

# Synthesis and antifungal assay of some Chlorosubstituted derivatives of 1,2,3-Triazoles

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## ABSTRACT

Literature survey reveals that the 1,2,3-triazole nucleus containing derivatives have a very broad spectrum of biological as well as physiological activities. The present segment of the study deals with the synthesis of some chlorosubstituted derivatives of 1,2,3-triazoles from azidobenzene . All the target molecules were supported by elemental analysis, FTIR, 1H-NMR spectral data. The titled compounds were assayed for their antifungal activity against *Aspergillus niger*, *Candida albicans*, *Pencillium chrysogenum* and *Tricoderma viridae* using Agar disc diffusion method. The antifungal results obtained are very encouraging.

**Keywords-**1,2,3-triazole; azidobenzene; antifungal activity.

## INTRODUCTION

Triazole is a five membered ring containing aromatic heterocycle that encompasses three nitrogen and two carbon atoms<sup>1</sup> having a molecular formula C<sub>2</sub>H<sub>3</sub>N<sub>3</sub>. The synthesis of high nitrogen containing heterocyclic systems has been increasing over the past decade due to their utility in various fields such as biological, agricultural as well as industrial sectors. In recent years, the chemistry of triazole and their fused heterocyclic derivatives has received a considerable attention owing to their synthetic and effective biological importance.

Triazole have been studied extensively due to its wide variety of activities<sup>2</sup>, low toxicity, good pharmacokinetics and pharmacodynamic profile. Triazole and its derivatives are an imperative type of compounds which possess environmental<sup>3</sup>, industrial<sup>4-5</sup>, agricultural<sup>6-7</sup> and biological activities<sup>8-9</sup>. Triazole and its derivatives embrace a vital session of biologically and pharmmocologically active compounds such as antibacterial<sup>10</sup>, antifungal<sup>11</sup>, antiviral<sup>12</sup>, antitumor<sup>13</sup>, antiparasitic<sup>14</sup>, anticancer<sup>15-16</sup>, antimicrobial<sup>17-18</sup>, antimalarial<sup>19</sup>, antidepressant<sup>20</sup>, fungicidal<sup>21-22</sup>, pesticidal<sup>23</sup>, insecticidal<sup>24</sup>, bactericidal<sup>25</sup> activities. In addition to these biological and agricultural applications the triazole derivatives are also of great utility in preparative organic chemistry. They find wide use to create dyes<sup>26</sup>, polymers<sup>27</sup>.

The broad spectrum of biological activities of 1,2,3-triazoles revealed that there is a wide scope of study in the synthesis of chlorosubstituted 1,2,3-triazoles. So, we thought it interesting to synthesize some new chlorosubstituted 1,2,3-triazoles and study their antifungal activity and their impact on the growth of some *rabbi crop* plants.

## EXPERIMENTAL

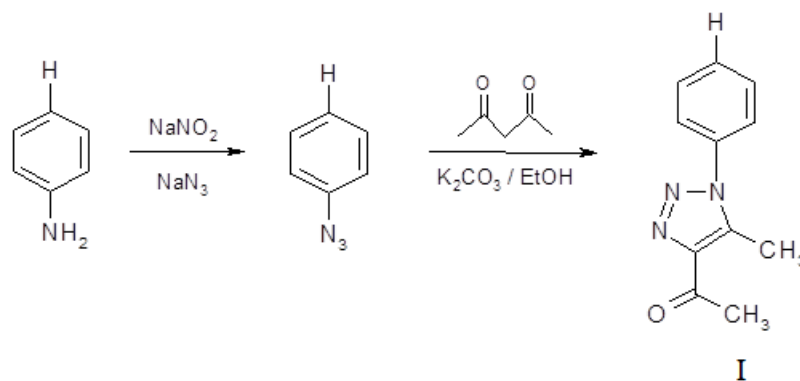
The present study deals with the synthesis of chlorosubstituted 1,2,3-triazoles from azidobenzene derivatives on reaction with acetyl acetone in presence of potassium carbonate in an alcoholic medium. All the synthesised compounds were characterised on the basis of their chemical properties, elemental analysis and spectral data. The melting point were determined by Thiels apparatus using capillary tubes which are uncorrected. The purity of the compounds were tested by TLC. The IR spectra scanned on FTIR spectrophotometer in KBr pellets.  $^1\text{H}$ NMR spectra were recorded on 400 Hz spectrophotometer in  $\text{CDCl}_3$  solvent. The elemental analysis and spectral analysis were carried out at SAIF, Punjab University, Chandigarh.

