International Journal of Pharmaceutical Science Invention
ISSN (Online): 2319 – 6718, ISSN (Print): 2319 – 670X
www.ijpsi.org || Volume 4 Issue 5|| May 2015 || PP.01-04

Microwave Assisted Synthesis, Structure, Spectral Characterization And Biological Studies Of (E)-N'-(4- Chloro Benzylidene)Hydrazinecarbothiohydrazide

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ABSTRACT : *Now a day's development of simple, efficient, environmentally benign and economically viable chemical process or methodologies for synthesis of organic compounds are in great demand. A (E)-N'-(4-chloro benzylidene) hydrazinecarbothiohydrazide (4-Chloro B)HCT has been synthesized by reacting 4-chloro benzaldehyde and thiocarbohydrazide under microwave irradiation without catalyst under solvent free condition, as a green chemistry approach. The reaction proceeds selectively within a couple of minutes giving high yields of the product. The compound was characterized by elemental, Uv-visible, IR, NMR and mass spectra. The compound was tested for the evaluation of antibacterial activity against S. aureus and E. coli and antifungal activity against A. niger and Rhizopus spe. The compound is biologically active in very low concentration.*

Keywords: *Thiocarbohydrazide, Green Chemistry, Antibacterial and Antifungal activity*

I. INTRODUCTION

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 and has considerable value in many useful applications such as the assessment process of the three-dimensional ultrastructure examination techniques of interphase nuclei and tissues, besides their therapeutic importance. They are also described for use as fogging agents and are considered as safe, storable, and cool-burning pyrotechnic compounds for dissemination of smoke, chemical warfare agents. On the other hand, thiocarbohydrazides are used in performing a highly selective heavy metal ion adsorbent and as complexing agents for the solvent extraction separation methods. Thiocarbohydrazide was used as a complexing agent for the solvent extraction separation of some bivalent metals such as Cd from Co, Cu, and Pb and of Pb from Ni and Pd and Cu from Zn and Hg and of Pb from Zn and Cd using various masking agents [1,2]. Thiocarbohydrazide, thiosemicarbazide, ethylenebis(thiosemicarbazide) and dithiobiurea are considered as safe, storable, and cool burning pyrotechnic compounds for dissemination of smoke, chemical warfare agents, etc [3].

Thiocarbohydrazide Schiff bases are a class of important compounds in medicinal and pharmaceutical field. They show biological activities including antibacterial [4-10], antifungal[11-14], anticancer [10-19], and herbicidal [12]activities. Furthermore, Schiff bases are utilized as starting materials in the synthesis of industrial [15-20] and biological compounds [14-25].

Microwave-assisted organic synthesis is characterized by the spectacular accelerations produced in many reactions as a consequence of the heating rate, which cannot be reproduced by thermal heating. Higher yields, milder reaction conditions, shorter reaction times can be used and many processes can be improved. The applications of microwave irradiation are used for carrying out chemical transformations, which are pollution free and eco-friendly. The basis of this technique of synthesis is much faster with higher yields compared to conventional heating. Reports on the synthesis of Schiff bases and their metal complexes by microwave methods have been comparatively less [26-31].

Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Schiff in 1864. The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R1, where R and R1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines. Several studies [32-38]showed that the presence of a lone pair of electrons in an sp2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance.

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. Mass spectra were recorded on YOKUDELNA-ES$^+$2000. 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

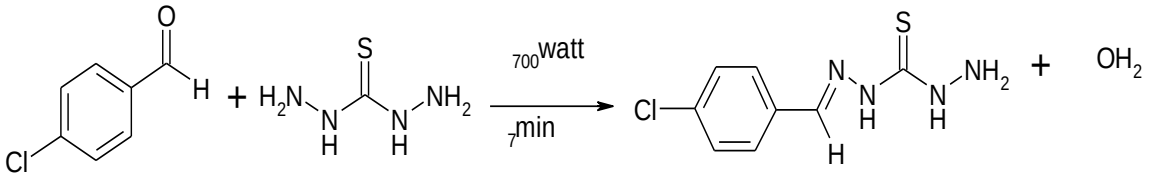
It is two step manufacturing process.

a. Preparation of thiocarbohydrazide (TCH) *– It is synthesized by various methods [39-41]); one of them is [41] as follows.*

