Available online at www.joac.info

ISSN: 2278-1862

Journal of Applicable Chemistry

2016, 5 (4): 871-876

(International Peer Reviewed Journal)

Synthesis and Characterizations of Substituted 1, 3, 5-triazine -2, 4, 6-triamines as Biological Potent Agents

D. M. Vashi*, K. B. Kurmi, T.V.Patel

Department of Chemistry, Narmada College of science & commerce, Bharuch, Gujarat, **INDIA**

Email: Talha.patel9@gmail.com

Accepted on 16th July 2016

ABSTRACT

Some novel 1, 3, 5-triazine-2, 4, 6- triamines have been synthesized and characterized by elemental analyses, IR and NMR. The products have been tested for their antibacterial activity against gram (+)ve and gram (-)ve bacteria.

Keywords: Sulfonamide, Substituted thiourea, Cyanuric chloride and antibacterial activity.

INTRODUCTION

Cyanuric chloride (2, 4, 6 trichloro 1,3,5 triazine) is an extremely important compounds that find wide spread application in dye chemistry[1], agriculture[2] textile industry. The displacement of chlorine atom by the nucleophile such as amine, alcohol and Phenol has been well documented [3] and wide substituted product prepared. The s triazine based chalcone and their derivatives have been their own important in heterocyclic chemistry due to their good biological activities [4]. Several derivatives of s- triazines show: antibacterial [5], Antimicrobial [6], herbicidal [7] activities. The replacement of a Cl atom in cyanuric chloride by basic group is greatly facillated by the ring N atom. The symmetrically build s triazine nucleus. The s triazine have been shows a wide range of therapeutic activities[8-11] such as antibacterial, fungicidal, anti malarial, anticancer, antiviral, antiulcer, antiarthritic, local anaesthetic, anticonvulsant, algaecide, disinfectant, hypoglycerimic, analgesic, sedative, anti-inflammatory, anthelmintic and antitubercular activities. Sulphonamides have a variety of biological activities such as antibacterial,[12-14] insulin releasing, [15] carbonic anhydrase inhibitory, [16-17] anti-inflammatory, [18] and antitumor[19] activities. These findings encouraged us to explore the synthesis of sulphonamides containing thiazole/benzothiazole moieties and to examine their antibacterial and antifungal properties. Thiourea is important organic compound: possess high biological activity, act as corrosion inhibitors and antioxidant, and are polymer components [20]. Thiourea and urea derivatives show a broad spectrum of biological activities as anti-HIV, antiviral, HDL-elevating, antibacterial and analgesic properties [21-24]. Acyl thiourea derivatives are well known for wide range of biological activities like bactericidal, fungicidal, herbicidal, insecticidal action and regulating activity for plant growth [25-26]. In this paper we present the syntheses, characterization and in-vitro antibacterial activity of the tri-substituted-1,3,5-triazine derivatives. The structures of these compounds have been confirmed from spectral analysis like FTIR, ^{1}H NMR (400 MHz) and elemental analysis.

We have already reported some of our work on the synthesis and biological properties of various cyanuric chloride derivatives [27-32]. These compounds were screened for their antibacterial and antifungal activities and it was found that some of them have moderate to good biological properties. The biological significance of this class of compounds impelled us to continue working on the synthesis of new cyanuric chloride derivatives.

MATERIALS AND METHODS

All the melting points were taken in open capillaries tube and are uncorrected. The purity of compounds was checked routinely by TLC (0.5 mm thickness) using silica gel – G coated Al – plates (Merck) and spots were visualized by exposing the dry plates in iodine vapors. IR spectra were recorded on FTIR spectrophotometer using KBr technique.^{1}H NMR spectra on a Varian 400 FT MHz NMR instrument at using $CDCl_3$ as solvent and TMS as internal reference..

Synthesis: The triazines described were synthesized starting from cyanuric chloride (2, 4, 6-trichloro-1, 3, 5-triazine) and different nucleophiles. The chlorine atoms of cyanuric chloride can be replaced successively by substituted or non– substituted different amino groups. The nucleophiles can selectively displace the different chlorines by controlling the reaction temperature.

In general, the first chlorine can be displaced while the temperature is maintained at 0-5^{0}C, the second between 27-50^{0}C and the third substitution happens at reflux temperature. Other important factors that have to be considered for the preparation of the different derivatives are the nature of the reactive group and the order of entry of the group.

