Synthesis of pyrrolidine homoazasugars and 3,4-dihydroxy-5-hydroxymethylprolines using aldol additions of metalated bislactim ethers to 2,4-*O*-ethylidene-D-erythroses

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Electronic Supplementary Information

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1. Computational methods.

The conformational space accessible to the models was analyzed first by using hybrid methods, considering a two-layer scheme (DFT:semiempirical) and the ONIOM method for the partition of the system.[1] The DFT description (B3LYP method, using LANL2DZ basis set [2]) was limited to an "inner layer" including the critical parts of the reacting system: the atoms directly involved in the breaking and forming bonds and other areas sensitive to electronic effects. For the low-level treatment of the entire system, we employed the semiempirical AM1 method [3] (see Figure S1). Thus, the conformational space accessible to the azaenolate moiety was sampled by considering three different rotamers for the isopropyl group (those with the tertiary carbon atom pointing to the metal atom, to the nucleophilic carbon atom or to the imidate moiety) and two rotamers for each of the methoxy groups (directed to or opposite to the imidate nitrogen). In addition, for the erythrose moiety, three different rotamers for the benzyloxy group were studied. Significative structures located with these conformational analyses were fully reoptimized at B3LYP/cc-pVDZ-PP level.

Figure S1. High-level (B3LYP/LANL2DZ) and low-level (AM1) layers for the ONIOM calculations.

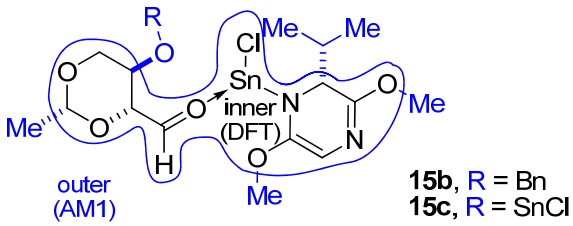

Figure S2. Felkin-Anh, modified-Cornforth and non-Anh models for azaenolate addition to 2,4-ethylidene-D-erythrose derivative.

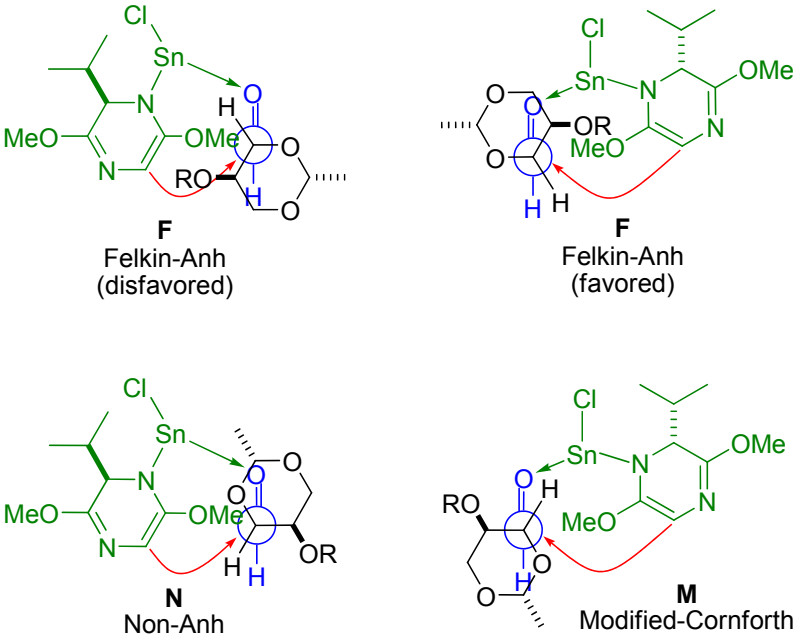

Figure S3. Chem3D representations of the most favored TSs located in the gas 3,6-*cis* diastereomeric pathways (at B3LYP/cc-pVDZ-PP level) for the reaction between azaenolate $SnCl^{+}$**10**$^{-}$ and benzylated erythrose ethylidene **11b**. Relative energies in THF (at B3LYP(SCRF)/cc-pVTZ-PP level using the PCM method) are shown in parenthesis in kcal mol^{-1}. Distances are in angstromgs. The hydrogen atoms are omitted for clarity except at chiral and reaction centers.

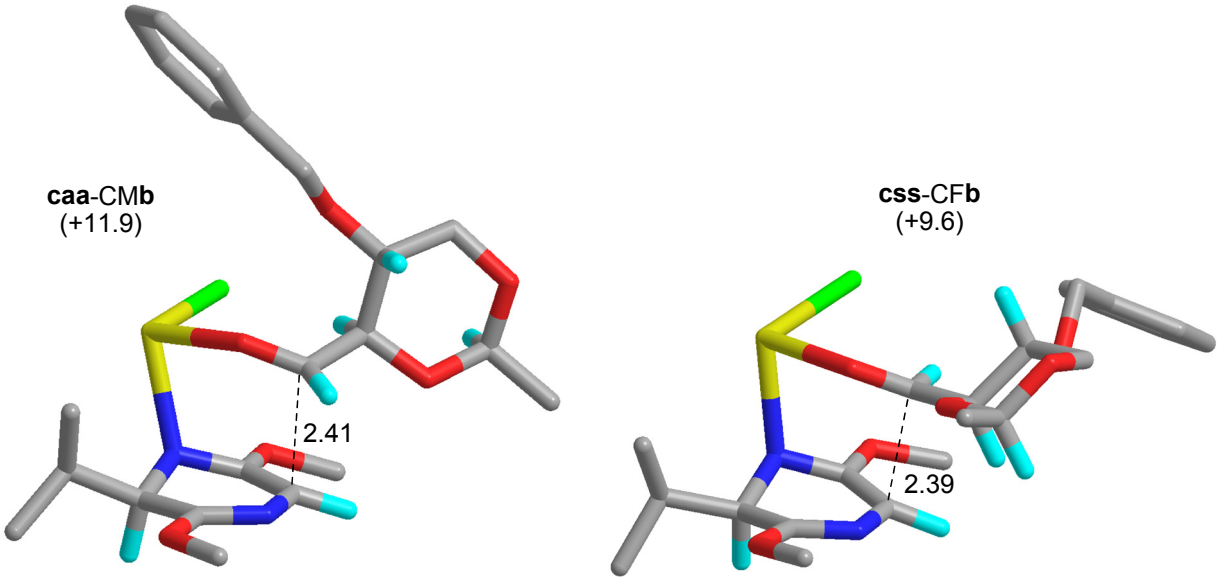

Figure S4. Chem3D representations of the most favored TSs located in the gas 3,6-*cis* diastereomeric pathways (at B3LYP/cc-pVDZ-PP level) for the reaction between azaenolate $SnCl^{+}$**10**$^{-}$ and "unprotected" erythrose ethylidene **11c**. Relative energies in THF (at B3LYP(SCRF)/cc-pVTZ-PP level using the PCM method) are shown in parenthesis in kcal mol^{-1}. Distances are in angstromgs. The hydrogen atoms are omitted for clarity except at chiral and reaction centers.

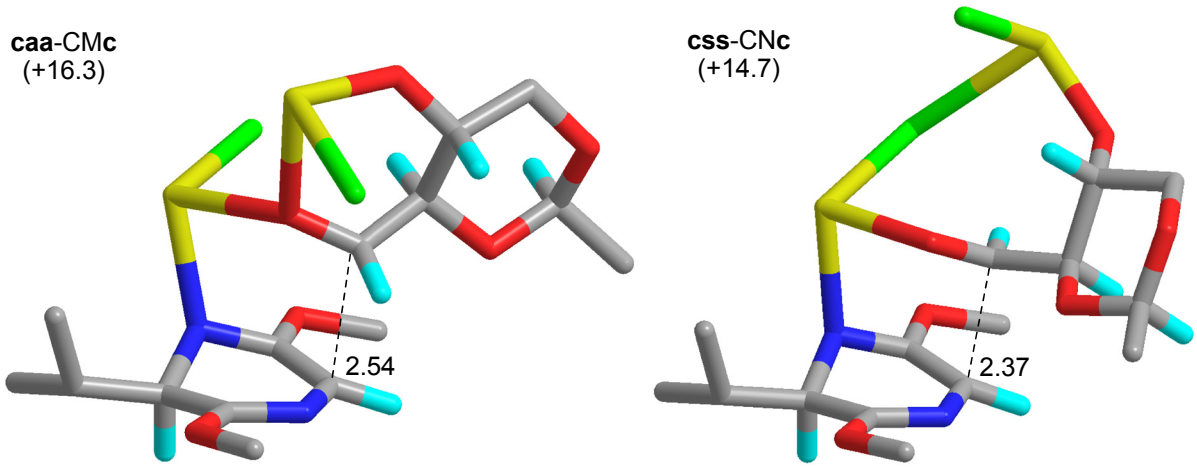

Table S1. Absolute energies (hartrees) and relative free energies (kcal/mol) calculated for most significative intermediate and TSs in the reaction of $SnCl^{+}$**10**$^{-}$ and **11b**.

	B3LYP/cc-pVDZ-PP			B3LYP(SCRF)/cc-pVTZ-PP	
model (*config*)[a]	E_{SCF}	N_{imag}	E_{cor}[b]	G	G_{rel}[c]
15b	–2092.53531729	0	0.457543	–2092.971201	–1.24
caa-CM**b**	–2092.51363190	1	0.458570	–2092.951269	+11.9
css-CF**b**	–2092.51365522	1	0.458572	–2092.954799	+9,6
tas-BN**b**	–2092.53470649	1	0.459266	–2092.968294	**0.0**
tsa-CM**b**	–2092.53198882	1	0.458695	–2092.966689	+0.65

[a] Legend: **caa**–cis,anti,anti; **css**–cis,syn,syn; **tas**–trans,anti,syn; **tsa**–trans,syn,anti; B–boat-like; C–chair-like; F–Felkin-Anh; M–Cornforth; N–non-Anh.
[b] Zero-point energy corrections with thermal and entropy effects at 195.15 K and 1.0 atm, scaled by 0.97.
[c] With zero-point energy corrections and thermal and entropy effects (calculated at B3LYP/cc-pVDZ-PP level).

Table S2. Absolute energies (hartrees) and relative free energies (kcal/mol) calculated for most significative intermediate and TSs in the reaction of $SnCl^{+}$**10**$^{-}$ and **11c**.

	B3LYP/cc-pVDZ-PP			B3LYP(SCRF)/cc-pVTZ-PP	
model (*config*)[a]	E_{SCF}	N_{imag}	E_{cor}[b]	G	G_{rel}[c]
15c	–2496.26419872	0	0.318559	–2496.648718	–8.38
caa-CM**c**	–2496.22535153	1	0.321745	–2496.612589	+16.3
css-CN**c**	–2496.22711105	1	0.323001	–2496.616406	+14.7
tas-BN**c**	–2496.24913566	1	0.324171	–2496.633866	+4.4
tsa-CM**c**	–2496.25656316	1	0.322848	–2496.639644	**0.0**

[a] Legend: **caa**–cis,anti,anti; **css**–cis,syn,syn; **tas**–trans,anti,syn; **tsa**–trans,syn,anti; B–boat-like; C–chair-like; F–Felkin-Anh; M–Cornforth; N–non-Anh.
[b] Zero-point energy corrections with thermal and entropy effects at 273.15 K and 1.0 atm, scaled by 0.97.
[c] With zero-point energy corrections and thermal and entropy effects (calculated at B3LYP/cc-pVDZ-PP level).

4. Cartesian coordinates of reported structures.

caa-CMb

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E(RB+HF-LYP) =  -2092.51363190
Zero-point correction=                           0.495398 (Hartree/Particle)
Thermal correction to Energy=                    0.512026
Thermal correction to Enthalpy=                  0.512644
Thermal correction to Gibbs Free Energy=         0.458570
Sum of electronic and zero-point Energies=          -2092.018234
Sum of electronic and thermal Energies=             -2092.001606
Sum of electronic and thermal Enthalpies=           -2092.000988
Sum of electronic and thermal Free Energies=        -2092.055062
----------------------------------------------------------------------
Variational PCM results
<psi(f)|   H    |psi(f)>                    (a.u.) =   -2092.969094
<psi(f)|H+V(f)/2|psi(f)>                    (a.u.) =   -2092.987302
Total free energy in solution:
 with all non electrostatic terms           (a.u.) =   -2092.951269
----------------------------------------------------------------------
Center     Atomic     Atomic              Coordinates (Angstroms)
Number     Number      Type              X           Y           Z
----------------------------------------------------------------------
   1          6             0        2.538246    1.599153    0.104909
   2          6             0        0.311937    1.102812    0.882916
   3          8             0        0.178831   -0.145027    0.685688
   4         50             0        0.269290   -1.493601   -1.148393
   5          7             0        2.327539   -0.491660   -1.062712
   6          6             0        2.259178    0.856796   -1.048240
   7          7             0        3.155909    0.995795    1.213493
   8          6             0        3.509022   -0.228295    1.098191
   9          8             0        4.130749   -0.870404    2.112823
  10          6             0        3.384523   -1.052792   -0.179319
  11          8             0        1.728478    1.377083   -2.173744
  12          6             0       -0.646639    2.095808    0.267943
  13          8             0       -0.132353    3.409136    0.500243
  14          6             0       -1.021606    4.447287    0.101008
  15          8             0       -2.242795    4.376664    0.799598
  16          6             0       -2.908090    3.146237    0.548554
  17          6             0       -2.028579    1.963454    0.969479
  18         17             0       -0.991249   -0.100829   -2.781959
  19          6             0        4.342669   -0.113104    3.310409
  20          6             0        1.695653    2.794677   -2.335033
  21          6             0        3.244912   -2.590557    0.010150
  22          6             0        4.618671   -3.268484    0.125347
  23          6             0        2.328693   -3.030514    1.168290
  24          6             0       -0.364977    5.770964    0.419799
  25          8             0       -2.657210    0.758211    0.581272
  26          6             0       -3.800984   -1.290730    1.107372
  27          6             0       -4.364476   -2.208295    2.007591
  28          6             0       -3.916806   -1.525670   -0.268353
  29          6             0       -5.031346   -3.342590    1.542418
  30          6             0       -4.585631   -2.664687   -0.732779
  31          6             0       -5.144339   -3.574904    0.166756
  32          6             0       -3.079269   -0.076768    1.649018
  33          1             0       -3.752183    0.480460    2.331825
  34          1             0       -5.465939   -4.047380    2.255417
  35          1             0       -4.667252   -2.836629   -1.808731
  36          1             0       -5.666520   -4.462023   -0.199092
  37          1             0       -1.223697    4.334336   -0.987911
  38          1             0        0.580113    5.874625   -0.132045
  39          1             0        2.552108    2.687191    0.102800
  40          1             0        1.215593    2.965884   -3.306500
  41          1             0        1.116477    3.283334   -1.538173
  42          1             0        2.719604    3.206508   -2.347580
  43          1             0        2.799752   -2.939389   -0.939937
  44          1             0        4.871295   -0.787929    3.995602
  45          1             0        3.383108    0.207589    3.744306
  46          1             0        4.944892    0.784278    3.102228
  47          1             0        4.502723   -4.359884    0.224871
  48          1             0        5.162180   -2.901148    1.008900
  49          1             0        5.238697   -3.076629   -0.765516
  50          1             0        1.981778   -4.064314    1.010017
  51          1             0        1.442307   -2.387359    1.281484
  52          1             0        2.868196   -2.991615    2.125120
  53          1             0        4.344493   -0.907700   -0.718846
  54          1             0        0.786731    1.427692    1.824212
  55          1             0       -0.789439    1.892423   -0.809082
  56          1             0       -3.158824    3.039441   -0.525410
  57          1             0       -3.844343    3.159890    1.124478
  58          1             0       -0.158141    5.824202    1.498811
  59          1             0       -1.037063    6.595315    0.142396
  60          1             0       -1.868683    2.007806    2.061931
  61          1             0       -4.281192   -2.033121    3.084647
  62          1             0       -3.482270   -0.815374   -0.971582
  63          1             0       -2.202069   -0.399369    2.243220
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css-CF**b**

E(RB+HF-LYP) = -2092.51365522
Zero-point correction= 0.495898 (Hartree/Particle)
Thermal correction to Energy= 0.512513
Thermal correction to Enthalpy= 0.513131
Thermal correction to Gibbs Free Energy= 0.458572
Sum of electronic and zero-point Energies= -2092.017758
Sum of electronic and thermal Energies= -2092.001142
Sum of electronic and thermal Enthalpies= -2092.000524
Sum of electronic and thermal Free Energies= -2092.055083

Variational PCM results
<psi(f)| H |psi(f)> (a.u.) = -2092.970168
<psi(f)|H+V(f)/2|psi(f)> (a.u.) = -2092.989822
Total free energy in solution:
with all non electrostatic terms (a.u.) = -2092.954799

