Supplementary Information for:

Esterase-Sensitive Prodrugs of a Potent Bisubstrate Inhibitor of Nicotinamide *N*-Methyltransferase (NNMT) Display Cellular Activity

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† These authors contributed equally to this work.

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Cellular MNA data

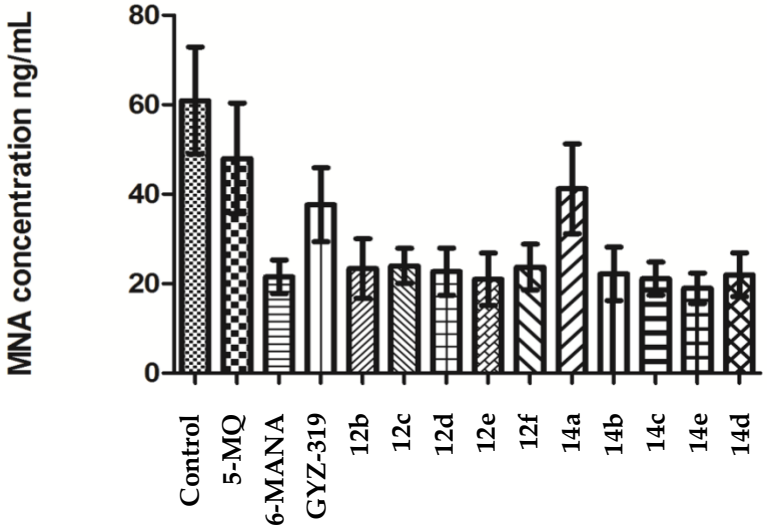
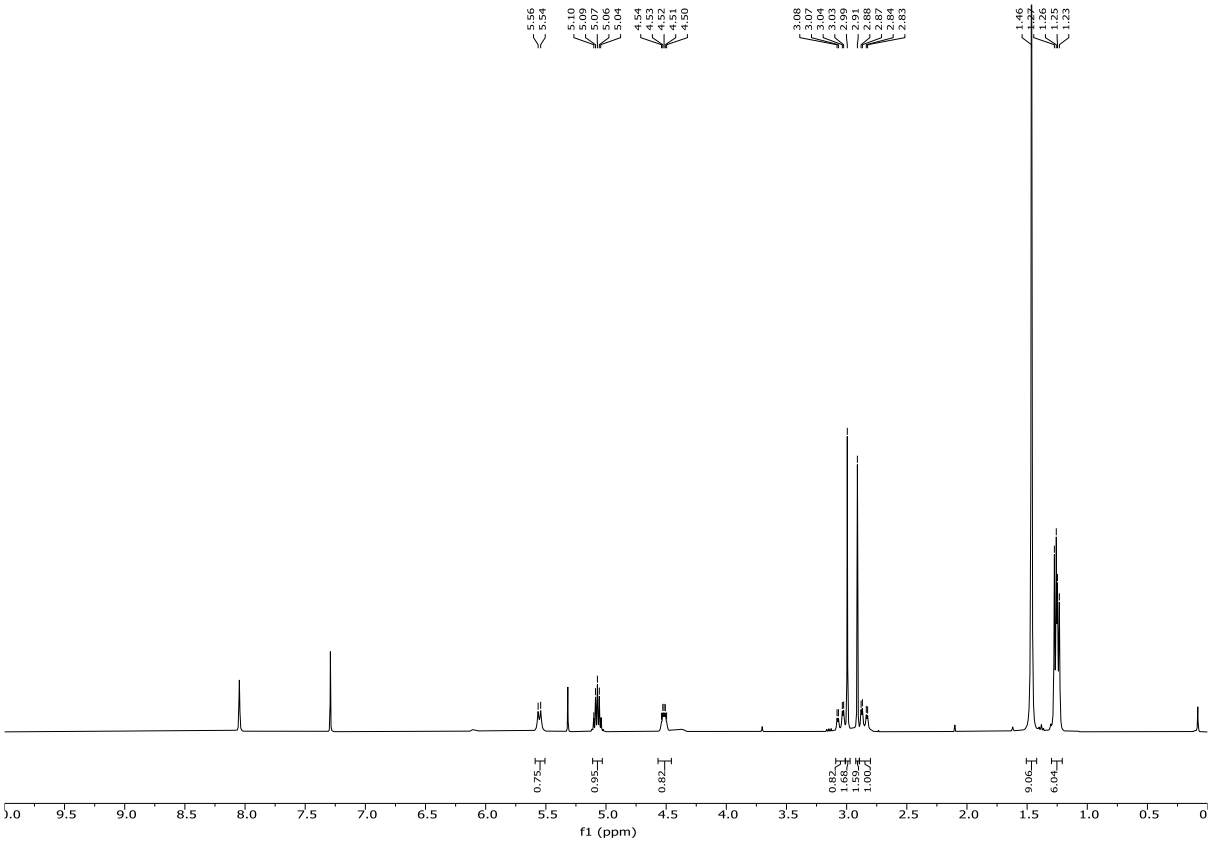


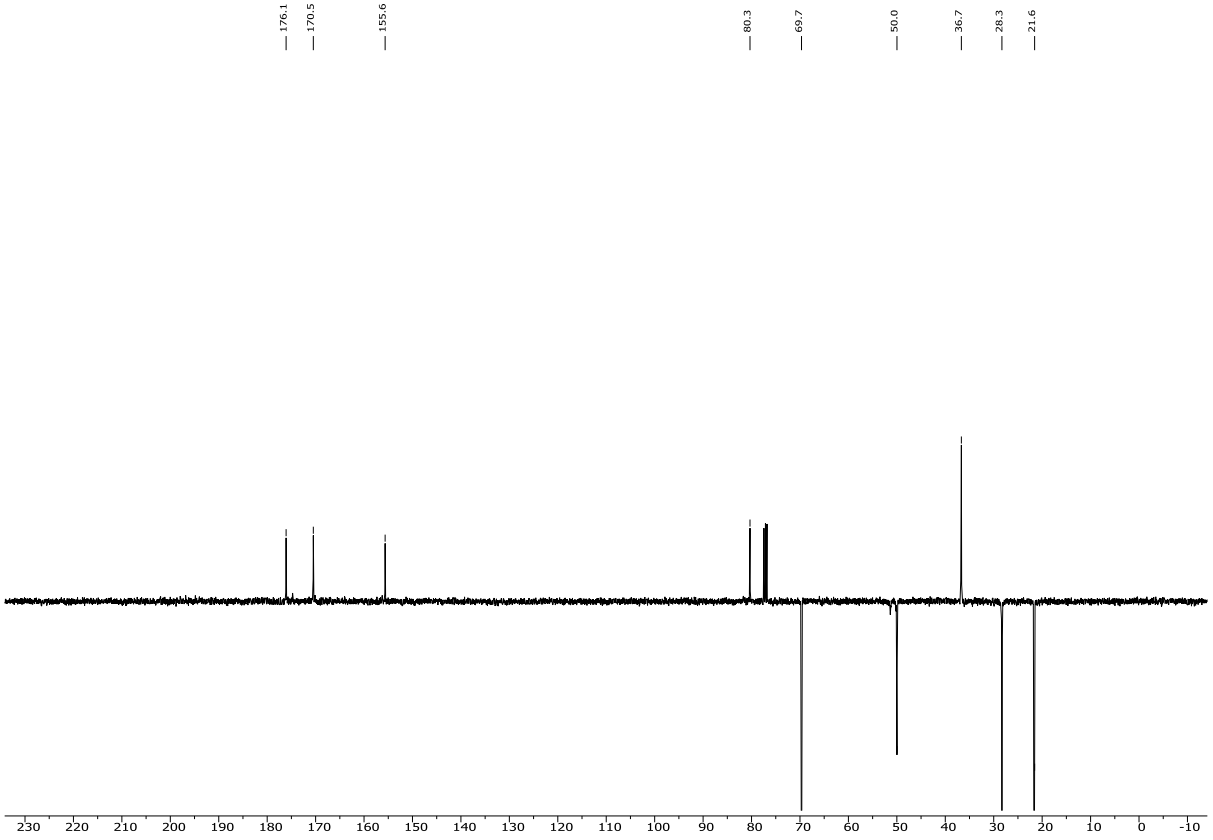
Figure S1. 1-methylnicotinamide (MNA) concentrations in endothelial HMEC-1 cells after 24-hour incubation with 10 μM of reference compounds 5-amino-methylquinolinium (5-MQ), 6-methylamino-nicotinamide (6-MANA), parent compound **GYZ-319** or prodrug compounds **12b**-**f** and **14a**-**e**.

NMR spectra

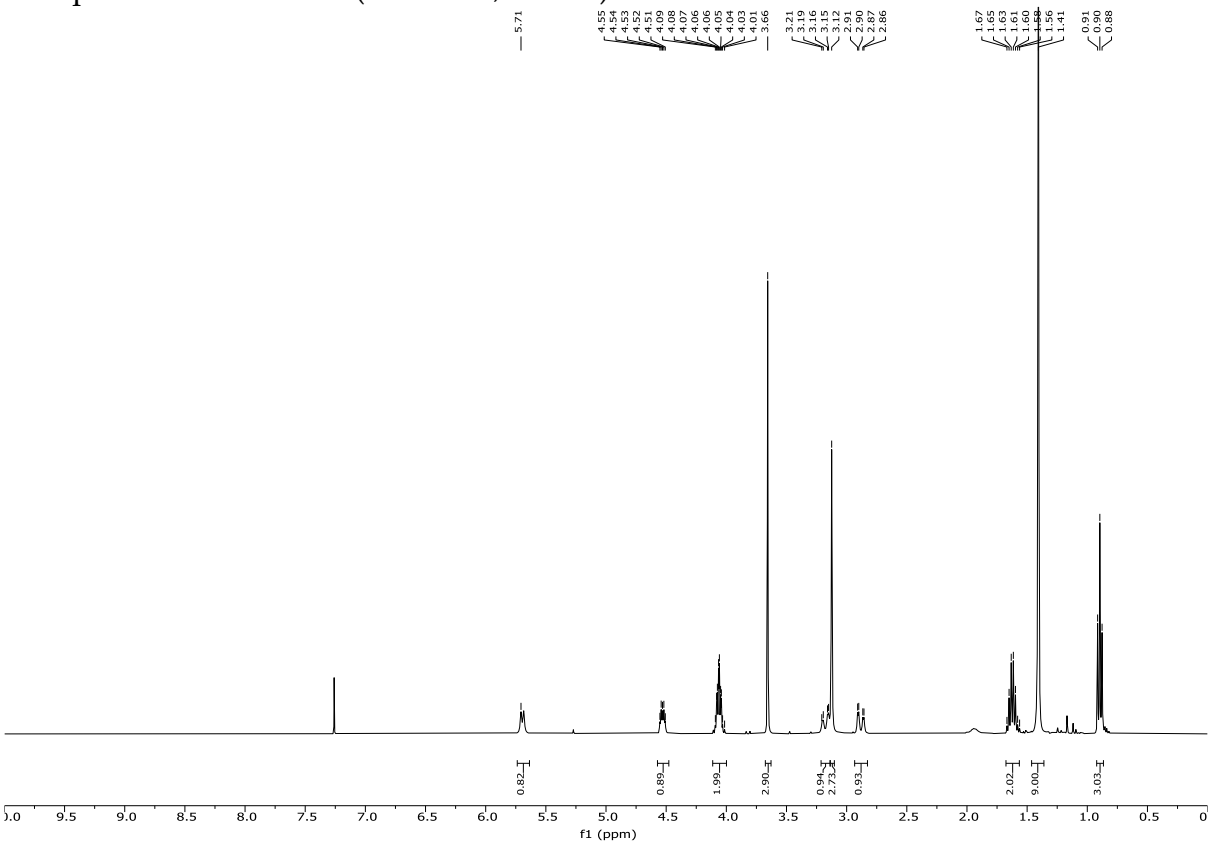
Compound **3e** ^{1}H NMR (400 MHz, $CDCl_3$)



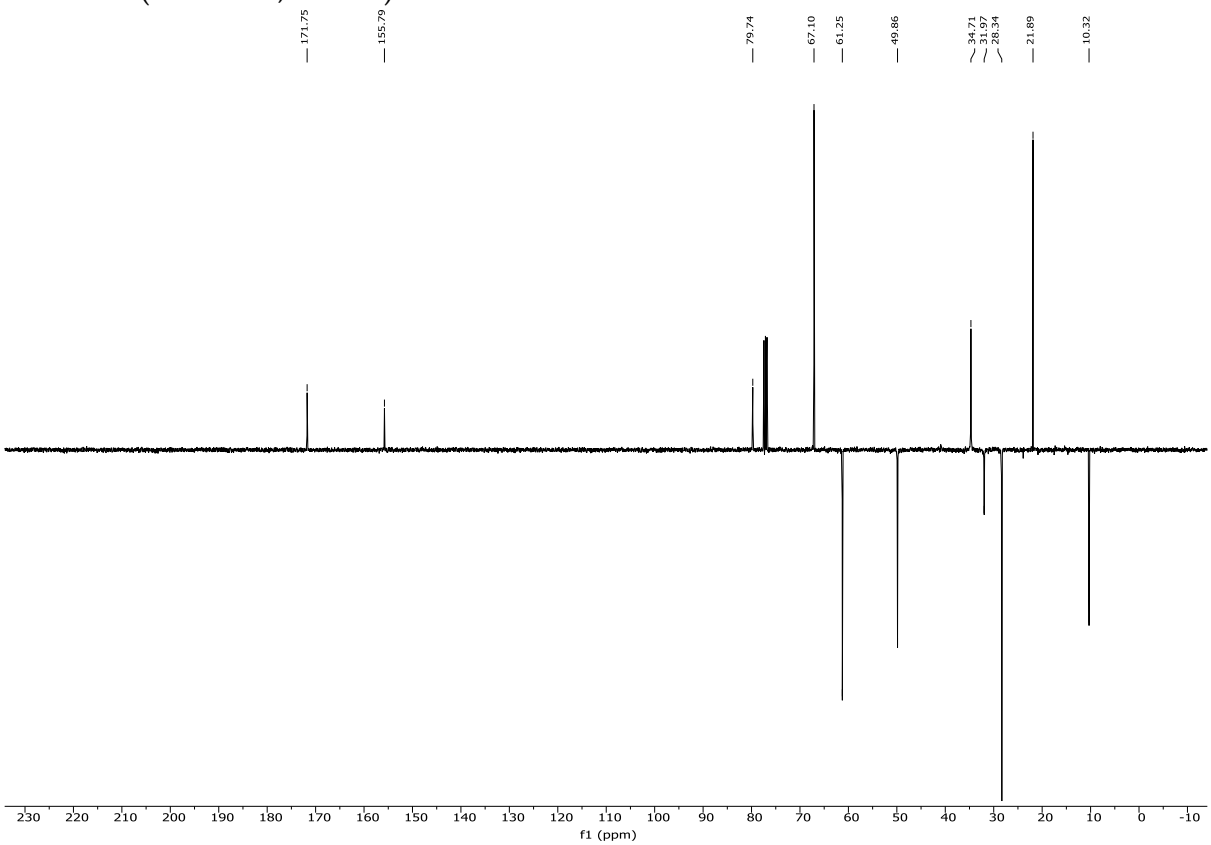
^{13}C NMR (101 MHz, $CDCl_3$)



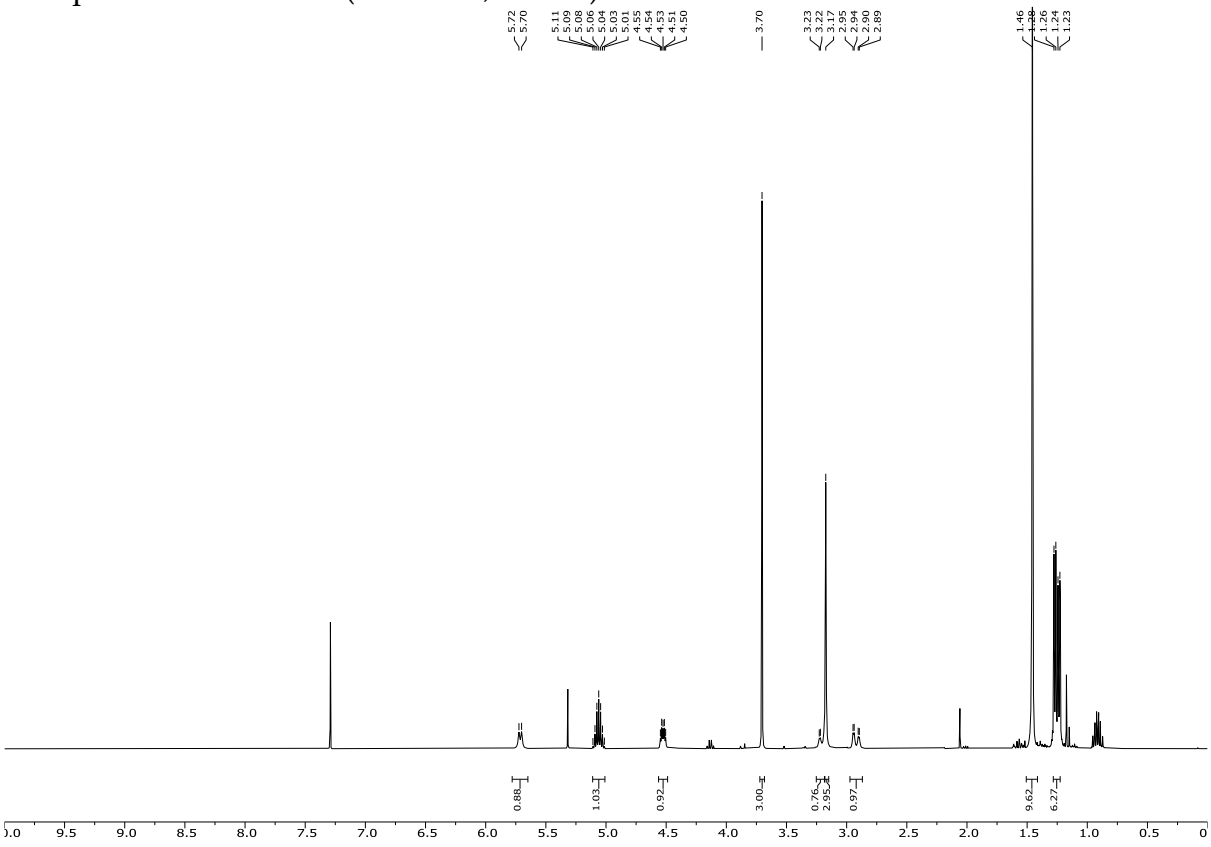
Compound **4d** 1H NMR (400 MHz, $CDCl_3$)



