SYNTHESIS AND CHARACTERIZATION OF NOVEL TRIAZINE COMPOUND AND THEIR BIOLOGICAL STUDIES

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ABSTRACT
Novel organic derivatives of 2,4,6 trichloro-1,3,5-triazine (cyanuric chloride) (2) moiety using condensation with various amines to get trisubstituted triazine (3a-h and 4a-h) have been reported. All the newly synthesized compounds are characterized by analytical and spectral tools. The novel synthesized compounds are accessed for their microbial activity.

Keywords: Cyanuric chloride, Simazine, Atrazine, Antimicrobial Activity, Spectral Studies.

INTRODUCTION
Triazine (1) is a class of agrochemical active ingredients that comprise derivatives having the same backbone with different functionalities to exhibit various herbicidal activities. Simazine, Atrazine, Propazine, cyanazine are well-known and largely produced herbicide derivatives. These derivatives are helpful for the better growth of crops like Corn and Sugarcane. It also inhibits the growth of unwanted weeds and annual grass. The potential activity of Triazine derivatives is due to various substituent groups attached to a 1,3,5-triazine moiety. Towards the search for new active derivatives of the Triazine class, we wish to report the synthesis and characterization of novel derivatives of Triazine along with their biological activity. Instead of basic Triazine moiety, further derivatization of existing potential herbicides like Simazine and Atrazine has been evaluated.1-2

Amongst all Triazine backbones, 1,3,5-Triazine derivatives are more active and extensively studied because of their symmetrical geometry. These Triazine derivatives can be synthesized using Cyanuric acid, melamine and cyanuric chloride as a key starting raw materials.3-5

Cyanuric chloride (2) is produced by the trimerization of chlorinated hydrocyanic acid. (Scheme-1) and the prompt reactivity towards nucleophilic aromatic substitution (SNAr) leads us to novel derivatives of the Triazine class.6-9

Numerous reports are available in the literature on the diversity of biological activities of substituted -1,3,5-triazine like anti-bacterial, anti-fungal, anti-HIV and other microbial activity.10-18

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substitution of three different nucleophiles on the same triazine core, which provides a vast variety of possible triazine derivatives and their application. Disubstituted triazines like Simazine and atrazine are a very important herbicide. It is used for preventing pre and postmergerence broadleaf weeds in a crop like maize and sugarcane.

**EXPERIMENTAL**

**Material and Methods**
Laboratory solvents were purchased from a commercial supplier, Ahmedabad in their pure form. The remaining facilitation was received from Suyog dye chime Pvt. Ltd Ankleshwar. Precoated silica aluminium plates of Merck were used for TLC.

**Characterization**
Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Shimadzu spectrometer and $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ with TMS as internal standard on a Brucker spectrometer at 400 MHz. ESI-MS of selected samples taken on Thermo Scientific Orbitrap Velos ProTM.

**General Procedure**
The compound 2, 4, 6-trichloro-1, 3, 5-triazine (cyanuric chloride) is prepared industrially by chlorination of hydrogen cyanide followed by cyclization. This compound is available commercially.

**Preparation of N, N'-Diethyl-N''-alkyl-[1,3,5]triazine-2,4,6-triamine (Compound-3 a-h)**
A flowing reaction scheme (Scheme-2) is adopted for the synthesis of N, N'-Diethyl-N''-alkyl-[1,3,5]triazine-2,4,6-triamine (compound-3 a-h).

