Synthesis Of 3-Substitutedimine-5-Substituted-Guanidino-1,2,4-Thiadiazoles

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Abstract - A novel series of 3-substitutedimine-5-substitutedguanidino-1,2,4-thiadiazoles (Xa-g) was synthesized by the oxidative cyclization of N-substituedformamidino-N'-substituediminothiocarbamides also called as 1-(N-substitutedcarbamimidoyl) 3-{N-(E)-substitutedmethylidenecarbamimidoyl}-thiourea (Va-g) respectively in chloroform medium using liquid bromine as oxidizing agent. The products were isolated in these reactions were characterised and justified on the basis of elemental analysis, chemical characteristics, and spectral data.

Keywords - 3-substitutedimine-5-substitutedguanidino-1,2,4-thiadiazoles, N-substituedformamidino-N'-substituediminothiocarbamides, 1-(N-substitutedcarbamimidoyl) 3-{N-(E)-substitutedmethylidenecarbamimidoyl}-thiourea etc

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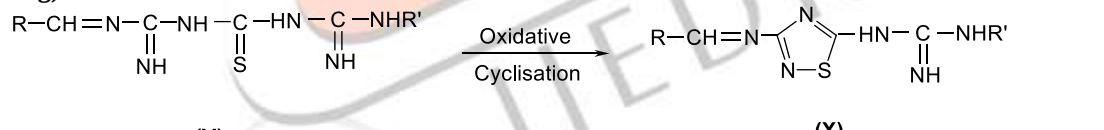
INTRODUCTION

Thiadiazoles and triazoles nucleus containing compounds possesses their own identity and importance in pharmaceutical, medicinal, agricultural, industrial, biochemical and biotechnological fields[1-7]. The compounds having thiadiazoles and triazoles as a parent nucleus are widely used in pharmaceutical, medicinal and biological sciences[8-9]. It was noticed that these drugs possesses antidiabetic[10], herbicidal[11], amoebicidal[12] and antibacterial[13-14] properties. Recently in this laboratory the oxidative cyclisation of some cyanoamidinothiocarbamides, diformamidino- thiocarbamides, substituted N-glucosides and thioglucosides were carried out by Waghmare[15], Panpaliya[16], Bhagwatkar[17] and Raghuwanshi[18] to isolate 1,2,4-thiadiazoles. Oxidative cyclisation for the synthesis of 1,3,4-thiadiazoles, 1,3,4-thiadiazolines and 1,2,4-triazoles have been studied by various researchers[19-25].

As a part of research work presently been undertaken in this laboratory in the synthesis of heteroacycles and heterocycles, it was thought interesting to investigate the cyclisation of N-substituedformamidino-N'-substituedimino-thiocarbamide also called as 1-(N-substitutedcarbamimidoyl)3-{N-(E)-substi-tutedmethylidenecarbamimidoyl}thiourea **(Va-g)** with liquid chloroform medium to obtain a novel series of 3-substitutedimine-5-substitutedguanidino-1,2,4-thiadiazoles **(Xa-g)** respectively which are hither to unknown. The present work describes suitable, convenient and somewhat direct method for the synthesis of **(Xa-g)**.



(V)

1-(N-substitutedcarbamimidoyl)3-{N-(E)-substitutedmethylidenecarbamimidoyl}thiourea

Where R & R' = -methyl, -ethyl, -allyl, -phenyl

(X)

3-Substitutedimine-5-substitutedguanidino-1,2,4-thiadiazoles

OR

1-Methyl-3-{[(E)-substitutedmethylidene]amino}-1,2,4-thiadiazol-5-yl)guanidines

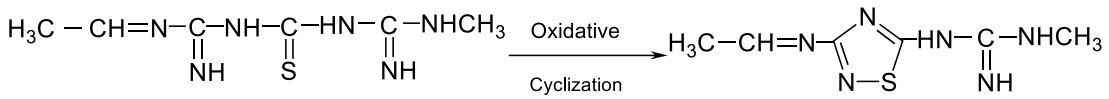
Scheme-1

EXPERIMENTAL

1. Synthesis of 3-methylimine-5-methylguanidino-1,2,4-thiadiazole (Xa):

3-Methylimine-5-methylguanidino-1,2,4-thiadiazole **(Xa)** was synthesized by the oxidative cyclisation of N-methylformamidino-N'-methylimino-thiocarbamide **(Va)** with liquid bromine in presence of chloroform. A paste of N-methylformami- dino-N'-methyliminothiocarbamide **(Va)** was prepared in chloroform. To it liquid bromine in chloroform was added with constant stirring. Initially the colour of bromine disappear the addition was continued till the colour of bromine persisted to the reaction mixture. The reaction mixture was allowed to stand for 8 hours, it afforded dark brown coloured product. It was crystallised from ethanol, yield 76%, m.p. 198^{0}C.

