

Synthesis and structure elucidation of 2-substitutedamino-4-(2-imino-4-thiobiureto-5-yl- carbamidino)-6-substitutedimino-1,3,5-thiadiazine

Shelke ME*

Associate Professor of Chemistry, H.V.P.M.'s College of Engineering and Technology
Amravati, Maharashtra, India.

*Corresponding Author: E-Mail: meshelke@rediffmail.com

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ABSTRACT

Novel series 2-substitutedamino-4-(2-imino-4-thiobiureto-5-yl- carbamidino)-6-substitutedimino-1,3,5-thiadiazine [3a(i) to 3f(iv)] have been obtained by the basification of their hydrochlorides [2a(i) to 2f(iv)] in presence of ammonium hydroxide solution, which were synthesized by the interaction of 1-formamidino-3-thioamido-N-substituted formamidinothiocarbamide(1a-f) with aryl/alkylisocyno-dichlorides in 1:1 molar ratio in carbon tetrachloride medium for 4 hrs. During heating evolution of hydrogen chloride gas was clearly noticed. After distillation of excess carbon tetrachloride, dark brown crystals were isolated. The structures of all these compounds were established on the basis of IR and PMR spectrum data and elemental analysis.

Keywords: 1,3- Diformamidinothiacarbamide, 1,3,5-thiadiazines, synthesis.

1. INTRODUCTION

The heterocyclic compounds having 1,3,5-thiadiazine enhanced pharmaceutical [1-3], medicinal [4-5], agricultural and industrial activities of the drugs and medicines. So the drugs or medicines containing thiadiazine nucleus are now used extensively in medical, biochemical and biotechnological faculties. The biological importance of the 1,3,5-thiadiazine derivatives is further emphasized by showing the presence of 1,3,5-thiadiazine ring in therapeutic agent [6] 1,3,5-thiadiazine have been shown to possess brightening and fiber finishing properties in textile industry [7-8] and used as fungicidal, [9-10] insecticidal [11] as well as medicinal compounds.

2. EXPERIMENTAL

All chemicals used were of analar grade. Aryl/alkylisothiocyanate, Aryl/alkylisocyanodichlorides were prepared according to literature method. [12] Melting points of all synthesized compounds were determined in open capillary. IR spectra were recorded on Perkin-Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded with TMS as internal standard using CDCl_3 and $\text{DMSO}-d_6$. TLC checked the purity of the compounds on silica gel-G plates with layer thickness of 0.3 mm. and result are cited in table 1.

3. RESULTS AND DISCUSSION

The parent compound 1-formamidino-3-thioamido-N-substituted formamidinothiocarbamide (1a-f) was prepared by refluxing the mixture of 1,3-Diformamidinothiacarbamide and phenylisothiocyanate in carbon tetrachloride medium for 4 hr. on water bath. The compound (1a-f) was then further reacted with N-substitutedisocyanodichlorides [12] in 1:1 molar proportion in carbon tetrachloride medium for 4 hrs. During heating evolution of hydrogen chloride gas was noticed as tested with moist blue litmus paper. Cooling the reaction mixture and distilling off excess solvent needle shape crystals were isolated. These were acidic to litmus and identified as monohydrochlorides of 2-substitutedamino-4-(2-imino-4-thiobiureto-5-yl-carbamidino)-6-substitutedimino-1,3,5-thiadiazine [2a(i) to 2f(iv)] which on basification with aqueous ammonium hydroxide solution afforded free bases [3a(i) to 3f(iv)].

3.1. Synthesis of 1-formamidino-3-thioamido-N-substitutedformamidinothiocarbamide (1a)

1-Formamidino-3-thioamido-2-phenylformamidino-thiocarbamide was prepared by refluxing the mixture of 1, 3-diformamidinothiacarbamide and

phenylisothiocyanate in carbon tetrachloride medium for 4 hrs on water bath. The solvent was distilled off, pale brown crystals were separated out. Which were washed with petroleum ether and recrystallized with aqueous ethanol, yield 80%, m.p. 264°C. ; IR spectram shows ν (N-H) 3356.6 cm^{-1} , (C-H)(Ar) 3131.3 cm^{-1} , ν (C=N) 1635.4 cm^{-1} , ν (C-N) 1297.7 cm^{-1} , ν (C=S) grouping 11197.7 cm^{-1} , ν (C-S) 777.9 cm^{-1} , ν (C=NH) grouping 1688.4 cm^{-1} . The PMR spectra of compounds showed signals due to N-H protons at δ 6.7776ppm, Ar-NH protons at δ 7.4657 ppm, Ar-H protons at δ 6.3 ppm.

