# Synthesis of some isoxazole derivatives by ring transformation of pyrone-2

**Gopal Jee[1], Rakesh Kumar Singh[2], Anjani Kumr Shukla[3] and Kumari Sweeti[4]**

**Department of Chemistry**

.[1,2]Ph.D.(Chemistry), B. R. A. Bihar University, Muzaffarpur(Bihar),
[3]Assistant Professor, S. N. S, College, Muzaffarpur(Bihar),
[4]Ph.D.(Chemistry), B. N. Mandal University, Madhepura(Bihar)

***Abstract :*** Heterocyclic compounds containing nitrogen and Oxygen as hetero atoms are an important class of compounds largely employed in pharmaceutical and therapeutic field. The present paper deals with the synthesis of 3, 5-disubstituted isoxazoles from substituted phenyl pyrone-2 on treatment with hydroxyl amine hydrochloride on irradiation in microwave. This method of ring transformation is a deviation from the classical synthetic procedure.

**Keyword:** Heterocyclic compounds, Pharmaceutical, pyrone-2, hydroxylamine hydrochloride, irradiation, isoxazole.

## I. INTRODUCTION

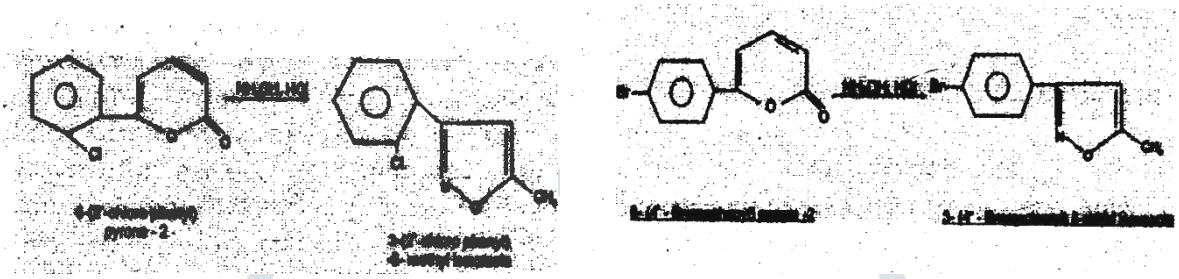
Heterocyclic compounds are woven into life processes. A variety of compounds aare naturally occurring heterocyclic Chemistry has its origin in organic synthesis, natural products chemistry and medicinal chemistry. These are present in more than 90 percent of the novel drugs. The isoxazole moiety is present in insecticidal, antibacterial, antibiotic, antitumour, antifungal, antituberculosis, anticancer and anti-ulcerogenic drugs. Many general methods of synthesis of substituted isoxazoles are known. Condensation- cyclisation of α, β- diketones with hydrdoxylamine yields isoxazoles. Ring transformation reactions include ring contraction, ring resension or ring expansion. Pyrones are taken as the starting material for the synthesis in the given research work. There are two pyrone to be known 2H-pyrone and 4H-pyrone. These compounds do not posses an aromatic sextet. Studies show that 2-pyrones bear higher order of activity. It is found that a number of nucleophilic centres in 2-yrone could alone or in combination be exploited for the generation of a variety of new heterocyclic products. These are present at C2, C4 and C6 centres. It is also found that in contrast to electrophilic substitution. Pyrones are easily attacked by nucleophilic reagents. Weak nucleophiles add at 2-position while strong ones at 6-position. The present work involves the treatment of 6-(substitutedphenyl) pyrone-2 with hydroxylamine hydrochloride under microwave irradiation for 5 minutes at 320W. the reaction proceeds via opening of the ring between N and C of carbonyl group after attack of th nucleophile on C atom followed by recyclisation to 3,5-disubstituted isoxazole derivatives. The substituent initially at position 6 in pyrone-2 is retained at position 3 of the isoxazole nucleus.

## II. EXPERIMENTAL

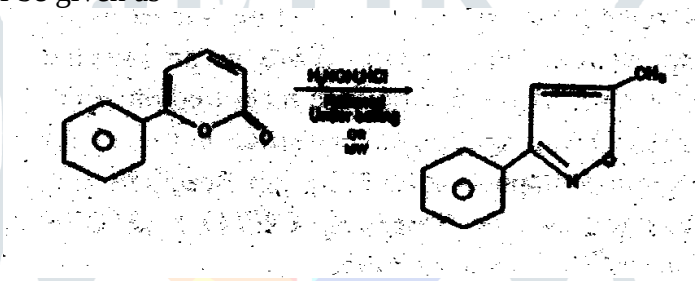
Melting points were uncorrected. Elemental analysis was carried out by elemental analyser vario EL III, I. R. Spectra (KBr) was performed by IR-Prestige 21 FTIR spectrum. The visible absorption spectra were recorded on UV-visible spectrophotometer. Perkin Elmer Lambda -25 and NMR spectra (CD $Cl_3$) on Varian A-60 spectrophotometer with TMS as an internal standard. Mass spectra were measured opn JEOL – JMS D-300 spectrometer. Silica gel used for chromatography was 60-120 CE 74 JD (800 W) unmodified domestic oven.

