

An Alternative Pathway to Ribonucleoside β -Hydroxy-Phosphonate Analogues and Related Prodrugs

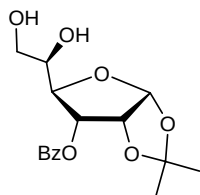
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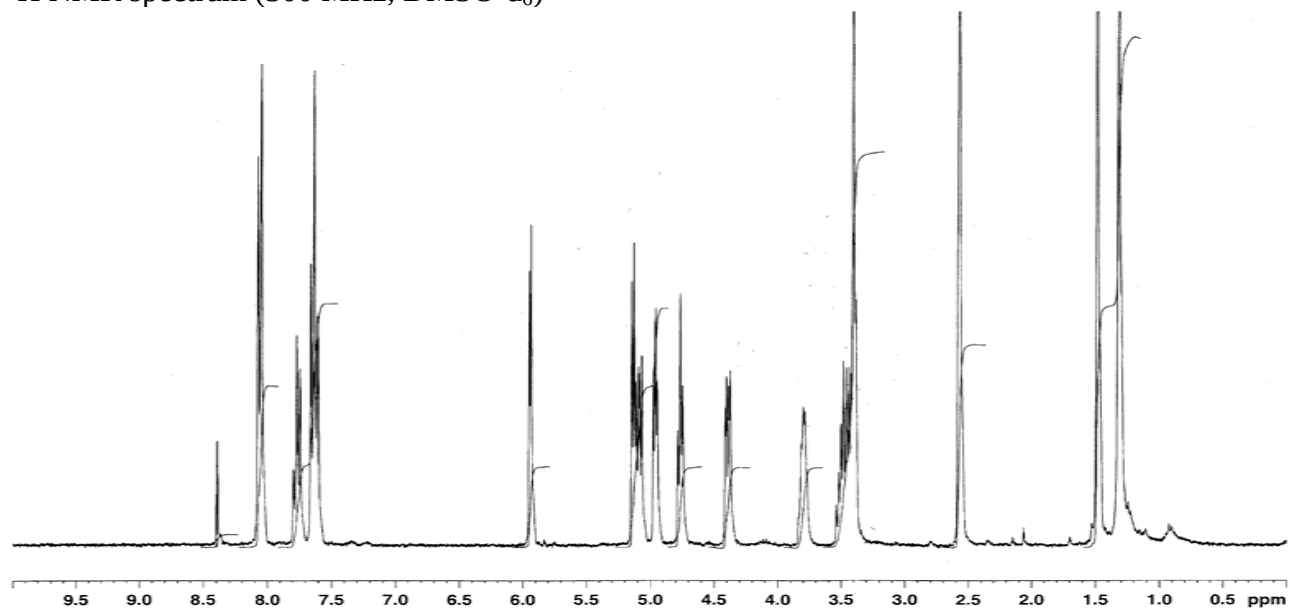
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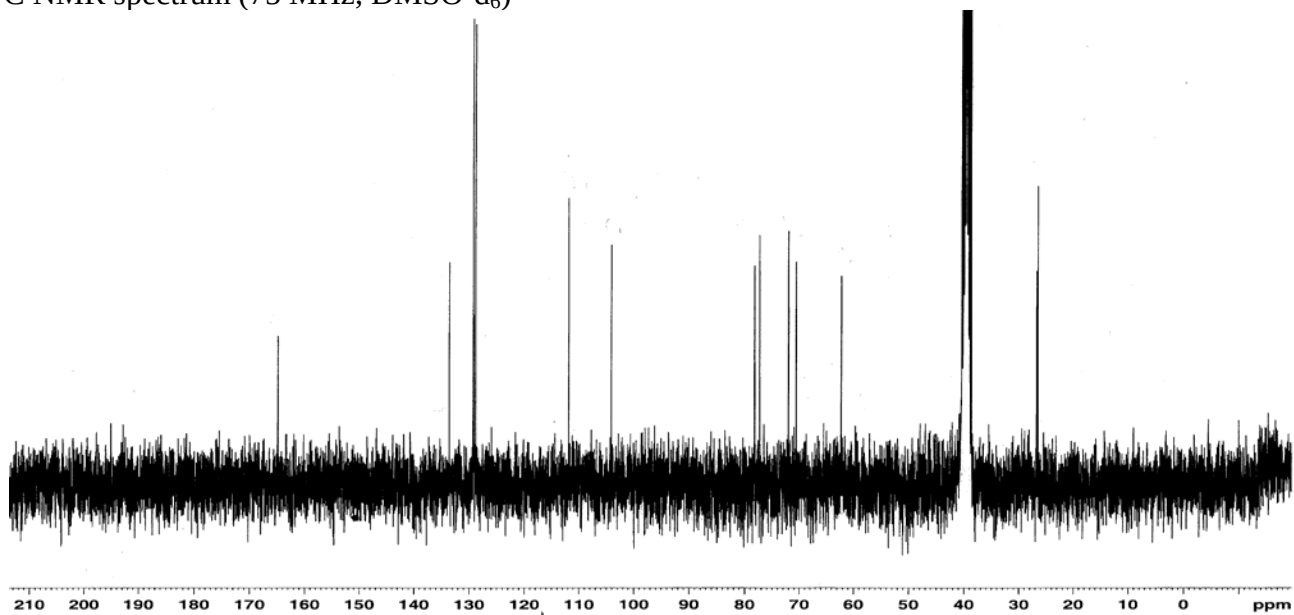


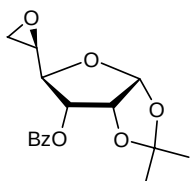
3-*O*-Benzoyl-1,2-*O*-isopropylidene-D-allofuranose (1)

^1H NMR spectrum (300 MHz, DMSO- d_6)



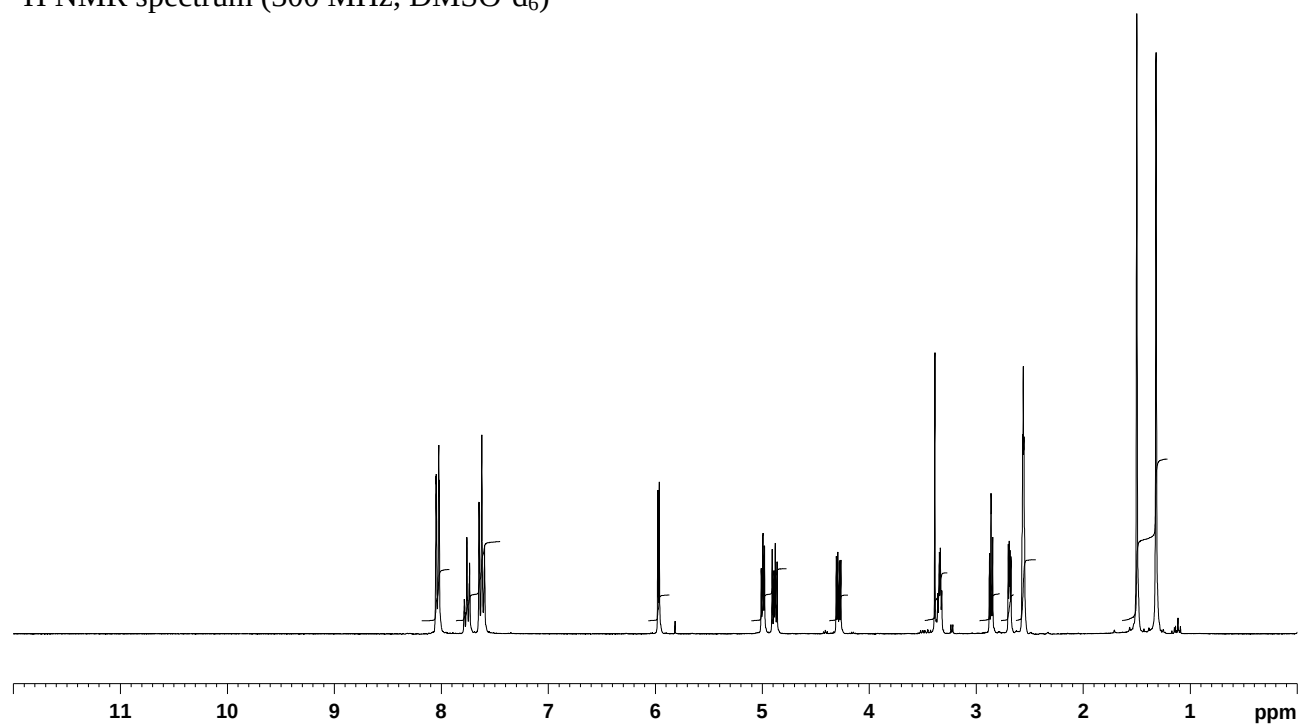
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



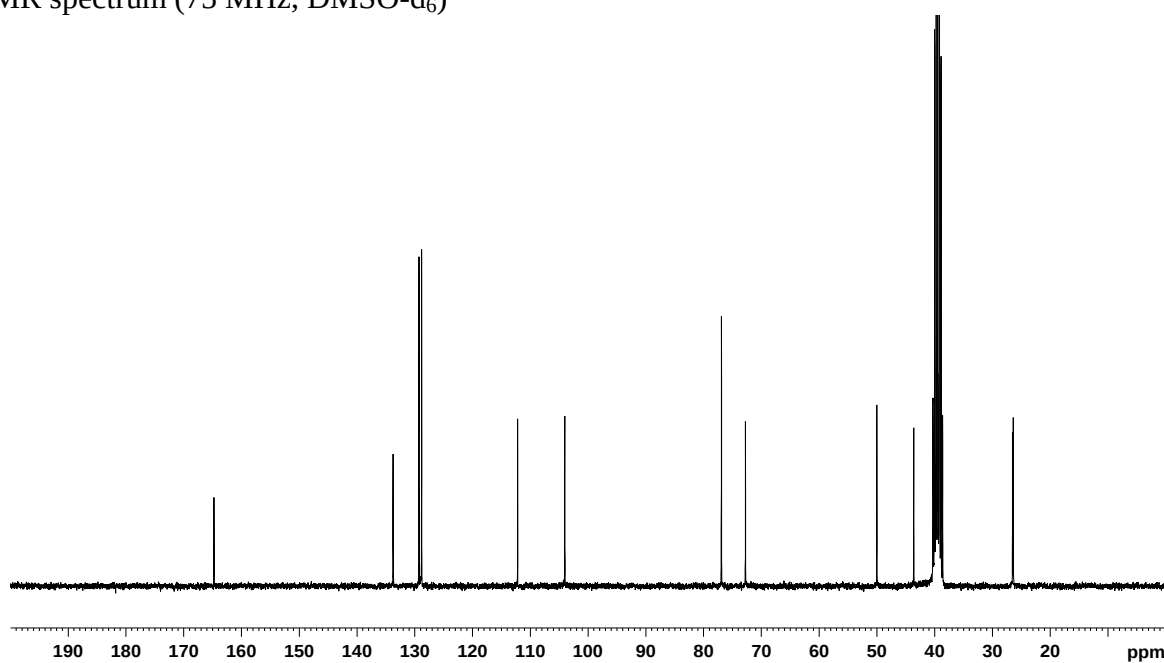


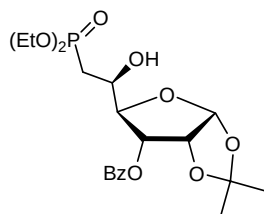
3-*O*-Benzoyl-1,2-*O*-isopropylidene-5,6-oxiran-D-allofuranose (2)

^1H NMR spectrum (300 MHz, DMSO- d_6)



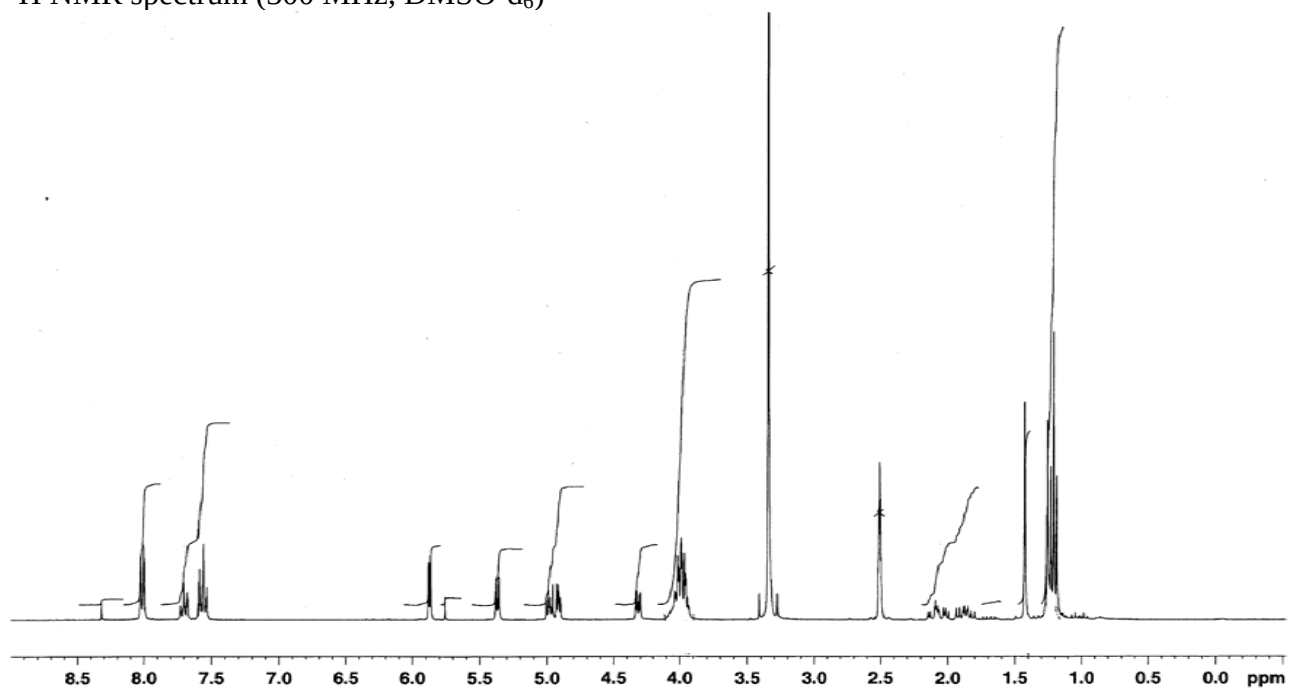
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



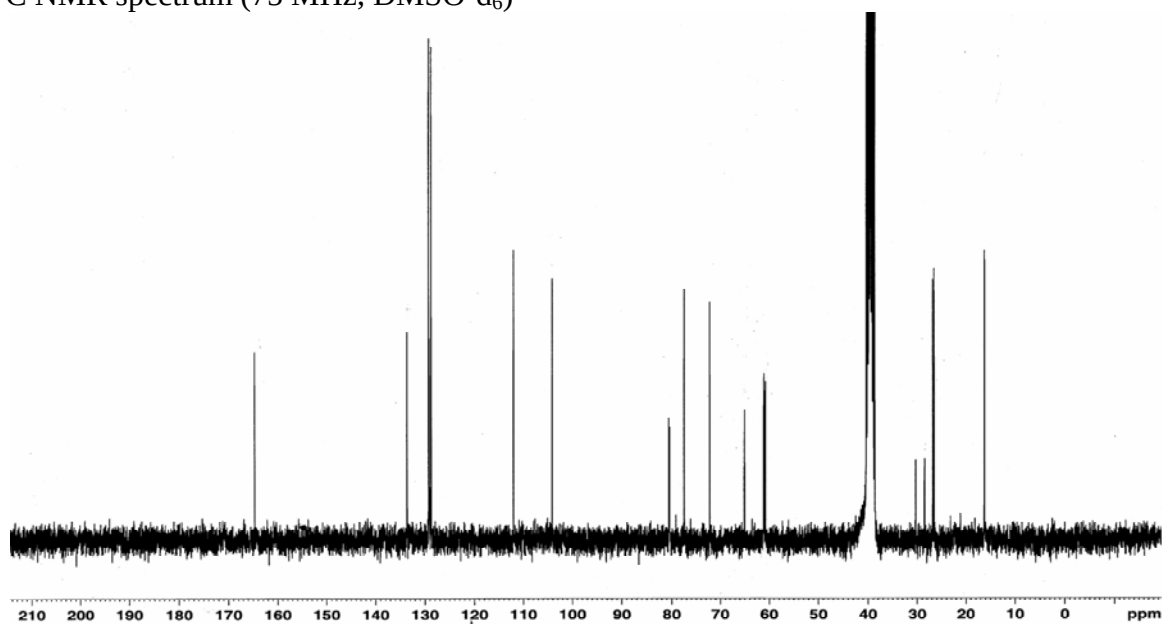


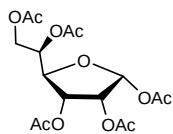
3-*O*-Benzoyl-6-deoxy-6-diethylphosphono-1,2-*O*-isopropylidene-D-allofuranose (3)

^1H NMR spectrum (300 MHz, DMSO-d_6)



^{13}C NMR spectrum (75 MHz, DMSO-d_6)

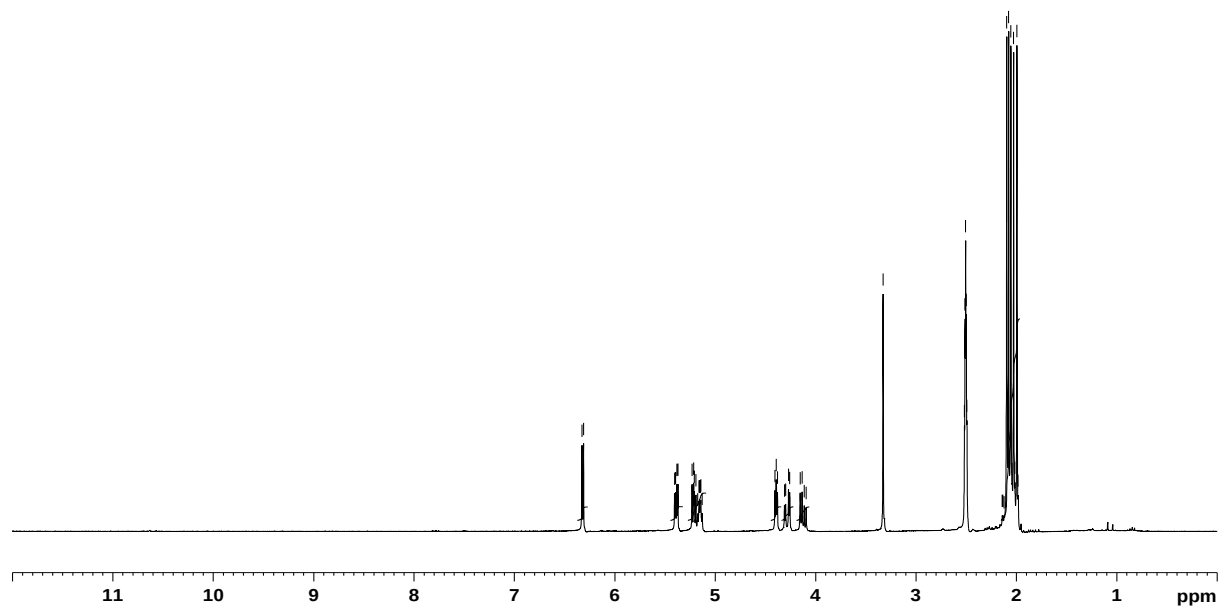




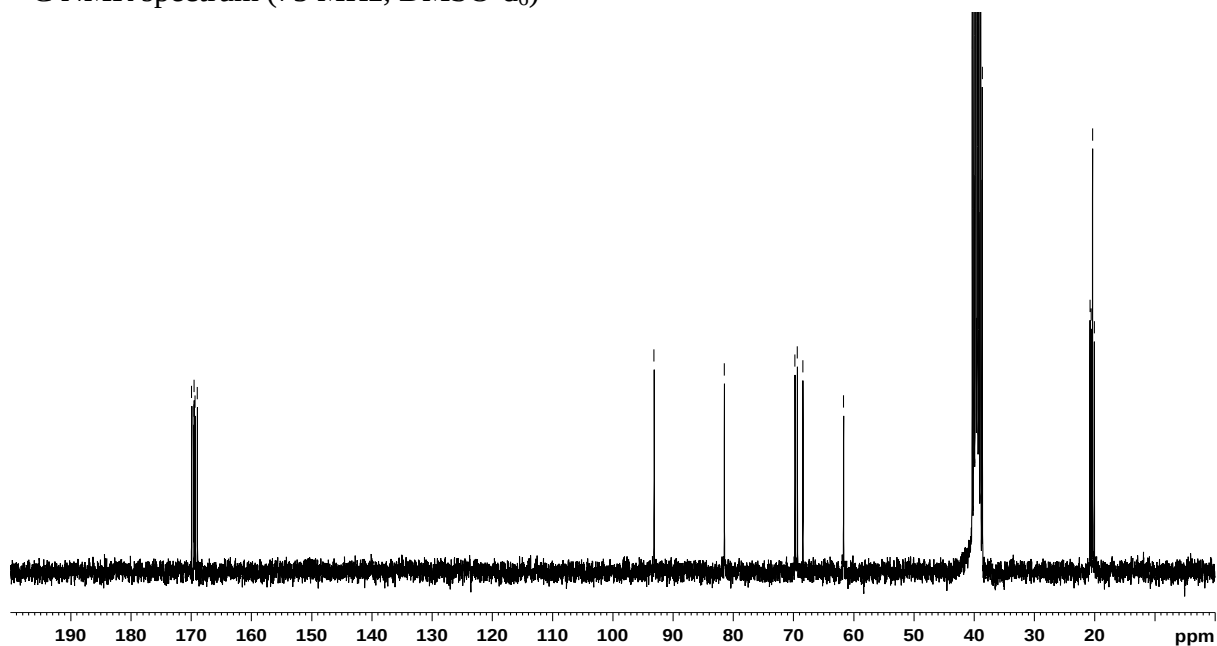
1,2,3,5,6-penta-*O*-Acetyl-(α,β)-D-allofuranose (4)

