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# Synthesis and Characterization of 2- and 4-Substituted Pyridine Carbothionamides and 2- and 4-Pyridinethio Carbonyl Ureas

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The four compounds, *viz.*, 2- and 4-N-(*n*-butyl)pyridine carbothionamides as well as 2- and 4-pyridine thiocarbonyl ureas were synthesized using 2- and 4-pyridine carbonitrile with *n*-butylamine and urea in the ratio 1 : 4 respectively in the presence of $H_2S$. The prepared compounds were characterized using IR, NMR and mass spectra and the structures were determined.

**Key Words: Synthesis, Substituted pyridine, Carbonyl ureas.**

## INTRODUCTION

Ethionamide is found to be converted *in vivo* to its S-oxide[1], during physiological transformations. Introduction of substituents in the alpha position in isonicotinamide increases the tuberculostatic activity both *in vitro* and *in vivo*[2]. Prothionamide and its S-oxide given orally at the same doses has approximately equal activity against M-leprae[3]. Antonini and co-workers[4] have established the significant antitumour activity of compounds containing N-N-S tridentate ligand system. The thionamide group[5] is a functional analytical group for bismuth and iron producing a yellow colour with bismuth and red or red-brown colour with iron. An ammonical absolute alcoholic solution of the nitrile when saturated with $H_2S$ and the resulting solution kept overnight at room temperature, the thionamide is precipitated out[6].

## EXPERIMENTAL

The compounds 2-4-N-(*n*-butyl)pyridine carbothionamides and 2-/4-thiocarbonylureas were synthesized using the various pyridine carbonitriles and the respective amines in the ratio of 1' : 4·2-N-(*n*-butyl)pyridine carbothionamide and 4-N-(*n*-butyl)pyridine carbothionamide were prepared using 20 mL of alcoholic *n*-butylamine with 5 mL of 2- or 4-cyanopyridine in 10–15 mL of 95% ethanol respectively. $H_2S$ gas was bubbled through the solution for 6 h at a slow rate. The resulting solution was diluted with water and kept overnight. The precipitate obtained was filtered, recrystallized and dried. 2- and 4-pyridine thiocarbonyl urea were prepared in the same way by taking 20 g of urea with 2- or 4-cyanopyridine.

The IR spectra of the compounds were recorded at 4000–400 $cm^{-1}$ using KBr pellets in a Perkin-Elmer spectrophotometer. Proton NMR spectra of the compounds were recorded on AV 300 instrument operating at 300 MHz. Tetramethylsilane was used as internal reference. Chemical shifts are reported in $\delta$ scale. The solvent employed was $CDCl_3$. Mass spectra were obtained using a QP-5000 instrument.

The C, H and N analyses of the samples were done using C, H, N analyzer at Indian Institute of Science, Bangalore and sulphur was estimated by gravimetric method by oxidizing to sulphate using $Br_2$ and conc. $HNO_3$ and precipitating as $BaSO_4$ using $BaCl_2$ solution.

## RESULTS AND DISCUSSION

The compounds were prepared and characterized using elemental analysis, IR, NMR and Mass spectra. The elemental data are given in Table-1.

In the IR spectra of the compounds, the typical bands in the region of 3300–3150 and 3020–2920 $cm^{-1}$ correspond to the $\nu$(N—H) and $\nu$(C—H) stretching vibrations respectively. The bands around 1590–1570, 990–950, 630–610 $cm^{-1}$ are indicative of ring vibrations, ring breathing and out of plane deformations of pyridine, respectively. The C—N vibration occurs at 1430–1400 $cm^{-1}$ while the $\nu$(C=S) stretching vibration occurs at 1060–1150 $cm^{-1}$ and bending occurs at 740–720 $cm^{-1}$.

A reliable assignment of $\nu$(C=S) stretching frequency in the spectra of thiocarbonyl compounds is of special significance. The $\nu$(C=S) stretching mode as a group frequency is poorly characterized. This arises from the incidence of coupling of C=S stretching vibrations with other molecular vibrations[7]. This is especially so when the C=S moiety is attached to a strongly mesomeric atom such as nitrogen. This results in a lowering of C=S bond order. The higher mass of sulphur and lower C=S bond order shift the C=S stretching vibrations to lower wavenumbers, conductive to coupling with other vibrations. The absence of a band in the 2600–2500 $cm^{-1}$ region[8] characteristic of the —SH group in the spectra of the above compounds, indicates that the compounds are in the thione form. The characteristic IR frequencies of the compounds are given in Table-1.

