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Studies on synthesis, antibacterial screening and the mass fragmentation of 1-(4,6-dimethylbenzothiazolyl)-3,5-disubstituted-1,2,4-1H-triazoles

***D. K. Swamy, **S. V. Kuberkar and ***M. V. Deshmukh**

**Department of Chemistry, Pratibha Niketan Mahavidyalaya, Nanded*
***Department of Chemistry, Yashwant College, Nanded*
****P.G. Department of Chemistry,Science College, Nanded*

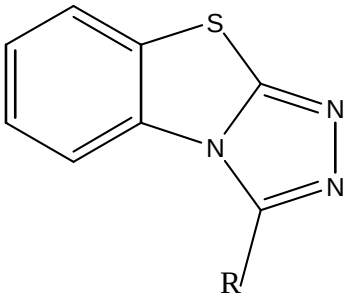
ABSTRACT

Some substituted benzothiazolyl triazoles are synthesized from 2-hydrazino-4,6-dimethylbenzothiazole treating this starting material with alkyl/aryl/heteryl nitrile in presence of anhydrous aluminium chloride yielded 1-(4,6-dimethylbenzothiazolyl)-3,5-alkyl/aryl or heteryl 1,2,4-1H triazole. Mechanism of reaction, its mass fragmentation pattern and antibacterial activity are reported.

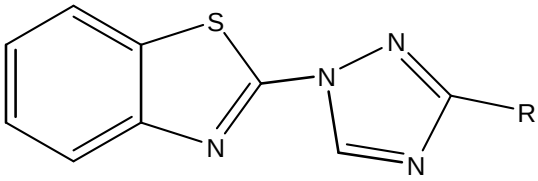
Key words: Hydrazino, benzothiazolyl, mass fragmentation and antibacterial activity.

INTRODUCTION

Enormous work is done on preparation and physiological activity of triazolobenzothiazole (Compound-1) and condensed tricyclic system [1]. Few scattered references are available on heteryl moiety attached to triazole system [2,3,4,5,6] (Compound-2).