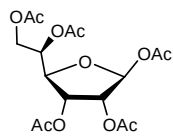
α -anomer

^1H NMR spectrum (300 MHz, DMSO- d_6)



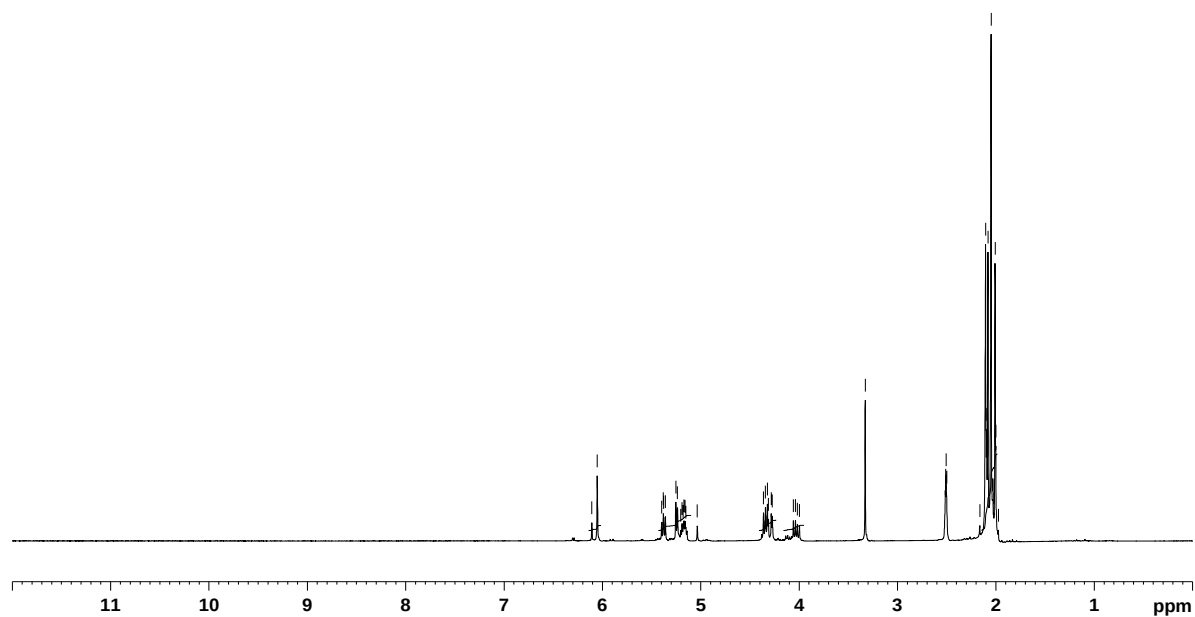
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



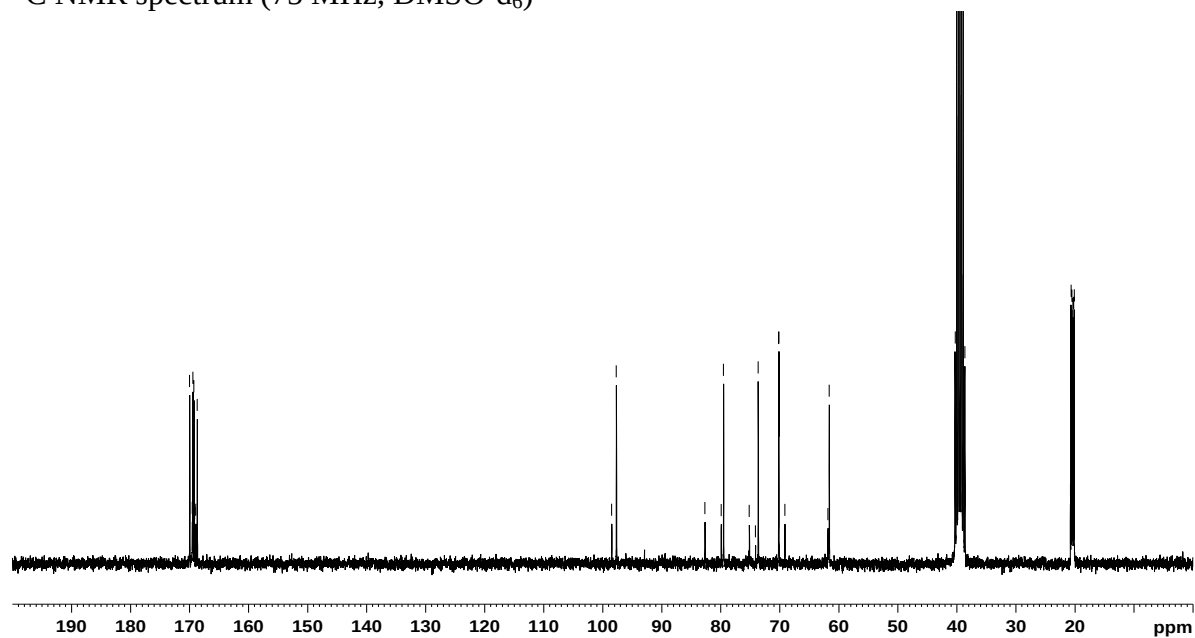


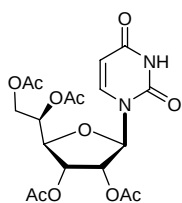
1,2,3,5,6-penta-*O*-Acetyl-(α,β)-D-allofuranose (4) **β -anomer (contaminated by α)**

^1H NMR spectrum (300 MHz, DMSO- d_6)



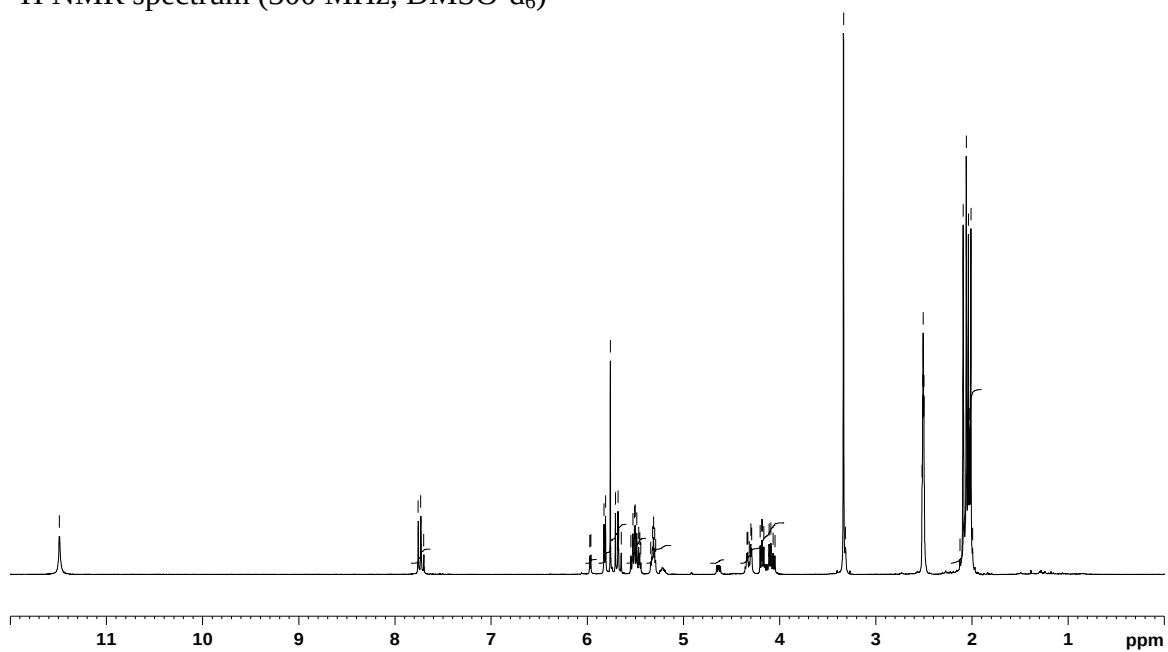
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



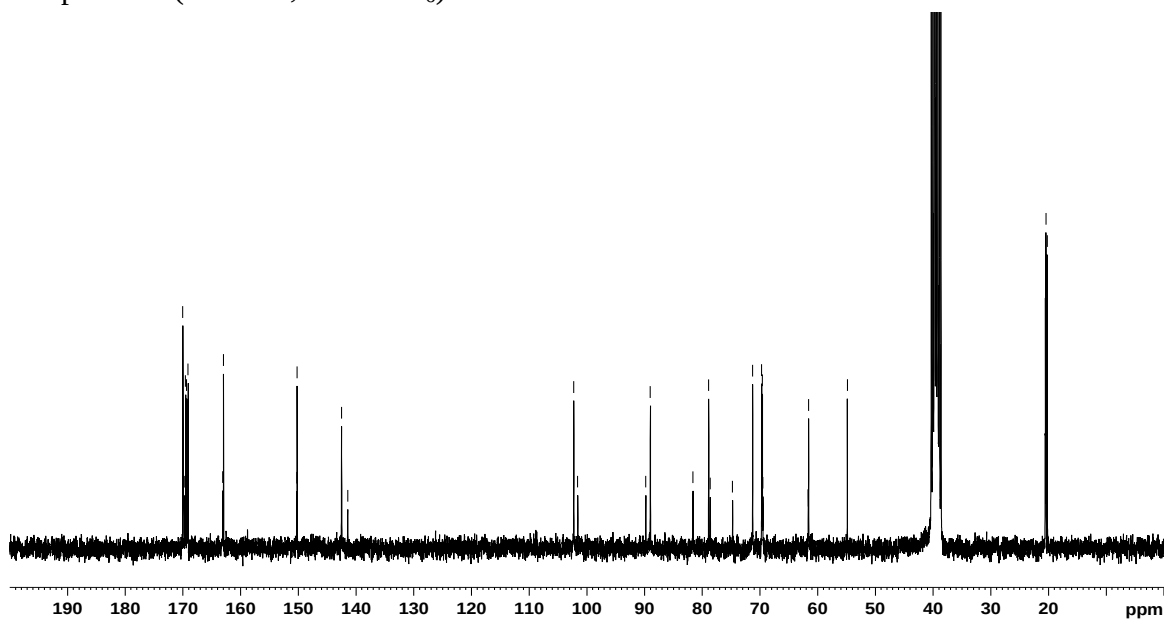


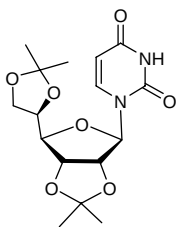
1-(2,3,5,6-tetra-*O*-Acetyl- α,β -D-ribo-(5*R*)-hexofuranosyl) uracil (5)

^1H NMR spectrum (300 MHz, DMSO- d_6)



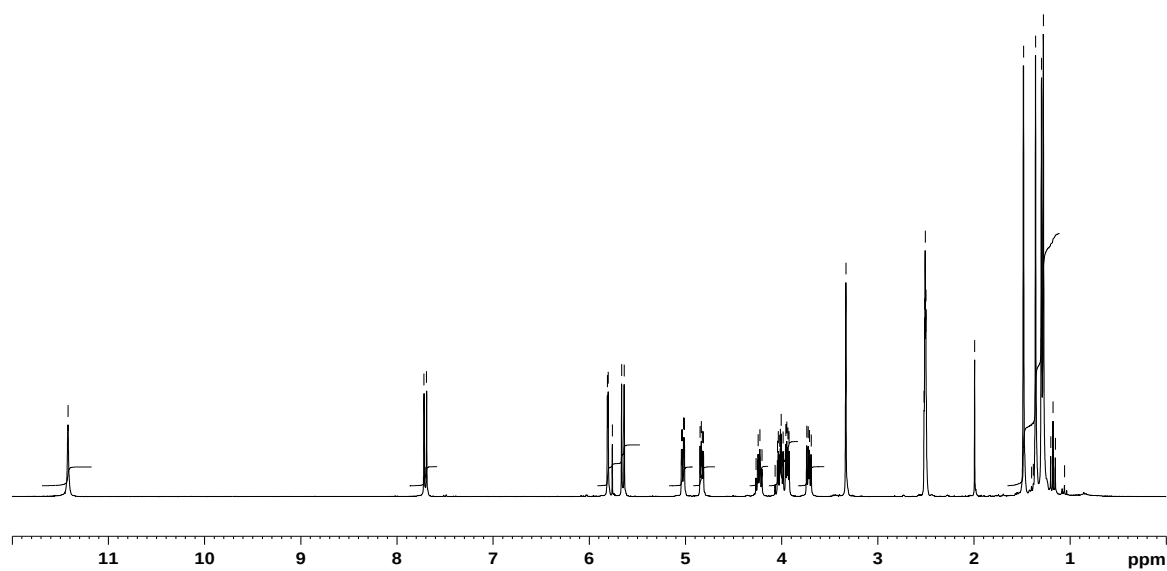
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



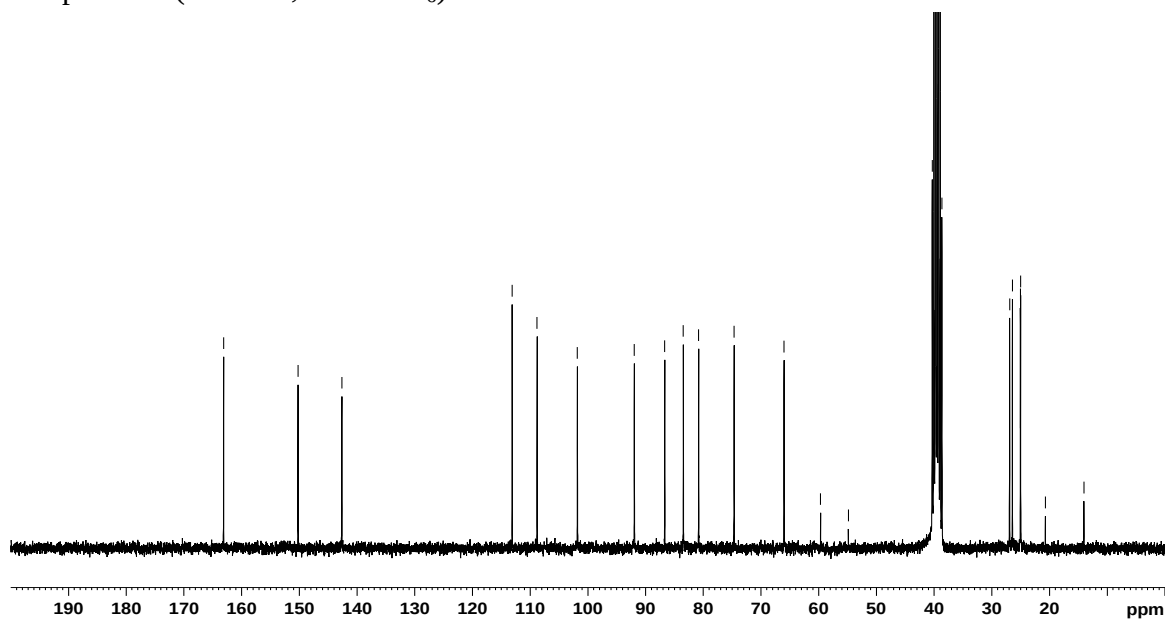


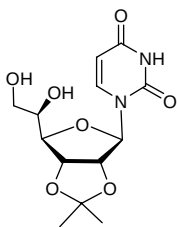
1-(2,3:5,6-di-*O*-Isopropylidene- β -D-ribo-(5'*R*)-hexofuranosyl) uracil (6)

^1H NMR spectrum (300 MHz, DMSO- d_6)



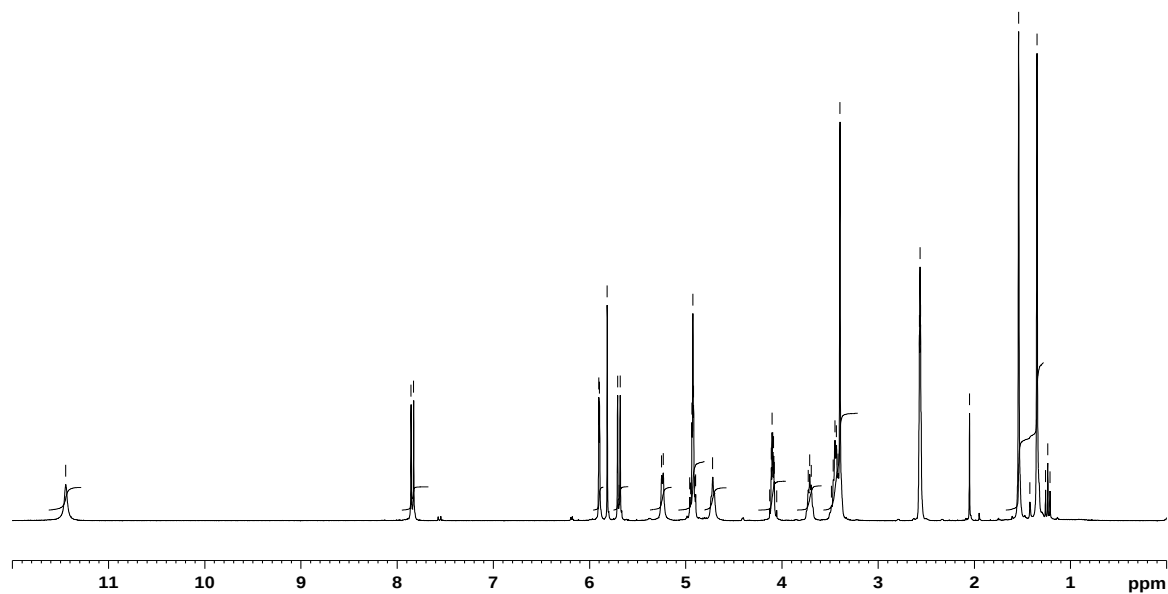
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



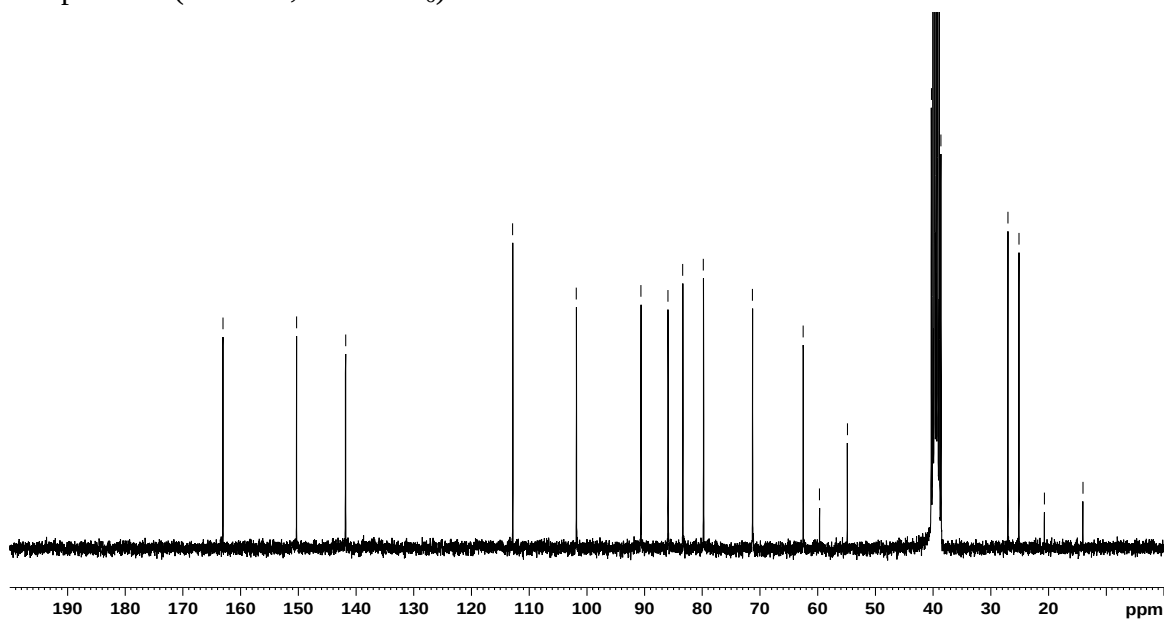


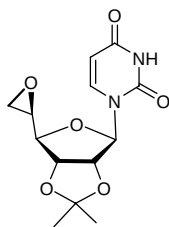
1-(2,3-*O*-Isopropylidene- β -D-ribo-(5*R*)-hexofuranosyl) uracil (7)

