Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2017, 9(5):140-144

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, Characterization and Biological Evaluation of Some Schiff's Base from 2-Amino Thiazole with Indole-3-Carbadehyde

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ABSTRACT

A novel Schiff's base derivatives were synthesized from some substituted Indole-3-carbaldehyde with substituted 2-aminothiazole. Which was 2-amino Thiazole synthesized by substituted phencyl bromide and thiaourea. All the synthesized compounds were confirmed their structures by elemental analysis, ^{1}H NMR, 13C NMR, Mass spectral data and also studied their biological activity.

Keywords: Substituted phenacylbromides; Thiourea; 2-aminothoazole; Schiff's bases

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INTRODUCTION

A Schiff's base (or azomethine) is a functional group that contains a carbon, nitrogen double bond with the nitrogen atom connected to an aryl (or) group but not hydrogen [1,2]. In this Schiff's base possess 2- aminothiazole and Indole-3-carbaldehyde. BOH of the compounds shows biological activity. This Schiff's base aromatic hetero bicyclic structure of Indole containing a strong Pharmaco dynamic nucleus where as 2- aminothiazole is five membered hetero cyclic ring. Both compounds of Schiff's base exhibit a wide spectrum of biological activities such as antimicrobial [3-5], antifungal [6], anticancer [7], analgesics [8-11], antioxidant activity [12], anticonvulsant [13]. Purity of compounds was ascertained by the thin layer chromatography (TLC), all the synthesized compounds gave satisfactory elemental analysis and ^{1}HNMR spectra were consistent with the assigned structures. The synthesized compounds scaffold was screened for antimicrobial activity, antifungal activity. 2-amino thiazole, Schiff's bases and its derivatives are synthesized in the present work.

EXPERIMENTAL SECTION

All the chemical and reagents were of synthetic grade and commercially procured from Merk and Sigma Aldrich chemicals. The melting point of all synthesized compounds was determined in open capilliary tube and is uncorrected. The ^{1}HNMR spectra ($CDCl_3$) were scanned on Brocker (400MHz) spectrometer using TMS as internal and also chemical shift expressed in δ ppm. Purity of all synthesized compounds were checked by thin layer chromotography and iodine was used as visualizing agent.

General Procedure of Synthesis of 2-amino Thaizole

A mixture of a substituted phencyl bromide (0.01 mol) and Thiourea (0.012 mol) was taken in mortor and mixture was grinded with pistle. After completion of the grinded with mixture, the sample of the mixture was monitored with thin layer chromotography using Ethyl acetate and n-hexane. The powder washed with base and extracted by ethyl acetate, the solvent removed by vaccum pump. Final product was obtained after purified from ethanol.

Characterization

2-Amino Thaizole (a):

Yield of the compound - 92%, White Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 7.78-7.45 (m,5H,Ar-H).7.37(s,1H,thiazol ring), 6.69(s,2H, NH_2).^{13}CNMR (100MHz, $CDCl_3$) δ in ppm: 166.9, 137.9, 132.9, 128.7, 128.1, 125.7, 108.0. LCMS (m/z): 176.24. Molecular formula: $C_9H_8N_2S$. Elemental analysis: Calculated: C-61.34, H-4.58, N-15.90,S-18.19 . Obtained: -61.36, H-4.56, N-15.89, S-18.17.

Methoxy-2-aminothiozoles (3b):

Yield of the compound - 93%, Pale Yellow Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 7.68-7.05 (m,4H, Ar-H). 7.04 (s,1H,thiazole ring), 6.62(s,2H,NH_2), 3.78 (s,3H ,-OCH_3). ^{13}CNMR (100MHz, $CDCl_3$) δ in ppm: 166.8, 160.6, 138.6, 128.4, 125.3, 114.3, 108.0, 54.9. LCMS (m/z): 206.09. Molecular formula: $C_{10}H_{10}N_2OS$. Elemental analysis: Calculated: C-58.23, H-4.89, N-13.55, O-7.76, S-15.55. Obtained: C-58.27, H-4.88, N-13.54, O-7.75, S-15.54.

