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Review Article

Oxazolones: A Review of Its Synthesis

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Abstract

Oxazolones or oxazolidinone or azlactones are five membered heterocyclic lactams derived from oxazole, also known as (4*H*)-oxazol 5-ones. Oxazolones have been very widely explored as important synthons for the synthesis of several biologically active molecules. Oxazolones derivatives have been used as starting materials for the synthesis of modified á-amino acids, peptides, other heterocycles, and biosensors. This review preesnts the various methods of synthesis of oxazolone derivatives.

Keywords: Oxazolone; Hippuric Acid; Benzoylglycine.

Introduction

Oxazolones represent an important class of heterocyclic compounds with the molecular formula $C_3H_3NO_2$. It was named in-line with the Hantzsch–Widman nomenclature and is part of a large family of oxazole based compounds. There are a total of 5 structural isomers of oxazolone, three according to the location of the carbonyl group and two according to the location of the double bond C=X (with X= N or C) i.e. 2-(3*H*)-oxazolone, 2-(5*H*)-oxazolone, 4-(5*H*)-oxazolone, 5-(2*H*)-oxazolone, 5-(4*H*)-oxazolone [1].

Oxazolones has a special place in the synthesis of several organic molecules including amino acids [2], thiamine [3], amides [4], peptides [5] and polyfunctional compounds [6]. Oxazolone (Natural or synthetic) including benzoxazolone derivatives possess important biological activities; such as antimicrobial [7,8], anti-inflammatory [9], anticancer [10], antiangiogenic [11], pesticidal [12], cardiotonic [13], immunomodulator [14], and antioxidant [15] activity.

The synthetic ways for the preparation of oxazolone ring can be classified into several groups: cyclization reaction of benzoylglycine/acetylglycine with aromatic aldehydes in presence of acetic anhydride and different catalysts, cyclization reaction of benzoylglycine/acetylglycine with aromatic aldehydes in presence of different catalyst without acetic anhydride, synthesis from carbamates, reaction of benzoylglycine /acetylglycine with reagents other than aromatic aldehydes.

Cyclization Reaction of Benzoylglycine/ Acetylglycine with Aromatic Aldehydes in Presence of Acetic Anhydride and Different Catalysts.

Large number of catalyst have been used to accelerate the reaction ranging from sodium acetate through microwave irradiations to functionalized sphere SiO_2 nanoparticles.

Calcium acetate [16 (a,b)], bismuth (III) acetate [17], lead acetate [18], potassium phosphate [19] and ytterbium (III) triflate [20] have been used in place of sodium acetate for synthesis of substituted oxazolone derivatives.

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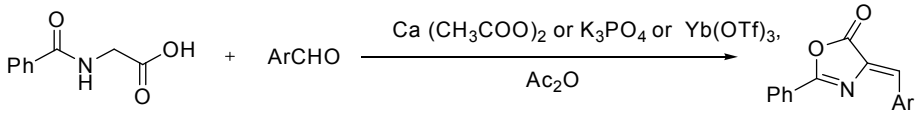
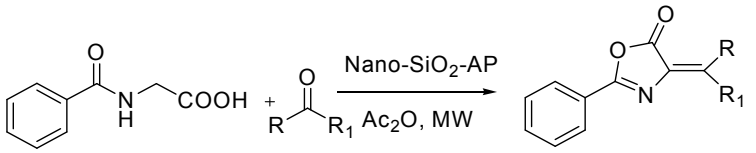
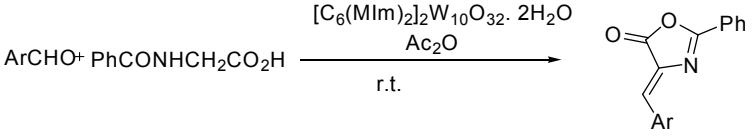


Akbar Mobinikhaledi *et. al.* have demonstrated effective use of microwave in presence of 2-aminopyridine-functionalized nano-sphere SiO_2 (nano-sphere SiO_2–AP) to synthesize oxazolone in good yield [21].

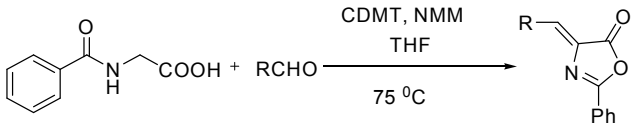


Use of $[C_6(MIm)_2]_2W_{10}O_{32}.2H_2O$ in ultrasonic conditions at room temperature has been explored by Mahboubeh Rostami *et. al.* [22] whereas Tikdari A. M. *et. al* has used three different catalyst (dodecatungstophosphoric acid ($H_3PW_{12}O_{40}$), samarium and ruthenium (^{222}) Chloride) to obtain substituted azalactones from hippuric acid and appropriate aldehydes or ketones under microwave irradiations [23].

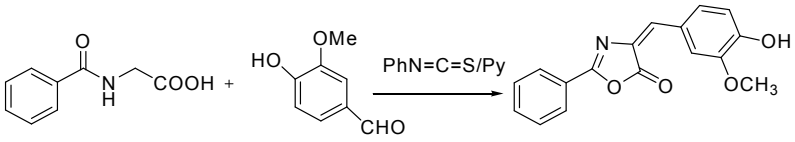


Cyclization Reaction of Benzoylglycine / Acetylglycine with Aromatic Aldehydes in Presence of Different Catalyst without Acetic Anhydride.

