Synthesis and biological activity of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones and their α -glucosides

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ABSTRACT
The 4-(4-hydroxybenzylidene)-2-methyl oxazol-5-ones 1 treated with various aldehydes in the presence of acetic acid to form 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones 2a-i which were glucosylated by using α-acetobromogluco as a glucosyl donor to afforded 4-(4-α-β-d-tetra-o-acytlyl- glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones 3a-i which was deacetylated by using Zinc acetate in absolute methanol to formed 4-(4-α-β-d-glucobybenzylidene)-2-(substituted styryl) oxazol-5-ones 4a-i. Compounds showed good antimicrobial and antifungal activity.

Keywords: Oxazolone, α - acetobromogluco, decetylation, α -glucosides, antimicrobial and antifungal activity.

INTRODUCTION
Heterocyclic compounds are widely distributed in nature and are essential for life. They play a vital role in the metabolism of all living cells. There are vast numbers of pharmacologically active heterocyclic compounds, many of which are in regular clinical use. Oxazoles play a very vital role in the manufacturing of various biologically active drugs as anti-inflammatory, antidepressant, fluorescent whitening agent, scintillator properties, analgesics, etc.1-8 Glucoconjugates and carbohydrates containing structure exhibit variety of biological and therapeutic properties.

Glycosides have a wide range of biological activities including antibacterial, antifungal, antiviral, anticancer, and antitumor activities.9-12 Thus keeping in view of pharmacological activity of oxazole, importance of glucoside in metabolism and continuation of our works13 4-(4-α-β-D-glucobybenzylidene)-2-(substituted styryl) oxazol-5-ones have been synthesized. Besides some of the compounds are evaluated for their biological activity.
RESULT AND DISCUSSION

The starting compound 4-(4-hydroxybenzylidene)-2-methyl oxazol-5-ones 1 have been synthesized by using known methods from acetylglycine and p-hydroxy benzaldehyde. Thus compound 1 reacted with various aldehyde in the presence of acetic acid to formed 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones 2a-i. The IR spectrum of 2a shows a broad peak 3430 (–OH), due to the presence of phenolic –OH group, 1510 (C=N), 1554 (C=C), 1701 (C=O), 3010, 3085 (Ar-CH).

1H-NMR δ 5.15 (s, 1H, Ar-CH, exchangeable with D2O), δ 5.20 (d, 1H, CH=CH-Ar), δ 6.80 (d, 1H, CH=CH-Ar), δ 7.20 the signal due to exocyclic vinylic proton.

Glucosylation of the product 2a-i were carried out by using α-glucopyranosyl bromide which was prepared from bromination of glucose pentacetate. The potassium salt of 2a-i has been carried out using argon atmosphere in dry acetonitrile in the presence of 18-crown-6 ether as a catalyst. The salt of aglycon and α-glucopyranosyl bromide use for the glucosylation to afford , 4-(4-O-β-D-tetra-O-acetylglucopyranosylidene)-2-(substituted styryl) oxazol-5-ones 3α-i. The compound obtained in good yield and it is confirmed by absence of phenolic -OH group at 3454 and the presence of 1610 (C=N), 1710 (C=O), 1088 was attributed to C-O-C stretch α-anomer of acetylated 3α is confirmed by 1H-NMR, the anomeric proton 1-H resonated as a doublet at δ 3.10 with coupling constant J1,2=3.2Hz establishing the α-stereochemistry of the glucosidic bond. Further, 4-(4-O-β-D-tetra-O-acetylglucopyranosylidene)-2-(substituted styryl) oxazol-5-ones undergo deacetylation by using zinc acetate and absolute methanol (Scheme-2) to form 4-(4-O-β-D-glucopyranosylidene)-2-(substituted styryl) oxazol-5-ones 4α-i. IR spectra of 4α showed broad band 3405 cm⁻¹ (imtramolecular –OH, broad, stretch) indicates the presence of carbohydrate hydroxyl group, 1612 (C=N) and C-N observed at 1252 cm⁻¹. The β-D-glucopyranosyl ring observed band at 1028 cm⁻¹ which confirmed the formation of α-glucosides. The 1H-NMR display a signal due to sugar proton between δ 3.1 to 4.0 ppm. The β-anomeric configuration was established by the appearance of doublet δ 5.2 ppm, aromatic ring proton between 7.4 to 8.20 ppm. 5.6 (1H, CH=CH-Ar), 6.6 ppm (1H, CH=CH-Ar), δ 7.20 (s, 1H, exocyclic vinylic). In EI-MS study of 4α, the molecular ion peak at m/z 453 (M), was dominated by 290 (100%) with the loss of 163 amu corresponding to the loss of sugar moiety. This fragmentation pattern is characteristic of α-glucosidically linked sugar. Also the molecular ion of m/z 453 (M) which confirmed the molecular formula of the corresponding glucoside 4α. All the compounds 4α-i gave satisfactory IR, NMR, optical rotation and elemental analysis data correlation with assigned structure.