4-chloro-2-aminothiazole (3c):

Yield of the compound - 92%, White solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 7.73-7.53(m, 4H, Ar-H), 7.07(s, 1H, thiazolring). ^{13}CNMR (100MHz, $CDCl_3$) δ in ppm: 166.8, 160.6, 138.6, 128.4, 125.3, 114.3, 108.0, 54.9. LCMS (m/z): 305.00. Molecular formula: $C_{18}H_{13}N_3S$ Elemental analysis: Calculated: C-71.26, H-4.32, N-13.85, S-10.70. Obtained: C-71.30, H-4.31, N-13.83, S-10.69.

General Procedure for the Synthesis of Schiff base

A mixture of equimolar quantities (0.01 mol) of substituted 2-aminothiozoles and substituted indole-3-carbaldehyde (0.01 mol) was dissolved in 20 ml of dry ethanol taken in RB flask and subsequently added 1 or 2 drops of concentrated sulfuric acid to be mixture. The RB flask put on the magnetic stirrer and heat at reflux 3-4 hours. The reaction was monitored by TLC. The mixture of the compound with extracted with ethyl acetate and washed with and solution of sodium bicarbonate. Finally product can be obtained by after re-crystallized from ethanol.

N-((1H-indol-3-yl)methylene)-5-Phenylthiazole-2-amine(5a):

Yield of the compound - 90%: (^{1}HNMR (400MHz, $CDCl_3$) δ in ppm: 11.15(s,1H,NH), 8.62 (s,1H, CH) ,8.18-7.07 (m,8H,Ar-H). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 165.8, 160.1, 143.1, 136.9, 132.6, 130.3, 128.6, 128.5, 128.1, 126.2, 125.7, 120.6, 119.8, 119.0, 111.1, 102.0. LCMS (m/z): 305.00 Molecular formula: $C_{18}H_{13}N_3S$ Elemental analysis: Calculated: C-71.26, H-4.32, N-13.85, S-10.70 . Obtained: C-71.30, H-4.31, N-13.83, S-10.69.

N-((5-methoxy-1H-indol-3-yl)methylene)-5-Phenylthiazole-2-amine(5b):

Yield of the compound - 93%, White solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.55(s,1H,NH), 8,71(s,1H,CH), 7.81-6.56(m,8H,Ar-H), 3.89 (s,3H,-OCH3).). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 170.2, 158.8, 148.6, 142.0, 133.1, 130.0, 129.2, 128.8, 128.2, 127.0, 125.7, 112.0, 111.6, 103.6, 101.2, 54.4. LCMS (m/z): 334.05. Molecular formula: $C_{19}H_{15}N_3OS$ Elemental analysis: Calculated: C-68.45, H-4.53, N-12.60, O-4.80, S-9.62. Obtained; 68.50, H-4.52, N-12.58, O-4.79, S-9.60.

N-((5-bromo-1H-indol-3-yl)methylene)-5-Phenylthiazole-2-amine(5C):

Yield of the compound - 92%. Pale red solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.09 (s,1H,NH),8.53 (s,1H,NH),7.86-7.13 (m,8H,Ar-H).). ^{13}CNMR (100MHz, $CDCl_3$) δ in ppm: 166.3, 159.8, 142.9, 135.4, 132.2, 129.7, 128.7, 128.5, 127.9, 126.1, 124.2, 120.1, 118.8, 113.1, 112.8, 102.1. LCMS (m/z): 382.97. Molecular formula: $C_{18}H_{12}BrN_3S$. Elemental analysis: Calculated: C-68.45, H-4.53, N-12.60, O-4.80, S-9.62. Obtained: C-68.50, H-4.52, N-12.58, O-4.79, S-9.60.

