Indian J.Sci.Res. 7(2) : 143-148, 2017

ISSN : 0976-2876 (Print)
ISSN : 2250-0138 (Online)

SYNTHESIS OF PHENYL-1, 3-THIAZOLE SUBSTITUTED AMINO S-TRIAZINES AND STUDYING THEIR BIOLOGICAL ACTIVITY

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ABSTRACT

Amino S-triazines exert antibacterial effects by non specific mechanism. A series of amino substituted S-triazines were synthesised and subsequently screened for their in vitro antibacterial activity against gram positive (*Bacillus anthracis*, *Clostridium tetani*, *Staphyloccocus epidermis*) and gram negative (*Acetobacter aceti*, *Vibrio cholera*, *Escherichia coli*) by broth dilution technique w. r. t. streptomycin. Compound and its derivatives showed good antibacterial activity.

KEYWORDS : Phenyl-1, 3-Thiazole, Amino S-Triazines, , Antibacterial

The introduction of antibiotics has changed the medical prognosis of both major and minor infections. Due to prolonged use of a particular antibiotic, the bacterial strains aquire resistance against them. The bacterial resistance towards a particular antibiotic pose a threat both to the hospitals and to the community.. Hence important antibacterial agents with better antibacterial property should be updated regularly, as new information becomes available, including the resistance patterns and development of new drugs.

During the past decade, the potential of S-triazine derivatives in agrochemicals and antibacterial activity has been much studied. It is found that amino substituted S triazine derivatives are associated with a number of prominent antibacterial activities, against gram positive (*Bacillus anthracis, Clostridium tetani, Staphyloccocus epidermis*) and gram negative (*Acetobacter aceti, Vibrio cholera, Escherichia coli*)strains. The biological activity is a function of physicochemical properties of the target molecule , and chemicals that might fit at the active site and thus making the enzyme inactive were used to block the active site. The physiological activity of the bacteria was thus hamphered. Cyanuric chloride and various amines with good antibacterial properties were used . Incorporation of the derivatives gave access to a wide range of different chemical structures, showing prominent antibacterial activities (Wise et al., 1998, Baker, 2006. Srinivas et al., 2006 and Zhu et. al., 2006)

MATERIALS AND METHODS

Phenyl-4-chlorophenyl and 4-Nitrophenyl thiazole-2-amine derivatives were synthesised, with the help of corresponding acetophenone, thiourea, thionyl chloride and bromine. The designed compounds were prepared in two steps.

STEP 1

Nucleophilic substitution of two chlorine in cyanuric chloride in presence of aqueous dioxane with various amines like diisopropylamine, morpholine and diphenylamine to synthesise diamino-S-triazine.

STEP 2

Further substitution of chlorine in presence of 1,4-dioxane with synthesised phenyl -1, 3- thiazole-2-amine to obtain a series of phenyl-1, 3-thiazole substituted amino S-triazine (Figure 1).

Synthesised compounds were subsequently screened for their in vitro antibacterial activity (MIC) against three gram positive (*Bacillus anthracis, Clostridium tetani, Staphyloccocus epidermi*s) and three gram negative (*Acetobacter aceti, Vibrio cholera, Escherichia coli*) micro organisms by broth dilution technique. Nutrient agar and nutrient broth were used. (Nishigaki et al., 1969, Gubernator and Bohn 1998,Weiner and William 1964 and WHO, 2005).

RESULTS AND DISCUSSION

The MIC values of synthesised compounds against test organism displayed significant activity with wide degree of variation.

