Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2017, 9(6):202-214

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Review Article on Synthesis of 1,3,4-Thiadiazole Derivatives and It's Biological Activity

Ketan C Parmar* and Nikita H Umrigar

Department of Chemistry, Sir PT Sarvajanik College of Science, Surat, Gujarat, India

---

ABSTRACT

The present review outlines the synthesis and different biological activities of 1,3,4 thiadiazole and its derivatives. 1,3,4 thiadiazole has been studied extensively because of its wide variety of biological activities such as antimicrobial, anti-inflammatory, analgesic, anti-cancer, anti-tubercular and diuretic etc. However, The wide range of therapeutic values of 1,3,4 thiadiazole has encouraged us to do advance research on it.

Keywords: 1,3,4-thiadiazole; Anti-microbial; Anti-inflammatory; Anti-tubercular; Anti-cancer

---

INTRODUCTION

Heterocyclic compounds are organic compounds that contain a ring structure containing atoms in addition to carbon, such as sulfur, oxygen or nitrogen, as the heteroatom. Several five membered aromatic systems having three hetero atoms at symmetrical position have been studied because of their interesting physiological properties [1-8], such as azole, pyrole, thiazole, thiadiazole, oxadiazole, triazene etc. and they also exhibits wide variety of biological activities. Thiadiazole is a heterocyclic compound featuring both two nitrogen atom and one sulfur atom as part of the aromatic five membered ring. Thiadiazole and related compounds are called 1, 3, 4-thiadiazole (two nitrogen and one other hetero atom in a five-membered ring). The others four isomeric forms of thiadiazole are occurred in nature as 1,2,3-thiadiazole; 1,2,5-thiadiazole; 1,2,4-thiadiazole. 1,3,4-thiadiazoles are important compounds in medicine, agriculture, and in many fields of technology. A large number of thiadiazoles have been patented in the medical field for the treatment of a wide variety of diseases and some of them have become commercial products. A large number of thiadiazoles have been patented in the medical field for the treatment of a wide variety of diseases and some of them have become commercial products compounds in medicinal chemistry because of its therapeutic values. It is also known to have unique antibacterial and anti-inflammatory activities. Differently substituted thiadiazole moieties have also been found to have other interesting activities such as analgesic, antimicrobial, anti-tubercular, anticonvulsant and anti-hepatitis B viral activities. Due to presence of –N=C-S moiety in its structure 1,3,4-thiadiazoles exhibit various biological activities [9].

REVIEW

Synthetic Review of Various 1,3,4-Thiadiazole Derivatives

P Chaturvedi et al. [10] synthesized 3, 6-disubstituted-1, 2, 4-triazolo [3, 4-b]-1, 3, 4-thiadiazoles derivatives. This was based upon the route of preparation of aryl acid hydrazide. Then compound was treated with the solution of potassium hydroxide and ethanol and formed 3-substituted-5-mercapto-1,3,4-oxadiazole. A suspension of this compound, water and hydrazine hydrate was mixed and refluxed for 6-7 hours with occasional shaking and formed 3-substituted-4-amino-5-mercapto-1,2, 4-triazoles). After that an equimolar mixture of and aromatic acids in

phosphorus oxychloride was refluxed for 5 h and final compound was obtained. The synthesized compounds were determined by ^{1}H NMR spectra and mass spectroscopy (Figure 1).

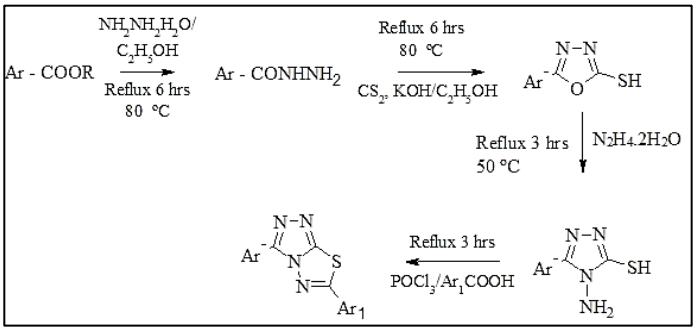


Figure 1: Synthesis of 3, 6-disubstituted-1, 2, 4-triazolo [3, 4-b]-1, 3, 4-thiadiazoles derivatives

MR Mahendrasingh et al. [11] has reported the synthesis of thiadiazole derivative from morphine. In this morpholine (0.1 mol), ethylchloroacetate (0.1 mol) and 0.3 g of potassium carbonate in 60 ml of acetone was stirred on magnetic stirrer for 10 hours. In the next step, resulting compound (0.08 mol) and thiosemicarbazide (0.08 mol) were taken in 50 ml of ethanol, stirred for 6 hours and then refluxed for 3 hours. The yellow coloured compound was obtained after recrystallization from the mixture of chloroform and hexane (9:1 V/V) (Figure 2).

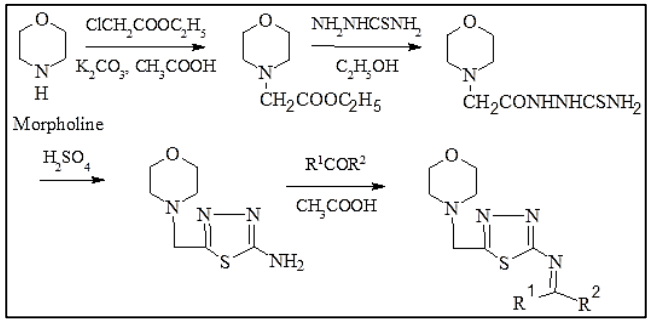


Figure 2: Synthesis of thiadiazole derivative from morphine

S Geogeta [12] has reported the synthesis of 2-R-5-formyl-1,3,4-thiadiazole derivatives. The aromatic and heterocyclic amines after treatment with carbon disulfide in ammonium hydroxide followed by refluxing with hydrazine hydrate in ethanol were converted to the thiosemicarbazides. After treatment with monochloracetyl chloride, the intermediary thiosemicarbazides were cyclized into the 2-R-5-chloromethyl-1,3,4-thiadiazoles 3a-das the result of a ring closing reaction (Figure 3).

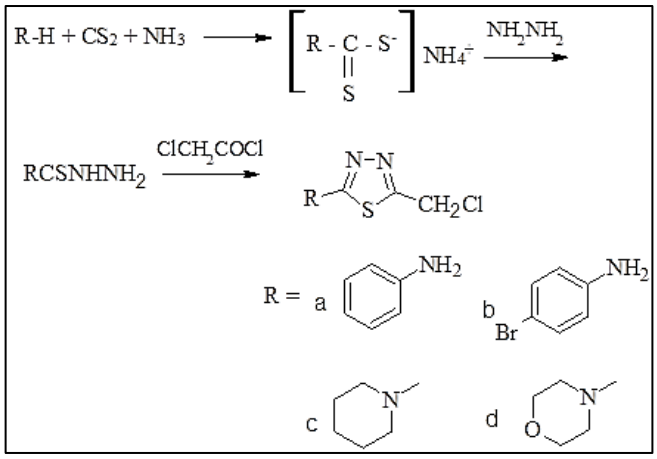


Figure 3: Synthesis of 2-R-5-formyl-1,3,4-thiadiazole derivatives

J Malgorzata et al. [13] synthesized 2-(4-chlorophenylamino)-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole. The compound was obtained from sulfinylbis (2,4-dihydroxythiobenzoyl) and 4-(3-chlorophenyl)-3-thiosemicarbazide or 4-(4-chlorophenyl)-3-thiosemicarbazide (Lancaster, Germany) via cyclization process (Figure 4).

