International Journal of Engineering Science Invention
ISSN (Online): 2319 – 6734, ISSN (Print): 2319 – 6726
www.ijesi.org ||Volume 6 Issue 9|| September 2017 || PP. 46-49

Synthesis, Characterization And Biological Studies Of N'',N'''-Bis[(E)-(4-Fluorophenyl) Methylidene] Thiocarbonohydrazide

Rekha Nalawade [1,2],Avinash Nalawade [2] ,Rajendra Shejwal[2], Mansing Anuse[1*]
[1] *Department of Chemistry, Shivaji University Kolhapur, India.*
[2] *Lal Bahadur Shastri College of Arts, Science and Commerce Satara, Maharashtra, India.*
**Corresponding author email: mansinganuse@yahoo.co.in*

Abstract: *The N'',N'''-bis[(E)-(4-fluorophenyl)methylidene] thiocarbonohydrazide viz. bis-(4-fluoro PM) TCH which is new symmetric derivative of thiocarbohydrazide has been synthesized by reacting thiocarbohydrazide with double equivalent amount p- fluoro benzaldehyde in ethanol medium at refluxing conditions. Elemental and spectral (Uv-visible, IR and NMR) analyses carried out for characterization of bis-(4-fluoroPM) TCH. This new derivative of thiocarbohydrazide was tested for the evaluation of antibacterial activity against Staphylococcus aureus and Escherichia coli and antifungal activity against Aspergillus niger and Rhizopus sps. This compound is biologically active in very low concentration.*

Keywords: *Thiocarbohydrazides, thiocarbohydrazones, TCH, antifungal activity, antibacterial activity*

Date of Submission: 22-08-2017 Date of acceptance: 09-09-2017

I. INTRODUCTION

Thiocarbohydrazide Schiff bases are important class of compounds in medicinal and pharmaceutical field. They show biological activities including antibacterial [1, 2, 3] antifungal [4,5] and anticancer activities [3-5]. The bioactive properties of Schiff bases of thiocarbohydrazide and their metal complexes motivated several researchers to explore their physical and chemical properties.

Study of thiocarbohydrazide and its derivatives is of great interest due to the wide use of these compounds and their valuable reactions.Thiocarbohydrazones are prepared by reaction between thiocarbohydrazides with aldehydes or ketones; or Thiocarbohydrazones are Schiff bases (C=N/ azomethine gr) formed by condensation of thiocarbohydrazides with aldehyde or ketones[6]. Thiocarbohydrazides are an important class of compounds which possess applications in many fields. The chemistry of thiocarbohydrazides has gained increased interest in both synthetic organic chemistry and biological fields.

Carbohydrazide and thiocarbohydrazide are hydrazine derivatives of carbonic and thiocarbonic acids. Thiocarbohydrazides are more widely used in heterocyclic synthesis as contain the functional group RNHCSNHR. Substituted thiocarbohydrazide (RNHCONHNHCSNHR) are key to the synthesis of many organic heterocyclic ring systems.

Thiocarbohydrazide derivatives have attracted much attention in recent years due to their applications in the synthesis of heterocyclic compounds[7], synthesis of transition metal complexes[8], and pharmacological studies[9].

Symmetric and asymmetric derivatives of thiocarbohydrazide have broadly been studied due to their potential utility as analytical reagents[10,11]. Symmetric Schiff base can be easily obtained by direct reaction while there have many troubles in obtaining asymmetric Schiff base[12]. The obvious difficulty in the synthesis of asymmetric Schiff base is that the straight condensation methodology used for symmetric Schiff base is no longer applicable when some symmetric diamines were adopted as the parent reactants in the condensation reaction[13].

Thiocarbohydrazones were used for analytical applications like determination of copper(II) from binary, ternary mixtures, food materials, micronutrient fertilizer, pesticides, pharmaceuticals etc.[14] and determination of mercury(II) from binary, ternary mixtures, water samples and pharmaceuticals etc.[15].

In present study we have synthesized new symmetric Schiff base derivatives of thiocarbohydrazide viz. N'',N'''-bis[(E)-(4-fluorophenyl)methylidene] thiocarbonohydrazide [bis-(4-fluoroPM)TCH] using symmetric diamine viz. symmetric thiocarbohydrazide. It was characterized by elemental, Uv-visible, IR and NMR spectra. The compounds were tested for the evaluation of antibacterial activity against Staphylococcus aureus and

Escherichia coli and antifungal activity against Aspergillus niger and Rhizopus sps. The compound is biologically active in very low concentration.

