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SYNTHESIS OF 3-SUBSTITUTEDIMINO-5-[2-ISOBUTOXY-5-(4-METH- YL-5-CARBOXY-1,3-THIAZO-2-YL)-PHENYLFORMAMIDINO]AMINO 1,2,4-DITHIAZOLES

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ABSTRACT

One step synthesis of 3-substitutedimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazoles were carried out by oxidative cyclisation of 2-(3-substituted-2,4-dithiobiureto- formamidino-4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3-thiazoles by making use of liquid bromine in chloroform medium as an oxidative cyclising agent. The products were isolated, characterized and justified on the basis of conventional elemental analysis, chemical characteristics and spectral studies.

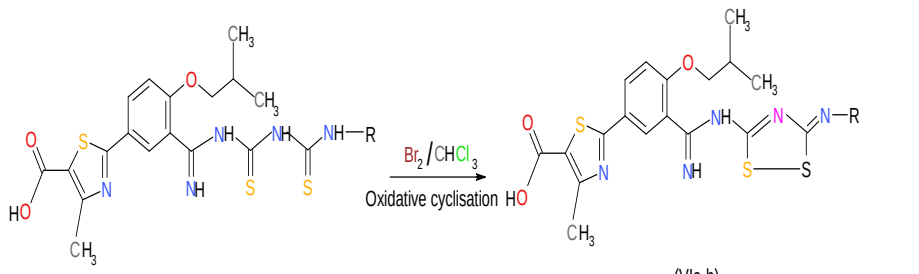
KEYWORDS: conventional elemental analysis, chemical characteristics and spectral studies.

INTRODUCTION

The heterocyclic compounds containing nitrogen, nitrogen and sulphur have gained immense important in human life. Nowadays dithiadiazole nucleus containing heterocycles are useful in pharmaceutical, industrial, biological, agricultural and medicinal fields.[1-13] These types of drugs showed a various range of physiological such as herbicidal, anti-tubercular, anti-fungal, anti-cancer, anti-oxidant, anti-inflammatory, anti-bacterial, amoebicidal and anti-diabetic properties.[14-22] Some were found to be active against different micro-organism like *E. coli, C. alibicans* and *S. Aureus*.[23-24] It was clearly noticed that thiadizoles are effective against copper corrosion[25] and are used as additive in lubricating oil.[23] Dabolkar and Ansari briefly investigated the oxidative cyclisation of cyanoamidinosubstitutedthiocarbamide and N-substituted-formamidinothiocarbamide.

As a part of research work presently being undertaken in the synthesis of various heteroacycles and heterocycles, it was thought interesting to investigate the oxidative cyclisation of 2- (3-substitutedamino-2,4-dithiobiuretoforma-midino- 4-isobutoxyphenyl)-4-methyl-5-carboxy-1, 3-thiazoles **(Va-h)** with liquid bromine in chloroform medium to obtained a novel series of 3-substitutedimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1, 3-thiazo-2-yl)-phenylformamidino]-amino-1,2, 4-dithiazoles **(VIa-h)** which are heither to unknown.

The present research work describes somewhat suitable, convenient, cheaper, more practical utility and one step direct method for the synthesis of 3-substitutedimino-5-[2-isobutoxy-5- (4-methyl-5-carboxy-1,3-thiazo-2-yl)-phenyl -formamidino]-amino-1,2,4-dithiazoles.



(Va-h)
2-(3-Substitutedamino-2,4-dithiabiuratoformamidino -4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3-thiazoles

(VIa-h)
3-Substitutedimino-5-[2-isobutoxy-4-(4-methyl-5-carboxy -1,3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazoles

Where R= -methyl, -ethyl, -t-butyl, -phenyl, p-chlorophenyl, -o-tolyl, -m-tolyl, -p-tolyl.

EXPERIMENTAL

All chemicals used were of AR grade (India make). The purity of the compounds were checked on Silica Gel-G plates by TLC with layer thickness of 0.3 mm. The carbon and hydrogen analysis were carried out on Carlo-Ebra-1106 analyser. Nitrogen estimations were carried out on Colman-N-analyser-29. IR spectra were recorded on Perkin-Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded on Bruker AC-400F spectrometer with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as solvent. MASS spectra were recorded on WATERS, Q-TOF micro mass (HR-MS).

RESULT AND DISCUSSION

Synthesis of 3-phenylimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazo -2-yl)-phenylformamidino]-amino-1,2,4-dithiazole (VIa)

3-Phenylimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1, 3-thiazo-2-yl)- phenylformamidino]-amino-1,2,4-dithiazole **(VIa)** was synthesized by the oxidative cyclisation of 2-(3-phenylamino-2,4-dithiobiuretoformamidino-4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3-thiazole **(Va)** using liquid bromine in presence of chloroform. In a china dish pest of 2-(3-phenylamino-2, 4-dithiobiuretoformamidino-4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3-thiazole **(Va)** was prepared by adding minimum amount of chloroform. To it liquid bromine in chloroform was added with constant stirring. Initially the colour of bromine disappear, the addition was continued till colour of bromine persisted to the reaction mixture. The reaction mixture was allowed to stand for 4 hours and then on basification with dilute ammonium hydroxide solution, afforded brownish products. Recrystalized from ethanol, yield 90%, m.p. 168^0C.

