Synthesis and Anti-bacterial Activities of 2,2'- Disulfanediyldibenzamides

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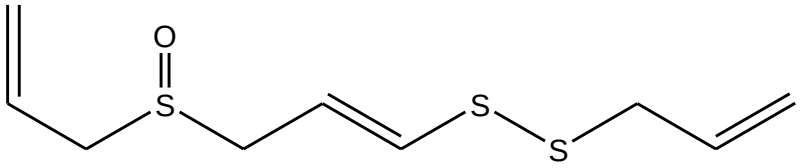
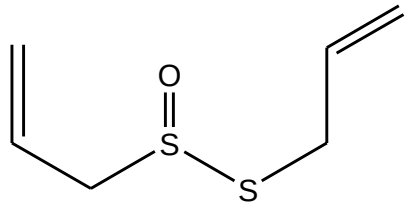
INTRODUCTION

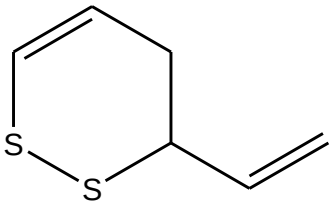
- Sulfur containing compounds have broad significance in organic, pharmaceutical and medicinal chemistry.
- Some common examples of natural disulfides which have exhibited important anti-microbial, anti-fungal and anti-cancer properties.



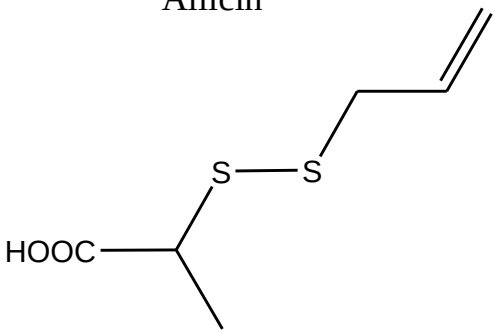
Ajoene



Allicin



Vinyl dithiin



S-Allylmercaptocysteine

INTRODUCTION

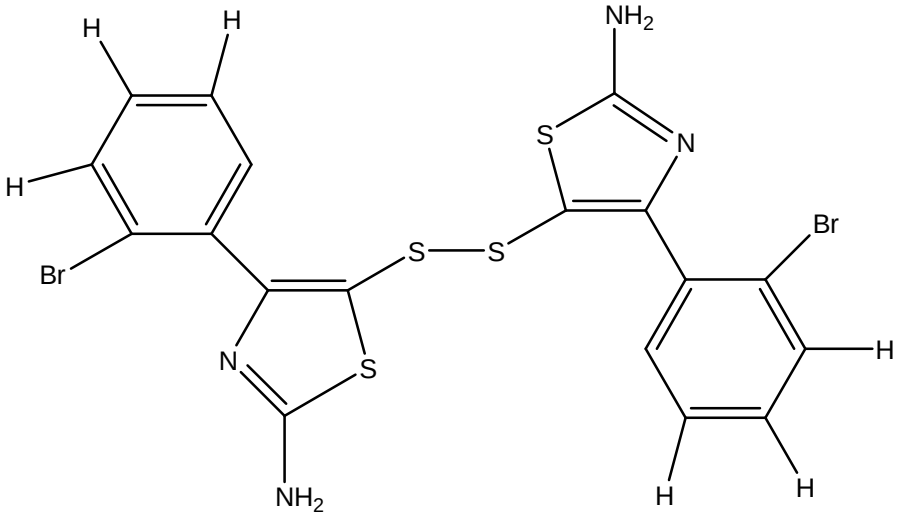
Organosulfur compounds are:

- Indispensable chemical substances to life.
- of great use in synthesis of biological macromolecules.
- Important in pharmaceutical industries, in the field of material science, and in solving sulfur-deposition problems in sour gas fields.

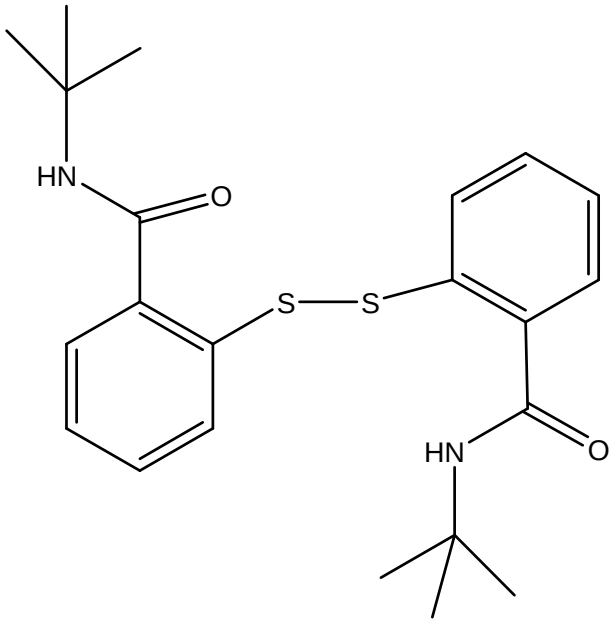
INTRODUCTION

A number of aryl sulfide compounds exhibit various biological properties such as anti-inflammatory, anti-tumor and anti-microbial

Examples of bio-active disulfide compounds



Inhibitory activities against *Bacillus cereus* and *Pseudomonas aeruginosa* *(*Hamid, et al., 2007**).**

