Supporting Information:

Novel Polyhydroxylated Cyclic Nitrones and *N*-Hydroxy-Pyrrolidines through BCl_3-Mediated Deprotection

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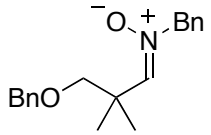
General Experimental Methods

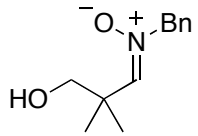
Reactions were performed under a positive pressure of dry argon in oven-dried, or flame-dried glassware equipped with a magnetic stir bar. Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents. Dichloromethane was freshly distilled over calcium hydride. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel plates. TLC spots were viewed under ultraviolet light and by heating the plate after treatment with either a 1% ethanolic solution of phosphomolybdic acid reagent or a 3% solution of potassium permanganate in 10% aqueous potassium hydroxyde (w/v) . Product purification by gravity column chromatography was performed using Silica Gel 60 (70-230 mesh). Melting points were determined in capillary tubes and are uncorrected. Infrared (IR) spectra were recorded on a Fourier Transform spectrometer as neat films, or as a thin film of a dichloromethane solution of the compound on sodium chloride discs. The data are reported in reciprocal centimeters (cm^{-1}) and are assigned as following: br (broad), s (strong), m (medium), w (weak). Chemical shifts for ^1H spectra are values downfield from tetramethylsilane in $CDCl_3$ (δ 0.00), HOD for D_2O (δ 4.79) or CD_3OD and are reported as follows: chemical shift (ppm), multiplicity, integration, and coupling constants (Hz). Mass spectra (MS) were recorded on a ion-trap spectrometer using DCI (ammonia/isobutane 63/37) or the electrospray techniques (ESI). High resolution mass spectra (HRMS) were recorded at the LCOSB, UMR 7613, Université Pierre et Marie Curie, Paris. Elemental analyses were performed at the Service d'Analyse Elementaire du Département de Chimie Moléculaire, Grenoble.

Typical procedure for the BCl_3 deprotection of polyalkoxy-substituted nitrones and *N*-hydroxypyrrolidines: To a stirred solution of polyalkoxy compound (0.1 mmol) in CH_2Cl_2 (10 mL) cooled to 0 °C, under argon, a solution of BCl_3 (1 M, 3 equivalents per alkoxy group) in hexanes was added at 0 °C. After 15 h, ethanol was added and the reaction mixture was concentrated under vacuum. The residue was dissolved in a minimum of water and neutralized with DOWEX 1X8 or DOWEX 1X4-50 (OH^- form). After filtration, the filtrate was lyophilized to afford the deprotected polyhydroxylated product, which was characterized without further purification.



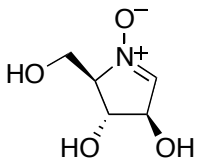
1

(*Z*)-*N*-(3-(Benzyloxy)-2,2-dimethylpropylidene)-1-phenylmethanamine oxide (1): To solution of 3-benzyloxy-2,2-dimethyl propanal (600 mg, 3.1 mmol) in dichloromethane (10 mL) were added excess $MgSO_4$ (1 g) and *N*-benzyl hydroxylamine (384 mg, 3.1 mmol) and the resulting suspension was stirred during 24 h at 20 °C. After filtration over celite, evaporation of the solvent, and purification by column chromatography (pentane:AcOEt 1/1, then 0/1) nitrone **1** was isolated as a white solid (562 mg, 61%): mp 93-94 °C; MS (ESI) *m/z* 298 $[M + H]^+$, 320 $[M + Na]^+$; IR ν (cm^{-1}) 3071 (m), 2954 (s), 2801 (s), 1576 (w); ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 6 H); 3.54 (s, 2 H); 4.46 (s, 2 H); 4.82 (s, 2 H); 6.60 (s, 1 H); 7.23-7.36 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0 (CH_3); 37.7 (Cq); 70.5 (CH_2); 73.1 (CH_2); 75.9 (CH_2); 127.2 (CH); 127.3 (CH); 128.2 (CH); 128.5 (CH); 128.6 (CH); 128.7 (CH); 133.5 (Cq); 138.5 (Cq); 142.7 (CH). Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 77.08; H, 7.96; N, 4.99.



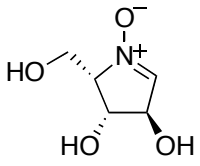
2

(*Z*)-*N*-(3-Hydroxy-2,2-dimethylpropylidene)-1-phenyl-methanamine oxide (2): prepared according to general procedure from nitrone **1** (89 mg, 0.3 mmol) and a 1 M solution of BCl_3 in hexane (0.9 mL, 0.9 mmol). After purification by chromatography (pentane:AcOEt 1/1, then 0/1) the deprotected nitrone **2** was obtained as a colorless solid (35 mg, 56%): mp 94-95 °C; MS (DCI) *m/z* (%) 208 (94) $[M + H]^+$, 192 (100) $[M + H - O]^+$; IR ν (cm^{-1}) 3240 (br), 3053 (s), 2968 (s), 2872 (s), 1596 (w); ^1H NMR (300 MHz, $CDCl_3$) δ 1.18 (s, 6 H); 3.60 (s, 2 H); 4.88 (s, 2 H); 6.50 (s, 1 H); 7.39 (s, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9 (CH_3); 39.7 (Cq); 69.3 (CH_2); 70.2 (CH_2); 128.8 (CH); 129.0 (CH); 132.8 (Cq); 146.1 (CH). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.80; H, 8.26; N, 6.36.



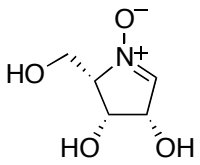
9

(2*R*,3*R*,4*R*)-3,4-Dihydroxy-2- hydroxymethyl l-3,4-dihydro-2*H*-pyrrole 1-oxide (9): prepared according to general procedure from nitrone **3** (78 mg, 0.19 mmol) and a 1 M solution of BCl_3 in hexane (1.7 mL, 1.70 mmol). The deprotected nitrone **9** was obtained as a colorless oil (27 mg, 97%); $[\alpha]^{20}_D$ = –45 (*c* 1.17, MeOH); MS (DCI) *m/z* (%) 130 (22) $[M + H - H_2O]^+$, 148 (100) $[M + H]^+$; IR ν (cm^{-1}) 3293 (br), 2932 (s), 2872 (s), 1595 (w); ^1H NMR (300 MHz, D_2O) δ 3.90 (dd, 1 H, *J* = 2.5, 12.5 Hz); 4.02-4.09 (m, 1 H); 4.24 (dd, 1 H, *J* = 3.0, 12.5 Hz); 4.84-4.87 (m, 1 H); 7.38 (br s, 1 H); ^{13}C NMR (75 MHz, D_2O) δ 56.6 (CH_2); 74.8 (CH); 76.4 (CH); 79.2 (CH); 141.7 (CH); HRMS (ESI) Calcd for $C_5H_9NNaO_4$: *m/z* = 170.04238 $[M + Na]^+$; Found *m/z* = 170.04239.



10

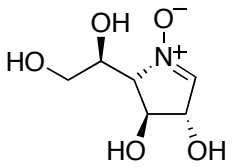
(2*R*,3*R*,4*S*)-3,4-Dihydroxy-2- hydroxymethyl l-3,4-dihydro-2*H*-pyrrole 1-oxide (10): prepared according to general procedure from nitrone **4** (57 mg, 0.14 mmol) and a 1 M solution of BCl_3 in hexane (1.2 mL, 1.20 mmol). The deprotected nitrone **10** was obtained as a colorless oil (17 mg, 85%); $[\alpha]^{20}_D$ = –46 (*c* 1.28, MeOH); MS (ESI) *m/z* 148 $[M + H]^+$, IR ν (cm^{-1}) 3180 (br), 2962 (s), 2921 (s), 2846 (s), 1621 (m); ^1H NMR (300 MHz, CD_3OD) δ 4.00 (dd, 2 H, *J* = 2.0, 3.0 Hz); 4.06-4.10 (m, 1 H); 4.39 (dd, 1 H, *J* = 4.5, 7.5 Hz); 4.73 (td, 1 H, *J* = 1.5, 4.5 Hz); 7.09 (br s, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 58.0 (CH_2); 77.2 (CH); 77.9 (CH); 79.2 (CH); 140.9 (CH); HRMS (ESI): Calcd for $C_5H_9NNaO_4$: *m/z* = 170.04238 $[M + Na]^+$; Found *m/z* = 170.04243.



11

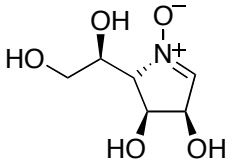
(2*S*,3*R*,4*S*)-3,4-Dihydroxy-2-(hydroxymethyl)-3,4-dihydro-2*H*-pyrrole 1-oxide (11): prepared according to the general procedure from nitrone **5** (200 mg, 0.48 mmol) and a 1 M solution of BCl_3 in hexane (4.32 mL, 4.32 mmol). The deprotected nitrone **11** was obtained as a beige solid (52 mg, 74%); m.p. 69-71°C; $[\alpha]^{20}_D$ = +15 (*c* 1.0, MeOH); MS (DCI) *m/z* (%) 148 (75) $[M + H]^+$, 130 (100)

$[M + H - H_2O]^+$; IR ν (cm^{-1}) 3358 (br), 2950 (s), 2877 (s), 1588 (w); ^1H NMR (300 MHz, D_2O) δ 3.97 (dd, 1 H, J = 3.0, 12.5 Hz); 4.08 (dd, 1 H, J = 4.0, 12.5 Hz); 4.22-4.25 (m, 1 H); 4.73-4.79 (m, 1 H); 4.88 (dd, 1 H, J = 2.0, 6.5 Hz); 7.41 (s, 1 H); ^{13}C NMR (75 MHz, D_2O) δ 55.5 (CH); 66.9 (CH); 69.8 (CH); 75.1 (CH); 141.6 (CH); HRMS (ESI) Calcd for $C_5H_9NNaO_4$: m/z = 170.04238 $[M + Na]^+$; Found m/z = 170.04239.



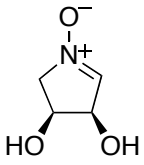
12

(2*S*,3*S*,4*S*)-2-((*S*)-1,2-Dihydroxyethyl)-3,4-dihydroxy-3,4-dihydro-2*H*-pyrrole 1-oxide (12): prepared according to the general procedure from nitrone **6** (150 mg, 0.28 mmol) and a 1 M solution of BCl_3 in hexane (3.35 mL, 3.35 mmol). The deprotected nitrone **12** was obtained as a brown oil (45 mg, 91%); $[\alpha]^{20}_D$ = +34 (*c* 0.9, MeOH); MS (ESI) m/z 178 $[M + H]^+$, 200 $[M + Na]^+$; IR ν (cm^{-1}) 3362 (br), 2942 (s), 2880 (s), 1593 (w); ^1H NMR (300 MHz, D_2O) δ 3.87-3.98 (m, 2 H); 4.14-4.21 (m, 2 H); 4.36 (t, 1 H, J = 3.5 Hz); 4.83 (br t, 1 H, J = 2.0 Hz); 7.39 (br s, 1 H); ^{13}C NMR (100 MHz, D_2O) δ 60.4 (CH_2); 67.9 (CH); 73.8 (CH); 74.2 (CH); 76.9 (CH); 139.6 (CH); HRMS (ESI) Calcd for $C_6H_{11}NNaO_5$: m/z = 200.05294 $[M + Na]^+$; Found m/z = 200.05307.



