

SUPPORTING INFORMATION

Chemoenzymatic Convergent Synthesis of 2'-O,4'-C-Methyleneribonucleosides

Vivek K. Sharma,^a Manish Kumar,^a Carl E. Olsen^b and Ashok K. Prasad^{a*}

^aBioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007, India; ^bFaculty of Life Sciences, Department of Plant and Environmental Sciences, University of Copenhagen, DK- 1871 Frederiksberg C, Denmark

*Corresponding Author

Ashok K. Prasad: Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007, India; Phone: 00-91-11-27662486; E-mail: ashokenzyme@yahoo.com.

Copy of ¹H- and ¹³C NMR spectra of 7-12, 13a-d, 14a-d and 15a-d are enclosed in this supporting information.

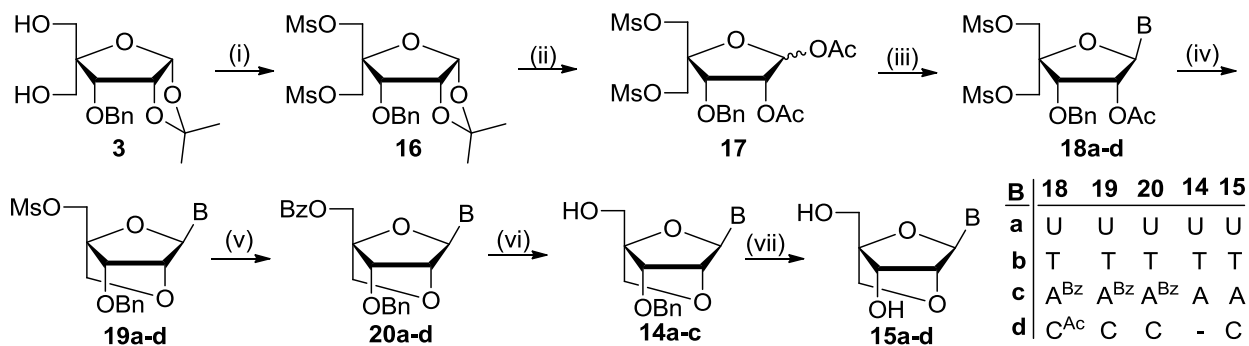
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General information

Reactions were conducted under an atmosphere of nitrogen when anhydrous solvents were used. The IR spectra were recorded by making KBr disc for solid samples and thin film for oils. The optical rotations were measured using light of 589 nm wavelegth. The ¹H- and ¹³C NMR spectra were recorded at 400 and 100.6 MHz, respectively, using TMS as internal standard. The chemical shift values are on δ scale and the coupling constants (*J*) are in Hz. Signals from OH and NH groups in ¹H NMR spectra recorded in DMSO-*d*₆ were verified by removing them by D₂O exchange method. Analytical TLCs were performed on pre-coated silica gel 60F₂₅₄ plates; the spots were detected either using UV light or by charring with 4% alcoholic sulfuric acid. Silica gel (100-200 mesh) was used for column chromatography.

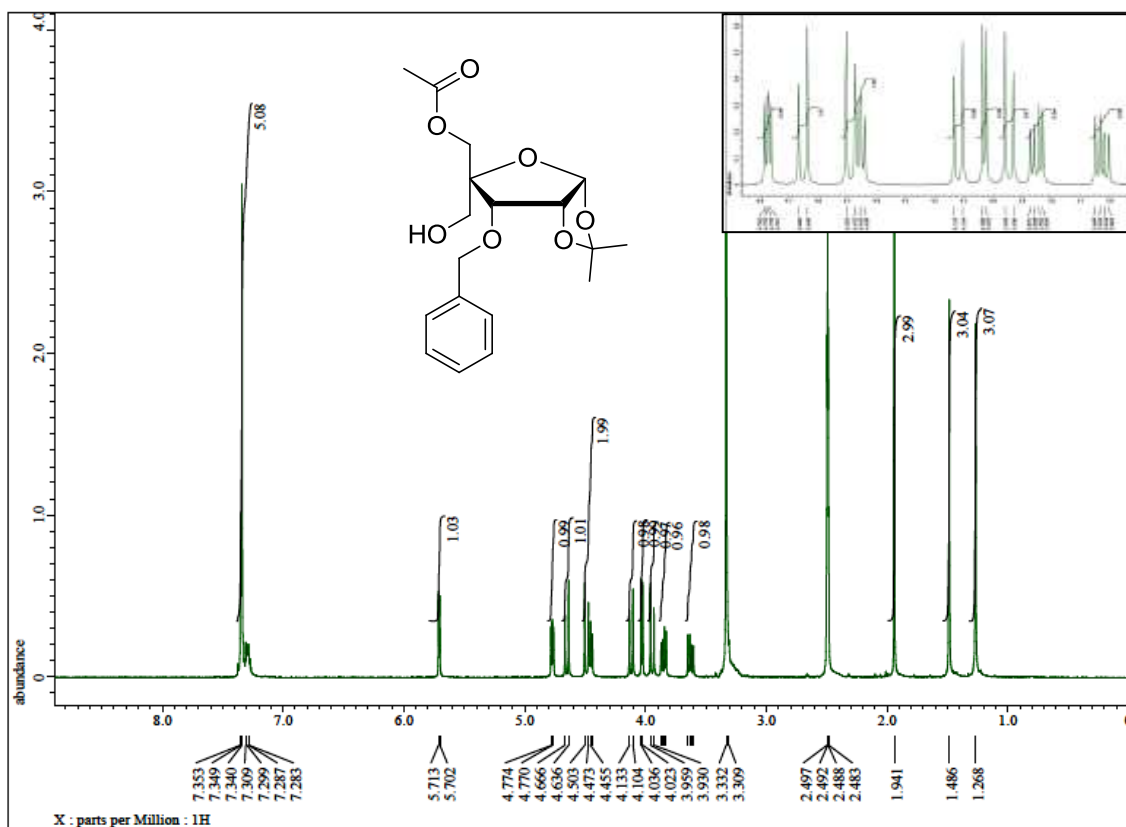
SI-Scheme 1. Literature convergent synthesis of LNA monomers.^{1,2}



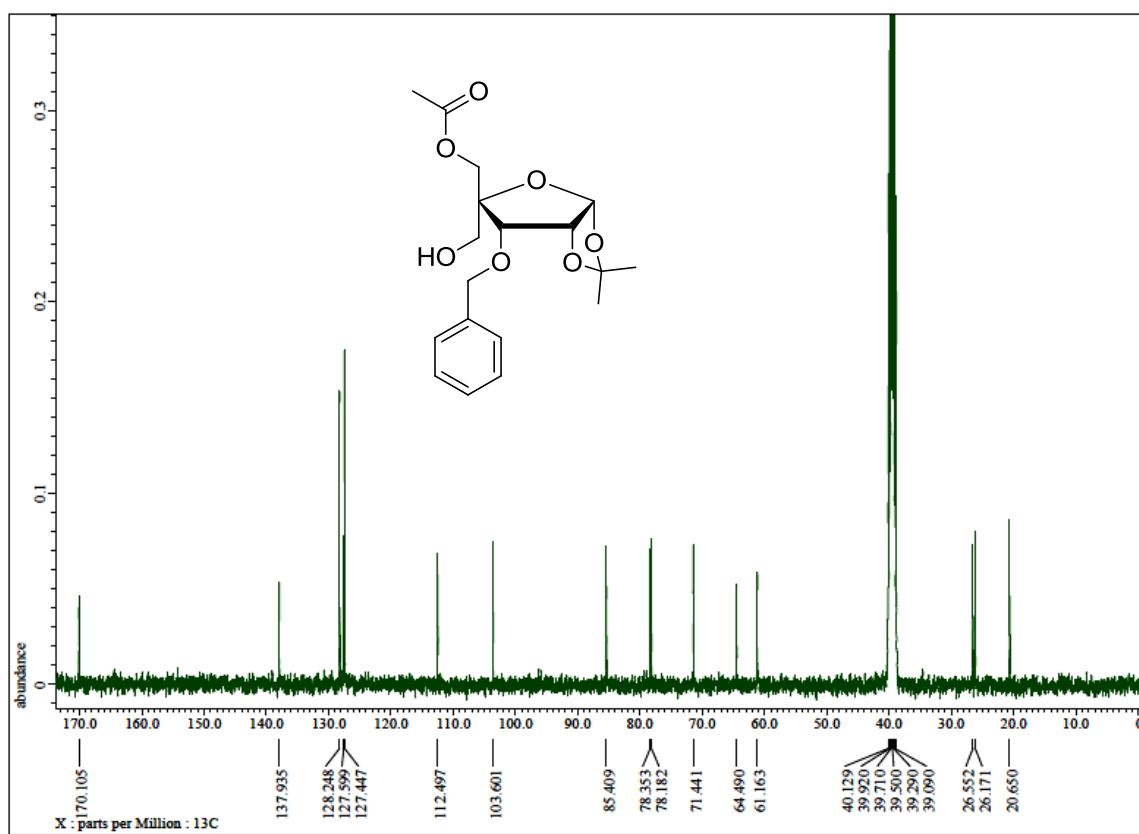
Reagents (% yields): (i) MsCl, pyridine, CH₂Cl₂ (98%); (ii) Ac₂O, AcOH, conc. H₂SO₄ (97%); (iii) nucleobase, *N,O*-bis(trimethylsilyl)acetamide, TMS-triflate, CH₃CN or 1,2-dichloroethane (**18a**, 90%; **18b**, 88%; **18c**, 68%; **18d**, 82%); (iv) aq. NaOH, THF or dioxane (**19a**, 97%; **19b**, 94%; **19c**, 78%; **19d**, 87%); (v) NaOBz, DMF (**20a**, 97%; **20b**, 86%; **20c**, 88%; **20d**, 93%); (vi) aq. NaOH, THF (**14a**, 95%; **14b**, 91%); NH₄OH, MeOH (**14c**, 86%); (a) 20% Pd(OH)₂/C, HCO₂NH₄, MeOH; (b) NH₄OH (**15d**, 77%); (vii) 20% Pd(OH)₂/C, 88% HCOOH, THF/MeOH (9:1) (**15a**, 91%); 20% Pd(OH)₂/C, HCO₂NH₄, MeOH/EtOH (**15b**, 83%; **15c**, 91%).

SI-Table 1. Comparison of overall yields of LNA monomers in literature convergent synthesis with modified chemo-enzymatic convergent synthesis.

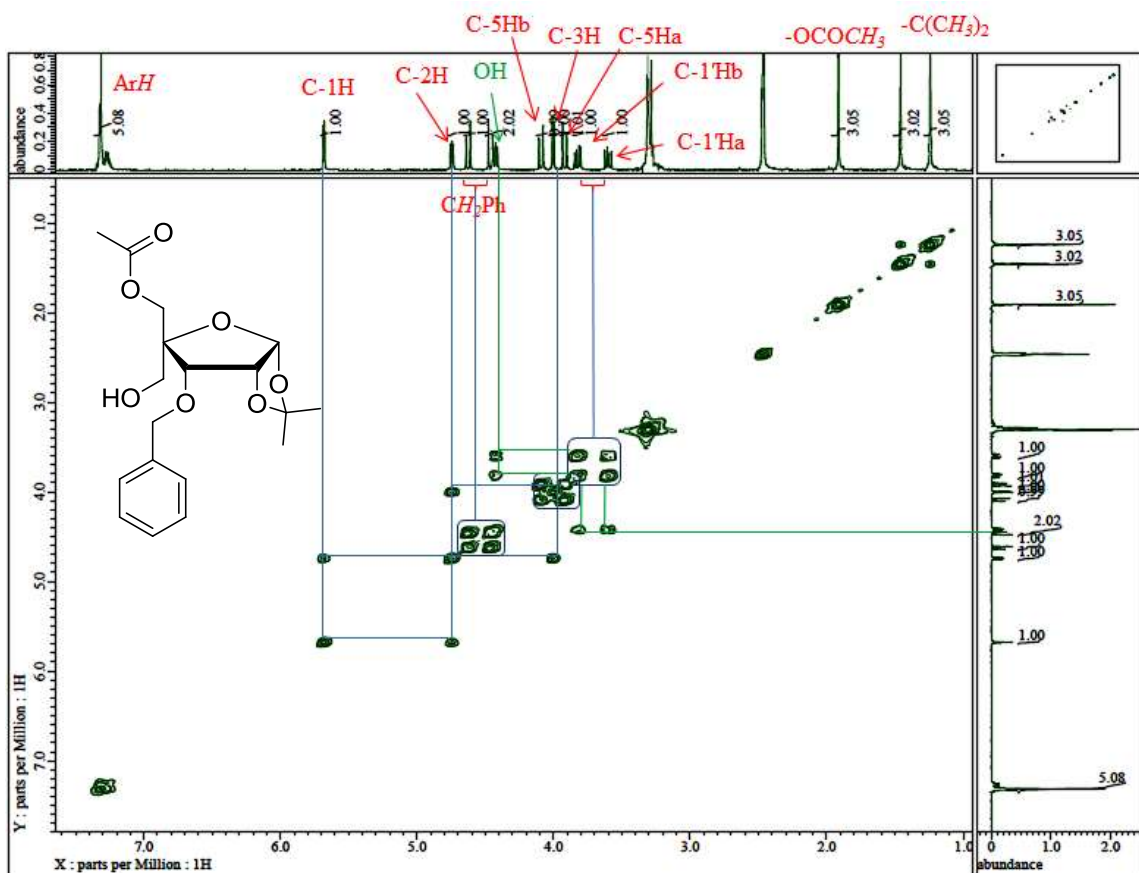
LNA monomer	Overall yield (%) (SI-Scheme 1)*	Overall yield (%) (Scheme 3)*
U; 15a	69.6	72.4
T; 15b	51.1	63.9
A; 15c	34.7	54.1
C; 15d	48.6	55.9