Two moles of hydrazine hydrate are refluxed for two hours in an aqueous medium with one mole of carbon disulphide to give thiocarbohydrazide (TCH).

b Microwave mediated synthesis of (E)-N'-(4-Chlorobenzylidene)hydrazinecarbothiohydrazide (4-Chloro B)HCT

It was synthesized from thiocarbohydrazide (0.05mol),and 4-Chloro benzaldehyde (0.05mol). They were mixed well with mortar-pestle and placed in small conical flask at room temperature. The mixture was then exposed to microwave irradiations for five minute with 30 sec. pause at 700 W. Separate out the product and recrystallize with ethyl alcohol. Completion of reaction was tested by single spot TLC.



2.3 ***Biological Evaluation***

Antibacterial and antifungal activity

Antibacterial and antifungal activity of (4-Chloro B)HCT was tested by serial dilution technique [42].Eight test tubes containing 5 ml of sterile nutrient / sabouraud broth were inoculated with 0.02ml of 24 h old culture of bacteria S. aureus and E. coli and fungi A. niger and Rhizopus spe. respectively. Different amounts of (4-Chloro B)HCT in ethanol were aseptically added with the help of sterile pipettes from the stock solution 100 µg/ml to 5 ml quantities of respective media so as to reach the concentration from 1µg/ml to 50µg/ml. All test tubes were inoculated at 37^{0}C 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 (4-Chloro B)HCT inhibiting the growth of organism was determined as MIC value.

III. RESULTS AND DISCUSSION

The microwave irradiated synthesis of (4-Chloro B)HCT is completed in a couple of minutes (~ 7min) giving 75% yield. The compound (4-Chloro B)HCT is colorless crystalline solid having sharp melting point 188^{0}C and soluble in common organic solvents. The compound gave satisfactory C,H ,N and S analyses data. The observed and calculated % of C, H ,N and S in the (4-Chloro B)HCT were found that C- 42.10 (42.10), H- 3.28(3.29) , N- 24.58(24.56) and S-14.05 (14.03).

3.1 ***Spectral analysis***

(E)-N'-(4- Chloro benzylidene)hydrazinecarbothiohydrazide)

IR (KBr) cm^{-1}: *C=N 1600, and N-H 3271.26, 3385.05.*
Other peaks 3160, 2966, 2806, 1697

^{1}HNMR (200 mHz, DMSO) δ ppm:
4.66 (d, 2H, NH_2), 7.29-7.76 (m, 4H, Aromatic), 7.94 (s, 1H, CH),
11.44 (s, 1H, NH), 9.56 (s, 1H, NH).

Mass(m/z): *228.51.*

Melting Point *: 200^{0}C*

3.2 ***Antibacterial and antifungal Activities***

The compound (4-Chloro B)HCT has been tested for the evaluation of antibacterial activity against S.aureus and E. coli and antifungal activity against A. niger and Rhizopus spe. The MIC values for the compound (4-Chloro B)HCT lie in the range 14-16 μg/ml for antibacterial activity and 8-12 μg/ml for antifungal activity. The compound (4-Chloro B)HCT exhibits prominent antifungal activity than antibacterial activity.

3.3 Electronic spectra

Electronic spectral data of compound (4-Chloro B)HCT were recorded in amyl acetate solutions. Compound (4-Chloro B)HCT shows several intense absorptions bands in the visible and ultraviolet regions. These wide range bands seem to be due to both the π→π and n→π* of benzene ring or azomethine (-C=N)groups [43-45]. The bands at the 216-297 nm region are assigned to intramolecular π→π* transitions and the bands at the 321-410 nm are attributed to n→π* transitions of benzene ring or azomethine (C=N) groups.The band at 382 nm corresponds to the transition of azomethine group [46].*

IV. CONCLUSION

Microwave mediated synthesis of (4-Chloro B)HCT is a convenient and rapid process resulting in good yield of the expected product. (4-Chloro B)HCT is obtained without catalyst under solvent free condition, as a green chemistry approach.The reaction rate of (4-Chloro B)HCT is too much faster than the rates of conventional method for synthesis of Schiff bases. The compound (4-Chloro B)HCT exhibit good antibacterial activity against S. aureus and E.coli and antifungal activity against A. niger and Rhizopus spe.. It shows better antifungal activity than antibacterial activity

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