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Research

Novel Synthesis of 5-Subtituted 1,3-Oxazole-Based Molecules Via Van Leusen Oxazole Synthesis as Anti-Microbial Activity

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Abstract:
Oxazole is heterocyclic five membered nucleus that explored improvement of novel mixtures with promising restorative exercises. In this manner, these mixtures have been blended as target structures by numerous analysts and were assessed for their natural exercises. Because of restricting with a far reaching range of receptors and chemicals effectively in natural frameworks through different communications, oxazole-based particles are turning into sort huge heterocyclic core, which stand out enough to be noticed from scientists worldwide, driving them to combine assorted oxazole subsidiaries.most suitable procedures to get ready oxazole-based restorative mixtures. In this survey, we sum up the new advances of the union of oxazole-containing particles using van Leusen oxazole combination expecting to search restorative mixtures, which are significant data revelation and amalgamation.
Keywords: *Anti-microbial, oxazole, microbial activity.*

Introduction:

Heterocyclic systems are a part of large number of drugs and biologically relevant molecules. Often the presence of hetero atoms or groupings imparts preferential specifcities in their biological responses. Te chemistry and biological study of heterocyclic compounds has been

interesting feld for a long time [1] and oxazole is one such moiety which has gained attention in recent times due to its increasing importance in the feld of medicinal chemistry. Oxazoles is a doubly unsaturated 5-membered ring having one oxygen atom at position 1 and a nitrogen at position 3 separated by a carbon in-between. It was frst prepared in 1947, has a boiling point of 69 °C and is a stable liquid at room temperature [2]. Substitution pattern in oxazole derivatives play a pivotal role in delineating the biological activities like antimicrobial [3], anticancer [4], antitubercular [5] anti-infammatory [6], antidiabetic [7], antiobesity [8] and antioxidant [9] etc. Oxazoles and its derivatives are a part of number of medicinal compounds (Fig. 1) which includes aleglitazar (1, antidiabetic), ditazole (2, platelets aggregation inhibitor), mubritinib (3, tyrosine kinase inhibitor), and oxaprozin (4, COX-2 inhibitor) [10,11].

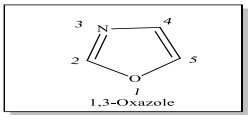


Fig.1:Oxazole

Amongst the class of planar heterocycles, the oxazole parental skeleton is found (scheme 1). Oxazole is unique in its structure and the scaffold is a constituent of several natural products with a good biological activity such as (-)hennoxazole A (antiviral) [1] and pimperinine (alkaloide) [2] (scheme 2). Also oxazole and its derivatives have been incorporated into a number of medicinally relevant compounds, both as exploratory and advanced drug candidates. Oxazole-containing compounds have been used as diabetes II treatment e.g. aleglitazar [3], platelets aggregation inhibitor e.g. ditazole [4], as part of tyrosine kinase inhibitor such as mubritinib [5], and as COX-2 inhibitors such as oxaprozin [6].

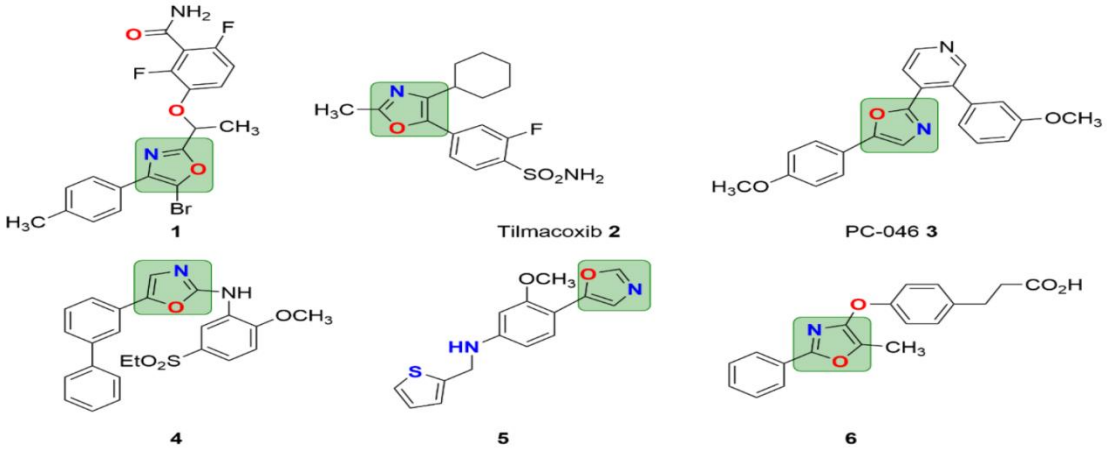
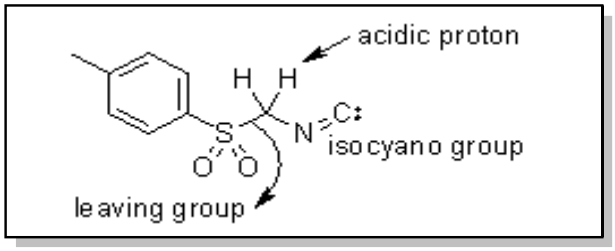


Fig.2 Different marketed product.

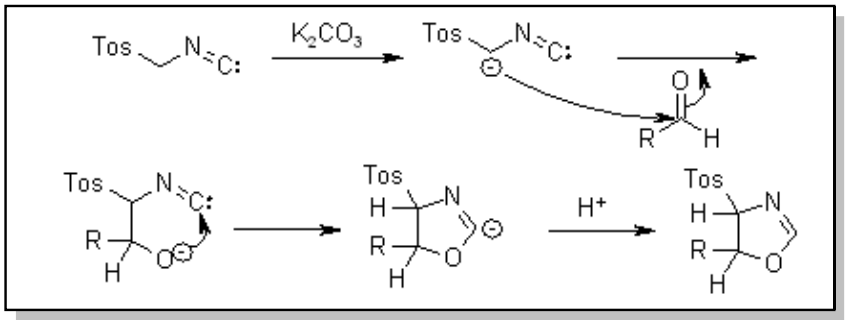
This review critically evaluates the pharmacological activity of the oxazole derivatives as antipathogenic agent that were reported recently in medicinal chemistry studies.

