Electronic Supplementary Material (ESI) for MedChemComm.

Synthesis of novel inhibitors of α-amylase based on thiazolidine-4-one skeleton containing pyrazole moiety and their configurational studies

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Synthesis of 2-(*p*-tolylimino)thiazolidin-4-one (**3**) [1]

It was prepared by a three component reaction of 1-*p*-tolylthiourea (1) (1.0 mmol), ethyl bromoacetate (1.0 mmol) and sodium acetate (2.0 mmol) in glacial acetic acid under the refluxing condition for 2 h. After completion of reaction, reaction was quenched using ice and the solid so formed was filtered under suction and recrystallized from ethanol.Yield 80%; M.pt:167-170°C.

Synthesis of 5-((3-(aryl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-(*p*-tolylimino)thiazoli din-4-one(5a-g) [1]

2-Arylimino-thiazolidin-4-ones **1** (0.5 mmol) and 1-phenyl-3-(p-substituted phenyl)-1*H*-pyrazole-4-carbaldehydes **2** (0.6 mmol) were dissolved in absolute ethanol. Piperidine (0.5 mmol) was added to the reaction mixture and the reaction mixture was stirred for 8 h at 60°C until precipitate formed. Then the mixture was cooled to room temperature, and the precipitates formed were filtered and washed with absolute ethanol to yield the final compound **5a-5g** in good to excellent yield.

Table S1: Percentage of peaks of *E* and *Z* isomers present in **5a-5g** in DMSO-d_6

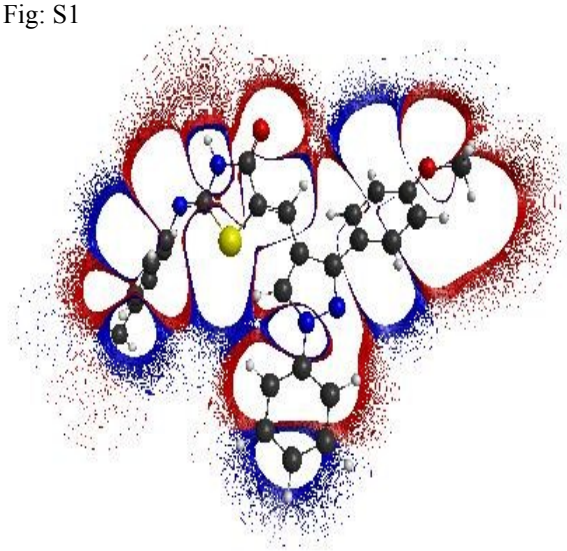
Compound	Pyr-H (H_{17})		$H_{10/12}$		$H_{28/32}$		C-CH_3 (C-14)	
	E-isomer	*Z*-isomer	*Z*-isomer	*E*-isomer	*E*-isomer	*Z*-isomer	*Z*-isomer	*E*-isomer
5a	8.61 (39.2%)	8.52 (61.7%)	[b] 7.19-7.21 (59.1%)	6.97 (40.8%)	7.96 (40.7%)	7.92 (59.3%)	2.31 (60.3%)	2.30 (39.6%)
5b	8.64 (39.8%)	8.54 (60.1%)	[b] 7.19-7.21 (59.1%)	6.96 (40.8%)	7.97 (40.6%)	7.93 (59.3%)	2.31 (60.0%)	2.30 (39.9%)
5c	8.30 (38.8%)	8.18 (61.1%)	[b] 6.93-6.98	6.74 (40%)	7.72 (37.7%)	7.66 (62.2%)	2.13 (62.9%)	2.11 (37.1%)
5d	8.58 (37.1%)	8.47 (62.8%)	[a]-	[a]-	7.93 (37.0%)	7.88 (62.2%)	2.31 (62.4%)	2.30 (37.5%)
5e	8.54 (28.1%)	8.42 (71.8%)	[a]-	[a]-	[a]-	[a]-	2.31 (62.6%)	2.30 (37.3%)
5f	8.56 (39.1%)	8.44 (60.8%)	[b] 7.11-7.18	6.93 (40%)	7.92 (42.3%)	7.87 (57.6%)	2.31 (61.2%)	2.30 (38.7%)
5g	8.61 (42.0%)	8.49 (58.4%)	[a] 7.14-7.16	6.91 (40%)	[b] 7.93-7.96	-	2.31 (61.2%)	2.30 (38.7%)

[a] Signals are not separated
[b] Mixed with multiplet

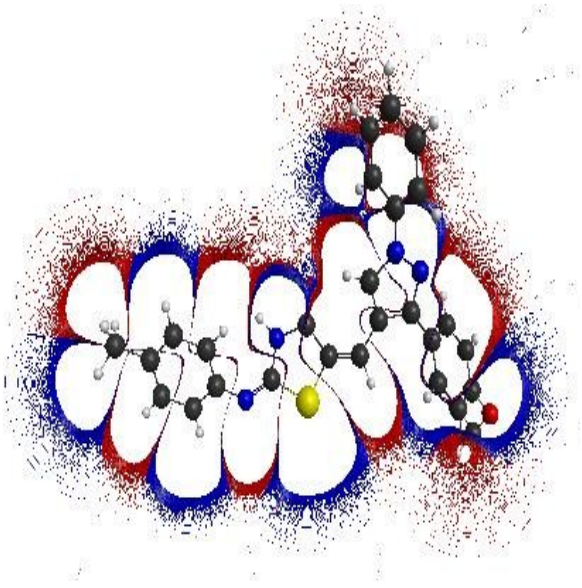
Table S2:DFT Calculationsfor different configuration of **5a**

Configuration	*2Z,5Z*	*2E,5E*	*2Z,5E*	*2E,5Z*
Dipole moment (Debye)	3.97	3.15	1.24	1.49
Difference in energy(kcal/mole)	0	71.04	60.14	2.08

