Int. J. Chem. Sci.: 14(4), 2016, 2723-2735
ISSN 0972-768X
www.sadgurupublications.com

SYNTHESIS, CHARACTERIZATION OF 1, 2, 4-TRIAZOLES AND ANTIMICROBIAL SCREENING

VEERA VENKATARAO, LAV KUMAR and ANJALI JHA*

Department of Chemistry, GIS, GITAM University, Rushikonda,
VISAKHAPATNAM – 530045 (A.P.) INDIA

ABSTRACT

An innovative progression of synthetic 1, 2, 4 triazole derivatives (5a-g) have been synthesized via usual process producing high-quality yield in methanol through cyclization reaction of N-Cyanoimidates (3a-g), by means of phenyl hydrazine. All the new compounds have been characterized by spectral data and subsequently evaluated for their anti-bacterial and anti fungal activity by using Disc Diffusion Method. Those prepared compounds had been screened for their antimicrobial activities, which give an idea about reasonable to good activity against a variety of strains of bacteria and fungi employed. These prepared compounds had been established with IR, ^{1}H NMR and mass spectral statistics.

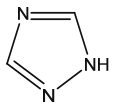
Key words: N-Cyanoimidates, Tri Azoles, Antibacterial, Antifungal agents.

INTRODUCTION

Heterocyclic chemistry is a chemistry involving the heterocyclic compounds, which has atoms of at least one different element as number of ring. The heterocyclic atoms may be inorganic, through the compound contains carbon atoms in the ring. The word hetero means "different from carbon and hydrogen". Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. Among five membered heterocyclestriazoles occupies significant position and is commonly found in a wide variety of natural products, synthetic pharmaceutical molecules and other function materials.

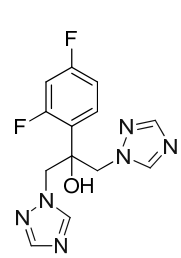
1,2,4-Triazole is one of a pair of isomeric chemical compounds with molecular formula $C_2H_3N_3$, called Tri azoles (Fig. 1), which have a five-membered ring of two carbon atoms and three nitrogen atoms. 1,2,4-Triazole is a basic aromatic hetero cycle. 1,2,4-Triazole derivatives find use in a wide variety of applications, most notably as Antifungals such as Flucanazole and Itraconazole (Fig. 2).

*Author for correspondence; E-mail: venkatorganic10@gmail.com

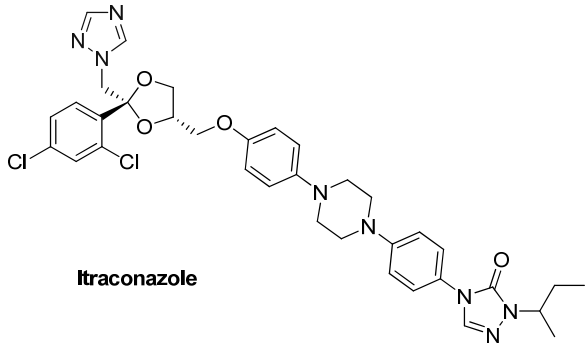


1,2,4 Tri Azole

Fig. 1: Structure of 1, 2, 4 Tri azole



Flucanazole



Itraconazole

Fig. 2: Structures of flucanazole, itraconazole drugs containing 1, 2, 4 tri azole core unit

Triazolic nucleus is now a day's considered an important moiety in the design and synthesis of bioactive compounds that are associated with numerous biological activities[1] such as antibacterial, antifungal[2], anti-inflammatory[3], anticonvulsant[4], anti-HIV[5], antineoplastic, and antiproliferative[6-13]. Additionally, there are review studies that indicate the fact that 1,2,4-triazoles occupy a distinctive place in the field of medicinal and pharmaceutical chemistry[14,15], as well as in industry[16]. Also, synthesis and complete characterization by both spectroscopic and thermal techniques were reported in literature for numerous derivatives bearing 1,2,4-tri azole moieties[17-20].

In search of bioactive molecules and in continuation of our previous work in developing synthesis of poly functionally substituted Heterocyclic compounds, we report an efficient synthesis of some novel 1, 2, 4-triazole amine derivatives 4(a-g). All the synthesized compounds 4(a-g) were evaluated for antimicrobial activity.

