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"Synthesis, Characterization and antimicrobial activity of novel Schiff bases containing Thiazole moiety"

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Abstract

Various functionalized heterocyclic compounds have verity of activities; we have synthesized such kind of molecule containing sulphur and nitrogen as hetero atom. The synthesized novel compounds, which has shown ability as anti-microbial as considerable inhabitation. N-(thiophene-2-ylmethylene)-4-(substituted phenyl)-thiazole-2-amine was synthesized from 2-amino-4-(substituted phenyl)-1,3 thiazole by condensation in acidic media with thiophene-2-carbaldehyde derivatives. All intermediates and final compounds were confirmed by ^{1}H-NMR, ^{13}C-NMR, Mass Spectroscopy analysis

Keywords: thiazole, Schiff Bases, Anti-bacterial

Introduction

Varity of biological activity is given by heterocyclic ring containing compounds like thiazole, triazole, pyrazole, triazoles, oxadiazole, tetrazole, coumarin etc. Thiazole is as one of nitrogen and sulphur containing ring compounds. This work is planned basically on thiazole containing molecules because of its various kinds of biological activities like antifungal, antimicrobial, anti-tuberculosis, anti-malarial, antioxidant, HIV inhibitor[1-4] etc.

The chemistry of the Schiff base current interest and encompasses a vast area of compounds and various aspects of organic chemistry. Schiff bases are easily prepared by condensation of aldehydes or ketones with amines[5]. The importance of Schiff base in organic chemistry, biomedical applications, supramolecular chemistry, catalysis and material science, separation and encapsulation processes, and formation of compounds with unusual properties and structures has been well recognized. Large numbers of Schiff bases have shown to exhibit a wide range of biological activities, including antitumor, anti-bacterial[6-8], fungicidal[9-10] and anti carcinogenic[11] properties. On the other hand, heterocyclic Schiff base attention of the chemist in current years to find applications as potential drugs, due to the presence of multifunctional groups. Thiazole molecule has attracted significant interest and gained special attention not only in structural chemistry of their multifunctional modes but also showed importance in medicinal and pharmaceutical field. This is because thiazoles moiety have a great pharmacological activity[12-14].

Many thiazole derivatives like sulfathiazole, blemycin, ritonavir, and tiazofurin are well known as potent highly biologically active compounds. Moreover, thiazoles are very important building blocks in medicinal chemistry and can be found in numerous natural products and biologically important compounds including anti-inflammatory, anti-microbial, anti-HIV, anti-hypertensive anticancer and cytotoxic activity that can be well illustrated by

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Saarth
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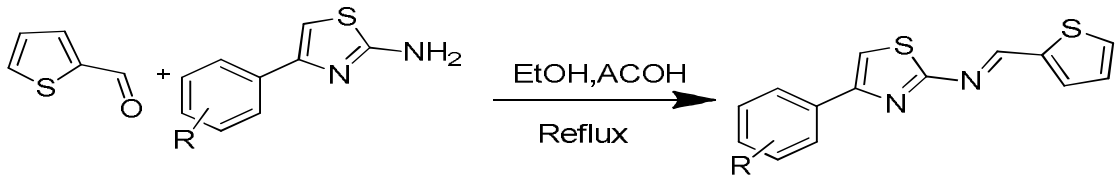
the many drugs in the market containing the moiety. Thiazole ring also found applications in polymer[15], liquid crystals[16-17], fluorescent dyes[18], photo-nucleases, antioxidants[19] and insecticides. Hereby we report the synthesis of a novel Schiff base N-(thiophene-2-ylmethylene)-4-(substituted phenyl)-thiazole-2-amine and their characterization by different spectroscopic techniques and their antibacterial, antifungal activity[20].

Results and Discussion

Chemistry

In our study, a new Schiff base of thiazole derivative has been synthesized by condensation of 2-amino-4-(substituted phenyl)-1,3 thiazole (0.01 mol) and thiophene-2-carbaldehyde (0.01 mol) in the presence of catalytic amount of glacial acetic acid with good yield of 80% as shown in Scheme-1. The purity of the current Schiff base was checked by running TLC on a silica gel coated plate using hexane- Ethyl acetate (80:20%) as the eluent. The formation of Schiff base were obtained from characteristic band positions in FT IR and resonance signals in ^{1}H NMR, Mass spectra and elemental analysis.



