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Synthesis And Antimicrobial Evaluation of some Novel (5Z)-5- (4-substitutedbenzylidene)-2- (4-nitrophenyl)[1,3] thiazolo [3,2-b] [1,2,4] triazol-6- (5H)-one derivatives

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Abstract

A series of [1,2,4] triazol-6- (5H)-one derivatives[A_{1-9}] has been synthesized by the cyclization of the 1-acyl-thiosemicarbazide (1) in alkaline medium followed by acidification with 37% HCl gives 5- (4-nitrophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (2). Mixture of 5-(4-nitrophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (2), chloroacetic acid, required aromatic aldehyde, anhydrous sodium acetate, acetic anhydride and acetic acid was refluxed for 6 hr. which gives (5Z)-5- (4-substitutedbenzylidene)-2- (4-nitrophenyl)[1,3] thiazolo[3,2-b] [1,2,4] triazol-6- (5H)-one derivatives (A_{1-9}) The crude products were recrystallized from methanol.

Keywords: Thiosemicarbazide, 1,2,4-triazoles, [1,2,4] triazol-6- (5H)-one derivatives, disc diffusion method, antifungal activity.

Introduction

In the last few decades, the chemistry of 1,2,4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. 1,2,4-triazoles represent important class of heterocyclic compounds. 1,2,4-triazoles possess a wide range of bioactivities viz. anti-inflammatory[1-2], anticancer[3-4], antimicrobial activity[5-9]. 1,2,4-triazoles has potential to bind with the receptors and enzymes to produce different pharmacological actions. The aim of present investigation is a trial to combine the structural features of with 1,2,4-triazoles. The target compounds which are structurally-related to previously reported pharmacologically-active compounds are expected to possess anti-inflammatory and antimicrobial activities. An attempt is to synthesize some Novel (5Z)-5- (4-substituted benzylidene)-2- (4-nitrophenyl)[1,3] thiazolo [3,2-b] [1,2,4] triazol-6- (5H)-one derivatives.

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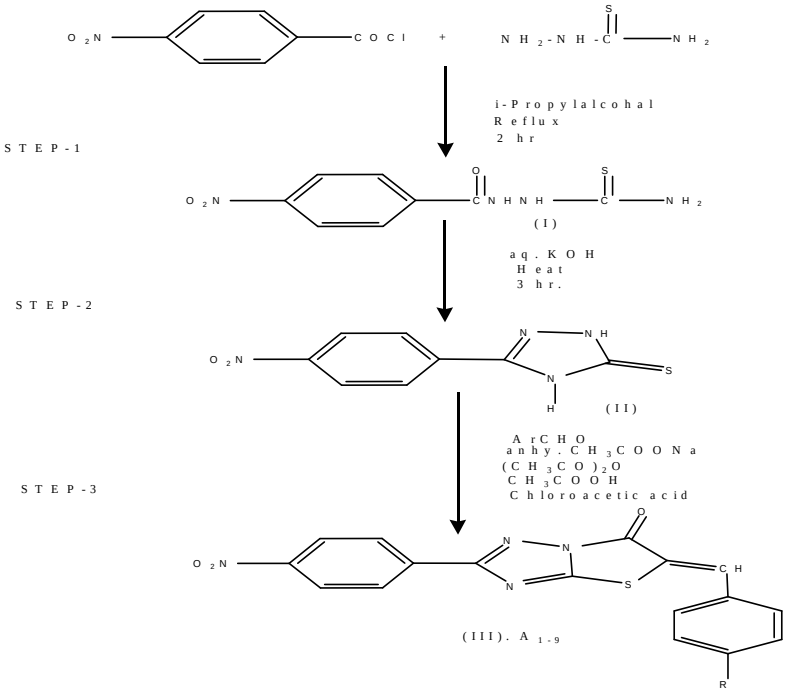
Material and Method

The chemicals used for the experimental work were commercially procured from various chemicals units like Hi Media (Mumbai), Loba chemicals, Qualigens (Mumbai), S.D. fine chemical (Mumbai), E. Merck (Mumbai), CDH (New Delhi) and Samar chemical India. The solvents and reagents were of AR grade and some were LR grade purified before the use. The commercially available grade of solvents and reagents were found to be of adequate purity. Melting points were taken by Thiel's melting point tube (capillary tube method) and m.p. apparatus and are uncorrected. The IR spectra were recorded in KBr on Perkin-Elmer-720 spectrophotometer. The synthesized compounds (A_1-A_9) have been screened for antimicrobial (antibacterial against *Staphylococcus aureus* (MTCC-96), *Escherichia coli* (MTCC-443) and antifungal activity *Candida albicans* (MTCC-227) by using Disc-Diffusion Method.