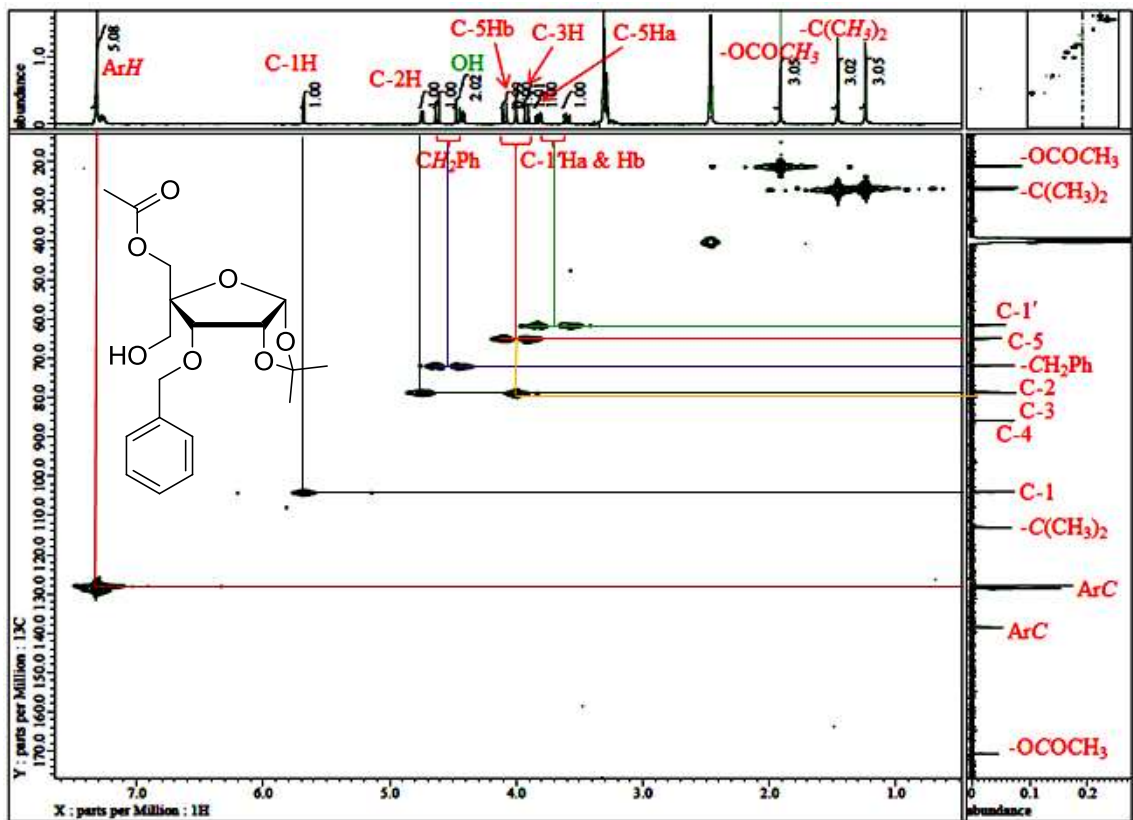
¹H NMR spectrum of compound 7 (400 MHz, DMSO-*d*₆)



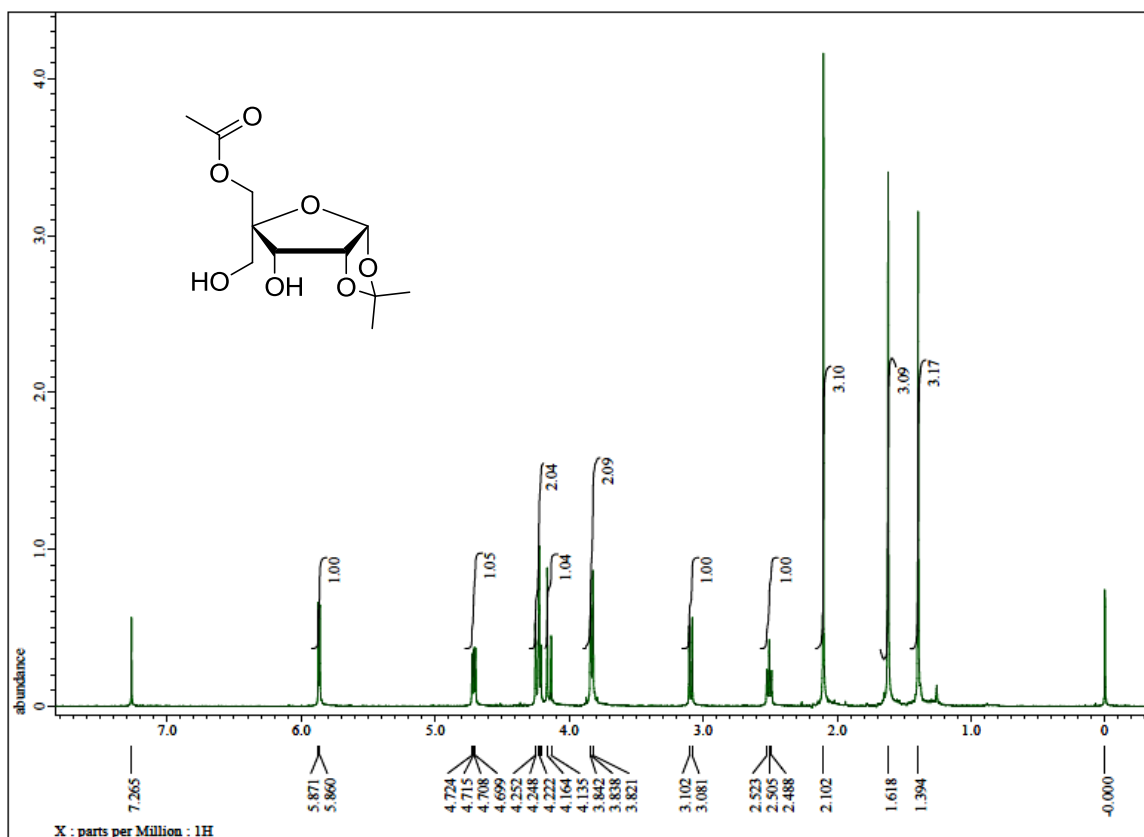
¹³C NMR spectrum of compound 7 (100.6 MHz, DMSO-*d*₆)



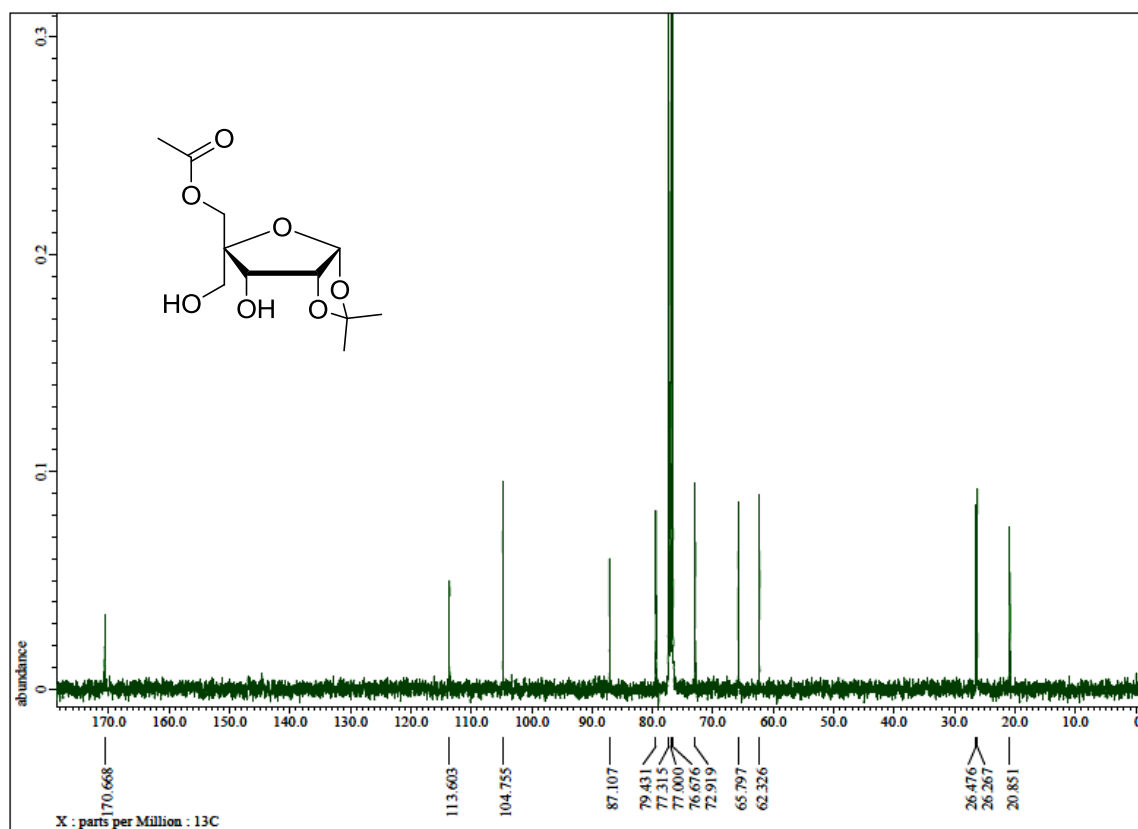
¹H-¹H COSY NMR spectrum of compound **7** (400 MHz, DMSO-*d*₆)



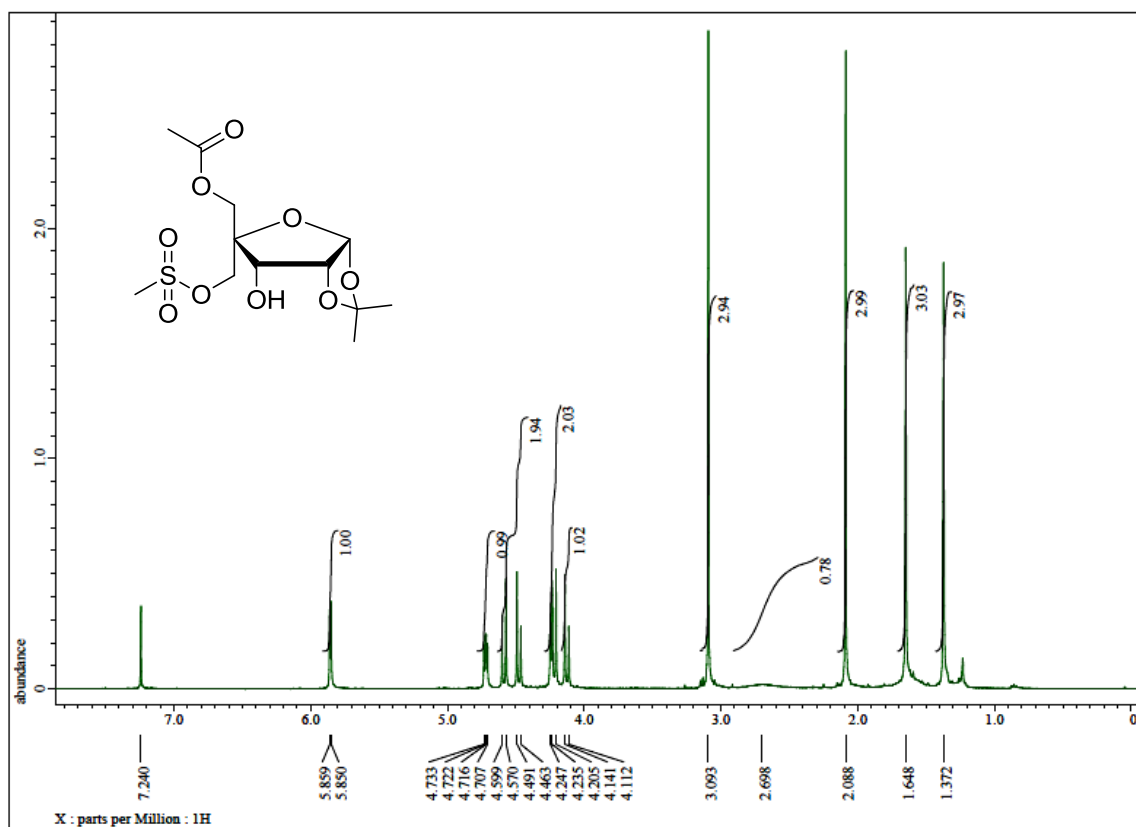
¹H-¹³C NMR HMQC spectrum of compound **7** (400 MHz, DMSO-*d*₆)



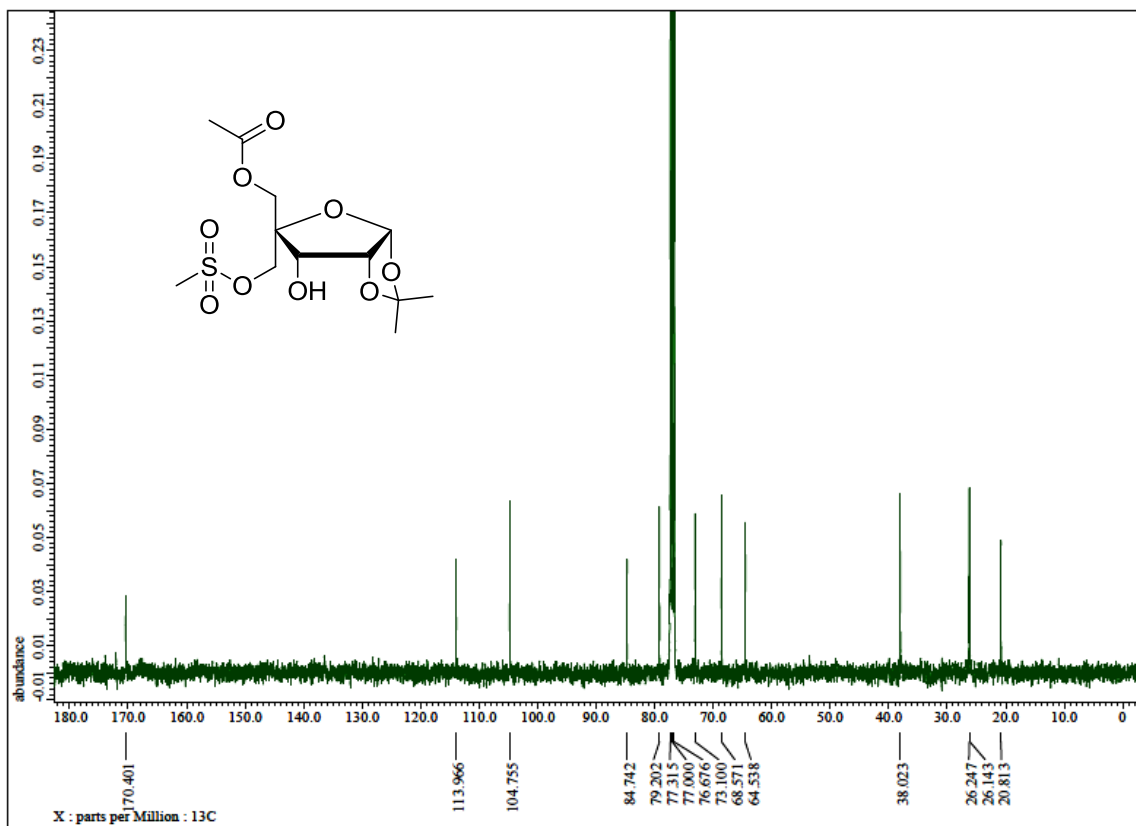
¹H NMR spectrum of compound **8** (400 MHz, CDCl₃)



