International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304
Vol.8, No.1, pp 80-87, 2015

A Review on Synthesis and Biological Significance Of Pyrazoles

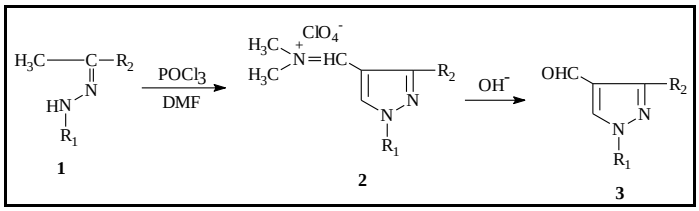
M.Jyothi* and Ramchander Merugu

University College of Science and Informatics, Mahatma Gandhi University, Nalgonda India

Abstract: Pyrazoles have their own importance in heterocyclic chemistry due to their good biological activities. Pyrazole is a heterocycle which is characterized by a 5-membered ring of three carbon atoms and two adjacent nitrogen atoms. Several derivatives of pyrazoles have been found to possess diverse types of biological activities including antibacterial, anti-inflammatory, analgesic, antifungal, antipyretic, ant arrhythmic, tranquilizing, psycho analeptic, anticonvulsant, muscle relaxing, anti diabetic, monoamine oxidase inhibiting and antibacterial activities. In view of biological significance of pyrazoles, the present communication discusses the various synthetic methods reported along with the biological activity of pyrazoles.
Key words: Pyrazoles, synthesis, biological activity.

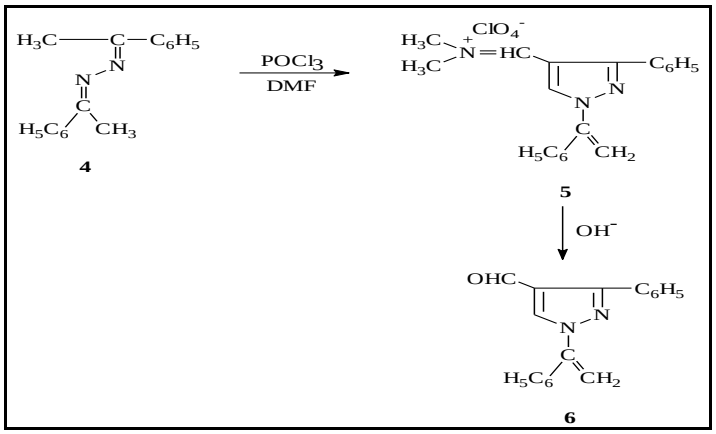
Introduction

Nitrogen containing heterocycles are compounds of biological interest. Numerous synthetic methods have been described in the literature for preparation of pyrazoles. A brief account of synthesis and biological significance of various pyrazoles is recorded below. Kira and co-workers[1] have reported that the Vilsmeier-Haack reaction on acetophenone/acetonehydrazones **1** affords the corresponding formylpyrazoles **3**.



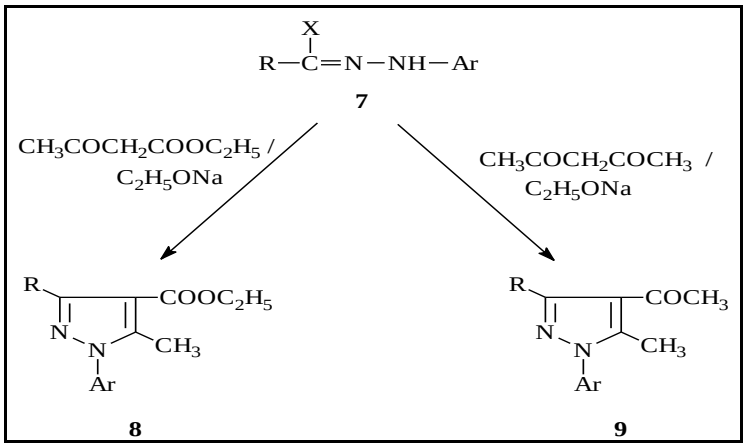
1 **2** **3**

The reaction of acetophenone azine **4** with two moles of $POCl_3$-DMF gave, via the perchlorate salt **5**, the pyrazole carboxaldehyde **6** in an almost quantitative yield.[2]

