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Synthesis and antifungal activity of D-glucopyranosyl ureas and D-glucofurano-imidazolidine-2-ones

Xuan Tang · Feng Xue · Hongju Ma · Xiufang Cao · Changshui Chen · Xuegang Li

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Abstract A series of *N*-*β*-D-glucopyranosyl-*N'*-substituted phenyl ureas were synthesized by reaction of glucosyl isocyanate with arylamines and glycosamine with aryl isocyanates, and a series of D-glucofurano-imidazolidine-2-ones were obtained via deacetylation of glycosylureas. Although some of the compounds have already been described, most were prepared for the first time in this work. The structures of all the compounds synthesized were confirmed by IR, ^{1}H NMR, and, in part, by ^{13}C NMR. Antifungal activity of the title compounds was determined against four kinds of plant pathogenic fungi, *Sclerotinia sclerotiorum*, *Fusarium graminearum*, *Fusarium oxysporum*, and *Bipolaris maydis*. Preliminary bioassay indicates that most of glycosylureas had some activity against *S. sclerotiorum*; for some, the antifungal activity was strong. However, most of the imidazolidine-2-ones had weak antifungal activity.

Keywords Glycosylureas · Imidazolinone · Synthesis · Antifungal activity

Introduction

Glucose, an energy source of living cells and an intermediate of metabolism, exists widely in nature and is important in biology. Because modification of medicines by glycosyl can not only prolong and enhance their effect but also efficiently reduce

X. Tang · F. Xue · X. Cao · C. Chen (✉) · X. Li (✉)
College of Science, Huazhong Agricultural University, Wuhan 430070, People's Republic of China
e-mail: chenchang@mail.hzau.edu.cn

X. Li
e-mail: lixuegang@mail.hzau.edu.cn

H. Ma
Department of Plant Protection, Huazhong Agricultural University, Wuhan, China

toxicity and side effects, they are widely used as bactericides [1, 2], fungicides [3, 4], insecticides [5], and antidiabetic agents [6].

Urea functionality is a well known attractive structural feature with a wide range of biological activity, for example, herbicidal [7], antifungal [8], antibacterial [9], and anti-HIV [10, 11]. Also, imidazolinone, a type of heterocyclic compound, has been reported to have a wide variety of biological properties, viz., antibacterial, antifungal [12, 13], anticancer [14], and antiviral [15].

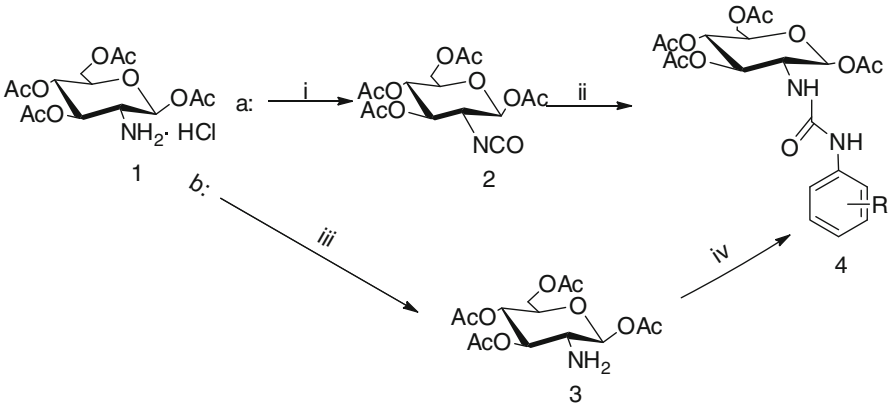
Fungal diseases, which cause extensive crop losses in yield and quality, are one of the most serious problems for cultivation [16]. Discovery of novel fungicides with high efficiency and low toxicity is, therefore, a trend in research and development. Encouraged by the above observations, herein we report the synthesis of some urea and imidazolinone derivatives containing, respectively, glucopyranosyl and glucofuranosyl. Although some have already been described, most have been prepared for the first time. The antifungal activity of the compounds has been evaluated and compared.

Results and discussion

Synthesis of *N*-(1,3,4,6-tetra-*O*-acetyl)-2-deoxy-*β*-D-glucopyranosyl-*N*'-substituted phenylureas **4s**–**4u**

The synthetic route adopted for preparation of *N*-(1,3,4,6-four-*O*-acetyl)-2-deoxy-*β*-D-glucopyranosyl-*N*'-substitutedphenyl urea derivatives is depicted in Scheme 1.

Traditionally, glycosylureas have been obtained by reaction of glycosylamine with aryl isocyanates in anhydrous solvents [17], but the yields were invariably low because of hydrolysis of the aryl isocyanates. Maya proposed a one-pot, two-phase procedure for preparation of glycosylureas starting from glycosyl isocyanate and

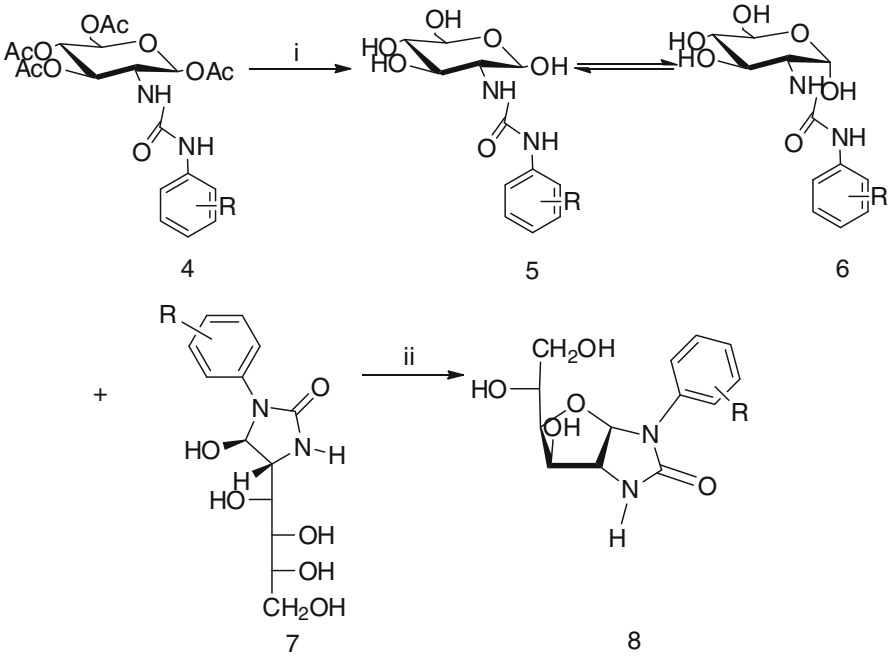


Scheme 1 General synthetic route for *N*-(1,3,4,6-four-*O*-acetyl)-2-deoxy-*β*-D-glucopyranosyl-*N*'-substituted phenylureas **4**. Reagents and conditions: **a** *i* BTC, dichloromethane, sat $NaHCO_3$, 0 °C, 1 h. *ii* Substituted aniline, dichloromethane/chloroform, 25/55 °C, 8/120 h. **b** *iii* CH_3COONa, water, 25 °C, 1 h. *iv* RNCO, 25 °C, dichloromethane, 4 h

aryl amines and using triphosgene in the isocyanation step; this was more convenient and the products were readily obtained [18]. In the work discussed in this paper, using different substituents on benzene, we used two different routes for synthesis of the target compounds. The first route to, **4a–q**, involves treatment of isocyanate **2** with aryl amines (Scheme 1a); the second, to **4r–u**, is reaction of glycosylamine **3** with aryl isocyanates (Scheme 1b, the reaction conditions and physical data of compounds **4** were listed in Table 1). Generally, most glycosylureas **4** can be synthesized by the first route, because of the relative stability to hydrolysis of isocyanate **2** and the aryl isocyanates. To obtain products in high yield, we separated the isocyanate **2** and, after purification, added the substituted aniline. But when an inactive aromatic amine participates in the reaction, it is necessary to pay attention to three key factors:

1 the isocyanate **2** must remove the water and the redundant hydrochloride as much as possible;
2 the temperature must be raised to 55 °C;
3 the reaction time must be prolonged to five days.

