

Synthesis, Characterisation and Antimicrobial Activity of Some New Thiosemicarbazones

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Four different thiosemicarbazones, viz., *m*-anisaldehyde thiosemicarbazone (**1a**), acetophenone-thiosemicarbazone (**2a**), 2-hydroxy-5-methyl benzene-1,3dicarbonyl thiosemicarbazone (**3a**) and 2,6-diacetyl-pyridine thiosemicarbazone (**4a**) have been synthesized by the reaction of different carbonyl compounds with thiosemicarbazide (**a**) and were characterized by their TLC, elemental analysis and IR spectral data. All compounds have been screened for their biocidal activity *in vitro* by serial dilution method against gram +ve bacteria *Staphylococcus aureus* and gram -ve *Escherichia coli* and two common fungi *Aspergillus niger* and *Aspergillus flavus*. All the thiosemicarbazones have shown several-fold increase in antimicrobial activity as compared to their constituting thiosemicarbazide and carbonyl compounds.

Key words: Synthesis, thiosemicarbazones, antimicrobial activity.

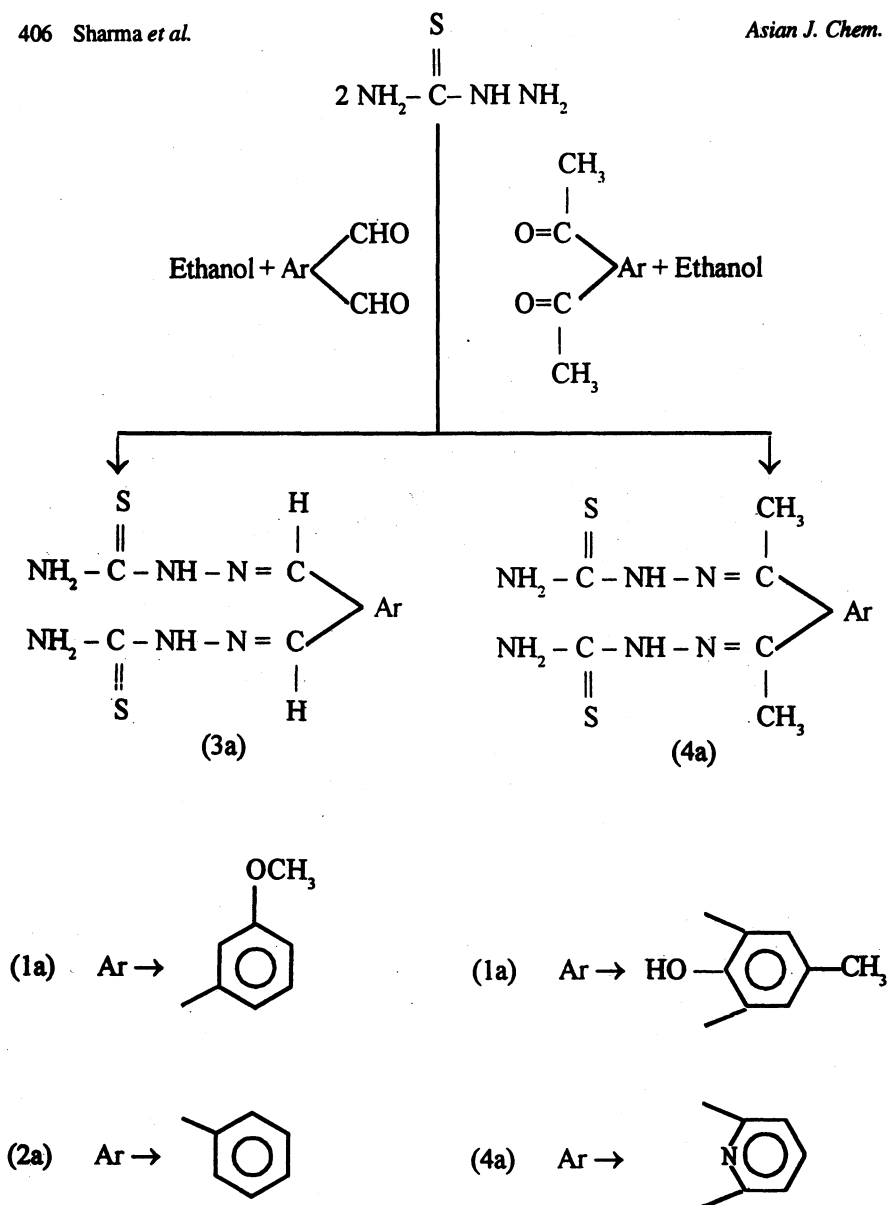
INTRODUCTION

A number of thiosemicarbazones have been reported to possess different biological activities¹⁻⁷. These compounds are synthesized from different carbonyl compounds with thiosemicarbazide, in which primary amino group undergoes condensation with carbonyl group resulting in the formation of respective thiosemicarbazones⁸. The thiosemicarbazones of α -N-ketones and aldehydes possess broad spectrum chemotherapeutic activities and are found to be potentially active⁹.

EXPERIMENTAL

All the chemicals used were of AR grade and the liquid chemicals were purified by distillation before use. The purity of compounds was judged by the repeated m.p. of the recrystallized products which was determined in open capillary using Toshniwal apparatus and by running TLC for single spot on silica gel.

(A) **Synthesis of thiosemimonocarbazones (1a and 2a):** 0.91 g (0.01 M) of thiosemicarbazide was dissolved in dry alcohol (20 mL), 1.1 mL (0.01 M) *m*-anisaldehyde/1.15 mL (0.01 M) acetophenone in dry alcohol (20 mL) were mixed together and then refluxed for 5 h over a water bath using water condenser. Crude products were obtained after cooling the reacting mixture in ice bath, filtered and dried. They were recrystallized from a mixture of 10 mL ethyl alcohol and 5 mL DMF, filtered and dried in vacuum desiccator over anhydrous CaCl₂ (yield: **1a**, 72% and **2a**, 68%).



