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Review Article

A SYSTEMIC REVIEW: MICROWAVE SYNTHESIS AS A PART OF GREEN CHEMISTRY FOR THE SYNTHESIS OF NOVEL 1, 2, 4- TRIAZOLE DERIVATIVES

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ABSTRACT

Microwave reactions are based on the basic principles of green chemistry, basically involve *"Go Green"* concept. Purpose of green synthesis is to proceed with all the synthetic procedures which are ecofriendly and economic. Great deal of better yield in lesser time than conventional methods are observed. In medicinal chemistry, 1,2,4- triazoles are the source for potent medicaments for different pharmacological activities. In connection with this, literature is being compiled up for the sake of synthesis of 1,2,4- triazoles derivatives by using microwave irradiations.

Keywords: Microwave synthesis, green chemistry, triazoles, pharmacology, synthesis.

INTRODUCTION

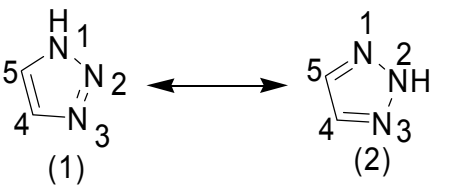
Organic synthesis is the preparation of a desired organic compound from available starting materials. The use of microwave irradiation in organic synthesis has become increasingly popular within the pharmaceutical and academic areas, because it is a new enabling technology for drug discovery and development. Microwave technology is an emerging alternative energy source powerful enough to accomplish chemical transformations in minutes, instead of hours or even days. For this reason, microwave irradiation is presently seeing an exponential increase in acceptance as a technique for enhancing chemical synthesis. A growing number of investigators are adopting microwave-assisted synthesis as a means to increase their productivity. Microwave assisted organic synthesis has been the foremost and one of the most researched applications of Microwaves in chemical reactions is an important part of green chemistry. Green chemistry is the design and implementation of processes and products that minimize or eliminate the use and generation of hazardous chemicals and solvents and other substances which may have an adverse effect on the environment and on human health. Green chemistry is a more eco-friendly green alternative to conventional chemistry practices. The green chemistry movement is part of a larger movement ultimately leading to a green economy- namely sustainable development, sustainable business and sustainable living practices. Green Chemistry encourages environmentally conscious behaviour, such as reducing and preventing pollution and the destruction of the planet.

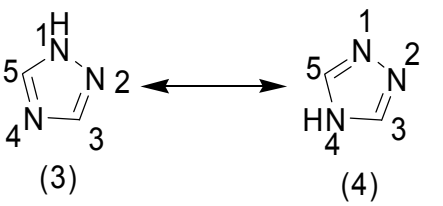
The term green chemistry was first used in 1990 by P. T. Anastas Green chemistry incorporates a new approach to the synthesis, processing and application of chemical substances in such a manner as to reduce threats to health and the environment. Green chemistry is also known as:

- Environmentally benign chemistry
- Clean chemistry
- Atom economy
- Benign-by-design chemistry[1]

In, inorganic chemistry, microwave technology was used since the late 1970s, while it has only implemented in organic chemistry since the mid-1980s. The first microwave-assisted organic syntheses, reported in 1986 by groups of Richard Gedye[2] and Raymond J. Giguere/George Majetich[3] attracted our attention. Considerably shorter reaction times than normal had been obtained for common organic transformations such as esterification, hydrolysis, etherification, addition, and rearrangement. This suggested that microwave heating could be advantageous for synthesis if it could be conducted safely. Scientists have demonstrated the potential of microwave -assisted organic synthesis using ionic liquids as solvent, cosolvent, additives and/or catalyst[4].

Triazoles are 5-membered rings, which contain two carbon and three nitrogen atoms. According to the position of nitrogen atoms, triazoles exist in isomeric forms *i.e.* 1,2,3-triazole and 1,2,4-triazole[5]. Two structural isomeric triazoles exists in two dissimilar tautomeric forms, are known the 1*H*-1,2,3-triazole (1) or 2*H*-1,2,3-triazole (2) and the 1*H*-1,2,4-triazole (3) or 4*H*-1,2,4-triazole (4) the former being known as *osotriazole*, and the latter as *triazole*[6].



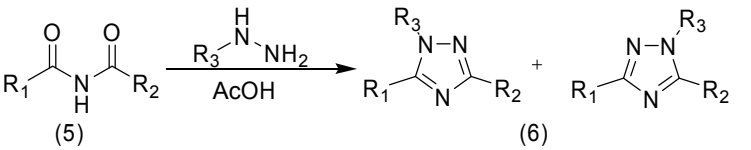


Out of the two triazoles, 1,2,4- triazole have drawn great attention to medicinal chemists from two decades due to its wide variety of activity[7], low toxicity and good pharmacokinetic and pharmacodynamic profiles. 1,2,4-triazole derivatives exhibit wide range of biological activities including antibacterial[8-10], antifungal[11,12], hypoglycaemic[13,14], antidepressant[15], analgesic[16], antitumor[17], anti-proliferative[18], antitubercular[19], anticonvulsant[20] activities.

GENERAL METHOD OF SYNTHESIS

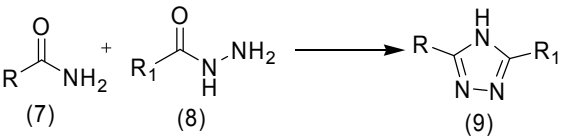
1,2,4-Triazoles are usually prepared using either of two reactions, *i.e.* the Einhorn–Brunner reaction or Pellizzari reaction[21].

The **Einhorn–Brunner** reaction occurs between an alkyl hydrazine and an imide (5) that give a mixture of isomeric 1,2,4-triazoles (6). This cyclization reaction is catalyzed by an organic acid, such as acetic acid (Scheme 1).



(Scheme 1)

In the **Pellizzari reaction**, an acyl hydrazide (8) is condensed with an amide (7) at high temperature and give substituted 1,2,4-triazole (9) (Scheme 2).

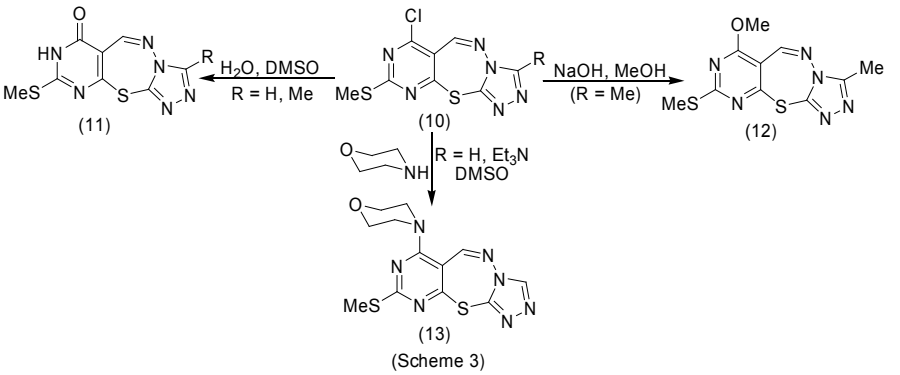


(Scheme 2)

CHEMISTRY OF THE 1,2,4-TRIAZOLES

Nucleophilic substitution and Rearrangement reaction

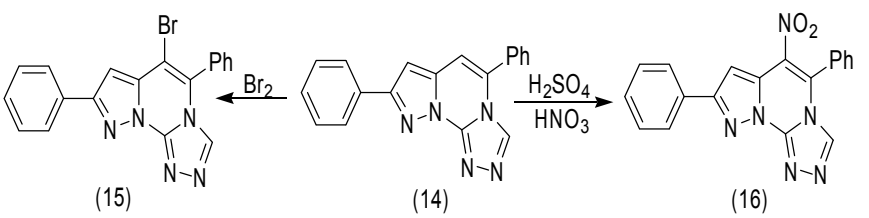
Nucleophilic substitution of 7-chloro-9-methylthio-3-substitutedpyrimido[5,4- *f*][1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazepines (10) with water gives 3-substituted 9-methylthio-7,8-dihydropyrimido[5,4-*f*][1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazepin-7-ones (11), sodium methoxide gives 7-Methoxy-3-methyl-9-methylthiopyrimido[5,4-*f*][1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazepines (12) and amines occurs with the formation of the corresponding 3-Substituted 7-(substituted amino)- 9-methylthiopyrimido[5,4-*f*][1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazepines (13)[22] (Scheme 3).



(Scheme 3)

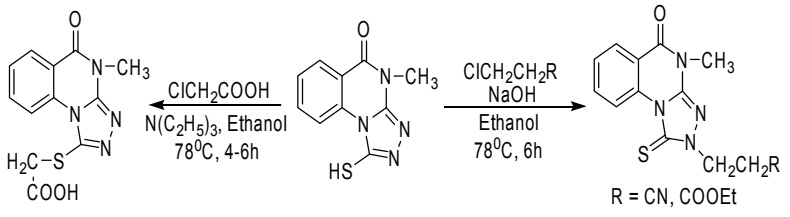
Electrophilic substitution reaction

The electrophilic substitution reactions of 5,8-Diphenylpyrazolo[1,5-*c*]-1,2,4-triazolo[4,3-*a*]pyrimidine (14) such as bromination with bromine and nitration with nitric and sulfuric acids in glacial acetic acid gave the respective 6-Bromo-5,8-diphenylpyrazolo[1,5-*c*]-1,2,4-triazolo[4,3-*a*]pyrimidine (15) and 6-Nitro-5,8-diphenylpyrazolo[1,5-*c*]-1,2,4-triazolo[4,3-*a*]pyrimidine (16) compound[23] (Scheme 4).



