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Review article

Triazines – A comprehensive review of their synthesis and diverse biological importance

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ABSTRACT

Triazine is a heterocyclic aromatic ring structure, with three isomers distinguished by positions of their nitrogen atoms. 1,2,3-triazine derivatives like tubercidin, toyocamycin, sangivamycin, 2-azaadenosine and 2-aza-2-desamino-5,8-dideazafolic acid are the important active moieties in pharmaceutical field while 6-azacytosine, 6-azauracil, azaribine, tirapazamine, dihydromethyl furalazine, vardenafil, apazone, lamotrigine, ceftriaxone, pymetrozine, fervenulin (planomycin), reumycin and toxoflavin (panthothricin) are 1,2,4-triazine moieties used in clinical practices. The triazine ring structure is also found in naturally occurring antibiotics like fervenulin, reumycin and toxoflavin. 1,3,5-Triazine isomer or s-triazine is an oldest known organic compound, broadly used as a lead structure in ammeline, aceto-guanide, acetoguanamine, cyanuric acid and melamine. Some s-triazine containing drugs are hexamethylmelamine (altretamine), 2-amino-4-morpholino-s-triazine, hydroxymethyl-pentamethyl melamine, triethylenemelamine (tretamine), dioxadet, irsogladine, cycloguanil, almitrine, S9788 and DW1865. Triazines have a high significance in the field of pharmaceutical chemistry with wide-spectrum of pharmacological activities so useful for design and formation of novel drugs. Some triazine analogues are recently screened in clinical trials which may lead to potent type drugs with no side effects as presently available pharmacological agents. This review outlines the biological importance and synthesis of various types of triazine derivatives from various heterocyclic and drugs containing triazine moiety.

INTRODUCTION

Heterocycles are the ring compounds that contain one or more diverse ring atoms (i.e. atom other than carbon like N, O, S, P, B, Si, As and Se). Five and six-membered compounds are the most important heterocyclic systems. These are main class compounds which include more than 50% of all well-known organic compounds. They can be drugs, vitamins and natural products (Morrison et al., 2004). In the ancient times, synthesis of heterocyclic compounds was important because of its broad application. Heterocyclic compounds obtained from nature are important to life (Khalil et al., 2011). In life science industry and industrial field's related to fine and special chemistry, heterocyclic compounds showed important role (Patel et al., 2007). They consist of a class of natural and synthetic products; some of them showed good pharmacological property (Elgazwy et al., 2006).

Triazines have a unique position in pharmaceutical chemistry. It is worked as protecting groups in natural chemistry. Triazines are reactive groups and flexible for different synthetic transformations (Dawane et al., 2010). Triazine is a six-membered heterocyclic compound with empirical formula $C_3H_3N_3$. Its structure is analogous to the benzene ring in which three carbons of the ring are substituted by nitrogen atoms. Due to different position of nitrogen atoms in the ring, triazine are found in three isomeric forms (Fig. 1)

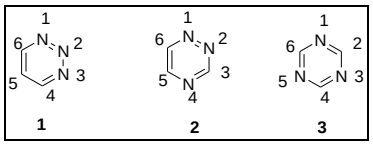


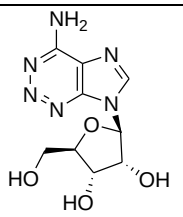
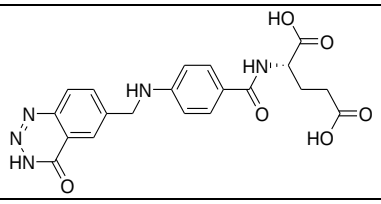
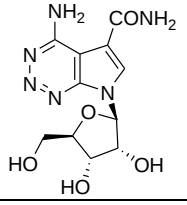
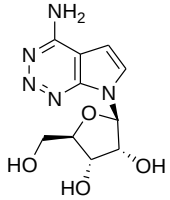
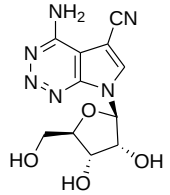
Fig. 1. Isomeric forms of triazine: **1** (1,2,3-triazine); **2** (1,2,4-triazine); **3** (1,3,5-triazine)

Pyridines (with one ring nitrogen atom), diazines (with two ring nitrogen atoms) and tetrazines (with four ring nitrogen atoms) are other aromatic nitrogen heterocyclic compounds. As compare to pyridine, Triazine compounds are weaker bases (Yu et al., 2008).

1,2,3-Triazine

1,2,3-Triazine derivatives are the new member of heterocyclic compounds. In older literature, V-triazine or β-triazine are also found along with 1,2,3-triazine isomer (Biesele, 1952, Simons et al., 1963). Heterocyclic moiety fused with 1,2,3-triazine-4-ones show high chemically-reactivity and biological activity (Stevens et al., 1976). As a comparison with 1,2,4- and 1,3,5-triazine isomers, the 1,2,3-triazine isomer is the least studied isomer because the nucleus of 1,2,3-triazine isomer is the least stable as compare to rest isomers and synthetic routes are also limited (Butler et al., 2006). Newly discovered 1,2,3-triazines are more effective drugs along with less adverse effects (Biesele, 1952; Simons et al., 1963). Tubercidin, toyocamycin, sangivamycin, 2-azaadenosine and 2-aza-2-desamino-5,8-dideazafolic acid are the 1,2,3-triazine moiety containing drugs which show different pharmacological activities. The drugs containing 1,2,3-triazine moiety and their biological activities are shown in Table 1.

