

SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL STILBENE DERIVATIVES DERIVED FROM SUBSTITUTED (PHENYL ACETIC ACID, BENZALDEHYDE, AMINES) TRIETHYL AMINE AND THIONYL CHLORIDE.

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ABSTRACT:

Stilbene derivatives are widely distributed in the nature and they possess various bioactivities that includes antimicrobial, antifungal, antioxidant, hepato protective, anti-HIV, cytotoxic, anti-inflammatory and antiplatelet. We have synthesized novel derivatives of stilbenes by reacting various substituted phenyl acetic acid with aldehydes in presence of acetic anhydride and triethyl amine. These derivatives were characterised by various spectral techniques and were evaluated for their antimicrobial activities.

Keywords: Stilbenes, phenyl acetic acid, Antimicrobial activity.

1. INTRODUCTION

Synthesis of functionalized stilbene have attracted immense attention over the past decades and have been reported in several research papers and reviews.¹⁻⁴

Stilbenes are biologically active secondary metabolites found in numerous families of plants and is derived from the greek word 'stilbos', which means shining. Chemically stilbenes are derivatives of 1, 2-diphenyl ethane. Stilbene itself does not occur in nature but hydroxylated and methylated stilbenes are found in medicinal plants. Stilbene derivatives such as diethylstilbestrol (DES), euvestin, 4,4' diaminostilbene and pinosylvin, have a variety of biological action, including hormonal, hypo cholesterolemic, sympathomimetic, antifungal, anti allergic, antibacterial, anti malarial and anticancer activities.⁵⁻⁸. DES is the most famous stilbene derivative, which was used medically for prostate and breast cancer and to prevent threatened abortions⁹⁻¹¹.

Resveratrol (4,3',5'- trihydroxy stilbene) which is found in grapes, peanuts, pine- apple and also grape products such as wine, exerts potent anti oxidant and anti inflammatory activities¹²⁻¹⁴.

The development of methods for their effective construction has attracted considerable attraction in organic synthesis. The synthesis of stilbene derivatives has been an important part and is aimed at modifying the action of drugs particularly to reduce the side-effect along with increasing the drug action. Thus in agreement with their role as anti-oxidant¹⁵⁻¹⁶, anti-inflammatory¹⁷⁻¹⁸, anti-cancer¹⁹. Our interest in the field of substituted stilbene, total synthesis of stilbene and their several analogues. In the light of the above discussion it was

thought important to undertake the synthesis of some novel stilbene derivatives and to characterize them by using various spectral techniques such as $^1\text{H-NMR}$, IR and elemental analysis.

2. EXPERIMENTAL PROCEDURE

$^1\text{H NMR}$ spectra were recorded on a Bruker Act 300 (300 Mz) spectrophotometer and elemental analyses were carried out at department of chemistry University Of Mumbai. Infrared spectra were recorded on Perkin Elmer FTIR-4200 spectrometer at V.G.Vaze college. All the melting points are uncorrected. Temperature was recorded in $^{\circ}\text{C}$.

Procedure for the preparation of some novel stilbene derivatives from substituted benzaldehyde, substituted phenyl acetic acid and triethyl amine.

1. Preparation of carboxylic acid.

A mixture of phenyl acetic acid, substituted benzaldehyde (equimolar) was refluxed along with triethyl amine for 24 hrs and the reaction mixture was broken in sodium carbonate solution and left for 24 hrs. The mixture was extracted with ether. The aqueous solution was acidified with dilute HCL and the ppt. was filtered and dried in vacuum and used without further purification.

2. Preparation of Substituted stilbene derivatives (Enamide) from carboxylic acid.

A mixture of carboxylic acid, thionyl chloride and benzene was refluxed for 6 hrs. Further it was treated with aqueous methyl amine solution. The precipitated product was filtered washed with very dilute NaOH solution and dried and used without further purification.

3. RESULT AND DISCUSSION.

Synthesized compounds PM-01 to PM-04, their theoretical and practical data of elemental analysis are in very good agreement as depicted in the table 1, which confirms formation of carboxylic acid and its amide derivatives.

IR Spectral data (cm^{-1}) and $^1\text{H NMR}$ Spectral data of the substituted stilbene and derivatives of stilbene is shown in the table 2.