^1H NMR spectrum (300 MHz, DMSO- d_6)



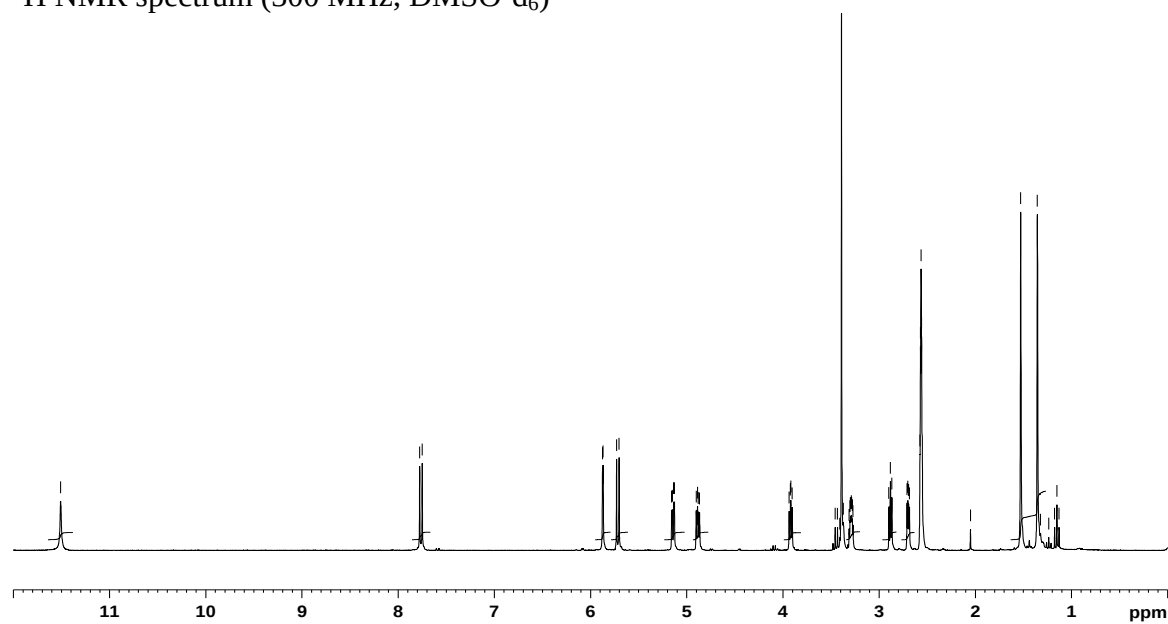
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



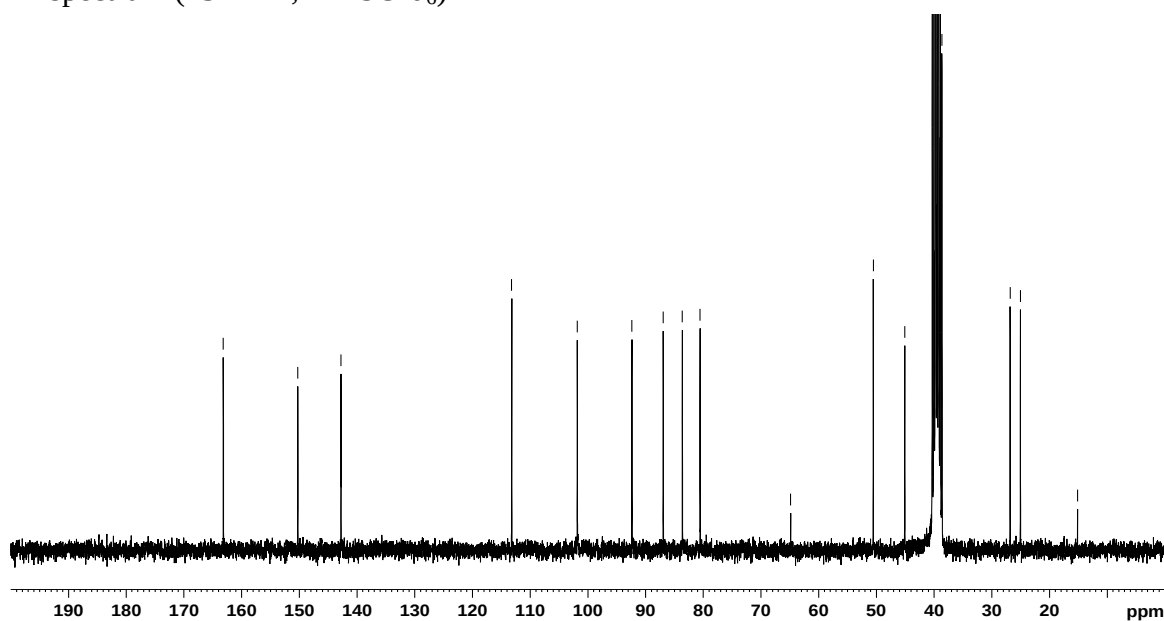


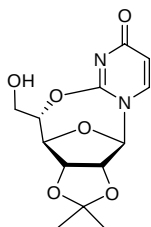
1-(2,3-*O*-Isopropylidene-5,6-oxiran- β -D-ribo-(5*R*)-hexofuranosyl) uracil (8)

^1H NMR spectrum (300 MHz, DMSO- d_6)



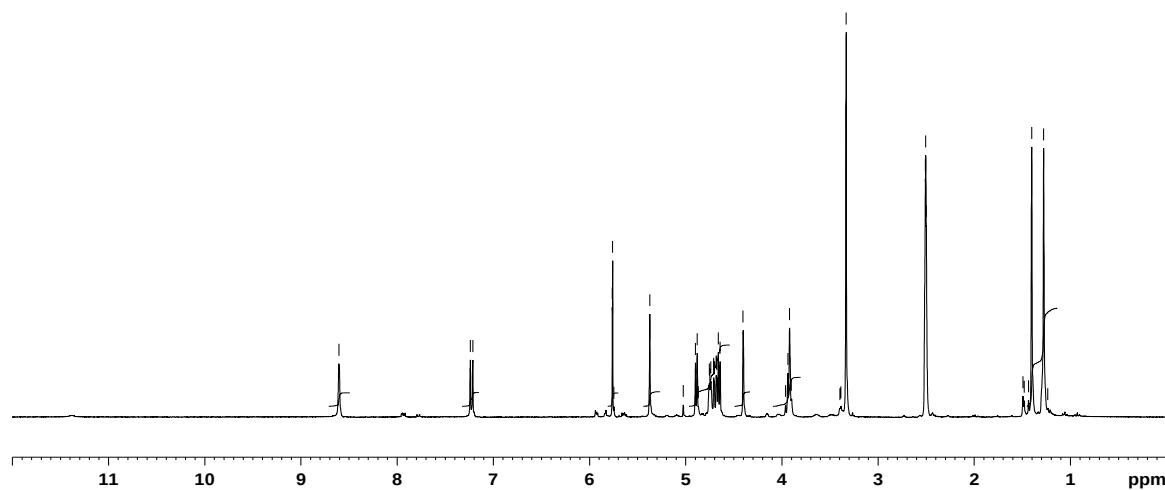
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



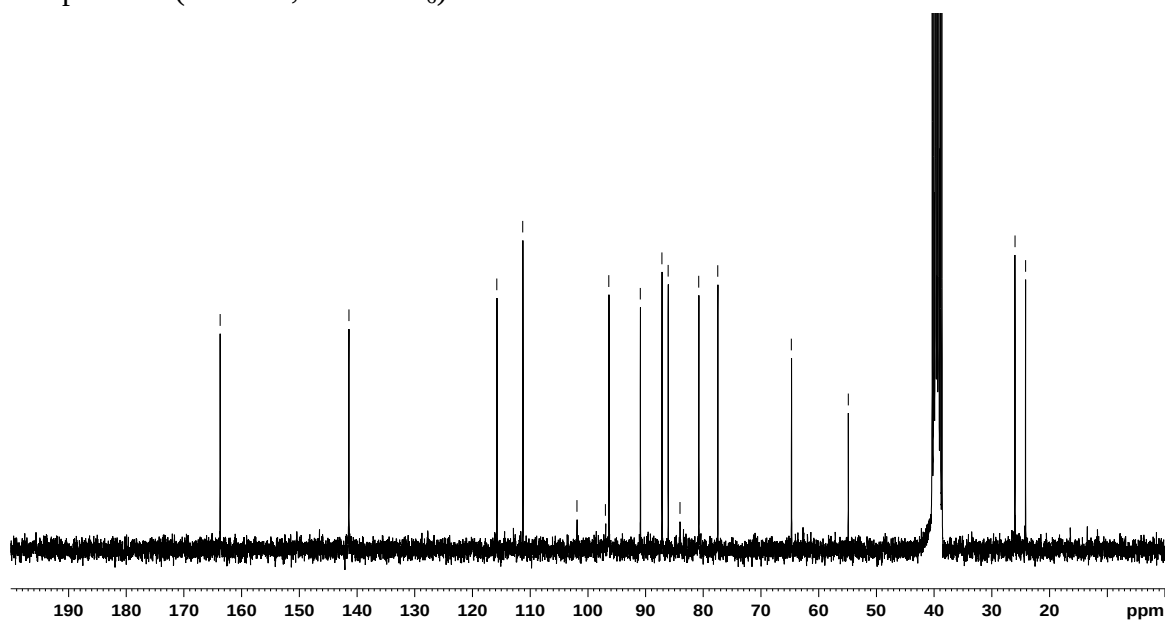


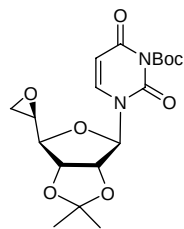
2,5'-Anhydro-1-(2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexofuranosyl) uracil (9)

^1H NMR spectrum (300 MHz, DMSO- d_6)



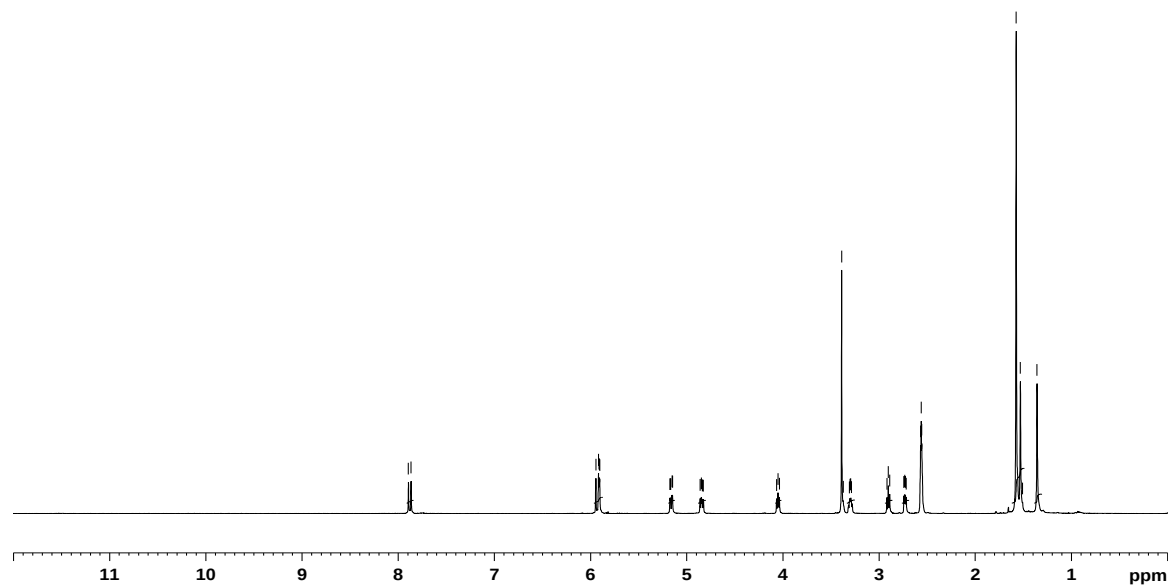
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



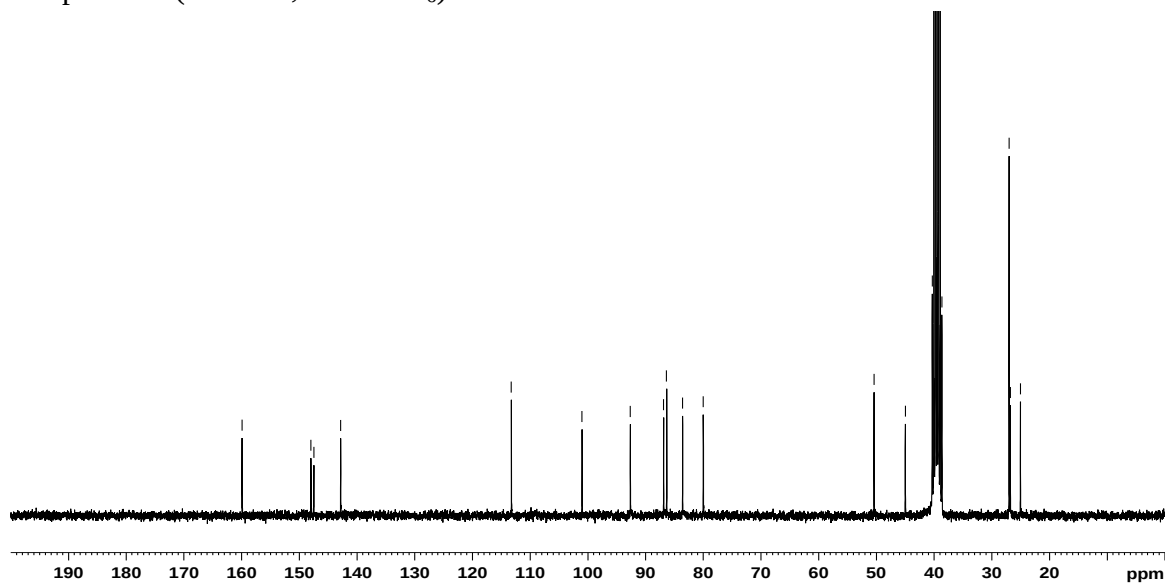


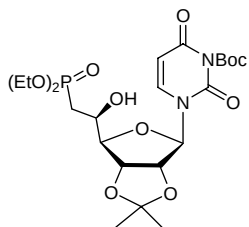
***N*-3-*tert*-Butyloxycarbonyl-1-(2,3-*O*-isopropylidene-5,6-oxiran- β -D-ribo-(5*R*)-hexofuranosyl) uracil (10)**

^1H NMR spectrum (300 MHz, DMSO- d_6)



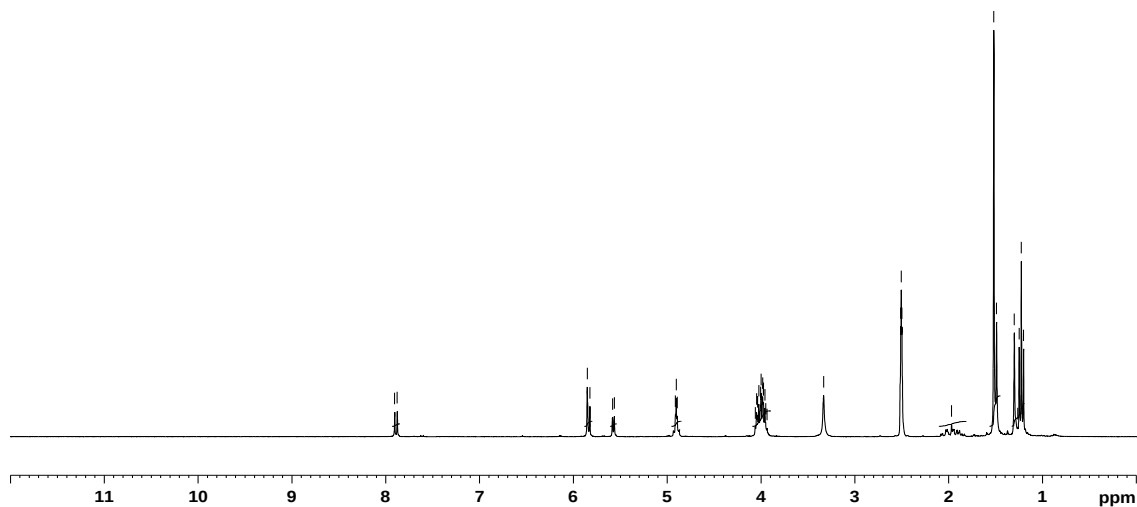
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



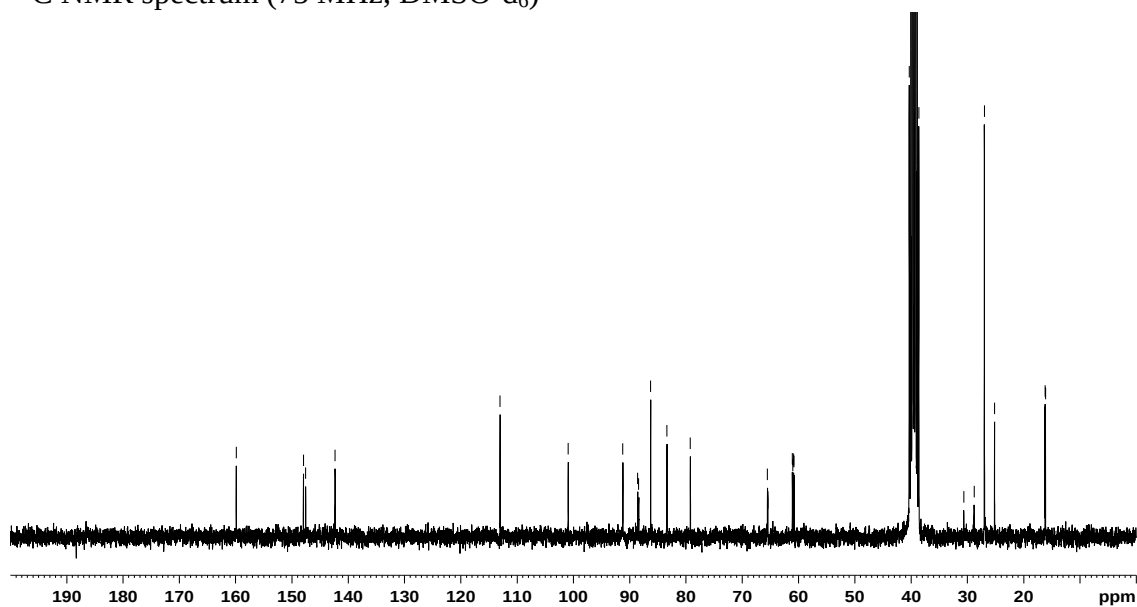


***N*-3-*tert*-Butyloxycarbonyl-1-(6-deoxy-6-diethylphosphono-2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexo furanosyl) uracil (11)**

