Supplementary Material

Synthesis and antimycobacterial screening of a novel series of α-amino acids containing thiazole linker

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Table S1. Experimentally determined anti-mycobacterial activity in % inhibition of the key compounds **5a-e** and **9a-d**

Comp.	*M. tuberculosis H37Ra* (Dormant Stage)[a]			*M. bovis BCG* (Dormant Stage)[a]		
	30 μg mL^{-1}	10 μg mL^{-1}	3 μg mL^{-1}	30 μg mL^{-1}	10 μg mL^{-1}	3 μg mL^{-1}
5a	68.8	40.4	49.8	50.86	40.78	36.14
5b	26.1	55.0	49.6	44.83	23.66	31.11
5c	52.8	43.4	28	**98.58**	**96.00**	**95.65**
5d	56.9	61.1	59.9	47.12	33.22	36.81
5e	2.9	36.1	59.2	64.37	33.91	21.49
9a	35.2	24.2	16.6	34.09	18.40	1.39
9b	40.6	39.8	21.4	70.23	9.19	-
9c	51.5	14.7	13.9	22.84	4.79	2.46
9d	49.7	22.4	13.5	**81.61**	41.36	19.68
Rifampicin[b]	99.5	98.0	96.4	99.0	96.8	94.6

a: % inhibition; b: at 0.5 μg mL^{-1} concentration; - : Not active

Table S2. Antibacterial screening in % inhibition of synthesized compounds **5a-e** and **9a-d**

	Gram-negative strains							Gram-positive strains	
Comp	*E.coli*			*P. flurescence*				*S. aureus*	
	30 μg mL^{-1}	10 μg mL^{-1}	3 μg mL^{-1}	30 μg mL^{-1}	10 μg mL^{-1}	3 μg mL^{-1}	30 μg mL^{-1}	10 μg mL^{-1}	3 μg mL^{-1}
5a	29.95	13.33	3.50	25.29	20.01	0.12	27.87	12.18	0.66
5b	75.22	62.93	60.40	72.79	62.63	56.54	74.05	69.63	59.82
5c	**97.98**	**92.62**	**86.05**	**99.28**	**94.30**	**86.13**	**97.13**	**92.96**	**87.12**
5d	60.27	47.19	35.61	52.56	40.94	36.52	59.35	43.91	34.84
5e	**83.79**	70.88	64.91	**88.96**	71.22	65.16	81.53	76.63	61.19
9a	27.58	11.35	4.30	26.27	16.85	2.51	26.32	14.56	2.01
9b	26.75	15.76	2.82	29.23	13.53	8.75	21.44	11.04	6.35
9c	24.87	15.59	6.69	28.36	15.66	9.63	20.39	13.43	6.44
9d	**92.68**	**88.53**	**83.13**	**94.26**	**90.45**	**83.27**	**97.20**	**93.27**	**89.33**
[a]AMP	**97.00**	**95.25**	**92.25**	**96.60**	**92.00**	**92.15**	**96.50**	**93.80**	**91.15**

[a]AMP : Ampicillin

Biological assay

Antitubercular assay. All the synthesized compounds were screened for their *in vitro* activity against *M. tuberculosis* H37Ra (ATCC 25177) and *M. bovis* BCG (ATCC 35743) using a two-fold dilution technique. Activity against MTB was determined through the XTT reduction menadione assay (XRMA) reading absorbance at 470 nm.[12]

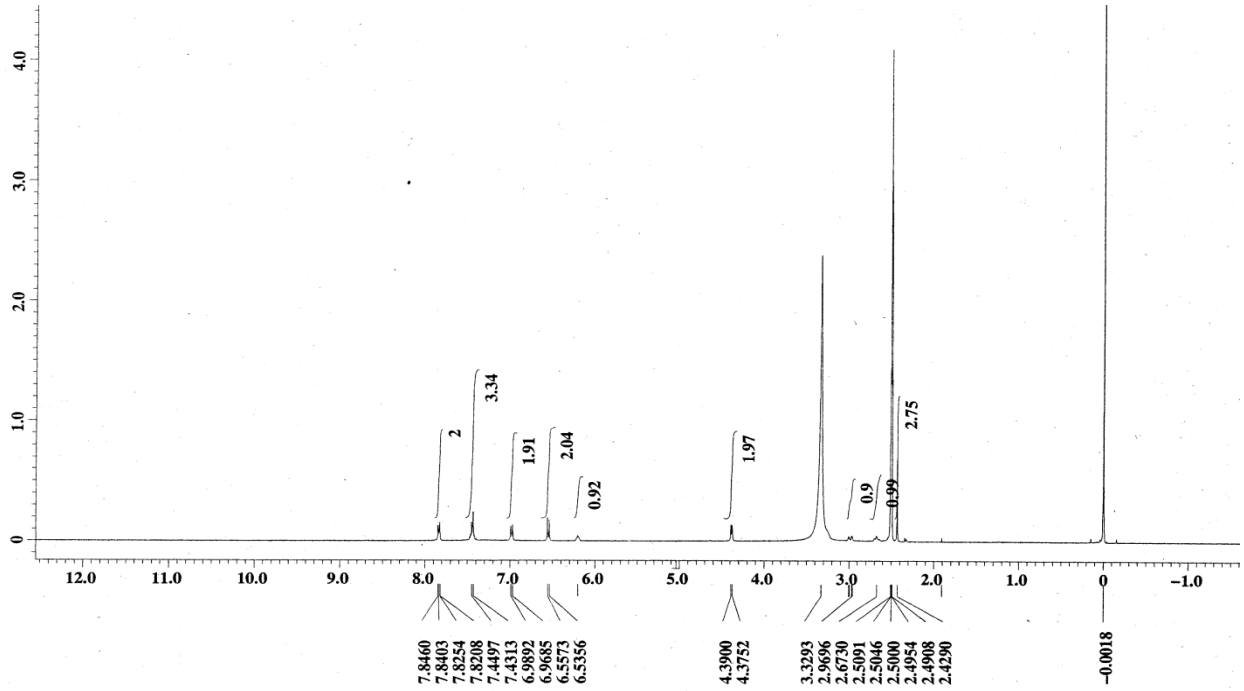
Cytotoxicity assay. To check the selectivity, selected (S)-2-amino-3-(4-(((4-methyl-2-arylthiazol-5-yl)methyl)amino)phenyl)propanoic acid (**5a-e**) and (S)-2-amino-3-(4-(((2-arylthiazol-4-yl)methyl)amino)phenyl)propanoic acid (**9a-d**) were assayed for their cytotoxic effects on HUVECs; primary Human umbilical vein endothelial cells, HeLa; cervix adenocarcinoma, and HCT 116; colon carcinoma using MTT assay. The cell lines were maintained under standard cell culture conditions under 5% CO_2 at 37 °C in a 95% air humidified environment. Each concentration was tested in duplicates in a single experiment. GI_{50} / GI_{90} values were calculated using Origin 8 Pro Software.