### Experiment No. 1

#### Synthesis of 1-phenyl-4-acetyl-5-methyl-1,2,3-triazole (I).

Aniline (0.144M) was dissolved in 1:1 ratio of HCl and water in a round bottom flask equipped with stirrer, the reaction mixture was made alcoholic until a clear solution was obtained. To this reaction mixture sodium nitrite (0.144M) dissolved in 51.30 ml of ice cold water was added dropwise sodium azide (0.144M) dissolved in 113.40 ml. of water was then added to above reaction mixture at  $0-5^\circ\text{C}$  dropwise for about half an hour. The precipitate thus formed was extracted with chloroform, washed with water. The organic layer was then dried over anhydrous sodium sulphate and excess solvent was evaporated using rotary evaporator to get azidobenzene.

The mixture of azidobenzene (0.018M), acetyl acetone (0.018M), potassium carbonate (0.057M) in 45 ml of ethanol in a round bottom flask was agitated at  $75^\circ\text{C}$  for 30 min. The solid product thus obtained was neutralized with 10% HCl solution. The product obtained was extracted with diethyl ether dried over sodium sulphate. The solid product thus obtained was recrystallized with ethanol to get the compound (I); yield 80%, m.p.  $137^\circ\text{C}$ .



**Properties and constitution of the compound (I)**

1. The compound (I) was pale yellow coloured crystalline solid with m.p. 137°C. Its alcoholic solution gave orange red precipitate with 2,4-dinitro-phenylhydrazine. It has given positive test for nitrogen by forming prussian blue coloured solution.

2. Thin layer chromatography results of the compound (I).

Compound	Solvent height (cm)	Solute height (cm)	Rf value
I	3.4	2.6	0.76

3. The elemental analysis of the compound (I)

Compound	Analysis	%Cl	%N	%S
I	Found	20.88	-	-
	Calculated	20.92	-	-

4. The analytical results of the compound (I) were in agreement with the molecular formula.

Compound	Molecular formula
I	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O

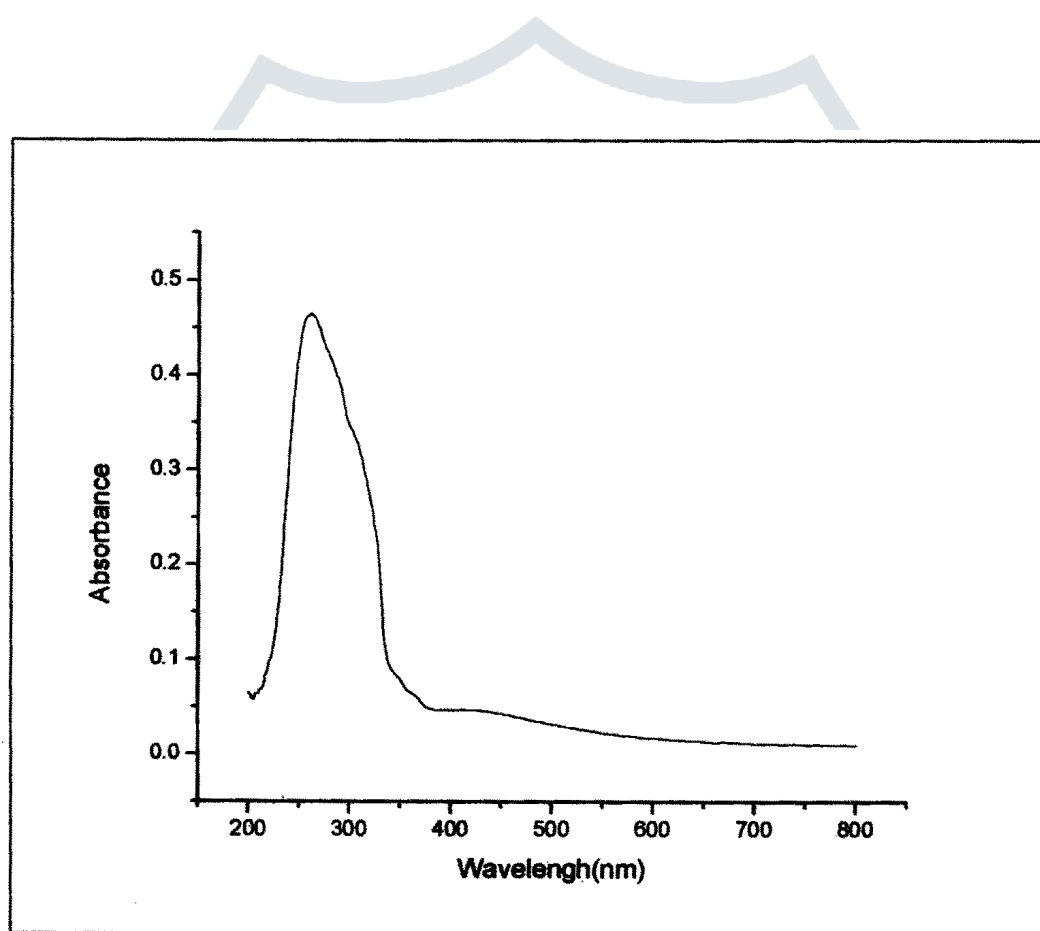
5. The UV-VIS spectrum of compound (I) (Spectrum No. 1) recorded in CDCl<sub>3</sub> showed  $\lambda_{max}$  value of 260nm corresponding to n  $\rightarrow$   $\pi^*$  transition.

