BIOLOGICAL STUDY OF 2-(2-AMINO-4-ARYL-6H-1,3-OXAZIN/THIAZIN -6-YL)-4-SUBSTITUTED-NAPHTHALEN-1-OL

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ABSTRACT

2-Acetyl- 4-substituted-1-naphthol have been synthesized from 4-substituted-1-naphthol by refluxing 4-substituted-1-naphthol with glacial acetic acid in presence of fused $ZnCl_2$. Chalcones were synthesized from from 2-acetyl-4-substituted -1-naphthol by condensing it with aromatic aldehydes. Then these chalcones were cyclized with urea/thiourea in the presence of alcoholic KOH to give titled oxazins/thiazins. The synthesized compounds were characterized by elemental analysis, 1H NMR, IR Spectroscopy. All Newly synthesized compound were scanned for their antimicrobial and antifungal activity and all newly synthesized compounds shows an excellent antimicrobial and antifungal activities.

Key Words: Oxazin, Thiazin, Antimicrobial activities , Antifungal activities.

INTRODUCTION

Oxazines are six membered heterocyclic compounds containing one oxygen and one nitrogen. The oxazine derivatives are an important class of heterocyclic compounds which are well known for their use as a monomer for polymer formation[1] , antibacterial[2,3], photochromic agents[4], antituberculor[5], antimalarial[6] , antitumor[7,8] and anti-HIV agents [9,10] . In addition, oxazine nucleus is a part of many biologically important natural products [11,12] and other synthetic bioactive molecules[13-16] including Efavirenz, a benzoxazinone derivative for the treatment of HIV-1 infections[17] .

Thiazines have attracted a great deal of attention from synthetic community due to their diverse type of biological activities[18-23]. Thiazines were prepared by cyclization with thiourea[24,25]. Various useful synthetic analogs with improved therapeutic properties can be obtained from various thiazine derivatives[26,27]. Many class of chemotherapeutic agents containing thiazine derivatives are in clinical use such as anti-inflammatory and analgesics agents[28,29]. Inspired from these observations it was planned to synthesize titled oxazin and thiazine derivatives to evaluate their antibacterial and antifungal activity.

EXPERIMENTAL

All the melting points were taken in silicon oil bath with open capillary tubes and are uncorrected. The structures of titled compounds were established on the basis of elemental analysis and spectral data. Thin Layer Chromatography on silica gel-G, was used to check the purity of the compounds.

The medium used throughout the experiment was HI-Media (Indian make) nutrient agar. For sterilization autoclave is used. The size of zones of inhibition were measured by antibiotic zone reader (Metzer Make).

RESULTS AND DISCUSSION

Synthesis of 2-Acetyl- 4-substituted-1-naphthol

2-Acetyl-4- substituted -1-naphthol was prepared by refluxing 4-substituted-1-naphthol with glacial acetic acid in presence of fused $ZnCl_2$.

Synthesis of 1-(4- substituted -1-hydroxynaphthalen-2yl)-2-aryl-prop-2-en-1-one

1-(4-substituted-1-hydroxy naphtha alen-2yl)-2-aryl-prop-2-en-1-one were synthesized from 2-acetyl-4-substituted -1-naphthol by condensing it with aromatic aldehydes.

Synthesis of 2-(2-amino-4-aryl-6H-1,3-thiazin-6-yl)-substituted-naphthalen-1-ol

Titled thiazine obtained by the action of thio urea with KOH in ethanol on 1-(4- substituted-1-hydroxynaphthalen-2yl)-2-aryl-prop-2-en-1-one.

Synthesis of 2-(2-amino-4-aryl-6H-1,3-oxazin-6-yl)-substituted-naphthalen-1-ol

Titled oxazine obtained by the action of urea with KOH in ethanol on 1-(4- substituted-1-hydroxynaphthalen-2yl)-2-aryl-prop-2-en-1-one.

Antimicrobial activity

All above oxazines and thiazines 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^{o} C and the zone of inhibition was measured after 24 hr. Most of these compounds were found active Activities of titled compounds are summarized in table 1

Antifungal activity

The compounds were taken for screening of antifungal activity against Candida albicans and Aspergillus niger grown on the potato-dextrose-agar medium using disc

diffusion method. The procedure followed for the preparation of test sample was same as that for antimicrobial evaluation. Activities of titled compounds are summarized in table 1

Table 1. PHYSICAL DATA OF SYNTHESIZED COMPOUNDS.

