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Synthesis, Structure, Spectral Characterization and Biological Studies of (E)-N'-(4methylbenzylidene) Hydrazinecarbothiohydrazide

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Abstract : Development of simple, efficient, environmentally begin and economically viable chemical process or methodologies for synthesis of organic compounds are in great demand.
A (E)-N'-(4-methylbenzylidene)hydrazinecarbothiohydrazide viz.(4-methyl B)HCT has been synthesized by reacting4-methyl 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, IR, NMR and mass spectra. The compound was tested for the evaluation of antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* and antifungal activity against *Aspergillusniger* and *Rhizopussps*. The compound is biologically active in very low concentration.
Keywords: Microwave mediated synthesis, thiocarbohydrazide, green chemistry, antibacterial and antifungal activity.

1. Introduction

Thiocarbohydrazide Schiff bases are a class of important compounds in medicinal and pharmaceutical field. They show biological activities including antibacterial [1],antifungal [2,3],anticarcinogenic [4] and antiviral [5] activities. Furthermore, Schiff bases are utilized as starting materials in the synthesis of industrial [6] and biological compounds [2,6].

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 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. ThiocarbohydrazideSchiff basewas used as a complexing agent for the solvent extraction separation of some bivalent metals such as Cu fromCo^{+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}using various masking agents [7,8].Thiocarbohydrazide, thiosemicarbazide, ethylenebis (thiosemicarbazide) and dithiobiurea are considered as safe, storable, and cool burning pyrotechnic compounds for dissemination of smoke, chemical warfare agents, etc[9].

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.With microwave method organic synthesisis carried out at higher yields, milder reaction conditionsand shorter reaction times. 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 reactions with higher yields compared to conventional heating.

In present work **,**we have reacted thiocarbohydrazide with equivalent amount of 4-methyl benzaldehyde in ethanol medium under microwave conditions to give (E)-N'-(4-methylbenzylidene) hydrazine carbothiohydrazide (4-methyl B)HCT in high yield, provided the reactant ratio was carefully controlled, the reaction could afforded the desired monosubstituted products in high selectivity and no 1,5-disubstitued byproducts were observed [10].(4-methyl B)HCT was characterized by elemental, IR, NMR and mass spectra. The compound was tested for the evaluation of antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* and antifungal activity against *Aspergillus niger* and *Rhizopussps.* The compound is biologically active in very low concentration.

2. Experimental

2.1 Instrumentation

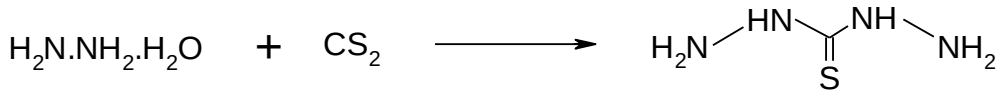
All chemicals used were of analytical grade, from SD Fine. IR spectra was recorded on Bruker FT- IR spectrophotometer by using KBr pellets technique. ^{1}HNMR was recorded on Bruker AMX 200 MHz spectrophotometer by using DMSO as solvent. Mass spectra was recorded on YOKUDELNA-ES^{+}2000. The microanalysis 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

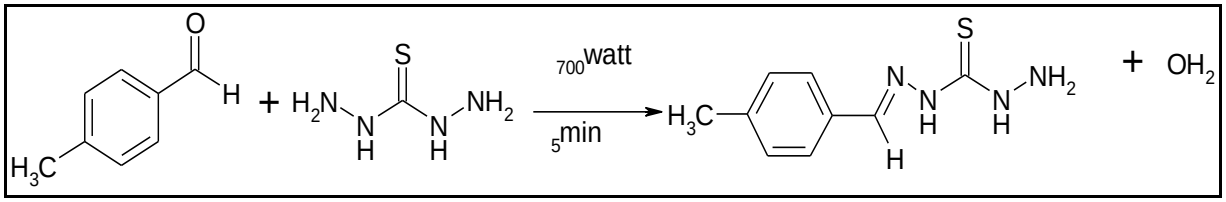
It is two step manufacturing process.

a. Preparation of thiocarbohydrazide (TCH) – It is synthesized by various methods [6, 10-12]; one of them is [10] 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-methylbenzylidene)hydrazinecarbothiohydrazide Itwas synthesized from thiocarbohydrazide (0.05mol)and 4-methyl benzaldehyde (0.05mol). They were mixed well with mortar-pestle and placed insmall conical flask at room temperature. The mixture was then exposed to microwaveirradiations for five minute with 30 sec. pause at 700 W. The product wasseparated out and recrystallized with ethyl alcohol.Completion of reaction was tested by single spot TLC.



