



Green Synthesis of 1-{N(1E)-substituted carbamimidoyl}3-{N-[(E)-substituted methylidene]carbamimidoyl}thiourea

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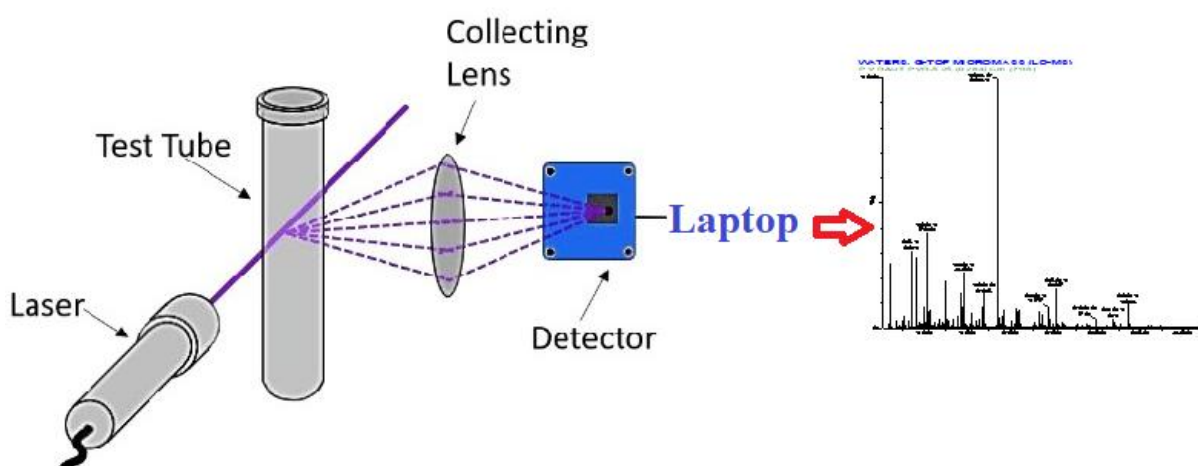
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ABSTRACT:

A novel series of 1-{N(1E)-substituted carbamimidoyl}3-{N-[(E)-substituted methylidene]carbamimidoyl}thiourea (VIa-e) were synthesized in this laboratory. 1-{N(1E)-substituted carbamimidoyl}3-{N-[(E)-substituted methylidene]carbamimidoyl}thiourea (VIa-e) were synthesized by the reaction of 1-(N-carbamimidoyl)-3-{N-(E)-substituted carbamimidoyl}thiourea (Va) with various aldehydes (IIa-e) in sulphuric acid in acetone-ethanol medium in 1:1 molar proportion for 20 minutes. The structures of all the synthesized compounds were justified on the basis of chemical characteristics, elemental analysis and spectral analysis.

Keywords: 1-(N-carbamimidoyl)-3-{N-(E)-substituted carbamimidoyl}thiourea, sulphuric acid, aldehydes, etc.

GRAPHICAL ABSTRACT



Background Information

Nitrogen and sulfur-containing heterocyclic and heterocyclic compounds developed their own character and significance in organic chemistry as a result of their numerous uses in a variety of industries. Biuretes, barbutaric acid, urethanes, imines, cyanoguanidine, thiocarbamides, cyanoaminothiocarbamides, and cyanoaminothiocarbamides all have industrial, agricultural, and medical relevance. Moreover, the synthesis of compounds with 5, 6, and 7 members uses these heterocycles as an intermediate. According to a literature review, heterocyclic compounds with the nucleus of imines, thiocarbamides, triazoles, thiadiazoles, thiazolidines, Hector's bases, 1,3,5-triazines, 1,3,5-thiadiazines, 1,3,5-dithiazines, and diazapines have distinct identities in medicine, pharmaceuticals, agriculture, industry, and biology. A comprehensive review of the literature revealed the distinct identification and importance of thiocarbamido, amidinothiocarbamido, and thioamido nucleus containing heterocycles and heterocycles compounds in pharmaceutical, medical, agricultural, and industrial sciences¹⁻¹². The potency and therapeutic value of that medicine are increased by these nucleus-containing molecules. Amazing qualities like anti-tumour and anti-cancer are present in these types of substances¹³⁻¹⁵. Moreover, the heterocyclic molecules in the thiocarbamido nucleus showed antiviral, antifungal, antibacterial, antitubercular, and anti-inflammatory properties¹⁶⁻²⁰. Tayade *et al*²¹⁻²² recently reported the synthesis series of thiadiazoles, thiadiazines, and dithiazines by experimenting with the synthetic application of -amino, -cyano, -halo, and other groups and investigated their antibacterial, antifungal, and physiochemical properties. In this laboratory, an alternate method for the synthesis of six member heterocycles was developed as part of a larger programme in the synthesis of nitrogen, nitrogen and sulphur-containing heterocycles and heterocycles, in light of the applicability and significance of these compounds in various fields.