II. MATERIALS AND METHODS

2.1 Instrumentation

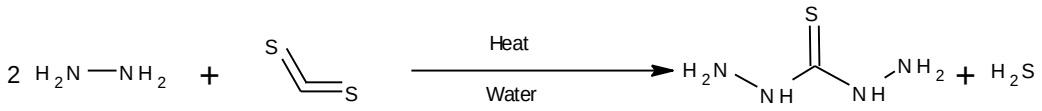
All chemicals used were of analytical grade, from SD Fine. IR spectra was recorded on Bruker FT- IR spectrophotometer by using KBr pellets technique. ^{1}HNMR was recorded on Bruker AMX 200 MHz spectrophotometer by using DMSO as solvent. The microanalysis of C, H, and N were estimated by elemental analyzer (Perkin Elmer 2400), at SAIF, CDRI, Lucknow, India.Microwave mediated reaction was carried out in conventional 25 DLX microwave oven.

2.2 Synthesis of Schiff base

It is two step manufacturing process.

(a)Preparation of thiocarbohydrazide (TCH) *– It is synthesized by various methods [6,16-18]; one of them [6] is as follows.*

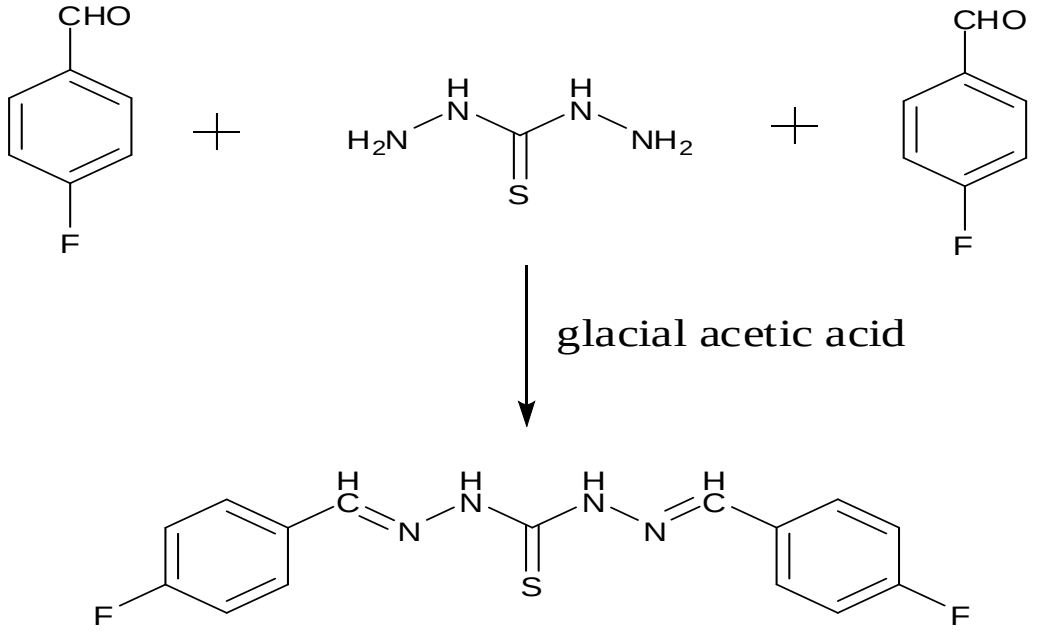
Initially 25 ml of hydrazine hydrate and 25ml water was placed in a 100 ml in round bottom flask .The temperature of solution was lowered to 10° C and 12.5 ml of carbon disulfide was dropped in round bottom flask. Now the above solution was refluxed by using water condenser about 1.5 hours. The temperature of flask was maintained about 80 to 85° C. Reaction was monitored with TLC. The temperature was then lowered to 10° C. Now the flask was cooled in ice cold water. The product obtained was filtered, recrystallised with hot water and washed with water.