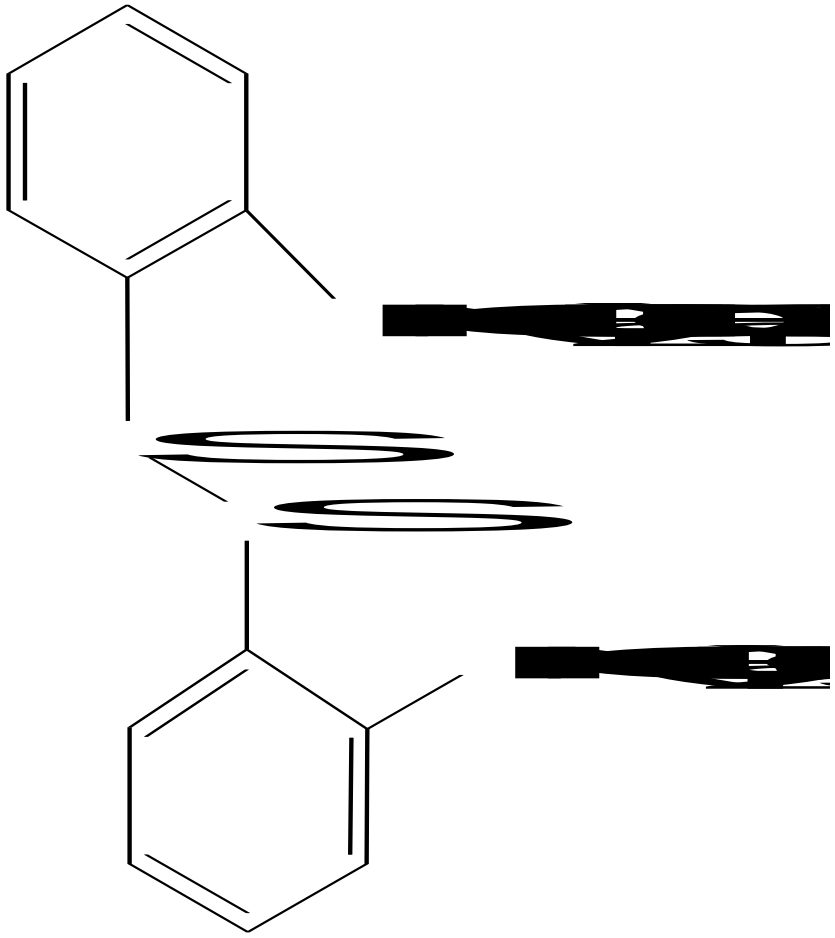


CETP inhibition in human plasma IC_{50} >500 (μM) (Hisashi & Kimiya, 2000)

