

5'-Methylene-Triazole-Substituted-Aminoribosyl Uridines as MraY Inhibitors: Synthesis, Biological Evaluation and Molecular Modeling

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Ana Amoroso,³ Bernard Joris,³ Dominique Mengin-Lecreulx,² Sandrine Calvet-Vitale^{1,*} and
Christine Gravier-Pelletier^{1,*}

ELECTRONIC SUPPLEMENTARY INFORMATION

¹H and ¹³C Spectra, HPLC purity of compounds **27a-n**

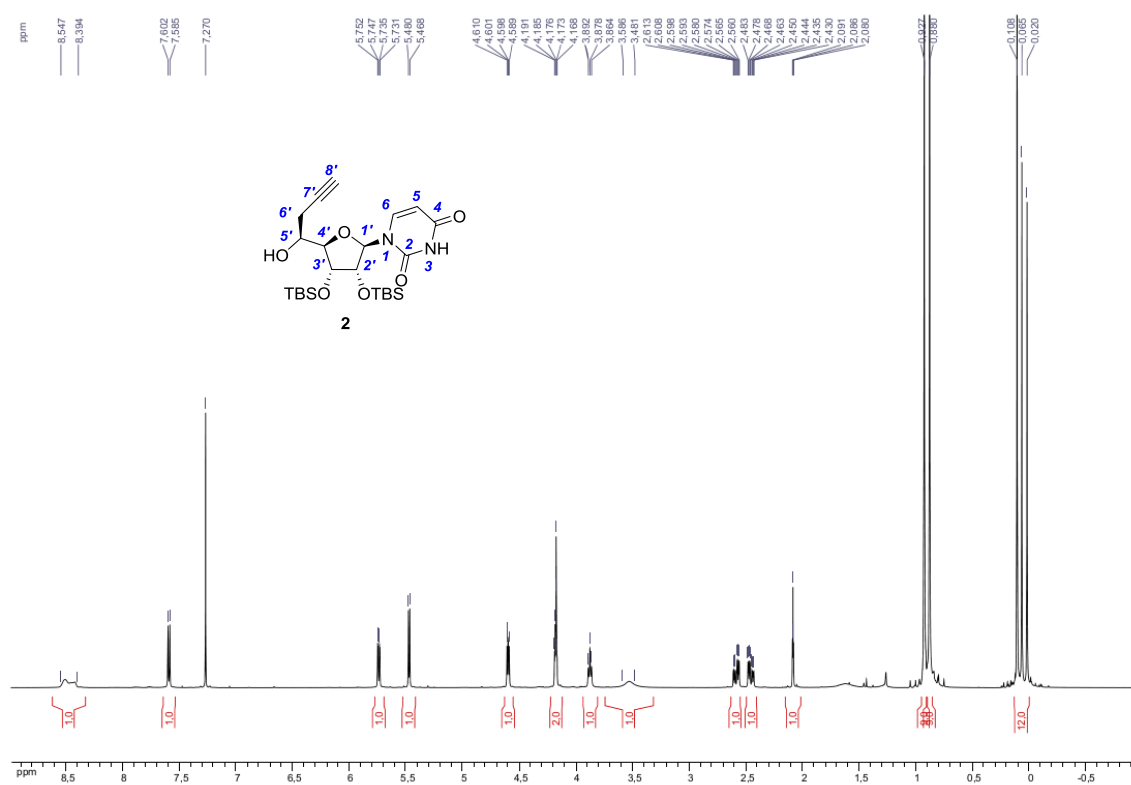
Compounds 2, 5, 6, 9-11, 13-22	1
Compounds 7b, d, f	16
Compounds 8b, d, f-h	19
Compounds 23a-h	24
Compounds 24a-h	32
Compounds 25a-h	40
Compounds 26a-h	48
Compounds 28, 29, 32-34	56
HPLC purity of compounds 27a-n .	61

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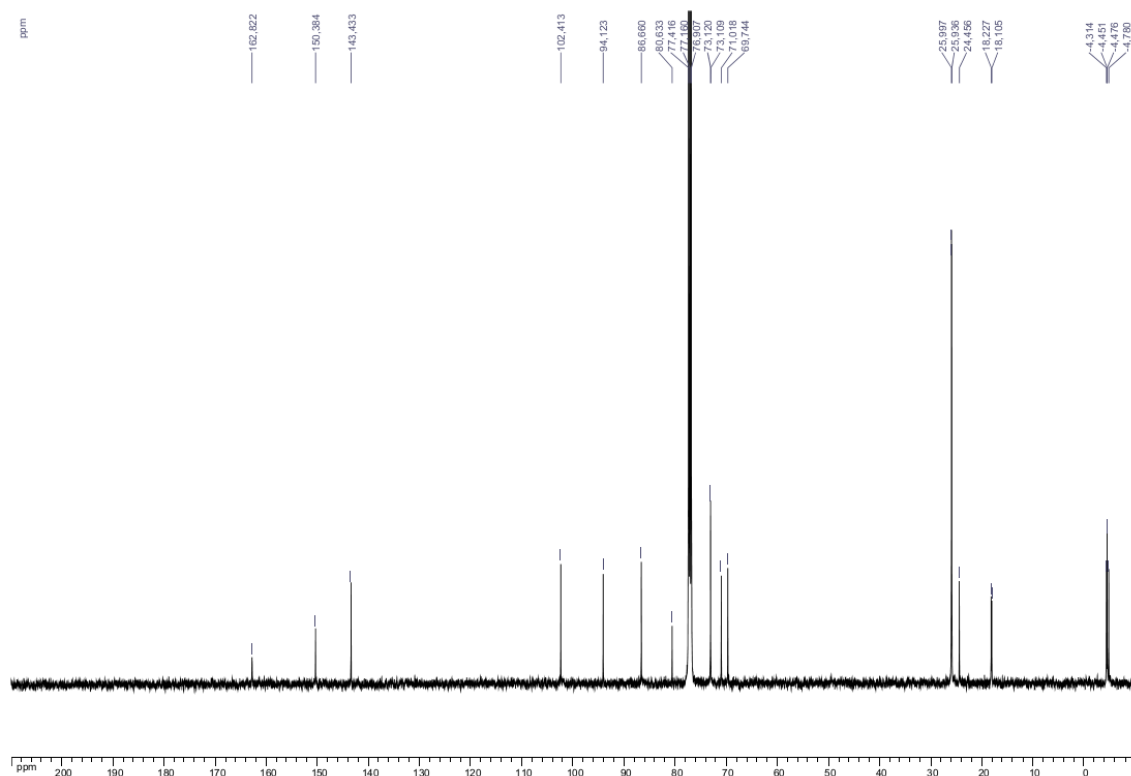
² Institute for Integrative Biology of the Cell (I2BC), CNRS, Université Paris Sud, CEA, F-91405, Orsay, France.

³ Unité de Physiologie et Génétique Bactériennes, Centre d'Ingénierie des Protéines, Département des Sciences de la Vie, Université de Liège, Sart Tilman, B4000 - Liège 1- Belgique.

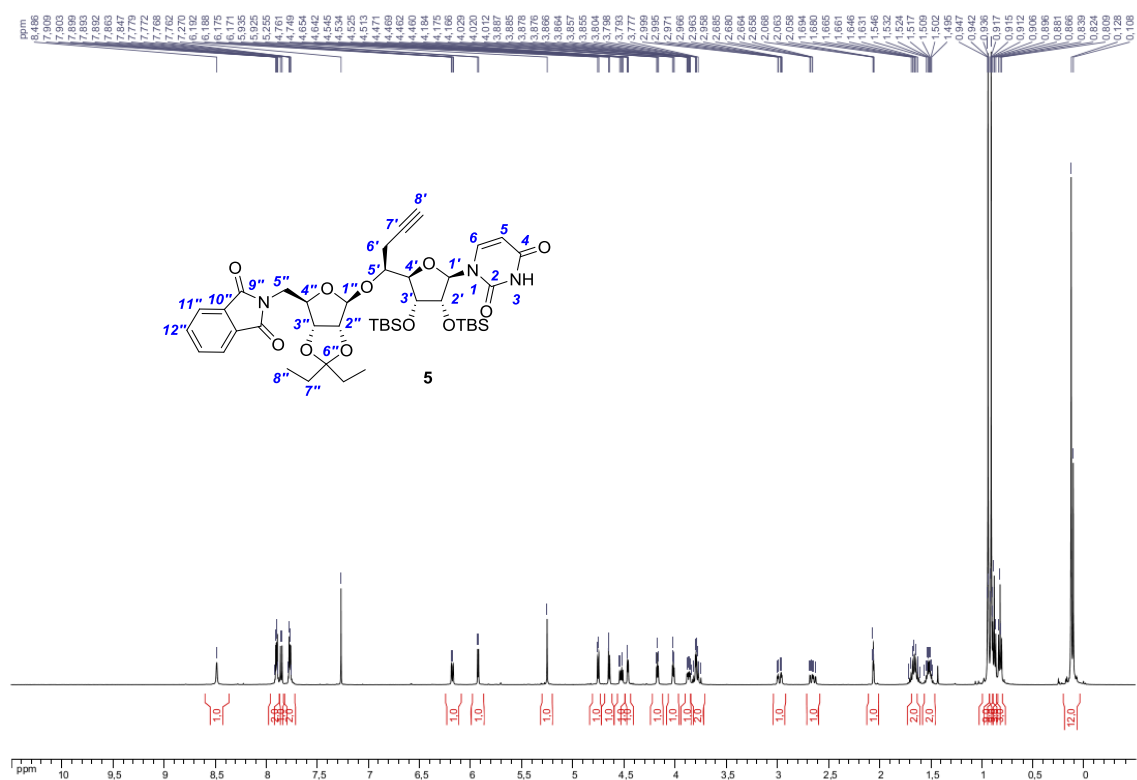
^1H NMR, 500 MHz (CDCl_3), compound **2**



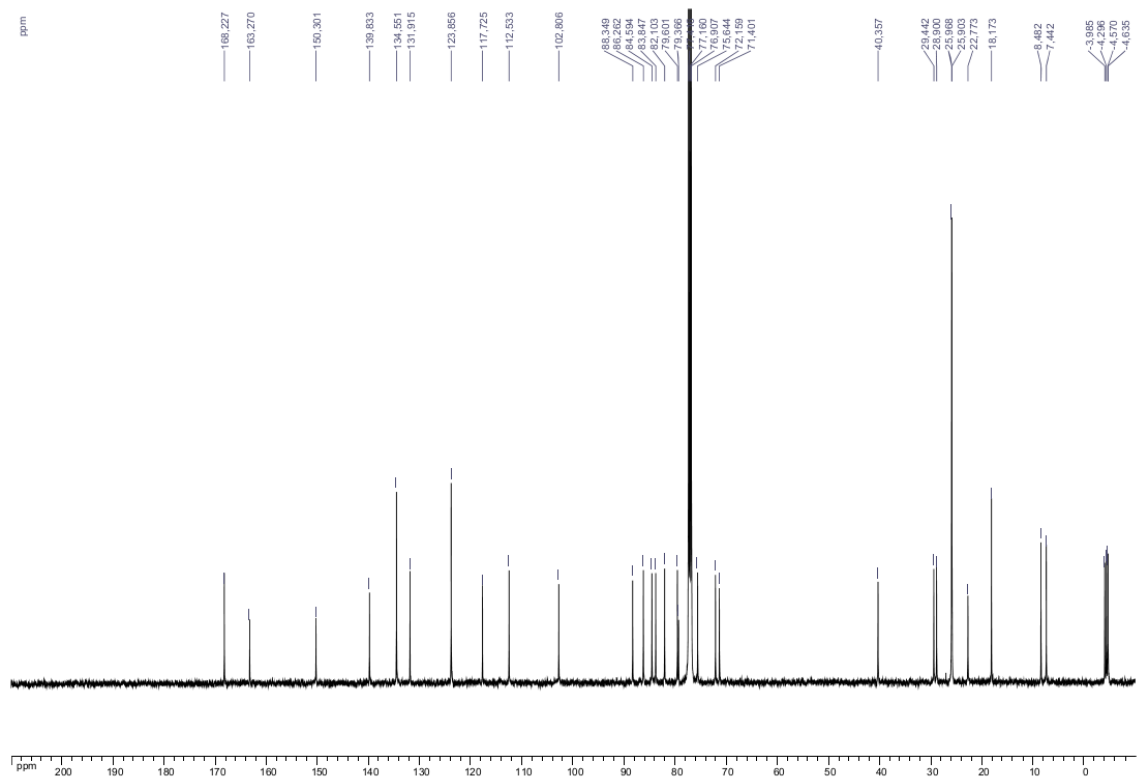
^{13}C NMR, 125 MHz (CDCl_3)



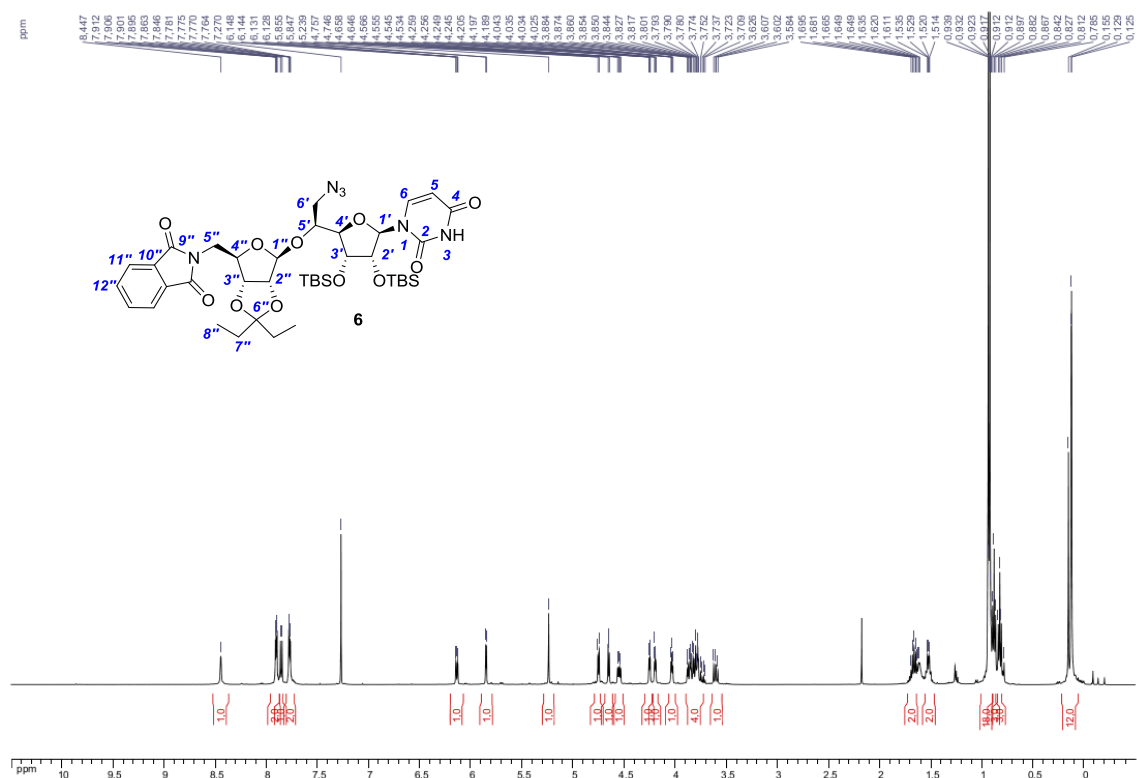
^1H NMR, 500 MHz (CDCl_3), compound **5**



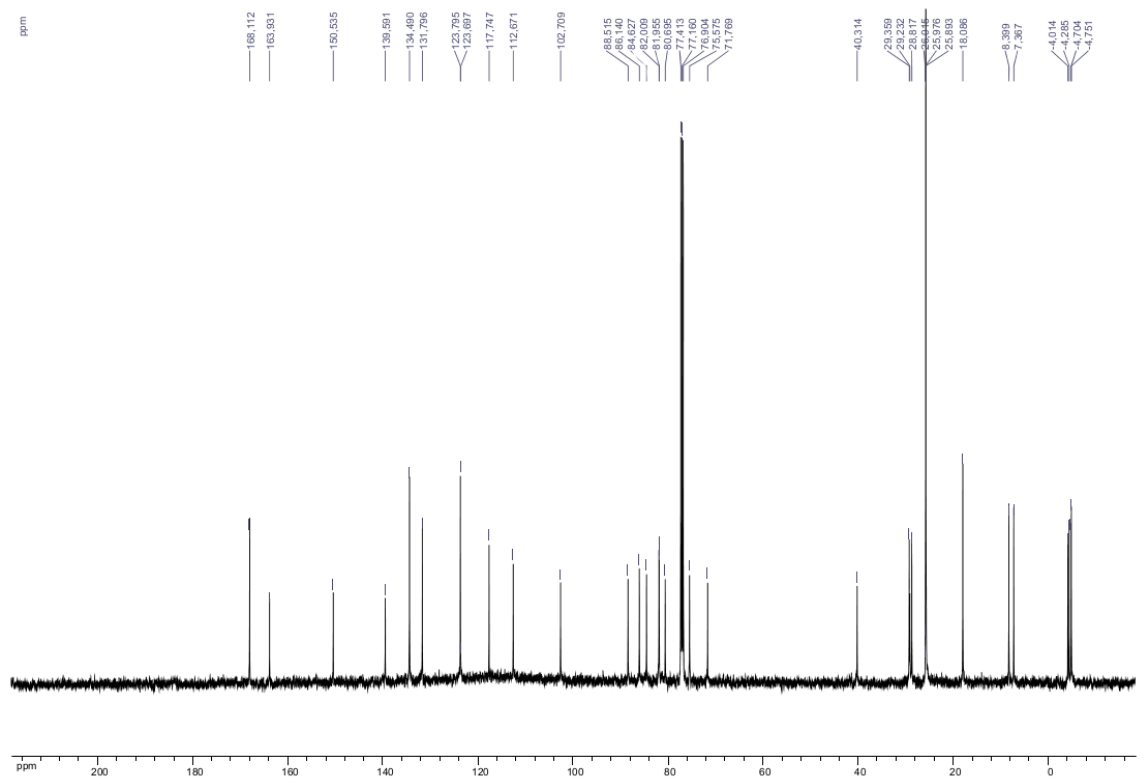
^{13}C NMR, 125 MHz (CDCl_3)



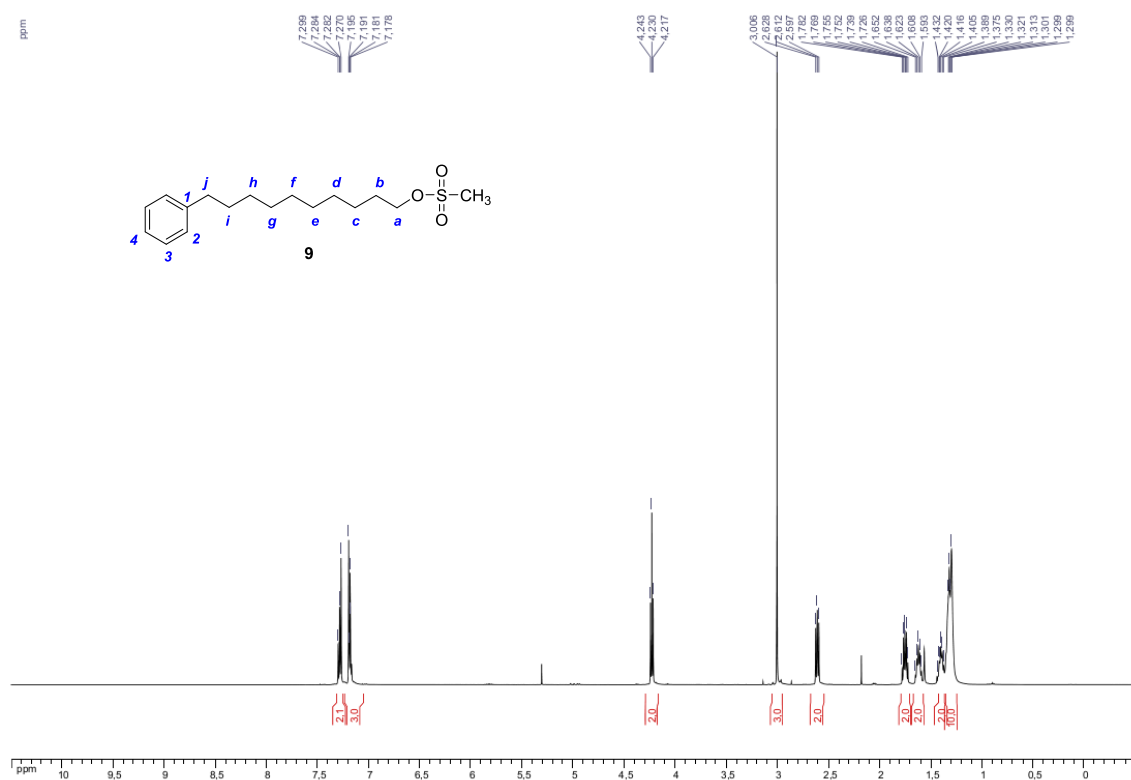
^1H NMR, 500 MHz (CDCl_3), compound **6**



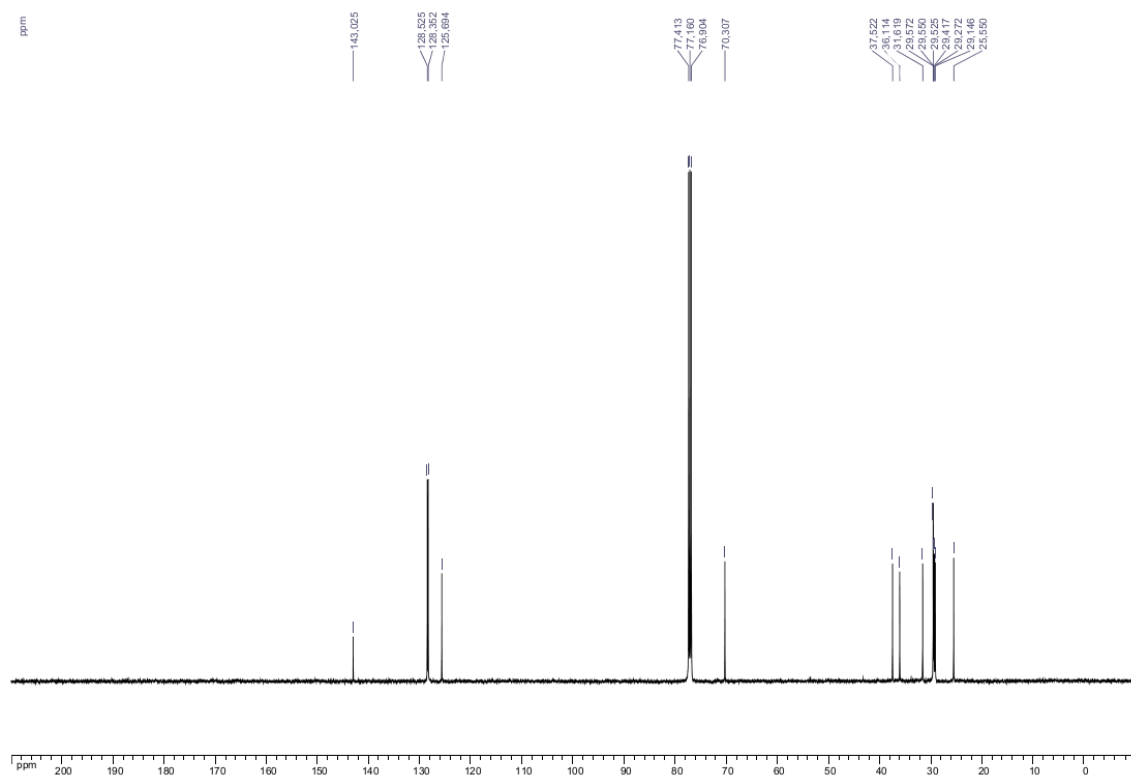
^{13}C NMR, 125 MHz (CDCl_3)

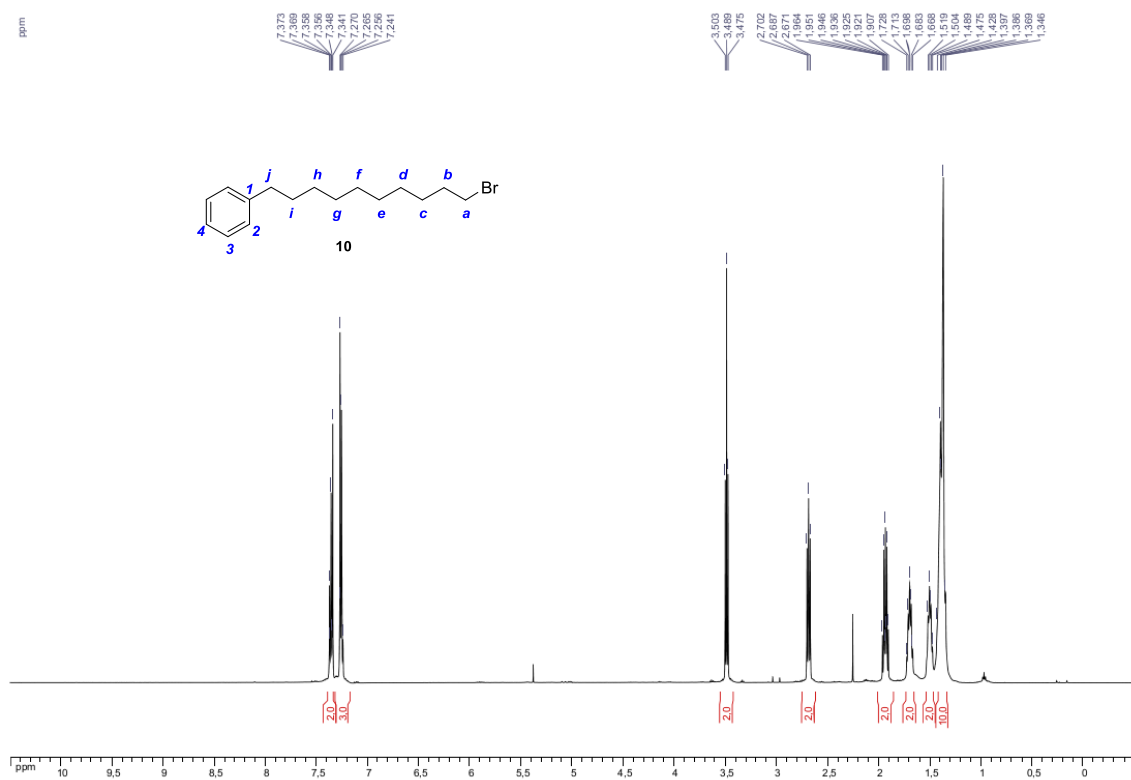
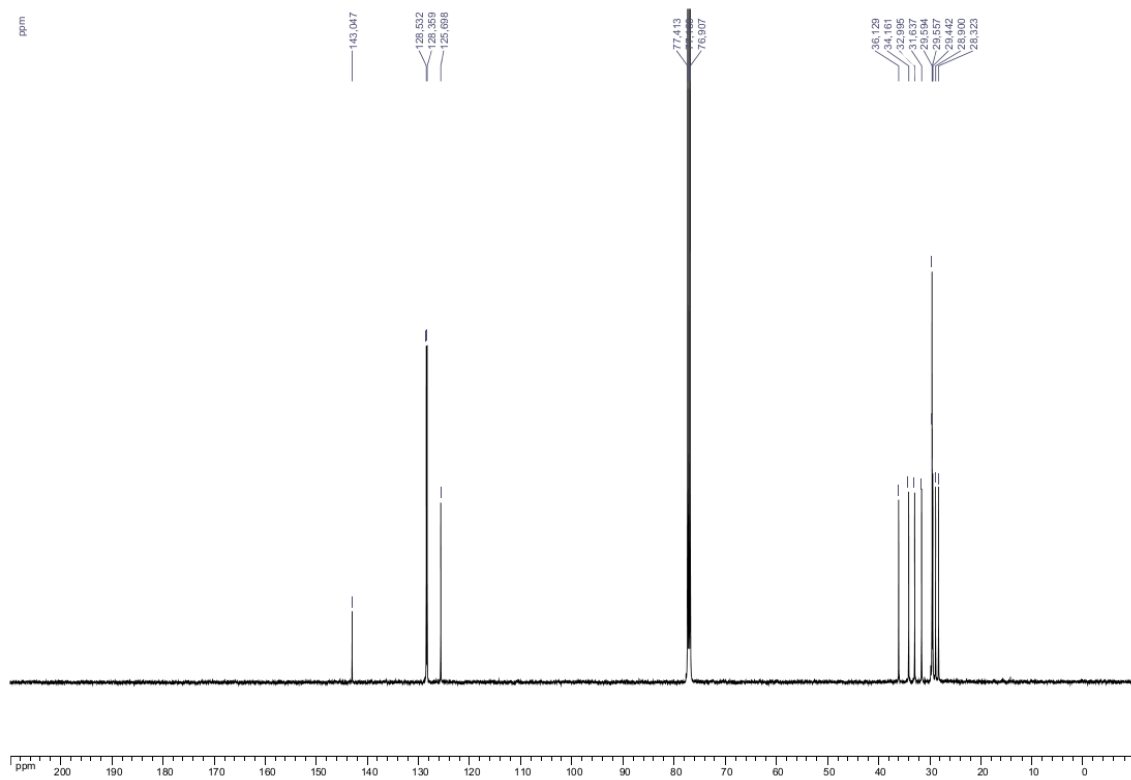


¹H NMR, 500 MHz (CDCl₃), compound **9**

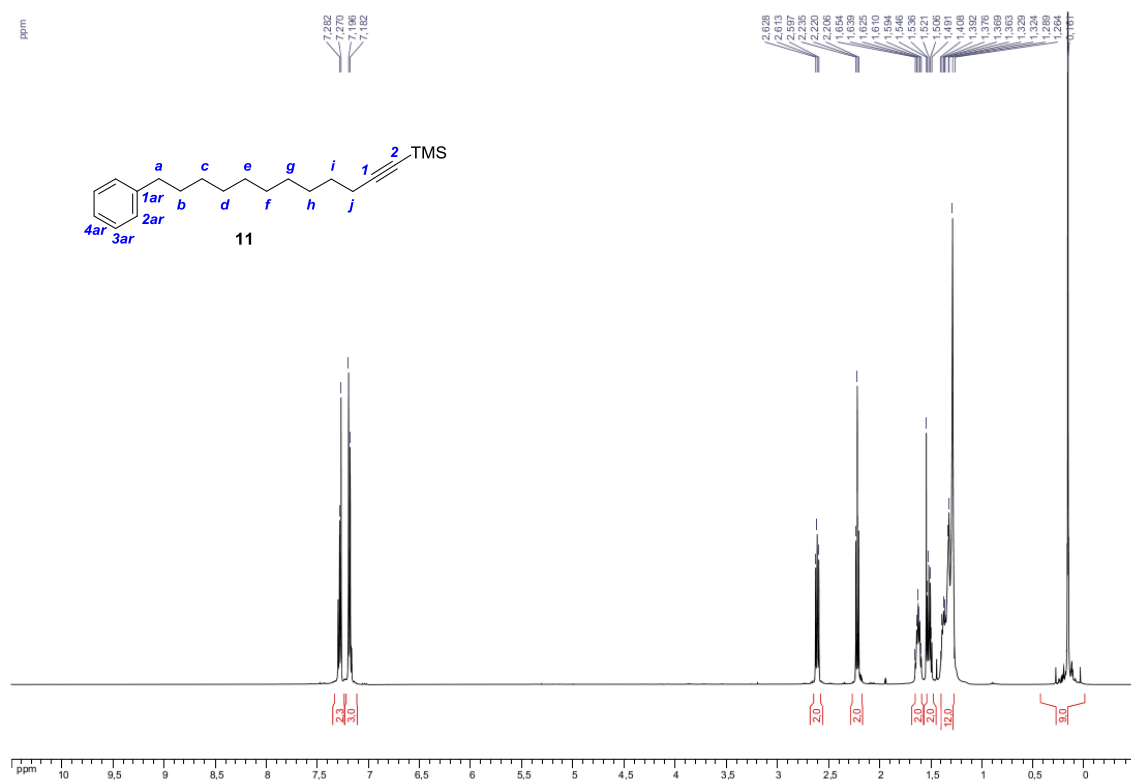


¹³C NMR, 125 MHz (CDCl₃)

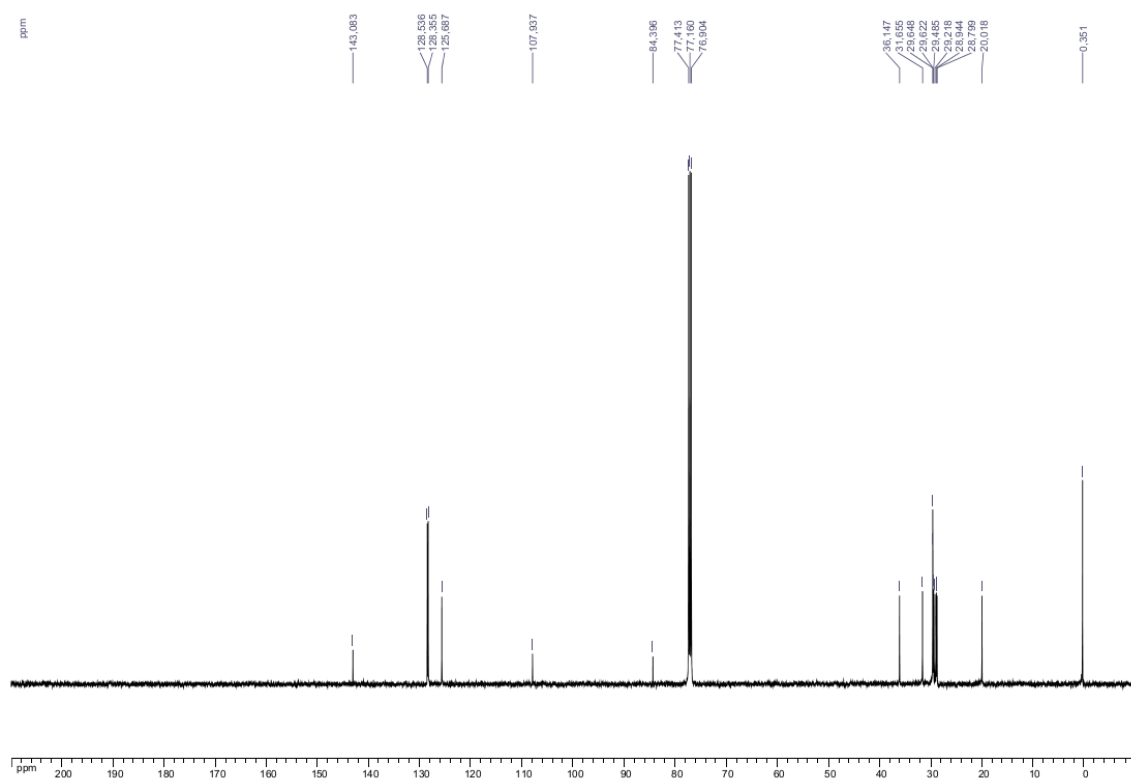


¹H NMR, 500 MHz (CDCl₃), compound **10** ^{13}C NMR, 125 MHz (CDCl_3)

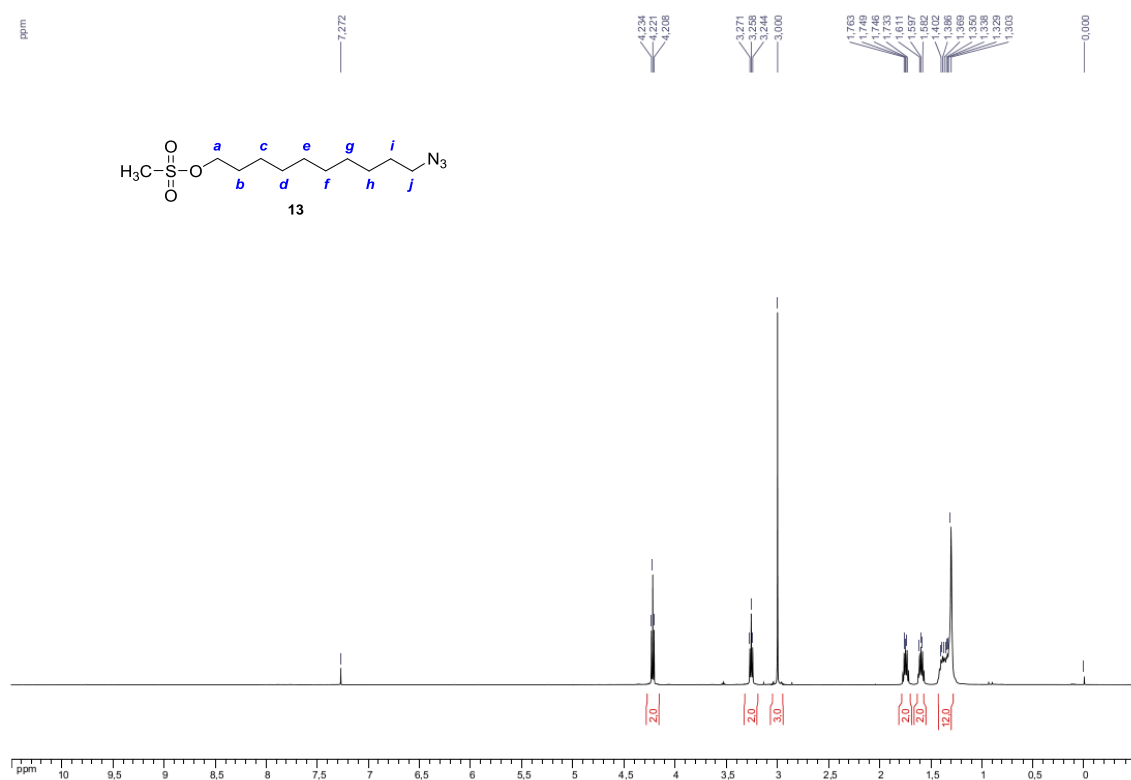
^1H NMR, 500 MHz (CDCl_3), compound **11**



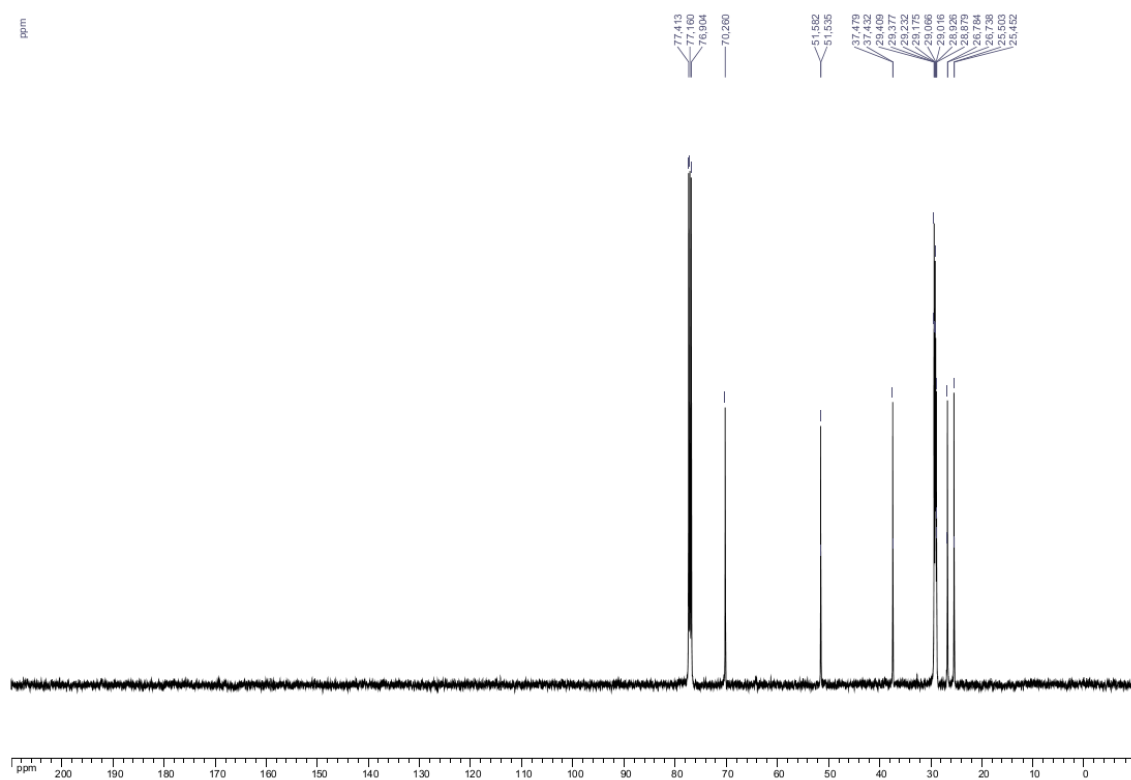
^{13}C NMR, 125 MHz (CDCl_3)



