Supplementary Information

Identification of optically active pyrimidine derivatives as selective 5-HT_{2C} modulators

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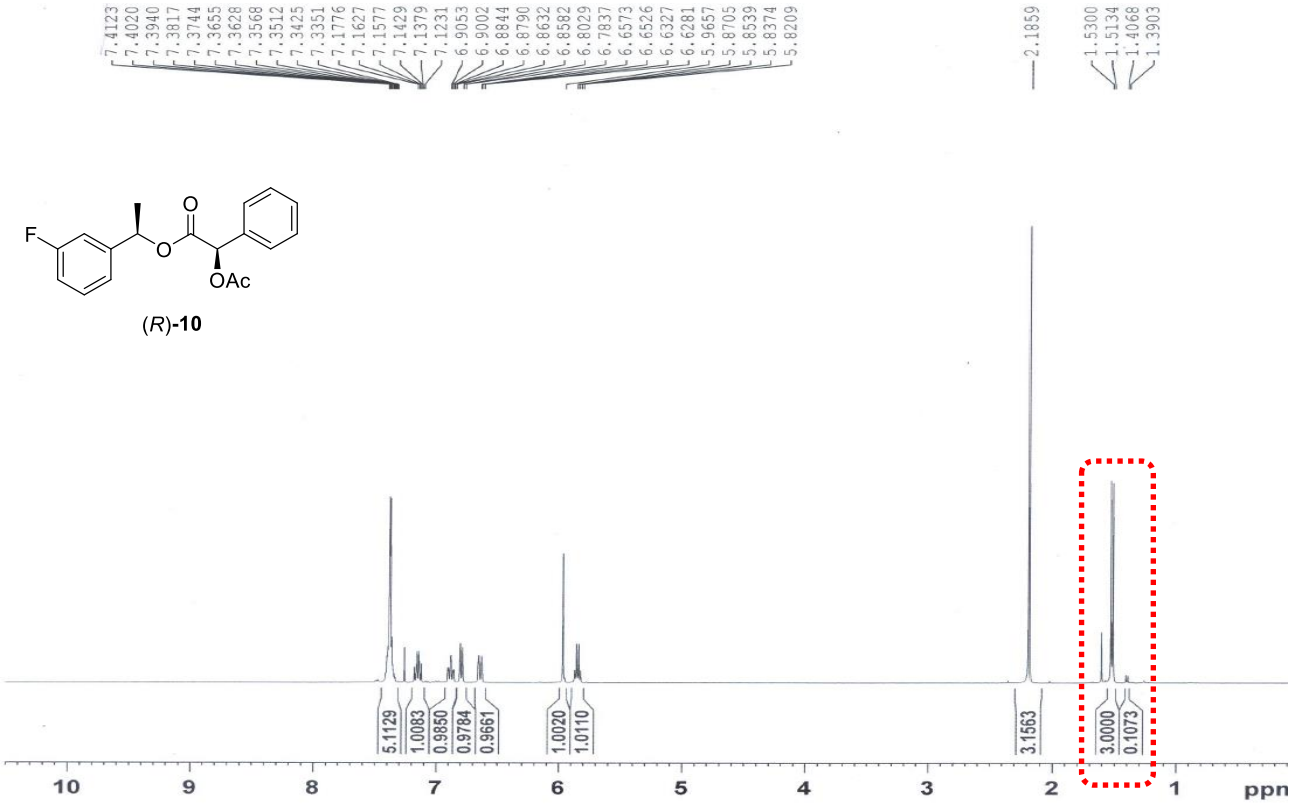
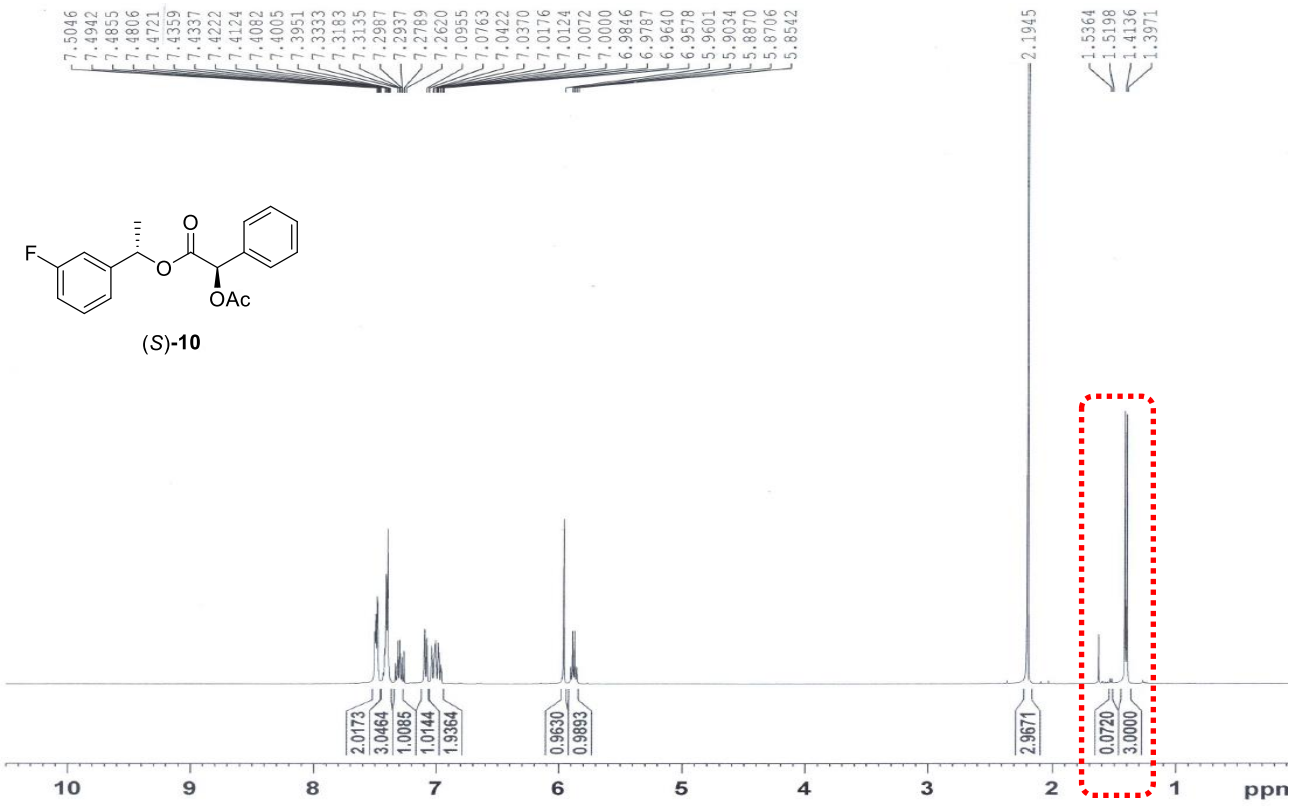
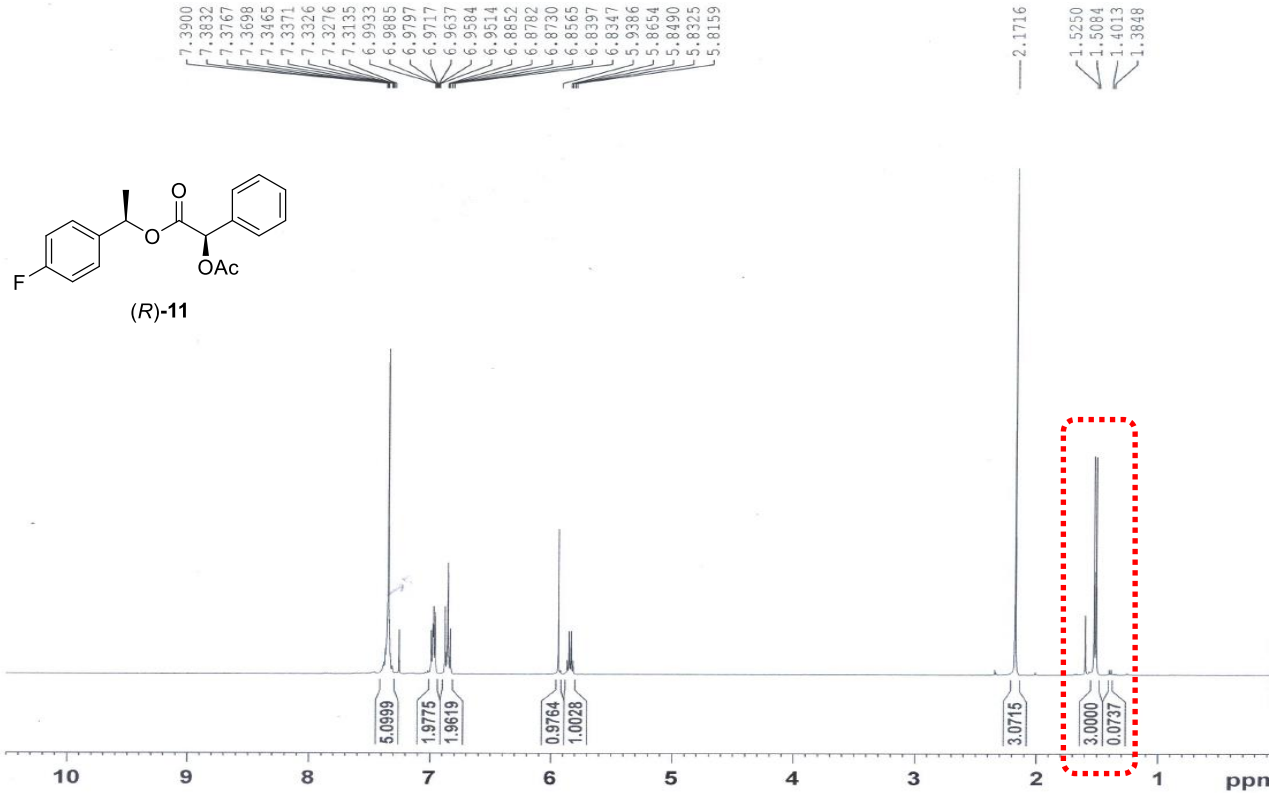
1. Determination of optical purities of compounds (*R*)/(*S*)-**5d** and **5e**



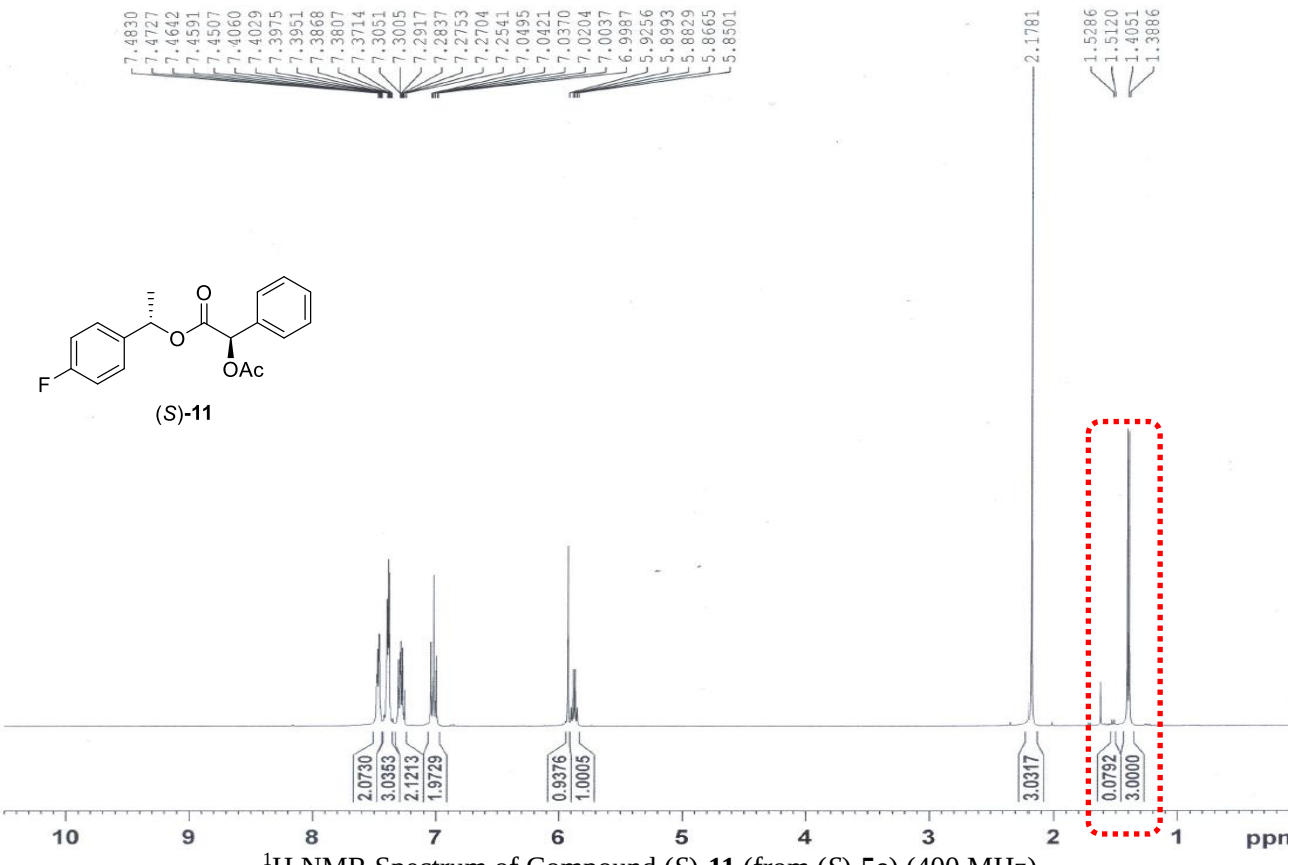
^{1}H NMR Spectrum of Compound (*R*)-**10** (from (*R*)-**5d**) (400 MHz)



^{1}H NMR Spectrum of Compound (*S*)-**10** (from (*S*)-**5d**) (400 MHz)



^{1}H NMR Spectrum of Compound (*R*)-**11** (from (*R*)-**5e**) (400 MHz)



^{1}H NMR Spectrum of Compound (*S*)-**11** (from (*S*)-**5e**) (400 MHz)

2. Radioligands and reference compounds for binding assay

Table S1. A list of 5-HT receptor radioligands and reference compounds for binding assay.

