Turk J Chem
33 (2009) , 295 – 305.

doi:10.3906/kim-0712-12

Synthesis and Biological Activity of 4-(4-Hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones and Their *o*-glucosides

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Received 24.12.2007

The 4-(4-hydroxybenzylidene)-2-methyl oxazol-5-ones **1** were 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 using α-acetobromoglucose as a glucosyl donor to afford 4-(4-*o*-β-d-tetra-*o*-acetyl-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones **3a-i**, which were deacetylated using zinc acetate in absolute methanol to form 4-(4-*o*-β-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones **4a-i**. The compounds showed good antimicrobial and antifungal activity.

Key Words: Oxazolone, α-acetobromoglucose, decetylation, *o*-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 vital role in the manufacture of various biologically active drugs as anti-inflammatory, antidepressant, fluorescent whitening agent, scintillator properties, analgesics, etc.[1−8] Glycoconjugates and carbohydrate containing structures have a variety of biological and therapeutic properties. Glycosides have a wide range of biological activities including antibacterial, antifungal, antiviral, anticancer, and antitumor activities.[9−12]

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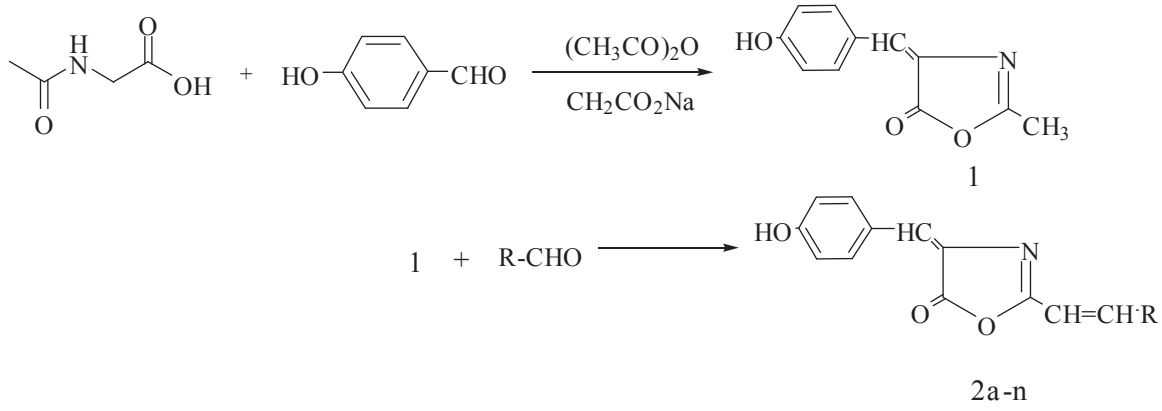
Thus, keeping in view the pharmacological activity of oxazole and the importance of glucoside in metabolism and in continuation of our work,[13] 4-(4-*o*-β-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones were synthesized. Moreover, some of the compounds were evaluated for their biological activity.

Results and Discussion

The starting compounds 4-(4-hydroxybenzylidene)-2-methyl oxazol-5-ones **1** were synthesized by known methods[14] from acetylglycine and *p*-hydroxy benzaldehyde. Thus compound **1** reacted with various aldehydes in the presence of acetic acid to form 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones **2a-i**. The IR spectrum of **2a** shows a broad peak at 3430 (-OH), due to the presence of phenolic –OH group, 1510 (C=N), 1554 (C=C), 1701 (C=O), 3010, 3085 (Ar-CH). ^{1}H-NMR δ 5.15 (s, 1H, Ar-OH, exchangeable with D_2O), 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.