Only in this way can the reaction occur, producing, for example, **4i**, **4m**, **4n**, **4o**. The temperature cannot exceed 65 °C, however, otherwise, the isocyanates will polymerize to gels, and the time cannot exceed seven days, or the isocyanates will decompose, furnishing *N*, *N*'-glycosyl urea. If a strong electron-withdrawing



Scheme 2 General synthetic route for 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-ones **8**. Reagents and conditions: *i* MeOH/MeONa, dichloromethane, methanol, 25 °C. *ii* Amberlite 732 (H^+ form), acetic acid (30 mL, 30 %), 100 °C, 30 min

substituent is on the aniline, however, the aniline will be too inactive to undergo nucleophilic substitution with isocyanate **2**, and the reaction will not proceed by the first route, so **4r**, **4s**, **4t**, **4u** cannot be obtained in this way. In these circumstances, glycosylureas were obtained by reaction of glycosylamine with aryl isocyanates in anhydrous solvents, in accordance with Scheme 1b. Alkyl isocyanates are freshly prepared and dropped into glycosylamine at 40 °C, to reduce condensation with themselves and avoid hydrolysis side reactions.

Deacetylation of compounds **4** gave anomeric mixtures of the α and β urea derivatives (**5**, **6**), together with monocyclic imidazolidin-2-ones **7**. In neutral medium, compounds **6** were slowly converted into monocyclic imidazolidin-2-ones **7** and this transformation proceeds rapidly in basic media. Then, under acidic conditions, both ureas and monocyclic compounds were transformed into furanoid bicyclic imidazolidin-2-ones **8** [19].

The deacetylation of compounds **4** has been reported by Ávalos, who used ammonia in ethanol as the deacetylating reagent [20]. Herein, we used sodium methoxide (Scheme 2) as the deacetylating reagent, which was more easy to perform in the laboratory. During the procedure, the pH of the reaction solution cannot exceed 10 and sodium methoxide must be added slowly; in more basic media, the reaction will cause epimerisation at C-2 of compound **7**.

Table 1 Respective different reaction conditions and physical data for compounds **4a–u**

Compound	*R*	Temperature (°C)	Time (h)	Yield (%)	M.P. (°C)
4a	H	25	8	74.5	203–205
4b	2-OCH_3Ph	25	8	74.2	202–203
4c	2-OC_2H_5Ph	25	8	58.3	202–203
4d	2-ClPh	25	8	64.1	187–189
4e	4-CH_3Ph	25	8	74.6	198–200
4f	4-OC_2H_5Ph	25	8	76.1	201–202
4g	4-ClPh	25	8	62.9	205–207
4h	4-BrPh	25	8	75.7	202–203
4i	2,6-di-F	55	120	56.4	212–214
4j	2,6-di-CH_3Ph	25	8	65.7	245–247
4k	3-OCH_3	25	8	72.5	210–212
4l	3,4-di-CH_3	25	8	68.3	217–219
4m	2-CH_3-4-NO_2	55	120	55.7	203–205
4n	4-CH_3-2-NO_2	55	120	58.4	229–231
4o	2-OCH_3-4-NO_2	55	120	52.5	224–226
4p	5-Cl-2-CH_3	25	8	82.4	202–204
4q	2,5-di-CH_3	25	8	70.3	229–231
4r	4-OF_3CPh	25	4	79.8	197–199
4s	2-NO_2	25	4	35.7	220–222
4t	3-NO_2	25	4	38.2	195–197
4u	3-CF_3	25	4	40.3	188–190

Table 2 Antifungal activity of compounds **4** and **8** against four kinds of plant pathogenic fungi

Compound	Inhibition % (100 mg/L)			
	S. sclerotiorum	*F. graminearum*	*F. oxysporm*	*B. maydis*
4a/8a	21.0 (±2.23)/18.4 (±1.69)	17.6 (±2.92)/11.7 (±1.68)	7.6 (±1.50)/9.8 (±0.84)	9.0 (±2.12)/8.2 (±1.45)
4b/8b	24.3 (±1.72)/20.3 (±2.34)	14.0 (±0.62)/12.9 (±1.00)	8.1 (±0.73)/7.7 (±1.88)	5.6 (±3.00)/8.7 (±1.64)
4c/8c	25.4 (±1.88)/22.8 (±1.84)	10.6 (±1.34)/ 9.9 (±0.22)	10.1 (±0.98)/11.2 (±0.61)	4.1 (±0.89)/7.9 (±1.61)
4d/8d	27.8 (±1.25)/24.3 (±0.98)	11.8 (±1.45)/10.5 (±1.22)	9.2 (±1.72)/10.2 (±2.09)	8.5 (±1.24)/7.7 (±2.67)
4e/8e	51.6 (±2.76)/21.6 (±1.54)	10.8 (±1.44)/11.4 (±0.95)	9.0 (±0.84)/8.8 (±1.68)	8.3 (±1.45)/7.5 (±2.52)
4f/8f	50.5 (±0.82)/18.9 (±1.62)	11.6 (±0.84)/10.6 (±1.53)	9.2 (±1.46)/9.8 (±0.87)	9.5 (±1.68)/9.3 (±3.03)
4g/8g	40.3 (±1.49)/23.3 (±1.36)	12.6 (±0.85)/11.2 (±1.62)	13.7 (±2.14)/12.3 (±0.55)	11.9 (±1.74)/10.6 (±1.32)
4h/8h	73.7 (±0.78)/24.1 (±0.43)	14.4 (±1.53)/15.5 (±0.94)	9.0 (±2.64)/11.2 (±2.14)	8.5 (±0.89)/9.9 (±1.25)
4i/8i	11.0 (±1.67)/12.2 (±2.06)	14.4 (±2.12)/11.5 (±2.65)	8.9 (±0.87)/7.3 (±1.92)	9.7 (±3.15)/8.8 (±2.16)
4j/8j	49.7 (±1.56)/17.8 (±1.88)	12.8 (±2.36)/13.7 (±0.91)	9.5 (±1.28)/9.3 (±2.72)	9.3 (±2.33)/8.4 (±2.62)
4k	43.4 (±0.64)	15.6 (±1.32)	11.5 (±1.67)	8.7 (±0.98)
4l	41.5 (±0.89)	12.8 (±1.58)	8.6 (±1.75)	10.2 (±1.54)
4m	62.8 (±1.12)	12.6 (±1.65)	12.9 (±0.84)	12.7 (±1.76)
4n	23.7 (±1.43)	13.2 (±1.32)	11.2 (±1.46)	17.5 (±2.65)
4o	36.6 (±1.42)	11.6 (±1.88)	7.0 (±2.88)	14.1 (±1.54)
4p	51.6 (±1.16)	10.4 (±0.87)	10.3 (±2.52)	10.7 (±0.94)
4q	68.0 (±2.08)	14.8 (±2.85)	4.5 (±1.76)	8.3 (±0.82)
4r/8r	70.2 (±2.42)/19.8 (±2.51)	18.2 (±2.42)/17.3 (±2.64)	9.2 (±1.34)/8.8 (±0.82)	12.7 (±1.16)/10.8 (±2.43)
4s/8s	62.3 (±1.65)/25.7 (±2.95)	10.8 (±3.11)/11.2 (±0.96)	12.6 (±0.62)/11.4 (±1.82)	2.9 (±2.63)/6.7 (±2.28)
4t	27.8 (±1.83)	16.0 (±3.24)	13.1 (±1.66)	19.5 (±2.21)
4u	72.0 (±2.62)	34.8 (±2.45)	20.3 (±3.12)	35.8 (±3.02)
Control	13.8 (±0.64)	11.6 (±0.77)	3.3 (±0.98)	5.1(±0.56)

