Executive Summary of UGC Minor Research Project

Topic: Green approaches towards selective oxidation of isoxazoles under phase transfer catalysis

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Conducted By

Dr. Raksha P. Dhankar

Assistant Professor

Department of Chemistry

Sardar Patel Mahavidyalaya,

Chandrapur (M.S.) 442 402

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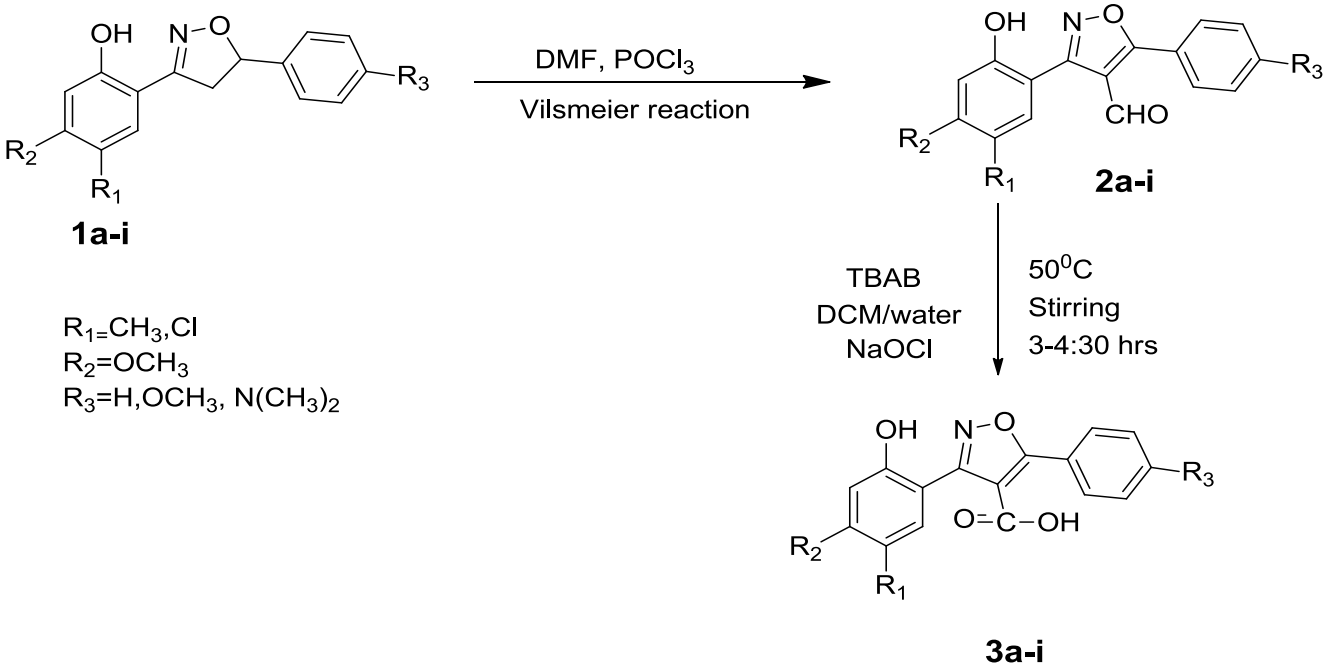
Heterocyclic compounds having oxygen and nitrogen atoms, because of their enormous biological applications are considered as a prominent class of compounds in medicinal chemistry. Use of simple and economical reagents for synthesis of various functionalized heterocyclic compound is a valuable contribution in the field of organic chemistry. Isoxazole is a five-membered heterocyclic ring structure composed of three carbon atoms, nitrogen and oxygen atom in its adjacent position.

The development of new synthetic methods that are more environmentally benign has been propelled by the growing importance of green chemistry protocols in organic synthesis. Green chemistry helps to design environmentally compatible chemical reactions, that offer the tools to approach pollution and sustainability concerns at the source. In order to be eco-friendly, or green, organic syntheses must meet, if not all, at least some of the following requirements: viz. avoiding waste generation, to be atom efficient, to avoid use and production of toxic and dangerous chemicals, to produce compounds which perform better or

equal to existing ones and are biodegradable, avoiding auxiliary substances (e.g., solvents), reducing energy requirements, to use renewable materials, using catalysts rather than stoichiometric reagents. It is very difficult for a new synthetic protocols to satisfy all principle. The use of water as a non-toxic reaction medium, together with the employment of catalysts appears to be promising.

A facile synthesis of isoxazoles derivatives with selective oxidation catalysed by phase transfer catalysts has been successfully explored by tetrabutyl ammonium bromide (TBAB) as PTC in DCM –water biphasic solvent system. Overall, mild reaction conditions, enhanced rates, improved efficiency of reaction with maximum atom economy, use of inexpensive catalysts, green solvent system and reduced reaction time are the remarkable features exhibited by this process. The process of catalysis was explored with various phase transfer catalysts as PEG 400, β cyclodextrin and TBAB through different oxidising agents such as potassium permanganate, hydrogen peroxide and sodium hypochlorite.



SCHEME I

A study of reference reaction involving 3-(2-hydroxyl-5-phenyl)-5-isoxazole-4- carbaldehyde (**2a**) and sodium hypochlorite acting as oxidizing agent, carried in DCM and water biphasic solvent system whereby they were subjected to catalytic reaction in presence of TBAB as phase transfer catalyst for synthesis of 3-(2-hydroxy-5- methylphenyl)-5-phenylisoxazole-4-carboxyllic acid(**3a)** at 50^{o}C for 3 hours stirring. Interestingly, TBAB phase transfer catalyst in CH_2Cl_2-water system proved to be exceptionally effective at enhancing the efficiency of the reaction. The reactant **2a** is soluble in organic phase at 50^{0}C in presence of TBAB and sodium hypochloride is soluble in water. The reaction was accomplished in 3hrs with 85% of yield. The reaction mixture was worked up in ice –cold water. The product was separated out and was filtered. The filtrate was evaporated to remove water leaving TBAB behind . The phase transfer catalyst (TBAB) was utilized for further synthetic cycles. The same procedure was repeated with other substituted carbaldehydes to get the substituted acid derivatives of isoxazoles (**3a-i**). The assigned structures were confirmed by IR, ^{1}HNMR, ^{13}CNMR, Mass, CHN analysis.