R =

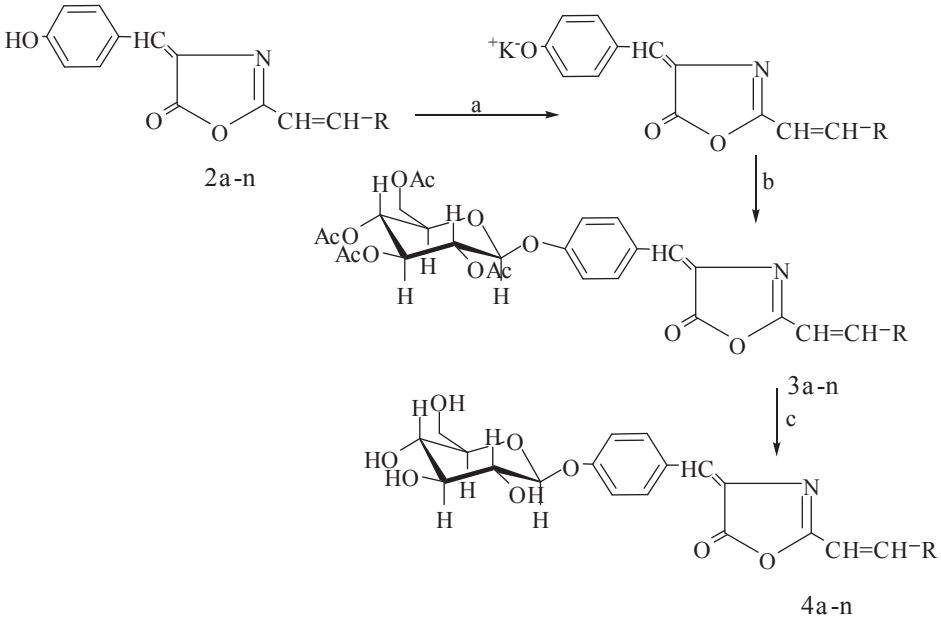
a) C_6H_5 b) 2-Cl C_6H_4 c) 3-Cl C_6H_4 d) 4-Cl C_6H_4

e) 2-(OCH_3) C_6H_4 f) 3-(OCH_3) C_6H_4 g) 4-(OCH_3) C_6H_4 h) 3-NO_2 C_6H_4, i) 4-N $(CH_3)_2C_6H_5$

Scheme 1. Synthesis of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones.

Glucosylation[15] of the product **2a-i** was carried out using α-glucopyranosyl bromide, which was prepared from bromination of glucose pentacetate. The potassium salt of **2a-i** was prepared 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 were used for the glucosylation to afford 4-(4-*o*-β-d-tetra-*o*-acetyl-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones **3a-i**. The compound was obtained in good yield and its structure was confirmed by the IR spectrum (absence of phenolic -OH group at 3454 cm^{-1} and the presence of C=N and C=O groups at 1610 cm^{-1} and 1710 cm^{-1}, respectively). The absorption peak at 1088 cm^{-1} was attributed to C-O-C stretching. The α-anomer of acetylated **3a** was confirmed by ^{1}H-NMR, and the anomeric proton 1-H resonated as a doublet at δ 5.10 with coupling constant $J_{1-2} = 3.2$ Hz, establishing the α-stereochemistry of the glucosidic bond. Further, 4-(4-*o*-β-d-tetra-*o*-acetyl-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones undergo deacetylation[16] using

zinc acetate and absolute methanol (Scheme 2) to form 4-(4-*o*-β-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones **4a-i**. IR spectra of **4a** showed a broad band at 3405 cm^{-1} (intramolecular –OH, broad, stretch). This indicates the presence of a carbohydrate hydroxyl group. The β-d-glucopyranosyl ring band was observed at 1028 cm^{-1}, which confirmed the formation of *o*-glucosides. ^{1}H-NMR displays a signal due to sugar proton between δ 3.1 and 4.0 ppm. The β-anomeric configuration was established by the appearance of doublet δ 5.2 ppm, aromatic ring proton between 7.4 and 8.20 ppm, 5.6 (1H, CH=CH-Ar), 6.6 ppm (1H, CH=CH-Ar), δ 7.20 (s, 1H, exocyclic vinylic). In the EI-MS study of **4a,** 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 *o*-glucosidically linked sugar. Also the molecular ion of m/z 453 (M) confirmed the molecular formula of the corresponding glucoside **4a**. All the compounds **4a-i** gave satisfactory IR, NMR, optical rotation, and elemental analysis data correlation with the assigned structure.



R =

a) C_6H_5 b) 2-Cl C_6H_4 c) 3-Cl C_6H_4 d) 4-Cl C_6H_4

e) 2-(OCH_3) C_6H_4 f) 3-(OCH_3) C_6H_4 g) 4-(OCH_3) C_6H_4 h) 3-NO_2 C_6H_4, i) 4-N $(CH_3)_2C_6H_5$

Scheme 2. 4-(4-*o*-β-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones (*a*) K_2CO_3, CH_3CN, argon atmosphere; (*b*)α-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 aerogenes* using the cup plate diffusion

method. The test compounds were dissolved in methanol at a concentration of 100 μg/mL using Ciprofloxacin and Sulphacetamide as standard drugs.

