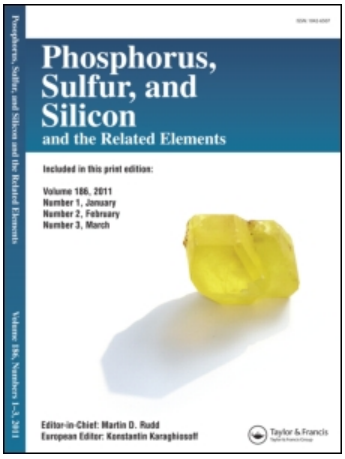

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A CONVENIENT SYNTHESIS OF GLYCOSYLATED HYDANTOINS AS POTENTIAL ANTIVIRAL AGENTS

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A CONVENIENT SYNTHESIS OF GLYCOSYLATED HYDANTOINS AS POTENTIAL ANTIVIRAL AGENTS

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Reaction of 5-arylidene-2-thiohydantoins **3a–d** with glycosyl halides **4a,b** under alkaline conditions gave the respective bisglycosylated derivatives **5a–h**. Deacetylation with ammonia in methanol caused a change of the S-glycosyl residue and gave the N-3 glycosylated analogues **7a–h**. S-Glycosylation also occured when N-3 substituted hydantoins **9a–h** were reacted.

Keywords: 2-Thiohydantoins; 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromides; monoglycosylated hydantoins; bisglycosylated hydantoins

INTRODUCTION

In continuation of the study on the synthesis of S-glucosylated hydantoins[1–3] the convenient syntheses of new glycosylated hydantoins with various heterocyclic side chains substituents at position 5 as potential antiviral agents are reported. Substituted hydantoins at C-5 are associated with a wide range of biological properties, including anticonvulsant[4], antidepressant[5], antiviral[6–8] and platelet inhibitory activities[9] and are a conspicuous structural feature of several inhibitors of aldose reductase[10]. Recently, the antiviral studies on a series of hydantoin nucleosides indicated that the most active compounds against both herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) were 5-(2-thienylidene)-3-aryl-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thiohydantoins[1]. Introduction of a furan-2-yl or thien-2-yl groups into the position 5 of 2′-deoxyuridine afforded compounds with marked activity against HSV-1[11,12].

RESULTS AND DISCUSSION

Heterocyclic aldehydes **2a–d** were condensed with 2-thiohydantoin **1** by refluxing in a solution of sodium acetate and acetic acid to give 5-arylidene-2-thiohydantoins **3a–d**. Compounds **3a–d** were reacted with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and D-galactopyranosyl bromides **4a,b**[13] in the presence of aqueous potassium carbonate to give 5-arylidene-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thiohydantoins **5a–d** and 5-arylidene-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-(2″,3″,4″,6″-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thiohydantoins **5e–h** respectively. When compound **1** was subjected to the reaction with **2a–d** and **4a,b** in the presence of alcoholic potassium carbonate, the corresponding hydantoin-2-thione glycosides **5a–h** were obtained. These compounds were shown to be the same as those obtained from the reaction of hydantoin-2-thiones **3a–d** with bromides **4a,b**. The structures of compounds **5** could be established and the reaction products confirmed on the basis of their elemental analysis and spectral data (IR, ^{1}H-NMR and MS). The IR spectrum of compound **5e** was characterized by the absence of signals for an NH group and the presence of acetoxy carbonyl groups at 1756 cm^{-1}. The ^{1}H-NMR spectrum of compound **5e** showed the presence of eight OAc. The doublet at δ 5.68 with spin-spin coupling constant 10.50 Hz which corresponds to the diaxial orientation of the H-1′ and H-2′ protons, indicating the presence of only the β-configuration[1]. Upon deprotection of **5a–h** with ammonia in methanol, the glycosylthio group was probably replaced by a methoxide group in a nucleophilic substitution reaction. Subsequent demethylation afforded the N-3 glycosyl hydantoin derivatives **7a–d**. This type of cleavage also explains the deprotection of the compounds **10a–p** in saturated methanolic ammonia was not successful. The structures of compounds **7a–d** could be established and confirmed for the reaction products on the basis of elemental analysis and spectral data (IR, ^{1}H-NMR and MS). The IR spectrum of compound **7e** was characterized by the absence of signals for an acetoxy group and the presence of OH and NH groups at 3400 cm^{-1}. The signal at 1767 cm^{-1} was due to C_2=O. The ^{1}H-NMR (DMSO-d_6) spectrum of 5-benzylidene-3-methylhydantoin has been reported to show N_1-H at 10.72 ppm while 5-benzylidene-1-methylhydantoin showed N_3-H at 11.38 ppm[14]. The ^{1}H-NMR (DMSO-d_6) spectrum of compound **7e** revealed the presence of a singlet at 10.68 ppm due to N_1-H, proving N-3 glycosylation. The singlet at δ 6.78 ppm assigned to the vinyl proton is an indication of the *Z*-configuration of the exocyclic double bond. The doublet at δ 4.82 ppm due to H-1′ with J = 9.50 Hz corresponds to the diaxial orientation of H-1′ and H-2′ protons, indicating the presence of the β-D-galactopyranose moiety. This proves the bisglycosylation

took place on reaction of **3a–d** with glycosyl halides **4a,b** under alkaline conditions at neither positions 2 and 3 nor positions 1 and 2.