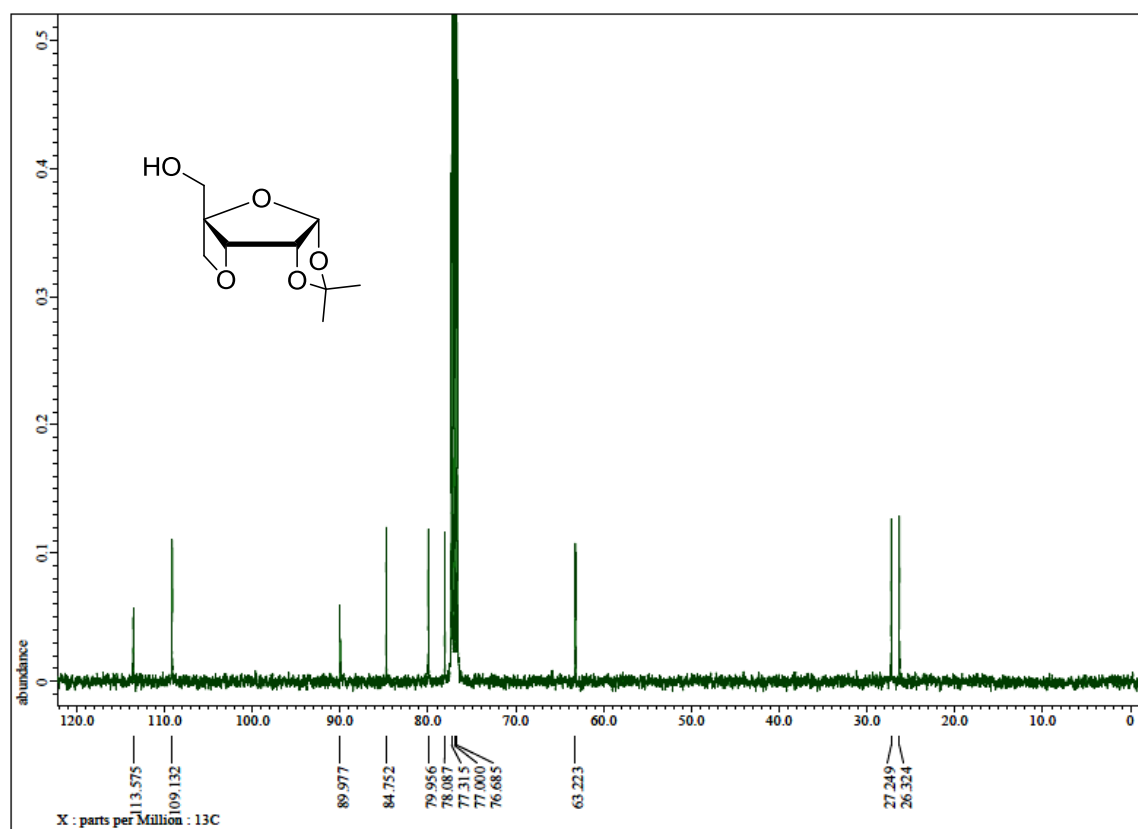
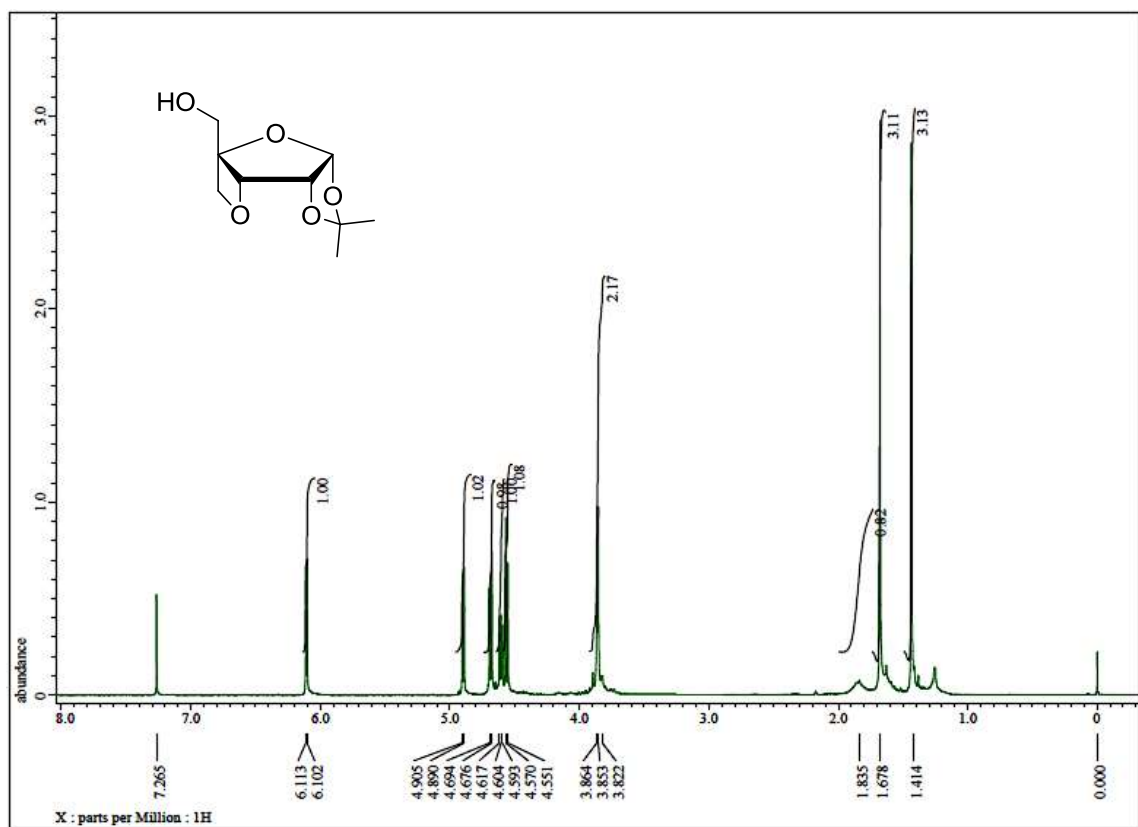
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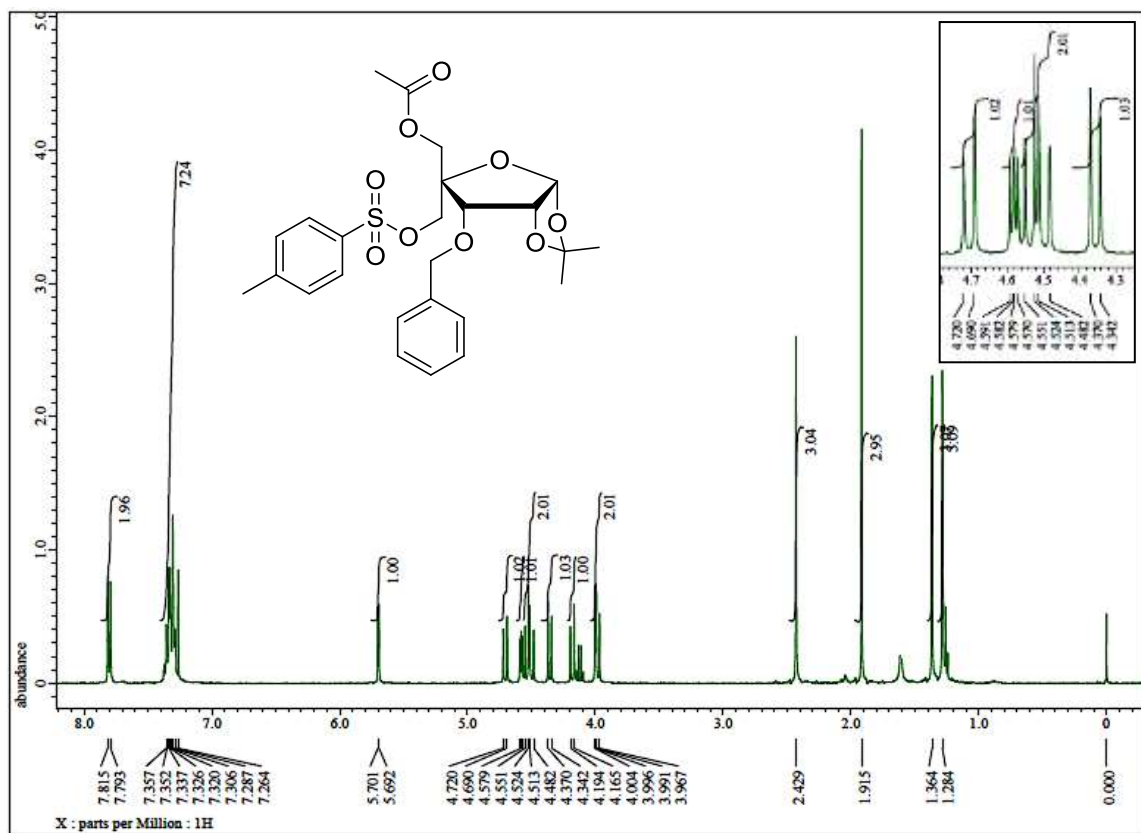


¹H NMR spectrum of compound **9** (400 MHz, CDCl₃)

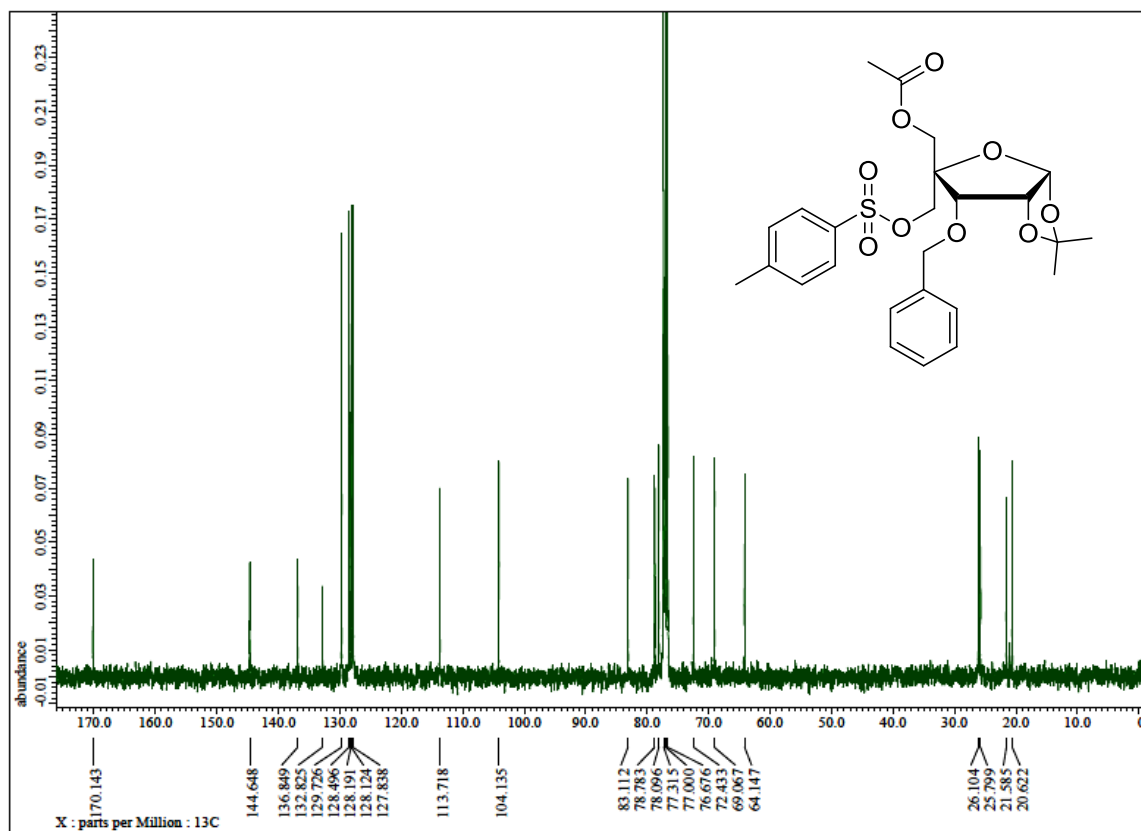


¹³C NMR spectrum of compound **9** (100.6 MHz, CDCl₃)

