JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF 4-(5-CHLORO-8-HYDROXY NAPHTHALEN-2-YL)-6-(4-METHOXY PHENYL)-5,6-DIHYDROPYRIMIDINE-2(1H)-ONE

[1]Dr. Vinod M. Sherekar and [2]Mr. Nilesh S. Padole
Assistant Professor, Department of Chemistry, Vinayak Vindhyan Mahavidyalaya Nandgaon (Kh), Amravati (M.S), India

ABSTRACT: -

1-(4- Chloro -1-hydroxynaphthalen-2-yl)-ethan-1-one was prepared by refluxing 4-chloronaphthalen-1-ol with glacial acetic acid in presence of fused $ZnCl_2$. By condensing 1-(4- Chloro -1-hydroxynaphthalen-2- yl)-ethan-1-ones with 4- methoxy benzaldehyde, to prepared by 1-(4- Chloro -1-hydroxynaphthalen-2-yl)-3-(4-methoxy phenyl)-prop-2-en-1-one were synthesized. 1-(4- Chloro -1-hydroxynaphthalen-2-yl)-3-(4-methoxy phenyl)-prop-2-en-1-one, urea and concentrated HCl in DMF were added and refluxed. Cool and pour in crushed ice. Treat it with cold NH4OH solution to obtain titled compounds. The compounds thus synthesized have been characterized by physical and spectral data. All of these titled synthesized compounds have been screened for antimicrobial study and are found to possess excellent antimicrobial activities.

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

INTRODUCTION: -

Numbers of Heterocyclic ring compounds plays key role in biological system and has significant role in the industrial sector for the development of drugs and medicine. In the same context, Dihydropyridine derivatives have significant attention in organic and medical chemistry as pharmacological and therapeutic properties[1,2]. In medical chemistry context a great potential in the search for new bioactive compounds and their biological properties specially as anti-infective agents[3,4].

Now a day's as per the demand of society, most of the researcher have engaged in the development of new and known multicomponent reactions as rapidly to intend simple synthesis to large number of novel compounds. As the time changes the chemistry of these compounds changes because these are one of the most advantaged medicinal pharmacophores which appears as an important structural part in many naturally occurring and synthetically prepared medicinal drugs. The synthesis of these heterocyclic compounds and their derivatives is a synthetic challenge in organic reaction[5,7]. In the view of these challenge, report the synthesis, characterization, and antimicrobial activity of the diaryl-substituted pyrimidine via a one-pot reaction[8]. Newly synthesized dihydropyridine derivative which play interesting biological activity such like that antibacterials[9], antimicrobial[10], antihypertensive[11], antitumor[12], calcium channel blockers[13], anticancer[14], antihypertensive[15], antifungal[l6], anti-inflammatory[17], analgesic[18] compound.

Their efforts are quite significant in literature hence considering the scope of dihydropyrimidine derivatives we have synthesized novel 4-(5-chloro-8-hydroxynaphthalen-2-yl)-6-(4-methoxy 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-Methoxy 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-methoxy phenyl)-prop-2-en-1-one. After that 1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-methoxy 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-(5-Chloro-8-hydroxy naphthalen-2-yl)-6-(4-methoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one.

DISCUSSION AND RESULT: -

Synthesis of 1-(4-Chloro -1-hydroxynaphthalen-2-yl)-ethan-1-one.

1-(4-Chloro-1-hydroxynaphthalen-2-yl) ethan-1-one was prepared by modified Nenchis 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-methoxy phenyl)-prop-2-en-1-one.

1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-methoxy phenyl)-prop-2-en-1-one were synthesized from 1-(4-Chloro-1-hydroxynaphthalen-2-yl) ethan-1-one by condensing it with 4-methoxy Benzaldehyde were added in ethanol solvent and KOH mixture.

Synthesis of 4-(5-Chloro-8-hydroxy naphthalen-2-yl)-6-(4-methoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one.