Table 1. Physical and Analytical data of the substituted stilbene and derivatives of stilbene.

Compound	Molecular formula	Molecular weight	% yield	Melting point	Colour	Carbon	Hydrogen	Nitrogen	Chlorine
PM-01	$\text{C}_{15}\text{H}_{11}\text{O}_2\text{Cl}$	258	70	170	White	69.49 (69.00)	4.24 (3.95)	–	13.70 (13.25)
PM-02	$\text{C}_{15}\text{H}_{13}\text{ON}_2\text{Cl}$	272	70	95	Yellow	66.17 (65.80)	4.77 (4.55)	10.29 (10.10)	13.05 (12.85)
PM-03	$\text{C}_{16}\text{H}_{14}\text{NOCl}$	271	63	112	White	70.84 (70.24)	5.16 (4.95)	5.16 (4.92)	13.09 (12.64)
PM-04	$\text{C}_{17}\text{H}_{16}\text{ONCl}$	258	68	290	White	79.06 (78.45)	6.20 (5.84)	5.42 (5.15)	13.75 (13.23)

Table 2 .IR Spectral data(cm-1) and ¹H NMR Spectral data of the substituted stilbene and derivatives of stilbene.

COMPOUND	IR SPECTRAL DATA (cm ⁻¹)						¹ H NMR Chemical Shift (δ ppm)				
	V (C-H) aromatic	V (C-H) aliphatic	V (C-O)	V (C=C)	V (C-C)	V (C-NH)	1H- COOH	1H- CH	9HAr- H	¹ H-NH	2H- NH ₂
C ₁₅ H ₁₁ O ₂ Cl(PM01)	3035	2925	1680	1620	550	-	10.25	7.38	7.31- 6.54	-	-
C ₁₅ H ₁₃ ON ₂ Cl(PM02)	3022	2924	1618	1591	548	3344- 3378		8.92	8.05- 6.93	12.95	5.38- 3.36
C ₁₆ H ₁₄ NOCl(PM03)	3095	2825	1605	1600	545	3350		8.90	7.76- 6.91	12.89	-
C ₁₇ H ₁₆ ONCl(PM04)	3040	2850	1700	1595	560	3300		8.25	7.25- 6.85	13.50	-

3.1. IR Spectra

Infrared spectra of the acid obtained from substituted phenyl acetic acid (PM01) and its amide derivatives (PM02-PM04) were compared. The spectra of derivatives show two sharp bands in the range of 3350 – 3378 cm⁻¹ which is assigned for NH- Stretching. This band was absent in PM-01 as depicted in the representative IR spectra of PM-01 where as PM-02 shows sharp band. The aromatic C-H stretching at 3022-3095 cm⁻¹, Aliphatic C-H stretching at 2825-2925 cm⁻¹. CO Stretching at 1605-1700 cm⁻¹, C=C stretching at 1591 – 1620 cm⁻¹, C-C stretching at 540 – 560 cm⁻¹ were assigned for PM01-PM04²⁰⁻²¹.

3.2. ¹H NMR Spectra

The ¹H NMR Spectra of the PM01 to PM04 were recorded in DMSO solvent and the assignment are detailed in the table. The signal appeared in the region of 10.25 ppm confirms presence of COOH as shown in the representative spectra of PM01. Absence of this signal in all other spectra and new peaks in the region of 12.95 to 13.50 ppm confirms presence of NH in PM02 to PM04. In PM02 new peak in the range of 5.38 to 3.36 ppm indicates –NH₂. The multiplets in the range of 6.50 to 7.70 ppm were assigned to aromatic proton²⁰⁻²¹.