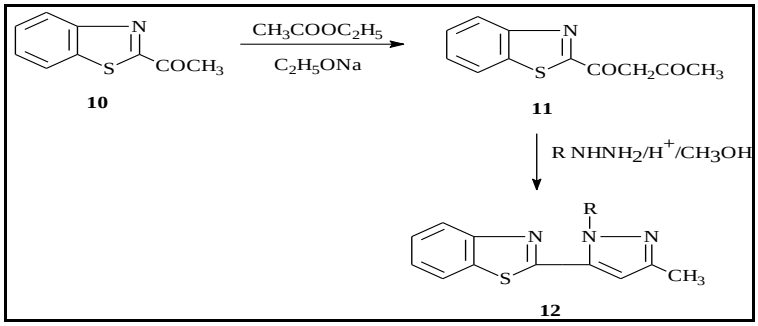


4 **5** **6**

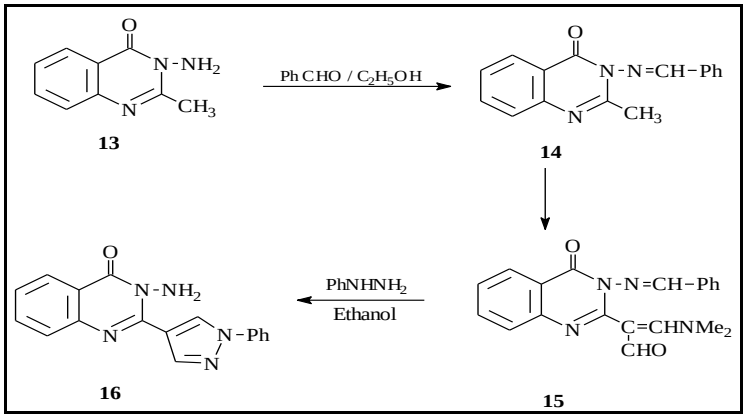
A series of C-ethoxycarbonyl and C-acetyl derivatives of hydrazidoyl halides **7** have been reacted with carbanions of active methylene compounds to afford substituted pyrazoles **8** and **9** in good yields.[3]



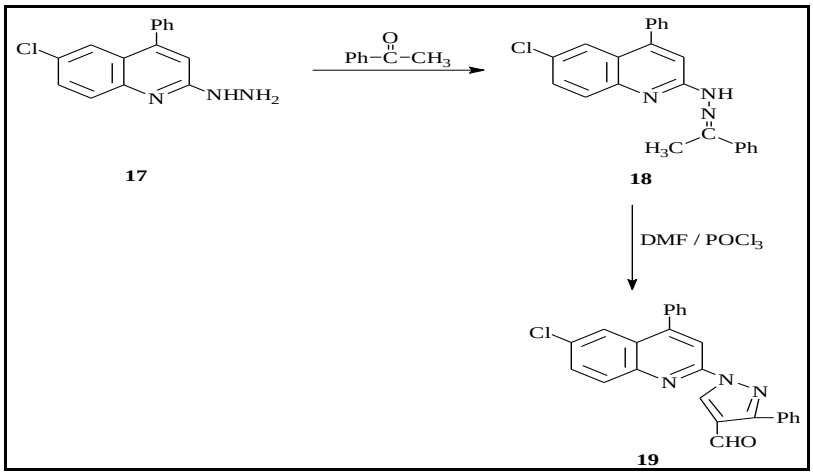
Singh *et al*.[4] have reported the synthesis of 2-(3′-methylpyrazol-5′-yl)benzothiazoles **12** by condensing 2-acetoacetylbenzothiazole **11** with hydrazines.