Fig: S1

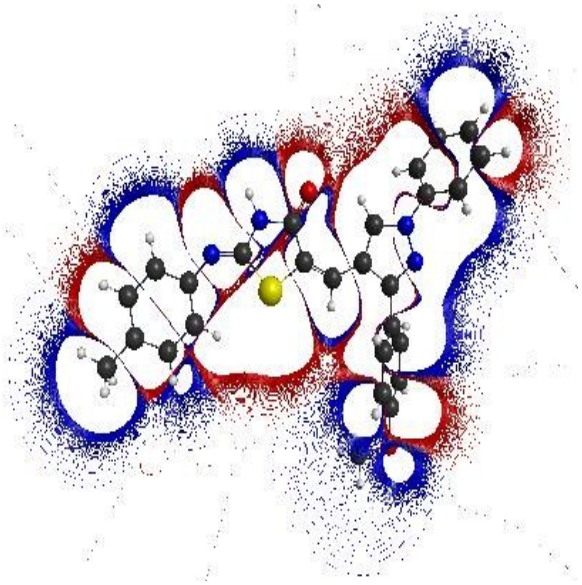


2D-Orbital Counter map of HOMO of *2Z,5Z*

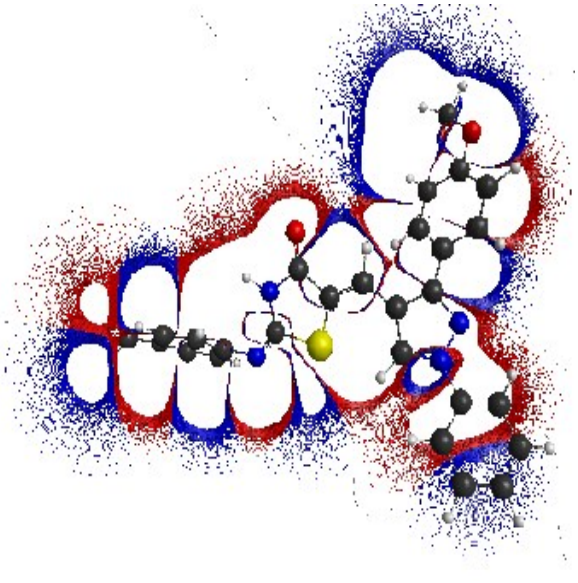


2D-Orbital Counter map of HOMO of *2E,5E*

Fig: S2

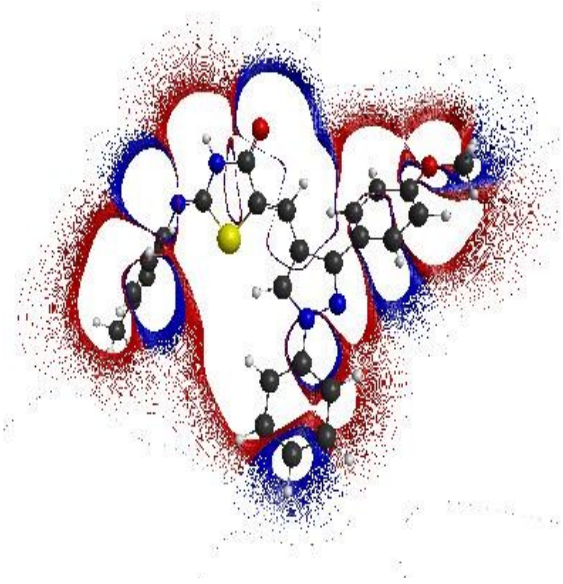


2D-Orbital Counter map of HOMO of *2Z,5E*

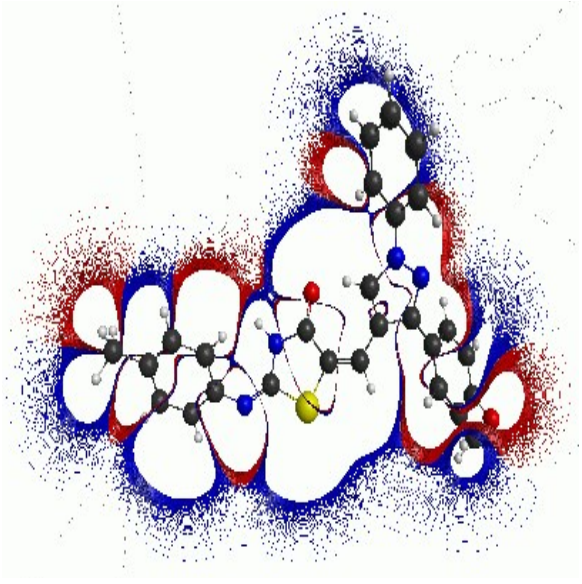


2D-Orbital Counter map of HOMO of *2E,5Z*

Fig: S3

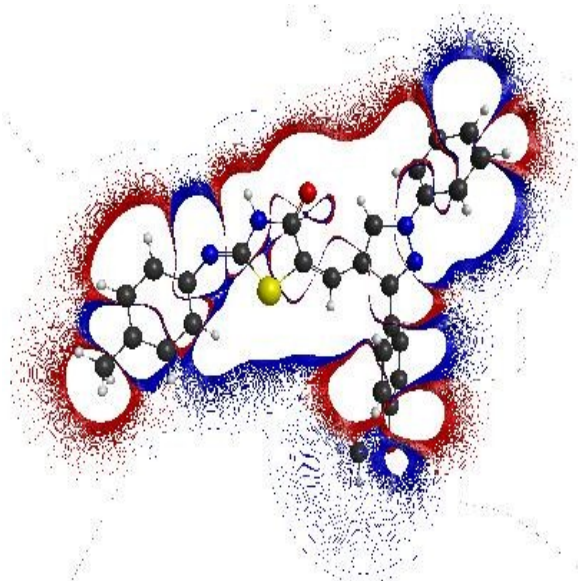


2D-Orbital Counter map of LUMO of *2Z,5Z*

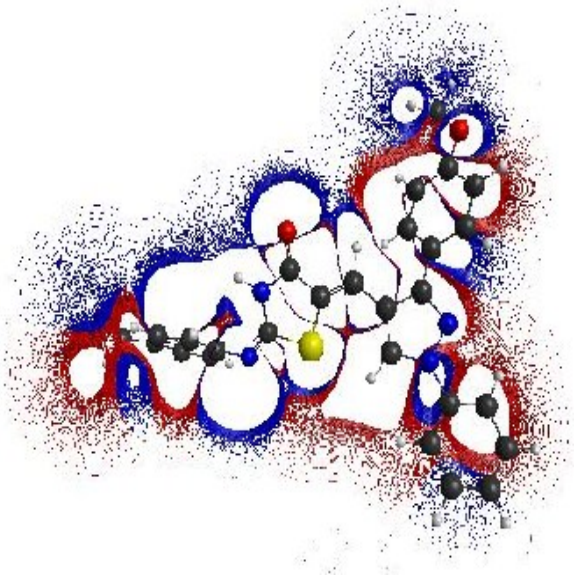


2D-Orbital Counter map of LUMO of *2E,5E*

Fig: S4

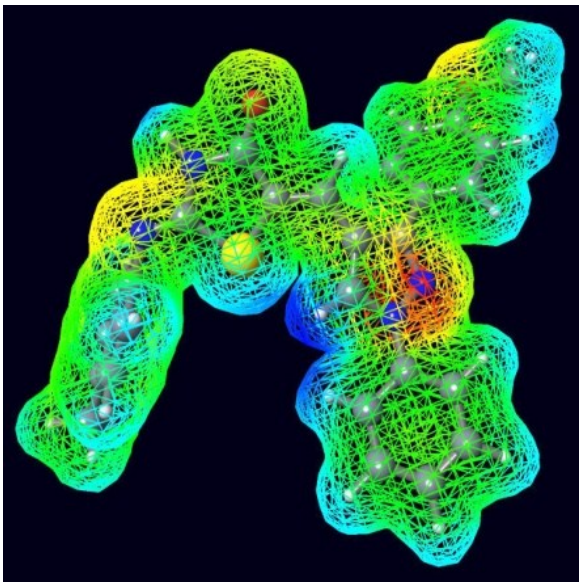


2D-Orbital Counter map of LUMO of *2Z,5E*

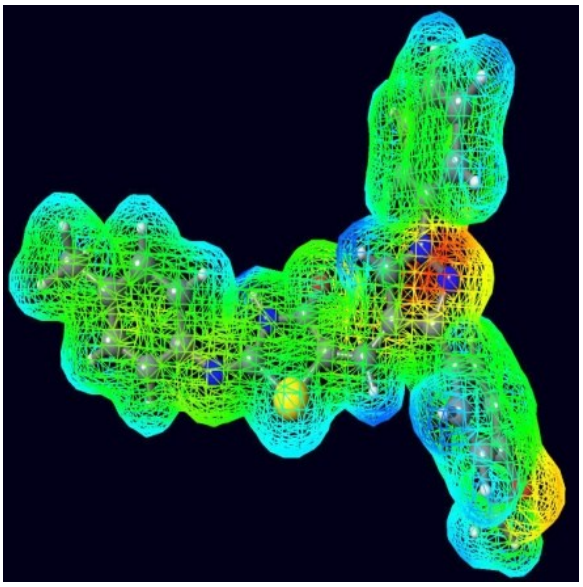


2D-Orbital Counter map of LUMO of *2E,5Z*

Fig: S5

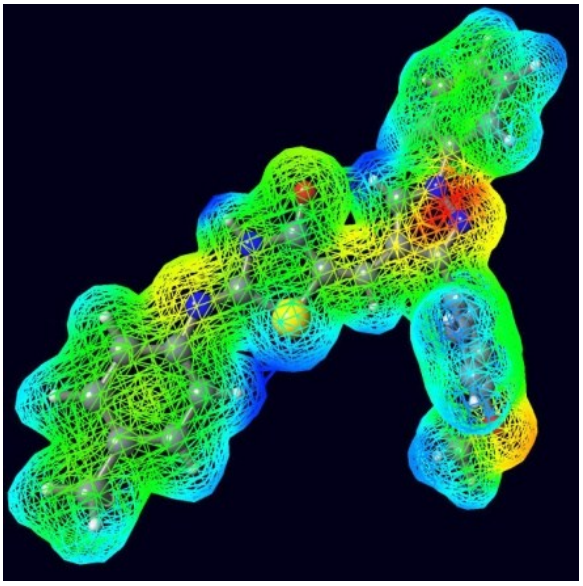


Molecular electrostatic potential surface at 0.01 of *2Z,5Z*

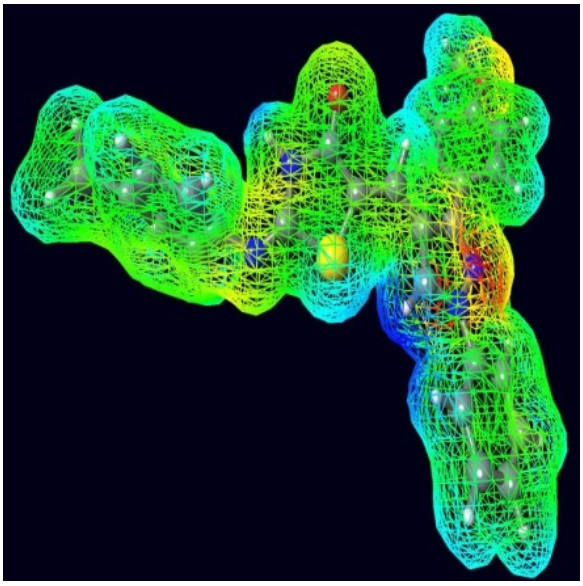


Molecular electrostatic potential surface at 0.01of *2E,5E*

Fig: S6

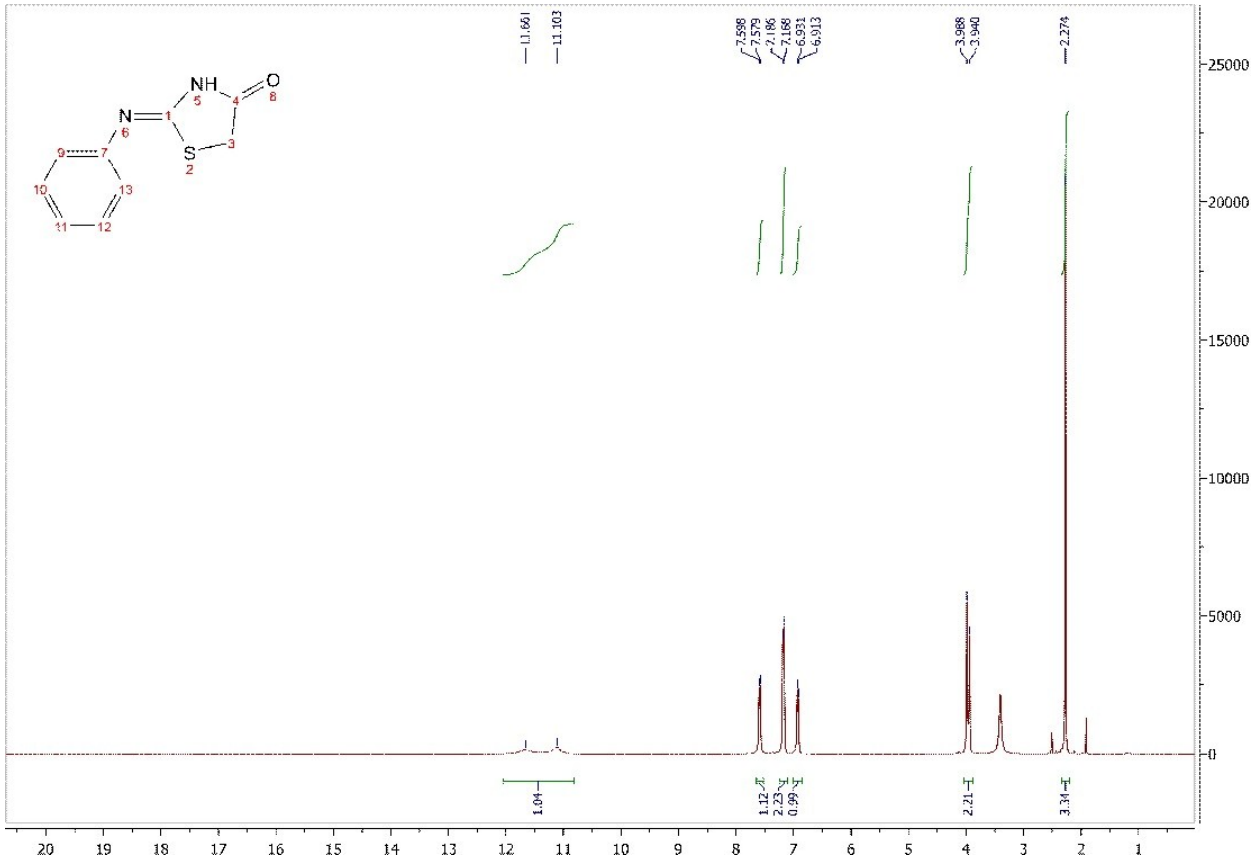


Molecular electrostatic potential surface at 0.01 of *2Z,5E*

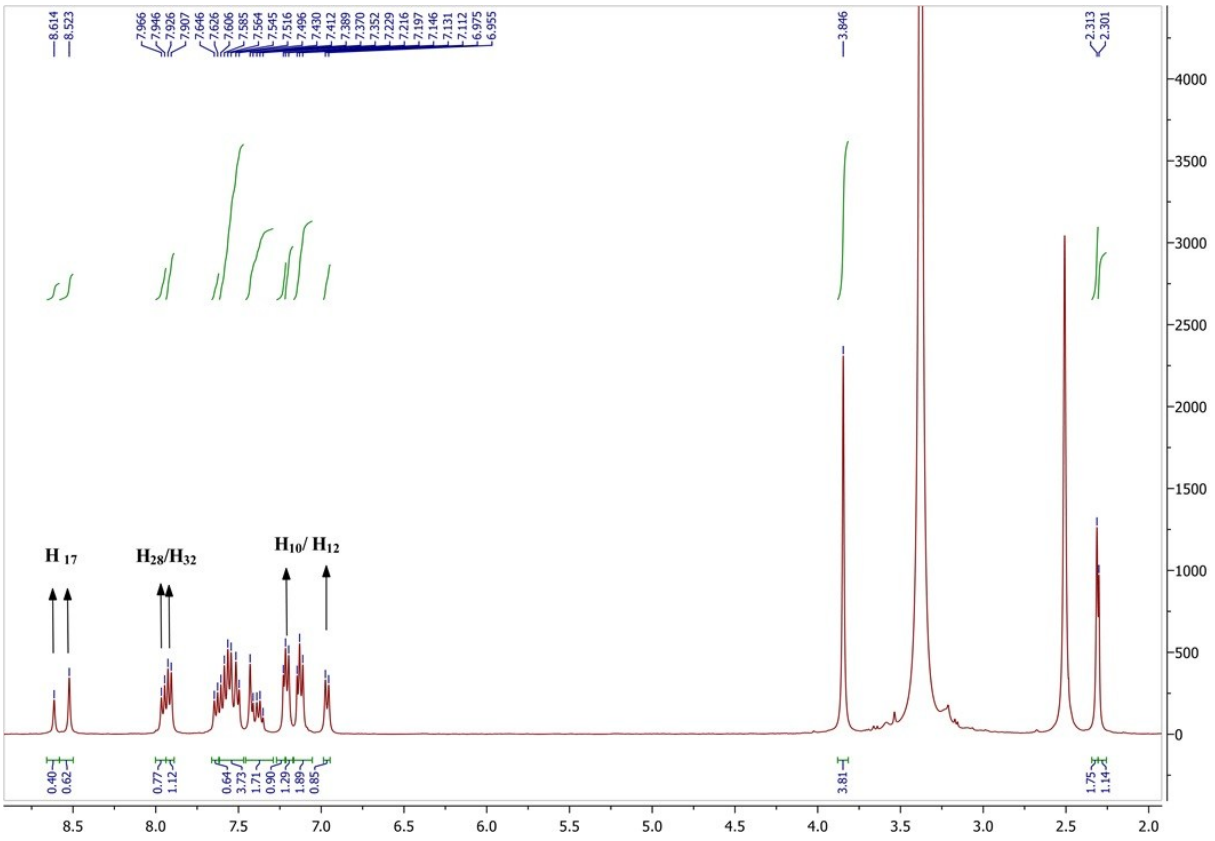


Molecular electrostatic potential surface at 0.01of *2E,5Z*

^{1}H NMR spectrum of 3



^{1}H NMR spectrum of **5a(1)(DMSO)**



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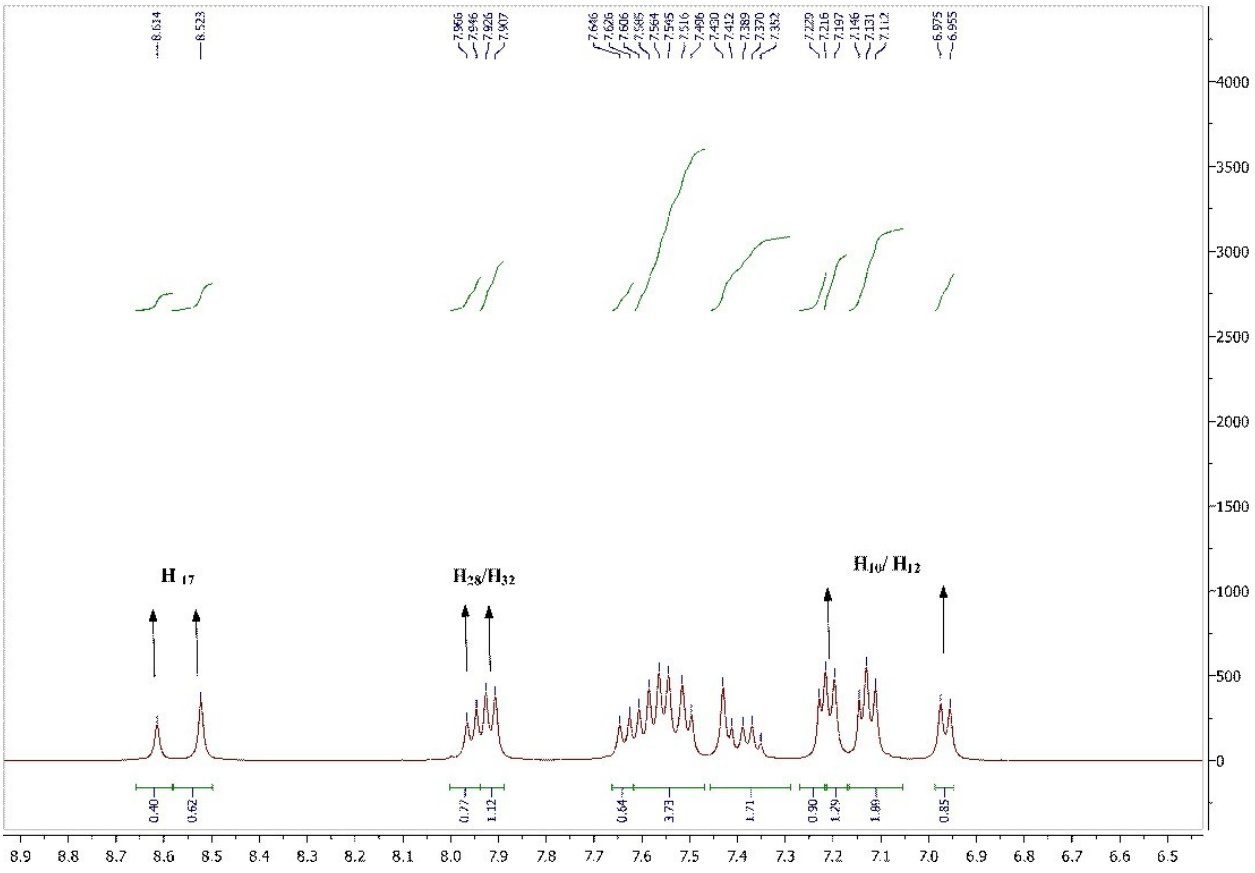
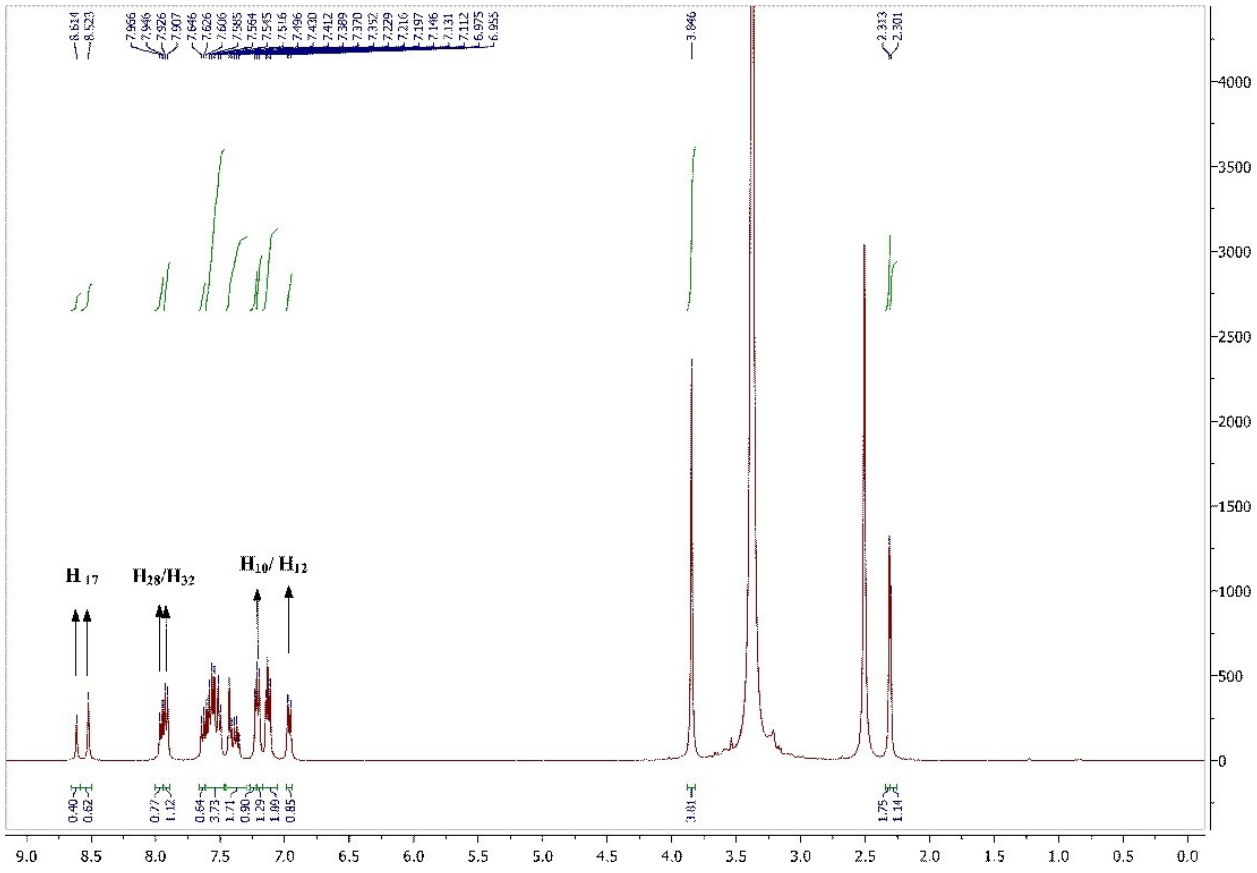
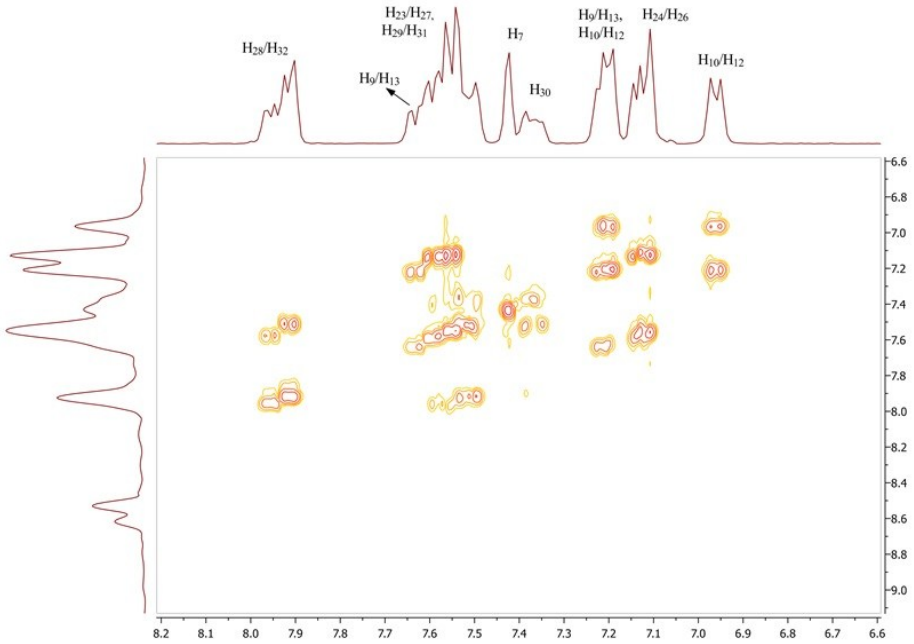


