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SYNTHESIS AND CHARACTERIZATION OF SOME UNIQUE OXAZOLONE ANALOGS

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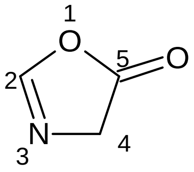
ABSTRACT

A series of oxazolone derivatives (3a-i) have been prepared by the condensation of {[(2*E*)-3-phenylprop-2-enoyl]amino}acetic acid with different aldehydes in presence of ethanol, acetic anhydride and sodium acetate. The structures of the newly synthesized compounds were confirmed by FT-IR, 1H-NMR and MASS spectral data.

KEYWORDS: Oxazolone, Erlenmeyer Reaction, Cinnamic Acid, Glycine.

1. INTRODUCTION

Heterocyclic compounds are acquiring more importance in recent years due to the pharmacological activities. Nitrogen, sulphur, oxygen containing five/six member heterocyclic compounds has occupied enormous significance in the field of medicinal chemistry. Oxazolones have five membered heterocyclic compound containing oxygen and nitrogen as hetero atoms (Fig .1). The C-4 and C-2 position are characterized for their different biological activities.[1]

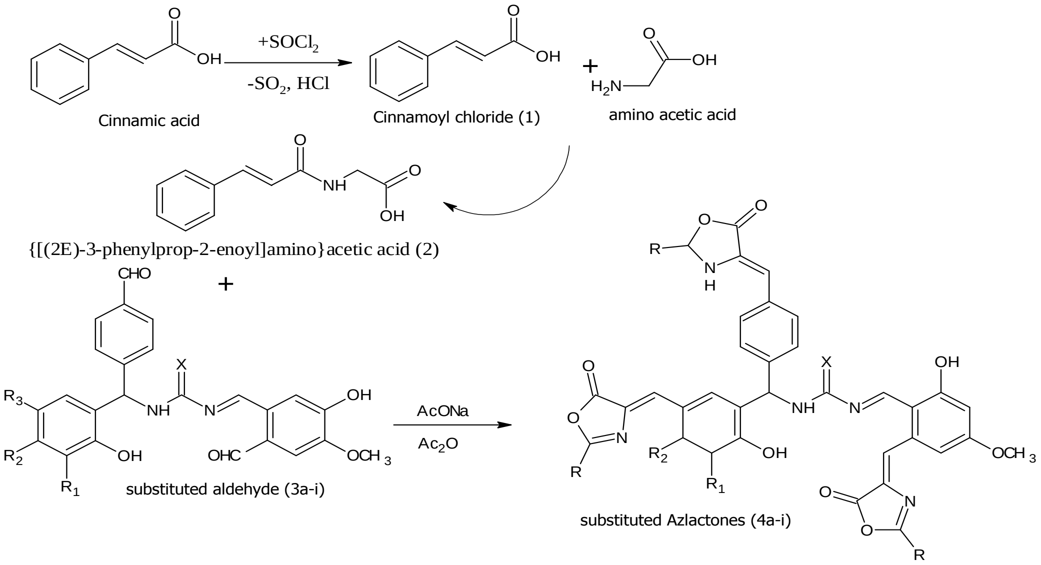


(Fig .1)

Various derivatives of Oxazolones show pharmacological activity, for example: anticancer[2] anti-diabetic,[3] antifungal,[4] anti-inflammatory[5] and immunomodulatory activity.[6] In view of this, it was of considerable interest to synthesize the title compound with a hope to obtain potent biologically active compound.

2. EXPERIMENTAL

The synthetic routes are outlined in scheme, the titled compounds 1- {1- [X-substituted-X'-hydroxy-X"- ({5- oxo- 2- [(*E*)- 2- phenylethenyl] -1, 3- oxazol-4(5*H*)-ylidene}methyl) phenyl/napthyl] – 4 - [(Z) -{5-oxo-2 [(E)-2-phenylethenyl] -1, 3- oxazol- 4 (5H) -ylidene} methylphenyl] methyl)-3 ((E){ (4-hydroxy-5-methoxy-2- {5- oxo- 2- [(E)-2-phenylethenyl] -1, 3- oxazol-4 (5H)-ylidene} methylphenyl) methylidene] thiourea /urea (4a-n) were synthesised by reacting {[(2*E*)-3-phenylprop- 2- enoyl] amino} acetic acid with aldehyde in presence of ethanol, acetic anhydride and sodium acetate. The melting points were taken in open capillary and are uncorrected. IR spectra were recorded on Shimadzu FTIR 8201 PC (4000-400 cm-1) and Perkin Elmer Spectrum RXI (4000-450 cm-1). 1H-NMR and 13C-NMR spectra were recorded on Bruker's ADVANCE –III 500 MHz FTNMR using CDCl3 and DMSO as an internal solvents respectively and TMS as an internal standard and mass spectra has been evaluated in GCMS system from Agilent.



