IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736.Volume 11, Issue 8 Ver. I (August. 2018), PP 27-32
www.iosrjournals.org

Synthesis, Charecterization And Antibacterial Activity of Some Novel Chalcones And Its Derivatives

M.Thamizhthendral And S. Syed Shafi*
Department of Chemistry, Thiruvalluvar University, Serkkadu, Vellore-632115, Tamil Nadu, India.
Corresponding Author: S. Syed Shafi

Abstract: *Chalcones, (E)-N-(4-(4,6-dichloro-1,3,5 –triazin-2-ylamino) phenyl)-3-(4-methoxyphenyl) acrylamide (4a-c) have been prepared according to Claisen-Schmidt condensation. Further these chalcones (4a-c) on reaction with malononitrile affords cyanopyridines (5a-c) and on reaction with hydrazine hydrate affords pyrazole (6a-c) respectively. The constitutions of newly synthesised compounds have been characterized on the basis of their IR and ^{1}H NMR, ^{13}C NMR spectral data.These synthesized compounds have been screened for their antibacterial activity.*

Keywords: *Chalcones, cyanopridines ,pyrazolines, antibacterial activity.*

Date of Submission: 20-08-2018 Date of acceptance: 03-09-2018

I. Introduction

Commonly α,β- unsaturated ketone is known as chalcones. These are coloured compounds because of the chromophore -CO-CH=CH-, which depends in the presence of other auxochromos. Different methods are available for the preparation of chalcones[1-3]. The most convenient method is the Claisen-Schimdt condensation. Chalcones are used to synthesize several derivatives like, cyanopyridines, pyrazolines, isoxazoles having different heterocyclic ring systems [4,5]. These are found to be effective as anti-inflammatory[6,7], anticancer[8-10], antifungal[11-13], cardiovascular[14], and antimalarial[15] agents.The well known stepwise reaction between cyanuric chloride and aminoacetanilide is very well defined, and high yields of aminodichlorotriazines were obtained. Cyanuric chloride is definitely an excellent starting compound for the straight forward preparation of highly structured multitopic molecules. Indeed,each chloride atom of 2,4,6 –trichloro-1,3,5-triazine can be substituted by any nucleophilic reactant. The first substitution is exothermic. Therefore, the temperature of the reaction mixture has to be maintained to 0 ºC. The substitution of the second step at room temperature, finally the third step is functionalized under reflux of the solvent. These observation led us to synthesize some new s-triazinyl based chalcones and it corresponding pyrazoline and cyanopyridine derivatives. (SCHEME-I).

II. Experimental

Materials and Methods:

Melting points were determined by Deep Vision instrument. The purity of the compounds was checked by TLC using silica gel coated plates and spots were visualized by exposing the dry plates in iodine vapours. IR Spectra were recorded in the solid state, as KBR dispersion by use of the FT-IR-Spectrometer. The ^{1}HNMR and ^{13}C NMR spectra of the compounds were carried out in Bruker AMX 400 MHZ. NMR instrument using $CDCl_3$ or DMSO as a solvent and TMS as internal reference (chemical shift in δ ppm). The mass spectrum was carried out in WATERS-Q-TOF premier-HAB213, electron spray ionization-MS electrode.

Synthesis of N-(4-(4,6-dichloro-1,3,5-triazin-2-yl amino)phenyl) acetamide (3):

4-amino acetanilide (0.01 mole) was added slowly to cyanuric chloride (0.01 mole) in acetone (30ml) with constant stirring over a period of 4 hr at 0 to 5º C Then ,sodium carbonate (0.05 mole) dissolved in water (10 ml) was added drop wise to neutralize HCl evolved during the reaction .Finally ,the contents were poured into crushed ice. The solid was separated out by filtration and washed with water. The product is dried, recrystallized from alcohol to give the product (3).

Synthesis of (E)-N-(4-(4,6-dichloro-1,3,5 –triazin-2-ylamino) phenyl)-3-(4-methoxyphenyl) acrylamide (4a):

Acetamide compound (3) (0.01 mole) was dissolved in Ethanol (30 ml) then 10% NaOH solution and 4- Methoxybenzaldehyde (0.01mole) was added to the reaction mixture with constant stirring over a period of 6 hrs .The reaction mixture was poured into crushed ice. The solid was separated out by filtration and washed with water. The product (4a) is dried, recrystallized from ethanol.