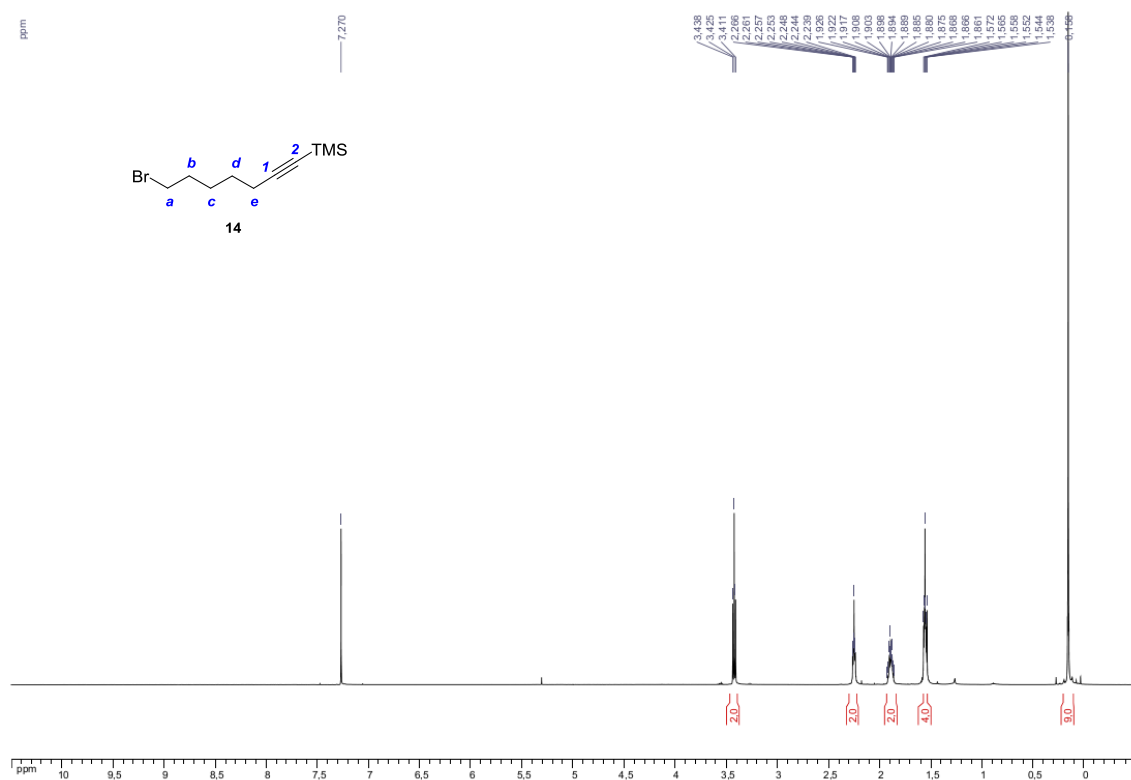
^1H NMR, 500 MHz (CDCl_3), compound **13**



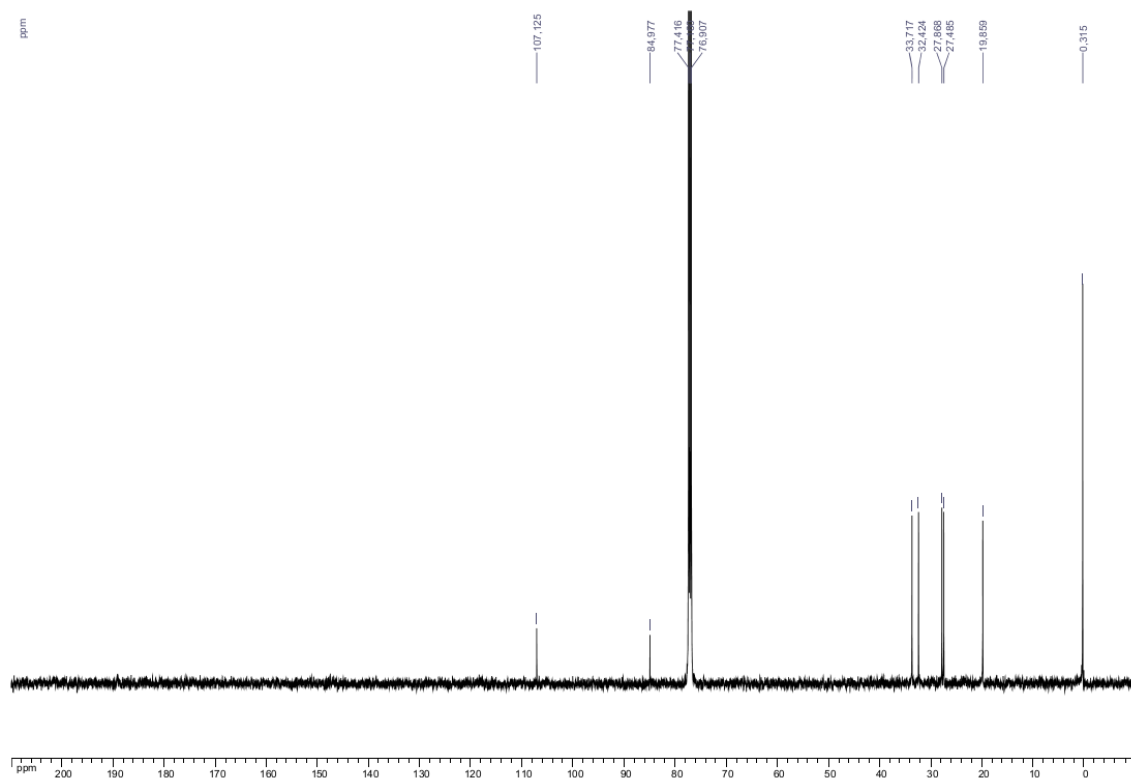
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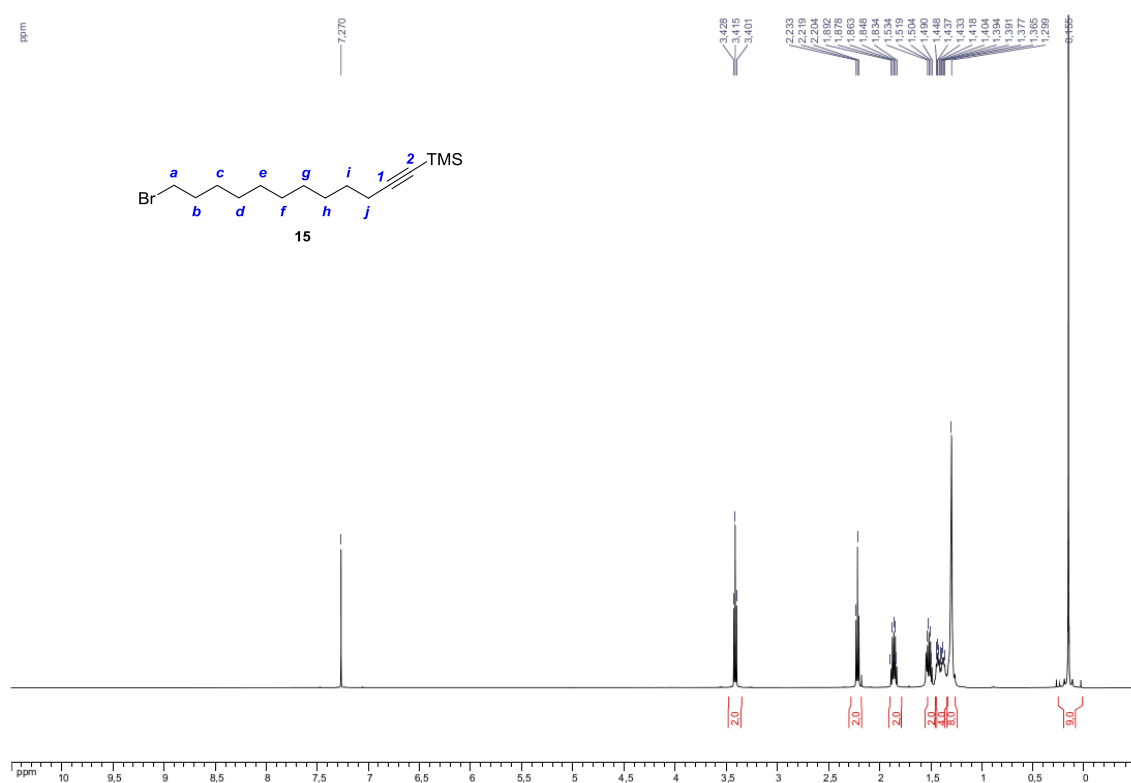
^1H NMR, 500 MHz (CDCl_3), compound **14**



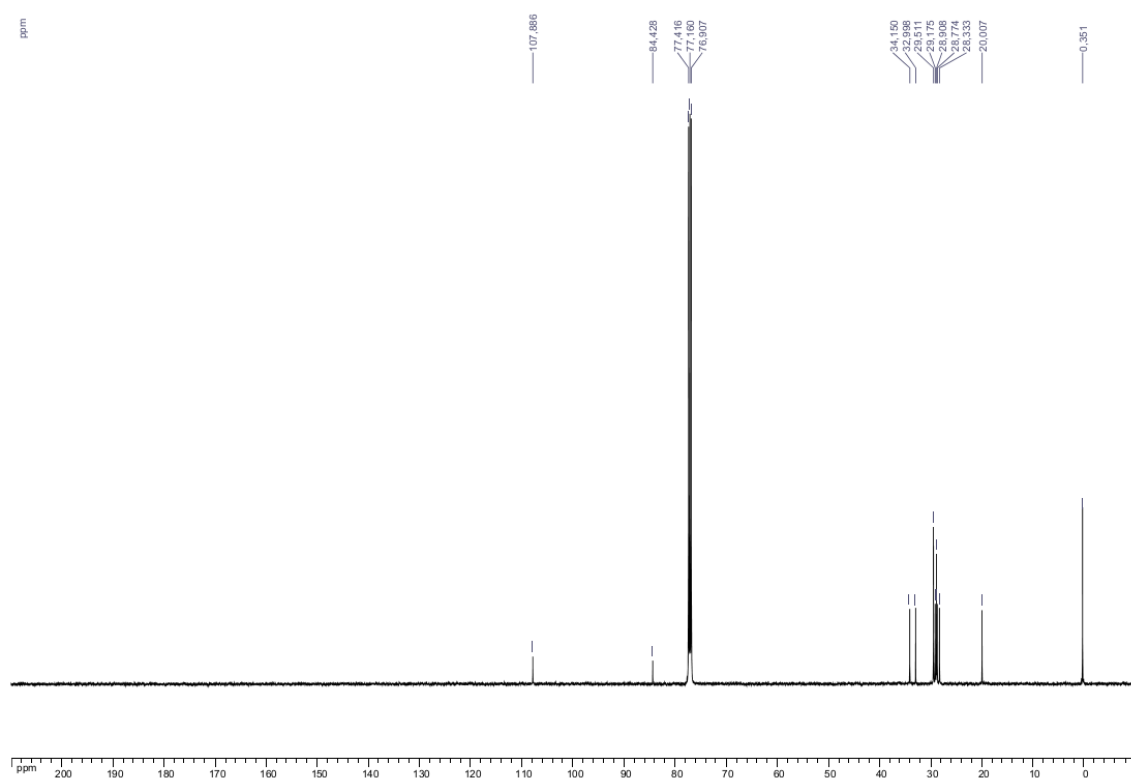
^{13}C NMR, 125 MHz (CDCl_3)



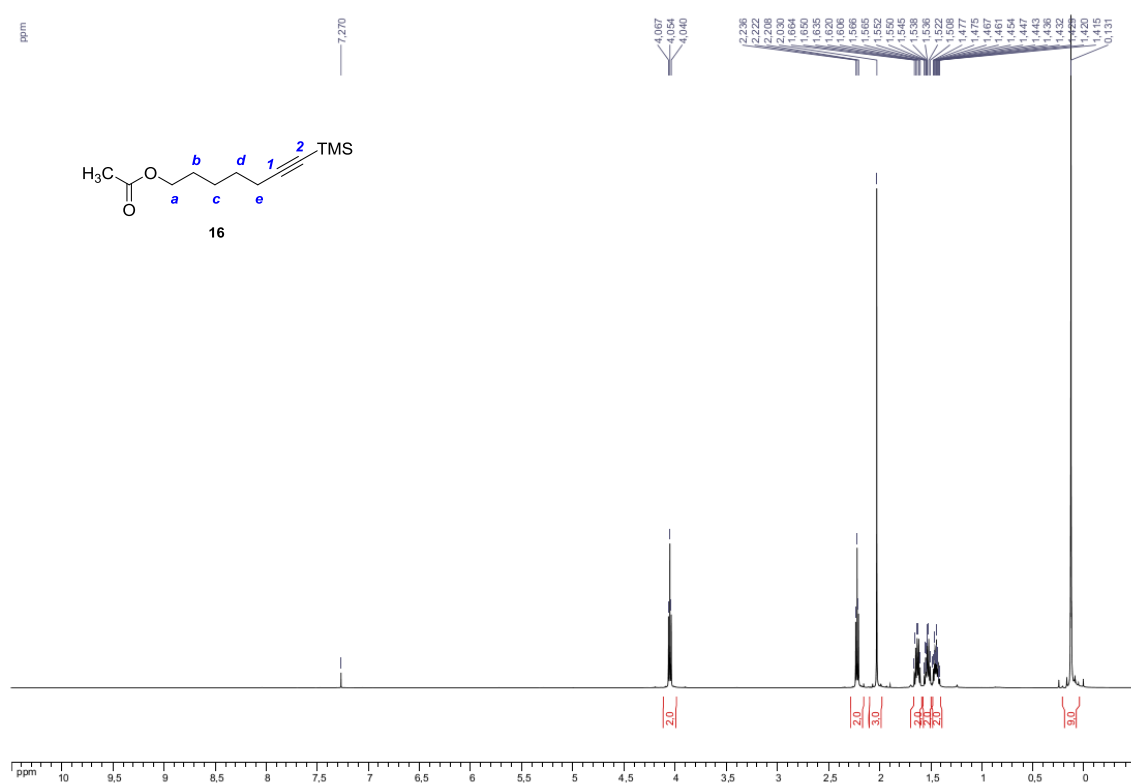
^1H NMR, 500 MHz (CDCl_3), compound **15**



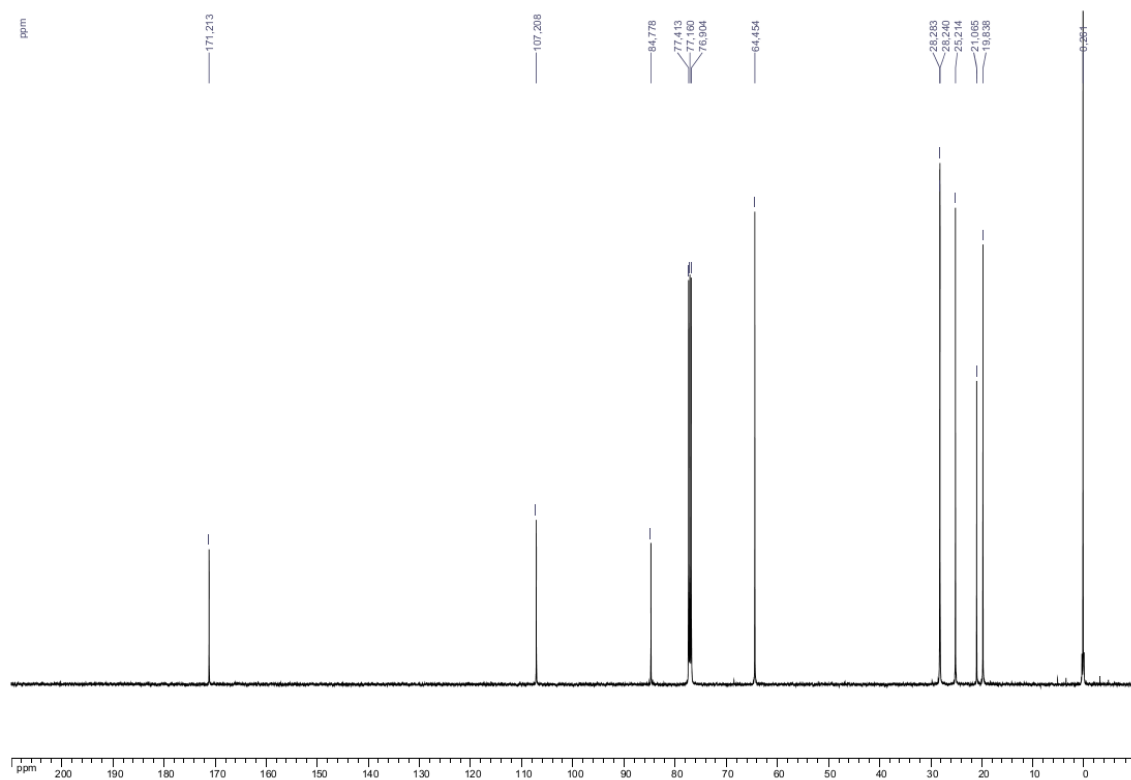
^{13}C NMR, 125 MHz (CDCl_3)



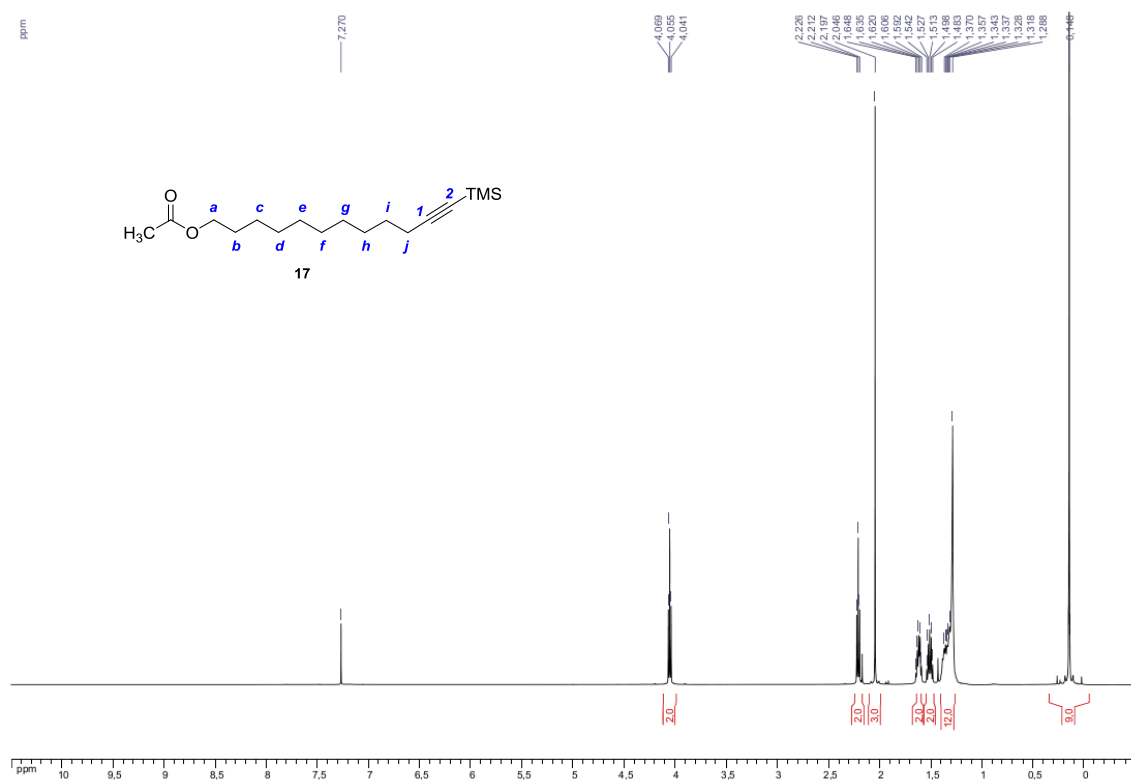
^1H NMR, 500 MHz (CDCl_3), compound **16**



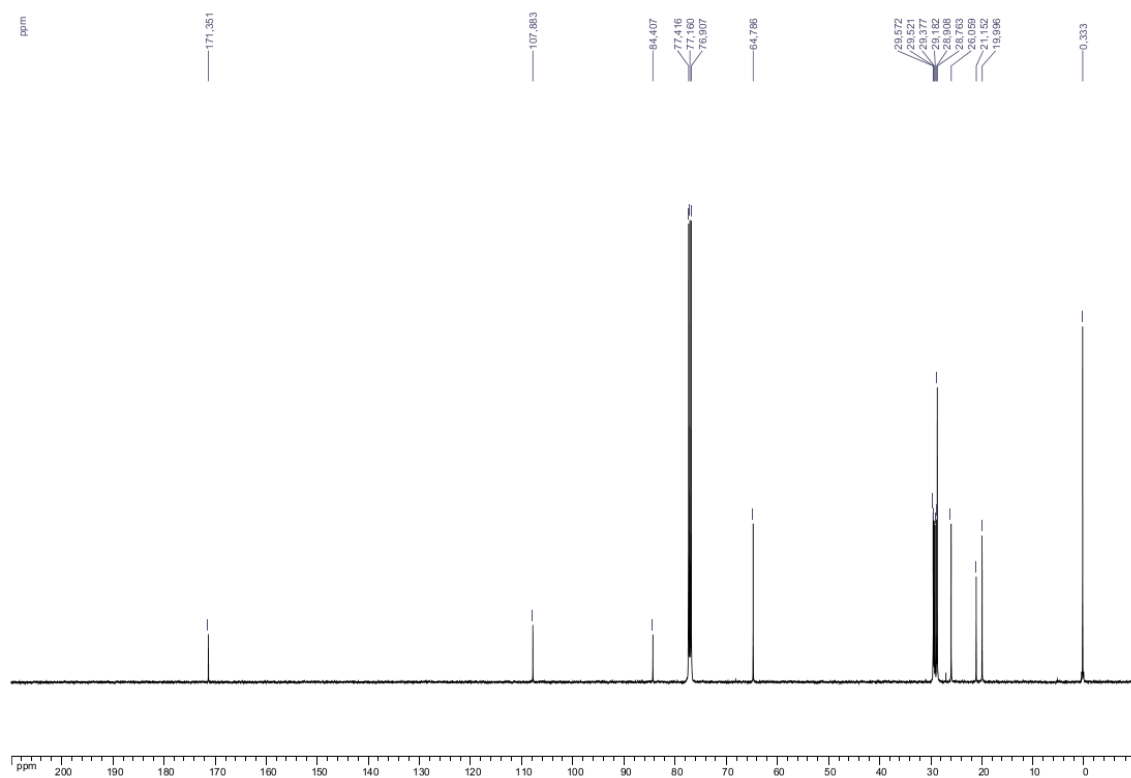
^{13}C NMR, 125 MHz (CDCl_3)



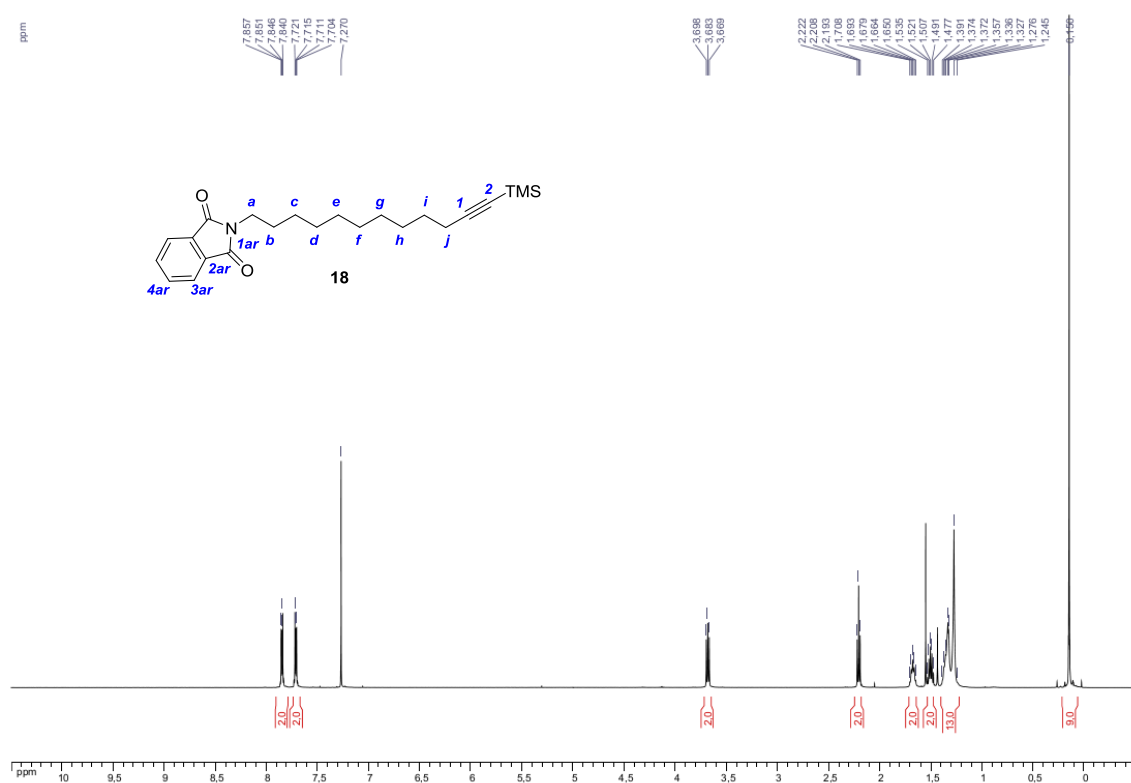
^1H NMR, 500 MHz (CDCl_3), compound **17**



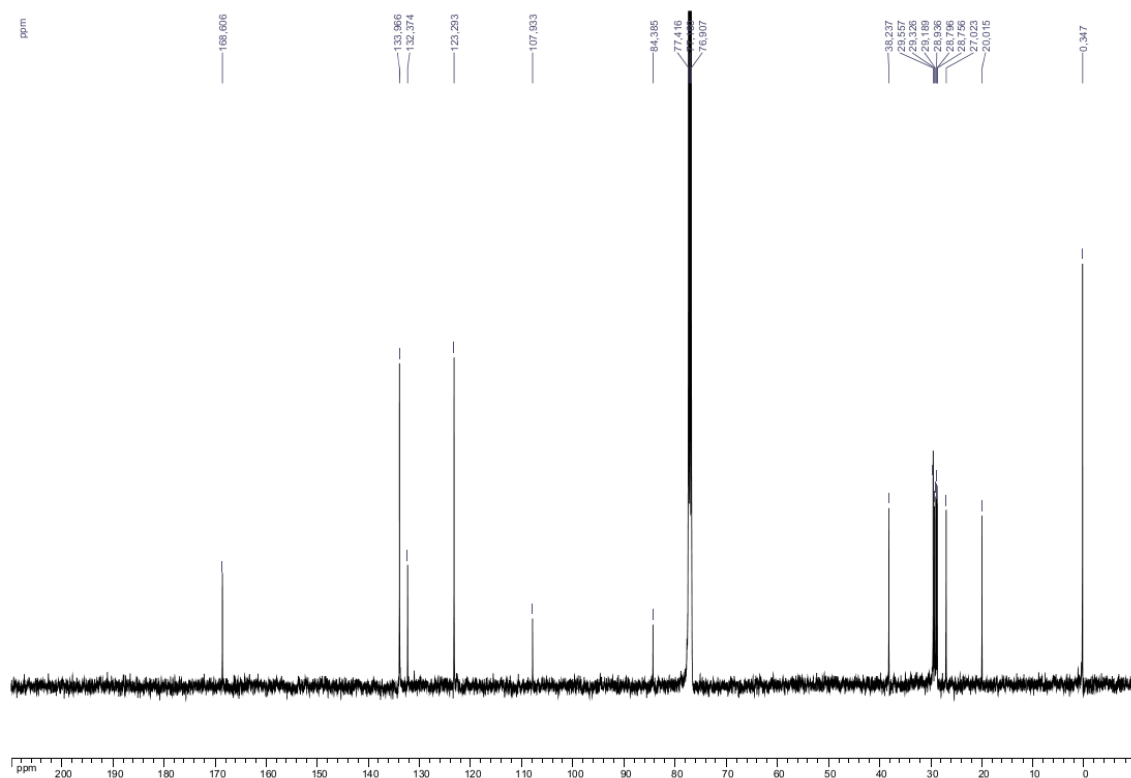
^{13}C NMR, 125 MHz (CDCl_3)

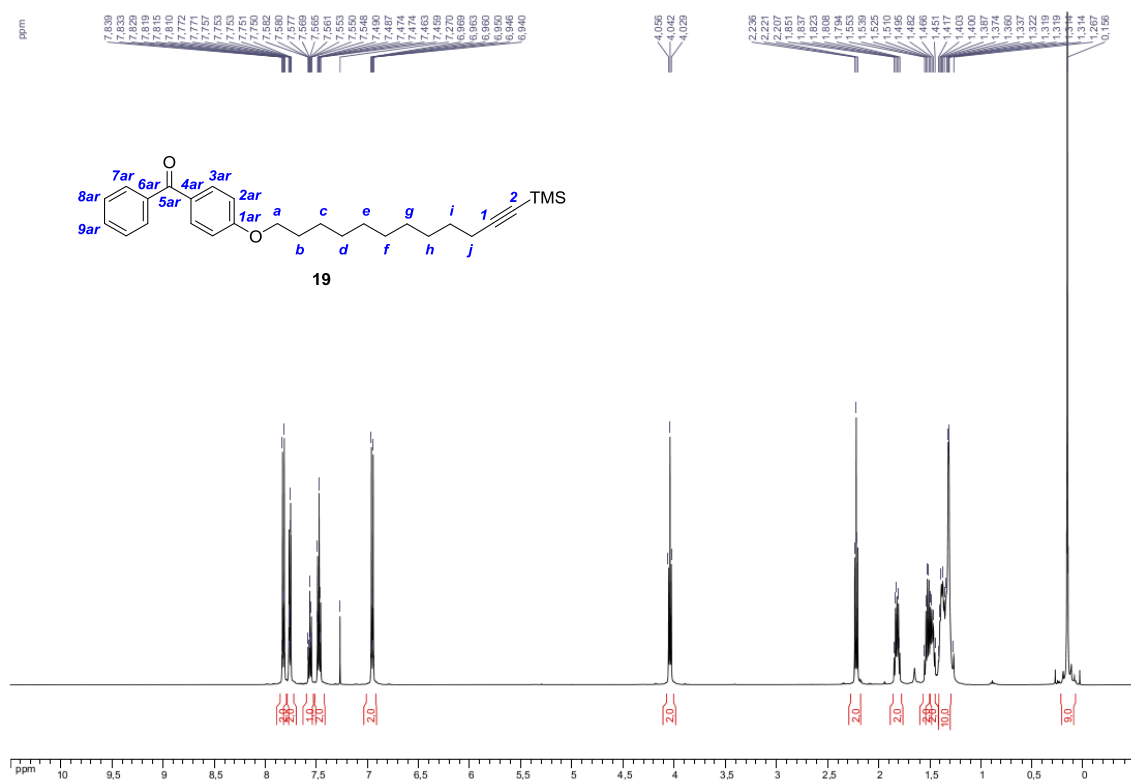
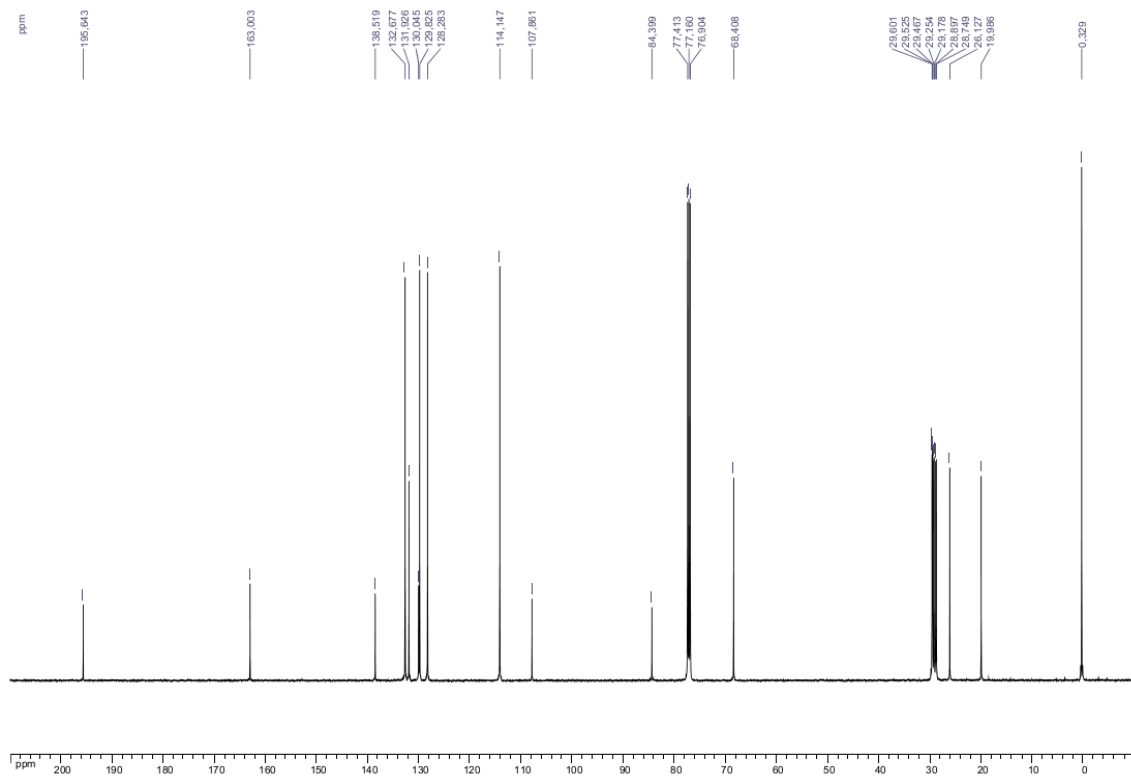


^1H NMR, 500 MHz (CDCl_3), compound **18**

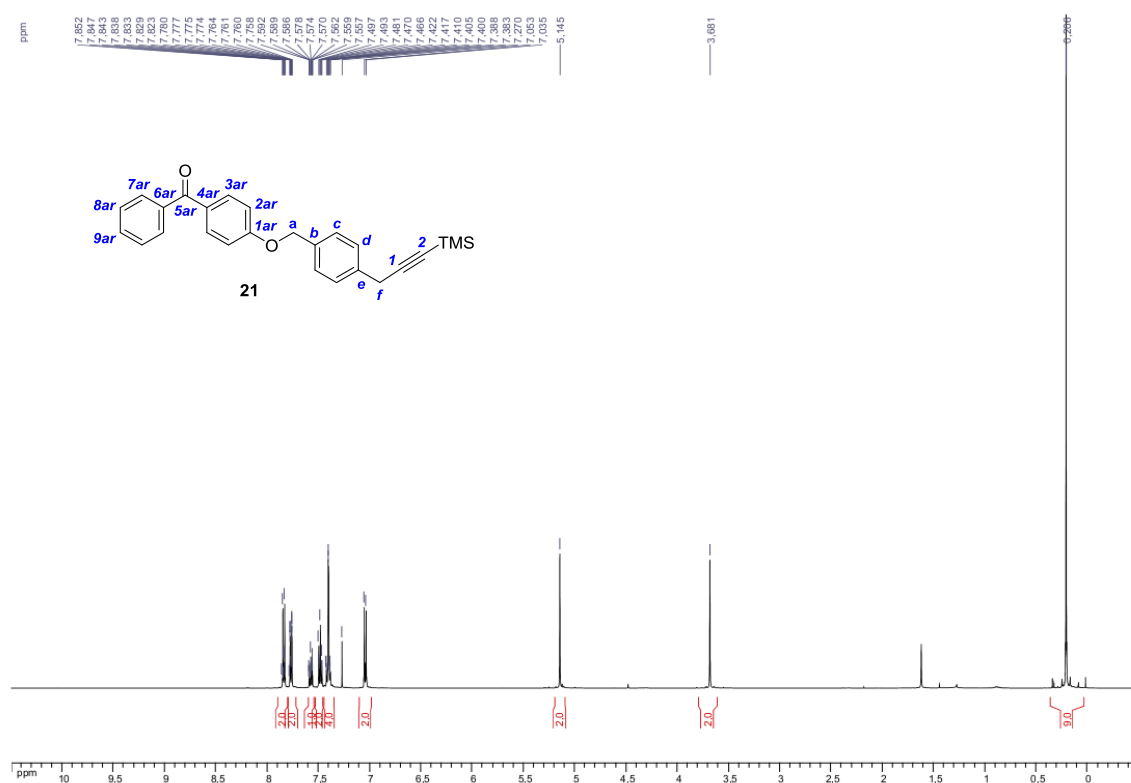


^{13}C NMR, 125 MHz (CDCl_3)

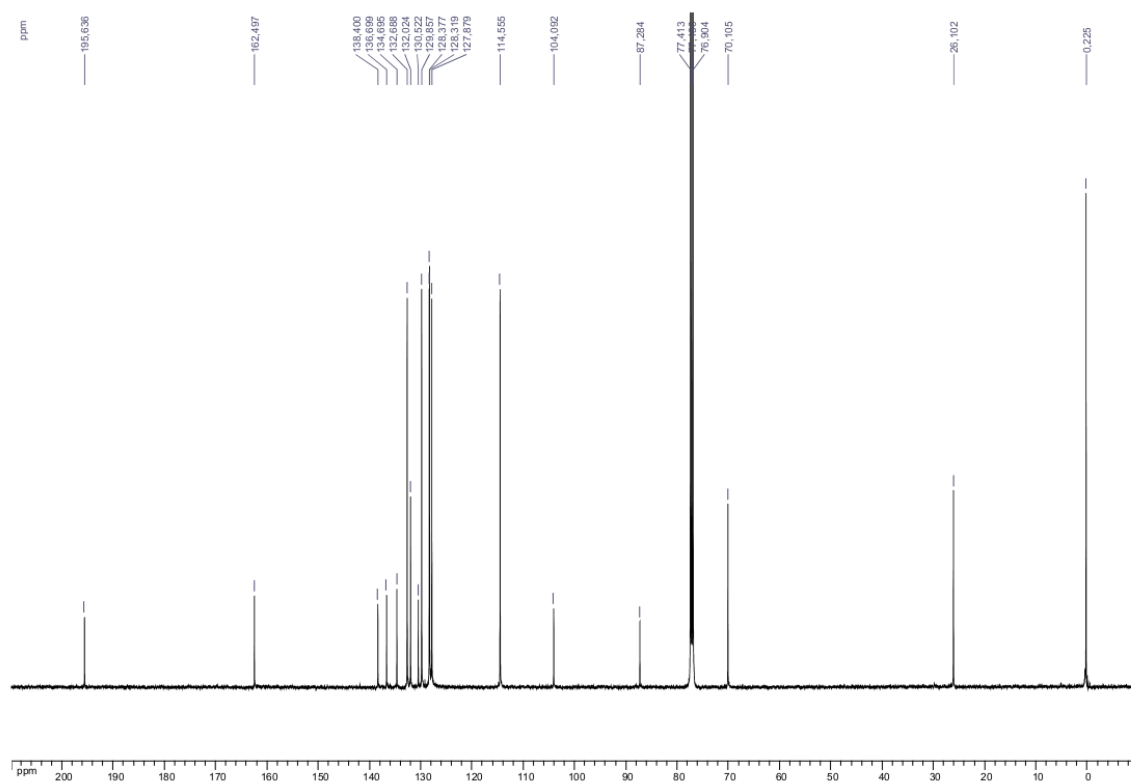


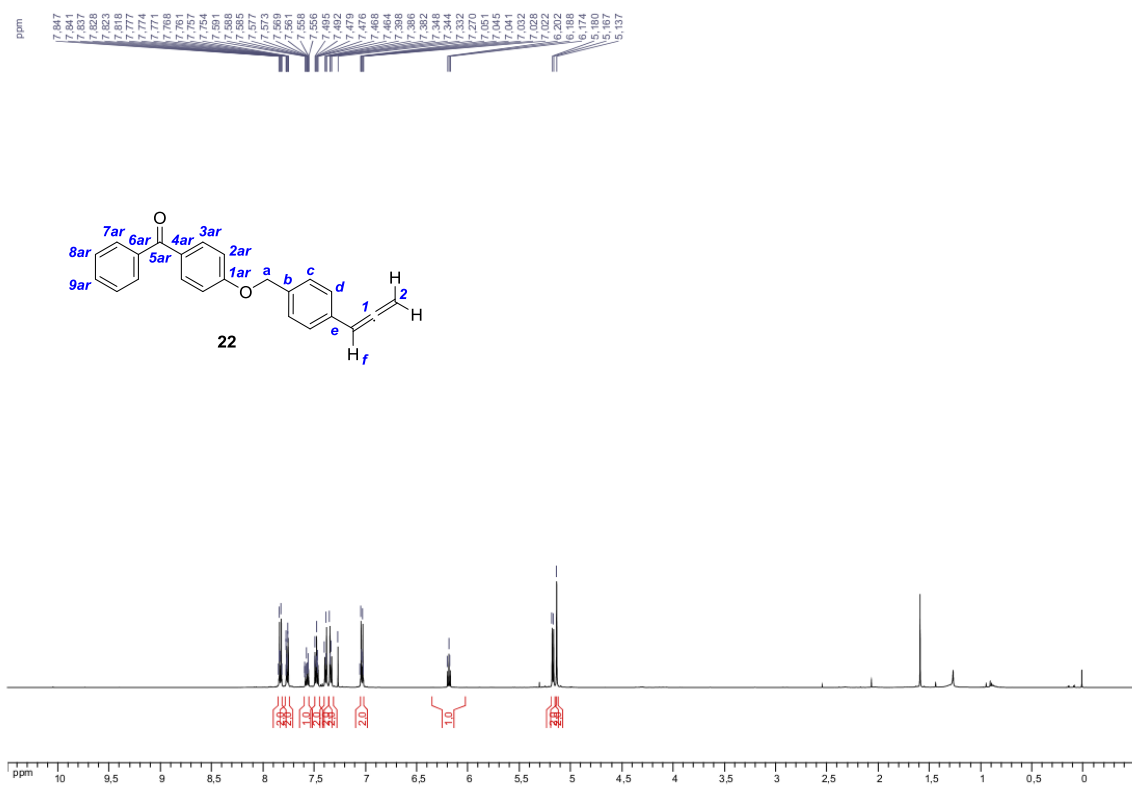
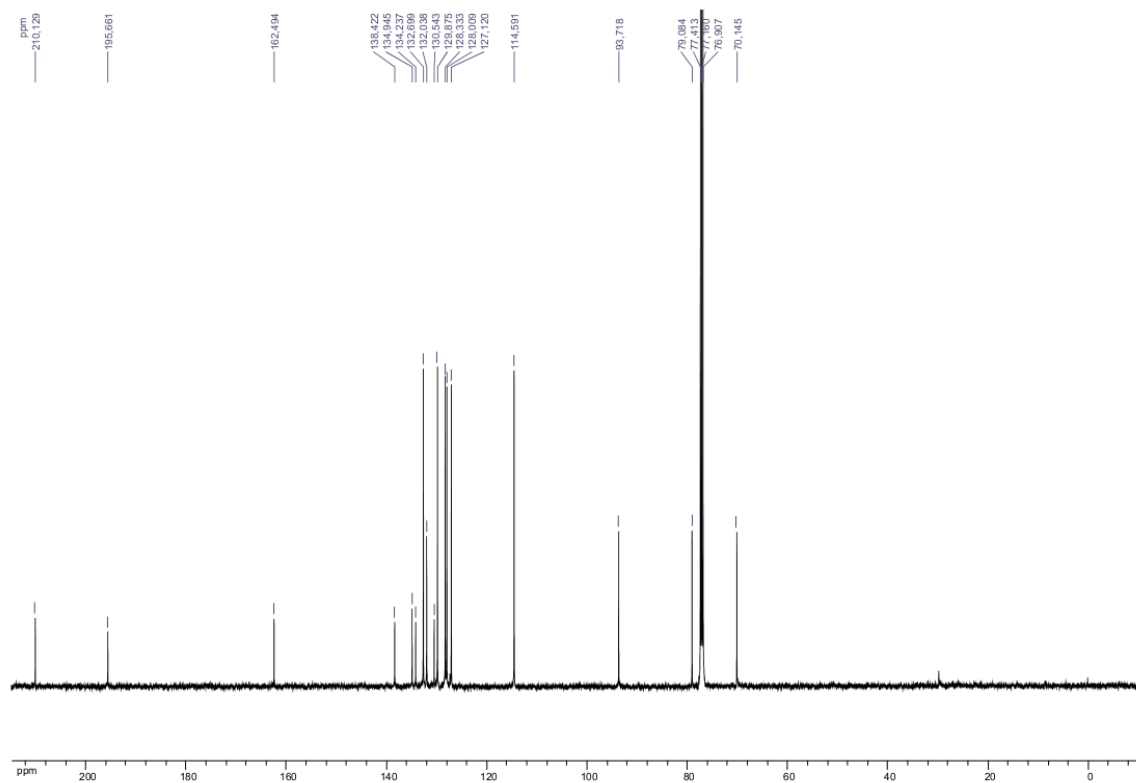
¹H NMR, 500 MHz (CDCl₃), compound **19** ^{13}C NMR, 125 MHz (CDCl_3)