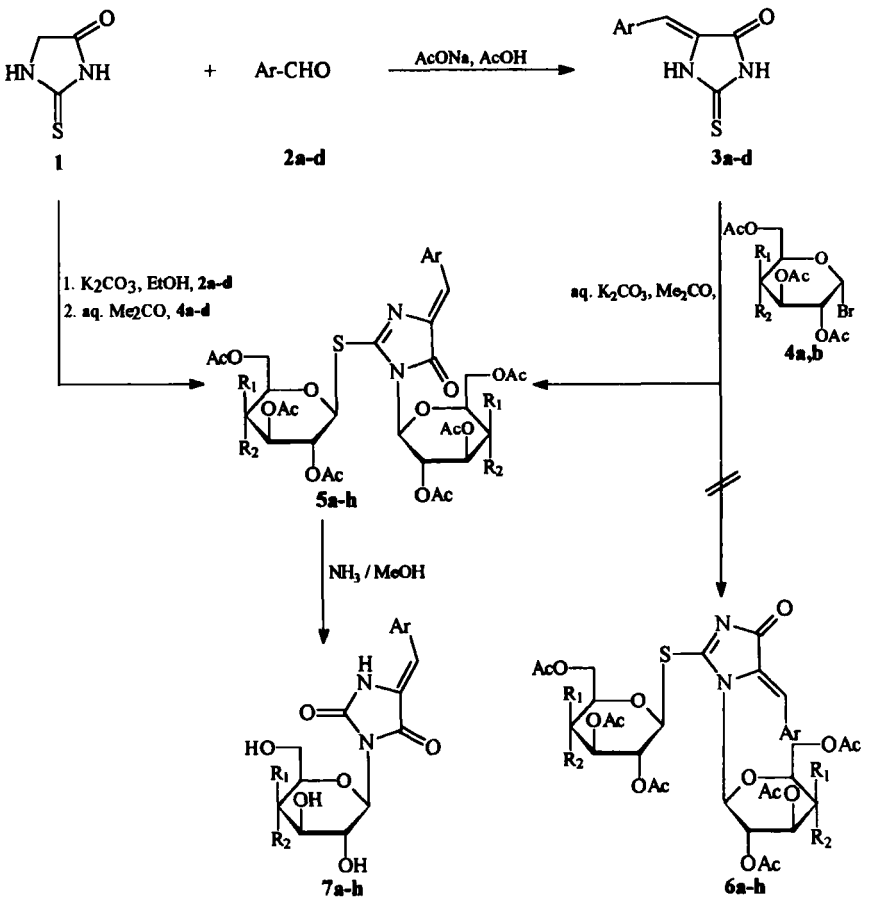
5-Arylidene-3-substituted-2-thiohydantoins **9a-h** were prepared from the condensation of **2a–d** with 3-substituted-2-thiohydantoins **8a,b** by refluxing in a solution of sodium acetate and acetic acid. Compounds **9a–h** were reacted with **4a,b** in the presence of aq. KOH to give 5-arylidene-3-substituted-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosyl)-2-thiohydantoins **10a–p**. When compounds **8a,b** were subjected to reaction with **2a–d** and **4a,b** in the presence of alcoholic KOH, the corresponding hydantoin-2-thione glycosides **10a–p** were obtained. These compounds were shown to be the same as those obtained from the reaction of hydantoin-2-thiones **9a–h** with bromides **4a,b**. The structure of compounds **10a–p** was established on the basis of elemental analysis and spectral data (IR, ^{1}H-NMR and MS). The IR spectrum of compound **10a** was characterized by the absence of a signal for an NH group and the presence of acetoxy carbonyl groups at 1756 cm^{-1}. The ^{1}H-NMR spectroscopy revealed the presence of a doublet at δ 6.00 ppm with spin-spin coupling constant 10.6 Hz which corresponds to the diaxial orientation of H-1′ and H-2′ protons, indicating the presence of only the β-configuration[1]. Treatment of **10a–p** with concentrated hydrochloric acid in refluxing ethanol afforded only the hydantoin derivatives **12a–h** as the unique product (a 2-thiohydantoin derivative is not formed) proving the existence of S-glycosides. This proves 5-arylidene-1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosyl)-3-substituted-2-thiohydantoins **11a–p** are not formed. The structure of compounds **12a–h** could be established and confirmed for the reaction products on the basis of elemental analysis and spectral data (IR and ^{1}H-NMR). The IR spectrum of compound **12a** was characterized by the absence of signals for an acetoxy carbonyl groups and the presence of N_1-H, C_2=O groups at 3290, 1717 cm^{-1}, respectively. The ^{1}H-NMR spectrum of **12a** revealed the presence of a singlet at δ 6.75 ppm assigned to vinyl proton indicating *Z*-configuration of the exocyclic double bond.

The antiviral activity of the prepared nucleosides is under biological evaluation studies.