(B) Synthesis of thiosemidicarbazones (3a and 4a): 1.82 g (0.02 M) thiosemicarbamide dissolved in dry ethanol (20 mL) and 1.64 g (0.01 M) 2-hydroxy-5-methyl-benzene-1,3-dicarbaldehyde/1.63 g (0.01 M) 2,6-diacetyl pyridine in dry alcohol (20 mL) were mixed together and refluxed for 5 h over a water bath using water condenser. The obtained solutions were concentrated to one-fourth of their original volume, then cooled overnight in freezing mixture and filtered. The resulting products were recrystallized from a hot mixture of 10 mL alcohol and 5 mL DMF, filtered and dried in vacuum desiccator over anhydrous CaCl_2 (yield: 3a, 70% and 4a, 67%).

Carbon, hydrogen and nitrogen analyses were carried out on Carlo-Erba

micro-analyser (model 1106) and sulphur was estimated as BaSO₄ by standard procedure¹⁰. IR spectra were recorded on a JASCO spectrophotometer-0087 in KBr medium.

Antimicrobial Activities: All the synthesized ligands were screened for their antimicrobial and antifungal activities against the bacteria *Staphylococcus aureus* (gram +ve) and *Escherichia coli* (gram -ve) and the fungi *Aspergillus niger* and *Aspergillus flavus* adopting serial dilution method¹¹ in suitable nutrient medium (6.0 g peptone, 3.0 g yeast extract, 1.5 g beef extract, 1.5 g agar for slant and 1.0 g dextrose in one litre distilled water for bacteria; and 10 g peptone, 20.5 g agar only for slant, 20.0 g dextrose in one litre distilled water for fungi). Graded diluted solutions for the test compounds were inoculated with the micro-organisms under examination using aseptic conditions and incubated at 37°C for 24 h in case of bacteria and 28°C for 96 h in case of fungi in a BOD incubator. The MIC values of the test compounds were determined by detecting the inhibition of the growth by minimum concentration of the test compound.

RESULTS AND DISCUSSION

The results of physical and analytical data of all the synthesized compounds have been presented in Table-1. In the IR spectra of all compounds, medium intensity bands in the regions of 3140–3120 cm⁻¹ and 3320–3310 cm⁻¹ have been

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF THIOSEMICARBAZONE COMPOUNDS

Compound (colour)	m.f.	m.w.	m.p. (°C)	% Analysis, found (calculated)			
				C	H	N	S
1a (Light yellow shiny crystals)	C ₉ H ₁₁ N ₃ OS	209	190	51.58 (51.67)	5.09 (5.26)	19.94 (20.09)	15.00 (15.31)
2a (Pale yellow amorphous)	C ₉ H ₁₁ N ₃ S	193	120	55.90 (55.96)	5.57 (5.69)	21.63 (21.76)	16.02 (16.58)
3a (Dark yellow crystals)	C ₁₀ H ₁₂ N ₆ OS ₂	296	146	40.48 (40.54)	3.98 (4.05)	27.38 (27.87)	21.12 (21.62)
4a (Cream shiny crystals)	C ₁₁ H ₁₅ N ₇ S ₂	300	230	42.64 (42.72)	4.77 (4.85)	31.62 (31.72)	20.15 (20.71)

obtained which may be due to stretching vibration of —NH and —NH₂ group respectively^{12, 13}. A weak intensity band in the region of 1270–1250 cm⁻¹ in the IR spectra of all compounds may be due to C=S group¹³. In the IR spectra of all thiosemicarbazones (**1a–4a**) a new band of sharp intensity in the region 1620–1610 cm⁻¹ has appeared which may be due to stretching vibration of azomethine group (>C=N—) group¹⁴. All thiosemicarbazones have shown a sharp intensity band in the region 3050–2980 cm⁻¹ due to —CH stretching vibration of aromatic ring¹⁵. In the IR spectra of compound **4a** two bands of medium sharp intensity at 630 cm⁻¹ and 420 cm⁻¹ are obtained which may be attributed to in-plane and out-of-plane pyridine ring deformation respectively¹². In the IR spectra of compounds **2a** and **3a**, a medium intensity band has been

obtained in the region 880–860 cm^{-1} which may be attributed to out-of-plane C—H deformation vibration¹⁶. The IR spectrum of compound **3a** has shown bands at 3580–3570 cm^{-1} and a sharp intensity band at 2960 cm^{-1} probably due to —C—OH and C—CH₃ groups respectively.

A comparative study of MIC values (Table-2) of thiosemicarbazones reveals the following activity order: **4a** > **3a** > **2a** > **1a**. These observations in general infer that antimicrobial activity of thiosemicarbazide has increased in the form of their thiosemicarbazone. The maximum activity of compound **4a** may be due to presence of additional heterocyclic moiety.

TABLE-2
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY DATA (MIC VALUES) IN MOLAR CONCENTRATION ($\times 10^{-5}$) OF THIOSEMICARBAZONES (**1a–4a**)

S.No.	Compound	Bacteria		Fungi	
		<i>S. aureus</i>	<i>E. coli</i>	<i>A. niger</i>	<i>A. flavus</i>
1.	1a	11.96	11.96	12.02	12.02
2.	2a	10.50	10.80	11.31	11.35
3.	3a	8.44	8.44	7.36	7.37
4.	4a	7.35	7.35	7.10	7.10

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