IJPAC : **13(1-2)**, (January-June 2018) ISSN: 0973-3876

Synthesis, Characterization, and Fungicidal Activities 3-Chloro-4 (3'-iodo-4'-hydroxy -5-methoxy)–2-azetidinone Derivatives

Dr. Jagmohan Singh Negi

Department of Chemistry, P. N. G.Govt P.G.Collage Ramnagar, Nainital, Uttarakhand (INDIA)
E-mail address: drjsn@rediffmail.com

ABSTRACT: The present study was conducted to evaluate the antimicrobial activity , many phenols and compounds with phenolic groups have antifungal potency A large number of fungicides are formulated as wettable powders; this is the form most commonly used for spray mixes.Nodern wettable powerders are easily wetted and disperse well in water . They simply inhibit fungus growth temporarily.If the fungus is freed from such substance, it would revive. Such a chemical is called a "fungistat" and the phenomenon of temporarily inhibiting the growth is "fungistasis" .Some other chemicals, like certain phenanthrene derivatives and Bordeaux mixture, may inhibit spore production without affecting the growth of vegetative fungistate hyphae.These are called "antisporulaaaaants". 2-amino 4-Phenyl Oxazoleis condensed with appropriate ethanol and piperidine aromatic was refluxed on water bath for 1 hr.Various. obtaining gave benzylidins and thiazolidones respectively and synthesized compounds showed moderate to good antifungal activity with respect to standard drugs

Keywords: 2-amino 4-Phenyl Oxazole , EtOH , anhydrous zink chloride , antifungal activity

INTRODUCTION

Schief bases appear to be an important intermediate in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate. One of the most important types of catalytic mechanism is the biochemical process which involves the condensation of a primary amine in an enzyme usually that of a lysine residue, with a carbonyl group of the substrate to form an imine, or Schiff base. Stereochemical investigation carried out with the aid of molecular model showed that Schiff base formed between methylglyoxal and the amino group of the lysine side chains of proteins can bent back in such a way towards the N atom of peptide groups that a charge transfer can occur between these groups and oxygen atoms of the Schiff bases . Heterocyclic chemistry is currently experiencing arenaissance because of the interest in Heterocyclic chemistry is currently experiencing arenaissance because of the interest in heterocyclic scaffolds as templates for combinatorial chemistry. They are known to possess variety of biological activities such as analgesic, anti-inflammatory, protein kinase C inhibitor.4 Many pyrazole derivatives possess remarkable antiepileptic and antimicrobial,5 antiamoebic,61Azetidinones, commonly known as beta-lactams, are wellknown heterocyclic compounds among the organic and medicinal chemists .The activity of the famous antibiotics such as penicillin, cephalosporin, monobactams and carbapenems are attributed to the presence of azetidinone ring in them. Azetidin can be prepared from Schiff's bases, which arethe condensation products of aldehydes and amino compounds. They are considered significant owing to their wide range of biological application. Recently, some other types of biological activity besides the antibacterial activity have been reported in compounds containing azetidinones ring. Such biological activities include antimicrobial, The structures of the various synthesizedcompounds were assigned on the basis of IR, 1H-NMR spectralNitrogen containing heterocyclic with sulfur atom is an important class of compounds in medicinal chemistry. Thiazoles being an integral part of many potent biologically active molecules such as sulfathiazole (Antimicrobial drug), Ritonavir (Antiretroviral

