National Conference on New Horizons in Material Science
© 2018 IJSRSET | Volume 4 | Issue 3 | Print ISSN: 2395-1990 | Online ISSN : 2394-4099
Themed Section : Engineering and Technology

Synthesis of Some Novel Tetrazole Derivatives & Evaluation of Their Biological Activity

Dhas A. K.[1], Shirsat A. J.[2],Rupnar B. D.[2], Bhagat S. S.[2], Kakade G. K.[3]
[1]Department of chemistry, Deogiri College, Aurangabad, Maharashtra, India
[2]Department of chemistry, R. B. Attal Arts, Commerce & Science College, Georai, Beed, Maharashtra, India
[3]Department of chemistry, Arts, Commerce & Science College, Kille- Dharur, Beed, Maharashtra, India

ABSTRACT

High efficient process for the preparation of novel tetrazole derivatives has been developed from aryl nitrile and sodium azide through [3+2] cycloaddition reaction. This method has the advantage of high yield and easy work up process.

Keywords: Tetrazole, Azide, Antimicrobial Activity.

I. INTRODUCTION

Recently compounds containing tetrazole moiety have gained considerable attention because they have a wide range of applications in material science and medicinal chemistry. Various biological activities of these compounds are reported such as antihypertensive, antifungal, antibacterial, anticancer, antidiabetic, anticonvulsant, anti-inflammatory etc[1-3]. They also play a very important role as a ligand in coordination chemistry.

Tetrazole derivatives can be prepared by different methods. Generally, the most convenient and versatile procedure for the preparation of tetrazole is the cycloaddition between nitriles and azide[4]. Several methods have been reported for the synthesis of 1/5-substituted tetrazole, unfortunately these methods have some drawbacks such as long reaction times, use of expensive and toxic reagents and harsh reaction conditions, low yield, tedious work-up, and even the need for excess amounts of highly toxic and explosive hydrazoic acid[5-6]. Therefore, in order to overcome these drawbacks, it is necessary to develop a simple, convenient and more efficient method for the synthesis of tetrazole derivatives also it is necessary to synthesis novel tetrazole derivatives & checks them for biological activity[7-8].

II. MATERIALS AND METHODS

All chemicals used for the synthesis of the compounds were obtained from Sigma Aldrich and SD fine chemicals. Proton magnetic resonance (^{1}HNMR) spectra were recorded in 400 MHZ NMR spectrophotometer by using Deuterated Dimethyl Sulfoxide (DMSO-d_6) as solvent and Tetramethylsilane (TMS) as an internal standard. The Infra-Red (IR) spectra were recorded using Fourier Transform Infrared (FT-IR) spectrophotometer Model RZX (Perkin Elmer). Using Thin Layer Chromatography (TLC) purity of the synthesized compounds was checked. TLC silica gel coated plates obtained from Merck as stationary phase and mobile phase were mixture of ethyl acetate/hexane (20:80).

General Procedure

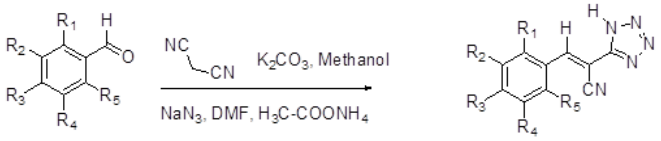
0.01 mole of aldehydes and 0.012 moles of malenonitrile was dissolved into 20 ml ethanol. In this reaction mixture 0.01 mole K_2CO_3 was added to initiate the reaction. The reaction mixture was reflux for 30 minutes. Solid was obtained that indicate completion of the reaction, further confirmed by thin layer chromatography. Then solid intermediate was isolated by filtration and then washed by using cold alcohol. The filtrate was dried at 60^0c in oven. In second step, 0.01 mole of above intermediate, 0.03 moles of sodium azide, 0.01mole sodium acetate and 20 ml dimethyl

formaamide was added as a solvent and heated at 100^0c for 6 hours. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction solvent was evaporated and 20 ml ethyl acetate was added into the flask to dissolve the residue obtained after the evaporation of dimethyl formaamide. Then the washing of 20 ml 10% hydrochloric acid was given to ethyl acetate layer. After washing ethyl acetate layer was dried over sodium sulphate and then ethyl acetate was evaporated to obtain tetrazole derivative. Using this typical procedure, other analogs of this series were prepared. Their structures have been confirmed by analyzing method such as ^{1}HNMR and IR spectra.

IR (1a) (cm-1): 1090 (C-Cl), 2350 (nitrile), 1585 (C=C), 1580 (C=N).

