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SYNTHESIS OF 1-FORMAMIDINO-3-SUBSTITUTED FORMAMIDINO THIOCARBAMIDES AND THEIR ANTIBACTERIAL SCREENING

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ABSTRACT

In the present work, a novel series of 1-formamidino-3-substituted formamidino thiocarbamides have been prepared by the interaction of dicyandiamide with thiourea in ether acetone medium. The justification of the structure of these newly synthesized compounds has been established on the basis of chemical characteristics, elemental analysis, IR, NMR and mass spectral analysis. Then synthesized compounds were screened for their antimicrobial activity against E. coli, S. typhi and P.aeruginosa. The synthesized compounds found to be good to moderate antimicrobial activity.

KEYWORDS: Thiocabamides, Dicyandiamide, Characteristics & Antimicrobial evaluation

INTRODUCTION

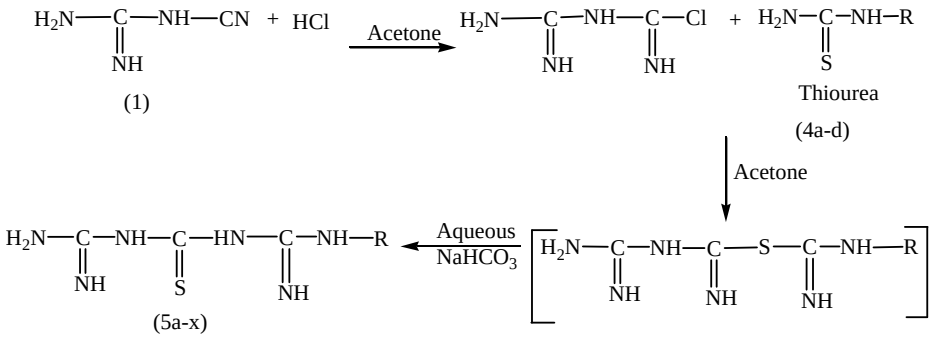
Glucosyl group or its derivatives when attached to the sulphur of the sulphur containing heteroacycles and heterocycles are commonly referred as "Thioglucosides."As evident from the structure of cyanoamidino substituted thiocarbamide, it was observed that there are various reactive sites in this molecule for the reactions. This molecule possesses -SH, -CN, -NH2 important reactive sites for the reactions. As a wider program of this laboratory in the synthesis of nitrogen, nitrogen and sulphur containing heteroacycles and heterocycles. The interactions of dicyandiamide with various thioureas and alkyl/arylisothiocycnates had been investigated in sufficient details in various reaction conditions [1-4]. Some of these compounds showed noticeable pharmaceutical and biological values [5-6]. These heteroacycles were also classified in 5 and 6 membered heterocycles viz. thiadiazoles, dithiazoles, hectors bases, thiadiazines and triazines. These heterocycles posses their own identity and significance in pharmaceutical, medicinal, agricultural, industrial and biotechnical sciences [7-10]. S-glucosides and N-glucosides had been found several applications in industry and also in medicinal chemistry [11-12]. Dicyandiamide is an important organic compound for its pharmaceutical, medicinal, biological, agricultural and industrial applications [13].

Dicyandiamide is a bifunctional molecule. It has basic formamidino group at position three and a cyano/nitrilo group at first position. This molecule, therefore, is expected to produce verities of certain interesting heterocycles and heterocycles containing nitrogen, nitrogen and sulphur, through its reactive basic amino group and cyano group. Interaction of cyanamide with various thioureas had been investigated in sufficient details. [14-15].

EXPERIMENTAL

1, 3-diformamidinothicarbamide (5a) was synthesized by refluxing a mixture of dicyandiamide dicyandiamide (0.1 M) thioureas (0.1 M), acetone (50 ml) and ethanol (50 ml) was taken. To this reaction mixture, dry hydrogen chloride gas was bubbled (NaCl 16 g and H_2SO_4 25 ml) for 20 minutes. This reaction mixture was refluxed for 10 hrs, during

boiling dicyandiamide went into the solution and new product was found to be gradually separated out. It was filtered in hot condition and recrystallized with aqueous ethanol, yield-70%, m.p. 187^{0}C.The probable reaction mechanism of the formation of is as depicted below.