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.754990	0.046904	1.926327
2	6	0	0.147547	0.581313	-0.221214
3	8	0	-0.846396	0.413529	-0.987938
4	50	0	-1.601851	-1.633346	-1.522679
5	7	0	-2.009504	-1.616865	0.730608
6	6	0	-0.905954	-1.255872	1.433184
7	7	0	-1.795253	0.976563	1.839186
8	6	0	-2.935241	0.544421	1.441984
9	8	0	-3.969736	1.388541	1.245766
10	6	0	-3.227421	-0.942192	1.265226
11	8	0	0.071542	-2.185560	1.430556
12	6	0	0.669830	1.977664	0.055060
13	8	0	-0.221806	2.957114	-0.446780
14	6	0	0.276609	4.273888	-0.269574
15	8	0	1.495800	4.461644	-0.961582
16	6	0	2.505486	3.577528	-0.495998
17	6	0	2.046718	2.120850	-0.637933
18	17	0	0.727834	-2.519331	-1.670057
19	6	0	-3.664546	2.785773	1.369475
20	6	0	1.300690	-1.897704	2.098609
21	6	0	-4.536355	-1.367325	0.548802
22	6	0	-5.719914	-1.310205	1.529973
23	6	0	-4.905919	-0.619297	-0.743848
24	6	0	-0.737104	5.242971	-0.832795
25	8	0	2.954402	1.230441	-0.003316
26	6	0	4.746218	-0.356623	-0.116043
27	6	0	4.558373	-1.743447	-0.195758
28	6	0	5.753960	0.147652	0.720404
29	6	0	5.373084	-2.612372	0.538366
30	6	0	6.564076	-0.717483	1.457946
31	6	0	6.376491	-2.101440	1.365843
32	6	0	3.869515	0.582387	-0.903408
33	1	0	4.485875	1.343664	-1.418307
34	1	0	0.453676	4.441615	0.817003
35	1	0	-1.689558	5.156750	-0.291069
36	1	0	0.064914	0.316860	2.591819
37	1	0	1.932689	-2.780557	1.946784
38	1	0	1.808333	-1.016174	1.675900
39	1	0	1.131214	-1.742144	3.177802
40	1	0	-4.367261	-2.429809	0.296035
41	1	0	-4.583466	3.314138	1.084672
42	1	0	-2.826976	3.047580	0.705766
43	1	0	-3.382269	3.030324	2.405225
44	1	0	-6.644537	-1.658626	1.042351
45	1	0	-5.889088	-0.278960	1.878116
46	1	0	-5.545315	-1.946607	2.412614
47	1	0	-5.743146	-1.134635	-1.242645
48	1	0	-4.082253	-0.576261	-1.473439
49	1	0	-5.210463	0.414149	-0.532847
50	1	0	-3.335002	-1.329897	2.299646
51	1	0	0.902094	-0.211228	-0.122772
52	1	0	0.832754	2.113135	1.140514
53	1	0	2.743651	3.769043	0.570226
54	1	0	3.406570	3.776759	-1.093862
55	1	0	-0.906122	5.016250	-1.895700
56	1	0	-0.360462	6.271439	-0.739864
57	1	0	1.923437	1.877255	-1.708616
58	1	0	3.767217	-2.145016	-0.834367
59	1	0	5.902100	1.228278	0.792160
60	1	0	5.221599	-3.691610	0.461675
61	1	0	7.347637	-0.313115	2.103129
62	1	0	7.014303	-2.779561	1.937766
63	1	0	3.303126	0.024961	-1.670756

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tas-BN**b**

E(RB+HF-LYP) = -2092.53470649
Zero-point correction= 0.496192 (Hartree/Particle)
Thermal correction to Energy= 0.512830
Thermal correction to Enthalpy= 0.513448
Thermal correction to Gibbs Free Energy= 0.459266
Sum of electronic and zero-point Energies= -2092.038514
Sum of electronic and thermal Energies= -2092.021876
Sum of electronic and thermal Enthalpies= -2092.021258
Sum of electronic and thermal Free Energies= -2092.075440

Variational PCM results
<psi(f)| H |psi(f)> (a.u.) = -2092.991772
<psi(f)|H+V(f)/2|psi(f)> (a.u.) = -2093.008172
Total free energy in solution:
with all non electrostatic terms (a.u.) = -2092.968294

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.555885	1.036352	1.640946
2	6	0	0.112118	1.026988	-0.084650
3	8	0	-0.379237	1.209673	-1.244788
4	50	0	-1.918913	-0.218409	-2.126517
5	7	0	-2.589544	-0.440779	0.038570
6	6	0	-2.412531	0.782191	0.565396
7	7	0	-1.038982	-0.027445	2.400254
8	6	0	-1.379059	-1.214140	2.047386
9	8	0	-0.887689	-2.303043	2.668529
10	6	0	-2.332808	-1.590900	0.924130
11	8	0	-2.951633	1.741283	-0.223304
12	6	0	1.089717	2.027062	0.487780
13	8	0	0.601767	3.355397	0.315636
14	6	0	1.498970	4.332388	0.830792
15	8	0	2.733404	4.296114	0.154091
16	6	0	3.371365	3.033640	0.295267
17	6	0	2.472592	1.901288	-0.210376
18	17	0	-0.404257	-2.200410	-1.941162
19	6	0	0.068886	-2.074334	3.710347
20	6	0	-2.716698	3.124598	0.081191
21	6	0	-3.646849	-2.231833	1.464213
22	6	0	-4.471494	-1.267556	2.324633
23	6	0	-4.478946	-2.804898	0.311898
24	6	0	0.882309	5.697009	0.626889
25	8	0	3.095829	0.672704	0.119061
26	6	0	3.928249	-1.498075	-0.482344
27	6	0	5.117976	-1.343446	0.245190
28	6	0	3.494500	-2.788930	-0.813192
29	6	0	5.865246	-2.460124	0.624914
30	6	0	4.248130	-3.906840	-0.440565
31	6	0	5.434994	-3.745934	0.278746
32	1	0	1.670537	4.112034	1.908837
33	1	0	-0.075632	5.767576	1.161709
34	1	0	-1.493615	2.020747	2.102196
35	1	0	-3.256533	3.685408	-0.692110
36	1	0	-3.136089	3.372607	1.069886
37	1	0	-1.643987	3.360589	0.046227
38	1	0	-3.314678	-3.069921	2.101951
39	1	0	0.336651	-3.069202	4.087398
40	1	0	-0.365389	-1.456757	4.511325
41	1	0	0.957347	-1.558992	3.313756
42	1	0	-5.338964	-1.786670	2.763673
43	1	0	-4.857282	-0.428081	1.722876
44	1	0	-3.879017	-0.848266	3.154225
45	1	0	-5.376978	-3.316818	0.693847
46	1	0	-3.900569	-3.532957	-0.280303
47	1	0	-4.812588	-2.002599	-0.366404
48	1	0	-1.819001	-2.368023	0.334962
49	1	0	0.224301	0.003949	0.310108
50	1	0	1.230848	1.792367	1.560207
51	1	0	3.629613	2.835358	1.355248
52	1	0	4.303219	3.075552	-0.285894
53	1	0	0.712126	5.863890	-0.446981
54	1	0	1.563714	6.472165	1.005083
55	1	0	2.317924	2.010422	-1.297843
56	1	0	5.447248	-0.340302	0.522134
57	1	0	2.557316	-2.919120	-1.360232
58	1	0	6.788988	-2.327332	1.193579
59	1	0	3.898703	-4.907381	-0.706168
60	1	0	6.021441	-4.619248	0.574124
61	6	0	3.139790	-0.293839	-0.937540
62	1	0	2.123028	-0.600787	-1.238341
63	1	0	3.622085	0.163772	-1.825329

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tsa-CM**b**

E(RB+HF-LYP) = -2092.53198882
Zero-point correction= 0.495771 (Hartree/Particle)
Thermal correction to Energy= 0.512392
Thermal correction to Enthalpy= 0.513010
Thermal correction to Gibbs Free Energy= 0.458695
Sum of electronic and zero-point Energies= -2092.036218
Sum of electronic and thermal Energies= -2092.019597
Sum of electronic and thermal Enthalpies= -2092.018979
Sum of electronic and thermal Free Energies= -2092.073294

Variational PCM results
<psi(f)| H |psi(f)> (a.u.) = -2092.988873
<psi(f)|H+V(f)/2|psi(f)> (a.u.) = -2093.006213
Total free energy in solution:
with all non electrostatic terms (a.u.) = -2092.966689

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.691964	1.286741	1.181240
2	6	0	0.071896	1.220167	-0.532225
3	8	0	0.242904	-0.028756	-0.672758
4	50	0	-1.256140	-1.364216	-1.745586
5	7	0	-2.499442	-0.647324	-0.004434
6	6	0	-2.489558	0.693183	0.200579
7	7	0	-0.982685	0.507892	2.105512
8	6	0	-1.179905	-0.758824	2.068247
9	8	0	-0.490748	-1.616425	2.848303
10	6	0	-2.197145	-1.460655	1.189800
11	8	0	-3.198910	1.377190	-0.720059
12	6	0	1.025715	2.039800	0.300255
13	8	0	0.553401	3.386149	0.223962
14	6	0	1.389421	4.313953	0.899144
15	8	0	2.684571	4.327064	0.341364
16	6	0	3.307958	3.056710	0.465447
17	6	0	2.484594	1.956197	-0.218966
18	17	0	-1.689664	0.367131	-3.447196
19	6	0	0.504668	-1.045967	3.708745
20	6	0	-3.192450	2.803669	-0.673637
21	6	0	-3.469251	-1.901022	1.977390
22	6	0	-4.272952	-0.725716	2.546868
23	6	0	-4.348722	-2.801782	1.102401
24	6	0	0.786822	5.691185	0.744499
25	8	0	3.032372	0.701041	0.142210
26	6	0	3.882435	-1.463052	-0.412763
27	6	0	2.927001	-2.179897	0.325904
28	6	0	5.122059	-2.057415	-0.677046
29	6	0	3.209782	-3.468309	0.782594
30	6	0	5.403685	-3.351655	-0.225930
31	6	0	4.448124	-4.059871	0.506048
32	6	0	3.557286	-0.082389	-0.929861
33	1	0	2.804984	-0.149727	-1.738043
34	1	0	4.464772	0.389653	-1.352400
35	1	0	1.460740	4.009337	1.967474
36	1	0	-0.219905	5.718343	1.185127
37	1	0	-1.747674	2.349505	1.406126
38	1	0	-3.763431	3.128942	-1.551676
39	1	0	-3.683256	3.168070	0.245211
40	1	0	-2.170032	3.211219	-0.724038
41	1	0	-3.087238	-2.500710	2.823701
42	1	0	0.894617	-1.882336	4.302425
43	1	0	0.063354	-0.276964	4.360251
44	1	0	1.311772	-0.588732	3.115022
45	1	0	-5.100489	-1.099108	3.171944
46	1	0	-4.715158	-0.118139	1.740779
47	1	0	-3.651447	-0.066114	3.172696
48	1	0	-5.230945	-3.151478	1.662097
49	1	0	-3.796922	-3.691677	0.755669
50	1	0	-4.701720	-2.253981	0.214317
51	1	0	-1.721141	-2.400367	0.853703
52	1	0	-0.510947	1.781302	-1.281775
53	1	0	1.021129	1.663334	1.340438
54	1	0	3.434484	2.780699	1.531610
55	1	0	4.304809	3.138322	0.009391
56	1	0	0.720783	5.942277	-0.324507
57	1	0	1.421528	6.434196	1.247823
58	1	0	2.495768	2.113928	-1.311859
59	1	0	1.963599	-1.713642	0.538582
60	1	0	5.877690	-1.503587	-1.241202
61	1	0	2.458358	-4.016014	1.356796
62	1	0	6.375281	-3.802478	-0.441409
63	1	0	4.667106	-5.068885	0.863218

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caa-CMc

```
 E(RB+HF-LYP) =  -2496.22535153
 Zero-point correction=                           0.380007 (Hartree/Particle)
 Thermal correction to Energy=                    0.407694
 Thermal correction to Enthalpy=                  0.408559
 Thermal correction to Gibbs Free Energy=         0.321745
 Sum of electronic and zero-point Energies=          -2495.845345
 Sum of electronic and thermal Energies=             -2495.817657
 Sum of electronic and thermal Enthalpies=           -2495.816792
 Sum of electronic and thermal Free Energies=        -2495.903606
-------------------------------------------------------------------
 Variational PCM results
 =======================
 <psi(f)|   H    |psi(f)>                   (a.u.) =   -2496.627799
 <psi(f)|H+V(f)/2|psi(f)>                   (a.u.) =   -2496.649001
 Total free energy in solution:
  with all non electrostatic terms          (a.u.) =   -2496.612589
 -------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
-------------------------------------------------------------------
    1          6             0        0.744268    1.802448    1.896172
    2          6             0       -0.838709    0.192516    0.732600
    3          8             0       -0.078572   -0.473429   -0.069132
    4         50             0        1.518748    0.211390   -1.726064
    5          7             0        2.227109    1.345168    0.061446
    6          6             0        1.267590    2.123757    0.641385
    7          7             0        1.235459    0.718709    2.634172
    8          6             0        2.328474    0.187072    2.221273
    9          8             0        2.858400   -0.896625    2.813825
   10          6             0        3.152002    0.795471    1.091811
   11          8             0        0.824963    3.112360   -0.154338
   12          6             0       -2.083001    0.814210    0.199755
   13          8             0       -2.605760    1.757663    1.124682
   14          6             0       -3.880865    2.265251    0.722446
   15          8             0       -4.836585    1.240202    0.631664
   16          6             0       -4.465444    0.253199   -0.324370
   17          6             0       -3.118548   -0.380513    0.046304
   18         17             0        0.007265    1.785278   -2.878480
   19          6             0        2.093885   -1.482479    3.881920
   20          6             0       -0.190423    3.992882    0.331981
   21          6             0        4.343849   -0.049860    0.588219
   22          6             0        4.021209   -1.439356    0.015639
   23          6             0        5.228957    0.757755   -0.371651
   24          6             0       -4.338731    3.254997    1.768845
   25          8             0       -2.732936   -1.279415   -0.941974
   26         17             0       -1.394671   -3.235310    1.554511
   27         50             0       -1.162918   -2.589251   -0.821659
   28          1             0       -5.330440    3.644562    1.498839
   29          1             0       -3.219102   -0.848613    1.044249
   30          1             0       -3.758638    2.740109   -0.276682
   31          1             0       -3.631575    4.093437    1.844511
   32          1             0        0.028370    2.443355    2.407241
   33          1             0       -0.426315    4.657676   -0.507845
   34          1             0       -1.088374    3.438776    0.643110
   35          1             0        0.190994    4.586963    1.180310
   36          1             0        4.927751   -0.225933    1.507854
   37          1             0        2.704707   -2.314006    4.254516
   38          1             0        1.127111   -1.849481    3.504819
   39          1             0        1.910311   -0.743489    4.675596
   40          1             0        4.943233   -2.041615   -0.032945
   41          1             0        3.630945   -1.391434   -1.014332
   42          1             0        3.300306   -1.984640    0.640271
   43          1             0        6.139576    0.191623   -0.624120
   44          1             0        5.538377    1.717139    0.073177
   45          1             0        4.708972    0.988065   -1.315801
   46          1             0        3.628733    1.687090    1.552709
   47          1             0       -0.819911   -0.078767    1.796912
   48          1             0       -1.917083    1.251531   -0.801628
   49          1             0       -4.396136    0.686711   -1.341811
   50          1             0       -5.252691   -0.513083   -0.320194
   51          1             0       -4.405853    2.750290    2.743802
 -------------------------------------------------------------------
```

css-CN**c**

```
E(RB+HF-LYP) =  -2496.22711105
Zero-point correction=                           0.380531 (Hartree/Particle)
Thermal correction to Energy=                    0.408022
Thermal correction to Enthalpy=                  0.408887
Thermal correction to Gibbs Free Energy=         0.323001
Sum of electronic and zero-point Energies=          -2495.846580
Sum of electronic and thermal Energies=             -2495.819089
Sum of electronic and thermal Enthalpies=           -2495.818224
Sum of electronic and thermal Free Energies=        -2495.904110
```

```
Variational PCM results
=======================
<psi(f)|   H    |psi(f)>                    (a.u.) =   -2496.631070
<psi(f)|H+V(f)/2|psi(f)>                    (a.u.) =   -2496.651855
Total free energy in solution:
 with all non electrostatic terms           (a.u.) =   -2496.616406
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.739330	1.026574	1.929612
2	6	0	0.191033	0.677196	0.599750
3	8	0	-0.327245	0.326944	-0.514403
4	50	0	-1.094349	-1.704757	-0.778991
5	7	0	-2.572979	-0.945281	0.819050
6	6	0	-1.896137	-0.370316	1.845564
7	7	0	-2.384939	1.874177	1.027762
8	6	0	-3.243198	1.340045	0.239398
9	8	0	-3.825844	2.042798	-0.749890
10	6	0	-3.729230	-0.091313	0.423494
11	8	0	-1.235524	-1.262500	2.617876
12	6	0	0.993756	1.940755	0.692223
13	8	0	0.415714	3.038421	0.013898
14	6	0	1.246213	4.189478	0.106062
15	8	0	2.501537	3.978481	-0.498628
16	6	0	3.212601	2.895443	0.095820
17	6	0	2.378894	1.611306	0.042811
18	17	0	0.925585	-2.620387	0.642713
19	6	0	-3.321096	3.375340	-0.947387
20	6	0	-0.499332	-0.790401	3.745163
21	6	0	-4.652538	-0.655228	-0.677163
22	6	0	-4.065526	-0.742687	-2.095067
23	6	0	-5.258478	-1.997491	-0.244746
24	6	0	0.558439	5.328141	-0.611169
25	8	0	3.025386	0.567020	0.725646
26	17	0	2.888694	-1.034211	-2.294028
27	50	0	3.495114	-1.337917	0.084846
28	1	0	2.173252	1.372004	-1.016091
29	1	0	1.399840	4.416964	1.186267
30	1	0	-0.422519	5.524609	-0.155709
31	1	0	-1.321054	1.507482	2.814023
32	1	0	-0.085537	-1.686273	4.223514
33	1	0	0.327417	-0.123465	3.450358
34	1	0	-1.160960	-0.261221	4.451288
35	1	0	-5.469366	0.085150	-0.727243
36	1	0	-3.812167	3.742927	-1.857215
37	1	0	-2.227128	3.353060	-1.057432
38	1	0	-3.574268	4.013176	-0.086461
39	1	0	-4.880371	-0.852111	-2.829492
40	1	0	-3.419920	-1.627495	-2.229746
41	1	0	-3.498323	0.159594	-2.365392
42	1	0	-5.983108	-2.356253	-0.992978
43	1	0	-5.783388	-1.910724	0.720307
44	1	0	-4.481144	-2.769373	-0.126837
45	1	0	-4.376370	-0.049878	1.325112
46	1	0	0.553400	-0.097843	1.285525
47	1	0	1.161161	2.177906	1.762427
48	1	0	3.473797	3.120690	1.150336
49	1	0	4.143889	2.773175	-0.475636
50	1	0	0.422134	5.062024	-1.669924
51	1	0	1.176546	6.235088	-0.549254

tas-BN**c**