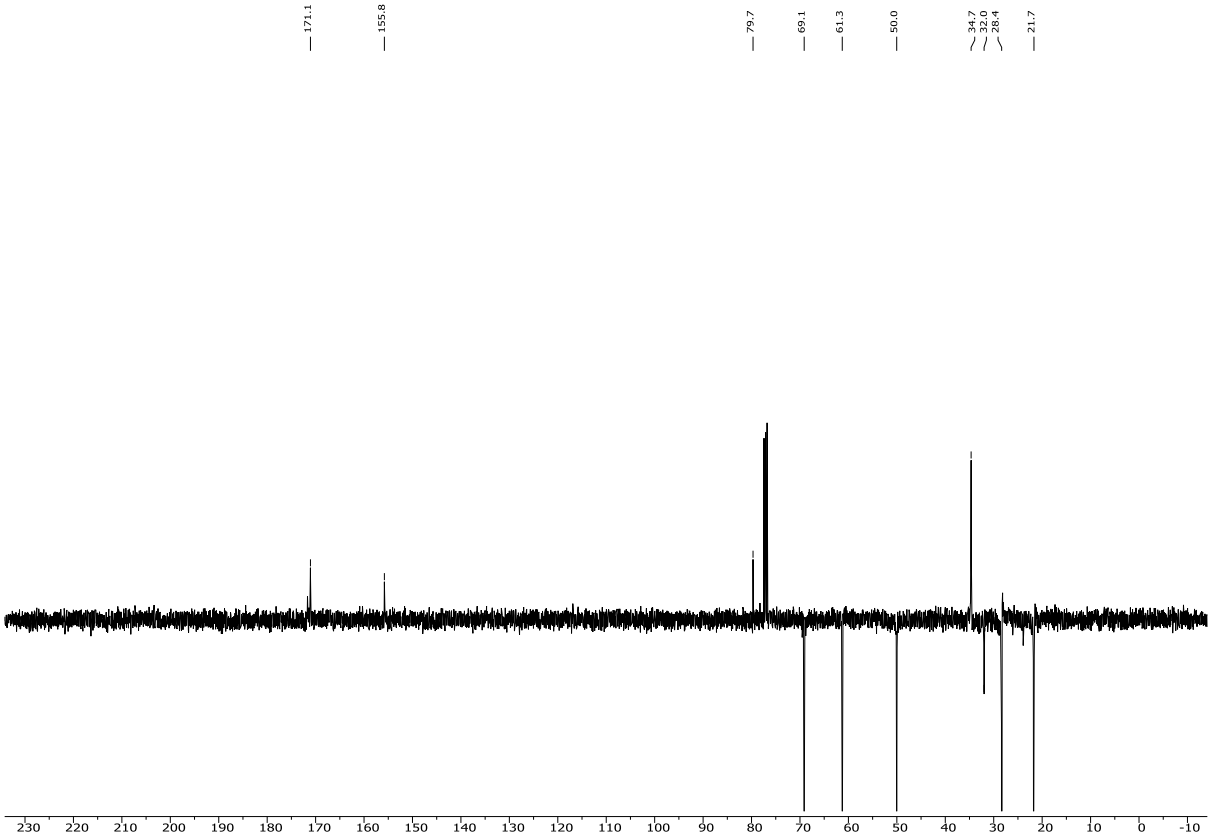
^{13}C NMR (101 MHz, $CDCl_3$)



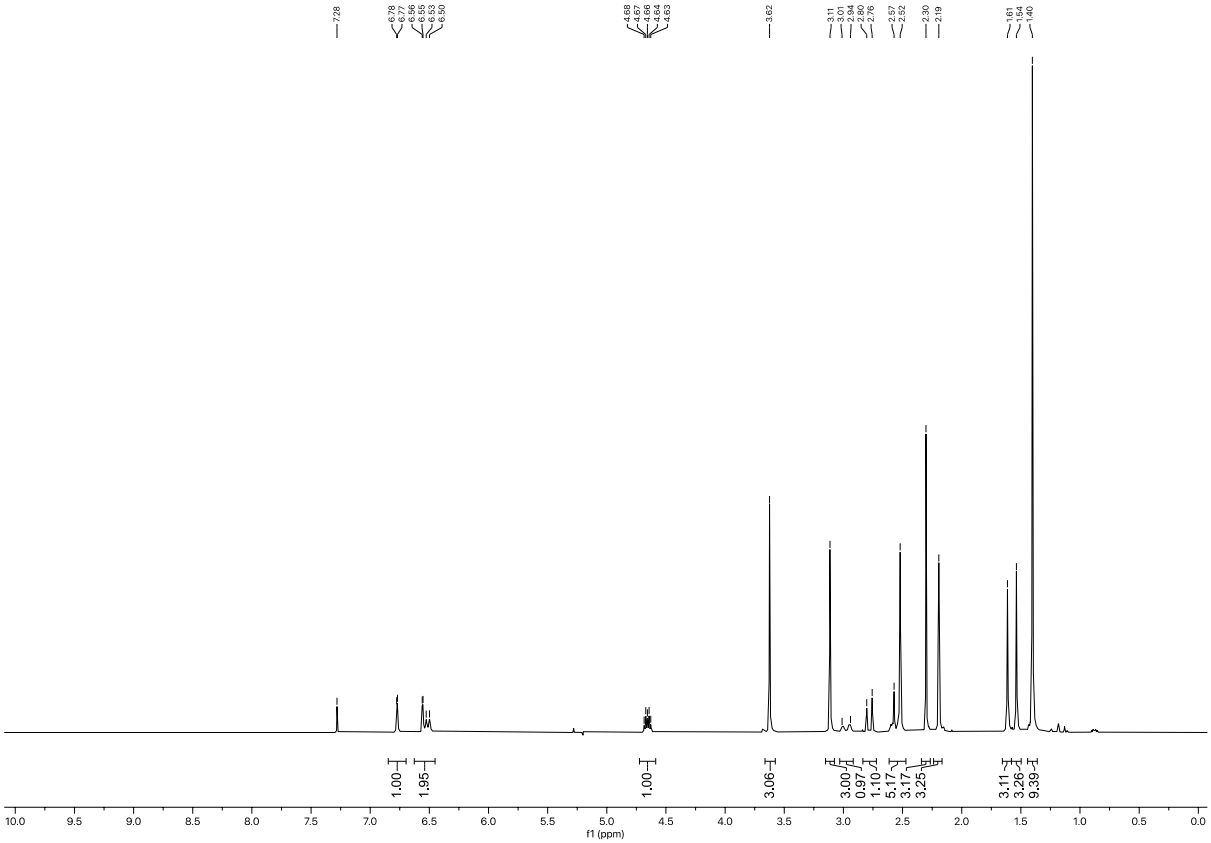
Compound **4e** ^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



Compound **8a** ^{1}H NMR (300 MHz, $CDCl_3$)



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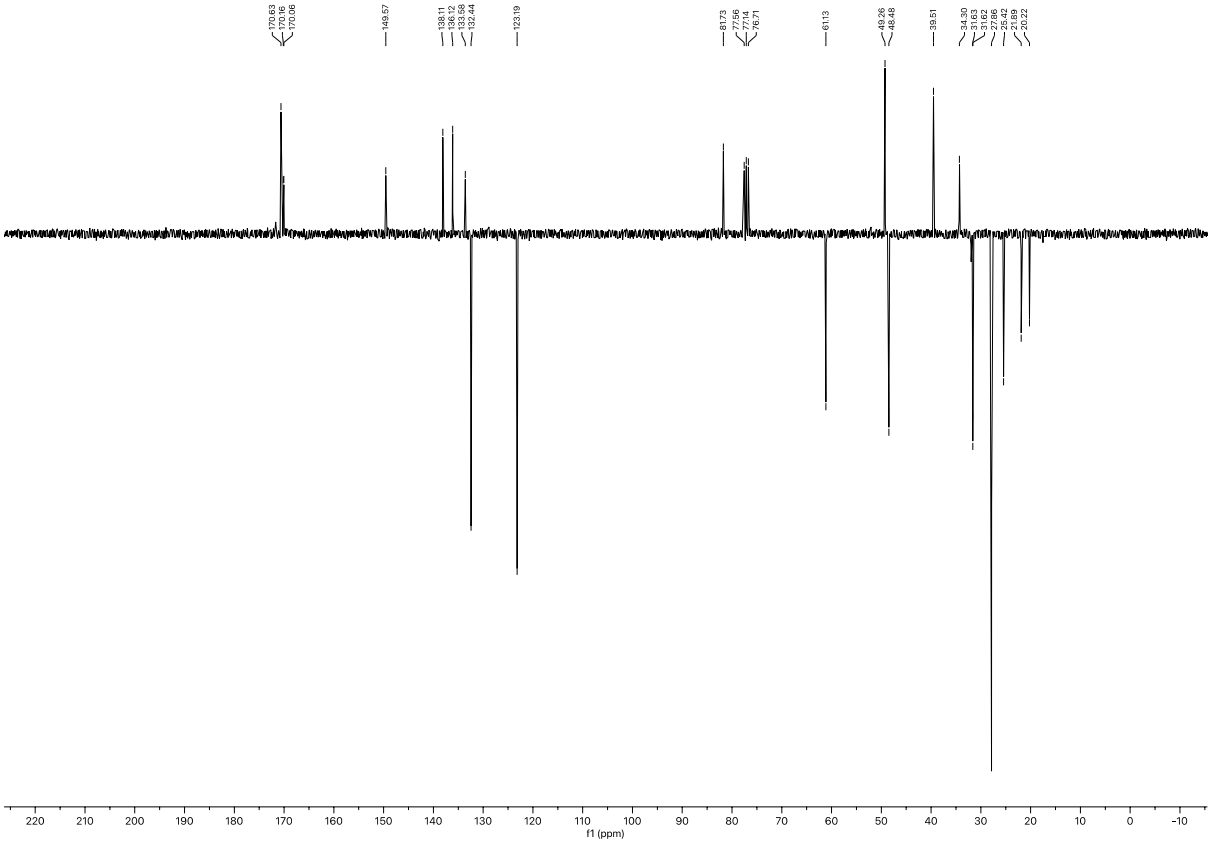
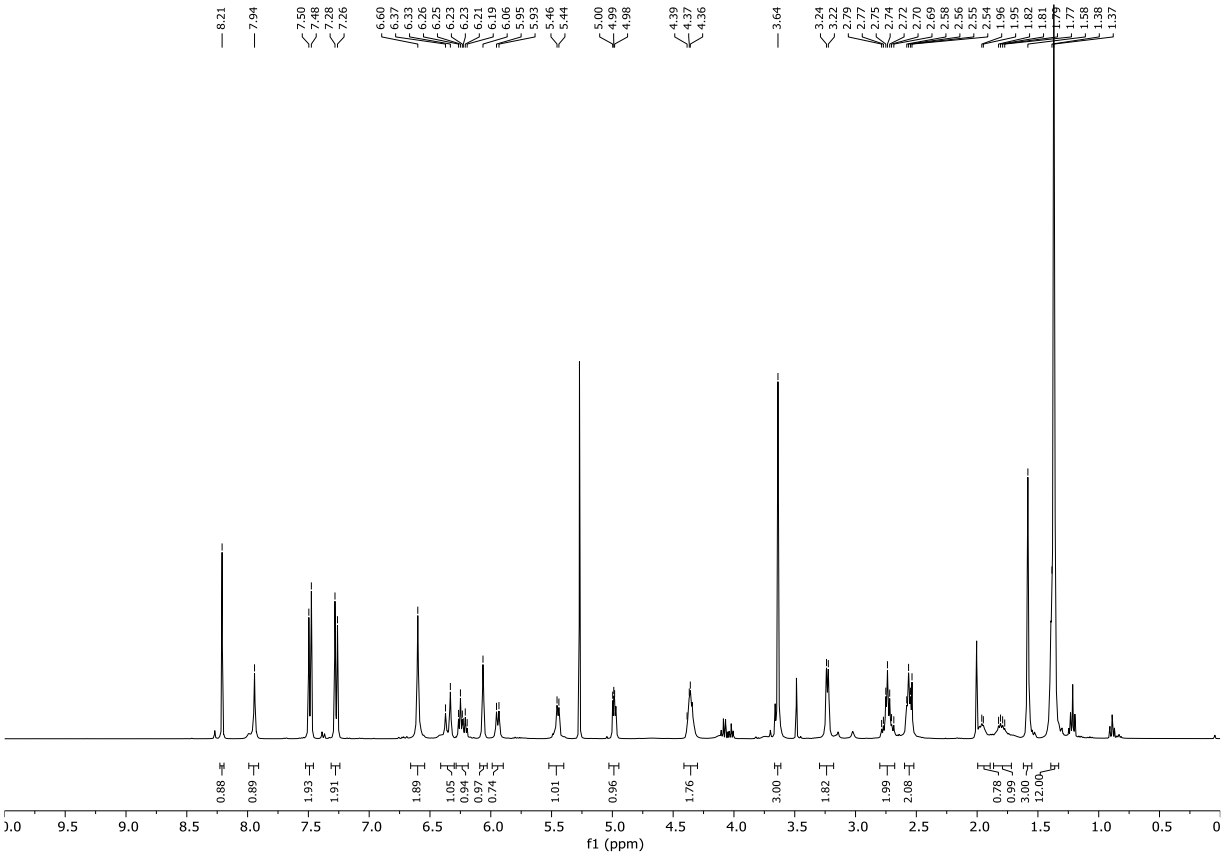
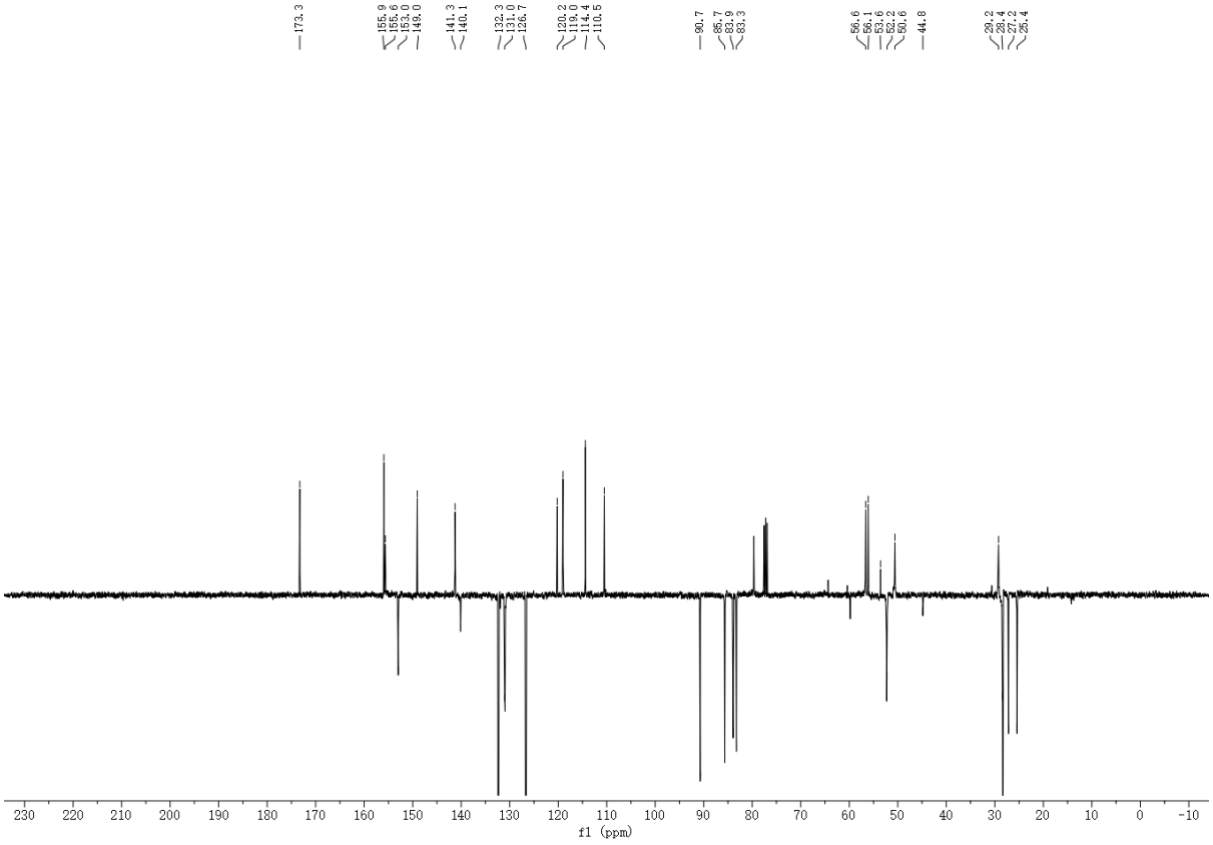


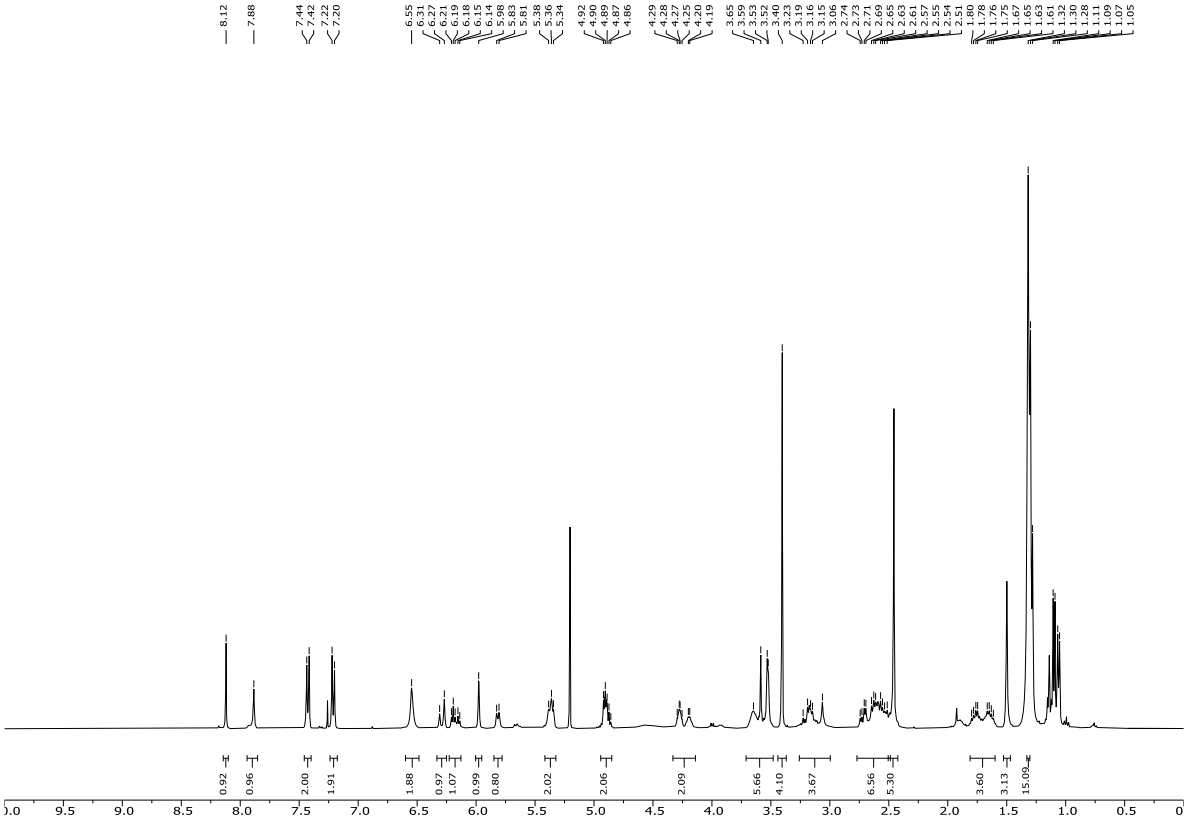
Compound **11b** ^{1}H NMR (400 MHz, $CDCl_3$)