Receptor subtype	Radioligand	Reference compound
1A	[^{3}H]8-OH-DPAT	Methysergide
1B	[^{3}H]GR125743	Ergotamine
1D	[^{3}H]GR125743	Ergotamine
1E	[^{3}H]5-HT	5-HT
2A	[^{3}H]Ketanserin	Chlorpromazine
2B	[^{3}H]LSD	5-HT
2C	[^{3}H]Mesulergine	Chlorpromazine
3	[^{3}H]LY278584	LY278584
5A	[^{3}H]LSD	Ergotamine
6	[^{3}H]LSD	Chlorpromazine
7	[^{3}H]LSD	Chlorpromazine

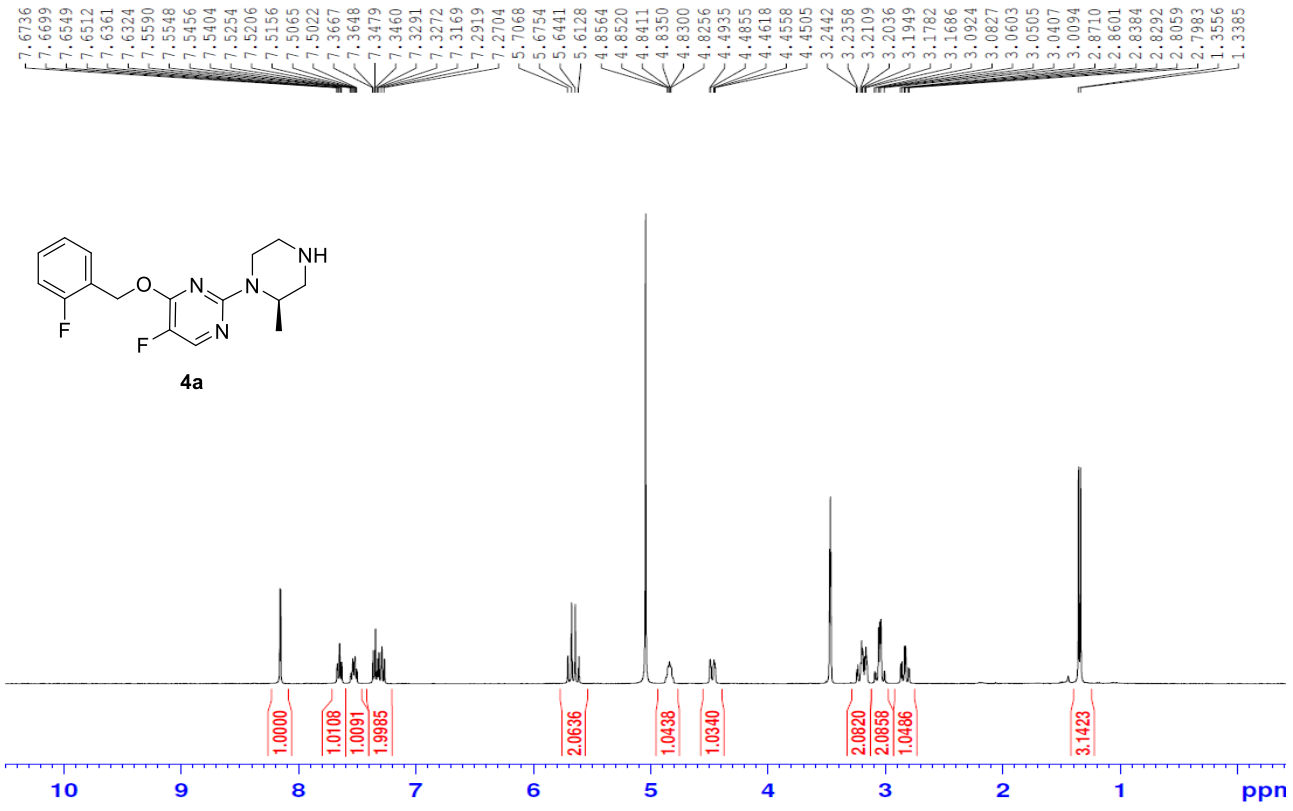
3. Binding affinity of (*R*,*R*)/(*S*,*R*)-**4d** and **4e** against 5-HT receptor subtypes

Table S2. Binding affinity evaluation of compounds (*R*,*R*)/(*S*,*R*)-**4d** and **4e** against 5-HT receptor subtypes[a]

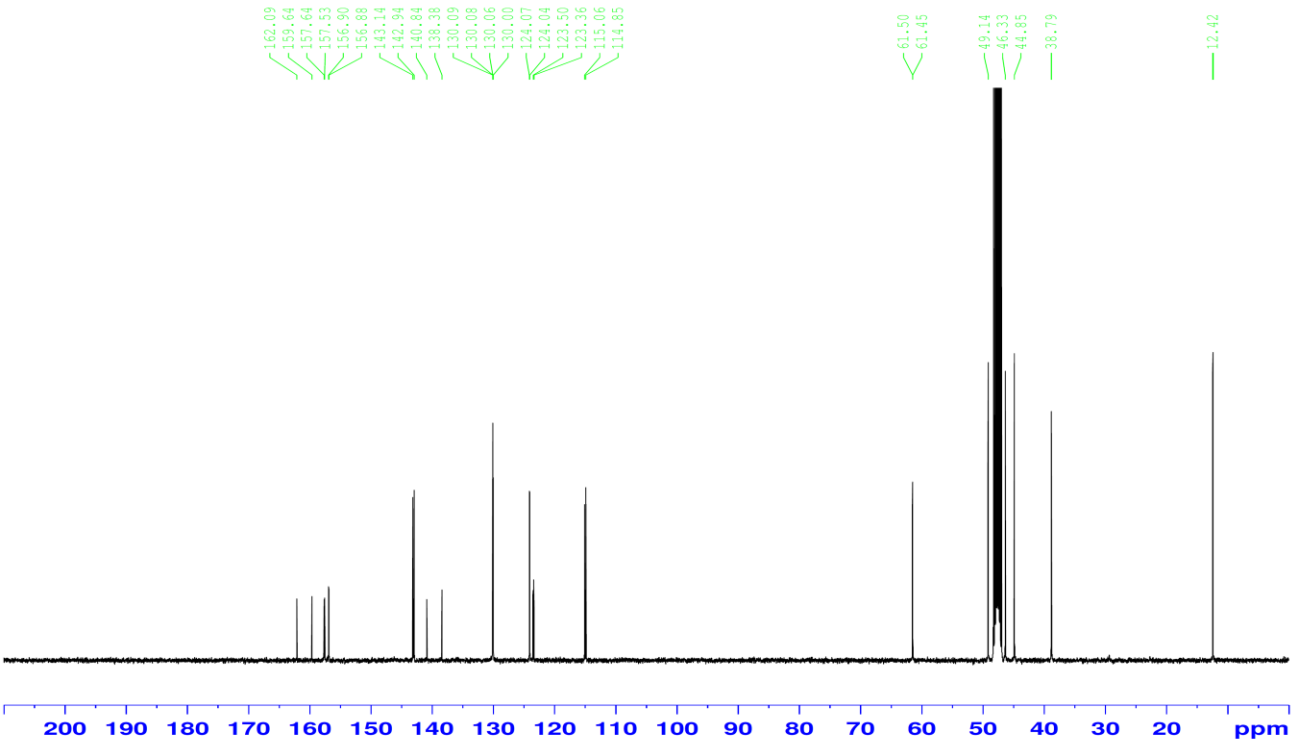
compd.	5-HT subtypes	**1A**	**1B**	**1D**	**1E**	**2A**	**2B**	**2C**	**3**	**5A**	**6**	**7**
(*R*,*R*)-**4d**	% binding at 10 μM	78.0	27.7	-6.8	67.5	93.3	100.2	**98.5**	89.4	28.1	95.7	84.4
	*K*i (nM)	98.0	-[b]	-[b]	1161.0	222.0	2.6	**1.2**	242.0	-[b]	57.0	444.0
(*S*,*R*)-**4d**	% binding at 10 μM	67.7	3.0	10.3	29.5	82.4	95.2	**97.7**	78.6	22.8	91.6	56.9
	*K*i (nM)	806.0	-[b]	-[b]	-[b]	475.0	67.0	**14.0**	501.0	-[b]	70.0	766.0
(*R*,*R*)-**4e**	% binding at 10 μM	10.0	6.4	-7.7	42.7	0.9	99.6	**94.2**	87.8	26.7	97.4	87.6
	*K*i (nM)	-[b]	-[b]	-[b]	-[b]	-[b]	19.0	**4.0**	242.0	-[b]	17.0	236.0
(*S*,*R*)-**4e**	% binding at 10 μM	67.3	17.9	40.4	-[c]	64.8	95.3	**97.8**	70.1	5.2	86.1	64.8
	*K*i (nM)	1117.0	-[b]	-[b]	-[b]	1024.0	128.0	**23.0**	1000.0	-[b]	116.0	946.0
3 (ref)	% binding at 10 μM	89.0	55.1	78.3	65.6	95.6	97.4	**98.2**	75.0	37.4	93.8	94.7
	*K*i (nM)	353.0	1780.0	542.0	1160.0	128.0	7.9	**0.7**	241.0	-[b]	43.0	84.0

[a] 5-HT receptor binding was determined by competitive binding assay using radioligands and reference compounds in Table S1. [b] Not determined due to low %binding. [c] Not determined

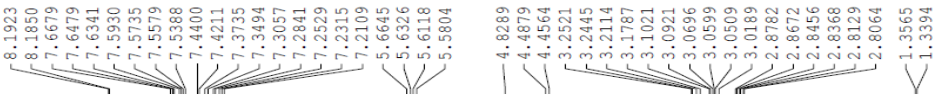
4. NMR spectral data of pyrimidine derivatives **4a**-**4i** and (*R*,*R*)/(*S*,*R*)-**4d** and **4e**

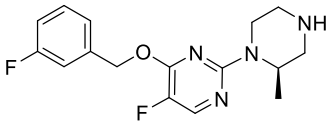


^{1}H NMR Spectrum of Compound **4a** (400 MHz)

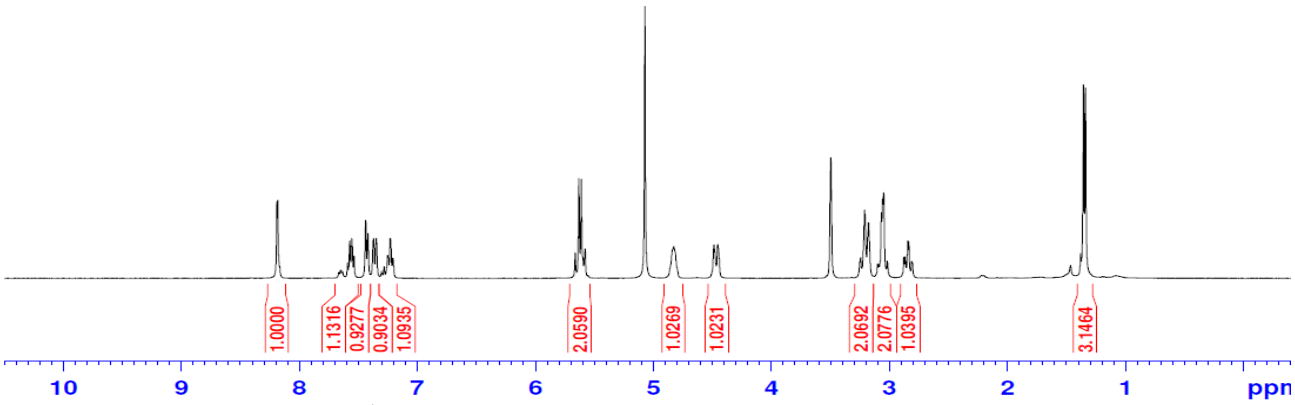


^{13}C NMR Spectrum of Compound **4a** (100 MHz)