(Scheme 4)

4-Methyl-1-thioxo-1,2,4,5-tetrahydro[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (17) reacts with alkyl halides under basic conditions (K_2CO_3, NEt_3) in presence of ethanol to produce the *S*-substituted products 2-[(4-Methyl-5-oxo-4,5-dihydro[1,2,4]triazolo[4,3-*a*]quinazolin-1-yl)sulfanyl]acetic acid (18) *via* an SN_2 reaction mechanism. On the other hand, when either 3-chloropropanenitrile or methyl-3-chloropropanoate were used, the reaction gave the N (2)-substituted products (19)[24] (Scheme 5).

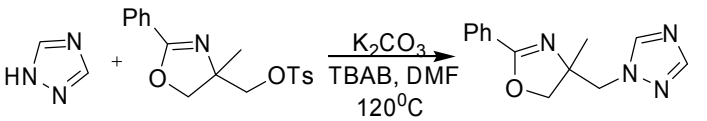


(18) (17) (19)

(Scheme 5)

Alkylation reaction

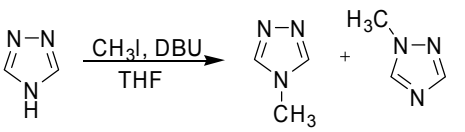
Alkylation of 1,2,4-triazole with alkyl halides and a variety of bases afforded the corresponding 1- and 4-alkylated isomers, with prevalence of the N1-isomer, but reaction of 1*H*-1,2,4-triazole (20) with *O*-tosyloxazoline derivative (21) and K_2CO_3, was carried out in the presence of a catalytic amount of tetra-*n*-butylammonium bromide (TBAB) in *N*,*N*' dimethylformamide at 120 °C for 12 hours afforded only the 1-substituted product, 4-((1*H*-1,2,4-Triazol-1-yl)methyl)-4-methyl-2-phenyl-4,5-dihydrooxazole (22)[25] (Scheme 6).



(20) (21) (22)

(Scheme 6)

The alkylation of 1,2,4-triazole with the help of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base synthetically allows for a convenient and high yielding synthesis of 1-substituted-1,2,4-triazoles. Hence, by applying these conditions to a range of alkylating agents like methyl iodide good yields of 4-methyl 1,2,4-triazole (24) was obtaind as compared to 1-methyl 1,2,4-triazole (25) with the regioselectivity of 86:14 up to 94:6 from 4*H*-1,2,4-triazole (23)[26] (Scheme 7).

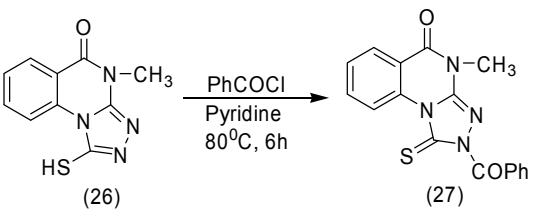


(23) (24) (25)

(Scheme 7)

Acylation reaction

4-Methyl-1-thioxo-1,2,4,5-tetrahydro[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (26) with benzoyl chloride gave only the N-acyl derivative *i.e.* 2-benzoyl-4-methyl-1-thioxo-1,2,4,5-tetrahydro[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (27)[24] (Scheme 8).

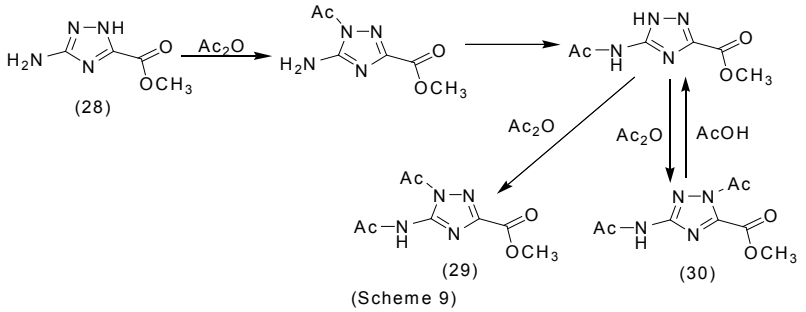


(26) (27)

(Scheme 8)

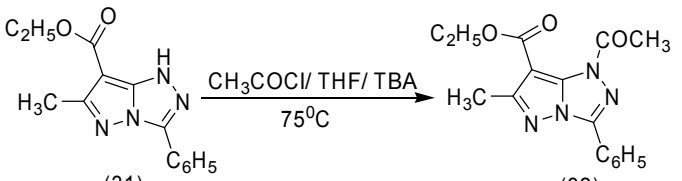
Acetylation reactions

Methyl 5-amino-1*H*-[1, 2, 4] triazole-3-carboxylate (28) undergoes acetylation with acetic anhydride to form two isomeric diacetylated products (29) and (30)[27] (Scheme 9).



(Scheme 9)

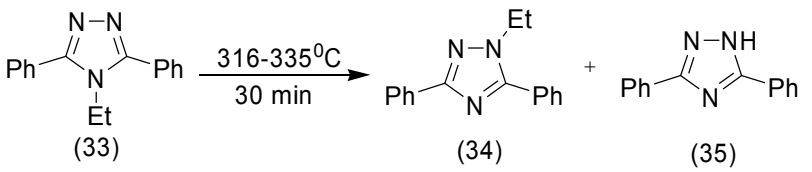
Acetylation of 7-ethoxycarbonyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole (31) with acetyl chloride in the presence of THF/ tributylamine, has led to the 1-acetyl-7-ethoxycarbonyl-6-methyl-3-phenyl-pyrazolo[5,1-*c*][1,2,4]triazole (32)[28] (Scheme 10) .



(Scheme 10)

Thermolysis

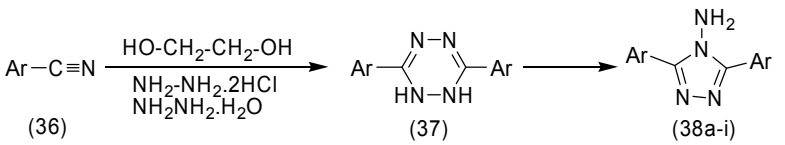
3,4,5-substituted-1,2,4-triazole (33) undergo thermolysis when heated at 316-335°C for 30 min and rearranged to yield 1-ethyl-3,5-diphenyl-1*H*-1,2,4-triazole (34) together with elimination of small amount of 3,5-diphenyl-1*H*-1,2,4-triazole derivative (35)[29] (Scheme 11).



(Scheme 11)

Synthesis of novel 1,2,4 triazole derivatives

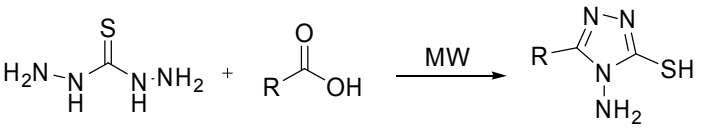
3,5-disubstituted 4-amino-1,2,4-triazoles (38a-i) was synthesized by the reaction of aromatic nitriles (36) on hydrazine dihydrochloride in the presence of an excess of hydrazine hydrate in ethylene glycol under microwave irradiation *via* formation of 1,2-dihydro-1,2,4,5-tetrazine (37)[30] (Scheme 12).



(Scheme 12)

Compound	Ar
38a	C_6H_5
38b	4-$CH_3C_6H_4$
38c	4-$NH_2C_6H_4$
38d	4-OHC_6H_4
38e	3-CH_3O, 4-OHC_6H_3
38f	4-$CH_3OC_6H_4$
38g	4-ClC_6H_4
38h	2-pyridyl
38i	4-pyridyl

3-substituted-4 amino-5-mercapto-1,2,4-triazole (41) derivatives was synthesized by condensation of thiocarbohydrazide (39) with different alkanoic acids (40) under microwave irradiation[31] (Scheme 13).

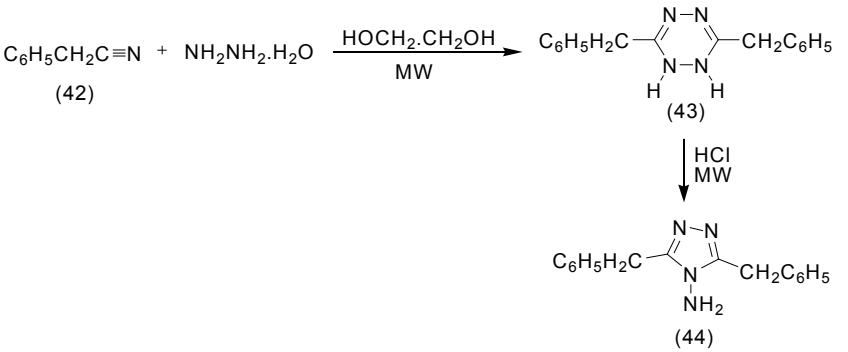


(39) (40) (41)

(Scheme 13)

R = H, CH_3, C_2H_5

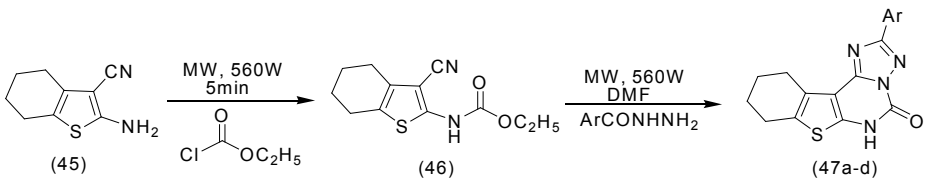
3,5-dibenzyl-4-amino-1,2,4-triazole (44) was synthesised from benzyl cyanide (42) in the presence of hydrazine hydrate and ethylene glycol *via* dihydro-1,2,4,5-tetrazine (43) which rearranged on treatment under acidic conditions into the product[32] (Scheme 14).



