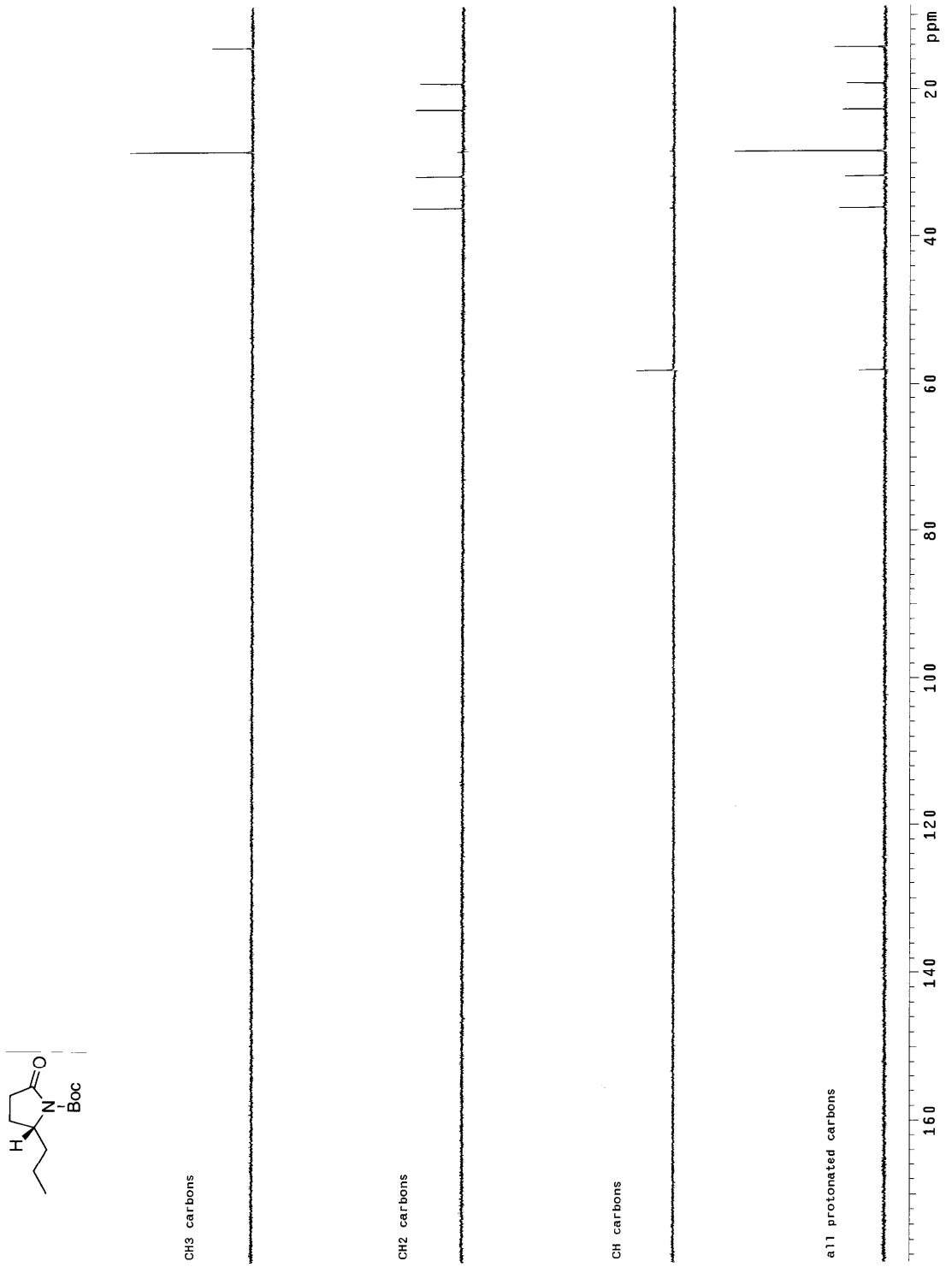

CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
20
40
60
80
100
120
140
160

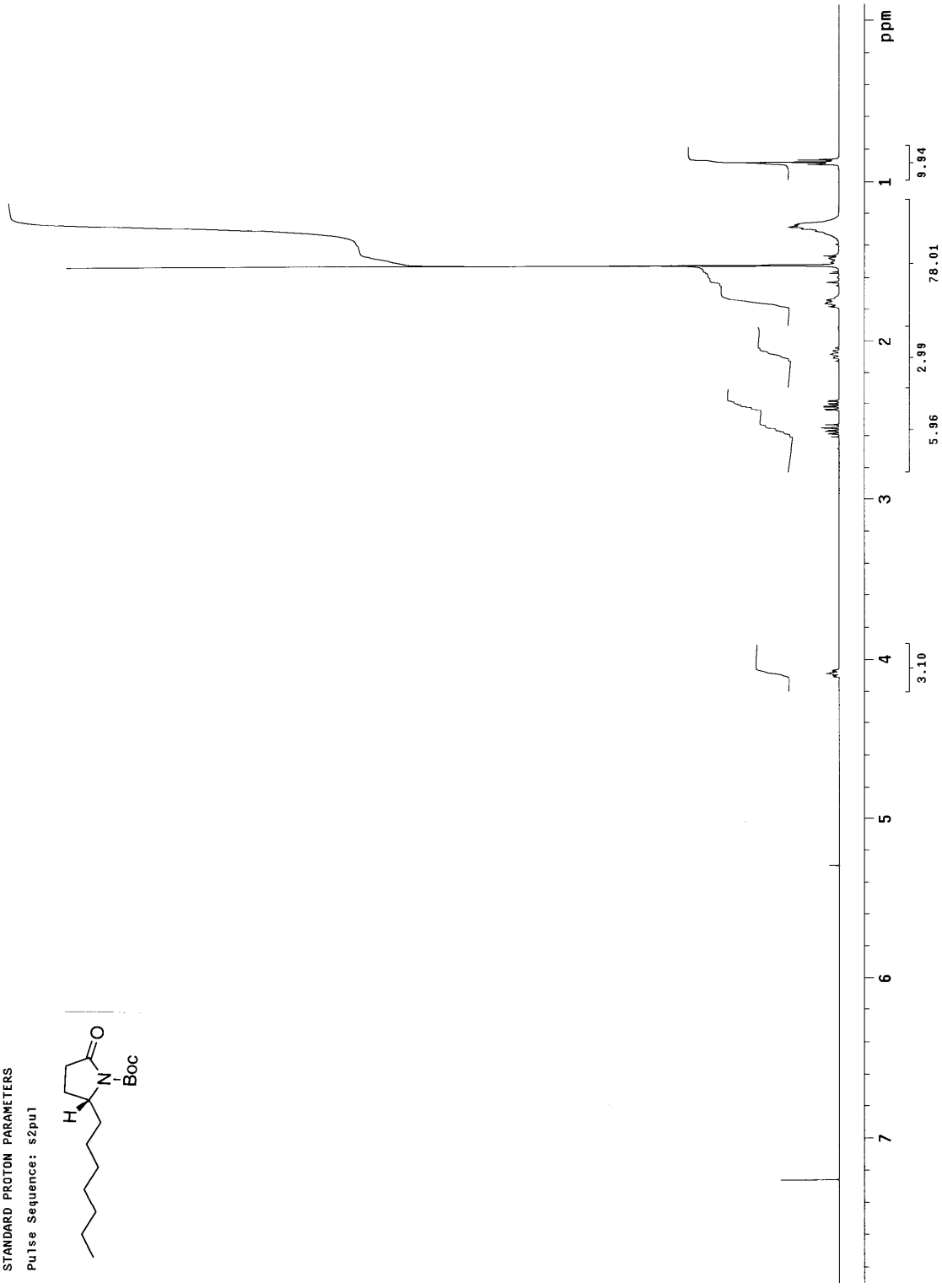

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
O
N
Boc
H
ppm
1
2
3
4
5
6
7
13.86
67.80
4.59
9.20
4.55

INDEX	FREQUENCY	PPM	HEIGHT
1	13113.715	173.802	10.8
2	11266.678	149.323	7.2
3	6188.243	82.016	11.7
4	5841.542	77.421	6.8
5	5809.802	77.000	6.7
6	5776.841	76.563	6.7
7	4328.999	57.374	23.4
8	2669.962	35.386	25.2
9	2337.911	30.985	23.2
10	2085.210	27.636	71.8
11	1667.704	22.103	24.7
12	1395.470	18.495	24.0
13	1024.354	13.576	24.1

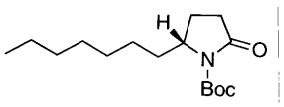


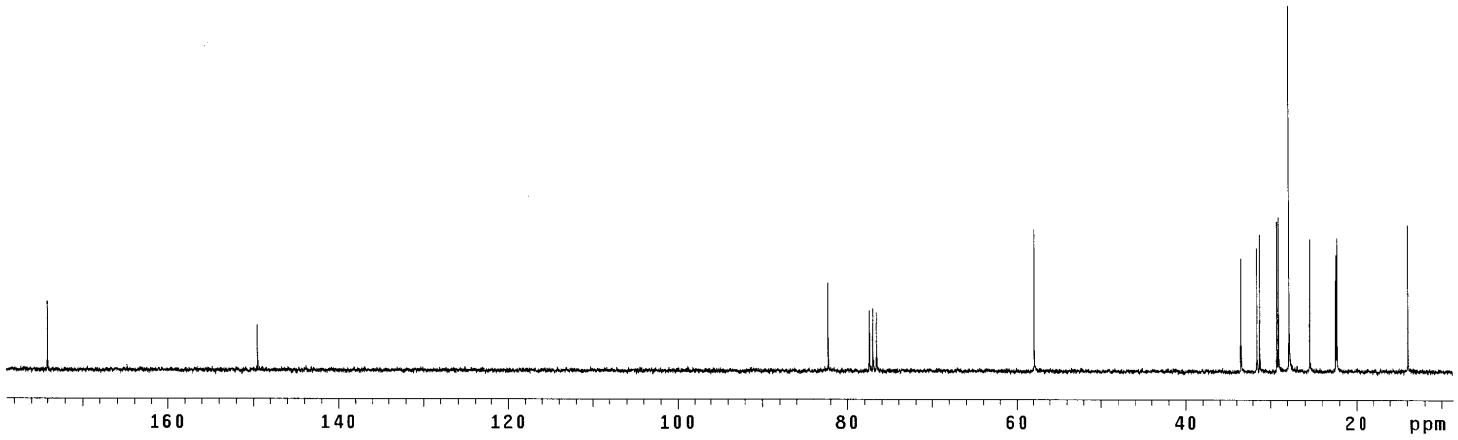


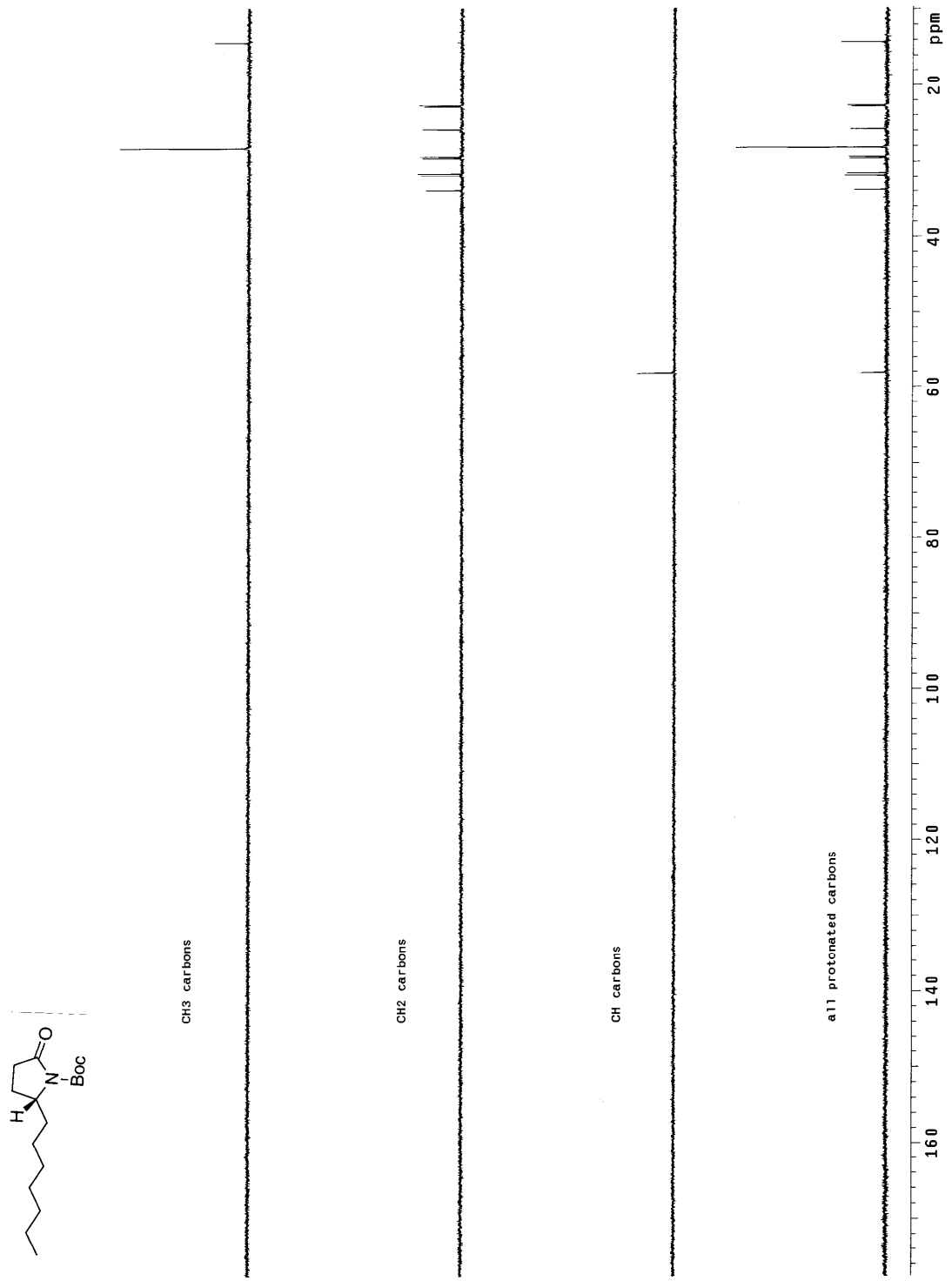

O
N
Boc
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
140
120
100
80
60
40
20
ppm

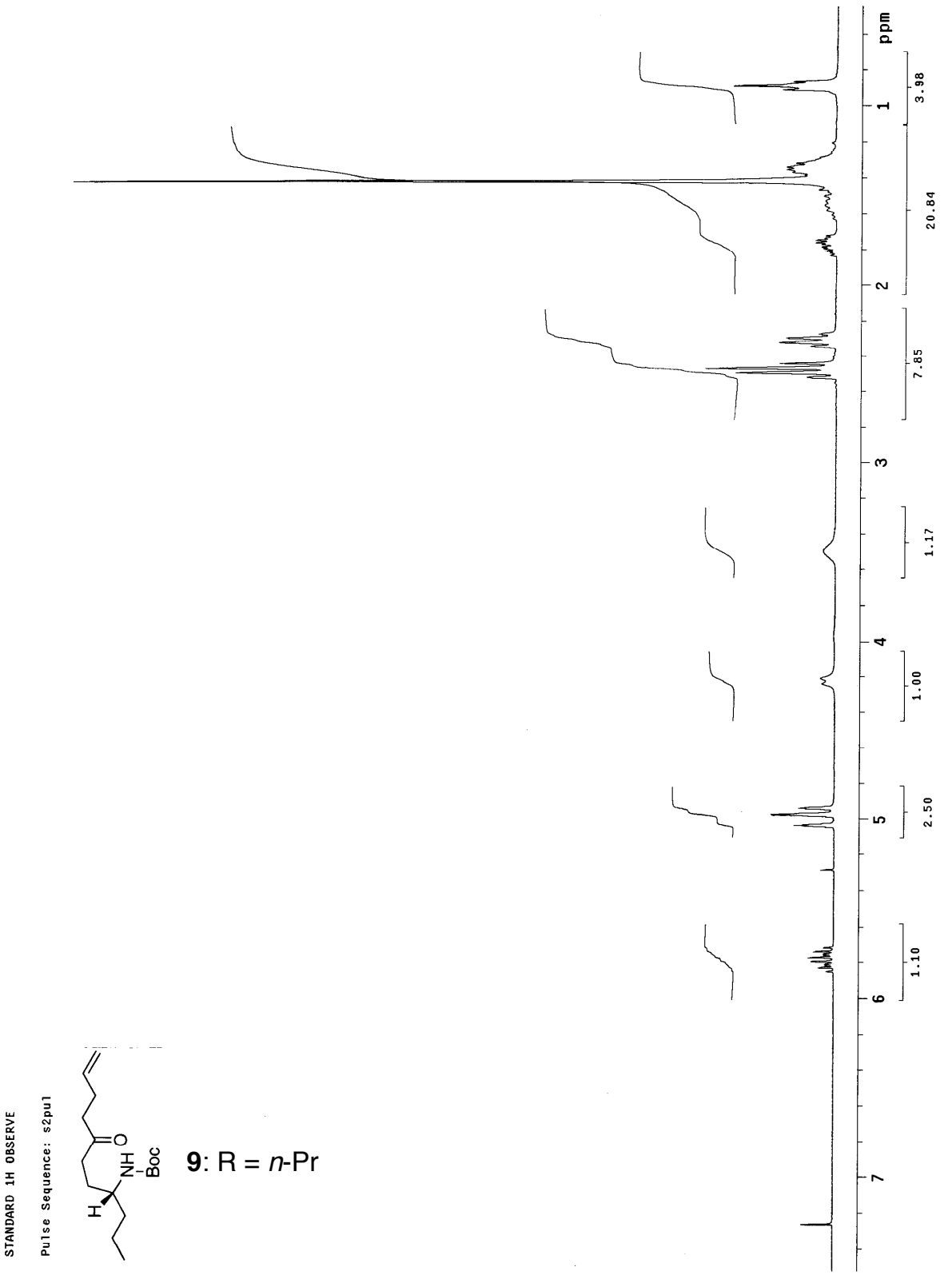

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
H
N
O
Boc
ppm
1
2
3
4
5
6
7
9.94
78.01
2.99
5.96
3.10

INDEX	FREQUENCY	PPM	HEIGHT
1	13128.364	173.996	11.9
2	11281.327	149.517	7.7
3	6202.892	82.210	15.1
4	5841.542	77.421	10.3
5	5809.802	77.000	10.7
6	5778.061	76.579	10.0
7	4361.959	57.811	24.4
8	2525.910	33.477	19.4
9	2376.975	31.503	21.2
10	2352.559	31.180	23.5
11	2202.404	29.189	25.8
12	2187.754	28.995	26.6
13	2098.638	27.814	63.2
14	1916.742	25.403	22.8
15	1689.677	22.394	20.0
16	1681.132	22.281	22.9
17	1047.548	13.884	25.3

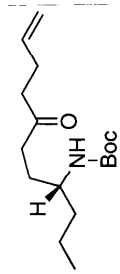





O
N
Boc
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
140
120
100
80
60
40
20
ppm

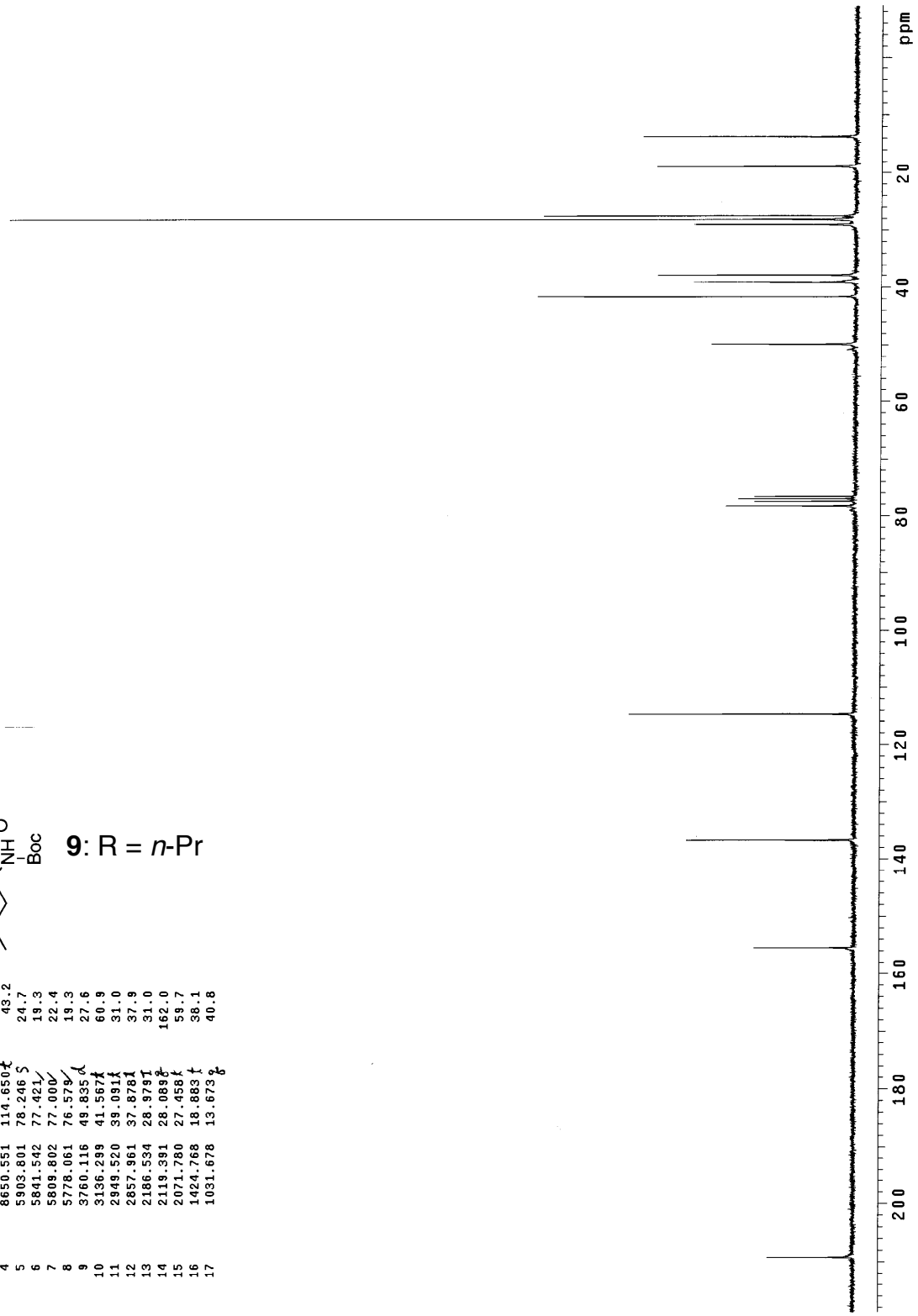

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
NH
O
Boc
H
ppm
1
2
3
4
5
6
7
3.98
20.84
7.85
1.17
1.00
2.50
1.10

9: R = *n*-Pr

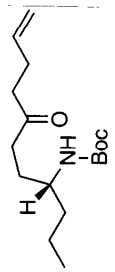


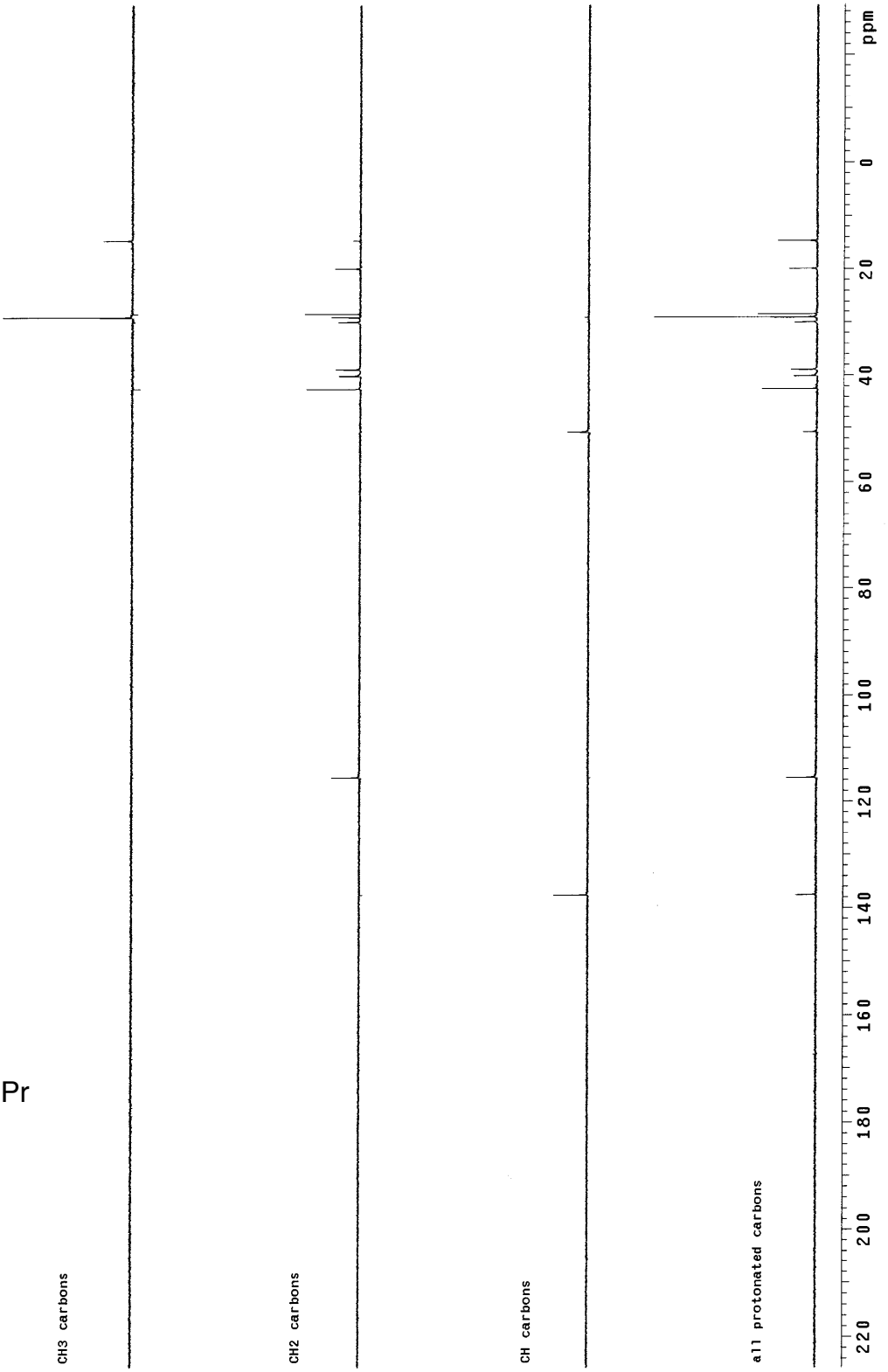
9: R = *n*-Pr

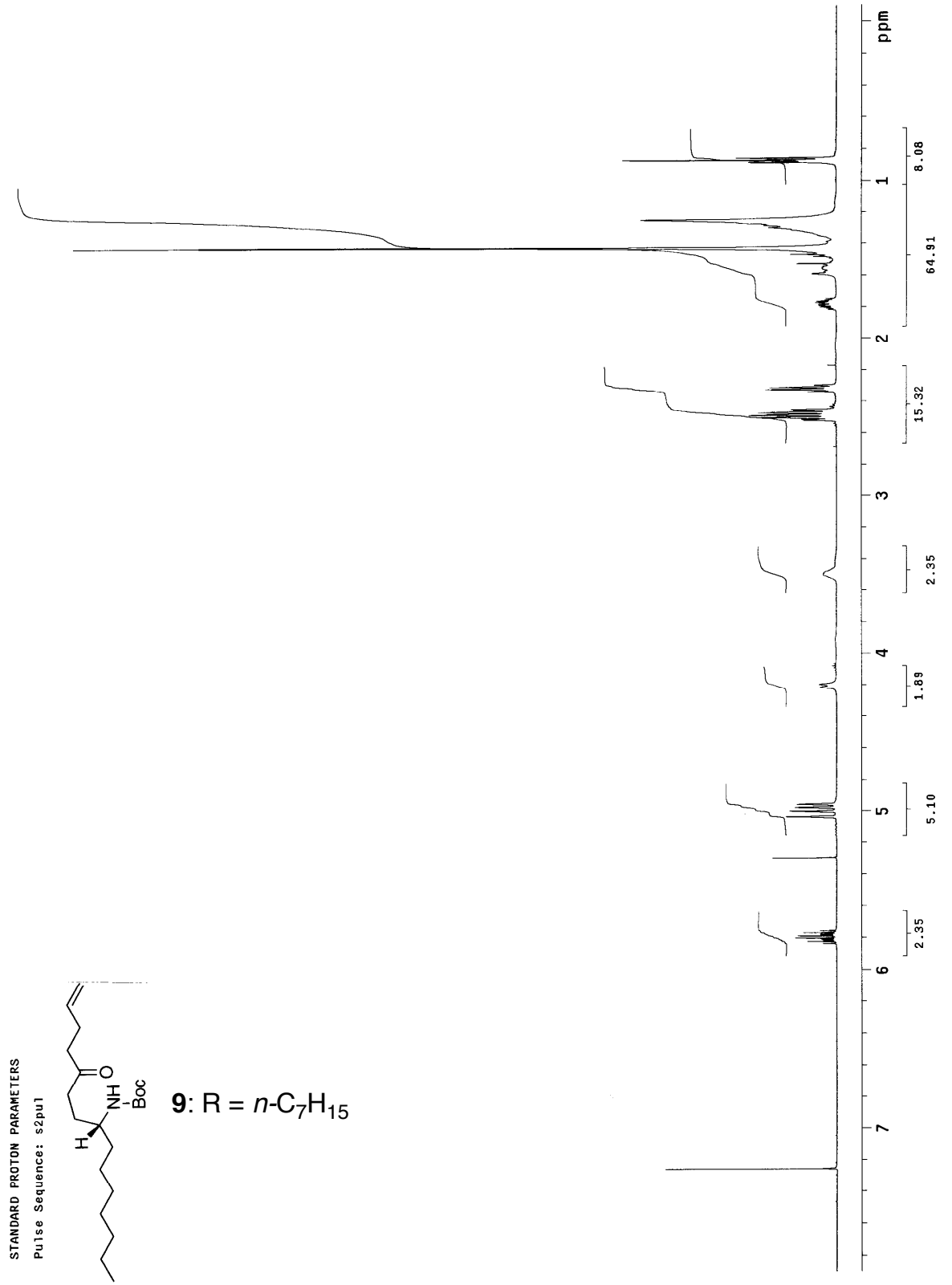
INDEX	FREQUENCY	PPM	HEIGHT
1	15787.217	209.235	16.3
2	11723.248	155.374	19.1
3	10309.588	136.638	32.1
4	8650.551	114.650	43.2
5	5903.801	78.246	24.7
6	5841.542	77.421	19.3
7	5809.802	77.000	22.4
8	5778.061	76.579	19.3
9	3760.116	49.835	27.6
10	3136.299	41.567	60.9
11	2949.520	39.091	31.0
12	2857.961	37.878	37.9
13	2186.534	28.979	31.0
14	2119.391	28.089	162.0
15	2071.780	27.458	59.7
16	1424.768	18.883	38.1
17	1031.678	13.673	40.8



9: R = *n*-Pr

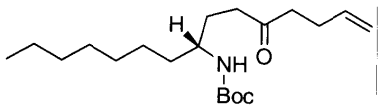

O
NH
Boc
H


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
220
200
180
160
140
120
100
80
60
40
20
0
ppm

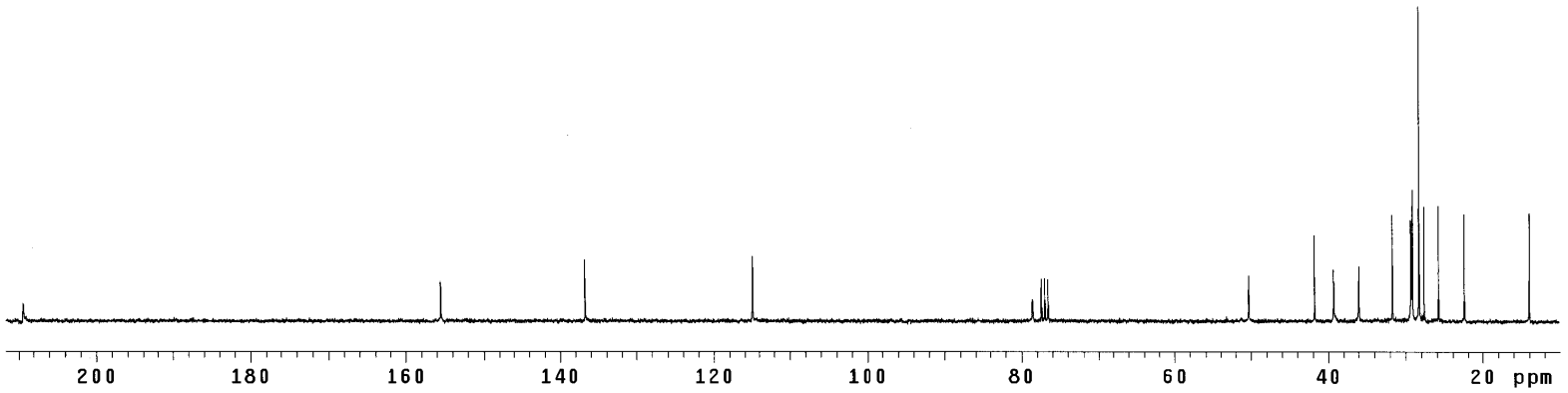

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
NH
O
Boc
H
ppm
1
2
3
4
5
6
7
8.08
64.91
15.32
2.35
1.89
5.10
2.35

9: R = *n*-C_7H_{15}

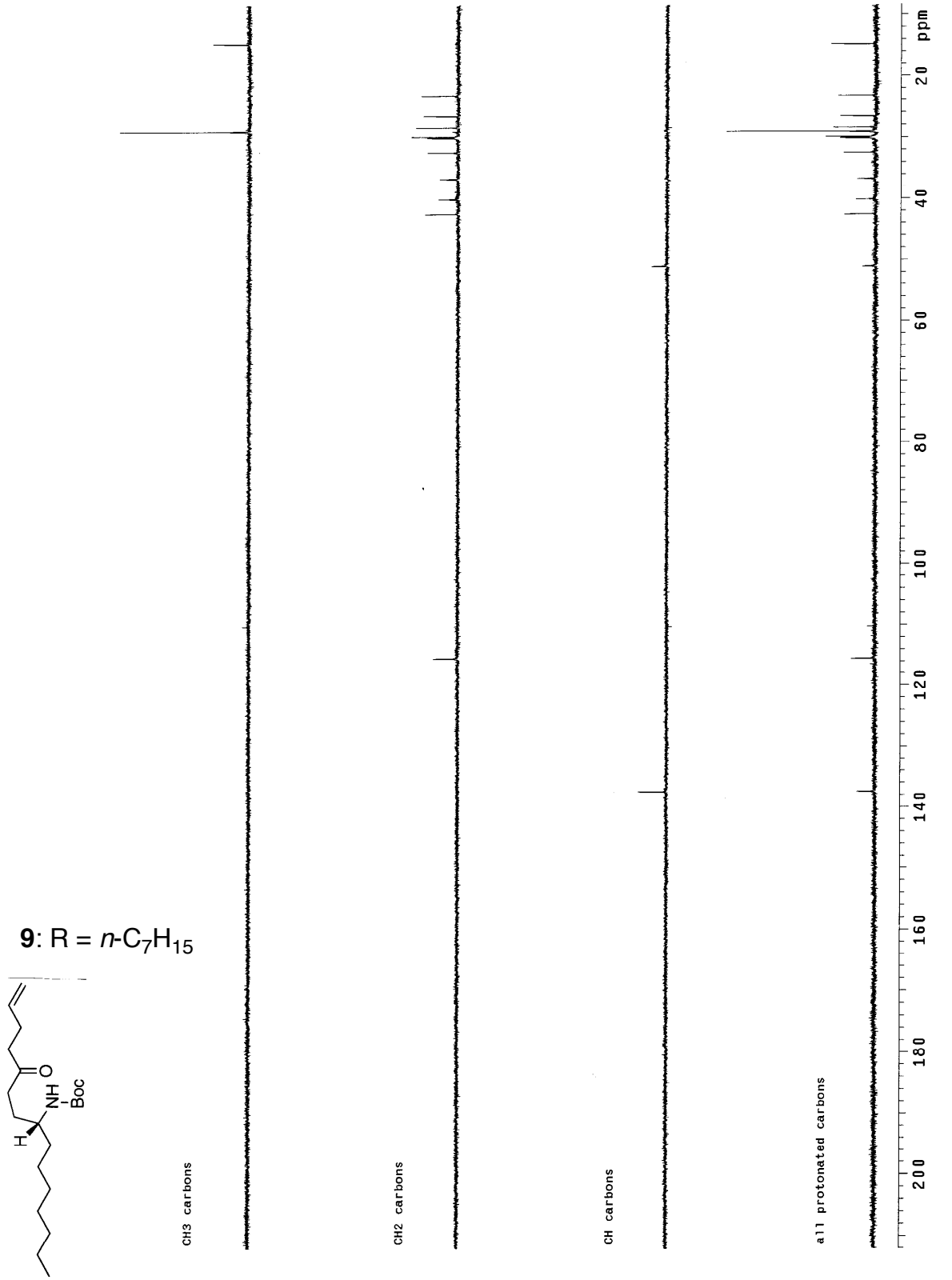
INDEX	FREQUENCY	PPM		HEIGHT
1	15803.087	209.446	S	2.7
2	11733.014	155.503	S	6.3
3	10320.574	136.783	d	9.7
4	8663.979	114.828	t	10.3
5	5928.217	78.569	S	3.4
6	5841.541	77.421		6.7
7	5809.801	77.000		6.8
8	5776.840	76.563		6.6
9	3793.076	50.271	d	7.2
10	3152.168	41.777	t	13.7
11	2966.610	39.318	t	8.2
12	2710.247	35.920	d	8.8
13	2386.741	31.633	t	17.0
14	2212.169	29.319	t	16.2
15	2199.962	29.157	t	11.9
16	2195.079	29.092	t	21.1
17	2131.598	28.251	q	50.7
18	2083.988	27.620	t	18.3
19	1946.040	25.792	t	18.4
20	1698.222	22.507	t	17.1
21	1053.651	13.965	q	17.3