EXPERIMENTAL

Materials and methods

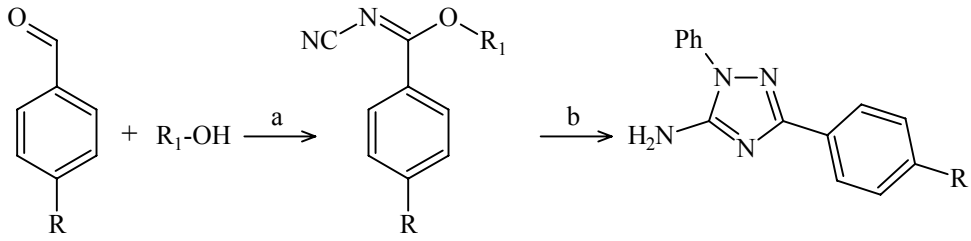
Melting points were determined in open-end capillaries and are uncorrected. Compounds were checked for their purity by TLC on silica gel G plates and spots were located by iodine vapors. ^{1}H NMR spectra were recorded on BRUKER ADVANCE II 400

NMR Spectrometer using TMS as internal standard. The mass spectra were obtained on a JEOL 5x102/DA-6000 mass spectrometer. The IR spectra were recorded on Perkin-Elmer spectrum RX IFT-IR System using KBr pellets.

All reactions were carried out under argon inoven-dried glassware with magnetic stirring. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. All solvents were reagent grade. THF was distilled from sodium benzophenoneketyl and degassed thoroughly with dry argon directly before use. Unless otherwise noted, organic extracts were dried with anhydrous Na_2SO_4, filtered through a fritted glass funnel, and concentrated with a rotary evaporator (20-30 Torr). Flash chromatography was performed with silica gel (200-300 mesh) by using the mobile phase indicated. The NMR spectra were measured with a 400 MHz Bruker Avance spectrometer at 400.1 and 100.6 MHz, for ^1H for ^{13}C, respectively, in $CDCl_3$ solution with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ) and are referenced to the residual proton resonances of the solvents. Proton and carbon magnetic resonance spectra (^1H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$-*d* or DMSO-*d*6 as the internal standard (^1H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm, DMSO at 2.50 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, DMSO at 40.00 ppm.

The synthetic route is depicted in Scheme **I**.

The title compounds 5(a-g) were synthesised in two sequential steps using different reagents and reaction conditions, the 5(a-g) were obtained in moderate yields. The structure were established by spectral (IR, ^1H-NMR, ^{13}C-NMR and mass) and analytical data.



(1) **(2)** **3(a-g)** **4(a-g)**

R = −OMe, −Cl, −F, −Br, $-NO_2$, −F, −H, $-CH_3$

R_1 = $-CH_3$

Scheme 1

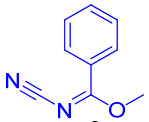
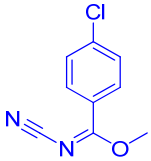
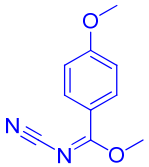
Reagents and reaction conditions: (a) Methanol, Cyanamide, t-BuONa, RT, Then NBS, 50^oC (b) Methanol, reflux

Experimental section

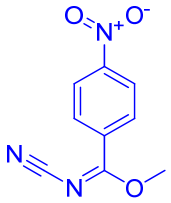
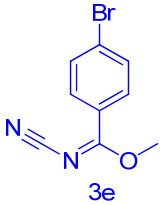
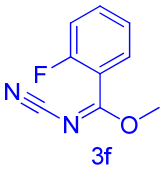
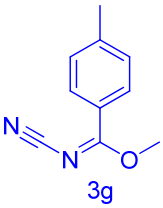
All reactions were carried out under argon in oven-dried glassware with magnetic stirring. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. All solvents were reagent grade. THF was distilled from sodium benzophenoneketyl and degassed thoroughly with dry argon directly before use. Unless otherwise noted, organic extracts were dried with anhydrous Na_2SO_4, filtered through a fritted glass funnel, and concentrated with a rotary evaporator (20-30 Torr). Flash chromatography was performed with silica gel (60-120 mesh) by using the mobile phase indicated. The NMR spectra were measured with a 400 MHz Bruker Avance spectrometer at 400.1 and 100.6 MHz, for ^1H, for ^{13}C, respectively, in $CDCl_3$ solution with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ) and are referenced to the residual proton resonances of the solvents.