13

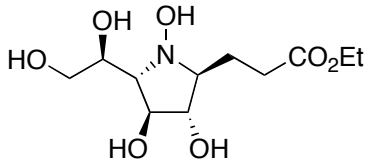
2-((*S*)-1,2-Dihydroxyethyl)-(2*S*,3*S*,4*R*)-3,4-dihydroxy-2*H*-pyrrole 1-oxide (13): prepared according to general procedure from nitrone **7** (103 mg, 0.40 mmol) and a 1 M solution of BCl_3 in hexane (4.8 mL, 4.80 mmol). The deprotected nitrone **13** was obtained as a colorless oil (63 mg, 88%); $[\alpha]^{20}_D$ = −72 (*c* 1.13, MeOH); MS (DCI) m/z (%) 178 (100) $[M + H]^+$; IR ν (cm^{-1}) 3300 (br), 2932 (s), 2884 (s), 1591 (w); ^1H NMR (300 MHz, CD_3OD) δ 3.71-3.82 (m, 2 H); 4.00-4.05 (m, 1 H); 4.07 (br s, 1 H); 4.41 (dd, 1 H, J = 1.5, 5.5 Hz); 4.90 (br d, 1 H, J = 1.5 Hz); 7.12 (br s, 1 H); ^{13}C NMR (75 MHz, D_2O): δ 62.7 (CH_2); 70.5 (CH); 71.0 (CH); 71.6 (CH); 81.3 (CH); 142.9 (CH); HRMS (ESI) Calcd for $C_6H_{11}NNaO_5$: m/z = 200.05294 $[M + Na]^+$; Found m/z = 200.05309.



14

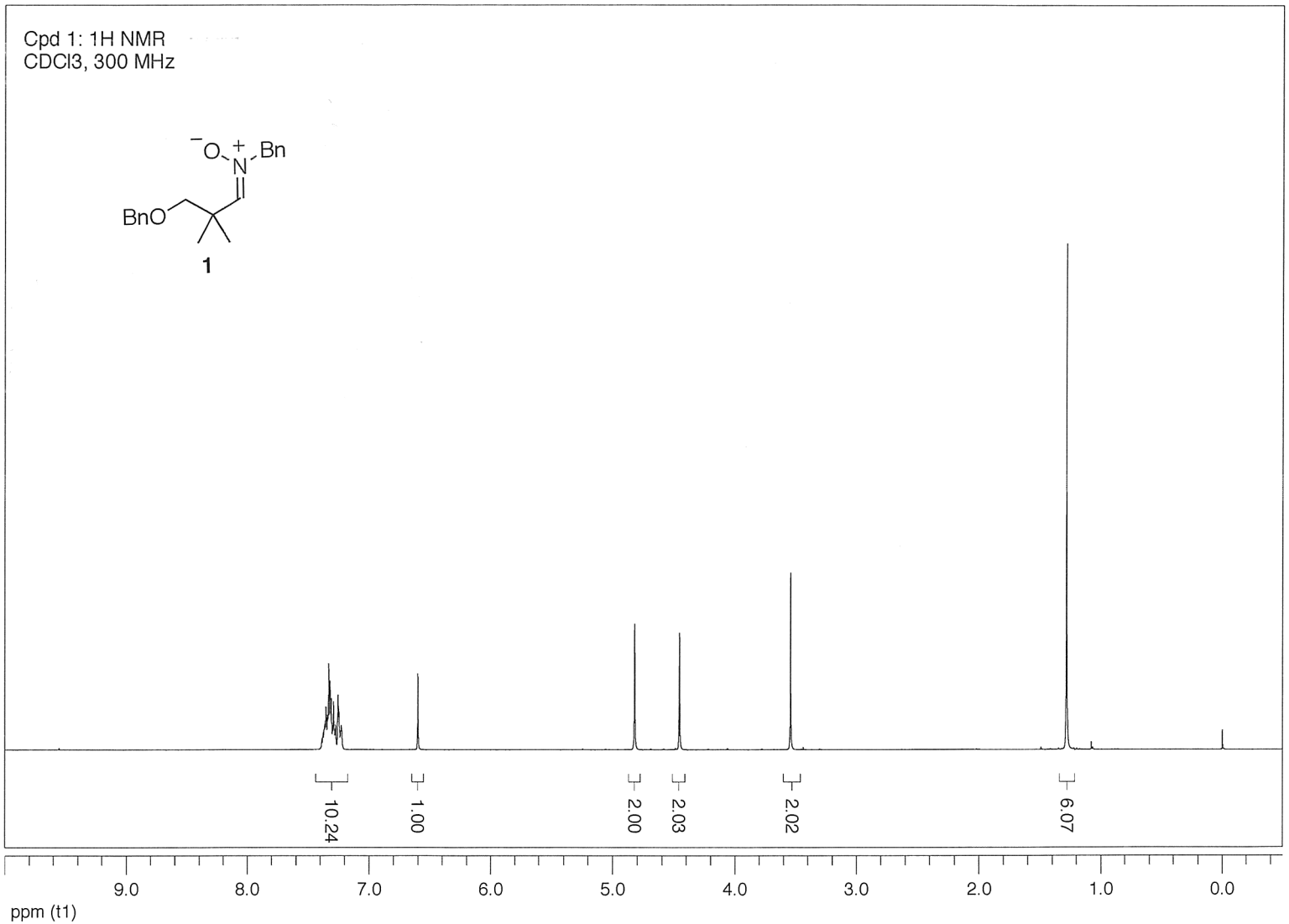
(3*S*,4*R*)-3,4-Dihydroxy-3,4-dihydro-2*H*-pyrrole 1-oxide (14): prepared according to the general procedure from nitrone **8** (60 mg, 0.38 mmol) and a 1 M solution of BCl_3 in hexane (2.26 mL, 2.26 mmol). The deprotected nitrone **14** was obtained as a brown oil (25 mg, 57%); $[\alpha]^{20}_D$ = −111 (*c* 1.04, MeOH); MS (DCI) m/z (%) 118 (100) $[M + H]^+$; IR ν (cm^{-1}) 3340 (br), 2968 (s), 2943 (s), 2833 (s),

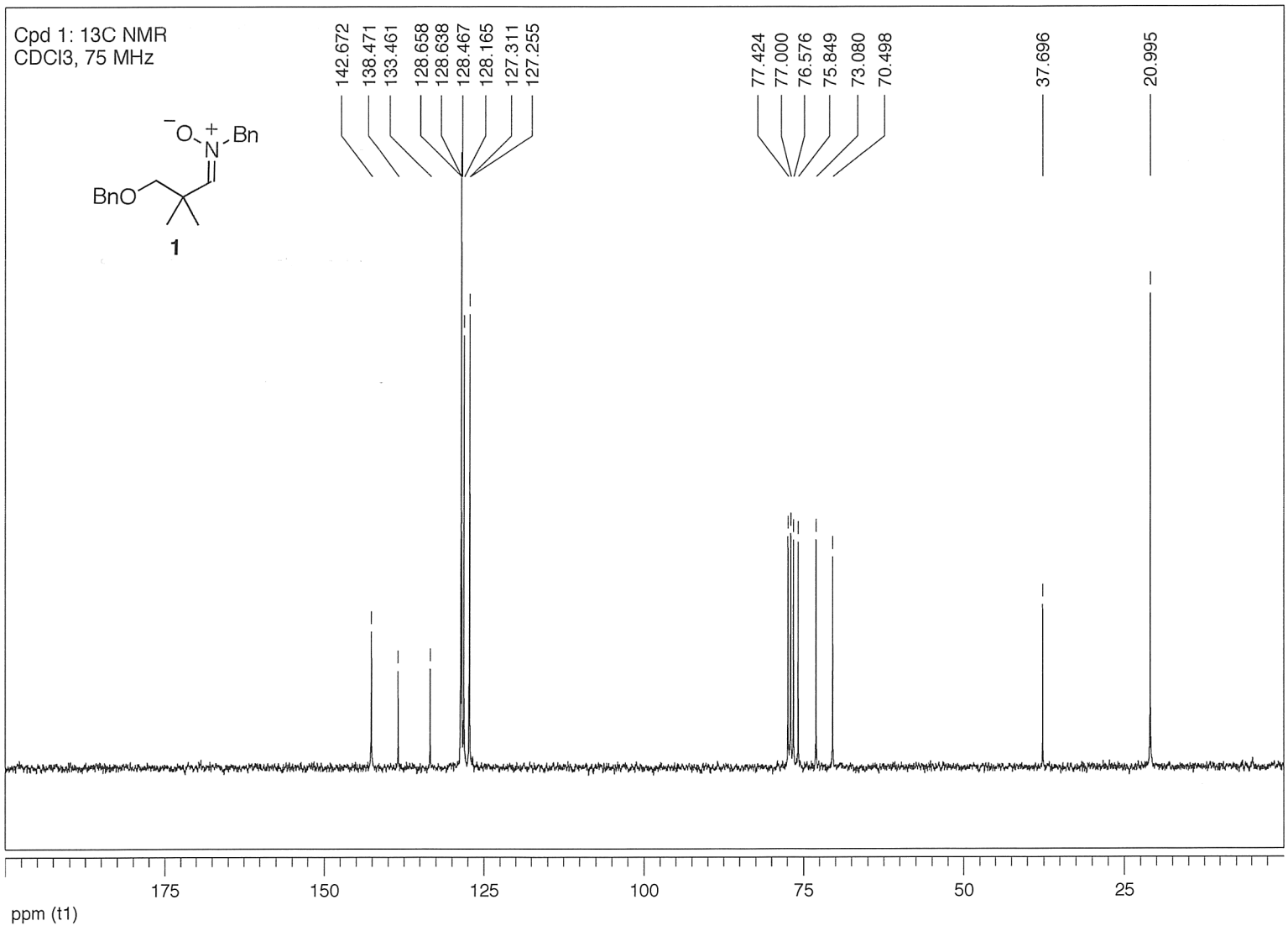
1595 (w); ^{1}H NMR (300 MHz, CD_3OD) δ 3.79 (ddd, 1H, *J* = 1.0, 2.0, 14.0 Hz); 4.0 (dddd, 1H, *J* = 1.0, 2.0, 5.5, 14.0 Hz); 4.50 (td, 1 H, *J* = 2.0, 5.5 Hz); 4.87 (br d, 1 H, *J* = 5.5 Hz); 7.06 (s, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 68.8 (CH); 69.8 (CH); 73.8 (CH); 140.6 (CH); HRMS (ESI) Calcd for $C_4H_7NNaO_3$: *m/z* = 140.03181 $[M + Na]^+$; Found *m/z* = 140.03175.