(42) (43) (44)

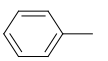
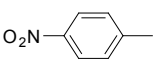
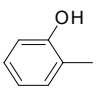
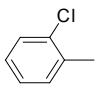
(Scheme 14)

8,9-cycloalkathieno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-5(6*H*)-ones (47a-d) was synthesized from 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carbonitrile (45) in ethyl chloroformate gives ethyl-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene-2-yl carbamate (46) which on condensation with aryl acid hydrazides under microwave-assisted conditions yield the final product[33] (Scheme 15).

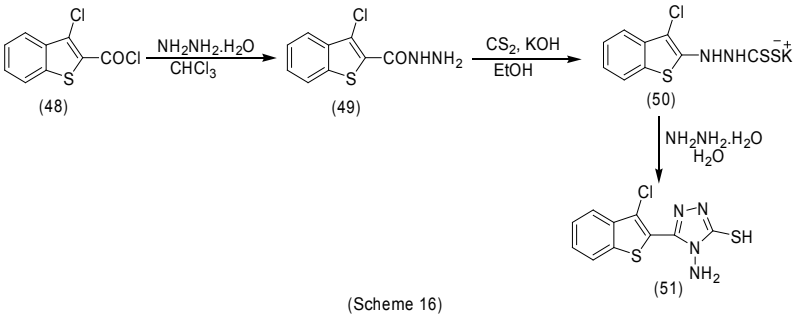


(45) (46) (47a-d)

(Scheme 15)

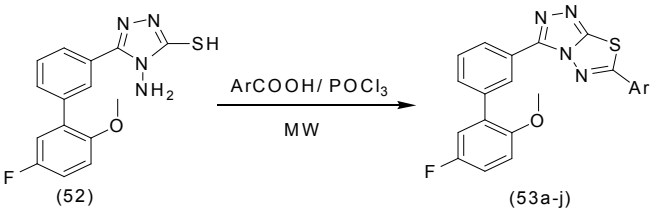
Compound	Ar
47a	
47b	
47c	
47d	

4-amino-5-(3-chlorobenzo[*b*]thien-2-yl)-3-mercapto-1,2,4-triazole (51) was synthesized from potassium dithiocarbazate (50) under microwave irradiation from 3-chloro-2-chlorocarbonylbenzo[*b*]thiophene (48) through an corresponding hydrazide intermediate (49), which on cyclisation with hydrazide gives the product[34] (Scheme 16).

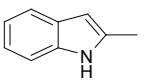
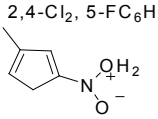


(Scheme 16)

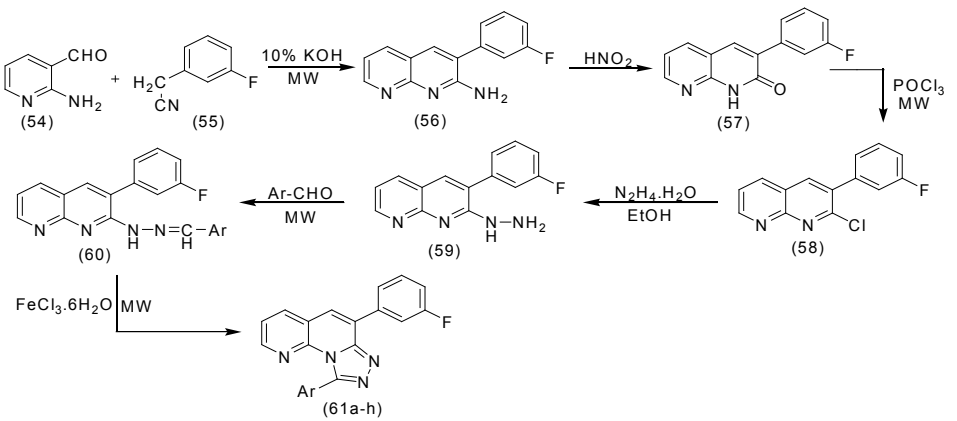
3-(5'-fluoro-2'-methoxybiphenyl-3-*yl*)-6-(substituted)[1,2,4]-triazolo[3,4-*b*][1,3,4] thiadiazole (53a-j) was synthesized from 4-amino-5-(5'-fluoro-2'-methoxybiphenyl-3-*yl*)-4*H*-1,2,4-triazole-3-thiol (52) subjected to MW irradiation using dry phosphorous oxychloride and carboxylic acid[35] (Scheme 17).



(Scheme 17)

Compound	Ar	Compound	Ar
53a	2-FC_6H_4	53f	2-Cl, 6-FC_6H_3
53b	4-F, 3-$CF_3C_6H_3$	53g	2-F, 5-$NO_2C_6H_3$
53c	4-IC_6H_4	53h	4-F, 3-$NO_2C_6H_3$
53d		53i	2,4-Cl_2, 5-FC_6H_2
53e		53j	

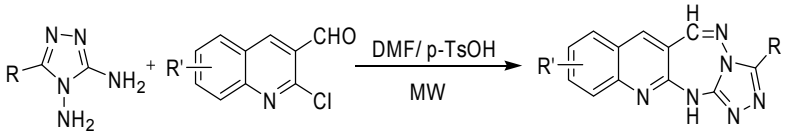
9-aryl-6-(3-fluorophenyl)-1,2,4-triazolo[4,3-*a*][1,8]naphthyridines (61a-h) was synthesized from aryl aldehyde 3-(3-fluorophenyl)-1,8-naphthyridine-2-ylhydrazones (60) using $FeCl_3.6H_2O$ under microwave irradiation[36] (Scheme 18).



(Scheme 18)

Compound	Ar
61a.	C_6H_5
61b.	4-$CH_3C_6H_4$
61c.	4-$CH_3OC_6H_4$
61d.	2-ClC_6H_4
61e.	4-ClC_6H_4
61f.	3-$NO_2C_6H_4$
61g.	4-$NO_2C_6H_4$
61h.	3,4-$(CH_3O)_2C_6H_3$

9-substituted-3-aryl-5*H*,13*aH*-quinolino[3,2-*f*][1,2,4]triazolo[4,3-*b*][1,2,4]triazepine (64a-j) was synthesized from 5-aryl-3,4-diamino-1,2,4-triazoles (62) and 2-chloro-3-formylquinoline (63) using catalytic amount of *p*-TsOH and N, N-dimethylforamide as an energy transfer medium using MW heating[37] (Scheme 19).

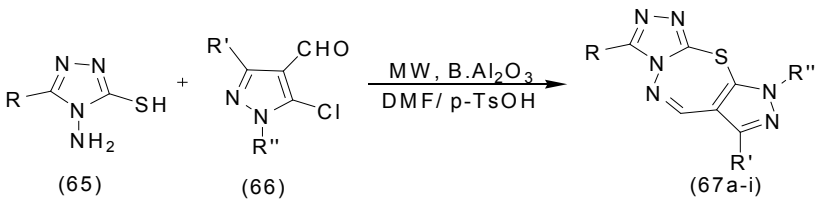


(62) (63) (64a-j)

(Scheme 19)

Compound	R	R'
64a	C_6H_5	H
64b	4-$NO_2C_6H_4$	H
64c	2-ClC_6H_4	3-CH_3
64d	4-$NO_2C_6H_4$	3-CH_3
64e	2-ClC_6H_4	4-OCH_3
64f	$CH_2C_6H_5$	4-CH_3
64g	C_6H_5	4-CH_3
64h	4-ClC_6H_4	4-OCH_3
64i	4-$NO_2C_6H_4$	4-OCH_3
64j	4-$NO_2C_6H_4$	4-CH_3

1-substituted-3,7-dialkyl/aryl-4*H*-pyrazolo[4,5-*f*]-[1,2,4]triazolo[3,4*b*][1,3,4]thiadiazep- ines (67a-i) were synthesized by condensation of 1-amino-2-mercapto-1,3,4-triazoles (65) and 5-chloro-4-formyl-1,2-pyrazoles (66) in the presence of N,N-dimethylforamide as an energy transfer medium, *p*-TsOH as catalyst and basic alumina as solid support under microwave irradiation[38] (Scheme 20).

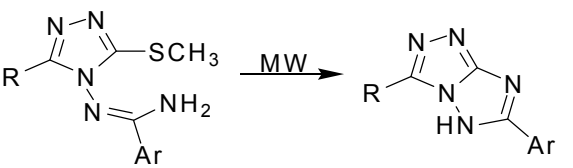


(65) (66) (67a-i)

(Scheme 20)

Compound	R	R'	R''
67a	CH_3	CH_3	H
67b	C_2H_5	CH_3	H
67c	n-C_3H_7	CH_3	H
67d	4-$OCH_3C_6H_4$	CH_3	H
67e	CH_3	4-$NO_2C_6H_4$	C_6H_5
67f	n-C_3H_7	4-$NO_2C_6H_4$	C_6H_5
67g	C_6H_5	4-BrC_6H_4	C_6H_5
67h	4-$OCH_3C_6H_4$	4-$NO_2C_6H_4$	C_6H_5
67i	4-ClC_6H_4	4-$NO_2C_6H_4$	C_6H_5

6-aryl-3-substituted-5*H*-[1,2,4]-triazolo[4,3-*b*][1,2,4]triazoles (69a-e) was synthesized by microwave assisted cyclization of N-(3-methylthio-5-substituted-4*H*-1,2,4-triazol-4-yl)benzenecarboximidamides (68)[39] (Scheme 21).