N-((5-nitro-1H-INDOL-3-yl)methylene)-5-PhenylThiazol-2-amine (5d):

Yield of the compound - 89%. White solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm): 11.35(s,1H,NH), 8.25 (s,1H,CH), 8.47(d,J=7.6,1H), 8.15-7.79 (m,2H,Ar-H), 7.69-7.40(m,5H,Ar-H), 7.38 (s,1H,thiazole ring). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 170.2, 159.7, 142.6, 142.3, 133.1, 131.3, 130.2, 129.0, 128.6, 126.9, 126.3, 125.8, 118.7, 114.3, 111.7, 102.3. LCMS (m/z):348.08. Molecular formula: $C_{18}H_{12}N_4O_2S$ .Elemental analysis: Calculated: C-62.06, H-3.47, N-16.08, O- 9.19, S-9.20; Obtained: C-62.12, H-3.46, N-16.07, 9.17, S-9.18.

N-((1H-indol-3-yl)methylene))-5-(4-methoxy phenyl)thiazole-2-amine(5e):

Yield of the compound - 91%,White solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.19(s,1H,NH), 8.70 (s,1H,CH),8.19-7.45(m,4H,Ar-H),7.37(s,1H,thiazole ring), 7.31-7.03 (s,4H,Ar-H). 3.75(s,3H,-OCH3). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 168.7, 160.5, 159.5, 142.9, 137.0, 129.2, 128.1, 126.2, 125.7, 121.1, 119.2, 118.9,

114.6, 111.0, 101.58, 55.4. LCMS (m/z): 334.05. Molecular formula: $C_{18}H_{12}N_3OS$ .Elemental analysis: Calculated: C-68.45, H-4.53, N-12.60, O-4.80, S-9.62. Obtained: C-68.50, H-4.52, N-12.59, O-4.78, S-9.60.

N-((5-methoxy-1H-indol-3-yl)methylene)-5-(4-methoxy phenyl)thiazol-2-amine (5f):
Yield of the compound - 93%, White solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.03(s, 1H, NH), 8.61(s, 1H, CH), 7.74-7.03 (m, 8H, Ar-H), 3.79(s, 6H, 2(OCH_3)). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: LCMS (m/z): 363.13. Molecular formula: $C_{20}H_{17}N_3O_2S$. Elemental analysis: Calculated: C-66.10, H-4.71, N-11.56, O-8.80, S-8.82. Obtained: C-66.14, H-4.70, N-11.55, O-8.79, S-8.81.

N-((5-bromo-1H-indol-3-yl)methylene)-5-(4-mehoxyPhenyl)thiazol-2-amine (5g):
Yield of the compound – 91%, Pale Red Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.25(s, 1H, NH), 8.70(s, 1H, CH), 7.73-7.05(m, 8H, Ar-H), 3.79(s, 3H, -OCH_3). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 172.1, 160.3, 158.9, 142.6, 132.9, 130.1, 128.2, 127.6, 125.4, 124.2, 120.5, 119.1, 114.5, 1131, 112.6, 101.4, 54.8. LCMS (m/z): 411.21. Molecular formula: $C_{19}H_{14}BrN_3OS$ .Elemental analysis: Calculated: C-55.35, H-3.42, Br-19.39, N-10.19, O-3.88, S-7.78. Obtained: C-55.42, H-3.41, Br-19.36, N-10.17, O-3.87, S-7.77.

5-(4-methoxyphenyl)-N-((5-nitro-1H-indol-3-yl)methylene)thiazol-2-amine (5h):
Yield of the compound - 92%, White Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.48 (s,1H,NH),8.50 (d,J=8.4Hz,1H), 8.19 (s,1H,CH), 8.09-7.06 (m,2H,Ar-H), 3.67 (s,3H,-CH3). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 170.3, 160.4, 160.1, 143.1, 142.8, 131.9, 130.3, 127.0, 126.2, 125.6, 119.1, 114.4, 111.9, 102.1, 55.6. LCMS (m/z): 378.86. Molecular formula: $C_{19}H_{14}N_4O_3S$ .Elemental analysis: Calculated: C-60.31, H-3.73, N-14.81, O-12.68, S-4.87. Obtained: C-60.35, H-3.72, N-14.80, O-12.67, S-8.46.