^1H NMR, 500 MHz (CDCl_3), compound **21**

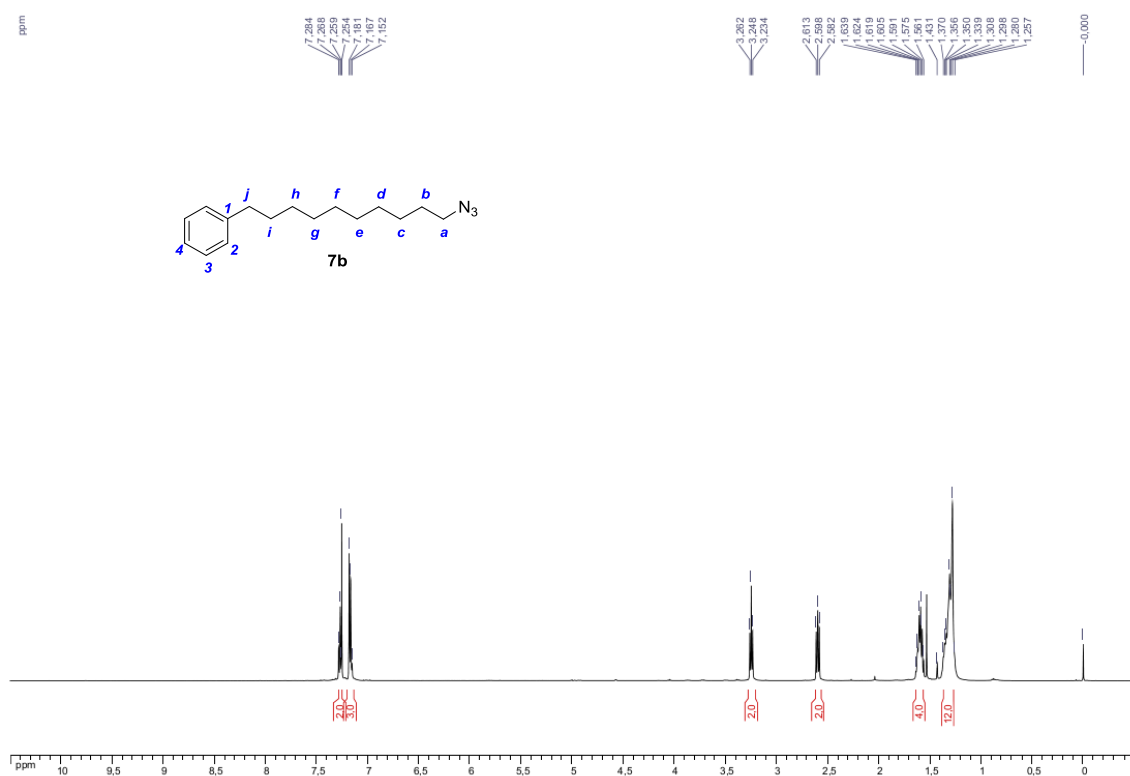


^{13}C NMR, 125 MHz (CDCl_3)

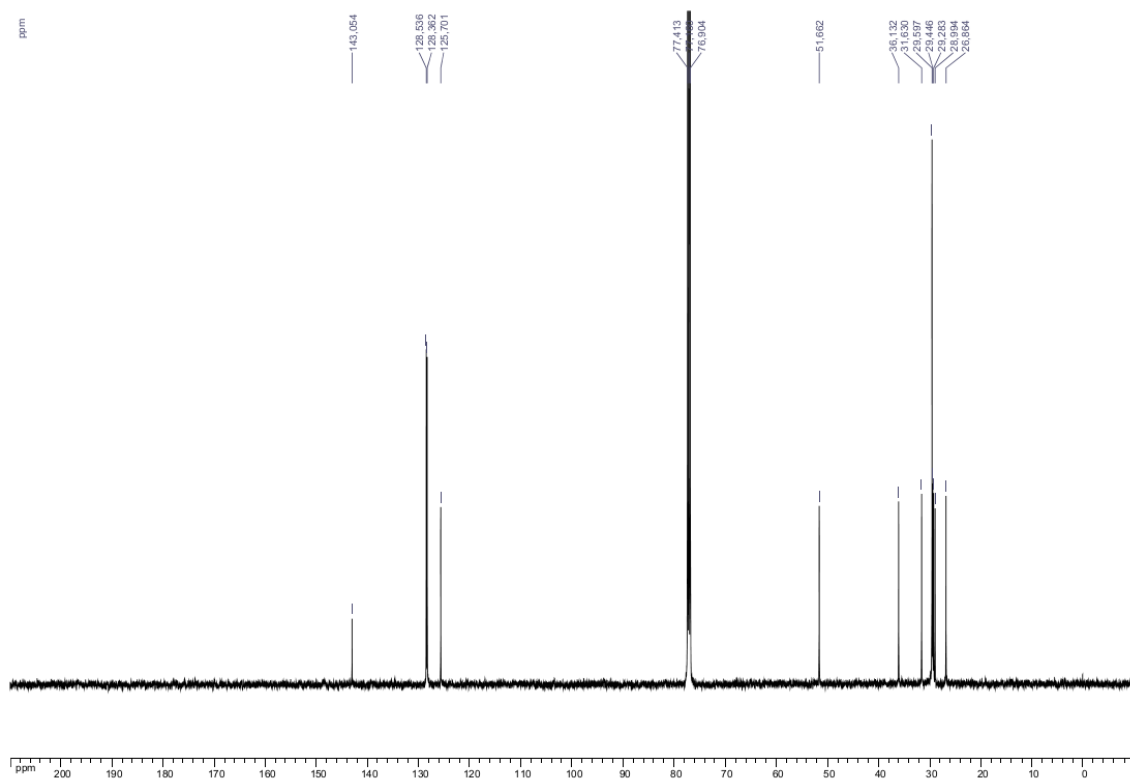


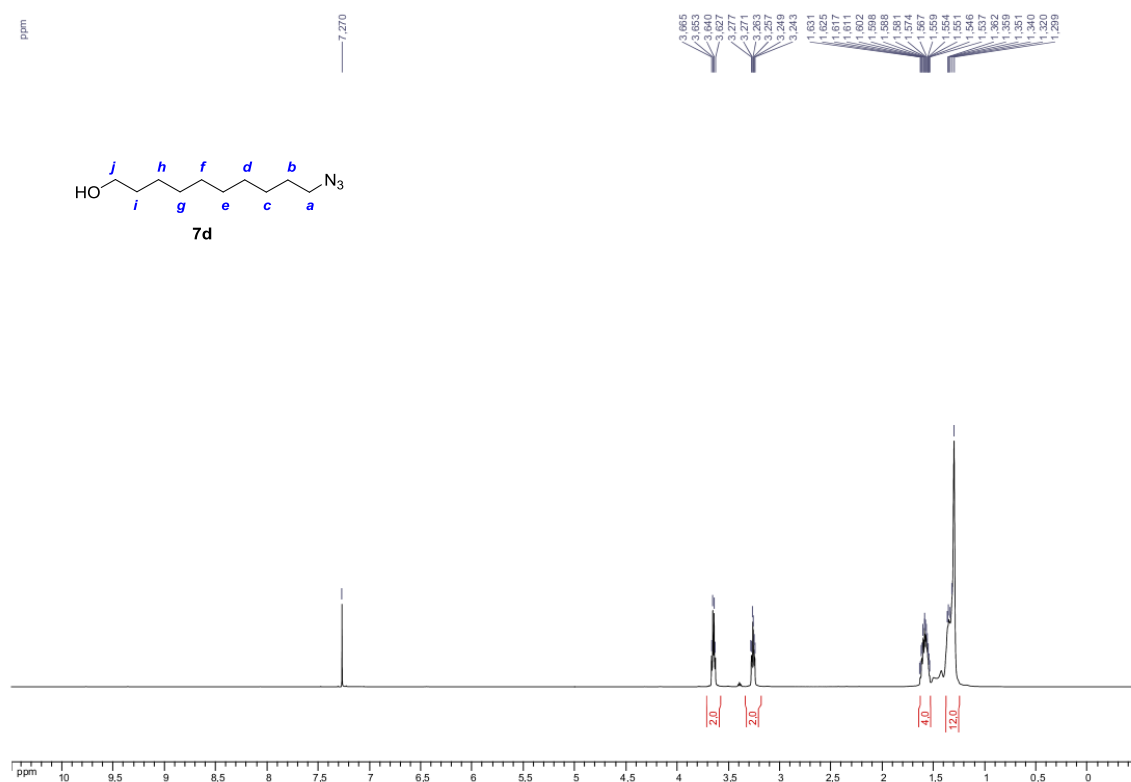
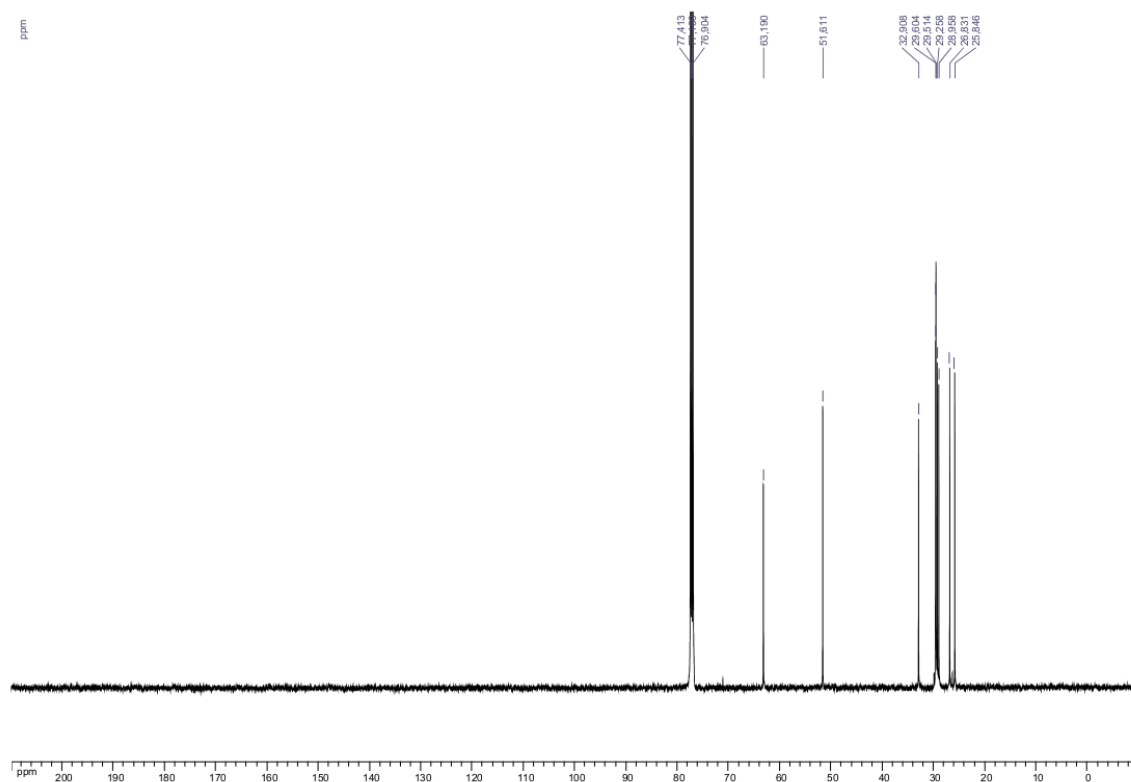
¹H NMR, 500 MHz (CDCl₃), compound **22** ^{13}C NMR, 125 MHz (CDCl_3)

^1H NMR, 500 MHz (CDCl_3), compound **7b**

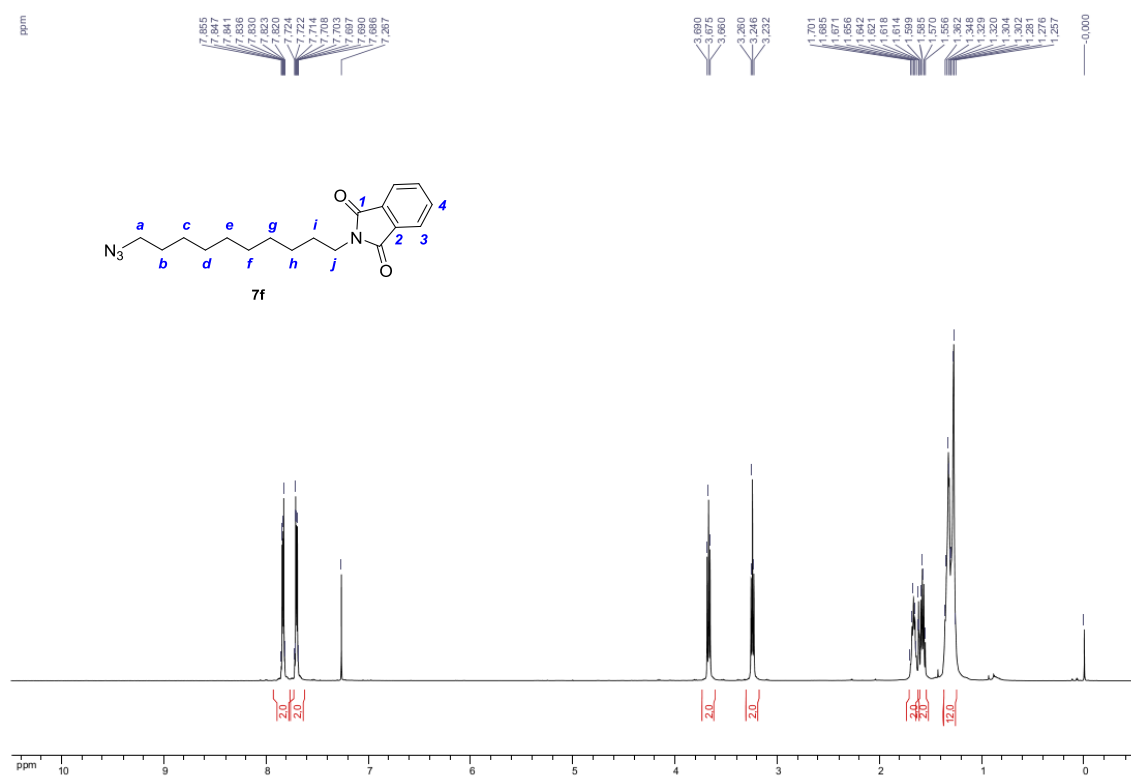


^{13}C NMR, 125 MHz (CDCl_3)

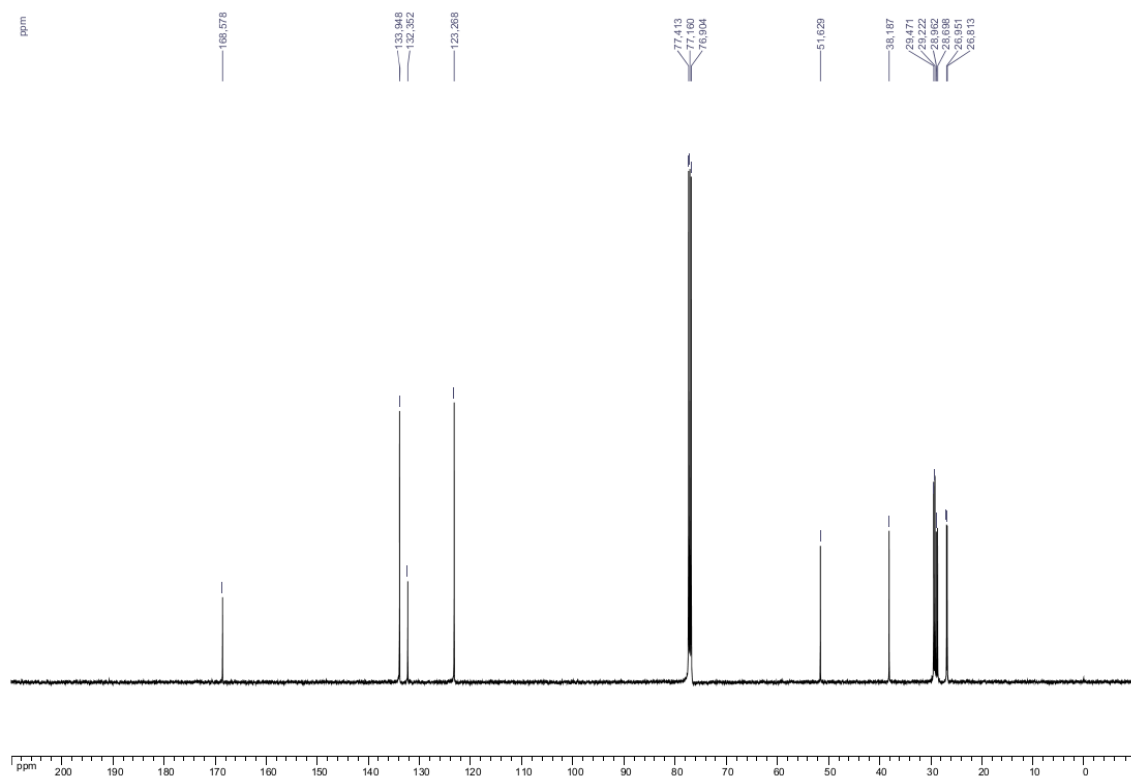


¹H NMR, 500 MHz (CDCl₃), compound **7d** ^{13}C NMR, 125 MHz (CDCl_3)

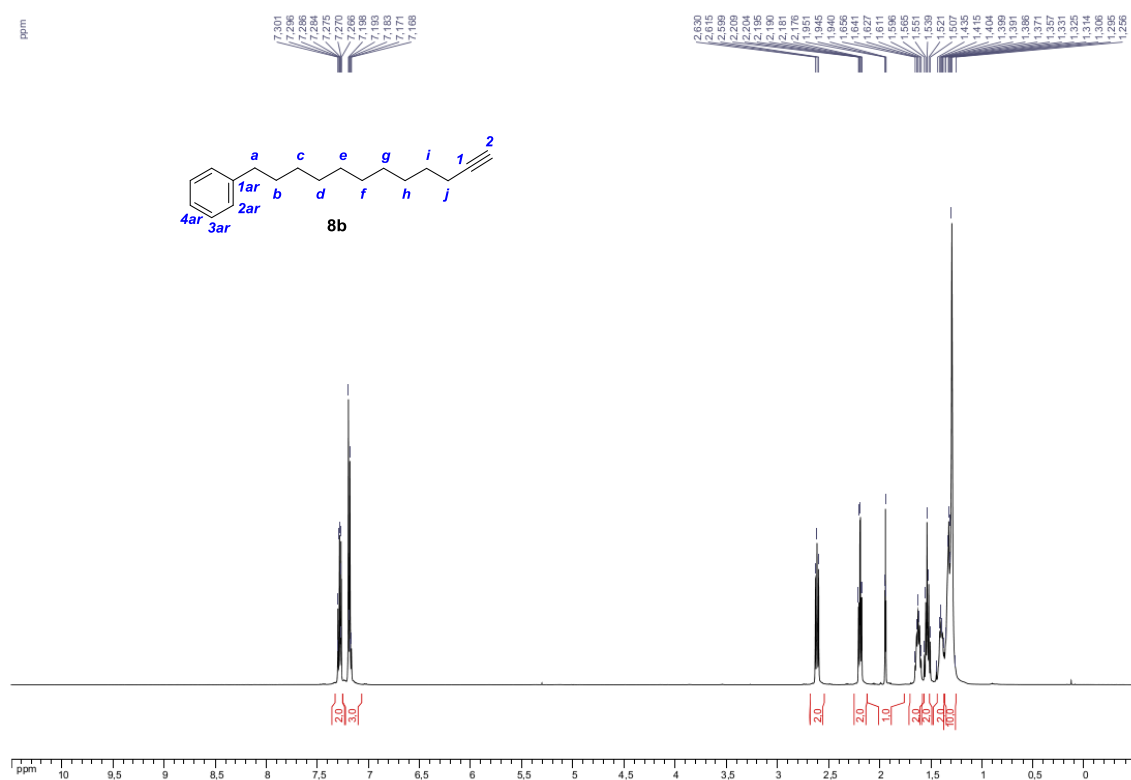
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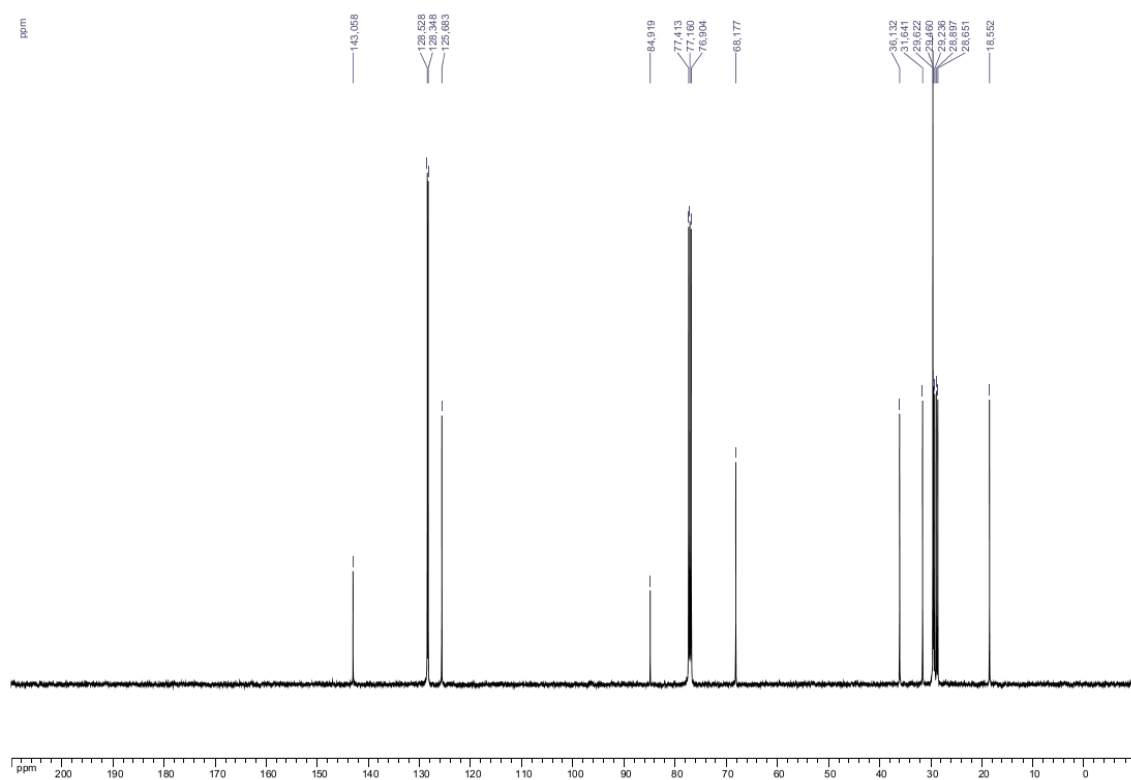
^{13}C NMR, 125 MHz (CDCl_3)



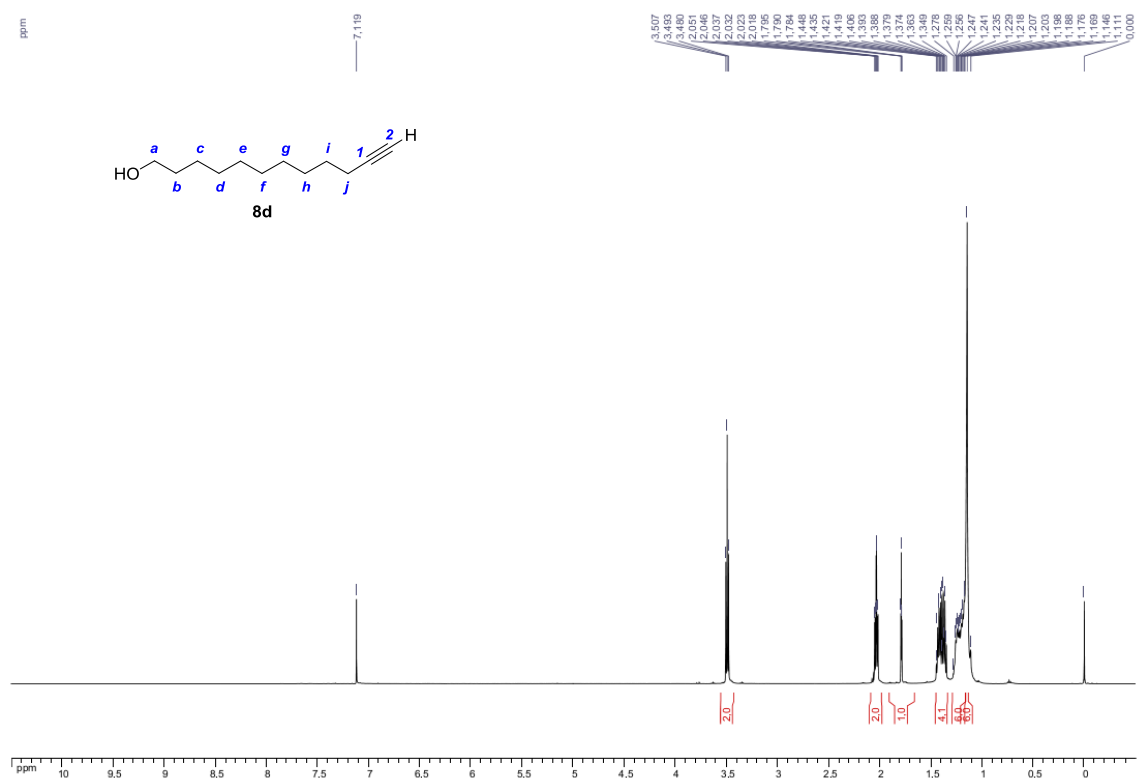
^1H NMR, 500 MHz (CDCl_3), compound **8b**



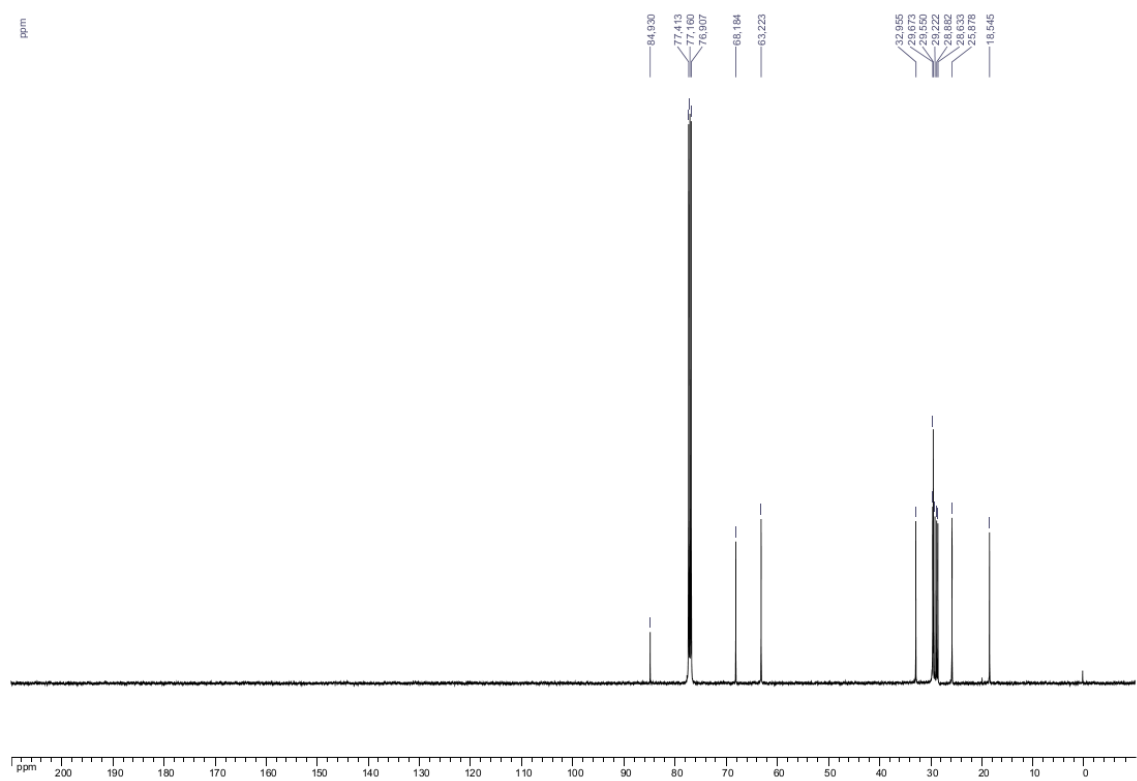
^{13}C NMR, 125 MHz (CDCl_3)



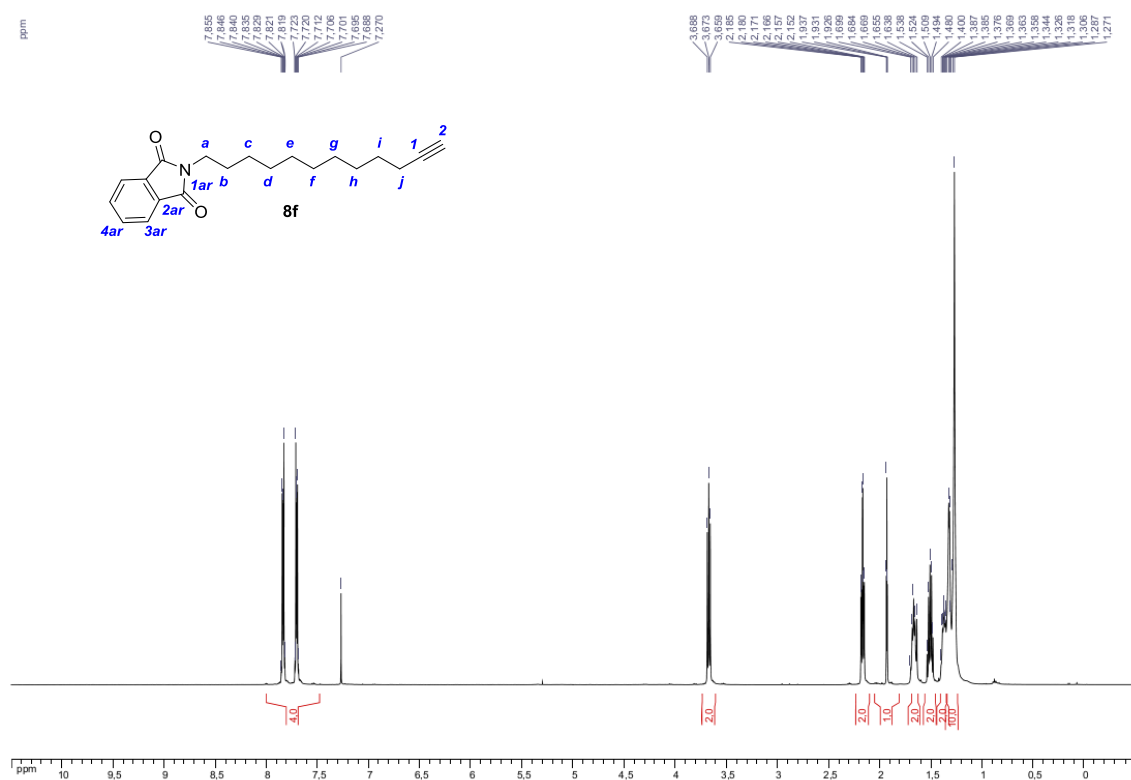
^1H NMR, 500 MHz (CDCl_3), compound **8d**



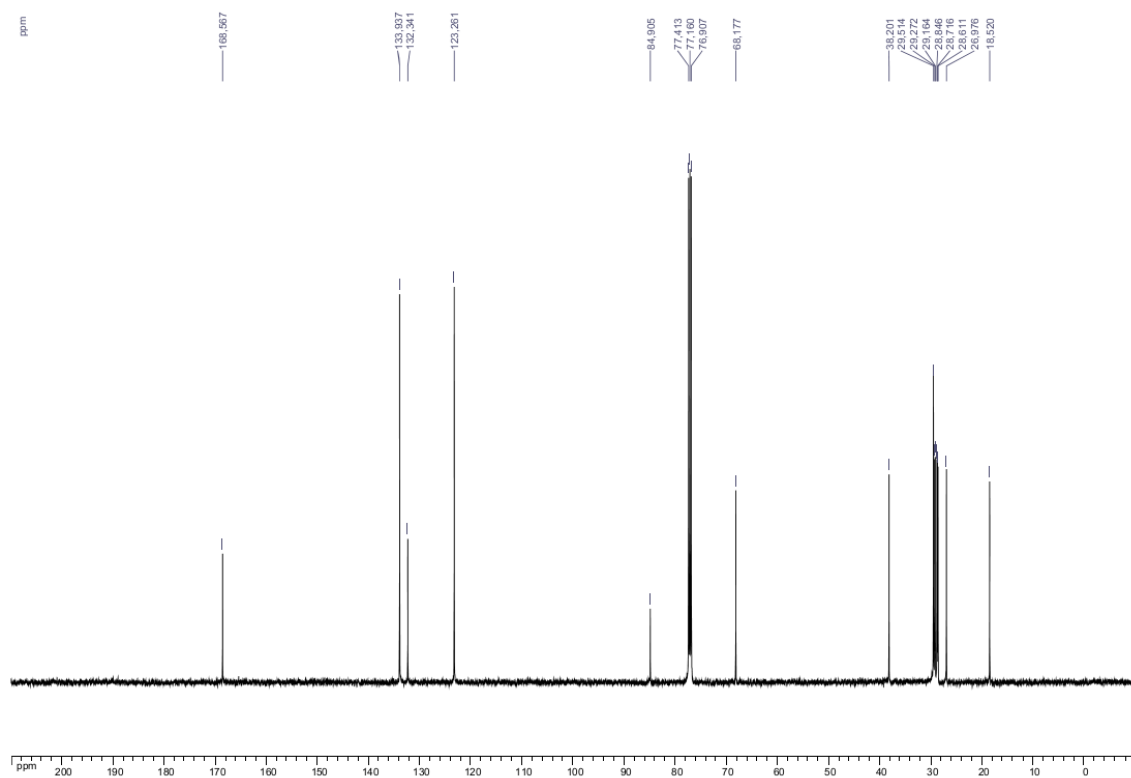
^{13}C NMR, 125 MHz (CDCl_3)



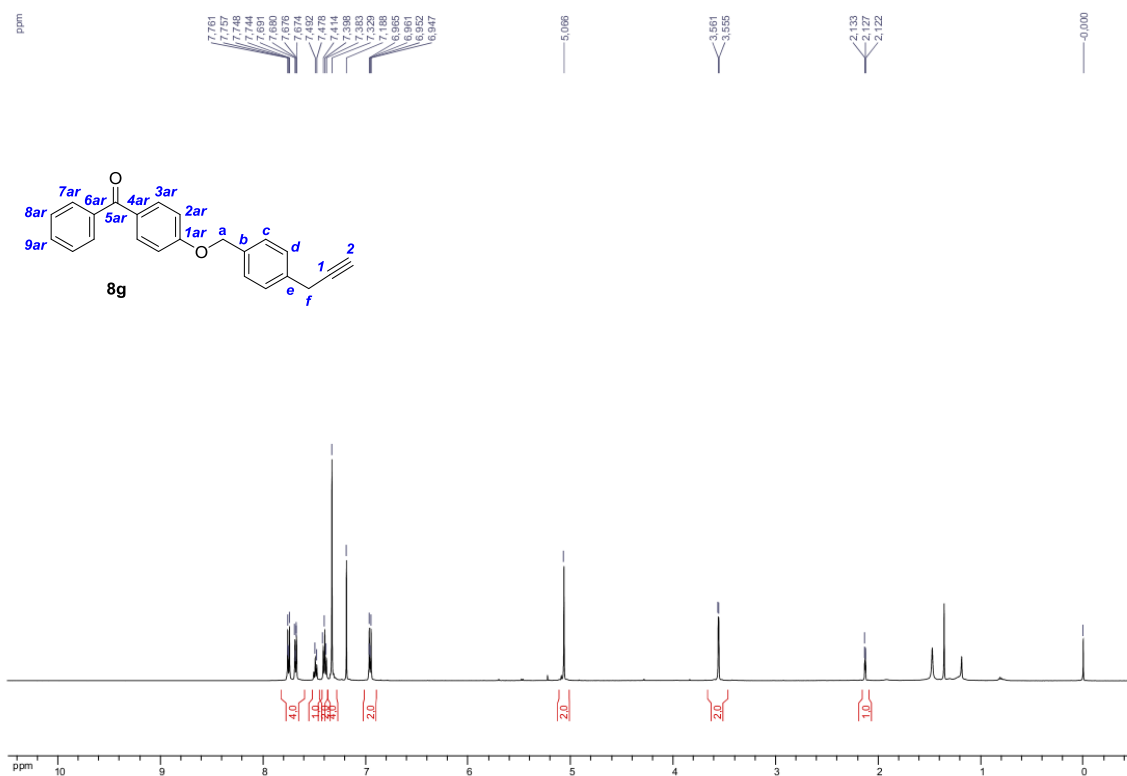
^1H NMR, 500 MHz (CDCl_3), compound **8f**



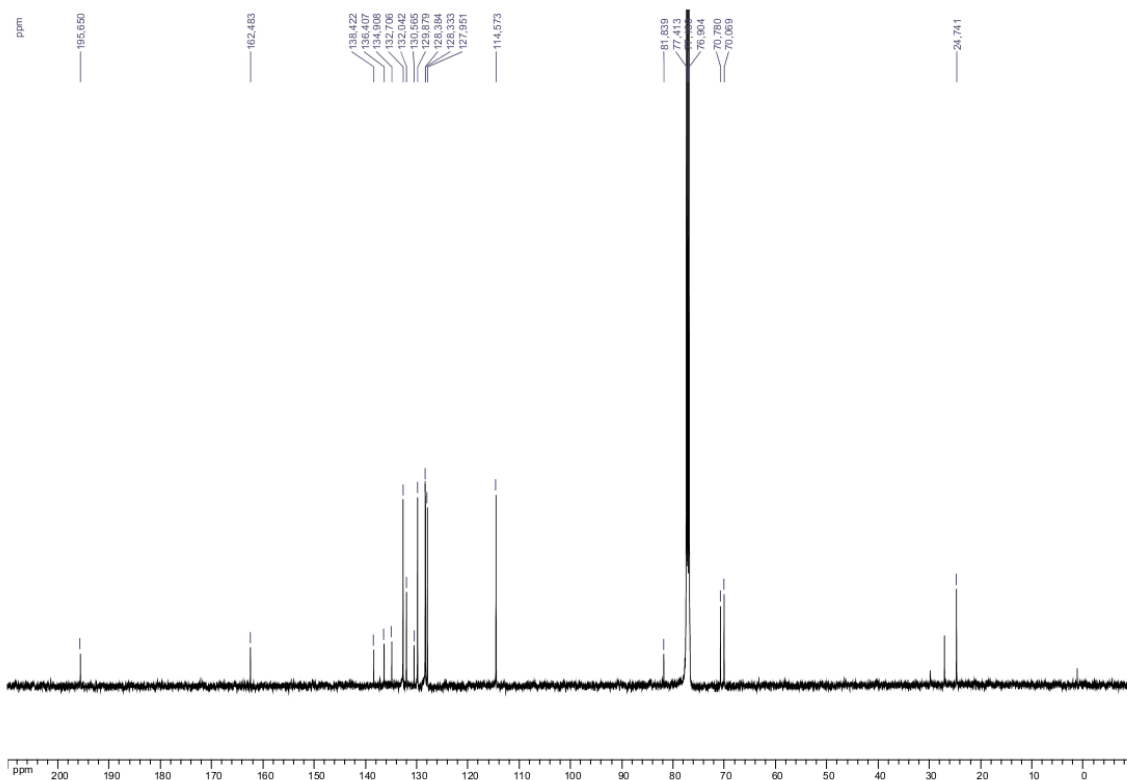
^{13}C NMR, 125 MHz (CDCl_3)