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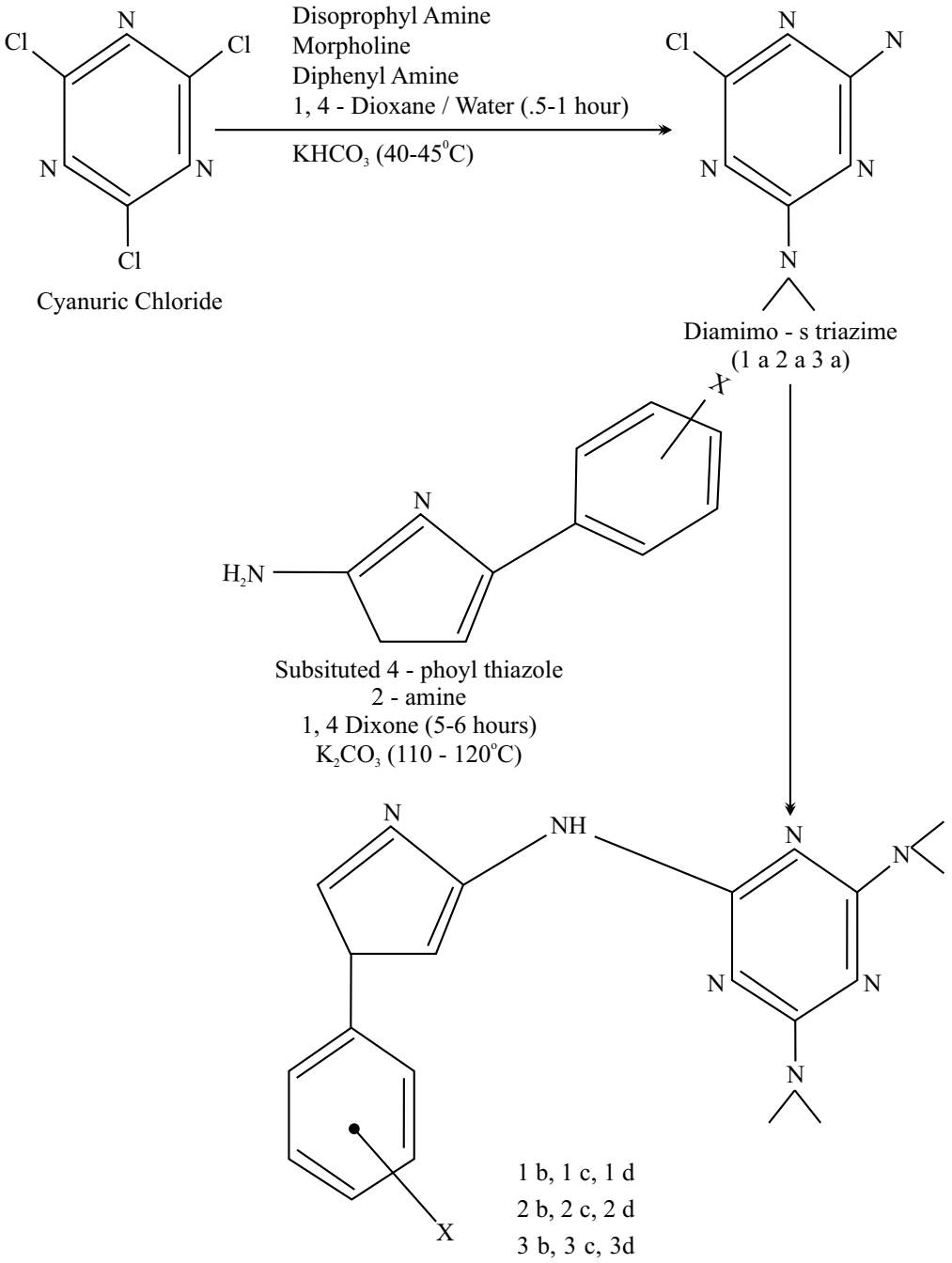
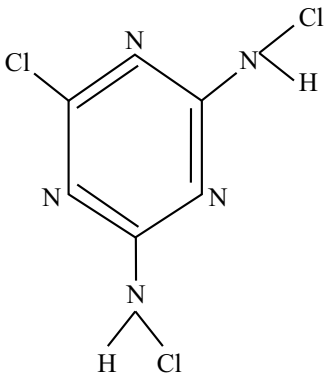