N-((1H-indol-3-yl)methylene)-5-(4-chlorophenyl)thiazol-2-amine (5i):
Yield of the compound – 91%, White Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.24(s, 1H, NH), 8.60(s, 1H, NH), 8.21-7.54(m, 5H, Ar-H), 7.38(s, 1H, thiazolring), 7.35-7.01(m, 4H, Ar-H). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 166.8, 160.1, 143.1, 136.9, 132.8, 130.3, 128.6, 128.5, 128.0, 126.6, 125.7, 120.6, 119.3, 118.9, 11.6, 102.0. LCMS (m/z): 338.05. Molecular formula: $C_{18}H_{12}ClN_3S$. Elemental analysis: Calculated: C-64.00, H-3.58, Cl-10.49, N-12.44, S-9.49. Obtained: C-64.07, H-3.56, Cl-10.46, N-12.41, S- 9.47.

5-(4-chlorophenyl-N-((5-methoxy-1H-indol-3-yl)methylene)thiazol-2-amine (5j):
Yield of the compound - 92%, White Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.14(s,1H,NH), 8.52(s,1H,CH), 7.76-7.42(m,7H,Ar-H), 7.35(s,1H,thiazol ring), 6.67(d, J=7.6Hz, 1H), 3.69(s,3H,-OCH_3). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 167.9, 158.5, 151.4, 142.6, 133.3, 130.9, 129.8, 128.9, 128.4, 126.5, 118.5, 111.7, 110.8, 103.8, 101.6, 54.92. LCMS (m/z): 469.5(M+2). Molecular formula: $C_{19}H_{14}ClN_3OS$. Elemental analysis: Calculated: C-62.04, H-3.84, Cl-9.64, N-14.42, O-4.35, S-8.72. Obtained: C-62.10, H-3.83, Cl-9.63, N-14.40, O-4.34, S-8.71.

N-((5-bromo-1H-indol-3-yl)methylene)-5-(4-chloro phenyl)thiazol-2-amine (5k):
Yield of the compound: ^{1}HNMR (400MHz, $CDCl_3$) δ in ppm: 11.29(s,1H,NH), 8.52(s,1H,CH), 8.20(d, J=8.0Hz,1H) 7.75-7.42(m, 4H, Ar-H), 7.38(s, 1H, thiazol ring), 7.35-7.26(m, 4H, Ar-H). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 169.5, 158.7, 142.6, 135.7, 134.1, 130.9, 130.1, 129.2, 128.5, 128.2, 124.0, 120.7, 118.7, 113.8, 113.7, 101.6. LCMS (m/z): 416.53. Molecular formula: $C_{18}H_{11}BrClN_3S$ .Elemental analysis: Calculated: C-51.88, H-2.66, Br-19.17, Cl-8.51, N-10.08, S-7.68. Obtained: C-51.93, H-2.65, Br-19.16, Cl-8.50, N-10.07, S-7.67.

5-(4-chlorophenyl)-N-((5-nitro-1H-indol-3-yl)methylene)thiazol-2-amine (5l):
Yield of the compound - 90%, White Solid: ^{1}HNMR (400 MHz, $CDCl_3$) δ in ppm: 11.43 (s,1H,NH), 8.62(s,1H,CH), 8.51(d,J=8.4Hz,1H) 7.98-7.31(m,8H,Ar-H), 7.10(s,1H,thiazole ring). ^{13}CNMR (100 MHz, $CDCl_3$) δ in ppm: 171.2, 160.0, 143.1, 142.8, 133.4, 130.9, 130.2, 129.1, 128.4, 127.2, 126.3, 119.1, 113.7, 112.9, 102.1. LCMS (m/z): 382.54. Molecular formula: $C_{18}H_{11}ClN_4O_2S$ .Elemental analysis: Calculated: C-56.47, H-2.90, Cl-9.46, N-14.64, O-8.36, S-8.38. Obtained: C-56.53, H-2.88, Cl-9.25, N-14.63, O-8.35, S-8.36.