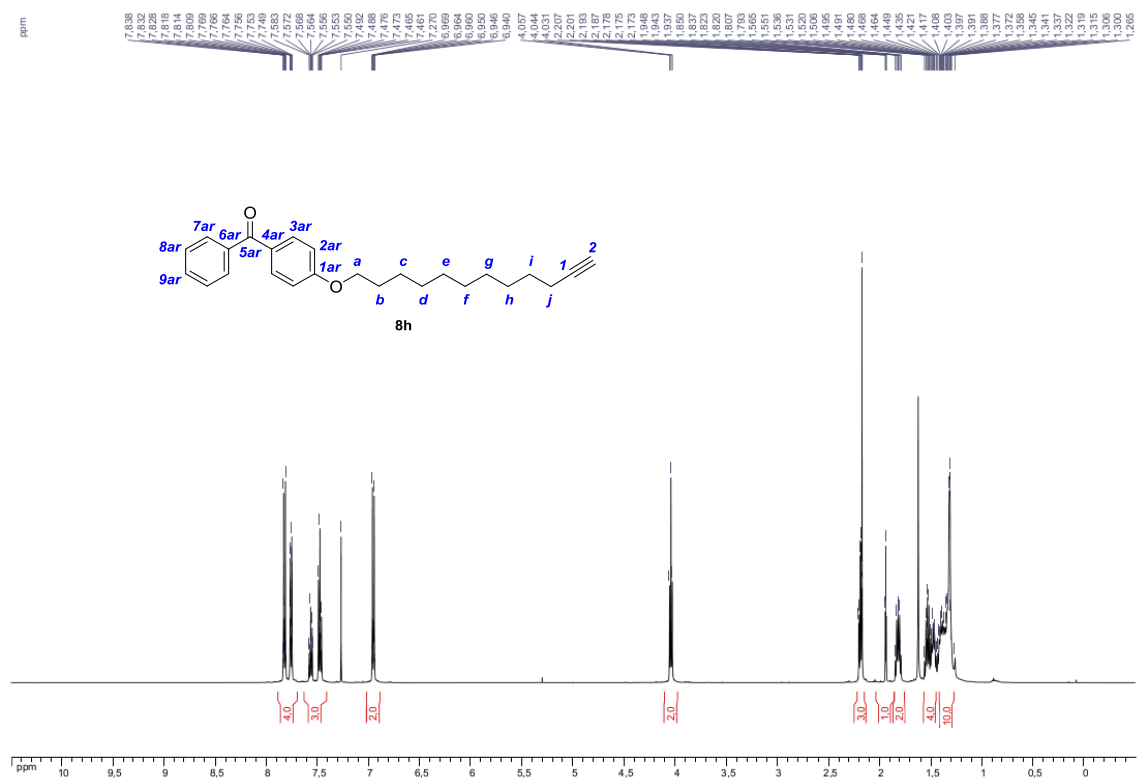
^1H NMR, 500 MHz (CDCl_3), compound **8g**



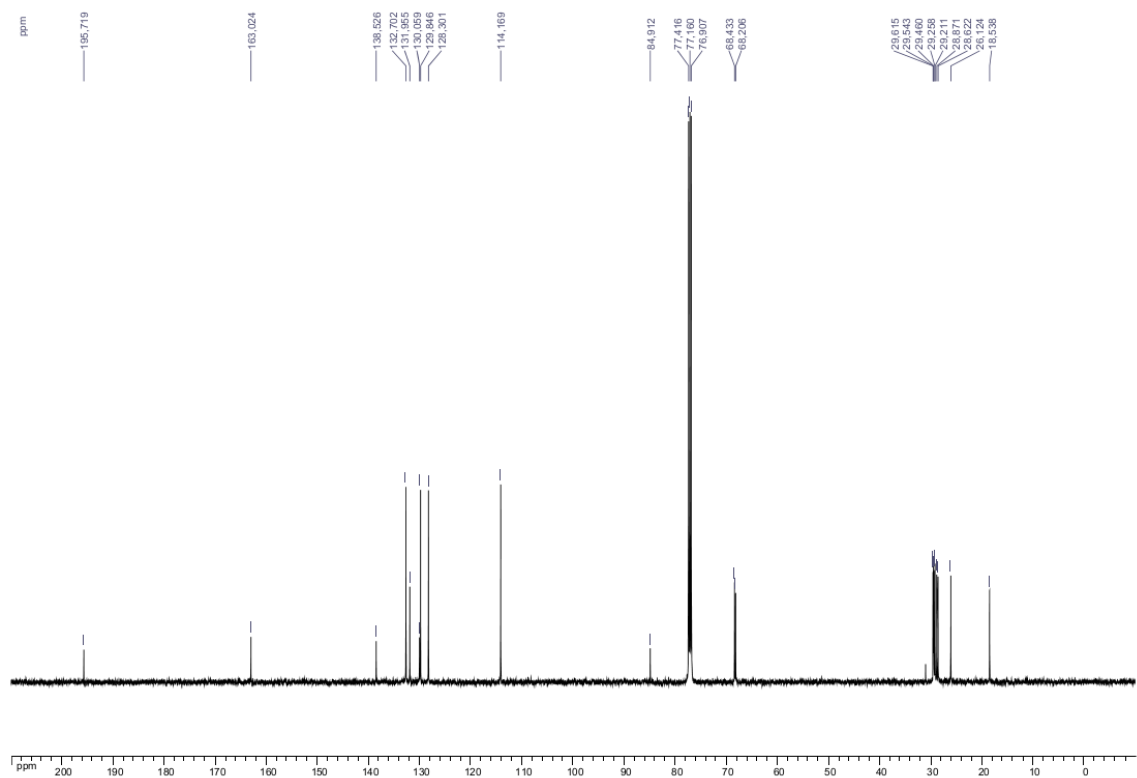
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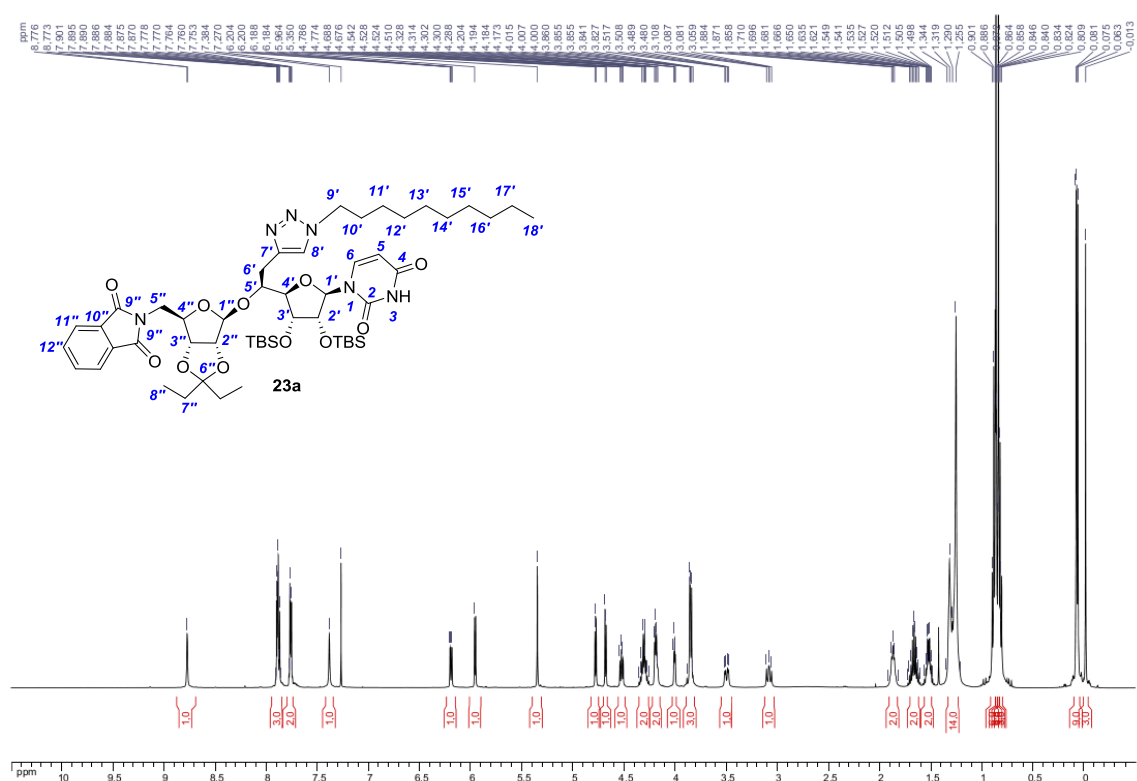
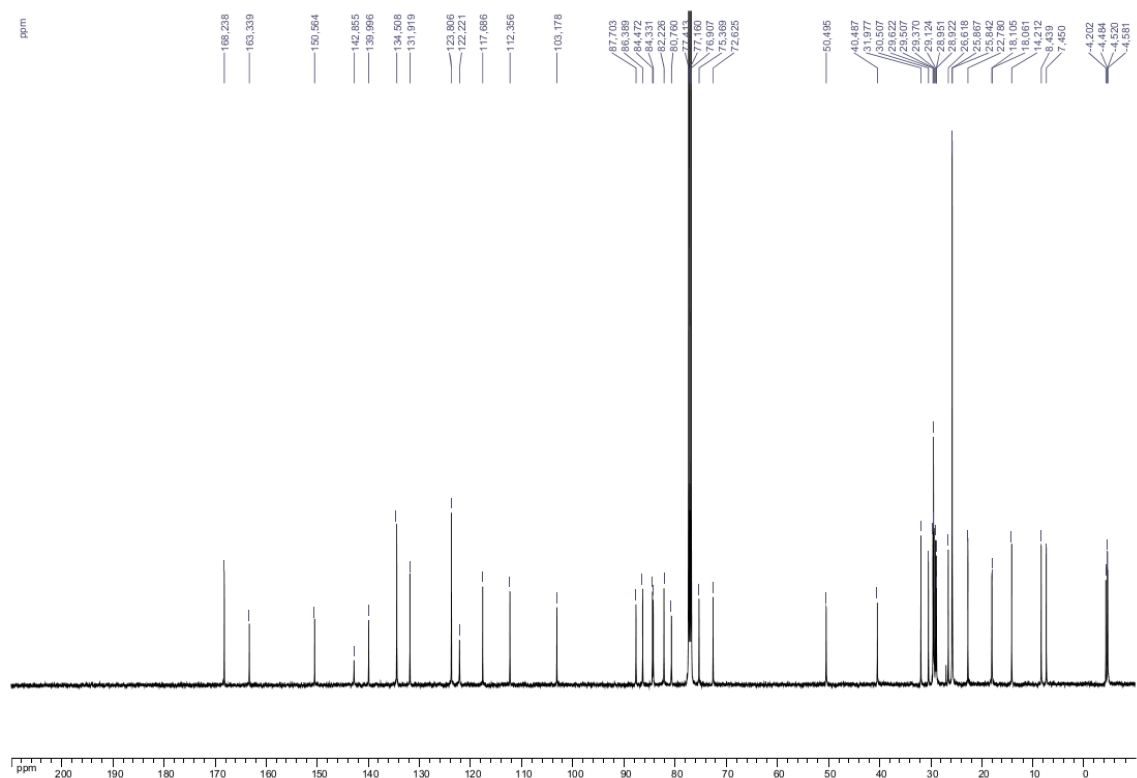


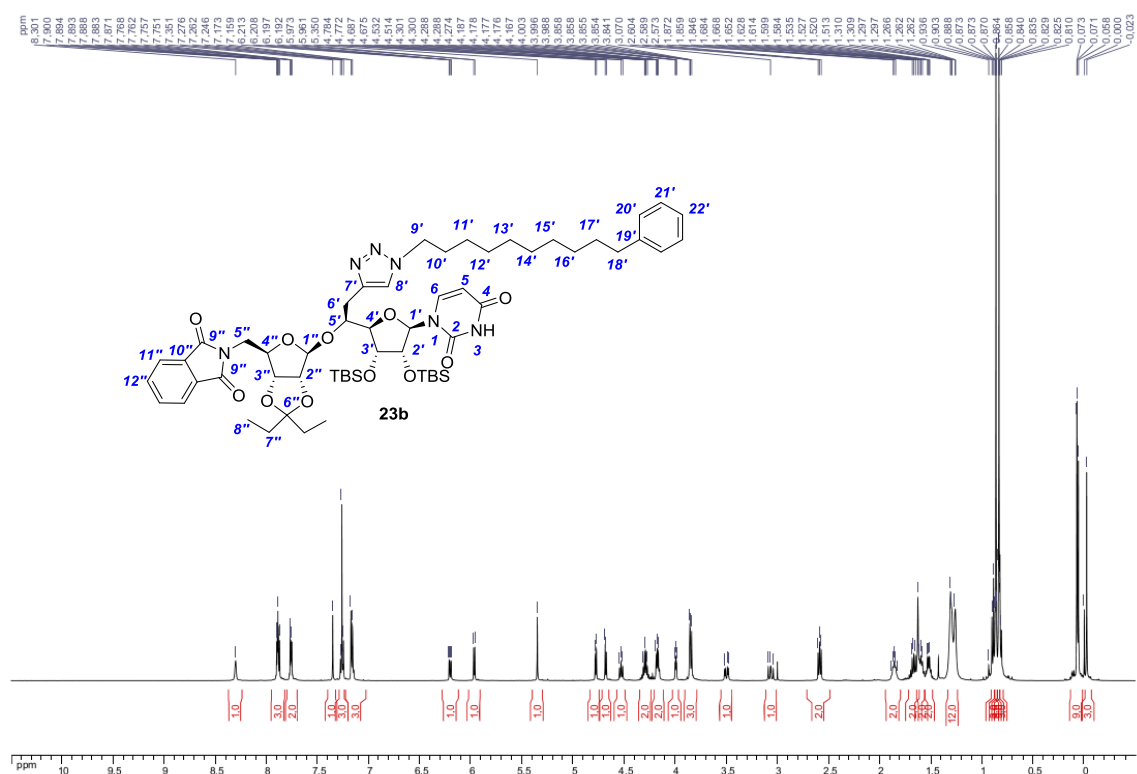
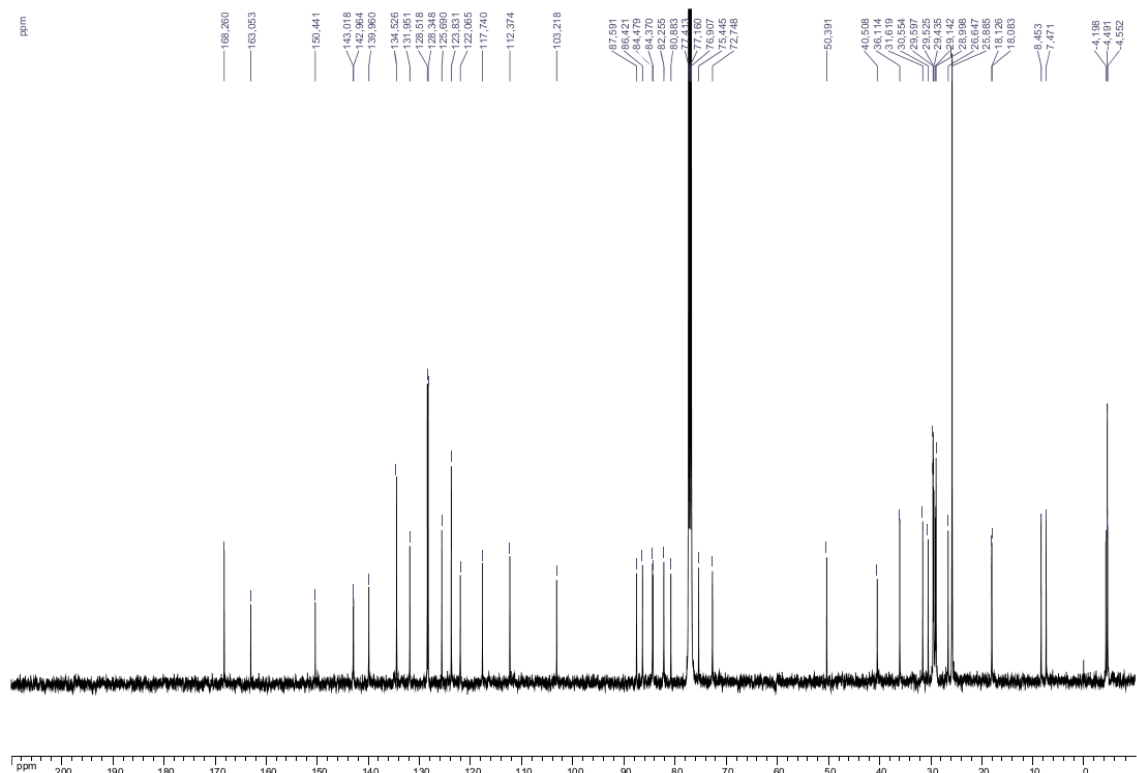
^1H NMR, 500 MHz (CDCl_3), compound **8h**



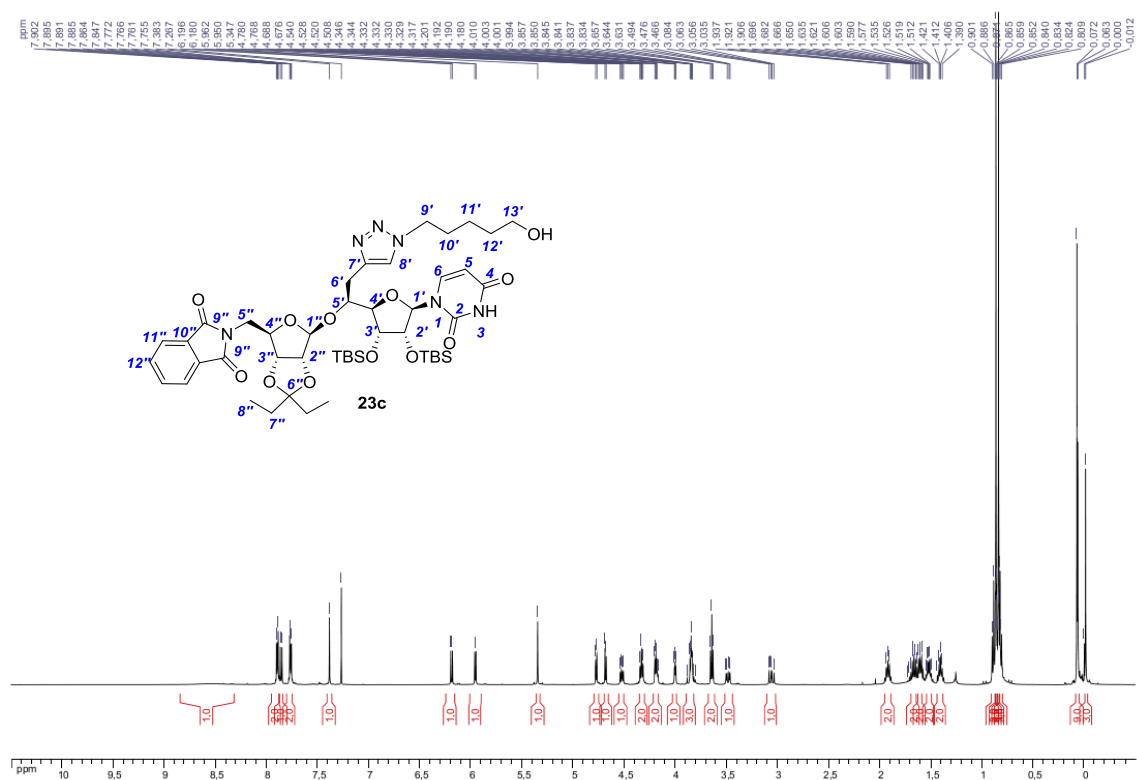
^{13}C NMR, 125 MHz (CDCl_3)



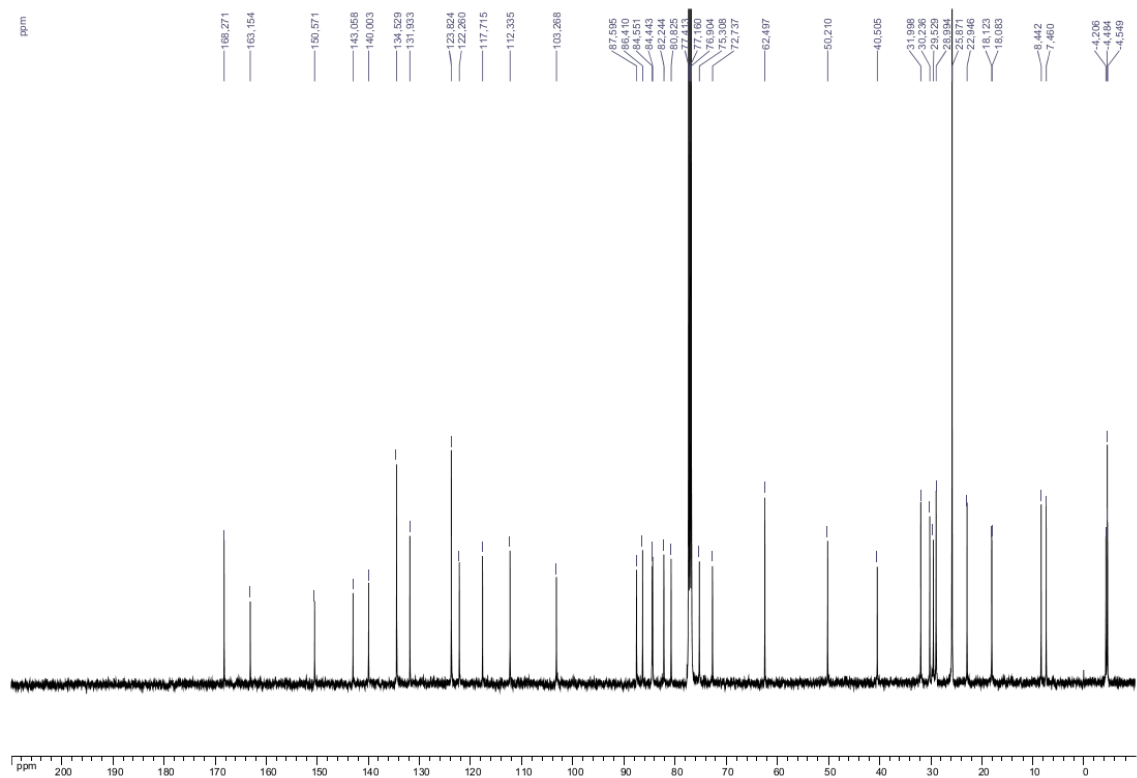
¹H NMR, 500 MHz (CDCl₃), compound **23a** ^{13}C NMR, 125 MHz (CDCl_3)

¹H NMR, 500 MHz (CDCl₃), compound **23b** ^{13}C NMR, 125 MHz (CDCl_3)

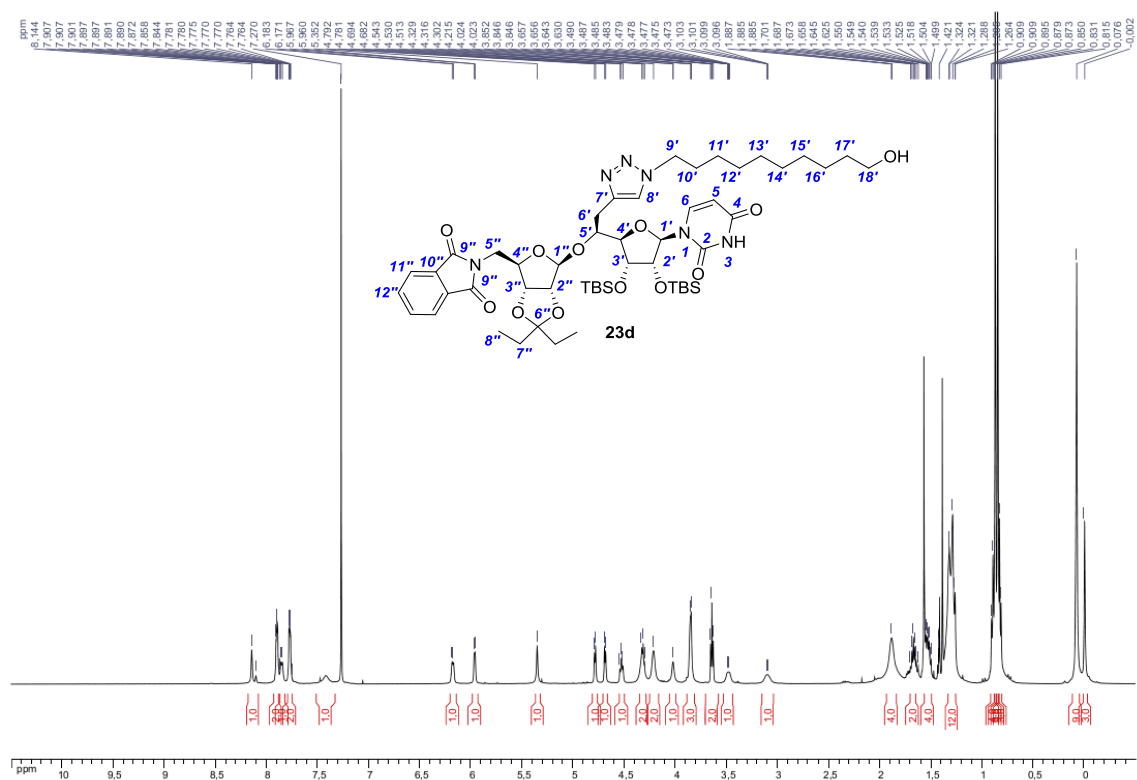
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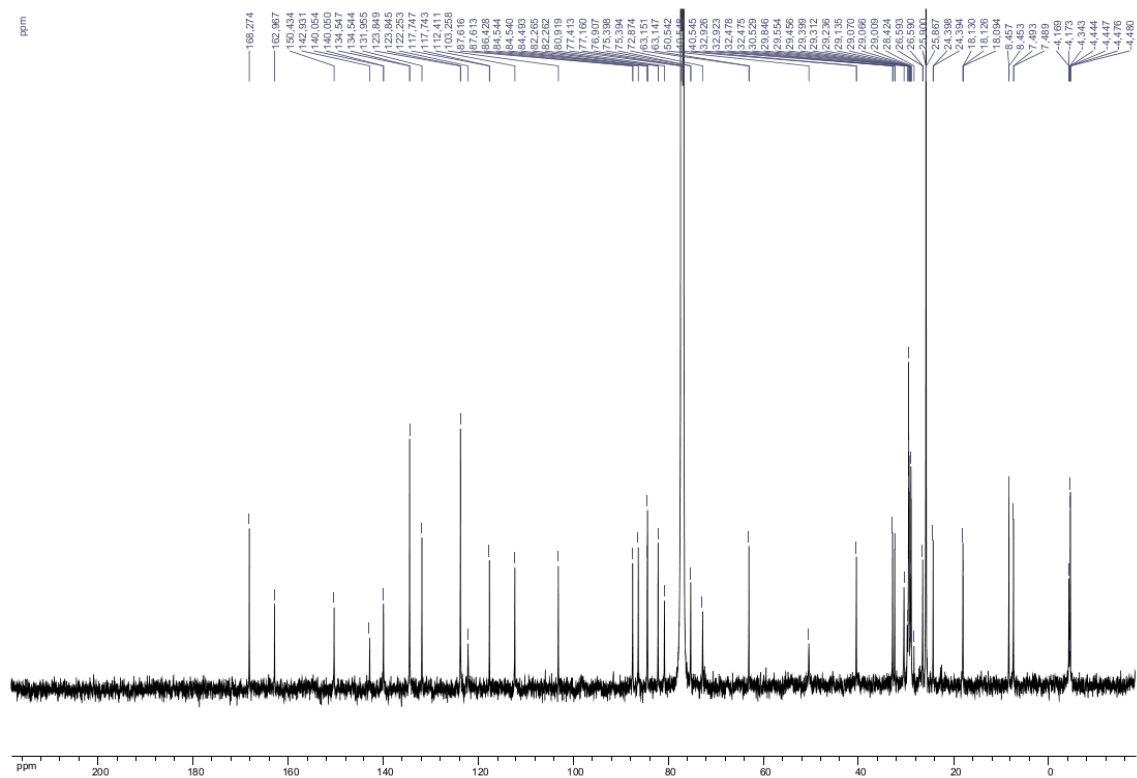
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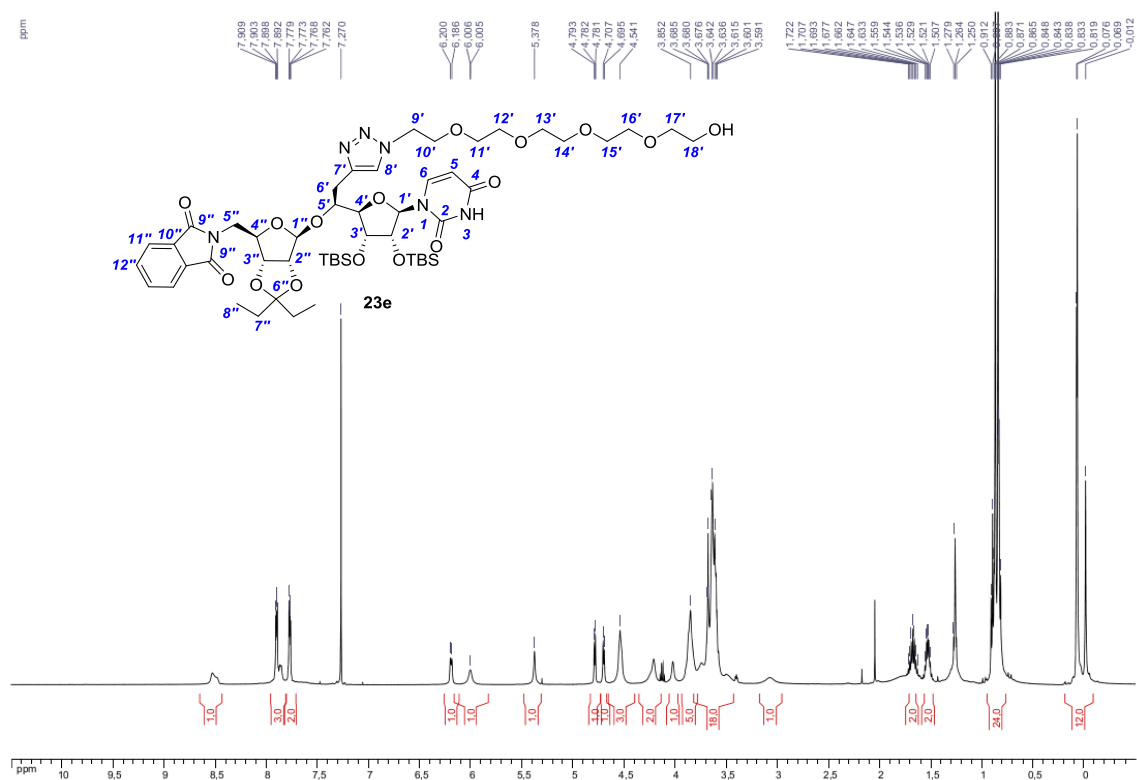
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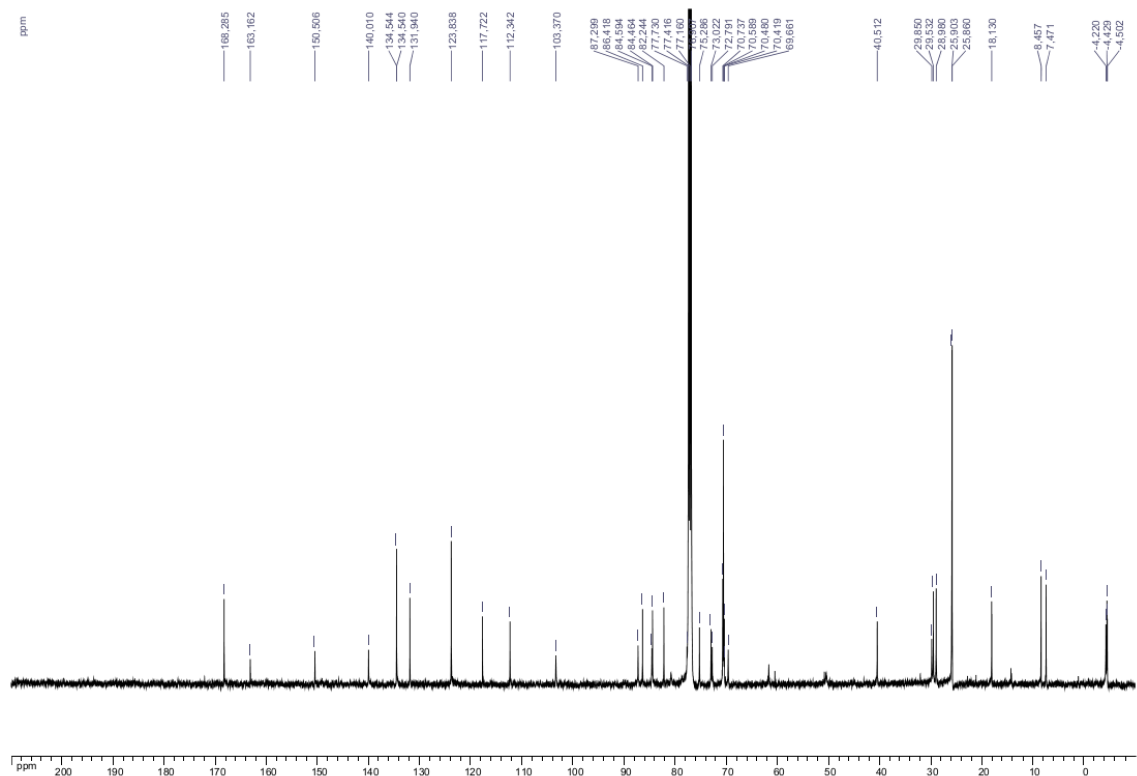
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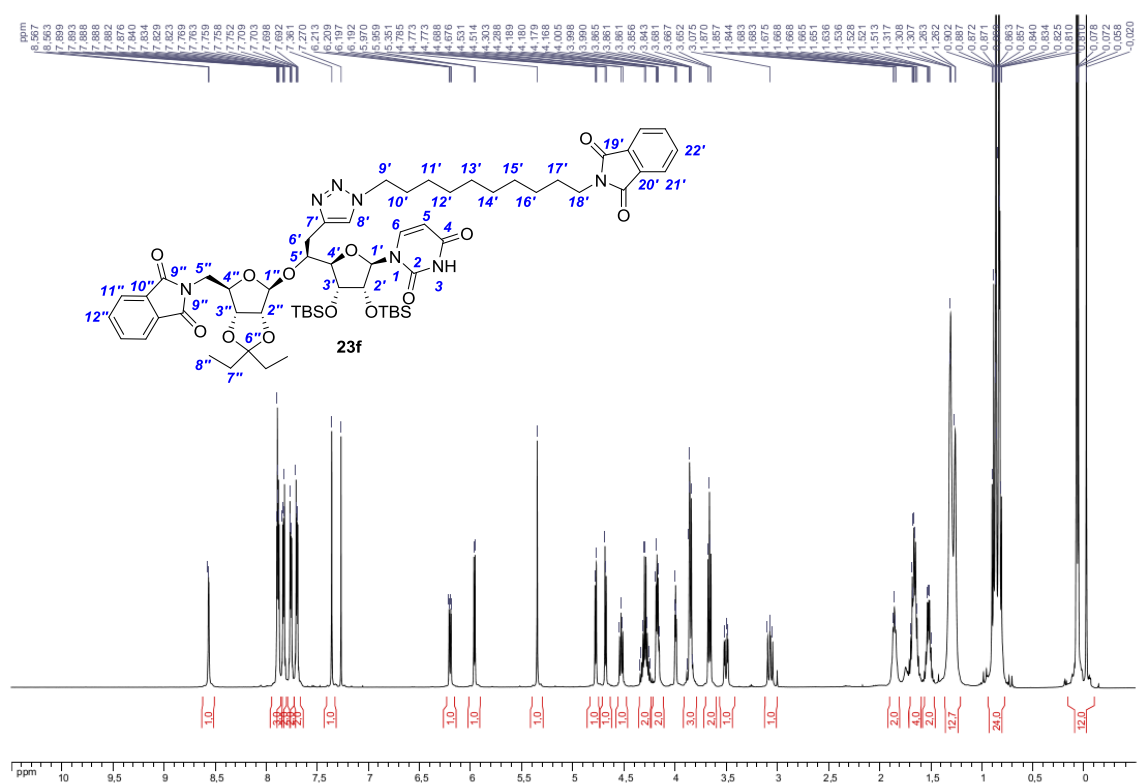
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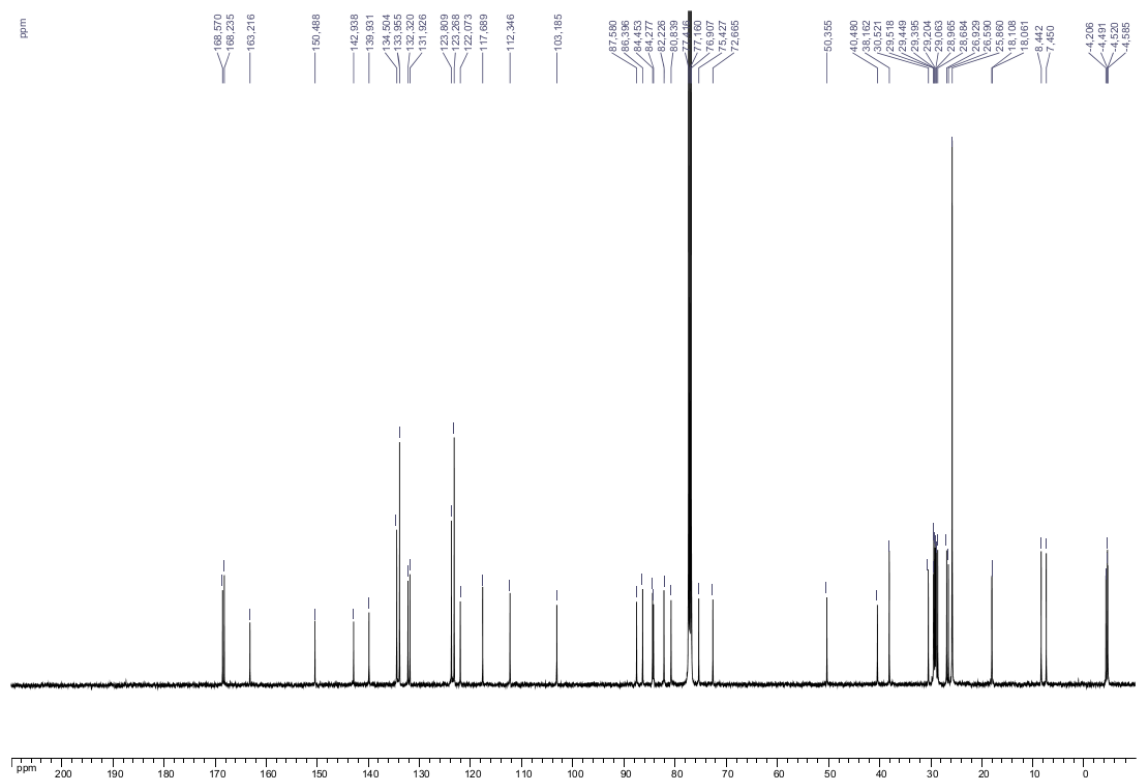
^{13}C NMR, 125 MHz (CDCl_3)

