WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 16, 512-518. Research Article ISSN 2277– 7105

SYNTHESIS, SPECTRAL AND BIOLOGICAL STUDIES OF SOME s-TRIAZINE DERIVATIVES OF 1-(1-(4METHXYPHENYL)ETHYL) CYCLOHEXANOL

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Article Received on
04 October 2017,

Revised on 25 October 2017,
Accepted on 15 Nov. 2017

DOI: 10.20959/wjpr201716-10039

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ABSTRACT

With the help of some new synthetic protocols a series of s-triazine derivatives with aliphatic and aromatic urea along with 1-(1-(4-methoxyphenyl)ethyl)cyclohexanol is prepared. All the synthesized compounds of this series were characterized by spectral analysis using IR, and ^{1}H NMR spectroscopy. Biological activities were evaluated for the selected synthesized derivatives. Some of the compounds were found good active against different gram positive, gram negative or fungal stains.

KEYWORDS: aromatic urea, s-triazine, antimicrobial activity, cyanuric chloride, antifungal.

INTRODUCTION

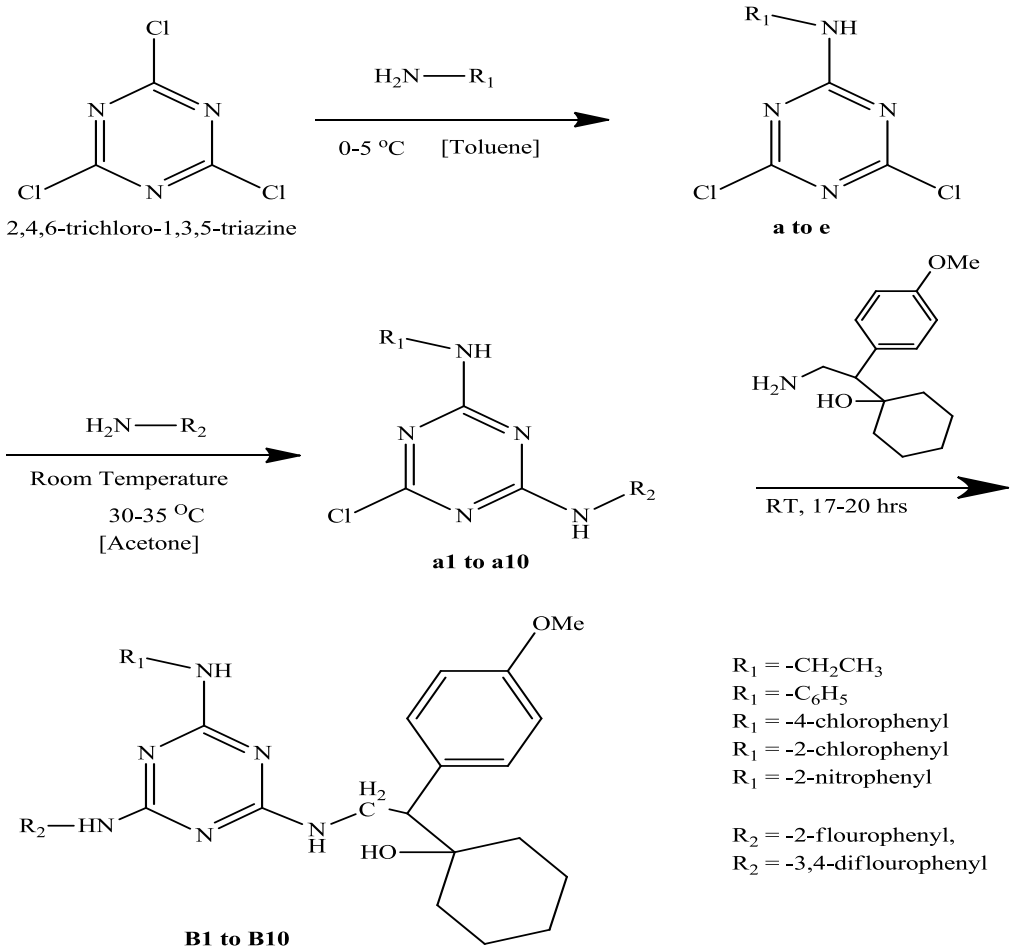
S-triazine derivatives are of great interest among the researchers in medicinal chemistry. It is due to their vital role in many biological processes and synthetic drugs. The replacement of all three chlorine atoms in the molecule of cyanuric chloride by basic groups is greatly facilitated by the ring nitrogen atoms of the symmetrically built s-triazine moiety. These derivatives of s-triazine are reported as antimalarials[1], anticancer agents[2], anti-protozoals[3], antimicrobials[4], antitumour[5], anti-inflammatory[6], antibacterial[7], antiviral[8] and many more. Due to these diversified activities in the present work we have synthesized a series of s-triazine derivatives and the compounds were evaluated for their biological activities.