Antifungal activity

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

Experimental

FT-IR spectra were recorded on a KBr disk on a Perkin-Elmer infrared spectrophotometer. ^{1}H-NMR and ^{13}C-NMR were obtained from a Bruker II-400 NMR spectrophotometer (^{1}H, 400 MHz and ^{13}C, 100 MHz) using TMS as an internal standard in DMSO-d_6. Mass spectra were recorded on a 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 performed using the FLASH EA 1112 CHN analyzer, Thermo Finnigan, Italy. The 4-(4-hydroxybenzylidene)-2-methyl oxazol-5-ones **1** was prepared by a known procedure.

General procedure for the preparation of 4-(4-hydroxybenzylidene)-2-(substituted styryl) oxazol-5-ones[17] **(2a)**. 4-(4-Hydroxybenzylidene)-2-methyl oxazol-5-ones **1** (0.01 mol) was refluxed with benzaldehyde (0.01 mol) in glacial acetic acid (10 mL) for 2 h on a sand bath. Completion of the reaction was tested by TLC. The reaction mixture was poured onto crushed ice; the residue was filtered, and washed with acetic acid. The crude product was crystallized 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=C), 1510 (C=N); ^{1}H-NMR (DMSO-d_6)δ ppm: 5.15 (s, 1H, Ar-OH, exchangeable with D_2O), 5.20 (d, 1H, CH=CH-Ar), 6.80 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic). Anal. Calcd for $C_{18}H_{13}NO_3$ (291) C, 74.22; H, 4.50; N, 4.81 found C, 74.26; H, 4.48; N, 4.82, R_f=0.68. Similarly, all the compounds **2a-i** were synthesized using this method and spectral data of 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); ^{1}H-NMR (DMSO-d_6)δ ppm: 5.05 (s, 1H, Ar-OH, exchangeable with D_2O), 5.16 (d, 1H, CH=CH-Ar), 6.84 (d, 1H, CH=CH-Ar), 7.12 (s, 1H, exocyclic vinylic); R_f=0.67. Anal. Calcd for $C_{18}H_{12}ClNO_3$ (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.); ^{1}H-NMR (DMSO-d_6)δ ppm: 4.85 (s, 1H, Ar-OH, exchangeable with D_2O), 5.12 (d, 1H, CH=CH-Ar), 6.80 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic); R_f=0.54. Anal. Calcd for $C_{18}H_{12}ClNO_3$ (325) C, 66.37; H, 3.71; N, 4.30 found C, 66.35; H, 3.69; N, 4.32.

Table. Biological activity 4 -(4-*o* -β-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones. Zone of Inhibition[b] (mm) (Activity Index)[std].

Zone of Inhibition[b] (mm) (Activity Index)[std]						
Entry	Antibacterial Activity				Antifungal Activity	
	Gram-positive		Gram-negative			
	S. aureus	*B. subtilis*	*E. coli*	*K. aerogenes*	*C. albicans*	*A. niger*
4a	29(0.85)* (0.93)#	28(0.96)* (1.07)#	24(0.68)* (0.82)#	18(0.81)* (0.85)#	16(0.76)* (0.69)#	24(0.96)* (1.00)#
4b	19(0.55)* (0.61)#	24(0.82)* (0.92)#	16(0.45)* (0.55)#	17(0.77)* (0.80)#	21(1.00)* (0.91)#	22(0.88)* (0.91)#
4c	23(0.67)* (0.74)#	15(0.51)* (0.57)#	23(0.65)* (0.79)#	19(0.86)* (0.90)#	22(1.04)* (0.95)#	21(0.84)* (0.87)#
4d	30(0.88)* (0.96)#	26(0.89)* (1.00)#	29(0.82)* (1.00)#	22(1.00)* (1.04)#	17(0.80)* (0.73)#	17(0.68)* (0.70)#
4e	12(0.35)* (0.38)#	15(0.51)* (0.57)#	18(0.51)* (0.62)#	20(0.90)* (1.95)#	11(0.52)* (0.47)#	21(0.84)* (0.87)#
4f	22(0.64)* (0.70)#	12(0.41)* (0.46)#	22(0.62)* (0.75)#	14(0.63)* (0.66)#	20(0.95)* (0.86)#	20(0.80)* (0.83)#
4g	12(0.35)* (0.38)#	14(0.48)* (0.53)#	12(034)* (0.41)#	16(0.72)* (0.76)#	18(0.85)* (0.78)#	21(0.84)* (0.87)#
4h	22(0.64)* (0.70)#	16(0.55)* (0.61)#	31(0.88)* (1.06)#	18(0.81)* (0.85)#	15(0.71)* (0.65)#	19(0.76)* (0.79)#
4i	14(0.41)* (0.45)#	18(0.62)* (0.69)#	21(0.60)* (0.72)#	12(0.54)* (0.57)#	16(0.76)* (0.69)#	15(0.60)* (0.62)#
Std.1	34	29	35	22	21	25
Std. 2	31	26	29	21	23	24