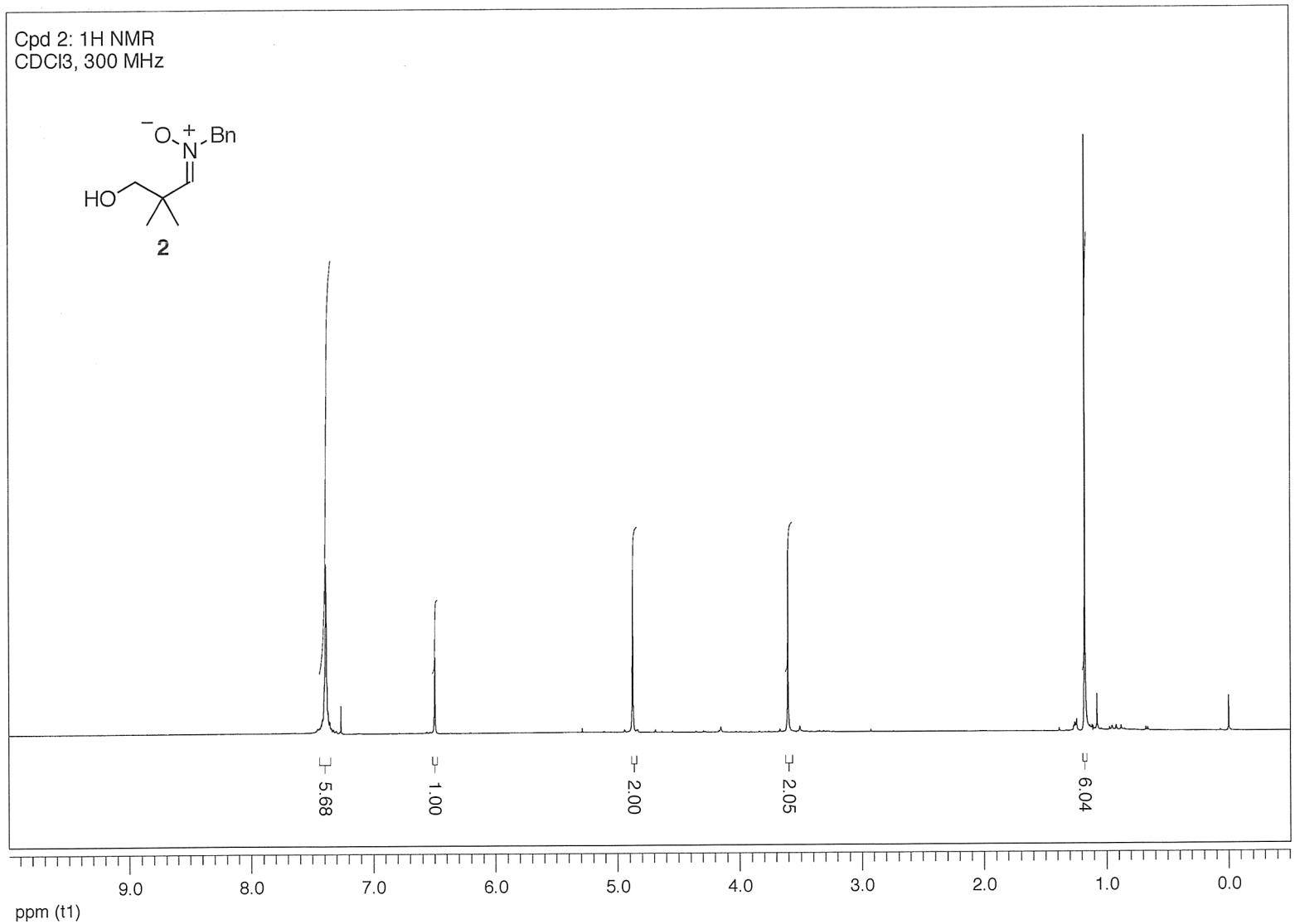


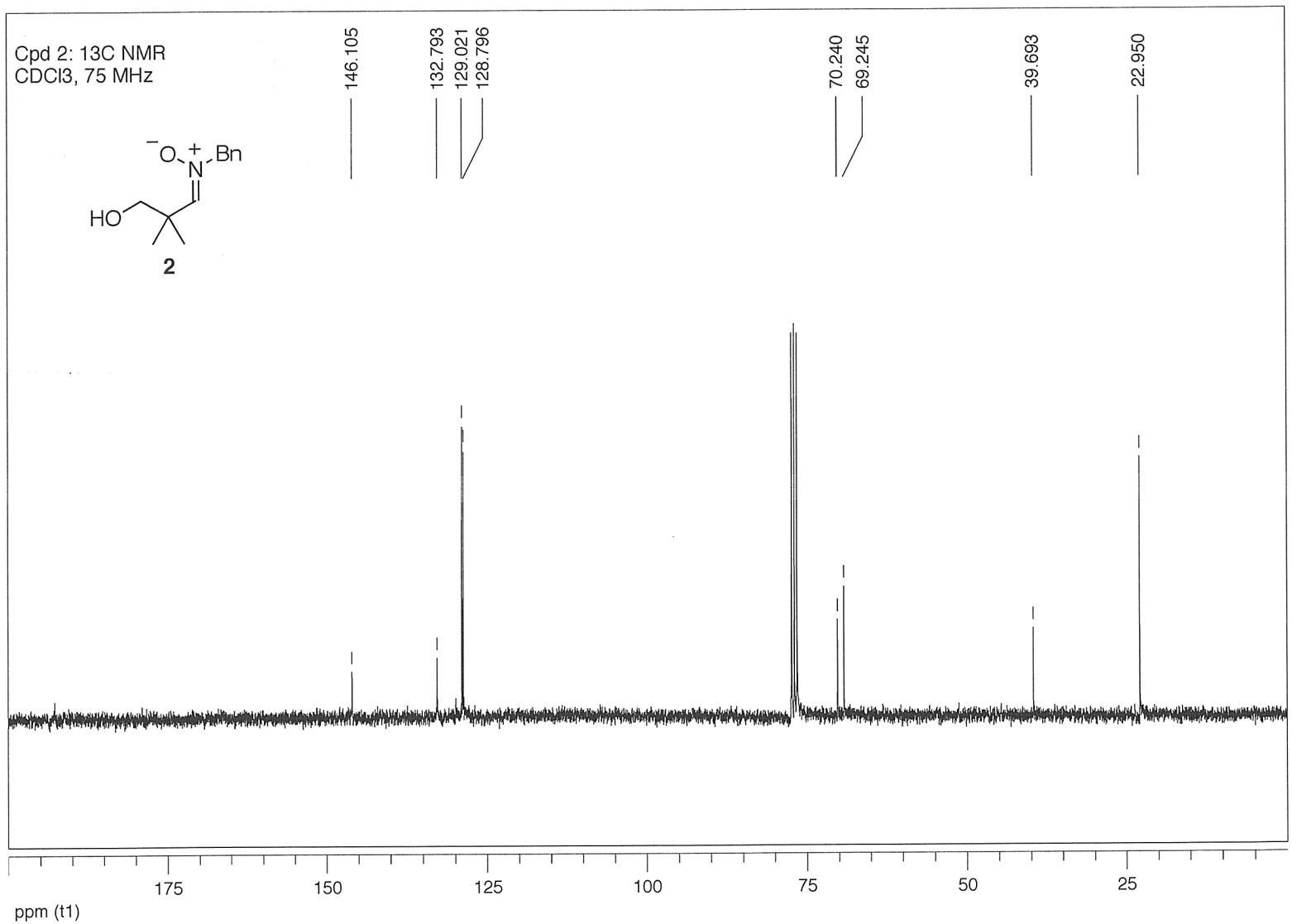
16

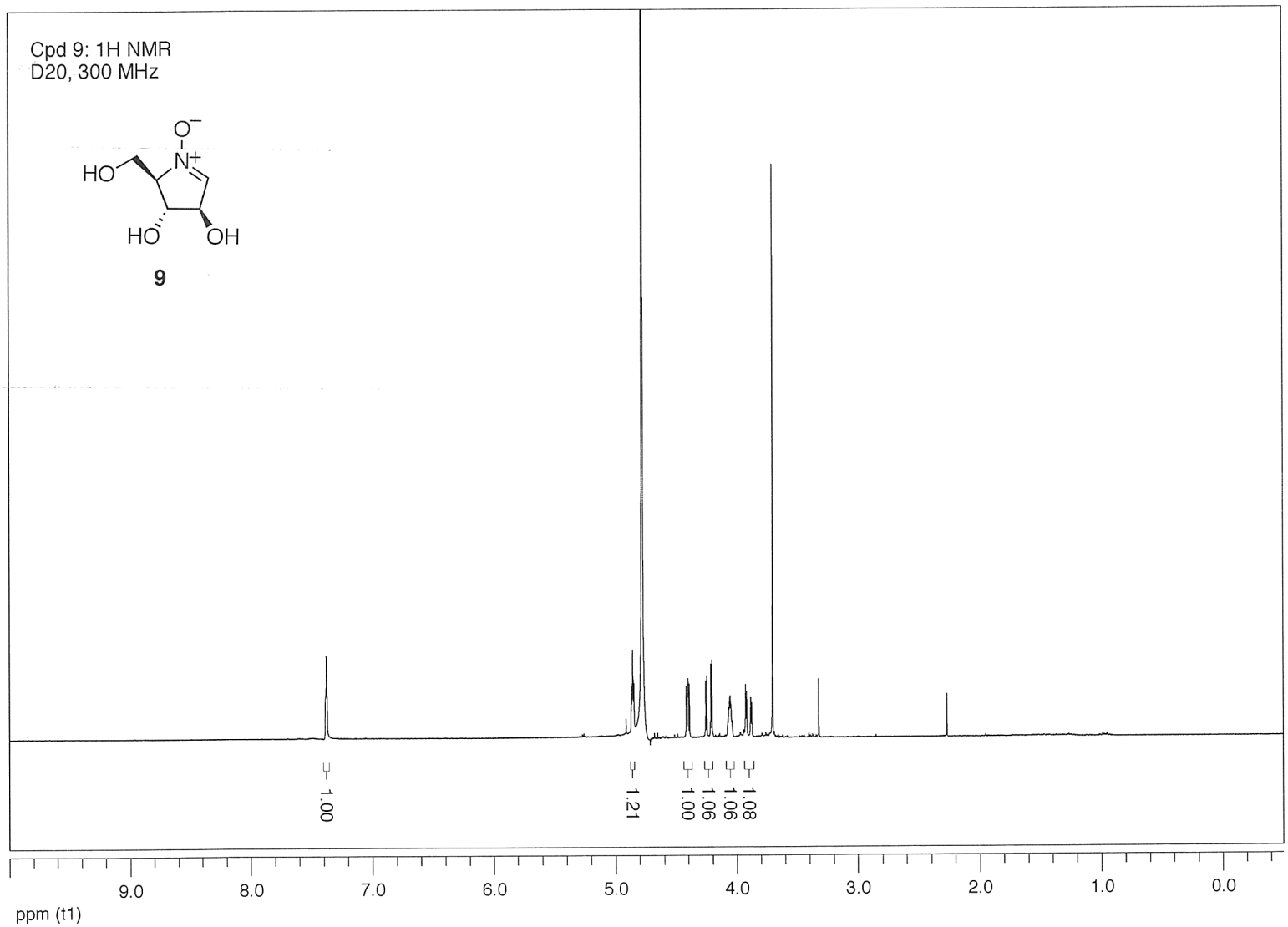
3-((2*S*,3*S*,4*S*,5*S*)-5-((*S*)-1,2- Dihydroxyethyl)-3,4- dihydroxy)-1-hydroxy-pyrrolidin-2-yl) propionic acid ethyl ester (16): prepared according to the general procedure from *N*-hydroxypyrrolidine **15** (20 mg, 0.03 mmol) and a 1 M solution of BCl_3 in hexane (380 μL, 0.38 mmol). After purification by chromatography (CH_2Cl_2/MeOH: 95/5, 90/10, then 80/20) the deprotected *N*-hydroxypyrrolidine **16** was obtained as a brown oil (8 mg; 92%); $[\alpha]^{20}_D = -7$ (*c* 1.1 ; MeOH); MS (ESI) *m/z* = 280 $[M + H]^+$, 264 $[M + H - H_2O]^+$; IR ν (cm^{-1}) 3349 (br), 2981 (s), 2932 (s), 1715 (s); ^{1}H NMR (300 MHz, CD_3OD) δ 1.21 (t, 3 H, *J* = 7 Hz); 1.85-2.00 (m, 1 H); 2.02-2.16 (m, 1 H); 2.43-2.64 (m, 2 H); 2.90-2.98 (m, 1 H); 3.04-3.12 (m, 1 H); 3.66-3.78 (m, 3 H); 3.88-3.98 (m, 2 H); 4.09 (q, 2 H, *J* = 7 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 14.5 (CH_3); 24.9 (CH_2); 32.4 (CH_2); 61.5 (CH_2); 65.4 (CH_2); 71.6 (CH); 73.0 (CH); 76.2 (CH); 80.1 (CH); 81.9 (CH); 175.7 (C=O).