The inhibition values were obtained by use of the formula $(D_{blank} - D_{test})/D_{blank} \times 100$

We synthesized the target compounds selectivity, because compounds **8** can generate rotational isomers because of substituents on benzene with different spatial positions. To afford the product exclusively, we chose the symmetric substituted aniline which had no isomer and the *ortho*-substitute aniline which had a large steric effect and resulted in a stable conformation.

Biological activity evaluation

The antifungal activity of the title compounds **4a**–**4u**, **8a**–**8j**, **8r**, and **8s** against four kinds of plant pathogenic fungi (*Sclerotinia sclerotiorum*, *Fusarium graminearum*, *Fusarium oxysporm*, and *Bipolaris maydis*) were investigated at dosages of 100 mg/L according to the method described in the "Antifungal activity testing" section; the results are shown in Table 2. To enable discussion of structure–activity relationships, for compounds with the same substituted phenyl we list the percentage inhibition values in the same row.

As shown in Table 2, Most of compounds **4** had some activity against *S. sclerotiorum*, some of the compounds, for example **4h**, **4m**, **4q**, **4r**, **4s**, **4u**, had somewhat stronger antifungal activity. However, most of compounds **4** had weak antifungal activity against the other three fungi; only compound **4u** had strong antifungal activity compared with the other compounds. Most imidazolidine-2-ones **8** had weak antifungal activity against the four fungi, weaker than compounds **4** with the same substituent on the benzene. The antifungal activity of deacetylated compounds **8** was not increased. It is possible compounds **8** cannot combine with the active site very well because of their rigid structure.

Conclusions

The title compounds **4** were designed, and synthesized by reaction of glucosyl isothiocyanates with a substituted aniline or by reaction of glycosylamine with aryl isocyanates. Compounds **8** were obtained by deacetylation of glycosylureas. Most of the compounds **4** had some activity against *S. sclerotiorum*, and most compounds **8** had weak antifungal activity against the four strains. Introduction of an acetylated glucopyranosyl group to the urea was useful for improvement of the antifungal activity against *S. sclerotiorm*. However, although introduction of a glucofuranosyl to imidazolinone can enhance water solubility and reduce toxicity, it cannot improve antifungal activity.

Experimental

Instrumentation and chemicals

All reagents were commercially available and all solvents and liquid reagents were dried by standard methods and distilled before use. Melting points were determined

with a digital melting-point apparatus and are uncorrected. FT-IR spectra were recorded in KBr. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM spectrometer at room temperature with tetramethylsilane (TMS) as internal standard and $CDCl_3$ or dimethyl sulfoxide (DMSO)-d_6 as solvent. The progress of reactions was monitored by TLC on silica gel plates visualized with UV light. Chemical shifts are reported in ppm units with the use of the δ scale.

General procedure for preparation of *N*-(1,3,4,6-tetra-*O*-acetyl)-2-deoxy-β-D-glucopyranosyl-*N'*-substituted phenylurea derivatives **4a–q**

To a vigorously stirred solution of BTC (bis(trichloromethyl) (2.5 mmol) in an 1:1 mixture of CH_2Cl_2 and saturated aqueous $NaHCO_3$ (60 mL) at 0 °C in an ice bath was added hydrohalides **1** (5 mmol), while maintaining stirring for 60 min. The organic layer was separated and then extracted three times with dichloromethane (20 mL). The combined organic fractions were washed with saturated aqueous $NaHCO_3$ and water successively, and dried over anhydrous magnesium sulfate. After drying, the substituted aniline in 30 mL dry dichloromethane was added dropwise to the separated liquid compound **2** while the reaction was monitored by TLC. After evaporation to dryness, the crude products were purified by recrystallization (water–acetone).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-phenyl-urea (**4a**)*

White crystals. IR (KBr) cm^{-1}: ν 3318 (N–H), 1756/1743 (C=O), 1637 (C=O), 1218 (O–C–O); ^{1}H NMR (600 MHz, $CDCl_3$), δ 7.31 (m, 4H, ArH), 7.11 (t, $J = 7.2$ Hz, 1H, ArH), 6.57 (br s, 1H, ArNH), 5.75 (d, $J = 8.4$ Hz, 1H, H-1), 5.17 (m, 2H, H-3, H-4), 4.91 (d, $J = 9.6$ Hz, 1H, gly–NH), 4.29 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.15 (m, 2H, H-2, H-6′), 3.82 (m, 1H, H-5), 2.14 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.04 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-methoxyphenyl)urea (**4b**)*

White crystals. IR (KBr) cm^{-1}: ν 3395 (N–H), 3329 (N'–H), 1758 (C=O), 1676 (C=O), 1225 (O–C–O); ^{1}H NMR (600 MHz, $CDCl_3$), δ 8.01 (d, $J = 7.8$ Hz, 1H, ArH), 7.00 (t, $J = 6.6$ Hz, $J = 7.8$ Hz, 1H, ArH), 6.93 (t, $J = 7.8$ Hz, $J = 7.2$ Hz, 1H, ArH), 6.88 (br s, 1H, ArNH), 6.84 (d, $J = 7.8$ Hz, 1H, ArH), 5.69 (d, $J = 9.0$ Hz, 1H, H-1), 5.16 (m, 2H, H-3, H-4), 4.90 (d, $J = 9.0$ Hz, 1H, gly–NH), 4.29 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.22 (m, 1H, H-2), 4.14 (m, 1H, H-6′), 3.83 (s, 4H, H-5, OCH_3), 2.12 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.05 (s, 6H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-ethoxylphenyl)urea (**4c**)*

White crystals. IR (KBr) cm^{-1}: ν 3387 (N–H), 3314 (N'–H), 1752 (C=O), 1643 (C=O), 1218 (O–C–O); ^{1}H NMR (600 MHz, $CDCl_3$), δ 8.00 (d, $J = 7.2$ Hz, 1H, ArH), 6.98 (m, 1H, ArH), 6.93 (t, $J = 7.8$ Hz, $J = 7.2$ Hz, 1H, ArH), 6.85 (d,

