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Synthesis and Biological Studies of 4-(4-chloro-1-hydroxynaphthalen-2-YL)-6- aryl-5,6-dihydropyrimidin-2(1H)-one

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ABSTRACT

1-(4- chloro -1-hydroxynaphthalen-2-yl)-ethanone were prepared by refluxing 4- chloro -naphthalen-1-ol with glacial acetic acid in presence of fused $ZnCl_2$ then 1-(4- chloro -1-hydroxynaphthalen-2yl)-2-aryl-prop-2-en-1-one were synthesized from 1-(4- chloro -1-hydroxynaphthalen-2-yl)-ethanones by condensing it with aromatic aldehydes. 1-(4- chloro -1-hydroxy-naphthalen-2-yl)-3-aryl-prop-2-en-1-ones, urea and concentrated HCl in DMF were added and refluxed. Cool & pour in crushed ice, it was then treated with cold NH_4OH solution to get titled compounds. The structure assignment of the new compounds is based on chemical and spectroscopic evidence. All of these titled synthesized compounds are found to posses excellent antimicrobial activities.

Keywords: Synthesis, Biological Studies, antimicrobial study, 4-(Chloro-Naphthalene-2-Yl)-6-Aryl-5, 6- Dihydropyrimidin-2(1h)-One.

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INTRODUCTION

Literature survey reveals that heterocyclic compounds like pyrazoles, pyrazolines, thiazoles, dihydropyrimidin-2-one etc having excellent antimicrobial and antifungal activities [1-5]. Urea is widely used in organic synthesis . urea can react directly with compounds such as acetaldehyde [6], formaldehyde [7], cinnamaldehyde [8] etc forming resins. It also reacts with formaldehyde, propionaldehyde or acetaldehyde to form sprayable sources of nitrogen in aqueous medium and prolonged fertilizer activity [9]. For construction of dihidropyrimidinione by Biginelli reaction is widely used reaction in multiple-component chemical reaction depending on Beta-dicarbonyl compounds, an aryl aldehyde and urea [10].

Dihydropyrimidin-2-one derivatives shows variety of pharmacological activities such as active and safe tumor anti-initiating and multi-potent blocking agent[11], potential calcium channel blockers [12] , analgesic activity [13] , anti-microbial activities [14,15] etc

Synthesis characterization and biological evaluation of titled compound becomes favorite field for many investigator. Their efforts are quite significant in literature. Hence, a series of novel 4-(chloro-naphthalene-2-yl)-6-aryl-5,6-dihydropyrimidin-2(1H)-one compounds from 4-chloro-naphthalen-1-ol has been synthesized and studied for their biological activities.

MATERIALS AND METHOD

The melting points (ºC) were recorded by open capillary method and are uncorrected. IR spectra (υ max in cm-1) were recorded on a Shimadzu FTIR 8300 spectrophotometer using KBr pellets. The 1H NMR spectra were recorded on DRX-300 (300 MHZ) instrument using $CDCl_3$ as solvent (chemical shift in δ ppm) and TMS as internal standard. Thin Layer Chromatography on silica gel-G, was used to check the purity of the compounds.

RESULTS AND DISCUSSION

Synthesis of 1-(4-chloro-1-hydroxynaphthalen-2-yl)-ethanone:

1-(4-Chloro-1-hydroxynaphthalen-2-yl)-ethanone (2) was prepared by refluxing 4- chloro -naphthalen-1-ol with glacial acetic acid in presence of fused ZnCl2.

Synthesis of 1-(4- chloro -1-hydroxy-naphthalen-2-yl)-3-aryl-prop-2-en-1-one (3-6) :

1-(4- Chloro -1-hydroxynaphthalen-2yl)-2-aryl-prop-2-en-1-one were synthesized from 1-(4-chloro -1-hydroxynaphthalen-2-yl)-ethanone by condensing it with aromatic aldehydes.

Synthesis of 4-(chloro-naphthalene-2-yl)-6-aryl-5,6-dihydropy rimidin-2(1h)-one (7-10) :

1-(4- Chloro -1-hydroxy-naphthalen-2-yl)-3-aryl-prop-2-en-1-ones , Urea and concentrated HCl in DMF were added and refluxed for 8 Hours. Cool & pour in crushed ice It was then treated with cold NH4OH Solution to get 4-(chloro-naphthalene-2-yl)-6-aryl-5,6-dihydropyrimidin-2(1H)-one

Spectral Analysis : Spectral interpretation of (9)

IR (ν_{max}) (cm^{-1}): 1699 (C=O, str), 3357 (NH_2, str), 2932 (CH aliphatic) 3092(CH str in Ar), 3230 (NH, bend), 1171 (C-O-C str)

NMR (δ ppm): 1.4-2.1 (m, 2H, -CH_2 of pyrimidinr), 3.8 (s, 3H, -OCH_3) 4.5 (t, 1H, CH of pyramidine),5.5 (s, 1H, NH exchangeable with D2O) , 7.6 – 8.6 (m, 9H, Ar-H)

Antimicrobial studies:

All above 4-(bromo-naphthalene-2-yl)-6-aryl-5,6-dihydropyrimidin-2(1H)-one have been studied for their antimicrobial activity against Escherichia coli, Proteus mirabilis, Staphylococcus aureas, Pseudomonas aeruginosa. The culture of each species was incubated at 37^0C and the zone of inhibition was measured after 24 hr. Results are tabulated in Table 2. Most of these compounds were found active.