Mechanism of the Van Leusen Oxazole Synthesis

The reaction is driven by the unique reactivity of TosMIC, which includes acidic protons, sulfinic acid as a leaving group and an isocyano group that contains an oxidizable carbon atom:



After adding the deprotonated TosMIC to the aldehyde and bond formation between the resulting hydroxy group and the isocyano group, an oxazoline results as an intermediate.

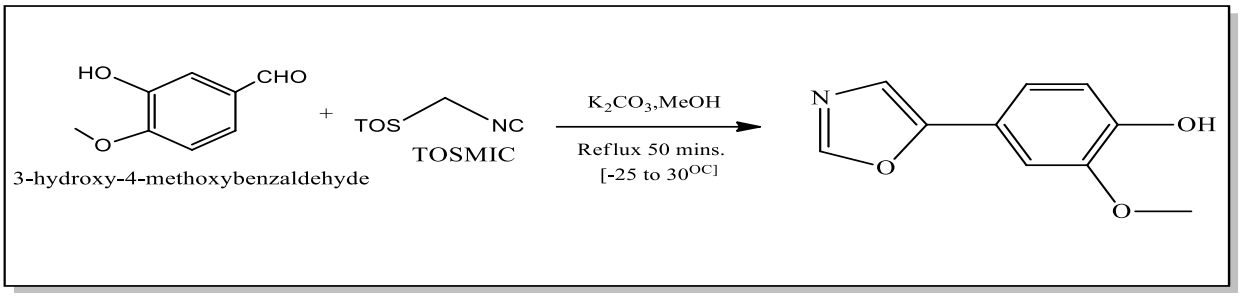


Within contrast to the Van-Leusen Reaction (synthesis of nitriles from ketones), the existence of a proton in the β-position to the sulfinyl group allows a base-promoted elimination.

Synthesis and Characterization of Oxazole:

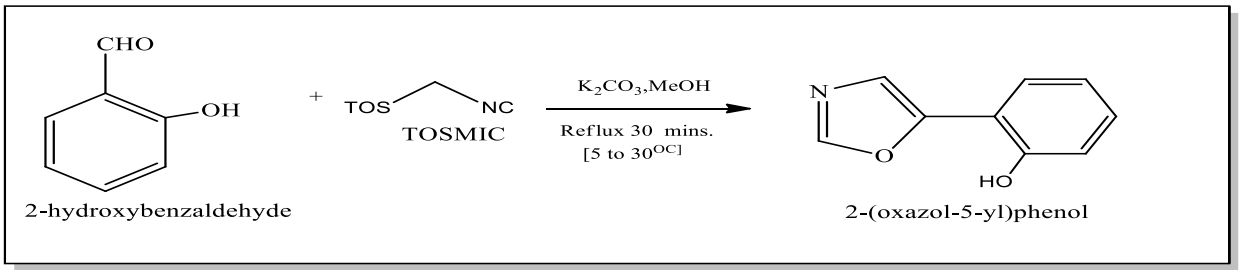
1. **Synthesis of Compound 2-methoxy-4-(oxazole-5-yl) Phenol**

I Took solution of tosylmethyl isocynide (Distilled with $LiAH_4$ 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 50^{OC}. Then a solution of 35 mmol of ***3-Hydroxy-4-methoxybenzaldehyde*** in 30-50 ml of dimethoxymethane mixture at 5 to 50^{OC}. methanol (90 ml) was added to the cold solution, which on heated to reflux 20 minutes resulted, Yield was found 68%.



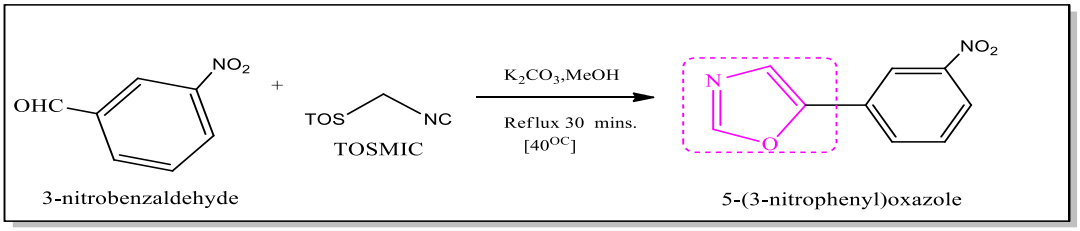
2. Synthesis of Compound 2-OXAZOLE-5-phenyl

I Took solution of tosyl-methyl isocynide (Distilled with $LiAH_4$ 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 50^{OC}.Solution of 35 mmol of ***Orthohydroxybenzaldehyde*** Compound synthesized (1g, 37mmol) in dimethoxyethane (100 ml) and acetic acid (4 ml), and extracted with dichloromethane. The extracts were washed with a saturated solution of $NaHC0_3$, dried (MgS04) and distilled, or distilled with steam. Yield was found 67%.



3. Synthesis of 5-(3-NITROPHENYL) OXAZOLE

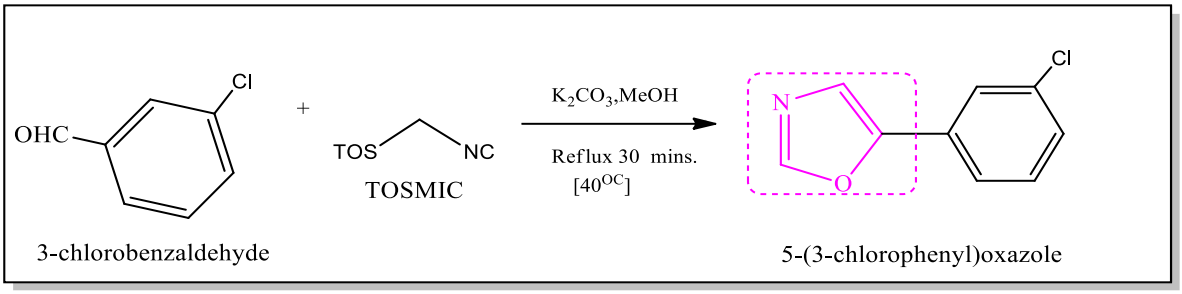
I Took solution of tosyl-methyl isocynide (Distilled with $LiAH_4$ 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Then a solution of 35 mmol of ***3nitro-benzaldehyde*** in 30-50 ml of dimethoxymethane was added dropwise to the mixture. After 60 min. methanol (90 ml) was added to the cold solution, which was then heated to reflux for 25 minutes. After removal of the solvent the residue was taken up in a mixture of water, in dimethoxyethane (100 ml) and acetic acid (5 ml), and extracted with dichloromethane. The extracts were washed with a saturated solution of $NaHC0_3$, dried (MgS04) and distilled, or distilled with steam. Yield was found 67%.