Table 1. Drugs containing 1,2,3-triazine moiety.

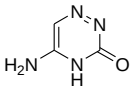
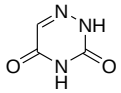
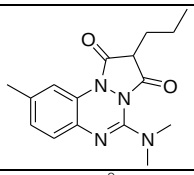
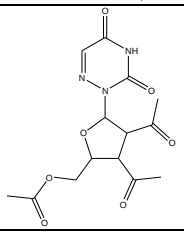
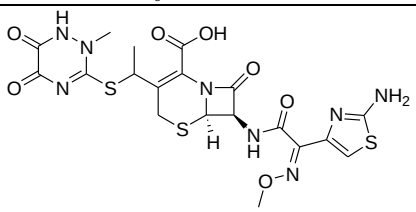
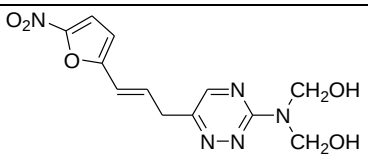
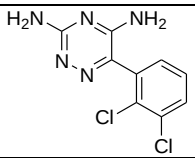
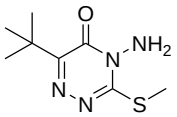
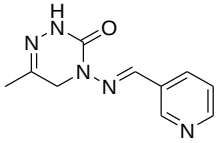
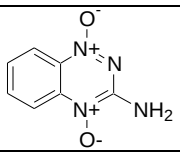
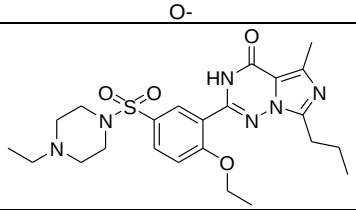
S.No.	Name of compound	Structure	Uses	Reference
1.	2-Azaadenosine		Cytotoxic agent	Montgomery and Thomas, 1972
2.	2-Aza-2-desamino-5,8-dideazafolic acid		Thymidylate synthase inhibitor	Roeowsky et al., 1992
3.	Sangivamycin		Anticancer agent	Brockman, 1983; Robins and Revankar, 1985
4.	Tubercidin		Antimicrobial activity by inhibiting DNA, RNA and protein synthesis	Nishimura et al., 1966; Bergstrom et al., 1984
5.	Toyocamycin (Antibiotic)		Anticancer agent	Cohen and Glazer, 1985; Renau et al., 1994

1,2,4-Triazine

The 1,2,4-triazine derivatives, obtained from synthetic and natural sources, have different biological activity (Simons et al., 1953). 1,2,4-Triazine compound and its condensed derivatives with the heterocyclic ring, showed the application in various fields as pharmaceuticals, agriculture, dyes, pesticides, and herbicides (Diana et al., 2002). 6-Azacytosine, 6-azauracil, azaribine, tirapazamine, dihydromethyl furalazine, vardenafil, apazone, lamotrigine, ceftriaxone, pymetrozine, fervenulin (planomycin), reumycin and toxoflavin (panthothricin) are 1,2,4-triazine moiety containing drugs which show different pharmacological activities. Naturally occurring antibiotics like fervenulin (planomycin), reumycin and toxoflavin (panthothricin) are N-methyl derivatives of 1,2,4-

triazines. The microwave assisted one-pot solvent-free synthesis of 3,5,6-trisubstituted-1,2,4-triazines was carried out from fatty acid hydrazides together with their antimicrobial activity (Rauf et al., 2007).

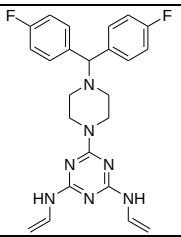
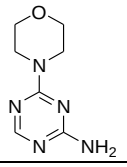
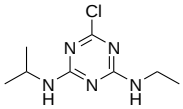
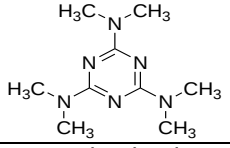
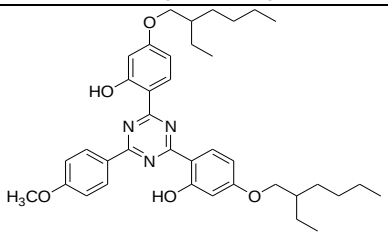
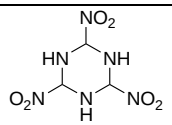
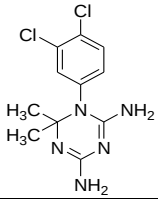
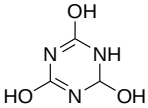
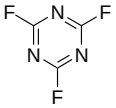
Table 2. Drugs containing 1,2,4-triazine moiety.

