# Synthesis of S-Triazine derivative using Ultrasonication and its antibacterial activity

A. A. Patil[1,a)], S. R. Patil[1,b)] and A. P. Manake[2,c)]

[1]*Department of Chemistry, MGSM's ASC College, Chopda. Dist-Jalgaon, Maharashtra, India.*
[2]Department of Chemistry, Pratap College, Amalner. Dist-Jalgaon. Maharashtra. Pin-425401, India.
[a)]Corresponding author: amitraopatil1@gmail.com
[b)]srpatil_001@rediffmail.com
[c)]apmanake@gmail.com

**Abstract.** The present study deals with the synthesis and biological evaluation of s-triazine derivatives bearing substituted aniline moiety ultrasonically. The strategy of the synthesis started with the substituted aniline which further reacted with cyanuric chloride furnished 1,3,5-triazine aniline based derivatives. The ultrasonication offered the compounds in higher yields and purity in shorter reaction time compared with the conventional method. All these compounds were characterized by spectroscopic techniques. The title compounds were screened for their antibacterial activity.

**Keywords**: Ultrasonicator; Cyanuric chloride; Aniline; s-triazine; antibacterial activity.

## INTRODUCTION

Cyanuric Chloride derivative have wide range of application in pharmaceutical industry, its reactivity is due to reactive -Cl atom hence its mono, di-and trisubstituted various derivative shows widespread application in Rubber, Plastic, Pesticide, dyestuff ,explosive and surface active agent. Several derivative of S-triazine shows antibacterial, antimicrobial, antitumor, and antifungal activities. Our aim is to develop new methodology by using green chemistry approach i.e. sonochemical synthesis, this technique is to promote reaction under the influence of sonic waves, which improve the yield in shorter reaction time. Number of reaction can be carried out in higher yield at milder conditions using ultrasound. Sonochemistry is attractive considerable research activity in synthetic chemistry, hence from last few decade sonochemical methods have widely used in organic synthesis.

## MATERIALS AND METHOD

Starting materials and solvents used for each reaction is of synthetic grade procured from S D Fine, and the products obtained were assessed for purity by physical constant determination, All the reactions were monitored using thin layer chromatography on pre- coated TLC plates (Silica gel 60-120#) using solvent system toluene:Ethyl acetate [8:2] for series-1 compounds and Dichloromethane: Ethyl acetate [9:1] for series-2 compounds. TLC was performed by ascending development in a chamber previously saturated with the solvent system. TLC plates were observed under long UV lamp in UV chamber for detection of spots. Final reactions were carried out on sonicator made by Dakshin ,Mumbai.

The synthesized compounds were purified by recrystallization and their structures were characterized by Physical constant and IR. They have shown single spot on TLC plate when observed under UV light; Melting points were taken in open capillaries on melting point apparatus and were uncorrected. Infrared spectroscopy was carried out using potassium bromide (KBr) pellet method on the SHIMADZU IR Affinity-1. . The characterization with IR

and 1HNMR spectra of the synthesized compounds, confirmed the anticipated structure. IUPAC names were confirmed with Chemdraw Ultra 8.0 (Chemoffice 2004,Cambridge Soft, Cambridge, USA).

# EXPERIMENTAL

## Conventional Method

*preparation of compound B- (4,6-dichloro-N-(4-chlorophenyl)-1,3,5-triazin-2-amine)*

Cyanuric chloride (0.01 mole) was added to acetone (25 ml) at 0– $5^0$C, then substituted Anilines (A1-5) (0.01 mole) was added dropwise with constant stirring for 3 hrs. Sodium carbonate solution (10%) was added slowly to neutralize HCl evolved during the reaction. Finally, the contents were poured into crushed ice. The solid separated, was filtered, washed with water, dried and recrystallized from ethanol to give compound B.

*Preparation of compound C- (6-chloro-N2,N4-bis(4-chlorophenyl)-1,3,5-triazine-2,4-diamine)*

Compound B (0.01 mole) was added to acetone (30 ml) at room temperature, then Substituted Anilines (A1-5) (0.01 mole) was added dropwise with constant stirring for 3 hrs. Sodium carbonate solution (10%) was added slowly to neutralize HCl evolved during the reaction. Finally, the contents were poured into crushed ice. The solid separated, was filtered, washed with water, dried and recrystallized from ethanol to give compound C.

