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# Synthesis Characterization and Biological Evaluation of Nitro Amidinothioureas

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**Abstract:** *The discovery of new bioactive compounds necessarily involves previously diversity studies, because by knowing the type of micro organisms that reside in a certain environment, it is possible to design cultivation techniques adapted for all the microbial communities Present in a certain ambience.*

*Marine organisms possess an inexhaustible source of useful chemical substances for the development of new drugs. The structure of the newly synthesized compounds were elucidated with elementary analysis with IR, <sup>1</sup>H NMR and mass spectral data. All the synthesized compounds show weak antioxidant activity and weak antimicrobial and antifungal activity against some bacteria and fungi.*

**Keywords:** *Amidinothiourea, Antibacterial activity and Anti fungal activity.*

## I. INTRODUCTION

The major classes of almost all antibiotics are encountering resistance in clinical applications. In order to overcome this rapid development of drug resistance, new agents should preferably consist of chemical characteristics that clearly differ from those of existing agents. Various heterocyclic nucleus acts as highly functionalized scaffold and used in biologically active molecules. The heterocyclic Amidinothiourea has attracted widespread attention due to their diverse biological activities, including antibacterial, antifungal activity.

In view of these observations, we herein report the synthesis of some new Amidinothiourea derivatives and evaluate their antimicrobial and antifungal activity. Over the decades guanidine and its derivatives have gained wide applications in organic synthesis, in the production of agrochemicals, pesticides, pharmaceutical industry and in rubber industry. Guanidine functional groups are found in numerous biologically active natural products and several drugs.

The target compounds were performed using the Agar Diffusion method. In addition many thiourea derivatives have shown significant pharmacological interest as antianxiety, antipyretic, analgesic and anti-inflammatory drugs. Moreover, they are well known for their remarkable antimicrobial antiparasitic and anti-cancer activities.

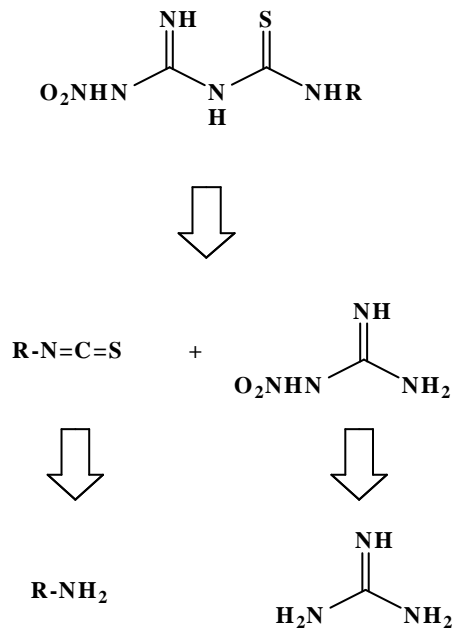
## II. EXPERIMENTAL SECTION

Melting points of the synthesized compounds were determined by open capillary method and are uncorrected and were determined by open capillary method using a immersion bath of silicon oil. The spectra were recorded on JEOL DRX 300 or DPX 300 NMR spectrometer (300 MHz for <sup>1</sup>H and 75 MHz for <sup>13</sup>C NMR Spectra), DMSO as the solvent. Tetra methyl silane as the internal standard and chemical shifts in (ppm) Follow up of the reacting checking the purity of the compounds were made by TLC on Silica gel coated on glass plates. The spots were visualized in iodine vapour or under UV light. The starting compounds was prepared according to literature procedure.

### A. General Procedure for 1-Alkyl/aryl-3-(N-nitroamidino)thioureas

Nitroguanidine (0.52 g, 5 mmol) was stirred with finely powdered potassium hydroxide (0.56 g, 10 mmol) in DMF (5 ml) for 15 min. when the solution becomes homogeneous, alkylisothiocyanate (5 mmol) was added with stirring during an hour. The mixture was then poured slowly with stirring into ice and water (50 ml) and filtered. The filtrate was acidified with dil. Hydrochloric acid (0.1 N).