The probable reaction for the formation of **(Xa)** is depicted below,



(Va)

1-(N-methylcarbamimidoyl)3-{N-(E)-methylmethylidenecarbamimidoyl}thiourea

(Xa)

3-Methylimine-5-methylguanidino-1,2,4-thiadiazoles

Scheme-2

Synthesis of 3-phenylimine-5-phenylguanidino-1,2,4-thiadiazole(Xc):

3-Phenylimine-5-phenylguanidino-1,2,4-thiadiazole **(Xc)** was synthesized by the oxidative cyclisation of N-phenylformamidino-N'-phenyliminothio-carbamide **(Vc)** with liquid bromine in presence of chloroform. A paste of N-phenylformamidino-N'-phenyliminothiocarbamide **(Vc)** was prepared in chloroform. To it liquid bromine in chloroform was added with constant stirring. Initially the colour of bromine disappear the addition was continued till the colour of bromine persisted to the reaction mixture. The reaction mixture was allowed to stand for 8 hours, it afforded dark brown coloured product. It was crystallised from ethanol, yield 85%, m.p. 168^0C.

The probable reaction for the formation of **(Xc)** is depicted below.

(Vc) (Xc)

Scheme-3

RESULT & DISCUSION

Properties of (Xa):

1) It was ivory crystalline solid having m.p. 198^0C.

2) It gave positive test for nitrogen and sulphur.

3) It was soluble in acetone, chloroform, carbontetrachloride while insoluble in water and petroleum ether.

4) It formed picrate having m.p. 143^0C.

5) Desulphurization was not observed when warm with silver nitrate, sodium plumbite solution indicating sulphur is blocked[26-28].

6) Elemental analysis: The result of elemental analysis is given in **Table No. 1**

Table No. 1

Element	Found (%)	Calculated (%)
Carbon	33.59	33.9516
Hydrogen	04.47	04.7487
Nitrogen	45.95	46.1928
Sulphur	15.01	15.1067

7) From the analytical data, the molecular formula was found to be $C_6H_{10}N_7S_1$.

8) IR Spectrum:

The IR spectrum of compound **(Xa)** was carried out in KBr pellets and is reproduce on **IR Plate No.- PVR-11**. The IR spectrum clearly indicated the important absorption bands can be correlated in **Table No. 2** as follows,

Table No. 2

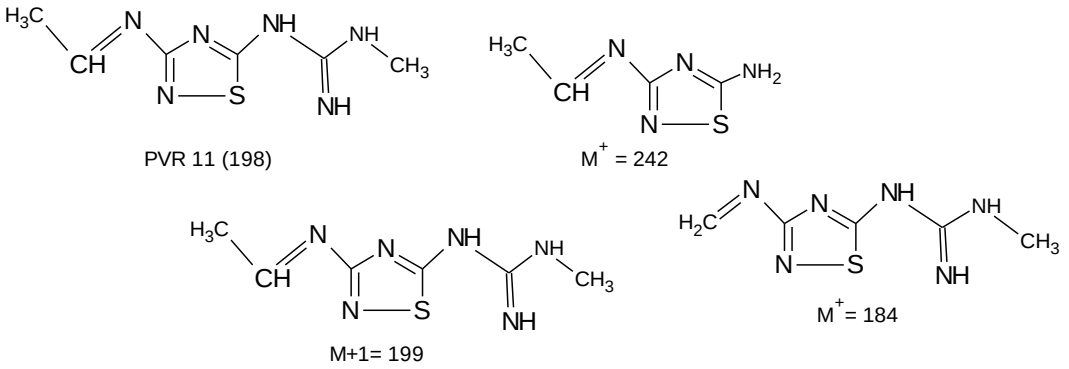
Absorption (cm^{-1})	Assignment Observed	Absorption Expected (cm^{-1})
1695.0	C=N[20] Stretching	1700-1400
1112.4	C-N[20] Stretching	1200-1000
630.5	C-S[21] Stretching	800-600
3357.0	N-H[20,24] Stretching	3450-3300

9) PMR Spectrum:

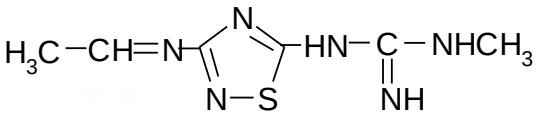
The PMR spectrum of compound **(Xa)** was carried out in DMSO-d_6 and $CDCl_3$. This spectrum distinctly displayed the signals due to –NH proton at δ 3.2297-3.2477 ppm[20,24], =NH proton at δ 2.6543 ppm[20,24] , –CH proton at δ 2.1465 ppm and CH_3 protons at δ 1.3306-1.7039 ppm.

