

## Diastereoselective Synthesis of C2'-Fluorinated Nucleoside Analogues using an Acyclic Strategy

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**Part I: Computational Data****DFT Method and Details**

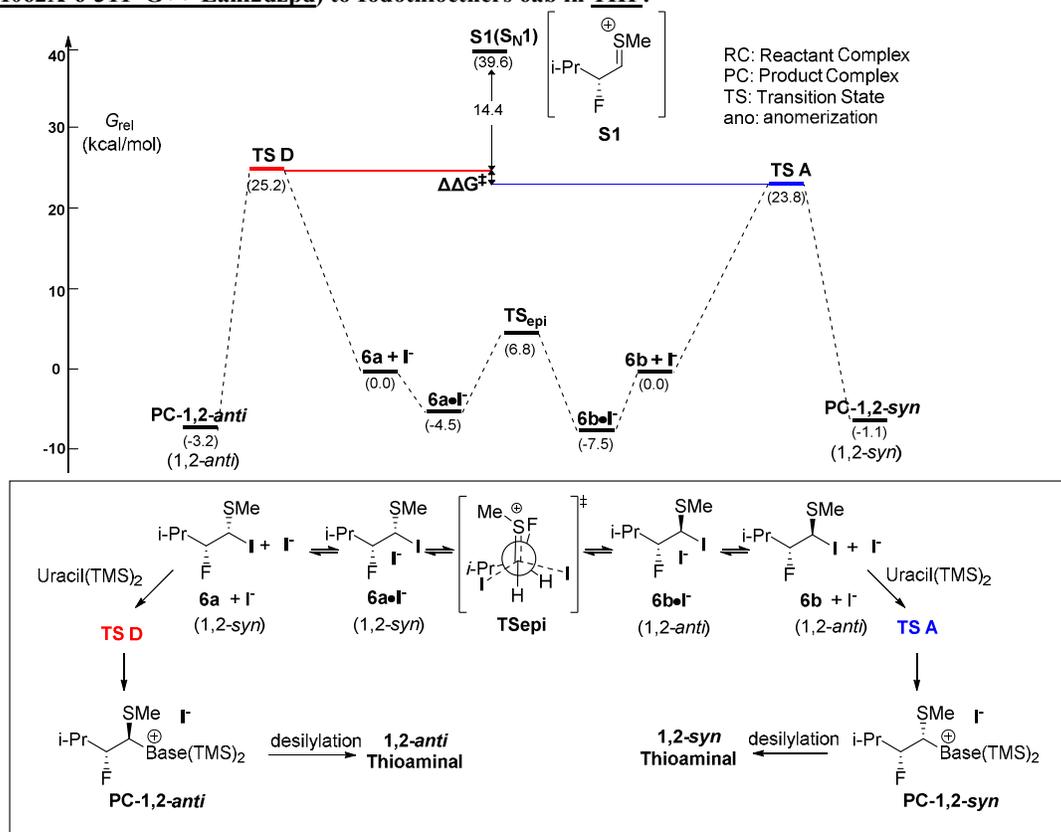
QM calculations were performed in Gaussian 09.<sup>1</sup> The geometry and transition state optimizations (Berny algorithm) were achieved with tight SCF convergence, an ultrafine integral grid and a fine CPHF grid (keywords: Int(Grid=Ultrafine) CPHF(Grid=Fine)). All the possible conformations of the C1-C2 bond and the isopropyl side chain were considered and optimized for the formation of the major and minor diastereoisomers. The energies presented in the paper and the supporting information are from fully optimized structures at the M062X<sup>2,3</sup> level of theory using the 6-311+G\*\* basis set with the LANL2DZpd<sup>4,5</sup> effective core potential. Calculation in solvents (THF) were performed with transition state or geometry using the polarizable continuum model (PCM).<sup>6</sup>

```
Pseudopotential for Iodine4,5:
****
I 0
LANL2DZ
P 1 1.00
   0.308000000E-01   1.00000000
D 1 1.00
   0.294000000   1.00000000
****
```

Frequency calculations were performed at 273.15 K (1 atm) on every optimized structure to determine their nature, transition states or intermediates, and to determine free energy values (1 Hartree = 627.5095 kcal mol<sup>-1</sup>). As mentioned in the manuscript, free energy corrections were applied using Truhlar's quasiharmonic approximation.<sup>7,8,9</sup> Intrinsic reaction coordinate calculations using the local quadratic approximation (LQA) ensured that the TS led either to reported product (or product complex) and reactant (or reactant complex) without encountering any energy barriers. The wave function stability was confirmed for all stationary structures. Orbital stabilization energies and Wiberg bond orders<sup>10</sup> were obtained from the NBO theory (version 3.1) implemented in Gaussian 09. Gibbs free energies of activation ( $\Delta\Delta G^\ddagger$ ) correspond to the energy difference between the lowest energy *anti*- and *syn*-predictive TS. The ratio of products was calculated from equation 1 ( $R=1.987204118\times 10^{-3}$  kcal mol<sup>-1</sup> K<sup>-1</sup>, T=273.15).

$$\Delta\Delta G^\ddagger = RT \ln \frac{[2,3\text{-anti}]}{[2,3\text{-syn}]} \quad (\text{eq 1})$$

**Gibbs Free Energy Profile for the Addition of Silylated Nucleobase (Uracil(TMS)<sub>2</sub>) (M062X-6-311\*G++-Lan12dzpd) to Iodothioethers 6ab in THF:**



**Free Gibbs Energies (Ha) Profile:**

Species (Gibbs Free Energies Relative to <b>6a</b> )		Gibbs Free Energies	
		(Ha)	(kcal/mol)
<b>TSepi</b>	<b>TS-epi</b> (-756.552435) - [ <b>6a</b> (-745.0479214) + $\Gamma$ (-11.515284)]	0.01077	6.76
<b>6a•<math>\Gamma</math></b>	<b>6a•<math>\Gamma</math></b> (-756.5703271) - [ <b>6a</b> (-745.0479214) + $\Gamma$ (-11.515284)]	-0.007121	-4.46
<b>6a</b>	<b>6a</b> (-745.0479214) and $\Gamma$ (-11.515284) (energies are represented relative to this energy point)	<b>0</b>	<b>0</b>
<b>TS D</b>	<b>TS D</b> (-1976.871609) - [ <b>6a</b> (-745.0479214) + <b>Uracil(TMS)<sub>2</sub></b> (-1231.863921)]	0.04023	25.2
<b>PC-1,2-anti</b>	<b>PC-1,2-anti</b> (-1976.916929) - [ <b>6a</b> (-745.0479214) + <b>Uracil(TMS)<sub>2</sub></b> (-1231.863921)]	-0.005086	-3.19
<b>6b•<math>\Gamma</math></b>	<b>6b•<math>\Gamma</math></b> (-756.5752276) - [ <b>6a</b> (-745.0479214) + $\Gamma$ (-11.515284)]	-0.01202	-7.54
<b>6b</b>	<b>6b</b> (-745.0478995) - [ <b>6a</b> (-745.0479214) + $\Gamma$ (-11.515284)]	-0.00002187	-0.01
<b>TS A</b>	<b>TS A</b> (-1976.873854) - [ <b>6a</b> (-745.0479214) + <b>Uracil(TMS)<sub>2</sub></b> (-1231.863921)]	0.03799	23.8
<b>PC-1,2-syn</b>	<b>PC-1,2-syn</b> (-1976.913611) - [ <b>6a</b> (-745.0479214) + <b>Uracil(TMS)<sub>2</sub></b> (-1231.863921)]	-0.001768	-1.11

**Energies (M06-2X/6-311+G\*\*/lanl2dzpd/PCM=THF) and Cartesian Coordinates****TSepi**

SCF energy: -756.68615467 hartree

zero-point correction: +0.171781 hartree

enthalpy correction: +0.185103 hartree

free energy correction: +0.130549 hartree

quasiharmonic free energy correction: +0.00317109 hartree

imaginary frequency: -38.8i cm<sup>-1</sup>

C	0.1919220	0.1756150	0.6776240
C	0.3027410	1.6610530	0.7448890
H	1.3254430	1.9116650	0.4371000
C	-0.6899260	2.4144060	-0.1452170
H	-1.6975520	2.0819950	0.1186680
S	0.1194960	-0.7148180	2.0568300
C	0.0570760	-2.3894250	1.3854960
H	0.9567610	-2.5442090	0.7876300
H	0.0315780	-3.0673360	2.2352840
H	-0.8469820	-2.4802300	0.7818480
H	0.1246670	-0.3145580	-0.2839980
I	-2.9672210	-0.7677800	-0.4980620
C	-0.5479190	3.9137750	0.1173520
H	-1.2556080	4.4613990	-0.5075040
H	-0.7465690	4.1619850	1.1599760
H	0.4612010	4.2538920	-0.1346730
C	-0.4193490	2.0883350	-1.6145110
H	0.6150670	2.3257100	-1.8811170
H	-0.6134600	1.0407460	-1.8496370
H	-1.0787760	2.6893310	-2.2432320
I	3.0800440	-0.5289150	-0.5806850
F	0.1628220	2.0509960	2.0722400

**6a•I<sup>-</sup>**

SCF energy: - 756.70624573 hartree  
 zero-point correction: + 0.173234hartree  
 enthalpy correction: + 0.185881 hartree  
 free energy correction: + 0.133857 hartree  
 quasiharmonic free energy correction: + 0.002061 hartree  
 imaginary frequency: none

C	0.8738590	0.1885090	0.2386630
C	1.2940020	1.5988560	-0.1634570
H	1.6805860	1.6006730	-1.1857170
C	0.1539720	2.6177630	-0.0598990
H	-0.4589470	2.3725480	0.8133290
S	0.7667200	0.0479540	2.0245430
C	-0.0689450	-1.5522210	2.1581930
H	0.5875680	-2.3461710	1.8014640
H	-0.2757020	-1.7010310	3.2172650
H	-1.0028080	-1.5385190	1.5973570
H	-0.0838680	-0.0742880	-0.2122640
I	-3.1507930	-0.4911750	-0.2041980
C	0.7128410	4.0321830	0.0965750
H	-0.1079270	4.7521970	0.0879130
H	1.2664870	4.1489420	1.0278510
H	1.3838100	4.2738730	-0.7335890
C	-0.7090700	2.5215880	-1.3201550
H	-0.1358820	2.8466870	-2.1940770
H	-1.0773190	1.5094370	-1.4956030
H	-1.5818400	3.1702360	-1.2250130
I	2.2585330	-1.2817540	-0.6540520
F	2.3653520	1.9714770	0.6551300

**6a**

SCF energy: - 745.18608518 hartree  
 zero-point correction: + 0.172758 hartree  
 enthalpy correction: + 0.184071 hartree  
 free energy correction: + 0.137203 hartree  
 quasiharmonic free energy correction: + 0.000961 hartree  
 imaginary frequency: none

C	-0.1638830	0.3454490	0.2479530
C	-1.2637120	-0.6572570	-0.0750190
H	-1.1410820	-1.5266380	0.5787730
C	-2.6866640	-0.1159580	0.0551280
H	-2.8227070	0.6353780	-0.7286270
S	-0.2468230	1.8033100	-0.7942030
C	0.8592390	2.8883900	0.1421750
H	1.8732870	2.4890190	0.1363690
H	0.8474210	3.8545650	-0.3594480
H	0.5021930	3.0064510	1.1649760
H	-0.2321850	0.6311710	1.2958870
C	-3.6786520	-1.2577660	-0.1714610

H	-4.7006270	-0.8743490	-0.1629020
H	-3.5057070	-1.7515890	-1.1284620
H	-3.5910090	-2.0039710	0.6240900
C	-2.9056320	0.5391430	1.4192430
H	-2.6235930	-0.1418160	2.2287270
H	-2.3340870	1.4636170	1.5255980
H	-3.9613640	0.7849530	1.5454600
I	1.7818410	-0.6775400	0.1647720
F	-1.0847910	-1.1069020	-1.3838000

**TS D**Optimized at **M06-2X/6-311+G\*\*/lanl2dzpd/Gas phase**

(solvation calculation PCM=THF performed on the final geometry)

SCF energy: - 1977.26130275 hartree

zero-point correction: + 0.463519 hartree

enthalpy correction: + 0.494607 hartree

free energy correction: + 0.402859 hartree

solvation energy: - 0.0204747 hartree

quasiharmonic free energy correction: + 0.007309 hartree

imaginary frequency: - 230.3i cm<sup>-1</sup>

O	-0.3048600	-0.3467730	0.8643660
C	2.0339970	1.4046830	0.1294360
H	1.6687060	0.5141520	-0.3783930
C	2.2626360	1.3297590	1.5931700
H	1.2989020	1.1220820	2.0631180
C	3.2663140	0.2259530	1.9678890
H	2.8870370	-0.6902690	1.5035830
S	2.6386010	2.6682660	-0.7522220
C	2.1627770	2.1808270	-2.4321910
H	1.0758310	2.1502830	-2.4969160
H	2.5635270	2.9392990	-3.1017680
H	2.5839250	1.1944560	-2.6426730
C	-1.0189840	0.6379100	0.3518500
N	-0.3465880	1.7655690	0.1288660
Si	-0.6976560	-2.0316940	0.9307300
I	2.8805800	-1.4717780	-1.5933200
C	-1.0341650	2.7832420	-0.3982490
H	-0.4678540	3.6942990	-0.5790430
C	-2.3728790	2.7020590	-0.6973120
H	-2.9387740	3.5178480	-1.1206330
N	-2.3189120	0.4462840	0.1112990
C	-2.9889750	1.4716960	-0.4085380
O	-4.2771800	1.3339450	-0.6616470
Si	-5.2990640	0.0324720	-0.1872650
C	4.6635440	0.5137550	1.4226600
H	5.0225600	1.4857640	1.7711450
H	4.6814920	0.4847980	0.3318740
H	5.3547260	-0.2525540	1.7776310
C	3.2725520	0.0745390	3.4891790
H	3.6286780	0.9898870	3.9678110

H	3.9383120	-0.7409900	3.7769720
H	2.2740160	-0.1488880	3.8737370
C	0.8185650	-2.7751300	1.7039680
H	0.6506420	-3.8347010	1.9167960
H	1.6707710	-2.6953370	1.0241130
H	1.0634630	-2.2801460	2.6479340
C	-2.1741840	-2.2386900	2.0595290
H	-3.0956000	-1.8813810	1.5997260
H	-2.3026760	-3.2960710	2.3086150
H	-2.0261500	-1.6946470	2.9965930
C	-1.0098810	-2.6111550	-0.8079260
H	-1.6943470	-1.9423420	-1.3343780
H	-0.0654460	-2.6417870	-1.3575160
H	-1.4483420	-3.6132590	-0.8082930
C	-4.7282370	-1.5548280	-0.9769470
H	-4.5383090	-1.4066360	-2.0434000
H	-3.8152550	-1.9361930	-0.5202160
H	-5.5065480	-2.3175840	-0.8823690
C	-5.3121170	-0.0122340	1.6778460
H	-5.8340950	0.8611550	2.0763110
H	-5.8272990	-0.9056120	2.0412340
H	-4.2984470	-0.0213610	2.0824770
C	-6.9443940	0.5662780	-0.8750340
H	-7.7256820	-0.1498280	-0.6072210
H	-7.2334770	1.5438630	-0.4832050
H	-6.9100020	0.6339100	-1.9647040
F	2.7074220	2.5607270	2.0594630

**PC-1,2-anti**

SCF energy: - 1977.33085841 hartree

zero-point correction: + 0.466715 hartree

enthalpy correction: + 0.497345 hartree

free energy correction: + 0.407710 hartree

quasiharmonic free energy correction: + 0.0062188 hartree

imaginary frequency: none

O	-0.1753140	-0.9295050	0.1190100
C	1.3393060	1.1869720	-0.6150560
H	1.6660860	0.2379250	-0.1910820
C	2.0199160	2.2952100	0.1798610
S	1.8658710	1.2274410	-2.3494740
C	1.3971420	-0.4731020	-2.7737890
H	0.3159410	-0.6049800	-2.7090190
H	1.7109770	-0.6362570	-3.8037950
H	1.9207190	-1.1667210	-2.1136070
C	-0.8614440	0.1299970	-0.1610510
N	-0.1441230	1.2312560	-0.5166490
Si	-0.7393680	-2.5887120	0.2492820
I	4.1992390	-1.1046200	0.2452400
C	-0.8134460	2.3671570	-0.8737650
H	-0.1914470	3.1961770	-1.1841180
C	-2.1655790	2.4208280	-0.8326810
H	-2.7139360	3.3101270	-1.1024150

N	-2.1832710	0.1279780	-0.1048770
C	-2.8406810	1.2434920	-0.4221640
O	-4.1376840	1.2613520	-0.3641480
Si	-5.2165190	0.0244210	0.2358080
H	3.0799470	2.0267930	0.2175070
C	1.4797930	2.5305610	1.5834480
H	0.4427280	2.8779770	1.4962430
C	2.3024680	3.6245950	2.2658220
H	1.8909720	3.8410150	3.2533650
H	2.3054720	4.5464580	1.6833000
H	3.3367130	3.2926090	2.3947950
C	1.5170710	1.2378130	2.4017640
H	1.2110900	1.4463540	3.4285990
H	2.5299510	0.8262580	2.4189450
H	0.8564340	0.4631160	2.0057400
C	0.8290730	-3.4964720	0.6209340
H	0.6271760	-4.5690760	0.6885480
H	1.5810000	-3.3321230	-0.1539810
H	1.2561730	-3.1669780	1.5708760
C	-1.4442300	-2.9816570	-1.4289110
H	-2.0200380	-3.9102410	-1.3897510
H	-2.1076290	-2.1912960	-1.7878660
H	-0.6397480	-3.1163790	-2.1560830
C	-1.9585500	-2.6788950	1.6489640
H	-1.5698820	-2.1571890	2.5277140
H	-2.9247280	-2.2478300	1.3888390
H	-2.1109570	-3.7263150	1.9239490
C	-4.9703300	-1.5145090	-0.7786740
H	-4.9760900	-1.2732260	-1.8450450
H	-4.0348030	-2.0217600	-0.5451960
H	-5.7945300	-2.2077720	-0.5890900
C	-6.8738490	0.7987270	-0.0750680
H	-7.6686880	0.1435260	0.2904540
H	-6.9610110	1.7578210	0.4398760
H	-7.0349060	0.9623820	-1.1428640
C	-4.8339760	-0.1617650	2.0474810
H	-5.1630790	0.7237690	2.5962980
H	-5.3587020	-1.0284700	2.4583700
H	-3.7653490	-0.2990390	2.2229480
F	1.9258400	3.4962330	-0.5445280

**6b•I<sup>-</sup>**

SCF energy: - 756.71062339 hartree

zero-point correction: + 0.173441 hartree

enthalpy correction: + 0.186726 hartree

free energy correction: + 0.133273 hartree

quasiharmonic free energy correction: + 0.00206095 hartree

imaginary frequency: none

C	-0.6377210	-0.2062920	0.3688700
C	-0.5967780	1.2057140	0.9285100
H	0.4216880	1.3362070	1.3164320

C	-0.9284380	2.3542750	-0.0135930
H	-1.9912740	2.2783900	-0.2641310
S	-0.3131590	-1.3966150	1.6718220
C	0.2288250	-2.7869640	0.6471910
H	1.0987490	-2.4914970	0.0602020
H	0.5000860	-3.5927540	1.3277940
H	-0.5856820	-3.1178550	0.0018170
H	0.1269960	-0.3060260	-0.4010750
I	-2.5231080	-0.6325870	-0.6936030
C	-0.6857890	3.6815790	0.7084050
H	-0.9885680	4.5156790	0.0723360
H	-1.2495000	3.7386120	1.6406440
H	0.3771910	3.8006570	0.9388860
C	-0.0951880	2.2732840	-1.2932820
H	0.9716890	2.2232650	-1.0574410
H	-0.3486700	1.3988260	-1.8968630
H	-0.2715410	3.1617790	-1.9029730
I	3.2093100	-0.1435910	-0.3051920
F	-1.4587580	1.2675970	2.0305270

**6b**

SCF energy: - 745.18633032 hartree

zero-point correction: + 0.172913 hartree

enthalpy correction: + 0.184130 hartree

free energy correction: + 0.137697 hartree

quasiharmonic free energy correction: + 0.00073348 hartree

imaginary frequency: none

C	-0.1264480	0.7043400	0.3390400
C	1.2880640	0.8997630	-0.1886440
H	1.6101200	1.8900430	0.1581950
C	2.3338900	-0.1322080	0.2105860
H	2.0674840	-1.0767690	-0.2727650
S	-1.1889470	2.0307260	-0.2488550
C	-2.5584590	1.8504770	0.9212300
H	-2.2065790	1.9603750	1.9464050
H	-3.2670200	2.6455060	0.6946330
H	-3.0459750	0.8849120	0.7863450
H	-0.1108440	0.7124450	1.4273060
I	-0.9121290	-1.2874090	-0.1476540
C	3.7038700	0.3146790	-0.3031470
H	4.4515780	-0.4511980	-0.0896050
H	3.6882500	0.4876180	-1.3798970
H	4.0164620	1.2393050	0.1914860
C	2.3558870	-0.3291370	1.7269740
H	2.4852070	0.6281920	2.2420560
H	1.4430740	-0.8019250	2.0958200
H	3.1945370	-0.9704970	2.0029670
F	1.2287620	0.9717270	-1.5813130

**TS A**

Optimized at M06-2X/6-311+G\*\*/lanl2dzpd/Gas phase

(solvation calculation PCM=THF performed on the final geometry)

SCF energy: - 1977.26329489 hartree  
zero-point correction: + 0.463257 hartree  
enthalpy correction: + 0.494453 hartree  
free energy correction: +0 .402192 hartree  
solvation energy: - 0.02015088 hartree  
quasiharmonic free energy correction: + 0.00739976 hartree  
imaginary frequency: -82.2i cm<sup>-1</sup>

O	-0.3048600	-0.3467730	0.8643660
C	2.0339970	1.4046830	0.1294360
H	1.6687060	0.5141520	-0.3783930
C	2.2626360	1.3297590	1.5931700
H	1.2989020	1.1220820	2.0631180
C	3.2663140	0.2259530	1.9678890
H	2.8870370	-0.6902690	1.5035830
S	2.6386010	2.6682660	-0.7522220
C	2.1627770	2.1808270	-2.4321910
H	1.0758310	2.1502830	-2.4969160
H	2.5635270	2.9392990	-3.1017680
H	2.5839250	1.1944560	-2.6426730
C	-1.0189840	0.6379100	0.3518500
N	-0.3465880	1.7655690	0.1288660
Si	-0.6976560	-2.0316940	0.9307300
I	2.8805800	-1.4717780	-1.5933200
C	-1.0341650	2.7832420	-0.3982490
H	-0.4678540	3.6942990	-0.5790430
C	-2.3728790	2.7020590	-0.6973120
H	-2.9387740	3.5178480	-1.1206330
N	-2.3189120	0.4462840	0.1112990
C	-2.9889750	1.4716960	-0.4085380
O	-4.2771800	1.3339450	-0.6616470
Si	-5.2990640	0.0324720	-0.1872650
C	4.6635440	0.5137550	1.4226600
H	5.0225600	1.4857640	1.7711450
H	4.6814920	0.4847980	0.3318740
H	5.3547260	-0.2525540	1.7776310
C	3.2725520	0.0745390	3.4891790
H	3.6286780	0.9898870	3.9678110
H	3.9383120	-0.7409900	3.7769720
H	2.2740160	-0.1488880	3.8737370
C	0.8185650	-2.7751300	1.7039680
H	0.6506420	-3.8347010	1.9167960
H	1.6707710	-2.6953370	1.0241130
H	1.0634630	-2.2801460	2.6479340
C	-2.1741840	-2.2386900	2.0595290
H	-3.0956000	-1.8813810	1.5997260
H	-2.3026760	-3.2960710	2.3086150
H	-2.0261500	-1.6946470	2.9965930
C	-1.0098810	-2.6111550	-0.8079260
H	-1.6943470	-1.9423420	-1.3343780

H	-0.0654460	-2.6417870	-1.3575160
H	-1.4483420	-3.6132590	-0.8082930
C	-4.7282370	-1.5548280	-0.9769470
H	-4.5383090	-1.4066360	-2.0434000
H	-3.8152550	-1.9361930	-0.5202160
H	-5.5065480	-2.3175840	-0.8823690
C	-5.3121170	-0.0122340	1.6778460
H	-5.8340950	0.8611550	2.0763110
H	-5.8272990	-0.9056120	2.0412340
H	-4.2984470	-0.0213610	2.0824770
C	-6.9443940	0.5662780	-0.8750340
H	-7.7256820	-0.1498280	-0.6072210
H	-7.2334770	1.5438630	-0.4832050
H	-6.9100020	0.6339100	-1.9647040
F	2.7074220	2.5607270	2.0594630

**PC-1,2-anti**

SCF energy: - 1977.32749868 hartree

zero-point correction: + 0.466735 hartree

enthalpy correction: + 0.497471 hartree

free energy correction: + 0.407186 hartree

quasiharmonic free energy correction: + 0.00621883 hartree

imaginary frequency: none

O	-0.0664200	-0.4235280	0.7800650
C	1.4409550	1.5639040	-0.0082010
H	1.7896950	0.5754060	-0.3201650
C	1.6937640	1.7389180	1.4995300
H	0.7678790	1.5349520	2.0421310
C	2.7961310	0.8396360	2.0413570
H	2.4737180	-0.1793720	1.7941580
S	2.3263440	2.8060600	-0.9721270
C	2.2125600	2.0128460	-2.6027940
H	1.1839170	2.0005270	-2.9654960
H	2.8199650	2.6169540	-3.2752610
H	2.6091230	0.9993420	-2.5520380
C	-0.7524260	0.4633800	0.1375830
N	-0.0443710	1.5515460	-0.2836360
Si	-0.5488570	-2.0359430	1.2879130
I	2.8499260	-1.8388200	-1.4256470
C	-0.7071600	2.5496770	-0.9244650
H	-0.1015240	3.3965460	-1.2198450
C	-2.0402440	2.4615240	-1.1648210
H	-2.5807170	3.2438380	-1.6749560
N	-2.0494860	0.3251400	-0.0676660
C	-2.7004950	1.2960760	-0.7107650
O	-3.9783650	1.1788220	-0.9224190
Si	-5.0821350	0.0019400	-0.2573480
C	4.1580620	1.0871710	1.3928860
H	4.4601610	2.1310490	1.5087890
H	4.1523730	0.8387340	0.3303810
H	4.9074510	0.4580990	1.8778440
C	2.8707170	0.9833660	3.5617670

H	3.1954920	1.9896570	3.8377740
H	3.5892610	0.2715300	3.9722260
H	1.9002550	0.7968720	4.0299650
C	0.9680980	-2.6052740	2.1858670
H	0.8220320	-3.6254870	2.5510490
H	1.8301970	-2.5974310	1.5142340
H	1.1778010	-1.9654810	3.0473380
C	-1.9995510	-1.8346690	2.4379790
H	-2.9258100	-1.6327450	1.9001850
H	-2.1310920	-2.7571100	3.0108340
H	-1.8265960	-1.0225940	3.1492240
C	-0.9439080	-2.9903890	-0.2561990
H	-1.5170150	-2.3827080	-0.9604900
H	-0.0229210	-3.3098580	-0.7472310
H	-1.5391920	-3.8734050	-0.0071000
C	-4.5328950	-1.7001760	-0.7657560
H	-4.2910240	-1.7237740	-1.8316510
H	-3.6566520	-2.0296830	-0.2075420
H	-5.3438710	-2.4125220	-0.5903380
C	-5.0804450	0.2958170	1.5816280
H	-5.5713160	1.2434400	1.8151090
H	-5.6218290	-0.5026920	2.0960320
H	-4.0641400	0.3251940	1.9795580
C	-6.6779380	0.4939060	-1.0659460
H	-7.4959730	-0.1291870	-0.6957090
H	-6.9201740	1.5366900	-0.8495880
H	-6.6218030	0.3688640	-2.1496290
F	1.9891720	3.0821690	1.7595170

**Uracil(TMS)<sub>2</sub> (low energy conformation, see reference [Guindon et al. JOC 2014](#))<sup>11</sup>**

SCF energy: - 1232.111083 hartree

zero-point correction: + 0.288779 hartree

enthalpy correction: + 0.308447 hartree

free energy correction: + 0.243323 hartree

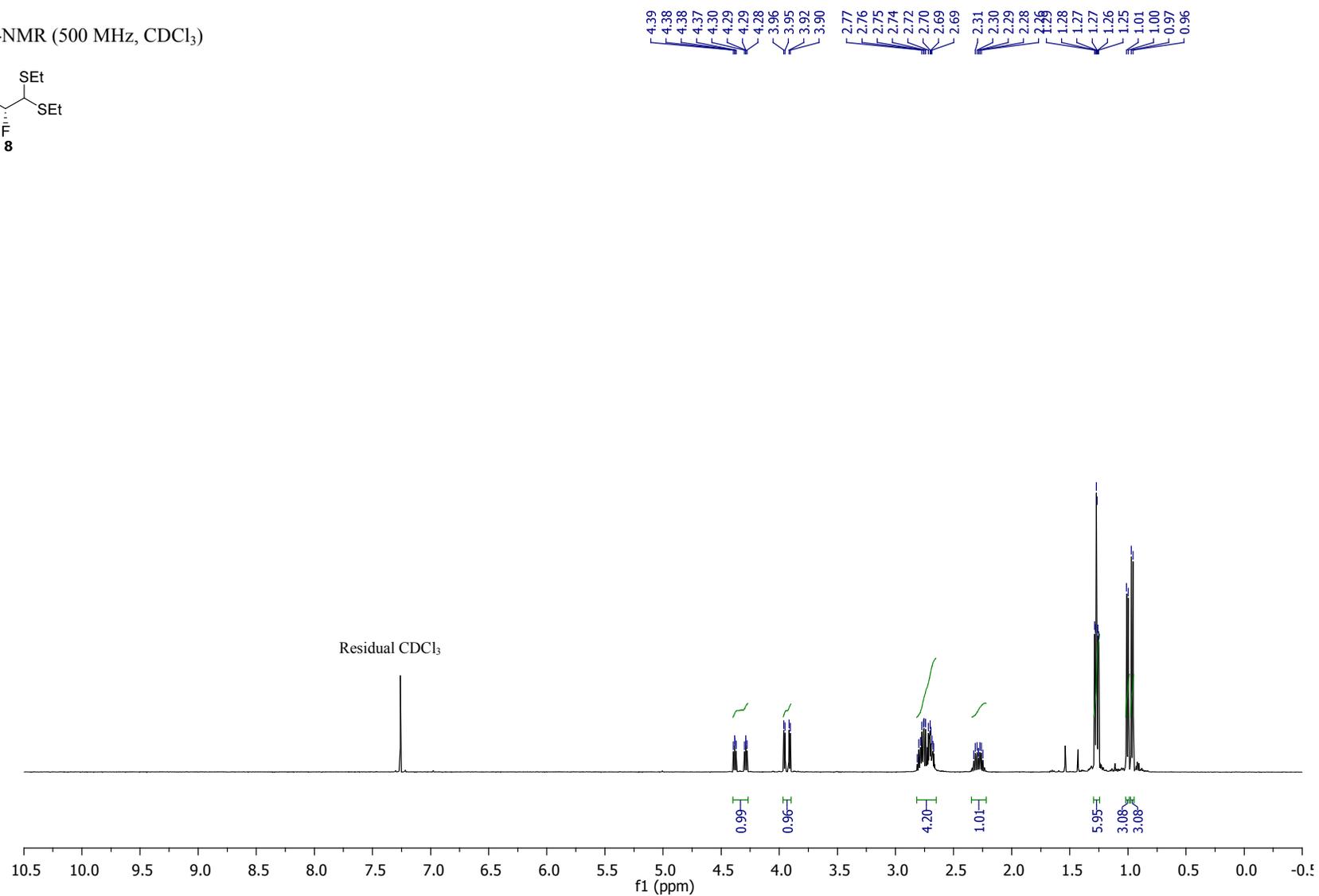
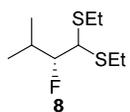
quasiharmonic free energy correction: + 0.00383851 hartree

imaginary frequency: none

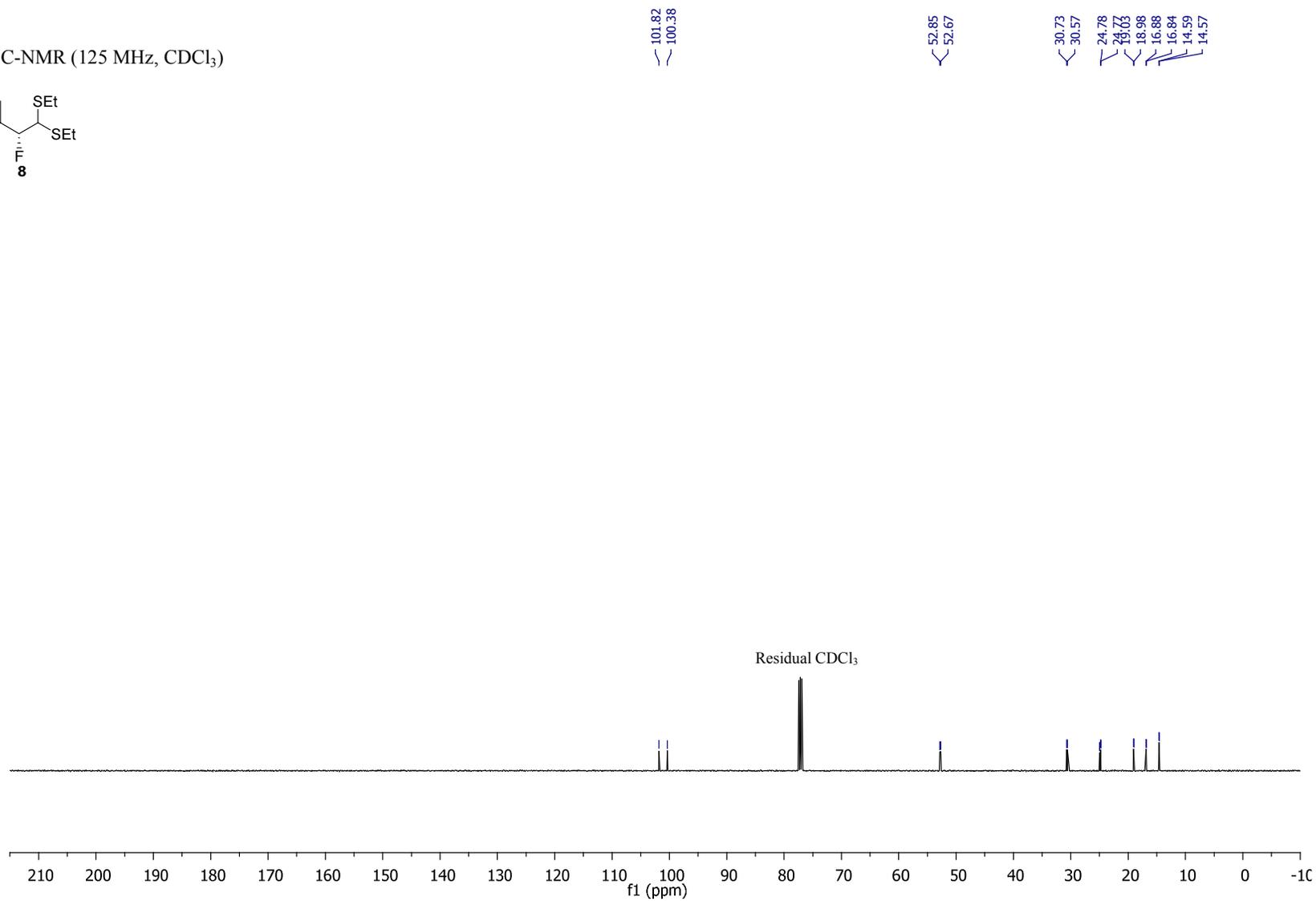
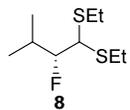
O	-1.6317410	-0.6162250	-0.0000900
C	-0.8251110	0.4403240	-0.0001370
N	-1.3732390	1.6501330	-0.0000230
Si	-3.3473670	-0.5753570	0.0000190
C	-0.5101520	2.6771330	0.0000570
H	-0.9497040	3.6695840	0.0001750
C	0.8564690	2.5166350	0.0000290
H	1.5467640	3.3467830	0.0001500
N	0.4794650	0.1565540	-0.0001760
C	1.3115130	1.1888900	-0.0001750
O	2.6168560	0.9504050	0.0000170
Si	3.3527880	-0.6077320	0.0000160
C	-3.7697350	-2.3902040	0.0000390
H	-3.3634960	-2.8850880	0.8852290
H	-4.8537020	-2.5313180	0.0000980
H	-3.3635920	-2.8850870	-0.8851950

C	-3.9509280	0.2588070	1.5535410
H	-3.5015160	-0.1999760	2.4379210
H	-3.7057090	1.3216960	1.5498000
H	-5.0363170	0.1516860	1.6353890
C	-3.9511340	0.2588190	-1.5534160
H	-3.7059610	1.3217180	-1.5496770
H	-3.5017960	-0.1999230	-2.4378560
H	-5.0365270	0.1516500	-1.6351500
C	5.1632390	-0.1689490	0.0005020
H	5.7751820	-1.0747540	0.0005290
H	5.4240890	0.4157920	-0.8847710
H	5.4236620	0.4155580	0.8860560
C	2.8740480	-1.5179060	1.5543710
H	1.8145630	-1.7775330	1.5485040
H	3.4578960	-2.4391350	1.6368420
H	3.0812570	-0.9095300	2.4384310
C	2.8748030	-1.5175740	-1.5547690
H	3.0824010	-0.9089880	-2.4385930
H	3.4587200	-2.4387650	-1.6371850
H	1.8153250	-1.7772310	-1.5494530

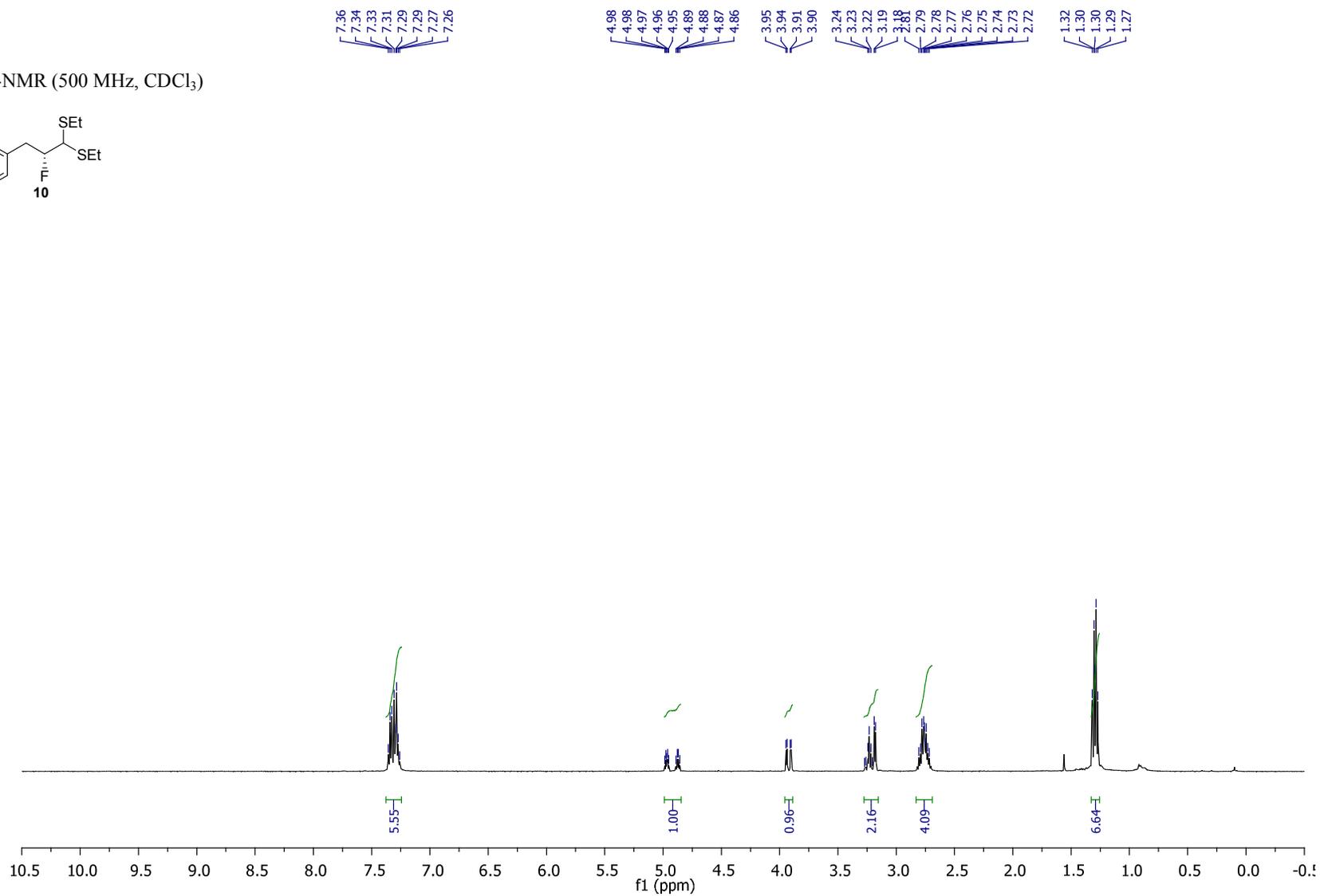
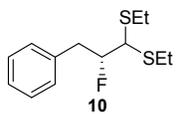
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)



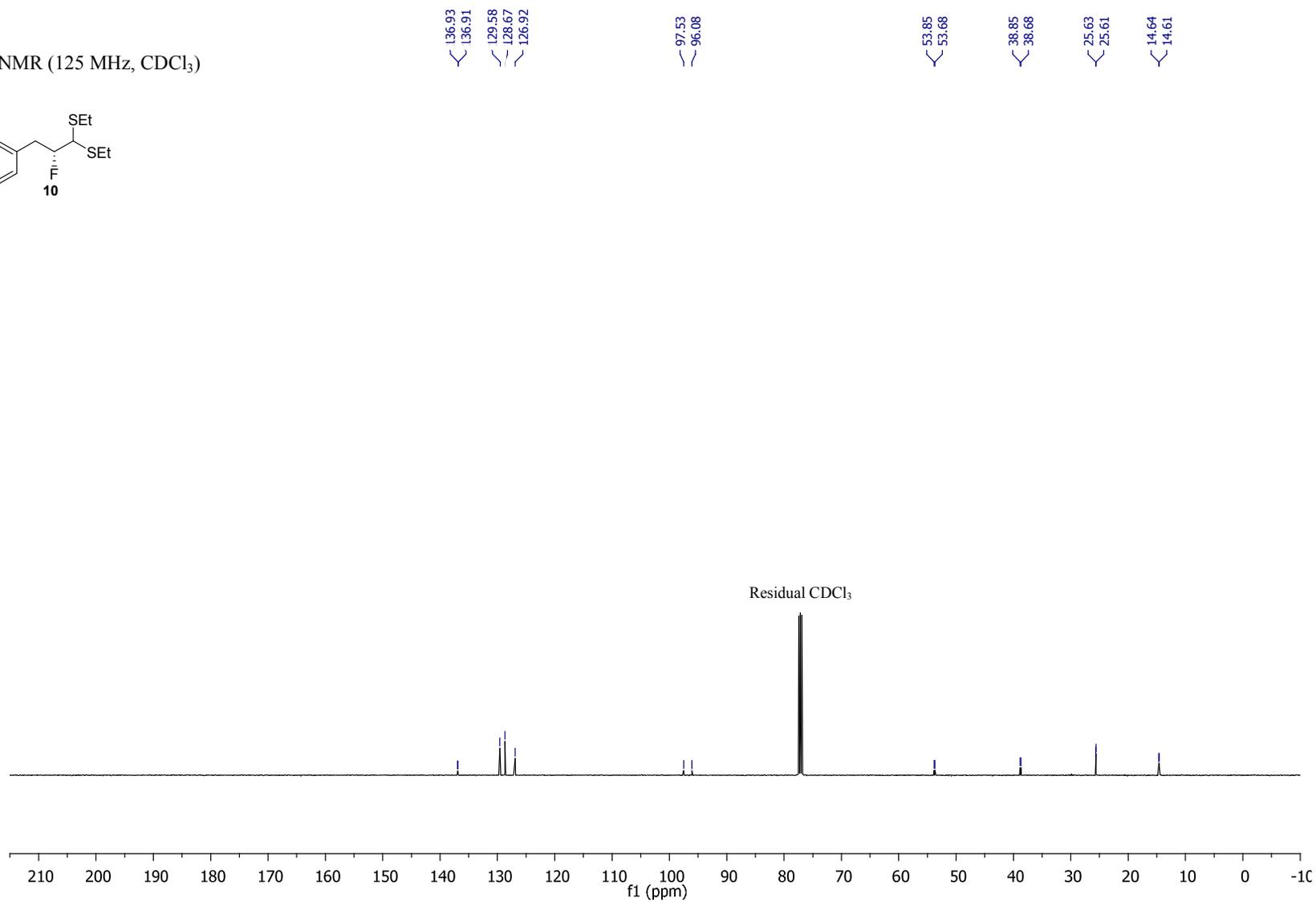
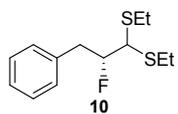
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

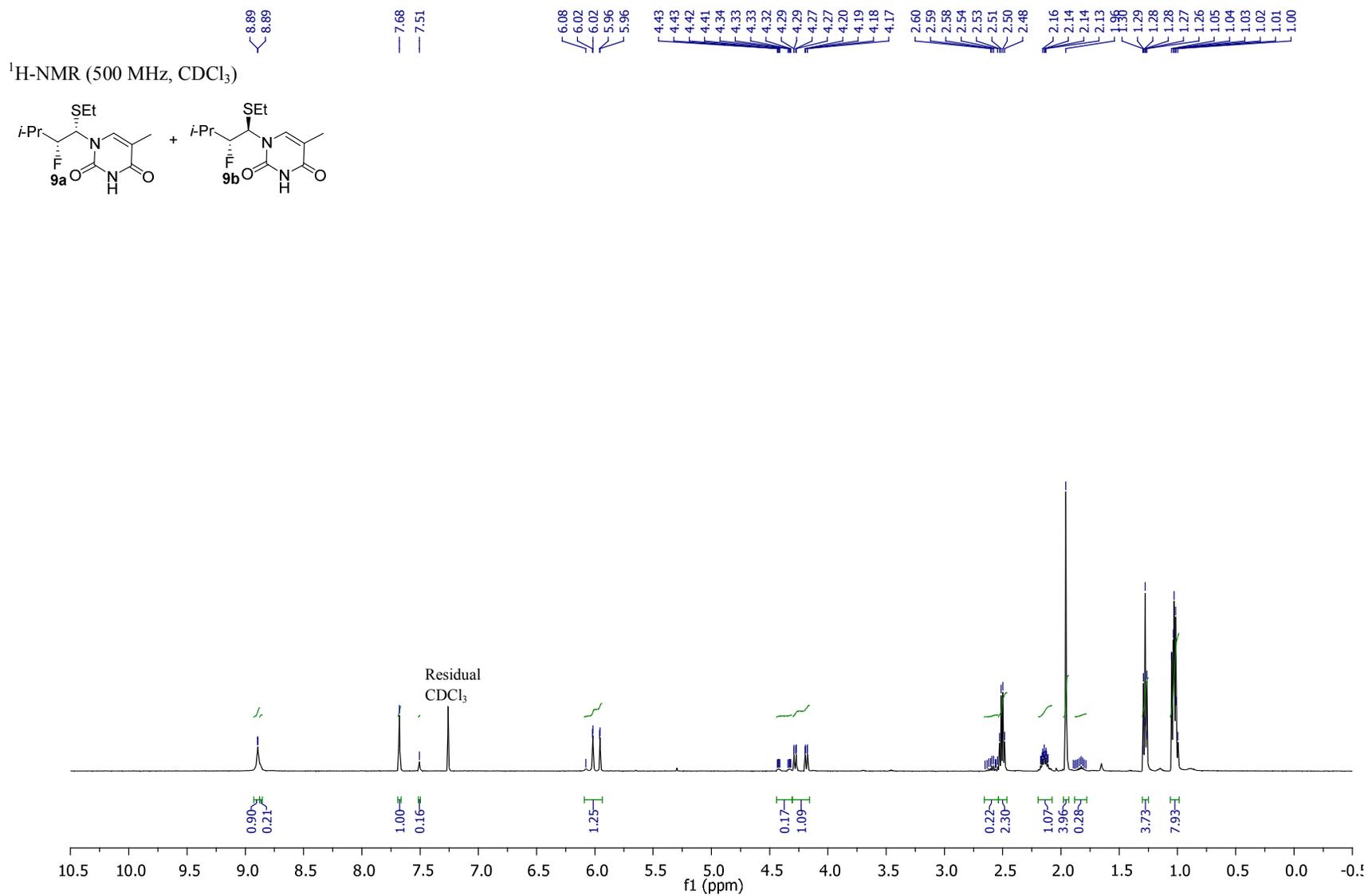


<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

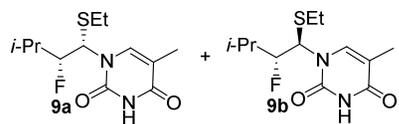


<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>)





<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>)



163.74  
163.74  
163.60

151.46  
151.46  
151.08  
151.08

137.99  
137.99  
137.95  
137.95  
137.79  
137.73

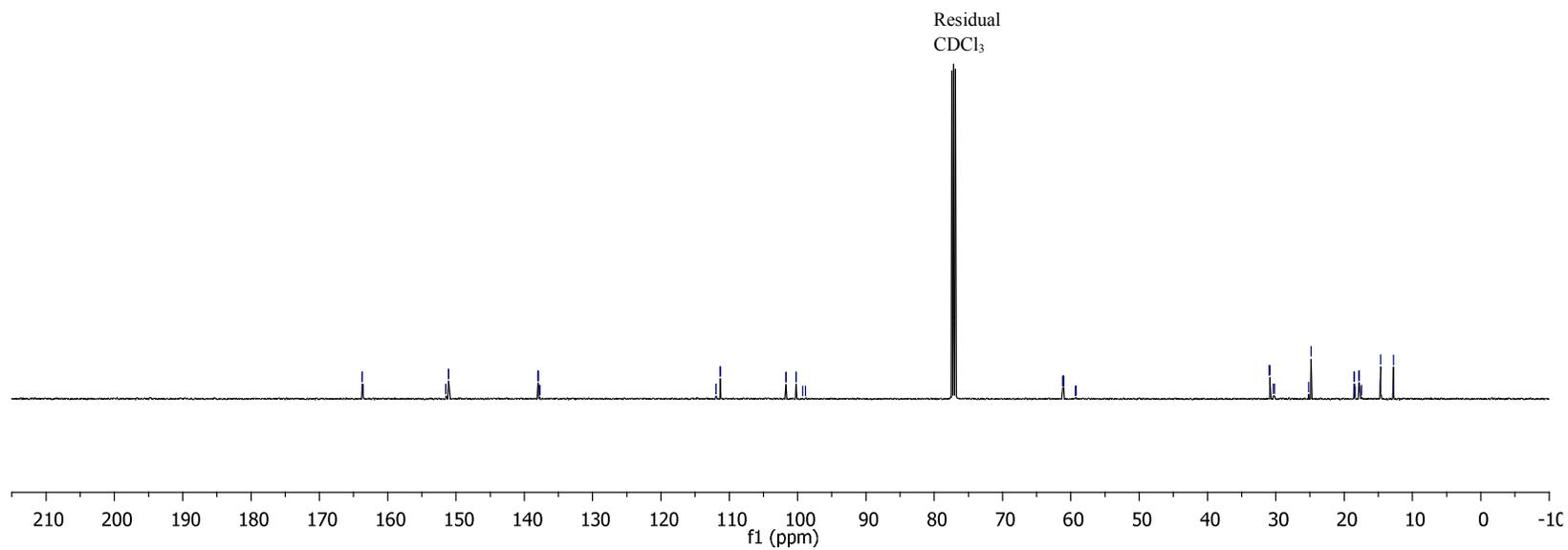
111.94  
111.94  
111.31  
111.31

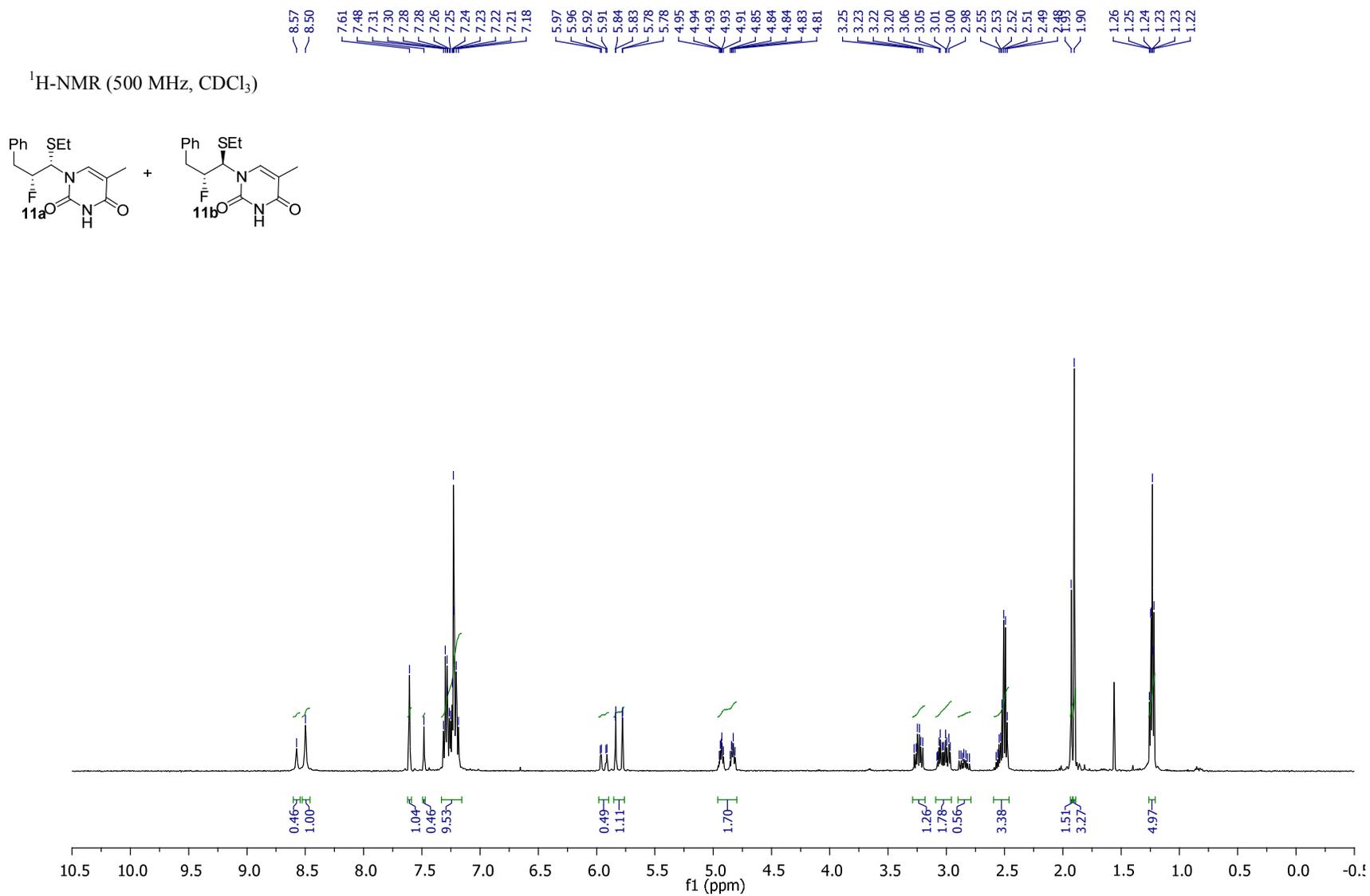
101.68  
101.68  
100.25  
100.25  
99.26  
98.84

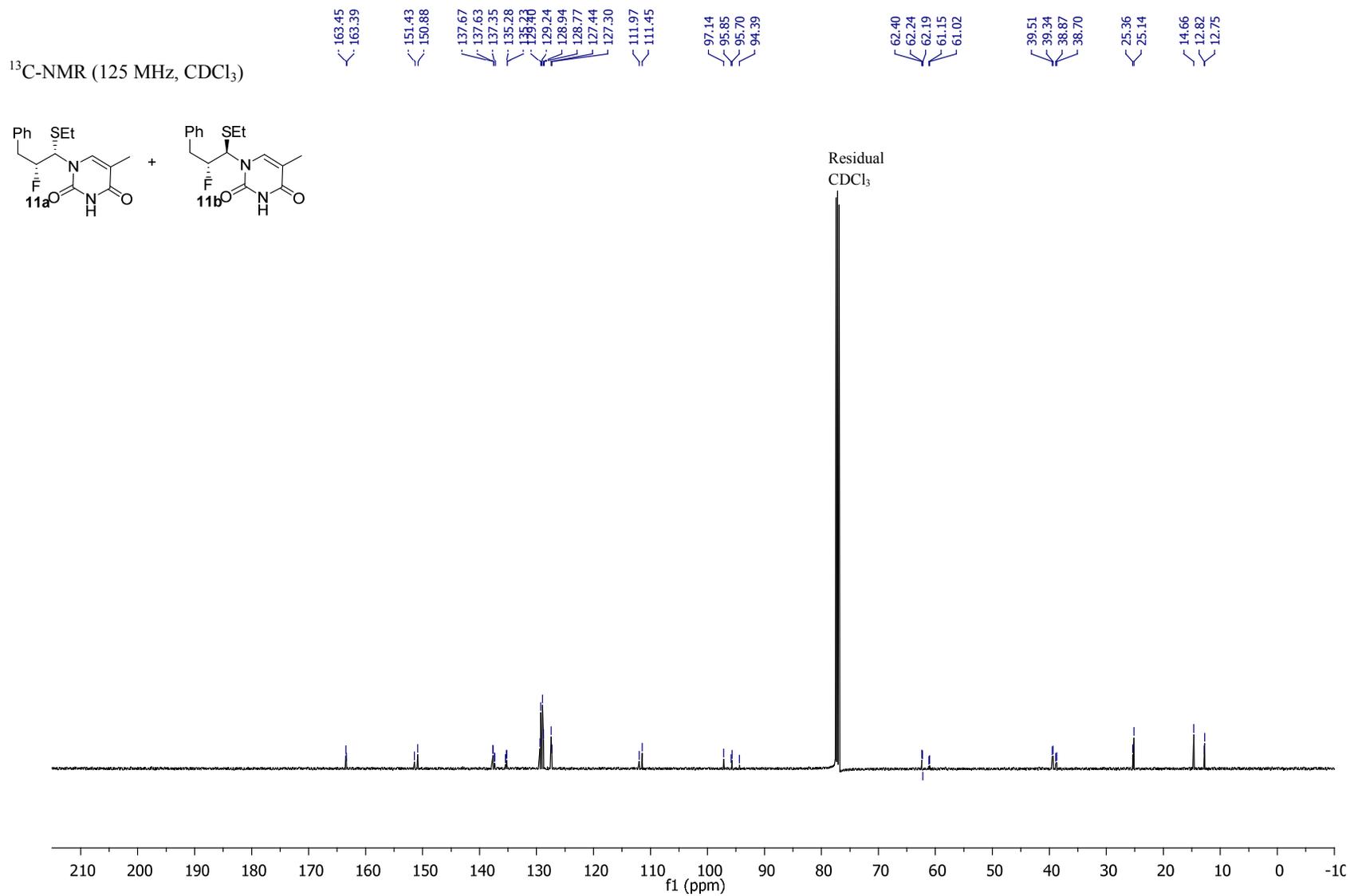
61.19  
61.18  
61.04  
61.03  
59.37  
59.20

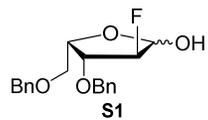
31.00  
30.85  
30.36  
30.21  
25.18  
24.86

18.55  
18.51  
18.48  
17.86  
17.79  
17.51  
17.45  
14.67  
14.65  
12.83  
12.76

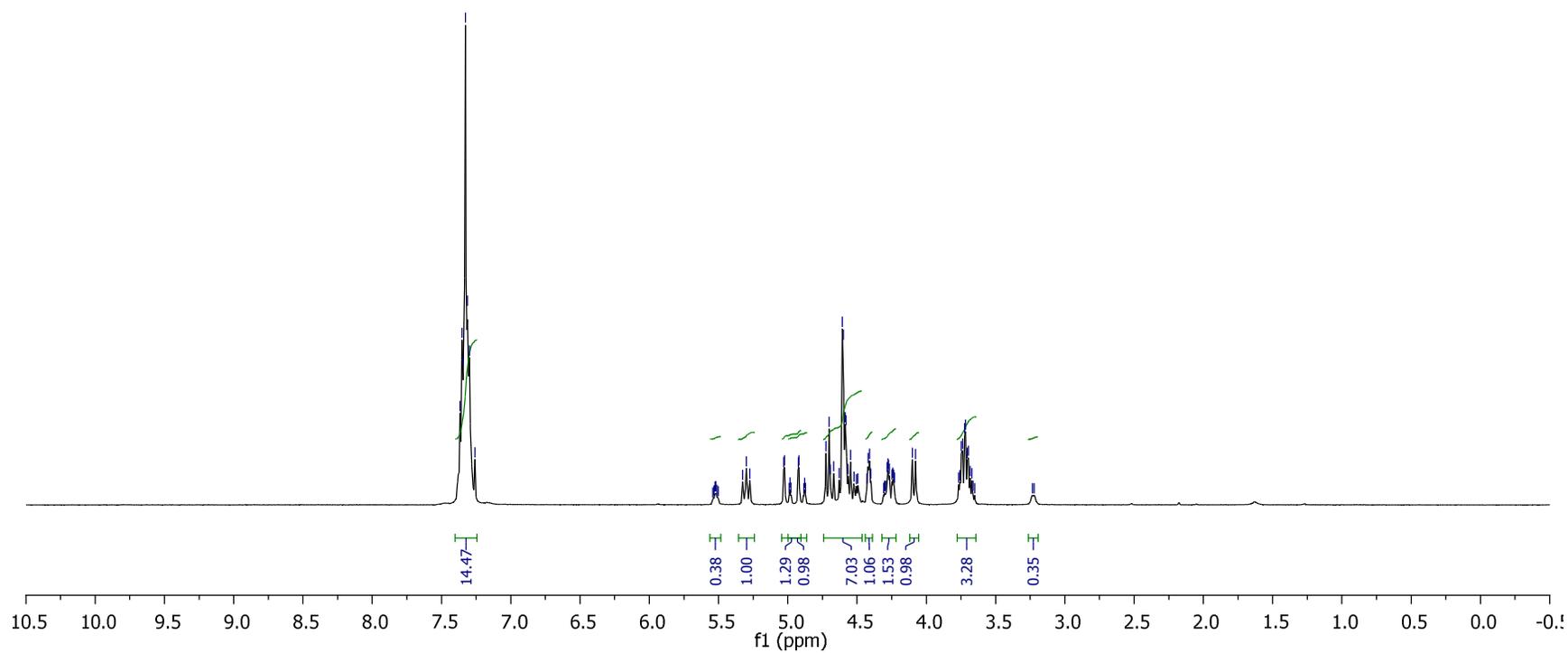


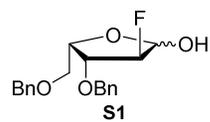




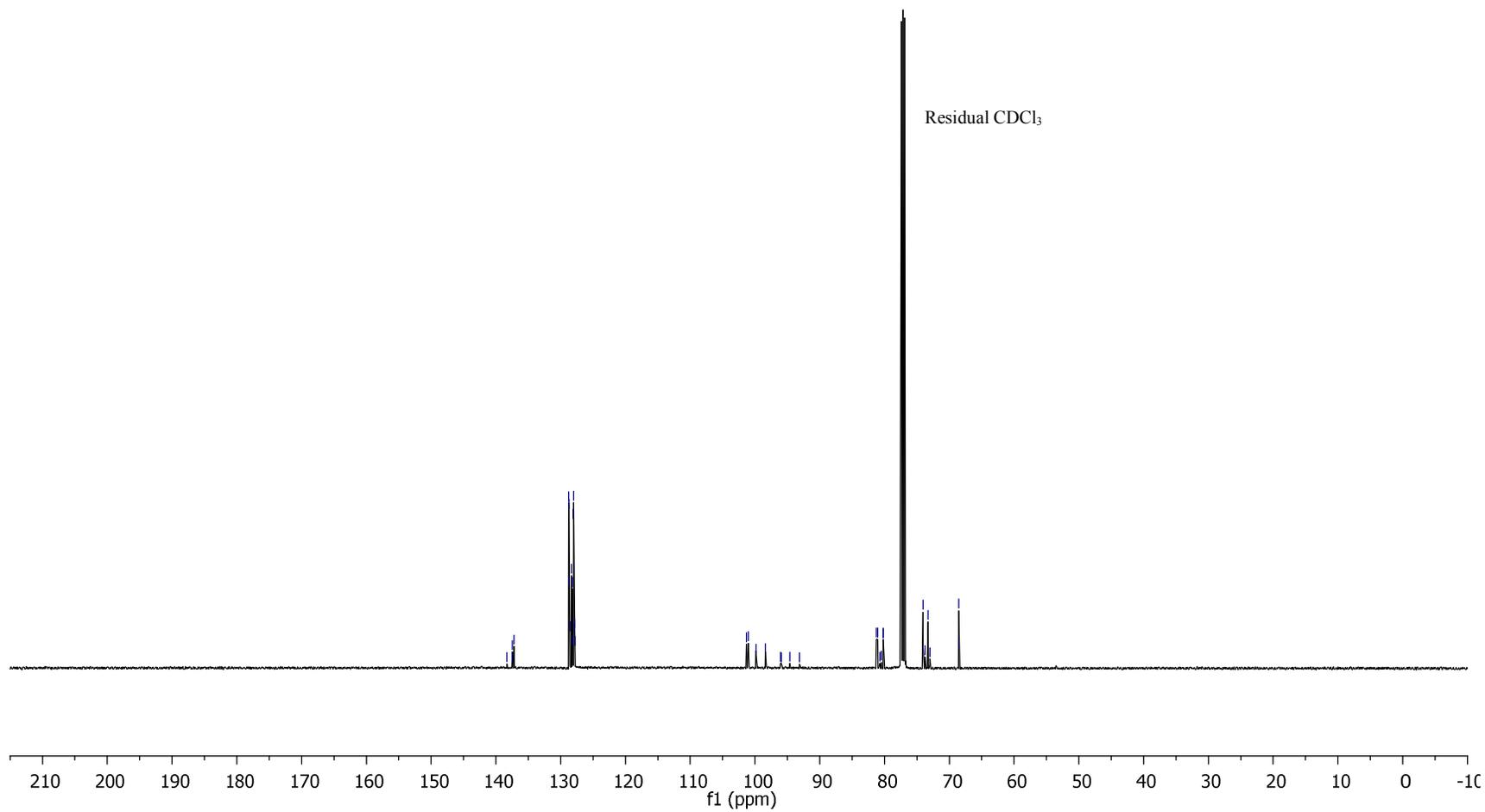
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

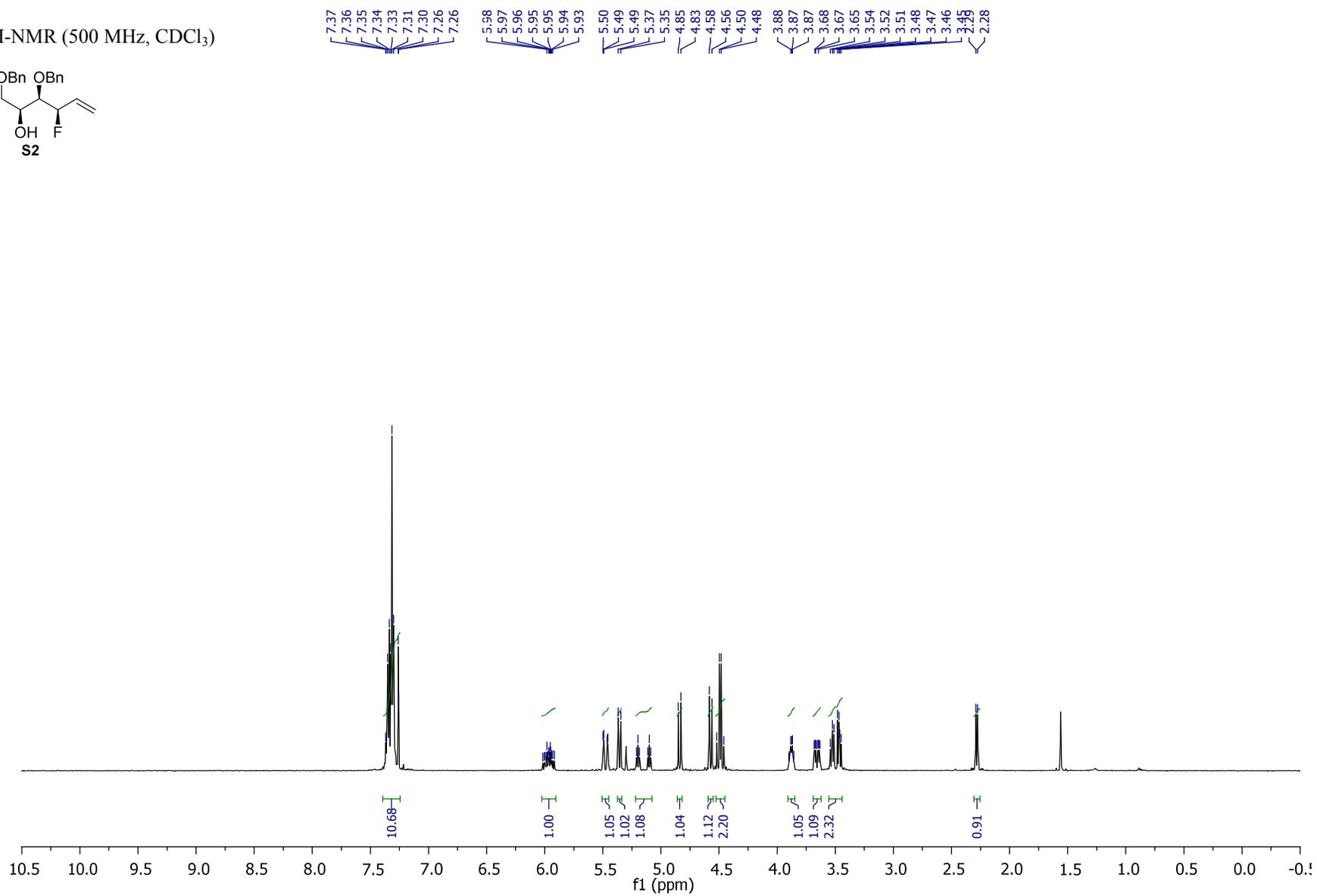
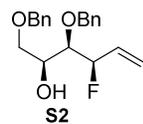
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7.335  
7.333  
7.331  
7.330  
7.226  
5.330  
5.03  
5.02  
4.92  
4.92  
4.73  
4.770  
4.67  
4.61  
4.60  
4.59  
4.58  
4.56  
4.55  
4.42  
4.41  
4.28  
4.28  
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4.27  
4.10  
4.08  
3.75  
3.74  
3.72  
3.72  
3.22

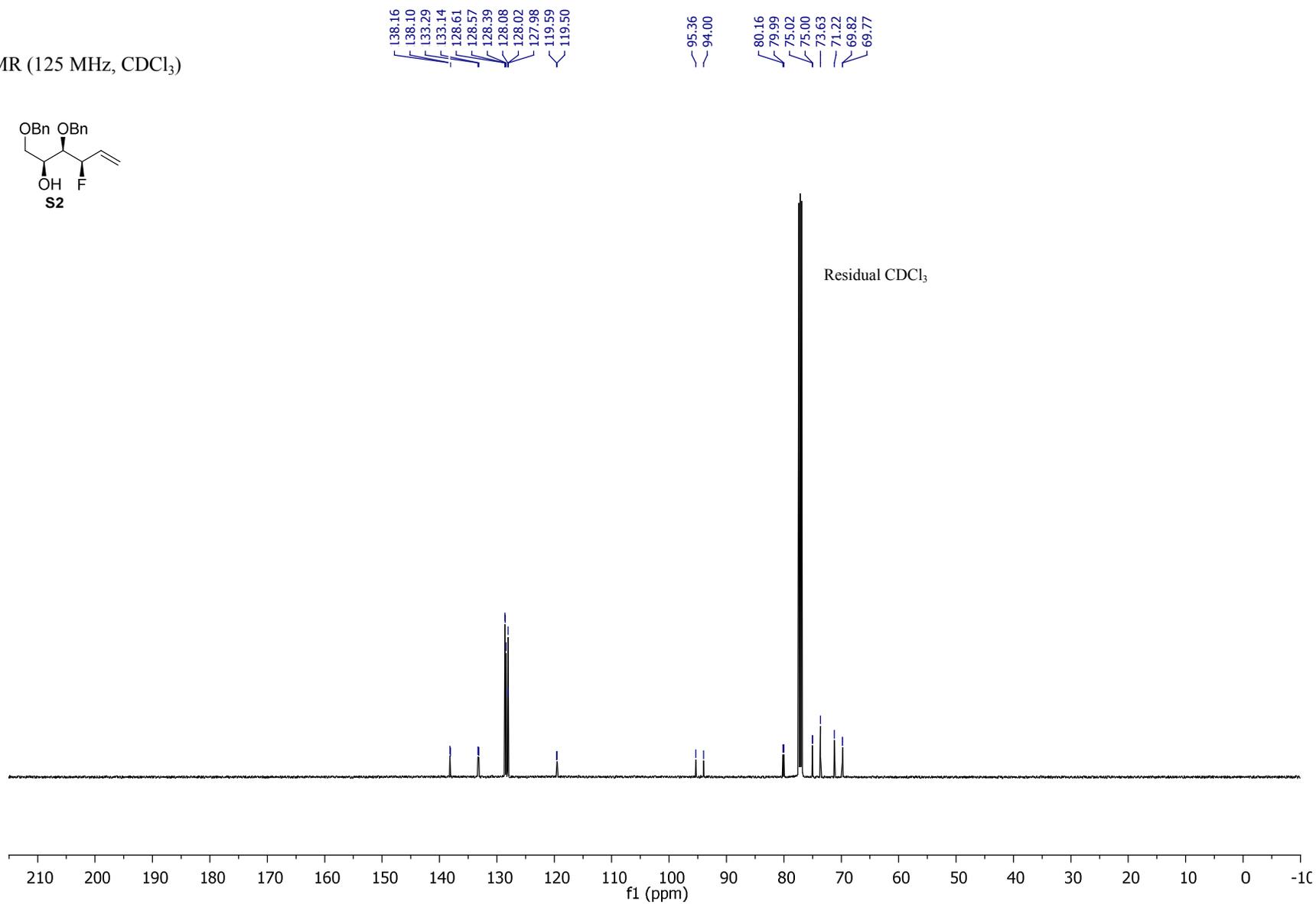
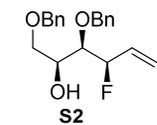


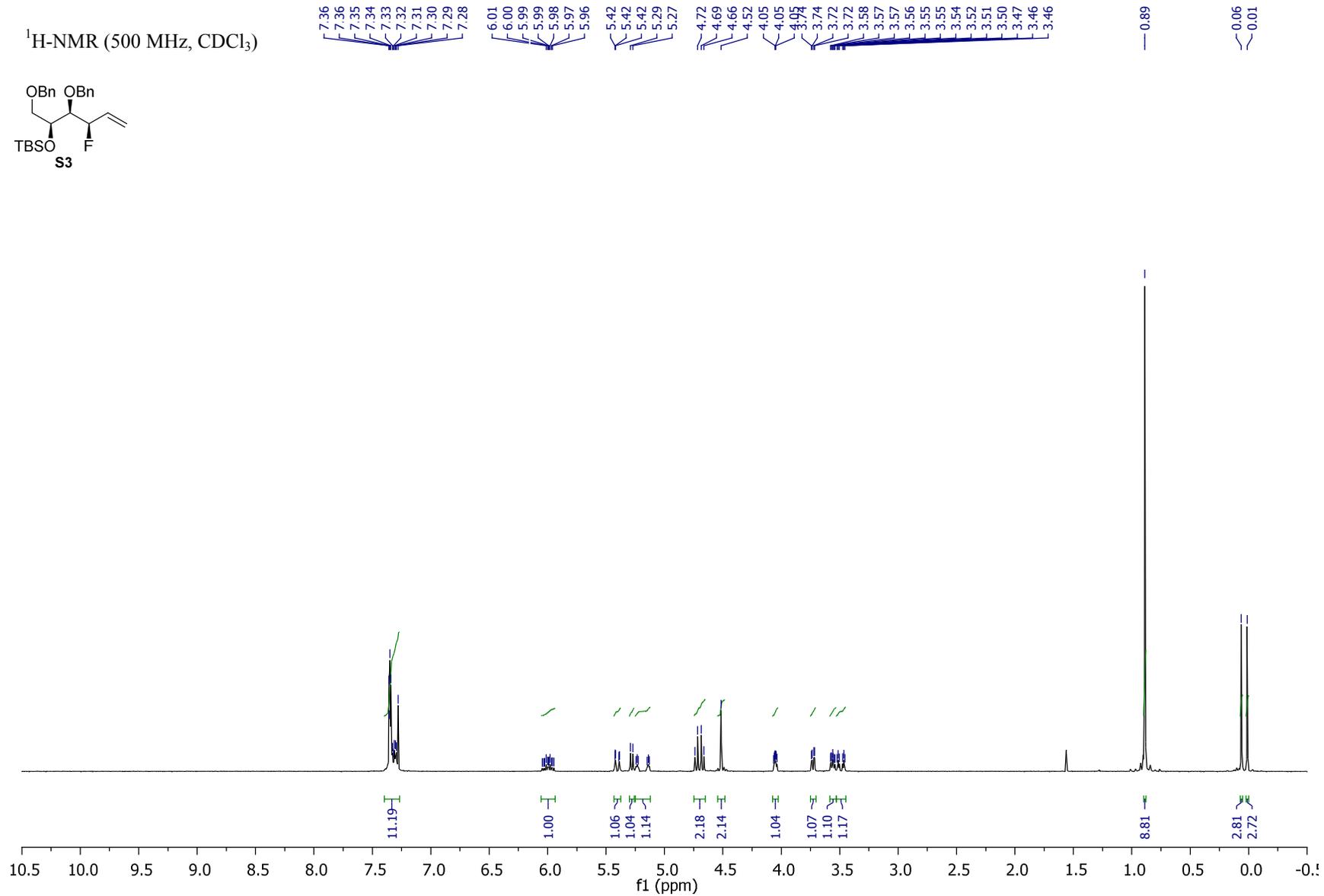
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

