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Research Article

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Synthesis and antimicrobial activity of 2-{4'-[(3"-aryl)-2"-propene-1"-N-(1,2,4-triazole) amino]}-6-[bis(2"'-chloro ethyl) amino]-4-methoxy-1,3,5-triazine

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ABSTRACT

The titled compounds (5a-5k) 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 4-amino -1,2,4 - triazole in alcohol. The biological activities of these compounds have been determined against various Gram +ve, Gram –ve bacteria and fungi. The constitutions of the products are supported by IR, ^{1}H NMR, Mass spectra and elemental analysis.

Keywords: Triazole, S-Triazine.

INTRODUCTION

Triazoles derivative possess broad spectrum of pharmacological activities which are reflected by their use as Fungicide[1], Antideprassant[2], Coronary vasodilator[3], Sedative-hypnotic [4], anti viral[5], antiallergic[6], etc. In view of getting potent therapeutic agents to synthesized titles compounds.

2-{4'-[(3"-aryl)-2"-propene-1"-n-(1,2,4-triazole) amino]}-6-[bis(2"'-chloro ethyl) amino]-4-methoxy-1, 3, 5-triazine (5a – 5k) 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 4-amino -1,2,4 - triazole in alcohol.

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.

EXPERIMENTAL SECTION

Antimicrobial activity

Triazoles (5a-5k) were evaluated in vitro for antimicrobial activity against *B. Mega*, *B. Subtillis*, *E. Coli*, *P. Fluoresences* and for antifungal activity against *A. awamori* using DMF as solvent at 50 µg concentration by cup-plate method[7]. After 24 hrs. of incubation at 37 ^{0}C temp., the zone or inhibition were measured in mm. The activity was compared with the known antibiotics viz. Ampicillin chloramphenicol, Norfloaxacin, Greseofulvin at same concentration which is represented in Table-I and comparable anti microbial activity represented in Table no. II

METHOD SECTION

All the melting points were taken in open glass capillaries and are uncorrected. IR absorption spectra were recorded on a Shimadza-FT-IR 8400 spectro-photometer using KBr pellet and ^{1}H NMR specra 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 get G.

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) and aq. NaOH solution till solution basic. The reaction mixture was stirring at 0 $^\circ$C temp. for 5 hrs. The content was poured into crushed ice, filltered and washed with water. The isolated product was crystallized from dioxane yield : 82%, MP. 112 $^\circ$C. (Found : C, 46.61 , H, 2.79, N, 19.75, $C_{11}H_8N_4OCl_2$ required C, 46.64, H, 2.82, N, 19.79%). IR : 2952 (C–H str. asym.), 2870 (C–H Str. Sym), 1420 (C–H def.), 3056 (C–H str. aromatic), 1509 (C=C str.), 1118 (C–N str.), 1620 (N–H bend), 768 (C–Cl Str.), 1700 (C=O str.) NMR : 3.10–3.20 (s, 3H, Ar–$COCH_3$); 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, filltered and wash with water. The isolated product was crystallized from dioxane. yield : 86%, M. P. 178^{0}C. (Found C, 51.65