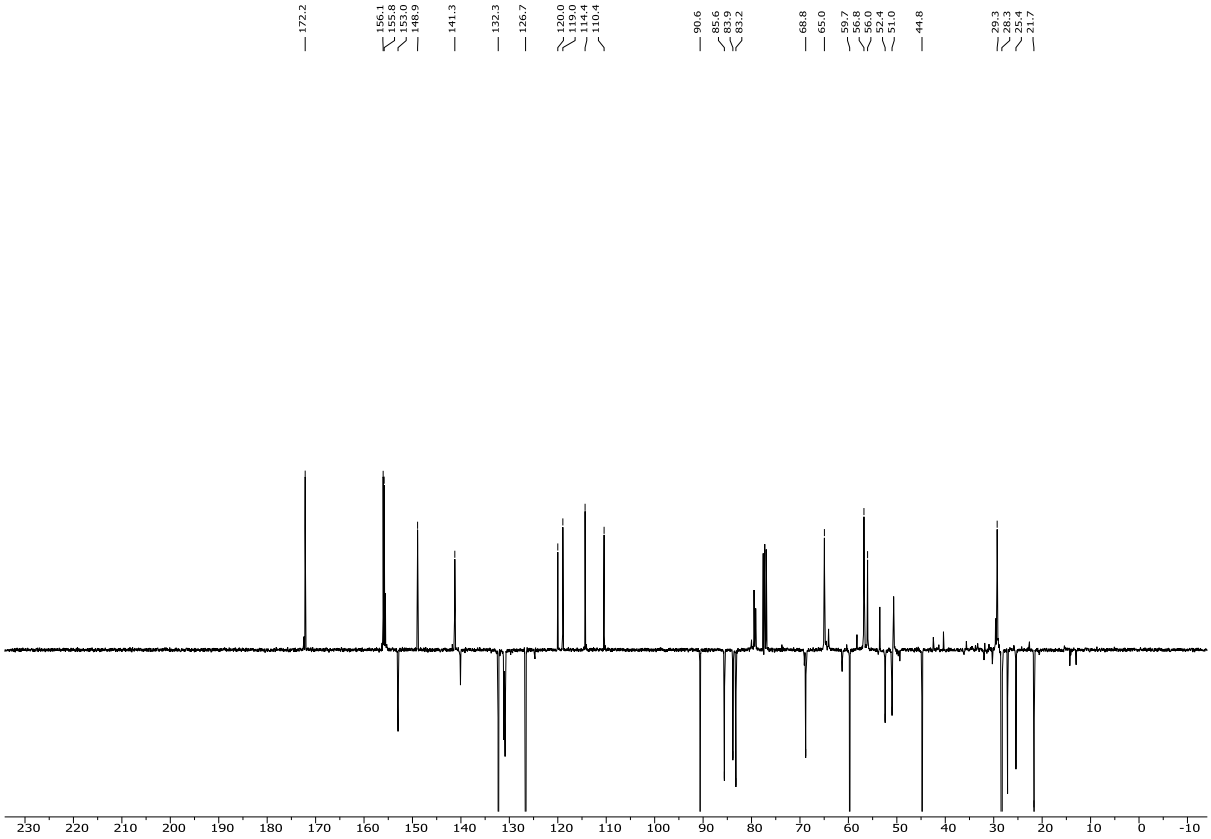
^{13}C NMR $CDCl_3$ (101 MHz, $CDCl_3$)



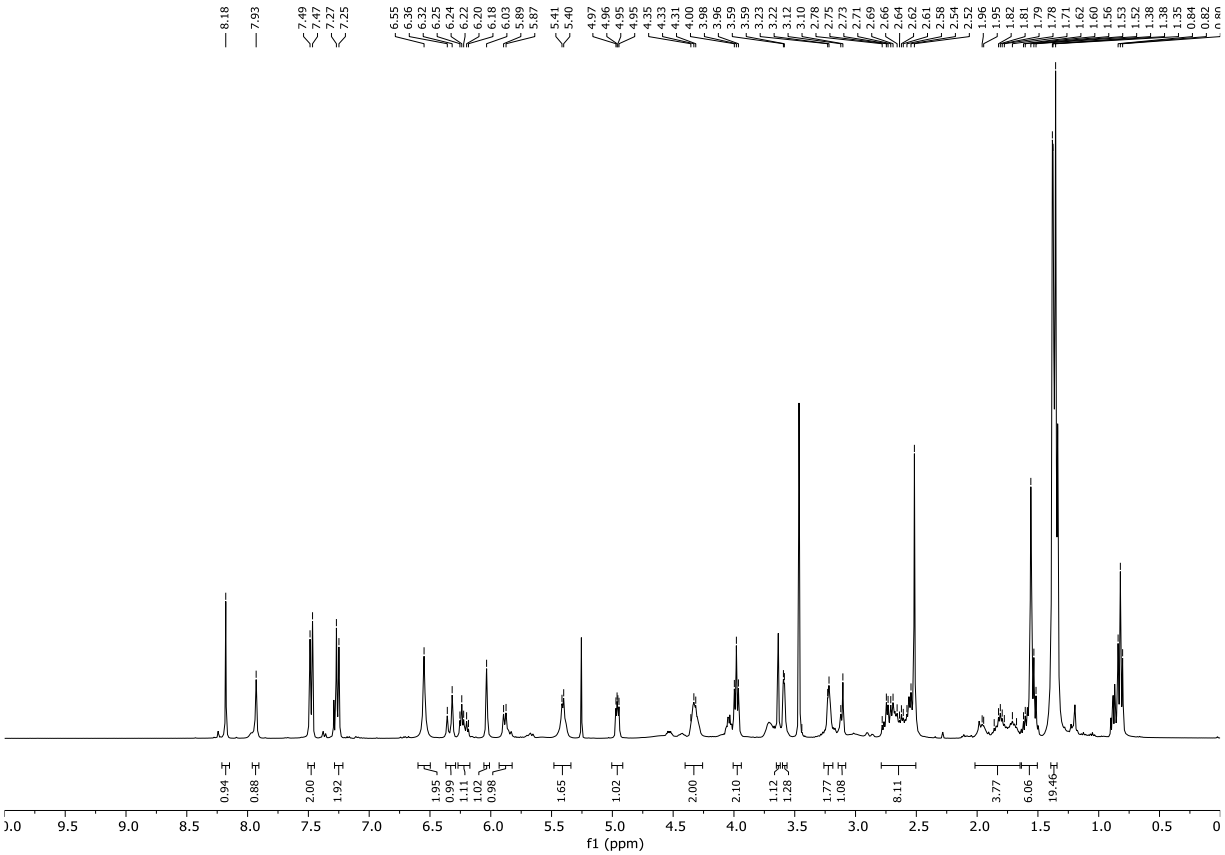
Compound **11c** ^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



Compound **11d** ^{1}H NMR (400 MHz, $CDCl_3$)



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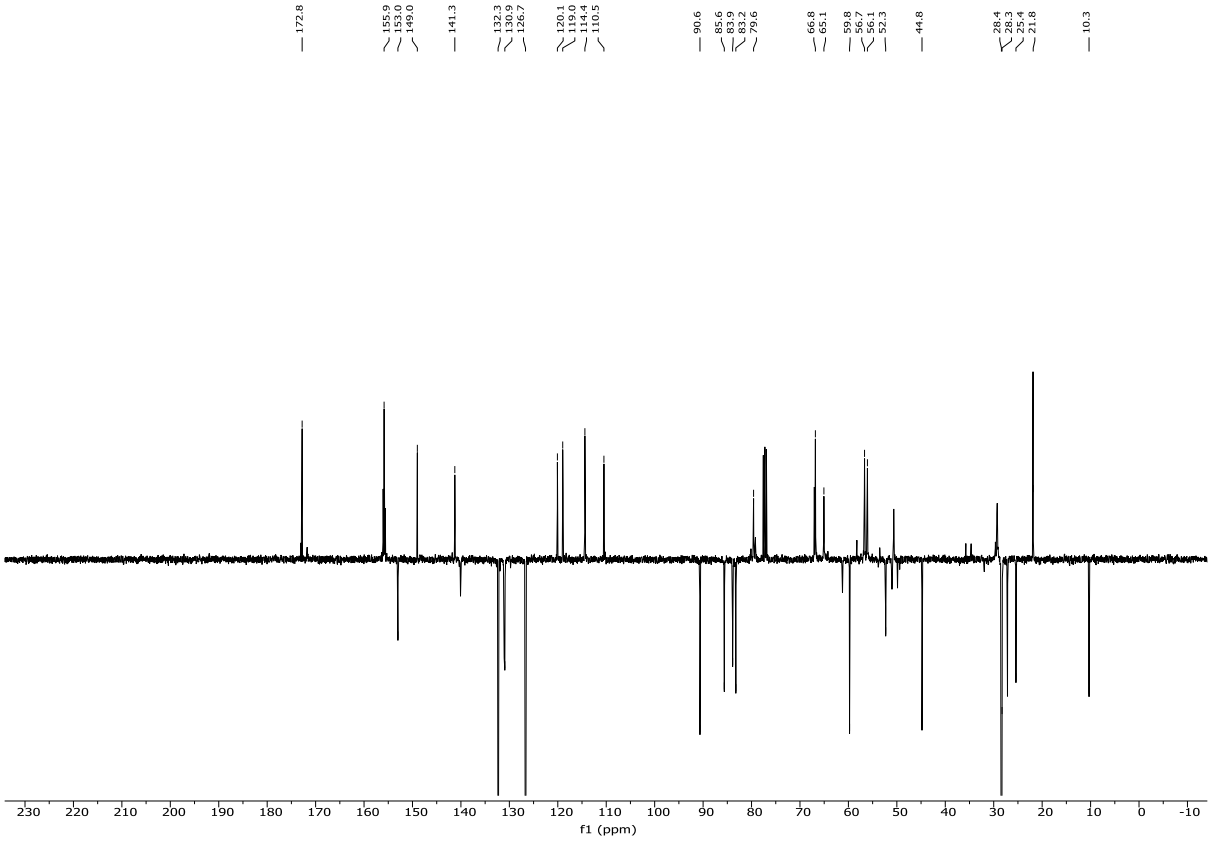
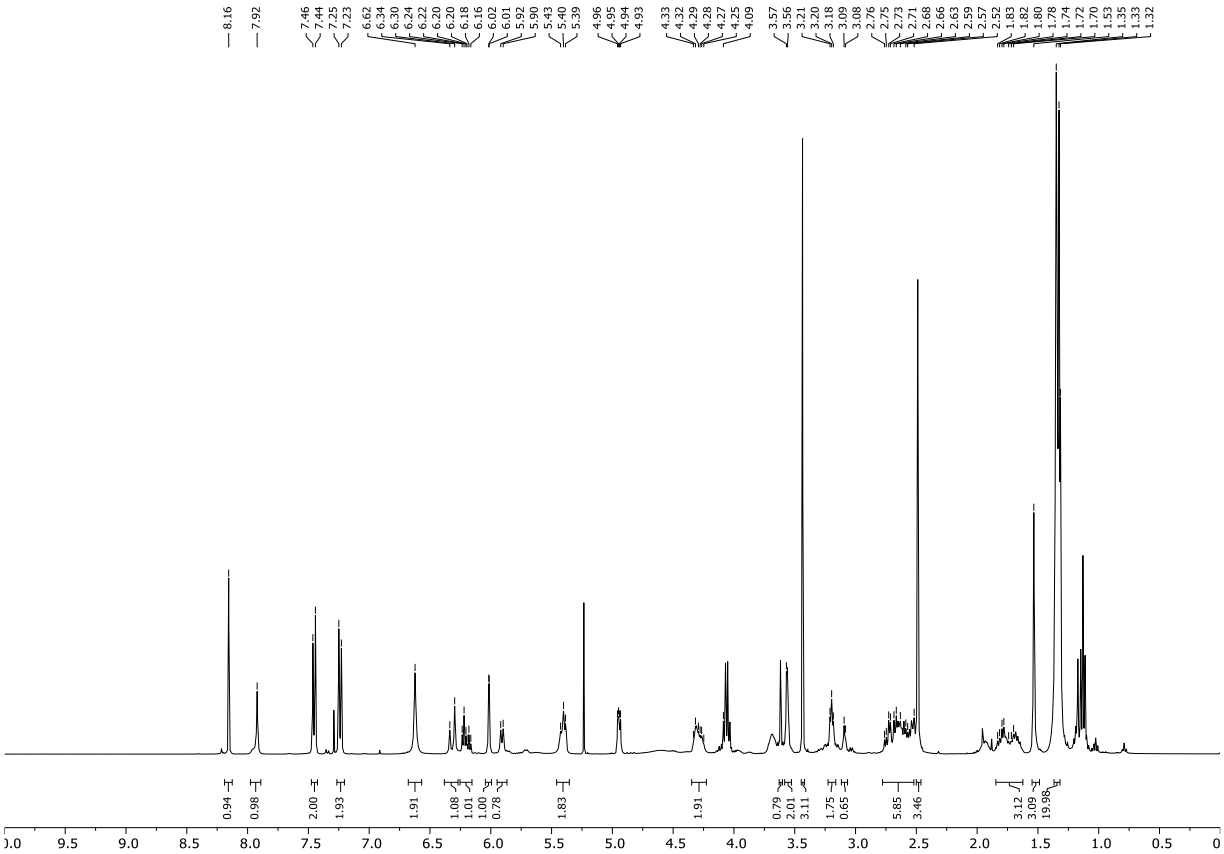
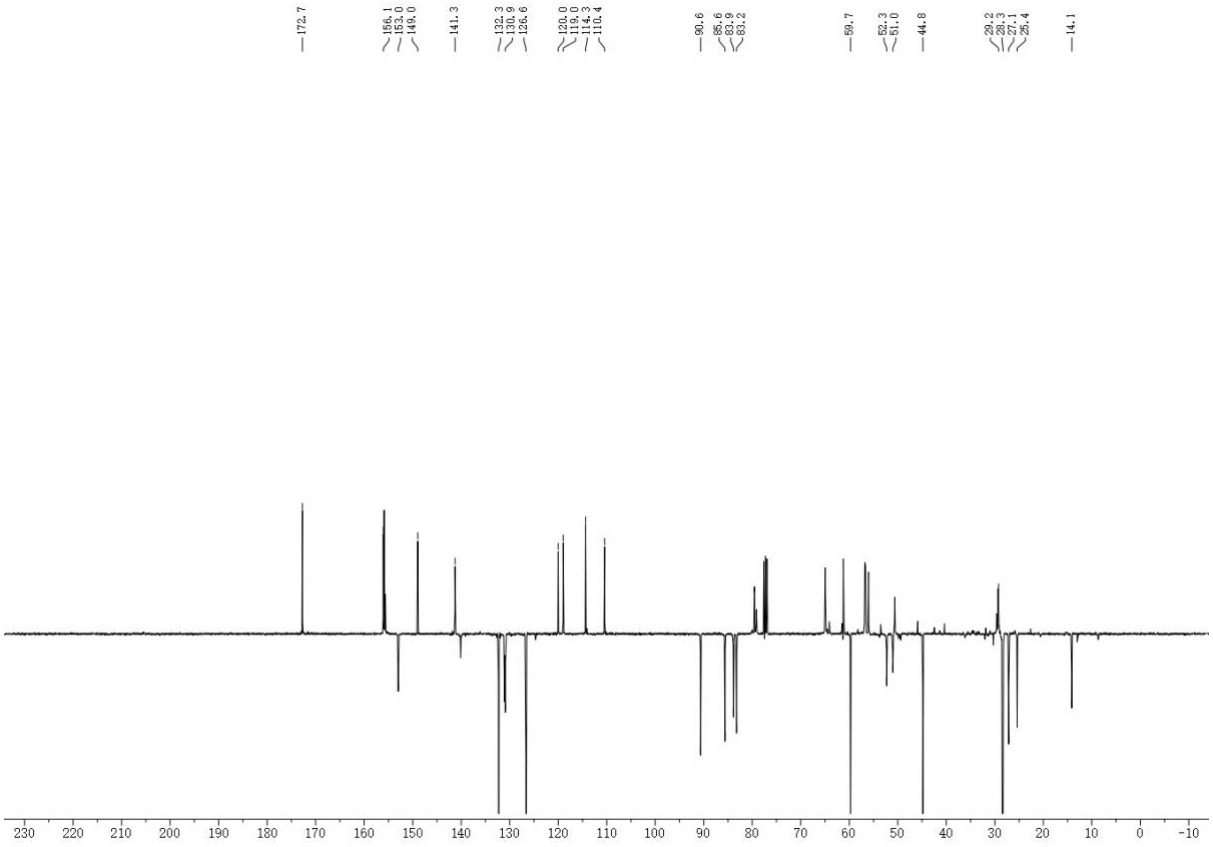


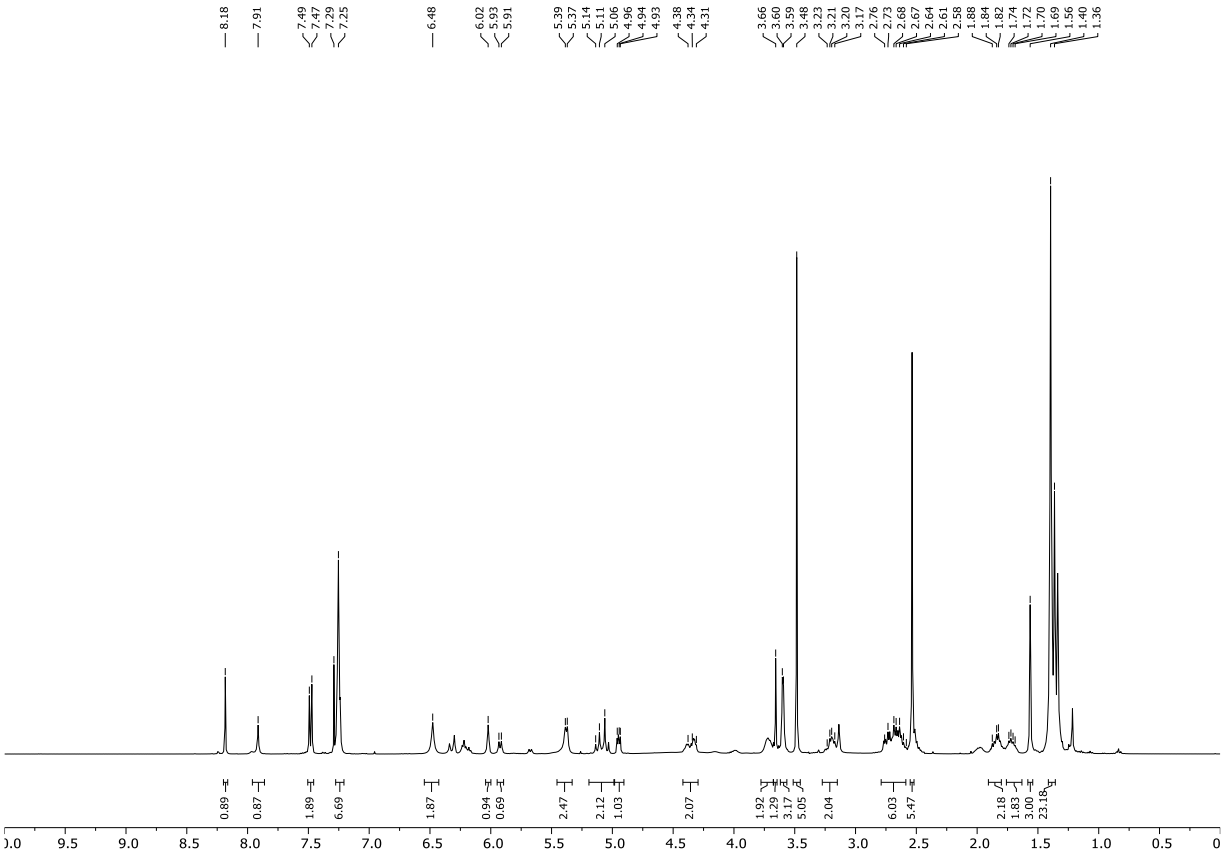
Compound **11e** ^{1}H NMR $CDCl_3$ (400 MHz, $CDCl_3$)



^{13}C NMR $CDCl_3$ (101 MHz, $CDCl_3$)



Compound **11f** ^{1}H NMR (400 MHz, $CDCl_3$)



