



SYNTHESIS AND CHARACTERIZATION OF SUBSTITUTED 1, 3, 4-THIADIAZOLE AND IT'S DERIVATIVES

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ABSTRACT

Substituted 1, 3, 4 –thiadiazole have been synthesized by the action of amines with isoniazid in presence of acid like HCl. The synthesized compounds have been characterized by spectral analysis and elemental analysis.

Key words : Thiadiazole, Amines, Isoniazid, Acid catalyst

INTRODUCTION

Heterocyclic compounds promote the formation of life on earth¹. They are widely distributed in nature and essential to life as they play a vital role in the metabolism of living cells. Heterocyclic ring system containing nitrogen and nitrogen-sulphur heteroatoms exhibited chemotherapeutic² and other medicinal uses.

On the basis of the history, some of the authors^{3,4} code it, as fused and pendant 1, 3, 4–thiadiazoles are ubiquitous feature of many pharmaceutical and agrochemical products. Thiadiazole nucleus is associated with various pharmacological activities like antimicrobial, antibacterial, antiviral, antifungal effects⁵ and CNS depressant⁶. Dendrodoine, a cytotoxic substance from marine tunicate is an example having medicinal value⁷.

Now-a-days, substituted 1, 3, 4 –thiadiazole nucleus is a common examples found in various marketed drugs. There are some other substituted 1, 3, 4 –thiadiazole entities that are very interesting components in terms of their biological properties. In them, antibacterial, antitubercula, herbicidal and plant growth regulator activities have been reported⁸⁻¹³. It has also an important application for the protection of human skin from

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harmful UV irradiation^{14,15} and corrosion inhibitor¹⁶.

Due to these valuable findings and its need, present work has been carried out on the precipitation of substituted 1, 3, 4 – thiadiazole and its derivatives.

EXPERIMENTAL

Synthesis of 1-naphthyl isothiocyanate

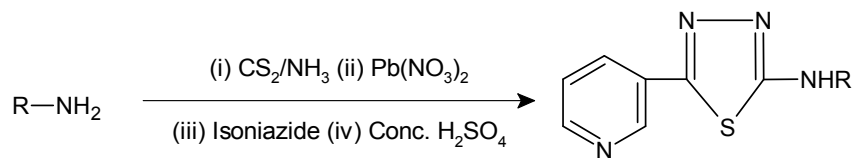
A mixture of 1-naphthyl amine (0.25 mol, 35.8 g), carbon disulphide (0.39 mol, 11.78 mL) and methanol (90 % 60 mL) was cooled to 10°C and then ammonia (6.1 mL) was added dropwise to the reaction mixture with continuous stirring. The mixture was allowed to stand overnight. The mixture was filtered and solid was then washed with 50 mL ether. The solid was dissolved in 250 mL of water. A solution of lead nitrate (0.25 mol, 8.27 g) was slowly added to this solution. The mixture was steam distilled to yield the product; M. P. (58°C).

Synthesis of 4-(1-naphthyl)-1-(isomeric pyridyl) thiosemicarbazide

Isoniazid (0.004 mol, 0.552 g) were dissolved in absolute ethanol (60 mL). The α -naphthyl isothiocyanate (0.004 mol) is separately dissolved in 30 mL ethanol. Then the solution was added to isoniazid with continuous stirring. The reaction mixture was then refluxed for 6 hours. It was cooled at room temperature to form white precipitate. White solid crystals were then filtered and dried.

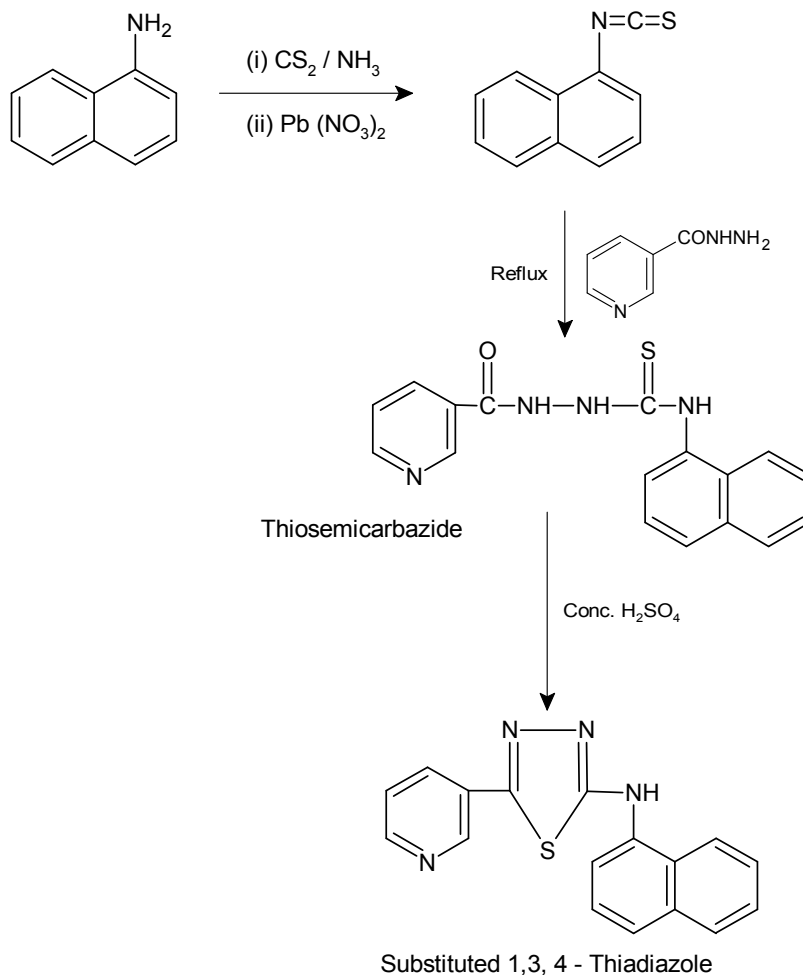
Synthesis of 4-(1-naphthyl amino) -5-(isomeric pyridyl) 1, 3, 4-thiadiazole