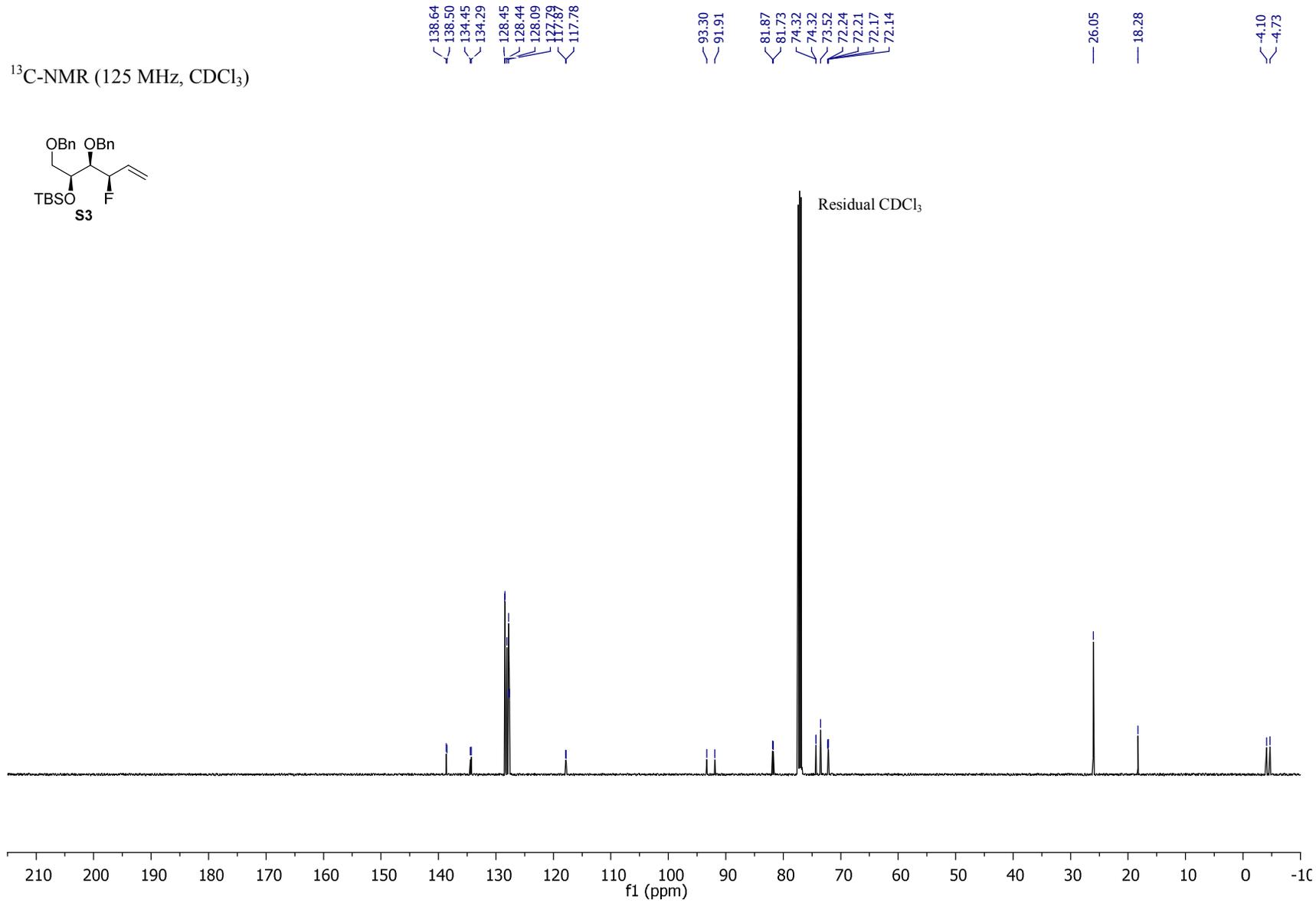
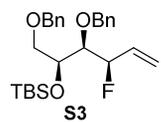
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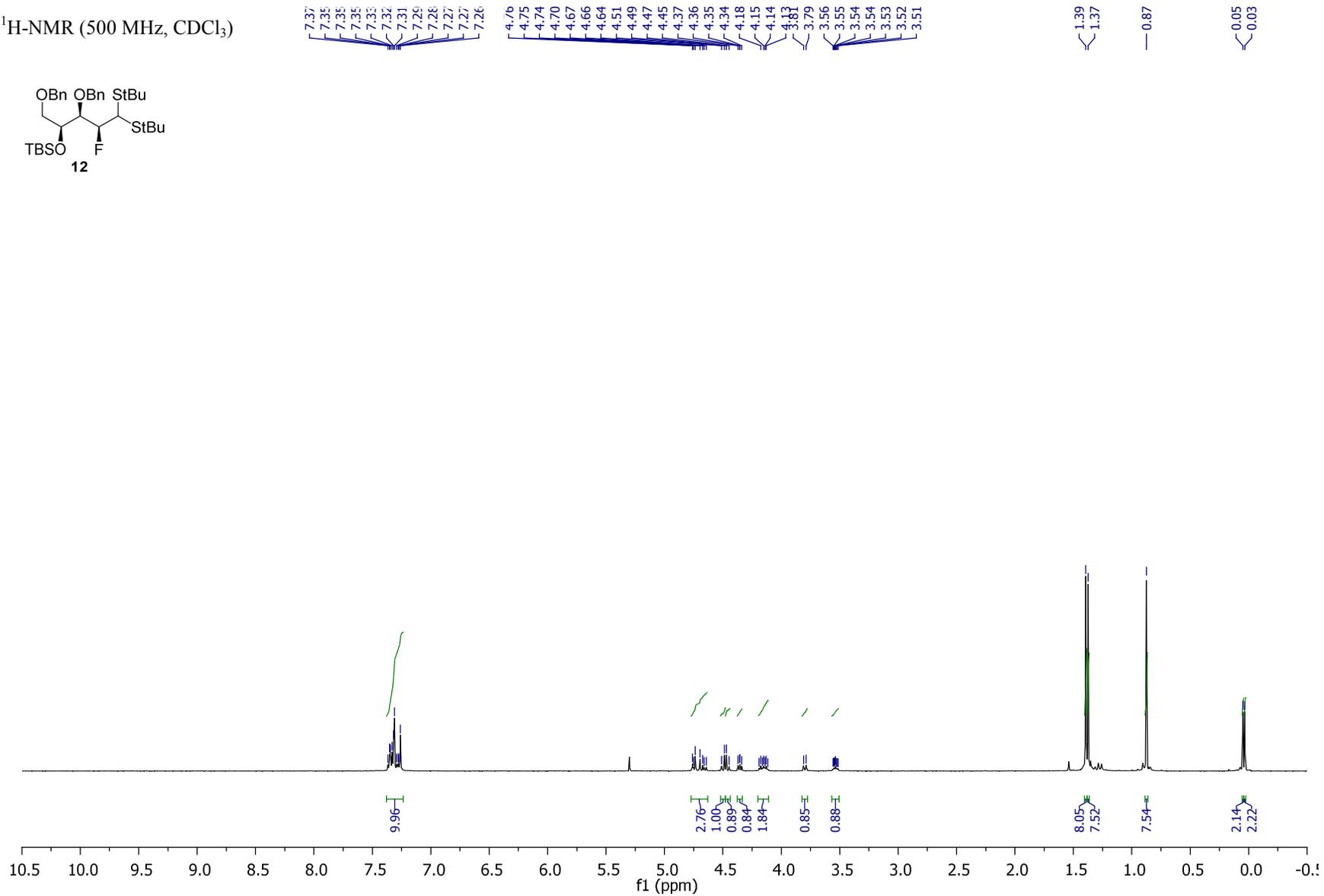
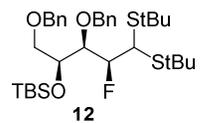


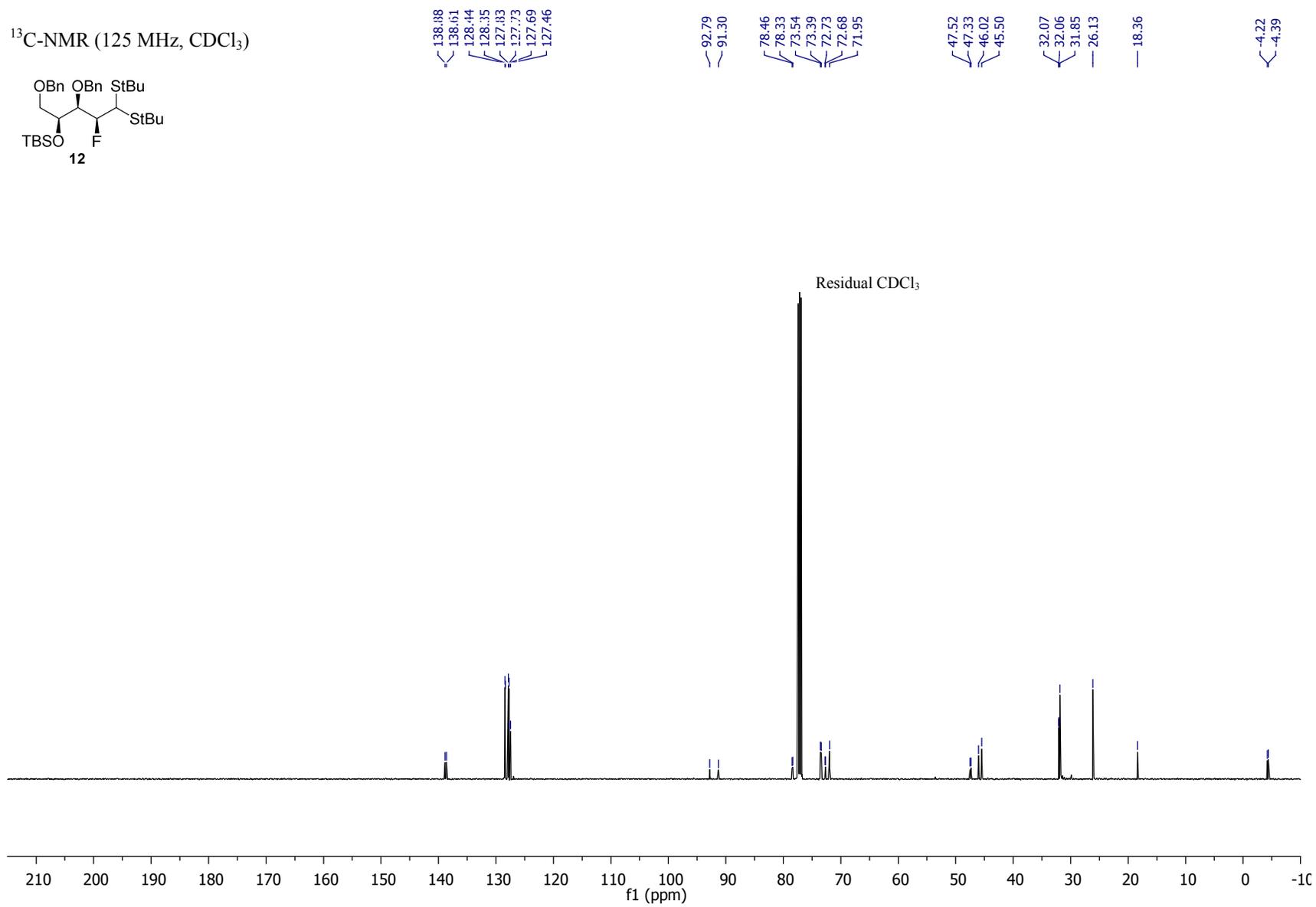
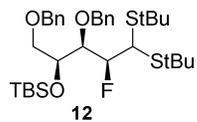
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )



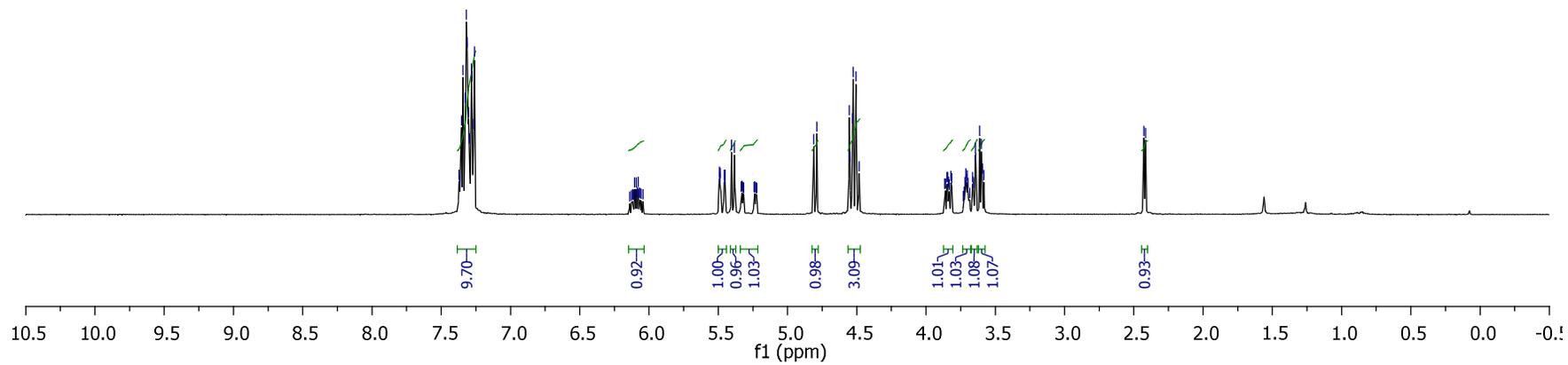
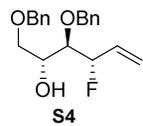
$^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ )

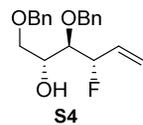
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

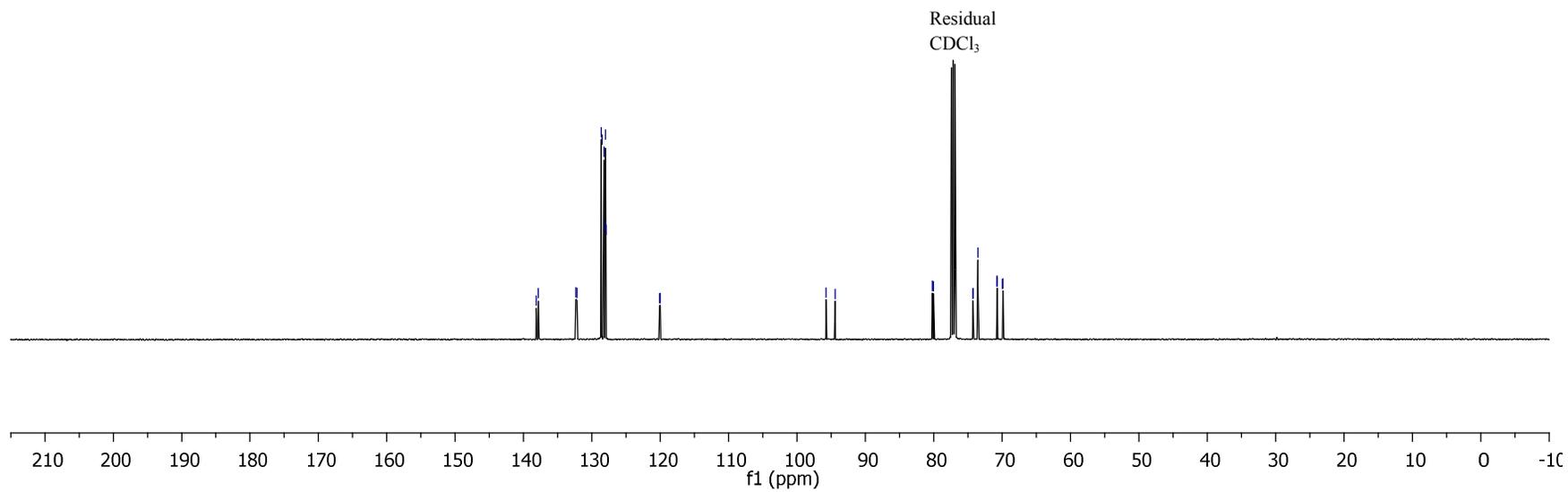
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

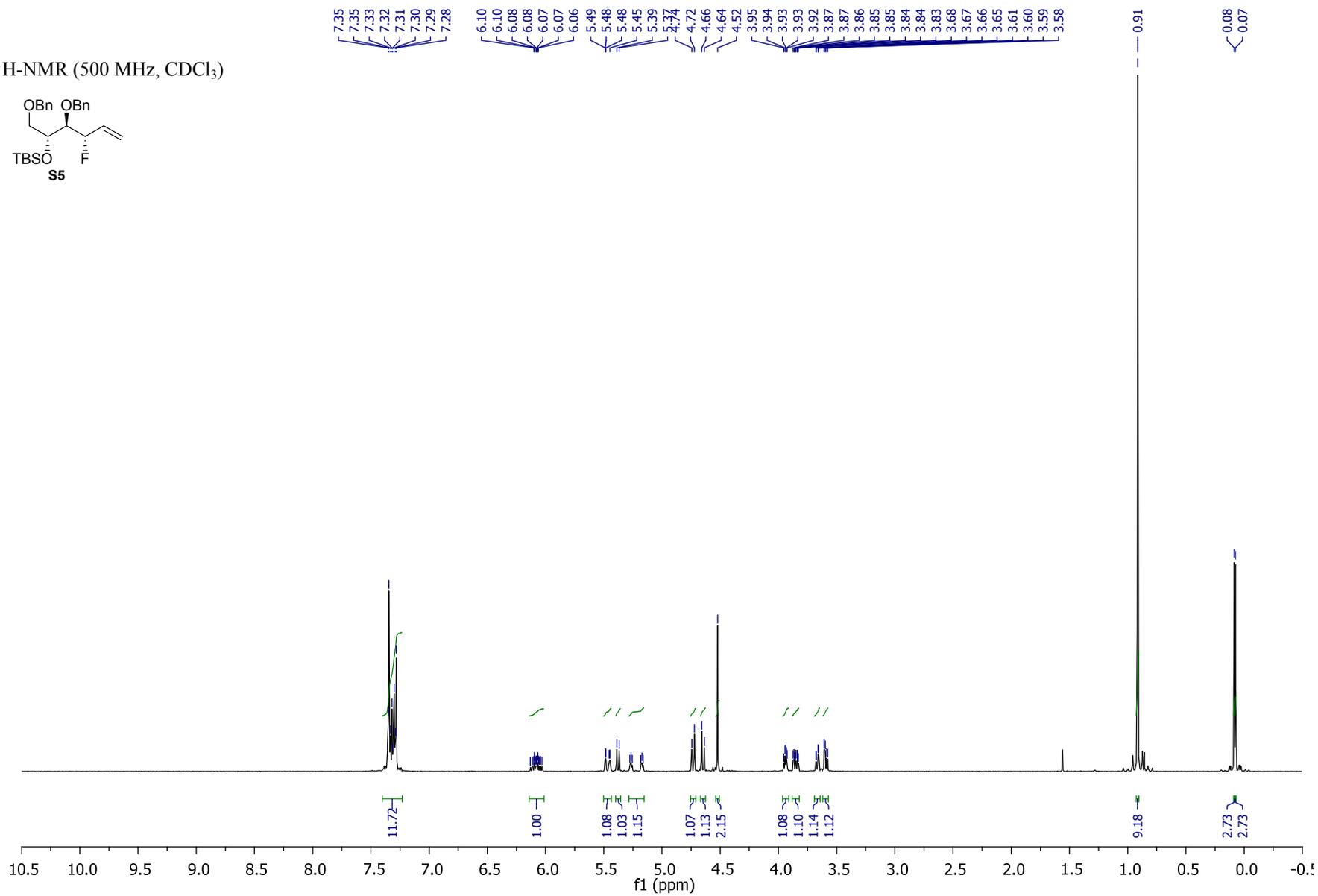
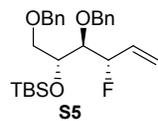
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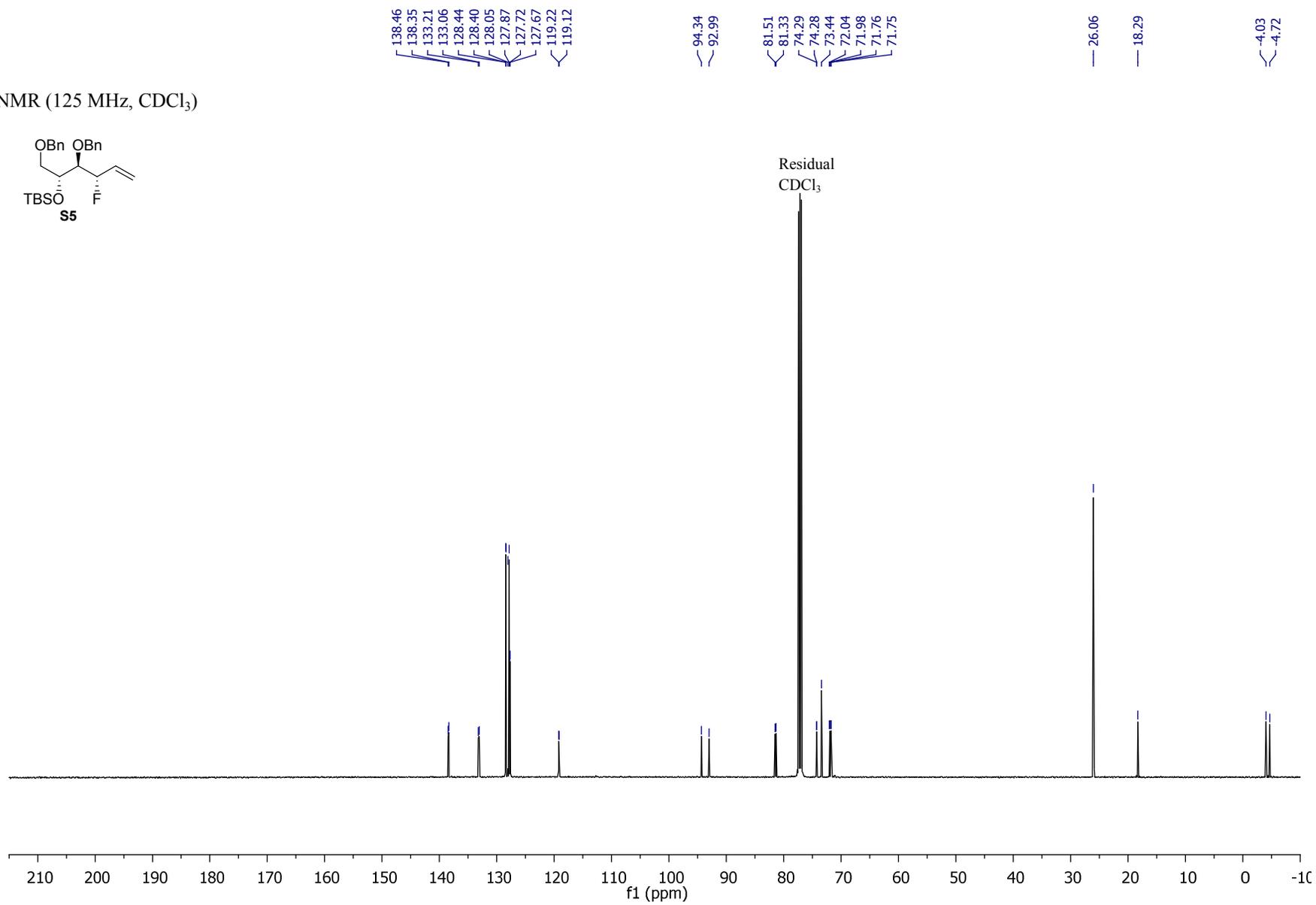
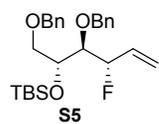


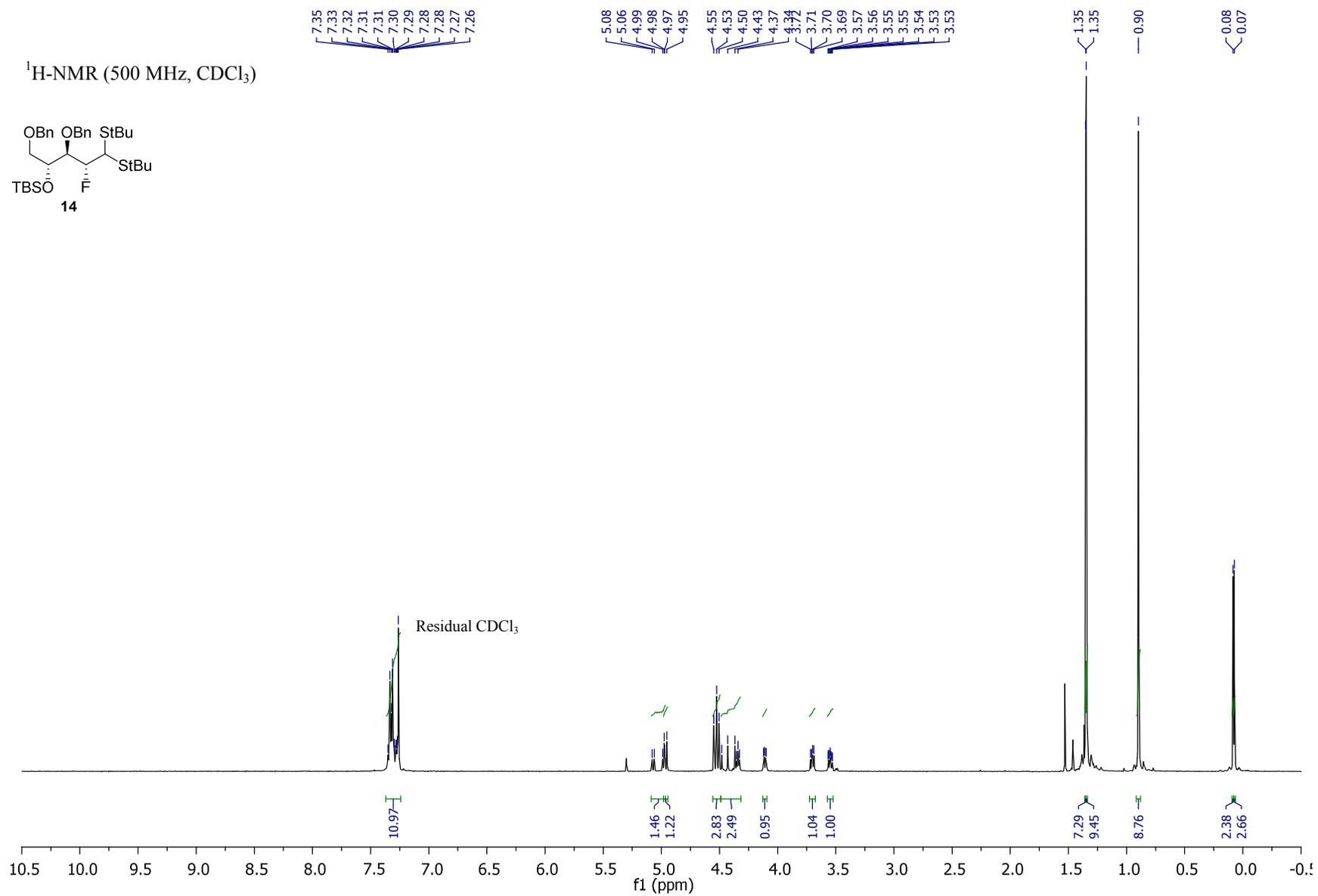
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

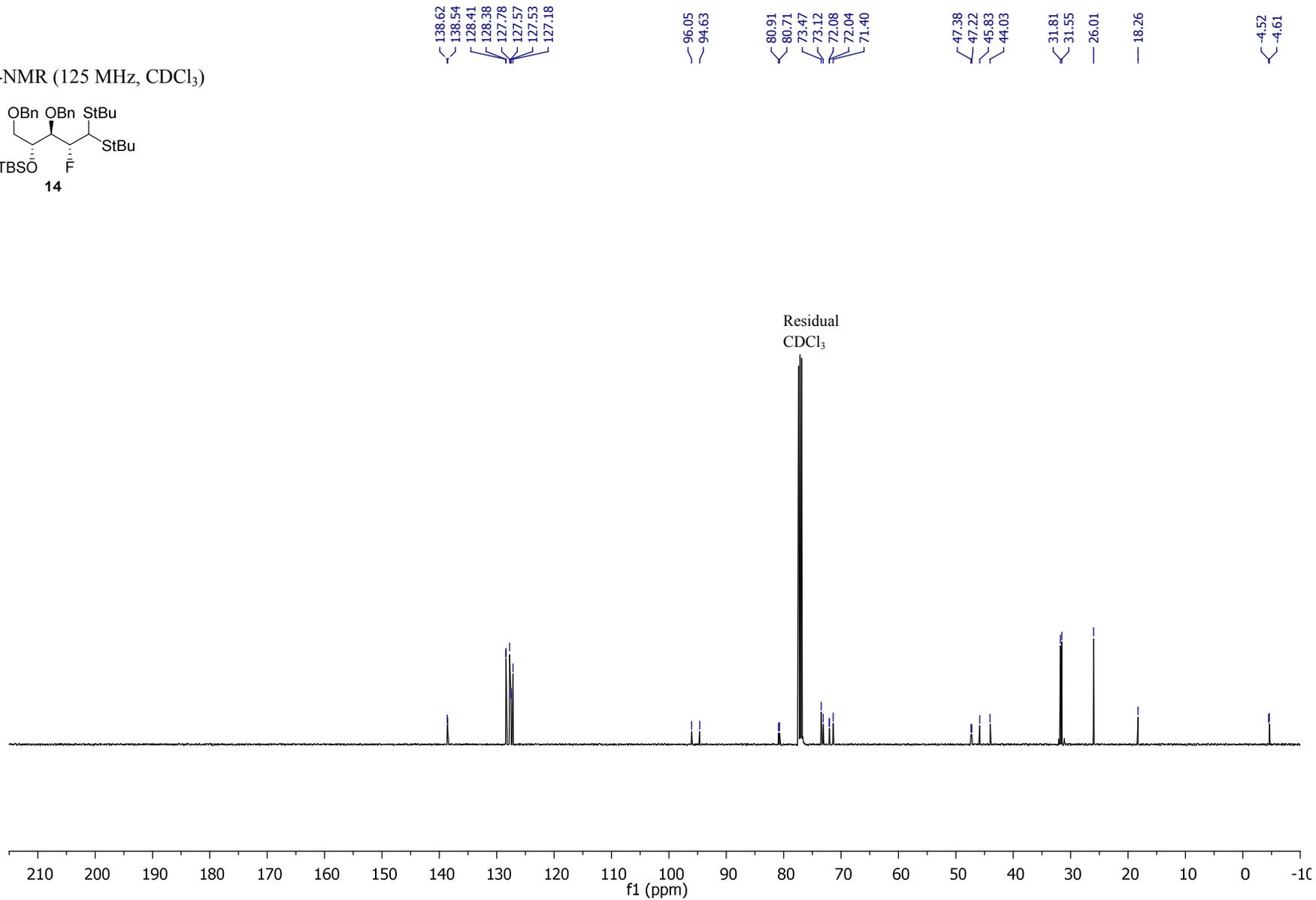
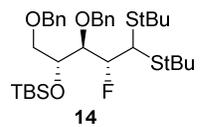
138.15  
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128.64  
128.50  
128.21  
128.08  
119.99  
95.77  
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80.05  
74.29  
74.27  
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69.95  
69.88

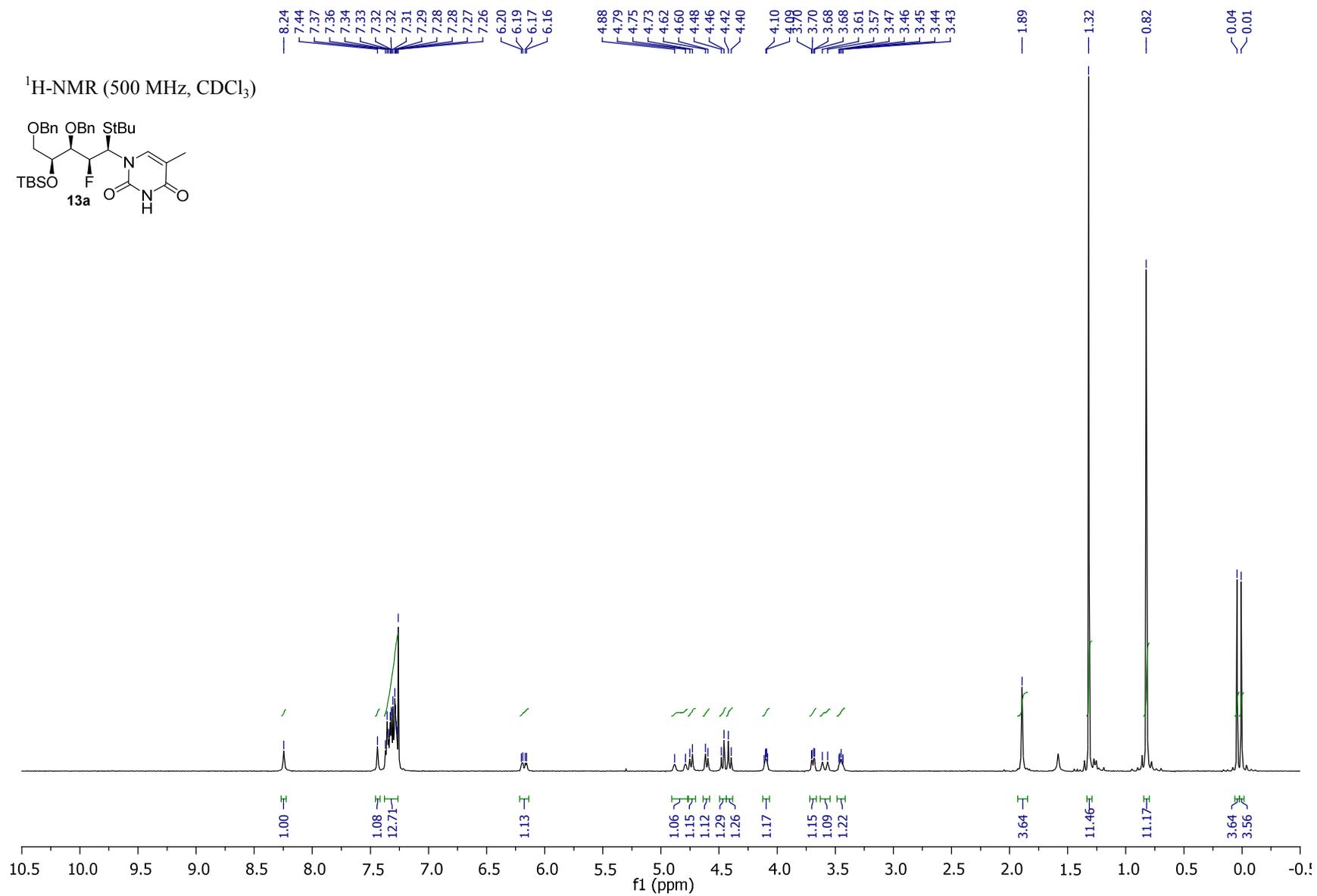


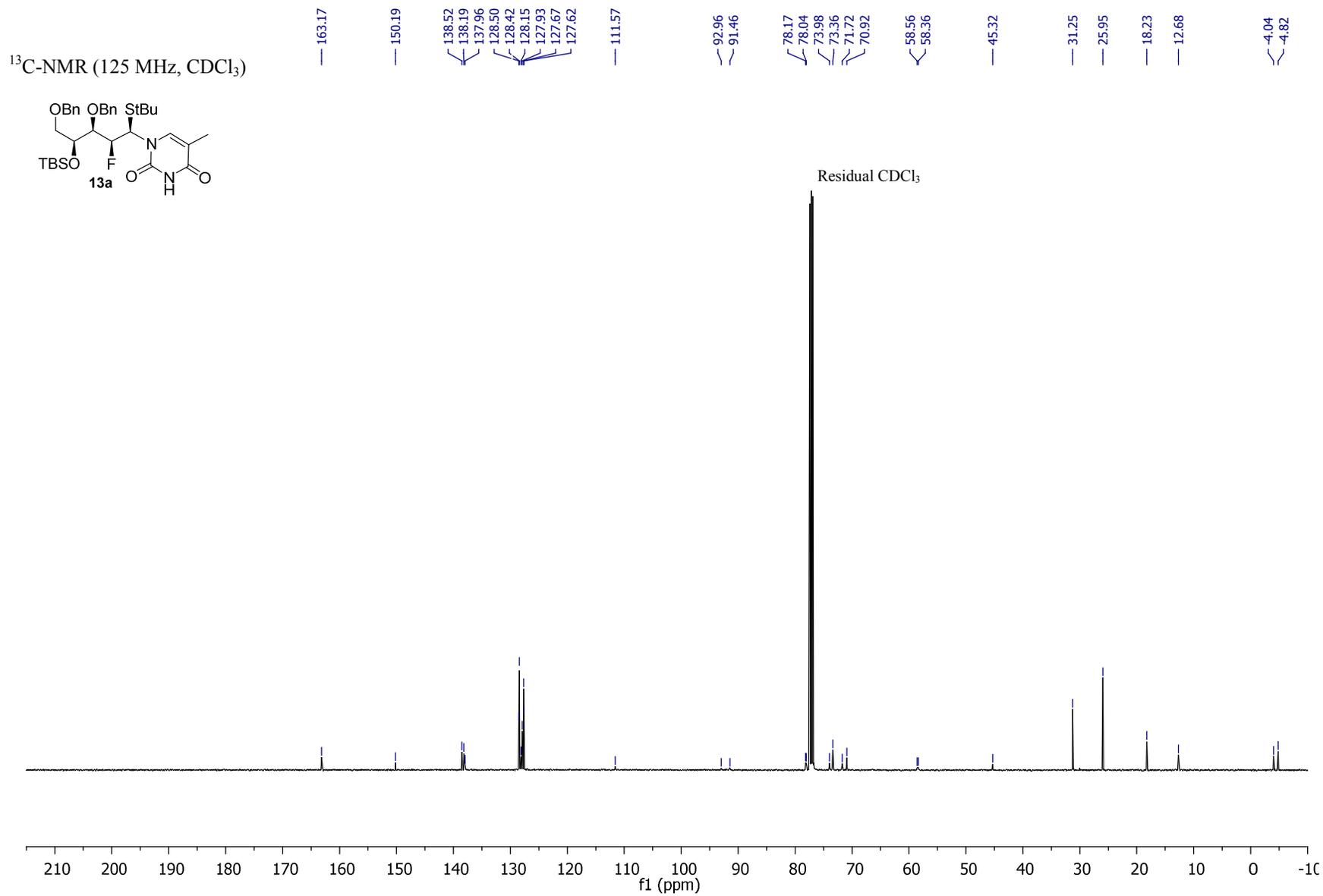
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

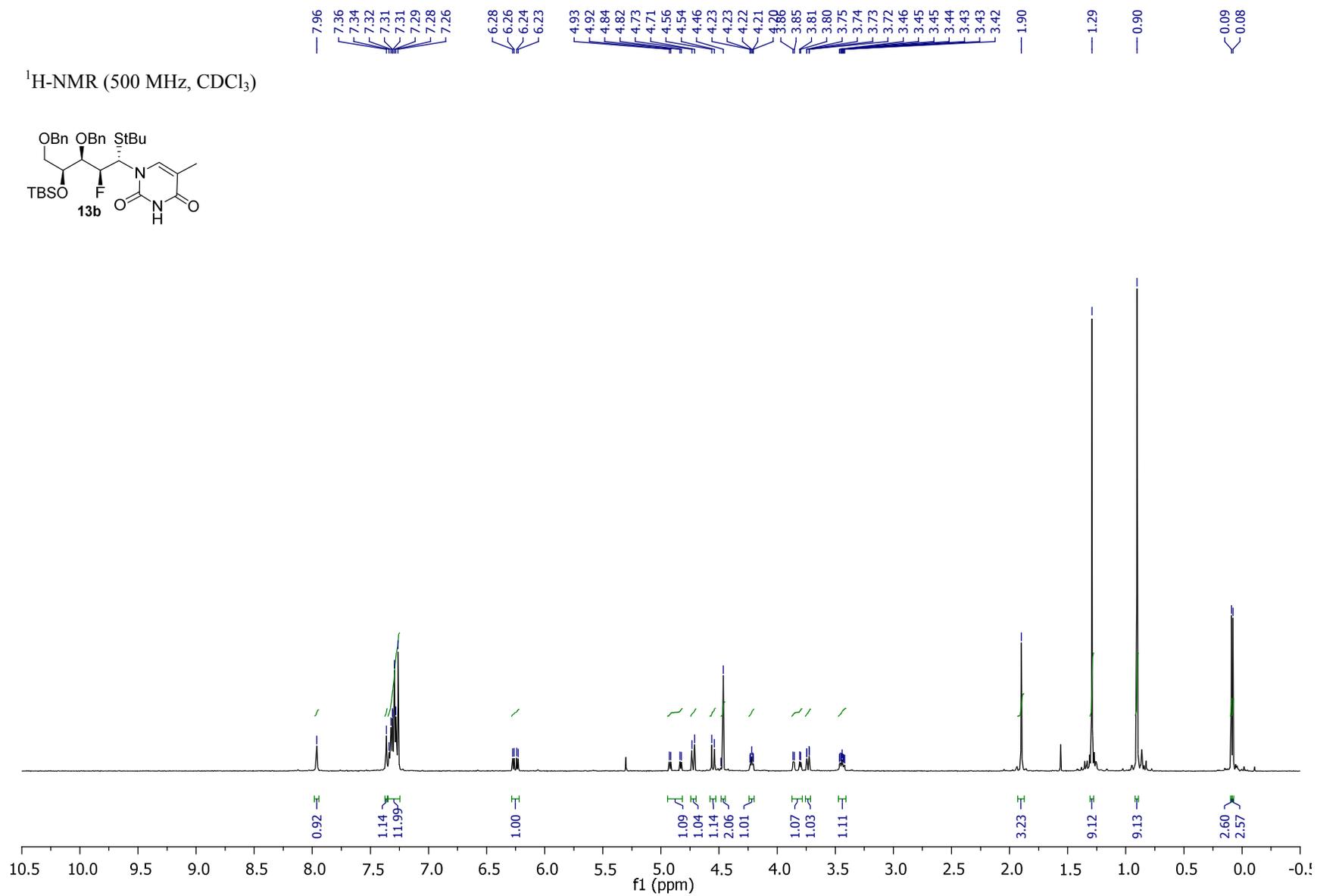
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

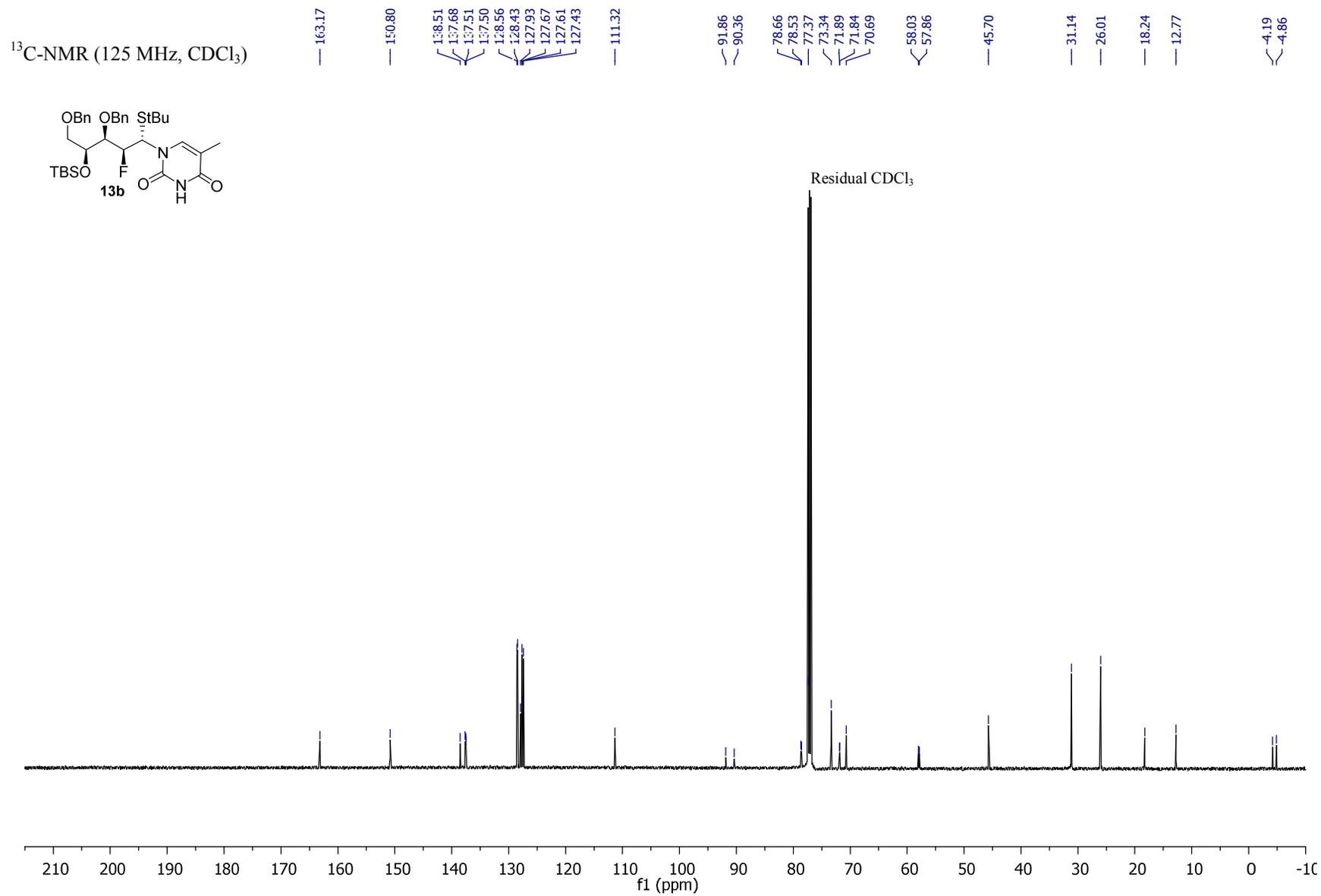


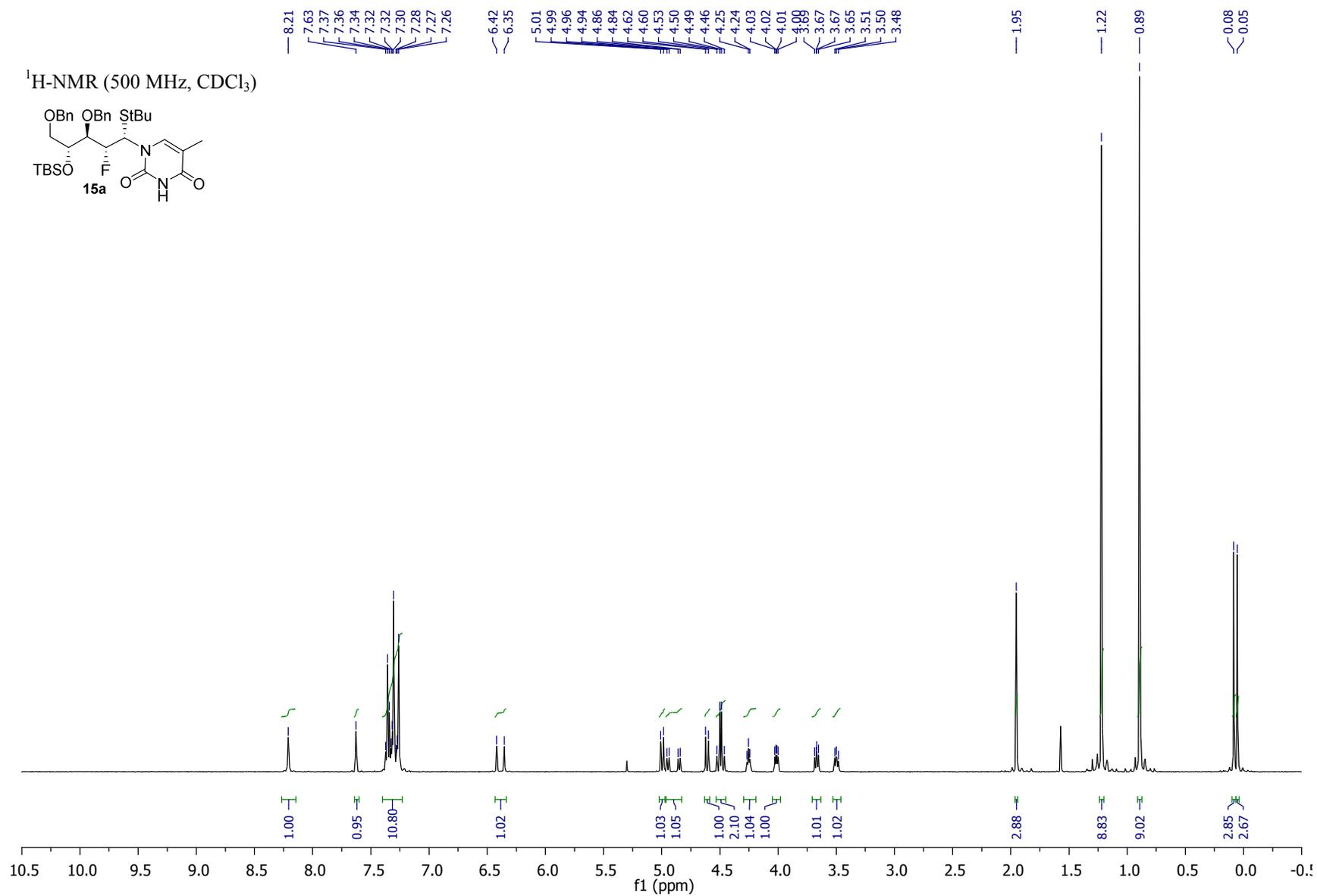
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

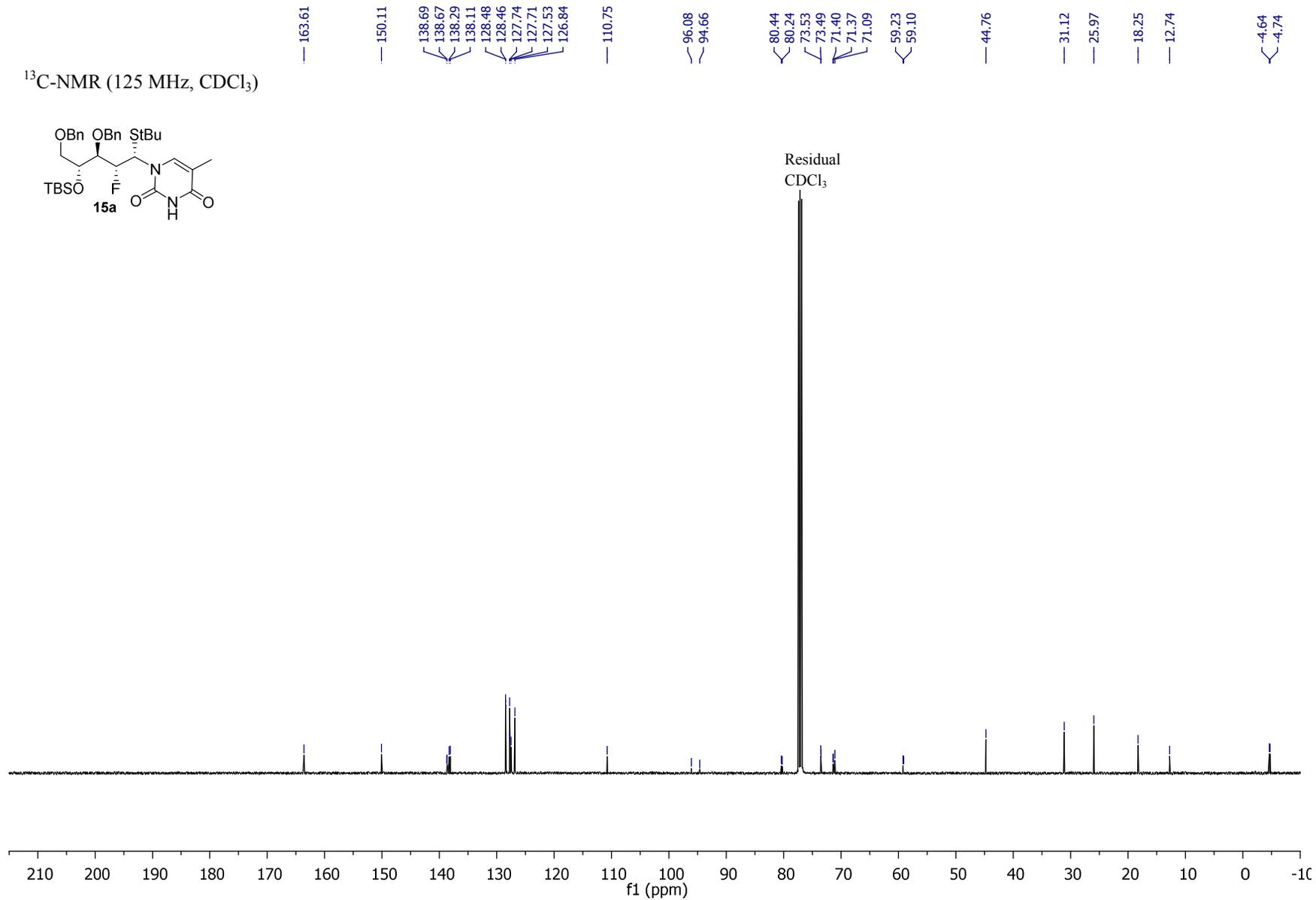
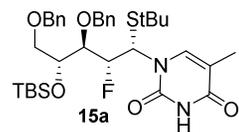


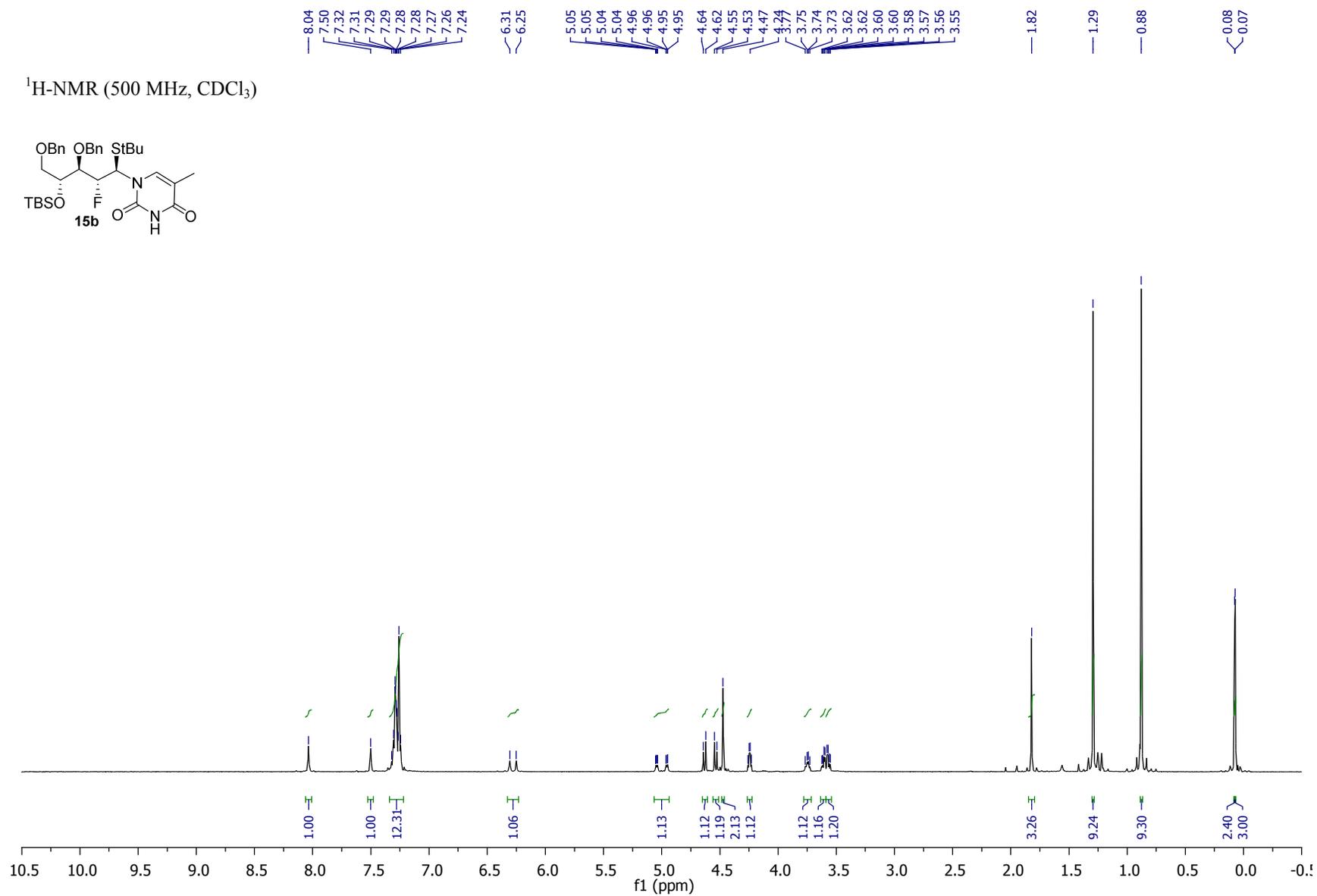
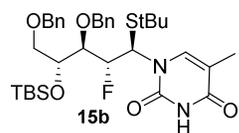


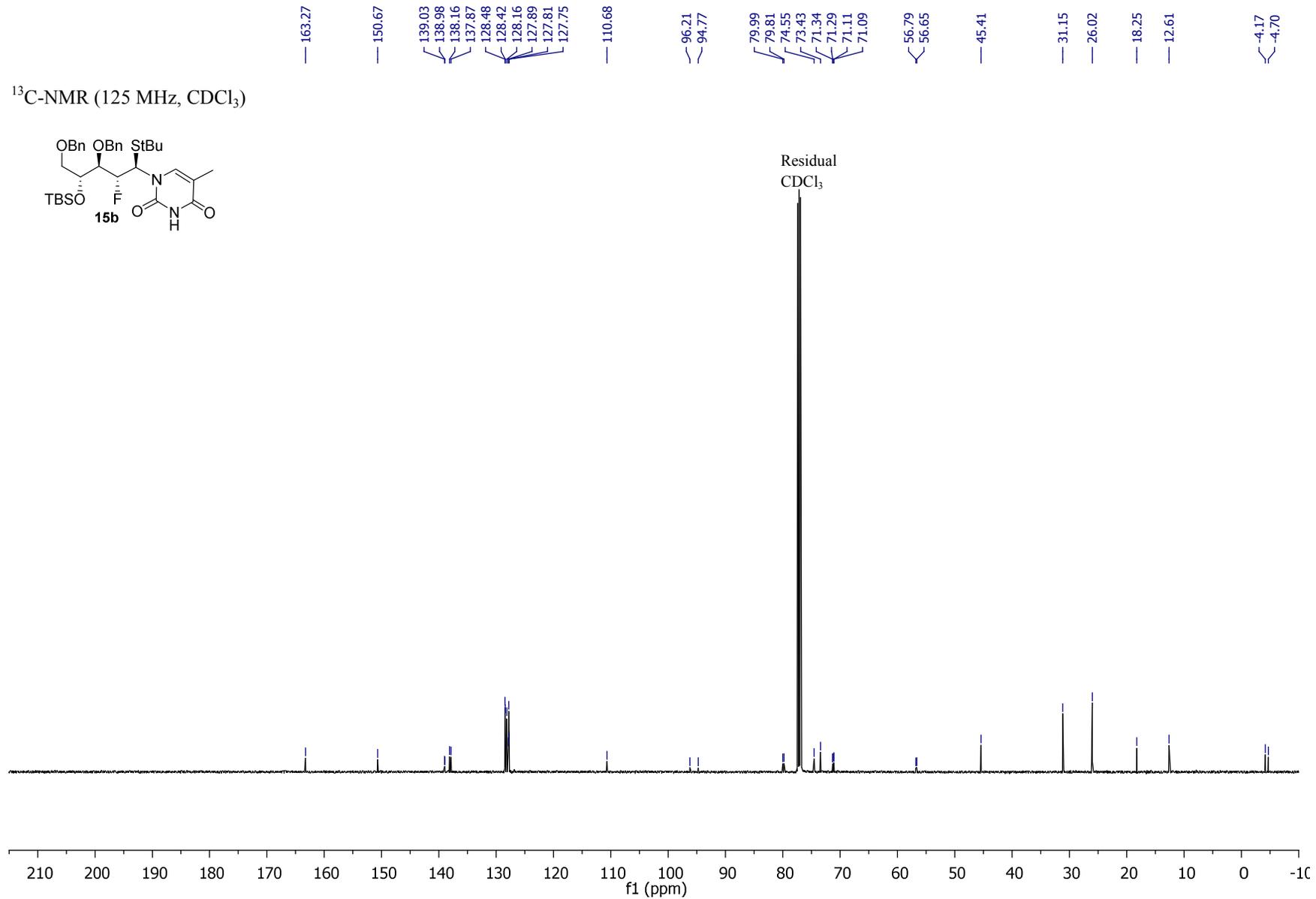


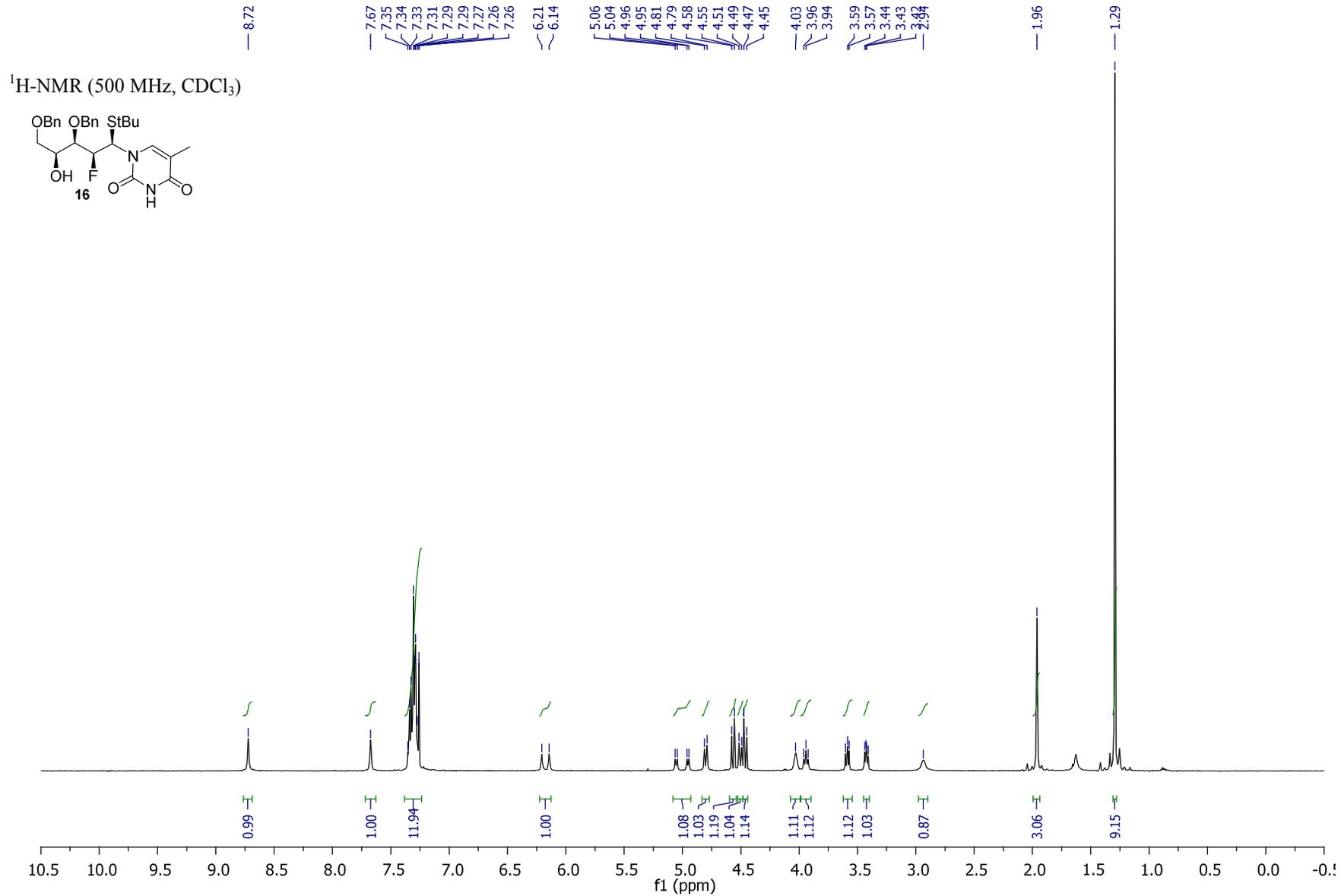


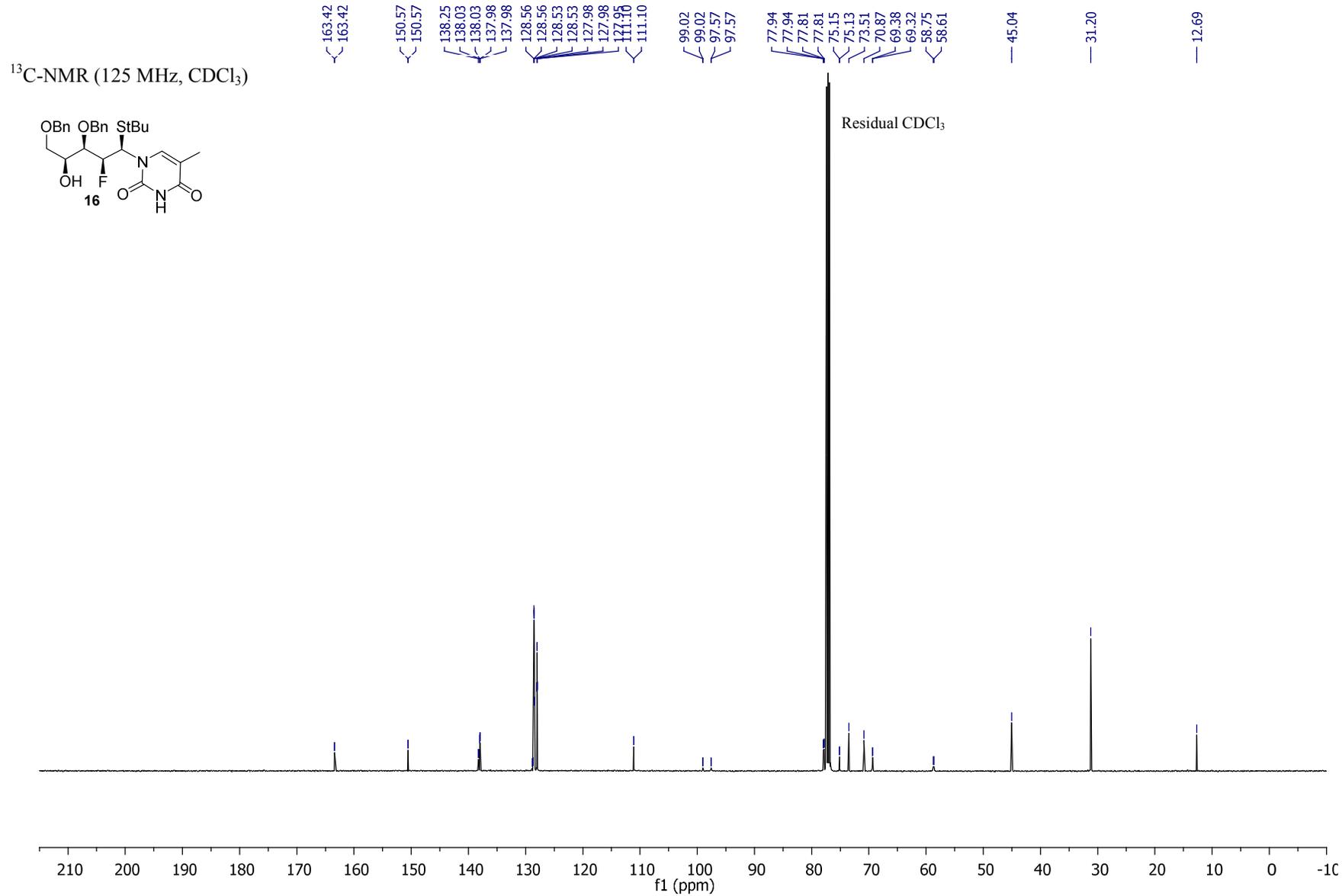


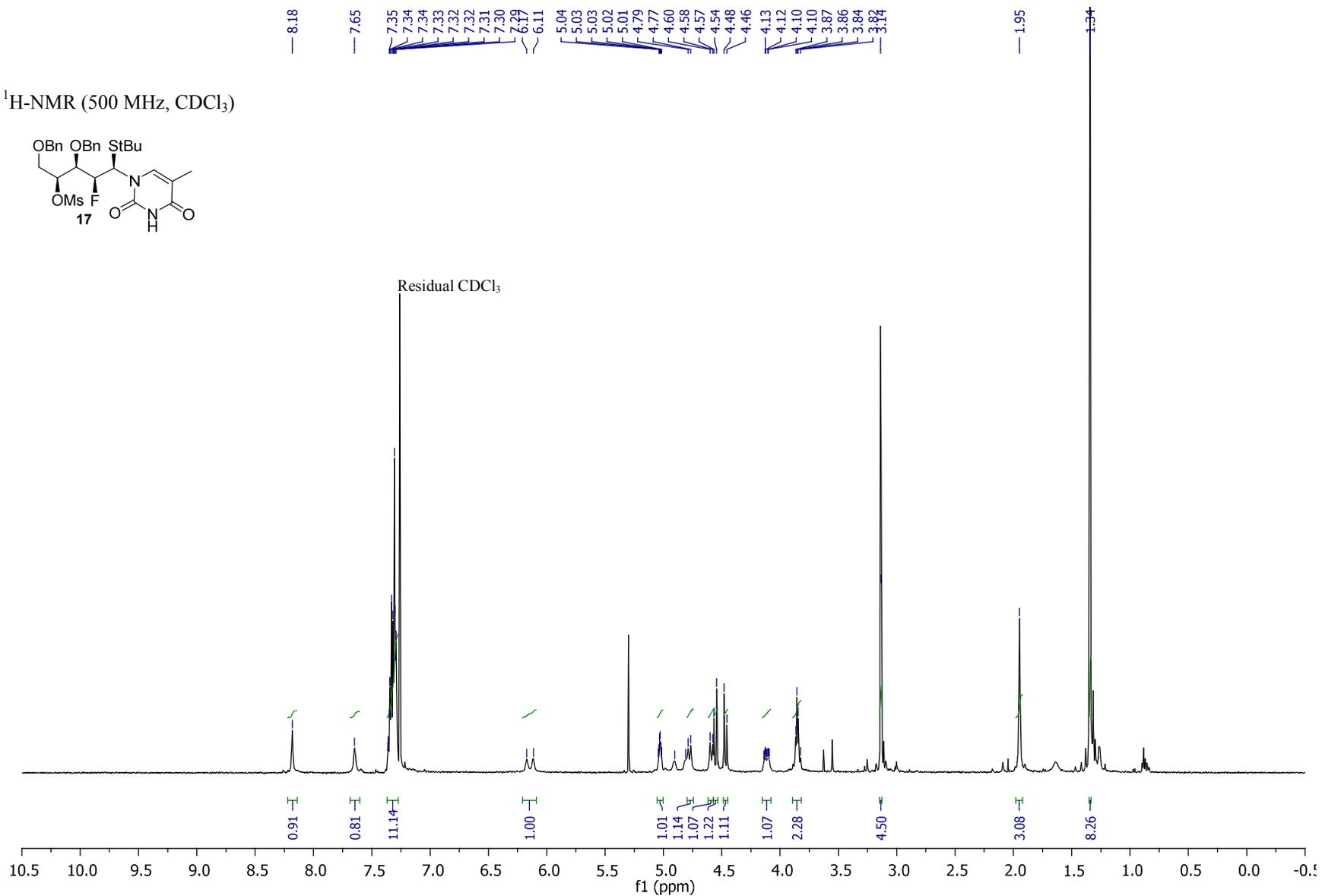
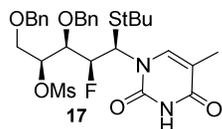
$^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ )

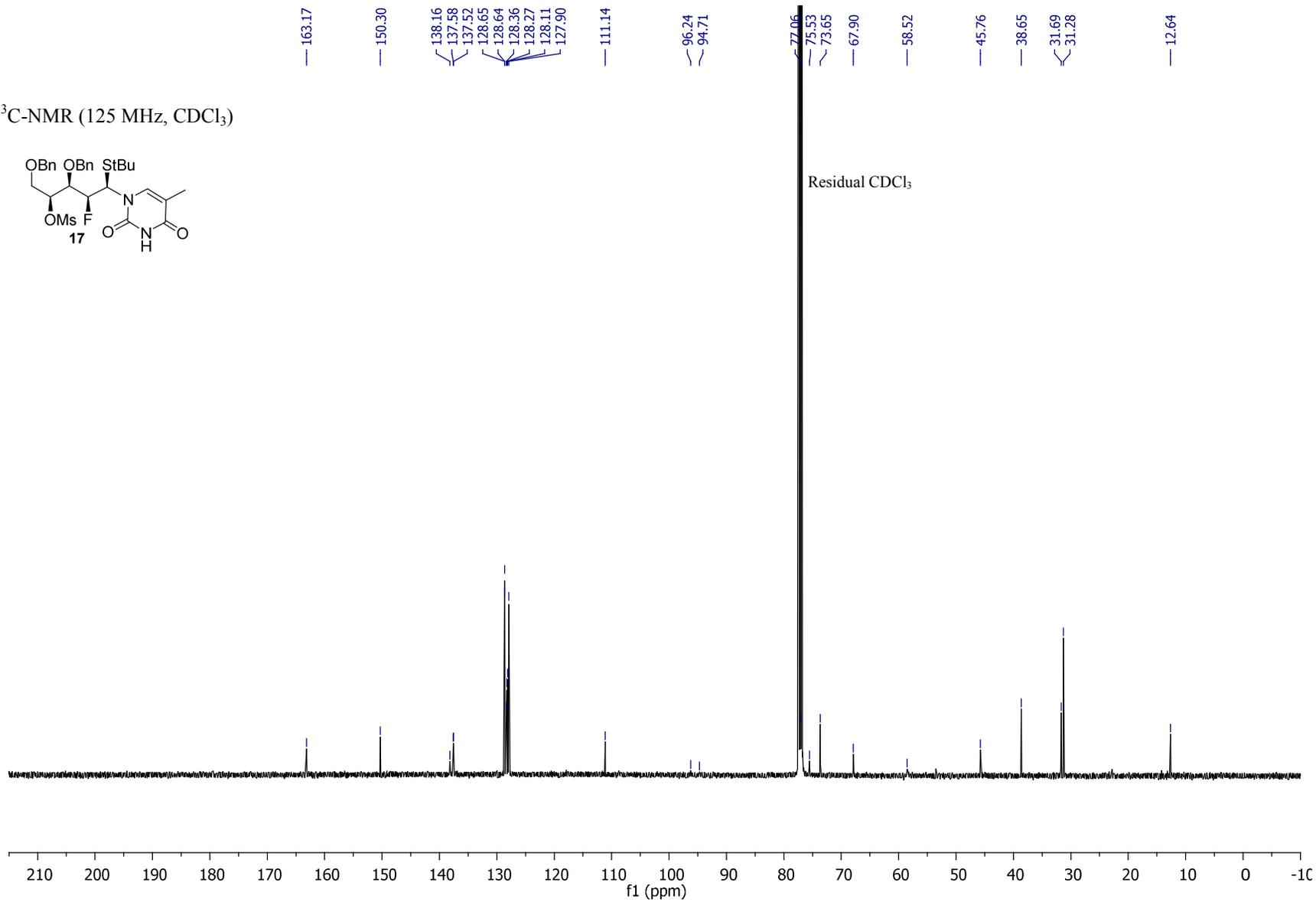
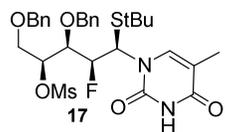
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