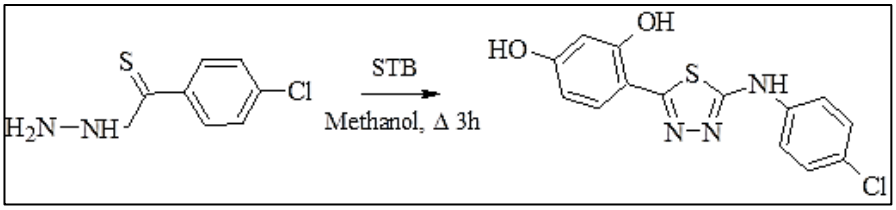


Figure 4: Synthesis of 2-(4-chlorophenylamino)-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole

AM Khedr et al. [14] has reported the preparation of the thiadiazole Schiff base ligands. The Schiff bases were prepared by the stoichiometric reaction of 2-amino-5-substituted-aryl-1,3,4-thiadiazole with the appropriate aldehydes in a molar ratio of 1:1 (amine: aldehyde). A mixture of 0.01 mol of 2-amino-5-substituted-aryl-1,3,4-thiadiazole in ethanol, 0.01 mol of the appropriate aldehydes and 2 drops of concentrated sulphuric acid was refluxed in water bath for 5 h. The progress of the reaction was monitored at time intervals of 30 min by thin layer chromatography (TLC) (Figure 5).

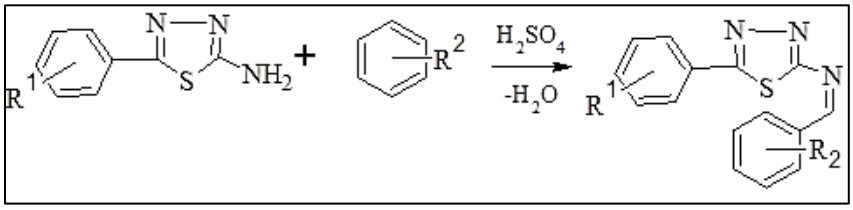


Figure 5: Preparation of the thiadiazole Schiff base ligands

MR Mahendrasinh et al. [15] synthesized thiadiazole derivatives by the reaction between benzoic acid 2-hydroxy benzoic acid with thiosemicarbazide using conc H_2SO_4 as oxidising agent. The synthesized compounds were characterized by IR. H^1NMR and nitrogen estimation and screened for their antibacterial and antifungal activities by paper disc diffusion technique. All the synthesized compounds showed moderate activity against bacteria and fungi (Figure 6).

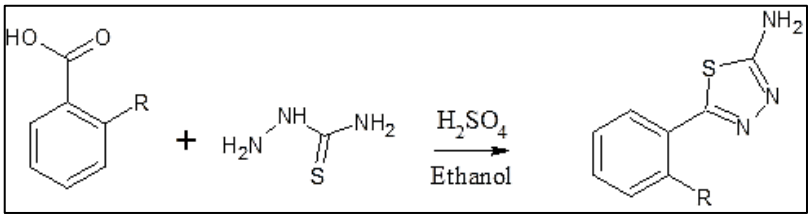


Figure 6: Synthesis of thiadiazole derivatives by the reaction between benzoic acid 2-hydroxy benzoic acid with thiosemicarbazide using conc. H_2SO_4

A Kumar et al. [16] synthesized thiadiazole from thiosemicarbazide. Thiosemicarbazide derivative on cyclization with different aromatic carboxylic acids in the presence of $POCl_3$ formed 1, 3, 4 thiadiazole derivatives which were characterized by elemental analysis, IR, H^1NMR and Mass spectral data's and screened for their antimicrobial activities and showed significant antimicrobial activities (Figure 7).

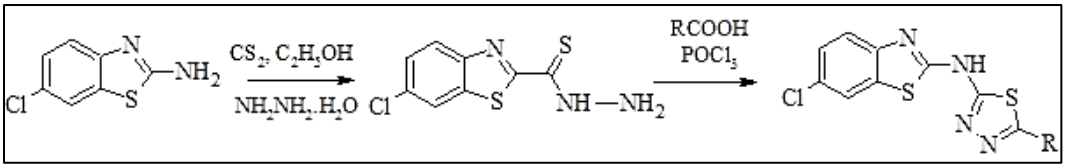


Figure 7: Synthesis of thiadiazole from thiosemicarbazide. Thiosemicarbazide derivative on cyclization with different aromatic carboxylic acids in the presence of $POCl_3$

SK Chitale et al. [17] synthesized thiadiazole from aromatic acid and thiosemicarbazide, and Schiff bases were prepared by reacting with different aldehydes and isatin using glacial acetic acid as catalyst. Elemental analysis, IR, H^1 NMR and mass spectral data elucidated structure of newly synthesized compounds and tested for *in vitro* antioxidant activity by testing nitric oxide and hydrogen peroxide scavenging activity. Some of these novel derivatives showed moderate to potent antioxidant activity (Figure 8).

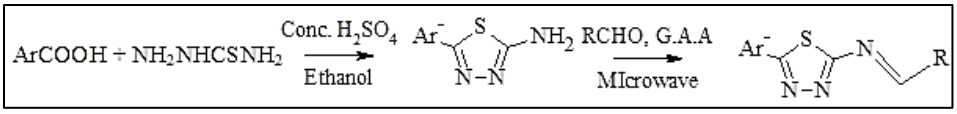


Figure 8: Synthesis of thiadiazole from aromatic acid and thiosemicarbazide

MS Yar et al. [18] synthesized a series of five membered heterocyclic compounds by the reaction between isoniazid and various substituted isothiocyanates and were tested for their anticonvulsant activity by determining their ability to provide protection against convulsions induced by electro convulsometer comparing with standard drug phenytoin sodium. Among the synthesized compounds, 2-(4-chlorophenyl) amino-5-(4-pyridyl)-1,3,4-thiadiazole and 2- (4-chlorophenyl)amino-5-(4-pyridyl)-1, 3, 4- oxadiazole were found promising compounds of the series (Figure 9).