^{1}H NMR spectrum of **5a(3)(DMSO)**



^{1}H-^{1}H 2D-1 spectrum of5a(DMSO)



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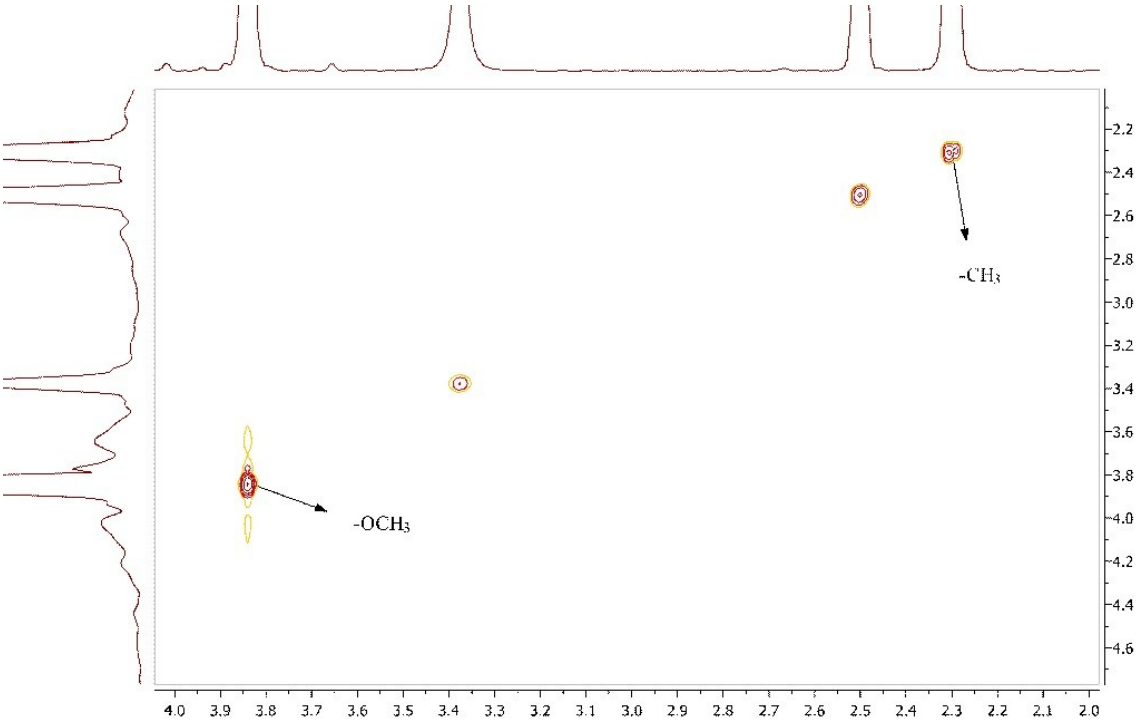
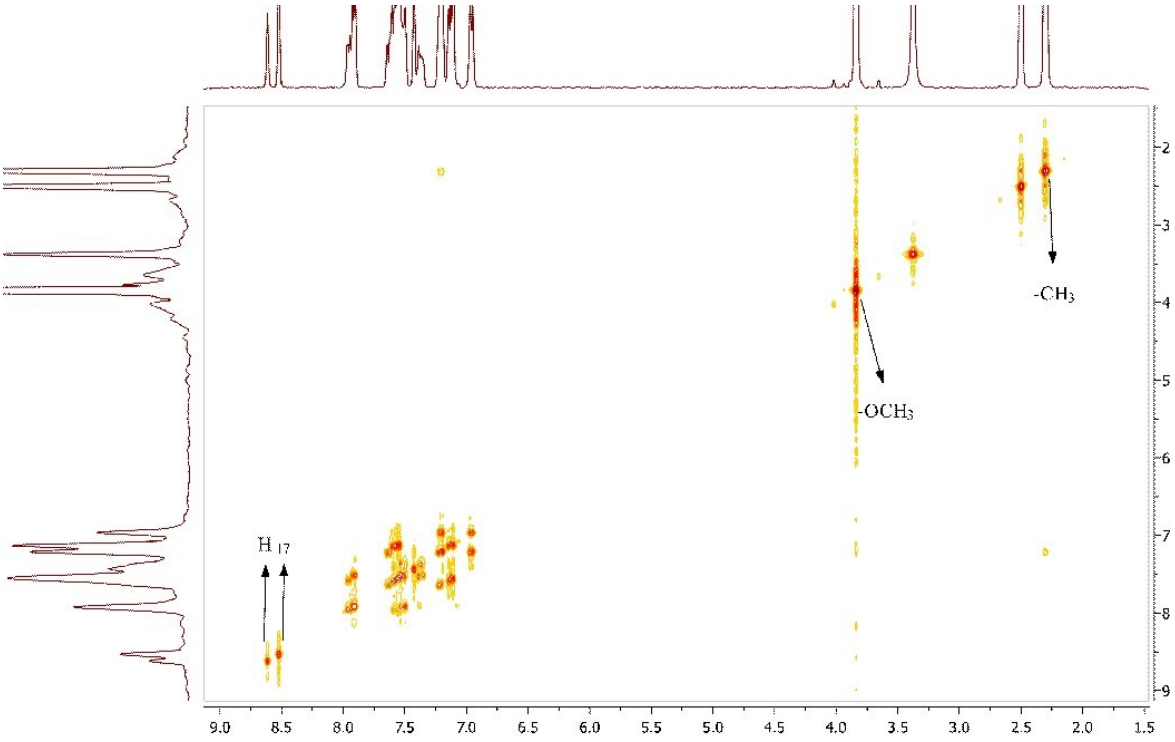


^{1}H-^{1}H 2D-3 spectrum of5a (DMSO)



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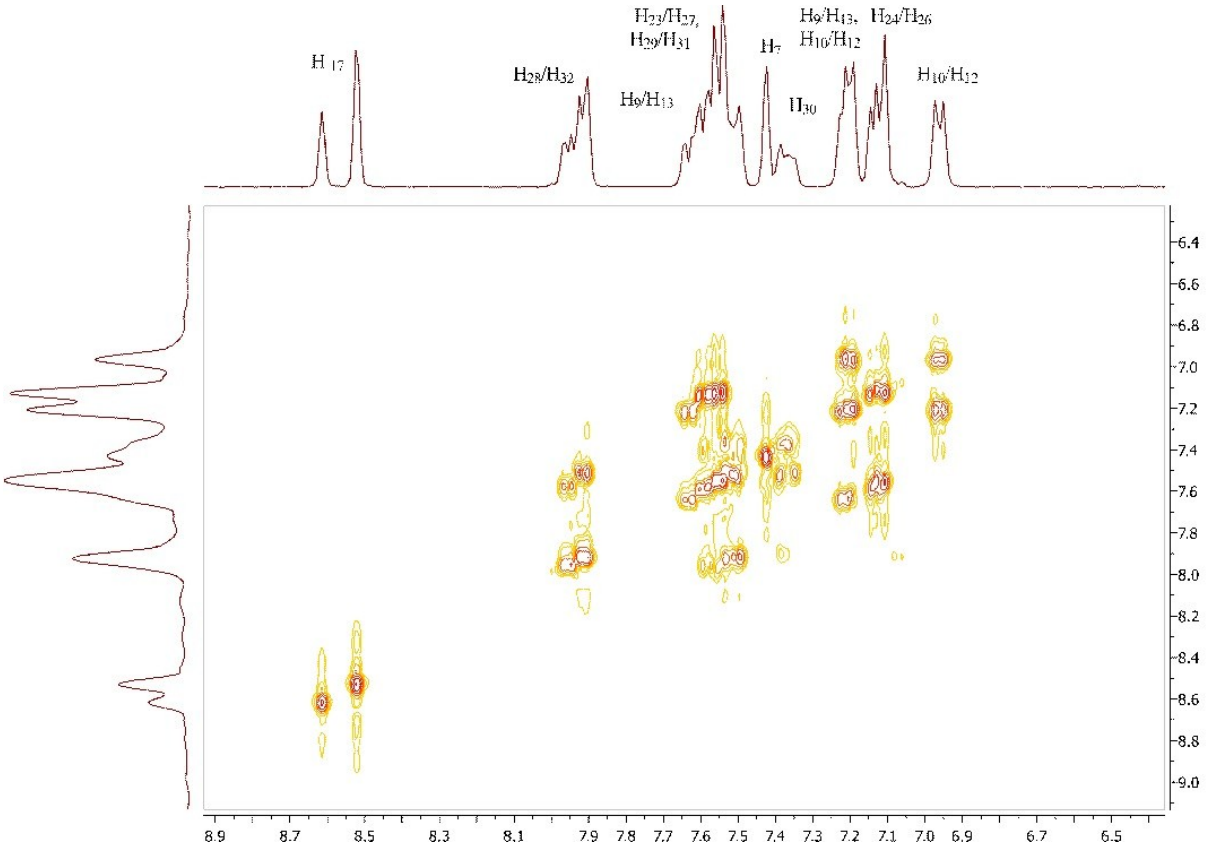
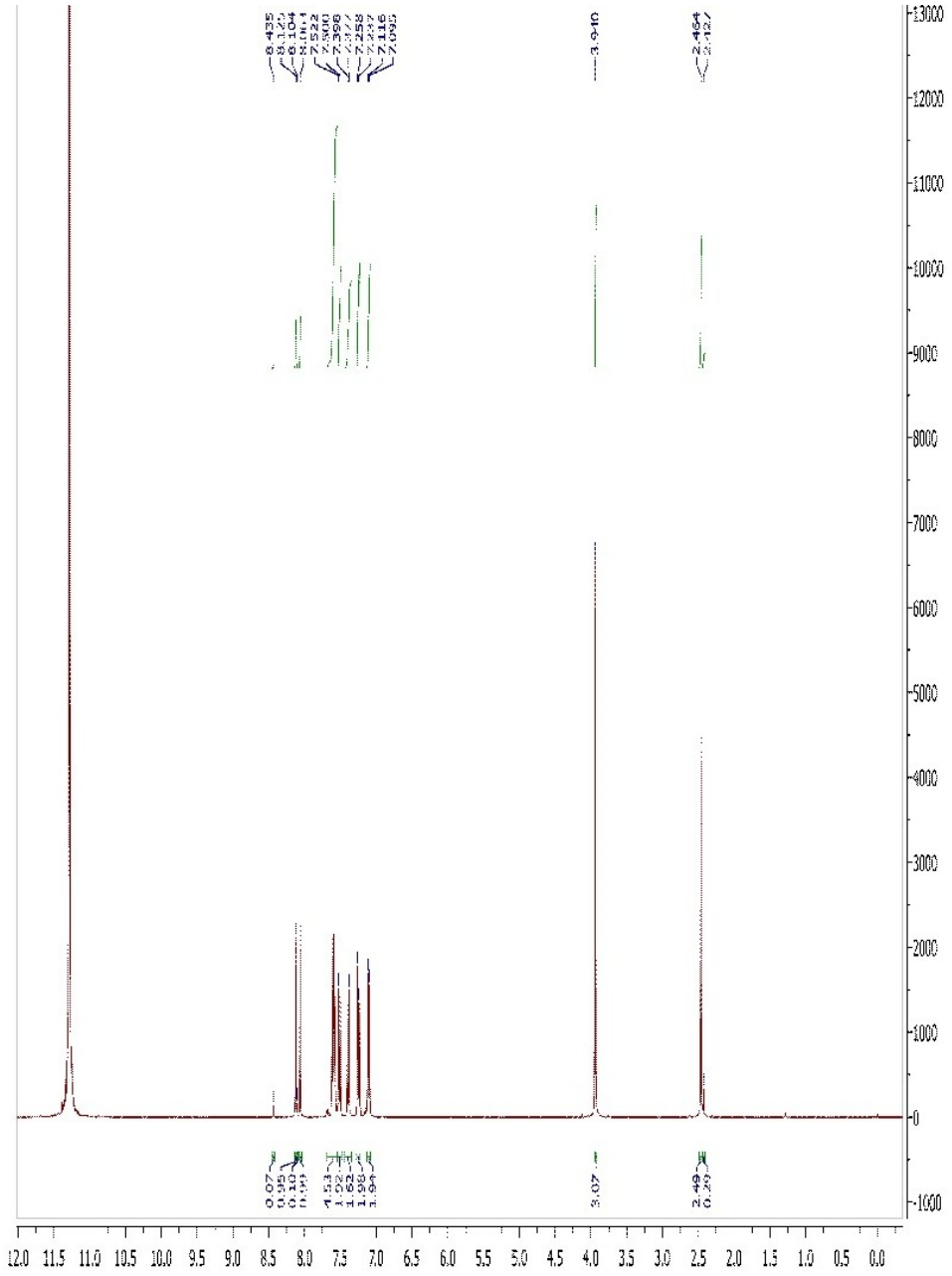
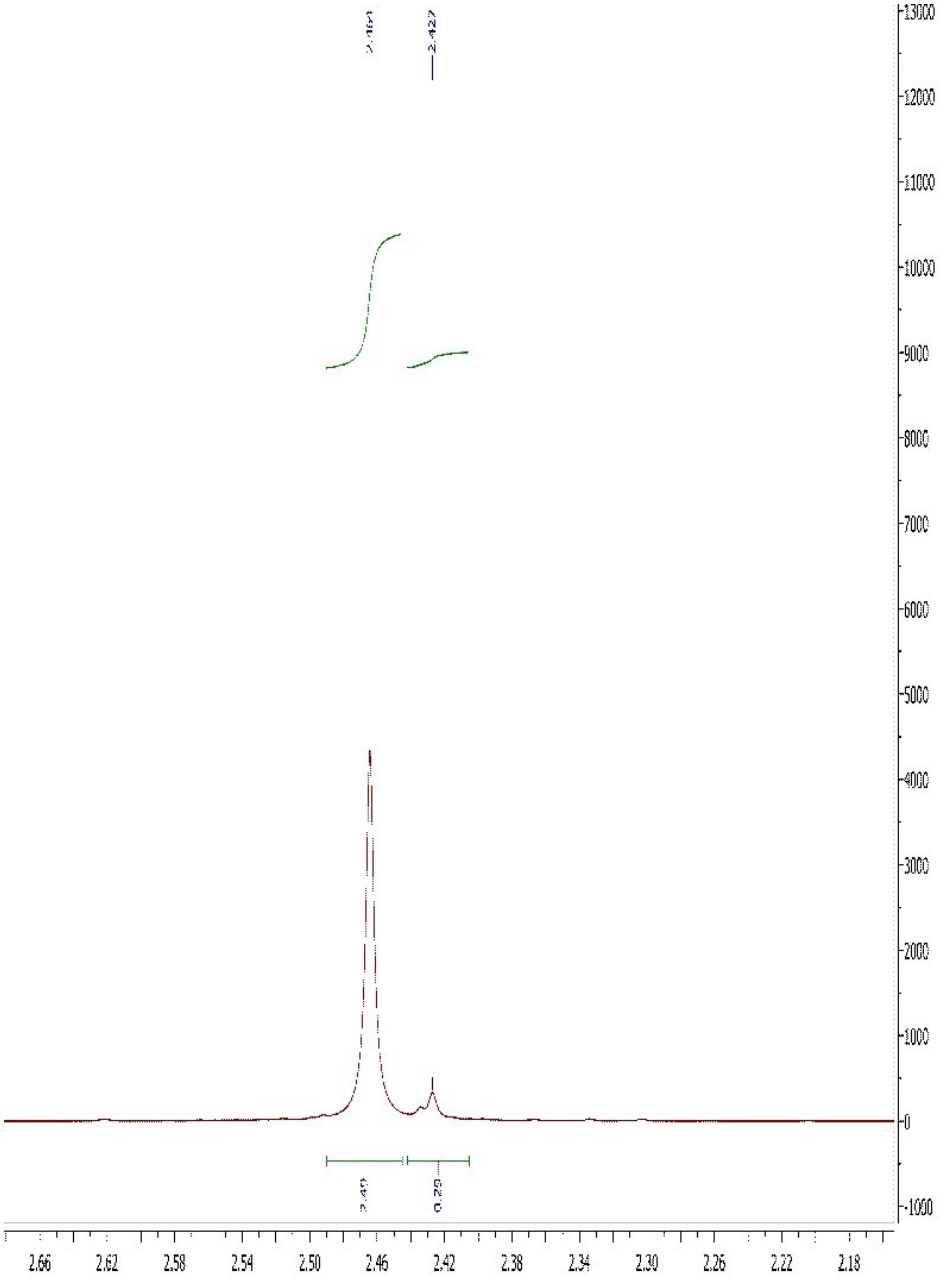