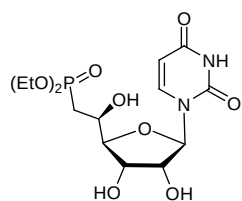
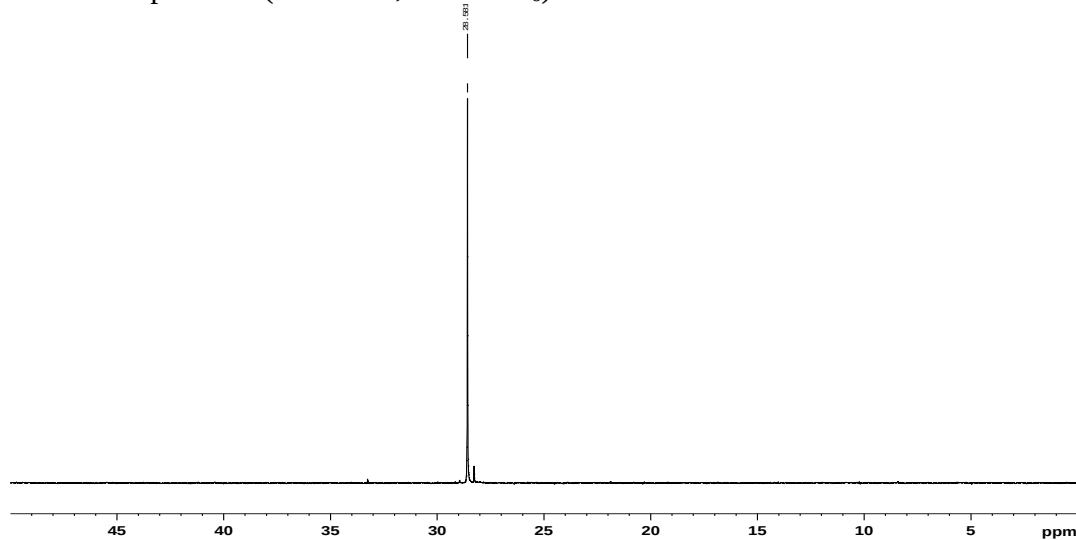
^1H NMR spectrum (300 MHz, DMSO- d_6)



^{13}C NMR spectrum (75 MHz, DMSO- d_6)

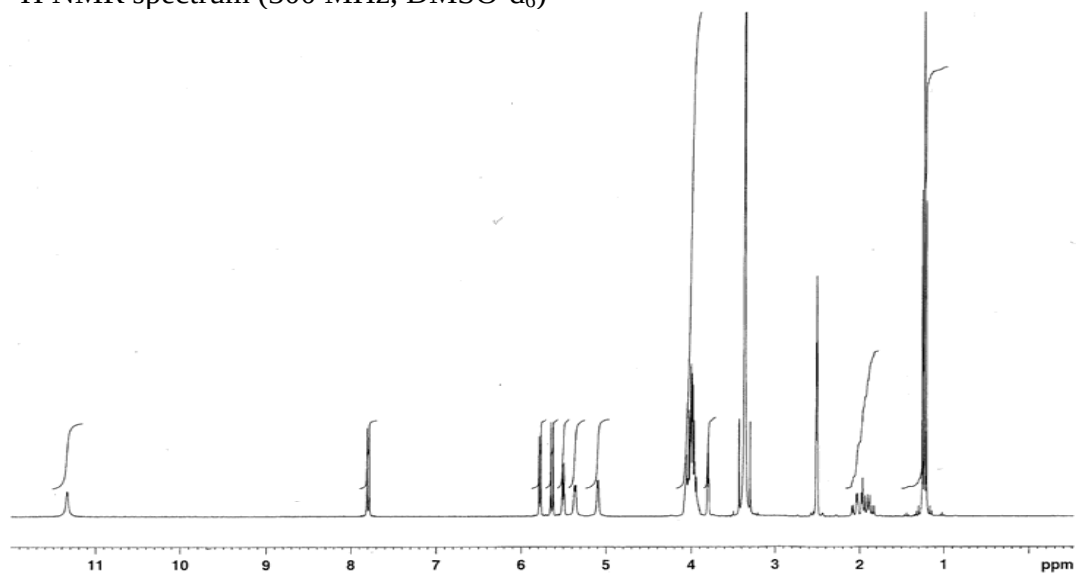


^{31}P NMR spectrum (121 MHz, DMSO- d_6)

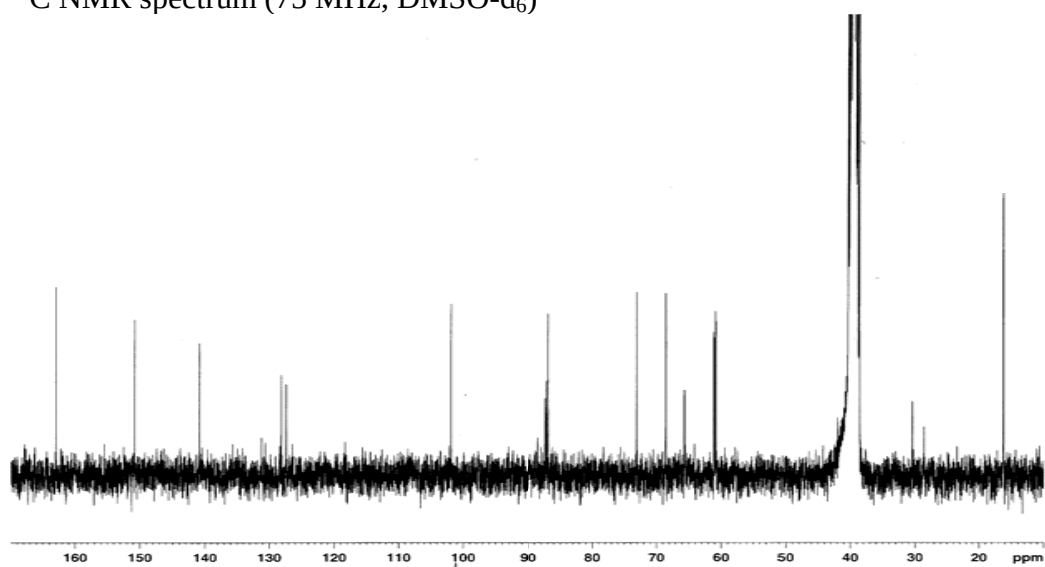


1-(6-Deoxy-6-diethylphosphono- β -D-ribo-(5S)-hexofuranosyl) uracil (12)

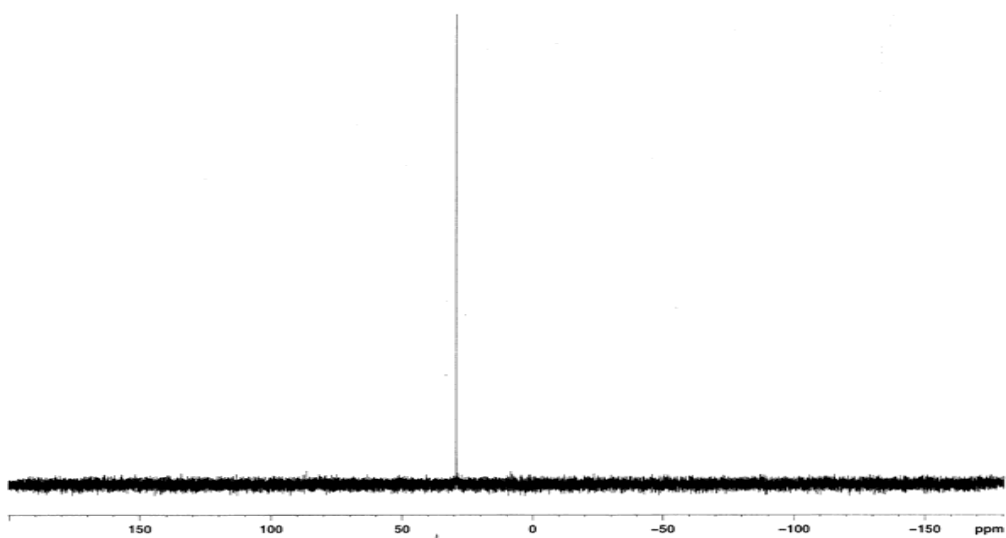
^1H NMR spectrum (300 MHz, DMSO- d_6)

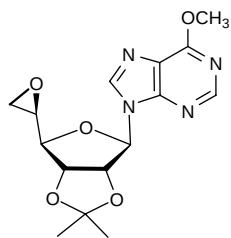


^{13}C NMR spectrum (75 MHz, DMSO- d_6)



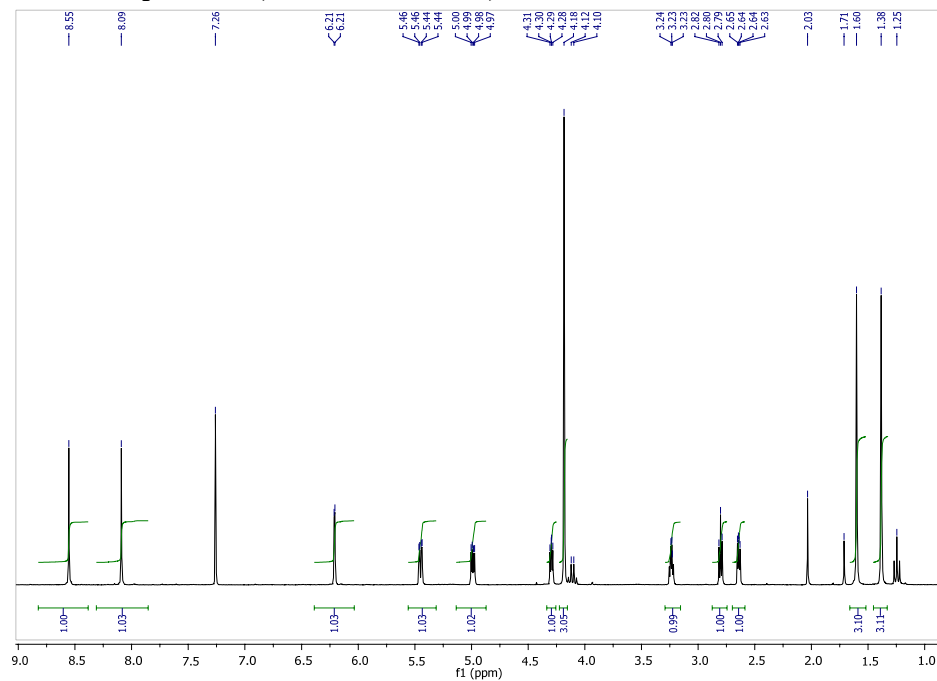
^{31}P NMR spectrum (121 MHz, DMSO- d_6)



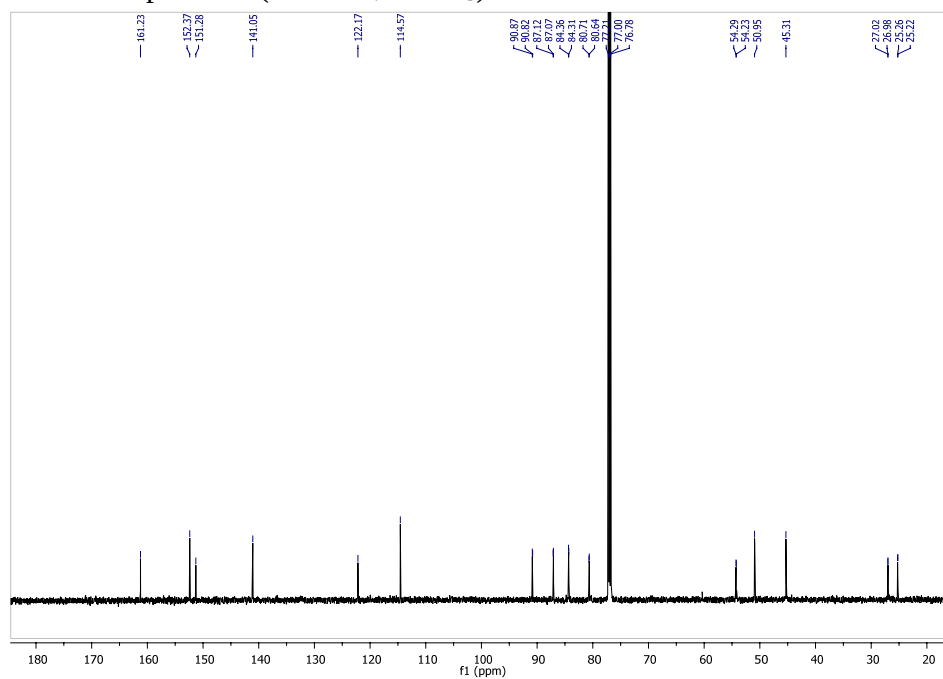


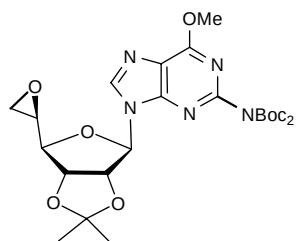
9-(2,3-*O*-Isopropylidene-5,6-oxiran- β -D-ribo-(5*R*)-hexofuranosyl)-6-*O*-methyl-purine (13a)

^1H NMR spectrum (300 MHz, CDCl_3)



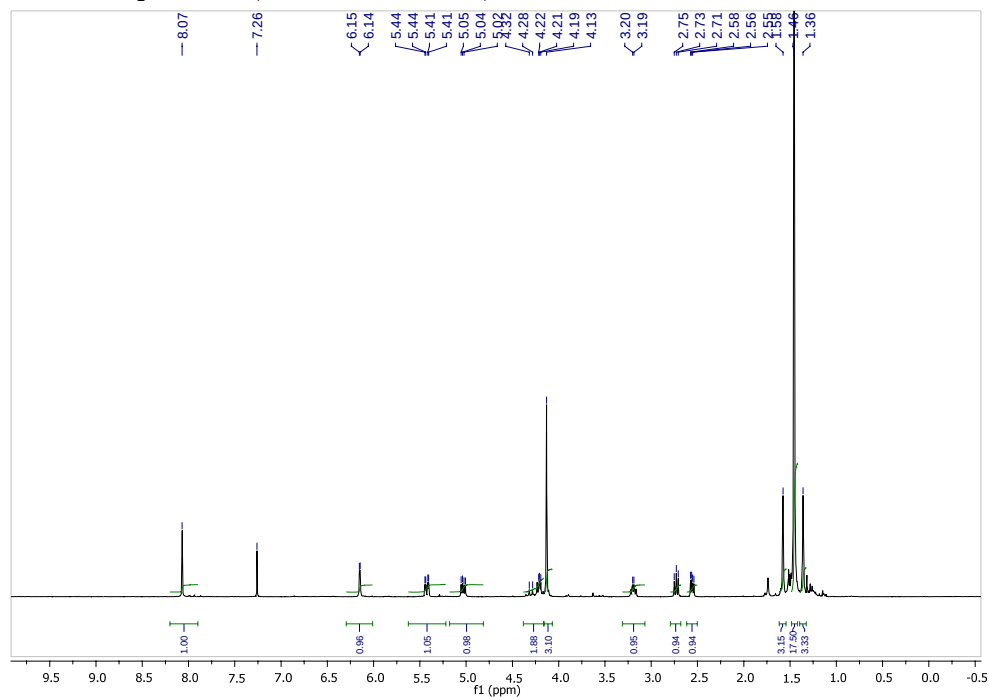
^{13}C NMR spectrum (75 MHz, CDCl_3)



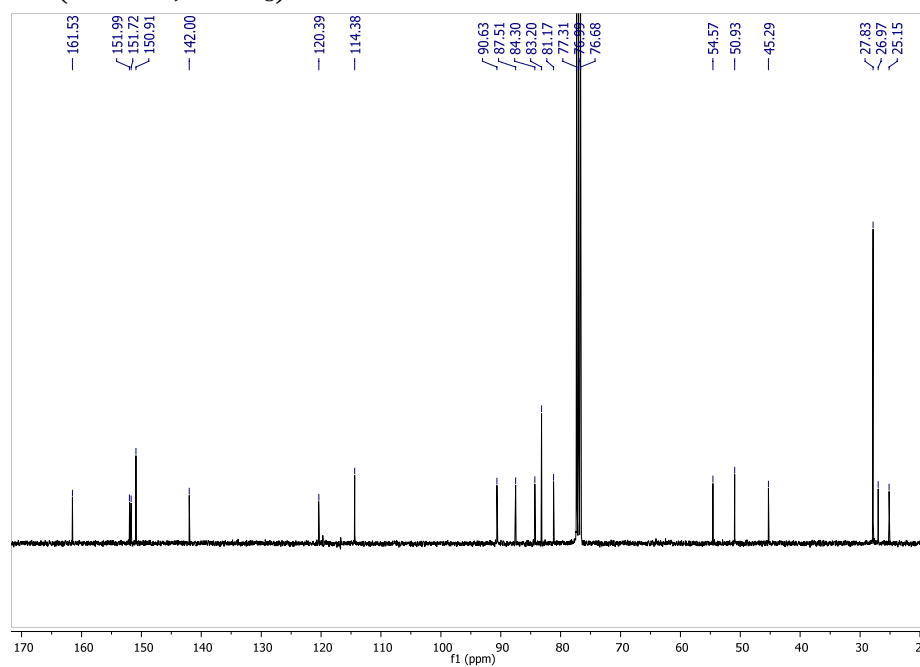


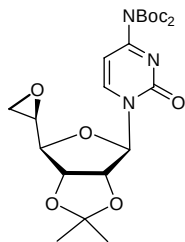
***N,N*-2(ditert-Butyloxycarbonyl)-9-(2,3-*O*-isopropylidene-5,6-oxiran- β -D-ribo-(5*R*)-hexofuran-osyl)-6-*O*-methyl-purine (13b)**

^1H NMR spectrum (300 MHz, CDCl_3)



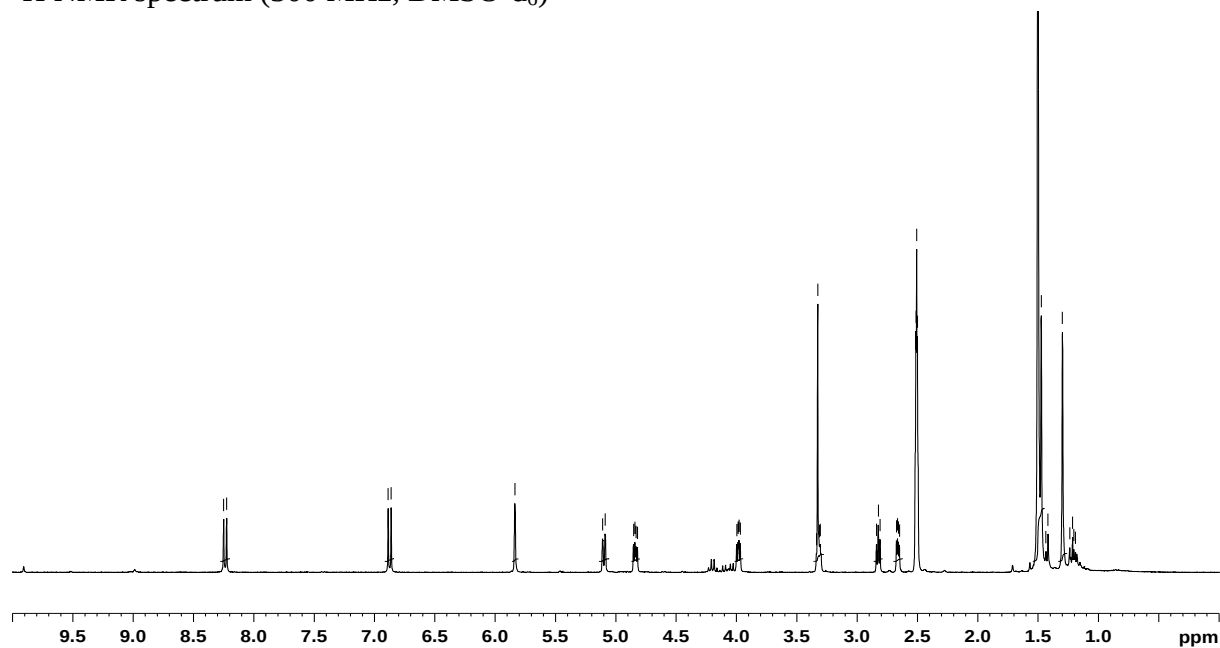
^{13}C NMR spectrum (75 MHz, CDCl_3)