Sr. No.	Compound	% Nitrogen		Antimicrobial activity				Antifungal activity	
		Found	Calculated	P. mirabilis	P. aeruginosa	S. aureus	E. coli	A. Niger	C. albicans
1	2-[2-amino-4-(4-nitrophenyl)-6H-1,3-oxazin-6-yl]-naphthalen-1-ol , Melting Point :158^{0}C, Yield : 45 % , Rf Value : 0.71	11.61	11.63	12	14	10	17	17	18
2	2-[2-amino-4-(3-nitrophenyl)-6H-1,3-oxazin-6-yl]-naphthalen-1-ol , Melting Point :163^{0}C, Yield : 41 % , Rf Value : 0.68	11.62	11.63	13	15	11	16	15	17
3	2-[2-amino-4-(2-nitrophenyl)-6H-1,3-oxazin-6-yl]-naphthalen-1-ol , Melting Point :173^{0}C, Yield : 43 % , Rf Value : 0.62	11.62	11.63	07	15	14	13	12	17
4	2-[2-amino-4-(4-fluorophenyl)-6H-1,3-oxazin-6-yl]-naphthalen-1-ol , Melting Point : 167^{0}C, Yield : 47 % , Rf Value : 0.71	8.61	8.64	14	17	17	16	18	17
5	2-[2-amino-4-(3-chlorophenyl)-6H-1,3-oxazin-6-yl]-naphthalen-1-ol , Melting Point : 169^{0}C, Yield : 45 % , Rf Value : 0.63	7.96	7.99	14	15	13	17	16	17
6	2-[2-amino-4-(2-chlorophenyl)-6H-1,3-oxazin-6-yl]-naphthalen-1-ol , Melting Point : 217^{0}C, Yield : 38 % , Rf Value : 0.58	7.97	7.99	13	12	-	17	18	15
7	2-[2-amino-4-(4-nitrophenyl)-6H-1,3-oxazin-6-yl]-4-chloro-naphthalen-1-ol , Melting Point : 203^{0}C, Yield : 47 % , Rf Value : 0.65	10.61	10.62	14	15	17	13	12	10
8	2-[2-amino-4-(3-nitrophenyl)-6H-1,3-oxazin-6-yl]-4-chloro-naphthalen-1-ol , Melting Point : 175^{0}C, Yield : 39 % , Rf Value : 0.63	10.60	10.62	09	12	13	16	15	17
9	2-[2-amino-4-(2-nitrophenyl)-6H-1,3-oxazin-6-yl]-4-chloro-naphthalen-1-ol , Melting	10.61	10.62	07	13	12	14	17	16

	Point : 221^{0}C, Yield : 48 % , Rf Value : 0.59								
10	2-[2-amino-4-(4-fluorophenyl)-6H-1,3-oxazin-6-yl]-4-chloro-naphthalen-1-ol , Melting Point : 162^{0}C, Yield : 42 % , Rf Value : 0.57	7.80	7.81	17	18	15	16	17	16
11	2-[2-amino-4-(3-chlorophenyl)-6H-1,3-oxazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point : 199^{0}C, Yield : 41 % , Rf Value : 0.58	7.26	7.27	14	12	16	16	17	15
12	2-[2-amino-4-(2-chlorophenyl)-6H-1,3-oxazin-6-yl]-4-chloro-naphthalen-1-ol, Melting Point : 251^{0}C, Yield : 37 % , Rf Value : 0.61	8.84	8.86	07	13	14	12	16	17
13	2-[2-amino-4-(4-nitrophenyl)-6H-1,3-thiazin-6-yl]-naphthalen-1-ol Melting Point: 204^{0}C, Yield : 45 , Rf Value : 0.69	11.13	11.14	08	12	13	14	16	15
14	2-[2-amino-4-(3-nitrophenyl)-6H-1,3-thiazin-6-yl]-naphthalen-1-ol Melting Point: 225^{0}C, Yield : 38 , Rf Value : 0.71	11.12	11.14	17	15	12	18	17	14
15	2-[2-amino-4-(2-nitrophenyl)-6H-1,3-thiazin-6-yl]-naphthalen-1-ol Melting Point: 198^{0}C, Yield : 40 , Rf Value : 0.67	11.13	11.14	12	13	12	11	15	16
16	2-[2-amino-4-(4-fluorophenyl)-6H-1,3-thiazin-6-yl]-naphthalen-1-ol Melting Point 147^{0}C, Yield :52 , Rf Value : 0.57	8.22	8.24	15	16	17	15	16	17
17	2-[2-amino-4-(3-chlorophenyl)-6H-1,3-thiazin-6-yl]-naphthalen-1-ol Melting Point: 158^{0}C, Yield : 39 , Rf Value : 0.68	7.63	7.64	-	15	16	12	11	14
18	2-[2-amino-4-(2-chlorophenyl)-6H-1,3-thiazin-6-yl]-naphthalen-1-ol Melting Point: 128^{0}C, Yield : 38 , Rf Value : 0.71	7.62	7.64	15	07	14	15	16	14
19	2-[2-amino-4-(4-	10.20	10.21	12	13	12	11	14	15