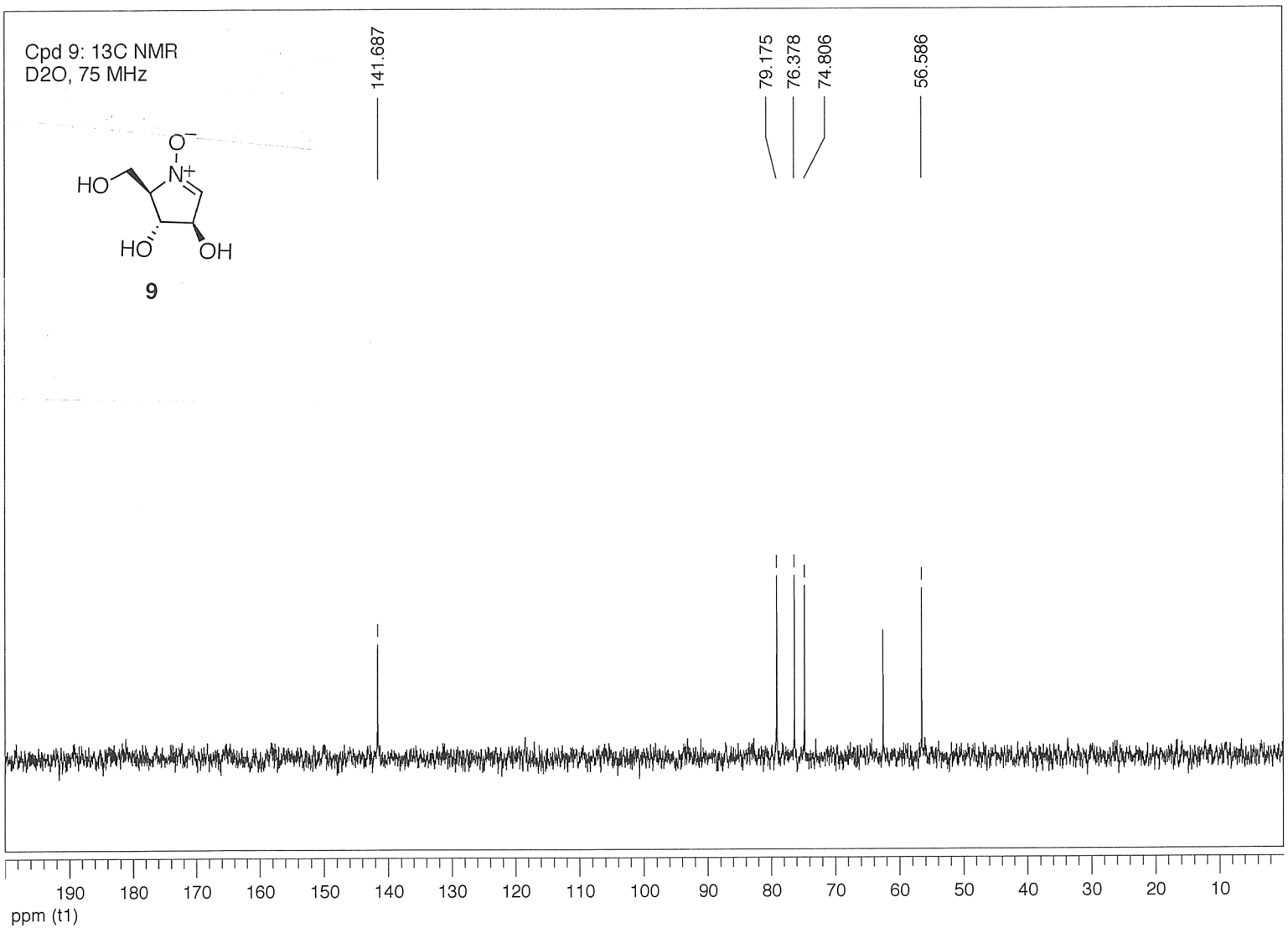

Cpd 1: 1H NMR
CDCl3, 300 MHz
BnO
Bn
1
10.24
1.00
2.00
2.03
2.02
6.07
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

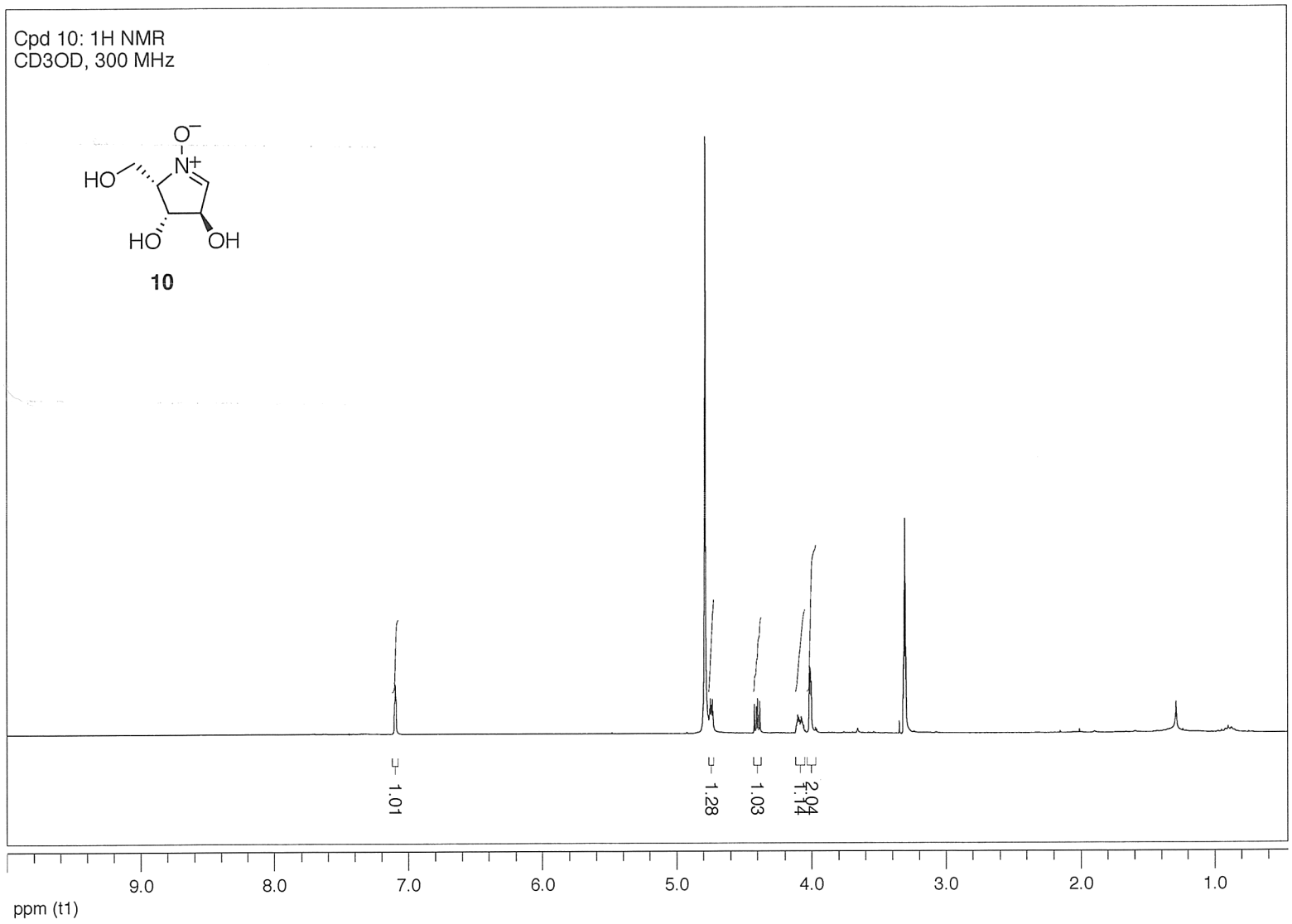

Cpd 1: 13C NMR
CDCl3, 75 MHz
142.672
138.471
133.461
128.658
128.638
128.467
128.165
127.311
127.255
77.424
77.000
76.576
75.849
73.080
70.498
37.696
20.995
BnO
Bn
1
175
150
125
100
75
50
25
ppm (t1)