4. Synthesis of 5-(3-NITROPHENYL) OXAZOLE

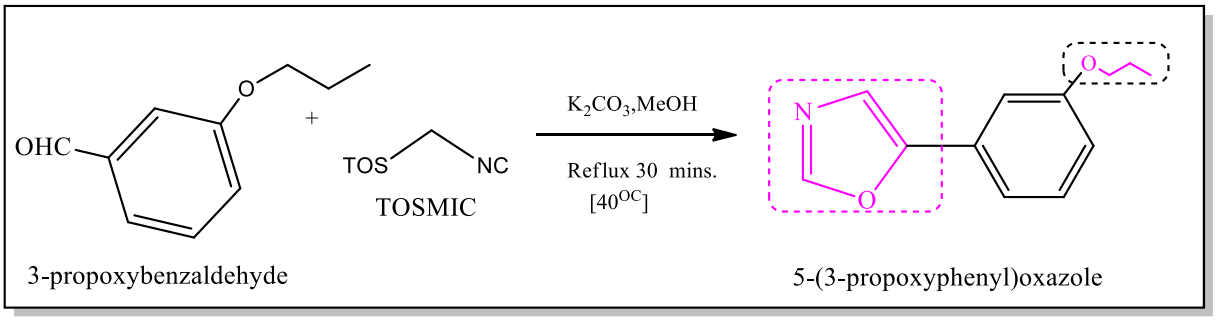
I took solution of tosyl-methyl isocynide (Distilled with LiAH4 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Then a solution of 35 mmol of 3-Chloro-benzaldehyde in 30-50 ml of dimethoxymethane was added dropwise to the mixture. After 60 min.

methanol (90 ml) was added to the cold solution, which was then heated to reflux for 25 minutes. After removal of the solvent the residue was taken up in a mixture of water, in dimethoxyethane (100 ml) and acetic acid (5 ml), and extracted with dichloromethane. The extracts were washed with a saturated solution of NaHC03, dried (MgS04) and distilled, or distilled with steam. Yield was found 63%.



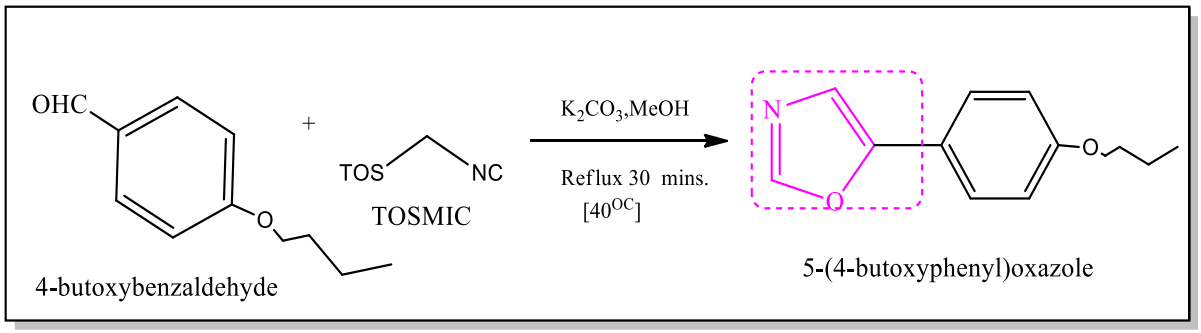
5. Synthesis of 5-(3-propoxyphenyl) Oxazole

I took solution of tosyl-methyl isocynide (Distilled with LiAH4 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Yield was found 73%.



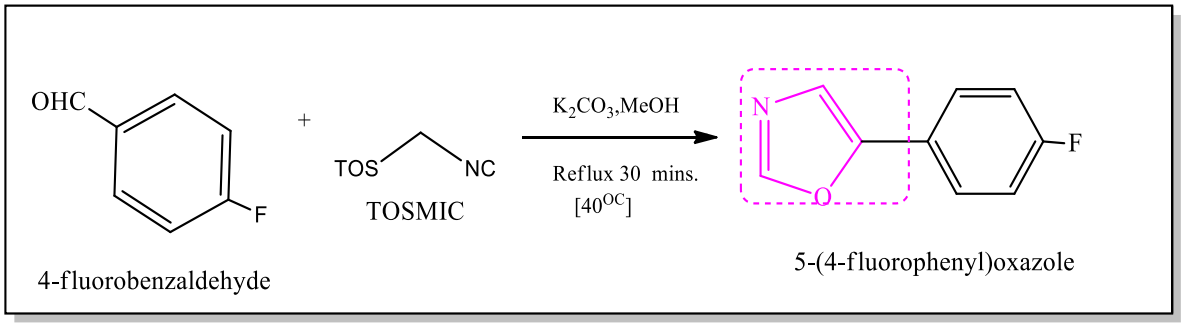
6. Synthesis of 5-(4-butoxyphenyl) oxazole

I took solution of tosyl-methyl isocynide (Distilled with LiAH4 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Yield was found 68%.



