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Novel Synthesis of 2-Chloro-4,6-Distitutedthiocarbamido-1,3,5-Triazines

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Abstract:

Recently in this laboratory a new route for the synthesis of 2-chloro-4, 6-distitutedthiocarbamido-1, 3, 5-triazines was developed to increase the yield of products by maintaining the purity of them and the time span required for the completion of reactions was also decreases. These are eco-friendly reactions. Novel green synthesis of-chloro-4,6-distitutedthiocarbamido-1,3,5-triazines ***(IIIa-e)*** *was successfully carried out by interacting cyanuryl chloride* ***(I)*** *with various thiourea in* ***(IIa-e)*** *in 1:2 molar ratio in ethanol-acetone medium. During the synthesis 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, substitutedthiourea, 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 various attempts were made for the interactions of cyanuric chloride with various thiourea in 1:1, 1:2 and 1:3 molar ratios was refluxed at 40^0C in acetone-ethanol medium on oil bath to synthesize 2-chloro-4,6-distitutedthiocarbamido-1,3,5-triazines, which is hither to unknown.

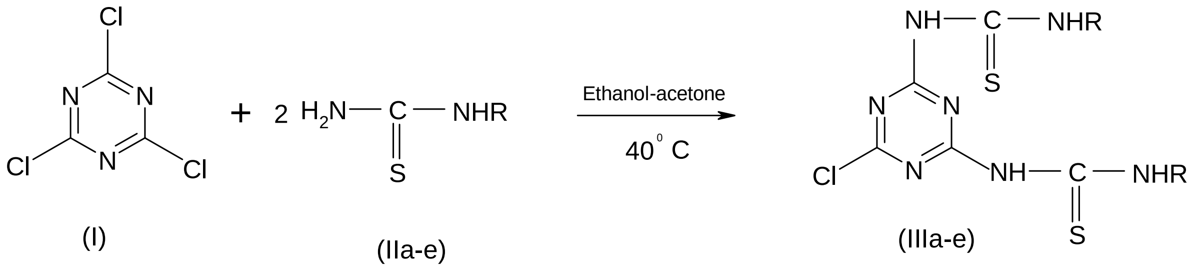
We developed the new route for this synthesis, in which the time span of the reactions decreases which maintain the green chemistry parameters i.e. we used 80% acetone-ethanol mixture, as a medium in which the percentage of acetone is only 20% which help one green chemistry parameter and we reduces the time span of the reactions by 6 hours; this is another parameter of green chemistry. At the same time yield of product is also increased by maintaining purity of products.

Experimental

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.

Synthesis of 2-Chloro-4,6-diethylthiocarbamido-1,3,5-triazine (IIIa)

A mixture of cyanuryl chloride (0.1 M) and ethylthiourea (0.2 M) in ethanol-acetone medium (80%, 15 ml) was refluxed at 40^0C in acetone-ethanol medium on oil bath for 1 hour then it was poured in water to obtained yellowish crystals of **(IIIa).** Yield 85%, melting point 215^0C.



(I) Cyanuryl chloride

(IIa-e) Substitutedthiourea

(IIIa-e) 2-chloro-4,6-disubstitutedthiocarbamido-1,3,5-triazine

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

Properties

It is yellow, crystalline solid. It gave positive test for nitrogen, sulphur and chlorine. Desulphurised by alkaline plumbite solution. It formed picrate, melting point 169^0C. Elemental analysis:- C [(found 32.17%) calculated 33.80], H [(found 3.28%) calculated 4.38%],N[(found 30.18%)calculated 30.67%],S[(found19.28%) calculated 20.03%]. 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 (Ar-H 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 proton at δ 10.2953-9.6331 ppm .The signal at δ 5.3282-3.8916 ppm is due to NH proton, The signal at δ 2.5658-2.1171 ppm is due to CH_2 protons and the signal at δ 1.4047-1.2438 ppm is due to CH_3 protons.

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 No. 1

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**).

Similarly 2-chloro-4,6-dimethylthiocarbamido-1,3,5-triazine **(IIIb),** 2-chloro-4,6-dithiocarbamido-1,3,5 -triazine **(IIIc),** 2-chloro-4,6-diallylthiocarbamido-1,3,5-triazine **(IIId)** and 2-chloro-4,6-diphenylthiocarbamido-1,3,5-triazine **(IIIe)** were synthesized by interacting cyanuric chloride **(I)** with methyl thiourea **(IIb),** thiourea **(IIc),** allyl thiourea **(IId)** and phenyl thiourea **(IIe)** in 1:2 molar ratio respectively by the above mentioned method. The results obtained are given in

Table No.2

Sr. No.	**Compd. No.**	**Expt. No.**	**2-Chloro-4,6-distitutedthiocarbamido-1,3,5-triazines**	**Yield (%)**	**M.P. (^{0}C)**
1	IIIb	2	------ dimethylthiocarbamido--------------	78	203
2	IIIc	3	------ dithiocarbamido---------------------	89	167
3	IIId	4	------- diallylthiocarbamido-----------------	82	192
4	IIIe	5	----------diphenylthiocarbamido-----------	83	124

Conclusion

Ethanol-acetone mixture is the best medium for the synthesis of 2-chloro-4,6-distitutedthiocarbamido-1,3,5-triazines, in which the yield is 85% 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 for maintaining green chemistry parameters.

As an evidence from the structure of cyanuric chloride this molecule looks like symmetrical, so reactivity of all three chlorine atoms must be identical which are present on 2,4,6 carbons of triazino nucleus. Hence various attempts were made for the interactions of cyanuric chloride with various thiourea in 1:1, 1:2 and 1:3 molar ratios at 40^0C in acetone-ethanol medium and it was observed during the reactions that only two groups were replaced in all three sets in various reaction conditions which is quite interesting. In 1:1 and 1:3 molar ratio's reactions of cyanuryl chloride with various thiourea contains only 2-chloro-4,6-distitutedthiocarbamido-1,3,5-triazines as a product with impurity of cyanuric chloride. From this it can be concluded that reactivity of all three chlorine atoms is different, it means this molecule is trifunctional molecule and replacement of chlorine group is totally dependent on temperature maintenance during the reaction. It means that at 40^0C only two chlorine groups were replaced to obtained 2-chloro-4,6-distitutedthiocarbamido-1,3,5-triazines**.**

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