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SYNTHESIS CHARACTERIZATION AND BIOLOGICAL EVALUATION OF N,1-DIPHENYL-1H-INDOLE-3-CARBOXAMIDE

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Abstract
Mannich base synthesis of N,1-diphenyl-1H-indole-3-carboxamide were synthesized by the condensation of azido(1-phenyl-1H-indol-3-yl)methanone with substituted aniline .The structure of these newly synthesized compounds were characterized by ^{1}H NMR,^{13}CNMR ,Mass ,IR, and elemental analysis.

Keywords;- Mannich Bases, DMF, Acetone, Substituted Aniline.

Indroduction

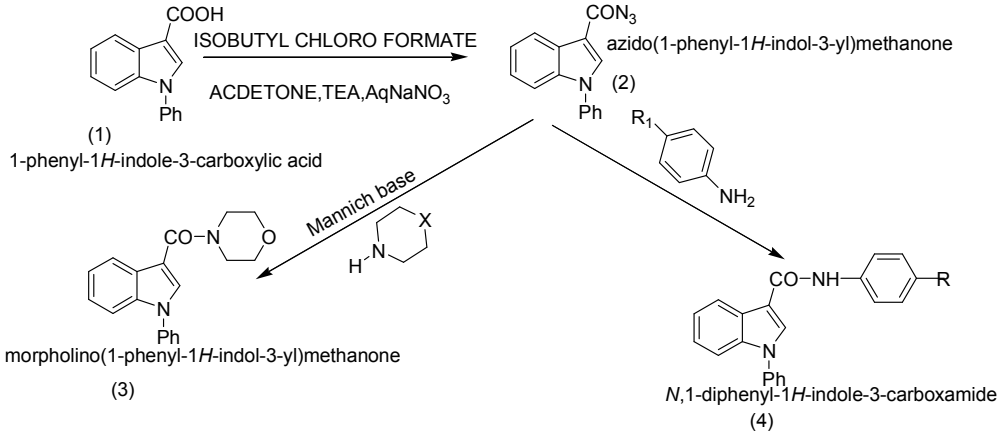
Heterocyclic compounds represent an important class of biological molecules. The hetero cyclic molecules which posses indole, pyrazole and azetidine moieties exhibit wide range of biological activities. Indoles are one of the most important alkaloids molecules found extensively in biological systems, which play vital role in many of the biochemical process. Indole ring constitutes an important basic skelton and development of the drug. The classical indole drugs are indomethacin and indoxole. Indole derivatives found to posses high which includes,antibacterial,analgesic,antipyretic,antifungal,antiflamatory,anthelmintic,cardiovascular,anticonvalsant and selective COX-2 inhibitary activities,anticonvalsant,and selective COX-2 inhibitary activities .

Dermatophytes are infections of keratinized tissue, that is, the epidermis, hair and nails, caused by a group of specialized fungi. The dermatophytes do not invade subcutaneous or deep tissue. *Dermytophyte- Trichophyton schoenleinii* was the first microorganism that was proven to cause an infectious disease of humans [1]. The dermatophytes species can be categorized as an ecological basic as being geophilic, zoophilic or anthrophilic [2]. The geophilic species are natural habitats in the soil, natural habitats of the zoophilic dermatophytes are domestic and wild animals [3]. *Geotrichum candidum* was believed to be part of the normal flora of human skin and gastrointestinal tract. *Geotrichum* is frequently isolated from milk and is recorded as a spoilage

organism on dairy products [4]. Some fungi are parasitic, especially on plants and others are symbiotic with roots and algae [5]. Fungi cells are quite different from plant cells not only by lacking chloroplasts but also by having a cell wall that contains chitin and not cellulose [6]. Indole and its derivatives have attracted much attention because of their unique structure and applications as antihypertensive,, antiallergic, antibiotic and anticonvulsant agents [7-14].

RESULTS AND DISCUSSION

The target compounds were synthesized via the route as shown in Scheme above. The synthon required for the synthesis of the target molecules indole-3-carbaldehyde was prepared by a reported method. Filtered and recrystallized from ethanol. These reactions are summarized in the scheme-1. Yields were moderate to fair(55-70%). The purity of the compounds was monitored by TLC.



