

## 1, 3, 4 OXADIAZOLE IN MEDICINAL CHEMISTRY: AN OVERVIEW

Deepak S Musmade<sup>1</sup>, Nachiket S Dighe\*<sup>1</sup>, Shashikant R Pattan<sup>1</sup>, Manjusha S Sanap<sup>1</sup>,  
Prerana A Chavan<sup>1</sup>, Manisha S Kedar<sup>1</sup>, Snehalata K Tambe<sup>1</sup> and Pramod J Shirote<sup>2</sup>

1-Department of Pharmaceutical Chemistry, Pravara Rural College of  
Pharmacy, Pravaranagar, MS, India, 413736.

2-Department of Pharmaceutical Chemistry, Bharati Vidyapeeth, Kolhapur.

### Summary

Five membered aromatic systems having three heteroatoms at symmetrical positions such as 1, 3, 4 Oxadiazole have been studied extensively owing to their interesting pharmacological activities. This review article covers the most active amino thiazole derivatives that have shown considerable biological actions such as antimicrobial, anti-inflammatory, anticancer, anticonvulsant, antidepressant, antioxidant, radioprotective and anti-leishmanial. This review also discusses the structure-activity relationship of the most potent compounds. It can act as an important tool for medicinal chemists to develop newer compounds possessing Oxadiazole moiety that could be better agents in terms of efficacy and safety.

**Key words:** 1, 3, 4 Oxadiazole, Biological activities, SAR, Total synthesis.

### Address for Correspondence:

**Mr. Nachiket S Dighe**

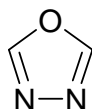
Assistant Professor & HOD

Department of Pharmaceutical Chemistry, Pravara Rural College of Pharmacy,  
Pravaranagar, A/P- Loni Bk. Taluka -Rahata, Dist-Ahmednagar 413736, India (MS).

[E-mail-nachiket1111@rediffmail.com](mailto:E-mail-nachiket1111@rediffmail.com)

### Introduction

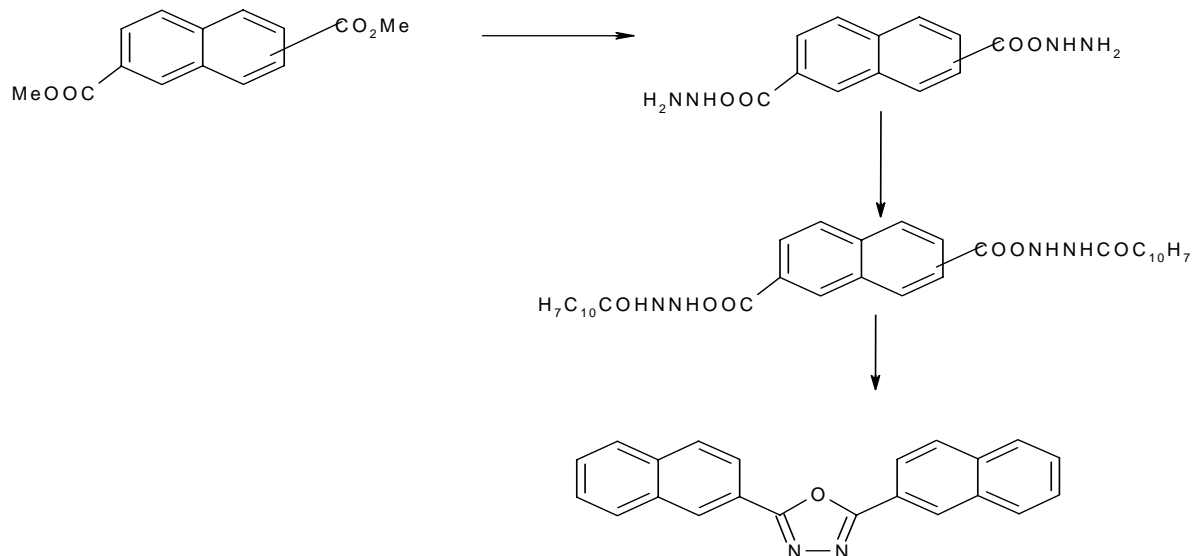
Oxadiazole is a cyclic compounds containing one oxygen and two nitrogen atoms in a five membered ring. 1,3,4 Oxadiazole are known from about eighty years and investigations in this field have intensified due to its applications in most diverse areas like dry synthesis, polymer as they give new aliphatic nitrogen compounds to other ring systems.