6. The IR spectrum of the compound (I) (Spectrum No. 2) which was recorded in KBr showed following main absorption bands.

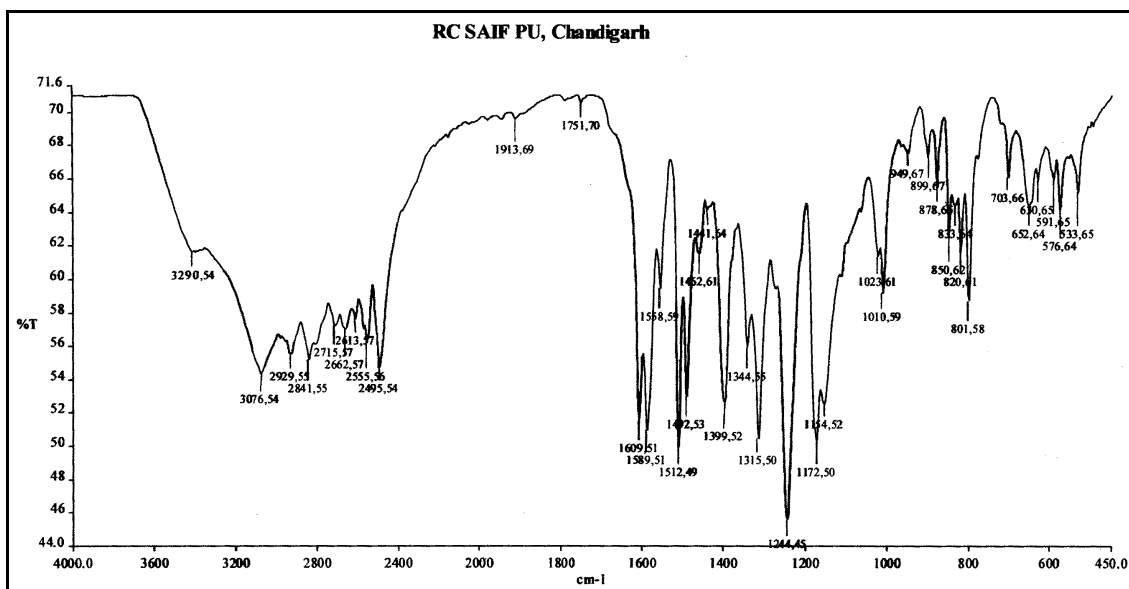
Compound	Frequency (cm <sup>-1</sup> )	Intensity	Correlation
(Spectrum No. 2)	3290	Vb	-N-H stretch
	3076	S	-C-H stretch (Aromatic)
	1751	W	>C=O stretch
	1558	S	N=N stretch