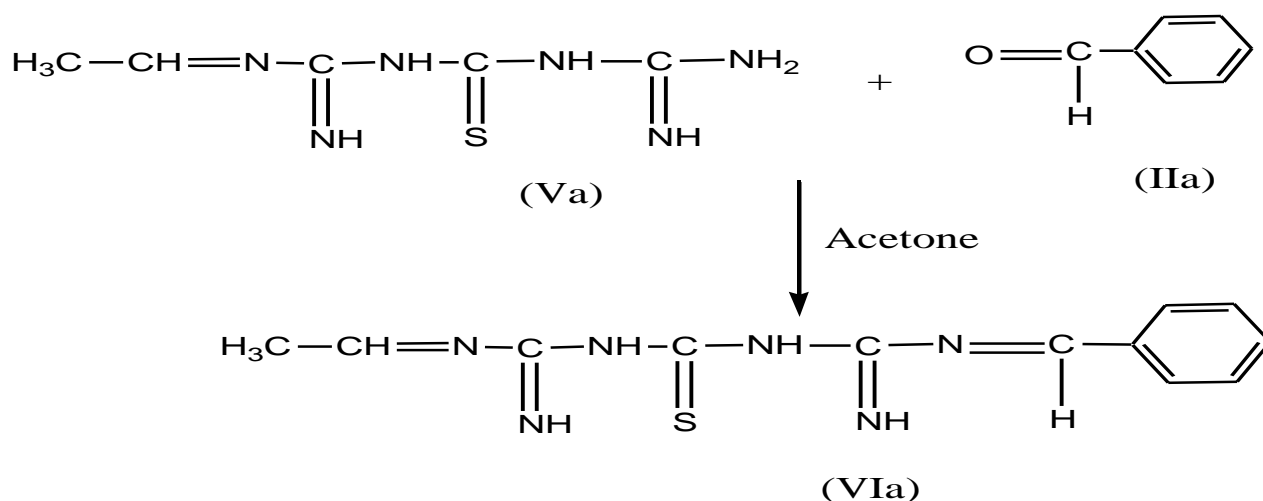
METHODS

Synthesis of 1-{N-(1E)-methyl carbamimidoyl}3-{N-[(E)-phenylmethylidene]carbamimidoyl}thiourea (VIa):

For 20 minutes, a reaction mixture of 1-(N-methylcarbamimidoyl)-3-N-(E) substituted carbamidoyl thiourea (Va) and acetaldehyde (IIa) in 60% ethanol-acetone in a 1:1 molar ratio was refluxed in H₂SO₄. The reaction mixture was then poured onto crushed ice

while being constantly stirred, yielding a white crystals product (VIa). The product was recrystallized from ethanol and yielded 86% (m.p. 205⁰C).

Fig 1 Synthesis of 1-{N-(1E)-methyl carbamimidoyl}3-{N-[(E)-phenylmethylidene] carbamimidoyl}thiourea (VIa):



RESULT AND DISCUSSION

Properties of (VIa):

- 1) It was a white crystalline solid with a melting point of 205 degrees Celsius.
- 2) It tested positive for nitrogen and sulphur.
- 3) It was discovered that boiling it with an alkaline plumbite solution desulphurized it.
- 4) It was soluble in alcohol, acetone, dioxane, and DMSO but not water or ether.
- 5) When a compound's benzene solution was treated with pure and dry carbon disulphide, a yellow colour developed, indicating the presence of a basic imino (=NH) group²².
- 6) It formed a picrate with a melting point of 133⁰ C.
- 7) **Elemental analysis:** Table 1 shows the results of the elemental analysis.