Scheme:

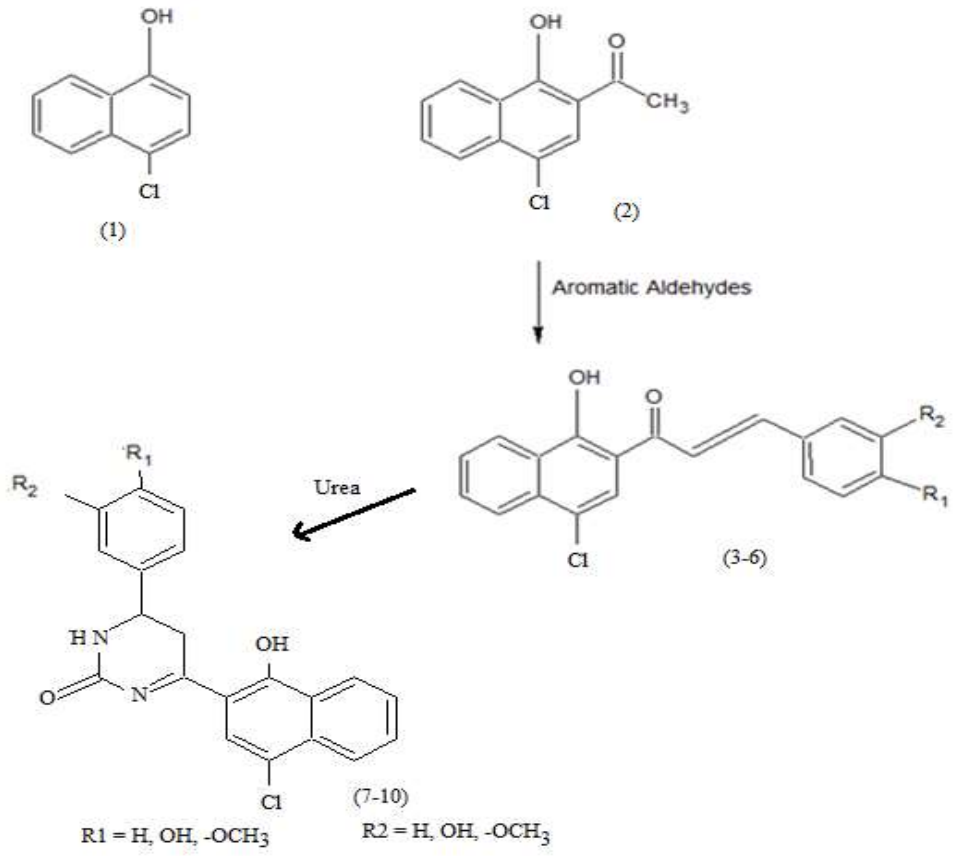

Table 1: Physical Data of Synthesized Compounds

Sr.No.	Compound No	R_1	R_2	Molecular formula	Melting Point ^0C	% Yield	% Nitrogen		R.F. Value
							Found	Calculated	
1	3	$-OCH_3$	-H	--	128^0C	60%	--	--	--
2	4	$-OCH_3$	$-OCH_3$	--	125^0C	58%	--	--	--
3	5	-H	-OH	--	143^0C	62%	--	--	--
4	6	-OH	-H	--	150^0C	57%	--	--	--
9	11	$-OCH_3$	-H	C21H17ClN2O3	245^0C	42%	7.35	7.36	0.55
10	12	$-OCH_3$	$-OCH_3$	C22H19ClN2O4	219^0C	45%	6.80	6.82	0.52
11	13	-H	-OH	C20H15ClN2O3	215^0C	48%	7.63	7.64	0.56
12	14	-OH	-H	C20H15ClN2O3	251^0C	42%	7.61	7.64	0.58

Table 2: Antimicrobial activity

Sr. No.	Compound Number	Antimicrobial activity			
		E-coli	Proteus mirabilis	Staphylococcus aureas	Pseudomonas aeruginosa
1	7	16	11	18	12
2	8	17	19	07	15
3	9	12	10	14	16
4	10	17	09	15	11

Strongly active, range 15-19 Weakly active, range 7-10 mm, Moderately active, range 11-14mm Inactive, -

CONCLUSION

Thus from above results it was observed that these heterocyclic compounds containing Chlorine atom were found effective against Escherichia coli, Proteus mirabilis, Staphylococcus aureas, Pseudomonas aeruginosa. So those compounds can be easily be used for the treatment of diseases caused by test pathogens, only when they does not have toxic and other side effects.

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