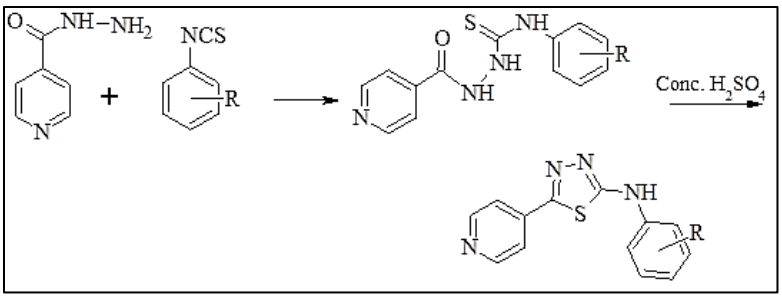


Figure 9: Synthesis of a series of five membered heterocyclic compounds

AK Verma et al. [19] synthesized N-phenyl thiosemicarbazide from aromatic amine by refluxing with CS_2 and hydrazine hydrate in ethanol and from phenyl isothiocyanate by reacting with hydrazine hydrate in ethanol. The synthesized thiosemicarbazides where condensed with aromatic carboxylic acid in presence of conc. H_2SO_4 to form thiadiazole analogues. The compounds were screened for anti-inflammatory activity by carageenan induced rat paw edema method and the compounds exhibited significant to moderate anti-inflammatory activity (Figure 10).

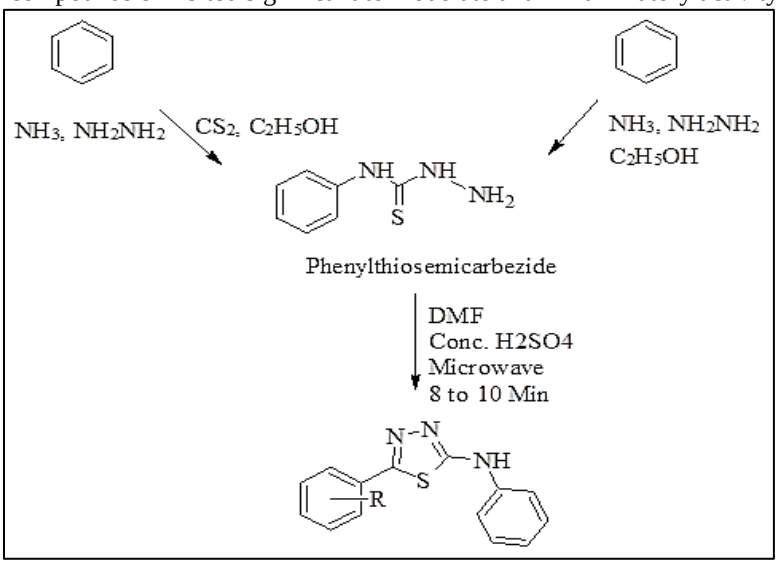


Figure 10: Synthesis of N-phenyl thiosemicarbazide from aromatic amine by refluxing with CS_2

DE Abdel Rahman et al. [20] synthesized substituted imidazo [2,1-b]-1, 3, 4 – thiadiazoles, substituted 1, 3, 4-thiadiazolo[3,2-a] pyrimidines and substituted thioureas. Structures elucidated by IR, NMR and mass spectroscopy. All the compounds were evaluated for their cytotoxic activity against tumor cell line A549 (non-small cell lung cancer cell line) using Sulfo-Rodamine B (SRB) standard method. Most of the tested compounds exhibited potent cytotoxicity. Docking studies were performed to explore the possible binding modes of these compounds with the binding site of fibroblast stromelysin-1 enzyme, which is involved in several pathological conditions including cancer (Figure 11).

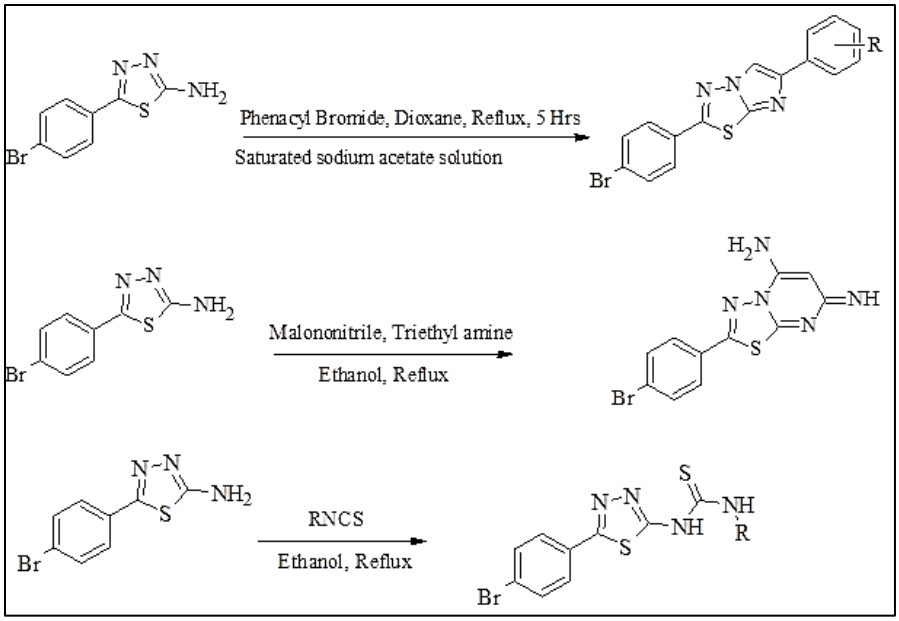


Figure 11: Synthesis of substituted imidazo [2,1-b]-1, 3, 4 – thiadiazoles, substituted 1, 3, 4- thiadiazolo[3,2-a] pyrimidines and substituted thioureas

A Naskar et al. [21] synthesized 2-amino-5- aryl -1,3,4- thiadiazoles by oxidative cyclization of thiosemicarbazones using $FeCl_3$ catalyst and from this Schiff bases were prepared by condensation with aldehyde and synthesized compounds were characterized by IR, NMR, and C, H and N analysis. Anticancer activity was evaluated using Ehrlich's Ascites carcinoma cells and all the compounds exhibited significant anticancer activity compared to control (Figure 12).

