



**SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NEWLY SYNTHESISED
THIAZOLO PYRIMIDO PYRIMIDO BENZOTHIAZOLES**

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ABSTRACT

Condensation of 2-amino -5-methyl thiazole (**1**) with bis (methylthio) methylene malononitrile (**2**) give 6-cyano-5-imino-2-methyl-7-(methylthio)-5*H*-thiazolo [3,2-*a*] pyrimidine (**3**). Which on further condensation with various 2-amino-1/2/3/4 – substituted benzothiazoles gives 12, 13-diimino-9-methyl- thiazolo [2,3-*a*]-4*H*-pyrimido [4,5-*d*]-4*H*- pyrimido [2,1-*b*] benzothiazole and their 1/3/4 substituted derivatives (**5a-g**). The chemical structure of the product was proved on the basis of their spectral IR, ¹H-NMR, ¹³C-NMR, Mass and analytical studies. Some of the newly synthesized compounds have been screened for antimicrobial and antioxidant activity.

KEYWORDS: Bis (methylthio) methylene malononitrile, thiazolo pyrimido pyrimido benzothiazoles, anhydrous K₂CO₃, DMF, bis (methylthio) methylene malononitrile and benzothiazoles.

INTRODUCTION

The fused pyrimido benzothiazole and its derivatives display a extensive range of activities like antibacterial,^[1] antitumor,^[2] antimicrobial activities,^[3] anti HIV^[4] and antiviral.^[5] In considering the reported pharmacological activities of this fused polycyclic heterocycles has caught the attention in recent years, which might be more potent. Consequently, in the present section pyrimidine and thiazole moiety are fused with pyrimido benzothiazoles to give the thiazolo pyrimido pyrimido benzothiazoles.

Due to the great interest in this class of biologically active compounds, our research group reported the synthesis of pyrido pyrimidoPyrimido Benzothiazoles⁶ compounds. . In this manuscript we report the synthesis of some novel 12, 13-diimino-9-methyl- thiazolo [2,3-*a*]-4*H*-pyrimido [4,5-*d*]-4*H*-pyrimido [2,1-*b*] benzothiazole derivatives and screened for their antimicrobial and antioxidant activity.

MATERIALS AND METHODS

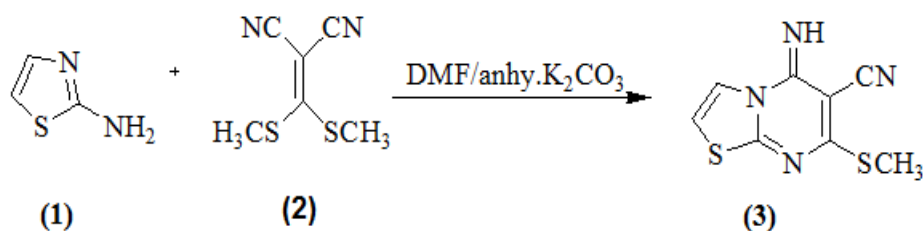
Melting point were determined by open capillary tubes and were uncorrected. Progress of reaction was monitored by thin layer chromatography carried out of aluminium silica plates using UV Chamber for detection. Infrared spectra were recorded in potassium bromide pallets on an infrared spectrophotometer, nuclear magnetic spectra were obtained on Bruckner advance

spectrophotometer; 400MHz mass spectra were recorded on ET-VC7070H mass

spectrophotometer with the use of EI technique at 70ev. All the reactions were carried out under ambient atmosphere