Synthesis of Cynoamidate derivatives 3(a-g)

To a 25 mL flask with a mixture of 4-Substituted benzaldehyde (1 m.mol) and H_2NCN (4 m.mol) and t-BuONa (4 m.mol) in MeOH (8 mL), the mixture was stirred for 0.5 h at room temperature, then NBS (4 m.mol) was added. The resulting mixture was stirred for 12 h at 50°C. Themixture was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (6:4) as eluent to give compounds 3 (a-g).

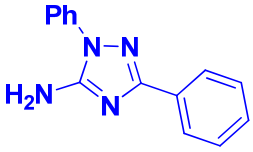
Compound name	Structure	Yield (%)
Methyl N-cyanobenzimidate	 3a	84
Methyl 4-chloro-N-cyanobenzimidate	 3b	85
Methyl N-cyano-4-methoxybenzimidate	 3c	80

Cont…

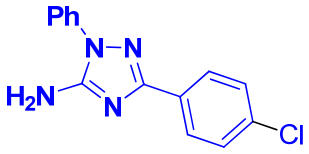
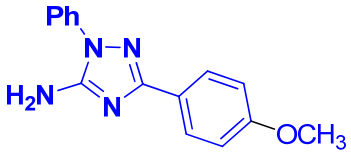
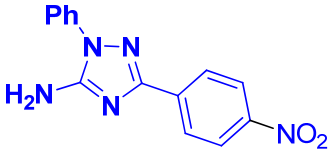
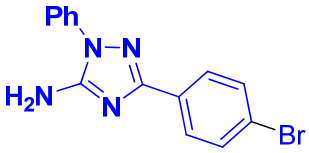
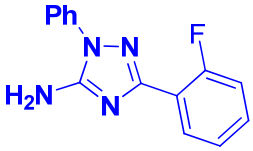
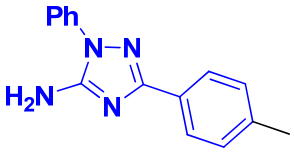
Compound name	Structure	Yield (%)
Methyl N-cyano-4-nitrobenzimidate	 3d	65
Methyl 4-bromo-N-cyanobenzimidate	 3e	75
N-cyano-2-fluorobenzimidate	 3f	87
Methyl N-cyano-4-methylbenzimidate	 3g	70

General procedure of 3-amino-l, 2, 4-triazole derivatives 4(a-g)

A mixture of N-Cyanoimidates (1 m.mol), phenylhydrazine (1.2 m.mol) and methanol (5 mL) was refluxed for 5 h. Then the reaction mixture was concentrated in vacuum and the residue was purified by flash chromatography to obtain the final product.

Compound name	Structure
1,3-diphenyl-1H-1,2,4-triazol-5-amine (4a)	

Cont…

Compound name	Structure
3-(4-chlorophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4b)	
3-(4-methoxyphenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4c)	
3-(4-nitrophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4d)	
3-(4-bromophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4e)	
3-(2-fluorophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4f)	
1-phenyl-3-p-tolyl-1H-1,2,4-triazol-5-amine (4 g)	

Analytical data of Compounds 4 (a-g)

1,3-diphenyl-1H-1,2,4-triazol-5-amine (4a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05-8.02 (m, 2H), 7.62-7.59 (m, 2H), 7.54-7.50 (m, 2H), 7.44-7.36 (m, 4H), 5.45 (br, 2H); M.p. 158-159^{o}C

3-(4-chlorophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01(s, 1H), 7.99 (s, 1H), 7.62-7.53 (m, 4H), 7.46-7.40 (m, 3H), 4.90 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 158.4, 154.4, 136.8, 135.0, 129.9, 129.5, 128.8, 128.3, 127.5, 123.5; MS (ESI): [M+H]+ 271.07482.