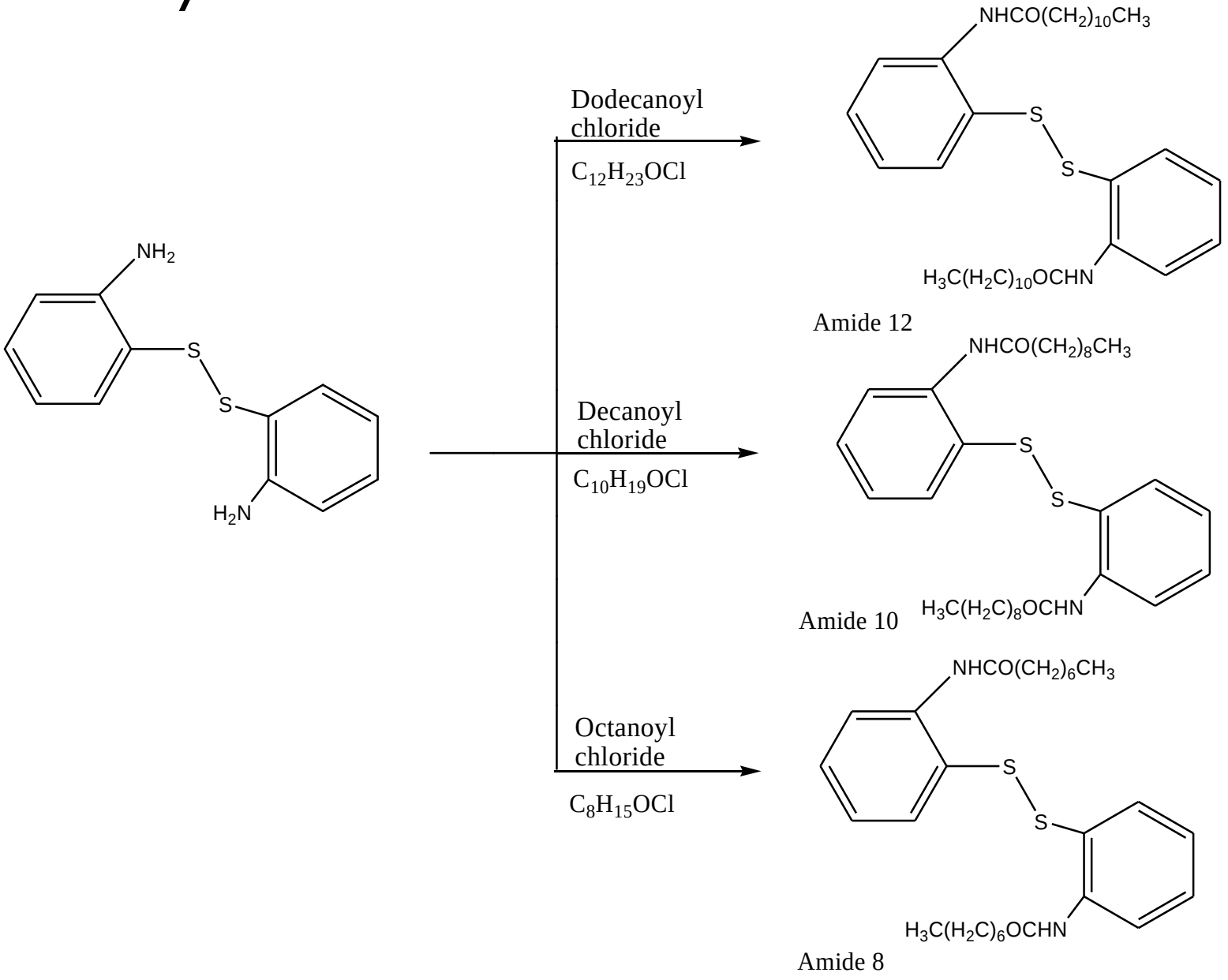
INTRODUCTION

- Lipophilicity is known to influence biological activity.
- Increasing alkyl chain length enhances the anti-bacterial properties.
- In continuation of our efforts in the synthesis of biologically active organo-sulfur compounds, the lipophilic character of diaryl disulfide compounds was increased by introducing long alkyl chain at amino end species which move effectively into the bacterial cell wall.

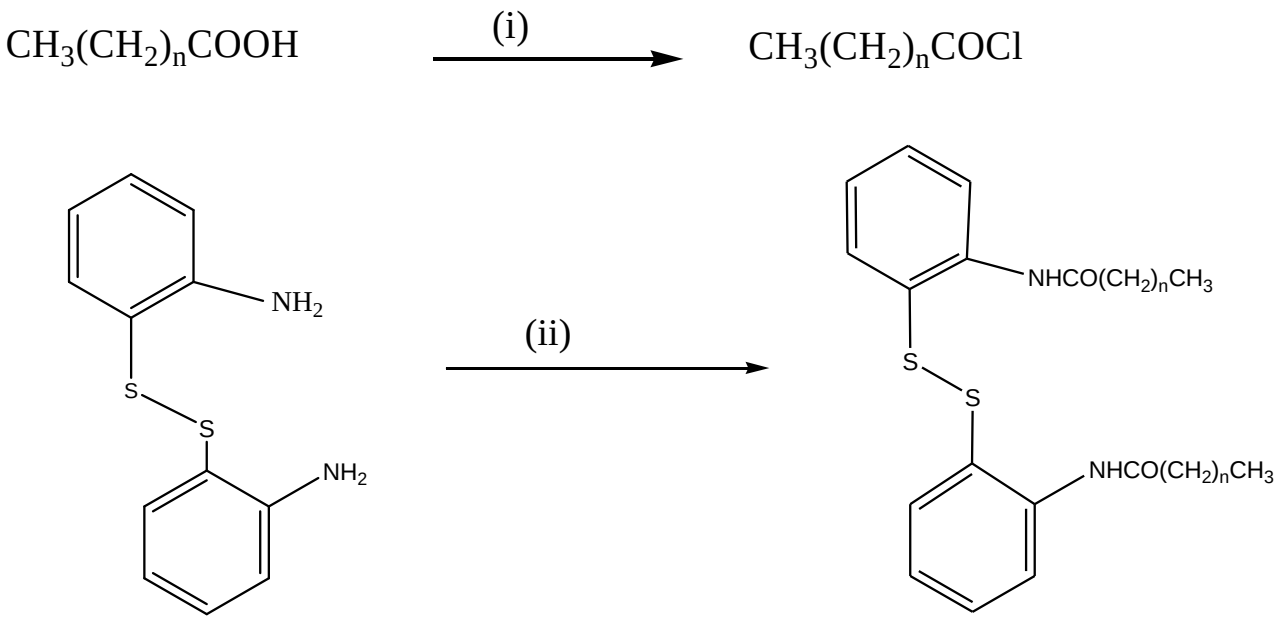
The syntheses of new dialkyl 2,2'-disulfanediyldibenzamides containing long alkyl chains are herein reported.



Synthesis of dialkyl amides from Bis-Amino Phenyl Disulfide



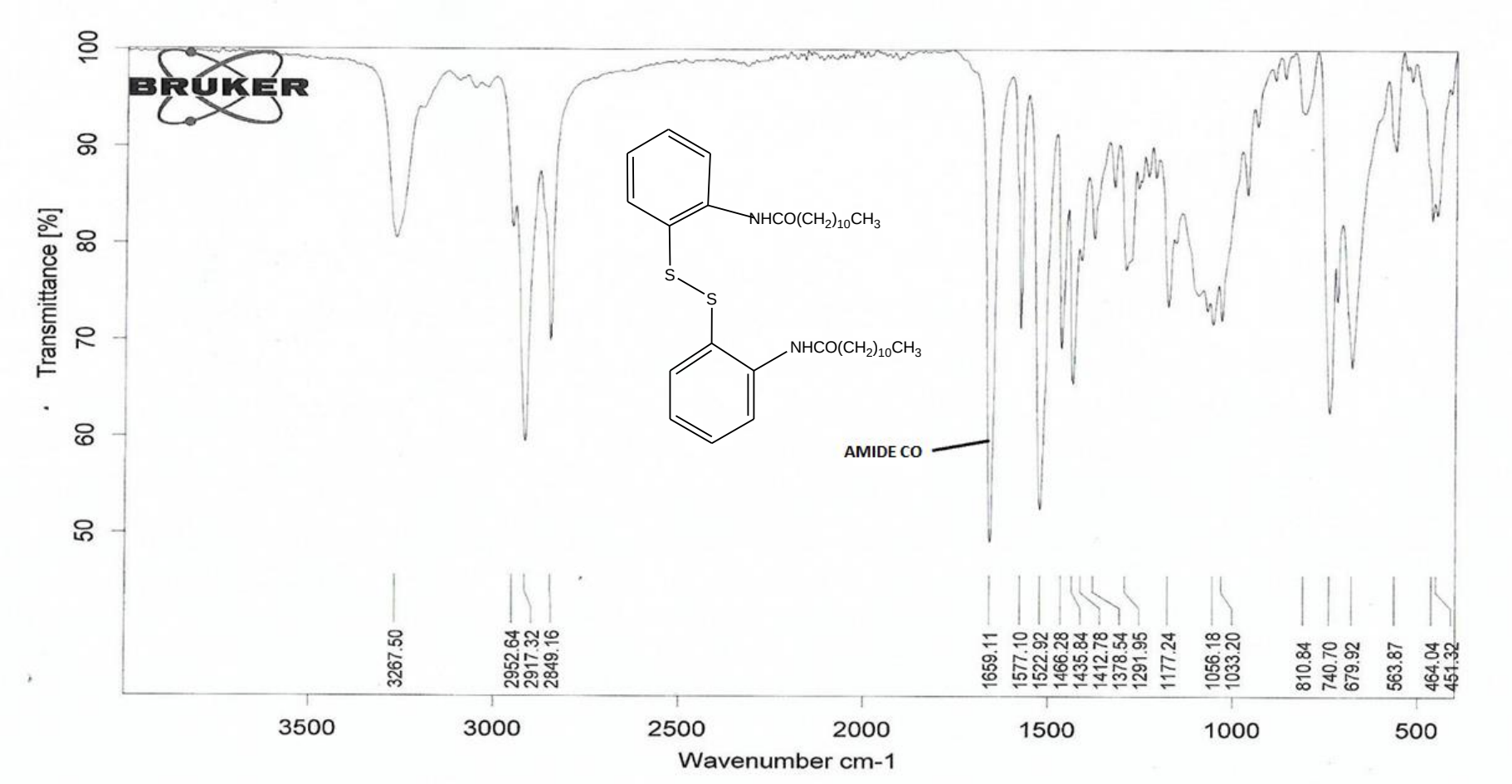
Didodecyl 2,2'-disulfanediyldibenzamides (Amide 12)