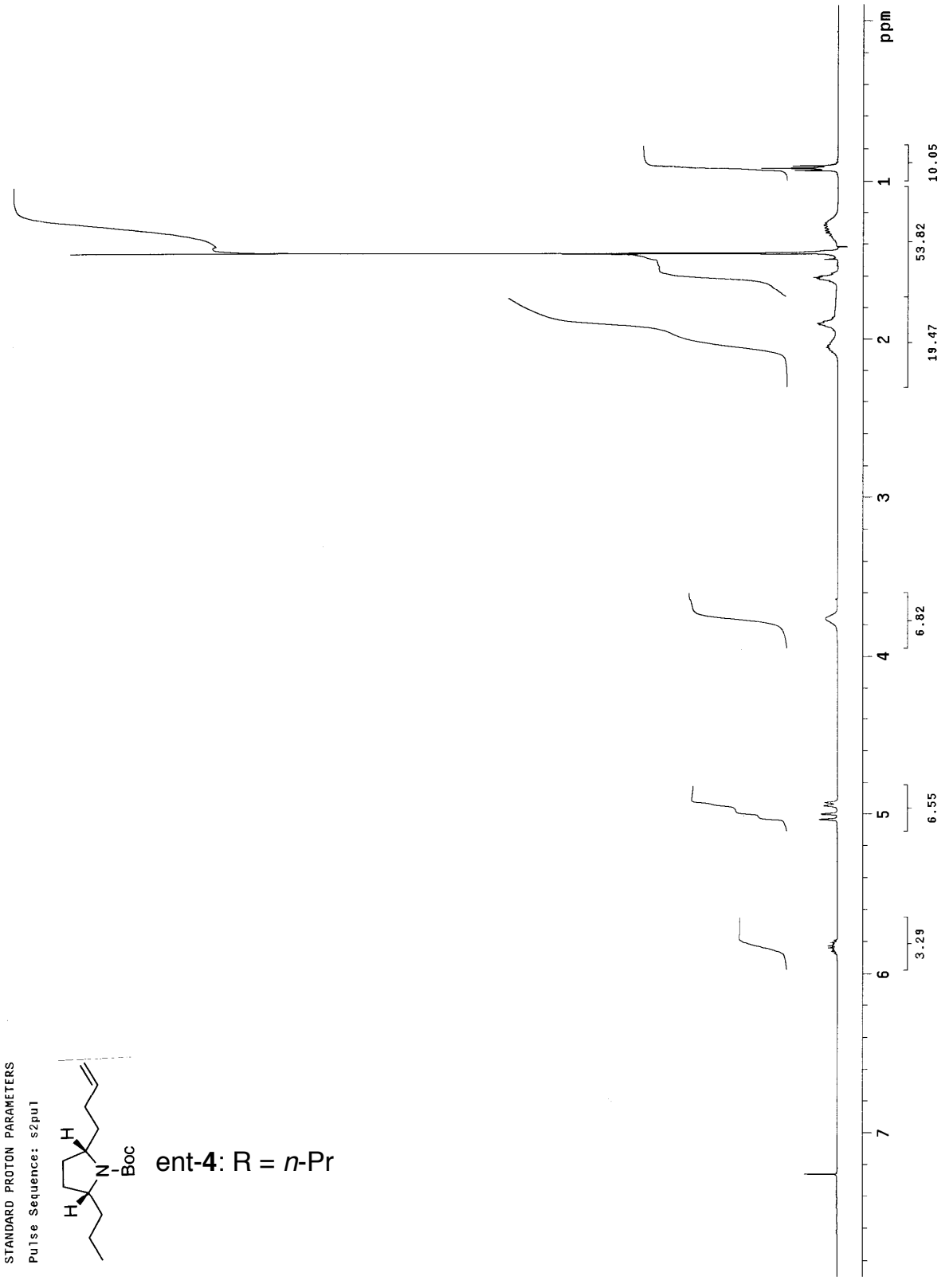


9: R = *n*-C_7H_{15}



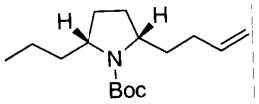
9: R = *n*-C_7H_{15}


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
200
180
160
140
120
100
80
60
40
20
O
NH
Boc
H

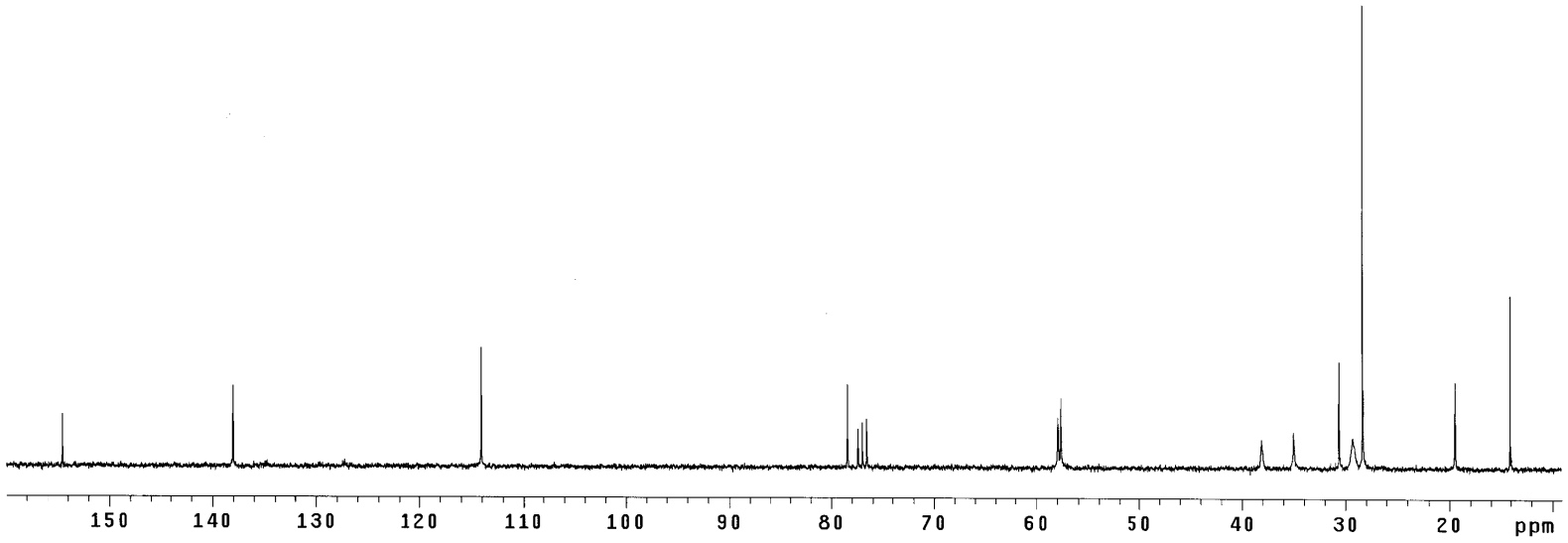

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
H
N-Boc
H
ppm
1
2
3
4
5
6
7
10.05
53.82
19.47
6.82
6.55
3.29

ent-**4**: R = *n*-Pr

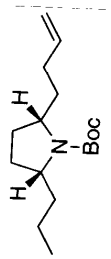
INDEX	FREQUENCY	PPM	HEIGHT
1	11654.885	154.468	8.3
2	10414.574	138.029	12.9
3	8606.603	114.067	19.2
4	5918.450	78.440	13.4
5	5841.541	77.421	6.2
6	5809.801	77.000	7.2
7	5778.061	76.579	7.8
8	4371.725	57.941	8.0
9	4349.751	57.649	11.2
10	2870.169	38.040	4.6
11	2639.442	34.982	5.8
12	2308.611	30.597	17.2
13	2208.507	29.270	4.8
14	2138.923	28.348	74.8
15	1467.495	19.449	14.0
16	1057.314	14.013	27.9

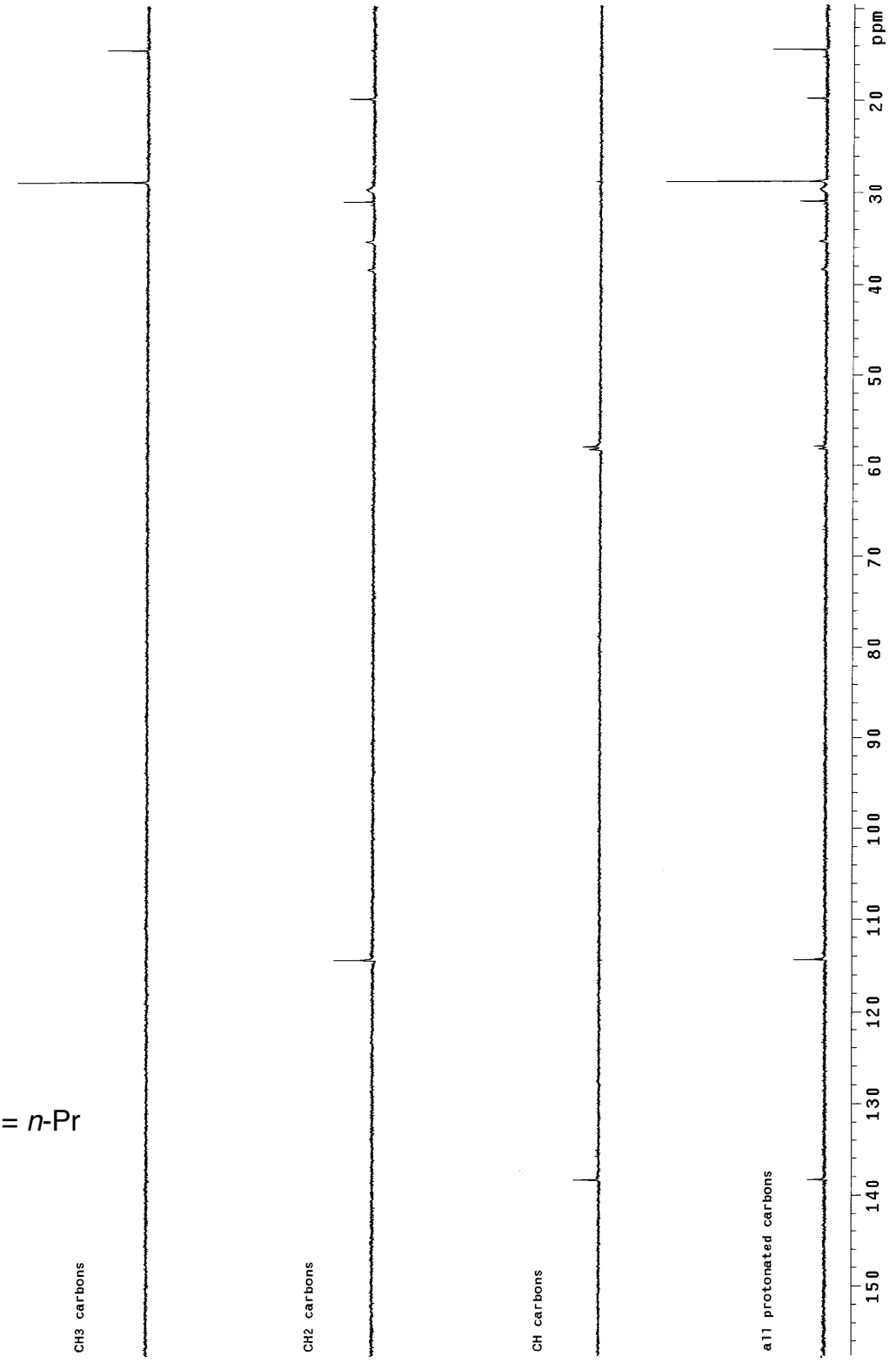


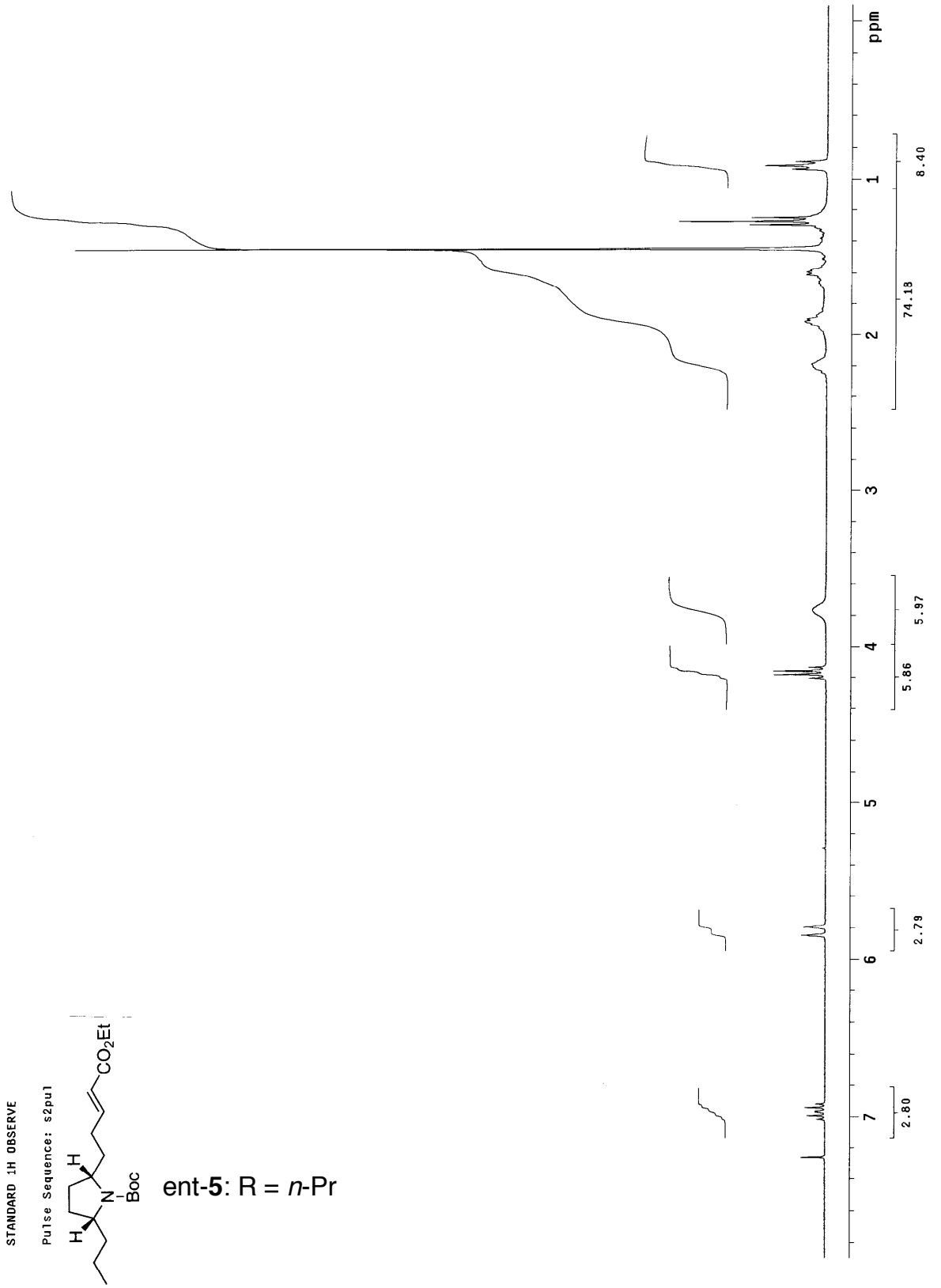
ent-4: R = *n*-Pr



ent-**4**: R = *n*-Pr

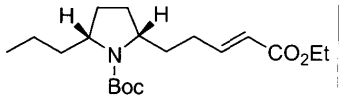

H
N
Boc
H


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

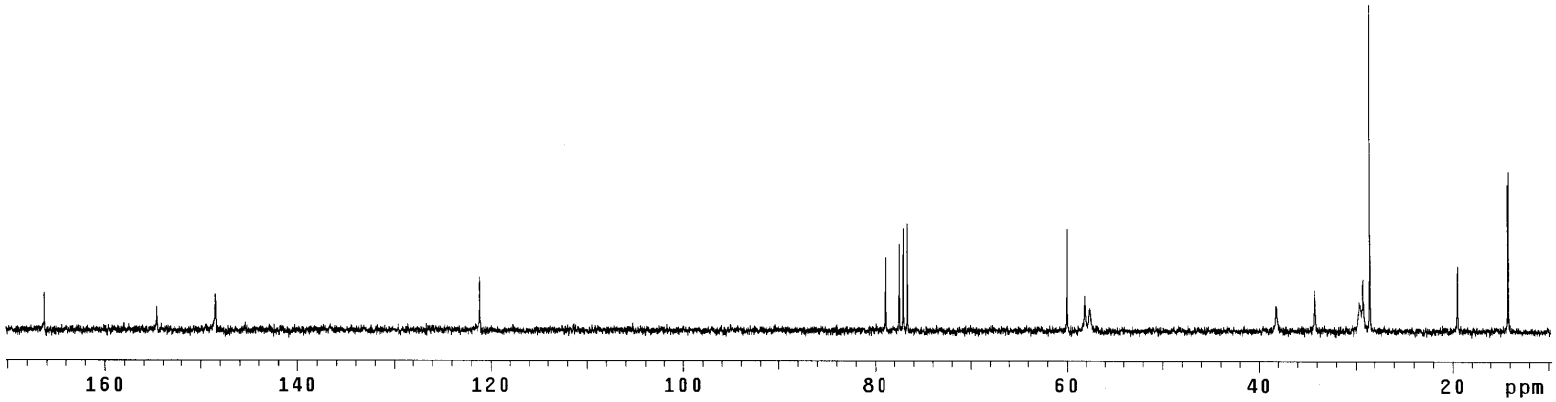

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
CO2Et
H
N
Boc
H
ppm
1
2
3
4
5
6
7
8.40
74.18
5.97
5.86
2.79
2.80

ent-**5**: R = *n*-Pr

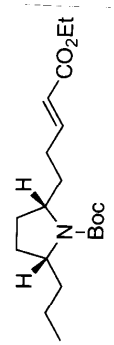
INDEX	FREQUENCY	PPM	HEIGHT
1	12542.390	166.230	6.0
2	11668.313	154.646	3.7
3	11200.755	148.449	5.9
4	9140.082	121.138	8.7
5	5948.970	78.844	12.0
6	5841.541	77.421	14.0
7	5809.801	77.000	16.6
8	5778.061	76.579	17.4
9	4524.322	59.963	16.5
10	4385.153	58.118	5.7
11	4346.089	57.601	3.7
12	2883.597	38.218	4.1
13	2580.844	34.205	6.6
14	2228.039	29.529	4.7
15	2198.741	29.141	8.5
16	2146.247	28.445	52.9
17	1472.378	19.514	10.6
18	1073.184	14.223	23.7
19	1064.638	14.110	25.8

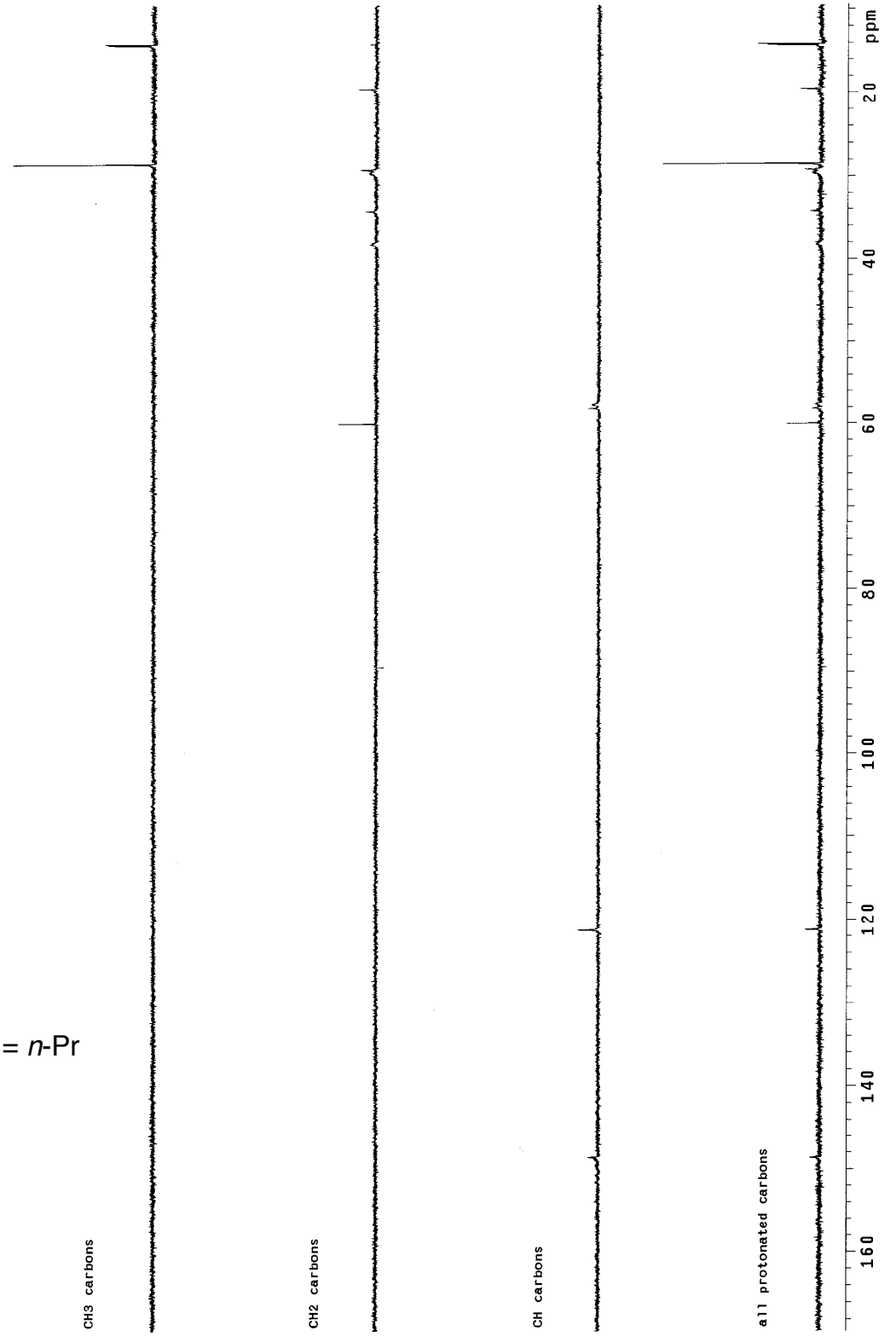


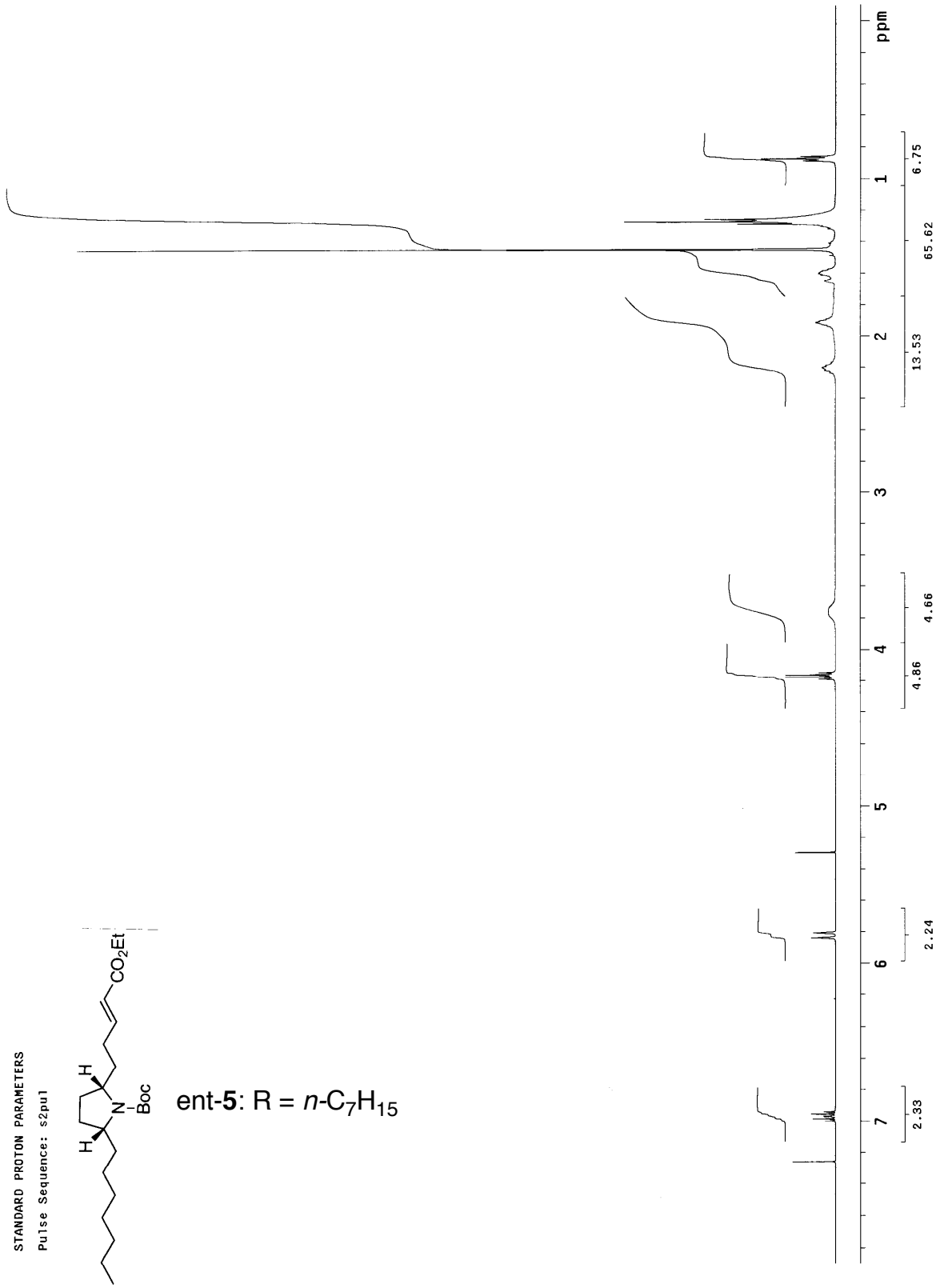
ent-5: R = *n*-Pr



ent-**5**: R = *n*-Pr

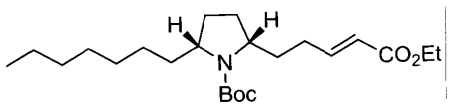

H
N
Boc
CO2Et


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
140
120
100
80
60
40
20
ppm

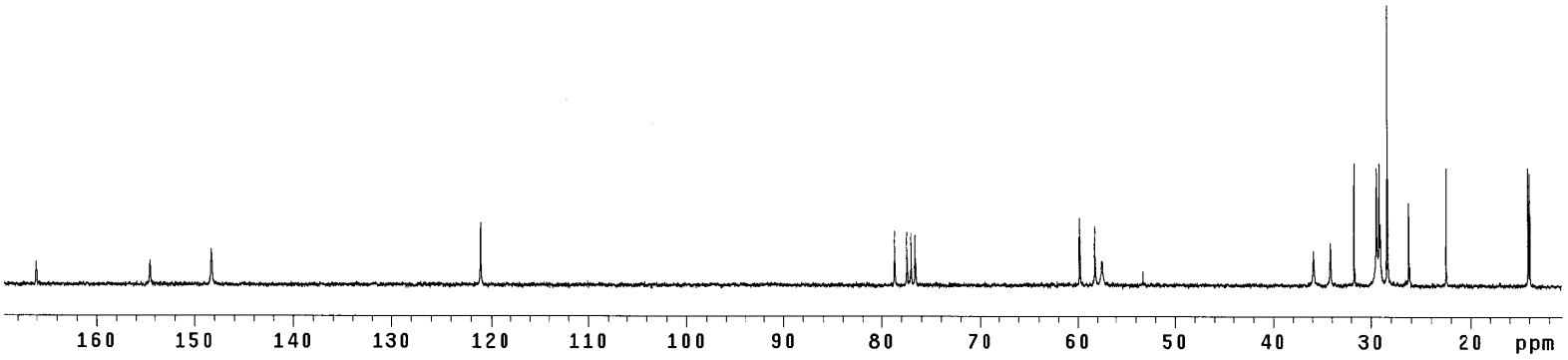


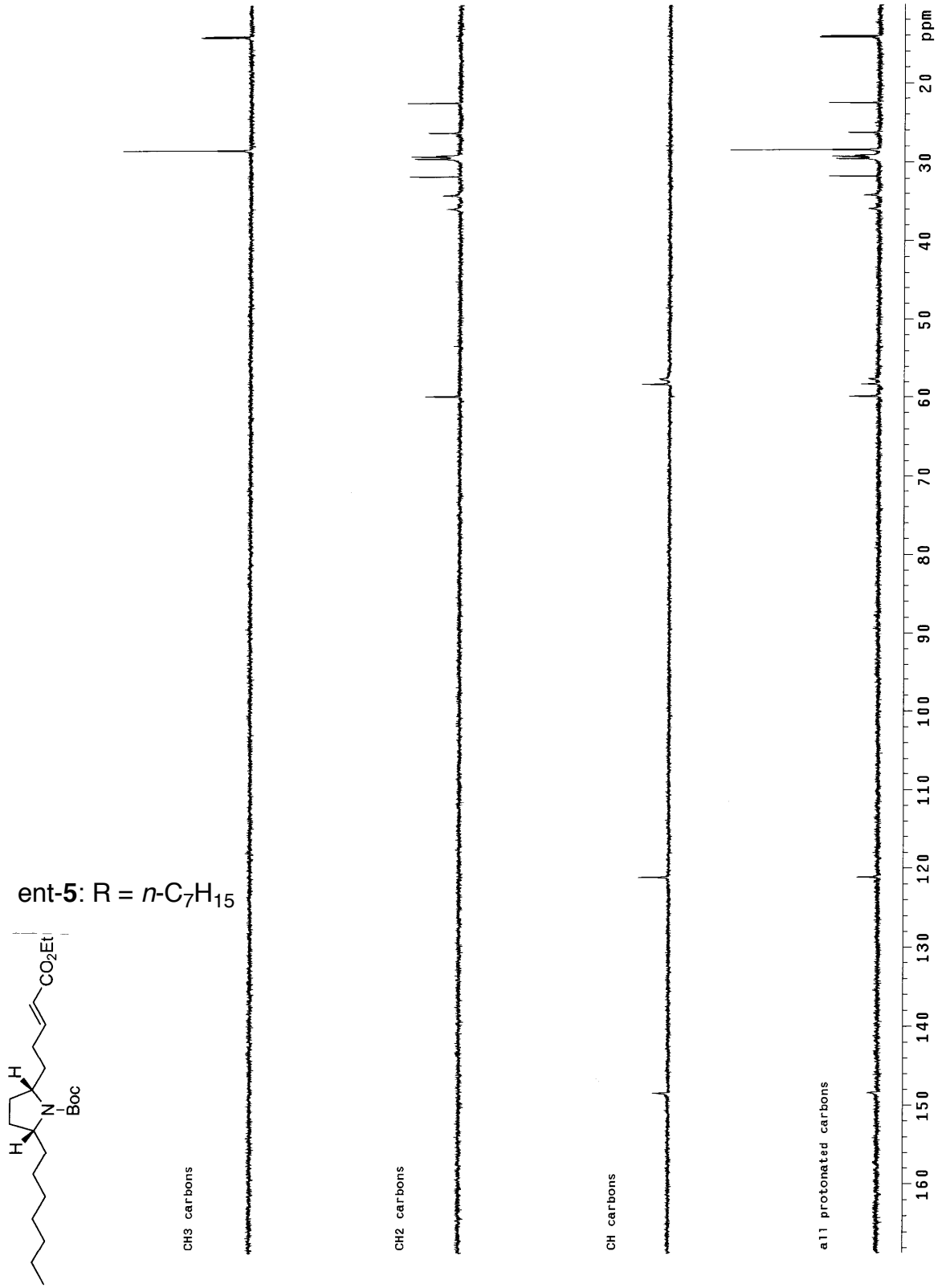
ent-**5**: R = *n*-C_7H_{15}

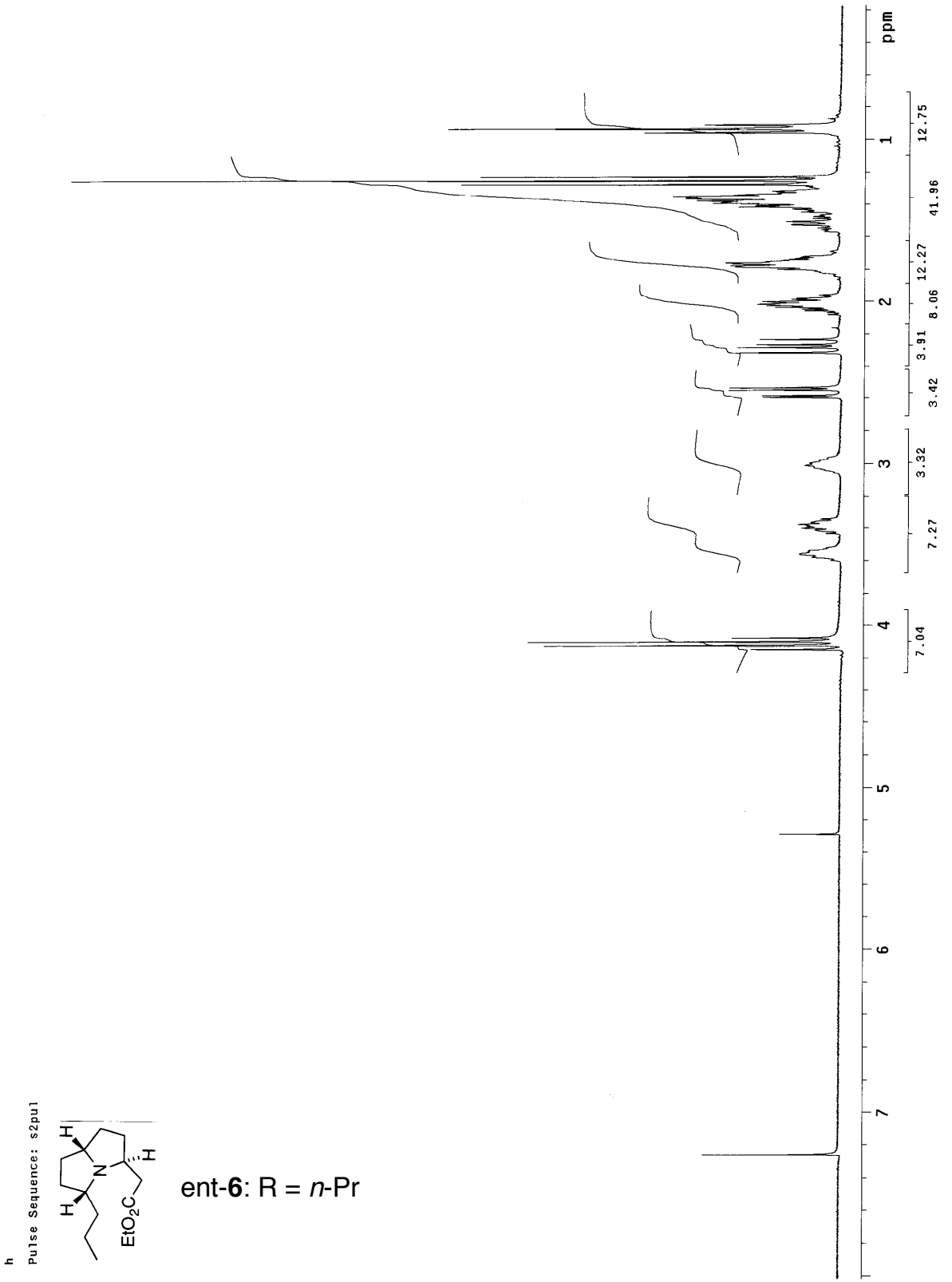
INDEX	FREQUENCY	PPM		HEIGHT
1	12528.961	166.052	S	3.6
2	11657.326	154.500	S	3.8
3	11187.327	148.271	d	5.6
4	9132.758	121.041	d	9.8
5	5936.762	78.683	S	8.6
6	5841.541	77.421	/	8.4
7	5809.801	77.000	/	8.2
8	5778.061	76.579	/	7.9
9	4512.115	59.801	t	10.7
10	4394.920	58.248	d	9.3
11	4339.985	57.520	d	3.8
12	4016.479	53.232	/	2.2
13	2705.364	35.855	t	5.4
14	2574.740	34.124	t	6.7
15	2386.741	31.633	t	19.5
16	2220.715	29.432	t	18.7
17	2199.962	29.157	t	19.4
18	2191.416	29.044	t	9.8
19	2137.702	28.332	q	45.0
20	1977.780	26.212	t	13.2
21	1695.781	22.475	t	18.7
22	1064.639	14.110	q	18.7
23	1052.431	13.948	q	17.9



ent-**5**: R = *n*-C_7H_{15}



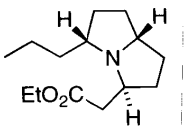

ent-5: R = n-C7H15
CO2Et
H
N
Boc
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


h
Pulse Sequence: s2pul
ppm
1
2
3
4
5
6
7
12.75
41.96
12.27
8.06
3.91
3.42
3.32
7.27
7.04

