ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 8, Issue, 12, pp. 22691-22695, December, 2017

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

SYNTHESIS AND BIOLOGICAL EVALUATION OF TETRAZOLE ANALOGUES OF PYRAZOLECARBALDEHYDE AS ANTIBACTERIAL AGENTS

Nagaraj A*., Aparna M., Nageswara Rao G., Ramesh Naik P and Raghuveer S

Department of Chemistry, Telangana University, Nizamabad, Telangana-503322 India

DOI: http://dx.doi.org/10.24327/ijrsr.2017.0812.1317

ARTICLE INFO

Article History:

Received 18th September, 2017
Received in revised form 10th October, 2017
Accepted 06th November, 2017
Published online 28th December, 2017

Key Words:

Pyrazole, Tetrazole,
Antibacterial activity.

ABSTRACT

A series of new 5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-aryl-1*H*-1,2,3,4-tetraazole 5(a-j) have been synthesized from *N*-[(*E*)-1-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)methylidene]-*N*-arylamine 4(a-j). The structures of the synthesized compounds have been confirmed *via* IR, ^{1}H NMR, ^{13}C NMR and MS spectral analyses. Further, all the synthesized new compounds 5(a-j) have been assayed for their antibacterial activity against Gram-positive bacteria *viz*. *Bacillus subtilis*, *Bacillus sphaericus* and *Staphylococcus aureus*, and Gram-negative bacteria *viz*. *Pseudomonas aeruginosa*, *Klobsinella aerogenes* and *Chromobacterium violaceum*. The antibacterial screening data reveal that, compounds 5 which contain 4-methoxyphenyl (5c), 4-fluorophenyl (5d) and 2,5-difluorophenyl (5h) moieties on tetrazole ring might be the reason for the significant inhibitory activity. Most of these new compounds showed appreciable activity against test bacteria and emerged as potential molecules for further development.

INTRODUCTION

The treatment of infectious diseases still remains an important and challenging problem because of a combination of factors including emerging infectious diseases and the increasing number of multi-drug resistant microbial pathogens. In spite of a large number of antibiotics and chemotherapeutics available for medical use, at the same time the emergence of old and new antibiotic resistance created in the last decades revealed a substantial medical need for new classes of antimicrobial agents.

Tetrazole derivatives have a potential pharmacological activities, such as antihypertensive (Ramakrishna *et al*, 2017), antimicrobial (Abdl *et al*, 2013), corrosion inhibitor (Mihit *et al*, 2010), anti-inflammatory (Sukumar *et al*, 2008), anticancer (Gorle *et al*, 2017), antioxidant (Julliano *et al*, 2017), analgesic (Shantaram *et al*, 2013), antiviral (Hutchinson *et al*, 1985), protein arginine deiminase inhibitor (Subramanian *et al*, 2015), anti allergic (Roger *et al*, 1986), dual selective serotonin and nor epinephrine reuptake inhibitors (Paudel *et al*, 2016) and HIV inhibitors (da Silva *et al*, 2009). Similarly, pyrazole and its derivatives possess a broad spectrum of biological effectiveness such as antiviral (Osama *et al*, 2009), antibacterial (Yu *et al*, 2015), antidepressants (Gamal *et al*, 2009), inhibitors of protein kinases (Persson *et al*, 2007), anticancer (Balbi *et al*, 2011), antiarthritic (Nugent *et al*, 1993), and herbicidal (Kudo *et al*, 1999). Some aryl pyrazoles (Mohd *et al*, 2016) were reported to have non-nucleoside HIV-1 reverse transcriptase inhibitors (Genin *et al*, 2000), COX-2 inhibitors (Habeeb *et al*, 2001), potent activator of the nitric oxide receptor and soluble guanylate cyclise (David *et al*, 2001). Besides, great interest in the pyrazole molecule has been stimulated by some promising pharmacological, agrochemical and analytical applications of its derivatives (Florence *et al*, 2013).