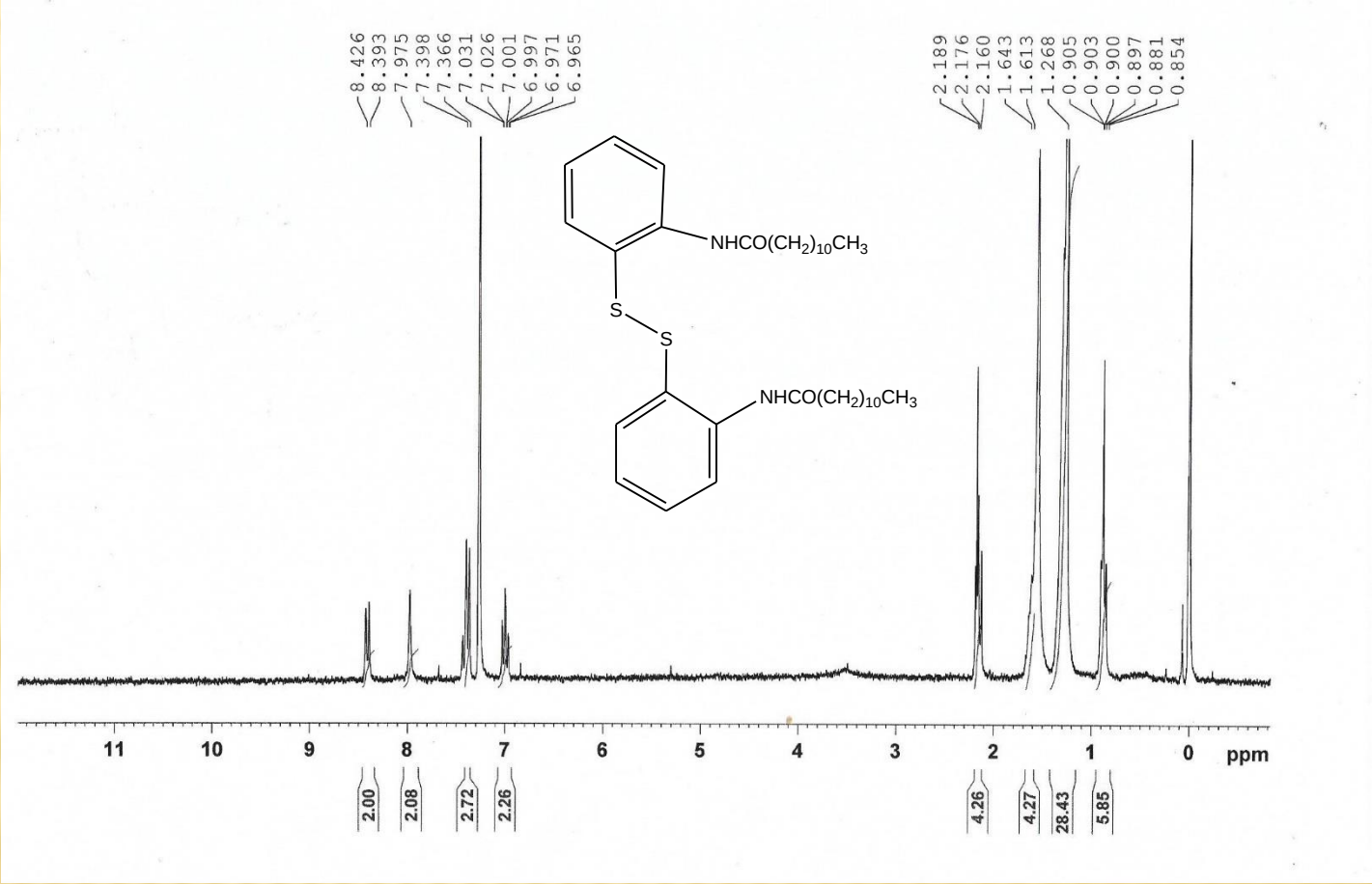
Reagents: (i) $SOCl_2$ in DCM; (ii) $CH_3(CH_2)_{10}COCl$ in THF