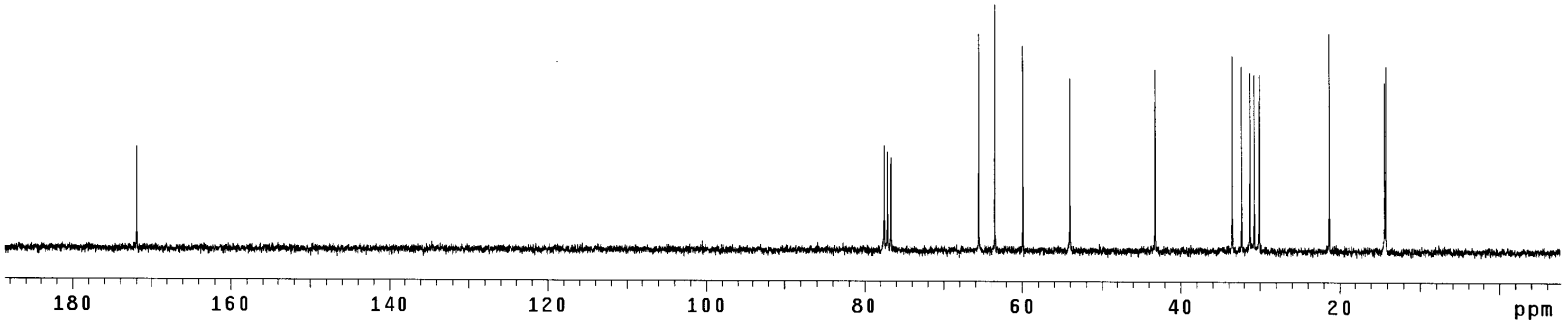
H
N
H
H
EtO2C

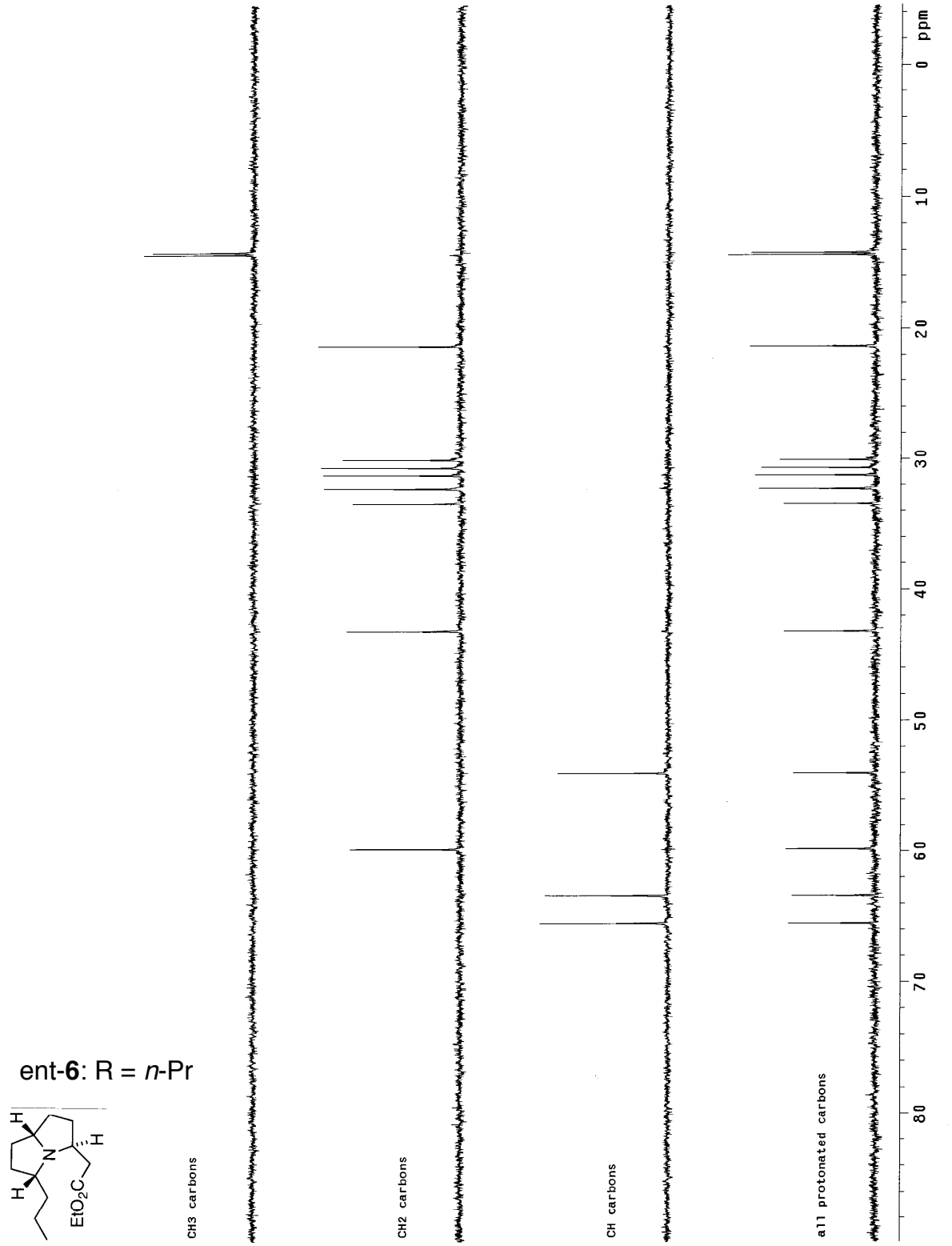
ent-**6**: R = *n*-Pr

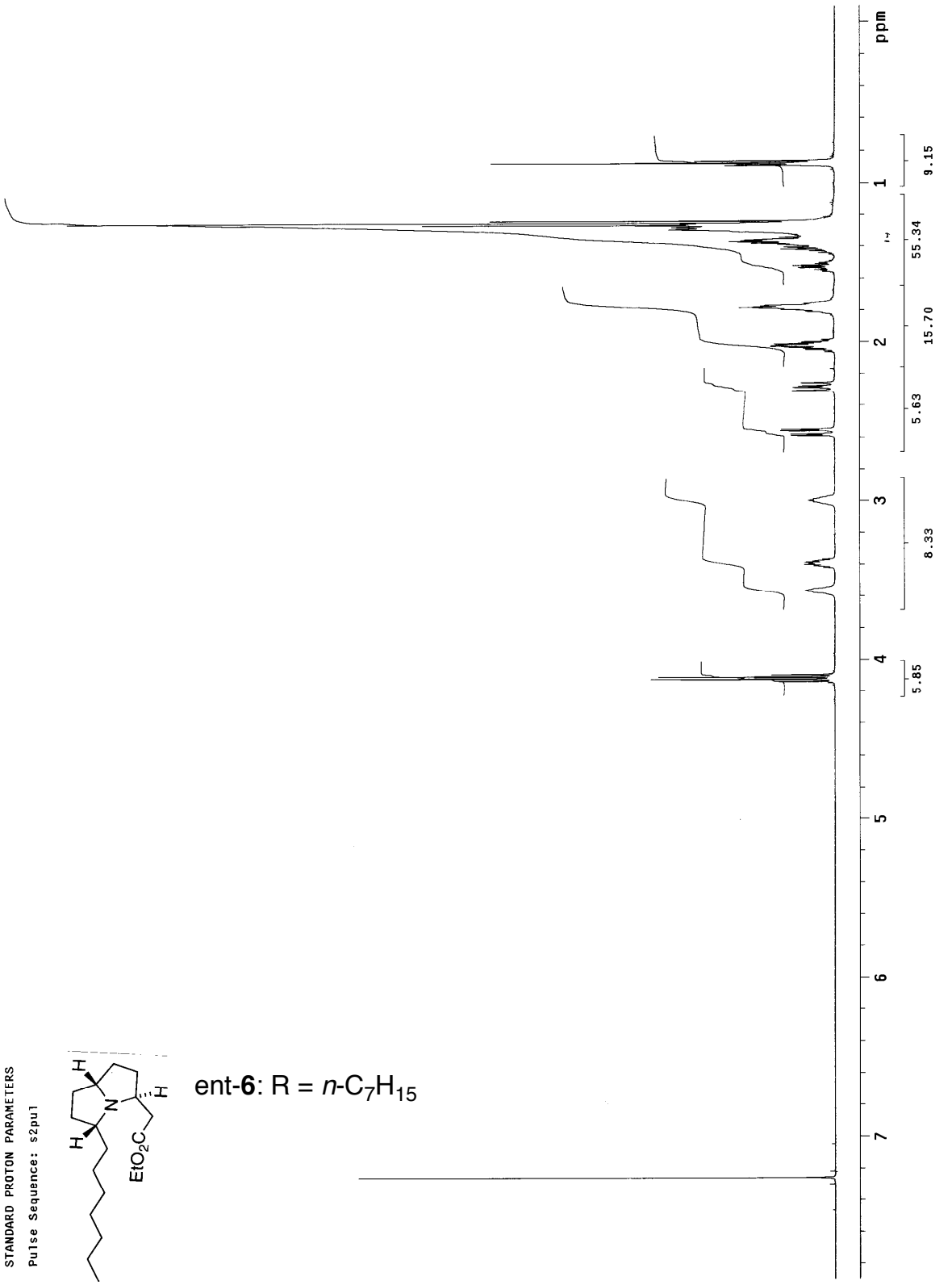
INDEX	FREQUENCY	PPM	HEIGHT
1	12972.103	171.925	16.5
2	5841.541	77.421	16.9
3	5809.801	77.000	15.9
4	5776.840	76.563	14.9
5	4943.049	65.513	35.0
6	4783.127	63.393	39.7
7	4518.218	59.882	33.0
8	4076.297	54.025	27.9
9	3255.934	43.152	29.3
10	2521.026	33.412	31.5
11	2434.351	32.264	29.8
12	2357.442	31.244	28.8
13	2314.715	30.678	28.4
14	2267.104	30.047	28.4
15	1606.664	21.294	35.1
16	1078.067	14.288	27.3
17	1067.080	14.143	29.9



ent-**6**: R = *n*-Pr

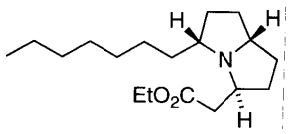



ent-6: R = n-Pr
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
0
10
20
30
40
50
60
70
80

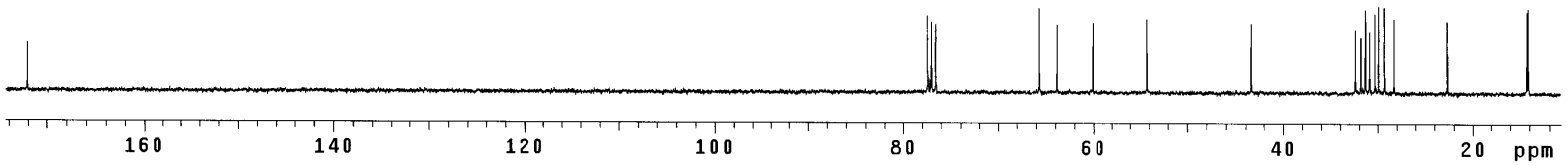


ent-**6**: R = *n*-C_7H_{15}

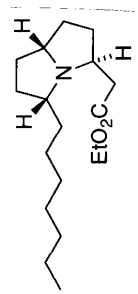
INDEX	FREQUENCY	PPM	HEIGHT
1	12985.532	172.103	7.9
2	5841.541	77.421	12.5
3	5824.450	77.194	2.3
4	5809.801	77.000	11.6
5	5776.840	76.563	11.2
6	4954.036	65.658	13.8
7	4814.867	63.814	11.1
8	4530.426	60.044	11.4
9	4087.283	54.171	12.0
10	3265.700	43.282	11.3
11	2444.117	32.393	10.4
12	2400.169	31.811	9.1
13	2365.987	31.358	13.6
14	2362.325	31.309	11.7
15	2324.480	30.807	10.1
16	2280.532	30.225	12.9
17	2253.675	29.869	14.2
18	2208.507	29.270	14.1
19	2135.260	28.300	12.1
20	1710.429	22.669	11.8
21	1076.846	14.272	13.3
22	1065.859	14.126	13.8

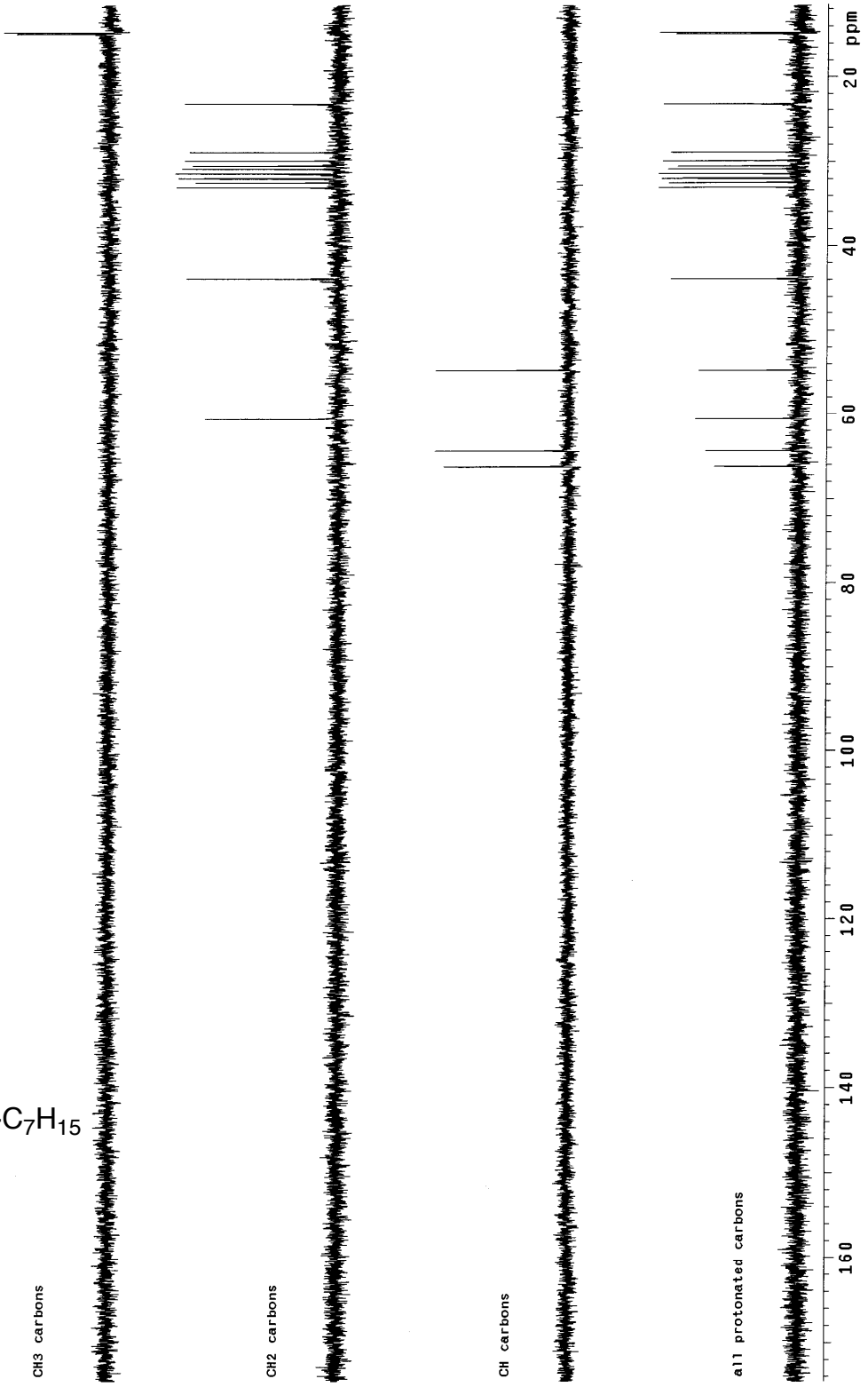


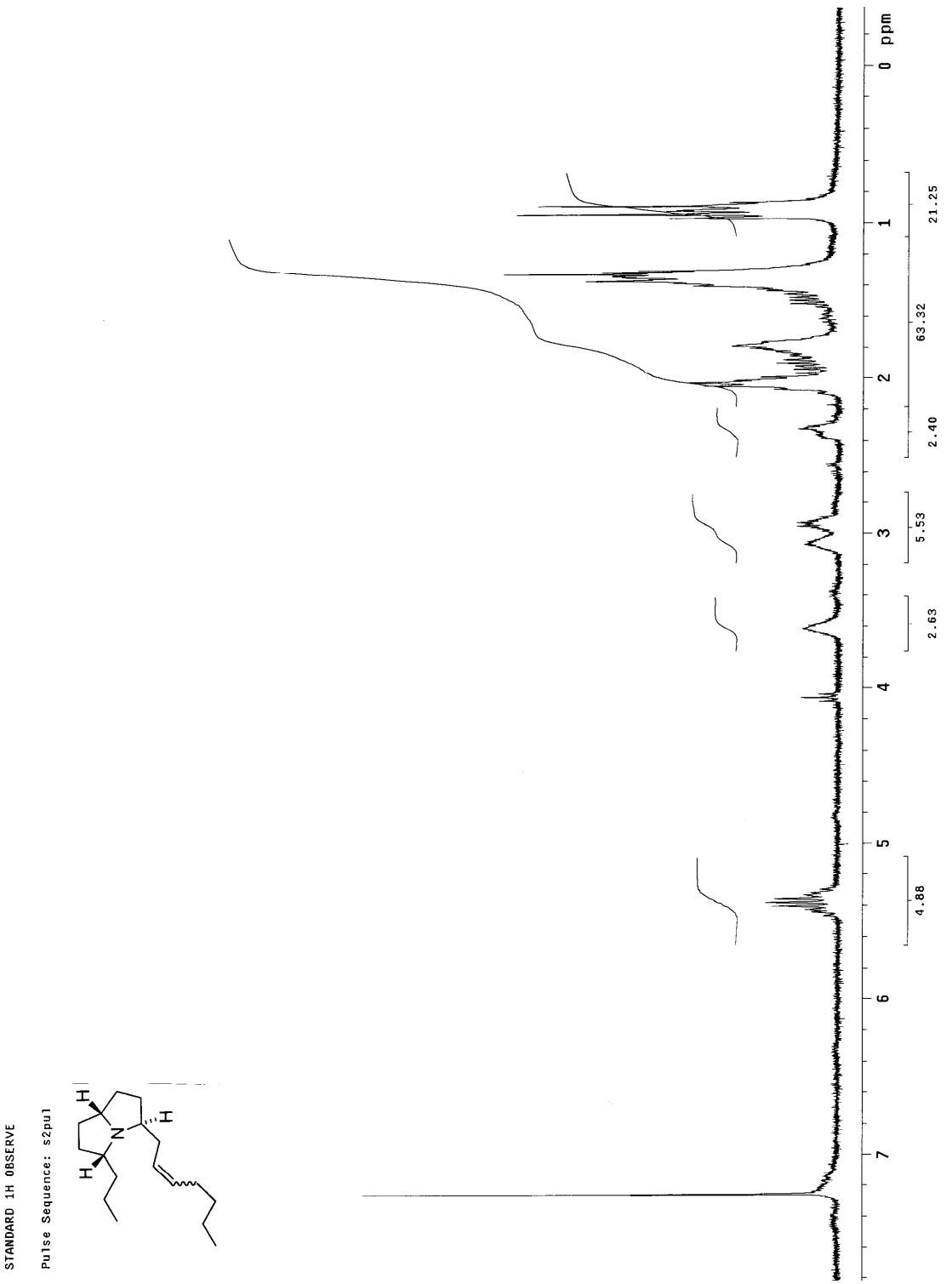
ent-**6**: R = *n*-C_7H_{15}

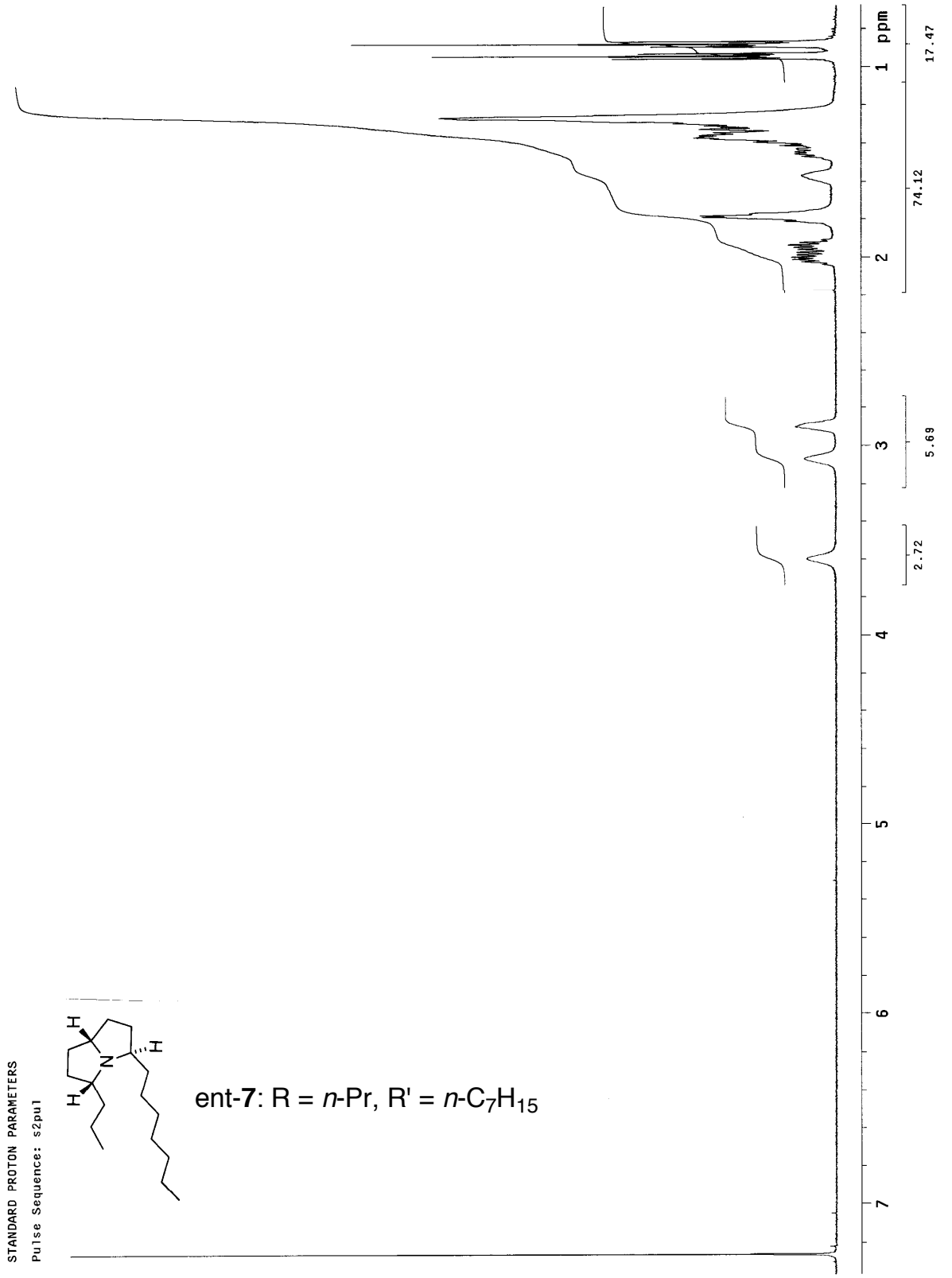


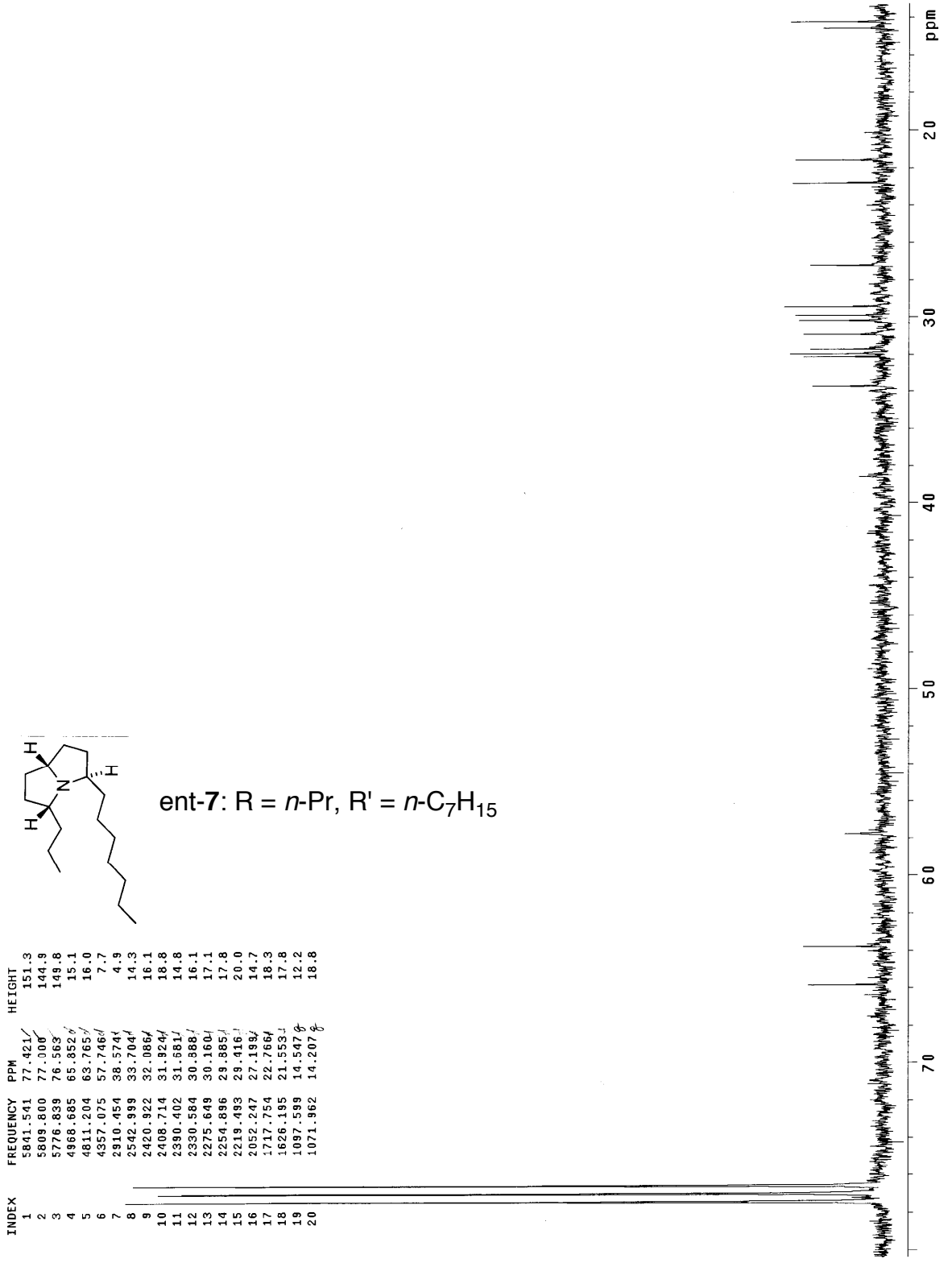
ent-**6**: R = *n*-C_7H_{15}



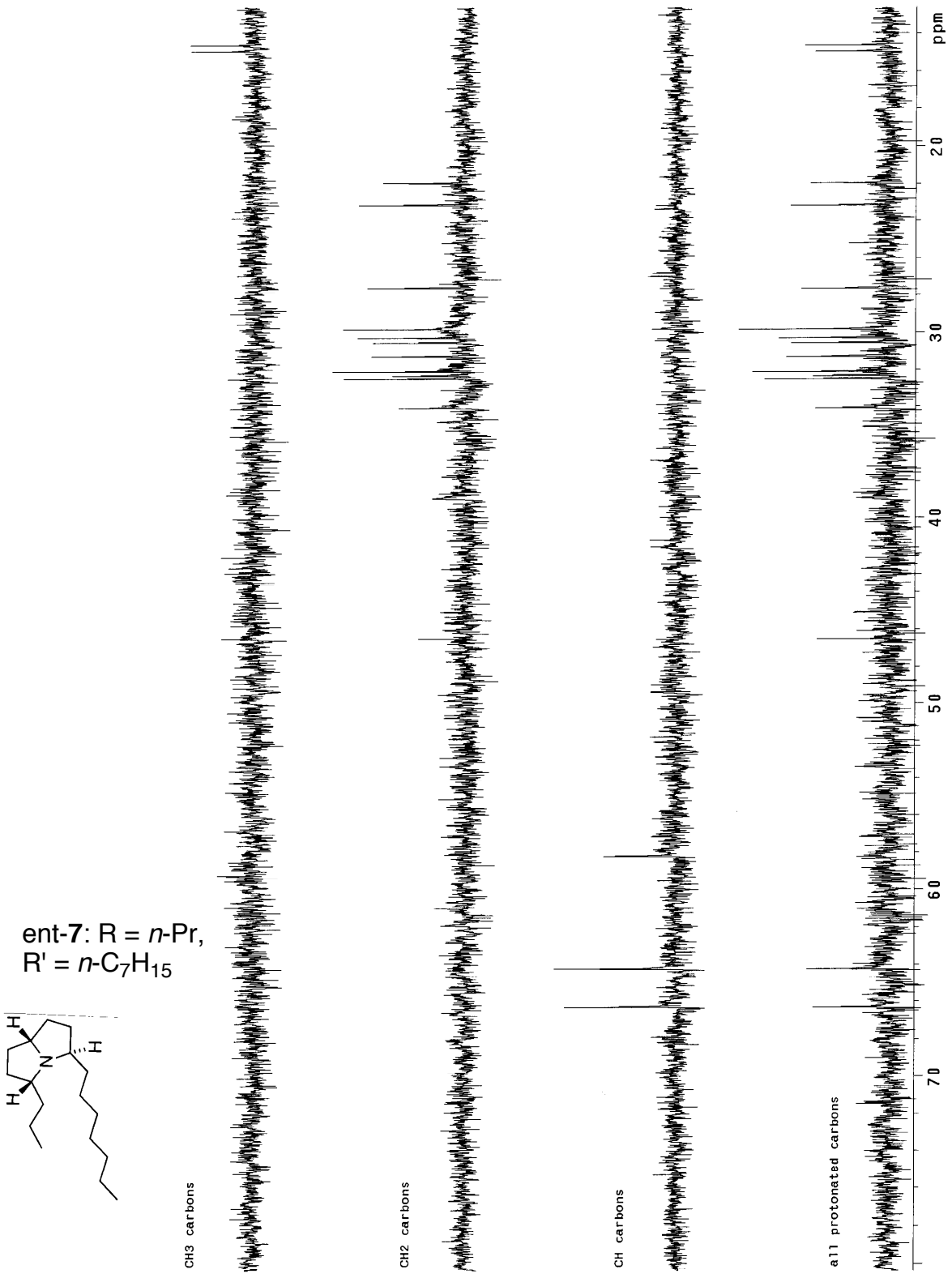


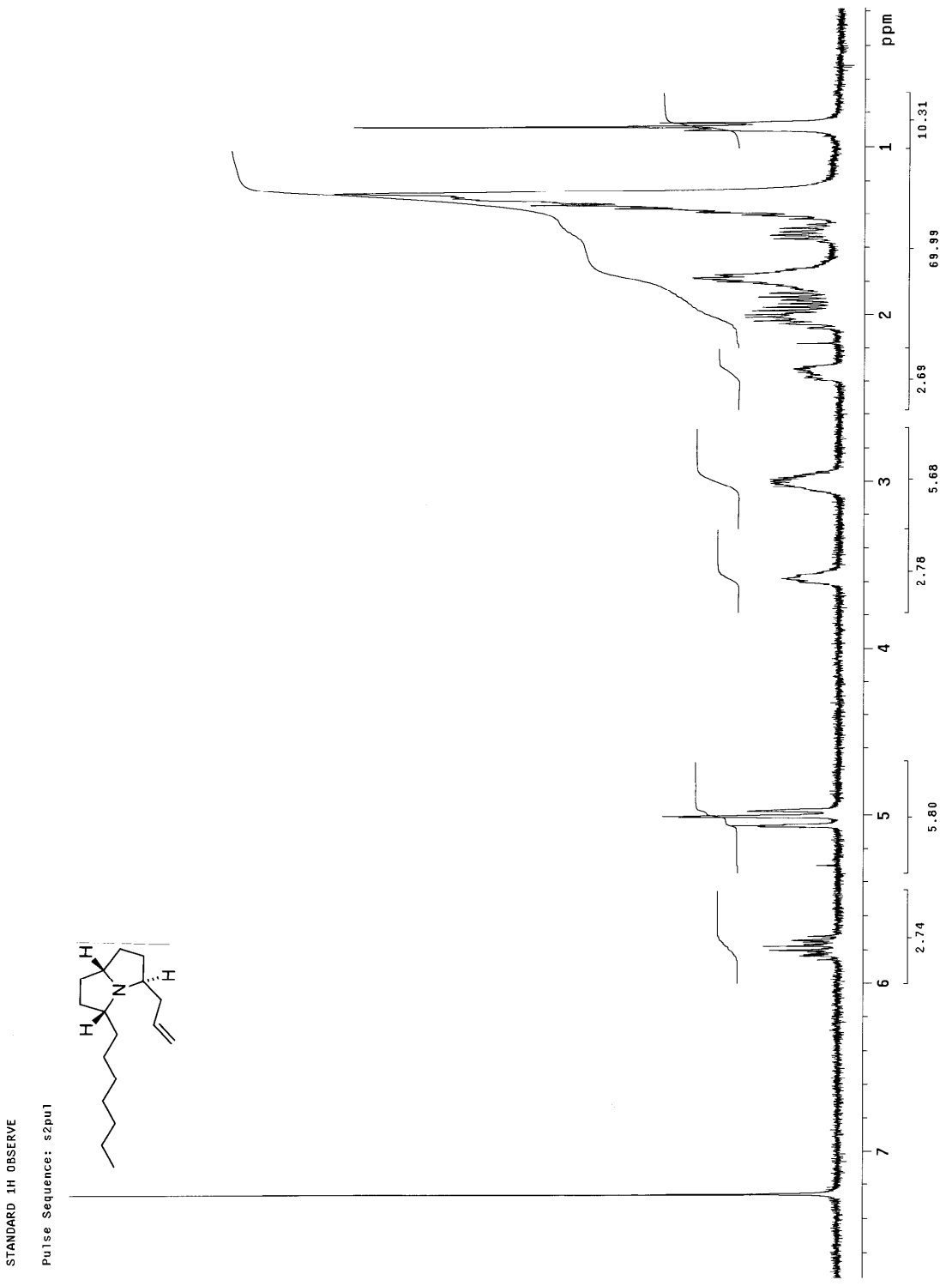

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
H
N
H
H
7
6
5
4
3
2
1
0 ppm
4.88
2.63
5.53
2.40
63.32
21.25


STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
ent-7: R = n-Pr, R' = n-C7H15
1 ppm
17.47
74.12
5.69
2.72

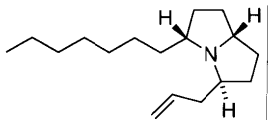


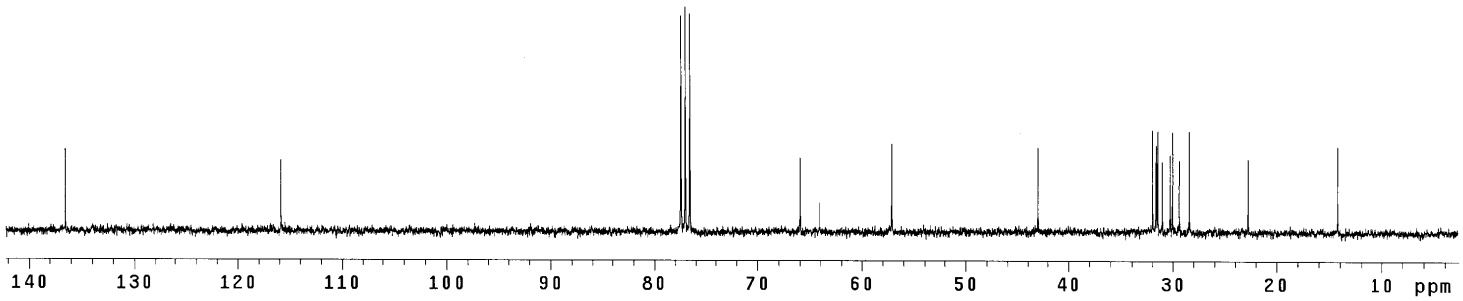
ent-**7**: R = *n*-Pr, R' = *n*-C_7H_{15}

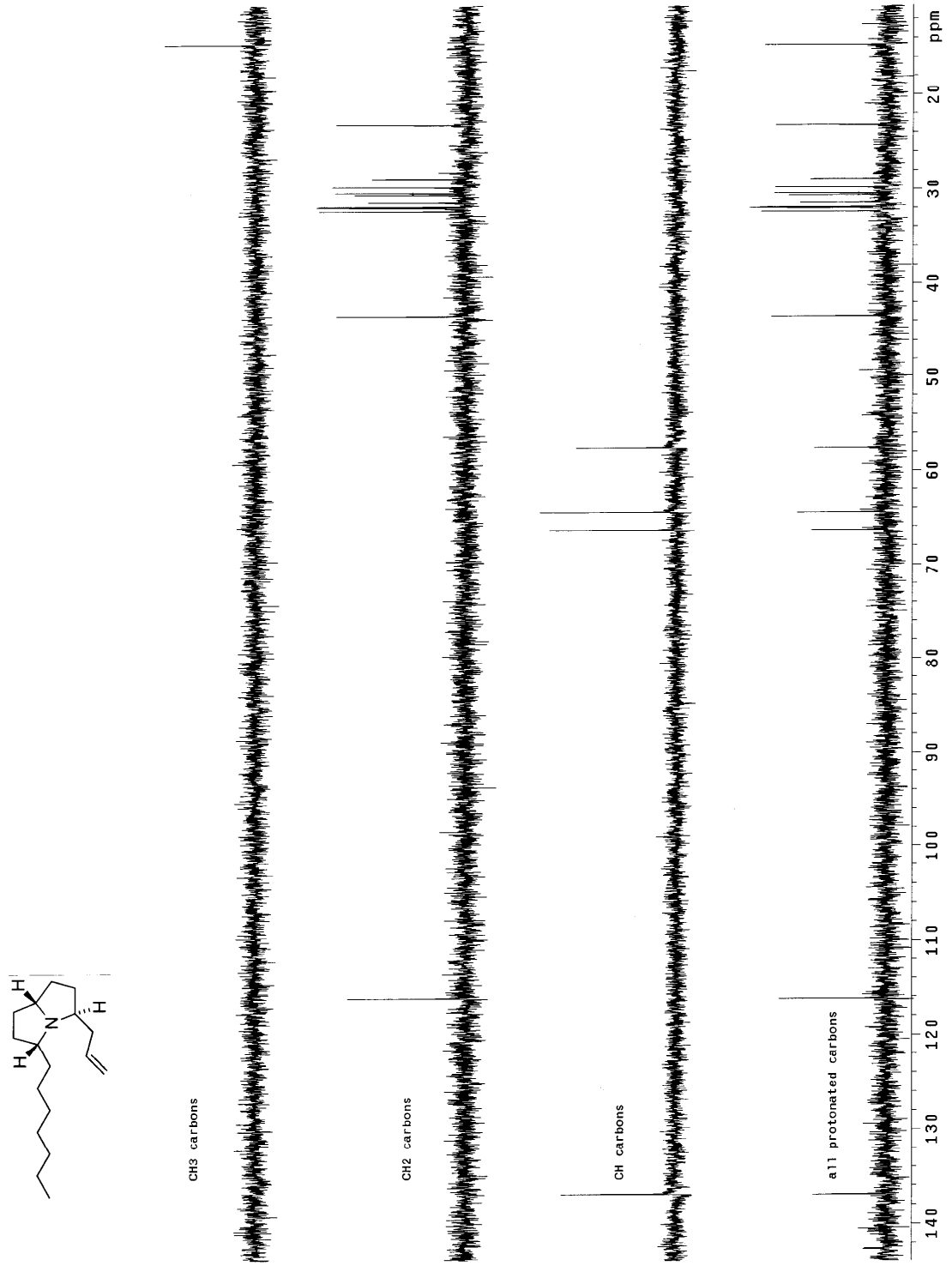

ent-7: R = n-Pr,
R' = n-C7H15
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
20
30
40
50
60
70

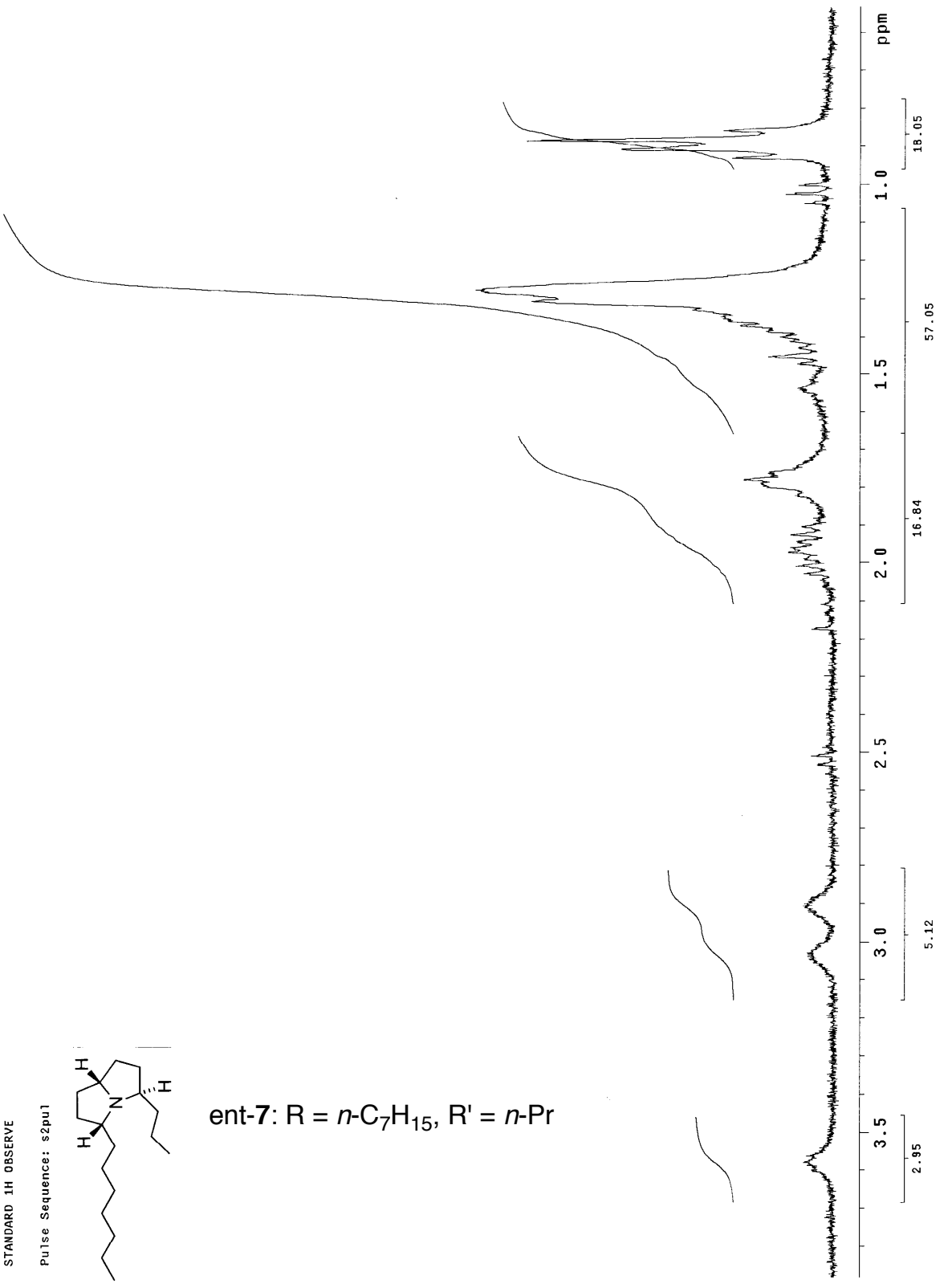

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
ppm
1
2
3
4
5
6
7
10.31
69.99
2.69
5.68
2.78
5.80
2.74

INDEX	FREQUENCY	PPM	HEIGHT
1	10302.262	136.541	14.0
2	8737.225	115.799	12.2
3	5841.541	77.421	37.3
4	5809.800	77.000	38.8
5	5778.060	76.579	37.6
6	4977.230	65.966	12.7
7	4831.958	64.040	17.0
8	4310.686	57.132	15.2
9	3246.167	43.023	14.6
10	2406.272	31.891	17.5
11	2380.636	31.552	14.9
12	2369.649	31.406	17.4
13	2335.467	30.953	12.1
14	2279.312	30.209	13.3
15	2262.221	29.982	17.2
16	2214.610	29.351	12.4
17	2143.805	28.413	17.4
18	1716.533	22.750	12.5
19	1071.962	14.207	14.7

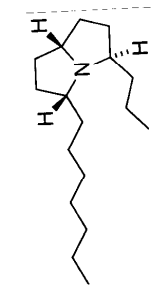





CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
140
130
120
110
100
90
80
70
60
50
40
30
20



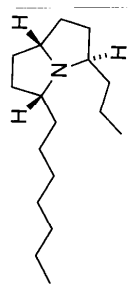
ent-**7**: R = *n*-C_7H_{15}, R' = *n*-Pr

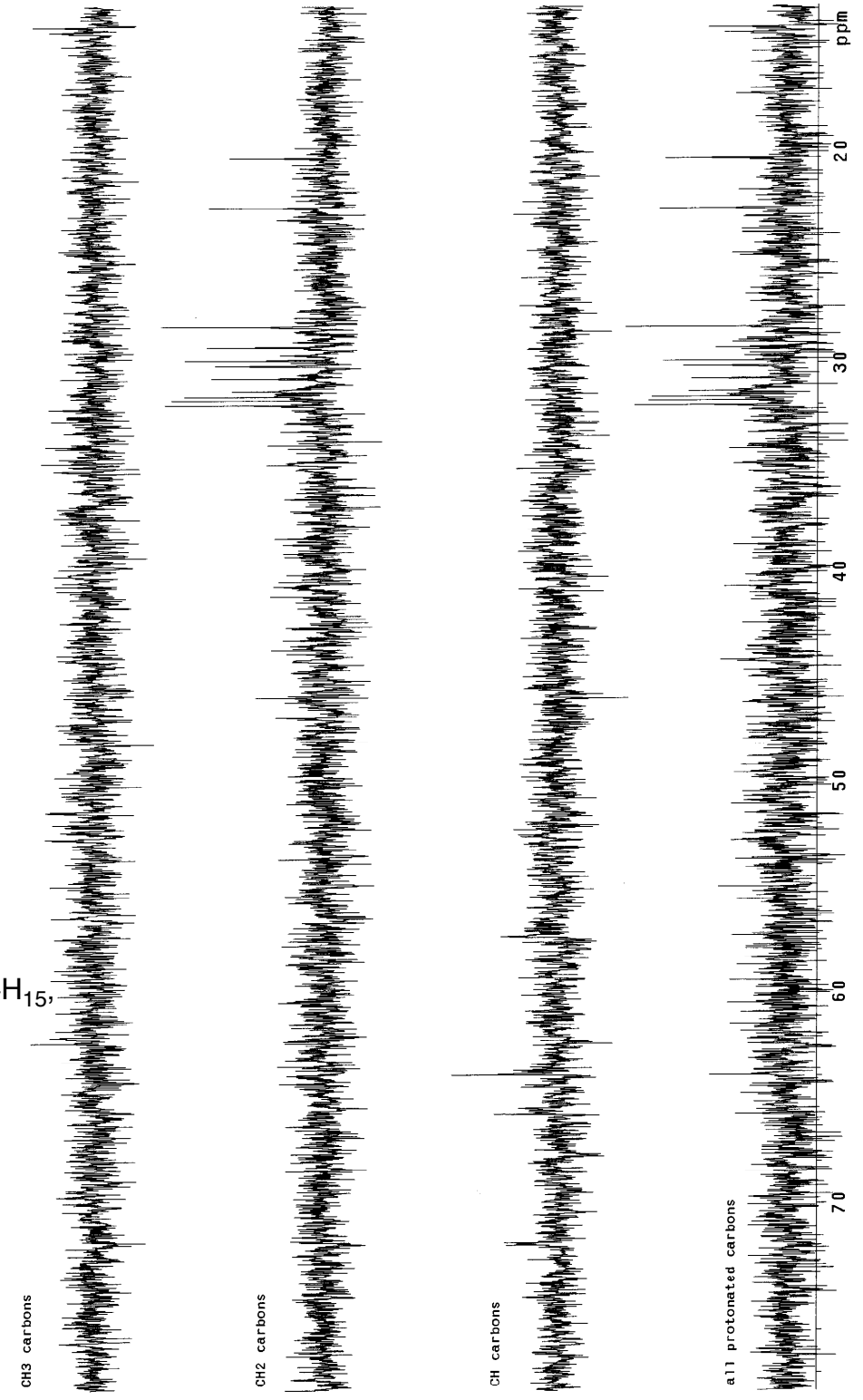


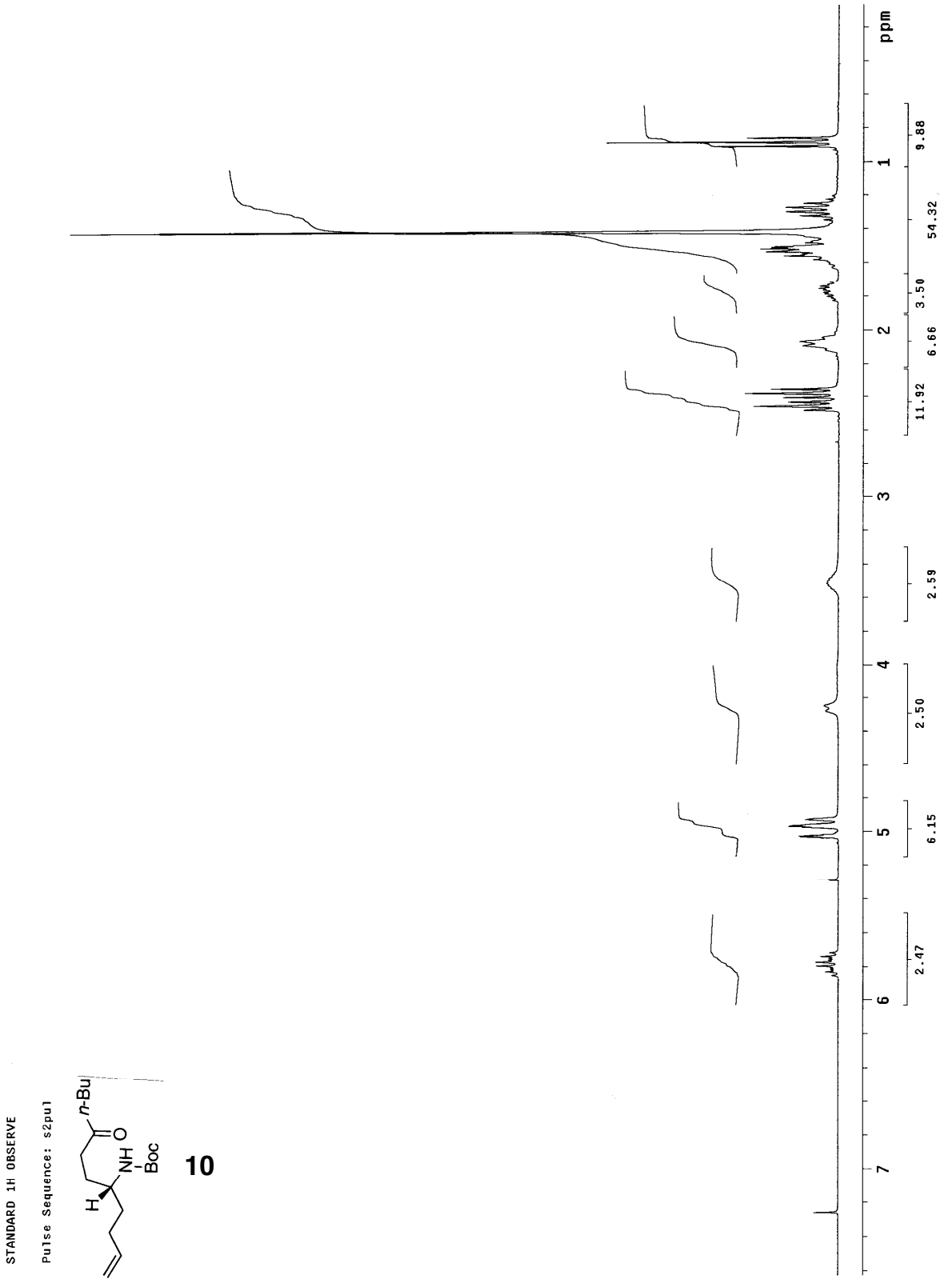
ent-**7**: R = *n*-C_7H_{15}, R' = *n*-Pr

INDEX	FREQUENCY	PPM	HEIGHT
1	5842.761	77.437	418.8
2	5825.670	77.210	23.3
3	5809.800	77.000	414.2
4	5778.060	76.579	437.3
5	4969.905	65.868	15.4
6	4831.957	64.040	19.7
7	2661.415	35.273	8.0
8	2425.805	32.150	22.7
9	2394.065	31.730	15.4
10	2330.584	30.888	9.4
11	2284.195	30.273	14.0
12	2263.441	29.998	21.1
13	2215.831	29.367	21.0
14	2143.805	28.413	17.3
15	1717.754	22.766	22.1
16	1540.741	20.420	13.7
17	1092.716	14.482	18.8
18	1073.183	14.223	19.0

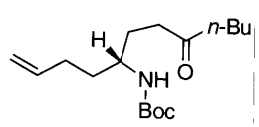
ent-**7**: R = *n*-C_7H_{15}, R' = *n*-Pr



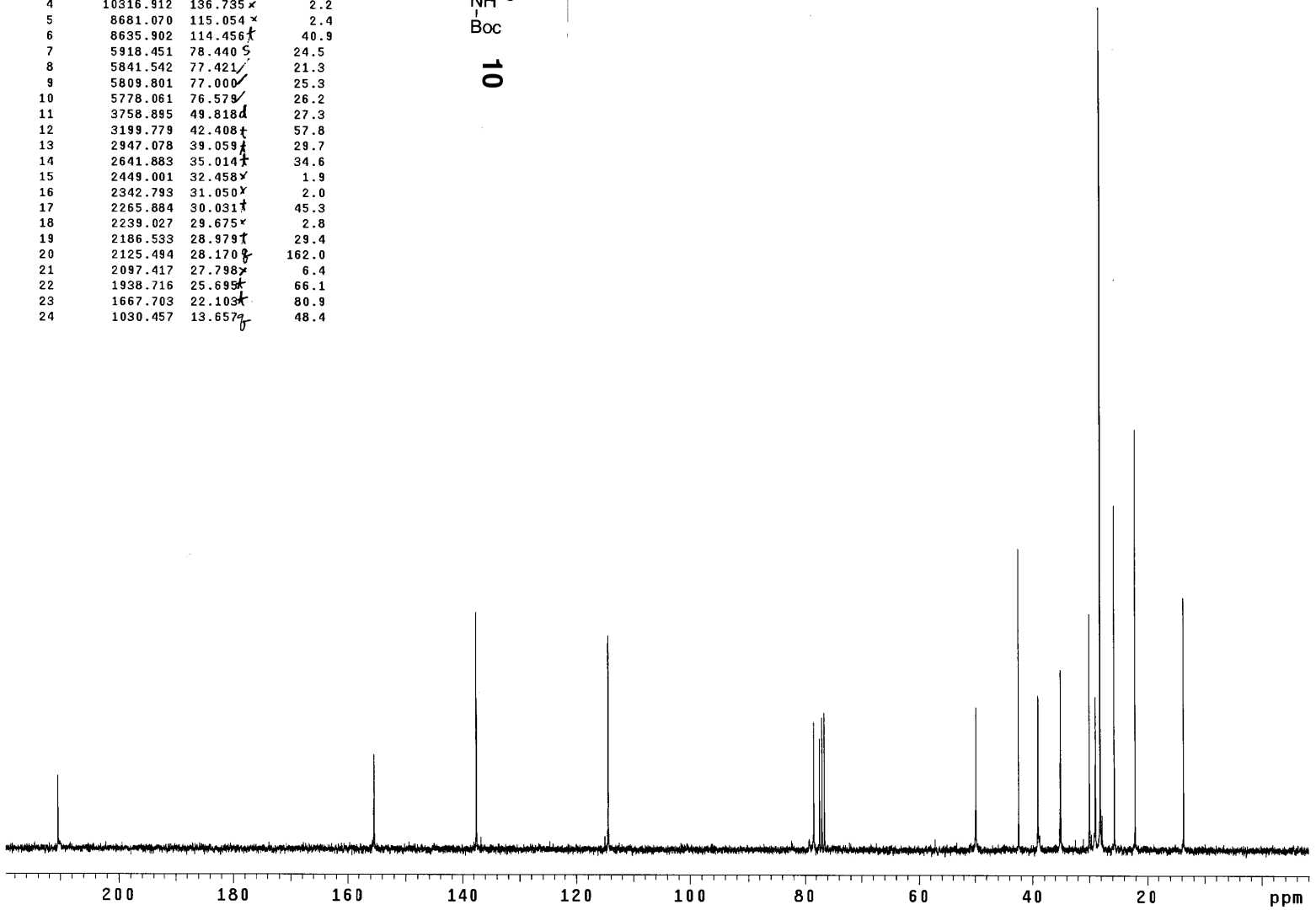


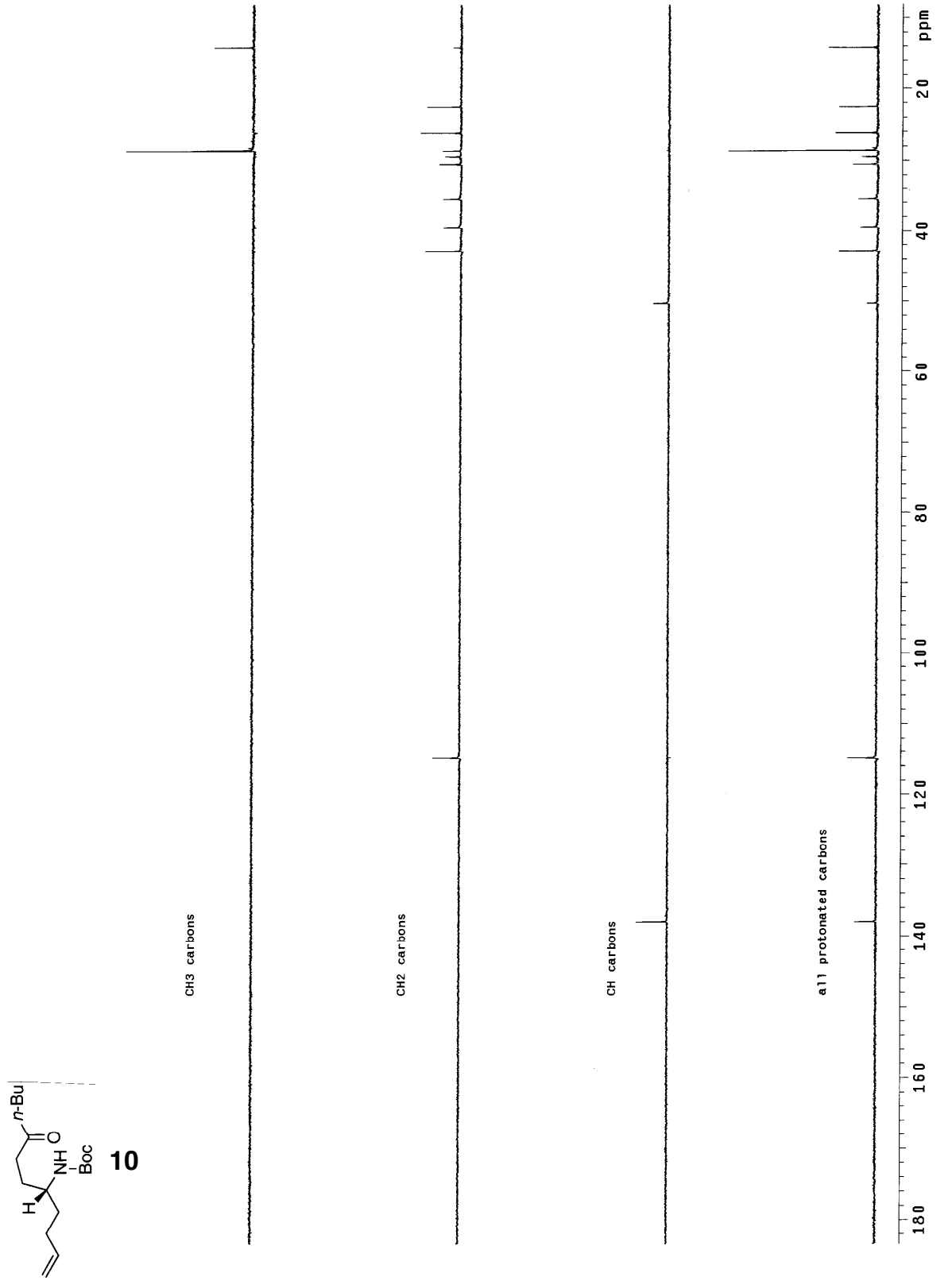

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
n-Bu
NH
O
Boc
H
10
ppm
1
2
3
4
5
6
7
9.88
54.32
3.50
6.66
11.92
2.59
2.50
6.15
2.47

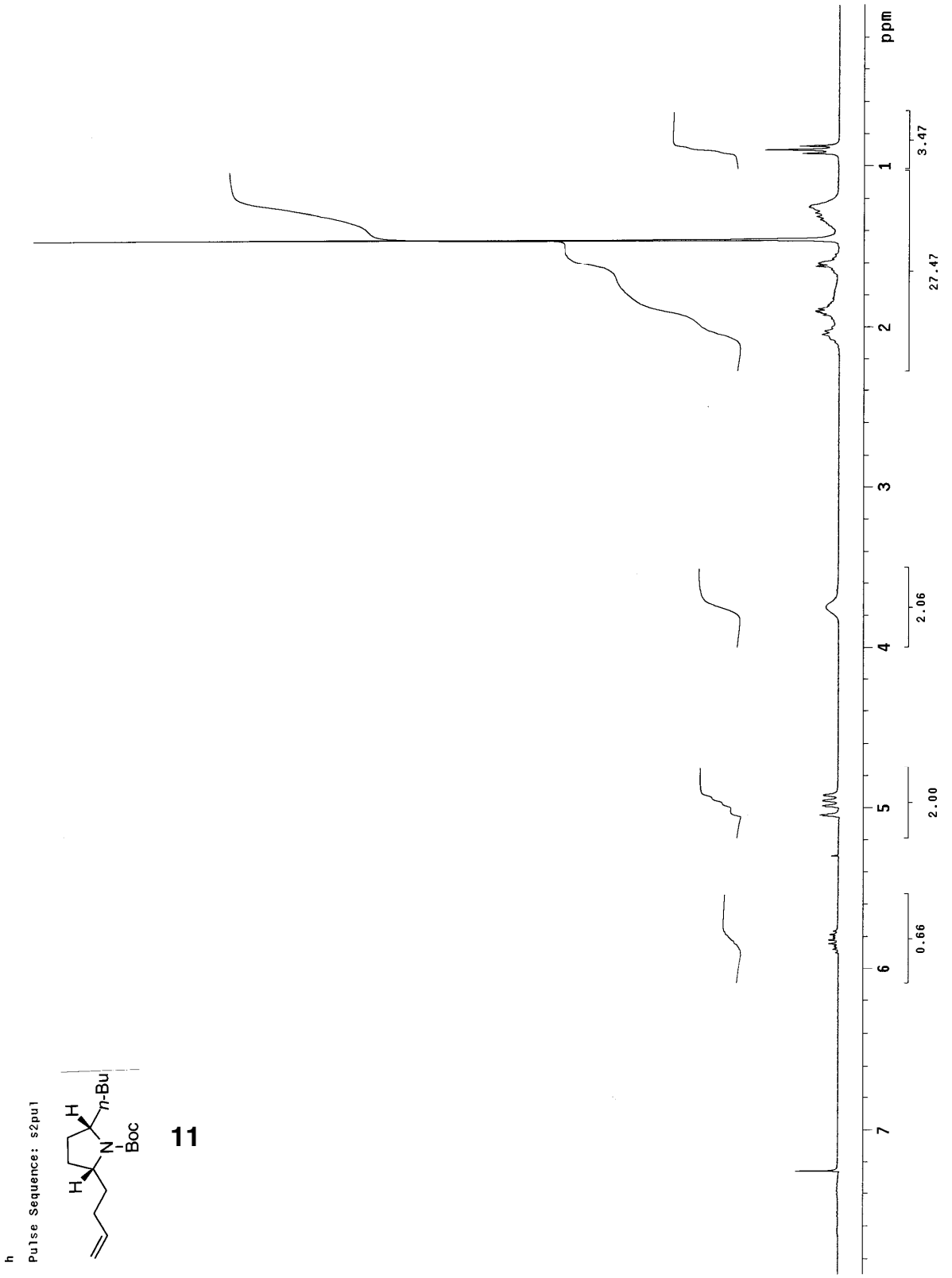
INDEX	FREQUENCY	PPM	HEIGHT
1	15872.671	210.368	13.9
2	11722.027	155.357	18.0
3	10379.172	137.560	45.4
4	10316.912	136.735	2.2
5	8681.070	115.054	2.4
6	8635.902	114.456	40.9
7	5918.451	78.440	24.5
8	5841.542	77.421	21.3
9	5809.801	77.000	25.3
10	5778.061	76.579	26.2
11	3758.885	49.818	27.3
12	3199.779	42.408	57.8
13	2947.078	39.059	29.7
14	2641.883	35.014	34.6
15	2449.001	32.458	1.9
16	2342.793	31.050	2.0
17	2265.884	30.031	45.3
18	2239.027	29.675	2.8
19	2186.533	28.979	29.4
20	2125.494	28.170	162.0
21	2097.417	27.798	6.4
22	1938.716	25.695	66.1
23	1667.703	22.103	80.9
24	1030.457	13.657	48.4



10

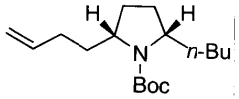



n-Bu
O
NH
Boc
H
10
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
180
160
140
120
100
80
60
40
20

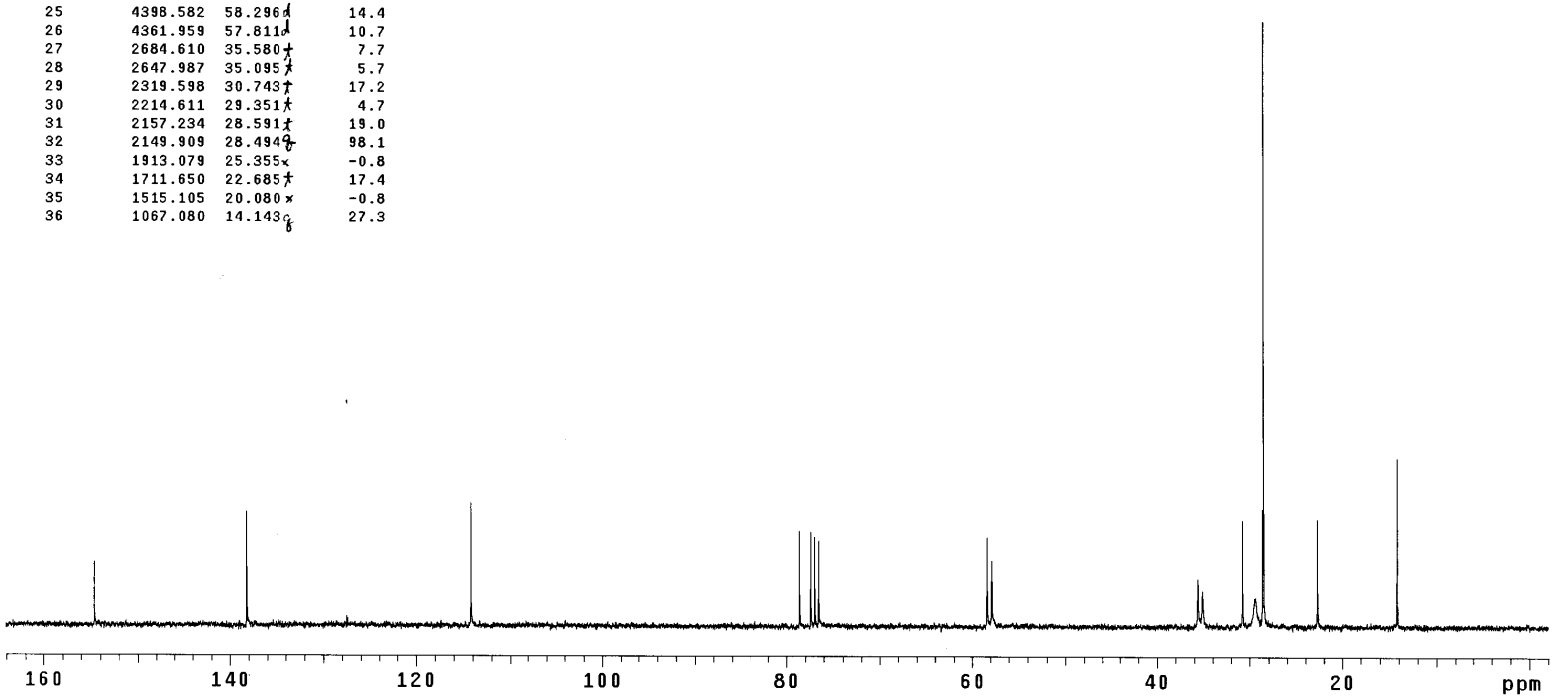

h
Pulse Sequence: s2pul
H
n-Bu
N
Boc
H
ppm
1
2
3
4
5
6
7
3.47
27.47
2.06
2.00
0.66