Owing to the immense importance and varied bioactivities exhibited by tetrrazole and pyrazole derivatives and in continuation of our ongoing research on the synthesis of new heterocyclic compounds (Nagaraj *et al*, 2015, 2017; Sanjeeva Reddy *et al*, 2015, 2016, 2017), it was thought of interest to accommodate tetrazole and pyrazole moieties in a single molecular frame and to obtain a new heterocyclic compounds with potential biological activity. In this article, we wish to report the synthesis of new class of tetrazole analogues of pyrazolecarbaldehyde 5(a-j) and evaluation of their *in vitro* antibacterial activity

MATARIALS AND METHODS

All reagents are commercial grade and were used as supplied. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F_{254} plates from Merck, and compounds

Corresponding author:* **Nagaraj A
Department of Chemistry, Telangana University, Nizamabad, Telangana-503322 India

visualized by exposure to UV light. Chromatographic columns 70-230 mesh silica gel for separations were used. Melting points were determined on a Fisher-Johns apparatus and are uncorrected. IR spectra were recorded using KBr disk on a Perkin-Elmer FTIR spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C). Chemical shifts are reported in δ ppm units with respect to TMS as internal standard and coupling constants (*J*) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer.

Synthesis of 3,5-dimethyl-1-phenyl-1*H*-pyrazole (2): A mixture of acetyl acetone **1** (0.02 mol), and phenyl hydrazine hydrochloride (0.02 mol) in ethanol (20 ml) was heated under reflux for 3 h on a water bath. After completion of the reaction ethanol was evaporated, the residue was dissolved in water, neutralized with sodium bicarbonate and extracted with ether. The solvent was evaporated under reduced pressure to get the compound **2** as yellow-brown liquid. Yield 90%; b.p. 270-272 ^{o}C; IR (KBr) ν_{max}: 3010, 2962, 1516, 1510 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 6.21 (s, 1H, Ar-H), 7.10-7.20 (m, 5H, ArH); MS: *m/z* 172 (M^+).

Synthesis of 3,5-dimethyl-1-phenyl-1*H*-4-pyrazolecarbaldehyde (3): To a cold solution of *N*,*N*-dimethylformamide (0.02 mol), freshly distilled phosphorous oxychloride (0.01 mol) was added with stirring over a period of 30 minutes. When formylation solution was obtained, a solution of compound **2** (0.01 mol) in *N*,*N*-dimethylformamide (5 ml) was added drop wise while maintaining the temperature 0-5 ^{o}C. The resulting mixture was heated under reflux for 1 h, cooled and poured with continuous stirring onto crushed ice and the formed yellow precipitate was filtered, crystallized from aqueous ethanol to get the pure compounds. Yield 86%, mp 124-126 ^{o}C; IR (KBr) ν_{max}: 3012, 2961, 2854, 1700, 1516, 1505 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.64 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 7.15-7.25 (m, 5H, Ar-H), 9.98 (s, 1H, CHO); MS: *m/z* 200 (M^+).

General procedure for the synthesis of Schiffs bases 4(a-j): A mixture of compound **3** (0.01 mol) and corresponding aryl amine (0.01 mol) in acetic acid (0.5 mL) was refluxed in toluene for 3 h using a Dean-Stark apparatus and the water formed was removed azeiotropically. The progress of the reaction was checked by TLC using toluene: ethyl acetate (4:1) as an eluent. After completion of the reaction, solvent was removed by distillation to give the solid, which was filtered, and recrystallized from methyl alcohol to get the pure compounds **4 (a-j)**.

***N*-[(*E*)-1-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)methylidene]-*N*-phenylamine (4a):** Yield 52%; m.p. 127-129^{o}C; IR (KBr) ν_{max}: 3052, 2932, 1616, 1584, 1523 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.32 (s, 3H, CH_3), 2.59 (s, 3H, CH_3), 7.10-7.25 (m, 10H, ArH), 8.19 (s, 1H, CH=N); MS: *m/z* 275 (M^+).