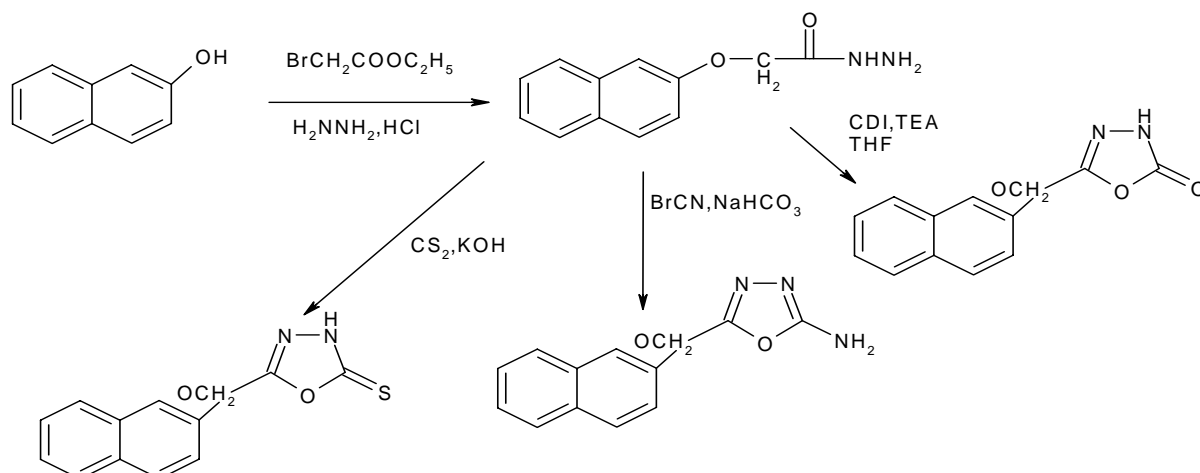
1,3,4 Oxadiazole

### Methods of Synthesis

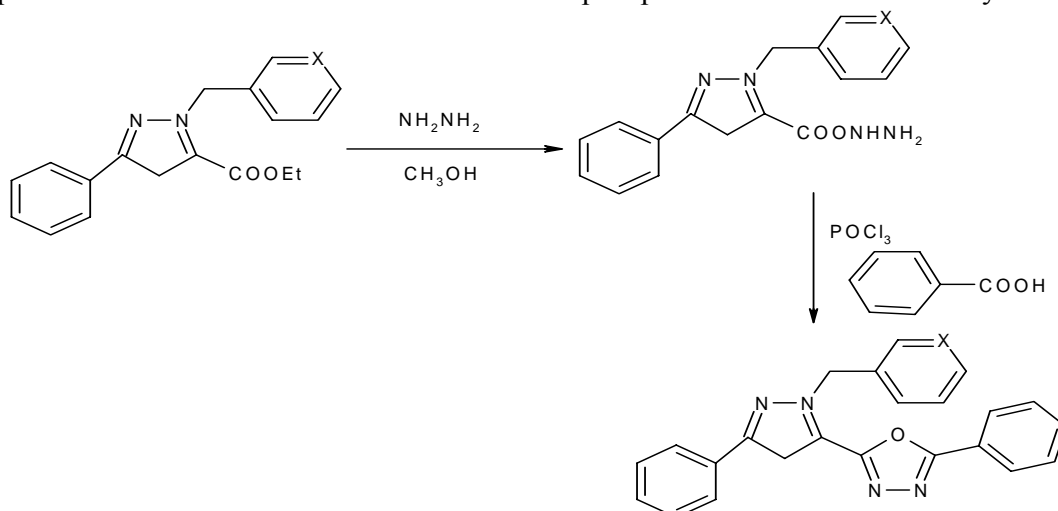
- Two types of naphthalene trimers linked by 1,3,4-oxadiazole spacers were synthesized and investigated for their physical and electronic properties. 2,6- and 2,7-isomers on central naphthalene moieties were obtained in the forms of pale yellow solids and colorless crystals, respectively.<sup>1</sup>