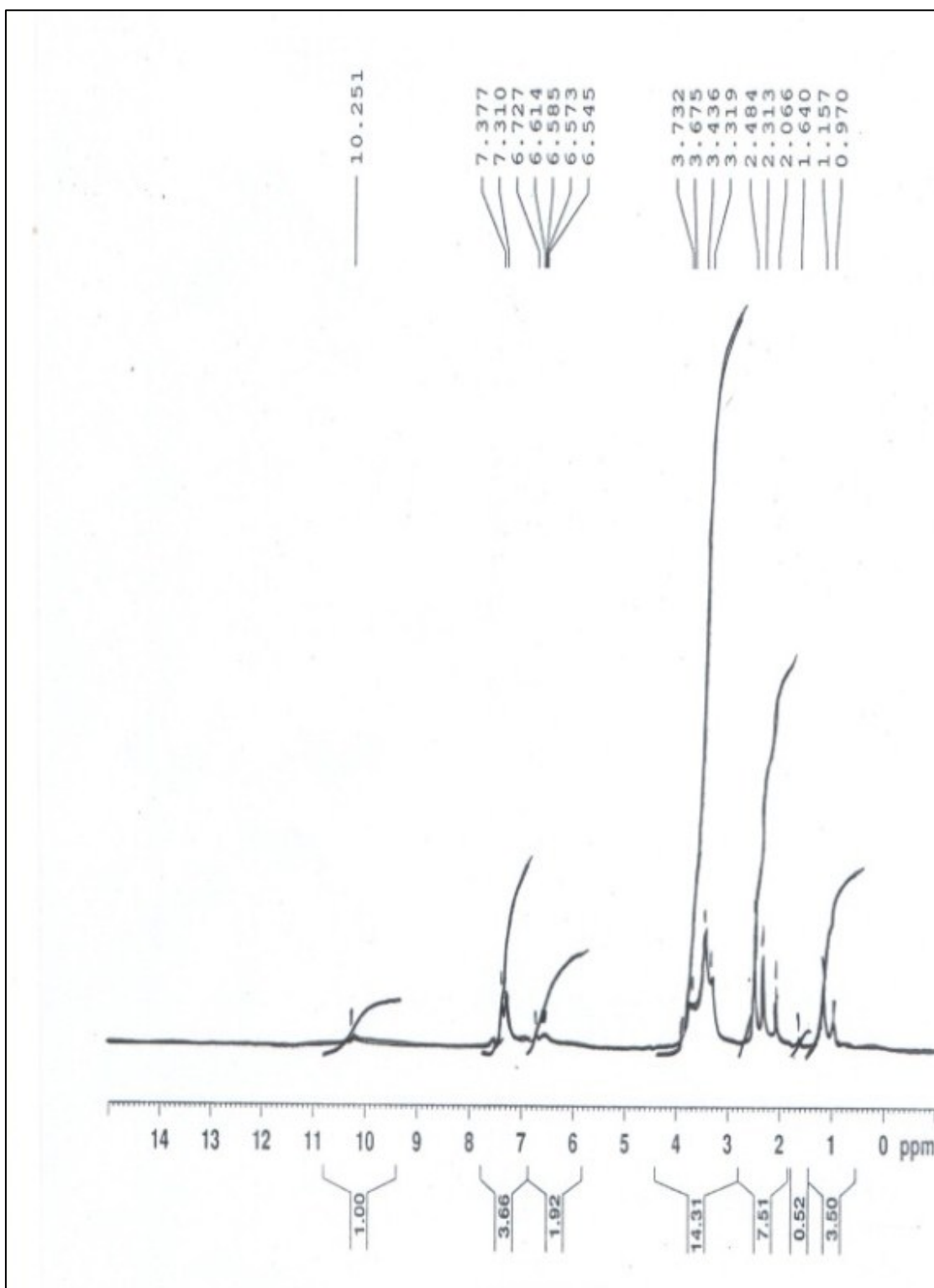


Fig.No. (1)