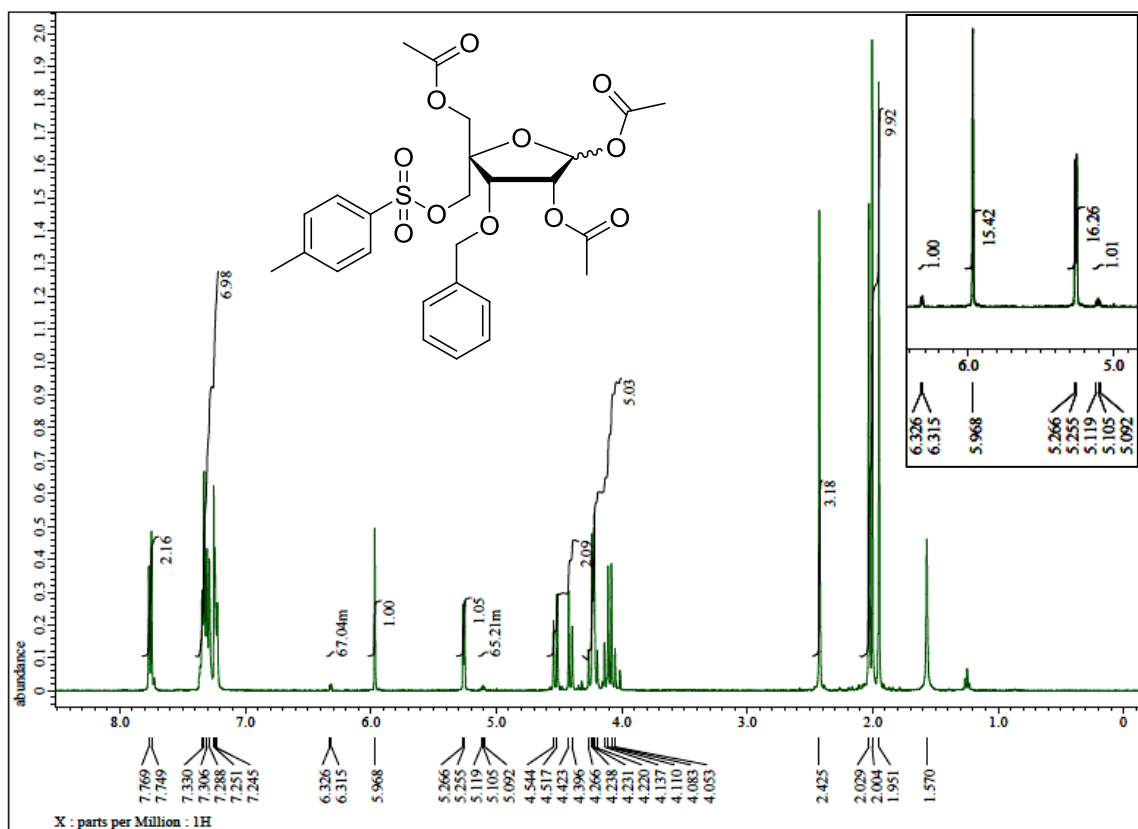




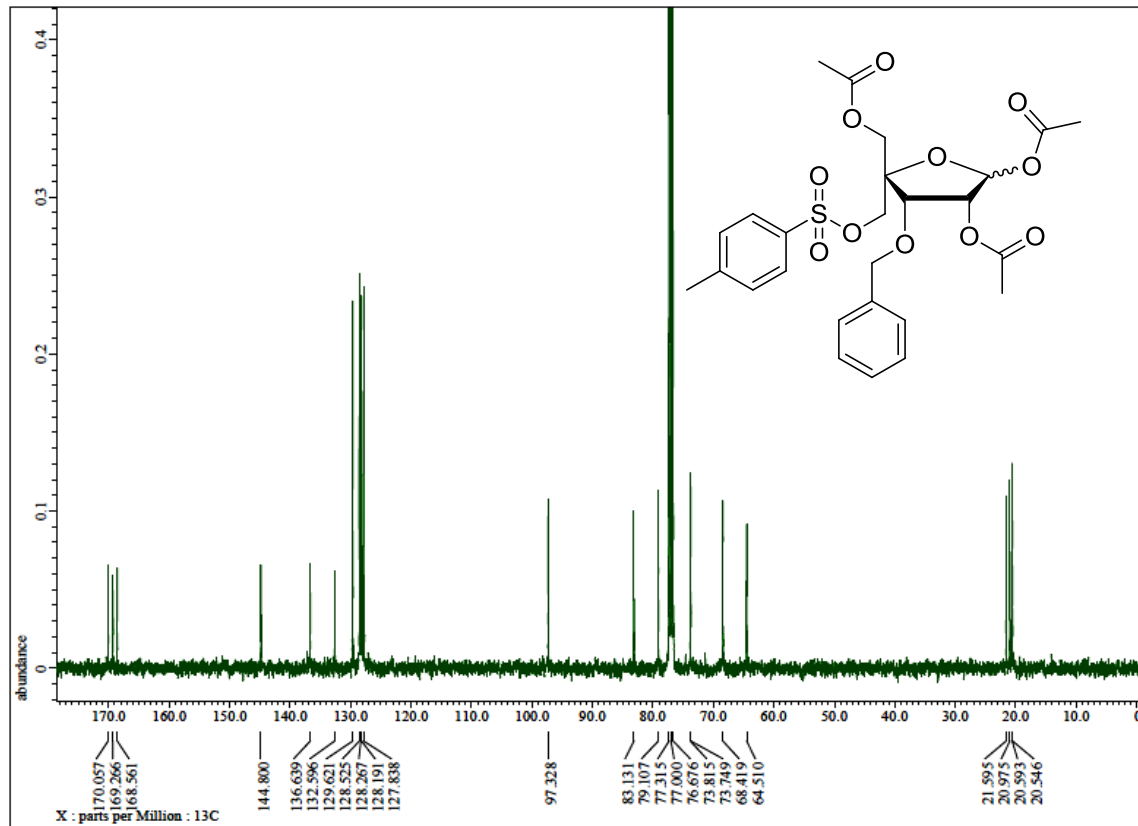
¹H NMR spectrum of compound **11** (400 MHz, CDCl₃)



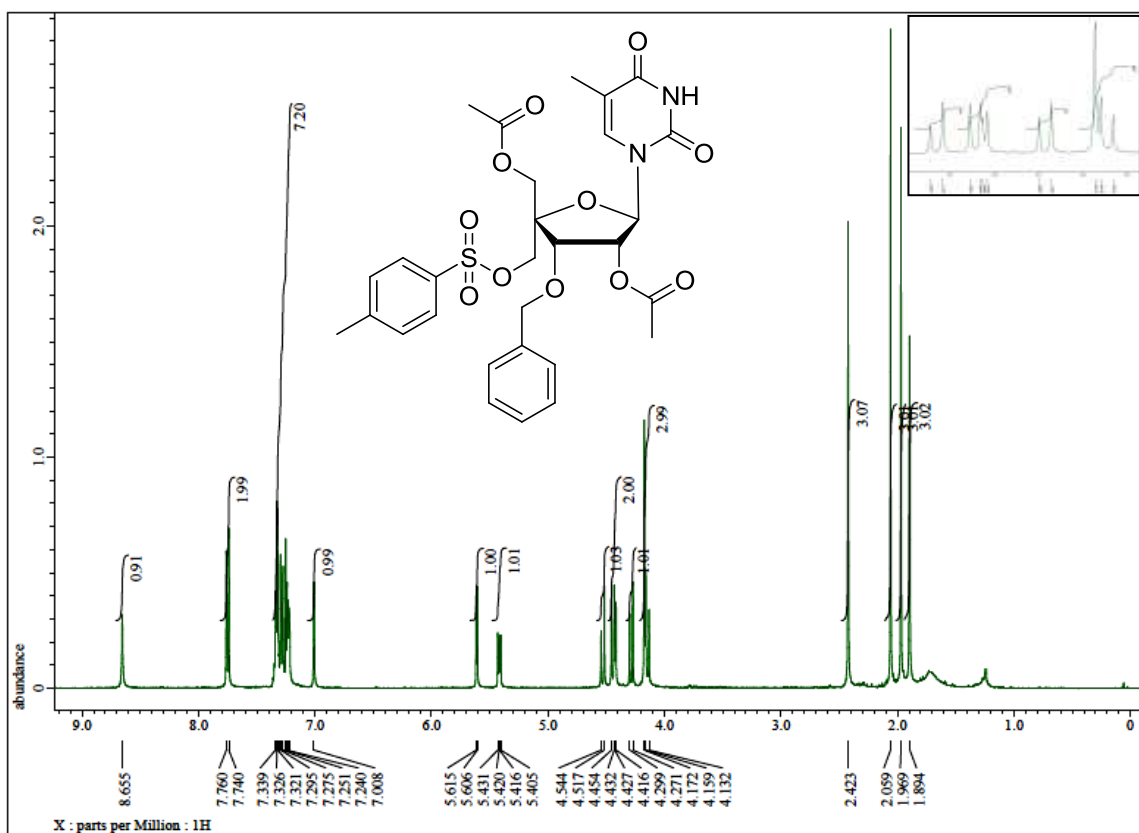
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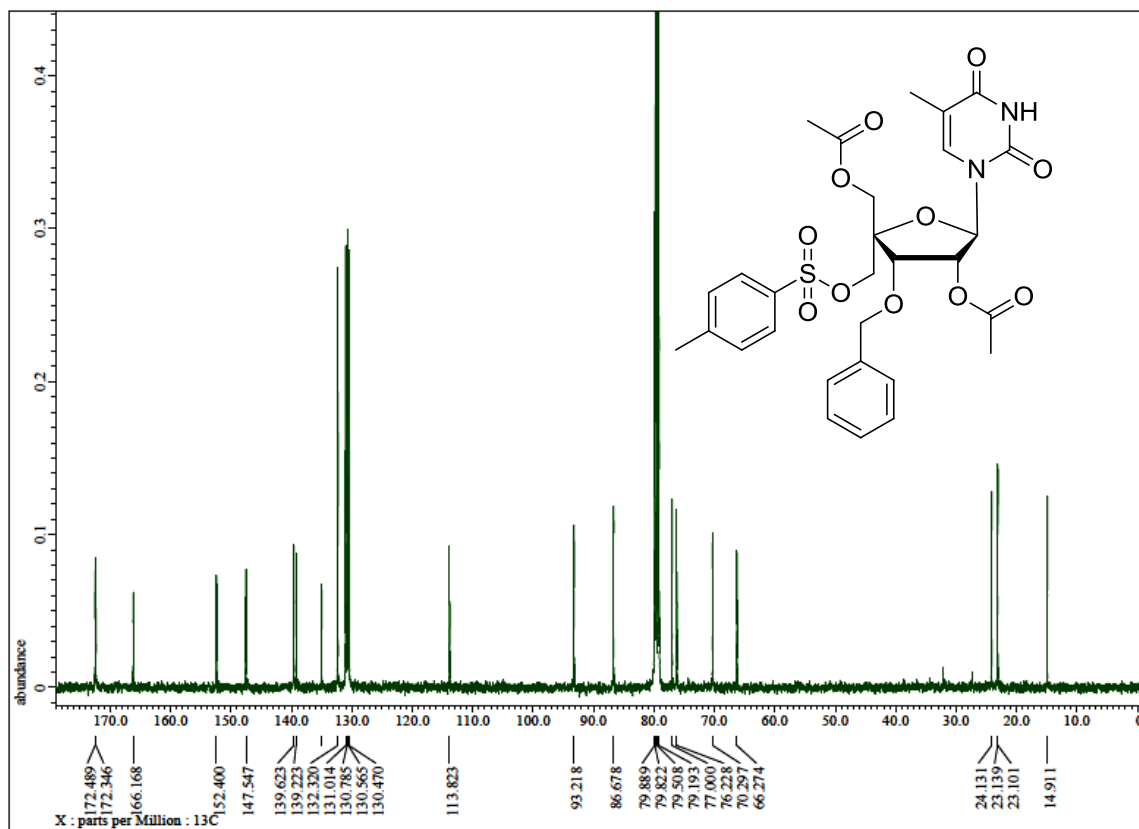
¹H NMR spectrum of compound **12** (400 MHz, CDCl₃)



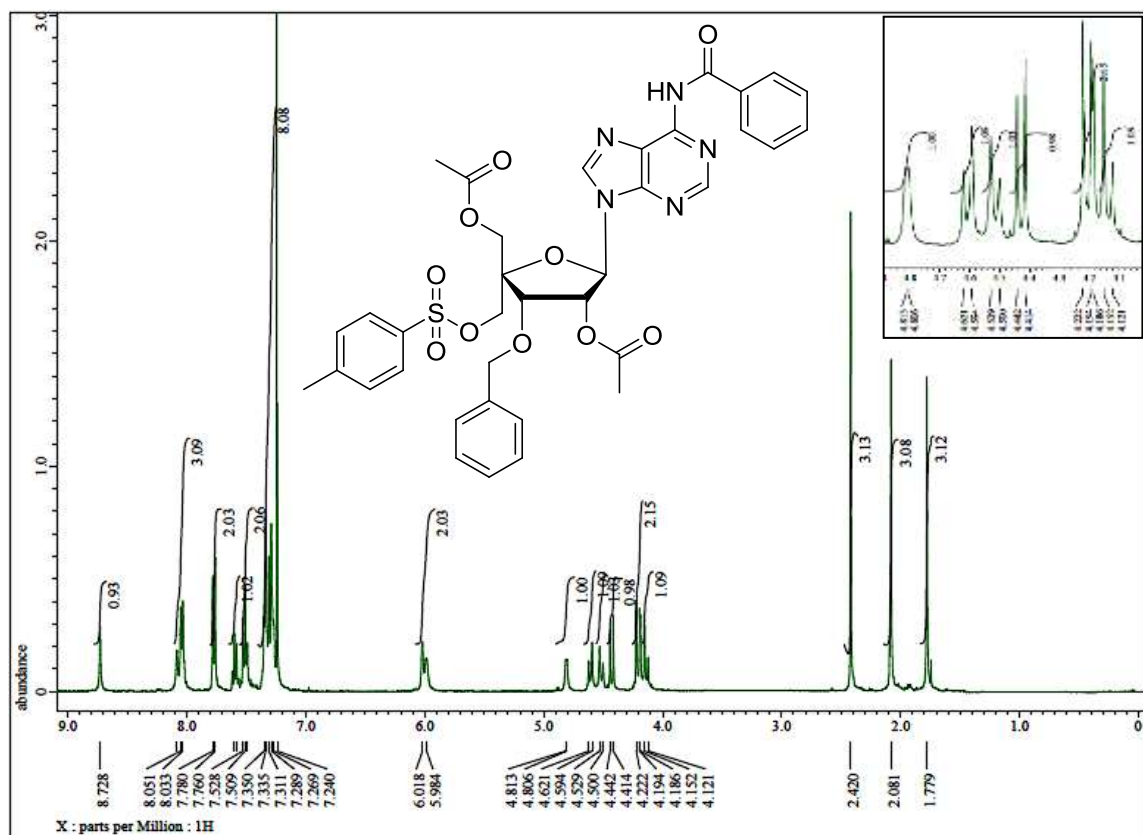
¹³C NMR spectrum of compound **12** (100.6 MHz, CDCl₃)



