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Synthesis of different α, β- unsaturated oxazolone derivatives

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ABSTRACT

Acetyl glycine were prepared from glycine acetic anhydride and then 2, 4-disubstituted Oxazol-5-one were prepared from acetyl glycine, substituted aldehydes, acetic anhydride, and sodium acetate as a catalyst. The formed product is evaluated and characterized by thin layer chromatography, infrared spectroscopy and melting point. The, β- unsaturated shows ability to react with various nucleophilic reagents for synthesis of new fused oxazole compounds.

Keywords: glycine, acetic anhydride, aldehyde Sodium acetate, Oxazolone, E. coli, Antibacterial Activity.

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INTRODUCTION

Oxazolone is a five member heterocyclic ring containing oxygen nitrogen in it. These five member heterocyclic ring act as pharmacophore for synthesis various biologically active chemical agents. Oxazolones are used as important precursor for the synthesis of various chemical compounds such as amino alcohols, amides[1], amino acid[2, 3], dyes[3, 4], heterocyclic precursors and various biologically active compounds.

Substituted Oxazole derivatives are found to be associated with various biological activities such as antibacterial[5], antifungal[6], antitubercular, and anti-inflammatory[7]. Oxazole's are well known as important structural units in a wide variety of biologically active natural products as well as useful synthetic intermediates[8-10]. The oxazolone ring occurs naturally and the total synthesis of natural products with a wide variety of biological activities containing oxazole moiety is an area of intense research. Other applications of oxazole derivatives include the use as pesticides, fluorescent whitening agents, lubricants, dyes and pigments[11-19]. Therefore, there is considerable interest of having available efficient routes to these heterocycles and better understand their reactivity. The ability of α, β-unsaturated ketones to react with various nucleophilic reagents prompted us to synthesis some new fused oxazole compounds.

METHOD & MATERIAL

Melting points of all synthesized compounds were determined in open capillary tubes on an electro thermal apparatus (Veego Model VMP DS) and are uncorrected.

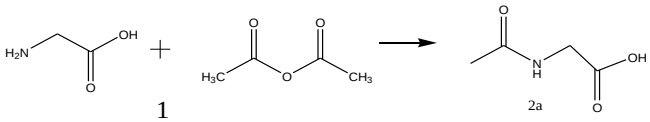
The purity of the compounds was monitored by thin layer chromatography on silica gel coated aluminum plate.

The infrared spectrometer used for the characterization of various oxazolone compounds was Perkin Elmer Spectrum 65. The KBr pellet technique is used for the characterization of oxazoles.

EXPERIMENTAL

Synthesis of Acetyl glycine

General Reaction: Acetyl glycine is prepared from glycine and acetic anhydride in presence of water.



1 2a

Procedure

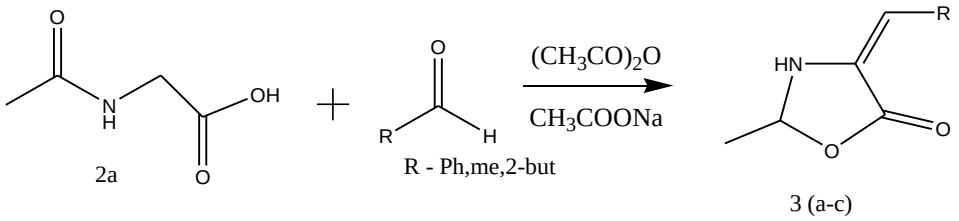
Place glycine and water together in a conical flask. Stir the content of conical flask vigorously until all the solid has completely dissolved. To the resulting solution add acetic anhydride in one portion and stir the solution vigorously for 15 to 20 minutes. After stirring the solution became hot and

some acetyl glycine may crystallize. Cool the solution in refrigerator for around overnight. Next morning collect the sample and filter it with the help of Buchner funnel. Collect the precipitate and wash with cold water and dry at 100c. The melting points of the formed product were found to be 207-208c. combine the filtrate and washings and evaporate it to dryness under reduced pressure on water bath at 50-60°c and with the help of boiling water recrystallize the residue. Collect the solid which separates, wash, and dry it as before. The second fraction of acetyl glycine.

(B) Synthesis of 2,4 disubstituted, 1-3 Oxazole 5-one

General Reaction

Acetyl glycine and different aldehydes with acetic unhydride in presence of sodium acetate treated with each other to get 2,4 disubstituted,1-3 oxazole 5-one.



Procedure

Take 1 gm of Acetyl glycine, 1.36 gms of various aldehydes, 0.51gm of anhydrous sodium acetate and 2.18gm of acetic unhydride in flak. Warm the content of flask with occasional stirring until solution is complete. Heat the solution for about1 hour, after completion of heating cool it and leave the content of flask overnight in a refrigerator. Next morning stir the solid mass of yellow crystals with cold water. Recrystallise it from carbon tetrachloride. Dry the product and take the resulting yield.

Biological Activity

Oxazolone is the five membered heterocyclic ring containing O and Nitrogen as heteroatom. Oxazolones having various pharmacological activities such as anticancer, ant diabetic, antifungal, antibacterial, Analgesic, Anti-inflammatory etc. But here we are mainly focusing on the Antibacterial activity of the synthesized compound[20-23].