The white precipitate thus obtained was filtered, washed with cold water and recrystallised from ethanol – water (2:1) to obtain white, crystalline 1 – alkyl– 3 – ( N – nitroamidino) thiourea.



### III. SPECTRAL DATA OF DIFFERENT DERIVATIVES

#### A. Synthesis of 3-(N-nitroamidino)-1-phenylthiourea (a)

Mol. Formula :  $\text{C}_8\text{H}_9\text{N}_5\text{O}_2\text{S}$ ; Mol. wt: 239.26; Yield 74.0%; mp 160-61°C; IR (KBr,  $\text{cm}^{-1}$ ) : 3333(N-H str.), 2951-3020(Aliphatic & ArC-H str.), 1654 (C=O str), 1580(C=C str.), 1330(C-N str.), 643(ArC-S str.); The  $^1\text{H NMR}(\delta, \text{ppm})$ : (DMSO- $d_6$ , 250 MHz): 7-58-7.791(m, 2ArH), 7.3-7.5(m, 3ArH), 1.589(s, 4NH).

#### B. Synthesis of 1-chlorophenyl -3-(N-nitroamidino)thiourea (b)

Mol. Formula :  $\text{C}_8\text{H}_8\text{ClN}_5\text{O}_2\text{S}$ , Mol. wt: 273.71, Yield 70%; mp 168-70°C, IR (KBr,  $\text{cm}^{-1}$ ) : 3373(N-H str.), 2941-3000(Aliphatic & ArC-H str.), 1667 (C=O str), 1580(C=C str.), 1383(C-N str.), 616(ArC-S str.); The  $^1\text{H NMR}(\delta, \text{ppm})$ : (DMSO- $d_6$ , 250 MHz): 7.550(d, J=6Hz, 2ArH), 7.464(d, J=8.4Hz, 2ArH), 1.836(s, 4NH).

#### C. Synthesis of 1-methylphenyl -3-(N-nitroamidino)thiourea (c)

Mol. Formula :  $\text{C}_9\text{H}_{11}\text{N}_5\text{O}_2\text{S}$ , Mol. wt: 253.28, Yield 82%; mp 168-69°C, IR (KBr,  $\text{cm}^{-1}$ ) : 3360(N-H str.), 2917-3033(Aliphatic & ArC-H str.), 1650 (C=O str), 1567(C=C str.), 1417(C-N str.), 600(ArC-S str.); The  $^1\text{H NMR}(\delta, \text{ppm})$ : (DMSO- $d_6$ , 250 MHz): 7.204-7.452(m, 4ArH), 3.321(s,  $\text{CH}_3$ ), 1.789(s, 4NH).

#### D. Synthesis of 1-methoxyphenyl -3-(N-nitroamidino)thiourea (d)

Mol. Formula :  $\text{C}_9\text{H}_{11}\text{N}_5\text{O}_3\text{S}$ , Mol. wt: 269.28, Yield 74.0%; mp 153-54°C, IR (KBr,  $\text{cm}^{-1}$ ) : 3319(N-H str.), 2935-3083(Aliphatic & ArC-H str.), 1633 (C=O str), 1583(C=C str.), 1417(C-N str.), 658(ArC-S str.); The  $^1\text{H NMR}(\delta, \text{ppm})$ : (DMSO- $d_6$ , 250 MHz): 7.144(d, J=9Hz, 2ArH), 6.864(d, J=17.1Hz, 2ArH), 3.344(s,  $\text{OCH}_3$ ), 1.578(s, 4NH).

#### E. Synthesis of 1-ethoxyphenyl -3-(N-nitroamidino)thiourea (e)

Mol. Formula :  $\text{C}_{10}\text{H}_{13}\text{N}_5\text{O}_3\text{S}$ , Mol. wt: 283.31, Yield 87.0%; mp 162-63°C, IR (KBr,  $\text{cm}^{-1}$ ) : 3299(N-H str.), 2925-3010(Aliphatic & ArC-H str.), 1634 (C=O str), 1572(C=C str.), 1378(C-N str.), 617(ArC-S str.); The  $^1\text{H NMR}(\delta, \text{ppm})$ : (DMSO- $d_6$ , 250 MHz): 7.139(d, J=8.7Hz, 2ArH), 6.864(d, J=1.7Hz, 2ArH), 4.01(q, J=1.8Hz,  $\text{CH}_2$ ), 1.40(t, J=1.3Hz,  $\text{CH}_3$ ), 1.636(s, 4NH).

