Synthesis and antimicrobial activity of [2"-ARYL(QUINOXALINE)-3-YL]-(METHYLENE PHENYL AMINO)-6-[BIS(2"'-CHLORO ETHYL) AMINO]-4-METHOXY-1,3,5-TRIAZINE

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ABSTRACT

The compounds 5d, 5e, 5g, 5i showed moderate antimicrobial activity then other synthesized compounds, compare with known standard drugs.

1. INTRODUCTION

Quinoxalines derivative possess broad spectrum of pharmacological activities which are reflected by their use as CNS depressant, Antitubercular, Antiulcer, Analgesic, Anxiolytic, Antihypertensive, Antitumor etc. In view of getting potent therapeutic agents to synthesized titles compounds.

2-{4"-[(4"-aryl)-3"-cyano-2"-methoxy-pyridine-6"-yl]-phenyl amino}–6-[Bis(2"'-chloro ethyl) amino]-4-methoxy-1,3,5-triazine have been synthesized by the condensation of 2–{4"–[(3"–aryl) – 2"–propene–1"–one phenyl amino}–6– [Bis(2"'–chloroethyl) amino– 4–methoxy–1,3,5 triazine with bromine in glacial acetic acid and o-phenylenediamine.

2–{4"–[(3"–aryl)–2"–propene–1"–one phenyl amino}–6–[(Bis(2"'–chloro ethyl)amino]–4–methoxy–1,3,5–triazine (4a – 4k) have been synthesized by the reaction of 2–(4"–acetyl phenyl amino)–6–Bis (2"'–chloro ethyl)amino]–4–methoxy–1,3,5–triazine (3) with aromatic aldehyde in the present of aq. NaOH solution.

2–(4"–acetyl phenyl amino)–6–Bis(2"'–chloro ethyl)amino]–4–methoxy–1,3,5–triazine (3) have been synthesized by the condensation of 2–(4"–acetyl phenyl amino)–6–chloro–4– methoxy–1,3,5–triazine (2) with 2,2’–dichlorodiethyl amine hydrochloride in the presence of aq. NaOH and dioxane at 110 °C temp.

2–(4"–Acetyl phenyl amino)–6–chloro–4–methoxy–1,3,5–triazine (2) have been synthesized by the reaction of 2–(4"–acetyl phenyl amino)–4,6–dichloro–1,3,5–triazine (1) with sodium methoxide in methanol at room temp.

2–(4"–Acetyl phenyl amino)–4,6–dichloro–1,3,5–triazine (1) have been synthesized by the condensation of 2,4,6–trichloro–S–triazine with 4–amino acetophenone in aq. NaOH and acetone at 0 °C temp.

2. MATERIALS AND METHODS

2.1 Antimicrobial activity
Quinoxalines (5a-5k) were evaluated in vitro for antimicrobial activity against B. Mega, B. Subtilis, E. Coli, P. Fluoresences and for antifungal activity against A. awamori using DMF as solvent at 50 µg concentration by cup-plate method. After 24 hrs. of incubation at 37 °C temp., the zone or inhibition were measured in mm. The activity was compared with the known antibiotics viz.
3. METHOD SECTION

All the melting points were taken in open glass capillaries and are uncorrected. IR absorption spectra were recorded on a Shimadzu-FT-IR 8400 spectro-photometer using KBr pellet and $^1$H NMR spectra on a Bruker DPX-200 spectrometer (300 MHz) using DMSO as solvent and TMS as internal standard. Purity of the compounds were routinely checked by TLC using silica gel G.

4. EXPERIMENTAL AND SPECTRAL SECTION

(A) 2–(4’–Acetyl phenyl amino)–4,6–dichloro–1,3,5–triazine (1):

A mixture of 2,4,6–trichloro–S–triazine (1.845 gm, 0.01 m), 4-amino acetophenone (1.35 gm, 0.01 m) in acetone (25 ml) andaq. NaOH solution till solution basic. The reaction mixture was stirring at 0 °C temp. for 5 hrs. The content was poured into crushed ice, filtered and washed with water. The isolated product was crystallized from dioxane. yield : 86%, M. P. 178 °C. (Found : C, 51.65, H, 3.91, N, 20.09, C_{12}H_{8}N_{4}O_{2}Cl required C, 51.70, H, 3.94, N, 20.10%) IR : 2950 (C–H str. asym), 2870 (C–H def.), 1420 (C–H def.), 3056 (C–H str. aromatic), 1510 (C=C str.), 1118 (C–N str.), 1620 (C=C str.), 768 (C–Cl str.), 1700 (C=O str.) NMR : 3.10–3.20 (s, 3H, Ar–Cl); 6.50–6.63 (m, 4H, Ar–H), 9.95 (s, 1H, N–H). Mass : (m/z) 77, 103, 139, 145, 172, 198, 221, 240, 259.