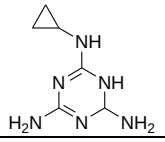
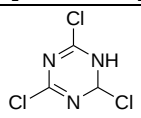
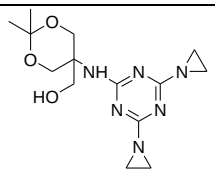
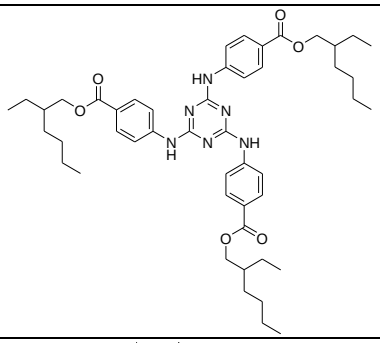
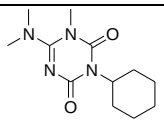
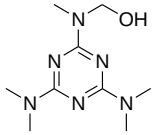
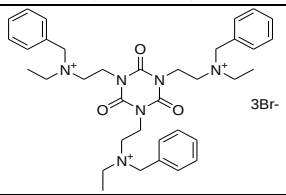
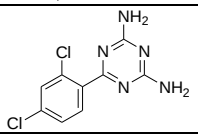
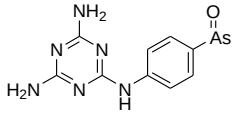
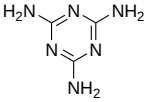
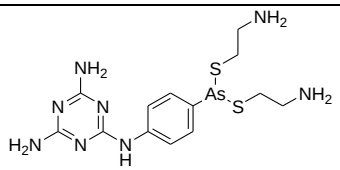
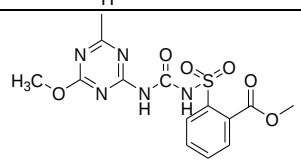
S.No.	Name of compound	Structure	Uses	Reference
1.	6-Azacytosine		Antiviral and antitumor activities	Sidwell et al., 1968; Falke and Rada, 1970; Creasey et al., 1963
2.	6-Azauracil		Antiviral and antitumor activities	Sidwell et al., 1968; Falke and Rada, 1970; Creasey et al., 1963
3.	Apazone		Anti-inflammatory and analgesic activities	Tripathi, 2003; Lemke et al., 2010
4.	Azaribine		Antiviral, antifungal agents and also in treatment of psoriasis	Negwer, 1987
5.	Ceftriaxone (Third generation cephalosporin antibiotic)		Broad spectrum antimicrobial agent	Lemke et al., 2010; Ucherek et al., 2008
6.	Dihydromethyl furalazine		Wide spectrum antibacterial agent	Kobari et al., 1970
7.	Lamotrigine		Anticonvulsant drug and also in the treatment of bipolar depression	Tripathi, 2003; Lemke et al., 2010
8.	Metribuzin		Herbicide	Curran, 1999
9.	Pymetrozine		Insecticide	Ucherek et al., 2008
10.	Tirapazamine		Anticancer agent by inducing DNA damage in poorly oxygenated tumour cells	Sarkar et al., 2010
11.	Vardenafil		Used for treatment of erectile dysfunction by inhibiting phosphor-diesterase-5	Arnold, 2004

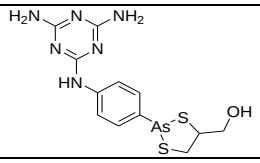
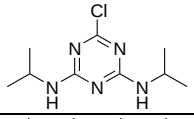
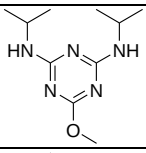
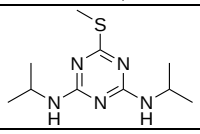
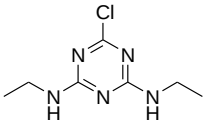
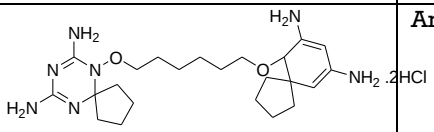
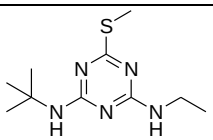
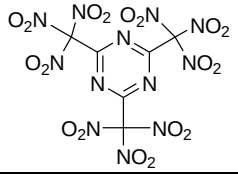
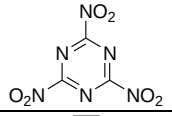
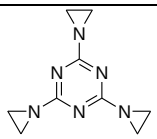
1,3,5-Triazine or s-triazine

1,3,5-triazine isomer also called as s-triazine due to the symmetry of three nitrogen in the ring. This isomer is an oldest known organic compound. 1,3,5-Triazines represent a broadly used lead structure with remarkable applications in various fields (Vora et al., 2009). s-Triazine derivatives are an important class of compounds showing many pharmacological activities (like antimicrobial activities) (Dawane et al., 2010). Ammeline, aceto-guanide, acetoguanamine, cyanuric acid, and melamine are the 1,3,5-triazine moiety-containing compounds (Simons et al., 1953). Due to various applications in different fields, 1,3,5-triazines are a well-known class of compounds from a long time and still continue of considerable interest (Afonso et al., 2006). Hexamethylmelamine (altretamine), 2-amino-4-morpholino-s-triazine, hydroxymethyl-pentamethylmelamine, dioxadet, irsogladine, triethylenemelamine (tretamine), cycloguanil, almitrine, S9788 and DW1865 are s-triazine containing drugs. The drugs containing 1,3,5-triazine moiety are given in Table 3.