```
E(RB+HF-LYP) =  -2496.24913566
Zero-point correction=                           0.381274 (Hartree/Particle)
Thermal correction to Energy=                    0.408651
Thermal correction to Enthalpy=                  0.409516
Thermal correction to Gibbs Free Energy=         0.324171
Sum of electronic and zero-point Energies=          -2495.867862
Sum of electronic and thermal Energies=             -2495.840485
Sum of electronic and thermal Enthalpies=           -2495.839620
Sum of electronic and thermal Free Energies=        -2495.924965
----------------------------------------------------------------------
Variational PCM results
=======================
<psi(f)|   H    |psi(f)>                    (a.u.) =   -2496.653303
<psi(f)|H+V(f)/2|psi(f)>                    (a.u.) =   -2496.672727
Total free energy in solution:
 with all non electrostatic terms           (a.u.) =   -2496.633866
----------------------------------------------------------------------
Center     Atomic     Atomic              Coordinates (Angstroms)
Number     Number      Type              X           Y           Z
----------------------------------------------------------------------
   1          6             0       -1.703166    2.064272    0.455976
   2          6             0        0.263953    0.900901    0.002206
   3          8             0        0.318580    0.482678   -1.211425
   4         50             0       -1.096823   -1.067707   -1.879254
   5          7             0       -2.589599    0.062474   -0.563630
   6          6             0       -2.170790    1.336888   -0.647977
   7          7             0       -1.941465    1.592363    1.759761
   8          6             0       -2.563183    0.475558    1.872126
   9          8             0       -2.789453   -0.088251    3.073188
  10          6             0       -3.124966   -0.372506    0.740029
  11          8             0       -1.992928    1.715653   -1.932232
  12          6             0        1.356504    1.801098    0.506794
  13          8             0        1.513132    2.962967   -0.302178
  14          6             0        2.587440    3.776305    0.167049
  15          8             0        3.814127    3.089253    0.133453
  16          6             0        3.801065    1.912887    0.942204
  17          6             0        2.675978    0.978476    0.490906
