Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2014, 6(6):2760-2764

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis and biological activity of some new thiazole based thiazolidinones

V. G. Patel*, Tulsigiri K. Goswami and Avirath R. Bhatt

Department of Chemistry, Municipal Arts and Urban Science College, Mehsana

---

ABSTRACT

The basic compound 5-methyl-N-[(1-substituted phenyl) methylene] – 1,3-thiazol-2-amine [A 1-10] have been synthesized by reaction of 5-methyl amino thiazole and aromatic aldehyde in presence of toluene and further react with thioglycolic acid gives 3-(5-Subtituted 1,3-thiazol-2-yl)-2- (Substitued phenyl)-1, 3-thiazolidin-4-ones [B 1-10]. The structure of the final product is confirmed by IR, and 1H NMR spectral data. All the synthesized compounds were evaluated for their antibacterial activity to gram-positive and gram-negative bacteria. All the synthesized compounds have exhibited selective and effective active against gram-positive and gram-negative bacteria. Antibacterial activities of the synthesized compounds have been compared with standard drugs.

Keywords: Schiffbases. Thioglycolic acid, 3-thiazolyl-2-aryl-1, 3-thiazolidin-4-ones.

INTRODUCTION

A number heterocyclic compounds are being used as therapeutic agents and they are essential of human life. Heterocyclic compounds containing thiazole moiety have a wide variety of pharmacological activity[1-3]. This stimulated our interest in the synthesis of a series of compounds containing thiazole ring system associated with β-Lactum ring and to evaluate their biopotency.

In the present investigation the synthesis of new series of Schiff bases derived from 2-amino thiazoles and different aldehydes has been undertaken Schiff bases are well known to have pronounced biological activities.[4-7] Their ready synthesis and myriad properties have contributed greatly to their popularity and to the study of many biological systems. Cylcoadition reactions of Schiff bases with mereapto acetic acid results into the formation of thiazolidinones.

These Thiazolidinone derivatives are associated with various kind of biological activities.[8-9] They were also exhibit 8 variety of pharmacological activities.[10] Thiazolidinones belong to an important group at position on 2-4 or 5 is the subject of extensive study : several substituted thiazolidinones biologically active compounds were prepared and found to have antibacterial[11-12] and antifungal[13] properties. It has also been found to possess antitubercular activity[14-15] as well as anticonvulsant[16-17], anti cancer[18] CNS-stimulant[19], analgesic[20], choleretic[21], antiphlogistic activities[22], anti tumer[23], anti inflammatory[24], anti-HIV[25], and antioxidant activity.[26]

EXPERIMENTAL SECTION

General Procedure for the preparation of 5-mathyl-N-[(1-substitued pheny) methylene]–1, 3-thiazole-2-amine [A1-10]

2- Amino thiazole (0.01 mole, 1.14gm) was dissolved in dry benzene (50 ml), Aldehyde (0.01 mole) was added in the reaction mixture. The contains were refluxed for 8-10 hrs. using the Dean & Stark separator and remove the water librated. Then distilled out the solvent U/reduce presser. The crude mass was poured in water. The resulting solid obtained was filtered and washed with petroleum ether; the product was recrystallized from ethanol as dark yellow needles.

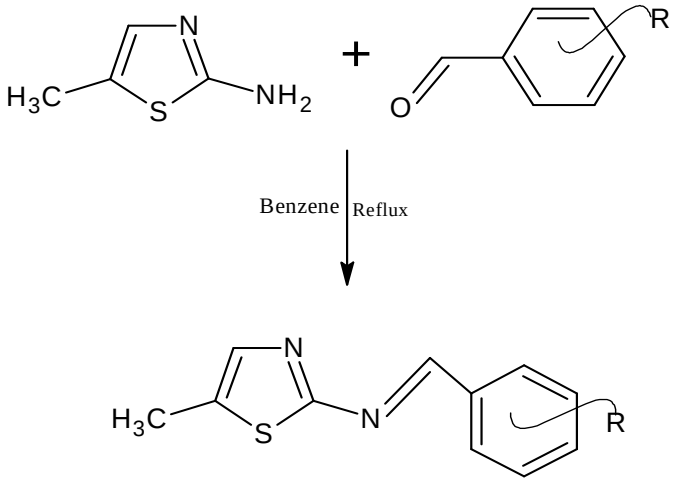
Similarly, all other compounds [A1-10] were synthesized. Their physical constant and antibacterial activities are recorded in Table-1.