R =

a) C6H5   b) 2-Cl C6H5   c) 3-Cl C6H5   d) 4-Cl C6H5

e) 2-(OCH3) C6H5   f) 3-(OCH3) C6H5   g)4-(OCH3) C6H5   h) 3-NO2 C6H5   i)4-N (CH3)2C6H5

SCHEME 1: Synthesis of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones.
Synthesis and biological activity of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones and their o-glucosides

R =

a) C₆H₅  b) 2-Cl C₆H₄  c) 3-Cl C₆H₄  d) 4-Cl C₆H₄  

e) 2-(OCH₃) C₆H₄  f) 3-(OCH₃) C₆H₄  g) 4-(OCH₃) C₆H₄  h) 3-NO₂ C₆H₄  i) 4-N (CH₃)₂C₆H₅  

**SCHEME 2:** 4-(4-o-β-D-glucopyranosyl benzylidene)-2-(substituted styryl) oxazol-5-ones (a) K₂CO₃, CH₃CN, argon atmosphere; (b) β-glucopyranosyl bromide, 18-crown-6;  (c) Zn(OAc)₂, MeOH.

**Biological Activity**

**Antibacterial Activity**
The synthesized compounds were screened for their antibacterial activities against pathogenic bacteria such as *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Klebsiella aerogens* using cup plate diffusion method. The test compounds were dissolved in methanol at concentration 100 µg/mL by using Ciprofloxacin, Sulfacetamide as a standard drug.

**Antifungal Activity**
The synthesized compounds were also screened for their antifungal activity against *Aspergillus niger* and *Candida albicans* using cup plate diffusion method by dissolving methanol at concentration 100 µg/mL. The zone of inhibition is at after 7 days and 20°C and it was compared with Gentamycin and Clotrimazole as a standard drug as shown in Table-1.

**Experimental**
FT-IR spectra recorded KBr disc on Perkin-Elmer infra red spectrophotometer, ¹H-NMR and ¹³C-NMR were obtained from Bruker II-400 NMR spectrophotometer (¹H, 400MHz and ¹³C, 100 MHz) using TMS as an internal standard in DMSO-d₆, Mass spectra recorded on Hitachi Perkins-Elmer RMU 6D mass spectrophotometer. Purity of the compounds was checked on silica gel G plates using iodine vapor as visualizing agent. Elemental analyses were determined using the FLASH EA 1112 CHN analyzer, Thermo Finning, Italy. The 4-(4-hydroxybenzylidene)-2-methyl oxazol-5-ones I was prepared by using known procedure.

**General procedure for the preparation of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones ² (2a)**
4-(4-Hydroxybenzylidene)-2-methyl oxazol-5-ones I (0.01mole) was refluxed with benzaldehyde (0.01mole) in glacial acetic acid (10 mL) for 2 h on sand bath. Completion of reaction was tested by TLC. The reaction mixture was poured on crushed ice; the residue was filtered, washed with acetic acid. The crude product was crystallize from methanol to get 4-(4-hydroxybenzylidene)-2-styryl oxazol-5-ones 2a yield 65%; mp 260°C. FT-IR (KBr) cm⁻¹: 3430 (-OH), due to the presence of phenolic –OH group, 3010, 3085(aromatic str.), 1701 (C=O),1554 (C=O), 1510 (C=N); ¹H-NMR (DMSO-d₆) δ ppm: 5.15 (s, 1H, Ar-OH,
exchangeable with D₂O), 5.20 (d, 1H, CH=CH-Ar), 6.80 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic). Anal. Calcd for C₁₉H₁₃NO₃ (291) C, 74.22; H, 4.50; N, 4.81 found C, 74.26; H, 4.48; N, 4.82, R²=0.68. Similarly, all the compound 2a-i was synthesized by using this method and spectral data some compounds are given as follows.

4-(4-hydroxybenzylidene)-2-(2-chloro styryl) oxazol-5-ones (2b)
Yield 70%; mp 238° C (methanol); FT-IR (KBr) cm⁻¹: 3450 (phenolic -OH), 2978, 3019 (aromatic str.), 1695 (C=O), 1532 (C=N) 1568 (C=C); ¹H-NMR (DMSO-d₆) δ ppm: 5.05 (s, 1H, Ar-OH, exchangeable with D₂O), 5.16 (d, 1H, CH=CH-Ar), 6.84 (d, 1H, CH=CH-Ar), 7.12 (s, 1H, exocyclic vinylic); R²=0.67. Anal. Calcd for C₁₉H₁₃CINO₃ (325) C, 66.37; H, 3.71; N, 4.30 found C, 66.30; H, 3.68; N, 4.35.