  18         17             0       -0.310393   -2.537267    0.122157
  19          6             0       -2.280126    0.608133    4.217991
  20          6             0       -1.340276    2.967452   -2.214804
  21          6             0       -4.683177   -0.408203    0.760180
  22          6             0       -5.311079    0.970063    0.522826
  23          6             0       -5.212266   -1.443029   -0.238647
  24          6             0        2.692743    4.984135   -0.735670
  25          8             0        2.566315   -0.134840    1.343488
  26         17             0        3.281041   -1.989873   -1.440950
  27         50             0        2.551996   -2.145303    0.912398
  28          1             0        2.859329    0.698407   -0.561729
  29          1             0        2.360478    4.064075    1.218961
  30          1             0        1.750217    5.550254   -0.727848
  31          1             0       -1.446145    3.119508    0.377631
  32          1             0       -1.287734    3.023256   -3.308912
  33          1             0       -1.949231    3.802761   -1.833971
  34          1             0       -0.330536    2.994948   -1.781379
  35          1             0       -4.949101   -0.741521    1.778667
  36          1             0       -2.571830    0.001930    5.084565
  37          1             0       -2.712399    1.618094    4.284352
  38          1             0       -1.184748    0.701335    4.159792
  39          1             0       -6.405500    0.920519    0.641338
  40          1             0       -5.103901    1.330471   -0.498154
  41          1             0       -4.932539    1.722530    1.233736
  42          1             0       -6.310800   -1.510714   -0.186829
  43          1             0       -4.804036   -2.446881   -0.034757
  44          1             0       -4.940853   -1.166743   -1.270568
  45          1             0       -2.780630   -1.402227    0.930202
  46          1             0       -0.157147    0.242173    0.775315
  47          1             0        1.118390    2.082008    1.551120
  48          1             0        3.666401    2.168824    2.012908
  49          1             0        4.781214    1.431166    0.817295
  50          1             0        2.910356    4.653831   -1.762223