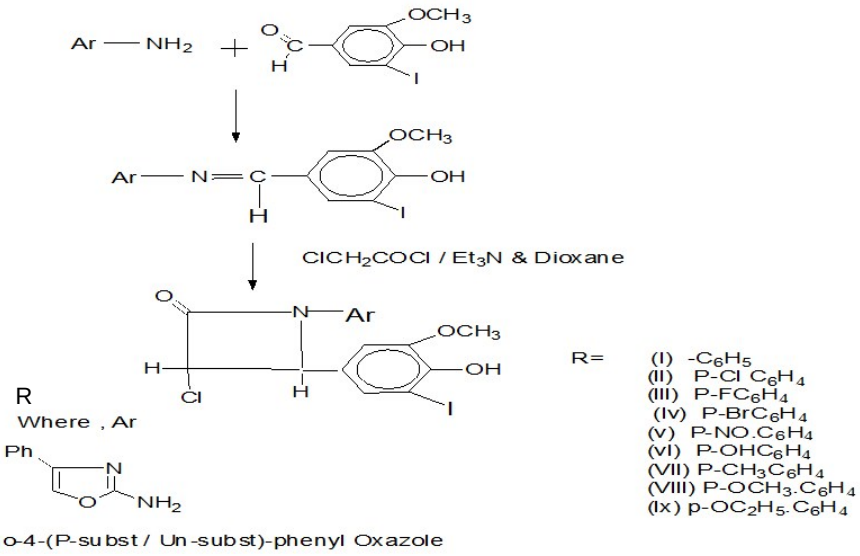
drug), Abafungin (Antifungal drug) with trade name Abase cream and Bleomycin and Tiazofurin (Antineoplastic drugs) have been explored previously

MATERIAL AND METHODS

Thiazoles are important class of natural and synthetic compounds. Thiazole derivatives display a wide range of biological activities such as cardiotonic,fungicidal,sedative, anesthetic ,bactericidal and anti-inflammatory.The synthesis of thiazole derivatives is important of their wide range of pharmaceutical and biological properties .A large number of fungicides are formulated as wettable powders; this is the form most commonly used for spray mixes.Nodern wettable powerders are easily wetted and disperse well in water.A wetting agent is usually present in most wettable powder formulations, but the adding of a spreader-sticker is sometimes desirable, especially on plants with glossy or waxy leaves Fungicide which is effective only if applied prior to fungal infection is called a protectant ; e.g.zaneb,sulpher, etc.On the other hand , fungicide which is capable of eradicating a fungus after it has caused infection and thereby "curing" the plant, is called atherapeutant 8-quinolinol, antibiotics like Aureofungin,etc.Eradicants are those which remove pathogenic fungi from an infection court some chemicals do not kill fungi. The IR spectra were recorded on IR affinity-1, DRS-8000A, Shimadzu, Ptc. Ltd., Japan spectrophotometer. The 1H-NMR was recorded in DMSO on Bruker Advance II 400 MHz spectrometer using TMS as an internal standard. Melting points were determined in open capillary tubes and are uncorrected. The purity of the compounds was checked by TLC-using Silica gel-G (Merck). Column chromatography was performed on silica gel. All the compounds were tested for their antibacterial and antifungal activities by broth dilution method. Nitrogen containing heterocyclic compounds has received considerable attention due to their wide range of pharmacological activity. The pyrazoles and the pyrimidines constitute interesting class of organic compounds with diverse chemical and biological application. They are known to possess variety of biological activities such as analgesic, anti-inflammatory, protein kinase inhibitor. Many pyrazole derivatives possess remarkable antiepileptic and antimicrobial, antiamoebic,.

[1] Synthesis of N-(4-Phenyl-2-Oxazolyl)-2-imino-((3- iodo-4-hydroxy -5- methoxy)benzylidine

A mixture of 2-Amino-4-phenyl Oxazolyl (0.01 mol) and vanillin 0.01 moles in ethanol 30 ml and piperidine 3-4 drops was refluxed on water bath for 1 hours . the reaction mixture was cooled and the solid separated was filtered and recrystallised from ethanol. Yield: (92%), m.p. 160^{0}C , IR(KBr) = 1210-1220 cm-1 (due toC-O-c) , 1665-1670 cm-1 ,(C=N) , 1590 - 1595 cm-1 (C=C) , 3000-3110 cm-1 (due to -OH) , 1640-1625 cm-1 and 1250 cm-1 (due to C=N and C-N) , PMR = δ 4.0-4.2(3H,s.OCH_3) , δ 7.1-7.6(8H, m, ArH) , δ 8.2-8.5(1H,s =CH) , δ 9.5-9.7(1H, s,-OH) Similarly , various N-[4-(P-subst/un-subst)-Phenyl-2-thiazolyl]-2-imino-(4'-Hydroxy-3'-methoxy benzylidine were prepared by using similar reaction procedure and their analytical data are incorporated in the table(l) respectively.