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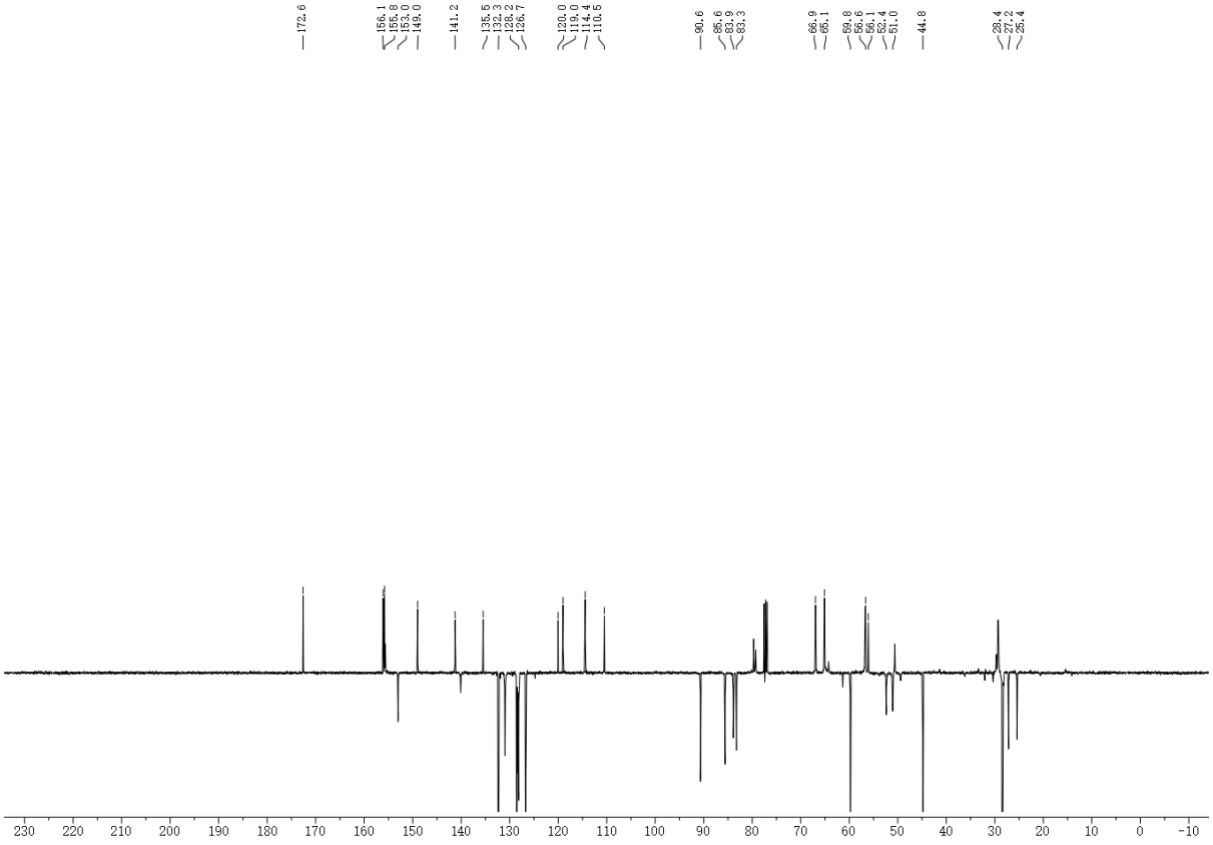
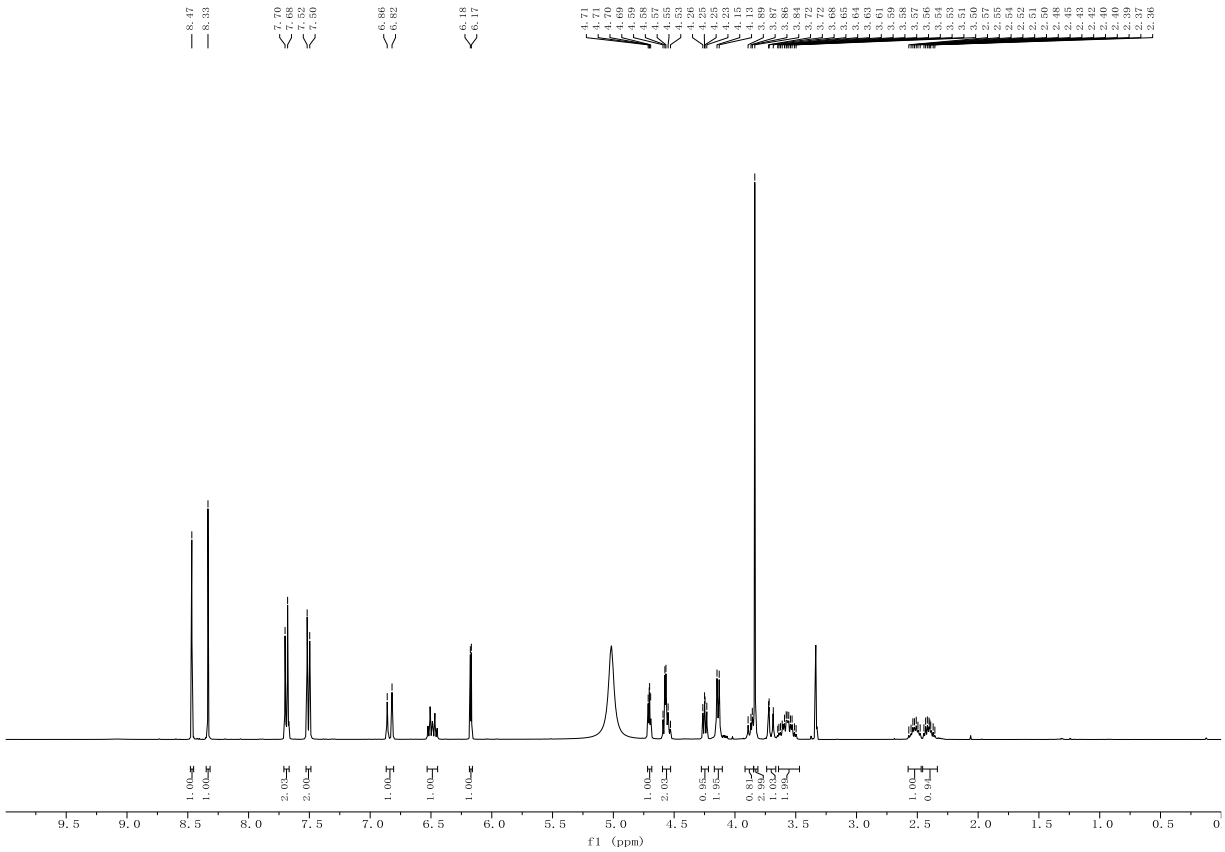


Compound **12b** ^{1}H NMR (400 MHz, CD_3OD)



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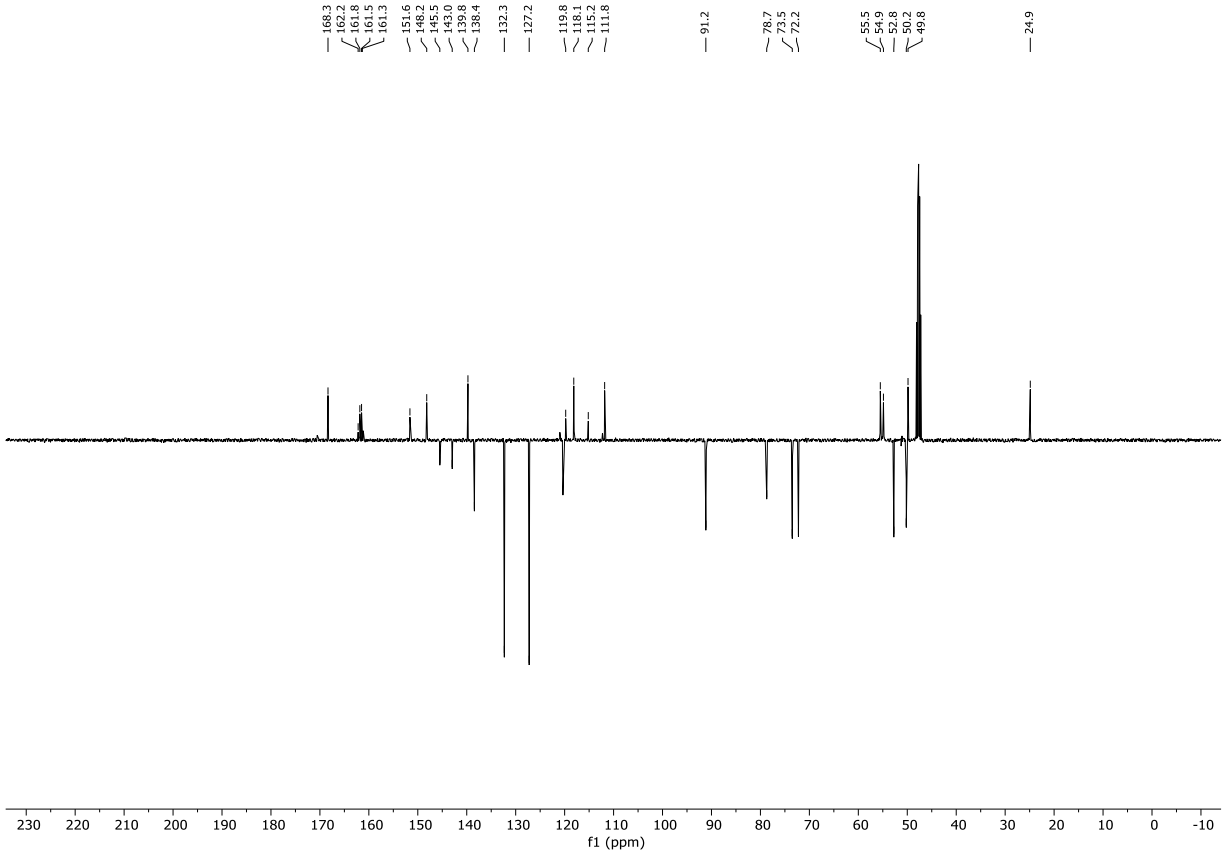
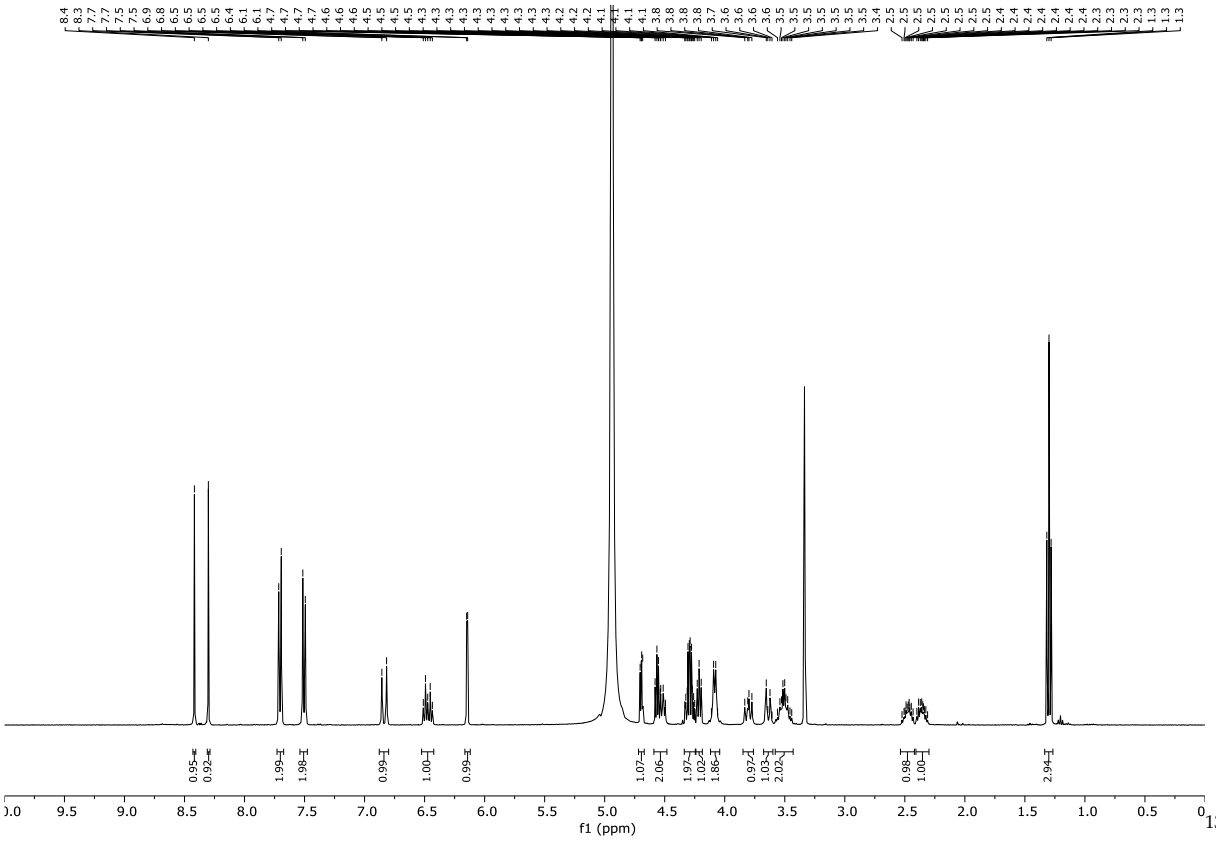


Compound **12c** ^{1}H NMR (400 MHz, CD_3OD)



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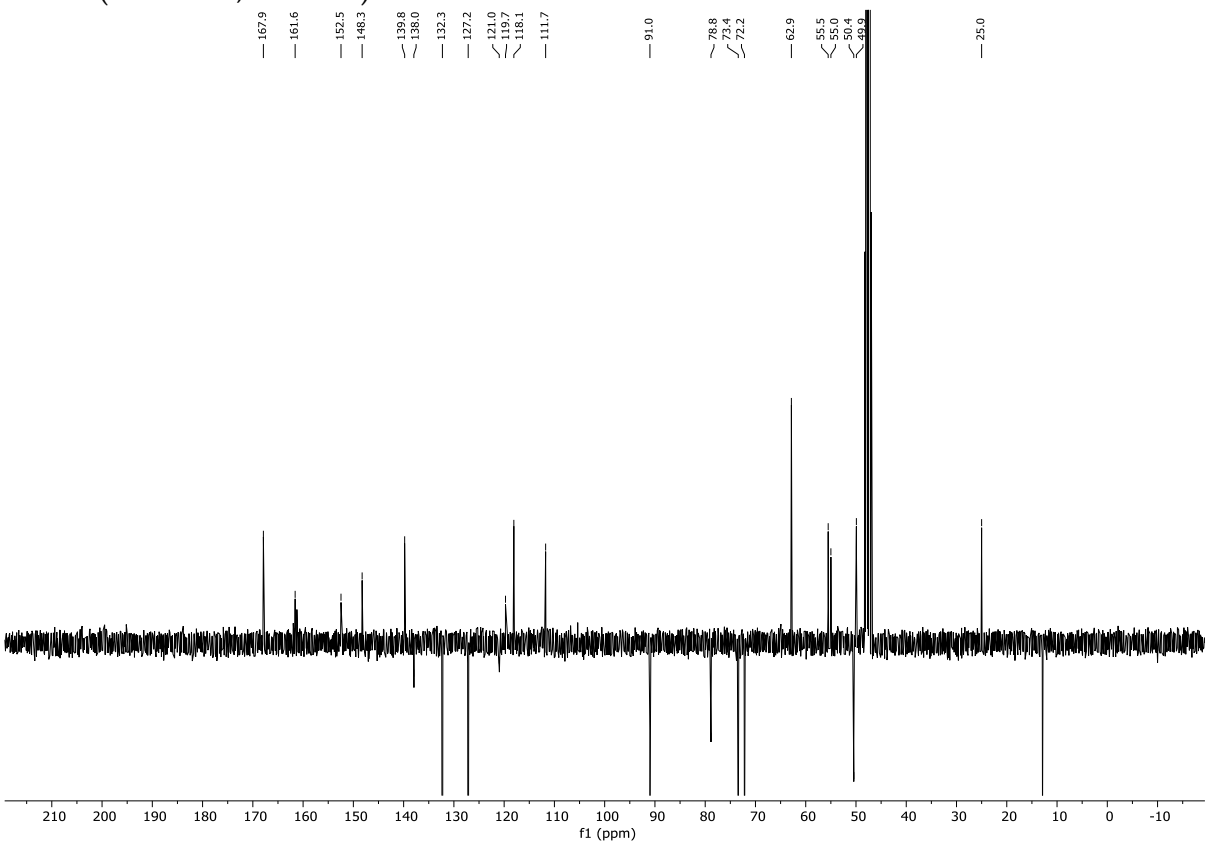

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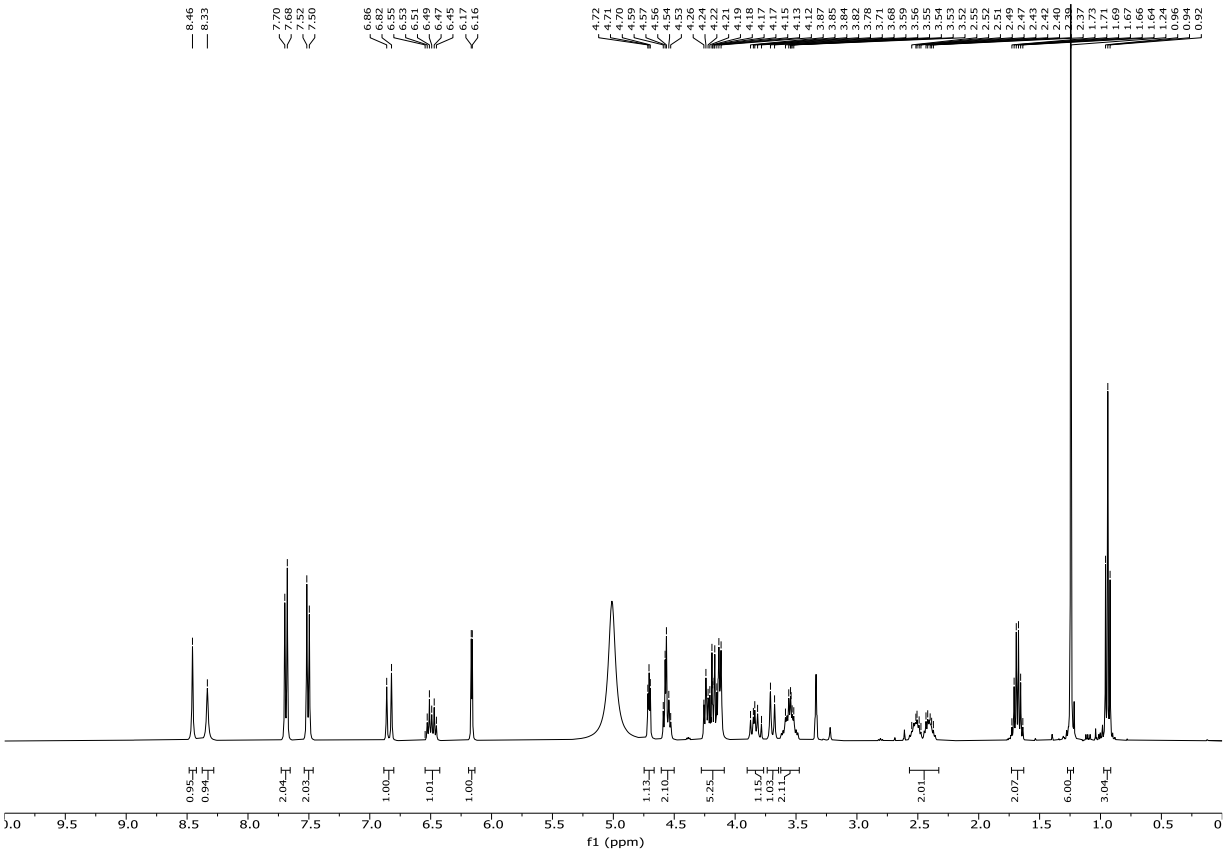