Figure 1 : Synthesis of Phenyl-1, 3-thiazole Substituted Amino-[1,3,5]-triazine

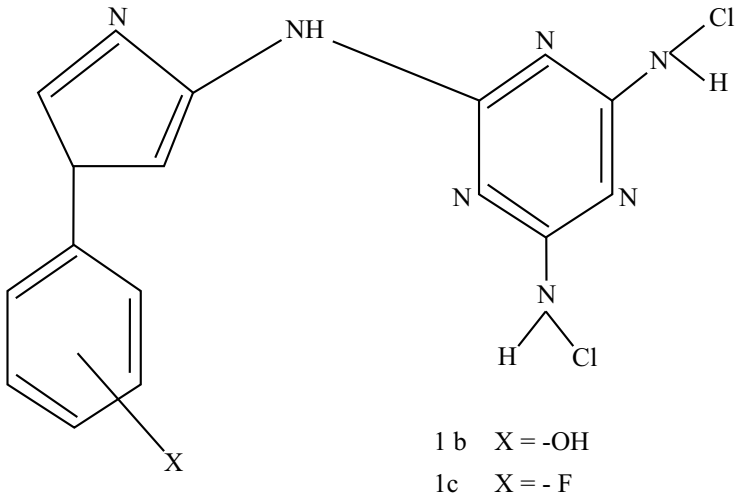
Data from these experiments was combined for MIC over control Streptomycin. The series of compounds have displayed good antibacterial results . Amongst them compound 2a and 3a were found equipotent to Streptomycin. Compound 3a have shown great activity. A decreased activity was reported in case of compound 1c . Rest of the compounds showed substantial to weak activity. Similarly greater to moderate activity was reported in case of S-triazine derivatives. Compound 3a showed prominent activity against *Bacillus anthracis* and *Clostridium tetani*. Rest of the compounds were found to have good activity to moderate activity against various strains of both the gram positive and gram negative strains of bacteria.

Table 1 : In *vitro* Antibacterial Activity of the Synthesized Compound

Compound	*Bacillus anthracis*	*Clostridium tetani*	MIC (µg/ml) *Staphyloccous epidermis*	*Acetobacter aceti*	*Vibrio cholera*	*Escherichil coli*
1 a	16	8	16	8	24	16
1 b	64	32	40	40	56	64
1 c	128	64	64	128	64	40
1 d	40	32	64	32	48	32
2 a	8	3	8	8	16	24
2 b	40	32	24	40	48	56
2 c	32	40	24	24	24	40
2 d	40	40	32	32	40	40
3 a	4	4	8	4	24	16
3 b	24	16	24	32	16	32
3 c	16	32	32	24	24	24
3 d	24	16	24	16	24	16
Streptamyim	8	4	8	2	2	2



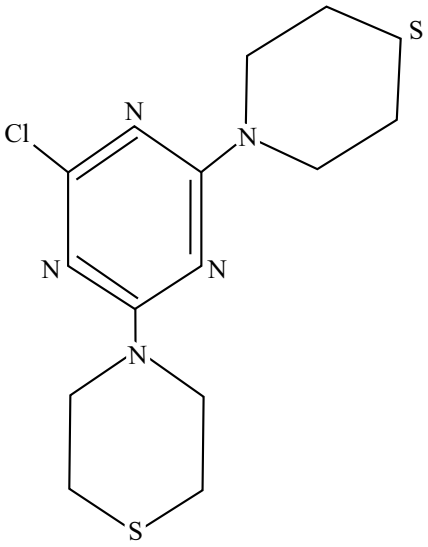
(1 a)



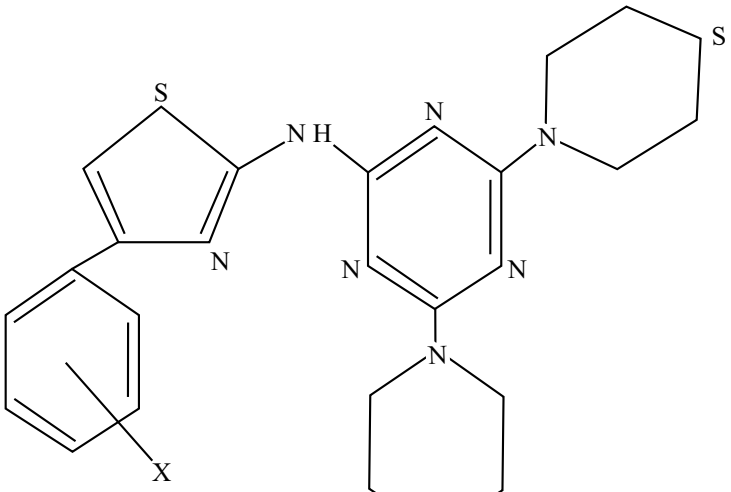
1 b X = -OH

1c X = - F

1d X = - SO_3H



(2 a)



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2 d X = - SO_3H

(2 a)