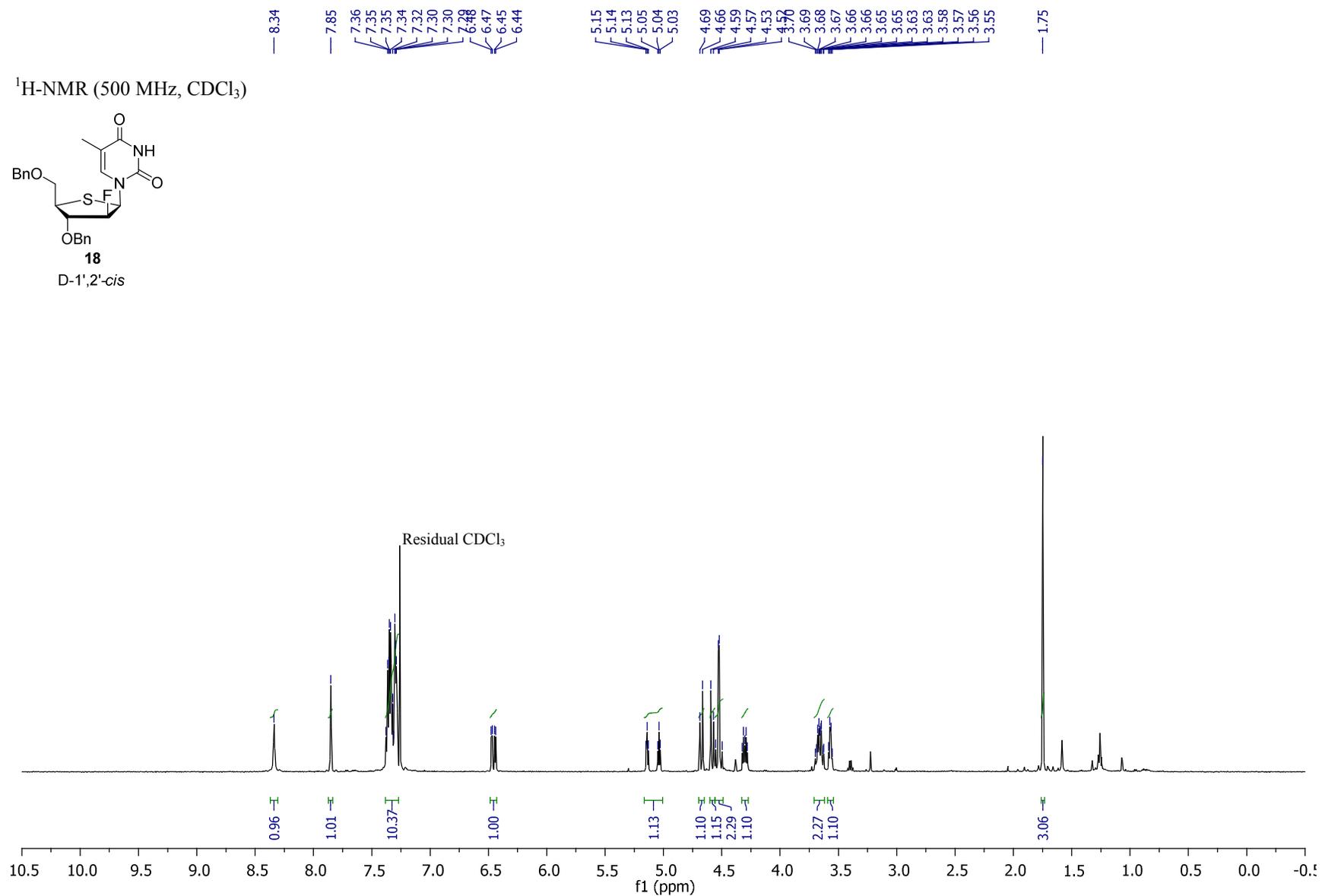


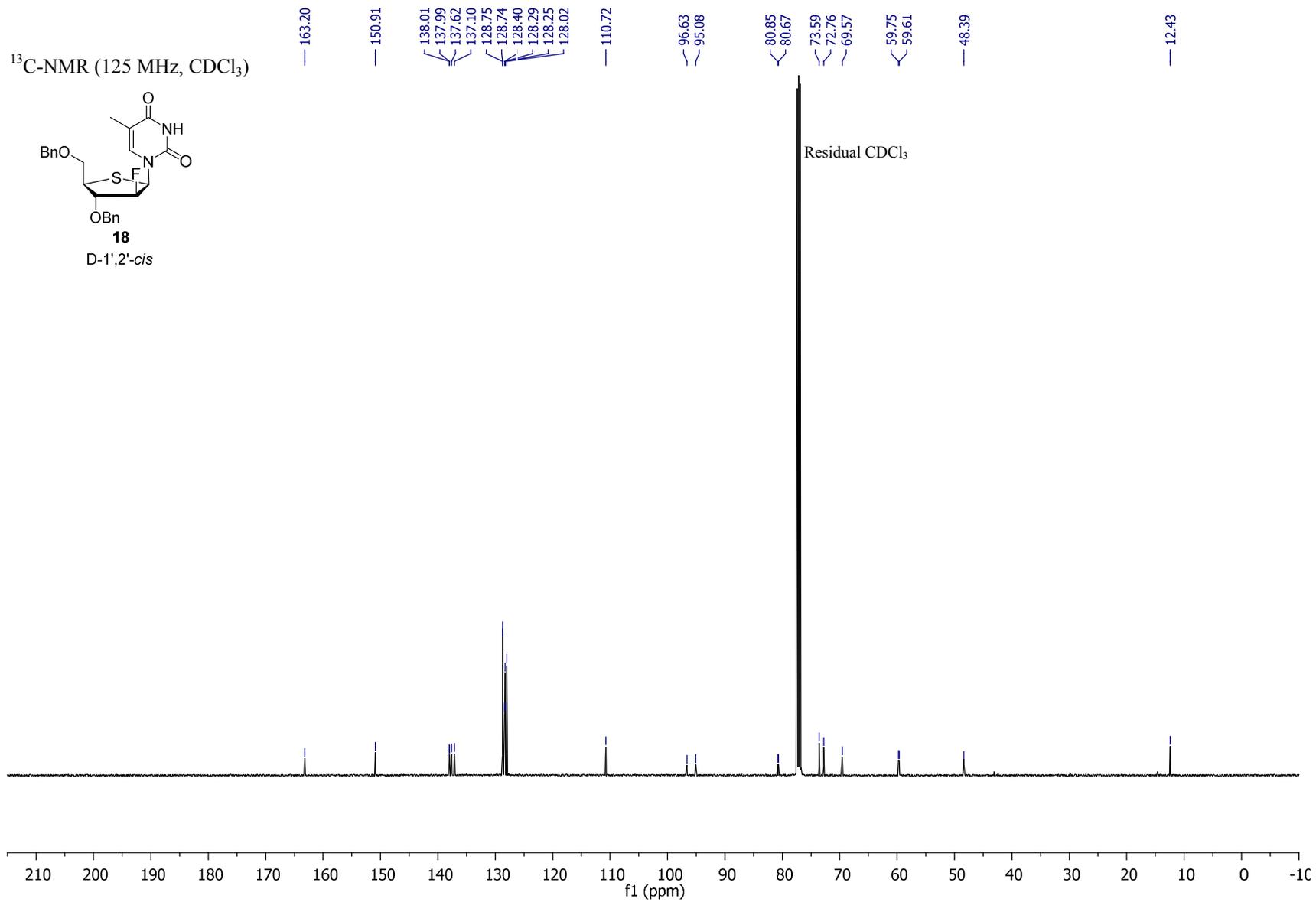


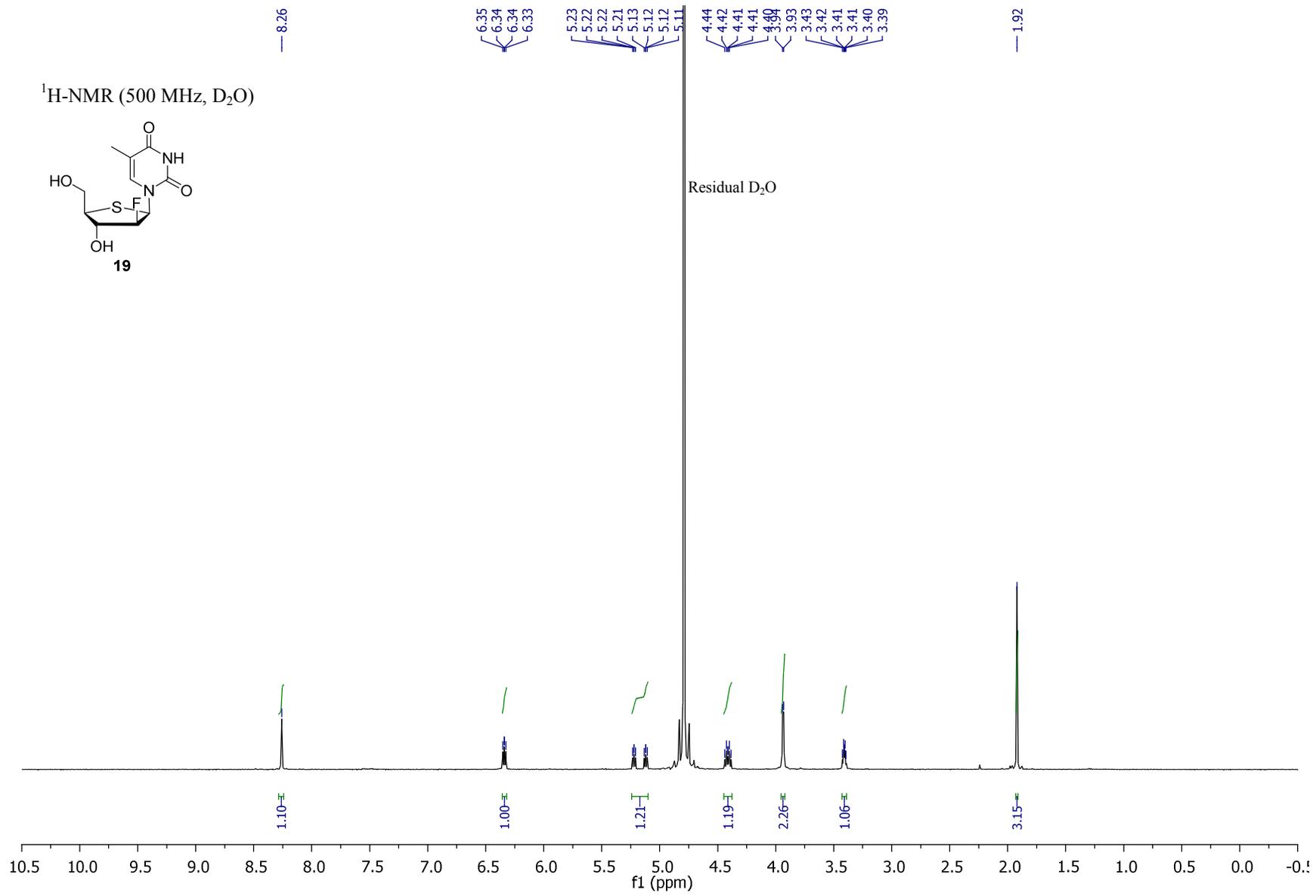


$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

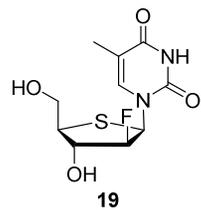
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )



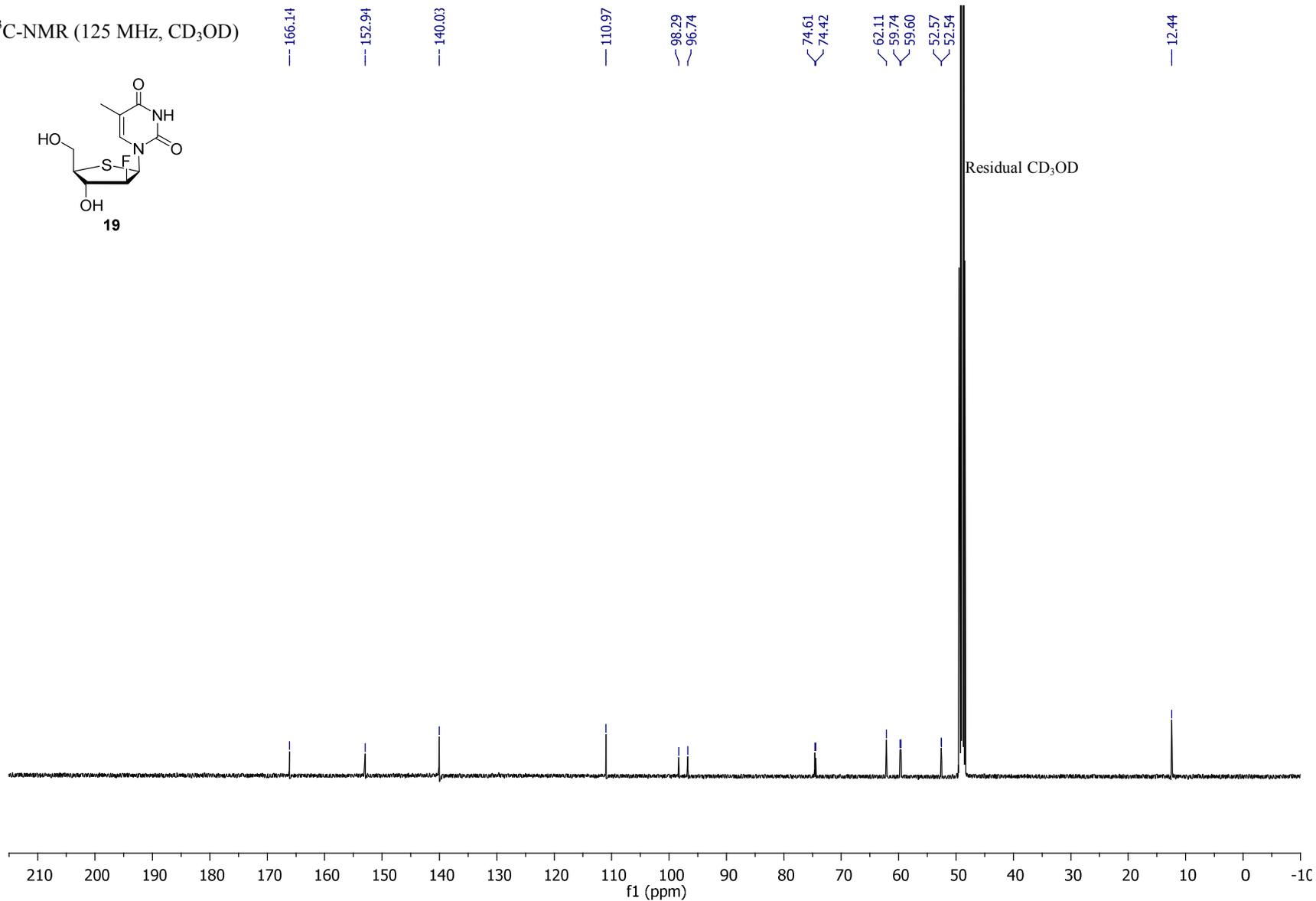


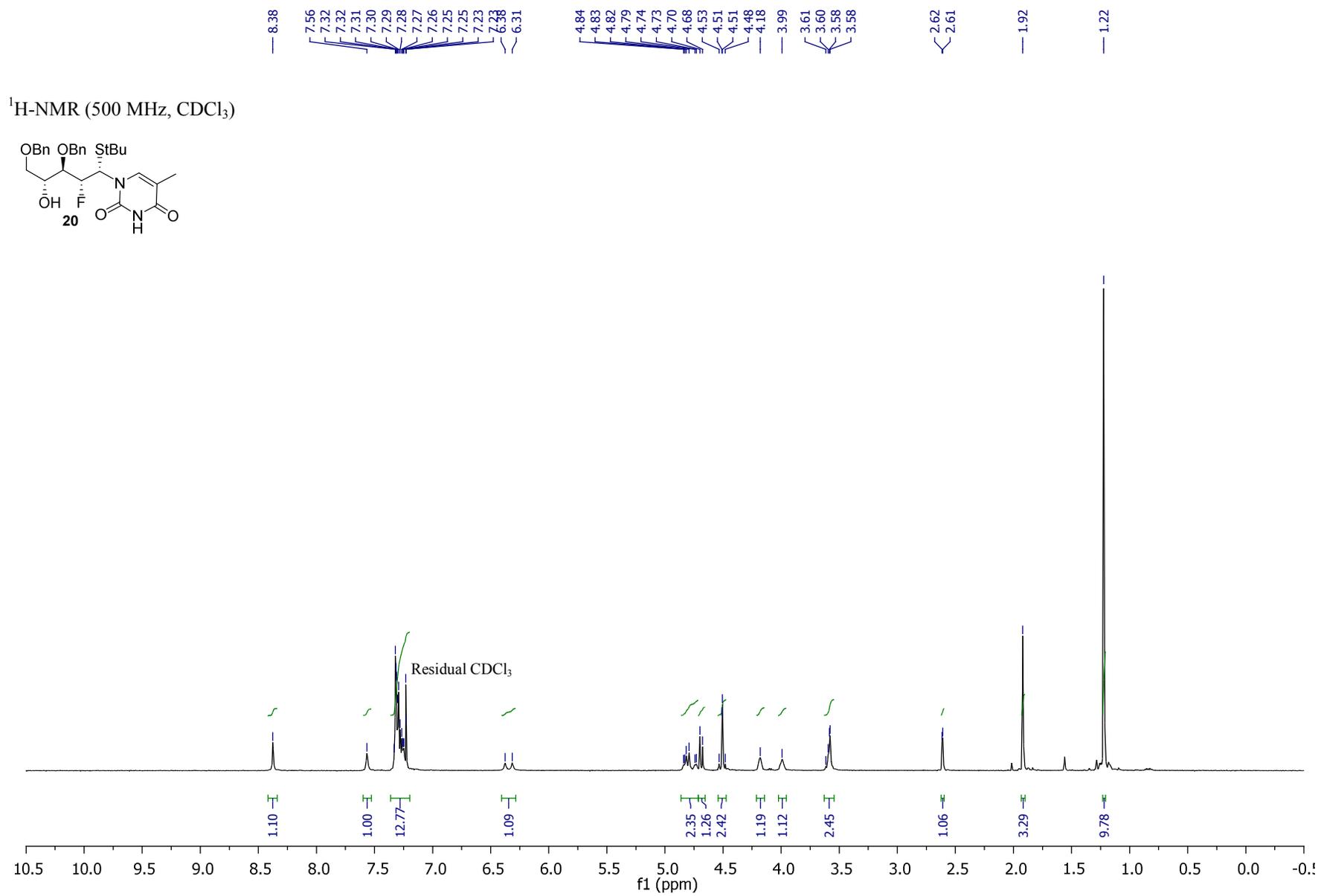


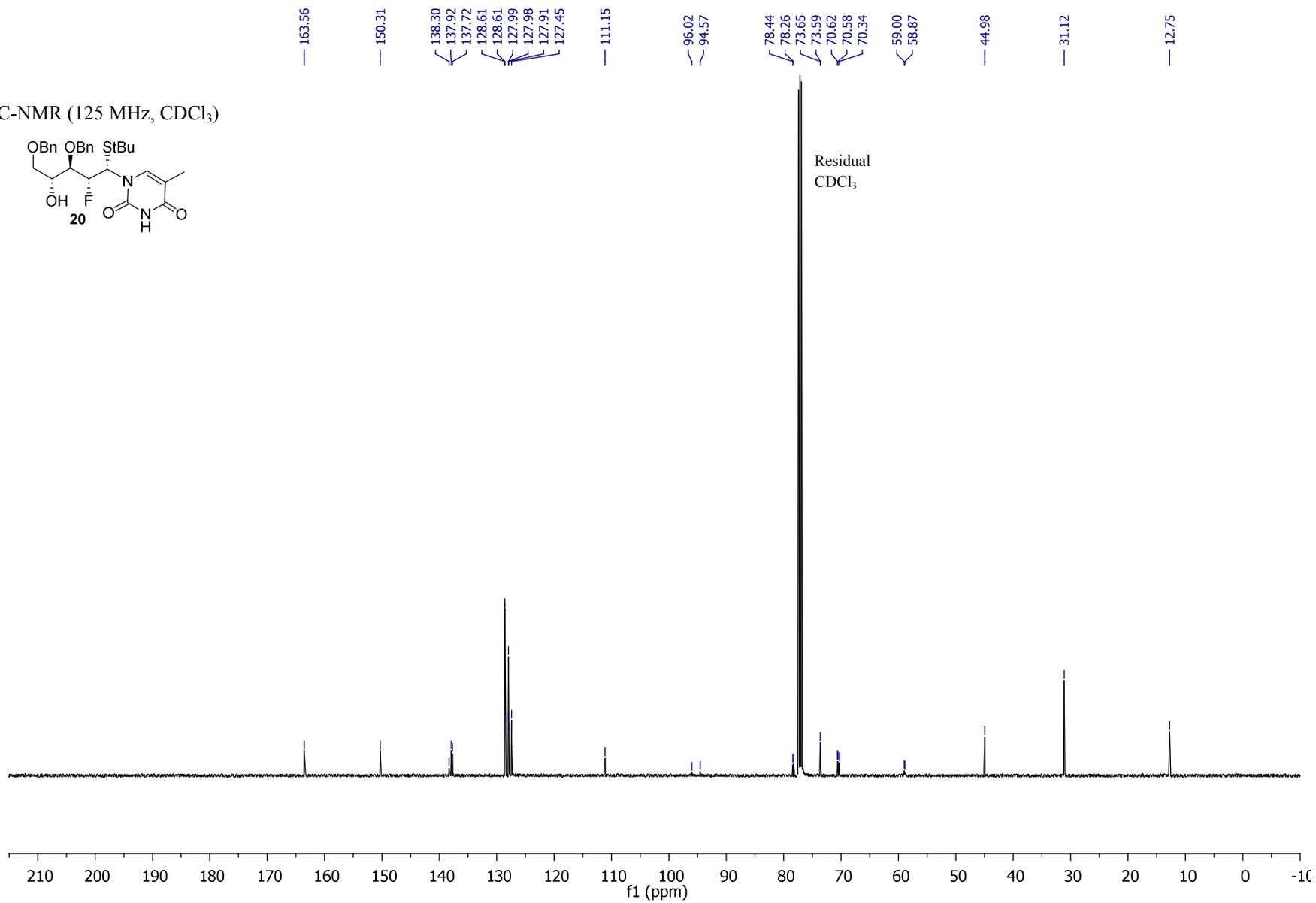
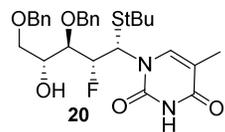
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CD}_3\text{OD}$ )

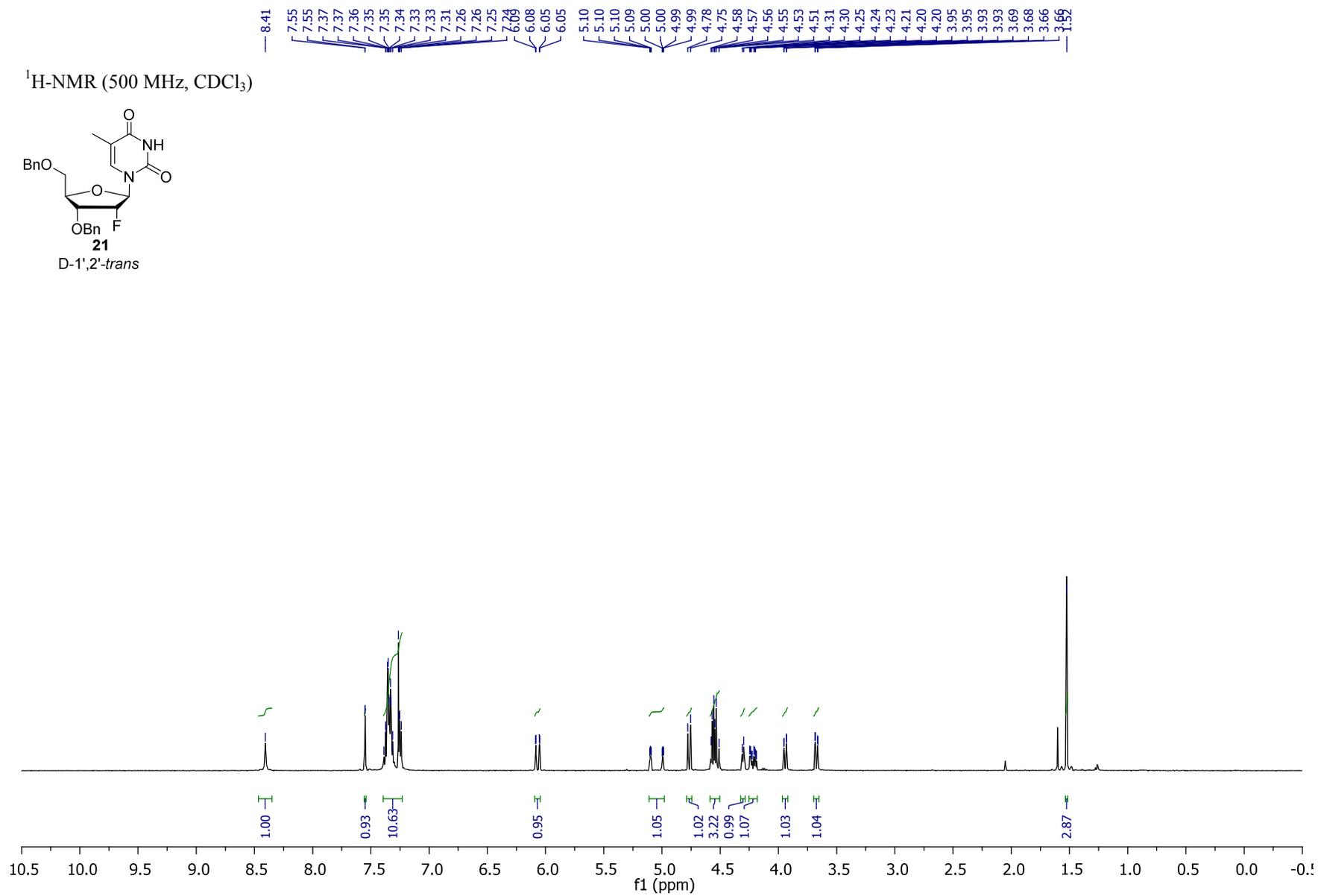
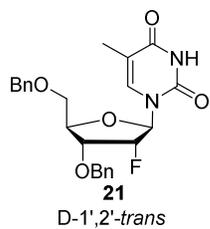


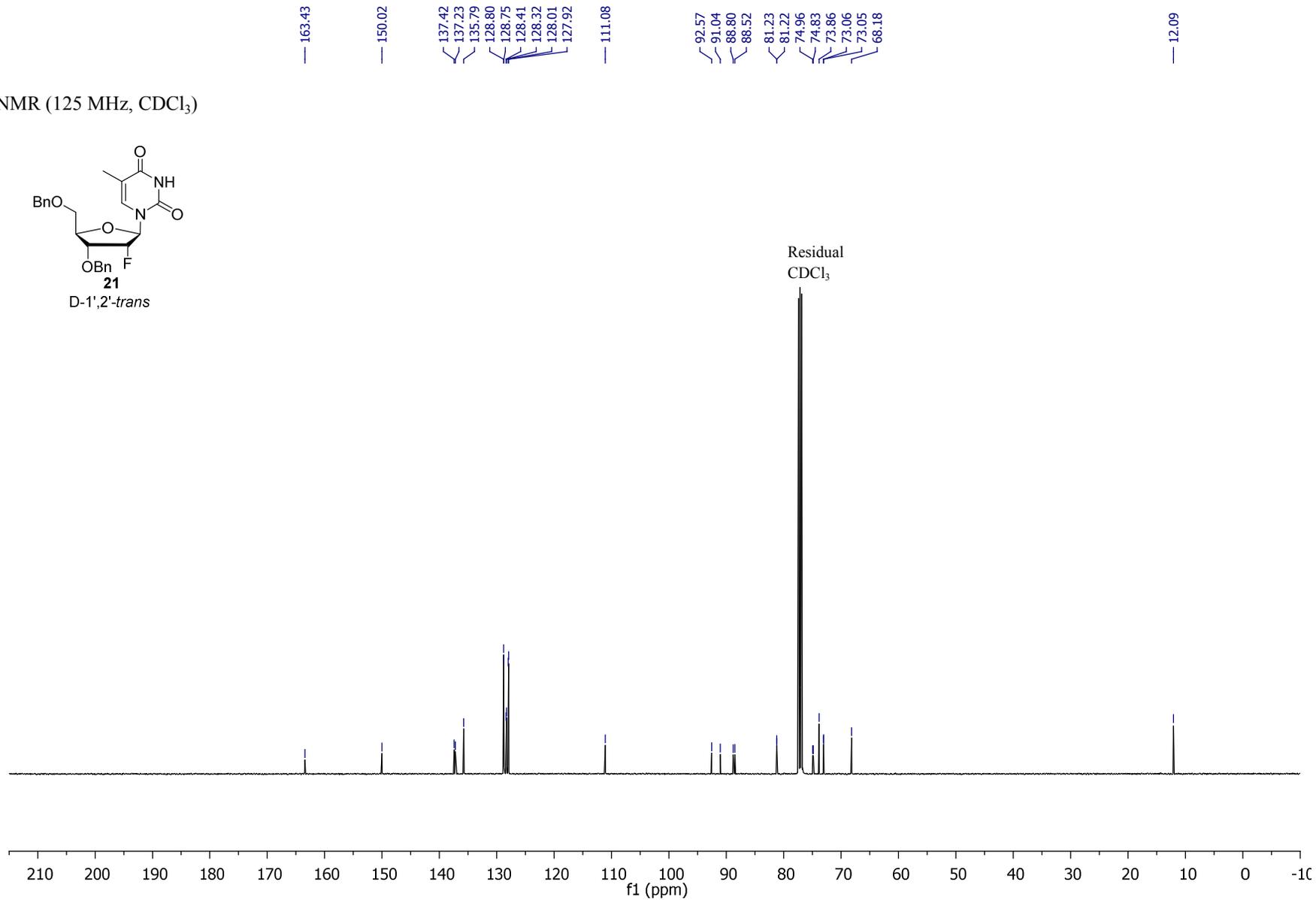
--- 166.14      --- 152.94      --- 140.03      --- 110.97      ~ 98.29      ~ 96.74      < 74.61      < 74.42      < 62.11      < 59.74      < 59.60      < 52.57      < 52.54      --- 12.44

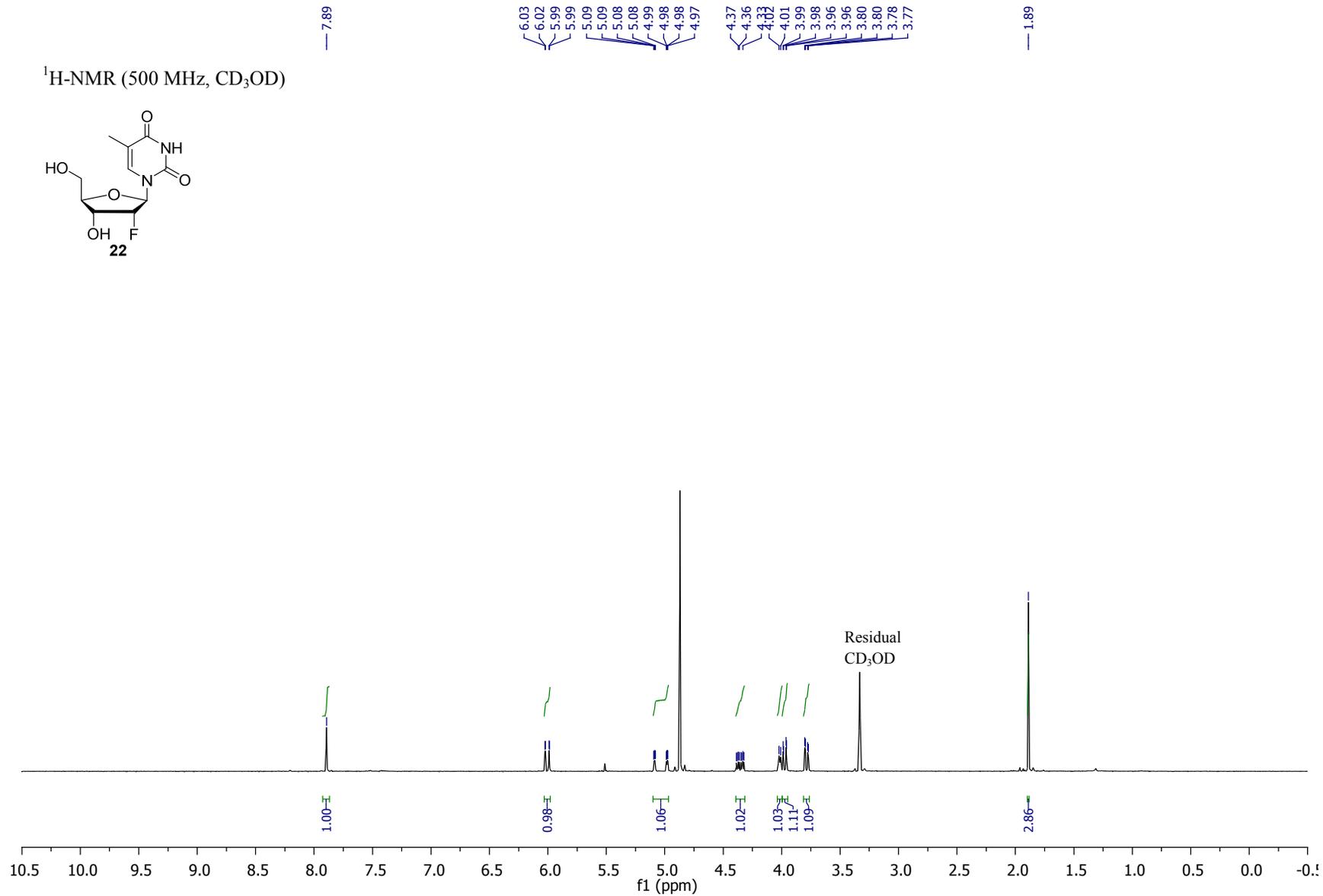
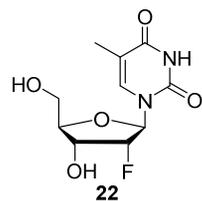


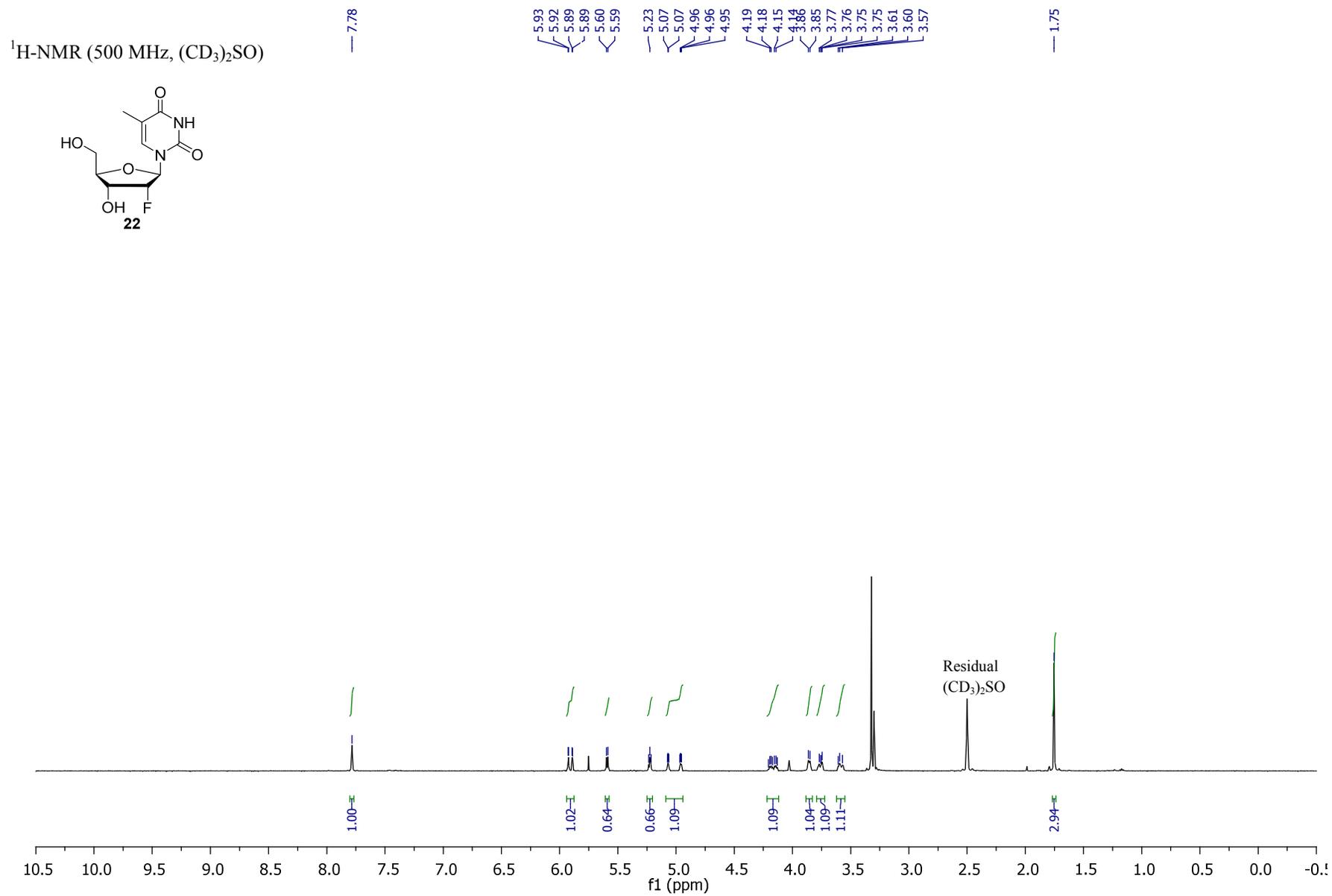


$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

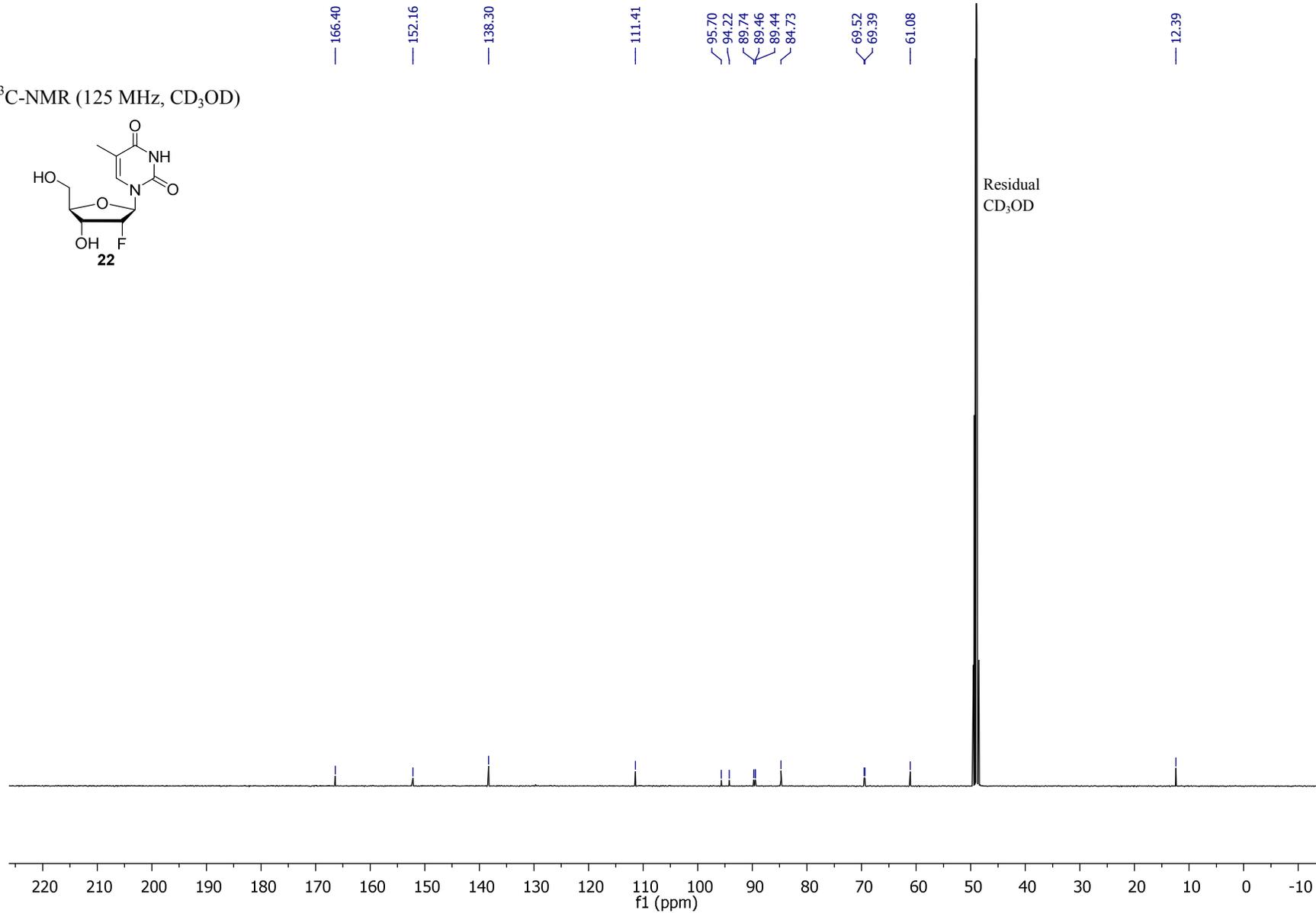
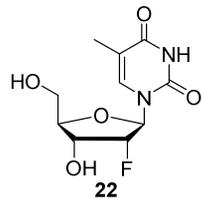
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

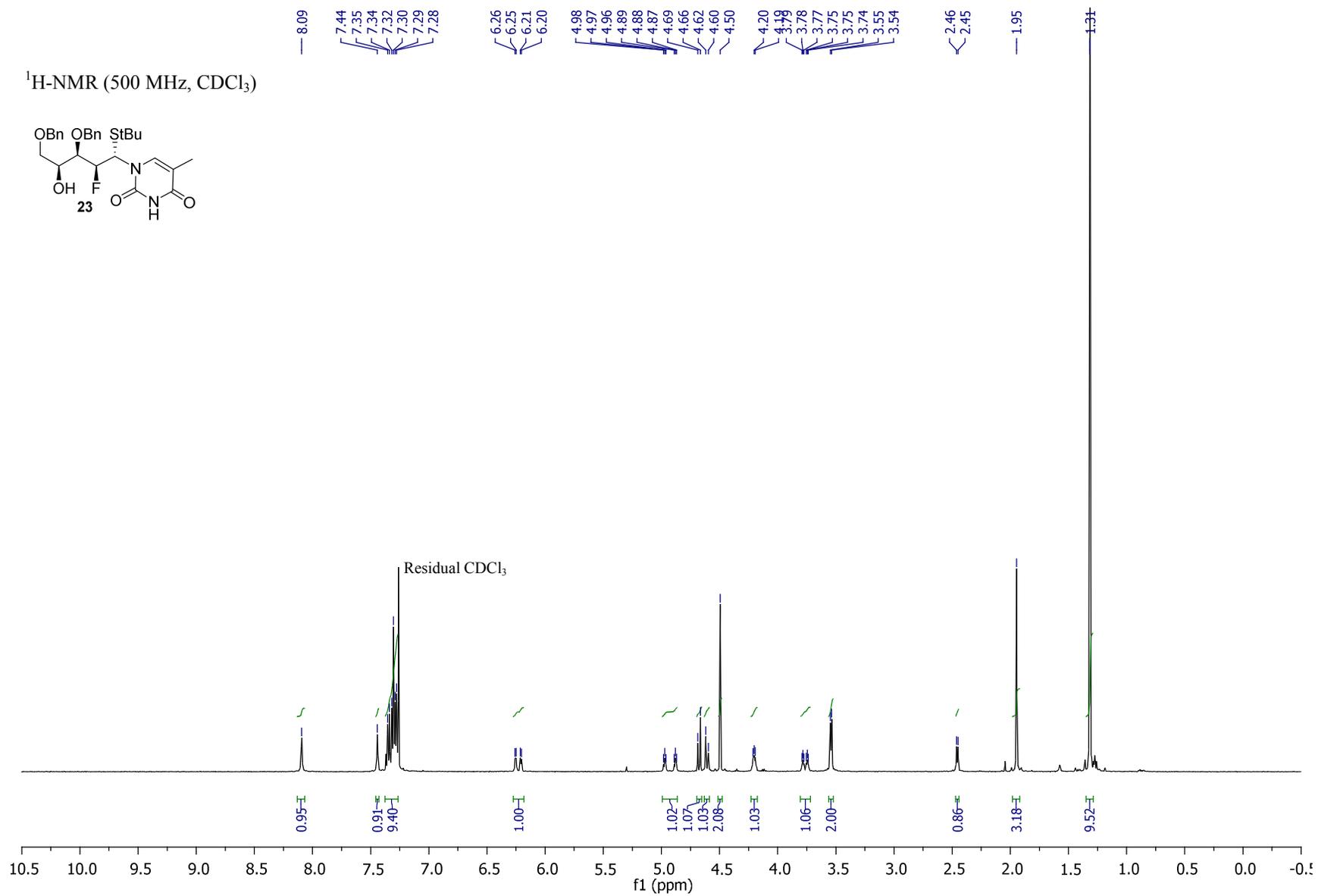
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

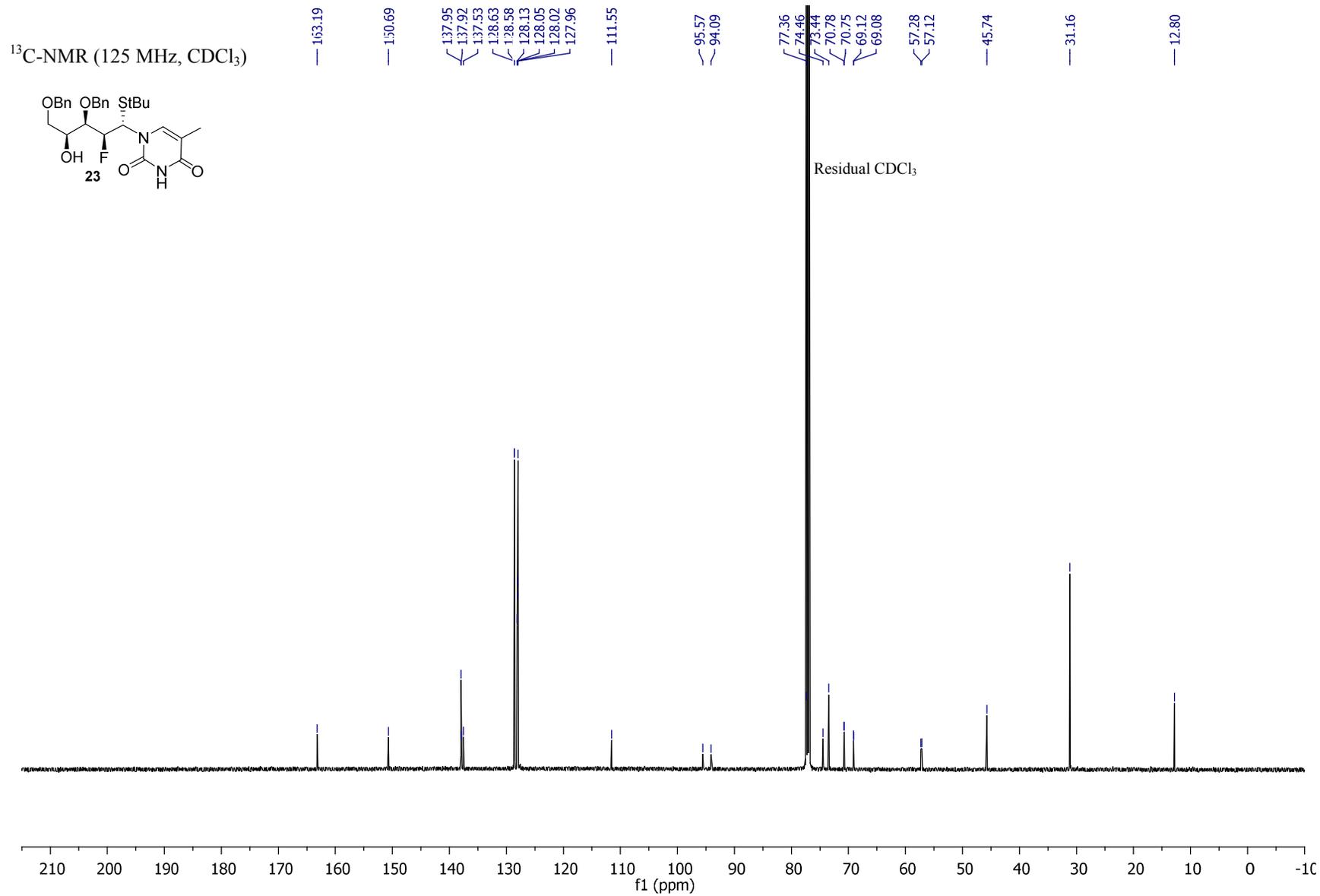
$^1\text{H-NMR}$  (500 MHz,  $\text{CD}_3\text{OD}$ )

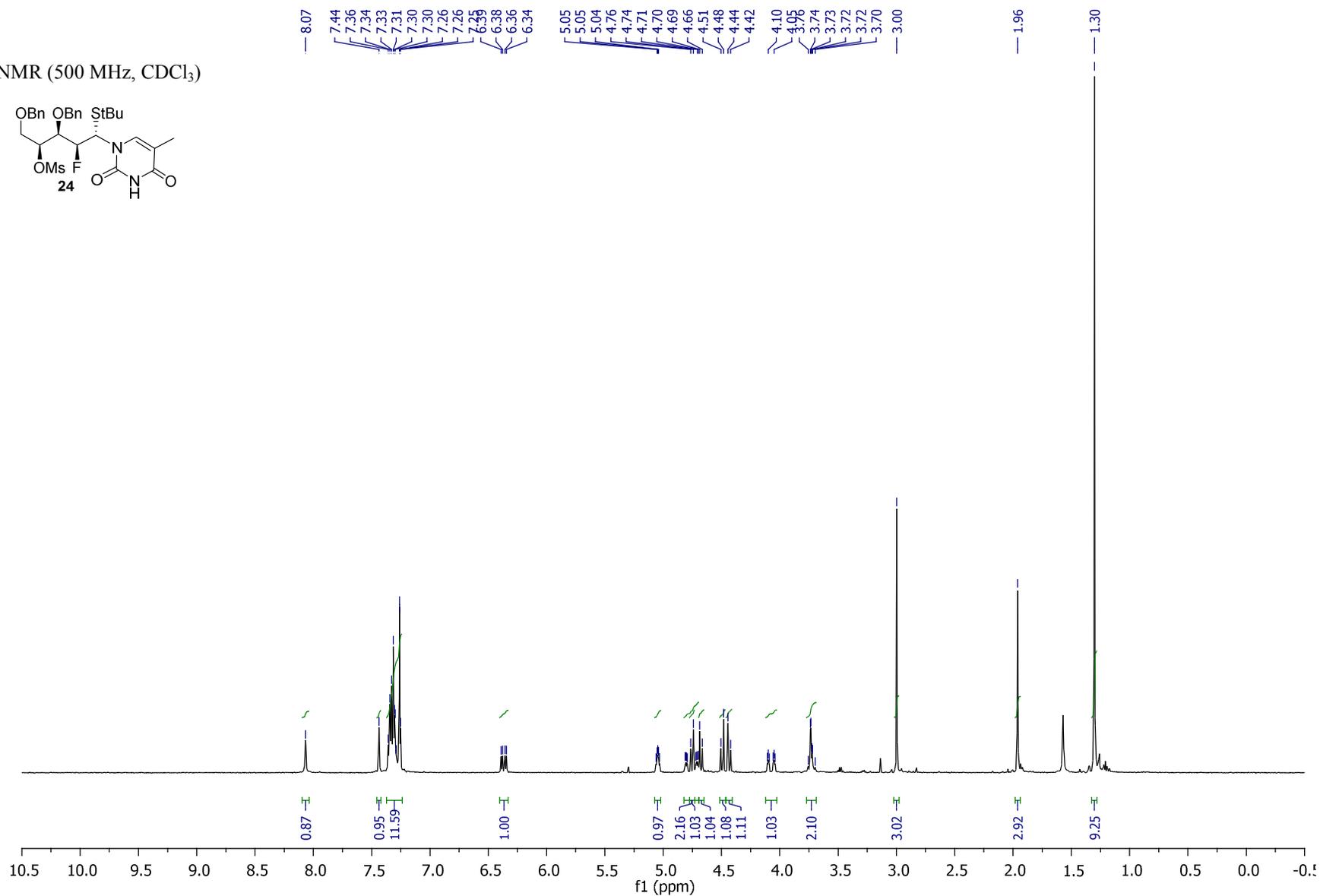
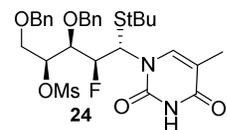


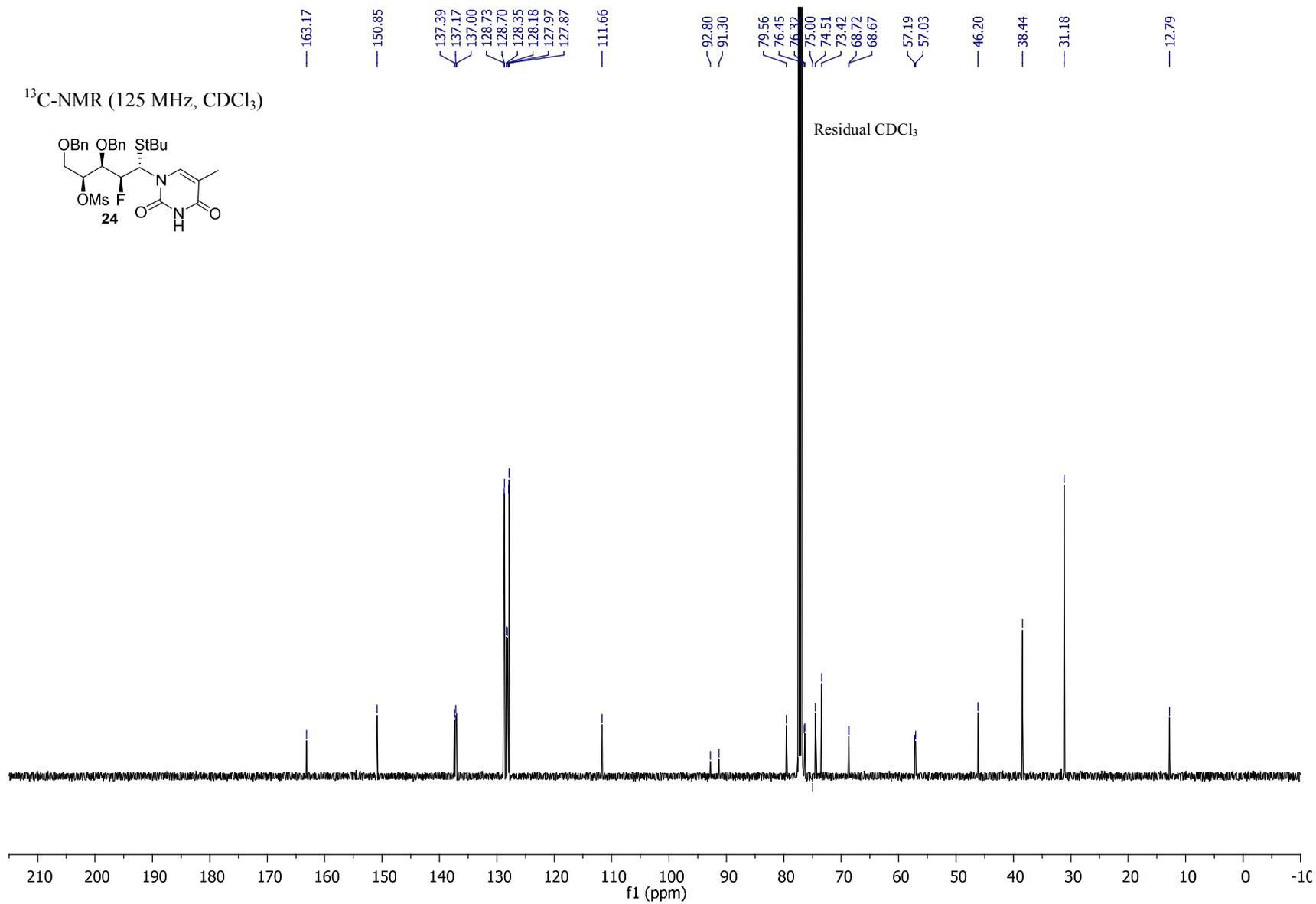
<sup>13</sup>C-NMR (125 MHz, CD<sub>3</sub>OD)

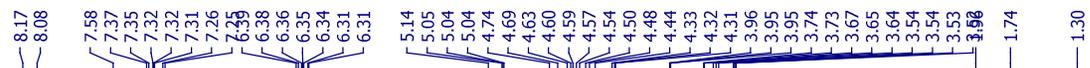
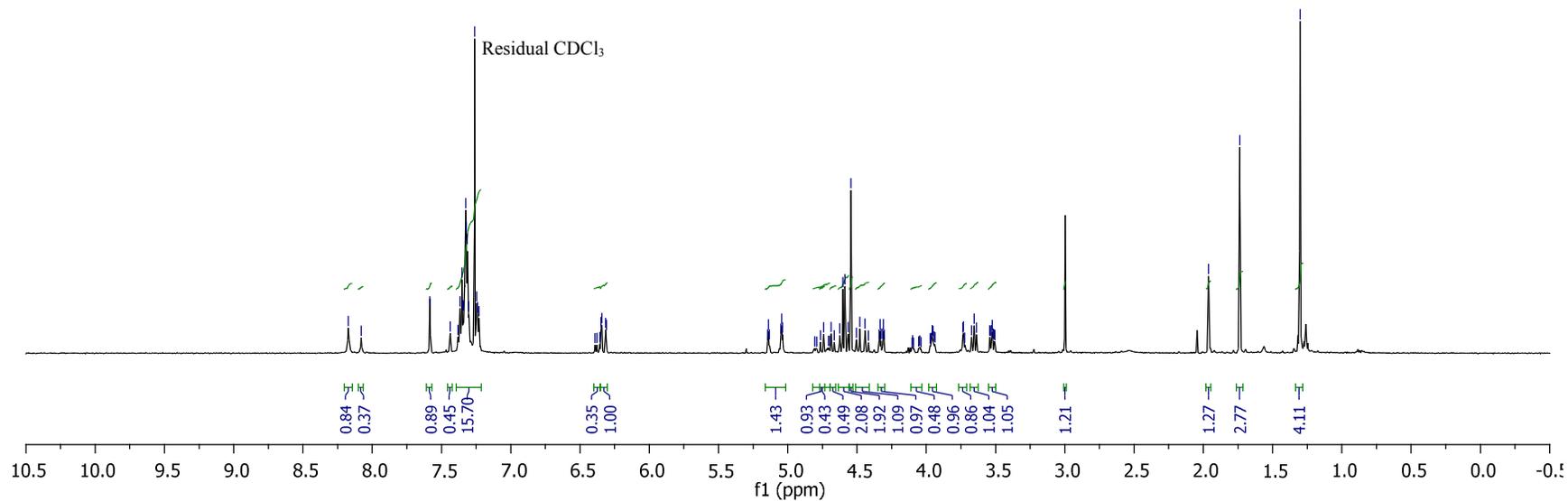
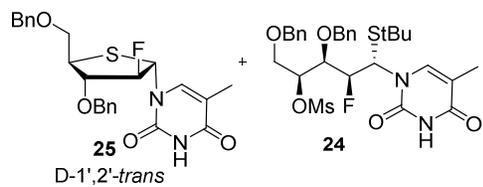


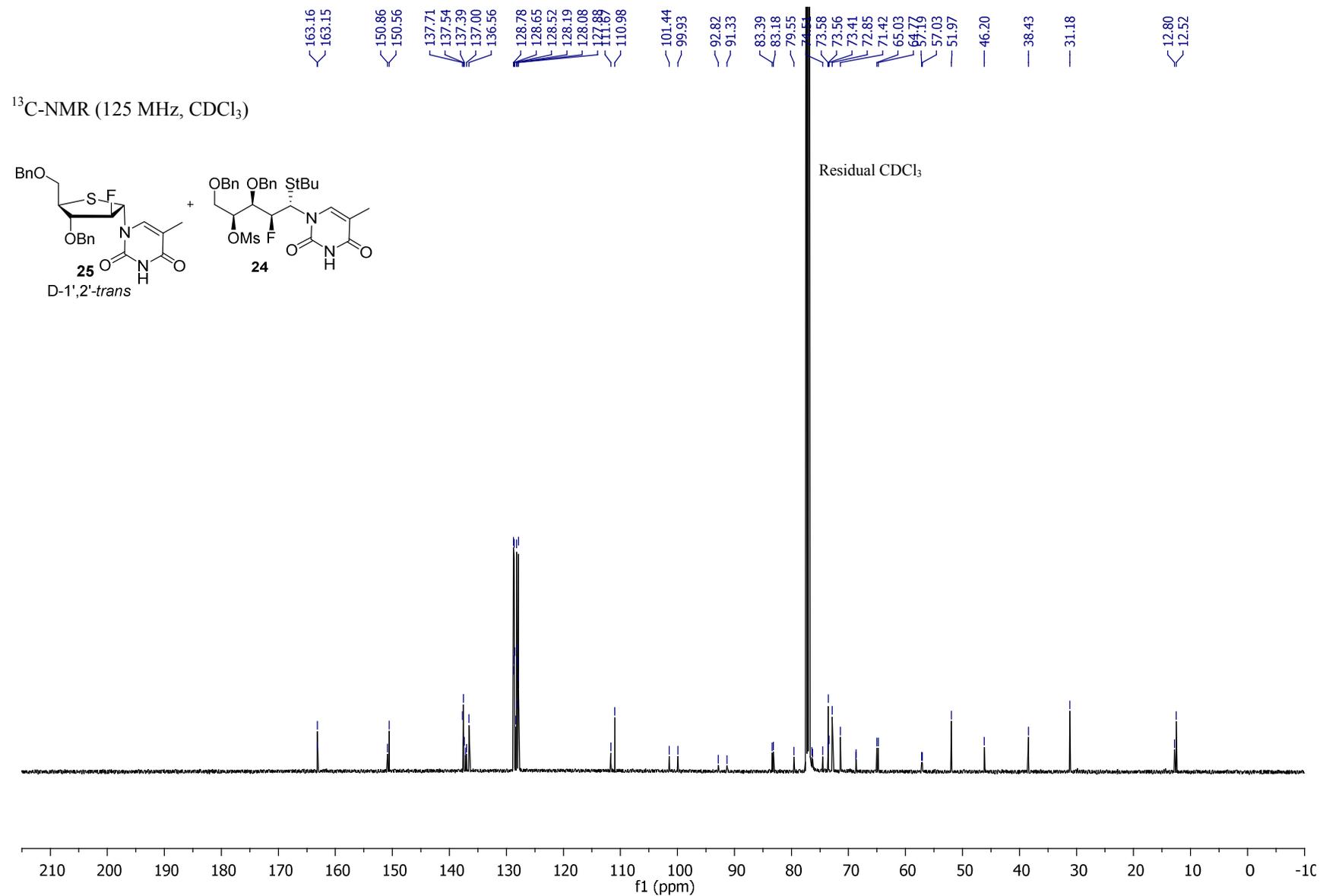


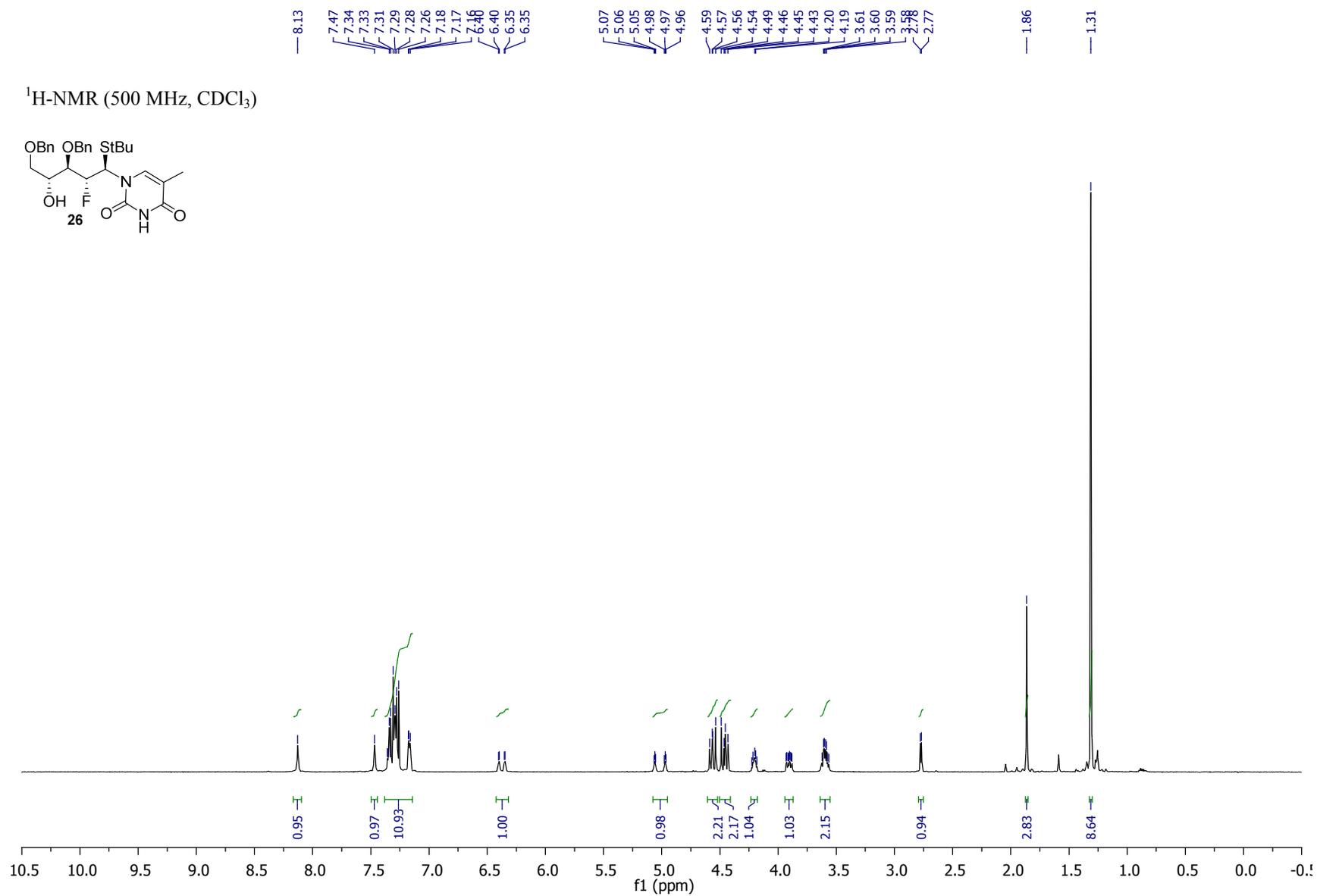


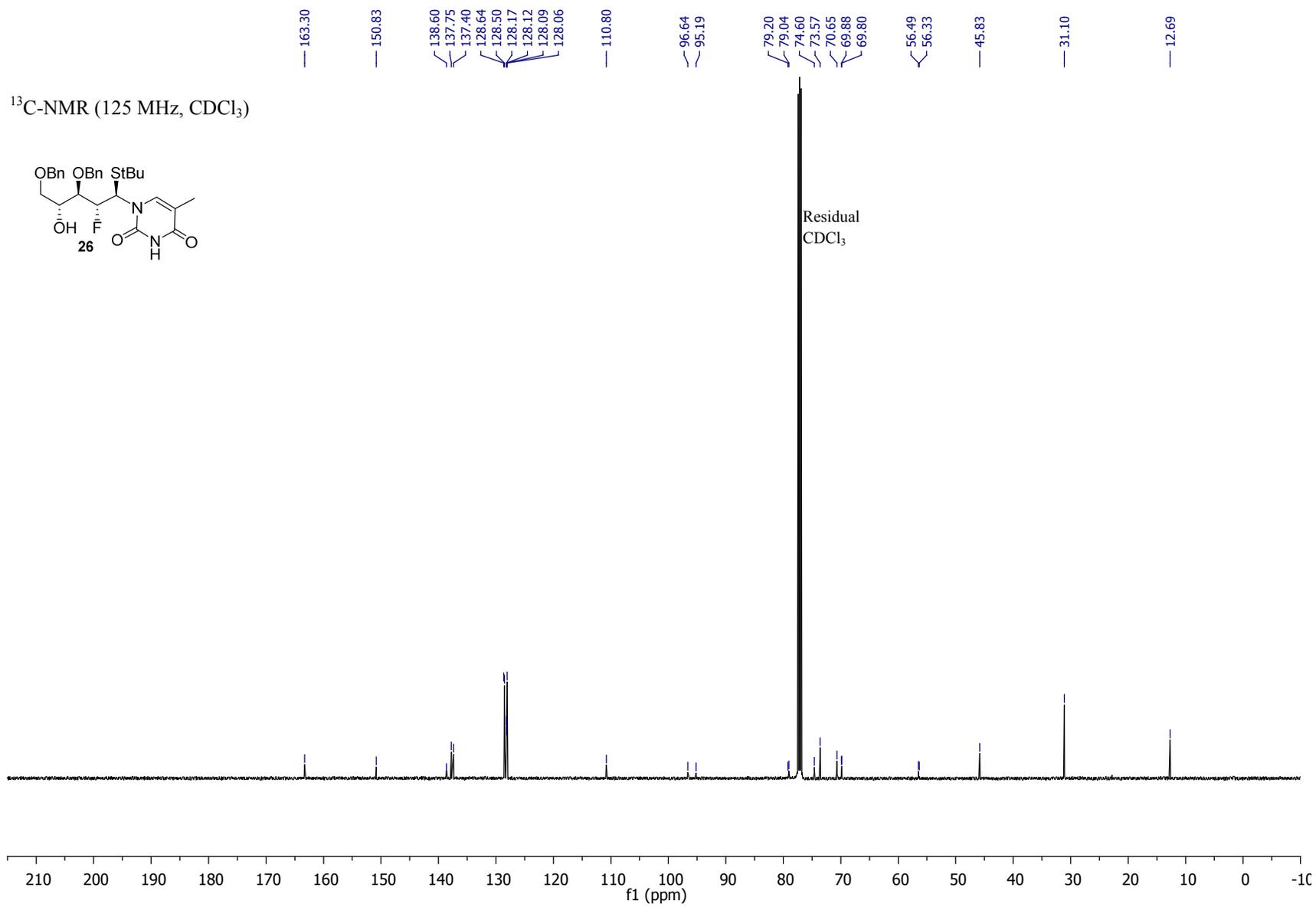
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

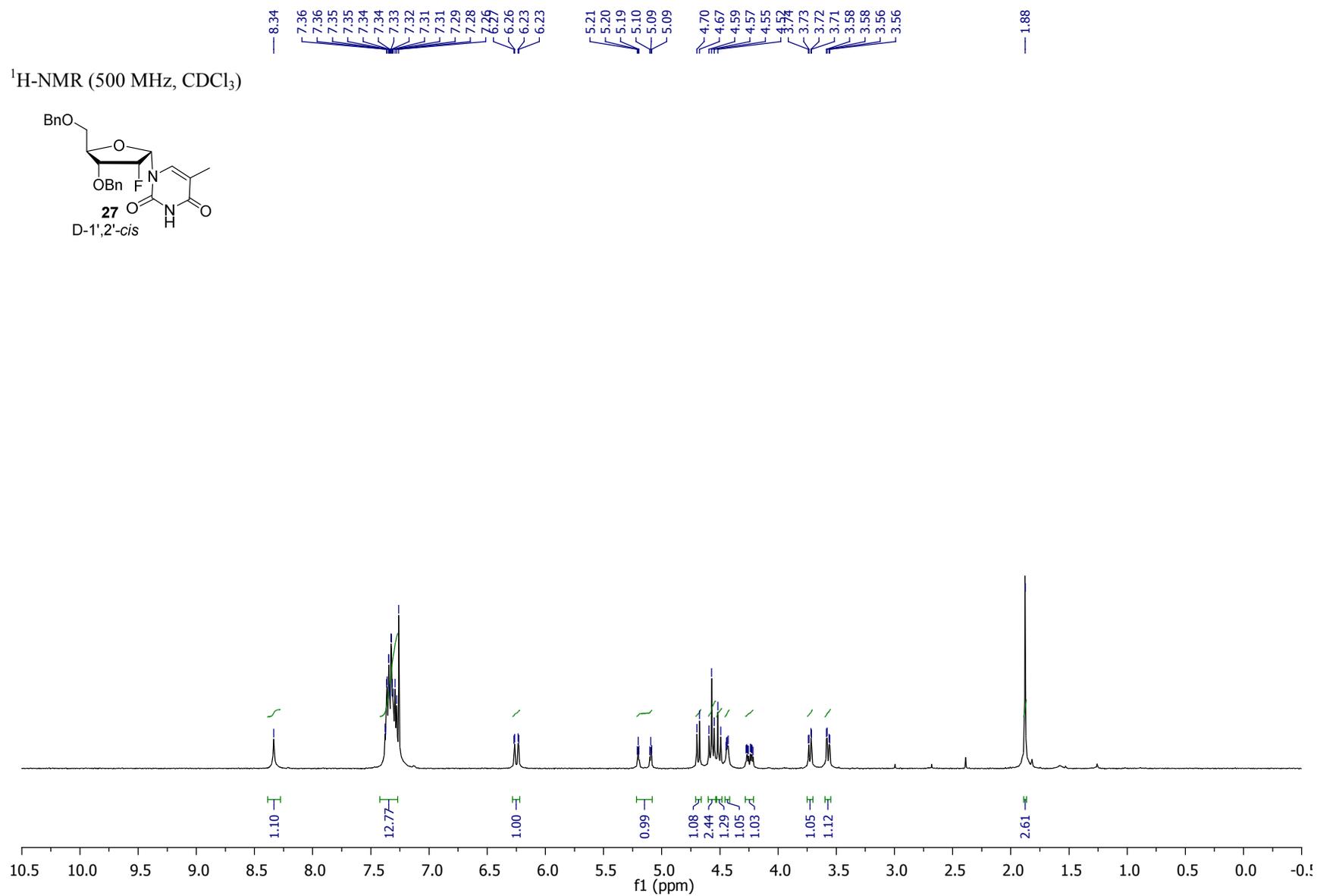
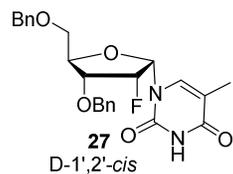


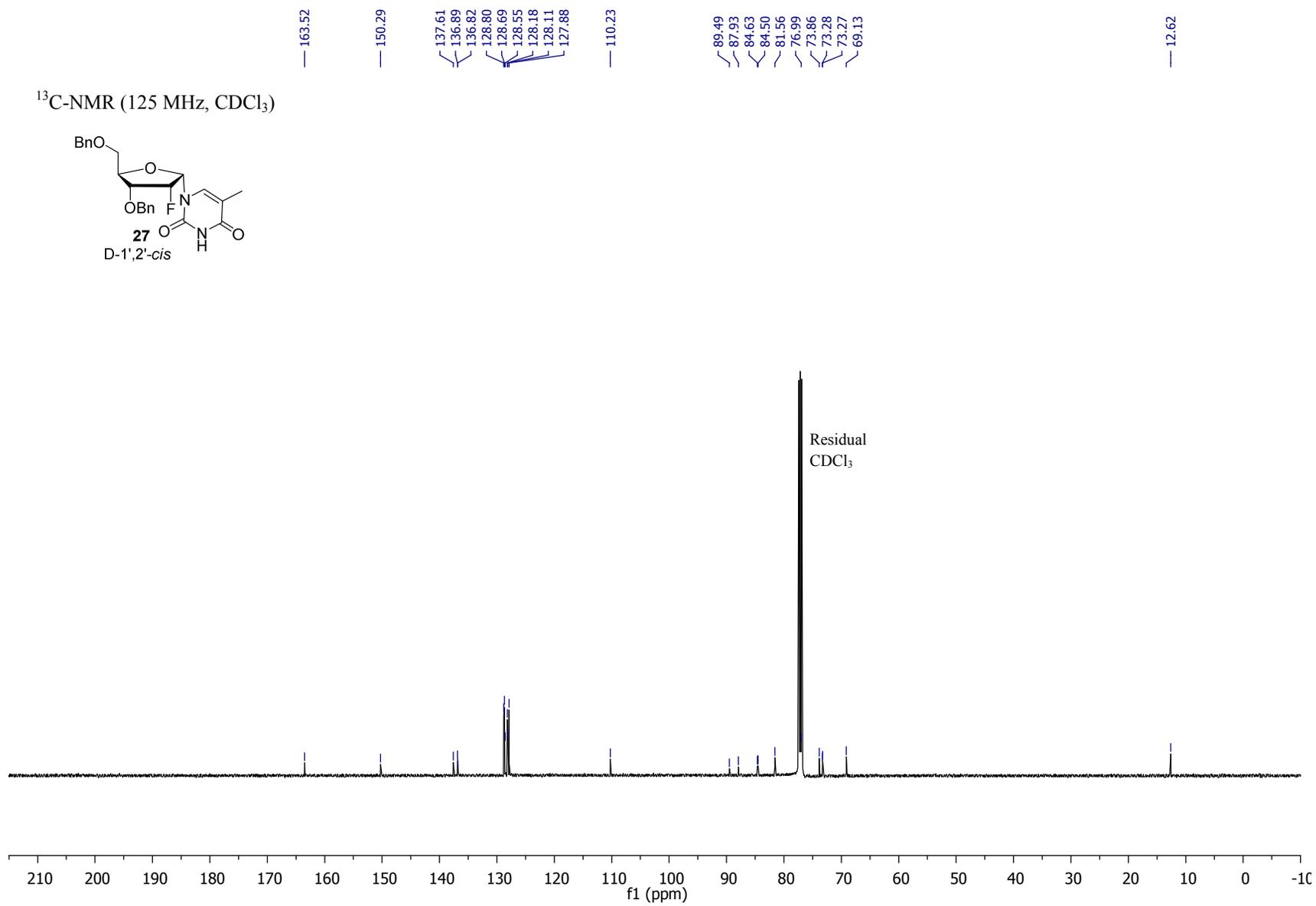
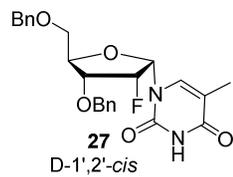
 $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



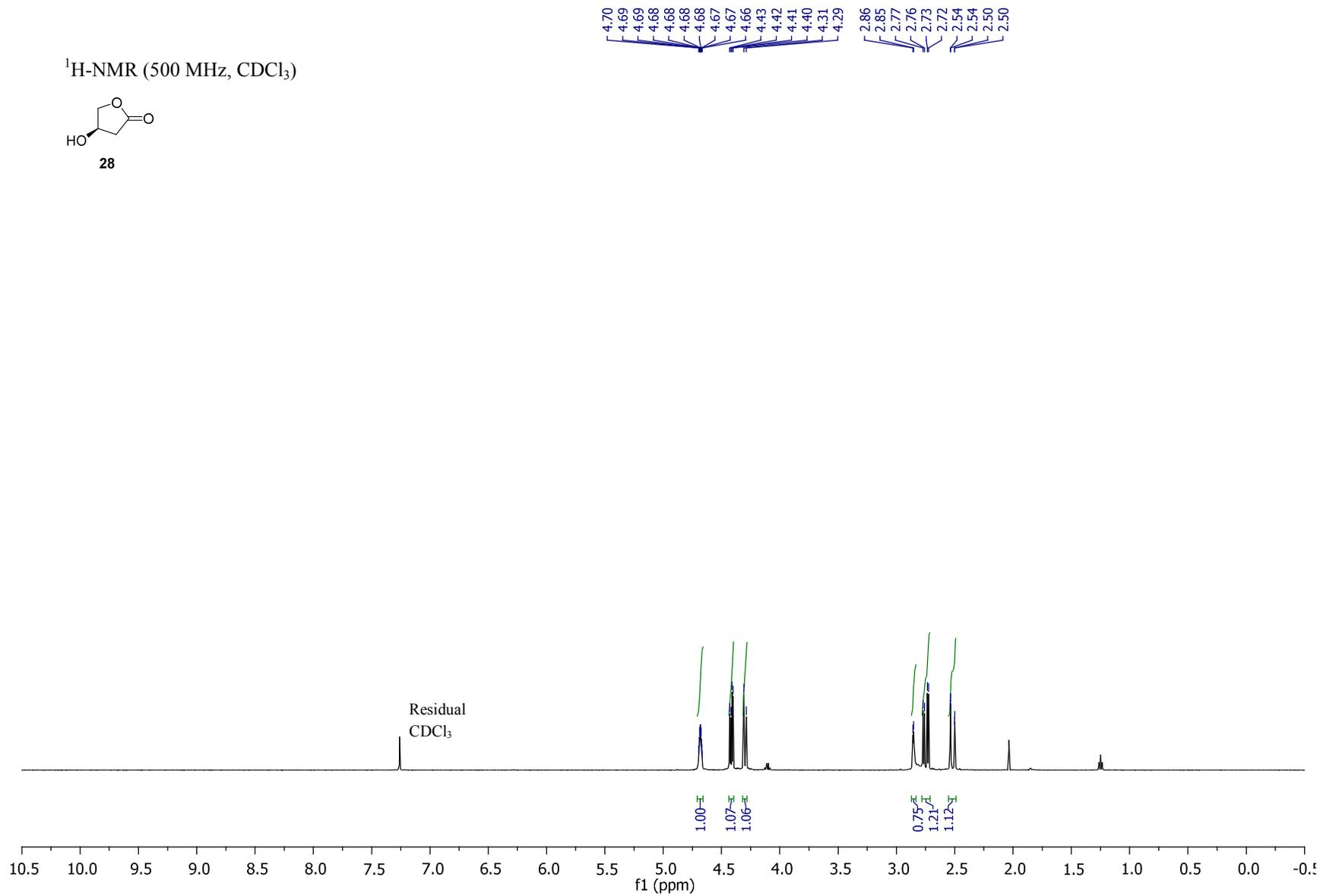
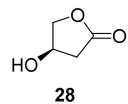