7. The  $^1\text{H}$ NMR spectrum of the compound (I) (Spectrum No. 3) was recorded in  $\text{CDCl}_3$  with TMS as an internal standard. The observed chemical shifts can be correlated as follows :

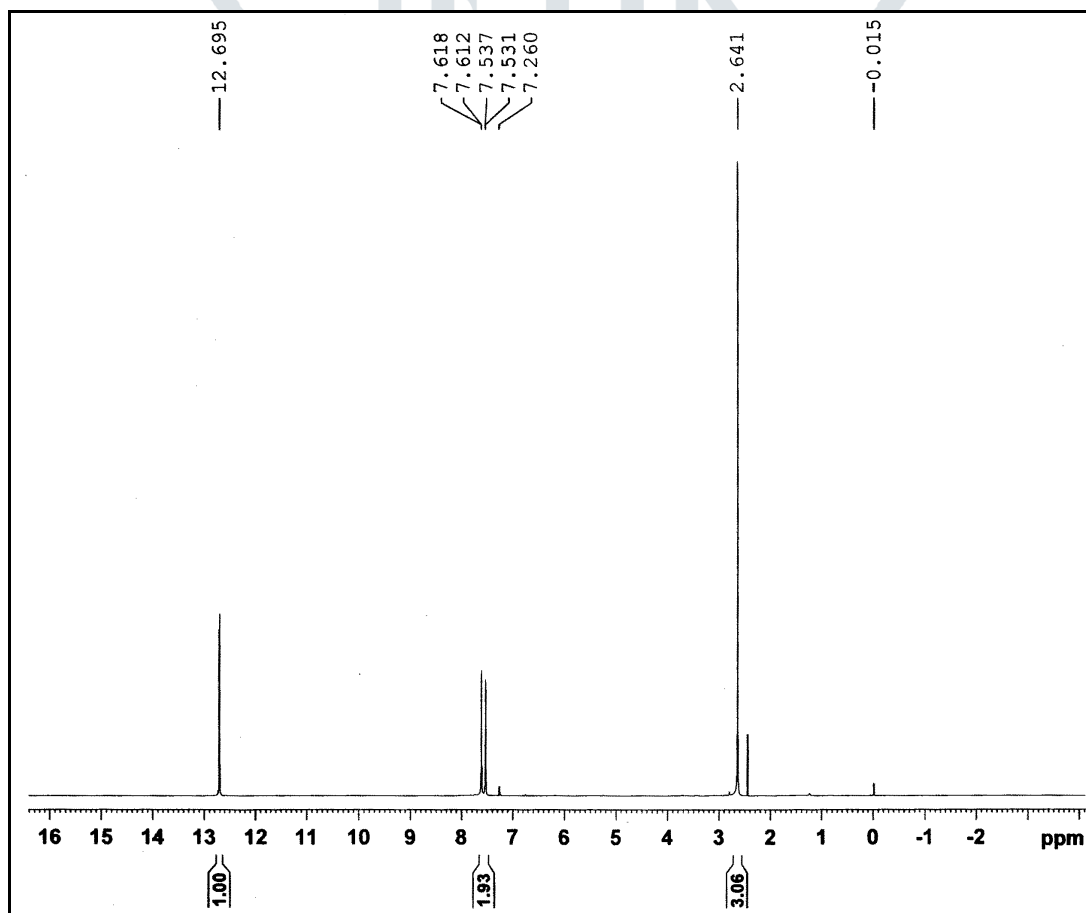
Compound	Chemical Shift $\delta$ ppm	Name of peak	No. of Protons	Types of Protons
I (Spectrum No. 3)	7.2 - 7.6	M	5H	Ar-H
	2.6	S	3H	-CH <sub>3</sub>
	2.3	S	3H	-CH <sub>3</sub>



SPECTRUM NO. 1

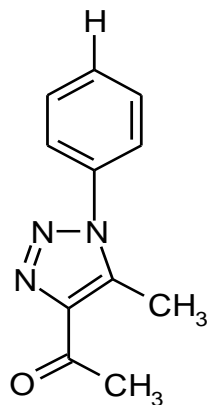


SPECTRUM NO. 2



SPECTRUM NO. 3

On the basis of chemical properties, elemental analysis and spectral analysis<sup>87-89</sup> the compound (I) has assigned the following structure.