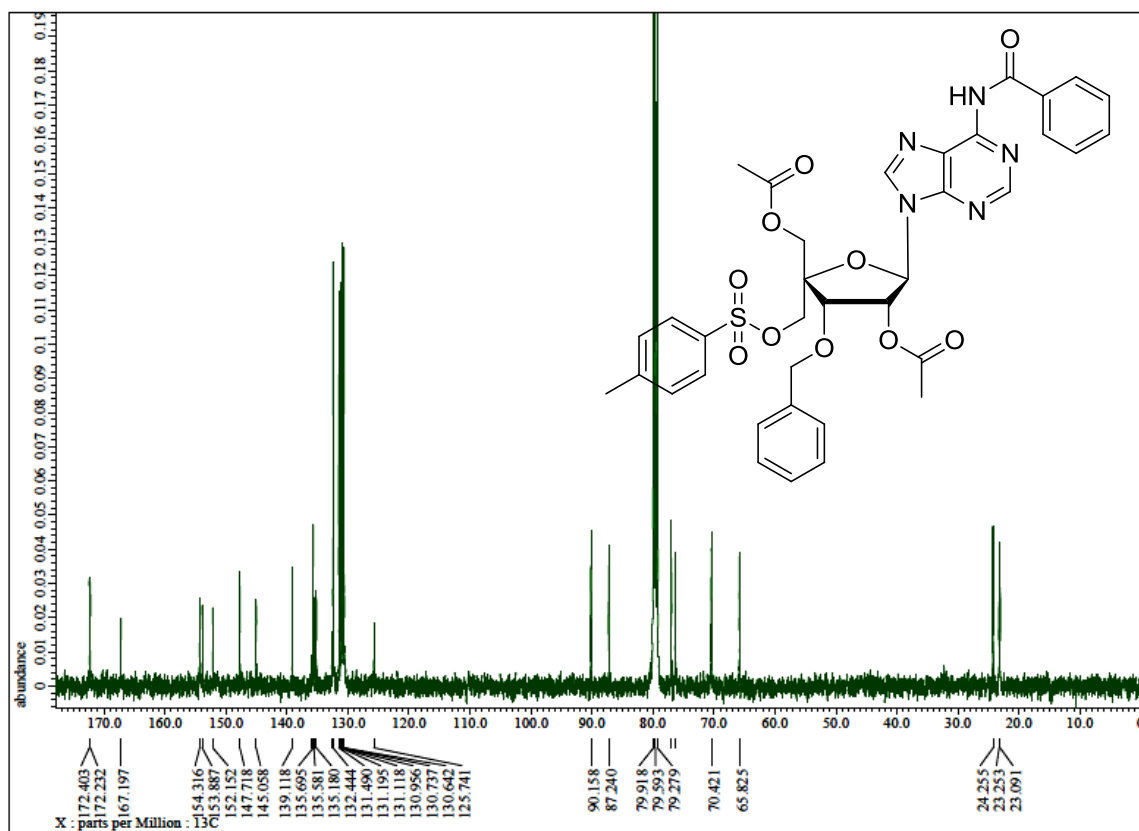
¹H NMR spectrum of compound **13b (400 MHz, CDCl₃)**



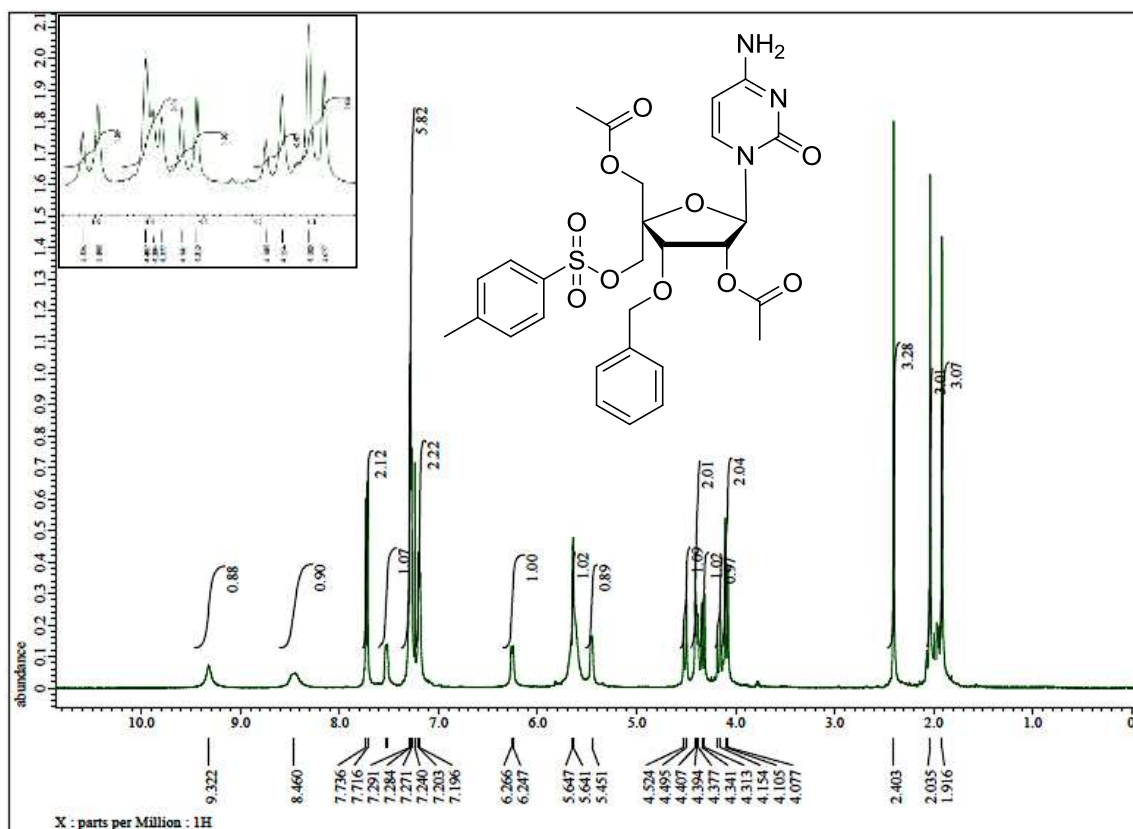
¹³C NMR spectrum of compound **13b (100.6 MHz, CDCl₃)**



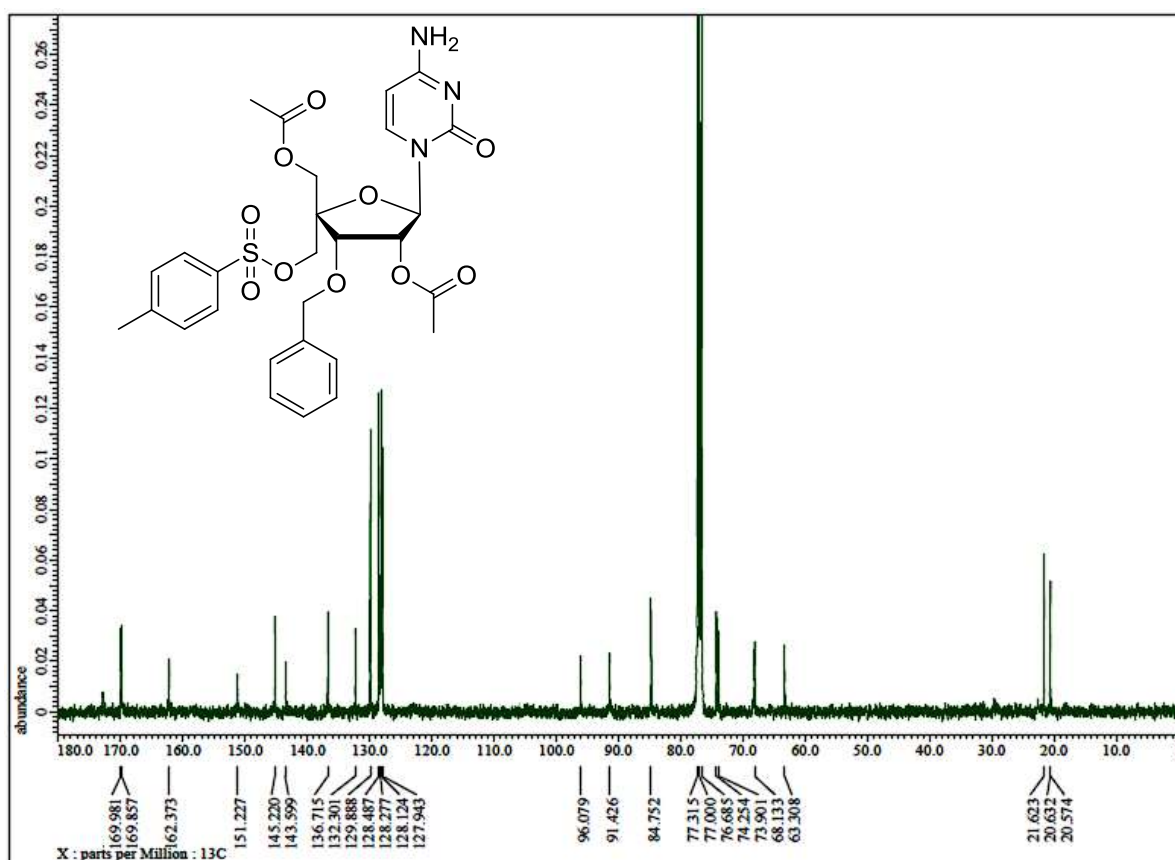
¹H NMR spectrum of compound **13c** (400 MHz, CDCl₃)



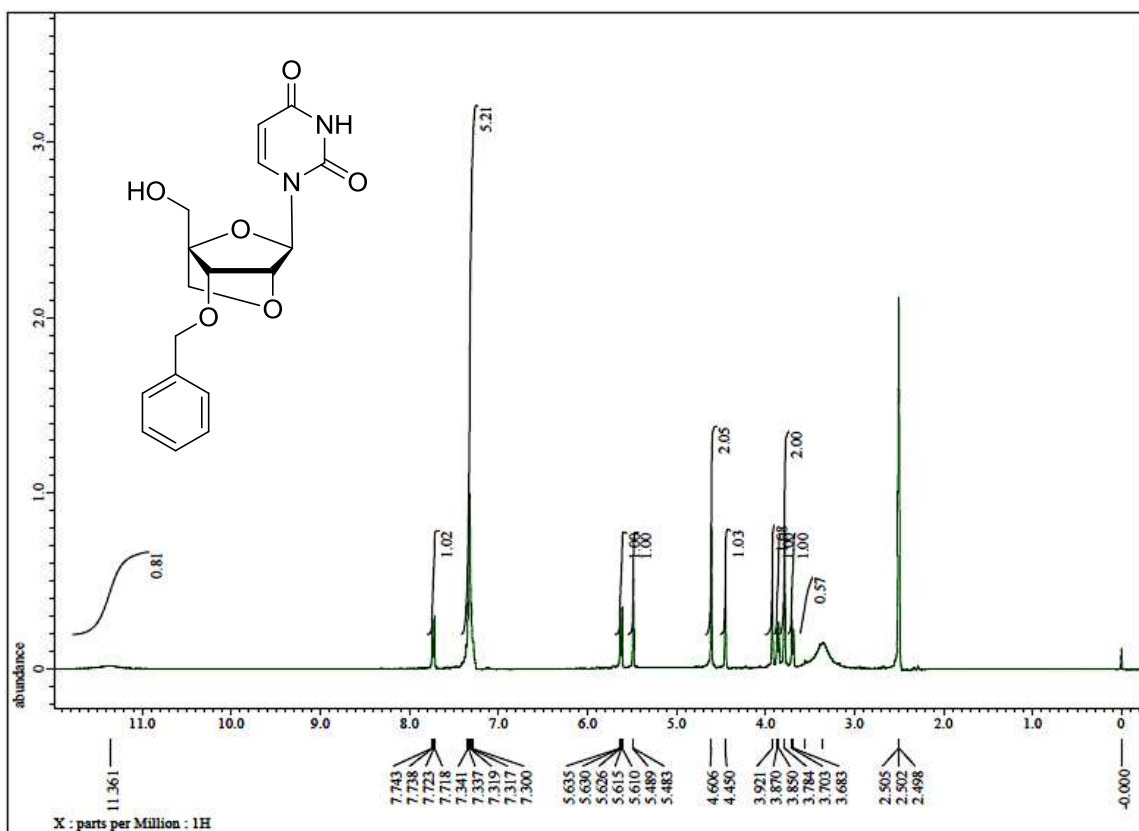
¹³C NMR spectrum of compound **13c** (100.6 MHz, CDCl₃)



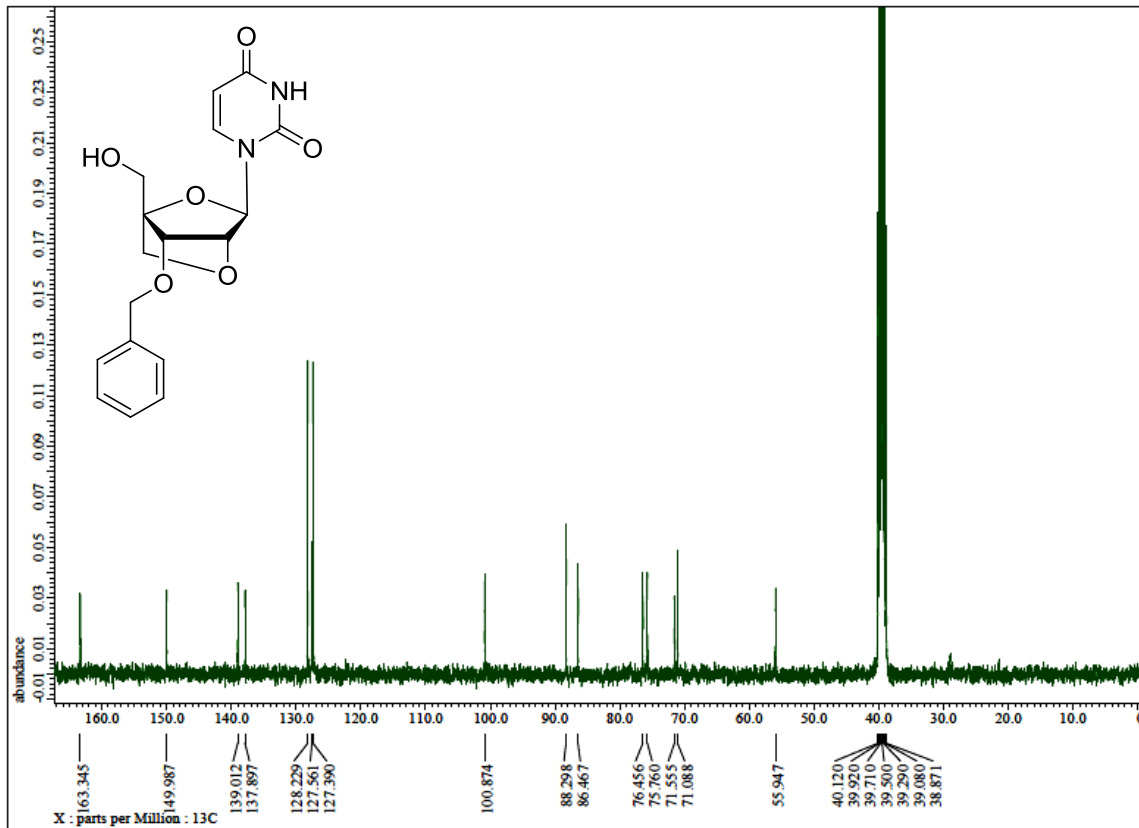
¹H NMR spectrum of compound **13d** (400 MHz, CDCl₃)