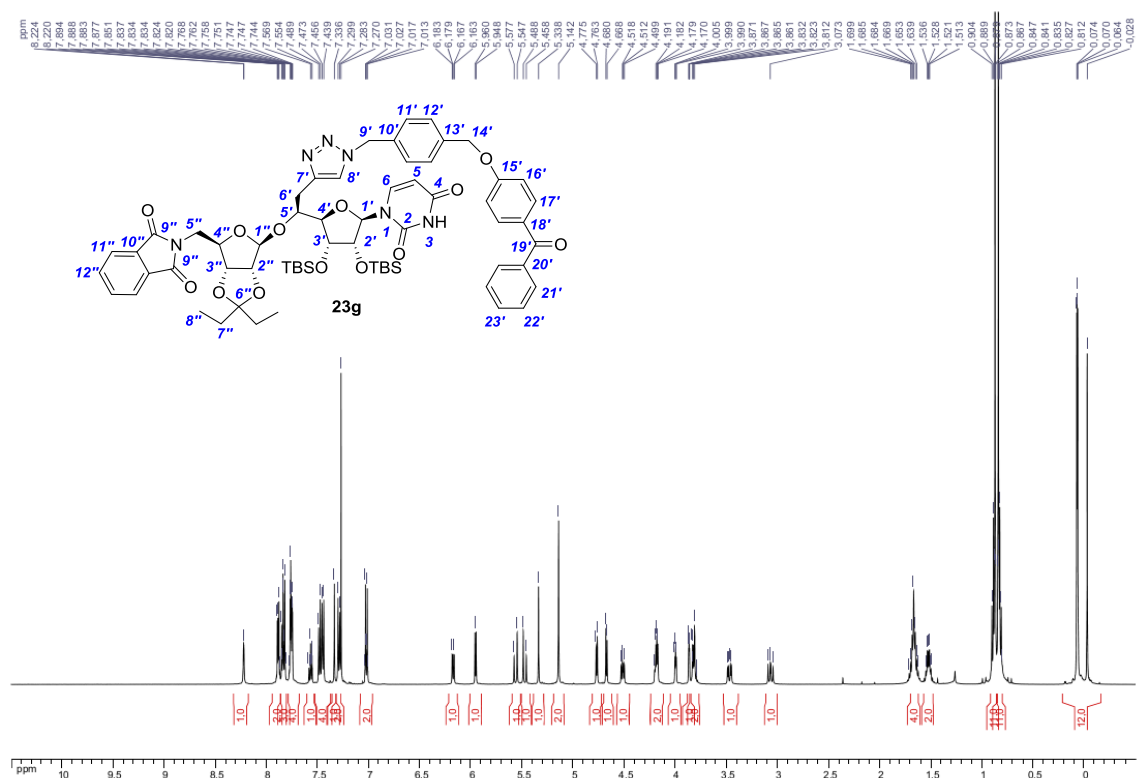
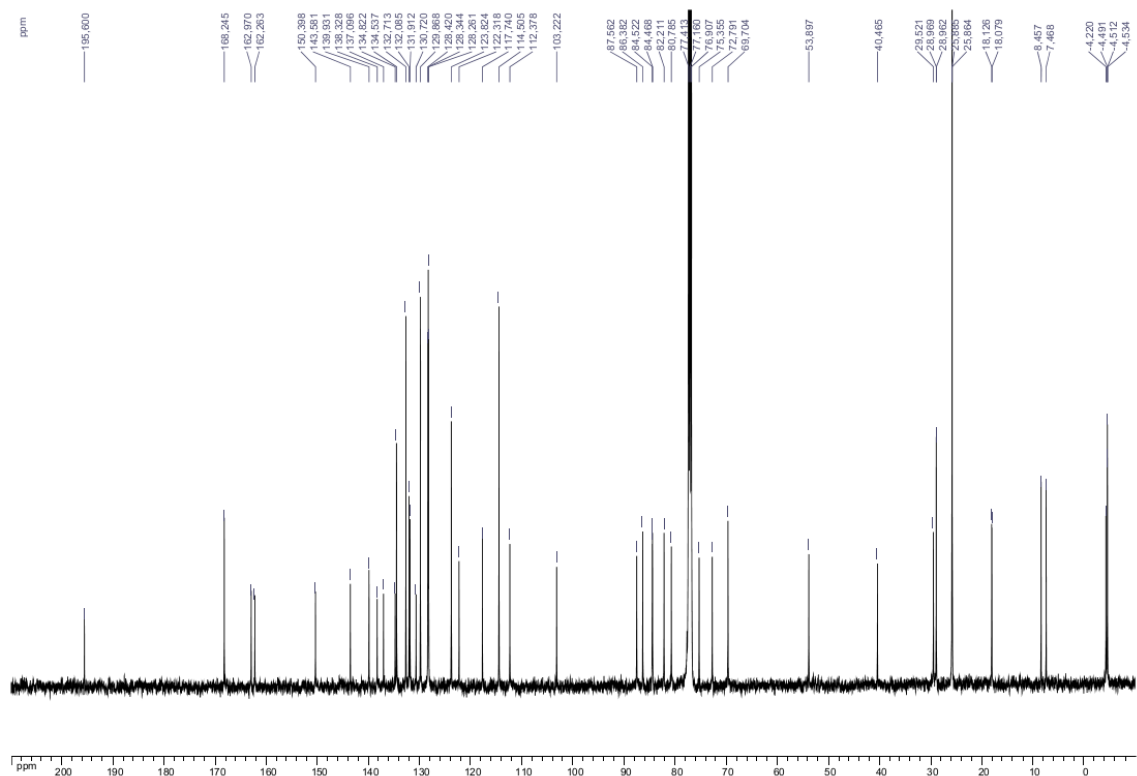


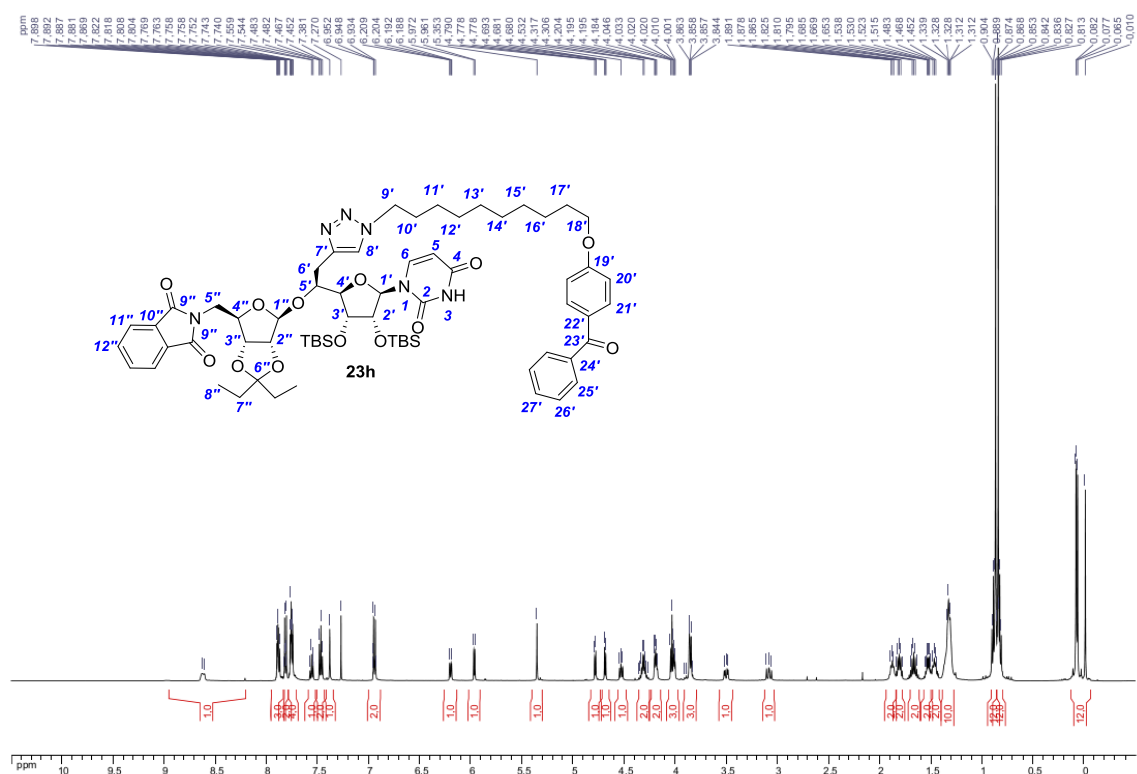
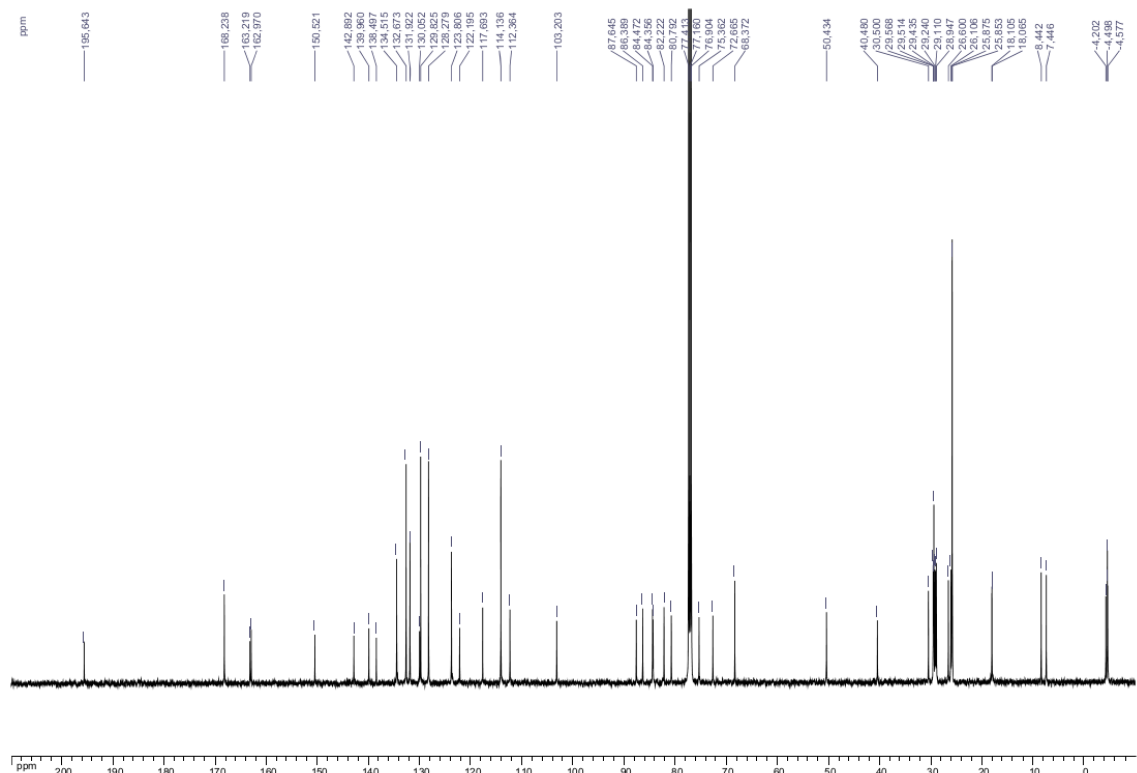
^1H NMR, 500 MHz (CDCl_3), compound **23f**

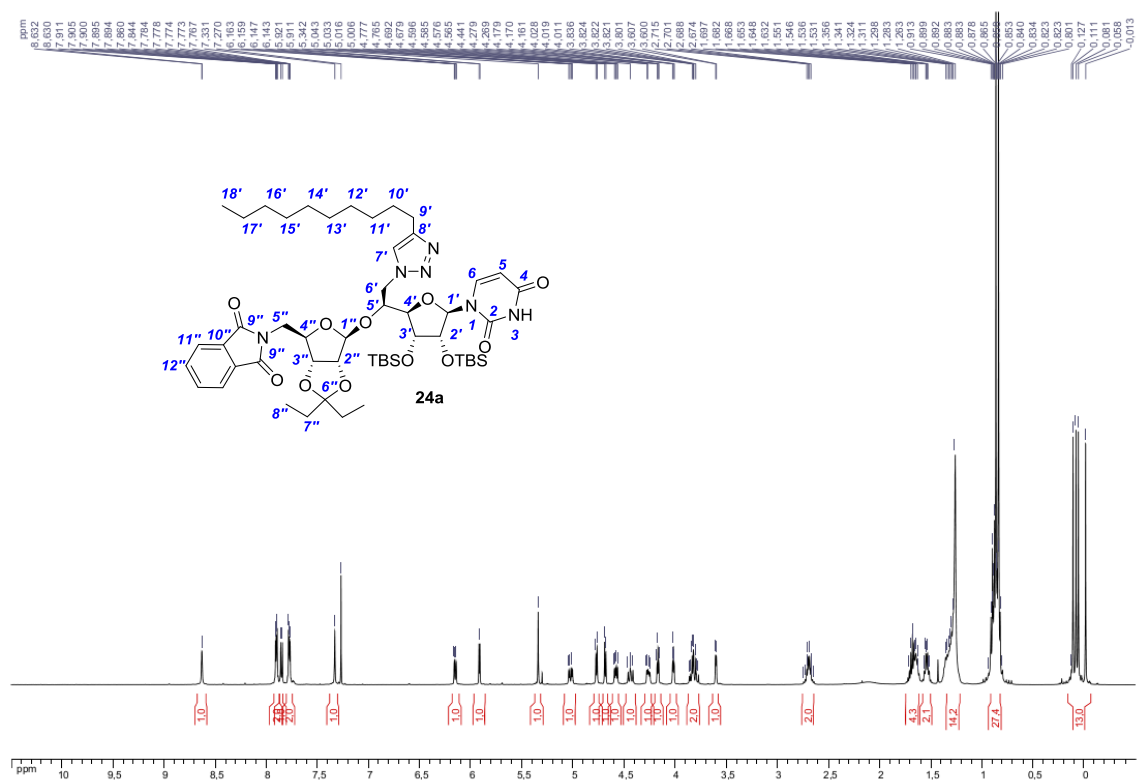
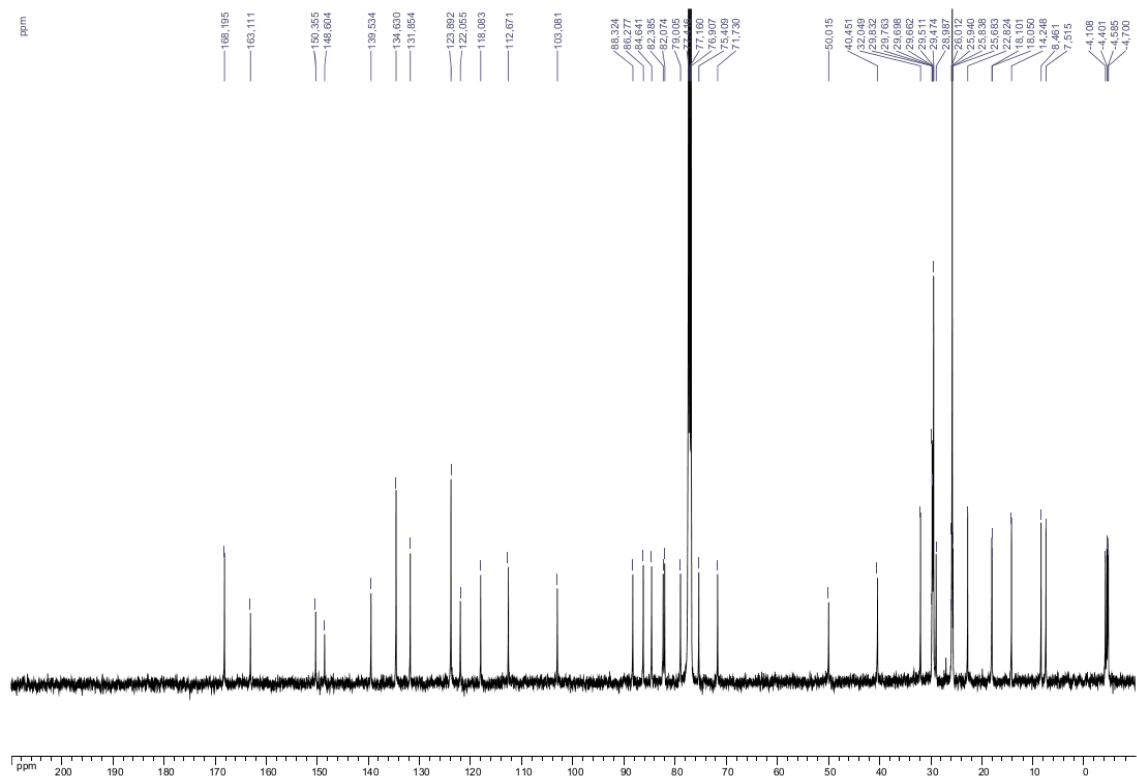


^{13}C NMR, 125 MHz (CDCl_3)

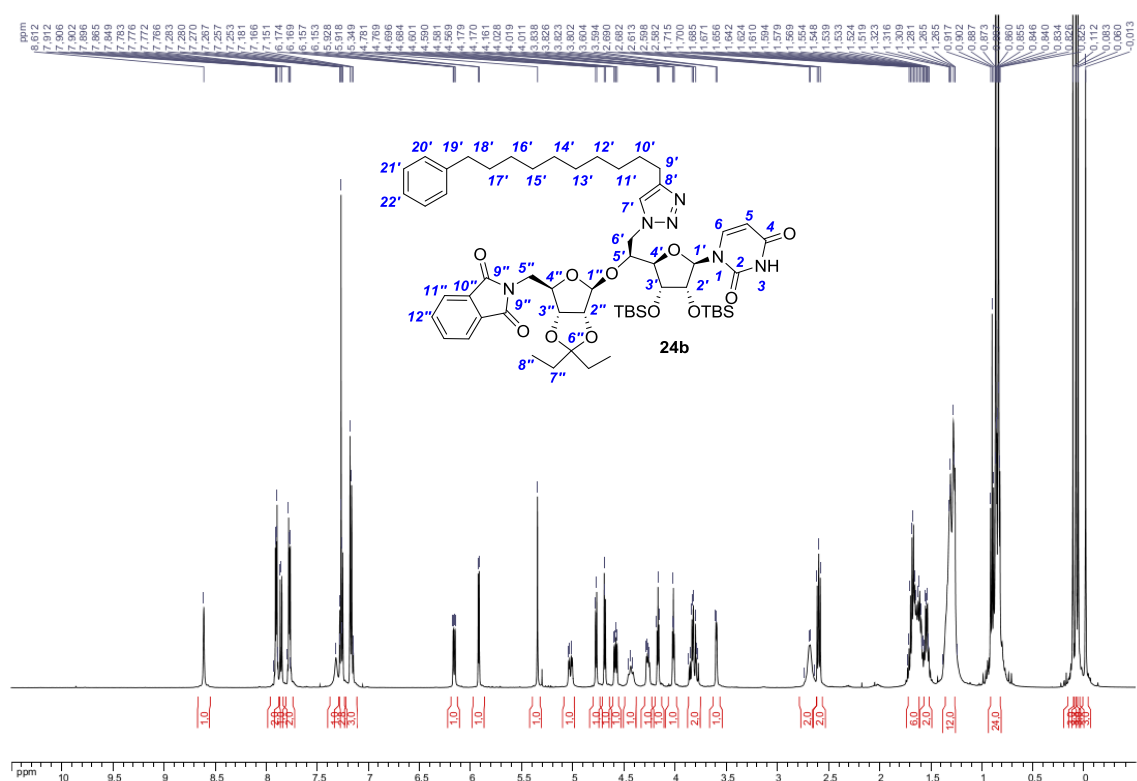


¹H NMR, 500 MHz (CDCl₃), compound **23g** ^{13}C NMR, 125 MHz (CDCl_3)

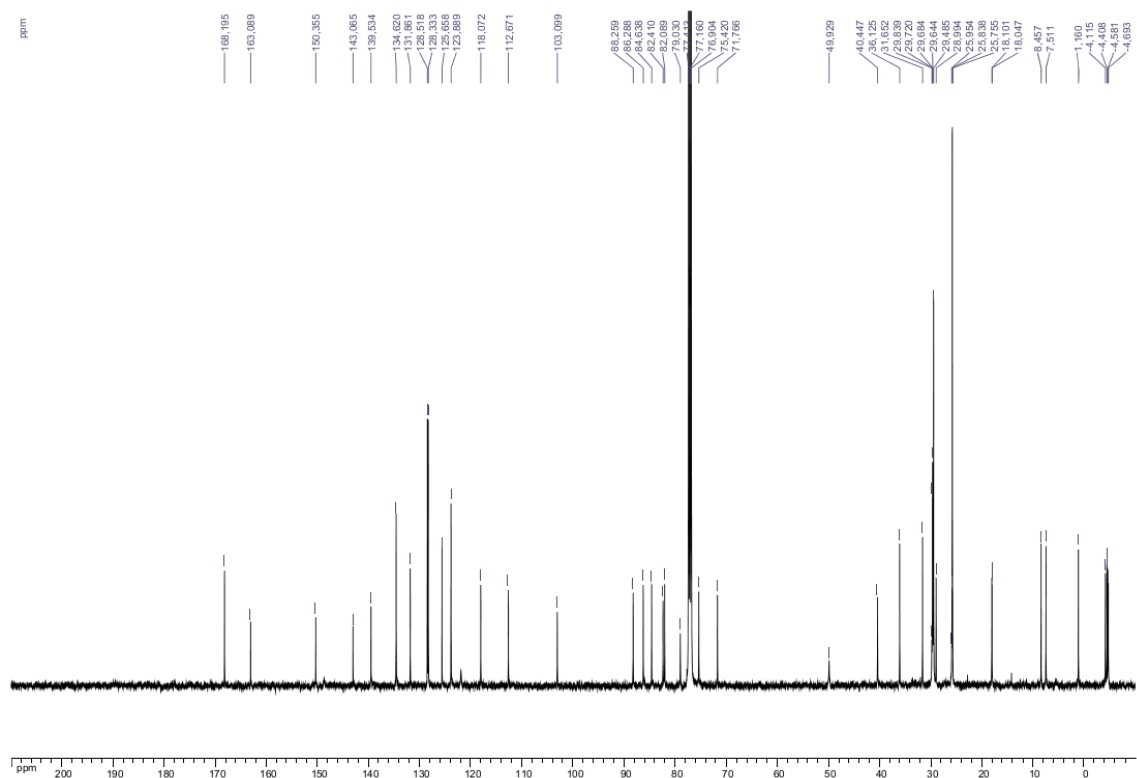
¹H NMR, 500 MHz (CDCl₃), compound **23h** ^{13}C NMR, 125 MHz (CDCl_3)

¹H NMR, 500 MHz (CDCl₃), compound **24a** ^{13}C NMR, 125 MHz (CDCl_3)

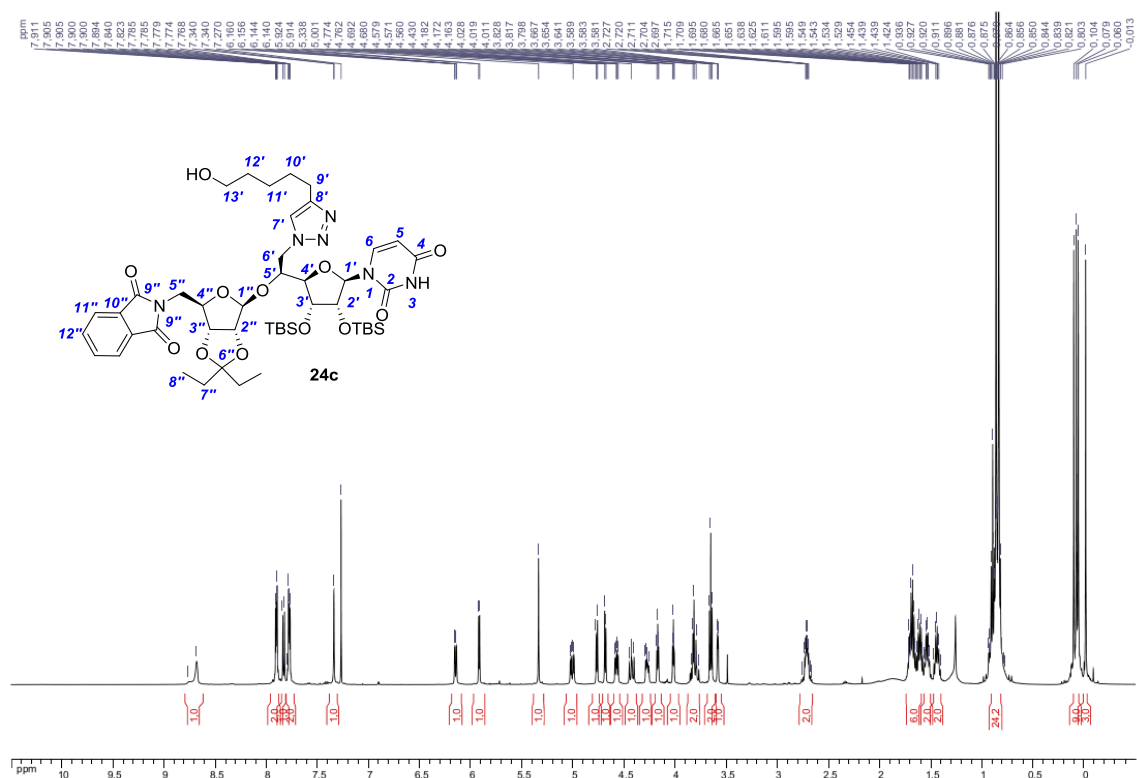
^1H NMR, 500 MHz (CDCl_3), compound **24b**



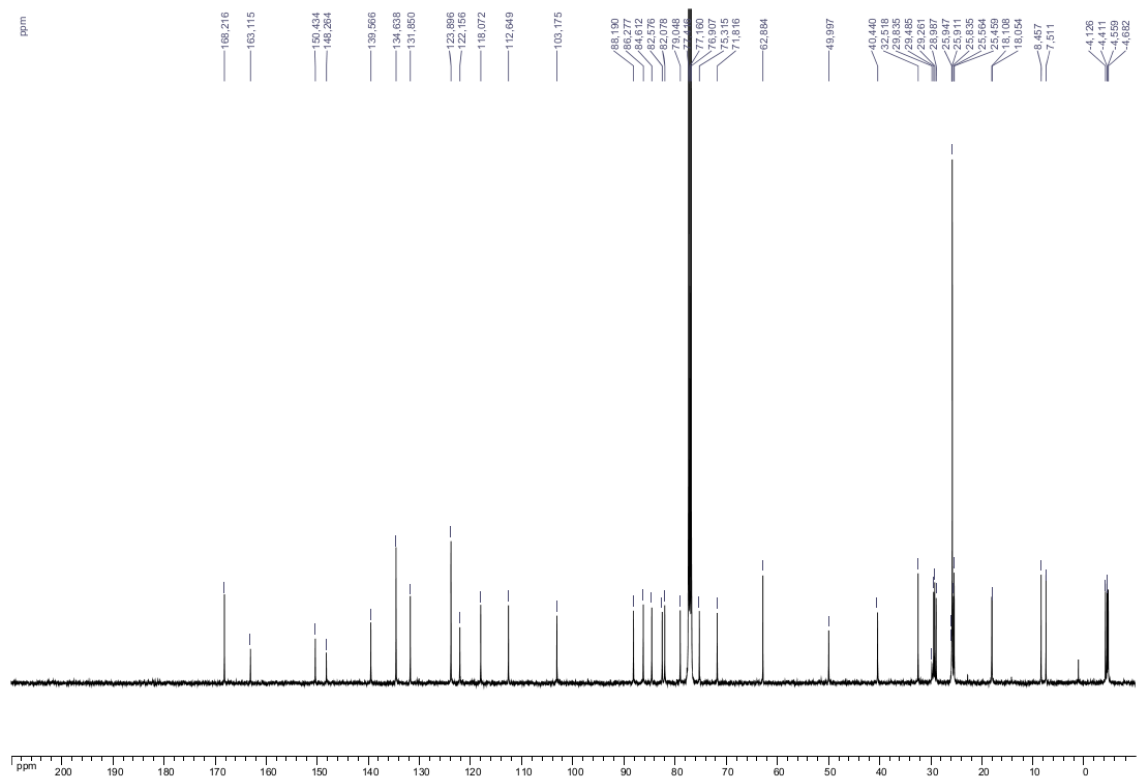
^{13}C NMR, 125 MHz (CDCl_3)



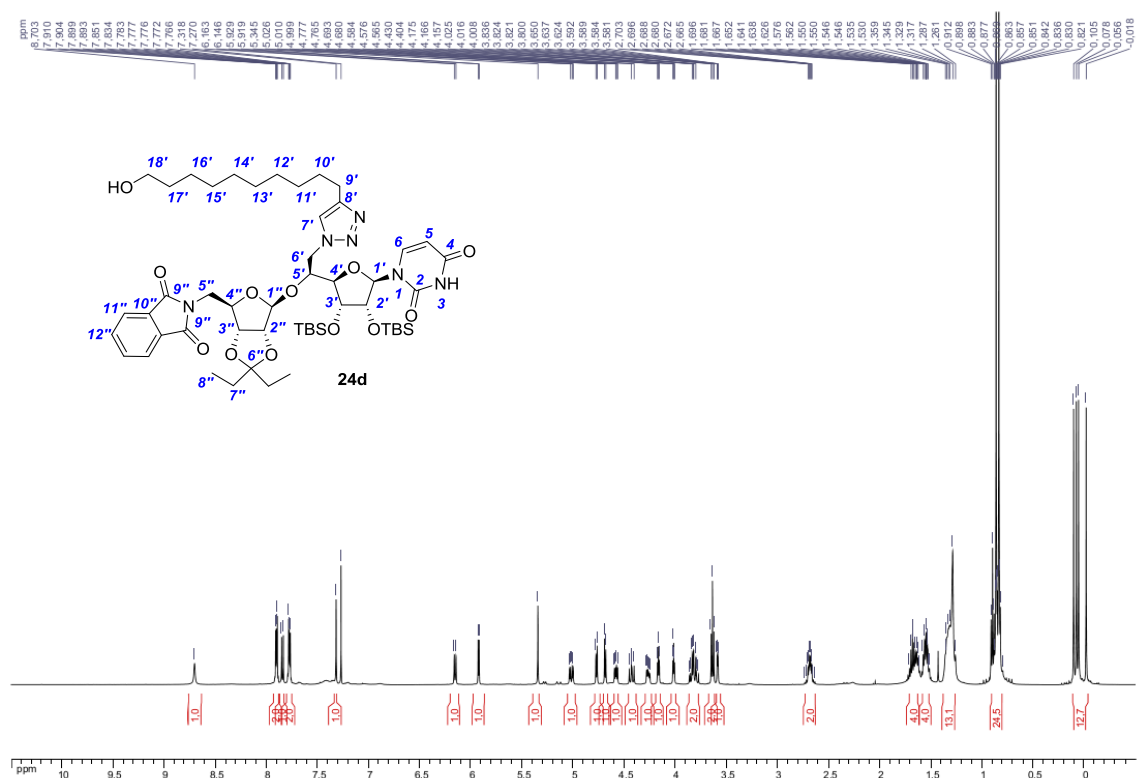
^1H NMR, 500 MHz (CDCl_3), compound **24c**



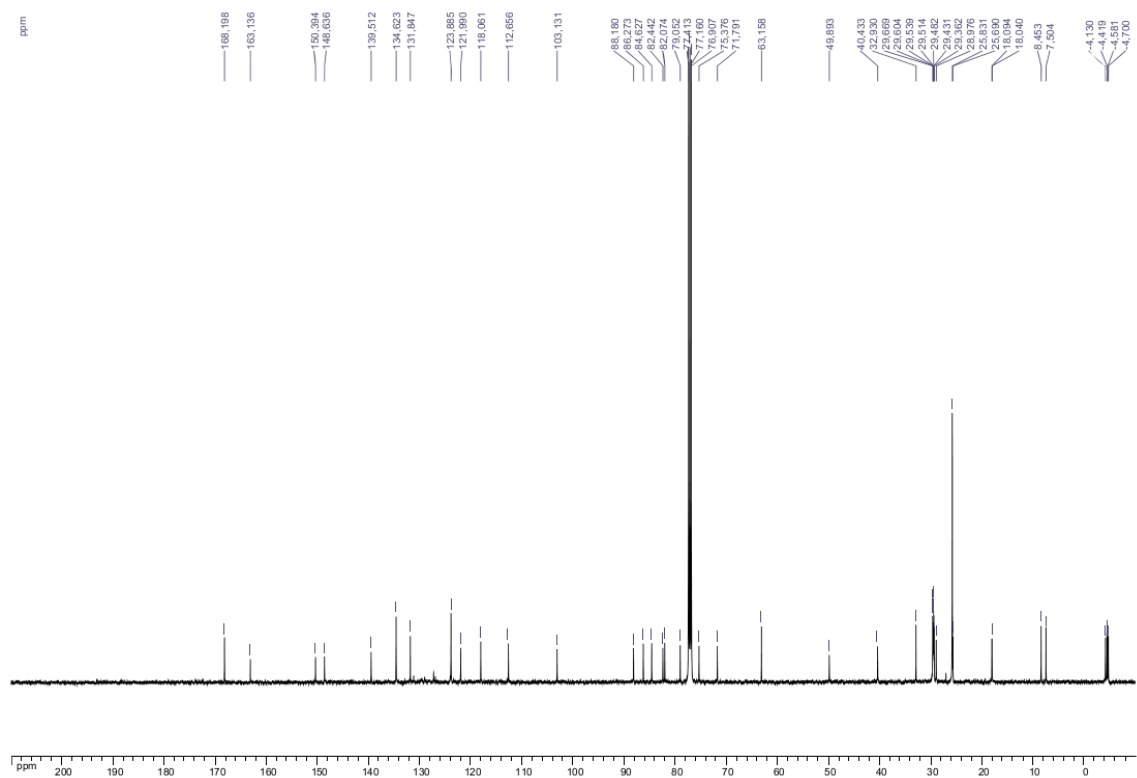
^{13}C NMR, 125 MHz (CDCl_3)



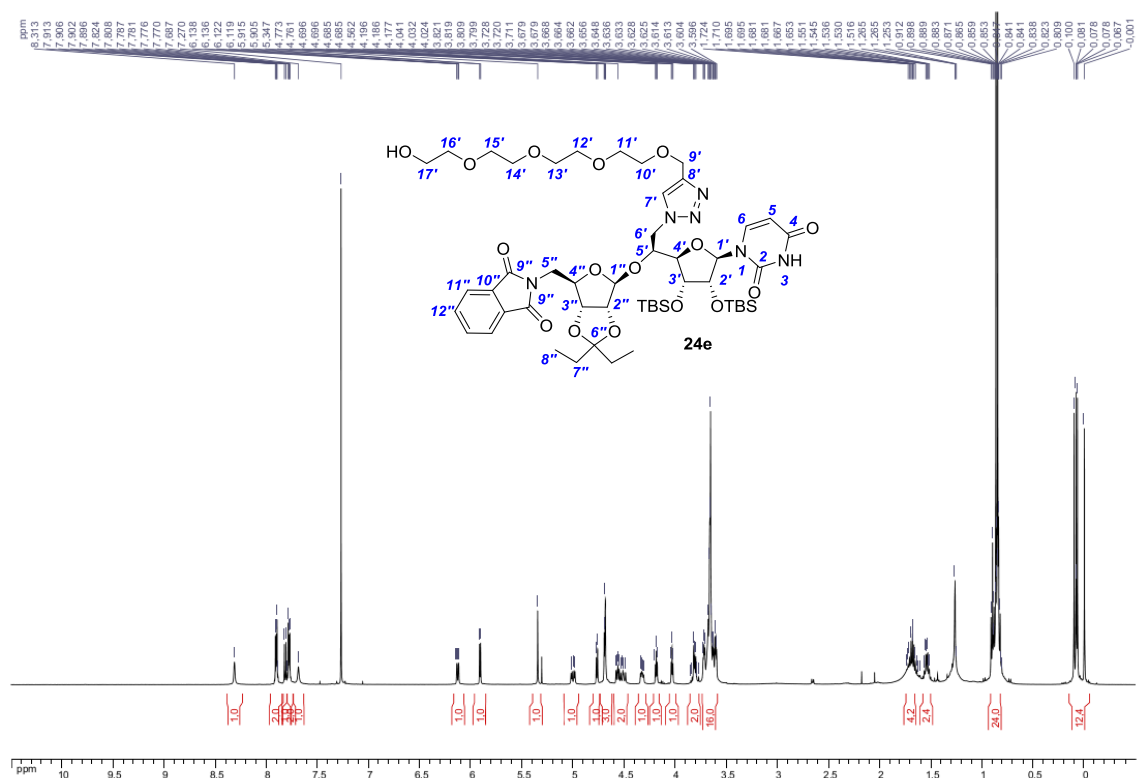
^1H NMR, 500 MHz (CDCl_3), compound **24d**



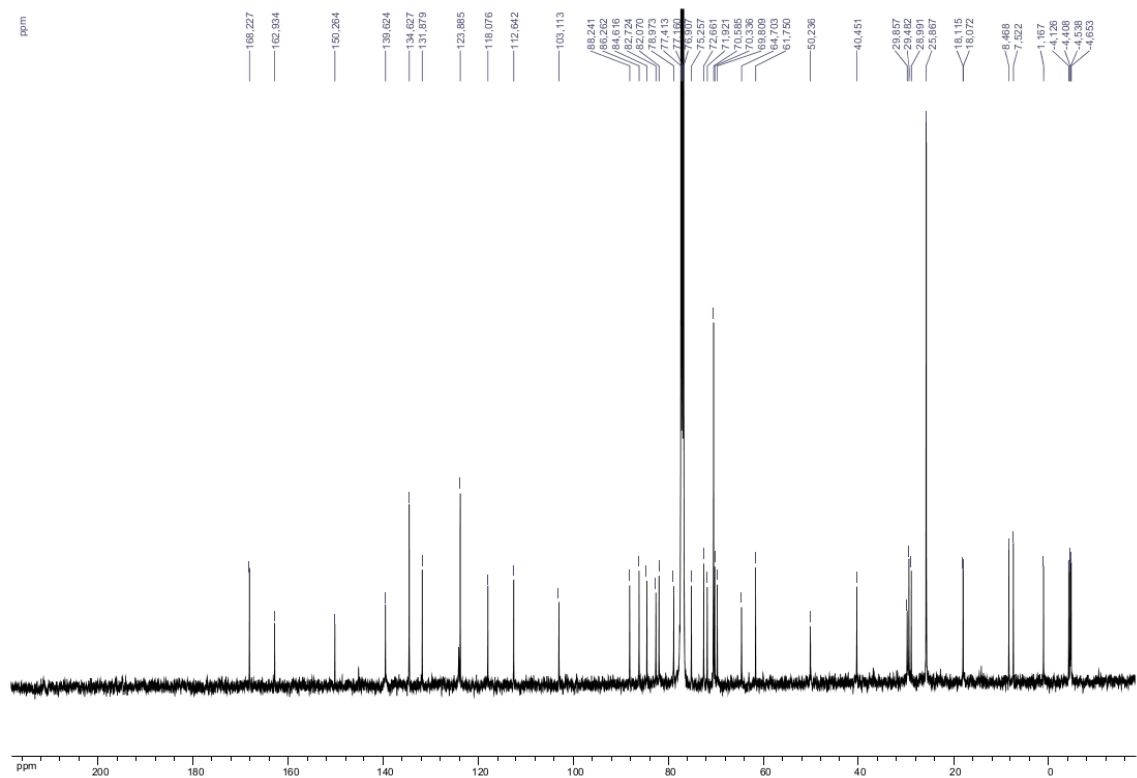
^{13}C NMR, 125 MHz (CDCl_3)

