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

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INTRODUCTION

Chalcones derivatives showed potent biological activities, these have been reported to be active as antidepressants, antibacterial, antifungal, antiviral, antiinflammatory, analgesics, and Bis (2–chloro ethyl) amine possess anticancer, anti-HIV activities. In order to achieving better potency to synthesize chalcone (4a – 4k). The constitution of the products delineated by IR, ^{1}H NMR, Mass spectral studies and TLC. The Products are evaluated their antimicrobial activity against Gram +ve bacteria, Gram –ve bacteria and Fungi.

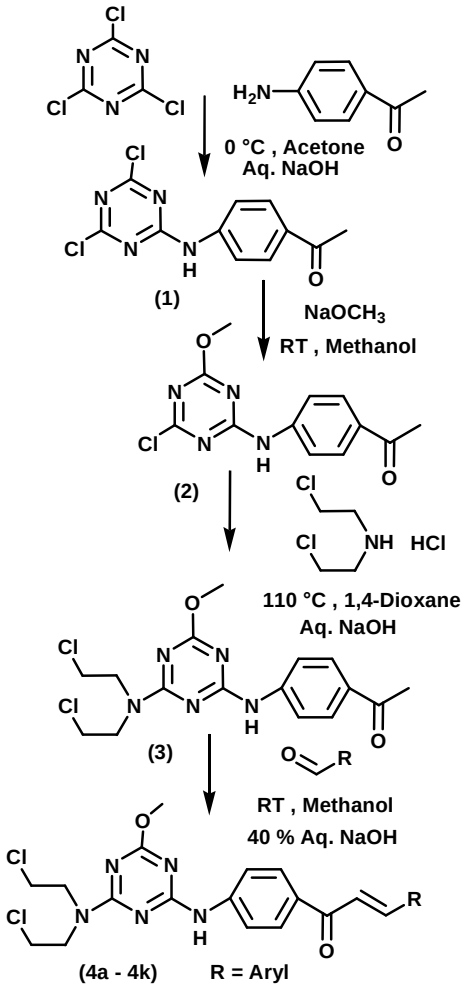
2,2'–Dichlorodiethyl amine and S–triazine molecules are well known in pharmaceutical chemistry. These molecules gave therapeutic activities, such as anti-inflammatory[1], anticonvulsant[2], antipyretic[3], antibacterial[4], fungicidal[5], antiviral[6], antileukemia[7], antitumor[8] etc.

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.

Reaction Scheme



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.

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ANTIMICROBIAL ACTIVITY

Chalcones (4a – 4k) were evaluated for their antimicrobial activity against *B. Megaterium, B. Subtillis, E. Coli, P. Fluorescens* and for antifungal activity against *A. Awamori*, using DMF as solvent at 50 µg concentration by cup-plate method[9]. After 24 hr of incubation at 37 °C, the zones of inhibition were measured in mm. The activity was compared with the known antibiotics, viz., Ampicillin, Chloramphenicol, Norfloxacin, and Greseofulvin at the same concentration and result are represented in TABLE 1 and comparable antimicrobial activity represented in TABLE 2.

EXPERIMENTAL

All the melting points were taken in open glass capillary tubes and are uncorrected. IR absorption spectra were recorded on a shimadzu IR-435 spectrophotometer. using KBr pellet method and ^{1}H NMR spectra on Bruker spectrometer (300 MHz) using DMSO–d_6 as solvent and TMS as internal standard (chemical shift in δ ppm), Purity of the compounds were checked by TLC using silica gel G.

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

A mixture of 2,4,6–trichloro–S–triazine (1.84 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 °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 °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–

TABLE 1 : The physical data and antimicrobial activity of compounds (4a - 4k)

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
4a	C_6H_5	$C_{23}H_{23}Cl_2N_5O_2$	218	70	14.83	14.80	16	13	18	19	17
4b	2-OH, C_6H_4	$C_{23}H_{23}Cl_2N_5O_3$	224	82	14.34	14.31	17	15	17	18	22
4c	3-OH C_6H_4	$C_{23}H_{23}Cl_2N_5O_3$	230	85	14.34	14.32	19	19	16	19	21
4d	4-OH C_6H_4	$C_{23}H_{23}Cl_2N_5O_3$	220	81	14.34	14.29	20	17	20	21	23
4e	4-OCH_3 C_6H_4	$C_{24}H_{25}Cl_2N_5O_3$	198	79	13.94	13.91	15	18	18	17	16
4f	4-OH, -3-OCH_3 C_6H_3	$C_{24}H_{25}Cl_2N_5O_4$	231	83	13.51	13.49	18	14	16	22	18
4g	4-Br C_6H_4	$C_{23}H_{22}Br\ Cl_2N_5O_2$	172	86	12.70	12.69	21	19	21	18	20
4h	3-NO_2 C_6H_4	$C_{23}H_{22}Cl_2N_6O_4$	222	89	16.24	16.22	17	16	18	19	17
4i	4-NO_2 C_6H_4	$C_{23}H_{22}Cl_2N_6O_4$	175	81	16.24	16.21	21	17	20	22	19
4j	4-N,N$(CH_3)_2$ C_6H_3	$C_{25}H_{28}Cl_2N_6O_2$	226	78	16.30	16.25	15	18	17	17	18
4k	C_4H_3O Furfuryl	$C_{21}H_{21}Cl_2N_5O_3$	238	83	15.15	15.10	14	15	16	19	17

*** Zone of inhibition in mm.**

TABLE 2 : Comparable antimicrobial activity

	Compd	B. Mega	B. Subtillis	E. Coil	P. Fluorescens	A. awamori
	4a-4k	4g, 4i	4c, 4e, 4j	4a, 4d, 4g, 4i	4d, 4f, 4i	4b, 4c, 4d, 4g
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

4–methoxy–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

(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 of 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 represented in TABLE 1.

CONCLUSION

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 and some of the compounds **(4c)**, **(4g)** and **(4i)** showed good remarkable antibacterial and antifungal activity with compare to known standard drugs e.g. ampicillin, chloramphenicol, norfloxacin and greseofulvin at same concentration 50µg/ml, which is represented in TABLE 2.

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