I J P A C
© Global Research Publications
ISSN : 0973-3876

Vol. 14 • No. 1-2 • January-June 2019
pp. 77-81

Synthesis and Fungicidal Activity of Some New Derivatives of N-[4-phenyl-5-diazophenyl thiazolyl]-3-Chloro-4-[4'-hydroxy-3-methoxy phenyl-2-azetidinones

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. In the present review, emphasis is given on diverse pharmacological properties associated with substituted thiazolidinones and structurally related thiazolidines. 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. They simply inhibit fungus growth temporarily.. 2-amino 4-phenyl-5-phenylazo thiazole is condensed with appropriate aromatic aldehyde in methanol was refluxed on water bath for 1 hr. Various. obtaining gave of N-[4-phenyl-5-diazophenyl thiazolyl]-3-Chloro-4-[4'-hydroxy-3-methoxy phenyl-2' azetidinones. and by reaction with chloroactyl chloride respectively and synthesized compounds showed moderate to good antifungal activity with respect to standard drugs.

Keywords: chloroactyl chloride, EtOH and Fungicidal activity.

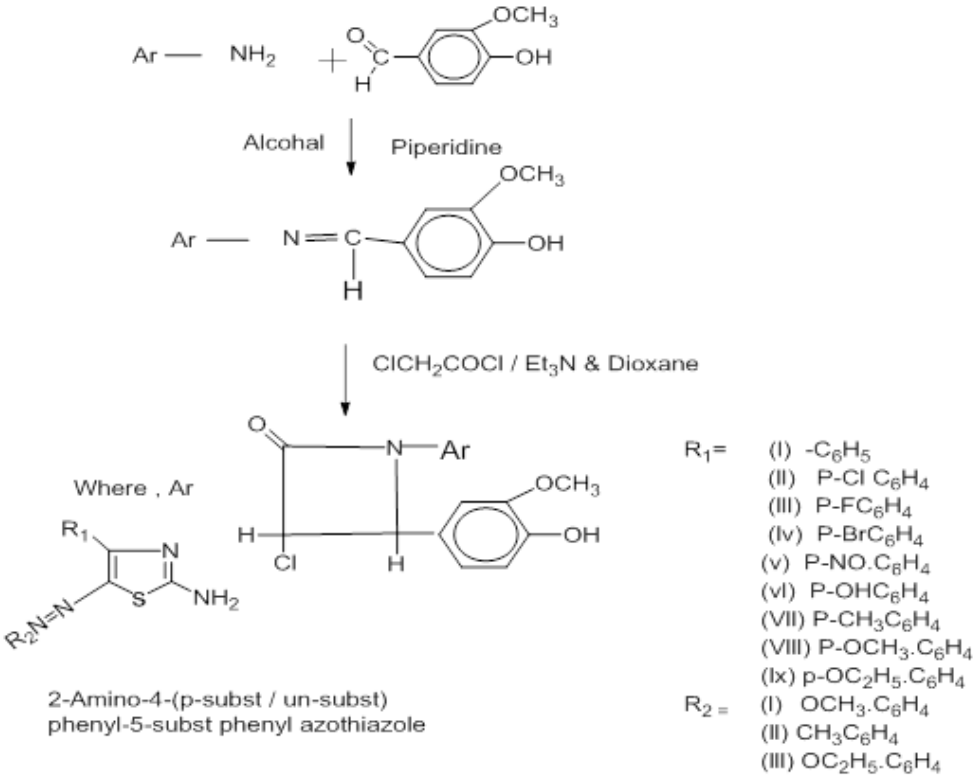
INTRODUCTION

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. The â-lactam heterocycles are still the most prescribed antibiotics used in medicine. They are considered as an important contribution of science to humanity The most widely used antibiotics such as the penicillins, cephalosporins, carumonam, aztreonam, thienamycine and the nocardicins all contain β-lactam rings Azetidinones, which are part of the antibiotic structure, are known to exhibit interesting biological activities . A large number of 3-chloro monocyclic β-lactams possess powerful antibacterial, antimicrobial, anti-inflammatory, anticonvulsant and antitubercular activity. They also function as en zyme inhibitors and are effective of the central nervous system. 2-Aminob nzothiazolesconstitute another class of heterocycles that possess antimicrobial and various other pharmacological activities like diuretic, antiulcer, antihistamine and anticancer properties. 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. 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 containingazetidinones ring. Such biological activities include antimicrobial, The structures of the variou synthesized compounds were assigned on the basis of IR, 1H-NMR spectral,showed excellent antibacterial activities. [15] Based on the previous results, to find out new compounds with better activities and investigate the effect of substituents on fungicidal activity, we decided to further functionalize the N2 atom of triazole. Because the synthesis of N2-substituted 1,2,3-triazole was relatively rare and desirable.