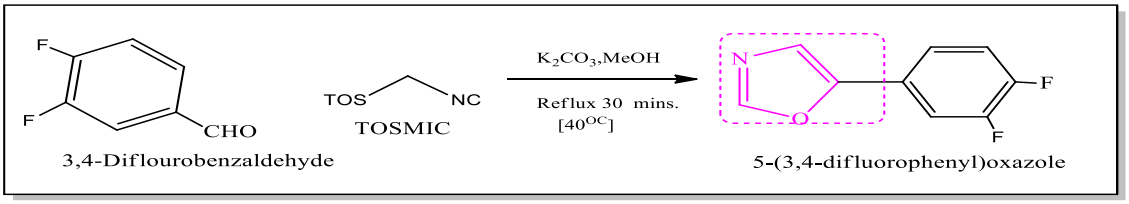
7. Synthesis of 5-(4-Flourophenyl) Oxazole

I took solution of tosyl-methyl isocynide (Distilled with LiAH4 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Then a solution of 30 mmol of 4-fluorobenzaldehyde in 30-50 ml of dimethoxymethane was added dropwise to the mixture, which was then heated to reflux for 25 minutes. After removal of the solvent the residue was taken up in a mixture of water, in dimethoxyethane (100 ml) and acetic acid (5 ml), and extracted with dichloromethane. The extracts were washed with a saturated solution of NaHC03, dried (MgS04) and distilled, or distilled with steam. Yield was found 63%.



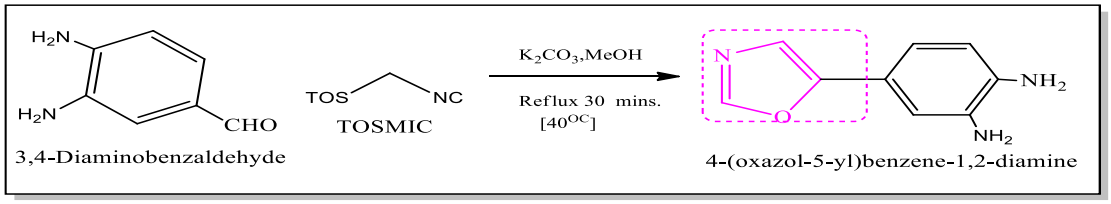
8. Synthesis of 5-(3,4-diflourophenyl)-oxazole

I took solution of tosyl-methyl isocynide (Distilled with LiAH4 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Then a solution of 30 mmol of 3,4-fluorobenzaldehyde in 30-60 ml dimethoxymethane was added mixture Yield was found 78%.

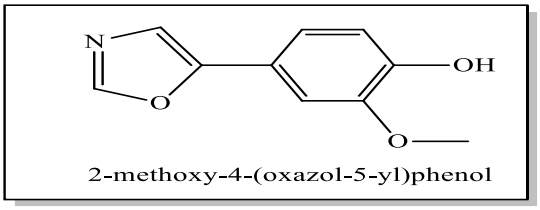


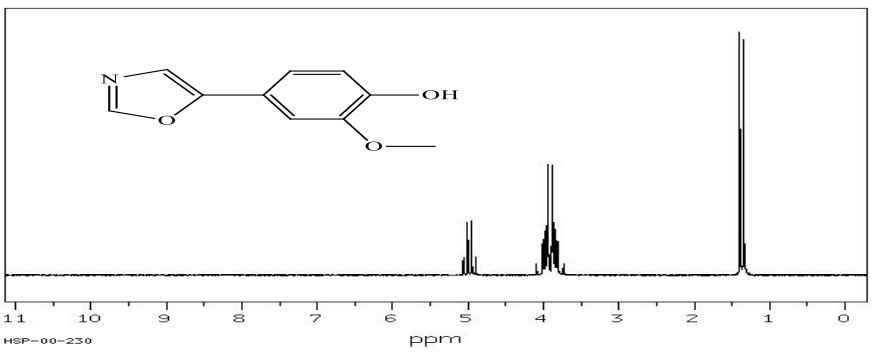
9. Synthesis of 4-(oxazole-5-yl) benzene 1,2-diamine

I took solution of tosyl-methyl isocynide (Distilled with LiAH4 30 ml) was pour dropwise and mixed by stirred suspension in 30ml of dimethoxymethane and kept below 45^{OC}. Then a solution of 30 mmol of 3,4-diaminbenzaldehyde in 30-50 ml of dimethoxymethane was added dropwise to the mixture, Yield was found 66 %.