4-(5-Chloro-8-hydroxy naphthalen-2-yl)-6-(4-methoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one were prepared from 1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-methoxy phenyl)-prop-2-en-1-one was reflux with urea and concentrated HCl in DMF. It was then treated with cold NH_4OH.

In present work the compounds under investigation are: -

Compound 1: - 4-(4-Chloro-1-hydroxy naphthalen-2-yl)-6-(4-methoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one.

Compound 2: - 4-(4-Chloro-1-hydroxy naphthalen-2-yl)-6-(3, 4-Dimethoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one.

Compound 3: - 4-(4-Chloro-1-hydroxy naphthalen-2-yl)-6-(3-Hydroxy phenyl)-5,6-dihydropyrimidine-2(1H)-one.

Compound 4: - 4-(5-Chloro-8-hydroxy naphthalen-2-yl)-6-(4-methoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one.

SCHEME: -

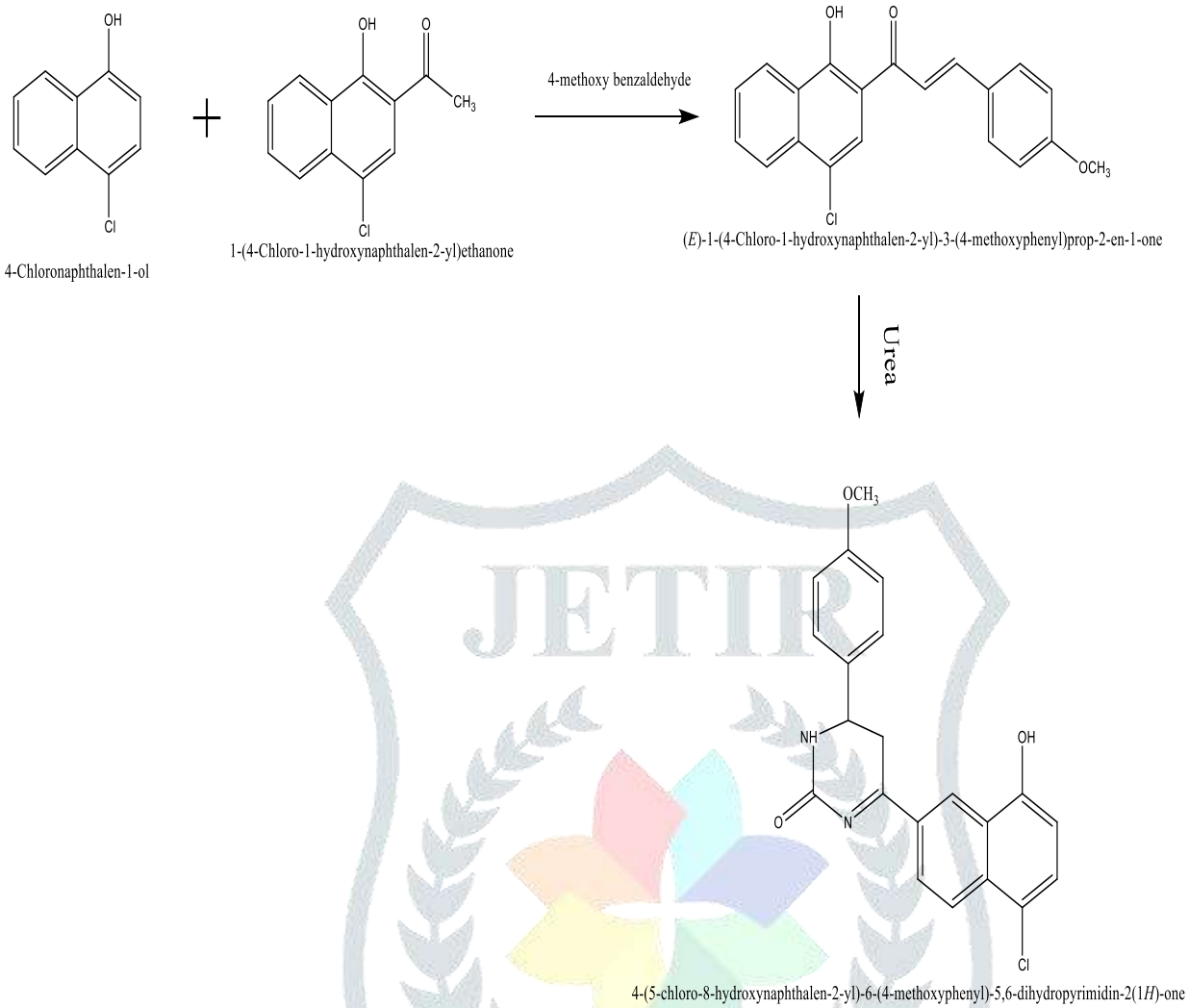
OH
Cl
4-Chloronaphthalen-1-ol
OH
O
CH3
Cl
1-(4-Chloro-1-hydroxynaphthalen-2-yl)ethanone
4-methoxy benzaldehyde
OH
O
OCH3
Cl
(E)-1-(4-Chloro-1-hydroxynaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one
Urea
OCH3
NH
O
N
OH
Cl
4-(5-chloro-8-hydroxynaphthalen-2-yl)-6-(4-methoxyphenyl)-5,6-dihydropyrimidin-2(1H)-one