The dialkyl amide compound was characterized by IR, ^{1}H NMR, ^{13}CNMR, DEPT and 2D NMR

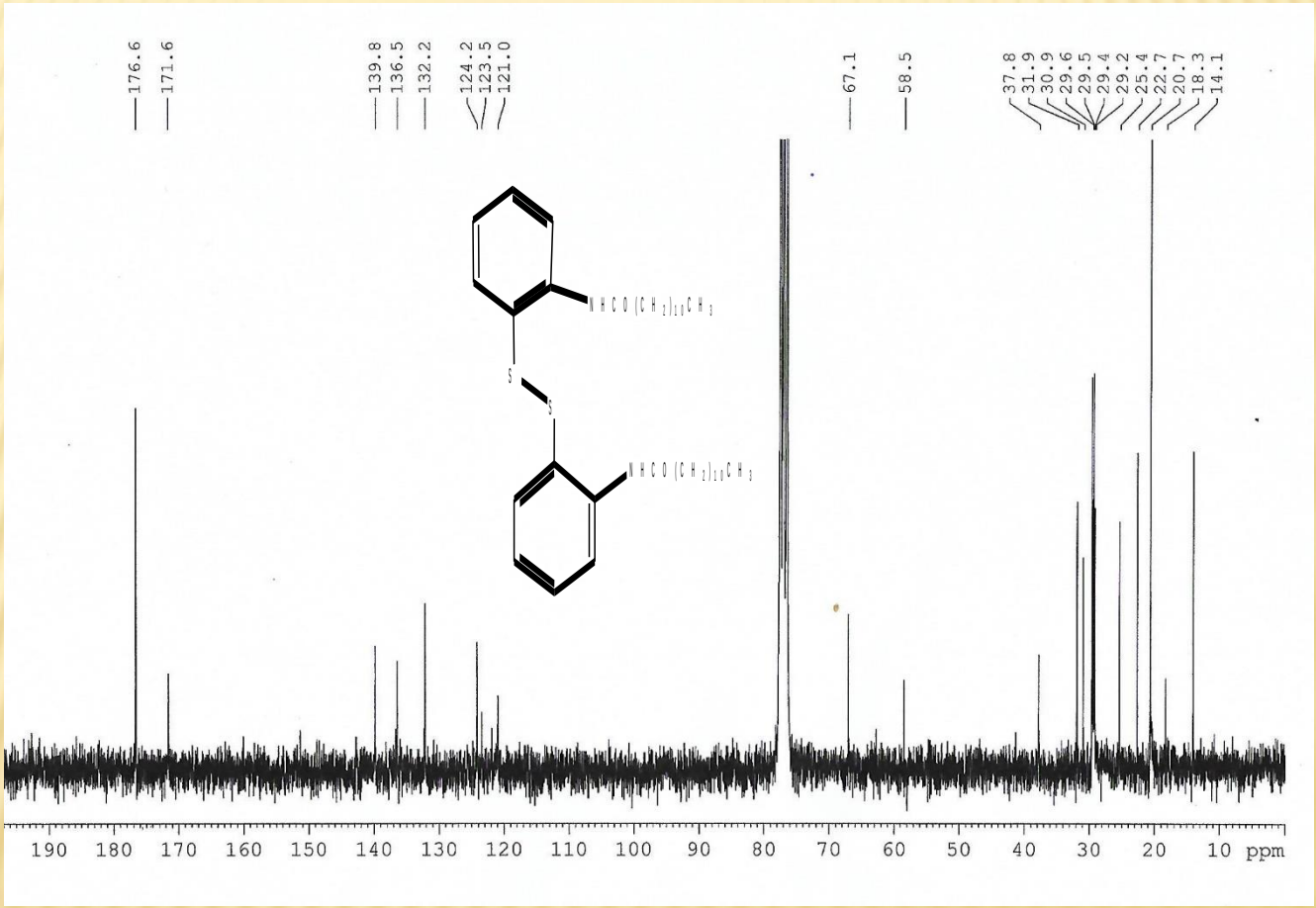
IR SPECTRUM OF AMIDE 12