Table 3. Drugs containing 1,3,5-triazine moiety.

S. No.	Name of compounds	Structure	Uses	Reference
1.	Almitrine (Duxil)		Respiratory stimulant	Dhainaut et al., 1996
2.	2-Amino-4-morpholino-s-triazine		Antitumor agent	Arya and Dandia, 2007
3.	Atrazine		Herbicide, production of some dyes and explosives.	Tomassetti et al., 2015
4.	Altretamine (Hexalen)		Antineoplastic agent	Lemke et al., 2010
5.	Bemotrizinol		Added to sunscreens to absorb UV rays	Ngan, 2012
6.	Cyclotrimethylenetrinitramine (or RDX)		Widely used as an explosive nitroamine widely used in military and industrial	Woody et al., 1986
7.	Cycloguanil		A cyclic metabolite of antimalarial drug proguanil which is plasmodial dihydrofolate reductase inhibitor	Tripathi, 2003
8.	Cyanuric acid		Precursor or a component of bleaches, disinfectants and herbicides.	Huthmacher and Most, 2005
9.	Cyanuric fluoride		Precursor for fibre-reactive dyes and as a fluorinating agent	Boudakian, 1994

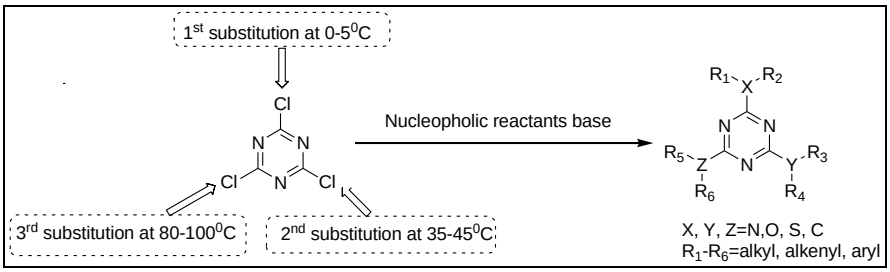
10.	Cyromazine (A cyclopropyl derivative of melamine)		Insecticide, acaricide and in veterinary medicine as ectoparasiticide.	Caldas, 1969
11.	Cyanuric chloride		A catalyst to develop new synthetic molecule; starting material for dyes and cross-linking agents; used to form triazine class pesticides, especially atrazine.	Huthmacher and Most, 2000
12.	Dioxadet		Antitumor agent	Bespalov et al., 2011
13.	Ethylhexyl triazine		Used in sunscreens to absorb UVB radiation	Herzog et al., 2009
14.	Hexazinone		A broad spectrum herbicide	Curran, 1999
15.	Hydroxymethylpentamethylmelamine		Major active form of Altretamine	Arya and Dandia, 2007
16.	Isocyuronium Bromide		Myorelaxation drug	Dobryanskii et al., 1998
17.	Irsogladine		Anti-gastric ulcer agent	Saczewski et al., 2006
18.	Melarsen oxide		Antitrypanosomal agent	Steverding, 2010
19.	Melamine		Pesticide, fire retardants in polymer resins	Ingelfinger, 2008
20.	Melarsomine (Melaminylthioarsenate)		Trypanocidal agent	Bonagura and Twedt, 2013
21.	Metsulfuron-methyl		Residual sulfonylurea herbicide	Appleby et al., 2002

22.	Melarsoprol		For the treatment of human African trypanosomiasis and Chagas disease	Steverding, 2010
23.	Propazine		Herbicide	Yang and Ngo, 2012
24.	Prometon		Herbicide	Yang and Ngo, 2012
25.	Prometryn		Herbicide	Fishel, 2016
26.	Simazine		Herbicide	Tomassetti et al., 2015
27.	SIPI 1029		Antitrypanosomal agent	Bacchi et al., 1998
28.	Terbutryn		Herbicide	Yang and Ngo, 2012
29.	2,4,6-Tris(trinitromethyl)-1,3,5-triazine		Used as an oxygen source, or added to oxygen-poor explosives to increase their power	Shastin, 2003
30.	Trinitrotriazine		Potential explosive	Li, 2008
31.	Triethylenemelamine		Used in Chemotherapy	Kar, 2010

Although triazine derivatives are aromatic compounds since their resonance energy is less than benzene. s-triazine shows more frequent nucleophilic aromatic substitution and difficult electrophilic aromatic substitution reactions. Triazine ring can be worked as a building block or linker for biologically active materials, dyeing, carbohydrate, protein modifiers, dendrimers, gene therapy and polymer synthesis. Selective nucleophilic displacement reactions of Cl atoms from 1,3,5-triazine by nitrogen (N), oxygen (O) or sulphur (S) are possible under temperature control (Pal et al., 2005).