4-(4-hydroxybenzylidene)-2-(3-chloro styryl) oxazol-5-ones (2c)
Yield 62%; mp 230° C (methanol); FT-IR (KBr) cm⁻¹: 3350 (phenolic -OH), 1666 (C=O), 1512 (C=N), 1568 (C=C) and 2755, 2885 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm: 4.85 (s, 1H, Ar-OH, exchangeable with D₂O), 5.12 (d, 1H, CH=CH-Ar), 6.80 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic); R²=0.54. Anal. Calcd for C₁₉H₁₃CINO₃ (325) C, 66.37; H, 3.71; N, 4.30 found C, 66.35; H, 3.69; N, 4.32.

4-(4-hydroxybenzylidene)-2-(4-chloro styryl) oxazol-5-ones (2d)
Yield 58%; mp 245° C (methanol); FT-IR (KBr) cm⁻¹: 3411 (phenolic -OH), 1675 (C=O), 1610 (C=C), 1511 (C=N) and 2988, 3068 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm: 4.86 (s, 1H, Ar-OH, exchangeable with D₂O), 5.10 (d, 1H, CH=CH-Ar), 6.17 (1H, CH=CH-Ar), 7.14 (s, 1H, exocyclic vinylic); R²=0.57. Anal. Calcd for C₁₉H₁₃CINO₃ (325) C, 66.37; H, 3.71; N, 4.30 found C, 66.38; H, 3.74; N, 4.33.

4-(4-hydroxybenzylidene)-2-(2-methoxy styryl) oxazol-5-ones (2e)
Yield 68%; mp 215° C (methanol); FT-IR (KBr) cm⁻¹: 3320 (phenolic -OH), 1545 (C=N), 1589 (C=C), 1670 (C=O) and 2764, 3078 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm : 4.85 (s, 1H, Ar-OH exchangeable with D₂O), 5.22 (d, 1H, CH=CH-Ar), 6.68 (1H, CH=CH-Ar), 7.2 (s, 1H, exocyclic vinylic); R²=0.55. Anal. Calcd for C₁₉H₁₃NO₅ (321) C, 71.02; H, 4.71; N, 4.36 found C, 71.05; H, 4.73; N, 4.32.

4-(4-hydroxybenzylidene)-2-(3-methoxy styryl) oxazol-5-ones (2f)
Yield 67%; mp 225° C (methanol); FT-IR (KBr) cm⁻¹: 3410 (phenolic -OH), 1555 (C=N), 1615 (C=O), 1676 (C=O) and 2812, 3019 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm : 5.15 (s, 1H, Ar-OH exchangeable with D₂O), 5.60 (d, 1H, CH=CH-Ar), 6.65 (1H, CH=CH-Ar), 7.18 (s, 1H, exocyclic vinylic); R²=0.58. Anal. Calcd for C₁₉H₁₃NO₅ (321) C, 71.02; H, 4.71; N, 4.36 found C, 71.00; H, 4.72; N, 4.40.

4-(4-hydroxybenzylidene)-2-(4-methoxy styryl) oxazol-5-ones (2g)
Yield 68%; mp 190° C (methanol); FT-IR (KBr) cm⁻¹: 3422 (phenolic -OH), 1706 (C=O), 1561 (C=N), 1620 (C=O) and 2824, 3020 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm : 5.10 (s, 1H, Ar-OH exchangeable with D₂O), 5.21 (d, 1H, CH=CH-Ar), 6.67 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic); R²=0.62. Anal. Calcd for C₁₉H₁₃NO₅ (321) C, 71.02; H, 4.71; N, 4.36 found C, 71.05; H, 4.71; N, 4.34.

4-(4-hydroxybenzylidene)-2-(3-nitro styryl) oxazol-5-ones (2h)
Yield 64%; mp 248° C (methanol); FT-IR (KBr) cm⁻¹: 3411 (phenolic -OH), 1665 (C=O), 1614 (C=C), 1535 (C=N) and 2754, 2995 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm : 5.25 (s, 1H, Ar-OH exchangeable with D₂O), 5.18 (d, 1H, CH=CH-Ar), 6.70 (1H, CH=CH-Ar), 7.12 (s, 1H, exocyclic vinylic); R²=0.48. Anal. Calcd for C₁₉H₁₂N₂O₅ (336) C, 64.29; H, 3.60; N, 8.33 found C, 64.32; H, 3.64; N, 8.32.