IR (KBR) cm^{-1}: C-N,s-triazine (829.90), N-H Bend (3419.04) , C─Cl (770.81).

Synthesis of (E)-N-(4-(4,6-dichloro-1,3,5 –triazin-2-ylamino) phenyl)-3-(4-flurophenyl) acrylamide (4b):

Acetamide compound (3) (0.01 mole) was dissolved in Ethanol (30 ml) then 10% NaOH solution and 4- Flurobenzaldehyde (0.01mole) was added to the reaction mixture with constant stirring over a period of 6 hrs .The reaction mixture was poured into crushed ice. The solid was separated out by filtration and washed with water. The product (4b) is dried, recrystallized from ethanol.
IR (KBR) cm^{-1}: C-N,s-triazine (809.95), N-H str (2926.45) , C─Cl (764.63).

Synthesis of (E)-N-(3-(4,6-dichloro-1,3,5 –triazin-2-ylamino) phenyl)-3-(benzo [d] [1,3] dioxol-5yl) acrylamide (4c):

Acetamide compound (3) (0.01 mole) was dissolved in Ethanol (30 ml) then 10% NaOH solution and piperonal (0.01mole) was added to the reaction mixture with constant stirring over a period of 6 hrs .The reaction mixture was poured into crushed ice. The solid was separated out by filtration and washed with water. The product is dried, recrystallized from ethanol .
IR (KBR) cm^{-1}: C-N,s-triazine (809.95), N-H str (2922.59) , C─Cl (657.60).

Synthesis of 5-(4-(4,6-dichloro-1,3,5 triazin-2ylamino)phenylamino)-2-amino-4-(4-methoxyphenyl) pyridine-3-carbonitrile (5a):

A mixture of a compound (4a) (0.01 mole) dissolved in 40 ml ethanol and added malononitrile (0.01 mole), ammonium acetate (0.08 mole) was refluxed for 8 hrs. Then the mixture was cooled and poured into crused ice .The product (5a) separated out was filtered washed and recrystallized from alcohol. IR(KBR) cm^{-1} : C-Cl (834.06),Ar C-Cl (1119.48) ,Ar-N str (1383.68), primary N-H (1509.07), C=C (1570.74), C=N (1613.16), N-H str (2853.17). ^{1}H NMR ($CDCl_3$) δ ppm : 3.734 (O-CH_3), 4. 311 to 4.349 (S,1H,s-triazine, Ar-C-NH), 6.986-7.437 (d, 4H,Ar-CH),7.688 (Ar-H), 9.896 (2-Py-Ar-1H). ^{13}C NMR ($CDCl_3$) δ ppm: Aliphatic-CH_3 (55.51), Ar-CH (119.52 to 121.12), 2-Py (134.85),1-imine (166.10), S- triazine (168.3).

Synthesis of 5-(4-(4,6-dichloro-1,3,5 triazin-2ylamino)phenylamino)-2-amino-4-(4-flurophenyl) pyridine-3-carbonitrile (5b):

A mixture of a compound (4b) (0.01 mole) dissolved in 40 ml ethanol and added malononitrile (0.01 mole), ammonium acetate (0.08 mole) was refluxed for 8 hrs. Then the mixture was cooled and poured into crused ice .The product (5b) separated out was filtered washed and recrystallized from alcohol. IR(KBR) cm^{-1} : C-Cl (776.208),Ar C-Cl (1129.12) ,Ar-N str (1380.78), primary N-H (1509.07),C=C (1626.66), N-H str (2918.73). ^{1}H NMR($CDCl_3$) δ ppm : 4.296 to 4.314 (S,1H,s-triazine Ar-C-NH) , 4.331 (S,1H,Ar-C-NH_2) 6.986-7.437 (d, 4H,Ar-CH),7.588 (Ar-H), 9.898 (2-Py-Ar-1H). ^{13}C NMR ($CDCl_3$) δ ppm: Ar-CH (119.40 to 121.02), 2-Py-CH (134.15 to135.28), S- triazine (168.20).