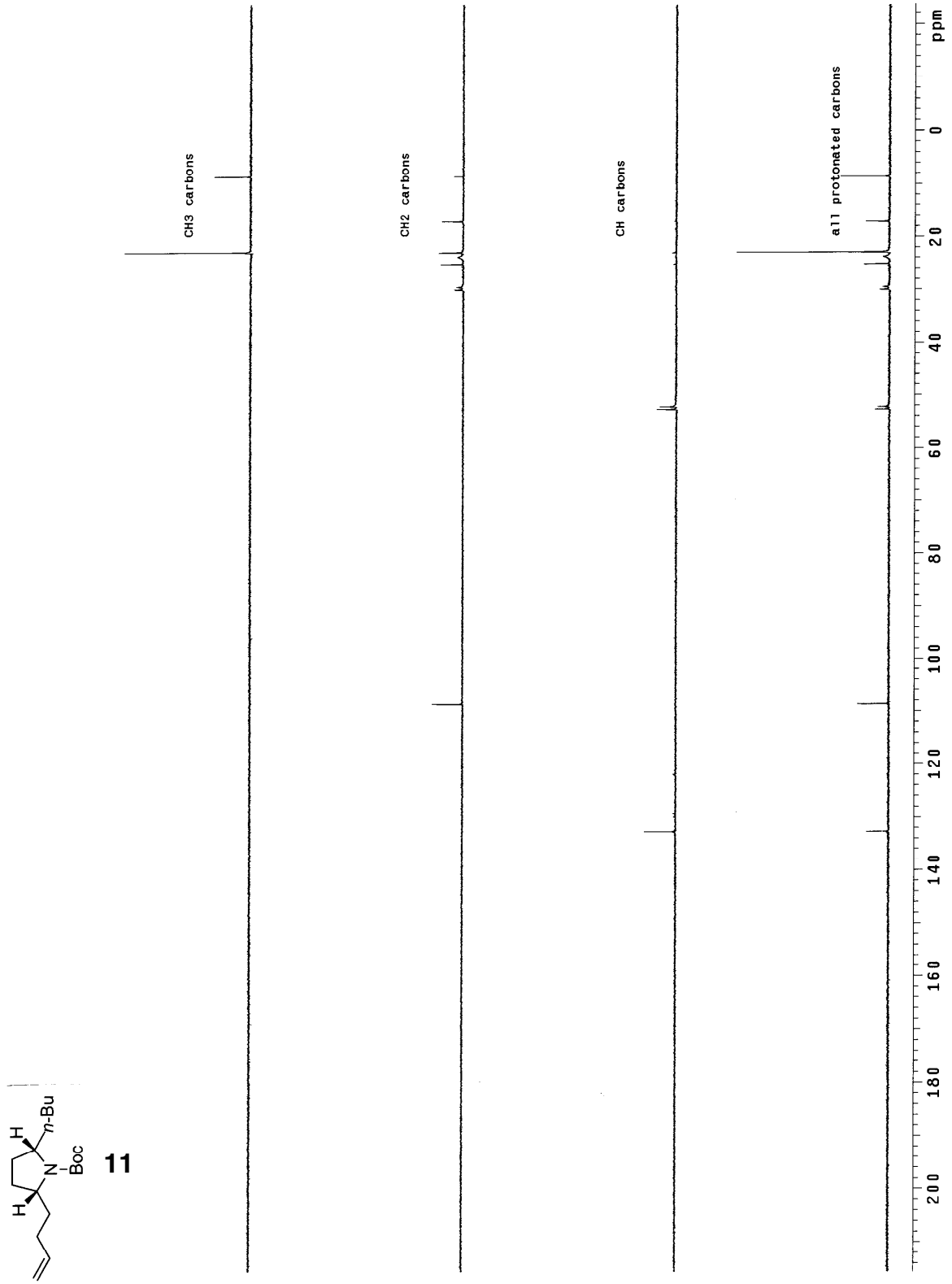
11

INDEX	FREQUENCY	PPM	HEIGHT
1	12317.766	163.253	-0.7
2	11667.092	154.629	10.2
3	11000.547	145.795	-0.7
4	10495.145	139.097	-0.8
5	10475.613	138.838	-0.8
6	10429.223	138.223	18.4
7	10258.315	135.958	-0.8
8	10170.419	134.793	0.8
9	9623.510	127.545	1.4
10	9614.965	127.432	1.1
11	8853.199	117.336	0.8
12	8707.927	115.410	-0.8
13	8616.369	114.197	19.9
14	7964.473	105.557	-0.8
15	7843.616	103.955	0.7
16	7589.695	100.590	-0.7
17	6534.943	86.611	-0.7
18	5931.879	78.618	15.4
19	5841.541	77.421	15.2
20	5809.801	77.000	14.4
21	5776.840	76.563	13.8
22	5035.828	66.742	-0.7
23	4779.465	63.344	-1.0
24	4496.244	59.591	-0.8
25	4398.582	58.296	14.4
26	4361.959	57.811	10.7
27	2684.610	35.580	7.7
28	2647.987	35.095	5.7
29	2319.598	30.743	17.2
30	2214.611	29.351	4.7
31	2157.234	28.591	19.0
32	2149.909	28.494	98.1
33	1913.079	25.355	-0.8
34	1711.650	22.685	17.4
35	1515.105	20.080	-0.8
36	1067.080	14.143	27.3

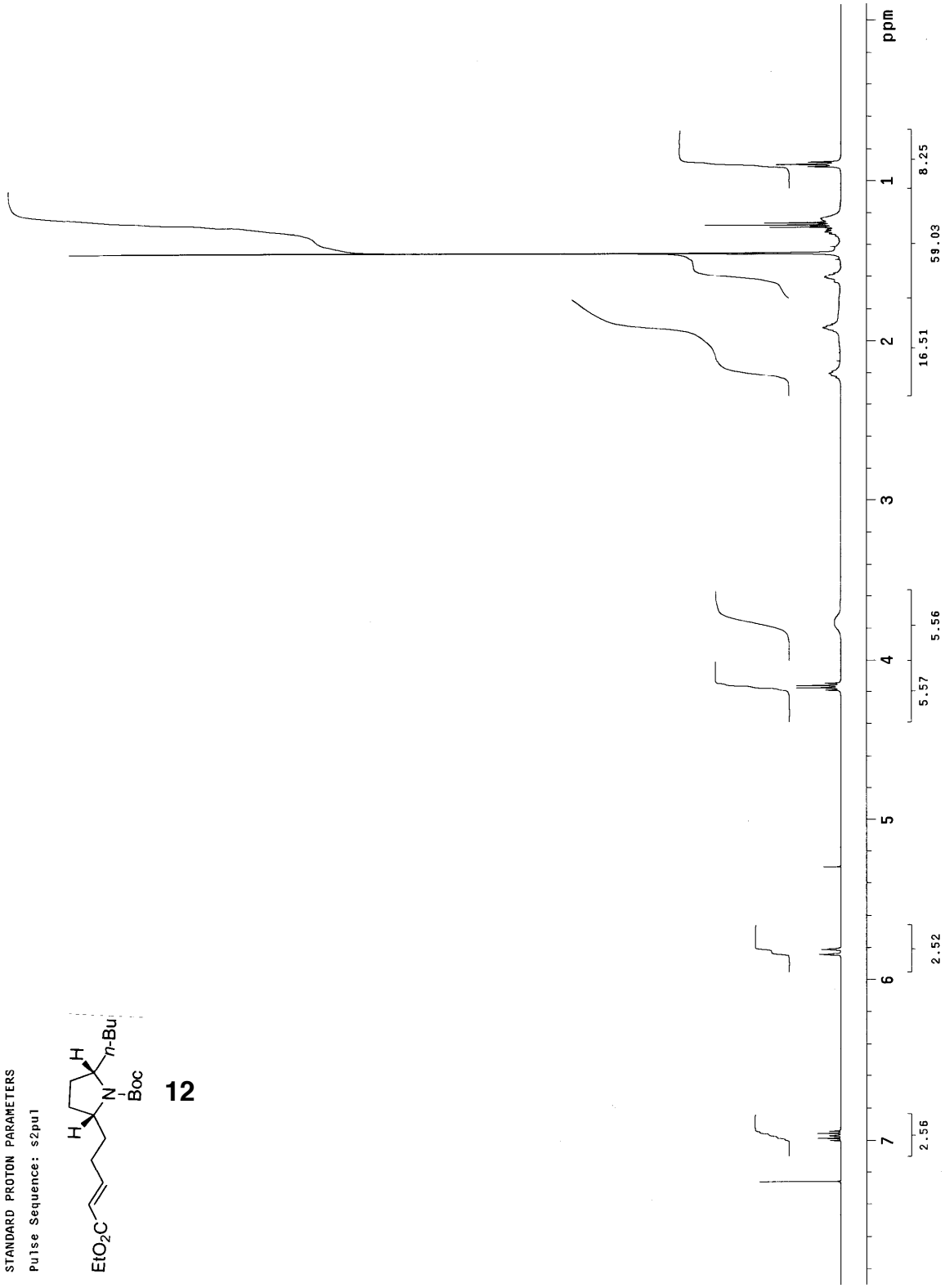


11

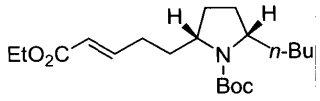



CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
200
180
160
140
120
100
80
60
40
20
0
H
n-Bu
N
Boc
H

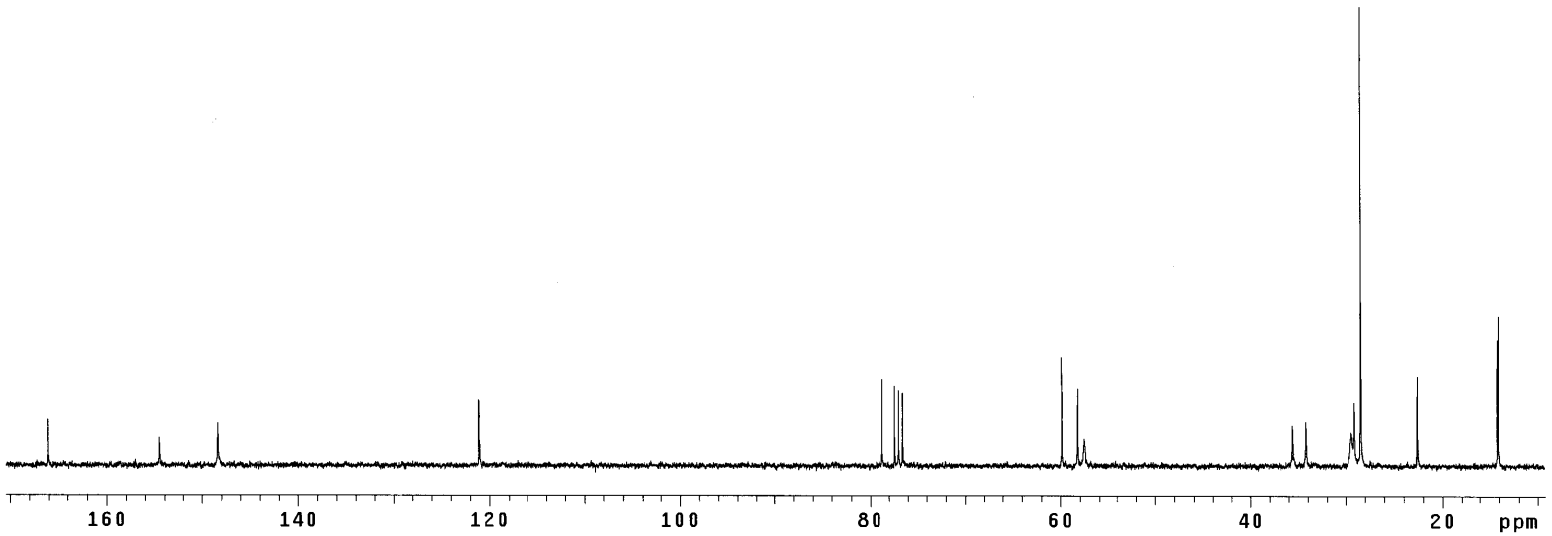
11

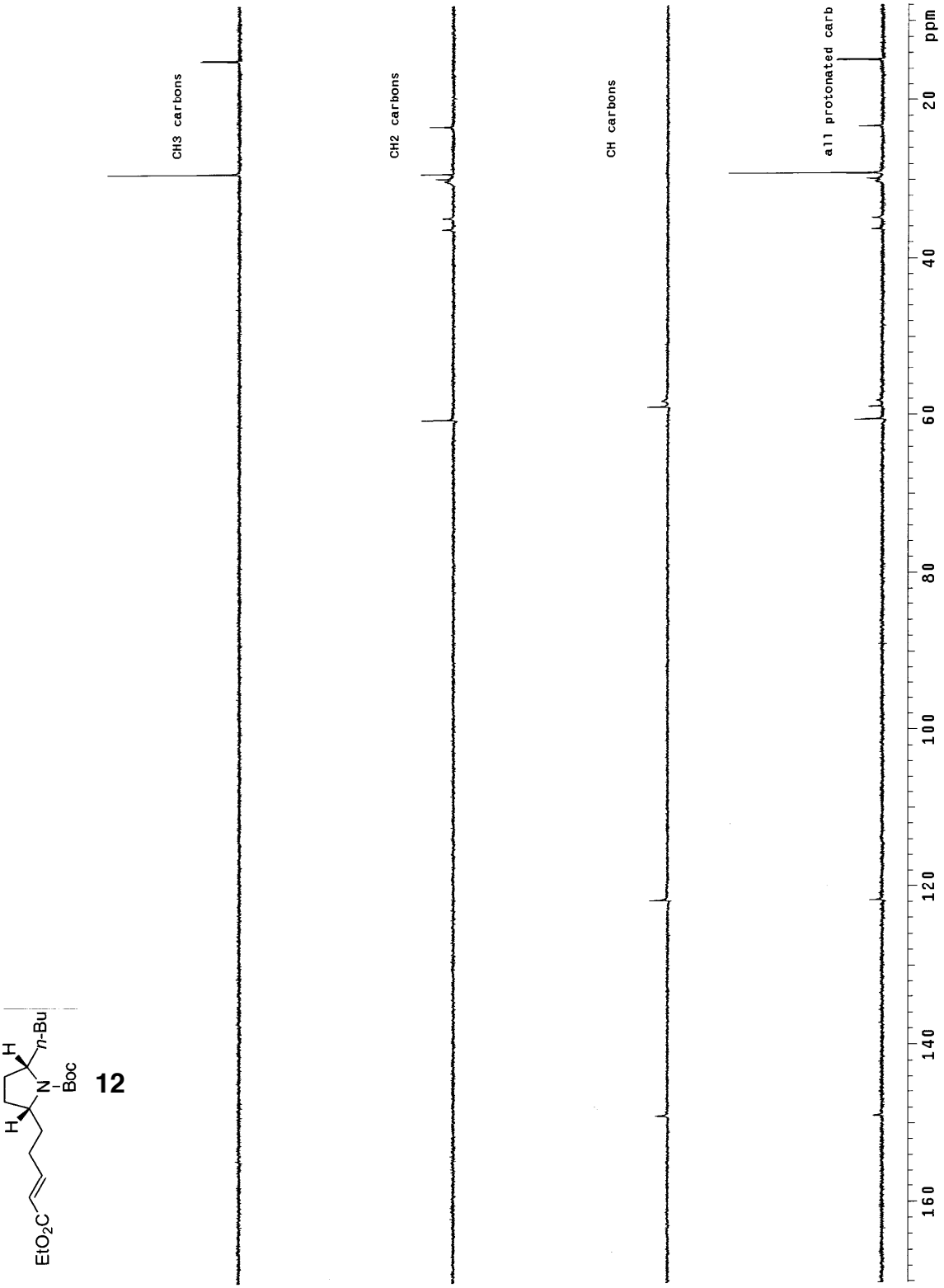

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
EtO2C
H
n-Bu
N
Boc
H
12
ppm
1
2
3
4
5
6
7
8.25
59.03
16.51
5.56
5.57
2.52
2.56

INDEX	FREQUENCY	PPM	HEIGHT
1	12533.844	166.117	7.4
2	11660.988	154.549	4.5
3	11192.210	148.336	6.9
4	9136.420	121.089	10.6
5	5941.645	78.747	14.1
6	5841.541	77.421	13.0
7	5809.801	77.000	12.2
8	5776.840	76.563	11.9
9	4516.998	59.866	17.6
10	4396.141	58.264	12.5
11	4343.647	57.568	4.4
12	2685.831	35.597	6.6
13	2577.182	34.157	7.2
14	2219.494	29.416	5.5
15	2193.858	29.076	10.4
16	2146.247	28.445	24.9
17	2141.364	28.380	74.6
18	1701.884	22.556	14.6
19	1067.080	14.143	20.5
20	1058.535	14.029	24.3

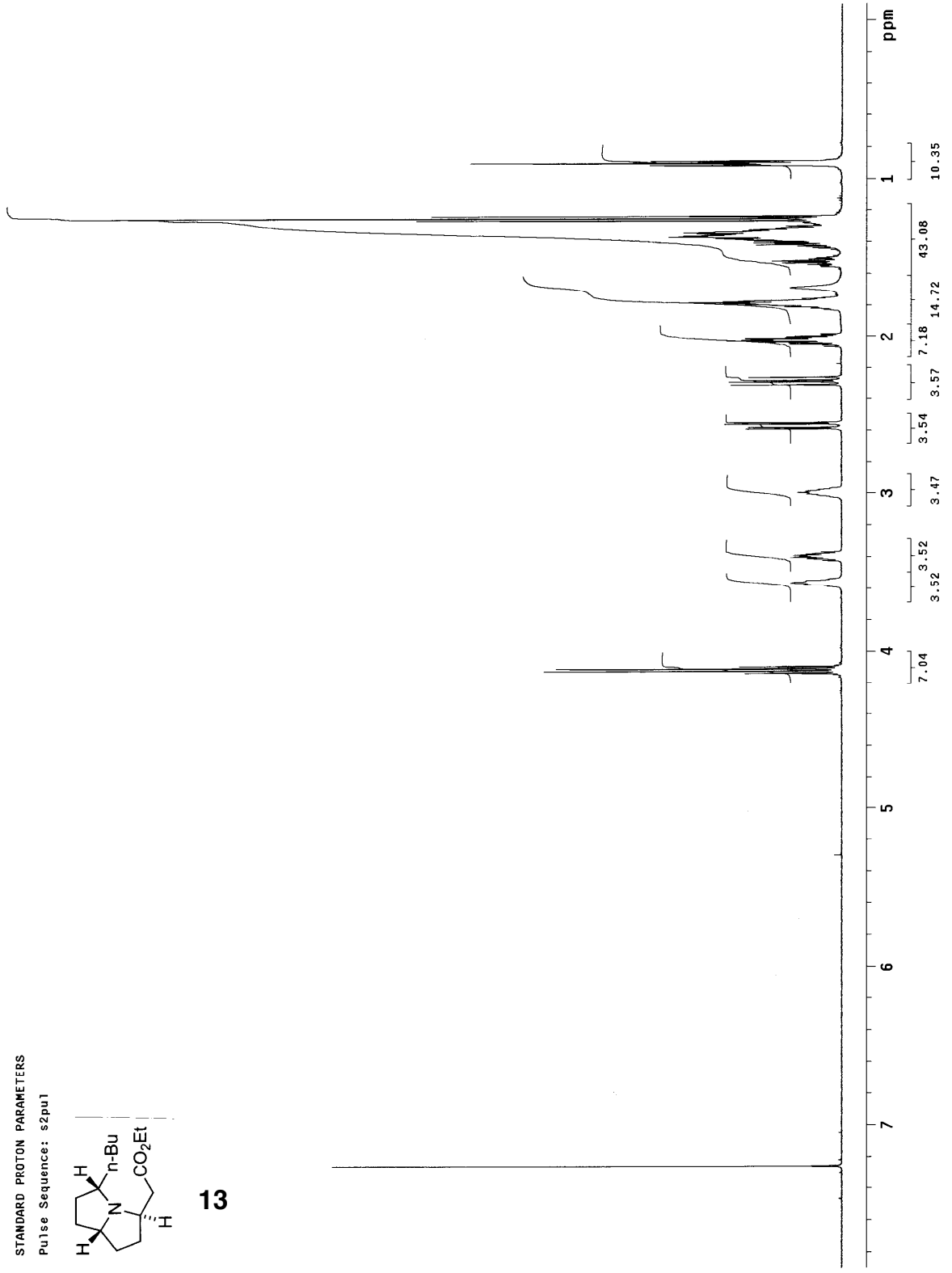


12

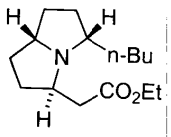



CH3 carbons
CH2 carbons
CH carbons
all protonated carb
ppm
160
140
120
100
80
60
40
20
H
n-Bu
N
Boc
H
EtO2C

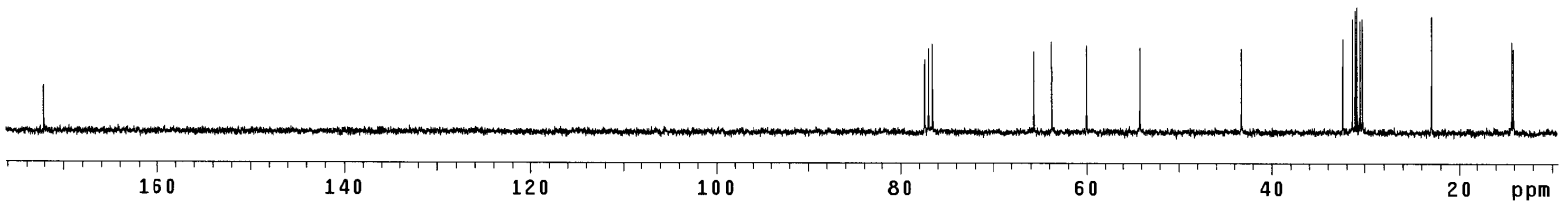
12


STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
n-Bu
CO2Et
H
N
H
H
13
ppm
7
6
5
4
3
2
1
7.04
3.52
3.52
3.47
3.54
3.57
7.18
14.72
43.08
10.35

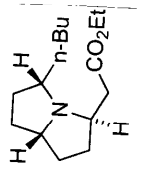
INDEX	FREQUENCY	PPM	HEIGHT
1	12981.869	172.055	7.3
2	5840.320	77.404	11.6
3	5808.580	76.984	13.4
4	5776.840	76.563	14.2
5	4950.373	65.610	12.9
6	4808.763	63.733	14.5
7	4527.984	60.011	13.9
8	4086.063	54.154	13.6
9	3260.817	43.217	13.4
10	2442.896	32.377	15.0
11	2364.766	31.341	18.2
12	2335.468	30.953	19.5
13	2320.818	30.759	20.1
14	2296.403	30.435	17.8
15	2278.091	30.193	18.2
16	1729.962	22.928	18.6
17	1074.404	14.240	14.5
18	1060.976	14.062	13.3

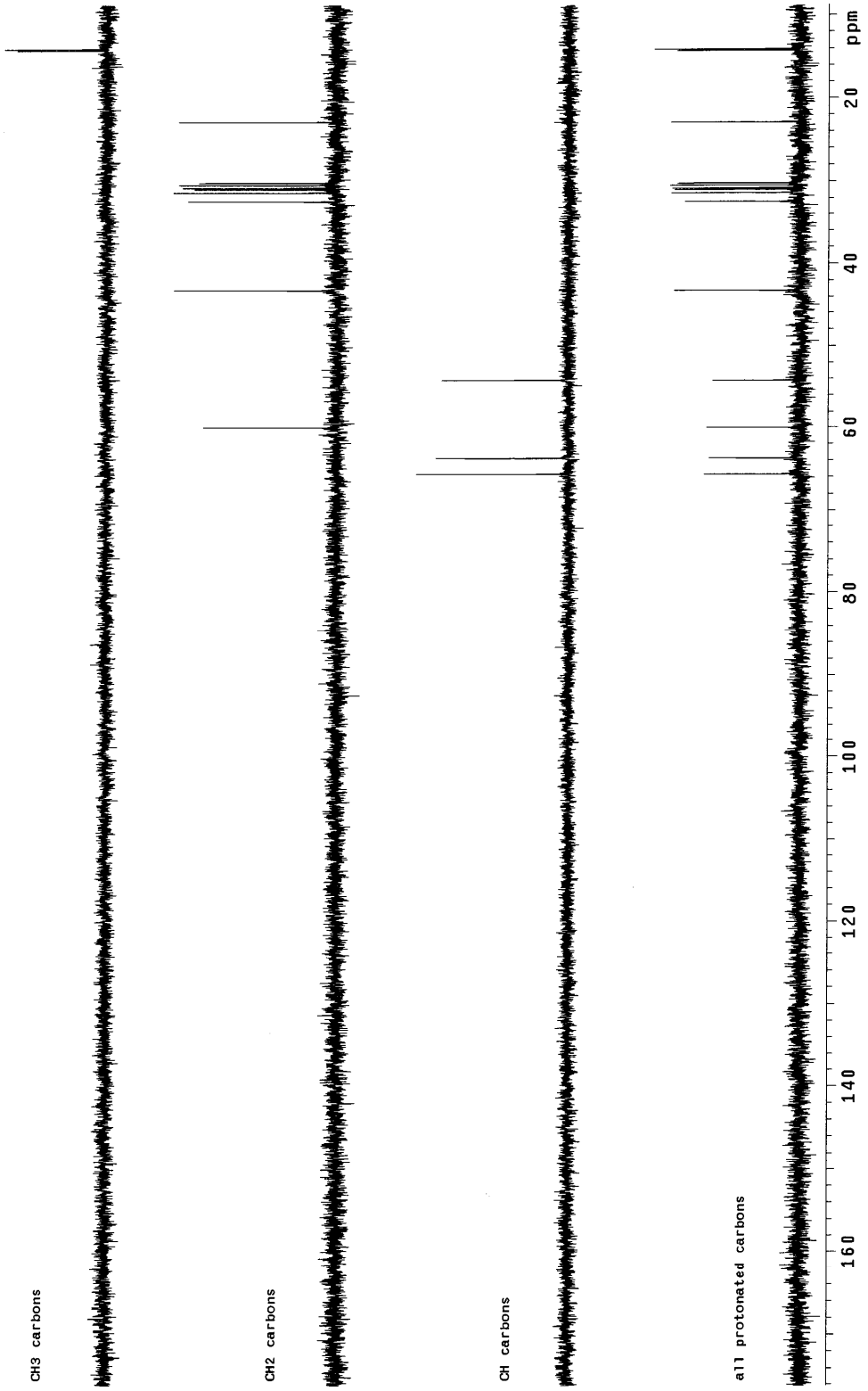


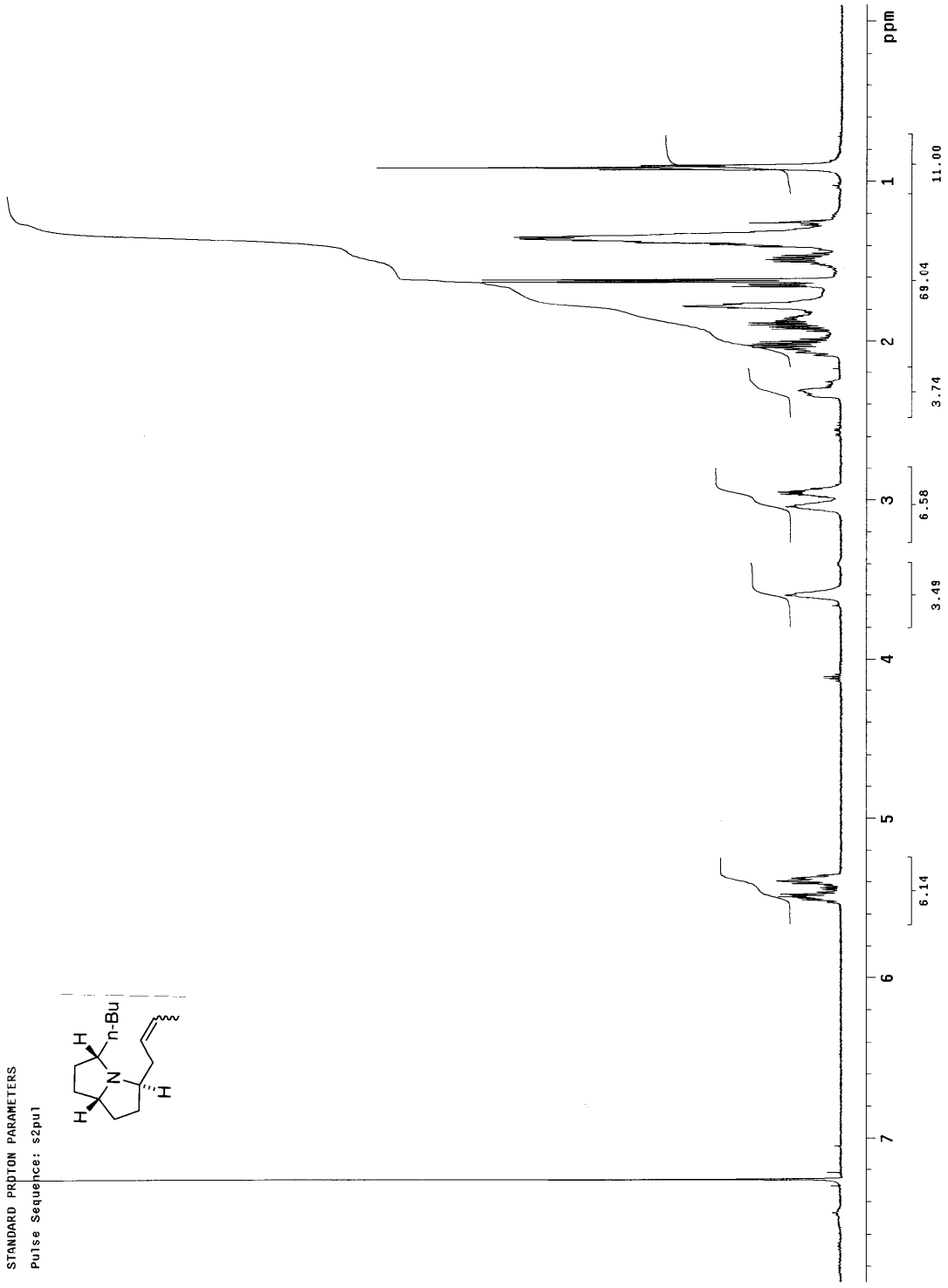
13

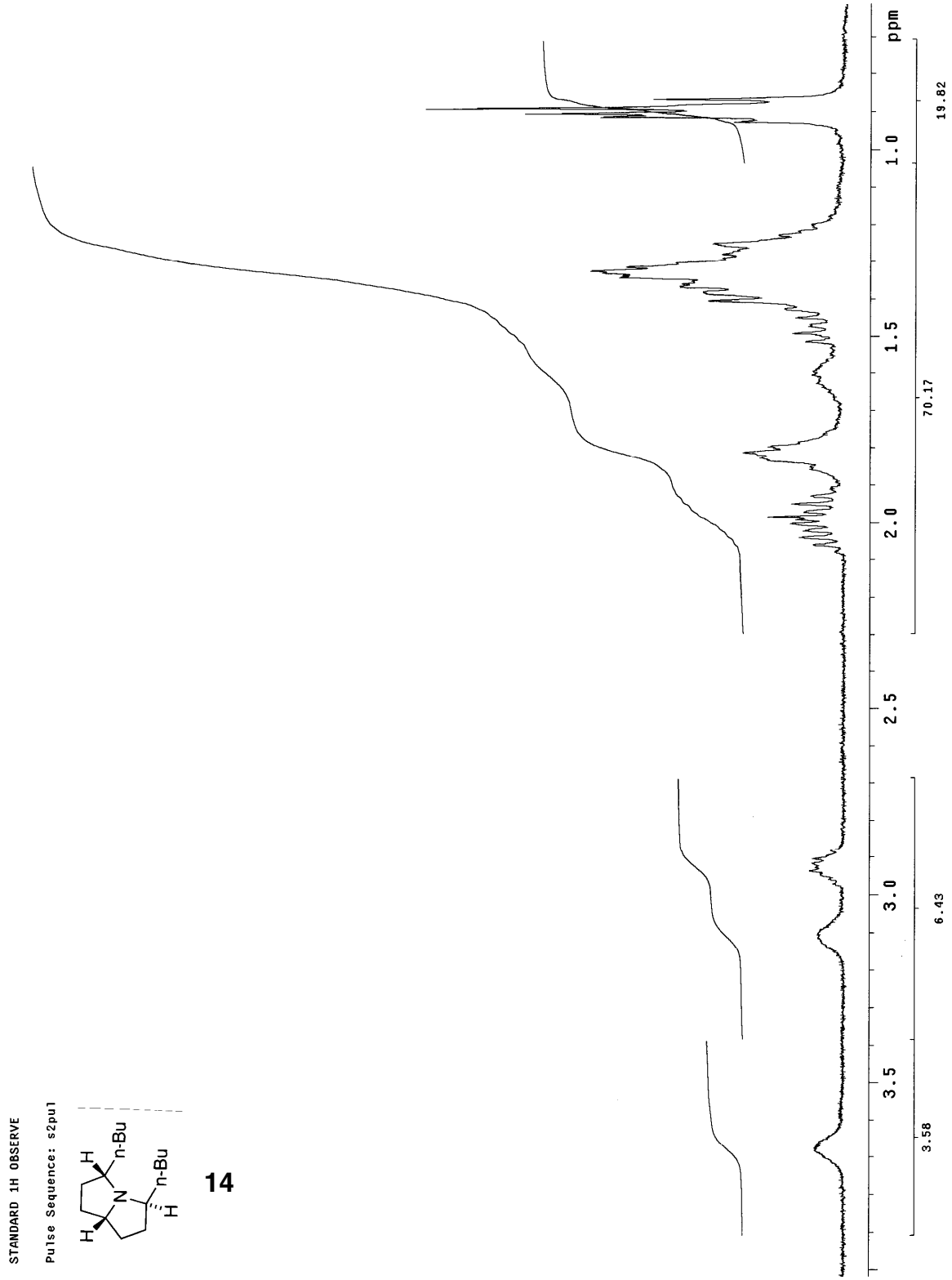


13

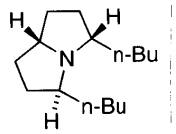

H
n-Bu
N
CO2Et
H
H


CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
140
120
100
80
60
40
20
ppm

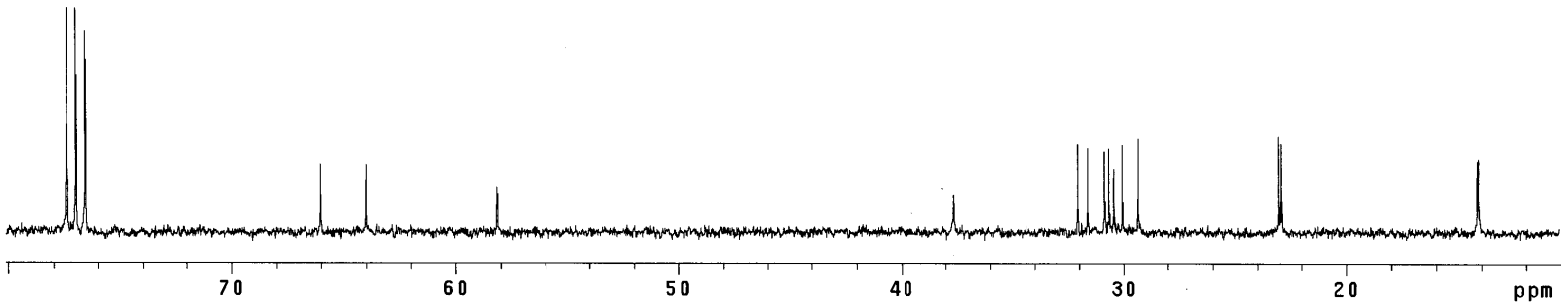

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
n-Bu
H
N
H
H
ppm
1
2
3
4
5
6
7
11.00
69.04
3.74
6.58
3.49
6.14