$J = 8.4$ Hz, 2H, ArH, ArNH), 5.70 (d, $J = 9.0$ Hz, 1H, H-1), 5.16 (m, 2H, H-3, H-4), 4.82 (d, $J = 9.6$ Hz, 1H, gly–NH), 4.28 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.0$ Hz, 1H, H-6), 4.22 (m, 1H, H-2), 4.16 (m, 1H, H-6′), 4.08 (m, 2H, OCH_2CH_3), 3.82 (m, 1H, H-5), 2.13 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.05 (s, 6H, OAc), 1.45 (t, $J = 7.2$ Hz, $J = 6.6$ Hz, 3H, OCH_2CH_3).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-chlorophenyl)urea (**4d**)*

White crystals. IR (KBr) cm^{-1}: *v* 3344 (N–H), 3310 (N'–H), 1762/1733(C=O), 1689 (C=O), 1222 (O–C=O); ^1H NMR (600 MHz, $CDCl_3$), δ 8.04 (d, $J = 7.8$ Hz, 1H, ArH), 7.34 (d, $J = 7.8$ Hz, 1H, ArH), 7.25 (d, $J = 8.4$ Hz, 1H, ArH), 7.01 (t, $J = 7.2$ Hz, 1H, ArH), 6.83 (br s, 1H, ArNH), 5.72 (d, $J = 8.4$ Hz,1H, H-1), 5.17 (m, 2H, H-3, H-4), 5.14 (d, $J = 9.0$ Hz, 1H, gly–NH), 4.30 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.20 (m, 1H, H-2), 4.14 (dd, $J_{5,6'} = 1.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6′), 3.83 (m, 1H, H-5), 2.15 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.06 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(4-methyphenyl)urea (**4e**)*

White crystals. IR (KBr) cm^{-1}: *v* 3389 (N–H), 3353 (N'–H), 1756/1734 (C=O), 1683 (C=O), 1231 (O–C–O); ^1H NMR (600 MHz, $CDCl_3$), δ 7.13 (br s, 4H, ArH), 6.44 (br s, 1H, ArNH), 5.73 (d, $J = 8.4$ Hz, 1H, H-1), 5.15 (m, 2H, H-3, H-4), 4.83 (d, $J = 9.6$ Hz, 1H, gly–NH), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.15 (m, 2H, H-2, H-6′), 3.80 (m, 1H, H-5), 2.32 (s, 3H, CH_3), 2.14 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(4-ethoxylphenyl)urea (**4f**)*

White crystals. IR (KBr) cm^{-1}: *v* 3310 (N–H), 1757 (C=O), 1637 (C=O), 1228 (O–C–O); ^1H NMR (600 MHz, $CDCl_3$), δ 7.16 (d, $J = 7.8$ Hz, 2H, ArH), 6.89 (br s, 1H, ArNH), 6.84 (d, $J = 7.8$ Hz, 2H, ArH), 5.80 (d, $J = 8.4$ Hz, 1H, H-1), 5.24 (m, 2H, H-3, H-4), 5.14 (d, $J = 6.6$ Hz, 1H, gly–NH), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.0$ Hz, 1H, H-6), 4.13 (m, 2H, H-2, H-6′), 4.01 (m, 2H, OCH_2CH_3), 3.86 (m, 1H, H-5), 2.11 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.41 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(4-chlorophenyl)urea (**4g**)*

White crystals. IR (KBr) cm^{-1}: *v* 3346 (N–H), 1755 (C=O), 1655 (C=O), 1234 (O–C–O); ^1H NMR (600 MHz, $CDCl_3$), δ 7.28 (d, $J = 7.8$ Hz, 2H, ArH), 7.25 (d, $J = 7.8$ Hz, 2H, ArH), 7.23 (br s, 1H, ArNH), 5.77 (d, $J = 8.4$ Hz, 1H, H-1), 5.70 (d, $J = 9.0$ Hz, 1H, gly–NH), 5.24 (t, $J = 9.6$ Hz, 1H, H-3), 5.15 (t, $J = 9.6$ Hz, 1H, H-4), 4.27 (m, 1H, H-6), 4.13 (m, 2H, H-2, H-6′), 3.86 (m, 1H, H-5), 2.10 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.04 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(4-bromomethyphenyl)urea (**4h**)*

White crystals. IR (KBr) cm^{-1}: *v* 3394 (N–H), 1750 (C=O), 1682 (C=O), 1237 (O–C–O); ^1H NMR (600 MHz, $CDCl_3$), δ 7.42 (d, $J = 7.8$ Hz, 2H, ArH), 7.24 (d, $J = 7.8$ Hz, 2H, ArH), 6.90 (br s, 1H, ArNH), 5.75 (d, $J = 8.4$ Hz, 1H, H-1), 5.18 (m, 2H, H-3, H-4), 5.15 (d, $J = 9.6$ Hz, 1H, gly–NH), 4.30 (m, 1H, H-6), 4.18 (m, 2H, H-2, H-6′), 3.84 (m 1H, H-5), 2.15 (s, 3H, OAc), 2.12 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2,6-difluorophenyl)urea (**4i**)*

White crystals. IR (KBr) cm^{-1}: *v* 3330 (N–H), 1746 (C=O), 1663 (C=O), 1221 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 7.15 (t, $J = 7.2$ Hz, 1H, ArH), 6.90 (t, $J = 7.2$ Hz, $J = 8.4$ Hz, 2H, ArH), 6.62 (br s, 1H, ArNH), 5.75 (d, $J = 9.0$ Hz, 1H, H-1), 5.41 (d, $J = 9.6$ Hz, 1H, gly–NH), 5.24 (t, $J = 9.6$ Hz, $J = 10.2$ Hz, 1H, H-3), 5.12 (t, $J = 9.6$ Hz, $J = 9.0$ Hz, 1H, H-4), 4.26 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.0$ Hz, 1H, H-6), 4.15 (m, 2H, H-2, H-6′), 3.86 (m, 1H, H-5), 2.13 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.04 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2,6-dimethyphenyl)urea (**4j**)*

White crystals. IR (KBr) cm^{-1}: *v* 3382 (N–H), 1743 (C=O), 1672 (C=O), 1225 (O–C=O); ^1H NMR (600 MHz, $CDCl_3$), δ 7.11 (m, 3H, ArH), 6.11 (br s, 1H, ArNH), 5.70 (d, $J = 6.6$ Hz, 1H, H-1), 5.16 (t, $J = 9.0$ Hz, $J = 9.6$ Hz, 1H, H-3), 5.07 (t, $J = 9.0$ Hz, $J = 9.6$ Hz, 1H, H-4), 4.24 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.0$ Hz, 1H, H-6), 4.08 (d, $J = 12.0$ Hz, 2H, H-2, H-6′), 3.78 (m, 1H, H-5), 2.19 (s, 6H, CH_3), 2.12 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.99 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(3-methoxyphenyl)urea (**4k**)*

White crystals. IR (KBr) cm^{-1}: *v* 3380 (N–H), 3328 (N'–H), 1750 (C=O), 1679 (C=O), 1224 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 7.30 (s, 1H, ArH), 7.17 (t, $J = 8.4$ Hz, 1H, ArH), 6.99 (br s, 1H, ArNH), 6.81 (d, $J = 8.4$ Hz, 1H, ArH), 6.60 (d, $J = 8.4$ Hz, 1H, ArH), 5.84 (d, $J = 8.4$ Hz, 1H, H-1), 5.53 (d, $J = 9.6$ Hz, 1H, gly–NH), 5.31 (t, $J = 9.6$ Hz, $J = 10.2$ Hz, 1H, H-3), 5.14 (t, $J = 9.6$ Hz, 1H, H-4), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.12 (m, 2H, H-2, H-6′), 3.88 (m, 1H, H-5), 3.76 (s, 3H, OCH_3), 2.12 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(3,4-dimethyphenyl)urea (**4l**)*