Synthesis of 5-(4-(4,6-dichloro-1,3,5 triazin-2ylamino)phenylamino)-2-amino-4-(benzo [d] [1,3] dioxol 4-yl pyridine-3-carbonitrile (5c):

A mixture of a compound (4c) (0.01 mole) dissolved in 40 ml ethanol and added malononitrile (0.01 mole), ammonium acetate(0.08 mole) was refluxed for 8 hrs. Then the mixture was cooled and poured into crused ice .The product (5c) separated out was filtered washed and recrystallized from alcohol. IR(KBR) cm^{-1} : C─Cl (813.61), C-O-C (1032.69), Ar C-Cl (1108.87) Ar-N (1334.50), primary N-H (1508.06), C=C (1578.45), C=N (1616.06), N-H str (2922.59), O-H str (3784.62). ^{1}H NMR($CDCl_3$) δ ppm : 4.427 (S,1H,s-triazine ,Ar-C-NH) , 5.276(S,1H,Ar-C-NH_2), 6.672 (d,1H,Ar-Py), 6.983-7.469 (d, 4H,Ar-CH),^{13}C NMR($CDCl_3$) δ ppm: Ar-CH (108.82 to121.53),2-Py-CH(134.65 to148.38), 1-imine (166.01), S- triazine (166.24).

Synthesis of N^1-(4-(4,6-dichloro-1,3,5-triazin-2-yl)-N^4-(4,5-dihydro-5-(4-methoxyphenyl-1H-pyrazol-3-yl) benzene-1,4-diamine (6a):

A mixture of a compound (4a) (0.01 mole) dissolved in 40 ml ethanol and added hydrazine hydrate (0.01 mole) was refluxed for 8 hrs. Then the mixture was cooled and poured into crused ice .The product (6a) separated out was filtered washed and recrystallized from alcohol. IR(KBR) cm^{-1} : C-Cl (779.101),Ar C-Cl (1119.48) ,Ar-N str (1383.68), primary N-H (1509.07), C=N (1630.52), N-H str (2919.70). ^{1}H NMR($CDCl_3$) δ ppm : 4.314 to 4.330 (S,1H,s-triazine Ar-C-NH), 7.522 to 7.587 (d, 4H,Ar-CH), 9.891 (2-Py-Ar-1H).
^{13}C NMR ($CDCl_3$) δ ppm: Ar-CH (119.40 to 121.50), 1-imine (166.02), S- triazine (168.25).

Synthesis of N^1-(4-(4,6-dichloro-1,3,5-triazin-2-yl)-N^4 –(5-(4-flurophenyl)-4,5-dihydro-1H-pyrazol-3yl) benzene-1,4-diamine (6b):

A mixture of a compound (4b)(0.01 mole) dissolved in 40 ml ethanol and added hydrazine hydrate (0.01 mole) was refluxed for 8 hrs. Then the mixture was cooled and poured into crused ice .The product (6b)

separated out was filtered washed and recrystallized from alcohol. IR(KBR) cm^{-1} : C-Cl (876.488),Ar C-Cl (1119.48) ,Ar-N str (1386.57), primary N-H (1509.07), C=C (1630.52), N-H str (2922.59). ^{1}H NMR ($CDCl_3$) δ ppm : 4.296 to 4.311 (S,1H,s-triazine Ar-C-NH) ,7.519 to 7.585 (d, 4H,Ar-CH), 9.894 (2-Py-Ar-1H). ^{13}C NMR ($CDCl_3$) δ ppm: Ar-CH (119.40 to 121.49), 1-imine (166.01), S- triazine (168.17).