3-(4-methoxyphenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4c)

^{1}H NMR (400 MHz, d_6-DMSO): δ 7.89-7.87(d, 2H, J = 8.4Hz), 7.63-7.61 (d, 2H, J = 8.0Hz), 7.55-7.51 (t, 2H, J = 7.6Hz), 7.40-7.37 (t, 2H, J = 7.2Hz), 7.01-6.99 (d, 1H, J = 8.4Hz), 6.21 (br, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 159.8, 158.1, 155.2, 137.3, 129.4, 127.0, 126.9, 124.0, 122.7, 113.9, 55.1; ESI for $[M+H]^+$267.12462

3-(4-nitrophenyl)-1-phenyl-1H-1, 2, 4-triazol-5-amine (4d)

^{1}H NMR (400 MHz, d_6-DMSO): δ 7.89-7.87(d, 2H, J = 8.4Hz), 7.63-7.61 (d, 2H, J = 8.0Hz), 7.55-7.51 (t, 2H, J = 7.6Hz), 7.40-7.37 (t, 2H, J = 7.2Hz), 7.01-6.99 (d, 1H, J = 8.4Hz), 6.21 (br, 2H); ^{13}C NMR (100 MHz, d_6-DMSO) δ 159.8, 158.1, 155.2, 137.3, 129.4, 127.0, 126.9, 124.0, 122.7, 113.9; ESI for $[M+H]^+$282.262.

3-(4-bromophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4e)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.99 (s, 1H), 7.62-7.53 (m, 4H), 7.46-7.40 (m, 3H), 4.90 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 158.4, 154.4, 136.8, 135.0, 129.9, 129.5, 128.8, 128.3, 127.5, 123.5; MS (ESI): [M+H]+ 315.16,317.16.

3-(2-fluorophenyl)-1-phenyl-1H-1,2,4-triazol-5-amine (4f):

^{1}H NMR (400 MHz, d_6-DMSO): δ 7.99-7.97 (t, 1H, J = 5.2Hz), 7.64-7.62 (d, 1H, J = 5.2Hz), 7.57-7.54 (t, 2H, J = 5.2Hz), 7.47-7.42 (m, 2H), 7.31-7.28 (m, 2H), 6.62 (s, 2H); ^{13}C NMR (100 MHz, d_6-DMSO): δ 160.3, 158.7, 155.0 , 154.9, 137.1, 130.6, 130.5, 129.7, 129.4, 127.2, 124.3, 123.0, 119.2, 119.2, 116.5, 116.4; ESI for: $[M+H]^+$ 255.10455.

1-phenyl-3-p-tolyl-1H-1, 2, 4-triazol-5-amine (4 g):

^{1}H NMR (400 MHz, d_6-DMSO): δ 7.87-7.84(d, 2H, J = 9.6Hz), 7.63-7.62(d,2H, J = 5.2Hz), 7.55-7.52(t, 2H, J = 9.6Hz), 7.40-7.38(t, 1H, J = 5.2Hz), 7.25-7.24(d, 2H, J =5.2Hz), 2.34(s, 3H); ESI for: $[M+H]^+$ 251.105.

Anti-microbial activity

Media and chemicals

Nutrient Broth, Nutrient agar and 5 mm diameter antibiotic assay were obtained from Hi-Media Laboratories Limited, India. Barium chloride dehydrate GR, concentrated sulphuric acid GR, Dimethyl sulphoxide GR, Sodium chloride AR and Potassiumdichromate were obtained from Ranbaxy Laboratories Ltd, Chemical Division, India. The standard bacterial and fungal strains were procured from National Centre from Cell Science (NCCS), Pune, India. The bacterial included two Gram positive bacterial isolates *Staphylococcus aureus* NCCS 2079 and Bacillus cereus NCCS 2106 and two Gram negative bacterial

isolates *Escherichia coli* NCCS2065 and *Pseudomonas aeruginosa* NCCS 2200. The fungicidal organisms included were *Aspergillus nigeri* NCCS 1196 (AN) and Candida albicans NCCS 3471(CA). The bacteria were grown and maintained on nutrient agar (Hi-Media, Mumbai) and were subculture when needed.

Glasswares and Apparatus

Glass petridish, Glass tubes, Beakers, Erlenmeyer flasks, bacterial loop and measuring cylinder. All the glass wares were of Borosilicate grade. Digital electronics balance (Shankar Scientific supplies, India), Yorco Horizontal Laminar air flow bench (Yorco sales Pvt. Ltd, New Delhi, India), Ausco incubator, Zone reader (Cintex industrial Corporation, India), hot air oven, autoclave and UV/Visible spectrophotometer (Shimadzu corporation, Japan).