2-Amino-4-(P-subst / Un-subst)-phenyl Oxazole

[2] Synthesis of N-[4-phenyl-2-oxazolyl]-2-chloro-4(3-iodo-4-hydroxy-5-methoxy)–2-azetidinone

The compound first is treated with equimolar quantities of triethy amine. Dissolved indioxane ,chloroacetyl chloride dropwise at 10^{0}C .The reaction mixture was refluxed on water bath for 7 hours . The solvent was removed by distillation and cooled separated solid was recrystallised from chloroform.. Yield 47, M.P 148^{0}c IR(KBr) = 3100 cm-1 (due to OH) , 1640-1625 cm-^{1} AND 1250 ,(C=N) , 1590 - 1595 cm^{-1} (C=C) , 3000-3110 cm-1 (due to -OH) , 1640-1625 cm^{-1} and 1250 cm^{-1} (due to C=N and C-N) , 1210-1220 CM^{-1}(due to C-O-C) , 1660-1670 cm^{-1} (due to C-S-C) 1685 cm$^-$ (due to cyclic > c=o), PMR = ä 3.82-3.86 (3H,s.OCH_3) , ä 9.85(1H, s,OHm), ä 4.15-(2H,s CH_2S) , ä 6.5-6.8(1H, s,-CH), ä 6.5-7.4(8H, M,-Ar-H), Similarly, various methoxy)–2-azetidinon were prepared by using similar reaction procedure and their Similarly , various N-[4-(P-subst/un-subst)-Phenyl-2-Oxazolyl]-2-chloro-(4(3-iodo-4-hydroxy-5 were prepared by using similar reaction procedure and their analytical data are incorporated in the table(ll) respectively .

Table-1 Analytical data of N-[4-(P-subst/un-subst)-Phenyl-2-thiazolyl] -2-imino-(4'-Hydroxy-3'-methoxy benzylidine.

S.N.	Nature of Ar	Molecular Formula	Yield%	M.P. ^{o}C	ELEMENTAL ANALYSIS % of N		% of S	
					Cald	Fond	Cald	Found
la	2-Amino-4-phenyl Oxazole	$C_{17}H_{15}N_2O_2SI$	42	138	09.03	09.00.	10.32	10.25
lb	2-Amino-4(p-chloro)-phenyl thiazole	$C_{18}H_{12}N_2O_2ClSI$	50	140	19.92	19.86	22.77	22.69
lc	2-Amino-4(p-fluoro)-phenyl Oxazole	$C_{17}H_{12}N_2O_2SFI$	52	145	08.53	08.50	09.75	09.70
ld	2-Amino-4(p-bromo)-phenyl Oxazole	$C_{17}H_{12}N_2O_4SBrI$	48	106	07.21	07.11	08.24	08.20
le	2-Amino-4(p-nitro)-phenyl Oxazole	$C_{18}H_{12}N_3O_4SI$	47	148	11.83	11.76	09.01	08.93
lf	2-Amino-4(p-hydroxy)-phenyl Oxazole	$C_{17}H_{13}N_2O_3SI$	48	165	08.53	08.49	09.75	09.73
lg	2-Amino-4(p-methyl)-phenyl Oxazole	$C_{20}H_{16}N_2O_3SI$	52	226	08.64	08.60	09.87	09.80
lh	2-Amino-4(p-methoxy)-phenyl Oxazole	$C_{18}H_{15}N_2O_3SI$	53	246	08.23	08.20	09.41	09.35
li	2-Amino-4(p-ethoxy)-phenyl Oxazole	$C_{20}H_{16}N_2O_3S$	50	250	07.90	07.80	09.03	09.00

Table-2 Analytical data N-[4-Phenyl-2-Oxazolyl]-2-Chloro-4(3-iodo-4-hydroxy-5-methoxy)–2-azetidinone