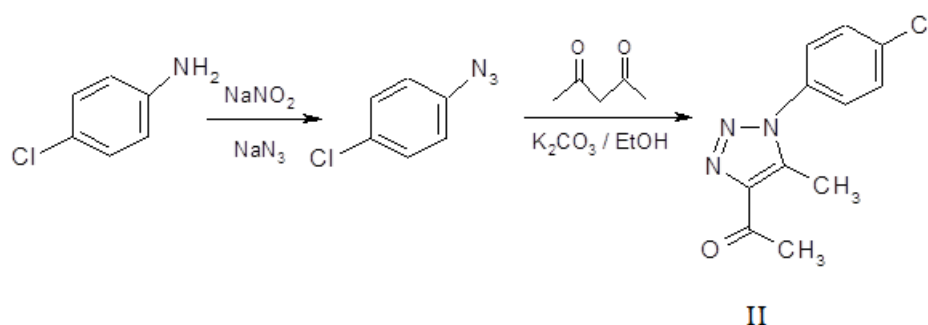
1-Phenyl-4-acetyl-5-methyl-1,2,3-triazole (I).

## Experiment No. 2

### Synthesis of 1-[4-(chlorophenyl)]-4-acetyl-5-methyl-1,2,3-triazole (II).

Chloroaniline (0.144M) was dissolved in 1:1 ratio of HCl and water in a round bottom flask equipped with stirrer, the reaction mixture was made alcoholic until a clear solution was obtained. The reaction mixture was fused with sodium nitrite (0.144M) dissolved in 51.30 ml of ice cold water to which a dropwise sodium azide (0.144M) dissolved in 113.40 ml of water was added. The reaction occurs at 0-5°C for about half an hour. The precipitate was extracted with chloroform which was washed with water and dried over anhydrous sodium sulphate. The solid obtained was recrystallized with ethanol to get 1-azido-4-chlorobenzene.

1-Azido-4-chlorobenzene (0.018M), acetyl acetone (0.018M), potassium carbonate (0.057M) were dissolved in 45 ml of ethanol in a round bottom flask. The reaction mixture was agitated at 75°C for 30 min. The solid product obtained was neutralized with 10% HCl solution. The product obtained was extracted with diethyl ether which was dried over sodium sulphate. The solid product obtained was recrystallized with ethanol to get the compound (II); yield 76%, m.p. 129°C.



II

**Properties and constitution of the compound (II)**

1. The compound (XV) was pale yellow coloured crystalline solid with m.p. 129°C. Its alcoholic solution gave orange red precipitate with 2,4-dinitro-phenylhydrazine. It gave positive test for nitrogen by forming prussian blue coloured solution. It gave Lossaigen's test for chlorine element.

2. Thin layer chromatography results of the compound (II).

Compound	Solvent height (cm)	Solute height (cm)	Rf value
II	2.9	2.3	0.79

3. The elemental analysis of the compound (II)

Compound	Analysis	%Cl	%N	%S
II	Found	15.04	17.83	-
	Calculated	15.14	17.93	-

4. The analytical results of the compound (II) were in agreement with the molecular formula.

Compound	Molecular formula
II	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O