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	-OCH3	-H	C17H17N2O2Cl	259^{0}C	45%	6.65	6.62	0.59
2	2	-OCH3	-OCH3	C17H19N2O4Cl	225^{0}C	48%	6.23	6.20	0.67
3	3	-H	-OH	C17H15N2OCl	228^{0}C	45%	6.90	6.85	0.56
4	4	-OH	-H	C17H15N2O2Cl	269^{0}C	51%	5.89	5.82	0.55

SPECTRAL ANALYSIS: -

IR(νmax) (cm^{-1}): 1625 (C=O, str), 3345 (NH, str), 1569 (C=N), 1171 (C-O-C),758(monosubstituted Benzene

NMR (δ ppm): 1.3-1.8 (m, 2H, -CH_2 of pyrimidine), 10.31 (s, 1H, -OH),3.62 (s, 3H, -OCH_3),2.53 (s, 3H, CH_3,)

ANTIMICROBIAL STUDIES: -

All above synthesized 4-(5-Chloro-8-hydroxy naphthalen-2-yl)-6-(4-methoxy phenyl)-5,6-dihydropyrimidine-2(1H)-one have been studied for their antimicrobial activity against Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Pseudomonas aeruginosa. The culture of each species was incubated at 370 C 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	Pseudomonas aeruginosa
1	1	18	17	18	10
2	2	16	09	17	14
3	3	17	13	13	17
4	4	14	14	10	13

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 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.

