



Green synthesis of Novel 2,4,6-Tri S[(5-Substituted)-2,4-Dithio Biureto]-1,3,5-Triazines

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ABSTRACT

Recently in this laboratory a new route for the synthesis of 2,4,6-tris[(5-substituted)-2,4-dithiobiureto]-1,3,5-triazines was developed to increase the yield of products by maintaining the purity of them and at the same time, the time span required for the completion of reactions was also decreases. These are eco-friendly reactions. Novel green synthesis of 2,4,6-tris[(5-substituted)-2,4-dithiobiureto]-1,3,5-triazines (**Va-e**) was successfully carried out by interacting 2,4,6-tris[substitutedthiocarbamido]-1,3,5-triazines (**IIIa-e**) with various isothiocyanates in 1:3 molar ratio in ethanol-acetone medium. Firstly cyanuryl chloride (**I**) was treated with various thiourea (**IIa-e**) in 1:3 molar ratio in ethanol-acetone medium for the isolation of (**IIIa-e**). During the synthesis two parameters of green chemistry are maintained. The justification and identification of the structure of these newly synthesized compounds had been established on the basis of chemical characteristics, elemental analysis and through spectral data.

Keywords: Green synthesis, cyanuryl chloride, 1,3,5-triazine, acetone-ethanol.

INTRODUCTION

Cyanuryl chloride is also referred as 'cyanuric chloride'. It is an interesting molecule whose behavior is most amazing. It is chlorinated analogue of 1,3,5-triazine. This molecule is used as an intermediate for the synthesis of important heterocycles. 1,3,5-triazine and thiocarbamido nucleus containing drugs created their own identity, importance and significances in pharmaceutical, medicinal, biochemical, industrial, and agricultural sciences. These drugs showed muscle relaxant [1], hypoglycemic [2], blood pressure depressant [3], anti-diabetic [4] properties. They also showed anti-tumor [5,6], anti-bacterial [7-9], anti-inflammatory [10], anti-cancer [11], hormone antagonists [12] and anti-psychotic properties [13]. Some of them are used in industries as finishing and brightening agents [14]. They are also been used as herbicidal [15-23], sea water algicidal [24], fungicidal [25], insecticidal [26] and pesticides [27]. As a wider programme of this laboratory in the synthesis of nitrogen, nitrogen and sulphur containing heterocycles and their cyclization into 5,6 and 7 member heterocycles viz. 1,2,4-thiadiazols, 1,2,4-dithiazols, 1,3,5-thiadiazines, 1,3,5-dithiazines, 1,3,5-triazines etc and synthetic applications of isocyanodichlorides, cyanoguanidine, and biuretes have been explored in sufficient details [28-30]. Hence interactions of

cyanuric chloride with various thiourea in 1:3 molar ratios at 90°C in acetone-ethanol medium were carried out to synthesize 2,4,6-tris[substituted thiocarbamido]-1,3,5-triazines. 2,4,6-tris[substituted thiocarbamido]-1,3,5-triazines were further interacted with various isothiocyanates in 1:3 molar ratio in ethanol-acetone medium to obtain 2,4,6-tris[(5-substituted)-2,4-dithiobiureto]-1,3,5-triazines which are hitherto unknown.

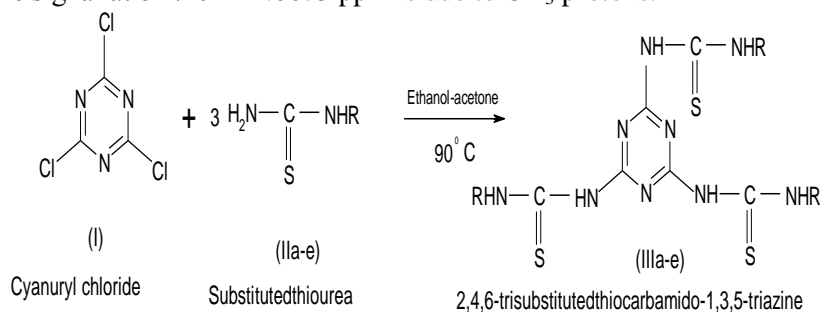
We developed the new route for this synthesis of 2,4-dithio biureto]-1,3,5-triazines, in which the time span of the reactions decreases which maintain the green chemistry parameters and we used 80% acetone-ethanol mixture, as a medium in which the percentage of acetone is only 20% which help another green chemistry parameter. At the same time yield of product is also increased by maintaining purity of products.