**General method for the synthesis of 3-(substitutedphenyl)-5-methylisoxazoles**

A mixture of 6-(o-chlorophenyl) pyrone-2 or 6-(o-bromophenyl) pyrone-2 (6g), hydroxylamine hydrochloride (1.7g) and pyridine (5ml) was taken in a conical flask and homogenous solution was prepared by shaking. It was allowed to irradiate in a microwave for 5 minutes at 320 W. after completion of the reaction pyridine was evaporated and to the residue chloroform was added, washed with water several times. It was dried and finally passed through column of silica gel and was eluted with benzene-ethylacetate and double run. The compound obtained was recrystallized from methanol and chloroform to furnish pure crystals of 3-(substitutedphenyl)-5-methylisoxazole. The 6-substitutedphenyl pyrones were earlier synthesized by Van Pechmann condensation. The following isoxazole derivatives were prepared by the above method



In general the reaction will be given as



3-(2-chlorophenyl)-5-methylisoxazole
Yellow crystals
Yield = 70%
Melting point: 122°C
Found N = 7.10%
Calculated N = 7.19%

**I.R Vmax(KBr disc):**

1660 $cm^{-1}$(for C=N stretching frequencies), 940$cm^{-1}$ (for N-O group), 3340 $cm^{-1}$ (phenyl substituted isoxazole ring), 3600 $cm^{-1}$ (for- C=N-O- grouping), 740$cm^{-1}$ (for aromatic C-Cl group), 720$cm^{-1}$ (for C-H bending for 1, 2- disubstituted benzene ring).

$^{1}$Hn. M. R. δH($CDCl_3$): (80, MHz) 1.84(1H,s), 7.27(2H, d, J8, HzArH), 7.54(2H, d, J8.1, Hz, Ar-H), 1.58(1H,s, -CH), 6.62(1H,s, 8H)

**Mass spectrum**

(m/z)+=193.5

**3-(4`-bromophenyl)-5-methylisoxazole**

Yellow crystals
Yield = 2.8g
Melting point= 182°C
Found N = 5.84%
Calculated N =5.88%

**I.R** Vmax(KBr disc) 1665 $cm^{-1}$ (for C=N-stretching frequency) 950 $cm^{-1}$ (for N-O group), 3340 $cm^{-1}$ (for aryl substituted isoxazole), 3360 $cm^{-1}$ (for C=N-O group), 750 $cm^{-1}$ (for C-H bending for 1,2- disbstituted benzene), 820 $cm^{-1}$ (for aromatic C-Br group).

**1H.N.M.R** δH($CDCl_3$), (80MHz)

1.84(1H,S). 7.26(2H, d, J8.1, Hz, Ar-H), 7.62 (2H,d, J8.1, Hz, Ar-H)

1.54(1H,s, - CH), 6.54(1H,S, 8H)

**Mass spectrum** (700ev)(m/z)- = 238,223

## III. CONCLUSION

The 3 and 5 di-dubstituted isoxazole derivatives were obtained by the transformation of corresponding substituted 2-pyrones in the presence of hydroxylamine hydrochloride which were further characterized by spectral studies. The IR rang of the synt6hesized compounds falls between 700-1670 $cm^{-1}$ which is within the range of isoxazole molecule. The values for substituted benzene ring is also in accordance with the actual range. The obtained NMR data helps in building the structure of the compound thus suggesting that values obtained are correct. Some deviations in the values may occur dxue to substitution at 3 and 5. These spectral studies help in revealing and identifying the structures of the synthesized isoxazoles derivatives.

## REFERENCES


**[1]** H.C Vander Plas and H.J. Den Hertog. *Rec. trav Chem* 81, 841(1996).

**[2]** The Chemistry of Heterocylic compounds, R. C., Elderfied (Ed.) Vol. V John Wiley and Sons new York (1956).

**[3]** K. M. Johnson and R.G. Schotter. *J.Chem. Sockl*, 1774, (1960).

**[4]** R.Justoni and R. Pesia, Gazz, Chim et.al., 85, 34, (1955).

**[5]** W.J. Wakefield, and D.J. Wright. *Adv. Hetercycl Chem.* 25, 147(1979).

**[6]** T. Shimizu, Y. Hayashi, N. Furukawa and K. Teramura *Bull., Chem. Soc. Japan* 64, 318, (1991).

**[7]** K. Sharavan Kumar, V. Chandrashekhar, V, Ravinder "N-Heterocycyclic carbon catalysed 1,3-dipolar cycloaddition reaction" *Org. Biomole* 9, 7869, (2011).

**[8]** Ajay Kumar, M. Govindraju and Vasant kumar "synthesis of isoxazole via 1,3-dipolar cycloaddition reaction and their antimicrobial activity ind. J. Het. Chem., 20, 183, 184,(2010).

**[9]** P. Jayroopa, Vasant Kumar, N. Renuka and Ajay Kumear "synthesis of new 3,5-diaryl dipolar cycloadditon reaction" *IQSR.J. APP. Chem.* 14, 20(2011).

**[10]** Ajay Kumar, K. Govindraju M. Jayarupa P. and Vasanth Kumar G., Nitrile Oxides; A key intermediate in organic synthesis. Int. *J. Chem. Bio, Sci*., 3(1), 91, (2013).

**[11]** V.S. Jamode, H.S.Chandak, P.R.Bhagat, D.H.Tambekar *Indian J. Heterocyclic Chem*. 12, 323,(2003).

**[12]** Vasant Kumar, P. Jayaroopa "synthesis of 3, 5-diarylisoxazolo-4-carbonitriles and their efficacy as antimicrobical agents" *Org. pharma chem*.., 4161, 2283(2012).