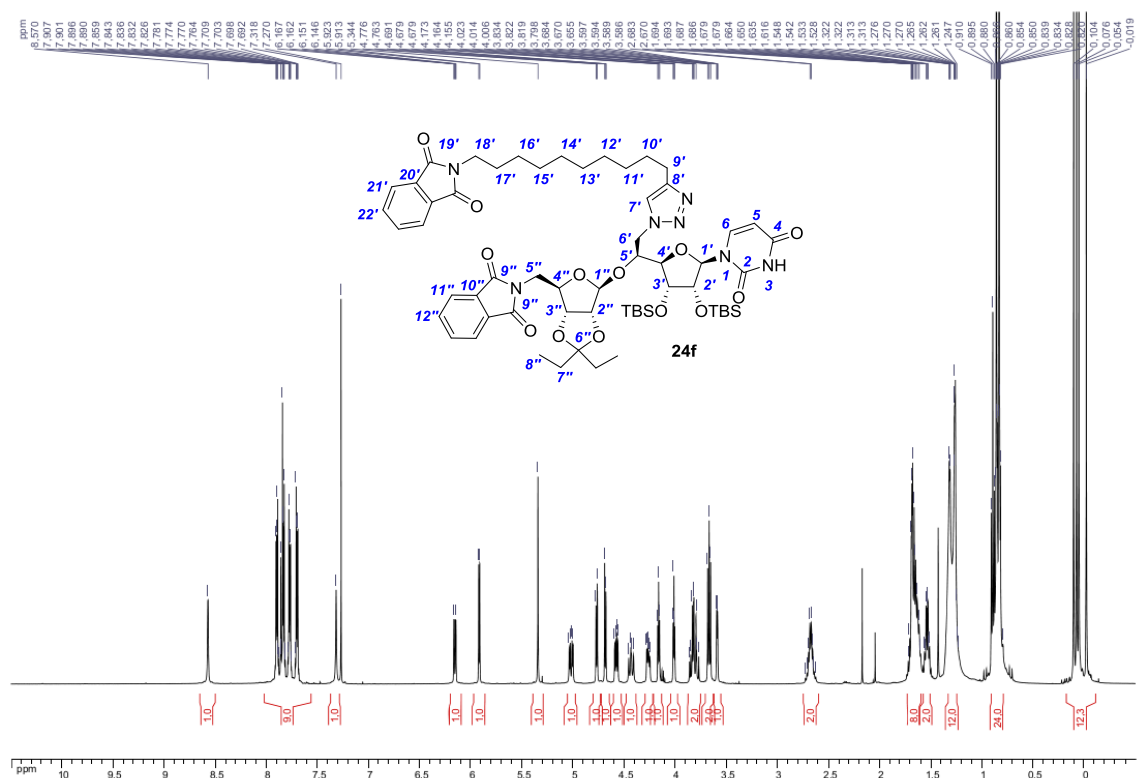
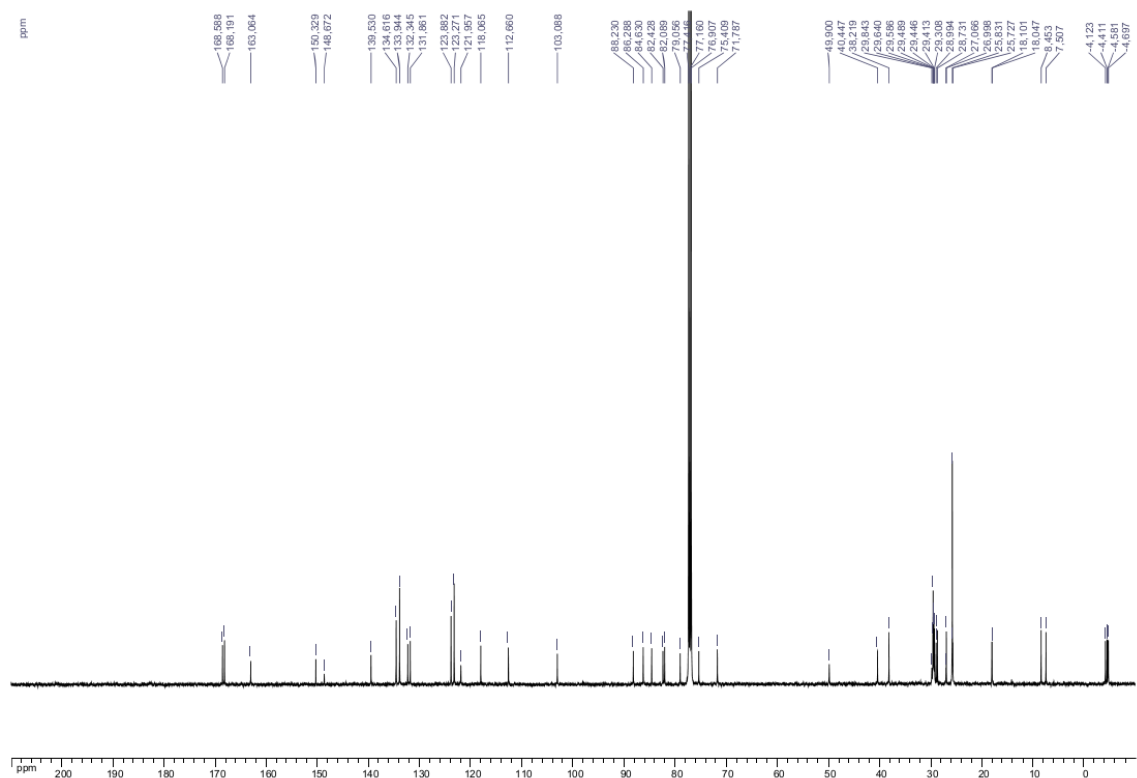


^1H NMR, 500 MHz (CDCl_3), compound **24e**

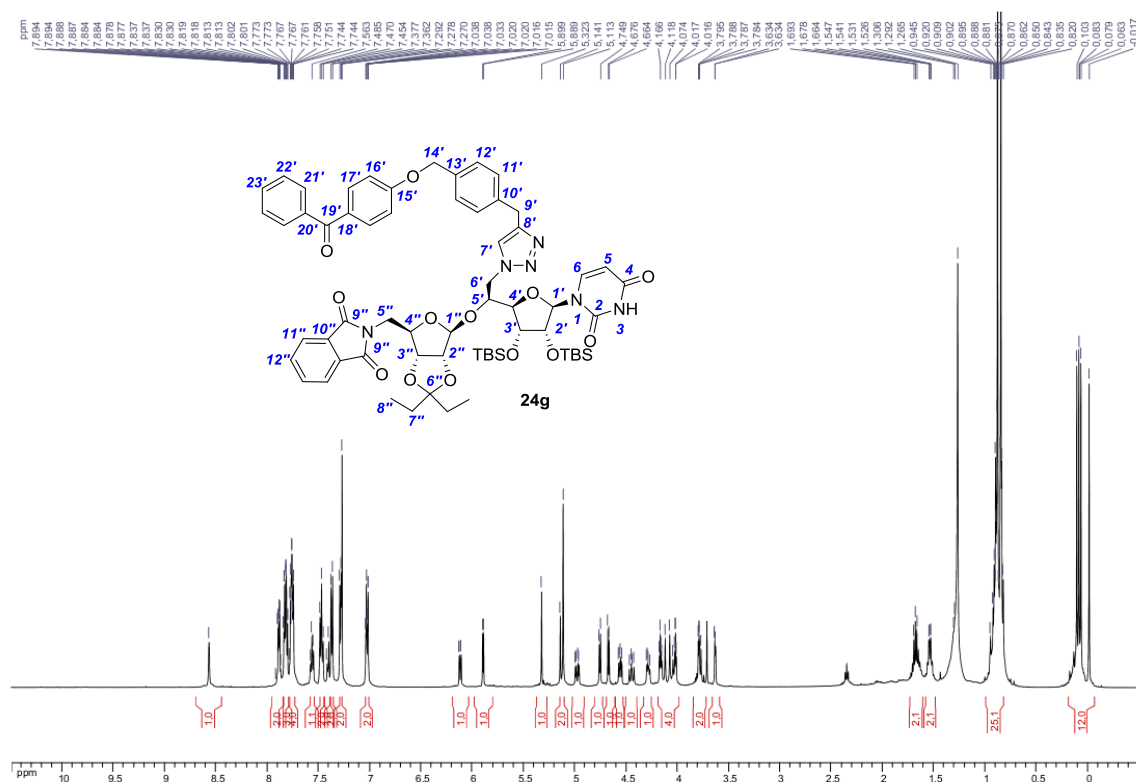


^{13}C NMR, 125 MHz (CDCl_3)

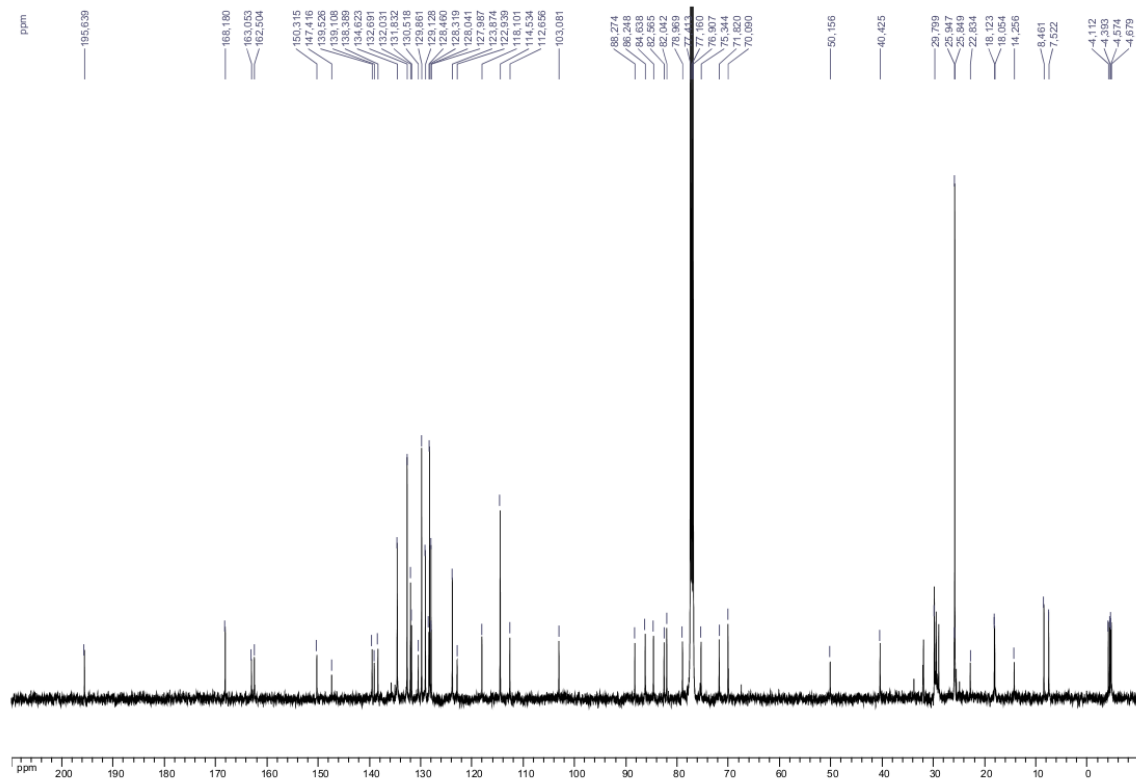


¹H NMR, 500 MHz (CDCl₃), compound **24f** ^{13}C NMR, 125 MHz (CDCl_3)

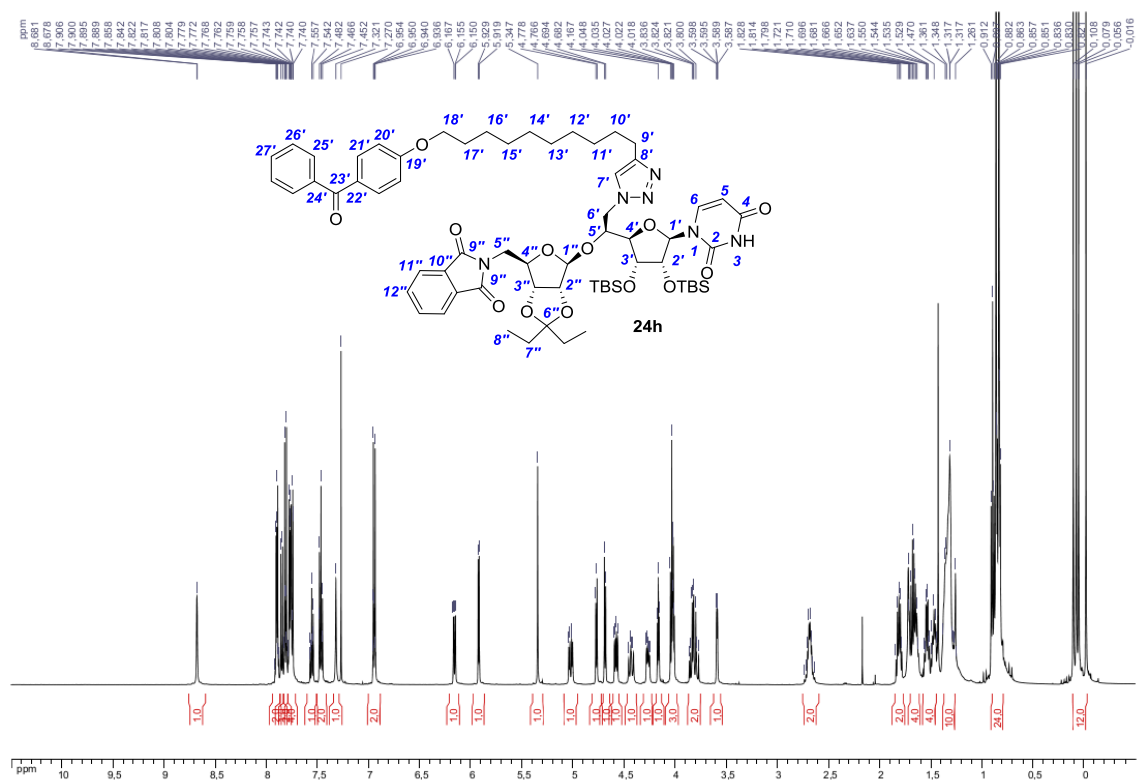
^1H NMR, 500 MHz (CDCl_3), compound **24g**

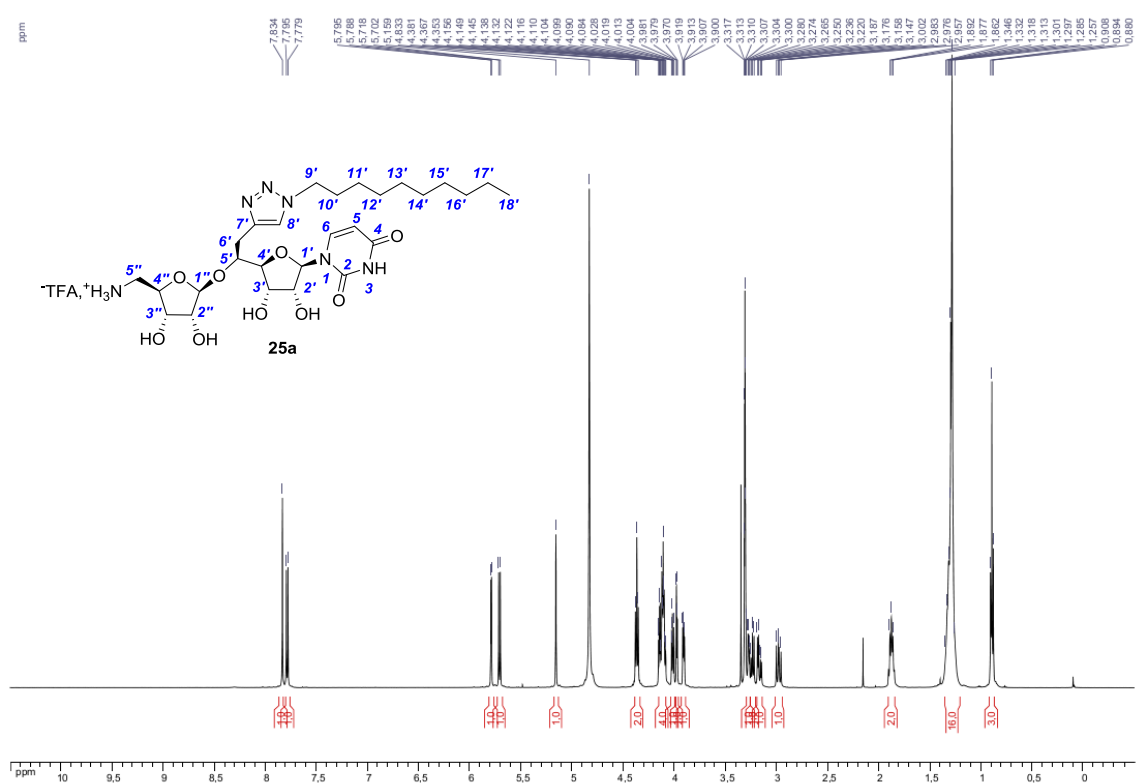
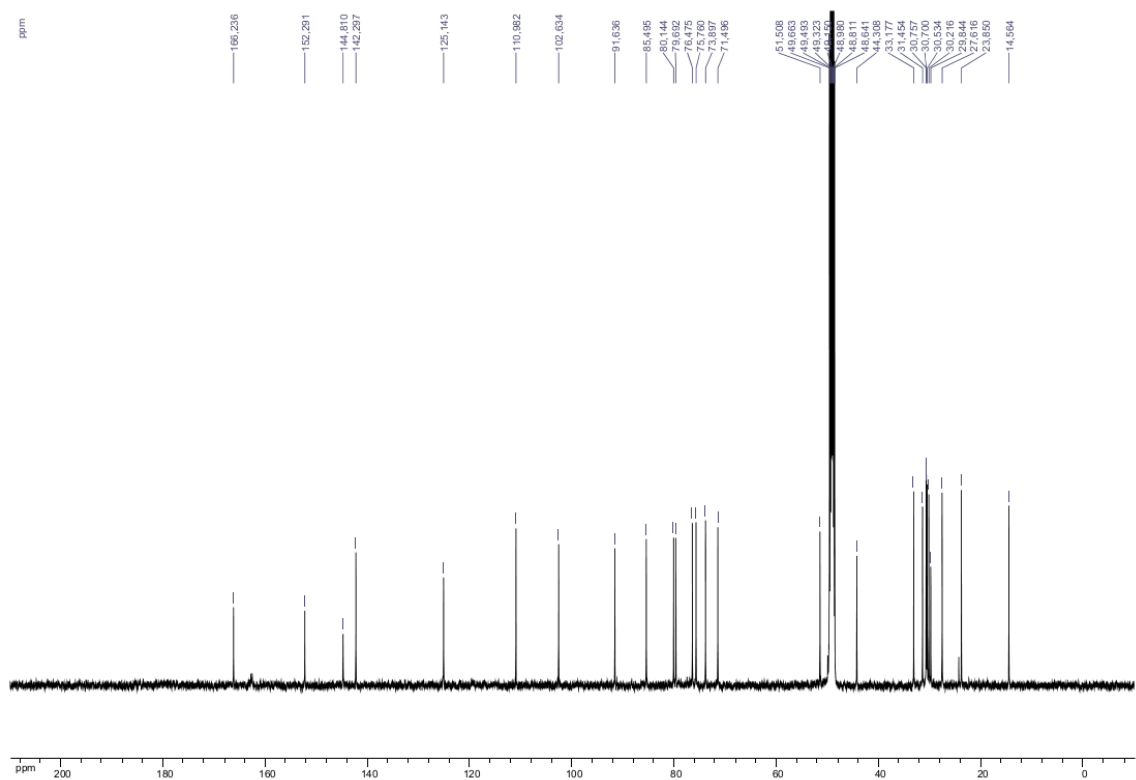


^{13}C NMR, 125 MHz (CDCl_3)

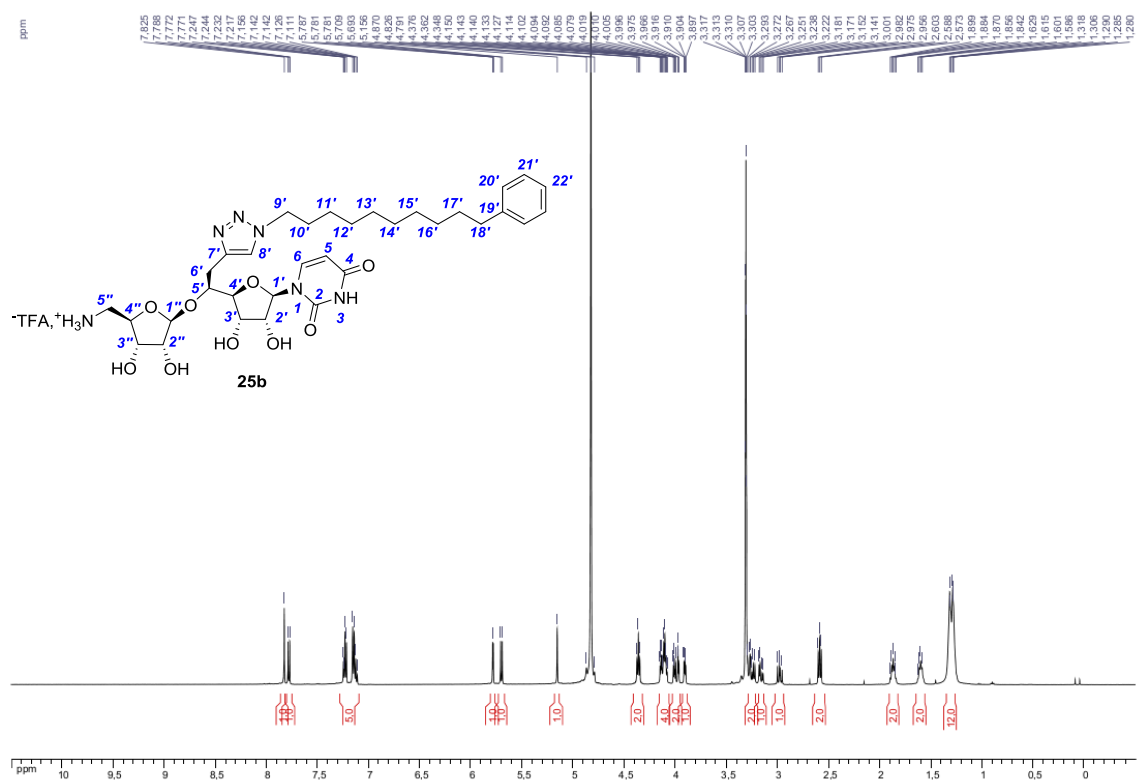


^1H NMR, 500 MHz (CDCl_3), compound **24h**

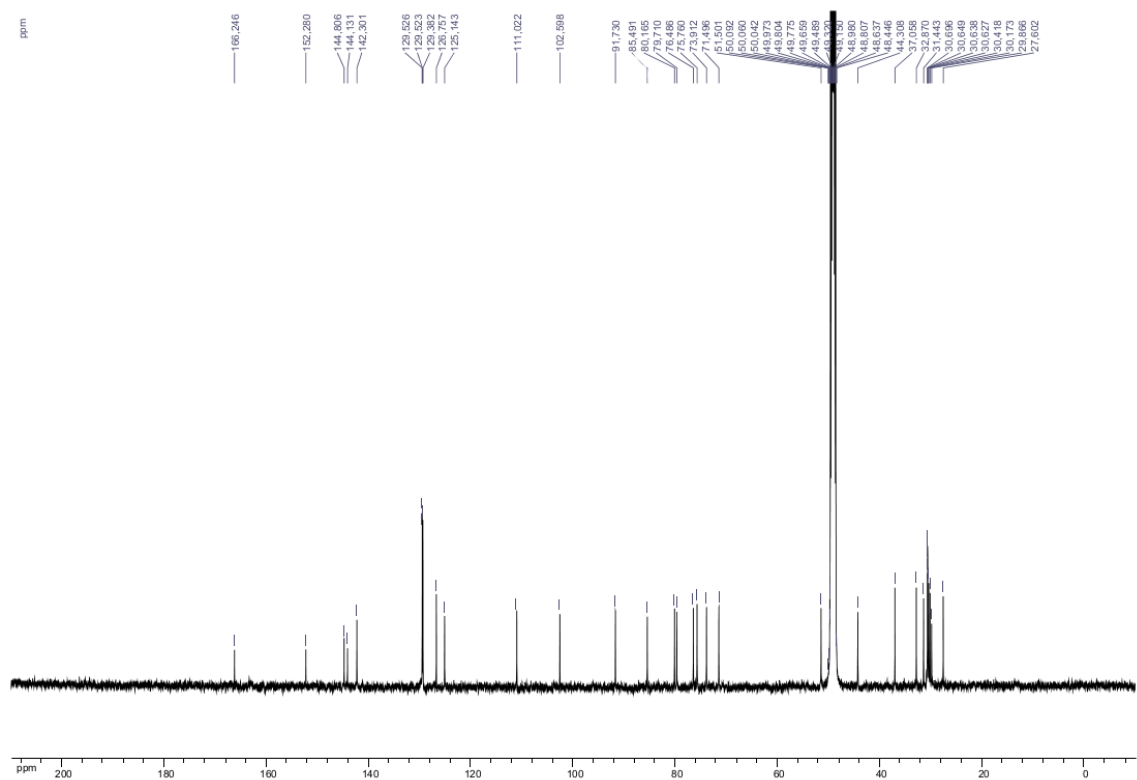


¹H NMR, 500 MHz (CD₃OD), compound **25a** ^{13}C NMR, 125 MHz (CD_3OD)

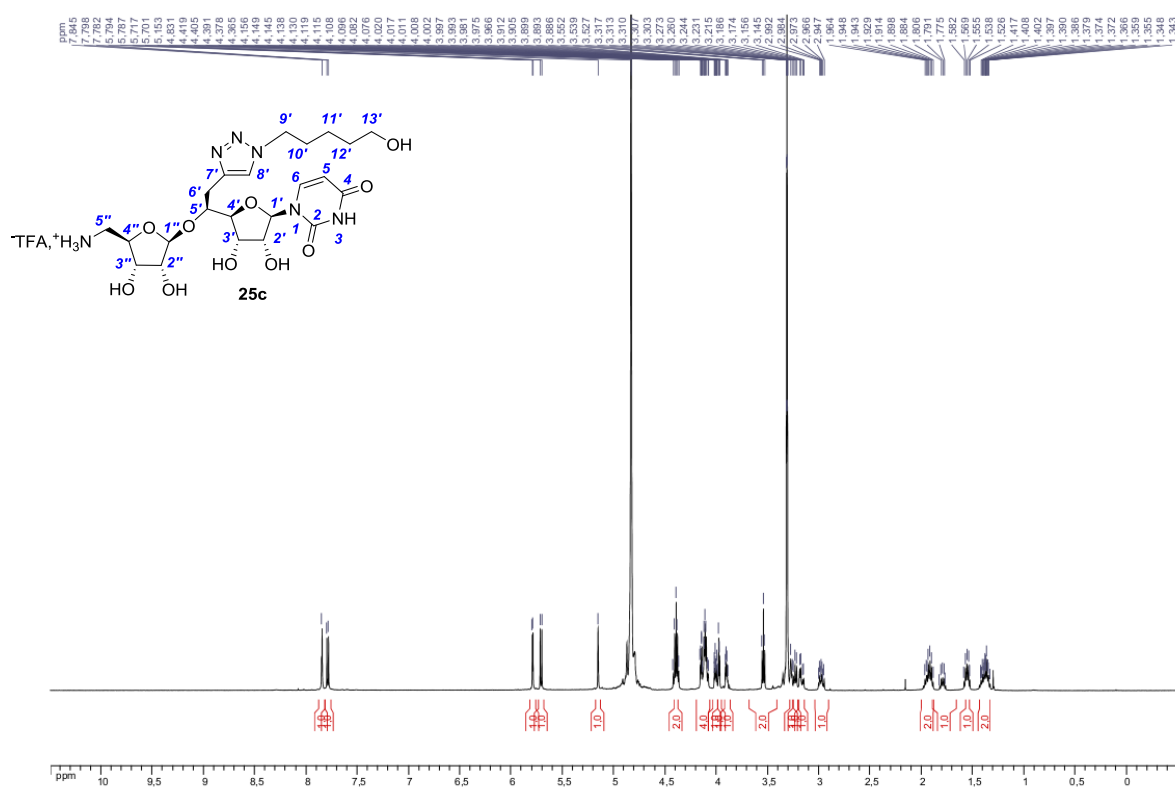
^1H NMR, 500 MHz (CD_3OD), compound **25b**

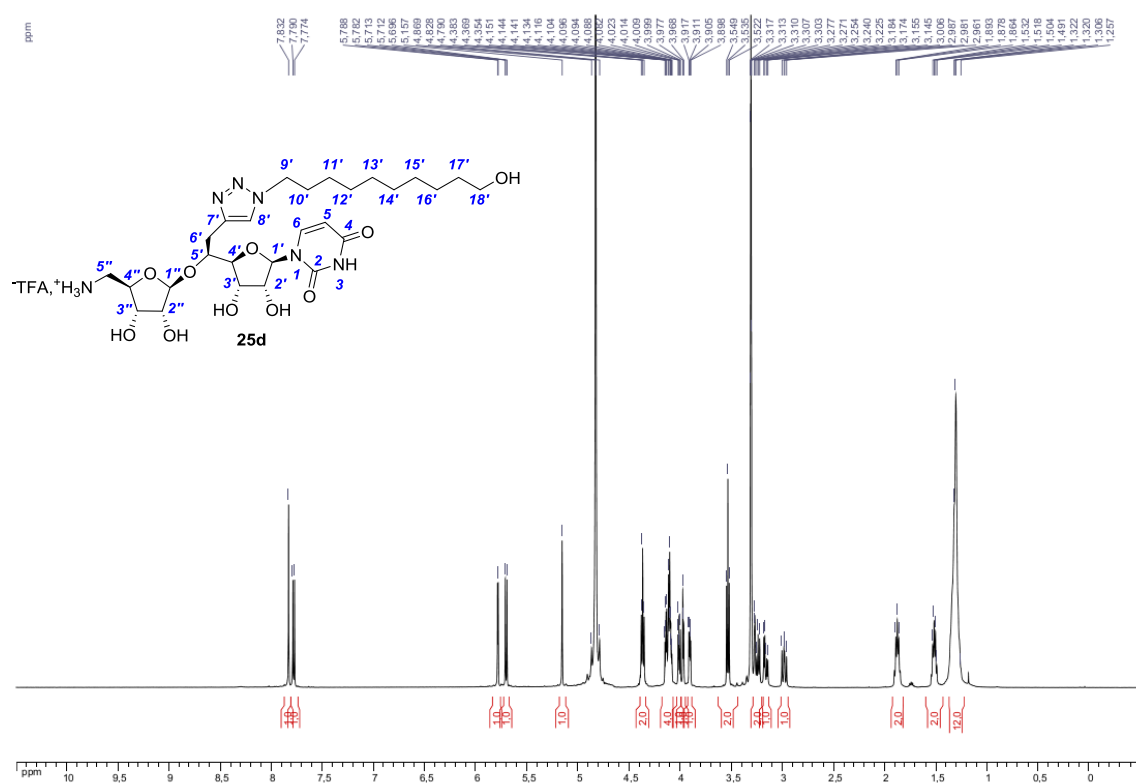
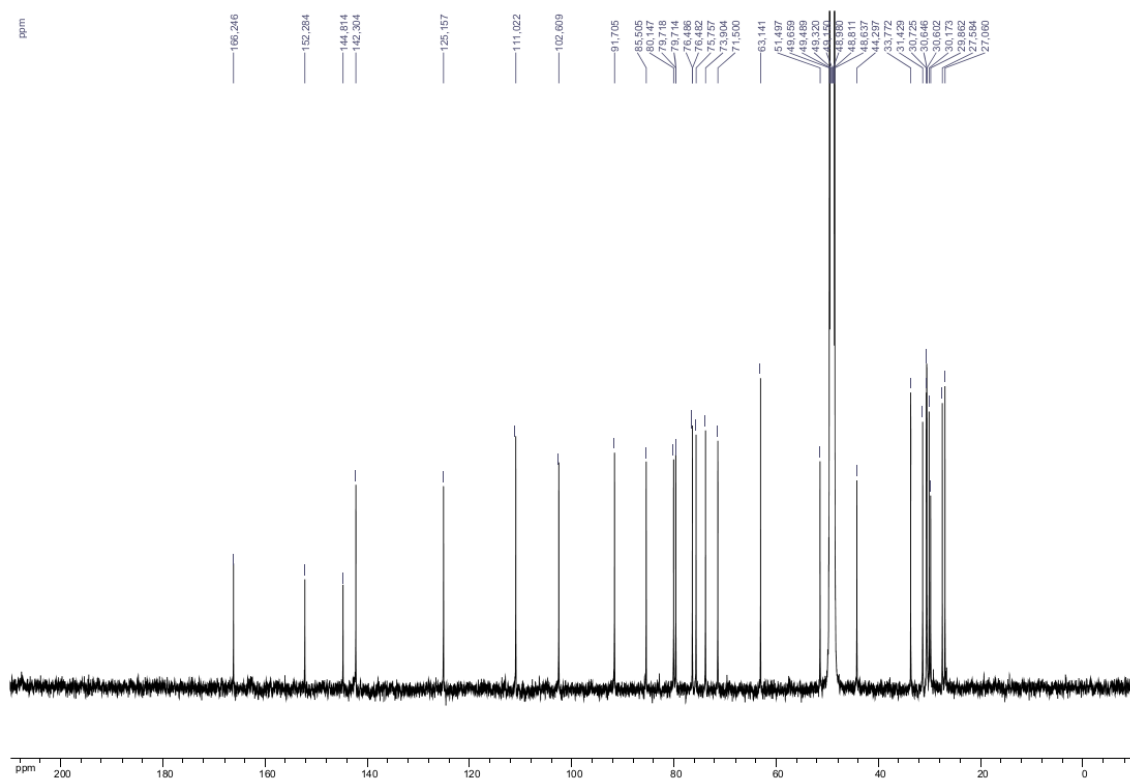


^{13}C NMR, 125 MHz (CD_3OD)

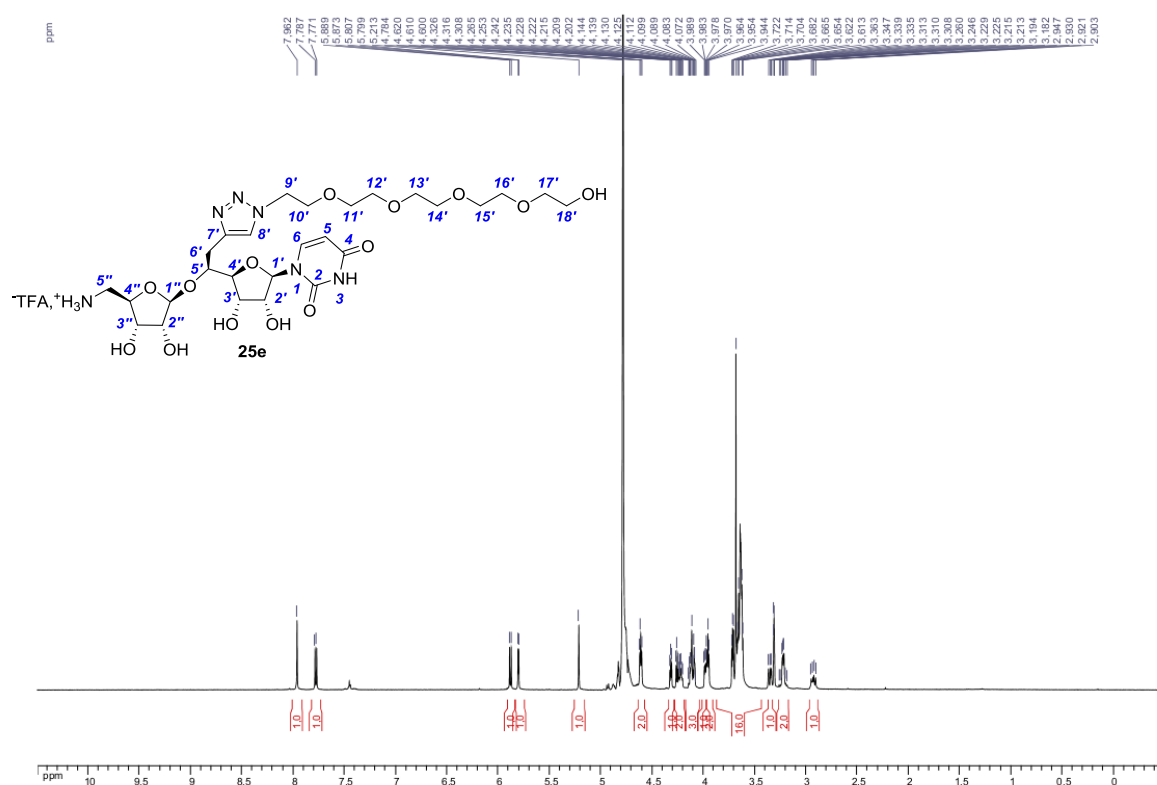


^1H NMR, 500 MHz (CD_3OD), compound **25c**

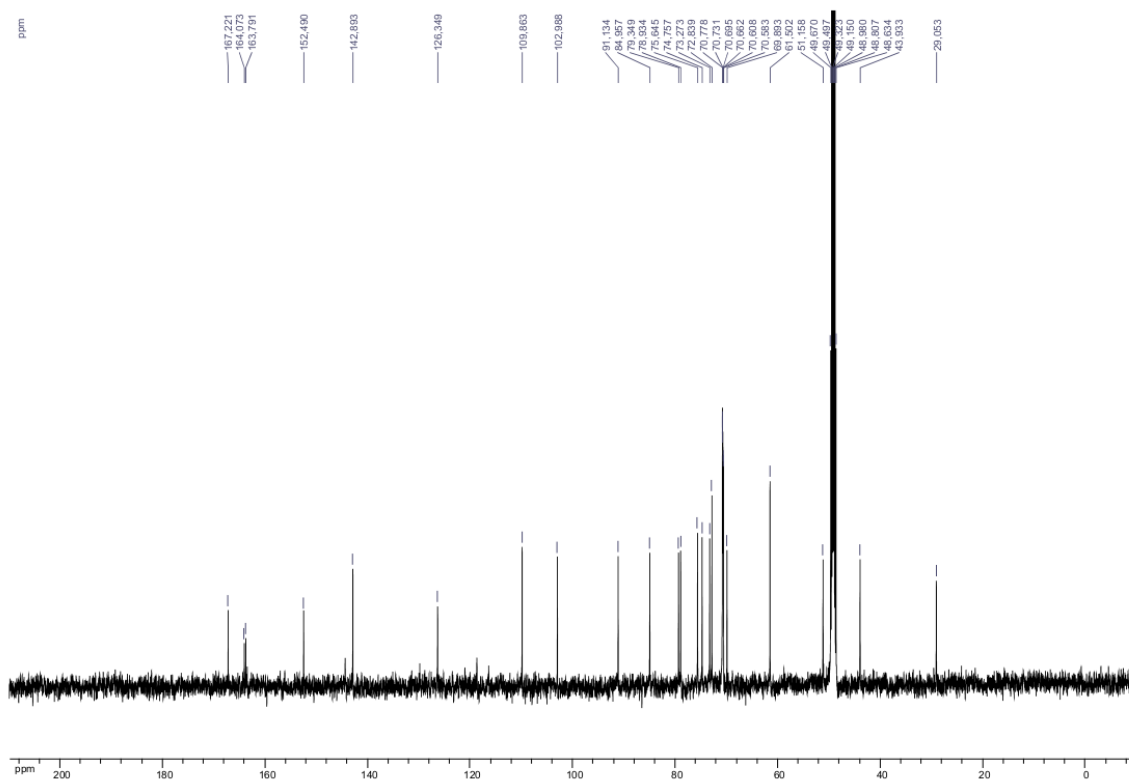


¹H NMR, 500 MHz (CD₃OD), compound **25d** ^{13}C NMR, 125 MHz (CD_3OD)

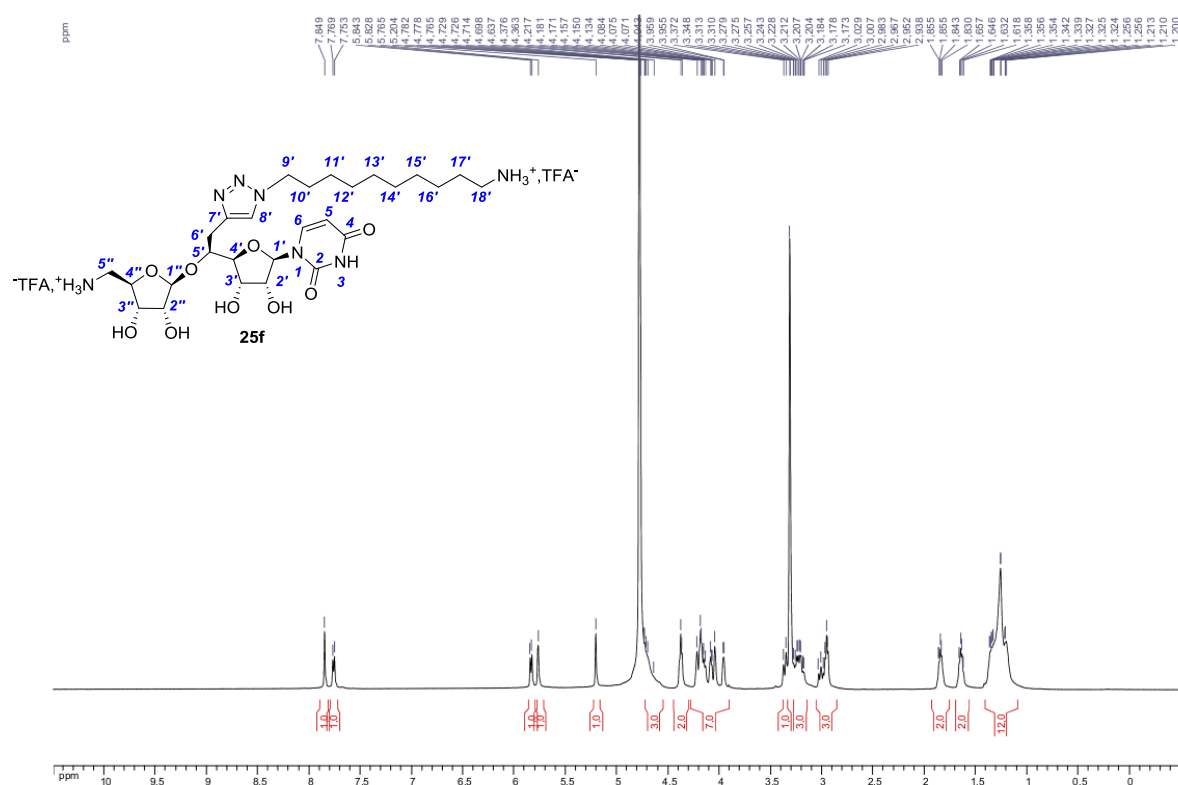
^1H NMR, 500 MHz ($\text{D}_2\text{O} + 50\mu\text{L CD}_3\text{OD}$), compound **25e**