REFERENCES: -

1. Malah-El-A. Mahmoud, Z. Salem, H.H. Abdou, A. Soliman, M. Hassan, R. 2021. Design, ecofriendly synthesis, anticancer and antimicrobial screening of innovative Biginelli dihydropyrimidines using β-aroylpyruvates as synthons. Green Chemistry Letters and Reviews, 14(2): 220-232.
2. Kheffache, O. Lopez-Olmos, C. Rodriguez-Ramos, I. Cherifi, O. 2020. Clean 3,4-Dihydropyrimidones Synthesis via Biginelli Reaction over Supported Molybdenum: Structural and Textural Characteristic of αMoO3. Bulletin of Chemical Reaction Engineering & Catalysis, 15(3): 698-713.
3. Garg, V. Jindal, D. Singh, R. 2020. Synthesis and Evaluation of antifungal activity of 4, 6-Diphenyl-3, 4- Dihydropyrimidine-2-(1h)-one derivatives. Tropical Journal of Pharmaceutical and Life Science, 7(6): 8-12.
4. Graebin, C. Ribeiro, F. Rogerio, K. Kummerle, A. 2019. Multicomponent Reactions for the Synthesis of Bioactive Compounds: A Review current organic synthesis, 16(6): 855-899.
5. Jain, P. Patil, A. 2018. Synthesis of Biologically and Pharmacologically Active dihydropyrimidones/thiones: a review. World Journal of Pharmaceutical Research, 7(11): 410-427.
6. Pisal, P. Sawant, A. Kamble, V. Varala, R. Adil, S. Khan, M. Siddiqui, M.R. 2020. ZrCl4-catalyzed one-pot multi-component synthesis of hexahydropyrano pyrimidinone derivatives. Organic Communication, 13(1): 28-32.
7. Pachore, S. Ambhaikar, N. Siddaiah, V. Khobare, S. kumar, S. Dahanukar, V. Kumar, S. 2018. Successful utilization of β-ketonitrile in Biginelli reaction: synthesis of 5-cyanodihydropyrimidine. Journal of Chemical Science,130(6): 69.
8. Mohammad, I. Abdullah Al-F, Geyer, A. 2017. One-pot synthesis and antimicrobial activity of new 4,6-disubstituted-3,4-dihydropyrimidine-2(1H)-thiones, European Journal of Chemistry. 8(1): 96-100.
9. Bukane, A. Jagdale, B. 2021. DFT Exploration on Molecular Characteristics of 6-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate, Journal of Advanced Chemical Science. 7(1):717-720.

10. Kim, T. Cho, S. Oh, H. Hur, J. Kim, H. Choi, Y.H. Jeon, S. Yang, Y.D. Kim, S.H. 2020. Design of Anticancer 2,4-Diaminopyrimidines as Novel Anoctamin 1 (ANO1) Ion Channel Blockers. Molecules. 25, 5180.

11. Morales, V.F. Medrano, E.A. Elias, J.G. Fierro, M.M. Marquez, E. Mora, J. 2019. Understanding the Lack of Reactivity of 2,4-Dihydroxybenzaldehyde Towards the Biginelli Adduct Using Density Functional Theory Molecular Modeling, Processes.7(8): 521.

12. Zhao, F. Jia, X. Li, P. Zhao, j. Huang, Li, H. Li, L. 2017. $FeCl_3 \cdot 6H_2O$/TMSBr-Catalyzed Rapid Synthesis of Dihydropyrimidinones and Dihydropyrimidinethiones under Microwave Irradiation, Molecules. 22(9): 1503.

13. Patil, V. Gidh, P. Salve, A. 2017. SiO2.TTC: Efficient Catalyst for Synthesis of 3,4-Dihydropyrimidine-2(1H)- ones/Thiones, Pelagia Research Library. 8(2): 247-253.

14. Pramanik, T. Maji, P. 2015. Microwave assisted green synthesis of pharmaceutically important dihydropyrimidinones in fruit juice medium, International Journal of Pharmacy and Pharmaceutical Science. 7(11): 0975-1491.

15. Hamouly, W.E. Amine, K. Tawfik, H. Dahood, D. 2013. Synthesis and antihypertensive activity of certain substituted dihydropyridines and pyrimidinones,
Egyptian Pharmaceutical Journal. 12(1): 20-27.

16. Esfahani, M.N. Montazerozohori, M. Mirrezaee, M.A. Kashi, H. 2014. Efficient and green catalytic synthesis of dihydropyrimidinone (thione) derivatives using cobalt nitrate in solvent-free conditions, Journal of the Chilean Chemical Society. 59(1): 75918-74831.

17. Gein, V. Zamaraeva, T. Gorgopina, E. Dmitriev, M. 2019. A Four Component Biginelli's Reaction, New Opportunities for Synthesis of Functionalized Pyrimidines, Journal of Scientific & Technical Research. 14(4): 10790-10796.

18. Patel, N. Pathan, S. Soni, H. 2019. 3,4-Dihydropyrimidin-2(1*H*)-One Analogues: Microwave irradiated Synthesis with Antimicrobial and Antituberculosis Study, Current Microwave Chemistry. 6(1): 61-70.