Solid thiosemicarbazide (0.6 mole, 0.2 g) was added in 25 mL of concentrated H₂SO₄ at 0°C with continuous stirring. The mixture was then stirred for 3 hours at room temperature. Then it was neutralized with dil. NaOH. Precipitate of brownish yellow solid was filtered and washed with small quantity of water. It was then recrystallized with acetic and water (1 : 1).



Where R = CH₃-, C₂H₅-, C₆H₅-, p-ClC₆H₄-, p-CH₃C₆H₄-, o-CH₃C₆H₄- and α -Naphthyl

General Reaction Scheme



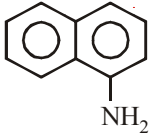
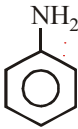
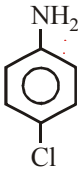
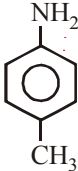
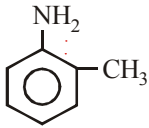
Reaction scheme (Representative)

RESULTS AND DISCUSSION

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Fourier Transform IR spectrophotometer (Shimadzu) using KBr disc method.

The purity of the test compounds was determined by thin layer chromatography. A single spot is obtained on TLC slide, which confirmed the purity of substituted 1, 3, 4 - thiadiazole. Physical data of the compounds are recorded in Table 1.

Table 1

Comp.	R (Amine)	Mol. formula	Solvent	Yield (%)	M. P. (°C)
1(a)		C ₁₇ H ₁₂ N ₄ S	Methanol	70	112
1(b)		C ₁₃ H ₁₀ N ₄ S	Methanol	72	109
1(c)		C ₁₃ H ₉ N ₄ SCl	Ethanol	75	106
1(d)		C ₁₄ H ₁₂ N ₄ S	Methanol	68	111
1(e)		C ₁₄ H ₁₂ N ₄ S	Methanol	69	116
1(f)	CH ₃ – NH ₂	C ₈ H ₈ N ₄ S	Ethanol	68	107
1(g)	C ₂ H ₅ – NH ₂	C ₉ H ₁₀ N ₄ S	Ethanol	65	109

Elemental analysis

These compounds were analyzed for C, H and N and the values were found to be within $\pm 0.4\%$ of calculated values.

Percentage of elements were recorded by elemental analysis at Wochardt Ltd. and are reported in Table 2.

Table 2

Comp.	Mol. formula	Mol. wt.	C (%)	H (%)	N (%)	S (%)	Cl (%)
1(a)	C ₁₇ H ₁₂ N ₄ S	304	67.10	3.94	18.42	10.52	-
1(b)	C ₁₃ H ₁₀ N ₄ S	254	61.41	3.93	22.04	12.50	-
1(c)	C ₁₃ H ₉ N ₄ SCl	270	60.93	3.33	20.74	11.85	6.29
1(d)	C ₁₄ H ₁₂ B ₄ S	260	64.61	4.61	21.53	12.30	-
1(e)	C ₁₄ H ₁₂ N ₄ S	260	64.61	4.61	21.53	12.30	-
1(f)	C ₈ H ₈ N ₄ S	192	50	4.16	29.16	16.66	-
1(g)	C ₉ H ₁₀ N ₄ S	206	52.42	4.85	27.18	12.30	-

In the present work, thiosemicarbazide were used as the key intermediate for the synthesis of the substituted 1, 3, 4 –thiadiazoles.

The acid catalyzed intramolecular cyclization of the thiosemicarbazide involving dehydration furnished substituted 1, 3, 4 –thiadiazoles. The IR of these compounds lacked carbonyl absorption; however, they show absorption band of N-H at 3423 cm⁻¹, which is only one band confirming secondary amine, C = N stretching at 1595 cm⁻¹ and C-N stretching at 1028 cm⁻¹ (aromatic).

Substituted 1, 3, 4 –thiadiazole and their derivatives are an important class of heterocyclic compounds with a diverse agricultural, industrial antitubercular, antifungal effect etc.

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