

Synthesis and characterization of substituted 1,2,4-Triazole and its derivatives

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ABSTRACT

Substituted 1,2,4 – Triazole have been synthesized by the action of base like dilute NaOH. The synthesized compound have been characterized by spectral and elemental analysis.

Key words: Triazole, amines, isoniazid, base catalyst.

INTRODUCTION

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

From the literature^{3,4}, it is revealed that pendant 1,2,4 – triazole are ubiquitous feature of many pharmaceutical and agrochemical products.

Triazole nucleus is associated with various pharmacological activities like antimicrobial, antibacterial, antiviral, antifungal effects⁵. Dendrodoine, a cytotoxic substance from marine tunicate is an example which have medicinal value⁶.

Now-a-days substituted 1,2,4 – triazole nucleus is a common example found in various marketed drugs. Such as Flucanazole⁷, teracanazole, rizatriptan, triazoleum which act as antifungal agent⁸.

There are some other substituted 1,2,4 – triazole entities that are very interesting components

in terms of their biological properties, such as antibacterial, antitubercular, herbicidal and plant growth regulator activities⁹.

RESULTS AND DISCUSSION

In the present work thiosemicarbazides were used as the key intermediate for the synthesis of the substituted 1,2,4 – triazoles.

The base catalysed intramolecular dehydrative cyclization of the thiosemicarbazide furnished substituted 1,2,4 – triazoles. The detailed reaction are depicted in scheme I. The IR spectra of the substituted 1,2,4 – triazole gives the significant peak in the region of 2557 cm^{-1} attributed to S – H stretching, C=N stretching 1665 cm^{-1} , C–N stretching at, 1185 cm^{-1} . The absence of C=S, N–H stretching and presence of S–H absorption established that the isolated triazoles are in thiol form and not in thione form.

Melting points were determined in open capillary tubes and were found uncorrected. IR spectra were recorded on 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 confirmed the purity of substituted 1,2,4 – triazole.

**Preparation of 1 – Naphthyl isothiocyanate:
(R=Naphthyl Group)**

A mixture of 1-naphthylamine (0.25 mol, 35.8 gm), carbon disulphide (0.39 mol, 11.78 ml)

Table 1: Physical Data of compounds recorded

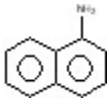
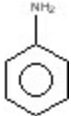
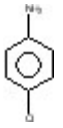
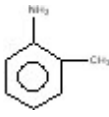
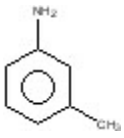
Compound	- R Amine	Molecular formula	Solvent	% yield	Melting point
1a		C ₁₇ H ₁₂ N ₄ S	Methanol	70%	89°C
1b		C ₁₃ H ₁₀ N ₄ S	Methanol	72%	88°C
1c		C ₁₃ H ₉ N ₄ SCl	Methanol	68%	88°C
1d		C ₁₄ H ₁₂ N ₄ S	Methanol	70%	92°C
1e		C ₁₄ H ₁₂ N ₄ S	Methanol	71%	90°C
1f	CH ₃ – NH ₂	C ₈ H ₈ N ₄ S	Ethanol	74%	87°C
1g	C ₂ H ₅ – NH ₂	C ₉ H ₁₀ N ₄ S	Ethanol	70%	88°C

Table 2: Results of elemental analyses*

Compound	Molecular formula	Molecular weight	% C	% H	% N	% S	% Cl
1a	C ₁₇ H ₁₂ N ₄ S	304	67.10	3.94	18.42	10.52	-
1b	C ₁₃ H ₁₀ N ₄ S	254	61.41	3.93	22.04	12.50	-
1c	C ₁₃ H ₉ N ₄ SCl	270	60.93	3.33	20.74	11.85	6.29
1d	C ₁₄ H ₁₂ N ₄ S	260	64.61	4.61	21.53	12.30	-
1e	C ₁₄ H ₁₂ N ₄ S	260	64.61	4.61	21.53	12.30	-
1f	C ₈ H ₈ N ₄ S	192	50.00	4.16	29.16	16.66	-
1g	C ₉ H ₁₀ N ₄ S	206	52.42	4.85	27.18	12.30	-