Antibacterial activity. All bacterial cultures were first grown in Luria Burtony media at 37 °C at 180 rpm. Once the culture reaches 1 O.D., it is used for the anti-bacterial assay. Bacterial strains *Escherichia coli* (NCIM 2576), *Pseudomonas flurescence* (NCIM 2059) as Gram-negative and *Staphylococcus aureus* (NCIM 2602), *Bacillus subtilis* (NCIM 2162) as Gram-positive were obtained from NCIM (NCL, Pune) and were grown in Luria Burtony medium from Hi Media, India. The assay was performed in 96 well plates after 8 hours and 12 hours for Gram-negative and Gram-positive bacteria, respectively. 0.1 % of 1 O.D. culture at 620 nm was used for screening inoculated culture was added into each well of 96 well plates containing the compounds to be tested. Optical density for each plate was measured at 620 nm after 8 hours for Gram-negative bacteria and after 12 hours for Gram-positive bacteria.[3,4]

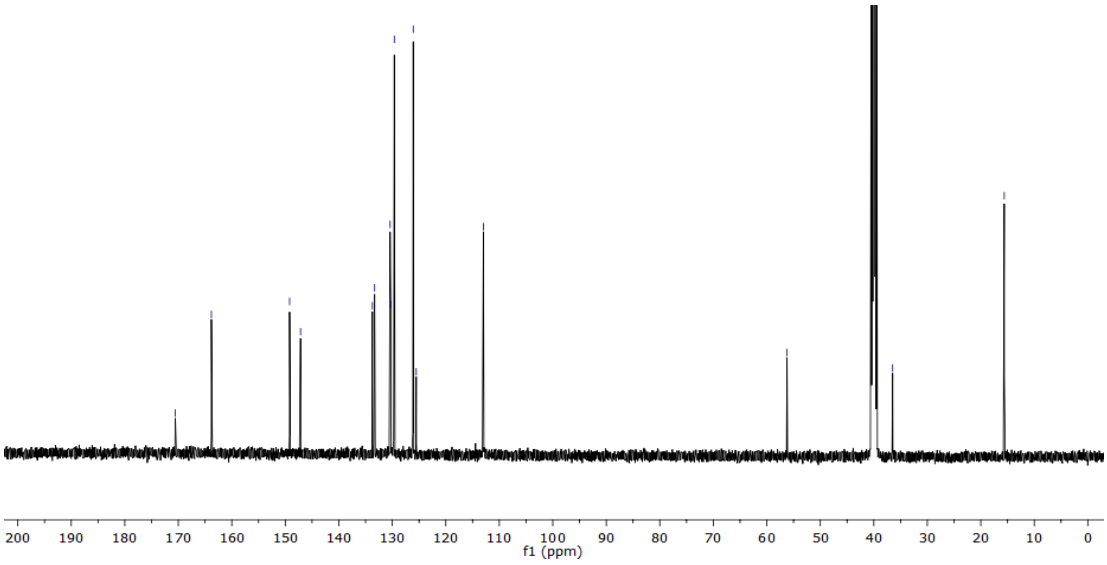
References

1. Singh, U.; Akhtar, S.; Mishra, A.; Sarkar, D. *J Microbiol Methods.* **2011,** 84, 202.
2. Khan, A.; Sarkar, D. *J Microbiol Methods,* **2008**, 73, 62.
3. Khan, A.; Sarkar, S.; Sarkar, D. *Int J Antimicrob Agents,* **2008,** *32*, 40.
4. Sarkar, S.; Sarkar, D. *J Biomol Screening*, **2012**, *17*, 966.

NMR spectra of representative compounds



^{1}H NMR (400 MHz, DMSO-d_6) spectrum of (S)-2-amino-3-(4-(((4-methyl-2-phenylthiazol-5-yl)methyl)amino)phenyl)propanoic acid, (**5a**)



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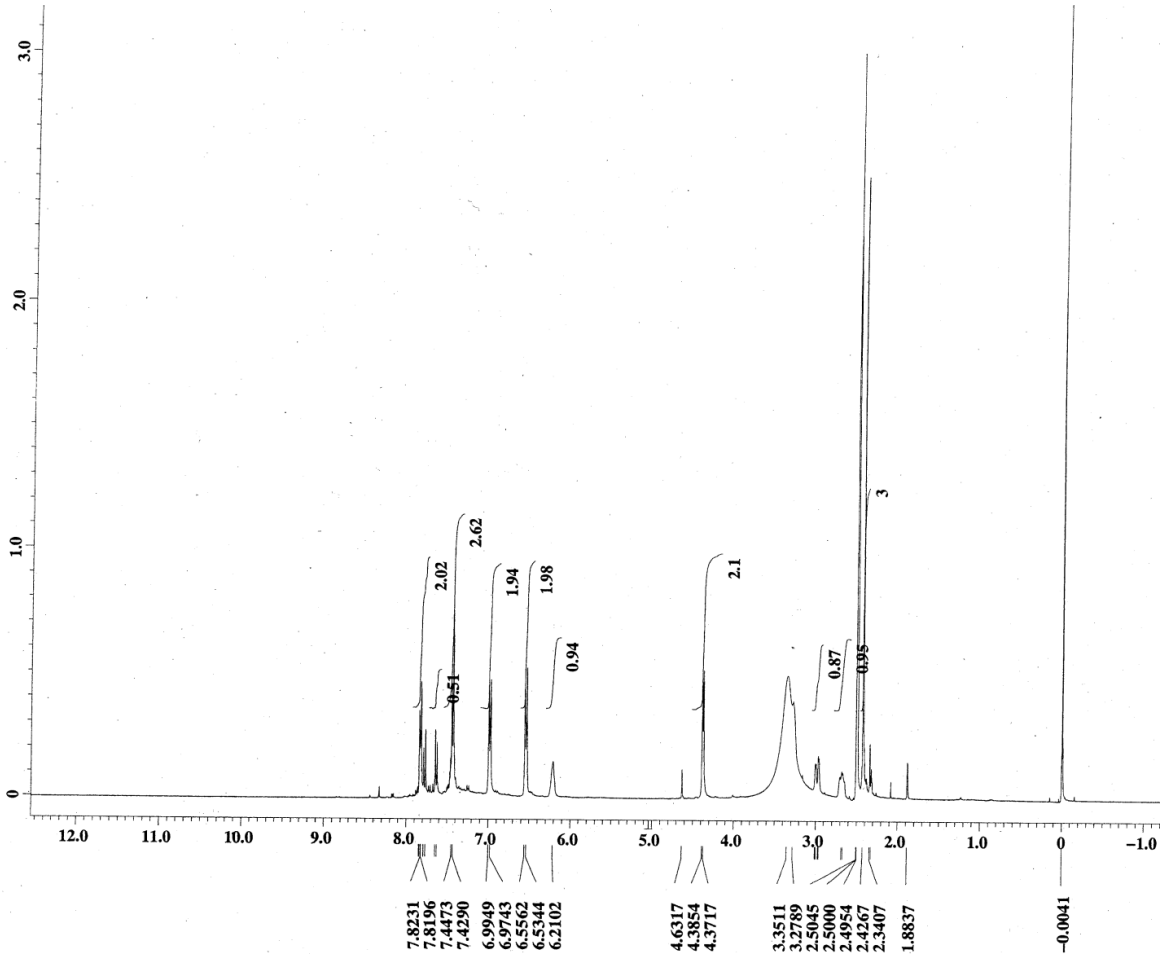
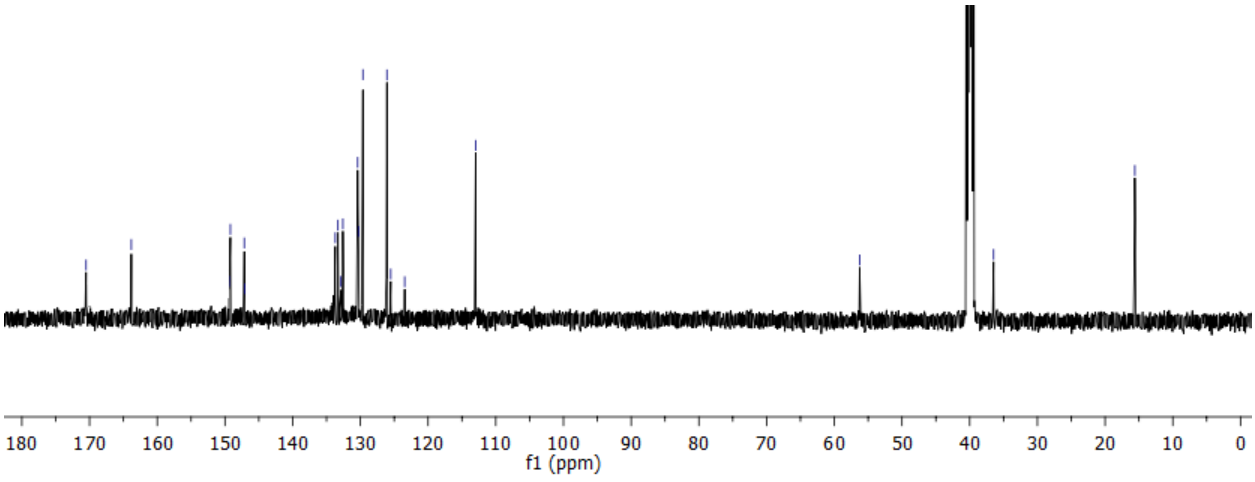