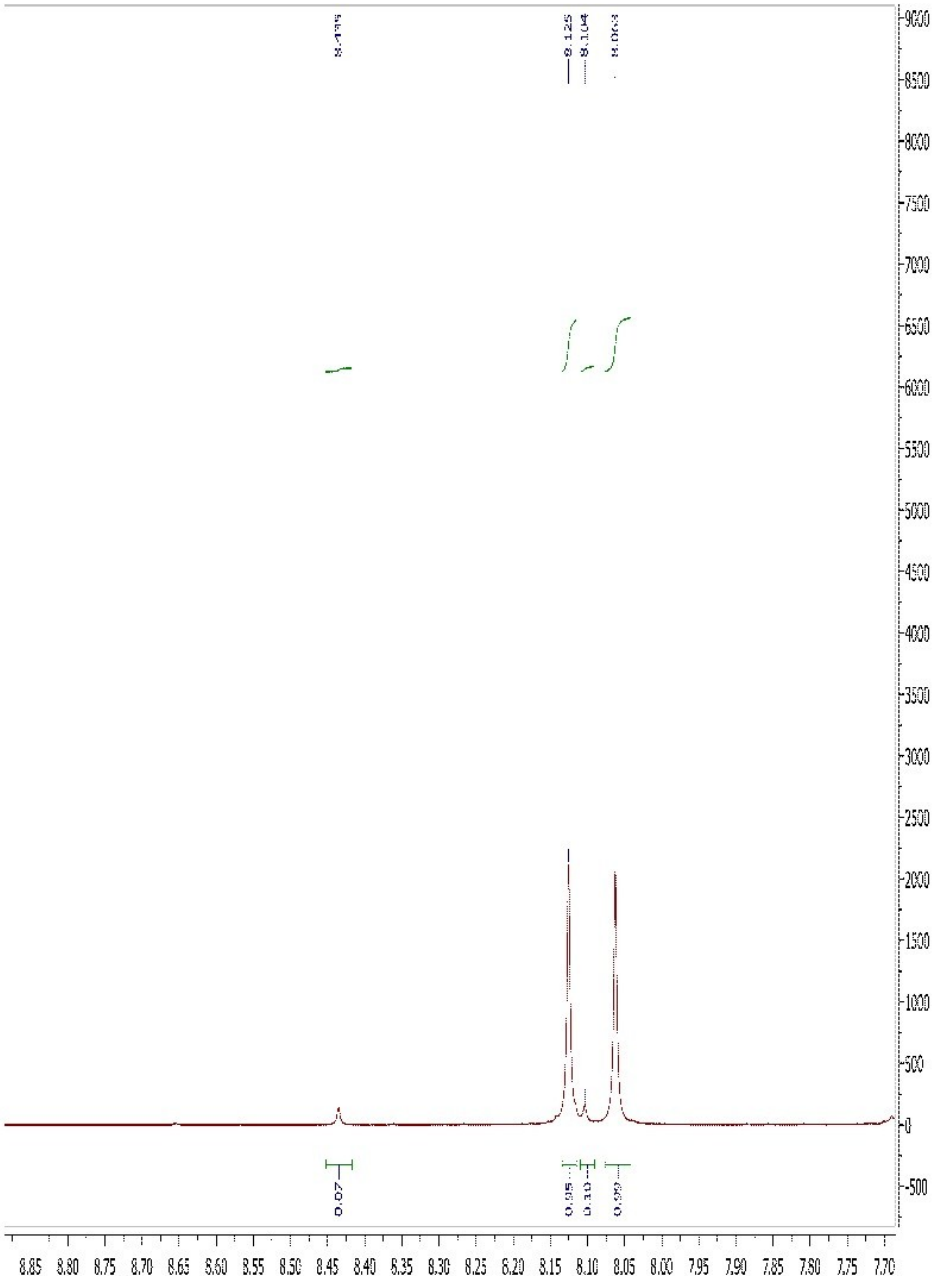
^{1}H NMR spectrum of 5a(1) (TFA)



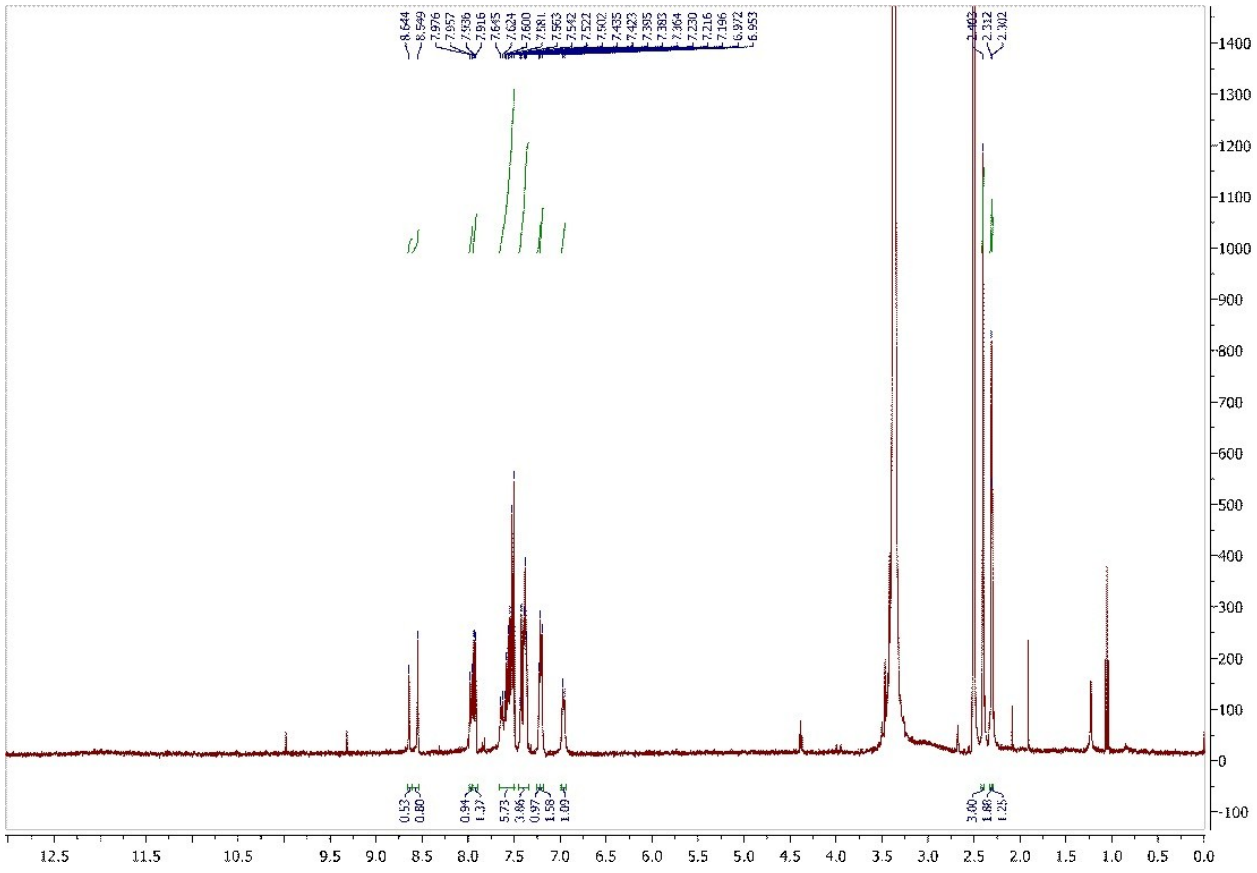
^{1}H NMR spectrum of 5a(2) (TFA)



^{1}H NMR spectrum of 5a(3) (TFA)



^{1}H NMR spectrum of 5b(1)



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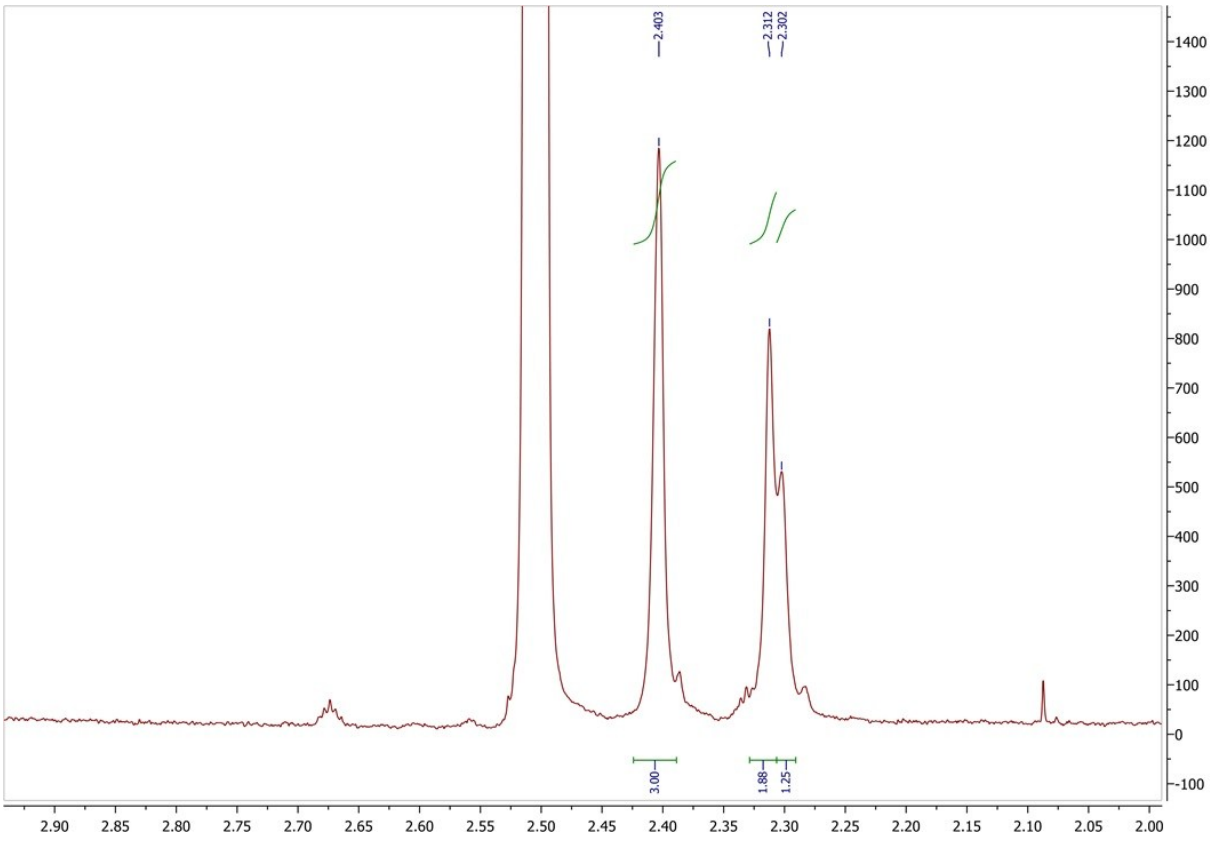