General Procedure for the preparation of 3-(5- Substitued 1, 3-thiazol-2-yl)-2– (substituted phenyl) -1, 3-thiazolidin – 4-ones [B1-10]

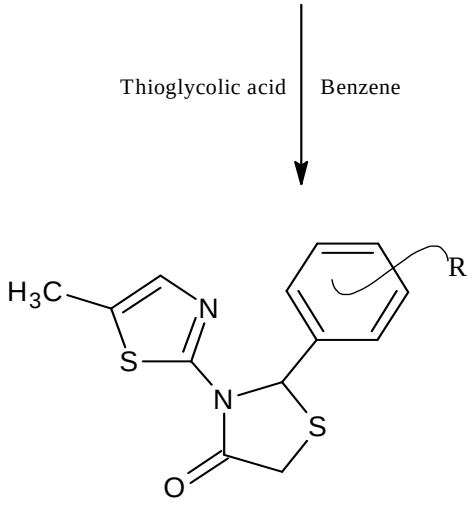
A mixture of compound A1 (0.01 mode) and thioglycolic acid (0.015 mole) were heated on oil bath at 160-170 0C for 3-4 hrs. then cool the reaction mixture and poured it in ice cold water. Further triturated with 20% sodium bicarbonate solution the product thus separated was filtered and washed with water and recrystallized from ethanol (95%) as pale yellow to white crystals.

Similarly, all other compounds [B1-10] were synthesized. Their physical constant and antibacterial activities are recorded in **Table-1.**

Reaction scheme



5-methyl-*N*-[(*E*)-phenylmethylidene]-1,3-thiazol-2-amine A1-10



3-(5-methyl-1,3-thiazol-2-yl)-2-phenyl-1,3-thiazolidin-4-one B1-10

Where R

1. 3, 4-dimethoxy,
2. 3, 4,5-try methoxy,
3. 2,5 di methyl-4- ethyl,
4. 2,5 di methyl-4- methyl,
5. 2-bromo-4,5-dimethoxy,
6. 2-nitro-4,5-dienthoxy,
7. 3-ethxy-4-methox,
8. 3-bromo-5-ethoxy-4-hydroxy
9. 4-methoxy,
10. 3-chloro

Spectroscopic data synthesized compound :
IR (KBr) cm-1 A1 : 2950 (C-H asym), 2850 (C-H sym) 755 (C-H bending) 1578 (C=C), 1635-1641 (-C=N), 765 (C-S), 1145 (C-O-C).

1H NMR (δ ppm) A10. 2.30 (d, 3H, -CH), 7.21 (qur, 1H, CH-CH3), 8.09-8.12 (m, 2H, Ar-H), 8.31-8.33 (m, 2H, Ar-H) 8.34-8, 38 (m, 1H, -N=CH)

Spectroscopic data of synthesized compounds :
IR (KBr) cm^{-1} A9 : 2950 (C-H asym), 2850 (C-H sym), 1578, 1615, 1516 (C=C), 1240 (C-O-C), 1660 (C=O), 1160 (C-N), 610 (C-S-C).

^{1}H NMR (δ ppm) A2 : 2.35 (d, 3H, -CH_3), 6.74 (qur, 1H, CH-CH_3), 7.10-7.14 (m, 2H, Ar-H), 4.9-5 (s, 1H, -N-CH). 3.84-3.87 (m, 3H, Ar-OCH_3), 6.44 (qur, 1H, CH-S-CH2), 6.74 (qur, 1H, CH-CH_3), 3.87-3.89 (s, 2H, S-CH_2-CO).

Melting points of all compounds were taken in open capillaries and are uncorrected. The 1R spectra were recorded on a Shimadzu FTIR 8400 spectrophotometer, PMR spectra were recorded on a BRUKER (300 MHz) spectrometer using TMS as internal standard. The purity of synthesized compounds has been checked by TLC.