![Scheme 2](image-url)

*Step-1*
Cyanuric chloride

$\text{Cl}_2\text{N}=\text{N}=\text{N}\text{Cl}$

**C$_2$Cl$_3$N$_3$**

**Mol. Wt.:** 184.41

**Step-2**
Ethyl amine

**TEA 0.10 °C**

**Ethyl amine 25-40 °C**

**Simazine**

CrH$_2$ClN$_5$

**Mol. Wt.:** 201.66

Where, R-NH$_2$ =

- (a) Propyl amine
- (b) Phenylethyl amine
- (c) Benzyl amine
- (d) Butyl amine
- (e) 4-Methoxy amine
- (f) 4-Methoxy phenylethyl amine
- (g) 3,4-Di Methoxy phenylethyl amine
- (h) 4-Hydroxy phenylethyl amine

Scheme 2
Stage-1: Preparation of 6-Chloro-N, N'-diethyl-1,3,5-triazine-2, 4-diamine (Simazine)
Charge 25 gm (0.136 mole) of cyanuric chloride and 100 ml of dioxane in 3 N RBF. Charge 30 gm (0.297 mole) of Triethyl amine. Cool to 0-5°C and stir for 15 minutes. Start addition of 15.5 gm (0.34 mole) of ethyl amine through addition funnel. After completion of addition stir reaction mass at 0-10°C for 3 hrs then stir it at 30-40°C for 6 hrs. The reaction is monitored by TLC (Mobile phase: Toluene: Ethyl acetate: 7:3). After completion of reaction dump reaction mixture. stir it for 3 hrs at 25-35°C. Filter the product and wash with 100 ml water. Dry the product at 70-80°C for 6 hrs in a hot air oven.

Stage-2: Preparation of N, N'-Diethyl-N''-alkyl - [1,3,5]triazine-2,4,6-triamine (Compound-3a-h)
Charge 5 gm (0.025 mole) of Simazine and 50 ml of dioxane in 3 N RBF under stirring. Charge 10 gm (0.1 mole) of Triethylamine and stir for 10 min. Start addition of alkyl amine (0.03 mole) at 25-35°C. Slowly raise temperature to 100-105°C and maintain above temperature for 6 hrs. The reaction is monitored by TLC (Mobile phase: Toluene: Ethyl acetate: 7:3). After completion of reaction cool to 25-35°C and quench reaction mass in 100 ml of water. Stir it for 2 hrs and filter it. Dry it at 60-70°C in hot air oven to get N, N'-Diethyl-N''-alkyl-[1,3,5]triazine-2,4,6-triamine (Compound-3a-h).

Preparation of N-Ethyl-N'-isopropyl-N''-propyl-[1,3,5]triazine-2,4,6-triamine (compounds 4a-h)
Flowing reaction scheme (Scheme-3) is adopted for synthesis N-Ethyl-N'-isopropyl-N''-propyl-[1,3,5]triazine-2,4,6-triamine (compounds 4a-h).

![Scheme-3](image)

Where R-NH₂ = (a) Propylamine (b) Phenylethylamine (c) Benzylamine (d) Butylamine (e) 4-Methoxy amine (f) 4-Methoxy phenylethylamine (g) 3,4-Di Methoxy phenylethylamine (h) 4-Hydroxy phenylethylamine

Stage-1: Preparation of 6-Chloro-N-ethyl N'- Isopropyl-1,3,5-triazine-2,4-diamine (Atrazine)
Charge 25 gm (0.136 mole) of cyanuric chloride and 100 ml of dioxane in 3 N RBF. Charge 30 gm (0.297 mole) of Triethylamine. Cool to 0-5°C and stir for 15 minutes. Start addition of 6.1 gm (0.136 mole) of ethyl amine through the addition funnel. After completion of addition stir reaction mass at 0-10°C for 3 hrs then allow coming at 25-35°C. Start addition of 8 gm (0.136 mole) of Isopropyl amine. Stir it at 30-40°C for 6 hrs then stir it at 30-40°C for 6 hrs. The reaction is monitored by TLC (Mobile phase: Toluene: Ethyl acetate: 7:3). After completion of reaction dump reaction mixture. Stir it for 3 hrs at 25-35°C. Filter the product and wash with 100 ml water. Dry the product at 70-80°C for 6 hrs in a hot air oven.
hrs. The reaction is monitored by TLC (Mobile phase: Toluene: Ethylacetate:: 7:3). After completion of reaction dump reaction mixture. Stir it for 3 hrs at 25-35°C. Filter the product and wash with 100 ml water. Dry the product at 70-80°C for 6 hrs in a hot air oven.