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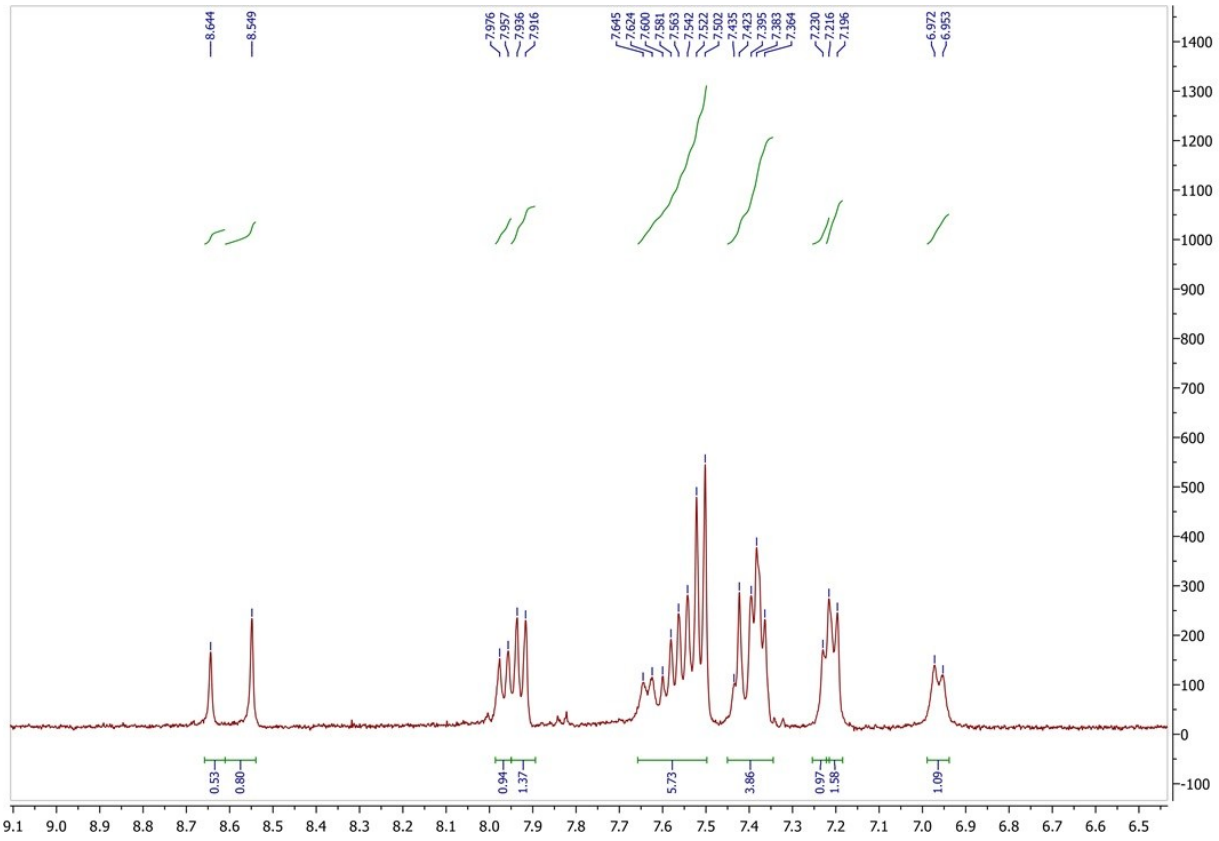
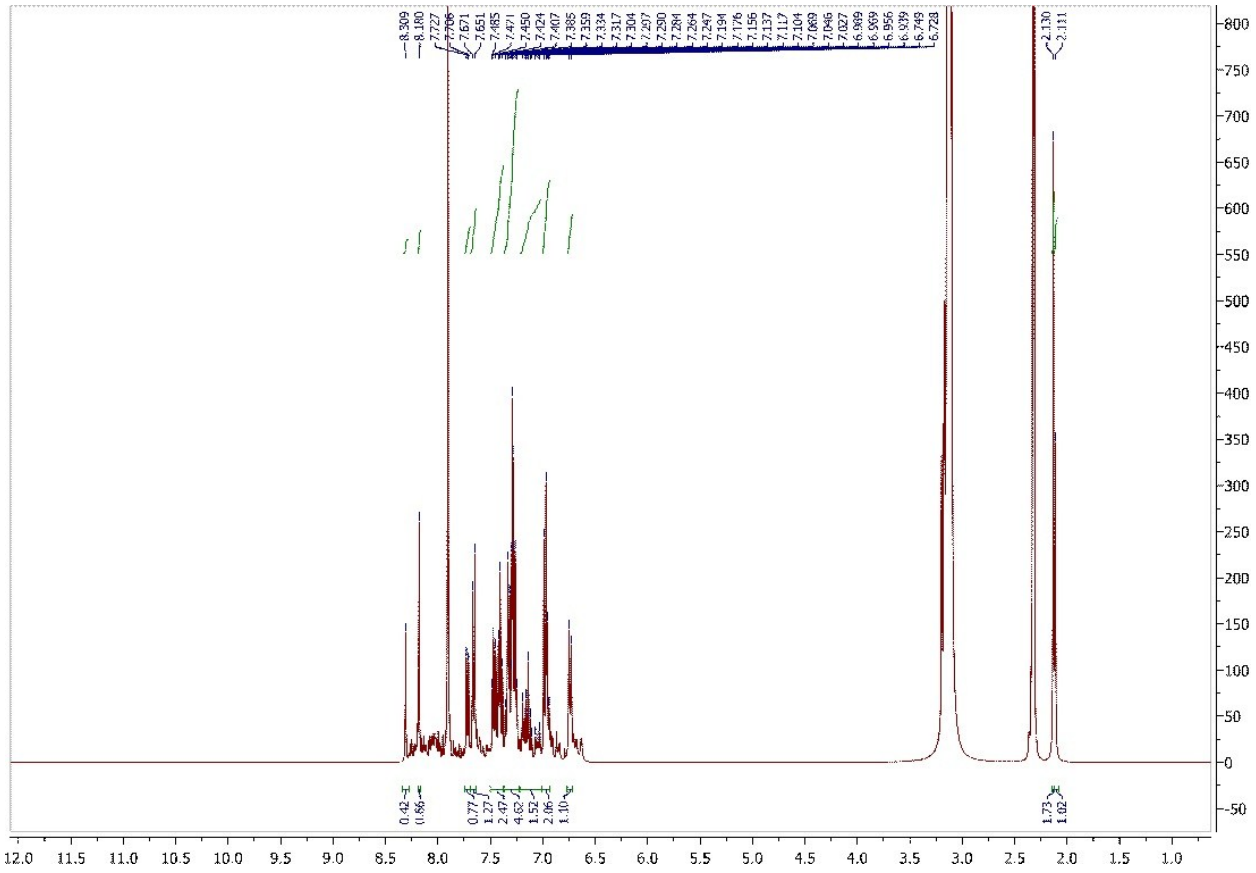


^{1}H NMR spectrum of 5c(1)



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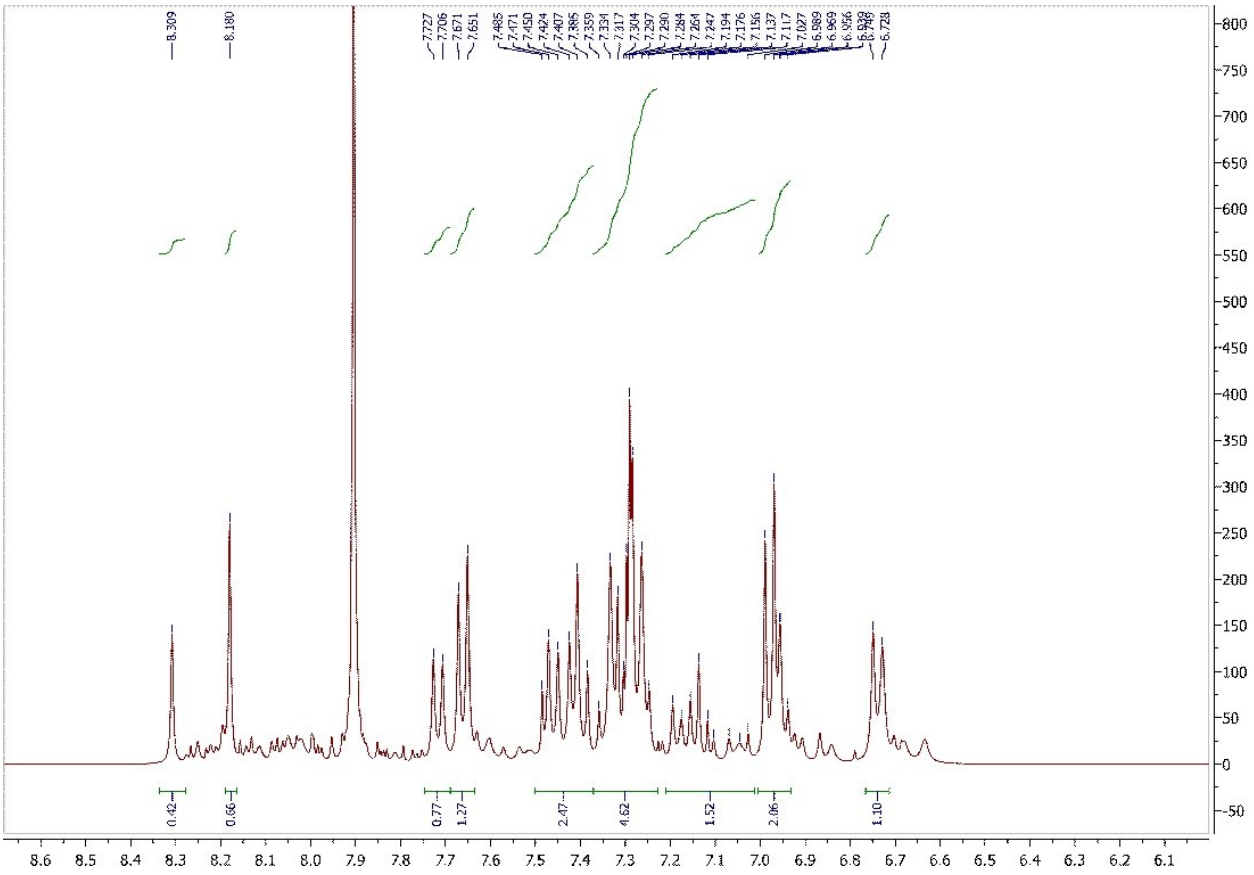

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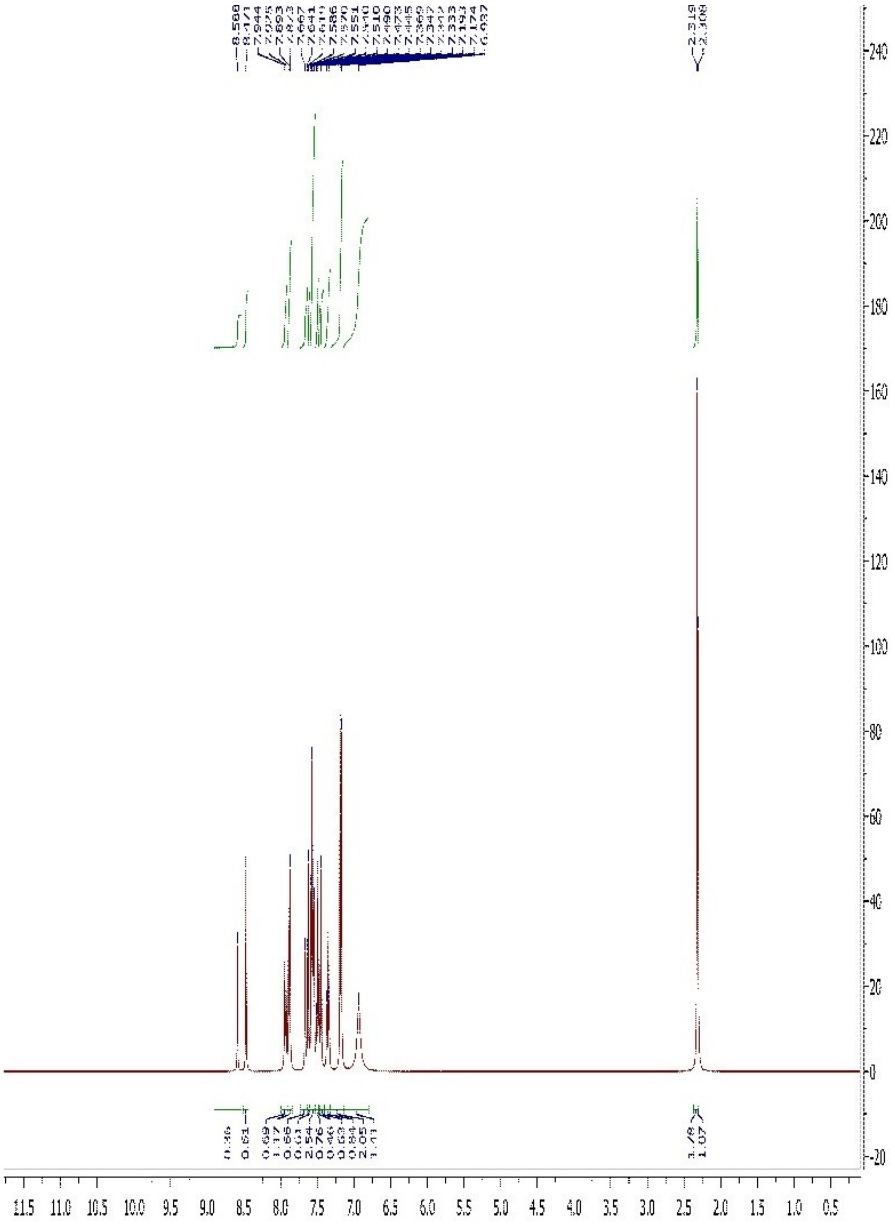
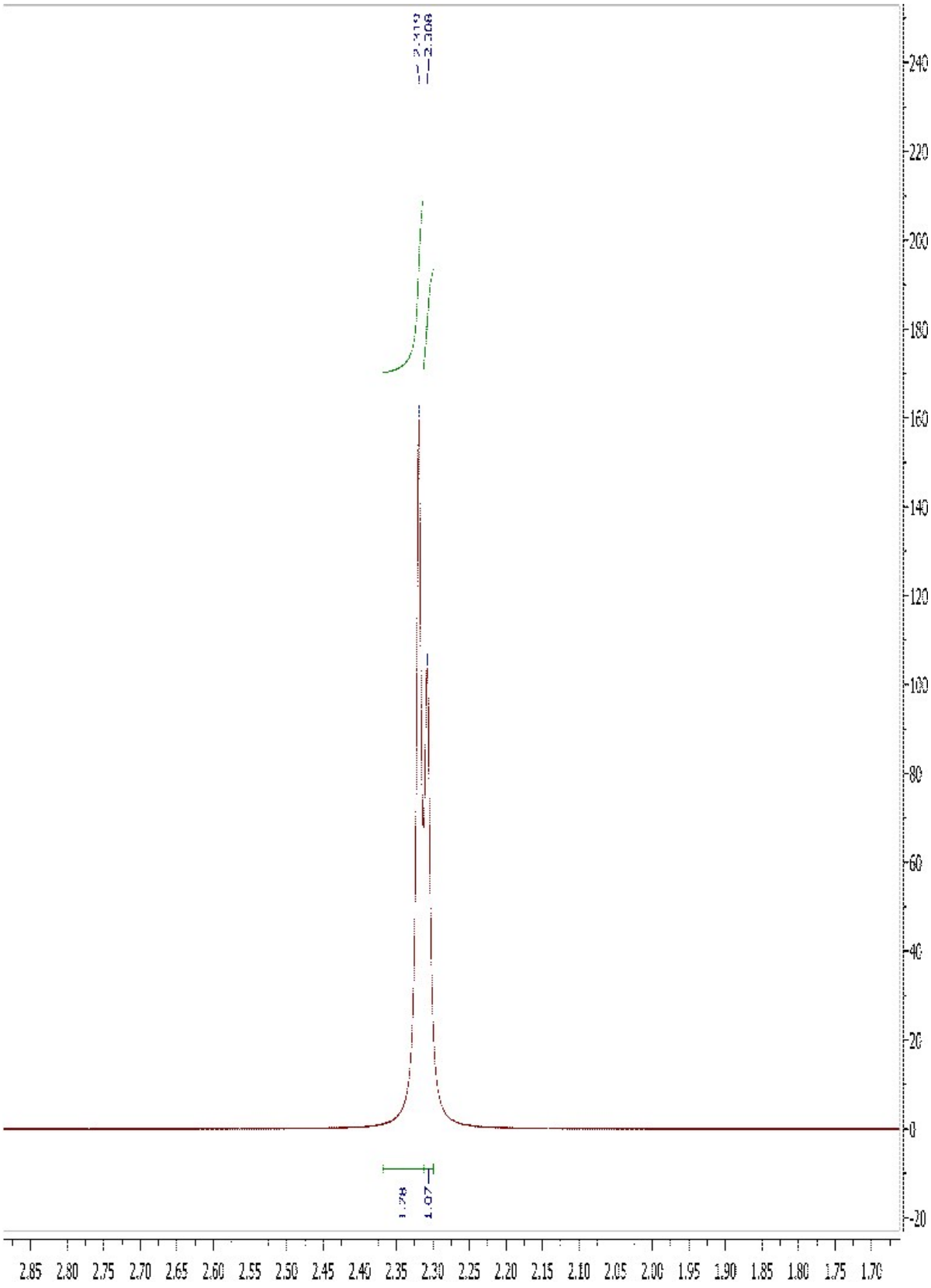