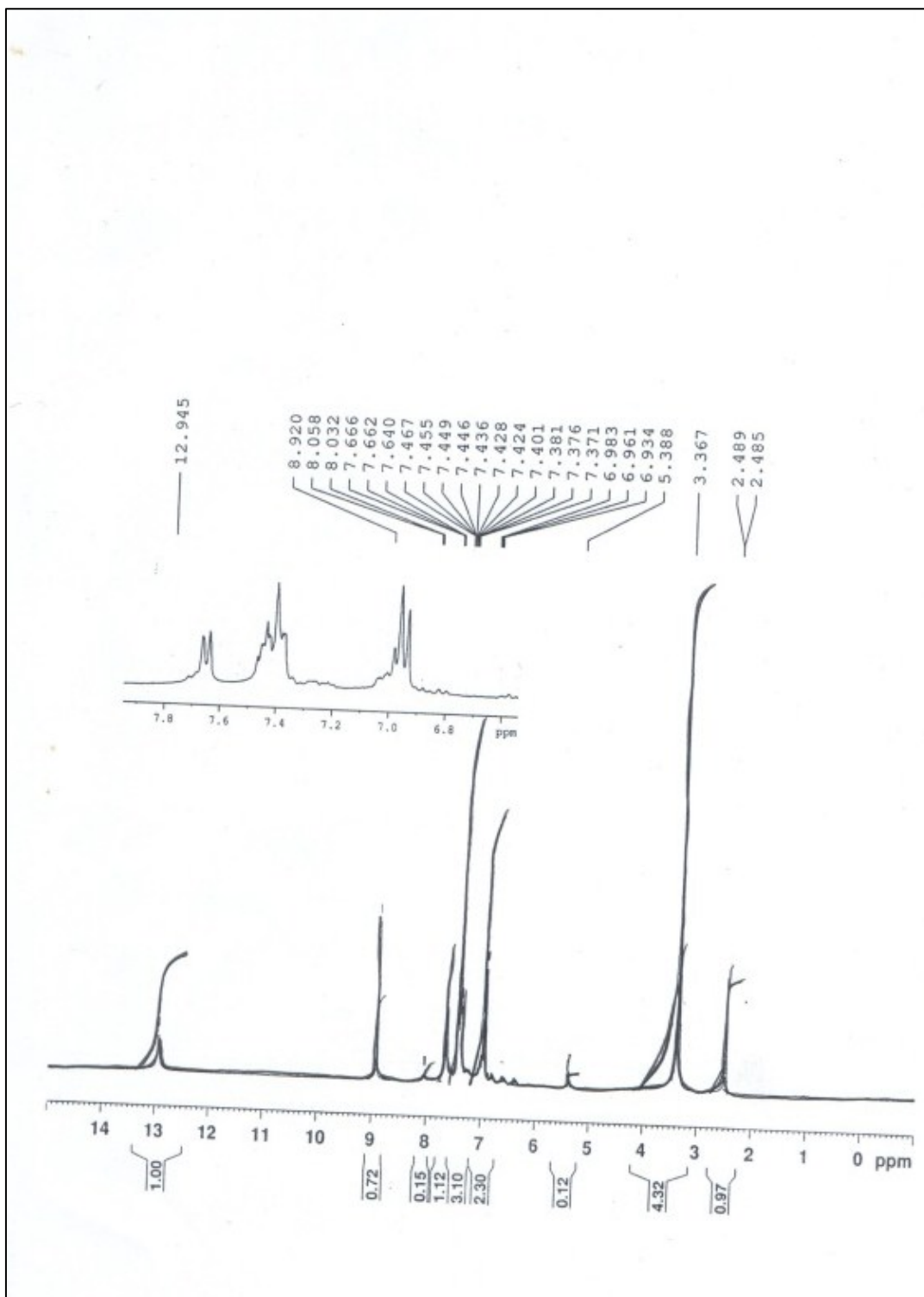


Fig.No.(2)

Fig No. (1) & (2) : ¹H-NMR Spectra of the compound PM-01 & PM-02

3.3. Antimicrobial activities:

Antimicrobial activities for all synthesized compounds were carried out by agar diffusion method and the average radius of the zone of inhibition was recovered. Among the other derivatives screened, the observations were made and compared with standard Norfloxacin (100µg/ml) as shown in Table 1.