White crystals. IR (KBr) cm^{-1}: *v* 3386 (N–H), 3353 (N'–H), 1755 (C=O), 1685 (C=O), 1227 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 7.09 (br s, 1H, ArNH), 7.04 (d, $J = 9.6$ Hz, 2H, ArH), 7.00 (d, $J = 7.8$ Hz, 1H, ArH), 5.82 (d, $J = 9.0$ Hz, 1H, H-1), 5.42 (d, $J = 9.6$ Hz, 1H, gly–NH), 5.29 (t, $J = 9.6$ Hz, $J = 10.2$ Hz, 1H, H-3), 5.12 (t, $J = 9.6$ Hz, 1H, H-4), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H,

H-6), 4.12 (d, $J = 12.6$ Hz, 1H, H-6′), 4.07 (m, 1H, H-2), 3.84 (m, 1H, H-5), 2.19 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 2.10 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.02 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-methyl-4-nitrophenyl)urea (**4m**)*

Yellow crystals. IR (KBr) cm^{-1}: *v* 3327 (N–H), 1756 (C=O), 1649 (C=O), 1217 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 8.11 (d, $J = 9.0$ Hz, 1H, ArH), 8.07 (m, 1H, ArH), 8.04 (s, 1H, ArH), 6.73 (br s, 1H, ArNH), 5.77 (d, $J = 8.4$ Hz, 1H, H-1), 5.42 (d, $J = 8.4$ Hz, 1H, gly–NH), 5.19 (m, 2H, H-3, H-4), 4.29 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.20 (m, 1H, H-2), 4.15 (d, $J = 12.6$ Hz, 1H, H-6′), 3.87 (m, 1H, H-5), 2.28 (s, 3H, CH_3), 2.14 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.06 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-nitro-4-methylphenyl)urea (**4n**)*

Yellow crystals. IR (KBr) cm^{-1}: *v* 3338 (N–H), 3276 (N'–H), 1760 (C=O), 1649 (C=O), 1222 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 9.59 (br s, 1H, ArNH), 8.46 (d, $J = 9.0$ Hz, 1H, ArH), 7.94 (s, 1H, ArH), 7.41 (d, $J = 9.0$ Hz, 1H, ArH), 5.92 (d, $J = 9.0$ Hz, 1H, H-1), 5.81 (d, $J = 9.0$ Hz, 1H, gly–NH), 5.34 (t, $J = 10.2$ Hz, 1H, H-3), 5.16 (t, $J = 9.6$ Hz, 1H, H-4), 4.31 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.23 (m, 1H, H-2), 4.17 (d, $J = 12.6$ Hz, 1H, H-6′), 3.93 (m, 1H, H-5), 2.35 (s, 3H, CH_3), 2.12 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.07 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-methoxy-4-nitrophenyl)urea (**4o**)*

Yellowish crystals. IR (KBr) cm^{-1}: *v* 3319 (N–H), 1758 (C=O), 1652 (C=O), 1228 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 8.37 (d, $J = 9.0$ Hz, 1H, ArH), 7.90 (m, 1H, ArH), 7.70 (d, $J = 2.4$ Hz, 1H, ArH), 7.29 (br s, 1H, ArNH), 5.72 (d, $J = 8.4$ Hz, 1H, H-1), 5.18 (m, 3H, H-3, H-4, gly–NH), 4.30 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.22 (m, 1H, H-2), 4.16 (dd, $J_{5,6'} = 2.4$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6′), 3.85 (m, 1H, H-5), 3.95 (s, 3H, OCH_3), 2.12 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.06 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-methyl-5-chlorophenyl)urea (**4p**)*

White crystals. IR (KBr) cm^{-1}: *v* 3324 (N–H), 1756 (C=O), 1648 (C=O), 1231 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 7.47 (s, 1H, ArH), 7.13 (d, $J = 8.4$ Hz, 1H, ArH), 7.10 (m, 1H, ArH), 6.23 (br s, 1H, ArNH), 5.78 (d, $J = 9.0$ Hz, 1H, H-1), 5.20 (t, $J = 9.6$ Hz, $J = 10.2$ Hz, 1H, H-3), 5.15 (t, $J = 9.6$ Hz, 1H, H-4), 4.83 (d, $J = 8.4$ Hz, 1H, gly–NH), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.12 (m, 2H, H-2, H-6′), 3.82 (m, 1H, H-5), 2.18 (s, 3H, CH_3), 2.15 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C NMR (125 MHz, $CDCl_3$), δ_C 171.1, 170.7, 169.5, 169.3, 155.3, 136.9, 132.0, 131.6, 129.3, 125.1, 124.1, 92.7, 72.7, 68.2, 63.1, 54.3, 21.0, 20.8, 20.6, 20.4, 17.2.

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2,5-dimethylphenyl) urea (**4q**)*

White crystals. IR (KBr) cm^{-1}: *v* 3399 (N–H), 3310 (N'–H), 1749 (C=O), 1665 (C=O), 1230 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 7.77 (s, 1H, ArH), 7.37 (br s, 1H, ArNH), 7.01 (d, $J = 7.8$ Hz, 1H, ArH), 6.77 (d, $J = 7.8$ Hz, 1H, ArH), 6.45 (d, $J = 9.0$ Hz, 1H, gly–NH), 5.86 (d, $J = 9.0$ Hz, 1H, H-1), 5.32 (t, $J = 9.6$ Hz, $J = 10.2$ Hz, 1H, H-3), 4.91 (t, $J = 9.6$ Hz, 1H, H-4), 4.20 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.08 (m, 1H, H-2), 4.01 (d, $J = 12.6$ Hz, 1H, H-6′), 3.89 (m, 1H, H-5), 2.22 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.06 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.95 (s, 3H, OAc).

General procedure for preparation of *N*-(1,3,4,6-tetra-*O*-acetyl)-2-deoxy-*β*-D-glucopyranosyl-*N'*-substituted phenylurea derivatives **4r–u**

To a solution of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-*β*-D-glucopyranose hydrohalide **1** (1.92 g, 5 mmol) in water (20 mL), sodium acetate (0.82 g, 10 mmol) was added, and the reaction was stirred for 60 min. Much white solid appeared. This was extracted three times with 20 mL CH_2Cl_2, and the extract was dried with anhydrous magnesium sulfate, filtered, and the liquid was added dropwise to a solution of aryl isocyanate (5 mmol) in dichloromethane (20 mL). The progress of the reaction was monitored by TLC. After evaporation to dryness, the crude product was purified by recrystallization (water–acetone).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(4-trifluoromethoxyphenyl) urea (**4r**)*

White crystals. IR (KBr) cm^{-1}: *v* 3339 (N–H), 1753 (C=O), 1681 (C=O), 1233 (O–C–O); ^1H NMR (600 MHz, $CDCl_3$), δ 7.32 (d, $J = 9.0$ Hz, 2H, ArH), 7.12 (d, $J = 9.0$ Hz, 2H, ArH), 7.02 (br s, 1H, ArNH), 5.77 (d, $J = 9.0$ Hz, 1H, H-1), 5.22 (m, 2H, gly–NH, H-3), 5.14 (t, $J = 9.6$ Hz, 1H, H-4), 4.28 (dd, $J_{5,6} = 4.8$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.13 (m, 2H, H-2, H-6′), 3.84 (m, 1H, H-5), 2.11 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(2-nitrophenyl)urea (**4s**)*

