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Synthesis of Some Novel Nitrogen Containing Pyrrole Derivatives and Their Antimicrobial Activity

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ABSTRACT

Heterocyclic molecules represent the most utilized scaffolds for the discovery of novel synthetic drug. As reported in recent communications, the pyrrole moiety can be found both in natural and synthetic pharmaceutical products. Pyrroles have been reported to play an important role as antibacterial, antiviral and anti-inflammatory activity.

New pyrrole derivatives were synthesized and screened for antimicrobial activity. The reaction was performed by using ordinary condensation type, which enabled to easy work-up and good yield. Synthesized compounds were screened for antimicrobial activity.

INTRODUCTION

Pyrrole and its derivatives are important heterocycles in organic and biochemistry and have been found in many pyrrole containing natural products such as heme, chlorophyll, vitamin B12 and bile pigments. There are extensive studies on the synthesis and reactivity of pyrrole derivatives. The most widely used methods for synthesis of pyrrole derivatives involve intramolecular cyclization of a heteroatom. Many pyrrole derivatives have shown interesting biological properties such as antibacterial, anti-inflammatory, antioxidant, antitumor, antifungal and immune suppressant activities. Pyrrole derivatives are prepared by using formamide and triethyl orthoformate reagent. These pyrrole derivatives are screened for antimicrobial activity.

MATERIALS AND METHODS

Materials

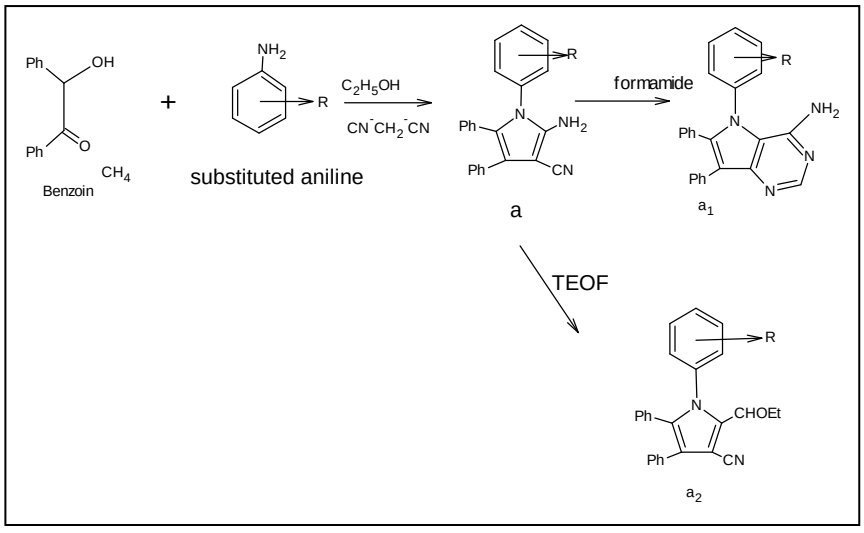
Benzoin, primary aromatic aniline, triethyl orthoformate, formamide, malanonitrile etc. purchased from Samarth Lab, Loba Research lab. All chemicals were of analyatical grade.

Methods

All products were synthesized by conventional method.

Experimental

Chemistry: Scheme of reaction:



Substituted aniline- p- chloro aniline

Step 1

Synthesis of 2-amino-4, 5-diphenyl-1-substituted-1H-pyrrole-3-carbonitriles (1)[4]

A mixture of benzoin (2 g, 0.01 mol), the appropriate primary amine p- chloro aniline (1.23 ml, 0.01 mol), and conc. HCl (6–8 drops) in ethanol (30 mL) was heated under reflux for 8 min and cooled. Malanonitrile (0.66 ml, 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.

Step 2

1) A mixture of the appropriate aminopyrrole (3.35 g, 0.01 mol), was heated in triethyl orthoformate (30 ml) were refluxed for 6 h. The solvent was removed under reduced pressure and the residue a_1 was recrystallized from methanol/ water to afford.

2) A mixture of appropriate aminopyrrole (3.49 g, 0.0 mol) and formamide (30 mL, 0.066 mol) was heated under reflux for 6 h, cooled and poured onto ice-water to give precipitates, which were filtered off, dried, and recrystallized from ethanol to yield compounds a_2.

Pharmacological studies [7]

Antimicrobial Activity

i) Antibacterial Activity

The compounds (1a-1b) were evaluated for their *in vitro* antibacterial activity against *E. coli*, *S. aureus*, *B. substilis* and *S. typhi* by disc diffusion method was performed using MacConkeys agar and Nutrient agar medium. Each compound was tested at concentration 600 µg/ml in DMSO. The zone of inhibition was measured after 24 h incubation at 37°C.