a= concentration of test compounds and standard 100 □g/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.

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 (aro-

matic str.); ^{1}H-NMR (DMSO-d_6)δ ppm: 4.86 (s, 1H, Ar-OH, exchangeable with D_2O), 5.10 (d, 1H, CH=CH-Ar), 6.17 (1H, CH=CH-Ar), 7.14 (s, 1H, exocyclic vinylic); R_f=0.57. Anal. Calcd for $C_{18}H_{12}ClNO_3$ (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.); ^{1}H-NMR (DMSO-d_6)δ ppm: 4.85 (s, 1H, Ar-OH exchangeable with D_2O), 5.22 (d, 1H, CH=CH-Ar), 6.68 (1H, CH=CH-Ar), 7.2 (s, 1H, exocyclic vinylic); R_f=0.55. Anal. Calcd for $C_{19}H_{15}NO_4$ (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=C), 1676 (C=O) and 2812, 3019 (aromatic str.); ^{1}H-NMR (DMSO-d_6)δ ppm: 5.15 (s, 1H, Ar-OH exchangeable with D_2O), 5.60 (d, 1H, CH=CH-Ar), 6.65 (1H, CH=CH-Ar), 7.18 (s, 1H, exocyclic vinylic); R_f=0.58. Anal. Calcd for $C_{19}H_{15}NO_4$ (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=C) and 2824, 3020 (aromatic str.); ^{1}H-NMR (DMSO-d_6)δ ppm: 5.10 (s, 1H, Ar-OH exchangeable with D_2O), 5.21 (d, 1H,CH=CH-Ar), 6.67 (1H, CH=CH-Ar), 7.20 (s, 1H, exocyclic vinylic); R_f=0.62. Anal. Calcd for $C_{19}H_{15}NO_4$ (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.); ^{1}H-NMR (DMSO-d_6)δ ppm: 5.25 (s, 1H, Ar-OH exchangeable with D_2O), 5.18 (d, 1H, CH=CH-Ar), 6.70 (1H, CH=CH-Ar), 7.12(s, 1H, exocyclic vinylic); R_f=0.48. Anal. Calcd for $C_{18}H_{12}N_2O_5$ (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-dimethyamino 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.); ^{1}H-NMR (DMSO-d_6)δ ppm: 4.82 (s, 1H, Ar-OH exchangeable with D_2O), 5.20 (d, 1H, CH=CH-Ar), 6.34 (1H, CH=CH-Ar), 7.22 (s, 1H, exocyclic vinylic); R_f=0.56. Anal. Calcd for $C_{20}H_{18}N_2O_3$ (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-*o*-acetyl-glucoxybenzylidene) 2-(substituted styryl) oxazol-5-ones (3a-i). A mixture of 4-(4-hydroxybenzylidene)-2-(substituted styryl-oxazol-5-ones, (0.39 mmol), K_2CO_3 (0.43 mmol), and acetonitrile (60 mL) was stirred at room temperature for 2 h under argon atmosphere. 18-Crown-6 (0.04 mmol) was added followed by α-glucopyranosyl bromide (0.58 mmol). After 5 h, it was poured onto ice cold water. It was neutralized with H_2SO_4 (1 mol/L). The product was extracted in ethyl acetate (50 mL × 4). Removal of the volatiles under reduce pressure afforded a brown semisolid.