*Preparation of Compound D- (1-(4-(4,6-bis(4-chlorophenylamino)-1,3,5-triazin-2-ylamino)phenyl)ethanone)*

Compound C (0.01 mole) and 4-Aminoacetophenone (0.01 mole) was added to acetone (40 ml). The reaction mixture was refluxed for 6 hrs. Sodium carbonate (10%) was added periodically and slowly to neutralize HCl evolved during the reaction. Finally, the reaction mixture was cooled and poured into crushed ice. The solid separated, was filtered, washed with water, dried and recrystallized from ethanol to give compound D.

## Ultrasonication Method

*Preparation of compound C- 6-chloro-$N^2$,$N^4$-bis(4-chlorophenyl)-1,3,5-triazine-2,4-diamine*

Cyanuric chloride (0.01 mole) was added to acetone (30 ml) at room temperature, then Substituted Anilines (A1-5) (0.02 mole) was added dropwise with constant stirring for few min.,then solution is subjected to sonication for about 25-35 min. the reaction progress monitored by using TLC after that Sodium carbonate solution (10%) was added slowly to neutralize HCl evolved during the reaction.Finally, the contents were poured into crushed ice. The solid separated, was filtered, washed with water, dried and recrystallized from ethanol to give compound C.

*Preparation of Compound D-1-(4-(4,6-bis(4-chlorophenylamino)-1,3,5-triazin-2-ylamino)phenyl)ethanone*

Compound C (0.01 mole) and 4-Aminoacetophenone (0.01 mole) was added to acetone (40 ml). The reaction mixture was subjected to sonication for 30-45min. Sodium carbonate (10%) was added periodically and slowly to neutralize HCl evolved during the reaction. Finally, the reaction mixture was cooled and poured into crushed ice. The solid separated, was filtered, washed with water, dried and recrystallized from ethanol to give compound D.

TABLE 1. Comparative study of Conventional and Ultrasonication Method

| Comp. | $R_1$ | Reac. time (min) Conventional | % Yield For Conventional | Reac. time (min) Ultrasonication | % Yield For Conventional | M.P. |
|---|---|---|---|---|---|---|
| D-1 | -Cl | 189 | 78 | 37 | 82 | 216$^{o}$C |
| D-2 | -OH | 195 | 74 | 35 | 84 | 230$^{O}$C |
| D-3 | -$OCH_3$ | 192 | 79 | 34 | 86 | 221$^{0}$C |
| D-4 | -2,4-$NO_2$ | 205 | 75 | 38 | 80 | 224$^{0}$ |
| D-5 | -$CH_3$ | 194 | 76 | 32 | 85 | 225$^{O}$c |