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of (S)-2-amino-3-(4-(((2-(4-bromophenyl)-4-methylthiazol-5-yl)methyl)amino)phenyl)propanoic acid, (**5b**)



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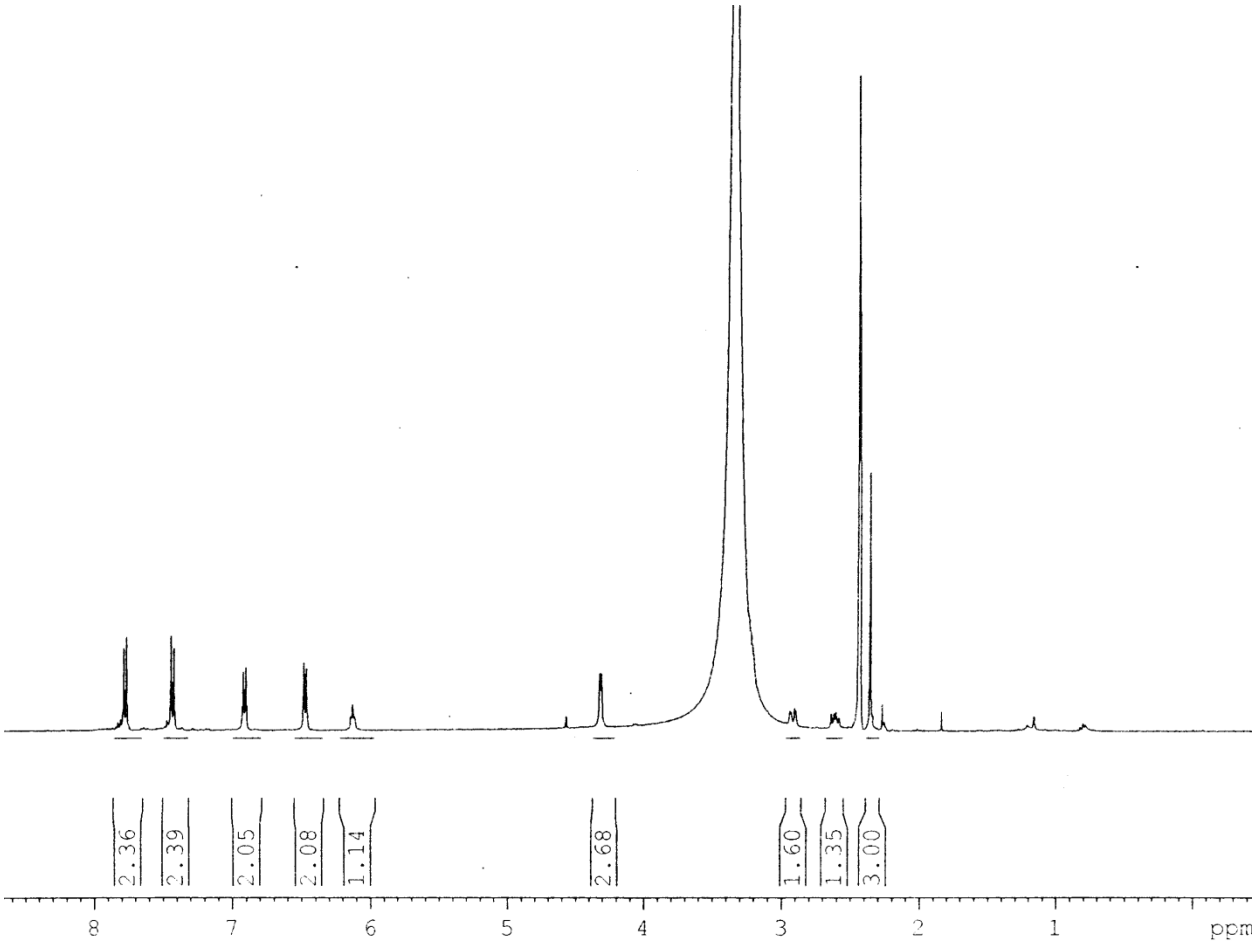