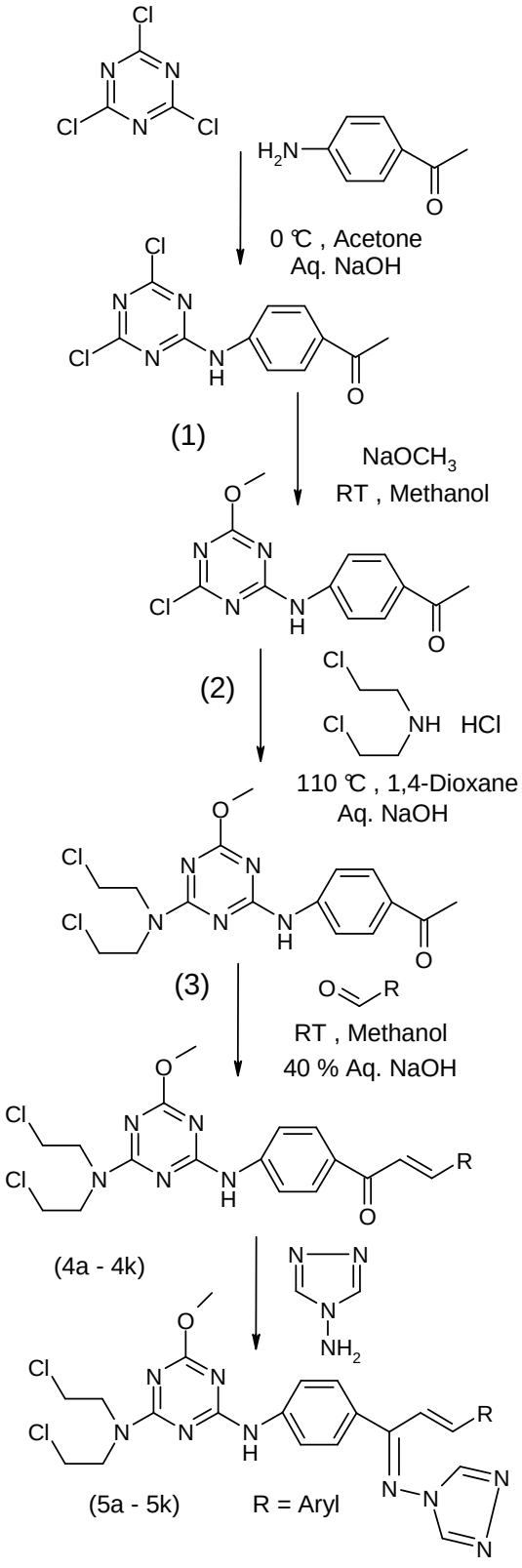
H, 3.91, N, 20.09, $C_{12}H_{11}N_4O_2Cl$ required C, 51.70, H, 3.94, N, 20.10%) IR : 2950 (C–H str. asym), 2871 (C–H Str. Sym.) 1421 (C–H def.), 3051 (C–H str. aromatic), 1510 (C=C str.) 1120

(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–$COCH_3$), 3.62–3.86 (s, 3H, Ar–OCH_3), 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. (3)** :

A mixture of 2–(4'–acetyl phenyl amino)–6–chloro–4–metholy–1,3,5–triazine (2.78 gm, 0.01 m), 2,2'–di chloro diethyl amine hydrochloride (1.43 gm, 0.01m); dioxane (25 ml) and aq. NaOH. The reaction mixture was refulx at 110 °C temp. for 6 hrs. The content was cooled and poured into crushed ice, Filltered 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, $C_{16}H_{19}N_5O_2Cl_2$ required C, 50.00, H, 4.94, N, 18.22%) IR : 2921 (C–H str. asym), 2850 (C–H str. sym.), 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–$COCH_3$), 3.62–3.86 (s, 3H, –OCH_3), 7.01–7.03 (D.D. 4H, (Ar-H), 4.79–4.80 (t, 4H, –CH_2–Cl), 9.95 (s, 1H, –NH), Mass : (m/z) 77, 103, 145, 172, 210, 228, 265, 282, 302, 326, 355, 370.

