Synthesis, Characterizations and Antimicrobial Activity of Naphtho imidazole Derivatives of Pyridine

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Abstract

Synthesis of series of some naphtha imidazole derivatives of pyridine under specific conditions. Synthesized compound were purified and studied by yield, melting point, IR, NMR, 1H and mass spectral analysis. The synthesized compound were studied by antimicrobial and antifungal activity by disc diffusion method. The compound were evaluated for antimicrobial activity against bacteria viz streptomyces, , Pseudomonas sp, Escherichia coli and and antifungal activity against various fungi viz Aspergillus niger, Penicillium sp.

Keyword: Naphthalenediamine, Spectral study, Antimicrobial Activity.

INTRODUCTION

Heterocyclic chemistry began in 1800's in step with development of organic chemistry. About half of six million compounds were recorded in chemical abstract are heterocyclic compounds. Nitrogen heterocyclic compounds are present in nucleic acids, proteins, vitamins and other biological important systems[1] . Pyridine studies in the heterocyclic field was studied [2,3]. They play a role in bioactive molecules[4,5]. Imodazole and its derivatives has great significance due to the role in biological system and co-ordination system[6]. Imidazole derivatives show wide pharmacological and therapeutic activities such as anticonvulsant[7], anti-parkinson[8,9] , mono-aminooxidase inhibiting activity[10] , antihistaminic and anti-hypertensive[11]. Histamine H_3 antagonist[12,13] , farnesyltransferase inhibitor[12,14], anti-tumor [15], anti-cancer and anti parasitic[16], herbicidal [17], analgesic[18], fungicidal[19], anti-inflammatory[20], antithrombotic activities[21]. Imidazole and its substituted imidazole has many applications in the field of science[12]. The pharmacological activity like an inhibiter against human and murine tumour cell[23-25], cytotoxicity towards murine tumour cell[26-27].

MATERIALS AND METHODS:

All used Chemicals are AR grade of laboratory chemicals. All melting points were determined by open capillary method. A laboratory oven was used in all experiments. IR spectra were obtained a KBR. 1H NMR spectra were recorded in DMSO with TMS as internal standard. Reactions monitor by TLC in Laboratory. (Ethyl acetate: n-hexane 3:1)

EXPERIMENTAL

Synthesis of 4-(1H-naphtho[2,3-d]imidazol-2-yl)benzenamine (compound 3)

Synthesis of compound 3 by equimolar quantity of naphthalene-2,3-diamine (0.01mol), 4-aminobenzoic acid (0.01mol) in polyphosphoric acid PPA (30 ml) was refluxed at 200^{0}C foe about 5 hrs. Reaction was monitored by TLC. The mixture was cooled and then diluted with distilled water and quenched by 10 % NaOH . It forms two layers aqueous layer was extracted with EtOAC and then concentrated it. It separate the brownish coloured product filter it and then was recrystallized from chloroform as desired compound 3. Measured the yield and melting point.

Synthesis of 3-(4-1-methyl-1-h-cyclopenta[b]naphthalene-2-yl)phenyl) thiazolidin-4-one (compound 4)

A Compound 3 ***4-(1H-naphtho[2,3-d]imidazol-2-yl)aniline*** (0.01mol) and of and Aromatic benzaldehyde **(a –e)** was refluxed for 16hr, in 20 mL of ethanol. The reaction mixture was cooled and concentrated obtained soild was recrystallized from ether: pentane. The crystals found was filtered and obtained as desired comp which was used as such next step without any purification and isolation. Compound 4 (0.01mol) and thioglycollic acid (0.01mol) dissolved in 1,4-dioxane (25 ml), anhydrous zinc chloride (0.5 mg) was added and reflux at 120^{0}C for 20 hrs. The reaction was monitored by TLC after consumption of starting material. Reaction was concentrated to half of solvent separated and yield 3-(4-1-methyl-1-h-cyclopenta[b]naphthalene-2-yl)phenyl) thiazolidin-4-one (compound 5). Synthesized yellowish compound was recrystallized from chloroform. Measured the yield and melting point .