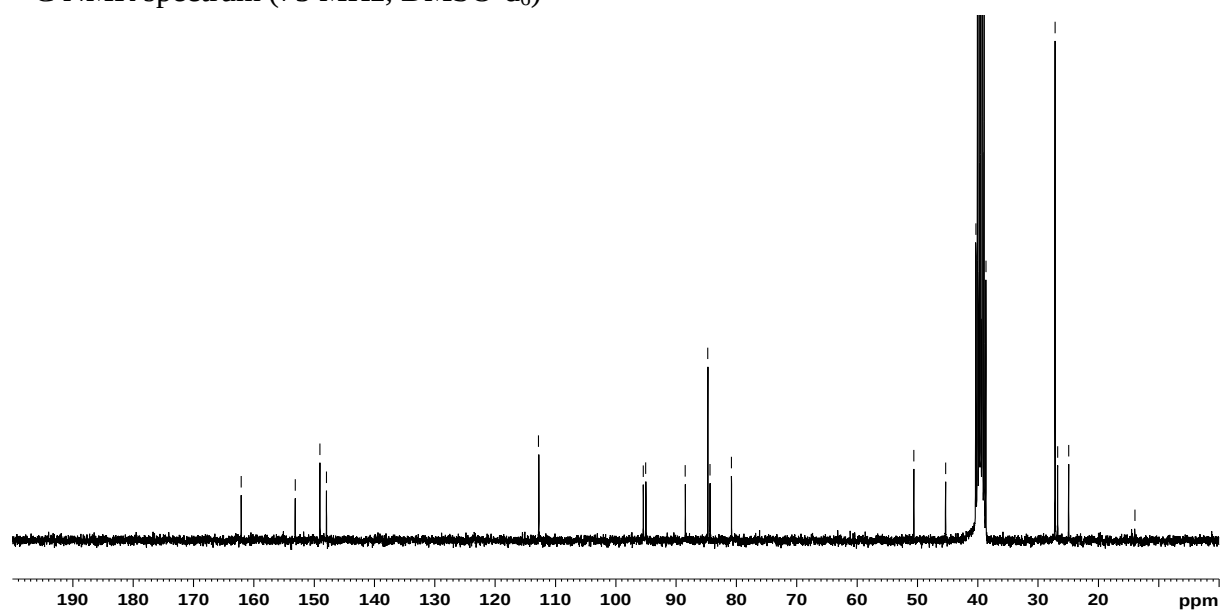


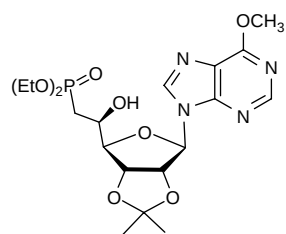
***N,N*-4-(di-*tert*-Butyloxycarbonyl)-1-(2,3-*O*-isopropylidene-5,6-oxiran- β -D-ribo-(5*R*)-hexofuran-*osyl*) cytosine (13c)**

^1H NMR spectrum (300 MHz, DMSO- d_6)



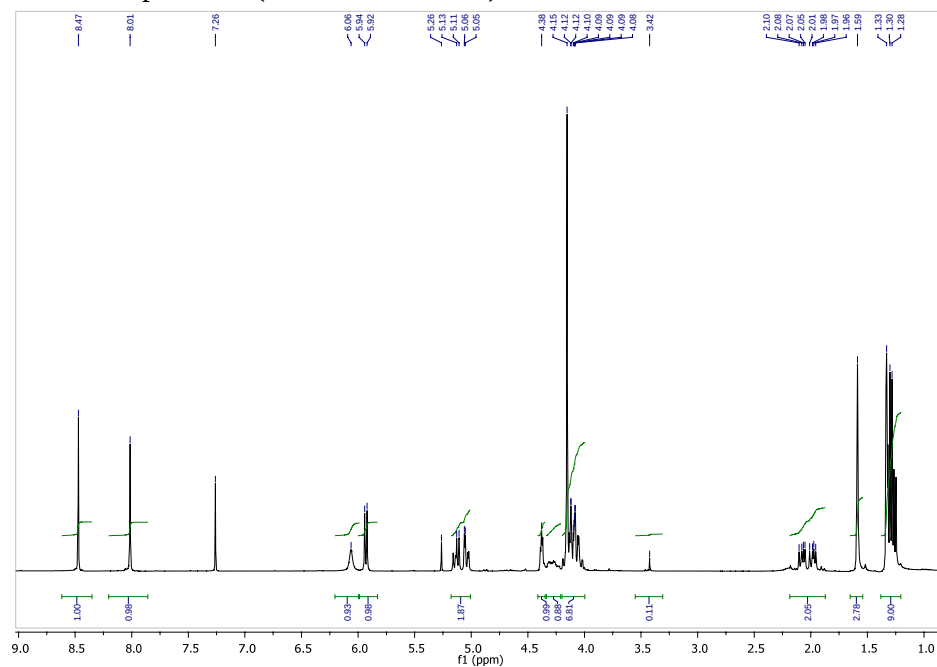
^{13}C NMR spectrum (75 MHz, DMSO- d_6)



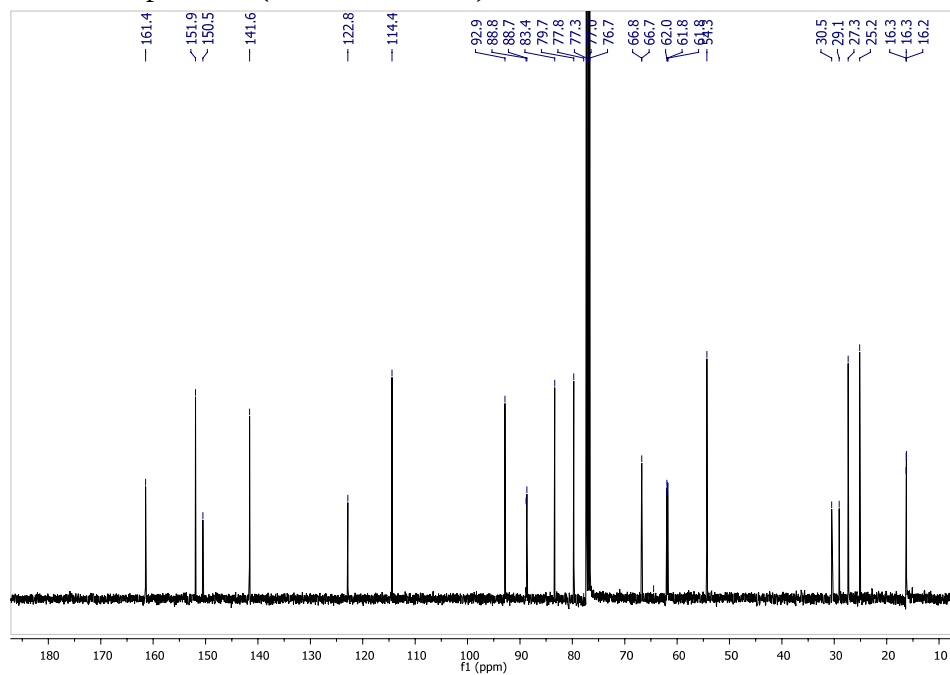


9-(6-Deoxy-6-diethylphosphono-2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexofuranosyl)-6-*O*-methyl-purine (14a)

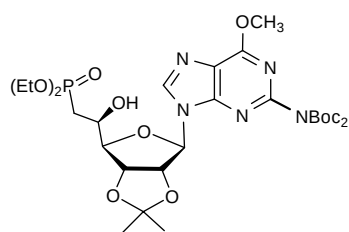
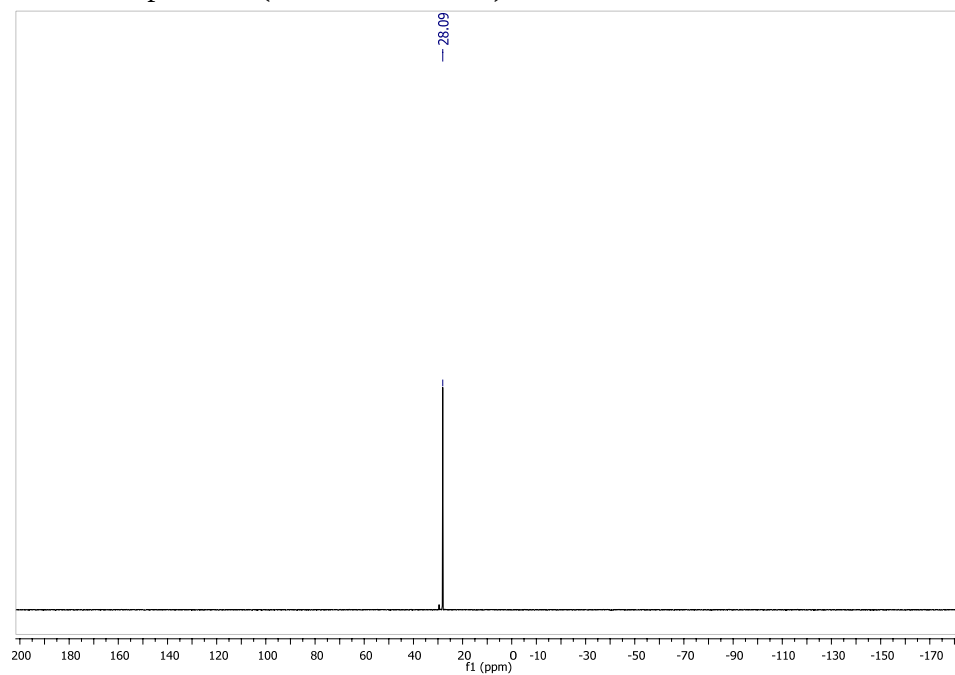
^1H NMR spectrum (300 MHz, CDCl_3)



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

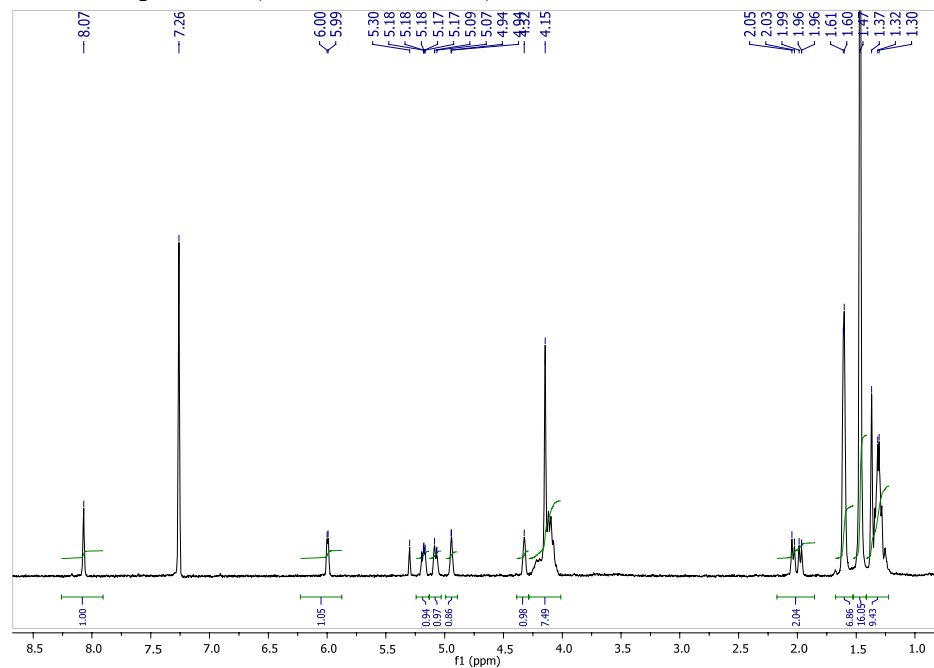


^{31}P NMR spectrum (121 MHz, CDCl_3)

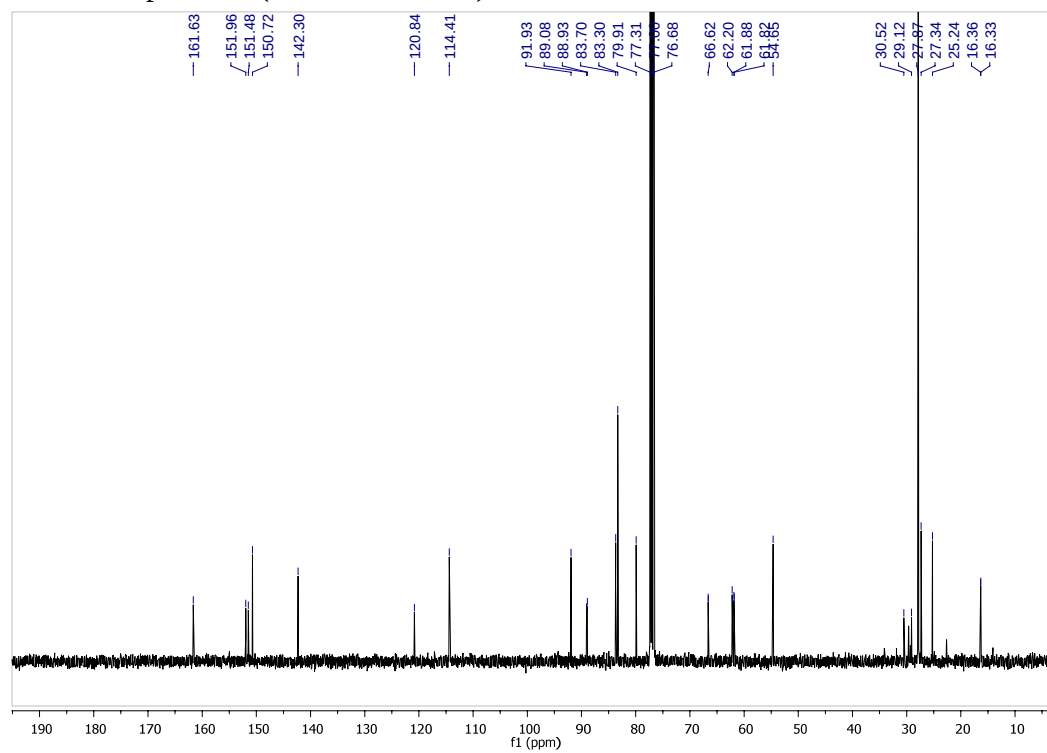


***N,N*-2(di-*tert*-Butyloxycarbonyl)-9-(6-deoxy-6-diethylphosphono-2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexofuranosyl)-6-*O*-methyl-purine (14b)**

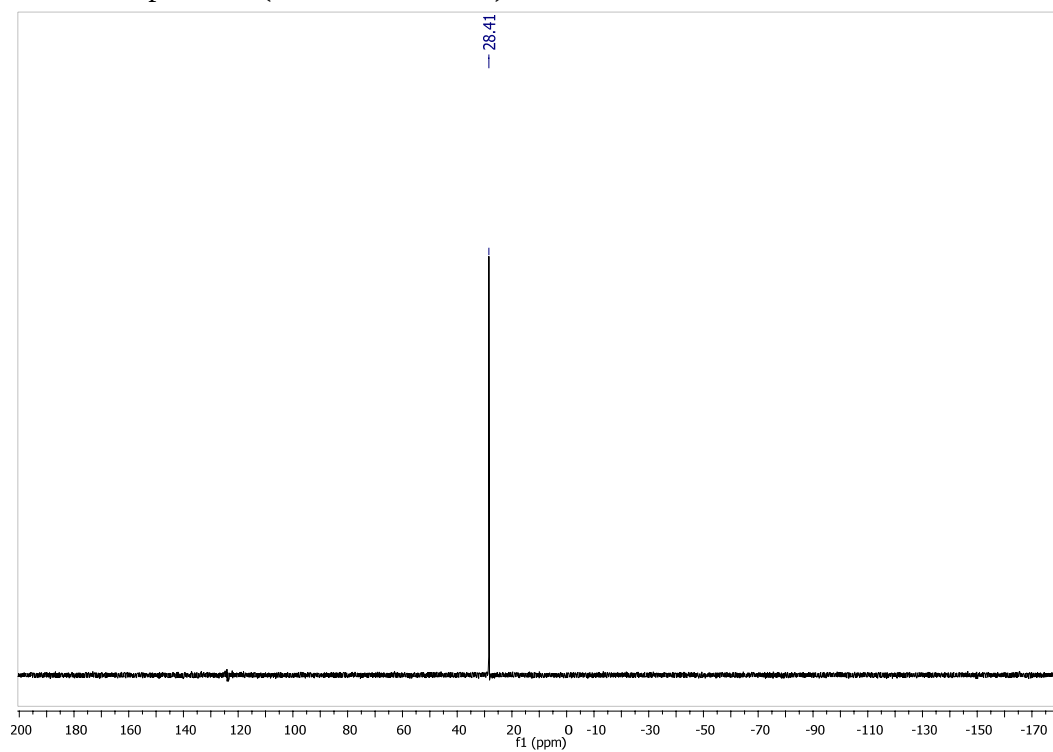
^1H NMR spectrum (300 MHz, CDCl_3)

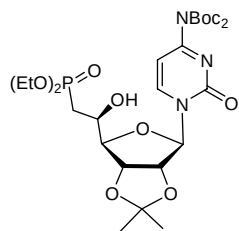


^{13}C NMR spectrum (75 MHz, CDCl_3)



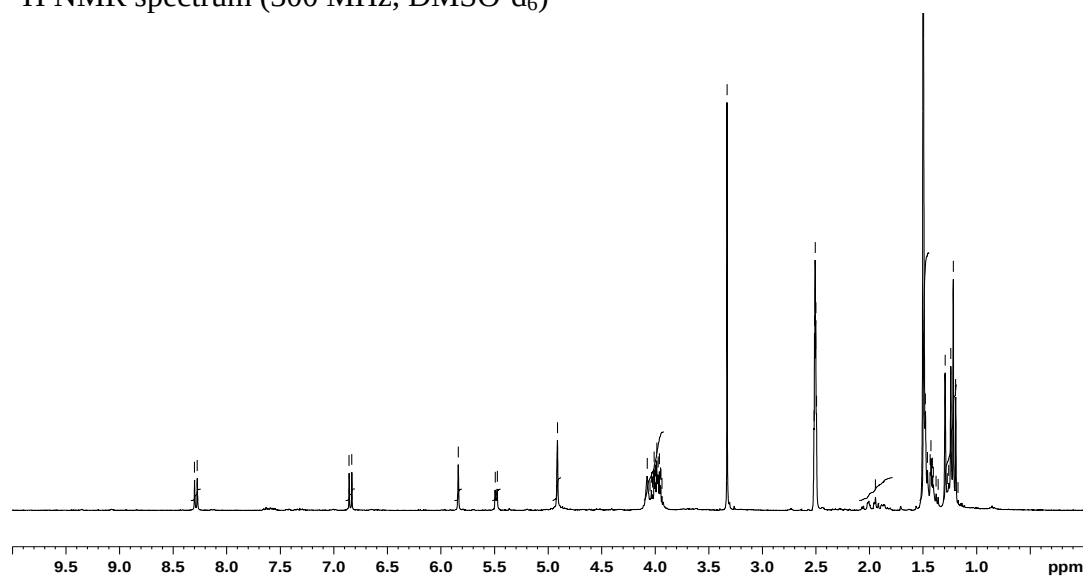
^{31}P NMR spectrum (121 MHz, CDCl_3)



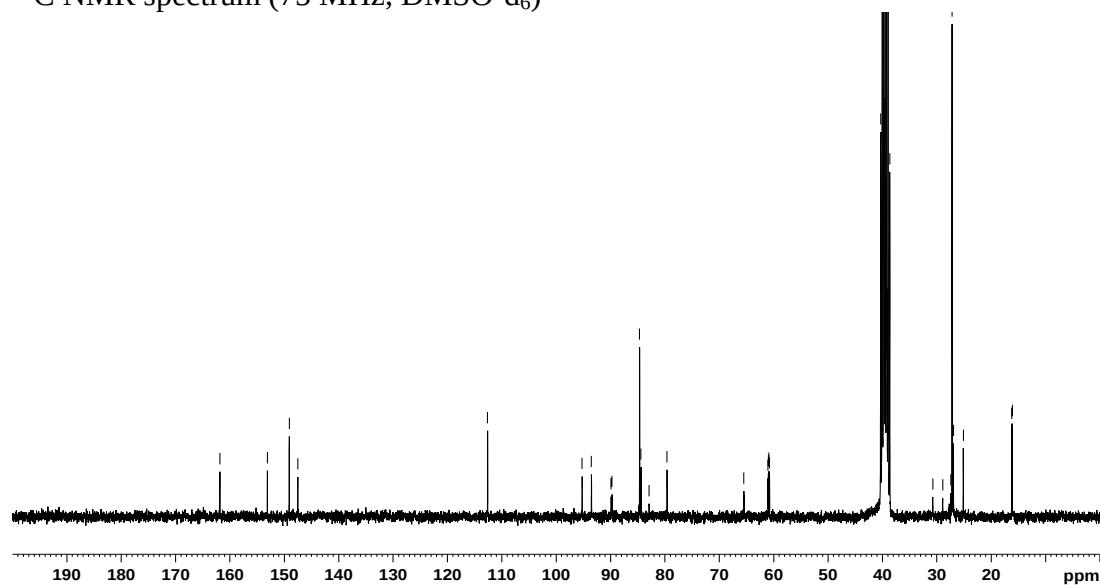


***N,N*-4-(di-*tert*-Butyloxycarbonyl)-1-(6-deoxy-6-diethylphosphono-2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexofuranosyl) ytosine (14c)**