*Elemental analysis of the given compounds were carried out, percentage of elements C, H and N are recorded at Wockhardt Pvt. Ltd.

and methanol (90%, 60 ml) were cooled at 10°C. Ammonia (6.1 ml) was added drop wise to the reaction mixture with continuous stirring. The mixture was filtered and the solid was then washed with 50 ml ether. The solid was dissolved in 250 ml of water. A solution of aqueous (32 ml) lead nitrate (0.25 mol, 8.27 gm) was slowly added to the solution. The mixture was then steam distilled to get the product.

Yield – 20 gm

Melting point = 58°C

% yield – 55.8%

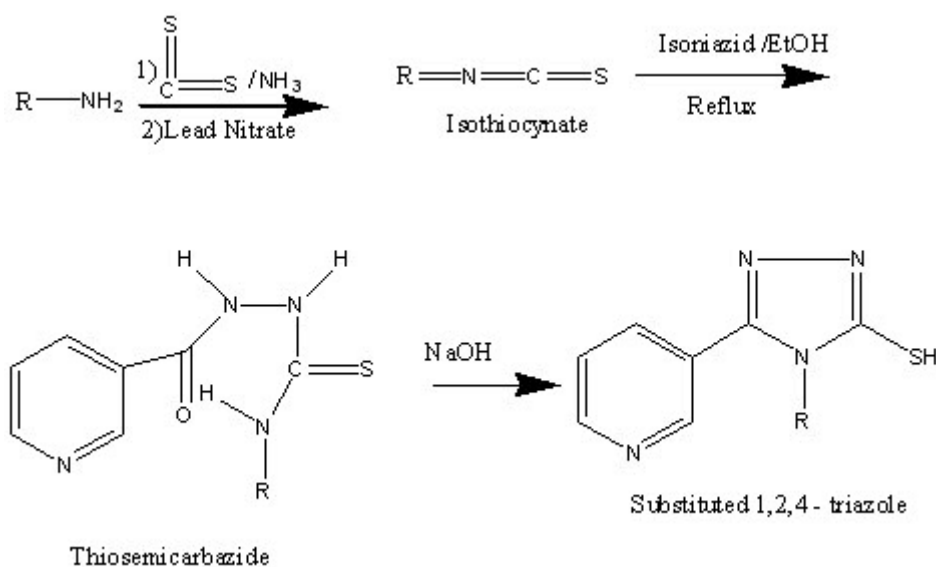
Synthesis of 4-(1-naphthyl)-1-(isomeric pyridyl) thiosemicarbazide

Isoniazide (0.004 mol, 0.552 gm) was dissolved in absolute ethanol (60 ml). The μ -naphthyl isothiocyanate (0.004 mol) was separately dissolved in 30ml ethanol. Then the solution was added to isoniazide with continuous stirring. The reaction mixture was then refluxed for 6 hours. It was cooled to room temperature to form precipitate. The white solid crystals was then filtered and dried.

Yield – 0.325 gm.

Melting point = 62°C

% yield = 58.387%



Scheme 1: General Reaction

Synthesis of 4-(1-naphthyl amino)-5-(isomeric pyridyl) 1,2,4-triazole- 3- thiol

Solid thiosemicarbazide (0.1 gm, 0.004 mol) was added portion wise to 15 ml of 2N NaOH solution. The reaction mixture was refluxed for 4 hours. It was then allowed to cool at room temperature and then filtered. Then it was acidified with 2N HCl. The precipitated yellow solid was filtered washed with water and recrystallised from ethanol: water (80 : 20)

Yield – 0.062 gm

Melting point = 87°C

% yield = 62.7%

CONCLUSION

Substituted 1,2,4-triazoles and their derivatives are an important class of organic compounds with an diverse agricultural, industrial, antitubercular, antiviral and antifungal effect etc.

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