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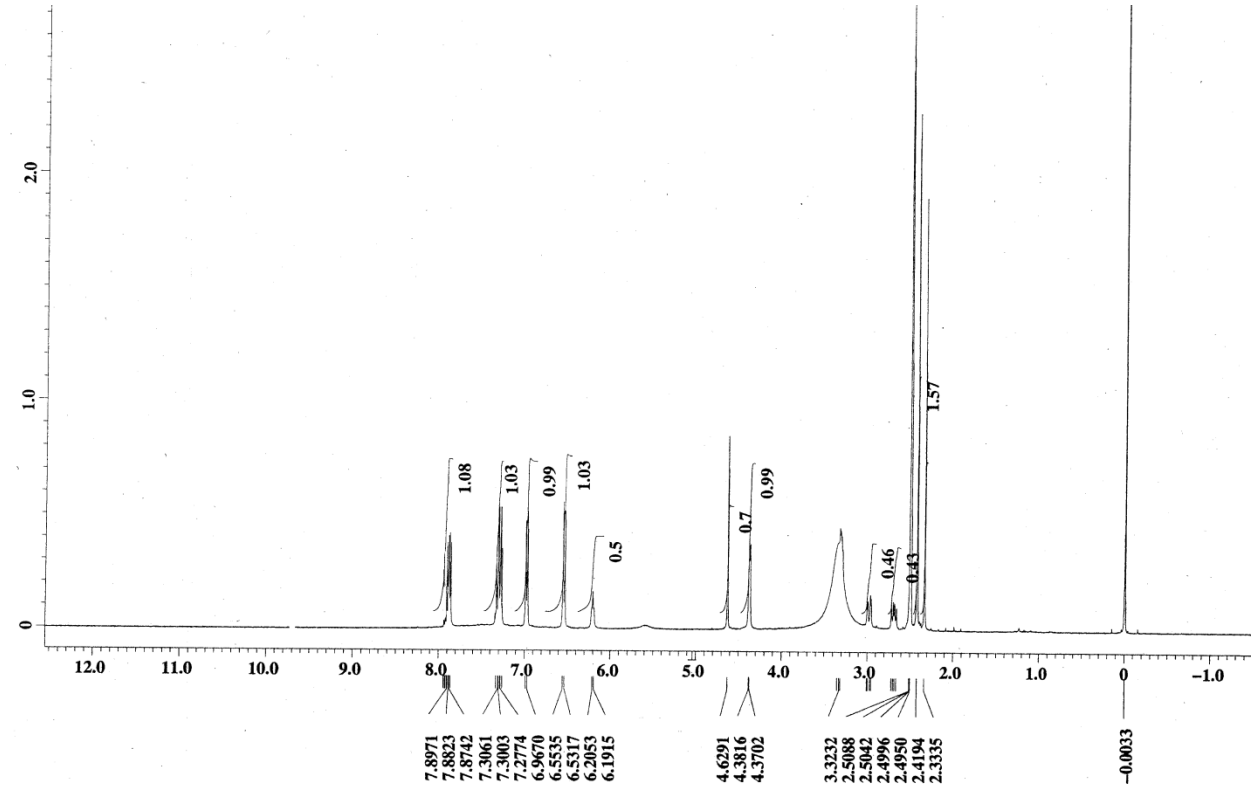

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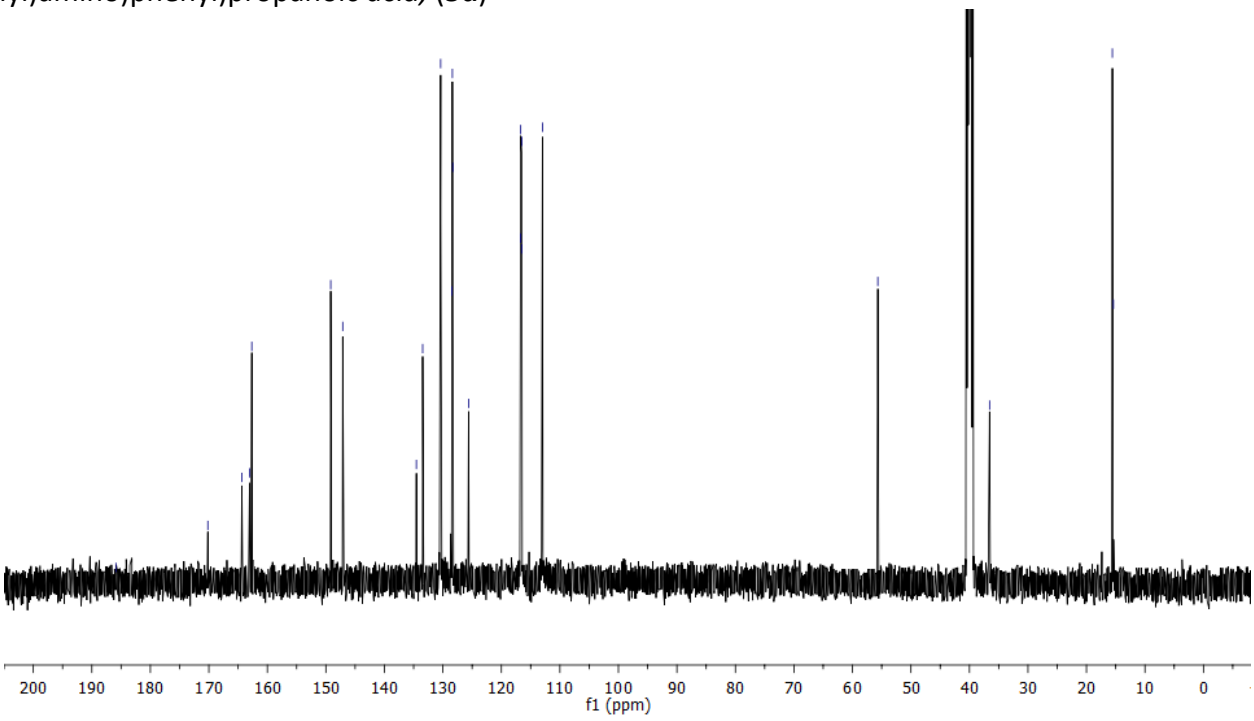

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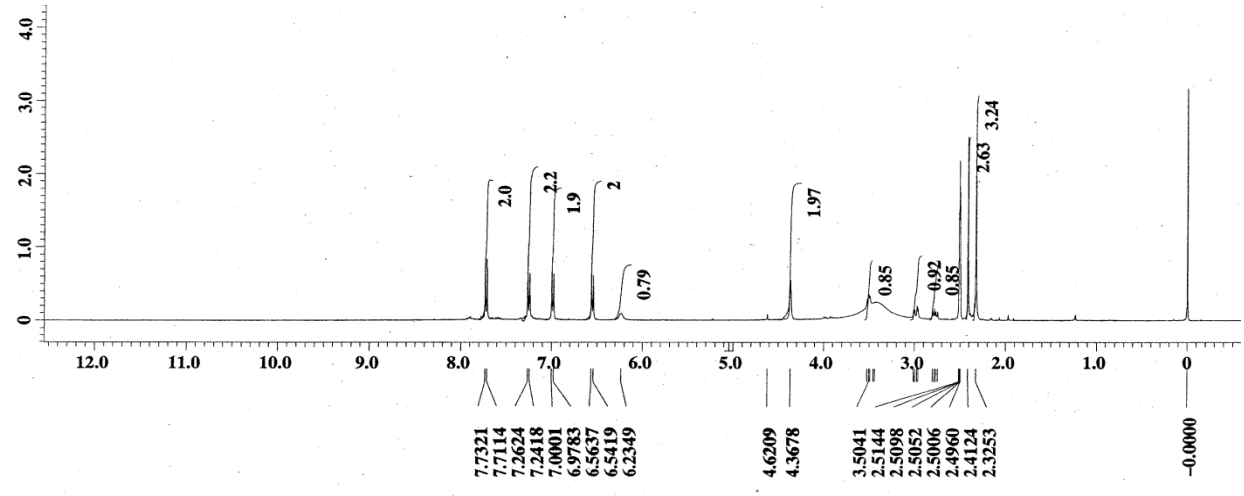

