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Synthesis and Microbial Screening of Some Novel 1, 3, 5-triphenyl -1H Pyrazoline

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Abstract

Nitrogen heterocycles has very important role in medicinal field due to their biological activities. One of the N heterocycle pyrazole having five membered ring structure like 1, 3, 5-triphenyl -1*H* Pyrazolines and their different derivatives have been synthesised. These compounds were characterized using IR, ^{1}H-NMR, Mass spectra and Elemental analysis. As per literature They possess some potent biological activities. Therefore biological screening of such novel comp is essential.

Keywords: *Heterocyclic, pyrazolines, Biological activity*

1.Introduction

Heterocycles are of inevitable part in the designing of drug moieties in that N – heterocycles constitute an important class of natural and synthetic products, many of which exhibited useful biological activities [1]. An interest in five member systems with two adjacent nitrogen atoms occurs from saturated and partially saturated pyrazoles in biologically active compounds and natural products [2,3]. Substituted pyrazolines and their derivatives embedded with different functional groups are important biological agents. Thus, a significant amount of research has been directed towards this class. In particular, they are used as a antibacterial, antifungal, anti-tumor, anti-tubercular anti-viral, anti-parasitic and insecticidal agents. In recent years, a significant portion of research in heterocyclic chemistry has been devoted to 2-pyrazolines containing different aryl groups as substituents, as evident in literature. Pyrazolines have been reported to show a broad spectrum of biological activities including anti- bacterial [4], antifungal [5], anti-inflammatory [6], and antidepressant activities [7]. The pyrazoline function is quite stable, and has inspired chemists to utilize this stable fragment in bioactive moieties to synthesize new compounds possessing biological activities. Several methods are employed in the synthesis of pyrazolines, including the condensation of chalcones with hydrazine, phenyl hydrazine, [8-12] and condensation of chalcones with thio-semi carbazide in ethanol under strong basic or acidic conditions [13] . The desired chalcones [14] were synthesized by reacting 6-(3-acetyl-phenylamino) pyridazin-3(2H)-one with substituted aromatic aldehydes in presence of

alkali. In a typical case, equimolar quantities of chalcones and phenyl hydrazine hydrochloride in presence of acetic acid and sodium acetate, led the formation of pyrazolines. As shown in scheme (4-6).

2. Result & Discussion

Different methods were reported for the preparation of pyrazoline class of compounds. After pioneering work of Fischer and Knoevengel in 19th century, the reaction of α, β-unsaturated aldehydes and ketones with phenyl hydrazine in acetic acid under reflux condition became the most popular method for the preparation of pyrazolines [14]. In 1998, Powers et al. [15] reported the reaction of chalcones and phenyl hydrazine hydrochloride in the presence of sodium hydroxide which was carried out in absolute ethanol at 70˚C, but; there are disadvantages such as longer the reaction time (8 h) etc. In 2005, the synthesis of 3,5-diaryl-2-pyra-zolines by the reaction of Chloro chalcones with phenyl hydrazine in acetic acid under reflux condition was reported for three hours. When the molar ratio of chalcones 3 and phenyl hydrazine hydrochloride was 1:1, the yield of 1,3,5-triphenyl pyrazoline obtained was very less. But by increasing the molar ratio to 1:2 and 1:3 the yield of products were also increased. It may be that sodium acetate is in favour the release of phenyl hydrazine from phenyl hydrazine hydrochloride [14]. So reaction condition we chose were the molar ratio of chalcone: phenyl hydrazine: sodium acetate was 1:2:0.15.