S.N.	Nature of Ar	Molecular Formula	Yield%	M.P. ^{o}C	ELEMENTAL ANALYSIS % of N		% of S	
					Cald	Fond	Cald	Found
lla	2-Amino-4-phenyl Oxazole	$C_{19}H_{13}N_2O_4ClI$	52	179	07.09	07.05	16.24	16.22
llb	2-Amino-4(p-chloro)-phenyl Oxazole	$C_{19}H_{12}N_2O_4Cl_2I$	53	190	06.50	06.45	14.93	14.90
llc	2-Amino-4(p-fluoro)-phenyl Oxazole	$C_{19}H_{12}N_2O_3ClIF$	50	185	06.54	06.50	15.05	15.00
lld	2-Amino-4(p-bromo)-phenyl Oxazole	$C_{19}H_{12}N_2O_4BrClI$	42	186	05.93	05.88	13.55	13.52
lle	2-Amino-4(p-nitro)-phenyl Oxazole	$C_{19}H_{12}N_3O_4SClI$	50	225	09.56	09.49	14.97	14.55
llf	2-Amino-4(p-hydroxy)-phenyl Oxazole	$C_{19}H_{13}N_2O_4SClI$	42	148	06.82	06.78	15.60	15.55
llg	2-Amino-4(p-methyl)-phenyl Oxazole	$C_{20}H_{15}N_2O_3SClI$	51	144	06.86	06.81	15.68	15.60
llh	2-Amino-4(p-methoxy)-phenyl Oxazole	$C_{19}H_{13}N_2O_4SClI$	50	141	06.60	06.55	15.09	14.55
lli	2-Amino-4(p-ethoxy)-phenyl Oxazole	$C_{21}H_{17}N_2O_4SClI$	54	145	06.39	06.20	14.61	14.02

ANTIFUNGAL SCREENING

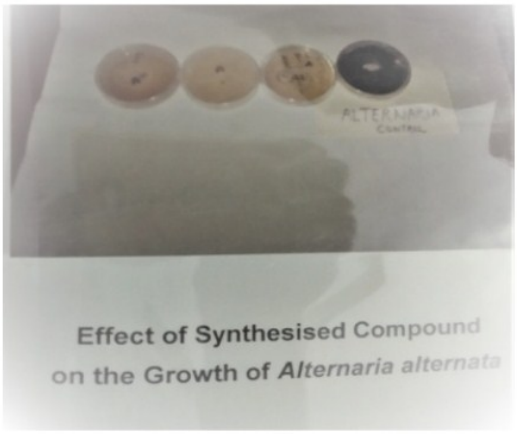
The newly synthesized compounds were evaluated against Alternaria alternate fungus at optimum temperature of 28± 1^{o}C (after 7 days incubation) was observed. After inoculation , All the petridishes were incubated at (25 ± 2^{0C}) for 7 days, the efficiency of varios ant-fungal was recorded by measuring the radial growth of the fungal colony (in mm). The percentage inhibition of fungus mycelia growth was calculated by the equation.

$$\% \text{ of Inhibition} = \frac{[(C- T) \times 100]}{C}$$

Where C and T are average colony diameters (in mm) of the fungal colony in control © and treated (T) plates respectively.

Table-3-Effect of Some Newly Synthesised Antifungal Compounds against *Alternaria alternata* at optimum temperature (After 7 days incubation)

Compound	Dose	Average colony diameter (in mm) in PDA medium	% Inhibition
Control		60.88	
la	0.20	2.8	95.39
lb	0.20	3.2	94.73
lc	0.20	4.0	93.42
ld	0.20	1.9	96.87
le	0.20	2.7	95.55
lf	0.20	2.8	95.39
lg	0.20	9.9	83.71
lh	0.20	3.0	95.06
li	0.20	3.2	94.73
lla	0.20	3.1	94.90
llb	0.20	2.7	95.55
llc	0.20	4.1	93.25
lld	0.20	3.5	94.24
lle	0.20	3.2	94.73
llf	0.20	2.8	95.39
llg	0.20	2.4	96.05
llh	0.20	1.7	97.20
lli	0.20	2.8	95.39
BAVISTIN(Std drug)	0.20	0.22	99.65



RESULT AND DISCUSSION

It is evident from fungal screening data that all the newly synthesized compound tested were found satisfactorially superior over control but inferior to that of standard antifungal (Bavistin) compoundmostly synthesized compound showed marked of the fungal growth in vitro test . It can also be concluded from the result that mostly synthesized compound are good antifungal and showed significant level of antifungal activity and .compound No(lg) showed moderate activity.