REACTION SCHEME



(D) **2–{4'–[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 contents were poured into crushed ice, acidified, filltered and crystalized from dioxane. yield 79%, M. P. : 198 °C. (Found C, 57.31, H, 4.90, N, 13.91, $C_{24}H_{25}O_3N_5Cl_2$ required C, 57.37, H, 4.98, N, 13.94%) IR : 2923 (C–H str. asym.), 2852 (C–H str. sym), 1436 (C–H str. asym), 1371 (C–H str. sym) 3097 (C–H str. aromatic) 1276 (C–H i.p. def.), 821 (C–H, o.o.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-OCH_3), 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'-[3"-(4""-Methoxyphenyl)-2"-propene-1"-n-(1,2,4-triazole) amino]}-6-[Bis(2"'-chloro ethyl) amino]-4-methoxy-1, 3, 5-triazine (5e) :**
A mixture of 2-{4'-[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, 0.01 M); 1-amino-1,3,4-triazole (0.76 gm; 0.01 M) and alcoholic KOH, the reaction mixture was refluxed fo 10 hrs. at 100º C. temp. The reaction mixture poured into crushed ice, filtered, dried and crystallized from dioxane, Yield : 79% ; M.P. 185º C. (Found : C : 54.90; H : 4.73; N : 22.15, $C_{26}H_{27}O_2N_9Cl_2$ required C : 54.92; H : 4.75; N : 22.18%). IR : 2947 (C–H str. asym), 2889 (C–H str. sym.) 1444 (C–H def. asym), 1363 (C–H def. sym.), 3024 (C–H str. aromatic) 1101 (C–H i. p. def.), 830 (C–H o.o.p. def.), 1450 (C=C str), 1149 (C–N str.), 1581 (C=N str.), 3413 (N–H str.), 1550 (N–H ben.), 1215 (C–O– C str. asym.), 1047 (C–O– C str. sym.), 792 (C–Cl str.), 3350 (N–H str.), 1676 (C–N str.), 1581 (N=N str.), 1298 (C–N ben.). NMR : 3.71-3.86 (s, 6H, Ar–OCH_3), 7.66-7.79 (DD, 4H, Ar-H_b), 7.99-8.12 (D.D. 4H, Ar–H_C), 4.79-4.84 (t, 4H, -CH_2–Cl), 2.50-2.89 (t, 4H, -NCH_2), 9.87-9.96 (s, 2H, Ar–NH), 4.81-4.84 (d, 2H CH=CH). Mass : (m/z) 114, 130, 151, 157, 189, 246, 279, 337, 372, 398, 457, 492, 584.

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

RESULTS AND DISCUSSION

Table-I: The physical data and antimicrobial activity of compounds (5a -5k)

Compd	R	Mol. Formula	M.P. ^{0}C	Yield (%)	N(%)		Antibacterial activity				Antifungal Activity
					Calc.	(Found)	*B. Mega*	*B. Subtillis*	*E. Coli.*	*P. Fluoroscens*	*A. awamori*
5a	C_6H_5	$C_{25}H_{25}Cl_2N_9O$	238	57	23.41	23.39	16	17	14	19	20
5b	2-OH C_6H_4	$C_{25}H_{25}Cl_2N_9O_2$	232	62	22.74	22.71	15	19	17	20	17
5c	3-OH C_6H_4	$C_{25}H_{25}Cl_2N_9O_2$	215	65	22.74	22.72	20	14	23	18	21
5d	4-OH C_6H_4	$C_{25}H_{25}Cl_2N_9O_2$	223	72	22.74	22.69	18	20	22	23	19
5e	4-OCH3 C_6H_4	$C_{26}H_{27}Cl_2N_9O_2$	185	79	22.18	22.15	19	12	13	20	19
5f	4-OH, 3-OCH_3 C_6H_4	$C_{26}H_{27}Cl_2N_9O_3$	222	74	21.57	21.53	19	15	18	18	16
5g	4-Br, C_6H_4	$C_{25}H_{24}BrCl_2N_9O$	120	80	20.42	20.41	16	14	17	17	14
5h	3-NO_2 C_6H_4	$C_{25}H_{24}Cl_2N_{10}O_3$	182	83	24.01	24.00	23	17	15	19	21
5i	4-NO_2 C_6H_4	$C_{25}H_{24}Cl_2N_{10}O_3$	193	69	24.01	23.99	24	21	14	21	16
5j	4-N,N$(CH_3)_2$ C_6H_4	$C_{27}H_{30}Cl_2N_{10}O$	169	72	24.09	24.05	15	15	19	18	17
5k	C_4H_3O Furfuryl)	$C_{23}H_{23}Cl_2N_9O_2$	242	95	23.86	23.81	13	17	18	17	22

** Zone of inhibition in mm.*

Table-II : Comparable antimicrobial activity

	Compd	*B. Mega*	*B. Subtillis*	*E. Coil*	*P. Fluorescens*	*A. awamori*
	5a-5k	5c, 5h, 5i	5b, 5d, 5i	5c, 5d, 5j	5b, 5d, 5i	5c, 5h, 5k
1	Ampicillin (50 µg)	23	18	17	27	-
2	Chloramphenicol (50 µg)	24	19	25	26	-
3	Norfloxacin (50 µg)	24	19	25	26	-
4	Greseofulvin (50 µg)	-	-	-	-	23

CONCLUSION

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

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