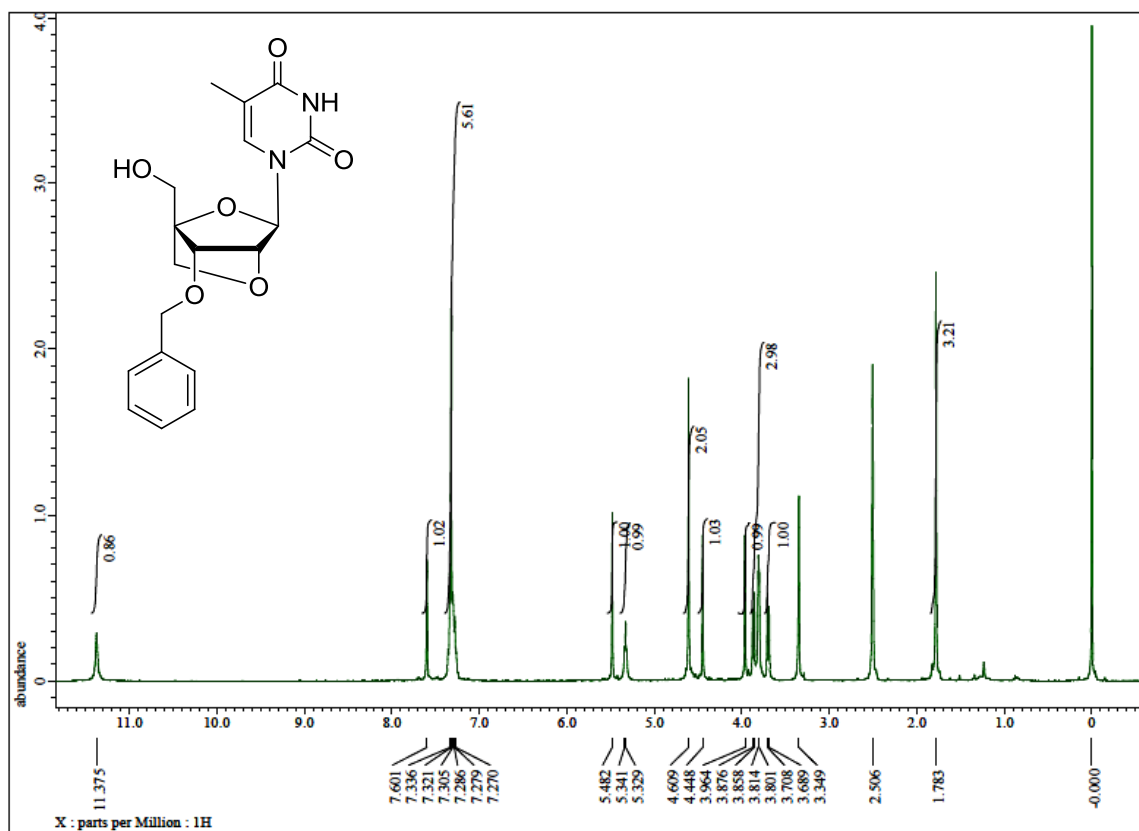
¹³C NMR spectrum of compound **13d** (100.6 MHz, CDCl₃)



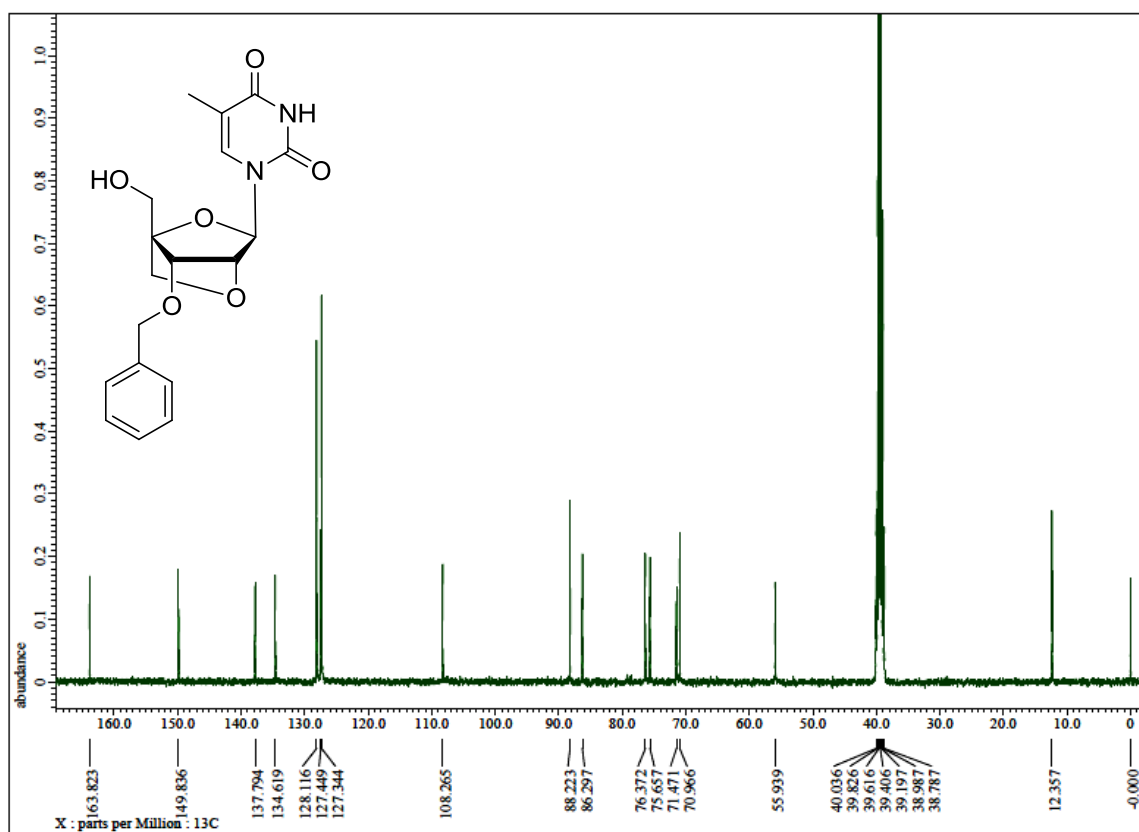
¹H NMR spectrum of compound **14a** (400 MHz, DMSO-*d*₆)