#### F. Synthesis of 1-ethyl -3-(N-nitroamidino)thiourea (f)

Mol. Formula :  $\text{C}_4\text{H}_9\text{N}_5\text{O}_2\text{S}$ , Mol. wt: 191.22, Yield 85.0%; mp 158-60°C, IR (KBr,  $\text{cm}^{-1}$ ) : 3283(N-H str.), 2928-3083(Aliphatic & ArC-H str.), 1654 (C=O str), 1546(C=C str.), 1326.46(C-N str.), 633(ArC-S str.); The  $^1\text{H NMR}(\delta, \text{ppm})$ : (DMSO- $d_6$ , 250 MHz): 5.789-5.95(m, CH), 5.25-5.60(m, 2 $\text{CH}_2$ ), 1.2650(s, 4NH).

**G. Synthesis of 3-(N-nitroamidino)-1-(n-propyl)thiourea (g)**

Mol.Formula:  $C_5H_{11}N_5O_2S$ , Mol.wt:205.24, Yield 75.0%; mp 160-61°C, IR (KBr,  $cm^{-1}$ ) : 3279(N-H str.), 2969-3100(Aliphatic & ArC-H str.), 1654 (C=O str), 1533(C=C str.), 1337(C-N str.),633(ArC-S str.); The  $^1H$ NMR( $\delta$ , ppm): (DMSO- $d_6$ , 250 MHz): 2.180(s,4NH), 1.542-1.67(m, $CH_2$ ), 1.312-1.460(m, $CH_2$ ), 0.952(t,J=7.2Hz, $CH_3$ ).

**H. Synthesis of 1-isopropyl-3-(N-nitroamidino)thiourea (h)**

Mol.Formula :  $C_5H_{11}N_5O_2S$ , Mol.wt:205.24, Yield 830%; mp162-163°C, IR (KBr,  $cm^{-1}$ ) : 3333(N-H str.), 2989-3049Aliphatic & ArC-H str.), 1650 (C=O str), 1539(C=C str.), 1371(C-N str.),629(ArC-S str.); The  $^1H$ NMR( $\delta$ , ppm): (DMSO- $d_6$ , 250 MHz): 1.147(d,J=1.3Hz,2 $CH_3$ ), 1.8(q,J=1.8Hz,ch), 2.142(s,4NH).

**I. Synthesis of 1-n-butyl-3-(N-nitroamidino)thiourea (i)**

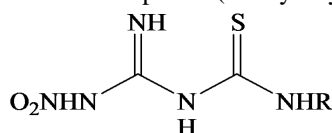
Mol.Formula :  $C_6H_{13}N_5O_2S$ , Mol.wt:219.27, Yield 80.0%; mp 148-49°C, IR (KBr,  $cm^{-1}$ ) : 3292(N-H str.), 2962-3067Aliphatic & ArC-H str.), 1654 (C=O str), 1546(C=C str.), 1337(C-N str.),6670(ArC-S str.); The  $^1H$ NMR( $\delta$ , ppm): (DMSO- $d_6$ , 250 MHz): 3.198-3.266(m,3 $CH_2$ ), 2.180(s,4NH), 0.991(t,J=4.2Hz, $CH_3$ ) :  $^{13}C$  NMR (75MHz,  $CDCl_3$ )  $\delta$ : 13.73(1C),20.09(2C),44.15(1C),181.54(1C).

**J. Synthesis of 1-allyl-3-(N-nitroamidino)thiourea (j)**

Mol.Formula :  $C_5H_9N_5O_2S$ , Mol.wt:203.23, Yield 86.0%; mp 149-50°C, IR (KBr,  $cm^{-1}$ ) : 3339(N-H str.), 2751-3083(Aliphatic & ArC-H str.), 1647 (C=O str), 1596(C=C str.), 1330(C-N str.),617(ArC-S str.); The  $^1H$ NMR( $\delta$ , ppm): (DMSO- $d_6$ , 250 MHz): 5.799-5.95(m,CH), 5.25-5.60(m,2 $CH_2$ ), 1.650(s,4NH).