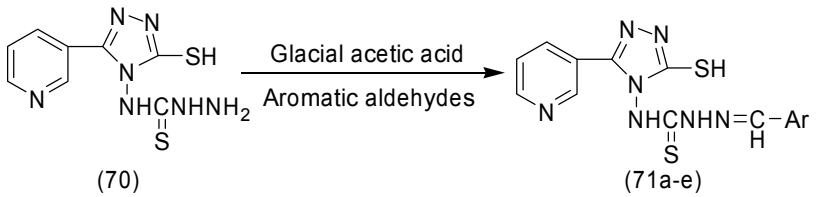


(68) (69a-e)

(Scheme 21)

Compound	R	Ar
69a	CH_3	C_6H_6
69b	CH_3	4-Cl-C_6H_4
69c	CH_3	4-Br-C_6H_4
69d	CH_3	4-CH_3-C_6H_4
69e	H	C_6H_5

Schiff's bases of 5-mercapto-3-(3'-pyridyl)-4*H*-1,2,4triazole-4-yl-thiosemicarbazide (70) was synthesized by reacting with different aromatic aldehyde to yield (71a-e)[40] (Scheme 22).

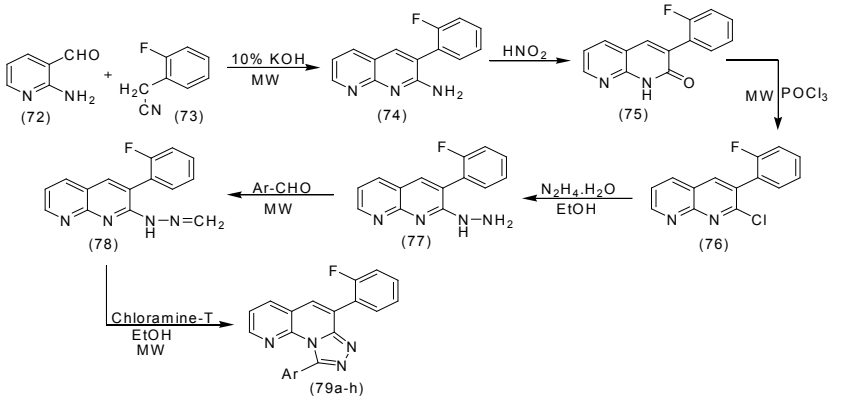


(70) (71a-e)

(Scheme 22)

Compound	Ar
71a	phenyl
71b	2-furyl
71c	2-hydroxyphenyl
71d	2-chlorophenyl
71e	4-methoxyphenyl

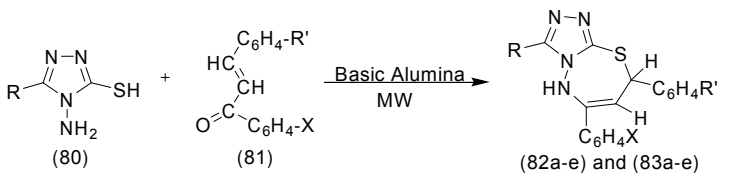
9-aryl-6-(2-fluorophenyl)-1,2,4-triazolo[4,3-*a*][1,8]naphthyridines (79a-h) was synthesized by oxidation of the corresponding aryl aldehyde 3-(2-fluorophenyl)-1,8-naphthyridin-2-ylhydrazones (78) with chloramines-T in ethanol under microwave irradiation[41] (Scheme 23).



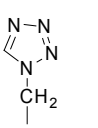
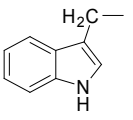
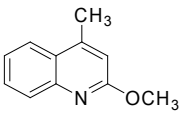
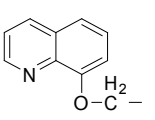
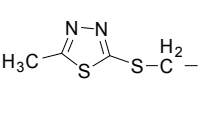
(Scheme 23)

Compound	Ar
79a	C_6H_5
79b	4-$CH_3C_6H_4$
79c	4-$CH_3OC_6H_4$
79d	2-ClC_6H_4
79e	4-ClC_6H_4
79f	3-$NO_2C_6H_4$
79g	4-$NO_2C_6H_4$
79h	3,4-$(CH_3O)_2C_6H_3$

5-substituted 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazeepines (82a-e) and **(83a-e)** was synthesized from the reaction of 1-amino-2-mercapto-5-substituted triazoles (80) and substituted chalcones (81) on basic alumina under microwave irradiation[42] (Scheme 24).

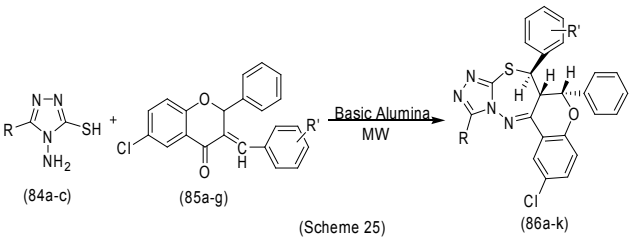


(Scheme 24)

Compound	a	b	c	d	e
R =					

	R'	X
(82a-e) =	4-OCH_3	H
(83a-e) =	3,4-OCH_2-O-	4-Br

Fluorine containing 3-alkyl-7-chloro-11a,12-dihydro-11-phenyl-12-(substituted aryl)-11*H*-benzopyrano[4,3-*e*][1,2,4]-triazolo[3,4-*b*][1,3,4]-thiadiazepines (86a–k) was synthesized using basic alumina as solid support from 4-Amino-5-alkyl-3-mercaptotriazoles (84a-c) and 6-chloro-3-(substituted-arylidene)-flavanones (85a-g) under microwaves irradiation[43] (Scheme 25).



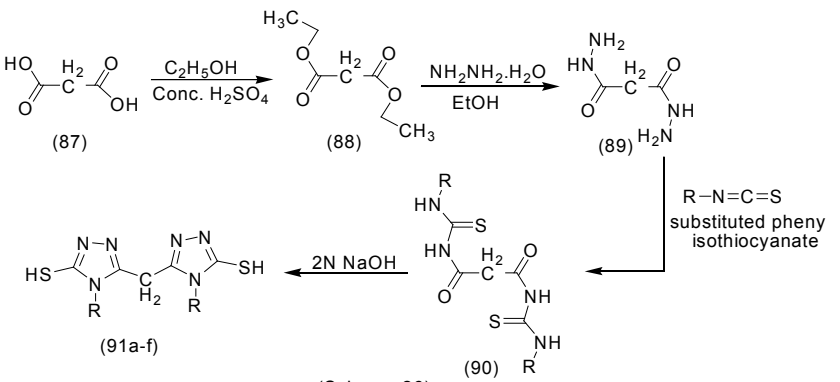
(Scheme 25)

Compound	R
84a	CH_3
84b	C_2H_5
84c	C_3H_7

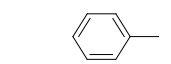
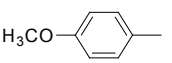
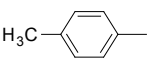
Compound	R'
85a	2-F
85b	4-OCF_3
85c	2-Cl
85d	H
85e	4-F
85f	2-Cl, 4-F
85g	3,4-diF

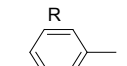
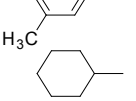
Compound	R	R'
86a	CH_3	2-F
86b	CH_3	4-OCF_3
86c	CH_3	2-Cl
86d	CH_3	H
86e	C_2H_5	4-F
86f	C_2H_5	2-Cl, 4-F
86g	C_2H_5	2-F
86h	C_2H_5	3,4-diF
86i	C_3H_7	2-F
86j	C_3H_7	4-OCF_3
86k	C_3H_7	2-Cl, 4-F

5, 5-methylenebis (4-substituted phenyl/alkyl-4*H*-1,2,4-triazole-3-thiol) (91a-f) was synthesized from malonic acid bisester (88) through malonic acid bis hydrazide (89), yield substituted bis thiosemicarbazide (90) which on addition of 2M sodium hydroxide solution gives series of bis-triazole derivatives[44] (Scheme 26).

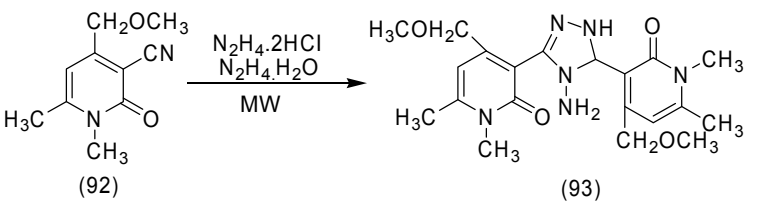


(Scheme 26)

Compound	R
91a	
91b	
91c	

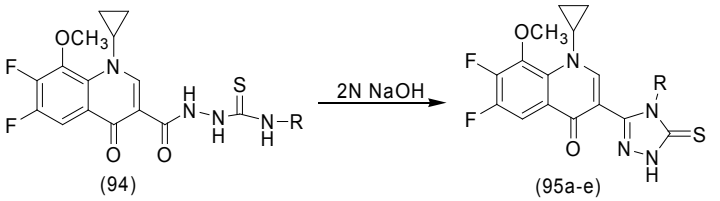
Compound	R
91d	
91e	
91f	$CH_3CH_2CH_2CH_2$-

4-amino-3,5-bis[6-(methoxymethyl)-3,4-dimethyl-2-oxo-1,2 dihydropyridine-1-yl]-1,2,4-triazole-2(*H*) (93) was synthesised by subjecting a mixture of 4-(methoxymethyl)-1,6-dimethyl-2-oxo-1,2-dihydropyridine-3- carbonitrile (92), hydrazine dihydrochloride and hydrazine hydrate in ethylene glycol in microwave reactor[45] (Scheme 27).