Stage-2: Preparation of N-Ethyl-N'-isopropyl-N''-alkyl-[1,3,5]triazine-2,4,6-triamine (Compound-4a-h)
Charge 5 gm (0.023 mole) of Atrazine and 50 ml of dioxane in 3 N RBF under stirring. Charge 5 gm (0.05 mole) of Triethylamine and stir for 10 min. Start addition of Alkyl amine (0.03 moles) at 25-35 °C slowly raise temperature to 100-105°C and maintain above temperature for 6 hrs. The reaction is monitored by TLC (Mobile phase: Toluene: Ethylacetate:: 7:3). After completion of reaction cool to 25-35°C and quench reaction mass in 100 ml water, stir for 2 hrs and filter. Dry it at 60-70°C in hot air oven to get N-Ethyl-N'-isopropyl-N''-alkyl-[1,3,5]triazine-2,4,6-triamine (Compound-4a-h).

Yield and Spectroscopic Data of Synthesized Compounds (3a-h and 4a-h)

N, N'-Diethyl-N''-propyl-[1,3,5]triazine-2,4,6-triamine (Compound-3a)
Yield: 57%, solid, m.p. 93-97°C. M.W.: 224.31; m/z : 225.

\[ \begin{align*}
\text{H NMR} (400 MHz, CDCl}_3: & \delta 0.907-0.956 (t,3H), 1.137-1.185 (t,6H), 1.498-1.615 (t,2H), 3.293-3.396 (q,6H), 5.126 (s,1H)
\end{align*} \]

\[ \begin{align*}
\text{C NMR} (400 MHz, CDCl}_3: & \delta 11.42, 15, 23, 35.48, 42.47, 165.48.
\end{align*} \]

FT-IR (In cm\(^{-1}\)): 1335.61 (C-H); 1516.91 (C-N); 2356.85 (C=N); 2965.35 (Aliphatic C-H); 3525.63 (N-H)

Anal. Calcd. for C\(_{10}\)H\(_{20}\)N\(_6\): C, 53.55; H, 8.99; N, 37.47; Found: C, 53.48; H, 8.91; N, 37.41.

N, N'-Diethyl-N''-phenethyl-[1,3,5]triazine-2,4,6-triamine (Compound-3b)
Yield: 61%, solid, m.p. 104-107°C. M.W.: 286.38; m/z : 287.

\[ \begin{align*}
\text{H NMR} (400 MHz, CDCl}_3: & \delta 0.1105-1.113 (t,6H), 2.78 (s,2H), 3.10 (t,4H), 7.1-7.21 (m,5H),
\end{align*} \]

\[ \begin{align*}
\text{C NMR} (400 MHz, CDCl}_3: & \delta 15.5, 37.3, 44.4, 53.7, 125.4, 127.4, 128.6, 140.2, 175.2.
\end{align*} \]

FT-IR (In cm\(^{-1}\)): 1335.61 (C-H); 1516.91 (C-N); 2356.85 (C=N); 2965.35 (Aliphatic C-H); 3030 (Aromatic C-H); 3525.63 (N-H)

Anal. Calcd. for C\(_{15}\)H\(_{22}\)N\(_6\): C, 62.91; H, 7.74; N, 29.35; Found: C, 62.83; H, 7.69; N, 29.49.