EXPERIMENTAL

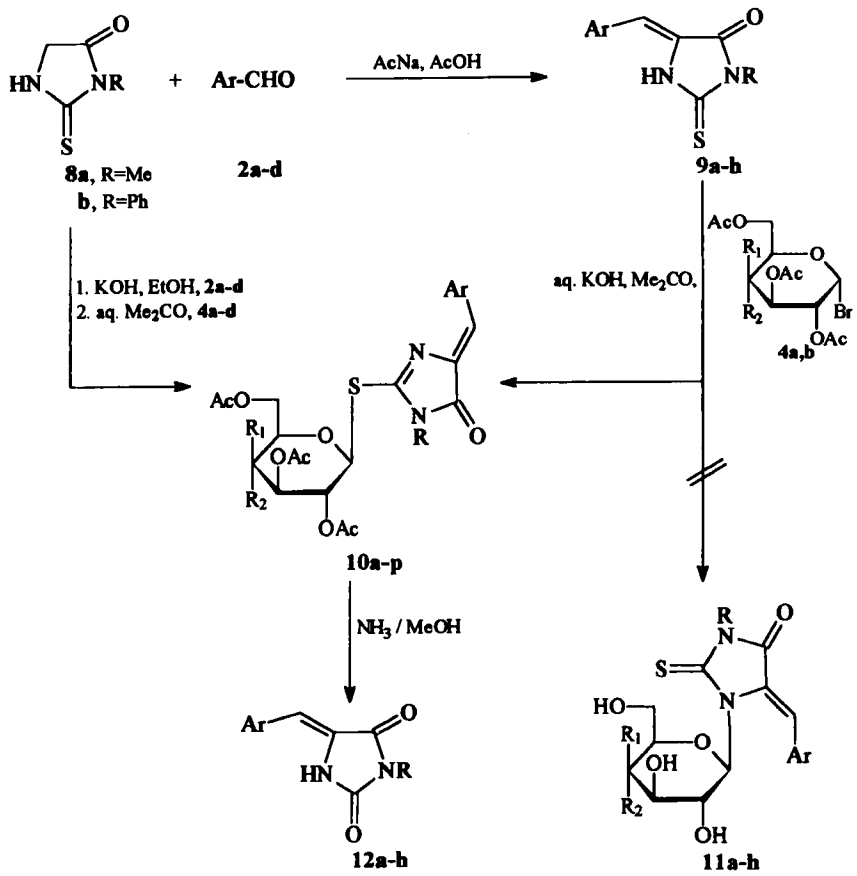
General Method

All Melting points are uncorrected. IR spectra (KBr disc) were obtained on Pye Unicom spectra-1000. ^{1}H-NMR spectra were measured on a Bruker A 250 FT



	Ar	R_1	R_2
3a	2-thienyl		
b	2-furyl		
c	3-indolyl		
d	2-pyridyl		
5a	2-thienyl	H	OAc
b	2-furyl	H	OAc
c	3-indolyl	H	OAc
d	2-pyridyl	H	OAc
e	2-thienyl	OAc	H
f	2-furyl	OAc	H

	Ar	R_1	R_2
g	3-indolyl	OAc	H
h	2-pyridyl	OAc	H
6,7a	2-thienyl	H	OH
b	2-furyl	H	OH
c	3-indolyl	H	OH
d	2-pyridyl	H	OH
e	2-thienyl	OH	H
f	2-furyl	OH	H
g	3-indolyl	OH	H
h	2-pyridyl	OH	H



	Ar	R	R_1	R_2
9,12a	2-thienyl	Me		
b	2-furyl	Me		
c	3-indolyl	Me		
d	2-pyridyl	Me		
e	2-thienyl	Ph		
f	2-furyl	Ph		
g	3-indolyl	Ph		
h	2-pyridyl	Ph		
10,11a	2-thienyl	Me	H	OAc
b	2-furyl	Me	H	OAc
c	3-indolyl	Me	H	OAc
d	2-pyridyl	Me	H	OAc

	Ar	R	R_1	R_2
e	2-thienyl	Me	OAc	H
f	2-furyl	Me	OAc	H
g	3-indolyl	Me	OAc	H
h	2-pyridyl	Me	OAc	H
i	2-thienyl	Ph	H	OAc
j	2-furyl	Ph	H	OAc
k	3-indolyl	Ph	H	OAc
l	2-pyridyl	Ph	H	OAc
m	2-thienyl	Ph	OAc	H
n	2-furyl	Ph	OAc	H
o	3-indolyl	Ph	OAc	H
p	2-pyridyl	Ph	OAc	H

NMR spectrometer for solutions in DMSO-d_6 using TMS as internal standard. Chemical shifts are expressed as (δ ppm). J values are given in Hz. Elementary analyses were performed at the Microanalytical Center of Cairo University. Aluminum sheets coated with silica gel 60 F_{254} (Merk) were used for TLC detection was effected by viewing under a short wavelength UV lamp.

5-Arylidene-2-thiohydantoins 3a–d

A mixture of the appropriate aldehyde **2a–d** (10 mmol), anhydrous sodium acetate (2.32 g, 28.3 mmol) and 2-thiohydantoin **1** (1.16 g, 10 mmol) in glacial acetic acid (14 ml) was refluxed for 2 h until the starting material was consumed (TLC with ether/benzene; 1:1). The reaction mixture was poured into cold water. The yellow solid obtained was filtered off and recrystallized from acetic acid to give the products **3a-d**.

5-(2-Thienylidene)-2-thiohydantoin 3a

Yield 1.72 g (89%); m.p. 248–249 °C (lit.[15] 245–247 °C).

5-(2-Furylidene)-2-thiohydantoin 3b

Yield 1.53 g (86%); m.p. 244–246 °C (lit.[15] 241–243 °C).