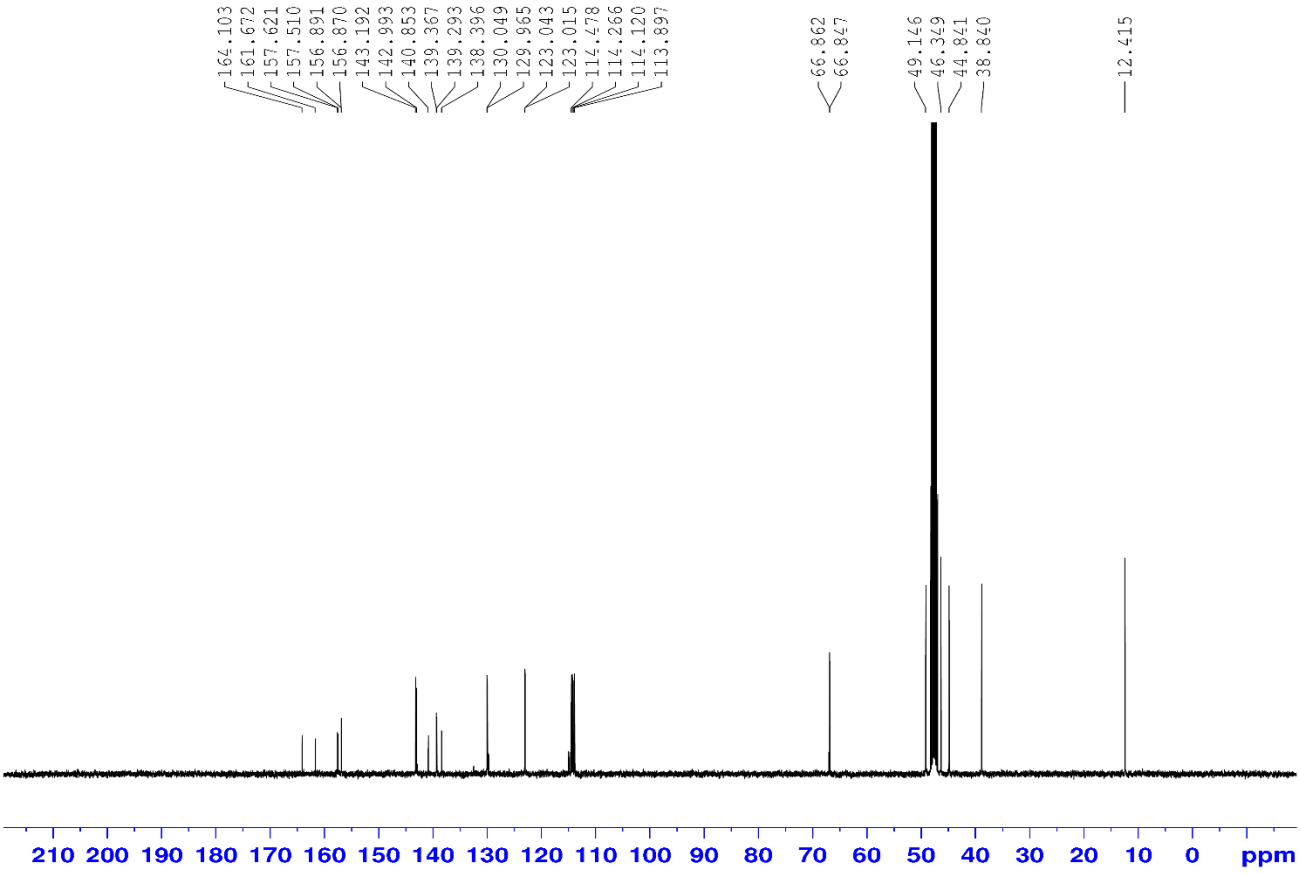




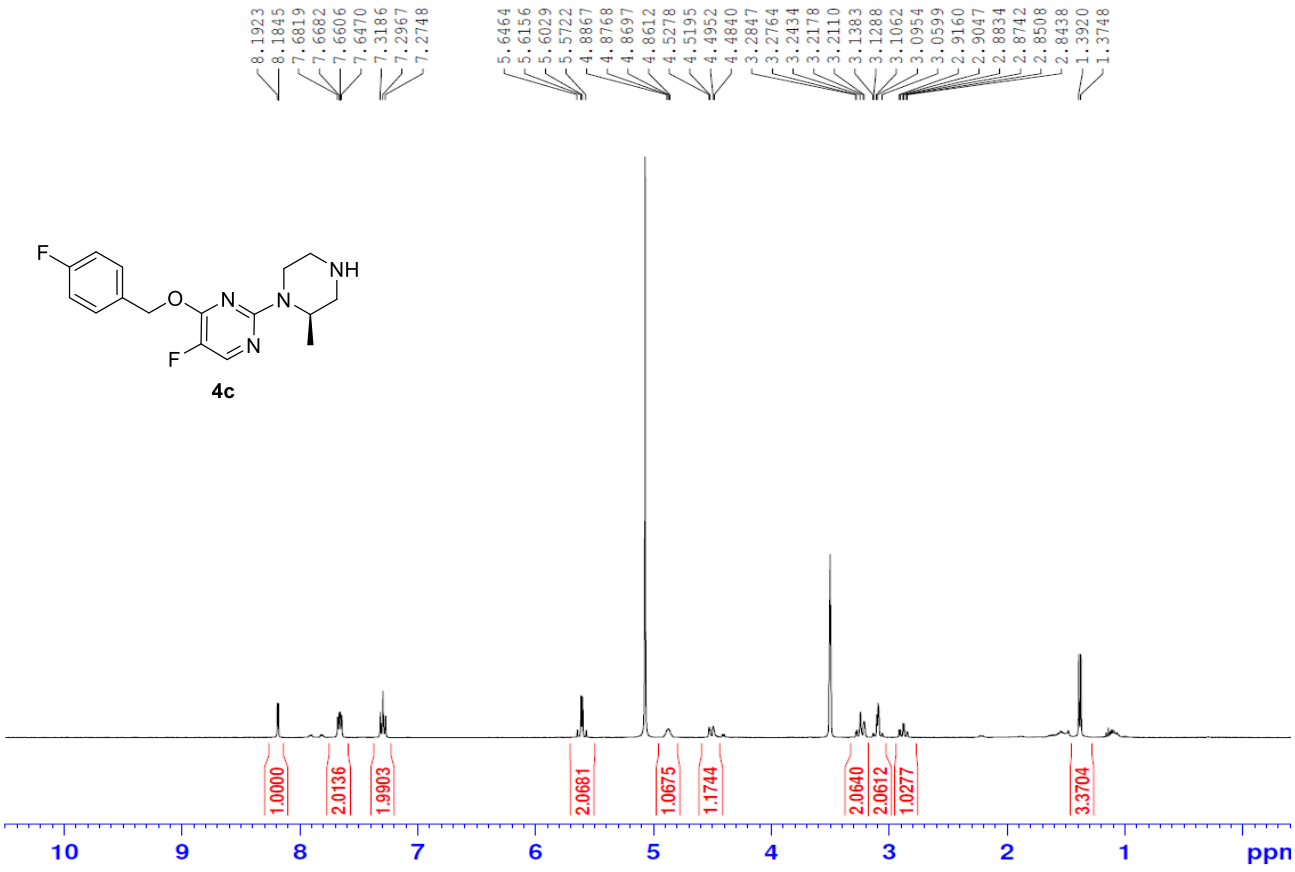
4b



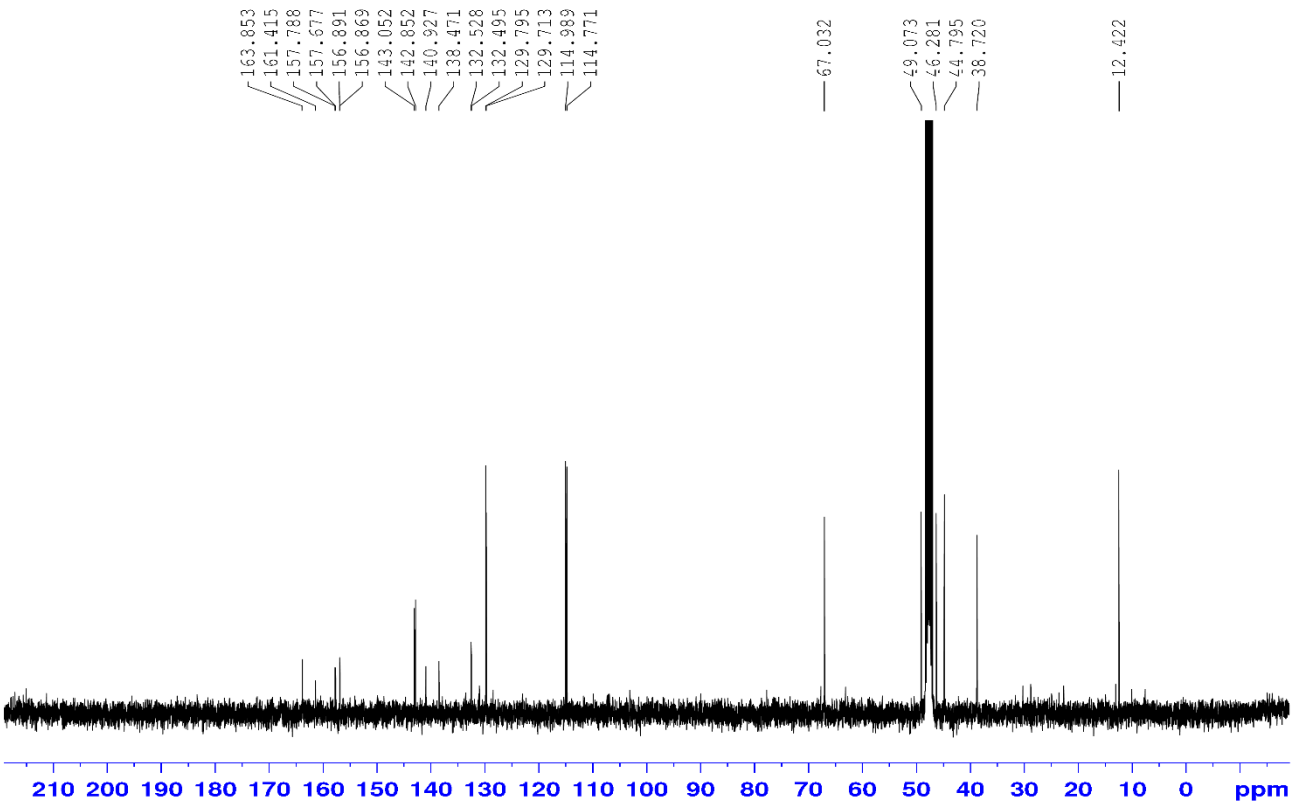
^{1}H NMR Spectrum of Compound **4b** (400 MHz)



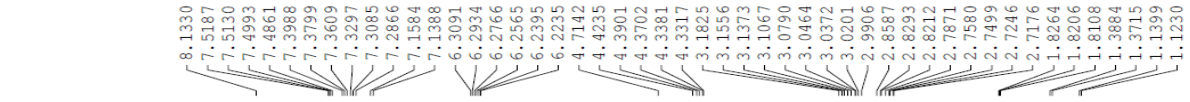
^{13}C NMR Spectrum of Compound **4b** (100 MHz)

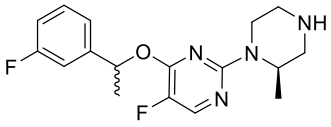


^{1}H NMR Spectrum of Compound **4c** (400 MHz)

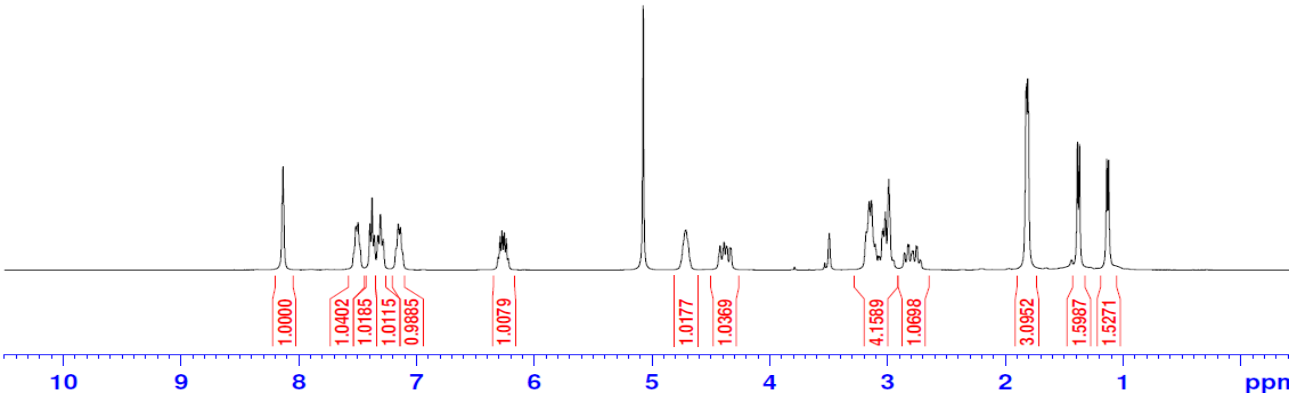


^{13}C NMR Spectrum of Compound **4c** (100 MHz)

