International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.4, No.2, pp 677-681, April-June 2012

Syntheses & studies of biological evaluation of certain s- triazine derived compounds

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Abstract: Some novel compounds are synthesized using the substitution of chlorine in 2,4,6-trichloro-s-triazine by some moieties having structural as well as biological importance like benzimidazole and benzotriazole, substituted urea what not which are anti infective agents. In this manner **10** novel compounds are prepared and they are subjected to antibacterial screening prior to this the synthesized compounds are duly characterized by spectral analysis. These compounds reveal substantive antibacterial activities against some randomly chosen both gram +ve & gram-ve bacteria. The promising results are in support of the fact that the compounds are worth to be optimized for some novel drugs in future. The newly synthesized compounds were characterized using **IR**, ^{1}**H-NMR**.
Keywords: - Benzimidazole, Substituted urea, Benzotriazole, Cyanuric chloride and Antimicrobial. activity.

Introduction:

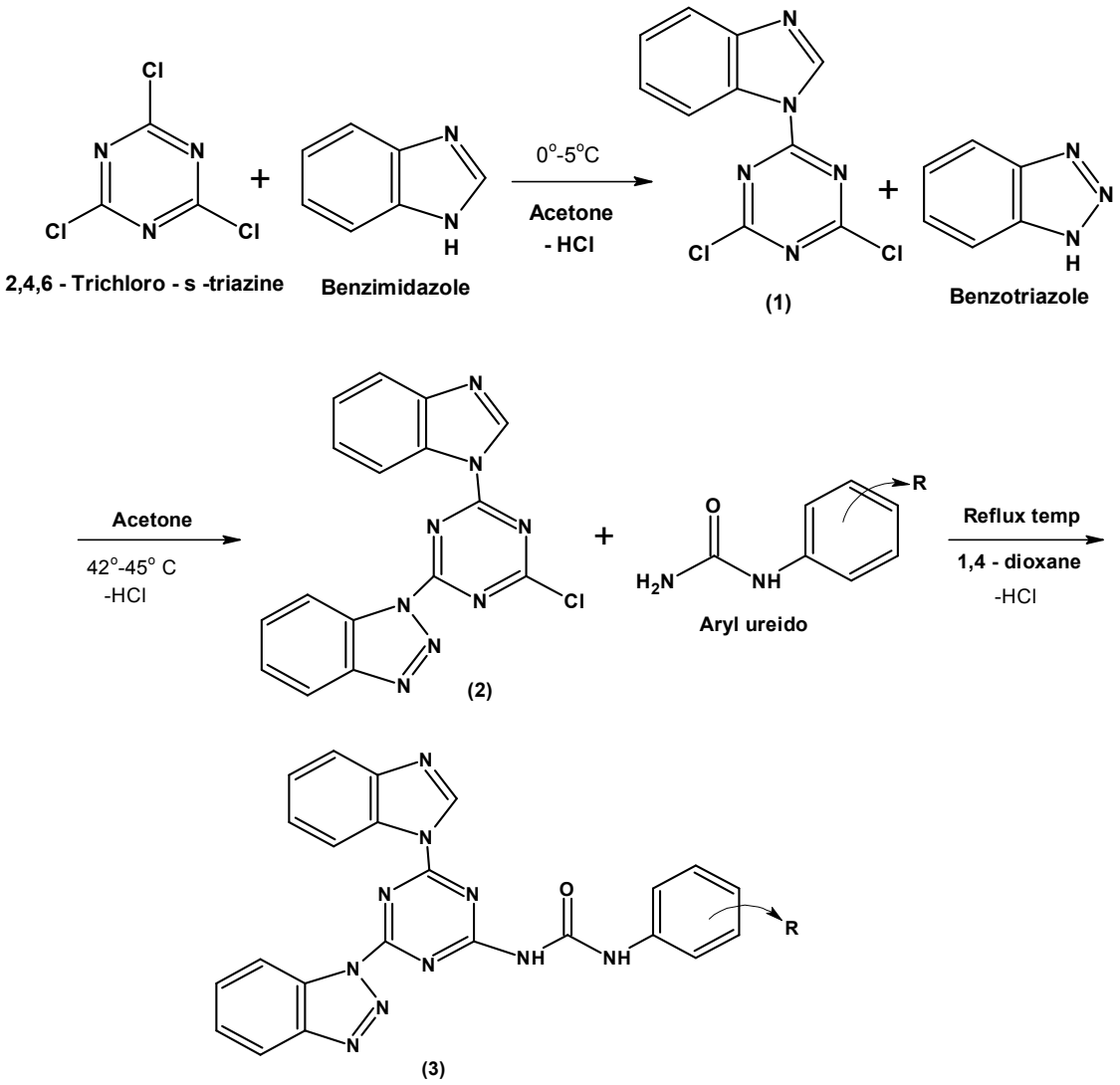
s-Triazine derivatives have important applications in the most significant fields of Organic Chemistry, including Medicinal[1,2], Materials[3-5]and Supramolecular Chemistry[6-10]. Cyanuric chloride (2,4,6-trichloro-1,3,5-triazine, TCT), is an inexpensive and mild reagent that has been widely used in organic reactions[11-16]. This reagent is available as a white powder of high purity and due to its specific structure and electronic properties, is used extensively in the dye and pharmaceutical industries[17]. Substituted s-triazine derivatives are an important class of compounds having anticancer[18], antitumor[19], antiviral[20] and antifungal[21] activities. These compounds have been used in the treatment of depression[22], and hence received a considerable therapeutics importance. These are valuable bases for estrogen receptor modulators[23] and also used as bridging agents to synthesize herbicides[24]. Further substituted s-triazines have been used as NLO materials, which have a wide range of applications in optoelectronics and telecommunications[25]. The preparation of *2-(Benz imidazol-1-yl)-4-(Benzotriazol-1-yl) -6-(aryl ureido) -s-triazine* using this reagent has not been reported to date.

