International Journal of Pharmaceutical Science and Practice.
Volume 3, Number 1 (2014) pp 13-18

http://www.ripublication.com

Synthesis and Antimicrobial Activity Study of Some Piprazino Methyl Imidazole Derivatives

Mr. A.N Ingle[1], Mr. Niraj Sinha, Mr. S.P Wate and Mr. K.P Bhusari

Sharad Pawar College of Pharmacy, wanadongri, Nagpur
amitingle2008@gmail.com

Abstract

Medicinal chemistry deals with study of structure and synthesis of drugs and there action of the body that is lots of works is done in clubbing of the molecules to get new pharmacological active drugs. In today's world of medicine we was tried to produced a novel and potent drug which was having verity of activities and stable motiy our emphasis to prepared simple and potent moties in world of medicine. So we prepared new 2-piprazinomethy imidazole derivatives this derivatives is prepared by mixing aminomathamine with benzoin to from 2-amino4, 5 diphenyl imidazole derivatives this imidazole derivatives is reacted with dicloromethane in etanolic KOH to give 2 –methyl amino imidiazole this 2-methyl imidazole finally reacted with 4-substituted piprazine in ethanolic KOH to give 2-piprazino methly imidazole derivatives. The identification of derivatives was done by thin layer chromatography and NMR spectra is also done to indentify the molecules. The prepared derivative is screen for antimicrobial activity and it is found that the molecules have good activity again gram positive and gram negative bacteria. We are trying to do incretion of 4-substituted piprazine ring at 2 position of imidazole ring and its successful attempted made the final molecules is stable and having potent other pharmacological activity like anti-inflammatory anthilmentic and antifungal.

keywords minomethamine, Benzoin and dichloromethane and substituted piprazine, agar for media

Introduction

Medicinal chemistry is disciplines which deal with study of structure and synthesis of novel moities in order to produce new and more effective drugs in today's world of chemistry our aim is to produce such moties which is easily available and easily

synthesized in normal temperature condition. our intention to produce a now combination so we try to club two major moties imdazole and piprazine together in order to get novel moties that is 2-piprazino methyl imdazole derivatives this approach are made to reduce the toxicity and increase the efficacy of drug the produce new moity having lots of good activity like antimicrobial, antifungal, anthalmantic and anti-inflamatory the moties is produce is stable at room tamprature and got in good yield. having good therapeutic activity.

Exprimental

Instrumentation:

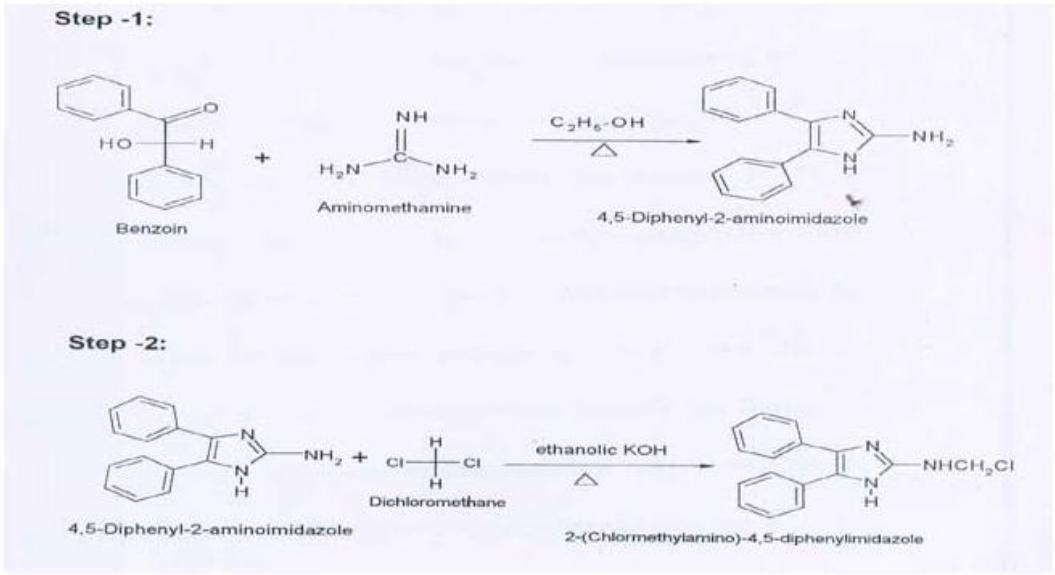
The Melting points of the synthesized compounds were determined in an in one-end-open capillary tubes using a melting point determination apparatus and are uncorrected. Completion of the reaction and the purity of the synthesized compounds were ascertained by TLC using Silica Gel 'G' plate (Merck) as stationary Phase and Chloroform: Methanol (9:1) as solvent system and the spots were detected by using iodine as indicator. IR spectra of the synthesized compounds were characterized by FT-IR (Model: MB 3000).