Examination of product

It is brown crystalline solid having melting point 168^0C. It gave positive test for nitrogen and sulphur. It gave positive test for carboxylic group. It does not desulphurized when boiled with sodium plumbite solution, which is clearly indicates that sulphur is not free and gets cyclised. It formed picrate having melting point 178^0C.

Elemental analysis

C **[(**found 53.64%) calculated 54.64**],** **H** [(found 3.76%) calculated 4.74%**],** N **[(**found 13.28%) calculated 14.28], **S** [(found 17.20%) calculated 17.20**].**

IR Spectra

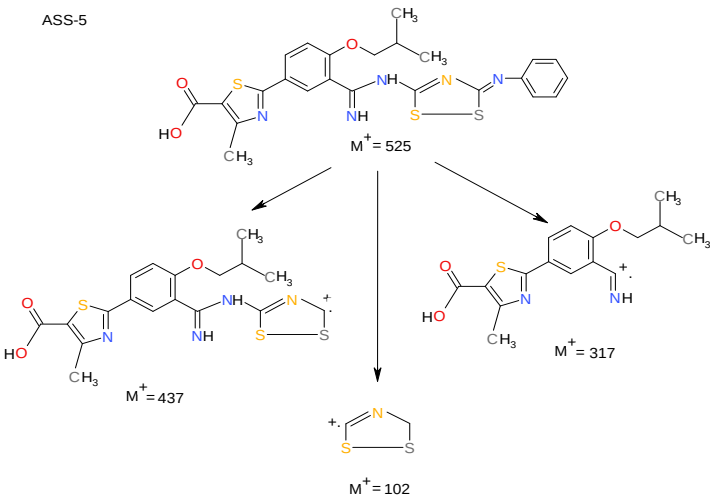
The IR spectra was carried out in KBr pellets and the important absorption can be correlated as (cm^{-1}): 3465.6 (N-H stretching), 3105.05 [C-H (Ar)] stretching, 2238.5, (S-C=N stretching), 1605.1 (=C=NH imino), 1059.18 (C-N stretching), 1427.0 (N=C=S) stretching.

PMR spectrum

The PMR spectrum of compound was carried out in $CDCl_3$ and DMSO-d_6 and reproduced on this spectrum distinctly displayed the signals due –COOH proton at δ 8.1934-8.2516 ppm, Ar-H protons at δ 7.3618-7.0539 ppm, –NH proton at δ 4.0015 ppm, =NH (imino) proton at δ 2.1233-2.1129 ppm, -CH_3 protons at δ 1.2399 ppm, -O-CH_2 protons at δ 2.5354-2.5271 ppm, -CH proton at δ 1.0376-1.0544 ppm.

Mass Spectrum

The Mass analysis of compound was carried out and reproduced on **t**he fragmentations occur during the analysis is given in below.



Synthesis of 3-tert-butylimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazole (VIb)

3-Tert-butylimino-5- [2-isobutoxy-5-(4-methyl-5-carboxy-1, 3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazole **(VIb)** was synthesized by the oxidative cyclisation of 2-(3-tert-butylaminodithiobiureto-4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3 thiazole **(Vb)** using liquid bromine in presence of chloroform. In a china dish pest of 3-tert-butylimino-5- [2-isobutoxy-5-(4-methyl- 5-carboxy-1, 3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazole **(Vb)** was

prepared by adding minimum amount of chloroform to it liquid bromine in chloroform was added with constant stirring. Initially the colour of bromine disappear, the addition was continued till colour of bromine persisted to the reaction mixture. The reaction mixture was allowed to stand for 4 hours and then on basification with dilute ammonium hydroxide solution, afforded brown products. Recrystalized from ethanol, yield 86%, m.p. 172^0C.

Examination of Product

It is brown crystalline solid having melting point 172^0C. It gave positive test for nitrogen, sulphur. It gave positive test for carboxylic group. It does not desulphurized when boiled with sodium plumbite solution, which is clearly indicates that sulphur is not free and gets cyclised. It formed picrate having melting point 168^0C.