General procedure for the synthesis of 5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-aryl-1*H*-1,2,3,4-tetraazole 5(a-j): A mixture of Schiffs base **4(a-j)** (0.01 mol) and PCl_5 (0.01 mol) was heated at 100 ^{0}C for one hour. When the evolution of fumes of HCl ceased, excess of PCl_5 was removed under reduced pressure and the residual imidoyl chloride was treated with an ice-cold solution of sodium azide (0.02 mol) and excess of sodium acetate in water (15 mL) and acetone (20 mL) with stirring. Stirring was continued for overnight, there after acetone was removed under reduced pressure. The remaining aqueous portion was extracted with chloroform was dried and recrystallized from ethanol to get the pure compounds **5(a-j)**.

5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-phenyl-1*H*-1,2,3,4-tetraazole (5a): Yield 42%; IR (KBr) ν_{max}: 3047, 2854, 1616, 1581, 1550, 1523 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.28 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 7.10-7.20 (m, 5H, ArH), 7.40-7.50 (m, 5H, ArH); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 11.2, 14.5, 115.2, 122.7, 127.6, 128.1, 123.7, 129.4, 133.1, 133.6, 135.1, 139.4, 139.7, 147.8; MS: *m/z* 316 (M^+).

5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-(4-methylphenyl)-1*H*-1,2,3,4-tetraazole (5b): Yield 51%; IR (KBr) ν_{max}: 3052, 2853, 1614, 1582, 1549, 1524 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.28 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 7.10-7.20 (m, 5H, ArH), 7.40-7.50 (m, 4H, ArH); MS: *m/z* 330 (M^+).

4-[5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1*H*-1,2,3,4-tetrazol-1-yl]phenylmethylether (5c): Yield 40%; IR (KBr) ν_{max}: 3053, 2851, 1610, 1583, 1549, 1524, 1071 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.29 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 7.10-7.20 (m, 7H, ArH), 7.47 (d, *J* = 7.2 Hz, 2H, ArH); MS: *m/z* 346 (M^+).

5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-(4-fluorophenyl)-1*H*-1,2,3,4-tetraazole (5d): Yield 45%; IR (KBr) ν_{max}: 3051, 2847, 1610, 1581, 1552, 1525 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.29 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 7.10-7.20 (m, 5H, ArH), 7.50-7.60 (m, 4H, ArH); MS: *m/z* 334 (M^+).

1-(4-bromophenyl)-5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1*H*-1,2,3,4-tetraazole (5e): Yield 44%; 3051, 2847, 1610, 1581, 1552, 1525, 585 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.30 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 7.10-7.20 (m, 5H, ArH), 7.40-7.50 (m, 2H, ArH), 7.81 (d, *J* = 8.5 Hz, 2H, ArH); MS: *m/z* 395 (M^+), 397 (M^++2).

5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-(3-nitrophenyl)-1*H*-1,2,3,4-tetraazole (5f): Yield 54%; 3032, 2878, 1615, 1581, 1551, 1533, 1379 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 7.10-7.20 (m, 5H, ArH), 7.80-7.90 (m, 3H, ArH), 8.67 (s, 1H, ArH); MS: *m/z* 361 (M^+).

5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-(4-nitrophenyl)-1*H*-1,2,3,4-tetraazole (5g): Yield 61%; 3047, 2912, 1617, 1594, 1559, 1541, 1368 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 7.10-7.25 (m, 7H, ArH), 8.33 (d, *J* = 8.2 Hz, 2H, ArH); MS: *m/z* 361 (M^+).

1-(2,5-difluorophenyl)-5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1*H*-1,2,3,4-tetraazole (5h): Yield 48%; 3031, 2872, 1611, 1590, 1544 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 7.00-7.20 (m, 7H, ArH), 7.63 (d, *J* = 8.1 Hz, 1H, ArH); MS: *m/z* 352 (M^+).