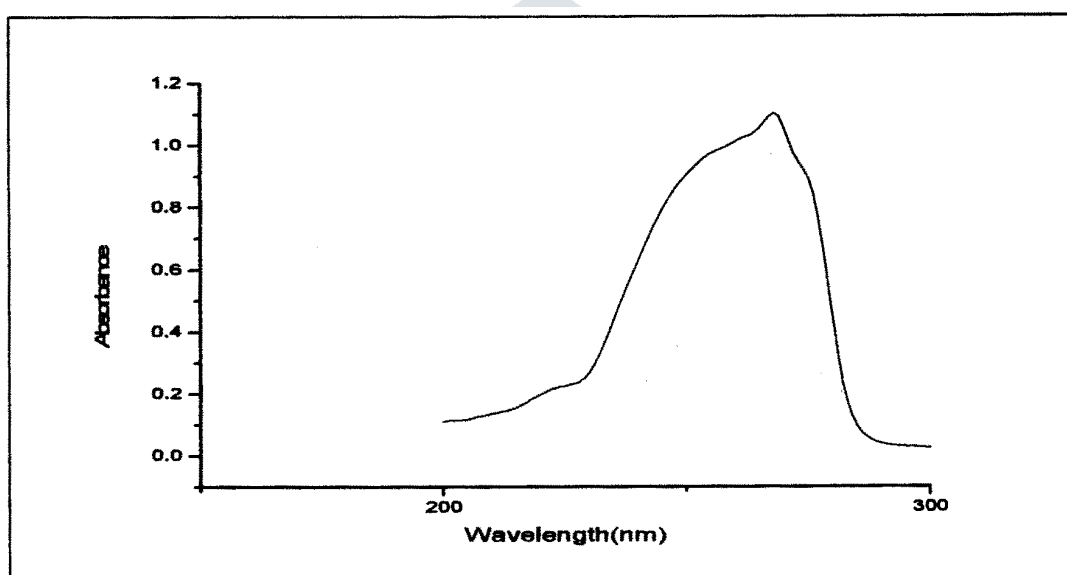
5. The UV-VIS spectrum of compound (II) (Spectrum No. 4) recorded in CDCl<sub>3</sub> showed  $\lambda_{max}$  value of 295nm corresponding to  $n \rightarrow \pi^*$  transition.

9. The IR spectrum of the compound (II) (Spectrum No. 5) which was recorded in KBr showed following main absorption bands.

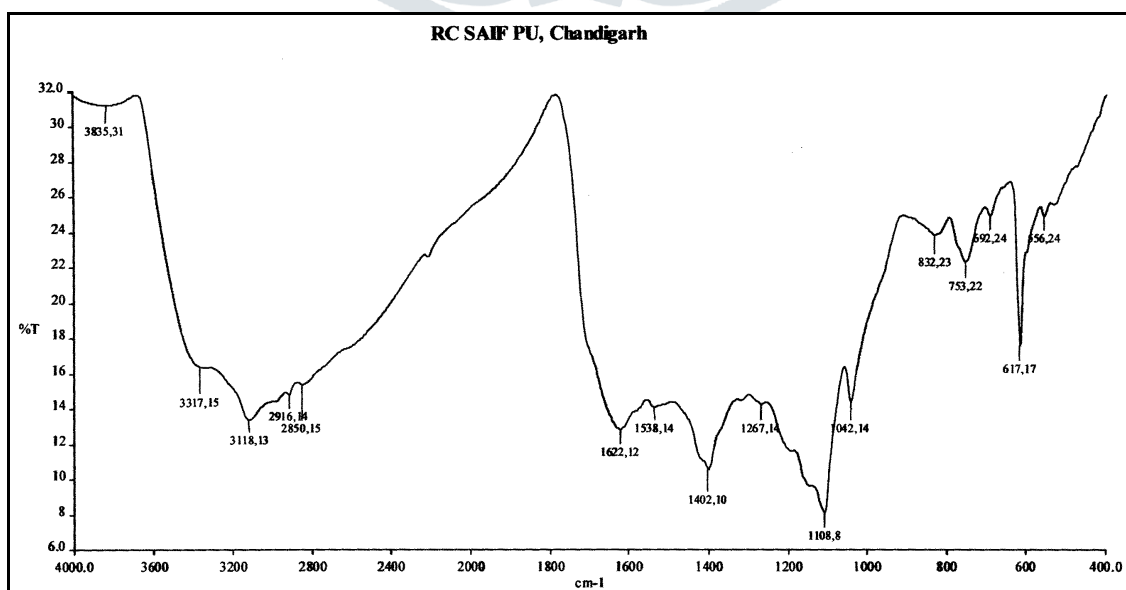
Compound	Frequency (cm <sup>-1</sup> )	Intensity	Correlation
II (Spectrum No. 5)	3317	W	-N-H stretch
	3118	S	-C-H stretch (Aromatic)
	1622	Vb	>C=O stretch
	1538	S	N=N stretch
	753	S	C-Cl stretch

10. The  $^1\text{H}$ NMR spectrum of the compound (II) (Spectrum No. 6) was recorded in  $\text{CDCl}_3$  with TMS as an internal standard. The observed chemical shifts can be correlated as follows :