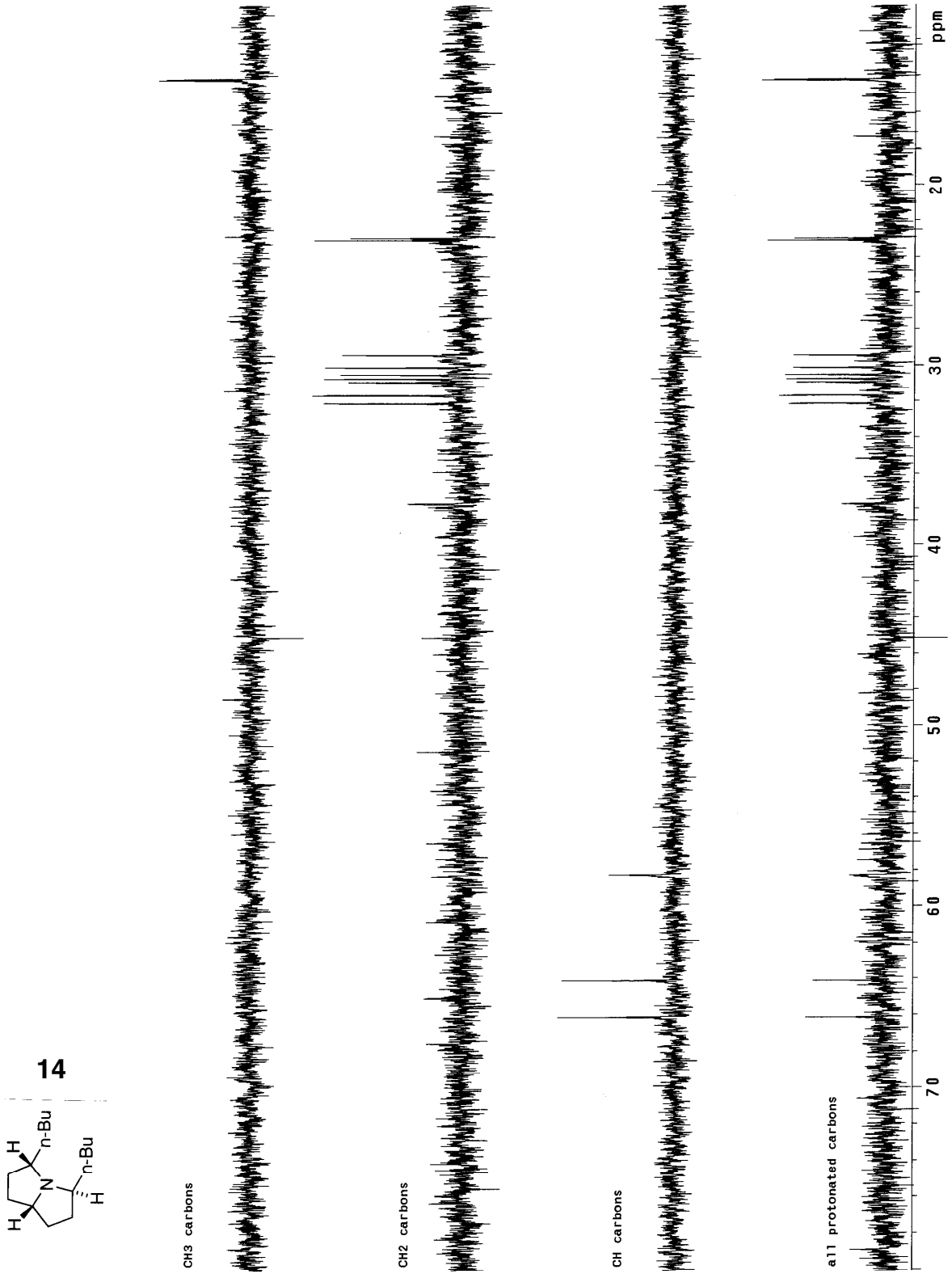

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
n-Bu
n-Bu
H
H
H
N
14
ppm
3.5
3.0
2.5
2.0
1.5
1.0
3.58
6.43
70.17
19.82

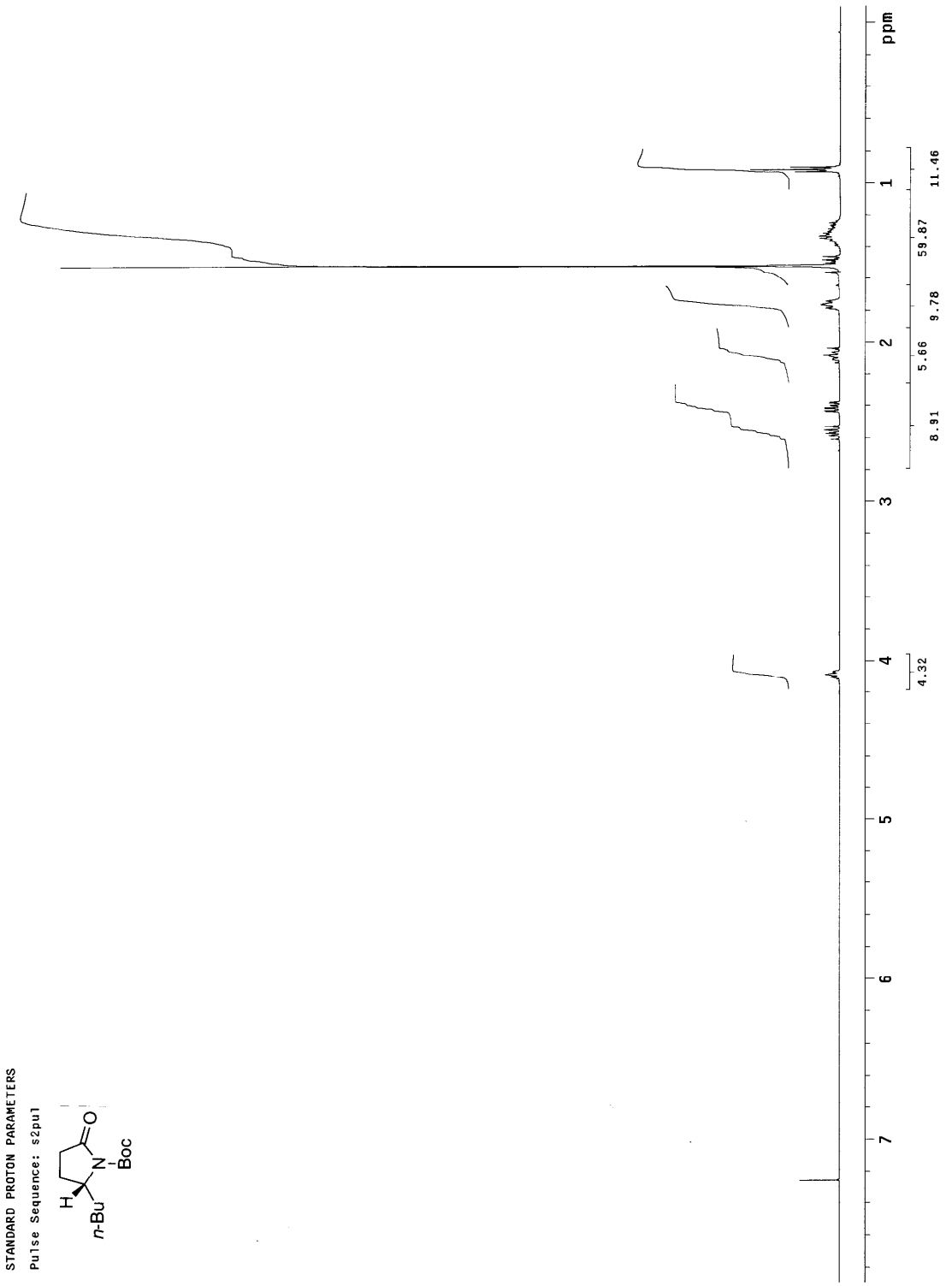
INDEX	FREQUENCY	PPM	HEIGHT
1	5841.541	77.421	36.1
2	5809.801	77.000	36.0
3	5778.060	76.579	32.4
4	4982.113	66.030	10.9
5	4829.516	64.008	10.8
6	4388.815	58.167	7.2
7	2839.649	37.635	6.0
8	2419.701	32.069	14.3
9	2385.519	31.616	13.6
10	2329.364	30.872	13.2
11	2313.493	30.662	13.5
12	2296.403	30.435	10.2
13	2267.104	30.047	14.1
14	2214.610	29.351	15.1
15	1736.066	23.009	15.5
16	1727.520	22.896	14.4
17	1069.521	14.175	11.5
18	1065.859	14.126	11.9



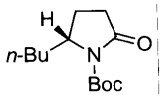
14

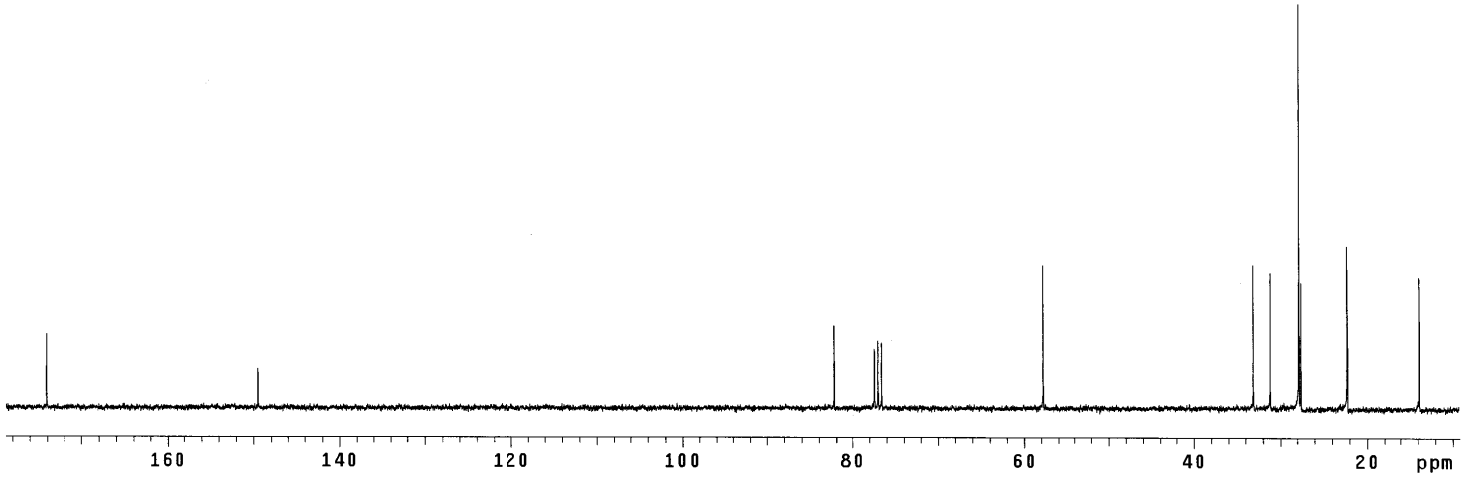


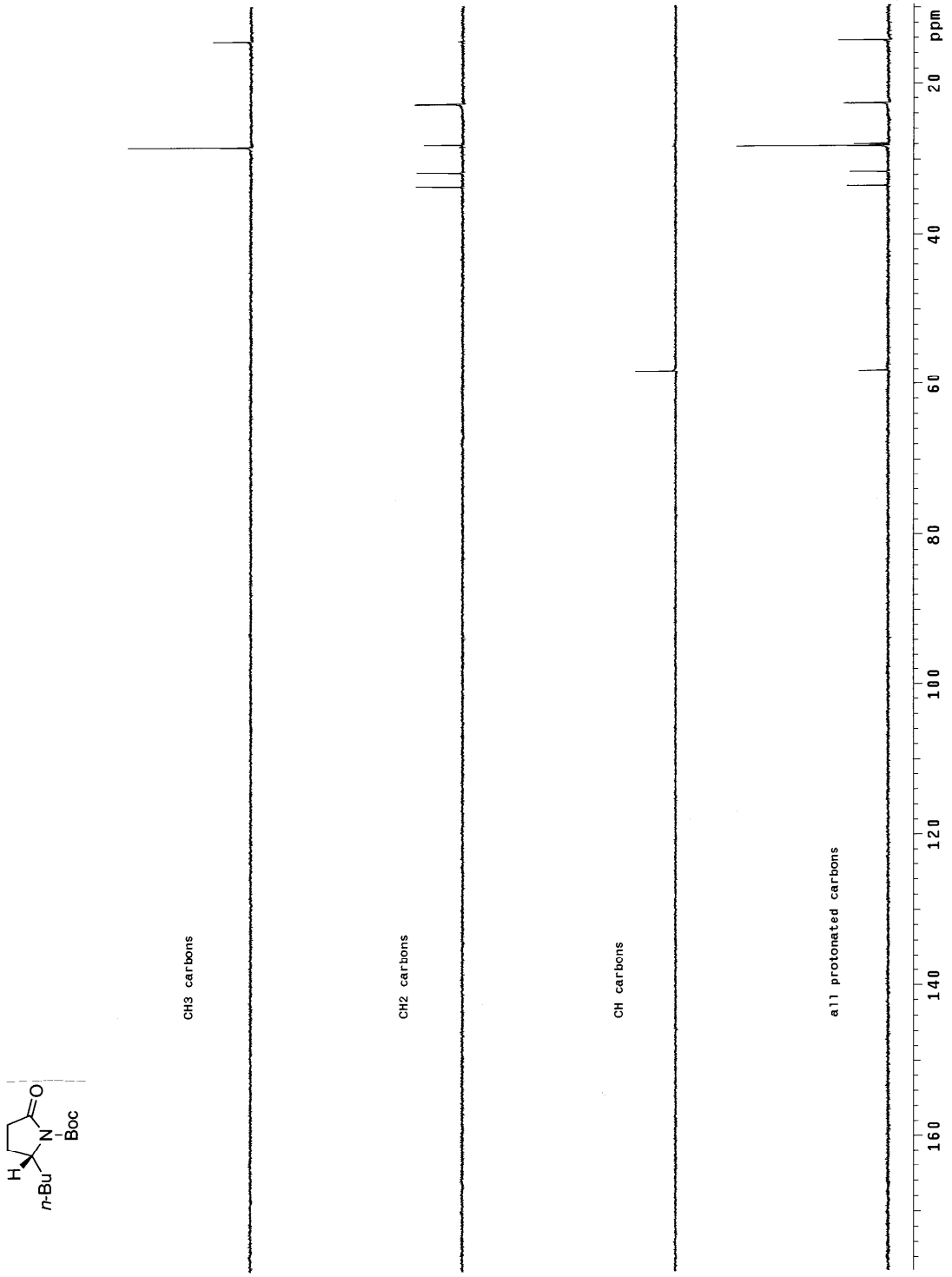

14
n-Bu
n-Bu
H
H
H
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
70
60
50
40
30
20
ppm

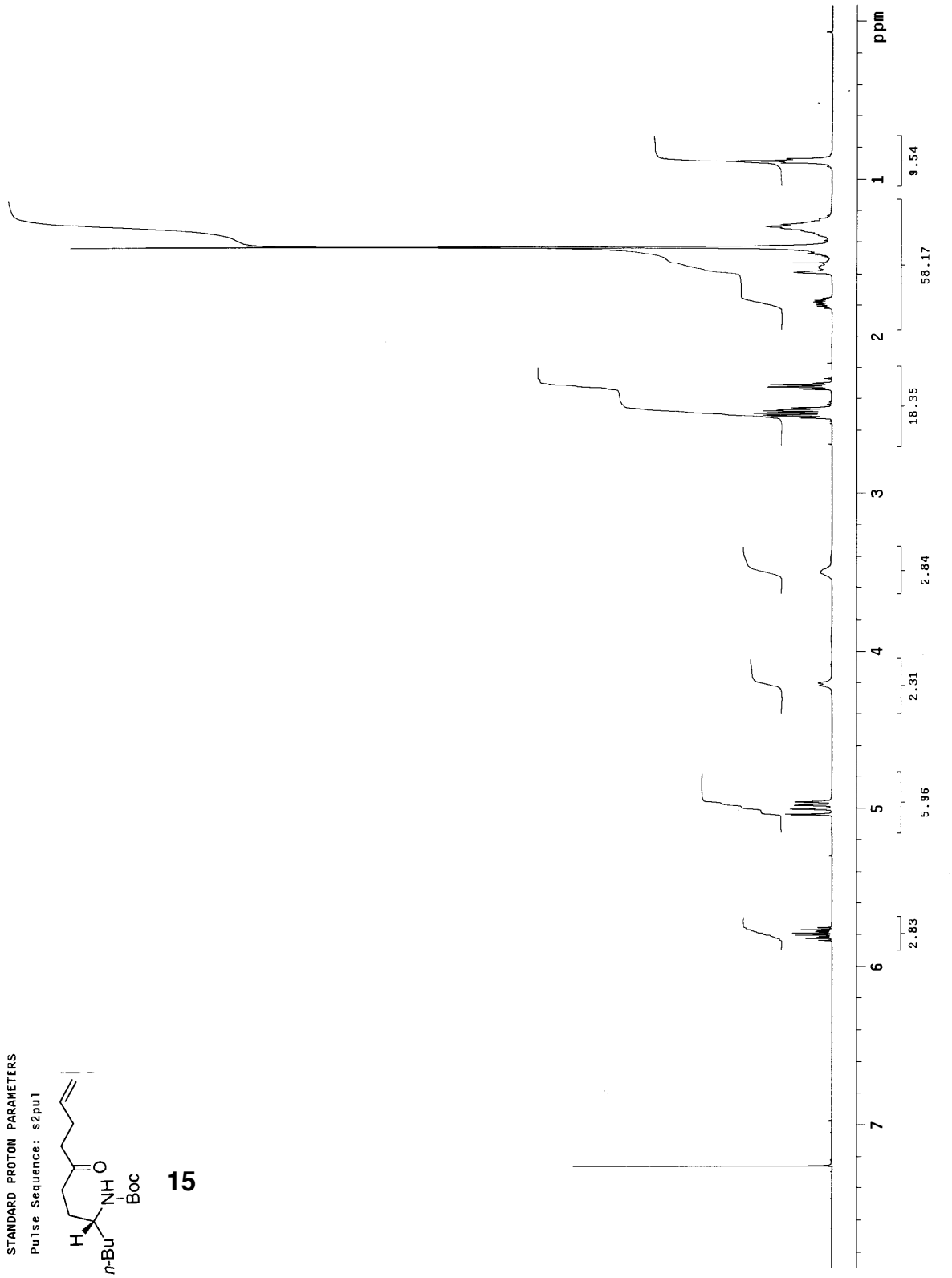

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
n-Bu
Boc
ppm
1
2
3
4
5
6
7
11.46
59.87
9.78
5.66
8.91
4.32

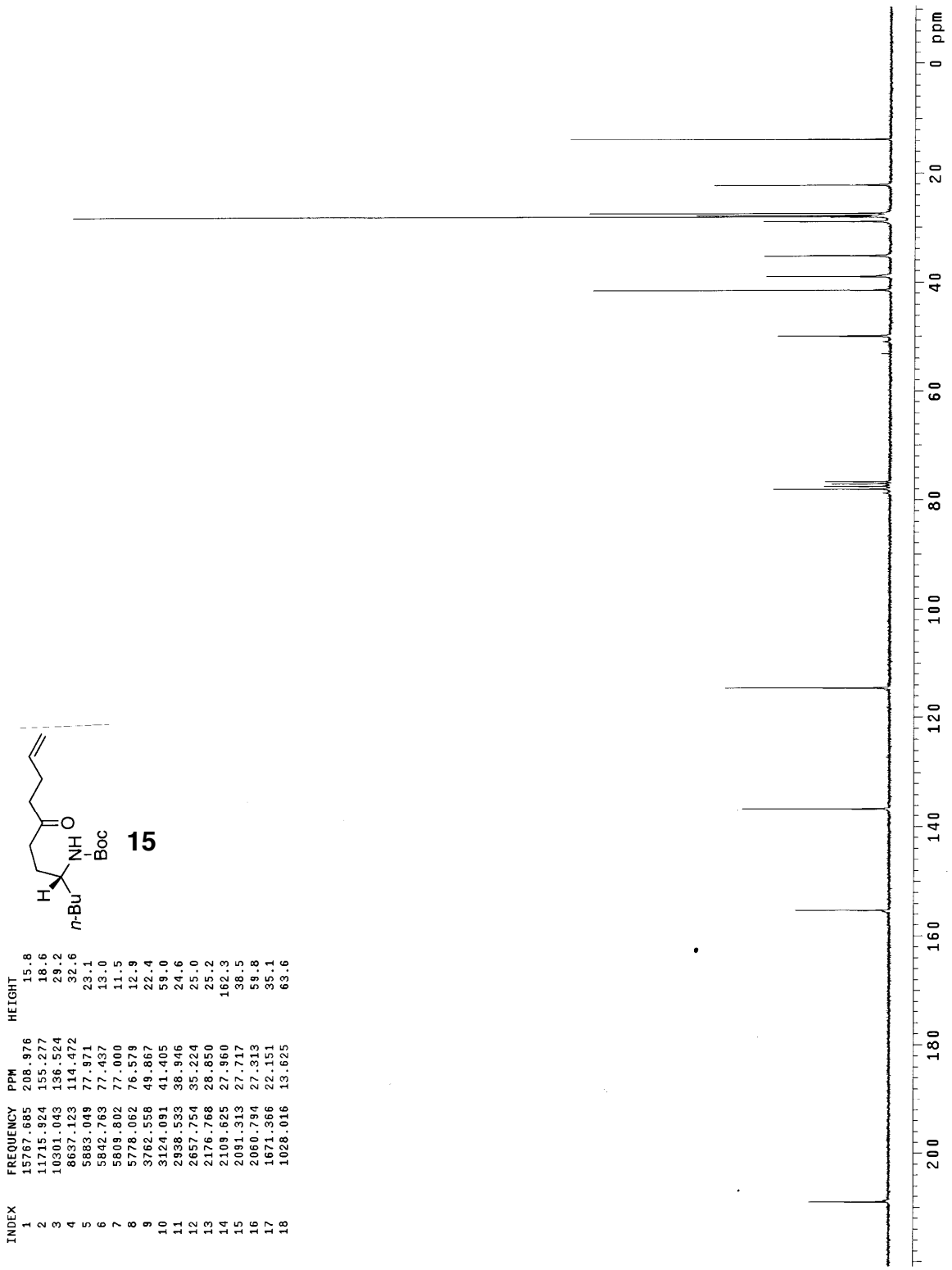
INDEX	FREQUENCY	PPM	HEIGHT
1	13130.805	174.029	12.5
2	11278.885	149.484	6.6
3	6202.892	82.210	14.1
4	5842.763	77.437	10.1
5	5809.802	77.000	11.5
6	5778.061	76.579	11.2
7	4359.518	57.779	24.7
8	2497.832	33.105	24.7
9	2350.118	31.147	23.3
10	2096.196	27.782	69.6
11	2075.443	27.507	21.6
12	1681.132	22.281	28.0
13	1677.469	22.232	24.0
14	1042.665	13.819	22.6





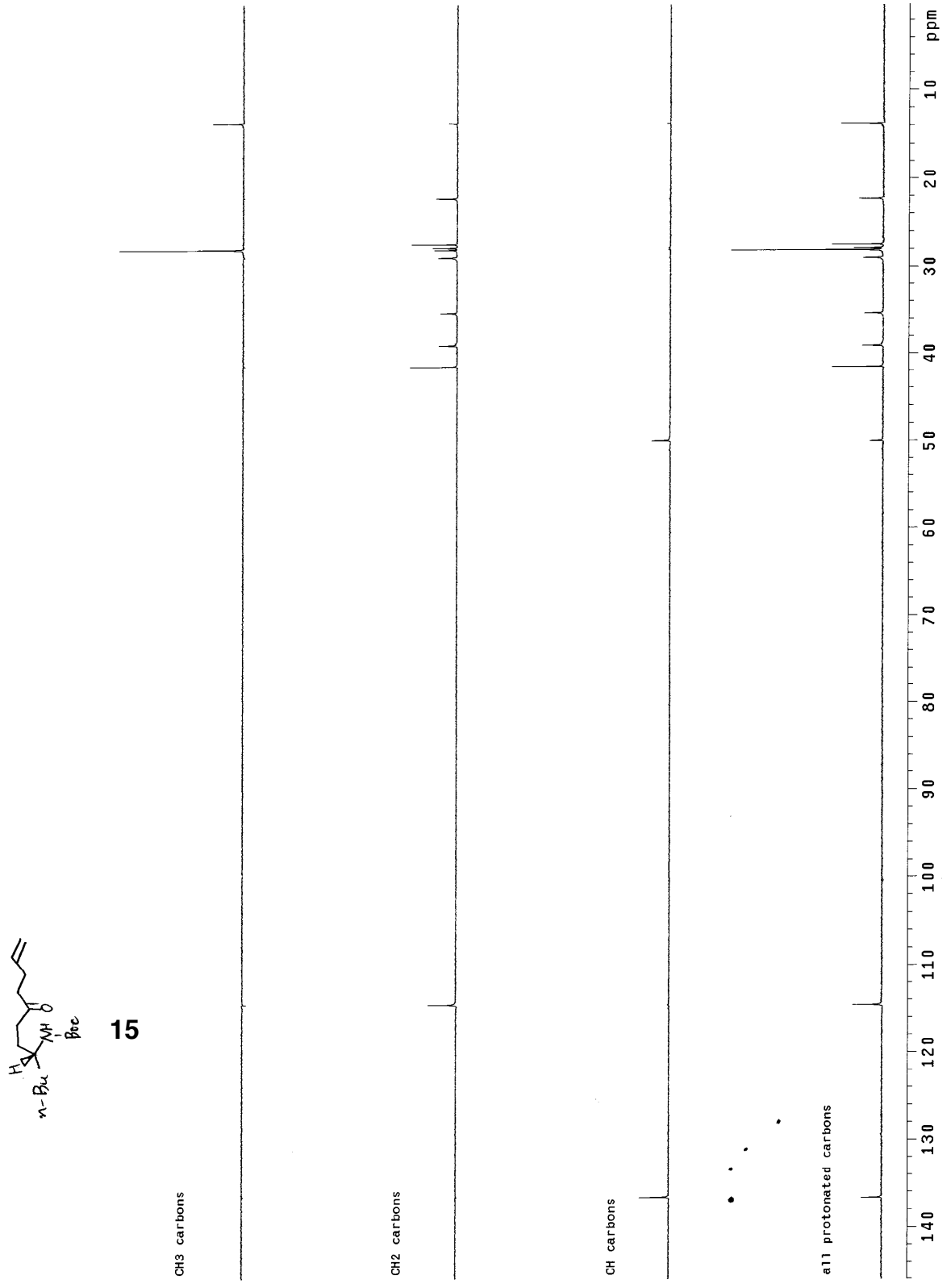

CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
20
40
60
80
100
120
140
160
O
N
Boc
H
n-Bu


STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
n-Bu
H
NH
Boc
O
15
ppm
1
2
3
4
5
6
7
9.54
58.17
18.35
2.84
2.31
5.96
2.83

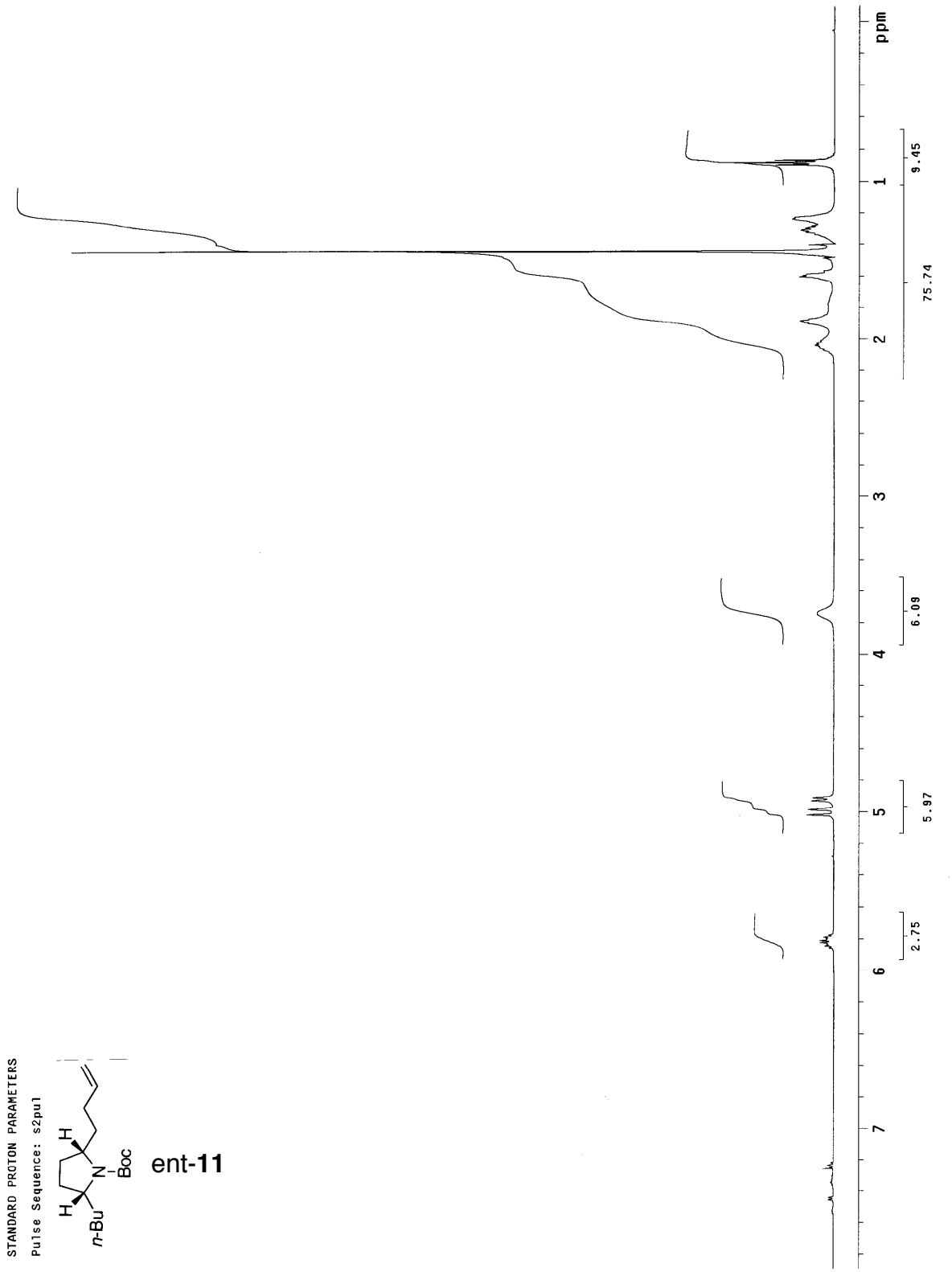


15

INDEX	FREQUENCY	PPM	HEIGHT
1	15767.685	208.976	15.8
2	11715.924	155.277	18.6
3	10301.043	136.524	29.2
4	8637.123	114.472	32.6
5	5883.049	77.971	23.1
6	5842.763	77.437	13.0
7	5809.802	77.000	11.5
8	5778.062	76.579	12.9
9	3762.558	49.867	22.4
10	3124.091	41.405	59.0
11	2938.533	38.946	24.6
12	2657.754	35.224	25.0
13	2176.768	28.850	25.2
14	2109.625	27.960	162.3
15	2091.313	27.717	38.5
16	2060.794	27.313	59.8
17	1671.366	22.151	35.1
18	1028.016	13.625	63.6

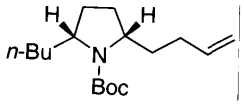

n-Bu
NH
O
Boc
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

15

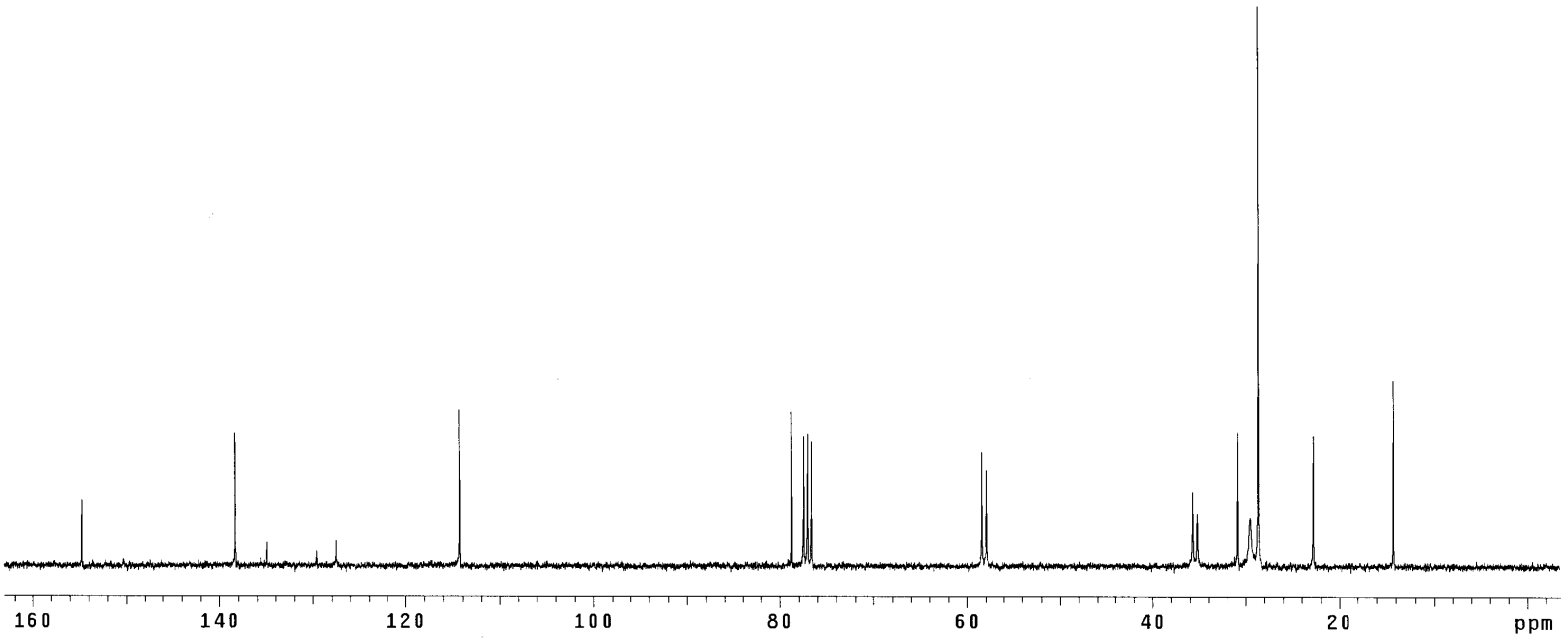

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
n-Bu
H
N
Boc
H
ppm
1
2
3
4
5
6
7
9.45
75.74
6.09
5.97
2.75