10) Mass spectrum:-

The Mass analysis of the compound was carried out and the fragmentation occurs during the analysis is given in **Mass Scheme-I.**



From the above properties and spectral analysis of the compound **(Xa)** was assigned the structure of 3-methylimine-5-methylguanidino-1,2,4-thiadiazole **(Xa)** as,



(Xa)

3-Methylimine-5-methylguanidino-

1,2,4-thiadiazoles

Properties of (Xc):

1) It was yellow crystalline solid having m.p. 168^{0}C.
2) It gave positive test for nitrogen and sulphur.
3) It was soluble in acetone, chloroform, carbontetrachloride while insoluble in water and petroleum ether.
4) It formed picrate derivative having m.p. 151^{0}C.
5) Desulphurization was not observed when warm with silver nitrate, sodium plumbite solution indicating sulphur is blocked[17].
6) **Elemental analysis:** The result of elemental analysis is given in **Table No. 4**

Table No4

Element	Found (%)	Calculated (%)
Carbon	58.93	59.62
Hydrogen	4.19	04.34
Nitrogen	25.42	26.08
Sulphur	09.28	09.93

7) From the analytical data, the molecular formula was found to be $C_{16}H_{14}N_6S_1$.
8) **IR Spectrum:**

The IR spectrum of compound **(Xc)** was carried out in KBr pellets and is reproduce on **IR Plate No.- PVR-12** The IR spectrum clearly indicated the important absorption bands can be correlated in **Table No7.5** as follows,

Table No7.5

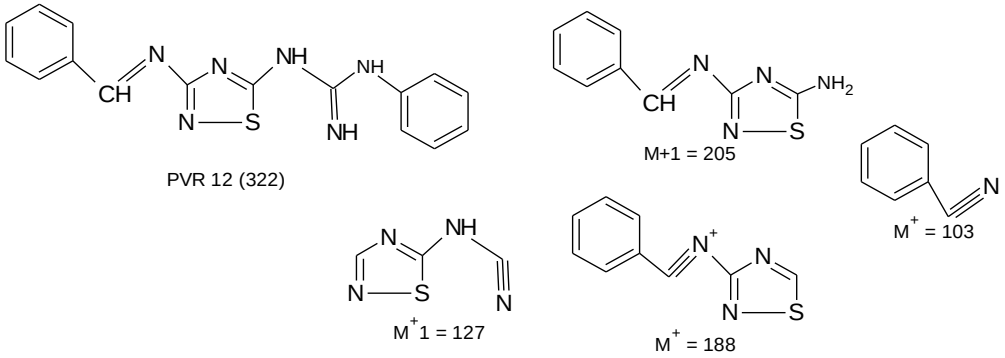
Absorption (cm^{-1})	Assignment Observed	Absorption Expected (cm^{-1})
1695.8	C=N Stretching[20]	1700-1400
1107.9	C-N Stretching[20]	1200-1000
1500	Ar C=C Stretching[19]	2950-2750
716.8	C-S Stretching[21]	800-600
3350	N-H Stretching[20,24]	3450-3300
3011.9	Ar-CH Stretching	3100-3000

9) **PMR Spectrum:**

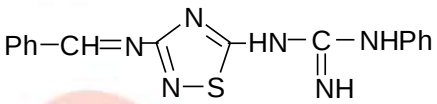
The PMR spectrum of compound **(Xc)**[19] was carried out in DMSO-d_6 and $CDCl_3$ and reproduce on **PMR Plate No.-PVR-12**. This spectrum distinctly displayed the signals due to Ar–H protons at δ 6.1354-9.9116 ppm, –NH protons at δ 5.9130 ppm, =NH protons at δ 2.7223-2.7898 ppm and =CH proton at δ 2.5997 ppm.

10)Mass spectrum:

The Mass analysis of the compound was carried out and reproduced on **Mass Plate No. PVR-12.** The fragmentation occurs during the analysis is given in **Mass Scheme-II.**



From the above properties and spectral analysis of the compound **(Xc)** was assigned the structure as 3-phenylimine-5-phenylguanidino-1,2,4-thiadiazole **(Xc).**



(Xd)

3-Phenylimine-5-phenylguanidino-

1,2,4-thiadiazoles

Similarly, N-methylformamidino-N'-phenyliminothiocarbamide **(Vb),** N-ethylformamidino-N'-phenyliminothiocarbamide **(Vd),** N-3-nitro-phenylformamidino-N'-phenyliminothiocarbamide **(Ve),** N-4-nitrophenyl-formamidino-N'-phenyliminothiocarbamide **(Vf)** and N-p-dimethyl phenyl-formamidino-N'-phenyliminothiocarbamide **(Vg)** were successfully oxidative cyclised with bromine in chloroform medium respectively by the above mentioned method in **Experiment No. 1-7.**

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