Standard: Ampicillin (600 µg/ml of DMSO).

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

Sr. No.	Compounds	Name of organism			
		E.Coli	*S. aureus*	*B.substalis*	*S.typhi*
1	a_1	6.1	3.2	8.4	6.1
2	a_2	9.2	8.4	8.4	6.1
Standard	Ampicillin	9.5	9.2	9.6	9.4

ii) Antifungal Activity

The compounds (1a-1b) were evaluated for their *in vitro* antifungal activity against*Candida albicans* and *Aspergillus niger* by disc diffusion method was performed using Saboraud's agar medium. Each compound was tested at concentration 600 µg/ml in DMSO. The zone of inhibition was measured after 48 hrs and 7 days incubation at 37ºC respectively.

Standard: Econazole 600 µg/ml of DMSO.

Sr. No.	Compounds	Name of organism	
		Candida albicans	***Aspergillus niger***
1	a_1	3.5	2.5
2	a_2	5.2	9.6
Standard	Econazole	9.7	9.8

Key to symbol

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

RESULTS AND DISCUSSION

Synthesis of pyrrole derivatives by the Paal- Knorr Condensation of benzoin with primary aromatic amines in refluxing ethanol resulted in the formation of α-aminoketone intermediates,

which were condensed, without isolation with melononitrile to yield the various 2-amino-4, 5-diphenyl-1-substituted-1H-pyrrole-3-carbonitriles (a).

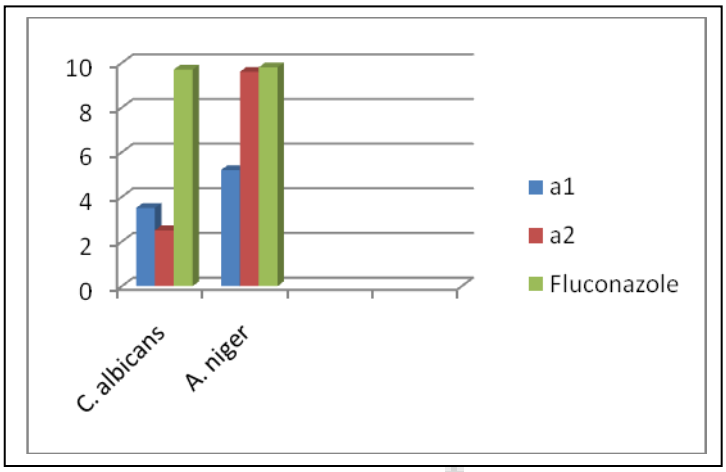


Fig. 1. antibacterial activity

The synthesized compounds were screened for their antimicrobial activity as shown in Fig.1

a_2 showed highly active compound against *E. coli*. a_1 showed moderately active compound against *E. coli*, *B. substalis*, compound a_2 showed moderately active compound against *E. coli*, *B. substalis*. Where Standard (ampicillin) showed highly active against *E. coli* and *B. substilis*, moderately active against *S. typhi*, *S. aureus*.

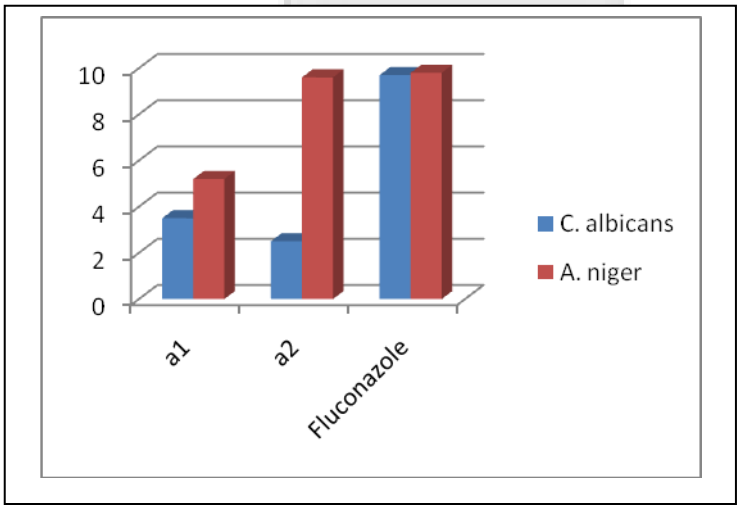


Fig. 2. anti- fungal activity

a_2 showed highly active compound against *Aspergillus niger*. a_1 showed moderately active compound against *Candida albicans*, *Aspergillus niger*. a_2 showed moderately active compound against *Aspergillus niger* , *Candida albicans*.

CONCLUSION

Pyrrole derivatives are synthesized by using Paal-Knorr condensation method through benzoin and aromatic primary amine gives good pharmacologically active compound.

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