Urea derivatives possess wide therapeutic activities, *i.e.,* antithyroidal[26], hypnotic and anesthetic[1][27], antibacterial[28], diuretic[29], anticancer[30], antimalarial[31], anticonvulsant[32] and anthelminitics activity.

Imidazole derivatives are effective drugs against hypertension, have good antibacterial and analgesics activity and reported exhibiting hypertensive properties. Some substituted imidazole derivatives have been prepared and used as antidiabetics, antihypertensive, antilipidemic and blood platelet aggregation inhibitors[33].

Material And Methods :

Melting points were determined by open glass capillary method and are uncorrected. The structures of these compounds have been confirmed from spectral analysis like FTIR, ^{1}H NMR (400 MHz).



Where R= Given in below table.

Table 1 :- Physical data of synthesized compounds:-

Compd	R	M.p.^{0}C	Yield %	Molecular Formula
3a	2-Cl	250	60.40	$C_{23}H_{15}ON_{10}Cl$
3b	3-Cl	265	59.70	$C_{23}H_{15}ON_{10}Cl$
3c	4-Cl	258	58.20	$C_{23}H_{15}ON_{10}Cl$
3d	H	270	59.15	$C_{23}H_{15}ON_{10}$
3e	4-Br	289	60.10	$C_{23}H_{15}ON_{10}Br$
3f	4-F	280	60.20	$C_{23}H_{15}ON_{10}F$
3g	2-OCH_3	140	59.20	$C_{23}H_{18}0_2N_{10}$
3h	4-OCH_3	145	58.80	$C_{23}H_{18}0_2N_{10}$
3i	2,4-Cl	262	59.25	$C_{23}H_{14}ON_{10}Cl_2$
3j	α-Naphthyl amine	272	61.25	$C_{27}H_{18}0N_{10}$

***2-(Benzimidazol-1- yl) -4,6,-dichloro-s-triazine* :**

To a stirred solution of cyanuric chloride (0.1 mole, 18.4 g.) in acetone (100 ml) at 0-5^{0}C, the solution of benzimidazole (0.1 mole, 11.8 g) in acetone (15 ml) was added and pH being maintained neutral by the addition of 10% sodium bicarbonate solution from time to time as per requirement of reaction condition. The stirring was continued at 0-5°C for 2 hours. After the completion of reaction the stirring was stopped and the solution was treated with crushed ice. The solid product obtained was filtered and dried. The crude product was purified by crystallization from absolute alcohol to get title compound.

