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MICROWAVE ASSISTED SYNTHESIS OF 1-FORMAMIDINO-3-SUBSTITUTEDFORMAMIDINOTHIOCARBAMIDES

D. T. Tayade and S. P. Ingole*

[1]Department of Chemistry, Govt. Vidarbha Institute of Science and Humanities, Amravati 444604.

***Corresponding Author: S. P. Ingole**

Department of Chemistry, Govt. Vidarbha Institute of Science and Humanities, Amravati 444604.

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ABSTRACT

One pot three component synthesis by non-conventional synthetic method has been carried out recently in this laboratory for the synthesis of 1, 3-diformamidinothiocarbamide and a series of 1-formamidino-5-substitutedformamidinothiocarbmides (IIIa-e) by the interactions of cyanoguanidine (I), concentrated hydrochloric acid and various thiourea (IIa-e) by making use of microwave irradiation. This synthetic method has revealed extensive applications as it is very efficient way to accelerate the course of many organic reactions, producing high yields, higher selectivity and lower quantities of side products consequently easier work-up and purification of the products.

KEYWORDS: Substituted thiourea, cyanogaunidine, microwave.

INTRODUCTION

In the recent years solvent free reaction condition had been studied.[1] The solvent free reactions are usually took shorter reaction time, simpler reactors, more efficient work up to procedure, easier separation and purification than conventional reaction condition.[2-3]

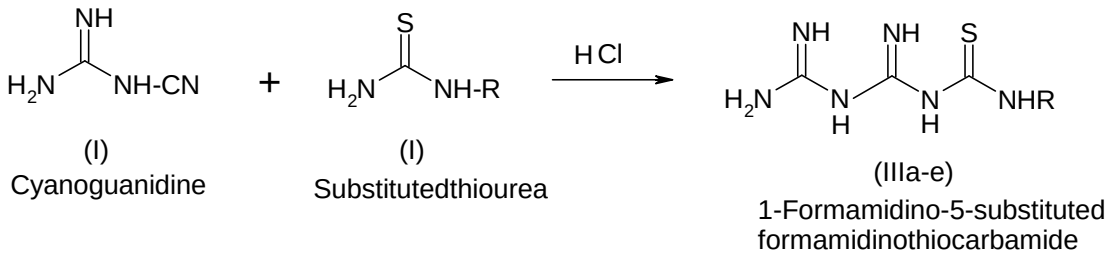
In recent era, an electromagnetic energy in the range of microwaves have achieved unique interest as regards the most various fields of utilization such as the alimentary (domestic ovens), analytical (small ovens devoted to the mineralization) and also biomedical applications.[4]

In synthetic chemistry, the main target is to explore an alternative reaction conditions to achieve the preferred chemical transformations with minimum byproducts or waste generation as well as to eliminate the use of conservative organic solvent. It also gave strict legal restrictions on pollution exposures. Again synthetic chemistry had been suffered either in the base research for the clear improvements which can lead to higher yields of cleaner products, minor energy consumption and environmental compatibility.

Thus microwave energy can be used as an activating agent in chemistry for the synthesis of a large number of compounds. Numerous organic reaction assisted by microwave heating have been explained in various articles and books.[5-6]

Thiocarbamides and their derivatives show strong antimicrobial activity and also versatile reagent in organic synthesis.[7] Although they have been known from long ago to be biologically active[8-10], their varied biological features are still of great scientific interest. Some derivatives of these possess anti-tuberculosis, anti-cancer, anti-tumor, anti-pyretic activites.[11-12] Recently in this laboratory Tayade *et al*[13-21] synthesized new series of thiadiazoles, thiadiazines and dithiazines by exploring the synthetic application of -amino,-cyano, -halo etc. groups successfully and also studied their antimicrobial, antifungal and physiochemical parameters.

The main objective of this work is to set up new solvent free reaction condition, reduce the time span of reactions and at the same time it was also thought to increase the yield of product by maintaining the purity. Cyanoguanidine, thiocarbamides and its derivatives had been pharmaceutical, agricultural, biological, medicinal and industrial significances and applications. We here in report the green synthesis of several 1-formamidino-5-substitutedformamidinothio- carbmides and 1,3-diformamidinothiocarbamide **(IIIa-e)** by the interactions of cyanoguanidine (I), concentrated hydrochloric acid and various thiourea **(IIa-e)** in microwave irradiation technique which is heither to unknown. The tentative reaction is depicted below **(Scheme-I)**



Where, R= H, ethyl, methyl, allyl, phenyl.