General method of preparation[8]:

Equimolar quantities of benzoic and aminomethamine (21g) and (6.5g) respectively were taken in (50ml) ethanol in round bottom flask. The reaction mixture was refluxed for 3 hrs, and was cooled and triturated with crushed ice. The product was allowed to separate. Then, it was filtered and washed thoroughly with small portions of cold water. After washing, the product 2-amino 4, 5-diphenylimidazole was dried, recrystalied from ethanol. Its melting point was found out

Synthesis of substituted benzoins were attempted using various substituted benzaldehydes and sodium cyanide.(step-1). Equimolar mixture of 4, 5-diphenyl-2-aminoimidazole and dichloromethane (25g)and (8g) respectively was taken in round bottomed flask to the mixture 5% ethanolic potassium hydroxide solution (50ml) was added this mixture was stirred well and refluxed on water bath for 3 hrs ethanol was removed by evaporation as much as possible. Residue was cooled with crushed ice the 2-methyl chloroamino4, 5 diphenyl imidazole was formed it was filtered and washed with small portions of cold water the product was recrystallised from ethanol, and was dried. Melting point was found out.(step-2)Equimolar mixture of 2-(chloromethyl amino)-4, 5-diphenylimidazole and Piperazine was taken in round bottomed flask to the mixture 5% ethanolic potassium hydroxide solution (50ml) was added this mixture was stirred well and refluxed on water bath for 3hrs Ethanol was removed by evaporation as much as possible. Residue was cooled with crushed ice. the 2-piprazino methyl imidazole was obtained it was filtered and washed with small portions of cold water the product was recrystallised in ethanol, and was dried (step-3)

Chemical reaction



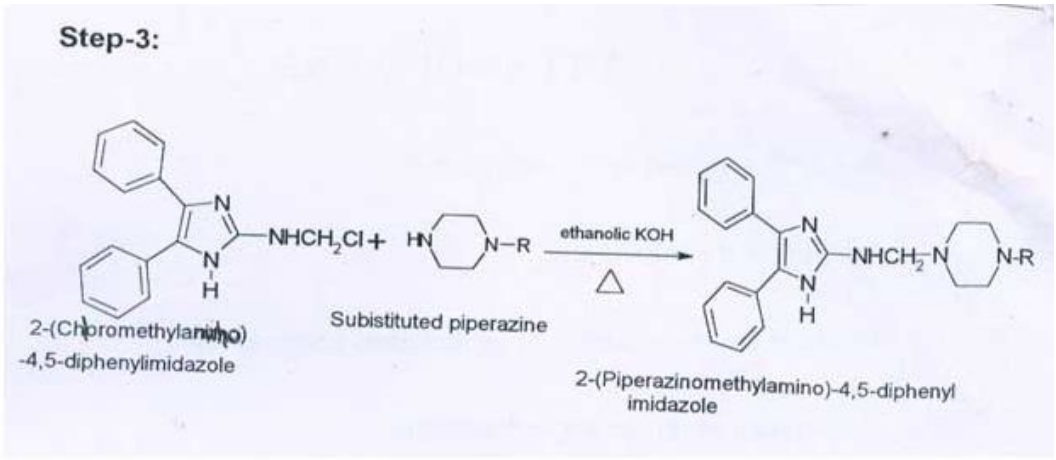


Table –I

Sr. No.	Name of derivatives	-R
3a	2-piprazinomethyamino4, 5-diphenyl imidazole	-H
3b	N-methyl-2-pipraznomethylamino4, 5-diphenyl imidazole	$-CH_3$
3c	N-ethyl-2-pipraznomethylamino4, 5-diphenyl imidazole	$-C_2H_5$
3d	N-acetyl 2-pipraznomethylamino4, 5-diphenyl imidazole	$-CO-CH_3$
3e	p-chloro-N-benzyl 2-pipraznomethylamino4, 5-diphenyl imidazole	$4-Cl-C_6H_5$
3f	N-benzoyl 2-pipraznomethylamino4, 5-diphenyl imidazole	$-COC_6H_5$
3g	p-amino-N-benzoyl 2-pipraznomethylamino4, 5-diphenyl imidazole	$4-NH_2-CO-C_6H_5$
3h	m-nitro-N-benzoyl 2-pipraznomethylamino4, 5-diphenyl imidazole	$3-NO_2-CO-C_6H_5$
3i	m-amino-N-benzoy 2-pipraznomethylamino4, 5-diphenyl imidazole	$3-NH_2-CO-C_6H_5$

2-(piperazinomethyl amino)-4, 5-diphenlyimidazole (3a)
The infra-red spectra (KBr): 3400cm^{-1}: N-H stretching, 3060-3040 cm ^{1}C-H stretching of aromatic ring, 2960-2840 cm^{-1}: stretching vibration of C-H bond in CH_2 group, 1960-1920 cm^{-1}: stretching vibration of substituted benzene, C=C and C=N, 1250 $^{cm-1}$: strong band of aromatic amine, 1200 cm^{-1}:bending vibration of C-N. ^{1}H-NMR spectra ($CDCI_3$): Triplet δ=7.25 ppm indicates the presence of two benzene ring, singlet δ=5.85 ppm: protons of methylene group, singlet δ=7.45 ppm: assigned the protons of piperazine ring, singlet at δ=7.85 ppm total protons of imidazole ring, singlet δ=4.40 ppm show single protons of piperazine ring.