RESULT AND DISCUSSION

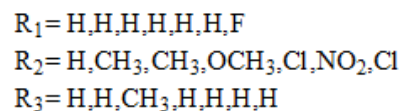
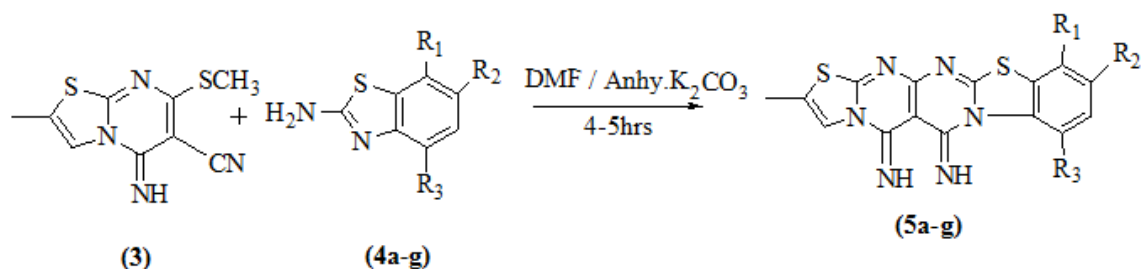
In the present investigation, we have reported synthesis of 12, 13-diimino-9-methyl- thiazolo [2,3-*a*]-4*H*-pyrimido [4,5-*d*]-4*H*- pyrimido [2,1-*b*] benzothiazole and their 1/3/4 substituted derivatives (**5a-g**).The reaction started with synthesis of 6-cyano-5-imino-2-methyl-7-(methylthio)-5*H*-thiazolo [3,2-*a*] pyrimidine (**3**) by condensation of 2-amino -5-methyl thiazole (**1**) with bis (methylthio) methylene malononitrile (**2**) in presence of DMF and anhydrous K₂CO₃ as catalyst. (**Scheme -1**).



Scheme 1

The compound (3) possesses replacable active methylthio group at 2-position and active cyano group at 3-position, due to this cyclisation takes place with substituted 2-amino benzothiazoles (4) in presence of DMF and pinch of K_2CO_3 to give (5a-g). Subsequently compound (3) refluxing with 2-amino benzothiazole, 2-

amino-6-methyl benzothiazole, 2-amino-6-methoxy benzothiazole, 2-amino-6-chloro benzothiazole, 2-amino-6-nitro benzothiazole, 2-amino-4,6-dimethyl benzothiazole, 2-amino-7-chloro-6-fluoro benzothiazole to obtain (5a-g) respectively (Scheme-2).



(Scheme 2).

ANTIOXIDANT ACTIVITY OF NEWLY SYNTHESIZED COMPOUNDS

DPPH assay

DPPH (2, 2, diphenyl-1-picrylhydrazyl) radical scavenging assay was carried out as per reported methods with slight modification (Kato et al., 1998). Briefly, 1ml of test solution (Test compound) added to equal quantity of 0.1mmol solution of DPPH in ethanol. After 20 min incubation at room temperature, the DPPH reductions were measured by reading the absorbance at 517 nm. Ascorbic acid used as reference compound.

Table No. 4: Antioxidant Activity of thiazolo pyrimido pyrimido benzothiazoles

Sr. No	Compound	DPPH radical scavenging activity (%)
1	5a	51 ± 0.49
2	5d	77 ± 0.76
3	5f	64 ± 0.63
4	Ascorbic Acid	86 ± 0.88

ANTIMICROBIAL ACTIVITY

Disc diffusion method

Kirby-Bauer method was followed for disc diffusion assay. In vitro antimicrobial activity was screened by

using Mueller Hinton Agar (MHA) obtained from Himedia (Mumbai). The MHA plates were prepared by pouring 15 mL of molten media into sterile petriplates. The plates were allowed to solidify for 5 min and 0.1 % inoculum suspension was swabbed uniformly and the inoculum was allowed to dry for 5 min. The concentration of compounds were set at (10 µg disc⁻¹) were loaded on 5 mm sterile individual discs. The loaded discs were placed on the surface of medium and the compound was allowed to diffuse for 5 min and the plates were kept for incubation at 37°C for 24 h. Penicillin (10 µg disc⁻¹) was used as positive control. At the end of incubation, inhibition zones formed around the disc were measured with transparent ruler in millimeter.

Table No. 4: Antimicrobial Activity of thiazolo pyrimido pyrimido benzothiazoles.

Sr.no.	Name of compound	Zone of inhibition in mm	
		<i>E. coli</i>	<i>B. subtilis</i>
1	5a	08	06
2	5d	14	16
3	5f	14	04
4	penicillin	26	28

NR: No Response

CONCLUSION

Simple and efficient synthesis of 12, 13-diimino-9-methyl- thiazolo [2,3-*a*]-4*H*-pyrimido [4,5-*d*]-4*H*-pyrimido [2,1-*b*] benzothiazole and their 1/3/4 substituted derivatives (**5a-g**). has been reported. Among these synthesized compounds (5d) showed remarkable antioxidant activity and compound (5d) exhibit promising antimicrobial activity against *B. subtilis*. The result of the present work demonstrated that thiazolo pyrimido pyrimido benzothiazoles are potent antioxidant and antimicrobial agents and it will attract researchers to design new potent pharmacological thiazolo pyrimido pyrimido benzothiazoles.

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