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Research Article

SYNTHESIS, STRUCTURE, SPECTRAL CHARACTERIZATION AND BIOLOGICAL STUDIES OF (E)-N'-(2-HYDROXYBENZYLIDENE) HYDRAZINE CARBOTHIOHYDRAZIDE

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ABSTRACT

A (E)-N'-(2-hydroxybenzylidene)-hydrazinecarbothiohydrazide viz. (2-hydroxy B) HCT has been produced using 2-hydroxy benzaldehyde and thiocarbohydrazide with the help of microwave light without utilization of solvents and catalysts, as an eco-friendly scheme. The reaction happens in very quick time giving high quantity of yield. Elemental, IR, NMR and mass spectra were used to characterize compound. Assessment of antibacterial action for *Staphylococcus aureus* and *Escherichia coli* and antifungal potential for *Aspergillus niger* and *Rhizopus sps* was completed for compound. Compound is bioactive even at very low quantities in solution.

Keywords: Microwave mediated synthesis, thiocarbohydrazide, green approach, Antibacterial and Antifungal activity

1. INTRODUCTION

There is need of development of simple, efficient, environment friendly and economic chemical methodology for synthesis of organic compounds.

Organic synthesis using microwave radiations is accelerated due to heating rate, which is not possible to attain by heating thermally. With microwave method, organic synthesis gives much more product, reaction proceeds under mild conditions with little reaction times. The uses of microwave illumination are utilized for doing chemical changes, which are pollution free and environment friendly. The premise of this method of combination is a lot quicker responses with higher yields contrasted with regular heating.

Schiff in 1864 reported first Schiff bases; condensation products of carbonyl compounds & primary amines. Azomethine group is the structural feature of Schiff base compounds with general representation RHC=N-R_1, R and R1 are alkyl or aryl or cycloalkyl or heterocyclic groups with various subtitites. Anils, imines or azomethines are other names for the same.

A few works [1-7] have demonstrated a lone pair of electrons on nitrogen atom from azomethine group is of impressive chemical and biological significance.

Thiocarbohydrazide Schiff bases are considered as notable compounds for medicinal as well as pharmaceutical field. Bioactivities like antibacterial [8], antifungal [9, 10], anticarcinogenic [11] and antiviral [12] activities are shown by them. Moreover, Schiff bases are used as precursor materials for obtaining industrial [13] as well as biological products [9, 13]. Thiocarbohydrazides are vital category of compounds that shows wide usefulness in several fields.

Thiocarbohydrazides chemistry has attracted much interest for both organic chemistry syntheses as well as for biological fields. They find applications in three-dimensional ultra structure assessment process study techniques of inter-phase nuclei and tissues, apart from their curative importance. They can also be employed as fogging agents and as they are safe, storable, as well, for cool-burning pyrotechnic compounds against dispersal of smoke, chemical warfare agents. Thiocarbohydrazides are used as adsorbent to highly selective heavy metal ion and in solvent extraction for complexing agents. Thiocarbohydrazide Schiff base was employed for complexing for the liquid-liquid extraction separation of divalent metals like Cu from Co^{+2}, Fe^{+3}, Ni^{+2}, Bi^{+2}, Al^{+3}, Zn^{+2}, Cd^{+2}, Pb^{+2}, Ag^{+}, Cr^{+3} and Au^{+3} and Hg from Fe^{+3}, Ni^{+2}, Bi^{+3}, Cr^{+3}, Al^{+3}, Zn^{+2}, Cd^{+2}, Pb^{+2}, Sn^{+2}, Sn^{+4},Se^{+4}, Te^{+4} with the help of various masking agents [14,15]. Thiocarbohydrazide, thiosemicarbazide, ethylenebis (thiosemicarbazide) as well as a dithiobiurea are employed as fogging agents and are safe, storable, as well

for cool-burning pyrotechnic compounds for dispersal of smoke, chemical warfare agents etc. [16].