2-Chloro-4,6-dimethoxy-1,3,5-triazine (CDMT) and N-Methylmorpholine (NMM) in tetrahydrofuran (THF) [24] has been utilized in place of sodium acetate and Acetic anhydride (Ac_2O) at room temperature (yield 65%) to obtain oxazolones from hippuric acid with aromatic aldehyde.

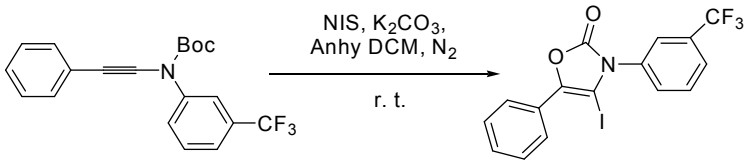


Isothiocyanate has also been utilized for cyclization of acetylglycine and aldehyde into oxazolones [25].

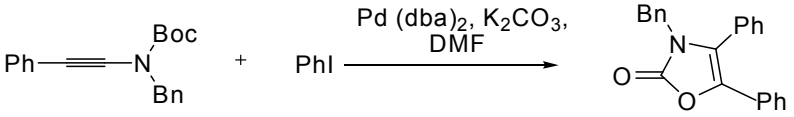


Synthesis from Carbamates

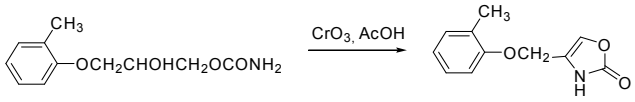
Oxazolones have been obtained from different carbamates using different catalyst in presence of base. *tert*-Butyl-*N*-phenyl-*N*-(phenylethynyl) carbamate and *tert*-butyl-2-phenylethynyl-(3-(trifluoromethyl) phenyl) carbamate has been used to obtain oxazolones by using palladium and *N*-iodosuccinimide respectively [26(a,b)].



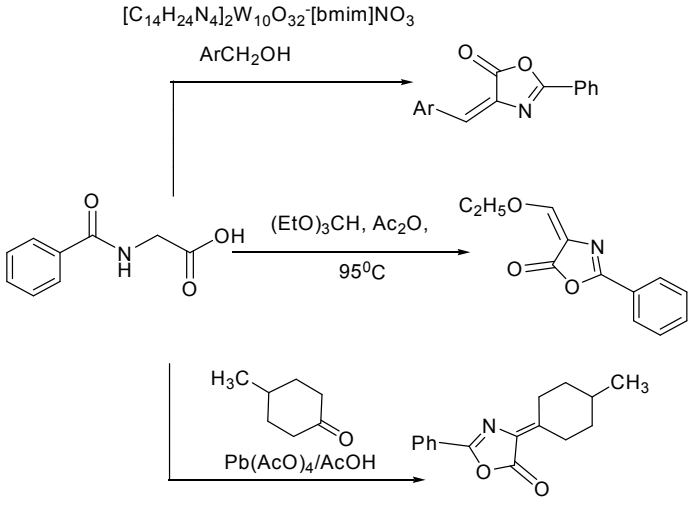
Zenghui Lu *et. al.* synthesized substituted oxazolones from *N*-alkynyl-*tert*-butyloxycarbamate with iodobenzene in presence of different Pd catalysts [$Pd(dba)_2$, $Pd(OAc)_2$, $Pd(PPh_3)_4$] along with different bases (Cs_2CO_3, Et_3N, *t*-BuOK, Na_2CO_3, K_2CO_3) and different ligands [(PPh_3), dppb, Xphos) in different solvents (DMF, DMSO, CH_3CN, dioxane, toluene). The combination of $Pd(dba)_2$, K_2CO_3, PPh_3 in DMF has been found to work best [27].



Mephenesin carbamate (2-hydroxy-3-(*o*-tolyloxy) propyl carbamate) a muscle relaxant has been converted to oxazolone by using CrO_3 and acetic acid [28].

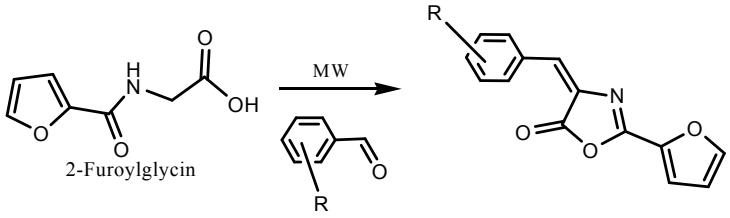


Reaction of benzoylglycine /acetylglycine with reagents other than aromatic aldehydes Oxazolones have been synthesized by replacing aromatic aldehyde with other reagents like triethyl-orthoformate with acetic anhydride [29] or aryl alcohol [30] or cyclic ketone [31] with immobilized $[(C_{14}H_{24}N_4)_2W_{10}O_{32}]$ on 1-*n*-butyl-3-methylimidazolium nitrate.



Microwave Assisted Synthesis [32]

Mariappan G et. al. has reported us of microwave to synthesize novel 4-(substituted benzyldiene)-2-furfurylidine oxazol-5-one and reported their antidiabetic activity.



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