Symmetric distribution of ring nitrogen atoms of 1,3,5-triazine nucleus facilitated substitution of a Cl atom of cyanuric chloride ($C_3Cl_3N_3$) by a basic group (Vora et al., 2009). Nature of any substituent and special characters of the ring are responsible for reactivity of triazines. In alkyl substituted triazines, electron withdrawing properties of triazine ring enhance acidity of the hydrogen (H) atoms in the α-methylene (-CH_2) group which allows alkylation, acylation, and condensation reactions to be performed on them (Shastin and GodoviKova, 1997).

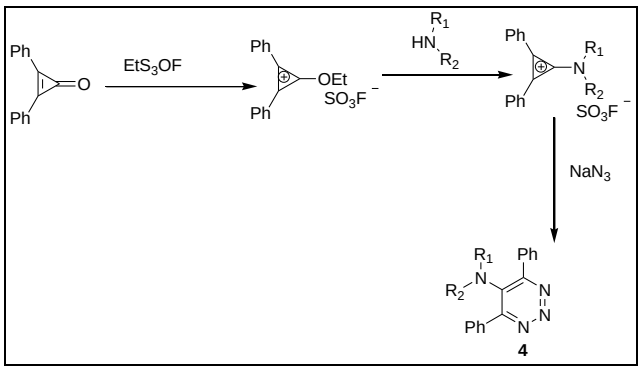
More restriction to the free rotation is caused by the formation of a stronger bond by an amino group (an electron-donating group) at positions 2, 4 or 6 of 1,3,5-triazine (Afonso et al., 2006). A reaction of the synthesis of 2,4,5-substituted s-triazine derivatives from cyanuric chloride is given in Scheme 1.



Scheme 1. Synthesis of 2,4,5-substituted s-triazine derivatives from cyanuric chloride.

General synthesis of 1,2,3-triazine derivatives

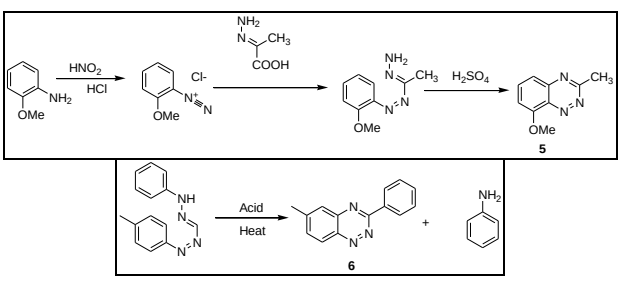
1. Aminodiethyl fluorosulfate prepared from diphenylcyclopropenone by ethylation with ethyl fluorosulfate, followed by treating with a secondary amine in one-pot operation (Scheme 2). The resulting salt reacted with sodium azide (NaN_3) to form 1,2,3-triazine derivatives (**4**) in a significant yield (Yoshida et al., 1985).



Scheme 2. Synthesis of 1,2,3-triazine derivatives from diphenylcyclopropenone.

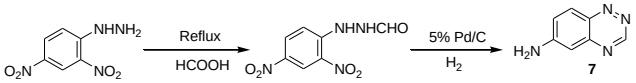
General synthesis of 1,2,4 triazine

1. Bamberger triazine synthesis - This is a classic method of triazine synthesis which was first reported by Eugen Bamberger in 1892. An aryl diazonium salt is formed by reaction between the corresponding aniline with $NaNO_2$, HCl and hydrazone of pyruvic acid. Then azo intermediate is converted into benzotriazine (**5**) with help of H_2SO_4 in CH_3COOH (Scheme 3). On the other hand, the phenyl azo derivative is converted into phenyl benzotriazine derivative (**6**) in the presence of acid (Hassner and Stumer, 2002).



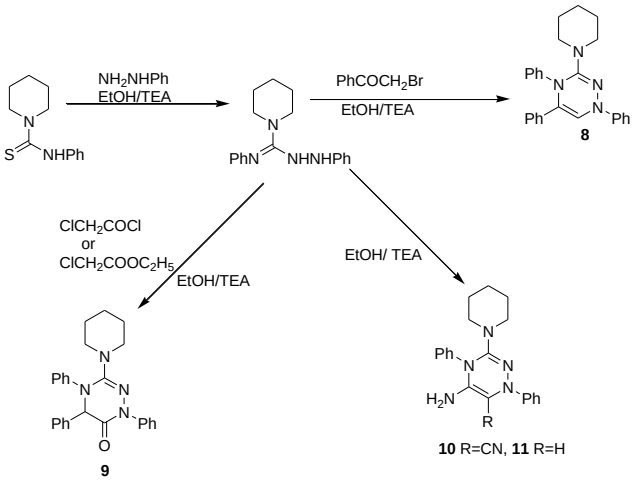
Scheme 3. Synthesis of benzotriazine derivatives.

2. Bischler triazine synthesis - Benzo[e][1,2,4]-triazin-6-amine (**7**) is prepared by ring closere of o-nitrophenylhydrazine via NO_2 to NH_2 reduction (Hassner and Namboothiri, 2012) (Scheme 4).



Scheme 4. Synthesis of 1,2,4-triazine derivatives.