  51          1             0        3.508409    5.635748   -0.391626
----------------------------------------------------------------------
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tsa-CM**c**

```
E(RB+HF-LYP) =  -2496.25656316
Zero-point correction=                           0.380471 (Hartree/Particle)
Thermal correction to Energy=                    0.408041
Thermal correction to Enthalpy=                  0.408906
Thermal correction to Gibbs Free Energy=         0.322848
Sum of electronic and zero-point Energies=          -2495.876092
Sum of electronic and thermal Energies=             -2495.848522
Sum of electronic and thermal Enthalpies=           -2495.847657
Sum of electronic and thermal Free Energies=        -2495.933715
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Variational PCM results
=======================
<psi(f)|   H    |psi(f)>                    (a.u.) =   -2496.659184
<psi(f)|H+V(f)/2|psi(f)>                    (a.u.) =   -2496.678287
Total free energy in solution:
 with all non electrostatic terms           (a.u.) =   -2496.639644
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.517066	2.369584	-0.221438
2	6	0	0.904433	0.602459	-0.604336
3	8	0	0.262073	-0.436905	-0.133627
4	50	0	-1.493860	-1.275554	-1.422399
5	7	0	-2.265841	0.749168	-0.583900
6	6	0	-1.419007	1.663188	-1.052325
7	7	0	-0.644292	2.308370	1.172147
8	6	0	-1.609960	1.600249	1.635648
9	8	0	-1.787688	1.429939	2.956326
10	6	0	-2.677695	0.895942	0.824258
11	8	0	-1.310812	1.643068	-2.408708
12	6	0	2.120126	1.127776	0.101141
13	8	0	2.557306	2.259270	-0.652044
14	6	0	3.778706	2.805683	-0.162388
15	8	0	4.818667	1.862405	-0.217340
16	6	0	4.534716	0.726658	0.594270
17	6	0	3.235249	0.038348	0.155935
18	17	0	-2.212136	-2.561842	0.575119
19	6	0	-0.839946	2.062077	3.826562
20	6	0	-0.499050	2.635954	-3.051339
21	6	0	-4.069966	1.583472	0.967789
22	6	0	-4.093325	3.024168	0.443448
23	6	0	-5.161558	0.731277	0.310438
24	6	0	4.148584	3.982846	-1.035435
25	8	0	2.916266	-0.952947	1.085817
26	17	0	1.466268	-3.110241	-1.306049
27	50	0	1.341773	-2.264012	1.072411
28	1	0	3.377182	-0.363263	-0.867269
29	1	0	3.618308	3.110362	0.896330
30	1	0	3.355359	4.743552	-1.007496
31	1	0	0.078810	3.197726	-0.599211
32	1	0	-0.588319	2.435791	-4.126084
33	1	0	-0.880791	3.645647	-2.829840
34	1	0	0.556735	2.567784	-2.745122