From the compound 4 the compound 5a, 5b, 5c and 5d was synthesized and then recrystallized.

Scheme:

Figure 1.

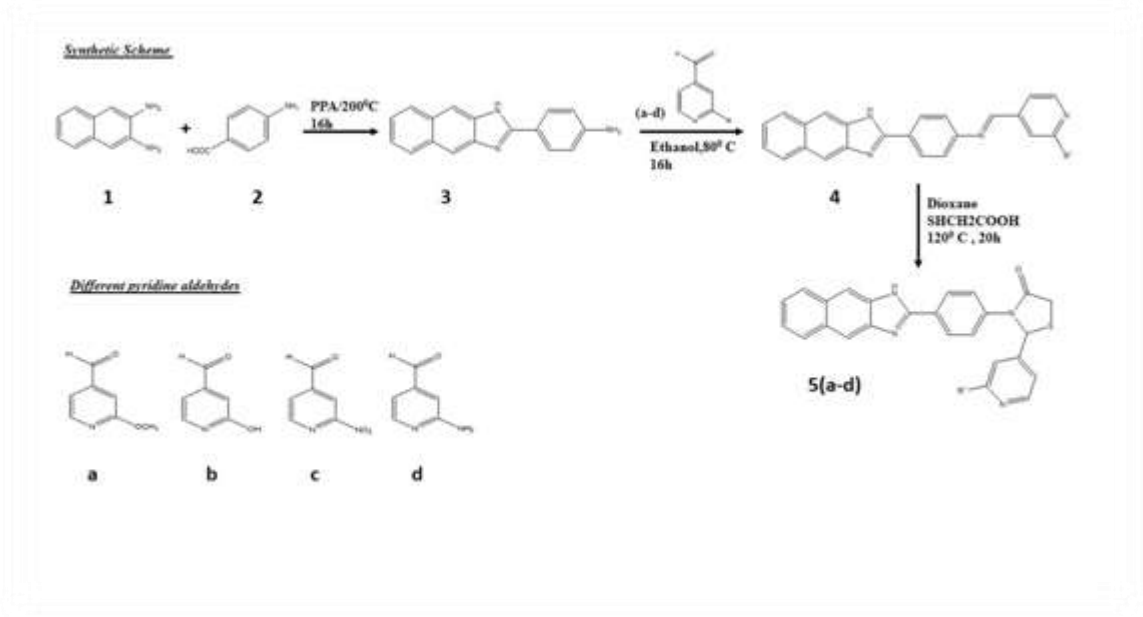
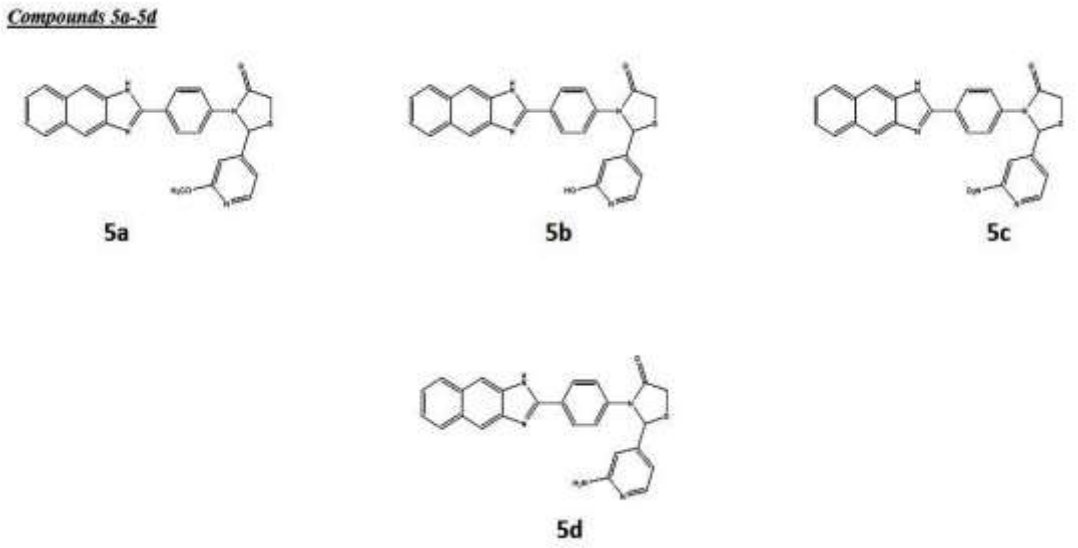