NMR spectrum of 5d(2)



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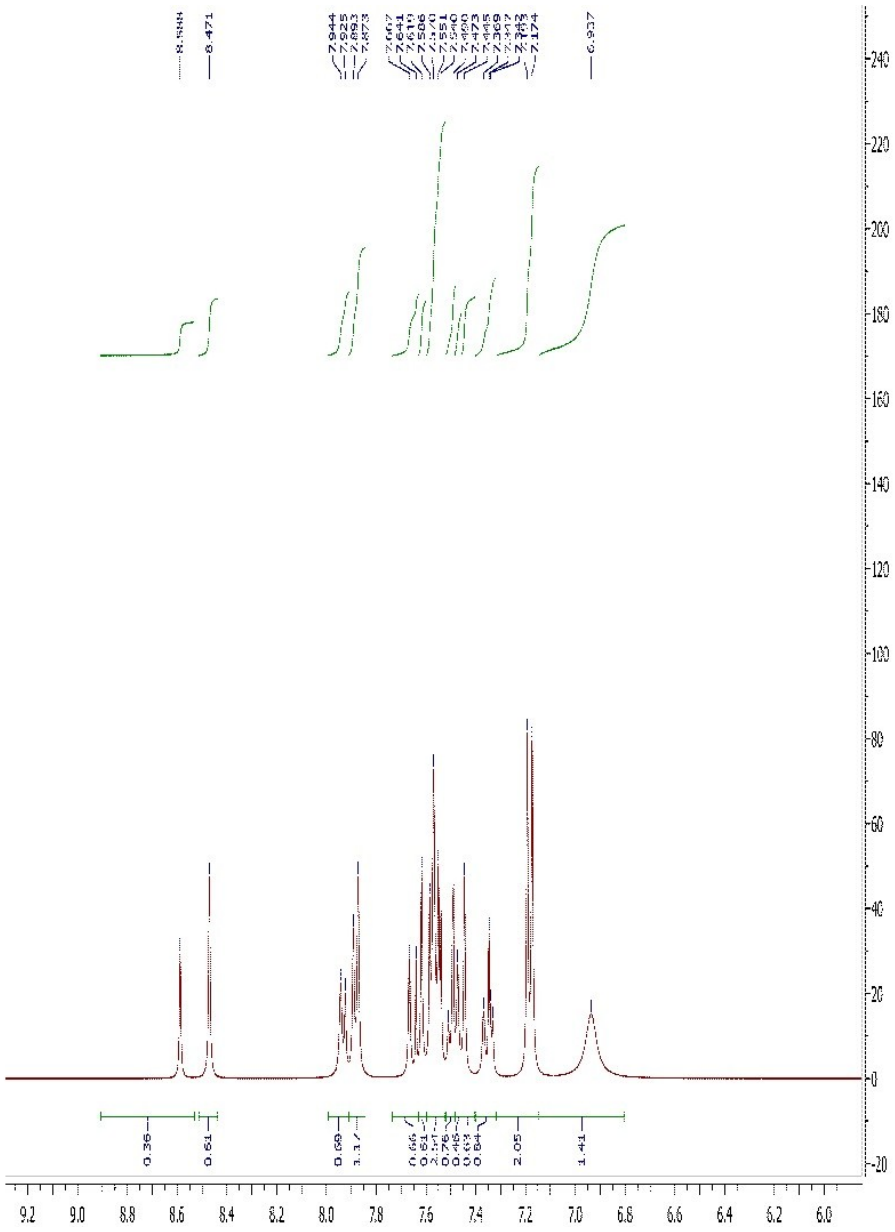

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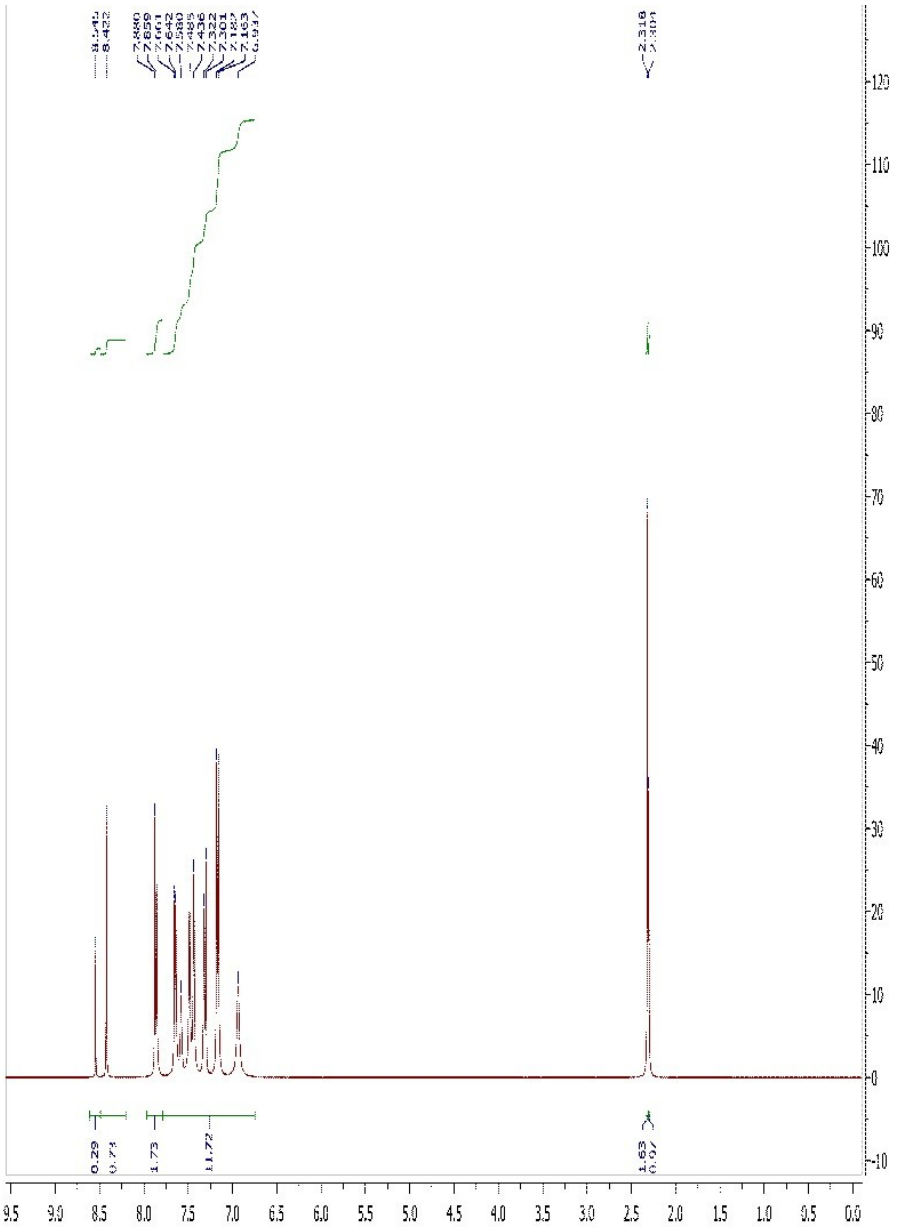

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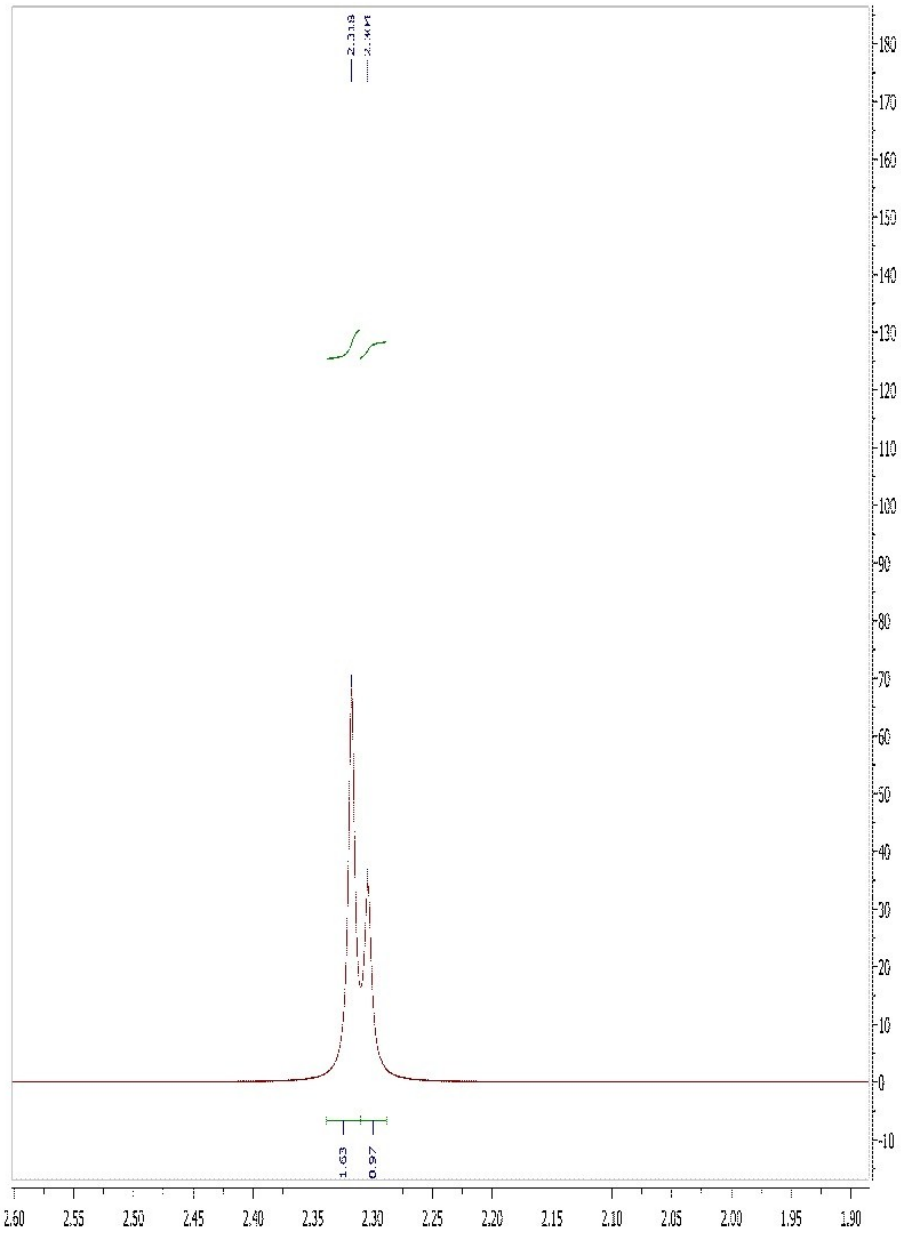