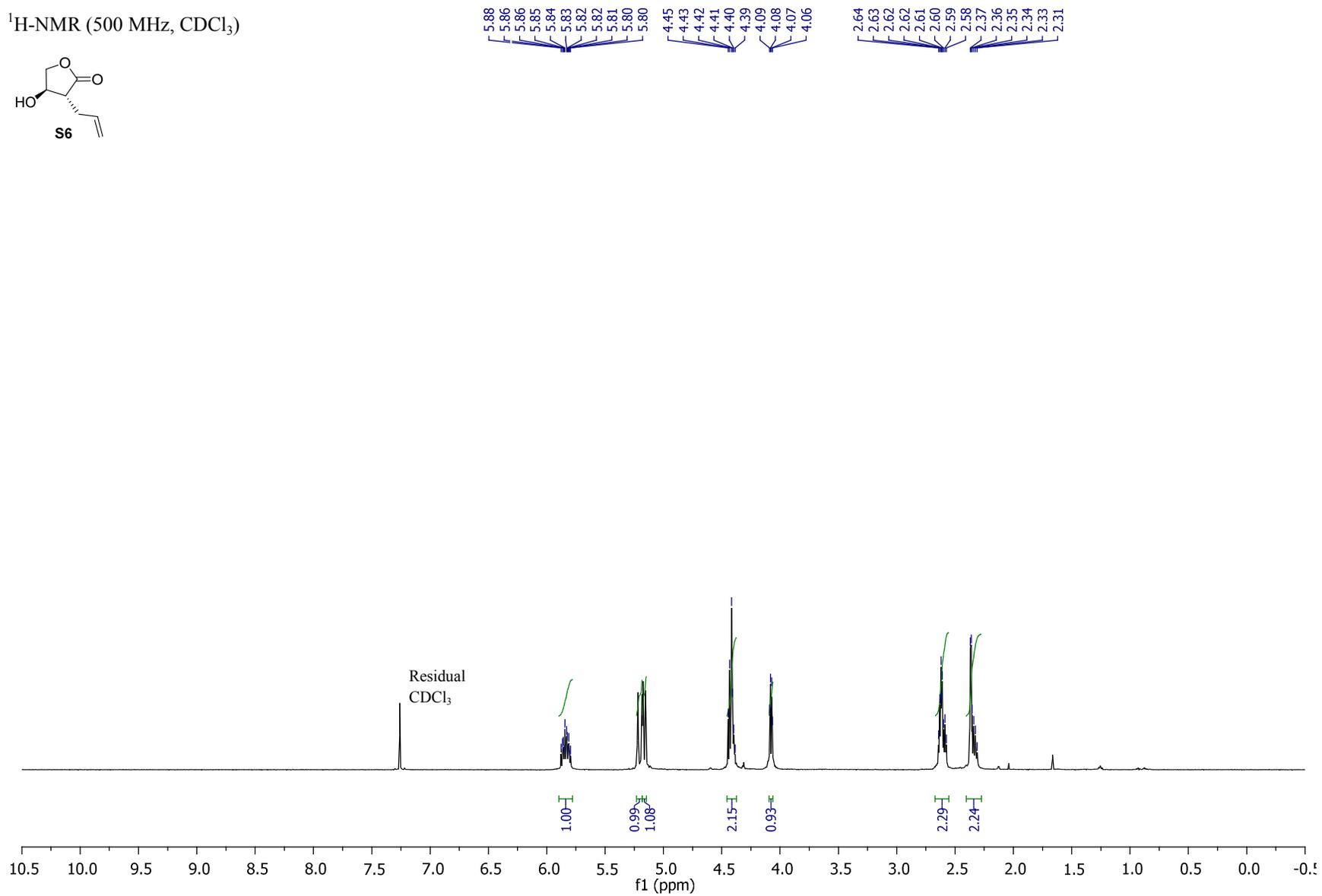
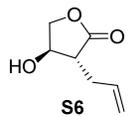


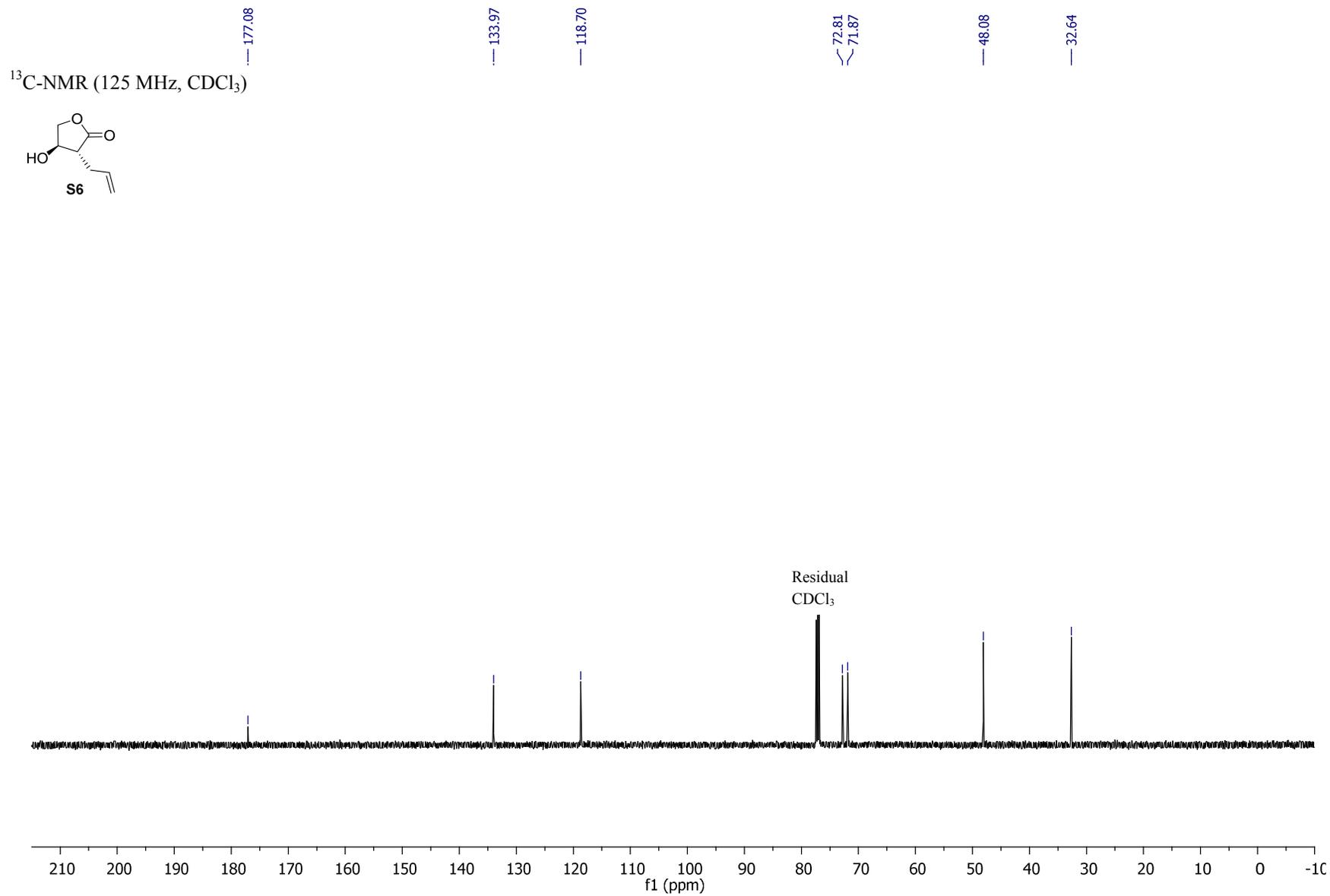
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

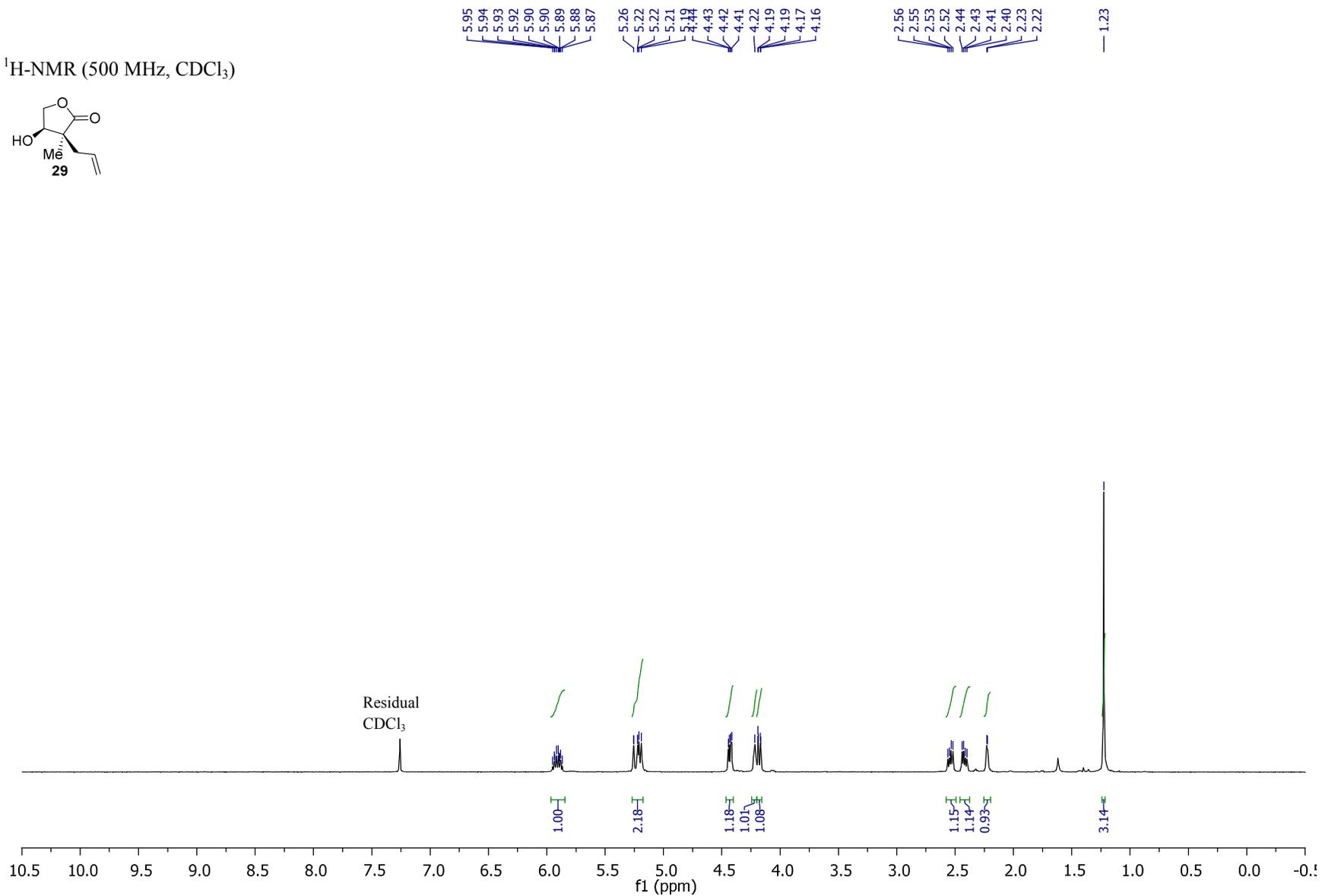
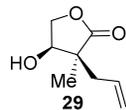
$^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ )

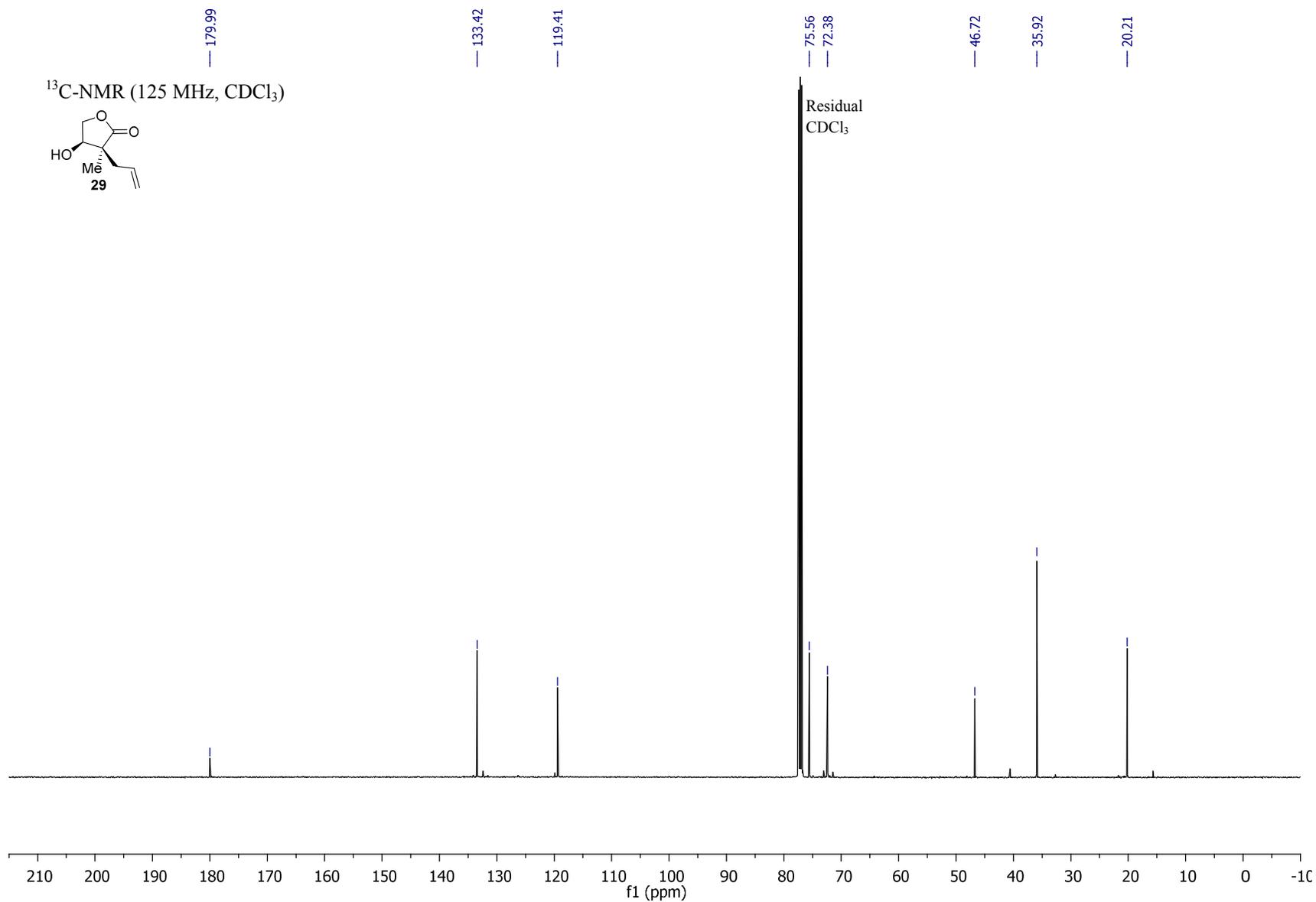
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

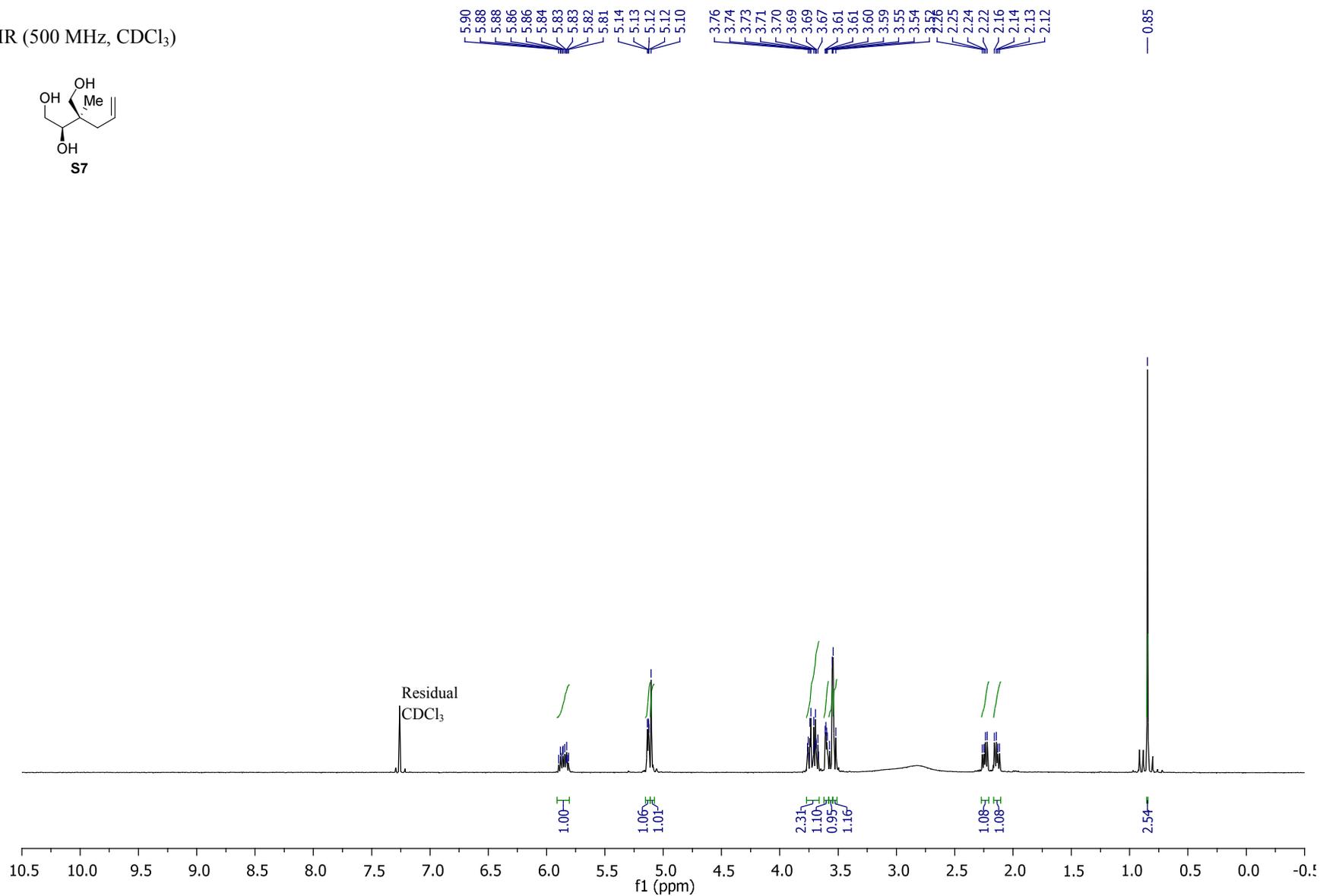
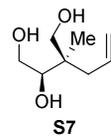


$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

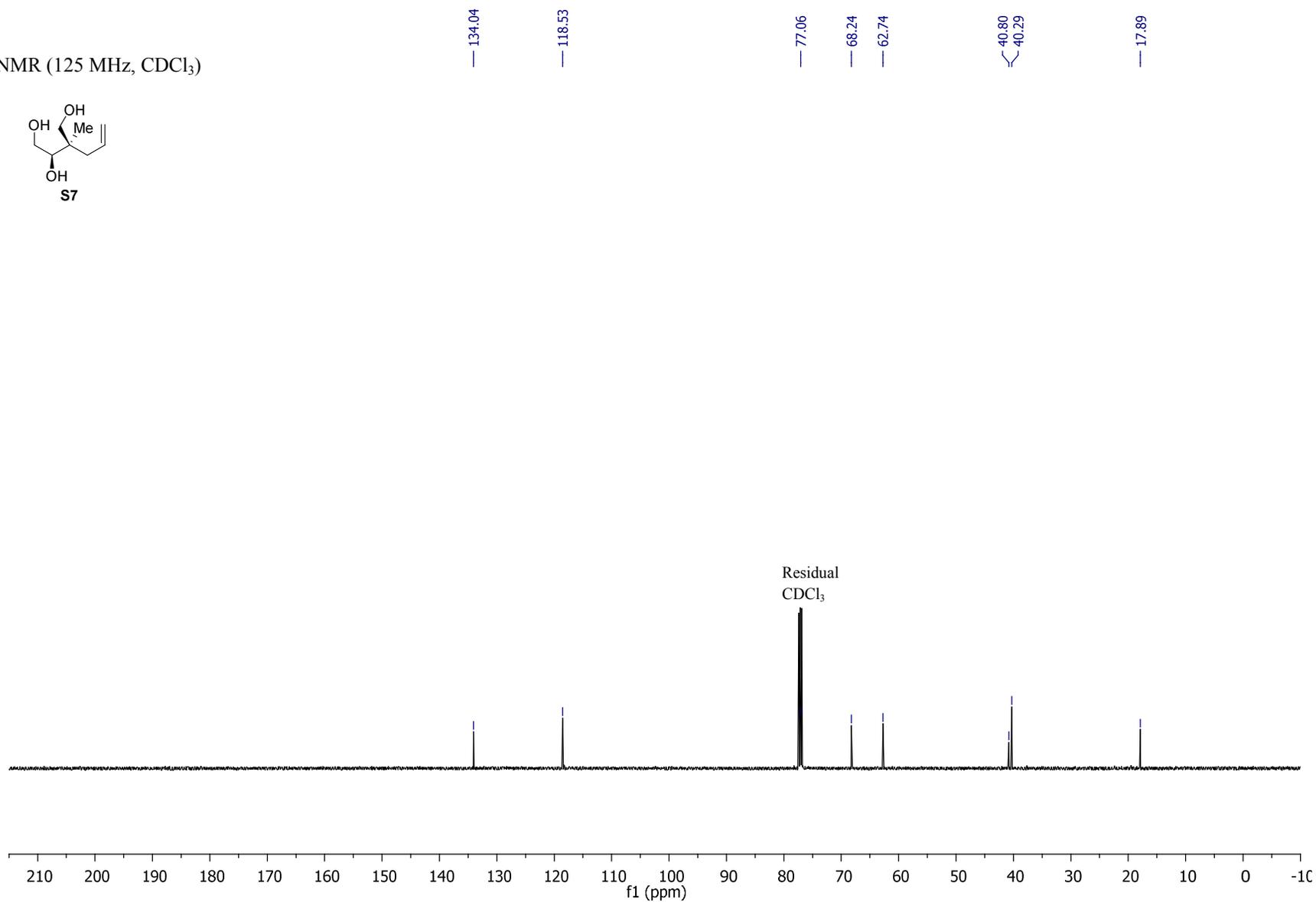
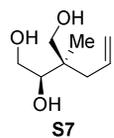


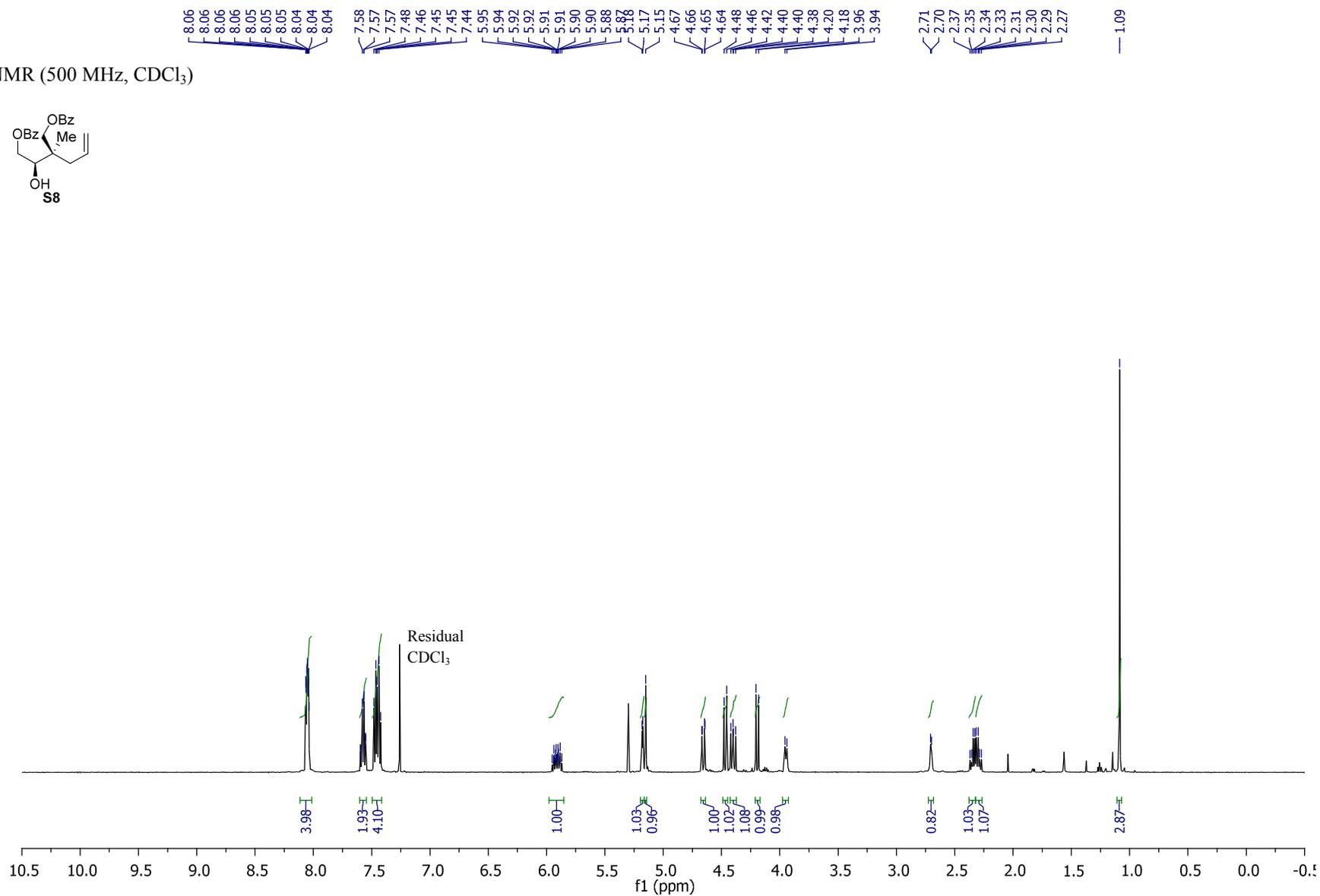
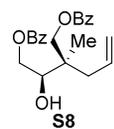
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

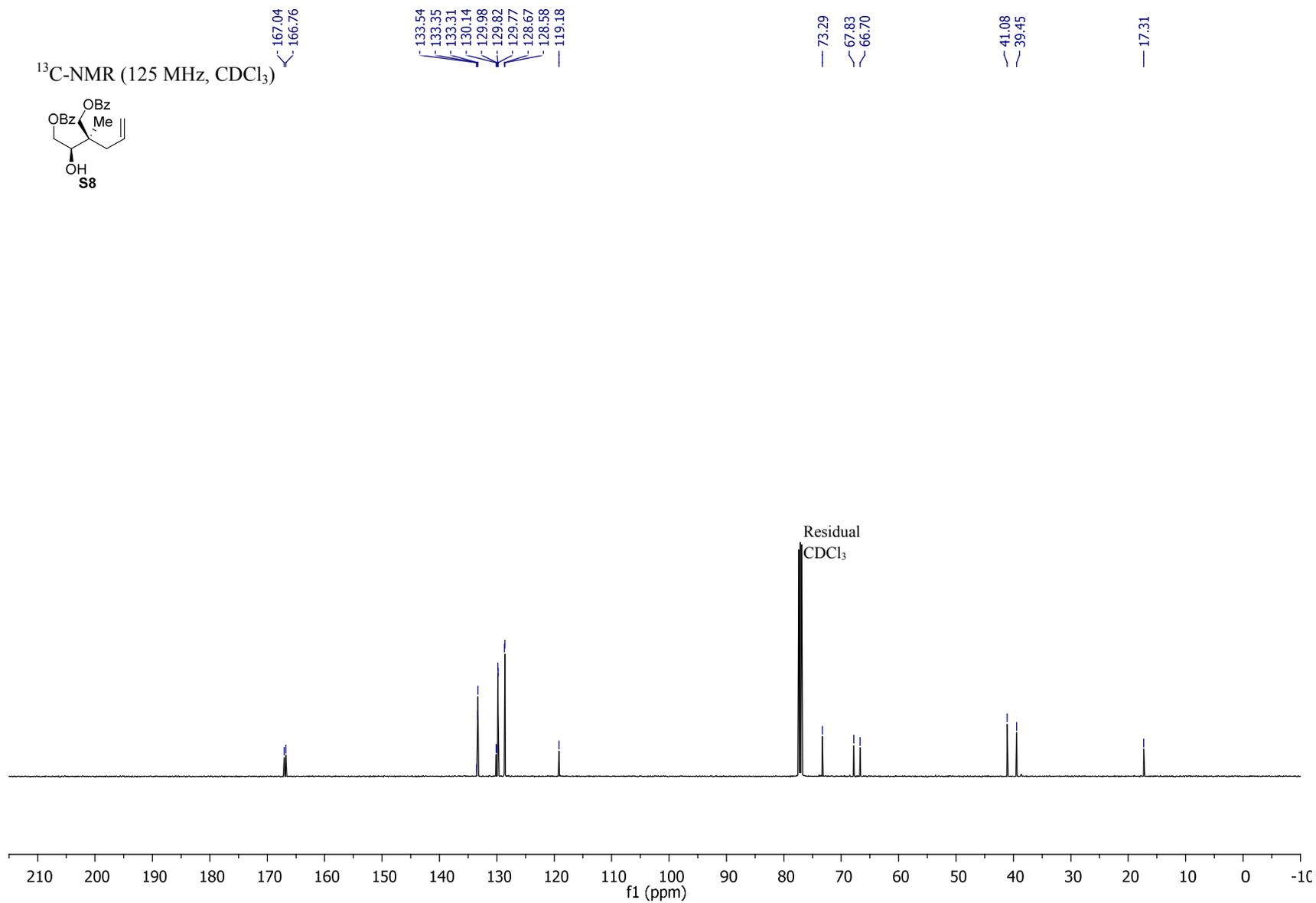


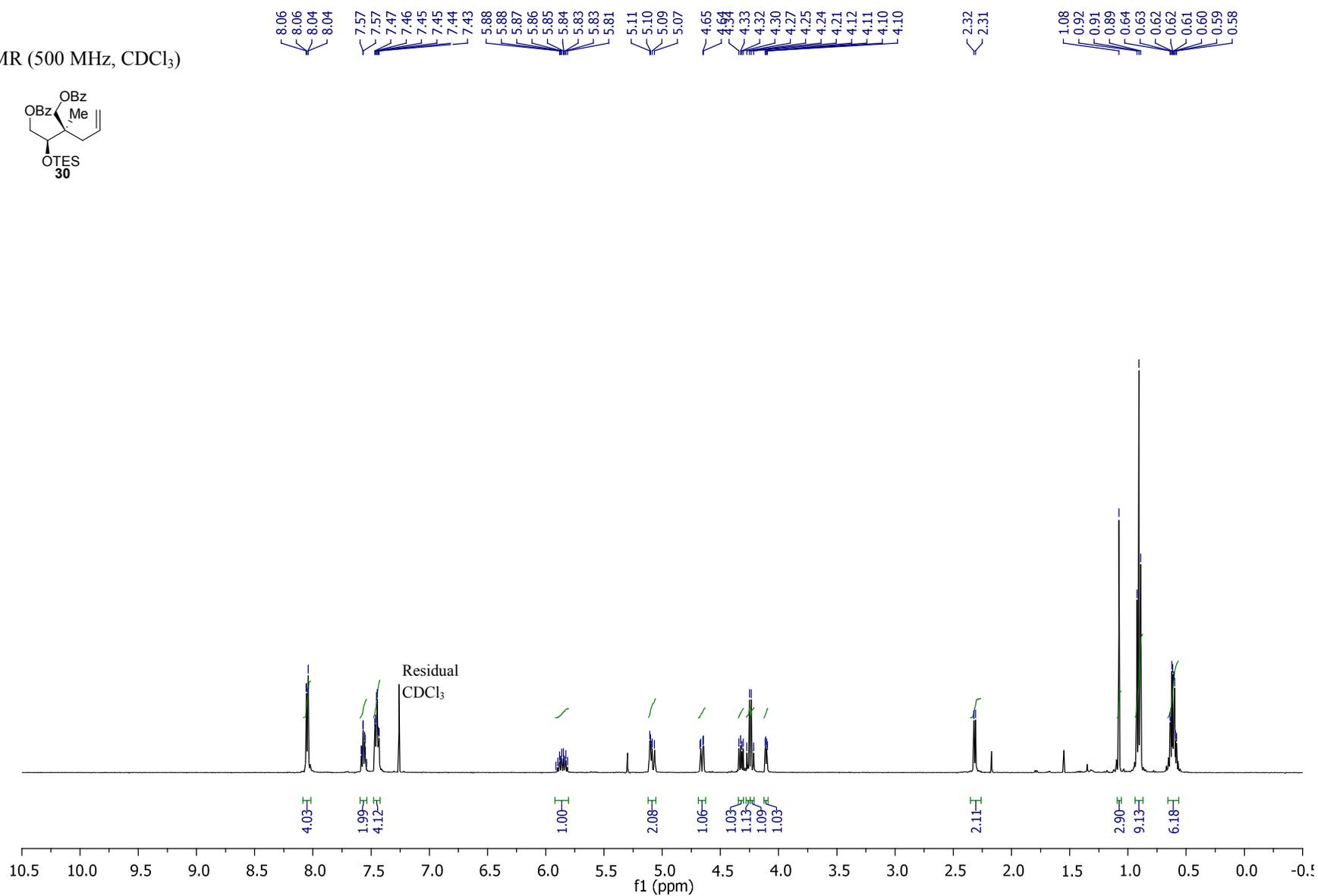
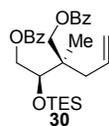
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

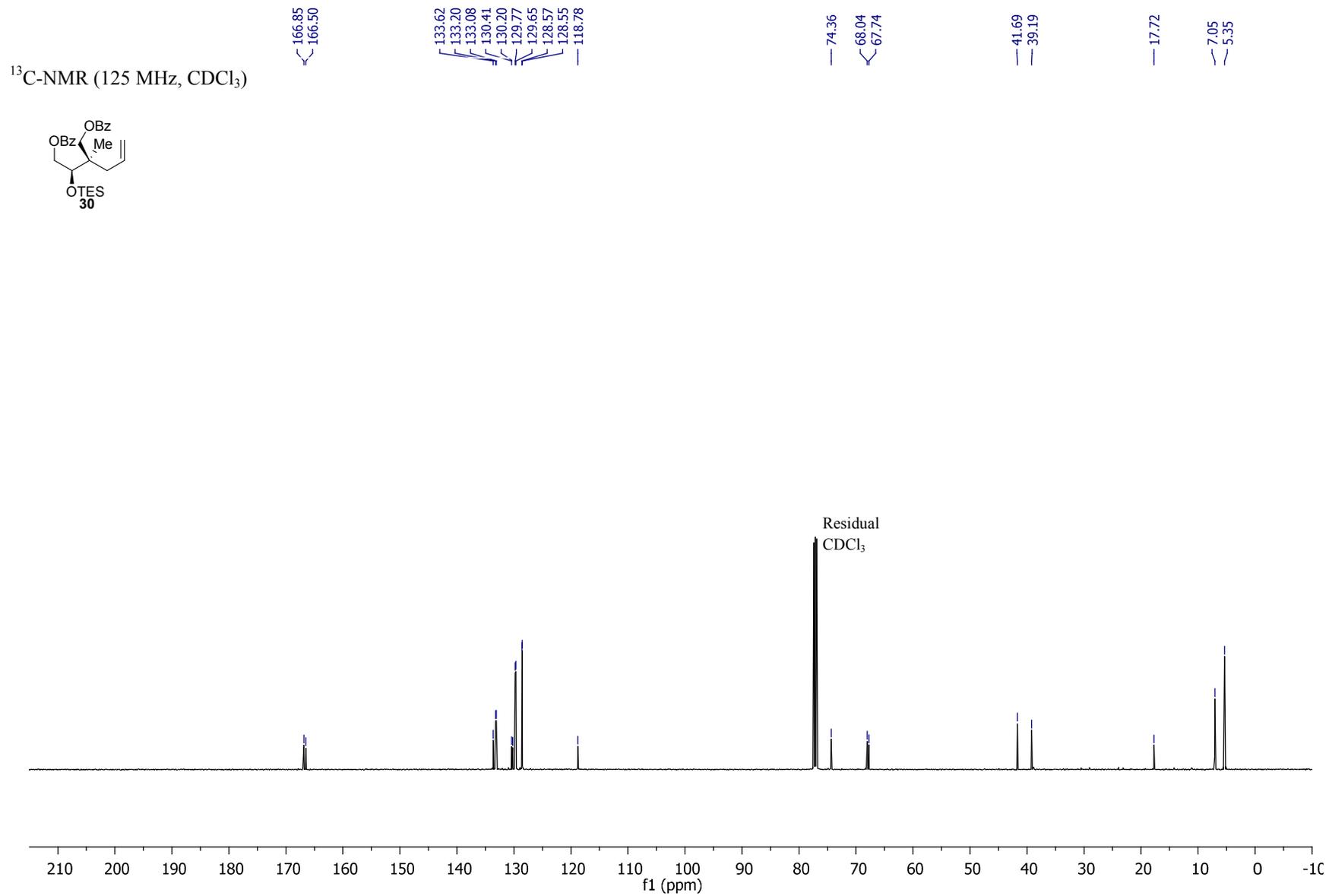
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

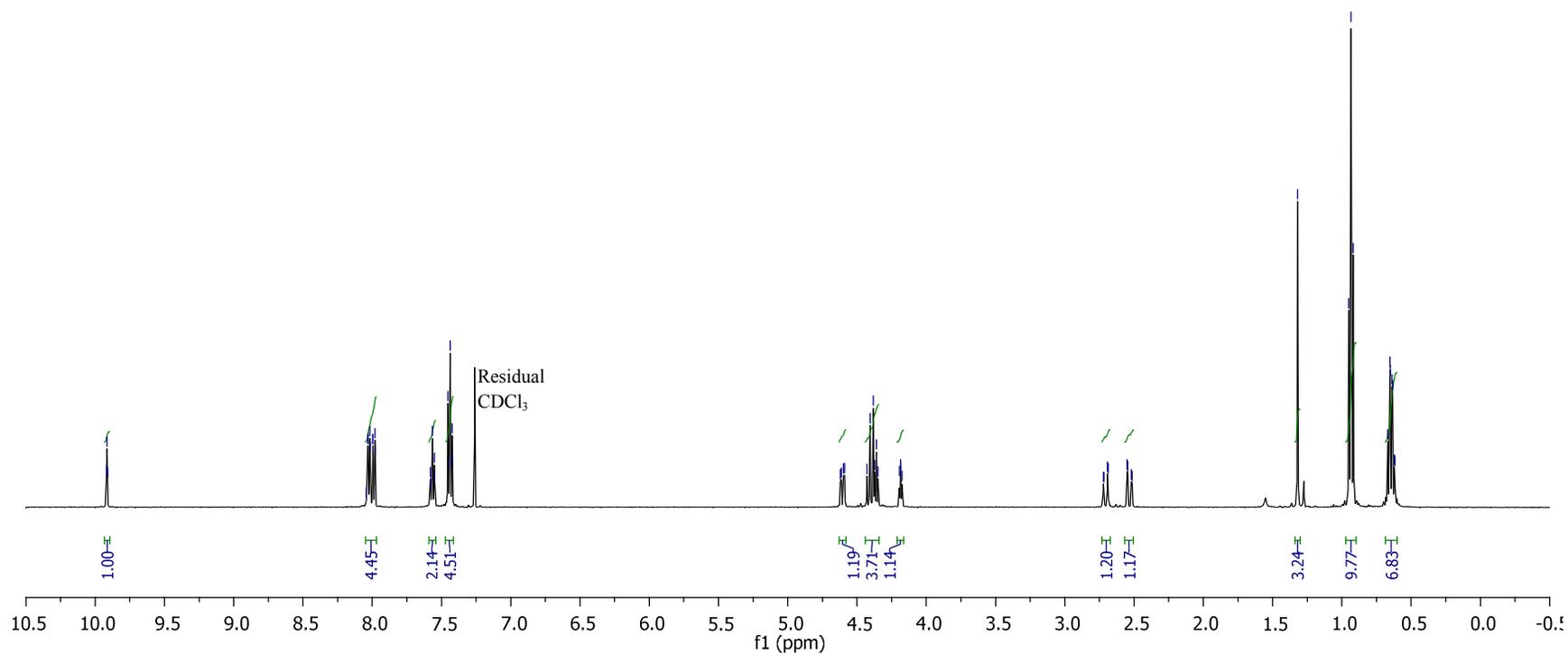
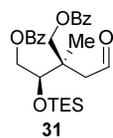


<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)



$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



9.92  
9.91  
9.918.04  
8.03  
8.02  
8.01  
8.00  
7.98  
7.98  
7.58  
7.58  
7.57  
7.55  
7.55  
7.45  
7.45  
7.44  
7.42  
7.424.62  
4.61  
4.60  
4.59  
4.43  
4.41  
4.38  
4.37  
4.36  
4.35  
4.19  
4.19  
4.18  
4.182.72  
2.72  
2.69  
2.69  
2.55  
2.55  
2.52  
2.511.32  
0.95  
0.93  
0.92  
0.67  
0.65  
0.65  
0.64  
0.63  
0.62  
0.62<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)



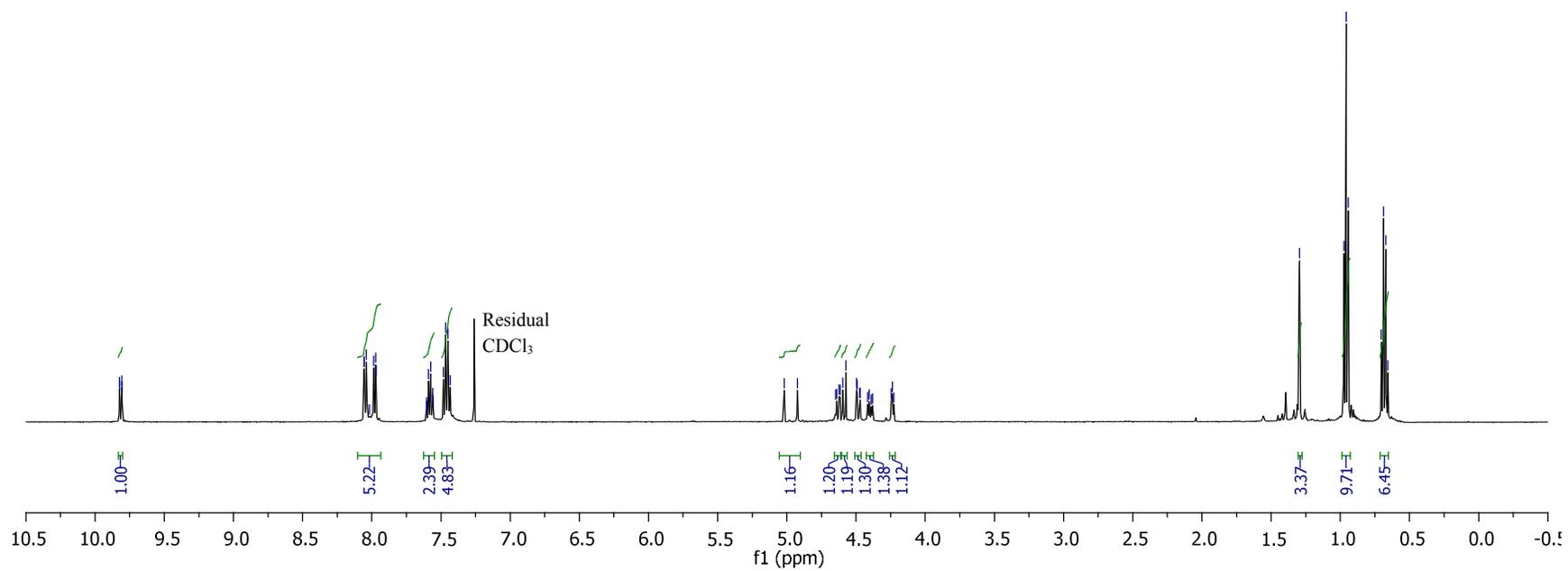
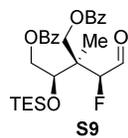
9.82  
9.82  
9.81  
9.81

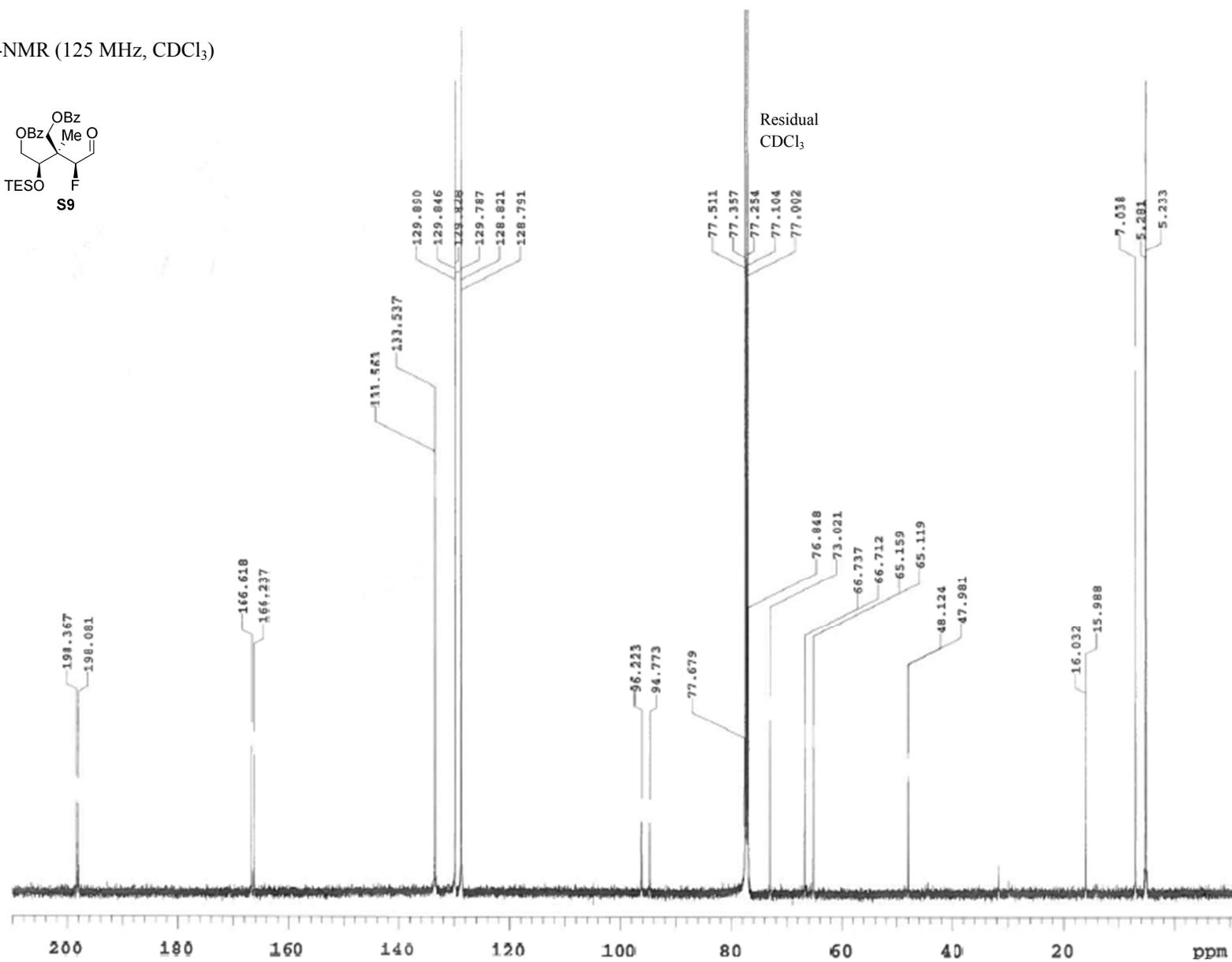
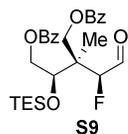
8.05  
8.05  
8.04  
8.02  
7.99  
7.97  
7.97  
7.61  
7.60  
7.60  
7.59  
7.57  
7.56  
7.56  
7.56  
7.48  
7.47  
7.45  
7.43

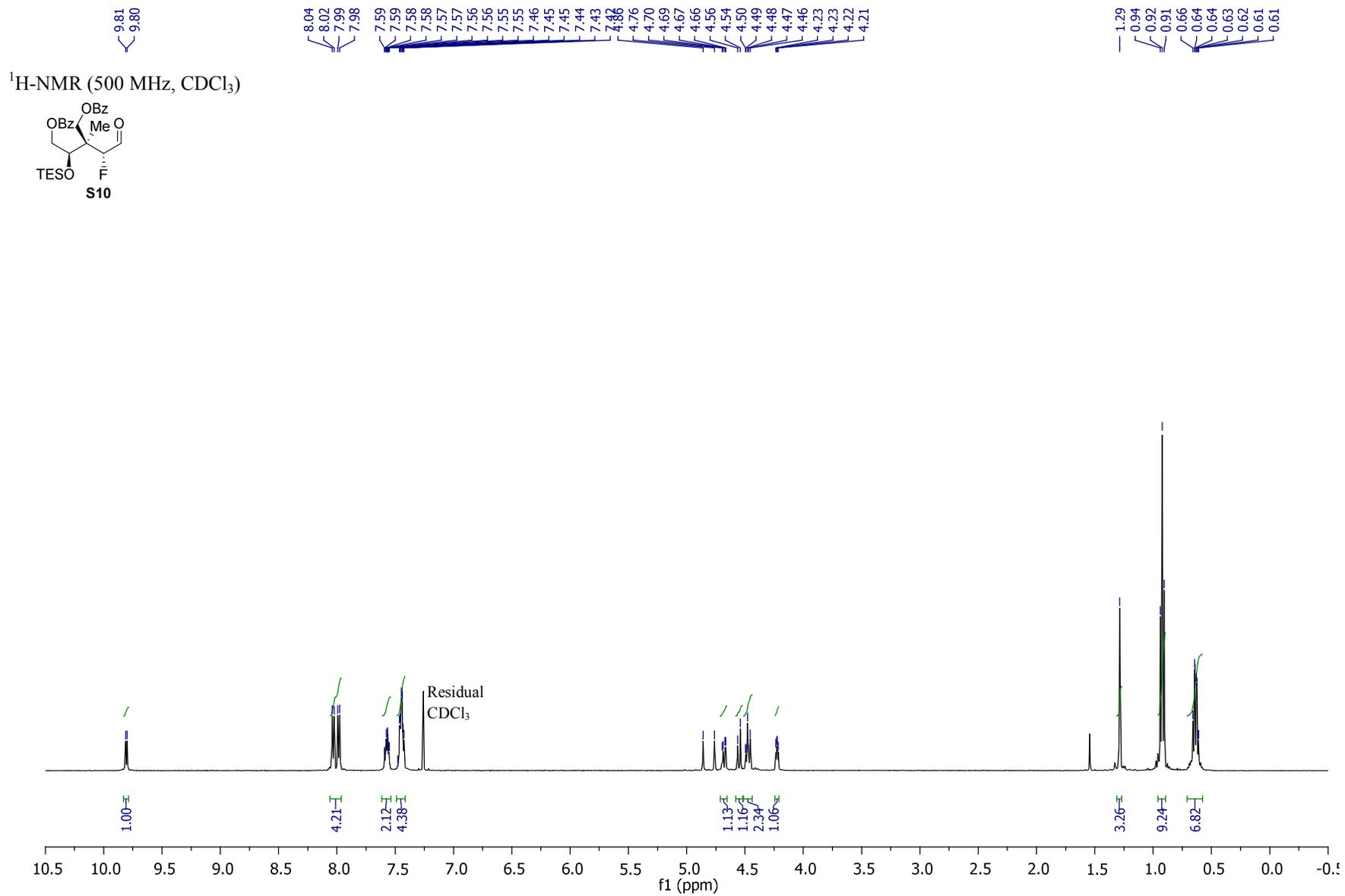
5.02  
4.92  
4.65  
4.64  
4.62  
4.62  
4.60  
4.57  
4.50  
4.49  
4.47  
4.47  
4.42  
4.41  
4.39  
4.38  
4.25  
4.24  
4.23

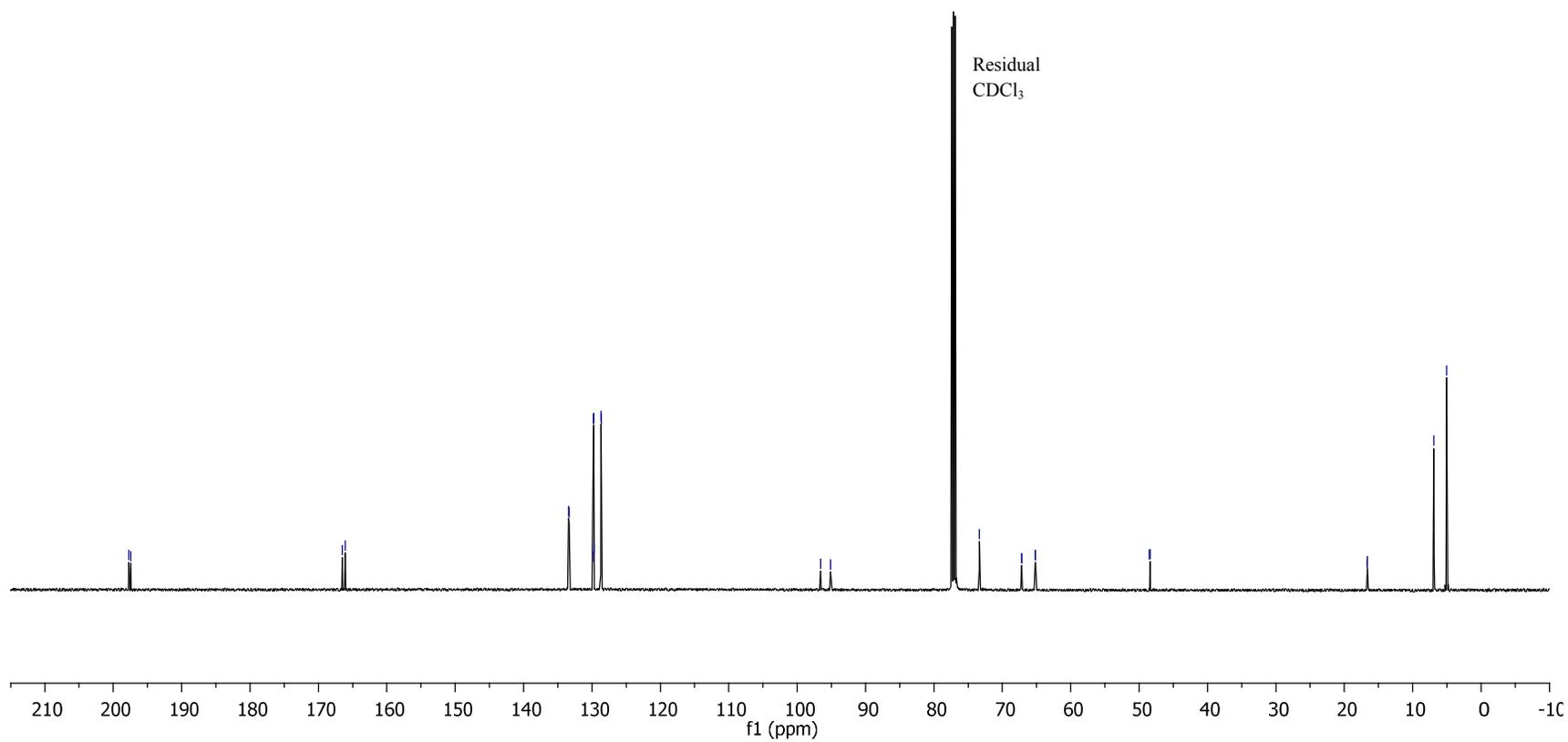
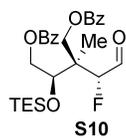
1.30  
0.97  
0.96  
0.94  
0.70  
0.69  
0.67  
0.66

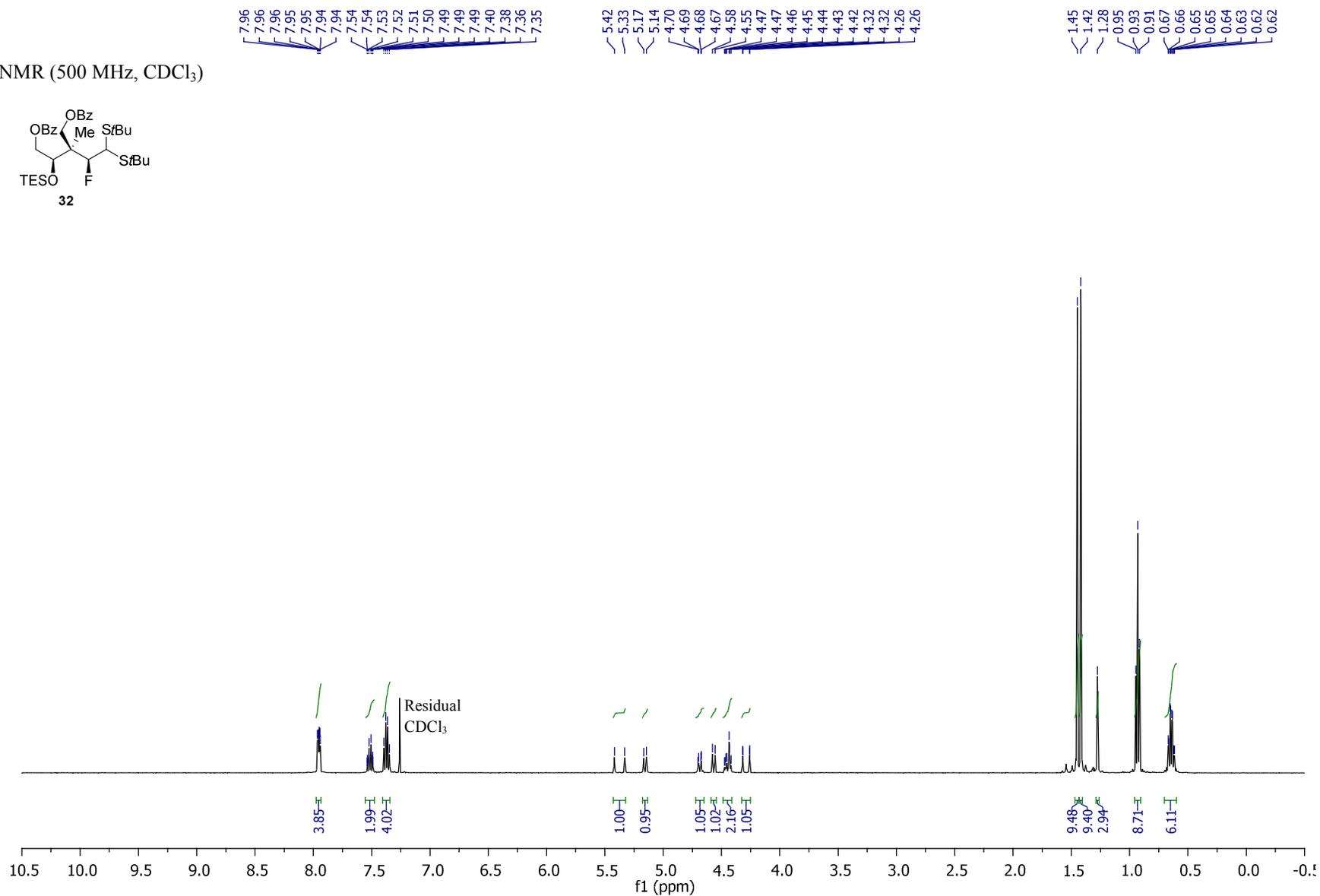
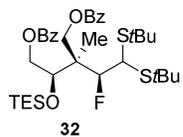
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

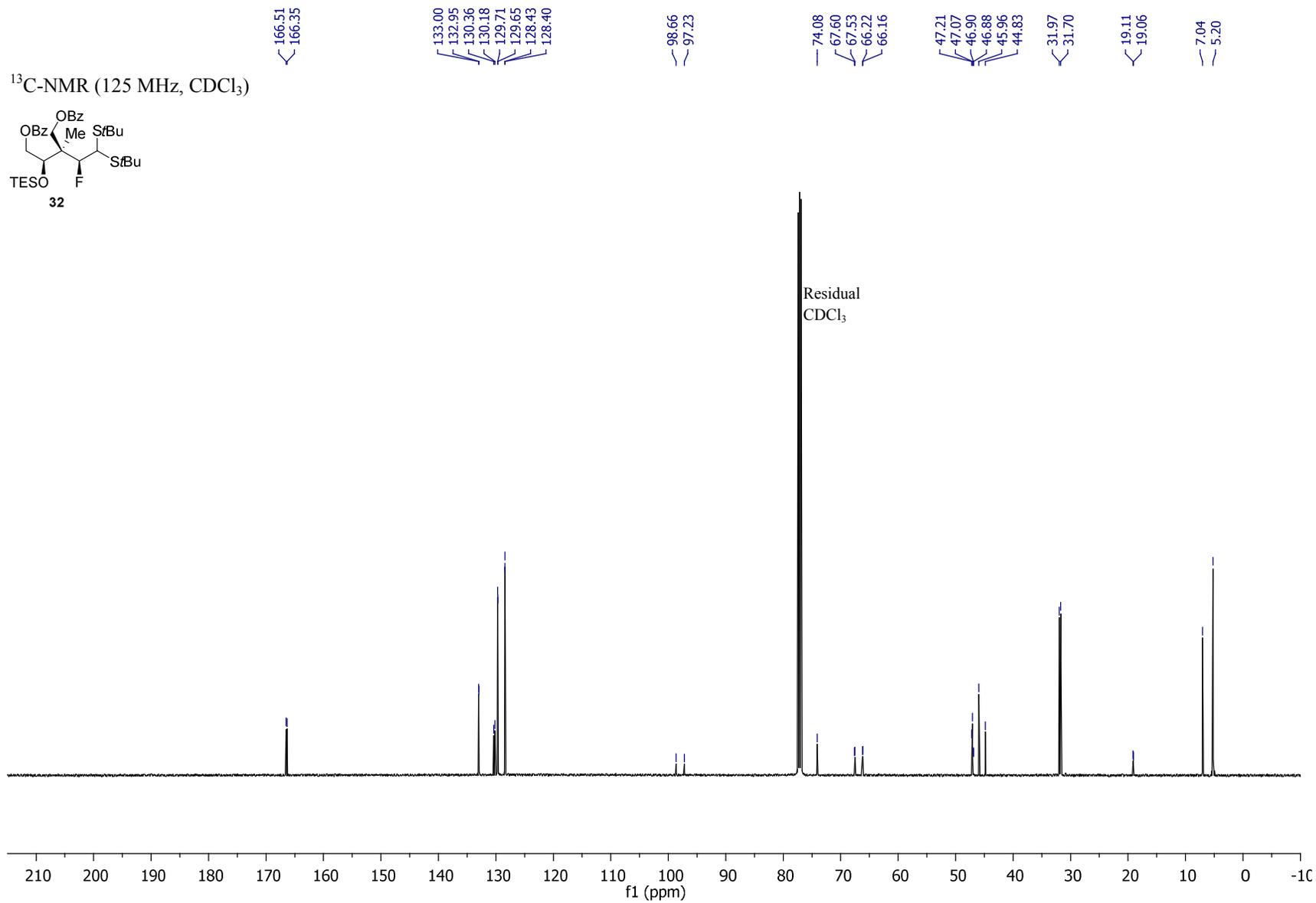


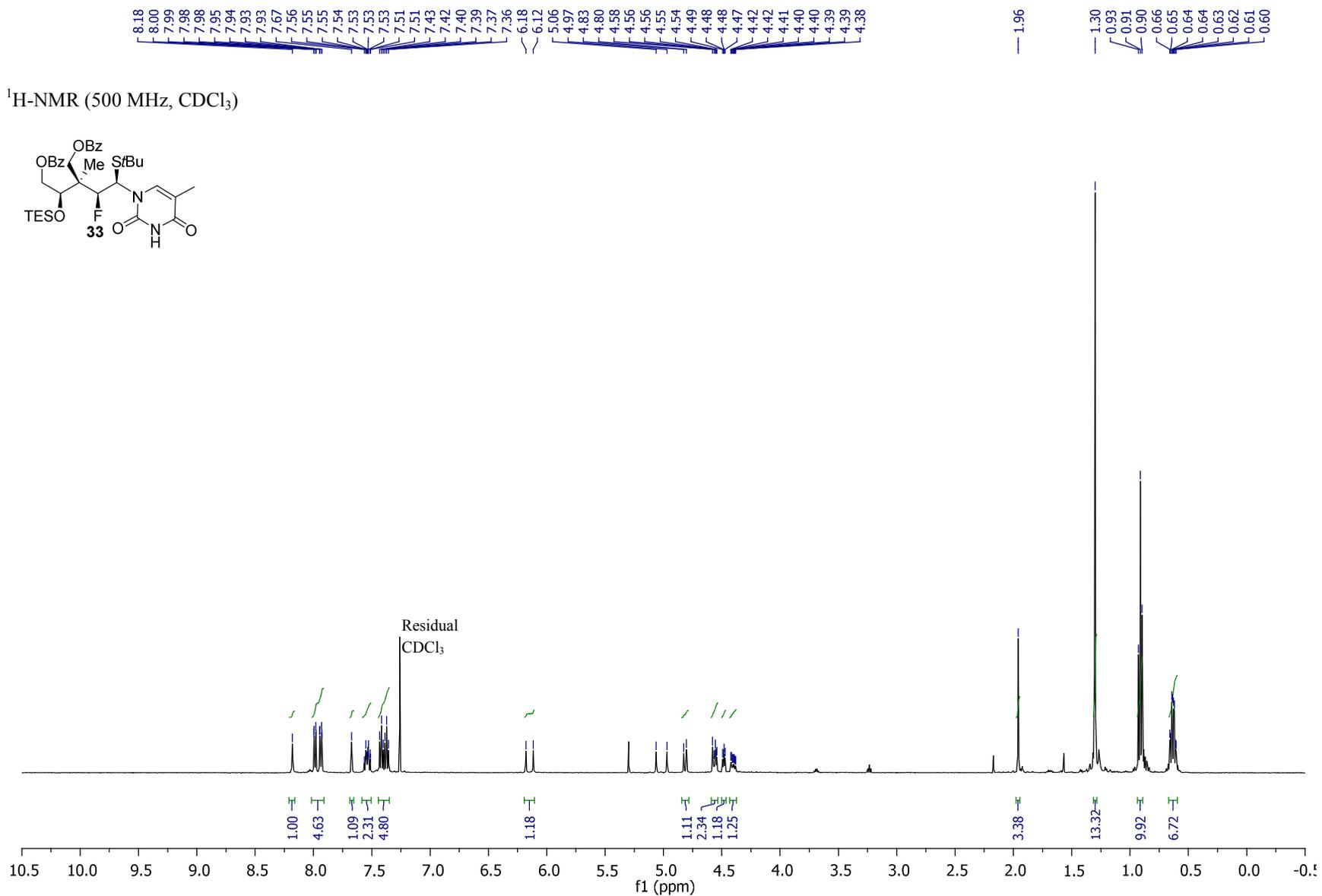
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

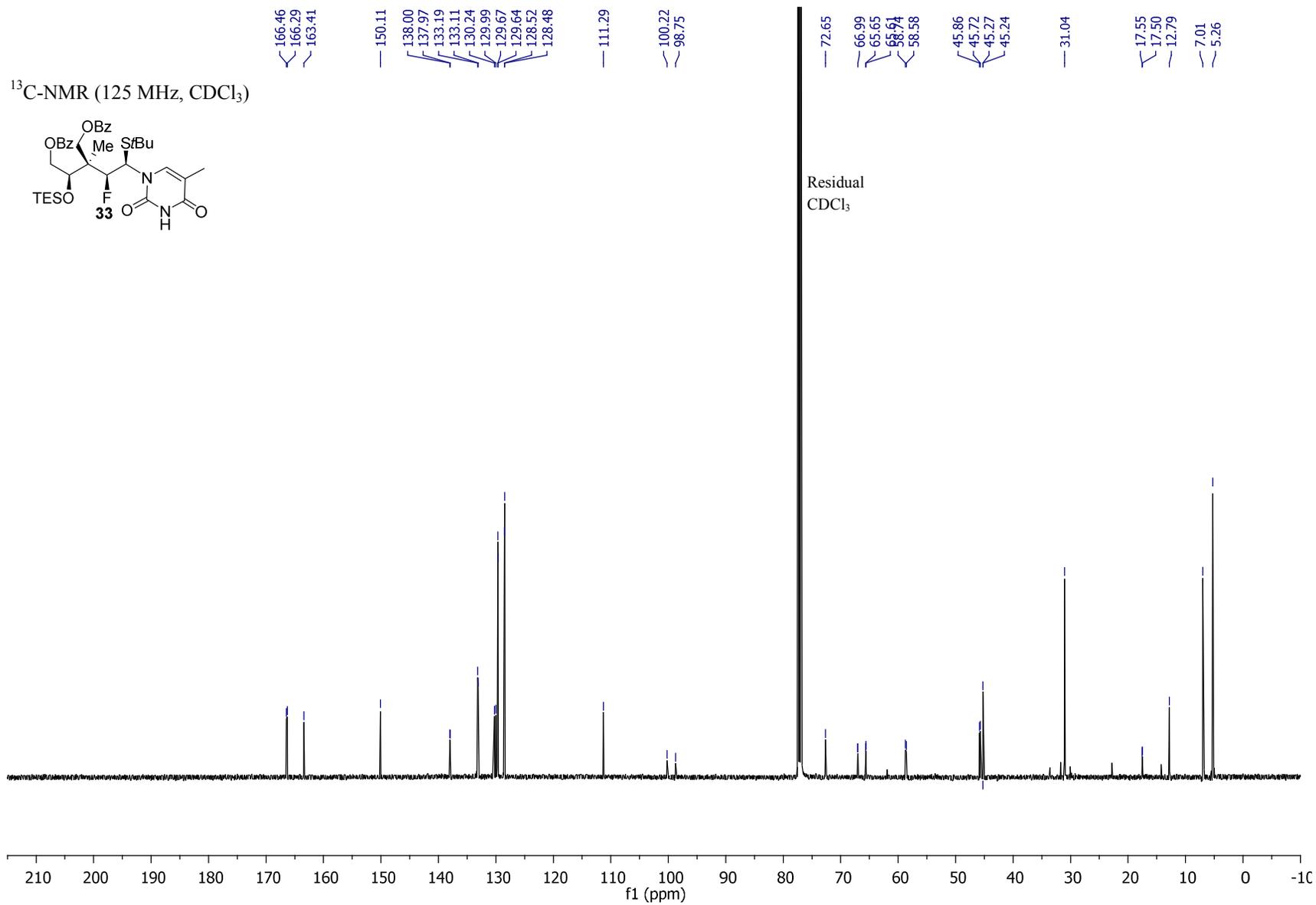


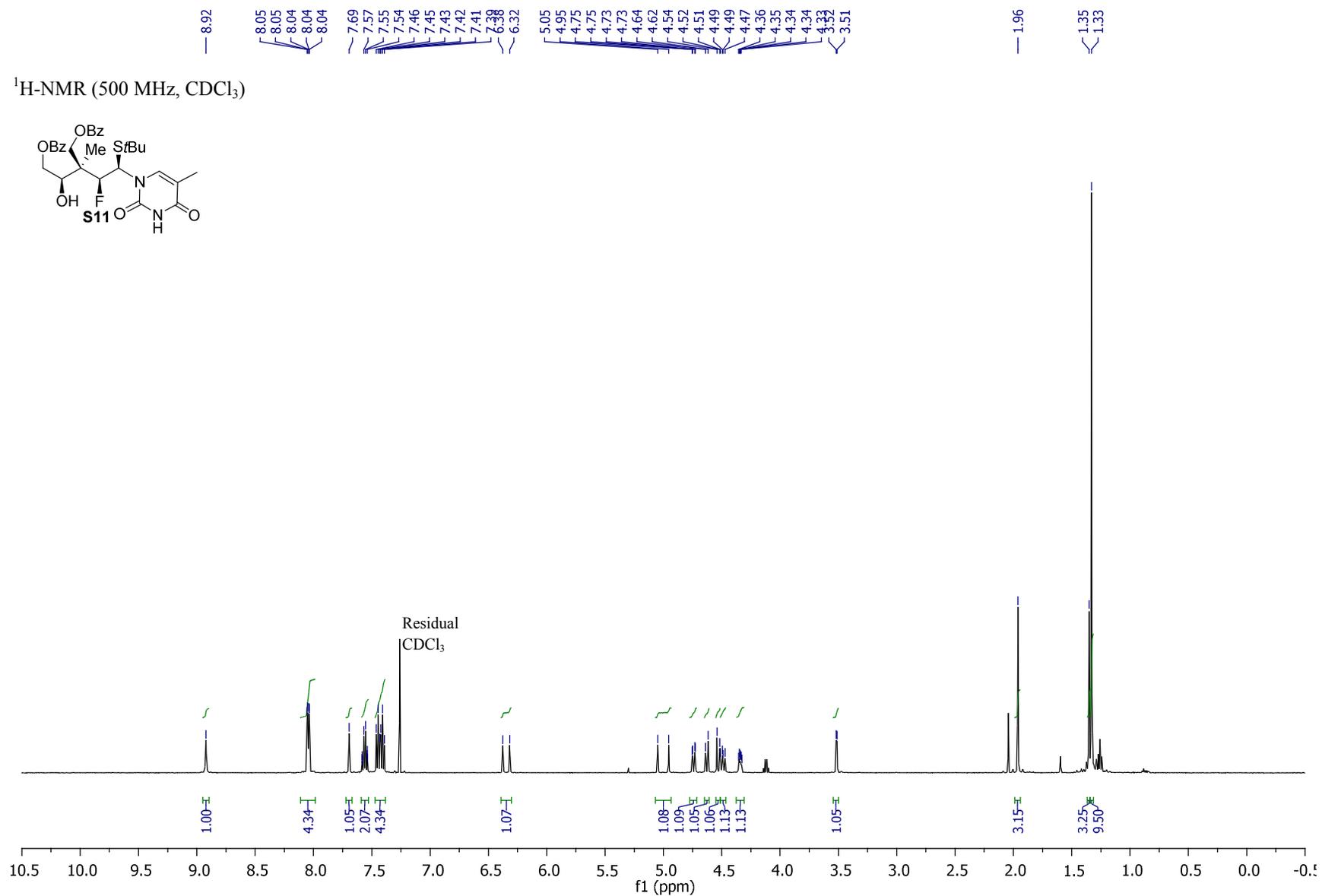
197.73  
197.44166.53  
166.07133.44  
133.35  
129.90  
129.79  
129.73  
129.70  
128.69  
128.6196.58  
95.1273.36  
67.19  
67.14  
65.20  
65.1648.53  
48.3816.67  
16.626.89  
5.05 $^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

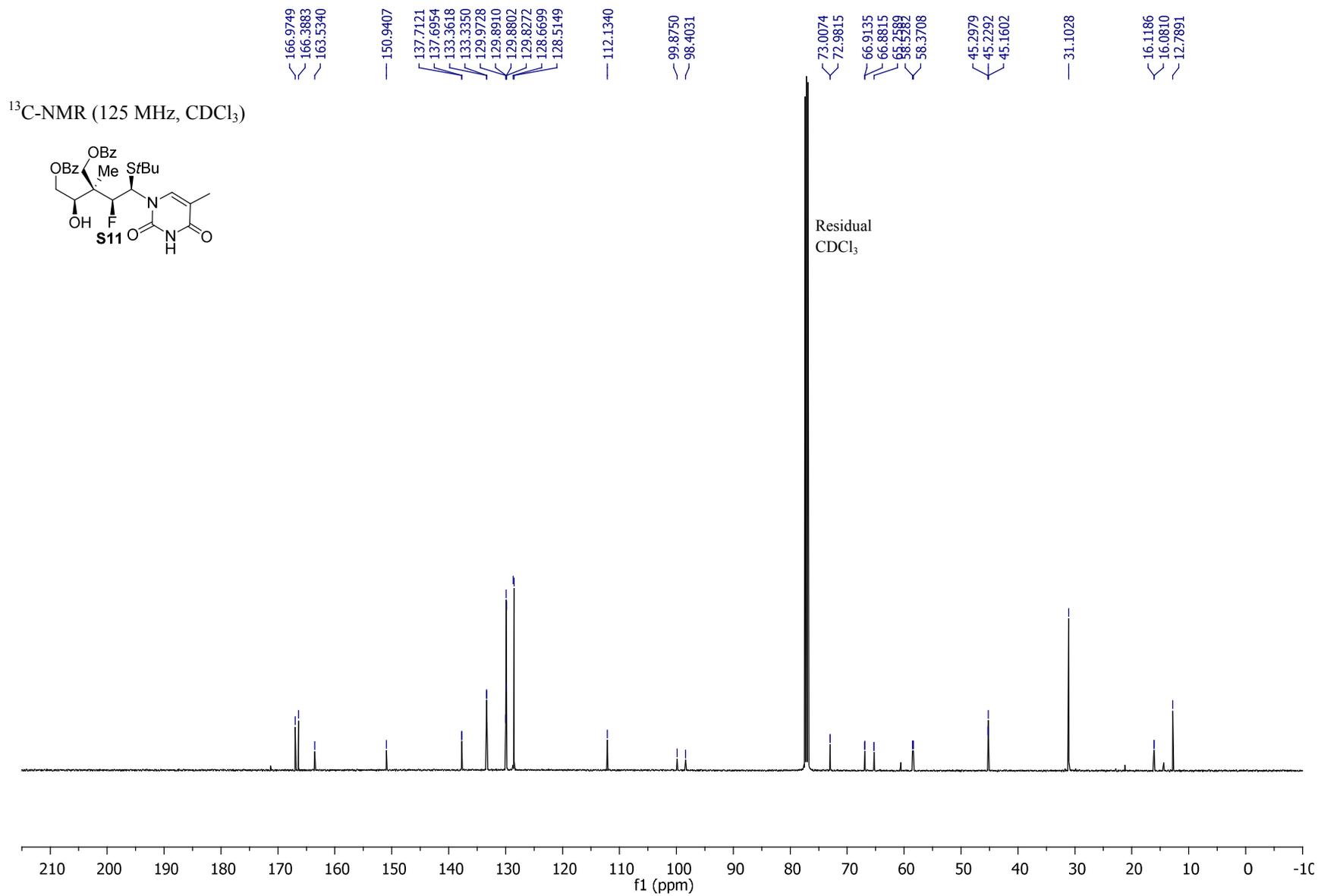
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