35	1	0	-4.259252	1.609144	2.055543
36	1	0	-1.184065	1.841841	4.844589
37	1	0	-0.810462	3.147527	3.648918
38	1	0	0.169215	1.653094	3.663360
39	1	0	-5.064809	3.495862	0.663041
40	1	0	-3.953440	3.055293	-0.649904
41	1	0	-3.309871	3.646114	0.906210
42	1	0	-6.155948	1.174824	0.479650
43	1	0	-5.172301	-0.293088	0.716084
44	1	0	-5.003073	0.662645	-0.777881
45	1	0	-2.783390	-0.112525	1.251380
46	1	0	0.946662	0.715514	-1.699386
47	1	0	1.869707	1.408416	1.142365
48	1	0	4.436657	1.017110	1.659806
49	1	0	5.384414	0.037293	0.497229
50	1	0	4.287085	3.639645	-2.071561
51	1	0	5.088691	4.427882	-0.680006

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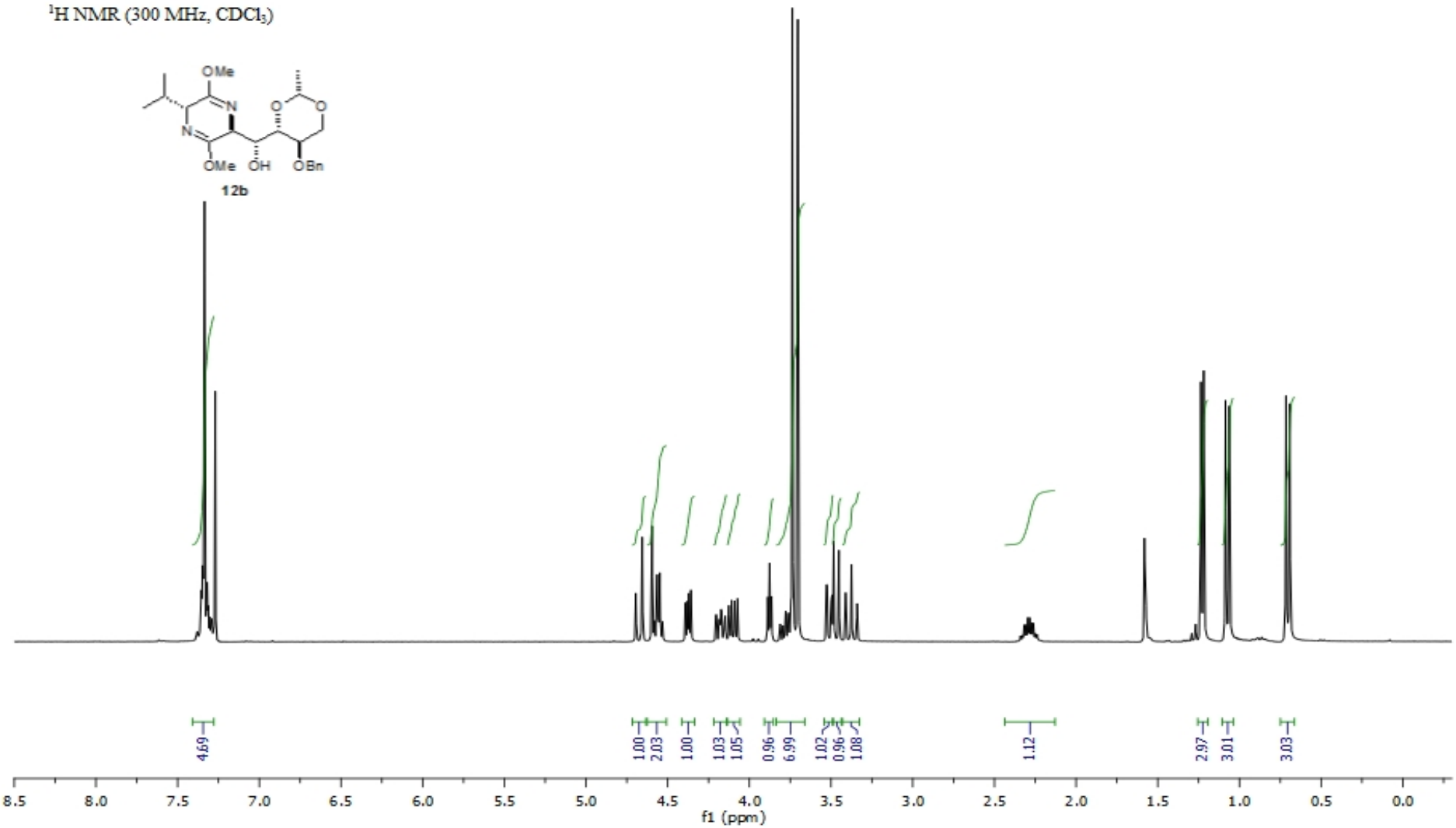
5. References.

(1) M. Svensson, S. Humbel, R. D. J. Froese, T. Matsubara, S. Sieber and K. Morokuma, *J. Phys. Chem.*, 1996, **100**, 19357–19363.

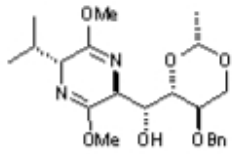
(2) (a) T. H. Dunning Jr. and P. J. Hay, in *Methods of Electronic Structure Theory, Vol. 2*, H. F. Schaefer III, ed., Plenum Press, 1977; (b) P. J. Hay and W. R. Wadt, *J. Chem. Phys.,* 1982, **82**, 270, 284 and 299.

(3) (a) M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902–3909; (b) M. J. S. Dewar and E. G. Zoebisch, *Teochem.*, 1988, **49**, 1–21; (c) M. J. S. Dewar and C. Jie, *Organometallics*, 1987, **6**, 1486–1490; (d) M. J. S. Dewar, E. F. Healy, D. R. Kuhn and A. J. Holder, *Organometallics*, 1991, **10**, 431–435.

6. NMR spectra.

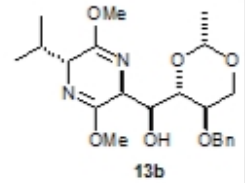


^{13}C NMR (75 MHz, $CDCl_3$)

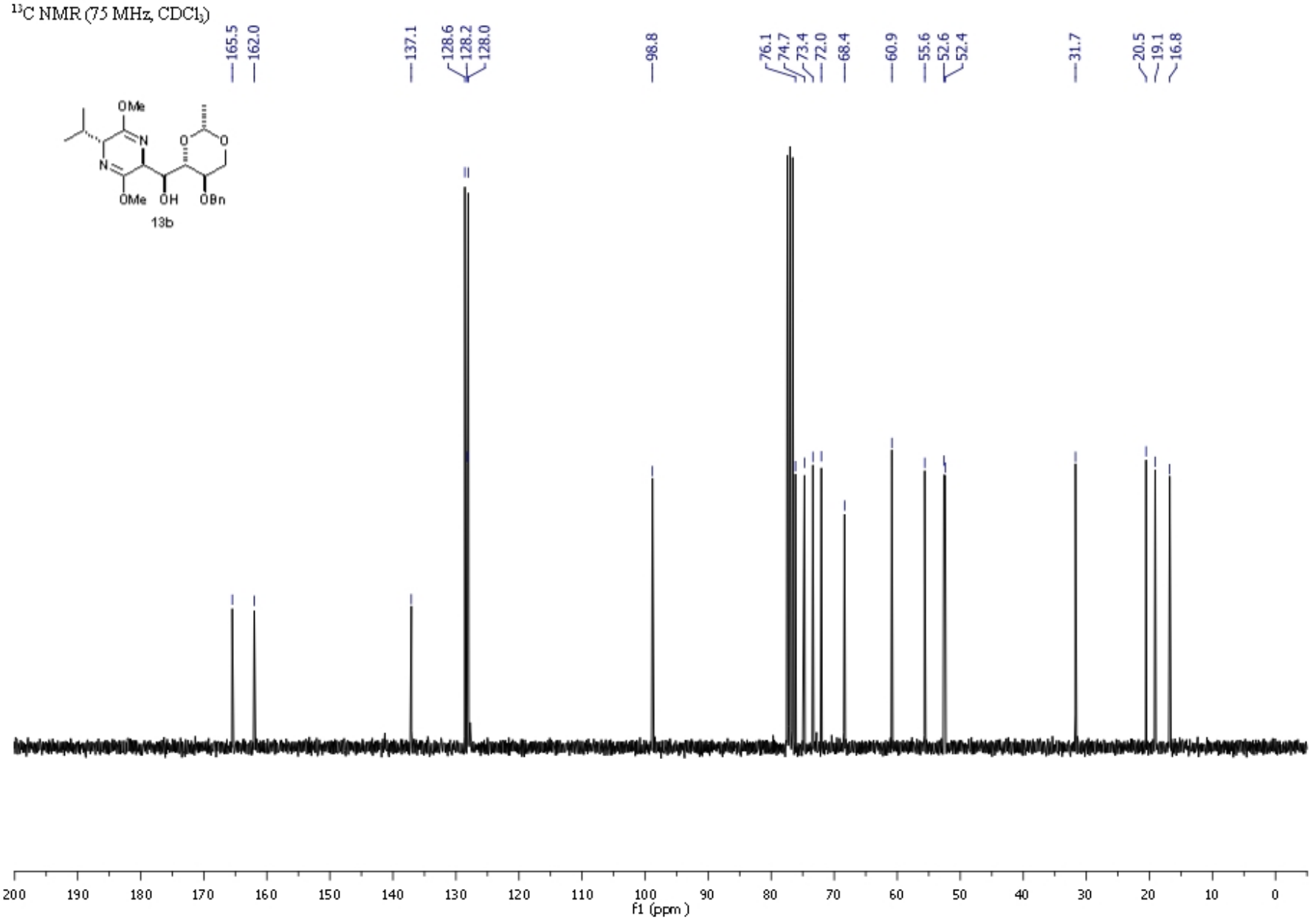


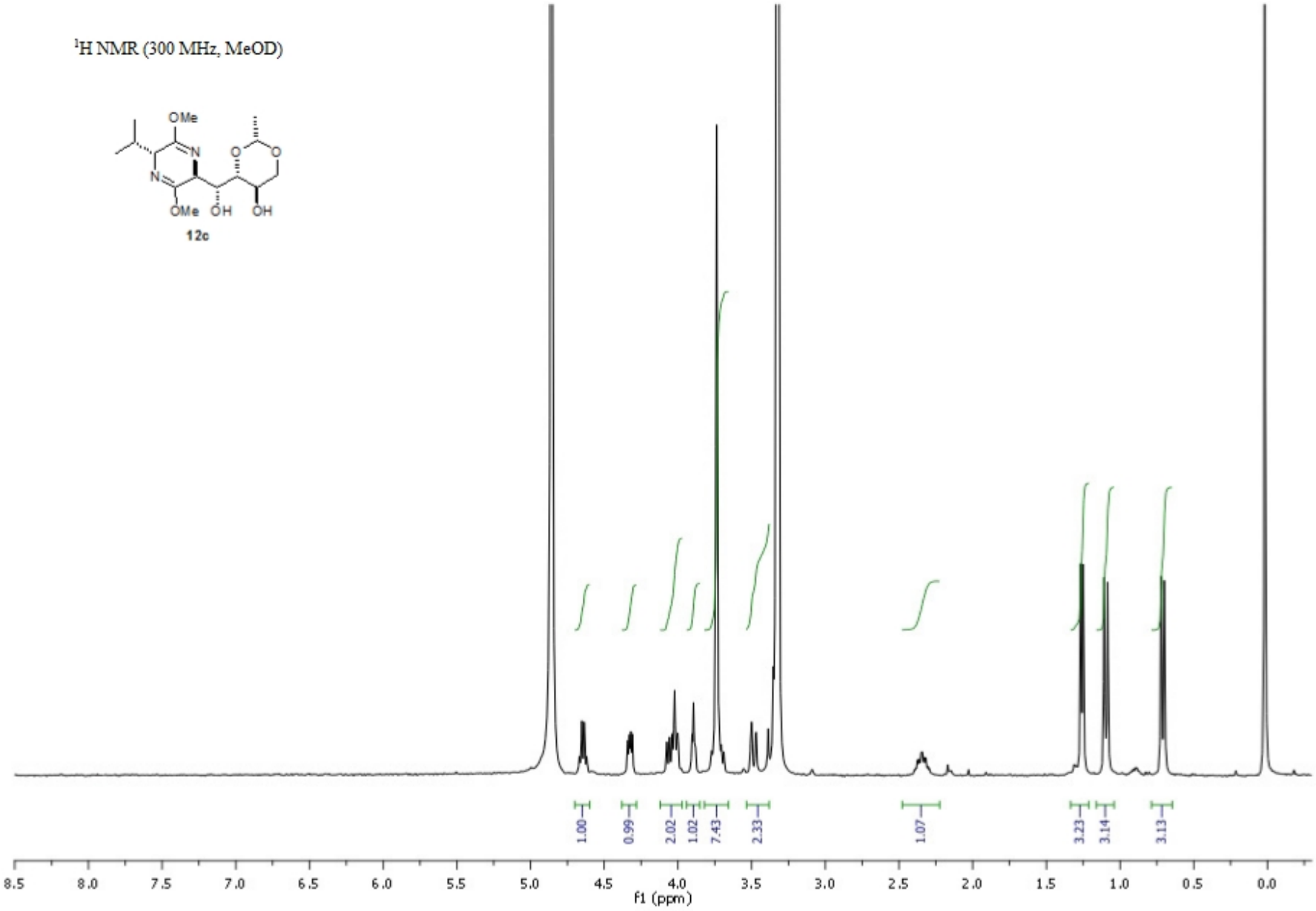
12b

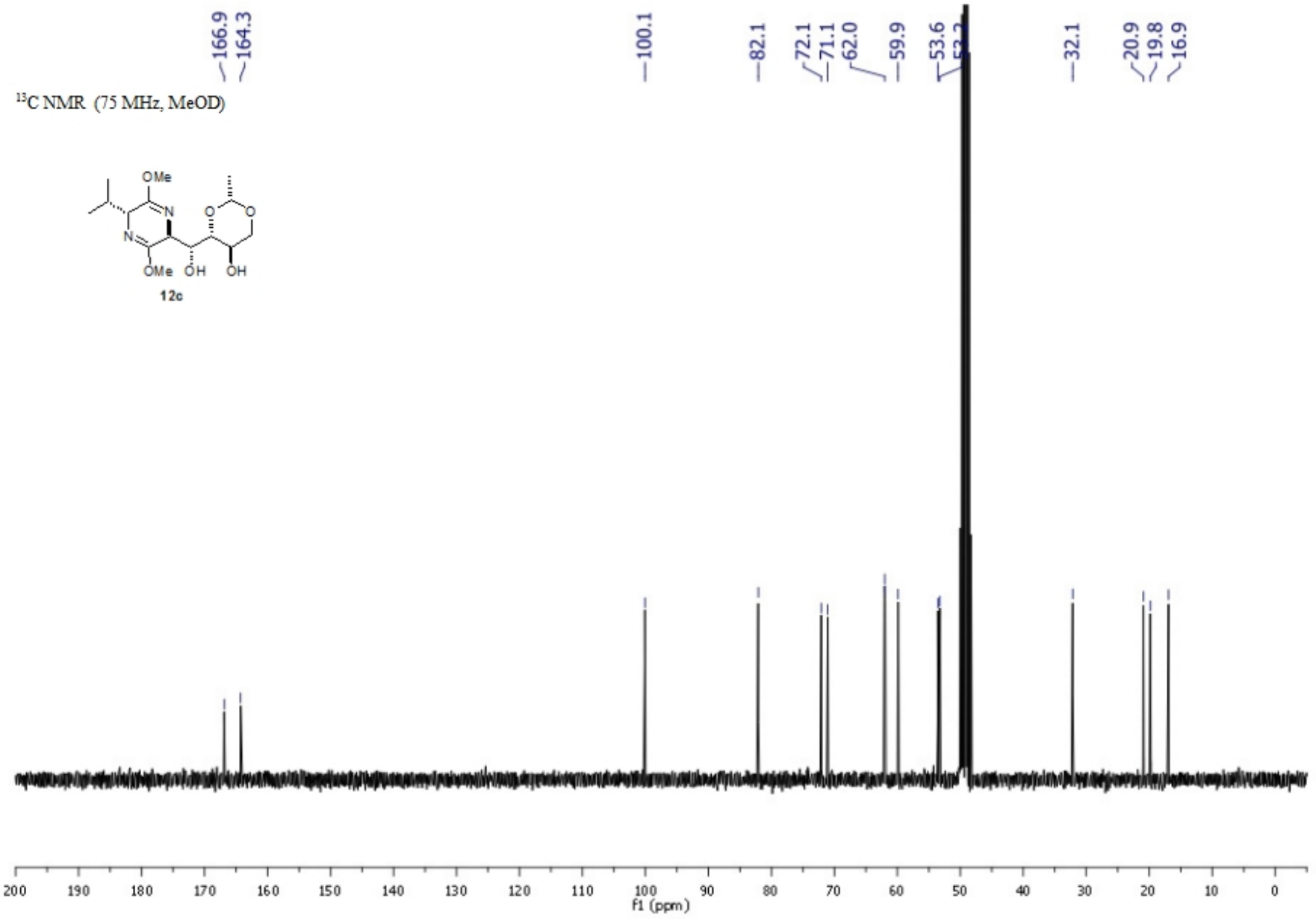
^{1}H NMR (300 MHz, $CDCl_3$)



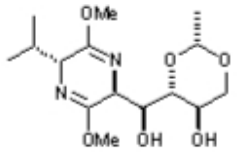
13b


^{13}C NMR (75 MHz, CDCl$_3$)
165.5
162.0
137.1
128.6
128.2
128.0
98.8
76.1
74.7
73.4
72.0
68.4
60.9
55.6
52.6
52.4
31.7
20.5
19.1
16.8
OMe
N
O
O
N
OMe
OH
OBn
13b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


^{1}H NMR (300 MHz, MeOD)
OMe
N
O
O
N
OMe
OH
OH
12c
1.00
0.99
2.02
1.02
7.43
2.33
1.07
3.23
3.14
3.13
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

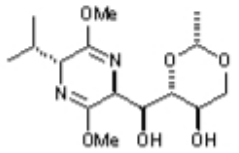

166.9
164.3
100.1
82.1
72.1
71.1
62.0
59.9
53.6
32.1
20.9
19.8
16.9
13C NMR (75 MHz, MeOD)
OMe
N
O
O
N
OMe
OH
OH
12c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (300 MHz, $CDCl_3$)

