IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

Synthesis and characterization of Schiff base battered benzothiazole derivatives and their metal complexes with antimicrobial activity

Trambak U. Kendre[1], M.A. Basser[2], P. A. Kulkarni[2]

1 Department of Chemistry, Toshniwal A.C.S. College, Sengaon

2 Department of Chemistry, Yeshwant Mahavidyalaya, Nanded

Abstract:

Two benzothiazoles Schiff bases namely A-N-(2-chlorobenzylidene)-6-ethoxybenzo(d)thiazole-2-amine (K5) and B- N-(2-bromo benzylidene)-6-ethoxybenzo(d)thiazole-2-amine (K6) and their metal complexes Pd(II), Cu(II), Ni(II) and Co(II) were synthesized. Ligand K5 and K6 along with metal complexes were characterized by elemental analysis, IR, NMR UV and TGA. Ligand and metal complexes were tested for antibacterial and antifungal activities. Synthesized benzothiazole containing pyrimidine derivatives and evaluated their antimicrobial activity by using 'disk diffusion method' and observed that all compounds show moderate to good antimicrobial activity. Synthesized benzothiazole derivatives (ligands) shows good activity than their metal complexes. It was observed that all synthesized compounds are active due to presence of substituents on Schiff base ligand, however they displayed moderate to good activities against antifungal strains. Therefore, benzothiazole derivatives are one of the most adaptable classes of compounds against microbes.

Keyword- Benzothiazole, Schiff base, antibacterial, complexes, IR, NMR.

Introduction:

Aromatic aldehydes especially with an effective conjugation system, form stable Schiff bases, where as those aliphatic aldehydes are unstable and readily polymerize[1]. Schiff base ligands with aldehydes are formed more readily than with ketone (carbonyl carbon)[2]. Schiff bases have very flexible and different structures[3]. A wide range of Schiff base compounds and their behaviour studied because these compounds have very flexible and diverse structure[4]. Schiff bases are generally are bi ,tri, or tetra-dentate chelate ligands and from very stable complexes with metal ions. Their chemical and physical properties in various field such as preparative uses, identification, or protection and determination of aldehyde or ketones, purification of carbonyl and amino compounds or production of these compounds in complex or sensitive reactions have studied by various workers[5,6] . Because of their ability to form complexes with transition metal ions, Schiff bases are considered

as a very important class of compounds[7]. Nitrogen- and Sulphur-containing heterocyclic compounds are attracting researchers due to their wide range of pharmacological activities[8]. Benzothiazole derivatives were attracted researchers due to their diverse biological activities including anticancer[9], antitubercular and anti-inflammatory[10]. Schiff base metal complexes have been studied extensively because of their remarkable chemical and physical properties[11]. Schiff base has great importance in a biological field due to their structural similarities with natural biological compounds[12]. Schiff base ligands are easily synthesized and form complexes with almost all metal ions, coordinating to metal ions via azomethine nitrogen[13-16]. Extensive discussions were reported for Fe(II), Mn(II), Co(II), Pd(II) ,Ni(II) and Cu(II) complexes with tetradentate, Schiff bases with two nitrogen and two oxygen donor atoms as oxygen carriers and catalysts for water splitting systems[17]. A great amount of attention has been given to the biological activity of metal complexes with tridentate Schiff bases which are of particular interest for giving variations to their donating properties[18-20].

Materials and equipment

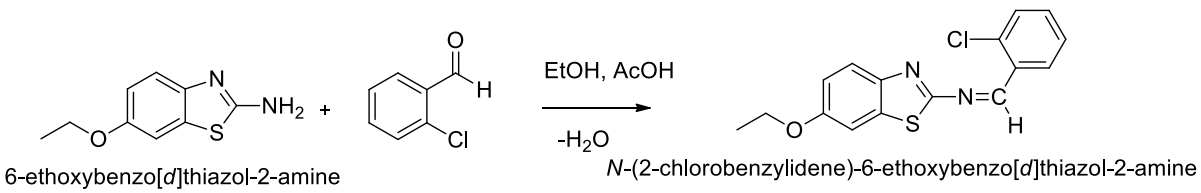
All the required chemicals were obtained from commercial sources and used as received without any further purification. The solvents used for synthesis and analytical measurements were used without further purification. The reactions were monitored by thin-layer chromatography (TLC) using 0.25mm E-Merck silica gel 60 F254 pre-coated plates, which were visualized with UV light. 1H NMR spectra were recorded on a 500 and 400 MHz. 13C NMR spectra were recorded on the 126 MHz instrument of Agilent Technology in $CDCl_3$ and DMSO-d6. The absorption spectra of the compounds were recorded on a Perkin Elmer Lambda-25 spectrophotometer at room temperature.