4-(4-*o*-β-d-tetra-*o*-acetyl-glucoxybenzylidene)-2-styryl oxazol-5-ones (3a). Yield 62%; $[\alpha]_D^{30}$=-10.55 (c 0.1, CH_3OH); 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) 5.32 (d, 1H, CH=CH-Ar), 6.16 (d, CH=CH-Ar), 7.10 (s, 1H, exocyclic vinylic), 7.4-7.9 (m, 9H, Ar-H). Anal. Calcd for $C_{32}H_{31}NO_{12}$ (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-*o*-acetyl-glucoxybenzylidene)-2-(2-chloro styryl) oxazol-5-ones (3b). Yield 70%; $[\alpha]_D^{30}$=+13.11(c 0.1, CH_3OH); 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 vinylic), 7.4-8.2 (m, 8H, Ar-H). Anal. Calcd for $C_{32}H_{30}ClNO_{12}$(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-*o*-acetyl-glucoxybenzylidene)-2-(3-chloro styryl) oxazol-5-ones (3c). Yield 68%; $[\alpha]_D^{30}$=+9.00 (c 0.1, CH_3OH); 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 vinylic), 7.4-8.5 (m, 8H, Ar-H). Anal. Calcd for $C_{32}H_{30}ClNO_{12}$(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-*o*-acetyl-glucoxybenzylidene)-2-(4-chloro styryl) oxazol-5-ones (3d). Yield 72%; $[\alpha]_D^{30}$=-14.12 (c 0.1, CH_3OH); 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 vinylic), 7.6 to 8.8 (m, 8H, Ar-H). Anal. Calcd for $C_{32}H_{30}ClNO_{12}$(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-*o*-acetyl-glucoxybenzylidene)-2-(2-methoxy styryl) oxazol-5-ones (3e). Yield 66%; $[\alpha]_D^{30}$=-21.44 (c 0.1, CH_3OH); 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 vinylic), 7.6 to 8.6 (m, 8H, Ar-H). Anal. Calcd for $C_{32}H_{33}NO_{13}$(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-*o*-acetyl-glucoxybenzylidene)-2-(3-methoxy styryl) oxazol-5-ones (3f). Yield 56%; $[\alpha]_D^{30}$=-20.11(c 0.1, CH_3OH); FT-IR (KBr) cm^{-1}: 2918,3035 (aromatic str.), 2858 (glucosidic-CH), 1518 (C=N),1610 (C=C),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 vinylic), 7.5 to 6.8 (m, 8H, Ar-H). Anal. Calcd for $C_{32}H_{33}NO_{13}$(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-*o*-acetyl-glucoxybenzylidene)-2-(4-methoxy styryl) oxazol-5-ones (3g). Yield 66%; $[\alpha]_D^{30}$=-19.68 (c 0.1, CH_3OH); 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); ^{1}H-NMR (400 MHz, DMSO-d_6)δ ppm: 2.01, 1.92, 1.93, 2.23 (s, 3H, OAc), 5.4 (d, 1H, anomeric 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 $C_{32}H_{33}NO_{13}$(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-glucoxybenzylidene)-2-(3-nitro styryl) oxazol-5-ones (3h). Yield 69%; $[\alpha]_D^{30}$=-14.25 (c 0.1, CH_3OH); FT-IR (KBr) cm^{-1}: 2912, 3108 (aromatic str.), 2871 (glucosidic-CH), 1615 (C=N), 1648 (C=C), 1710 (C=O), 1088 (C-O-C); ^{1}H-NMR (400 MHz, DMSO-d_6)δ ppm: 2.02, 1.95, 1.97,

2.19 (s, 3H, OAc), 5.6 (d, 1H, anomeric 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 $C_{32}H_{30}N_2O_{14}$(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-glucoxybenzylidene)-2-(4-dimethyamino styryl) oxazol-5-ones (3i). Yield 62%; $[\alpha]_D^{30}$=-16.40 (c 0.1, CH_3OH); FT-IR (KBr) cm^{-1}: 2922, 3034 (aromatic str.), 2880 (glucosidic-CH), 1627 (C=N), 1635 (C=C), 1768 (C=O), 1079 (C-O-C); ^{1}H-NMR (400 MHz, DMSO-d_6)δ ppm: 2.11, 1.97, 1.95, 2.10 (s, 3H, OAc), 5.5 (d, 1H, anomeric 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 $C_{34}H_{36}N_2O_{12}$(664) C, 61.44; H, 5.46; N, 4.21 found C, 61.47; H, 5.48; N, 4.28.

General preparation of 4-(4-*o*-β-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones (4a-i). A mixture of 4-(4-*o*-β-d-tetra-*o*-acetyl-glucoxybenzylidene)-2-styryl oxazol-5-ones (0.109 mmol), dry methanol (2 mL), and anhydrous zinc acetate (0.126 mmol) was refluxed for 7 h. After being cooled down at room temperature, it was filtered through cation exchanged resin; the solvent was removed under vacuum. The residue was purified by silica gel chromatography ($CHCl_3$, MeOH, 12:1 v/v) to get the title compound in brown semisolid form.