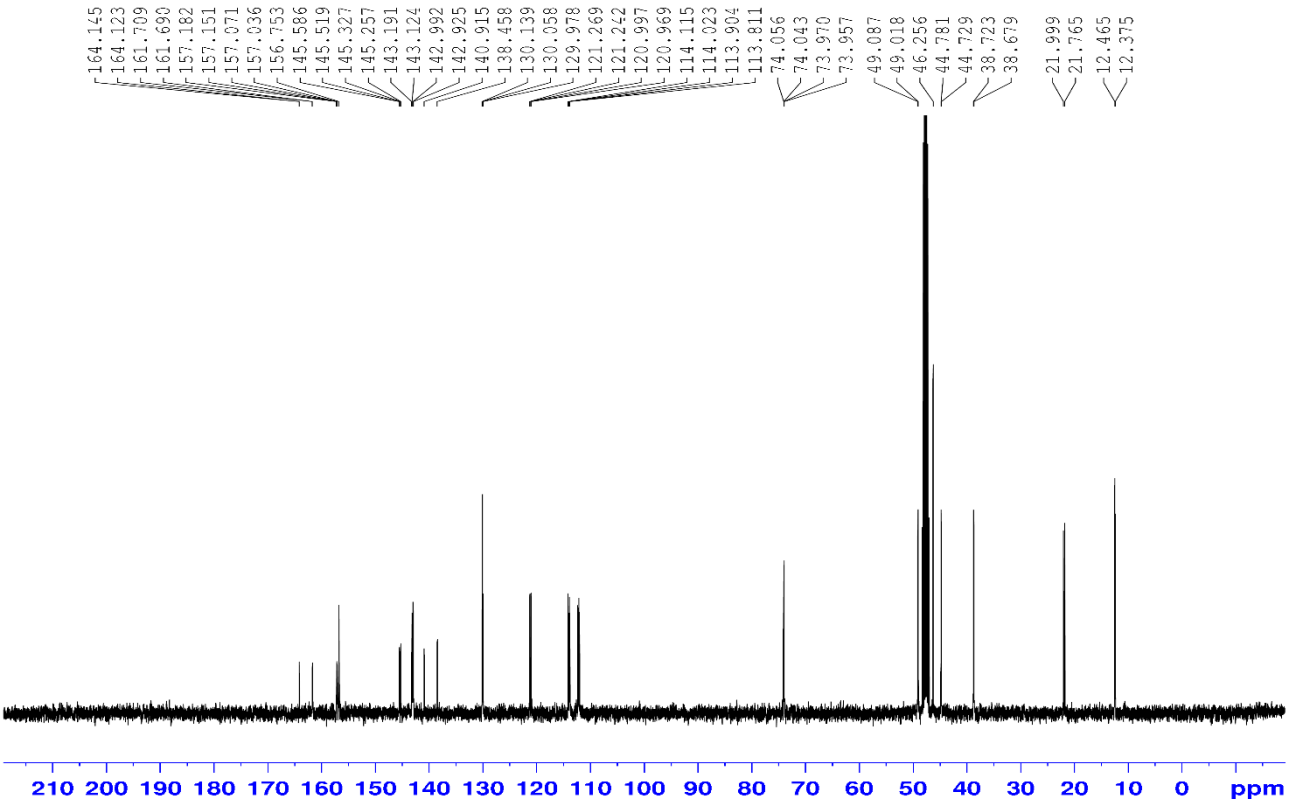




4d



^{1}H NMR Spectrum of Compound **4d** (400 MHz)



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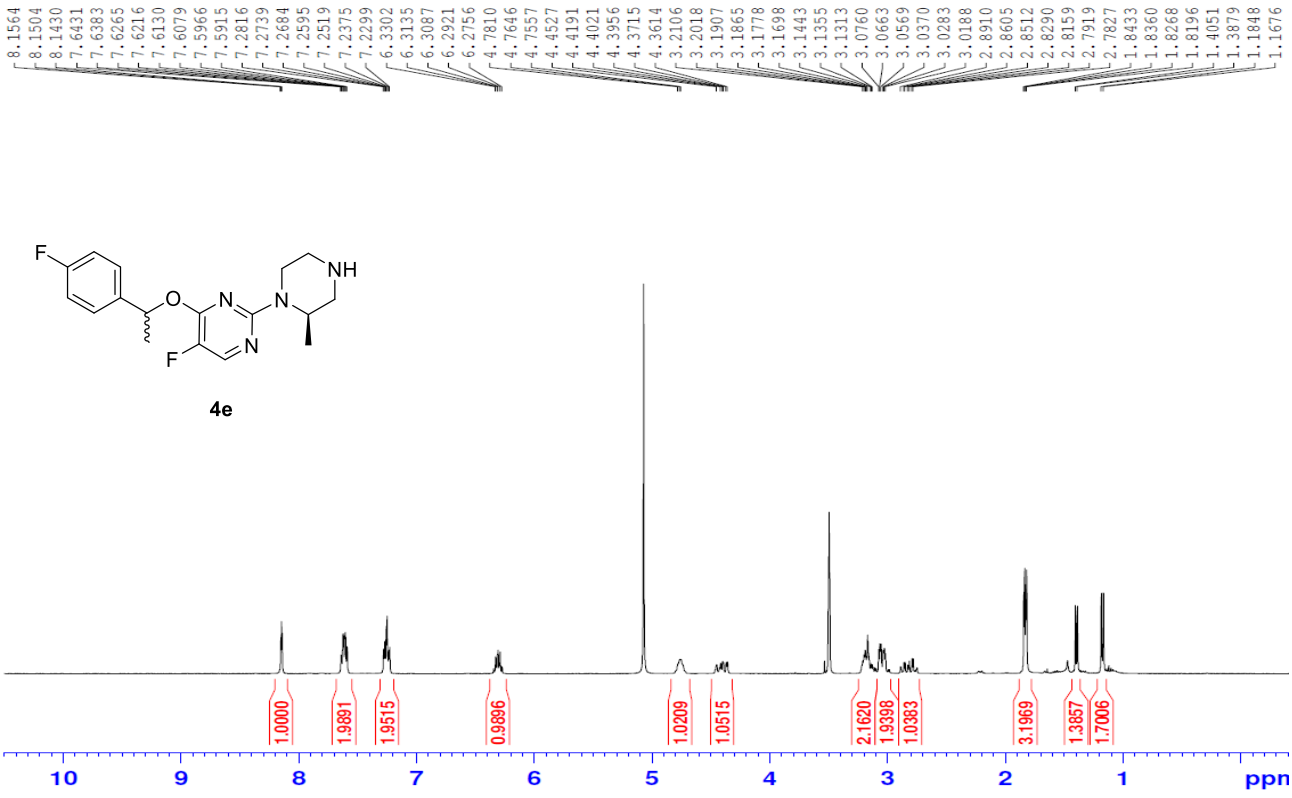
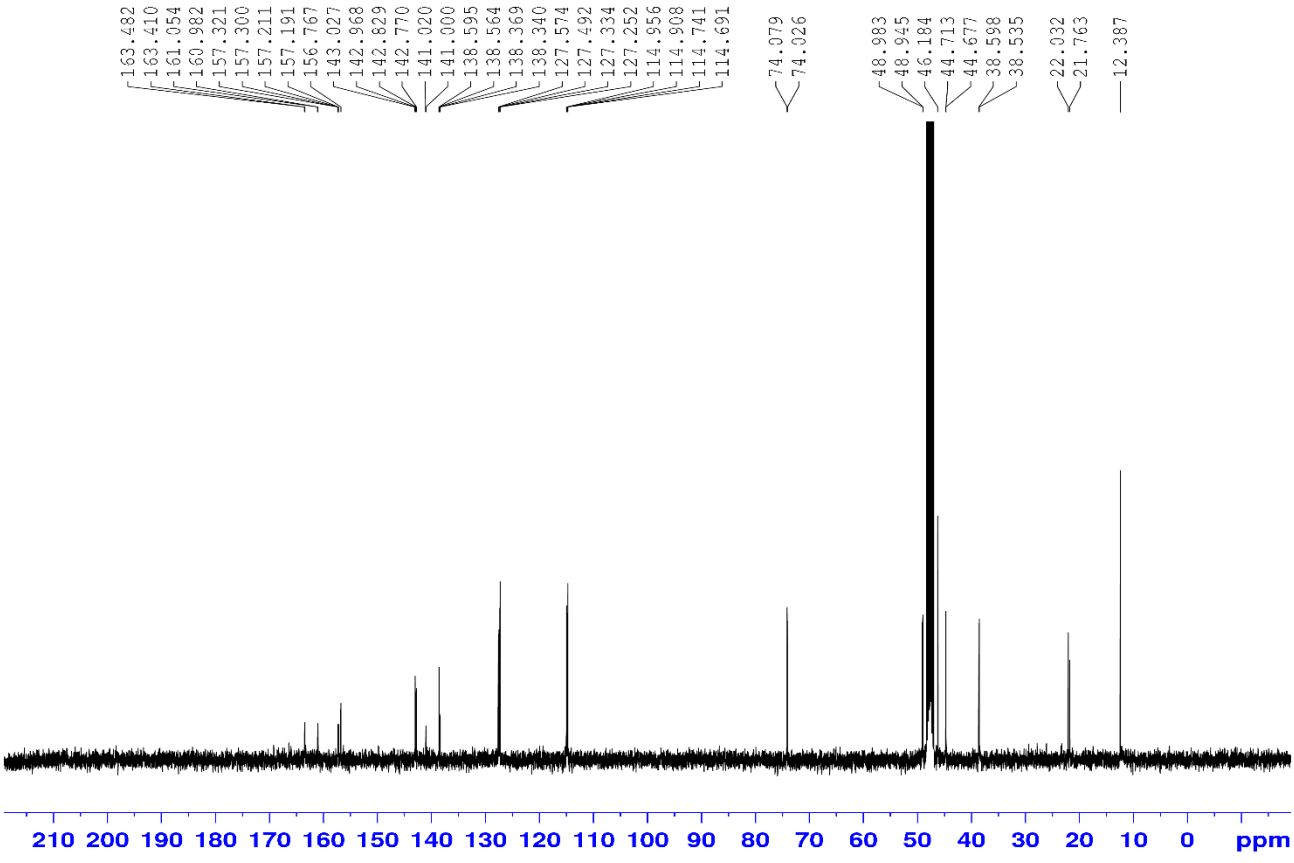
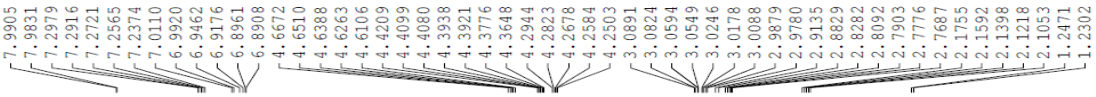
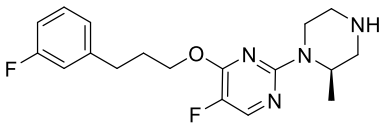


^{1}H NMR Spectrum of Compound **4e** (400 MHz)

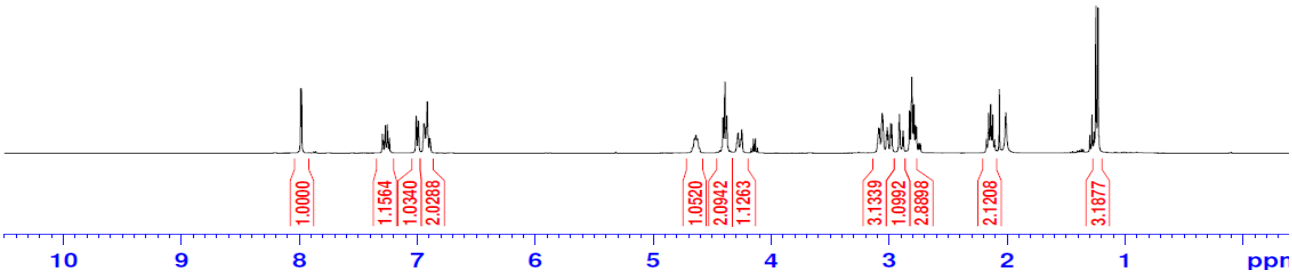


^{13}C NMR Spectrum of Compound **4e** (100 MHz)