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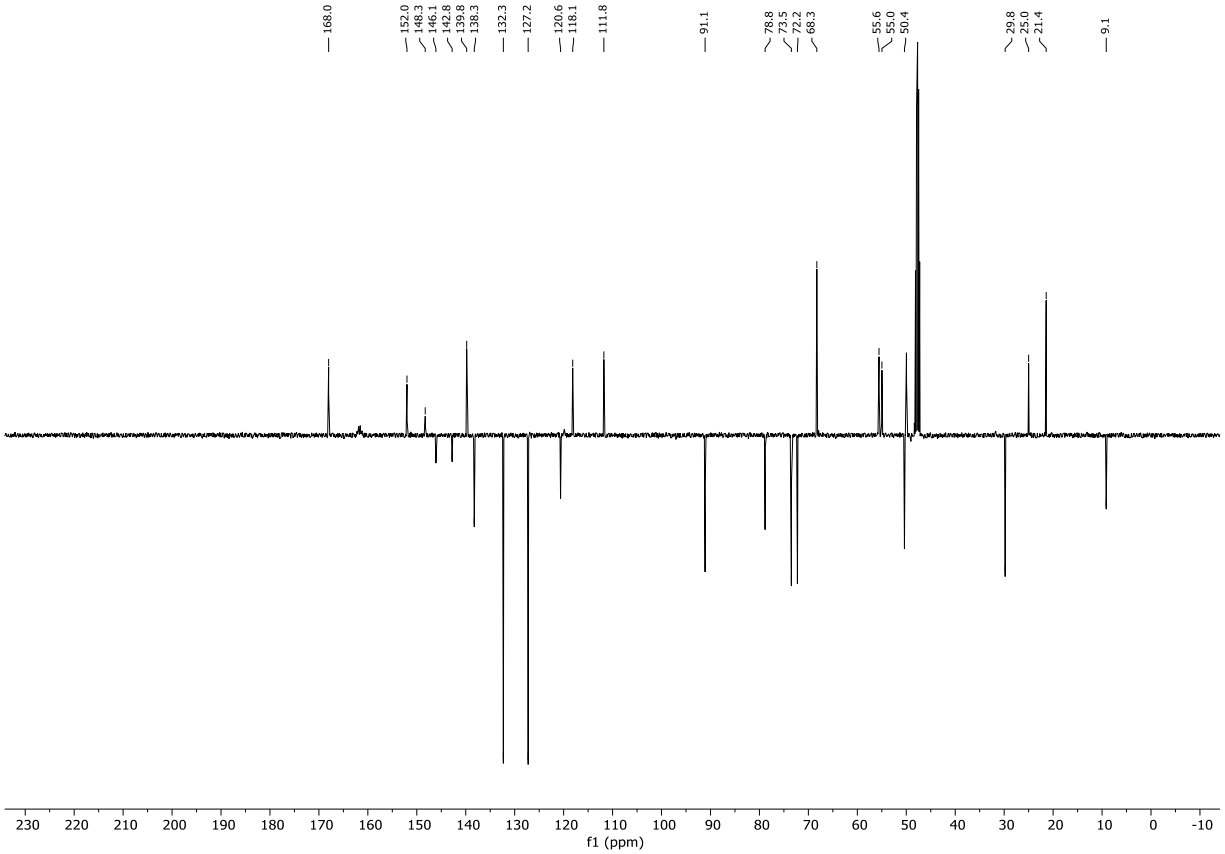

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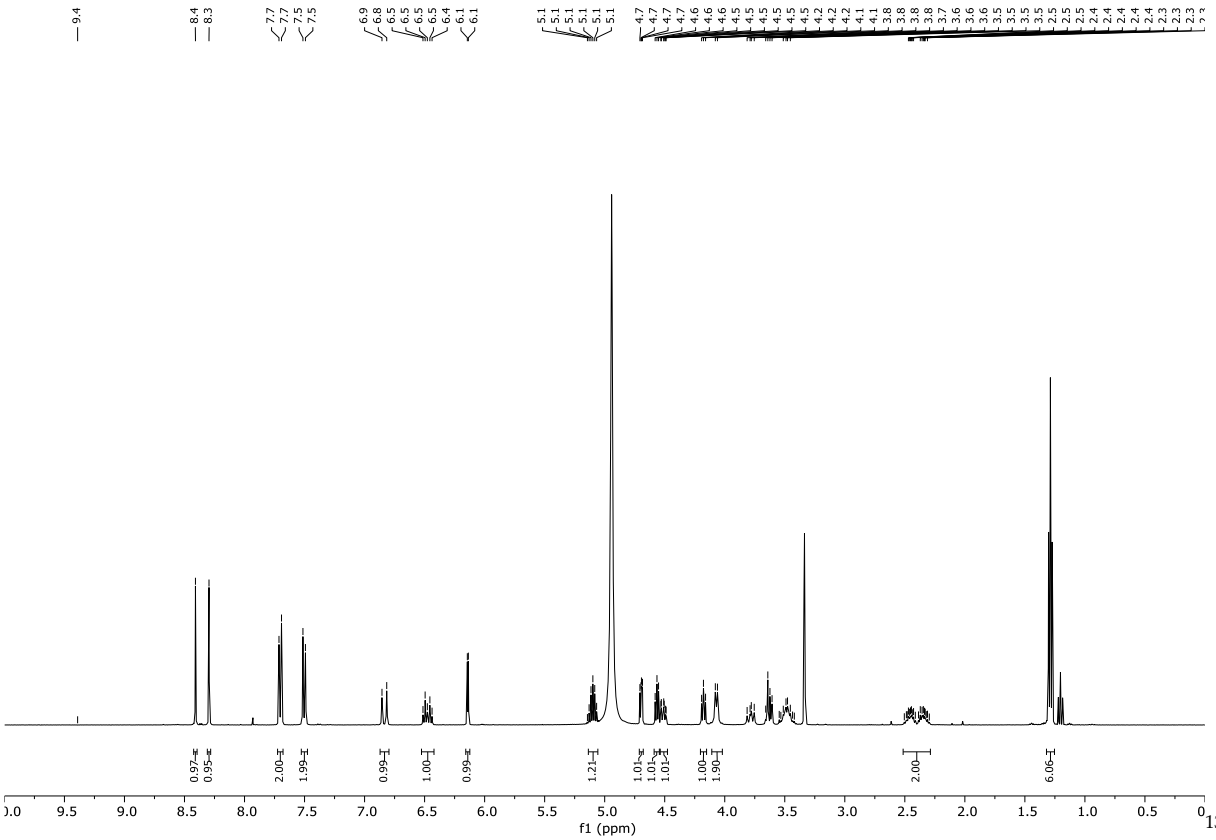

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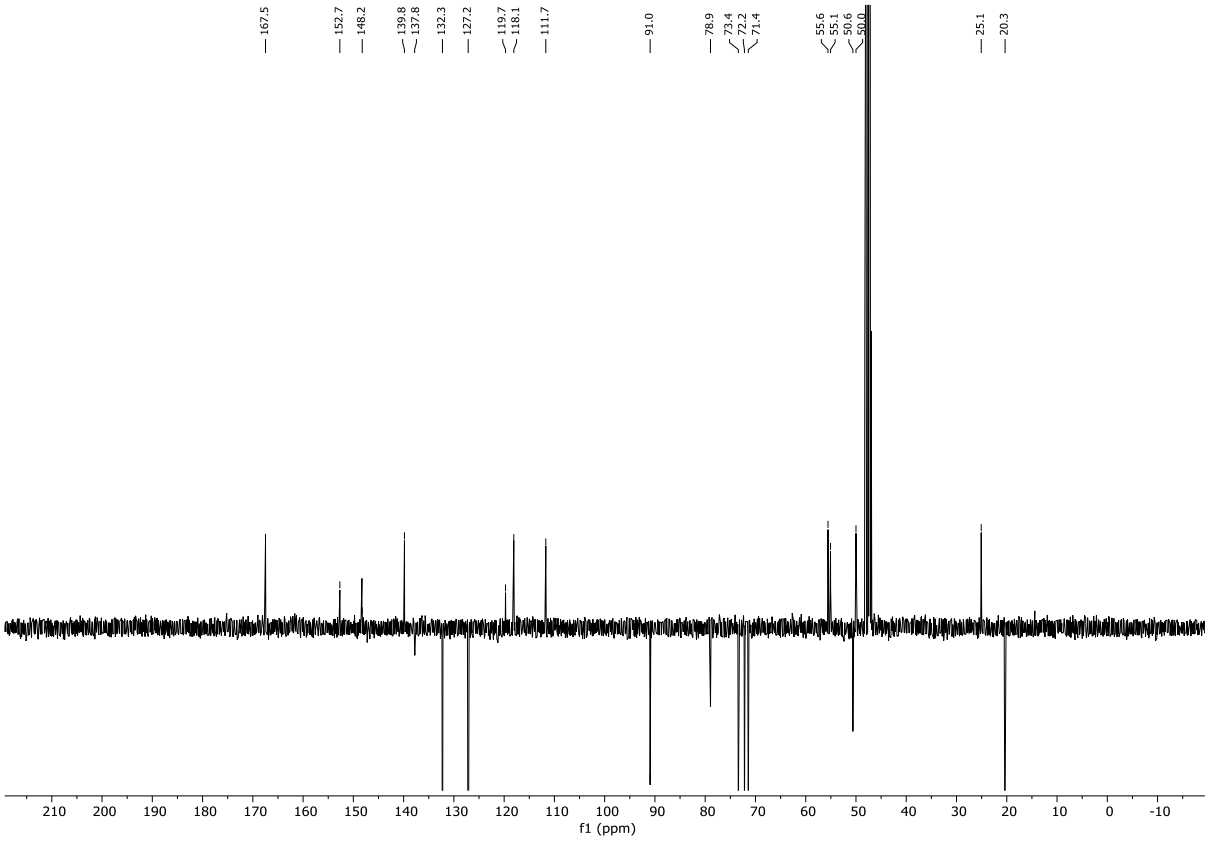
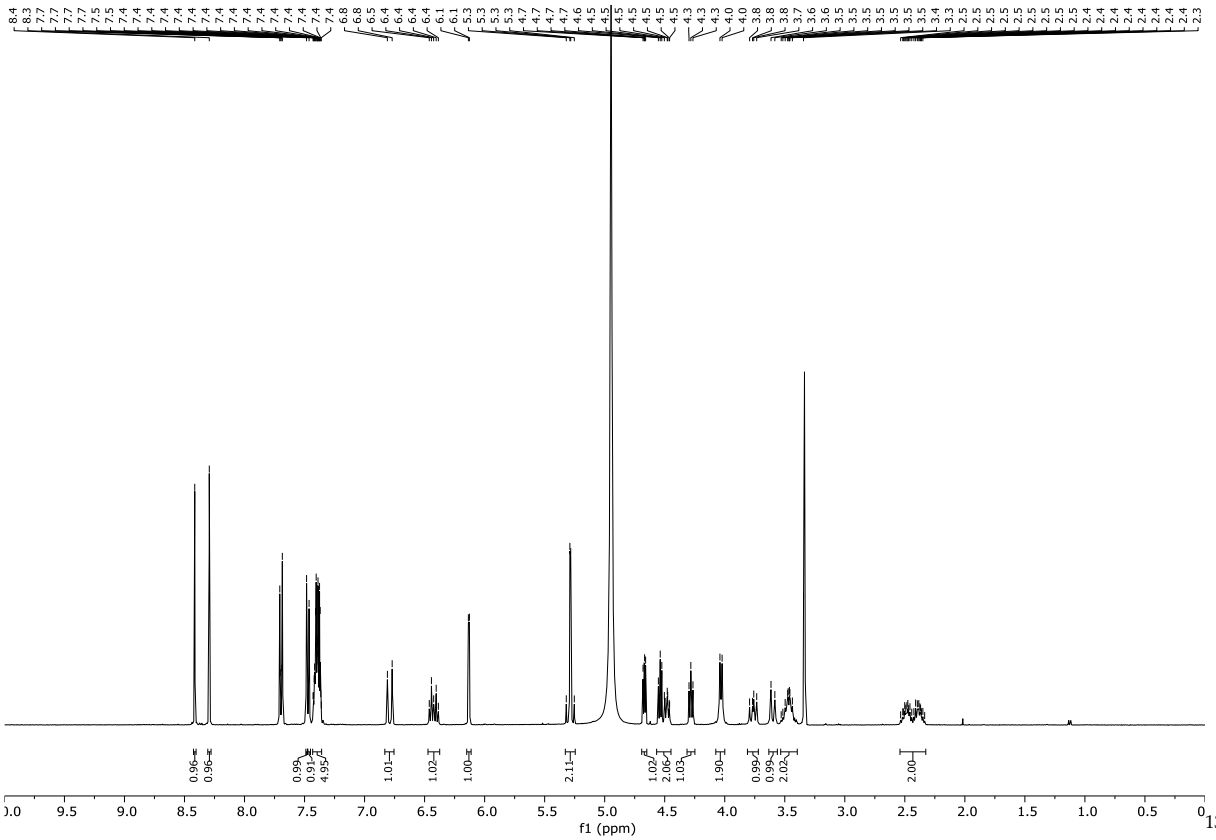


Compound **12f** ^{1}H NMR (400 MHz, CD_3OD)



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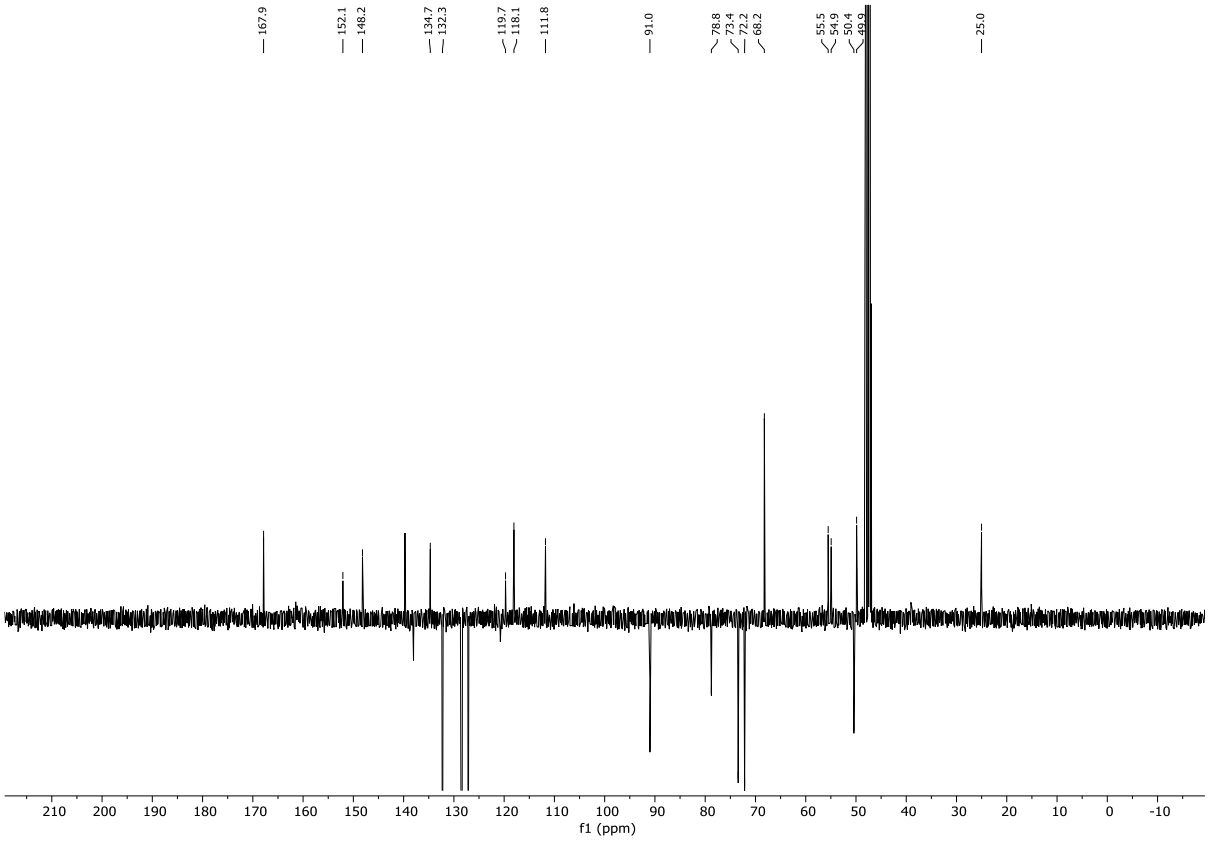
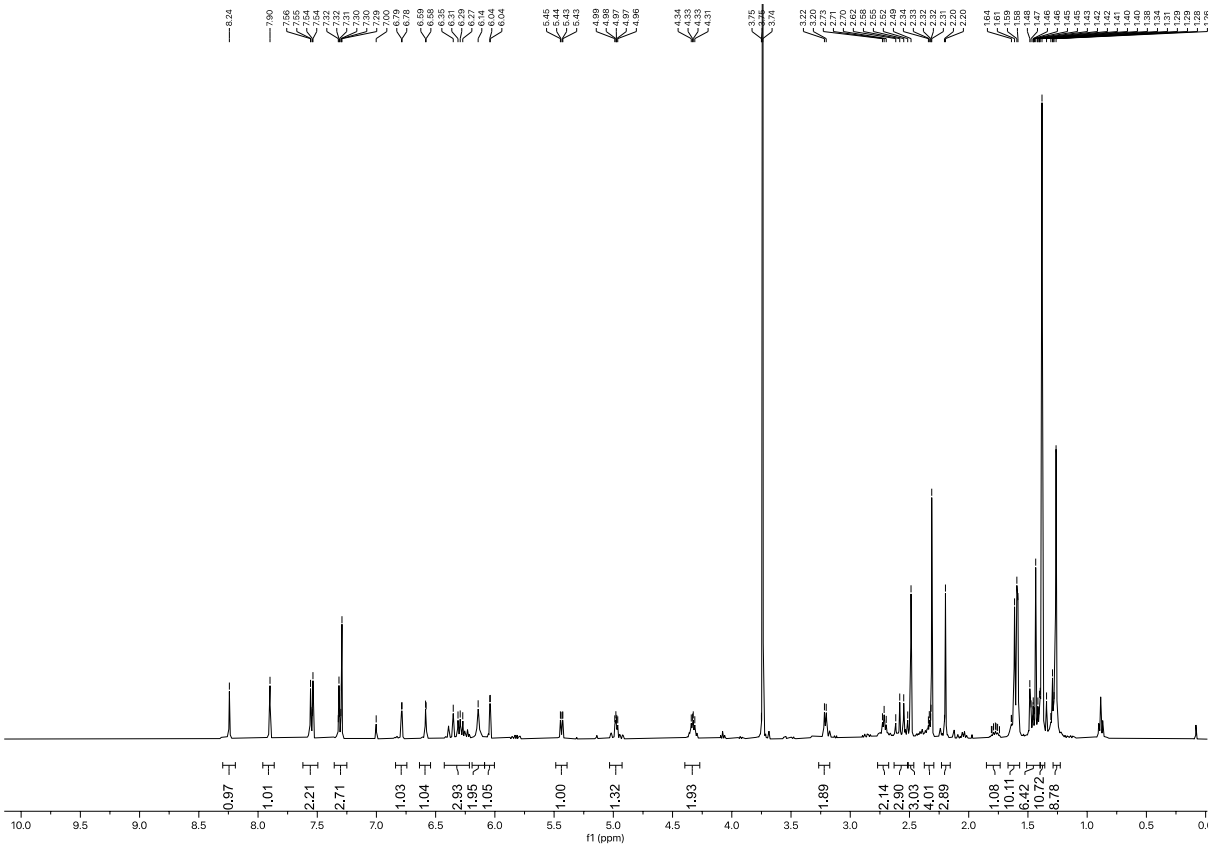
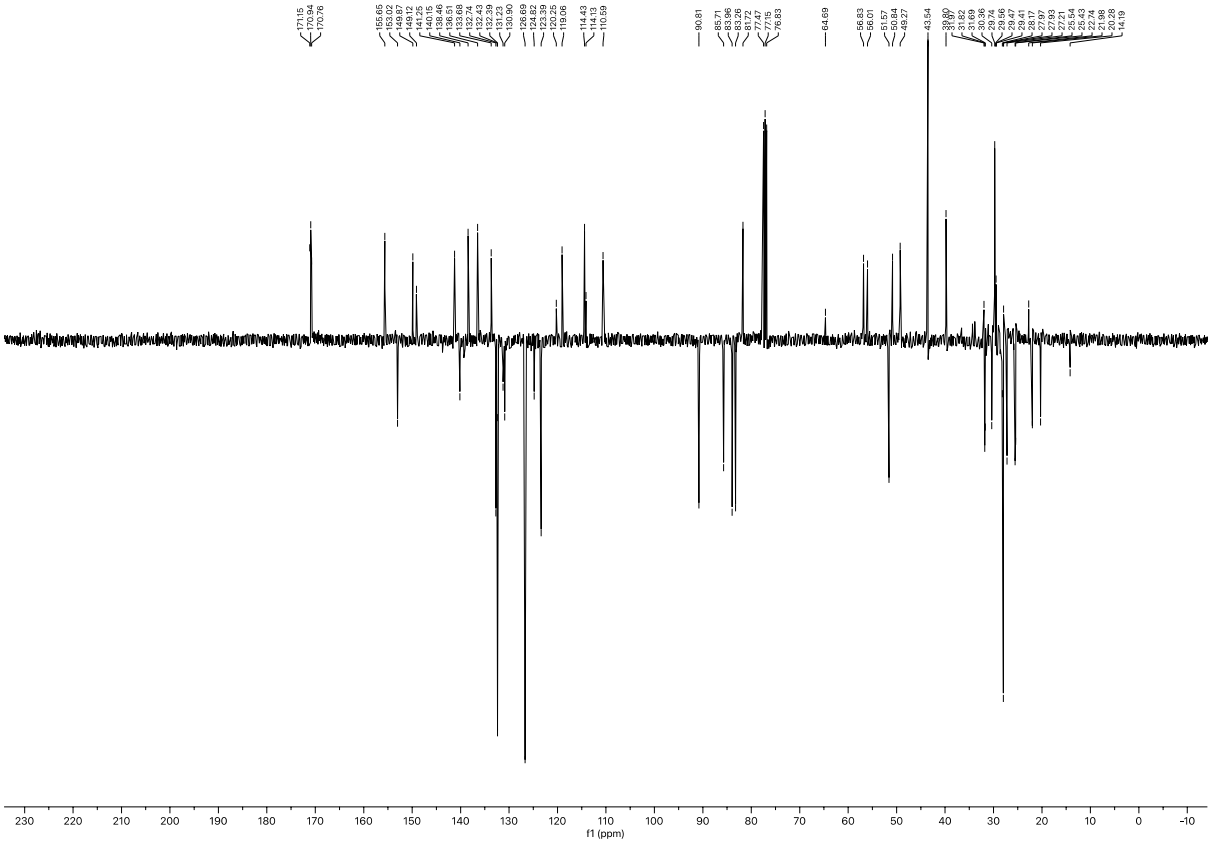