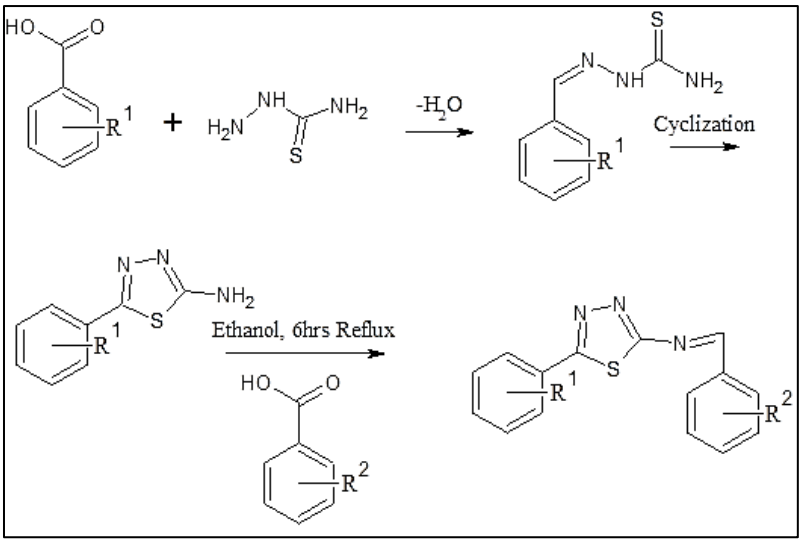


Figure 12: Synthesis of 2-amino-5- aryl -1,3,4- thiadiazoles by oxidative cyclization of thiosemicarbazones using $FeCl_3$

M Asif et al. [22] syntheszed 2,4- diphenyl-5-imino-1,3,4-thiadiazole derivatives by cyclization of α-chlorobenzalphenylhydrazone derivatives using potassium thiocyanate. A-chlorobenzalphenylhydrazone derivatives were synthesized by chlorination of hydrazonyl derivatives using PCl_5 which in turn was synthesized from benzoyl chloride and phenyl hydrazine in pyridine. The thiadiazole derivatives synthesized were characterized by IR, H^1NMR and elemental analysis and screened for *in vivo* anti-inflammatory activity by carageenan induced paw oedema and a few of them showed promising activity when compared to standard drug diclofenac sodium (Figure 13).

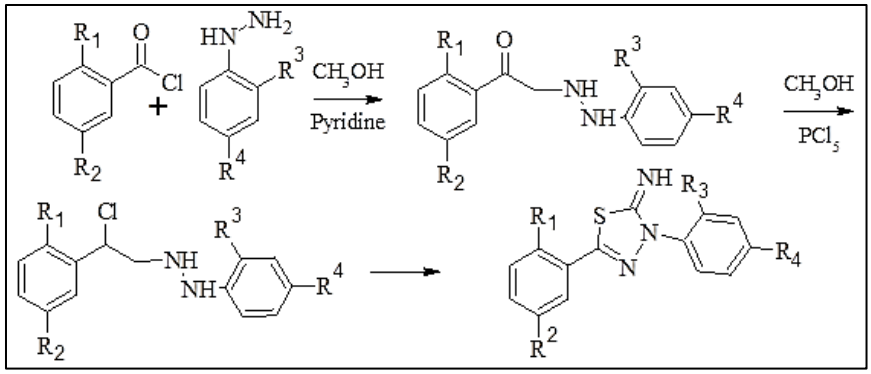


Figure 13: Synthesis of 2,4- diphenyl-5-imino-1,3,4-thiadiazole derivatives by cyclization of α-chlorobenzalphenylhydrazone derivatives using potassium thiocyanate

S Banerjee et al. [23] synthesized thiadiazole derivatives with new amino group by refluxing furan-2-carboxylic acid with thiosemicarbazide in presence of conc. H_2SO_4 and then different Schiff bases were prepared by reacting with various substituted aldehydes in presence of few drops of glacial acetic acid. The structures of the synthesized compounds were confirmed by spectral data's. Screening for *in vitro* anticancer activity was carried out using MTT (3-[4,5- dimethylthiazol-2-yl]-2,5-diphenyl terazolium bromide) assay on HT-29 colorectal cancer cell line. The compounds had shown significant activity at very less concentration (Figure 14).

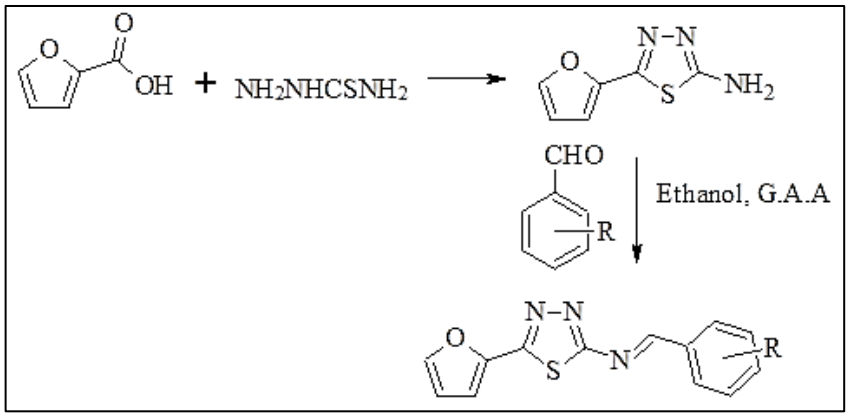


Figure 14: Synthesis of thiadiazole derivatives with new amino group by refluxing furan-2-carboxylic acid with thiosemicarbazide in presence of conc. H_2SO_4

Mahendrasinh et al. [24] synthesized novel 1, 3,4thiadiazole derivatives for their antimicrobial activities. Novel Thiadiazoles were synthesized by reaction of benzoic and 2-hydroxybenzoic acid with thiosemicarbazide to synthesize 5-phenyl-1,3,4-thiadiazol-2-amineand 2-(5-amino-1,3,4-thiadiazole-2-yl) phenol. From these compounds various derivatives of1,3,4-Thiadiazole derivatives have been synthesized. The chemical structures of the synthesized compounds were confirmed by means of IR, ^{1}H NMR, and nitrogen estimation (Figure 15).