Synthesis of N^1-(5-(benzo[d][1,3]dioxol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)-N^4-(4,6-dichloro-1,3,5-triazin-2-yl)benzene-1,4-diamine(6c):

A mixture of a compound (4c) (0.01 mole) dissolved in 40 ml ethanol and added hydrazine hydrate (0.01 mole) was refluxed for 8 hrs. Then the mixture was cooled and poured into crused ice .The product (6c) separated out was filtered washed and recrystallized from alcohol. IR(KBR) cm^{-1} : C-Cl (837.91),Ar C-Cl (1126.22) ,Ar-N str (1411.68), primary N-H (1505.17), C=C (1602.56), C=N (1661.37), N-H str (2985.27). ^{1}H NMR($CDCl_3$) δ ppm : 2.33(S,Ali-CH_2), 4.339 to 4.357 (S,1H,s-triazine Ar-C-NH), 4.392 (1,3-dioxole), 7.364-7.543 (d, 4H,Ar-CH),7.72 (Ar-H). ^{13}C NMR ($CDCl_3$) δ ppm: Ar-CH (128.71to 132.58), 1-imine (164.00), S- triazine (167.51).

III. Result And Discussion

The interest of organic chemistry in 2,4,6-trichloro-1,3,5-triazine as a starting material is due to temperature dependent reactivity of one chlorine atom that allow a sequential introduction of various substituent's. In the present artical we have reported the synthesis, characterization and antibacterial activity of some novel s-triazine based cyanopyridine, pyrazoline derivatives.

Table- 1: Physical data of the synthesized compounds (4a-c), (5a-c) and (6a-c)

Compound code	R	Mol. Formula	Mol. weight	MP(ºC)	Yield (%)	R_f value
4a	$C_6H_4OCH_3$	$C_{19}H_{15}C1_2N_5O_2$	416.26	190-191 ºC	89%	0.61
4b	C_6H_4F	$C_{17}H_{13}Cl_2FN_5O$	404.23	194-196 ºC	75%	0.70
4c	$C_7H_5O_2$	$C_{19}H_{13}Cl_2N_5O_3$	430.24	206-208º C	83%	0.53
5a	$C_6H_4OCH_3$	$C_{22}H_{16}Cl_2N_8O$	479.32	115-120 ºC	70 %	0.55
5b	C_6H_4F	$C_{17}H_{13}Cl_2FN_8$	467.29	138-140º C	75%	0.65
5c	$C_7H_5O_2$	$C_{22}H_{14}Cl_2N_8O_2$	493.30	123-125º C	62 %	0.61
6a	$C_6H_4OCH_3$	$C_{18}H_{16}Cl_2N_7O$	430.30	188-192º C	65%	0.62
6b	C_6H_4F	$C_{18}H_{14}Cl_2FN_7$	418.26	222-224 ºC	68%	0.72
6c	$C_7H_5O_2$	$C_{19}H_{14}Cl_2N_7O_2$	444.27	188-192ºC	72%	0.60

