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A REVIEW ON S-TRIAZINE SUBSTITUTIONS AND THEIR STRUCTURAL EFFECTS

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ABSTRACT

The substitution of the three chlorine atoms in 2,4,6-trichlorotriazine (TCT) with other N-heterocycles or amines is a critical undertaking with numerous applications. It is a privileged core capable of successive nucleophilic substitution processes to replace chlorine atoms with mono, di, or tri-substitution. The purpose of this review is to go over the advancements and effects of substitutes of the s-triazine core in recent decades' research.

INTRODUCTION

1,3,5-triazines, previously known as symmetric or s-triazines, have been known for more than 200 years and, like many heterocyclic compounds, are frequently referred to by innocuous names. Many nations have outlawed its use due of its contentious risks to humans and animals.[1] Contrary to the widespread use of melamine (2,4,6-triaminos-triazine)-based dendrimers in biological therapy for cancer, antimicrobial, amtimalarial, antiinflamatory etc. Bann and Miller studied the chemistry of 1,3,5-triazines, cyanuric acid, and cyanuric halides.[1] Bredereck evaluated 1,3,5-triazine and substituted 1,3,5-triazines synthesis.[2] Because of the simple nucleophilic substitution of chlorine atoms in 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride), it is a key chemical in 1,3,5-triazine study. It can be utilized as a bioconjugation cross-linking agent, a dehydrating agent, and a starting material for the synthesis of different s-triazine derivatives.[3] The 1,3,5-triazine moiety continues to draw a lot of interest as a building block for new substances and materials with a variety of beneficial features, from biological activity to liquid crystals.[4] Triazine has three isomers. Its symmetrical and asymmetrical isomers are often identified by how the three nitrogens in the benzene ring are arranged[6] (1,2,3, 1,2,4, and 1,3,5-triazine, or s-triazine) in (Fig 1). The six-membered heterocyclic ring 1,3,5-triazine is one of the first types of organic compounds. Due to their intriguing pharmacological properties, which include anticancer, herbicidal, insecticidal, anti- HIV, antimalarial, antibacterial, antimycobacterial, and antimicrobial activity,[7] it is still utilized in numerous chemotherapeutic treatments.

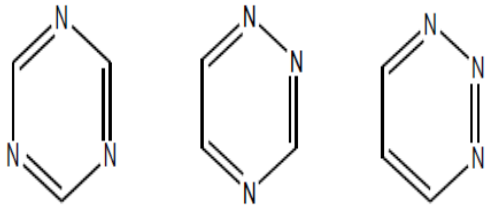


Fig. 1: Isomers of triazine.

Mono, Di, Tri-substitution of s-triazine Sequential nucleophilic substitution reactions occur with s-triazine, but the order of the nucleophiles is extremely important.[8] Once amine is added to s-triazine, it is exceedingly difficult to substitute any nucleophile other than the amine.

A mono substitution reaction route similar to the one outlined for this process may be imagined for imidates.[9] It would also entail opening the triazine ring and recyclization with the addition of the reagent residue, as described below. The cyclization process, in this case, corresponds to the one proposed for the trimerization of imidates to s-triazines.

Di substituted triazine reactions are outlined and were prepared to keep the temperature more than that of the first step reaction.