We have performed the reaction of chalcone with phenyl hydrazine hydrochloride or hydrazine hydrate by refluxing at 210˚C the yield of pyrazoline was 52% - 75% (Table 1). From the results, the optimum reaction condition was chosen: Chalcone (3 mmol), phenyl hydrazine hydro chlo- ride (6 mmol), Sodium acetate (0.3 mmol). Under this reaction system, a series of experiments for synthesis of pyridazin-3(2H)-one derivative were performed. initially starting material chalcone was prepared by the reflux reaction of 3,6-dichloro pyridazine with 4- amino acetophenone in ethanol for 4h. a new chloro pyridazine acetophenone was produced it is the on oxidation in the AR grade acetic acid solvent a new ketone is generated is 6-[(4-acetylphenyl) amino] pyridazin-3(2*H*)-one it on reacting with different aldehydes produces corresponding chalcones for pyrazoline compound

3.Experimental

Melting points were determined by open tube capillary method and are uncorrected the purity of compound was checked on thin layer chromatography (TLC) plates (silica gel) in the solvent system n-hexane– ethyl acetate 4 : 6 the spots were detected in iodine chamber.

General procedure:

1. 1-{4-[(6-chloropyridazin-3-yl) amino] phenyl} ethanone

0.01 mole of 3,6 di chloro pyridazine and 4-amino acetophenone on condensation in ethanol solvent for four hours the reaction mixture is then poured in ice cold water the solid compound was obtained is filtered and dried by IR lamp then recrystallised by using ethanol solvent.

2. 6-[(4-acetylphenyl) amino] pyridazin-3(2*H*)-one

The product obtained in first step on reflux for 4h. in glacial acetic acid solvent oxidised product poured in ice cold water and filtered and recrystallised in ethanol solvent.

3. *N*-{4-[(1*E*)-3-oxo-3-{4-[(6-oxo-1,6-dihydropyridazin-3-yl)amino]phenyl}prop-1-en-1-yl]phenyl}methanimine *N*-oxide

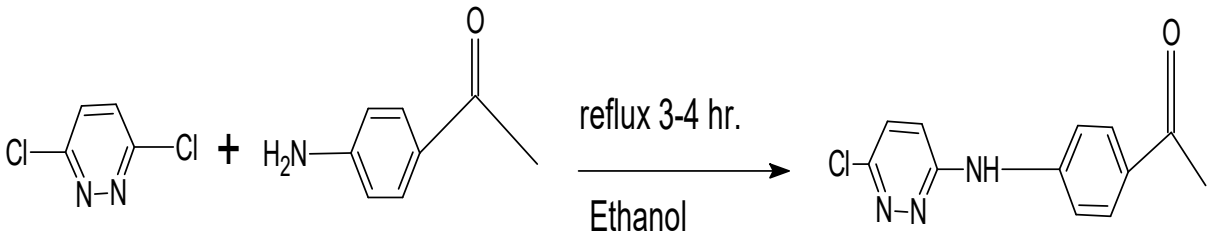
0.001 mole of 6-[(4-acetylphenyl) amino] pyridazin-3(2*H*)-one and 0.001 mole of para nitro benzaldehyde in 7ml of ethanol 10% 5ml sodium hydroxide on stirring over night the formed product is neutralised with 2N HCl then poured in ice cold water the solid obtained is filtered then recrystallised in ethanol.

4.6-{4-[5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole-Carbonyl]anilino]Phenyl]}pyridazin-3(2*H*)-one

0.0005moleofN-{4-[(1E)-3-oxo-3-{4-[(6-oxo-1,6-dihydropyridazin-3-yl)amino]phenyl}prop-1-en-1-yl]phenyl}methanimine N-oxide and 0.001 mole of phenyl hydrazine in the solvent of 10ml glacial acetic acid and pinch off sodium acetate is added and the reaction mixture is reflux for 3.30 min then the formed product is mixed in ice cold water the solid obtained is filtered through suction pump and dried by using IR lamp and recrystallised in the solvent of ethanol

Present Work:

Scheme -1.