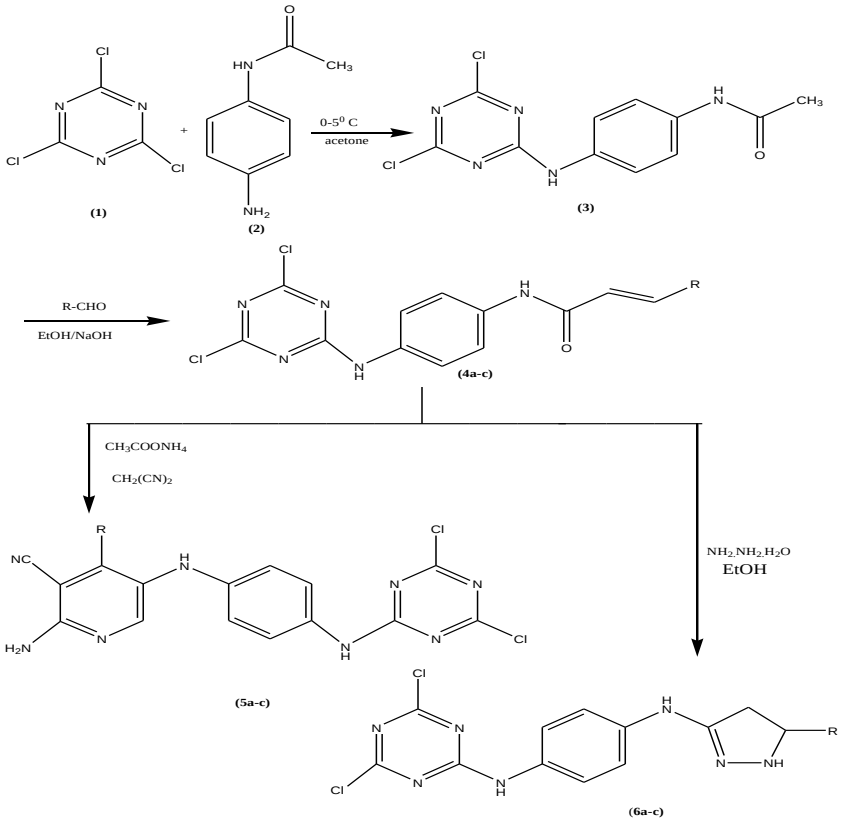

Figure 1. Scheme for synthesis of Chalcones (4a-c) and its derivatives (5a-c and 6a-c)

Antibacterial activity

All the synthesized compounds were screened for their antibacterial activity by using agar diffusion method against S. aureus and B.subtilis (Gram positive bacteria) and E.coli, S.Typi (Gram negative bacteria) by using agar medium.Ciprofloxacin was used as standard drugs for the comparison of antibacterial activity by visualizing activity data it could be observed that compounds (5a-c) and (6a-c) were found to be active or inactive against all bacterial strain.(Table-No.2)

Table-2: Antibacterial activity data of compounds (5a-c) and (6a-c)

S.No	Microorganism	Control	5a	5b	5c	6a	6b	6c	Ciprofloxacin
1.	Enterococcus faecalis	-	10	8	9	9	10	9	35
2.	Staphylococcus aureus	-	8	9	7	8	9	6	18
3.	Salmonella typhi	-	10	15	12	9	14	9	30
4.	Escherichia coli	-	10	7	9	8	9	7	15