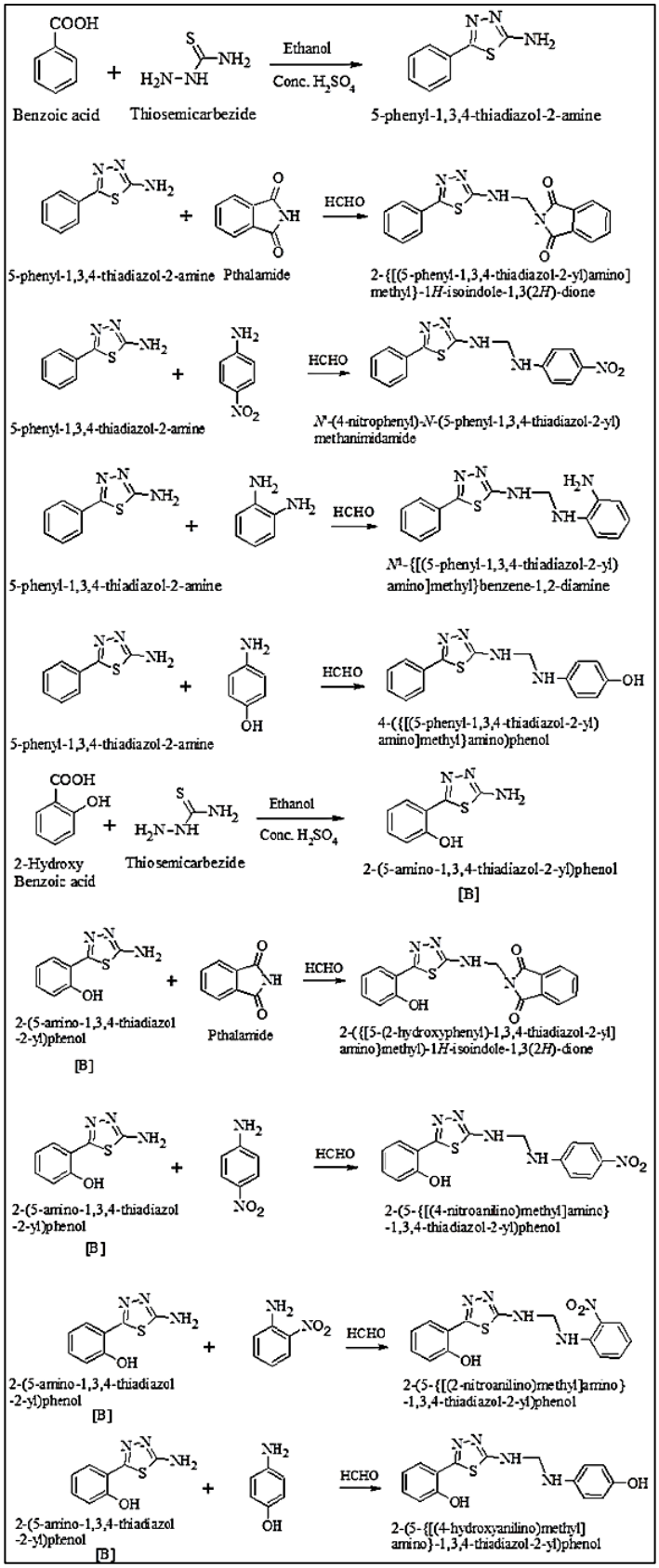


Figure 15: Synthesis of novel 1, 3,4 thiadiazole derivatives for their antimicrobial activities

AK Gadad [25] synthesised a series of 2-sulfonamido/trifluoromethyl-6-(4'-substitutedaryl/heteroaryl) imidazo[2,1-b]-1,3,4-thiadiazole derivatives have been synthesized by reaction of 2-amino-5-sulfonamido/trifluoromethyl-1,3,4-thiadiazoles and an appropriate a-halo- aryl/heteroaryl ketones. Further 5-bromo, 5-thiocyanato, 5-gaunylhydrazone derivatives were synthesized in order to study the effect of these substituents on biological activity (Figure 16).

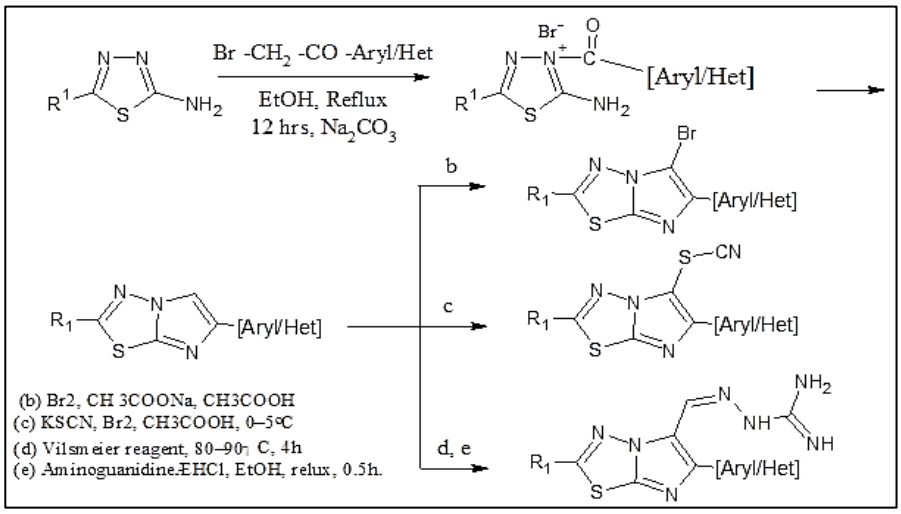


Figure 16: Synthesis of a series of 2-sulfonamido/trifluoromethyl-6-(4'-substitutedaryl/heteroaryl) imidazo[2,1-b]-1,3,4-thiadiazole derivatives

S Schenone et al. [26] synthized series of N-[5-oxo-4-(arylsulfonyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]-amides and tested *in vivo* for their analgesic and anti-inflammatory activities. All the new synthesized compounds possess good antalgic action in the acetic acid writhing test and some terms of the series showed also fair anti-inflammatory activity in the carrageenan rat paw edema test (Figure 17).

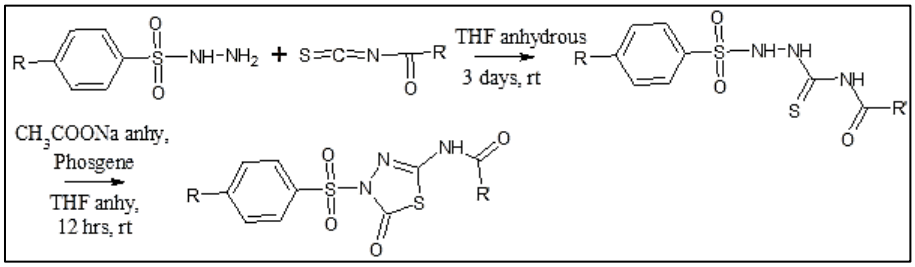
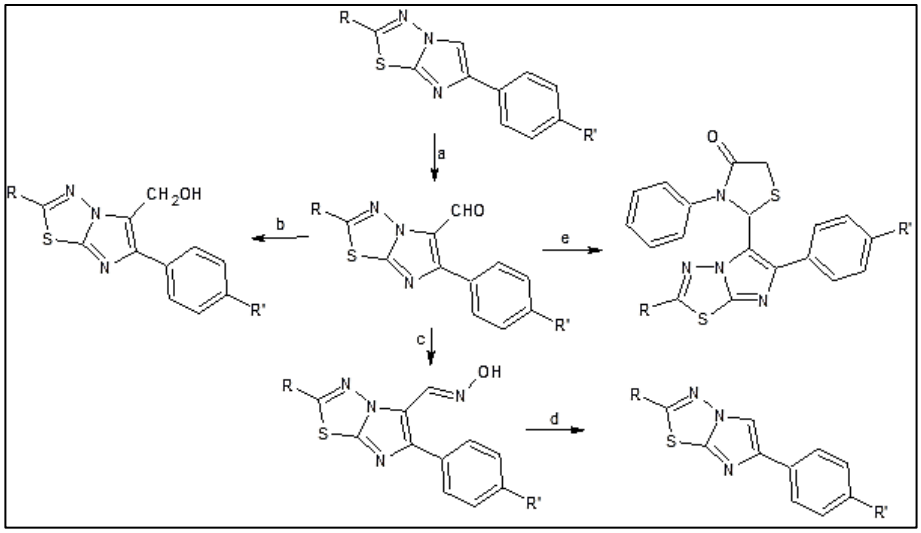


Figure 17: Synthesis of series of N-[5-oxo-4-(arylsulfonyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]-amides

G Kolavi et al. [27] synthesized a series of 2,6-disubstuted and 2,5,6- trisubstuted imidazo[2,1-b][1,3,5]thiadiazoles were synthesized and screened for anti-tubercular activity and some compounds show the good inhibitor activity (Figure 18).