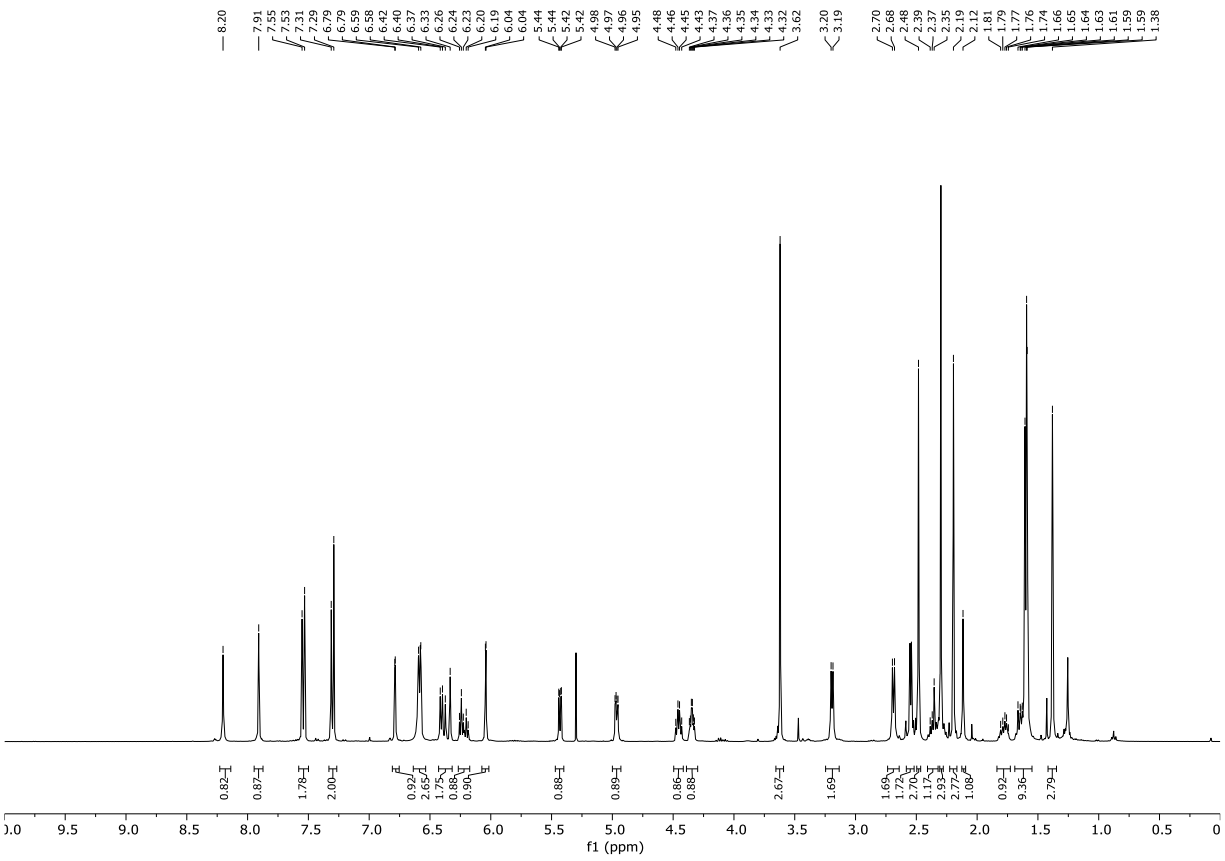
Compound **13a** ^{1}H NMR (400 MHz, $CDCl_3$)



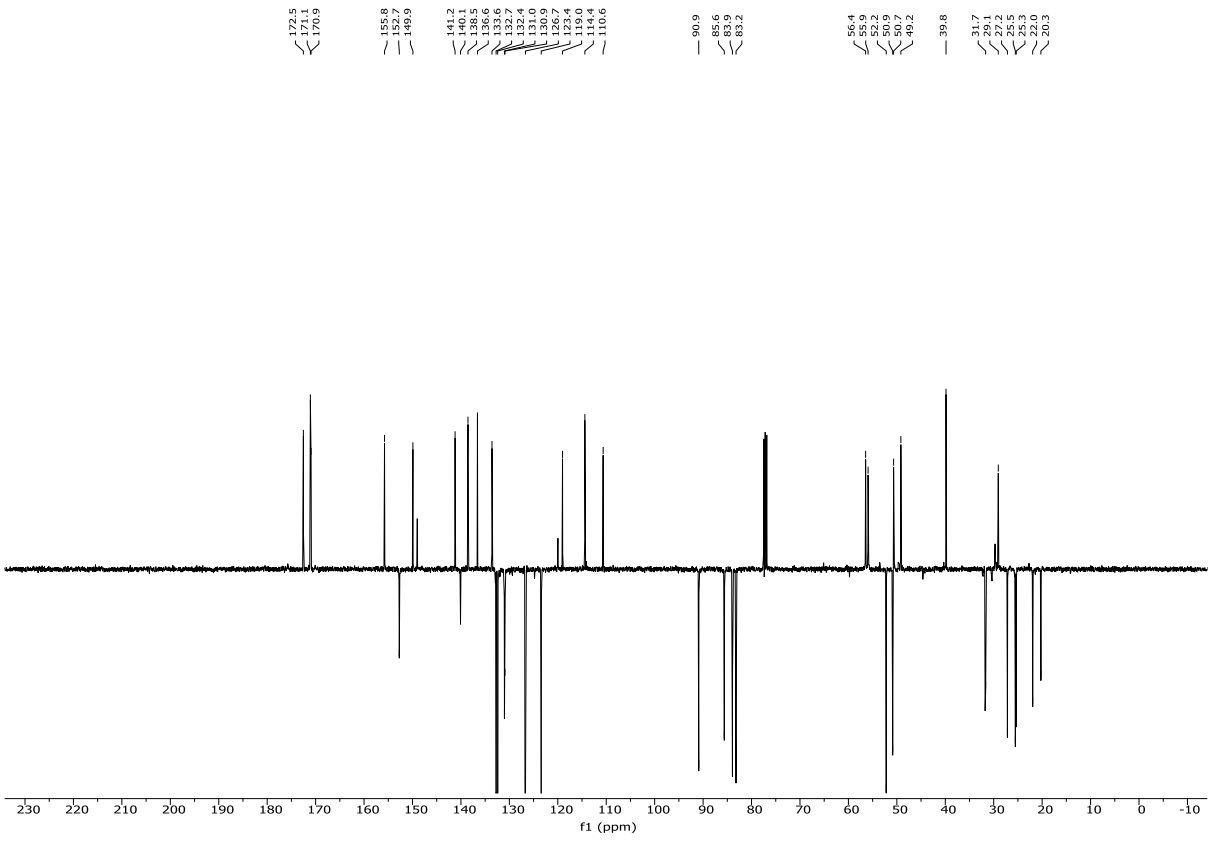
^{13}C NMR (101 MHz, $CDCl_3$)



Compound **13b** ^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



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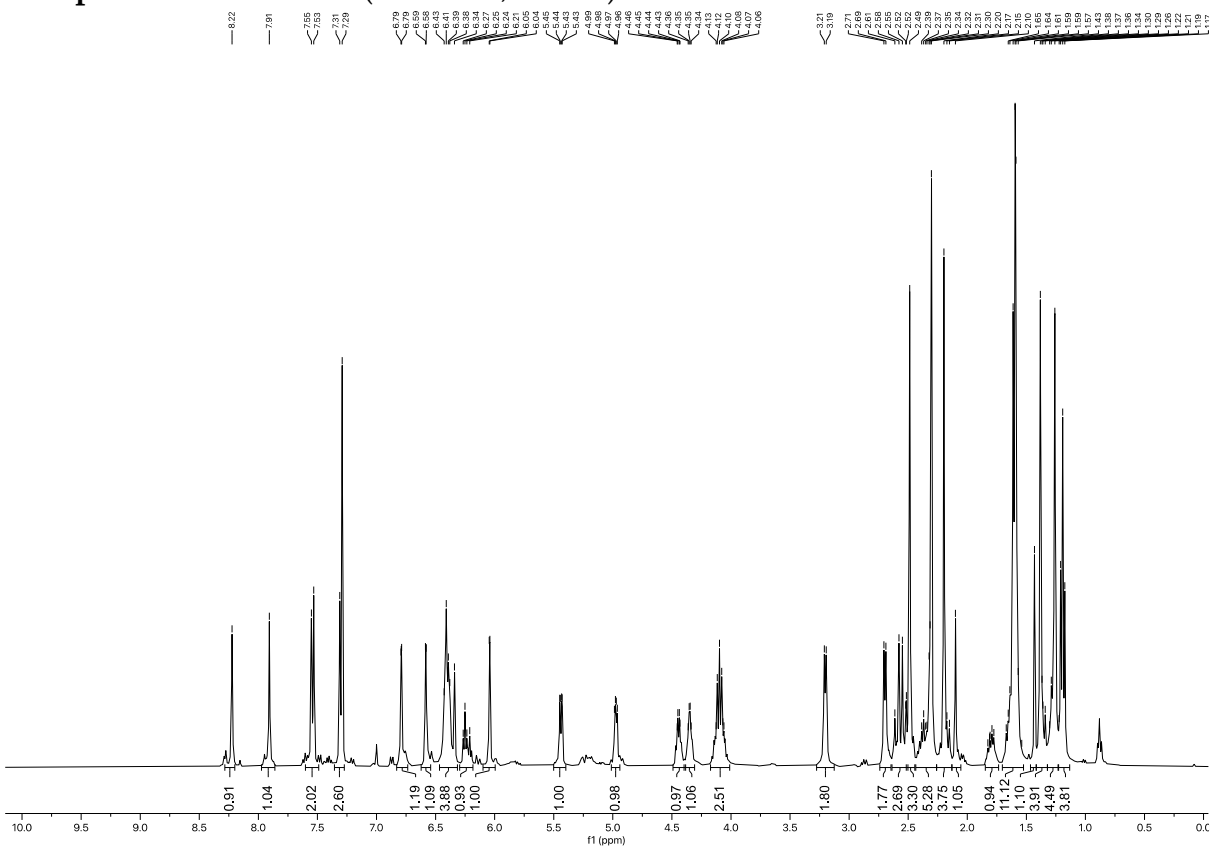

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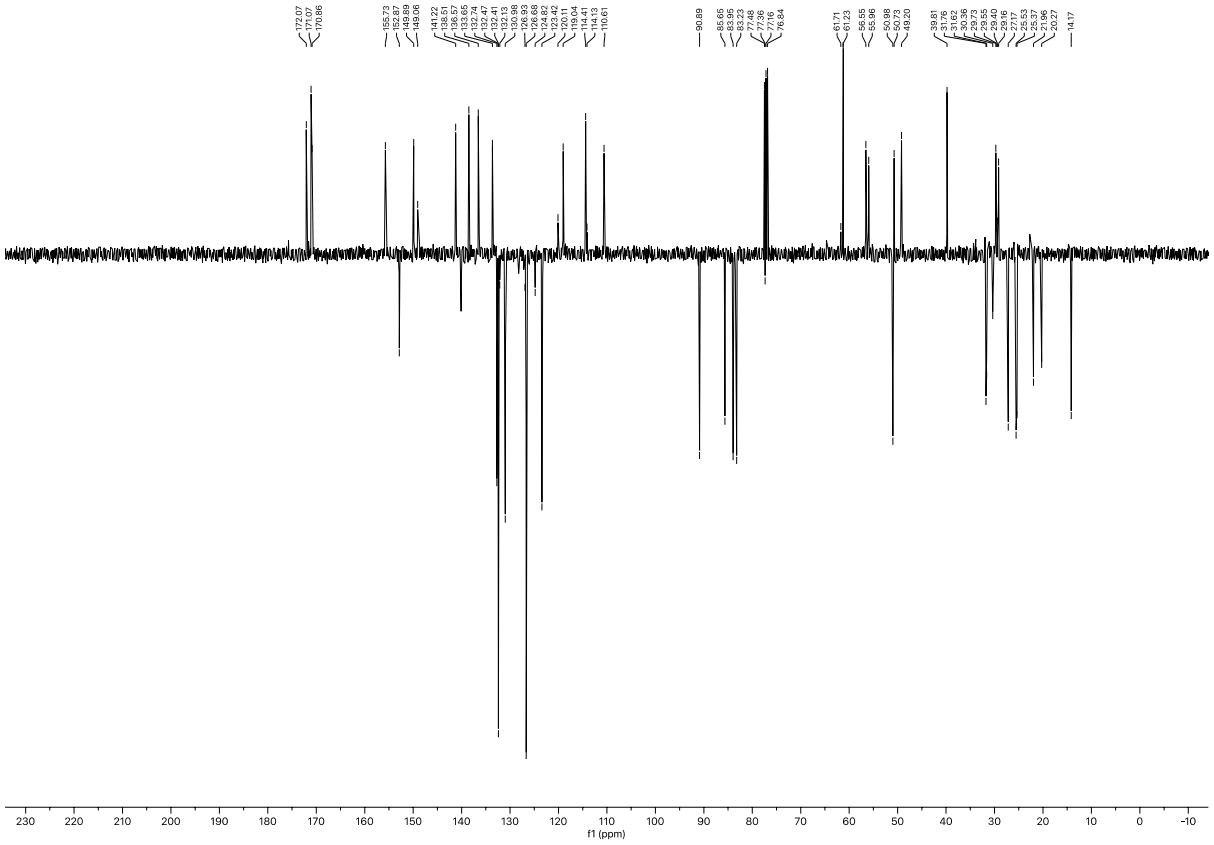
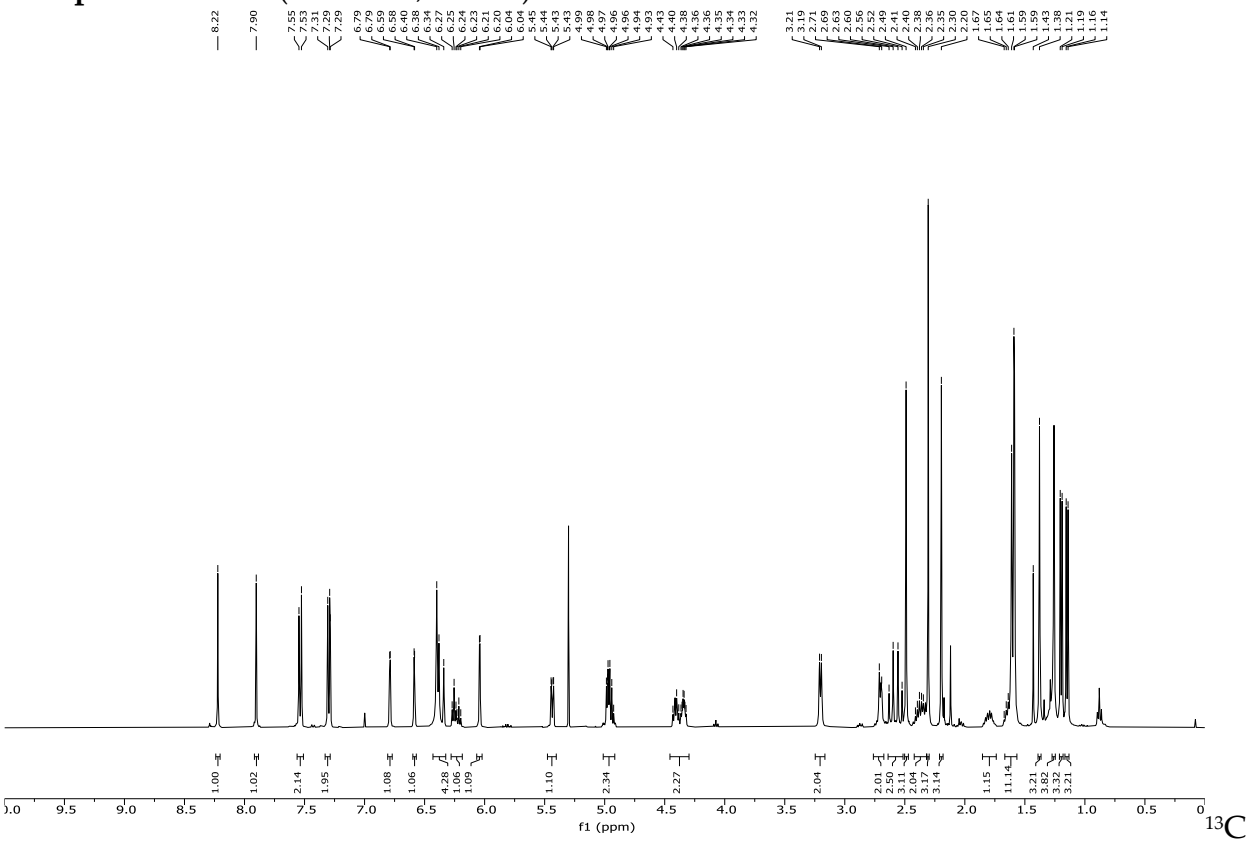


Compound 13e ^{1}H (400 MHz, $CDCl_3$)