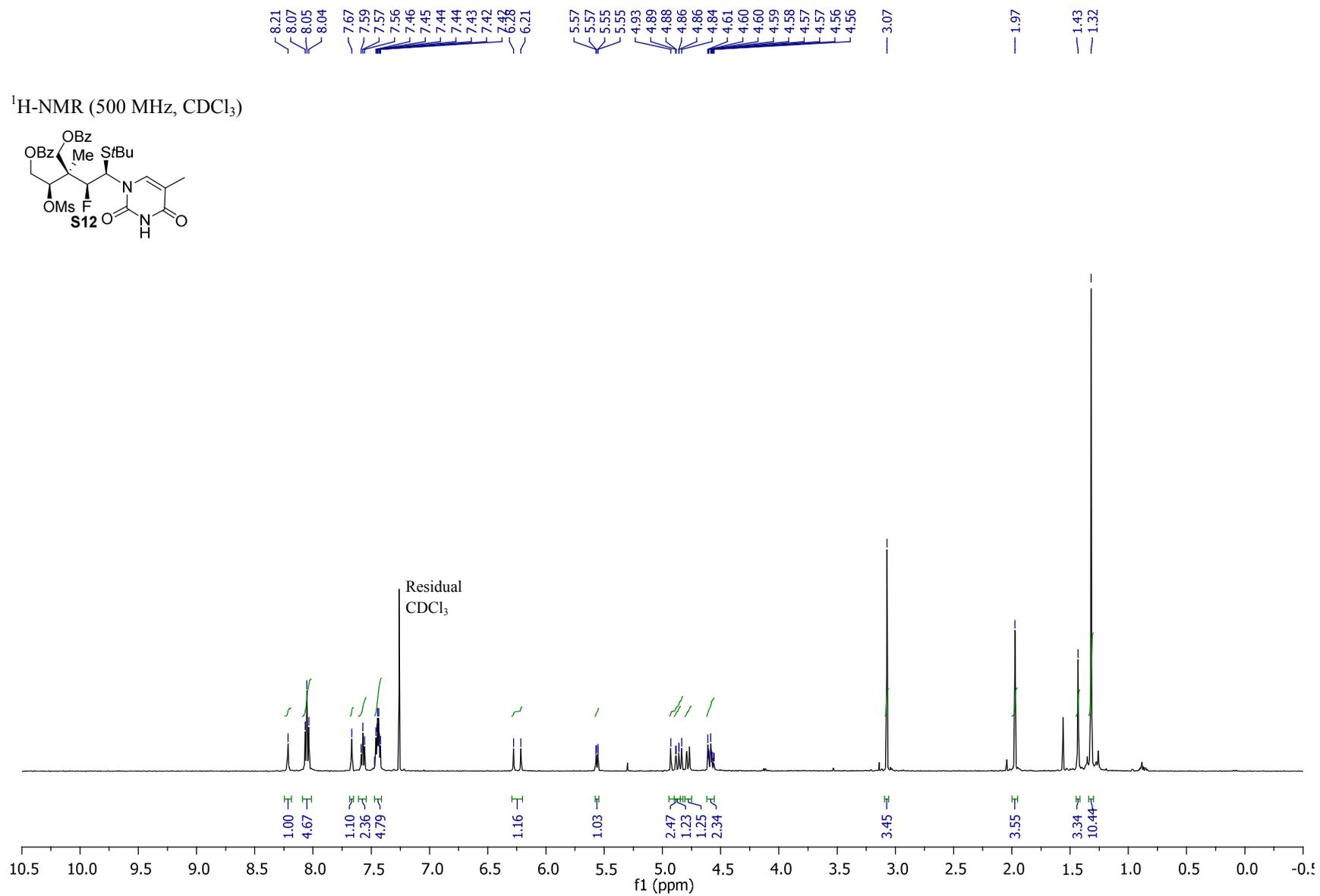


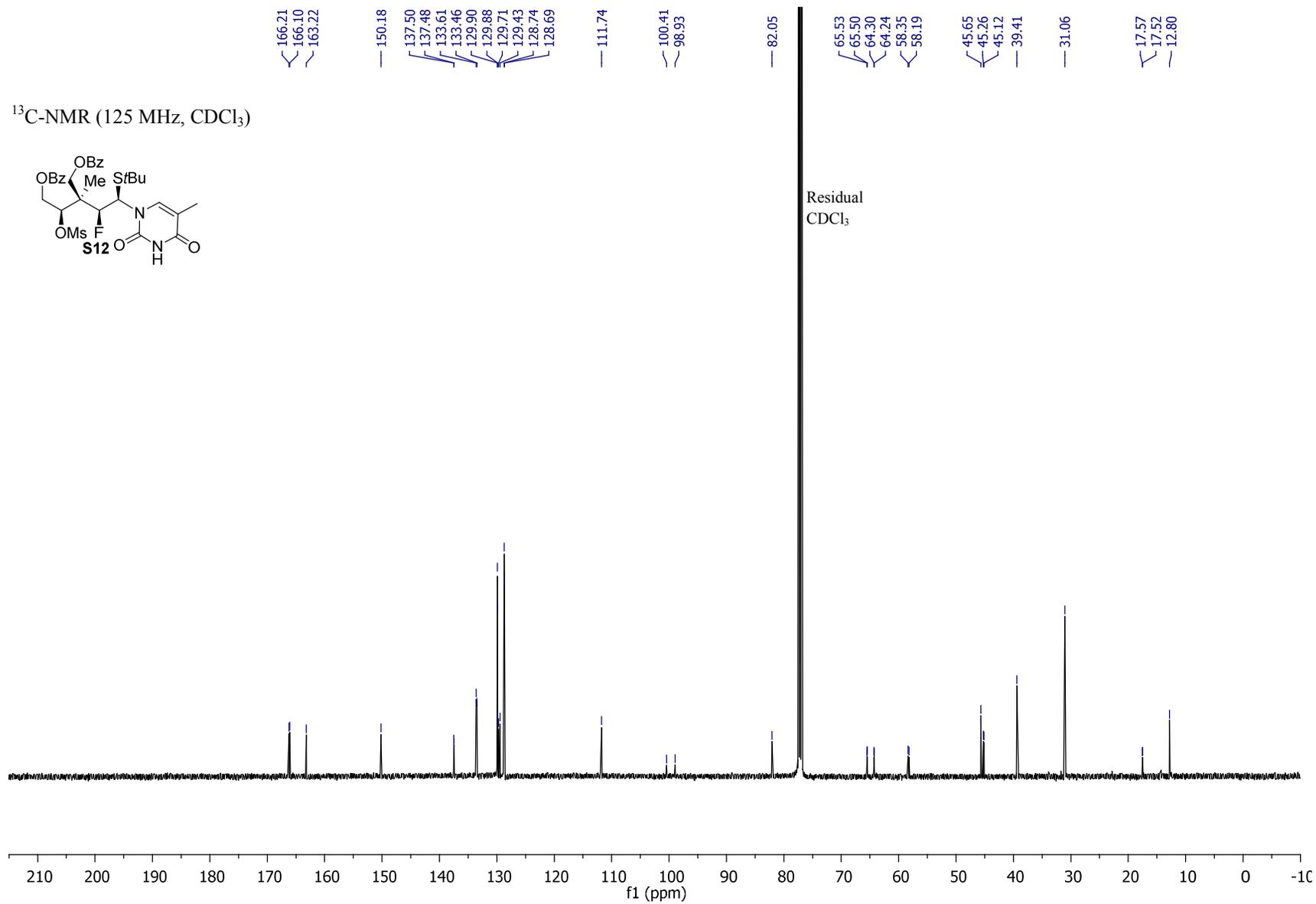


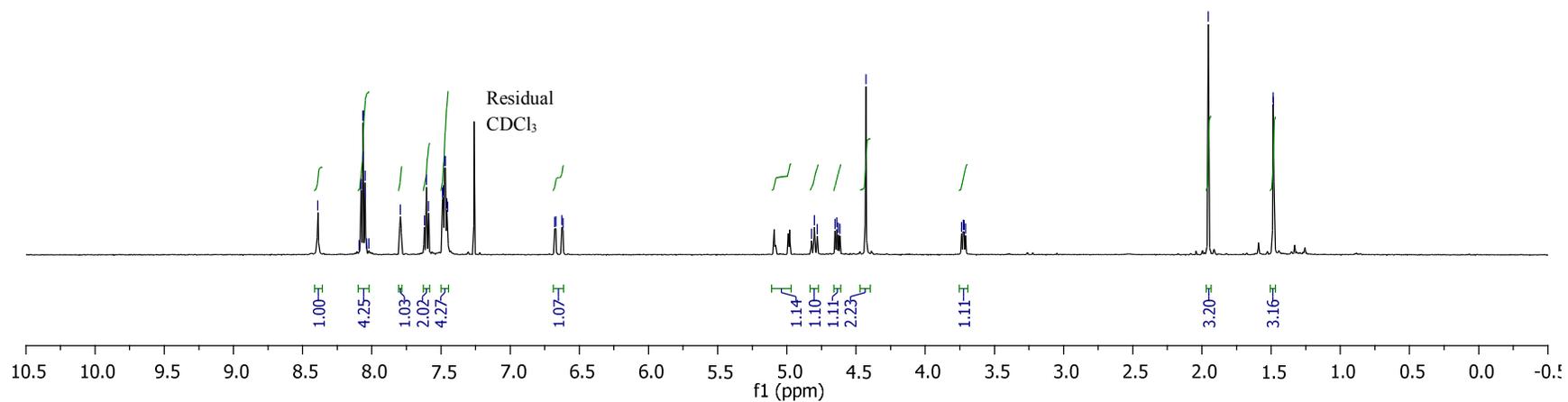
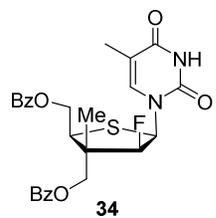


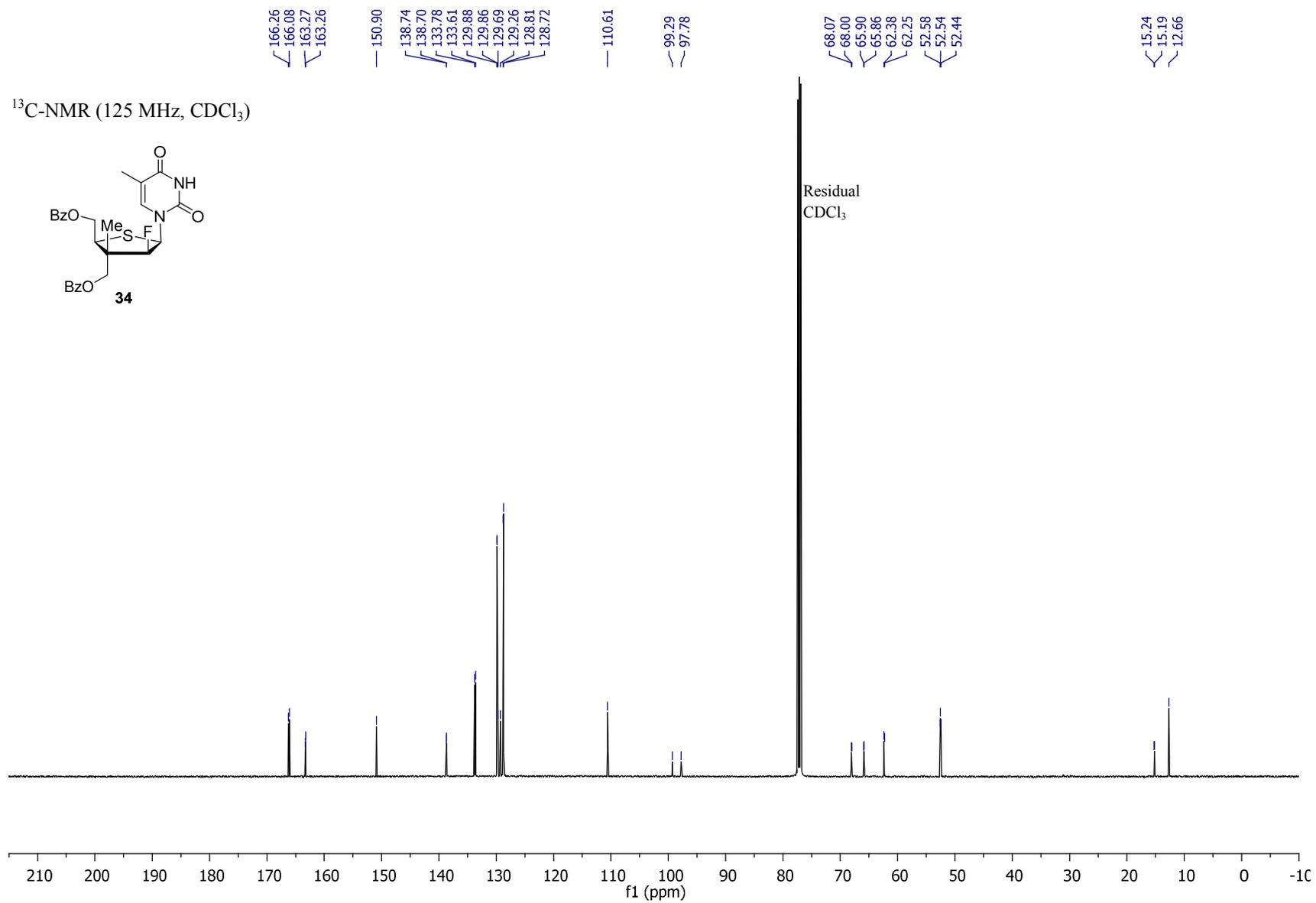




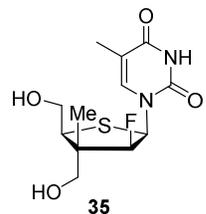




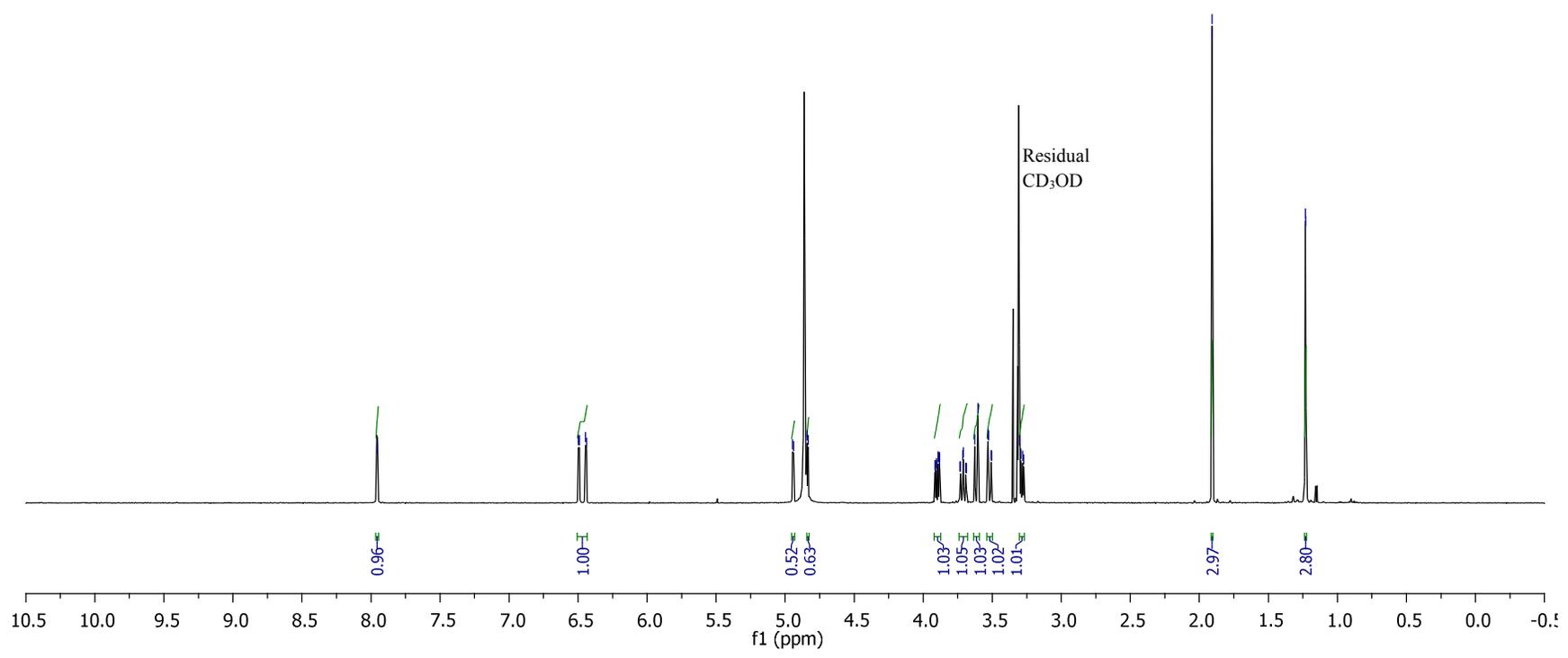
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

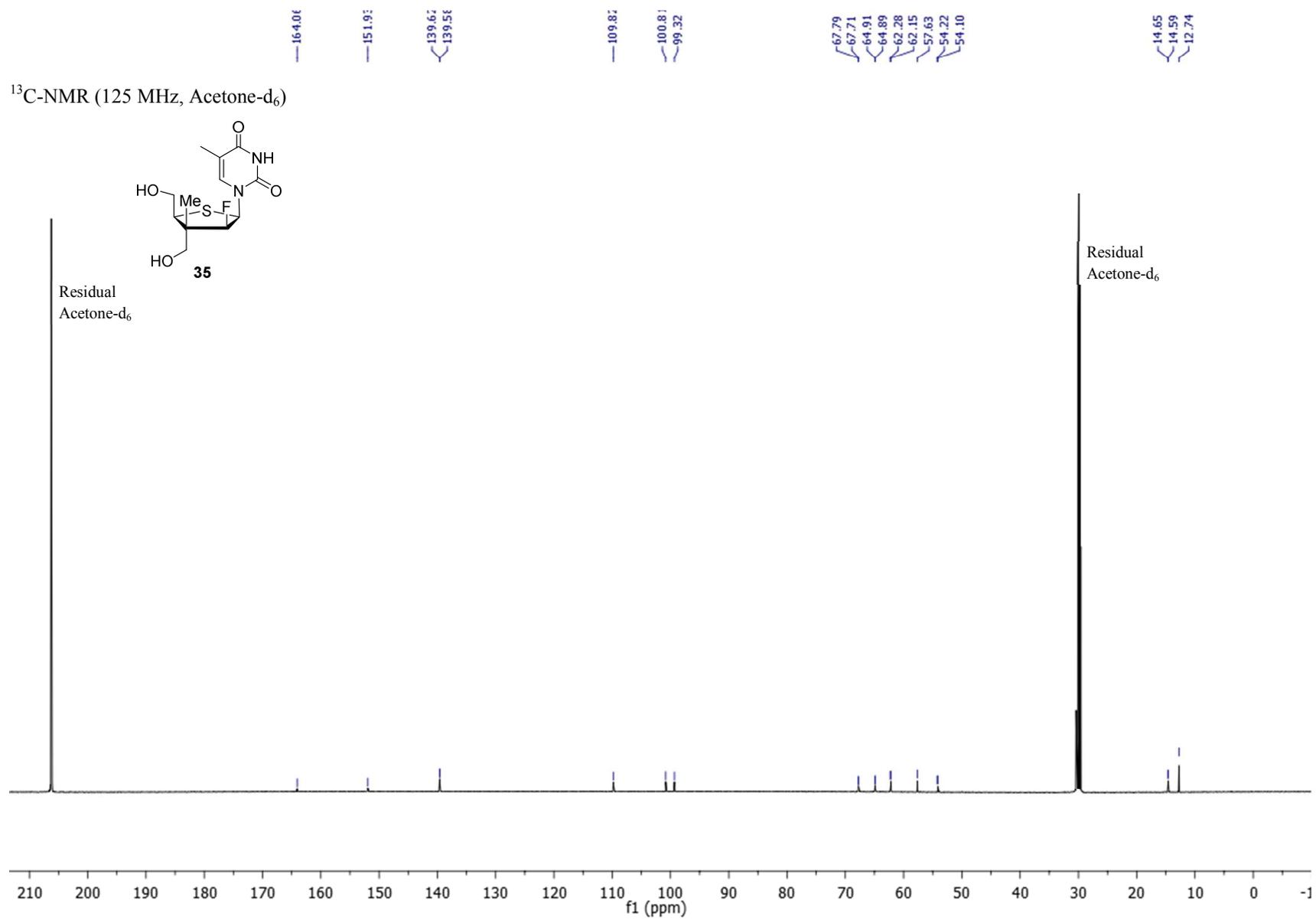


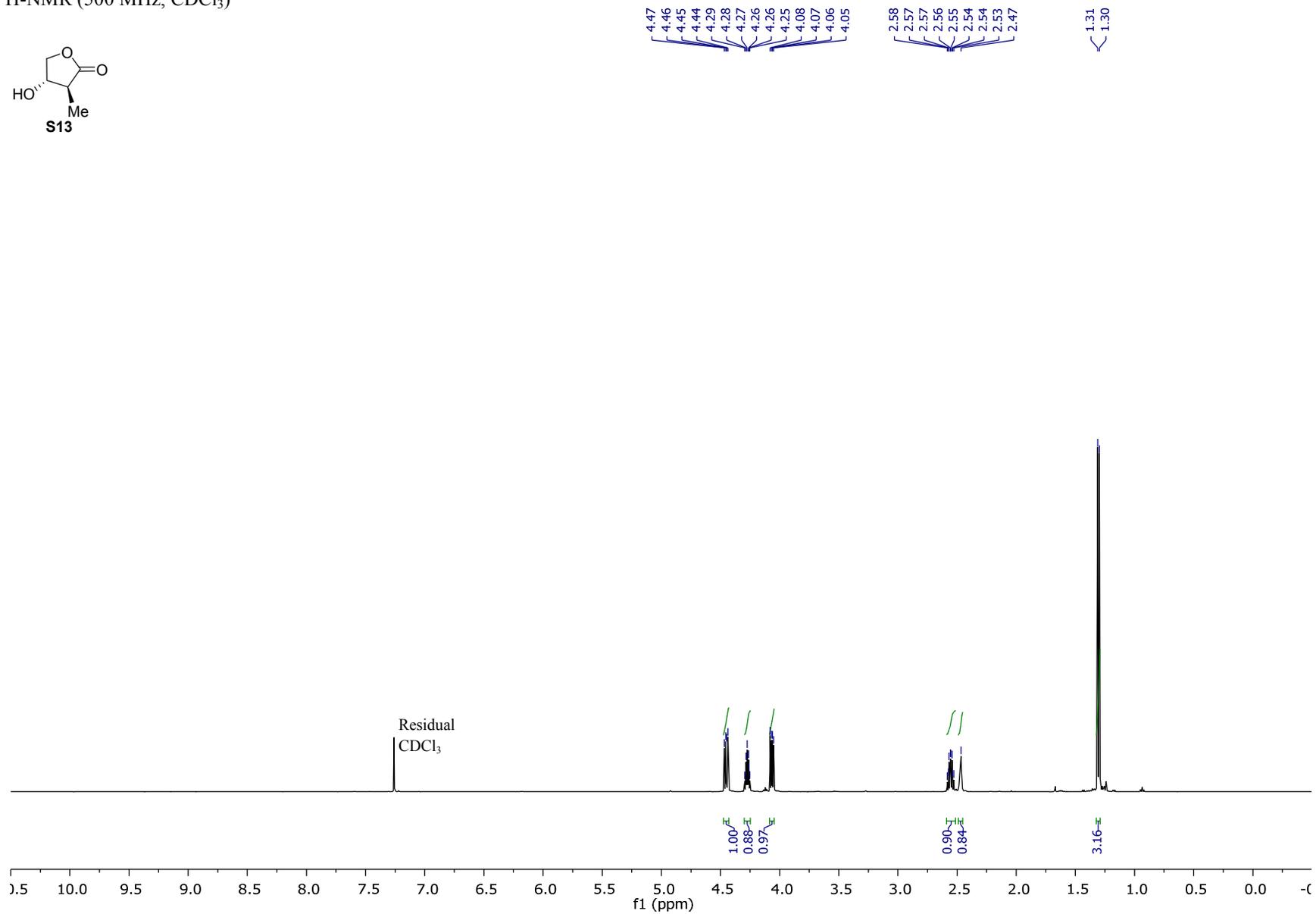
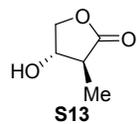
<sup>1</sup>H-NMR (500 MHz, CD<sub>3</sub>OD)



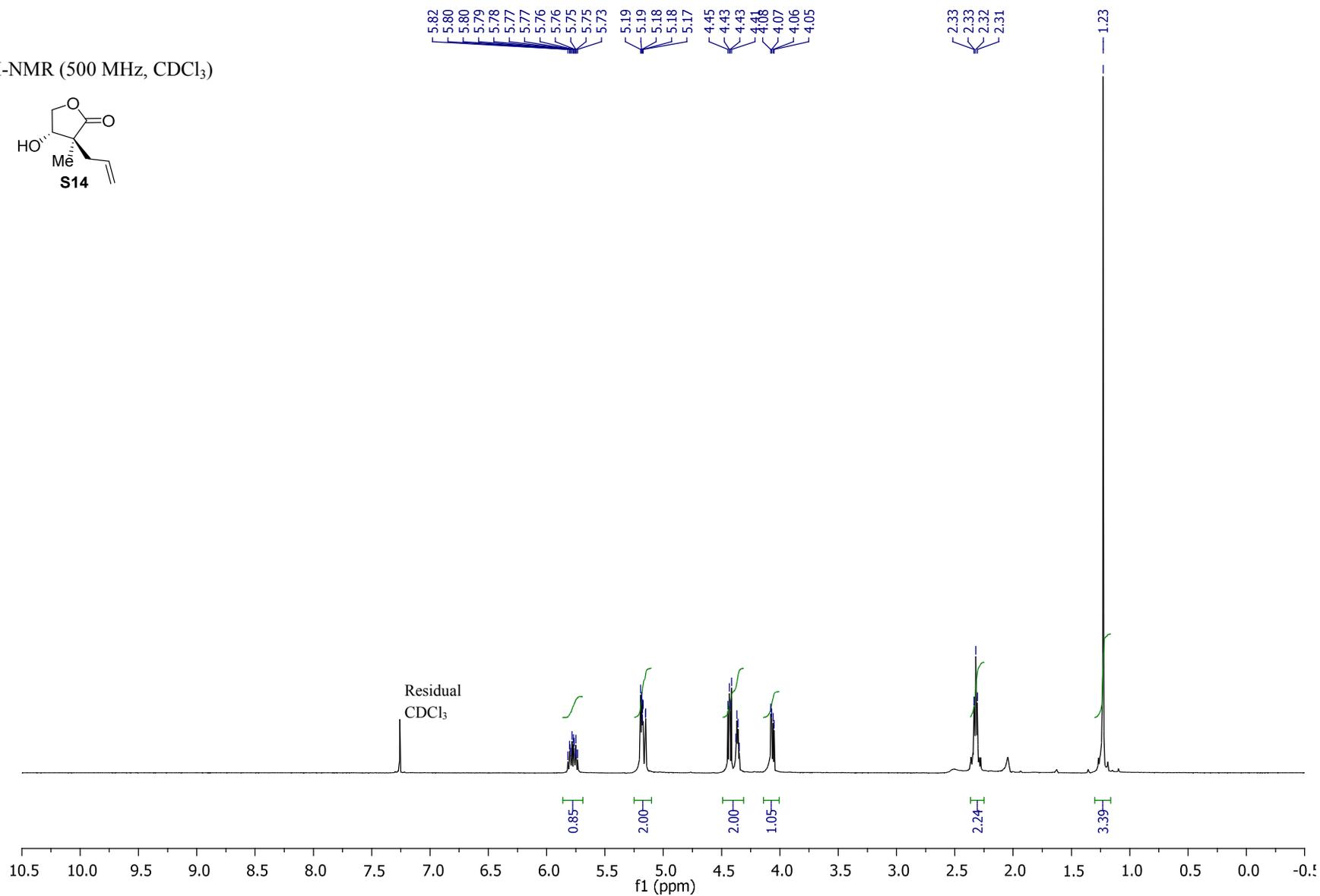
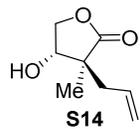
7.96  
6.50  
6.49  
6.45  
6.44  
4.95  
4.94  
4.84  
4.83  
3.91  
3.90  
3.90  
3.89  
3.88  
3.88  
3.71  
3.71  
3.63  
3.60  
3.53  
3.53  
3.51  
3.50  
3.30  
3.29  
3.28  
3.27  
1.91  
1.23  
1.23



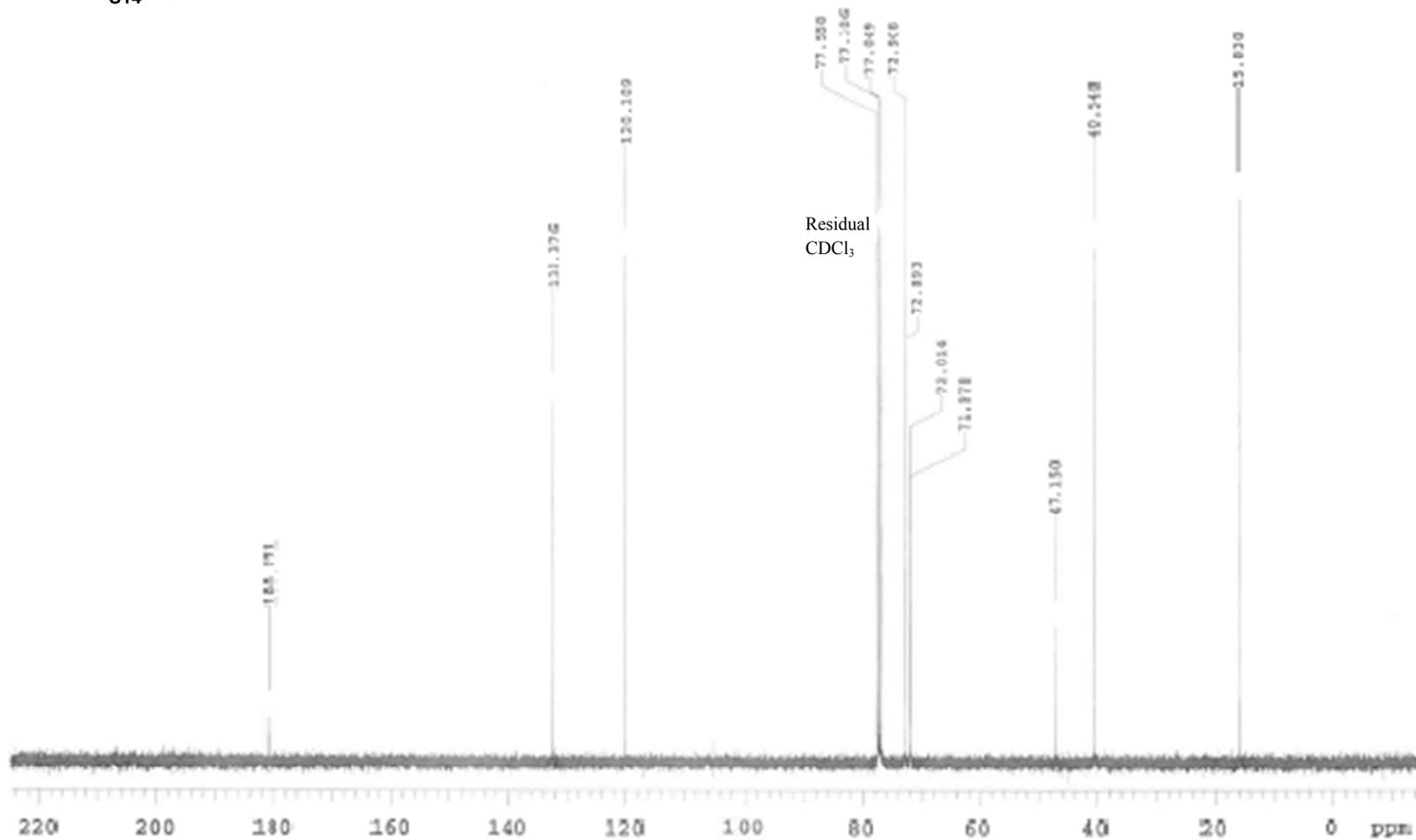
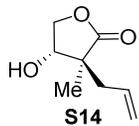


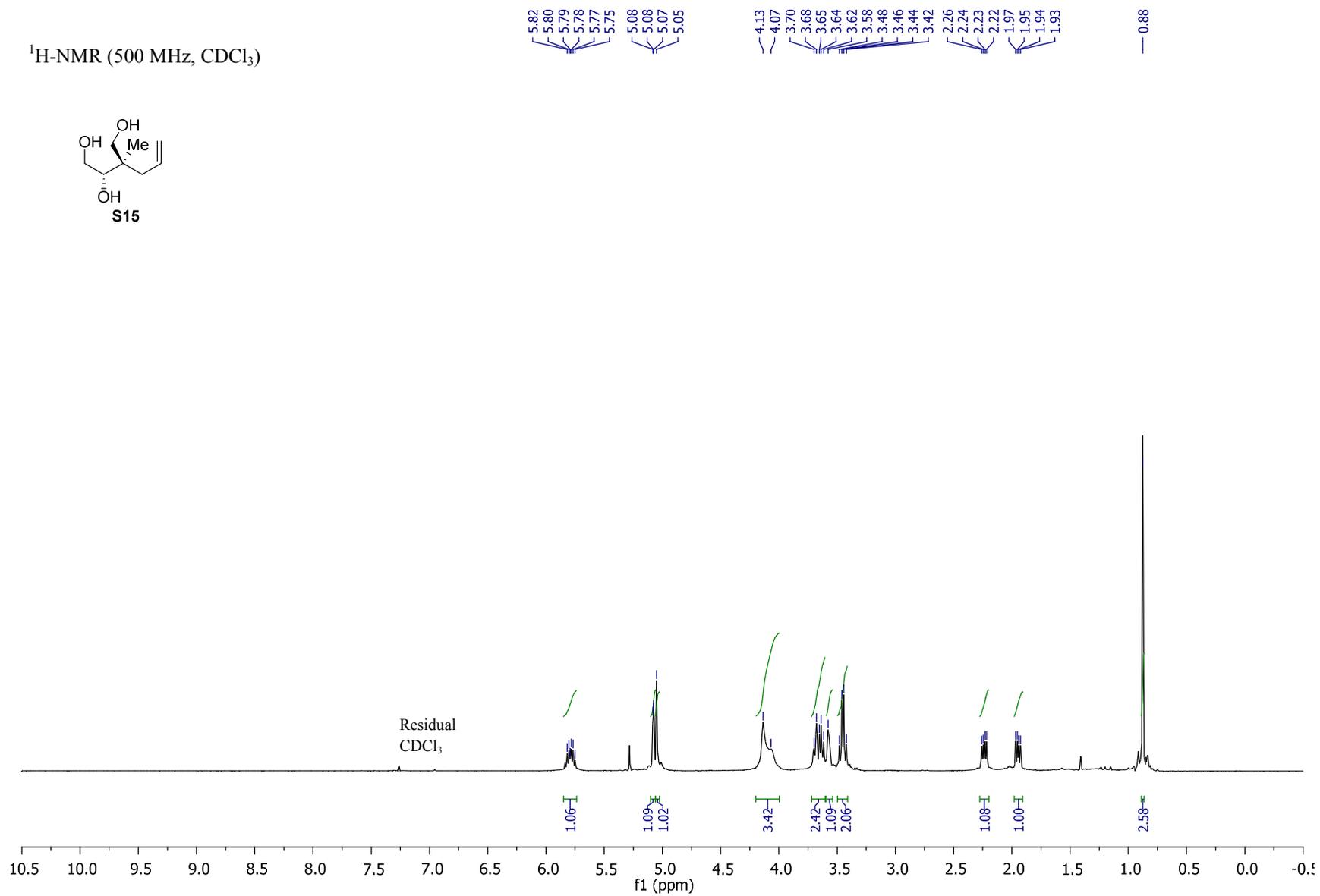
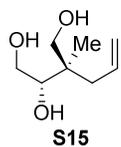
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

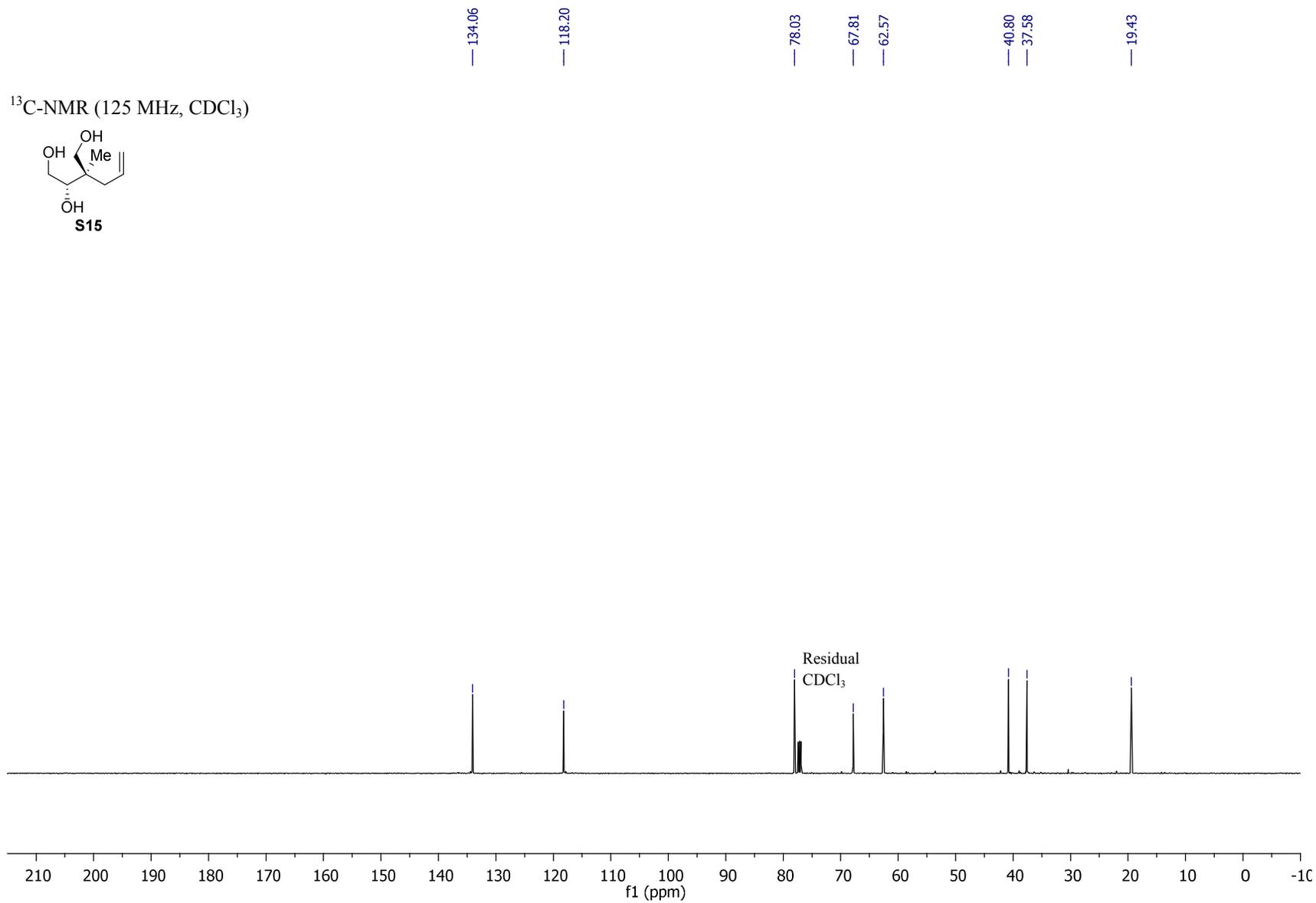
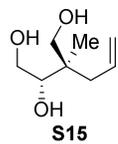
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

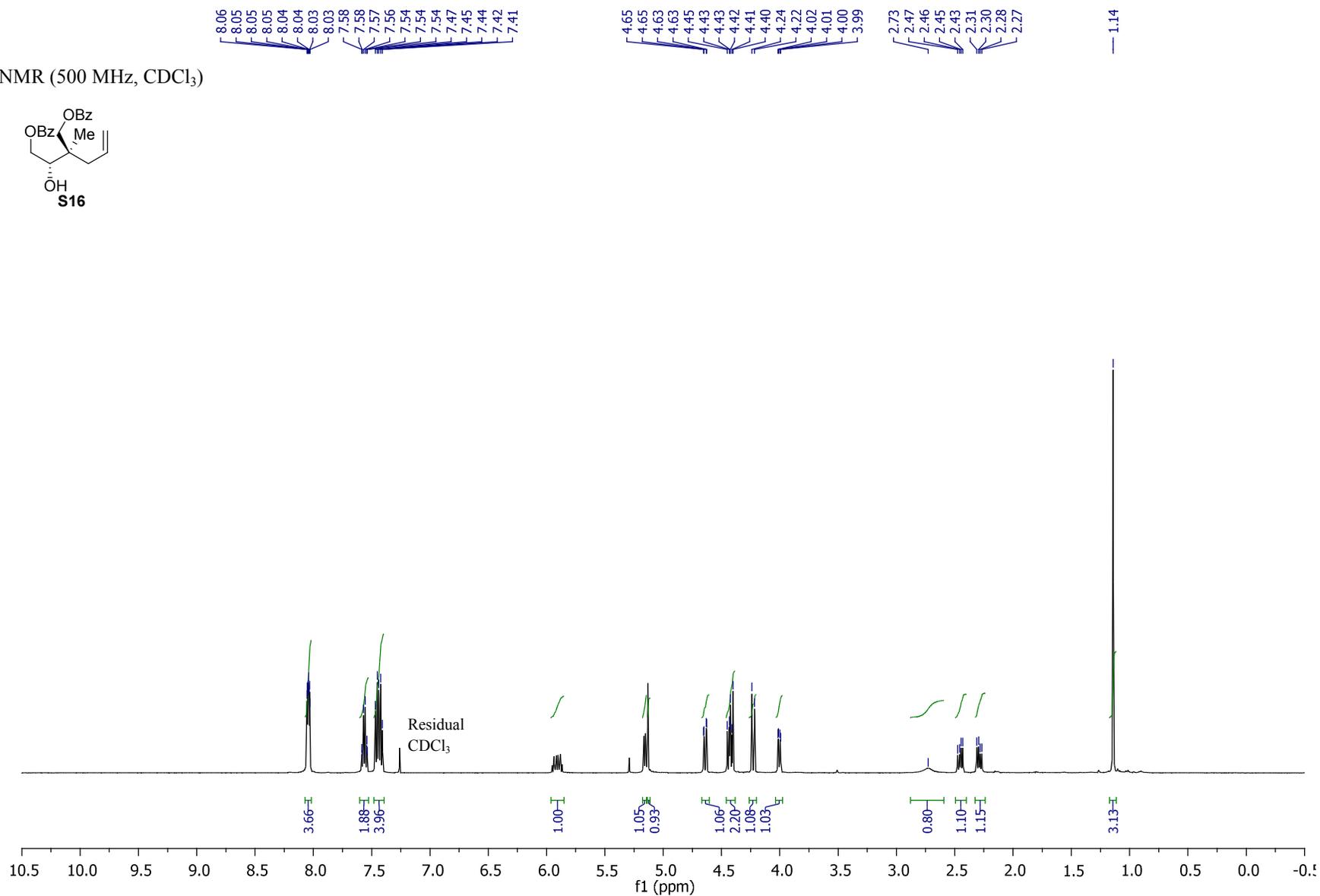
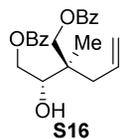


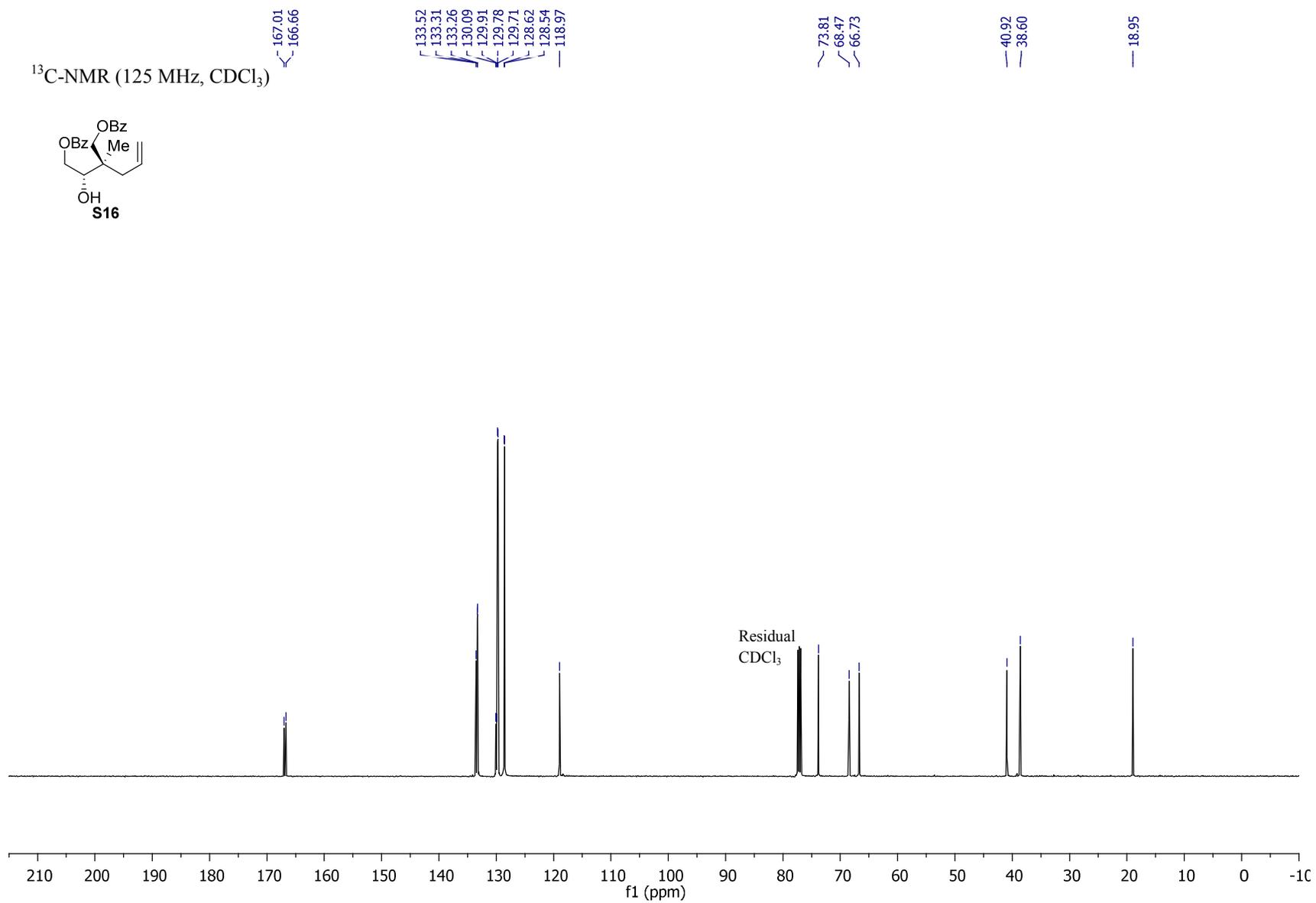
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

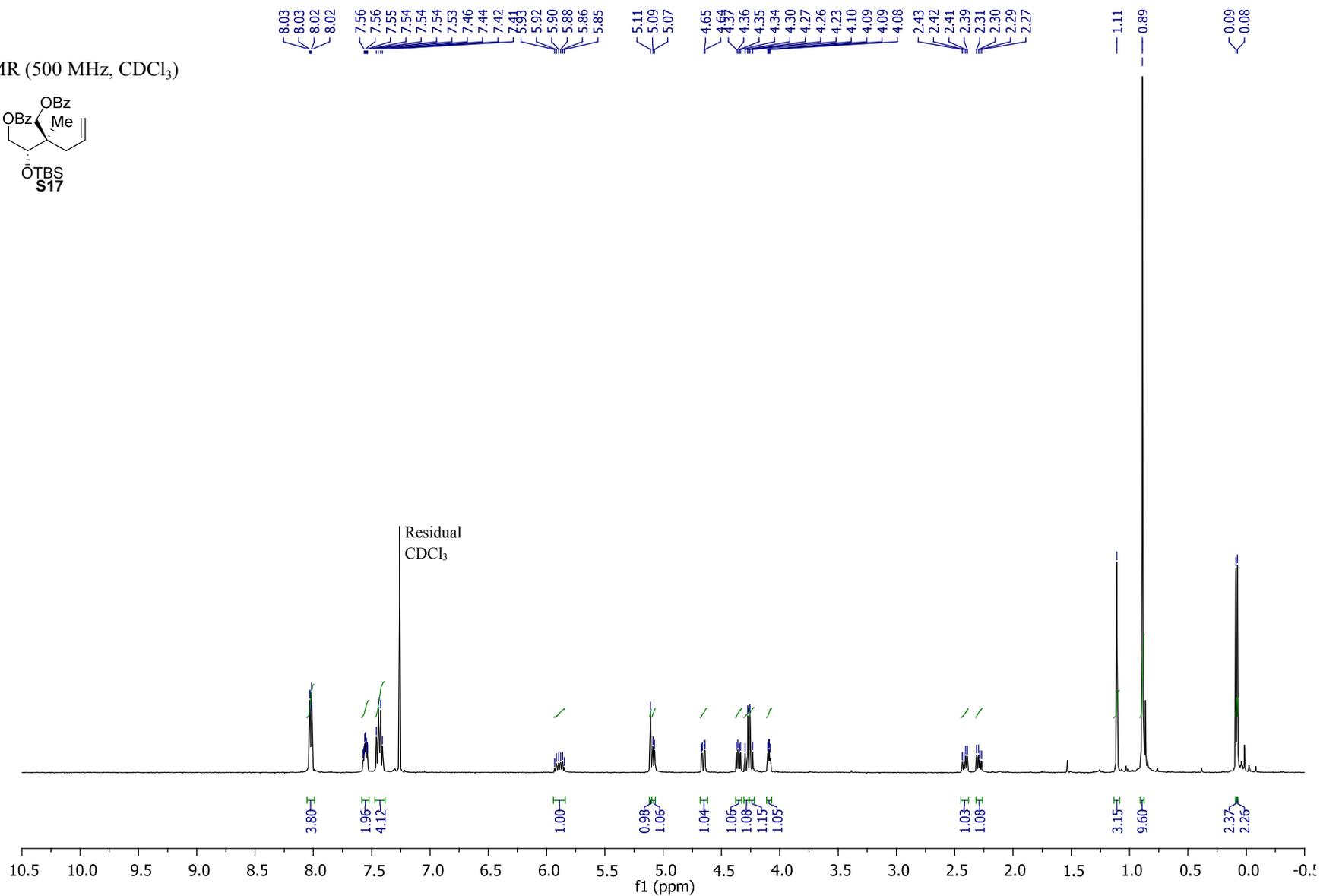
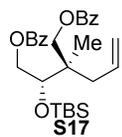


$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

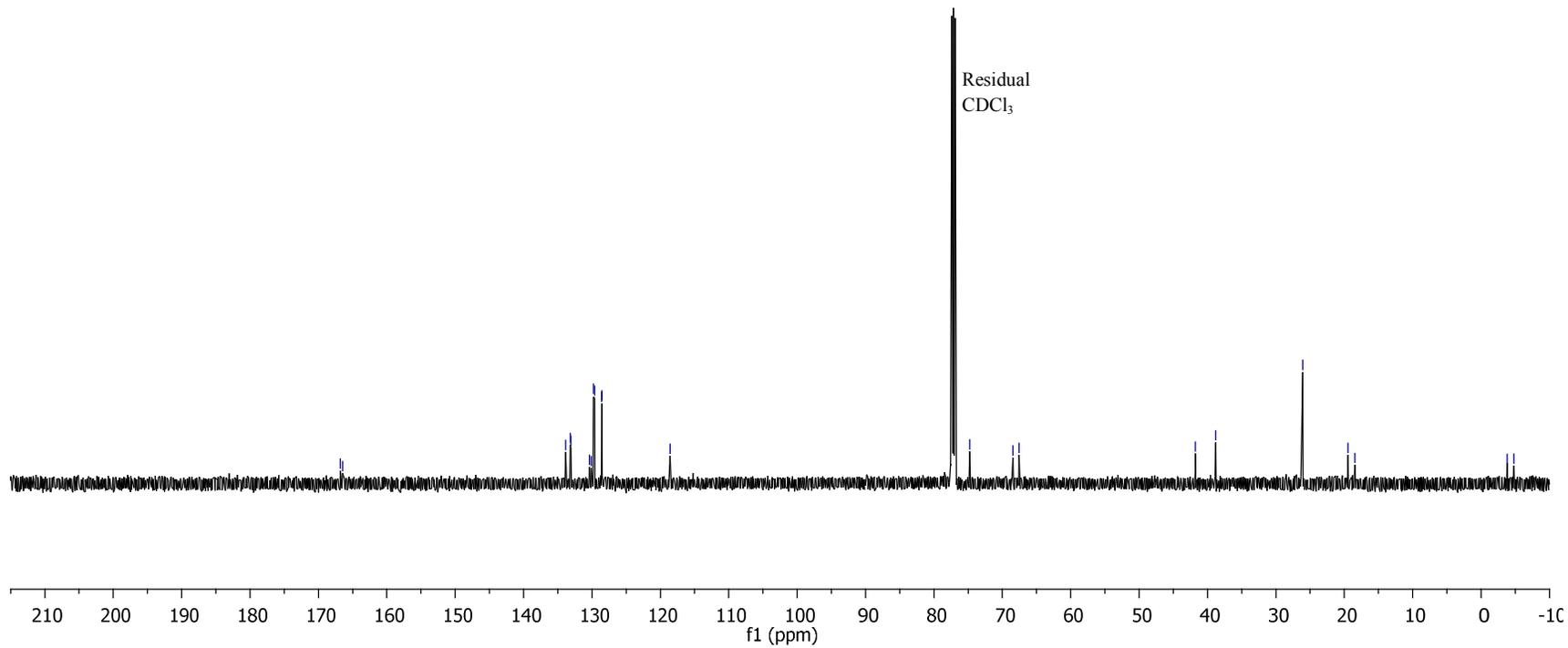
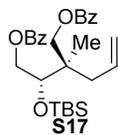
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



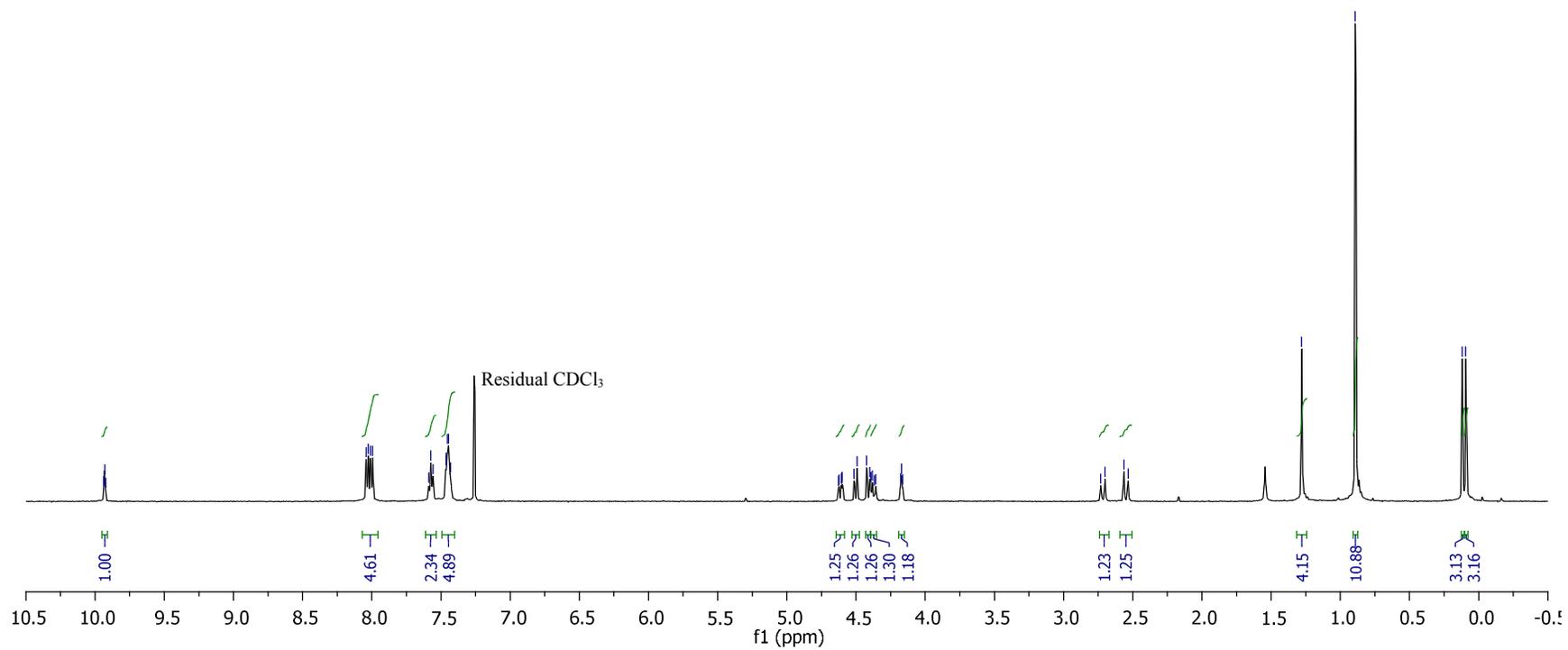
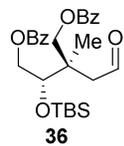
<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>)



9.94  
9.93  
9.928.04  
8.02  
8.01  
7.99  
7.59  
7.57  
7.56  
7.46  
7.46  
7.45  
7.44  
7.434.63  
4.62  
4.61  
4.60  
4.60  
4.51  
4.49  
4.42  
4.40  
4.39  
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2.70  
2.56  
2.53

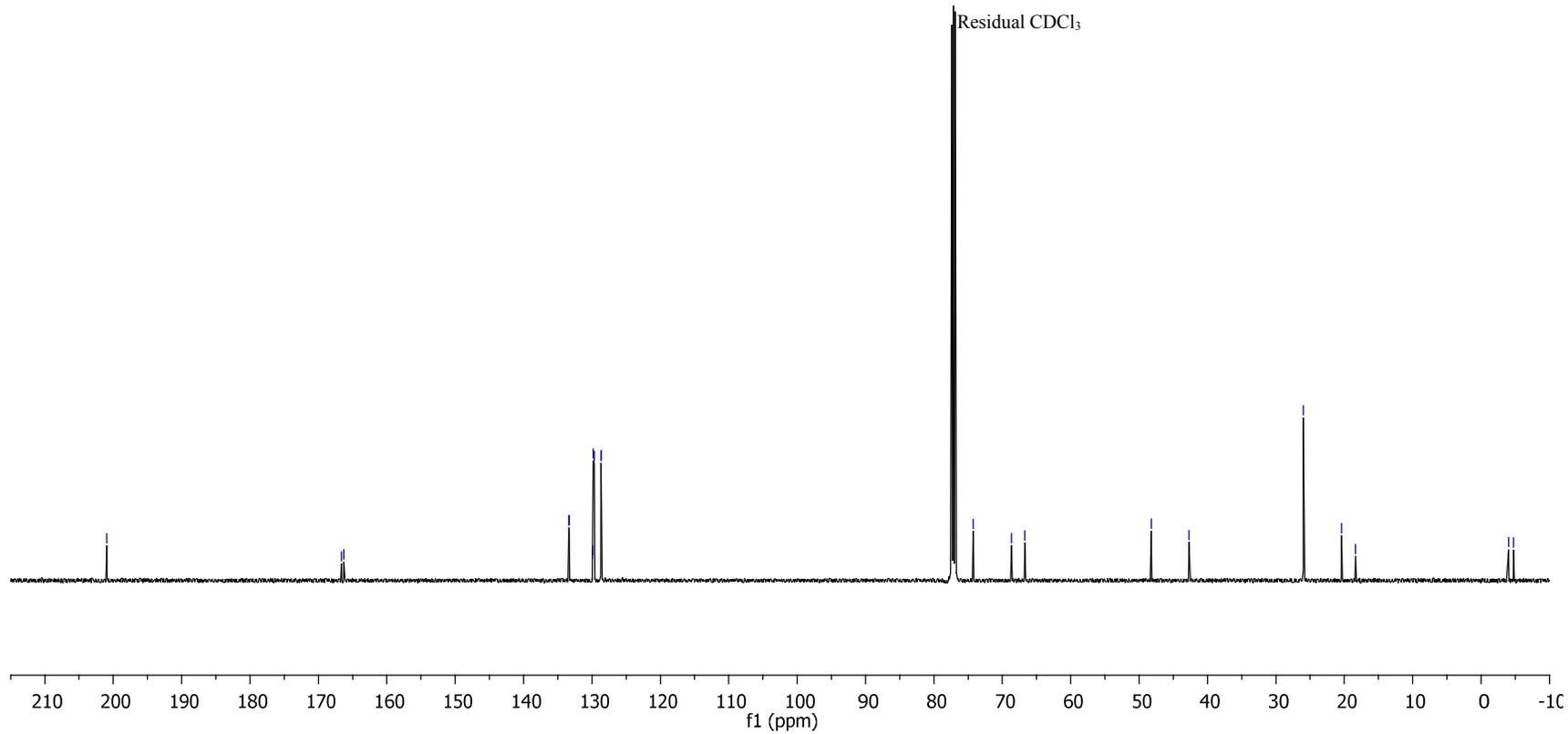
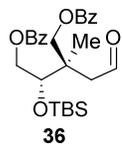
1.28

0.89

0.12  
0.09 $^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



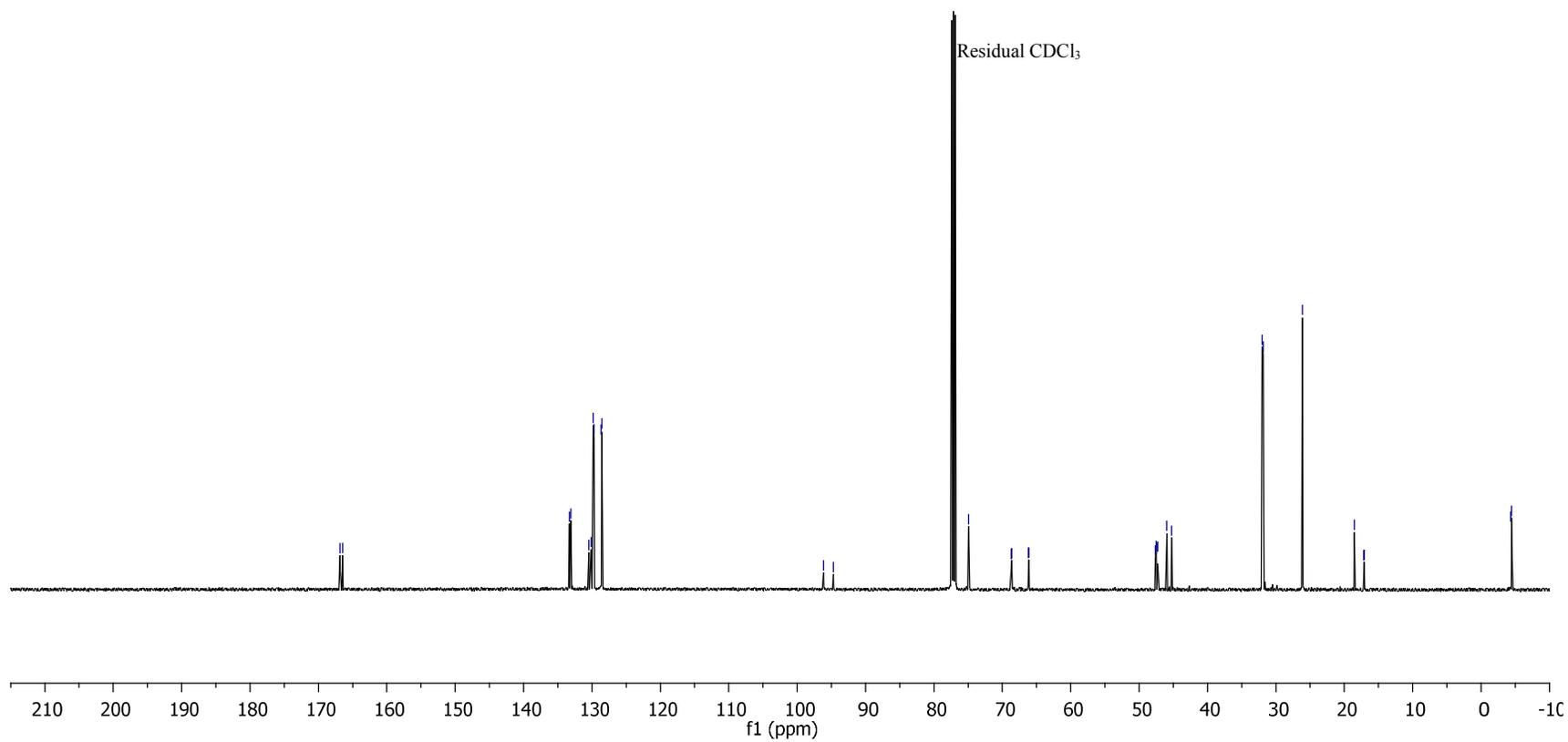
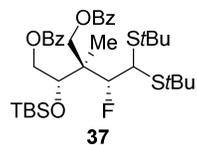
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

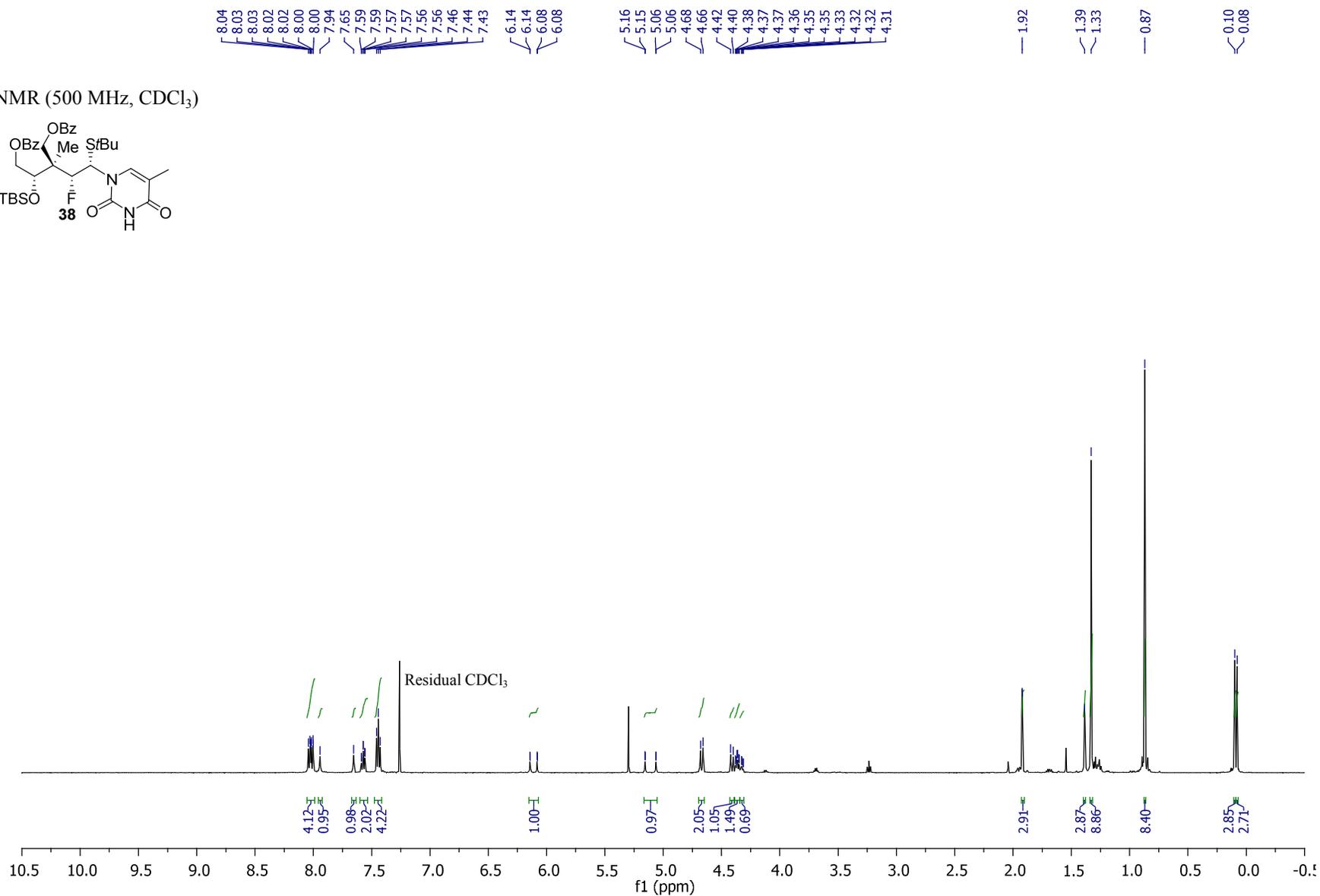
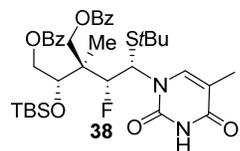


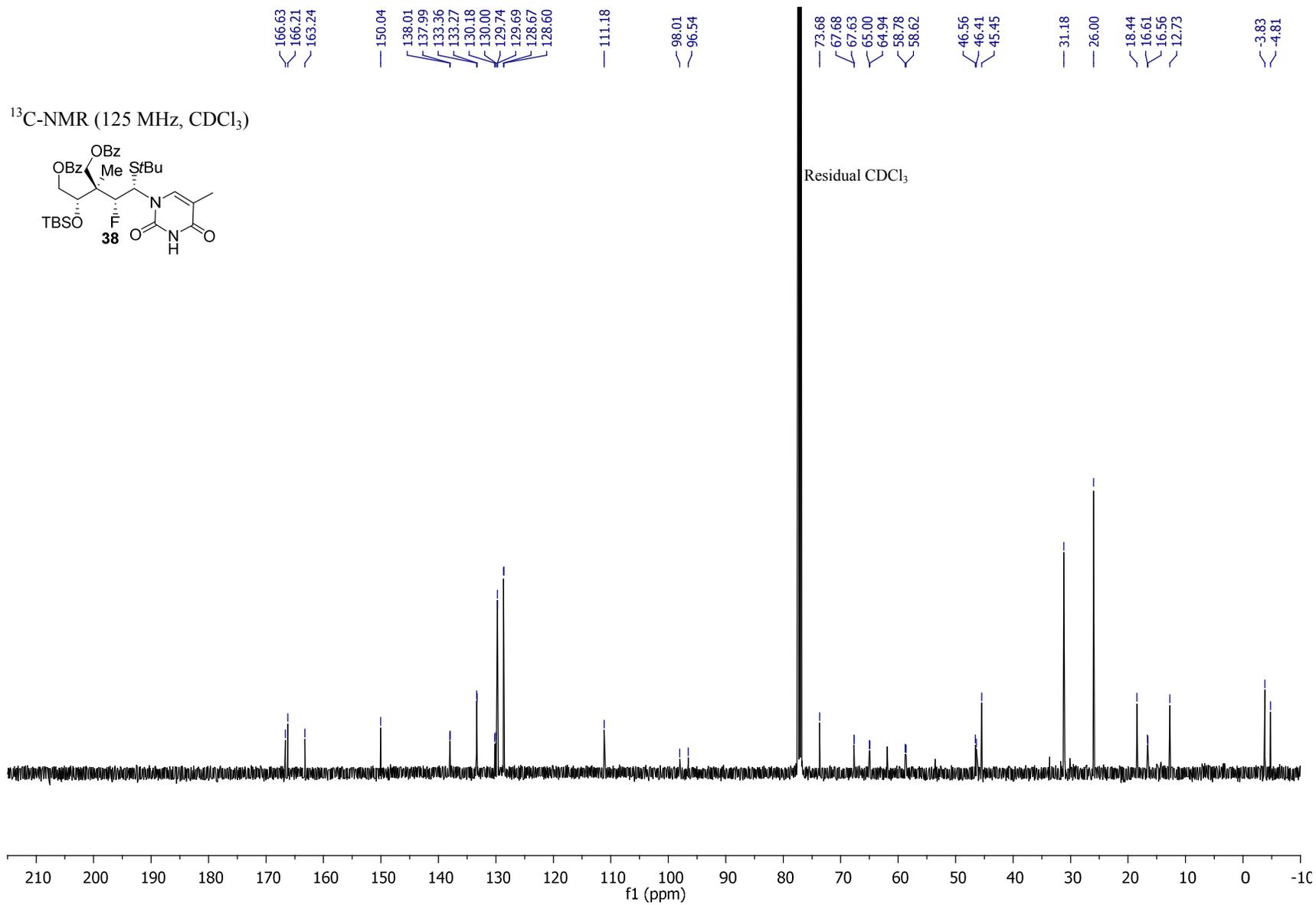
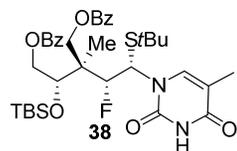




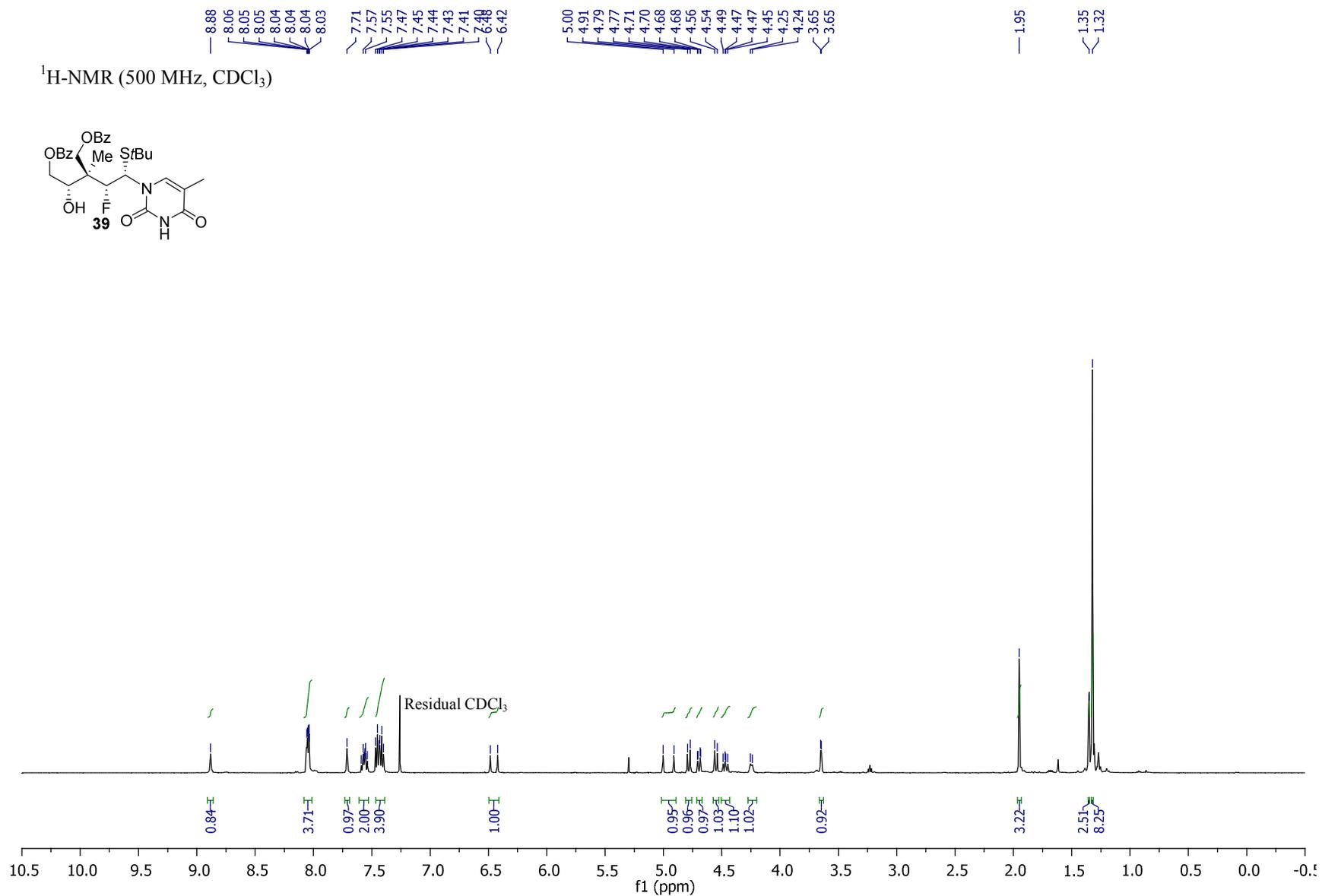
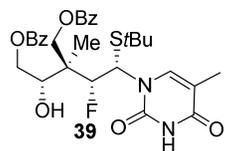
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