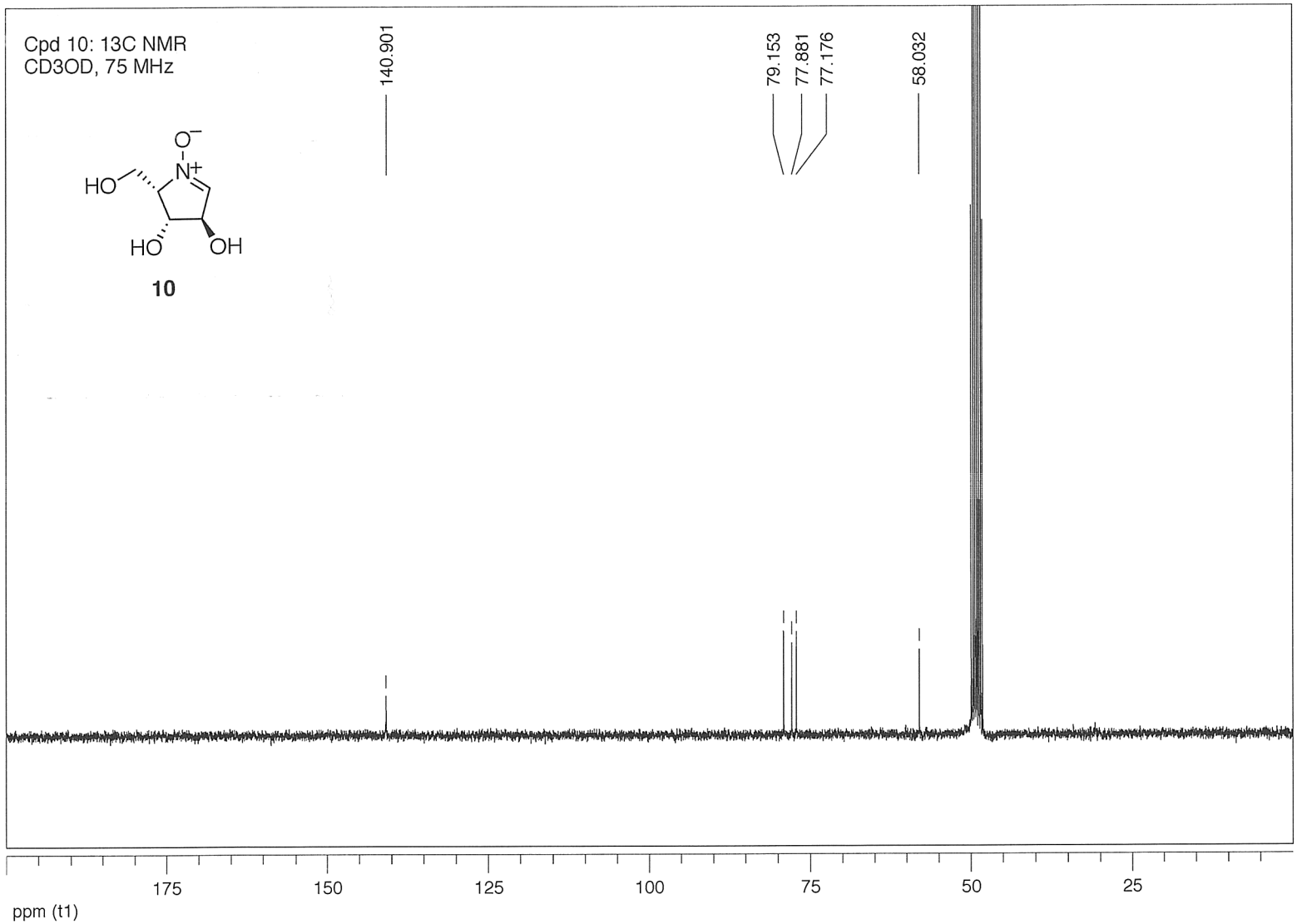

Cpd 2: 1H NMR
CDCl3, 300 MHz
HO
Bn
2
5.68
1.00
2.00
2.05
6.04
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

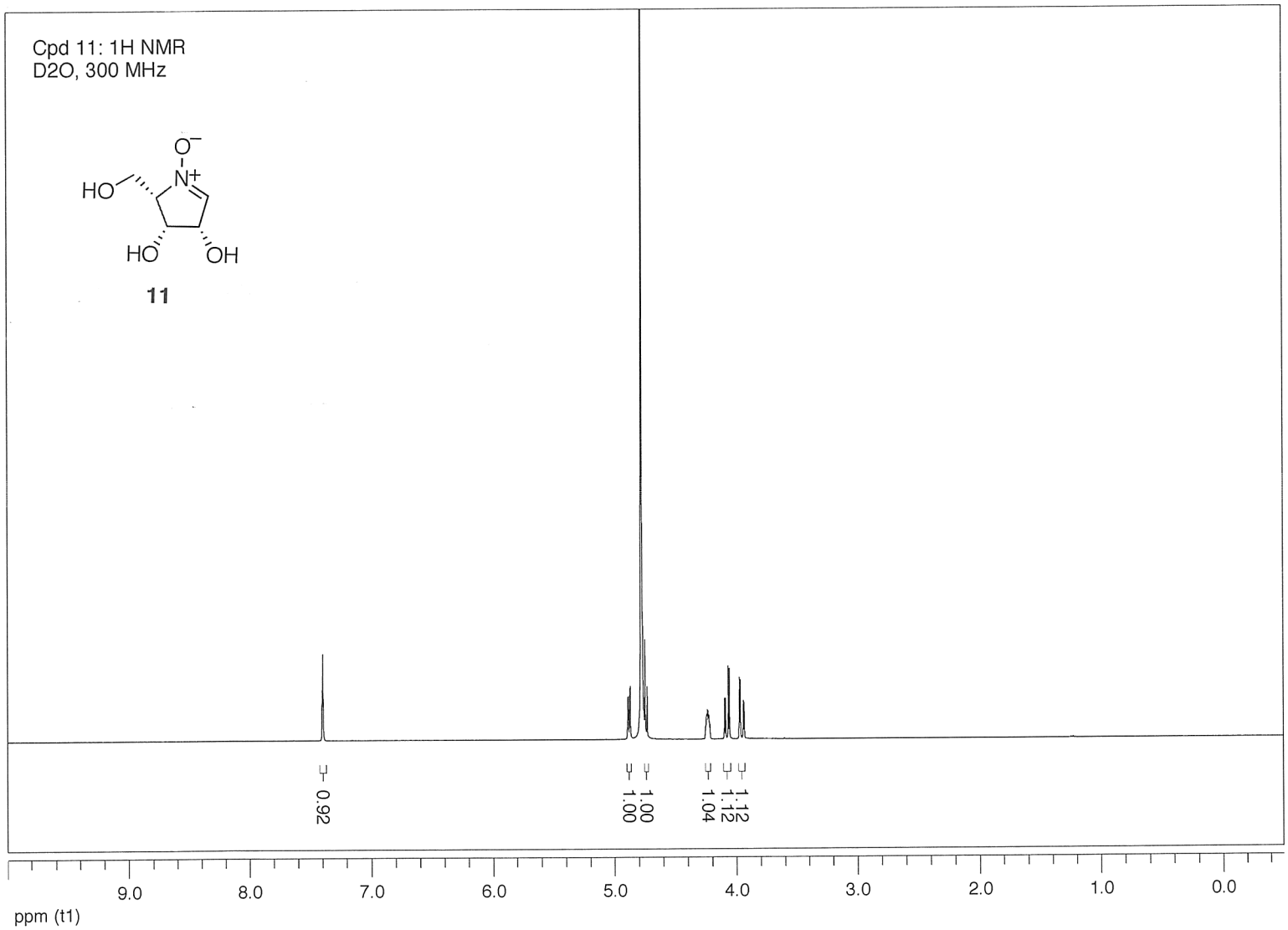

Cpd 2: 13C NMR
CDCl3, 75 MHz
146.105
132.793
129.021
128.796
70.240
69.245
39.693
22.950
HO
Bn
2
175
150
125
100
75
50
25
ppm (t1)

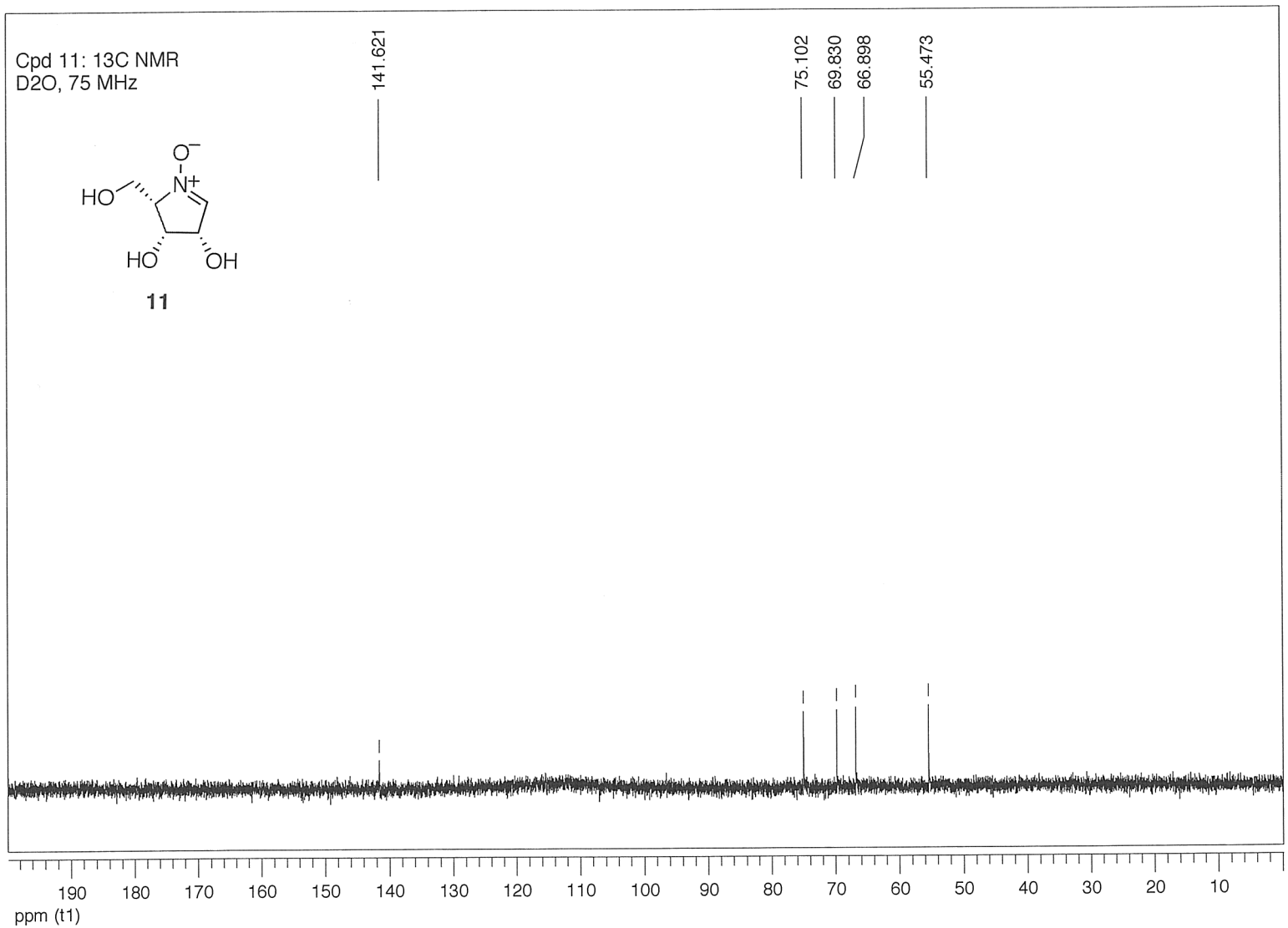

Cpd 9: 1H NMR
D20, 300 MHz
HO
HO
OH
9
1.00
1.21
1.00
1.06
1.06
1.08
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

