International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 5(4): July-August 2015

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Research Article……!!!

Received: 05-06-2015; Revised: 29-08-2015; Accepted: 30-08-2015

SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF PYRROLE DERIVATIVES

Dipali Mote*, Madhuri Nimbalkar, Shital Chalke, Puja Kamble, Chandrakant Magdum

Department of Pharmaceutical Chemistry, Rajarambapu College of Pharmacy, Kasegaon, Tal:-Walwa Dist- Sangli, India.

Keywords:

Paal-Knorr Reaction, 3-Carbonitrile, Pyrrole , Antibacterial Activity

For Correspondence:

Dipali Mote

Department of Pharmaceutical Chemistry, Rajarambapu College of Pharmacy, Kasegaon, Tal:-Walwa Dist-Sangli, India.

E-mail:

dipalipharma91@gmail.com

ABSTRACT

New pyrrole derivatives were synthesized using paal -knorr mechanism. The reaction was performed by using benzoin with primary amine in refluxing ethanol resulted in the formation of α –amino ketone intermediates, which where condensed ,without isolation, with malonitrile to yield the 2-amino-4,5- diphynyl pyrrole -3-carbonitrile. Pyrrole are reacted with reagent like- hydroxyl amine hydrochloride and formamide solution. Pyrrole derivatives examined for their antibacterial activity.

INTRODUCTION

Medicinal chemistry has occupied the central position in drug discovery and play the important role in designing and developing pharmaceutical drugs.[1] These are chemical compounds that may be used in diagnosis, treatment, cure and mitigation of disease or other abnormal condition. Heterocycles and medicines are both interrelated because humans are totally dependent on the drugs derived from heterocyclic rings. Nitrogen heterocycles are of special interest as they constitute an important class of natural andnon-natural products, many of which exhibit useful biological activities.[2] Pyrroles and their derivatives exhibit different important biological activities like antibacterial, antioxidant, cytotoxic, insecticidal, anti-inflammatory,anticoagulant, antiallergic, antiarhythmic, hypotensive and anticonvulsant.The newly synthesized compounds were evaluatedas antimicrobial agents against gram positive and gram negative bacteria.[2-5]

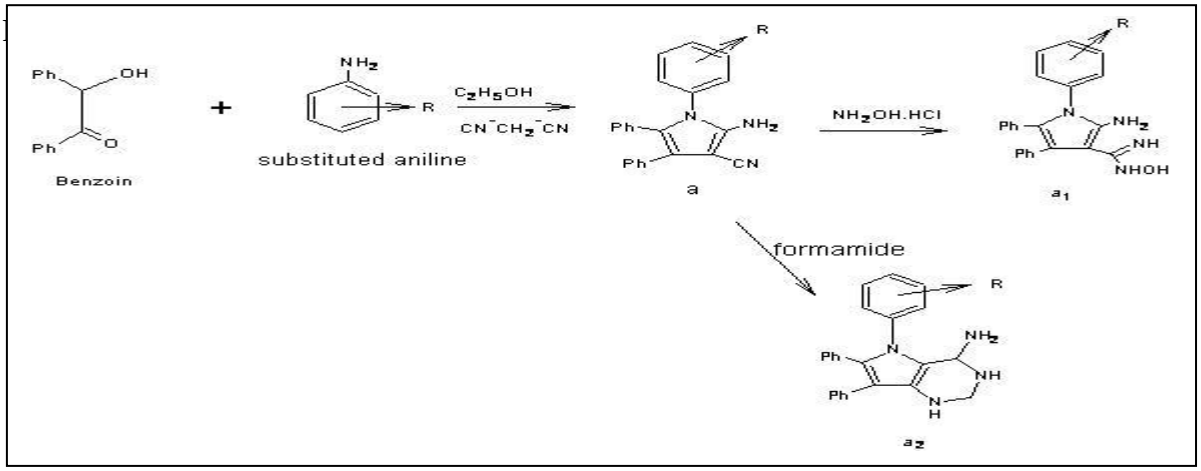
MATERIAL AND METHOD

Materials- Benzoin, primary aromatic aniline, hydroxyl amine hydrochloride ,formamide, malanonitrile were procured from Loba Research lab, Mumbai. All chemicals used were of AR grade.

Methods- Conventional Method.

Experimental Work :

Melting points of all compounds was determined by open tube capillary method and was uncorrected. Completion of reaction is determined by thin layer chromatography by using suitable mobile phase.



Where- Substituted aniline = P-bromo aniline.

Conventional Method:-

Synthesis of 2-amino-4, 5-diphenyl-1-substituted-1H-pyrrole-3-carbonitriles (a) [6]

A mixture of benzoin (2 g, 0.01 mol), the appropriate primary amine p-bromo aniline (1.72 g, 0.01mole) and conc. HCl (6–8 drops) in ethanol (50 mL) was heated under reflux for 8hr and cooled. Malanonitrile (1ml, 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 compounds **a**. Yield: 51%; M.P. 142-144.

Synthesis of 2-amino-1-(4-bromophenyl)N-Hydroxy-4,5-diphenyl-1*H*-p Carboximidamide (a_1)[8]

The appropriate cyanopyrrole (4.13 g, 0.01 mol) , hydroxyl amine hydrochloride (0.33 g, 0.01 mol) and anhydrous sodium carbonate (5.3 g, 0.05 mol) in absolute ethanol (40 mL) was refluxed for 4 h, filtered while hot and the residue was washed with hot ethanol. The collected filtrate was cooled, poured onto ice-water to yield precipitates, which were filtered, dried, and recrystallized from methanol. 57%,M.P. 140-142.

