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Synthesis and Antimicrobial Activity of Piperazine Derivatives

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ABSTRACT

Ethyl piperazine is treated with 4- chloro nitrobenzene in presence of anhydrous potassium carbonate and methanol is used as a solvent forms 1 ethyl -4-[4-nitrophenyl] piperazine, then it is treated with iron dust in presence of hydrochloric acid and neutralized with sodium carbonate to form the 4-[4-ethyl piperazine-1-yl] anilline, it is reacted with n-chloro acetyl aryl amine in presence of anhydrous potassium carbonate forms the final product 1-[2-(aryl amino -2-oxoethyl) - amino -4-(n-ethyl piperazine)] benzene derivatives were synthesized, the synthesized compounds were screened for their antibacterial activates against *s. aures* and *e.coli* by cup plates method . From screening results of some compounds found highly active against both gram – positive and gram – negative bacteria while other compounds possess moderate activity.

Keywords: Ethyl Piperazine, Potassium Carbonate, N-Chloro Acetyl Aryl Amine.

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INTRODUCTION

In recent decades, the problems of multi-drug resistant microorganisms have reached on alarming level in many countries around the world. Several antibiotics have been prescribed and found to be effective on various infectious disorders. For the treatment of these intractable infections, the Piperazine is a hetero cyclic atom and which is belongs to the family of medicines called anthelmentics. Anthelmentics are used in the treatment of worm infections. Piperazines derivatives have also been shown to a large number of antibiotics contain amide linkage. Several derivatives of amides were prepared and found to possess antimicrobial activities. Literature survey reveals that various drugs e.g. penicillin (antibacterial), pyrazinamide (ant tubercular), indinavir, ritonavir etc.(protease inhibitors as anti AIDS) contains their particular activities due to the amide linkage present in their structures. Diverse biological properties including Antihistamine, Anti-convoulsant, Anti HIV1 and as potential cocaine abuse therapeutic agent. The present investigation describes the synthesis of a series of benzeneno derivatives of N-alkyl and N-aryl piperazine. The derivatives so prepared were characterized by employing various spectroscopic techniques such as 1H NMR, 13CNMR, mass spectroscopy etc. The derivatives were assessed for their antimicrobial activity (zone of inhibition and minimum inhibitory concentration (MIC) activity) against a number of bacterial strains[1-8].

MATERIAL AND METHODS:-

Step -1: Preparation of 1-ethyl-4-(4-nitrophenyl) piperazine[2-17].

A mixture of N-ethyl piperazine (0.01 mile), 4-chloro nitrobenzene (0.01 mile), and anhydrous potassium carbonate in methanol was refluxed for three hour with stirring. After the competition of reaction the resultant mixture was cooled at room temperature. Then it was poured into ice cold water with constant stirring. The solid separated was purified by recrystallization. M.P.220-222˚C.IR is1321 cm^{-1}C – N Stretch, 2925 cm^{-1} Aromatic C-H Stretch, 1593 cm^{-1} Aromatic C=C Stretch, 1088 cm^{-1}, NMR is 1.61-1.26-NH, 7.50-7.8 -Are-H, 8.68-CONH.

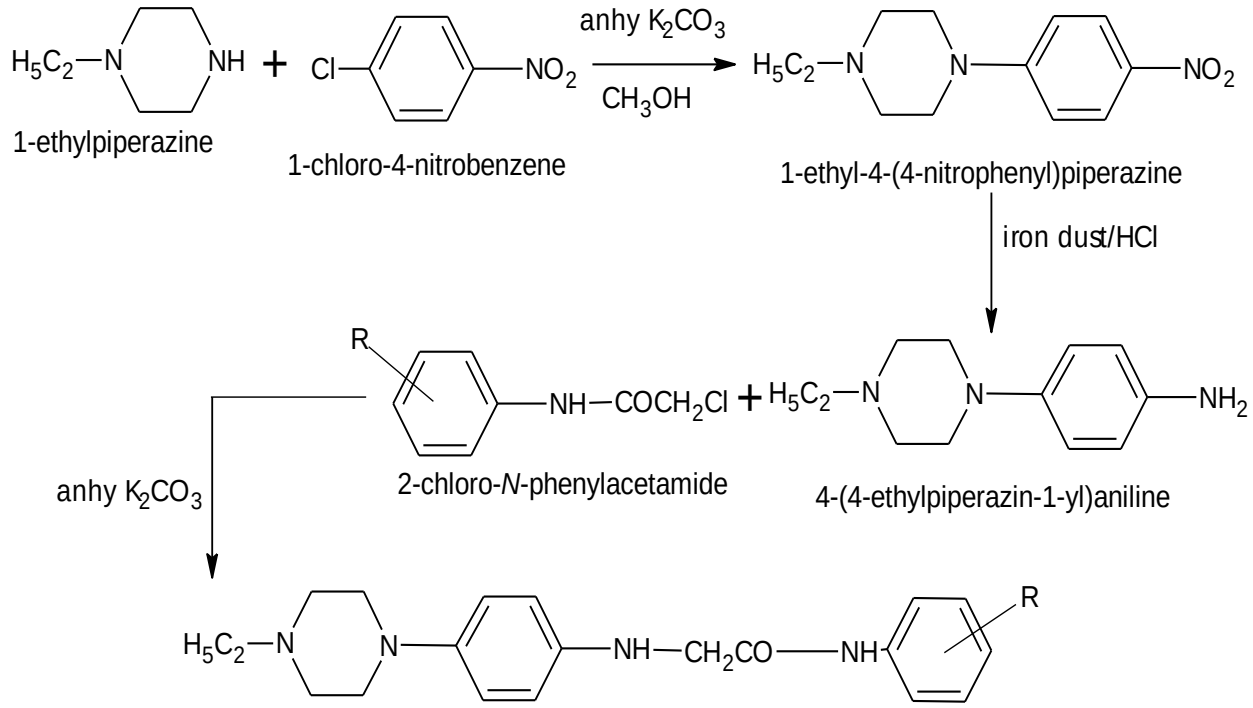
Step -2: Preparation of 4-(4-ethyl piperazine-1-yl) aniline.