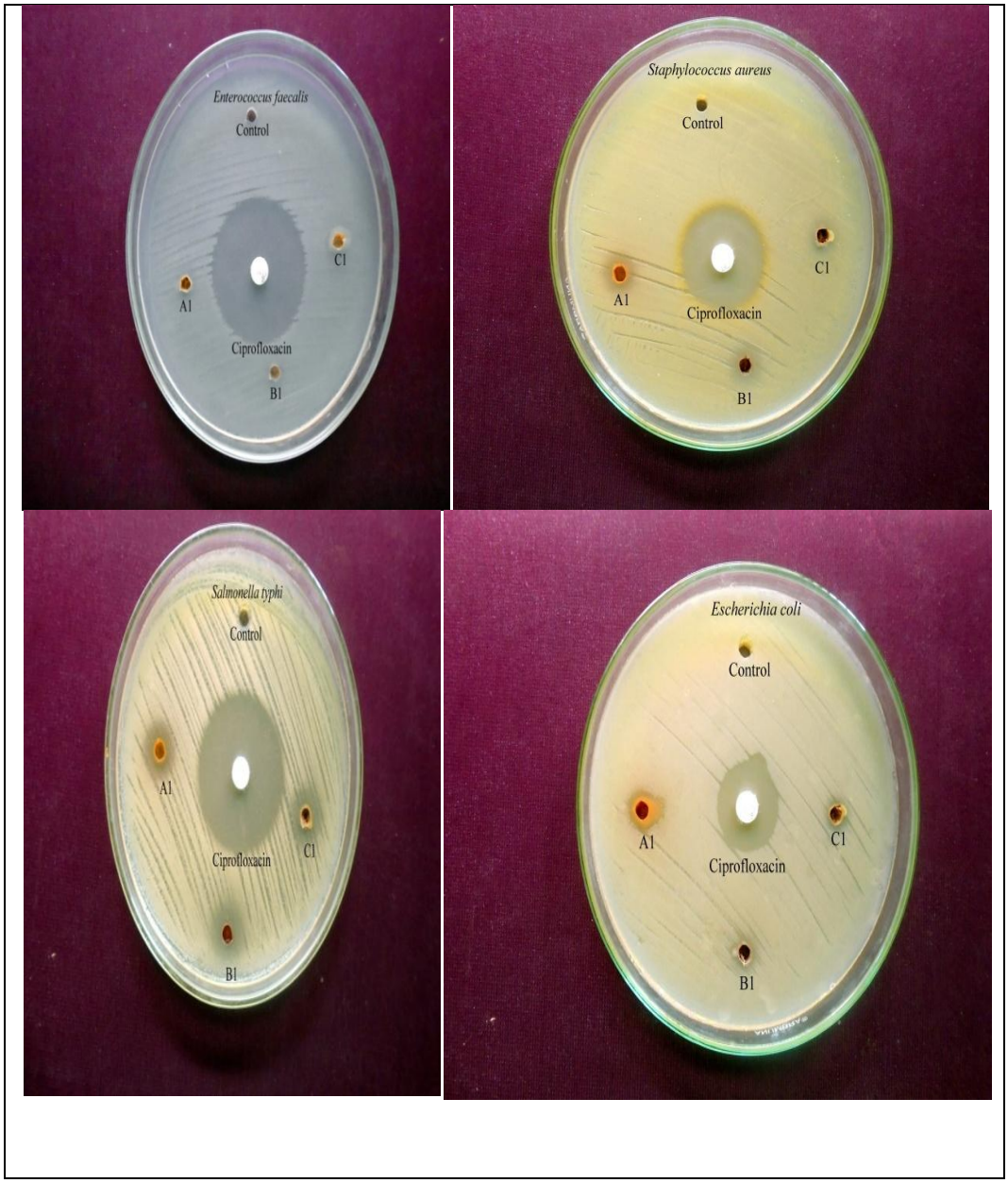

Figure 2. In vitro antibacterial activity data of s-triazine derivatives against tested organisms.

IV. Conclusion

We have successfully synthesizes a new series of chalcone derivatives and moreover, some compounds contains bioactive heterocyclic moiety. The antibacterial screening suggests that all the newly synthesized compounds showed moderate to good activity against the tested organism.

Acknowledgement

The author's wishes to express their thanks to, Department of chemistry, Thiruvalluvar university for providing laboratory facilities and also pondicherry university for spectral studies.

References

[1]. Dhar DN. Chem. Review 1981.
[2]. Bardia R, Rao JT. Asian. J. chem. 2004,16,1194.
[3]. Hussian MA. Indian J. Chem. 2001,40A, 324.
[4]. Ishida S, Matsuda A, Kawamura A. Chemotherapy.1960, 146.
[5]. Salvie D, Richard F, John A. Bio Org. Med. Chem. Lett.1998, 9, 8.
[6]. Vanstone AE , Maile GK, Nalbantoglu LK. Ger. Offen. DE. 1986, 3, 537, 207.
[7]. Prescott . Int. J. Clin. Pharmacol. Bio. Pharm.,1975,11(4), 332.
[8]. De vincenzo R, Seambla G, Panici P, Benedess, Remelletti FO. Anticancer. Drug Des. 1995, 10(6), 481-490.
[9]. Ahluwalia VK, Nayal L, Kaila N, Bala S, Tahim AK. India. J. Chem.1987, 26B, 384.
[10]. Modzelewska A, Pettit C, Achanta G, Davidson NE, Hunag P, Khan SR. Anticancer activities of novel chalcone and bischalcone. Bioorg. Med. chem. 2006, 14:10, 3491-3495.
[11]. Mehta KJ, Patel VS, Parikh AR. J. Indian chem. Soc.1978, 50, 241.
[12]. Pedersen AK, Fitzgereald GA, J. Pharm. Sci. 1985,74(2), 188.
[13]. Mishra SS, Kowhwaha CS. Indian. J.Chem. Soc.1977, 64, 640.
[14]. Brzozowski z, Kaminski Z. And Angielski S, Acta Pol. Chem. Abstr. 1980,93, 204525e.
[15]. Tomcufak AS, Wilkson RG, Child RG. German Patent .1975, 2502490.

IOSR Journal of Applied Chemistry (IOSR-JAC) is UGC approved Journal with Sl. No. 4031, Journal no. 44190.

M.Thamizhthendral. " Synthesis, Charecterization And Antibacterial Activity of Some Novel Chalcones And Its Derivatives." IOSR Journal of Applied Chemistry (IOSR-JAC) 11.8 (2018): 27-32.