4-(4-hydroxybenzylidene)-2-(4-dimethylamino styryl) oxazol-5-ones (2i)
Yield 55%; mp 187° C (methanol); FT-IR (KBr) cm⁻¹: 3387 (phenolic -OH), 1634 (C=O), 1552 (C=N), 1576 (C=C) and 2789, 2981 (aromatic str.); ¹H-NMR (DMSO-d₆) δ ppm : 4.82 (s, 1H, Ar-OH exchangeable with D₂O), 5.20 (d, 1H, CH=CH-Ar), 6.34 (1H, CH=CH-Ar), 7.22 (s, 1H, exocyclic vinylic); R²=0.56. Anal. Calcd for...
C$_{20}$H$_{22}$N$_2$O$_3$ (334) C, 71.84; H, 5.43; N, 8.33 found C, 71.82; H, 5.45; N, 8.40.

**General preparation of 4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(substituted styryl) oxazol-5-ones (3a-i)**

A mixture of 4-(4-hydroxybenzylidene)-2-(substituted styryl)-oxazol-5-ones, (0.39mmole), K$_2$CO$_3$ (0.43mmole) and acetonitrile (60 mL) was stirred at room temperature for 2 h under argon atmosphere. 18-Crown-6 (0.04 mmole) was added followed by [α]-glucopyranosyl bromide (0.58 mmole). After 5h, it was poured on to ice cold water. It was neutralized with H$_2$SO$_4$ (1 mole/L). The product was extracted in ethyl acetate (50 mL x 4). Remove of the volatiles under reduce pressure afforded a brown semisolid.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-styryl oxazol-5-ones (3a)**

Yield 62%; $[α]_{D}^{20}$=10.55 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2910, 3030 (aromatic str.), 2868 (glucosidic-CH), 1610 (C=N), 1710 (C=O), 1088 (C-O-C); $^1$H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.02, 1.92, 1.96, 2.15 (s, 3H, OAc), 5.10 (d, 1H, anomeric proton) 3.21 (d, 1H, CH=CH-Ar), 6.16 (d, CH=CH-Ar), 7.10 (s, 1H, exocyclic vinyl), 7.4 - 7.9 (m, 9H, Ar-H). Anal. Caled for C$_{32}$H$_{37}$NO$_2$ (621) C, 61.83; H, 5.03; N, 2.25 found C, 61.80; H, 3.02; N, 2.28.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(2-chloro styryl) oxazol-5-ones (3b)**

Yield 70%; $[α]_{D}^{20}$=+13.11 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2924, 3028 (aromatic str.), 2876 (glucosidic-CH), 1609 (C=N), 1625(C=C),1710 (C=O), 1089 (C-O-C); $^1$H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.04, 1.93, 1.96, 2.17 (s, 3H, OAc), 5.4 (d, 1H, anomeric proton), 5.78 (d, 1H, CH=CH-Ar), 6.52 (d, CH=CH-Ar), 7.14 (s, 1H, exocyclic vinyl), 7.4 - 8.2 (m, 8H, Ar-H). Anal. Caled for C$_{32}$H$_{36}$ClNO$_2$ (656) C, 58.59; H, 4.61; N, 2.14 found C, 58.60; H, 4.64; N, 2.16.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(3-chloro styryl) oxazol-5-ones (3c)**

Yield 68%; $[α]_{D}^{20}$=+9.00 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2945, 3038 (aromatic str.), 2870 (glucosidic-CH), 1612 (C=N), 1560(C=C), 1722 (C=O), 1078 (C-O-C); $^1$H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.04, 1.94, 1.97, 2.20 (s, 3H, OAc), 5.10 (d, 1H, anomeric proton), 5.54 (d, 1H, CH=CH-Ar), 6.12 (d, CH=CH-Ar), 7.15 (s, 1H, exocyclic vinyl), 7.4 - 8.5 (m, 8H, Ar-H). Anal. Caled for C$_{32}$H$_{36}$ClNO$_2$ (656) C, 58.59; H, 4.61; N, 2.14 found C, 58.62; H, 4.62; N, 2.18.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(4-chloro styryl) oxazol-5-ones (3d)**

Yield 72%; $[α]_{D}^{20}$=-14.12 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2905, 3011 (aromatic str.), 2878 (glucosidic-CH), 1620 (C=N), 1726 (C=O), 1080 (C-O-C); $^1$H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.00, 1.94, 1.96, 2.45 (s, 3H, OAc), 5.50 (d, 1H, anomeric proton), 5.88 (d, 1H, CH=CH-Ar), 6.35 (d, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinyl), 7.6 to 8.8 (m, 8H, Ar-H). Anal. Caled for C$_{32}$H$_{36}$ClNO$_2$ (656) C, 58.59; H, 4.61; N, 2.14 found C, 58.64; H, 4.63; N, 2.19.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(2-methoxy styryl) oxazol-5-ones (3e)**