3-[5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1*H*-1,2,3,4-tetrazol-1-yl]phenol (5i): Yield 51%; 3342, 3032, 2873, 1612, 1589, 1544 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.29 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 5.29 (s, 1H, OH), 6.80-6.90 (1H, ArH), 7.00-7.25 (m, 8H, ArH); MS: *m/z* 332 (M^+).

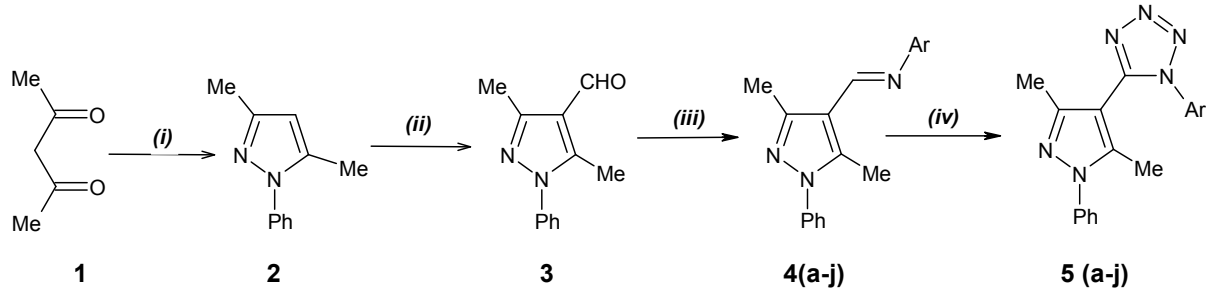
4-[5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1*H*-1,2,3,4-tetrazol-1-yl]phenol (5j): Yield 53%; 3341, 3033, 2873, 1612,

1589, 1547 cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.27 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 5.09 (s, 1H, OH), 7.10-7.20 (m, 6H, ArH), 7.47 (d, J = 7.8 Hz, 2H, ArH); MS: m/z 332 (M^+).

RESULTS AND DISCUSSION

The cyclo-condensation of ethylacetoacetate 1 with phenyl-hydrazine in ethanol at reflux temperature for 3 h gave the 3,5-dimethyl-1-aryl-1*H*-pyrazole 2 in good yields. Formylation of 2 with DMF in phosphorous oxychloride, at reflux for 1 h, gave the 3,5-dimethyl-1-aryl-1*H*-4-pyrazolecarbaldehyde 3 in 86% of yield (Sanjeeva Reddy *et al*, 2010). Further, condensation of compound 3 with corresponding arylamine in presence of acetic acid in toluene at reflux temperature for 3 h, gave *N*-[(*E*) -1-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)methyldene]-*N*-aryl-amine 4(a-j) in good yields (Nagaraj *et al*, 2017). Compounds 4(a-j) were treated with phosphorous pentachloride and heated at 100 ^{0}C for 1 h to get *in situ* imidoyl chloride intermediate which was treated with an ice-cold solution of sodium azide and excess of sodium acetate in water and acetone with stirring overnight (Muralikrishna *et al*, 2013), gave 5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-aryl-1*H*-1,2,3,4-tetraazole 5(a-j) in good yields (Scheme 1). The structures of the synthesized compounds were elucidated by IR, ^{1}H, ^{13}C NMR and MS spectral analysis.

Scheme 1 Schematic route for the synthesis of compounds 5(a-j)



1 **2** **3** **4(a-j)** **5 (a-j)**

Table 1 Antibacterial activity of compounds 5(a-j)

Compound	zone inhibition at 50 μg/mL (mm)					
	B. subtilis	*B. sphaericus*	*S. aureus*	*P. aeruginosa*	*K. aerogenes*	*C. violaceum*
5a	13	23	16	16	18	22
5b	10	17	18	15	22	20
5c	25	29	26	28	24	31
5d	28	30	30	29	25	26
5e	19	14	21	23	15	21
5f	18	17	15	20	15	19
5g	22	19	27	25	21	23
5h	25	32	30	30	27	30
5i	16	21	19	18	20	19
5j	19	20	21	15	12	11
Streptomycin	25	30	30	30	25	30