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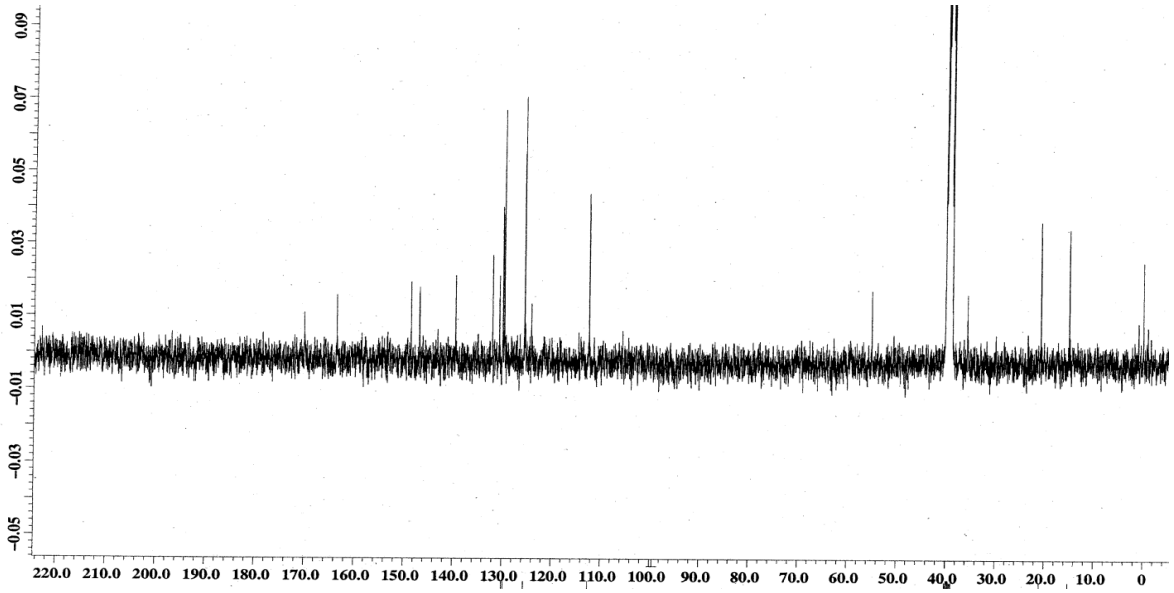

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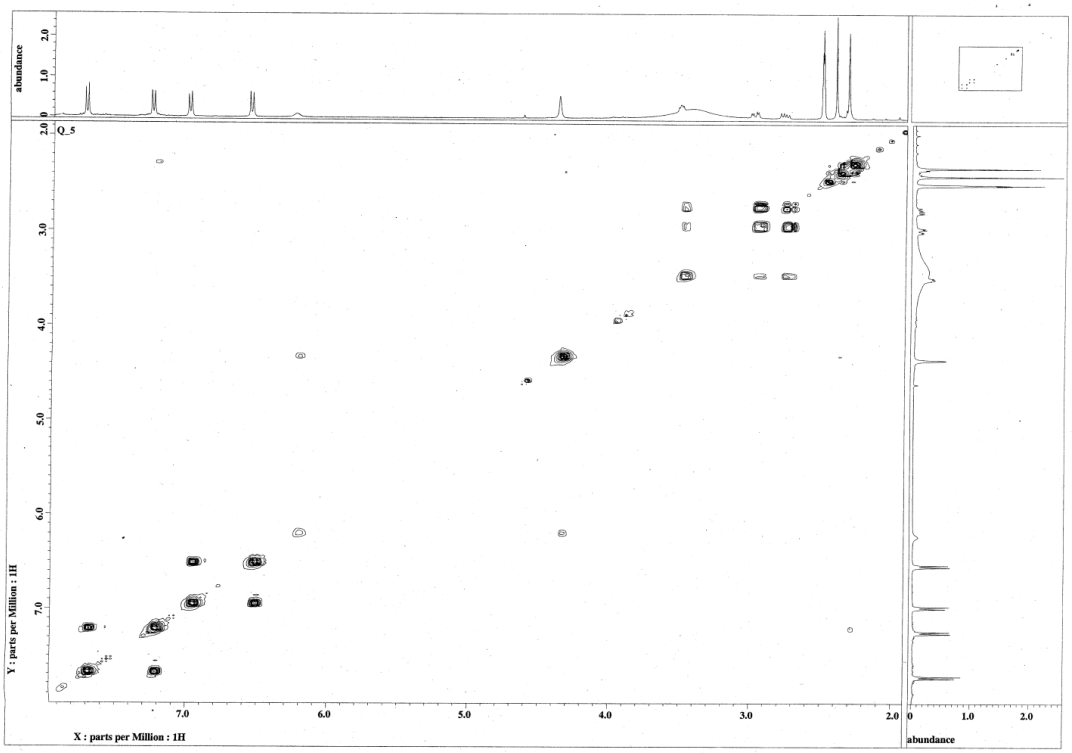

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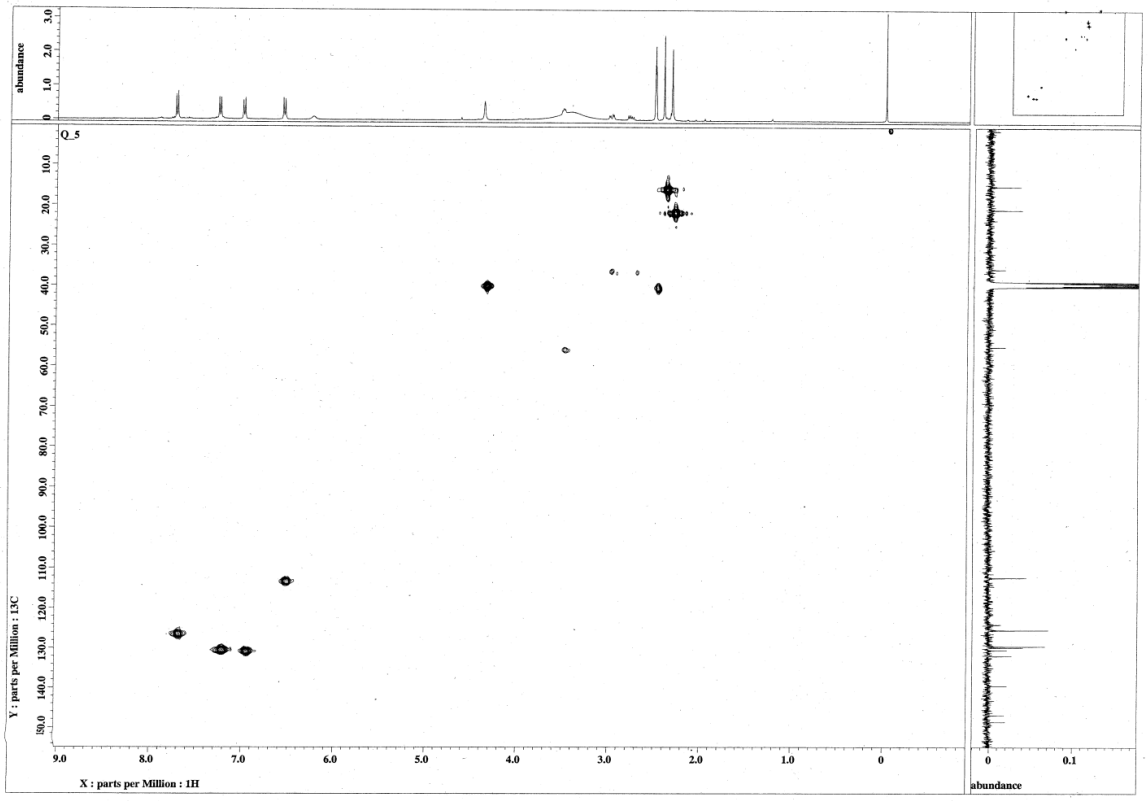