Antibacterial activity

The antibacterial activity of synthesized compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram-positive bacterial screened were *Staphylococcus aureus* NCCS 2079 (SA) and *Bacillus cereus* NCCS 2106 (BC). The gram negative bacterial screened were *Escherichia coli* NCCS 2065 (EC) and *Pseudomonas aeruginosa* NCCS 2200 (PA). The synthesized compounds were used at the concentration of 250 µg/mL and 500 µg/mL using DMSO as a solvent. The amoxicillin 10 µg/disc and Streptomycin 30 µg/disc were used as a standard (Himedia Laboratories Limited, Mumbai).

Disc diffusion method

A suspension of *Staphylococcus aureus* (SA) was added to sterile nutrient agar at 45ºC. The mixture was transferred to sterile petridishes to give a depth of 3 to 4 mm and allowed to solidify. Precautions were observed to reduce uniform layer of medium on the plate. Sterile discs 5 mm in diameter (made from Whatman Filter paper) were immersed in the solutions of synthesized compounds (250 µg/mL) and maintain an untreated control sample for comparison. Leave the plates to stand for 1 hour at room temperature as a period of preincubation diffusion to minimize the effects of variations in different time. Then the plates were incubated at 37ºC for 24 hours and observed for antibacterial activity. The diameter of the zone of inhibition was measured for each plate in which the zone of inhibition was observed. The average zone of inhibition was calculated and compared with that of standard. A similar procedure was adopted for studying the antibacterial activity against the other organisms.

Antifungal activity

The antifungal activity 3 of synthesized compounds were studied by disc diffusion method against the organisms of *Aspergillus nigeri* NCCS 1196 (AN) and *Candida albicans*

NCCS 3471 (CA). Compounds were treated at the concentrations of 250 µg/mL using DMSO as a solvent. The standard used was Ketaconazole 50 µg/mL and Griseofulvin 50 µg/mL against both the organisms.

Disc diffusion method

A suspension of *Aspergills nigeri* NCCS 1196 (AN) was added to a sterile sabouraud dextrose agar at 45ºC. The mixture was transferred to sterile petridishes and allowed to solidify. Sterile discs 5 mm in diameter (made from Whatmann Filter paper) immersed in the solutions of synthesized comopounds and control were placed on the surface of agar medium with forceps and pressed gently to ensure even contact. Leave the plates to stand for 1 hour at room temperature as a period of preincubation diffusion to minimize the effects of variation at 37ºC for 13 hours and observed for antibacterial activity. The diameters of the zone of inhibition were measured for the plates in which the zone of inhibition was observed. The average zone of inhibition was calculated with that of standard. The Novel 1, 2, 4 triazolederivates containing fluoro (4f) and nitro (4d) showed more activity than other substituent's. The order of activity was –

$$4f > 4d > 4e > 4b > 4c > 4g > 4a$$

Antimicrobial evaluation of Novel compounds 4(a-g).

Table 3: Antimicrobial activity and antifungal activity of synthesized compounds 4(a-g)

Compd. No	Zone of inhibition in mm					
	Antibacterial activity			Antifungal activity		
	S.aureus	***E.coli***	***P.aeruginosa***	***C. albicans***	***A. flavus***	***A.fumigatus***
4a	18	15	16	9	9	10
4b	21	18	19	10	9	10
4c	20	17	18	10	9	10
4d	23	21	22	11	9	10
4e	22	20	21	10	9	10
4f	20	17	18	10	9	10
4g	19	17	17	11	10	11
Ampicillin	20	21	22	21	-	-
Flucanazole	22	20	23	22	-	--

RESULTS AND DISCUSSION

Characterization

The IR spectrum of the title Compounds 4(a-h) has given stretching vibration at 3100 cm^{-1}, due to the stretching vibration corresponding to Ar-H Stretching vibrations. The absorption peak at 2935 cm^{-1} is due to the stretching vibration corresponding to the SP^3 C-H (methyl gp). The strong Intensity absorption at 1350 & 1530 cm^{-1} is due to The stretching vibration of -N-O Stretching in Nitro group, 1360 cm^{-1} is due to The stretching vibration of C-F bond.760 cm^{-1} is due to The stretching vibration of C-Cl bond. 560 cm^{-1} is due to The stretching vibration of C-Br bond. The weak Intensity absorption at 1620 cm^{-1} corresponds to a C=N Stretching vibration.1150 cm^{-1} corresponding to C-O Stretching.