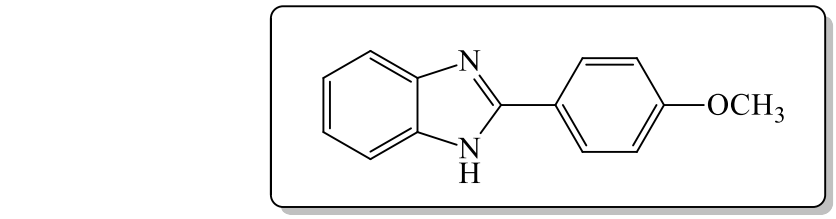


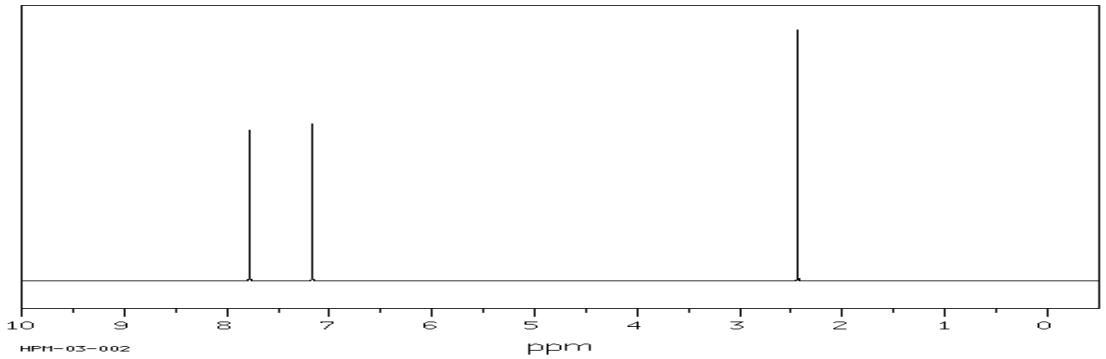
1. NMR SPECTRA OF A1 SCAFFOLD



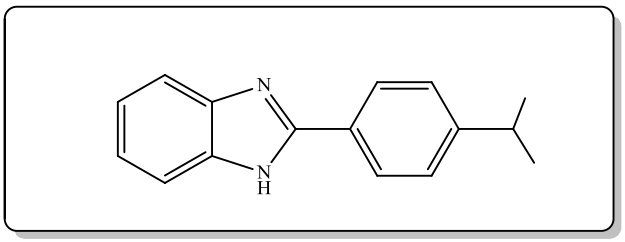


2. Proton NMR of A2 compound

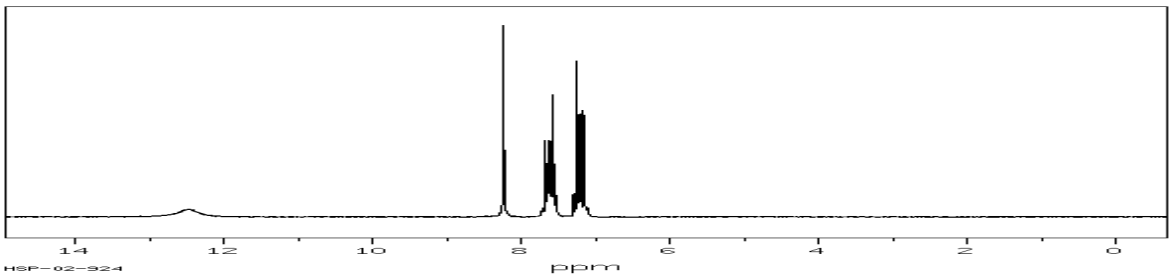




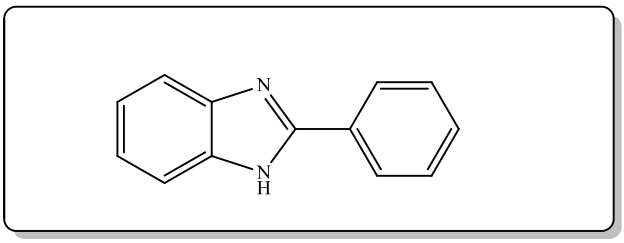
3. Proton NMR of A3 compound



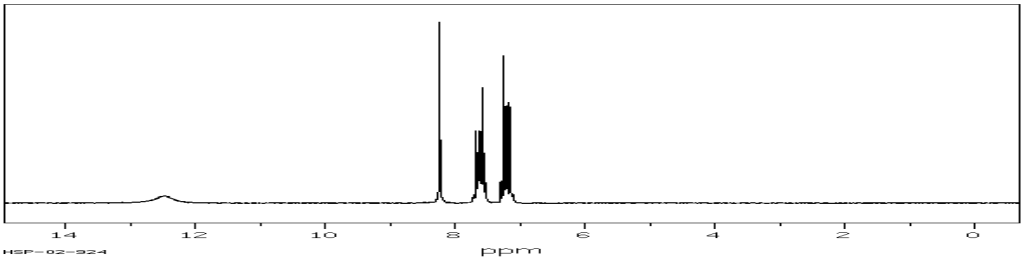
2-(4-isopropylphenyl)-1*H*-benzo[*d*]imidazole



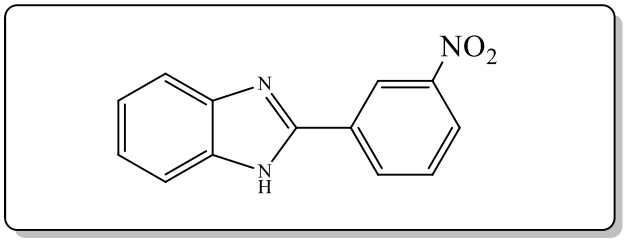
4. Proton NMR of A4 compound



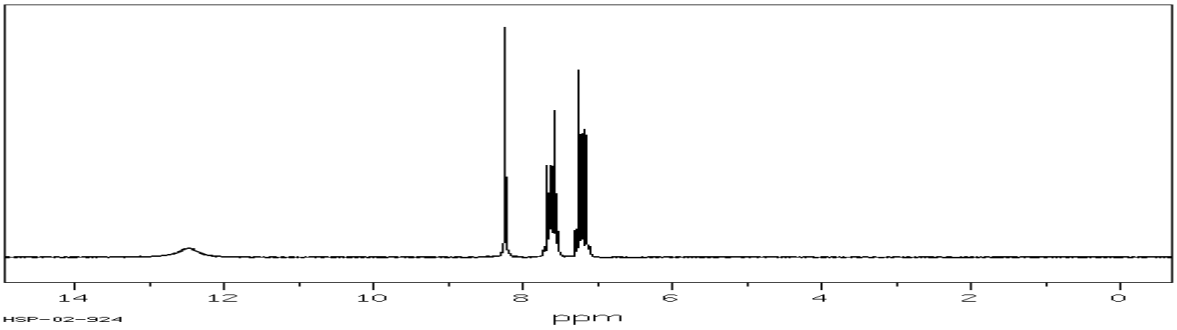
2-phenyl-1*H*-benzo[*d*]imidazole



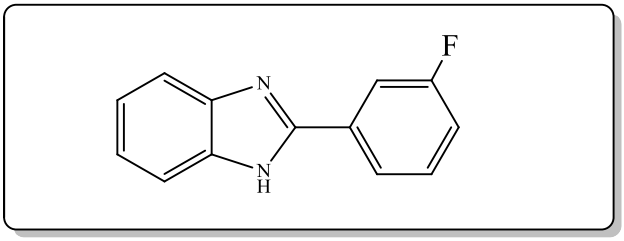
5. Proton NMR of A5 compound



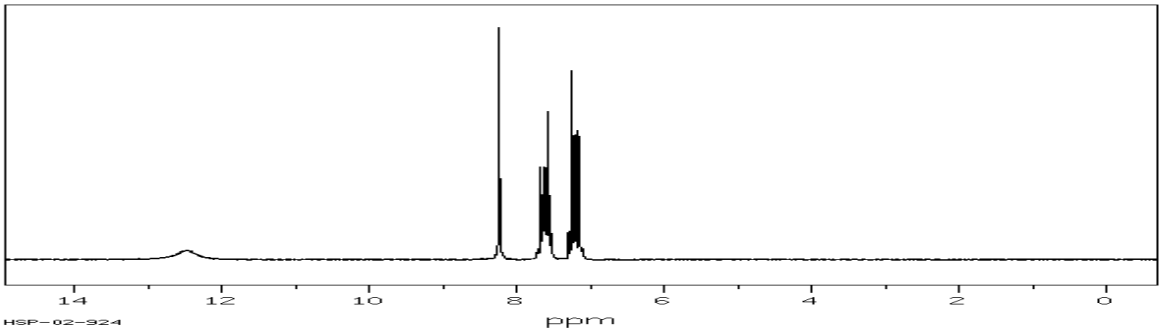
2-(3-nitrophenyl)-1*H*-benzo[*d*]imidazole