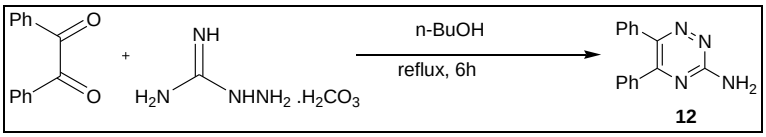
3. N,N-Diphenylpiperidine-1-carbohydrazonamide with phenacyl bromide, ethyl chloroacetate, or chloroacetyl chloride, bromomalononitrile, chloroacetonitrile formed 1,4,5-triphenyl-3-(piperidin-1-yl)-1,4-dihydro-1,2,4-triazine (**8**), 1,4,5-triphenyl-3-(piperidin-1-yl)-4,5-dihydro-1,2,4-triazin-6(1H)-one (**9**), 5-amino-1,4-diphenyl-3-(piperidin-1-yl)-1,4-dihydro-1,2,4-triazine-6-carbonitrile (**10**) and **1**,4-diphenyl-3-(piperidin-1-yl)-1,4-dihydro-1,2,4-triazin-5-amine (**11**), respectively (Omran and Amer, 2006) (Scheme 5).



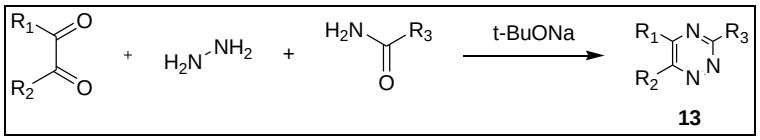
Scheme 5. Synthesis of 1,2,4-triazine derivatives from N,N-diphenylpiperidine-1-carbohydrazonamide.

4. 3-Amino-5,6-diphenyl-1,2,4-triazine (**12**) was synthesised by refluxing dibenzoyl with aminoguanidine bicarbonate in normal butanol followed by washing of a precipitate with a mixture of diethyl ether and hexane (50%) (Scheme 6). This method is a simple and efficient (Musatov et al., 2008).

5. 1,2,4-Triazine derivatives (**13**) were synthesised from alkyl amide (R_3CONH_2), hydrazine (NH_2NH_2) and 1,2-dicarbonyl compounds in the presence of a base (Phucho et al., 2008) (Scheme 7).

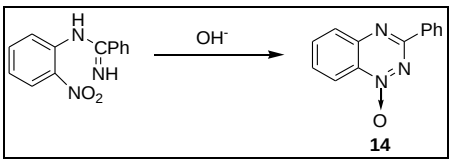


Scheme 6. Synthesis of 3-amino-5,6-diphenyl-1,2,4-triazine.



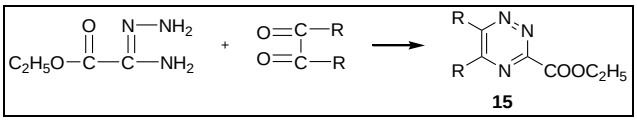
Scheme 7. Synthesis of 1,2,4-triazines derivatives.

6. 3-Phenyl-benzo-1,2,4-triazine 1-oxide (**14**) was synthesized from N-o-nitrophenylbenzamide in basic medium (Robbins et al., 1957) (Scheme 8).



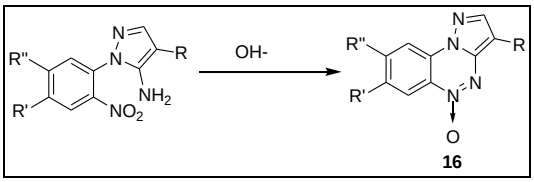
Scheme 8. Synthesis of 3-phenyl-benzo-1,2,4-triazine 1-oxide.

7. 1,2,4-Triazine derivatives (**15**) were formed by condensation of ethyl oxalamidrazonate with diketo derivatives (R=H, $COOC_2H_5$) (Paudler et al., 1966) (Scheme 9).



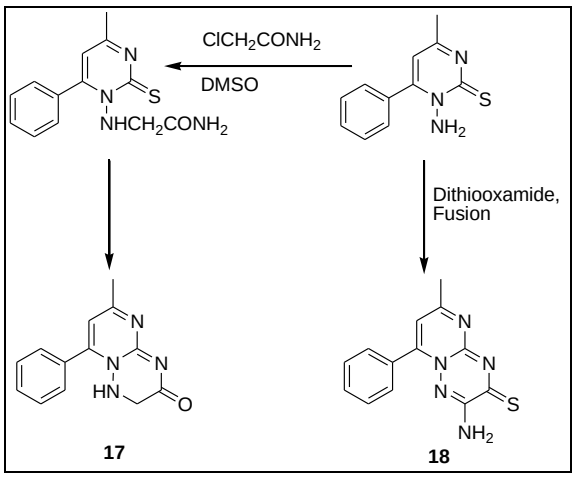
Scheme 9. Synthesis of 1,2,4-triazine derivatives.

8. Pyrazolo[5,1-*c*][1,2,4]benzotriazine 5-oxide (**16**) was prepared from 1-(2-nitrophenyl)-5-amino-pyrazole by cyclization in 10% sodium hydroxide solution at room temperature (Costanzo et al., 1994) (Scheme 10).