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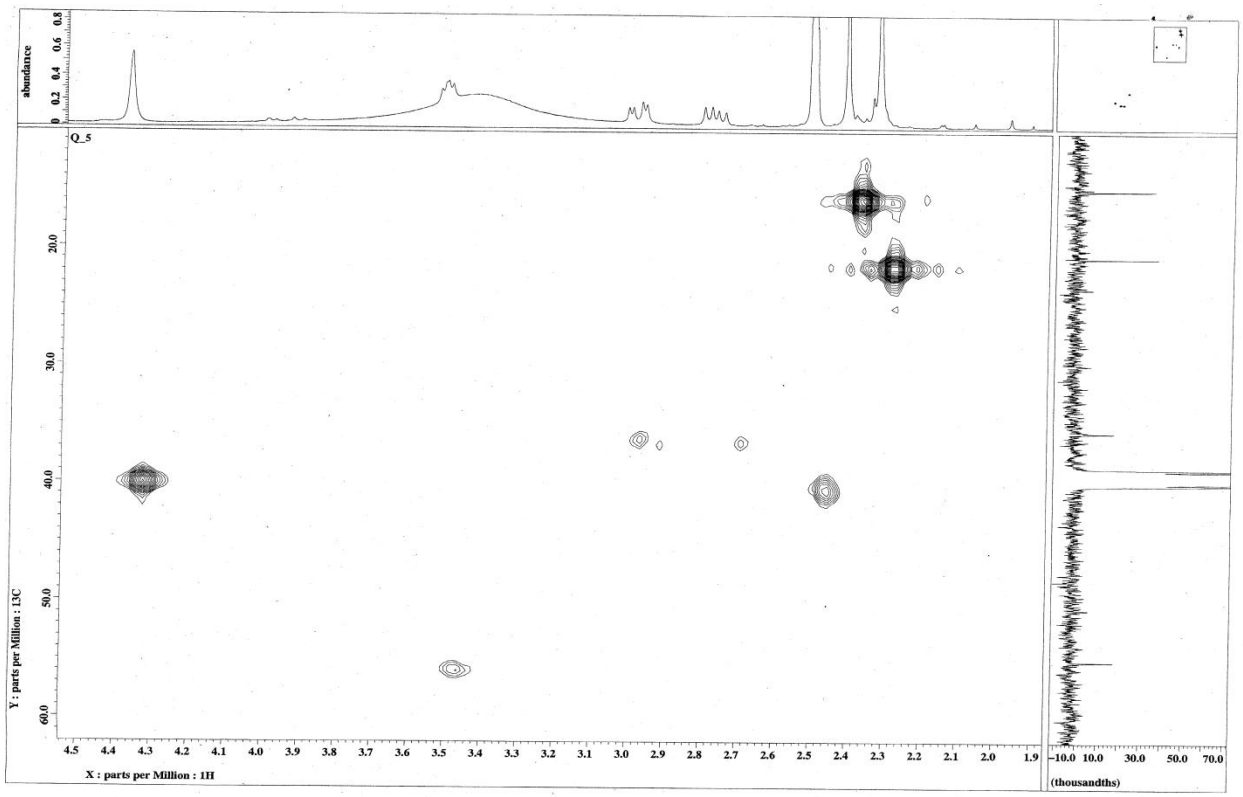

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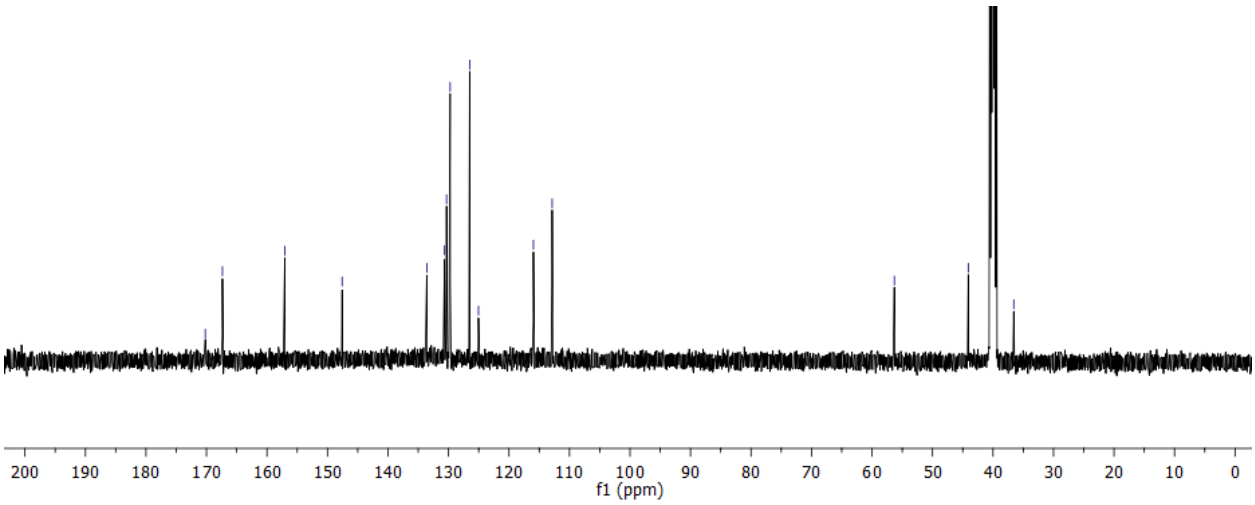