Elemental analysis

C **[(**found 51.00%) calculated 52.07]**,** **H** [(found 5.60%) calculated 5.71%**],** N **[(**found 13.80%) calculated 14.80], **S** [(found 17.90%) calculated 17.90]**.**

IR Spectra

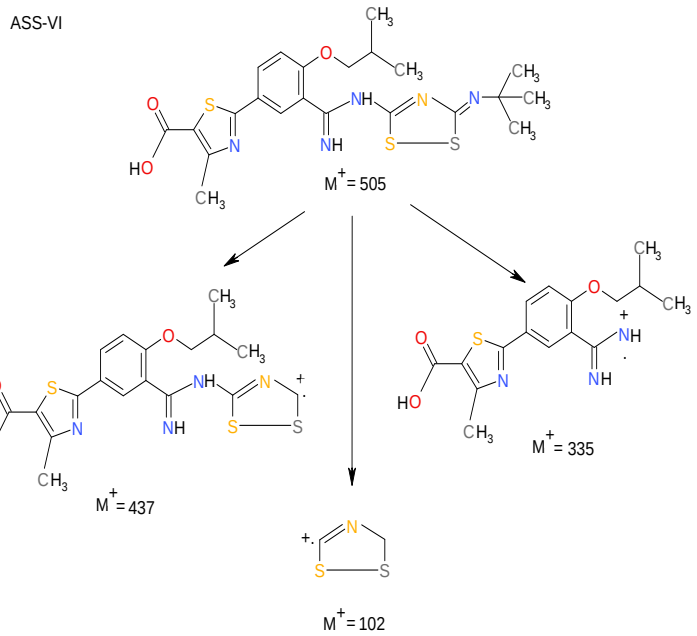
The IR spectra was carried out in KBr pellets and the important absorption can be correlated as (cm^{-1}): 3346.1 (N-H stretching), 3105.05 [C-H(Ar)] stretching, 2228.21, (S-C=N stretching), 1624.3 (=C=NH imino), 1160.5 (C-N stretching), 1476.0 (N=C=S) stretching.

PMR spectrum

The PMR spectrum of compound was carried out in $CDCl_3$ and DMSO-d_6 reproduced on **t**his spectrum distinctly displayed the signals due to –COOH proton at δ 8.2411-8.1764 ppm, Ar-H protons at δ 7.3539-7.0393 ppm, –NH proton at δ 5.4664-5.0228 ppm, -O-CH_2 protons at δ 2.5134-2.4865 ppm, =NH (imino) proton at δ 1.8989-1.4431 ppm, -CH proton at δ 1.1444-1.1028 ppm, -CH_3 protons at δ 1.0215-1.0107 ppm.

Mass spectrum

The Mass analysis of compound **VIb** was carried out and reproduced on the fragmentations occur during the analysis is given in below.



Simillarly, 3-methylimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazo-2-yl)- phenylformamidino]-amino-1,2,4-dithiazole **(VIc)**, 3-ethylimino-5-[2-isobutoxy- 5-(4-methyl- 5-carboxy- 1,3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazole **(VId),** 3-p-chlorophenylimino-5- [2-isobutoxy- 5-(4-methyl-5-carboxy-1,3-thiazo-2-yl)- phenylformamidino]-amino-1,2,4-dithiazole **(VIe),** 3-o-tolylimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1, 3-thiazo-2-yl)-phenylformamidino]-amino-1,2, 4-dithiazole **(VIf),** 3-m-tolylimino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1, 3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazole **(VIg)** 3-p-tolylimino-5-[2-isobutoxy-5- (4-methyl-5-carboxy-1,3-thiazo-2-yl)- phenylformamidino]-amino-1,2,4-dithiazole**(VIh)** were synthesized by oxidative cyclisation of 2-(3-methylaminodithiobiureto-4-isobutoxyphenyl)-4-methyl-5-carboxy- 1,3-thiazole **(Vc),** 2-(3-ethylaminodithiobiureto-4-isobuto-xyphenyl)-4-methyl-5-carboxy-1,3-thiazole **(Vd),** 2-(3-p-chlorophenylamino-dithiobiureto-4-isobutoxyphenyl)- 4-methyl-5-carboxy-1,3-thiazole **(Ve)** 2-(3-o-tolylaminodithio biureto-4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3-thiazole **(Vf)** 2-(3-m-tolyl-aminodithiobiureto-4-isobutoxyphenyl)-4-methyl-5-carboxy- 1,3-thiazole **(Vg)** 2-(3-p-tolylaminodithiobiureto-4-isobutoxyphenyl)-4-methyl-5-carboxy-1,3-thiazole **(Vh)** by the liquid bromine in chloroform medium respectively by the above mentioned in **Table No.1.**

Table No.1

Sr. No.	3-**Substituted**imino-5-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazo-2-yl)-phenylformamidino]-amino-1,2,4-dithiazole	Yield (%)	M.P. ^{0}C
1.	3-**Methylamino**----------	90	160
2.	3-**Ethylamino**-5----------	88	164
3.	3-**Chlorophenylamino**-5----------	80	200
4.	3-**o-Tolyl**-5----------	86	158
5.	3-**m-Tolyl**-5----------	78	152
6.	3-**p-Tolyl**-5----------	82	185

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