A mixture of 1-ethyl-4-(4-nitrophenyl) piperazine (0.01 mile), iron dust (0.01 mile), in presence of hydrochloric acid (0.01 mile), and water 2 ml was refluxed for 4-5 hour with stirring. After the competition of the reaction it was filtered, washed with water and add the for neutralize with sodium carbonate. The solid precipitate is separated and purified by recrystallisation.M.P.65-69 C˚. IR is 1310 cm^{-1}C – N Stretch, 2955 cm^{-1} Aromatic C-H Stretch, 1550 cm^{-1} Aromatic C=C Stretch, 1064 cm^{-1}, NMR is 1.64-1.25-NH, 7.58-7.9 -Are-H, 7.-CONH.

Step-3: Preparation of 1-[2-(Aryl Amino -2-Oxoethyl) - amino -4-(N-ethyl Piperazine)] Benzene.

A mixture of 4-(4-ethyl piperazine-1-yl) aniline (0.01 M 1.91 gm), 2-chloro N-phenylacetamide (0.01 M), in presence of anhydrous potassium carbonate relaxed for 4-5 hour with costant stirring. After the competition of reaction the resulting mixture was cooled to room temperature. Then it was poured into ice cold water with constant stirring. The solid precipitate was purified by recrystallization from ethanol. M.P. 230-232˚C. IR is 1356 cm^{-1}C – N Stretch, 2980 cm^{-1} Aromatic C-H Stretch, 1600 cm^{-1} Aromatic C=C Stretch, 1068 cm^{-1}, NMR is 1.64-1.25-NH, 7.5-7.9 -Ar-H, 7.2.-CONH.

Scheme[1, 2, 3, 4, 5]:-



1-[2-(aryl amino-2-oxoethyl)-amino-4-(N-ethyl piperazinol)-benzene

Where R = Cl, OCH_3, CH_3, H, OH, F, NO_2, Br, Mannish bases and coupling agents.

RESULTS AND DISCUSSION:-

The entire synthesized compounds were screened for their antibacterial activities against *S.aures* and *E.coli* by cup plate method. Gentamycin and chloramphenicol were used as standard drugs. The compound was tested at the concentration of 40 mg/ml and DMF as a solvent. From screening result it is observed that the some compounds shows highly active against Gram-positive and Gram-negative bacteria respectively.

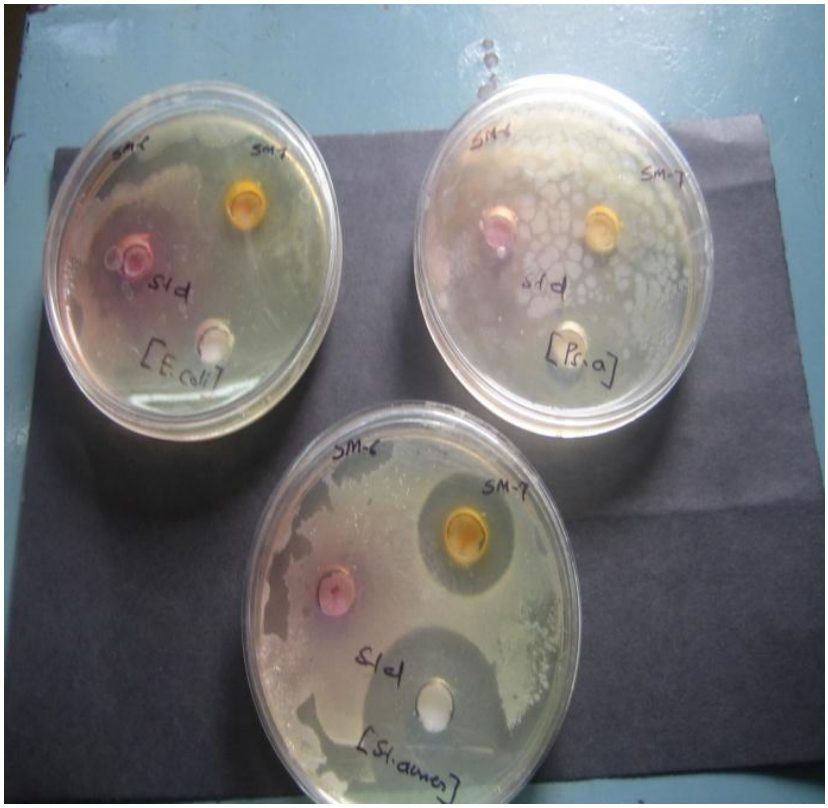


Figure 1:Minimum inhibitation concentration of piperazine derivatives

Table 1 :- Antibacterial activity of newly synthesized compound.

Compound no	Zone of inhibition in mm at 40 µg/ml conc.	
	E.coli	S.aureus
1.	-	12
2.	12	12
3.	08	-
4.	12	08
5.	08	06
6.	10	10
7.	10	11
8.	-	-
9.	08	09
10.Standard	13	11
Gentamycin	15	19
Chloramphenicol	18	25

CONCLUSION:-

From screening result it was observed that the compounds 2, 4, 6, 7, and 10 found highly active against both Gram-positive and Gram-negative bacteria while other compounds possess feeble to modern activity. Compounds 2 and 10 showed maximum zone of inhibition respectively. For *E.coli* while compounds two and ten showed maximum zone of inhibition for *S.aures*. So the compounds two and ten used for the antibacterial activity.

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