Compound	Chemical Shift $\delta$ ppm	Name of peak	No. of Protons	Types of Protons
II (Spectrum No. 6)	7.4 - 7.6	M	4H	Ar-H
	2.6	S	3H	$-\text{CH}_3$
	2.3	S	3H	$-\text{CH}_3$

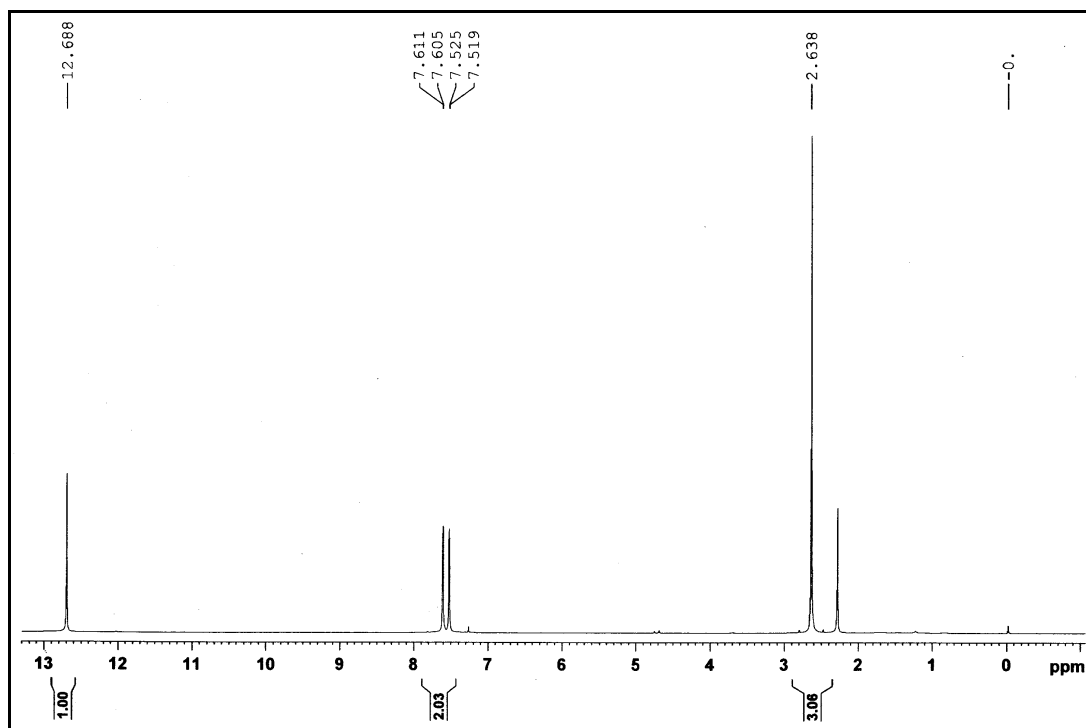


SPECTRUM NO. 4



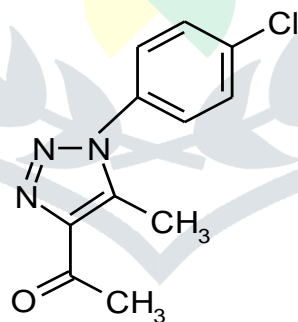
SPECTRUM NO. 5





SPECTRUM NO. 6

On the basis of chemical properties, elemental analysis and spectral analysis the compound (II) has assigned the following structure.



1-[4-(Chlorophenyl)]-4-acetyl-5-methyl-1,2,3-triazole (II).

## Result and discussion

The synthesised compounds were screened for their antifungal activity against some fungi *i.e.* *Aspergillus niger*, *Candida albican*, *Pencillium chrysogenum* and *Tricoderma viridae* using agar diffusion method. The compounds I and II shows activity against all the tested fungi.

## CONCLUSION

The newly synthesised chlorosubstituted compounds were characterized for their structural determination. Various chemical and spectral data supported the structures. Antifungal activities of newly synthesised chlorosubstituted compounds I and II were screened against various fungal species and it is concluded that the compounds showed significant activity against the tested species above 500ug.

### Acknowledgement

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