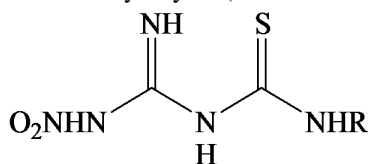
Table-1

Physical data of Different Synthesized Compound (1-alkyl/aryl-3-(N-nitroamidino)thioureas)



Compd.	R	M. P. (C)	Yield [%]	Molecular Formula	M. W.
a	phenyl	160-61	74	$C_8H_9N_5O_2S$	239.26
b	4-chlorophenyl	168-70	70	$C_8H_8ClN_5O_2S$	273.71
c	4-methylphenyl	168-69	82	$C_9H_{11}N_5O_2S$	253.28
d	4-methoxyphenyl	153-54	74	$C_9H_{11}N_5O_3S$	269.28
e	4-ethoxyphenyl	162-63	87	$C_{10}H_{13}N_5O_3S$	283.31
f	ethyl	158-60	85	$C_4H_9N_5O_2S$	191.22
g	n-propyl	160-61	75	$C_5H_{11}N_5O_2S$	205.24
h	isopropyl	162-63	83	$C_5H_{11}N_5O_2S$	205.24
i	n-butyl	148-49	80	$C_6H_{13}N_5O_2S$	219.27
j	allyl	149-50	86	$C_5H_9N_5O_2S$	203.23

Table 2  
Elemental data of 1-alkyl/aryl-3-(N-nitroamidino)thioureas



Compd.	R	Analysis [%]					
		Found			Calculated		
		C	H	N	C	H	N
<b>8a</b>	phenyl	39.94	3.64	29.03	40.16	3.79	29.27
<b>8b</b>	4-chlorophenyl	34.96	3.00	25.39	35.10	2.95	25.59
<b>8c</b>	4-methylphenyl	42.50	4.48	27.88	42.68	4.38	27.65
<b>8d</b>	4-methoxyphenyl	40.36	4.00	26.20	40.14	4.12	26.01
<b>8e</b>	4-ethoxyphenyl	42.53	4.77	24.86	42.39	4.62	24.72
<b>8f</b>	ethyl	25.34	4.60	36.84	25.12	4.74	36.63
<b>8g</b>	n-propyl	29.14	5.26	33.91	29.26	5.40	34.12
<b>8h</b>	isopropyl	29.07	5.24	34.01	29.26	5.40	34.12
<b>8i</b>	n-butyl	32.58	6.15	32.13	32.86	5.98	31.94
<b>8j</b>	allyl	29.68	4.25	34.27	29.55	4.46	34.46

#### IV. BIOLOGICAL EVALUATION

Test organisms utilized were staphylococcus as an example of gram positive bacteria, Escherichiacoli and an example of gram negative bacteria and candida albicans as representatives of fungi none of the tested compounds were able to exert significant anti bacterial anti fungal activities.

The compounds were tested in-vitro for their antibacterial activity against three micro-organisms viz, Escherichacoli, staphylococcus aureus and klebsiella pneumonia. The compounds were tested in vitro for their antifungal activity against candida albicans and Asper gillus niger.

#### V. CONCLUSION

This study reports the successful synthesis of the nitroamidinothiourea compounds in good yield and characterized by Elemental analysis, IR, 1H-NMR and 13C-NMR spectral analysis. All the novel compounds were tested for biological study.

The results of antibacterial study shows that the Aryl series, phenyl compound (a) exhibits moderate antibacterial activity towards staphylococcus aureus. But in the Alkyl series propyl compound (f) shows maximum activity towards the same microbe staphylococcus aureus. The Alkyl series showed mamimum activity against E.Coli when compared to Aryl series.

The results of antifungal study shows that the Alkyl series exhibit maximum activity towards candida albicans and moderate activity against Aspergillusniger.

## VI. ACKNOWLEDGEMENT

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