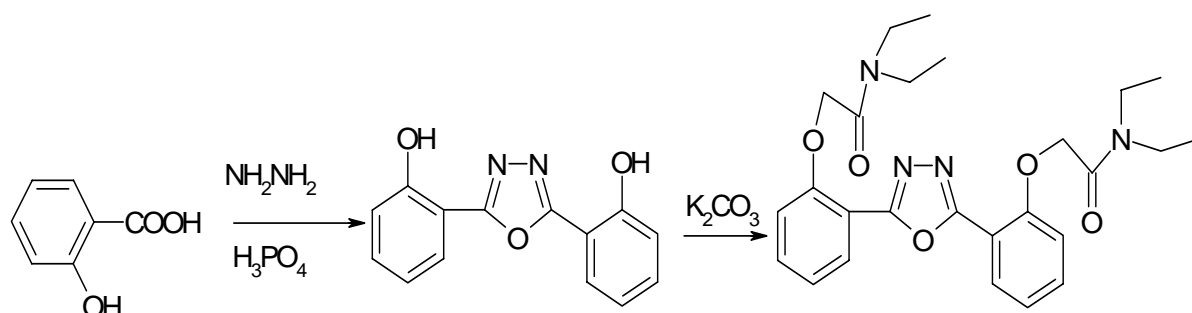
- Six new 5-(1-/2-naphthyloxymethyl)-1,3,4-oxadiazole-2(3*H*)-thione, 2-amino-5-(1-/2-naphthyloxymethyl)-1,3,4-oxadiazole, 5-(1-/2-naphthyloxymethyl)-1,3,4-oxadiazole-2(3*H*)-one derivatives have been synthesized from 1-and/or 2-naphthol.<sup>2</sup>



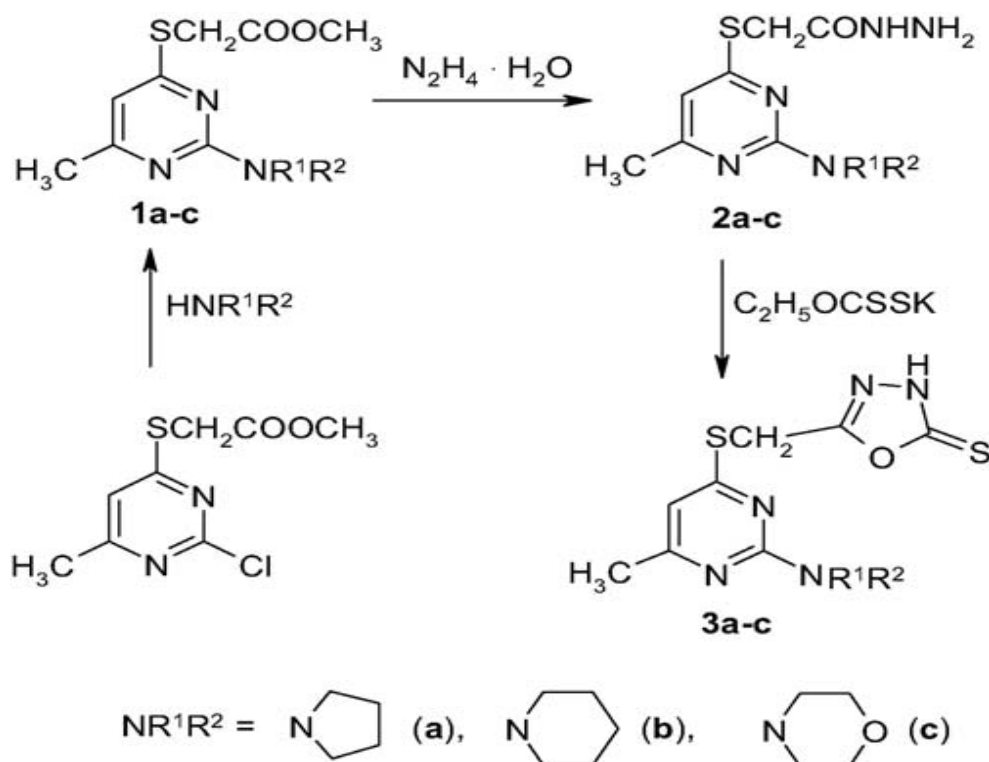
3. A series of novel substituted pyrazoly 1,3,4-oxadiazole derivatives were synthesized by the reaction of substituted pyrazole-5-carbohydrazide with substituted benzoic acid in the presence of phosphorus oxychloride.<sup>3</sup>