MATERIALS AND METHODS

Melting pVanillin was condensed with different substituted aromatic amines yielding Schiff bases which on cyclization with chloroacetyl chloride and a mixture of Schiff,s bases in Et_3N and dioxane affored various 2-azetidines. The purity of the All the compounds were tested for their The antifungal activities of the prepared compounds were tested against different to standard fungi



2-Amino-4-(p-subst / un-subst) phenyl-5-subst phenyl azothiazole

[I]SYNTHESIS OF 2-[4'-HYDROXY-3'-METHOXY BENZAL IMINO]4-PHENYL-5-DIAZOPHENYL THIAZOLE.

An equimolar quantity of 2-Amino-4-phenyl-5-phenylazo thiazole was react with Vanillin in ethanol (30ml) and piperidine (3-4 drops) was refluxed on water bath for 2 hours . The reaction mixture was cooled and solid separated was filtered and recrystallised from ethanol. respectively. The yield of the product was 52% and the product melts at 145^{0}C. Found:, N(13.90%), S(7.90), Calcd. N(13.93), S(7.96), IR(KBr) 1210-1220cm^{-1} (due to C-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), 1590-1575 cm-1 (due to –N=N). PMR = δ 4.0-402 (3H, s.OCH_3), δ 7.1 – 7.6 (13H, m, ArH), δ 8.2-8.5(1H, s =CH), δ 9.5-9.7(1H, s, -OH) Similarly, various 2-[4'- hydroxy-3'-methoxybenzal imino] 4 (p-subst/ un-subst) phenyl-5-diazophenyl thiazole were prepared by using similar reaction procedure and their analytical data are incorporated in the table (l) respectively

Analytical data of 2-[4'- hydroxy-3'-methoxy benzal imino]4-(p-subst/un-subst) phenyl-5-(p-subst/un-subst) diazophenyl thiazole.

S.N.	Nature of Ar	Molecular Formula	Yield %	M.P. ^{O}C	ELEMENTAL ANALYSIS			
					% of N		% of S	
					Cald	Fond	Cald	Found
I_i	2-Amino-4-phenyl -5-phenyl azo thiazole	$C_{23}H_{18}N_4O_2S$	52	145	13.52	13.50	7.72	7.70
Iii	2-Amino-4(p-chloro)pheny-5-phenyl azo thiazole	$C_{23}H_{17}N_4O_2SCl$	50	140	12.48	12.46	7.13	7.10
Iii	2-Amino-4(p-fluoro)pheny-5-phenyl azo thiazole	$C_{23}H_{17}N_4O_2SF$	52	145	12.96	12.92	7.40	7.38
Iiv	2-Amino-4(p-bromo)pheny-5-phenyl azo thiazole	$C_{23}H_{17}N_4O_2SBr$	48	106	11.38	11.35	6.50	6.48
Iv	2-Amino-4(p-nitro)pheny-5-phenyl azo thiazole	$C_{23}H_{17}N_5O_4S$	47	148	15.25	15.23	6.97	6.95
Ivi	2-Amino-4(p-hydroxy)pheny-5-phenyl azo thiazole	$C_{23}H_{19}N_4O_3S$	48	210	13.02	13.00	7.44	7.40
Ivii	2-Amino-4(p-methyl)pheny-5-phenyl azo thiazolepheny	$C_{24}H_{20}N_4O_2S$	52	140	13.08	13.05	7.47	7.45
Iviii	2-Amino-4(p-methoxy)-phenyl-5-phenyl azo thiazole	$C_{24}H_{20}N_4O_3S$	53	210	12.61	12.60	7.20	7.18
Iix	2-Amino-4-pheny-5-(p-methoxy) phenyl azo thiazole	$C_{24}H_{20}N_4O_3S$	51	162	12.61	12.60	7.20	7.19
Ix	2-Amino-4-(P-methyl))-phenyl-5phenyl azo thiazole	$C_{24}H_{20}N_4O_2S$	52	125	13.08	13.04	7.47	7.44
Ixi	2-Amino-4-pheny-5(p-ethoxy))-phenyl azo thiazolepheny	$C_{25}H_{23}N_4O_3S$	52	135	12.20	12.19	6.97	6.95