2.3 Biological Evaluation

2.3.1 Antibacterial and antifungal activity

Antibacterial and antifungal activity of (4-methyl B)HCTwas tested by serial dilution technique [13].Eight test tubes containing 5 ml of sterile nutrient / sabouraud broth were inoculated with 0.02mlof 24 h old culture of bacteria *Staphylococcus aureus* and *Escherichia coli*and fungi *Aspergillus niger* and *Rhizopus sps*.respectively. Different amounts of (4-methyl B)HCT in ethanol were aseptically added with the help ofsterile pipettes from the stock solution 200 µg/ml to 5 ml quantities of respective media so as toreach the concentration from 1µg/ml to 20µg/ml. All test tubes were inoculated at 37^0C and atroom temperature for bacteria and fungi respectively. Test tubes inoculated with organism wereobserved for presence of turbidity after 24h and 48h respectively. The lowest concentration ofin(4-methyl B)HCTinhibiting the growth of organism was determined as MIC value.

3. Results and Discussion

The microwave irradiated synthesis of (4-methyl B)HCTis completed in a couple of minutes (~ 5min) giving 75% yield. The compound (4-methyl B)HCT is colorless crystalline solid having sharp meltingpoint 188^0C and soluble in common organic solvents. The compound gave satisfactory C,H ,Nand S analyses data. The observed and calculated % of C, H ,N and S in the (4-methyl B)HCT were found that C- 51.94 (51.92), H- 5.76 (5.76) , N- 26.93 (26.92) and 15.39(15.38).

3.1 *Spectral analysis*

IR (KBr) cm^{-1}: The value of ν(C=N) stretching vibration in IR spectra of (4-methyl B)HCT, show band at 1613 cm^{-1} indicates that expected C=N (azomethine gr) in imino compound formed by condensation of thiocarbohydrazide (TCH) with 4-methyl benzaldehyde.

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

^{1}HNMR (DMSO) δ ppm : The single peak at 7.95 ppm in compound (4-methyl B)HCT are due to CH=N, azomethine proton showing formation of Schiff bases, which were formed by condensation of thiocarbohydrazide (TCH) with 4-methyl benzaldehyde. Doublet at 3.50-3.43 in compound (4-methyl B)HCT are due to NH_2 proton in thiocarbohydrazide.

11.64 (s, 1H, NH). 11.33 (s, 1H, NH).7.29-7.1 (m, 4H ,Aromatic), 3.50-3.43 (d, 2H,NH_2), 7.95 (s, 1H, CH),;2.3(s, 3H,CH_3);

Mass: 208.06.

3.2 Antibacterial and antifungal Activities

The compound (4-methyl B)HCT has been tested for the evaluation of antibacterial activity against*Staphylococcus aureus* and *Escherichia coli*and antifungal activity against*Aspergillus niger* and *Rhizopus sps.* respectively. The MIC valuesfor the compound (4-methyl B)HCT lie in the range 16-20 µg/mlfor antibacterial activity and 12-16 µg/mlfor antifungal activity. The compound (4-methyl B)HCT exhibits prominent antifungal activity thanantibacterial activityAntifungal and antibacterial activity is shown in following table 1.

Table 1 Antibacterial and antifungal activity of (4-methyl B)HCT

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 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

Microwave mediated synthesis of(4-methyl B)HCTis a convenient and rapid process resulting ingood yield of the expected product. (4-methyl B)HCT is obtained without catalyst under solvent free condition, as a green chemistry approach.The reaction rate of(4-methyl B)HCT is too much faster than the rates ofconventional method for synthesis of Schiff bases.The compound (4-methyl B)HCTexhibit good antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*and antifungal activity against *Aspergillus niger* and *Rhizopus sps*.It shows better antifungal activitythan antibacterial activity.

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