Experimental Work:

Synthesis of Schiff Base

The two Schiff bases namely K5: N-(4-bromo-2-hydroxy benzylidene)-6-ethoxybenzo(d)Thiazole-2-amine K6: N-(2-chlorobenzylidene)-6-ethoxybenzo(d)Thiazole-2-amine and were synthesized by same method. To a ethanolic solution of 0.01 mol 4-bromo -2-hydroxybenzaldehyde, another ethanolic solution of 0.01 mol 6-ethoxybenzo(d) thiazole was added. Further, the mixture was heated for two hours. After the accomplishment of the reaction, yellow colour solid was obtained the solvent was evaporated precipitate was filtered off from the reaction mixture. The solid parted was recrystallized using ethanol as solvent. The synthesis of the Schiff base ligand is shown in Scheme1.

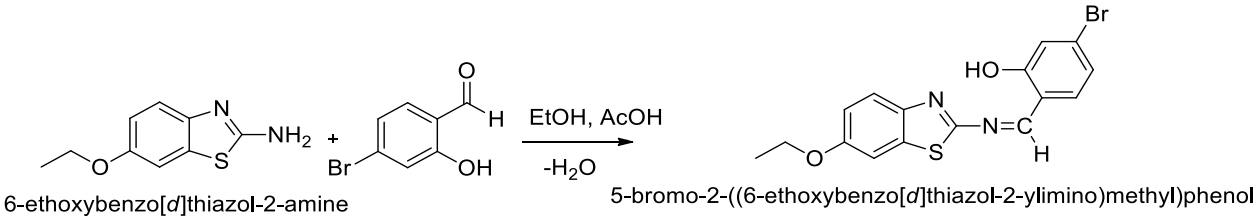
Similar procedure was applied for the synthesis of K6 Schiff base from 2-chlorobenzaldehyde and 6-ethoxybenzo(d) thiazole.



6-ethoxybenzo[*d*]thiazol-2-amine

N-(2-chlorobenzylidene)-6-ethoxybenzo[*d*]thiazol-2-amine

Scheme-1



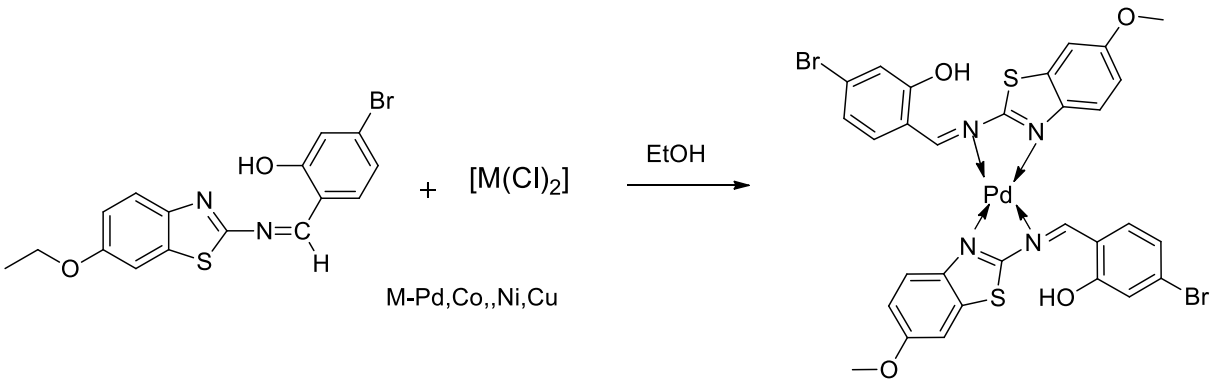
Scheme-2

N-(2-chlorobenzylidene)-5-ethoxybenzo[d]thiazol-2-amine: M.P. 190ºC, Solid, Yellow IR Cm^{-1} (KBR): 3442 (N-H), 1603 (C=N), ^1H NMR studies ($CDCl_3$) ppm: 8.40 (1H, s, N=CH), 7.01-7.91 (6H, m, Ar-H), 4.11 (2H, q) and 1.49 (3H, t). 13C NMR ($CDCl_3$) ppm: 174, 160, 153, 140, 136, 134, 132, 124, 122, 121, 119, 116, 114, 105, 64 and 18.LCMS m/z (%) 185 (100%) [M+1].