Biological Activity
The anti bacterial and antifungal activity of the target compound were examined by cup plate method against the following strains: *Stapylococcus aureus*, *Bacillus subtills*, *Escherichia coli*, *Salmonella typhi*, *U maydis* and *Aspergillus Niger* standard drugs Siprofloxin and Fluconazole for bacterial and fungal growth respectively. Evaluation of antibacterial and antifungal activity was done by the agar dilution method. All bacteria were grown on

Mueller-Hinton Agar (Hi media) plates (37°C, 24 hrs) and fungi were grown on sabouraud dextrose agar (Hi-media) plates (26°C, 48-72 hrs). The synthesized compounds were subject to antimicrobial screening by copulate method for zone of inhibition as follows the Table 1.

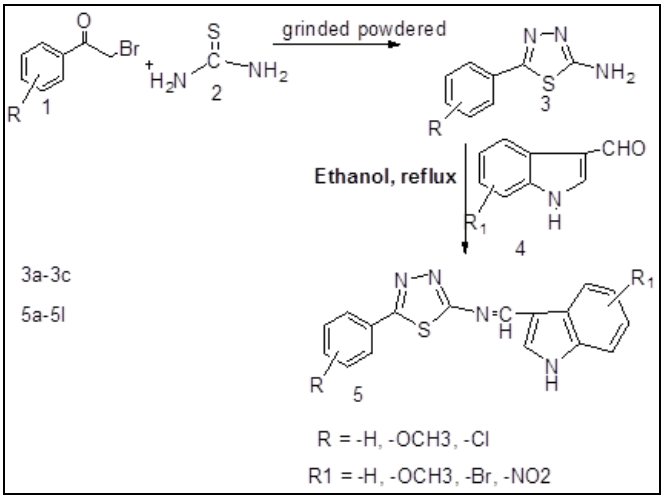
Table 1: Antimicrobial screening

Compound Code	*Zone of inhibition in (mm)					
	Bacteria				Fungi	
	Gram +ve		Gram -ve		*A. niger*	*U.maydis*
	S.aureus	*B.substills*	*E.coli*	*S.typhi*		
5a	++	++	++	++	++	++
5b	++	++	++	++	++	++
5c	+++	+++	+++	+++	+++	+++
5d	+	+	+	+	+	+
5e	++	++	++	++	++	++
5f	++	++	++	++	++	++
5g	+++	+++	+++	+++	+++	+++
5h	+	+	+	+	+	+
5i	++	++	++	++	++	++
5j	++	++	++	++	++	++
5k	++++	++++	++++	++++	+++	+++
5l	+	+	+	+	+	+
STD_1	++++	++++	++++	++++	-	-
STD_2	_	_	_	_	+++	+++

+=8-13(poor activity); ++ = 14-17(moderate activity); +++ = 18-21(good activity); ++++ = 20-25(strong activity); STD_1=Ciprofloxacin; STD_2 =Fluconazole

RESULTS AND DISCUSSION

The target compounds were synthesized via the root of as shown in scheme 1. All synthesized compounds were purified by successive re-crystallization using suitable solvents. The purity of the target compounds were checked by TLC and also determining melting points, the target compounds characterized by spectral analysis as ^{1}HNMR, ^{13}CNMR and mass spectra to conform the structures.



Scheme 1: Synthesis of target compounds

CONCLUSION

In this paper we presented Schiff's base from 2-aminothiozoles and indole-3-carboldehyde. The compounds can be characterized by spectral data and studied by the anti bacterial activity.

ACKNOWLEDGEMENT

The authors are thankful to the Dr. M.S. Surendra Babu, GITAM University, Hyderabad for keen interest to conduct the experiment.

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