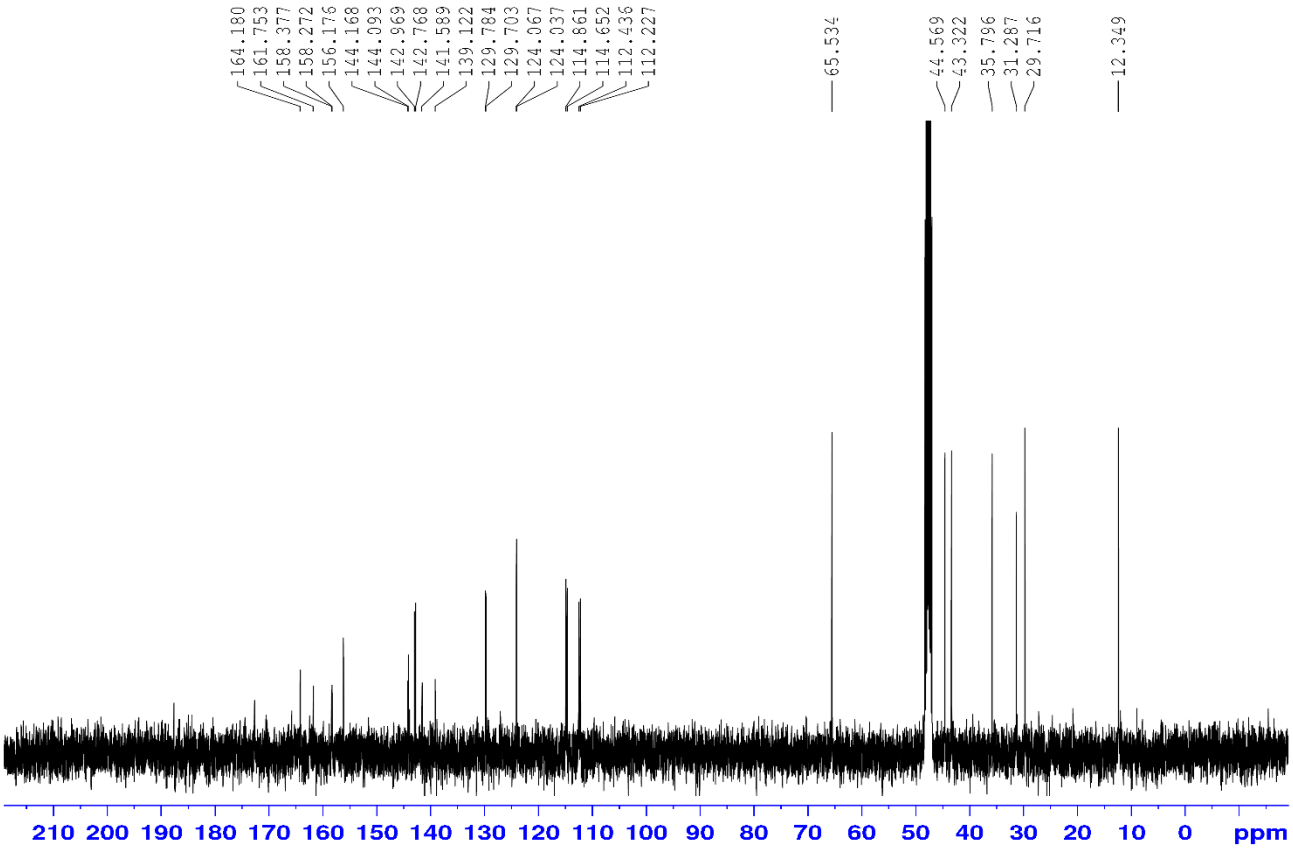




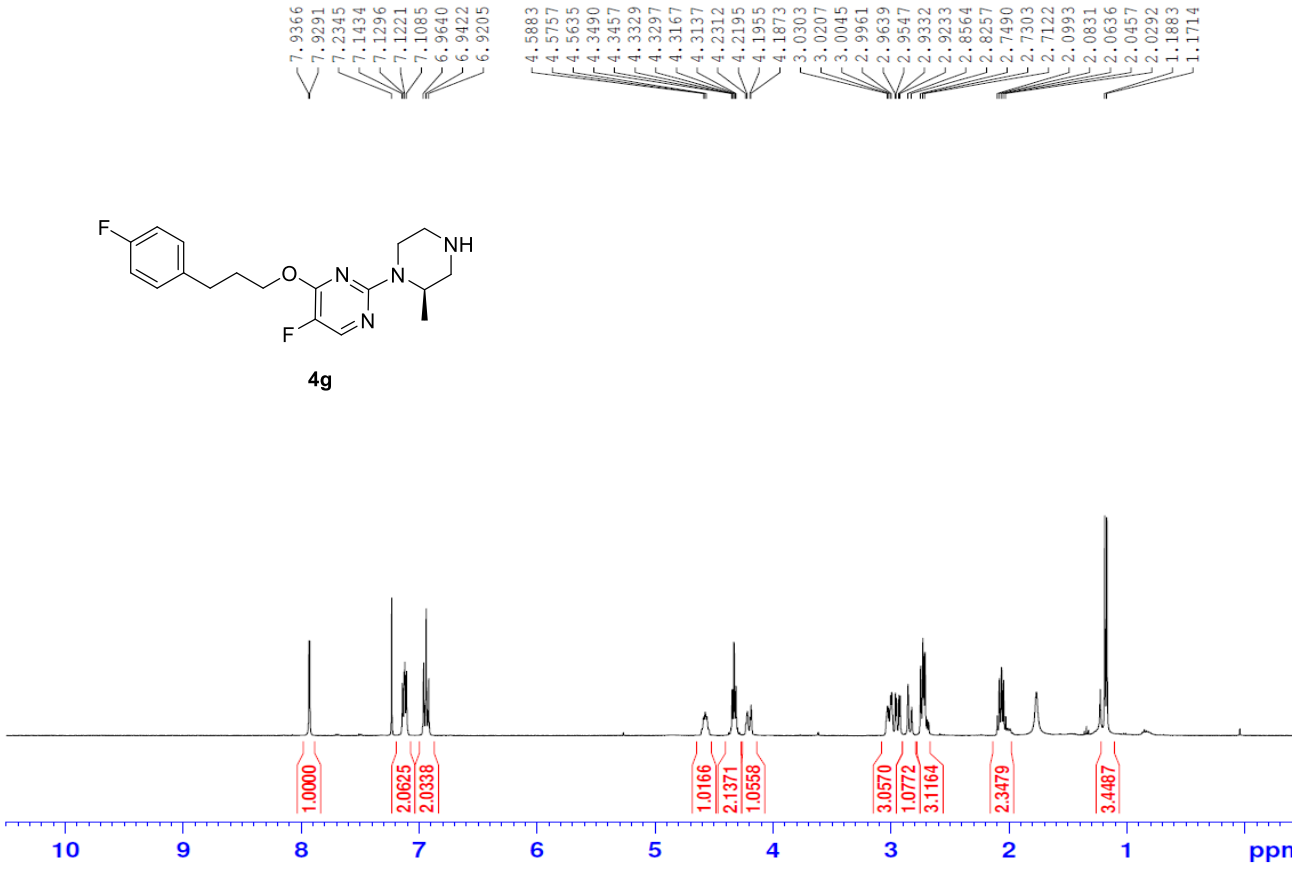
4f



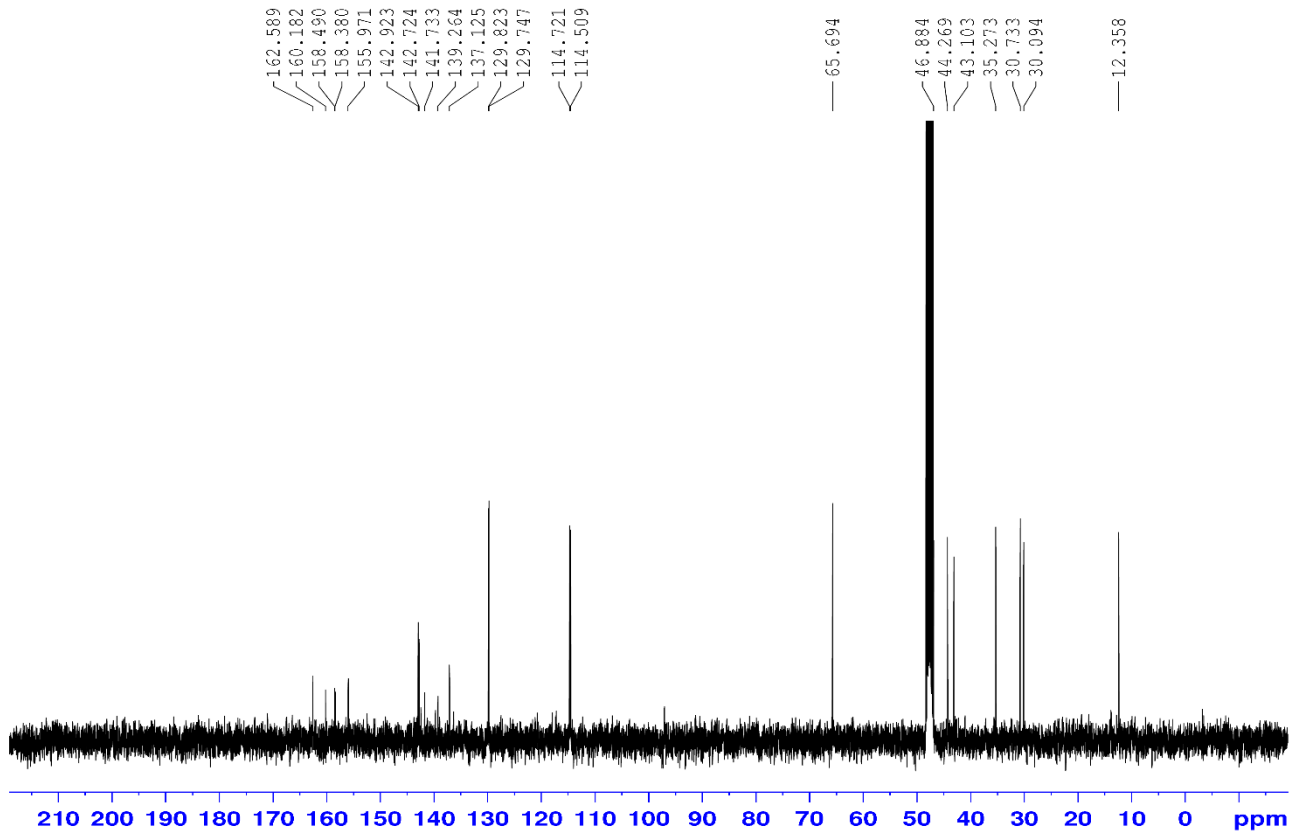
^{1}H NMR Spectrum of Compound **4f** (400 MHz)



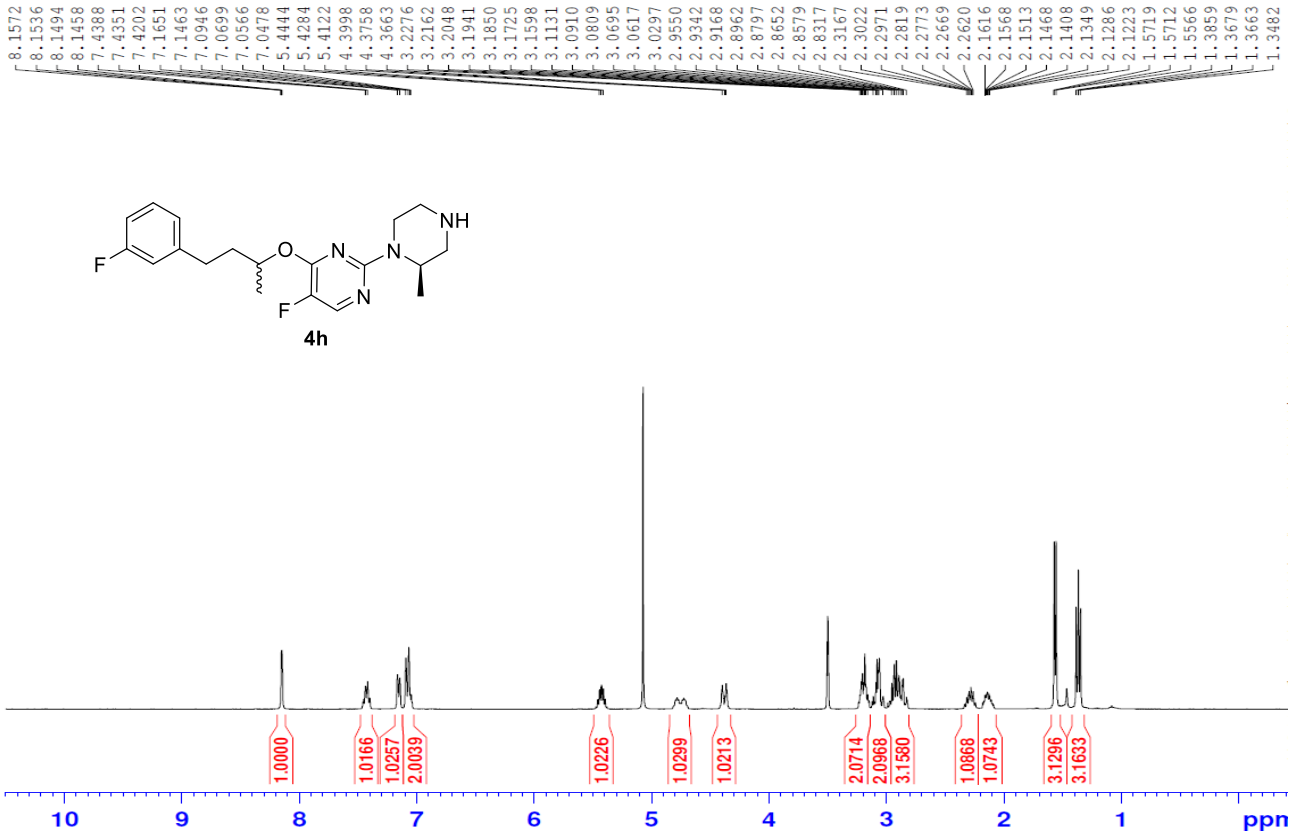
^{13}C NMR Spectrum of Compound **4f** (100 MHz)