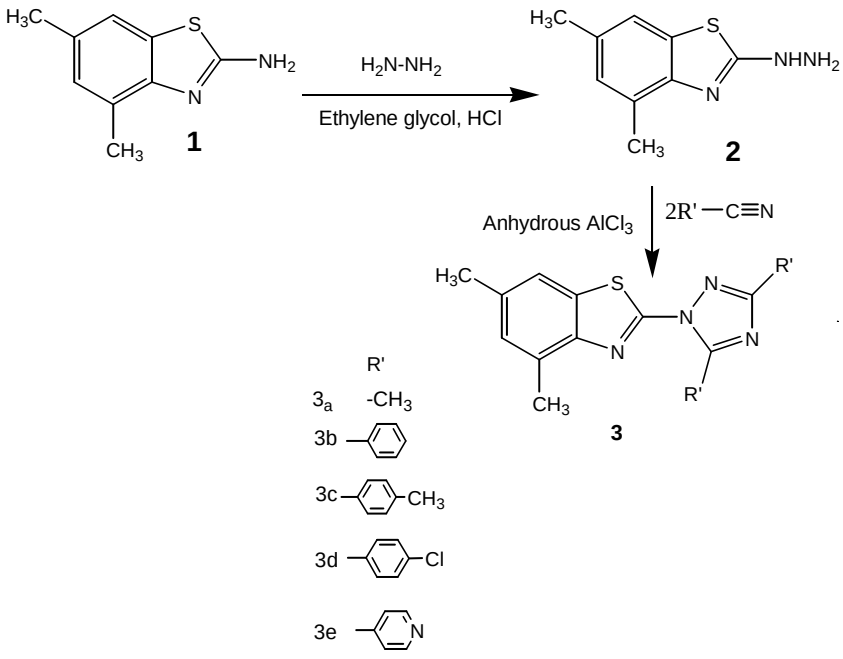


Compound-1



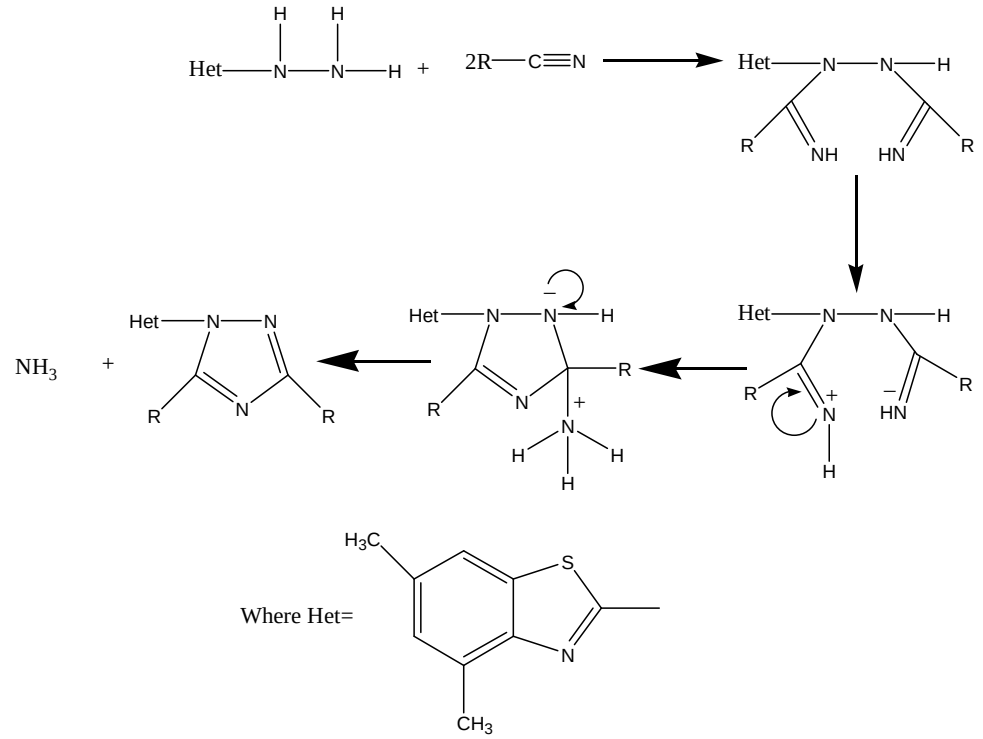
Compound-2

Since we did not come across any reference on the preparation of dimethyl benzothiazolyl 1,2,4-1H triazole compounds the applicability of this procedure was considered. These efforts brought some fruitful results. In the present work, we have synthesized some substituted dimethylbenzothiazolyl-3,5-disubstituted triazoles and their derivatives (Scheme-1) and also evaluated the antibacterial activity of these compounds.



Scheme-1

Proposed mechanism for the reaction.



Scheme-2

EXPERIMENTAL SECTION

Antibacterial activity of 1-(4,6-dimethyl benzothiazolyl)-3,5-disubstituted-1,2,4-1H-triazoles:

For bacteria nutrient agar medium was used. Nutrient medium was sterilized in autoclave at 120 $^{\circ}$C for 20 minutes. A suitable dilution growth culture of test bacteria was spread over media. Filter paper disc loaded with appropriate dilution after 24 hrs. incubation. The degree of sensitivity was determined by measuring growth inhibition zones in mm around the disc. The compounds (3_a-3_e) were tested for their antibacterial activity against *Xanthomonas*, *Erwinia* and *E-Coli* (gram–ve) using *ampicillin* as a standard antibacterial compound for comparison.
Refer Table **1**.

Melting points were determined in open capillaries and were found uncorrected, purity of compounds checked by TLC. IR spectra (KBr discs) were recorded on FTIR- SCHIMADZU 84005 and Thermo Nicolet Nexus 670 Spectrophotometer and absorption was expressed in cm^{-1}. NMR spectra were recorded on Gemini 200 MHz spectrometer with Tetra methyl silane as an internal standard. Chemical shift values were mentioned in δ ppm. Mass spectra were recorded on a FT VG-7070 H Mass spectrophotometer using the EI technique at 70 ev. The progress of all reactions was monitored by TLC on 2x5 cm pre-coated silica gel 60 F254 plates of thickness of 0.25 mm (Merck) and spots were visualized under UV 254-366 nm and iodine chamber. The compounds were analyzed for C, H and N and the elemental percentage reported.