Scheme 10. Synthesis of pyrazolo [5,1-*c*] [1,2,4]benzotriazine 5-oxide.

9. Triazine analogue **17** was synthesised by refluxing 1-amino-4-methyl-6-phenyl pyrimidin-2-thione with chloroacetamide. Triazine derivative **18** was formed by fusing dithiooxamide with 1-amino-4-methyl-6-phenyl pyrimidin-2-thione at 175 °C for 4 h (Al-Issa, 2013). A synthesis of pyrimido[3,2-b]-1,2,4-triazine analogs is given in Scheme 11.



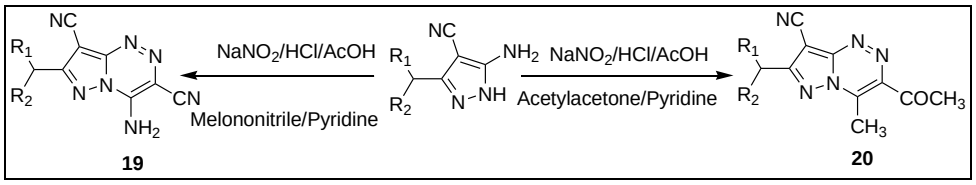
Scheme 11. Synthesis of pyrimido[3,2-b]-1,2,4-triazine analogs.

10. 5-Aminopyrazoles with $NaNO_2$ and concentrated HCl were diazotized to corresponding hydrazonium chloride. Then, it was reacted with acetylacetone and malononitrile in pyridine to form corresponding hydrazono derivatives. In presence of glacial acetic acid, these hydrazone derivatives were converted into compounds **19** and **20** (Al-Adiwish et al., 2013). A synthesis of pyrazolo[5,1-c][1,2,4]triazines (**19** and **20**) is given in Scheme 12.

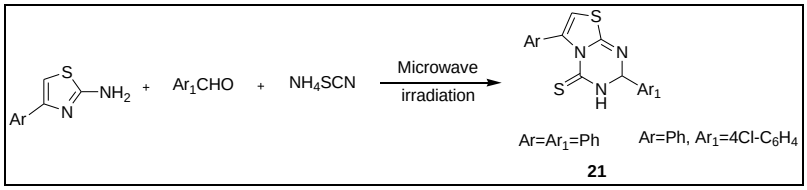
General synthesis of 1,3,5 triazine

1. Thiazolo-s-triazine nucleobases (**21**) were formed by reaction of -amino-4-arylthiazoles, Ar_1CHO and NH_4SCN in microwave irradiation (Yadav et al., 2007) (Scheme 13).

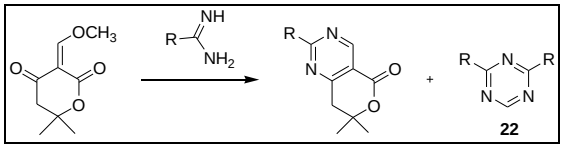
2. When 3,4-dihydropyrane-2,4-diones reacted with aromatic amidines, 2,4-diaryl-1,3,5-triazines (**22**) and pyrano(4,3-d)pyrimidines were formed (Wessing et al., 1995). A synthesis of thiazolo-s-triazine nucleobases is given in Scheme 14.



Scheme 12. Synthesis of pyrazolo[5,1-c][1,2,4]triazines

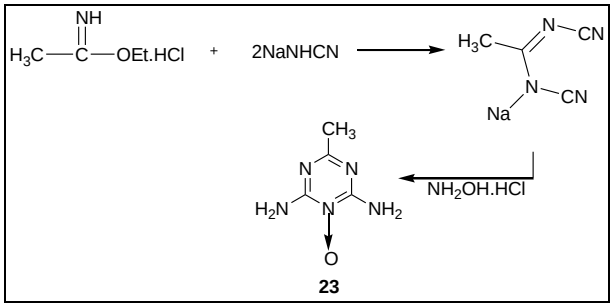


Scheme 13. Synthesis of thiazolo-s-triazine nucleobases.



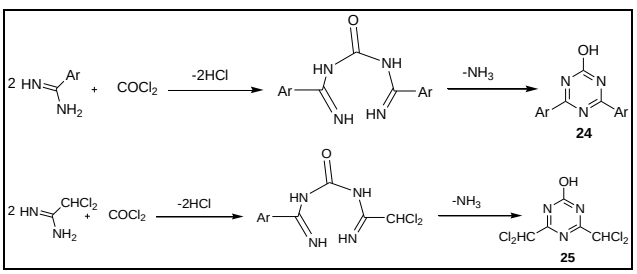
Scheme 14. Synthesis of 2,4-diaryl-1,3,5-triazines.

3. Ethyl acetimidate hydrochloride was reacted with two moles of monosodium cyanamide to give sodium dicyanoacetamidine (Scheme 15). This dicyano derivative was reacted with hydroxylamine hydrochloride to form s-triazine derivative (**23**) (Shaw, 1962).