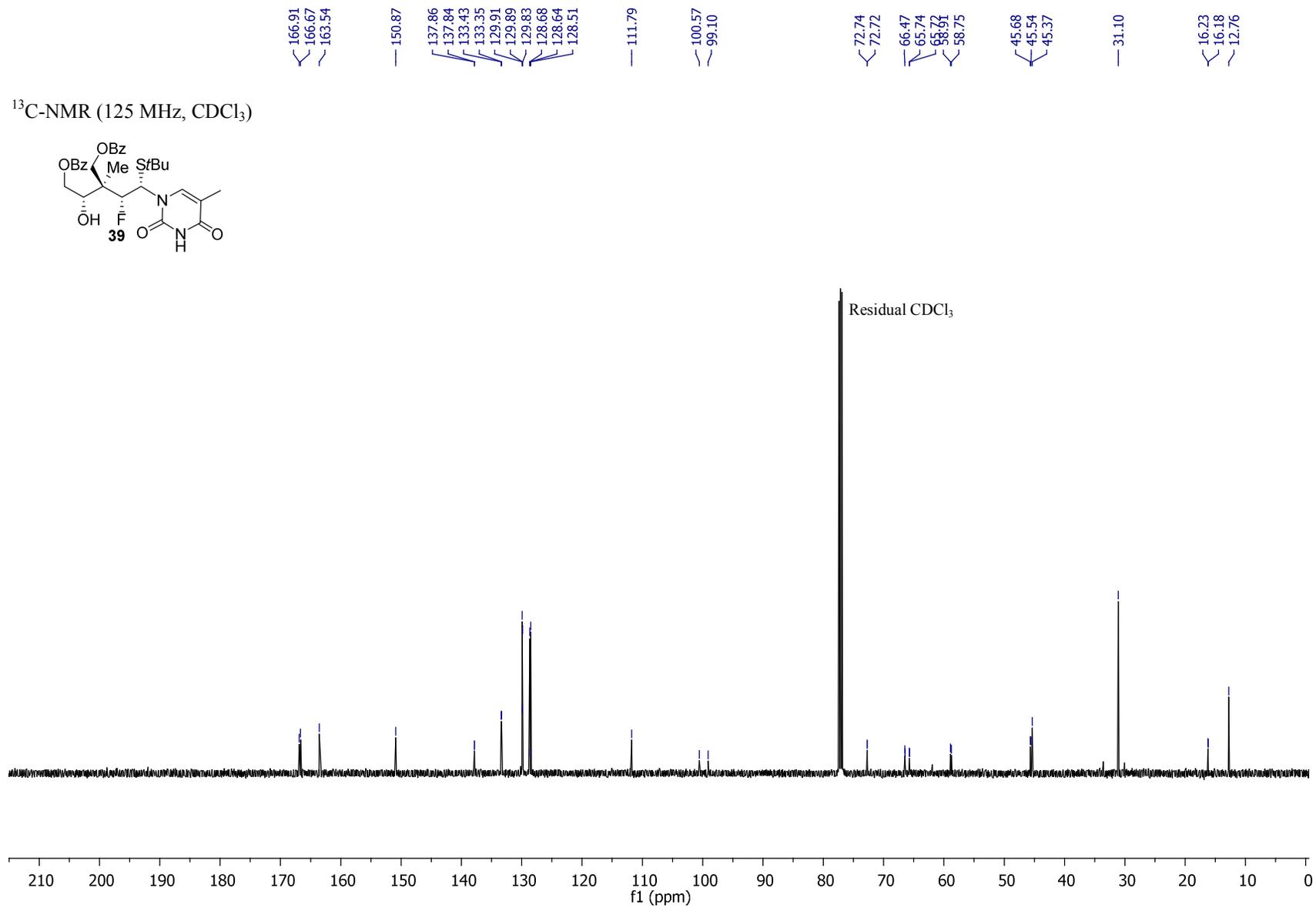


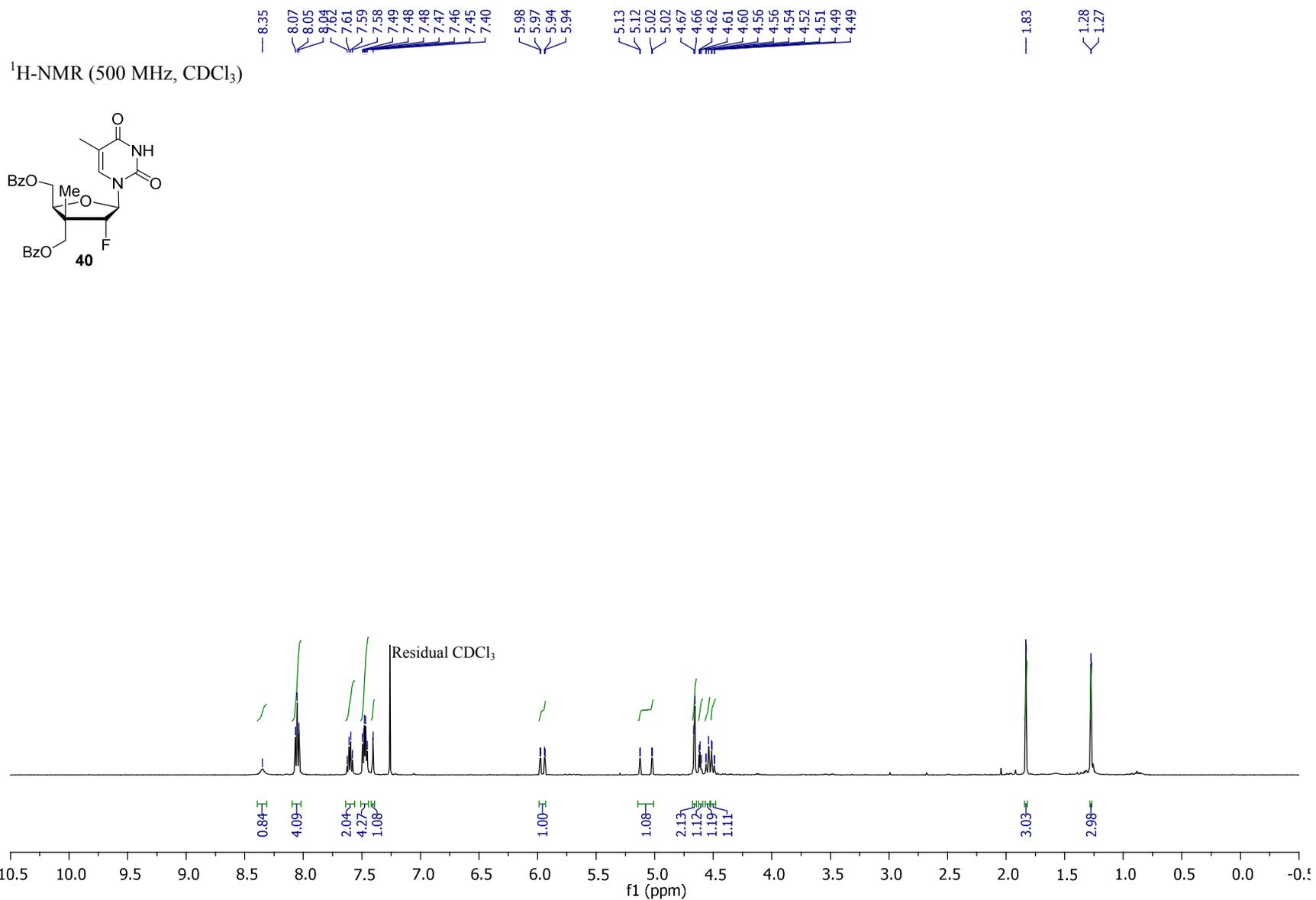
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

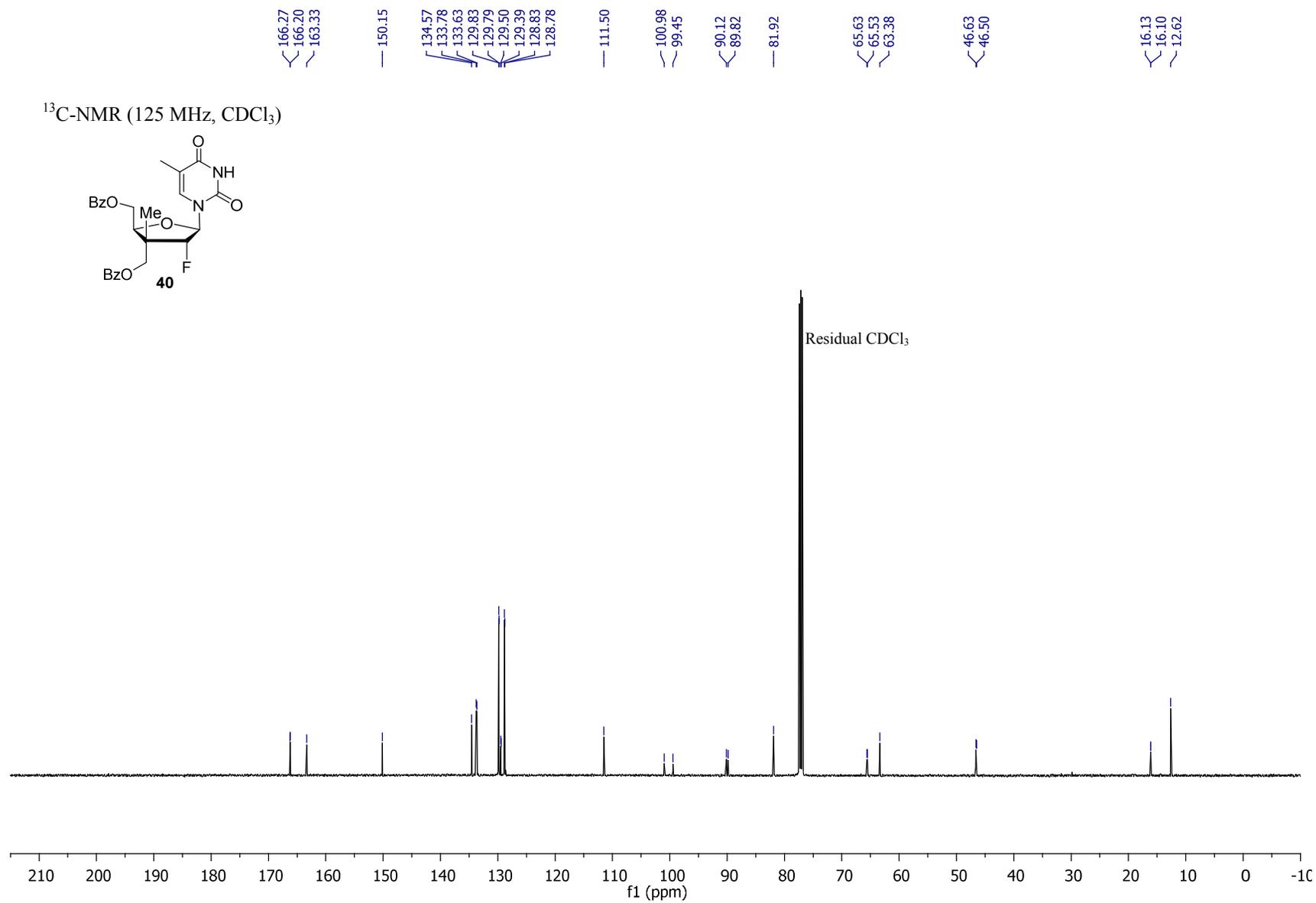
$^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ )

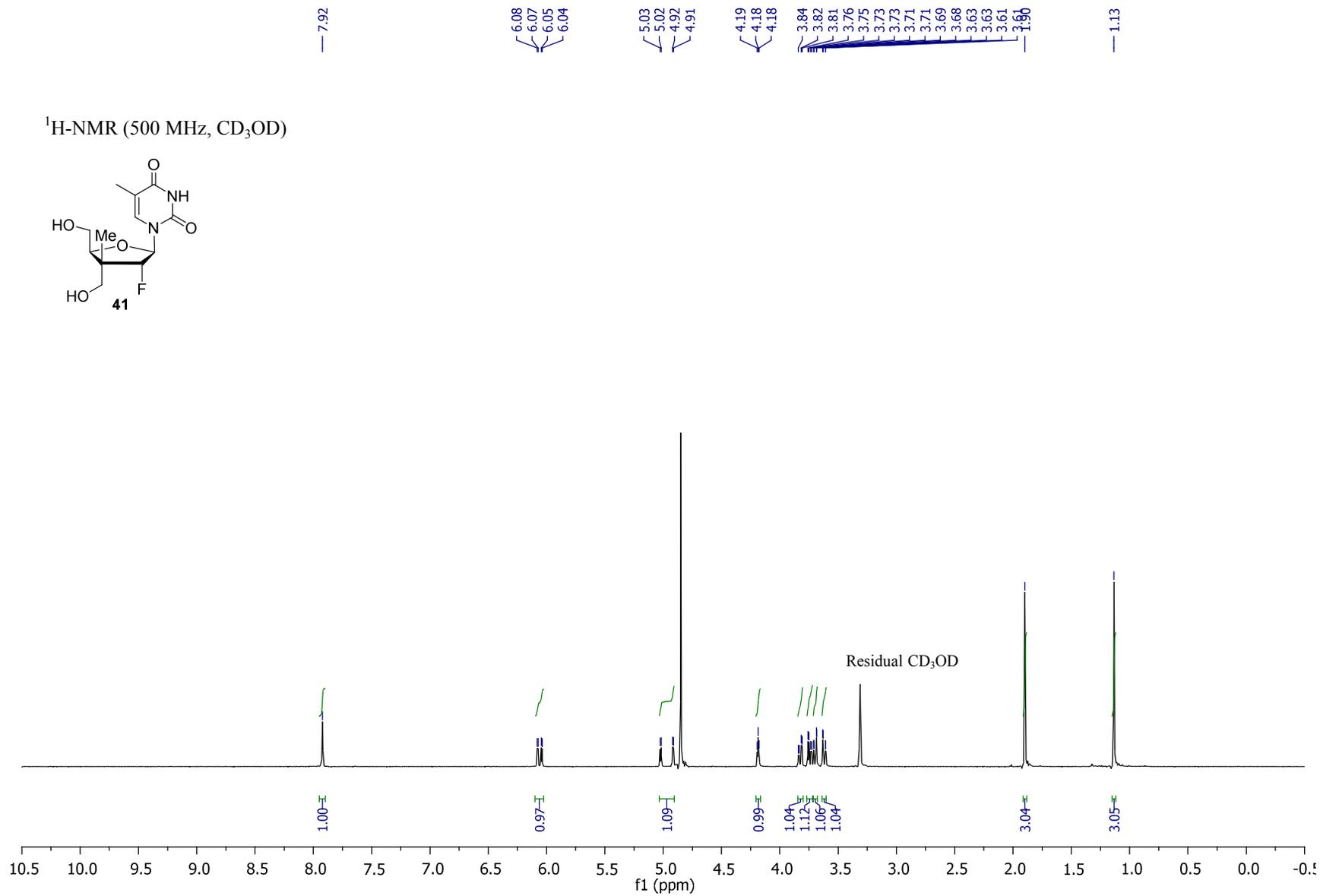
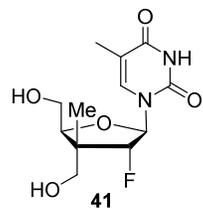
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

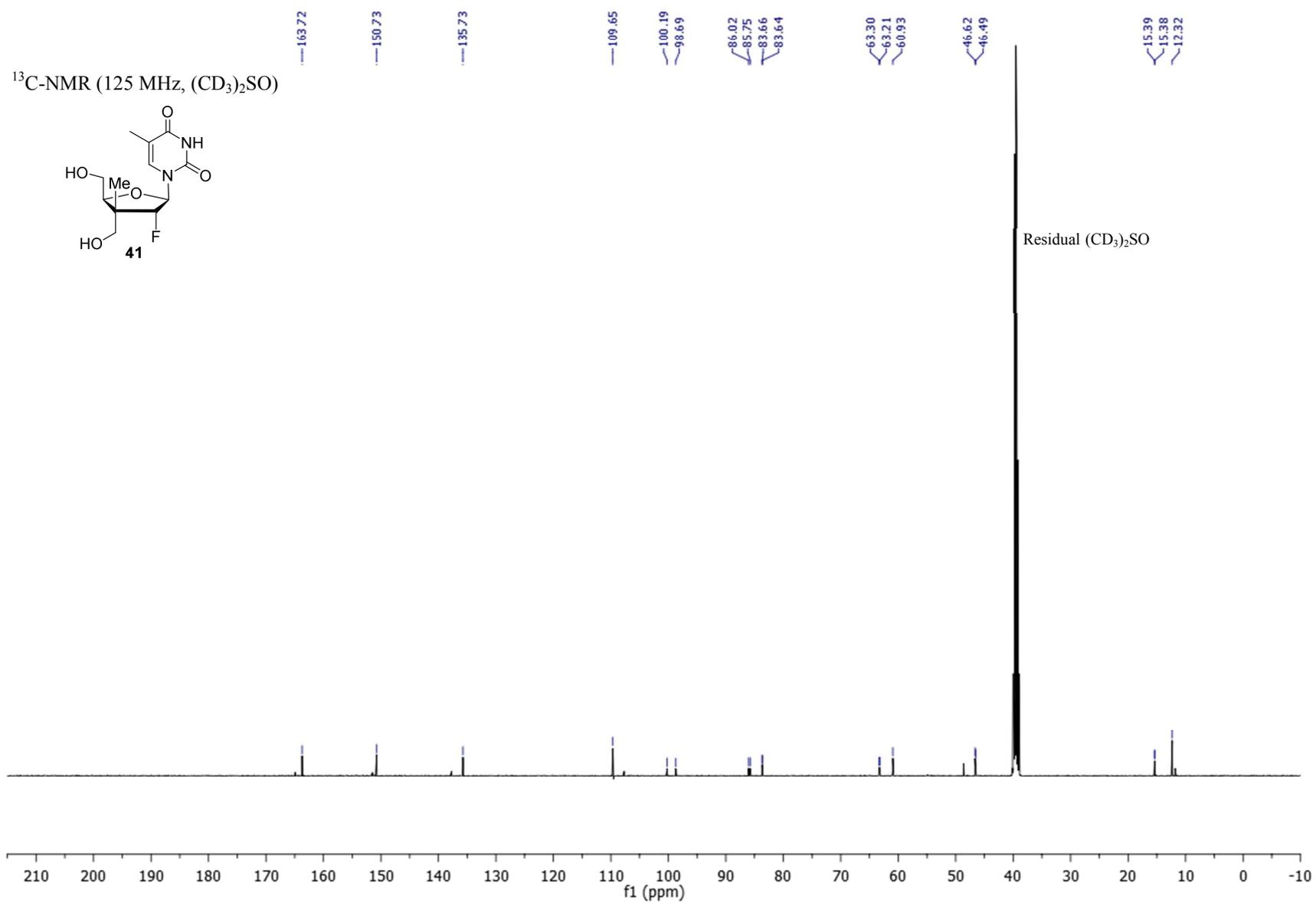


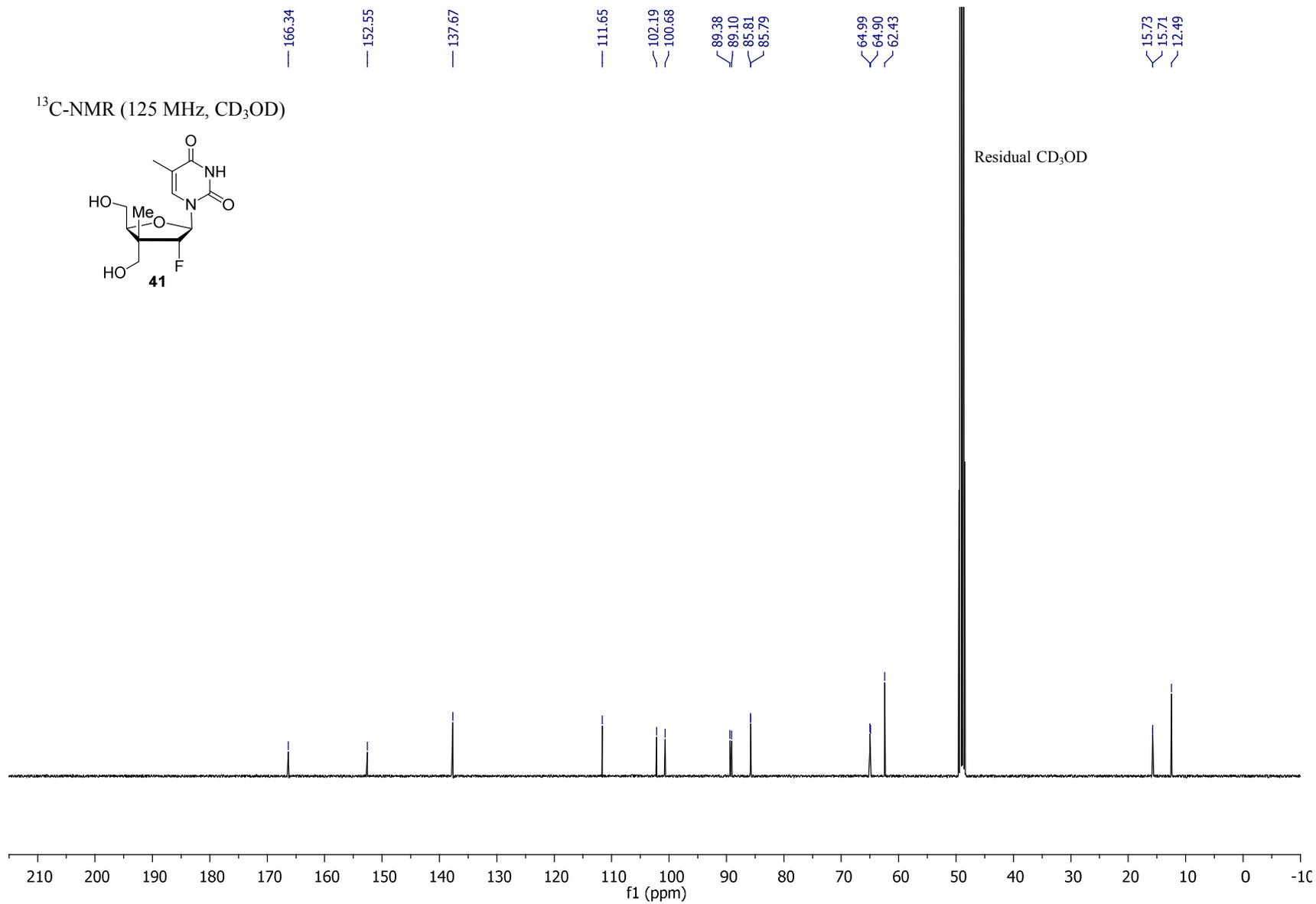






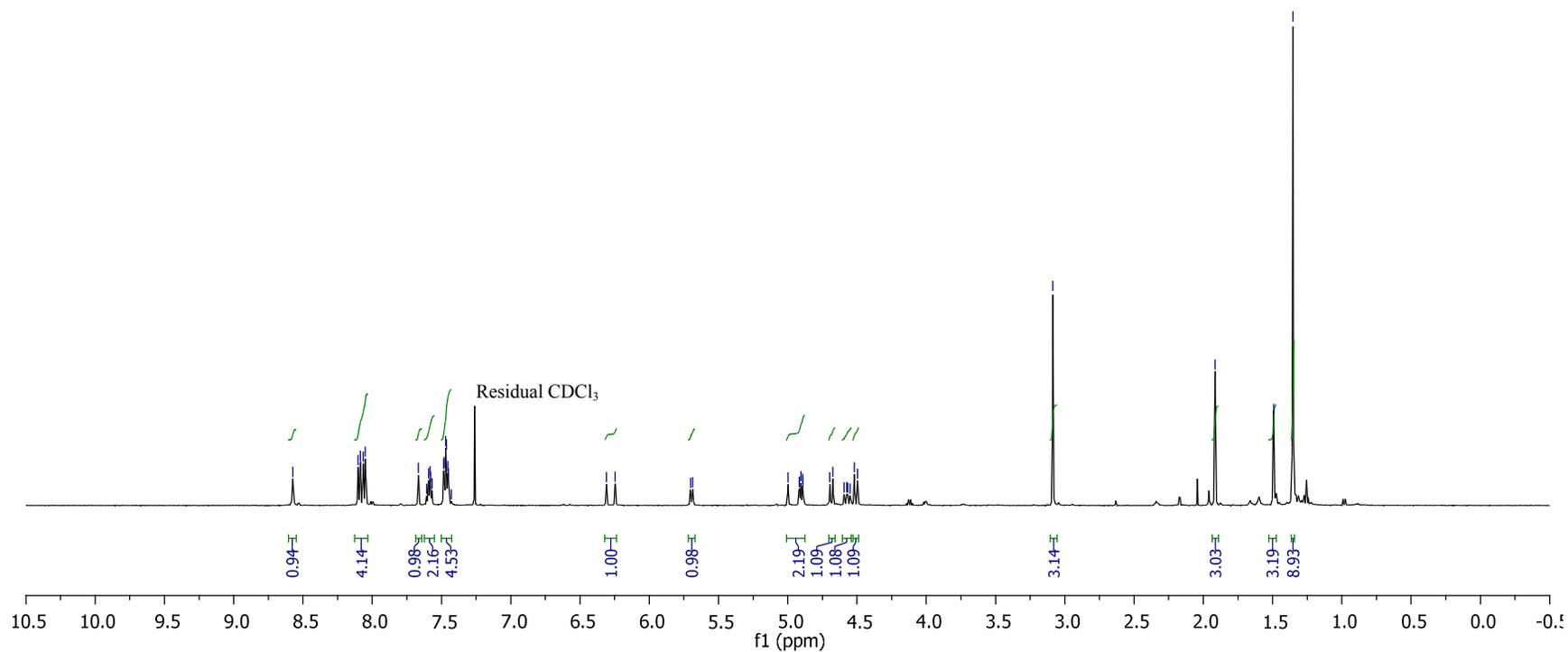
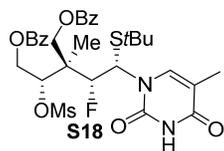
$^1\text{H-NMR}$  (500 MHz,  $\text{CD}_3\text{OD}$ )





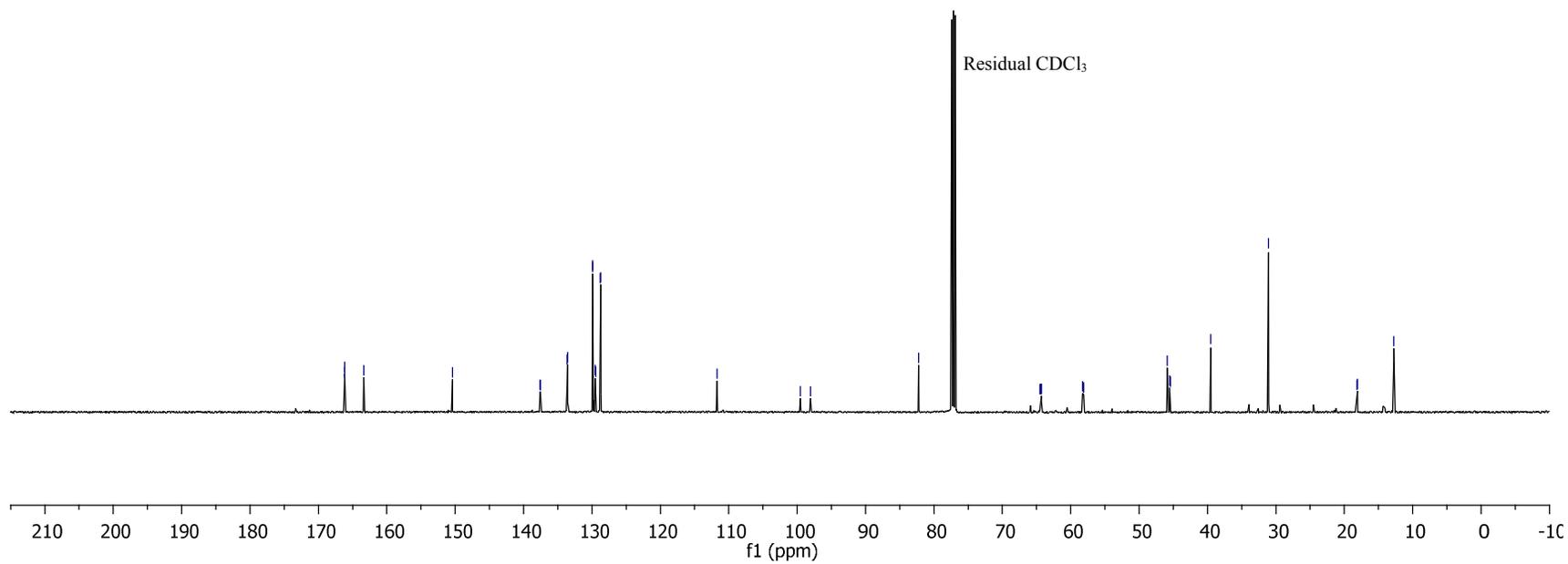
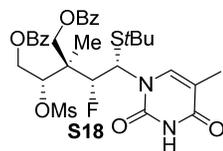


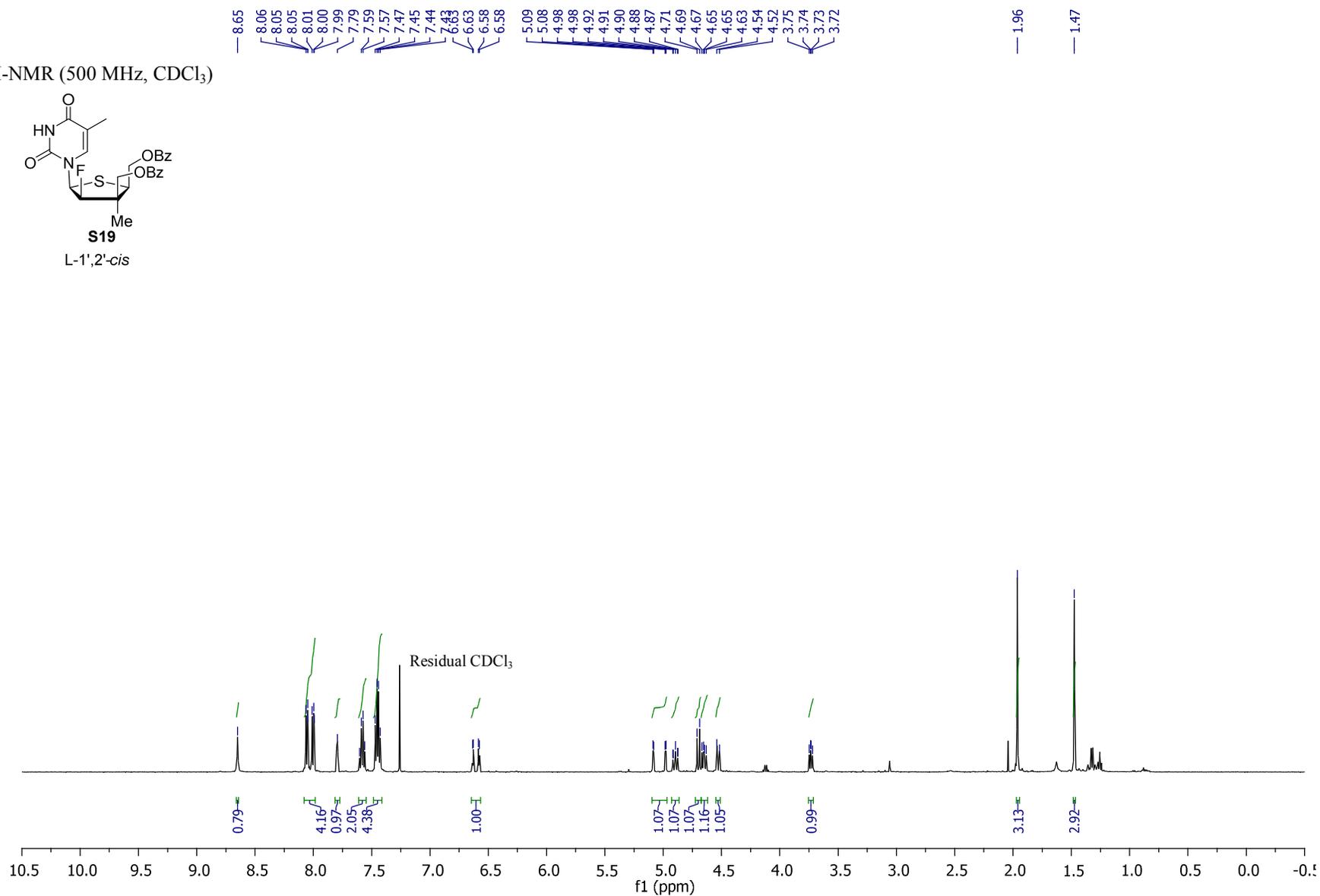
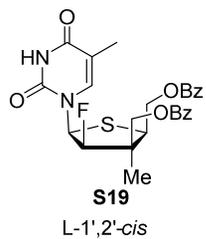
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

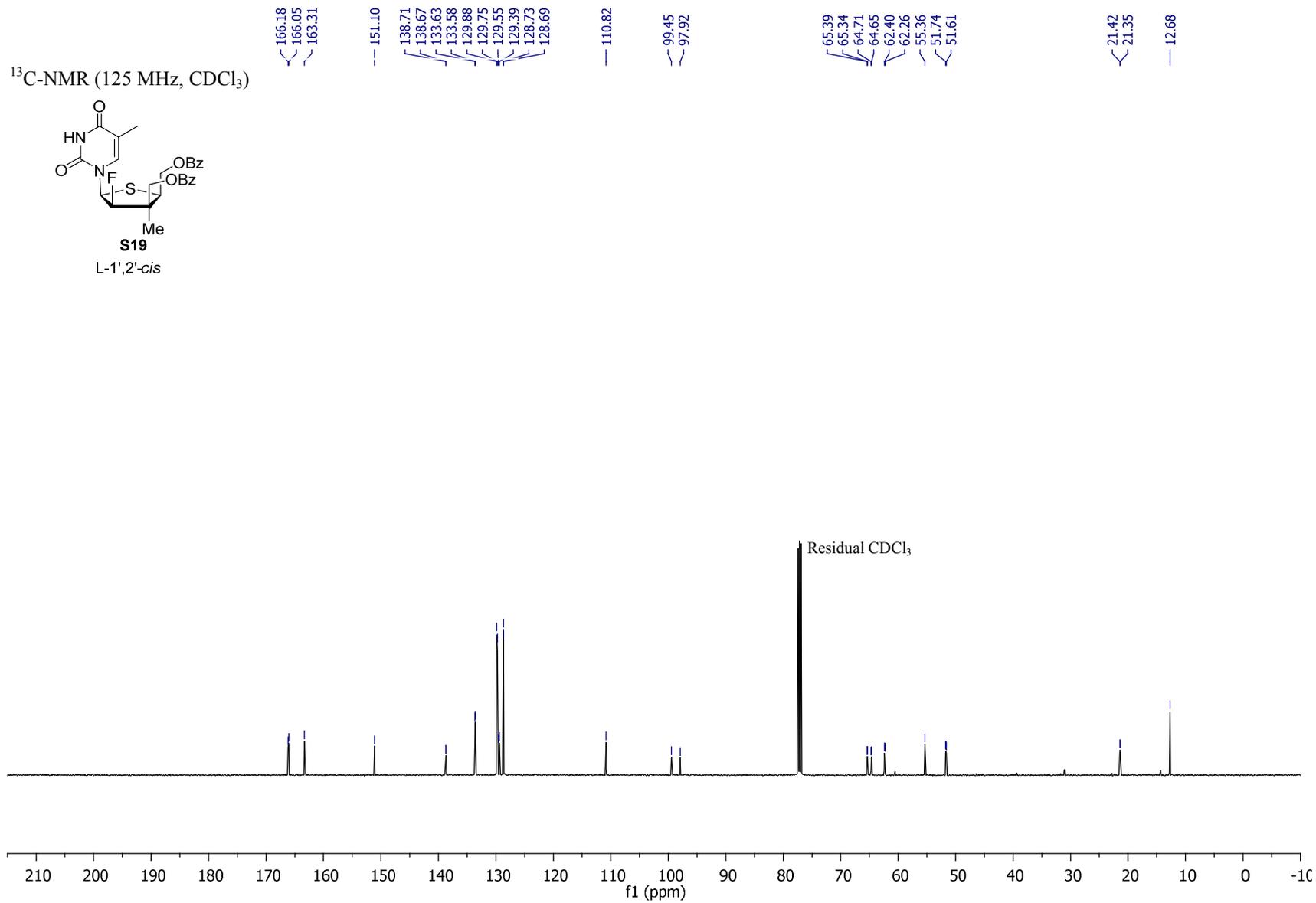


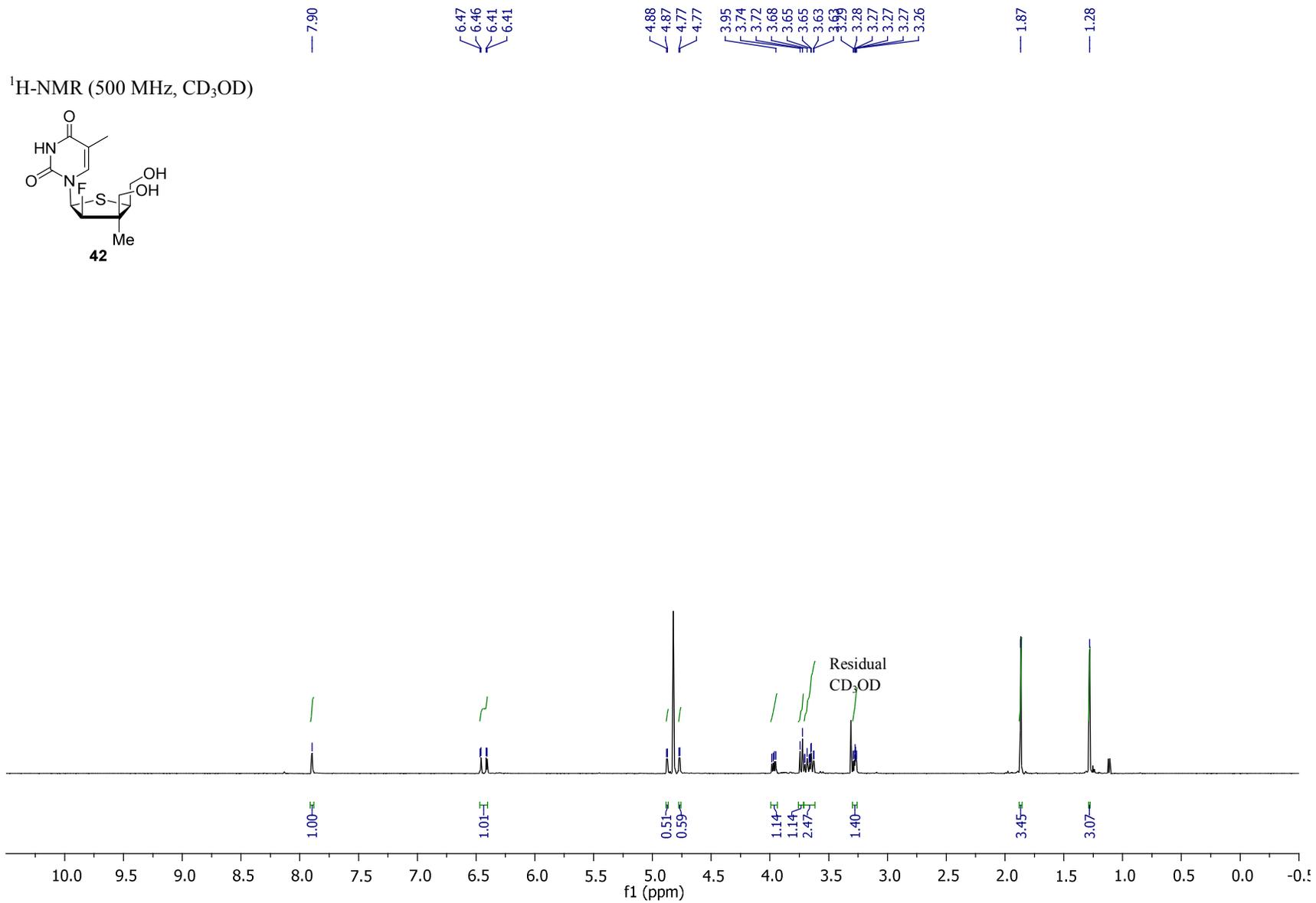


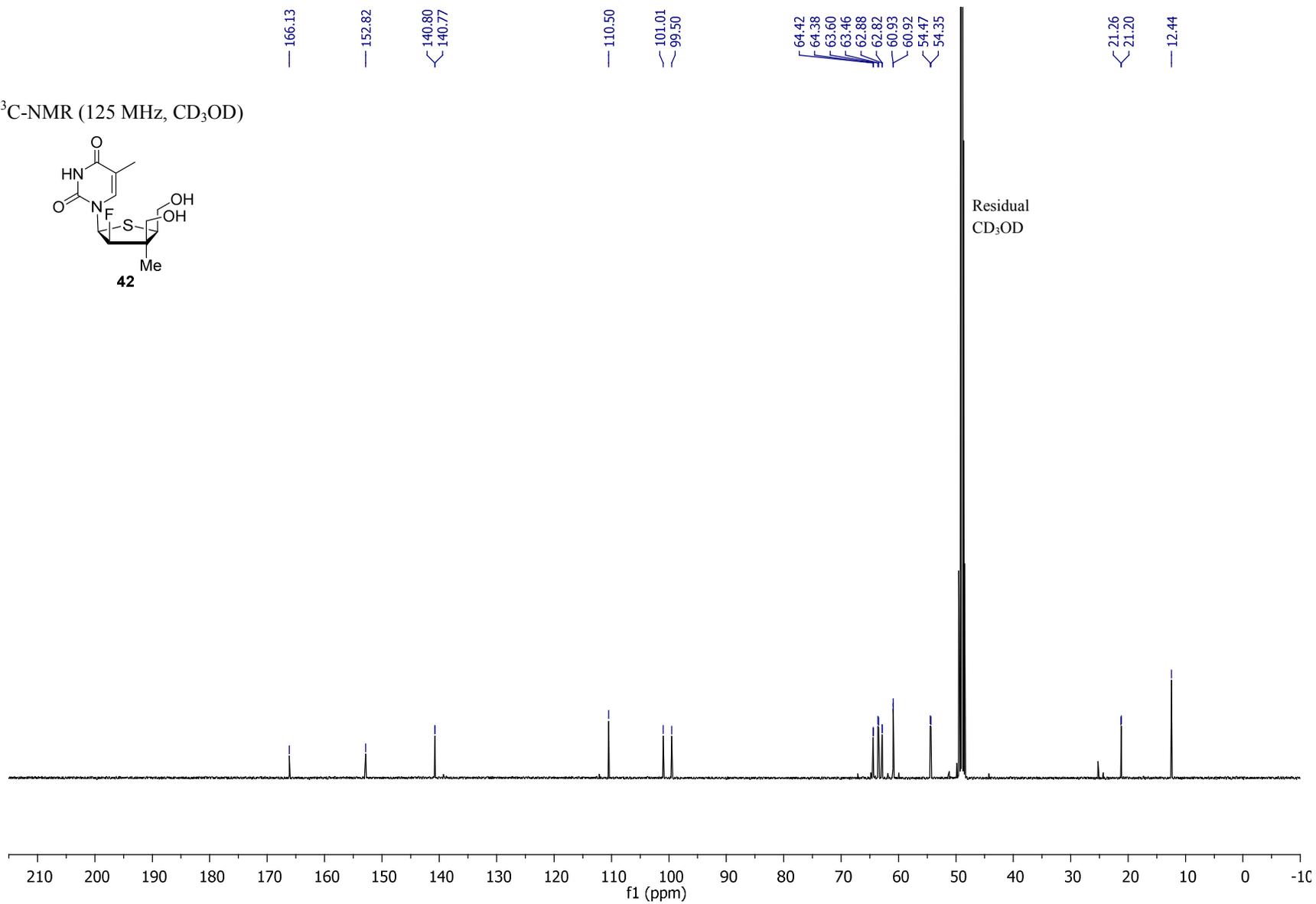
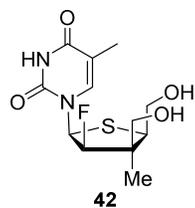
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

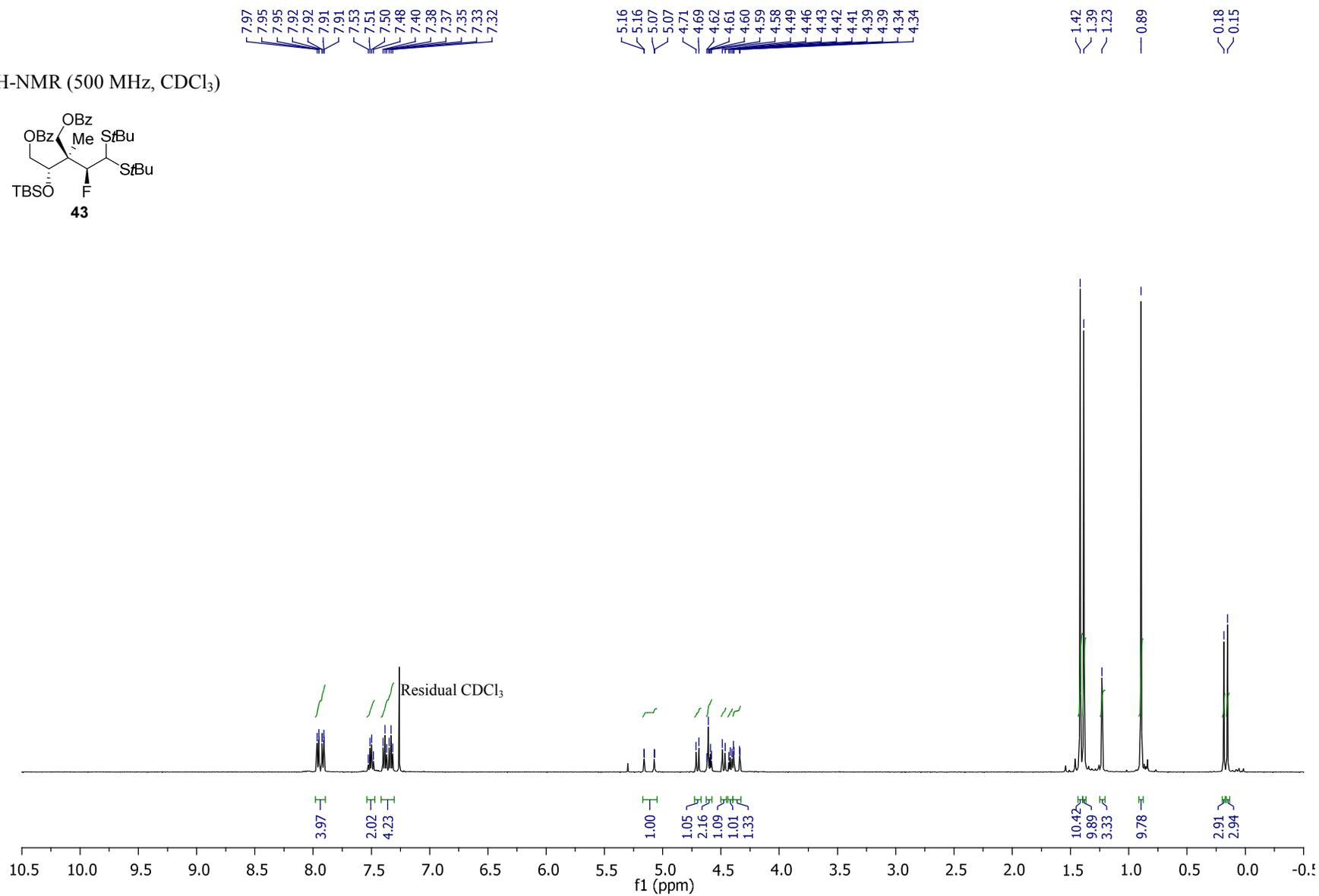
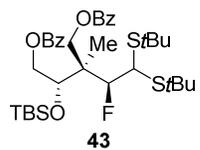


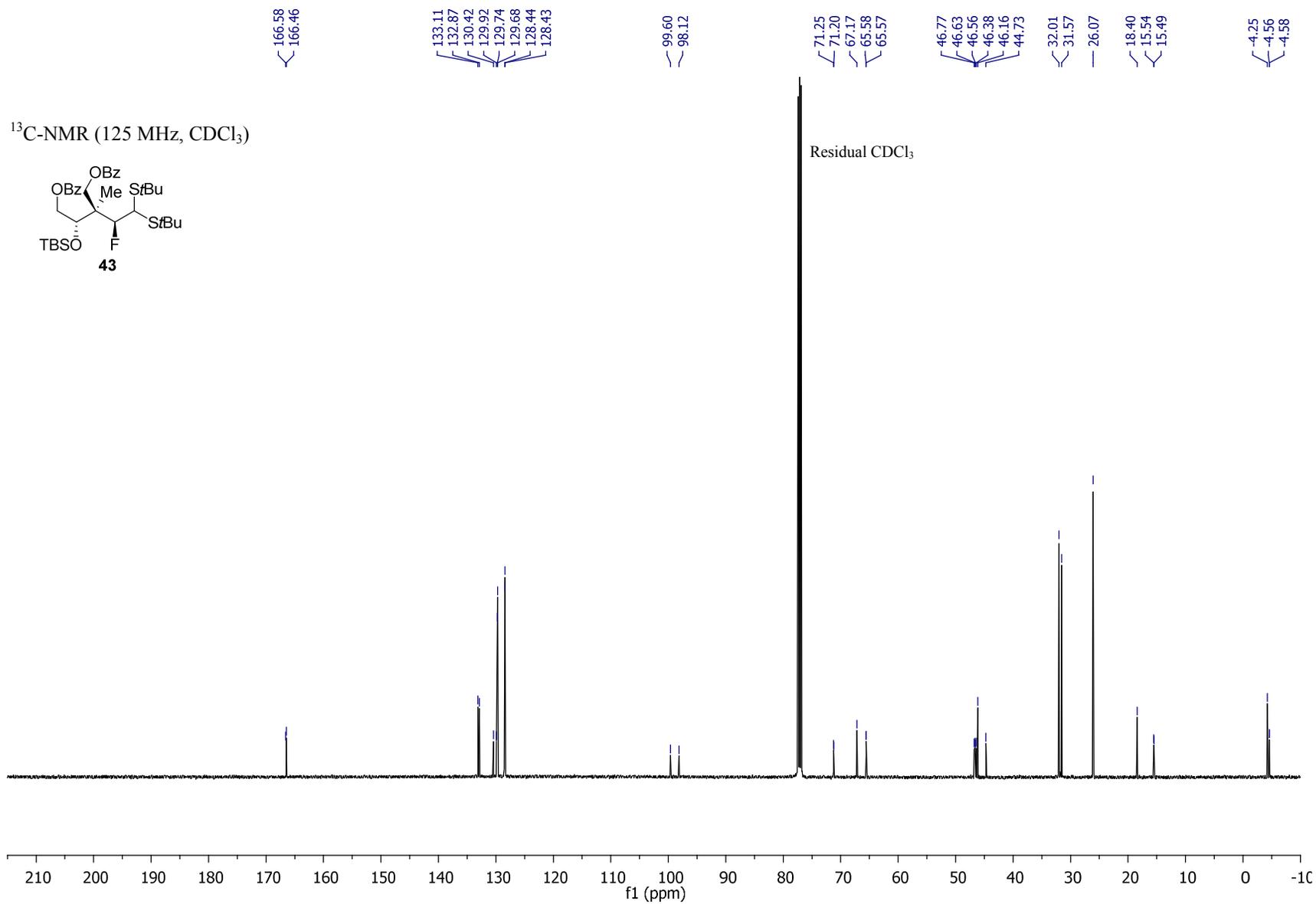
<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)

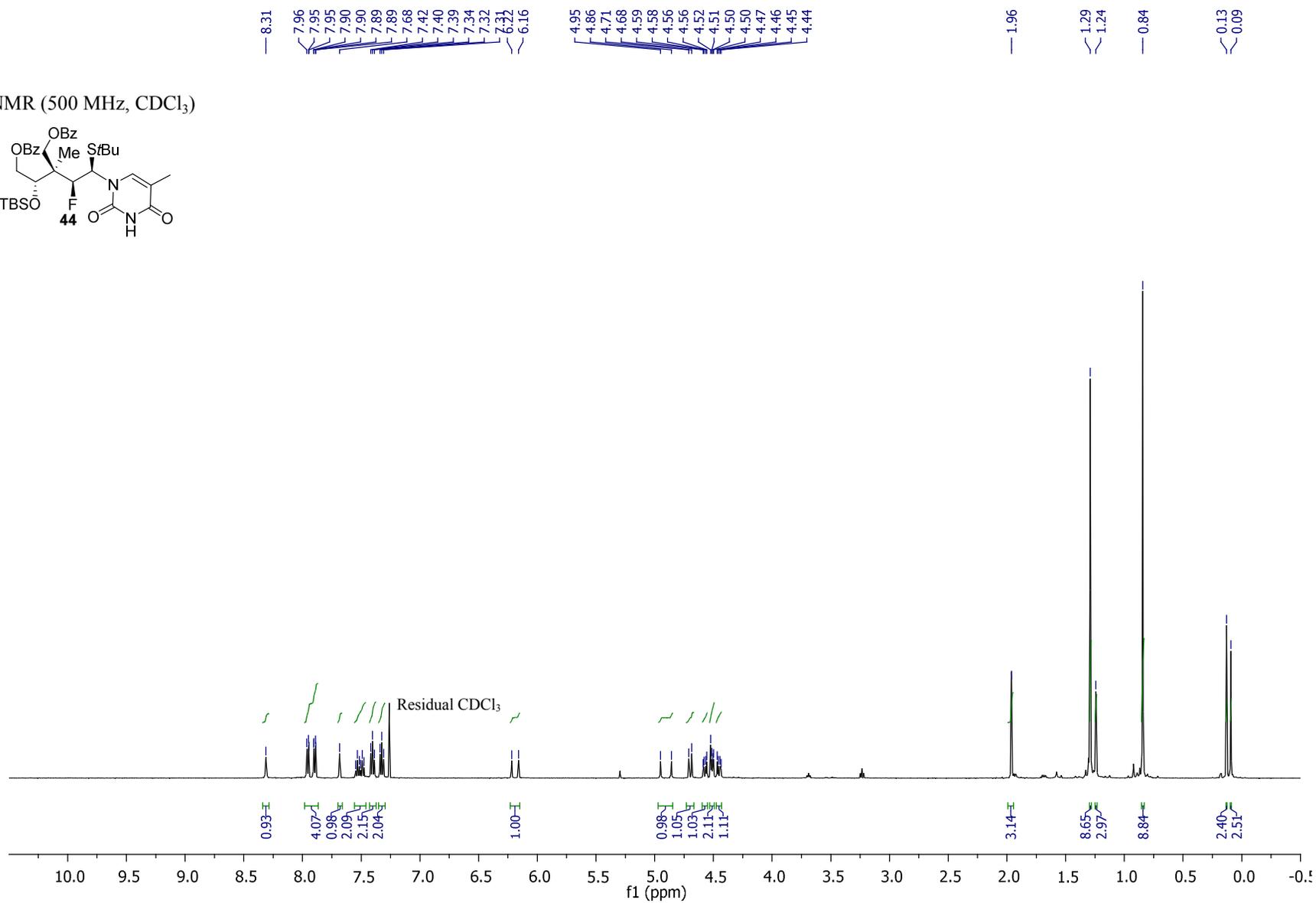
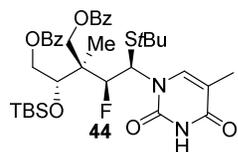


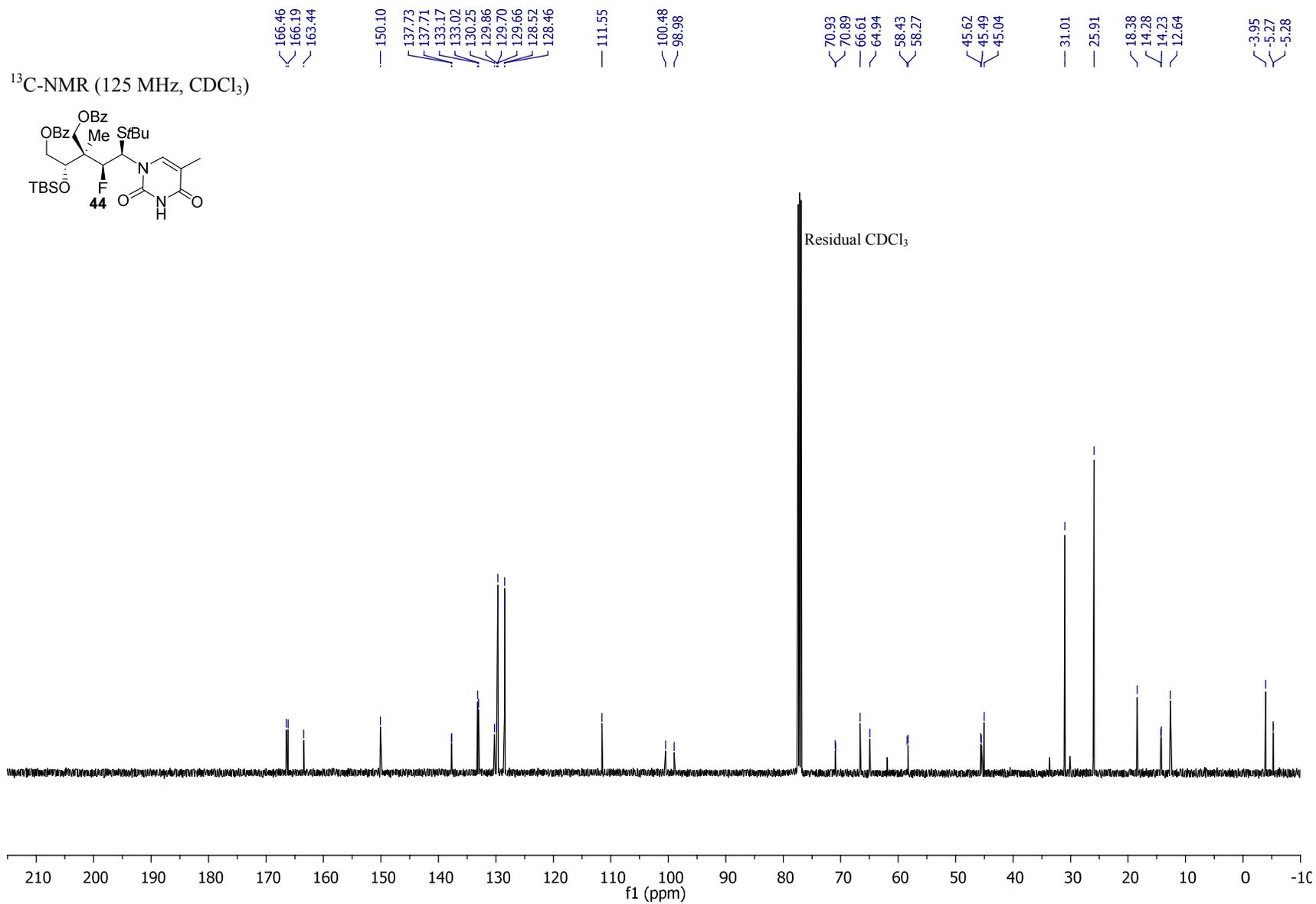


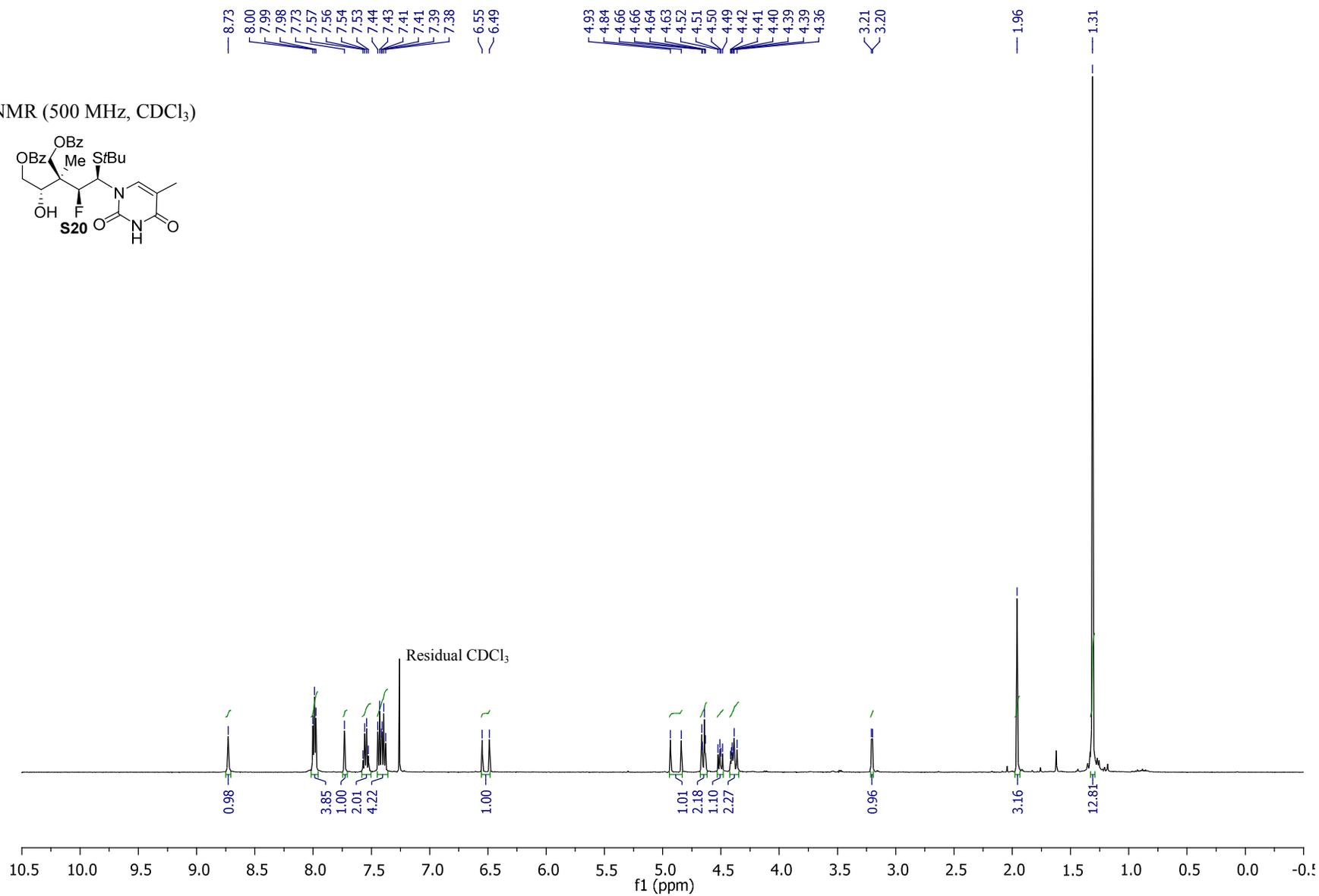
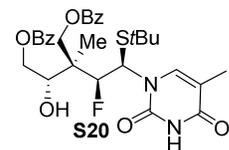
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CD}_3\text{OD}$ )

$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



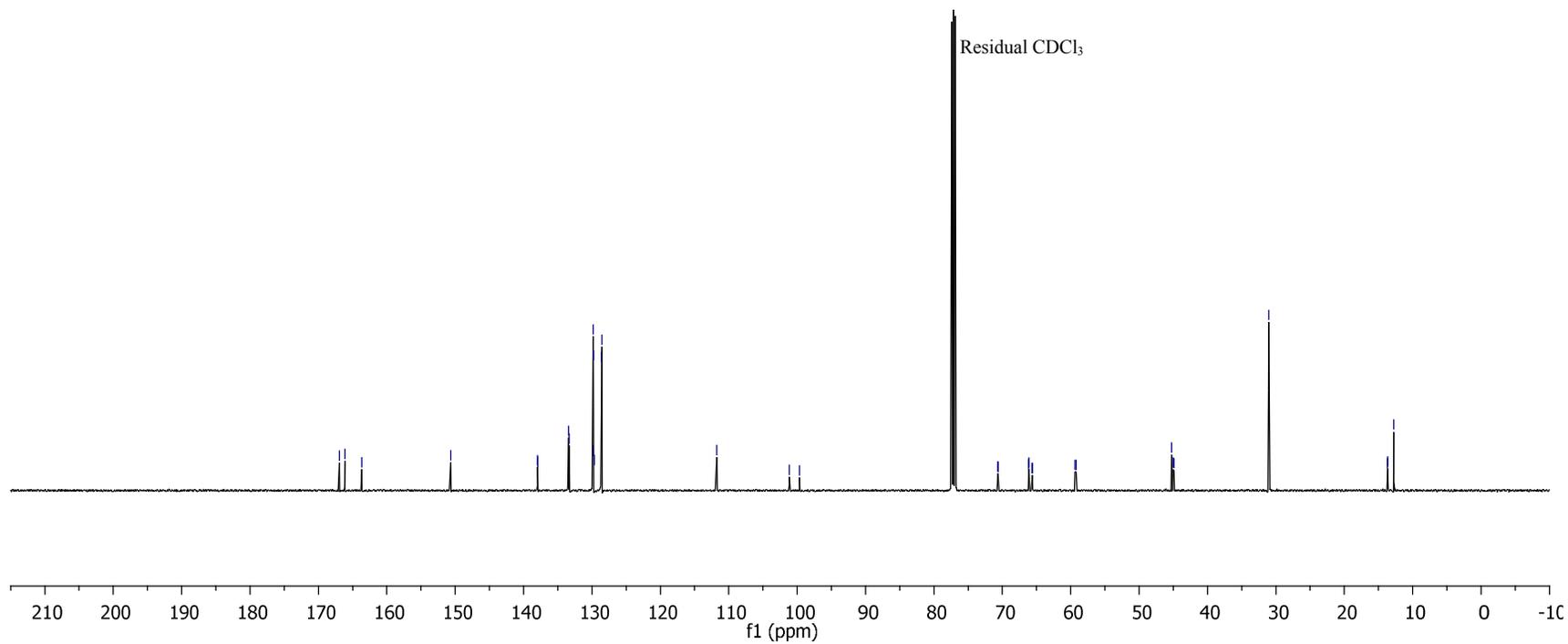
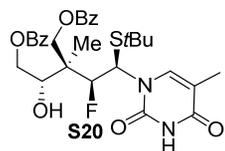
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

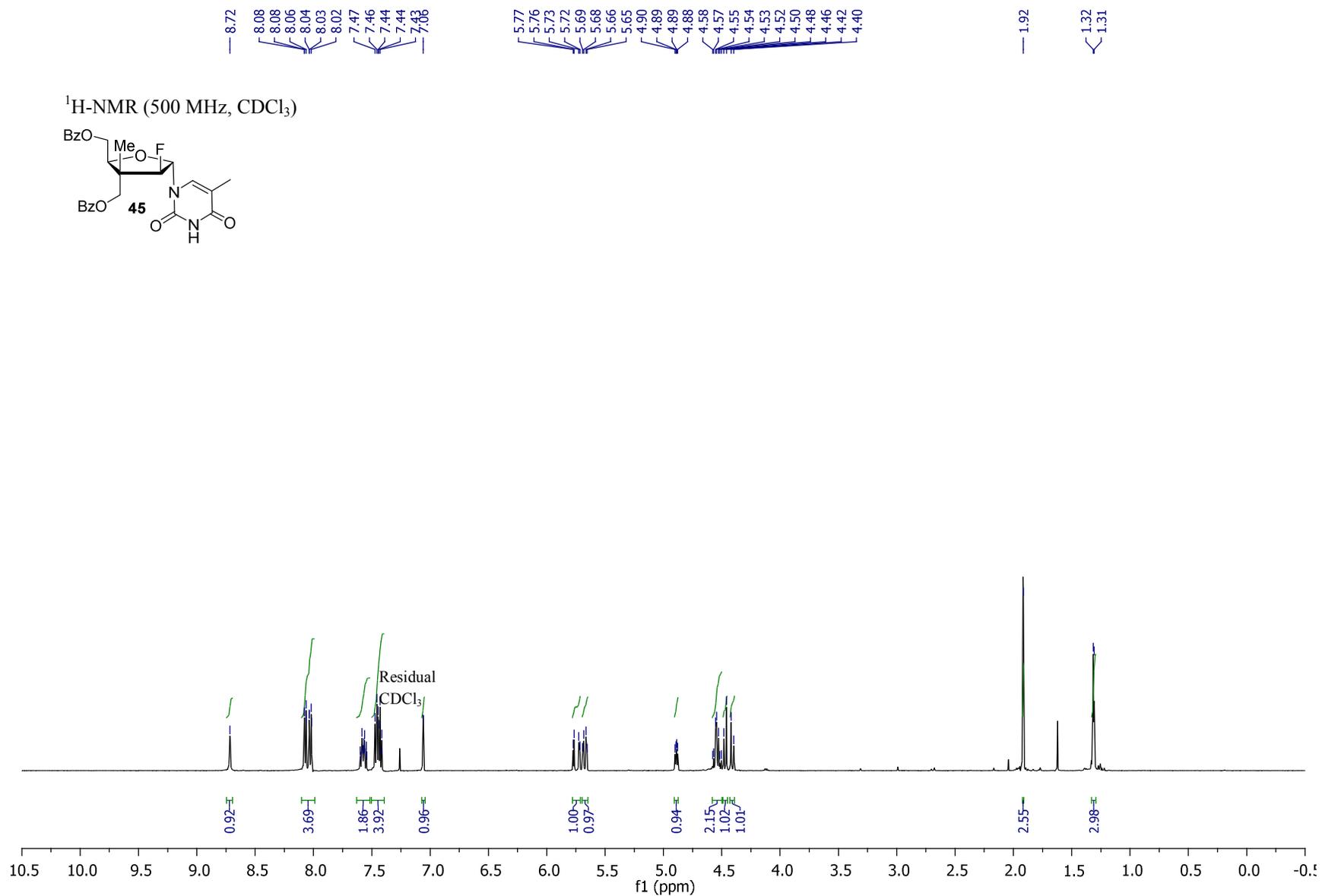


<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>)



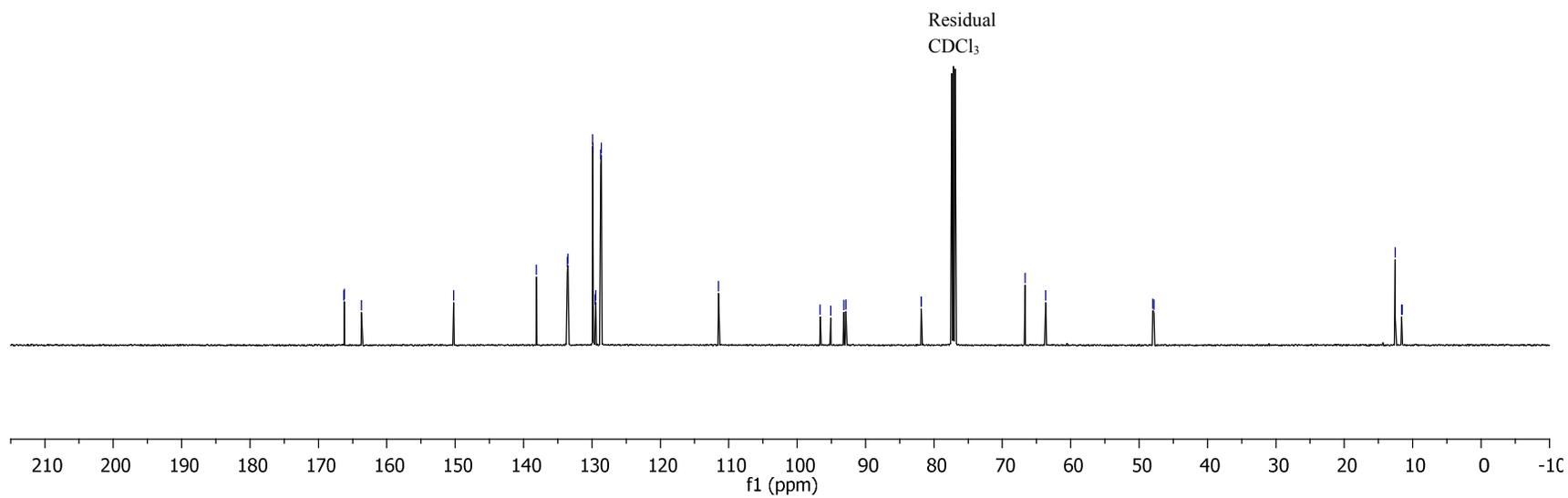
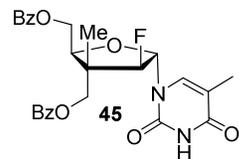
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

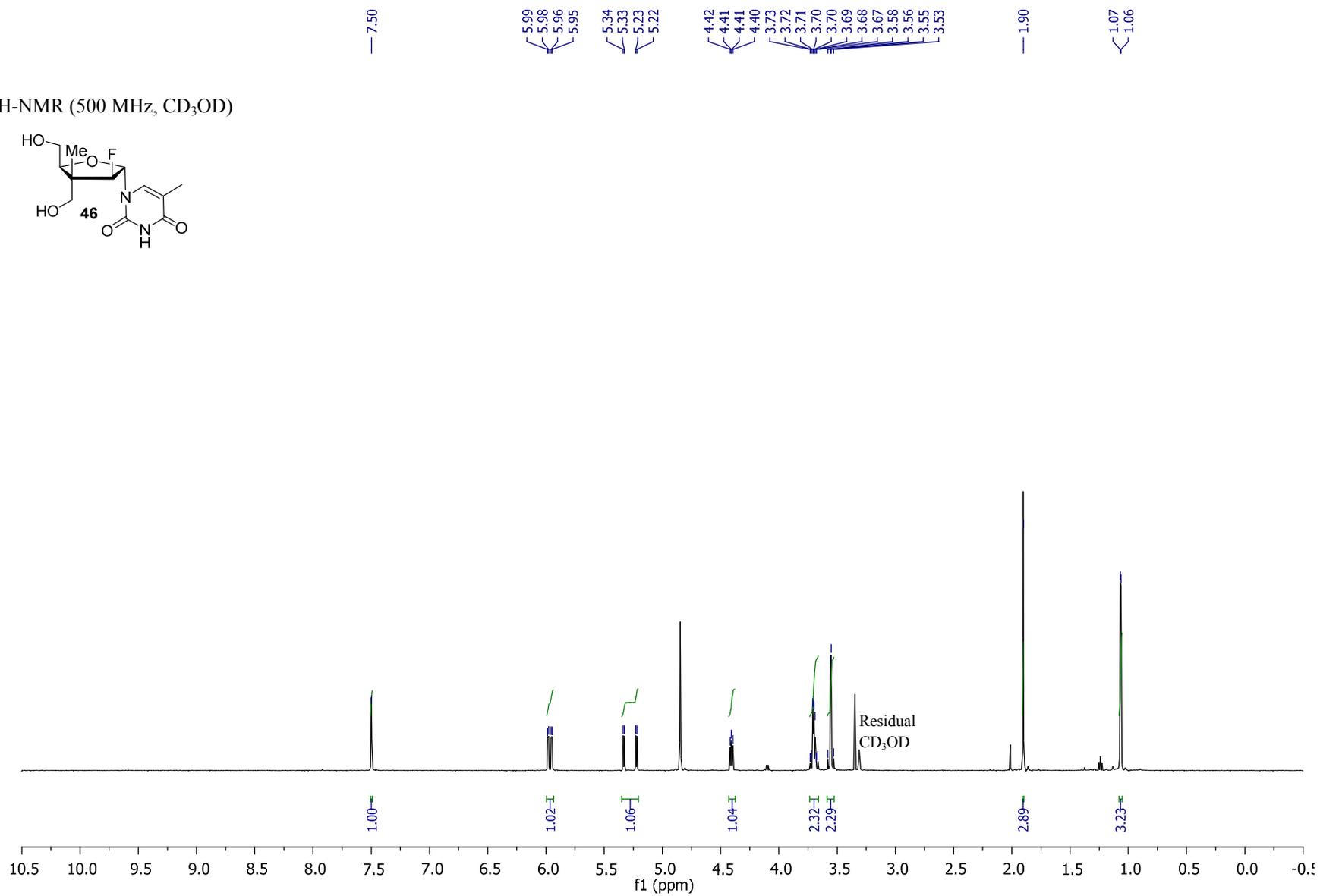
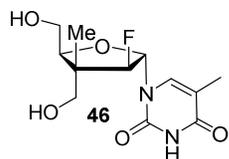




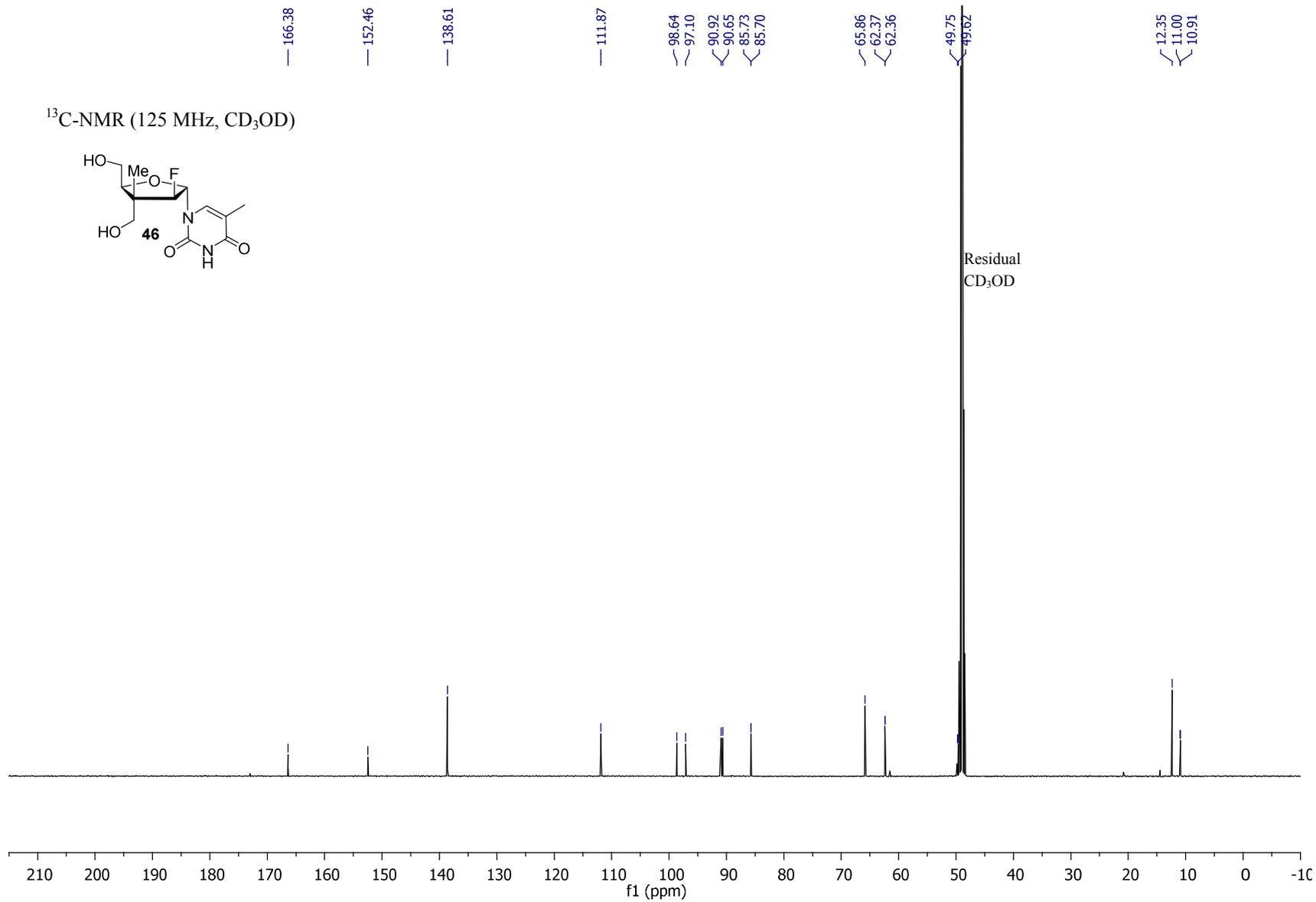
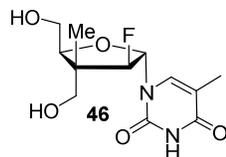


