ORIGINAL RESEARCH ARTICLES

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW 1,3,4-OXADIAZOLES, 1,2,4-TRIAZOLES AND 1,3,4-THIADIAZOLES

Laddi U. V.* and Desai S. R.

(Received 19 October 2015) (Accepted 08 February 2016)

ABSTRACT

Some new 5-[((α-phenyl/methyl)benzylidene)amino)oxy]methyl/ethyl-2-[4-(substituted aryl)/allyl)] amino-1,3,4-oxadiazoles (4a-p), 3-[((α-phenyl/methyl)- benzylidene) amino)oxy]methyl/ethyl-4-(4-substitutedaryl)/allyl-5-mercapto-1,2,4-triazoles (5a-p) and 5-[((α-phenyl/methyl)-benzylidene)amino) oxy]- methyl/ethyl-2-[4-(substituted aryl)/allyl)]amino-1,3,4-thiadiazoles (6a-p) were prepared starting from α/β-[((α-(phenyl/methyl)benzylidene)amino)oxy acetic/propionic acid hydrazides (1a-d). The structures of all the compounds have been established by elemental and spectral (IR, ^{1}HNMR and mass) analysis. All the newly synthesised compounds have been screened for their antimicrobial activity against *Escherichia coli, Bacillus cirroflagellosus, Aspergillus niger and Rhizoctonia bataticola.* Some of the newly synthesised compounds have been evaluated for antituberculosis activity against *Mycobacterium tuberculosis H37Rv* strain by BACTEC radiometric system at Southern Research Institute, Birmingham, AL and Frederick Research Centre, Frederick, MD. Significant antimicrobial activity is observed against *Escherichia coli* and *Rhizoctonia bataticola.* A few compounds also exhibited interesting antitubercular activity against *Mycobacterium tuberculosis H37Rv strain.*

Keywords: 1,2,4-triazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, aminoxy methyl/ethyl moiety, antituberculosis and antimicrobial, activity.

Multidrug-resistant organisms have emerged as a major threat, because of the abundant and often inappropriate use of broad-spectrum antibiotics. The multidrug resistance is a new challenge to our current therapeutic armamentarium and hence there is more responsibility on researchers for developing new and effective antibiotics.

Compounds with 1,3,4-oxadiazole moiety have been reported from our laboratory to possess antimicrobial activities[1,2]. Thiosemicarbazides, 1,3,4-oxadiazoles and 1,3,4-thiadiazoles are reported to possess antimicrobial activities[3,4] anticonvulsant[5,6], antiviral[7], antiinflammatory[8] and antitumor[9] activities. In view of these reports and in continuation of our search for 'nitrogen heterocycles of pharmacological interest[10-12], we report herein the synthesis, antimicrobial and antitubercular activities of some new 1,3,4-oxadiazoles, 1,2,4-triazoles and 1,3,4-thiadiazoles with "methylene amino oxy methyl moiety" (MAOM) a biologically active "biostere"[10] at the 2nd position of 1,3,4-oxadiazole and 1,3,4-thiadiazole rings and 3rd position of 1,2,4-triazole ring, respectively. The synthetic route to the title compounds is depicted as Scheme 1. All the newly synthesised compounds have been screened for their antimicrobial activity against *Escherichia coli*, *Bacillus cirroflagellosus*, *Aspergillus niger* and *Rhizoctonia bataticola*. Some of the newly synthesised compounds have been evaluated for antituberculosis activity against, *Mycobacterium tuberculosis H37Rv.*

For Correspondance:
Department Of Chemistry,
Channabasaveshwara Institute of Technology,
N.H. 206, B.H. Road,
Gubbi, Tumkur-572 216, Karnataka, India
E-mail: dr.umesh1969@gmail.com

MATERIALS AND METHODS

Physicochemical properties and spectral characterisation:

Melting points were determined in open capillaries and are uncorrected. IR spectra in KBr were recorded on a Perkin Elmer spectrophotometer and ^{1}HNMR spectra on a Varian 300 MHz NMR spectrometer using TMS as an internal standard (chemical shifts in δ ppm). Mass spectra were recorded on a Finnig Mat 8230 spectrometer.