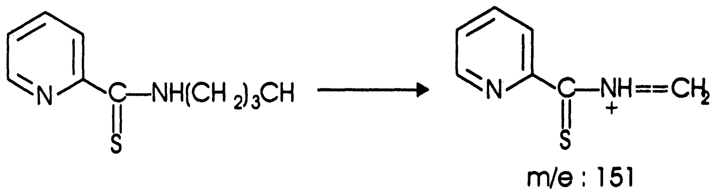
$^1$H NMR spectral data of **I** to **IV** are given in Table-1. In **I** and **II**, the peaks characteristic of methyl protons are found centred around 0.9 $\delta$ while those of $\alpha$-methylene and $\beta,\gamma$-methylene are observed around 3.88 and 1.68 $\delta$ respectively. The N—H protons are observed as broad peak in 8.48 and 10.18 $\delta$ region depending on the nature and position of the substituent present. The spectra of **III** and **IV** indicate the presence of peaks centred at about 9.5 and 9.4 $\delta$ characteristic of $—NH_2$ protons while the N—H protons are expected to be observed further downfield. In general, 3 sets of peaks are observed for the pyridine ring protons for the 2-substituted compounds (centred around 7.4, 7.8 and 8.5 $\delta$) and 2 sets of peaks centred at 7.5 and 8.5 $\delta$ for 4-substituted compounds, as would be expected from symmetry considerations.

In the mass spectra, the compound **I** has the molecular ion peak m/e 194 with less intensity while the compound **II** has an intense peak at m/e 194 due to

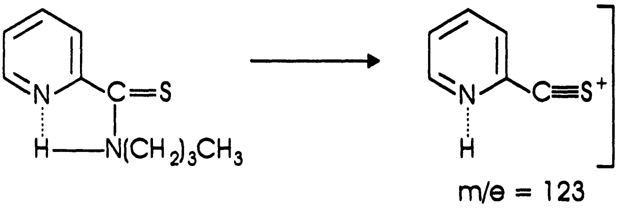
TABLE-1
PHYSICAL AND SPECTRAL DATA OF COMPOUNDS I–IV

| Compound | m.p. (°C) | % Elements (Calc.) | m.f. (yield %) | IR ($\nu_{max}$, cm$^{-1}$) | $^1$H NMR ($\delta_{ppm}$) |
|---|---|---|---|---|---|
| **I** | 130 | C 39.7 (40.82)<br>H 4.66 (4.76)<br>N 9.52 (9.4)<br>S 10.6 (10.88) | $C_{10}H_{14}N_2S$<br>(90) | 3278.1 (NH Str.), 15.89 (py ring vib.)<br>1521.9 (NH bend.), 1406.7 (CN vib.)<br>1071.5 (C═S str.), 954.4 (ring breathing)<br>745.4 (C═S bend), 616.0 (py ring out of plane bending) | 0.99 (—$CH_3$), 1.5 (β, γ—$CH_2$)<br>3.8 (α $CH_2$), 7.4 (py ring H)<br>7.8 (py ring H), 8.5 (py ring H)<br>10.1 (—NH) |
| **II** | 75 | C 39.82 (40.82)<br>H 4.68 (4.76)<br>N 9.46 (9.52)<br>S 10.42 (10.88) | $C_{10}H_{14}N_2S$<br>(73) | 3160.2 (NH Str.), 1598.1 (py ring vib.)<br>1553.1 (NH bend.), 1411.9 (CN vib.)<br>1062.7 (C═S str.), 951.7 (ring breathing)<br>730.0 (C═S bend), 623.4 (py ring out of plane bending) | 0.98 (—$CH_3$), 1.6 (β, γ—$CH_2$)<br>3.8 (α $CH_2$), 7.5 (py ring H)<br>8.5 (py ring H),<br>8.4 (—NH) |
| **III** | 125 | C 55.32 (55.63)<br>H 4.52 (4.64)<br>N 18.52 (18.54)<br>S 20.82 (21.19) | $C_7H_7N_2S$<br>(57) | 3148.8 (NH str.), 1581.4 (py ring vib.)<br>1566.5 (NH bend.), 1407.6 (CN vib.)<br>1145.9 (C═S str.), 994.1 (ring breathing)<br>725.5 (C═S bend.), 624.5 (py ring out of plane bending) | 7.4 (py ring H), 7.8 (py ring H),<br>8.6 (py ring H), 9.5 (—$NH_2$) |
| **IV** | 185 | C 54.82 (55.63)<br>H 4.56 (4.64)<br>N 17.96 (18.54)<br>S 20.92 (21.19) | $C_7H_7N_2S$<br>(33) | 3240.7 (NH Str.), 1598.6 (py ring vib.)<br>1555.6 (NH bend.), 1425.2 (CN vib.)<br>1150.0 (C═S str.), 997.7 (ring breathing)<br>725.5 (C═S bend), 682.7 (py ring out of plane bending) | 7.6 (py ring H), 8.6 (py ring H),<br>9.4 (—$NH_2$) |