Thiocarbohydrazide (TCH)

(b) Synthesis of N'', N'''-bis[(E)-(4-fluorophenyl)methylidene]thiocarbonohydrazide [bis-(4- fluoroPM)TCH]

1:2 molar solutions of TCH and p- fluoro benzaldyde refluxed in alcohol as a solvent and glacial acetic acid as a catalyst to give N",N'"-bis[(E)-(4-fluorophenyl)methylidene] thiocarbonohydrazide [bis-(4-fluoroPM)TCH]. Purity of the bis-(4-fluoroPM)TCH was tested by melting point, TLC, IR and NMR.



bis-(4-fluoroPM)TCH

2.3 Antibacterial and antifungal activity

Antibacterial and antifungal activity of [bis-(4-fluoroPM)TCH]were tested by serial dilution technique [19]. Eight test tubes containing 5 ml of sterile nutrient / sabouraud broth were inoculated with 0.02ml of 24 h old culture of bacteria Staphylococcus aureus and Escherichia coli and fungi Aspergillus niger and Rhizopus sps. respectively. Different amounts of [bis-(4-fluoroPM)TCH] in ethanol were aseptically added with the help of sterile pipettes from the stock solution 200 µg/ml to 5 ml quantities of respective media so as to reach the concentration from 1µg/ml to 20µg/ml. All test tubes were inoculated at 37^0C and at room temperature for bacteria and fungi respectively. Test tubes inoculated with organism were observed for presence of turbidity after 24h and 48h respectively. The lowest concentration of in [bis-(4-fluoroPM)TCH] inhibiting the growth of organism was determined as MIC value.

III. RESULTS AND DISCUSSION

When hydrazine hydrate taken twice moles as compared with the carbon disulphide and refluxed in water thiocarbohydrazide (TCH) is formed. Solutions of TCH and p-fluoro benzaldyde(1:2) refluxed in alcohol as a solvent and glacial acetic acid as a catalyst. The reaction went very smoothly to afford the schiff bases of thiocarbohydrazide(thiocarbohydrazone)viz.N'',N'''-bis[(E)-(4-fluorophenyl)methylidene]thiocarbonohydrazide, bis-(4-fluoroPM)TCH. The elemental analysis data(C,H,N,S and X) of thiocarbohydrazone showed that it may be represented by the formula $C_{15}H_{12}N_4SF_2$. The purity and structure of bis-(4-fluoroPM)TCH was confirmed by TLC, melting point, IR, NMR spectra. Melting point: 234^0C

3.1 ***Spectral analysis***

*3.1.1 IR (KBr) cm^{-1}***:** *C=N 1602, and N-H 3434.33 and 3648.42 .*

It was noted that a pair of bands at 3434.33 cm^{-1} and 3648.42 cm^{-1} in compound are corresponding to $\nu(NH_2)$ are present in the spectra of the thiocarbohydrazones. The value of ν(C=N) stretching vibration in IR spectra of thiocarbohydrazones, show band at 1602 cm^{-1} indicates that expected C=N (azomethine gr) in imino compound formed by condensation of thiocarbohydrazide (TCH) with aromatic aldehyde.

3.1.2 ^{1}HNMR (DMSO) δ ppm:

4.72 (d, 2H, NH_2), 7.58-7.75 (m, 4H, aromatic), 8.04-8.59 (m, 4H, aromatic),8.53 (s, 1H, CH), 8.59 (s, 1H, CH), 11.51 (s, 1H, NH). 11.92 (s, 1H, NH).

3.1.3 Elemental Analysis: Observed and calculated % of C, H, N, and S were as follows
C-(56.92) 56.96 , H-(3.80) 3.79, N-(17.70) 17.72, S-(1015) 10.13

3.1.4 Electronic spectra

Electronic spectral data of the thiocarbohydrazones were recorded in amyl acetate solutions. Each thiocarbohydrazones derivative shows several intense absorptions bands in the visible and ultraviolet regions. These wide range bands seem to be due to both the $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ of benzene ring or azomethine (-C=N)groups [20]. The bands at the 216-297 nm region are assigned to intramolecular $\pi\rightarrow\pi^*$ transitions and the bands at the 321-410 nm are attributed to $n\rightarrow\pi^*$ transitions of benzene ring or azomethine (-C=N) groups. The band at 382 nm corresponds to the transition of azomethine group [21].

3.2 Antibacterial and antifungal activity

The antibacterial and antifungal activities for bis-(4-fluoroPM)TCH are shown in table (1).The bis-(4-fluoroPM)TCH shows antibacterial and antifungal activity.