R = Cyclohexyl, 2-furyl, 2-thienyl, R' = H, Br

(a) DMF/POCl3, Na2CO3, (b) NaBH4, MeOH, rt, (c) NH2OH.HCl, Pyridine reflux, (d) SoCl2, digest 10 min, (e) (i)PhNH2, EtOH, reflux, (ii) Thioglycolic acid, benzene, reflux

Figure 18: Synthesis of a series of 2,6-disubstuted and 2,5,6- trisubstuted imidazo[2,1-b][1,3,5]thiadiazoles

P Zhan et al. [28] discover novel synthetic route for 2-(4-(2,4-dibromophenyl)-1,2,3-thidiazole-5-ylthio)acetamide derivatives. The entire synthesized compound subjected to anti-HIV activity evolution and most of the compound showed good range of activity (Figure 19).

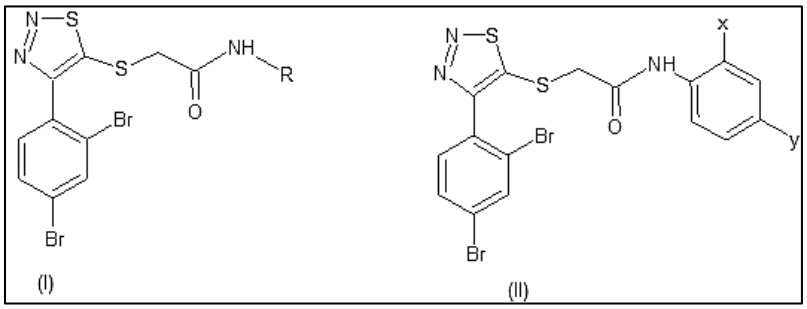


Figure 19: Novel synthetic route for 2-(4-(2,4-dibromophenyl)-1,2,3-thidiazole-5-ylthio)acetamide derivatives

MN Noolvi et al. [29] synthesized a series of 2,5,6-trisubstitutrd imidzo[2,1-b][1,3,4] thidiazole derivative. Furthermore 5-bromo and 5-thiocyanato derivative were synthesized. Some of this compound was tested for anticancer activity (Figure 20).

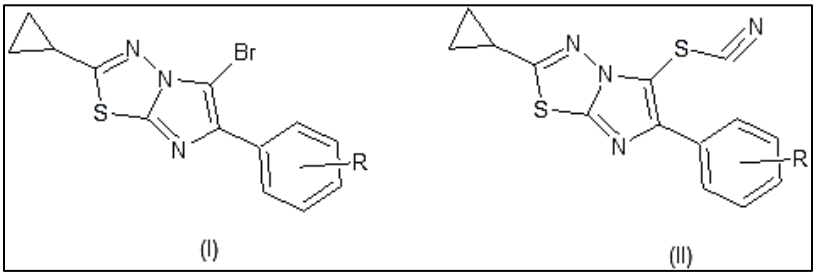


Figure 20: Series of 2,5,6-trisubstitutrd imidzo[2,1-b][1,3,4] thidiazole derivative

NMA El-Rahman et al. [30] used both conventional and ultrasonic method to synthesize 1,3,4 – thiadiazole and bi(1,3,4 - thiadiazole) derivative (Figure 21).

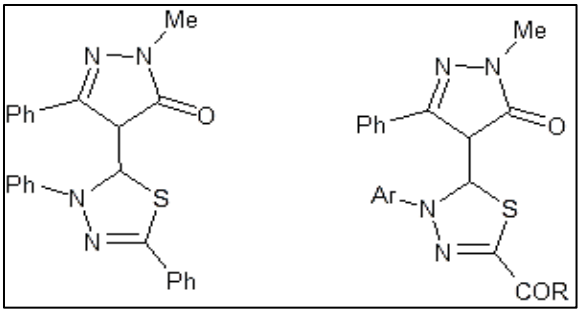
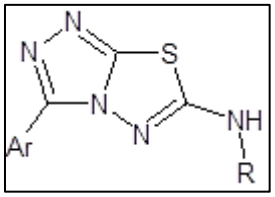


Figure 21: Thiadiazole and bi(1,3,4 - thiadiazole) derivative

M Amir et al. [31] used one pot synthetic route to synthesize series of 3,6 disubstituted-1,2,4-triazolo-[3,4,b]-1,3,4-thidiazoles. Some of this synthesized compound was tested for anti-inflammatory activity.



DA Ibrahim et al. [32] synthesized 3,6 disubstituted-triazolo-[3,4,b]-thidiazoles. The newly synthesizd compound were evaluated for their Cytotoxic acivity against a panel of 60 human cancer cell lines by National Cancer Institute (Figure 22).

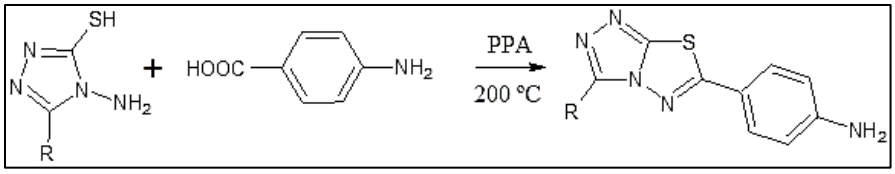


Figure 22: Synthesis of 3,6 disubstituted-triazolo-[3,4,b]-thidiazoles

SS Karki et al. [33] substituted different alkyl group (side chain) on imidazothidiazole of Levamisole. The entire snthesized compound was tested for cytotoxicity. Among them some compound showed string cytotoxicity (Figure 23).