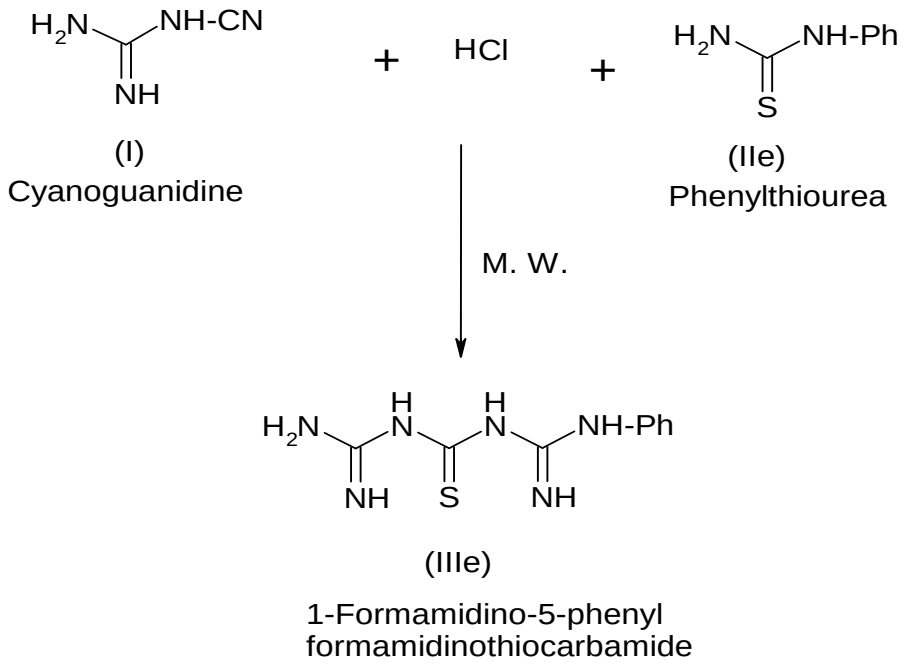
Scheme-I

Experimental

The melting point of the all synthesized compounds was recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra1106 analyzer. Nitrogen estimation was carried out on Colman-N-analyzer-29. IR spectra were recorded on Perkin Elmer Spectrometer in range 4000-400cm^{-1} in KBr pellets. PMR spectra were recorded on Brucker400F spectrometer with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as solvent. The purity of compound was checked on silica Gel-G Pellets by TLC with layer thickness of 0.3mm. All chemicals used were AR-grade.

A) Synthesis of 1-formamidino-3-phenylformamidinothiocarbamide

A reaction mixture of cyanoguanidine (I), concentrated hydrochloric acid and phenylthiourea (IIb) in 1:1:1 molar ratio was kept in microwave for 1 minute. Then the reaction mixture was poured into ice cold water, with vigorous stirring white granular crystals were separated out. Recrystallized from aqueous ethanol. Yield 96%, melting point 168^{0}C. The probable reaction and mechanism for the formation of (IIe) is depicted below,



Properties:- It is yellow crystalline solid having melting point 147^{0}C. It gave positive test for nitrogen and sulphur. It was desulpurized by alkaline plumbite solution. It formed picrate having melting point 160^{0}C.

Elemental Analysis: C[(found 44.56%) calculated 45.56], H[(found 04.48%) calculated 05.48], N[(found 35.40%) calculated 35.44], S[(found 12.35%) calculated13.50]. **IR spectrum** (cm^{-1}): The IR spectrum was carried out in KBr-pellets: 3305.12 (N-H stretching), 3175.12 (Ar-CH stretching), 1694.13(C=S stretching), 1593.11(C=NH imino group),1545.17(N-C=S stretching), 1076.39(C-N stretching), 0697.35(monosubstitutedbenzene).

NMR Spectrum: The NMR spectrum of compound was carried out in $CDCl_3$ and DMSO-d_6**.** This spectrum distinctly displayed the signals due to Ar-H protons at δ 9.2847-6.8660 ppm, NH_2 proton at δ 4.0283 ppm, -NH protons at δ 2.5645-2.5569 ppm, imino (=NH) proton at δ1.6550-1.3931 ppm.

Similarly, 1-formamidino-5-substitutedformamidinothiocarbamide**(IIIa),**1-formamidino-5-phenylformamidinothiocarbamide**(IIIb),**

1-formamidino-5-methylformamidinothiocarbamide **(IIIc),** 1-formamidino-5-ethylformamidinothiocarbamide **(IIId),** 1-formamidino-5-allylforma midinothiocarbamide **(IIIe)** were synthesized by the interactions of cyanoguanidine **(I)** with thiourea**(IIa),** phenylthiourea**(IIb)** methylthiourea **(IIc),** ethylthiourea **(IId),** allylthiourea **(IIe)** respectively by the above mentioned and enlisted in **Table No.1**

Table No. -1

Sr.No.	1-Formamidino-5-**substituted**forma midinothiocarbamide	Yield (%)	M.P.˚C
1.	1-Formamidino-5-**methyl**formamidino thiocarbamide	96	172
2.	1-Formamidino-5-**ethyl**formamidino thiocarbamide	98	97
3.	1-Formamidino-5-**allyl**formamidino thiocarbamide	94	178

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