It has been observed from chemical structure of compound 4(a-h) that different pair of protons. The protons of methyl group, which is attached to benzene ring appeared as a singlet at δ = 2.3 ppm. The protons of Methoxygroup appeared as a Singlet at δ = 3.8 ppm. The protons attached benzene ring appeared between δ = 7.2-8.03 ppm, respectively.

The chemical shifts of the final compound carbon vary from δ = 175 to 23 ppm. The carbon nucleus under the influence of a strong electronegative environment appeared down field. The carbon chemical shift of the methyl group at δ = 23 ppm. The carbon chemicalshift of the methoxy group at δ = 55 ppm.

Readily available starting materials and simple synthesizing procedures make this method very attractive and convenient for the synthesis of 1,2,4 tri azole derivatives. Formation of products was confirmed by recording their Elemental analysis, ^1H NMR, ^{13}C, FT-IR, mass spectra.

Biological activity screening

The results of biologicalstudies of newly synthesized compounds reveal that the compounds possess significant anti-bacterial and anti-fungalactivities. The results of these studies are given in Table 3. From Anti-bacterial and Anti-fungalactivity screening results, it has been observed that compounds **4f, 4d** possess good activity.

CONCLUSION

We have described an efficient procedure for the preparation of 2-amino-1,2,4-tri azoles from cynamidates and Phenyl hydrazine in methanol. The conditions are simple, mild, non-toxic, environmentally benign, scalable and thus it is one of the Good method available

for the preparation of 2-amino-1,2,4-tri azoles. From anti-bacterial and anti-fungal activity screening results, it has been observed that compounds **4f, 4d** possess good activity compared to standard drugs.

ACKNOWLEDGMENT

Author (VV) is thankful to Research Supervisor Dr. Lav Kumar and Dr. Anjali Jha for providing required facilities and motivation for completion of the research work. We also extend our gratitude towards Department of Chemistry, GIS, GITAM University for providing us facilities for characterization of synthesized compounds.

REFERENCES

1. S. H. Sumrra and Z. H. Chohan, Metal Based New Triazoles: Their Synthesis, Characterization and Antibacterial/Antifungal Activities, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, **98**, 53-61 (2012).
2. P. Zoumpoulakis, C. Camoutsis, G. Pairas et al., Synthesis of Novel Sulfonamide-1,2,4-Triazoles, 1,3,4-Thiadiazoles and 1,3,4- Oxadiazoles, as Potential Antibacterial and Antifungal Agents. Biological Evaluation and Conformational Analysis Studies, Bioorg. Med. Chem., **20(4)**, 1569-1583 (2012).
3. E. S. Al-Aabdullah, H. H. Asiri, S. Lahsasni, E. E. Habib, T. M. Ibrahim and A. A. El-Emam, Synthesis, Antimicrobial, and Anti-Inflammatory Activity, of Novel s-Substituted and n-Substituted 5-(1-Adamantyl)-1,2,4-triazole-3-thiols, Drug Design, Development and Therapy, **8**, 505-517 (**2014)**.
4. X.-Q. Deng, M.-X. Song, Y. Zheng and Z.-S. Quan, Design, Synthesis and Evaluation of the Antidepressant and Anticonvulsant Activities of Triazole-Containing Quinolinones, European J. Med. Chem., **73**, 217-224 (2014).
5. Z. Li, Y. Cao, P. Zhan et al., Arylazolylthioacetanilide, Part 11, Design, Synthesis and Biological Evaluation of 1,2,4-Triazole Thioacetanilide Derivatives as Novel Non-Nucleoside HIV-1 Reverse Transcriptase Inhibitors, Med. Chem., **9(7)**, 968-973 (2013).
6. G. Celik, P. Khloya, D. Vullo, C. T. Supuran and P. K. Sharma, Benzenesulfonamide Bearing 1,2,4-Triazole Scaffolds as Potent Inhibitors of Tumor Associated Carbonic Anhydrase Isoforms hCA IX and hCA XII, Bioorg. Med. Chem., **22(6)**, 1873-1882 (2014).