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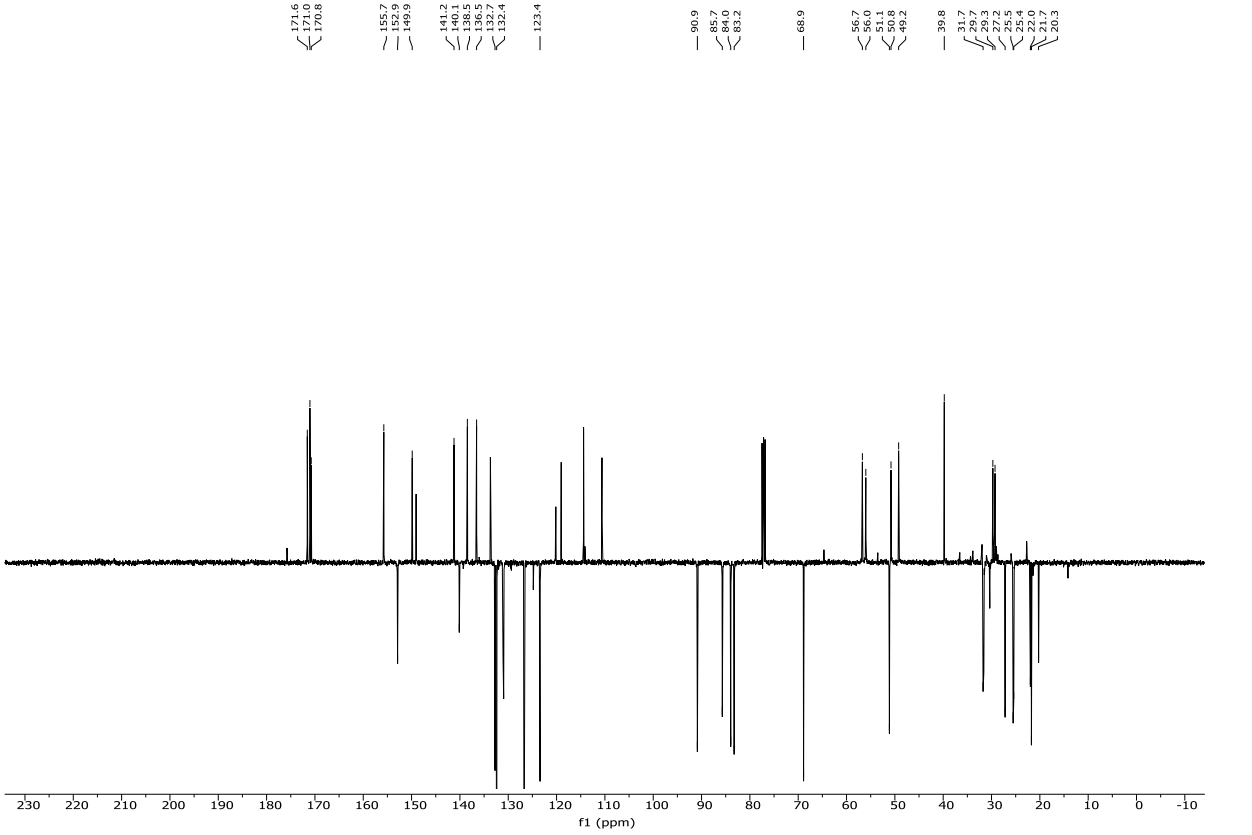
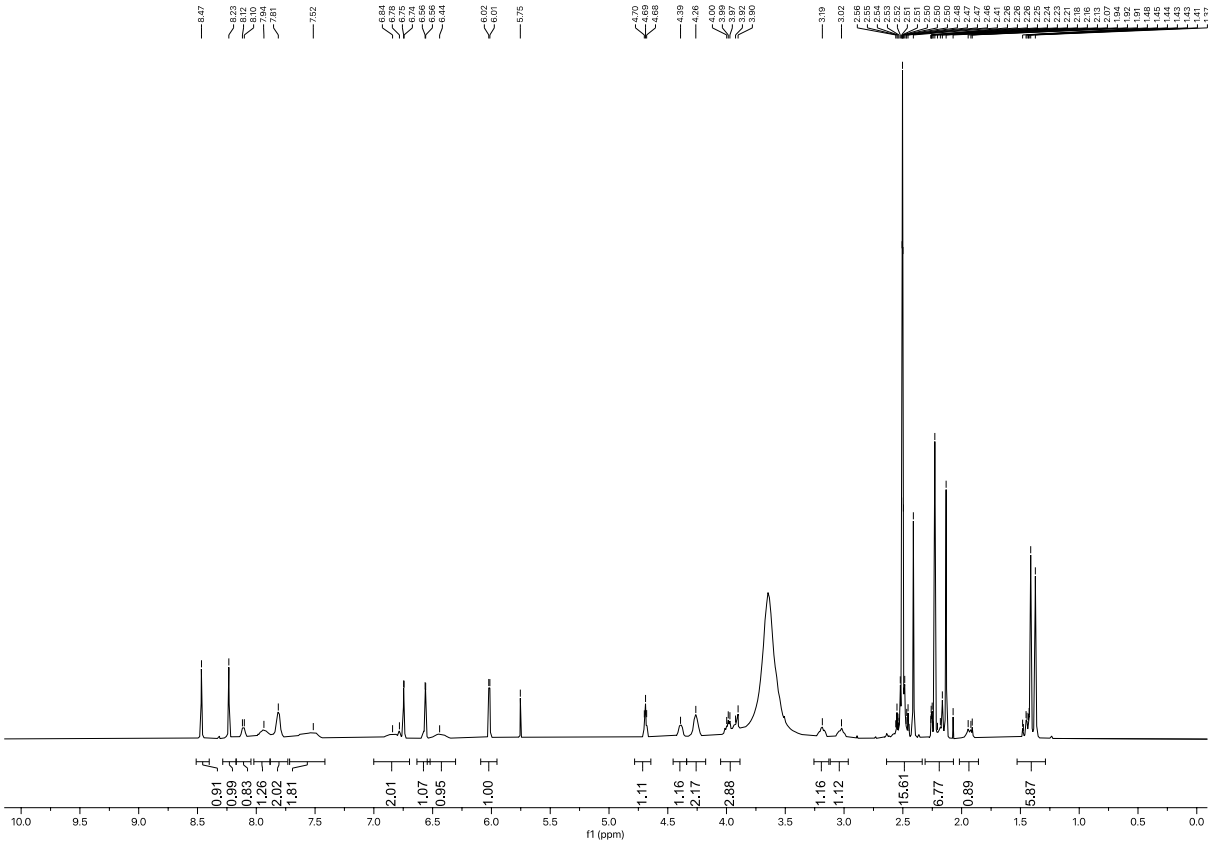
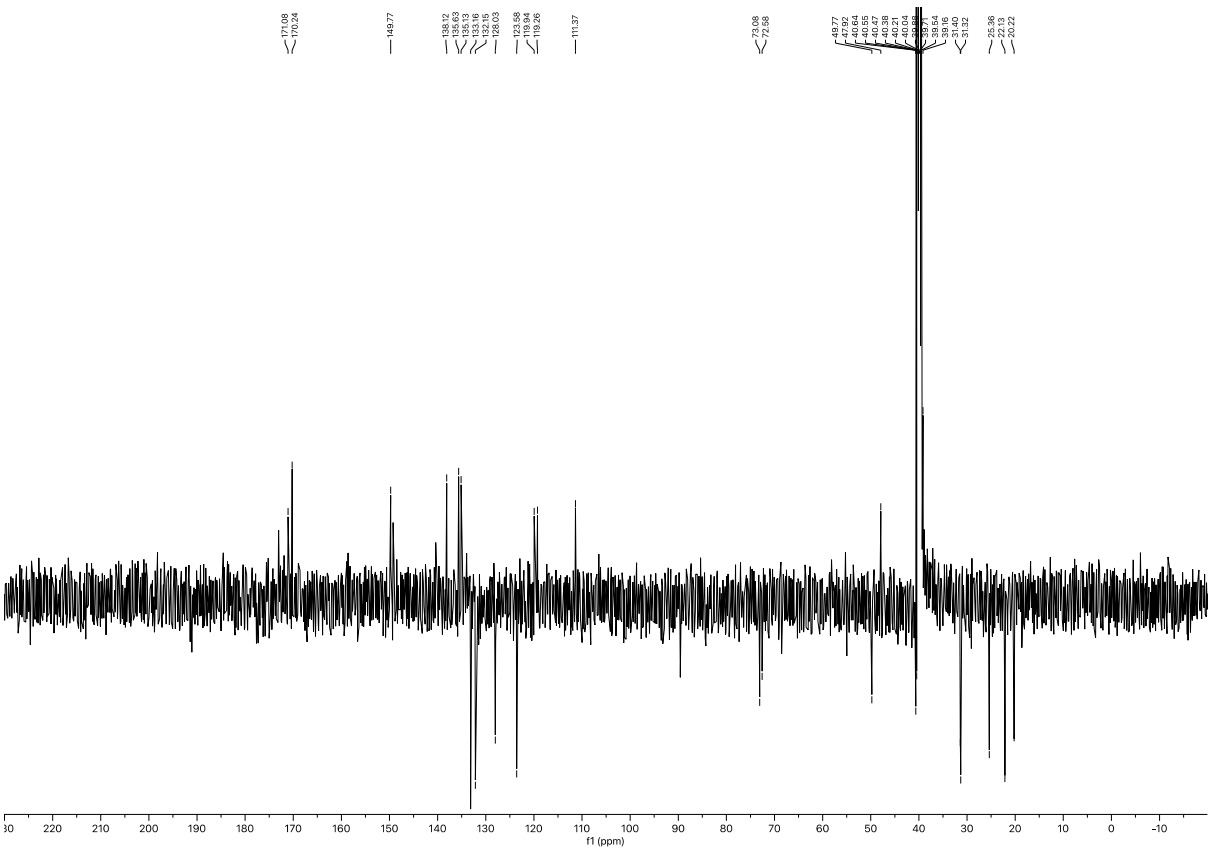


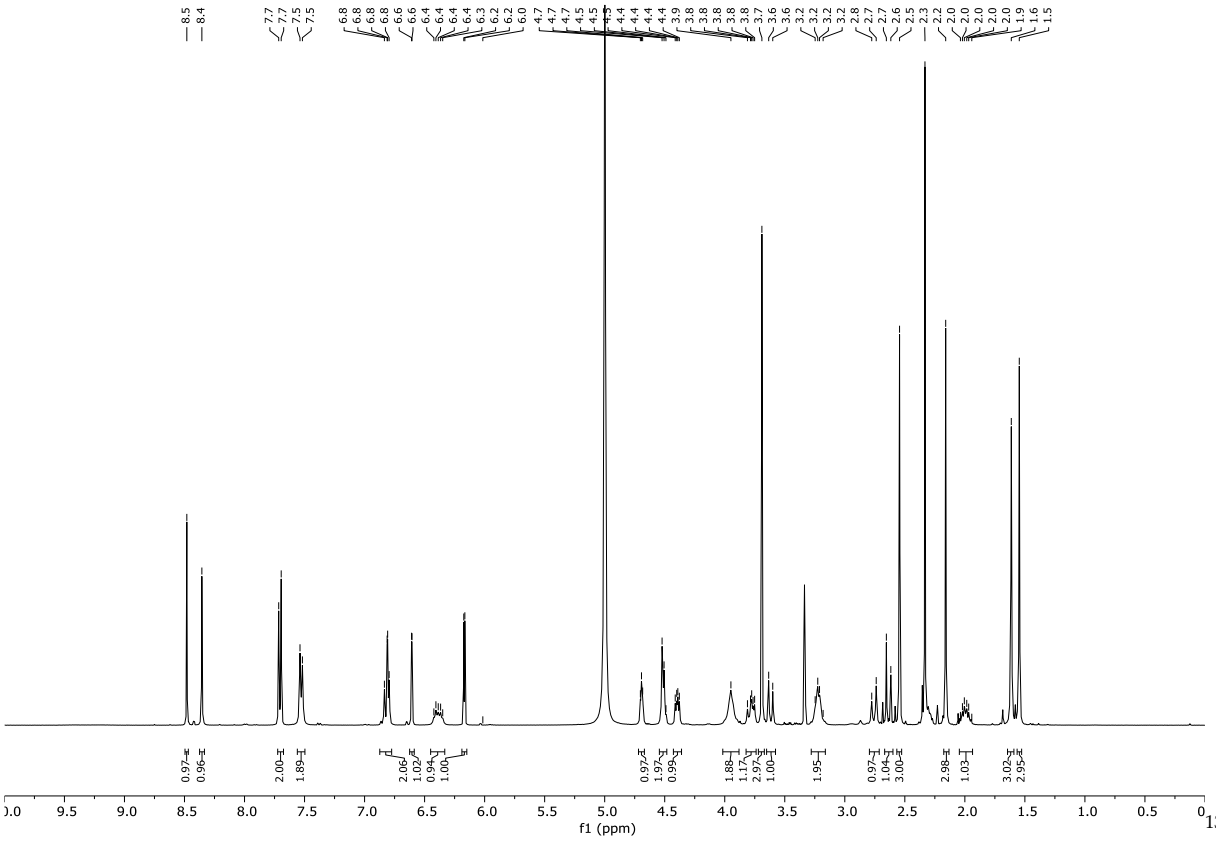
Compound **14a** ^{1}H (400 MHz, $CDCl_3$)



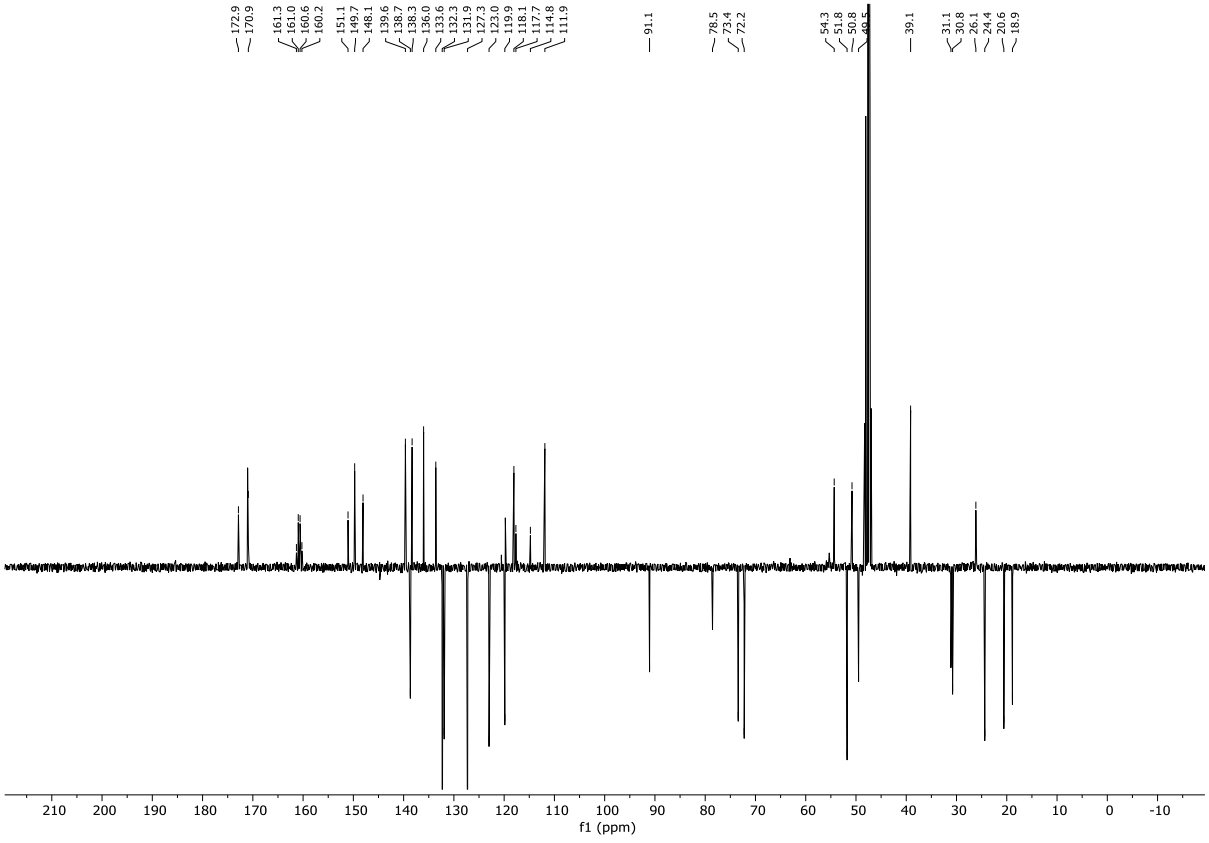
^{13}C NMR (101 MHz, $CDCl_3$)



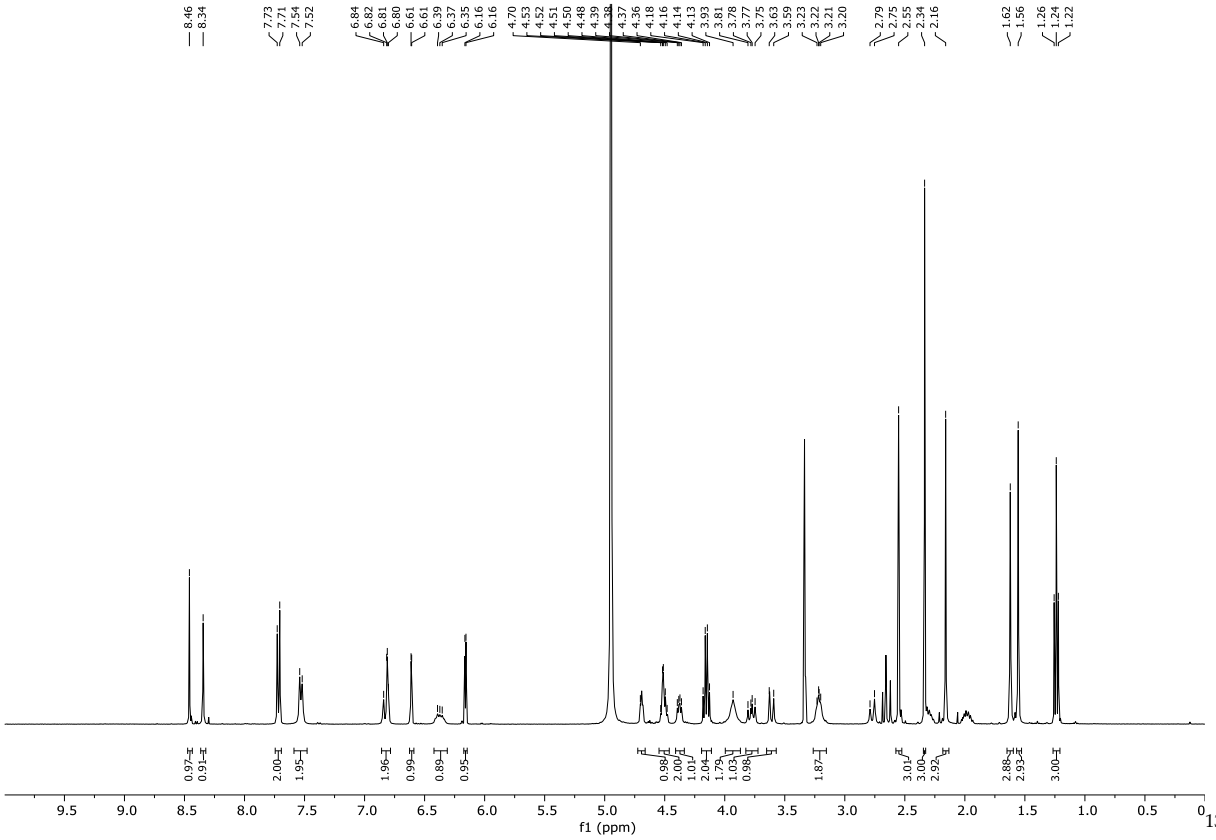
Compound **14b** ^{1}H NMR (400 MHz, CD_3OD)