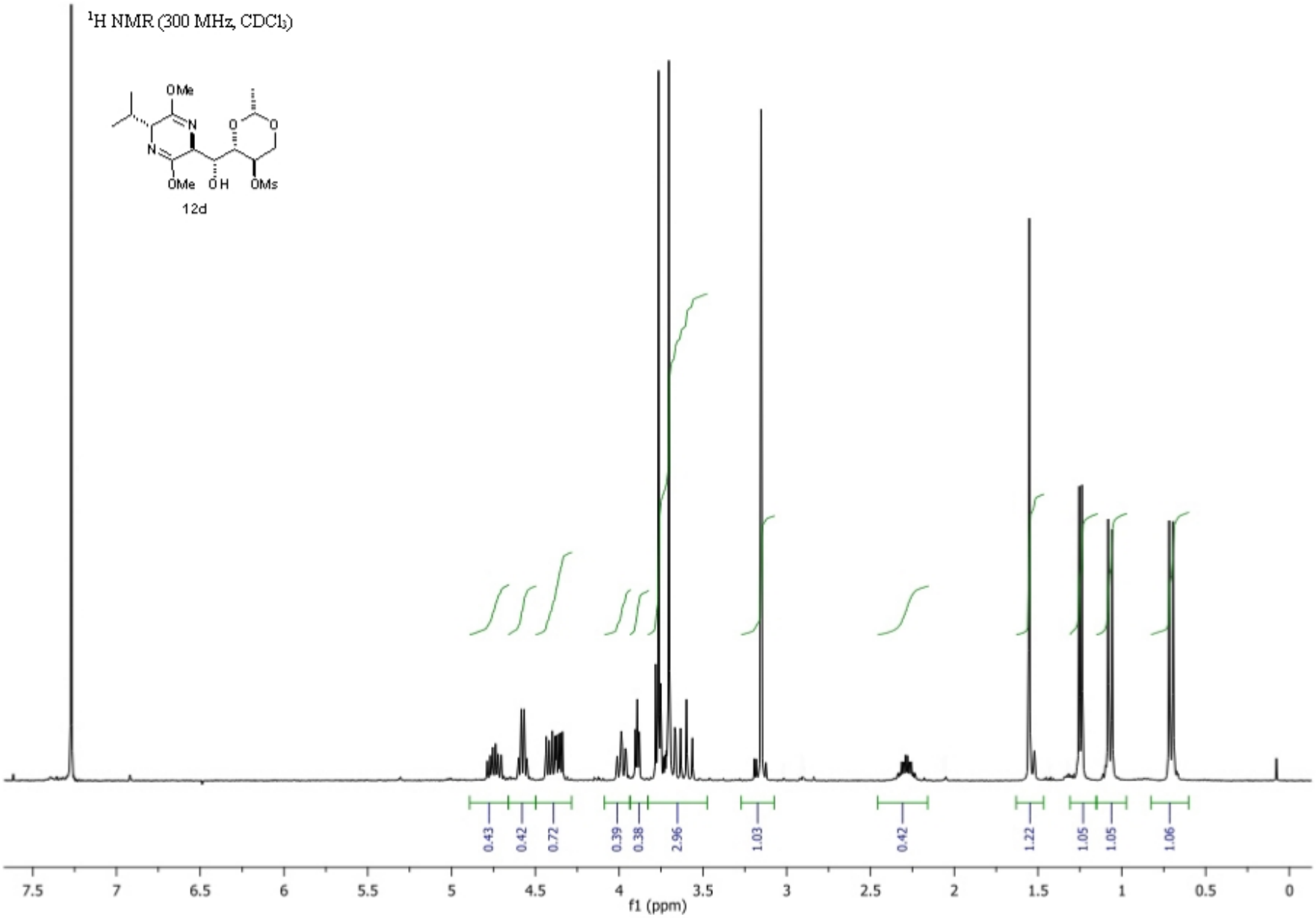


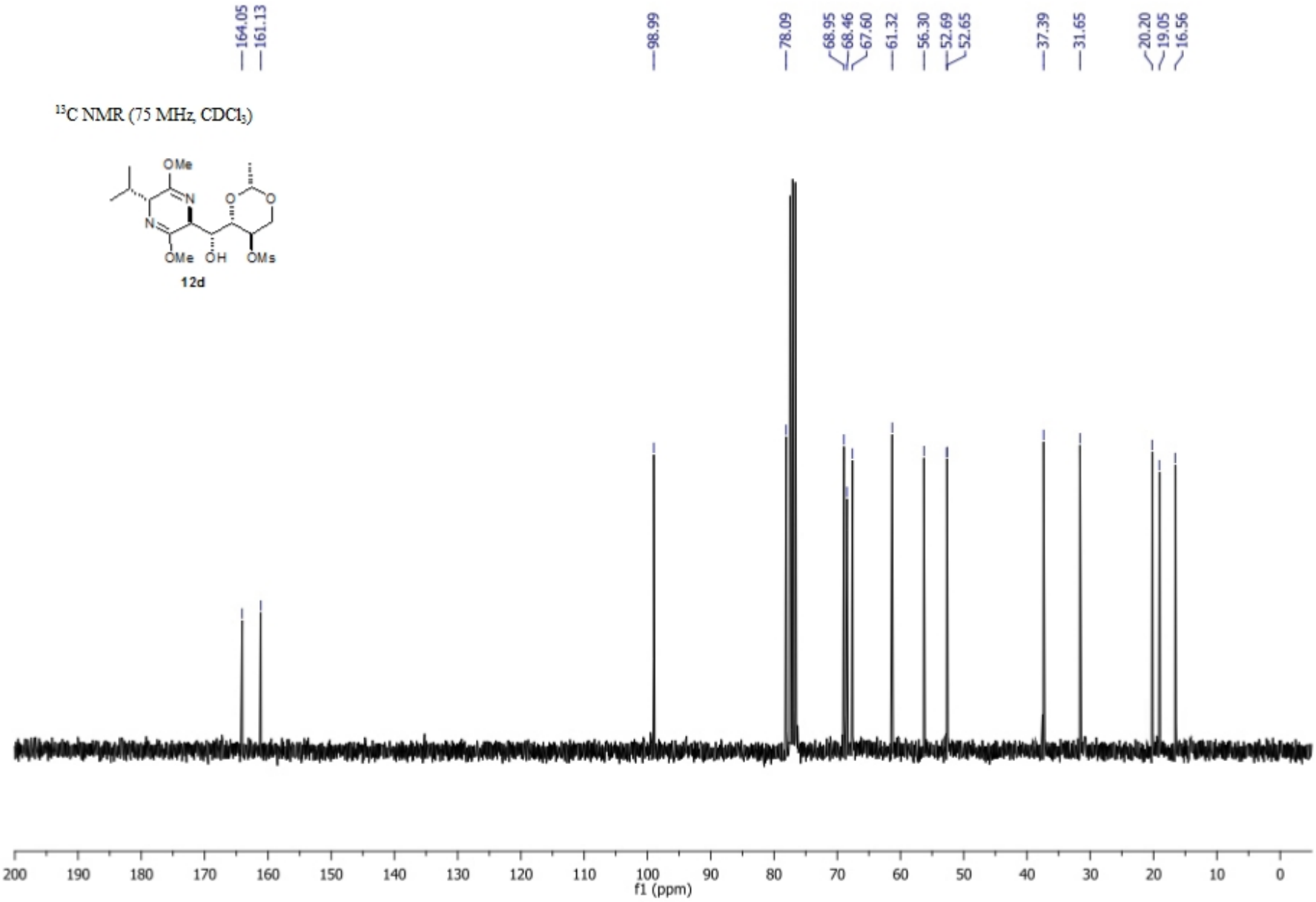
13c

^{13}C NMR (75 MHz, $CDCl_3$)

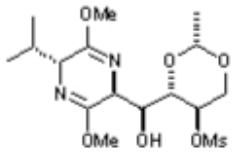


13c

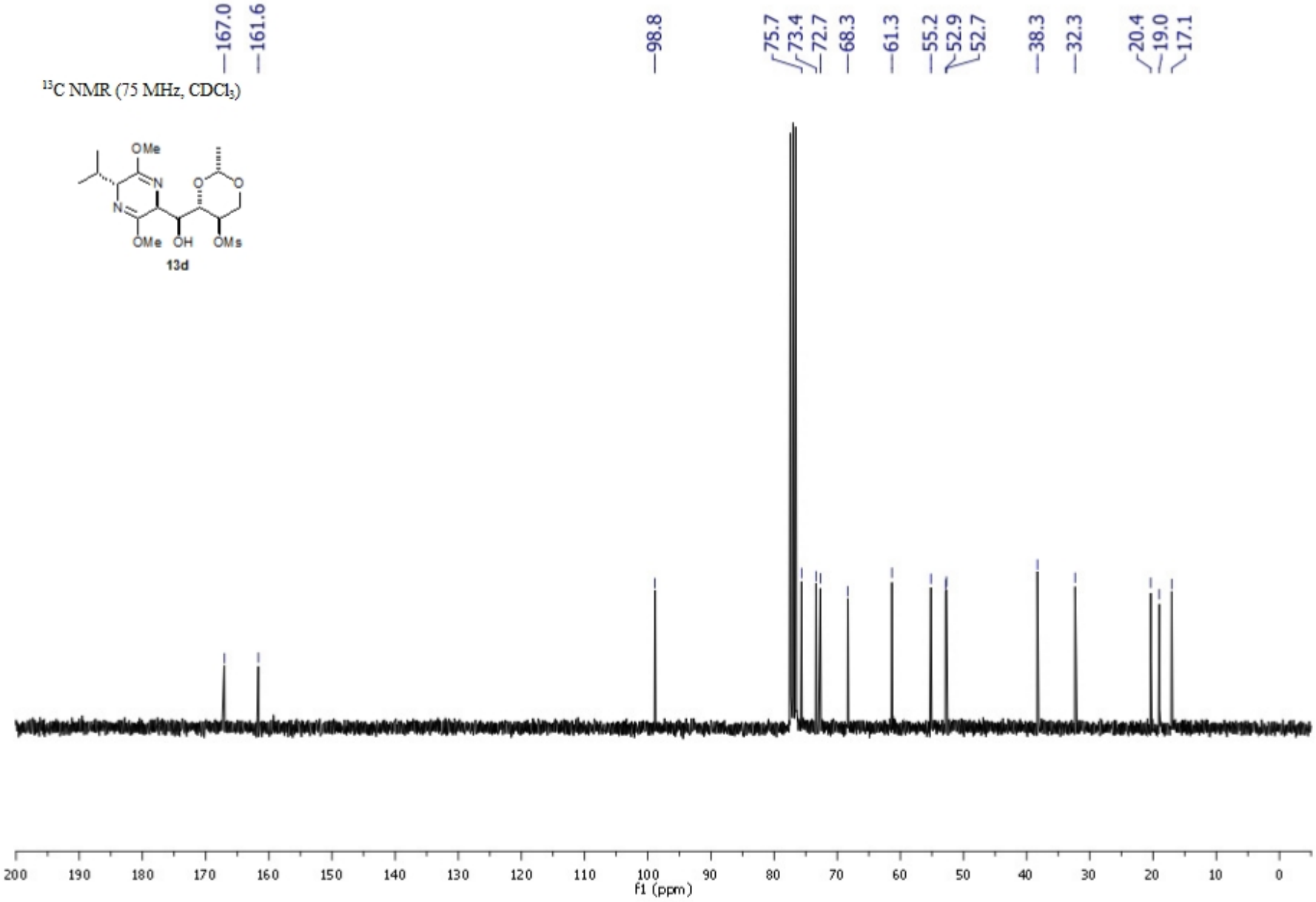

^{1}H NMR (300 MHz, CDCl$_3$)
OMe
N
N
O
O
OMe
OH
OMs
12d
0.43
0.42
0.72
0.39
0.38
2.96
1.03
0.42
1.22
1.05
1.05
1.06
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
f1 (ppm)


164.05
161.13
98.99
78.09
68.95
68.46
67.60
61.32
56.30
52.69
52.65
37.39
31.65
20.20
19.05
16.56
13C NMR (75 MHz, CDCl3)
OMe
N
O
O
N
OMe
OH
OMs
12d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

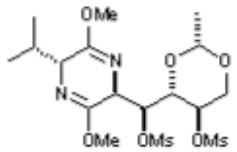
^{1}H NMR (300 MHz, $CDCl_3$)

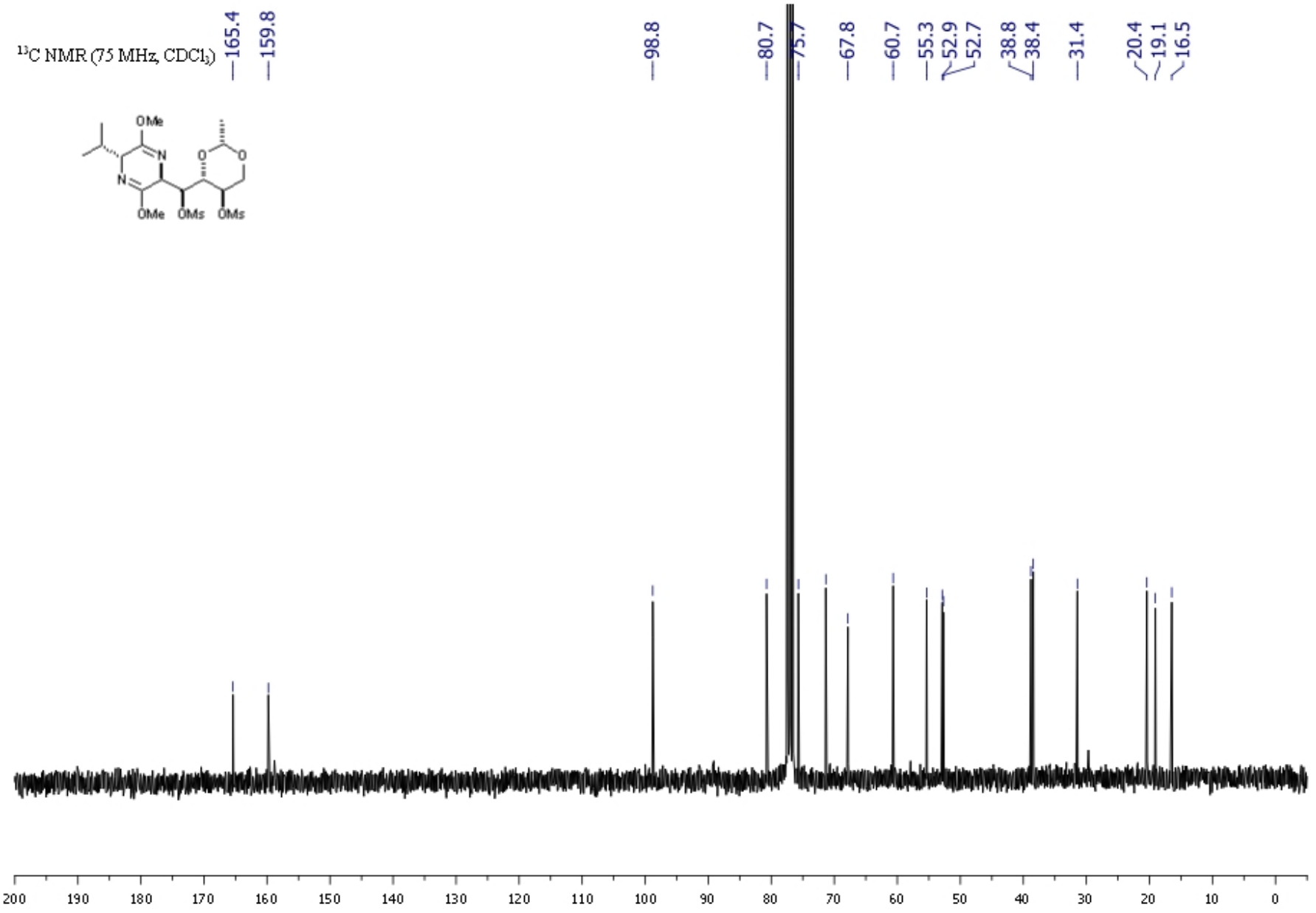


13d

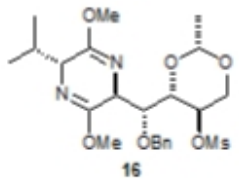

167.0
161.6
98.8
75.7
73.4
72.7
68.3
61.3
55.2
52.9
52.7
38.3
32.3
20.4
19.0
17.1
^{13}C NMR (75 MHz, $CDCl_3$)
OMe
N
O
O
N
OMe
OH
OMs
13d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (300 MHz, $CDCl_3$)

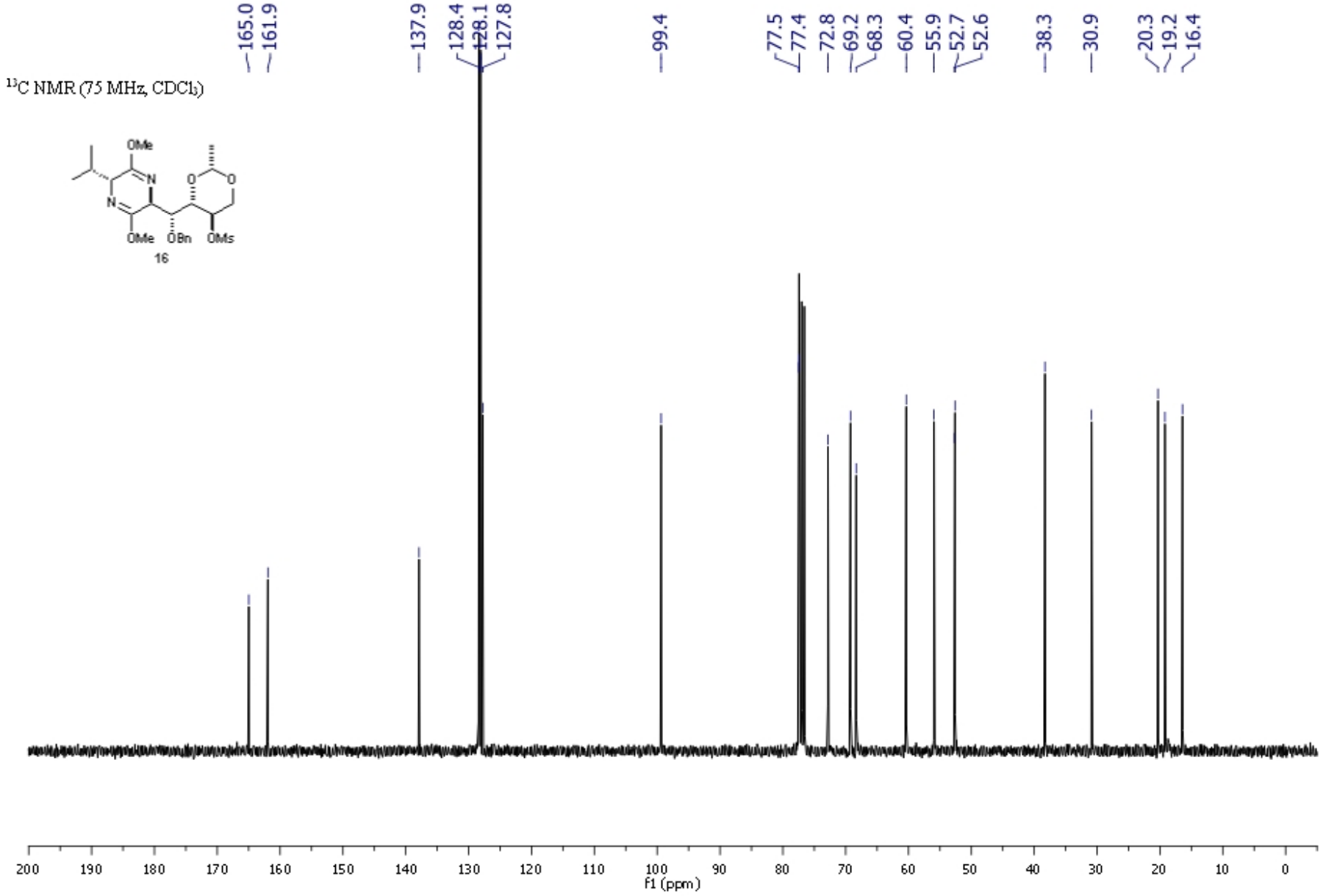


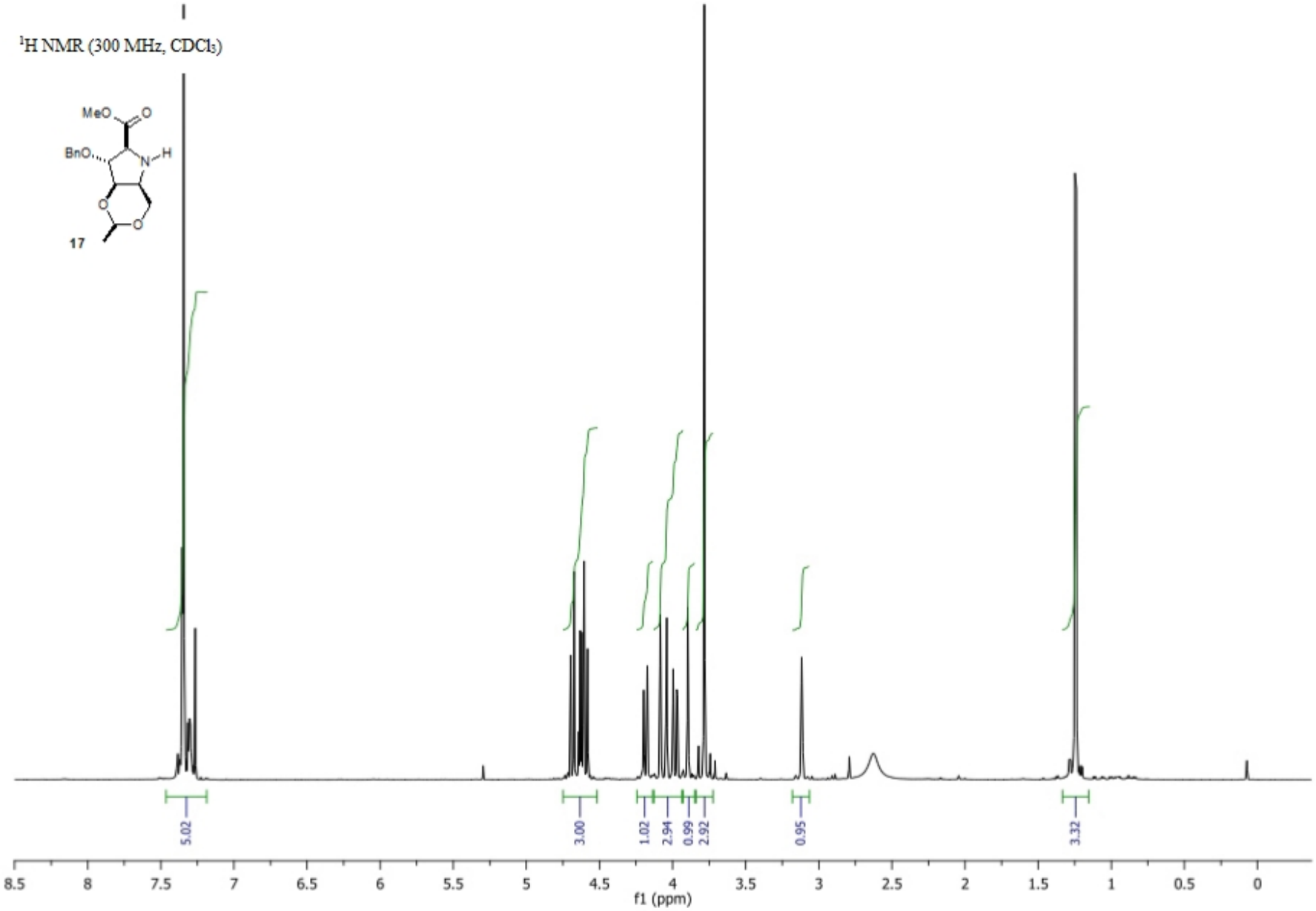

^{13}C NMR (75 MHz, CDCl$_3$)
165.4
159.8
98.8
80.7
75.7
67.8
60.7
55.3
52.9
52.7
38.8
38.4
31.4
20.4
19.1
16.5
OMe
OMe
OMs
OMs
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

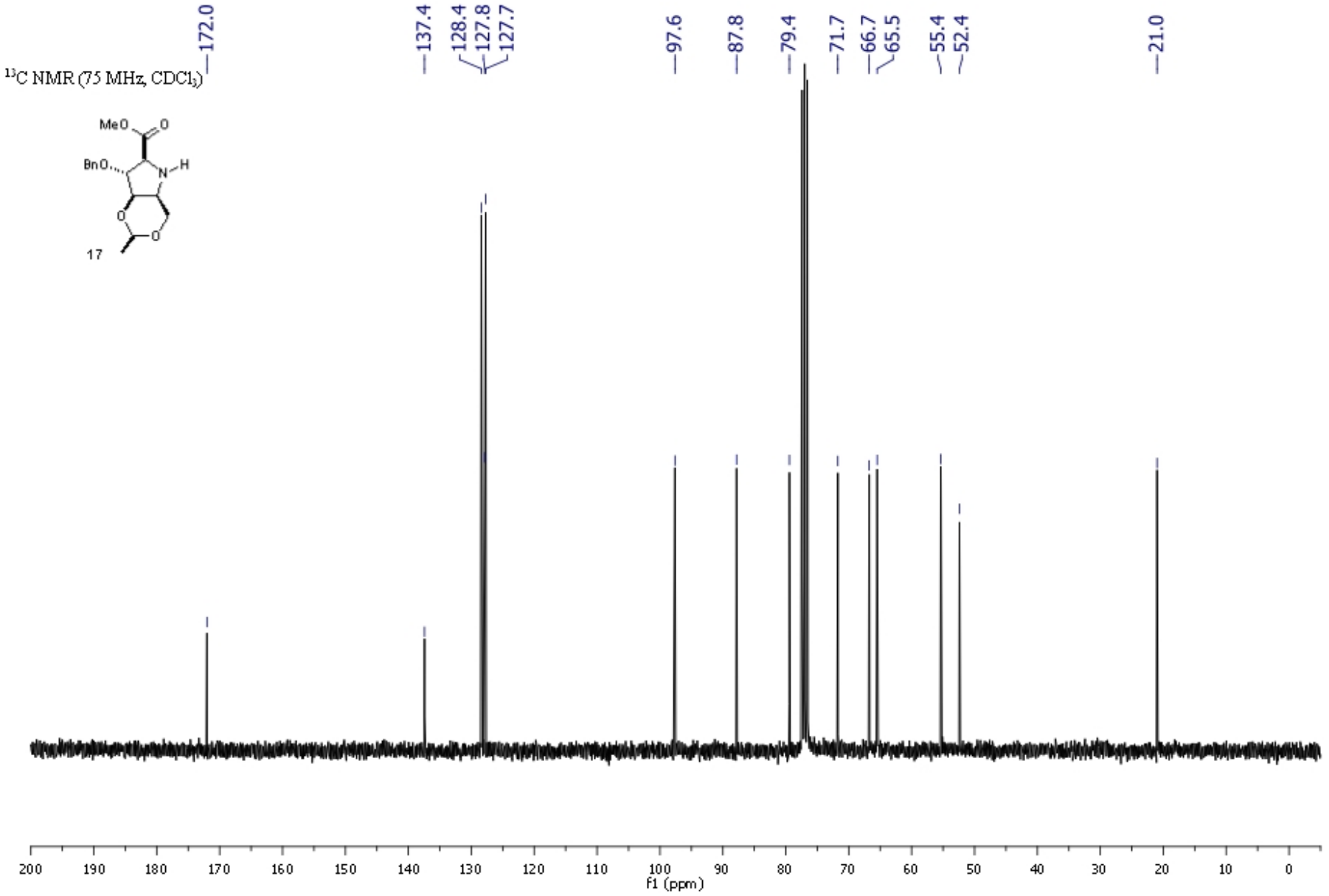
^{1}H NMR (300 MHz, $CDCl_3$)



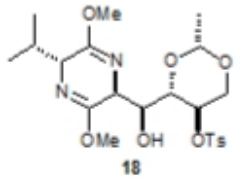
16


165.0
161.9
137.9
128.4
128.1
127.8
99.4
77.5
77.4
72.8
69.2
68.3
60.4
55.9
52.7
52.6
38.3
30.9
20.3
19.2
16.4
^{13}C NMR (75 MHz, CDCl$_3$)
OMe
N
O
O
N
OMe
OBn
OMs
16
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

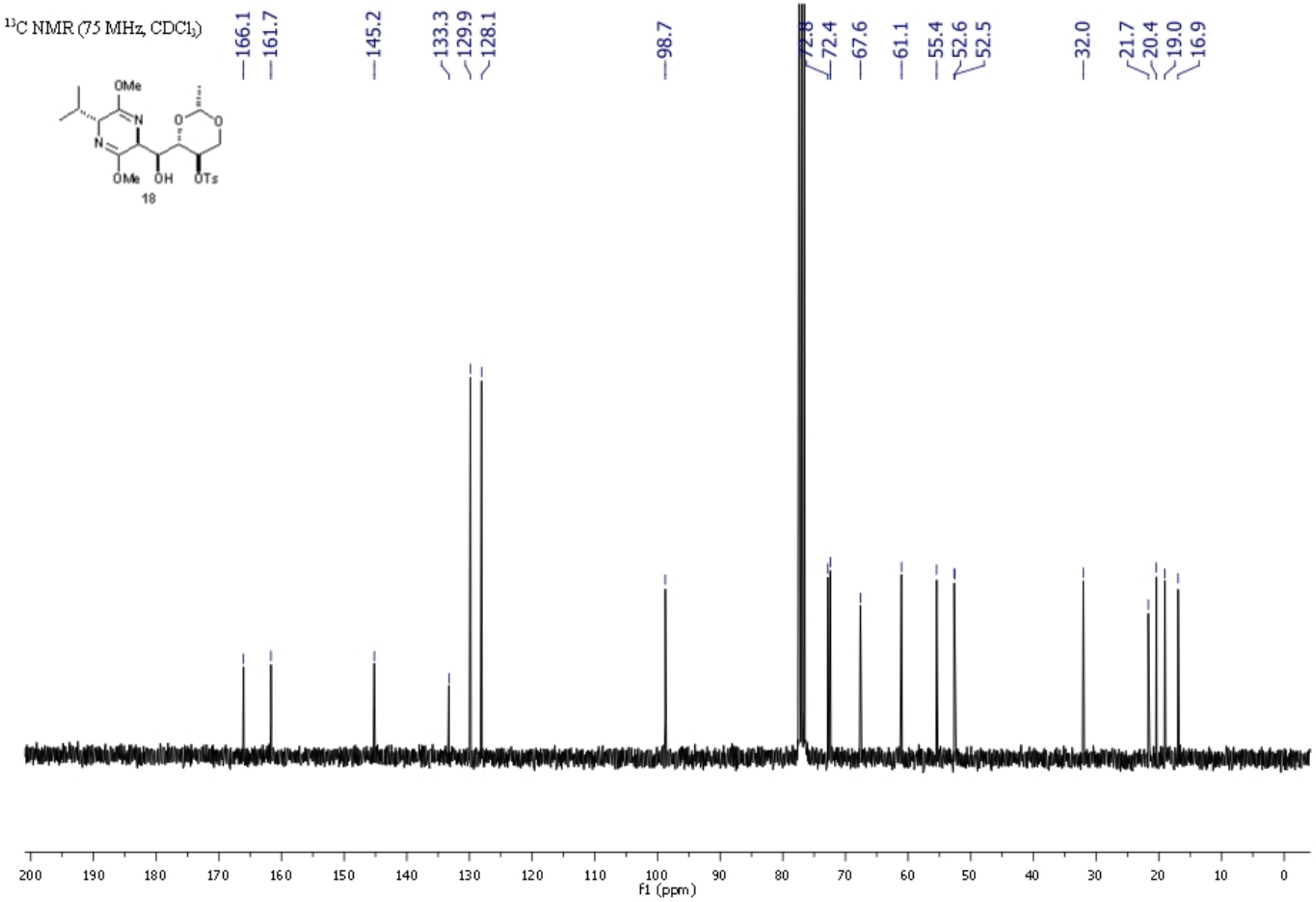

^{1}H NMR (300 MHz, $CDCl_3$)
MeO
O
BnO
N
H
O
O
17
5.02
3.00
1.02
2.94
0.99
2.92
0.95
3.32
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
f1 (ppm)


^{13}C NMR (75 MHz, CDCl$_3$)
172.0
137.4
128.4
127.8
127.7
97.6
87.8
79.4
71.7
66.7
65.5
55.4
52.4
21.0
MeO
O
BnO
N
H
O
O
17
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

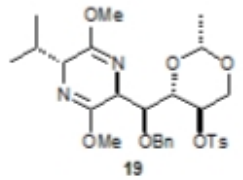
^{1}H NMR (300 MHz, $CDCl_3$)



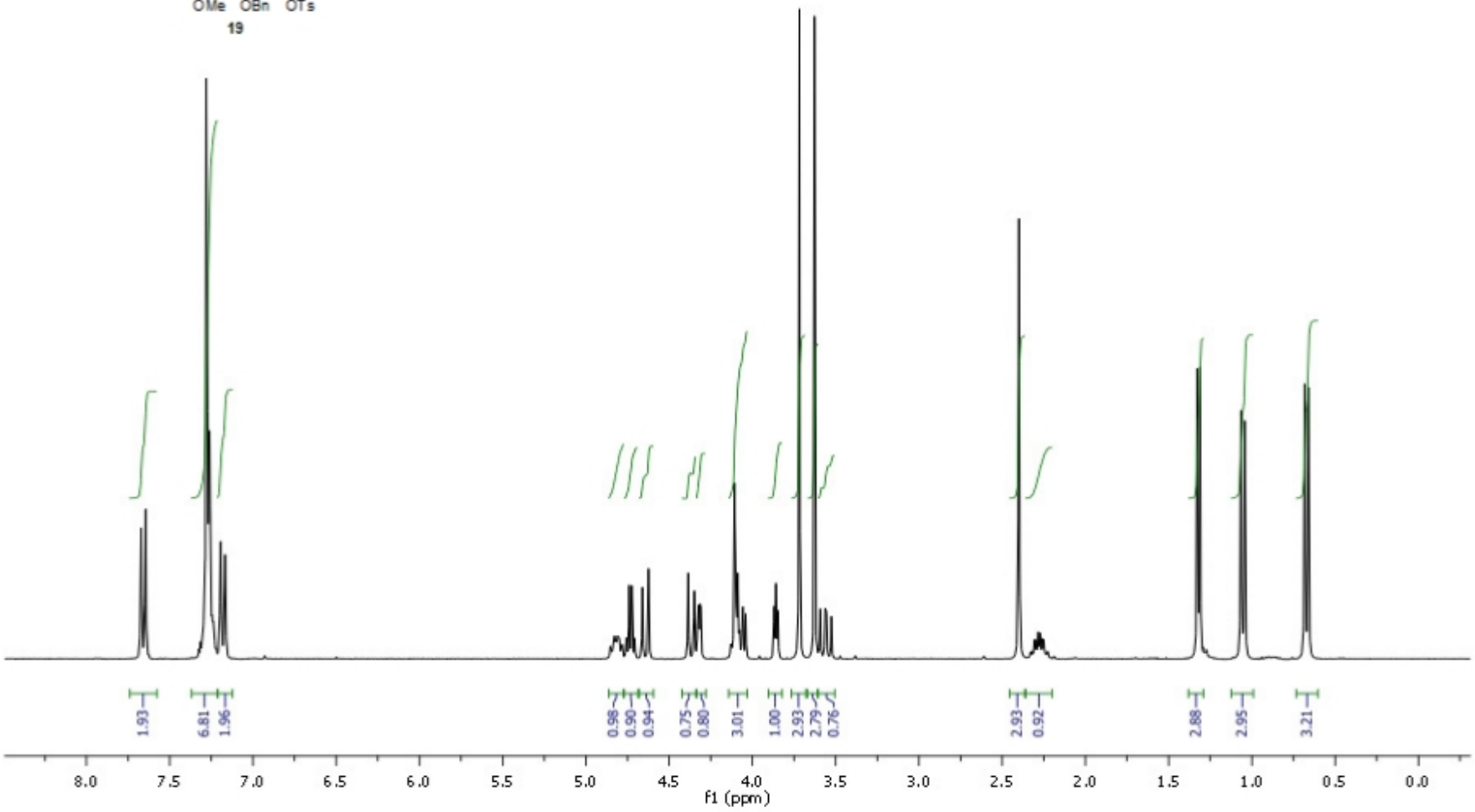
18

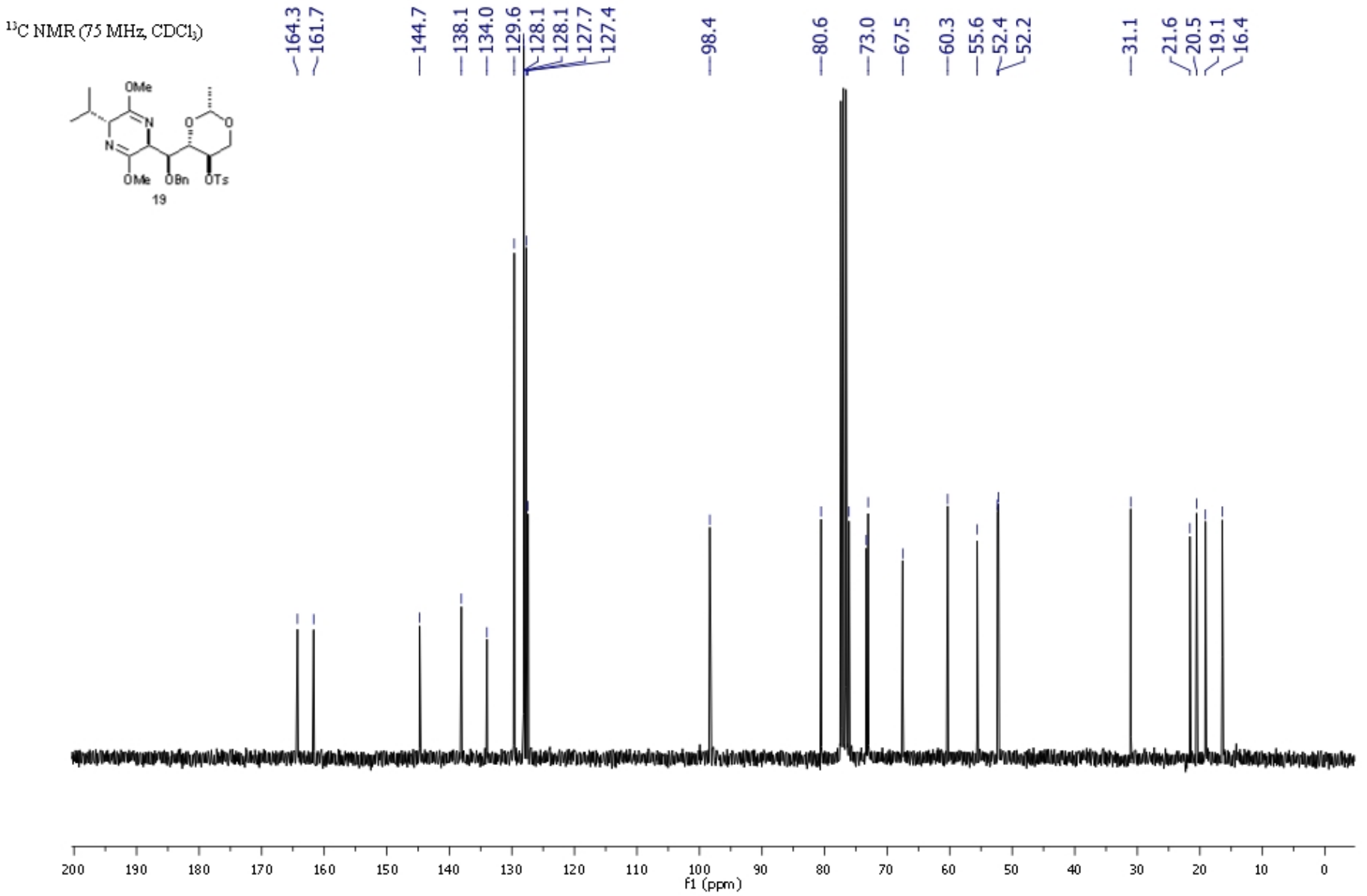

^{13}C NMR (75 MHz, CDCl$_3$)
166.1
161.7
145.2
133.3
129.9
128.1
98.7
72.8
72.4
67.6
61.1
55.4
52.6
52.5
32.0
21.7
20.4
19.0
16.9
OMe
N
O
O
N
OMe
OH
OTs
18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (300 MHz, $CDCl_3$)