Table- 2 N-[4-(subst/un-subst)phenyl-5-(subst/un-subst) diazophenyl thiazolyl]-3-Chloro-4-[4'-hydroxy-3-methoxy phenyl-2'azetidinones

S.N.	Nature of Ar	Molecular Formula	Yield	%M.P. ^{O}C	ELEMENTAL ANALYSIS			
					% of N		% of S	
					Cald	Fond	Cald	Found
Iii	2-Amino-4-phenyl -5-phenyl azo thiazole	$C_{24}H_{19}N_4O_3SCl$	46	144	11.70	11.68	6.68	6.65
II.ii	2-Amino-4(p-chloro)pheny-5-phenyl azo thiazole	$C_{24}H_{18}N_4O_3SCl$	44	140	10.93	10.90	6.25	6.24
II.iii	2-Amino-4(p-fluoro)pheny-5-phenyl azo thiazole	$C_{24}H_{18}N_4O_3SFCl_2$	48	142	12.45	12.43	6.44	6.42
II.iv	2-Amino-4(p-bromo)pheny-5-phenyl azo thiazole	$C_{24}H_{18}N_4OSBrCl$	42	145	10.06	10.04	5.75	5.73
II.v	2-Amino-4(p-nitro)pheny-5-phenyl azo thiazole	$C_{24}H_{18}N_5O_5SCl$	50	150	13.37	13.35	6.11	6.09
II.vi	2-Amino-4(p-hydroxy)pheny-5-phenyl azo thiazole	$C_{24}H_{18}N_5O_5SCl$	48	154	11.32	11.30	6.47	6.45
II.vii	2-Amino-4(p-methyl)pheny-5-phenyl azo thiazolepheny	$C_{24}H_{19}N_4O_4SCl$	60	126	11.37	11.35	6.29	6.25
II.viii	2-Amino-4(p-methoxy)-phenyl-5-phenyl azo thiazole	$C_{24}H_{21}N_4O_4SCl$	51	162	11.01	11.00	6.29	6.25
II.ix	2-Amino-4-pheny-5-(p-methoxy) phenyl azo thiazole	$C_{24}H_{21}N_4O_4SCl$	64	176	10.71	10.68	6.12	6.10
II.x	2-Amino-4-pheny-5(pmethyl))pheny azo thiazole	$C_{24}H_{19}N_4O_4SCl$	44	140	11.01	11.00	6.29	6.24
II.xi	2-Amino-4-pheny-5(p-ethoxy))-phenyl azo thiazolepheny	$C_{26}H_{23}N_4O_4SCl$	64	176	10.71	10.65	6.12	6.09

[2]N-[4-PHENYL-5-DIAZOPHENYL THIAZOLYL]-3-CHLORO-4-[4'-HYDROXY-3-METHOXY PHENYL-2'AZETIDINONES

An equimolar quantity of compound(I) and triethylamine dissolved in dioxane (25 ml), Chloro-acetyl chloride (0.12) was added dropwise at10^{0}, The reaction mixture was refluxed for 6 hours. Thenhalf of the solvent was removed bydistiiation and cooled, separated solid was recrystallised from chloroform respectively. The yield of the product was 62% and the product melts at 153^{0}C. Found:, N(11.10), S(6.31), Calcd.N (11.13) S(6.36), IR (KBr) 1210-1220 cm^{-1} (due to C-O-C). 1760 cm-1 (due to C=O), 1610 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 3.85 (3H, s.OCH_3), δ 7.1 – 7.6 (13H, m, ArH), δ 8.2-8.5(1H, s -CH), δ 9.5-9.7 (1H, s, -OH), δ 4.53 (1H, s.OCl). Similarly, N-[4-(subst/un-subst)phenyl-5-(subst/un-subst) diazophenyl thiazolyl]-3-Chloro-4-[4'-hydroxy-3-methoxyphenyl-2'azetidinones were prepared by using similar reaction procedure and their analytical data are incorporated in the

ANTIFUNGAL SCREENING

The newly synthesized compounds were evaluated against Alternaria alternate fungus at optimum temperature of 28± 1°C (after 7 days incubation) was observed. After inoculation , All the petridishes were incubated at (25 ± 2°C) 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 (c) and treated (T) plates respectively.