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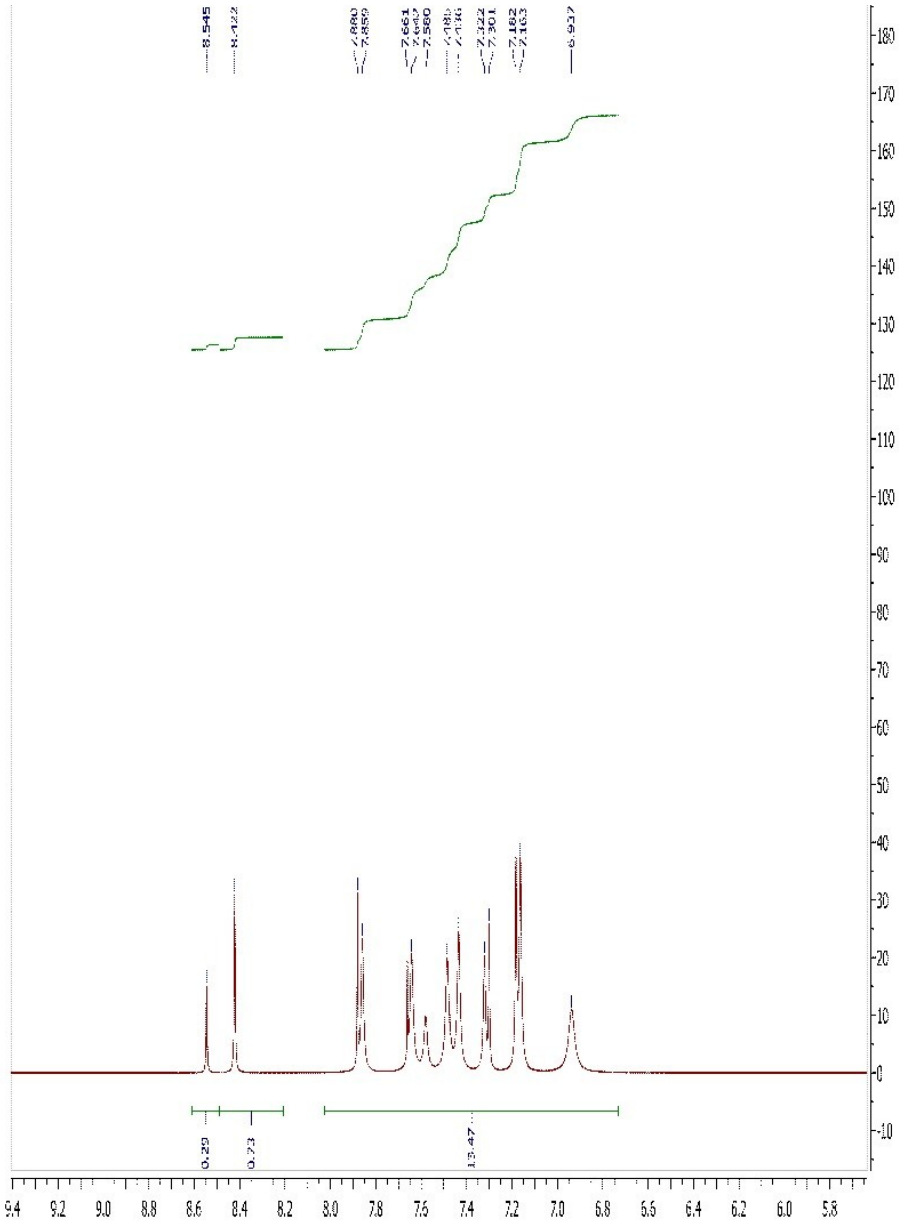
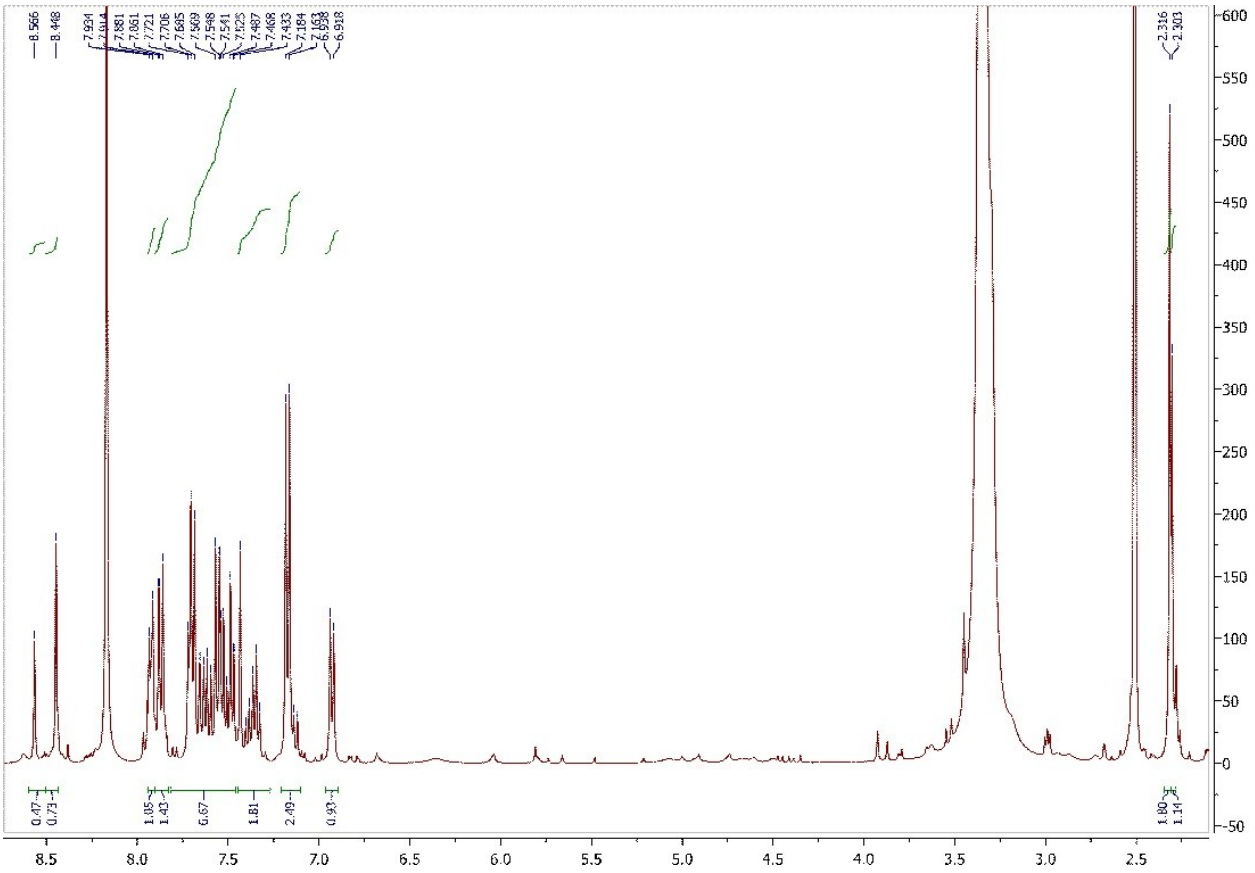


^{1}H NMR spectrum of 5f(1)



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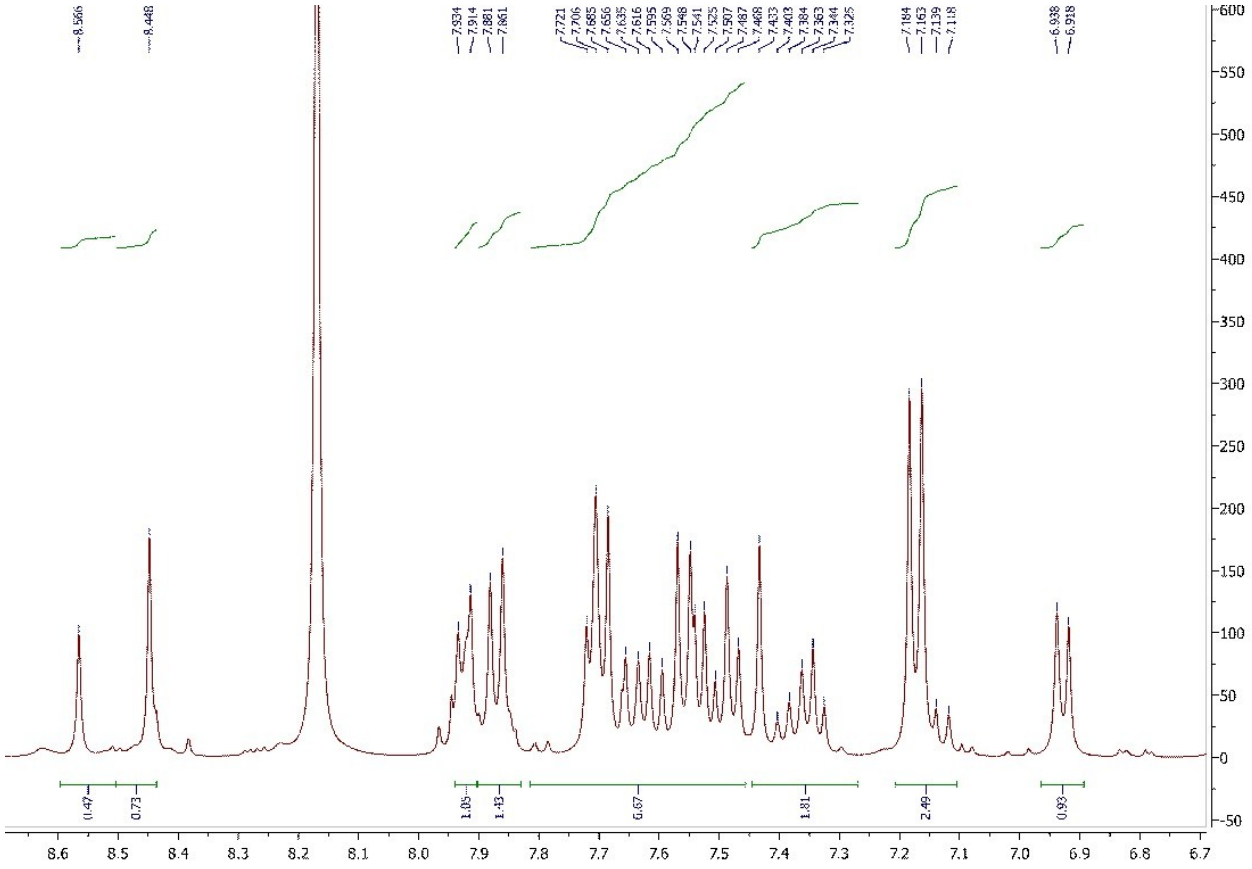
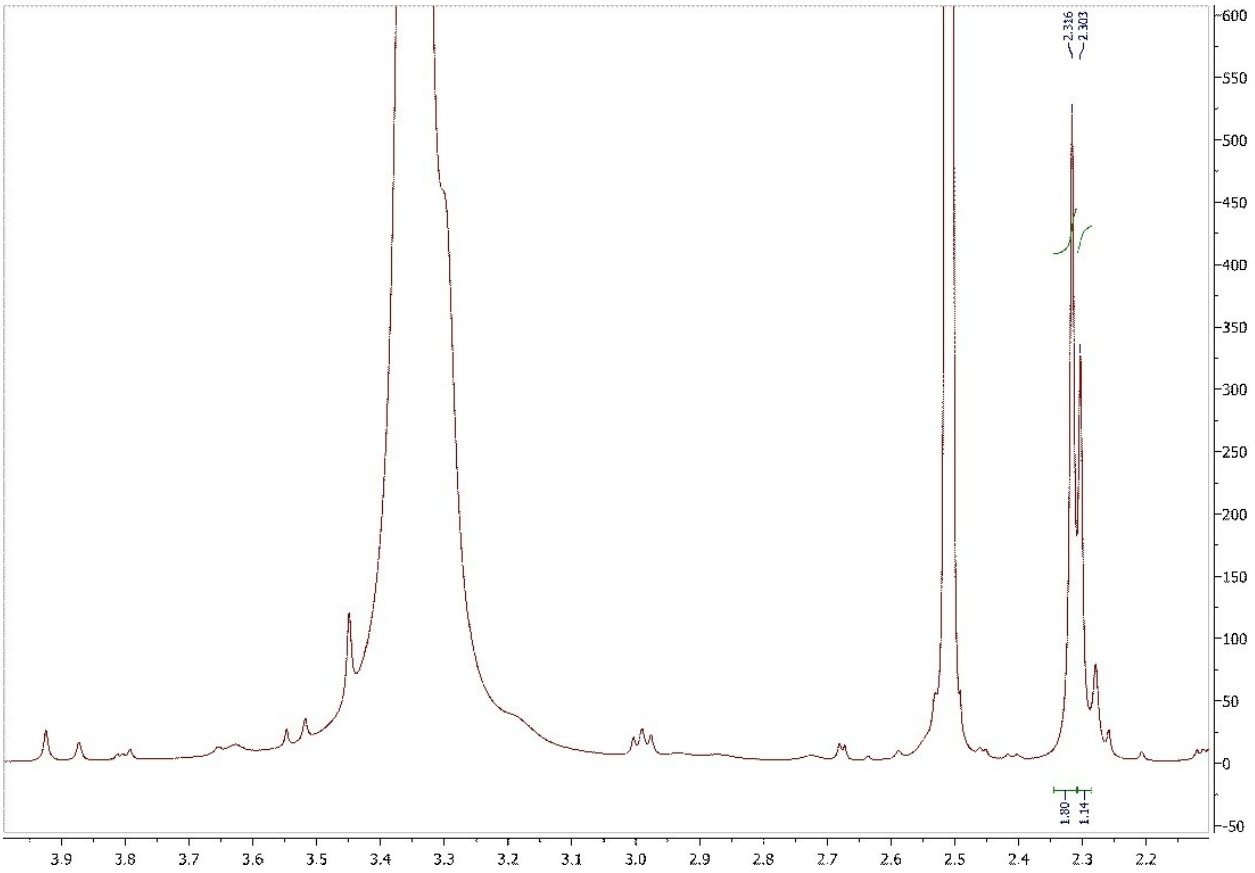
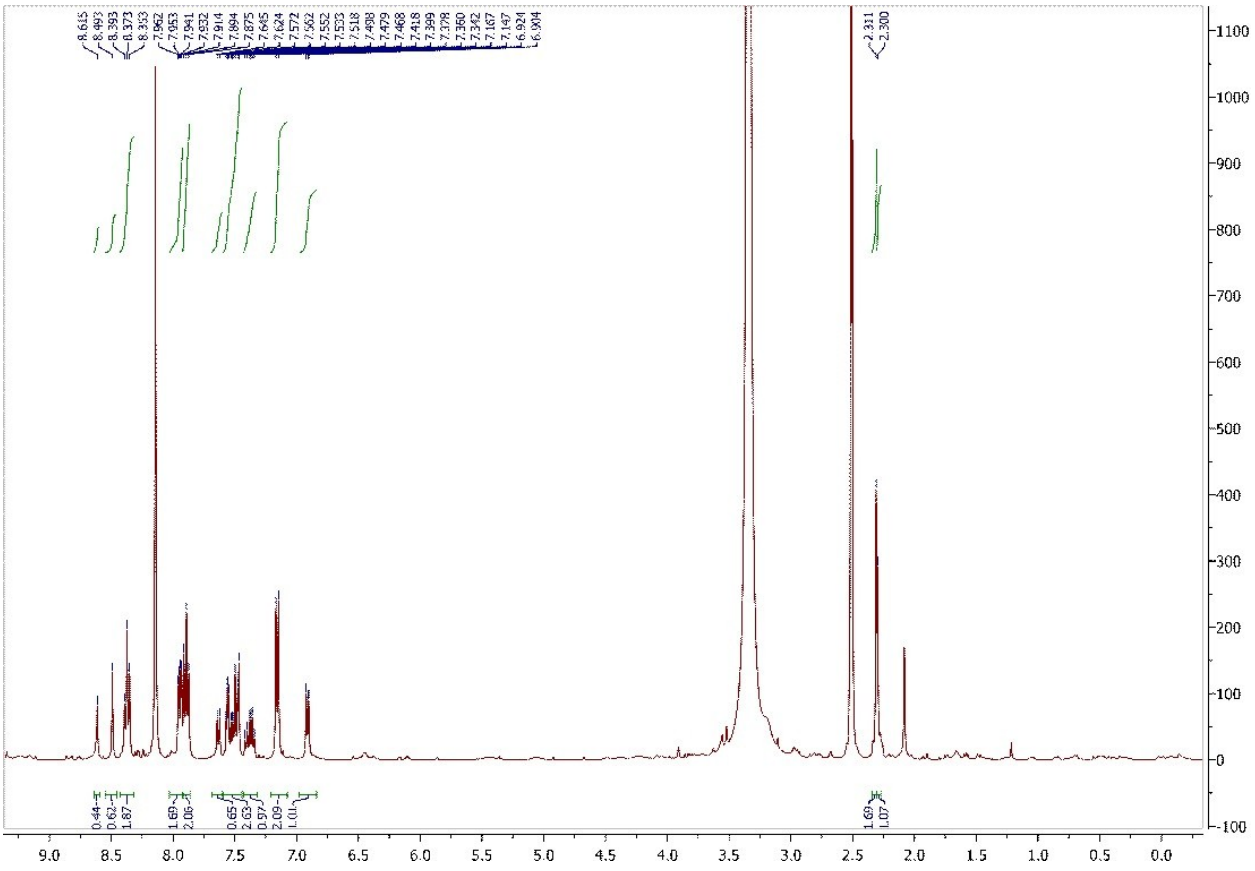


