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Design and Synthesis of substituted oxazolones and their anti-bacterial activity.

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Abstract: A great deal of work has been done on the synthesis of oxazolones. We have obtained 5(4*H*)-oxazolones by condensing anthracene-10-carbaldehyde & furan-2-carbaldehyde with a number of substituted benzoyl glycines, and tried to design new and effective anti-bacterial agents.

Keywords: Substituted oxazolones, substituted benzoyl glycines, substituted aromatic aldehydes, anti-bacterial activity.

Introduction: During the past few decades many results have been published in the area of the synthesis and the study of physical and chemical properties of heterocyclic compounds containing a furan & anthracene rings connected with different heterocyclic systems. The most common method for their preparation is the Erlenmeyer-Polchi reaction, a cyclodehydration-condensation of the appropriate aldehyde and hippuric acid in dry acetic anhydride catalyzed by acetate anion (using sodium or calcium acetate as a support/catalyst) [1-4].

Carter [5], Cornforth [6] and Baltzii [7] have adequately reviewed the chemistry and applications of 5(4) oxazolones. Their role in the development of Penicillin chemistry has also been described in the literature [8].The great biodiversity of oxazolone is reported in

medicinal field. Tandel et al [9] and Moxley et.al.[10] have reported anti-bacterial, anti-fungal, anti-inflammatoryactivity. They also possess properties like analgesic[11], anti-cancer[12-13], anti-diabetic, antiobesity[14-15]. Tikdari et al [16] synthesized some new 4-arylidene-5(4*H*)-oxazolone azo dyes and evaluated them for solvatochromic behaviour. We aimed to design novel derivatives containing furan and anthracene moiety directly connected with heterocyclic ring. These reports of interesting biological activities associated with oxazolones prompted us to synthesize a new series and to screen these new compounds for anti-bacterial activity.

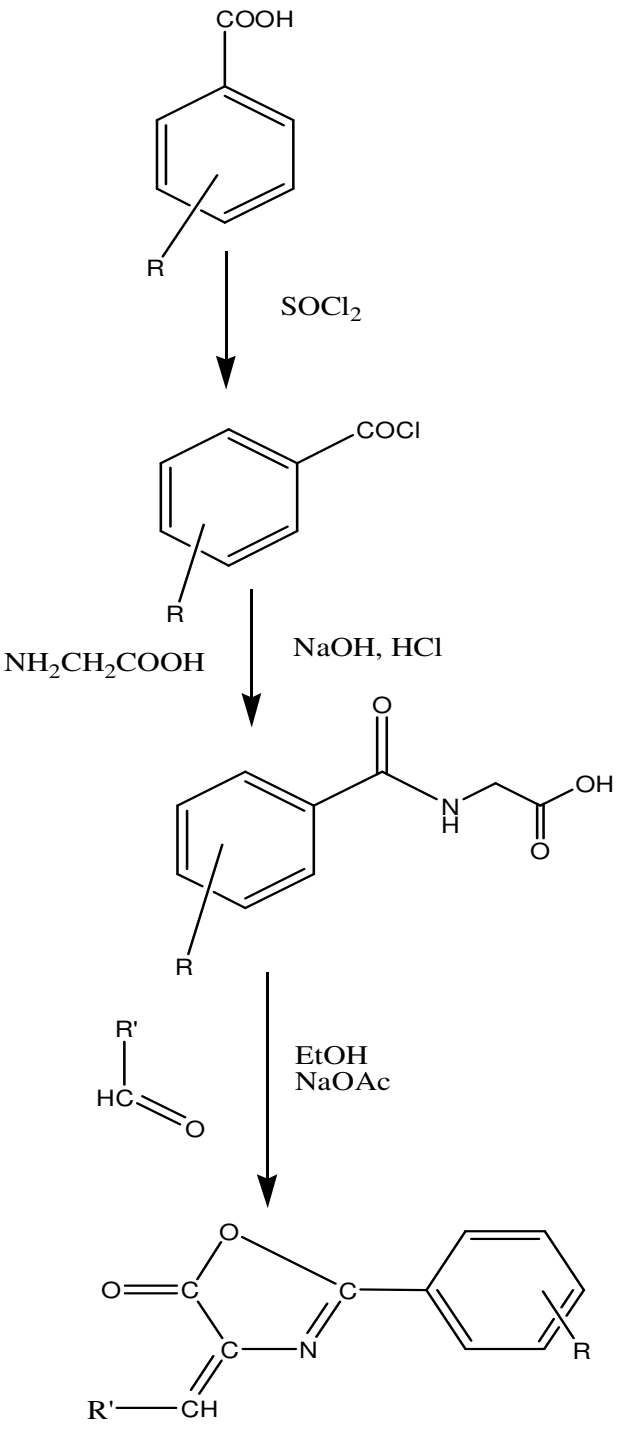
Results & Discussion: All condensation products are stable solids, which are rather sparingly soluble in common solvents and with high melting points. They displayed characteristic color. The characteristic bands found in the IR spectra correspond to the carbon-carbon double bond (1646-1642cm^{-1}) and C=O lactone (1793-1789cm^{-1}).
The ^{1}H-NMR spectra of the synthesized compounds I & II displayed signals of the aldehydic proton which gets resonate in the 7.35 & 7.59 ppm range corresponding to CH protons.