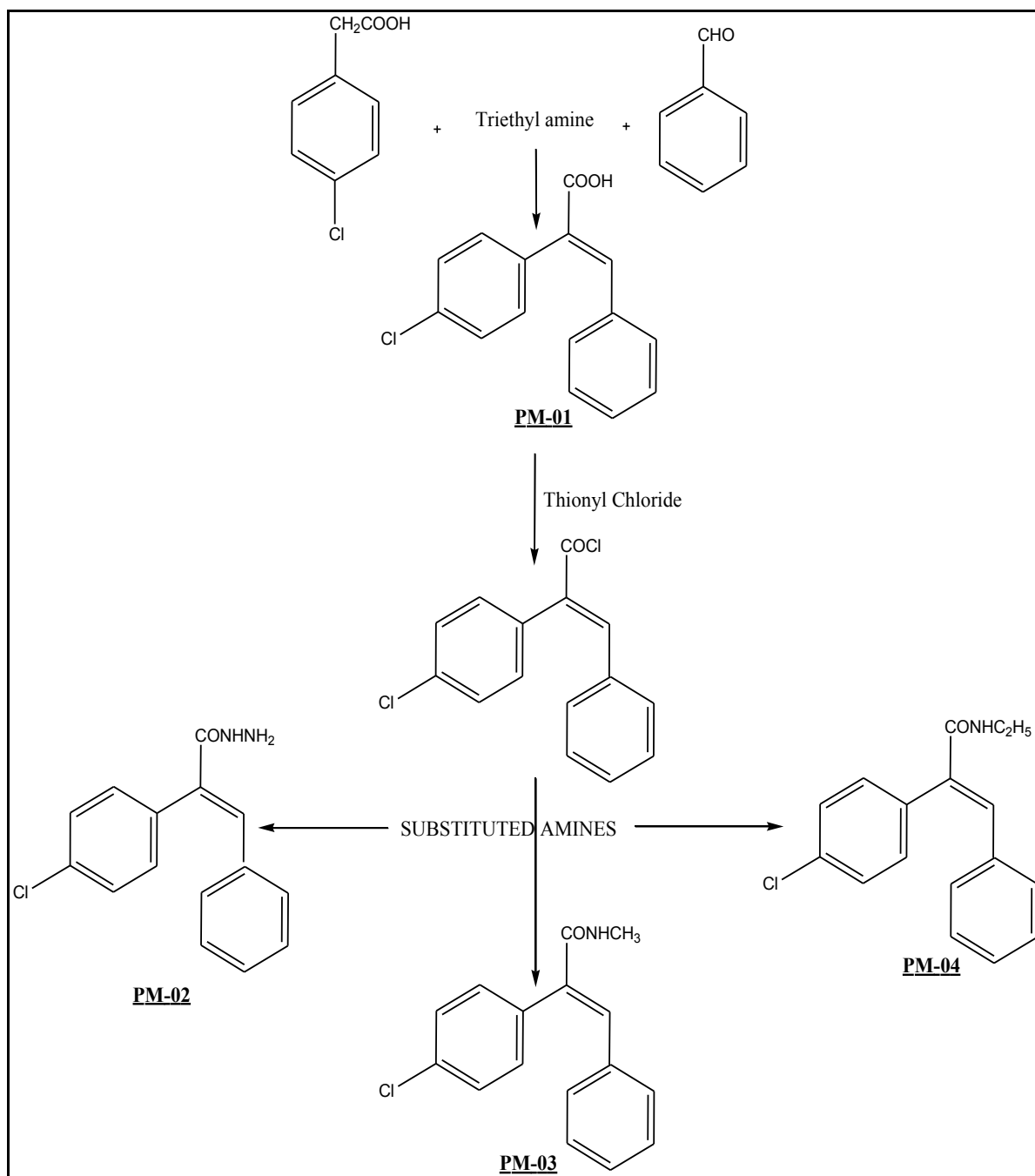
All the synthesized derivatives showed antibacterial activity against both gram positive and gram negative bacteria at a concentration of 100µg/ml. Best results in terms of antibacterial activity was shown by compounds PM01, PM03, PM04 where as moderate results is shown by PM02 .

Table 3 : Antibacterial activity of some substituted stilbene derivatives

Code no.of compounds	Concentration(µg/ml)	Zone of inhibition (In mm)		
		E.coli	S.aureus	B.subtilis
PM01	100	11.2	14.2	13.0
PM02		11.8	11.2	13.2
PM03		16.3	16.8	16.1
PM04		14.5	14.9	12.8
Standard (Norfloxacin)		100	23.90	23.8

CONCLUSION:

In conclusion, it is for the first time that a very simple methodology has been employed for the synthesis of novel stilbene derivatives. All the structures are well supported by ¹H NMR, IR and Elemental analysis. On the basis of above studies we are proposing following structure.



Structures of stilbene derivatives .