Yield 66%; $[α]_{D}^{20}$=-21.44 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2912, 3035 (aromatic str.), 2855 (glucosidic-CH), 1614 (C=N), 1714 (C=O), 1091 (C-O-C); $^1$H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.04, 1.90, 1.95, 2.18 (s, 3H, OAc), 5.6 (d, 1H, anomeric proton), 5.92 (d, CH=CH-Ar), 6.69 (d, 1H, CH=CH-Ar), 7.18 (s, 1H, exocyclic vinyl), 7.6 to 8.6 (m, 8H, Ar-H). Anal. Caled for C$_{32}$H$_{36}$O$_2$N (651) C, 60.83; H, 5.10; N, 2.15 found C, 60.85; H, 5.10; N, 2.12.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(3-methoxy styryl) oxazol-5-ones (3f)**

Yield 56%; $[α]_{D}^{20}$=-20.11 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2918,3035 (aromatic str.), 2858 (glucosidic-CH), 1518 (C=N),1610(C=N),1733(C=O), 1089 (C-O-C); $^1$H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.05, 1.92, 1.96, 2.20 (s, 3H, OAc), 5.7 (d, 1H, anomeric proton), 5.95 (d, 1H, CH=CH-Ar), 6.58 (d, CH=CH-Ar), 7.14 (s, 1H, exocyclic vinyl), 7.5 to 6.8 (m, 8H, Ar-H). Anal. Caled for C$_{32}$H$_{36}$O$_3$N (651) C, 60.83; H, 5.10; N, 2.15 found C, 60.83; H, 5.11; N, 2.11.

**4-(4-o-β-d-tetra-α-acetyl-glucopyranosylidene)-2-(4-methoxy styryl) oxazol-5-ones (3g)**

Yield 66%; $[α]_{D}^{20}$=-19.68 (c 0.1, CH$_2$OH); FT-IR(KBr) cm$^{-1}$: 2902,3030 (aromatic str.), 2852 (glucosidic-CH), 1612 (C=N),1646(C=C),1740(C=O), 1109 (C-O-C);...
1H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.01, 1.92, 1.93, 2.23 (s, 3H, OAc), 5.4 (d, 1H, anemic proton), 5.78 (d, 1H, CH=CH-Ar), 6.56 (d, CH=CH-Ar), 7.15 (s, 1H, exocyclic vinylic), 7.3 to 8.2 (m, 8H, Ar-H). Anal. Calcd for C$_{32}$H$_{34}$NO$_1$ (651) C, 60.83; H, 5.10; N, 2.15 found C, 60.80; H, 5.10; N, 2.19.

4-(4-o-β-d-tetra-o-acetyl-glucopyranosylidene)-2-(3-nitro styryl) oxazol-5-ones (3h) Yield 69%[α]$_D^{25}$=–14.25 (c 0.1, CH$_3$OH); FT-IR(KBr) cm$^{-1}$: 2912, 3108 (aromatic str.), 2871 (glucosidic-CH), 1615 (C=O), 1648(C=C),1710 (C=O), 1088 (C=O-C); 1H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.02, 1.95, 1.97, 2.19 (s, 3H, OAc), 5.6 (d, 1H, anemic proton), 5.88 (d, 1H, CH=CH-Ar), 6.30 (d, CH=CH-Ar), 7.22 (s, 1H, exocyclic vinylic), 7.8 to 8.5 (m, 8H, Ar-H). Anal. Calcd for C$_{32}$H$_{34}$NO$_1$(666) C, 57.66; H, 4.54; N, 4.20 found C, 57.68; H, 4.56; N, 4.22.

4-(4-o-β-d-tetra-o-acetyl-glucopyranosylidene)-2-(4-dimethylamino styryl) oxazol-5-ones (3i) Yield 62%[α]$_D^{25}$=–16.40 (c 0.1, CH$_3$OH); FT-IR(KBr) cm$^{-1}$: 2922,3034 (aromatic str.), 2880 (glucosidic-CH), 1627 (C=O),1635(C=C),1768 (C=O), 1079 (C=O-C); 1H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 2.11, 1.97, 1.95, 2.10 (s, 3H, OAc), 5.5 (d, 1H, anemic proton), 5.94 (d, 1H, CH=CH-Ar), 6.68 (d, CH=CH-Ar), 7.18 (s, 1H, exocyclic vinylic), 7.6 to 8.5 (m, 8H, Ar-H). Anal. Calcd for C$_{32}$H$_{36}$N$_2$O$_{12}$ (664) C, 61.44; H, 5.46; N, 4.21 found C, 61.47; H, 5.48; N, 4.48.