^{1}H-NMR (1a) (DMSO-d6) δ ppm: 7.24 (dd, 1H, Ar-H, J=2.5 &8.84 Hz), 7.21(dd, 1H, Ar-H, J=3.5 & 7.4 Hz), 7.22 (dd, 1H, Ar-H, J=3.5 &7.4 Hz), 7.24 (m, 1H, Ar-H), 7.54 (s, 1H, =C-H), 4.2 (s, 1H, N-H).

The reaction scheme for synthesis of novel tetrazole derivatives [1(a-i)] have been
Presented below in scheme 1.



Scheme 1

Table 1. Substituent attached to the aromatic ring of scheme 1.

Compound	R_1	R_2	R_3	R_4	R_5
1a	H	H	Cl	H	H
1b	OH	H	H	H	H
1c	H	OH	H	H	H
1d	H	H	OH	H	H
1e	H	H	OCH_3	OCH_3	H
1f	H	H	H	H	H
1g	H	H	OH	OCH_3	H
1h	H	H	F	H	H
1i	H	H	Br	H	H

III. RESULTS AND DISCUSSION

The novel tetrazole derivatives were synthesized successfully having good yields. The newly synthesized compounds were analyzed from ^{1}H-NMR and IR spectral analysis. Using disc diffusion method, newly synthesized compounds were screened for antimicrobial activity.

Antimicrobial activity

Compounds 1(a-i) were screened for their antimicrobial activity against Pseudomonas aeruginosa (ATCC 27853), Escherichia coli (ATCC 25922), Staphylococcus aureus (ATCC 25923) by paper disc diffusion method using gentamycin as a reference standard drug. At 100 µg/ml concentration, all the tests were evaluated. The culture media was Muller Hinton agar. After 24 h of incubation at 37°C the zone of inhibition was measured in mm. Microbial data for 1(a-i) as summarized in Table 2.

Table 2. Antimicrobial analysis data of compounds 1(a-j)

Sr. No.	Compound number	Pseudomonas aeruginosa (ATCC 27853)	Escherichia coli (ATCC 25922)	Staphylococcus aureus (ATCC 25923)
1	1a	No Zone	No Zone	No Zone
2	1b	No Zone	No Zone	No Zone
3	1c	No Zone	No Zone	No Zone
4	1d	No Zone	No Zone	No Zone

5	1e	No Zone	No Zone	No Zone
6	1f	No Zone	No Zone	No Zone
7	1g	No Zone	No Zone	No Zone
8	1h	No Zone	No Zone	No Zone
9	1i	No Zone	No Zone	No Zone
10	1j	No Zone	No Zone	No Zone
11	Gentamycin	23 mm	28 mm	32 mm

IV. CONCLUSION

The newly synthesized compounds were screened for their antimicrobial activity against Candida sp., and Gram-negative as well as Gram-positive bacterial strains. The synthesized compounds do not shown any activity as compared to standard drug. Chalcones are intermediate in the biosynthesis of flavonoid. They are a very valuable compounds whether from bioactivity aspects or from organic synthesis aspects. Chalcones exhibit diverse pharmacological activities and can serve as synthons for synthesis of heterocyclic compounds. Due to these reasons, various preparation procedures were developed by many working Scientist and groups, including ecofriendly protocol.

V. ACKNOWLEDGEMENT

The authors are thankful to UGC, WRO, Pune for financial support & The Principal of Deogiri college, Aurangabad for providing laboratory facilities.

VI. REFERENCES

[1]. T. S. Lin, W. H. Prusoff, J. Med. Chem. 1978, 21, 109-112.
[2]. Zablocky, J. A.; Miyano, M.; Sashidhar, N. R.; Panzer-Knodle, S.; Nicholson, N.;
[3]. Feigen, L. J. Med. Chem. 1992, 35, 4914-4917.
[4]. B. Das, C. R. Reddy, D. N. Kumar, M. Krishnaiah, R. Narender, Synlett, 2010, 391-394.
[5]. Kumar, A.; Narayanan, R.; Shechter, H. J. Org. Chem. 1996, 61, 4462-4465.
[6]. Sreedhar, B.; Kumar, A. S.; Yada, D. Tetrahedron Lett. 2011, 3565-3569.
[7]. Mohite P.B., Bhaskar V.H. International Journal of Pharm Tech Research Vol.3, No.3,pp 1557-1566,
[8]. Lang, L.; Li, B.; Liu, W.; Jiang, L.; Xu, Z.; Yin, G. Chem. Commun. 2010, 448-450.