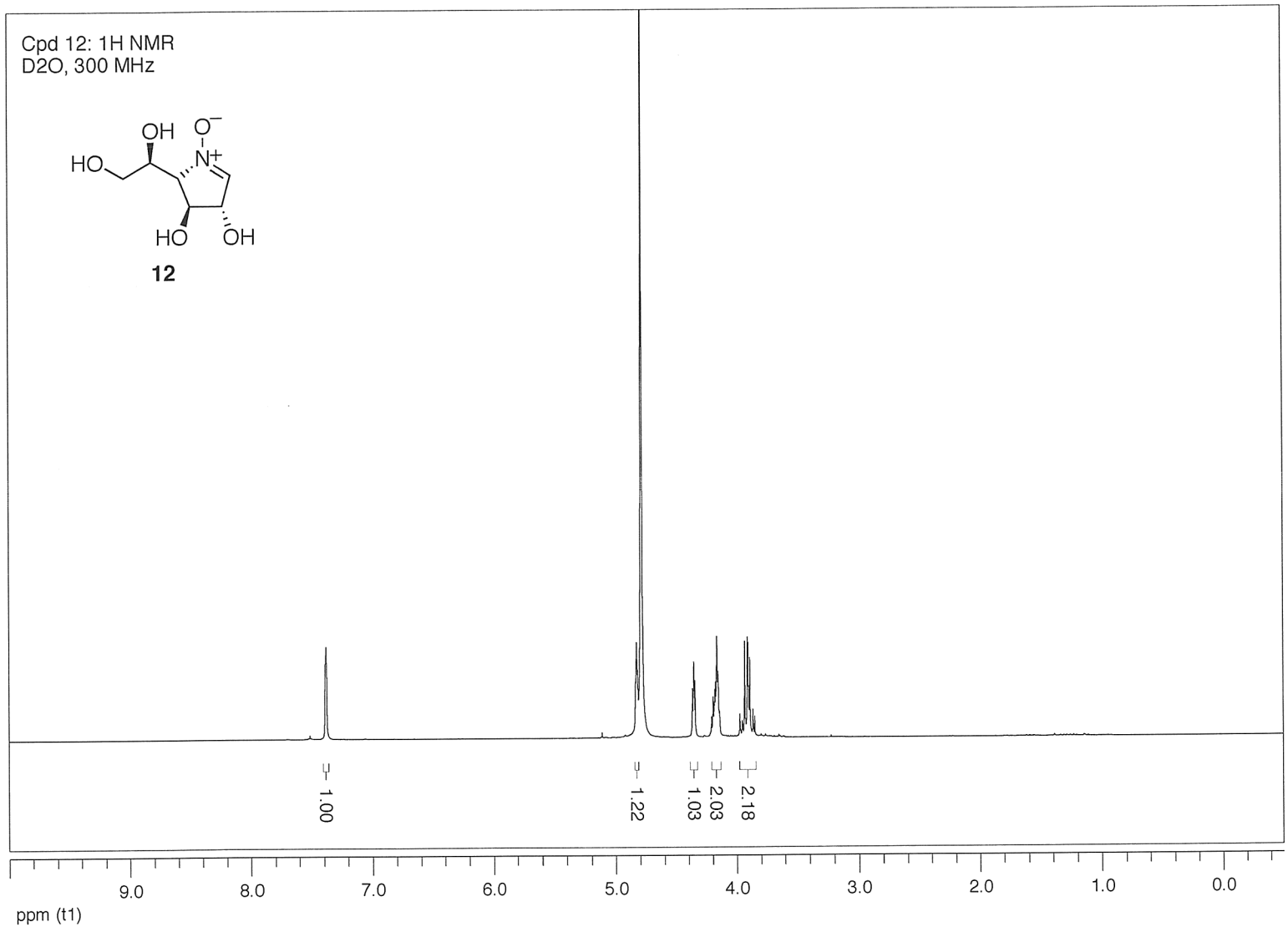

Cpd 9: 13C NMR
D2O, 75 MHz
141.687
79.175
76.378
74.806
56.586
HO
N+
O−
HO
OH
9
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

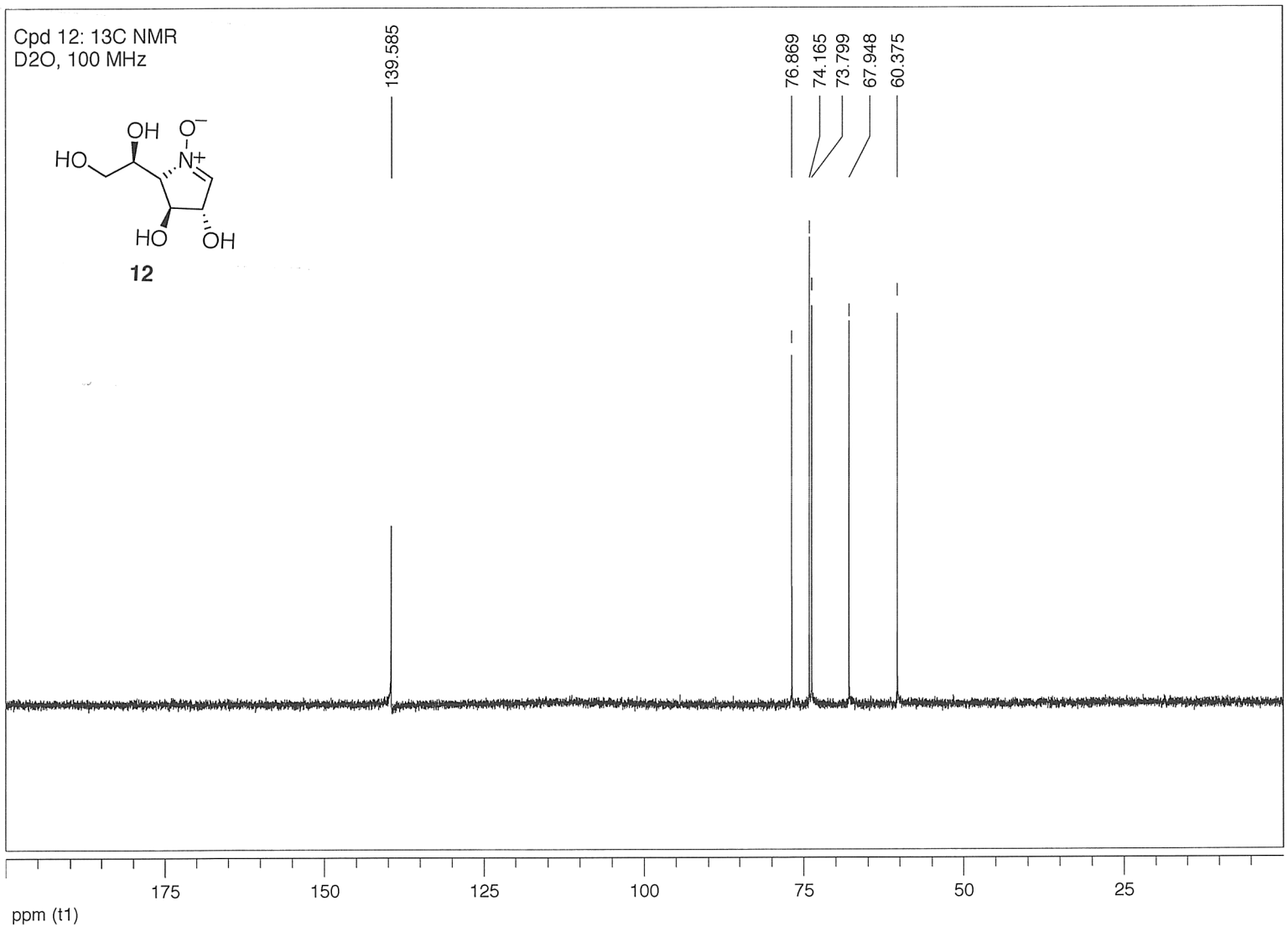

Cpd 10: 1H NMR
CD3OD, 300 MHz
HO
HO
OH
10
1.01
1.28
1.03
2.04
1.14
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

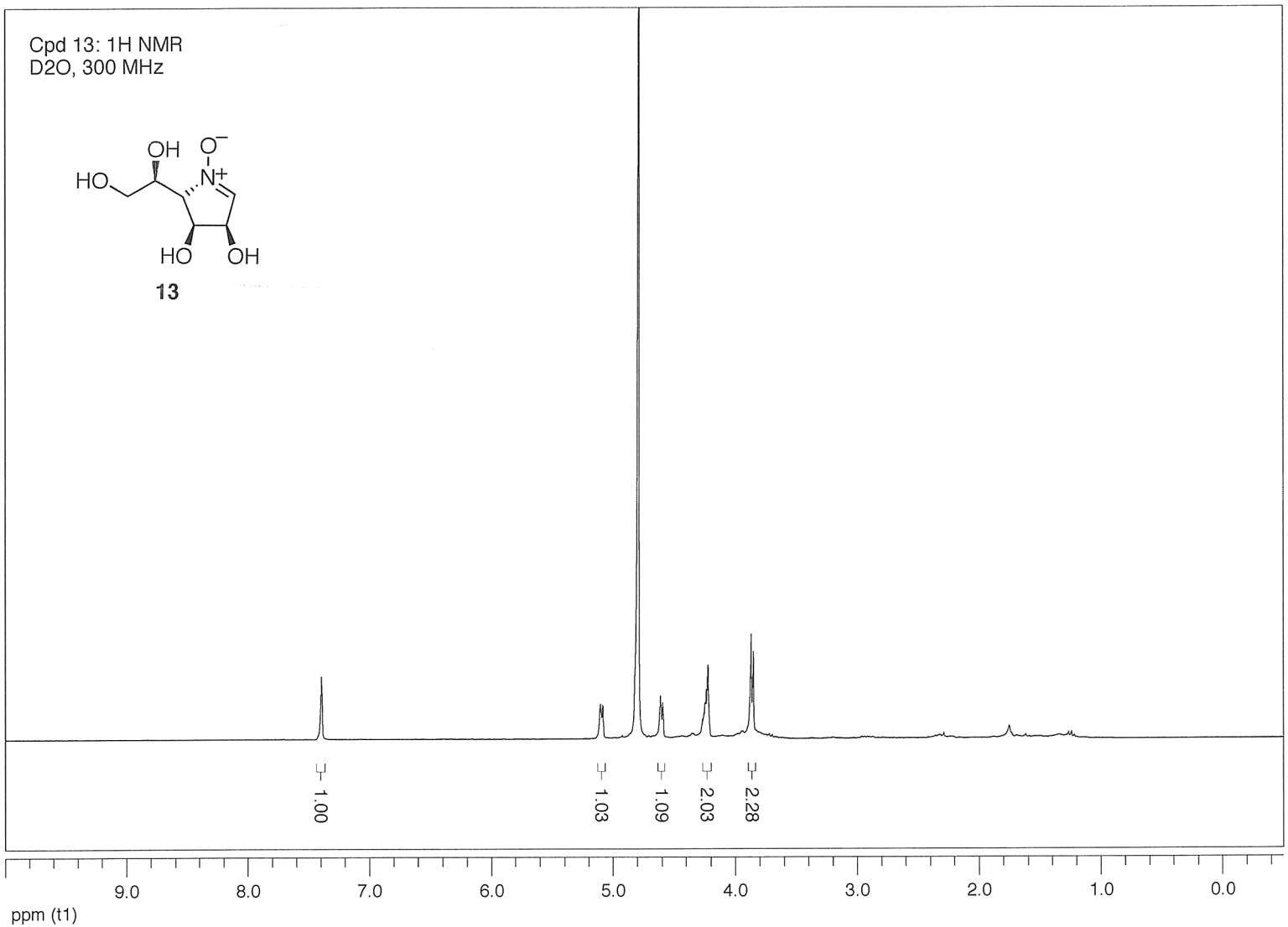

Cpd 10: 13C NMR
CD3OD, 75 MHz
140.901
79.153
77.881
77.176
58.032
HO
HO
OH
10
175
150
125
100
75
50
25
ppm (t1)