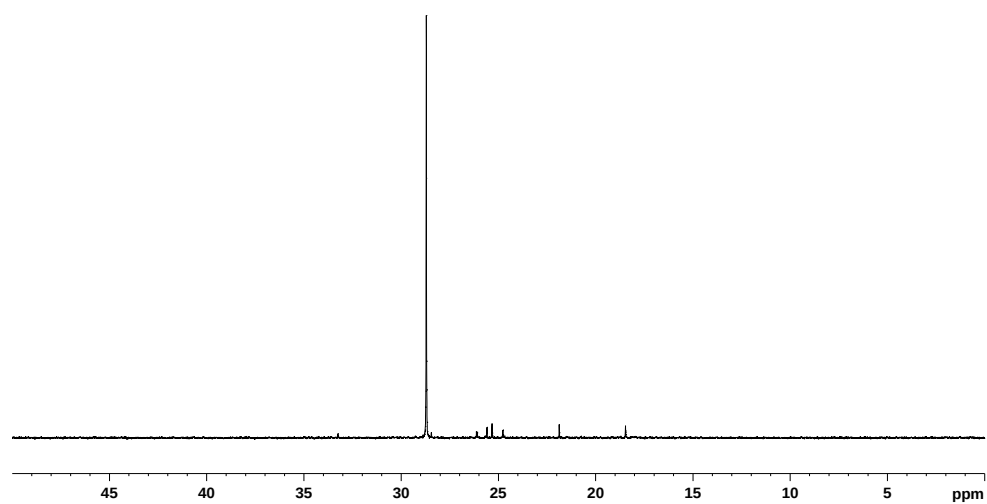
^1H NMR spectrum (300 MHz, DMSO- d_6)

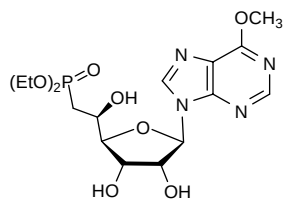


^{13}C NMR spectrum (75 MHz, DMSO- d_6)



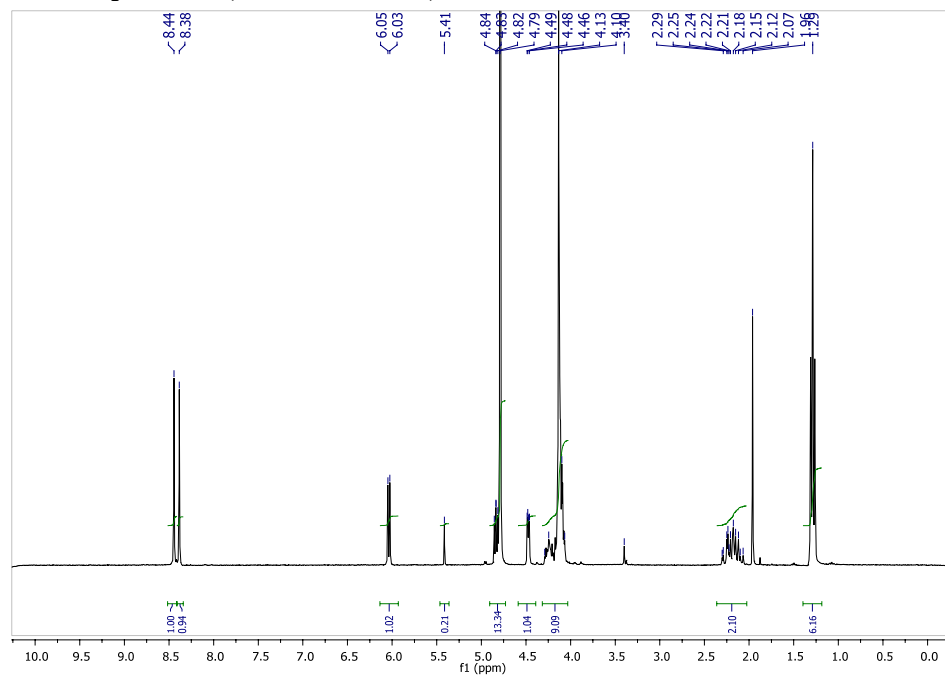
^{31}P NMR spectrum (121 MHz, DMSO- d_6)



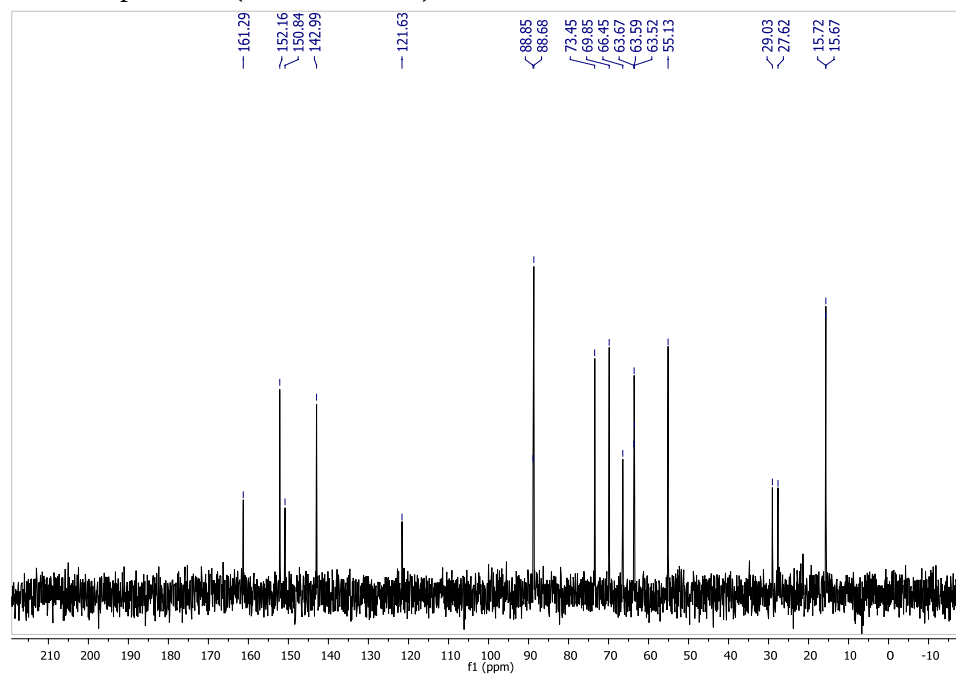


9-(6-Deoxy-6-diethylphosphono- β -D-ribo-(5S)-hexofuranosyl)-6-O-methyl-purine (15a)

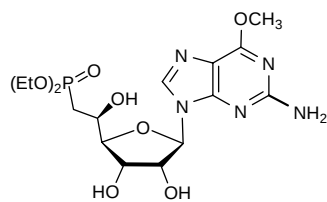
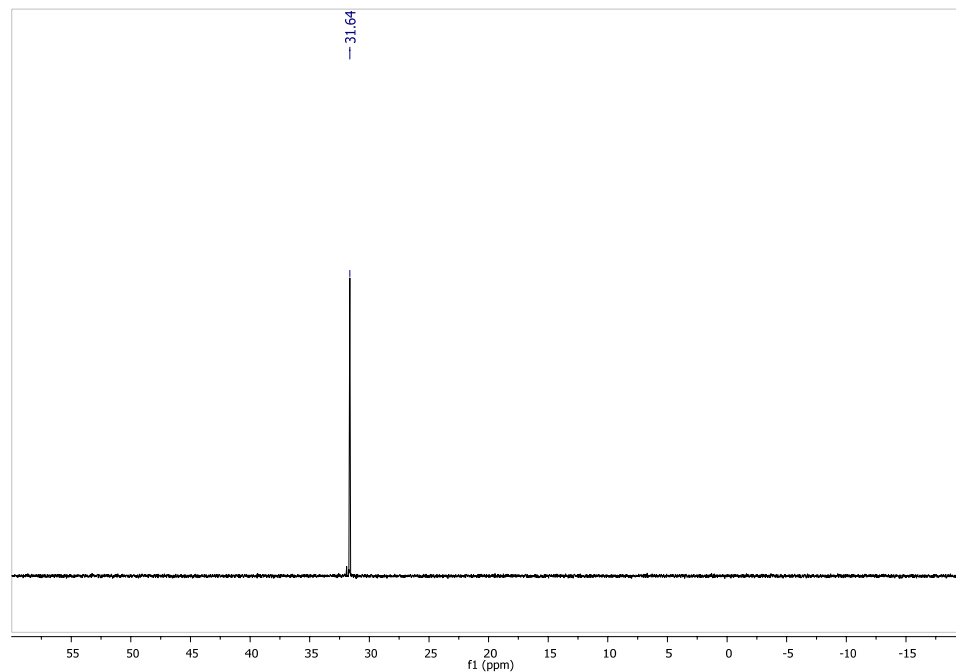
^1H NMR spectrum (300 MHz, D_2O)



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

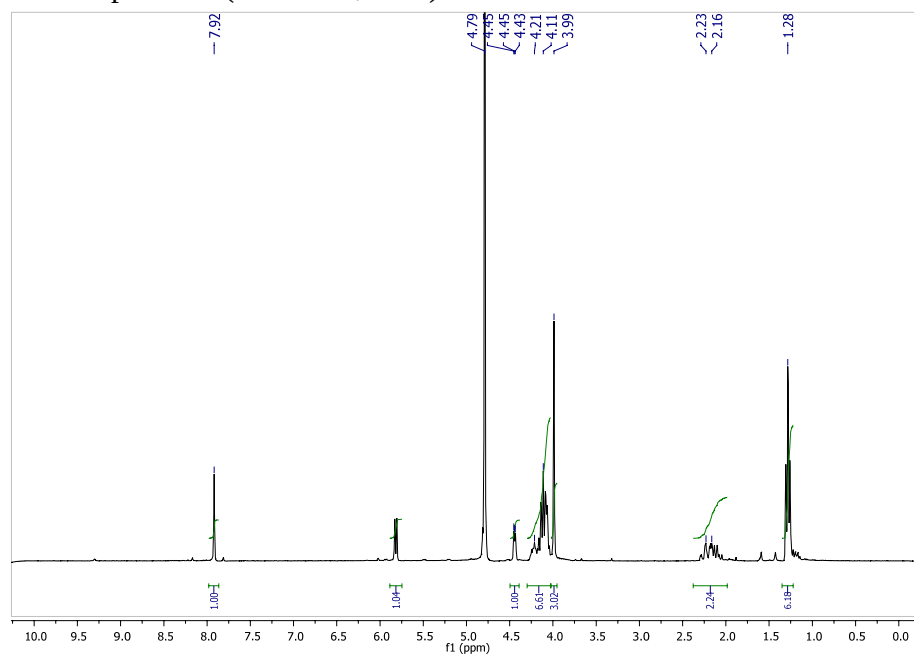


^{31}P NMR spectrum (121 MHz, D_2O)

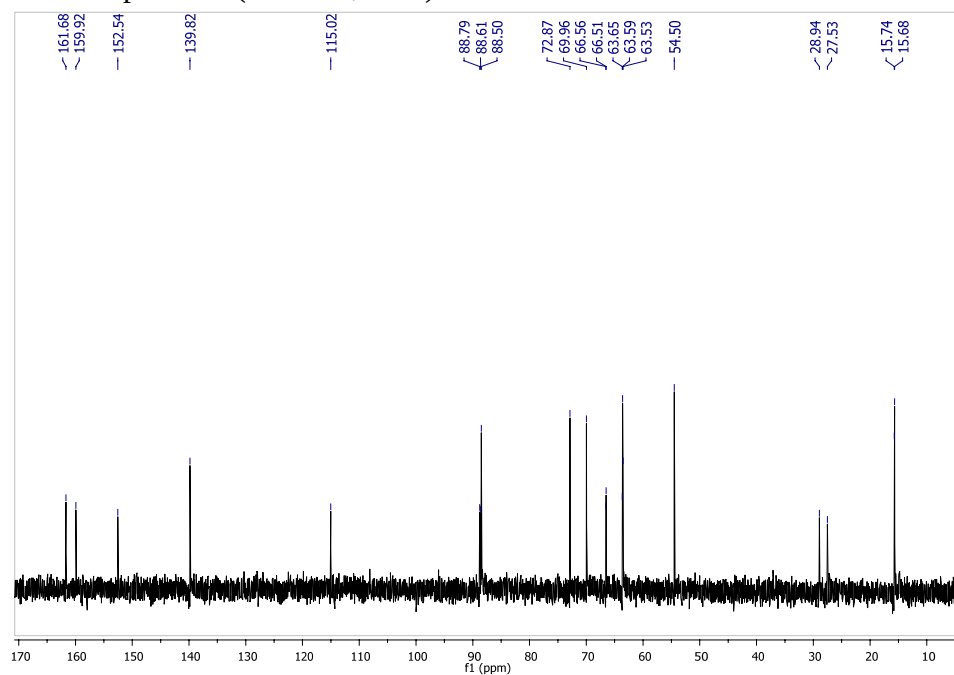


2-Amino-9-(6-deoxy-6-diethylphosphono- β -D-ribo-(5S)-hexofuranosyl)-6-O-methyl-purine (15b)

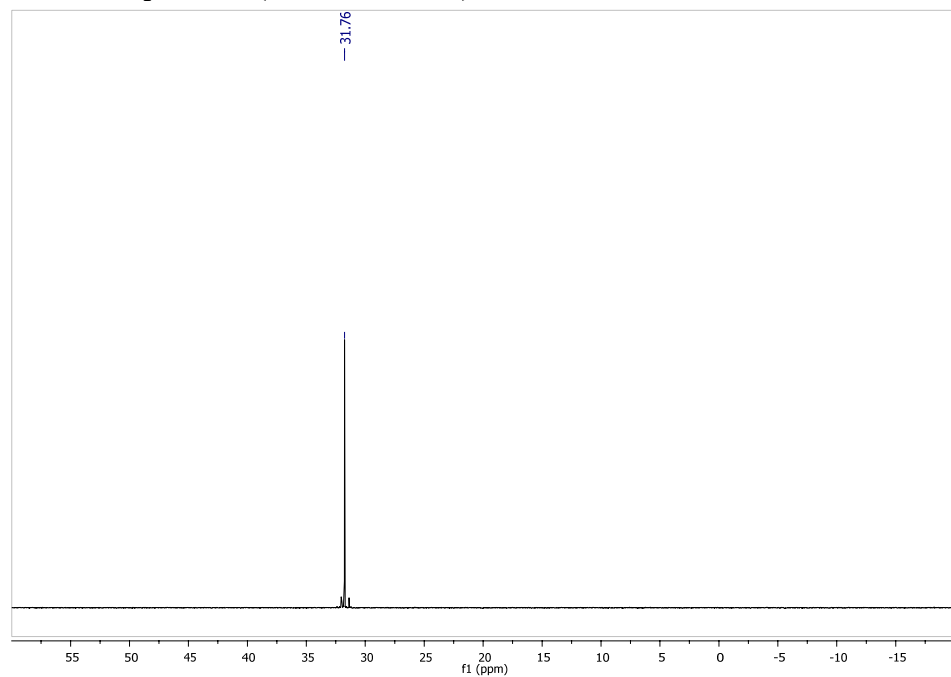
^1H NMR spectrum (300 MHz, D_2O)



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



^{31}P NMR spectrum (121 MHz, D_2O)





¹H NMR spectrum of compound **6d** in CDCl₃. The x-axis represents chemical shift in ppm, ranging from 0.0 to 9.5. The spectrum displays several peaks corresponding to different proton environments:

- Aromatic protons (NH) around 7.8 ppm.
- Amino protons (NH₂) between 7.2 and 7.4 ppm.
- Hydroxyl protons (OH) between 5.5 and 5.7 ppm.
- Methylene protons (CH₂) between 3.5 and 4.0 ppm.
- Methyl protons (CH₃) between 1.0 and 1.5 ppm.

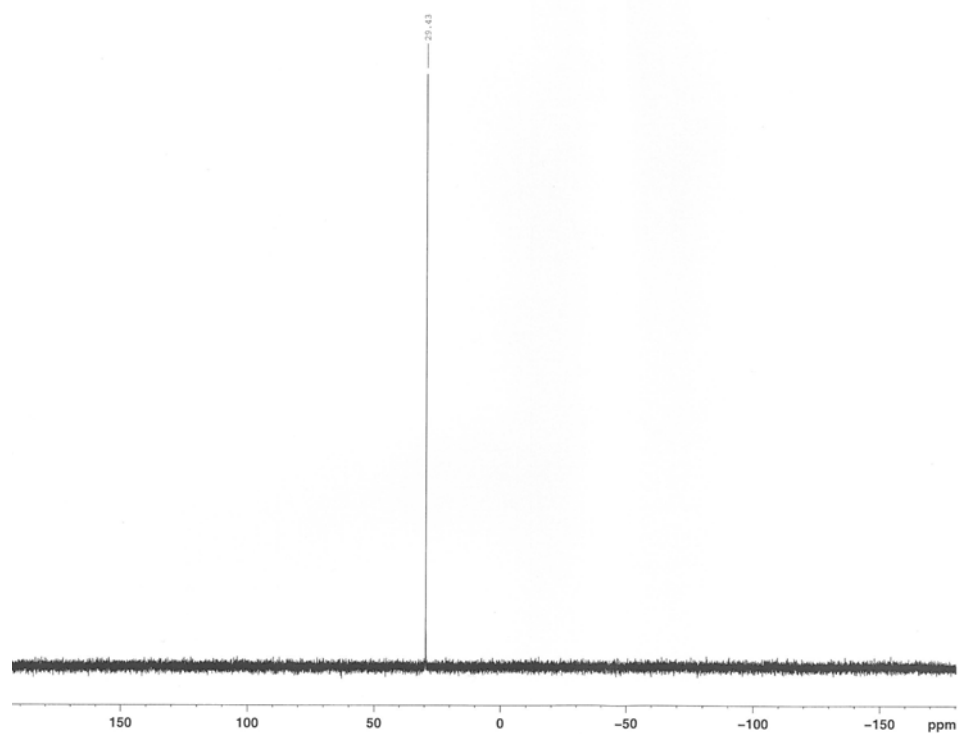
The integration values indicated below the baseline are as follows:

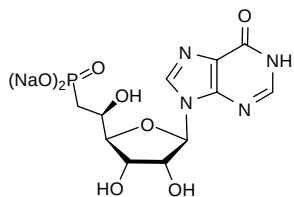
Chemical Shift Range (ppm)	Integration Value
~7.8	1.00
7.2 - 7.4	2.01
5.5 - 5.7	2.06
5.5 - 5.7	3.01
3.5 - 4.0	7.08
3.5 - 4.0	1.01
1.0 - 1.5	2.02
1.0 - 1.5	6.13

¹³C NMR spectrum (75 MHz, DMSO-d₆) of compound 10a. The spectrum displays several sharp peaks in the aromatic and aliphatic regions. The chemical shifts (ppm) are listed below the spectrum:

- 165.50
- 156.44
- 142.00
- 94.06
- 88.73
- 86.55
- 73.30
- 69.64
- 65.64
- 61.20
- 60.02
- 60.74
- 40.28
- 40.00
- 39.45
- 38.89
- 30.51
- 28.42
- 16.24
- 16.16

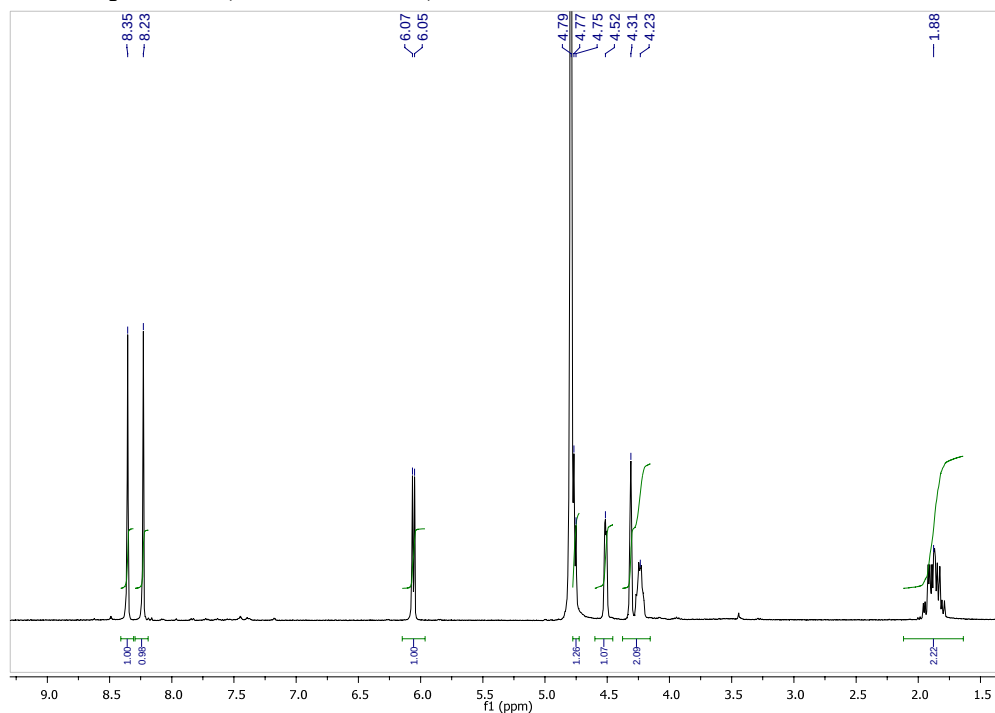
^{31}P NMR spectrum (121 MHz, DMSO- d_6)