Effect of Some Newly Synthesised Antifungal Compounds against *Alternaria alternata* and Fusarium solan in at optimum temperature (After 7 days incubation)

Compound	Dose	Average colony diameter (in mm) in PDA medium	% Inhibition
Control		60.88	
la	0.20	2.7	94.39
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
lla	0.20	3.1	94.90
llb	0.20	2.6	94.55
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
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, for providing necessary facilities the antimicrobial activityand also thankful to CDRI Lucknow for providing IR spectra and micro-care laboratory.

REFERENCES

1. Krishna, R., Pande, B. R., Bharthwal, S. P., Parmar, S. S., Eur. J.Med. Chem., **1980**, 15, 567
2. Heckmann, G., Bach, T., Angew. Chem. Int. Ed. **2005**, 44, 1199. 6Millan, S. E., Nicholas, D. P., Bioorg. Med. Chem. Lett., **2009**, 19, 222.
3. Chinnasamy, R.P., Sundararajan, R., Govindaraj, S. Synthesis, characterization and analgesic activity of novel Schiff base of isatin derivatives, J. Adv. Pharm. Technol. Res., 2010, 1, 342–347.
4. Baselt. T; Rehse. K. Archived der pharmazie., 2008, 24, 645-654.

   1-Ashok, K., Rathod, IDiseant. J. PharmTech. Res. **2011**, 3(1), 435.
5. El-Faham, A., Hozzein, W.N., Wadaan, M.A.M., Khattab, S.N., Ghabbour, H.A., Fun, H.K., Siddiqui, M.R. Microwave synthesis, characterization and antimicrobial activity of some novel isatin derivatives, J. Chem. 2015, 1–8, DOI: 10.1155/2015/716987; (b) Patel. A., Bari, S., Talele, G., Patel, J., Sarangapani, M. Synthesis and antimicrobial activity of some new isatin derivatives, Iranian J. Pharm. Res., 2006, 4, 249–254, (c) Aanandhi, M.V., George, S., Vaidhyalingam,

V. Synthesis and antimicrobial activities of 1-(5-substituted-2- oxo-indolin-3-ylidene)-4-(substituted pyridin-2-yl) thiosemicarbazide, Arkivoc, 2008, 11, 187–194.

6. Fan, Z.J., Yang, Z.K., Zhang, H.K., Mi, N., Wang, H.A., Cai, F., Zuo, X., Zheng, Q.X., Song, H.B. Synthesis, crystal structure, and biological activity of 4-methyl1,2,3-thiadiazole-containing 1,2,4-triazolo[3,4-b] [1,3,4] thiadiazoles, J. Agric. Food Chem., 2010, 58, 2630–2636.
7. Singh, G., Sharma, A., Kaur, H., Ishar, M. Chromanylisoxazolidines as antibacterial agents: Synthesis, biological evaluation, quantitative structure activity relationship, and molecular docking studies, Chem. Biol. Drug. Des., 2016, 87, 213–223
8. Tang, Z.L., Xia, Z.W., Chang, S.H., Wang, Z.X. Synthesis and fungicidal activity of novel 2-aryl-3- (1,3,4-thiadiazolyl)-6(8)-methyl-1,3-benzoxazines, Bioorg. Med. Chem. Lett., 2015, 25, 3378–3381.
9. Li, Y.X., Lei, S.F., Chen, D.Z., Liu, Y.L., Wei, D.C. Preparation of benzene ring containing halogenated triazole compounds as fungicides, Chem. Abstr., 2016, 165, 317154.
10. Faraq, A.A. Synthesis and antimicrobial activityof 5-(morpholinosulphonyl)isatin derivatives incorporating a thiazole moiety, Drug Res., 2015, 65, 373–379, (b). Chaithanya, B., Kasiviswanath, I.V., Chary,D.P.Synthesis and pharmacological screening of isatin-3-[N2-(benzimidazol-1-acetyl)]hydrazone, Bull. Chem. Soc. Ethiop., 2019, 33, 321–329. (c). Yadav, M., Sachan, N., Kumar, S., Husain, A. Syntheses and pharmacological activities of isatin derivatives, J. Drug Deliv. Ther., 2019, 9, 744–748.
11. Thanh, N.D., SonHai, D., Bich, V.T., Hien, P.T., Duyen, N.T., Mai, N.T., Dung, T.T., Toan, V.N., Kim Van, H.T., Dang, L.H., Toan, D.N., Thanh Van, T.T. Efficient click chemistry towards novel 1H-1,2,3- triazole-tethered 4H-chromene-d-glucose conjugates: Design, synthesis and evaluation of in vitro antibacterial, MRSA and antifungal activities, Eur J Med Chem., 2019, 167, 454–471