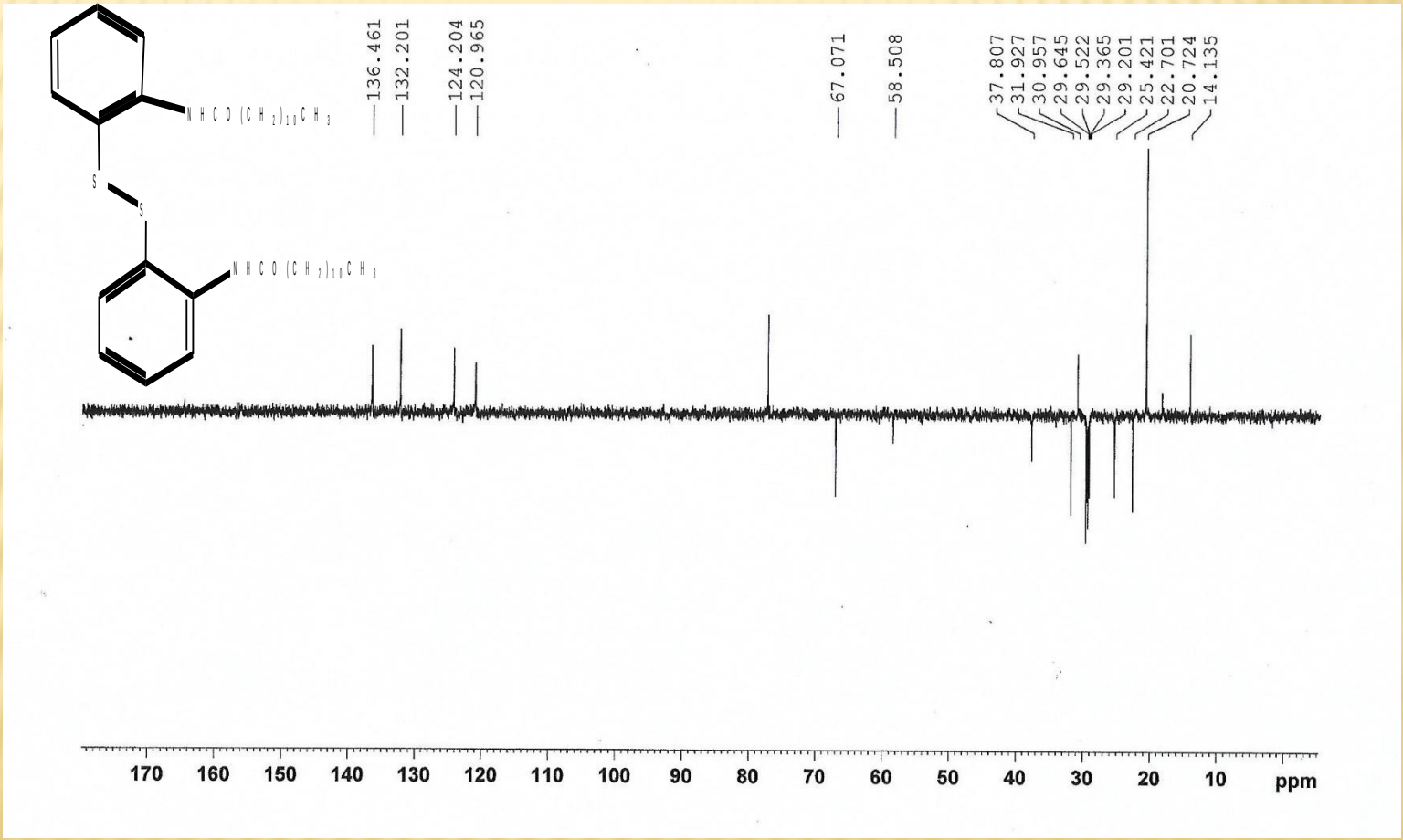
^{1}HNMR SPECTRUM OF AMIDE 12



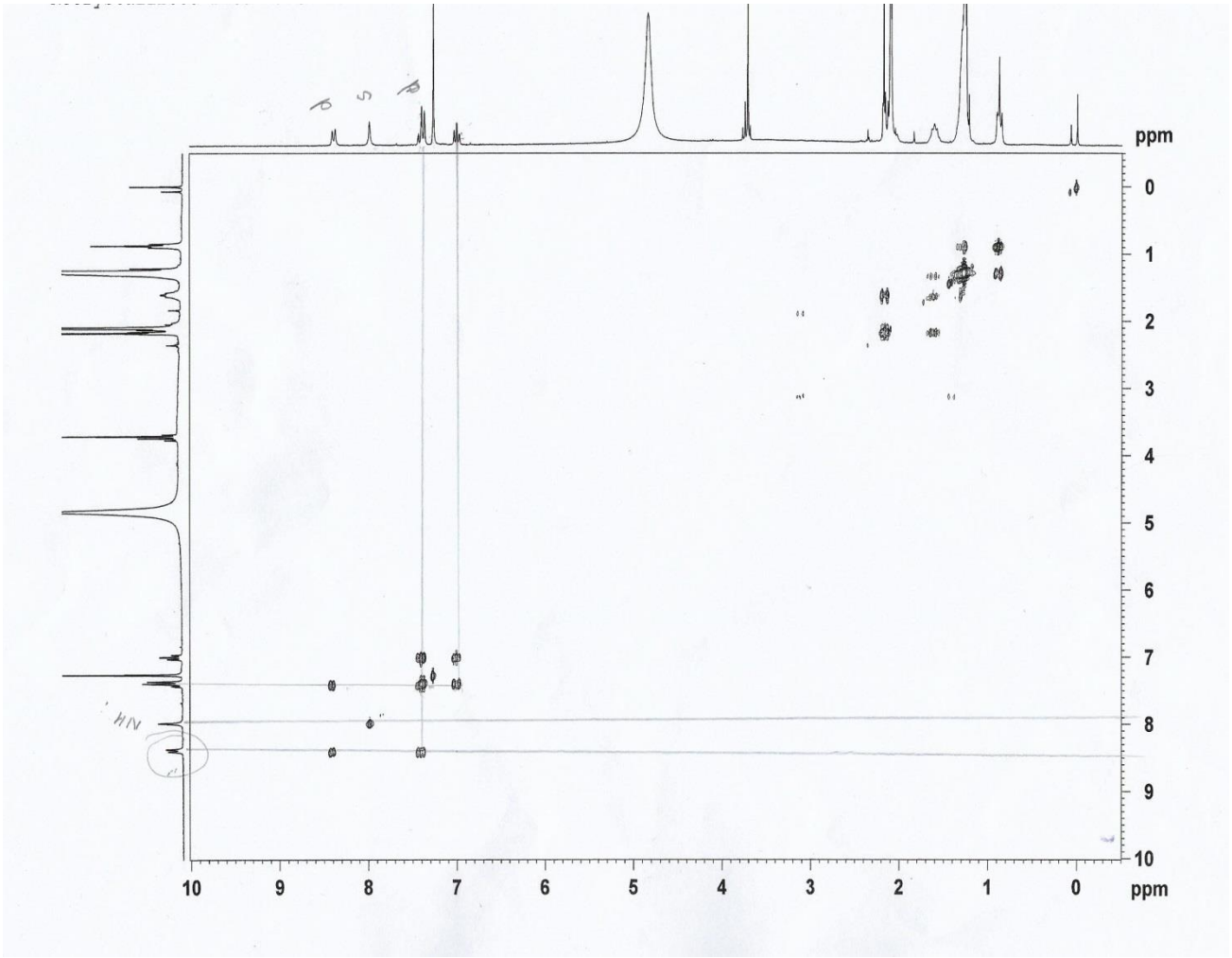
^{13}CNMR OF AMIDE 12



DEPT OF AMIDE 12