Yellowish crystals. IR (KBr) cm^{-1}: *v* 3353 (N–H), 3275 (N'–H), 1760 (C=O), 1651 (C=O), 1213 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 9.72 (br s, 1H, ArNH), 8.61 (d, $J = 8.4$ Hz, 1H, ArH), 8.14 (d, $J = 8.4$ Hz, 1H, ArH), 7.59 (t, $J = 7.8$ Hz, 1H, ArH), 7.06 (t, $J = 7.8$ Hz, 1H, ArH), 6.24 (s, 1H, gly–NH), 5.82 (d, $J = 9.0$ Hz, 1H, H-1), 5.37 (t, $J = 9.6$ Hz, $J = 10.2$ Hz, 1H, H-3), 5.17 (t, $J = 9.6$ Hz, 1H, H-4), 4.32 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.26 (m, 1H, H-2), 4.18 (d, $J = 12.6$ Hz, 1H, H-6′), 3.95 (m, 1H, H-5), 2.13 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.08 (s, 3H, OAc).

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(3-nitrophenyl)urea (**4t**)*

Yellowish crystals. IR (KBr) cm^{-1}: *v* 3359 (N–H), 3275 (N'–H), 1752 (C=O), 1655 (C=O), 1231 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 8.09 (s, 1H, ArH), 7.83 (d, $J = 7.8$ Hz, 1H, ArH), 7.79 (d, $J = 7.8$ Hz, 1H, ArH), 7.58 (br s, 1H, ArNH), 7.41 (t, $J = 8.4$ Hz, $J = 7.8$ Hz, 1H, ArH), 5.89 (d, $J = 8.4$ Hz, 1H, H-1), 5.54 (d, $J = 8.4$ Hz, 1H, gly–NH), 5.34 (t, $J = 10.2$ Hz, $J = 9.0$ Hz, 1H, H-3), 5.18 (t, $J = 9.6$ Hz, 1H, H-4), 4.31 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.0$ Hz, 1H, H-6), 4.19 (m, 2H, H-2, H-6′), 3.95(m, 1H, H-5), 2.15 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.06 (s, 3H, OAc); ^{13}C NMR (125 MHz, $CDCl_3$), δ_C 171.4, 170.8, 169.7, 169.5, 154.5, 148.4, 140.0, 131.3, 129.7, 125.0, 92.9, 72.7, 70.1, 62.4, 54.7, 21.0, 20.9, 20.6, 20.5.

*N-(1,3,4,6-tetra-O-acetyl)-2-deoxy-β-D-glucosyl-N'-(3-trifluoromethylphenyl)urea (**4u**)*

White crystals. IR (KBr) cm^{-1}: *v* 3371 (N–H), 1754 (C=O), 1677 (C=O), 1228 (C–O–C); ^1H NMR (600 MHz, $CDCl_3$), δ 7.59 (s, 1H, ArH), 7.55 (d, $J = 6.6$ Hz, 1H, ArH), 7.39 (t, $J = 7.2$ Hz, 1H, ArH), 7.29 (d, $J = 7.8$ Hz, 1H, ArH), 7.17 (br s, 1H, ArNH), 5.81 (d, $J = 8.4$ Hz, 1H, H-1), 5.24 (t, $J = 10.8$ Hz, $J = 9.6$ Hz, 2H, H-3, gly–NH), 5.17 (t, $J = 9.0$ Hz, $J = 9.6$ Hz, 1H, H-4), 4.29 (dd, $J_{5,6} = 4.2$ Hz, $J_{6,6'} = 12.6$ Hz, 1H, H-6), 4.16 (m, 2H, H-2, H-6′), 3.87 (m, 1H, H-5), 2.14 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc).

General procedure for preparation of 1-aryl-(1,2-dideoxy-α-D-glucofurano)-[2,1-*d*] imidazolidine-2-one derivatives **8a–j**, **8r**, and **8s**

To a solution *N*-(1,3,4,6-four-*O*-acetyl)-2-deoxy-*β*-D-glucopyranosyl-*N'*-substituted phenylureas **4** (2.5 mmol) in an 2:1 mixture of dichloromethane (40 mL) and methanol (20 mL) at 25 °C, a solution of sodium methoxide (135 mg, 2.5 mmol) in methanol (50 mL) was slowly added with stirring. The reaction was controlled by TLC (acetic ether–petroleum ether = 3:1). After the reaction was complete, the solution was neutralized by addition of Amberlite 732 (H^+ form). The resulting solution was filtered, washed with MeOH, and the filtrate was evaporated, then treated with aqueous acetic acid (30 mL, 30 %) and heated at 100 °C (external bath), for 30 min. After evaporation to dryness, the solid was crystallized from 96 % ethanol, affording **8**.

*1-(Phenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8a**)*

White crystals, yield 51 %, m.p. 212–215 °C. IR (KBr) cm^{-1}: *v* 3,400–3,100 (OH, NH), 1662 (C=O), 1074, 1023 (C–O); ^1H NMR (600 MHz, DMSO-d_6), δ 7.60 (d, $J = 8.0$ Hz, 2H, ArH), 7.53 (s, 1H, NH), 7.31 (t, $J = 7.8$ Hz, 2H, ArH), 7.05 (t, $J = 7.2$ Hz, 1H, ArH), 5.95 (d, $J = 6.0$ Hz, 1H, H-1), 4.08 (m, 1H, H-2), 3.98 (br d, $J = 6.0$ Hz, 1H, H-3), 3.75 (m, 1H, H-5), 3.68 (dd, $J_{3,4} = 1.6$ Hz, $J_{4,5} = 8.4$ Hz, 1H, H-4), 3.57 (dd, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 11.2$ Hz, 1H, H-6), 3.35 (m, 1H, H-6′).

*1-(2-Methoxyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8b**)*

White crystals, yield 43 %, m.p. 226–229 °C. IR (KBr) cm^{-1}: *v* 3,500–3,000 (OH, NH), 1686 (C=O), 1068, 1024 (C–O); ^{1}H NMR (600 MHz, DMSO-d_6), δ 7.27 (t, $J = 7.5$ Hz,1H, ArH), 7.19 (s, 1H, NH), 7.14 (d, $J = 7.8$ Hz, 1H, ArH), 7.05 (d, $J = 8.4$ Hz, 1H, ArH), 6.92 (t, $J = 7.5$ Hz, 1H, ArH), 5.73 (d, $J = 6.0$ Hz, 1H, H-1), 4.01 (br s,1H, H-2), 3.96 (br d, $J = 6.0$ Hz, 1H, H-3), 3.76 (s, 3H, OCH_3), 3.69 (m, 2H, H-4, H-5), 3.47 (d, $J = 10.8$ Hz,1H, H-6), 3.30 (m, 1H, H-6′); ^{13}C NMR (125 MHz, DMSO-d_6), δ_C 158.2, 155.5, 130.3, 128.2, 125.7, 120.2, 112.0, 89.8, 79.1, 74.5, 68.4, 64.0, 61.4, 55.5.

