RESEARCH PAPER

STUDY IN THE SYNTHESIS OF 4 - (5-SUBSTITUTEDAMINO) - 1,2,4-THIADIAZOLOPYRIDINES (IIIa-e)

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Abstract:

One step synthesis of 4-(5-substitutedamino)-1,2,4-thiadiazolopyridine **(IIIa-e)** was carried out by ox-dative cyclisation of 1-substituted-3-(4-pyridineimino)thiocarbamides **(Ia-e)** using liquid bromine in chloroform medium as an oxidizing agent. The products were isolated, characterized and justified on the basis of conventional elemental analysis, chemical characteristics and spectral studies.

Introduction:

Thiadiazolo nucleus containing heterocycles possesses their own identity in pharmaceutical, industrial, biological, agricultural and medicinal sciences[1-7]. Hence, medicines containing thiadiazole nucleus is now used extensively in medicinal, pharmaceutical and biological sciences[8-9]. Since from four decades it was observed that these drugs possesses a diverse range of physiological activities, herbicidal, antitubercular, antifungal, anticancer, antioxidant, anti-inflammatory, antibacterial, amoebicidal, antidiabetic, properties[10-15]. Some were found to be active against microorganism like *E. coli, C. alibicans* and *S. aureus*[16]. The literature survey reveals that the heterocyclic compounds containing nitrogen and nitrogen and sulphur have gained immense important in human life. It was also noticed that thiadiazoles are also effective against copper corrosion[17] and also used as additive in lubricating oil[18]. The oxidative cyclisation of cyanomidinosubstitutedthiocarbamide and N-substitutedformidinothiocarbamides had been extensively investigated by Dabolkar and Ansari[19]. Iminosubstitutedthiadiazolo-pyridine possesses noticeable pharmaceutical and medicinal activities.

As a part of research work presently been undertaken in this laboratory in the synthesis of heteroacycles and heterocycles, it was thought interesting to investigate the oxidative cyclisation of 1-substituted-3-(4-pyridineimino)thiocarbamides **(Ia-e)** with liquid bromine in chloroform medium to obtained a novel series of 4-(5-iminosubstituted-1,2,4-thiadiazolo)pyridine **(IIIa-e)** which is heither to unknown. The present work describes somewhat suitable, convenient, cheaper, more practical utility and one step direct method for the synthesis of **(IIIa-e).**

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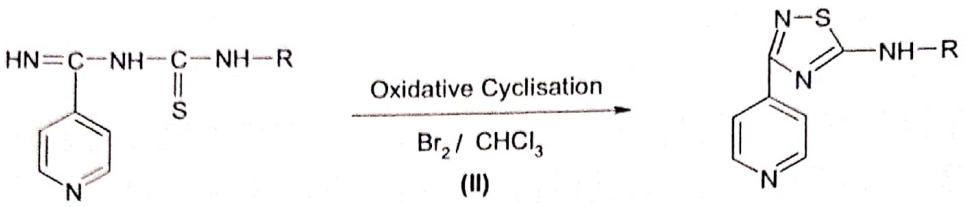

(Ia-e)

1-Substituted-3-(4-pyridineimino)thiocarbamides

(IIIa-e)

4-(5-Substitutedamino)-1,2,4-thiadiazolopyridines

Where, R = -H, -methyl, -ethyl, -allyl, -phenyl

Experimental:-

The melting points of all the synthesized compounds were recorded using hot paraffin bath and are uncorrected. The carbon and hydrogen analysis was carried out on Carlo-Ebra-1106 analyser, nitrogen estimation was carried out on Colman-N-analyser-29. IR spectra were recorded on Perkin-Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded on Bruker AC-300F spectrometer with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as solvent. The purity of the compounds was checked on Silica Gel-G plates by TLC with layer thickness of 0.3 mm. All chemicals used were of AR grade.

Result and Discussion:

A) Synthesis of 4-(5-ethylamino)-1,2,4-thiadiazolopyridine (IIIc):

4-(5-Ethylamino)-1,2,4-thiadiazolopyridine **(IIIc)** was synthesized by the oxidative cyclisation of 1-ethyl-3-(4-pyridinimino)thiocarbamide **(Ic)** using liquid bromine in presence of chloroform. In china dish the pest of 1-ethyl-3-(4-pyridinimino)-thiocarbamide **(Ic)** was prepared in chloroform. To it liquid bromine in chloroform was added with constant stirring. Initially the colour of bromine disappear, the addition was continued till colour of bromine persisted to the reaction mixture. The reaction mixture was allowed to stand for 4 hours and then on basification with dilute ammonium hydroxide solution, it afforded yellowish coloured products. It was recrystallized from ethanol, yield 90%, m.p. 158°C.

Properties of (IIIc): It is dark yellow crystalline solid having melting point 158°C. It gave positive test for nitrogen, sulphur. Desulphurization was not observed when warm with silver nitrate, sodium plumbite solution[19-20] clearly indicating sulphur is blocked in a ring. The benzene solution of compound when treated with pure and dry carbon disulphide then colourless solution was obtained indicating =NH (imino) group is not present[20]. It formed picrate having melting point 177°C. **Elemental Analysis: C [(found** 51.94%) **calculated** 52.42%], **H [(found** 04.26%) **calculated** 04.85%], **N [(found** 26.89%) **calculated** 27.18%], **S [(found** 15.53%) **calculated** 15.53%]. **IR Spectra:-The IR spectra was carried out in KBr pellets and the important absorption can be correlated as (cm^{-1})** 3409.10 (NH stretching), 2614.40 (C-H stretching), 2063.30 (N-C=S stretching), 1633.80 (N-C=N grouping showing Hexocyclic ring), 1555.24 [C = N stretching (Ring)], 1406.70 (C=N stretching), 1094.39 (C-N stretching). **NMR Spectra:-The spectrum was carried out in $CDCl_3$ and DMSO-d_6.** This spectrum distinctly displayed the signals due to pyridino proton at δ 7.1868-8.2506 ppm, NH proton at δ 3.6667 ppm, N-CH_2 proton at δ 2.5624 ppm and CH_3 proton at δ 1.2453 ppm.

Similarly 4-(5-amino)-1,2,4-thiadiazolopyridine **(IIIa),** 4-(5-methyl amino)-1,2,4-thiadiazolopyridine **(IIIb),** 4-(5-allylamino)-1,2,4-thiadiazolopyridine **(IIId),** 4-(5-phenyl-

amino)-1,2,4-thiadiazolopyridine **(IIIe)** were synthesized from 3-(4-pyridineimino)-thiocarbamides **(Ia)**, 1-methyl-3-(4-pyridineimino)thiocarbamide **(Ib)**, 1-allyl-3-(4-pyridine-imino)thiocarbamide **(Id)**, 1-phenyl-3-(4-pyridineimino)thiocarbamide **(Ie)** by the oxidative cyclisation with liquid bromine in chloroform medium respectively by the above mentioned method in **Experiment No. 2 to 5** and enlisted in **Table No. I**

Table No. I

Sr. No.	Expt. No.	4-(5-**Substitutedamino**)-1,2,4-thiadiazolopyridine**(IVa-e)**	Yield (%)	M.P. ^{0}C
1.	2	.....**amino**.....	86	142
2.	3	.....**methylamino**.....	87	146
3.	4	.....**allylamino**.....	89	167
4	5	.....**phenylamino**.....	82	140

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