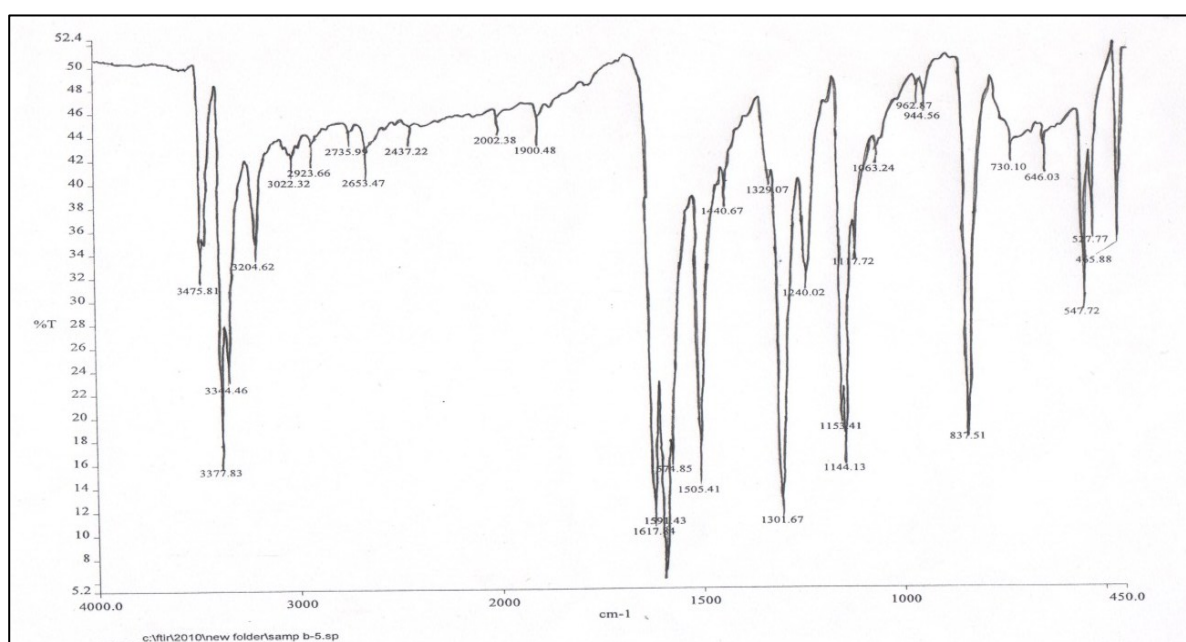
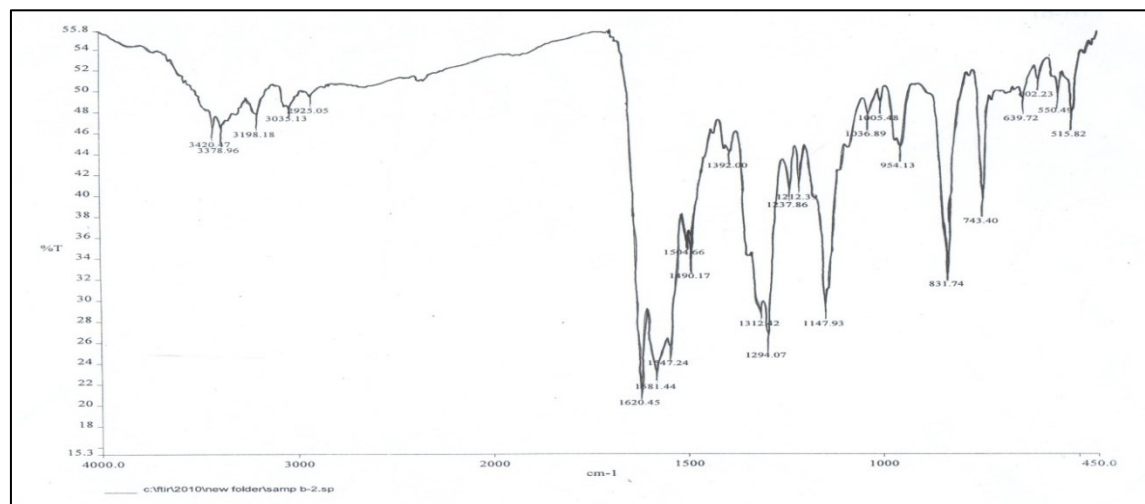


Fig. No. (4) : IR Spectra of the compound PM-02

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