*1-(2-Ethoxylphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8c**)*

White crystals, yield 54 %, m.p. 234–236 °C. IR (KBr) cm^{-1}: *v* 3,400–3,100 (OH, NH), 1662 (C=O), 1086, 1025 (C–O); ^{1}H NMR (600 MHz, DMSO-d_6), δ 7.24 (t, $J = 7.8$ Hz, 1H, ArH), 7.20 (s, 1H, NH), 7.13 (d, $J = 7.8$ Hz, 1H, ArH), 7.04 (d, $J = 8.4$ Hz, 1H, ArH), 6.91 (t, $J = 7.8$ Hz, 1H, ArH), 5.81 (d, $J = 6.0$ Hz, 1H, H-1), 5.45 (br s, 1H, C3-OH), 5.05 (br s, 1H, C5-OH), 4.47 (br s, 1H, C6-OH), 4.05–4.00 (m, 3H, H-2, OCH_2CH_3), 3.96 (br d, $J = 6.0$ Hz, 1H, H-3), 3.72 (br d, $J = 8.4$ Hz, 1H, H-4), 3.68 (m, 1H, H-5), 3.45 (br d, $J = 10.2$ Hz, 1H, H-6), 3.28 (m, 1H, H-6′), 1.31 (t, $J = 6.6$ Hz, 3H, OCH_2CH_3).

*1-(2-Chlorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8d**)*

White crystals, yield 34 %, m.p. 257–260 °C. IR (KBr) cm^{-1}: *v* 3,600–3,100 (OH, NH), 1669 (C=O), 1085, 1036 (C–O); ^{1}H NMR (600 MHz, DMSO-d_6), δ 7.53 (m, 1H, ArH), 7.37 (m, 4H, ArH, NH), 5.76 (d, $J = 6.4$ Hz, 1H, H-1), 4.03 (m, 2H, H-2, H-3), 3.81 (dd, $J_{3,4} = 1.2$ Hz, $J_{4,5} = 8.8$ Hz, 1H, H-4), 3.71 (m, 1H, H-5), 3.51 (dd, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 10.8$ Hz, 1H, H-6), 3.35 (m, 1H, H-6′).

*1-(4-Methyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8e**)*

White crystals, yield 38 %, m.p. 226–228 °C. IR (KBr) cm^{-1}: *v* 3,450–3,100 (OH, NH), 1666 (C=O), 1084, 1037 (C–O); ^{1}H NMR (600 MHz, DMSO-d_6), δ 7.47 (s, 1H, NH), 7.44 (d, $J = 6.4$ Hz, 2H, ArH) 7.11 (d, $J = 8.0$ Hz, 2H, ArH), 5.91 (d, $J = 6.0$ Hz, 1H, H-1), 4.05 (m, 1H, H-2), 3.97 (br d, $J = 6.0$ Hz, 1H, H-3), 3.74 (m, 1H, H-5), 3.68 (dd, $J_{3,4} = 1.2$ Hz, $J_{4,5} = 8.0$ Hz, 1H, H-4), 3.56 (dd, $J_{5,6} = 2.0$ Hz, $J_{6,6'} = 11.2$ Hz, 1H, H-6), 3.40 (m, 1H, H-6′), 2.25 (s, 3H, CH_3).

*1-(4-Ethoxyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8f**)*

White crystals, yield 58 %, m.p. 227–229 °C. IR (KBr) cm^{-1}: *v* 3391, 3261 (OH, NH), 1661 (C=O), 1084, 1025 (C–O); ^{1}H NMR (600 MHz, DMSO-d_6), δ 7.42 (d, $J = 8.4$ Hz, 2H, ArH), 7.36 (s, 1H, NH), 6.88 (d, $J = 9.0$ Hz, 2H, ArH), 5.84 (d, $J = 6.0$ Hz, 1H, H-1), 5.39 (br s, 1H, C3-OH), 4.89 (br s, 1H, C5-OH), 4.51 (br s, 1H, C6-OH), 4.03(m, 2H, H-2, H-3), 3.98 (t, $J = 6.9$ Hz, 2H, OCH_2CH_3), 3.95

(m, 1H, H-4), 3.73 (m, 1H, H-5), 3.68 (br d, $J = 8.4$ Hz, 1H, H-6), 3.57 (m, 1H, H-6′), 1.30 (t, $J = 6.9$ Hz, 3H, OCH_2CH_3); ^{13}C NMR (125 MHz, DMSO-d_6), δ_C 157.5, 154.8, 132.0, 128.2, 122.0, 114.3, 90.1, 79.2, 74.2, 68.5, 63.8, 63.1, 60.6, 14.7.

*1-(4-Chlorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8g**)*

White crystals, yield 37%, m.p. 216–220 °C. IR (KBr) cm^{-1}: ν 3,450–3,100(OH, NH), 1689 (C=O), 1081, 1028 (C–O); ^1H NMR (600 MHz, DMSO-d_6), δ 7.62 (d, $J = 7.8$ Hz, 2H, ArH), 7.60 (s, 1H, NH), 7.37 (d, $J = 9.0$ Hz, 2H, ArH), 5.97 (d, $J = 6.0$ Hz, 1H, H-1), 5.32 (br s, 1H, C3–OH), 4.74 (br s, 1H, C5-OH), 4.54 (br s, 1H, C6-OH), 4.05(m, 1H, H-2), 3.93 (m, 1H, H-3), 3.74 (m, 1H, H-4), 3.69 (m, 1H, H-5), 3.56 (m, 1H, H-6), 3.36 (m, 1H, H-6′).

*1-(4-Bromophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8h**)*

White crystals, yield 36 %, m.p. 236–238 °C. IR (KBr) cm^{-1}: ν 3412, 3279 (OH, NH), 1670 (C=O), 1085, 1020 (C–O); ^1H NMR (600 MHz, DMSO-d_6), δ 7.66 (s, 1H, NH), 7.57 (d, $J = 8.4$ Hz, 2H, ArH), 7.49 (d, $J = 8.4$ Hz, 2H, ArH), 5.95 (d, $J = 6.6$ Hz, 1H, H-1), 4.06 (br s, 1H, H-2), 3.96 (br d, $J = 5.4$ Hz, 1H, H-3), 3.73 (m, 1H, H-5), 3.64 (br d, $J = 8.4$ Hz, 1H, H-4), 3.53 (br d, $J = 11.4$ Hz, H-6), 3.32 (m, 1H, H-6′).

*1-(2,6-Difluorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8i**)*

White crystals, yield 38 %, m.p. 236–238 °C. IR (KBr) cm^{-1}: ν 3,500–3,100 (OH, NH), 1693 (C=O), 1086, 1025 (C–O); ^1H NMR (600 MHz, DMSO-d_6), δ 7.59 (s, 1H, NH), 7.44 (m, 1H, ArH), 7.20 (d, $J = 7.2$ Hz, 2H, ArH), 5.71 (d, $J = 6.0$ Hz, 1H, H-1), 5.31 (d, $J = 4.2$ Hz, 1H, C3-OH), 4.83 (br s, 1H, C5-OH), 4.44 (br s, 1H, C6-OH), 4.09 (br d, $J = 6.0$ Hz, 1H, H-2), 4.03 (m, 1H, H-3), 3.71 (m, 2H, H-4, H-5), 3.47 (br d, $J = 10.8$ Hz, 1H, H-6), 3.25 (m, 1H, H-6′).