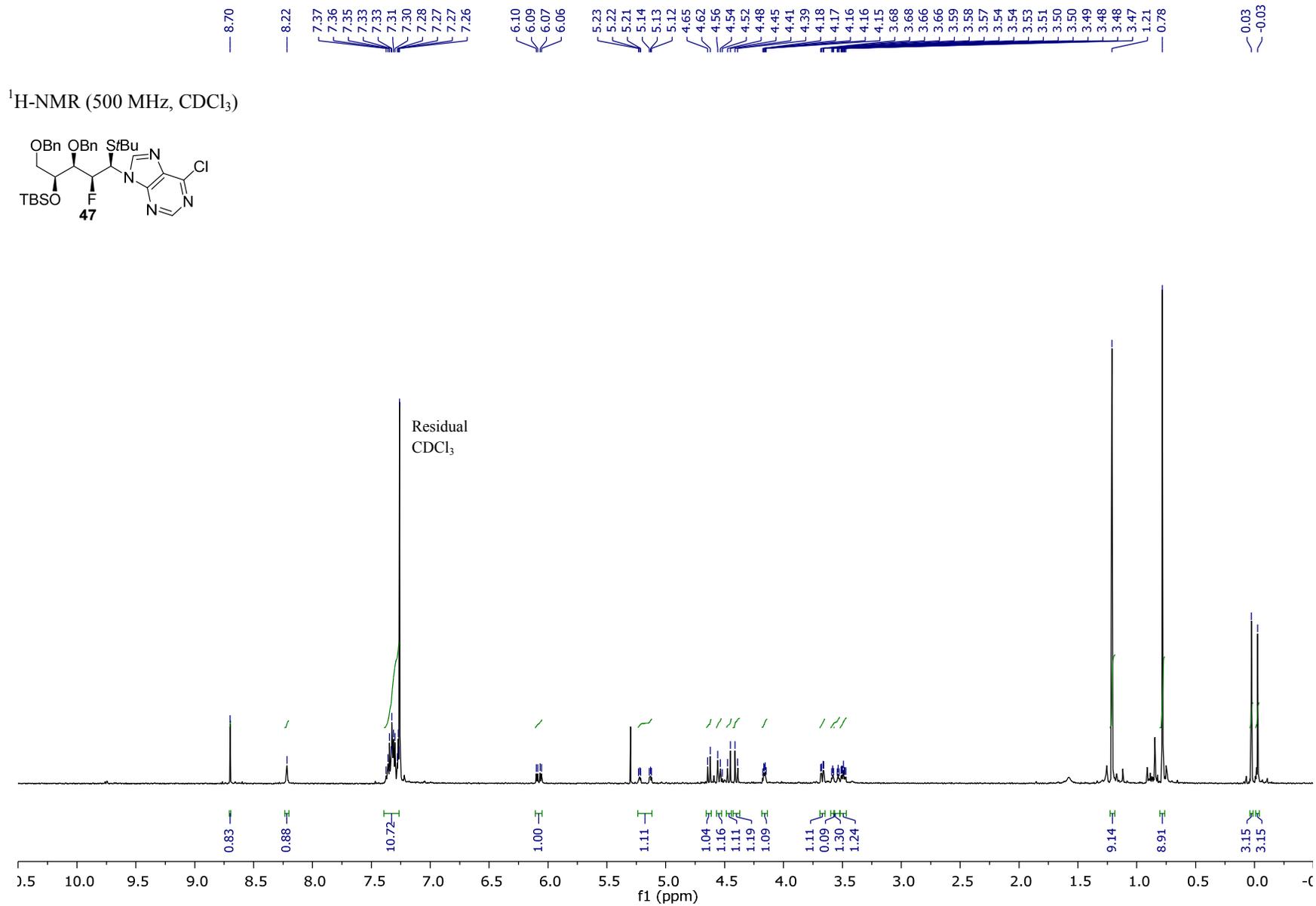
<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>)

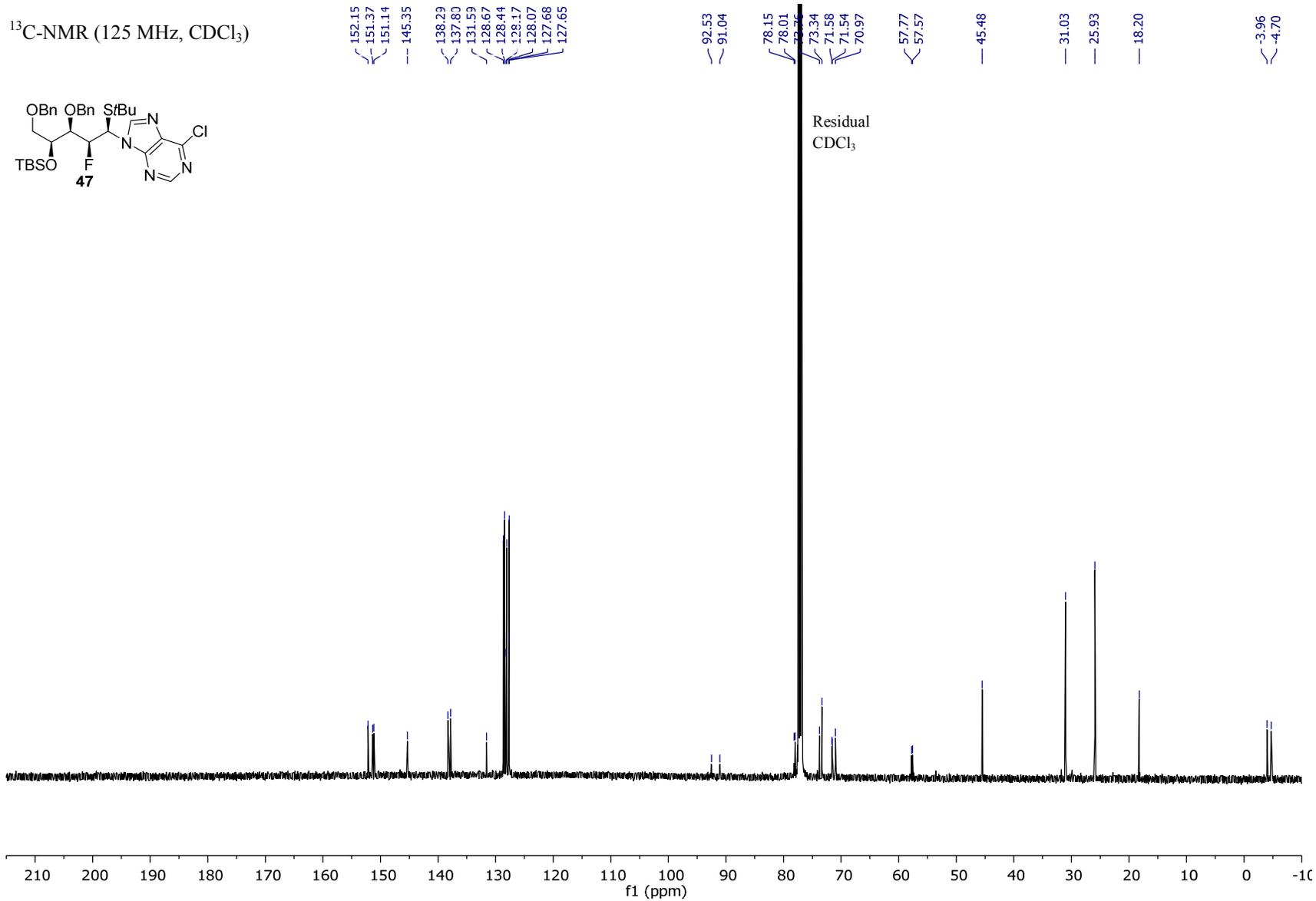


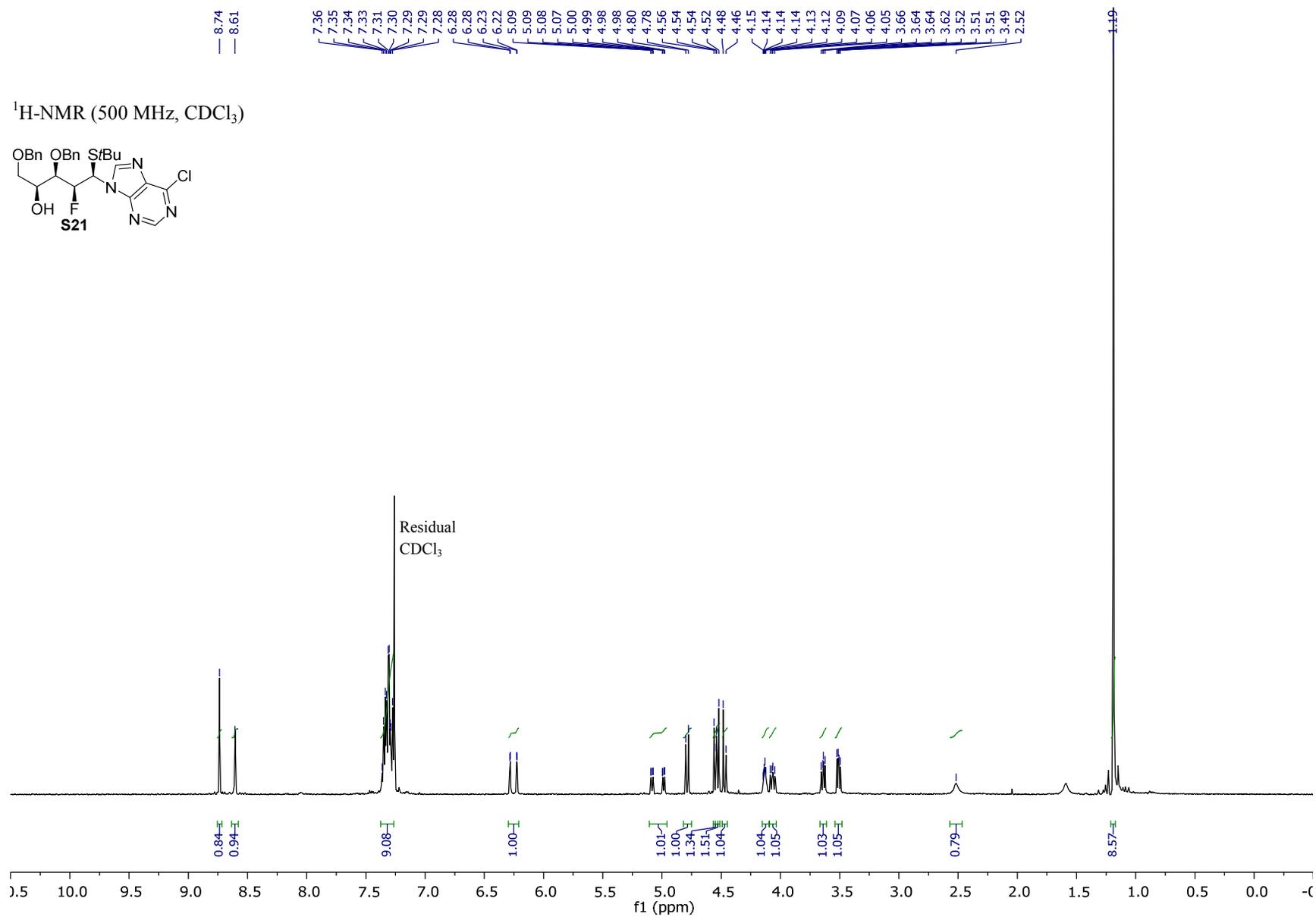
<sup>1</sup>H-NMR (500 MHz, CD<sub>3</sub>OD)

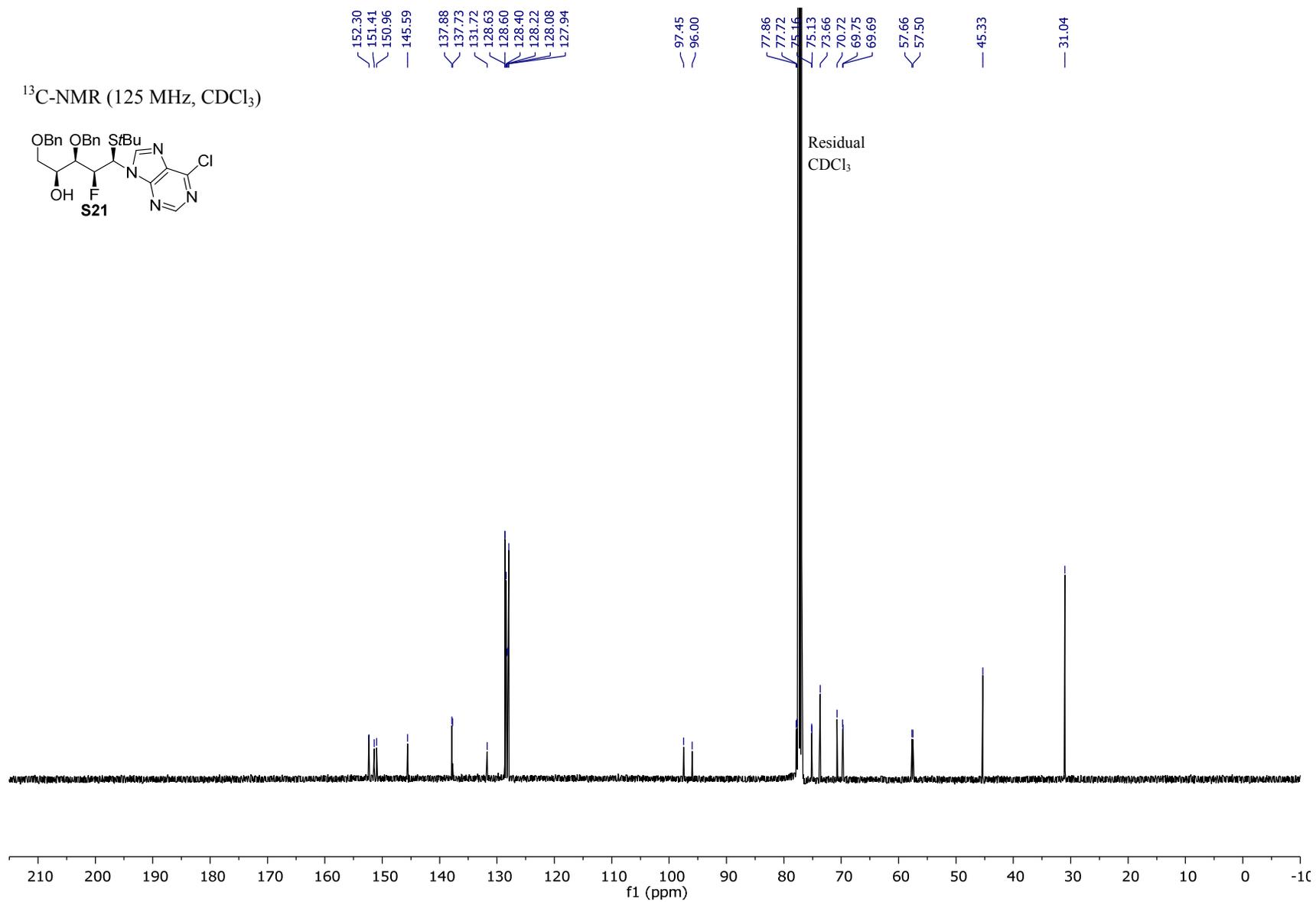
<sup>13</sup>C-NMR (125 MHz, CD<sub>3</sub>OD)

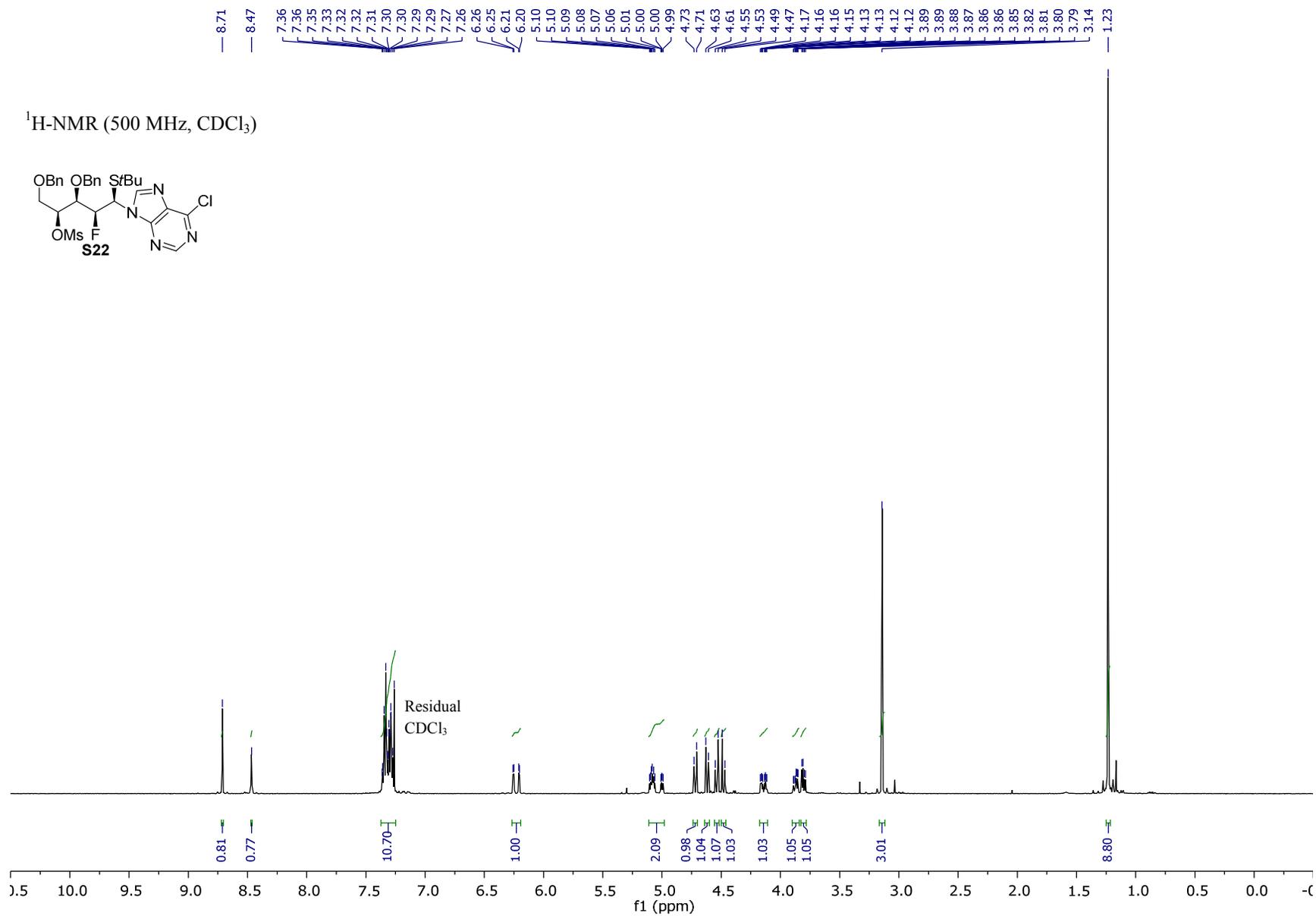


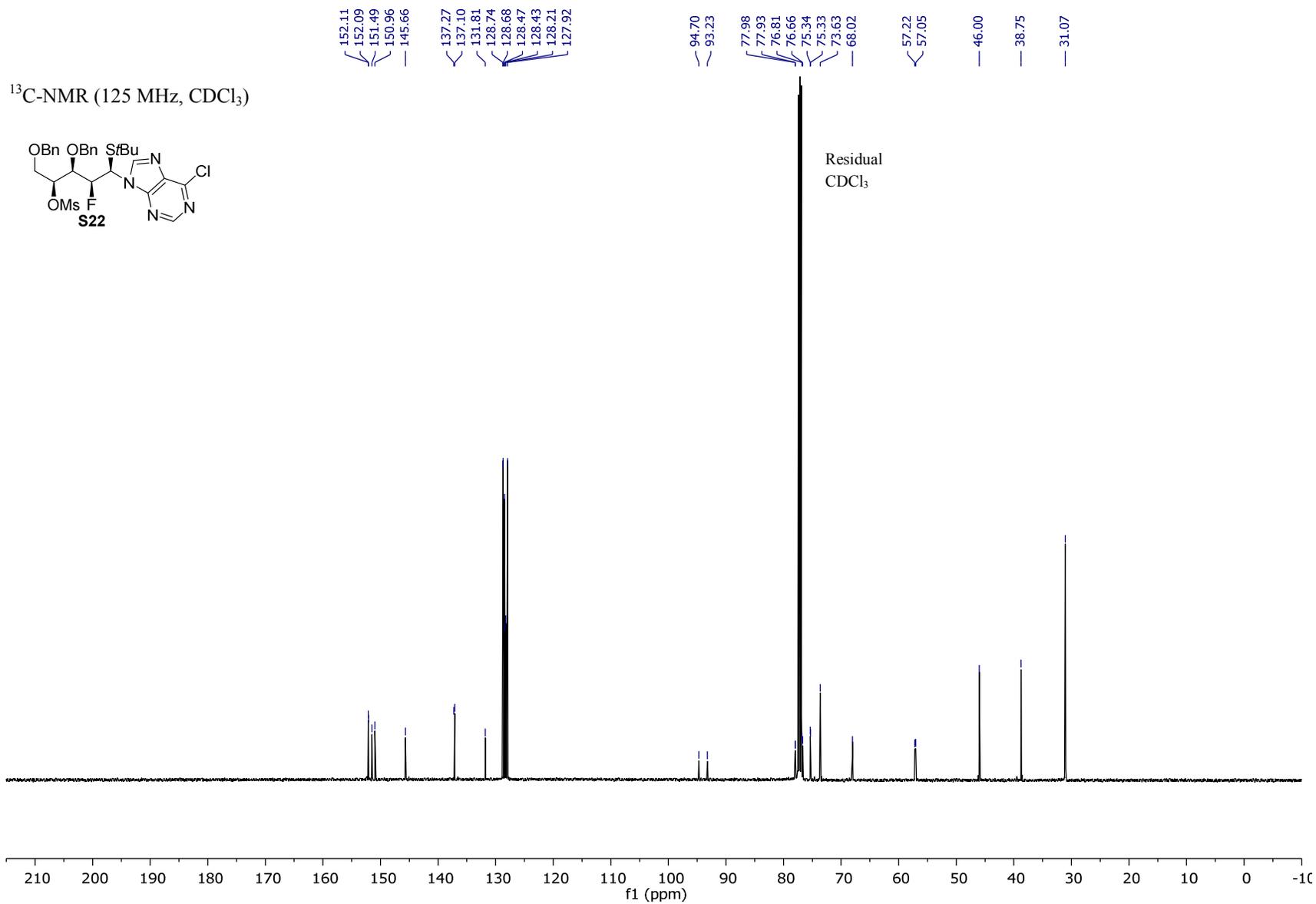
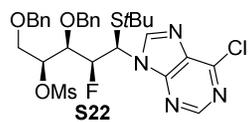


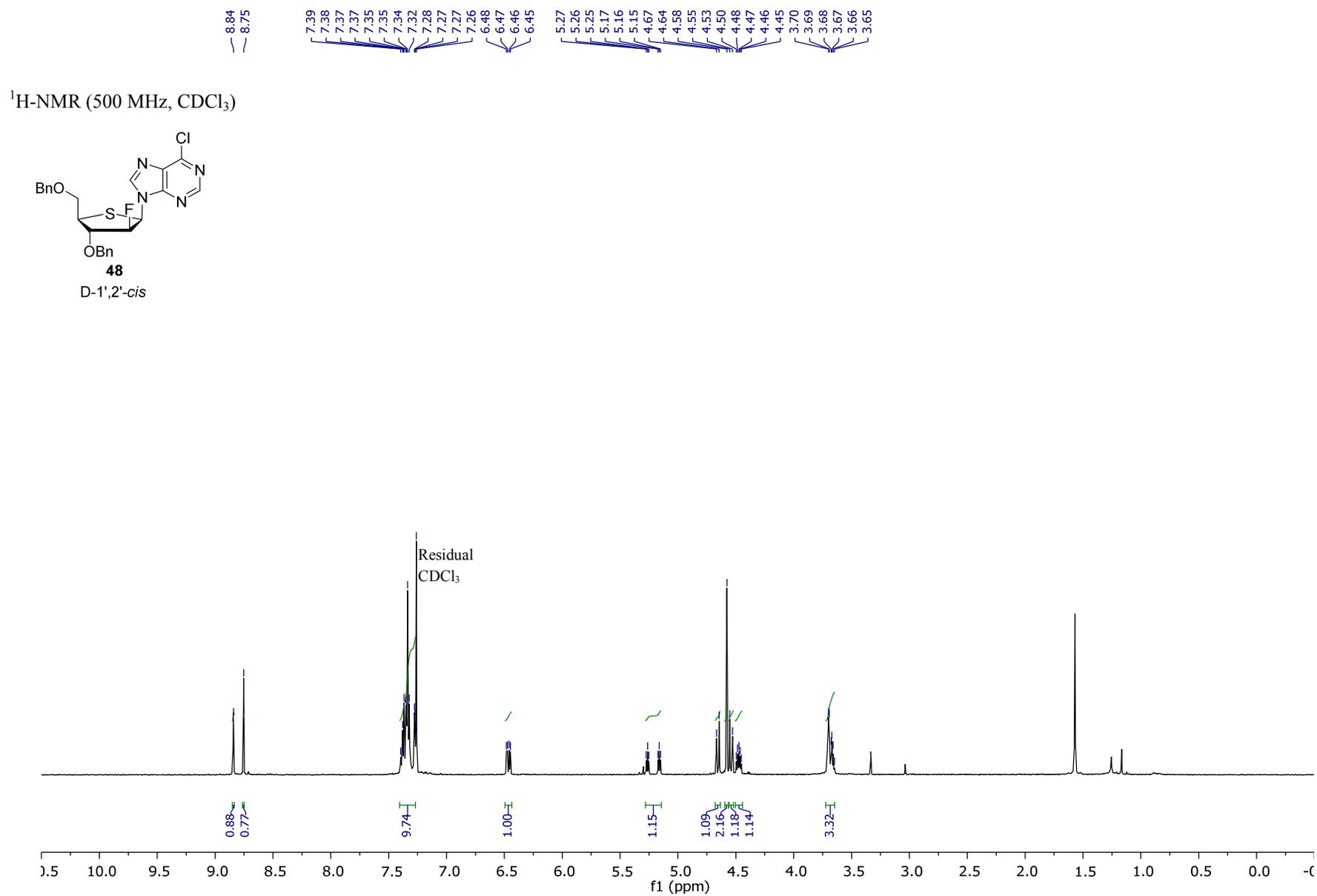


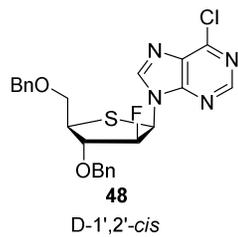






$^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C-NMR}$  (125 MHz,  $\text{CDCl}_3$ )

152.26  
152.23  
151.32  
145.70  
137.36  
136.91  
131.88  
128.77  
128.48  
128.31  
128.30  
128.10

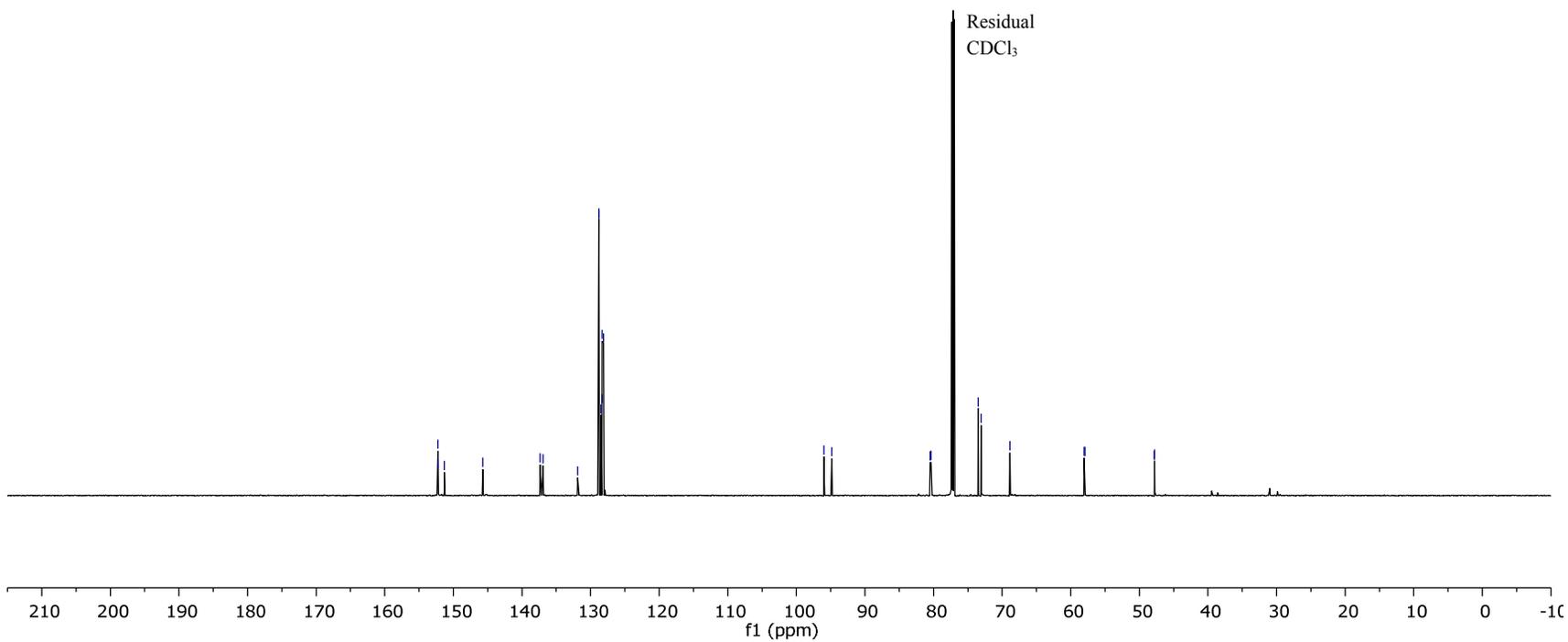
95.97  
94.86

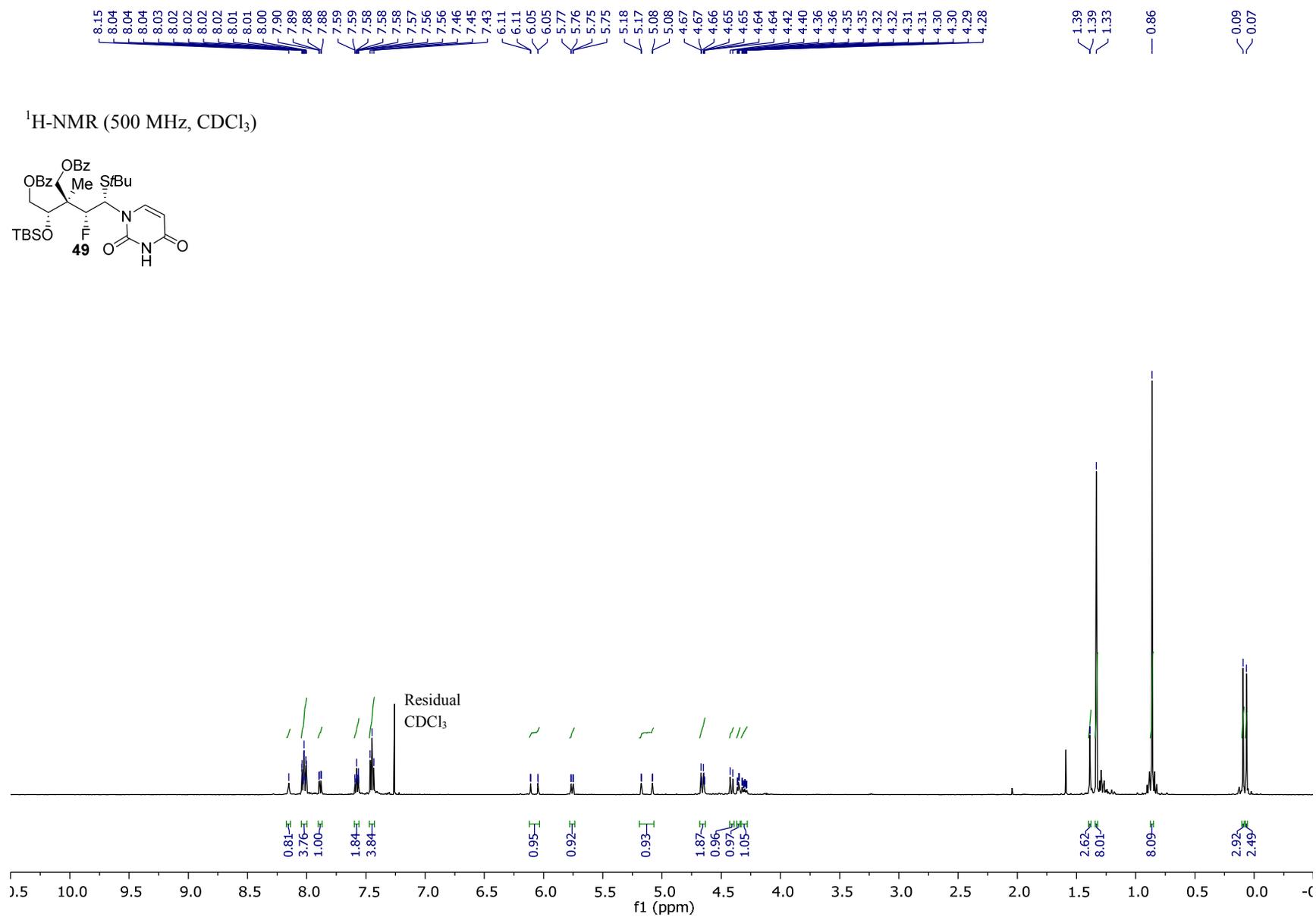
80.50  
80.38

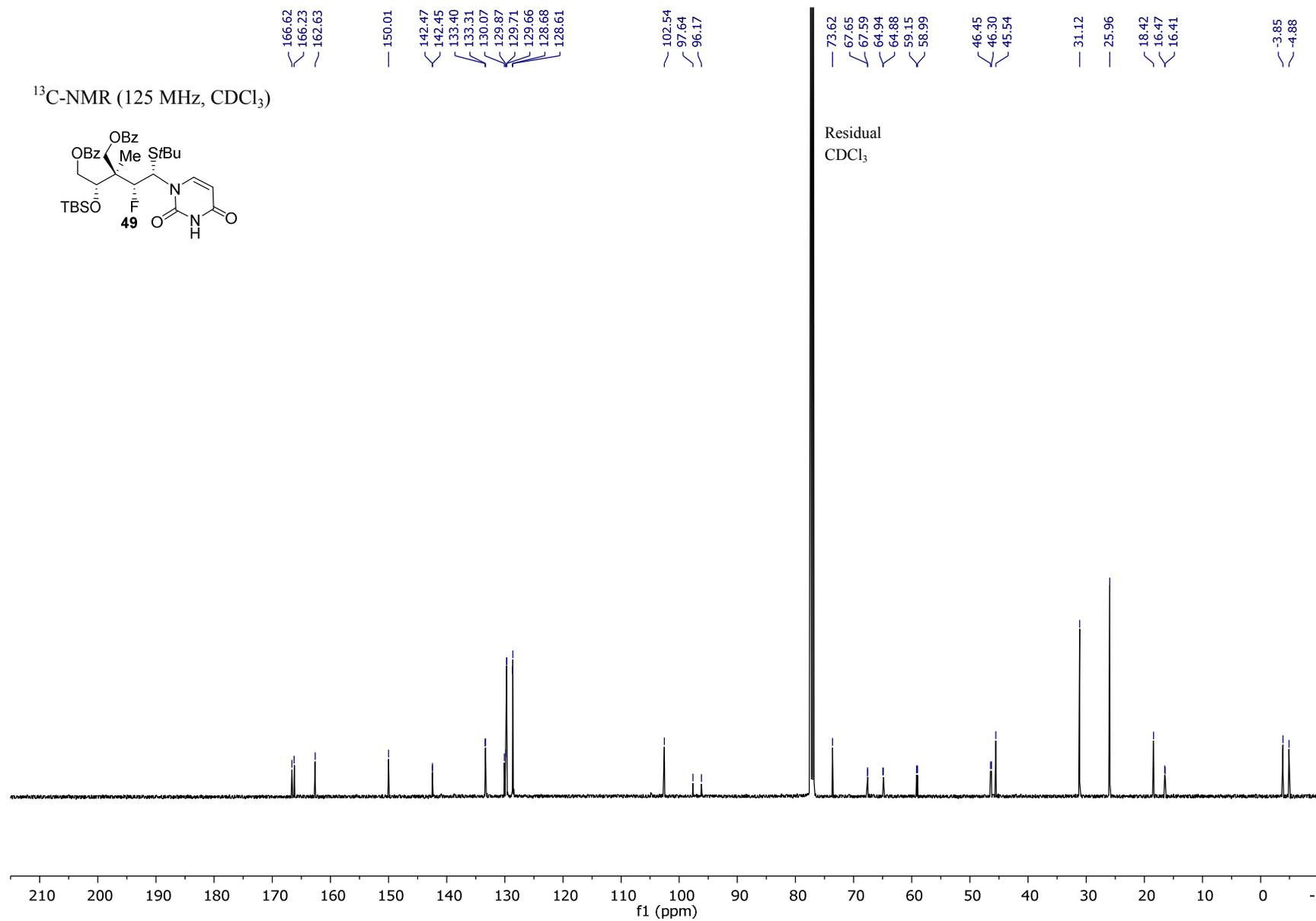
73.50  
73.05  
68.87

58.04  
57.94

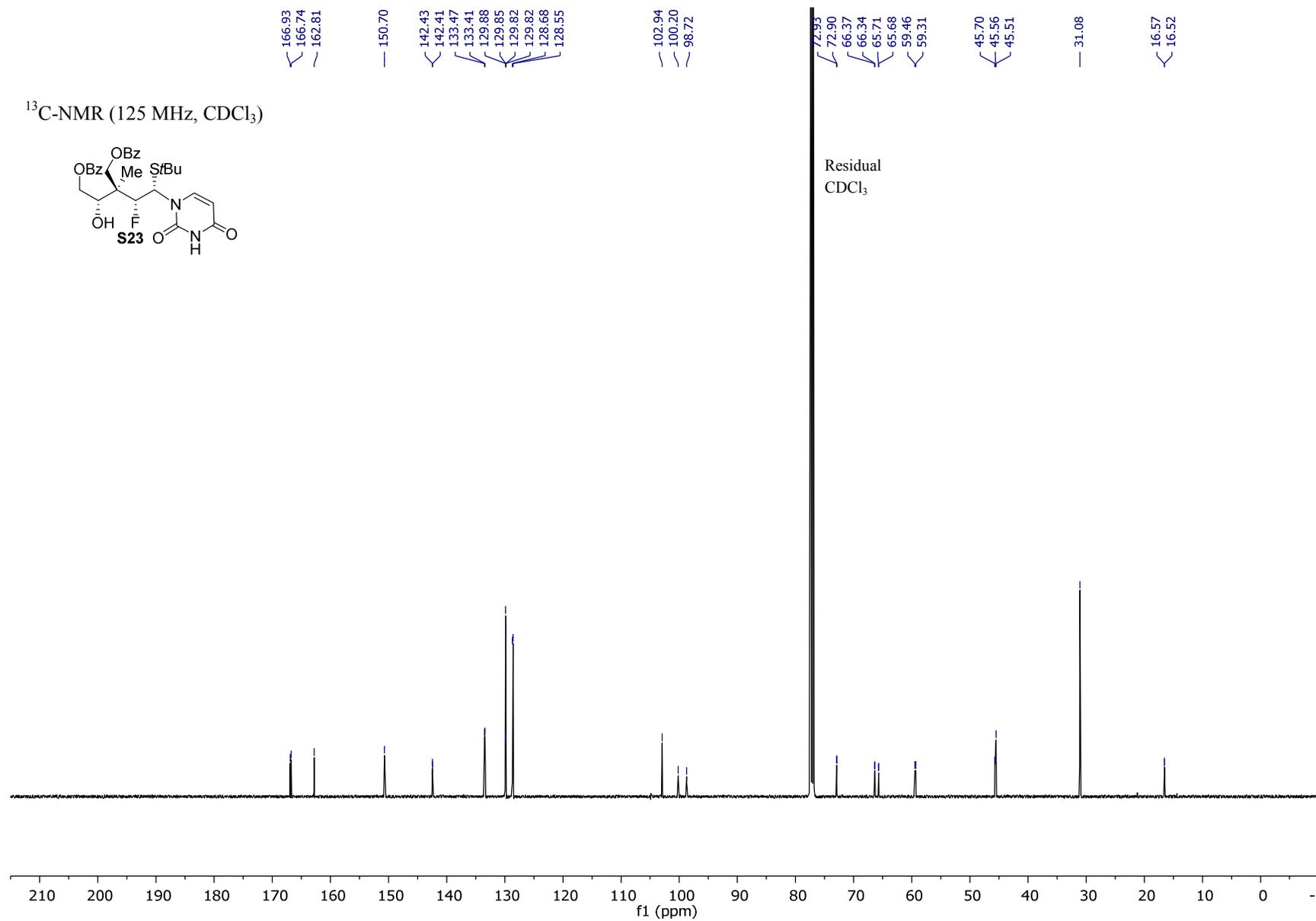
47.80  
47.78





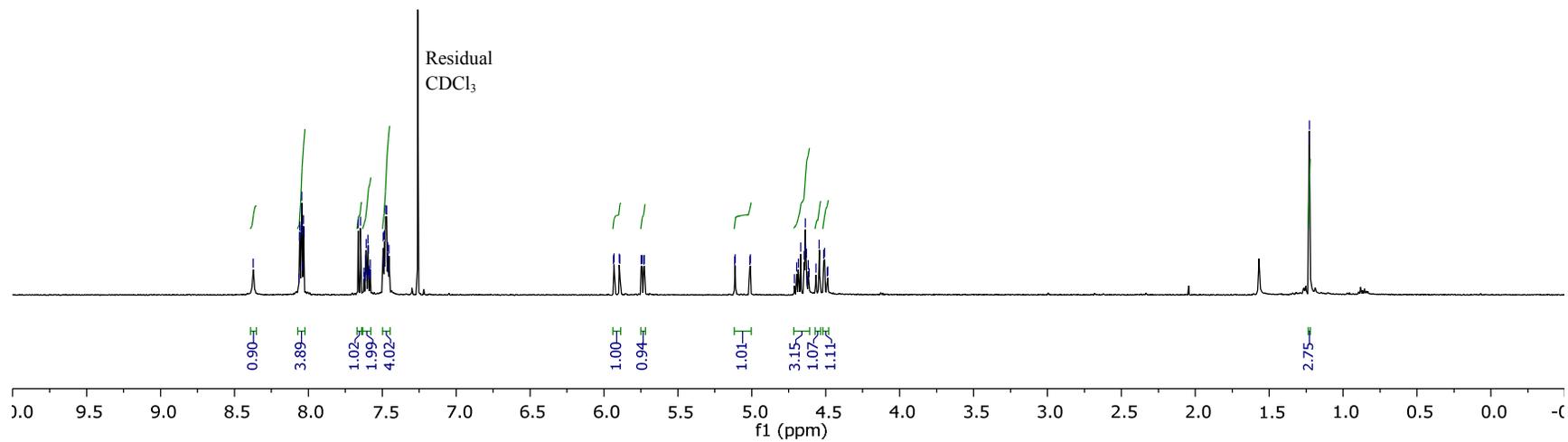
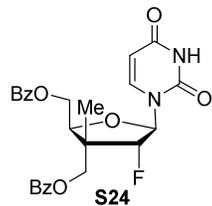


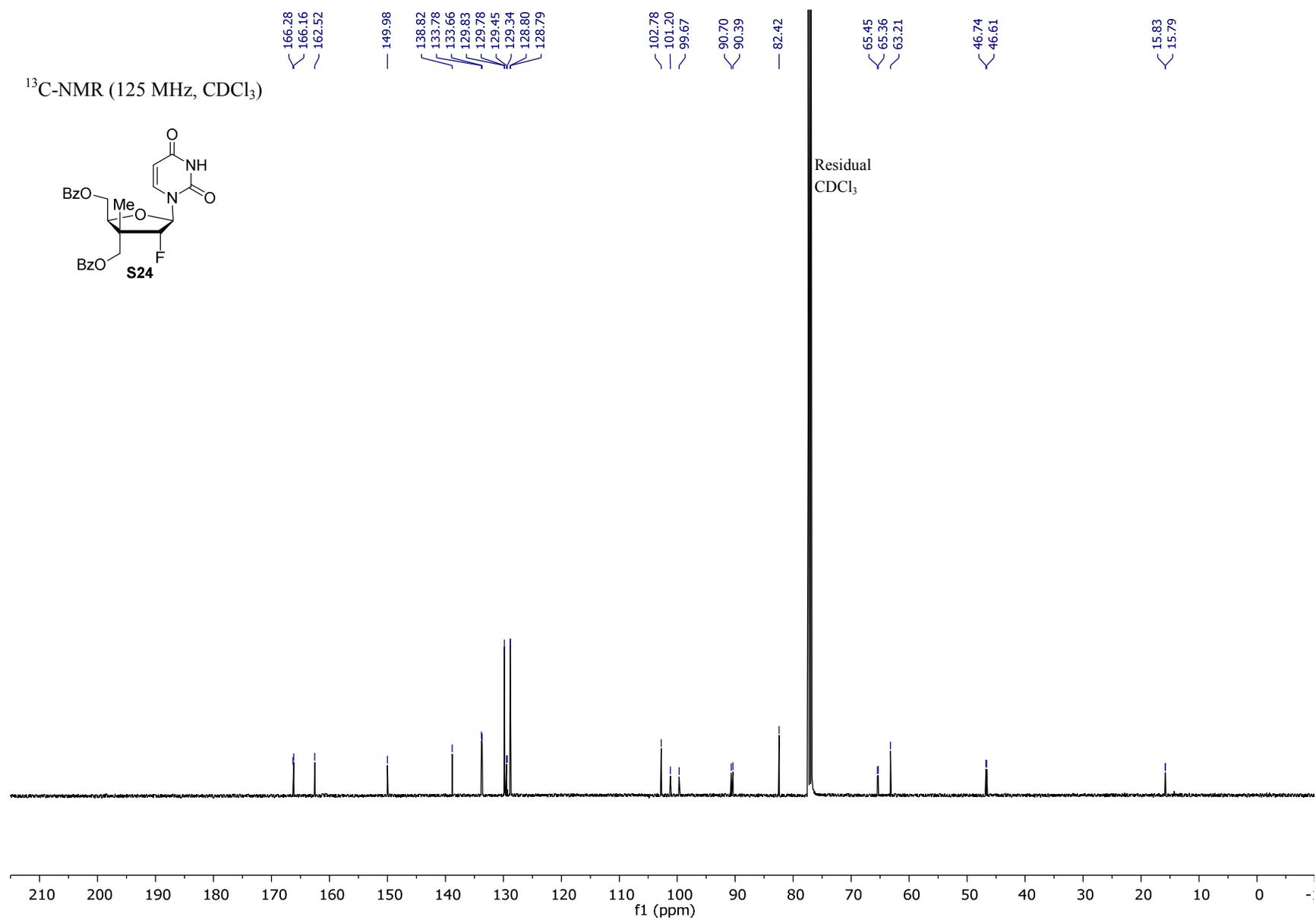


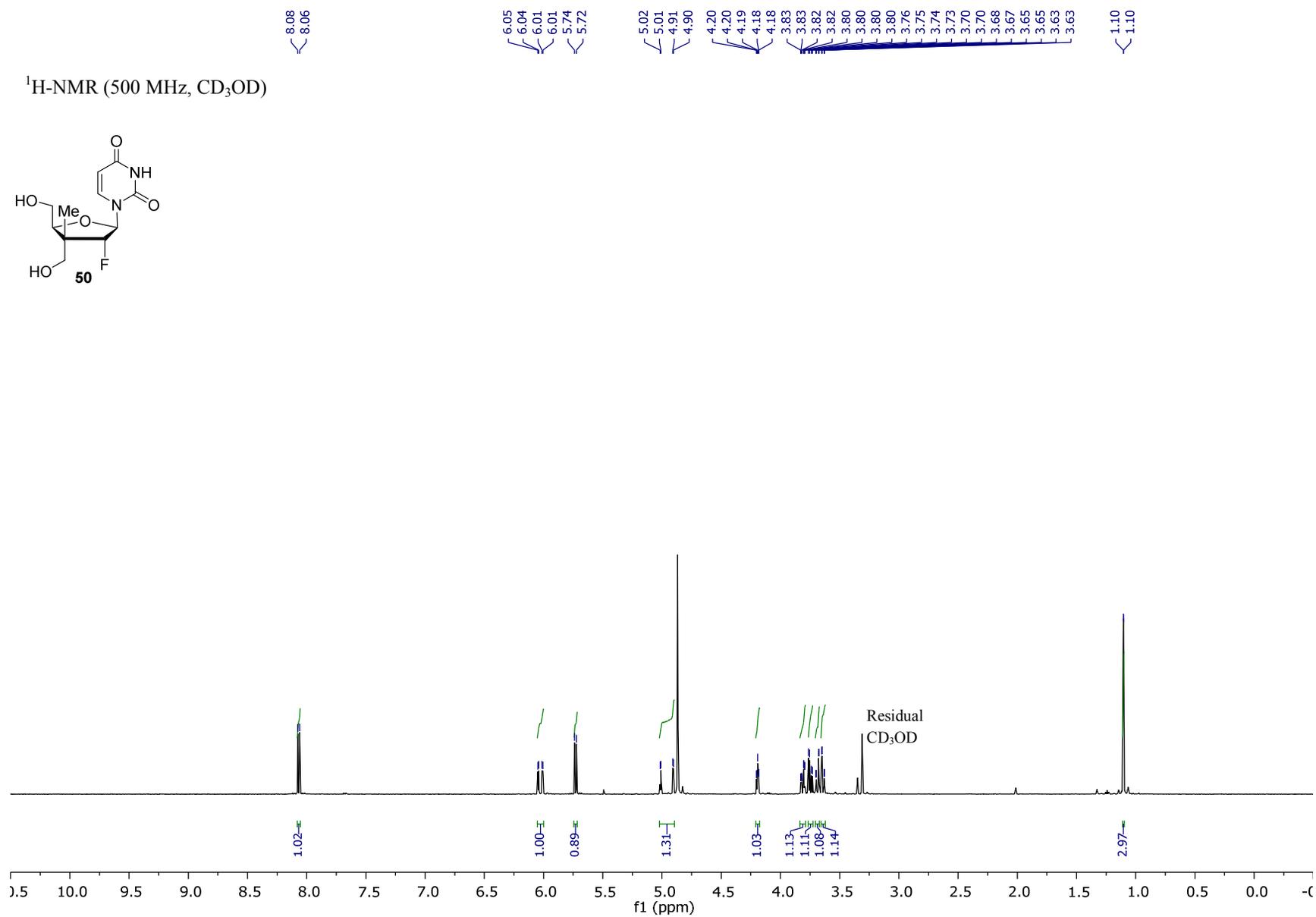


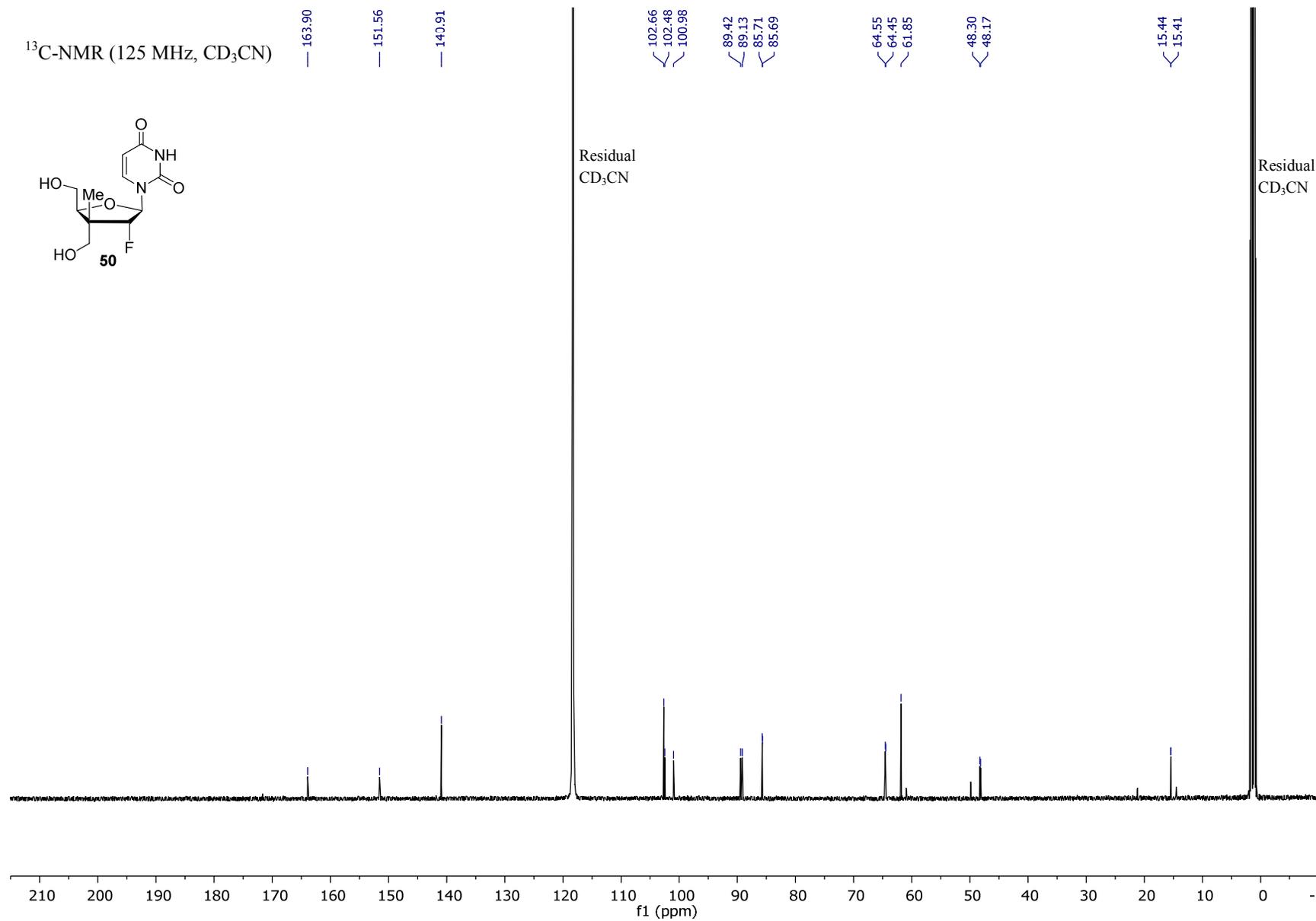


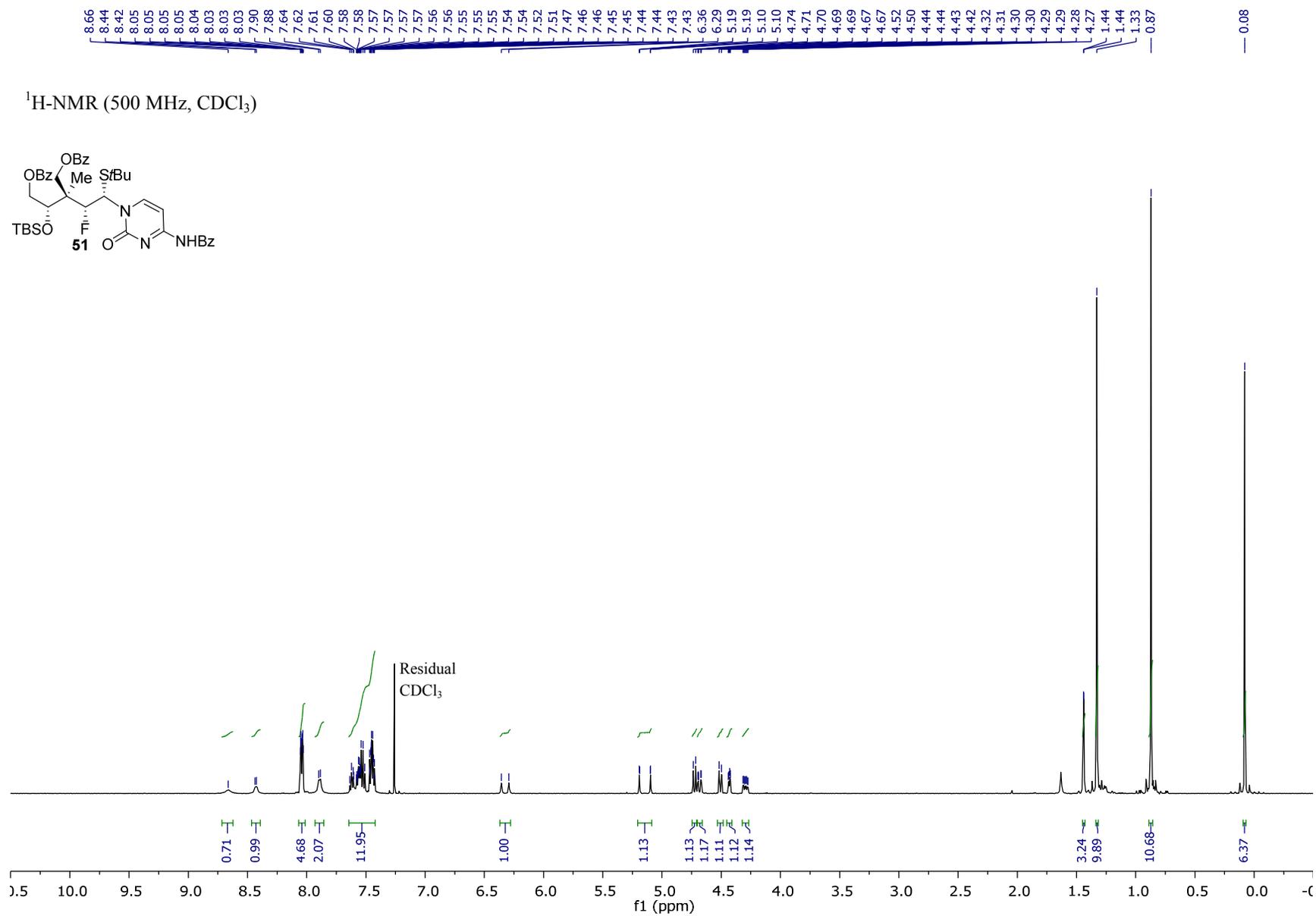
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

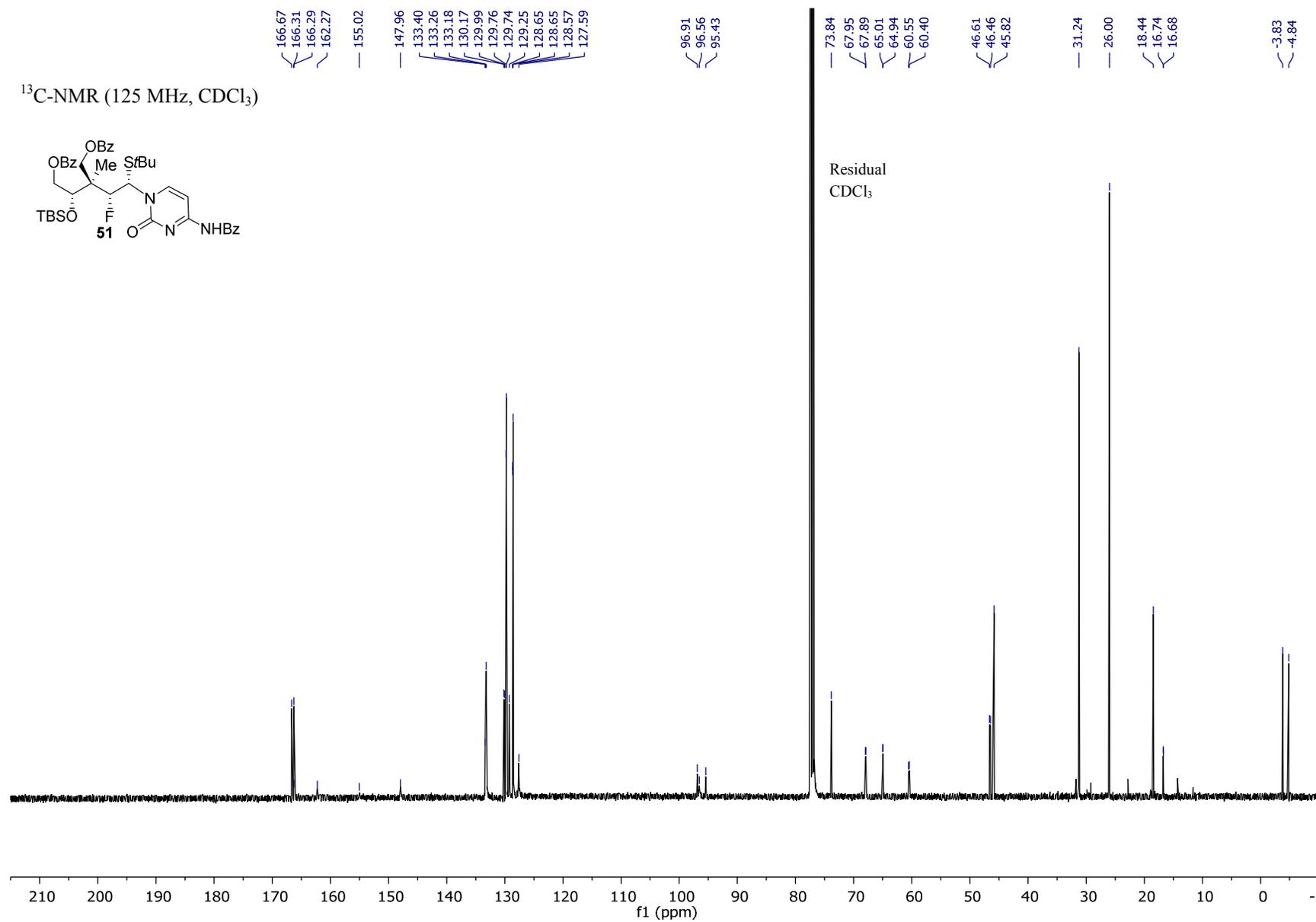


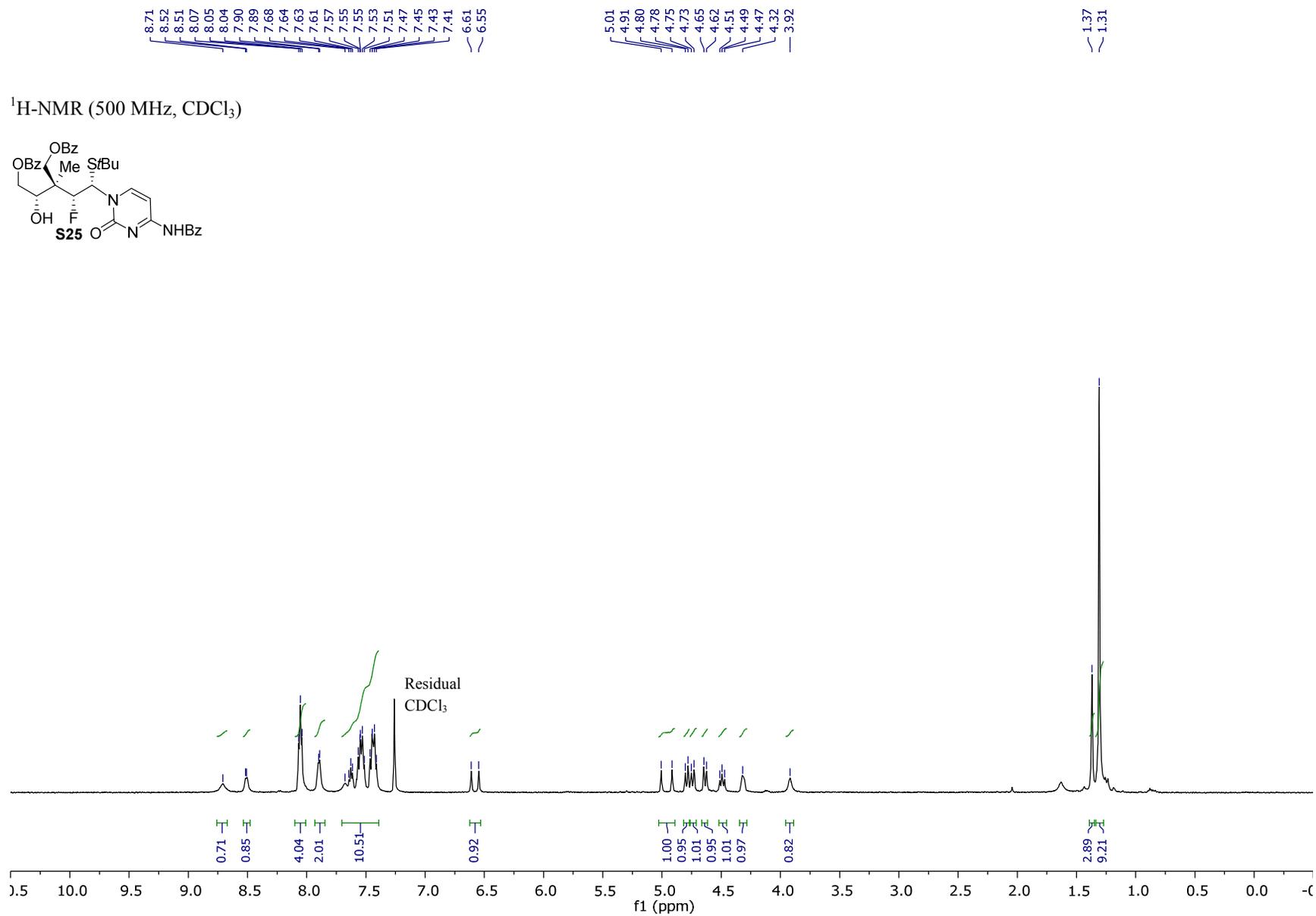


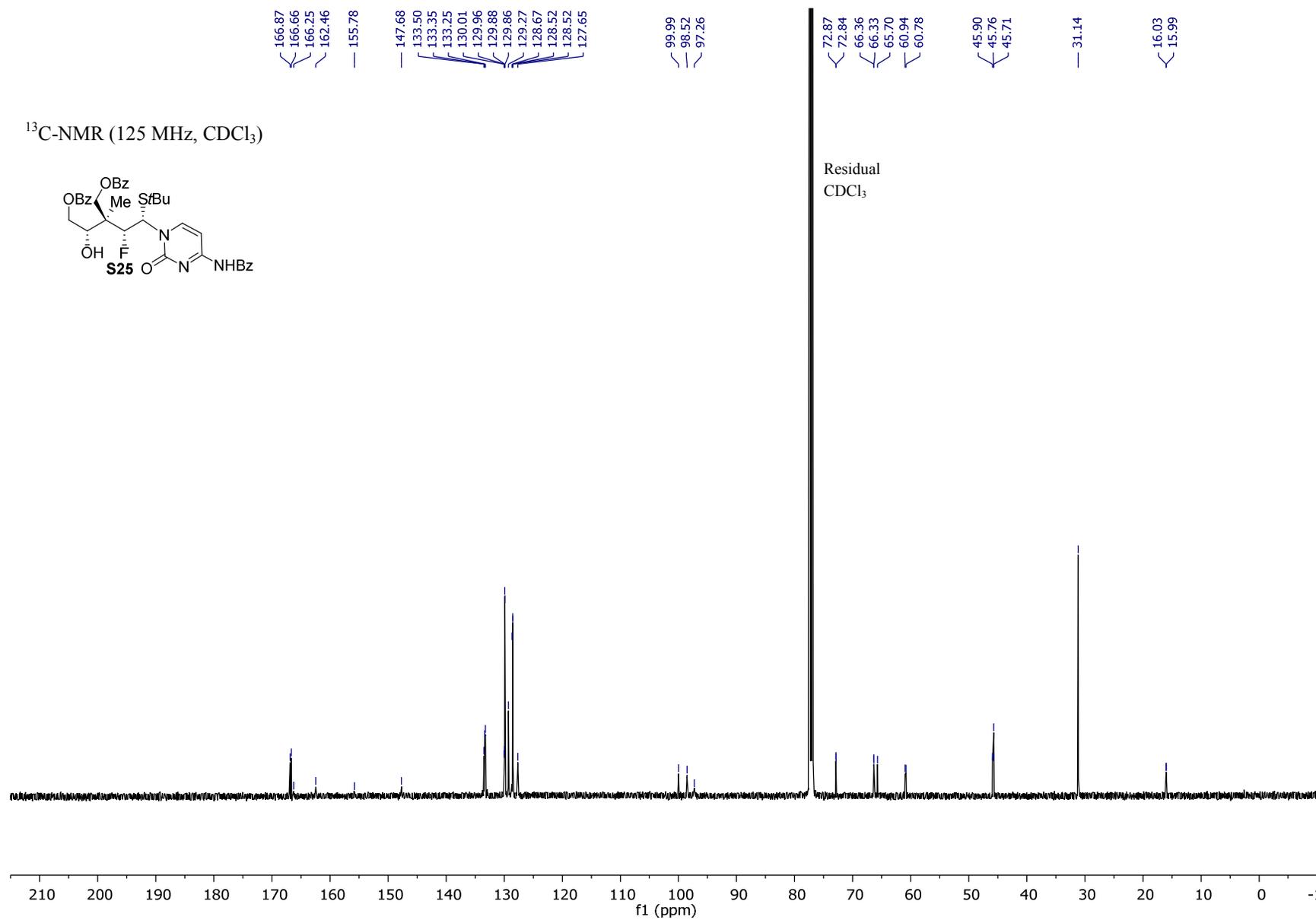


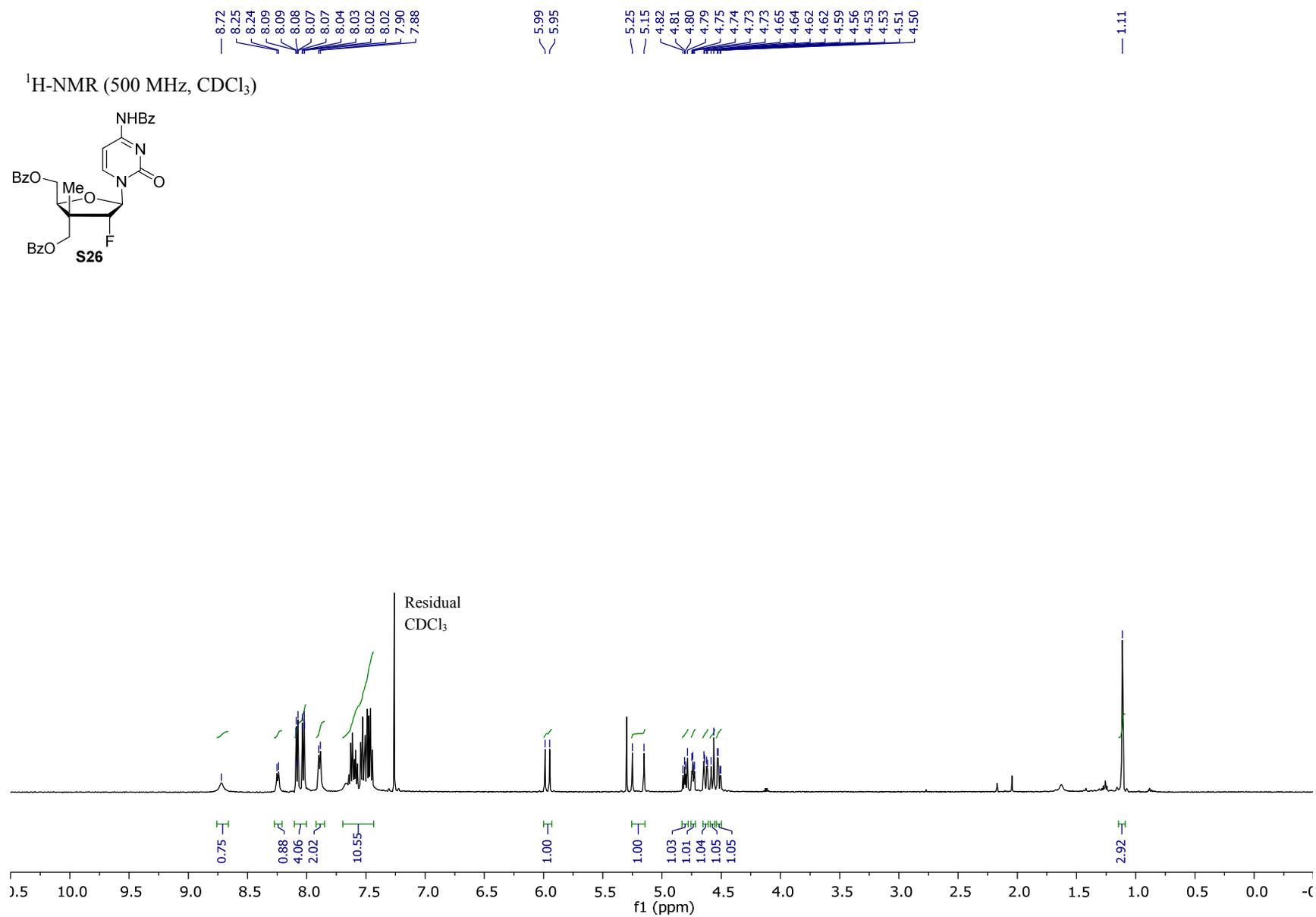




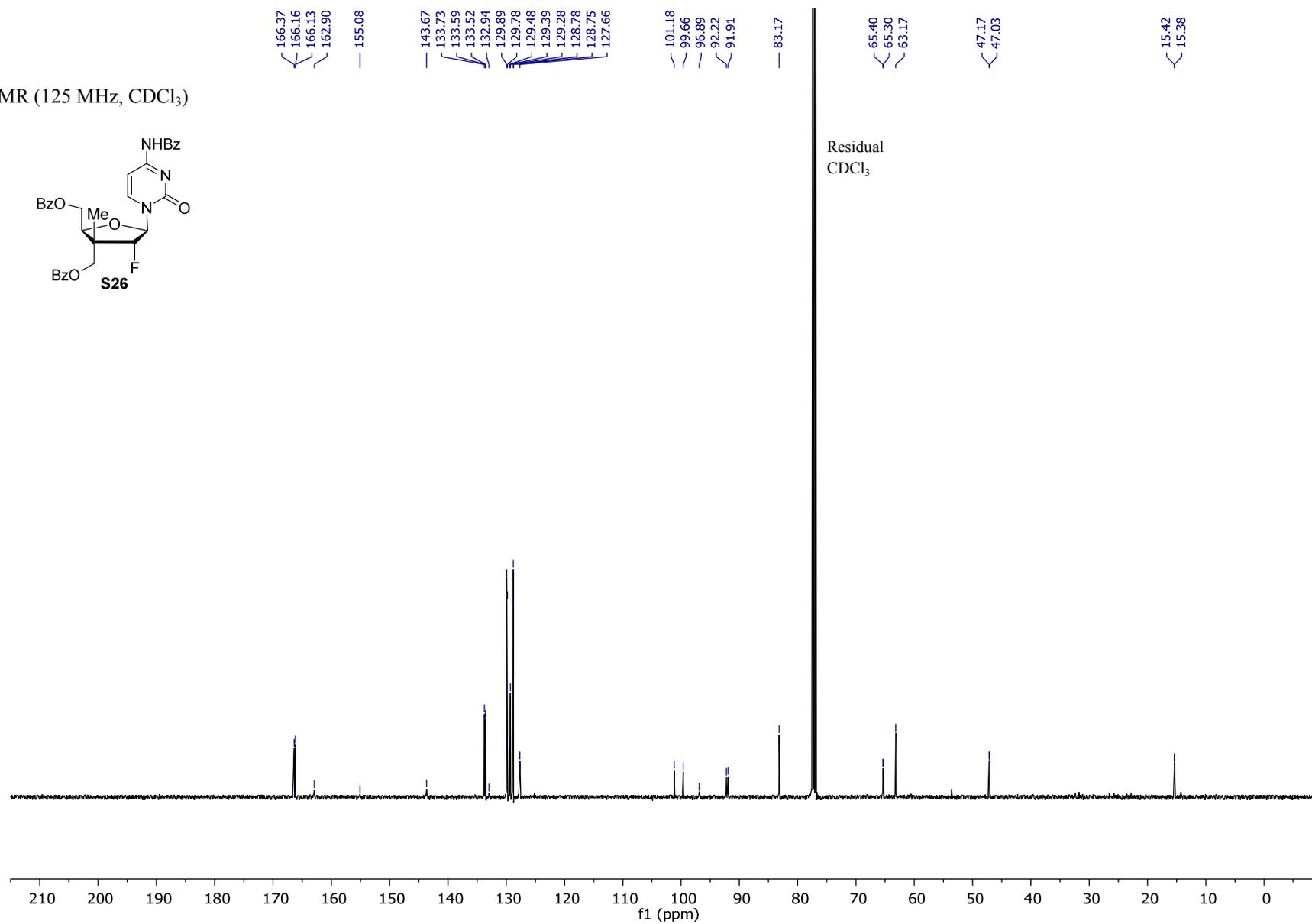
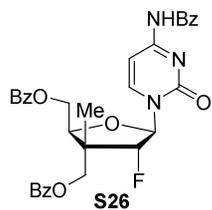