Reagents and Conditions: i) Ph-NH-NH_2/EtOH, reflux, 3 h; ii) $POCl_3$/DMF, reflux, 1 h; iii) Ar-NH_2/AcOH/toluene, reflux, 3 h; iv) PCl_5/NaN_3/Et_3N/dioxane

5: Ar = a) phenyl; b) 4-methylphenyl; c) 4-methoxyphenyl; d) 4-fluorophenyl; e) 4-bromophenyl; f) 3-nitrophenyl; g) 4-nitrophenyl; h) 2,5--difluorophenyl; i) 3-hydroxyphehyl; j) 4-hydroxyphenyl.

The IR spectrum of compound 5a showed absorption bands in the region of 1523 (N=N), 1616 (C=N) and 1550 (C-N) of tetrazole ring. Its ^{1}H NMR spectra showed the signals at δ 2.28 and 2.47 ppm as singlet, integrating three protons in each corresponding methyl groups at 3rd and 5th position of pyrazole ring. All the other aromatic protons were observed at the expected regions. In the ^{13}C NMR spectrum, the prominent signals corresponding to the C-3, C-4 and C-5 carbons of pyrazole ring is observed at 147.8, 115.2 and 135.1 ppm respectively, the C-5 carbon of tetrazole ring is observed at 139.7 ppm, are proof of further evidence of its structure.

Antibacterial Activity

All the newly synthesized compounds 5(a-j) were screened for their antibacterial activity against Gram-positive bacteria *viz*. *Bacillus subtilis* (MTCC 441), *Bacillus sphaericus* (MTCC 11) and *Staphylococcus aureus* (MTCC 96), and Gram-negative bacteria *viz*. *Pseudomonas aeruginosa* (MTCC 741), *Klobsinella aerogenes* (MTCC 39) and *Chromobacterium violaceum* (MTCC 2656) by disc diffusion method (NCCLS, 1982). For the antibacterial assay standard inoculums (1-2 × 10^7 c.f.u/mL 0.5 Mc Farland standards) were introduced on to the surface of sterile agar plates, and a sterile glass spreader was used for even distribution of the inoculums. The discs measuring 6.26 mm in diameter were prepared from Whatman no.1 filter paper and sterilized by dry heat at 140 ^{o}C for 1 h. The sterile discs previously soaked in a known concentration of the test compounds were placed in nutrient agar medium. The plates were inverted and incubated for 24 h at 37 ^{o}C. The inhibition zones were measured and compared with the standard drug streptomycin. The zones of inhibition are presented in Table 1.

The antibacterial screening data reveal that all the tested compounds 5(a-j) showed moderate to good inhibition towards all the tested strains. Compounds 5c, 5d and 5h exhibited potent inhibitory activity compared to standard drug at the tested concentrations. The results also reveal that the presence of 4-methoxyphenyl (5c) or 4-fluorophenyl (5d) or 2,5-difluorophenyl (5h) substituent on tetrazole ring might be the reason for the significant inhibitory activity. Most of these new compounds showed appreciable activity against test bacteria and emerged as potential molecules for further development.

CONCLUSION

A new series of 5-(3,5-dimethyl-1-phenyl-1*H*-4-pyrazolyl)-1-aryl-1*H*-1,2,3,4-tetraazole 5(a-j) have been synthesized and evaluated for their antibacterial activity against various bacterial strains. The screened compounds 5c, 5d and 5h exhibited potent antibacterial activity compared to standard drug at the tested concentrations. The other compounds also showed appreciable activity against the test bacteria and emerged as potential molecules for further development.

Acknowledgements

The authors are thankful to the Director, Indian Institute of Chemical Technology, Hyderabad, India, for providing NMR and mass spectral data. Financial assistance from the UGC, New Delhi, India, in the form of UGC-National Fellowship for Higher Education (NFHE) is gratefully acknowledged.