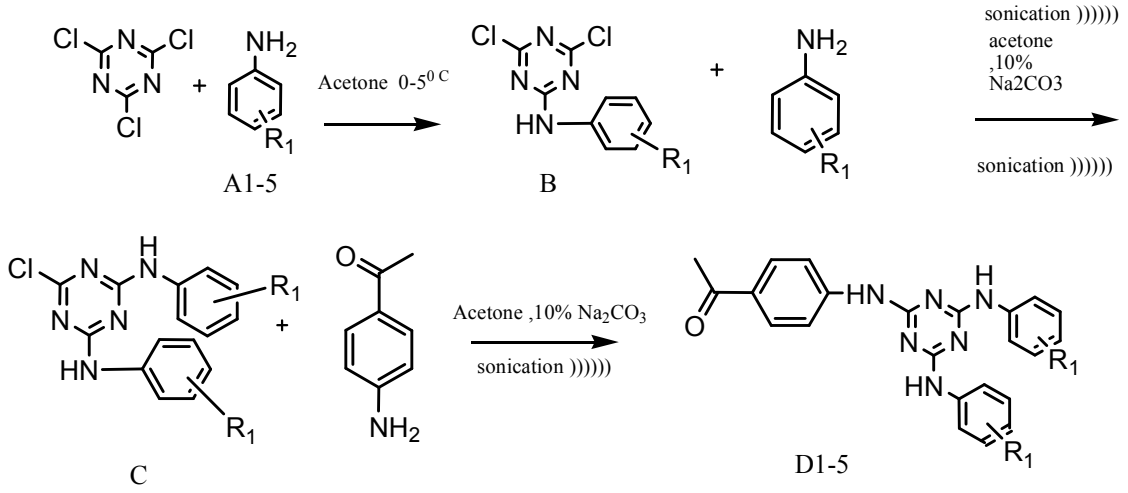


Figure 1. Scheme

## BIOLOGICAL ACTIVITY (ANTIBACTERIAL ACTIVITY)

All the synthesized compounds were screened for their minimum inhibitory concentration (MIC, µg/mL) against two gram-positive (Staphylococcus aureus and S.Pyogenus) and two gram-negative (Escherichia coli and Pseudomonas aeruginosa ) bacteria by the broth dilution method as recommended by the institute of virology. Penicillin and streptomycin were used as standard antibacterial agents. Solutions of the tested compounds and reference drugs were dissolved in dimethylsulfoxide (DMSO) at prepared concentrations of 1000, 500, 200, 100,50,25 and 12.5 µg/mL. The chemical compound– broth medium in serial test tube dilution inoculated with each bacterium was incubated on a rotary shaker at 37°C for 24h at 150 rpm.

**TABLE 2.** Antibacterial activity against synthesized compounds

| Compound No. | Escherichia coli | Pseudomonas aeruginosa | Staphylococcus aureus | S.Pyogenus |
|---|---|---|---|---|
| D-1 | 25 | 250 | 100 | 500 |
| D-2 | 50 | 250 | 500 | 250 |
| D-3 | 100 | 500 | 250 | 250 |
| D-4 | 100 | 500 | 100 | 500 |
| D-5 | 25 | 100 | 250 | 500 |

For antibacterial activity, in present protocol 100 µg/mL is considered as moderately active, 50 µg/mLis considered as good activity and 25 µg/mL is considered as active as compared to the standard drug gentamycin.Compounds D-3, D-4 were found to be moderately active, D-2 found to be active against E.coli where as compound D-1, D-5 found to be good active against S. aureus This is because of the presence of chloro, methoxy, nitro, and hydroxy in the s-triazine derivative.

## RESULT AND DISCUSSION

**TABLE 3.** $^{1}$H NMR and I.R. spectra of synthesized Compound.

| Compound No. | I. R. | $^{1}$H NMR (DMSO) ∂ ppm |
|---|---|---|
| D-1 | 3254 (N-H),1383(C=N),2978(ArCH),1699(C=O), 806(C-N,s-triazine),791(Ar-Cl) | 2.6 ((S,3H,-$CH_3$),7.08-7.6(M,12H,Ar-H), 7.4(S,3H,N-H) |
| D-2 | 3254(NH),1383(C=N),2978(ArCH),1695(C=O), 806(C-N,s-triazine),3671(Ar-OH) | 7.04-7.9(M,12H,Ar-H), 4.5(S,3H,N-H),2.2(S,3H,$CH_3$),5.2(Ar-OH) |
| D-3 | 3254(NH),1383(C=N),2978(ArCH),1691(C=O), 806(C-N,s-triazine) | 2.5((S,3H,-$CH_3$),6.3-7.6(M,12H,Ar-H), 4.5(S,3H,NH),3.8(S,3H,$CH_3$) |
| D-4 | 3254 (N-H),1383(C=N),2978(ArCH),1704(C=O), 806(C-N,s-triazine),1370 (-$NO_2$) | 2.6 ((S,3H,-$CH_3$),7.08-8.8(M,12H,Ar-H), 3.8(S,3H,N-H). |
| D-5 | 3254 (N-H),1383(C=N),2978(ArCH),1699(C=O), 806(C-N,s-triazine) | 2.6 ((S,3H,-$CH_3$),6.3-7.6(M,12H,Ar-H), 3.8(S,3H,NH),2.3(S,6H,$CH_3$) |

## CONCLUSION

The target products (D-1 to D-5) were prepared using conventional heating and ultrasonic irradiation. The ultrasonic irradiation affords the products in higher yields and purity in shorter reaction time. The biological activity i.e. antibacterial activity shown by the compound.

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