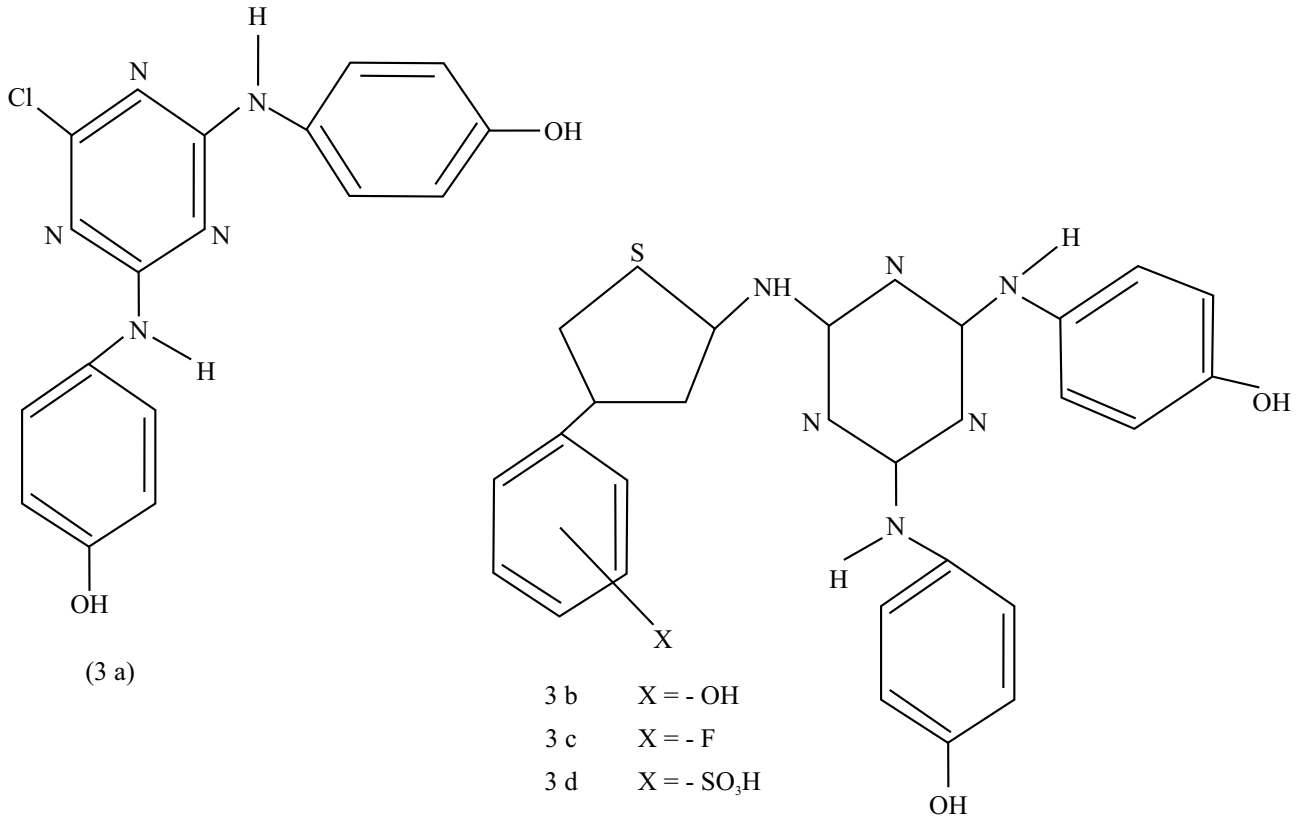

Figure 2 : Phenyl-1, 3-thiazole Substituted Amino-[1,3,5]-triazine

Several other substituents will be synthesised in future and their antimicrobial activity will be further explored (Blotny 2006).

Areview of the data revealed that compounds having fluoro group in thiazole skeleton showed maximum antibacterial activity for gram positive bacteria. This is because of good bonding of fluoro group with the target. Thiazole substitutes S-triazine derivatives emphasised the importance of incorporating lyophilic groups. All of the biologically active substituted amino-S-triazine derivatives show lyophilic traits.(Metwally et al., 2004,Yamaguchi et al.1999, Dikey et al., 1959 and Modha et al., 2001; Wise et al., 1990).

Series of Synthesised Phenyl-1,3-thiazole Substituted Amino-s-triazine (Figure 2).

In *Vitro* Antibacterial Activity of the Synthesised Compounds (Table 1).

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