(Scheme 27)

1-cyclopropyl-6,7–difluoro-8-methoxy-3-(4-substitutedphenyl-5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl) quinolin-4(1*H*)-one (95a-e) was synthesized from 1-(1-cyclopropyl-6,7–difluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carbonyl)-4-substitutedphenylthiosemi-carbazides (94) in 2N NaOH under microwave irradiation[46] (Scheme 28).

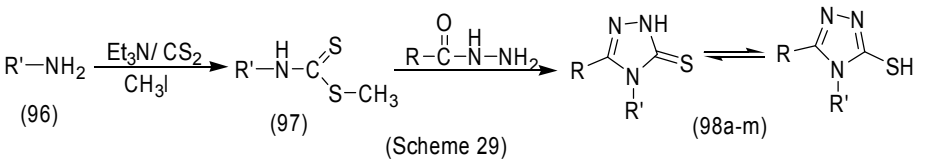


(94) (95a-e)

(Scheme 28)

Compound	R
95a	3-$OCH_3C_6H_4$
95b	3-ClC_6H_4
95c	C_6H_5
95d	1-$CH_3C_6H_4$
95e	2-$CH_3C_6H_4$

4-*N*, *N*-Dimethylamino/ 4-Cycloamino-Substituted 1,2,4-Triazole-3-thiones (98a-m) was synthesized from substituted methyl dithiocarbazates (97) and benzhydrazides under microwave irradiations. Methyl dithiocarbazates were obtained by the treatment of N,Ndimethylhydrazine, N-aminopiperidine, N-aminomorpholine, and N-methyl-1-aminopiperazine with carbon disulfide in the presence of triethylamine, followed by methylation with methyl iodide[47] (Scheme 29).

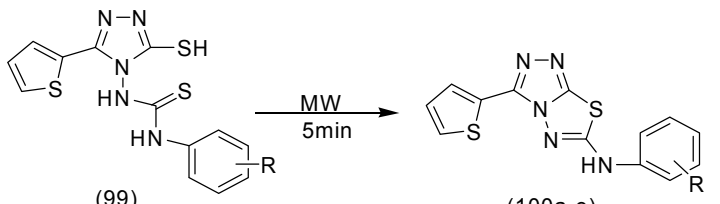


(96) (97) (98a-m)

(Scheme 29)

Compound	R	R'
98a	C_6H_5	$N(CH_3)_2$
98b	C_6H_5	Piperidine
98c	C_6H_5	Morpholine
98d	4-ClC_6H_4	$N(CH_3)_2$
98e	4-ClC_6H_4	Piperidine
98f	4-ClC_6H_4	Morpholine
98g	4-FC_6H_4	Morpholine
98h	4-$NH_2C_6H_4$	$N(CH_3)_2$
98i	4-$NH_2C_6H_4$	Piperidine
98j	4-$NH_2C_6H_4$	Morpholine
98k	4-$OCH_3C_6H_4$	Morpholine
98l	3,4-$Cl_2C_6H_3$	$N(CH_3)_2$
98m	3,5-$(OCH_3)_2C_6H_3$	4-Methylpiperazine

2-Arylamino-5-(2-thienyl)-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles derivatives (100a-e) was synthesized from dehydrosulphurization of N-[3-Mercapto-5-(2-thienyl)-1,2,4-triazol-4-yl]-N' arylthioureas (99) *via* exposure to microwave irradiation for 5 min[48] (Scheme 30).

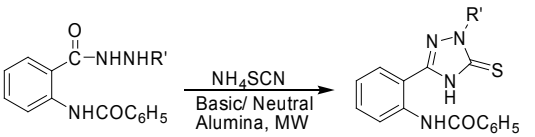


(99) (100a-e)

(Scheme 30)

Compound	R
100a	H
100b	3-F
100c	4-F
100d	4-Cl
100e	4-Br

3-[(2-benzoylamino) phenyl]-1,2,4-triazolin-5-thione (102) was synthesized from 2-(benzoylamino) benzoic hydrazide/ 2-benzoylaminobenzoic phenylhydrazide (101) and ammonium thiocyanate in ethanol using different solid supports under microwave irridation[49] (Scheme 31).



(101) (102)

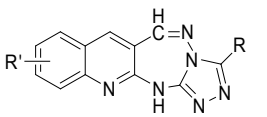
(Scheme 31)

R' = H, C_6H_5

PHARMACOLOGICAL ACTIVITIES

Antifungal Activity

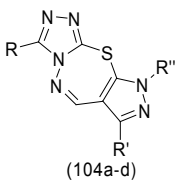
9-substituted -3-aryl-5*H*, 13*aH*-quinolino[3,2-*f*][1,2,4]triazolo[4,3-*b*][1,2,4]triazepine (103a-d) were screened for anti-fungal activity against *Aspergillus flavus, Aspergillus niger*, *Rhizopus* species and *Pencillum notatum* species by paper disc method at conc. 500 µg/ml and 1000 µg/ml using fluconazole as standard. Compounds showed excellent activity against *Aspergillus niger* at 1000 µg conc. and *Pencillum notatum* at 500 µg as well as 1000µg/ml conc whereas they showed good to moderate activity against *Aspergillus flavus and Rhizopus* species at both conc[37].



(103a-d)

Compound	R	R'
103a	C_6H_5	H
103b	4-$NO_2C_6H_4$	H
103c	2-ClC_6H_4	3-CH_3
103d	4-$NO_2C_6H_4$	3-CH_3

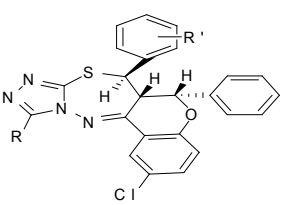
1-substituted-3,7-dialkyl/aryl-4*H*-pyrazolo[4,5-*f*]-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiaze- pines (104a-d) were evaluated for anti-fungal activity against *Aspergillus flavus, Aspergillus niger, Rhizopus species and Penicillum species* by paper disc method at concentrations 500µg/ml and 1000µg/ml using fluconazole as standard. Compounds showed good to moderate activity except *penicillum* species[38].



(104a-d)

Compound	R	R'	R''
104a	CH_3	CH_3	H
104b	n-C_3H_7	CH_3	H
104c	4-$OCH_3C_6H_4$	4-$NO_2C_6H_4$	C_6H_5
104d	4-ClC_6H_4	4-$NO_2C_6H_4$	C_6H_5

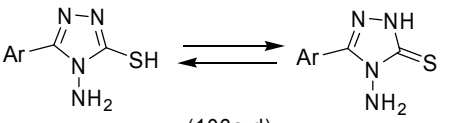
Fluorine containing 3-alkyl- 7-chloro-11a,12-dihydro-11-phenyl-12-(substituted aryl)-11*H*-benzopyrano[4,3-*e*][1,2,4]-triazolo[3,4-*b*][1,3,4]-thiadiazepines (105a–i) were screened for *in vitro* anti-fungal activity against *Rhizoctonia solani, Fusarium oxysporum* and *Collectotrichum capsici*. Compounds have shown good activity against these pathogens[43].



105(a-i)

Compound	R	R'
105a	CH_3	2-F
105b	CH_3	4-OCF_3
105c	CH_3	2-Cl
105d	CH_3	H
105e	C_2H_5	4-F
105f	C_2H_5	3,4-diF
105g	C_3H_7	2-F
105h	C_3H_7	4-OCF_3
105i	C_3H_7	2-Cl, 4-F

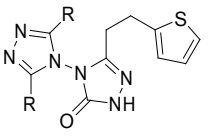
4-amino-3-mercapto-1,2,4 triazoles (106a-d) was evaluated as antifungal agents against *Candida albicans* and *Candida tropicalis* by the disk diffusion method. Compounds exhibit high activity against *Candida albicans* and *Candida tropicalis*[50].



(106a-d)

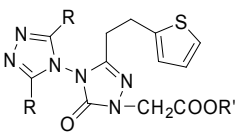
Compound	Ar
106a	C_6H_5
106b	$CH_2C_6H_5$
106c	*p*-Cl-C_6H_4
106d	*p*-CH_3-C_6H_4

4-(3,5-disubstitue-4*H*-1,2,4-triazol-4-yl)-5-(thiophen-2-yl-methyl)-2*H*-1,2,4-triazol-3(4*H*)- ones (107a-c) and 4-(3,5-disubstitue-4*H*-1,2,4-triazol-4-yl)-2-(2-oxo-2-arylethyl)-5-(thiophen-2-ylmethyl)-2*H*-1,2,4-triazol-3(4*H*)-ones (108a-f) were evaluated for antifungal activity against *Penicillum* spp., and *Aspergillus* spp. by agar-well diffusion method using fluconazole (5 μg) as standard drug. Compounds showed potent activity[51].



(107a-c)

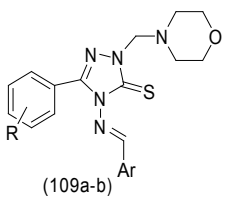
Compound	R
107a	H
107b	CH_3
107c	C_2H_5



(108a-f)

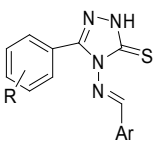
Compound	R	R'
108a	H	C_6H_5
108b	CH_3	C_6H_5
108c	C_2H_5	C_6H_5
108d	H	C_2H_5
108e	CH_3	C_2H_5
108f	C_2H_5	C_2H_5

4-(4-substituted benzylideneamino)-2-(morpholinomethyl)-5(substitutedphenyl)-2*H*-1,2,4-triazole-3(4*H*)-thione (109a-b) and 4-(4-substitutedbenzylideneamino)-5(substitutedphenyl)-2*H*-1,2,4-triazole-3(4*H*)thione (110a-e) were evaluated for anti-fungal activity against *Candida albicans, Candida tropicalis* and *Aspergillus niger* by tube dilution/turbidity method using fluconazole as standard. All compounds showed very good activity[52].