(5Z)-5- (4-substitutedbenzylidene)-2- (4-nitrophenyl)[1,3] thiazolo [3,2-b] [1,2,4] triazol-6-(5H)-one (A_{1-9}) **(General Method).**

A mixture of 2.7mmol 5- (4-nitrophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione (II), 4.1 mmol chloroacetic acid, 2.7mmol various aromatic aldehyde, 0.54 g of anhydrous sodium acetate, 4 ml of acetic anhydride and 5.5 ml of acetic acid was refluxed for 6 hr. which gives (5Z)-5- (4-substitutedbenzylidene)-2- (4-nitrophenyl)[1,3]thiazolo [3,2-b] [1,2,4] triazol-6-(5H)-one derivatives (A_1-A_9) The crude products were recrystallized from methanol. The physical and IR spectral data of all the synthesized compounds are given in Table-I & Table-II.

Reaction Scheme



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Biological Activity

Antimicrobial activities[10] (antibacterial and antifungal) of all the compounds A_1 to A_8 were screened against bacteria such as *Staphylococcus aureus* (MTCC-96), *Escherichia Coli* (MTCC-443) and against human pathogenic fungus *Candida Albicans* (MTCC-227) using agar disc diffusion method. Ciprofloxacin for bacteria and fluconazole for fungus were as reference drugs. Sterilized cork bore with 1.3 cm outer diameter was used to cut cups in the petridish contains the seeded agar media. The solution of synthesized compound (0.5 ml) was added aseptically to the cups. The dishes with the bacterial culture were incubated at 37°C for 24 hours. Whereas the dishes with fungal culture were kept at room temperature for 72 hours to facilitate growth. The zone of inhibition were observed then measured and compared that of standard. The microbial growth inhibitions were shown in Table-III.

% inhibition = (C-T) x 100/C

Where C and T are diameter (in mm) of fungus colony in control and treated plates respectively.

Results and Discussion

All the compounds A_1-A_9 were screened for antimicrobial activity and evaluated by agar disc diffusion method using *S. Aureus*, *E. Coli* and *C. Albicans* by known method[7] at the three concentration of 100 ppm. The screening data of compounds are listed in Table III**.** Results were compared with commercial fungicide miconazole tested under similar conditions. The percentage inhibition has been calculated by the formula

% inhibition = (C-T) x 100/C

Where C and T are diameter (in mm) of fungus colony in control and treated plates respectively.

Table 1.Physical Data of the Compounds Synthesized- (A_1-A_9)

Comp. No.	R	R’	M.P. (^{0}C)	Yield (%)	Molecular Formula	R_f
A_1	*p*-$NO_2C_6H_5$	-C_6H_5CHO	218^{0}C	68.57	$C_{17}H_{10}N_4O_3S$	0.4
A_2	*p*-$NO_2C_6H_5$	*p*-ClC_6H_4CHO	204^{0}C	79.36	$C_{17}H_9ClN_4O_3S$	0.3
A_3	*p*-$NO_2C_6H_5$	*p*-OHC_6H_4CHO	227^{0}C	58.82	$C_{17}H_{10}N_4O_4S$	0.5
A_4	*p*-$NO_2C_6H_5$	*p*-$CH_3C_6H_4CHO$	213^{0}C	66.00	$C_{18}H_{12}N_4O_3S$	0.4
A_5	*p*-$NO_2C_6H_5$	*p*-$OCH_3C_6H_4CHO$	211^{0}C	68.85	$C_{18}H_{12}N_4O_4S$	0.3
A_6	*p*-$NO_2C_6H_5$	*p*-$NO_2C_6H_4CHO$	209^{0}C	51.42	$C_{17}H_9N_5O_5S$	0.2
A_7	*p*-$NO_2C_6H_5$	3,4-Di-$OCH_3C_6H_3CHO$	232^{0}C	51.51	$C_{19}H_{14}N_4O_5S$	0.6
A_8	*p*-$NO_2C_6H_5$	*p*-Di-$CH_3NH_2C_6H_2CHO$	247^{0}C	55.85	$C_{19}H_{15}N_5O_3S$	0.5
A_9	*p*-$NO_2C_6H_5$	4-OH-3-$OCH_3C_6H_3CHO$	219^{0}C	45.71	$C_{18}H_{12}N_4O_5S$	0.4

Table 2.Spectral Data of the Compounds Synthesized (A_1-A_9)