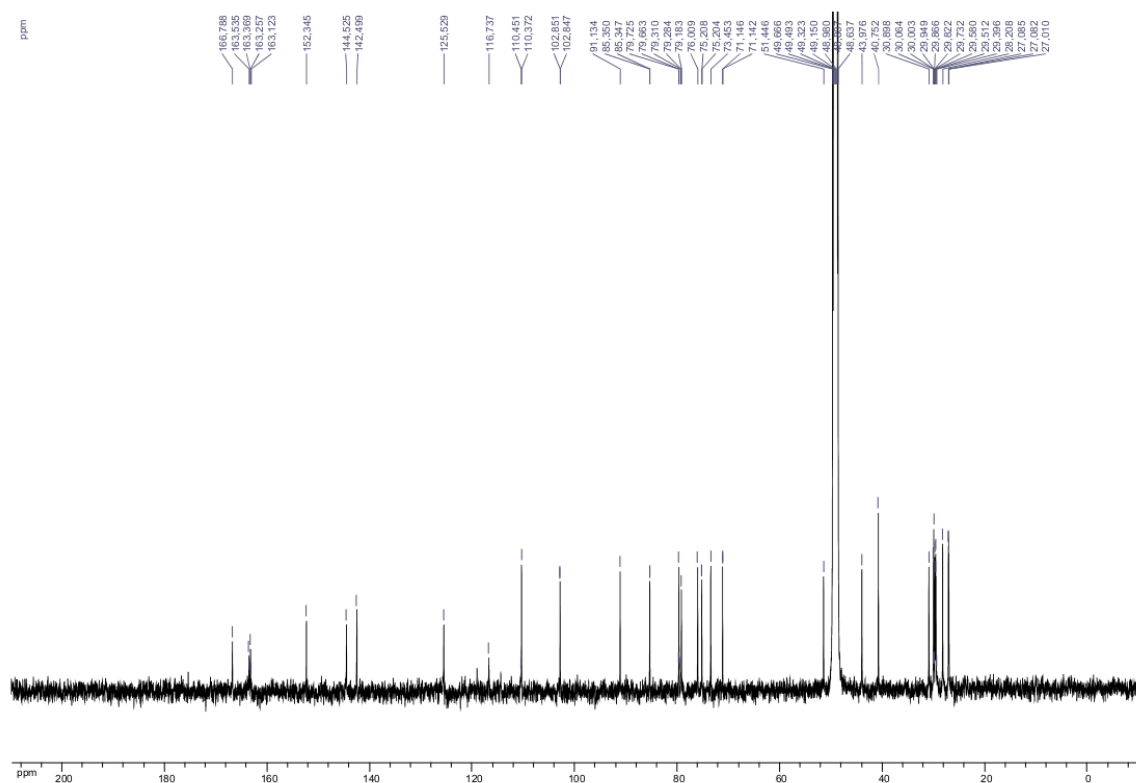
^{13}C NMR, 125 MHz ($\text{D}_2\text{O} + 50\mu\text{L CD}_3\text{OD}$)



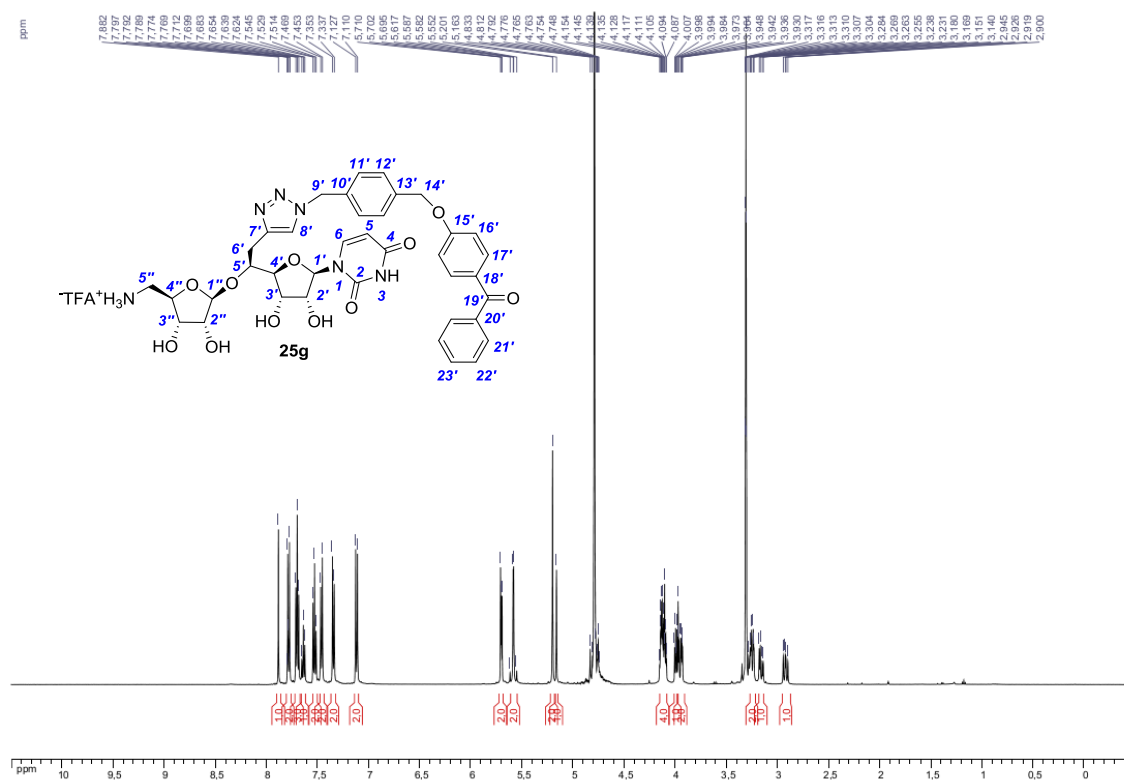
^1H NMR, 500 MHz ($\text{CD}_3\text{OD} : \text{D}_2\text{O}$ 1:1), compound **25f**



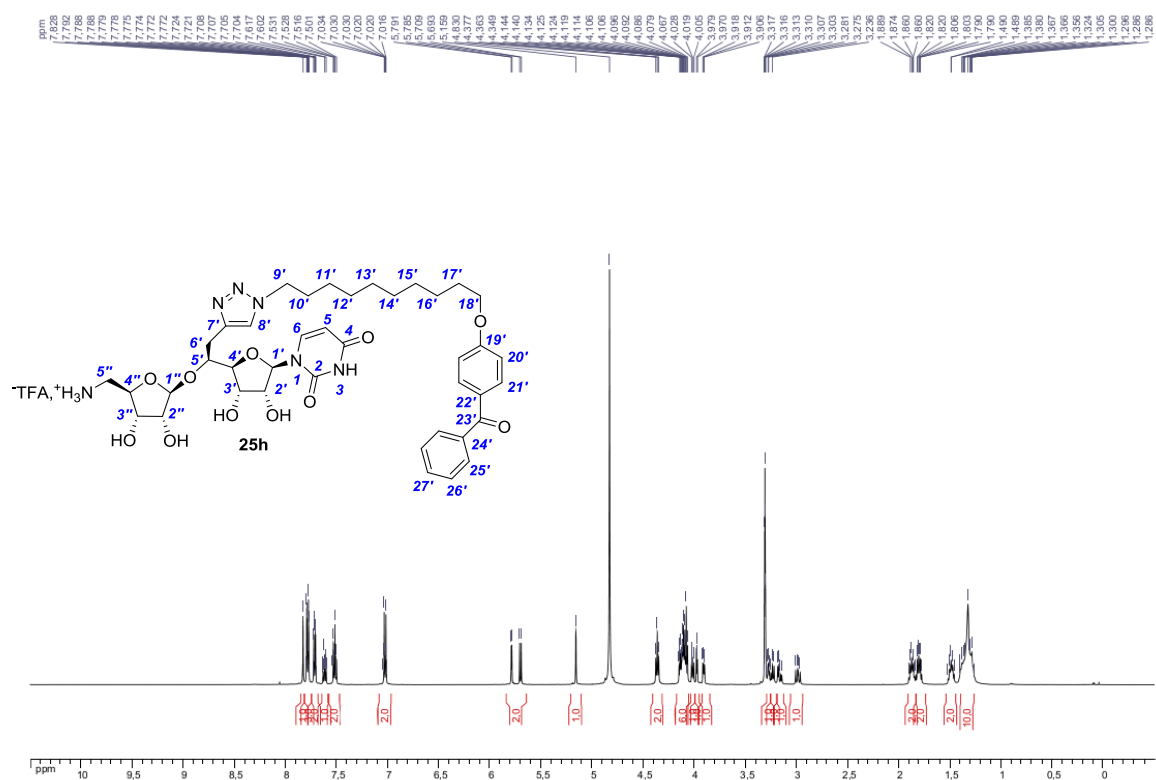
^{13}C NMR, 125 MHz ($\text{CD}_3\text{OD} : \text{D}_2\text{O}$ 1:1)

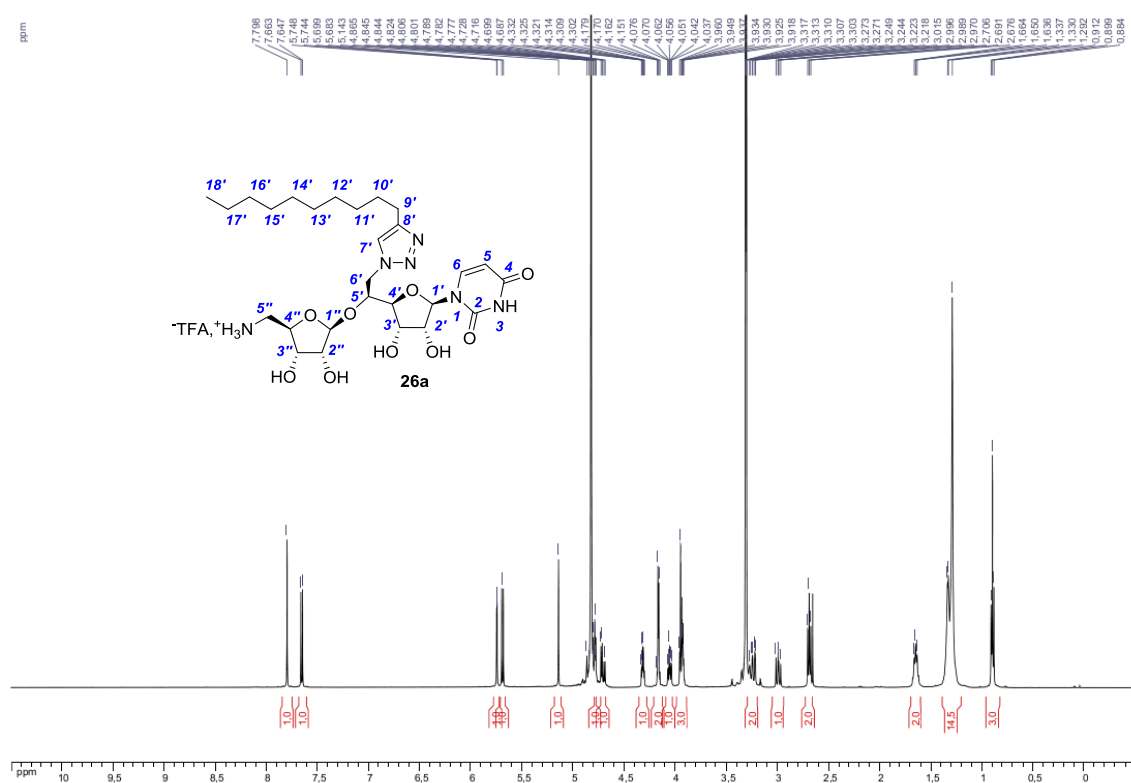
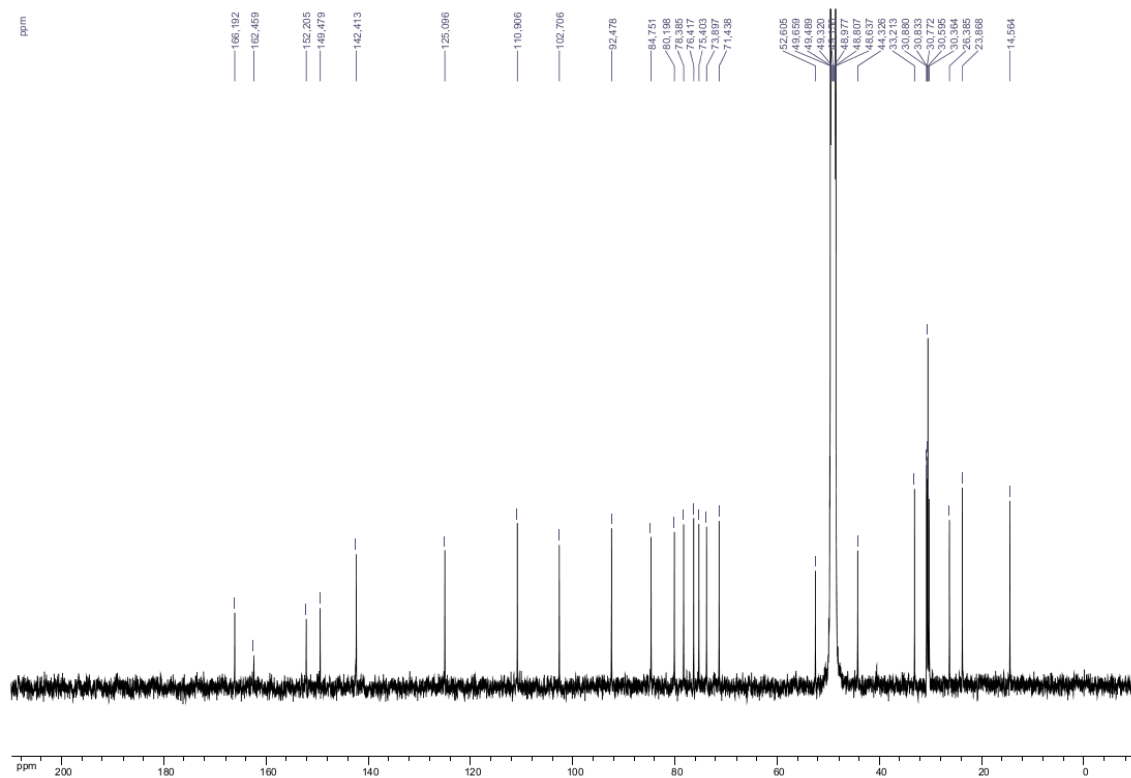


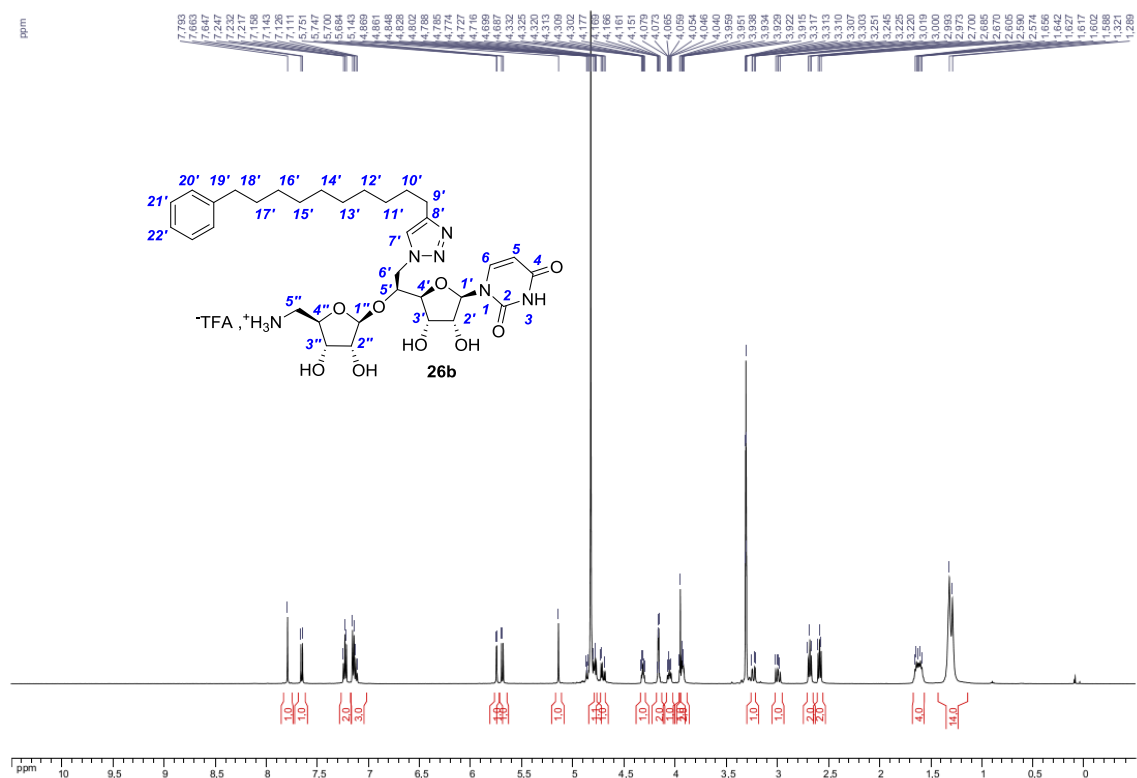
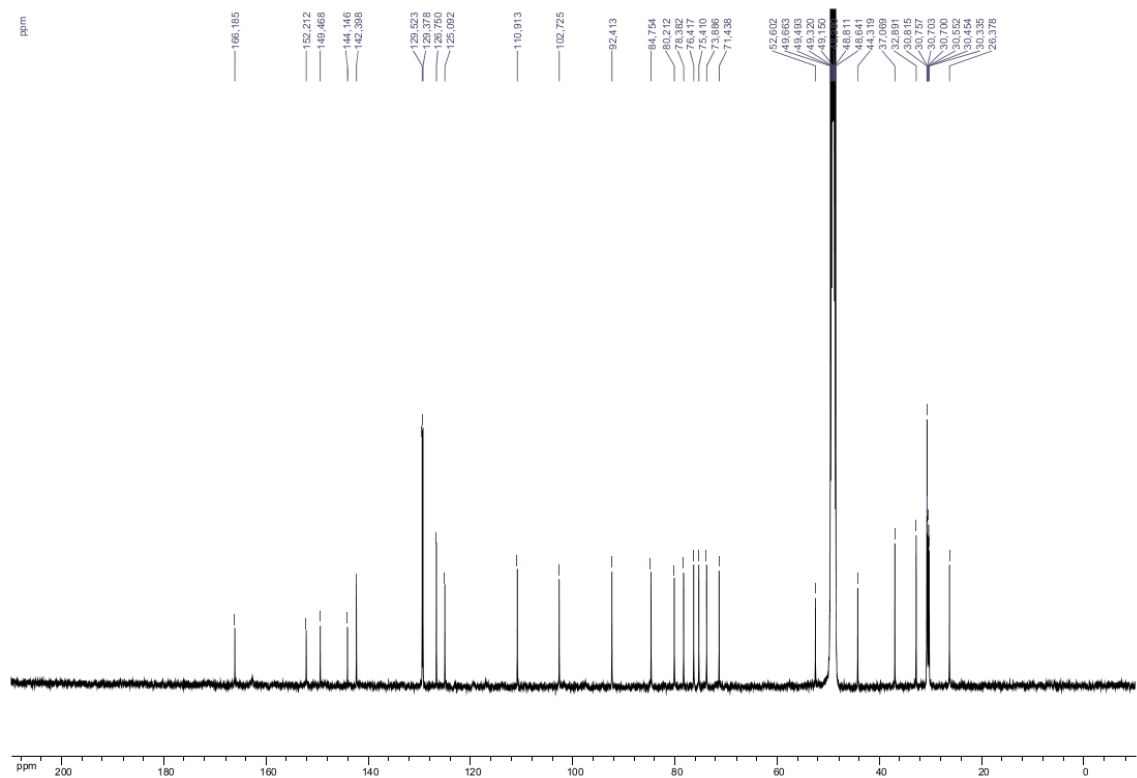
^1H NMR, 500 MHz (CD_3OD), compound **25g**



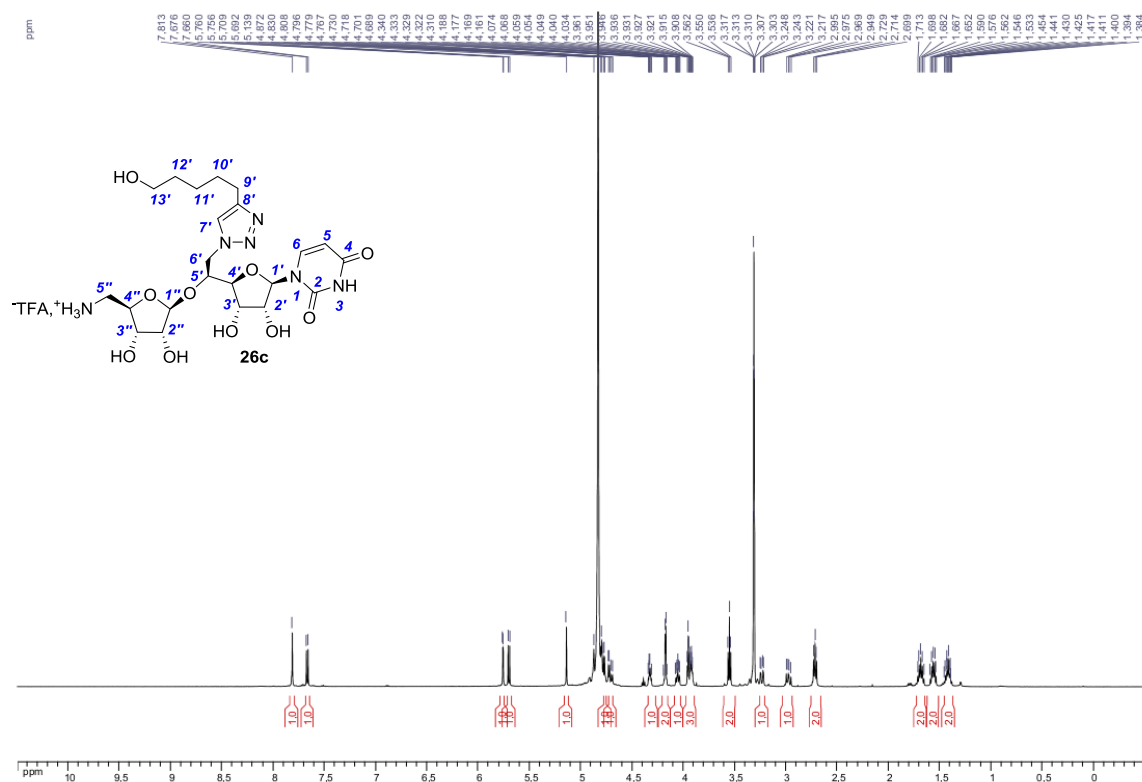
^1H NMR, 500 MHz (CD_3OD), compound **25h**



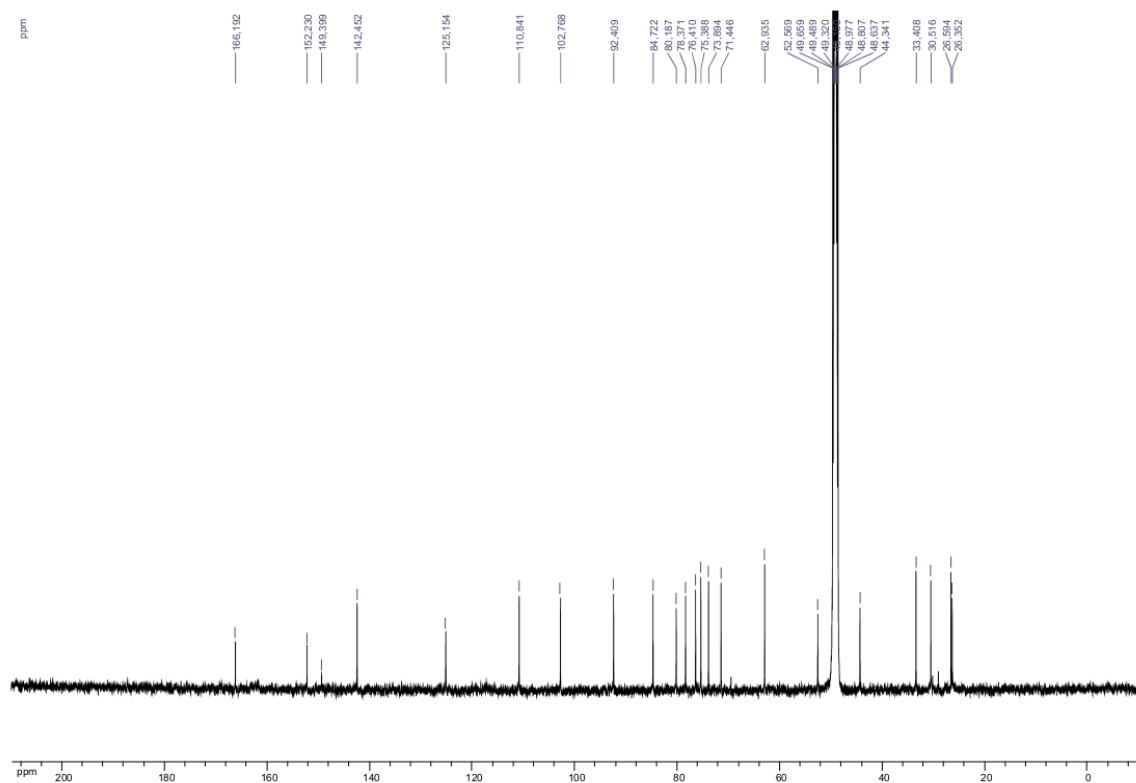
¹H NMR, 500 MHz (CD₃OD), compound **26a** ^{13}C NMR, 125 MHz (CD_3OD)

¹H NMR, 500 MHz (CD₃OD), compound **26b** ^{13}C NMR, 125 MHz (CD_3OD)

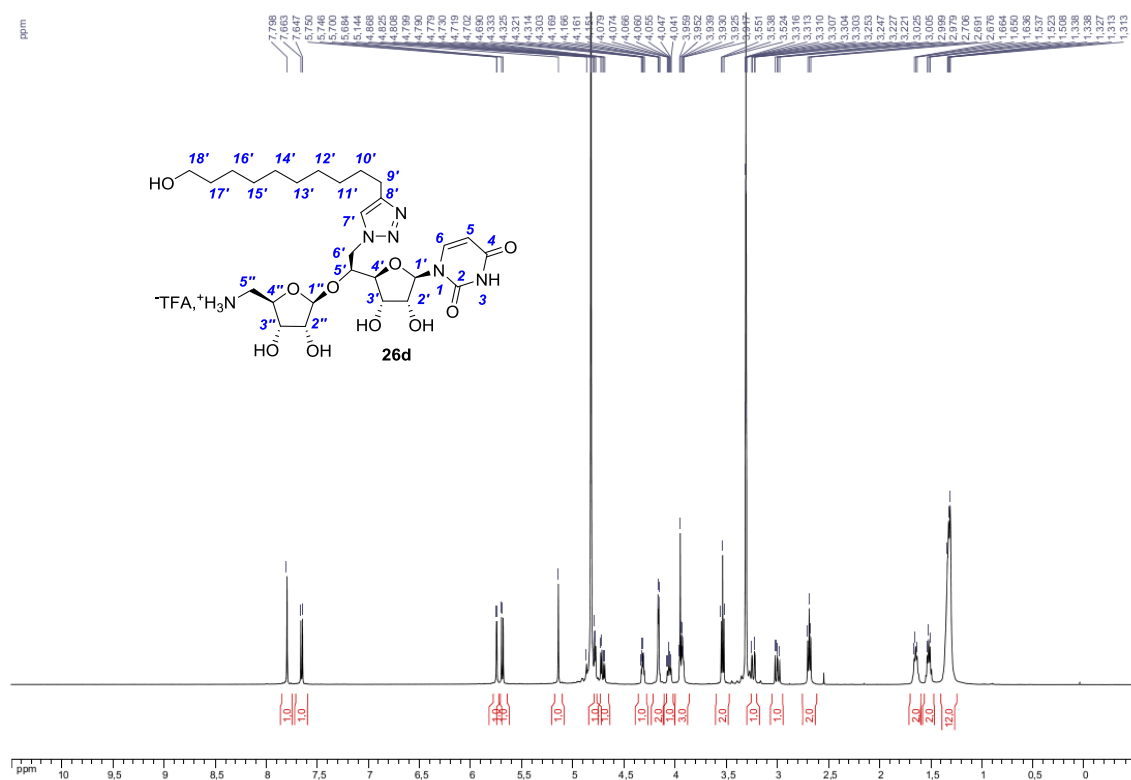
^1H NMR, 500 MHz (CD_3OD), compound **26c**



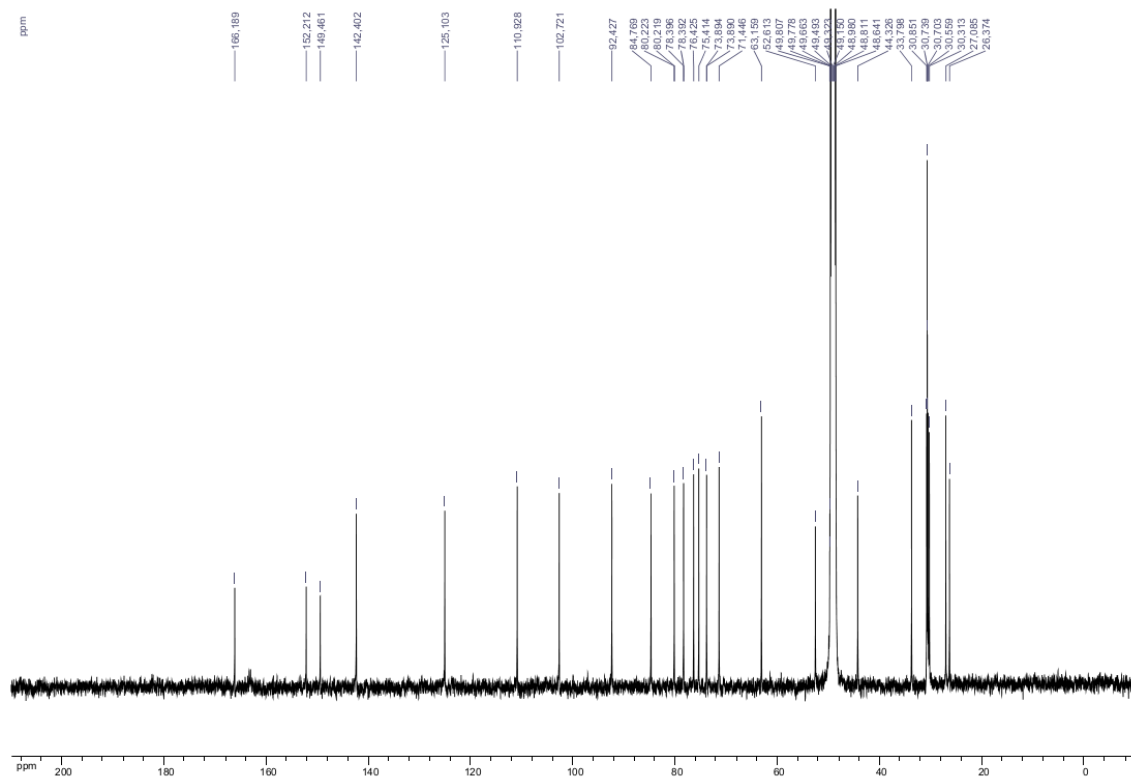
^{13}C NMR, 125 MHz (CD_3OD)

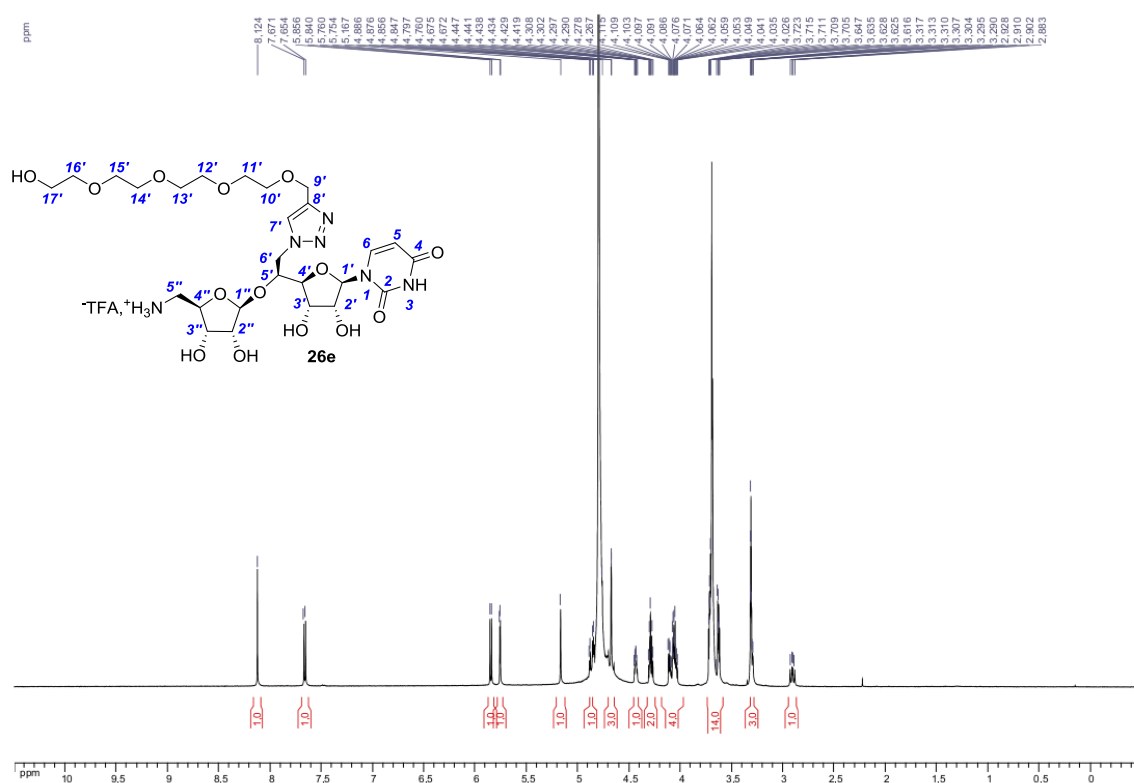
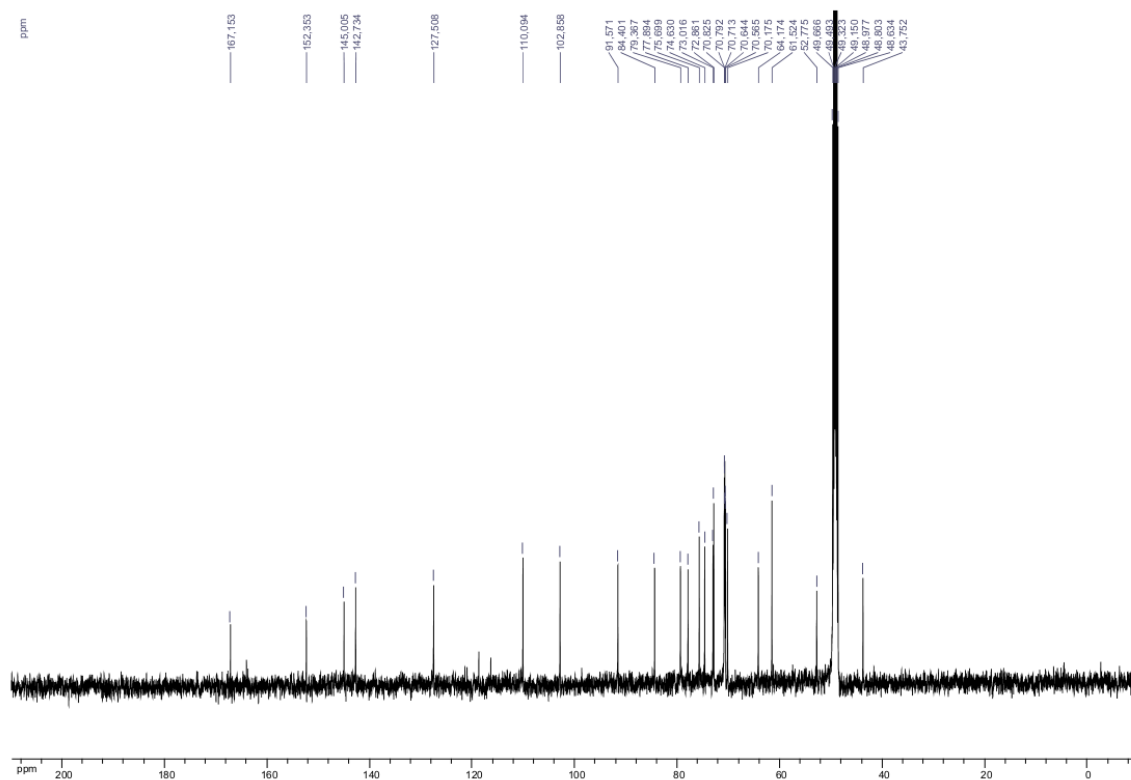


^1H NMR, 500 MHz (CD_3OD), compound **26d**

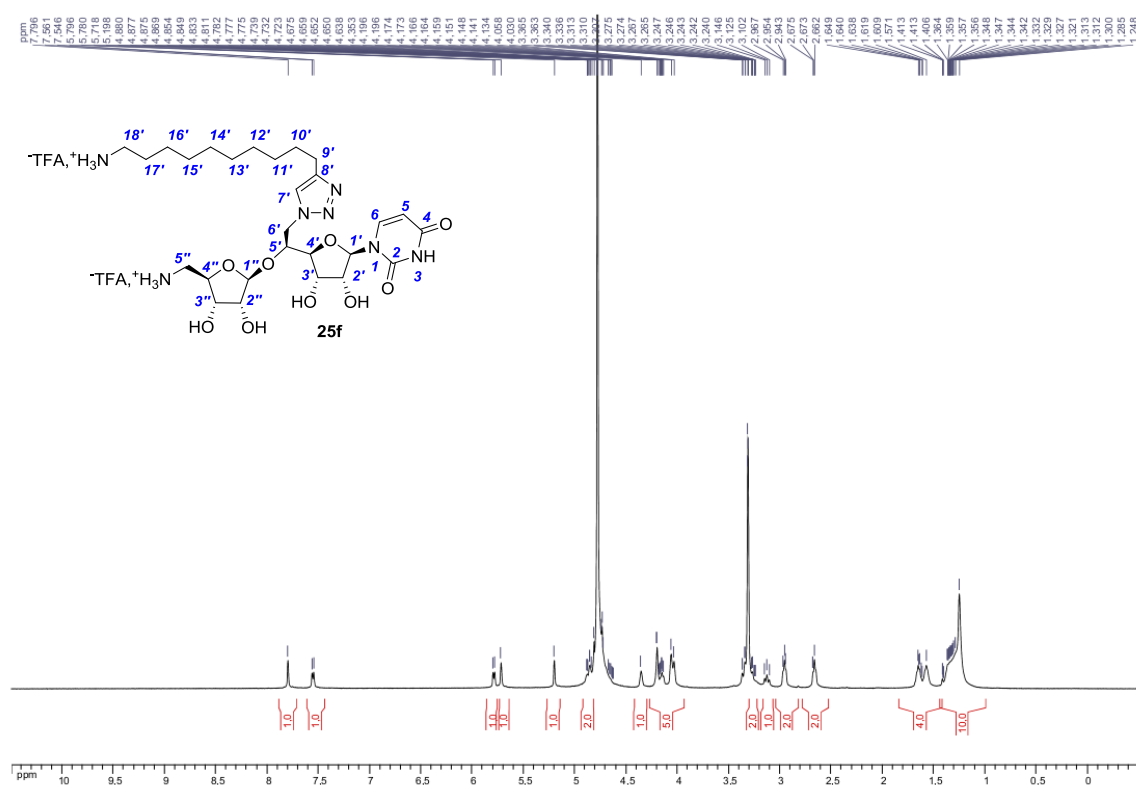


^{13}C NMR, 125 MHz (CD_3OD)

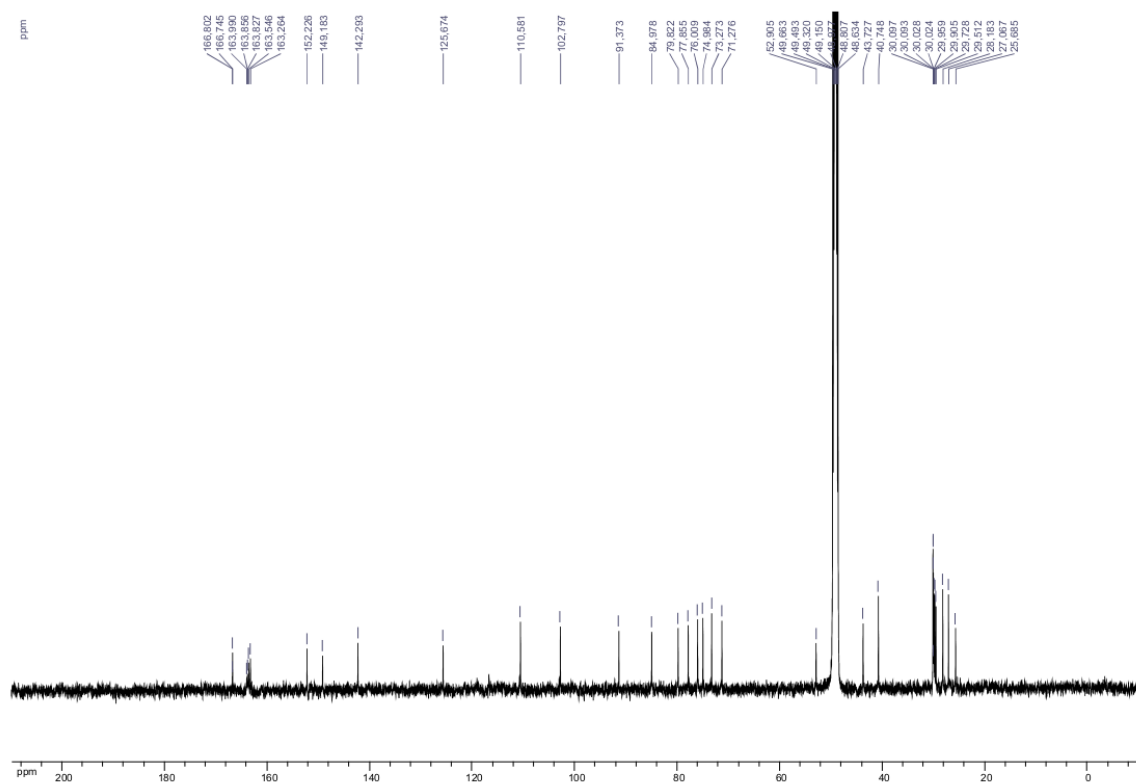


¹H NMR, 500 MHz (D₂O + 50 μL CD₃OD), compound **26e**¹³C NMR, 125 MHz (D₂O + 50 μL CD₃OD)