Microbial study:

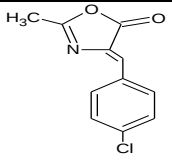
Modified agar well diffusion method was used to determine antimicrobial activity of the synthesized oxazolone derivatives. For evaluating antimicrobial activity we use culture of E.coli as Gram negative microorganism respectively[20,22]. Here first we prepared nutrient agar plates these nutrient agar plates were seeded with 0.2 ml of 24 h broth culture of E.coli. The plates were set for solidification after solidification of agar, wells were cut at equal distance in each plate by using a sterile 8mm borer. The dilutions of the synthesized compounds were prepared like 100µg/ml, 250µg/ml, 500µg/ml, and 750µg/ml. The wells of the plates were filled with near about 0.5ml of the dilution. After that plates were incubated for about 24hours at 37°C. After 24 hours the antibacterial activity was evaluated by measuring zone of inhibition in cm[24,25]. After evaluation it has been found that compound 3e shows highest antibacterial activity 3c show least Activity[26,27].

Table 1: Evaluation of biological Activity

Sr.no	Name of Compound	Zone of Inhibition in mm			
		100µg/ml	250µg/ml	500µg/ml	750µg/ml
3a	4-(4-Chlorobenzylidene)-2-methyl-1,3-oxazol-5-one	10	12	14	16
3b	4-(4-flurobenzylidene)-2-methyl-1,3-oxazol-5-one	11	13	15	17
3c	4-(4-hydroxy-3-methoxybenzylidene)-2-methyl-1,3-oxazol-5-one	7	09	11	13
3d	4-(4-ethylidene)-2-methyl-1,3-oxazol-5-one	8	10	12	14
3e	(4)-4-benzylidene-2-methyl-1,3-oxazol-5-one	12	15	17	18
3f	4-(4-methoxybenzylidene)-2-methyl-1,3-oxazol-5-one	10	12	14	15

RESULTS AND DISCUSSION

Table 2: Name, Structure, Physical Characteristic and Yield of the synthesized compound.

Sr.No	Name of Product	Starting Material	% yeild	Colour
3a	 (4*Z*)-4-(4-chlorobenzylidene)-2-methyl-1,3-oxazol-5(4*H*)-one	4-Chlorobenzaldehyde	73.52%	Yellow

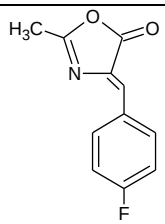
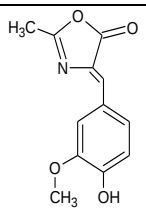
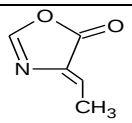
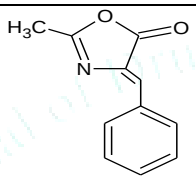
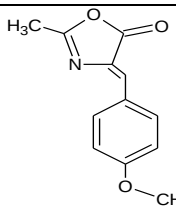
3b	 (4*Z*)-4-(4-fluorobenzylidene)-2-methyl-1,3-oxazol-5(4*H*)-one	4-Flurobenzaldehyde	85.14%	White
3c	 (4*Z*)-4-(4-hydroxy-3-methoxybenzylidene)-2-methyl-1,3-oxazol-5(4*H*)-one	vanillin	80.58%	yellow
3d	 (4*Z*)-4-ethylidene-1,3-oxazol-5(4*H*)-one	Acetaldehyde	87.1%	white
3e	 (4*Z*)-4-benzylidene-2-methyl-1,3-oxazol-5(4*H*)-one	Benzaldehyde	75.75%	white
3f	 (4*Z*)-4-(4-methoxybenzylidene)-2-methyl-1,3-oxazol-5(4*H*)-on	4-Methoxy Benzaldehyde	77.22%	white

Table 3: Characterization of the synthesised compound

Sr. no	Name of Compound	Melting Point	IR frequencies (cm^{-1})
3a	4-(4-Chlorobenzylidene)-2-methyl-1,3-oxazol-5-one	205˚c	C=O -1719.36 NH-3351.91 C-F-852.76 C-N 1136.19
3b	4-(4-flurobenzylidene)-2-methyl-1,3-oxazol-5-one	201˚c	C=O -1720.11 NH-3348.86 C-Cl-745 C-N 1136.40
3c	4-(4-hydroxy-3-methoxybenzylidene)-2-methyl-1,3-oxazol-5-one	199˚c	C=O -1720.12 NH-3351.99 C-N 1136.21
3d	4-(4-ethylidene)-2-methyl-1,3-oxazol-5-one	207˚c	C=O -1722.93 NH-3351.76 C-N 1137.00
3e	(4)-4-benzylidene-2-methyl-1,3-oxazol-5-one	210.7˚c	C=O -1766.89 NH-3352.27 C-N 1121.09
3f	4-(4-methoxybenzylidene)-2-methyl-1,3-oxazol-5-one	207.7˚c	C=O -1720.46 NH-3351.59 C-N 1136.25

During the course of our studies we found that glycine reacted efficiently with acetic anhydride, to provide acetyl glycine regioselectively in 90.14% yield (2a). In order to compare the present method with the one the reaction of **3a-f** with **2a** was carried out in acetic anhydride under refluxing condition with different aldehyde in presence of sodium acetate for 2h when **3a** was isolated in 85.14% yield. **3b** was isolated in 73.52% yield **3c** was isolated in 80.58% yield **3d** was isolated in 87.1% **3e** was isolated in 75.75% **3f** was isolated in 77.22 % yield.

CONCLUSION

The presented research work is an important development in the synthesis of biologically active oxygen containing heterocycles i.e. oxazolones. This method has various advantages such as easy work up, high yield and short reaction time. All the compound were evaluated for antimicrobial activity & it has been found that (4)-4-benzylidene-2-methyl-1, 3-oxazol-5-one shows highest antimicrobial activity.

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