(109a-b)

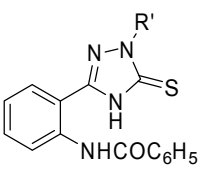
Comound	R	Ar
109a	4-Cl	4-ClC_6H_4
109b	2,4-Cl	4-ClC_6H_4



(110a-e)

Comound	R	Ar
110a	4-Cl	4-ClC_6H_4
110b	2,4-Cl	4-ClC_6H_4
110c	4-Cl	3,4,5-$(OCH_3)_3C_6H_2$
110d	4-Cl	4-$CH_3C_6H_4$
110e	2,4-OH	4-ClC_6H_4

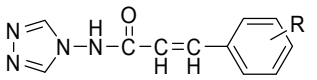
3-[(2-benzoylamino)phenyl]-1,2,4-triazolin-5-thione (111) were screened for their antifungal activity against *Aspergillus niger* and *Aspergillus flavus* by the paper disc diffusion method and compared to standard salicylic acid. Both compounds have shown good activity against both fungi[53].



R' = H, C_6H_5

(111)

3-(substitutedphenyl)-N-(4*H*-1,2,4-triazol-4-yl)acrylamide (112a-c) were studied for their in-vitro antifungal activity against *Mucor, Aspergillus niger* and *Penicillium* strains by the turbidometry method. Compounds 112a and 112c gives comparable activity of fluconazole[54].

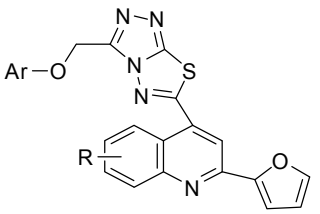


(112a-c)

Compound	R
112a	4-$N(CH_3)_2$
112d	3-OCH_3
112c	2-OH

Antibacterial Activity

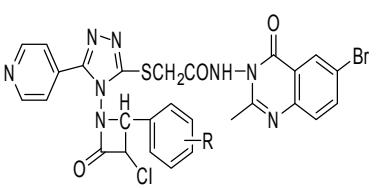
2-(2-furyl)-4-(3-aryloxymethyl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazol-6-yl)quinolines (113a-k) were screened for their anti-bacterial activities against *Escherichia coli, Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa* using furacin as standard by serial dilution method. All the compounds showed moderate to excellent activity compared with the standard drug, furacin[55] .



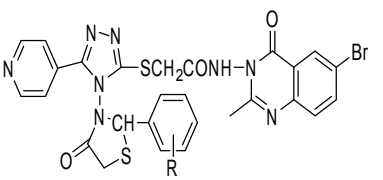
(113a-k)

Compound	R	Ar
113a	Br	4-ClC_6H_4
113b	Br	3-ClC_6H_4
113c	Br	4-$CH_3C_6H_4$
113d	Br	3-$CH_3C_6H_4$
113e	CH_3	4-ClC_6H_4
113f	CH_3	3-ClC_6H_4
113g	CH_3	4-$CH_3C_6H_4$
113h	CH_3	3-$CH_3C_6H_4$
113i	H	4-ClC_6H_4
113j	H	4-$CH_3C_6H_4$
113k	H	3-$CH_3C_6H_4$

N-(6-bromo-2-methyl-4-oxoquinazolin-3(4*H*)-yl)-2-(4-(3-chloro-2-(substitutedphenyl)-4- oxoazetidin-1-yl)-5-(pyridin-4-yl)-5-thio)acetamido-1,2,4-triazoles (114a-g), N-(6- bromo-2-methyl-4-oxoquinazolin-3(4*H*)-yl)-2-(4-(2-(substitutedphenyl)-4-oxothiazolidin -3-yl)-5-(pyridin-4-yl)- 3-thio)acetamido-1,2,4-triazoles (115a-g) were screened for antibacterial activity against *Escherichia coli, Staphylococcus aureus*, *Pseudomonas vulgaris* and *Klebsilla pneumoniae*. Among azetidinones 114a-g, compound 114b exhibited promising antibacterial activity. Among the compounds 115a-g, compounds 115b and 115c showed better activity against *S. aureus, E.coli and P.vulgaris*, 115e exhibited equipotent while 115a, 115d, 115f and 115g showed good antibacterial activity compared to that standard drugs ampicillin and gattifloxacine[56].



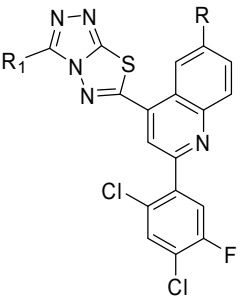
(114a-g)



(115a-g)

Compound	R
a	4-OH, 3-OCH_3
b	2,4-Cl
c	2,6-Cl
d	2,4-Br
e	2,6-Br
f	2-OH
g	$N(CH_3)_2$

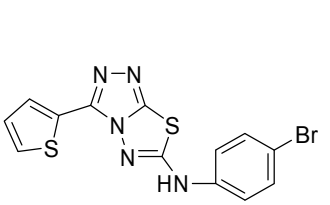
3-Substituted-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazol-6-yl-2-(2,4-dichloro-5-fluorophenyl) quinolines (116a-e) were screened for their in-vitro anti-bacterial activity aganist *Escherichia coli, Staphylococcus aureus* and *Bacillus subtilis* by serial dilution method using Nitrofurazone (furacin) as standard drug. All compounds showed very good activity[57].



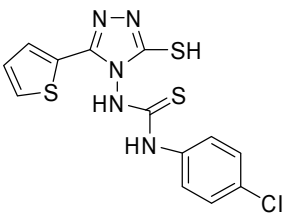
(116a-e)

Compound	R	R_1
116a	H	2-$ClC_6H_4OCH_2$
116b	H	2,4-$Cl_2C_6H_3OCH_2$
116c	Br	2-$ClC_6H_4OCH_2$
116d	Br	2,4-$Cl_2C_6H_3OCH_2$
116e	Br	4-Cl-3-$CH_3C_6H_3OCH_2$

***N*-(4-bromophenyl)-3-(thiophen-2-yl)-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-amine (117) and 1-(4-chlorophenyl)-3-(3-mercapto-5-(thiophen-2-yl)-4*H*-1,2,4-triazol-4-yl)thiourea (118)** was tested for their *in vitro* anti-bacterial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeuroginosa* using Ampicillin trihydrate antibiotic as standard by the agar disc-diffusion method. Compound display marked activity[48].

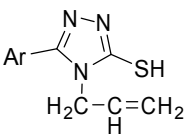


(117)

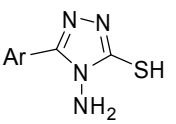


(118)

4-allyl/amino-5-aryl-1,2,4-triazoles (119a-f) was tested for anti-bacterial activity against *Escherichia coli*, *Bacillus subtilis, Salmonella enteritidis* and *Staphylococcus aureus* by filter paper disc method. Free NH_2 groups in the 4 position (119c-f) showed the greatest inhibitory activity. The 4-amino-5- (4-hydroxyphenyl)-1,2,4-triazole (119d) showed the highest inhibition zone diameter against *Staphylococcus aureus* (28 mm), than all the other tested organisms and compounds[58].



(119a-b)

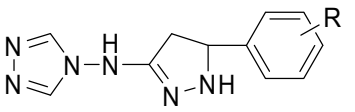


(119c-f)

Ar:

119a = 4-OH-C_6H_4-
119b = 2-OH-5-Cl-C_6H_4-
119c = 2-OH-C_6H_4-
119d = 4-OH-C_6H_4-
119e = 4-OH-C_6H_4-CH_2-
119f = 4-C_2H_5O-C_6H_4-CH_2-

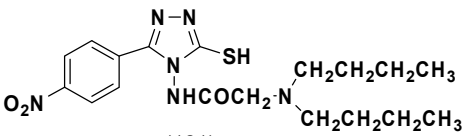
N-(5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)-4*H*-1,2,4-triazol-4-amine (120a-c) were screened for their *in-vitro* antibacterial activity against *Bacillus megaterium, Bacillus subtilus, Micrococcus luteus, Staphylococcus aureus, Eschericha coli, Enterobacter, Proteus vulgaris* and *Pseudomonas aeruginos* by the agar well diffusion method using standard antibiotic chloramphenicol. All compounds showed significant activity[59].



(120a-c)

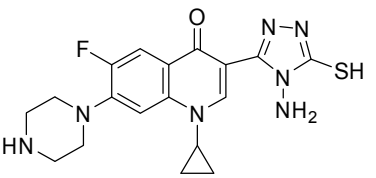
Compound	R
120a	4-$N(CH_3)_2$
120b	3-OCH_3
120c	2-OH

4-[N-dibutylamine]acetylamino-3-mercapto-5-(4-nitro)phenyl-1,2,4-triazole (121) were screened for antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa* and *Escherichia coli* by disc diffusion method using vancomycin and amikacin as standard. The compound display very good activity[60].



(121)

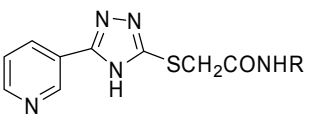
3-(4-amino-5-mercapto-4*H*-1,2,4-triazol-3-yl)-1-cyclopropyl-6-fluoro-7-(piperazin-1-yl) quinolin-4(1*H*)-one (122) was screened for their antibacterial activity against *Bacillus subtilis*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* by cup plate method. The compound exhibited good effect towards *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* but moderate activity against *Bacillus subtilis*[61].