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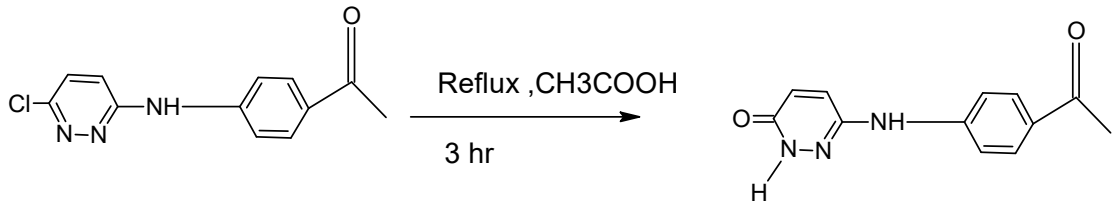
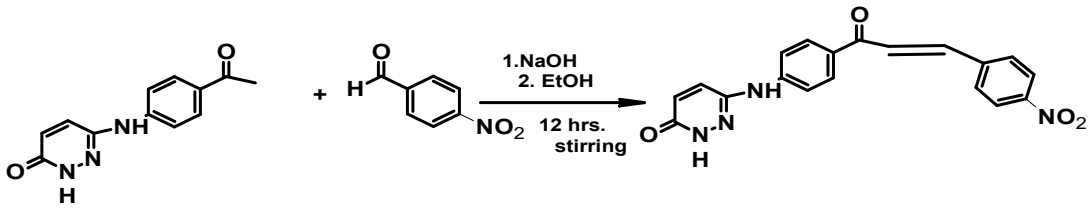
Scheme-2.



Scheme-3.



Scheme- 4.

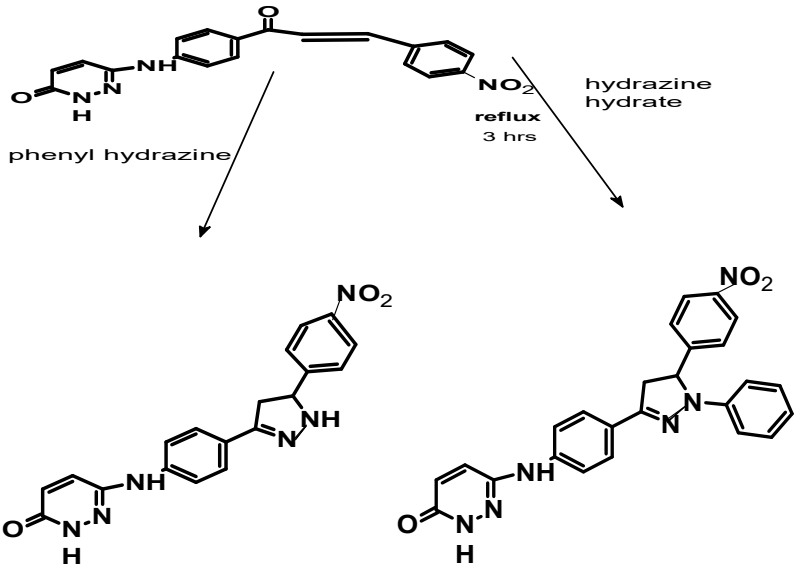
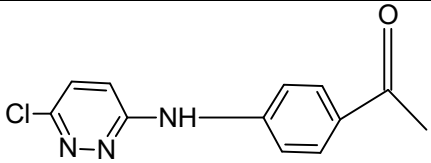
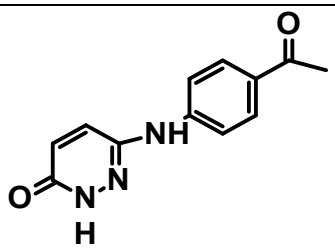
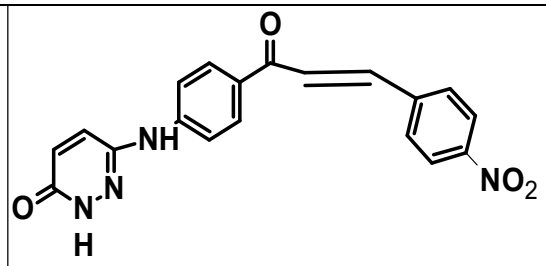
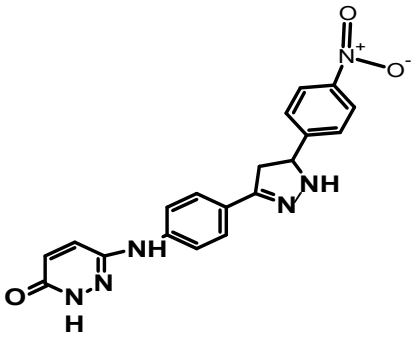
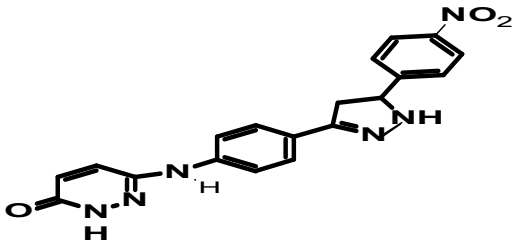