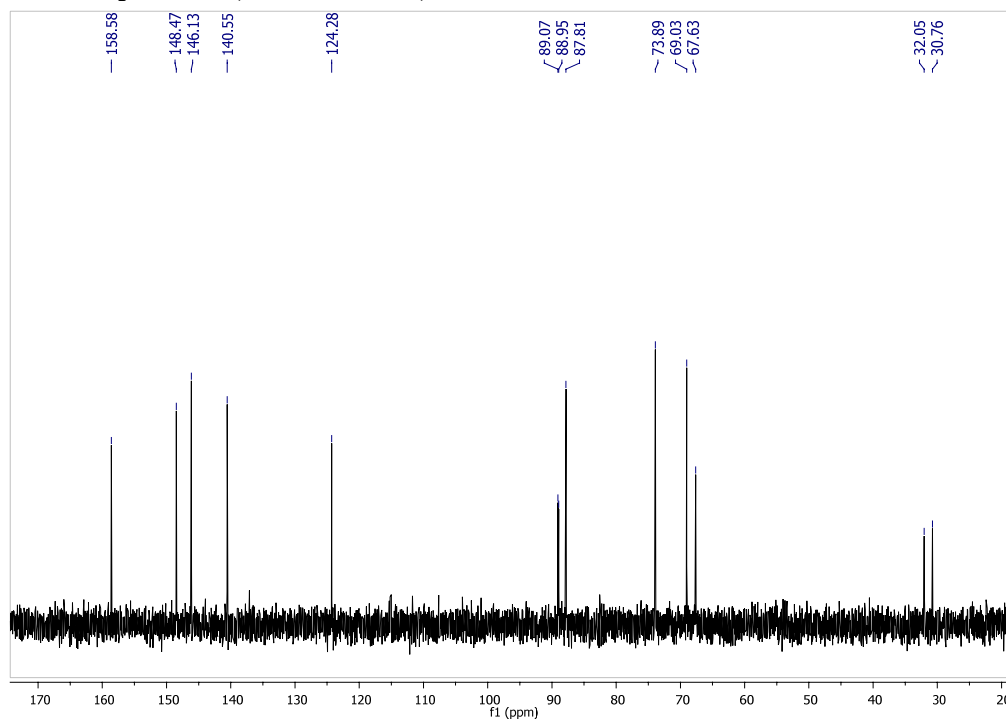


9-(6-Deoxy-6-phosphono- β -D-ribo-(5S)-hexofuranosyl) hypoxanthine, sodium salt (16a)

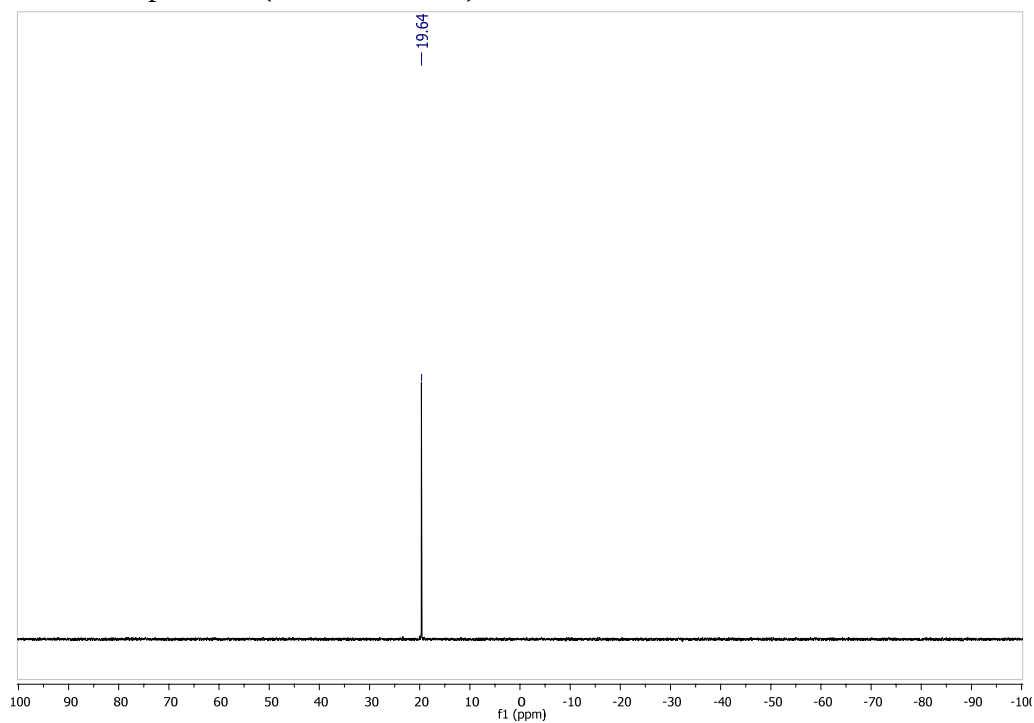
^1H NMR spectrum (300 MHz, D_2O)



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

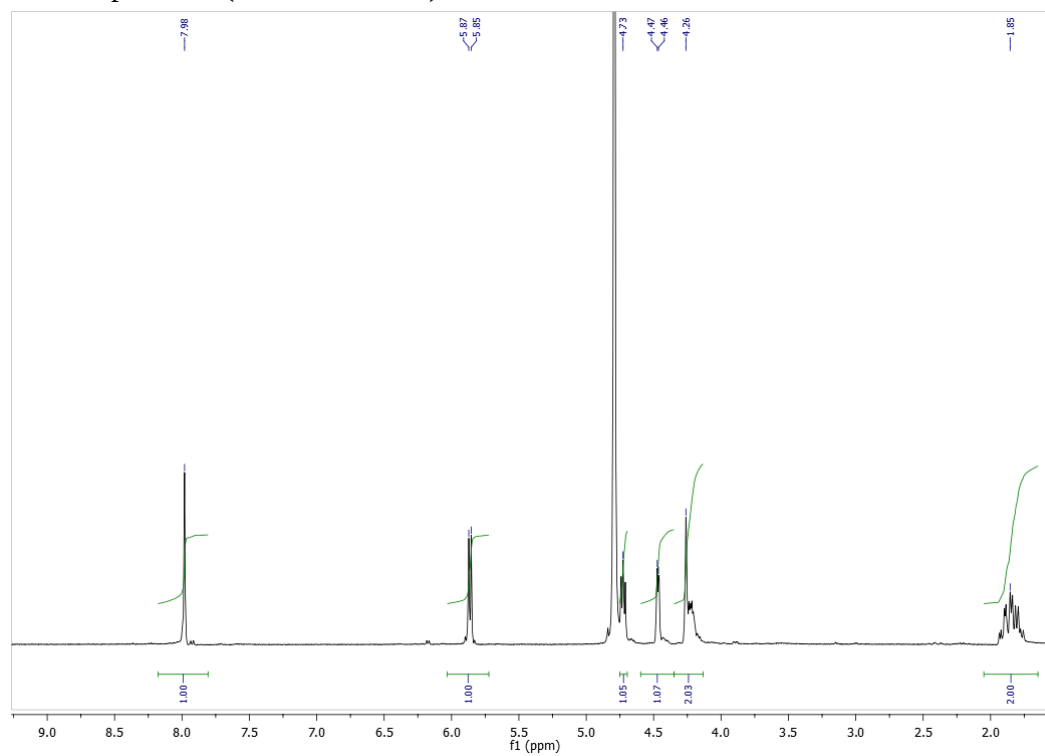


^{31}P NMR spectrum (121 MHz, D_2O)

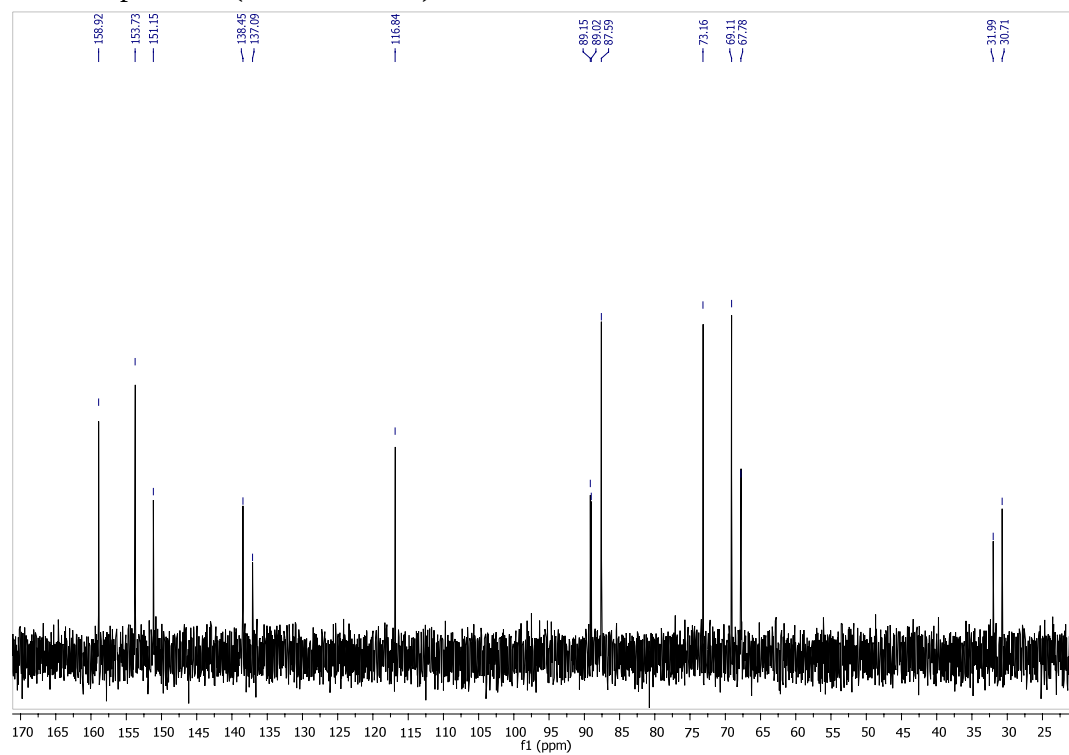


9-(6-Deoxy-6-phosphono- β -D-ribo-(5S)-hexofuranosyl) guanine, sodium salt (16b)

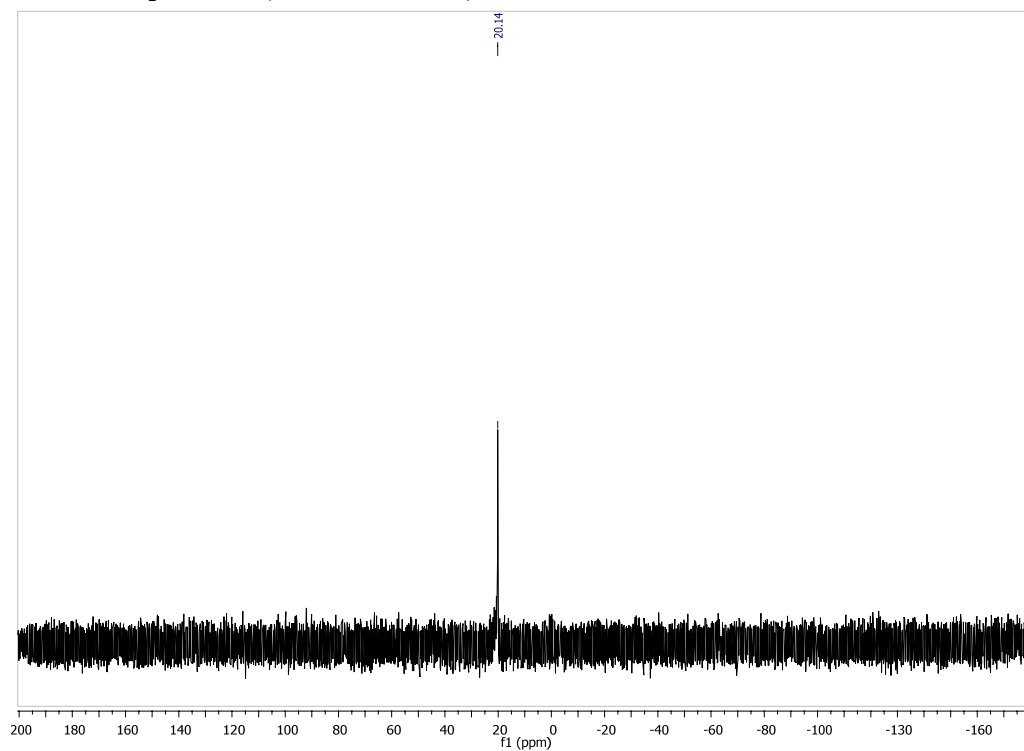
^1H NMR spectrum (300 MHz, D_2O)

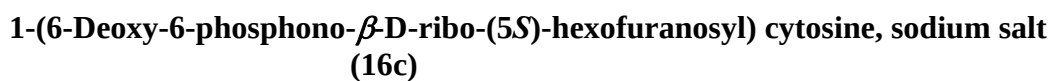


^{13}C NMR spectrum (75 MHz, D_2O)



^{31}P NMR spectrum (121 MHz, D_2O)





7.893
7.868

6.087
6.062
5.975
5.957
4.933
4.865
4.799
4.732
4.652
4.369
4.351
4.338
4.311
4.294
4.260
4.248
4.232
4.215
4.199
4.186
4.171
4.128
4.116
4.104
2.911
2.905
1.965
1.945
1.935
1.916
1.900
1.886
1.859
1.831
1.809
1.780

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

1.00
1.99
4.02
16.36

¹³C NMR spectrum (75 °C MHz, D₂O)

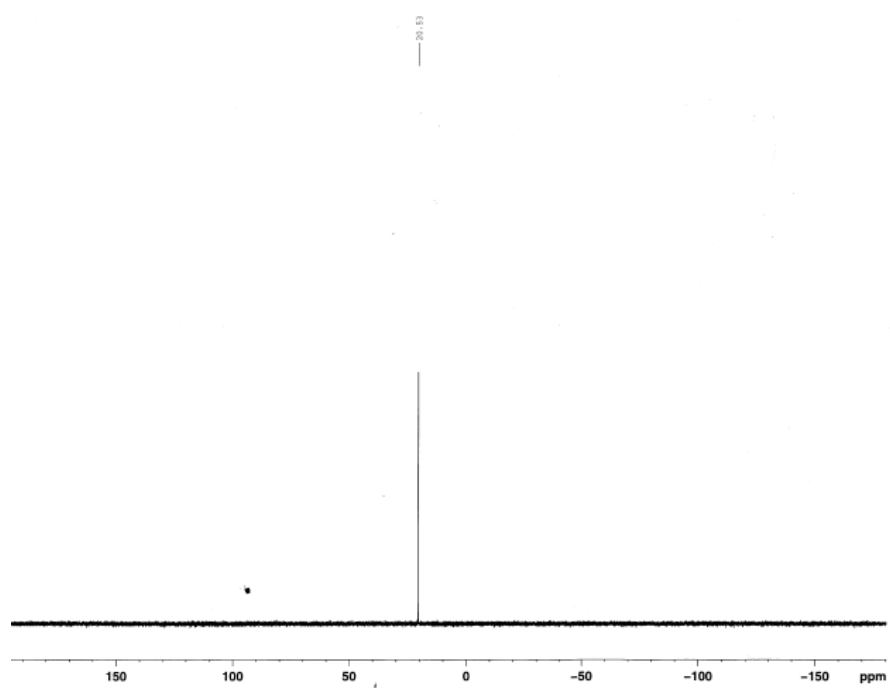
Chemical structure of compound 1 is shown above the spectrum:

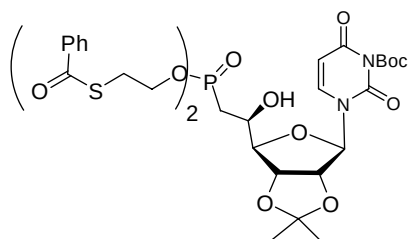
O=C1C(=O)C(=O)C(=O)C1

Peak list (ppm):

Peak (ppm)
166.050
157.777
141.889
96.52
88.88
87.71
87.00
73.73
71.75
67.05
67.24
32.77
30.05

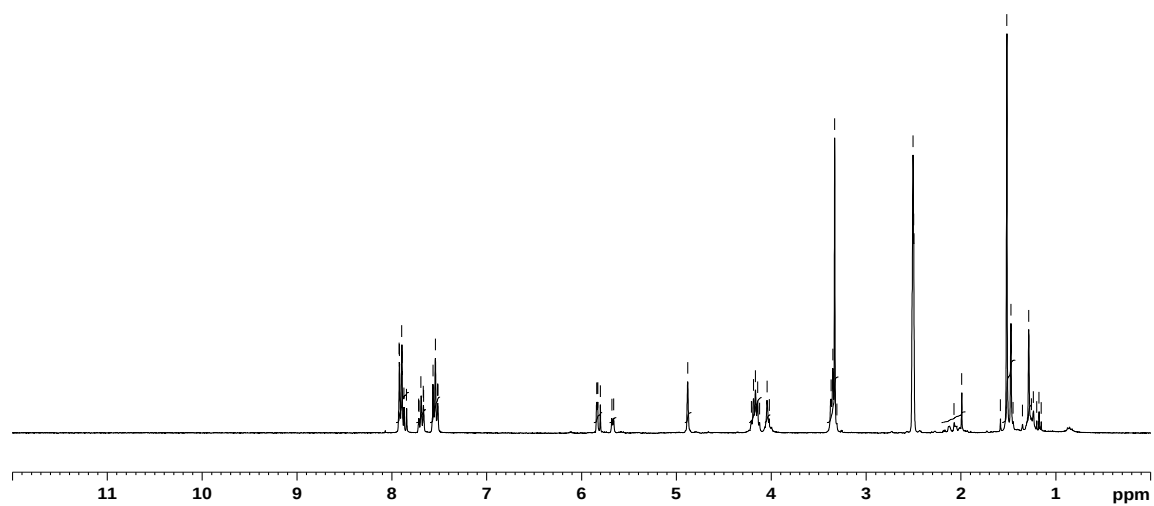
^{31}P NMR spectrum (121 MHz, D_2O)



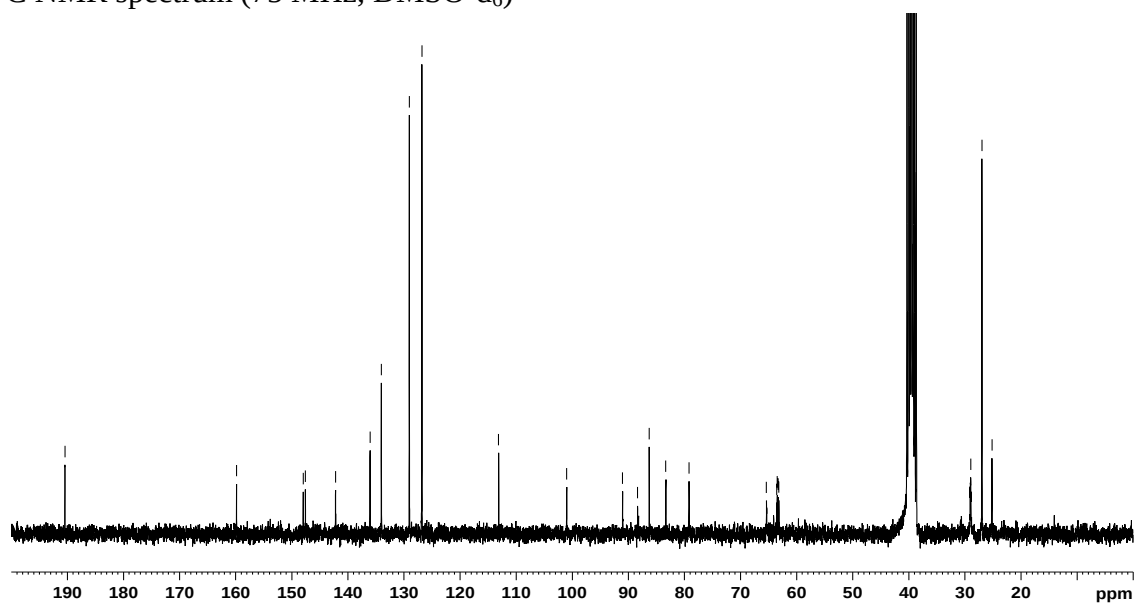


***N*-3-*tert*-Butyloxycarbonyl-1-(6-deoxy-6-di(*S*-benzoylthio)ethylphosphono-2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexofuranosyl) uracil (17)**