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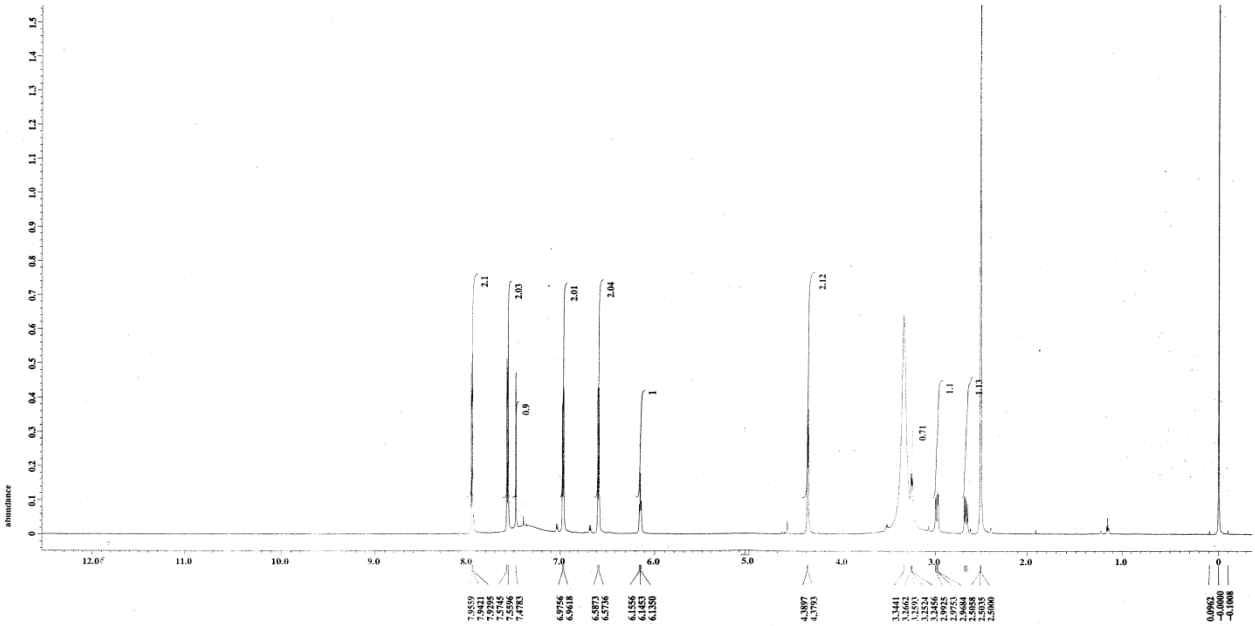

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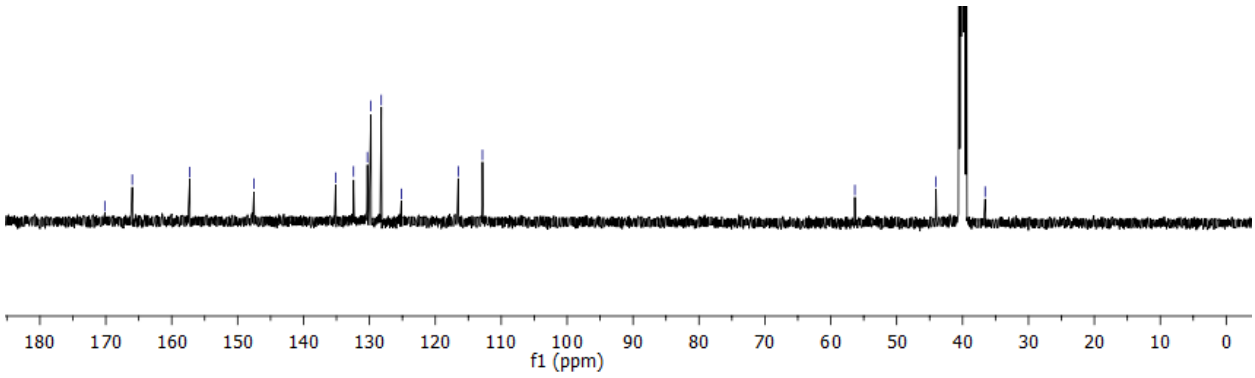

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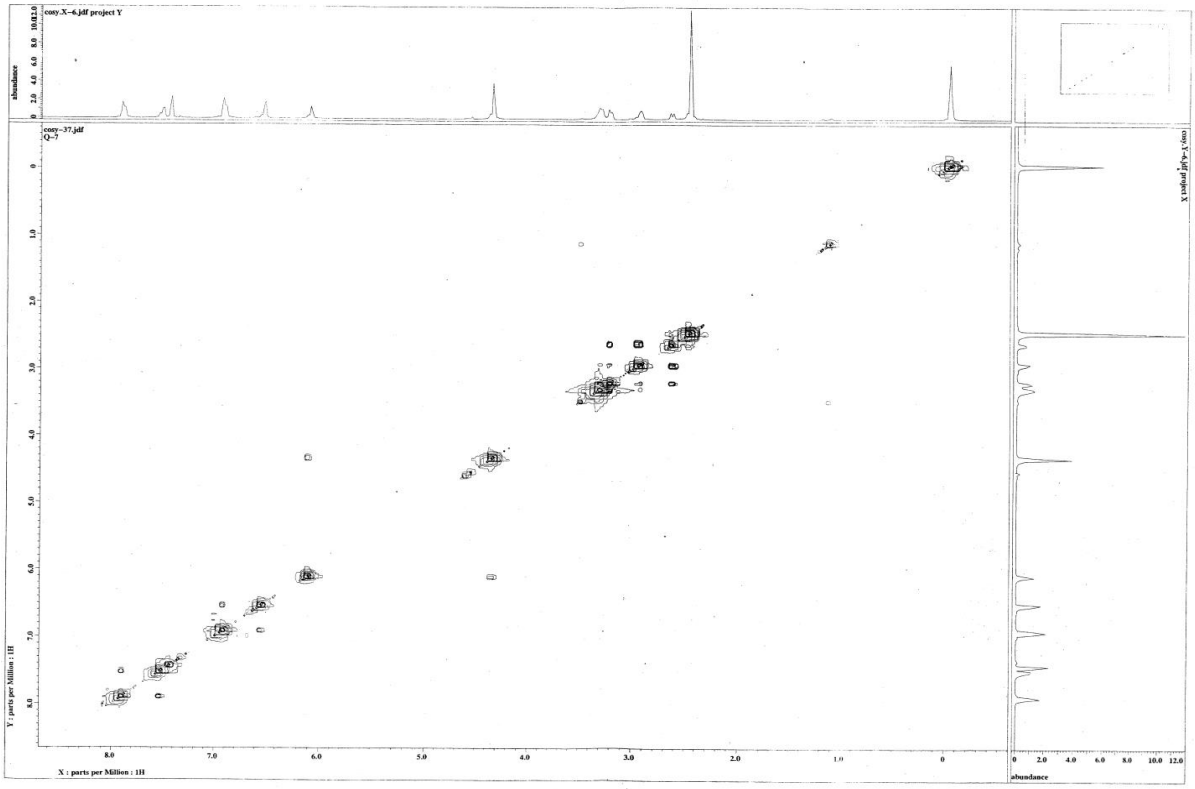