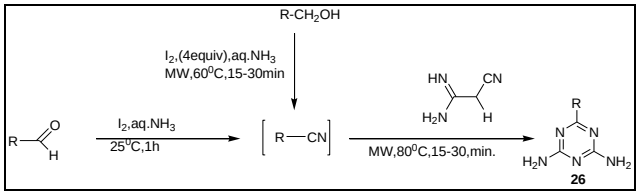
Scheme 15. Synthesis of 1,3,5-triazine derivatives from ethyl acetimidate hydrochloride.

4. Pinner triazine synthesis- 2-Hydroxy-4,6-diaryl-s-triazine derivatives (**24** and **25**) were synthesised by the interaction of aryl amidines and halogenated aliphatic amidines with phosgene, respectively (Pinner, 1890) (Scheme 16).



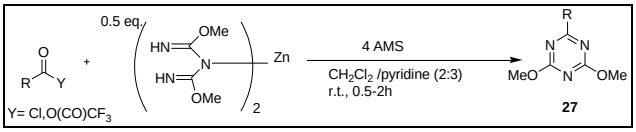
Scheme 16. Synthesis of 2-hydroxy-4,6-diaryl-s-triazines.

5. Under microwave irradiation when primary alcohols or aldehydes reacted with iodine in ammonia water to give intermediate nitriles, which interact with cyandiamide and N_3Na to form corresponding s-triazines (**26**) with good yield (Shie et al., 2007) (Scheme 17).



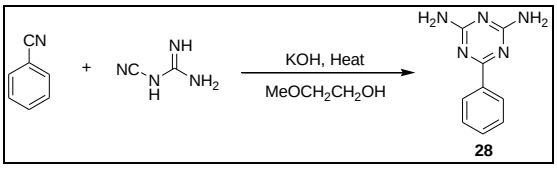
Scheme 17. Synthesis of 1,3,5-triazine derivatives from primary alcohols and aldehydes.

6. Activated carboxylic acid compounds treated zinc dimethyl imidodicarbonimidate in CH_2Cl_2-pyridine, 4,6-dimethoxy-1,3,5-triazine derivatives (**27**) were formed in good yield (Oudir et al., 2006). A synthesis of 4,6-dimethoxy-1,3,5-triazines is given in Scheme 18.



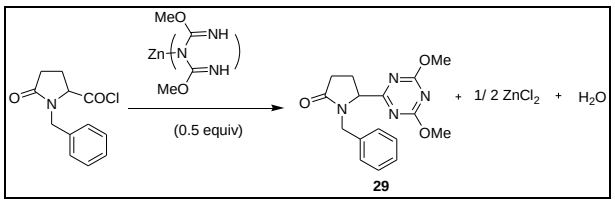
Scheme 18: Synthesis of 4,6-dimethoxy-1,3,5-triazines.

7. Cyanimide or cyanogen chloride was trimerized to 1,3,5-triazines. Benzoguanamine (**28**) was synthesised from benzonitrile and dicyandiamide in dimethoxyethane with KOH (Simons and Saxton, 1953) (Scheme 19).



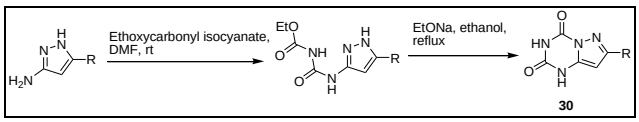
Scheme 19: Synthesis of Benzoguanamine from benzonitrile.

8. 6-Substituted 2,4-dimethoxy-1,3,5-triazines (**29**) were formed by reacting activated carboxy groups (acid chlorides, anhydrides, acylimidazolides) with zinc dimethyl imidodicarbonimidates. In this method, conversion speed of activated carboxy group was low yields (Scheme 20). Good yields were only obtained when a very large excess of the carboxylic acid derivative was used. Under similar experimental conditions, acid chloride reacted with zinc salt to form the corresponding triazine in a moderate 53% yield. Higher yields were obtained when acid chloride was condensed with salt in $4A^0$ molecular sieves and pyridine as co-solvent (Oudir et al., 2006).



Scheme 20. Synthesis of 6-substituted 2,4-dimethoxy-1,3,5-triazines.

9. 5-Substituted-1H-pyrazol-3-amine derivatives were reacted with ethoxycarbonyl isocyanate at room temperature in anhydrous DMF to give N-ethoxycarbonyl-N'-(pyrazol-3-yl)urea derivatives with significant yields. Then, this was followed by an intramolecular ring annulation reaction under catalysis of C_2H_5ONa to generate the pyrazolo[1,5-a][1,3,5]triazine compounds (**30**) (Lingyi et al., 2013) (Scheme 21).



Scheme 21. Synthesis of pyrazolo[1,5-a][1,3,5]triazine derivatives.

CONCLUSION

Triazines have a high significance in the field of medicinal chemistry with broad-spectrum of pharmacological activities. Thus triazine can be useful for design and formation of novel drugs. Some triazine derivatives are currently being evaluated in clinical trials. Triazine may lead to potent type drugs with no or fewer side effects as compared to presently available pharmacological agents.

ACKNOWLEDGMENT

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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