5-(3-Indolylidene)-2-thiohydantoin 3c

Yield 2.21 g (91%); m.p. 315–317 °C (lit.[1] 310–312 °C).

5-(2-Pyridylidene)-2-thiohydantoin 3d

Yield 1.68 g (82%); m.p. 248–250 °C. IR (KBr): ν 3298 cm^{-1} (NH), 1725 cm^{-1} (CO), 1478 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 6.70 (1H, s, =CH), 7.60–8.66 (4H, m, Ar-H), 11.30 (1H, s, N_1-H), 12.40 (1H, s, N_3-H). Calculated for $C_9H_7N_3OS$ (205.23): C, 52.67; H, 3.44; N, 20.47. Found: C, 53.04; H, 3.27; N, 20.40.

***5-Arylidene-2-(2',3',4',6'-tetra-O-acetyl-β-D-gluco- and D-galactopyranosyl)-3-(2",3",4",6"-tetra-O-acetyl-β-D-gluco- and D-galactopyranosyl)-2-thiohydantoins* 5a–h**

To a solution of 2-thiohydantoins **3a–d** (5 mmol) in aqueous potassium carbonate (0.7 g, 5 mmol, in distilled water 3 ml) was added a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-gluco- or D-galactopyranosyl bromides **4a,b** (4.52 g, 11 mmol) in acetone (30 ml).The reaction mixture was stirred 12 h at room temperature until the starting material was consumed (TLC with ether/petroleum ether, 40–60 °C; 1:1). The mixture was evaporated under reduced pressure at 40 °C and the residue was washed with distilled water to remove the potassium bromide formed. The solid product was dried and crystallized from absolute ethanol to give the products **5a–h**.

***5-(2-Thienylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-2",3",-4",6"-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin* 5a**

Yield 3.12 g (72%); m.p. 121–123 °C (lit.[1] yield 18%; m.p. 120–122 °C).

***5-(2-Furylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-(2",3",4",-6"-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin* 5b**

Yield 2.87 g (67%); m.p. 116–118 °C. IR (KBr): ν 1760, 1740 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 1.78, 1.88, 1.97, 2.00, 2.02, 2.03, 2.06, 2.08 (24H, 8s, 8Ac), 3.65–3.92 (2H, m, H-5', H-5"), 3.90–4.12 (4H, m, 2 × H-6', 2 × H-6"), 4.98–5.20 (2H, m, H-4', H-4"), 5.30–5.40 (4H, m, H-3', H-3", H-2", H-1"), 5.43 (1H, t, J = 9.1 Hz, H-2'), 5.64 (1H, d, J = 10.3 Hz, H-1'), 6.48 (1H, s, =CH), 7.10–7.75 (4H, m, Ar-H). Calculated for $C_{36}H_{42}N_3O_{20}S$ (868.80): C, 49.77; H, 4.87; N, 4.84. Found: C, 50.02; H, 5.14; N, 4.67.

***5-(2-Indolylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-(2",3",-4",6"-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin* 5c**

Yield 3.30 g (77%); m.p. 123–125 °C. IR (KBr): ν 1758, 1735 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 1.72, 1.86, 1.95, 2.00, 2.04, 2.05, 2.07 (24H, 7 s, 8Ac), 3.82–4.30 (6H, m, H-5', H-5", 2 × H-6', 2 × H-6"), 4.98–5.20 (2H, m, H-4', H-4"), 5.30–5.42 (4H, m, H-3', H-3", H-2", H-1"), 5.60 (1H, t, J = 9.2 Hz, H-2'), 5.82 (1H, d, J = 10.2 Hz, H-1'), 7.10–8.60 (6H, m, =CH, Ar-H). Cal-

culated for $C_{40}H_{45}N_3O_{19}S$ (903.87): C, 53.15; H, 5.02; N 4.65. Found: C, 53.55; H, 4.81; N, 4.90.

***5-(2-Pyridylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-(2'',3'',-4'',6''-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin* 5d**

Yield 3.27 g (76%); m.p. 106–108 °C. IR (KBr): ν 1760, 1730 cm^{-1} (2CO). Calculated for $C_{37}H_{43}N_3O_{19}S$ (865.82): C, 51.33; H, 5.01; N, 4.85. Found: C, 51.05; H, 5.23; N, 5.20.

***5-(2-Thienylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-(2'',-3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiohydantoin* 5e**

Yield 3.25 g (75%); m.p. 127–129 °C. IR (KBr): ν 1756, 1725 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6) δ 1.75, 1.86, 1.98, 2.02, 2.04, 2.05, 2.07, 2.12 (24H, 8s, 8Ac), 3.64–4.22 (6H, m, H-5', H-5'', 2 × H-6', 2 × H-6''), 4.86–5.20 (2H, m, H-4', H-4''), 5.30–5.42 (4H, m, H-3', H-3'', H-2'', H-1''), 5.56 (1H, t, J = 9.1 Hz, H-2'), 5.68 (1H, d, J = 10.5 Hz, H-1'), 7.10–7.75 (4H, m, =CH, Ar-H). Calculated for $C_{36}H_{42}N_3O_{19}S_2$ (884.86): C, 48.87; H, 4.78; N, 4.75. Found: C, 48.56; H, 4.72; N, 4.98.