MATERIALS AND METHODS

The melting points of all the synthesized compounds were recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra 1106 analyzer. Nitrogen estimation was carried out on Colman-N-analyzer-29. IR spectra were recorded on Perkin Elmer Spectrometer in range 4000-400 cm⁻¹ in KBr pellets. PMR spectra were recorded on Bruker Ac 400 F Spectrometer with TMS as internal standard using CDCl₃ and DMSO-d₆ as a solvent. The purity of compounds was checked on silica Gel-G Pellets by TLC with layer thickness of 0.3 mm. All chemicals used were of AR-grade.

Synthesis of 2,4,6-tris[ethylthiocarbamido]-1,3,5-triazine (IIIa): A mixture of cyanuric chloride (0.1 M) and ethyl thiourea (0.3 M) in ethanol-acetone medium (80%, 15 ml) was refluxed on oil bath at 90°C for 1 hour then it was poured in water to obtain yellowish crystals of (IIIa). Yield 89%, melting point 228°C. (Scheme I)

Properties: It is yellow, crystalline solid. It gave positive test for nitrogen and sulphur. Desulphurised by alkaline plumbite solution. It formed picrate, melting point 192°C. Elemental analysis:- C [(found 36.68%) calculated 37.20], H [(found 4.19%) calculated 5.42%], N [(found 32.44%) calculated 32.55%], S [(found 23.95%) calculated 24.80%]. IR Spectra:- The IR spectra was carried out in KBr pellets and the important absorption can be correlated as (cm⁻¹) 3272 (N-H stretching), 1660 (C=N stretching), 1412 (C=S stretching). PMR Spectra:- The spectrum was carried out in CDCl₃ and DMSO-d₆. This spectrum distinctly displayed the signals due to triazino-NH proton at δ 10.2926-9.1762 ppm. The signal at δ 5.3636-3.5910 ppm is due to -NH protons. The signal at δ 2.5592-2.1133 ppm is due to CH₂ protons and the signal at δ 1.4012-1.0673 ppm is due to CH₃ protons.



where R = -C₂H₅, -CH₃, -H, -CH₂-CH=CH₂, -C₆H₅

Scheme I

Similarly, 2,4,6-tris[methylthiocarbamido]-1,3,5-triazine (IIIb), 2,4,6-tris[thiocarbamido]-1,3,5-triazine (IIIc), 2,4,6-tris[allylthiocarbamido]-1,3,5-triazine (IIId) and 2,4,6-tris[phenylthiocarbamido]-1,3,5-triazine (IIIe) were synthesized by interacting cyanuric chloride (I)

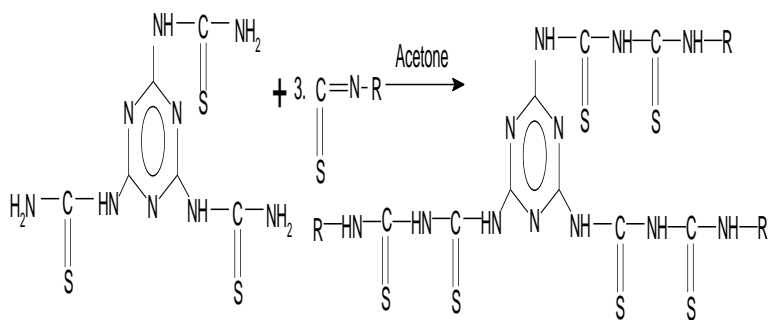
with thiourea (**IIb**), methyl thiourea (**IIc**), allyl thiourea (**IIId**) and phenyl thiourea (**IIe**) in 1:1 molar ratio respectively by the above mentioned method. The results obtained are given in table 1.

Table 1

| Sr. No. | Compd. No. | Expt. No. | 2,4,6-tris[substituted thiocarbamido]-1,3,5-triazines | Yield (%) | M.P. (°C) |
|---------|--------------|-----------|---|-----------|-----------|
| 1 | IIIb | 2 | ----- H ----- | 91 | 149 |
| 2 | IIIc | 3 | ----- -methyl ----- | 87 | 198 |
| 3 | IIIId | 4 | - ----- -allyl ----- | 82 | 129 |
| 4 | IIIe | 5 | ----- -phenyl- ----- | 89 | 193 |

Synthesis of 2,4,6-tris[(5-ethyl)-2,4-dithiobiureto]-1,3,5-triazine(Vb): A mixture of 2,4,6-tris[thiocarbamido]-1,3,5-triazine (**IIIb**) (0.1 M) and ethyl isothiocyanate (**IVa**) (0.3 M) in ethanol-acetone medium (80%, 15 ml) was refluxed on water bath for 1 hour during refluxing (**IIIb**) went into solvent and after half our the yellowish needle shaped crystals of (**IVa**) were isolated out. It was filtered and dried. Yield 76%, melting point 148°C (**Scheme II**).