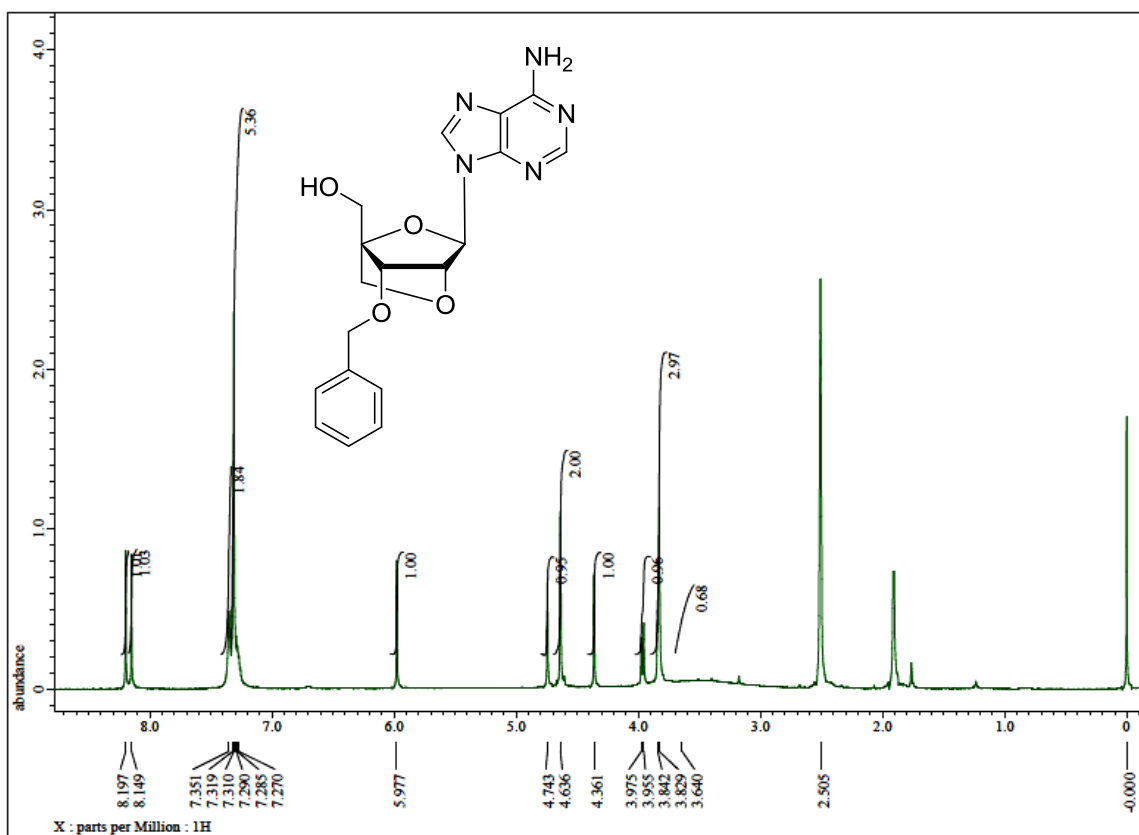
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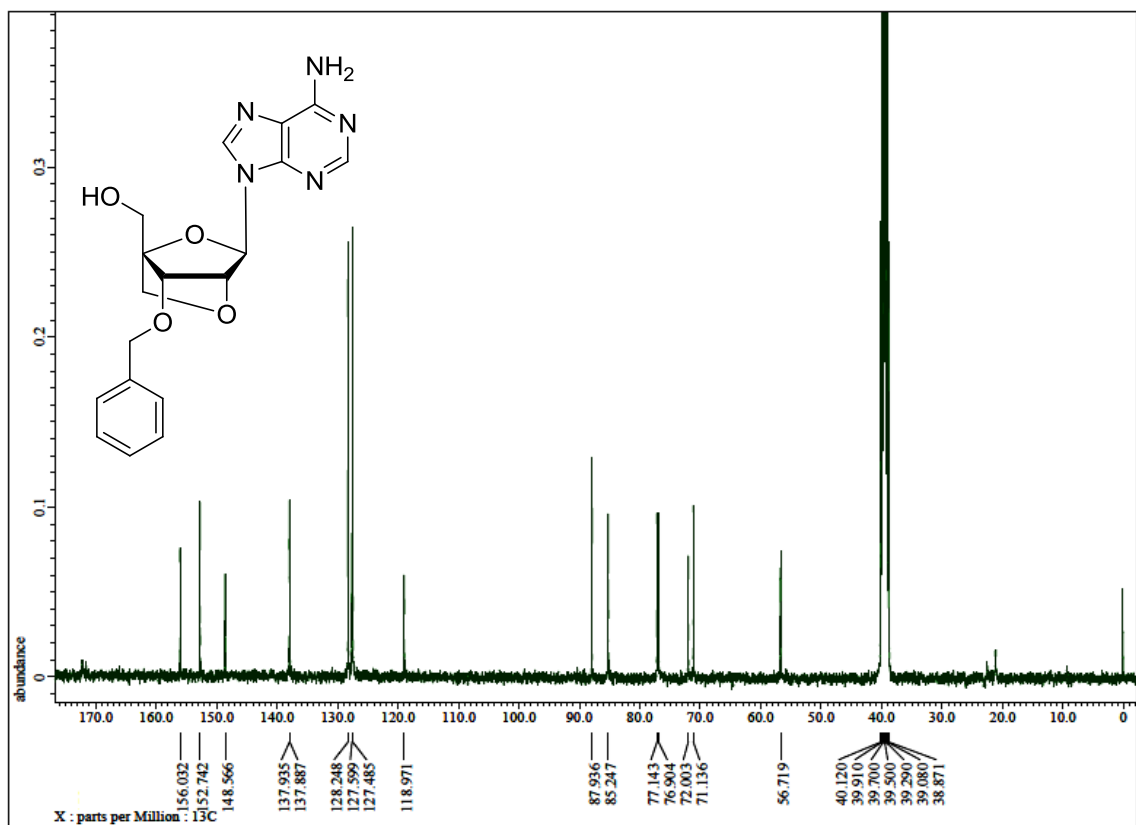
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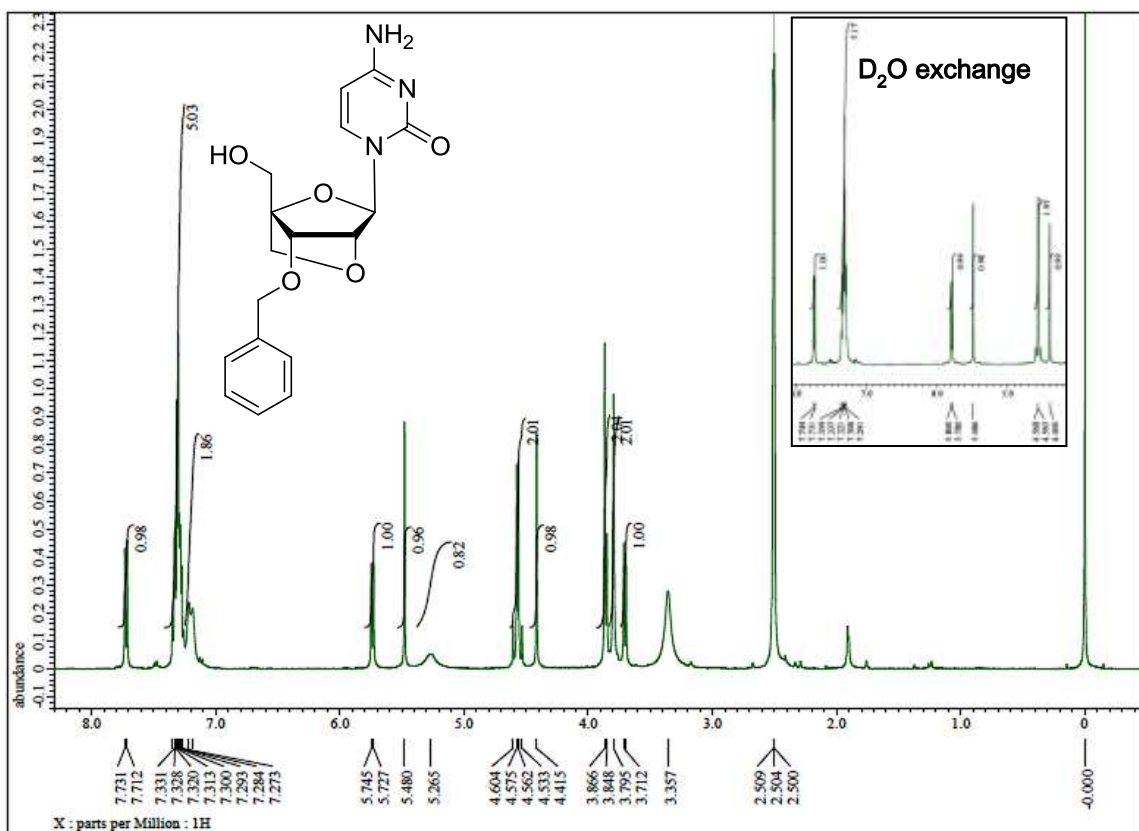
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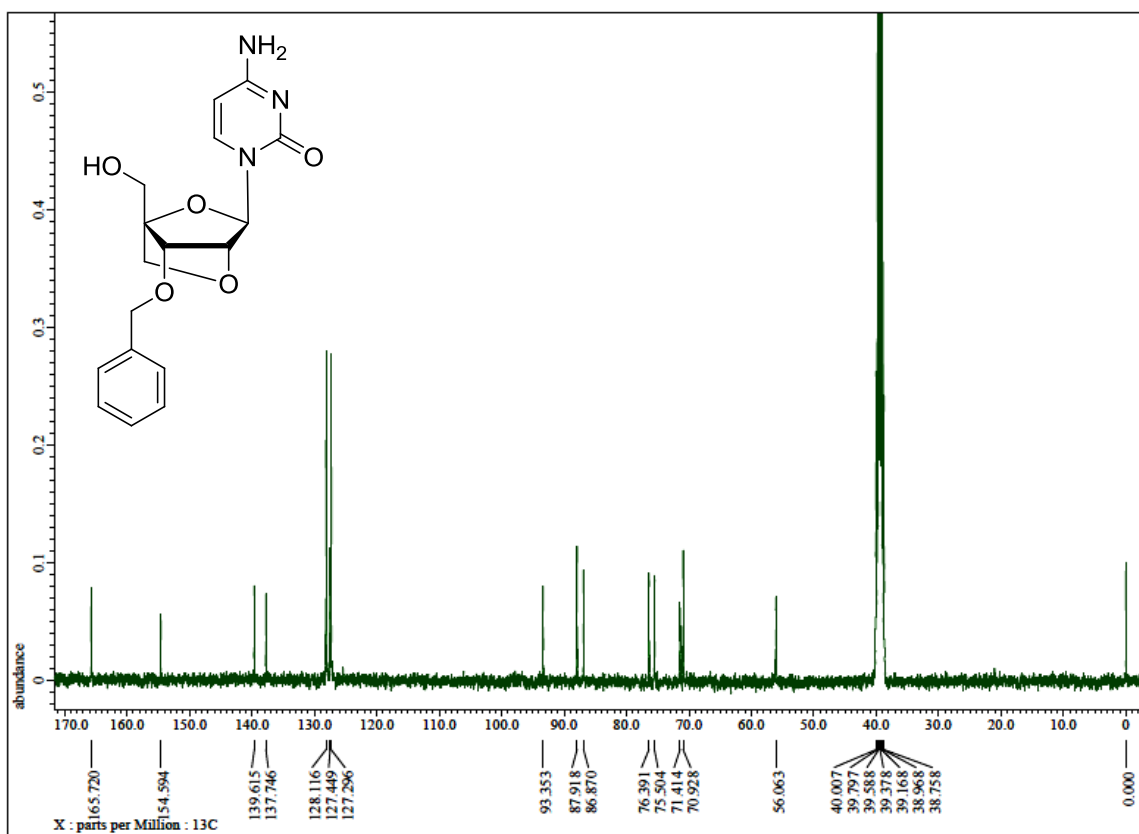
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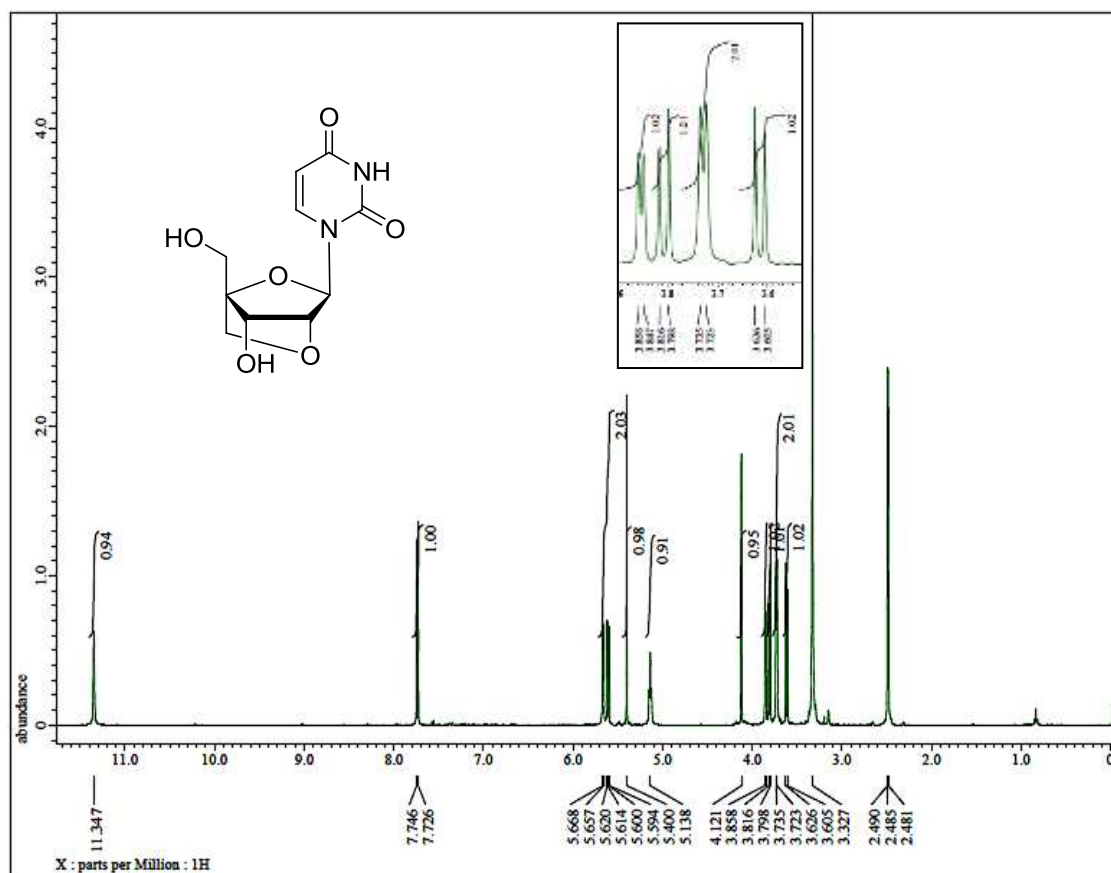
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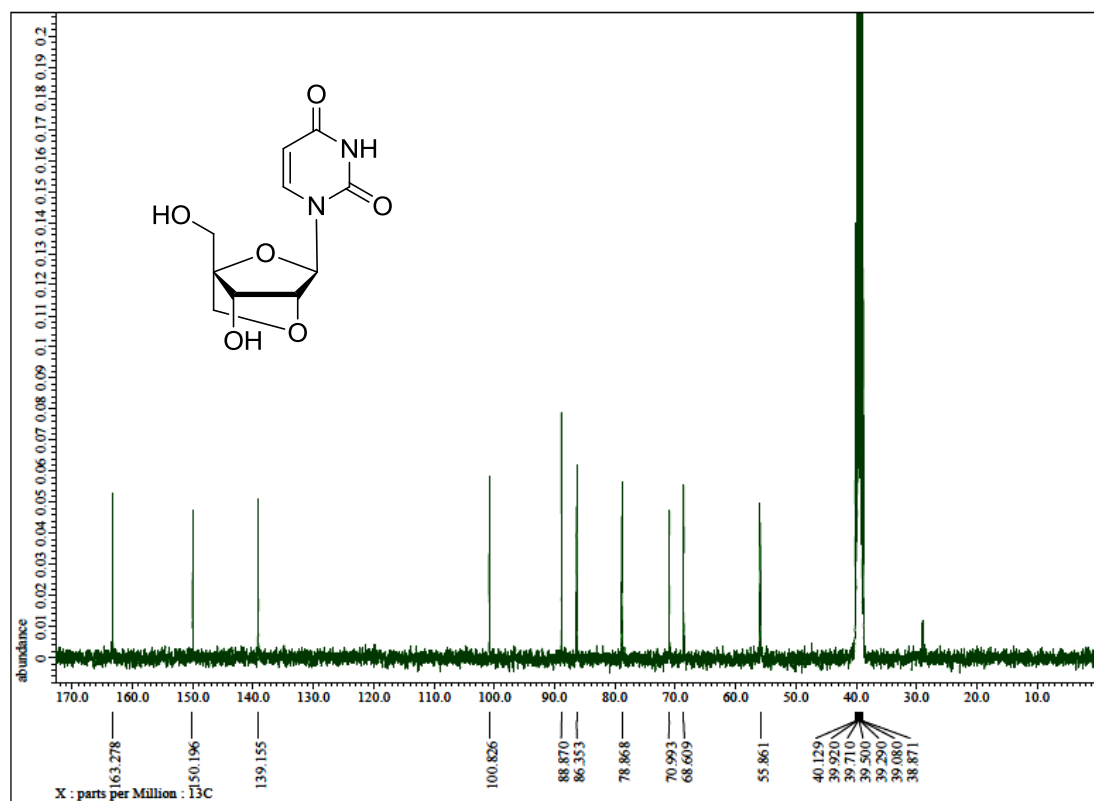
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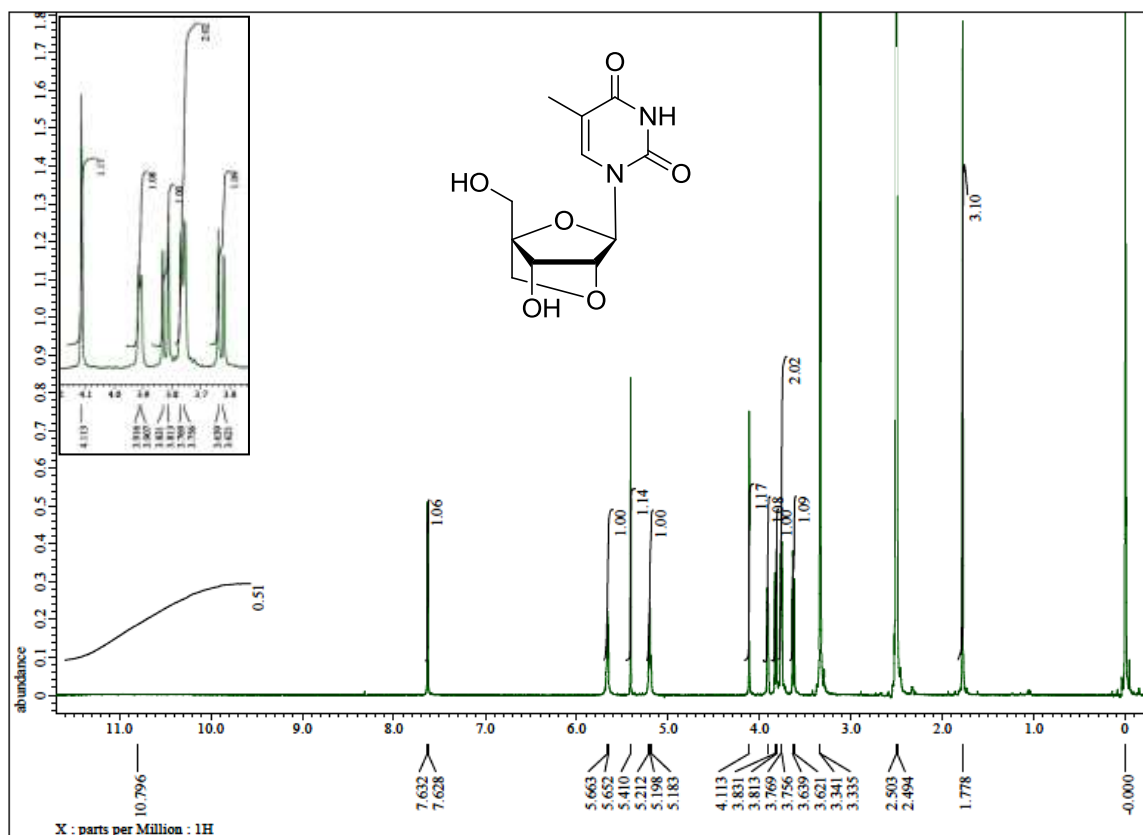
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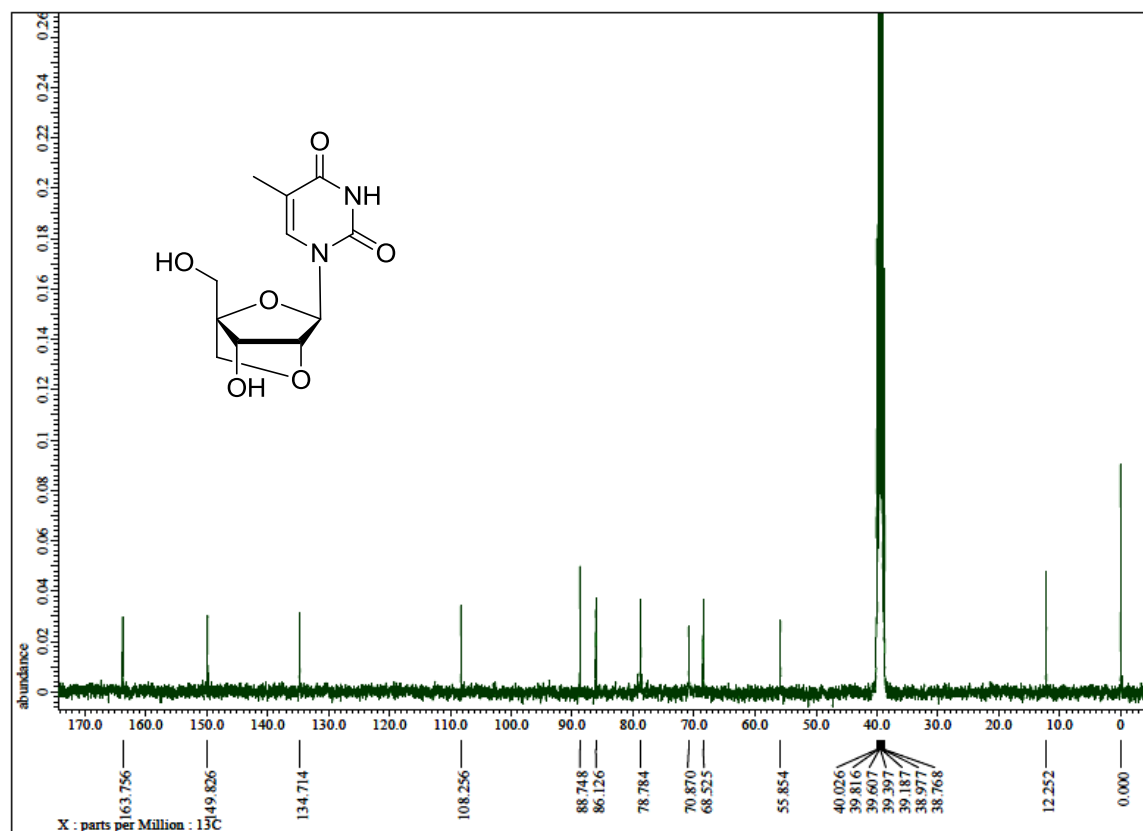
¹H NMR spectrum of compound **15a** (400 MHz, DMSO-*d*₆)