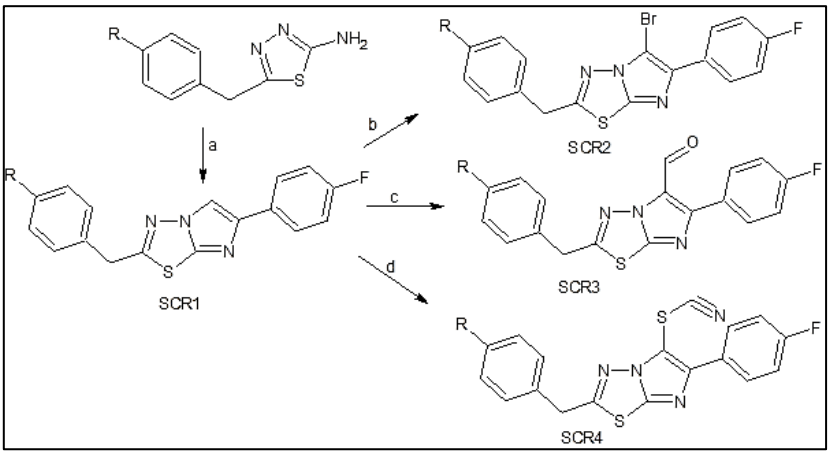
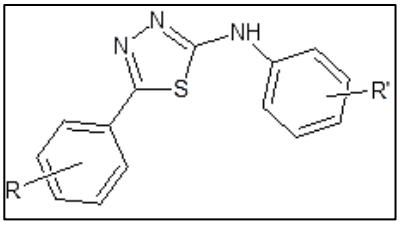


Figure 23: (a) (i) F-C_6H_4-$COCH_2Br$, EtOH, (ii) Na_2CO_3, (b) Br_2, gl. acetic acid, (c) $POCl_3$, DMF, 80-90°C (d) KSCN, gl.Acetic acid, Br_2 in gl.Acetic acid. 0-5°C

I Khan et al. [34] prepared a new series of 4,5-disubstituted 2,4-dihydro-3H-1,2,4-triazole-3-thiones and 2,5-disubstituted-1,3,5-thidiazoles by dehydrative cyclization of hydrazine carbothioamide derivatives by refluxing in 4N aqueous sodium hydroxide by overnight reaction with phosphoric acid. The entire synthesised compound was tested for antioxidant activity.



RS Lamani et al. [35] synthesized novel methylene bridged benzisoxazolyl imidazole [2,1-b] [1,3,4]thidiazole by using benzisoxazolyl-3-acetic acid and thiosemicarbezide. All the synthesized compounds were screened for antimicrobial activity (Figure 24).

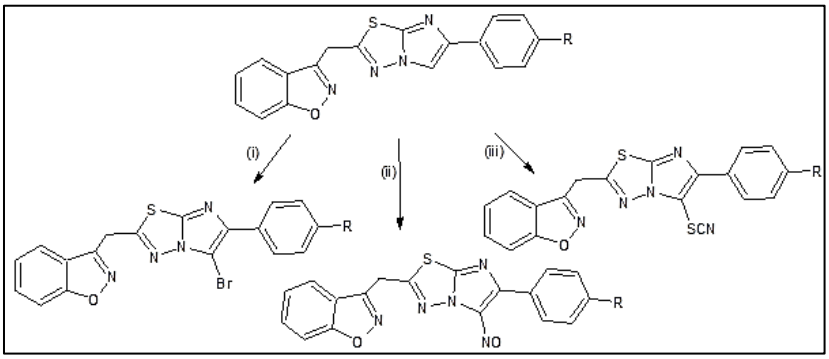


Figure 24: (i) Br_2/AcOH. sodium acetate, (ii) $NaNO_2$, AcOH, Reflux, 2 hr, (iii) Br_2, KSCN, AcOH

SK Srivastava et al. [36] synthesized 2-[2-{2-(Substitutedphenyl)-4-oxo-5-(substitutedaryliden)-1,3-thiazolidin}-acetylimino]-mercapto-5-methyl-1,3,4-thiadiazole from 2-(2-hydrazinoacetyl)-mercapto-5-methyl-1,3,4-thiadiazole, using 2-mercapto-5-methyl-1,3,4-thiadiazole as the starting material. All the synthesized products were evaluated for their and antibacterial activity against *B. substilis, E. coli. K. Pneumonia* and *S. aureus* bacteria and antifungal activity against *A. niger*, *A. flavus*, *F. oxisporium* and *T. viride* fungi respectively. The structures of all the synthesized compounds have been determined by their spectral and micro analytical data (Figure 25).

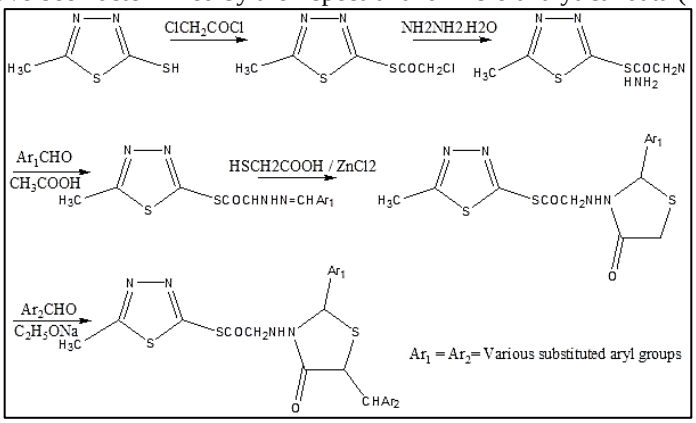


Figure 25: Synthesis of 2-[2-{2-(Substitutedphenyl)-4-oxo-5-(substitutedaryliden)-1,3-thiazolidin}-acetylimino]-mercapto-5-methyl-1,3,4-thiadiazole

M Al-Ghorbani [37] synthesized 3-(2-aroylaryloxy) methyl-5-mercapto-4-phenyl-4H-1,2,4-triazole analogues (6a-e) and using Substituted phenyl benzoates as starting material. Synthesized compounds were evaluated by DPPH, nitric oxide and hydrogen peroxide radical scavenging methods. The investigation of antioxidant screening revealed that some of the tested compounds showed good to moderate antioxidant activity. Interestingly, the results show that the compounds containing electron releasing groups like methyl and methoxy exhibit good activities (Figure 26).

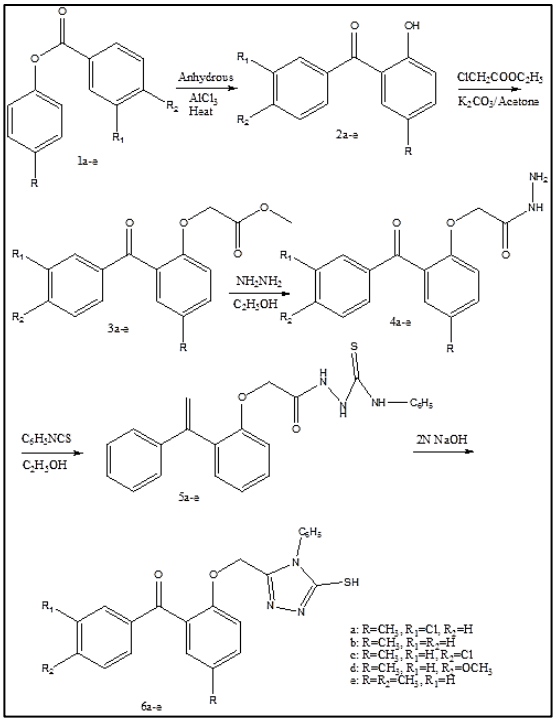


Figure 26: Synthesis of 3-(2-aroylaryloxy) methyl-5-mercapto-4-phenyl-4H-1,2,4-triazole analogues

DT Tayade and SA Waghmare [38] developed Single step synthesis of (2E)-1-[4-(3-substitutedimino-1,2,4-dithiazolo) aminophenyl] -3- (3,4- dimethoxyphenyl) prop-2-en-1-one using liquid bromine in chloroform medium as an oxidizing agent. The products were isolated, characterized and justified on the basis of conventional elemental analysis, chemical characteristics and spectral studies (Figure 27).