2-(Benzimidazol-1-yl) -4-(benzotriazol-1-yl)-6-chloro-s-triazine:

To a stirred solution of 2-(Benzimidazol-1–yl)-4,6,-dichloro-s-triazine (0.1 mole, 26.6g) in acetone (100 ml) was added, the solution of benzotriazole (0.1 mole, 11.9) in acetone (25 ml) was added drop wise maintaining the temperature 40°C, the pH being maintained neutral by the addition of 10% sodium bi-carbonate solution from time to time as per requirement of reaction condition. The temperature was gradually raised to 45°C during two hours. After the completion of reaction, the resultant content was poured into ice cold water. The solid product obtained was filtered and dried. The crude product was purified by crystallization from absolute alcohol to get the title compound.

2-(Benzimidazol-1-yl)-4-(Benzotriazol-1-yl) -6-(aryl ureido)-s-triazine:

A mixture of 2-(Benzimidazol-1-yl) - 4-(benzotriazol-1-yl)-6-chloro-s-triazine (0.01 mole, 3.48g) and fluoro urea (0.01 mole) in 1,4-dioxane (22ml) was refluxed in oil bath. The temperature was gradually raised to 110-115^{0}C during four hours, the pH being maintained neutral by the addition of 10% sodium bicarbonate solution from time to time as per requirement of reaction condition. After the completion of reaction, the refluxed content was added to cold water. The solid product obtained was filtered and dried. The crude product was purified by crystallization from absolute alcohol.

(3a) IR (KBr,cm^{-1}) : 1598.7 cm^{-1} (-C=O- stretching in urea), 3298.7 cm^{-1} (-NH- stretching in urea), 1568.0 cm^{-1} (-NH- deformation in urea), 808.1 cm^{-1}(-C=N- stretching in s-triazine), 835.2 cm^{-1} (1,4- Disubstituted benzene), 1347.0 cm^{-1} (>N- stretching in 3^0 amine), 743.5 cm^{-1} (-C-Cl- stretching in aromatic ring). **) ^{1}H-NMR:δ** 9.10 (1H, s, NH), 7.96 (1H, s , NH), 7.0- 7.94 (12H, m, Ar-H).

(3c) IR (KBr,cm^{-1}) : 1591.3 cm^{-1} (-C=O- stretching in urea), 3310.1 cm^{-1} (-NH- stretching in urea), 1566.5 cm^{-1} (-NH- deformation in urea), 798.4 cm^{-1}(-C=N- stretching in s-triazine), 822.4 cm^{-1} (1,4- Disubstituted benzene), 1367.0 cm^{-1} (>N- stretching in 3^0 amine), 748.8 cm^{-1} (-C-Cl- stretching in aromatic ring). **) ^{1}H-NMR:δ** 9.12 (1H, s, NH), 7.82 (1H, s , NH), 7.27-7.70 (12H, m, Ar-H).

(3d) IR (KBr,cm^{-1}) : 1596.7 cm^{-1} (-C=O- stretching in urea), 3290.7 cm^{-1} (-NH- stretching in urea), 1560.0 cm^{-1} (-NH- deformation in urea), 808.6 cm^{-1}(-C=N- stretching in s-triazine), 830.2 cm^{-1} (1,4- Disubstituted benzene), 1344.0 cm^{-1} (>N- stretching in 3^0 amine), **^{1}H-NMR:δ** 9.08 (1H, s, NH), 7.93 (1H, s , NH), 7.01-7.91 (12H, m, Ar-H).