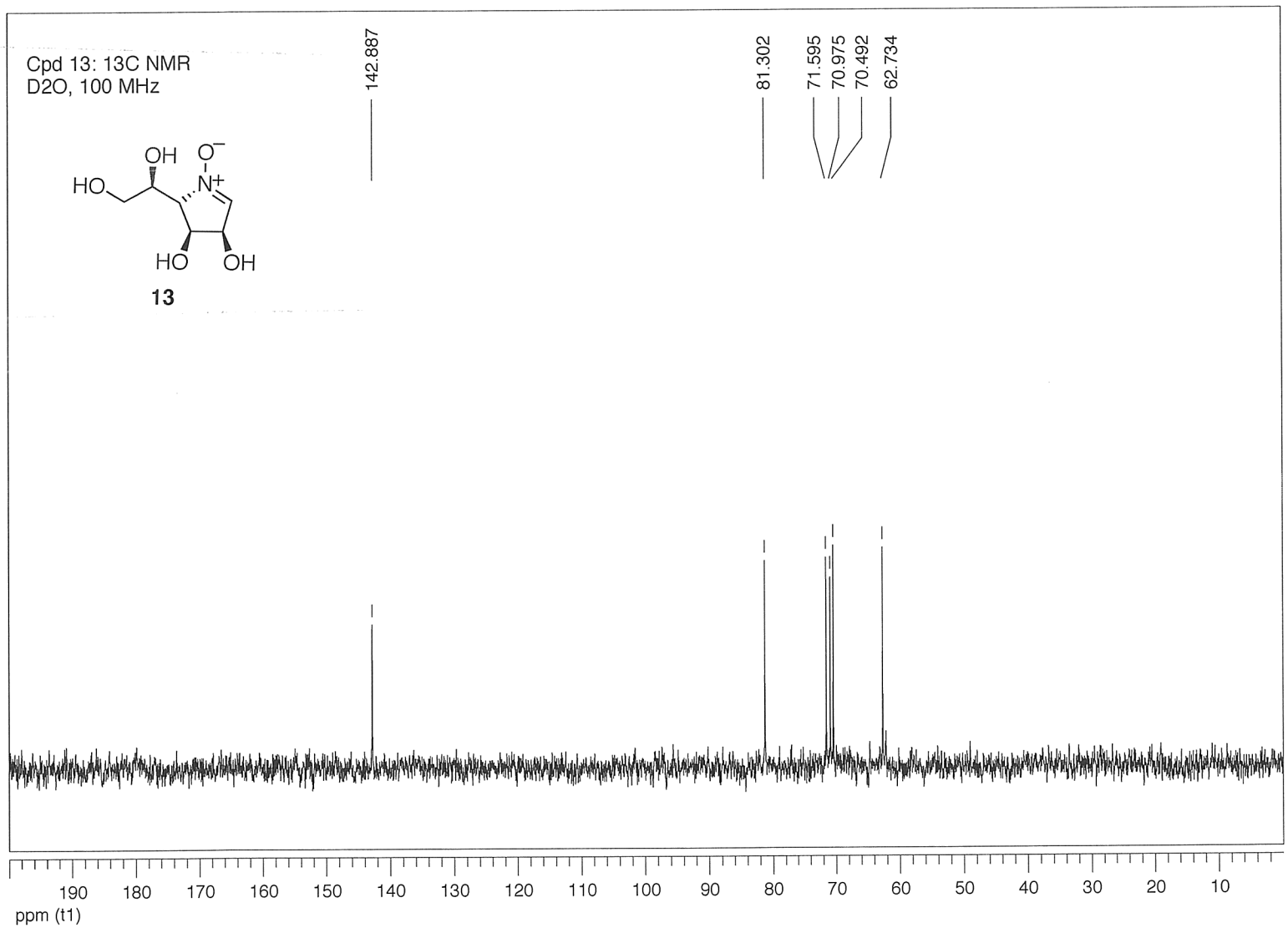

Cpd 11: 1H NMR
D2O, 300 MHz
HO
HO
OH
11
0.92
1.00
1.00
1.04
1.12
1.12
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

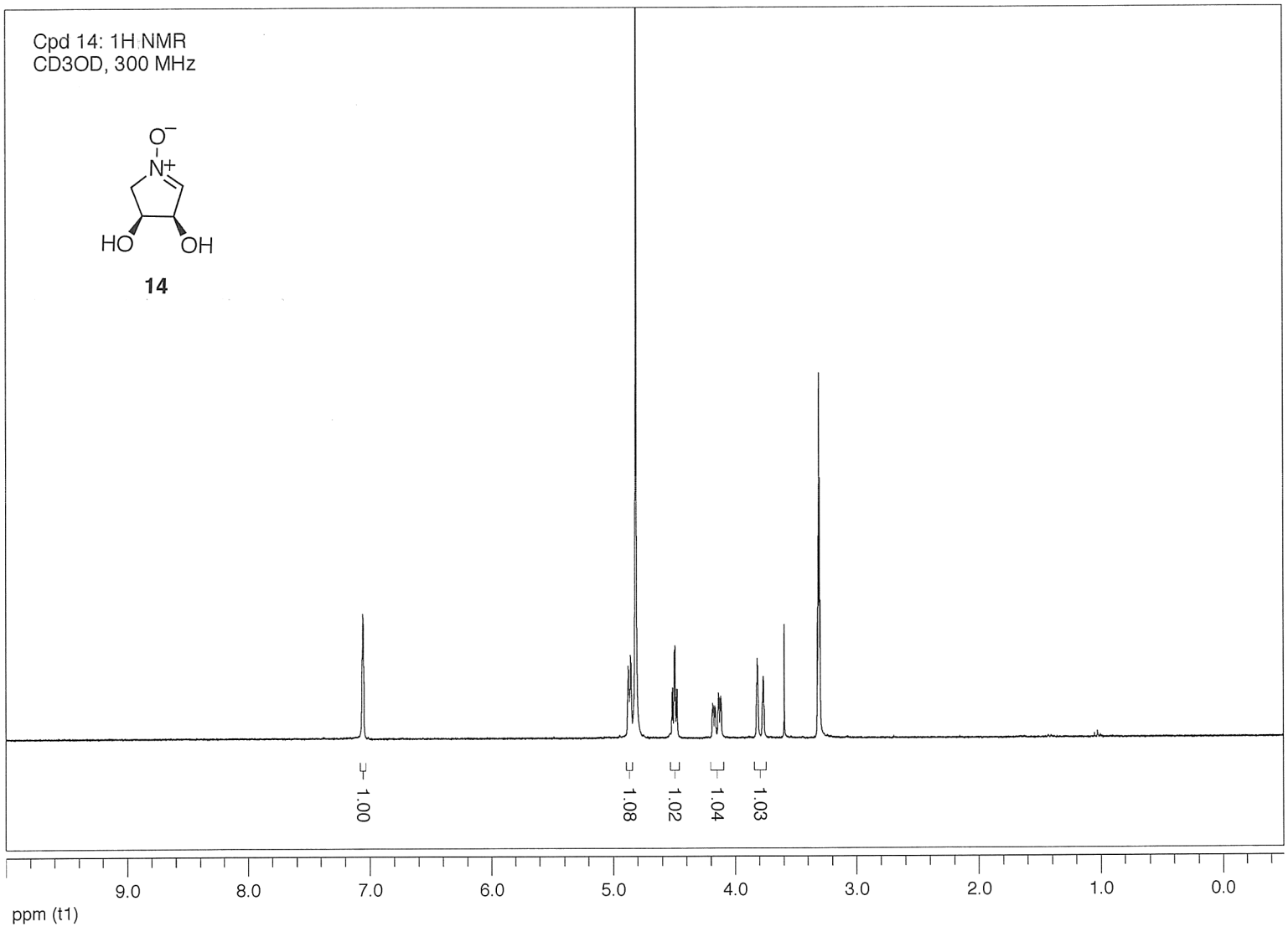

Cpd 11: 13C NMR
D2O, 75 MHz
141.621
75.102
69.830
66.898
55.473
HO
HO
OH
11
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