Compd	4a	4b	4c	4d	4e	4f
R	-H	$-CH_3$	$-OCH_3$	-Cl	$-NO_2$	$-CF_3$
X	-O-	-O-	-O-	-O-	-O-	-O-

Synthesis of azido(1-phenyl-1H-indol-3-yl)methanone(2)

At this instance to a solution of 4-nitrobenzoyl azide (2)(1eq) in acetone, TEA (3eq) was added and stirred at -150C for 20min.To this reaction mixture Isobutyl Chloro Formate (1:1eq) was added and stirred for 30 min.To the above reaction mixture aq NaN3(3eq) was added and stirred for 20min at 0^0C. The progress of the rection was monitered by TLC with acetone. Ethyl acetate (6:4) as mobile phase .The reaction mixture was cooled poured on ice cold water(20ml),extracted with 10ml diethyl ether (5timesThe organic layer was separated, washed with water, dried over anhydrous Na2SO4 . The dried organic layer was filtered and evaporated under vaccum to give crude oil. The crude oil was purified by column chromatography by using 60- 120 mesh silica gel. The 10% ethyl acetate-pet Ether solvent mixture was used as eluent. After the evaporation of the solvent under vaccum it affords pure 4-nitrobenzoyl azide.

Synthesis of morpholino(1-phenyl-1H-indol-3-yl)methanone (3)

A solution of (2) (0.01mol) and mannich base (0.018mol) in ethanol(20ml) was refluxed for 5hrs. The reaction mixture was cooled and poured in to ice cold water with stirring. The

separated solid was filtered, washed with water and recrystalised from ethanol to afford morpholino(1-phenyl-1H-indol-3-yl)methanone (3)

Synthesis of N,1-diphenyl-1H-indole-3-carboxamide(4)

To a mixture of pure of N,1-diphenyl-1H-indole-3-carboxamide(4) [3] (1eq), in benzene (1eq) was added and refluxed for 16hrs.progress of the reaction was monitored by TLC with acetone. Ethyl acetate (6:4) as mobile phase. After completion of reaction solvent was evaporated under vacuum to give crude residue, purified by column chromatography 60-120 mesh silica gel to give 4-nitro-Nphenylbenzamide(4).

The structures of this newly synthesized compounds 4(a-f) were characterized by1 H-NMR and IR spectral data.

1H NMR spectra (300MHZ, (CD)2 SO,TMS): 8.55 (S, 1H, due to the-NH attached to keto group), 6.75-7.75 (m,5H attached to the indole ring),6.55-7.45(s,4H attached to aniline ring),6.33-7.33(m,5Hdue to phenyl ring.

IR spedtra: The compound (4) shows signals at, 1690 (C=N), 1720 (-C=O), 3150(-NH)

Anti-Bacterial Actillity

The anti bacterial activity of synthesized compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram-positive bacteria screened were staphylococococcus aureas nccs 2079 and bacillus cereus nccs 2106. The gram negative bacteria.screened were Escherichia chia coli nccs 2065 and pseudomonas argunisaNCCS 2200.

The synthesized compounds were used at the concentration of 250 uglml and 500uglml using DMSO as a solvent **Chloromphenicol(5)** disc was used as a standard .(himedia laboratories ltd, Mumbai)

The test results presented in the table -1, suggest that exhibit high activity against the tested bacteria, the rest of the compounds were found to be moderate active against the tested microorganisms.

Antifungal activity

The antifungal activity of synthesized compounds were studied by disc diffusion against the organisms of aspergillus niger NCCS1196 and cadida albicas NCCS34471

Compounds were treated at the counteractions of 500uglm and 1000uglml using DMSO as solicit. The standard used was clot rigmarole 50uglml against both organisms. the test results were presented in the table-2.

TABLE.- Antibacterial activity by disc diffusion method of indole 4(a.f)

Compound	Zone of inhibition (mm)			
	Staphylococcus aures	Bacillus cereus	Escherichia coli	Pseudomonas aeruginosa
4a	15	15	12	17
4b	14	12	18	10

4c	12	12	10	09
4d	16	17	12	11
4e	18	19	18	12
4f	14	15	13	16
Chloromphenicol(5)	28	29	25	17

.Table-;2 Antifungal activity by disc diffusion method for of indole 4(a-f).

Compound	Zone of inhibition (mm)	
	Aspergillums Niger	Candida alb cans
4a	14	16
4b	15	13
4c	17	15
4d	18	17
4e	23	21
4f	15	13
Ketocanazole(50)	21	19

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