Table 1. Antibacterial and antifungal activity of bis-(4-fluoroPM)TCH

Antibacterial activity				Antifungal activity			
Quantity of Stock Solution	Conc. in µg/ml	Growth(+)/ Inhibition (-) for		Quantity of Stock Solution	Conc. in µg/ml	Growth(+)/ Inhibition (-) for	
		Staphylococcus aureus	*Escherichia coli*			*Aspergillus niger*	*Rhizopus sps*
0.05	2	+	+	0.05	2	+	+
0.1	4	+	+	0.1	4	+	+
0.2	8	+	+	0.2	8	+	+
0.3	12	-	+	0.3	12	-	-
0.4	16	-	-	0.4	16	-	-
0.5	20	-	_	0.5	20	-	-

IV. CONCLUSION

The present method for the synthesis of reagent bis-(4-fluoroPM) TCH or schiff bases of thiocarbohydrazide is easy, clean and efficient. Preparation and purification of thiocarbohydrazone is easy and rapid; it requires low cost of chemicals. Greater percentage yield (99.0%) is obtained in ethanol medium. The compound bis-(4-fluoroPM) TCH show better antibacterial and antifungal activity.

REFERENCES

[1] A. H. El-masry, H.H. Fahmy, S.H. Abdelwahed, Molecules, 5, 2000, 1429-1433.
[2] M. A. Baseer, V.D. Jadhav, R.M.Phule, Y.V.Archana, Y.B.Vibhute, Orient. J. Chem., 16, 2000, 553-557.
[3] E. M. Hodnett, W.J. Dunn, J. Med. Chem., 13,1970, 768-775.
[4] S. Samadhiya, A. Halve, Orient. J. Chem., 17, 2001,119-123.
[5] A. K. Nandi, S. Chaudhri, S.K. Mazumdah, S. Ghosh, J. Chem. Soc. Perkin Trans., 2(11), 1984, 1729-1733.
[6] Z. Li. , F. Xu, Y. Zhao, J.Het Chem., 45,2008, 1489-1492.
[7] M. S. Chande, M. A. Pankhi, S. B. Ambhaikar, Indian J. Chem., 39B, 2000 ,603-605.
[8] K.S. Siddiqi , Sadaf Khan , Shahab A.A. Nami , M.M. El-ajaily, Spectrochimica Acta Part A, 67 (2007) 995–1002.
[9] M. M. Suni, V.A. Nair and C. P.Joshua, Tetrahedron , 57,2001, 2003-2009.
[10] R.E. Sánchenz, J L. Gomez Ariza, A. Guiraúm Pérze et. al., J. molecular stru., 143,1986, 509 – 512.
[11] F. J. Barragan de la rosa, J. L.Gómezariza, F.Pino et al., Talanta, 30(8),1983, 555-564.
[12] Y. Xiaozeng, M. Qingjin, H. Wanshu., J. Progress in coordination Chemistry, Beijing: Higher education press., 2000,17-28.
[13] K. Yao, Ling. L., L. Shen, Science in China(series B) 2, 2003 ,75-83.
[14] R.A. Nalawade, A.M. Nalawade, G.S. Kamble, M.A. Anuse, Spectrochimica Acta Part A, 146,2015, 297–306.
[15] R.A. Nalawade, A.M. Nalawade , A.N. Kokare, S.B. Zanje, M.D. Jamdar, A.A. Ghare, M. A. Anuse, Intern. J. of Pharm. Sci. Invention , 6(1), 2017, 50-62.
[16] M. A. Metwally, M. E Khalifa, M. Koketsu, Am. J. Chem., 22, 2012, 38-51.
[17] Authenrith, Hefner, Ber.,58 ,1925; 2151, US 4172092 A.
[18] F. Kurzer, M. Wilkinson, Chem. Rev. 113, US 5376451 A (1969).
[19] D.I. Spooner, Sykes G., Methods in Microbiology, Academic Press, London (1972).
[20] R.L. Carlin, Transition Metal Chemistry, Vol. 1, Marcel Dekker, Inc., New York, p. 239 (1965) .
[21] A.B.P. Lever, Inorganic Electronic Spectroscopy, 2nd Ed., Elsevier; Amsterdam(1984).

International Journal of Engineering Science Invention (IJESI) is UGC approved Journal with Sl. No. 3822, Journal no. 43302.

Rekha Nalawade . "Synthesis, Characterization And Biological Studies Of N",N'"-Bis[(E)-(4-Fluorophenyl) Methylidene] Thiocarbonohydrazide." International Journal of Engineering Science Invention (IJESI), vol. 6, no. 9, 2017, pp. 46–49.