General preparation of 4-(4-o-β-d glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones (4a-i)

The mixture of 4-(4-β-D-tetra-o-acetyl-glucopyranosylidene)-2-styryl oxazol-5-ones (0.109 mmole), dry methanol (2 mL) and anhydrous zinc acetate (0.126 mmole) was refluxed for 7 h. After cooled down at room temperature, it was filtered through cation exchanged resin; the solvent was removed under vaccum. The residue was purified by silica gel chromatography (CHCl$_3$, MeOH, 12:1 v/v) to get title compound in brown semisolid form.

4-(4-o-β-d-glucooxybenzylidene)-2-styryl oxazol-5-ones (4a) Yield 66%; [α]$_D^{30}$=–14.11(c 0.1, DMSO); FT-IR(KBr) cm$^{-1}$: 3405 (intramolecular –OH, broad, carbohydrate group), 2956 (glucosidic –CH), 2789 (Ar-CH), 1612 (C=O), 1645(C=C), 1252 (C-N), 1028 (C-O-C); 1H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 3.0: (1H,5’H), 3.6 (1H,4’H), 3.5 (1H,3’H), 3.9 (1H,2’H), 5.2 (s,1H) anemic proton, 5.60 (d, 1H, =CH-Ar), 6.60 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic), 7.40 to 8.22 (m, 8H, Ar-H); 13C-NMR (100 MHz, DMSO-d$_6$) δ ppm : 138- 115 (Ar-C), sugar moiety: δ 102.2 (s, C-1’) anemic carbon, 82 (s, C-6’), 74 (s, C-5’), 69.5 (s, C-4’), 70.0 (s, C-3’), 61(s, C-2’); MS (El,70ev): 453 (M) (5%), 290 (100%) base peak, 273 (18%), 188 (14%), 163 (6%), 80(13%). Anal. Calcd for C$_{32}$H$_{36}$N$_2$O$_{14}$ (453) C, 63.57; H, 5.11; N, 3.09 found C, 63.50; H, 5.10; N, 3.31.

4-(4-o-β-d-glucooxybenzylidene)-2-(2-chloro styryl) oxazol-5-ones (4b) Yield 76%; [α]$_D^{30}$=+15.35(c 0.1, DMSO); FT-IR(KBr) cm$^{-1}$: 3415 (intramolecular –OH, broad, carbohydrate group), 2926 (glucosidic –CH), 2785 (Ar-CH), 1610 (C=N), 1632(C=C), 1244 (C-N), 1033 (C-O-C); 1H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 3.2: (1H,5’H), 3.8 (1H,4’H), 3.4 (1H,3’H), 3.9 (1H,2’H), 5.52 (s,1H) anemic proton, 5.90 (d, 1H,CH =CH-Ar), 6.45 (1H, CH=CH-Ar), 7.12 (s, 1H, exocyclic vinylic), 7.4 to 8.6 (m, 8H, Ar-H); 13C-NMR (100 MHz, DMSO-d$_6$) δ ppm : 131.2-116.6 (Ar-C), sugar moiety: δ 100.8 (s, C-1’) anemic carbon,77 (s, C-6’), 72 (s, C-5’), 70.5 (s, C-4’), 72.4 (s, C-3’), 64 (s, C-2’); MS (El,70ev): 487 (M) (15%), 324 (15%), 180 (100%) base peak ,165 (15%), 163 (10%), 79 (31%). Anal. Calcd for C$_{32}$H$_{22}$ClN$_2$O$_{8}$ (487) C, 59.08; H, 4.55; N, 2.87 found C, 59.10; H, 4.58; N, 2.85.

4-(4-o-β-d-glucooxybenzylidene)-2-(3-chloro styryl) oxazol-5-ones (4c) Yield 71%; [α]$_D^{30}$=–10.11(c 0.1, DMSO); FT-IR(KBr) cm$^{-1}$: 3420 (intramolecular –OH, broad, carbohydrate group), 2928 (glucosidic –CH), 2788 (Ar-CH), 1621 (C=N),1655(C=C), 1245 (C-N), 1034 (C-O-C); 1H-NMR (400 MHz, DMSO-d$_6$) δ ppm: 3.2: (1H,5’H), 3.7 (1H,4’H), 3.4 (1H,3’H), 3.8 (1H,2’H), 5.25 (s,1H) anemic proton, 5.84 (d,1H,CH=CH-Ar), 6.42 (1H,CH=CH-Ar), 7.15 (s, 1H, exocyclic vinylic), 7.3 to 8.4 (m, 8H, Ar-H); 13C-NMR (100 MHz, DMSO-d$_6$) δ ppm : 132.4-115 (Ar-C), sugar moiety: δ 101.0(s, C-1’) anemic carbon,75 (s, C-6’), 71 (s, C-5’), 70.5 (s, C-4’), 72.6 (s, C-3’),
Synthesis and biological activity of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones and their o-glucosides

65 (s, C-2'); MS (El, 70ev): 487 (M) (10%), 326 (11%), 181 (100%) base peak, 160 (18%), 163 (14%), 78 (30%). Anal. Calcld for C_{29}H_{2}_ClNO_8 (487) C, 59.08; H, 4.55; N, 2.87 found C, 59.05; H, 4.55; N, 2.83.