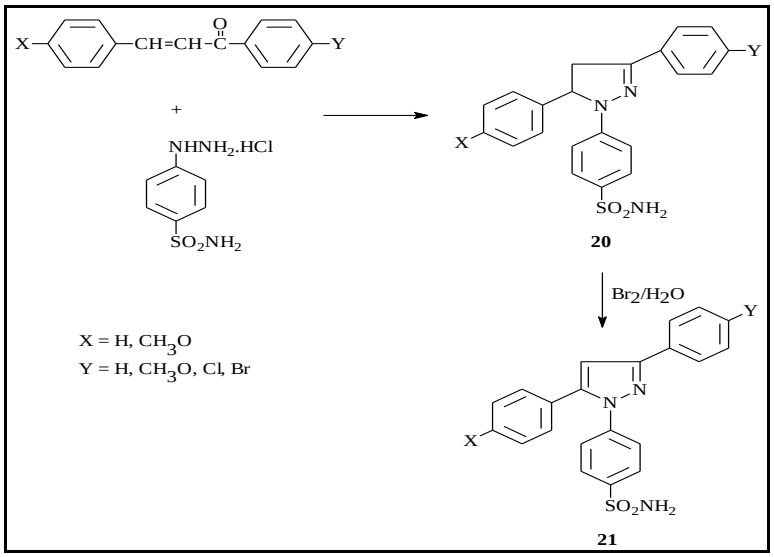
The Vilsmeier reaction on 3-benzalamino-2-methyl-4-quinazolone **14** using DMF-$POCl_3$ gave the aminoacrolein derivative **15**, which was converted into 3-amino-2-(1'-phenylpyrazol-3'-y1)-4-quinazolone **16** by reaction with phenylhydrazine in ethanol[5].



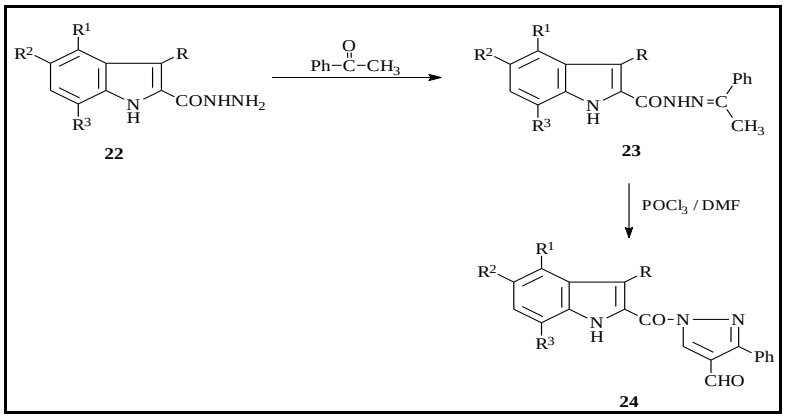
N′-(6-Chloro-4-phenylquinolin-2-yl)acetophenonehydrazone **18** on treatment with Vilsmeier reagent ($POCl_3$-DMF) gave 6-chloro-2-(4-formyl-3-phenylpyrazol-1-yl)-4-phenylquinoline **19** in an excellent yield. The hydrazone **18** was prepared by the condensation of 6-chloro-2-hydrazino-4-phenylquinoline **17**[6] with acetophenone.



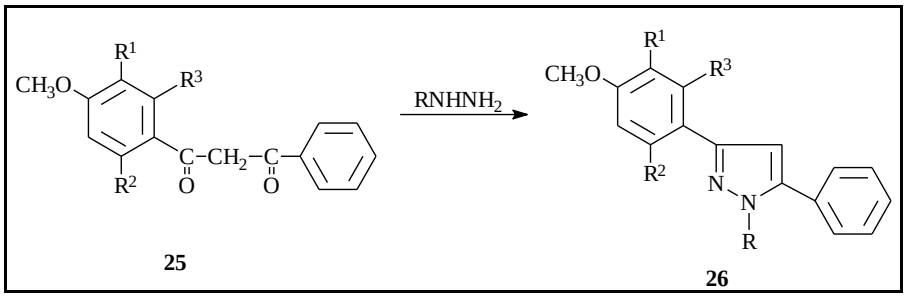
Condensation of *p*-sulphamylphenylhydrazine hydrochloride with different chalcones afforded 3,5-disubstituted-1-(*p*-sulphamylphenyl-Δ^2-pyrazolines **20**, which on oxidation with bromine water furnished the corresponding 3,5-disubstituted-1-(*p*-sulphamylphenyl)pyrazoles **21.**[7]