R : $C_6H_5CH=CH$-

R_1: H, Cl, CH_3, CHO

R_2: H, OH, CH_3, CHO

R_3: H, Cl, NH_2, CHO

X: O, S

Scheme.

Table 1: Characterstic Data of Azlactone Derivatives.

Compound code	Molecular formula	Molar mass	M.P (degree Celcius)	Color	Element. Anal. Calculation (%)
4a	$C_{58}H_{42}N_6O_9S$	999.05	110	Pink	C: 69.73 H:4.24 N:8.41 O: 14.41 S:3.21
4b	$C_{58}H_{40}ClN_5O_9S$	1018.49	123	Pink	C:68.40 H: 3.96 Cl: 3.48 N: 6.88 O:14.14 S: 3.15
4c	$C_{59}H_{43}N_5O_9S$	998.06	118	pink	C: 71.00 H: 4.34 N:7.01 O: 14.43 S: 3.21
4d	$C_{58}H_{41}N_5O_{10}S$	1000.04	125	pink	C: 69.66 H:4.13 N:7.00 O: 16.00 S:3.21
4e	$C_{86}H_{59}N_7O_{13}S$	1430.49	113	pink	C:72.21 H:4.16 N:6.85 O:14.54 S:2.24
4f	$C_{58}H_{40}ClN_5O_{10}$	1002.42	117	pink	C:69.49 H: 4.02 N: 6.99 O:15.96

4g	$C_{59}H_{43}N_5O_{10}$	982	121	pink	C:72.16 H: 4.41 N: 7.13 O:16.29
4h	$C_{58}H_{41}N_5O_{11}$	983.97	112	pink	C: 70.80 H: 4.20 N: 7.12 O: 17.89

Spectroscopic data of Azlactone Derivatives.

