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**Research Article.....!!!**

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## **ON THE ENERGY EFFICIENCY OF MICROWAVE ASSISTED SYNTHESIS OF NOVEL 1, 4, 5- TRIPHENYL SUBSTITUTED PYRROLE DERIVATIVES**

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### **ABSTRACT**

Novel series of 1, 4, 5 triphenyl substituted pyrrole derivatives have been synthesized using environmentally being procedure and evaluated for their antimicrobial activity. Neat reaction on microwave irradiation resulted in enhancement of yields and reaction rates. Pyrrole derivatives are more potent and less side effect. Benzoin and primary aromatic amine refluxing in ethanol resulted the formation of  $\alpha$ - aminoketone intermediates, which are condensed without isolation with malononitrile to yield various 2-amino-4, 5-diphenyl-1-substituted-1H-pyrrole-3-carbonitriles (1). Pyrrole (1) further reacted with triethyl orthoformate and alcoholic sodium hydroxide gives respective pyrrole derivatives (1a-1b). The synthesized compound were confirmed through spectral characterization using IR (JASCO 4100-FT/IR), Mass (QP 2013 Shimadzu) and  $H^1$  NMR. Result indicate that microwave method is more eco-friendly than conventional method and compound shows promising antimicrobial activity.

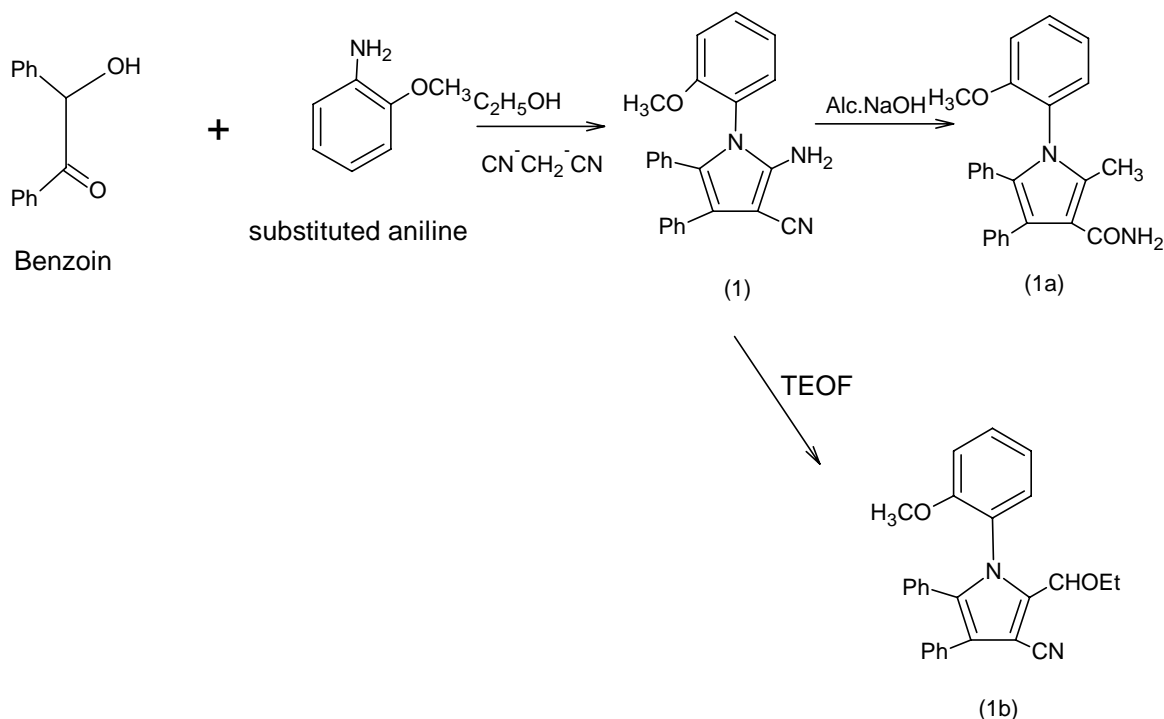
## INTRODUCTION

Pyrrole and its derivatives are important heterocycles in organic and bio-chemistry and have been found in many pyrrole containing natural products such as heme, chlorophyll, vitamin B<sup>12</sup> and bile pigments. The pyrrole derivatives are widespread in numerous natural products, and many of them display diverse biological activities. Besides, Pyrrole is one common structural unit in many organic materials. In the preparation of Pyrrole derivatives, however, many disadvantages including harsh reaction conditions and poor yields limit the application of classical methods, such as Knorr reaction and Paal-Knorr reaction. Although some novel strategies have been developed to synthesize Pyrrole derivatives recently. Pyrrole and the simple alkyl Pyrrole are colorless liquids, with relatively weak odors rather like that of aniline, which also like anilines, darkens by auto oxidation<sup>[1]</sup>. The pyrrole scaffold is an useful structural pattern for exhibiting chemical functionality in biologically active molecules. It has established broad application in drug development for the treatment as antibacterial, anti-inflammatory, antiviral, antitumor, and antioxidant agent<sup>[2]</sup>. The most widely used method is Paal-Knorr synthesis, which involves the cyclo condensation reaction of 1, 4- dicarbonyl compounds with primary amines to produce substituted Pyrroles<sup>[3]</sup>.

## MATERIAL AND METHOD

**Materials**-Benzoin, primary aromatic aniline, triethyl orthoformate, alcoholic sodium hydroxide, malononitrile etc. purchased from Samarth Lab, Loba Research lab. All chemicals are analytical grade.