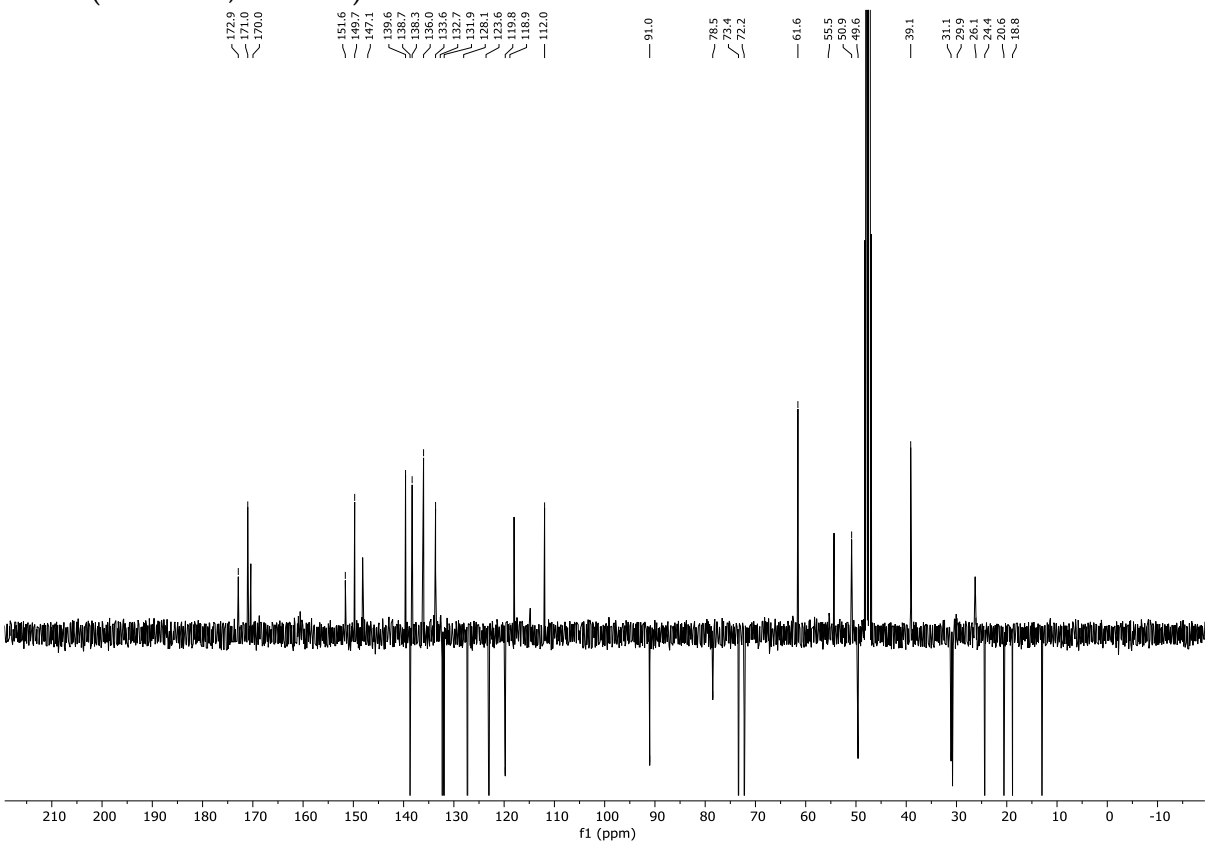
^{13}C NMR (400 MHz, CD_3OD)



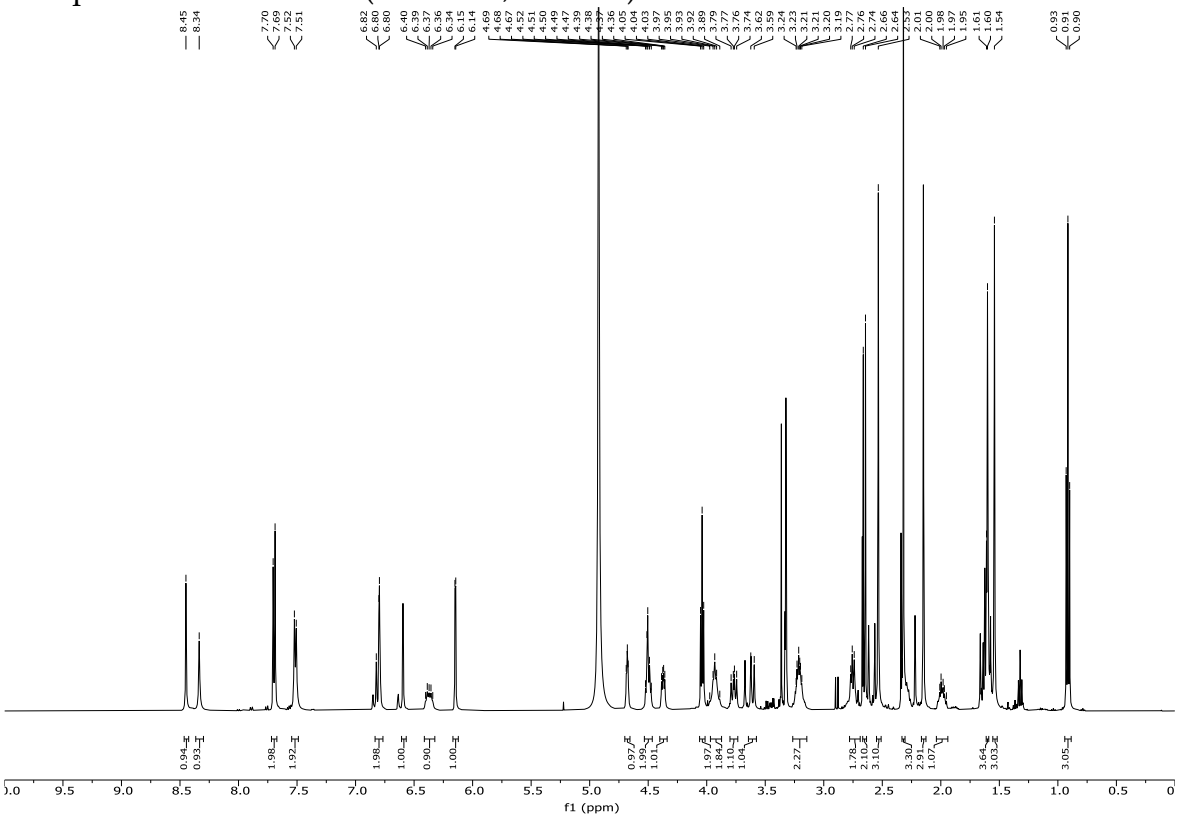
Compound **14c** ^{1}H NMR (400 MHz, CD_3OD)



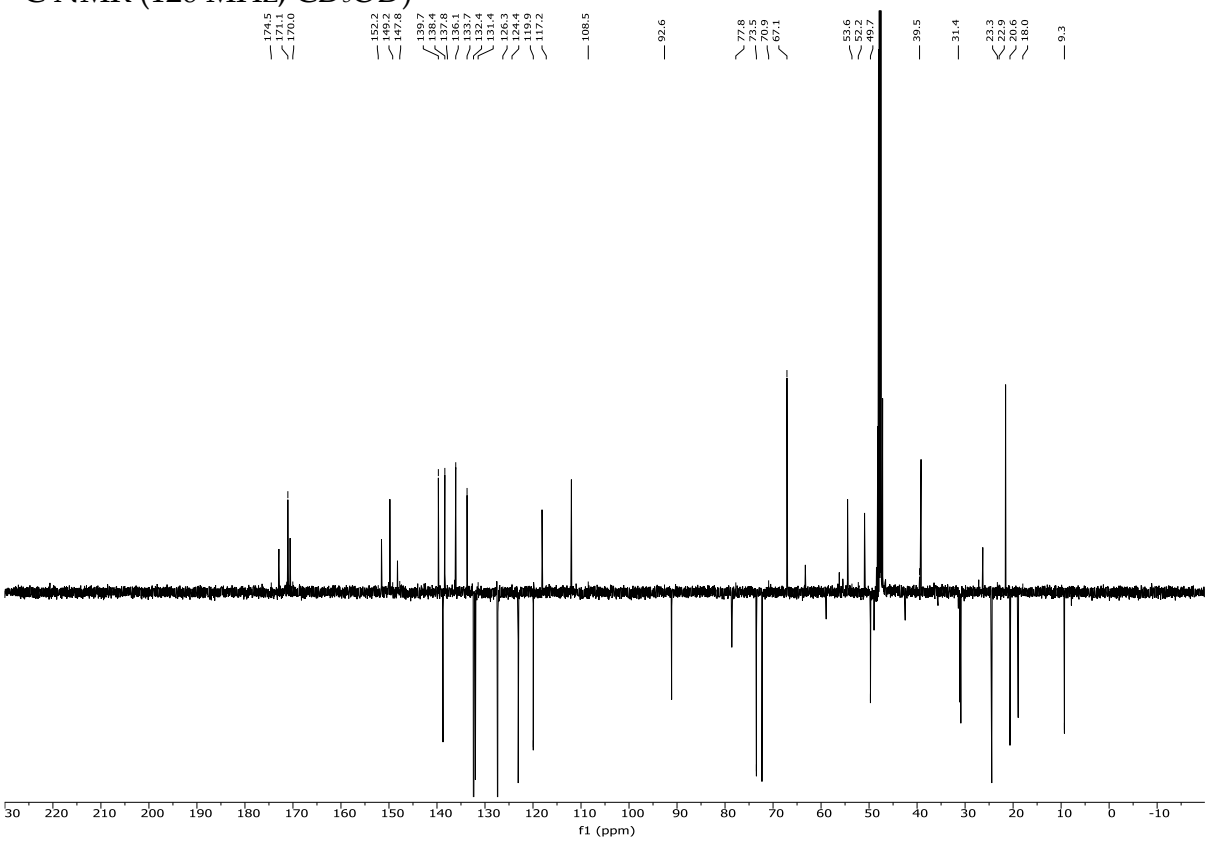
^{13}C NMR (400 MHz, CD_3OD)



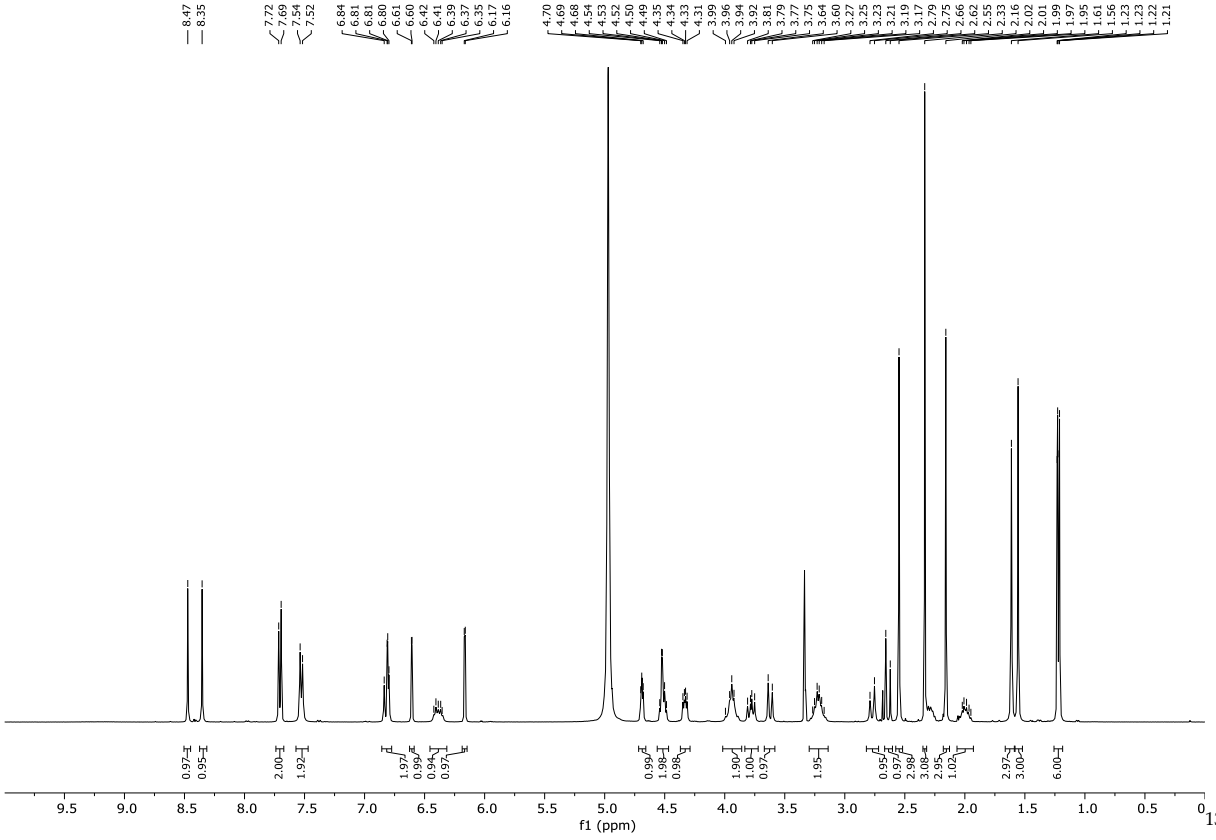
Compound **14d** ^{1}H NMR (500 MHz, CD_3OD)



^{13}C NMR (126 MHz, CD_3OD)



Compound **14e** ^{1}H NMR (400 MHz, CD_3OD)



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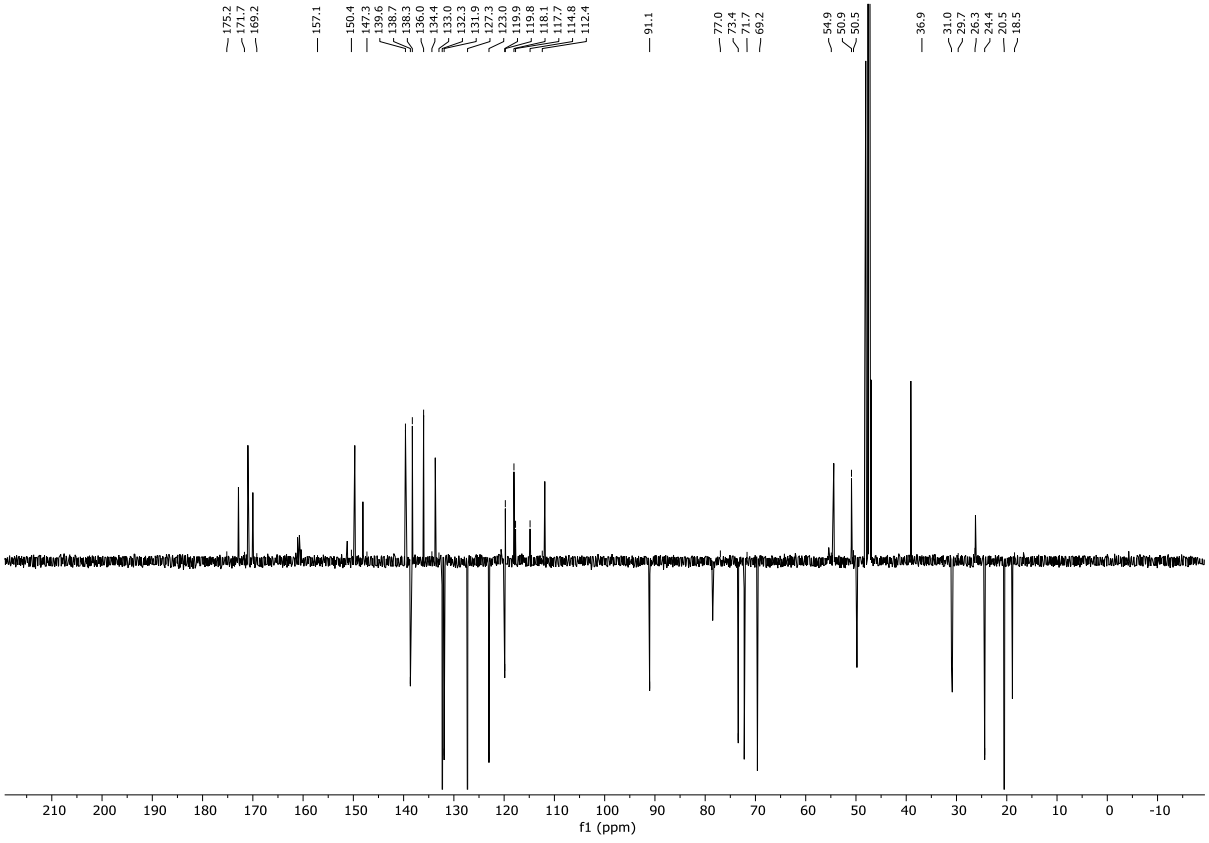
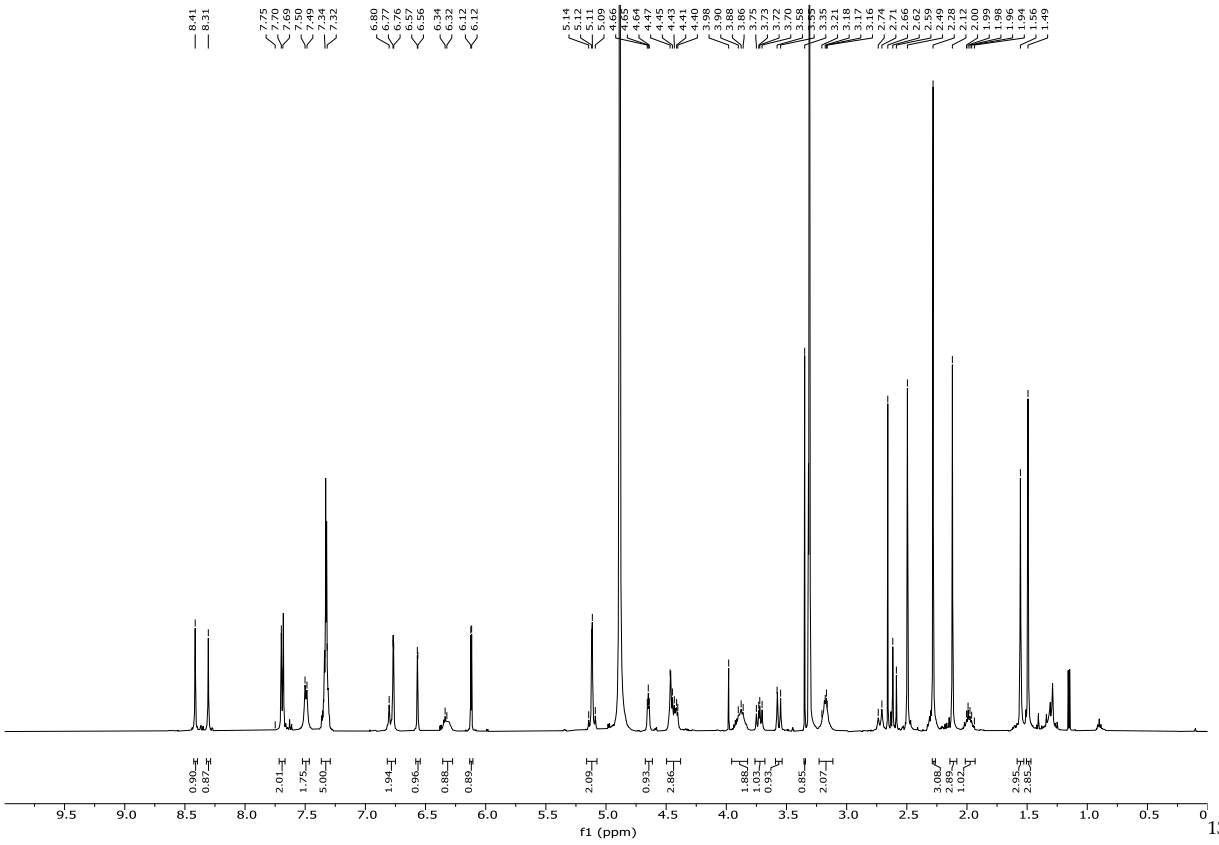


Compound **14f** ^{1}H NMR (500 MHz, CD_3OD)



^{13}C NMR (126 MHz, CD_3OD)