ACKNOWLEDGEMENTS

The authors are thankful to the Dr.Adarsh Pandey , Head Department of Botany , G.F.P.G.College Shahjahapur ,U.P for providing necessary facilities the antimicrobial activityand also thankful to CDRI Lucknow for providing IR spectra and micro-care laboratory

REFERENCES

1. B.Das and M.k.Rout. J Indian .Chem.Soc.1955.32.668.
2. L.F.Firser," Experiments in Organic Chemistry "

D.C.Health and CompanyBoston ,. 1957 ,3rd Edn.p 180.

3. Y.L.Nene , Fungicidal Plant diseases Control Oxford and I.B.H. Publishing Company , New Delhi , 1971.
4. A.L. Barry; " The antimicrobial succeptibility Test Principal and Practices, Edicted by Illus lea. and Fabiger 180, Bio. Abstr. 64 (1976). 25183.
5. Ulusoy. N; Kiraz. M; Kucukbasmaci. O. Monatshefte fur chemie., 2002, 133, 1305-1315.
7. Kaplancikli. Z. A; Zitouni. G. T; Revial. G; Guven. K. Arch pharm Res.,. 2004, 27, 10811085
8. Al-Saddi. M. S; Faidallah. H. M; Rostom. S. A. F. Arch. Pharm.Che. Life Sci., 2008, 341,9.42.
9. Tripathi. K. D. Essential of medical pharmacology., 2003, 5th edition, 627-686.
10. Karpov K. A; Nazarenko A.V; Pekarevskii B.V; potekhin. V. M Russian journal of applied chemist 2001, 74, 998-1001.
11. Baselt. T; Rehse. K. Archived der pharmazie., 2008, 24, 645-654.
12. Ashok, K., Rathod, IDiseant. J. PharmTech. Res.**2011**, 3(1), 435.
13. Abid, M., Azam, A., Bioorg. Med. Chem. Lett., **2006**, 16(10), 2812.
14. Amr, Ael-G., Abdel-Lalif, N. A., Abdalla, M. M., Bioorg. Med. Chem., 2006, 14(2), 373.
15. Anandarajagopal, K., Sunilson, A. J., Illavarasu, A., Thangavelpandian,N., R., Int. J. ChemTech. Res., **2010**, 2(1), 45.
16. Doherty, A. M., Ann. Rep. Med.
17. Eichenberger, K., Schweizer, E., Schimdt, P., US Patent
18. Hansford, K. A., Zanzarova, V.,. Dorr, A., Lubell, W. D., J Comb. Chem. **2004**, 6, 893.
19. Heckmann, G., Bach, T., Angew. Chem. Int. Ed. **2005**, 44, 1199. 6 Millan, S. E., Nicholas, D. P., Bioorg. Med. Chem. Lett., **2009**, 19, 222.
20. Krishna, R., Pande, B. R.,. Bharthwal, S. P., Parmar, S. S., Eur. J. Med. Chem., **1980**, 15, 567.
21. Lester A., Itschep M. and Foye, Principle of Medicinal Chemistry, **5**, 833 **(2002).**
22. Regaila, H. A., El-Bayonk, A. K., Hammad, M., Egypt J. . Chem., **1979**, 20, 197.
23. Sharma H.L., Principle of Pharmacology, **2**, 748-752 **(2008).**
24. Schimdt, P., Eichenberger, K., Schweizer, E., German Offen., 196908479, Chem. Abstr. **1970**, 72, 31837u .
25. Satoskar R.S. and Bhandarkar S.D., Pharmacology and Pharmacotherapeutics, **2**, **2641-651 (2007).**
26. Marchant R.Jaysukhal and D.S Chothia .J.Med.Chem, 1970. 13.335: M. S. Shinagare and
27. D.B.Ingle.J.Indian chem..Soc.1976.53.1036.

This document was created with the Win2PDF “print to PDF” printer available at
http://www.win2pdf.com

This version of Win2PDF 10 is for evaluation and non-commercial use only.

This page will not be added after purchasing Win2PDF.

http://www.win2pdf.com/purchase/