Indian Journal of Chemistry
Vol. 52B, August 2013, pp 1176-1181

Note

Synthesis and antimicrobial activities of some new 1,2,4-triazole derivatives

Shobha Desai*[a], Umesh Laddi[b], Rajani Bennur[c] & Shankar Bennur[c]

[a]Department of Chemistry, SS Arts College and T P Science Institute, Sankeshwar 591 313, India

[b]Department of Chemistry, Channabasaveshwar Institute of Technology, NH 206 (BH Road), Gubbi 572 216, India

[c]Department of Chemistry, Karnatak University, Dharwad 580 003, India

E-mail: dr.shobha.desai@gmail.com

Received 6 September 2011; accepted (revised) 13 May 2013

The triazole nucleus is one of the most important and well known heterocycle which is a common and integral feature of a variety of natural products and medicinal agents. The wide spectrum of antimicrobial, antiviral and potent pharmacological activities of triazole and their derivatives has established them as medicinally significant scaffolds. In view of these reports and in continuation of the search for triazole derivatives with better antimicrobial activities, herein is reported the synthesis and antimicrobial activities of some new triazole derivatives with biologically active sulphonamide moiety at the 3rd position. The structures of the newly synthesised compounds have been established on the basis of their spectrochemical data and elemental analysis. All the compounds have been screened for antimicrobial activities against *Escherichia coli*, *Bacillus cirroflagellosus*, *Aspergillus niger* and *Colletotrichum capsici* by cup plate method using Cotrimoxazole and Diflucan as standards.

Keywords: 1,2,4-Triazoles, antimicrobial activity, sulphonamide, pharmacophore, biologically active

It is well known that, azoles are an emerging class of drugs, wherein either an imidazole or a triazole group is joined to an asymmetric carbon atom as their functional pharmacophore (*e.g.*, *Ketaconazole*, *Fluconazole*, *Itraconazole*, *Ravuconazole*, *Voriconazole* and *Posaconazole*). Encouraged by these systematic serendipitous reports, established pharmacological activities such as antimicrobial[1-3,6], antiinflammatory[4,5], analgesic[6], anticancer[7] activities and in continuation of the search for triazole derivatives with better antimicrobial activities[8-10], herein is reported the synthesis and antimicrobial activities of some new 1,2,4-triazole derivatives. All the compounds were screened for their antimicrobial activities against *Escherichia coli*, *Bacillus cirroflagellosus*, *Aspergillus niger* and *Colletotrichum capsici* by cup plate method using Cotrimoxazole (Trimethoprim 500 mg and Sulphamethoxazole 800 mg) and Diflucan as standards. The synthetic route for the same is depicted as **Scheme I**.

In the present investigation, 3-β-[(N-benzene-sulphonyl/tosyl)-4-(un)substituted anilino] ethyl-4-anilino-5-mercapto-1,2,4-triazoles **3a-f**, were obtained by refluxing potassium salts of β-[(N-benzene-sulphonyl/tosyl)-4-(un)substituted anilino]propionyl dithiocarbazinates[11] with phenyl hydrazine. Condensation of triazoles **2a-f** (Ref 11) with aliphatic/aromatic acids in phosphoryl chloride yielded 3-β-[(N-benzenesulphonyl/tosyl)-4-(un)-substituted anilino]ethyl-6-H/CH_3/C_6H_5/*p*-$NO_2C_6H_4$-*s*-triazolo(3,4-*b*)(1,3,4)thiadiazoles **4a-d'**. Condensation of two moles of triazoles **2a-f**, with one mole of oxalic acid in phosphoryl chloride yielded 6,6'-bis-{β-[(N-benzenesulphonyl/tosyl)-4-(un)substituted anilino]ethyl-*s*-triazolo(3,4-*b*)(1,3,4) thiadiazoles} **5a-f**. The reaction of triazoles **2a-f**, with hydrazine hydrate, yielded 3-β-[(N-benzenesulphonyl/tosyl)-4-(un)-substituted anilino]ethyl-4-amino-5-hydrazino-1,2,4-triazoles **6a-f**. 3-β-[(N-Benzenesulphonyl/tosyl)-4-(un)substituted anilino]ethyl-*s*-triazolo(3,4-*b*)(1,3,4) thiadiazole-6-(5*H*)-thiones **7a-f**, were obtained by refluxing triazoles **2a-f**, with alcoholic potassium hydroxide and carbon disulphide. Cyclocondensation of triazoles **2a-f**, with benzoin yielded 5(*H*)-3-β-[(N-benzenesulphonyl/tosyl)-4-(un)substituted anilino]-ethyl-6,7-diphenyl-*s*-triazolo(3,4-*b*)(1,3,4)thiadiazines **8a-f**. 3-β-[(N-Benzenesulphonyl/tosyl)-4-(un)substituted anilino]ethyl-6-phenyl-*s*-triazolo(3,4-*b*)(1,3,4)-thiadiazines **9a-f**, were obtained by cyclocondensation of triazoles **2a-f**, with phenacyl bromide. Synthetic route to the title compounds is depicted in **Scheme I**. The structures of the newly synthesised compounds were confirmed by elemental and spectral (IR, ^{1}H NMR and mass) analysis.

Antimicrobial Activity

After establishing the physicochemical properties, all the compounds were screened for antimicrobial activities against *Gram negative* bacterium *Escherichia coli*, *Gram positive* bacterium *Bacillus cirroflagellosus* and fungi *Aspergillus niger* and