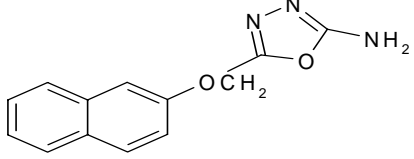
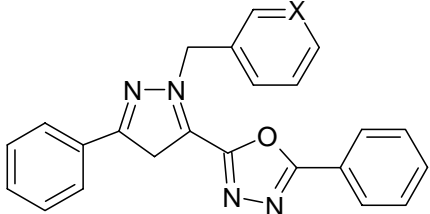
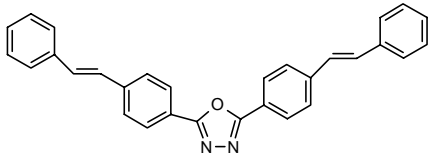
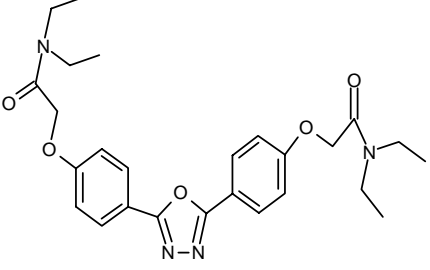
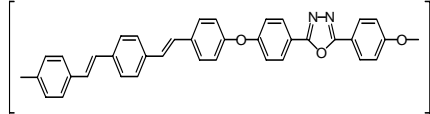
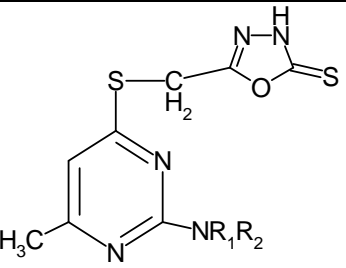
4. new amide-based 1,3,4-oxadiazole derivative ligand 2,5-bis[2-(*N,N*-diethyl-1-oxopropylamide)phenyl]-1,3,4-oxadiazole (L) and its complexes,  $\text{Ln}(\text{NO}_3)_3\text{L}$  ( $\text{Ln} = \text{La}, \text{Eu}, \text{Gd}, \text{Tb}, \text{Er}$ ), were synthesized. The complexes were characterized by elemental analysis, infrared spectra and conductivity. The lanthanide ions were coordinated by O atoms from C O. The fluorescence properties of  $\text{Eu}(\text{NO}_3)_3\text{L}$  and  $\text{Tb}(\text{NO}_3)_3\text{L}$  in the solid state and in different solvents were investigated. Under the excitation of UV light, these complexes exhibit characteristic fluorescence of europium and terbium ions.<sup>4</sup>

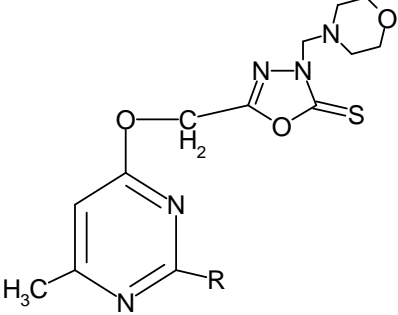
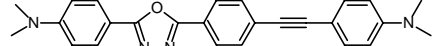
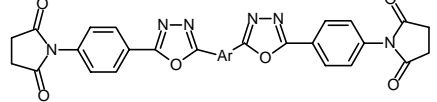
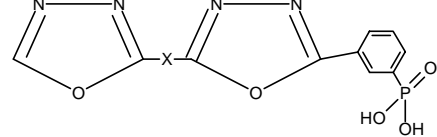
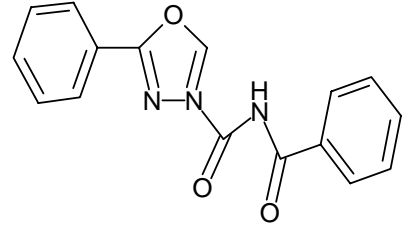
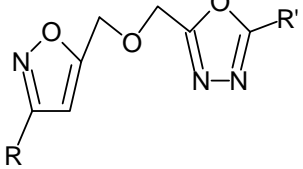
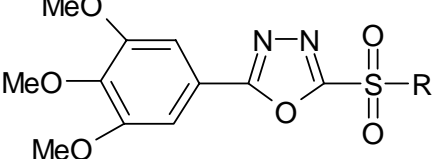
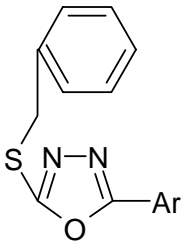