When different amino groups are introduced; the less reactive one is introduced before the more reactive one. The reactions, in most cases, are carried out in aqueous suspensions, since the products precipitate from solution, simplifying their isolation. To increase the reactivity and the yield, the cyanuric chloride is previously dissolved in acetone and then poured into ice-water to get a very fine suspension. The reaction of cyanuric chloride with different amines gives 2-sustituted-4,6-dichloro-1,3,5-triazines[33]. The 2,4-disubstituted-6-chloro-1,3,5-triazines are obtained by reaction of a further amine with the 2-substituted-4,6-dichloro-1,3,5-triazine in the presence of base. The displacement of the last chlorine is carried out at reflux temperature affording the product in good yields .The product had a low solubility in most organic solvents, except DMSO. However, purification was achieved by recrystalization from methanol-water solution. The elegance of this method lies in its simplicity in use and handling to achieve the desired target. The reaction process is shown in fig. 1 and obtained various products presented in table 1.

Table 1: Various Substituted compounds

Compounds	R1	R2	R3
1a	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	4-Cl
1b	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	2-Cl
1c	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	2-CH_3
1d	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	3-CH_3
1e	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	4-CH_3
1f	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	4-Br
1g	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	4-OCH_3
1h	*N*-(4-sulfamoylphenyl)benzamide	4-(dipropylamino)-3,5-dinitrobenzenesulfonamide	4-F

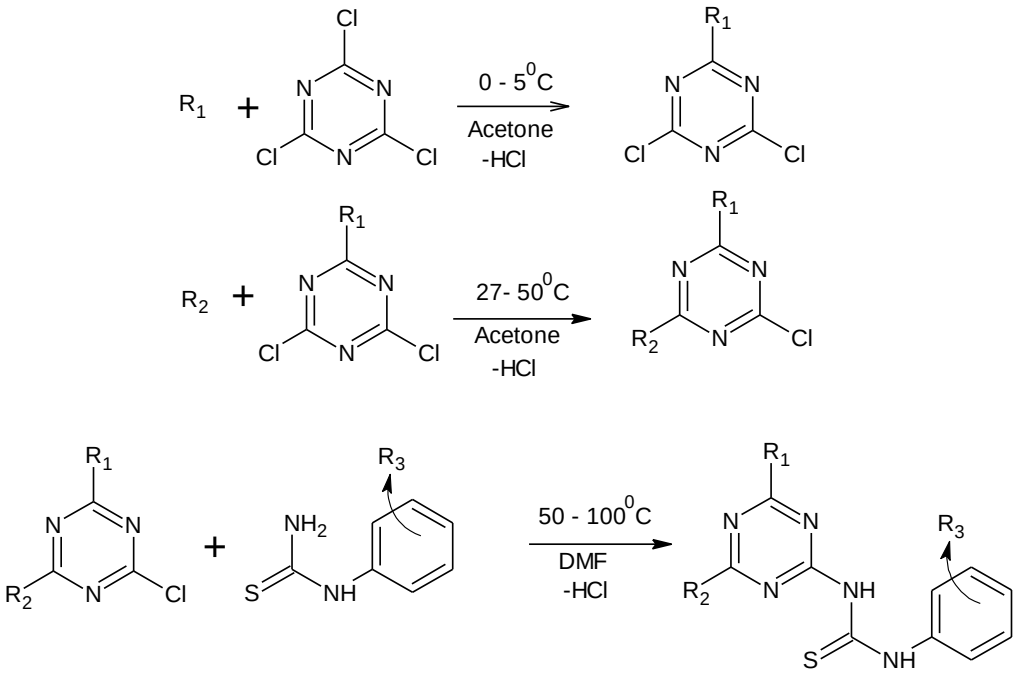

Fig 1. Reaction procedure

RESULTS AND DISCUSSION

Cyanuric chloride derivatives were synthesized and characterized for their structure elucidation. The Physical and Analytical data is given in table 2. Various chemical and spectral data supported the structures thought of. From the zone of inhibition of different compounds, it is obvious that the compound 1g and1h is the strongest of all. The above all activities are quiet interesting and further study on the molecule is essential.

Table 2: Physical and Analytical Data

Comp no	MP ^{0}C	Yield %	M.F	Calcd (%) Observed (%) C	H	N	IR(in KBr) Wave number in cm^{-1}	^{1}H NMR In $CDCl_3$ (δppm)
1a	181-183^{0}C	69.40	$C_{35}H_{34}ClN_{11}O_9S_3$	47.53 47.50	3.88 3.85	17.42 17.40	780.4 cm^{-1} (-C=N stretching in S-triazine) 3392.2 cm^{-1} (-NH- stretching in secondary amine 750.4 cm^{-1} (-C-Cl- stretching in aromatic ring)	7.02 to 7.98 aromatic protons 9.92 –NH Singlet 1H
1b	177-179^{0}C	68.20	$C_{35}H_{34}ClN_{11}O_9S_3$	47.53 47.51	3.88 3.84	17.42 17.39	776.2 cm^{-1} (-C=N stretching in S-triazine) 3389.6 cm^{-1} (-NH- stretching in secondary amine 748.5 cm^{-1} (-C-Cl- stretching in aromatic ring)	6.94 to 7.96 aromatic protons 9.87 –NH Singlet 1H
1c	158-160^{0}C	71.18	$C_{36}H_{37}N_{11}O_9S_3$	50.05 50.01	4.32 4.27	17.83 17.79	783.4 cm^{-1} (-C=N stretching in S-triazine) 3392.4 cm^{-1} (-NH- stretching in secondary amine 2921.5 cm^{-1} (-C-CH_3 stretching in aromatic ring)	7.02 to 7.98 aromatic protons 9.87 –NH Singlet 1H 2.54 -3H, Singlet CH_3,