	IR SPECTRA	^{1}HNMR ($CDCl_3$) δ (ppm)	13CNMR (DMSO) δ (ppm)	MASS FRAGMENTATION
4a	O-H stretching (3872.14 cm^{-1}), N-H stretching 2^0 (3740.14 cm^{-1}), C=O stretching for oxazolone ring (1759.68 cm^{-1}), C=N stretching for imine (11631.36 cm^{-1}), C=N stretching for oxazolone ring (1693.57 cm^{-1}), C-O-C stretch (1314.11 cm^{-1}), 3 bands for C=S (1502.14 cm^{-1}, 1452.28 cm^{-1}, 862.53 cm^{-1}), methoxy C-H stretch (2834.73 cm^{-1})	3.55 (s, 3H, OCH_3), 9.34 (s, 1H, C-OH), 6.61 (d, 2H, CH=CH, cinnamoyl), 6.43 (s, 1H, CH=C, methylidene of oxazolone ring), 7.54 (d, 1H, NH), 8.47 (s, 1H, N=CH, imine), 1.58 (d, 1H, CH), 6.84, 6.75 (m, 2H, C_6H_2), 7.64, 7.56, 7.51, 7.50 (m, 5H, C_6H_4).	37.12 (2C, CH-NH-CH), 59.58 (1C, OCH_3) 131.32, 132.27, 129.42, 129.88, 128.11, 128.90 (6C, C_6H_4), 159.23 (1C, HC=N of imine), 162.12 (1C, C=N of oxazolone ring), 185.55 (1C, C-O, oxazolone), 195.33 (3C, C=O, lactone).	989.3 [M +H], 801.2 [M - $C_6H_5CH=CH$ $C_4H_3NO_2$], 742.3 [M – C_5H_4], 698.1 [M - C_3H_3], 684.3 [M – OH], 588.5 [M – $C_4H_2NO_4$], 572.6 [M – NH_2], 498.3 [M – C_6H_5], 396.2 [M - $C_6H_5CH=CH$], 300.7 [M - $C_4H_3NO_2$], 223.8 [M – C_6H_5], 164.1 [M – CHNHS]
4d	O-H stretching (3814.43 cm^{-1}), N-H stretching 2^0 (3742.65 cm^{-1}), C=O stretching for oxazolone ring (1762.12 cm^{-1}), C=N stretching for imine (1629.04 cm^{-1}), C=N stretching for oxazolone ring (1692.28 cm^{-1}), C-O-C stretch (1317.15 cm^{-1}), 3 bands for C=S (1501.32 cm^{-1}, 1458.38 cm^{-1}, 866.51 cm^{-1}), methoxy C-H stretch (2856.84 cm^{-1}).	3.57 (s, 3H, OCH_3), 9.38 (s, 1H, C-OH), 6.69 (d, 2H, CH=CH, cinnamoyl), 6.52 (s, 1H, CH=C, methylidene of oxazolone), 7.56 (d, 1H, NH), 8.49 (s, 1H, N=CH, imine), 1.60 (d, 1H, CH), 6.92, 6.82 (m, 2H, C_6H_2), 7.68, 7.59, 7.55, 7.52 (m, 5H, C_6H_4).	37.65 (2C, CH-NH-CH), 59.98 (1C, OCH_3) 131.43, 132.45, 129.11, 129.24, 128.09, 128.76 (6C, C_6H_4), 159.34 (1C, HC=N of imine), 162.65 (1C, C=N of oxazolone ring), 185.21 (1C, C-O of oxazolone ring), 195.33 (3C, C=O, lactone).	984.76 [M +H], 802.12 [M - $C_6H_5CH=CH$ $C_4H_3NO_2$], 743.23 [M - C_6H_5], 700.7 [M - C_3H_3], 683.5 [M – OH], 587.5 [M – $C_4H_2NO_4$], 563.4 [M – COH], 501.3 [M – C_5H_5], 395.4 [M - $C_6H_5CH=CH$], 301.2 [M - $C_4H_3NO_2$], 241.2 [M – C_5H_5], 163.2 [M – CHNHS].
4h	O-H stretching (3812.42 cm^{-1}), N-H stretching 2^0 (3746.43 cm^{-1}), C=O stretching for oxazolone ring (1761.33 cm^{-1}), C-N stretching 2^0 (1114.21 cm^{-1}), C=N stretching for imine (1626.87 cm^{-1}), C=N stretching for oxazolone ring (1695.23 cm^{-1}), C-O-C stretch (1312.67 cm^{-1}), 3 bands for C=S (1505.76 cm^{-1}, 1457.75 cm^{-1}, 869.65 cm^{-1}), methoxy C-H stretch (2855.73 cm^{-1})	3.43 (s, 3H, OCH_3), 9.26 (s, 1H, C-OH), 6.65 (d, 2H, CH=CH, cinnamoyl), 6.54 (s, 1H, CH=C, methylidene of oxazolone), 7.56 (d, 1H, NH), 8.41 (s, 1H, N=CH, imine), 1.50 (d, 1H, CH), 6.97, 6.93 (m, 2H, C_6H_2), 7.62, 7.57, 7.52, 7.48 (m, 5H, C_6H_4).	38.17 (2C, CH-NH-CH), 58.12 (1C, OCH_3) 130.12, 131.23, 129.76, 129.63, 128.89, 128.54 (6C, C_6H_4), 158.22 (1C, HC=N of imine), 163.05 (1C, C=N of oxazolone ring), 189.16 (1C, C-O, of oxazolone ring), 197.00 (3C, C=O, lactone).	984.79 [M +H], 802.12 [M - $C_6H_5CH=CH$ $C_4H_3NO_2$], 743.23 [M - C_6H_5], 700.7 [M - C_3H_3], 683.5 [M - OH], 587.5 [M - $C_4H_2NO_4$], 563.4 [M - COH], 501.3 [M - C_5H_5], 395.4 [M - $C_6H_5CH=CH$], 301.2 [M - $C_4H_3NO_2$], 241.2 [M - C_5H_5], 163.2 [M - CHNHS].