5-bromo-2-(((5-ethoxybenzo[d]thiazol-2-yl)imino)methyl)phenol: M.P. 180ºC, Solid, Yellow. IR Cm^{-1} (KBR): 3429 (N-H), 1639 (C=N), 3631 (Ar-OH). ^1H NMR studies ($CDCl_3$) ppm: 9.46 (1H, s, Ar-OH), 8.40 (1H, s, N=CH), 7.01-7.91 (6H, m, Ar-H), 4.11 (2H, q) and 1.49 (3H, t). 13C NMR ($CDCl_3$) ppm: 174, 160, 153, 140, 136, 134, 132, 124, 122, 121, 119, 116, 114, 105, 64 and 18.LCMS m/z (%) 378.8 (100%) [M+1].

Synthesis of metal complexes:

An ethanolic solution of metal (II) chloride and another ethanolic solution of Schiff base(2mmol) which was containing a few drops of triethylamine stirred with each other. This mixture was stirred magnetically and refluxed for 4 hours. The resulting solution was kept in a water bath and was reduced to one-third. A solid complex was precipitated which was filtered and then washed with ethanol, further it was dried in a vacuum



Scheme-3

Characterization of Ligand and metal complexes:

Elemental Analysis:

Comp.	Empirical Formula	Yield (%)	Colour	Found (Calculated) (%)				Formula weight	$h_M\Lambda$)	μeff
				M	C	H	N /S	g/mol	cm2/ mol	(B.M.)
K5	(C16H13N2SOBr)	70	Yellow	-	53.2	3.6	7.75/ 8.87	361.23	-	-
[PdK5] Cl	[pd(C16H13N2OSBr]$_2$ Cl	66	Black	12.8	46.4	3.16	6.76/ 7.14	828.88	112	4.2
[CoK5] Cl	[CoC6H13N2OSBr]$_2$ Cl	72	Red	7.54	49.18	3.35	7.17/ 8.21	781.39	100	3.52
[NiK5] Cl	Ni(C16H13N2OSBr]$_2$Cl	70	Green	7.51	49.2	3.55	7.17/ 8.21	781.15	99	4.2
[CuK5] Cl	Cu(C16H13N2OSBr]$_2$ Cl	46	Brown	8.08	48.89	3.33	7.13	786.01	123	1.9

Antimicrobial studies

All synthesized compounds were evaluated for antibacterial and antifungal screenings using the micro-broth dilution method. The MIC values were calculated for all compounds on four bacterial and one fungal strain. The totals of nine dilutions of each compound were prepared using the BHI (brain heart infusion). For facultative anaerobes, tubes were incubated at 37ºC for 48–72 h in CO_2 Jar. For strict anaerobes, tubes were incubated in anaerobic jars for 48–72 h. The details of the whole assay protocol are in Supplementary On the other hand, the Schiff base has great importance in a biological field due to their structural similarities with natural biological compounds. Schiff base has also attracted researchers due to their wide range of pharmacological activities including antibacterial antifungal.

Antibacterial activity:

For their antibacterial activity against various pathogenic bacteria such as *Escherichia coli, Pseudomonas aeruginosa*, *Bacillus subtilis,* and *Staphylococcus aureus,* the Schiff base ligand and their complexes have been screened[42]. The standard used for bacterial studies was *Tetracycline*. It has been observed that the activity of metal ions is higher than that of the free ligand. Probably, the grater lipophilic nature of the complexes is responsible for this. The faster diffusion of metal complexes through the cell membrane is responsible for the increase in antibacterial activity[43]. This can also be due to the combined activity effect of the metal and ligand. The increased activity of metal complexes can be explained on the basis of the Overtone concept[16] and the Tweedy chelation theory[44]. Overtone's concept of cell permeability denotes that the lipid membrane that surrounds the cell supports only the passage of materials that are soluble in lipids; due to this, lipo solubility is an important factor that controls antimicrobial activity. The polarity of the metal ion will be reduced to a larger extent on chelation. This is due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it raises the delocalization of ʌ-electrons over

the chelate ring and develops the lipophilicity of the complex. This increase in lipophilicity leads to the breakdown of the permeability barrier of the cell due to which the normal cell processes retards.