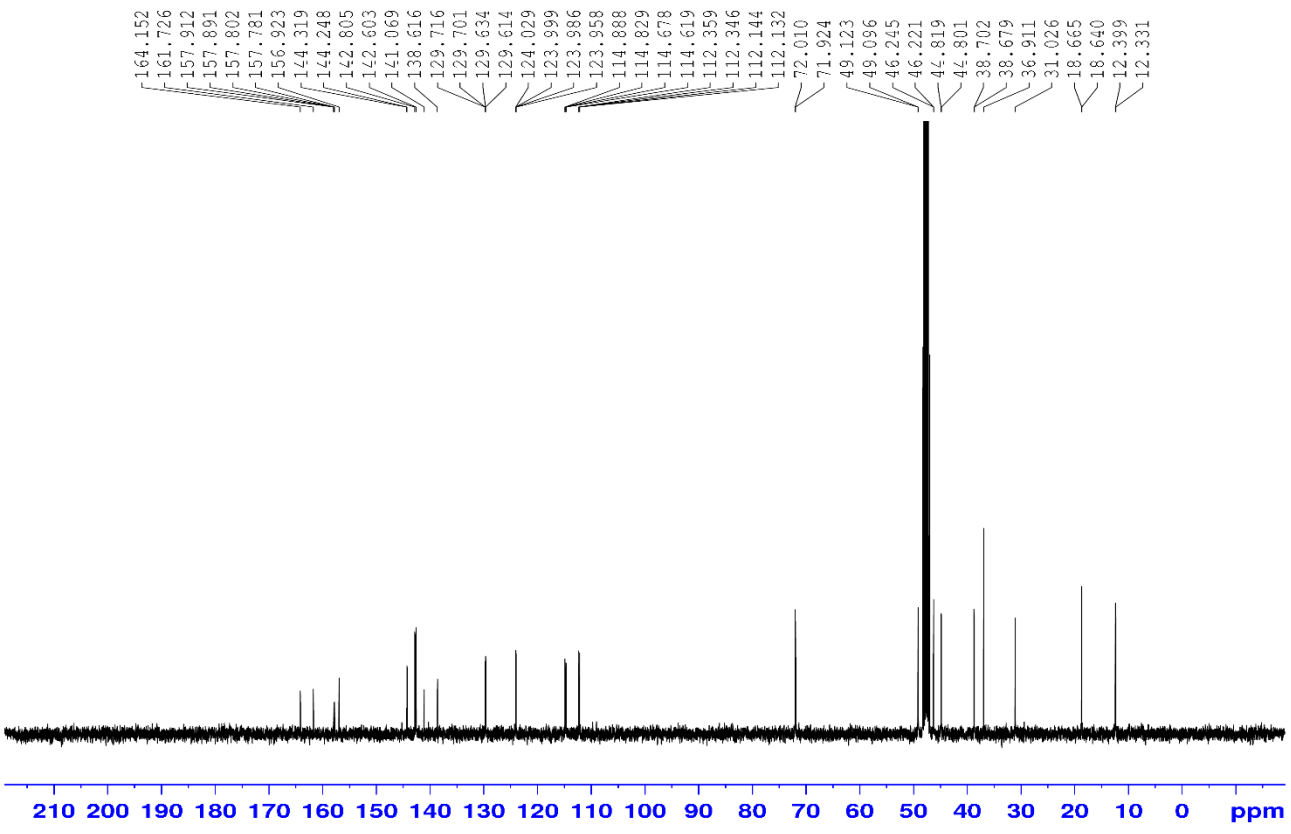
^{1}H NMR Spectrum of Compound **4g** (400 MHz)



^{13}C NMR Spectrum of Compound **4g** (100 MHz)



^{1}H NMR Spectrum of Compound **4h** (400 MHz)



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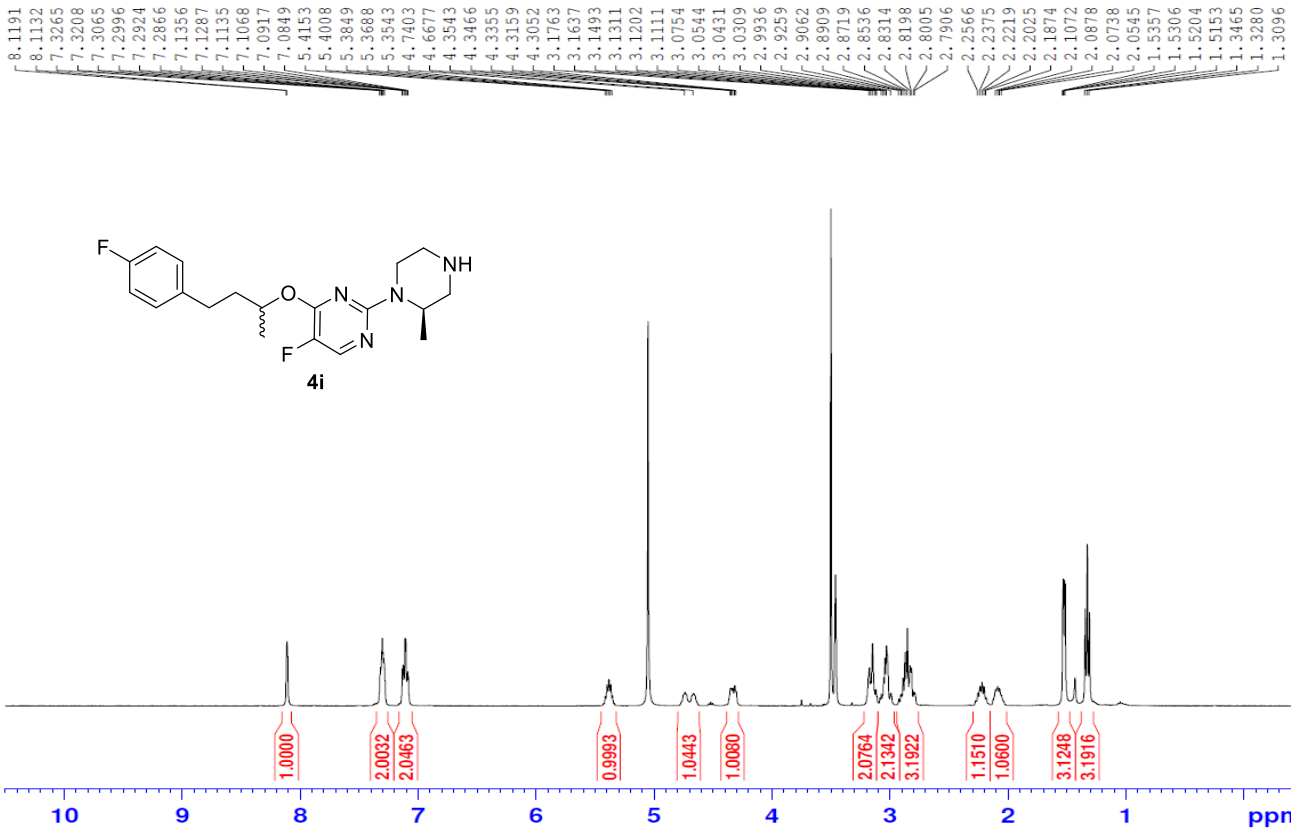
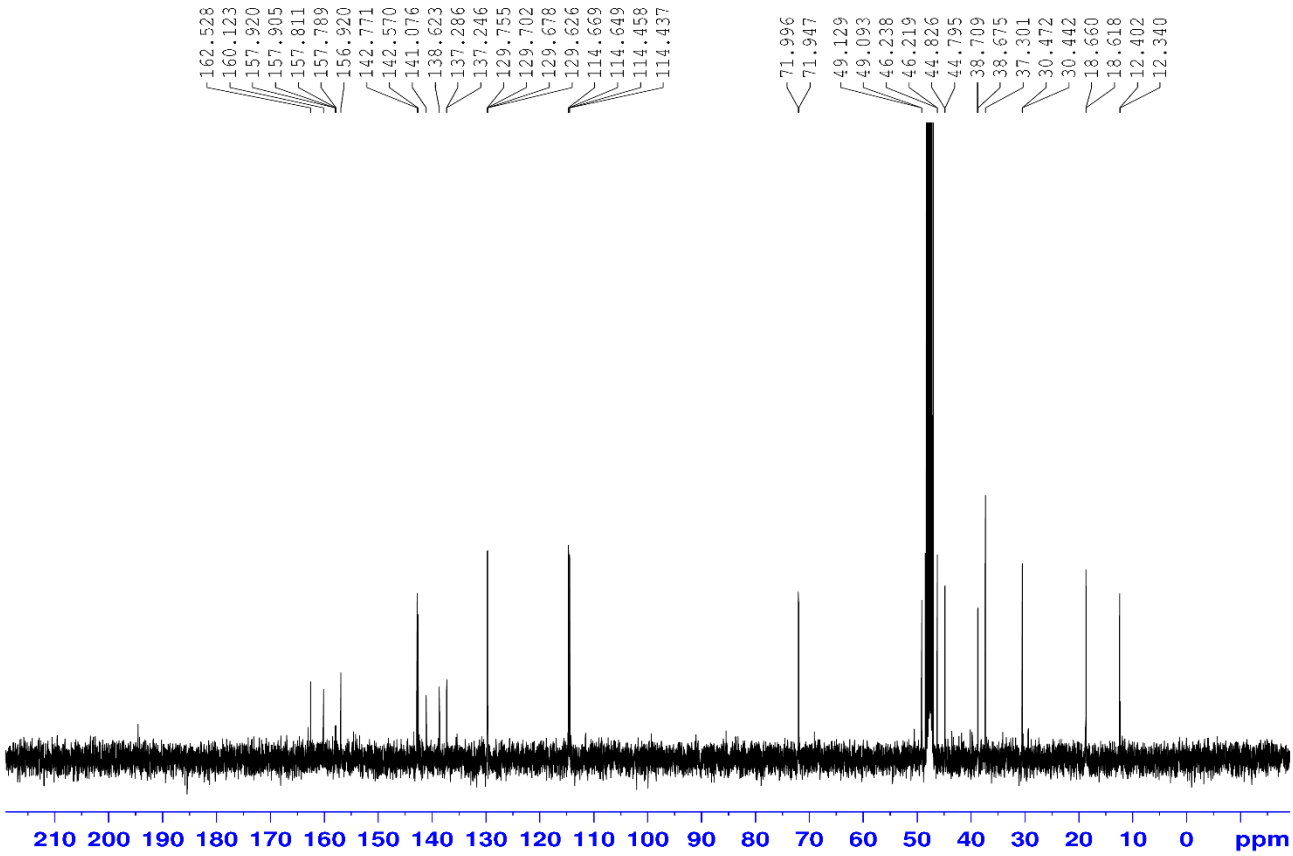


^{1}H NMR Spectrum of Compound **4i** (400 MHz)