Table-1. Physical constants of synthesized compounds

Compound No.	R	Molecular Formula	M.W	M.P.^{0}C	% of Yield	Rf Value
B1	3,4-di $OCH_3C_6H_3$	$C_{15}H_{16}N_2O_3S_2$	336	120	75%	0.45
B2	3,4,5-tri $OCH_3C_6H_2$	$C_{16}H_{18}N_2O_4S_2$	366	116	75%	0.50
B3	2,5 di OCH_3, 4-$OC_2H_5C_6H_2$	$C_{17}H_{20}N_2O_3S_2$	364	175	78%	0.55
B4	2,5-di OCH_3 4-$OCH_3C_6H_2$	$C_{16}H_{18}N_2O_3S_2$	350	205	70%	0.55
B5	2-Br. 4.5-di $OCH_3C_6H_2$	$C_{15}H_{15}B1N_2O_3S_2$	415	120	80%	0.52
B6	2-NO_2 4.5-di $OC_2H_5C_6H_2$	$C_{17}H_{19}N_3O_5S_2$	409	176	70%	0.47
B7	3-CO_2H_5 4-$OCH_3C_6H_3$	$C_{16}H_{18}N_2O_3S_2$	350	184	75%	0.47
B8	3-Br, 5-C_2H_5, 4-OH C_6H_2	$C_{15}H_{15}B1N_5O_3S_2$	415	130	75%	0.48
B9	4-$OCH_3C_6H_4$	$C_{14}H_{14}N_2O_2S_2$	306	127	72%	0.41
B10	3-Cl C_6H_4	$C_{13}H_{13}ClN_2OS_2$	310.5	170	75%	0.43

TLC Solvent system : - Toluene : Ethyl acetate (9 : 1)

Table -2. Antibacterial activity of synthesized compounds

Comp. No.	*S.aureus*	Antibacterial Activity (Zone of inhibition in mm)		*S.typhi*
		B.subtilis	*E.coli*	
A1	20	18	12	15
A2	20	18	13	15
A3	20	16	13	14
A4	18	15	11	13
A5	20	19	12	12
A6	19	12	10	11
A7	18	15	12	12
A8	18	19	12	12
A9	13	12	15	13
A10	19	20	12	14
B1	11	15	12	11
B2	12	13	13	12
B3	12	12	15	12
B4	13	13	15	13
B5	20	18	13	15
B6	20	18	11	15
B7	18	16	12	14
B8	20	15	10	13
B9	19	13	12	12
B10	18	12	12	11
Standard drugs				
Amoxicillin	22	23	24	24
Ciprofloxacin	26	25	24	25

Antibacterial Activity
The synthesized compounds were screened for the antibacterial activity against gram-positive bacteria S.aureus and B.subtilis and gram-negative bacteria E.coli and S.typhi. Applying the cup borer method27 at a concentration of 50 µg/ml in DMF and incubated for 24-36 hr at 37 ^{0}C. The result shows that most of the synthesized compounds shows

moderately active against gram-positive and gram-negative bacteria. The antibacterial activities of the synthesized compounds have been compared with standard drugs like Amoxicillin and Ciprofloxacin. DMF was used as a solvent. The antibacterial activities are summarized in the Table-2.

RESULTS AND DISCUSSION

IR spectra of the Schiff base exhibits C=N stretch, in the range of 1635-1641 cm-1. There is also C-S stretching peak observed at 765 cm-1. Thiazolidinone derivatives is confirmed by presence of cyclic ketone observed at 1660 cm-1 and C-S band at 610 cm-1. In addition to above mentioned peaks, spectrum of Schiff base and thiazolidinone also consists peaks corresponding to other common banding-stretching vibration.
In NMR spectra of Schiff base proton (N=CH) gives sharp singlet at 8.34 δ ppm. In thiazolidinone S-CH, CO displayed at 3.87 δ ppm and CH-S-CH2 showed as qurteret 6.44-6.49 δ ppm.

The synthesized compound A-5,8 and 10 having halogen group present at phenyl nucleus showed excellent activity against gram positive bacterial strains. Substiuent in ring B of the thiazolidinone derivatives, electro donating group present is responsible for high activity of the synthesized compounds. The influence of halogen subsistent present and β-lactom nucleus are explored to improve the antibacterial activity of our compounds. Rest of the compounds showed good to poor anti bacterial activity compared to standard drugs like Amoxicillin and Ciprofloxacin.

Acknowledgement
We are grateful to the authorities and Principal of Municipal Arts and Urban Science College, Mehsana for providing facilities. We are extremely thankful to CDRI, Luck now for IR and NMR Spectra.