Figure 2.



Antimicrobial and Antifungal Activity

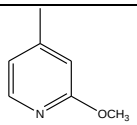
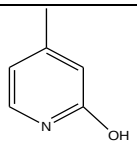
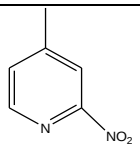
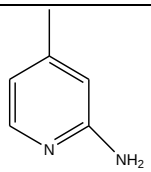
General method for the preparation of cultural media

The antimicrobial activities of some of the synthesized compounds were determined by the agar diffusion method, Nutrient agar (antibacterial activity) and sabouraud's dextrose agar medium (antifungal activity) was prepared and sterilized by an autoclave (121°C and 15 Ibs for 20 min) and transferred to previously sterilized petri dishes (9 cm in diameter). After solidification, petri plates were inoculated with bacterial organisms in sterile nutrient agar medium at 45^{o}C, organisms in sterile sabouraud's dextrose agar medium at45^{o}C in aseptic condition. Sterile Whatmann filter paper discs (previously sterilized in U.V. lamp) were impregnated with synthesized compounds at a concentration of 10µg/ml and 30µg/ml were placed in the organism-impregnated petri plate sunder sterile condition. The plates were left for 30 min to allow the diffusion of compounds at room temperature. Antibiotic discs of streptomycin Std was used as positive control, while DMSO used as negative control. Then the plates were incubated for 24 h at 37 ± 1°C for antibacterial activity and48 h at 37±1°C for antifungal activity. The zone of inhibition was calculated by measuring the minimum dimension of the zone of no microbial growth around the each disc. The synthesized compounds were screened for both antifungal and antimicrobial activity by zone of inhibition method. Antibacterial activity was observed for all the compounds using two strains of Gram (-ve) bacteria *Pseudomonas* sp and *Escherchia Coli* (-ve). The concentrations taken were 10µg/mL.for antifungal activity against *Aspergillus niger*, *Penicillium* sp at same concentration 10µg/mL, all above synthesized nicotinamide compound shows moderate antifungal and antibacterial activity against respective stains. Some shows little bit less than positive control and some shows higher

RESULT AND DISCUSSION

Table 1:

Physico-chemical data of Synthesized compounds

Sr .No	R	% Yield	Molecular Weight	Molecular Formula	Melting Point
4		75	332	$C_{19}H_{14}N_3OS$	215 - 221 ^{0}C
4 a		62	440	$C_{25}H_{20}N_4O_2S$	242 - 247 ^{0}C
4 b		70	426	$C_{24}H_{18}N_4O_2S$	240 - 242 ^{0}C
4 c		69	455	$C_{24}H_{17}N_5O_3S$	252 - 257 ^{0}C
4 d		71	426	$C_{24}H_{20}N_5OS$	248 - 251 ^{0}C

Spectral and Analytical Data

3-(4-1-methyl-1-h-cyclopenta[b]naphthalene-2-yl)phenyl) thiazolidin-4-one

Yellowish solid : Yield 75 % ; MP: 215 - 221^{0}C; 1H NMR data (DMSO), δ (ppm) Aromatic proton-7.69-7.70 (d,2H), 7.72-7.65 (s,2H), 8.11-8.15 (d,2H), 8.0 (dd,2H), 7.43 (dd, 2H), 7.83 (dd,2H), 6.83 (dd,2H), NH 12.56 (bs,1H) N 10.30 (bs), CH 6.44 (s,1H), CH_2 4.02 (s,2H) MS : m/z 452 (M^+)