Table-1

Elements	Found (%)	Calculated (%)
Carbon	52.5041	52.5355
Hydrogen	5.1094	5.14359
Nitrogen	30.6569	30.63306
Sulphur	11.6788	11.68785

- 8) From the analytical data, the molecular formula was found to be C₁₂H₁₄N₆S₁.

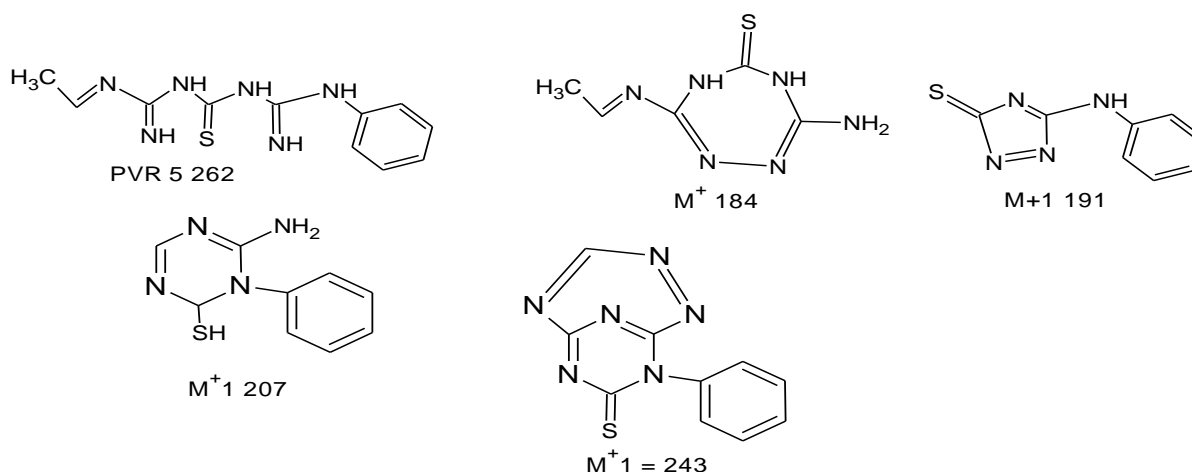
- 9) **IR Spectrum of compound:** IR spectrum of the compound was carried out in KBr pellets and reproduced on **Plate No. PVR-5**, an important absorption correlated in **Table No-2** as follows,

Table No-2

Absorption observed in cm^{-1}	Assignment	Absorption Expected in cm^{-1}
2860	C-H stretching ²³	2962-2853
1637.4	C=N stretching ²⁴	1750-1450
1343.12	C-N stretching ²⁴	1360-1000
1085	-N-C=S stretching ²⁴	1200-1050
1199.1	-C=S stretching	1600-1100
668.13	Mono-substituted ring	800-600

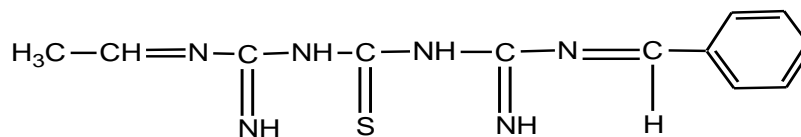
- 10) **PMR-Spectrum:** The PMR spectrum of the compound was carried out in CDCl_3 and DMSO-d_6 and reproduced on **PMR Plate No. PVR-5**. This spectrum distinctly displayed the signals due to Ar-H protons at δ 9.9950-6.5974 ppm, =NH protons at δ 3.6 ppm, =CH proton at δ 2.5903-2.5854 ppm and $-\text{CH}_3$ protons at δ 1.4796 ppm.
- 11) **Mass spectrum:-** The Mass analysis of the compound was carried out and reproduced on **Mass Plate No. PVR-5**. The fragmentation that occurs during the analysis is given in

Fig.2 Mass Scheme-I.