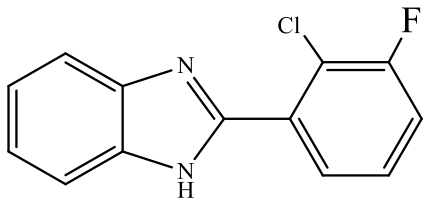
6. Proton NMR of A6 compound

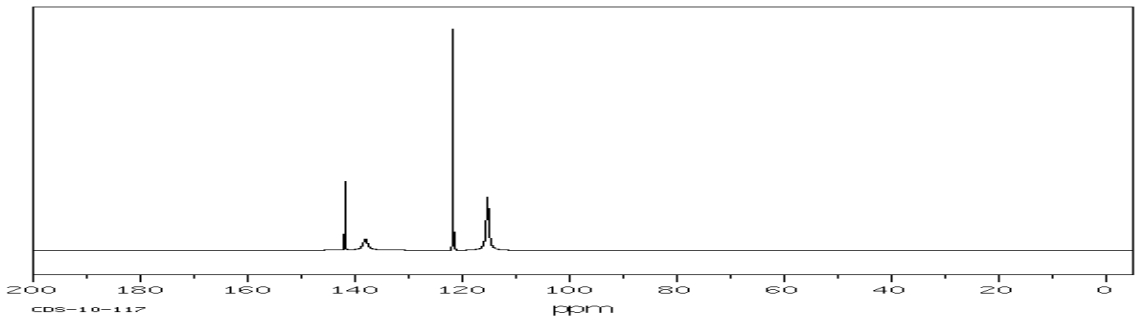


2-(3-fluorophenyl)-1*H*-benzo[*d*]imidazole

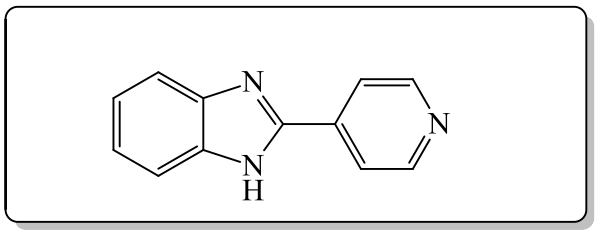


7. Proton NMR of A7 compound

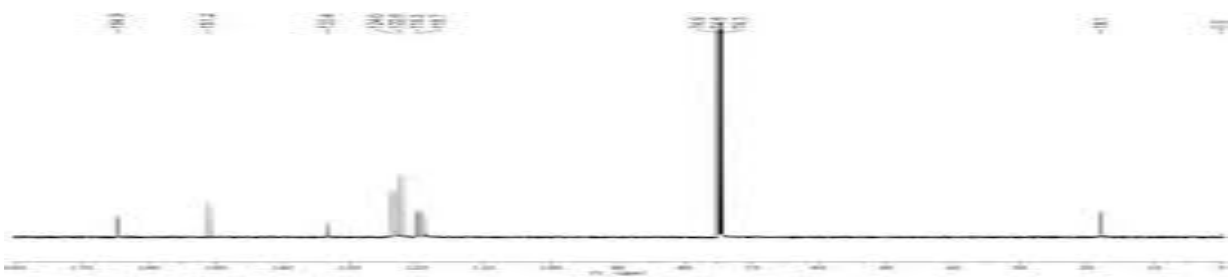




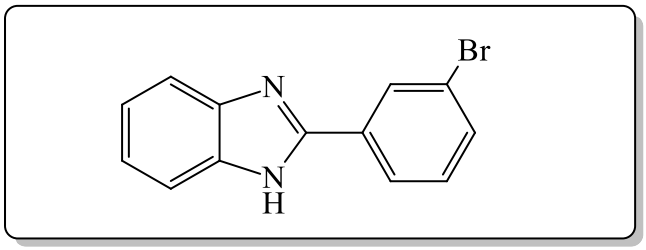
8. Proton NMR of A8 compound:



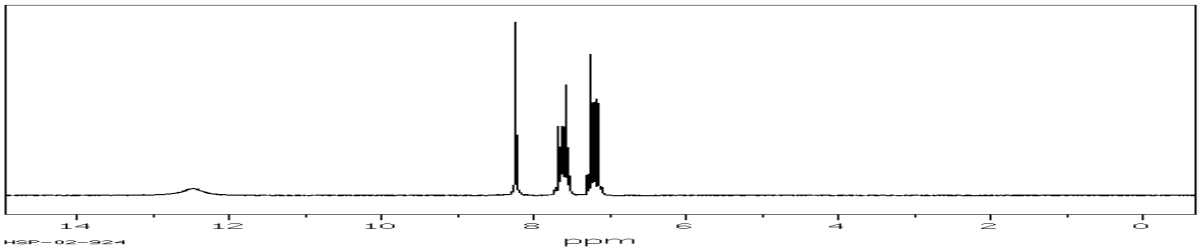
2-(pyridin-4-yl)-1*H*-benzo[*d*]imidazole