N, N'-Diethyl-N''-benzyl-[1,3,5]triazine-2,4,6-triamine (Compound-3c)
Yield: 63%, solid, m.p. 114-116°C. M.W.: 272.35; m/z : 273.

\[ \begin{align*}
\text{H NMR} (400 MHz, CDCl}_3: & \delta 1.105-1.113 (t,6H), 3.10 (q,4H), 4.4 (s,2H), 7.1-7.21 (m,5H),
\end{align*} \]

\[ \begin{align*}
\text{C NMR} (400 MHz, CDCl}_3: & \delta 15.5, 44.4, 57.1, 126.5, 127.1, 128.3, 142.2, 175.2.
\end{align*} \]

FT-IR (In cm\(^{-1}\)): 1330.61 (C-H); 1518.91 (C-N); 2335.85 (C=N); 2930.35 (Aliphatic C-H); 3030 (Aromatic C-H); 3525.63 (N-H)

Anal. Calcd. for C\(_{15}\)H\(_{22}\)N\(_6\): C, 61.74; H, 7.40; N, 30.86; Found: C, 61.68; H, 7.31; N, 30.81.

N,N'-Diethyl-N''-butyl-[1,3,5]triazine-2,4,6-triamine (Compound-3d)
Yield: 68%, solid, m.p. 122-124°C. M.W.: 238.33; m/z : 239.

\[ \begin{align*}
\text{H NMR} (400 MHz, CDCl}_3: & \delta 1.105-1.113 (t,6H), 1.3-1.5 (m,4H), 3.10-3.20 (m,6H),
\end{align*} \]

\[ \begin{align*}
\text{C NMR} (400 MHz, CDCl}_3: & \delta 14, 15.5, 20.5, 34, 44.4, 51.3, 175.2.
\end{align*} \]

FT-IR (In cm\(^{-1}\)): 1331.61 (C-H); 1518.91 (C-N); 2335.85 (C=N); 2935 (Aliphatic C-H); 3030 (Aromatic C-H); 3525.63 (N-H)

Anal. Calcd. for C\(_{11}\)H\(_{22}\)N\(_6\): C, 55.43; H, 9.30; N, 35.26; Found: C, 55.38; H, 9.22; N, 35.21.

N,N'-Diethyl-N''-(4-methoxy-benzyl)-[1,3,5]triazine-2,4,6-triamine (Compound-3e)
Yield: 72%, solid, m.p. 132-136°C. M.W.: 302.37; m/z : 303.

\[ \begin{align*}
\text{H NMR} (400 MHz, CDCl}_3: & \delta 1.105-1.113 (t,6H), 3.10 (q,4H), 3.73 (s,3H), 6.8-7.2 (m,6H),
\end{align*} \]

\[ \begin{align*}
\text{C NMR} (400 MHz, CDCl}_3: & \delta 15.5, 44.4, 57.1, 126.5, 127.1, 128.3, 142.2, 175.2.
\end{align*} \]

FT-IR (In cm\(^{-1}\)): 1320.61 (C-O); 1518.91 (C-N); 2335 (Aliphatic C-H); 3035 (Aromatic C-H); 3525.63 (N-H)

Anal. Calcd. for C\(_{15}\)H\(_{22}\)N\(_6\)O: C, 59.58; H, 7.33; N, 27.79; Found: C, 59.51; H, 7.24; N, 27.71.
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N, N'-Diethyl-N''-[2-(3,4-dimethoxy-phenyl)-ethyl]-[1,3,5]triazine-2,4,6-triamine (Compound-3g)
Yield: 63%, solid, m.p.121-127°C. M.W.: 346.4m/z : 347,

1H NMR (400 MHz,CDCl3): δ 1.105-1.113 (t,6H), 2.75-2.8 (m,2H) 3.10 (q,4H), 3.37-3.40(t,2H), 7.08-7.12 (m,5H)

13C NMR (400 MHz,CDCl3): δ 1325.61 (C-O); 1518.91(C-N); 2356.85 (C-N); 2964.39 (Aliphatic C-H); 3020 (Aromatic C-H) 3535.63(N-H), Anal. Calcd. for C16H22N6O2: C, 57.11; H, 7.99; N, 29.38; Found: C, 57.08; H, 7.85; N, 29.25.