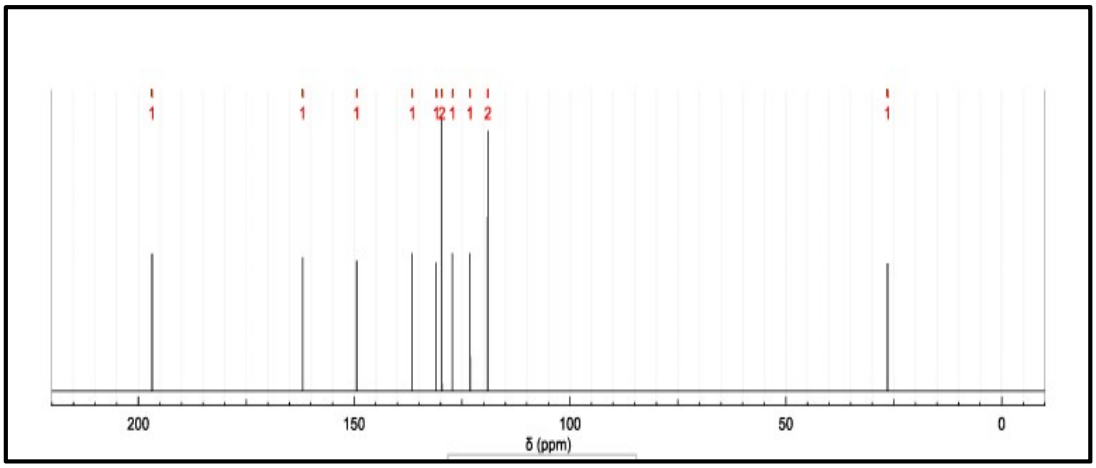
Table 1. synthesised various compounds.

Sr.no.	Product	M. P.	Yield
1)		260 ^{0}C	78 %
2)		350 ^{0}C	68%

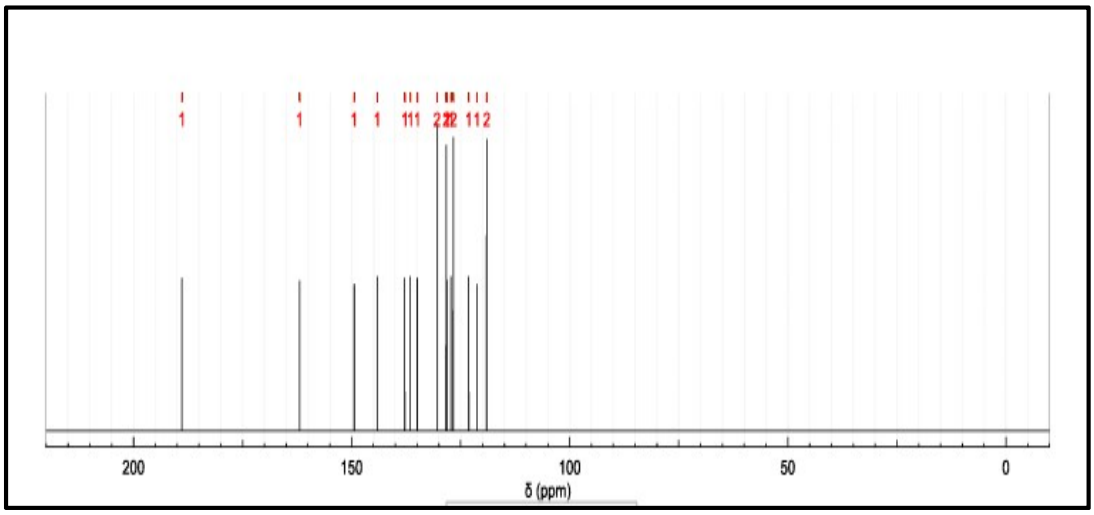
3)		260 ^{0}C	76%
4)		175 ^{0}C	68%
5)		205 ^{0}C	74 %