***5-(2-Furylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-(2'',3'',-4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiohydantoin* 5f**

Yield 3.30 g (77%); m.p. 115–117 °C. IR (KBr): ν 1760, 1738 cm^{-1} (2CO). Calculated for $C_{36}H_{42}N_3O_{20}S$ (868.80): C, 49.77; H, 4.87; N, 4.84. Found: C, 50.15; H, 5.01; N, 4.57.

***5-(3-Indolylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-(2'',-3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiohydantoin* 5g**

Yield 3.16 g (74%); m.p. 130–132 °C. IR (KBr): ν 1756, 1737 cm^{-1} (2CO). Calculated for $C_{40}H_{45}N_3O_{19}S$ (903.87): C, 53.15; H, 5.02; N 4.65. Found: C 53.40; H 5.23; N 4.86.

***5-(2-Pyridylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-(2'',-3'',4'',6''-tetra-O-acetyl-β-D-galactopyranosyl)-2-thiohydantoin* 5h**

Yield 3.23 g (75%); m.p. 111–113 °C. IR (KBr): ν 1760, 1730 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 1.77, 1.86, 1.98, 2.02, 2.03, 2.05, 2.08, 2.12 (24H, 8s,

8Ac), 3.62–4.24 (6H, m, H-5′, H-5″, 2 × H-6′, 2 × H-6″), 4.85–5.22 (6H, m, H-4′, H-4″, H-3′, H-3″, H-2″, H-1″), 5.45 (1H, t, J = 9.1 Hz, H-2′), 5.64 (1H, d, J = 10.5 Hz, H-1′), 7.10 (1H, s, =CH), 7.60–8.70 (4H, m, Ar-H). Calculated for $C_{37}H_{43}N_3O_{19}S$ (865.82): C, 51.33; H, 5.01; N, 4.85. Found: C, 51.63; H, 5.15; N, 4.98.

5-Arylidene-3-(β-D-gluco- and D-galactopyranosyl)hydantoins 7a–h

The protected nucleoside **5** (2.5 mmol) was stirred in saturated NH_3/MeOH (50 ml) at room temperature for 1 day. The solvent was removed *in vacuo* at 40 °C to give a solid residue, which was crystallized from methanol to give the products **7a–h**.

5-(2-Thienylidene)-3-(β-D-glucopyranosyl)hydantoin 7a

Yield 0.68 g (76%); m.p. 216–218 °C (lit.[1] 213–215 °C).

5-(2-Furylidene)-3-(β-D-glucopyranosyl)hydantoin 7b

Yield 0.62 g (73%); m.p. 188–190 °C. IR (KBr): ν 3400 (OH, NH), 1768, 1720 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6) δ 3.12 (1H, m, H-4′), 3.25 (1H, m, H-3′), 3.45 (2H, m, H-6′, 6″), 3.70 (1H, dd, J = 5.6, 10.6 Hz, H-5′), 4.22 (1H, m, H-2′), 4.50 (1H, t, J = 5.6 Hz, 6′-OH), 4.86 (1H, d, J = 9.2 Hz, H-1′), 5.00 (1H, d, J = 5.2 Hz, 4′-OH), 5.10 (1H, d, J = 5.0 Hz, 3′-OH), 5.30 (1H, d, J = 4.8 Hz, 2′-OH), 6.38 (1H, s, =CH), 7.08 (1H, dd, J = 1.7, 3.3 Hz, H-4 furyl), 7.38 (1H, d, J = 3.2 Hz, H-3 furyl), 7.74 (1H, d, J = 1.8 Hz, H-5 furyl), 10.86 (1H, s, N_1-H). Calculated for $C_{14}H_{16}N_2O_8$ (340.29): C, 49.41; H, 4.74; N, 8.23. Found: C, 49.70; H, 4.91; N, 8.45.

5-(3-Indolylidene)-3-(β-D-glucopyranosyl)hydantoin 7c

Yield 0.73 g (75%); m.p. 221–223 °C. IR (KBr): ν 3408 cm^{-1} (OH, NH), 1770, 1730 cm^{-1} (2CO). Calculated for $C_{18}H_{19}N_3O_7$ (389.36): C, 55.53; H, 4.92; N, 10.79. Found: C, 55.80; H, 4.76; N, 11.14.

5-(2-Pyridylidene)-3-(β-D-glucopyranosyl)hydantoin 7d

Yield 0.65 g (74%); m.p. 179–181 °C. IR (KBr): ν 3402 cm^{-1} (OH, NH), 1767, 1725 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.10 (1H, m, H-4′), 3.20 (1H, m, H-3′), 3.42 (2H m, H-6′, 6″), 3.70 (1H, dd, J = 5.7, 10.6 Hz, H-5′), 4.21 (1H,

m, H-2′), 4.58 (1H, t, J = 5.8 Hz, 6′-OH), 4.86 (1H, d, J = 9.6 Hz, H-1′), 5.00 (1H, d, J = 5.1 Hz, 4′-OH), 5.08 (1H, d, J = 5.0 Hz, 3′-OH), 5.30 (1H, d, J = 4.8 Hz, 2′-OH), 6.75 (1H, s, =CH), 7.60–8.70 (4H, m, Ar-H), 10.50 (1H, s, N_1-H). Calculated for $C_{15}H_{17}N_3O_7$ (351.32): C, 51.28; H 4.88; N 11.96. Found: C, 51.68; H, 5.17; N, 11.66.