References

Adel, A. H., Abdel, R.; Omar, M. A., Amira, A. S. and Abdel, M. (2013): Synthesis and antimicrobial activity of new tetrazoles incorporating isoindone-1,3-dione moiety and their sugar derivatives, *Journal of Hetero-cyclic Chemistry*, 50(3): 484-489.

Balbi, A., Anzaldi, M., Maccio, C., Aiello, C., Mazzei, M., Gangemi, R., Castagnola, P., Miele, M., Rosano, C. and Viale, M. (2011): Synthesis and biological evaluation of novel pyrazole derivatives with anticancer activity, *European Journal of Medicinal Chemistry*, 46(11): 5293-5309.

David, L, S., David, G. B., Joanna, B., Guillaume, E. B., Richard, O. C., Surinder, S. C., Ian, G. C., Patricia, A. F., Robert, C. G., Maria, C. G., Adrian, J. H., Marcel, R. K. Quan, L., David, J. M., Sylvie, M., Kenneth, L. P., Karen, R., Graham, D. S., Jeremy, N. S., Mark, A. T., Kerry, A. W., Grant, W. and Chi, K. W. (2001): Synthesis and biological evaluation of novel pyrazoles and indazoles as activators of the nitric oxide receptor, soluble guanylate cyclase, *Journal of Medicinal Chemistry*, 44(1): 78-93.

da Silva, F. D. C., de Souza, M. C. B. V., Frugulhetti, I. I. P. Castro, H. C., de O Souza, S. I., de Souza, T. M. I., Rodrigues, D. Q., Souza, A. M. T. Abreu, P. A., Passamani, F, Rodrigues, C. R. and Ferreira, V. F. (2009): Synthesis, HIV-RT inhibitory activity and SAR of 1-benzyl-1*H*-1,2,3-triazole derivatives of carbohydrate, *European Journal of Medicinal Chemistry*, 44(1): 373-383.

Florence, G., Sergiy, P., Lars, R., Norber, L., Jean, P. V. and Frederic R. L. (2013): Synthesis of diversely fluorinated pyrazoles as novel active agrochemical ingredients, *Journal of Fluorine Chemistry*, 152(8): 2-11.

Gamal, M. A. A., Din, G. E., Rahma, A. A. and Hassan, A. A. (2009): Synthesis of novel pyrazole derivatives and evaluation of their antidepressant and anticonvulsant activities, *European Journal of Medicinal Chemistry*, 44(9): 3480-3487.

Genin, M. J., Biles, C., Keise, B. J., Poppe, S. M., Swaney, S. M., Tarpley, W. G., Yagi, Y. and Romero, D. L. (2000): Novel 1,5-diphenylpyrazole nonnucleoside HIV-1 reverse transcriptase inhibitors with enhanced activity versus the delavirdine-resistant P236L mutant: Lead identification and SAR of 3- and 4-substituted derivatives, *Journal of Medicinal Chemistry*, 43(5): 1034-1040.

Gorle, S., Maddila, S., Maddila, S. N., Naicker, K., Singh, M., Singh, P. and Jonnalgadda, S. B. (2017): Molecular docking study and *in vitro* anticancer activity of tetrazole linked benzochromene derivatives, *Anticancer Agents Medicinal Chemistry*, 17(3): 464-470.

Habeeb, A. G., Praveen Rao, P. N. and Enaus, E. E. (2001): Design and synthesis of Celecoxib and Rofecoxib analogues as selective cyclooxygenase-2 (COX-2) inhibitors: Replacement of sulfonamide and methyl-sulfonyl pharmacophores by an azido bioisostere, *Journal of Medicinal Chemistry*, 44(18): 3039-3042.

Hutchinson, D. W. and Naylor, M. (1985): The antiviral activity of tetrazole phosphonic acids and their analogues, *Nucleic Acids Research*, 13(9): 8519-8530.