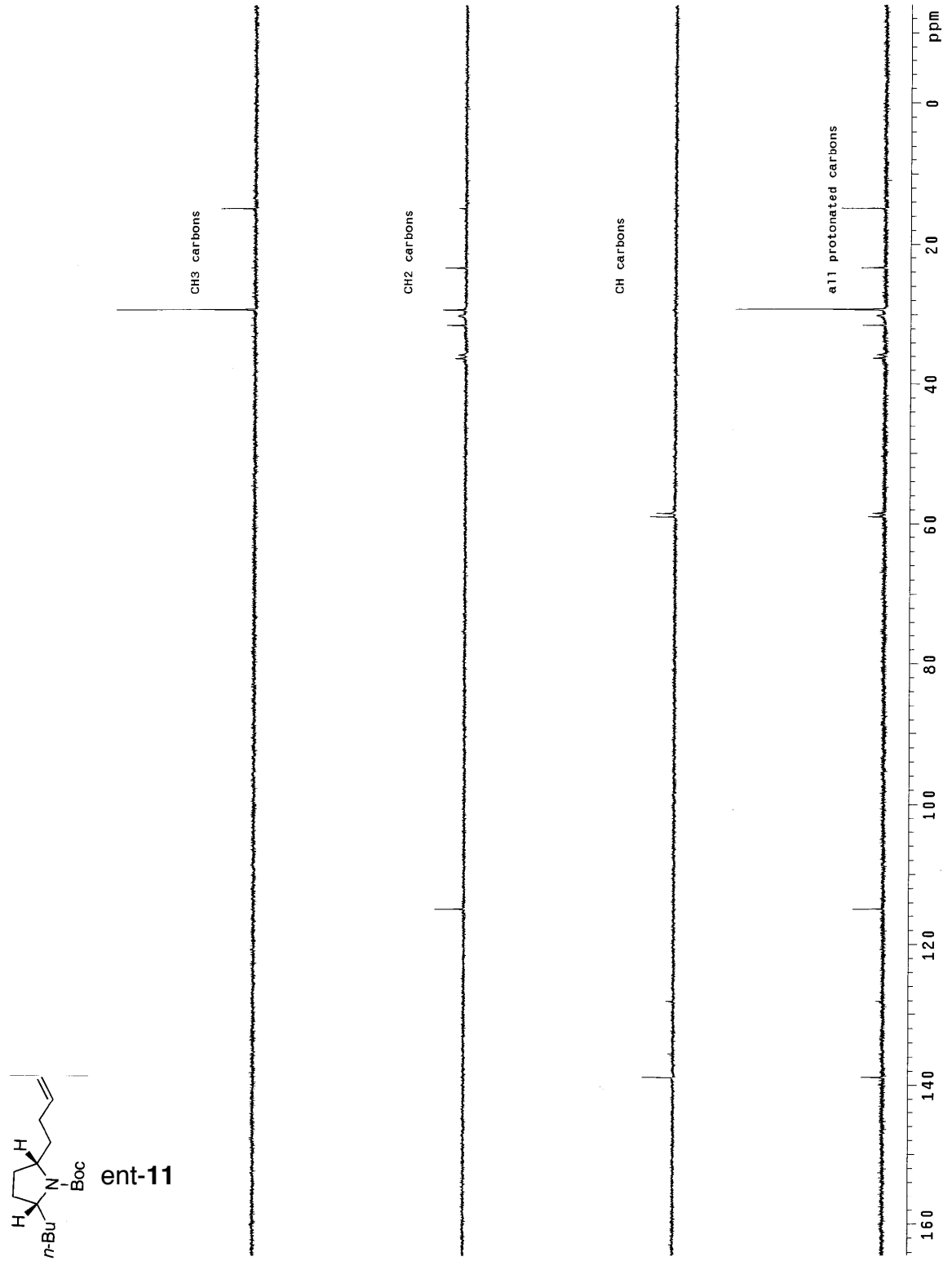
ent-**11**

INDEX	FREQUENCY	PPM	HEIGHT
1	11673.196	154.710	10.5
2	10437.769	138.337	21.3
3	10183.847	134.971	3.7
4	9778.549	129.600	2.3
5	9619.848	127.496	4.0
6	8621.252	114.261	25.1
7	5939.203	78.715	24.9
8	5841.541	77.421	20.9
9	5809.801	77.000	21.3
10	5778.060	76.579	20.1
11	4403.465	58.361	18.4
12	4366.841	57.876	15.5
13	2690.714	35.661	12.0
14	2652.870	35.160	8.5
15	2324.480	30.807	21.6
16	2223.156	29.465	7.8
17	2162.117	28.656	27.4
18	2156.013	28.575	90.1
19	1716.533	22.750	21.1
20	1071.963	14.207	30.0

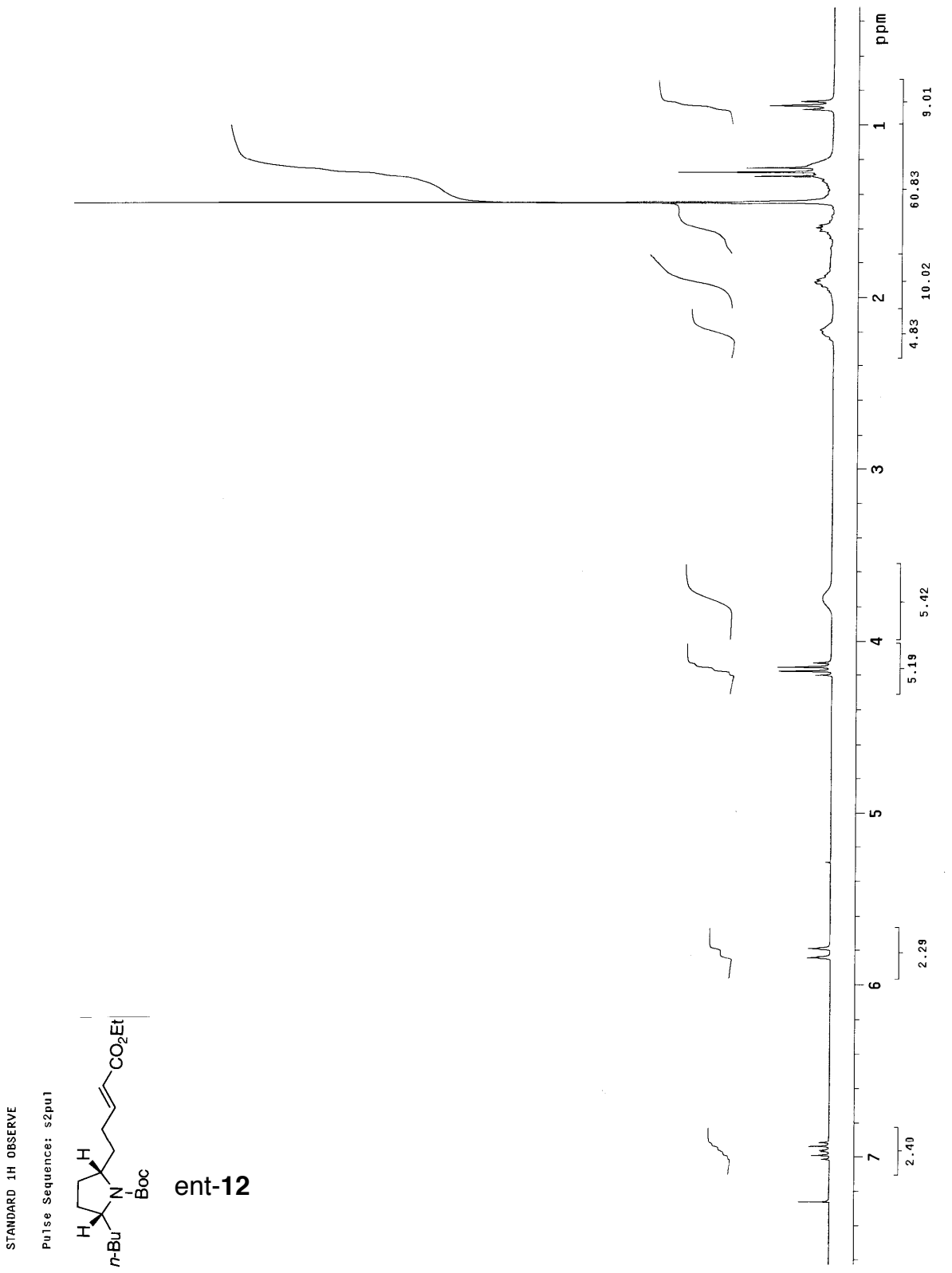


ent-11



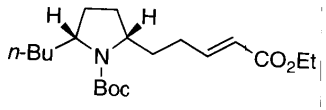

CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
0
20
40
60
80
100
120
140
160
H
N
Boc
n-Bu
H

ent-**11**

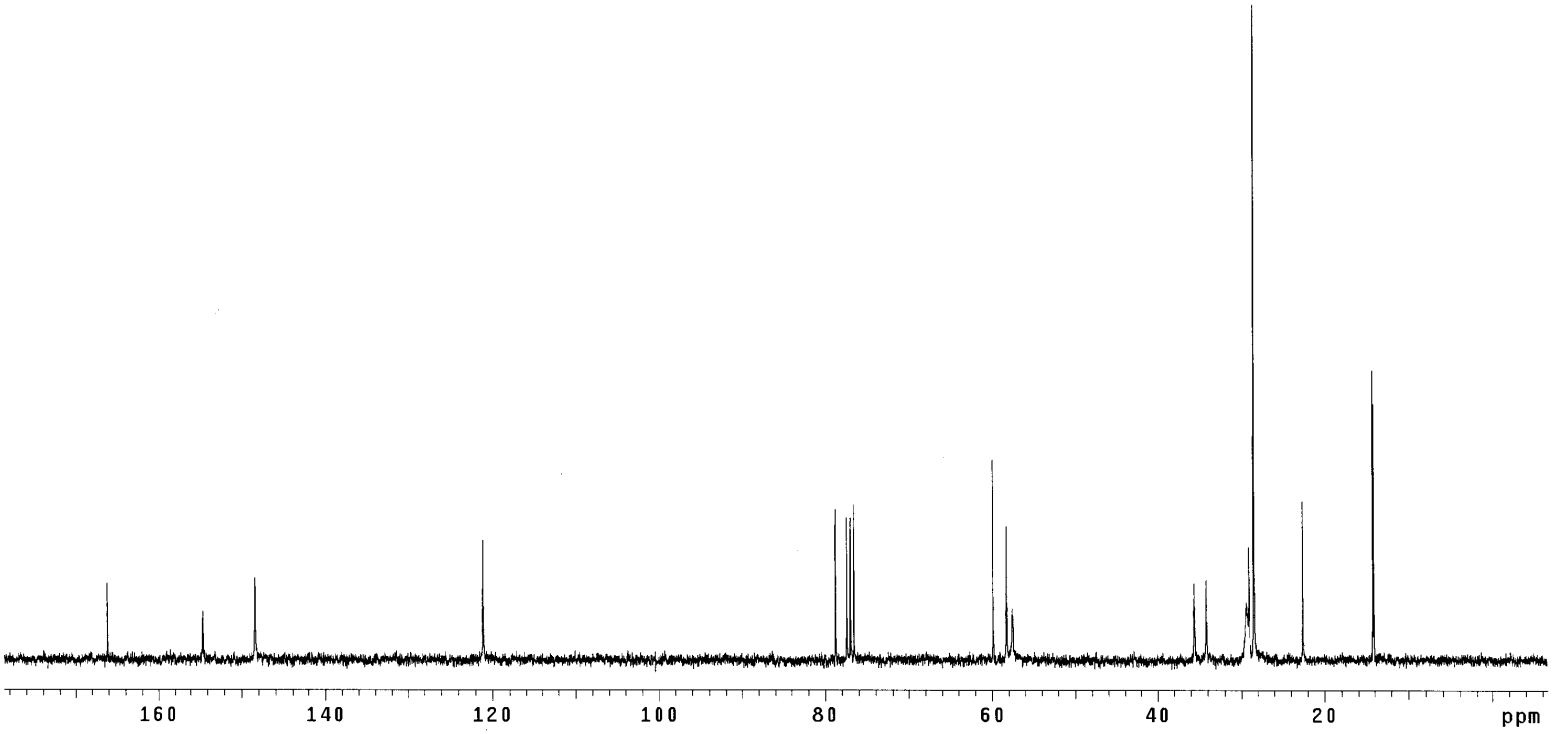

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
n-Bu
Boc
CO2Et
ppm
2.40
2.29
5.19
5.42
4.83
10.02
60.83
9.01

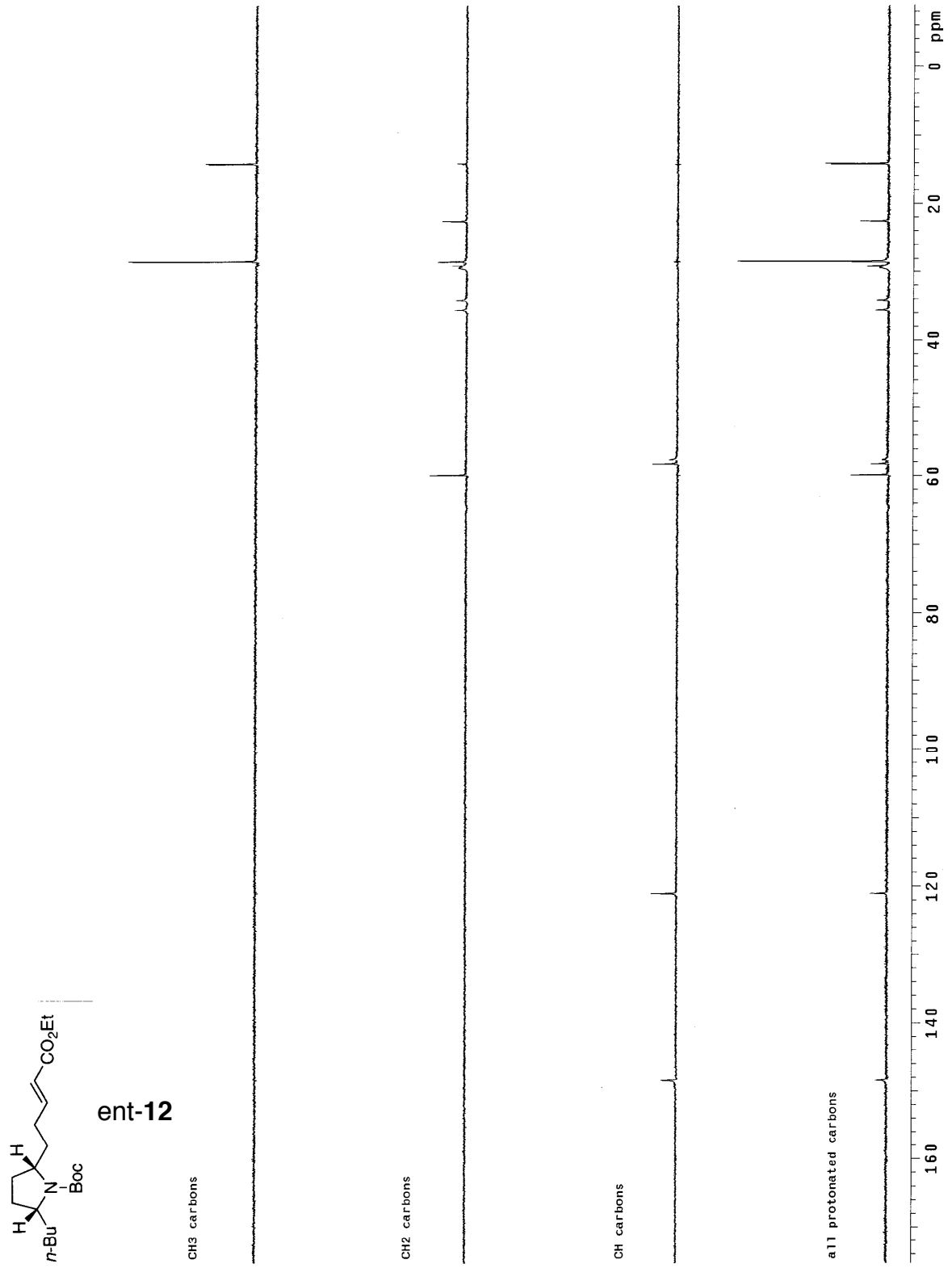
ent-**12**

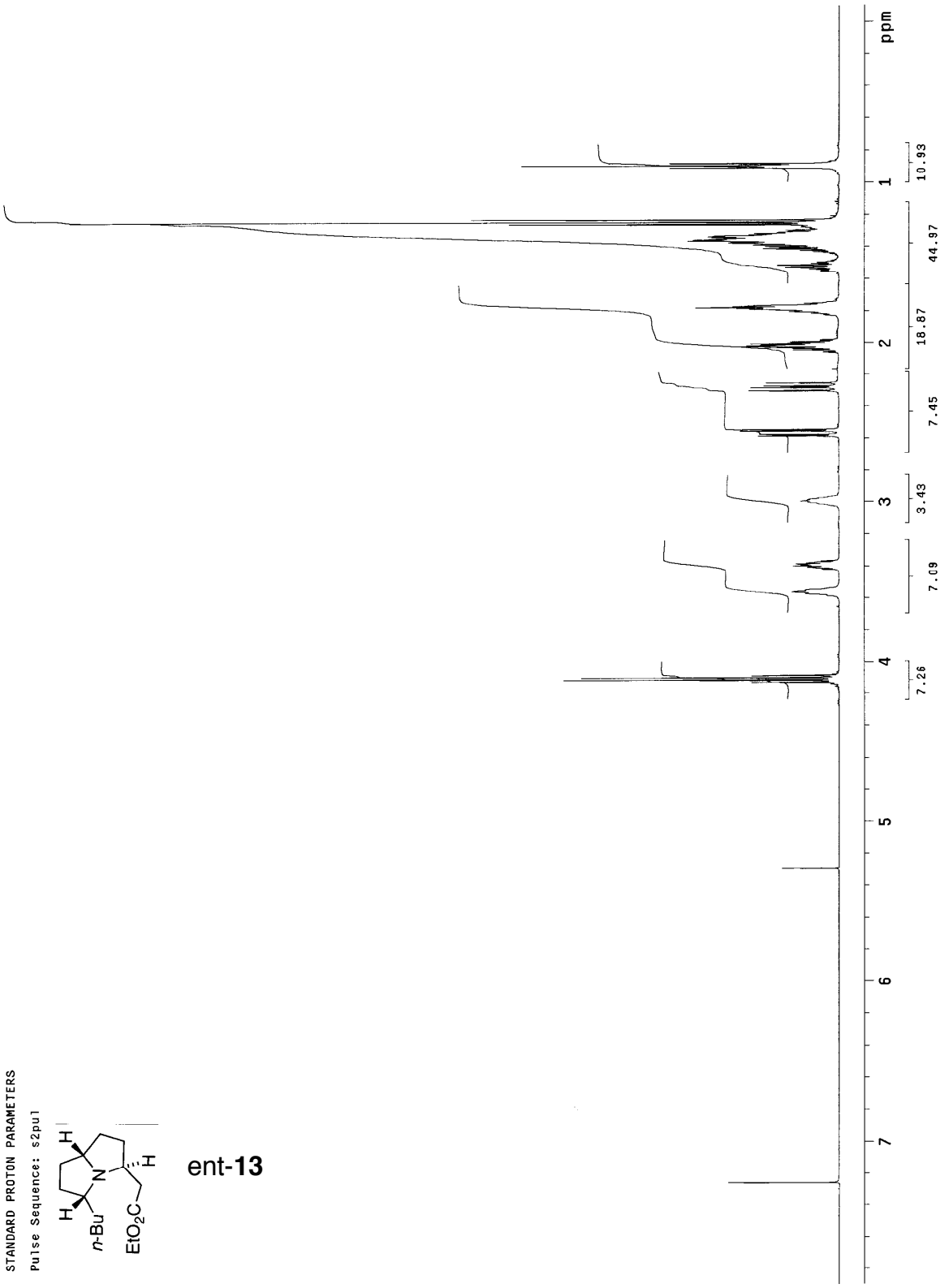
INDEX	FREQUENCY	PPM	HEIGHT
1	12536.286	166.149	12.2
2	11663.430	154.581	7.7
3	11194.651	148.368	13.2
4	9136.420	121.089	19.4
5	5942.866	78.764	24.5
6	5842.762	77.437	23.1
7	5809.801	77.000	23.1
8	5778.061	76.579	25.3
9	4519.439	59.898	32.4
10	4397.361	58.280	21.7
11	4344.868	57.585	8.2
12	2685.831	35.597	12.3
13	2578.403	34.173	12.9
14	2220.715	29.432	9.3
15	2196.299	29.109	18.3
16	2147.468	28.461	37.5
17	2142.585	28.397	106.1
18	1704.326	22.588	25.9
19	1069.521	14.175	46.9
20	1060.976	14.062	41.5



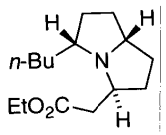
ent-12



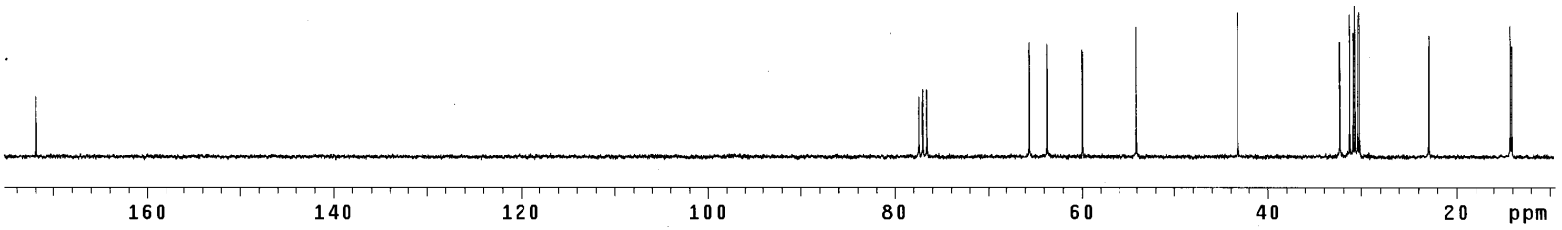

CO2Et
H
N
Boc
H
n-Bu
ent-12
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
160
140
120
100
80
60
40
20
0 ppm

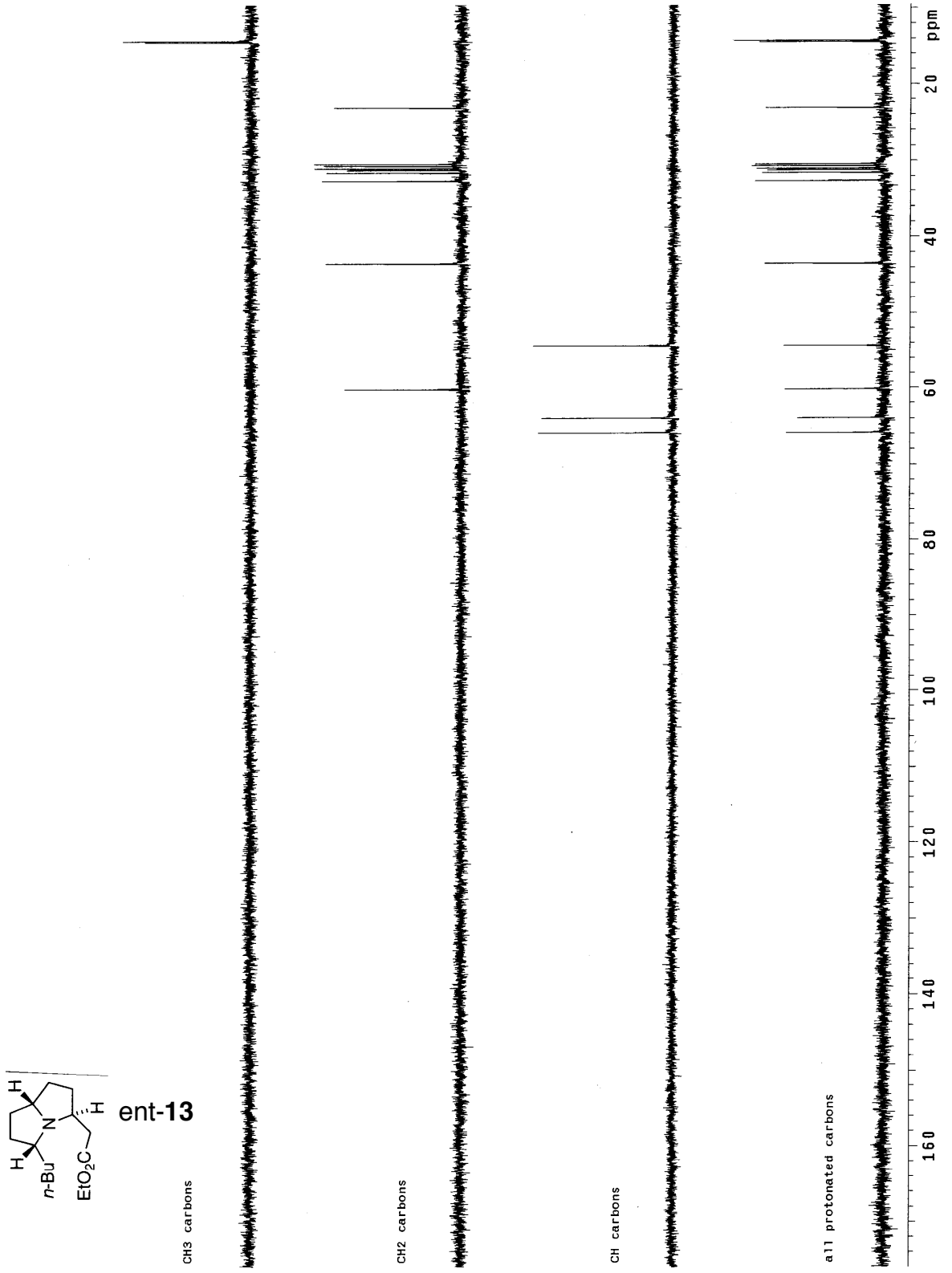

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
ent-13
ppm
1
2
3
4
5
6
7
10.93
44.97
18.87
7.45
3.43
7.09
7.26

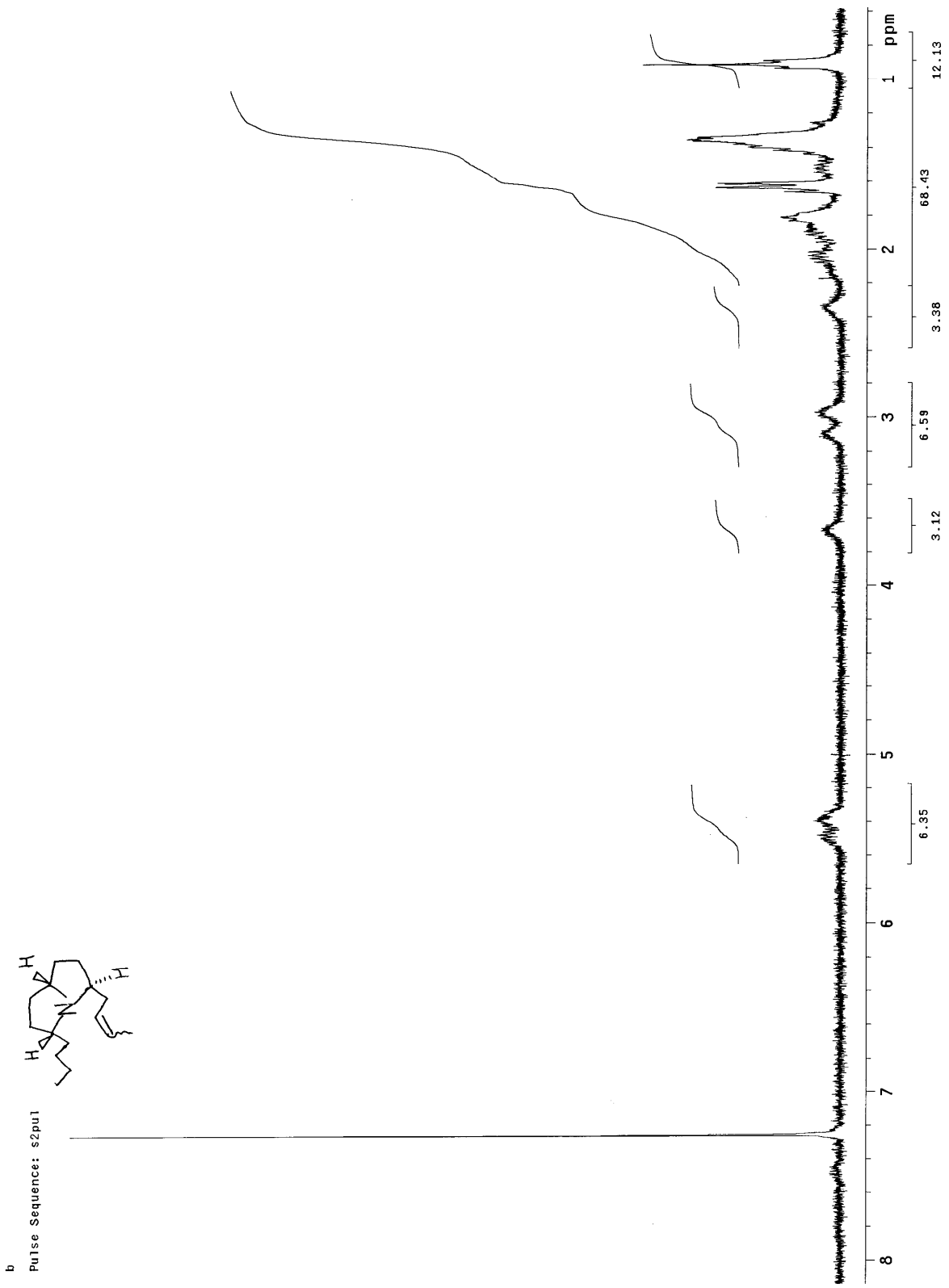
INDEX	FREQUENCY	PPM	HEIGHT
1	12973.324	171.942	9.7
2	5841.541	77.421	9.6
3	5809.801	77.000	10.8
4	5778.061	76.579	10.7
5	4944.270	65.529	18.4
6	4801.439	63.636	18.2
7	4520.660	59.914	17.2
8	4077.517	54.041	20.9
9	3257.155	43.169	23.2
10	2436.792	32.296	18.5
11	2358.663	31.260	23.0
12	2329.364	30.872	19.9
13	2314.715	30.678	24.4
14	2291.520	30.371	22.9
15	2273.208	30.128	23.4
16	1723.858	22.847	19.5
17	1068.301	14.159	21.1
18	1056.093	13.997	17.7

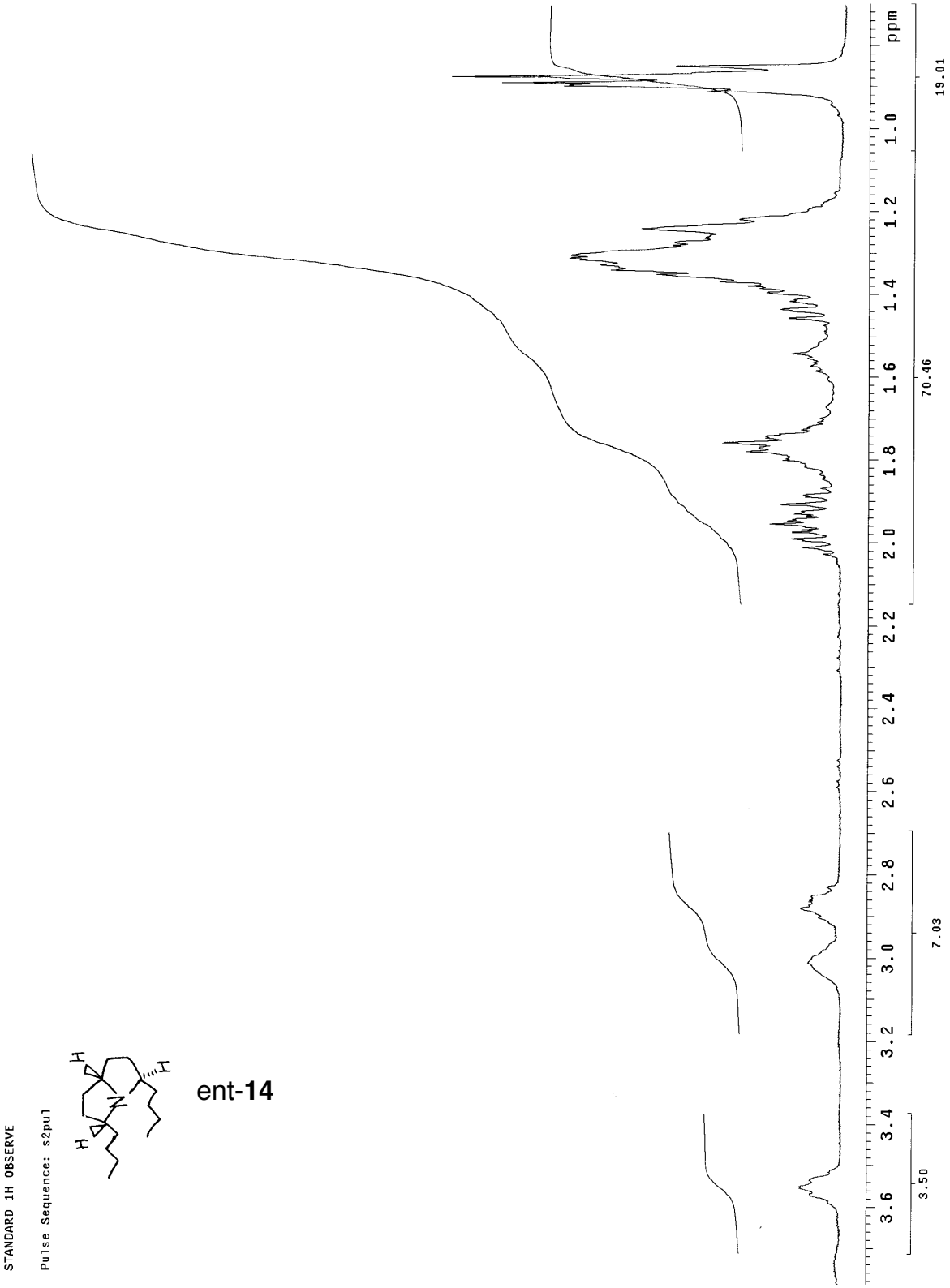


ent-13

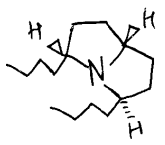



ent-13
n-Bu
EtO2C
CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
160
140
120
100
80
60
40
20

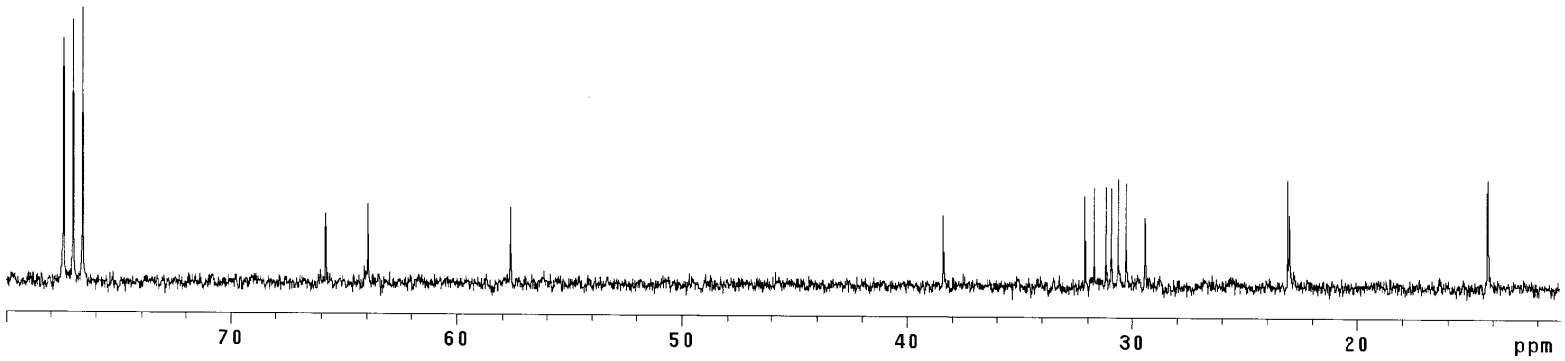

b
Pulse Sequence: s2pul
H
H
H
N
8
7
6
5
4
3
2
1
ppm
6.35
3.12
6.59
3.38
68.43
12.13


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
ent-14
ppm
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
3.50
7.03
70.46
19.01

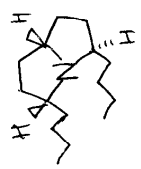
INDEX	FREQUENCY	PPM	HEIGHT
1	5841.541	77.421	39.0
2	5809.800	77.000	42.0
3	5778.060	76.579	43.9
4	4963.802	65.788	11.1
5	4824.633	63.943	12.7
6	4344.867	57.585	12.2
7	2897.025	38.396	11.2
8	2422.143	32.102	14.4
9	2391.623	31.697	15.9
10	2352.558	31.180	15.9
11	2331.805	30.905	15.7
12	2308.610	30.597	17.2
13	2281.753	30.241	16.5
14	2218.273	29.400	11.1
15	1740.949	23.074	17.1
16	1736.065	23.009	11.5
17	1073.183	14.223	15.3
18	1069.521	14.175	17.3