Where, R=H, Phenyl, methyl, ethyl, allyl

1, 3-diformamidinothiocarbamides (5a) was synthesized by refluxed Chemicals and solvents were reagent grade and used without further purification. Melting points were determined on a capillary melting point apparatus and are uncorrected. 1H NMR spectra were recorded in the indicated solvent on Bruker WM 400 MHz spectrometer with TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer spectrophotometer.

RESULT AND DISCUSSIONS

A mixture of dicyandiamide (0.1 M), various thioureas (0.1 M), acetone (50 ml) and ethanol (50 ml) was taken. To this reaction mixture, dry hydrogen chloride gas was bubbled (NaCl 16 g and H_2SO_4 25 ml) for 20 minutes. This reaction mixture was refluxed for 10 hrs, during boiling dicyandiamide went into the solution and new product was found to be gradually separated out. It was filtered in hot condition and recrystallized. The chemical and spectral data of the compounds (5a-e) are given in Tables 1 and 2.

Table 1: Chemical Data of the Compounds (5a-E)

Comp.	R	Formula	m. p.(°C)	Yield (%)
5a	Hydrogen	$C_9H_{12}N_6S$	182	72
5b	Phenyl	$C_4H_{10}N_6S$	123	53
5c	Methyl	$C_6H_{12}N_6S$	203	69
5d	Ethyl	$C_7H_{14}N_6S$	189	65
5e	Allyl	$C_7H_{12}N_6S$	191	55

Elemental analyses for C, H, N are within ± 0.4% of the theoretical values.

The IR spectrum was carried out in KBr pellets and is reproduced on Plate no. IR-1.2. Figure 1 shows the FT-IR spectrum of formamidino thiocarbamides whereas the table 1 shows the major absorption peaks. The important absorption can be correlated as follows-

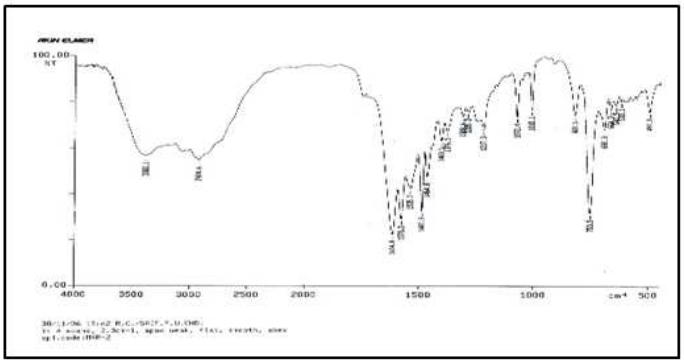


Figure 1: FT-IR Spectrum of 1, 3-Diformamidino Thiocarbamides

Table 2: Major Absorption Peak in FT-IR Formamidino Thiocarbamides

Absorption Observed (cm^{-1})	Assignment	Absorption Expected(Cm^{-1})
3184.8	NH stretching	3500-3000[16]
2931.3	C-H (Ar) Stretching	3150-2900[17]
1533.8	C=NH Stretching	1789-1478[18]
1496.3	C=N stretching	1789-1471[18]
1324.5	C-N stretching	1324-1250[19]
839.0	Glucopyranosyl ring	844+8[19]
746.2	C-S stretching	800-600[20]

The PMR spectrum of compound 1, 3-diformamidinothiocarbamide (5a) was carried out in DMSO-d6 and Ar. This spectrum distinctly displayed the signals due to NH protons at 2.5-2.6 ppm, ArNH protons at □7.1 (Silversteiry) ppm. Protons at δ 7.77 - 7.01 ppm, the signals at δ 6.99 – 6.27 ppm are due to protons of pyranosyl ring.