Scheme 1: Synthesis of Schiff base

Table-1 Physical data of Schiff base (2 a to 2 f)

Sr. No.	Compound	Substitution	% yield	MP (^{o}C)
1	2 a	H	88	178
2	2 b	3-bromo	80	188
3	2 c	3-methyl	82	205
4	2 d	2-chloro	82	185
5	2 e	4-methyl	80	169
6	2 f	4-chloro	78	173

Pharmacology

Antimicrobial activities

The biological activities of the synthesize Schiff bases were studied under antibacterial and antifungal activities by disc and well diffusion method respectively. The in vitro antibacterial activities of the compounds be tested against two Gram Positive P.aeruginosa (mtcc 109) and staphylococcus aureus (mtcc 3160) and two-gram negative kl. Pneumonia (MTCC 109) and Escherichia coli (MTCC 46) bacteria. The in vitro antifungal an activity

Saarth
E-Journal of Research
ISSN NO: 2395-339X

was carried out against Candida albicans (MTCC 227), fungi. The stock solution of the test chemicals (1 mg mL-1) was prepared by dissolving 10 mg of each test compound in 15 ml of distilled DMSO solvent. The different concentration of the test compounds (100, 75, 50 and 25 µg mL-1) prepared by diluting the stock solution with the required amount of freshly distilled DMSO. In addition, a controlled experiment was carried out by using freshly distilled DMSO solvent alone.

Antifungal screening

Potato dextrose agar media was used for the antifungal screening. The following ingredients were used prepare of media: potatoes 200 g, agar 20 g, and dextrose 20 g in 1000 mL distilled water. The pure cultures Candida albicans, and Aspergillus Niger were inoculated on Potato dextrose agar slants. These slants were incubated at 320C for 7 days. To these 7 days old slants of fungal strains, 50 mL of 0.1% tween-80 solution were added, and the culture were scraped with sterilized inoculating loop to get uniform spore suspension. The agar plates are prepared by using the above Potato dextrose agar media of antifungal and wells were related dug with the help of 6 mm sterile metallic cork bore. Each plate was inoculated with 7 days old spore suspension of each fungal culture using a spread and micropipette regularly using bent glass rod on each plate. Next each well was incorporated with the test compound solution of different concentrations. The drug Fluconazole is used as standard. All the inoculated plates were incubated at 320C for 48 hrs. Soon after the completion of incubation period the diameter of the inhibition zone generated by each test compound against fungal growth is measured activity of antibiogram zone measuring scale.

Table 2 ANTIBACTERIAL / FUNGAL ACTIVITY TABLE [microgram/ml]

MINIMAL INHIBITION CONCENTRATION						
SR. NO	**CODE**	**E. COLI**	**P. AERUGINOSA**	**KL. PNEUMONIAE**	**S. AUREUS**	**Candida albicans**
		MTCC 46	**MTCC 1688**	**MTCC 109**	**MTCC 3160**	**MTCC 227**
1	2 a	25	50	100	50	500
2	2 b	50	50	100	25	250
3	2 c	100	25	50	50	100
4	2 d	50	50	25	50	100
5	2 e	25	12.5	25	100	250
6	2 f	25	50	25	50	100
11	**Furacin**	25	25	50	50	-
12	**Fluconazole**	-	-	-	-	100

Saarth
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Antibacterial activity of N-(thiophene-2-ylmethylene)-4-(substituted phenyl)-thiazole-2-amine derivatives was appraised against E. coli, P. aeruginosa, Kl. Pneumoniae, P. marneffeiS. aureus, (anti-fungal activity) using ltraconozoleasand Furacinstandard drugs. Minimum bacterial inhibitory concentration values were resolved by Broth dilution technique. Dimethyl sulfoxide was used as diluent. MIC values of the appraised compounds are recorded in (Table 2). Majority of the prepared compounds displayed less MIC activity than standard drug Furacin and ltraconozole against E. Coli, P. aeruginosa, Kl. Pneumoniae, S. aureus, P. marneffei.

Experimental Section

Synthesis of (E)-4-phenyl-N-(thiophen-2-ylmethylene)thiazol-2-amine

Synthesis of Schiff base was summarized in Scheme 1. An equi molar mixture of 3-(2-aminothiazol-4-yl)benzene-1-ylium (0.01 mol) and thiophene-2-carbaldehyde (0.01 mol) with a catalytic amount of glacial acetic acid (1-2 drops) in ethanol (25 ml) was refluxed on a water bath for about 4-5 hrs. The reaction was monitored by thin-layer chromatography. The brown solid separates were filtered, washed with little ethanol, dried and recrystallized from alcohol. Melting point was (180-190°C) yield 88%; molecular weight (270) g per mol M.F C14H10N2S2, Elemental analysis: found (calc.): C, 62.19; H, 3.73; N, 10.36; S, 23.72.

spectral data

Synthesis of (E)-4-phenyl-N-(thiophen-2-ylmethylene)thiazol-2-amine(2 a)

^{1}HNMR (400MHz,$CDCl_3$-d)δ 9.032(s,1H,),8.747(d,1H),8.012-7.275(d,1H),8.012-7.275(M,7H),13C NMR (100 MHz, $CDCl_3$-d) δ 163.38 (s), 154.69 (s), 147.77 (s), 141.80 (s), 134.62 (s), 131.65 – 125.07 (m), 114.15 (s) yield 88%; molecular weight (270) g per mol M.F C14H10N2S2, Elemental analysis: found (calc.): C, 62.19; H, 3.73; N, 10.36; S, 23.72.