^{1}H-^{1}H COSY OF AMIDE 12



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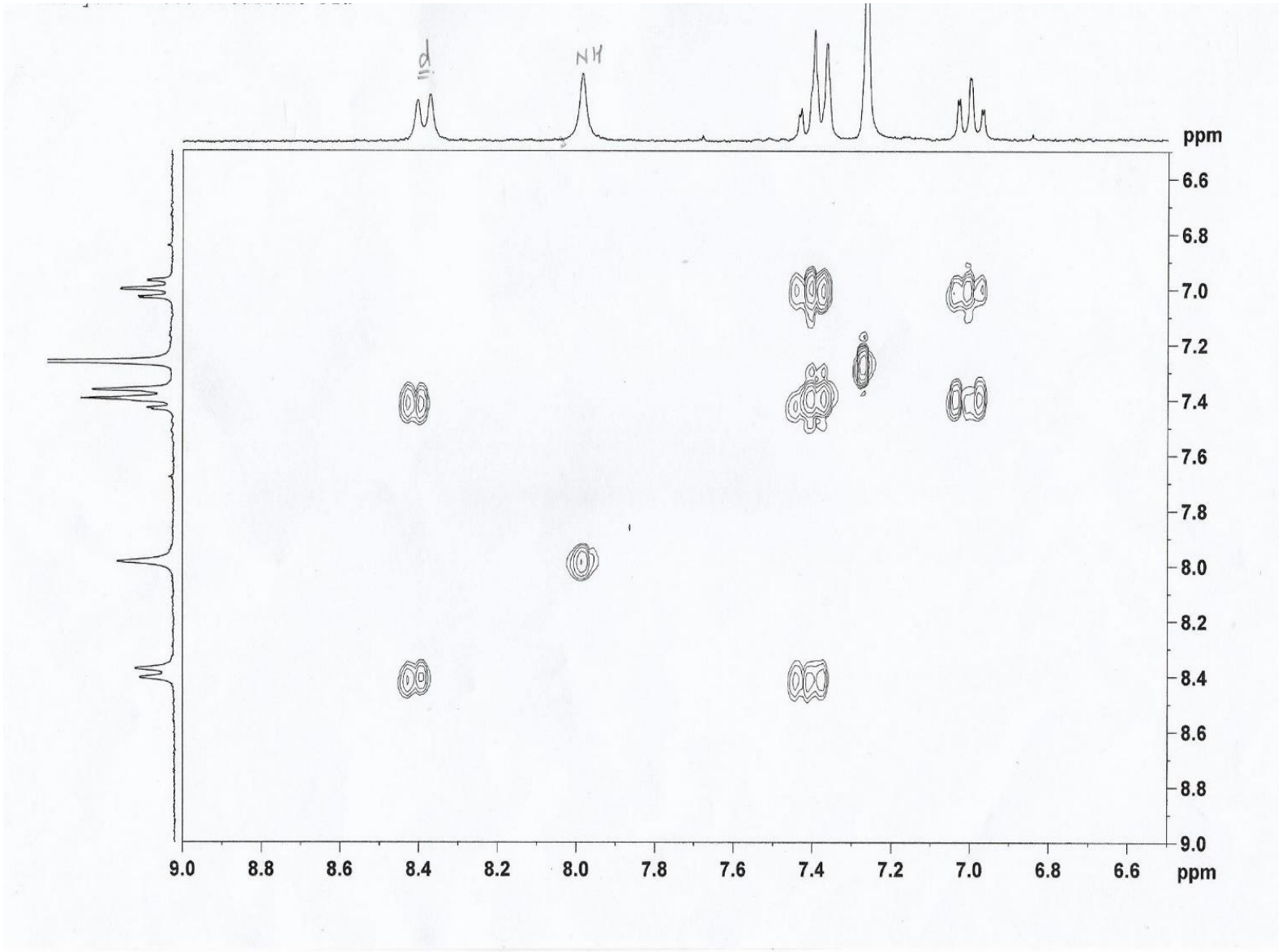
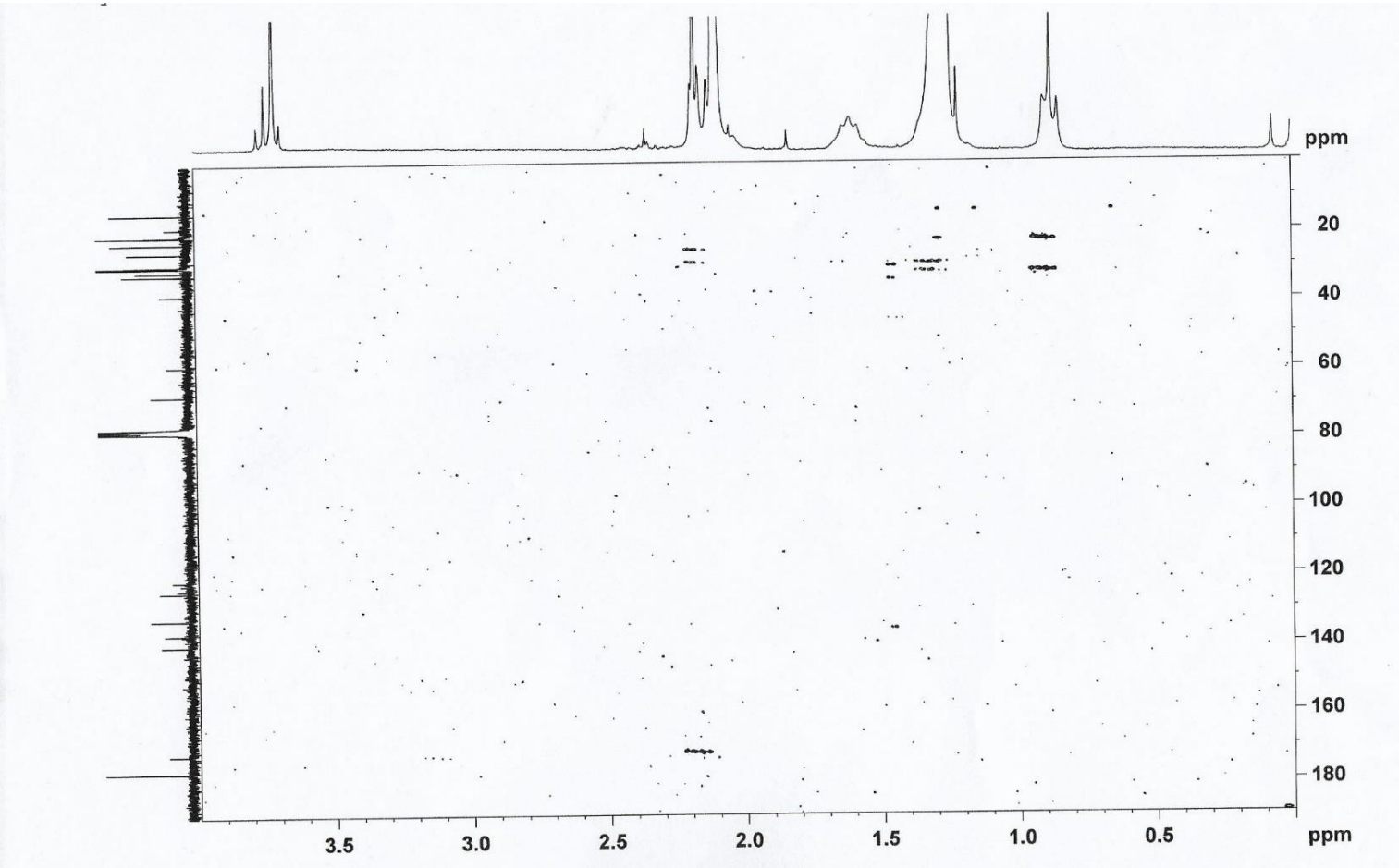