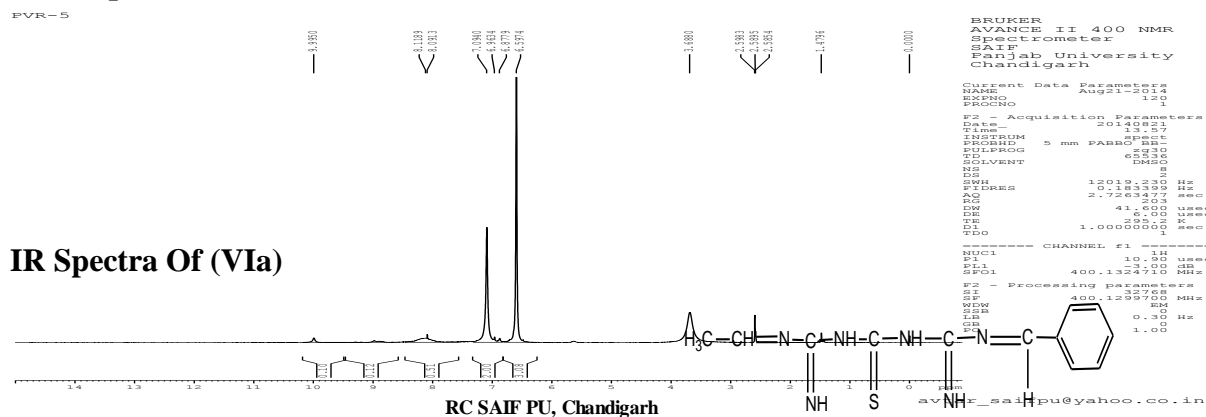
From the above properties and spectral analysis of the compound (**VIa**) was assigned the structure as 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-phenylmethylidene]carbamimidoyl}thiourea.

Fig.3 Spectral analysis of the compound (**VIa**)

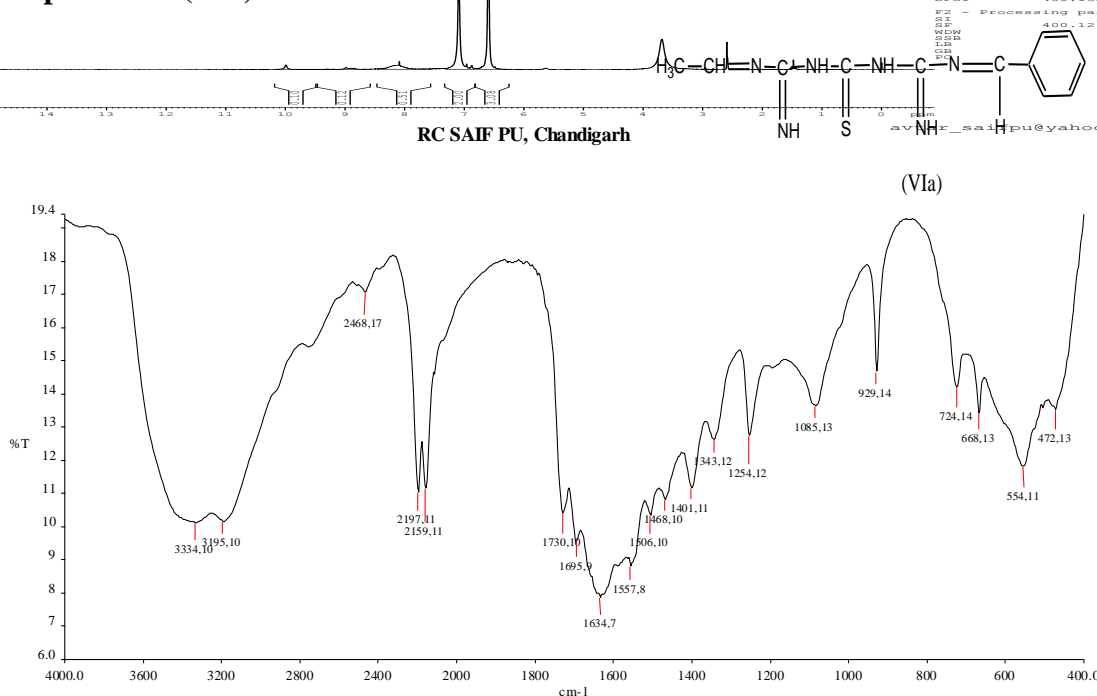


(VIa)

