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Green Synthesis of Novel 2-(5-Substituted)-2,4-Dithiobiureto-4,6-Dichloro-1,3,5-Triazines

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Abstract

Recently in this laboratory a new route for the synthesis of 2-(5-substituted)-2,4-dithiobiureto-4,6-dichloro-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-(5-substituted)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines (Va-e) was successfully carried out by interacting 2,4-dichloro-6-substitutedthiocarbamido-1,3,5-triazines (IIIa-e) with various isothiocynates in 1:1 molar ratio in ethanol-acetone medium. Firstly cyanuryl chloride (I) was treated with various thiourea (IIa-e) in 1:1 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-Triazino 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 pesticidals[27].

As a wider programme of this laboratory in the synthesis of nitrogen, nitrogen and sulphur containing heteroacycles 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 1:1 molar ratios at 0-5^{0}C in acetone-ethanol medium were carried out to synthesize 2,4-dichloro-6-substitutedthiocarbamido-1,3,5-triazines. 2,4-Dichloro-6-substitutedthiocarbamido-1,3,5-triazines were further interacted with various isothiocynates in 1:1 molar ratio in ethanol-acetone medium to obtained 2-(5-substituted)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines which are hither to unknown.

We developed the new route for this synthesis, 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 one green chemistry parameter. At the same time yield of product is also increased by maintaining purity of products.

Material 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 Brucker Ac 400 F Spectrometer with TMS as internal standard using $CDCl_3$ and DMSO-d_6 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.

2,4-Dichloro-6-ethylthiocarbamido--1,3,5-triazine (IIIa): A mixture of cyanuryl chloride (0.1 M) and ethylthiourea (0.1 M) in 1:1 molar ratio in ethanol-acetone medium (80%, 15 ml) was kept at 0-5^{0}C in ice bath for 1 hour then it was poured in water to obtained yellowish crystals of (IIIa). Yield 87%, melting point 167^{0}C.

Similarly, 2,4-dichloro-6-thiocarbamido-1,3,5-triazine (IIIb), 2,4-dichloro-6-methylthiocarbamido-1,3,5-triazine (IIIc), 2,4-dichloro-6-allylthiocarbamido-1,3,5-triazine (IIId) and 2,4-dichloro-6-phenylthiocarbamido-1,3,5-triazines (IIIe) were

synthesized by interacting cyanuric chloride (I) with thiourea (IIb), methyl thiourea (IIc), allyl thiourea (IId) 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
Synthesis Results of 2,4-Dichloro-6-substitutedthiocarbamido -1,3,5-triazines

Compd. No.	Expt. No.	2,4-Dichloro-6-substitutedthiocarbamido-1,3,5-triazines	Yield (%)	MP (^{0}C)
IIIb	2	-- ------ -H ----------	81	135
IIIc	3	-------- -methyl - --------	87	123
IIId	4	- ------- -allyl----------	89	182
IIIe	5	------- -phenyl----------	93	172

Synthesis of 2-(5-ethyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines Va: 2-(5-Ethyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazine was synthesized by refluxing the mixture of 2-thiocarbamido-4,6-dichloro-1,3,5-triazine IIIb with ethyl isothiocyanate IVb in 1:1 molar ratio in acetone medium for 1 hour on water bath, lemon yellow coloured crystals were separated out. They were filtered and dried at room condition, Recrystallized by ethanol, yield 80%, m.p. 189^{0}C.

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-2.

Table-2
Synthesis Results of with different solvents

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

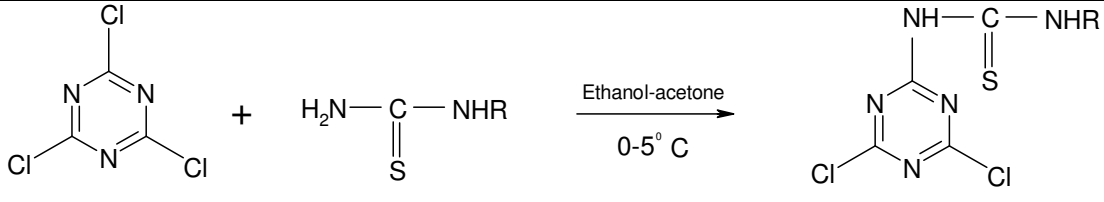
*Known literature medium.