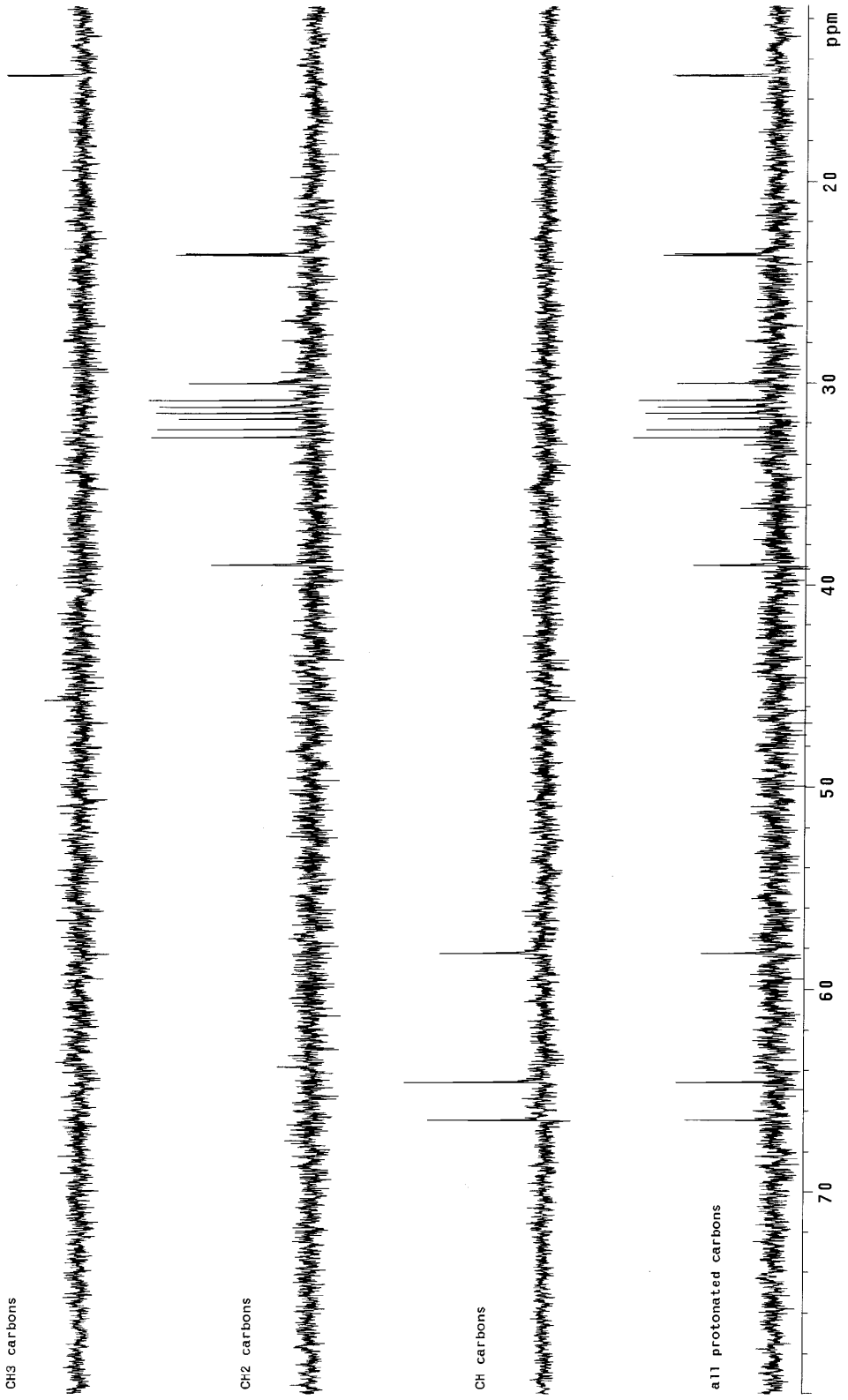


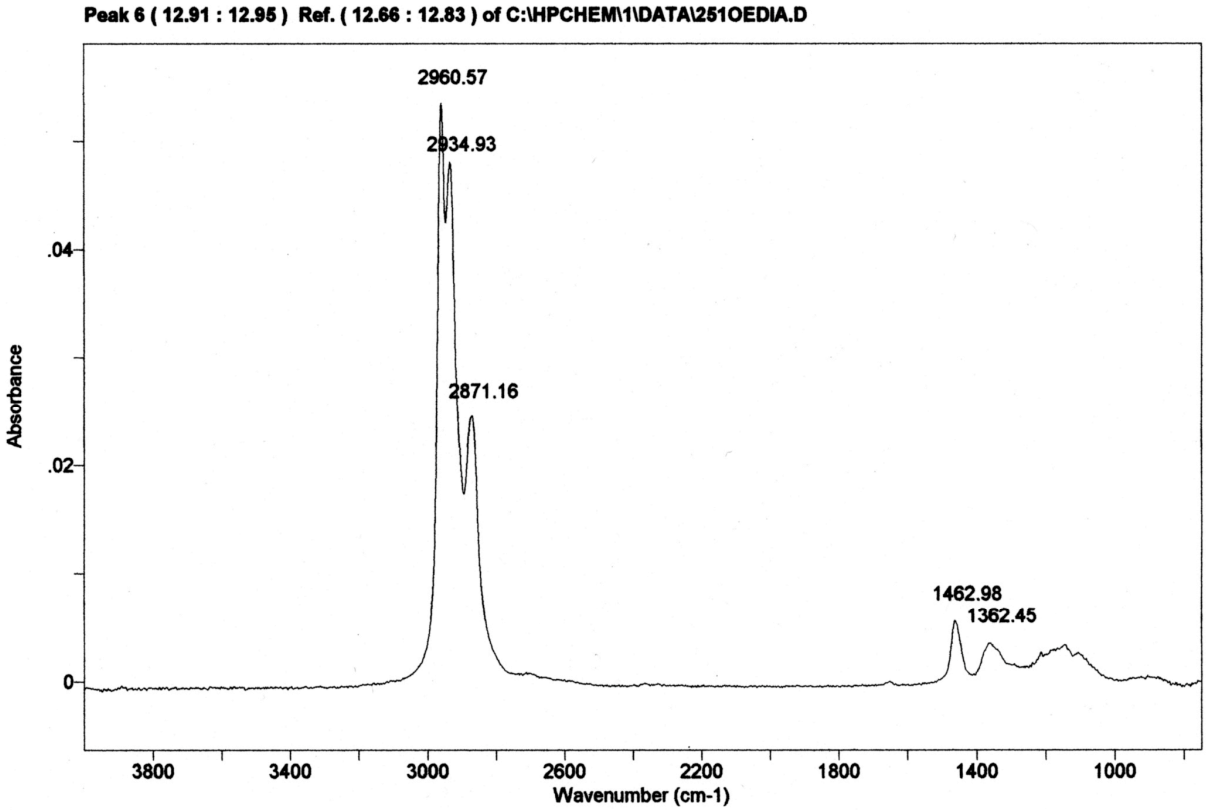
ent-14



ent-**14**

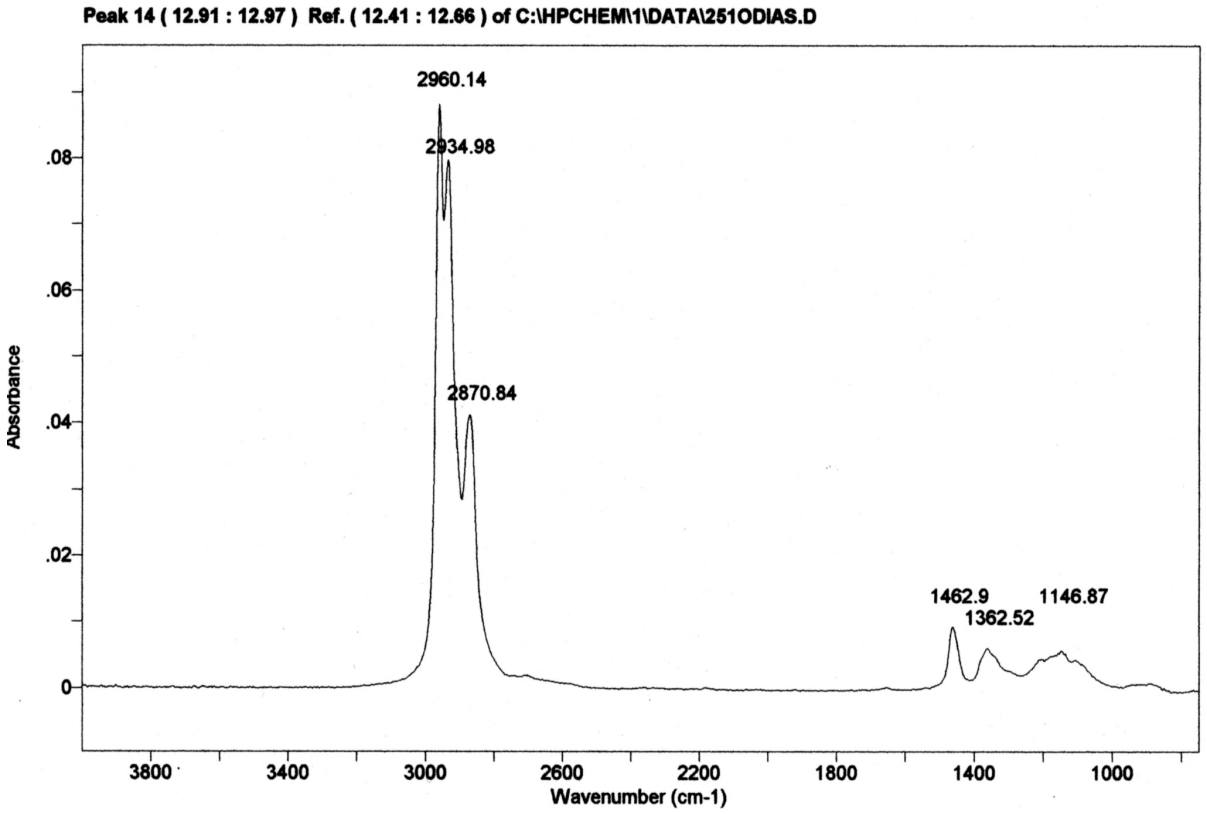



CH3 carbons
CH2 carbons
CH carbons
all protonated carbons
ppm
70
60
50
40
30
20



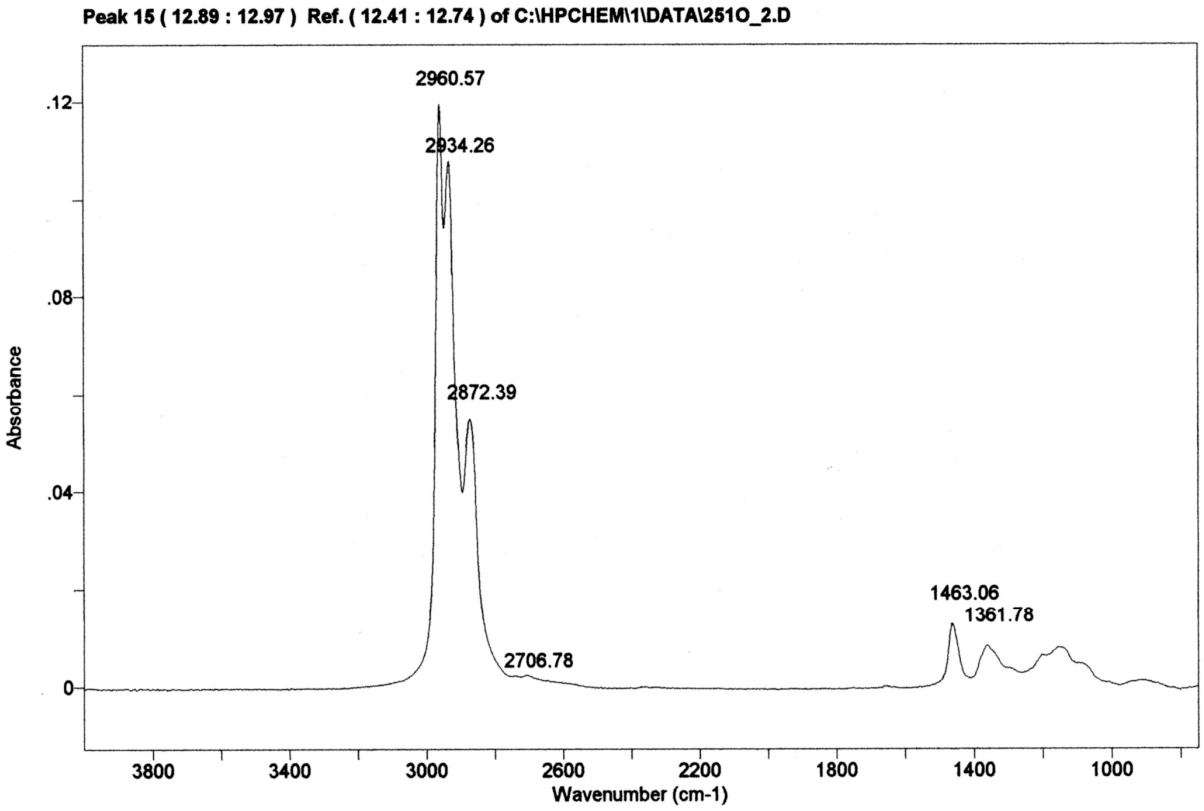
FT-IR spectrum of 7 (R = *n*-C_7H_{15}, R' = *n*-Pr)

The peak at around 2872 cm^{-1} (2871.16 cm^{-1}) is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}), but is identical with both FTIRs of *M. baroni* (2870.93 cm^{-1}) and *M. bernhardi* (2870.98 cm^{-1}). The shape between 1050 cm^{-1} and 1250 cm^{-1} is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}), but is identical with both FTIRs of *M. baroni* and *M. bernhardi*.



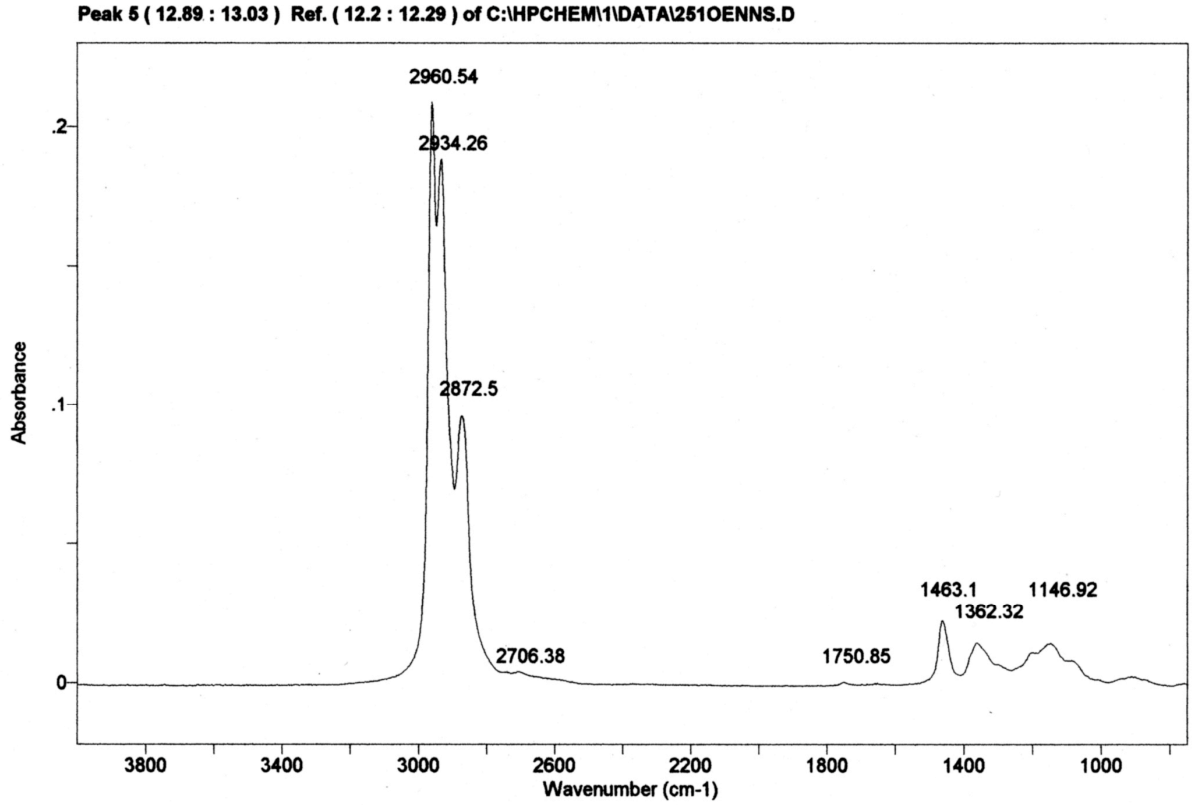
FT-IR spectrum of ent-7 (R = *n*-C_7H_{15}, R' = *n*-Pr)

The peak at around 2872 cm^{-1} (2870.84 cm^{-1}) is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}), but is identical with both FTIRs of *M. baroni* (2870.93 cm^{-1}) and *M. bernhardi* (2870.98 cm^{-1}). The shape between 1050 cm^{-1} and 1250 cm^{-1} is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}), but is identical with both FTIRs of *M. baroni* and *M. bernhardi*.



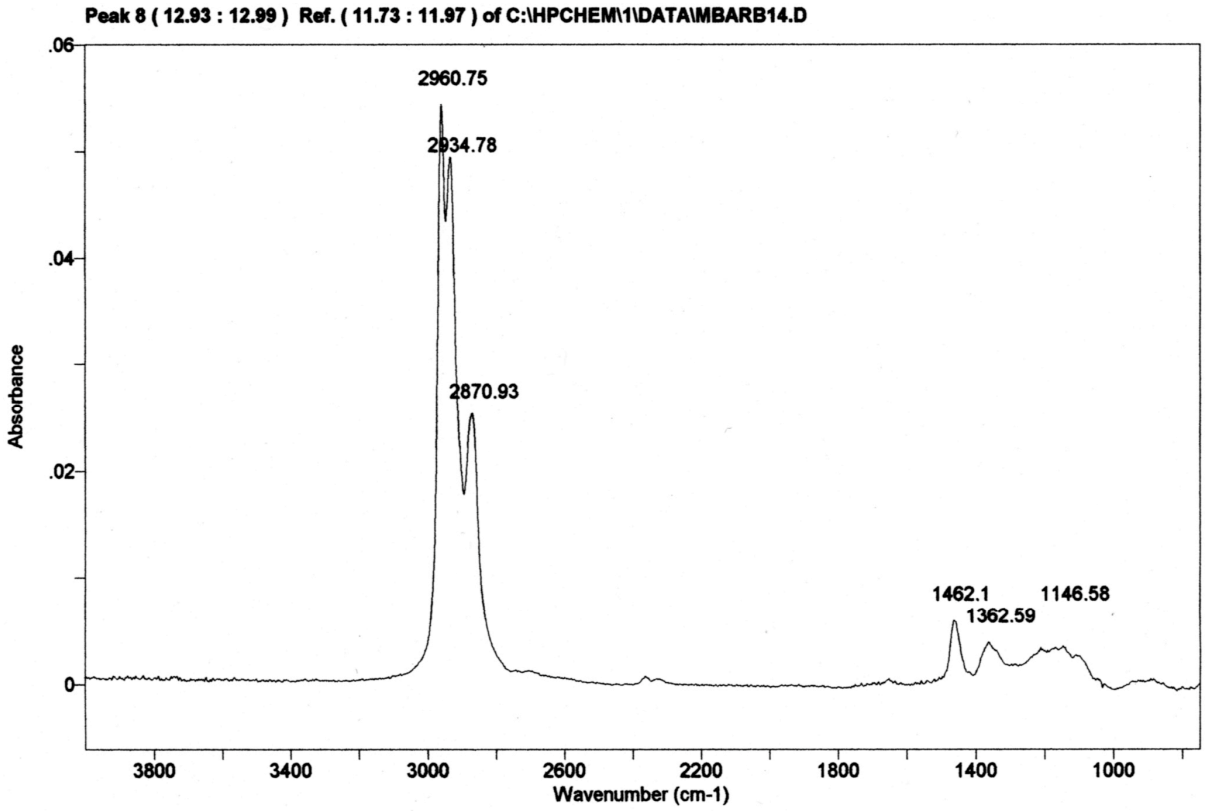
FT-IR spectrum of 7 (R = *n*-Pr, R' = *n*-C_7H_{15})

The peak at around 2872 cm^{-1} (2872.39 cm^{-1}) is different from both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2871.16 cm^{-1}) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2870.84 cm^{-1}), and is also different from both FTIRs of *M. baroni* (2870.93 cm^{-1}) and *M. bernhardi* (2870.98 cm^{-1}). The shape between 1050 cm^{-1} and 1250 cm^{-1} is different from both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr), and is also defferent from both FTIRs of *M. baroni* and *M. bernhardi*.



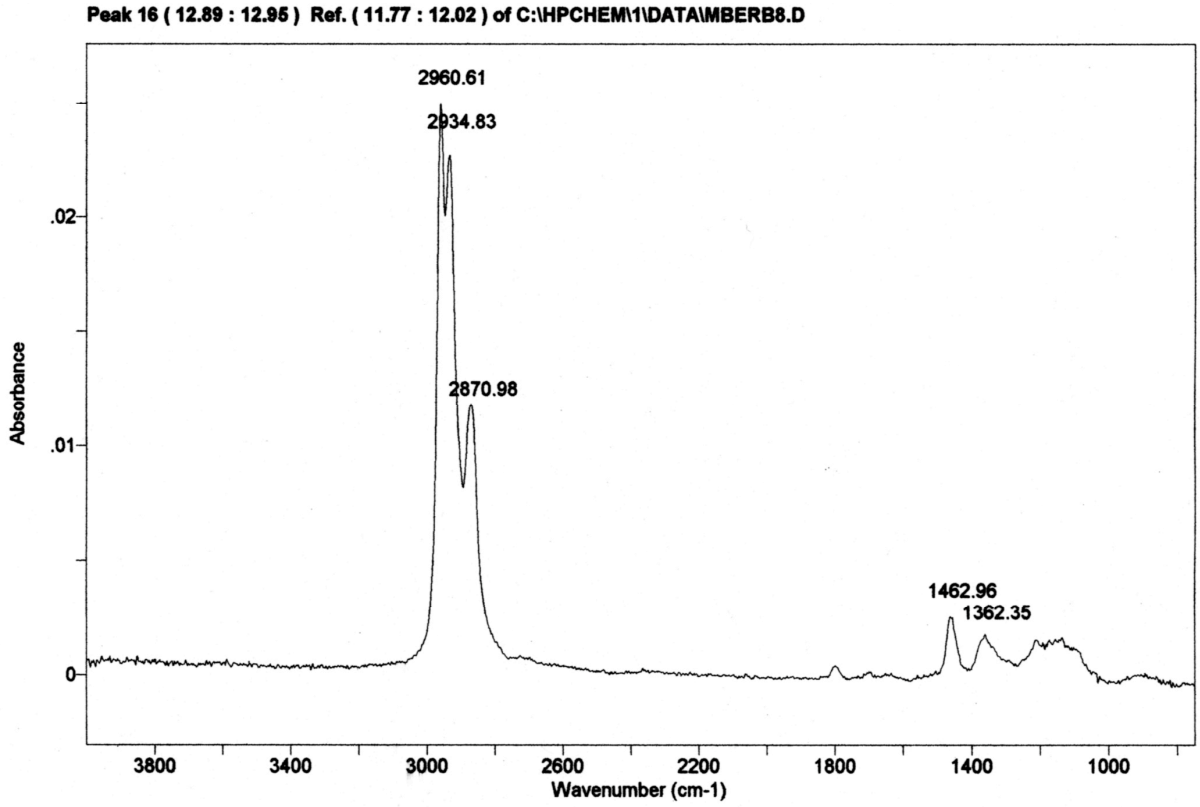
FT-IR spectrum of ent-7 (R = *n*-Pr, R' = *n*-C_7H_{15})

The peak at around 2872 cm^{-1} (2872.5 cm^{-1}) is different from both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2871.16 cm^{-1}) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2870.84 cm^{-1}), and is also different from both FTIRs of *M. baroni* (2870.93 cm^{-1}) and *M. bernhardi* (2870.98 cm^{-1}). The shape between 1050 cm^{-1} and 1250 cm^{-1} is different from both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr), and is also different from both FTIRs of *M. baroni* and *M. bernhardi*.



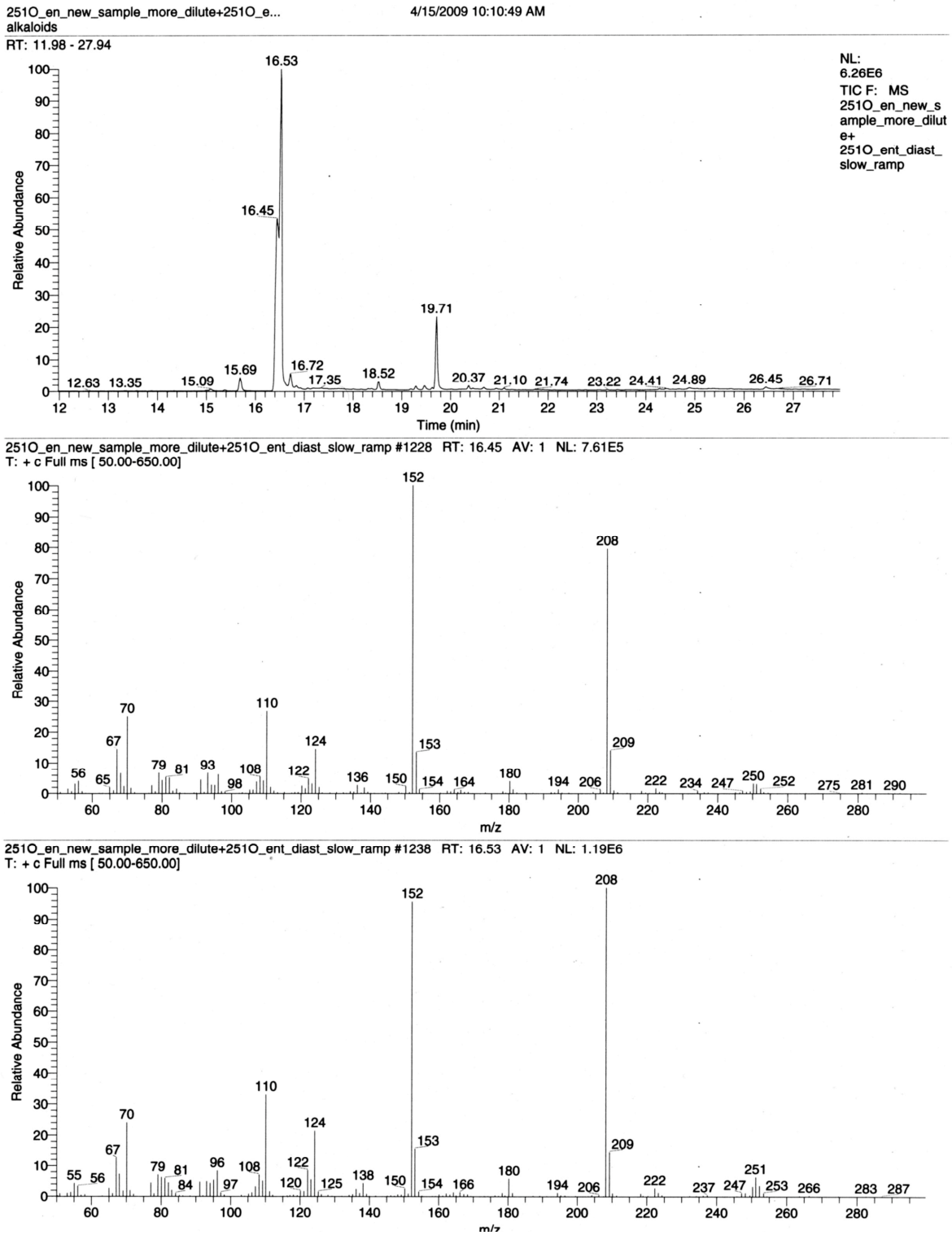
FT-IR spectrum of *M. baroni*

The peak at around 2872 cm^{-1} (2870.93 cm^{-1}) is identical with both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2871.16 cm^{-1}) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2870.84 cm^{-1}), but is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}, 2872.39 cm^{-1}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}, 2872.5 cm^{-1}). The shape between 1050 cm^{-1} and 1250 cm^{-1} is identical with both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr), but is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}).

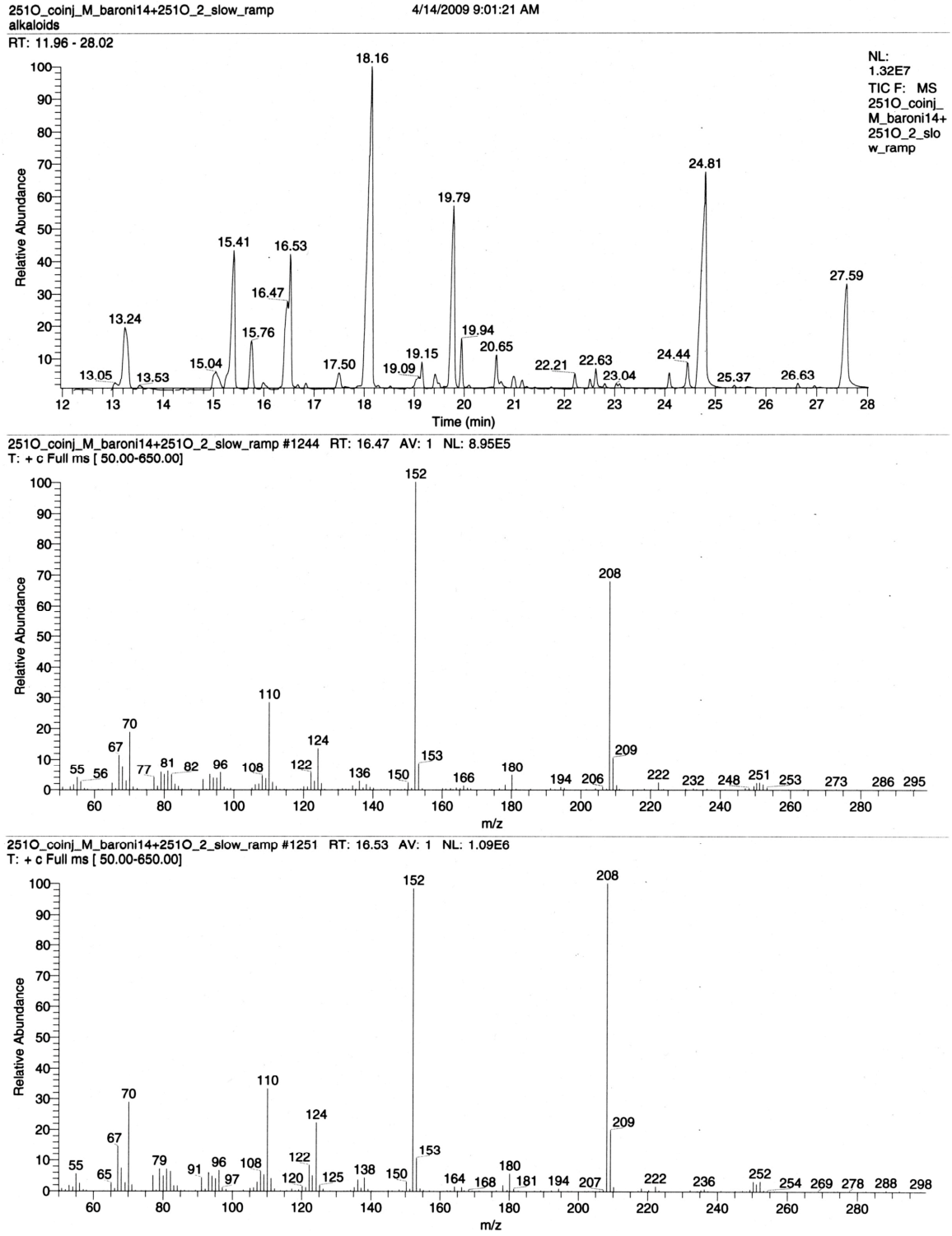


FT-IR spectrum of *M. bernhardi*

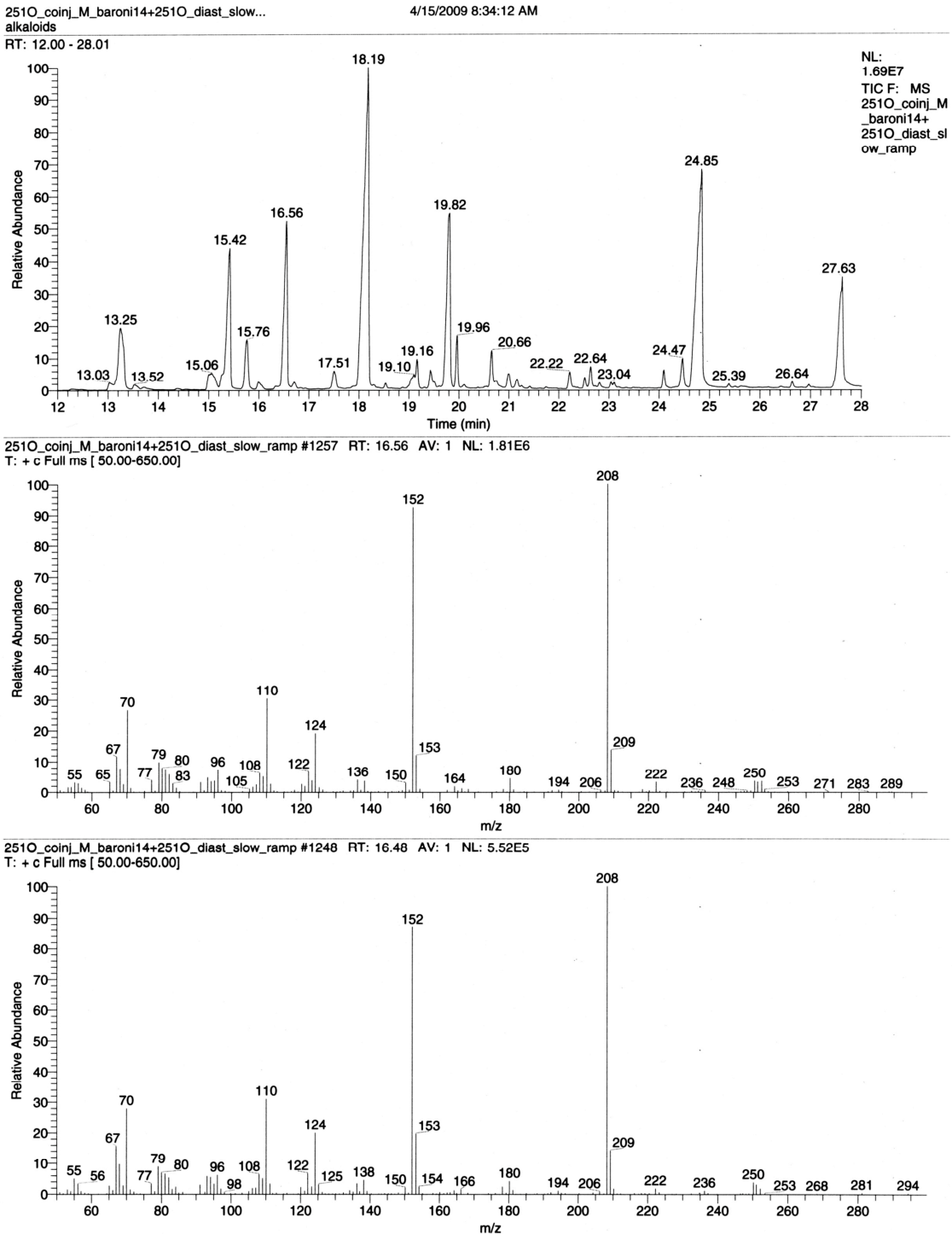
The peak at around 2872 cm^{-1} (2870.98 cm^{-1}) is identical with both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2871.16 cm^{-1}) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr, 2870.84 cm^{-1}), but is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}, 2872.39 cm^{-1}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}, 2872.5 cm^{-1}). The shape between 1050 cm^{-1} and 1250 cm^{-1} is identical with both FTIRs of **7** (R = *n*-C_7H_{15}, R' = *n*-Pr) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr), but is different from both FTIRs of **7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}).



GC-MS of a coinjection of ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr). They showed different Rt, and the fragment at m/z 208 is larger for ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr, Rt = 16.53 min).



GC-MS of a coinjection of ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}) and an extract of *M. baroni*. They showed different Rt (ent-**7** (R = *n*-Pr, R' = *n*-C_7H_{15}), Rt = 16.47 min, an extract of *M. baroni*, 16.53 min. The two mass spectra showed the same difference for the fragment at m/z 208.



GC-MS of a coinjection of ent-**7** (R = *n*-C_7H_{15}, R' = *n*-Pr) and an extract of *M. baroni*. The samples coeluted with Rt = 16.56 min, indicating that this is the right diastereomer for natural **251O**. Also the mass spec showed the large fragment at m/z 208. The second spectrum was taken at the start of the peak (16.48 min) and still showed large m/z 208. There is nothing here of the other diastereomer (ent-**7** (R = *n*-Pr, R' = C_7H_{15})).