Synthesis of 5-(4- substituted phenyl)-6-7-diphenyl5H-pyrolo(3,2-d) pyrimidine 4-amine (a_2)[7]

A mixture of the appropriate aminopyrrole **a** (4.13 g, 0.01 mol), 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. 59%,M.P. 138-140.

Pharmacological Studies [9,10]

Antibacterial Activity-

The compounds (a_1-a_2) were evaluated for their *in vitro* Antibacterial Activity against *E. coli, S. aureus, B. substilis 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 and the results were shown in table 1. The synthesized compounds were compared with standard antimicrobial drug Ampicillin (10mg/1ml of DMSO).

Table 1- Antibacterial screening result of synthesized compound measuring the zone of inhibition in millimeter

Sr. No.	Compound	Name of organism			
		E.coli	*S. aureus*	*B.substalis*	*S.typhi*
1	a_1	++	++	-	+++
2	a_2	++	++	+++	-
Standard	Ampicillin	+++	++	+++	+++

Key to symbol-

Highly active= +++ (inhibition zone>9mm)

Moderately active= ++ (inhibition zone 6-8mm)

Slightly active= + (inhibition zone 3-5mm)

Inactive = - (inhibition zone < 3)

RESULTS AND DISCUSSION

1] Study of conventional method-

An efficient 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). Pyrroles a reacted with different reagents such hydroxyl amine hydrochloride and formamide yield compound (a_1-a_2). The yield of product (a_1-a_2) in the range 57-59% by conventional method and time required4hr,6hr.

2] Pharmacological screening of synthesized derivatives-

Synthesized compounds were screened for their antimicrobial activity as shown in figure 1.

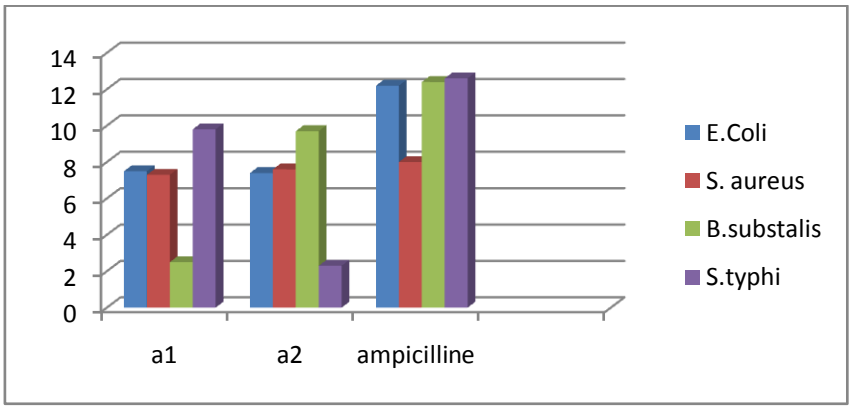


Fig 1: Antimicrobial activity of synthesized compounds

a_1 showed moderately active compound against e.coli, compound a_2 showed moderately active against e.coli . a_1 showed moderately active compound against S. aureus . a_2 showed

moderately active compound against S. aureus. a_1 showed Slightly active compound against B.substalis . a_2 showed highly active compound against B.substalis. . a_2 showed highly active compound against S.typhi. a_2 showed Slightly active compound against S.typhi. Where Standard (ampicilin) showed highly active against E.coli, S.typhi and B.Substilis, moderately active against S. aureus

CONCLUSION

In conclusion the present procedure for synthesis of pyrrole derivative by paal- knorr condensation .through benzoin and aromatic primary amine gives good pharmacological active compound. All synthesized compounds showed good anti- bacterial activity.

REFERENCES

1. Thomas L. Lemke , David A. Willimans, Victoria F. Roche and S. Willaman Zito, FOEY'S Principales of Medicinal Chemistry,6th edition,2008,4.
2. Kokila Parmar et.al., reported Synthesis and antimicrobial activity of substituted 2H-Pyrrole-2-Ones derivatives based on 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP) Journal of Chemical and Pharmaceutical Research4(7), 2012, 3478-3482.
3. Tarunkumar M. Patel et.al., Study of Novel Pyrrole Derivatives, International Journal Of Pharmaceutical Research & Allied Sciences 1(4),201, 36-39
4. Dorota Krajewska et.al., Synthessis and antimicrobial activity of de- thetro-1-(1 Methylsulfonyl pyyrole-3-yl)-2difluoactamidopropane-1,3-diol Acta Polonia Pharmaceutical n Drug Research, Vol. 66 No. 1 pp. 69-72, 2009.
5. P.B. Khulpe Synthesis and Characterization of 5, 6 Diphenyl Pyrrole Derivatives and it's Pharmacological Profile,Journal of Current Pharma Research 4(3), 2014, 1181-1185.
6. Sandip P. Dholaki et.al., Synthesis and Antimocrobial Screening of Novel 2-Amino-4,5 Diphynyl- 1-H-Pyrrole -3- Carbonitrile, American Journal Of Pharmatech Research,3(5). 2013,2249-338.
7. M. S. Mohamed et al. Synthesis of certain pyrrole derivatives as antimicrobial agent, Acta pharm.2009; 59, 145-158.
8. M. S. Mohamed , Synthesis and Evaluation of Novel Pyrroles and Pyrrolopyrimidines as Anti-Hyperglycemic Agents, BioMed Research International ,2014,1-13.
9. A.Idhahyadhulla et al. Synthesis of some new pyrrole derivatives and their antimicrobial activity, Der pharma chemica, 3(4),2011, 210-218.
10. Samar S. Fathallah et al. Synthesis and evaluation of novel pyrrole and pyrrolopyrimidine as anti-hyperglycemic agent, Biomed Research International Journal, 2014; 1-13.