Antibacterial activity: All compounds were screened for their in vitro anti-bacterial activity against *E. coli* and *Xanthomonas citri* by cup-plate method [17]. The concentration of test compounds is 1,000µg/ml. After 48 hr incubation at 37 ^{o}C, zone of inhibition produced by each compound is measured in mm as shown in Table 1. Streptomycin is used as the reference drug and Dimethyl formamide as a control. Compounds were found to possess moderate activity against both bacteria. Further investigation is in progress.

Table- 1 Antibacterial activity of the compounds I-VII

S. No	Compound No.	*E. coli*	*Xanthomonas citri*
1	I	++	+
2	II	+	R
3	III	R	R
4	IV	+	+
5	V	+	R
6	VI	++	+
7	VII	+	+
8.	Streptomycin	+ + +	+ + +

Key to symbols: Resistance = R; slightly active = + (inhibition zone 6-9mm); moderately active = + + (inhibition zone 9-12 mm); highly active = + + + (inhibition zone> 12 mm).



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Scheme-1

Where R= 2-Cl-4-NO_2, H, 2-Cl, 2- NO_2, 3,5-Di NO_2, 2-OCH_3 and 4- OCH_3

R'= furfuralaldehyde and anthranaldehyde

Experimental: The melting points were taken in open capillary and are uncorrected .the purity of the compounds was checked by TLC. IR spectra were recorded using KBr pellets. ^{1}H NMR spectra using TMS as an internal standard.

General procedure: A mixture of aldehydes (0.002mol) fused sodium acetate (0.16g, 0.002mol) substituted benzoyl glycines (0.002mol) and acetic anhydride (0.6ml, 0.006mol) was heated on a water bath for 2 hours. The contents were cooled and treated with water (10ml), filtered and washed with water. Product was purified by recrystalisation from absolute ethanol and ethyl acetate.

2-(2-chloro-4-nitrophenyl)-4-(cyclopenta-1, 3-dienylmethylene)oxazol-one ***(I)*** *:* Dark magenta crystal; Yield: 86.73%; m.p: 234°C; IR(KBr) (cm^{-1}): 3105 Furan ring (C-H, stret.), 3015 Aromatic (-C-H, stret.), 1793 (C=O, stret.), 1642 (-C=N, stret, oxazolone ring.), 1523 (ArC-NO_2, stret.) 1143 Oxazolone ring (-C-O-C-, stret.), 1070 (ArC-Cl, stret.), 984 (HC=C<, (C-H), stret., Def. out of plane); ^{1}H-NMR (300 MHz, DMSO-d_6): 7.24-7.25 ($CDCl_3$), 6.72-7.74 (m, 3H, furan ring), 7.75-8.44(m, 3H, Ar-H), 7.35 (s, 1H, CH methylene proton).; Anal. Calc. for $C_{14}H_7N_2O_5Cl$: C 52.74, H 2.19, N 8.79; Found: C 52.75, H 2.16, N 8.84.

4-(anthracen-9-ylmethlene)-2-(2-chlorophenyl) oxazol-5(4H)-one ***(II)*** *:* Dark orange, Yield: 88.43%; m.p:222^{o}C; IR(KBr) (cm^{-1}): 3042 Aromatic (-C-H, stret.), 1789 (C=O, stret.), 1646 (C=C & C=N, Stret), 1254 Oxazolone ring (-C-O-C-, Stret.), 1046 (ArC-Cl), 980 (CH=C<, (C-H), stret.); ^{1}H-NMR (300 MHz, DMSO-d_6): 7.26 ($CDCl_3$), 6.90-8.24 (m, 13H, Ar-H), 7.59 (s, 1H, CH methylene proton); Anal. Calc. for $C_{24}H_{14}NO_2Cl$: N 3.65; Found: N 3.66.

4-(anthracen-9-ylmethlene)-2-(4-nitrophenyl) oxazol-5(4H)-one ***(III)*** *:* Orange; Yield: 22.78% , m.p: 98^{o}C; Anal. Calc. for $C_{24}H_{14}N_2O_4Cl$: N 7.10; Found: N 7.14.

4-(anthracen-9-ylmethlene)-2-(3, 4-dinitrophenyl) oxazol-5(4H)-one ***(IV)*** *:* Dark brown; Yield: 77.05%, m.p: 244^{o}C Anal. Calc. for $C_{24}H_{13}N_3O_6$: C 66.60, H 3.18, N 9.56; Found: C 65.69, H 3.19, N 9.55.

4-(anthracen-9-ylmethlene)-2-(2-methoxyphenyl) oxazol-5(4H)-one ***(V):*** Yellow; Yield: 85.22%, m.p: 90^{o}C; Anal. Calc. for $C_{25}H_{17}NO_3$: N 3.69; Found: N 3.64.

4-(anthracen-9-ylmethlene)-2-(4-methoxyphenyl) oxazol-5(4H)-one ***(VI):*** Orangish Yellow; Yield:23.86%; m.p: 263^{o}C; Anal. Calc. for $C_{25}H_{17}NO_3$: N 3.69; Found: N 3.70.

4-(anthracen-9-ylmethlene)-2-(phenyl) oxazol-5(4H)-one ***(VII):*** Yellow: Yield:38.57%; m.p:228^{o}C; Anal. Calc. for $C_{24}H_{15}NO_2$: C 82.52, H 4.29, N 4.01; Found: C 82.57, H 4.32, N 4.09.

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