4i	O-H stretching (3798.12 cm^{-1}), N-H stretching 2^0 (3702.23 cm^{-1}), C=O stretching for oxazolone ring (1760.06 cm^{-1}), C-N stretching 2^0 (1113.32 cm^{-1}), C=N stretching for imine (1623.54 cm^{-1}), C=N stretching for oxazolone ring (1694.78 cm^{-1}), C-O-C stretch (1311.78 cm^{-1}), 3 bands for C=S (1503.43 cm^{-1}, 1458.36 cm^{-1}, 879.12 cm^{-1}), methoxy C-H stretch (2854.56 cm^{-1})	3.42 (s, 3H, OCH_3), 9.29 (s, 1H, C-OH), 6.68 (d, 2H, CH=CH, cinnamoyl), 6.61 (s, 1H, CH=C, methylidene of oxazolone), 7.54 (d, 1H, NH), 8.39 (s, 1H, N=CH, imine), 1.55 (d, 1H, CH), 6.98, 6.91 (m, 2H, C_6H_2).	38.17 (2C, CH-NH-CH), 58.12 (1C, OCH_3) 130.12, 131.23, 129.76, 129.63, 128.89, 128.54 (6C, C_6H_4), 158.22 (1C, HC=N of imine), 163.05 (1C, C=N of oxazolone ring), 189.16 (1C, C-O, of oxazolone ring), 197.00 (3C, C=O, lactone).	1394.8 [M – OH], 1307.7 [M – $C_6H_5CH=CH$], 1209.5 [M – $C_4H_3NO_2$], 1119.5[M – $C_6H_5CH=CH$], 1031. 4 [M – $C_3H_2NO_2$], 945.4 [M – $C_6H_5CH=CH$], 905.4 [M – CO], 815.3 [M – C_3H_4NO], 785.3 [M – C_3H_3], 757.3 [M – C_2H_2], 743.3 [M – CH_2], 721.3 [M – C_2H_2], 662.3 [M – CHNO2], 637.2 [M – C_2H_2], 627.12 [M – CH_2], 587.2 [M – C_3H_3], 541.1 [M – C_4H_3], 521.1 [M-CH_2], 432.1 [M – $C_4H_3NO_2$], 416.2 [M – CH_2], 389.3 [M – C_2H_2], 357.3 [M – CH_2OH], 326.2 [M – C_3H_3], 301.2 [M - C_2H_2], 193.2 [M – C_6H_5CH].

Synthesis of (2E)-3-phenylprop-2-enoyl chloride (1)
Cinnamic acid (1 gm) and thionyl chloride (2ml) were taken in a 100ml round bottom flask having a calcium chloride guard tube attached to the top of condenser. The contents were refluxed on a boiling water bath for three hours until the evolution of hydrogen chloride and sulphurdioxide ceased. Excess of thionyl chloride was removed by distillation.

Synthesis of {[(2E) -3- phenylprop -2-enoyl]amino}acetic acid (2)
Amino acetic acid i.e. glycine (2gm) was dissolved in aqueous sodium hydroxide (16.67 ml, 10%) and (2E)-3-phenylprop-2-enoyl chloride in five fractions. The contents were shaken vigorously after each addition, until all the acid chloride reacted. The cleared solution was transferred to a beaker, crushed ice was added and acidified with concentrated hydrochloric acid, the solid thus obtained was collected and recrystallise from hot water.

Synthesis of [1-(1-{2,4-dihydroxy-5-[(E)-{5-oxo-2 [(E)-2-phenylethenyl] -1, 3- oxazol- 4(5H)-ylidene} methylphenyl] {4-[(Z)-{5-oxo-2 [(E)-2-phenylethenyl]-1,3-oxazol-4 (5H)-ylidene} methylphenyl]methyl)-3((E) {(4-hydroxy-5-methoxy-2-{5-oxo-2- [(E)-2-phenylethenyl] -1, 3-oxazol -4 (5H)-ylidene}methylphenyl) methylidene]thiourea (4d)
An intimate mixture of 1- [1- (5- formyl- 2, 4-dihydroxyphenyl) (4-formylphenyl) methyl] -3- [(*E*) - (2-formyl-4-hydroxy-3-methoxyphenyl) methylidene] thiourea (0.01mole), {[(2*E*)-3-phenylprop-2-enoyl] amino} acetic acid and acetic anhydride were taken in a round bottom flask fitted with a reflux condenser. The contents were heated on steam bath for about 2 hrs. contents were cooled, treated with aqueous ethanol and the solid was filtered the product was recrystallize from aqueous ethanol in pink needles.

All new titled compounds (**4a-i**) were synthesized by following the same procedure (see *Scheme*).

3. RESULT

The characterisation and spectral data of titled compounds is summarized in *Table 1 and 2* respectively. These data confirms the synthesis of novel azlactone derivatives.

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