2-(N-methyl piperazino methyl amino)-4, 5-diphenlyimidazole (3b)
^{1}H-NMR spectra ($CDCI_3$): Triplet δ=7.25 ppm indicates tge oresebce if two benzene ring, singlet δ = 7.85ppm indicate the total protons of imidazole ring, singlet δ =4.56 ppm show total protons of methyl group.

2-(N-ethyl piperazino methyl amino)-4, 5-diphenylimidazole (3c)
The infra-red spectra (KBr): 3400 cm^{-1}: N-H stretching, 3060-3040 cm^{1}:C-H stretching in aromatic region, 296-2840 cm^{-1}: stretching vibration of C-H bond in CH_2 group, 1960-1920 cm^{-1}: stretching vibration of substituted benzene, C=C and C=N, 2960-2840 cm^{-1}: stretching vibration indicate the merging of ethyl group. ^{1}H-NMR spectra ($CDCI_3$): Triplet δ=7.25 ppm indicated the presence of two benzene ring, singlet δ=5.85 ppm: protons of methylene group, singlet δ = 7.45 ppm: assigned the protons of piperazine ring, singlet at δ = 7.85 ppm indicated the total protons of imidazole ring, singlet δ = 4.6 ppm assigned the total protons of ethyl group.

2-(N-acetylpiperazino methyl amino)-4, 5-diphenylimidazole (3d)
The infra-red spectra (KBr):3400 cm^{-1}: N-H stretching, 3060-3040 cm-^{1}:C-H stretching Ar-C-H, 2960-2840 cm^{-1}:stretching vibration of C-H bond in CH_2 group, 1960-1920 cm-^{1}: stretching vibration of substituted benzene, C=C and C=N, 1760 cm^{-1}: stretching vibration indicated the presence of carbonyl group, 2960-2840 cm^{-1}: stretching vibration indicated the merging of methyl group.

2-(N-benzoyl piperazino methyl amino)-4, 5-diphenylimidazole (3f)
The infra-red spectra (KBr): 3400 cm^{-1}: N-H stretching, 3060-3040 cm^{-1}:C-H stretching Ar-C-H, 2960-2840 cm^{-1}: stretching vibration of C-H bond in CH_2 group, 1960-1920 cm^{-1}: stretching vibration of substituted benzene, C=C and C=N, 1760 cm^{-1}: stretching vibration indicate the presence of carbonyl group, 3060-3040 cm^{-1}: indicated presence of benzene ring at aromatic region

Result and discussion
The antibacterial activities[9, 11] of compounds 3a-3j have been studied against gram negative *E. coli* and gram positive *S.aureus* by using cup plate method the nytrient agar medium (20ml) was poured into the sterile petri-dishes. In the solidified plates, wells were made using a sterile cork borer, 8 mm in diameter. Subculture bacteria

were innoculated in the petri-plates with a sterile cotton swab dipped in the nutrient broth medium. After innoculating, the compounds were dissolved separately in dimethylformamide and poured into the wells with the concentration of 100 µM using a micropipette using stander as *cefotaxime.*

Table-II

Sr.no.	Comp No.	Zone of inhibition	
		S. aureus	*E. coli*
i	3a	28	14
ii	3b	30	22
iii	3c	29	25
iv	3d	23	23
v	3e	25	15
vi	3f	24	18
vii	3g	21	13
viii	3h	29	18
xi	3i	30	11
Std	Cefotaxime	35	25

In the present study, an attempt has been made to design some 2-(piperazinomethylamino)-4, 5-diphenylimidazole derivatives and study their pharmacological activities. From the literature survey it was found that imidazole ring has various activities such as antimicrobial, antifungal, anti-inflammatory while piperazine moiety in the present work piperazine and 4-substituted piperazines was clubbed with 2-amino-4, 5-diphenylimidazole at-'2-' position to obtain compounds 3a-3j. 2-Amino-4, 5-diphenylimidazole itself was synthesized from benzoin and aminomethamine (step-1). The synthesized compounds were tested for various activites. 2-Amino-4, 5-diphenylimidazole was further used for synthesis of 2-(Chloromethylamino)-4, 5-diphenylimidazole with dichloromethane. (step-2). 2-(Choromethylamino)-4, 5-diphenylimidazole was further reacted with substituted piperazines in presence of potassium hydroxide to obtain 2-(piperazinomethylamino)-4, 5-diphenylimidazole. (step-3). The purity and homogeneity of the products was ascertained by thin layer chromatography. Amongst the synthesized compounds 3a and 3j showed highest antibacterial activity against *S. aureus* but less activity against *E.coli.* The compounds 3j and 3c were moderately active. Amongst the synthesized compounds 3a and 3j showed highest antibacterial activity against *S. aureus* but less activity against *E.coli.* The compounds 3j and 3c were moderately active.

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