(B) 2–(4’–Acetyl phenyl amino)–6–chloro–4–methoxy–1,3,5–triazine (2):

A mixture of 2–(4’–acetyl phenyl amino)–4,6–dichloro–1,3,5–triazine (2.83 gm, 0.01 m); sodium methoxide (0.56 gm, 0.01 m) in methanol. The reaction mixture was stirring at room temp. for 7 hrs. The content was poured into crushed ice, filtered and wash with water. The isolated product was crystallized from dioxane. yield : 86%, M. P. 178°C. (Found C, 51.65, H, 3.91, N, 20.09, C_{12}H_{8}N_{4}O_{2}Cl required C, 51.70, H, 3.94, N, 20.10%) IR : 2950 (C–H str. asym), 2871 (C–H def.), 1421 (C–H def.), 3051 (C–H str. aromatic), 1510 (C=C str.) 1120 (C–N str.), 1618 (–NH str.), 1244 (C–O–C str.), 761(C–Cl str.), 1702 (C=O str.) NMR : 3.10–3.20 (s, 3H, Ar–COCH3); 3.62–3.86 (s, 3H, Ar–OCH3); 7.10–7.03 (D.D. 4H Ar Hb, Hc), 9.95 (s, 1H, N–Hf) Mass : (m/z) 77, 103, 136, 145, 174, 202, 221, 240, 264, 278.

(C) 2–(4’–Acetyl phenyl amino)–6–[Bis (2”–chloroethyl) amino]–4–methoxy–1,3,5 triazine.

A mixture of 2–(4’–acetyl phenyl amino)–6–chloro–4–methoxy–1,3,5–triazine (2.78 gm, 0.01 m), 2,2’–di chloro diethyl amine hydrochloride (1.43 gm, 0.01 m); dioxane (25 ml) andaq. NaOH. The reaction mixture was reflux at 110 °C temp. for 6 hrs. The content was cooled and poured into crushed ice, Filtered and washed with water. The isolated product was crystallized from dioxane. yield 79%, M. P. 249 °C. (Found : C, 49.88, H, 4.91, N, 18.19, C_{16}H_{10}N_{4}O_{2}Cl required C, 50.00, H, 4.94, N, 18.22%) IR : 2921 (C–H str. asym), 1431 (C–H def.), 3062 (C–H str. aromatic), 1166 (C–H i.p. def.), 842 (C–H, o.p. def.), 1511 (C=C Str.) 1121 (C–N str.), 3342 (N–H Str.) 1242 (C–O–C str.), 1702 (C=O str.) NMR : 3.10–3.22 (s, 3H, Ar–COCH3), 3.62–3.86 (s, 3H, Ar–OCH3), 7.01–7.03 (D.D. 4H, (Ar–H), 4.79–4.80 (t, 4H, –CH2–Cl), 9.95 (s, 1H, –NH), Mass : (m/z) 77, 103, 145, 172, 210, 228, 265, 282, 302, 326, 355, 370.
(D) 2-4\prime-[3''-(4''''-Methoxy phenyl)-2''-propene-1''-one]phenyl amino}-6-[Bis(2''-chloro ethyl amino)-4-methoxy-1,3,5-triazine. (4e):

A mixture or 2-(4'-acetyl phenyl amino)-6-[Bis(2''-chloro ethyl amino)-4-methoxy-1,3,5-triazine( (3.84 gm, 0.01 m), 4-methoxy benzaldehyde (1.36 gm, 0.01 m), methanol (25 ml), and 40% aq. NaOH solution till becomes basic medium. The reaction mixture was stirring 24 hrs. at room temp. The mixture was poured into crushed ice, acidified, filtered and crystallized from dioxane. Yield : 69%, M. P. : 198°C. (Found C, 57.31, H, 4.90, N, 13.91, C_{24}H_{25}O_{3}N_{3}Cl_{2} required C, 57.37, H, 4.98, N, 13.94%) IR : 2923 (C-H str. asym), 1070 (C-O str.), 1118 (C=O str. sym), 1608 (C=N str.), 3311 (N-H str.) 3097 (C-H str. aromatic) 1276 (C-H i.p. def.), 1677 (C=O str.), 1118 (C-N str.), 3311 (N-H str.) 3045 (C=C str.), 1245 (C-O-C str.), 768 (C-Cl str.) NMR : 3.62-3.86 (s, 6H, Ar-CH_{2}), 7.01-7.03 (D. D. 4H, Ar–Hb), 8.08-8.72 (D. D. 4H, Ar–Hc), 4.79-4.80 (t, 4H, CH_{2}–Cl), 2.50-2.51 (t, 4H, -NCH_{2}), 9.95 (s, 1H, -NHf), 4.80-4.83 (s, 2H, CH=CHg) Mass : (m/z) 112, 130, 156, 212, 262, 271, 280, 285, 325, 335, 371, 428, 461, 502.