Julliano, G. L., Andre, C. S., Joao, C. P. M., Silvio, T. S., Debora, F. G., Felix, A. A. S., Bernardo, A. I., Davi, F. B., Oscar, E. D. R. And Luciano D. (2017): Synthesis and electrochemical and antioxidant properties of chalcogenocyanate oxadiazole and 5-heteroarylchalco genomethyl-1*H*-tetrazole derivatives, *New Journal of Chemistry*, 41: 5875-5883.

Kudo, N. and Furuta, S. (1999): Synthesis and herbicidal activity of 1,5-diarylpyrazole derivatives, *Chemical and Pharmaceutical Bulletin*, 47(6): 857-868.

Mihit, M., Laarej, K., Makarim, H. A. E., Bazzi, L., Salghi, R. and Hammouti, B. (2010): Study of the inhibition of the corrosion of copper and zinc in HNO_3 solution by electro- chemical technique and quantum chemical calculations, *Arabian Journal of Chemistry*, 3(1): 55-60.

Muralikrishna, S., Raveendrareddy, P., Ravindranath, L. K. Harikrishna, S. And Jagadeeswara Rao, P. (2013): Synthesis characterization and antitumor activity of thiazole derivatives containing indole moiety bearing-tetrazole, *Der Pharma Chemica*, 5(6): 87-93.

Mohd. J. N., Ozair, A., Farah, N., Mohd, J. A. and Perwaiz, A. (2016): Current status of pyrazole and its biological activities, *Journal of Pharmaceutical and Biological Allied Science*, 8(1): 2-17.

Nagaraj, A., Aparna, M., Ramesh Naik, P., Raghuveer, S. and Nageswara Rao, G. (2017): Synthesis and antibacterial evaluation of new thiazolo[4,5-*c*]isoxazole bearing morpholine, *Journal of Chemistry and Chemical Sciences*, 7(12): 1087-1096.

Nagaraj, A., Sunitha, M., Sanjeeva Rao, L., Vani Devi, M. and Sanjeeva Reddy, Ch. (2015): Synthesis and biological evaluation of 3-benzyl/piperazinomethyl-1,2,3-triazol-4-yl)-2,3-dihydro-1,3,4-thiadiazole-2-thione, *Organic Communications,* 8(3): 70-77.

Nagaraj, A., Aparna, M., Ramesh Naik, P., Raghuveer, S. And Nageswara Rao, G. (2017): Synthesis and antibacterial evaluation of new thiazolo[4,5-*c*]isoxazole bearing morpholine, *Journal of Chemistry and Chemical Sciences*, 7(12): 1087-1096.

National **C**ommittee for Clinical Laboratory Standards (NCCLS), (1982): Standard methods for dilution antimicrobial susceptibility tests for bacteria, which grows aerobically. *Nat. Comm. Lab. Stands*. Villanova, pp. 242.

Nugent, R. A., Murphy, M., Schlachter, S. T., Dunn, C. J., Smith, R. J., Staite, N. D., Galinet, L. A., Shields, S. K., Aspar, D. G. Richard, K. A. and Rohloff, N. A. (1993): Pyrazoline bisphosphonate esters as novel antiinflammatory and antiarthritic agents, *Journal of Medicinal Chemistry*, 36(1): 134-139.

Osama, I. E. S., Mohamed, M. B., Samy, M. I., Christophe, P., Graciela, A., Robert, S., Jan B. And Adel A. R. (2009): Synthesis and antiviral activity of new pyrazole and thiazole derivatives, *European Journal of Medicinal Chemistry*, 44(9): 3746-3753.

Paudel, S., Acharya, S., Yoon, G., Kim, K. M. And Cheon, S. H. (2016): Exploration of substituted arylpiperazine-tetrazoles as promising dual norepinephrine and dopamide, *Bioorganic and Medicinal Chemistry*, 24(21): 5546-5555.