4-(4-o-β-d-glucopyranosylidene)-2-(4-chlorostyryl) oxazol-5-ones (4d)
Yield 59%; [α]_D^25 = -18.25 (c 0.1, DMSO); FT-IR(KBr) cm\(^{-1}\): 3510 (intramolecular –OH, broad, carbohydrate group), 2930 (glucosidic –CH), 2780 (Ar-CH), 1612 (C=N), 1578(C=C), 1245 (C-N), 1035 (C-O-C); \(^1\)H-NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm: 3.2 (1H,5'H), 3.7 (1H,4'H), 3.4 (1H,3'H), 3.8 (1H,2'H), 5.28 (s,1H) anomeric proton, 5.58 (d, 1H,CH=CH-Ar), 6.62 (1H,CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic), 7.5 to 8.3 (m, 8H, Ar-H); \(^1^3\)C-NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) ppm: 132-117.2 (Ar-C), sugar moiety: \(\delta\) 102.0 (s, C-1') anomeric carbon, 75 (s, C-6'), 72 (s, C-5'), 70.4 (s, C-4'), 71.4 (s, C-3'), 68 (s, C-2'); MS (El, 70ev); 487 (M) (18%), 322 (26%), 130 (100%) base peak, 168 (10%), 163 (14%), 77 (31%). Anal. Calcld for C_{29}H_{2}_ClNO_8 (487) C, 59.08; H, 4.55; N, 2.87 found C, 59.05; H, 4.55; N, 2.83.

4-(4-o-β-d-glucopyranosylidene)-2-(2-methoxystyryl) oxazol-5-ones (4e)
Yield 78%; [α]_D^20 = -28.34 (c 0.1, DMSO); FT-IR(KBr) cm\(^{-1}\): 3505 (intramolecular –OH, broad, carbohydrate group), 2966 (glucosidic –CH), 2785 (Ar-CH), 1618 (C=N), 1625(C=C), 1238 (C-N), 1055 (C-O-C); \(^1\)H-NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm: 3.3 (1H,5'H), 3.6 (1H,4'H), 3.5 (1H,3'H), 3.8 (1H,2'H), 5.2 (s,1H) anomeric proton, 5.9 (d, 1H, CH=CH-Ar), 6.65 (1H, CH=CH-Ar), 7.24 (s, 1H, exocyclic vinylic), 7.5 to 8.8 (m, 8H, Ar-H); \(^1^3\)C-NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) ppm: 107-130 (Ar-C), sugar moiety: \(\delta\) 101.4 (s, C-1') anomeric carbon, 70 (s, C-6'), 74 (s, C-5'), 75 (s, C-4'), 78.5 (s, C-3'), 65 (s, C-2'); MS (El, 70ev); 483 (M) (22%), 320 (15%), 188 (21%), 165 (100%) base peak, 118 (12%), 77(20%). Anal. Calcld for C_{29}H_{2}_NO_9 (483) C, 62.11; H, 5.21; N, 2.90 found C, 62.14; H, 5.19; N, 2.89.

4-(4-o-β-d-glucopyranosylidene)-2-(3-nitrostyryl) oxazol-5-ones (4h)
Yield 72%; [α]_D^20 = -15.10 (c 0.1, DMSO); FT-IR(KBr) cm\(^{-1}\): 3410 (intramolecular –OH, broad, carbohydrate group), 2950 (glucosidic –CH), 2807 (Ar-CH), 1616 (C=N), 1612(C=C), 1249 (C-N), 1068 (C-O-C); \(^1\)H-NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) ppm: 2.9 (1H,5'H), 3.0 (1H,4'H), 3.4 (1H,3'H), 3.9 (1H,2'H), 5.40 (s,1H) anomeric proton, 5.82 (d, 1H,CH=CH-Ar), 6.56 (1H, CH=CH-Ar), 7.12 (s, 1H, exocyclic vinylic), 7.7 to 8.7 (m, 8H, Ar-H); \(^1^3\)C-NMR (100 MHz, DMSO-\(d_6\)) \(\delta\) ppm: 110-134 (Ar-C), sugar moiety: \(\delta\) 103.0 (s, C-1') anomeric carbon, 78 (s,C-3'), 64 (s, C-2'); MS (El,70ev); 498 (M)
(15%), 336 (100%) base peak, 292 (13%), 190 (15%), 163 (8%), 78 (11%). Anal. Calcd for C_{24}H_{22}N_{10}O_{10} (498) C, 57.83; H, 4.45; N, 5.62 found C, 57.85; H, 4.48; N, 5.65.