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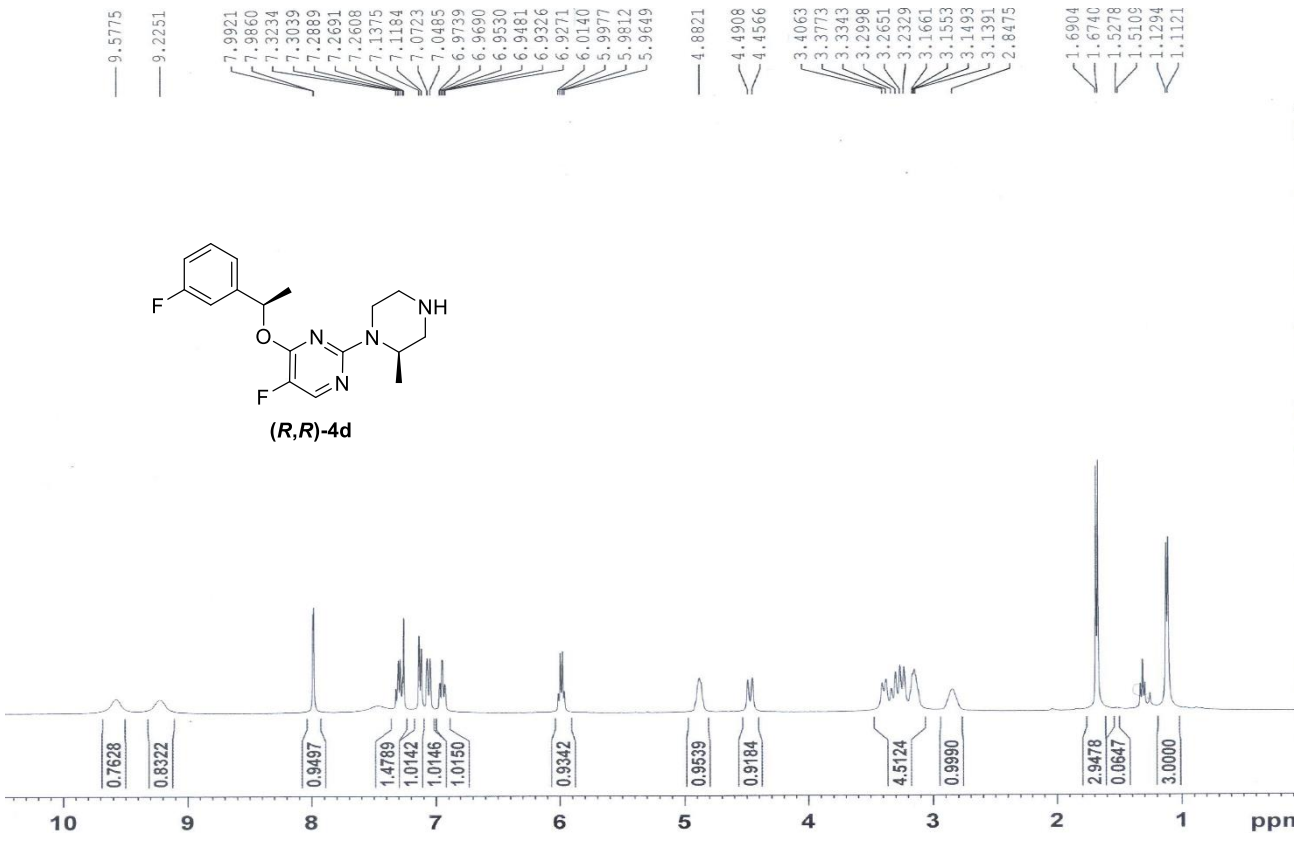
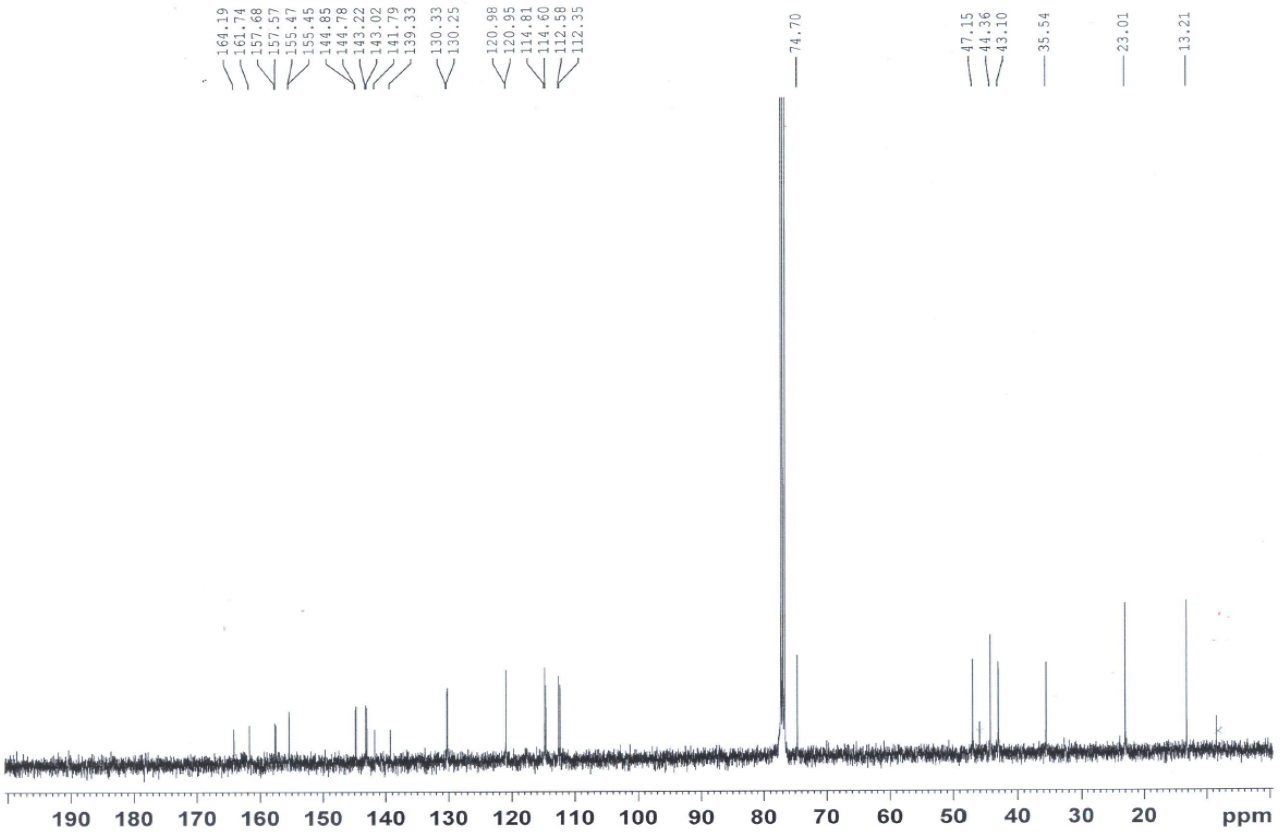
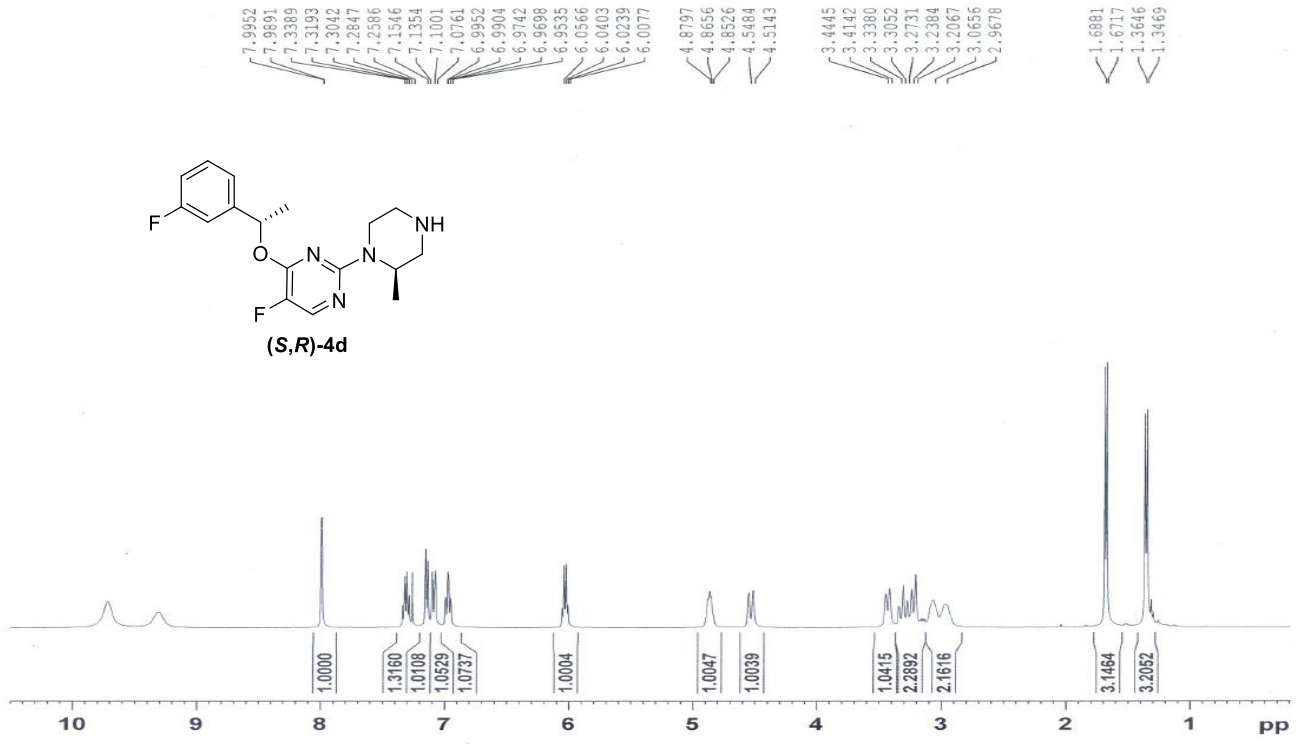


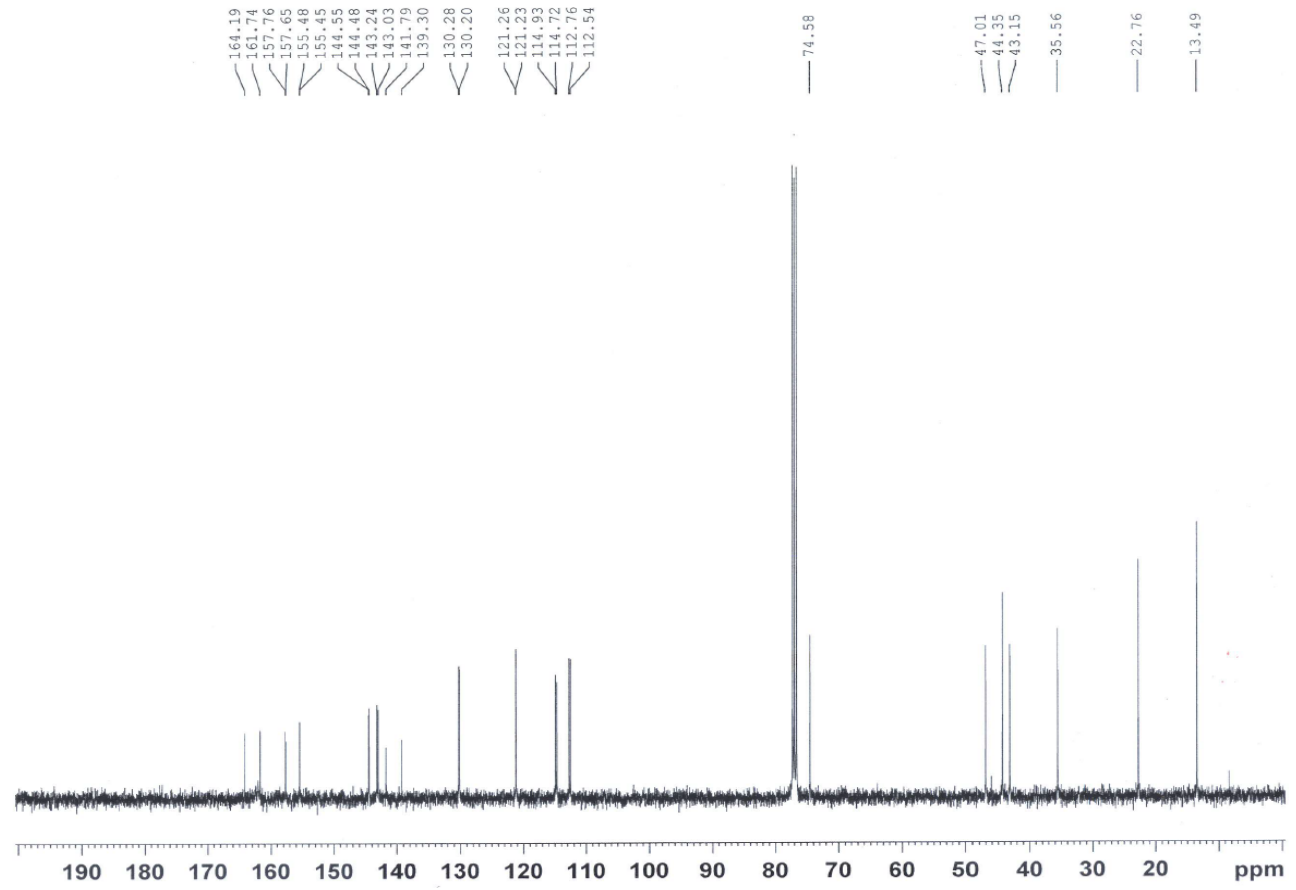
^{1}H NMR Spectrum of Compound (*R*,*R*)-**4d** (400 MHz)