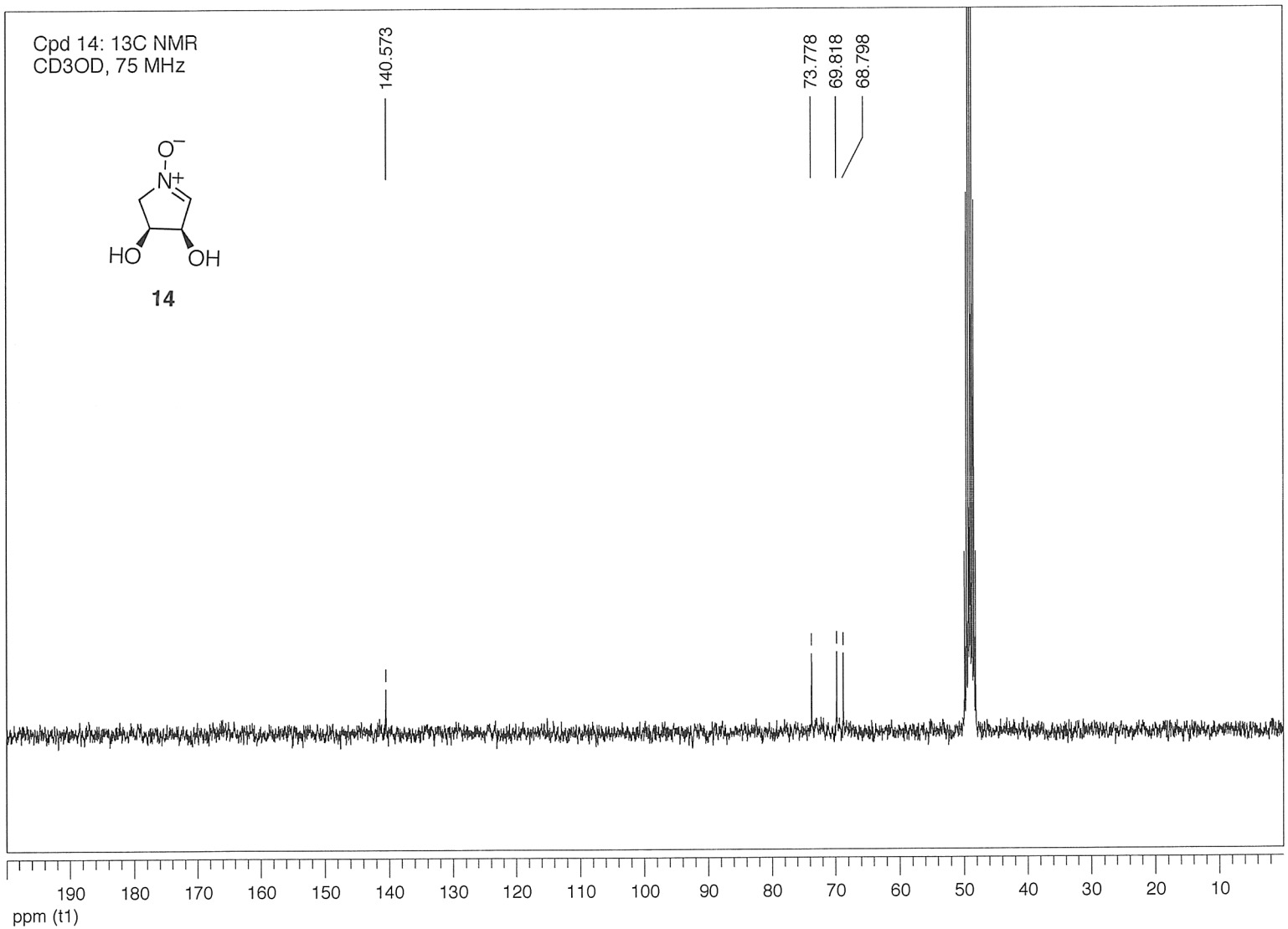

Cpd 12: 1H NMR
D2O, 300 MHz
OH
O
HO
N
HO
OH
12
1.00
1.22
1.03
2.03
2.18
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

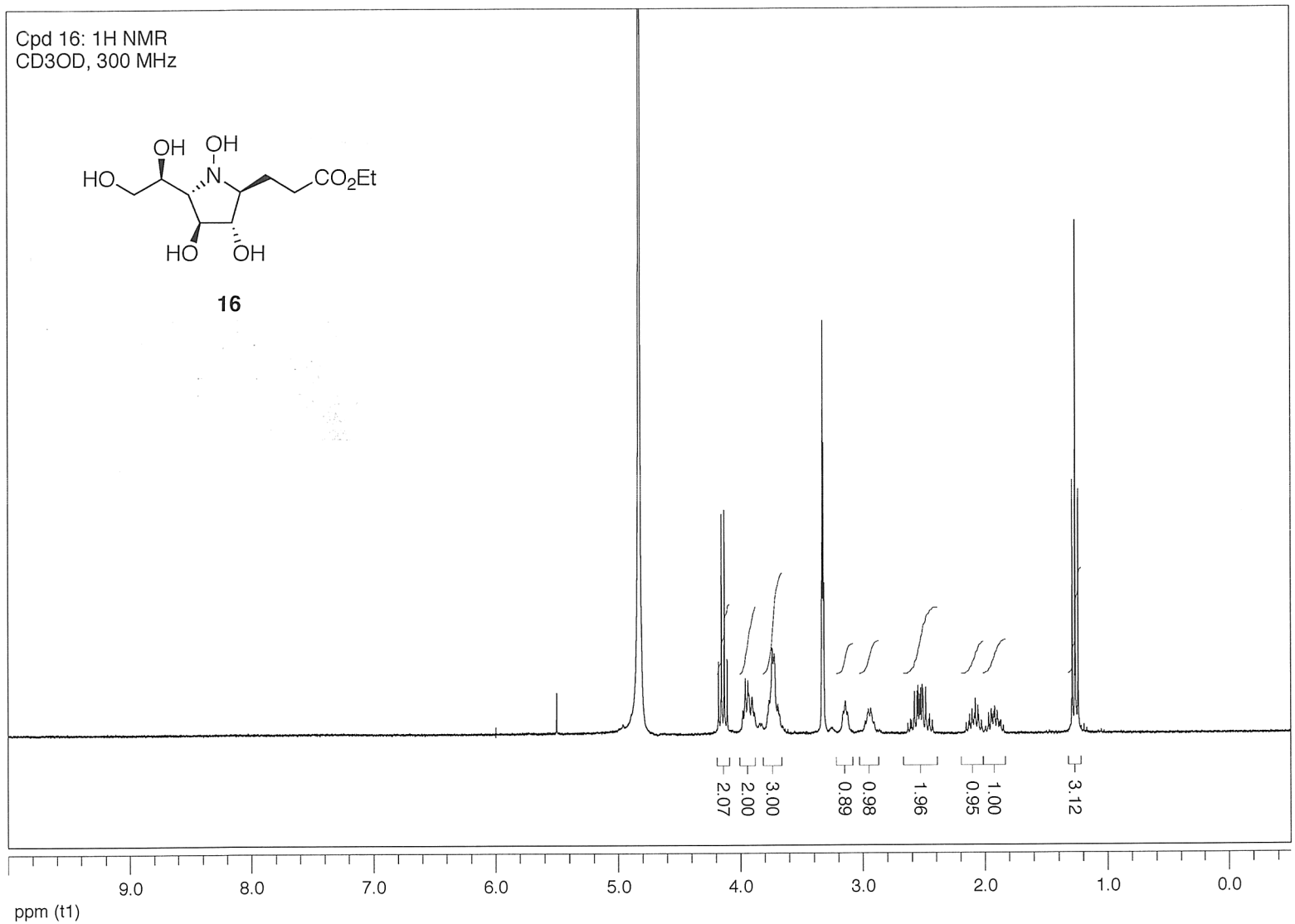

Cpd 12: 13C NMR
D2O, 100 MHz
139.585
76.869
74.165
73.799
67.948
60.375
OH
O⁻
HO
N+
HO
OH
12
175
150
125
100
75
50
25
ppm (t1)

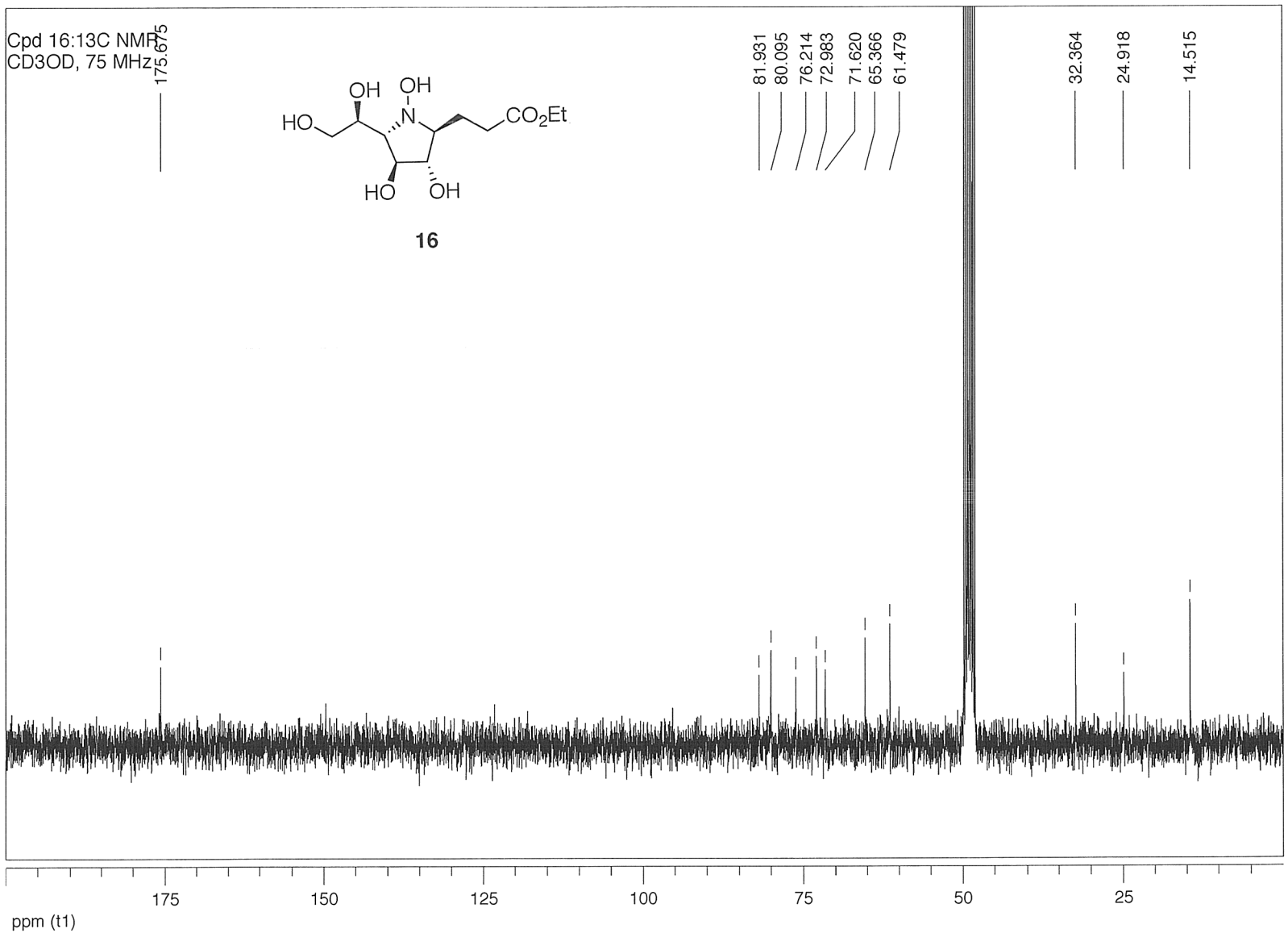

Cpd 13: 1H NMR
D2O, 300 MHz
OH
O⁻
HO
N⁺
HO
OH
13
1.00
1.03
1.09
2.03
2.28
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


Cpd 13: 13C NMR
D2O, 100 MHz
142.887
81.302
71.595
70.975
70.492
62.734
OH
O⁻
HO
N⁺
HO
OH
13
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


Cpd 14: 1H NMR
CD3OD, 300 MHz
HO
OH
14
1.00
1.08
1.02
1.04
1.03
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


Cpd 14: 13C NMR
CD3OD, 75 MHz
140.573
73.778
69.818
68.798
HO
OH
14
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


Cpd 16: 1H NMR
CD3OD, 300 MHz
OH
OH
HO
N
CO2Et
HO
OH
16
2.07
2.00
3.00
0.89
0.98
1.96
0.95
1.00
3.12
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


Cpd 16:13C NMR
CD3OD, 75 MHz
175.675
81.931
80.095
76.214
72.983
71.620
65.366
61.479
32.364
24.918
14.515
OH
OH
N
HO
CO2Et
HO
OH
16
175
150
125
100
75
50
25
ppm (t1)