MATERIAL AND METHODS

All the chemicals and reagents used in the work were of analytical grade and used without further purification. All the melting points were determined on SUNBIM apparatus by open glass capillary method and were uncorrected. The reactions were monitored by thin layer chromatography (TLC) using silica gel-G coated standard aluminum plates and spots were visualized under UV radiation. IR spectra were recorded on Bruker ALPHA FTIR spectrophotometer in KBr pellets. The H-NMR spectra were recorded on Bruker Avance II spectrometer in d-DMSO. Chemical shifts relative to TMS used as internal standard were obtained in d unit.

EXPERIMENTAL

As cyanuric chloride contains three chloro groups which can replaced by three different amine groups at three different temperatures viz. 0-5^{O}C, room Temperature and at 45-50^{O}C. The synthesis work was carried out in three steps.



Scheme: Synthesis of s-triazine derivatives of 1-(1-(4-methoxyphenyl)ethyl) cyclohexanol.

Step-1*: Preparation of 4,6-dichloro-N(substituted phenyl)-1,3,5-triazin-2-amine*

In the ice bath at 0-5^{o}C mixture of toluene and cyanuric chloride was stiired and then allowed to react with different amines with adjusting pH by bicarbonate solution. Getting reaction completion indication from TLC, reaction mass was added in crushed ice. This mixture is further stirred for half an hour and separated solids **(a to e)** were filtered and re-crystallized in absolute ethanol.

Step-II*: Preparation of aromatic floroamine derivatives of 4,6-dichloro-N(substituted phenyl)-1,3,5-triazin-2-amine*

In the second step products **(a to e)** were treated with aromatic flouro-amines(equimolecular) at room temperature in acetone for 17-20 hours with constant stirring. After completing the TLC check reaction was stopped for each compound and reaction mass was poured in to the ice cold water the solid product **(a1 to a10)** were filtered washed and purified.

Step-III*: Preparation of aromatic floroamine derivatives of 4,6-dichloro-N(substituted phenyl)-1,3,5-triazin-2-amine with 1-(2-amino-1-(4-methoxyphenyl)ethyl)cyclohexanol.*

Products of step-II (**a1** to **a10)** were taken in 80 ml acetone in an RBF and added 1-(2-amino-1-(4-methoxyphenyl) ethyl)cyclohexanol the mass was refluxed at 50 to 60 ^{o}C with constant stirring on heating mental. The pH was kept neutral by using diluted bicarbonate solution. After TLC check the reaction mass was poured in chilled distilled water. Again the pH of the solution was made 7. After constant stirring about half an hour the solid products were obtained. All the compounds **(B1 to B10)** were filtered, washed and re-crystallized in pure ethanol. physical properties of compounds prepared in this work are given in the table-1.

Table 1: Physical properties of compounds.

Compound	MF (MW)	M.P.	Yield (%)	Elemental Analysis		
				C% Cal., (found)	H% Cal., (found)	N% Cal., (found)
B1	$C_{26}H_{33}FN_6O_2$ 480.58	138	61	64.98, (64.99)	6.92, (6.91)	17.49, (17.50)
B2	$C_{30}H_{31}FN_6O_2$ 528.62	125	56	68.16, (68.16)	6.29, (6.31)	15.90, (15.90)
B3	$C_{30}H_{32}ClFN_6O_2$ 562.23	167	47	63.99, (63.98)	5.73, (5.74)	14.93, (14.92)
B4	$C_{30}H_{33}FN_6O_2$ 563.07	154	55	63.99, (63.97)	5.73, (5.75)	14.93, (14.94)
B5	$C_{30}H_{32}FN_7O_4$ 573.62	98	41	62.82, (62.81)	5.62, (5.63)	17.09, (17.08)
B6	$C_{26}H_{32}F_2N_6O_2$	106	65	62.64, (62.65)	6.47, (6.46)	16.86, (16.86)

	498.57					
B7	$C_{30}H_{32}F_2N_6O_2$ 546.61	89	43	65.92, (65.50)	5.90, (5.92)	15.37, (15.35)
B8	$C_{30}H_{31}ClF_2N_6O_2$ 581.06	118	56	62.01, (62.02)	5.38, (5.38)	14.46, (14.45)
B9	$C_{30}H_{31}ClF_2N_6O_2$ 581.06	97	58	62.01, (62.02)	5.38, (5.37)	14.46, (14.46)
B10	$C_{30}H_{31}F_2N_7O_4$ 591.61	151	51	60.91, (60.91)	5.28, (5.28)	16.57, (16.57)

RESULTS AND DISCUSSIONS

The results of characterization of the synthesized compounds are as follows.