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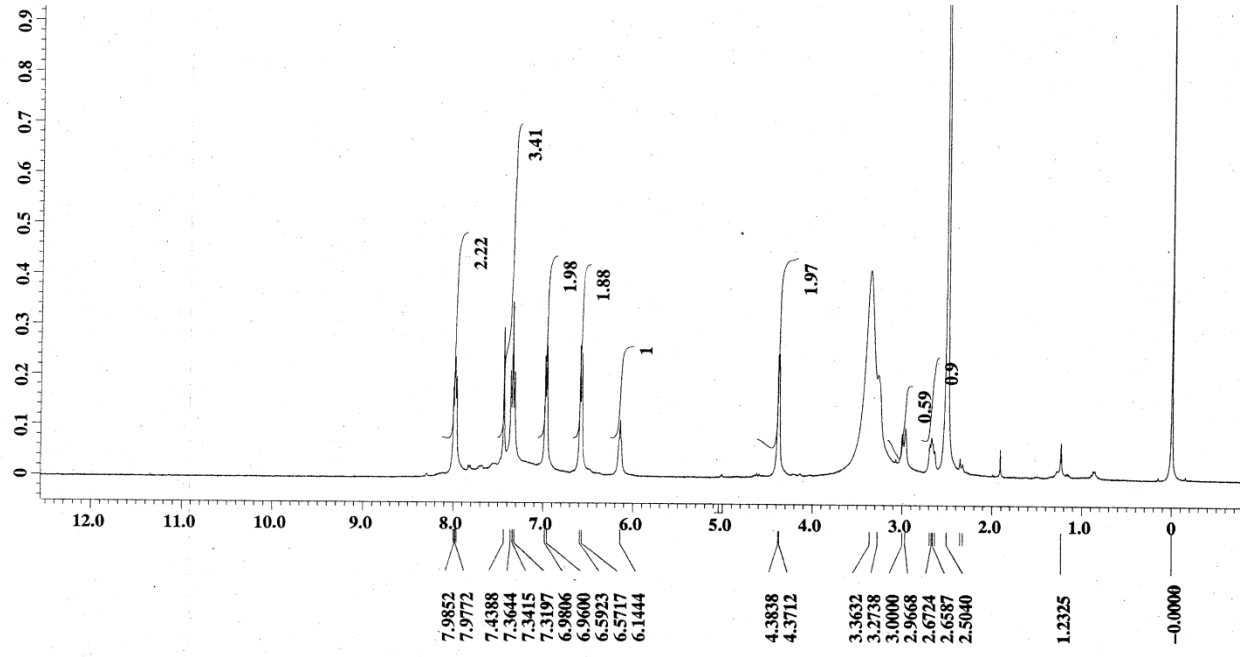

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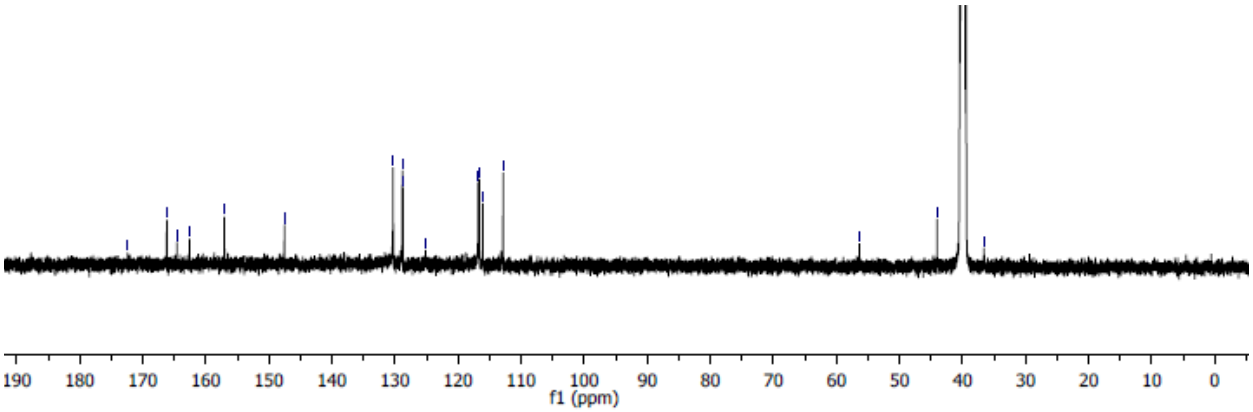

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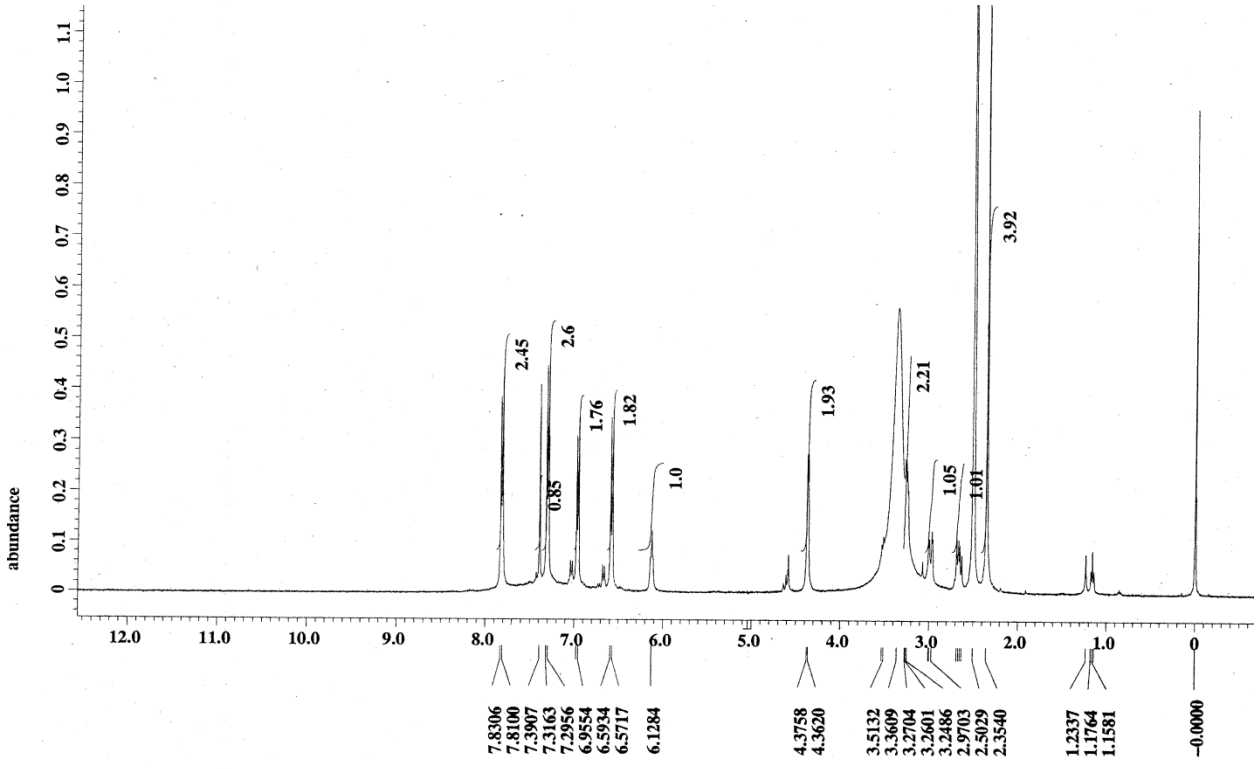

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