3-(4-(1H-naphtho[2,3-d]imidazol-2-yl)phenyl)-2-(2-methoxypyridin-4-yl) thiazolidin-4-one

Offwhite solid : Yield 62 % ; MP: 242 - 247^{0}C; 1H NMR data (DMSO), δ (ppm) aromatic proton-7.69-7.70 (d,2H), 7.72-7.65 (s,2H), 8.22-8.25 (d,2H), 8.5 (dd,2H), 7.43 (dd,2H), 7.83 (dd,2H), 6.83 (dd,2H), NH 12.56 (bs,1H) N 10.30 (bs), CH 6.46 (s,1H), CH_2 4.02 (s,2H) OCH_3 3.81 (s,3H), MS : m/z 499 (M^+)

3-(4-(1H-naphtho[2,3-d]imidazol-2-yl)phenyl)-2-(2-hydroxylpyridin-4-yl) thiazolidin-4-one

whitish solid : Yield 70 % ; MP: 240 - 242^{0}C; 1H NMR data (DMSO), δ (ppm) aromatic proton-7.69-7.70 (d,2H), 7.72-7.65 (s,2H), 8.22-8.25 (d,2H), 8.5 (dd,2H), 7.43

(dd,2H), 7.83 (dd,2H), 6.83 (dd,2H), NH 12.56 (bs,1H) N 10.30 (bs), CH 6.46 (s,1H), CH_2 4.02 (s,2H) OH 1.59 (s,1H), MS : m/z 401 (M^+)

3-(4-(1H-naphtho[2,3-d]imidazol-2-yl)phenyl)-2-(2-nitropyridin-4-yl) thiazolidin-4-one

Brownishwhite solid : Yield 69 % ; MP: 252 - 242^0 C; 1H NMR data (DMSO), δ (ppm) aromatic proton-7.69-7.70 (d,2H), 7.72-7.65 (s,2H), 8.22-8.25 (d,2H), 8.5 (dd,2H), 7.43 (dd,2H), 7.83 (dd,2H), 6.83 (dd,2H), NH 12.56 (bs,1H) N 10.30 (bs), CH 6.46 (s,1H), CH_2 4.02 (s,2H) NO 1.01 (s,1H), MS : m/z 501 (M^+)

3-(4-(1H-naphtho[2,3-d]imidazol-2-yl)phenyl)-2-(2-aminopyridin-4-yl) thiazolidin-4-one

Brownish solid : Yield 69 % ; MP: 252 - 242^0 C; 1H NMR data (DMSO), δ (ppm) aromatic proton-7.69-7.70 (d,2H), 7.72-7.65 (s,2H), 8.22-8.25 (d,2H), 8.5 (dd,2H), 7.43 (dd,2H), 7.83 (dd,2H), 6.83 (dd,2H), NH 12.56 (bs,1H) N 10.30 (bs), CH 6.46 (s,1H), CH_2 4.02 (s,2H) NH 2.35 (s,2H), MS : m/z 469 (M^+)

Table 2: Antimicrobial Activity of the compounds using streptomycin std

Compound No	**Antibacterial**		**Antifungal**	
	***Pseudomonas* sp**	***Escherchia Coli***	***Aspergillus niger***	***Penicillium* sp**
4 a	3.9	4.2	4.9	4.1
4 b	3.7	3.8	5.0	3.9
4 c	4.1	3.4	4.8	4.7
4 d	3.3	3.9	4.3	3.6
streptomycin	4.2	4.8	5.1	5.7

All derivatives were active against all tested microorganisms**.** The electron donating group like -OCH_3, were found to increase the antimicrobial properties. The synthesized compounds exhibited significant antibacterial activity and also antifungal activity.

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