***5-(2-Thienylidene)-3-(β-D-galactopyranosyl)hydantoin* 7e**

Yield 0.60 g (67%); m.p. 218–220 °C. IR (KBr): ν 3400 cm^{-1} (OH, NH), 1763, 1719 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.08 (1H, m, H-4′), 3.22 (1H, m, H-3′), 3.45 (2H, m, H-6′, 6″), 3.70 (1H, dd, J = 5.6, 11.0 Hz, H-5′), 4.20 (1H, m, H-2′), 4.60 (1H, t, J = 5.8 Hz, 6′-OH), 4.82 (1H, d, J = 9.5 Hz, H-1′), 5.00 (1H, d, J = 5.1 Hz, 4′-OH), 5.10 (1H, d, J = 5.0 Hz, 3′-OH), 5.30 (1H, d, J = 4.8 Hz, 2′-OH), 6.78 (1H, s, =CH), 7.20 (1H, dd, J = 4.0, 5.0 Hz, H-4 thienyl), 7.65 (1H, d, J = 3.7 Hz, H-3 thienyl), 7.76 (1H, d, J = 3.7 Hz, H-5 thienyl), 10.68 (1H, s, N_1-H). Calculated for $C_{14}H_{16}N_2O_7S$ (356.35): C, 47.19; H, 4.53; N, 7.86. Found: C, 47.54; H, 4.30; N, 8.05.

***5-(2-Furylidene)-3-(β-D-galactopyranosyl)hydantoin* 7f**

Yield 0.66 g (78%); m.p. 201–203 °C. IR (KBr): ν 3390 cm^{-1} (OH, NH), 1770, 1720 cm^{-1} (2CO). Calculated for $C_{14}H_{16}N_2O_8$ (340.29): C, 49.41; H, 4.74; N, 8.23. Found: C 49.63; H 4.86; N 7.98.

***5-(3-Indolylidene)-3-(β-D-galactopyranosyl)hydantoin* 7g**

Yield 0.75 g (77%); m.p. 224–226 °C. IR (KBr): ν 3386 cm^{-1} (OH, NH), 1767, 1728 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.12 (1H, m, H-4′), 3.26 (1H, m, H-3′), 3.43 (2H, m, H-6′, 6″), 3.72 (1H, dd, J = 5.6, 10.6 Hz, H-5′), 4.22 (1H, m, H-2′), 4.55 (1H, t, J = 5.6 Hz, 6′-OH), 4.83 (1H, d, J = 9.4 Hz, H-1′), 5.00 (1H, d, J = 5.2 Hz, 4′-OH), 5.10 (1H, d, J = 4.7 Hz, 3′-OH), 5.30 (1H, d, J = 4.9 Hz, 2′-OH), 6.75 (1H, s, =CH), 7.10–7.26 (3H, m, H-4, H-5, H-6 indole), 8.12 (1H, d, H-7 indole), 8.38 (1H, d, H-2 indole), 10.60 (1H, s, N_1-H). Calculated for $C_{18}H_{19}N_3O_7$ (389.36): C, 55.53; H, 4.92; N, 10.79. Found: C, 55.91; H, 4.85; N, 11.02.

***5-(2-Pyridylidene)-3-(β-D-galactopyranosyl)hydantoin* 7h**

Yield 0.66 g (75%); m.p. 193–195 °C. IR (KBr): ν 3390 cm^{-1} (OH, NH), 1770, 1720 cm^{-1} (2CO). Calculated for $C_{15}H_{17}N_3O_7$ (351.32): C, 51.28; H 4.88; N 11.96. Found: C 51.64; H 5.06; N 12.20.

5-Arylidene-3-substituted-2-thiohydantoins **9a–h**

A mixture of aldehyde **2** (10 mmol), anhydrous sodium acetate (2.32 g, 28.3 mmol) and the appropriate 3-substituted-2-thiohydantoins **8a,b** (10 mmol) in glacial acetic acid (14 ml) was refluxed for 2 h until the starting material was consumed (TLC with ether/benzene; 1 : 1). The reaction mixture was poured into cold water. The yellow solid obtained was filtered off and recrystallized from acetic acid to give the products **9a–h**.

5-(2-Thienylidene)-3-methyl-2-thiohydantoin **9a**

Yield 1.90 g (85%); m.p. 235–237 °C. IR (KBr): ν 3300 cm^{-1} (NH), 1720 cm^{-1} (CO), 1490 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 3.00 (1H, s, Me), 6.72 (1H, s, =CH), 7.20–7.86 (3H, m, Ar-H), 12.20 (1H, s, N_1-H). Calculated for $C_9H_8N_2OS_2$ (224.30): C, 48.19; H, 3.60; N, 12.49. Found: C, 48.06; H 3.35; N 12.78.

5-(2-Furylidene)-3-methyl-2-thiohydantoin **9b**

Yield 1.87 g (90%); m.p. 226–228 °C. IR (KBr): ν 3298 cm^{-1} (NH), 1722 cm^{-1} (CO), 1500 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 2.98 (1H, s, Me), 6.45 (1H, s, =CH), 6.70–7.90 (3H, m, Ar-H), 12.05 (1H, s, N_1-H). Calculated for $C_9H_8N_2O_2S$ (208.23): C, 51.91; H, 3.87; N, 13.45. Found: C, 52.02; H, 3.96; N, 13.38.