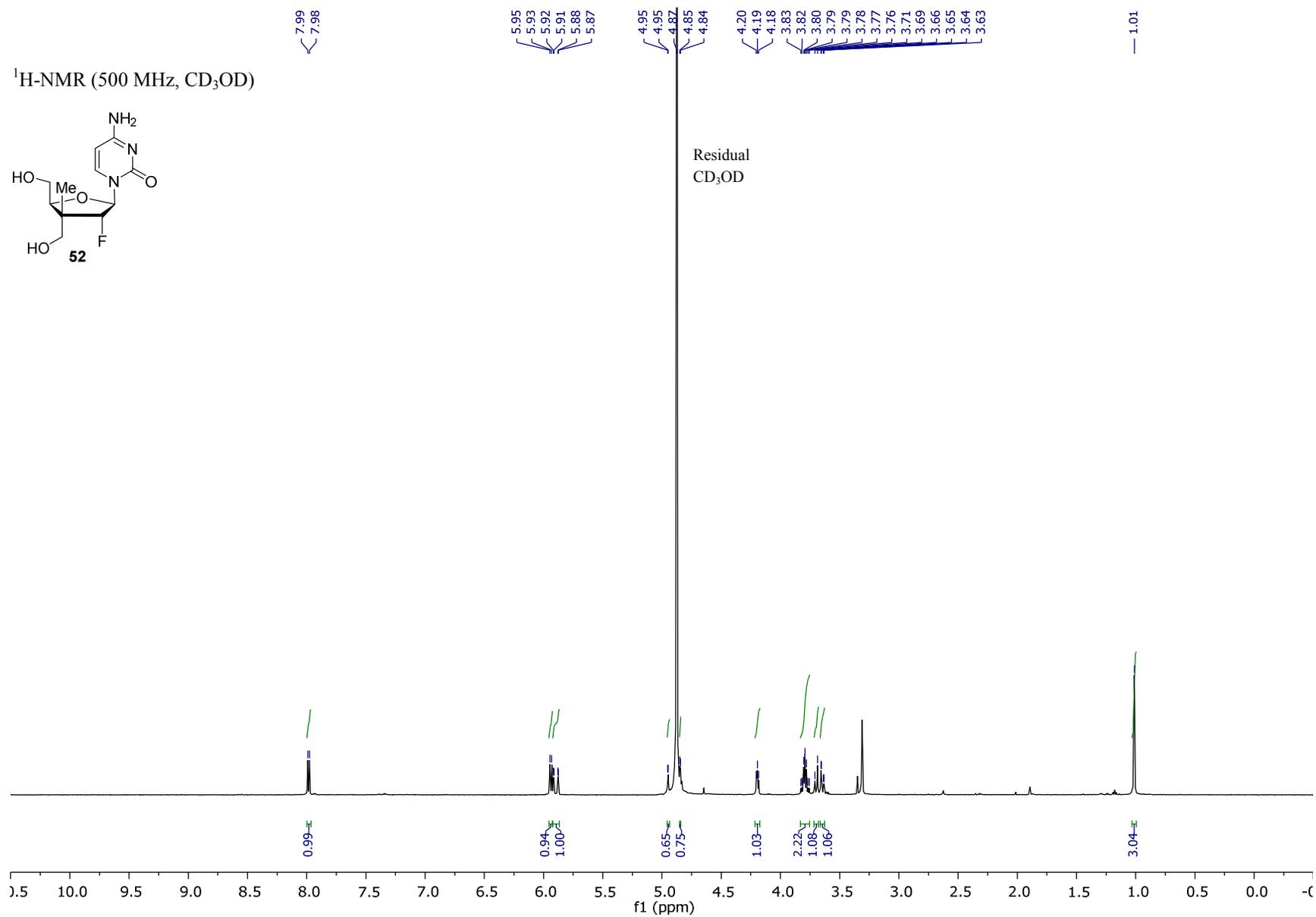




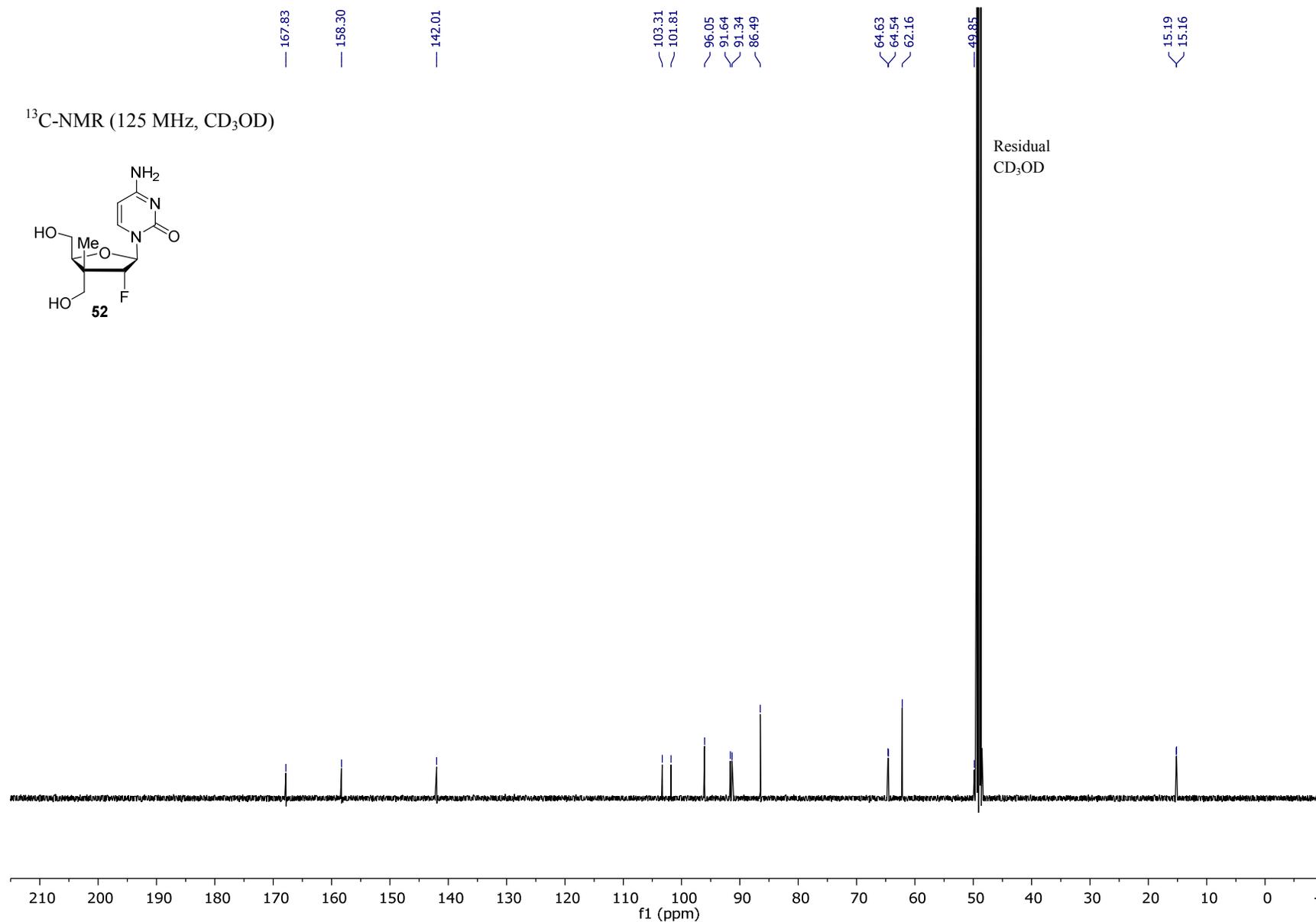
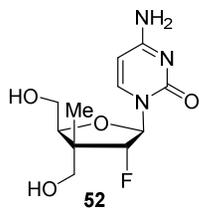


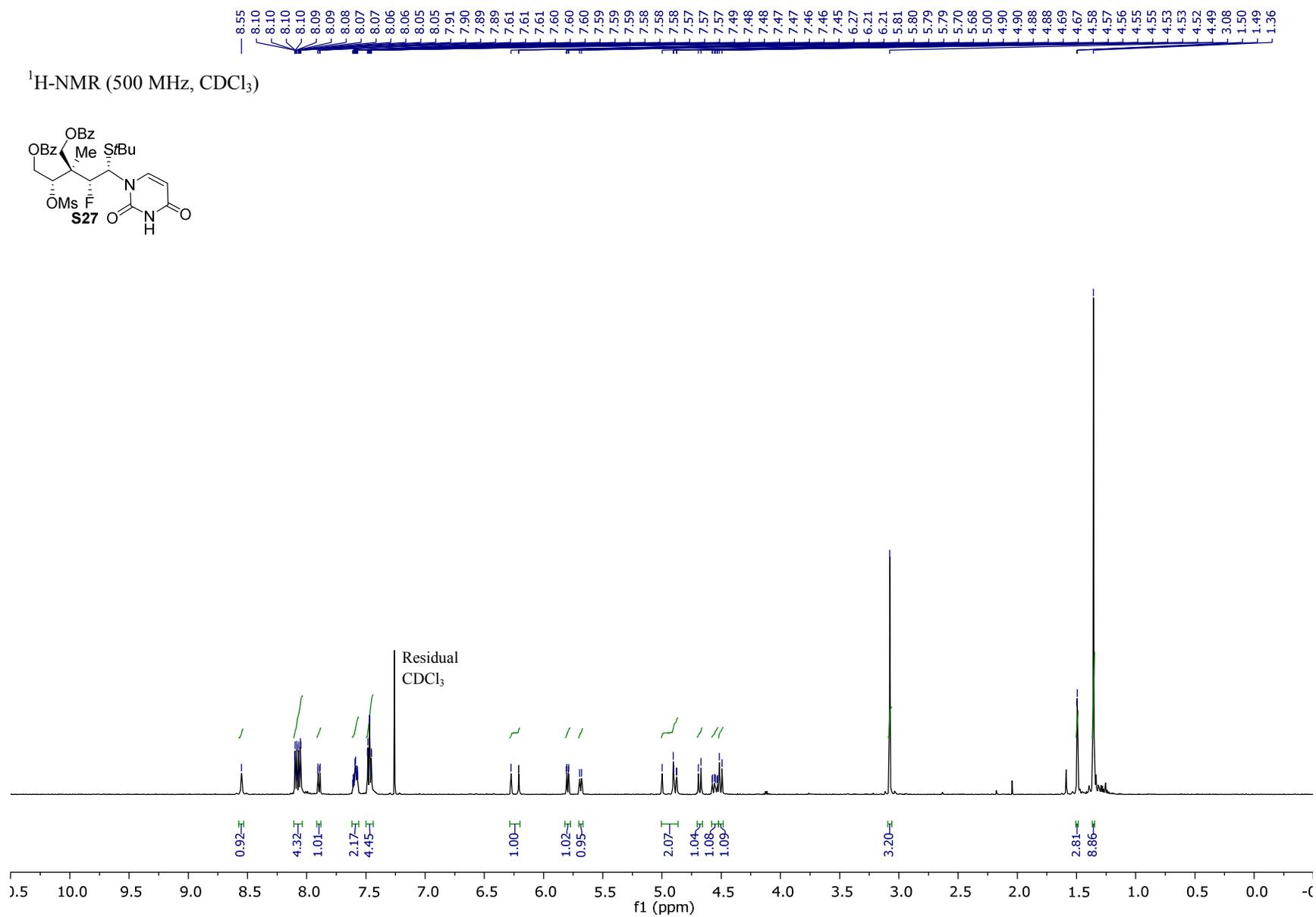
$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ )

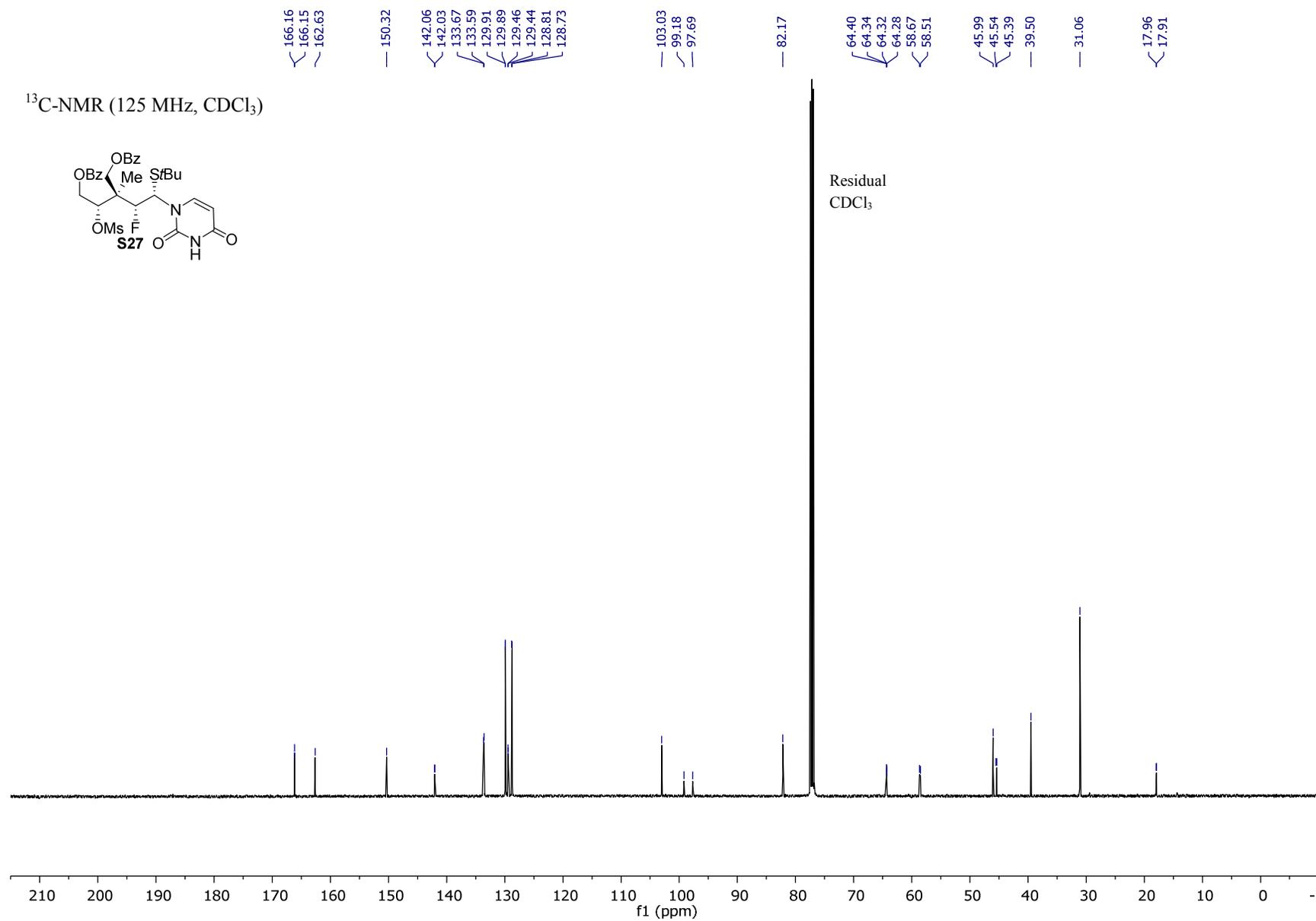




<sup>13</sup>C-NMR (125 MHz, CD<sub>3</sub>OD)

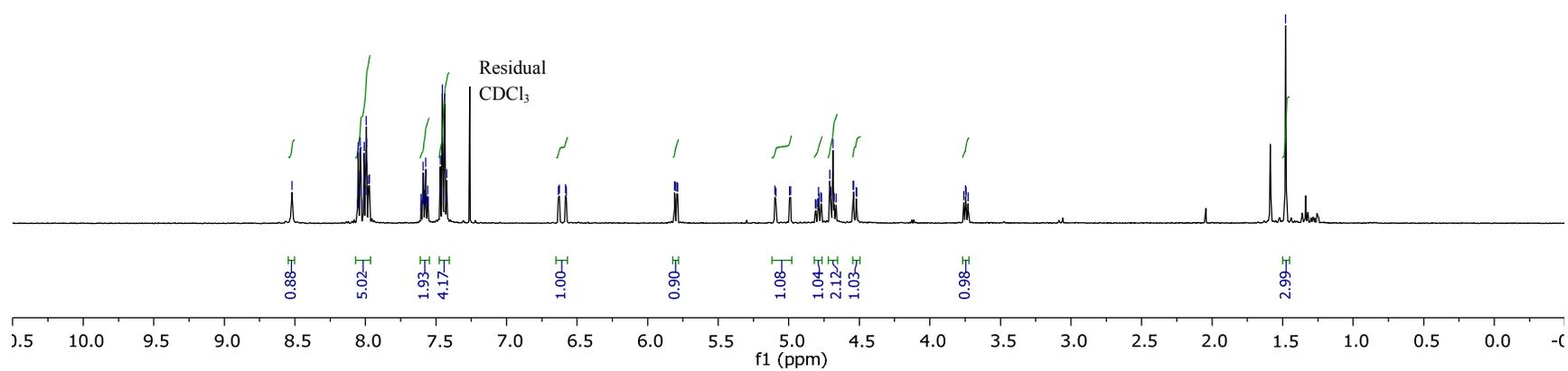
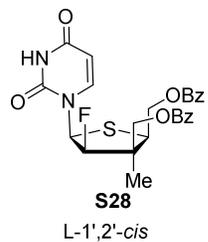


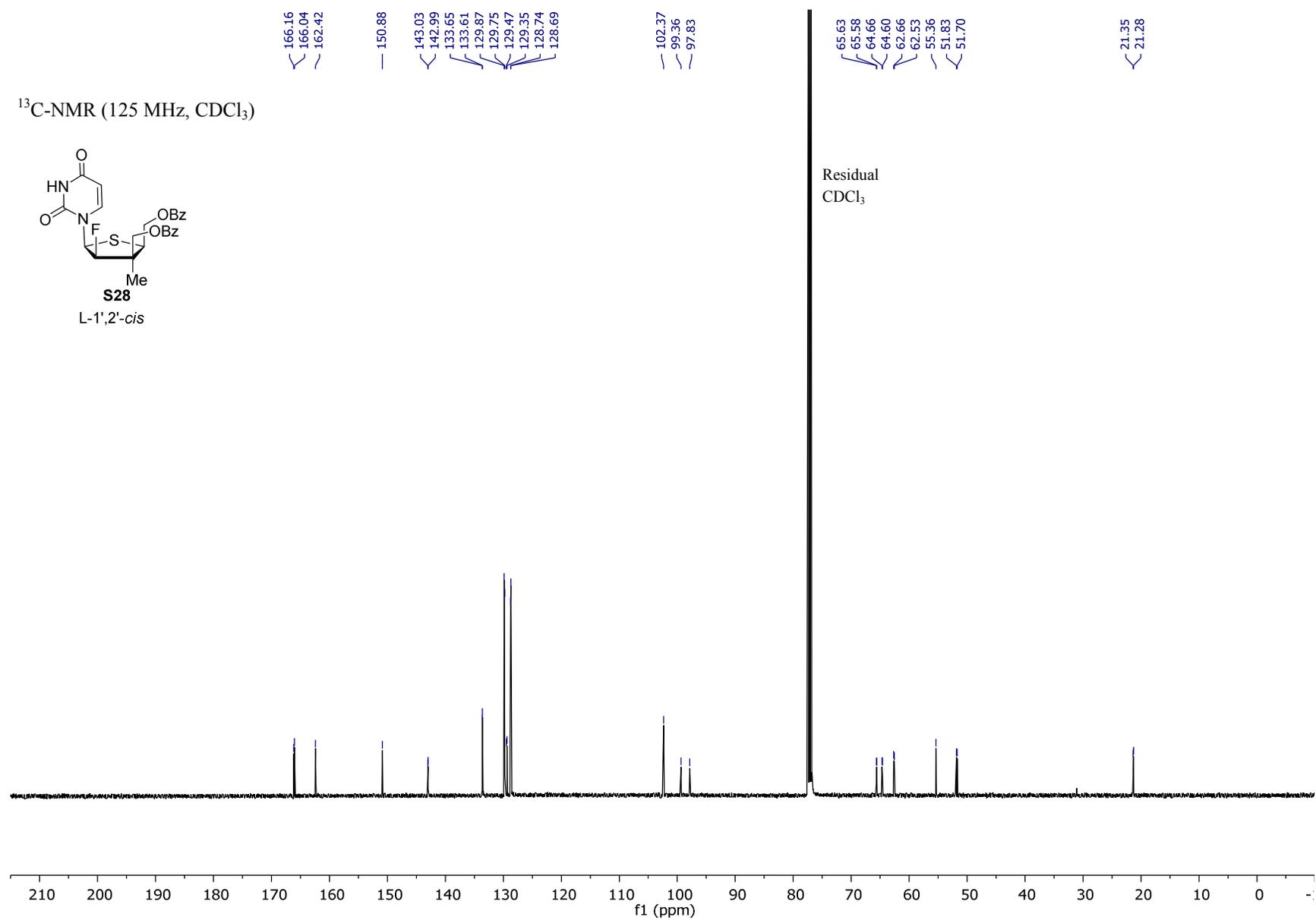


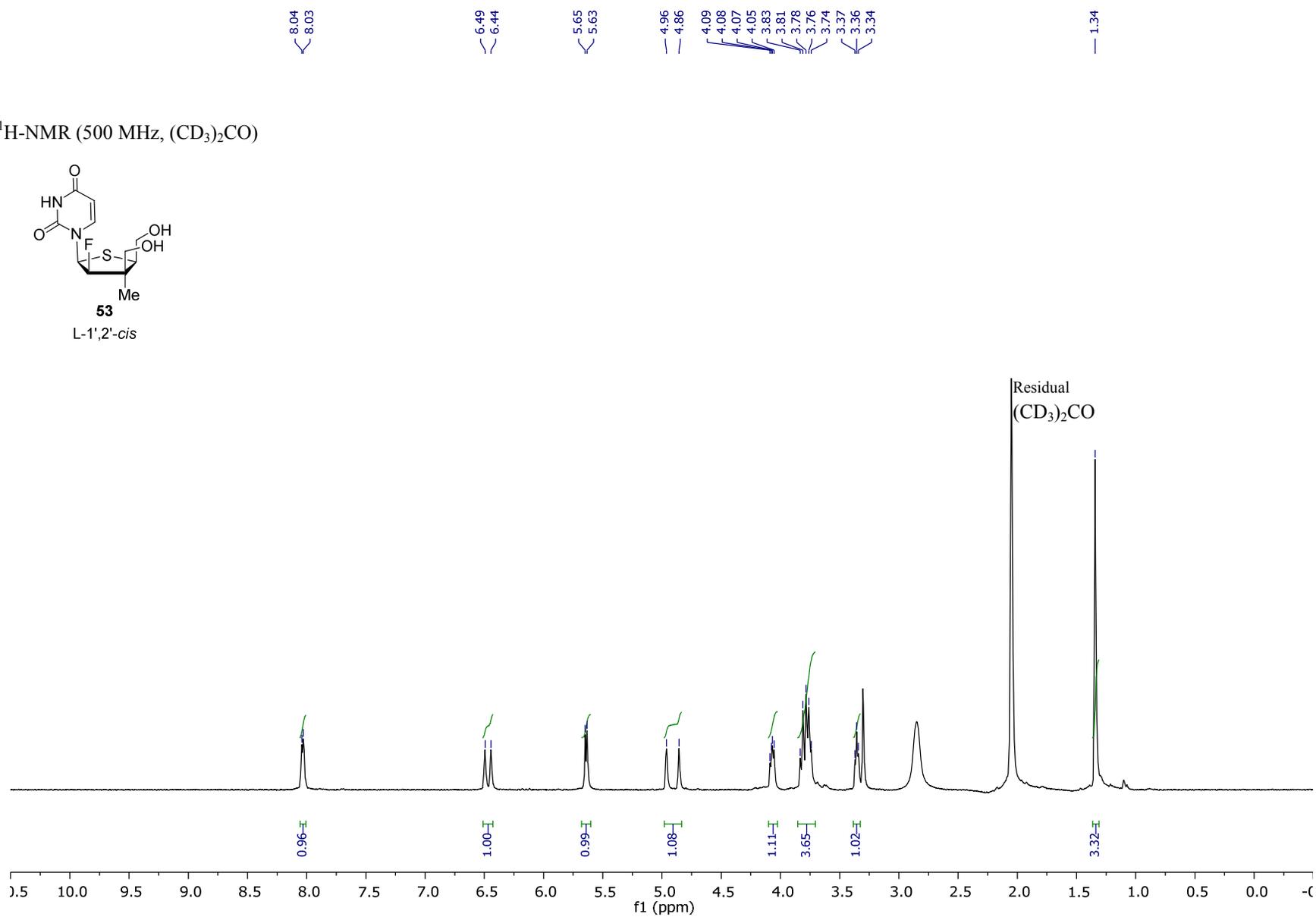
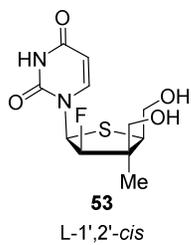


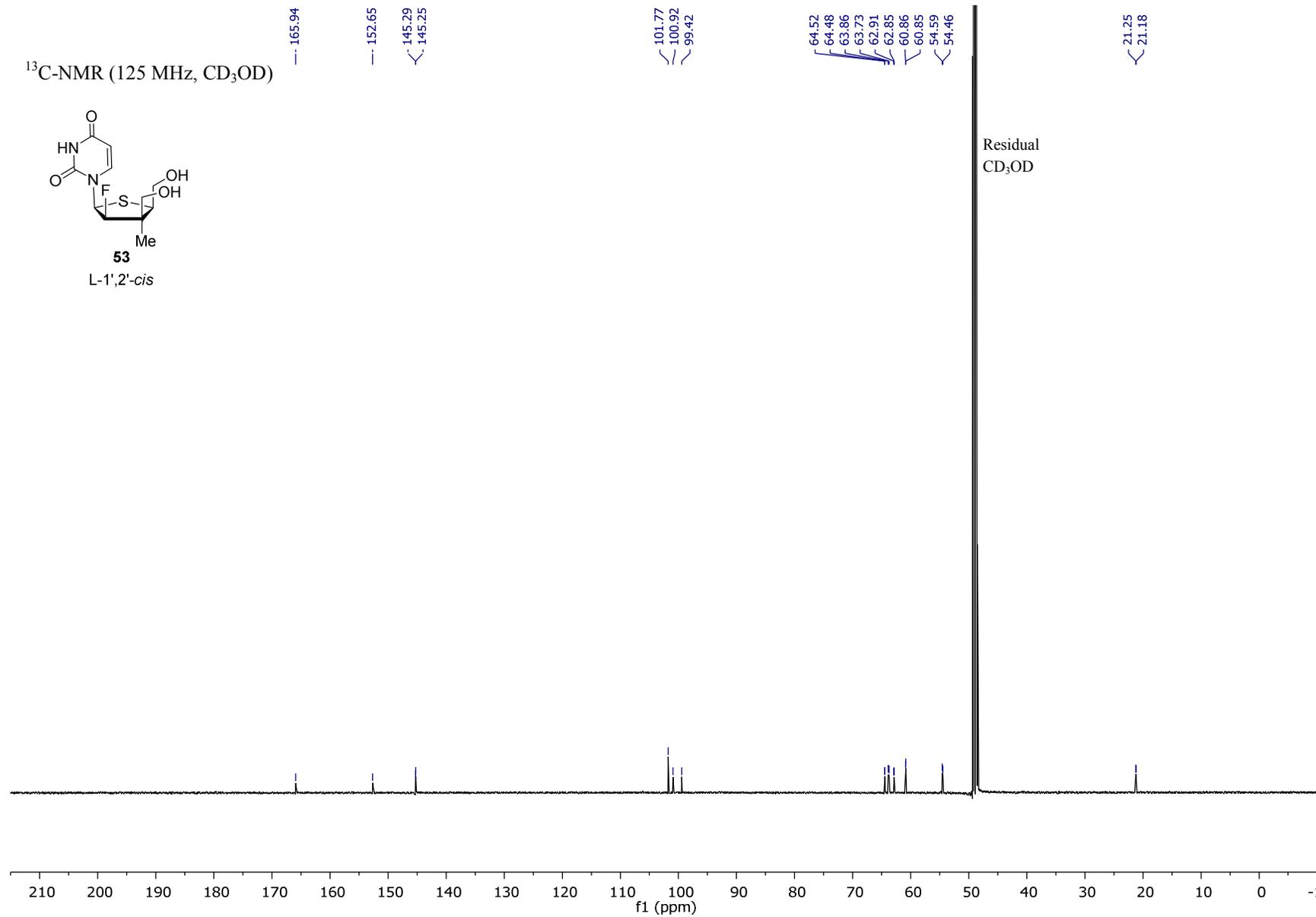
8.52  
8.06  
8.05  
8.05  
8.05  
8.04  
8.04  
8.03  
8.01  
8.01  
8.01  
8.00  
8.00  
7.99  
7.99  
7.98  
7.97  
7.61  
7.60  
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7.42  
7.42  
6.63  
6.63  
6.58  
6.58  
5.81  
5.80  
5.79  
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5.10  
5.09  
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1.48

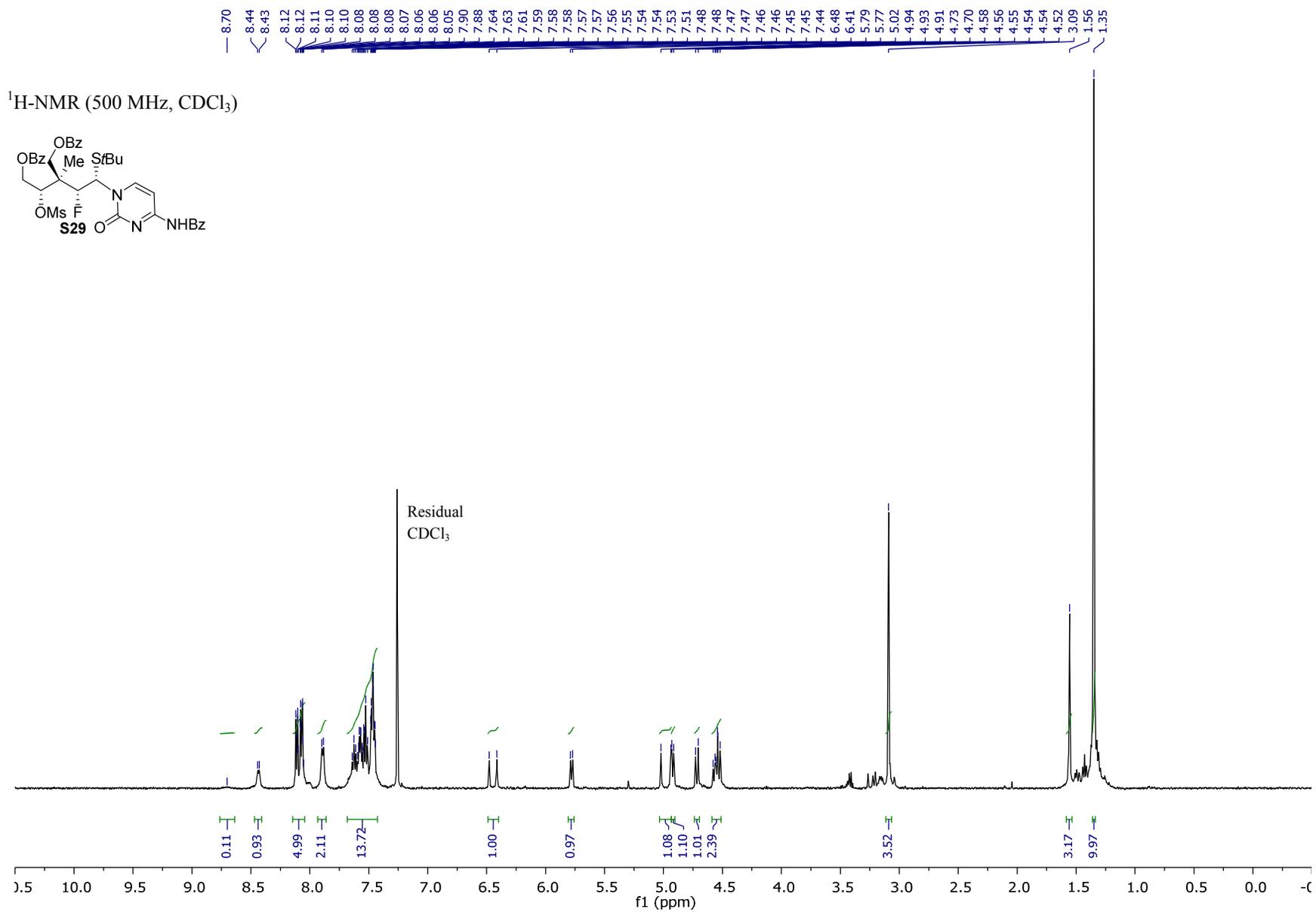
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )

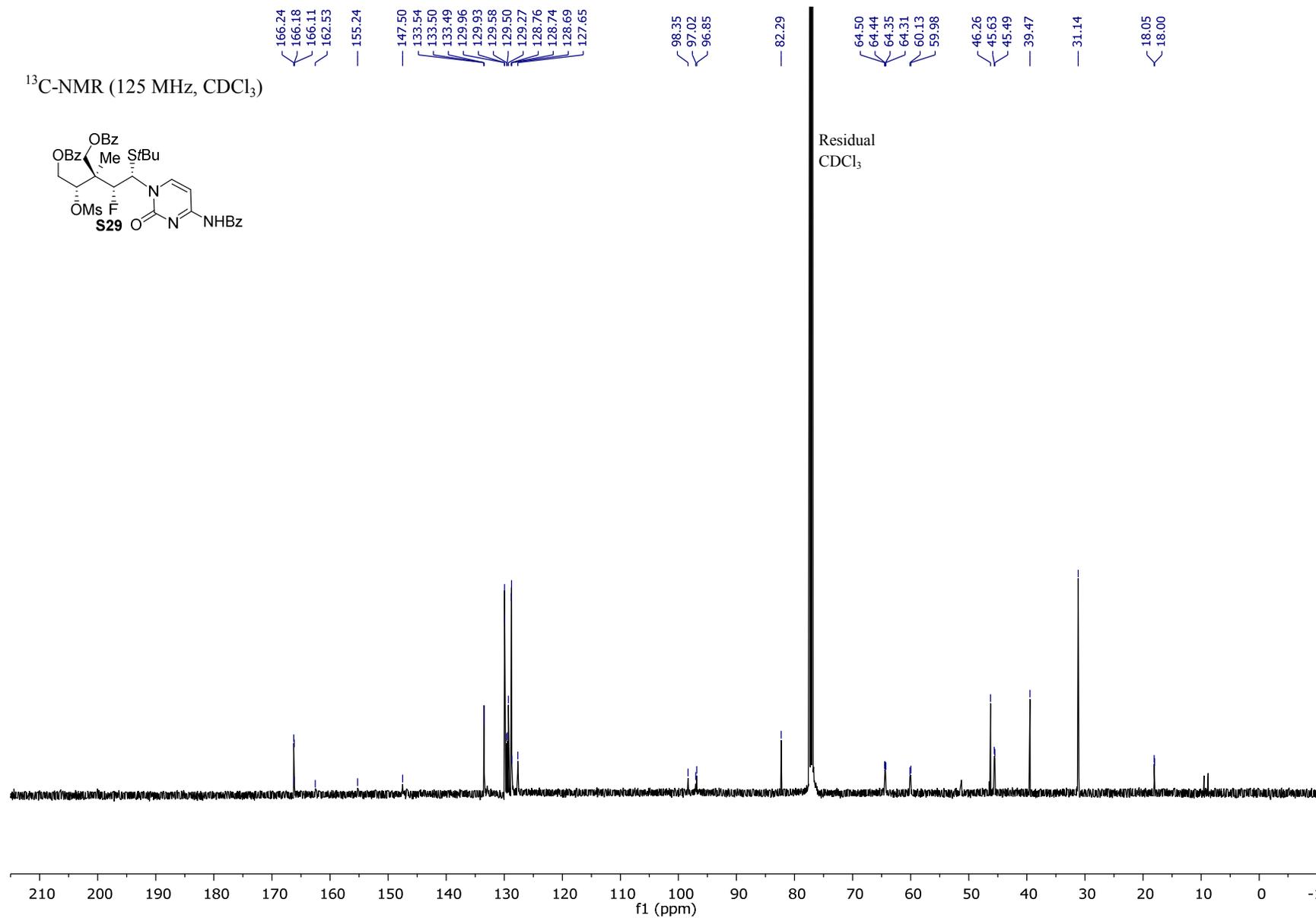


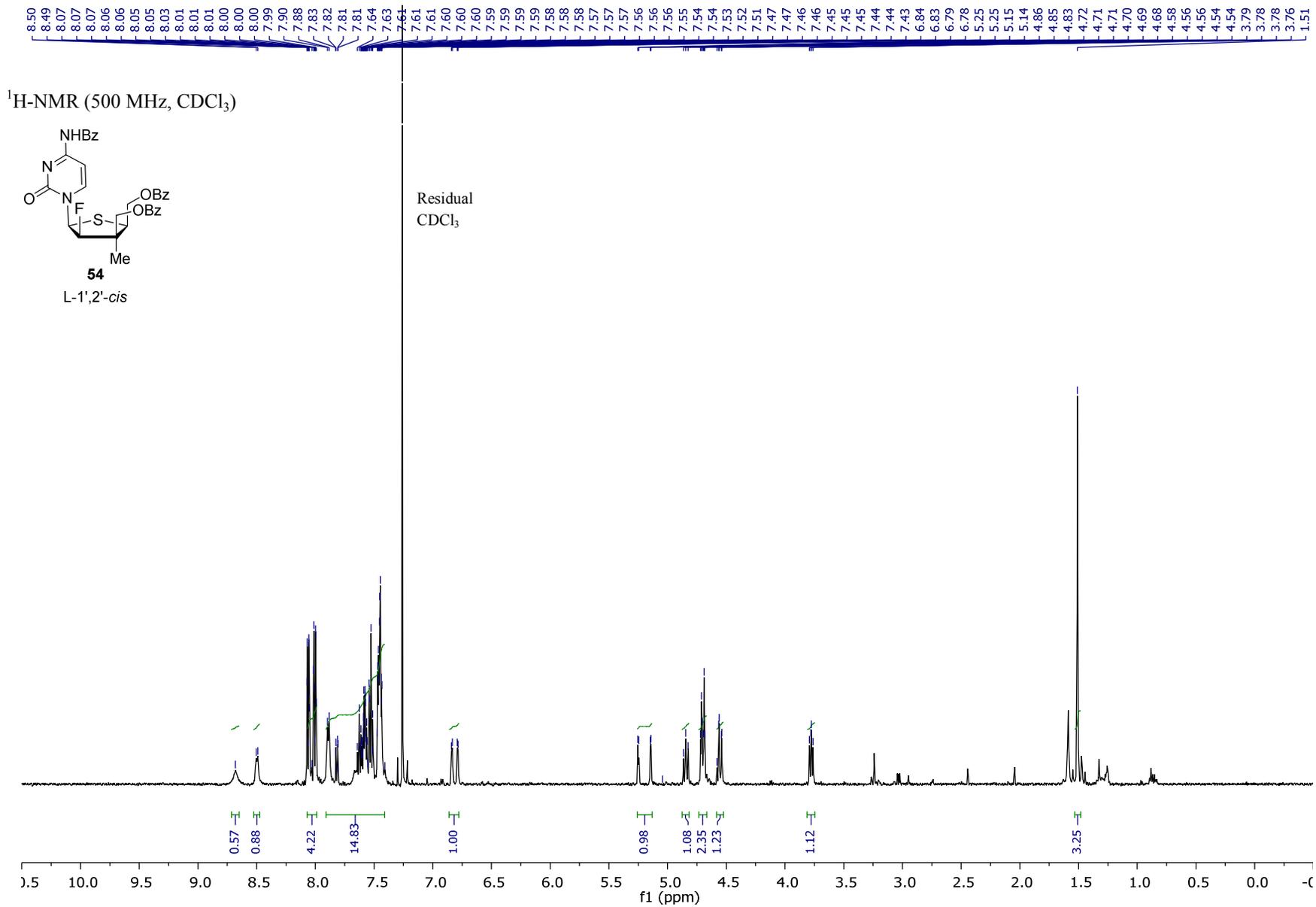


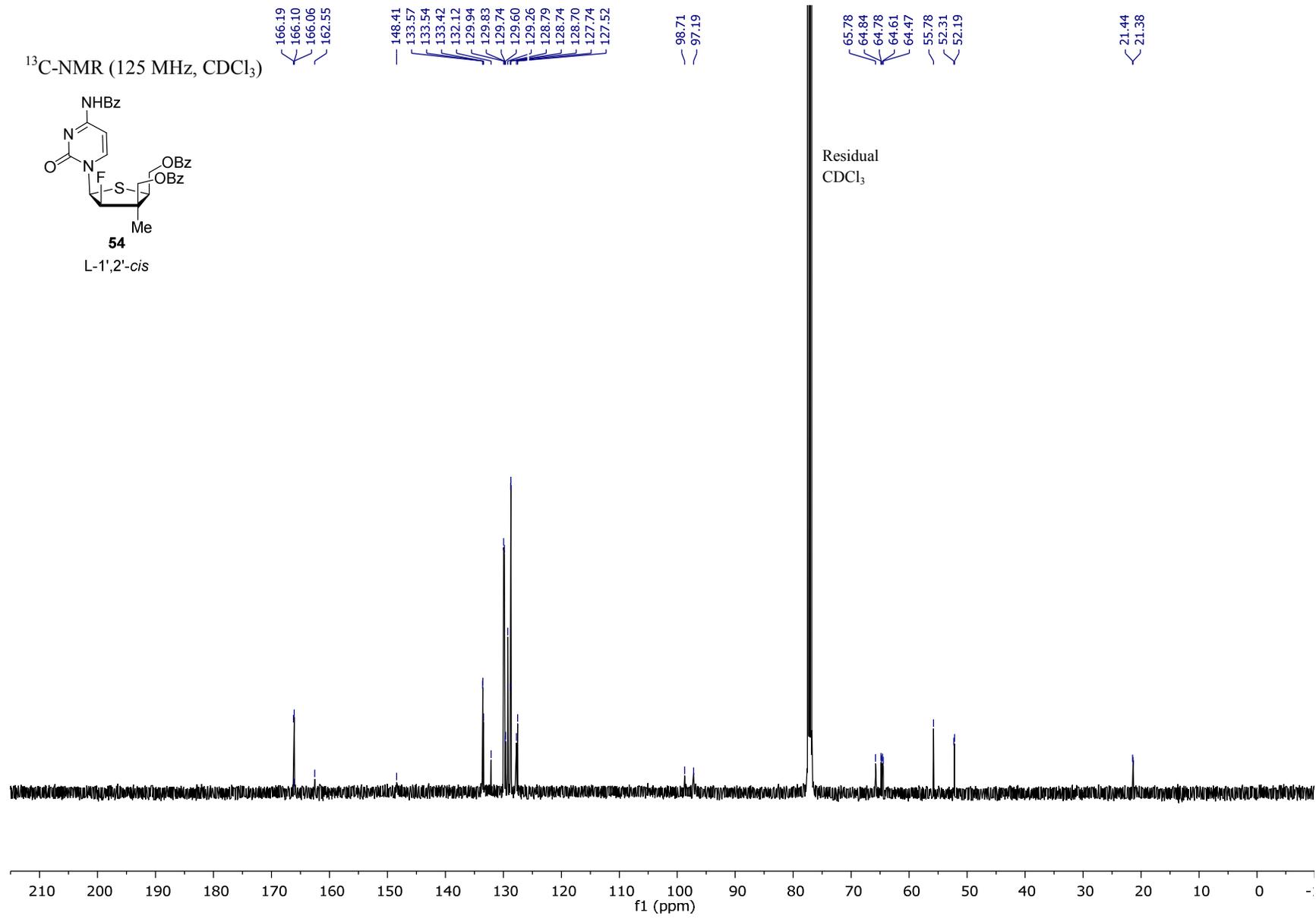
$^1\text{H-NMR}$  (500 MHz,  $(\text{CD}_3)_2\text{CO}$ )

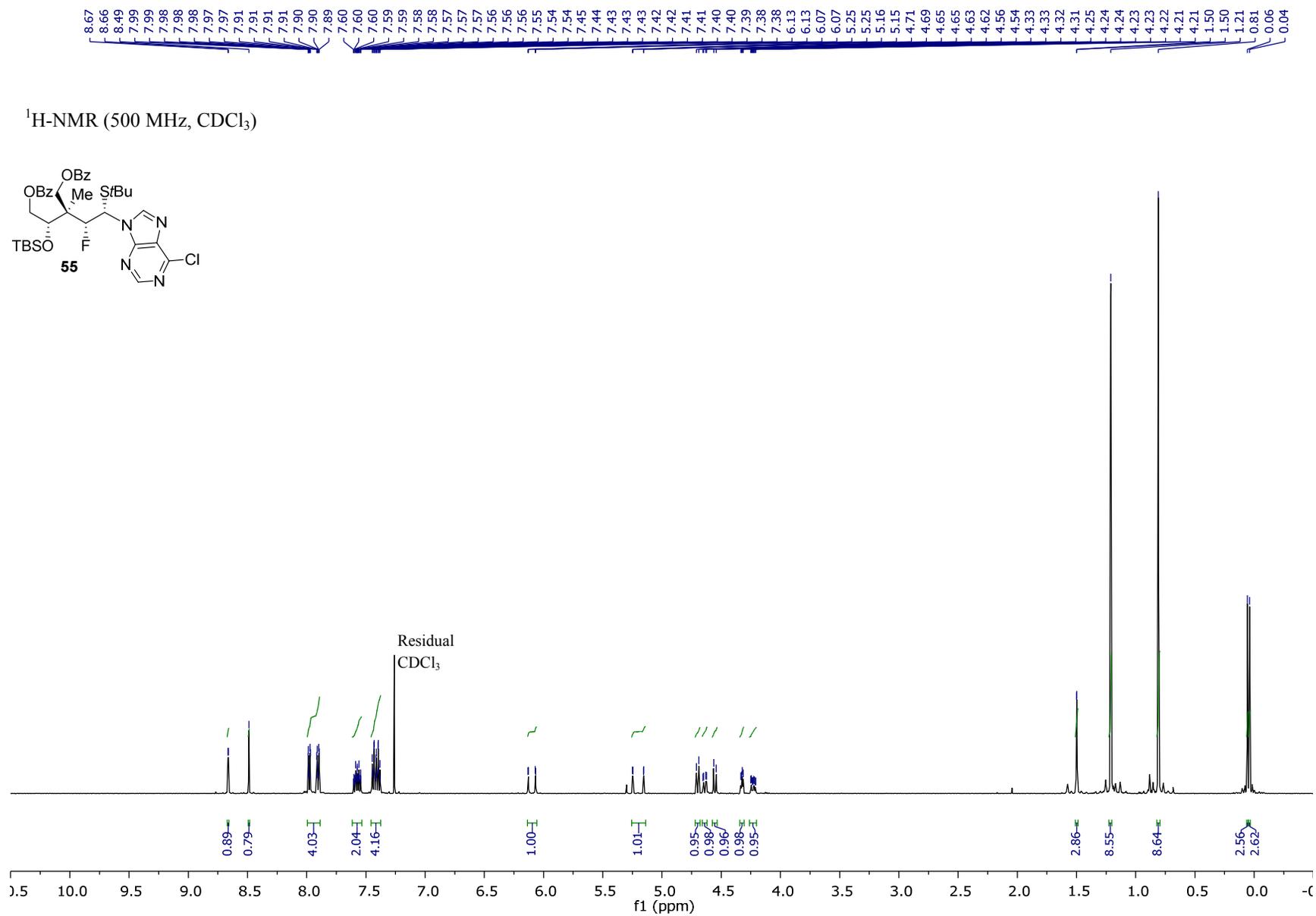


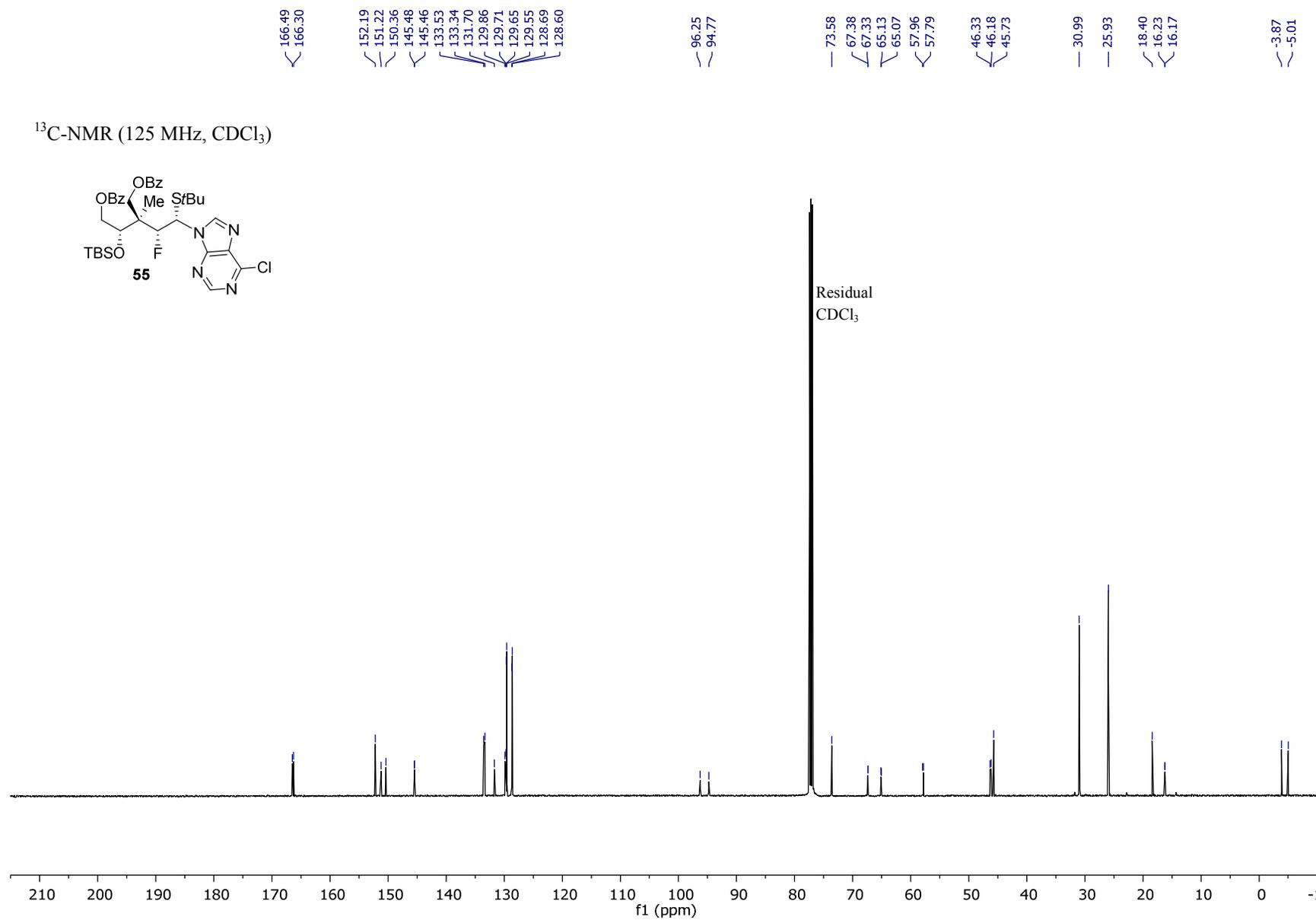


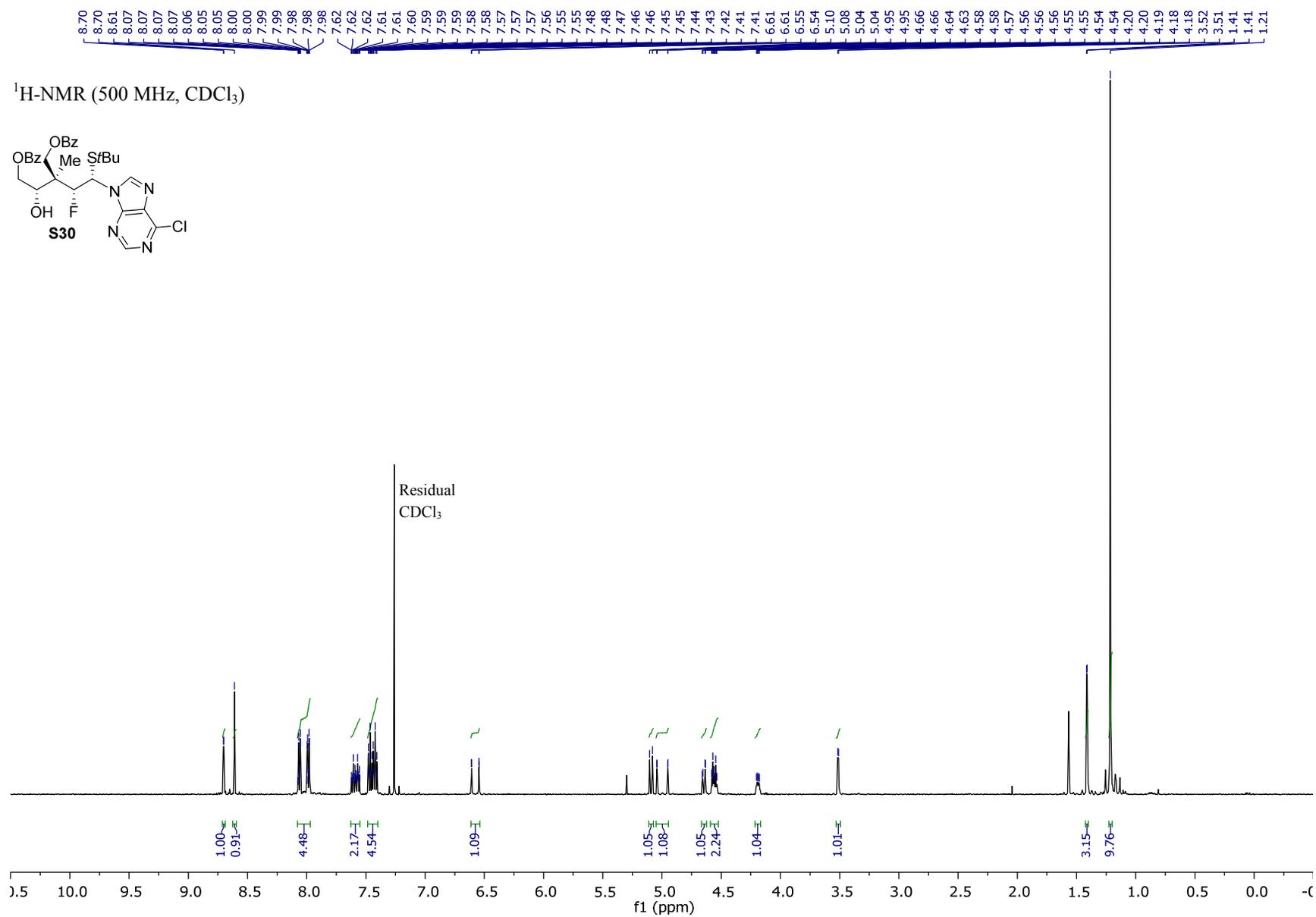




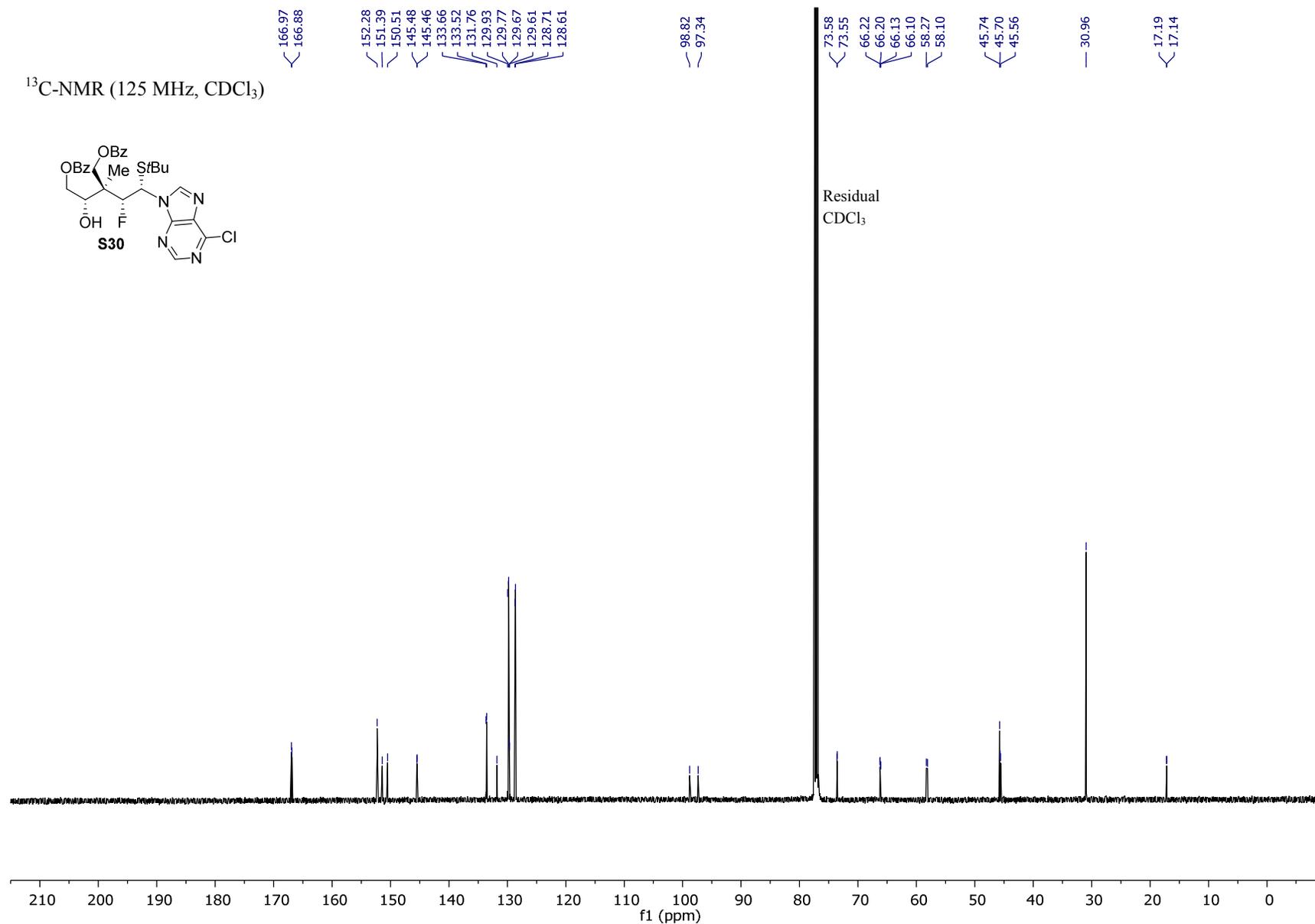
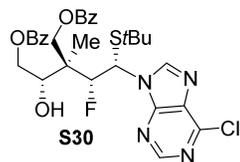






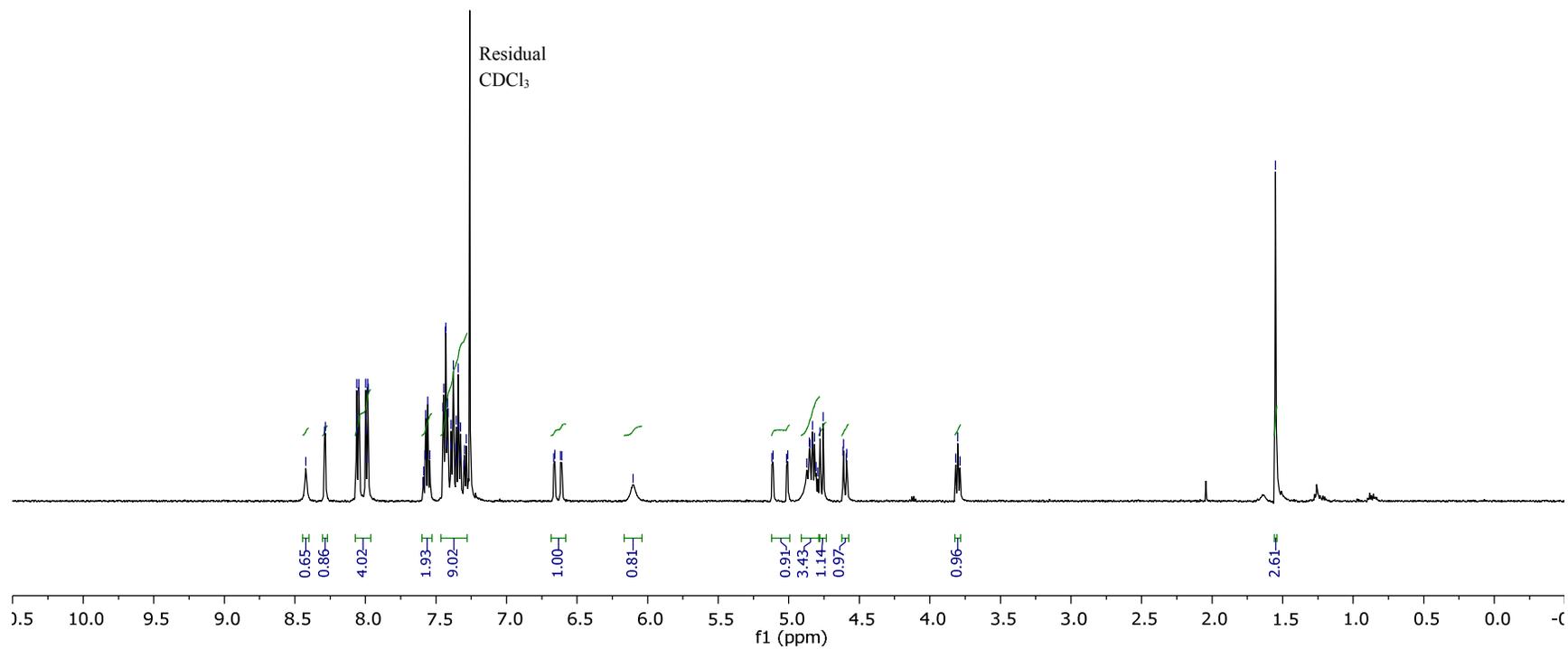
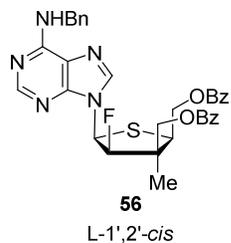


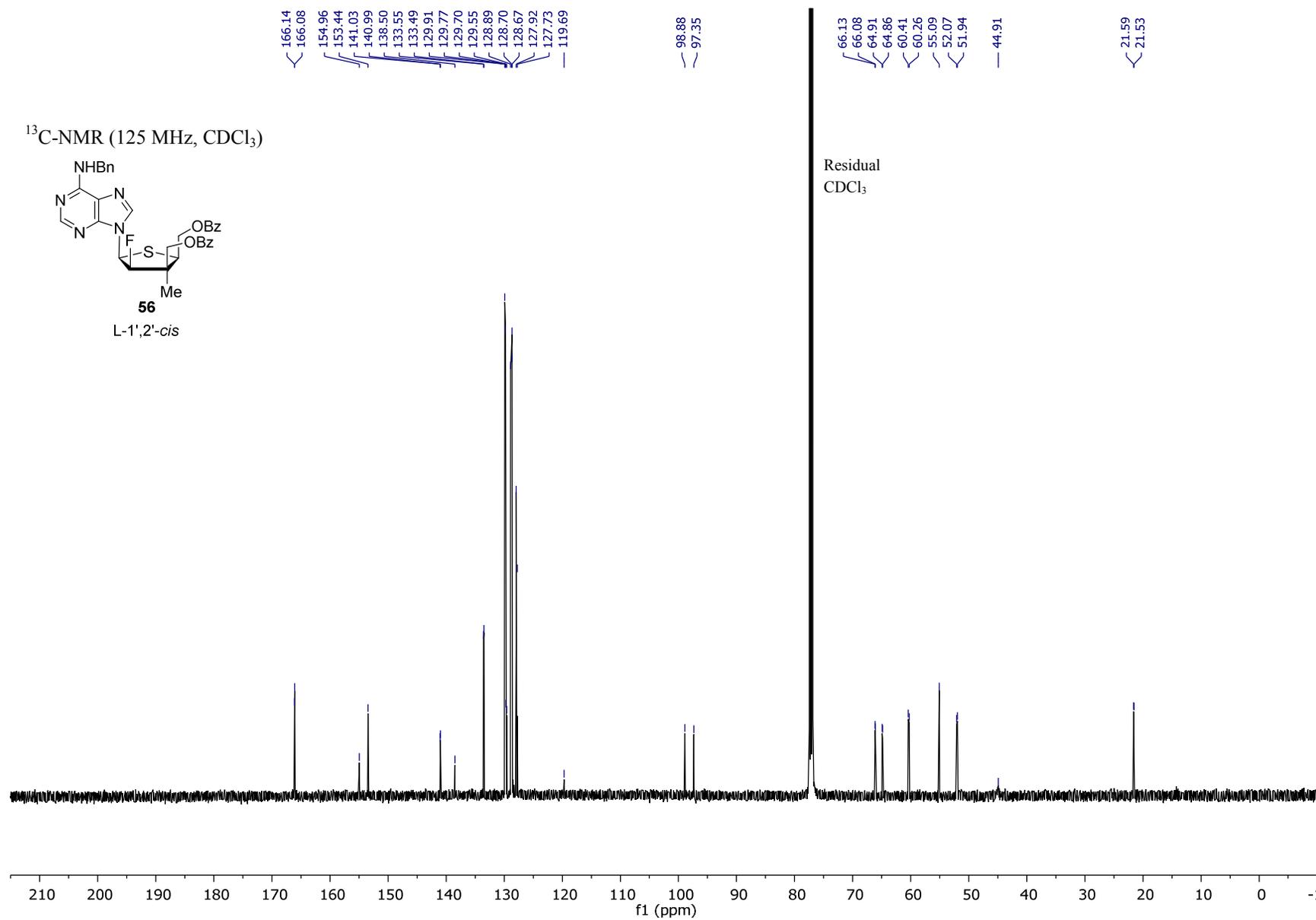
<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>)





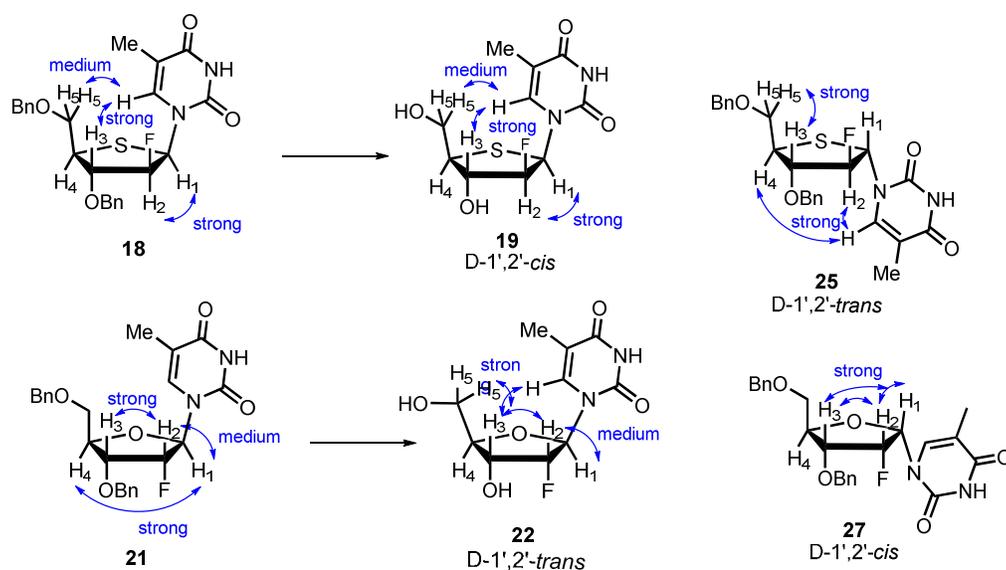
$^1\text{H-NMR}$  (500 MHz,  $\text{CDCl}_3$ )



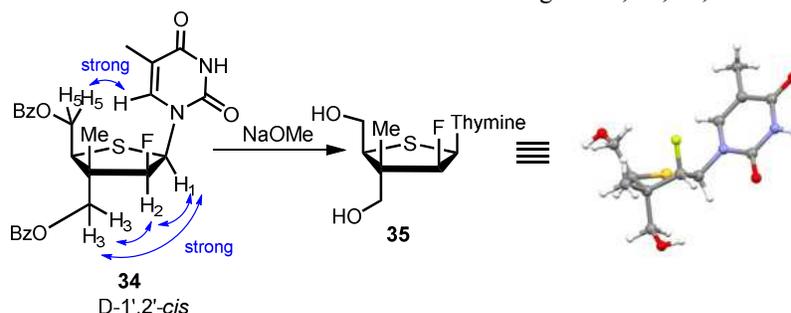


### Part III : Stereochemical Proofs

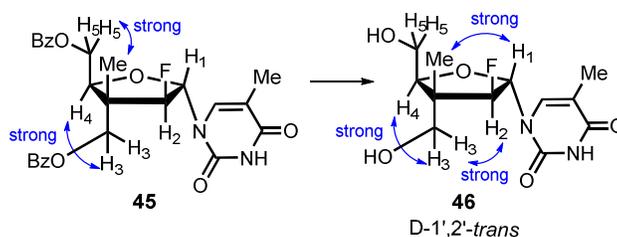
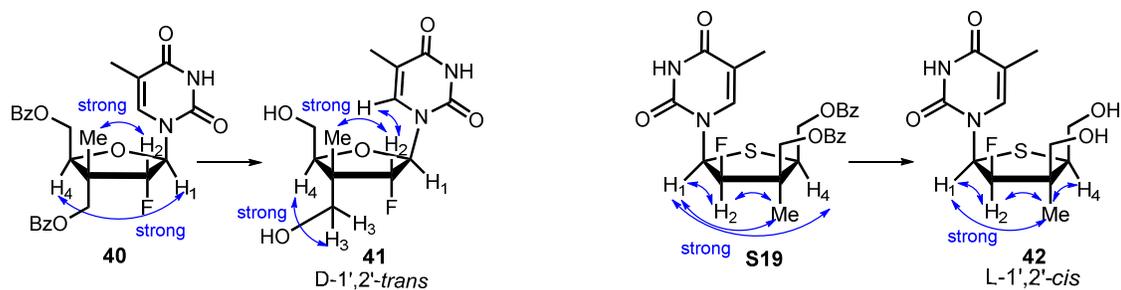
In all cases, the selectivities were determined by  $^1\text{H}$  NMR spectroscopic analysis of the unpurified reaction mixtures. The C1'–C2' relative configurations of the synthesized nucleoside analogues were determined by relevant nuclear Overhauser effect (NOE) enhancements (2D NOESY),  $^1\text{H}$  NMR coupling constant data and correlations of chemical shifts. The peaks in the  $^1\text{H}$  NMR spectra were assigned using  $^1\text{H}/^1\text{H}$  COSY experiments, chemical shifts, and coupling constants. Proof of structure for the C1'-C2' relative stereochemistry were provided by NOESY experiments. Nucleoside analogues **19**<sup>12</sup> and **22**<sup>13</sup> are known compounds.



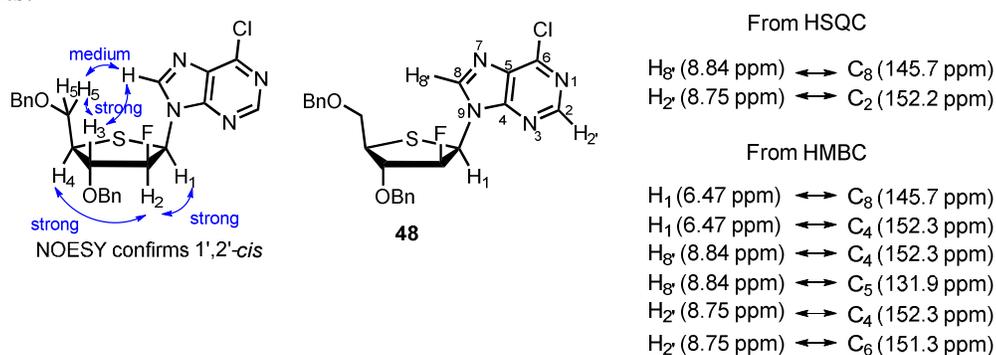
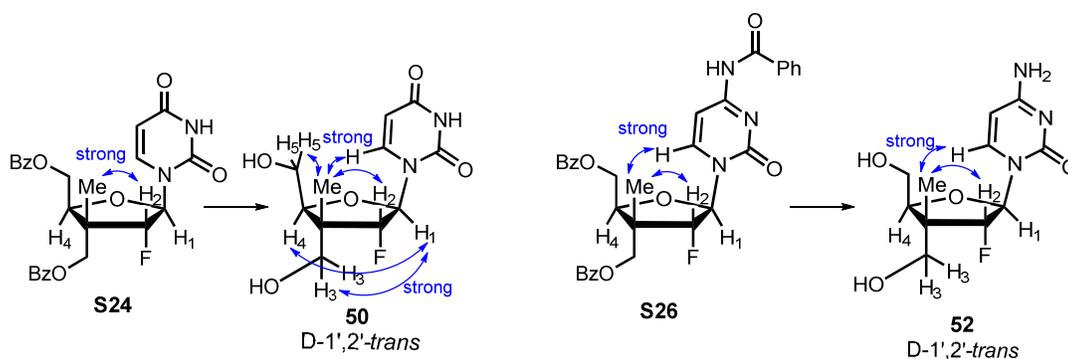
Relevant NOESY data for nucleoside analogues **19**, **22**, **25**, **27**.

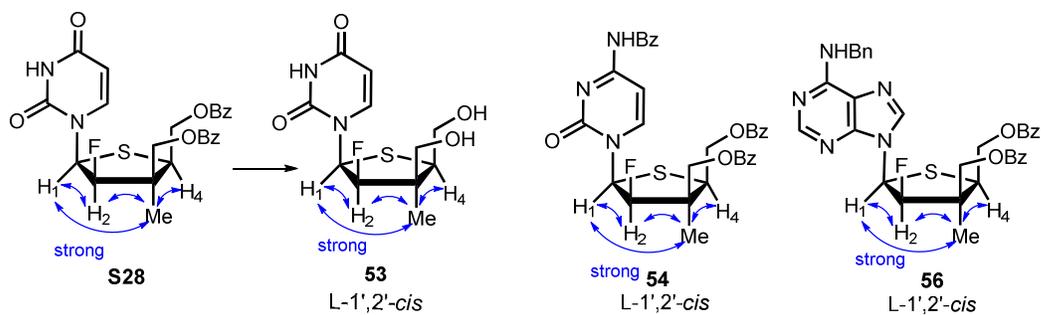


Relevant NOESY data for nucleoside analogue **35** including its X-ray.

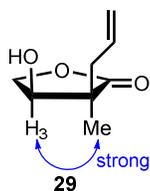
Relevant NOESY data for nucleoside analogues **41**, **42**, and **46**.

Proof of N9 regiochemistry of the 6-Cl-purine ring was determined from HSQC and HMBC experiments.

Relevant HSQC, HMBC and NOESY data for nucleoside analogues **48**.Relevant NOESY data for nucleoside analogues **50** and **52**.

Relevant NOESY data for nucleoside analogues **53**, **54** and **56**.

A strong coupling between H3 and the C2-Me group was confirmed by NOESY for compound **29**.



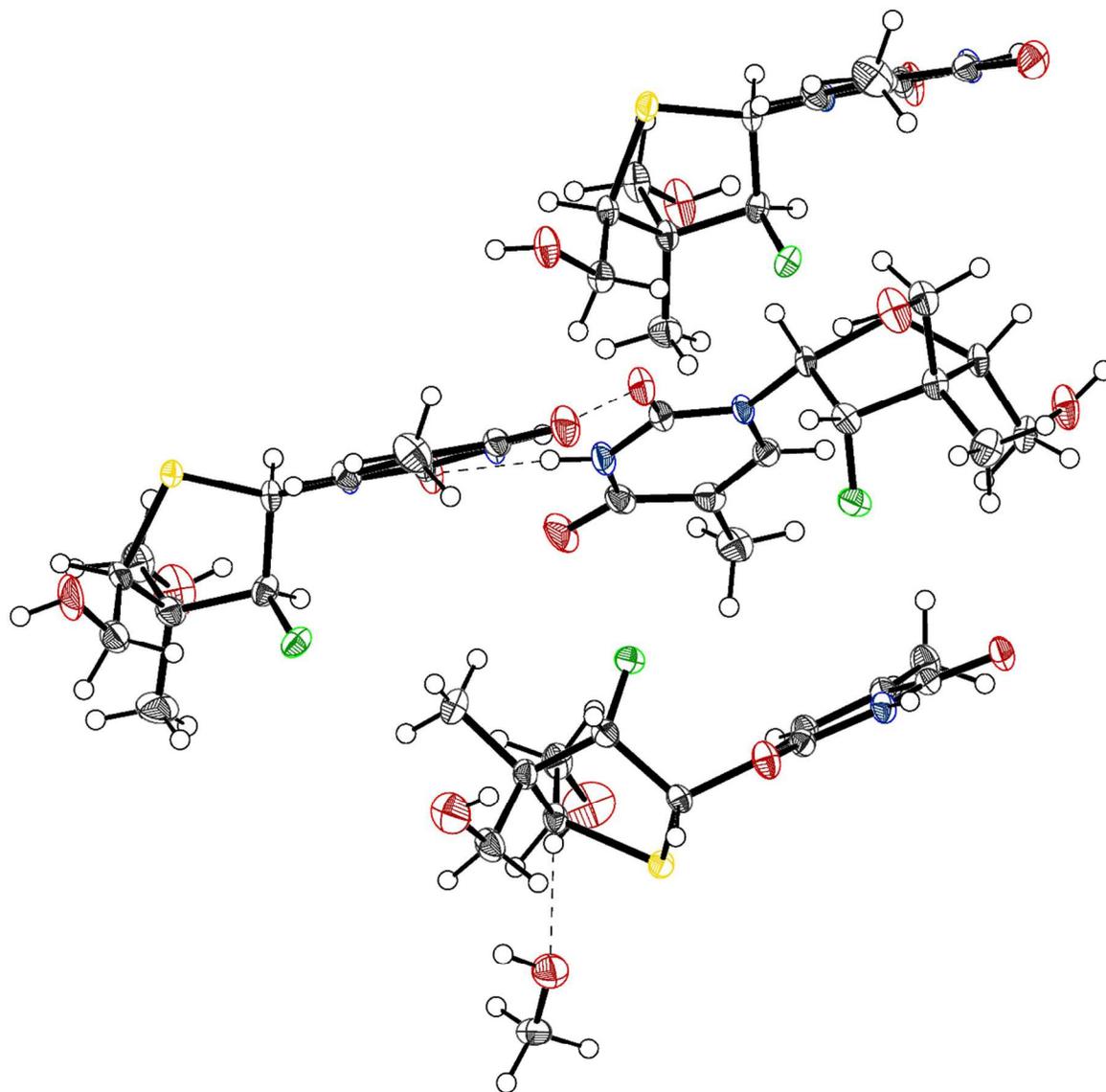
**Part IV. X-ray information for compound 35**

Single crystals of  $C_{48.5}H_{70}F_4N_8O_{16.5}S_4$  were prepared from a mixture of ethyl acetate, methanol and hexanes. A suitable crystal was selected and mounted on a diffractometer. The crystal was kept at 100 K during data collection. Using Olex2,<sup>14</sup> the structure was solved with the XT<sup>15</sup> structure solution program using Direct Methods and refined with the XL<sup>16</sup> refinement package using Least Squares minimization.

Crystal Data for  $C_{48.5}H_{70}F_4N_8O_{16.5}S_4$  (M = 1233.36 g/mol): monoclinic, space group P2<sub>1</sub> (no. 4), a = 11.8937(3) Å, b = 14.4166(4) Å, c = 16.4236(4) Å, β = 95.3690(10)°, V = 2803.75(13) Å<sup>3</sup>, Z = 2, T = 100 K, μ(GaKα) = 1.510 mm<sup>-1</sup>, D<sub>calc</sub> = 1.461 g/cm<sup>3</sup>, 97530 reflections measured (4.702° ≤ 2θ ≤ 121.444°), 12729 unique (R<sub>int</sub> = 0.0393, R<sub>sigma</sub> = 0.0238) which were used in all calculations. The final R<sub>1</sub> was 0.0347 (I > 2σ(I)) and wR<sub>2</sub> was 0.0964 (all data). Four molecules and a half methanol were found by asymmetric unit.

Empirical formula	$C_{48.5}H_{70}F_4N_8O_{16.5}S_4$
Formula weight	1233.36
Temperature/K	100
Crystal system	monoclinic
Space group	P2 <sub>1</sub>
a/Å	11.8937(3)
b/Å	14.4166(4)
c/Å	16.4236(4)
α/°	90
β/°	95.3690(10)
γ/°	90
Volume/Å <sup>3</sup>	2803.75(13)
Z	2
ρ <sub>calc</sub> /g/cm <sup>3</sup>	1.461
μ/mm <sup>-1</sup>	1.510
F(000)	1298.0
Crystal size/mm <sup>3</sup>	0.32 × 0.31 × 0.11
Radiation	GaKα (λ = 1.34139)
2θ range for data collection/°	4.702 to 121.444
Index ranges	-15 ≤ h ≤ 15, -17 ≤ k ≤ 18, -21 ≤ l ≤ 21
Reflections collected	97530
Independent reflections	12729 [R <sub>int</sub> = 0.0393, R <sub>sigma</sub> = 0.0238]

Data/restraints/parameters	12729/1/757
Goodness-of-fit on $F^2$	1.073
Final R indexes [ $I \geq 2\sigma(I)$ ]	$R_1 = 0.0347$ , $wR_2 = 0.0956$
Final R indexes [all data]	$R_1 = 0.0353$ , $wR_2 = 0.0964$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.50/-0.34
Flack parameter	0.014(4)



Thermal ellipsoid plot of the X-ray diffraction structure of compound **35**. Ellipsoid contour percent probability = 50%.

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