**Methods**-All product are synthesized by microwave (Catalyst) methods. Melting point of synthesized by open capillary tube method. The IR spectra were recorded on JASCO 4100-FT/IR spectrophotometer. The NMR spectra recorded on Bruker-NMR 400 mhz using dimethyl sulphoxide (DMSO) and chemical shift were recorded in part per million (ppm) and tetra methyl silane (TMS) used as reference standard in NMR spectroscopy. Purity of synthesized compounds was checked by thin layer chromatography (TLC) using silica gel (G) as adsorbent and visualization was detected by iodine vapour.

**EXPERIMENTAL****Chemistry: Scheme of reaction**<sup>[4, 5, 6]</sup>:-**Step 1: Synthesis of 2-amino-4, 5-diphenyl-1-substituted-1H-pyrrole-3-carbonitriles (1)**<sup>[4]</sup>

A mixture of benzoin (2 g, 0.01 mol), the appropriate primary amine 2- methoxy aniline (1.23 ml, 0.01 mol), and conc. HCl (6–8 drops) in ethanol (30 mL) was heated under reflux for 8min and cooled. Malanitrile (0.66ml 0.01 mol) was added, followed by a catalytic amount (0.5 mL) of pyridine portion wise and left to reflux until a solid was formed. The solvent was evaporated under reduced pressure and the residue was recrystallized from methanol to give compound(1). Yield: 80-85 %; M.P. 130-134.

**Step 2: Synthesis of 2-propanal-1,4,5-triphenyl-1H-substituted pyrrole-3-carbamide (1a)**<sup>[6]</sup>

Compound (1) (3.65g, 0.01 mol) was heated at reflux temperature in 20 ml of alcoholic sodium hydroxide solution for 03min the solvent was evaporated under reduced pressure, and the residue was poured into ice water to give a precipitate which was filtered, dried, and recrystallized from ethanol to afford 1a. Yield: 80-85%; M.P. 162-166 °C.

**Synthesis of 2 methyl-1, 4, 5-triphenyl-1H-3-carbonitriles (1b)**<sup>[5]</sup>

Compound (1) (3.65g, 0.01mol) was heated in triethyl orthoformate (30ml) were refluxed for 07min. The solvent was removed under reduced pressure and the residue was recrystallized from methanol to afford 1b. Yield: 85-90%; M.P. 116-118 °C.

**Table no: 1 Properties of Synthesized compound**

Name	Molecular formula	Rf value	% yield	Melting point
1a	C <sub>25</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	0.8	80-85%	162-166 °C
1b	C <sub>27</sub> H <sub>23</sub> N <sub>2</sub> O <sub>2</sub>	0.6	85-90%	116-118 °C

**Pharmacological studies:**<sup>[7]</sup>**Antimicrobial Activity-**

The compounds (1a-1b) were evaluated for their *in vitro* antimicrobial activity against E. coli, S. aureus, B. subtilis and S. typhi by disk diffusion method was performed using MacConkeys agar and Nutrient agar medium. Each compound was tested at concentration at 100µg/ml in DMSO. The zone of inhibition was measured after 24h incubation at 37°C.

Standard: Ampicilline (10mg/1ml of DM)

**Table no: 2 Antimicrobial screening result of synthesized compound measuring the zone of inhibition in millimeter**

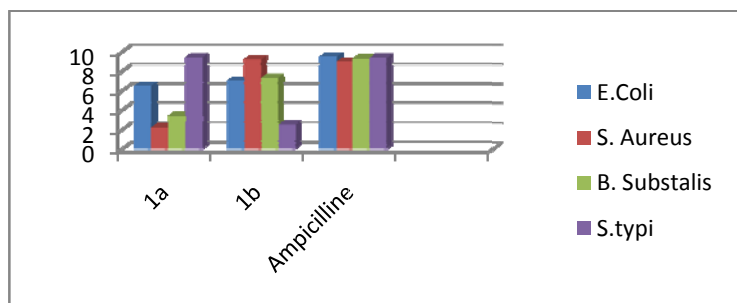
Sr. No.	Compound	Name of organism			
		<i>E.coli</i>	<i>S. aureus</i>	<i>B.subtilis</i>	<i>S.typhi</i>
1	1a	++	-	+	+++
2	1b	++	+++	++	
Standard	Ampicilline	+++	++	++	+++

**Key to symbol-**

Highly active= +++ (inhibition zone >9mm), Moderately active= ++ (inhibition zone 6-8mm), Slightly active= + (inhibition zone 3-5mm), Inactive = - (inhibition zone < 3)

**RESULT AND DISCUSSION****Experimental**

The compound were synthesized by “Paal-Knorr reaction” which shows good percentage yield and their physical data is given in table no. 1. The structural elucidation of the synthesized compound was done by interpretation of IR, MASS, NMR spectra's. All the compound shows satisfactory IR, MASS, NMR. The purity of the compound evaluated by TLC method.

**Antimicrobial activity-****Fig No.1: Antimicrobial activity of synthesized compounds**

1a showed moderately active compound and 1b showed moderately active compounds against E.coli. 1b showed highly active compound and 1a showed inactive compound against S.Aureus. 1a showed slightly active compound and 1b showed moderately active against B.Subtilis. 1a showed highly active compound and 1b showed inactive compounds against S.typhi. Where Standard (ampicilin) showed highly active against E.coli, S.aureus, B.Subtilis, and S.typhi.

## CONCLUSION

It may be reasonably concluded that the present procedure for synthesis of 1, 4, 5- triphenyl N-substituted pyrrole through benzoin and aromatic primary amine gives good pharmacological active compound. Microwave method is more suitable than conventional method. Advantages of microwave method with respect to simplicity of operation, yield of product and less reaction time as compare to conventional. The antimicrobial activity of synthesized compound were to obtain zone of inhibition by disk diffusion method. All synthesized compounds showed good anti- microbial activity.

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