1-(2-((4-(ethylamino)-6-((2-fluorophenyl)amino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxy phenyl)ethyl)cyclohexanol (B1): IR(KBr)cm^{-1}: 3463(O-H str), 3351 (N-H str) 2969(C-H aromatic), 1410 (C-C), 1130(C-O-C methoxy), 1020(C-F). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.14(t, 3H), 1.49-1.68(m, 10H), 3.08(t, 1H), 3.46(m, 2H), 3.48(d, 2H) 3.65(s, 1H), 3.83(s, 3H), 6.78-7.79 (m, 8H) 9.67(t, 1H), 13.58 (s, 2H).

1-(2-((4-((2-fluorophenyl)amino)-6-(phenylamino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B2): IR(KBr)cm^{-1} : 3484(O-H str), 3356 (N-H str) 2963(C-H aromatic), 1423 (C-C), 1143(C-O-C methoxy), 1032(C-F). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.29-1.39(m, 10H), 3.08(t, 1H), 3.47(d, 2H) 3.67(s, 1H), 3.88(s, 3H), 6.61-7.63(m, 13H) 9.98(t, 1H), 14.18 (s, 2H).

1-(2-((4-((4-chlorophenyl)amino)-6-((2-fluorophenyl)amino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B3): 3455(O-H str), 3361(N-H str) 2923(C-H aromatic), 1442 (C-C), 1142(C-O-C methoxy), 1027(C-F), 693(C-Cl). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.21(t, 2H), 2.21-2.50(m, 10H), 3.28(t, 1H), 3.81(s, 3H), 4.23(s, 1H), 6.98-8.32(m, 12H) 9.63(t, 1H), 11.37 (s, 2H).

1-(2-((4-((2-chlorophenyl)amino)-6-((2-fluorophenyl)amino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B4): 3469(O-H str), 3366(N-H str) 2930(C-H aromatic), 1449 (C-C), 1153(C-O-C methoxy), 1029(C-F), 701(C-Cl). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.22(t, 2H), 2.25-2.53(m, 10H), 3.29(t, 1H), 3.78(s, 3H), 4.41(s, 1H), 6.61-8.20(m, 12H) 9.71(t, 1H), 13.81(s, 2H).

1-(2-((4-((2-fluorophenyl)amino)-6-((2-nitrophenyl) amino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B5): 3510(O-H str), 3385(N-H str) 2927C-H aromatic), 1451 (C-C), 1140(C-O-C methoxy), 1034(C-F). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.13(t, 2H), 2.09-2.33(m, 10H), 3.09(t, 1H), 3.88(s, 3H), 4.12(s, 1H), 6.56-8.05(m, 12H) 10.02(t, 1H), 14.11(s, 2H).

1-(2-((4-((3,4-difluorophenyl)amino)-6-(ethylamino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B6): 3445(O-H str), 3363 (N-H str) 2958(C-H aromatic), 1435 (C-C), 1134(C-O-C methoxy), 1017(C-F). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.16(t, 3H), 1.43-1.63(m, 10H), 3.07(t, 1H), 3.41(m, 2H), 3.45(d, 2H) 3.70(s, 1H), 3.88(s, 3H), 6.55-7.39 (m, 7H) 9.77(t, 1H), 12.98 (s, 2H).

1-(2-((4-((3,4-difluorophenyl)amino)-6-(phenylamino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B7): 3464(O-H str), 3348 (N-H str) 2957(C-H aromatic), 1438 (C-C), 1167(C-O-C methoxy), 1041(C-F). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.43-1.68(m, 10H), 3.11(t, 1H), 3.47-3.50(d, 2H) 3.68(s, 1H), 3.71(s, 3H), 6.54-7.61(m, 12H) 9.77(t, 1H), 13.76 (s, 2H).

1-(2-((4-((4-chlorophenyl)amino)-6-((3,4-difluorophenyl)amino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B8): 3474(O-H str), 3358(N-H str) 2944(C-H aromatic), 1452 (C-C), 1139(C-O-C methoxy), 1013(C-F), 695(C-Cl). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.23(t, 2H), 2.19-2.35(m, 10H), 3.21(t, 1H), 3.83(s, 3H), 4.13(s, 1H), 6.55-7.79(m, 11H) 9.88(t, 1H), 12.96 (s, 2H).