Similarly other chalcones (4a – 4k) where prepared and their physical data and antimicrobial activities data published in other journal.

(E) 2''-(4''''-Methoxy phenyl)-(quinoxaline)-3-yl)-(methylene phenyl amino)-6-[Bis(2''-chloro ethyl amino)-4-methoxy-1,3,5-triazine (5e):

A mixture of 2-4\prime-[3''-(4''''-methoxy Phenyl) – 2'' – Propene – 1''-one] Phenyl amino)-6-[Bis (2''-chloro ethyl amino)-4-methoxy – 1,3,5 – triazine (5.02 gm, 0.01M and o-phenylene diamine (1.08 gm, 0.01 M) taken in methanol (25 ml). A few drops of conc. H_{2}SO_{4} & bromine in glacial acetic acid was added. The reaction mixture was heated at 90\degree C. for 1 hr. in water bath. The reaction mixture poured into crushed ice, filtered, dried and crystallised from dioxane. Yield : 69%, M. P. 239\degree C (Found C : 61.00; H : 4.89; N : 16.58; C_{30}H_{29}O_{2}N_{7}Cl_{2} required C : 61.01; H : 4.91; N : 16.60%). IR : 2900 (C-H str. asym), 2881 (C-H str. sym.) 1450 (C-H def. asym), 1369 (C-H def. sym.), 1450 (CH_{2} str.), 3058 (C-H str. aromatic) 1265 (C-H i.p. def.), 800 (C-H o.o.p. def.), 1487 (C=C str), 1070 (C-N str), 1598 (C=N str), 3315 (N-H str), 1558 (N-H ben.), 1625 (C-O-C str. asym), 1070 (C-O-C str. sym), 800 (C-Cl str.), 1608 (C=N str.), 1089 (C-N str.) NMR : 3.60-4.00 (s, 6H, Ar–OCH_{3}), 7.94-7.98 (DD, 4H, Ar-Hb), 8.07-8.40 (D.D. 4H, Ar–Hc), 4.10-4.14 (t, 4H, -CH_{2}–Cl), 2.77 (t, 4H, -NCH_{2}), 10.23 (s, 1H, Ar–NH), 7.34 (s, 2H, Ar-H), 7.28-8.07 (m, 4H, Ar-H). Mass : (m/z) 137, 144, 167, 179, 188, 255, 271, 340, 358, 384, 432, 462, 590.

Similarly other (5a – 5k) have been synthesized and their physical data represented in Table no. I.
REACTION SCHEME:

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\begin{align*}
\text{Cl} & \quad \text{Cl} \\
\text{Cl} & \quad \text{N} \quad \text{C} \quad \text{N} \\
\text{Cl} & \quad \text{N} \quad \text{N} \\
\text{Cl} & \quad \text{O} \\
\text{N} & \quad \text{H} \\
\text{O} & \quad \text{N} \\
\text{Cl} & \quad \text{N} \\
\text{N} & \quad \text{N} \\
\text{Cl} & \quad \text{N} \\
\text{Cl} & \quad \text{O} \\
\text{N} & \quad \text{H} \\
\text{O} & \quad \text{N} \\
\end{align*}
\]

(1) \( R = \text{Aryl} \)

(2) \( R = \text{Br} \)

(3) \( R = \text{gl. CH}_3\text{COOH} \)

(4a - 4k) \( R = \text{Aryl} \)

(5a - 5k) \( R = \text{Aryl} \)
5. RESULTS AND DISCUSSION:

The physical data and antimicrobial activity of compounds (5a -5k).

Table-I

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<th>Compound</th>
<th>R</th>
<th>E. coli</th>
<th>S. Roper</th>
<th>E. Staph</th>
<th>P. Fluorescens</th>
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* Zone of inhibition in mm.
Table-II
Comparable antimicrobial activity.

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<th>Compd</th>
<th>B. Megzi</th>
<th>E. Coli</th>
<th>P. Fluorescens</th>
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6. CONCLUSION

The compounds 5d, 5e, 5g, 5i showed moderate antimicrobial activity then other synthesized compounds, compare with known standard drugs.

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References

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