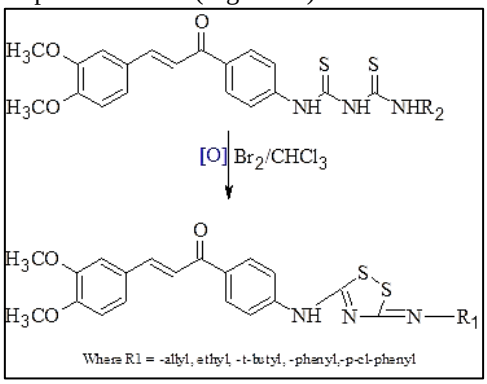


Figure 27: Single step synthesis of (2E)-1-[4-(3-substitutedimino-1,2,4-dithiazolo) aminophenyl] -3- (3,4- dimethoxyphenyl) prop-2-en-1-one

REFERENCE

[1] NS Mahajan; SR Pattan; RL Jadhav; NV Pimpodkar; AM Manikrao. *Int J Chem Sci*. **2008**, 6(2), 800-806.
[2] T Karabasanagouda; AV Adhikari; D Ramgopal; G Parameshwarappa. *Indian J Chem*. **2008**, 47B, 144-152.
[3] KM Basavaraja; B Somasekhar; S Appalaraju. *Indian J Heterocycl Chem*. **2008**, 18, 69-72.
[4] TF Abbs; F Reji; SKC Devi; KK Thomas; KG Sreejalekshmi; SL Manju; M Francis; SK Philip; A Bharathan; KN Rajasekharan. *Indian J Chem*. **2008**, 47B, 1145-1150.
[5] AA Chowki; CS Magdum; PL Ladda; SK Mohite. *Int J Chem Sci*. **2008**, 6(3), 1600-1605.
[6] R Basawaraj; M Suresh; SS Sangapure. *Indian J Heterocycl Chem*. **2005**, 15,153-156.
[7] A Hetzhein; A Mockel. *Adv Heterocycle Chem*. **1996**, **7**, 183.

[8] J Sandstrom. *Adv Heterocycle Chem*. **1968**.
[9] A Mavrova; D Wesselinova; YA Tsenov; P Denkova. *Eur J Med Chem*. **2009**, 44, 63-69.
[10] P Chaturvedi; P Valentina; P Kamaria. *Der Pharmacia Lettr*. **2013**, 5(4), 344-350.
[11] MR Mahendrasinh; PV Hemul; MR Lata; KP Naynika. *Int J Res Chem Environ*. **2013**, 3, 9-15.
[12] S Geogeta, CUC Stela, E Egri, Anamaria. Salvan Farmacia, **2010**, 58, 6.
[13] J Malgorzata; J Matysiak; N Andrzej; WojciechRzeski. *Folia Histochemicatcytobiologica*. **2011**, 49, 436-444.
[14] MK Abdalla; MM Hadi. *Int J Electrochem Sci*. **2012**, 10074-10093.
[15] MM Raj; HV Patel; LM Raj; NK Patel. *Int J Pharm Chem Biol Sci*. **2013**, 3(3), 814-820.
[16] A Kumar; MA Ali; SA Khan. *Indian J Chem*. **2009**, 4813, 1288-1293
[17] SK Chitale; B Ramesh; CM Bhalgat; V Jaishree; C Puttaraj; DR Bharathi. *Res J Pharm Technol*. **2011**, 4(10), 1540-1544.
[18] M Shaharyar; MW Akhter. *Acta Poloniae Pharmaceutica Drug Res*. **2009**, 66(4), 393-397.
[19] AK Verma; A Martin. *Int J Pharm Arch*. **2014**, 3(9), 1-5.
[20] A Rahman; AK Shakya; S Wahab; NH Ansari. *Bulgarian Chem Commun*. **2014**, 46(4), 750-756.
[21] A Naskar; T Singha; T Guria; J Singh; AB Kumar; TK Maity. *Int J Pharmacy Pharm Sci*. **2015**, 7(3), 397-402
[22] M Asif; C Asthana. *Int J Chem Tech Res*. **2009**, 1(4), 1200-1205.
[23] S Banerjee; TVSS Swaroop; IC Ferdy; A Singh; SM Lakshmi; S Mohan. *J Indo Am J Pharm Res*. **2014**, 2(2), 1074-1082.
[24] MR Mahendrasinh; VP Hemul; MR Lata; KP Naynika. *IJPCBS*. **2013**, 3(3), 814-819.
[25] AK Gadad; MN Noolvi; RV Karpoormath. *Bioorgan Med Chem*. **2004**, 12, 5651-5659.
[26] S Schenone; C Brullo; O Bruno; G Falcone. *Bioorgan Med Chem*. **2006**, 14, 1698-1705.
[27] G Kolavi; V Hegde; AK Imtiyaz; P Gadad, *Bioorgan Med Chem*. **2006**, 14, 3069-3080.
[28] P Zhan; X Liu; Z Li; D Wang; ED Clercq. *Bioorgan Med Chem*. **2009**, 17, 5920-5927.
[29] MN Noolvi; HM Patel; N Singh; AK Gadad. *Eur J Med Chem*. **2011**, 46, 4411-4418.
[30] NMA EL-Rahman; TS Saleh; MF Mady. *Ultrasonic Sonochem*. **2009**, 16, 70-74.
[31] M Amir; H Kumar; SA Javed. *Eur J Med Chem*. **2008**, 43, 2056-2066.
[32] DA Ibrahim. *Eur J Med Chem*. **2009**, 44, 2776-2781.
[33] SS Karki; K Panjamurthy; S Kumar; M Nambiar; KK Chiruvella; SS Raghavan. *Eur J Med Chem*. **2011**, 46, 2109-2116.
[34] I Khan; S Ali; S Hameed; NH Rama; MT Hussain; R Uddin; A Khan; MI Chaudhary. *Eur J Med Chem*. **2010**, 45, 5200-5207.
[35] RS Lamani; NS Shetty; RR Kamble; IAM Khazi. *Eur J Med Chem*. **2009**, 44, 2828-2833.
[36] SK Srivastava; S Verma; SD Srivastava. *J Chem Pharm Res*. **2010**, 2(5), 270-276.
[37] M Al-Ghorbani; VR Lakshmi; T Prashanth; A Bushra Begum; P Naveen; SA Khanum. *J Chem Pharm Res*. **2013**, 5(7), 246-250.
[38] DT Tayade; SA Waghmare. *J Chem Pharm Res*. **2016**, 8(5): 934-937.