Synthesis of (E)-4-(4-methylphenyl)-N-(thiophen-2-ylmethylene)thiazol-2-amine (2 e)

^{1}HNMR(400MHz,$CDCl_3$-d)δδ 10.681(s,1H), 8.836(s,1H),8.741(s,1H), 7.905-7.273(m,5H),2.717(s,3H) 2.540(s,3H). 163.03 (s), 154.69 (s), 13C NMR (100 MHz, $CDCl_3$-d) δ 147.34 (s), 141.80 (s), 137.38 – 126.15 (m), 103.27 (s), 21.14 (d, J 14.2).LCMS (m/z): 298.Elemental Analysis: C, 64.39; H, 4.73; N, 9.39; S, 21.49Chemical Formula: C16H14N2S2.

Conclusions

All the final compounds 9a-j were successfully synthesized. Characterized by different spectroscopically techniques like ^{1}H NMR, ^{13}C NMR and MS analysis, all the compounds were carried out for their antibacterial and anti fungal activity using gram positive and gram negative bacteria as well as two fungal stain. From this study we came to know that all the compounds emerged out as potent antibacterial and anti fungal agents.

REFERENCES

1 Yoshio,J.Pharm. Soc. Japan, **71**, 709 (1951)
2 Schmitt. Contrib, Boyce Thomson Inst; **16**, 261 (1951)
3 J.G. Horsfull and S. Rich, Cotrib, Boyce Thompson Inst; **16**, 313 (1951)
4 Varsha Trivedi and J. T. Rao, J. Inst. Chemists (India), **69**, 75 (1997)
5 Schiff H, *Ann*, **131**, 118 (1864).
6 Santoskar R S & Bhandarkar S D, “Pharmacology and Pharmacotheraputics”, Popular Prakashan Pvt Ltd, Bombay, 648 (1993).

Saarth
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7 Khan J A & Sayed Shafi S, Asian J Chem, 15(3), 1443 (2003).
8 Mohan S & Sarvan J, Asian J Chem, 15(2), 625 (2003).
9 Kumar Vinod & Dhakarey Rajesh, J Ind Council Chemists, 20(1), 46 (2003).
10 Mashelkar V C, Bade A A & Teli C R, J Ind Council Chemists, 18(1), 49 (2001).
11 Sinha C, Bag K & Das D, Ind J Chem (Sec - B), 39B, 787 (2000).
12 Scott, K.A.; Njardarson, J.T. Analysis of US FDA-Approved Drugs Containing Sulfur Atoms. Top. Curr. Chem. 2018, 376, 5.
13 Sharma, P.C.; Bansal, K.K.; Sharma, A.; Sharma, D.; Deep, A. Thiazole-containing compounds as therapeutic targets for cancer therapy. Eur. J. Med. Chem. 2020, 188, 112016.
14 Pola, S. Significance of Thiazole-based Heterocycles for Bioactive Systems. In Scope of Selective Heterocycles from Organic and Pharmaceutical Perspective; Varala, R., Ed.; InTech: Rijeka, Croatia, 2016; pp. 1–47.
15 Milne GWA. Handbook of Antineoplastic Agents. London, UK: Gower/Ashgate; 2000
16 Kiryanov AA, Sampson P, Seed AJ. Synthesis of 2-alkoxysubstituted thiophenes, 1,3-thiazoles, and related S-heterocycles via Lawesson's reagent-mediated cyclization under microwave irradiation: Applications for liquid crystal synthesis. The Journal of Organic Chemistry. 2001;66:7925
17 Mori A, Sekiguchi A, Masui K, Shimada T, Horie M, Osakada K, et al. Facile synthesis of 2,5-diarylthiazoles via palladium-catalyzed tandem C−H substitutions. Design of tunable light emission and liquid crystalline characteristics. Journal of the American Chemical Society. 2003;125:1700
18 Metwally MA, Abdel-Latif E, Amer FA, Kaupp G. Synthesis of new 5-thiazolyl azo-disperse dyes for dyeing polyester fabrics. Dyes and Pigments. 2004;609(3):249-264
19 Kurt BZ, Gazioglu I, Sonmez F, Kucukislamoglu M. Synthesis, antioxidant and anticholinesterase activities of novel coumarylthiazole derivatives. Bioorganic Chemistry. 2015;59:80-90
20 Zayed EM, Zayed MA. Synthesis of novel Schiff's bases of highly potential biological activities and their structure investigation. SpectrochimActa A MolBiomolSpectrosc. 2015;143:81-90. http://dx.doi.org/10.1016/j. saa.2015.02.024.