1. **Spectral Analysis:**

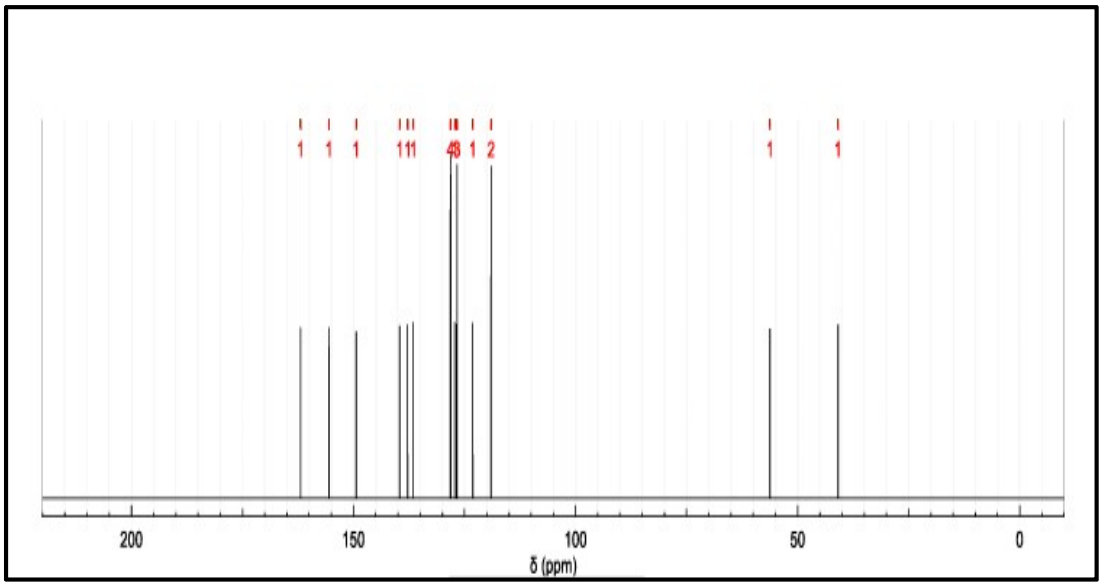
Compound(2) : Yield 68 %, M. P. 350°C; ^{13}C NMR: δ 126.94 (1C, s), 119.0 (2C, s), 123.2 (1C, s), 127.2 (1C, s), 129.7 (2C, s), 130.9 (1C, s), 136.5 (1C, s), 149.4 (1C, s), 161,9 (1C, s), 196.8 (1C, s).