In present work**,** we have reacted thiocarbohydrazide with equivalent amount of 2- hydroxy benzaldehyde in ethanol medium under microwave conditions to give (E)-N'-(2-hydroxybenzylidene)hydrazinecarbothiohydrazide {(2-hydroxy B) HCT} in high amount, with careful control of reactant ratio, the reaction could afforded the required monosubstituted products in high selectivity and no 1,5-disubstitued byproducts were observed [17]. (2-hydroxy B) HCT was analyzed using elemental, Infrared, NMR and mass spectrum. Tests of compound were also done for bactericide activity against *Staphylococcus aureus* and *Escherichia coli* and fungicidal activity against *Aspergillus niger* and *Rhizopus sps*. Compound showed bioactivity in very minimal quantity.

2. EXPERIMENTAL

2.1. Instrumentation

Analytical grade chemicals were used for obtaining product. IR spectrum was obtained using Bruker-FT-IR spectrophotometer with KBr pallets method. ^{1}HNMR was recorded with DMSO as solvent on Bruker-AMX 200-MHz spectrophotometer. A mass spectrum was recorded using YOKUDELNA-ES^{+}-2000. The microanalysis of C, H and N were done by using elemental analyzer (Perkin Elmer 2400), from SAIF, CDRI, Lucknow, India. Reaction was carried out in conventional 25-DLX microwave.

2.2. Synthesis of Schiff base

It is two step manufacturing process.

2.2.1. *Synthesis of thiocarbohydrazide(TCH)*

Which is obtained by number of methods [13, 17-19]; one from which is as given below [17]:

Hydrazine hydrate (two moles) & one mole of carbon disulphide are refluxed in an aqueous medium for two hours which give thiocarbohydrazide (TCH).

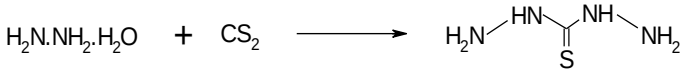

Fig. 1: Synthesis of thiocarbohydrazide

2.2.2. *Microwave mediated synthesis of (E)-N'-(2-hydroxybenzylidene) hydrazinecarbothiohydra-zide*

Equimolar quantity (0.05mol) of thiocarbohydrazide and 2- hydroxy benzaldehyde were mixed well using mortar-pestle and then taken in small sized conical flask. The combination of both was then exposed to 700 W microwave radiations for 5 minute with time interval of 30 seconds. The separated product was then recrystallized using ethyl alcohol. Single spot TLC was used to test completion of reaction.

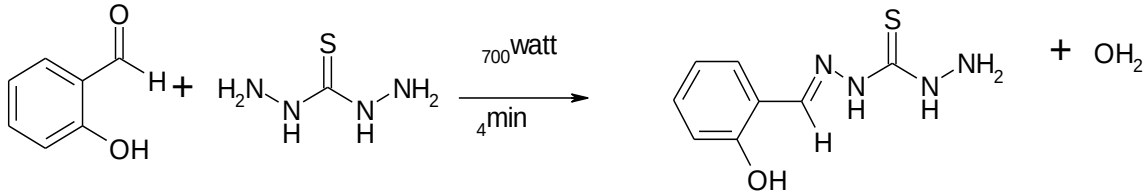

Fig. 2: ***Microwave mediated synthesis of (E)-N'-(2-hydroxybenzylidene) hydrazinecarbothiohydrazide***

2.3. Biological Evaluation

2.3.1. Bactericide and Fungicide activity

Test for (2-hydroxy B) HCT against bacteria and fungus was done by using serial dilution technique [13]. 0.02ml of 24 hour old bacteriological cultures of *Staphylococcus aureus* and *Escherichia coli* and fungi *Aspergillus niger* and *Rhizopus sps.* were inoculated in eight test tubes with 5 ml of sterile nutrient / sabouraud broth. Separate quantities of (2-hydroxy B) HCT in ethanol were aseptically mixed using sterile pipettes from stock solution of 200 µg/ml to 5 ml quantities of respective media so as to obtain the concentration from range of 1µg/ml to 20µg/ml. Inoculation of all test tubes was carried out at 37°C and as well as at room temperature for bacteria and fungi respectively. Presence of turbidity in inoculated test tubes with organism was observed after 24-hours and 48-hours. Minimum concentration of in (2-hydroxy B) HCT that hindering the development of organism was determined as MIC value.