The hydrazones **23** obtained from hydrazides **22** and acetophenone on reaction with $POCl_3$ and DMF produced the substituted 2-(4′-formyl-3′-phenylpyrazole-1′-carbonyl)-indoles **24**.[8]

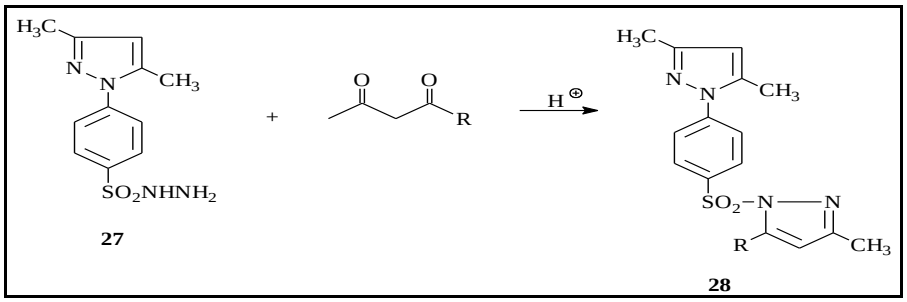


Ahluwalia *et al*.[9] have reported the synthesis and antimicrobial activities of some new 1-substituted-3-aryl-5-phenylpyrazoles **26** by condensing β-diketones **25** with hydrazine hydrate and substituted hydrazines.



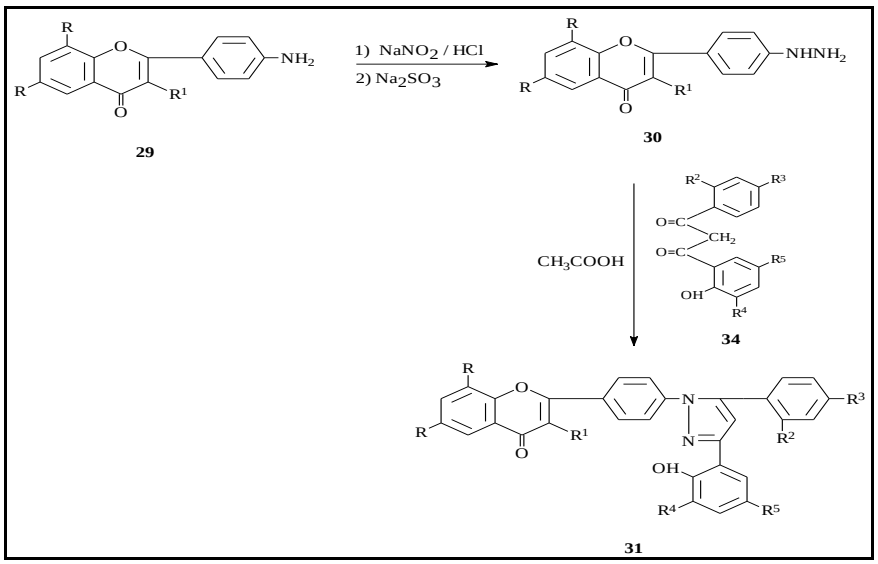
25 **26**

Patel and Fernandes[10] reported the synthesis and antibacterial activity of some new 1*H*-sulphonylpyrazoles **28**.



