RESEARCH PAPER

A NOVEL SYNTHESIS OF 1-SUBSTITUTED - 3 - (4-PYRIDINEIMINO)THIOCARBAMIDES

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Abstract : Recently in this laboratory a new series of 1-substituted-3-(4-pyridineimino)thiocarbamides (3a-e) was synthesised by the interactions of 4-cyanopyridine (1) with various thiourea (2a-e) in acetone, ethanol , acetone-ethanol mediums at various reaction conditions, for creating a new sutaible route for the synthesis of 1-substituted-3-(4-pyridineimino)thiocarbamides which increases the yield of products as well as maintain the purity of them. At the same time it was also considered to help indirectely to maintain the parameters of green chemistry by decreasing the time duration of the reactions, maintioned in literature. The synthesized compounds were recrystalised and their structures were established on the basis of elemental analysis,chemical characteristics and spectral studies.

Keyword : 4-Cyanopyridine, substitutedthiocarbamides, acetone, ethanol, etc.

Introduction : Cyanopyridine and their analogues are used as anti-depressant drugs in pharmaceutical and medicinal sciences [1-4]. The thiadiazolo and triazino derivatives of cyanopyridine showed remarkable anti-fungal [5],anti-bacterial[6],anti-tumor and anti-cancer[7], anti-material[8], anti-tuburcular[9], ant-inflammatory and anti-pyretic properties.[10,11]. Some amino derivatives of cyanopyridine are also used for the synthesis of paints, dyes, insecticides and herbicides. Hence the heterocycles containing such type of nuclei have their own importance in medicinal, pharmaceutical and chemical sciences. Recently in this laboratory Tayade et al [12-19] synthesized new series of thiadiazoles, thidiazines and dithiazines by exploring the synthetic applications of amino, cyno, halo, etc. groups successfully and also studied their antimicrobial, antifungal and physiochemical parameters. As 4-cyanopyridine, thadiazole, thiocarbamide, dithiazine and their derivatives showed pharmaceutical, medicinal, agricultural, biological and industrial significances and applications. Taking all these facts into consideration this research scheme was designed. During designing this scheme it was also planned to develop a new route for the synthesis of pyridinosubstitutedthiocarbamides by the interactions of 4-cyanopyridine(1) with various thioure(2a-e) in acetone, ethanol ,acetone-ethanol mediums (changing the previous reaction conditions mentioned in literature) with various composition and ratio Literature survey also revealed that the

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reaction of amino compound with thiocarbamides were performed in acetone, ethanol, 2-butanol and 2-propanol only and the time span required for the completion of reaction was in between 8 to 10 hours. Hence taking all these facts into consideration it was thought interesting to perform these reactions in various solvents.

The main objective of the work is to synthesize a novel series of pyridinosubstituted-thiocarbamides and also to investigate a new reaction medium for such type of reaction and also to set up new reaction condition to reduce the time span of such type of reaction and at the same time it was thougth to increase the yield of product by maintaining purity. It was observed during the study, that the (60%) acetone-ethanol solvent was the best solvent which curtails the time span and also maintain green chemistry parameters. This work is useful to incoming researcher in organic chemistry and medicinal as well as pharmaceutical sciences. The newly synthesized drug will be expected to posses more practical utility and also the new thiocarbamido substituent may enhance the potency of the drug.

Experimental:- All the chemicals used for the synthesis were purified. The melting points of all synthesize compounds were recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra-1106 analyzer, Nitrogen estimations were carried out by colmon N-analyzer-29. IR spectra were recorded with Perkin Elmer spectrometer in the range 4000-400 $cm.^{-1}$ PMR spectra were recorded on Bruker-AC-300 F spectrometer with TMS as internal standard solvent.

Synthesis of 1-phenyl-3-(4-pyridineimino) thiocarbamide (3e) :- This compound was synthesised by refluxing 4-cyanopyridine (1) with phenylthiourea (2e) in acetone-ethanol(60%) medium on water bath for 4 hours. During refluxing there is elimination of hydrogen chloride gas. It was filtered in hot condition and the filtrate was concentrated by distillation of solvent when brown crystals separated out on cooling, which were collected by filtration, washed several times with ether, recryestallised with ethonal and dried. Yield 97%, m.p. 147°C.

Same reaction was performing in various solvents at various reaction conditions and also the reaction time span were changed to improve the percentage yield of the products and also to maintain the purity. It was observed in 60% acetone-ethanol medium we get maximum yield and also the time span of the reaction is also reduce up to 4 hours. This is our main achievement of this work. This reaction was also carried out in microwave (solvent free reaction condition) at various time spans, but we get various impurities in the products and as the reaction were carried on micro-scale, hence it became very difficult to separate these impurities. The results are depicted in Table No-1.

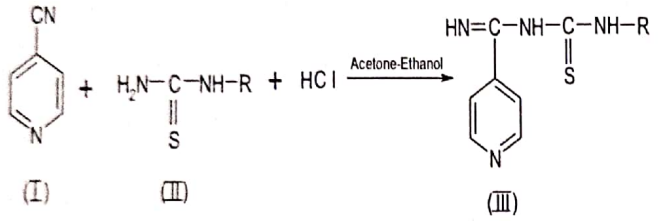
Properties of (3e): The compound is yellowish crystalline in colour having melting point 147° C. It gave positive test for nitrogen and sulphur (negative test for chloride which clearly indicated removal of chlorine) The compound(3e) was desulphurised by alkaline plumbite solution and it also gave positive test for imino group [20] these two test clearly indicated thiocarbamido group is condensed to 4-cyanopyridine through nitrogen while sulphur is present in the form of =S (double bonding) in the molecule. **Elemental analysis:- C [(found 55.17%) calculated 56.89], H [(found 4.98) calculated 5.17%], N [(found 24.11%) calculated 24.13], S[(found 13.78%) calculated 13.79].IR Spectra:- The IR spectra was carried out in KBr pellets an important absorption can be correlated as(cm^{-1}) 3393.26 (N-H stretching),1611.48 (C-N stretching), 1594.74 (=C=NH imino), 1193.11(C-N stretching), 1083.61 (N=C=S). PMR Spectra:-The spectrum was carried out in $CDCl_3$ and DMSO-d_6 .This spectrum distinctly displayed the signals due to Ar-H protons at δ8.8456-8.8601 ppm,**

pyridino protons at δ7.0483-7.6908 ppm, Ar-NH proton at δ7.0483-7.3989 ppm.

Table No-1 Solvents and reaction condition for the synthesis of(3e)

Sr No	Solvent	Time span in hrs	Yield (%)
1	Acetone*	16	67
2	Ethanol*	16	58
3	Benzene	18	48
4	Carbontetrachloride	18	48
5	Acetone- Ethanol(40%)	10	62
6	Acetone - Ethanol(50%)	10	78
7	Acetone- Ethanol(60%)	04	97
8	Acetone- Ethanol(70%)	10	74
9	Acetone- Ethanol(80%)	10	64
10	Acetone- Ethanol(90%)	10	62

Scheme-I



Cyanopyridine Substituted thiourea 4-Pyridinosubstitutedthiocarbamides

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

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