HMBC OF AMIDE 12



SPECTRAL DATA OF Amide 12

Atom	^{1}HMNR	^{13}CNMR	DEPT	^{1}H-^{1}H COSY	^{1}H/^{13}C HMBC
1		139.8			
2	7.39 (2H, d, J= 8 Hz)	120.9	120.9	3	4, 6
3	7.33 (2H, t, J=8 Hz)	124.2	124.2	2, 4	1,5
4	7.00 (2H, t, J=8 Hz)	136.4	136.4	3, 5	2, 6
5	8.40 (2H, d, J=8 Hz)	132.2	132.2	4	1, 3
6	-	123.5	-		
7	-	171.6	-		
8	2.17 (4H,t, J=7)	67.1	67.1	9	7
9	1.61(4H, t, J=7)	58.5	-		
10-17	1.27 (32, m)	37.8, 31.9, 29.6, 29.5, 29.3, 29.2, 25.4, 22.7	37.8, 31.9 , 29.6, 29.5, 29.3, 29.2, 25.4, 22.7	-	-
18	0.89 (6H, t, J=7)	14.1	14.1	17	
N-H	7.97 (2H, s)			2	

Compd	COLOR	IR(cm^{-1})				^{1}HNMR (ppm)			^{13}CNMR (ppm)		
			Amide I	Amide II	Amide III	Aromatic	Aliphatic	Amide	Aromatic	Aliphatic	Amide CO
AMIDE 8	Brown	ν_{NHCO}	1654	1520	1324	7.0-7.9	1.2-2.2	8.4	120-139.9	22.6-37.8	171.5
		ν_{S-S}	464								
		$\nu_{CH\ aliph}$	2852, 2922								
		$\nu_{CH\ arom}$	2953								
		ν_{NH}	3267								
AMIDE 10	Brown	ν_{NHCO}	1659	1522	1378	7.0-7.9	1.2-2.2	8.4	120-139.9	25.4-37.8	171.4
		ν_{S-S}	464								
		$\nu_{CH\ aliph}$	2849, 2917								
		$\nu_{CH\ arom}$	2952								
		ν_{NH}	3267								
		ν_{NHCO}	1659	1522	1377						

Antibacterial Properties of amides 8 & 12

MIC values (mM) of amides 8 & 12

Amide	*S. Aureus* ATTC 25923	*S. epidemitis* ATTC 1228	*B. Cerus* ATTC 11778	*Klebsiella* ATTC 13883	*E. Coli* ATTC 22922
8	2.50	5.00	2.50	2.50	2.5
12	2.04	1.02	0.03	2.10	2.04

Amide 12 showed better anti-bacterial activity

THANK YOU