1d	162-164^{0}C	69.80	$C_{36}H_{37}N_{11}O_9S_3$	50.05 50.02	4.32 4.28	17.83 17.79	781.3 cm^{-1} (-C=N stretching in S-triazine) 3387.2 cm^{-1} (-NH- stretching in secondary amine 2926.3 cm^{-1} (-C-CH_3 stretching in aromatic ring)	7.04 to 7.96 aromatic protons 9.87 –NH Singlet 1H 2.57 -CH_3, Singlet 3H,
1e	168-170^{0}C	67.15	$C_{36}H_{37}N_{11}O_9S_3$	50.05 50.03	4.32 4.29	17.83 17.80	778.4 cm^{-1} (-C=N stretching in S-triazine) 3394.7 cm^{-1} (-NH- stretching in secondary amine 2928.8 cm^{-1} (-C-CH_3 stretching in aromatic ring)	7.03 to 7.92 aromatic protons 9.87 –NH Singlet 1H 2.57 -CH_3, Singlet 3H
1f	188-190^{0}C	71.40	$C_{35}H_{34}BrN_{11}O_9S_3$	45.26 45.24	3.69 3.66	16.59 16.55	782.8 cm^{-1} (-C=N stretching in S-triazine) 3393.2 cm^{-1} (-NH- stretching in secondary amine 584.1 cm^{-1} (-C-Br stretching in aromatic ring)	6.98 to 7.96 aromatic protons 9.80 –NH Singlet 1H
1g	149-151^{0}C	66.90	$C_{36}H_{37}N_{11}O_{10}S_3$	49.14 49.11	4.24 4.20	17.51 17.48	774.9 cm^{-1} (-C=N stretching in S-triazine) 3391.4 cm^{-1} (-NH- stretching in secondary amine	7.01 to 7.97 aromatic protons 9.83 –NH Singlet 1H 3.93 (3H, Singlet -OCH3)
1h	157-159^{0}C	68.67	$C_{35}H_{34}FN_{11}O_9S_3$	48.44 48.40	3.95 3.91	17.75 17.72	783.5 cm^{-1} (-C=N stretching in S-triazine) 3390.3 cm^{-1} (-NH- stretching in secondary amine 1114.1 cm^{-1} (-C-F stretching in aromatic ring)	6.98 to 7.99 aromatic protons 9.82 –NH Singlet 1H

APPLICATIONS

Antibacterial Screening: The in-vitro antibacterial activities of the above synthesized compounds are done against Gram +ve strains and against Gram –ve strains using agar cup method. The zone of inhibition was measured in mm. All the compounds reported in table-2 are tested at 2mg mL^{-1} concentration under similarly controlled condition of experiments carried out by using Chloramphenicol (50µg mL^{-1}) as a standard for a comparison and the results are shown in table 3.

Table 3: In-vitro antibacterial activity of trisubstituted-s-triazines. Zone of inhibition in mm (Concentration: 50 µg mL^{-1})

Compound	E-coli	S-typhae	B.Subtilis
1a	12	14	14
1b	14	16	24
1c	12	12	25
1e	16	14	22
1f	18	26	28
1g	16	24	32
1h	14	22	20
(Standard drug) Chloramphenicol (50µg mL^{-1})	18	24	20

ACKNOWLEDGEMENTS

The authors would like to thanks to the department of Chemistry, Narmada College of science & commerce, Bharuch, for providing necessary infrastructure to carry out the syntheses & also thanks to Norrish Pharma Company for antibacterial screening. We are also grateful to S.A.I.F. Division, Punjab University, and Chandigarh for getting different spectra on subsidized payment.