**4-(4-α - β - d -glucoxybenzylidene) -2-(4-dimethyamino styryl) oxazol-5-ones (4i)**

Yield 60%; [α]_D^20 = -18.65 (c 0.1, DMSO); FT-IR(KBr) cm⁻¹: 3385 (intramolecular –OH, broad, carbohydrate group), 2960 (glycosidic –CH), 2778 (Ar-CH), 1610 (C=N), 1624=C=C),1255 (C-N), 1088 (C-O-C); ¹H-NMR (400 MHz, DMSO-d₆) δ ppm: 3.1 (1H,5'H), 3.7 (1H,4'H), 3.6 (1H,3'H), 3.9 (1H,2'H), 5.2 (s,1H) anomic proton, 5.7 (d, 1H, CH=CH-Ar), 6.12 (1H, CH=CH-Ar), 7.25 (s, 1H, exocyclic vinyl),7.5 to 8.7 (m, 8H, Ar-H); ¹C-NMR (100 MHz, DMSO-d₆) δ ppm : 114-128 (Ar-C), sugar moiety: δ 105.0 (s, C-1') anomic carbon, 78 (s,C-6'), 76 (s, C-5'), 70.5 (s, C-4'), 70.0 (s, C-3'), 63 (s, C-2'); MS (EI,70ev): 496 (M) (15%), 332 (16%), 270 (28%), 185 (100%) base peak, 163 (6%), 74 (10%). Anal. Calcd for C_{26}H_{28}N_{8}O_{8} (496) C, 62.89; H, 5.68; N, 5.64 found C, 62.87; H, 5.60; N, 5.61.

### TABLE I: Biological activity 4-(4-α - β -d -glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones

<table>
<thead>
<tr>
<th>Zone of Inhibition (mm) (Activity Index)</th>
<th>Antibacterial Activity</th>
<th>Antifungal Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Entry</strong></td>
<td><strong>S. aureus</strong></td>
<td><strong>B. subtilis</strong></td>
</tr>
<tr>
<td>4a</td>
<td>29(0.85)*</td>
<td>28(0.96)*</td>
</tr>
<tr>
<td></td>
<td>(0.93)*</td>
<td>(1.07)*</td>
</tr>
<tr>
<td>4b</td>
<td>19(0.55)*</td>
<td>24(0.82)*</td>
</tr>
<tr>
<td></td>
<td>(0.61)*</td>
<td>(0.92)*</td>
</tr>
<tr>
<td>4c</td>
<td>23(0.67)*</td>
<td>15(0.51)*</td>
</tr>
<tr>
<td></td>
<td>(0.74)*</td>
<td>(0.57)*</td>
</tr>
<tr>
<td>4d</td>
<td>30(0.88)*</td>
<td>26(0.89)*</td>
</tr>
<tr>
<td></td>
<td>(0.96)*</td>
<td>(1.00)*</td>
</tr>
<tr>
<td>4e</td>
<td>12(0.35)*</td>
<td>15(0.51)*</td>
</tr>
<tr>
<td></td>
<td>(0.38)*</td>
<td>(0.57)*</td>
</tr>
<tr>
<td>4f</td>
<td>22(0.64)*</td>
<td>12(0.41)*</td>
</tr>
<tr>
<td></td>
<td>(0.70)*</td>
<td>(0.46)*</td>
</tr>
<tr>
<td>4g</td>
<td>12(0.35)*</td>
<td>14(0.48)*</td>
</tr>
<tr>
<td></td>
<td>(0.38)*</td>
<td>(0.53)*</td>
</tr>
<tr>
<td>4h</td>
<td>22(0.64)*</td>
<td>16(0.55)*</td>
</tr>
<tr>
<td></td>
<td>(0.70)*</td>
<td>(0.61)*</td>
</tr>
<tr>
<td>4i</td>
<td>14(0.41)*</td>
<td>18(0.62)*</td>
</tr>
<tr>
<td></td>
<td>(0.45)*</td>
<td>(0.69)*</td>
</tr>
</tbody>
</table>

**Std.1** | 34 | 29 | 35 | 22 | 21 | 25 |
| **Std. 2** | 31 | 26 | 29 | 21 | 23 | 24 |

a= concentration of test compounds and standard 100 µg/mL, 
b= average zone of inhibition in mm, 
(Activity index) = Inhibition zone of the sample / Inhibition zone of the standard, 
* = Activity index against std. 1, 
# = Activity index against std. 2, 
for antibacterial activity: Std. 1 = Ciprofloxacin and Std. 2 = Sulphacetamide, for antifungal activity: Std. 1 = Gentamycin and Std. 2 = Clotrimazole.

**REFERENCES**

Synthesis and biological activity of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones and their o-glucosides