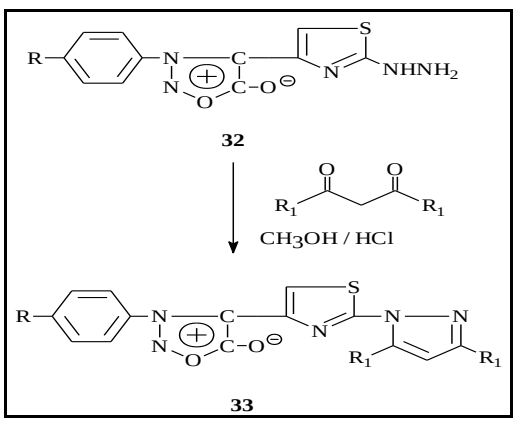
27 **28**

The synthesis of some new pyrazoles **31** from 4′-aminochromones **29** was reported by Mazumdar *et al*.[11]



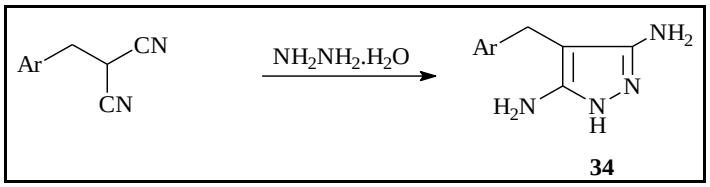
29 **30** **34** **31**

The condensation of 3-aryl-4-(2-hydrazino-4-thiazolyl)-sydnones **32** with 1,3-dicarbonyl compounds (acetylacetone, and dibenzoylmethane) in the presence of hydrochloric acid afforded 3-aryl-4-[2-(3,5-dimethyl/ phenylpyrazol-1-yl)-sydnones **33**.[12]



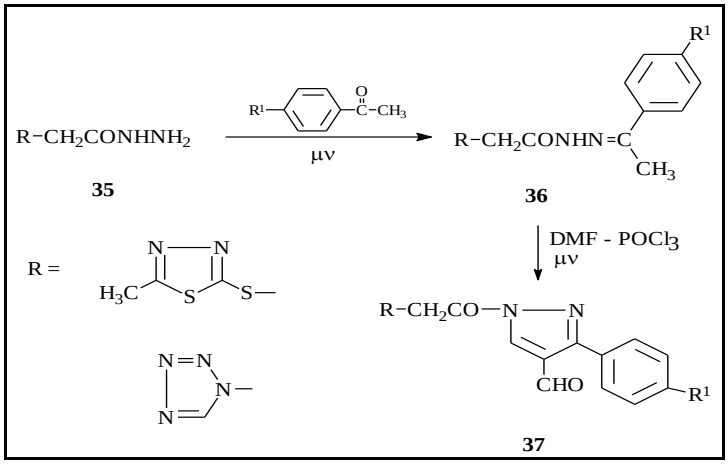
32 **33**

Ram and coworkers[13] have reported the synthesis and antimalarial activity of some new pyrazoles **34** by condensing benzylmalononitrile with hydrazine hydrate.



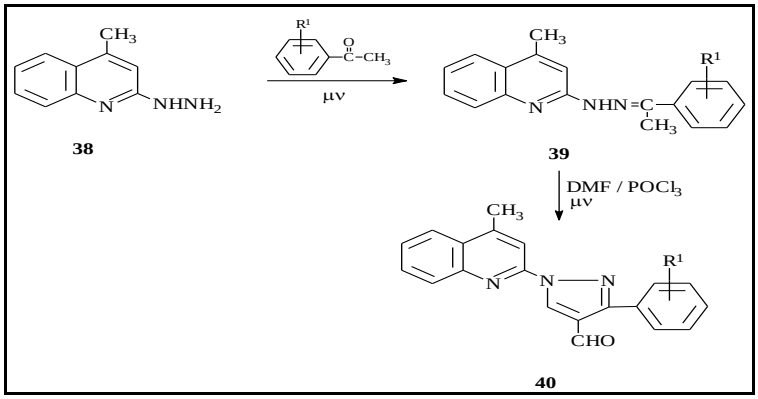
34

The reaction of substituted acetophenones with 5-methyl-1,3,4-thiadiazol-2-ylthio/tetrazol-1-ylacetic acid hydrazides **35** afforded corresponding hydrazones **36**. The hydrazones **36** on treatment with DMF/$POCl_3$ under microwave irradiation (MWI) afforded corresponding pyrazoles **37**.[14]