(122)

Anti-tubercular Activity

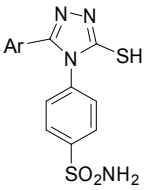
5-(N-substituted carboxamidomethylthio)–3-(3'-pyridyl)-1,2,4-triazoles (123a-f) were evaluated for in-vitro anti-tubercular activity at 50 µg/mL against *Mycobacterium tuberculosis* H_{37} Rv using rifampicin as standard. All compound exhibited excellent anti-TB activity[62].



(123a-f)

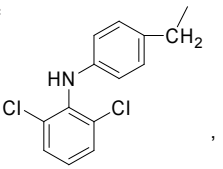
Compound	R
123a	4-BrC_6H_4
123b	4-ClC_6H_4
123c	4-$NO_2C_6H_4$
123d	3-$NO_2C_6H_4$
123e	2,6-ClC_6H_3
123f	2,6-$CH_3C_6H_3$

4-(3-mercapto-5-substituted-4*H*-1,2,4-triazol-4-yl)benzenesulfonamide (124) was evaluated for anti-tubercular activity aganist *Mycobacterium tuberculosis* $H_{37}Rv$ strain at 25µg/ml, 50µg/ml, 100µg/ml by Middlebrook 7H9 agar medium using Streptomycin as standard drug. Both compound have shown significant activity at all concentrations[63].



(124)

Ar =



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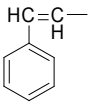
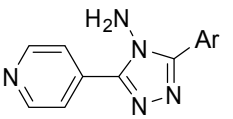


Anti-inflammatory Activity

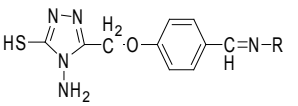
5-substituted-3-pyridine-1,2,4-triazole (125a-b) was studied for *in-vivo* anti-inflammatory activity using indomethacin as control by Carrageenan- induced hind paw odema model in rat. Compounds have shown good activity[64].



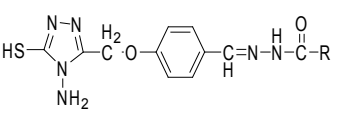
(125a-b)

Compoun	Ar
125a	4-C_2H_4-C_6H_4
125b	4-NH_2-C_6H_4

Schiff bases of 4-amino-3-substituted-5-mercapto-1,2,4-triazoles (126a-f) were investigated for anti-inflammatory activity by carrageenan induced rat paw oedema method and showed significant activity comparable to standard drug (Ibuprofen)[65].



(126a-d)

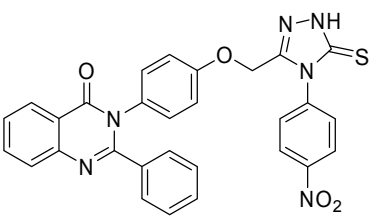


(126e-f)

Compound	R
126a	4-Chloro phenyl
126b	4-methyl phenyl
126c	2-fluoro phenyl
126d	4-hydroxy phenyl
126e	2(4'-isobutyl phenyl) propionyl carboxamido
126f	2(5'-methoxy naphthyl) propionylcarboxamido

Antimalarial Activity

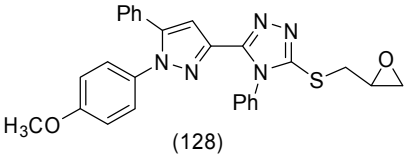
3-{4-[4-(4-fluoro-phenyl)-4*H*-[1,2,4]triazol-3-yl-methoxy]-phenyl}-2-phenyl-3*H*-quinazo- lin-4-one (127) was evaluated against chloroquine-resistant Plasmodium falciparum malarial parasite using the tritiated Hypoxanthine incorporation assay. The compound was found to be most active against Plasmodium falciparum strains[66].



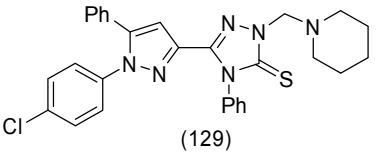
(127)

Anticancer Activity

3-(1-(4-methoxyphenyl)-5-phenyl-1*H*-pyrazol-3-yl)-5-(oxiran-2-ylmethylthio)-4-phenyl-4*H*-1,2,4-triazole (128), 5-(1-(4-Chlorophenyl)-5-phenyl-1*H*-pyrazole-3-yl)-4-phenyl-2-(piperidin-1-yl)methyl)-2*H*-1,2,4-triazole-3(4*H*)-thione (129) were screened for their anticancer activities against breast carcinoma (MCF7) and cervix carcinoma (HELA) human cell lines compared with Doxorubicin positive control. Compounds showed good activity against both types of carcinoma cell lines than that obtained by doxorubicin[67].

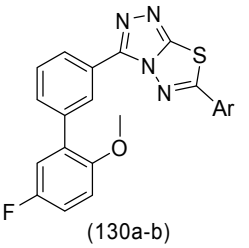


(128)



(129)

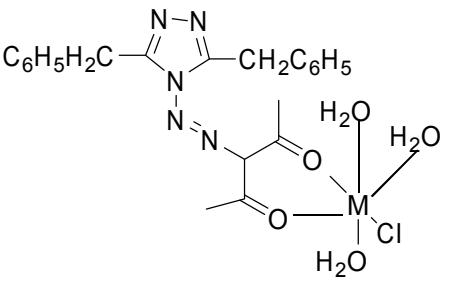
3-(5'-fluoro-2'-methoxybiphenyl-3-yl)-6-(substituted)[1,2,4]-triazolo[3,4-*b*][1,3,4]-thiadiazole (130) were screened for their anticancer activity against cancer cell lines HT29 (human adenocarcinoma), K293 (human kidney cancer) and MDA231 (human breast cancer) by using the MTT assay. Compounds exhibited significant activity comparable to 5-flurouracil[35].



(130a-b)

Compound	Ar
130a	4-F, 3-$CF_3C_6H_3$
130b	2-F, 5-$NO_2C_6H_3$

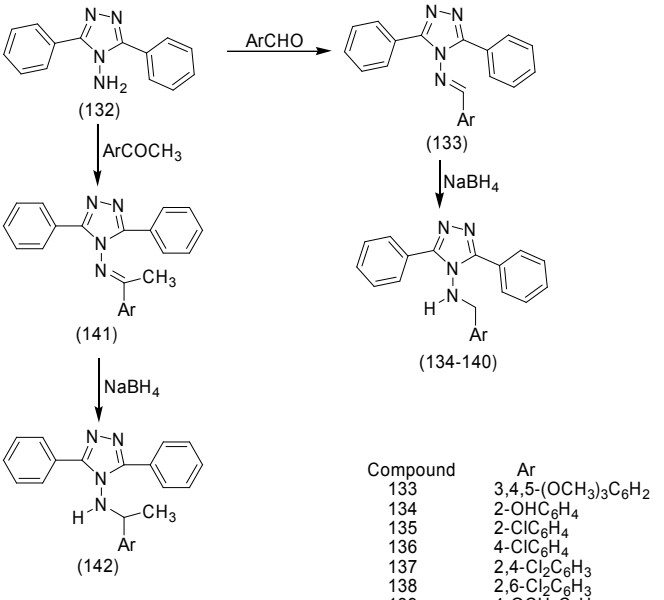
3,5-dibenzyl-4-amino-1,2,4-triazole (131) was screened for anticancer activity on Jurkat, Raji & PBMC cell lines. Ruthenium complexes showed potential anticancer activities[32].



M = Ni, Cu, Ru

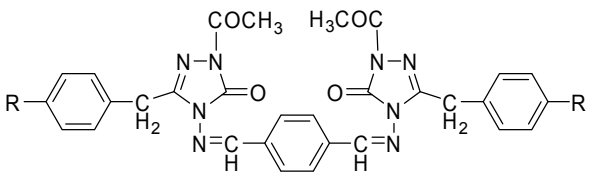
(131)

4-arylidenamino-4*H*-1,2,4-triazoles (133), 4-arylmethylamino-4*H*-1,2,4-triazoles (134-140), 4-(1-aryl) ethylidenamino-4*H*-1,2,4-triazoles (141) and 4-(1-aryl)ethylamino-4*H*-1,2,4-triazoles (142) were screened on three human tumor cell lines, breast cancer (MCF7), non small cell lung cancer (NCI-H460) and CNS cancer (SF-268) at National Cancer Institute (NIH), USA. The compounds showed low antiproliferative activity in the anticancer tests[68].



Compound	Ar
133	3,4,5-$(OCH_3)_3C_6H_2$
134	2-OHC_6H_4
135	2-ClC_6H_4
136	4-ClC_6H_4
137	2,4-$Cl_2C_6H_3$
138	2,6-$Cl_2C_6H_3$
139	4-$OCH_3C_6H_4$
140	2,4,6-$(OCH_3)_3C_6H_2$
141	4-$OCH_3C_6H_4$
142	4-$OCH_3C_6H_4$

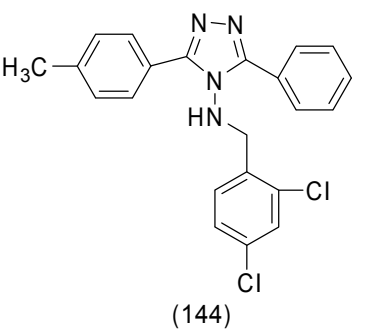
N,N'-bis(3-alkyl-4,5-dihydro-1*H*-1,2,4-triazol-5-on-4-yl)-1,4-xylenediimines (143) were screened for antitumor activities using cell lines derived from human solid tumors (lung, colon, melanoma, renal, ovarian, CNS, prostste, breast and leukemia). Compound showed weak cytostatic activity[69].