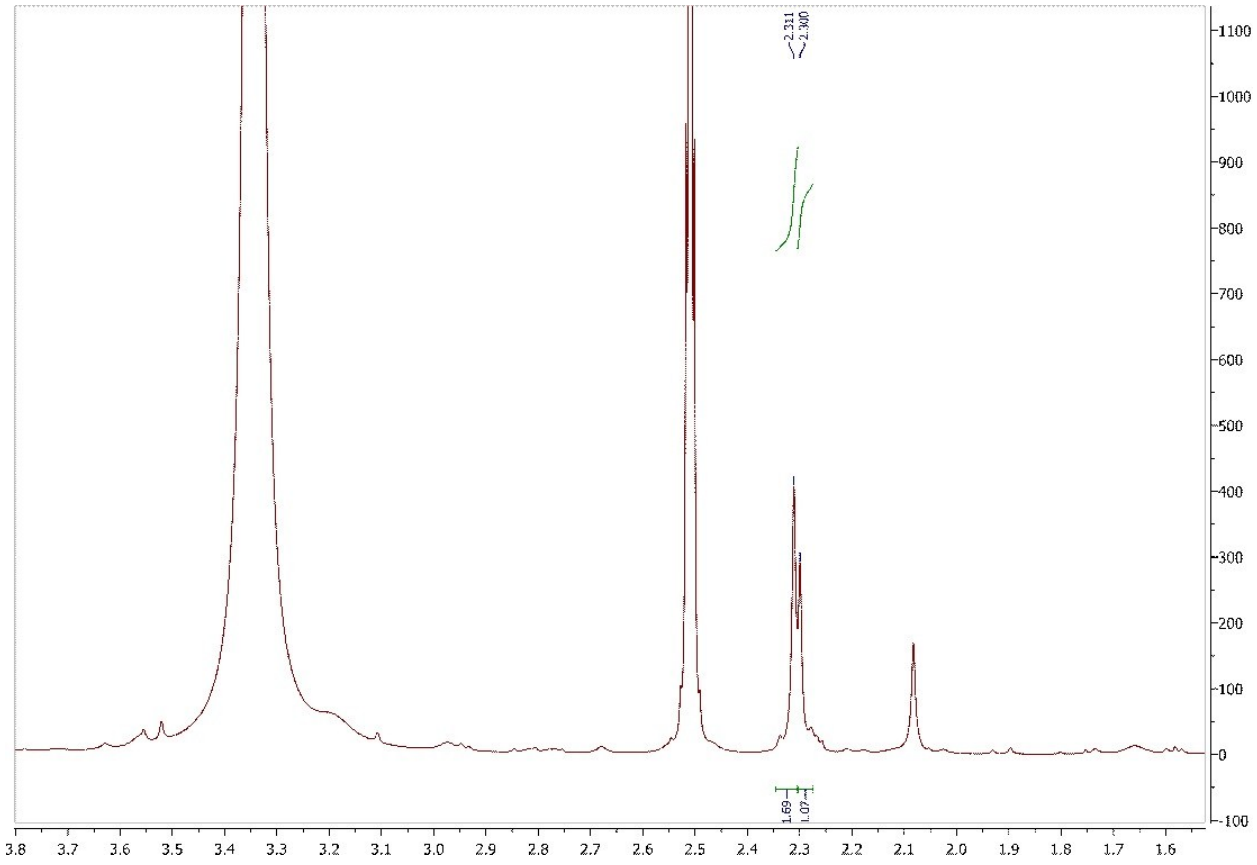
[1]H NMR spectrum of 5f(3)



^{1}H NMR spectrum of 5g(1)



^{1}H NMR spectrum of 5g(2)



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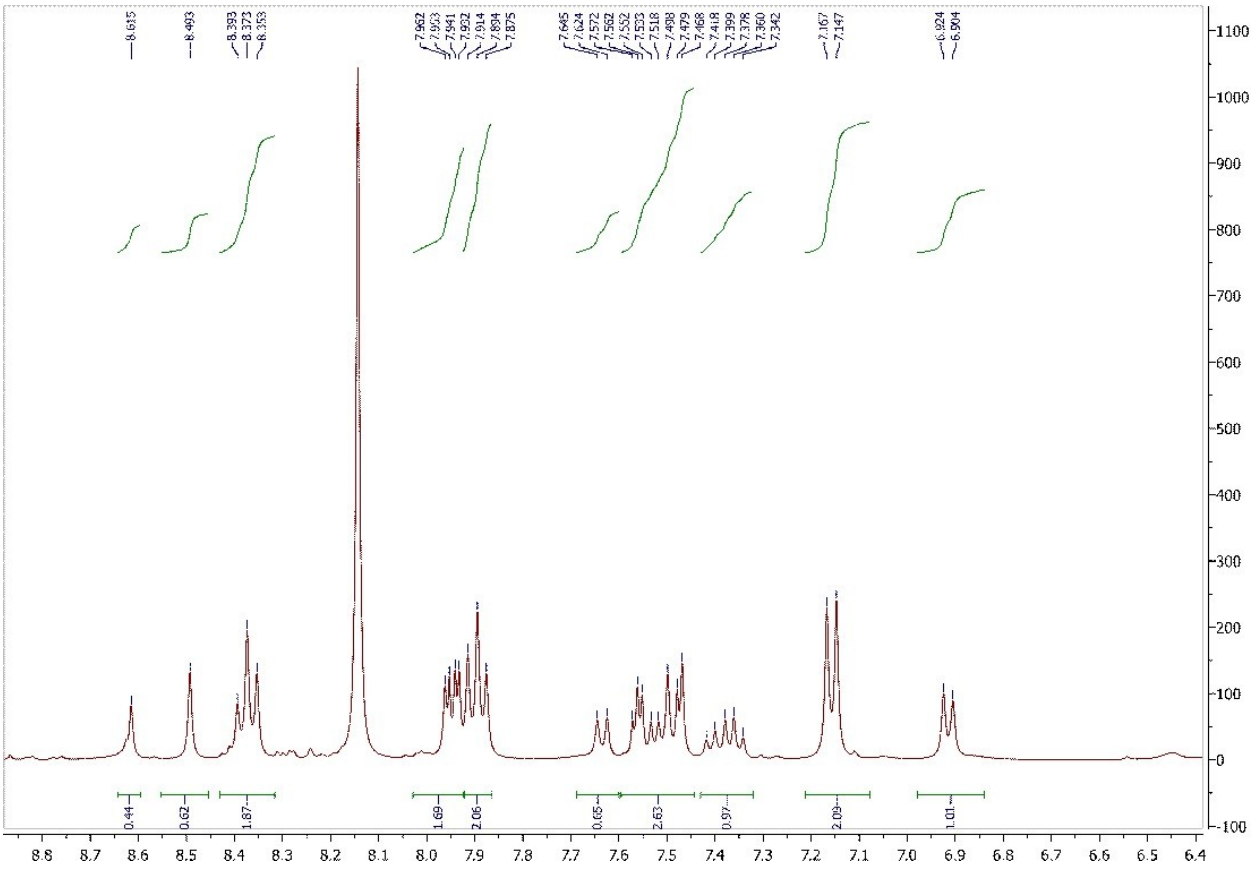
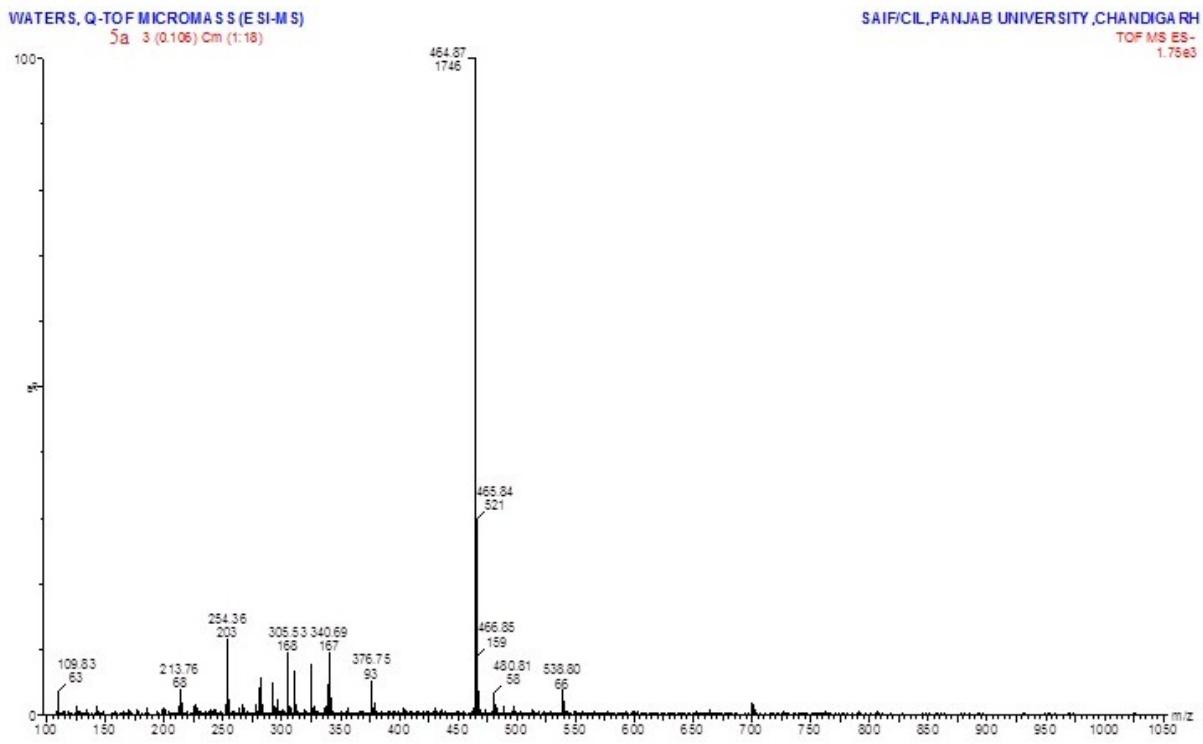
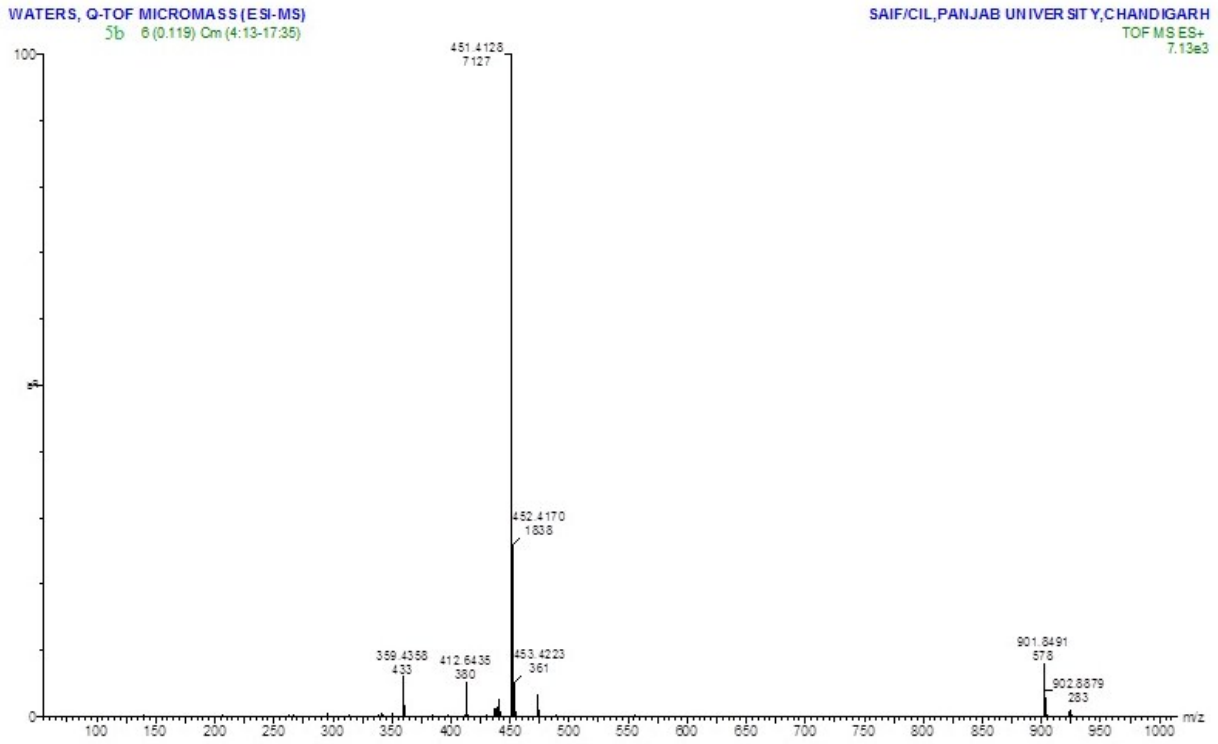


ESI-MS (m/z) of 5a(1)



ESI-MS (m/z) of 5b(1)



Reference

1. H. Zhou, S. Wu, S. Zhai, A. Liu, Y. Sun, R. Li, Y. Zhang, S. Ekins, P. W. Swaan, B. Fang, B. Zhang and B. Yan, Design, *J. Med. Chem.*, 2008, **51**, 1242-1251.