4-(4-*o*-β-d-glucoxybenzylidene)-2-styryl oxazol-5-ones (4a). Yield 66%; $[\alpha]_D^{30}$=-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=N), 1645 (C=C), 1252 (C-N), 1028 (C-O-C); ^{1}H-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) anomeric 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); ^{13}C-NMR (100 MHz, DMSO-d_6) δ ppm: 138-115 (Ar-C), sugar moiety: δ 102.2 (s, C-1') anomeric 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, 70 ev): 453 (M) (15%), 290 (100%) base peak, 273 (18%), 188 (14%), 163 (6%), 80(13%). Anal. Calcd for $C_{24}H_{23}NO_8$(453) C, 63.57; H, 5.11; N, 3.09 found C, 63.50; H, 5.10; N, 3.11.

4-(4-*o*-β-d-glucoxybenzylidene)-2-(2-chloro styryl) oxazol-5-ones (4b). Yield 76%; $[\alpha]_D^{30}$= +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); ^{1}H-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) anomeric 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); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 131.2-116.6 (Ar-C), sugar moiety: δ 100.8 (s, C-1') anomeric 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, 70 ev): 487 (M) (15%), 324 (15%), 180 (100%) base peak, 165 (15%), 163 (10%), 79 (31%). Anal. Calcd for $C_{24}H_{22}ClNO_8$(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-glucoxybenzylidene)-2-(3-chloro styryl) oxazol-5-ones (4c). Yield 71%; $[\alpha]_D^{30}$=-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); ^{1}H-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) anomeric 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); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 132.4-115 (Ar-C), sugar moiety: δ 101.0 (s, C-1') anomeric carbon, 75 (s, C-6'), 71

(s, C-5'), 70.5 (s, C-4'), 72.6 (s, C-3'), 65 (s, C-2'); MS (El, 70 ev): 487 (M) (10%), 326 (11%), 181 (100%) base peak, 160 (18%), 163 (14%), 78 (30%). Anal. Calcd for $C_{24}H_{22}ClNO_8$ (487) C, 59.08; H, 4.55; N, 2.87 found C, 59.11; H, 4.52; N, 2.87.

4-(4-*o*-β-d-glucoxybenzylidene)-2-(4-chloro styryl) oxazol-5-ones (4d). Yield 59%; $[\alpha]_D^{30}$=-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)δ 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); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 132-117.2 (Ar-C), sugar moiety: δ 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, 70 ev): 487 (M) (18%), 322 (26%), 130 (100%) base peak, 168 (10%), 163 (14%), 77 (31%). Anal. Calcd for $C_{24}H_{22}ClNO_8$ (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-glucoxybenzylidene)-2-(2-methoxy styryl) oxazol-5-ones (4e). Yield 78%; $[\alpha]_D^{30}$=-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)δ 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);^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 107-130 (Ar-C), sugar moiety: δ 101.4 (s, C-1') anomeric carbon, 78 (s, C-6'), 73 (s, C-5'), 72.5 (s, C-4'), 73.1 (s, C-3'), 62 (s, C-2'); MS (El, 70ev): 483 (M) (11%), 320 (15%), 215 (100%) base peak, 185 (28%), 130 (10%), 118 (24%). Anal. Calcd for $C_{25}H_{25}NO_9$ (483) C, 62.11; H, 5.21; N, 2.90 found C, 62.08; H, 5.24; N, 2.85.

4-(4-*o*-β-d-glucoxybenzylidene)-2-(3-methoxy styryl) oxazol-5-ones (4f). Yield 74%; $[\alpha]_D^{30}$=-26.56 (c 0.1, DMSO); FT-IR(KBr) cm^{-1}: 3420 (intramolecular –OH, broad, carbohydrate group), 2968 (glucosidic –CH), 2780 (Ar-CH), 1622 (C=N), 1620 (C=C), 1236 (C-N), 1056 (C-O-C);^{1}H-NMR (400 MHz, DMSO-d_6)δ ppm: 3.2 (1H, 5'H), 3.4 (1H, 4'H), 3.5 (1H, 3'H), 3.6 (1H, 2'H), 5.30 (s, 1H) anomeric proton, 5.82 (d, 1H, CH=CH-Ar), 6.66 (1H, CH=CH-Ar), 7.18 (s, 1H, exocyclic vinylic), 7.4 to 8.7 (m, 8H, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 107-128 (Ar-C), sugar moiety: δ 103.5 (s, C-1') anomeric carbon, 78 (s, C-6'), 74 (s, C-5'), 73.5 (s, C-4'), 75.1 (s, C-3'), 64 (s, C-2'); MS (El, 70ev): 483 (M) (20%), 320 (18%), 175 (30%), 145 (100%) base peak, 130 (12%), 116 (0.8%). Anal. Calcd for $C_{25}H_{25}NO_9$ (483) C, 62.11; H, 5.21; N, 2.90 found C, 62.14; H, 5.19; N, 2.86.