5-(3-Indolylidene)-3-methyl-2-thiohydantoin **9c**

Yield 2.46 g (89%); m.p. 280–282 °C. IR (KBr): ν 3300 (NH), 1725 cm^{-1} (CO), 1498 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 3.10 (1H, s, Me), 6.92 (1H, s,=CH), 7.20–8.90 (5H, m, Ar-H), 12.20 (2H, s, N-H indole, N_1-H). Calculated for $C_{13}H_{11}N_3OS$ (257.31): C, 60.68; H, 4.31; N, 16.33. Found: C, 61.00; H, 4.25; N, 16.47.

5-(2-Pyridylidene)-3-methyl-2-thiohydantoin **9d**

Yield 1.88 g (86%); m.p. 176–178 °C. IR (KBr): ν 3300 cm^{-1} (NH), 1720 cm^{-1} (CO), 1480 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 3.10 (1H, s, Me), 6.75 (1H, s, =CH), 7.60–8.70 (4H, m, Ar-H), 12.45 (1H, s, N_1-H). Calculated for $C_{10}H_9N_3OS$ (219.26): C, 54.78; H, 4.14; N, 19.16. Found: C, 54.95; H, 4.08; N, 19.22.

5-(2-Thienylidene)-3-phenyl-2-thiohydantoin **9e**

Yield 2.66 g (93%); m.p. 241–243°C (lit.[14] 239–241°C).

5-(2-Furylidene)-3-phenyl-2-thiohydantoin **9f**

Yield 2.53 g (94%); m.p. 238–240°C. IR (KBr): ν 3300 cm^{-1} (NH), 1718 cm^{-1} (CO), 1500 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 6.44 (1H, s,=CH), 6.70–7.90 (8H, m, Ar-H), 12.12 (1H, s, N_1-H). Calculated for. $C_{14}H_{10}N_2O_2S$ 270.31): C, 62.21; H, 3.73; N, 10.36. Found: C, 62.32; H, 3.79; N, 10.30.

5-(3-Indolylidene)-3-phenyl-2-thiohydantoin **9g**

Yield 2.81 g (88%); m.p. 301–303°C (lit.[1] 298–300°C).

5-(2-Pyridylidene)-3-phenyl-2-thiohydantoin **9h**

Yield 2.67 g (95%); m.p. 258°C. IR (KBr): ν 3280 cm^{-1} (NH), 1730 cm^{-1} (CO), 1500 cm^{-1} (CS). ^{1}H-NMR (DMSO-d_6): δ 6.80 (1H, s,=CH), 7.40–8.70 (9H, m, Ar-H), 12.32 (1H, s, N_1-H). Calculated for $C_{15}H_{11}N_3OS$ (281.33): C, 64.04; H, 3.94; N, 14.94. Found: C, 63.80; H, 3.76; N, 15.08.

5-Arylidene-2-(2',3',4',6'-tetra-O-acetyl-β-D-gluco- and D-galactopyranosyl)-3-substituted-2-thiohydantoins **10a–p**

To a solution of 5-arylidene-3-substituted-2-thiohydantoins **9a–h** (5 mmol) in aqueous potassium hydroxide (0.28 g, 5 mmol, in distilled water 3 ml) was added a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-gluco- or D-galactopyranosyl bromides **4a,b** (2.26 g, 5.5 mmol) in acetone (20 ml). The reaction mixture was stirred 6 h at room temperature until the starting material was consumed (TLC with ether/petroleum ether, 40–60°C; 1 : 1). The mixture was evaporated under reduced pressure at 40°C and the residue was washed with distilled water to remove the sodium bromide formed. The solid product was dried and crystallized from absolute ethanol to give the products **10a–p**.

5-(2-Thienylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-methyl-2-thiohydantoin **10a**

Yield 4.82 g (87%); m.p. 182–184°C. IR (KBr): ν 1756 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.70, 1.97, 2.02, 2.12 (12H, 4s, 4Ac), 3.06 (1H, s, Me), 4.00–4.16 (2H, m, H-6', 6''), 4.50 (1H, t, J = 6.2 Hz, H-5'), 5.22 (1H, t, J = 10.3 Hz,

H-4'), 5.40 (1H, d, J = 3.4 Hz, H-2'), 5.54 (1H, dd, J = 3.6, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.6 Hz, H-1'), 7.18 (1H, t, J = 3.8 Hz, H-4 thienyl), 7.36 (1H, s, =CH), 7.72 (1H, d, J = 3.4 Hz, H-3 thienyl), 7.86 (1H, d, J = 5.2 Hz, H-5 thienyl). Calculated for $C_{23}H_{26}N_2O_{10}S_2$ (554.59): C, 49.81; H, 4.73; N, 5.05. Found: C, 50.23; H, 4.90; N, 5.35.