COMP.	IR (cm^{-1})
A_1	1736.9 (C=O), 1593.6 (C=N), 1580.6 (C=C), 1670.9 (N=O), 1112.6 (C-S-C) str, 3027.1 (C-H)
A_2	1748.1 (C=O), 1595.9 (C=N), 1489.3 (C=C), 1670.9 (N=O), 1218.6 (C-S-C), 787.7 (C-Cl), 3085.5 (C-H)
A_3	1752.1 (C=O), 1600.4 (C=N), 1525.5 (C=C), 1115.0 (C-S-C) str, 3021.7 (C-H), 3431.0 (O-H)
A_4	3030.7 (Ar-H), 2856.2 (C-H), 1670.9 (N=O), 1580.6 (C=C)
A_5	3021.0 (C-H), 1216.2 (C=O), 1589.7 (C=N), 1512.8 (C=C)
A_6	1736.9 (C=O), 1593.6 (C=N), 1580.6 (C=C), 1112.6 (C-S-C)
A_7	1734.7 (C=O), 1589.7 (C=C), 3021.0 (C-H),1589.7 (C=N), 1512.8 (N=O)
A_8	1748.1 (C=O), 1489.3 (C=C), 3268.4 (N-H),1595.9 (C=N), 1525.5 (N=O)
A_9	1216.2 (C=O), 1114.1 (C-S-C), 1589.7 (C=N), 3431.0 (O-H)

Table 3.Screening Result of Antimicrobial Activity

S. No.	Compound	Activity at 100µ/ml concentration		
		Gm (+) ve	Gm (-) ve	Fungus
		E.Coli	*S.aureus*	*C. Albicans*
1	**A_3**	++	+	++
2	**A_5**	+++	+	++
3	**A_6**	+++	+++	++
4	**A_8**	+	++	++++
5	**Standard**	+++	+++	+++

[++++ means very good; +++ means good, ++ moderate activity, +least activity]

References

1. Wade P.C., Vogt B. R., Kissick T. S., Simpkins L. M., Palmer D.M.,"1-Acyltriazoles as anti-inflammatory agents", J. Med. Chem.,1982, 25, 331-333.
2. Tozkoparan Birsen, Gokhan Nesrin, Aktay Goknur, Yesilada Erdem, Ertan Mevlut, "6-Benzylidenethiazolo [3,2-b]-1,2,4-triazole-5H (6H)-ones substituted with ibuprofen: synthesis, characterization and evaluation of anti-inflammatory activity", Eur. J. Med. Chem., 2000 35, 743-750.
3. Holla B. S., Veerendra B., Shivananda M. K., Boojary B., "Synthesis, characterization and anticancer studies on some Mannich bases derived from 1,2,4-triazoles", Eur. J. Med. Chem., 2003 39, 759-767.
4. Duran H., N., Dogan S.R., "Synthesis and preliminary anticancer activity of some new 1,4-dihydro-3- (3-hydroxy-2-naphthyl)-4-substituted-5H-1,2,4-triazoline-5thiones", ILFarma co, 2002,57, 559-564A.

5. Tehranchian S., Akbarzadeh T., Fazeli M. R., Jamalfar H., Shafiee A., “Synthesis and antibacterial activity of 1-[1,2,4-triazol-3-yl] and 1-[1,3,4-thiadiazol-2-yl]-3-methylthio-6,7-dihydrobenzo[c]thiophen-4- (5H)ones”, Bioorg. Med. Chem. Letter, 2005, 15, 1023-1025.
6. Gulerman N. N., Dogan H, N., Rollas S., Johanssan C., Celik C., “Synthesis and structure elucidation of some new thioether derivatives of 1,2,4-triazoline-3-thiones and their antimicrobial activites”, IL Farmaco, 2001, 56, 953-958.
7. Karthikeyan M. S., Prasad D. J., Boojary B., Bhat K. S., Holla B. S., Kumari N.S. “Synthesis and biological activity of Schiff and Mannich bases bearing 2,4-dichloroo-fluorphenyl moiety”, Bioorg. Med. Chem. 2006, 14, 7482-7489.
8. Wujee Monika I, Joanna Stefa-Ska2, Agata Siwek1 and Magorzata Tatarc Zak, “Synthesis, lipophilicity and antifungal activity of new derivatives of thiosemicarbazides and 1,2,4-triazoline-5-thione”, Acta Poloniac pharmaceutica n Drug Research, 200966 (1), 73-82.
9. Turan-Zitouni G., Kaplancikli Z. A., Yildiz M. T., Chevallet P., Kaya D., “Synthesis and antimicrobial activity of 4-phenyl/cyclohexyl -5- (l- phenoxy ethyl) -3-[N-- (2- thiazolyl) acetamido] thio-4-H-l,2,4-triazole derivatives”, Eur. J. Med.Chem. 2005, 40, 607-613.
10. Peljar Michael J., Chan E. C. S., Noel R. Krieg, “Microbiology”, Tata Mc Graw-Hill Publishing Company Limited New Delhi 5th ed., 1993, 532-537.