4-(4-*o*-β-d-glucoxybenzylidene)-2-(4-methoxy styryl) oxazol-5-ones (4g). Yield 66%; $[\alpha]_D^{30}$=-22.19 (c 0.1, DMSO); FT-IR (KBr) cm^{-1}: 3368 (intramolecular –OH, broad, carbohydrate group), 2980 (glucosidic –CH), 2778 (Ar-CH), 1620 (C=N), 1644 (C=C), 1242 (C-N), 1058 (C-O-C); ^{1}H-NMR (400 MHz, DMSO-d_6)δ ppm: 3.2 (1H, 5'H), 3.4 (1H, 4'H), 3.6 (1H, 3'H), 3.7 (1H, 2'H), 5.42 (s, 1H) anomeric proton, 5.94 (d, 1H, CH=CH-Ar), 6.65 (1H, CH=CH-Ar), 7.16 (s, 1H, exocyclic vinylic),7.4 to 8.6 (m, 8H, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 107-128 (Ar-C), sugar moiety: δ 102.0 (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, 70 ev): 483 (M) (22%), 320 (15%), 188 (21%), 165 (100%) base peak, 118 (12%), 77 (20%). Anal. Calcd for $C_{25}H_{25}NO_9$ (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-glucoxybenzylidene)-2-(3-nitro styryl) oxazol-5-ones (4h). Yield 72%; $[\alpha]_D^{30}$=-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)δ 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); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 110-134 (Ar-C), sugar moiety: δ 103.0 (s, C-1') anomeric carbon, 78 (s, C-3'), 64 (s, C-2'); MS (El, 70 ev): 498 (M) (15%), 336 (100%) base peak, 292 (13%), 190 (15%), 163 (8%), 78 (11%). Anal. Calcd for $C_{24}H_{22}N_2O_{10}$(498) C, 57.83; H, 4.45; N, 5.62 found C, 57.85; H, 4.48; N, 5.65.

4-(4-*o*-β-d-glucoxybenzylidene)-2-(4-dimethyamino styryl) oxazol-5-ones (4i). Yield 60%; $[\alpha]_D^{30}$=-18.65 (c 0.1, DMSO); FT-IR (KBr) cm^{-1}: 3385 (intramolecular –OH, broad, carbohydrate group), 2960 (glucosidic –CH), 2778 (Ar-CH), 1610 (C=N), 1624 (C=C), 1255 (C-N), 1088 (C-O-C); ^{1}H-NMR (400 MHz, DMSO-d_6)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) anomeric proton, 5.7 (d, 1H, CH=CH-Ar), 6.12 (1H, CH=CH-Ar), 7.25 (s, 1H, exocyclic vinylic), 7.5 to 8.7 (m, 8H, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6)δ ppm: 114-128 (Ar-C), sugar moiety: δ 105.0 (s, C-1') anomeric carbon, 78 (s, C-6'), 76 (s, C-5'), 70.5 (s, C-4'), 70.0 (s, C-3'), 63 (s, C-2'); MS (El, 70 ev): 496 (M) (15%), 332 (16%), 270 (28%), 185 (100%) base peak, 163 (6%), 74 (10%). Anal. Calcd for $C_{26}H_{28}N_2O_8$(496) C, 62.89; H, 5.68; N, 5.64 found C, 62.87; H, 5.60; N, 5.61.

Acknowledgments

The authors are thankful to Dr. H.D. Juneja, Head of Department of Chemistry, R.T.M. Nagpur University for providing the necessary facilities, and to the Head of the Department of Pharmacy for help with the biological activity. Thanks are due to SAIF Chandigarh and IIT-Powai for providing spectral analysis.

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