International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Synthesis, Characterization and Biological Evaluation of 6-(5-Chloro-8-Hydroxynapthalene-2-yl)-4(4-Hydroxyphenyl)-4-5-Dihydroxypyrimidin-2(1h)-One

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ABSTRACT:
1-(4- Chloro -1-hydroxynaphthalen-2-yl)-ethanone was prepared by refluxing 4-chloronaphthalen-1-ol with glacial acetic acid in presence of fused $ZnCl_2$. From this synthesized compound weprepared 1-(4-Chloro -1- hydroxynaphthalen-2-yl)-3-(4-hydroxy phenyl)-prop-2-en-1-one from condensing 1-(4-Chloro -1-hydroxynaphthalen-2- yl)-ethenone, The final product 6-(5-chloro-8-hydroxynapthalene-2-yl)-4(4-hydroxyphenyl)-4-5-dihydroxypyrimidin-2(1h)-one, bycondensation in presence of urea and concentrated HCl in DMF. The compounds thus synthesized have been characterized by physical and spectral data. This titled synthesized compoundwas screened for antimicrobial study and are found to possess excellent antimicrobial activities due to presence of chlorine as a substituent on main nucleus.

KEYWORDS: Antimicrobial activities, cold NH_4OH solution, concentrated HCl in DMF.

INTRODUCTION:

Dihydropyrimidine-2(1H)- one is classified as heterocyclic compoundscontaining pyrimidine ring with nitrogen atoms in the six-member ring[1-2]. From the last two decades synthesis of dihydropyrimidine-2(1H) one and their derivatives being ainteresting field of research because it have wide spectrum and useful building blocks for designing new compounds with ample of biological and pharmacological application[3,7].

Synthesis of dihydropyrimidine-2(1H) oneand their analogue is increasing tremendously in passes few years.The dihydropyrimidine-2(1H) one and their derivatives have attracted great attention recently in synthetic organic chemistry as it is widely used in the field of drug research as related medical chemistry is an applied science with fundamental roots originated from all branch of chemistry[8]. The term of medical chemistry where the corresponding of drugs to materials useful in pharmacy the term of pharmaceutical science in chemical synthesis as they have been associated with diverse range therapeutic and medical properties[9,10]. The simplest and most common method for the synthesis one pot

three component reaction involving the condensation reaction with benzaldehyde, ethylacetoacetate and urea[11-12].

The newly synthesized chloro-substitituted dihydropyridine derivative have an interesting biological activity such as antitumor[13], anticancer[14], antihypertensive[15], antifungal[16], calcium channel blockers[17],antioxidant[18],anti-microbial[19], anti-inflammatory[20], analgesic compound. Their efforts are quite significant in literature hence considering the scope of dihydropyridine derivatives we have synthesized novel 4-(4-chloro-1-hydroxy naphthalen-2-yl)-6-(4-hydroxy phenyl)-5,6-dihydropyrimidine-2(1h)-one from 4-chloronaphthalen-1-ol and studied for their biological activities.

MATERIALS AND METHOD: -

In a hot glacial acetic acid (80 ml) fused $ZnCl_2$ (50 gm) was added and refluxed till dissolved, then powdered substituted 4-Chloronaphthalen-1-ol (0.01 mole) was added and the mixture was refluxed for about 8 hours then cooled and poured in acidulated water. The solid obtained was filtered, washed, dried and recrystallized from rectified spirit to obtain the product. It was filtered, washed, dried and recrystallized from rectified spirit to obtain 1-(4-Chloro-1-hydroxynaphthalen-2-yl) ethan-1-one. 1-(4-Chloro-1-hydroxynaphthalen-2-yl) ethan-1-one (0.01mole) and 4-hydroxy benzaldehyde (0.02 mole) were added in ethanol solvent (20 ml). To this mixture KOH (10%, 10 ml) solution was added drop wise with constant stirring. The reaction mixture was kept overnight. Then the mixture was poured over crushed ice and little HCl. The product was filtered and recrystallized from ethanol to obtain 1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-hydroxy phenyl)-prop-2-en-1-one. After that 1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-hydroxy phenyl)-prop-2-en-1-one (0.01 mole), urea (0.01 mole) and concentrated HCl in DMF were added and refluxed for 8 hours. Cool and pour in crushed ice. It was then treated with cold NH_4OH solution to get 4-(4-Chloro-1-hydroxy naphthalen-2-yl)-6-(4-hydroxy phenyl)-5,6-dihydropyrimidine-2(1H).

Material and Method -

Synthesisof 1-(4-chloro-1-hydroxynapthalene2-yl)ethanone

1-(4-Chloro-1-hydroxynaphthalen-2-yl) ethan-1-one was prepared by modified Nencki method in which 4-chloro- naphthalen-1-ol was refluxed with glacial acidic acid in presence of fused $ZnCl_2$.

Synthesis of 1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-hydroxy phenyl)-prop-2-en-1-one.

The compound was synthesized from 1-(4-Chloro-1-hydroxynaphthalen-2-yl) ethan-1-one by condensing it with 4-hydroyxbenzaldehyde were added in ethanol solvent and KOH mixture.

Synthesis of 6-(5-chloro-8-hydroxynapthalene-2-yl)-4(4-hydroxyphenyl)-4-5-dihydroxypyrimidin-2(1h)-one

This compound was prepared from 1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-hydroxy phenyl)-prop-2-en-1-one was reflux with urea and concentrated HCl in DMF. It was then treated with cold NH_4OH.

***Table 1. PHYSICAL DATA OF SYNTHESIZED COMPOUNDS**

Sr. no	Compound no	R1	R2	Molecular formula	Melting Point 0C	% Yield	% Nitrogen		R.F Value
							Found	Calculated	
1	1	-OH	-OH	C16H15N2O3Cl	258^{0}C	43%	6.64	6.61	0.58
2	2	-OCH3	-H	C16H17N2O3Cl	224^{0}C	47%	6.24	6.21	0.67
3	3	-H	-OH	C17H15N2OCl	224^{0}C	46%	6.92	6.84	0.54
4	4	-OH	-H	C17H15N2O2Cl	267^{0}C	50%	5.88	5.83	0.55

SCHEME:

DISCUSSIONAND RESULT: -

SPECTRAL ANALYSIS: -

IR(νmax) (cm^{-1}): 1624 (C=O, str), 3346 (NH, str), 1568 (C=N),1172(C-O-C),758(monosubstituted Benzene)

NMR (δ ppm): 1.3-1.8 (m, 2H, -CH_2 of pyrimidine), 10.32 (s, 1H, -OH),3.61 (s, 3H, -OCH_3),2.54 (s, 3H, CH_3,)

ANTIMICROBIAL STUDIES:

All above synthesized 4-(4-Chloro-1-hydroxy naphthalen-2-yl)-6-(4-hydroxy phenyl)-5,6-dihydropyrimidine-2(1H)-onehave been studied for their antimicrobial activity against Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Pseudomonas aeruginosa. The culture of each species was incubated at 370C and the zone of inhibition was measured after 24 hr. Results are tabulated in Table 2. Most of these compounds were found active.

Sr. no	Compound Number	Antimicrobial Activity			
		E-coli	Proteus mirabilis	Staphylococcus aureus	Pseudomonasa eruginosa
1	1	18	17	18	12
2	2	15	10	16	14
3	3	17	13	14	18

4	4	13	15	10	14

Strongly active, range 15-19 mm 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 aureus, Pseudomonas aeruginosa. So those compounds can be easily be used for the treatment of diseases caused by test pathogens, only when they do not have toxic and other side effects.

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