PMR Spectrum Of (VIa)

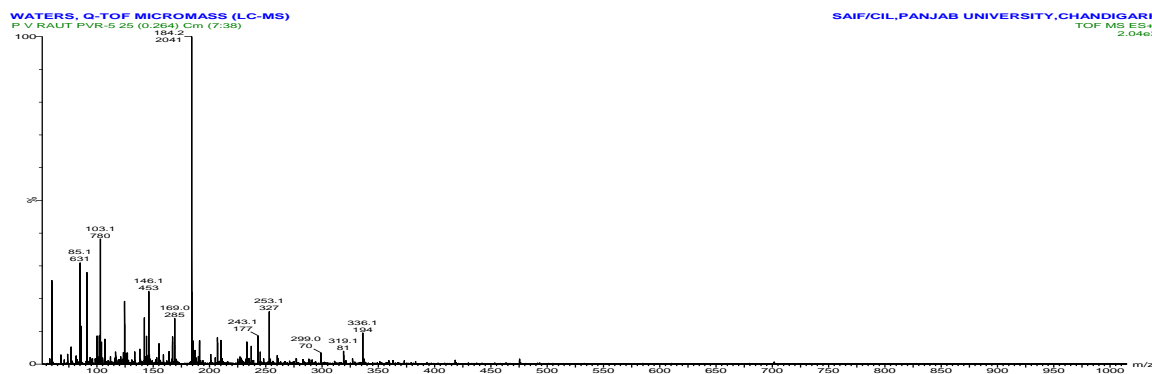


IR Spectra Of (VIa)

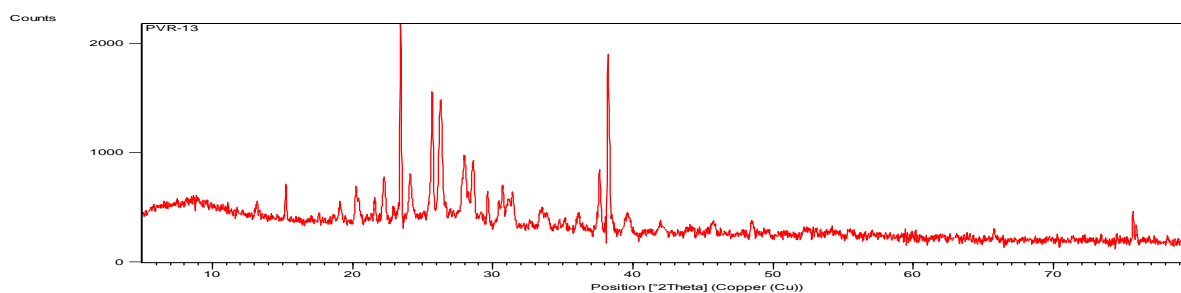


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MASS Spectrum of (VIa):



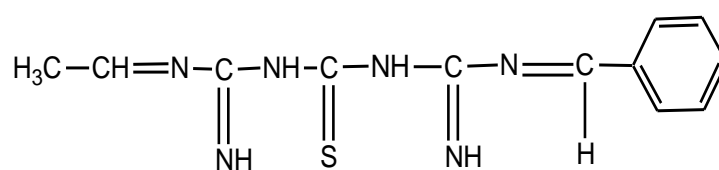
XRD Spectrum of (VIa)



Similarly, 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-methylmethylidene] carbamimidoyl} thiourea (VIb), 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-ethylmethylidene] carbamimidoyl} thiourea (VIc), 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-3-nitrophenylmethylidene] carbamimidoyl} thiourea (VI d) and 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-4-nitrophenylmethylidene] carbamimidoyl} thiourea (VIe) were synthesized by the interactions of 1-(N-methylcarbamimidoyl)-3-{N-(E)-carbamimidoyl} thiourea (Va) with acetaldehyde (IIb), propanaldehyde (IIc), 3-nitrobenzaldehyde (IId) and 4-nitrobenzaldehyde (IIE) respectively in H₂SO₄ in the ethanol-acetone medium in 1:1 molar proportion by the above-mentioned method, described in **Experiment No. 2-5**.