N, N'-Diethyl-N''-[2-(4-hydroxy-phenyl)-ethyl]-[1,3,5]triazine-2,4,6-triamine (Compound-4a)
Yield: 67%, solid, m.p.121-127°C. M.W.: 300.40/m/z : 301,

1H NMR (400 MHz,CDCl3): δ 0.934-0.965 (t,3H), 1.112-1.137 (d,6H),3.10 (q,2H),3.270-3.419 (sq,1H),3.4 (t,2H), 7.08 (t,1H) 7.12-7.22 (d,4H)

13C NMR (400 MHz,CDCl3): δ 1325.61 (C-O); 1518.91(C-N); 2356.85 (C-N); 2964.39 (Aliphatic C-H); 3311.55 (N-H), Anal. Calcd. for C16H22N6O2: C, 55.43; H, 9.30; N, 35.26; Found: C, 55.38; H, 9.22; N, 35.21.

N-Ethyl-N'-isopropyl-N''-propyl-[1,3,5]triazine-2,4,6-triamine (Compound-4f)
Yield: 67%, solid, m.p.121-127°C. M.W.: 252.36/m/z : 253,

1H NMR (400 MHz,CDCl3): δ 0.934-0.965 (t,6H), 1.102-1.117 (d,6H),1.30-1.33 (m,2H) ,1.50-1.52 (t,2H) 3.10 (q,2H),3.270-3.419 (sq,1H), 4.32(s,2H)

7.08-7.14 (m,5H)

13C NMR (400 MHz,CDCl3): δ 1325.61 (C-O); 1518.91(C-N); 2356.85 (C-N); 2964.39 (Aliphatic C-H); 3311.55 (N-H), Anal. Calcd. for C16H22N6O2: C, 57.11; H, 9.59; N, 33.30; Found: C, 57.08; H, 9.51; N, 35.21.

N-Ethyl-N'-isopropyl-N''-(4-methoxy-benzyl)-[1,3,5]triazine-2,4,6-triamine (Compound-4h)
Yield: 72%, solid, m.p.131-133°C. M.W.: 316.40/m/z : 317,

1H NMR (400 MHz,CDCl3): δ 0.934-0.965 (t,3H), 1.102-1.117 (d,6H), 3.10 (q,2H),3.270-3.419 (sq,1H),3.73(s,3H), 4.32(s,2H) 6.8-7.02 (m,4H)
NMR (400 MHz, CDCl3): δ 15.5, 23.8, 44.4, 49.8, 56.1, 57.1, 113.9, 128.1, 134.7, 154.7, 165.05, 165.82, 166.2 FT-IR (in cm⁻¹): 1320.61 (C-O); 1518.91 (C-N), 2935.35 (Aliphatic C-H); 3035 (Aromatic C-H) 3535.63 (N-H), Anal. Calcd. for C12H24N6: C, 60.74; H, 7.65; N, 26.56; Found: C, 60.68; H, 7.62; N, 26.52.

N-Ethyl-N'-isopropyl-N''-[2-(4-methoxy-phenyl)-ethyl]-[1,3,5]triazine-2,4,6-triamine (Compound-4f)

Yield: 61%, solid, m.p. 139-141°C. M.W.: 330.43; m/z: 330.2

1H NMR (400 MHz, CDCl3): δ 0.934-0.965 (t, 3H), 1.102-1.117 (d, 6H), 2.76-2.79 (t, 2H) 3.10 (q, 2H), 3.39 (t, 2H) 3.270-3.419 (s, 1H), 3.73 (s, 3H), 6.8-7.02 (m, 4H)

13C NMR (400 MHz, CDCl3): δ 15.5, 23.8, 37.3, 44.4, 56.0, 114.0, 128.9, 132.5, 165.05, 165.82, 166.2 FT-IR (in cm⁻¹): 1320.61 (C-O); 1518.91 (C-N), 2935.35 (Aliphatic C-H); 3035 (Aromatic C-H) 3535.63 (N-H), Anal. Calcd. for C17H26N6O2: C, 61.79; H, 7.93; N, 25.43; Found: C, 61.72; H, 7.87; N, 25.41.