Properties: It is yellow, crystalline solid. It gave positive test for nitrogen and sulphur. Desulphurised by alkaline plumbite solution. It formed picrate, melting point 138°C. Elemental analysis:- C [(found 30.32%) calculated 31.91], H [(found 3.98%) calculated 4.25%],N[(found 29.00%)calculated 29.78%],S[(found33.58%) calculated 34.04%]. IR Spectra:-The IR spectra was carried out in KBr pellets and The important absorption can be correlated as (cm⁻¹) 3213 (N-H stretching), 1698 (C=N stretching), 1398(C=S stretching). PMR Spectra:-The spectrum was carried out in CDCl₃ and DMSO-d₆. This spectrum distinctly displayed the signals due to triazino-NH proton at δ 10.1282-9.2670 ppm, The signal at δ 2.5402-2.1012 ppm is due to CH₂ protons and the signal at δ 1.3948-1.0508ppm is due to CH₃ protons. Similarly 2,4,6-tris[thiocarbamido]-1,3,5-triazine (**IIIb**) was interacted with phenyl isothiocyanate (**IVb**), p-Cl-phenyl isothiocyanate (**IVc**), methyl isothiocyanate (**IVd**), and t-butyl isothiocyanate (**IVe**), in 1:3 molar ratio respectively by the above mentioned method. The results obtained are given in table 2.



Where R = -phenyl, -p-Cl-phenyl, -methyl, -ethyl, t-butyl

Scheme II

Table 2.

| Sr. No. | Compd. No. | Expt. No. | 2,4,6-Tris[(5-substituted)-2,4-dithiobiureto]-1,3,5-triazines | Yield (%) | M.P. (°C) |
|---------|------------|-----------|---|-----------|-----------|
| 1 | Vb | 2 | -- ----- phenyl ----- - | 89 | 197 |
| 2 | Vc | 3 | ----- p-chlorophenyl - ----- ----- | 87 | 174 |
| 3 | Vd | 4 | - ----- methyl ----- - | 79 | 127 |
| 4 | Ve | 5 | ----- - t-butyl ----- | 72 | 183 |

This reaction was studied in various solvents and percent ratio of solvents for improving the yield and purity of the products as well as to maintain green chemistry parameters. The results are depicted in table 3

Table 3.

| Sr. No. | Solvent used | Quantity (ml) | Time Span (hours) | Yield (%) |
|---------|------------------------------|---------------|-------------------|-----------|
| 1 | Water | 50 | No reaction | -- |
| 2 | Acetone | 50 | 4 | 52 |
| 3 | Ethanol* | 50 | 4 | 57 |
| 4 | Methanol | 50 | 5 | 42 |
| 5 | Isopropanol | 50 | 8 | 35 |
| 6 | Benzene | No reaction | -- | -- |
| 7 | Dioxane | 50 | 10 | 20 |
| 8 | Acetone-ethanol (20%) | 30 | 7 | 60 |
| 9 | Acetone-ethanol (40%) | 30 | 5 | 65 |
| 10 | Acetone-ethanol (60%) | 30 | 4 | 71 |
| 11 | Acetone-ethanol (80%) | 15 | 1 | 87 |

* Known literature medium

This medium is used for the synthesis of all compounds (**IIIb-IIIe**) and (**Vb-Ve**).

APPLICATIONS

We developed the new route for the synthesis of 2,4-dithio biureto]-1,3,5-triazines, in which the time span of the reactions decreases which maintain the green chemistry parameters and used 80% acetone-ethanol mixture, as a medium in which the percentage of acetone (20%) which help another green chemistry parameter.

CONCLUSIONS

Ethanol-acetone mixture is the best medium for the synthesis of 2,4,6-tris[(5-substituted)-2,4-dithiobiureto]-1,3,5-triazines in which the yield is maximum and the solvent required for the condensation is only 15 ml while the reaction is completed in 1 hour. Known literature medium is acetone which required minimum 4 hours for completion of reactions and we are using 80% ethanol-acetone medium and quantity required is only 15 ml and % of acetone which is more toxic is only 20% in the reaction so our approach is towards maintain green chemistry parameters.

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