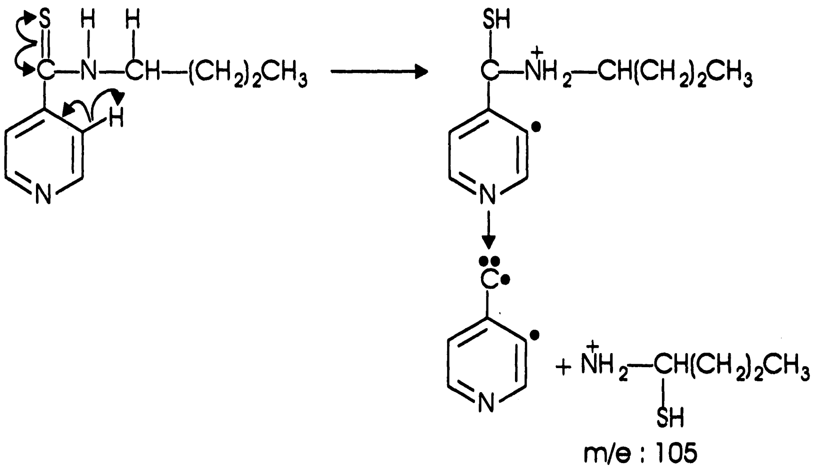
stabilization of positive charge by π electrons. Some of the peaks are discussed below.



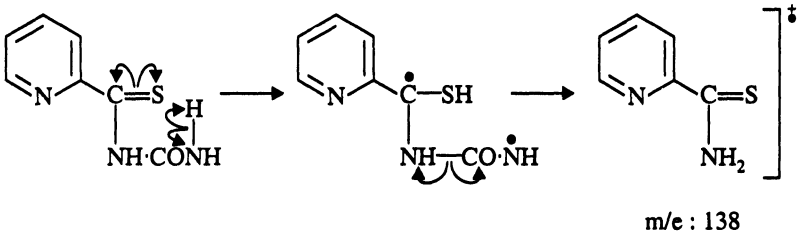
The m/e 123 fragment in **I** is found to be the base peak m/e and m/e 122 fragment in **II** is the base peak revealing the greater stability of these ions.



In **I** and **II**, the peak at m/e 105 may be due to



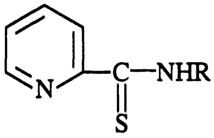
m/e 78 of compounds **I** and **II** may be due to the pyridine ring and m/e 51 may be due to $C_4H_3^{+}$. In case of compounds **III** and **IV**, the peak at m/e 138 may be due to:



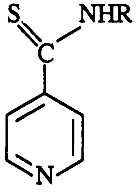
The peak at m/e 60 may be due to the formation of urea. The base peak at m/e 79 in compound **III** may be due to intramolecular hydrogen bonding between pyridine nitrogen and —NH proton.

## Structure of the Compound

The data obtained from the spectral studies indicate that the structure of the compounds may be:



and



where R = $—CH_2CH_2CH_2CH_3$ or $—CONH_2$

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