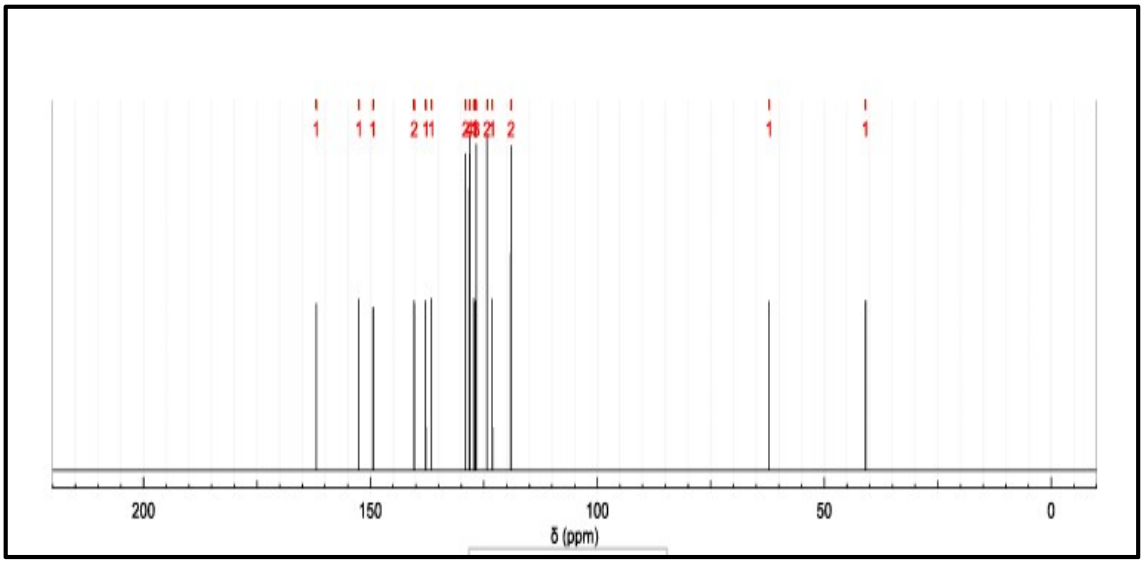
Compound (3) : Yield 76 %, M. P. 260˚C; ^{13}C NMR: δ 119.0 (2C, s),121.3 (1C, s), 123.2 (1C, s), 126.7 (2C, s), 127.2 (1C, s), 128.1 (1C, s), 128.3 (2C, s), 130.4 (2C, s), 134.9 (1C, s), 136.5 (1C, s), 137.8 (1C, s), 144.1 (1C, s), 149.4 (1C, s), 161.9 (1C, s), 188.9 (1C, s).



Compound(4) : Yield 68 %, M. P. 175˚C; ^{13}C NMR: δ 40.9 (1C, s), 56.2.(1C, s), 119.0 (2C, s), 123.2 (1C, s), 126.6-126.8 (3C, 126.7(s)),126.8 (s)),127.2 (1C, s), 128.0-128.2 (4C,128.1 (s),128.2 (s)), 136.5(1C, s) 137.8 (1C, s), 134.9 (s), 136.5 (1C, s), 139.6 (1C, s), 149.4 (1C, s), 155.5 (1C, s)161.9(1C, s).



Compound(5) : Yield 74 %, M. P. 205˚C; ^{13}C NMR: δ 40.9 (1C, s), 62.1.(1C, s), 119.0 (2C, s), 123.2 (1C, s), 124.3 (2C, s).126.6-126.8 (3C, 126.7(s)),126.8 (s)),127.0 127.2 (1C, s), 128.0-128.2 (4C,128.1 (s),128.2 (s)), 129.0(2C, s), 136.5 (1C, s), 137.8 (1C, s), 140.3-140.5 (2C, 140.3 (s) 140.4(s)), 149.4 (1C, s), 152.5 (1C, s)161.9(1C, s).



Conclusion.

In conclusion I have synthesised 1,3,5-Triphenyl-1H-pyrazoles containing 6-aminopyridazin-3(2H)-one derivatives from newly prepared acetophenone yield obtained in all the steps in this transformation are satisfactory and it has significant medicinal importance

REFERENCES:

[1] J. F. Swinbourne, H. J. Hunt and G. Klinkert, "An Efficient One Pot Synthesis of 4H-Pyrrolo[3,2,ij]quinolines," Advances in Heterocyclic Chemistry, Vol. 23, 1987, pp. 103-170. doi:10.1016/S0065-2725(08)60842-9

[2] J. V. Greenhill, "In Comprehensive Heterocyclic Chemistry," A. R. Katritzky and C. W. Rees, Eds., Pergamon Press, London, Vol. 5, 1984, p. 302.

[3] J. Elguero, "Evaluation of Antidepressant Effect of 2- Pyrazoline Derivatives," In: A. R. Katritzky and C. W. Rees, Eds., Comprehensive Heterocyclic Chemistry, Per- gamon Press, London, Vol. 3, 1996, p. 1.