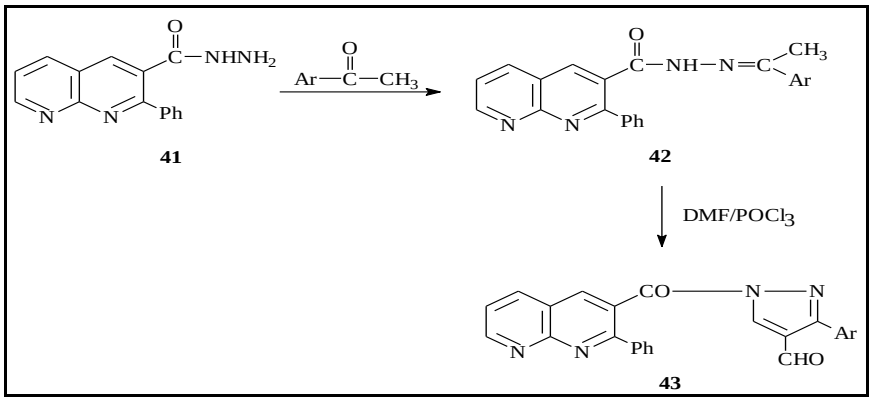
35 **36** **37**

Kidwai *et al*.[15] have reported the microwave assisted synthesis and antifungal activity of 4-methyl-2-[3′-substituted phenyl-4′-formylpyrazolyl]-quinolines **40**.



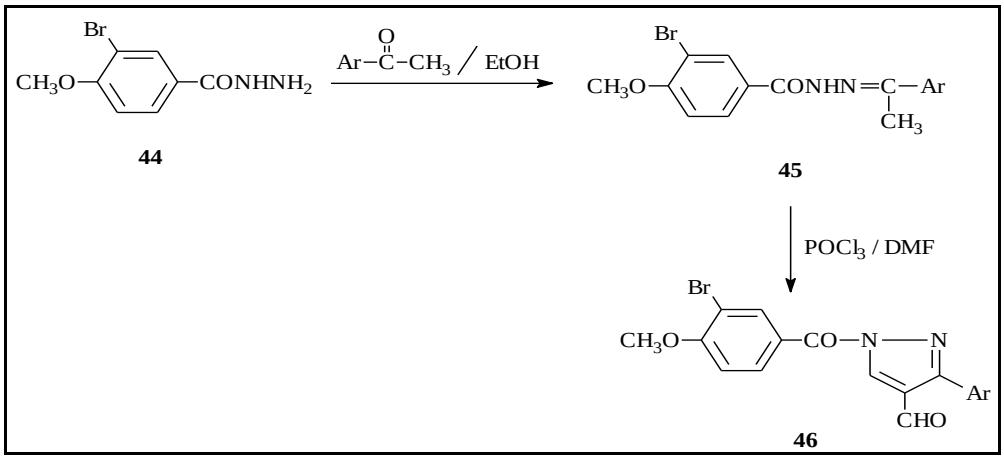
38 **39** **40**

Mogilaiah *et al*.[16] have reported the synthesis and antibacterial activity of 3-(3-aryl-4-formylpyrazole-1-carbonyl)-2-phenyl-1,8-naphthyridines **43**.