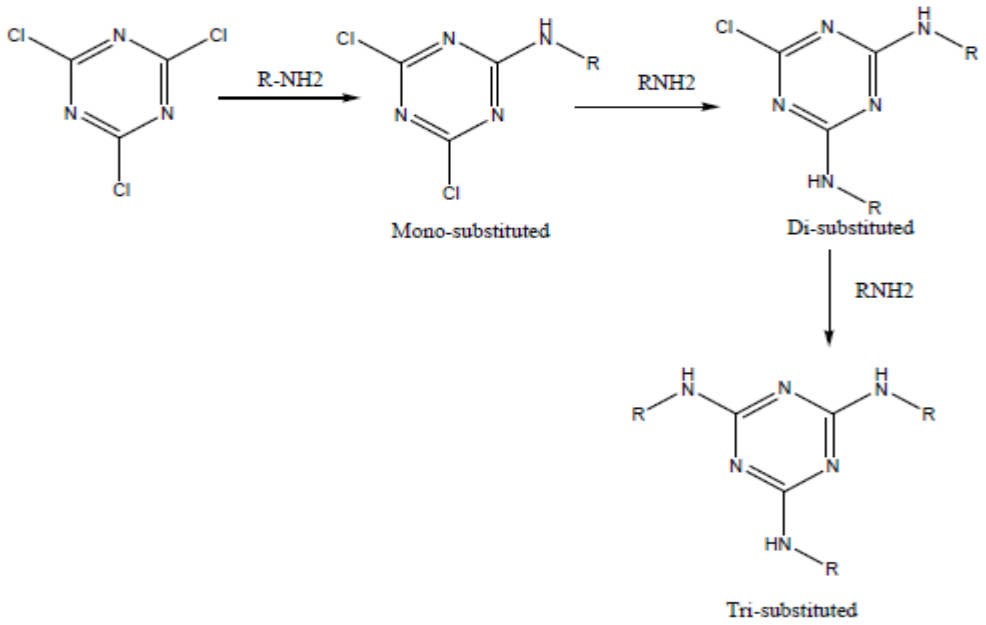


Fig. 2: General Scheme of chlorine replacement.

According to basicity or temperature gradient the scheme is designed with various methods of addition or substitution.[10]

For replacement of third chlorine atom it need a high degree of temperature so that it can replace quickly. Removal of third chlorine lead to formation of a tri-substituted s-triazine which shows maximum efficacy as compared to mono and di-substituted s-triazine. The third replacement basically contain the targeted compounds.[11] Among the trisubstituted 1,3,5-triazines, uncondensed derivatives bearing one or more amino groups at positions 2, 4 or 6 have been widely described as anticancer compounds with different mechanisms of action.[21]

Substitutions and Its effects

Substituents in functionalized 1,2,4triazines have an effect on the orientation of cyclization processes depending on their type.

Ammonia and s-triazine appear to react, but the anticipated product, formamidine[12] which is known to be unstable as a free base appear to suffer rapid additional breakdown, leading to the development of dark, untractable tars. The general equation is used to describe the ring cleavage of the s-triazine itself with primary amines is as follows- C3H3N3 + 6RNH2 + 3NH3 + 3R-NHCH=N-R

Any primary amines have a functional group is possible to behave ring closure reaction with s-triazine and they have atleast one hydrogen atom to it.

When a secondary amine is reacted to striazine i.e o-aminophenol and thiophenol. Tertiary amines were treated with cyanogen halides to produce quaternary salts with strongly electron-withdrawing nitrile groups, which promptly dissolved with the liberation of suitable haloalkane.[13] Nacylammonium[14] salts were also freely available, but unstable and susceptible to dealkylative breakdown.[15] Tertiary amines like 4-methylmorpholine, triethylamine, tri-n-propylamine, and tri-nbutylamine were substituted.

The groups that provided the most reactive halides (benzyl allyl > methyl > alkyl) were the most prone to replacement; however, substitution involving the phenyl group was never identified.[16]

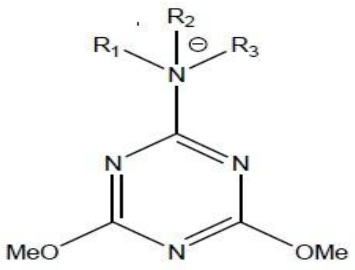


Fig. 3: Quaternary ammonium chloride.

The synthesis and characterization of two novel compounds based on an s-triazine privileged structure with three distinct moieties such as pyrazole, piperidine, and an aniline derivative. The compound in Fig 4 is a derivative which is biologically active. It consist of aniline, pyrazole and piperidine., the targeted compound is synthesized.[17]

Having a thiophenol moiety appeared to have superior antibacterial action. A halogen substitution at the para position of the thio-phenol ring gives good antibacterial activity against Gram +ve bacteria.