Biological Screening

Antibacterial Activity

Antibacterial activities of all the compounds were studied against gram-positive bacteria (Staphylococci) and gram-negative bacteria (E. coli, and P. aeruginosa) at a concentration of 50 μg/ml by agar cup plate method. The methanol system was used as a control in this method. Under similar conditions using streptomycin as a standard for comparison carried out control experiment. The area of inhibition of zone measured in mm. and found value is tabulated in Table (Tabel-1).

Table-1: Antibacterial Activity of Compounds (3a-h and 4a-h)

| Compound | Minimal Inhibition Concentration of Bacterial Strains (MIC) in μg/ml |
|----------|---------------------------------------------------------------|
|          | Gram Negative Strains                                         | Gram Positive Strains |
|          | E. coli MTCC-443                                              | P. aeruginosa MTCC-1688 | B. subtilis MTCC-441 | S. aureus MTCC-96 |
| 3a       | 1.0                                                          | 8.0                      | 16.0                 | 16.0               |
| 3b       | 4.0                                                          | 4.0                      | 16.0                 | 32.0               |
| 3c       | 0.5                                                          | 8.0                      | 16.0                 | 16.0               |
| 3d       | 4.0                                                          | 8.0                      | 32.0                 | 16.0               |
| 3e       | 4.0                                                          | 8.0                      | 4.0                  | 16.0               |
| 3f       | 4.0                                                          | 4.0                      | 8.0                  | 8.0                |
| 3g       | 2.0                                                          | 2.0                      | 8.0                  | 4.0                |
| 3h       | 8.0                                                          | 4.0                      | 4.0                  | 16.0               |
| 4a       | 4.0                                                          | 4.0                      | 8.0                  | 16.0               |
| 4b       | 1.0                                                          | 1.0                      | 2.0                  | 2.0                |
| 4c       | 8.0                                                          | 8.0                      | 16.0                 | 8.0                |
Antifungal Activity
The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were \textit{(Aspergillusniger)} The antifungal activity of all the compounds (3a-h and 4-h) was measured and tabulated in the table (Tabel-2).

Table-2: Antifungal Activity of Compounds (3a-h and 4a-h)

| Compound | Minimal Inhibition Concentration of Bacterial Strains (MIC) in µg/ml | Fungal Strains |
|----------|---------------------------------------------------------------|----------------|
|          |                                                               | \textit{A. niger} | MTCC-282 |
| 3a       | 256.0                                                         |                |
| 3b       | 128.0                                                         |                |
| 3c       | 512.0                                                         |                |
| 3d       | 128.0                                                         |                |
| 3e       | 512.0                                                         |                |
| 3f       | 128.0                                                         |                |
| 3g       | 256.0                                                         |                |
| 3h       | 256.0                                                         |                |
| 4a       | 512.0                                                         |                |
| 4b       | 64.0                                                          |                |
| 4c       | 512.0                                                         |                |
| 4d       | 256.0                                                         |                |
| 4e       | 128.0                                                         |                |
| 4f       | 256.0                                                         |                |
| 4g       | 64.0                                                          |                |
| 4h       | 64.0                                                          |                |
| Streptomycin | \textbf{0.25} | \textbf{0.5} | \textbf{0.25} | \textbf{0.25} |
| Kanamycin | \textbf{4.0}                                                        |                |

RESULTS AND DISCUSSION
It was observed that 2,4,6 -trichloro 1,3,5-triazine (1) on condensation with a various amine to get tri substituted triazine (compound3 a-h and 4a-h). The is confirmed by various analysis like elemental analysis and spectroscopical analysis (ESI-MS,1H NMR,13 C NMR and IR). The C, H, N analysis and \textsuperscript{1}H-NMR data of all compounds are presented above.

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