Table: antibacterial activity for ligand and complexes

Compound	*E. coli*			*P. aeruginosa*			*B. subtilis*			*S. aureus*		
	20µg	40µg	60µL	20µg	40µg	60µg	20µg	40µg	60µg	20µg	40µg	60µg
K5	15	16	24	9	20	21	12	17	23	-	12	25
[Pdk5]Cl	11	15	16	14	18	18	11	12	14	-	12	13
[Cok5]Cl	14	18	22	-	13	14	10	15	20	15	17	20
[Nik5]Cl	11	14	18	14	19	19	-	12	13	-	-	10
[Cuk5]Cl	12	14	16	14	19	19	10	12	14	-	12	14
Steptomycin (Standard Drug)	26.2			20.0			21.2			26.4		

Conclusion:

Schiff bases are interesting ligands due to their simple preparation and ease of complex formation with varied metal ions having variable denticity. Various Schiff bases have gained medicinal importance due to the presence of bioactive azomethine core. Versatile applications of Schiff bases and their metal complexes in the treatment of diseases opened a new era in medicinal science. In the human body trace and ultratrace amounts of transition metal ions are supplemented by the use of metal complexes of Schiff bases. Metal complexes exhibited stronger antimicrobial efficiency than their corresponding Schiff base ligands.Due to this strength of the ligand, the complexes formed are having square planar geometry. All the complexes formed were characterized by the NMR, IR, and the UV spectra, that resulted in the confirmation of the structure. Further, the ligand and the complexes were screened for antibacterial and antifungal activity. Here, the ligands showed good microbial activity as compared to the complexes.

References

1. 1.M.A. Ashraf, K. Mahmood, A. Wajid. Int. Proc. Chem. Biol. Environ. Eng., 10, 1 (2011).
2. P.A. Vigato, S. Tamburini. Coord. Chem. Rev., 248, 1717 (2004).
3. A. Salvat, L. Antonnacci, R.H. Fortunato, E.Y. Suarez, H.M. Godoy. Lett. Appl. Microbiol., 32, 293 (2001).
4. H. Schiff. Ann. Chem. Pharm., 131, 118 (1864).
5. D.N. Dhar, C.L. Taploo. J. Sci. Ind. Res., 41, 501 (1982).
6. Akhtar, J., Khan, A. A., Ali, Z., Haider, R., & Yar, M. S. (2017). Eur. J. Med. Chem. 125, 143–1810.1016/j.ejmech.2016.09.023
7. Alafeefy, A. M., Bakht, M. A., Ganaie, M. A., Ansarie, M. N., El-Sayed, N. N.,& Awaad, A. S. (2015). Chemistry Letters, 25, 179–183. doi10.1016/j.bmcl.2014.11.088
8. Al-Salihi, S., Israa, A., Israa, A., & Fournier, J. (2019). Biological activity Energy Procedia, 157, 296–306. doi:10.1016/ j.egypro.2018.11.194

9. Arafath, M. A., Adam, F., Al-Suede, F. S. R., Razali, M. R., Ahamed, M. B. K., Abdul Majid, A. M. S., … Abubakar, S. (2017). Journal of Molecular Structure, 1149, 216–228. doi:10.1016/ j.molstruc.2017.07.092
10. D.E. Goldberg, V. Sharma, A. Oksman, I.Y. Gluzman, J. Biol. Chem. 272 (1997) 6567–6572.
11. A.E. Tai, E.J. Lien, M.M.C. Lai, T.A.K Khawaja, J. Med. Chem. 27 (1984) 238.
12. P.H. Wang, G.J. Keck, E.J. Lien, M.M.C. Lai, J. Med. Chem. 33 (1990) 608.
13. A. Pasini, L. Casella, J. Inorg. Nucl. Chem. 36 (1974) 2133.
14. H. Luo, P.E. Fanwick, M.A. Green, Inorg. Chem. 37 (1998) 1127–1130.
15. A. Prakash, B.K. Singh, N. Bhojak, D. Adhikari, Spectrochim. Acta A 76 (2010) 356–362.
16. M. El-Behery, H. El-Twigry, Spectrochim. Acta A 66 (2007) 28–36.
17. Z. Afrasiabi, E. Sinn, W. Lin, Y. Ma, C. Campana, S. Padhye, J. Inorg. Biochem. 99
18. Crowe, A. J. In: B. Keppler (Ed.), *Metal Complexes in Cancer Chemotherapy*; VCH: Weinheim and New York, **1993,** 369-380.
19. Malhotra, R.; Mehta, J.; Bala, K.; Sharma, A. K. *Indian J. Chem.* **2008,** 47A, 58-61.
20. Malhotra, N.; Asijaa, S.; Malhotra, R. *Phosphorus Sulfur Silicon Relat. Elem*. **2011,** 186, 1449-1459.