From the above properties and spectral analysis of the compound (VIa) was assigned the structure as Bis[methylimino]thiocarbamides.

Fig.4 Structure as Bis[methylimino]thiocarbamides



(VIa)

Table No.-3

Sr. No.	Expt. No.	1-{N-(1E)-carbamimidoyl}3-{N-[(E)-substituted methylidene] carbamimidoyl} thiourea (VIb-e)	Yield (%)	m.p. (°C)
1	2methyl.....	86	205
2	3ethyl.....	79	166
3	43-nitrophenyl.....	91	120

4	54-nitrophenyl.....	83	127
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Experiment No.-2

Synthesis of 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-methylmethylidene]carbamimidoyl}thiourea (VIb) :

A reaction mixture of 1-(N-methylcarbamimidoyl)-3-{N-(E)-carbamimidoyl} thiourea (Va) (0.1M) with acetaldehyde (IIb) (0.1M) in H₂SO₄ (1ml) in ethanol-acetone (60%) in 1:1 molar ratio was refluxed for 20 minutes. The reaction mixture was then poured on crushed ice with constant stirring, giving white crystals of the product (VIb). The product was recrystallised from ethanol, 86%, m.p. 205⁰C

Experiment No.-3

Synthesis of 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-ethylmethylidene]carbamimidoyl}thiourea (VIc):

A reaction mixture of 1-(N-methylcarbamimidoyl)-3-{N-(E)-carbamimidoyl} thiourea (Va) (0.1M) with propanaldehyde (IIc) (0.1M) in H₂SO₄ (1ml) in ethanol-acetone (60%) in 1:1 molar ratio was refluxed for 20 minutes. The reaction mixture was then poured on crushed ice with constant stirring, giving white crystals of the product (VIc). The product was recrystallised from ethanol, yielding 79%, m.p. 166⁰C.

Experiment No.-4

Synthesis of 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-3-nitrophenylmethylidene]carbamimidoyl}thiourea (VIId):

A reaction mixture of 1-(N-methylcarbamimidoyl)-3-{N-(E)-carbamimidoyl} thiourea (Va) (0.1M) with 3-nitrobenzaldehyde (IIId) (0.1M) in H₂SO₄ (1ml) in ethanol-acetone (60%) in 1:1 molar ratio was refluxed for 20 minutes. The reaction mixture was then poured on crushed ice with constant stirring, giving white crystals of the product (VIId). The product was recrystallised from ethanol, yielding 86%, m.p. 138⁰C.

Experiment No.-5

Synthesis of 1-{N-(1E)-carbamimidoyl}3-{N-[(E)-4-nitrophenylmethylidene]carbamimidoyl}thiourea (VIE):

A reaction mixture of 1-(N-methylcarbamimidoyl)-3-{N-(E)-carbamimidoyl} thiourea (Va) (0.1M) with 4-nitrobenzaldehyde (IIe) (0.1M) in H₂SO₄ (1ml) in ethanol-acetone (60%) in 1:1 molar ratio was refluxed for 20 minutes. The reaction mixture was then poured on

crushed ice with constant stirring, giving white crystals of the product (VIe). The product was recrystallised from ethanol, yielding 91%, m.p. 120⁰C.

CONCLUSION:-

Green chemistry has long piqued the scientific imagination. It is a novel philosophical viewpoint with the potential to significantly advance chemistry, the chemical industry, and environmental protection through the introduction and application of its ideas. Green Chemistry ideas should be taught to the next generation of chemists, and they should have the skills and values to put them into effect.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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