Table 1

Compound	Diameter in mm of zone of inhibition at 25 µg/disc		
	Xanthomonas	*Erwinia*	*E-Coli*
3_a	34	32	11
3_b	11	10	NA
3_c	22	23	12
3_d	NA	NA	NA
3_e	17	22	14
Ampicilin 1mg/ml	18	16	08

NA= Not active

General procedure:

A mixture of 2-hydrazinobenzothiazole (0.02 mole), powdered anhydrous aluminium chloride (6 g) and the appropriate nitrile (0.045 mole) was heated in an oil bath at 160-180 °C for three hours and the product was decomposed with ice cold hydrochloric acid. It was kept overnight and nitrile removed by steam distillation. The solid compound obtained was filtered and crystallized from ethanol to give (**3_{a-e}**). Characterization data of the compounds thus synthesized are given below.

1-(4,6-Dimethyl benzotiazolyl)-3,5-di-methyl- 1,2,4-1H-triazole (3_a): Yield 0.921g, 72%, mp 300 °C; ir (KBr): C-H stretch of $-CH_3$ 3005, C=N 1635, C-N 1263 cm^{-1}. ^1H nmr ($CDCl_3$): δ 1.7 (s, 6H, CH_3), 2.1 (s, 6H, Ar-CH_3), 7.2-7.5 (d, 2H, Ar-H). ms: m/z 258(M^+). *Anal*. Calcd. for $C_{13}H_{14}N_4S$: C, 60.46; H, 5.42; N, 21.70. Found: C, 60.21; H, 5.08; N, 21.13.

1-(4,6-Dimethylbenzothiazolyl)-3,5-di-phenyl-1,2,4-1H-triazole (3_b): Yield 0.665g, 70%, mp 240 °C; ir (KBr): C-H stretch of $-CH_3$ 3013, C=N 1560, C-N 1280 cm^{-1}; ^1H nmr ($CDCl_3$): δ 2.4 (s, 6H, Ar-CH_3), 7.1-7.9 (m, 12H, Ar-H). ms: m/z 382(M^+). *Anal*. Calcd. for $C_{23}H_{18}N_4S$: C, 72.25; H, 4.71; N, 14.65. Found: C, 72.00; H, 4.13; N, 14.38.

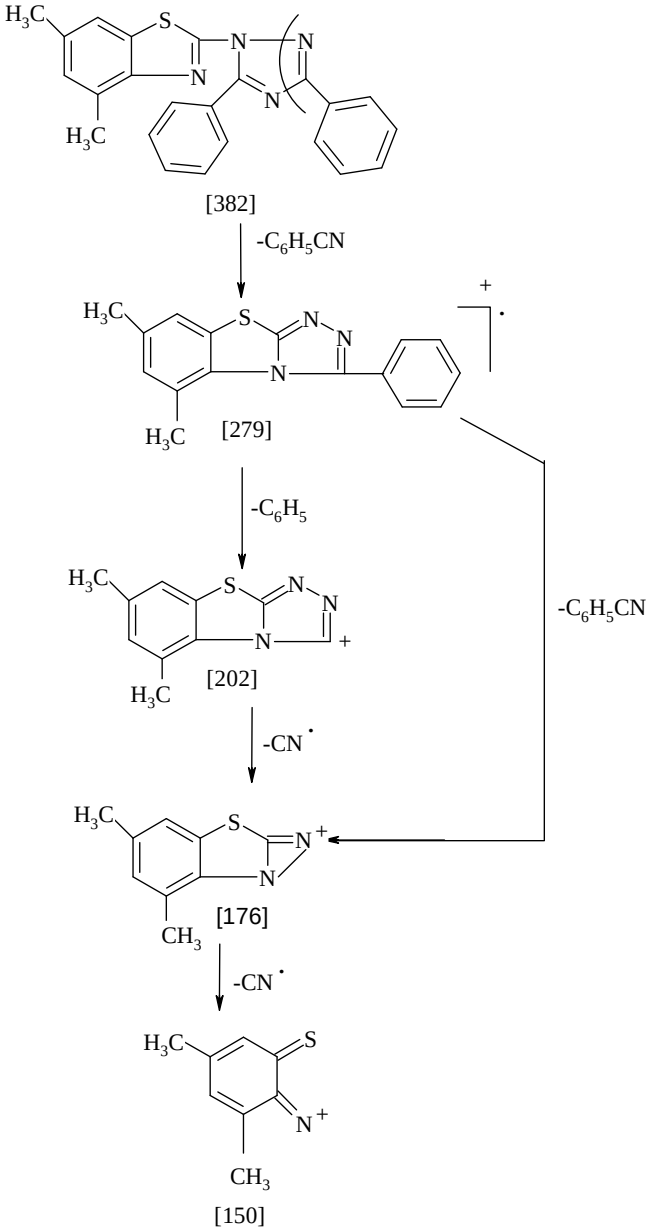
1-(4,6-Dimethyl benzothiazolyl)-3,5-di-4-tolyl-1,2,4-1H-triazole (3_c): Yield 0.534 g, 68%, mp 270 °C; ir (KBr): C-H stretch of $-CH_3$ 3045, C=N 1560, C-N 1271 cm^{-1}; ^1H nmr ($CDCl_3$): δ 2.5 (m, 12H, Ar-CH_3), 7.2-7.9 (m, 10H, Ar-H). ms: m/z 410(M^+). *Anal*. Calcd. for $C_{25}H_{22}N_4S$: C, 73.17; H, 5.36; N, 13.65. Found: C, 73.05; H, 5.17: N, 13.31.