	nitrophenyl)-6H-1,3-thiazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point: 167^{0}C, Yield : 40 , Rf Value : 0.64								
20	2-[2-amino-4-(3-nitrophenyl)-6H-1,3-thiazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point: 171^{0}C, Yield : 43 , Rf Value : 0.65	10.21	10.21	09	13	14	13	14	17
21	2-[2-amino-4-(2-nitrophenyl)-6H-1,3-thiazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point: 187^{0}C, Yield : 42 , Rf Value : 0.57	10.19	10.21	11	14	13	16	17	18
22	2-[2-amino-4-(4-fluorophenyl)-6H-1,3-thiazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point: 141^{0}C, Yield : 47 , Rf Value : 0.59	6.87	6.89	15	16	17	18	16	17
23	2-[2-amino-4-(3-chlorophenyl)-6H-1,3-thiazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point: 177^{0}C, Yield : 45 , Rf Value : 0.65	6.96	6.98	12	11	14	17	14	16
24	2-[2-amino-4-(2-chlorophenyl)-6H-1,3-thiazin-6-yl]-4-chloro-naphthalen-1-ol Melting Point: 173^{0}C, Yield : 44 , Rf Value : 0.62	6.97	6.98	13	09	11	16	17	14

Strongly active , range 15-18 **Weakly active, range 7-10 mm**

Moderately active, range 11-14mm **Inactive, -**

CONCLUSION

Thus from above results it was observed that most of heterocyclic were found more or less effective against *Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans* and *Aspergillus niger.* 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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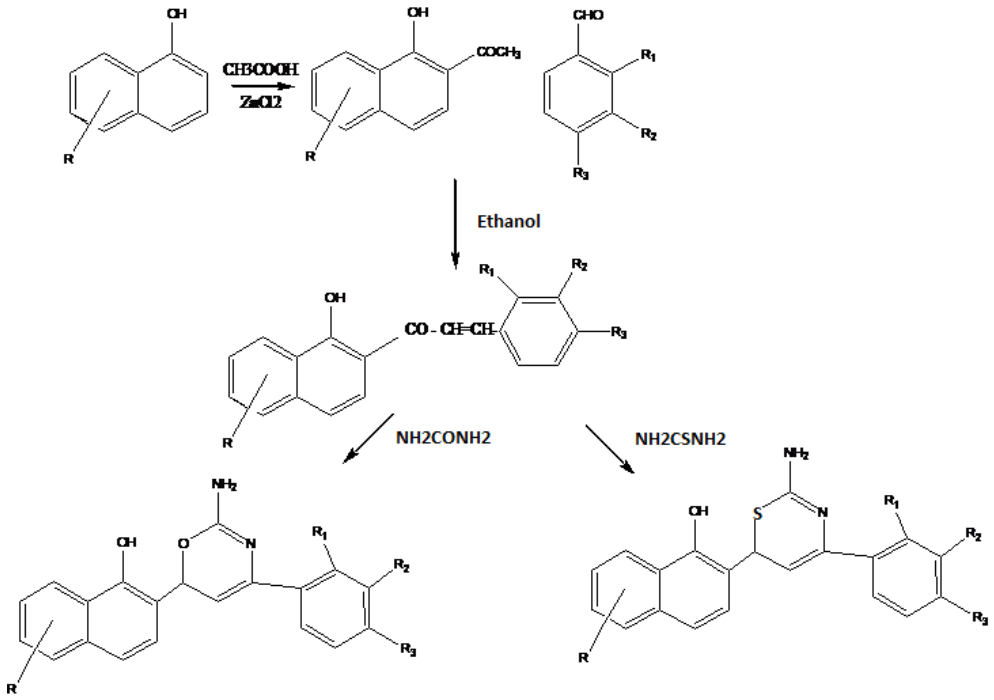

R=H,Cl R_1 = H, NO_2,Cl R_2 = H, NO_2, F R_3= H, NO_2,Cl