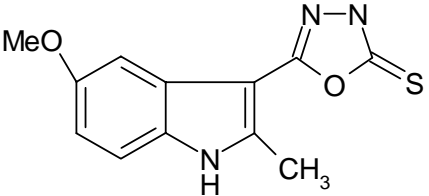
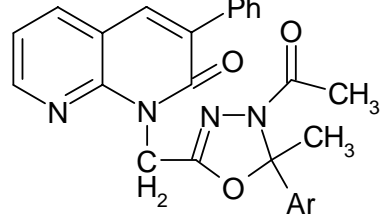
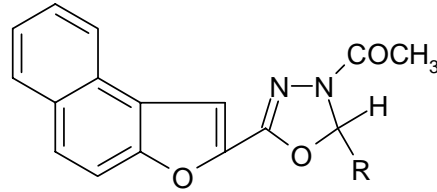
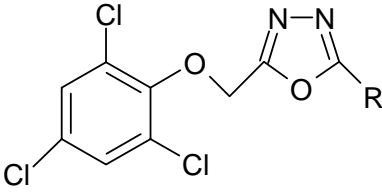
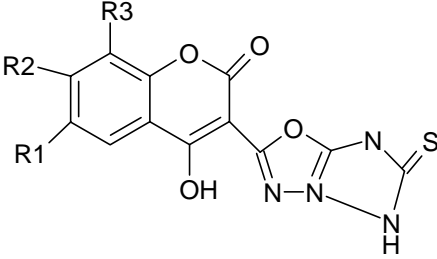
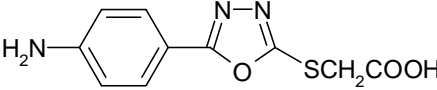
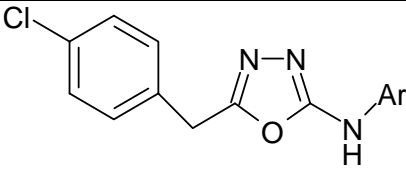
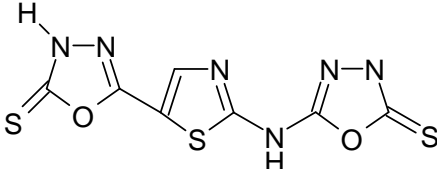
5. Synthesis and results of anti-inflammatory activity *in vivo* of 5-[(2-disubstitutedamino-6-methyl-pyrimidin-4-yl)-sulfanylmethyl]-3H-1,3,4-oxadiazole-2-thiones and their *S*-alkyl-, *N*3-acyl- and *N*3-aminomethyl derivatives are described. All the tested compounds possess anti-inflammatory activity comparable to that of acetylsalicylic acid and some derivatives of 5-[(6-methyl-2-piperidin-1-yl-pyrimidin-4-yl)-sulfanylmethyl]-3H-1,3,4-oxadiazole-2-thione were found to be much more active than ibuprofen.<sup>7</sup>

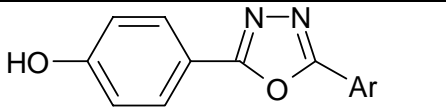
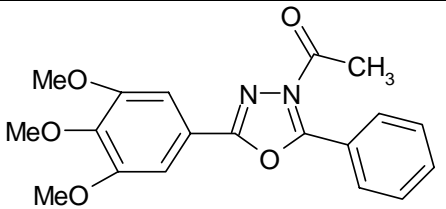


## Pharmacological actions of 1, 3, 4 Oxadiazole

Sr.no	Structure	Activity	Reference
1		Antimicrobial Activity	2
2		optical properties	3
3		optical properties	4
4		Spectroscopic properties	5
5		Organic electroluminisant	6
6		anti-inflammatory activity	7

7		anti-inflammatory activity	8
8		Photo-luminescent	9
9		high-performance bismaleimide resins.	10
10		Proton conductivity	11
11		MAO inhibitors	12
12		anti-inflammatory and analgesic activity	13
13		antifungal activity	14
14		glycogen synthase kinase-3β inhibitors	15

15		Antimicrobial activity	16
16		Antibacterial activity	17
17		Antimicrobial and anti-inflammatory activity	18
18		Anti-inflammatory activity	19
19		anti-inflammatory and analgesic activity	20
20		Anticancer activity	21
21		Antibacterial activity	22
22		Antimicrobial activity	23

23		Antitubercular activity	24
24		Anticancer activity	25

### Conclusion

The plethora of research subscribed in this review indicates a wide spectrum of pharmacological activities exhibited by 1,3,4 Oxadiazole derivatives. The biological profiles of these new generations of 1,3,4 Oxadiazole would represent a fruitful matrix for further development of better medicinal agents.