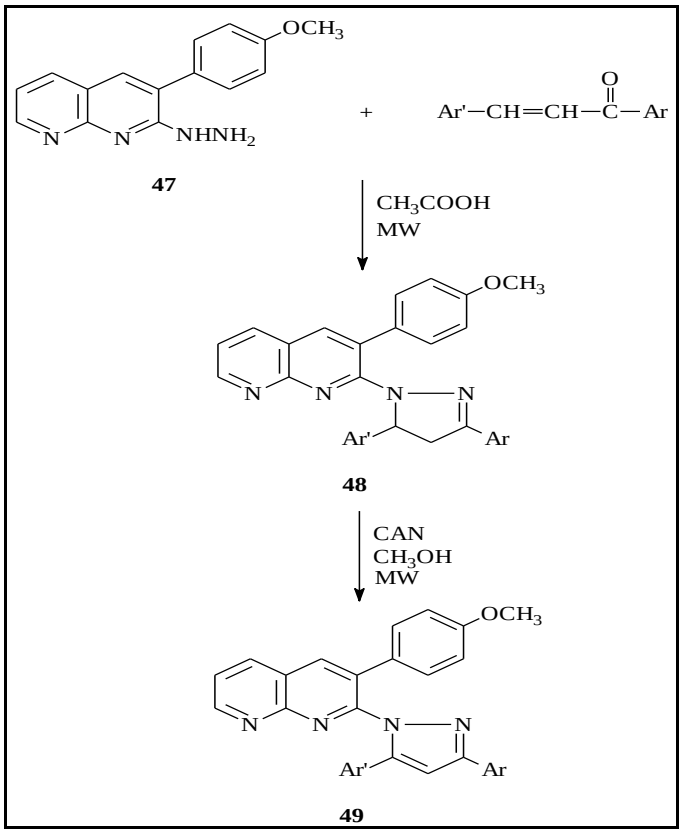


41 **42** **43**

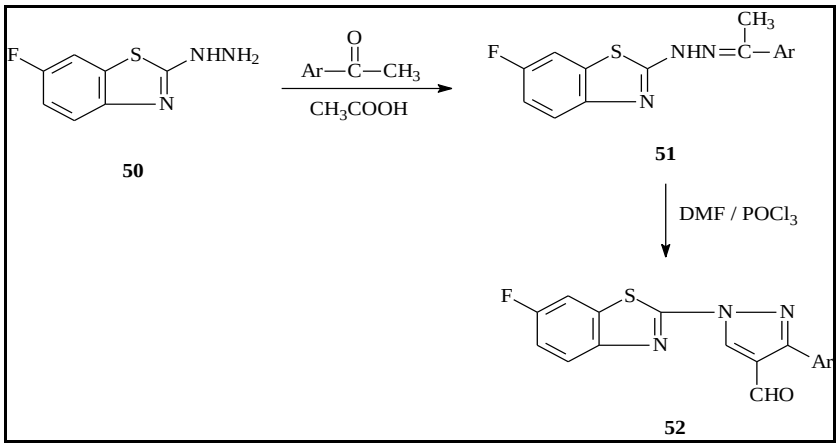
Havaldar and Mishra[17] have reported the synthesis and biological activity of 1-(3'-bromo-4'-methoxybenzoyl)-4-formyl-3-(substituted phenyl) pyrazoles **46**.



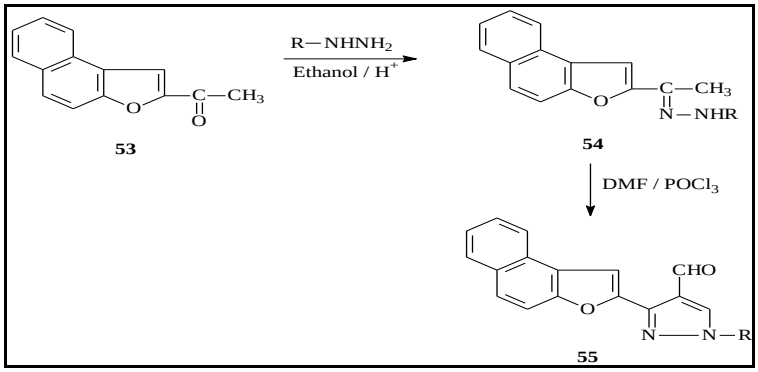
Mogilaiah *et al*.[18] have described a mild and efficient oxidation of pyrazolinyl-1,8-naphthyridines **48** to pyrazolyl-1,8-naphthyridines **49** mediated by cerium(IV) ammonium nitrate (CAN) under microwave irradiation.