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

Similarly, 2-(5-methyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazine (Vb), 2-(5-t-butyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazine (Vc), 2-(5-phenyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazine (Vd) and 2-(5-p-Cl-phenyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazine (Ve) were synthesized by interacting of 2-thiocarbamido-4,6-dichloro-1,3,5-triazine (IIIb) with methylisothiocyanate IVa, t-butylisothiocyanate IVc, phenylisothiocyanate IVd and p-chlorophenylisothiocyanate IVe in 1:1 molar ratio respectively by the above mentioned method. The results obtained are given in table-3.

Table-3
Synthesis results of 2-(5-Substituted)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines

Sr. No.	Compd. No.	Expt. No.	2-(5-Substituted)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines	Yield (%)	M.P. (^{0}C)
1	Vb	2	-- ------ methyl----------	78	132
2	Vc	3	-------- t-butyl- ----------	82	146
3	Vd	4	- ------- phenyl----------	87	186
4	Ve	5	------- -p-chlorophenyl----------	75	179



(I) Cyanuryl chloride

(IIa-e) Substitutedthiourea

(IIIa-e) 2,4-Dichloro-6-substitutedthiocarbamido-1,3,5-triazine

where R = $-C_2H_5$, $-CH_3$, -H, $-CH_2-CH=CH_2$, $-C_6H_5$

Scheme-1
Preparation of 2,4-Dichloro-6-substitutedithiocarbamido-1,3,5-Triazine

Results and Discussion

2,4-Dichloro-6-ethylthiocarbamido--1,3,5-triazine (IIIa): It is yellow, crystalline solid. It gave positive test for nitrogen, sulphur and chlorine. Desulphurised by alkaline plumbite solution. It formed picrate, melting point 124^0C. Elemental analysis**:** C [(found 27.86%) calculated 28.68%]**,** H [(found 2.16%) calculated 2.39%], N [(found 27.80%) calculated 27.88%], S[(found 12.74%) calculated 12.74%], Cl[(found 27.46%) calculated 28.28%]. IR Spectra: The IR spectra was carried out in KBr pellets and the important absorption can be correlated as (cm^{-1}) 3435.6 (N-H stretching), 3038 (Triazino stretching), 1623.6 (C=N stretching), 1319(C=S stretching). PMR Spectra: The spectrum was carried out in $CDCl_3$ and DMSO-d_6.This spectrum distinctly displayed the signals due to triazino-NH at δ 10.2716 – 9.8989 ppm. The signal at δ 4.0619 ppm 6.51-7.5 is due to –NH protons, the signal at δ 2.5629-2.1172 ppm is due to -CH_2 protons and the signal at δ 1.4053-1.2444 ppm is due to -CH_3 protons.

Synthesis of 2-(5-ethyl)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines Va: It is lemon yellow crystalline solid having m. p. 189^0C. It gave positive test for nitrogen, sulphur and chlorine elements. It was desulphurized by alkaline plumbite solution.It was soluble in DMSO, dioxane, ethanol, acetone while insoluble in benzene, carbontetra, chloride. It formed picrate having m.p. 132^0C. Elemental analysis**:** C [(found 26.12%) calculated 27.00%]**,** H [(found 1.98%) calculated 2.57%], N[(found 27.00%)calculated 27.00%], S[(found 19.15%) calculated 20.57%], Cl[(found 21.28%) calculated 22.82%]. IR Spectra:-The IR spectra was carried out in KBr pellets and the important absorption can be correlated as (cm^{-1}) 3413 (N-H stretching), 3024 (Triazino stretching), 1718 (C=N stretching), 1396(C=S stretching). PMR Spectra: The spectrum was carried out in $CDCl_3$ and DMSO-d_6 .This spectrum distinctly displayed the signals due to triazino-NH at δ 10.0699 – 9.8667 ppm. The signal at δ 4.2517 ppm is due to –NH protons, the signal at δ 2.5327-2.0993 ppm is due to -CH_2 protons and the signal at δ 1.3937-1.2389 ppm is due to -CH_3 protons.

Conclusion

Ethanol-acetone mixture is the best medium for the 2-(5-Substituted)-2,4-dithiobiureto-4,6-dichloro-1,3,5-triazines in which the yield is 80% and the medium required for the condensation is only 15 ml while the reaction is completed in 1 hour. Known literature medium is acetone 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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