REFERENCES

[1] AR Katrizy. CW Rees; comprehensive Heterocyclic Chemistry (Pergamon Press, New York), **1982**; 6, 233.
[2] L Troisi, L Ronzini, C Granito, LD Vitis, E Pindinelli.; *Tetrahedron*, Feb **2006**; 1-2.
[3] AS Kalgulkar, BC Crews, LJ Marnett. *Biochemistry*, **1996**; 35, 9076.
[4] EM Hodnett, WJ Dunn. *J. Med. Chem*, **1970**; 13, 768.
[5] AA Sanrilli, AR Fieber, Dong Han Kin, *J.Pharm. Sc*i.**1974**; 63, 449.
[6] S Vnos Erik, Knodel, H Marvin, Radford, Cynthia L, and Berger, J Bradley, *BMC Microbiology*, **2004**; 32.33, 16-17.
[7] S.S Tiwari, N.I Husain and G.C Srvastava; *J. Indian Chem. Soc*. **1980**; 19B, 1017-1023.
[8] K.P Roda, R.N Vabsdadua and H Parekh; *J. Indian Chem. Soc*, **1986**; 63, 594.
[9] P Kumar, A Gulati, and K.P Bhargaya, *Indian. J. Pharma, Sci*. **1982**;44, 141.
[10] A.R Survey and R.A Culter, *J. Am. Chem. Soc*. **1958**; 80, 578.
[11] Sawale, A Archana, Bendre, S Ratnmala, Patil, R Pradip, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, **2012**; 3(3), 415-420.
[12] Prasad, Ashok, K. S Nimayat, K.B Vyas; *Journal of Chemical and Pharmaceutical Research*.**2012**; 4(6). 2959-2963.
[13] Pati, Anita Sahu, Shankarshan, Patra, Manabendra, Majumdar, Poulomi; Behera. Ajaya Kumar; *Journal of the Indian Chemical Society*, **2012**; 89(5), 637-645.
[14] G Kolavi, V Hegde, L.A Khazi, P Gadad ; *Bioorganic & Medicinal Chemistry*, **2006**; 2-8 .
[15] P Vicini, A Geronikaki, K Anastasia, M Incerti,v Zani ; *Bioorganic & Medicinal Chemistry*, **2006** ;15-23.
[16] S.H.A EFeky. and Z.K Abd El-Samii; *Arch Pharm*, **1991**; 324-381.
[17] S.H.A EFeky ; *Pharmazie*, **1993**; 48, 894.
[18] S Grasso, Vintonyak, V Viktor, Warburg, Karin, Over, Bjoern, Huebel, Katja, Rauh, Daniel, Waldmann, Herbert, *Tetrahedron*, **2011**; 67(35), 6713-6729.
[19] H.D Troutman, M.M abd Long, *J. Amer. Chem. Soc.* **1948** ; 10, 3436.
[20] G Fench, Atti, Soc, Palorifajic Sci, *Fix. Mat. Nat*, 1965; 11, 117.
[21] G. U.S Saitzinger, Pat, **1963**; 3,072,671. Chemical Abs, 5F, **1963**; 412571.
[22] Warner Lambert, Pharma Co, Ger, Pat, Chemical Abs; **1964** ; 61, 4361.
[23] Vintonyak, V Viktor, Warburg, Karin, Over, Bjoern, Huebel, Katja, Rauh, Daniel, Waldmann, Herbert, *Tetrahedron*; **2011** ; 67(35), 6713-6729.
[24] S Rekha, U Shantharam , Chandy, Vineet, *International Research Journal of Pharmacy*; **2011**; 2(9), 81-84.
[25] Li, Xiaoliu, Chen, Hua; Zhanx, Hongzhi, Qin, Zhanbin, Zhang, Pingzhu, Yin, Qingmet, Zhang, Jinchao, Faming Zhuanli henqing, CN; 2012 102417515 A 20120418,
[26] Cacic, Milan, Molnar, Maja, Zeitschrift fuer Naturforschung, B, *A Journal of Chemical Sciences*; **2011** ; 66(2), 177-183.

[27] A. L Barry, The antiBacterial susceptibility test , Principle and practives edited by lllus leu and febiger (Phjiladelphia Pel USA); 180, Boil. Abstr; **1976** ; 64 25783.