1-(4,6-Dimethylbenzothiazolyl)-3,5-(di-4-chlorophenyl)-1,2,4-1H-triazole (3_d): Yield 0.896g, 65%, mp 120 °C; ir (KBr): C-H stretch of $-CH_3$ 3030, C=N 1600, C-N 1280 cm^{-1}; ^1H nmr ($CDCl_3$): δ 2.3 (s, 6H, Ar-CH_3), 7.1-7.8 (m, 10H, Ar-H). ms: m/z 451(M^+). *Anal*. Calcd. for $C_{23}H_{16}N_4SCl_2$: C, 61.19; H, 3.54; N, 12.41. Found; C, 61.02; H, 3.15; N, 12.28.

1-(4,6-Dimethylbenzothiazolyl)-3,5-di-4-pyridyl-1,2,4-1H-triazole (3_e): Yield 0.589g, 63%, mp 280 °C; ir (KBr): C-H stretch of $-CH_3$ 3080, C=N 1660, C-N 1250 cm^{-1}. ^1H nmr ($CDCl_3$): δ 2.4 (s, 6H, Ar-CH_3), 7.3-8.0 (m, 2H, Ar-H and 4H-Py-H). ms: m/z 384(M^+). *Anal*. Calcd. for $C_{21}H_{16}N_6S$: C, 65.62; H, 4.16; N, 21.87. Found: C, 65.11; H, 4.01; N, 21.20.

RESULTS AND DISCUSSION

The result in table 1 show that the compound tested against the test bacteria varied. The maximum activity shown by 1-(4,6-dimethyl benzothiazolyl)-3,5-dimethyl-1,2,4-1H-triazole against *Xanthomonas*, even in case with *Erwinia*. Whereas the maximum activity was observed with 1-(4,6-dimethyl benzothiazolyl)-3,5-diphenyl-1,2,4-1H-triazole compound against *Xanthomonas* as well as with *Erwinia*. In case of *E-Coli* maximum activity was shown by 1-(4,6-dimethyl benzothiazolyl)-3,5-dipyridyl-1,2,4-1H-triazole whereas the minimum activity was shown by 1-(4,6-dimethylbenzothiazolyl)-3,5-dimethyl-1,2,4-1H-triazole compound.



Scheme-3

As regards mass fragmentation pattern of 1-(4,6-dimethyl benzothiazolyl)-3,5-diphenyl-1,2,4-1H-triazole (Scheme-5) indicates that dimethylbenzothiazolyl ring is stable under electron impact whereas diphenyl triazole system undergoes fission. The special features of mass fragmentation are though contiguous nitrogen present that does not participate in primary cleavage C-S bond breakage.

Which is observed in triazolo benzothiazole is not found here. The benzothiazolyl triazole after cleavage and elimination of Ph.CN rearranges to fused triazolobenzothiazole rare phenomenon. Base peak is not molecular ion but rearranges the fragment to tricyclic which indicates that the benzothiazole system is very stable to electron impact in the initial stages in this case.

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