7. Ł. Popiołek, J. Rzymowska, U. Kosikowska, A. Hordyjewska, M. Wujec and A. Malm, Synthesis, Antiproliferative and Antimicrobial Activity of New Mannich Bases Bearing 1,2,4-Triazole Moiety, J. Enzyme Inhibition Med. Chem., **29(6)**, 786-795 (2014).

8. H. N. Nagesh, N. Suresh, G. V. S. B. Prakash, S. Gupta, J. V. Rao and K. V. G. C. Sekhar, Synthesis and Biological Evaluation of Novel Phenanthridinylpiperazine-triazoles Via Click Chemistry as Anti-Proliferative Agents, Med. Chem. Res., **24(2)**, 523-532 (2015).

9. N. Ahmed, N. K. Konduru, S. Ahmad and M. Owais, Design, Synthesis and Antiproliferative Activity of Functionalized Flavone-Triazole-Tetrahydropyran Conjugates Against Human Cancer Cell Lines, European J. Med. Chem., **82**, 552-564 (2014).

10. G. Revelant, C. Gadais, V. Mathieu, G. Kirsch and S. Hesse, Synthesis and Antiproliferative Studies of 5-aryl-2-(3-thienylamino)-1,3,4-thiadiazoles, Bioorg. Med. Chem. Lett., **24(12)**, 2724-2727 (2014).

11. M. W. Pertino, V. Verdugo, C. Theoduloz and G. Schmeda Hirschmann, Synthesis and Antiproliferative Activity of some Novel Triazole Derivatives from Dehydroabietic Acid, Molecules, **19(2)**, 2523-2535 (2014).

12. B. N. P. Kumar, K. N. Mohana and L. Mallesha, Synthesis and Antiproliferative Activity of some New Fluorinated Schiff Bases Derived from 1,2,4-Triazoles, J. Fluorine Chem., **156**, 15-20 (2013).

13. M. Abdel-Aziz, G. E.-D. A. A. Abuo-Rahma, E. A. M. Beshr and T. F. S. Ali, New Nitric Oxide Donating 1,2,4-Triazole/Oxime Hybrids: Synthesis, Investigation of Anti-Inflammatory, Ulceroginic Liability and Antiproliferative Activities, Bioorg. Med. Chem., **21(13)**, 3839-3849 (2013).

14. S. Maddila, R. Pagadala and S. B. Jonnalagadda, 1,2,4-Triazoles: A Review of Synthetic Approaches and the Biological Activity, Lett. Org. Chem., **10(10)**, 693-714 (2013).

15. M. M. Antonijevic and M. B. Petrovic, Copper Corrosion Inhibitors, A Review, Int. J. Electrochem. Sci., **3(1)**, 1-28 (2008).

16. L. Calu, M. Badea, D. Falcescu, D. Duca, D. Marinescu and R. Olar, Thermal Study on Complexes with Schiff Base Derived from 1,2,4-Triazole as Potential Antimicrobial Agents, J. Thermal Anal. Calorimetry, **111(3)**, 1725-1730 (2013).

17. M. Badea, L. Calu, M. C. Chifiriuc et al., Thermal Behaviour of some Novel Antimicrobials Based on Complexes with a Schiff Base Bearing 1,2,4-Triazole Pharmacophore, J. Thermal Anal. Calorimetry, **118(2)**, 1145-1157 (2014).

18. X. J. Du, X. D. Li, M. S. Zou, R. J. Yang and S. P. Pang, Thermal Kinetic Study of 1-Amino-1,2,3-Triazolium Nitrate, J. Thermal Anal. Calorimetry, **115(2)**, 1195-1203 (2014).

19. I. Ledet¸i, A. Fulias, G. Vlase, T. Vlase, V. Bercean and N. Doca, Thermal Behaviour and Kinetic Study of some Triazoles as Potential Anti-Inflammatory Agents, J. Thermal Anal. Calorimetry, **114(3)**, 1295-1305 (2013).

20. J. Sharma, S. Ahmad, and A. M. Shamsher, Bioactive Triazoles: A Potential Review, J. Chem. Pharmaceut. Res., **4(12)**, 5157-5164 (2012).

Revised : 15.10.2016 *Accepted : 18.10.2016*