9. Proton NMR of A9 compound :

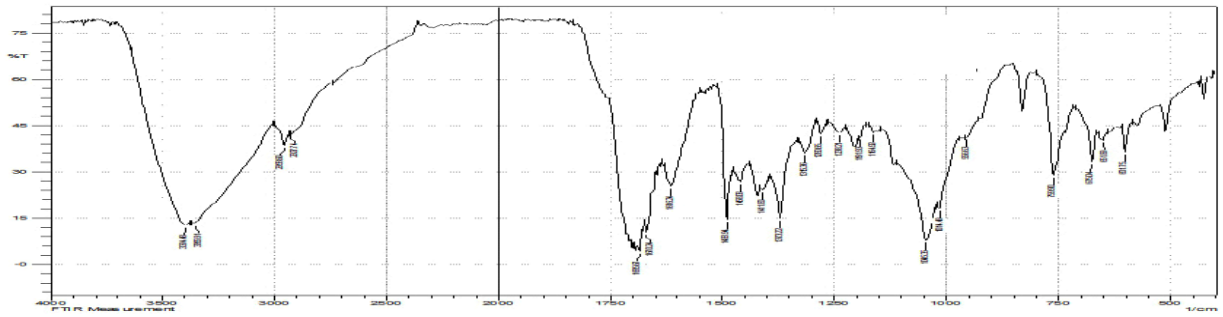


2-(3-bromophenyl)-1*H*-benzo[*d*]imidazole

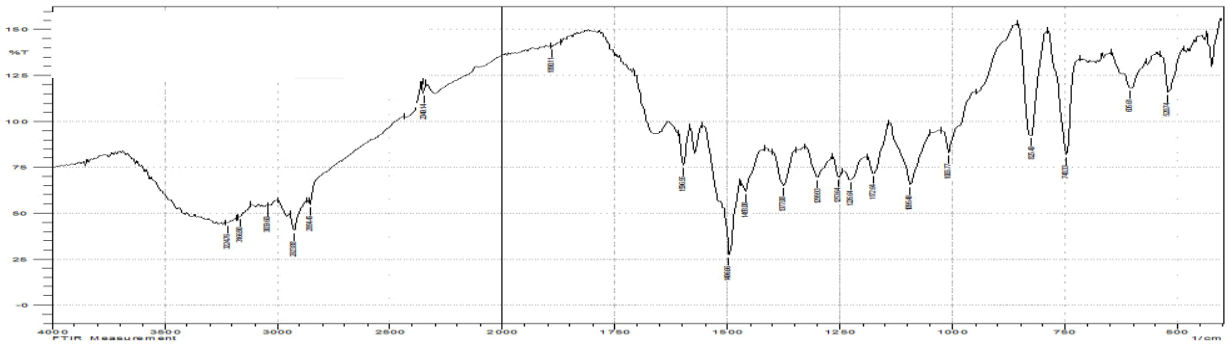


IR SPECTRA OF SYNTHESIZED COMPOUNDS:

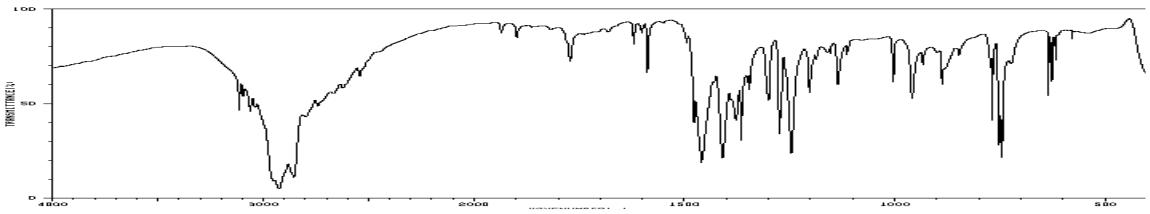
1. **IR of A1 COMPOUNDS :**



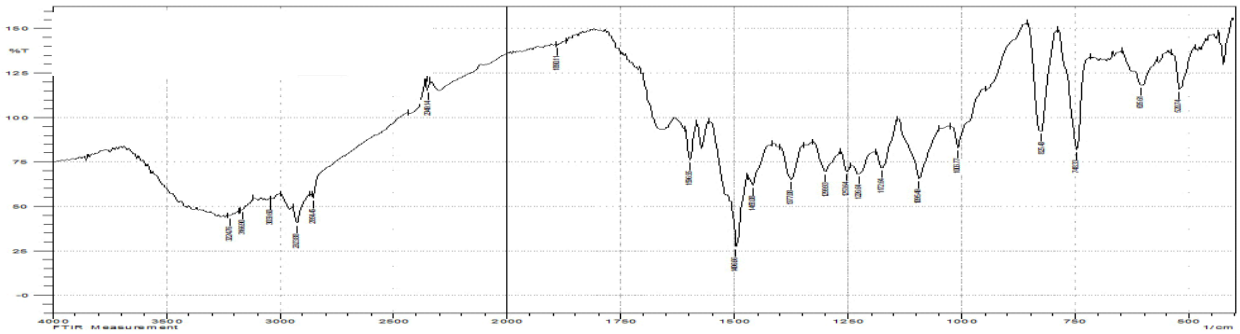
2. **IR of A2 COMPOUNDS :**



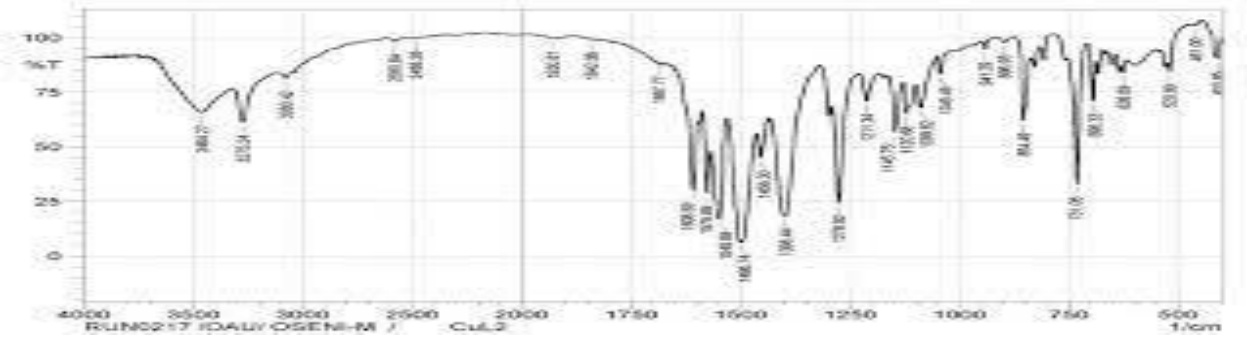
3. **IR OF A3 COMPOUNDS**



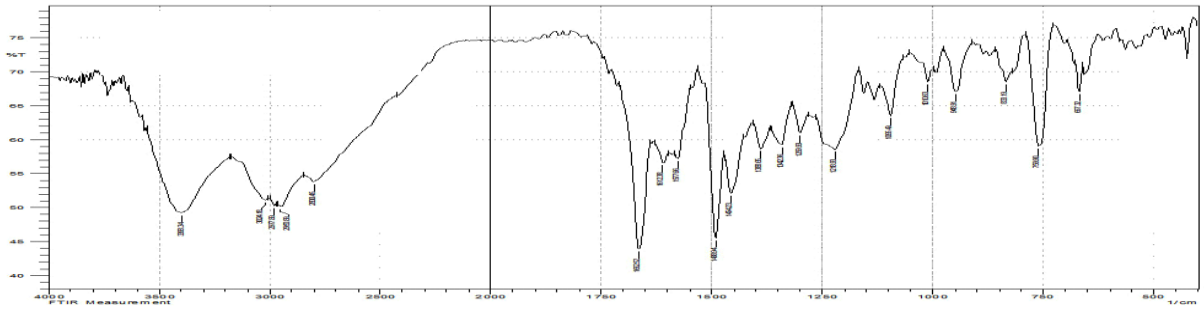
4. **IR SPECTRA OF A4 COMPOUND**



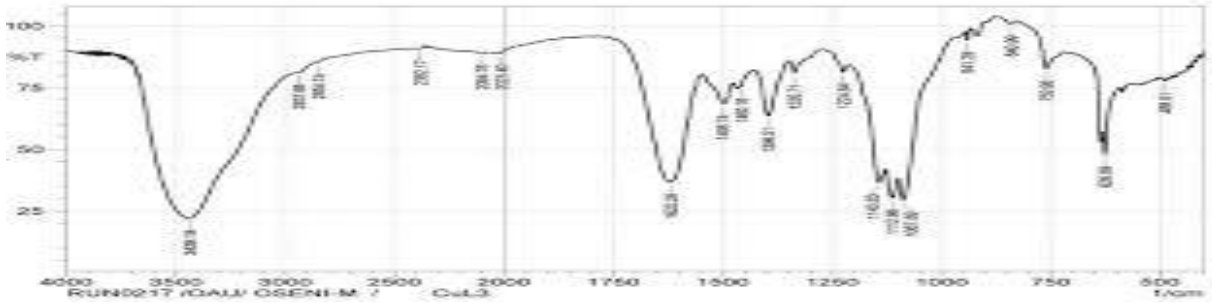
5. IR SPECTRA OF A5 COMPOUND



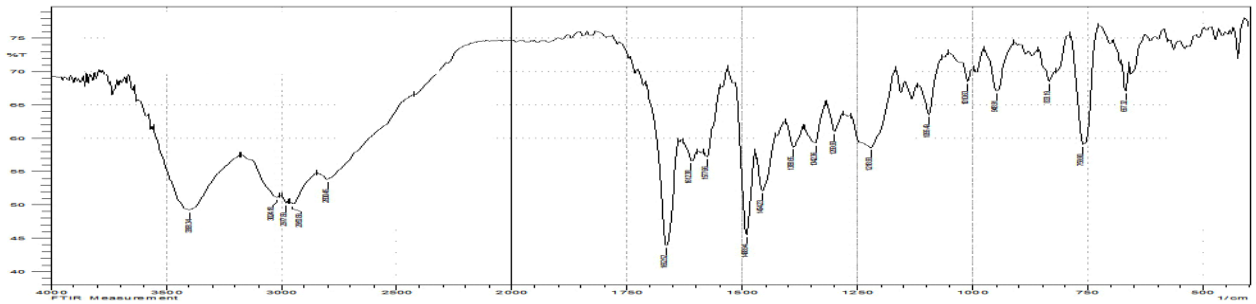
6. IR SPECTRA OF A6 COMPOUND



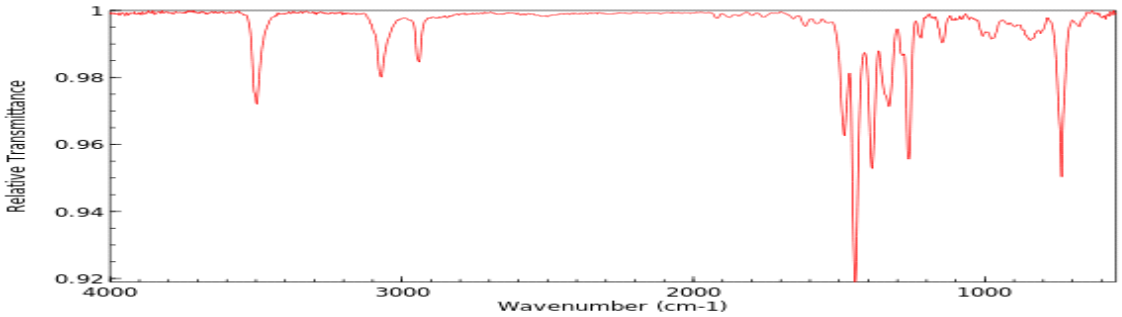
7. IR SPECTRA OF A7 COMPOUND



8. IR SPECTRA OF A8 COMPOUND:



9. IR SPECTRA OF A9 COMPOUND:



Conclusion and future Perspective

The utility of oxazole as intermediates for the blend of new engineered components in supportive science have been extended in the past several years. Oxazole is a huge heterocyclic center having many natural activities which drew the thought of researchers round the globe to coordinate different oxazole auxiliaries and screen them for their different normal activities. work covered helpful conceivable outcomes of oxazole subordinates which are critical for clinical applications during new thousand years. This study article relies upon consolidated oxazole subordinates which dis plays extensive variety of normal opportunities for instance antagonistic to bacterial, torment alleviating, relieving, energizer, anticancer, antimicrobial, antidiabetic, against heftiness, malignant growth counteraction specialist, adrenergic receptor ligand, antiprogesterone development, prostacyclin receptor miscreant, T-type calcium channel blocker and transthyretin amyloid fibril inhibitory. The heterocyclic moiety being so adaptable in nature offers the supportive researcher to explore more about it in helpful field and the data referenced in this article will be a phenomenal help to planned experts working around here for extra examination of this platform. Oxazole moiety is a huge heterocyclic com pound as they are being a basic constituent of colossal number of advanced drugs. Having such grouped scope of regular activities, oxazoles might conceivably be explored for more exceptional supportive.

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