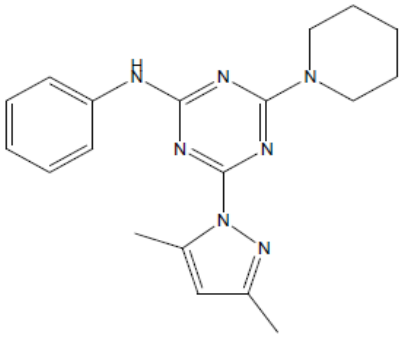


Fig. 4: Aniline substituted s-triazine.

When this substituent was substituted with meta, it demonstrated potential action against Gram ve bacterial strains. The inclusion of two nitrogen atoms in the piperazine ring, along with an electron withdrawing acetyl group, boosts the biological potential of the chemical over aniline and phenol substituted compounds.[18]

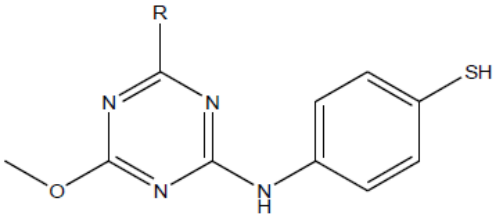


Fig. 5: Thiophenol derivative.

Triorthogonality has been proven utilising the nucleophiles azide, thiol, and phenol. Alcohol's concourse (due to its weak reactivity and the aromatic ring's deactivation as a result of its electrondonating behaviour). In the biological field, TCT with amines as substituents is a major participant.[19] Their finding was the first proof that the theory regarding the appropriateness of phenol to increase reactivity was correct.

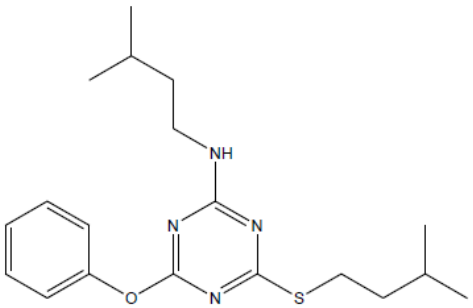


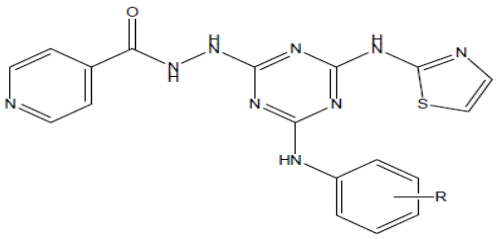
Fig. 6: Phenol substituted s-triazine.

TCT's reactivity toward different nucleophiles, including the three most relevant physiologically (S, O, N), has not been studied, nor has the effect of "-Cl" substitution with electron-donating groups (derived from nucleophiles) on TCT's reactivity been investigated.[20] The basic character of the entering nucleophile that substitutes the

third chlorine is known to be diminished due to the current substituents in TCT of the triazine ring through loss of - bond electron removal of a chlorine atom and gain of -orbital electronic donation of the additional nucleophiles.

Trihaloisocyanuric acids (TXCA) have recently been found to be effective halogenating agents due to their capacity to transfer halonium atoms[22] to unsaturated substrates. The synthesis of chloroalkenes during the chlorofluorination of styrene and a-methylstyrene suggests the presence of a b-chlorinated carbocation intermediate that can be deprotonated to yield the corresponding allyl or vinyl chlorides.

Particularly derivatives with electronwithdrawing groups such as fluoro and nitro, were discovered as antimicrobial active against tested bacteria. They have concluded that derivatives with fluoro and nitro substituents are the best chemicals for achieving the best antibacterial spectrum. As a result, it may be regarded as a promising lead for future design and development of novel chemical entities.[23]



R (-4-NO_2, -2-NO_2, -4-F)

Fig. 7: Thiazole substituted s-triazine.

CONCLUSION

To a desirable extent in terms of new molecular designs, the synthesis of striazine compounds in their substituted form may give successful results in medicinal chemistry. The hybrid derivatives of all substituents are well active towards desired activities. The presence of primary amines, and secondary amines leads to an active moiety against microbes. When the chain length increases more the 7folds activity slowly decreases. Fluoro and nitro substituted s-riazine have better activity than other methyl or ethyl substitutes.

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