3.2. Synthesis of 2-phenylamino-4-(2-imino-4-thiobiureto-5-yl-carbami-dino)-6-phenylimino-1,3,5-thiadiazine [3a(i)]

A reaction mixture of 1-formamidino-3-thioamido-N-phenylformamidinothiocarbamide (1a) and phenylisocyanodichlorides in 1:1 molar ratio was refluxed in carbon tetrachloride medium for 4 hrs. During heating the evolution of hydrogen chloride gas was observed and tested

with moist blue litmus paper. After cooling the reaction mixture distilled off excess solvent, the solid crystals were separated out. And crystallized from aqueous Ethanol, dark brown crystals were isolated; yield 88%, m.p. 210°C. It gives effervesces with sodium bicarbonate and acidic to litmus. Equivalent weight was found to be monohydrochlorides of [2a (i)] which on basification with dilute ammonium hydroxide solution afforded light brown crystals of [3a (i)].

Similarly other compounds [2a (ii)] to [2f (iv)] were synthesized from (1a-1f) and which on basification yielded [3a (ii)] to [3f (iv)] by above mention method and enlisted in table 1.

3.3. Properties of Compound [3a (i)]

It is light brown crystalline solid having m.p. 195 °c. From analytical data; molecular formula is C₁₇H₁₆N₈S₂; IR spectra of compound shows ν (N-H) 3359.5 cm^{-1} , (C-H)(Ar) 2924.7 cm^{-1} , ν (C=N) 1642.2 cm^{-1} , ν (C-N) 1294.3 cm^{-1} , ν (C=S) grouping 1173.7 cm^{-1} , ν (C-S) 778.3 cm^{-1} , ν (C=NH) grouping 1506.1 cm^{-1} .

Table - 1: Physical data of the compounds [3a (i) to 3f (iv)]

| Compd | R | R ₁ | Yield | m.p. (°C) |
|-----------|------------------------|------------------------|-------|-----------|
| [3a(i)] | Phenyl | Phenyl | 68 | 195 |
| [3a(ii)] | Phenyl | <i>p</i> -Chlorophenyl | 72 | 202 |
| [3a(iii)] | Phenyl | Ethyl | 76 | 192 |
| [3a(iv)] | Phenyl | <i>t</i> -butyl | 65 | 182 |
| [3b(i)] | Ethyl | Phenyl | 62 | 190 |
| [3b(ii)] | Ethyl | <i>p</i> -Chlorophenyl | 68 | 189 |
| [3b(iii)] | Ethyl | Ethyl | 73 | 177 |
| [3b(iv)] | Ethyl | <i>t</i> -butyl | 72 | 172 |
| [3c(i)] | <i>p</i> -Chlorophenyl | Phenyl | 68 | 207 |
| [3c(ii)] | <i>p</i> -Chlorophenyl | <i>p</i> -Chlorophenyl | 76 | 219 |
| [3c(iii)] | <i>p</i> -Chlorophenyl | Ethyl | 74 | 191 |
| [3c(iv)] | <i>p</i> -Chlorophenyl | <i>t</i> -butyl | 68 | 187 |
| [3d(i)] | <i>p</i> -Tolyl | Phenyl | 72 | 203 |
| [3d(ii)] | <i>p</i> -Tolyl | <i>p</i> -Chlorophenyl | 76 | 227 |
| [3d(iii)] | <i>p</i> -Tolyl | Ethyl | 59 | 187 |
| [3d(iv)] | <i>p</i> -Tolyl | <i>t</i> -butyl | 54 | 181 |
| [3e(i)] | Methyl | Phenyl | 62 | 184 |
| [3e(ii)] | Methyl | <i>p</i> -Chlorophenyl | 69 | 189 |
| [3e(iii)] | Methyl | Ethyl | 76 | 172 |
| [3e(iv)] | Methyl | <i>t</i> -butyl | 72 | 176 |
| [3f(i)] | <i>t</i> -Butyl | Phenyl | 77 | 184 |
| [3f(ii)] | <i>t</i> -Butyl | <i>p</i> -Chlorophenyl | 72 | 192 |
| [3f(iii)] | <i>t</i> -Butyl | Ethyl | 61 | 168 |
| [3f(iv)] | <i>t</i> -Butyl | <i>t</i> -butyl | 59 | 176 |

* All Compounds gave satisfactory C, H, N, and S analysis.

The PMR spectrum of compound [3a (i)] was carried out in DMSO-*d*₆ and CDCl₃. This spectrum distinctly displayed signals due to Ar-H protons at δ 7.04-7.71 ppm, Ar-NH protons at δ 6.48-6.87 ppm, and NH protons at δ 4.2-4.3 ppm. The signals at δ 2.7-3.1 ppm is due to moisture in DMSO-*d*₆ and 0.75-2.26 ppm is due to DMSO. From these spectral and chemical data the compound [3a (i)] is 2-phenylamino-4-(2-imino-4-thiobiureto-5-yl-carbamidino)-6-phenylimino-1,3,5-thiadiazine

4. CONCLUSION

As outline in synthesis process, important novel 1, 3, 5-thiadiazine has been synthesized. All the structure of the above compounds was in good agreement with Spectral and Analytical data.

5. REFERENCES

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