1-(2-((4-((2-chlorophenyl)amino)-6-((3,4-difluorophenyl)amino)-1,3,5-triazin-2-yl) amino) -1-(4-methoxyphenyl)ethyl)cyclohexanol (B9): 3478(O-H str), 3386(N-H str) 2947(C-H aromatic), 1438 (C-C), 1123(C-O-C methoxy), 1015(C-F), 699(C-Cl). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.21(t, 2H), 2.15-2.44(m, 10H), 3.33(t, 1H), 3.62(s, 3H), 4.22(s, 1H), 6.68-8.11(m, 11H) 9.55(t, 1H), 12.92(s, 2H).

1-(2-((4-((3,4-difluorophenyl)amino)-6-((2-nitrophenyl)amino)-1,3,5-triazin-2-yl)amino)-1-(4-methoxyphenyl)ethyl)cyclohexanol (B10): 3525(O-H str), 3377(N-H str) 2954(C-H aromatic), 1434 (C-C), 1121(C-O-C methoxy), 1066(C-F). **^{1}H NMR (DMSO-d$_6$, δ) ppm**: 1.28(t, 2H), 2.39-2.53(m, 10H), 3.18(t, 1H), 3.69(s, 3H), 4.31(s, 1H), 6.56-7.89(m, 11H) 9.91(t, 1H), 13.31(s, 2H).

BIOLOGICAL ACTIVITIES

Selected synthesized compounds were evaluated for their antimicrobial potential against two selected gram +ve bacterial organism (E. coli & P. aeruginosa), two selected gram –ve bacterial organisms (S. aureus & S. pyogenus) as well as three selected fungal organisms (C. albicans, A. niger & A. clavatus) by Broth dilution method. The minimal inhibition concentrations(MIC) of synthesized molecules and the reference standard drugs are given in the Table-2. The effects of the synthesized molecules were compared with the reference drugs like Ampicillin, Chloramphenicol, & Ciprofloxacin for antibacterial tests and Nystatin & Greseofulvin for anti fungal activity tests.

Table 2: Antibacterial activities for the selected compounds.

Compound	Minimal Inhibition Concentration (µg/mL)						
	E. coli	***P. aeruginosa***	***S. aureus***	***S. pyogenus***	***C. albicans***	***A. niger***	***A. clavatus***
B3	200	200	250	100	1000	>1000	>1000
B4	125	250	100	250	1000	>1000	>1000
B7	100	62.5	200	200	1000	>1000	>1000
B9	100	250	250	200	>1000	500	500
B10	250	200	100	200	500	500	1000
Ampicillin	100	--	250	100	--	--	--
Chloramphenicol	50	50	50	50	--	--	--
Ciprofloxacin	25	25	50	50	--	--	--
Nystatin	--	--	--	--	100	100	100
Greseofulvin	--	--	--	--	500	100	100

CONCLUSION

The series of the selected compounds was synthesized with good to moderate yields. From the biological data it was come to know that compound B7 contains potential activity against ***P. aeruginosa.*** *and* ***E. coli*** while all other compounds are moderate to less active against selected species. In the case of fungicidal effects compound B10 found moderate active against ***C. albicans***. All other compounds are lees active or inactive against selected fungal species.

ACKNOWLEDGEMENT

The authors are thankful to the Principal and Head Department of Chemistry and Library of B. K. M. Science College, Valsad for laboratory facilities and library Facilities, VGEC Chandkheda for IR spectral analysis, Central Instrumentation Laboratory Chandigarh for elemental analysis and Micro Care Laboratory for biological evaluation.

REFERENCES

1. Agarwal, A., Srivastava, K., Puri, S.K., Chauhan, P.M.S., Bioorg. *Med. Chem. Lett*, 2005; 15: 531–533.
2. Menicagli, R., Samaritani, S., Signore, G., Vaglini, F., Via, L.D., *J. Med. Chem.*, 2004; 47: 4649–4652.
3. Balini A., Bueno G.J., Stewart M. L., Yardley V., Brun R., Barrett P. M. *J. Med. Chem.*, 2005; 48: 5570–5579.
4. Koc Z. E., Bingol H., Saf A. O., Torlak E. and Coskum A. *J. Hazard. Mater*, 2010; 183: 251–255.
5. Menicagli R., Samatani S., Signore G., Valgini F. and Via L. D., *J. Med. Chem.*, 2004; 47: 4649.
6. El-Massry A. M., *Heterocycl Commun*, 1999; 5: 555.
7. Jyoti M., Shirodkar V., and Mulwad V., *Indian J. Chem.*, 2003; 42B: 621-626.
8. Cinranesh E., *Rev. Chem. (Bucharest)*, 1954; 5: 425.