*1-(2,6-Dimethyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8j**)*

White crystals, yield 37 %, m.p. 246–248 °C. IR (KBr) cm^{-1}: ν 3483, 3387, 3252 (OH, NH), 1665 (C=O), 1084, 1037 (C–O); ^1H NMR (600 MHz, DMSO-d_6), δ 7.25 (s, 1H, NH), 7.13 (t, $J = 7.8$ Hz, $J = 7.2$ Hz, 1H, ArH), 7.09 (t, $J = 7.8$ Hz, 2H, ArH), 5.64 (d, $J = 6.0$ Hz, 1H, H-1), 4.10 (m, 2H, H-2, H-3), 3.83 (br d, $J = 9.0$ Hz, 1H, H-4), 3.72 (m, 1H, H-5), 3.55 (m, 1H, H-6), 3.32 (m, 1H, H-6′), 2.17 (s, 3H, CH_3), 2.12 (s, 3H, CH_3).

*1-(4-Trifluoromethoxy)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8r**)*

White crystals, yield 42 %, m.p. 214–216 °C. IR (KBr) cm^{-1}: ν 3419, 3278 (OH, NH), 1640 (C=O), 1084, 1023 (C–O); ^1H NMR (600 MHz, DMSO-d_6), δ 7.71 (d,

$J = 9.0$ Hz, 2H, ArH), 7.68 (s, 1H, NH), 7.33 (d, $J = 8.4$ Hz, 2H, ArH), 5.98 (d, $J = 6.6$ Hz, 1H, H-1), 4.08 (br s, 1H, H-2), 3.97 (br d, $J = 6.0$ Hz, 1H, H-3), 3.75 (m, 1H, H-4), 3.65 (m, 1H, H-5), 3.55 (m, 1H, H-6), 3.34 (m, 1H, H-6′).

*1-(2-Nitrophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d]imidazolidine-2-one (**8s**)*

White crystals, yield 43 %, m.p. 236–238 °C. IR (KBr) cm^{-1}: ν 3,430–3,300 (OH, NH), 1696 (C=O), 1526, 1359 (NO_2), 1083, 1024 (C–O); ^{1}H NMR (600 MHz, DMSO-d_6), δ 7.92 (d, $J = 7.8$ Hz, 1H, ArH), 7.74 (t, $J = 8.1$ Hz, 1H, ArH), 7.66(d, $J = 7.2$ Hz, 2H, ArH, NH), 7.46 (t, $J = 7.5$ Hz, 1H, ArH), 6.02 (d, $J = 6.0$ Hz, 1H, H-1), 5.28 (d, $J = 4.8$ Hz, 1H, C3-OH), 4.73 (d, $J = 5.4$ Hz, 1H, C5-OH), 4.46 (t, $J = 5.4$ Hz, 1H, C6-OH), 4.06–4.03 (m, 2H, H-2, H-3), 3.85 (dd, $J_{3,4} = 1.8$ Hz, $J_{4,5} = 9.6$ Hz, 1H, H-4), 3.76 (m, 1H, H-5), 3.58 (m, 1H, H-6), 3.41 (m, 1H, H-6′); ^{13}C NMR (125 MHz, DMSO-d_6), δ_C 156.6, 145.3, 133.8, 131.0, 127.3, 126.7, 125.0, 90.1, 79.6, 74.1, 68.4, 64.0, 61.8.

Antifungal activity testing

The antifungal activity of compounds **4** and **8** against four kinds of plant pathogenic fungi (*S. sclerotiorum*, *F. graminearum*, *F. oxysporm* and *B. maydis*) was tested in a greenhouse, at 27 °C, for 1–3 days. Solutions of the title compounds in a small amount of DMSO were diluted to a concentration of 1,000 mg/L with distilled water containing 0.1 % Tween 80. The agar medium (9.9 mL) which had been autoclaved at 121 °C for 20 min and kept at 55 °C was then poured into culture dishes containing 0.1 mL (1000 mg/L) of the synthesized compounds, allowed to solidify, then inoculated. A mixture of the same amount of water, DMSO, and Tween 80 was used as the control. Strains treated with water were the blank test. Each treatment was repeated three times and the diameters of inhibition zone in each dish were measured by the crossing method. The inhibition observed is summarized in Table 2.

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References

1. C. Bartolucci, L. Cellai, C. Martuccio, A. Rossi, A.L. Segre, S.R. Savu, L. Silvestro, Helv. Chim. Acta **79**, 1611 (1996)
2. H.A. El-Sayed, A.H. Moustafa, A.Z. Haikal, E.S.H. El-Ashry, Nucleoside Nucleotide Nucl. Acids **28**, 184 (2009)
3. C.W.T. Chang, C.K. Evans, J.Y. Takemoto, U.S. Patent 0,130, 357 2011
4. N. Ding, W. Zhang, G.K. Lv, Y.X. Li, Arch. Pharm. Chem. Life Sci. **344**, 786 (2011)
5. Z. Wimmer, L. Pechová, L. SIŻle, D. Šaman, P. Jedlička, M. Wimmerová, E. Kolehmainen, Bioorg. Med. Chem. **15**, 7126 (2007)
6. C.R. Kumar, C.H. Tsai, Y.S. Chao, J.C. Lee, Chem. Eur. J. **17**, 8696 (2011)

7. P.A. Yonova, G.M. Stoilkova, J. Plant Growth Regul. **23**, 280 (2004)
8. R.H. Tale, A.H. Rodge, G.D. Hatnapure, A.P. Keche, Bioorg. Med. Chem. Lett. **21**, 4648 (2011)
9. S.A. Khan, N. Singh, K. Saleem, Eur. J. Med. Chem. **43**, 2272 (2008)
10. M.S. Duan, J. Peckham, M. Edelstein, R. Ferris, W.M. Kazmierski, A. Spaltenstein, P. Wheelan, Z.P. Xiong, Bioorg. Med. Chem. Lett. **20**, 7397 (2010)
11. M. Vijjulatha, S.S. Kanth, Cent. Eur. J. Chem. **5**, 1064 (2007)
12. E.R. El-Sawy, F.A. Bassyouni, S.H. Abu-Bakr, H.M. Rady, M.M. Abdlla, Acta Pharm. **60**, 55 (2010)
13. Z. Moussa, M.A.M.Sh. El-Sharief, A.M.Sh. El-Sharief, Eur. J. Med. Chem. **46**, 2280 (2011)
14. A.M.Sh. El-Sharief, Z. Moussa, Eur. J. Med. Chem. **44**, 4315 (2009)
15. J.H. Chern, C.S. Chang, C.L. Tai, Y.C. Lee, C.C. Lee, I.J. Kang, C.Y. Lee, S.R. Shih, Bioorg. Med. Chem. Lett. **15**, 4206 (2005)
16. M.D.H. Aly, N.S. El-Mougy, M.M. Abdel-Kader, J Plant Pathol Microbiol. **1**, 4172 (2010)
17. Ó. López, S. Maza, I. Maya, J. Fuentes, J.G. Fernández-Bolaños, Tetrahedron **61**, 9058 (2005)
18. I. Maya, Ó. López, S. Maza, J.G. Fernández-Bolaños, J. Fuentes, Tetrahedron Lett. **44**, 8539 (2003)
19. M. Ávalos, R. Babiano, P. Cintas, J.L. Jiménez, J.C. Palacios, C. Valencia, Tetrahedron **49**, 2668 (1993)
20. M. Ávalos, R. Babiano, P. Cintas, M.B. Hursthouse, J.L. Jiménez, M.E. Light, J.C. Palacios, G. Silvero, Tetrahedron **61**, 7931 (2005)