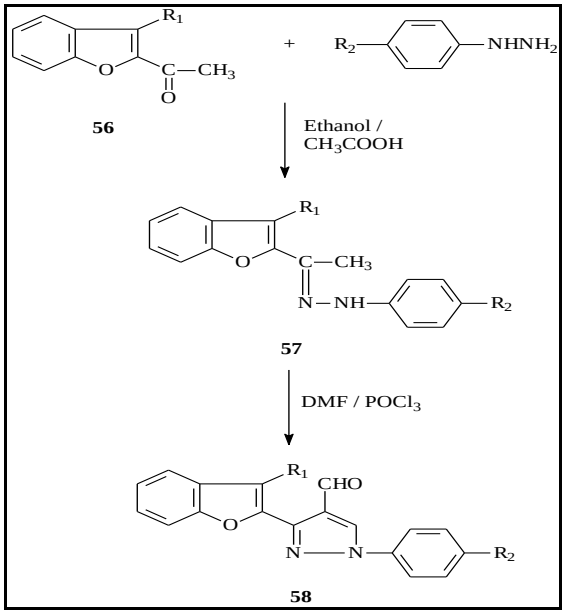
Bawa and Kumar[19] have described the synthesis and antibacterial activity of 6-fluoro-2-(4-formyl-3-(substitutedphenyl)pyrazol-1-yl]benzo-thiazoles **52**.



Nagaraja *et al*.[20] have reported the synthesis and antimicrobial activity of naphtho[2,1-*b*]furopyrazoles **55**.



Kumar *et al*.[21] have described the synthesis, antibacterial and antifungal activities of 1-aryl-3-(1-benzofuran-2-yl)-1*H*-pyrazole-4-carbaldehydes **58**.



References

1. Kira M A, Abdel-Rahman M O, Gadalla K Z, *Tetrahedron Lett*, 2, 1969, 109.
2. Kira M A, Nofal Z M, Gadalla K Z, *Tetrahedron Lett*, 48, 1970, 4215.
3. Tewari R S, Parihar P, *Indian J Chem*, 19B, 1980, 217.
4. Singh S P, Prakash I, Tomer R K, Prakash O, Sawhney S N, *Indian J Chem*, 22B, 1983, 43.
5. Barnela S B, Seshadri S, *Indian J Chem*, 23B, 1984, 161.

6. Prabhu V S, Seshadri S, *Indian J Chem*, 24B, 1985, 137.
7. Faid-Allah H M, Mokhtar H M, *Indian J Chem*, 27B, 1988, 245.
8. Hiremath S P, Ullagaddi A, Raja Sekhar K, Purohit M G,*Indian J Chem*, 27B, 1988, 758.
9. Ahluwalia V K, Mittal B, Singh R P, Singh R P, Mann R R, Singh S B, *Indian J Chem*, 28B, 1989, 150.
10. Patel H P, Fernandes P S, *J Indian Chem Soc*, 67, 1990, 321.
11. Mazumdar A K D, Das S C, Karmakar P K, Saha N K, Banerji K D, *J Indian Chem Soc*, 69, 1992, 761.
12. Yelamaggad C V, Hiremath U S, Badami B V, *Indian J Chem*, 33B, 1994, 674.
13. Ram V J, Nath M, Chandra S, *Indian J Chem*, 33B, 1994, 1048.
14. Kidwai M, Kumar P, Goel Y, Kumar K, *Indian J Chem*, 36B, 1997, 175.
15. Kidwai M, Goel Y, Kumar R, *Indian J Chem*, 37B, 1998, 174.
16. Mogilaiah K, Chowdary D S, Rao R B, *Indian J Chem*, 40B, 2001, 43.
17. Havaldar F H, Mishra S K J, *Indian J Heterocycl Chem*, 13, 2003, 165.
18. Mogilaiah K, Reddy N V, Rao R B, *Indian J Chem*, 42B, 2003, 2618.
19. Bawa S, Kumar H, *Indian J Heterocycl Chem*, 14, 2005, 249.
20. Nagaraja G K, Kumaraswamy M N, Mahadevan K M, *Indian J Heterocycl Chem*, 16, 2006, 89.
21. Kumar D M A, Prakash G K, Kumaraswamy M N, Nandeshwarappa B P, Sherigara B S, Mahadevan K M, *Indian J Chem*, 46B, 2007, 336.

*****