REFERENCES

[1] A Johnson, *The theory of colourisation of textile society of dyes and colourists*. *U.K*, **1989.**
[2] D H Hutsaon, T R Robert, *Progress in a pesticide biochemistry and toxicology, Wiley, Tornoto*, **1987**.
[3] H E Fierz Daviel and M Matter, *J Soci. Dyes Colour*, **1937**, 53, 424.
[4] D Dhake, *Indian J. Chem.* **1971**, 9, 1415.
[5] A S Gajare, S Shingarem, *Indian J.Chem.* **1998**, 37B, 510.
[6] P S Desai, K R Desai, *Indian Chem. Soci*, **1994**, 77, 155.
[7] N Nishimura, A Kato, *Carbohyd. Res.*, **2001**, 77, 331.
[8] S R Dighade, S D Patil, M M Chincholkar, N R Dighade, *Asian.Chem*, **2003**, 15(2), 1184.
[9] A Solanki, I Thakur, *Indian J .Chem*, **2006**, 45B, 513.
[10] A Solanki, J Patel, *Indian J.Chem*, **2004**, 43B, 1588, 2004.
[11] K R Desai, R B Patel, P S Desai, K H Chikhalia, *J. Indian Chem. Soci*, **2003**, 80, 138.
[12] A.K.Gadad,C.S. Mahajanshetti,S. Nimbalkar,A. Raichurkar, *Eur . J. Med.Chem*, **2000**, *35(9), 853.*
[13] V.S.Misra,V.K. Saxena, R.J. Srivastava, *Indian Chem. Soc*, **1982**, *59*, 781.
[14] F. Zani, P.Vicini, *Arch. Pharm*. **1998**, *331*, 219.
[15] T.H. Maren, *Ann. Rev. Pharmacol. Toxicol.* **1976,** *16*, 309.
[16] C.T. Supuran,A, Scozzafava, B.C. Jurca,M.A. Iiies, *Eur. J. Med. Chem*, **1998**, *33*, 8.
[17] G.Renzi,A. Scozzafava, C.T. Supuran, *Bioorg. Med. Chem. Lett*, **2000**, *10(7*), 673.
[18] J. J.Li,D. Anderson, E.J.Burton, K.Seibert,A.W. Veenhuizem, Y. Zang, D.B. Reitz, *J.Med. Chem*, **1995**, 38, 4570.
[19] H.YoshinoUeda, N. Niijma, J. Sugumi, H. Kotake, Y. Koyanagi, N.Yoshimatsu, *Med. Chem*.**1992**, *35*, 2496.
[20] A. R. Katritzky and M. F. Gordeev, *J. Chem. Soc., Perkin* **1991**, 1: 2199-2203.
[21] M. Struga, J. Kossakowski, E. Kedzierska, S. Fidecka and J. Stefanska, *Chem. Pharm. Bull*, **2007**, 55(5): 796-799.
[22] A. D. Desai, D. H. Mahajan and K. H. Chikhalia, *Ind. J. of Chem.*, **2007**, 46B: 1169-1173.
[23] R. B. Patel, K. H. Chikhalia, C. Pannecouque and E. D. Clercq, *J. Braz. Chem. Soc*., **2007**, 18(2): 312-321.

[24] G. A. Kilcigil and N. Altanlar, *Turk J. Chem.*, **2006**, 30: 223-228.
[25] S. Xue, J. Shan Zou and H. Yong, *Chin. Chem. Letters*, **2000**, 11(1), 19-20.
[26] C. Fengling, C. Yanrui, L. Hongxia, Y. Xiaojun, F. Jing and L. Yan, *Chinese Science Bulletin*, **2006**, 51(18): 2201-2207.
[27] K. N. Sarmah, T. V. Patel, *Scholars research library ,Archives of Applied Science Research*, **2011**, 3 (6):428-436.
[28] K. N. Sarmah, N. K. Sarmah, T. V. Patel, K. V. Kurmi, *International Journal Of Computational Engineering Research , IJCER*, **2012**, 2, 2, 289-229.
[29] N. K. Sarmah, K. N. Sarmah, T. V. Patel, K. V. Kurmi, *Scholars research library, Archives of Applied Science Research*, **2012**, 4 (2):805-808.
[30] K. N. Sarmah, N. K. Sarmah, T. V. Patel, K. V. Kurmi, *International Journal of Chem Tech Research*, **2012**, 4, 2, 677-681.
[31] K. N. Sarmah, N. K. Sarmah, T. V. Patel, K. V. Kurmi, *Pelagia Research Library, Advances in Applied Science Research*, **2012**, 3 (3):1459-1462.
[32] N. K. Sarmah, K. N. Sarmah and Talha V. Patel, *Journal of Applicable Chemistry*, **2014,** 3 (5):1936-1944.
[33] O. Diels, Zur Kenntnis der cyanurverbindungen, *Ber. Dtsch.Chem..Ges*, **1899**, 32, 691 702.

AUTHOR ADDRESS

1. **D. M. Vashi**
Department of Chemistry,
Narmada College of science & commerce,
Bharuch, Gujarat, INDIA
E-mail: Talha.patel9@gmail.com