(3f) IR (KBr,cm^{-1}) : 1599.7 cm^{-1} (-C=O- stretching in urea), 3293.7 cm^{-1} (-NH- stretching in urea), 1565.0 cm^{-1} (-NH- deformation in urea), 808.1 cm^{-1} (-C=N- stretching in s-triazine), 832.2cm^{-1} (1,4- Disubstituted benzene), 1345.0 cm^{-1} (>N- stretching in 3^0 amine),1074.6 cm^{-1} (-C-F- stretching in aromatic ring). **^{1}H-NMR:δ** 9.08 (1H, s, NH), 7.93 (1H, s , NH), 7.01-7.91 (12H, m, Ar-H).

(3i) IR (KBr,cm^{-1}) : 1588.2 cm^{-1} (-C=O- stretching in urea), 3300.1 cm^{-1} (-NH- stretching in urea), 1560.5 cm^{-1} (-NH- deformation in urea), 800.4 cm^{-1}(-C=N- stretching in s-triazine), 820.7 cm^{-1} (2,4- Disubstituted benzene), 1360.0 cm^{-1} (>N- stretching in 3^0 amine), 740.8 cm^{-1} (-C-Cl- stretching in aromatic ring). **) ^{1}H-NMR:δ** 9.25 (1H, s, NH), 7.85 (1H, s , NH), 7.20-7.60 (11H, m, Ar-H).

Antimicrobial Activity

For the testing antimicrobial activity various microorganism were used for the study. The **agar plate** method was used for this study. Following general procedure is adopted. The antimicrobial activity of all the compounds was studies at 1000 ppm concentration *in vitro*. The different types of microorganism used were some gram negative bacteria [*Escherichia coli, STB*] gram positive bacteria [*Bacillus subtilis*, *Staphylococcus aureus*].

80% DMSO are used as solvent to dissolve compound 1a to 1i to 10**(μg/ml).**

Table 2 :- MIC Results for different compounds

compound	R	Bacterial Strains		Bacterial Strains	
		S.aureus	B.subtilis	E-coli	STB
3a	2-Cl	15 µg/ml	40 µg/ml	10 µg/ml	15 µg/ml
3b	3-Cl	20 µg/ml	50 µg/ml	15 µg/ml	20µg/ml
3c	4-Cl	-	-	200µg/ml	300 µg/ml
3d	H	500 µg/ml	-	400 µg/ml	-
3e	4-Br	-	-	300 µg/ml	-
3f	4-F	200 µg/ml	-	150 µg/ml	200 µg/ml
3g	2-OCH_3	20 µg/ml	50 µg/ml	20 µg/ml	25 µg/ml
3h	4-OCH_3	300µg/ml	400 µg/ml	350 µg/ml	-
3i	2,4-Cl	15 µg/ml	50 µg/ml	15 µg/ml	20µg/ml
3j	α-Naphthyl amine	80 µg/ml	-	100 µg/ml	
Std drug	Chloramphenicol	20 µg/ml	60 µg/ml	20 µg/ml	30 µg/ml
Std drug	Tetracyline	25 µg/ml	50 µg/ml	20 µg/ml	20 µg/ml

Results and discussion :

Benzimidazole was condensed with 2,4,6-trichloro-s-triazine, which was further condensed with benzotriazole and the later on condensed with various aryl urea. The physical and analytical data are presented in Table 1. Antibacterial activities of the compounds were determined by Agar diffusion method[17]. The results are presented in Table 2. Among the compounds 3a was found to be more active against other all compounds. The aryl urea and benzimidazole moieties create structural crowding and various allosteric sites. On the other hand all three groups are providing sufficient electronic pressure to make it more active.

Acknowledgements: The authors would like to thanks to the department of Chemistry, Shree Jayendrapuri Arts & Science College, Bharuch, for providing necessary infrastructure to carry out the syntheses & thanks are also due to the Department of Micro-Biology for antibacterial screening. We are also grateful to S.A.I.F. Division, Punjab University, Chandigarh for getting different spectra on subsidized payment.

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