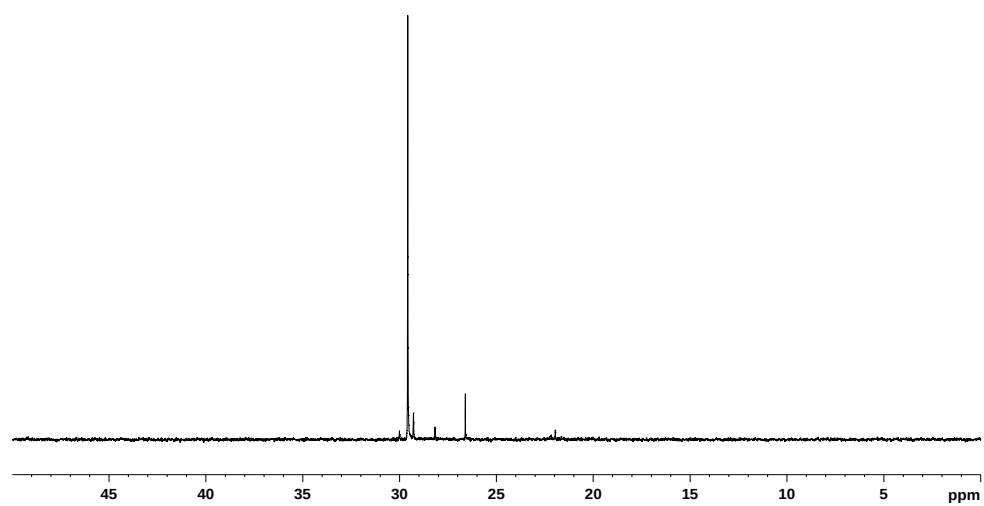
^1H NMR spectrum (300 MHz, DMSO- d_6)

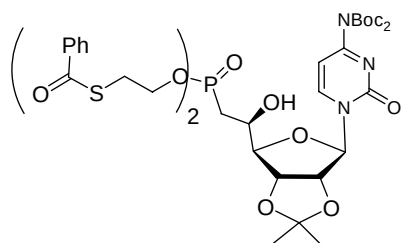


^{13}C NMR spectrum (75 MHz, DMSO- d_6)



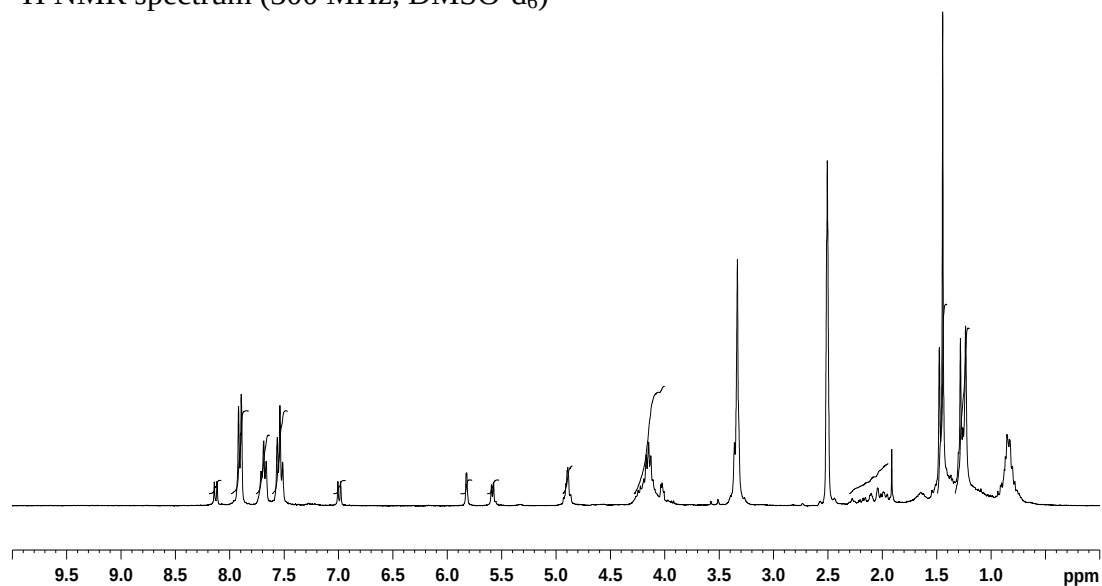
^{31}P NMR spectrum (121 MHz, DMSO- d_6)



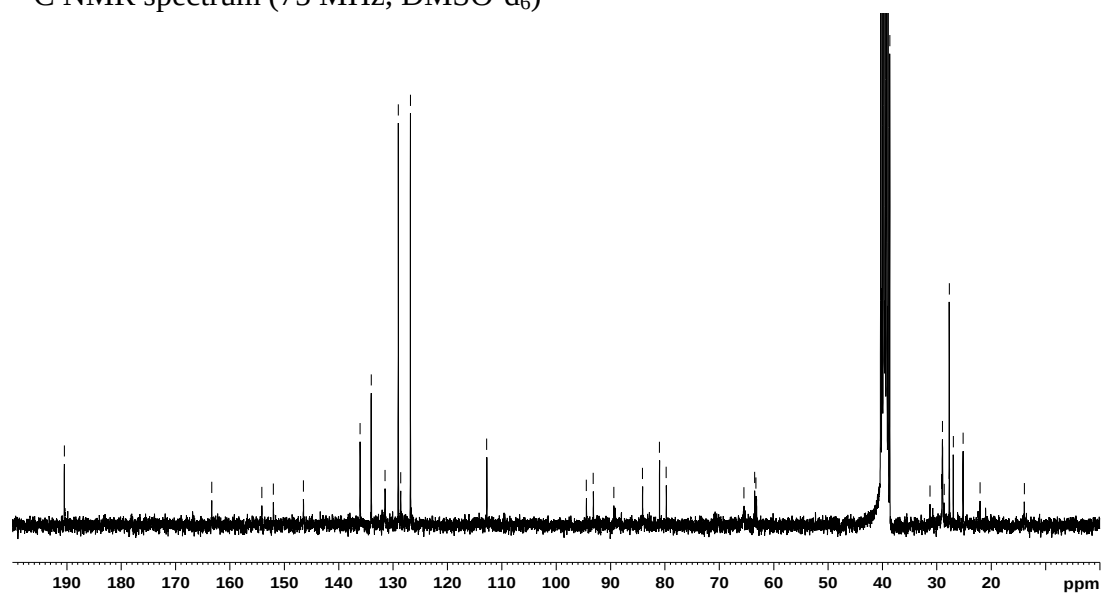


***N*-4(*tert*-Butyloxycarbonyl)-1-(6-deoxy-6-di-(*S*-benzoylthio)ethylphosphono-2,3-*O*-isopropylidene- β -D-ribo-(5*S*)-hexofuranosyl) cytosine (18)**

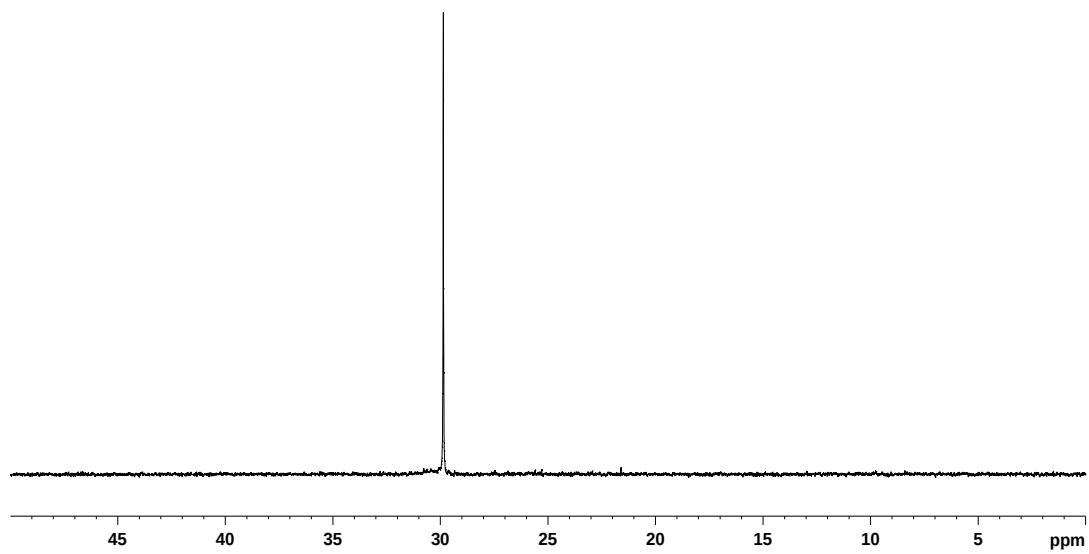
^1H NMR spectrum (300 MHz, DMSO- d_6)

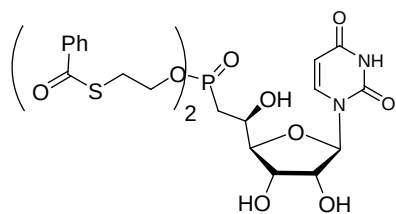


^{13}C NMR spectrum (75 MHz, DMSO- d_6)



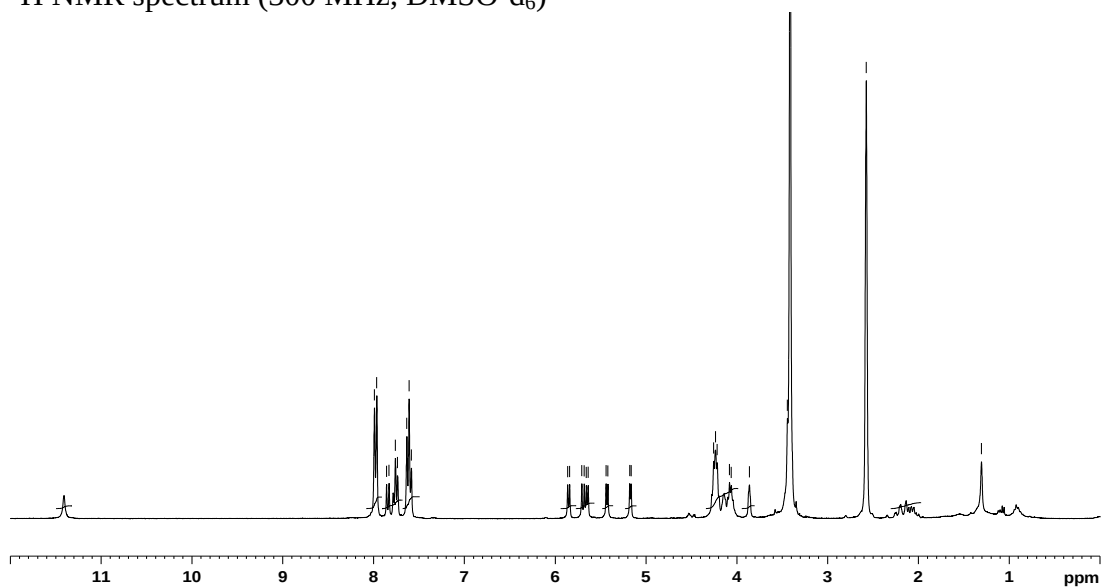
^{31}P NMR spectrum (121 MHz, DMSO- d_6)



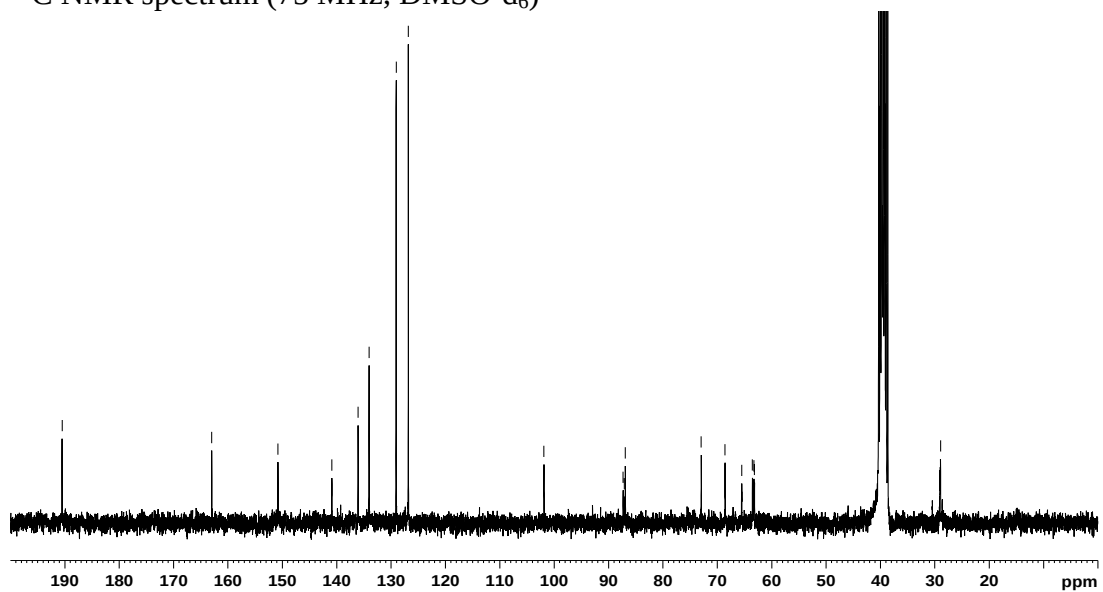


1-(6-Deoxy-6- di(*S*-benzoylthio)ethylphosphono- β -D-ribo-(5*S*)-hexofuranosyl) uracil (19)

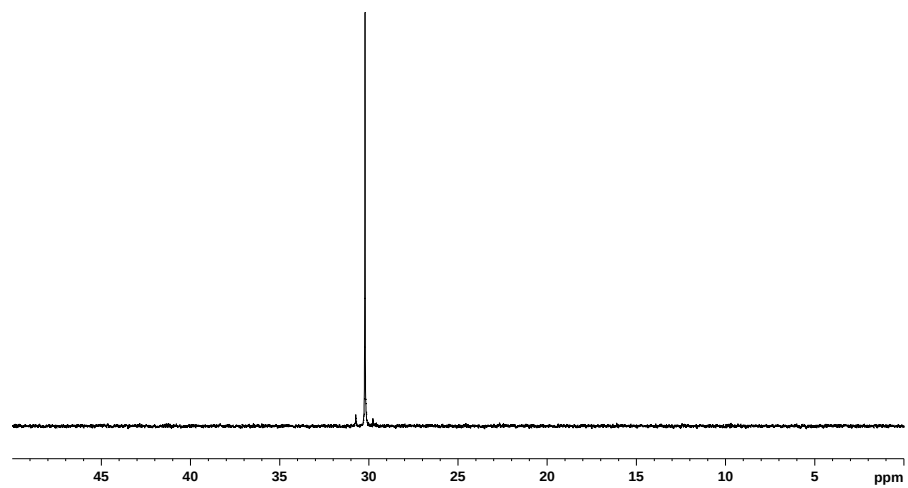
^1H NMR spectrum (300 MHz, DMSO- d_6)

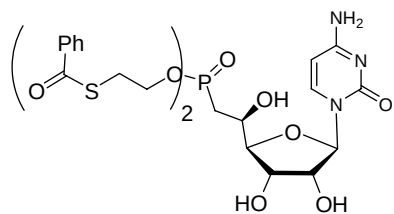


^{13}C NMR spectrum (75 MHz, DMSO- d_6)



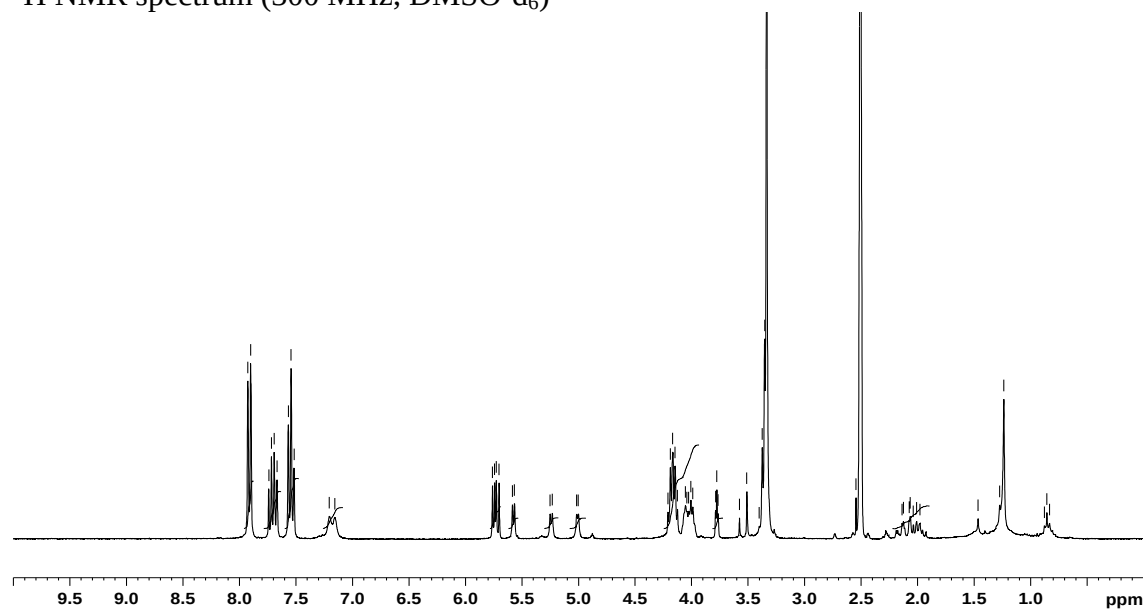
^{31}P NMR spectrum (121 MHz, DMSO- d_6)



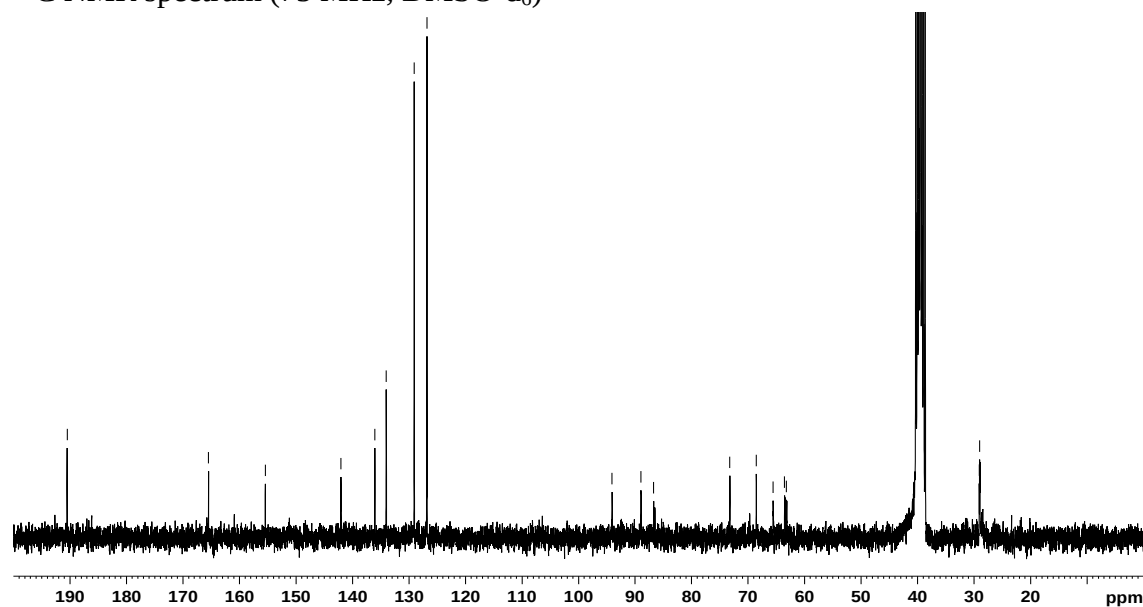


1-(6-Deoxy-6-di(*S*-benzoylthio)ethylphosphono- β -D-ribo-(5*S*)-hexofuranosyl) cytosine (20)

^1H NMR spectrum (300 MHz, DMSO- d_6)



^{13}C NMR spectrum (75 MHz, DMSO- d_6)



^{31}P NMR spectrum (121 MHz, DMSO- d_6)