[4] D. Nauduri and G. B. Reddy, "Synthesis and Activity of 2-Pyrazoline Derivatives," Chemical & Pharmaceutical Bulletin, Tokyo, Vol. 46, 1998, pp. 1254-1260. doi:10.1248/cpb.46.1254

[5] S. S. Korgaokar, P. H. Patil, M. T. Shah and H. H. Parekh, Studies on Pyrazolines: Preparation and Antimicrobial Activity of 3-(3'(p-Chloro phenyl sulphonamide phenyl)-5-aryl-acetyl pyrazolines," Indian Journal of Pharmaceuti- cal Sciences, Vol. 58, No. 6, 1996, pp. 222-225.

[6] R. H. Udupi, A. R. Kushnoor and A. R Bhat, "Synthesis and Biological Evaluation of Certain Pyrazoline Derivative of 2-(6-Methoxynaphthyl)-propionic Acid," Indian Journal of Heterocyclic Chemistry, Vol. 8, No. 1, 1998,
pp. 63-66.

[7] A. A. Bilgin, E. Palaska and R. Sunal, "Arzeimforsch; Evaluation of Antidepressant Effect of Pyrazoline Deri- vatives," Drug Research, Vol. 43, 1993, pp. 1041-1044.

[8] D. Azarifer and H. Ghasemnejad, "Microwave-Assisted Synthesis of Some 3,5-Arylated 2-Pyrazolines," Molecules, Vol. 8, No. 8, 2003, pp. 642-648. doi:10.3390/80800642

[9] D. Azarifer and M. Shaebanzadeh, "Synthesis and Char- acterization of New 3,5-Dinaphthyl Substituted 2-Pyra-zolines and Study of Their Antimicrobial Activity," Molecules, Vol. 7, No. 12, 2002, pp. 885-895. doi:10.3390/71200885

[10] M. A. Ali, A. A. Siddiqui and M. S. Synthesis, "Structural Activity Relationship and Anti-Tubercular Activity of Novel Pyrazolines Derivatives," European Journal of Medicinal Chemistry, Vol. 42, No. 2, 2007, pp. 268-275. doi:10.1016/j.ejmech.2006.08.004

[11] M. Amir, H. Kumar and S. A. Khan, "Synthesis and Pharmacological Evaluation of Pyrazoline Derivatives as New Anti-Inflammatory and Analgesic Agents," Bioorganic & Medicinal Chemistry Letters, Vol. 18, No. 3, 2008, pp. 918-922. doi:10.1016/j.bmcl.2007.12.043

[12] L. Knorr, "Notizuber die Pyrazoline reaction," Berichte der Deutschen Chemischen Gesellschaft, Vol. 26, No. 1, 1893, pp. 100-103. doi:10.1002/cber.18930260123

[13] V. Malhotra, S. Pathak, R. Nath, D. Mukerjee and K. Shankar, "Substituted Imidazole Derivatives as Novel Cardiovascular Agents," Indian Journal of Chemistry, Vol. 41B, 2002, p. 1310.

[14] T. L. Ji, H. Z. Xiao and P. L. B. Zhi, "An Improved Syn- thesis of 1,3,5-Triaryl-2-pyrazolines in Acetic Acid Aqueous Solution under Ultrasound Irradiation," The Journal of Organic Chemistry, Vol. 3, No. 1, 2007, pp. 13-16.

[15] A. Levai, "Synthesis of Chlorinated 3,5-Diaryl-2-pyra- zolines by the Reaction of Chloro chalcones with Hydra- zines," Arkivoc, 2005, pp. 344-352.

[16] R. J. Grayer and J. B. Harborne, "A Survey of Antifungal Compounds from Higher Plants," Phyto chemistry, Vol. 37, No. 1, 1994, pp. 19-42. doi:10.1016/0031-9422(94)85005-4

[17] O. N. Irob, M. Moo-Young and W. A. Anderson, "Anti- microbial Activity of Annatto Extract," International Journal of Pharmaceutics, Vol. 34, No. 2, 1996, pp. 87- 90. doi:10.1076/phbi.34.2.87.13201