(143)

R = H, 4-Cl

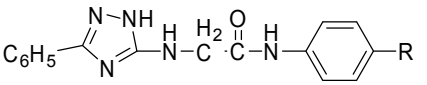
3-Phenyl-5-p-tolyl-4-(2,6-dichlorobenzylamino)-4*H*-1,2,4-triazole (144) was tested for anticancer activitiy. Compound showed higher anticancer activity in the preliminary tests with the cancer cell lines of breast cancer (MCF7), non-small cell lung cancer (NCI-H460) and CNS cancer (SF-268) and exhibited remarkable anticancer potential in screening tests with 60 human cancer cell lines[70].



(144)

Anticonvulsant Activity

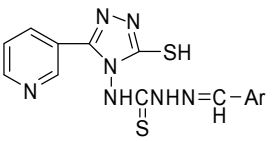
N-(substituted phenyl)-2-[5-phenyl-2*H*-1,2,4-triazol-3ylamino] acetamide (145) was tested for anticonvulsant activity by MES method using phenytoin as standard anticonvulsant drug in screening. The compounds were found to be active as they reduced the time of extensor phase compared to control[71].



(145a-b)

Compound	R
145a	NO_2
145b	Cl

Thiosemicarbazide derivatives of 5-mercapto-3-(3'- pyridyl)-4*H*-1,2,4-triazole (146a-e) were screened for anticonvulsant activity by Maximum Electroshock (MES) method. The compounds have shown good activity[40].

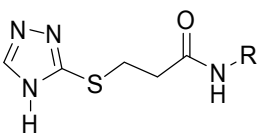


146a-e

Compound	Ar
146a	phenyl
146b	2-furyl
146c	2-hydroxyphenyl
146d	2-chlorophenyl
146e	4-methoxyphenyl

Anxiolytic Activity

3-(N-substituted carboxamidoethylthio)-(4*H*)-1,2,4-triazoles (147a-h) were screened for anxiolytic activity by Elevated plus maze, using diazepam at the dose of 2mg/kg as standard. All compounds showed significant activity[72].

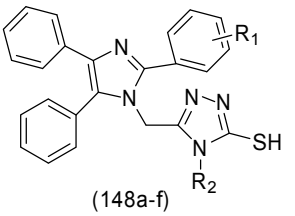


147a-h

Compound	R
147a	C_6H_5
147b	4-ClC_6H_4
147c	4-$NO_2C_6H_4$
147d	3-ClC_6H_4
147e	3-$NO_2C_6H_4$
147f	2-$CH_3C_6H_4$
147g	4-$OCH_3C_6H_4$
147h	$CH_2C_6H_5$

Anthelmintic Activity

Imidazole containing triazole derivatives (148a-f) were screened for their anthelmintic activity against Indian adult earthworms (*pheretima posthuma*) at different concentrations of 0.150% and 0.300% w/v by using albendazole as standard drug. Compound 148d was found to be the most potent, whereas compounds like 148b and 148f showed high activity, while 148a, 148c and 148e showed moderate athelmintic activity when compared with standard drug albendazole[73].

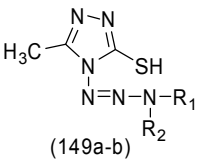


(148a-f)

Compound	R_1	R_2
148a	4-F	C_6H_5
148b	4-NO_2	C_6H_5
148c	4-F	4-ClC_6H_4
148d	4-NO_2	4-ClC_6H_4
148e	4-F	4-$CH_3C_6H_4$
148f	4-NO_2	4-$CH_3C_6H_4$

Analgesic Activity

3-substituted -4*H*-1, 2, 4- triazoles (149a-b) were evaluated for their analgesic activity using hot plate method. The compound were exhibit higher activity than the standard drug (aspirin)[74].

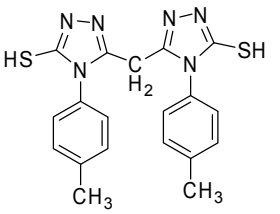


(149a-b)

Compound	R_1	R_2
149a	H	4-$OCH_3C_6H_4$
149b	C_6H_5	C_6H_5

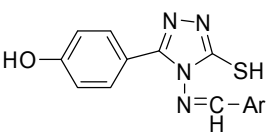
Antioxidant Activity

5, 5-methylene bis [4-(4-methylphenyl)-4*H*-1, 2, 4-triazole-3-thiol (150) was for their antioxidant activity by DPPH method. The compound was found to having potent antioxidant activity[44].



(150)

Schiff's bases of 3-substituted 1,2,4-triazo -5 thione (151a-e) were evaluated for its antioxidant activity by hydrogen peroxide scavenging method. All compounds have significant antioxidant activity[75].

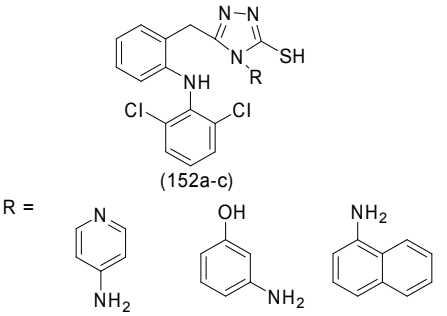


(151a-e)

Compound	Ar
151a	C_6H_5
151b	3-OHC_6H_4
151c	2-ClC_6H_4
151d	2-$NO_2C_6H_4$
151e	3-$NO_2C_6H_4$

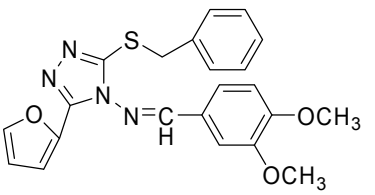
Antiulcer Activity

3-mercapto-1,2,4-triazole derivatives (152a-c) were screened for their ulcerogenic activity using diclofenac potassium as standard. Gastro intestinal tolerance of these compounds is better than that of Diclofenac potassium at 10mg/kg therapeutic dose[76].



Antiviral Activity

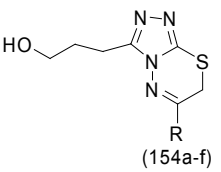
4-(3,4-Dimethoxylphenylidene)amino-3-(2-furyl)-5-benzylthio-4*H*-1,2,4-triazole (153) was assayed for anti-HIV-1 activity by examination of their inhibition of HIV-1-induced cytopathogenicity in MT-4 cells and by determination of their inhibitory effect on HIV-1 reverse transcriptase. Compound was found to be the most active inhibitor against HIV-1 replication in cell culture (EC50 = 12 μM) and against HIV-1 reverse transcriptase (IC50 = 43.5 μM)[77].



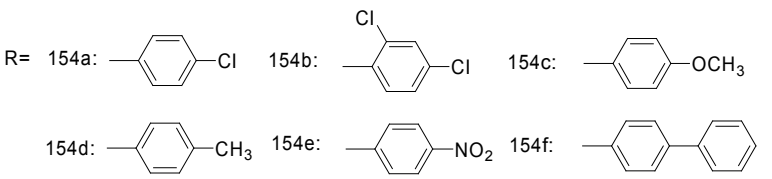
(153)

Plant Growth Regulating Activitiy

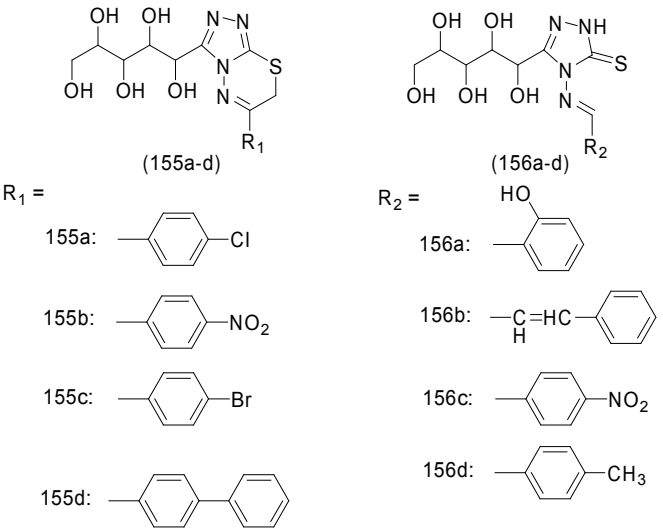
6-aryl-3-(3-hydroxypropyl)-7*H*-1,2,4-triazolo[3,4-*b*][1,3,4]-thiadiazines (154a-f) was investigated on sprouting of wheat and radish seeds. All compounds display remarkable inhibitory activities on the growth of radish and wheat[78].



(154a-f)



6-aryl-3-(D-galactopentitol-1-yl)- 7*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines (155a-d) and 4-(arylmethylidene)amino-5-(D-galactopentitol-1-yl)-3-mercapto-4*H*-1,2,4-triazoles (156a-d) was investigated on sprouting of wheat and radish seeds. These compounds have remarkable effects on the growth of radish and wheat[79].



CONCLUSION

The literature survey reveals that 1,2,4-triazole is a unique template that is associated with several biological activities, and the easy synthetic routes for synthesis have taken attention of the chemists, pharmacologists and researchers. The dynamic microwave power system employed offered an efficient heating of the material, thus reduced chemical reactions times and increased reaction yields were observed in most of the most of the literature quoted in this paper. In this respect, it can be concluded that 1,2,4-triazole derivatives show various activity against antimicrobial, anti-inflammatory, analgesic, antitubercular, anticancer *etc*. The possible improvements in the activity can be further achieved by slight modifications in the substituents which are undisclosed till date.

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