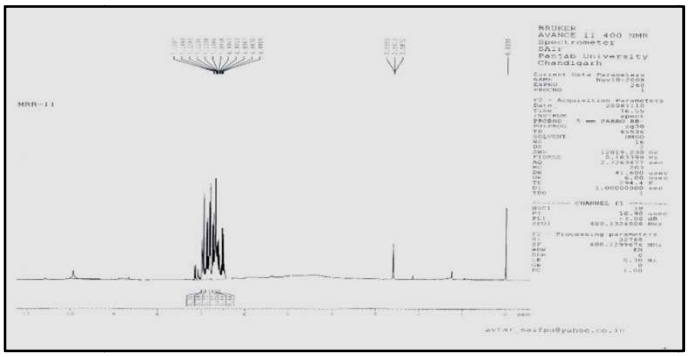


Figure 2: PMR Spectra of 1,3-Diformaamidinothiocarbamide (5a)

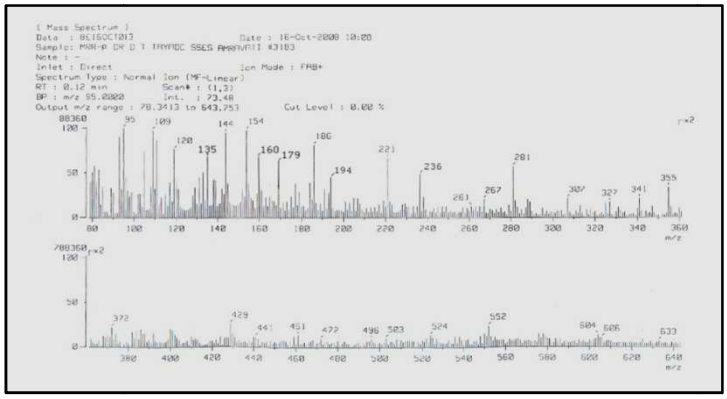


Figure 3: Mass Spectrograph of 1, 3-Diformamidino Thiocarbamide (5a)

The FAB mass spectrum of 1, 3-diformamidinothiocarbamide shown in figure, was recorded at room temperature by using Meta nitrobenzyl alcohol as the matrix m+ peak as well as other temperature fragment peaks and the probable fragmentation pattern of the molecular ion. While the mass spectrum is reproduced on plate No. Mass – 2.1

Antimicrobial Activity

Most of the synthesized compoundswere screened in vitro for their antimicrobial activities against E. coli, S. typhi, P.aerogenosa using disc diffusion method what man filter paprer No. 1 disks of 5mm diameter were sterilized in autoclave and soaked in sample solution, blotted on sterile filter paper. 0.1ml of the inoculums of test organism was spread using sterile glass spreader on the surface of nutrient agar. DMSO was used as a solvent and streptomycin was used as a control. The inhibition zones were measured in millimeter by the end of the incubation period (24 hrs. at 370C for bacteria).The results are presented in Table No.-2.

Table 3: Antibacterial Activity of Newely Synthesized of 1-Formamidino-3-Substituted Formamidino Thiocarbamides (5a-5e)

Compound R	Antibacterial Activity (Inhibition Zone in mm)		
	E. Coli	S. Typhi	P.aerogenosa
5a -H	10±0.3	8±0.3	-
5b Phenyl	9±0.3	10±0.6	-
5c methyl	6±0.6	8±0.3	-
5d Ethyl	-	8±0.3	-
5e Allyl	8±0.6	-	-
Std. Streptomycin	10±0.6	12±0.4	-

Antibacterial studies of these compounds indicated that compounds (5a) and(5b) were found to be active against E.coli and rest of were found to be moderately active.(5a) and (5b)exhibited most moderately activity against E. Coli and S. typhi.

Form the data it is clear that most of the compounds are highly effective against S. typhi and E. Coli while inactive against P. aerogenosa.

CONCLUSIONS

The compound 1-formamidino-3-substituted formamidino thiocarbamides (5a-e) which successfully prepared pale yellow crystalline solid having m.p.265-266(d).The synthesized sample was characterized by FT-IR,PMR and mass spectrograph indicating the formation of desired product. The compound was studied for their antimicrobial activity and all the pathogen tested during analysis. From the result it was clear that compound show remarkable and considerable antimicrobial activity against organism. The activity of compound was tested against all pathogen by disc diffusion method.

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