Persson, T., Yde, C. W., Rasmussen, J. E., Rasmussen, T. L., Guerra, B., Issinger, O. G. and Nielsen, J. (2007): Pyrazole carboxamides and carboxylic acids as protein kinase inhibitors in aberrant eukaryotic signal transduction: induction of growth arrest in MCF-7 cancer cells, *Organic and Biomolecular Chemistry*, 5(24): 3963-3970.

Ramakrishna, V., Sai, L. And Ravindranath, L. K. (2017): Novel route for synthesis of antihypertensive activity of tetrazole analogues as a carbamate and urea derivatives, *Medicinal Chemistry*, 7(8): 239-246.

Roger, E. F., Phillip, K., Edward, L., Stuart, M. M., Audrey, J. P., Christopher, A. R., Anthony, J. H. S., Joyce, L. W. and Derek, E. W. (1986): Synthesis and quantitative structure-activity relationship of antiallergic 2-hydroxy-*N*-(1*H*-tetrazole-5-yl)benzamides & *N*-(2-hydroxyphenyl)-1*H*-tetrazole-5-carboxamides, *Journal of Medicinal Chemistry*, 29(4): 538-549.

Sanjeeva Reddy, Ch., Chandrasekhar Rao, D., Kalyani1, B. and Nagaraj, A. (2017): Synthesis and antibacterial activity of bis-heterocycles containing pyrimidine and morpholine, *Journal of Chemistry and Chemical Sciences*, 7(11): 1011-1021.

Sanjeeva Reddy, Ch., Vani Devi, M., Sunitha, M., Kalyani, B. and Nagaraj, A. (2016): Synthesis and antibacterial activity of di-heteryl substituted[1,24]triazolo[3,4-*b*]thiadiazoles, *Indian Journal of Chemistry*, 55B(5): 590-597.

Sanjeeva Reddy, Ch., Sanjeeva Rao, L., Sunitha, B. and Nagaraj, A. (2015): Synthesis and antibacterial activity of *N*-substituted-[1,2,4]triazoles and 1,2,4-triazole[3,4-*b*][1,3,4] thiadiazine, *Indian Journal of Chemistry*, 54B(10): 1283-1289.

Sanjeeva Reddy, Ch., Vani Devi, M., Sunitha, M. And Nagaraj, A. (2010): Synthesis and antimicrobial study of linked heterocyclics containing pyrazole-pyrimidine-thiazolidin-4-one, *Chemical and Pharmaceutical Bulletin*, 58(12): 1622-1626.

Sukumar, B., Biplab, K. D., Sitesh, C. B., Joydev, K. K., Abu, S. S. R. And Bidyut K. D. (2008): Anti-inflammatory activity of indanyltetrazole derivatives, *Pakistan Journal of Pharmaceutical Science*, 21(3): 295-298.

Shantaram, G. K., Appala, R., Popat, B. M. And Ramdas, B. P. (2013): Analgesic activity of some 1,2,4-traizole heterocycles clubbed with pyrazole, tetrazole, isoxazole and pyrimidine, *Advanced Pharmaceutical Bulletin*, 3(1): 13-18.

Subramanian, V., Knight, J. S., Parelkar, S., Anguish, L. and Coonrod, S. A. (2015): Design, synthesis and biological evaluation of tetrazole analogues of CI-amidine as protein arginine deiminase inhibitors, *Journal of Medicinal Chemistry*, 58: 1337-1344.

Yu, L. G., Ni, T. F., Gao, W., He, Y., Wand, Y. Y., Cui, H. W., Yang, C. G. and Qiu, W. W. (2015): The synthesis and antibacterial activity of pyrazole-fused tricyclic diterpene derivatives, *European Journal of Medicinal Chemistry*, 90(1): 10-20.

How to cite this article:

Nagaraj A *et al*.2017, Synthesis And Biological Evaluation of Tetrazole Analogues of Pyrazolecarbaldehyde As Antibacterial Agents. *Int J Recent Sci Res.* 8(12), pp. 22691-22695. DOI: http://dx.doi.org/10.24327/ijrsr.2017.0812.1317

****