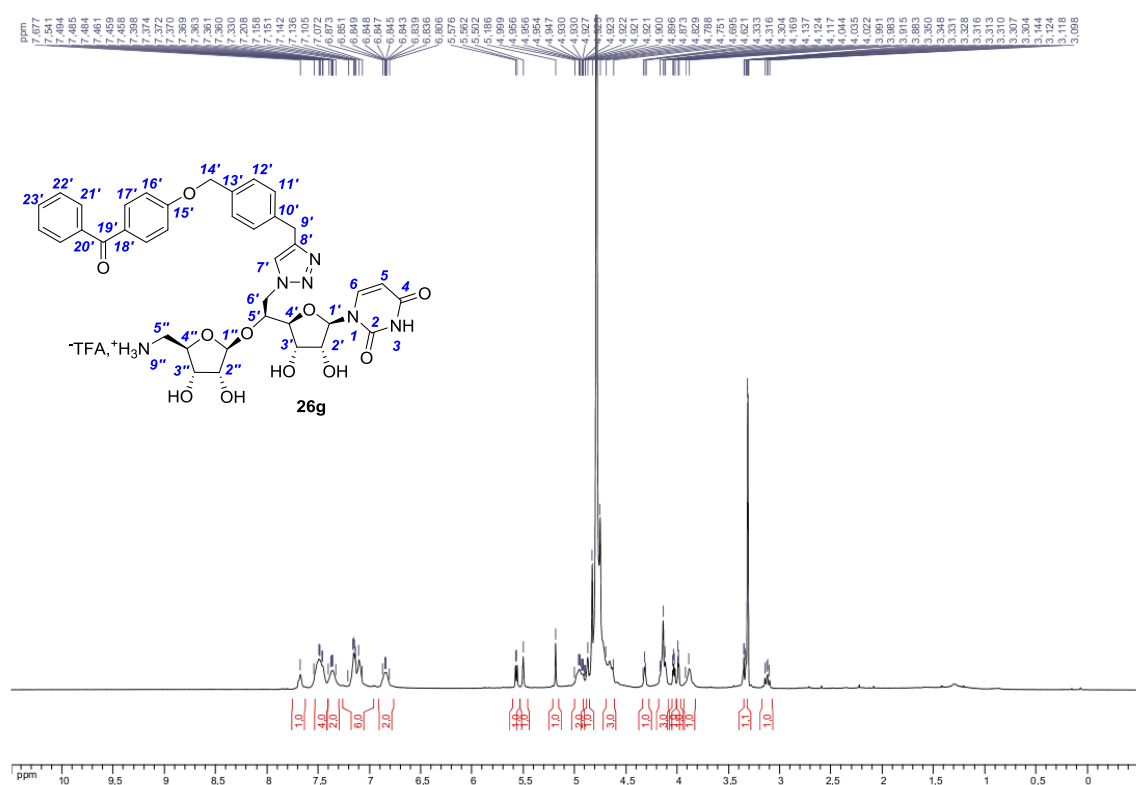
^1H NMR, 500 MHz ($\text{CD}_3\text{OD} : \text{D}_2\text{O}$ 1:1), compound **26f**



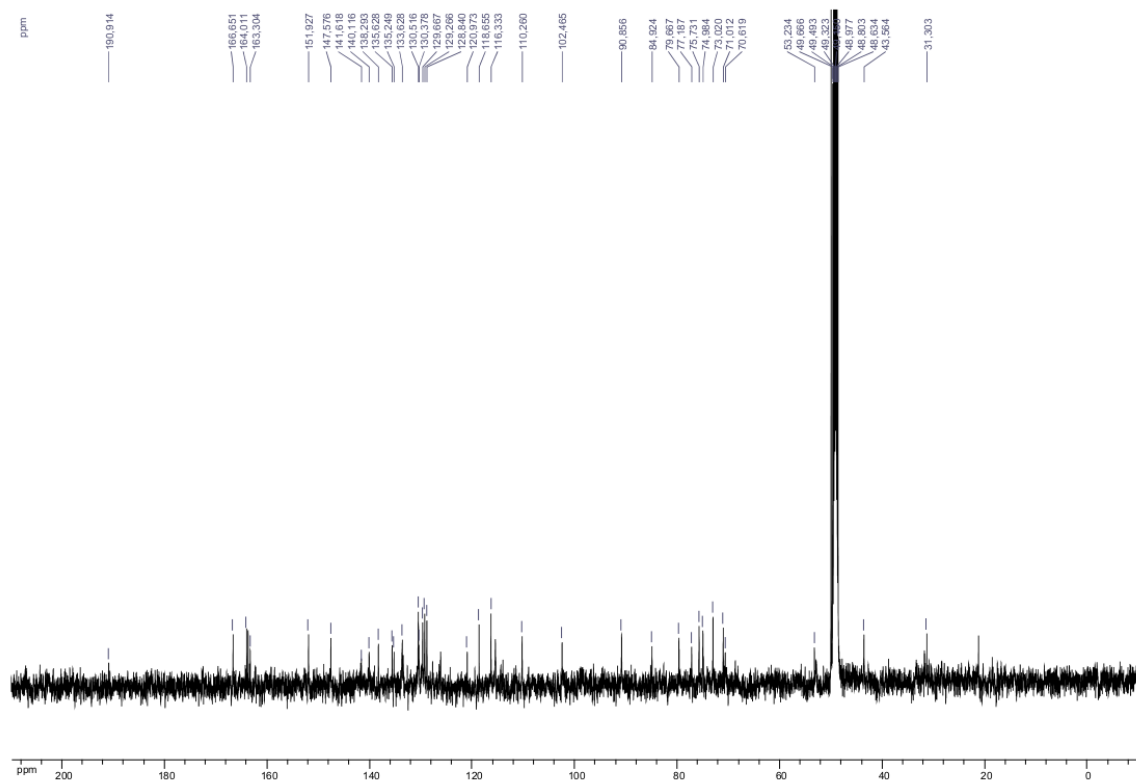
^{13}C NMR, 125 MHz ($\text{CD}_3\text{OD} : \text{D}_2\text{O}$ 1:1)

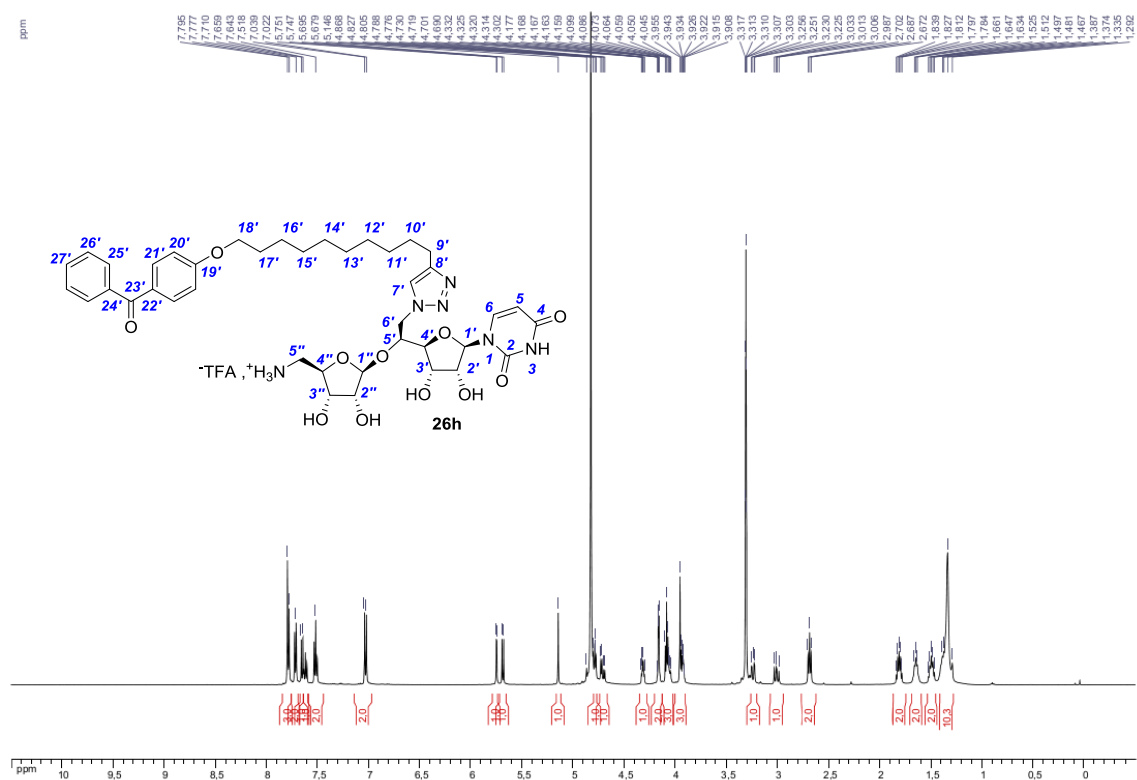
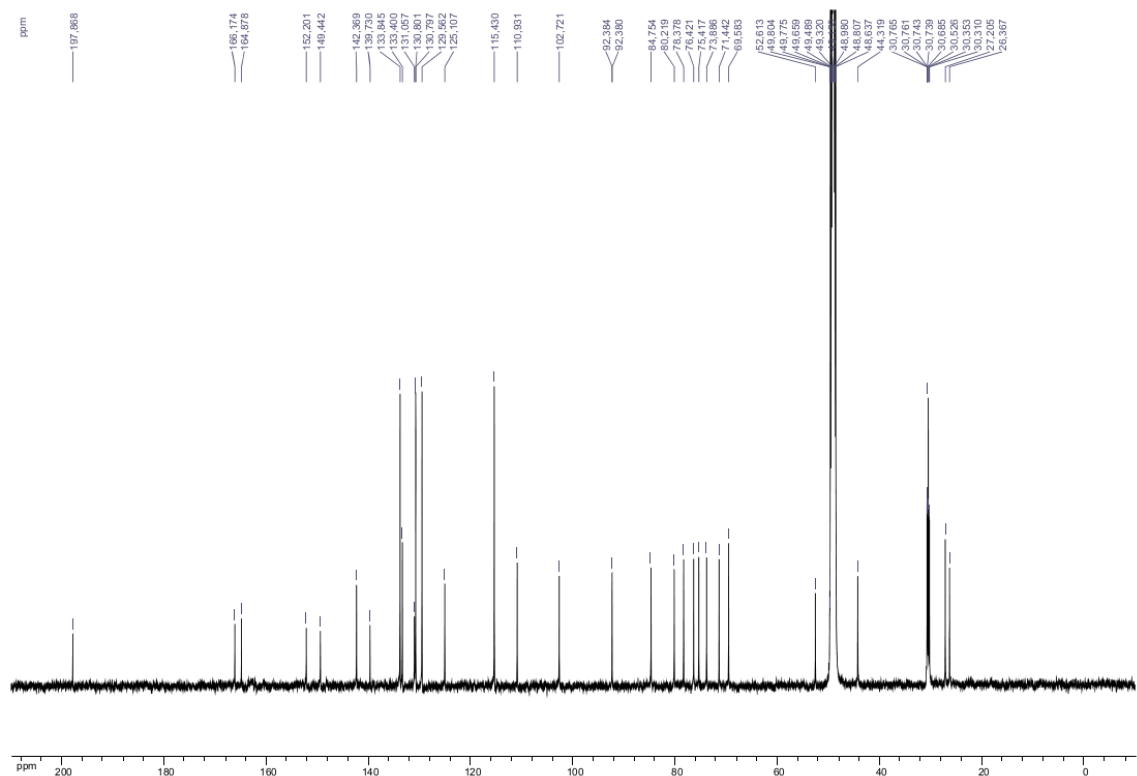


^1H NMR, 500 MHz ($\text{CD}_3\text{OD}/\text{D}_2\text{O}$ 1:1), compound **26g**

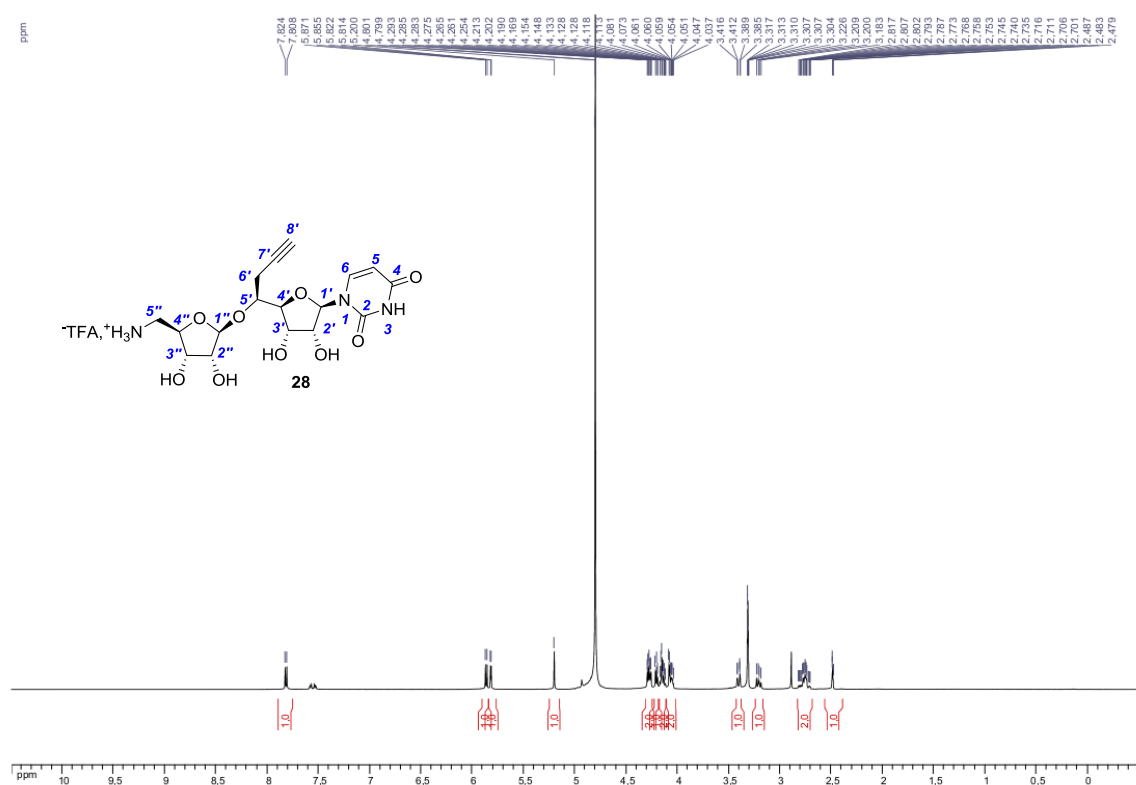


^{13}C NMR, 125 MHz ($\text{CD}_3\text{OD}/\text{D}_2\text{O}$ 1:1)

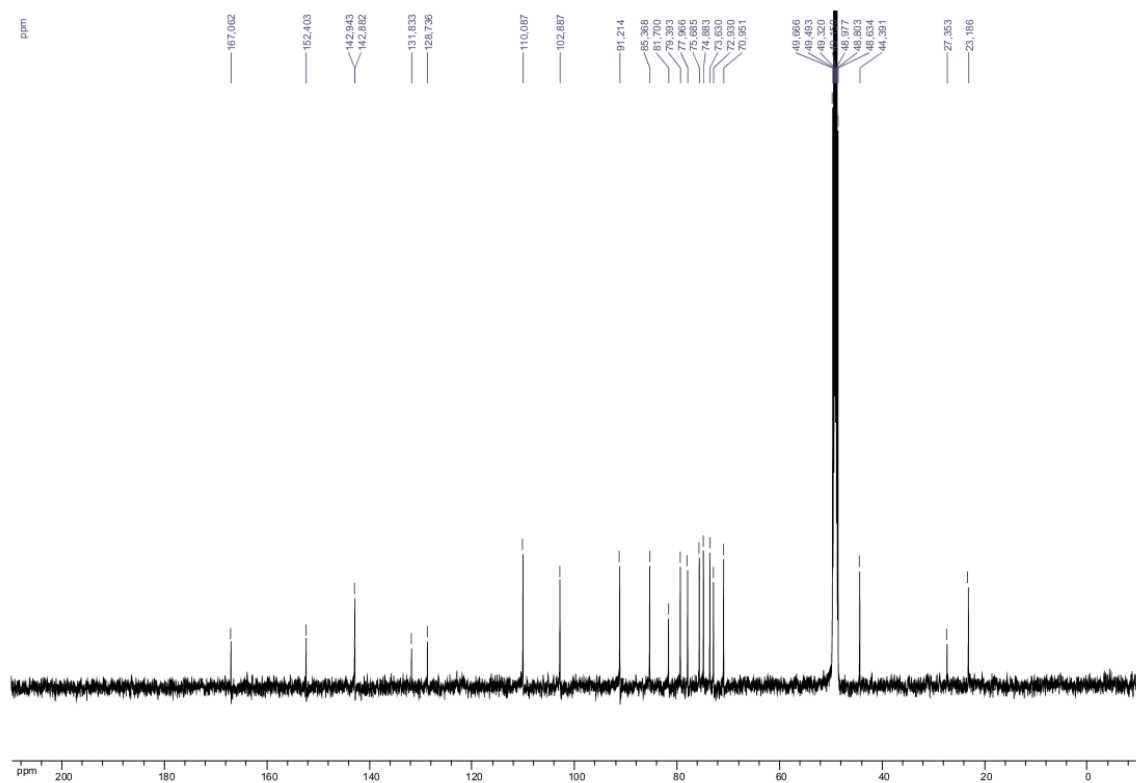


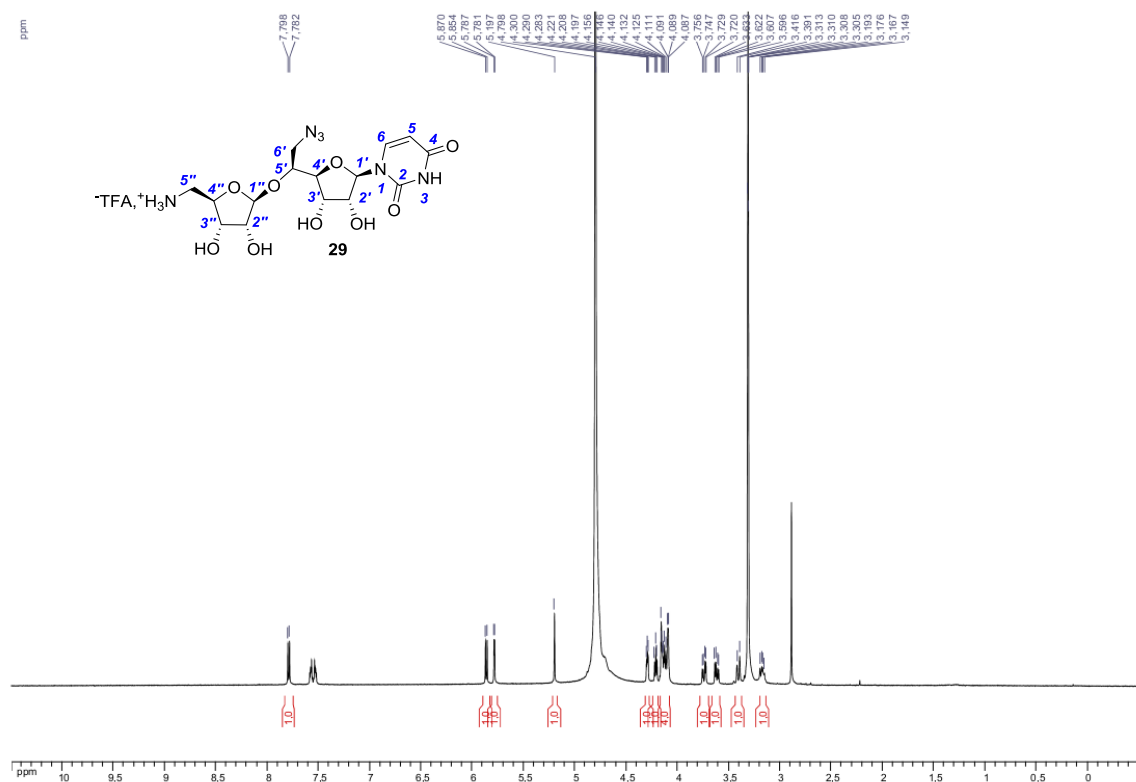
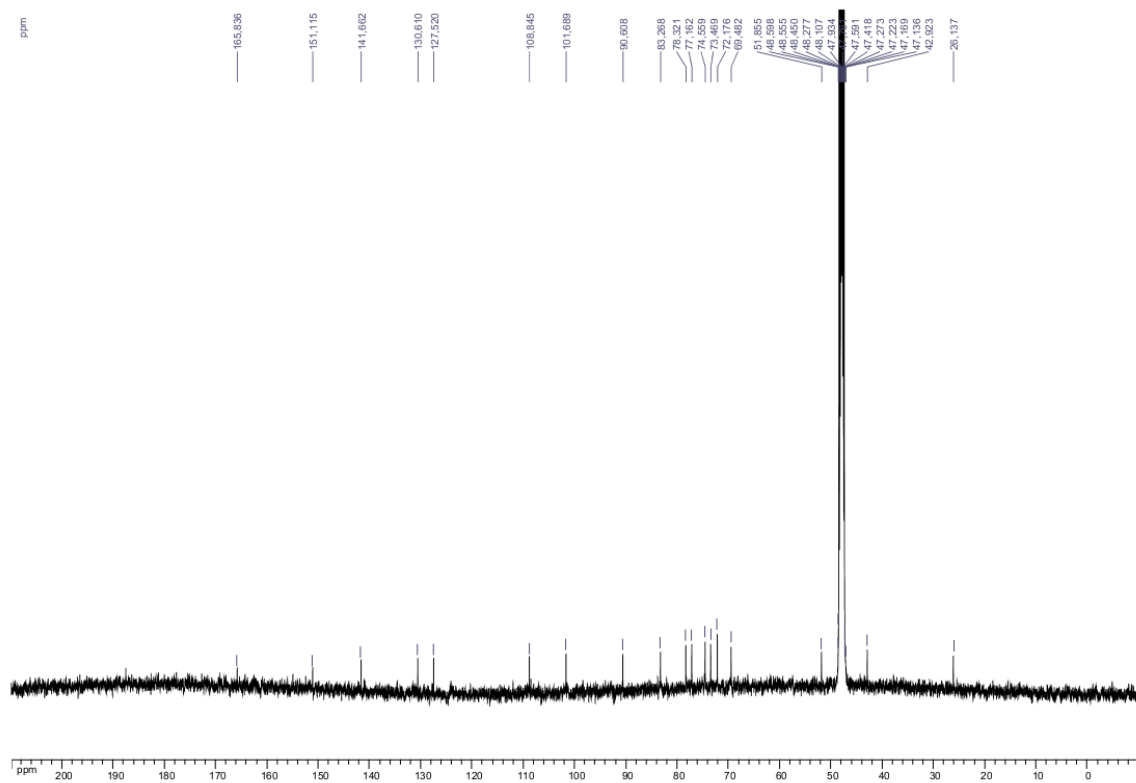
¹H NMR, 500 MHz (CD₃OD), compound **26h** ^{13}C NMR, 125 MHz (CD_3OD)

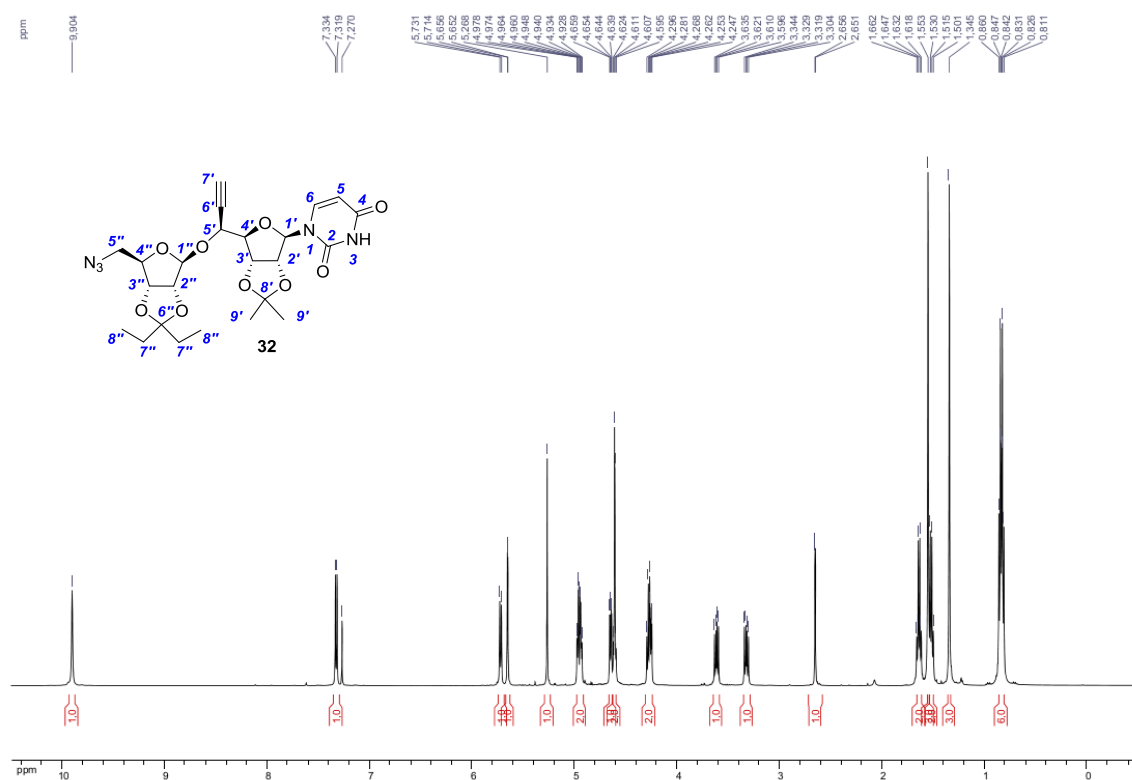
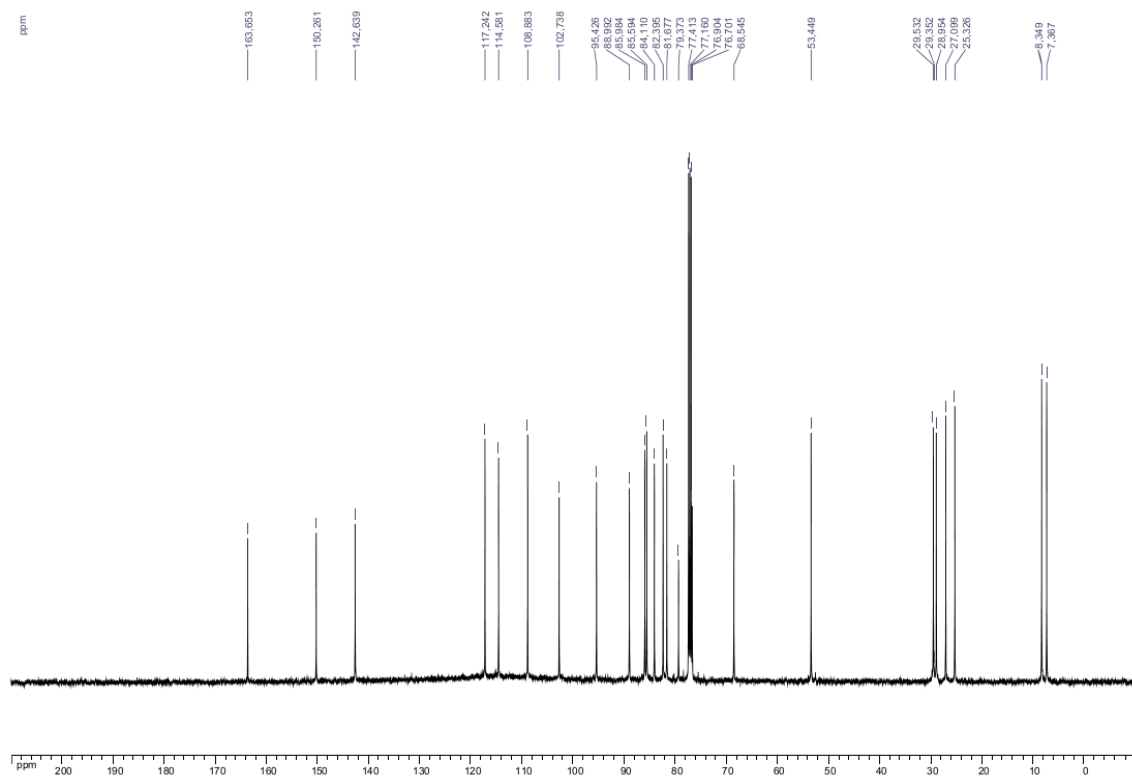
^1H NMR, 500 MHz (D_2O + 50 μL CD_3OD), compound **28**



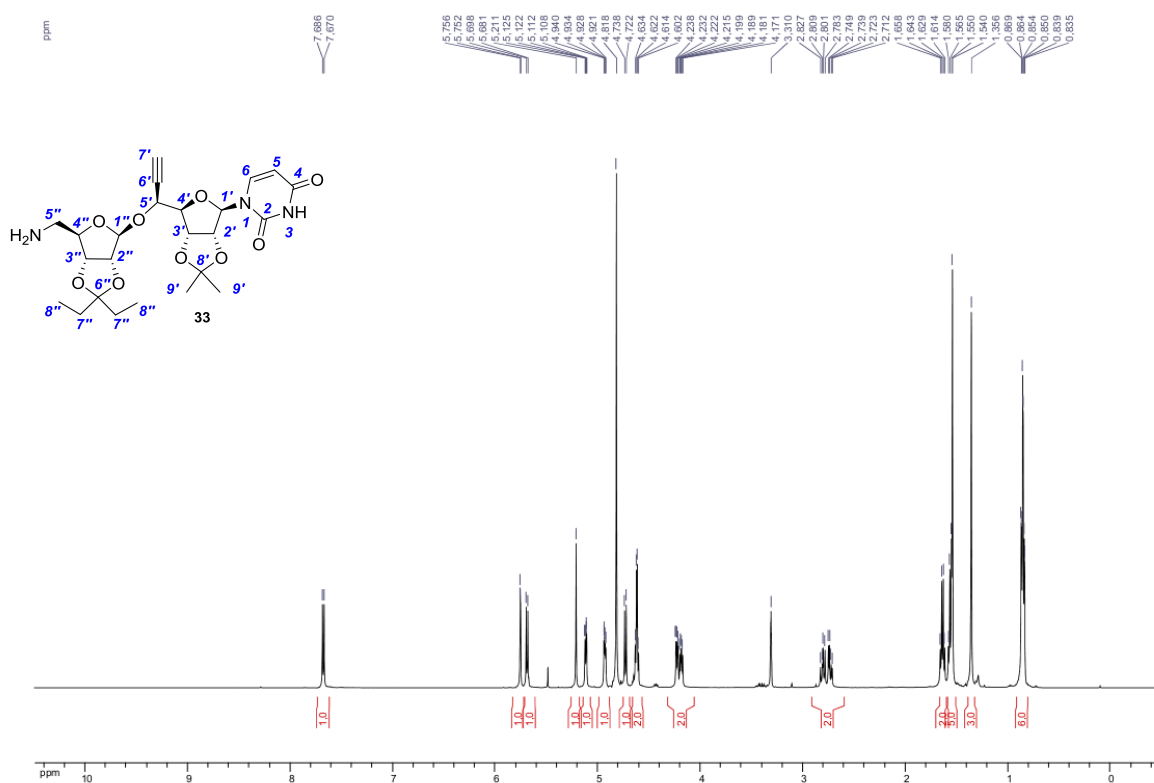
^{13}C NMR, 125 MHz (D_2O + 50 μL CD_3OD),



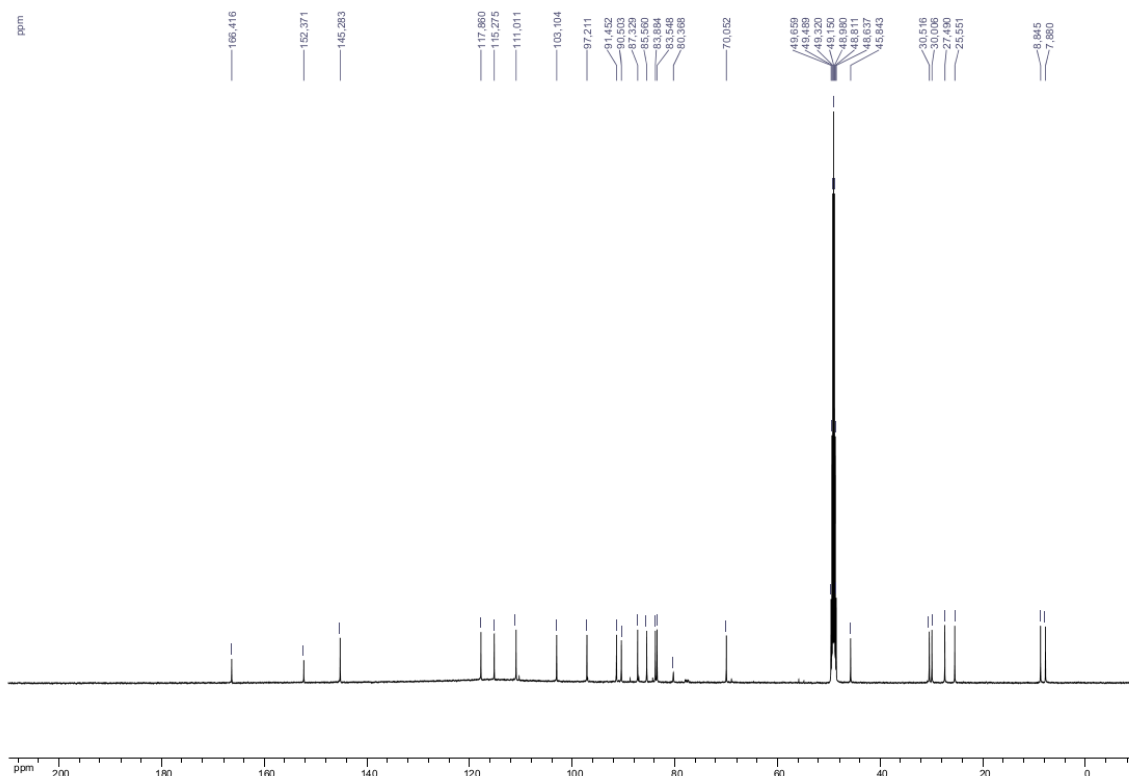
¹H NMR, 500 MHz (CD₃OD), compound **29** ^{13}C NMR, 125 MHz (CD_3OD)

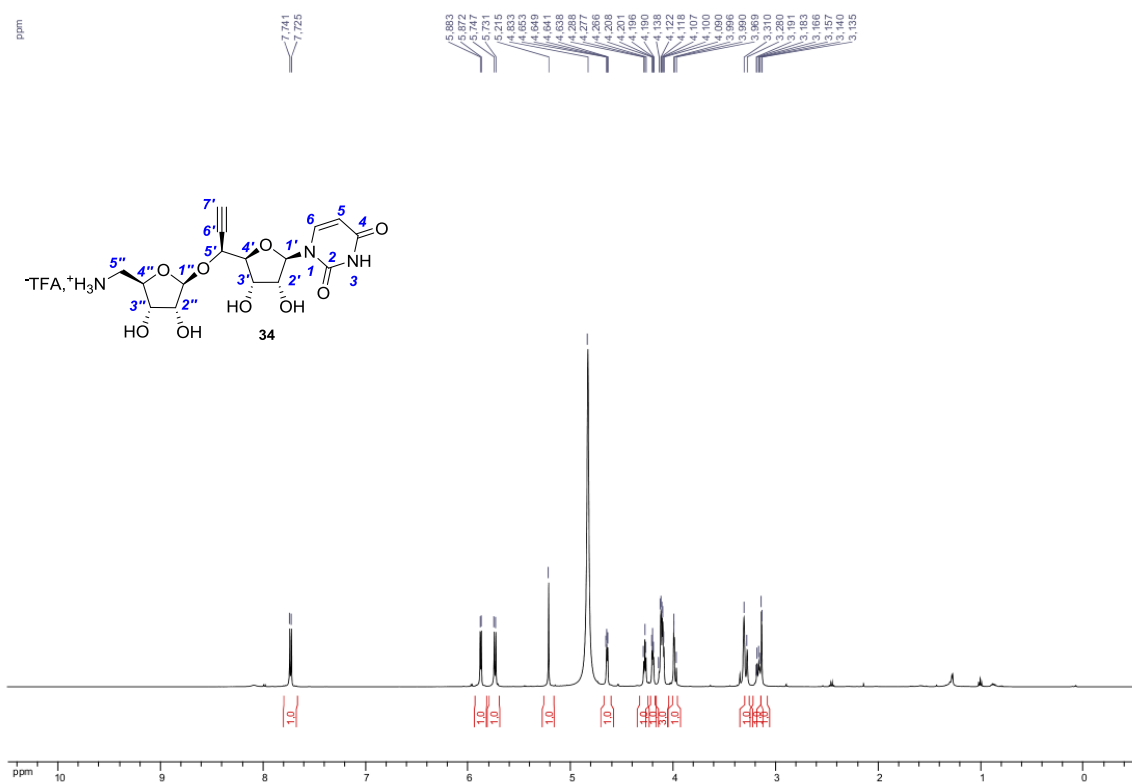
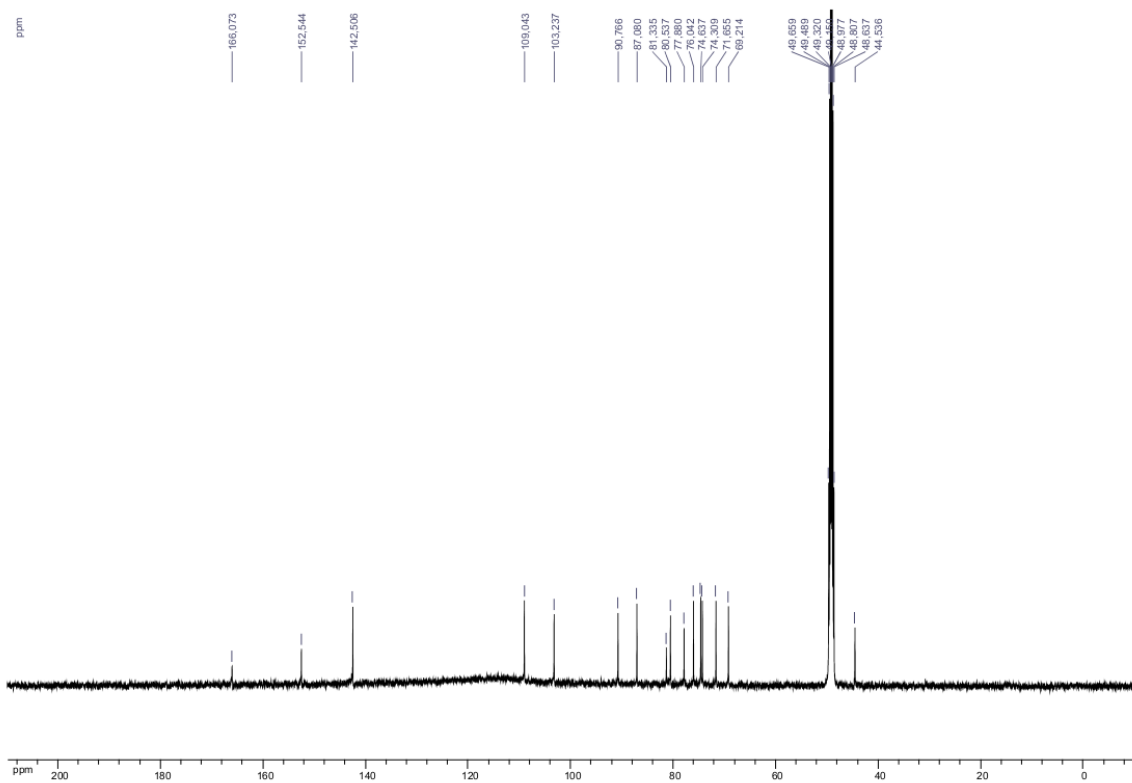
¹H NMR, 500 MHz (CDCl₃), compound **32** ^{13}C NMR, 125 MHz (CDCl_3)

^1H NMR, 500 MHz (CDCl_3), compound **33**



^{13}C NMR, 125 MHz (CDCl_3)



¹H NMR, 500 MHz (CD₃OD), compound **34**¹³C NMR, 125 MHz (CD₃OD)

HPLC purity of compounds **27a-n**

Compound	Method	t_R (min)	Purity (%)
27a	C	12.82	95
27b	C	5.81	99
27c	C	8.01	95
27d	C	9.69	96
27e	D	2.43	99
27f	D	2.49	99
27g	D	3.01	99
27h	D	2.82	99
27i	D	2.74	99
27j	C	3.59	97
27k	C	9.11	98
27l	C	10.71	95
27m	C	14.93	98
27n	C	11.45	97