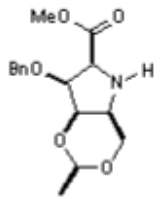


19

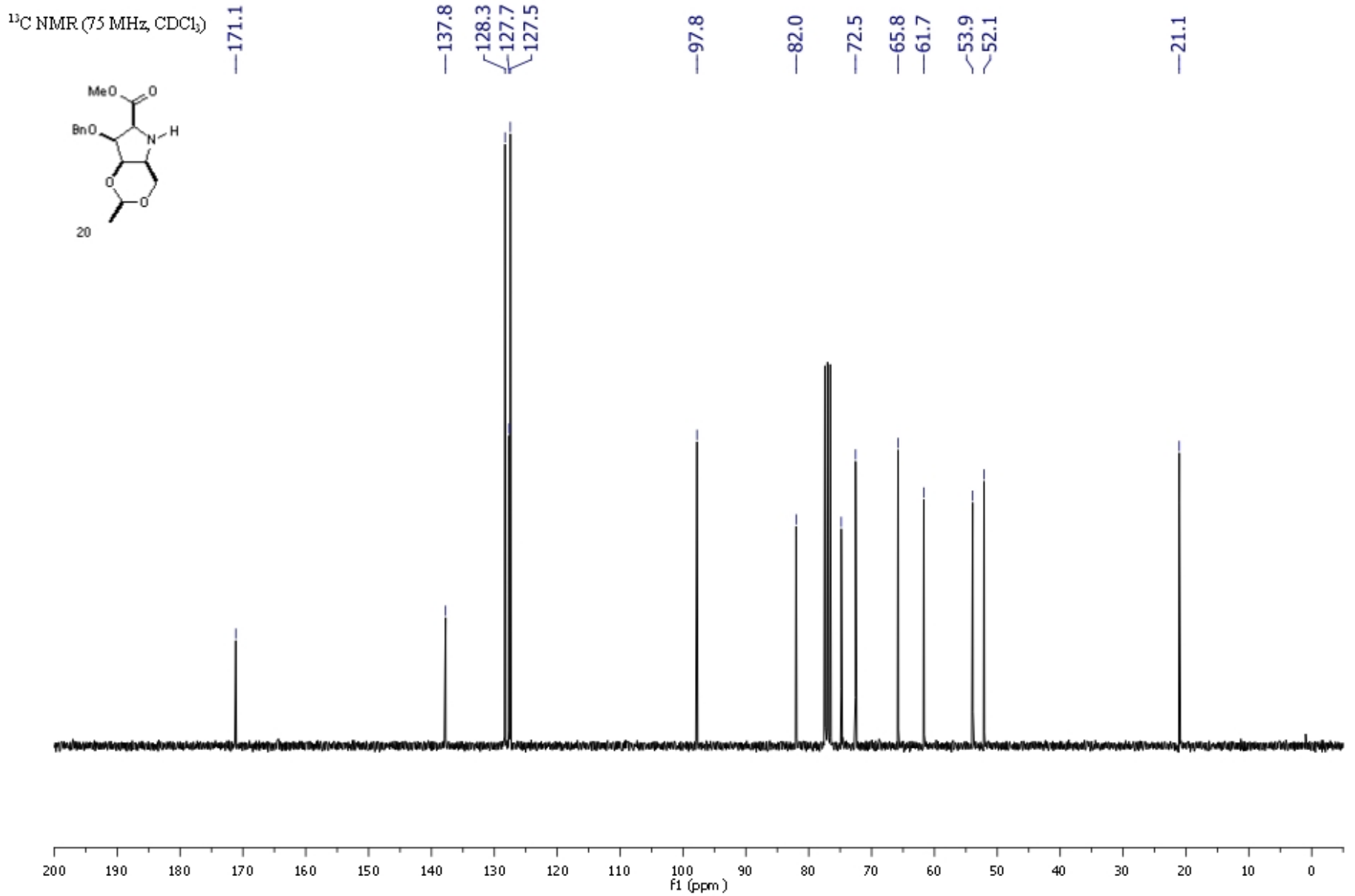



^{13}C NMR (75 MHz, CDCl$_3$)
164.3
161.7
144.7
138.1
134.0
129.6
128.1
128.1
127.7
127.4
98.4
80.6
73.0
67.5
60.3
55.6
52.4
52.2
31.1
21.6
20.5
19.1
16.4
OMe
N
N
O
O
OMe
OBn
OTs
19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

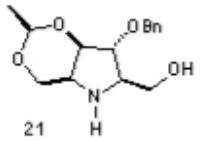
^{1}H NMR (300 MHz, $CDCl_3$)



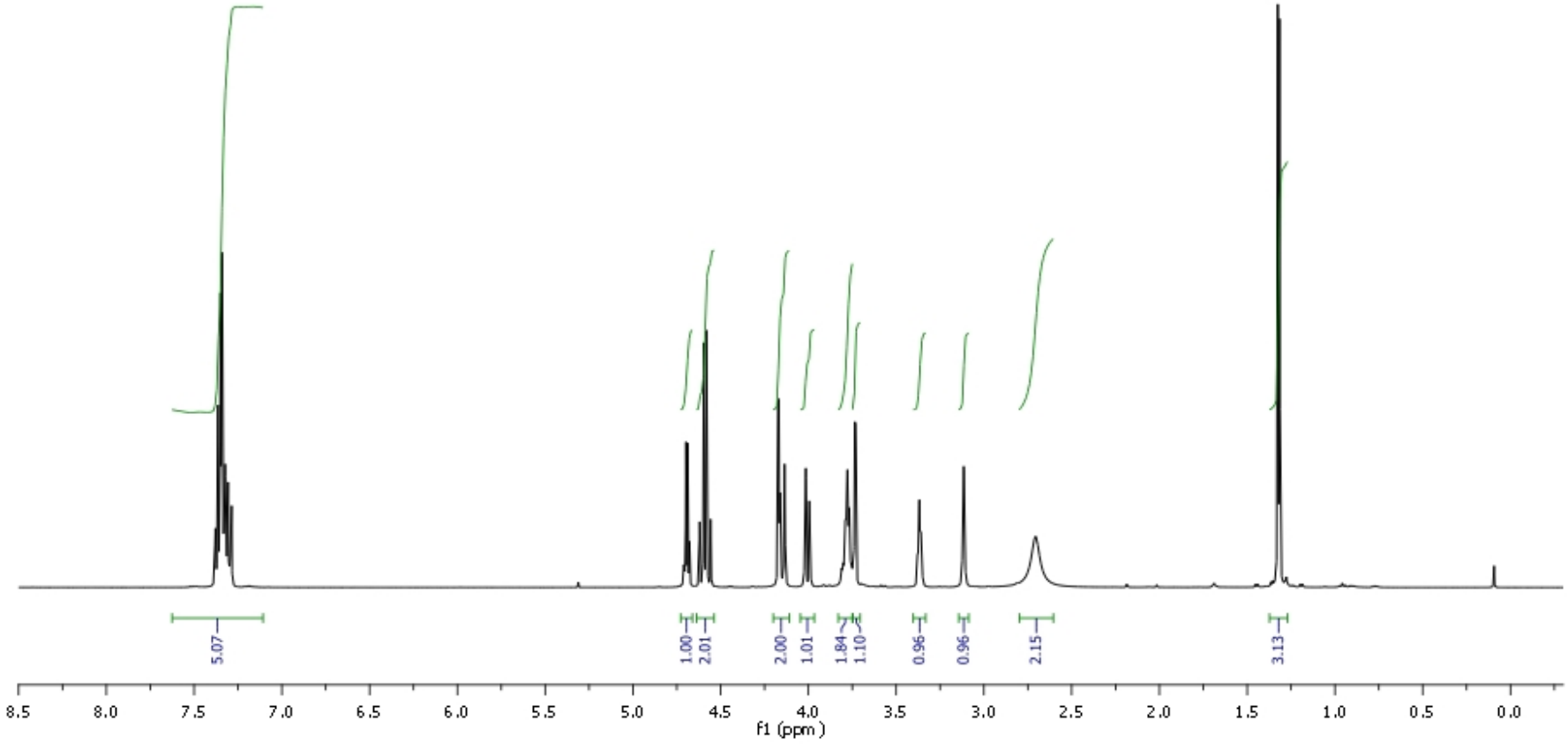
20

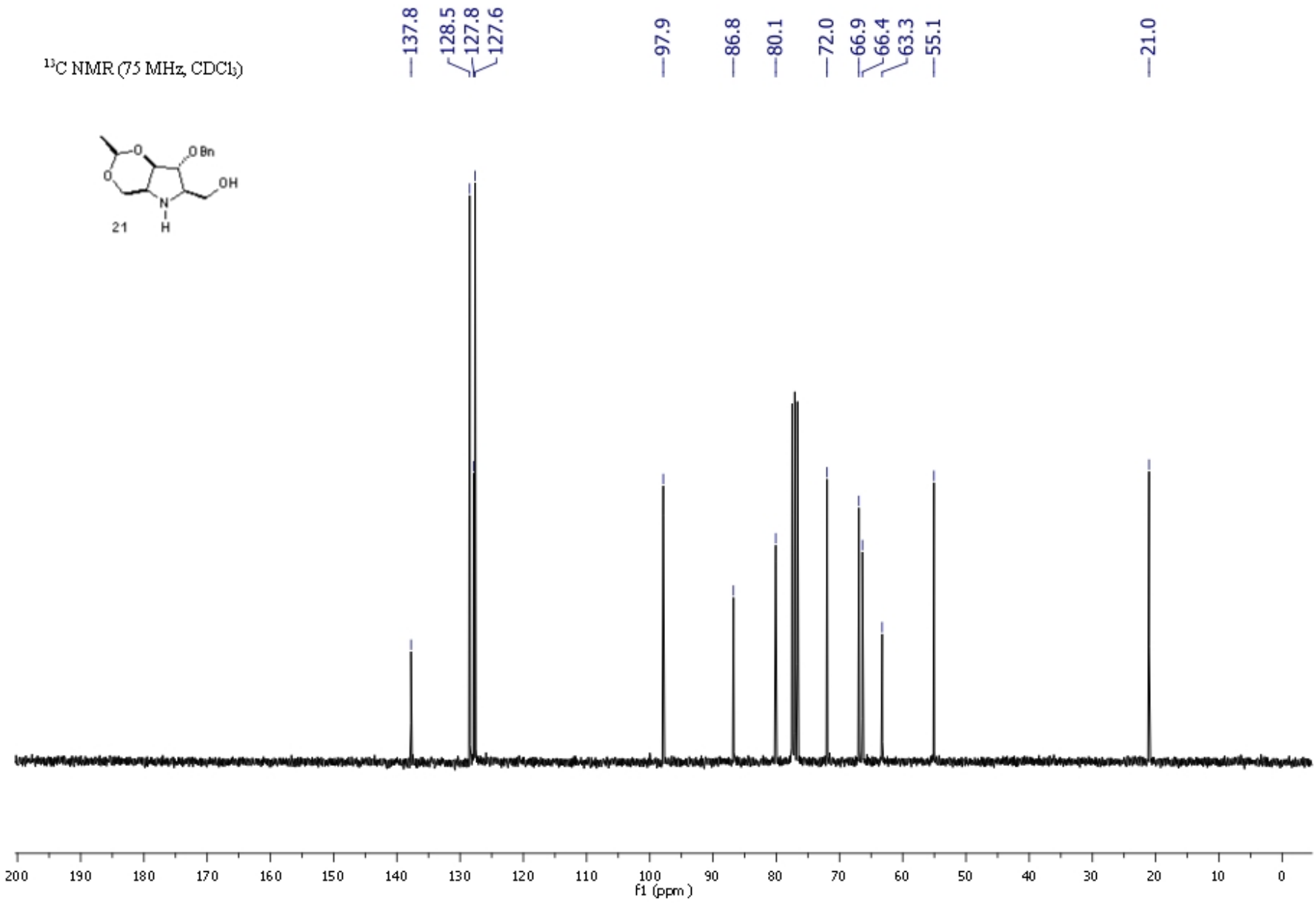

^{13}C NMR (75 MHz, CDCl$_3$)
171.1
137.8
128.3
127.7
127.5
97.8
82.0
72.5
65.8
61.7
53.9
52.1
21.1
MeO
O
BnO
N
H
O
O
20
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR (300 MHz, CDCl$_3$)

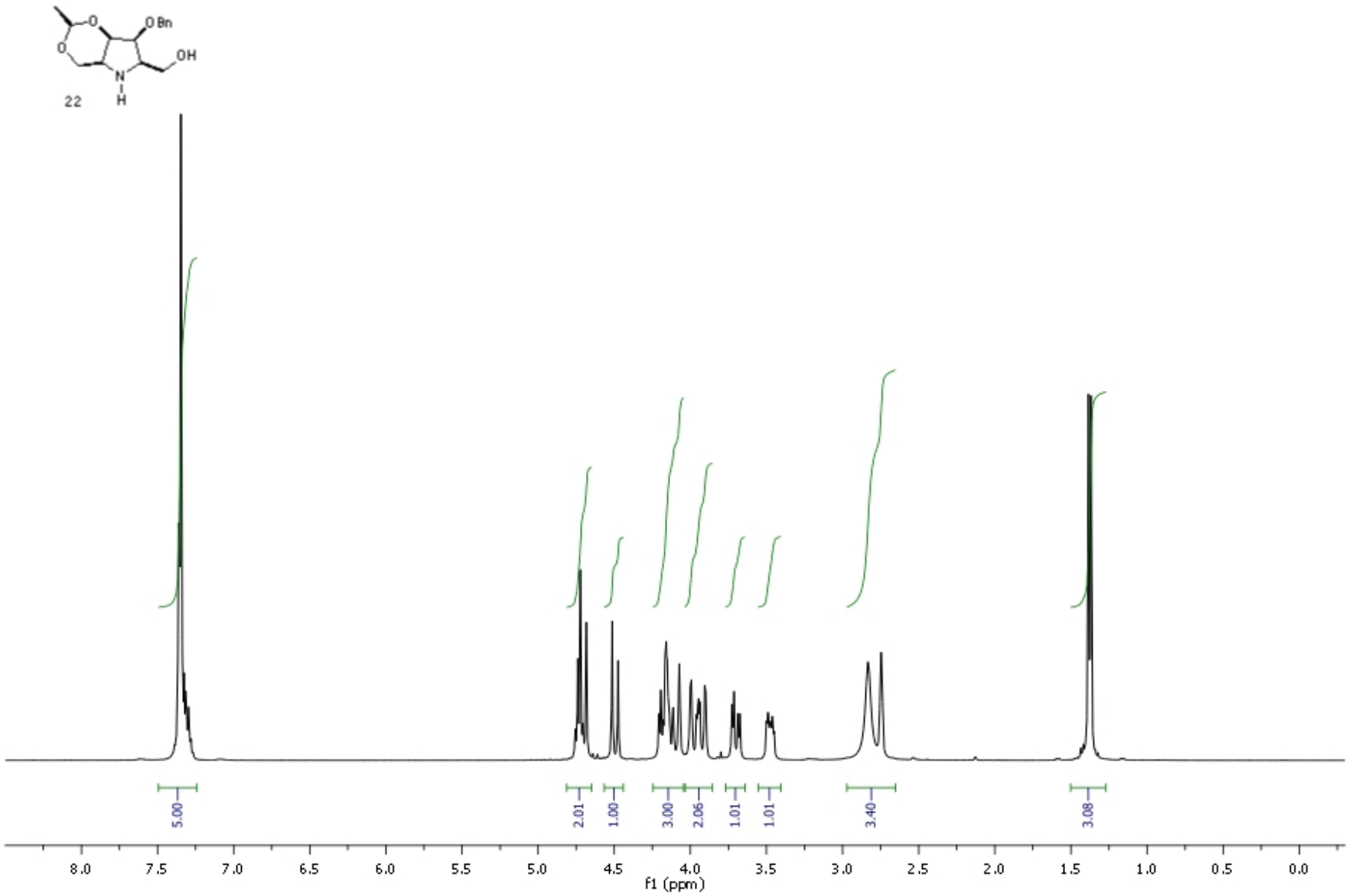


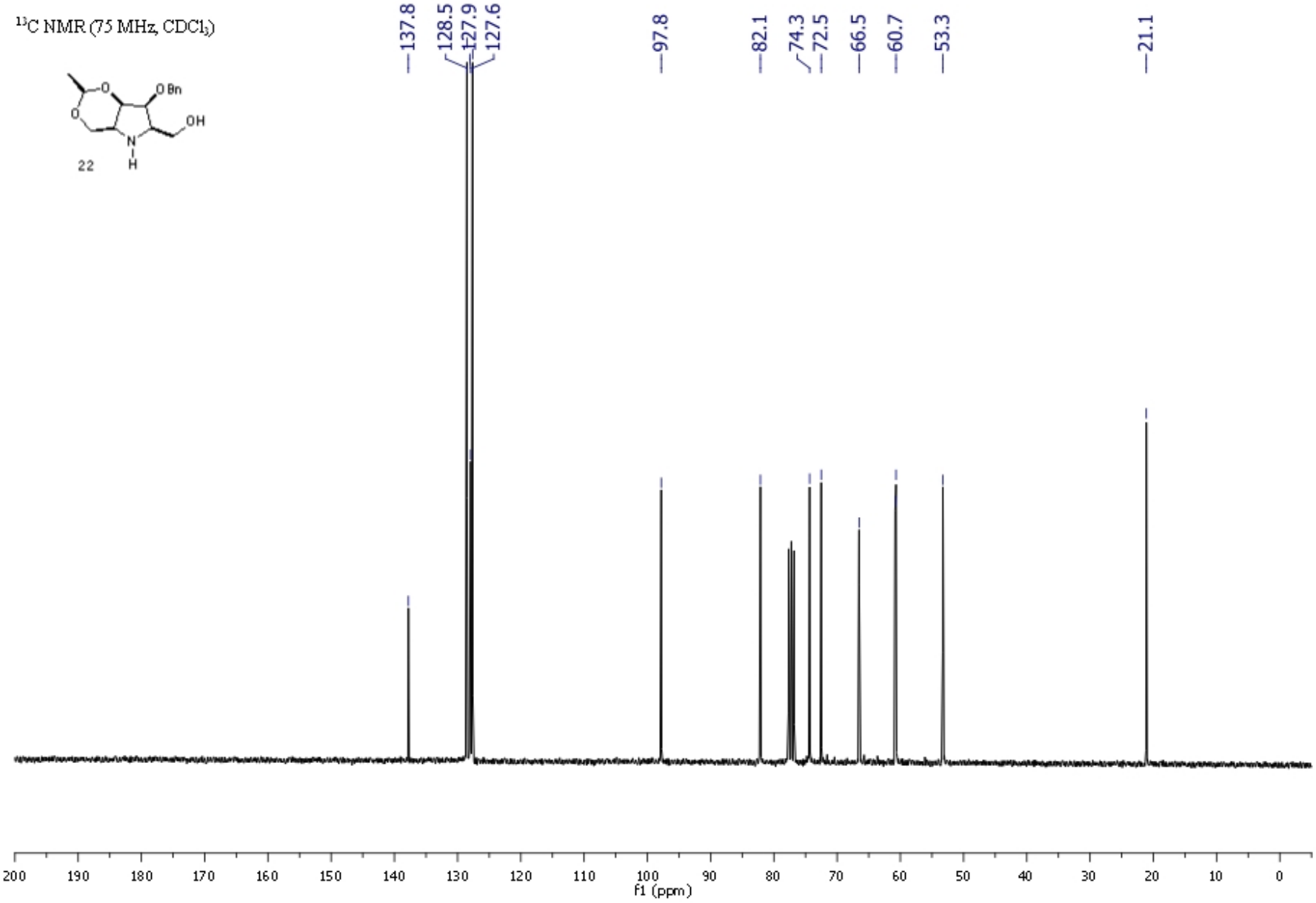
21

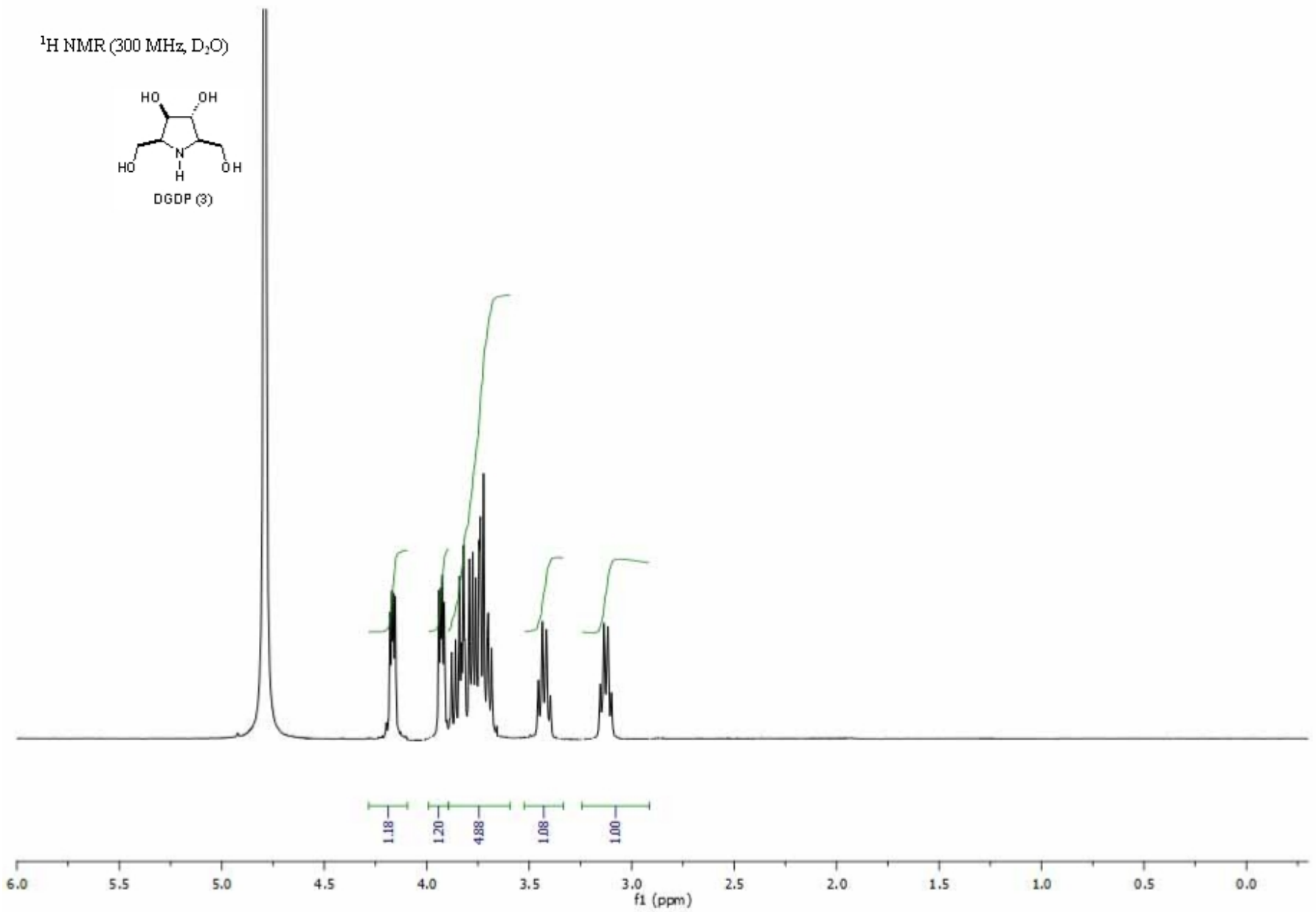



^{13}C NMR (75 MHz, CDCl$_3$)
137.8
128.5
127.8
127.6
97.9
86.8
80.1
72.0
66.9
66.4
63.3
55.1
21.0
OBn
OH
N
H
21
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

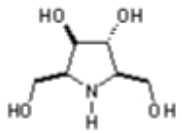
^{1}H NMR (300 MHz, $CDCl_3$)



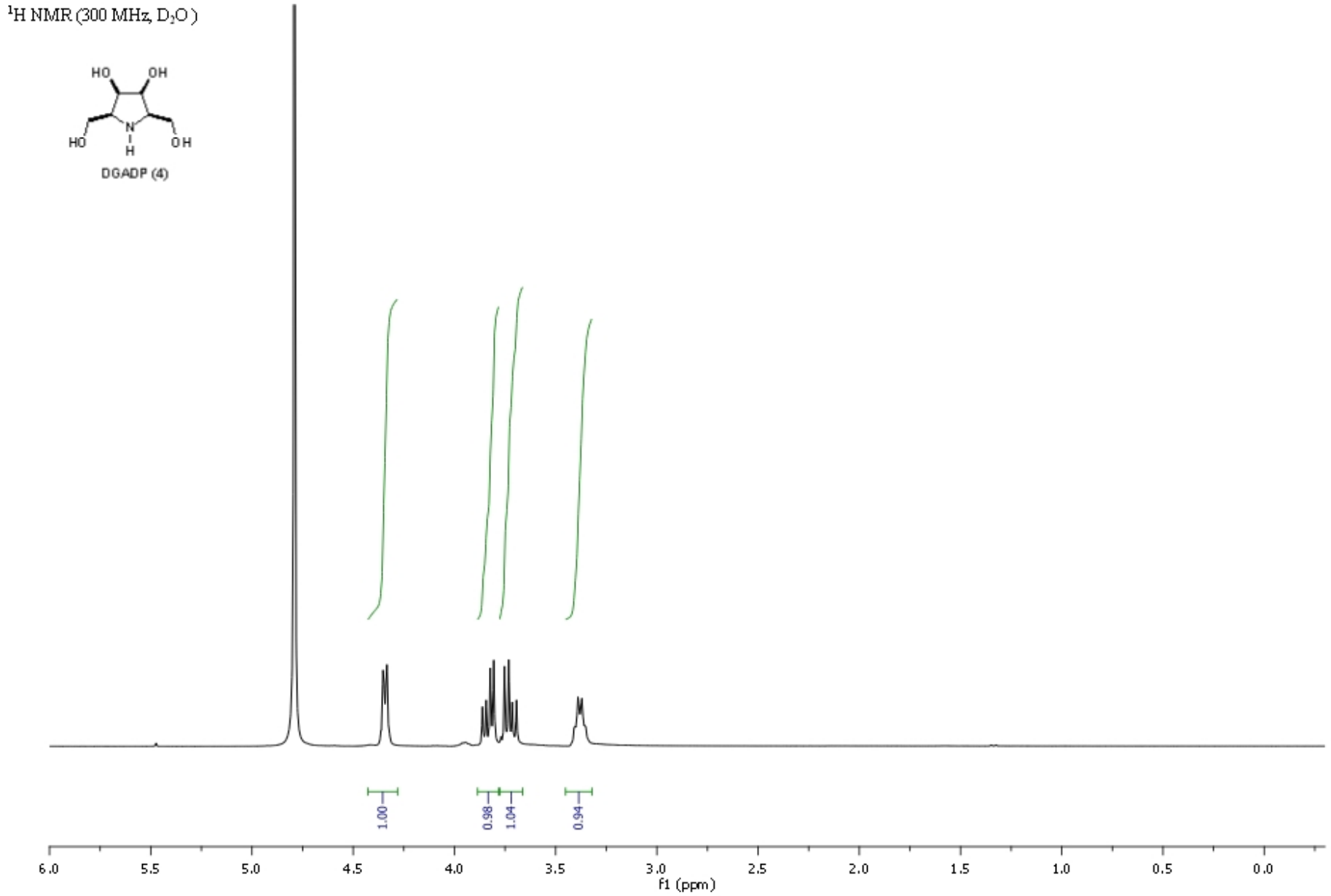

^{13}C NMR (75 MHz, $CDCl_3$)
137.8
128.5
127.9
127.6
97.8
82.1
74.3
72.5
66.5
60.7
53.3
21.1
OBn
OH
N
H
22
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


^{1}H NMR (300 MHz, D_2O)
HO
OH
HO
N
H
OH
DGDP (3)
1.18
1.20
4.88
1.08
1.00
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

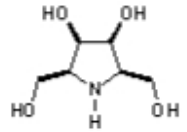
^{13}C NMR (75 MHz, D_2O)



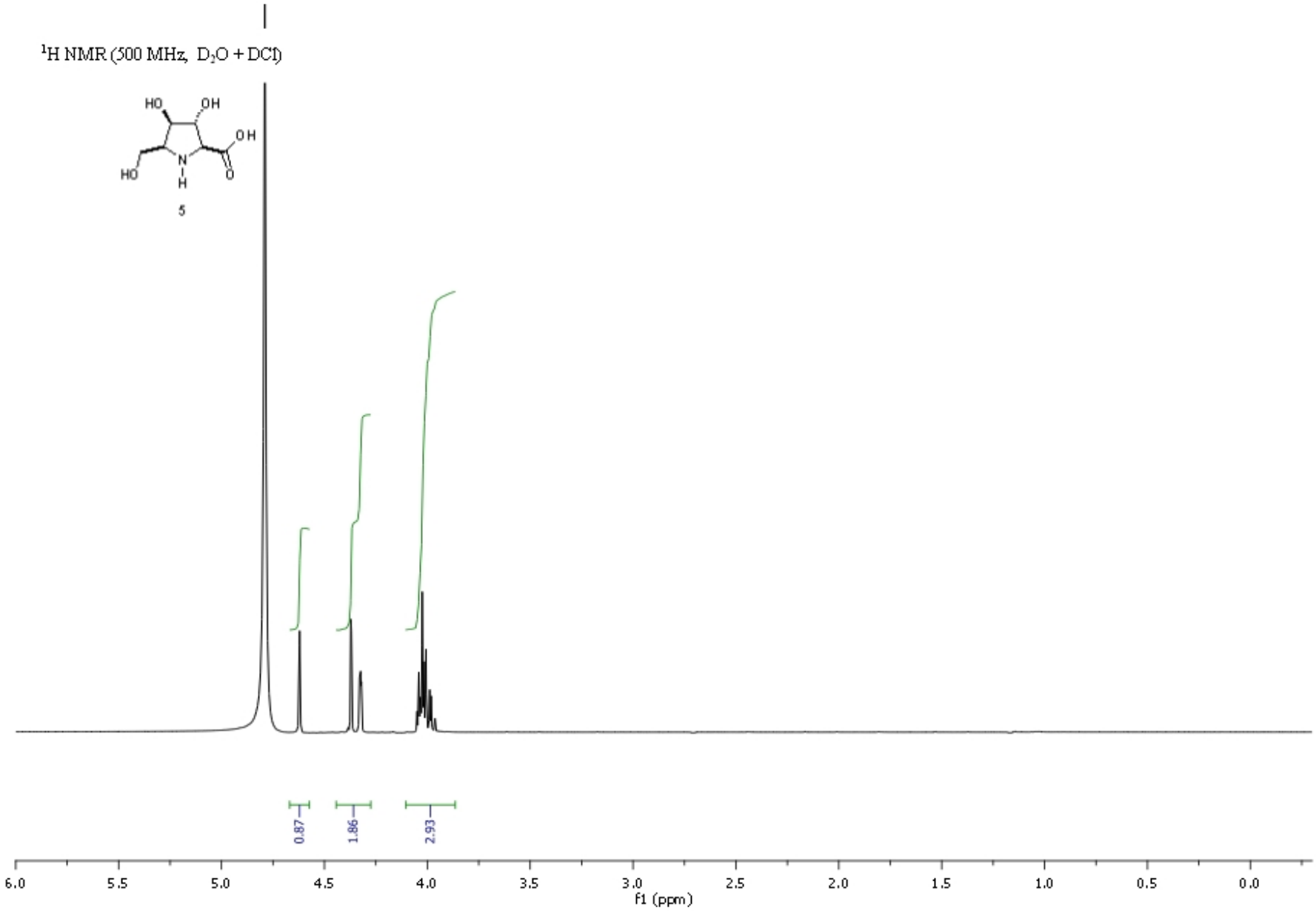
DGDP (3)

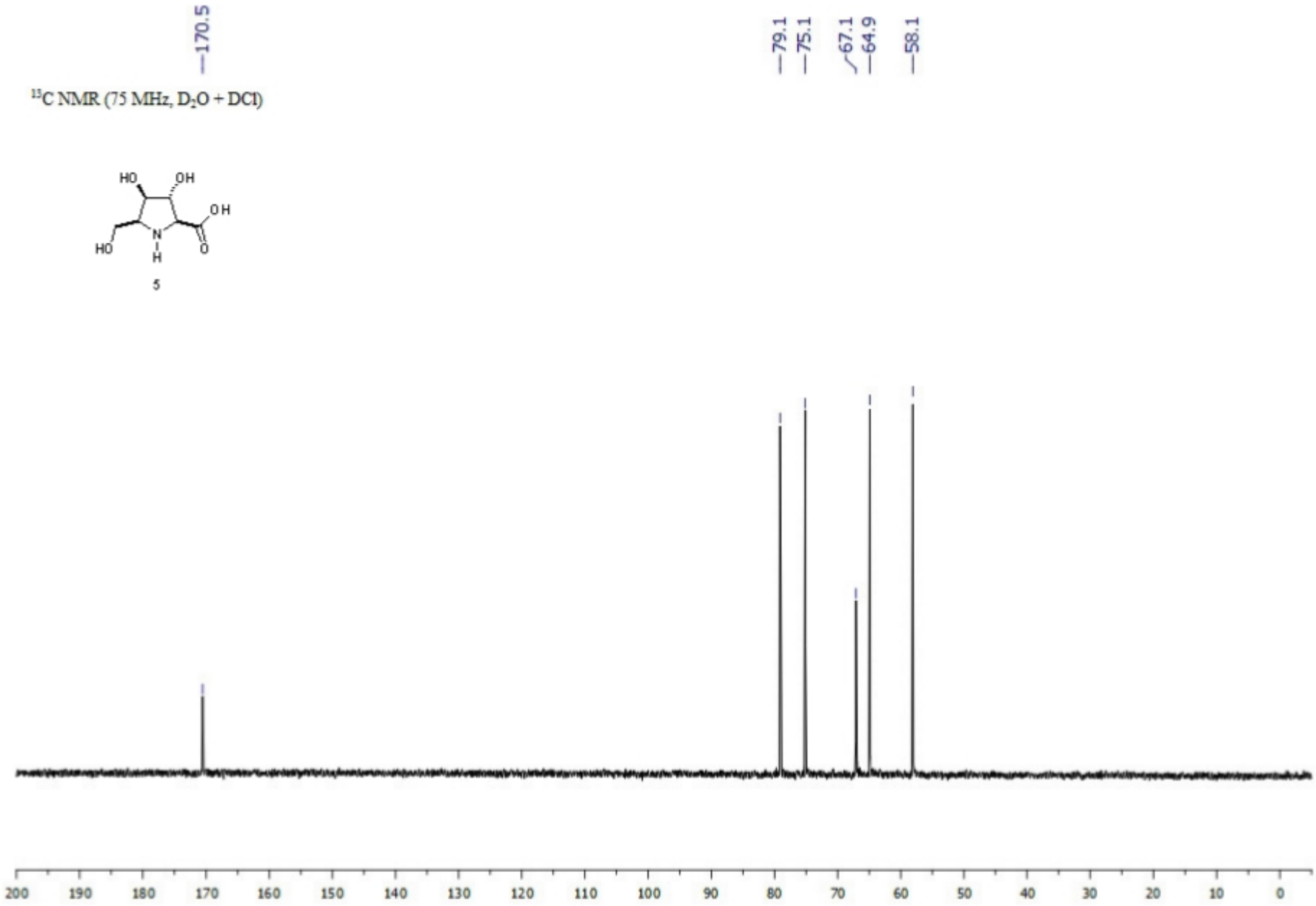

1H NMR (300 MHz, D2O)
HO
OH
HO
N
H
OH
DGADP (4)
1.00
0.98
1.04
0.94
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

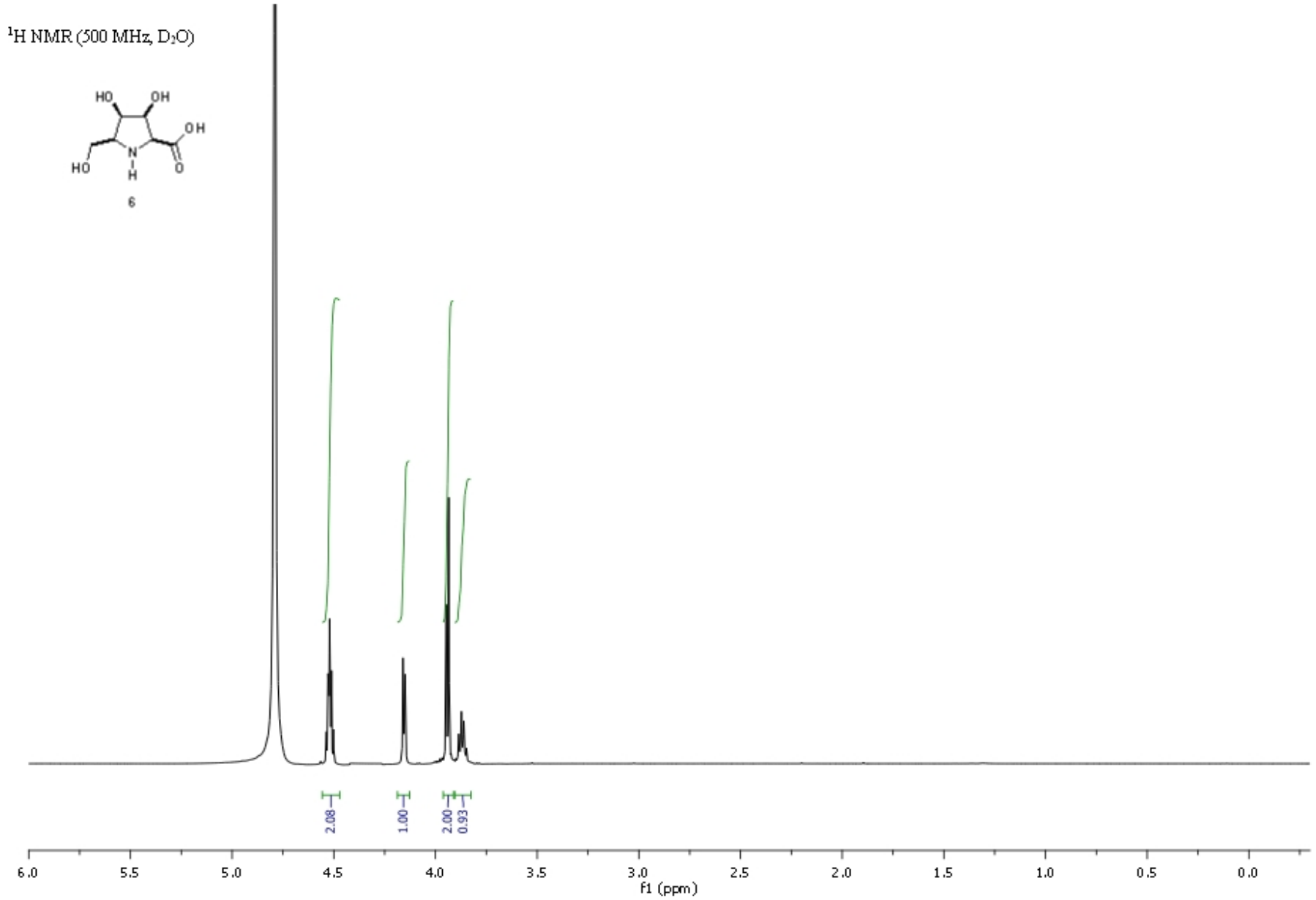
^{13}C NMR (75 MHz, D_2O)

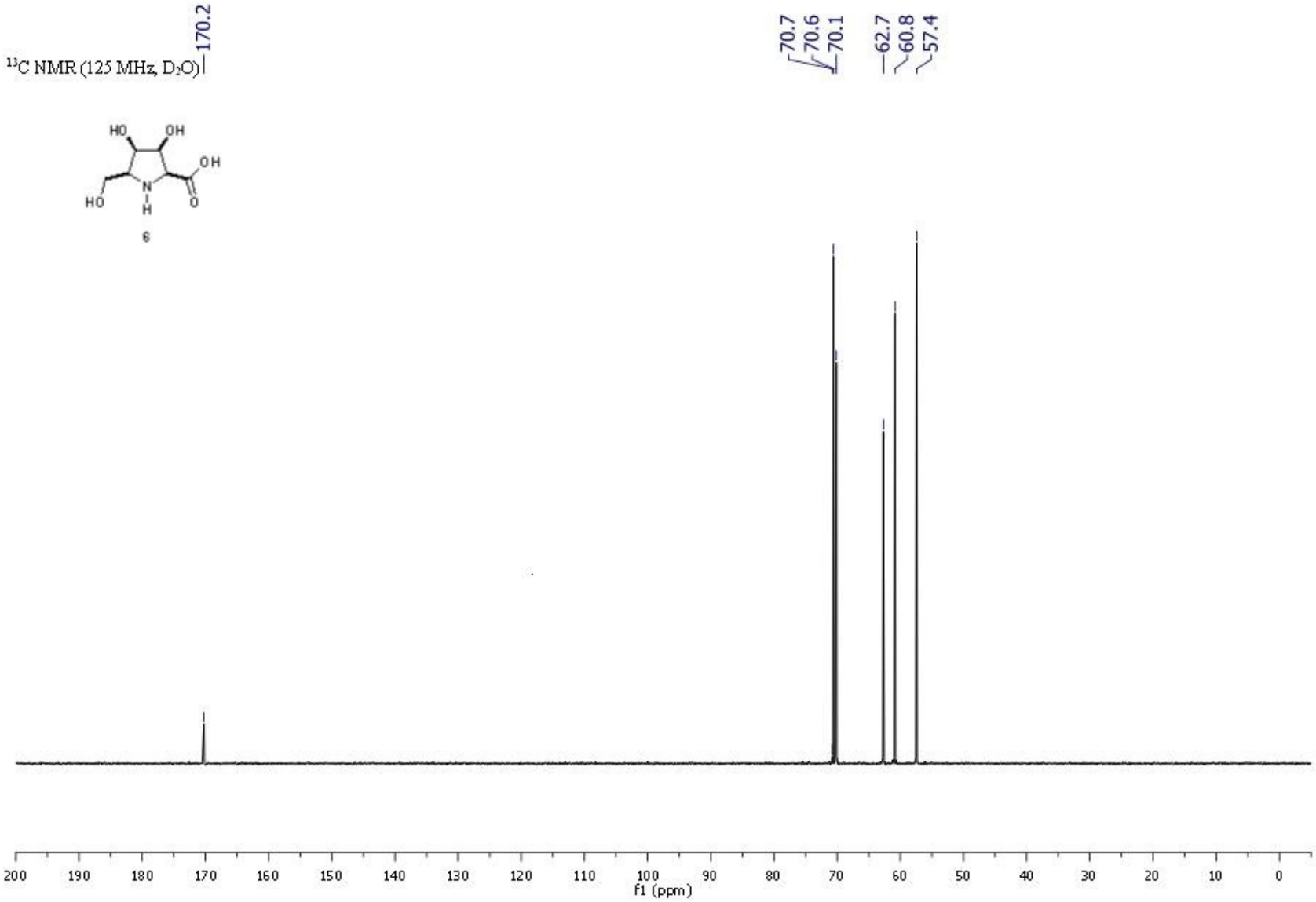


DGADP (4)


^{1}H NMR (500 MHz, D_2O + DCl)
HO
OH
OH
HO
N
H
O
5
0.87
1.86
2.93
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170.5
79.1
75.1
67.1
64.9
58.1
13C NMR (75 MHz, D2O + DCl)
HO
OH
OH
HO
N
H
O
5
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


^{1}H NMR (500 MHz, D_2O)
HO
OH
OH
HO
N
H
O
6
2.08
1.00
2.00
0.93
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


^{13}C NMR (125 MHz, D$_2$O)
170.2
70.7
70.6
70.1
62.7
60.8
57.4
HO
OH
OH
HO
N
H
O
6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)