### References

1. Katsuhiko Ono, Synthesis and properties of naphthalene trimers linked by 1, 3, 4-oxadiazole spacers, *Tetrahedron Letters* 49 (2008) 5816–5819.
2. Erhan Palaska, Synthesis and antimicrobial activity of some 1, 3, 4-oxadiazole derivatives, *Il Farmaco* 57 (2002) 539–542.
3. Hong-Shui Lv, The synthesis, characterization and optical properties of novel, substituted, pyrazoly 1,3,4-oxadiazole derivatives, *Dyes and Pigments* xxx (2009) 1e7.
4. Dao-Hang He, Synthesis and optical properties of two novel stilbene derivatives containing 1,3,4-oxadiazole moiety, *Spectrochimica Acta Part A* 72 (2009) 417–420.
5. Wei-Sheng Liu, Synthesis, infrared and fluorescence spectra of lanthanide complexes with a new amide-based 1,3,4-oxadiazole derivative, *Spectrochimica Acta Part A* 68 (2007) 349–353.
6. Yen chun, Aromatic polyethers containing distyrylbenzene and 1,3,4 oxadiazole chromophores: synthesis and electrochemical properties, *Synthetic metals*, 125, 2002; 379-387.
7. Milda Malvina Burbuliene, Synthesis and anti-inflammatory activity of derivatives of 5-[(2-disubstitutedamino-6-methyl-pyrimidin-4-yl)-sulfanylmethyl]-3H-1,3,4-oxadiazole-2-thiones, *IL FARMACO* 59 (2004) 767–774.
8. Virginija Jakubkiene, Synthesis and anti-inflammatory activity of 5-(6-methyl-2-substituted 4-pyrimidinylloxymethyl)-1,3,4-oxadiazole-2-thiones and their 3-morpholinomethyl derivatives, *Il Farmaco* 58 (2003) 323- 328.



9. Jie Han, Yong-Heng Wei, Synthesis, Single Crystal Structure and Photo-luminescent Property of Bipolar Compounds Containing 1,3,4-Oxadiazole and Carbazolyl Units, *Journal of Molecular Structure*,2010.
10. Xinghe Fan, Synthesis and properties of 1,3,4-oxadiazole-containing high-performance bismaleimide resins, *Polymer* 48 (2007) 129-138.
11. Yakov S. Vygodskii, Novel phosphonated poly(1,3,4-oxadiazole)s: Synthesis in ionic liquid and characterization, *Reactive & Functional Polymers* 68 (2008) 208–224.
12. Zhong Li, Xuhong Qian, 1,3,4-Oxadiazole-3(2H)-carboxamide derivatives as potential novel class of monoamine oxidase (MAO) inhibitors: Synthesis, evaluation, and role of urea moiety, *Bioorganic & Medicinal Chemistry* 16 (2008) 7565–7572.
13. B. Jayashankar, Synthesis and pharmacological evaluation of 1,3,4-oxadiazole bearing bis(heterocycle) derivatives as anti-inflammatory and analgesic agents, *Journal of Medicinal Chemistry* 44 (2009) 3898–3902.
14. Cai-Jun Chen, Bao-An Song, Synthesis and antifungal activities of 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-thiadiazole and 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-oxadiazole derivatives, *Bioorganic & Medicinal Chemistry* 15 (2007) 3981–3989.
15. Morihisa Saitoh, Jun Kunitomo, Design, synthesis and structure–activity relationships of 1,3,4-oxadiazole derivatives as novel inhibitors of glycogen synthase kinase-3b, *Bioorganic & Medicinal Chemistry* 17 (2009) 2017–2029.
16. Dundappa S Dondawade, *Indian J Chem*,45B,Mar.2006,689-696.
17. K.Mogilaian, *Indian J Chem*, 45B,Aug.2006,1905-1908.
18. H.M.Vagdevi, *Indian J Chem*,45B,Nov.2006,2506-11.
19. Mohd.Amir, *Indian J Chem*,46B,Jun.2007,1014-19.
20. Airody V.Adhikari, *Indian J Chem*,47B,Mar.2008,439-448.
21. T.K.Maity, *Indian J Chem*,47B,Mar.2008,460-462.
22. N.C.Desai, *Indian J Chem*,47B,Apr.2008,579-589.
23. BHM Mruthyunjayaswamy, *Indian J Chem*,48B,Sep.2009,1274-1278.
24. Shashikant R Pattan, *Indian J Chem*,48B,Oct.2009,1453-56.
25. Baoan Song, Synthesis, structure, and bioactivity of N0-substituted benzylidene-3,4,5-trimethoxybenzohydrazide and 3-acetyl-2-substituted phenyl-5-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole derivatives, *Bioorganic & Medicinal Chemistry Letters* 16 (2006) 5036–5040.