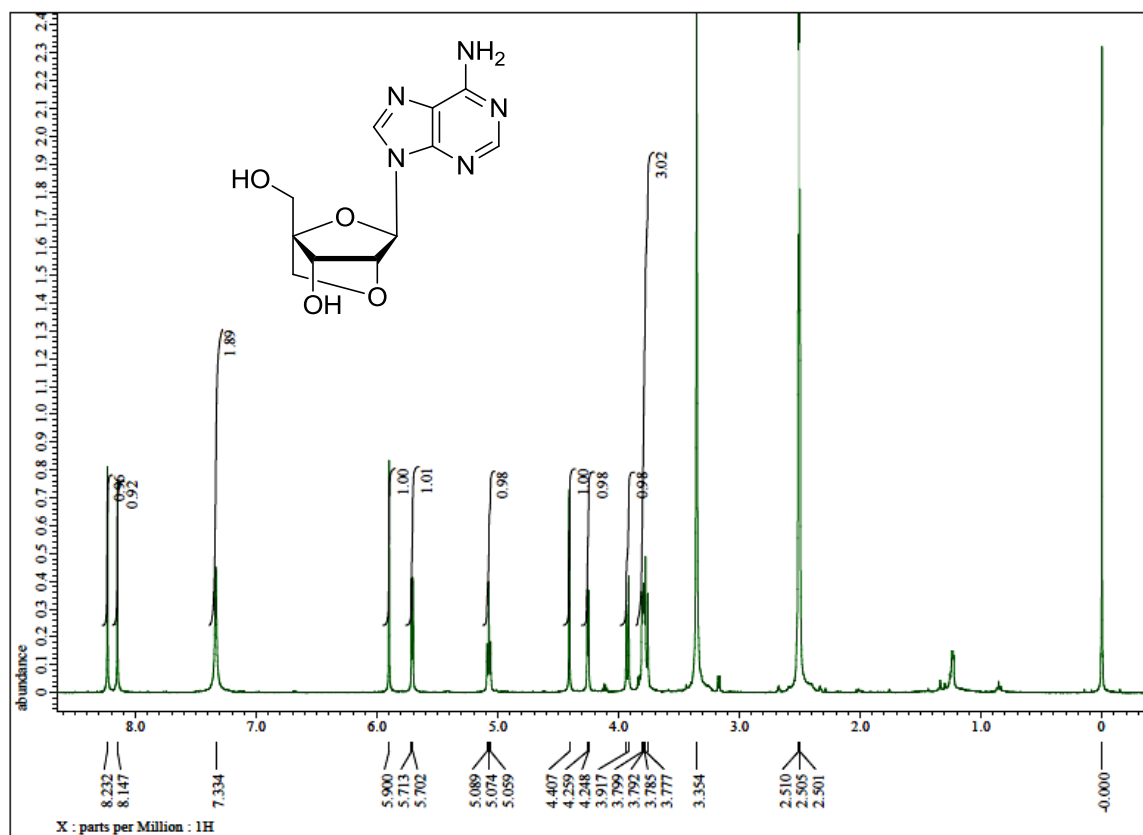
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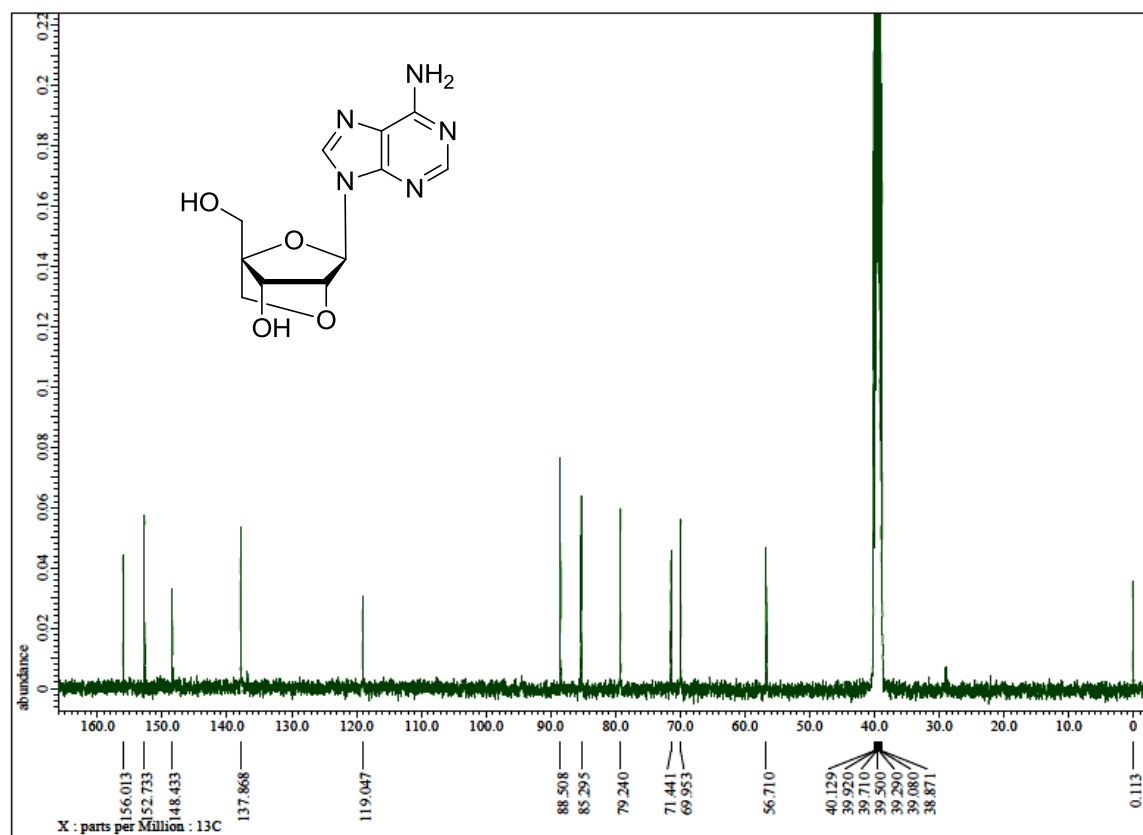
¹H NMR spectrum of compound **15b** (400 MHz, DMSO-*d*₆)



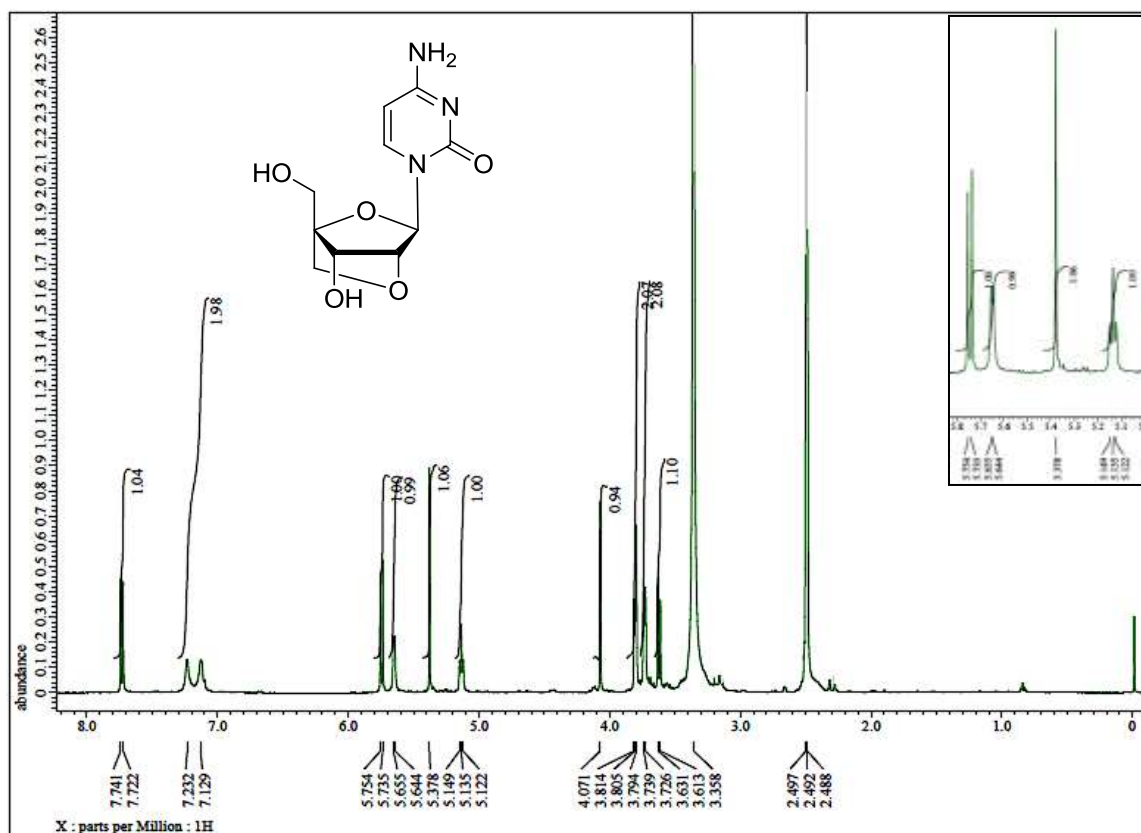
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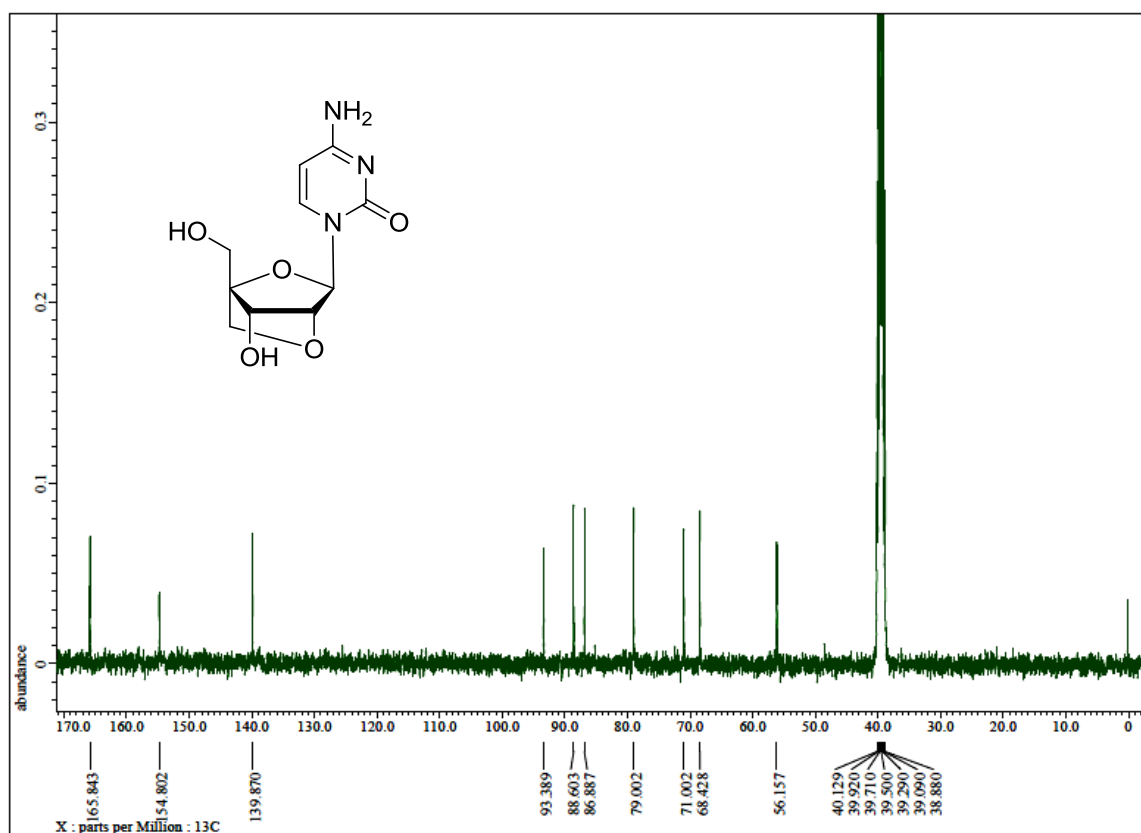
¹H NMR spectrum of compound **15c** (400 MHz, DMSO-*d*₆)



¹³C NMR spectrum of compound **15c** (100.6 MHz, DMSO-*d*₆)



¹H NMR spectrum of compound **15d** (400 MHz, DMSO-*d*₆)



¹³C NMR spectrum of compound **15d** (100.6 MHz, DMSO-*d*₆)

References:

- (1) Kumar, T. S.; Kumar, P.; Sharma, P. K.; Hrdlicka P. J. *Tetrahedron Lett.* **2008**, 49, 7168.
- (2) A. A. Koshkin, J. Fensholdt, H. M. Pfundheller and C. Lomholt, *J. Org. Chem.*, 2001, **66**, 8504.