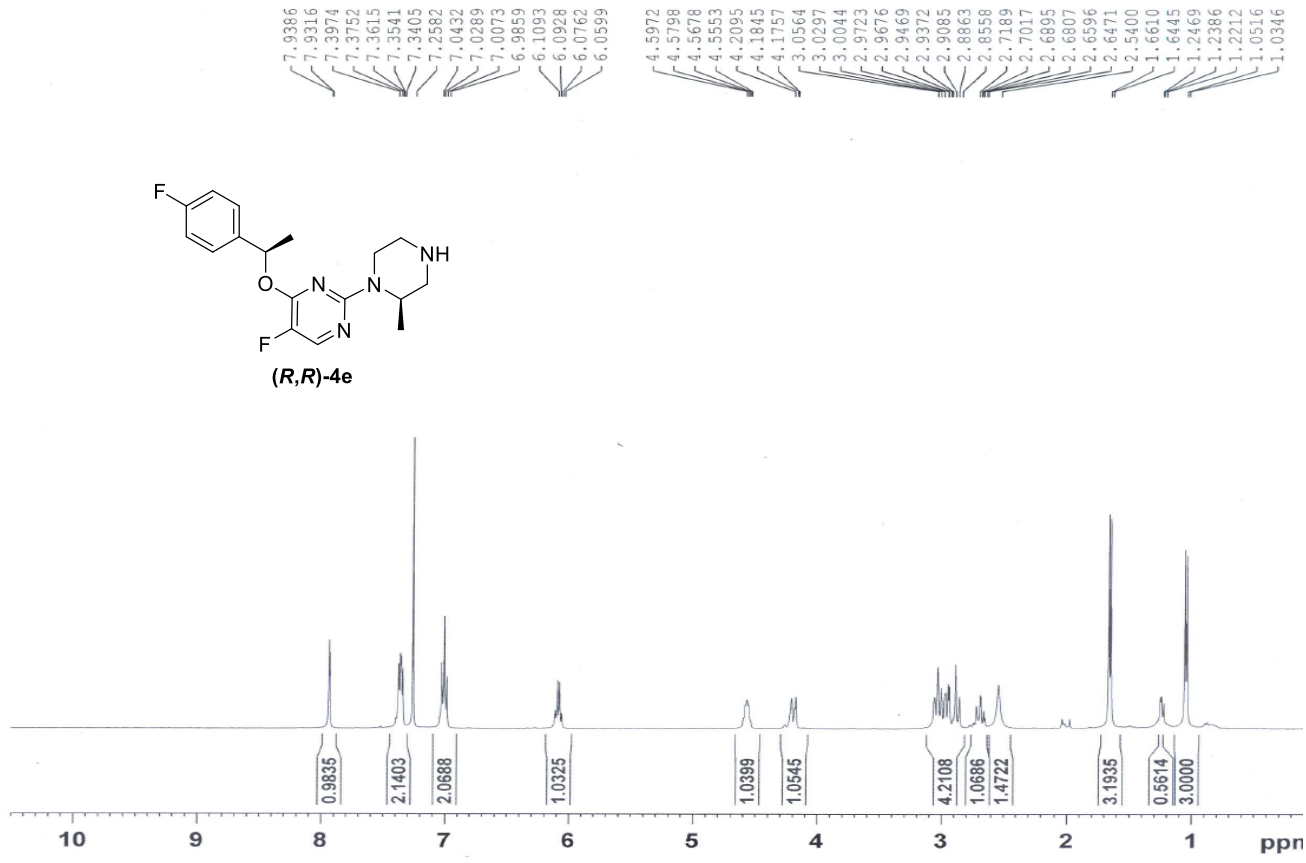
^{13}C NMR Spectrum of Compound (*R*,*R*)-**4d** (100 MHz)



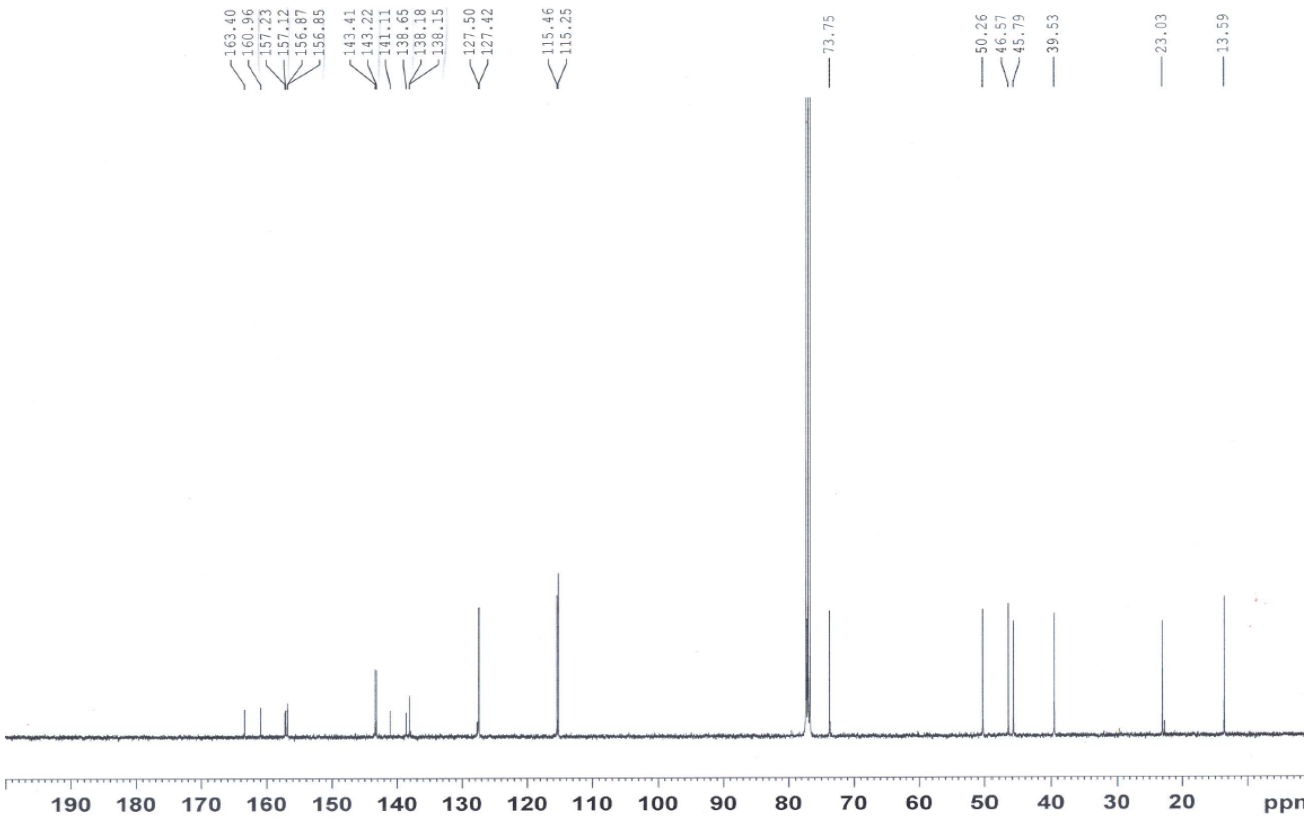
^{1}H NMR Spectrum of Compound (*S*,*R*)-**4d** (400 MHz)



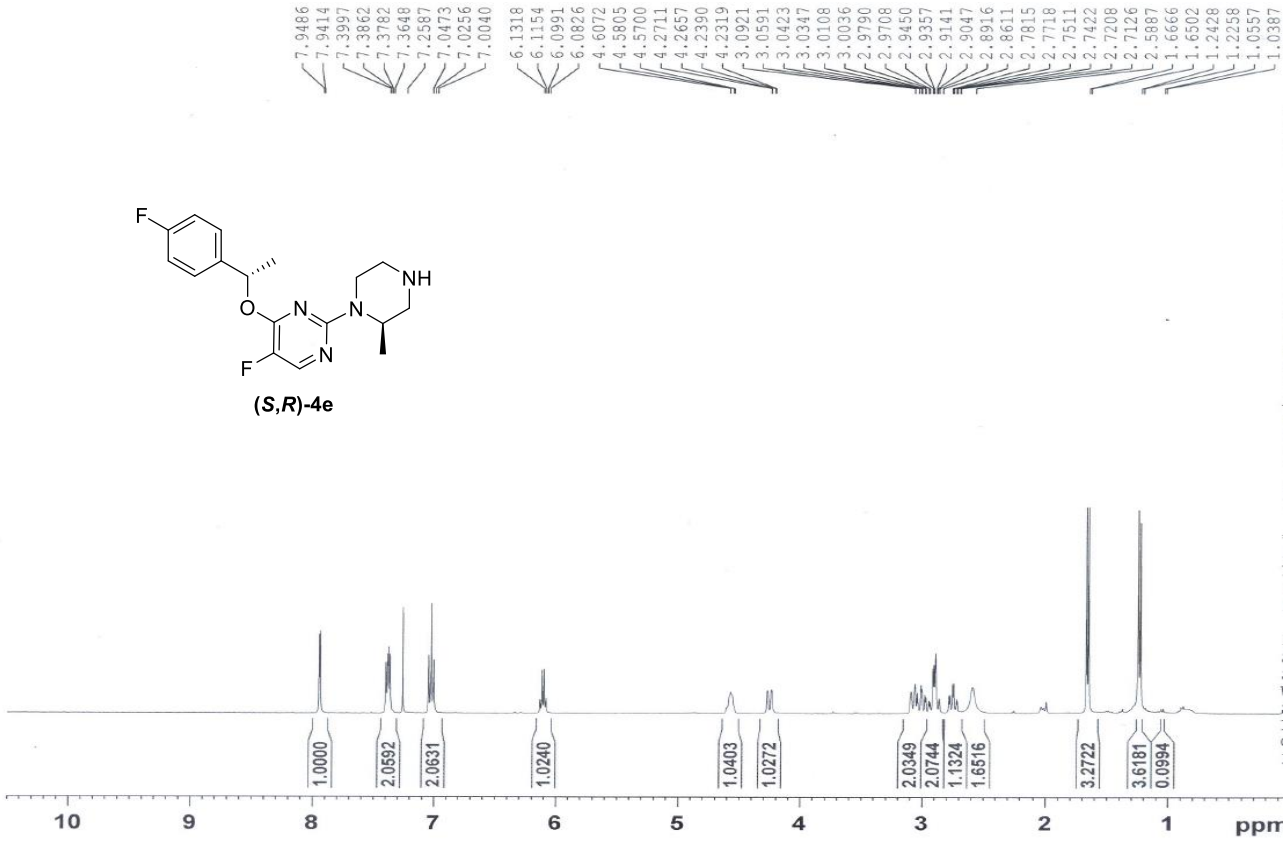
^{13}C NMR Spectrum of Compound (*S*,*R*)-**4d** (100 MHz)



^{1}H NMR Spectrum of Compound (*R*,*R*)-**4e** (400 MHz)



^{13}C NMR Spectrum of Compound (*R*,*R*)-**4e** (100 MHz)



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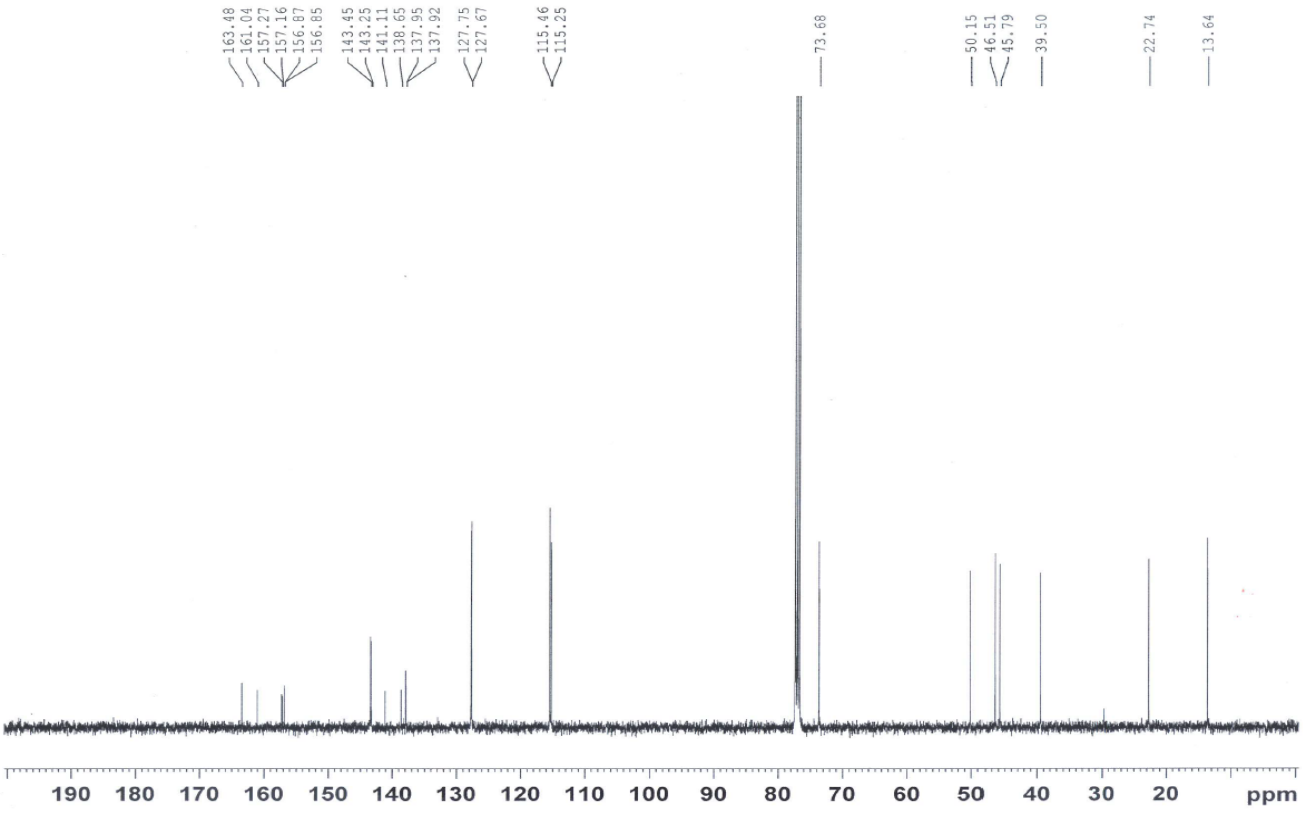

^{13}C NMR Spectrum of Compound (*S*,*R*)-**4e** (100 MHz)