3. RESULTS AND DISCUSSION

(2-hydroxy B) HCT, obtained with microwave method in a very short time (4min) gave about 77% yield. Compound (2-hydroxy B) HCT is with no color and is a crystalline solid which sharp melting point *i.e.* 193°C and soluble in common organic solvents. Analyses data for C, H, N and S of compound were found satisfactory. The observed and calculated % of C, H, N

and S in the (2-hydroxy B) HCT is as C- 45.70 (45.71), H- 4.76 (4.76) , N- 26.62 (26.66) and S-15.23(15.23).

3.1. Spectral analysis

IR (KBr) cm^{-1}: The value of ν(C=N) stretching vibration in IR spectra of (2-hydoxy B) HCT, showed band at 1613 cm^{-1} indicates that expected C=N (azomethine gr) in imino compound was formed by condensation of thiocarbohydrazide (TCH) with 2-hydroxy benzaldehyde.

C=N 1613 and N-H 3266 and 3153.

Other peaks- 2980, 2799, 1589, 1513, 1484, 1399, 1250, 1068, 874, 816, 724, 608, 508.

^{1}HNMR (DMSO) δ ppm: The single peak at 7.90 ppm in compound (2-hydroxy B) HCT are due to CH=N, azomethine proton showing formation of Schiff bases, which were formed by condensation of thiocarbohydrazide (TCH) with 2-hydroxy benzaldehyde. Broad singlet at 4.50 in compound (2-hydroxy B) HCT is due to NH_2 proton in thiocarbohydrazide.

12.03 (s, 1H, NH), 11.65 (s, 1H, NH), 6.93-6.78 (m, 4H, Aromatic), 4.50 (bs, 2H, NH_2), 7.90 (s, 1H, CH), 11.40 (bs, 1H,OH), Mass: 238.06, mp: 193°C.

3.2. *Antibacterial and antifungal Activities*

(2-hydroxy B) HCT had been tested for its bioactivity for bacteria against *Staphylococcus aureus* and *Escherichia coli* and for activity for fungus against *Aspergillus niger* and *Rhizopus sps.,* respectively. The (2-hydroxy B) HCT showed 16-20 μg/ml MIC value range for bactericidal activity and 12-16 μg/ml MIC value range for fungicidal activity. Compound (2-hydroxyn B) HCT showed outstanding activity against bacteria than activity against fungus. Both activities are shown in table 1.

Table 1: Antibacterial and antifungal activity of (2-hydroxy B) HCT

Antibacterial activity				Antifungal activity			
Quantity of Stock Solution	Conc. (μg/ml)	Growth (+)/ Inhibition (-)		Quantity of Stock Solution	Conc. (μg/ml)	Growth(+)/ Inhibition (-)	
		S. aureus	*E. coli*			*A. niger*	*Rhizopus spe*
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	-	-

4. CONCLUSION

(2-hydroxy B) HCT was obtained using microwave method which is convenient and gives good amount of expected product in very short time. (2-hydroxy B) HCT was obtained in absence of catalyst without use of solvent, following green approach. The rate of reaction of (2-hydroxy B) HCT is too much higher as compared to rates of traditional method. Compound (2-hydroxy B) HCT exhibited excellent activity against bacteria like *Staphylococcus aureus* and *Escherichia coli* and excellent activity against fungus like *Aspergillus niger* and *Rhizopus sps*. It indicates better fungicide activity than bactericide activity.

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