***5-(2-Furylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-methyl-2-thiohydantoin* 10b**

Yield 4.76 (88%); m.p. 174–176°C. IR (KBr): ν 1752 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.80, 1.95, 2.00, 2.02 (12H, 4s, 4Ac), 3.00 (1H s, Me), 4.00–4.17 (2H, m, H-6', 6''), 4.48 (1H, t, J = 6.1 Hz, H-5'), 5.15 (1H, t, J = 10.2 Hz, H-4'), 5.37 (1H, d, J = 3.4 Hz, H-2'), 5.55 (1H, dd, J = 3.5, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.2 Hz, H-1'), 6.45 (1H, s, =CH), 6.72 (1H s, H-4 furyl), 7.20 (1H, d, J = 3.4 Hz, H-3 furyl), 7.89 (1H, s, H-5 furyl). Calculated for $C_{23}H_{26}N_2O_{11}S$ (538.53): C, 51.30; H, 4.87; N, 5.20. Found: C, 51.63; H, 4.80; N, 5.52.

***5-(3-Indolylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-methyl-2-thiohydantoin* 10c**

Yield 5.00 g (85%); m.p. 187–189°C. IR (KBr): ν 1755 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.62, 1.90, 2.03, 2.08 (12H, 4s, 4Ac), 3.10 (1H, s, Me), 4.00–4.18 (2H, m, H-6', 6''), 4.55 (1H, t, J = 6.8 Hz, H-5'), 5.20 (1H, t, J = 10.0 Hz, H-4'), 5.40 (1H, d, J = 3.4 Hz, H-2'), 5.65 (1H, dd, J = 3.6, 10.0 Hz, H-3'), 6.00 (1H, d, J = 10.3 Hz, H-1'), 7.20–8.66 (11H, m,=CH Ar-H). Calculated for $C_{27}H_{29}N_3O_{10}S$ (587.60): C, 55.14; H, 4.97; N, 7.15. Found: C, 55.51; H, 5.20; N, 7.36.

***5-(2-Pyridylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-methyl-2-thiohydantoin* 10d**

Yield 4.72 (86%); m.p. 186–188°C. IR (KBr): ν 1753 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.70, 1.96, 2.03, 2.09 (12H, 4s, 4Ac), 3.02 (1H, s, Me), 4.00–4.15 (2H, m, H-6', 6''), 4.53 (1H, t, J = 6.2 Hz, H-5'), 5.22 (1H, t, J = 10.0 Hz, H-4'), 5.40 (1H, d, J = 3.5 Hz, H-2'), 5.56 (1H, dd, J = 3.4, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.4 Hz, H-1'), 7.60–8.66 (4H, m, Ar-H). Calculated for $C_{24}H_{27}N_3O_{10}S$ (549.55): C, 52.45; H, 4.95; N, 7.65. Found: C, 52.68; H, 5.12; N, 7.90.

***5-(2-Thienylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-phenyl-2-thiohydantoin* 10e**

Yield 5.6 g (91%); m.p. 192–193°C (lit.[1] 188–190°C).

***5-(2-Furylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-phenyl-2-thiohydantoin* 10f**

Yield 5.24 g (85%); m.p. 184–186°C. IR (KBr): ν 1752 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.81, 1.96, 2.00, 2.03 (12H, 4s, 4Ac), 4.02–4.22 (2H, m, H-6', 6''), 4.48 (1H, t, J = 6.1 Hz, H-5'), 5.15 (1H, t, J = 10.2 Hz, H-4'), 5.36 (1H, d, J = 3.4 Hz, H-2'), 5.55 (1H, dd, J = 3.5, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.2 Hz, H-1'), 6.45 (1H, s, =CH), 6.70–8.00 (8H, m, Ar-H). Calculated for $C_{28}H_{28}N_2O_{11}S$ (600.60): C, 56.00; H, 4.70; N, 4.66. Found: C, 56.26; H, 4.86; N, 5.00.

***5-(3-Indolylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-phenyl-2-thiohydantoin* 10g**

Yield 5.32 g (82%); m.p. 215–217 °C (lit.[1] 213–215 °C).

***5-(2-Pyridylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-3-phenyl-2-thiohydantoin* 10h**

Yield 5.25 g (86%); m.p. 190–191 °C. IR (KBr): ν 1755 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.82, 1.96, 2.00, 2.04 (12H, 4s, 4Ac), 4.02–4.20 (2H, m, H-6', 6''), 4.48 (1H, t, J = 6.1 Hz, H-5'), 5.13 (1H, t, J = 9.7 Hz, H-4'), 5.37 (1H, d, J = 3.4 Hz, H-2'), 5.55 (1H, dd, J = 3.6, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.3 Hz, H-1'), 7.10–8.86 (9H, m,=CH Ar-H). Calculated for $C_{29}H_{29}N_3O_{10}S$ (611.62): C, 56.95; H, 4.78; N, 6.87. Found: C, 57.28; H, 4.99; N, 7.07.

***5-(2-Thienylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-methyl-2-thiohydantoin* 10i**

Yield 4.65 g (87%); m.p. 188–190 °C. IR (KBr): ν 1755 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.72, 1.98, 2.04, 2.16 (12H, 4s, 4Ac), 3.06 (1H s, Me), 4.00–4.15 (2H, m, H-6', 6''), 4.50 (1H, t, J = 6.1 Hz, H-5'), 5.20 (1H, t, J = 10.2 Hz, H-4'), 5.42 (1H, d, J = 3.4 Hz, H-2'), 5.56 (1H, dd, J = 3.5, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.6 Hz, H-1'), 7.16 (1H, t, J = 3.8 Hz, H-4 thienyl), 7.36 (1H, s,

=CH), 7.72 (1H, d, J = 3.4 Hz, H-3 thienyl), 7.86 (1H, d, J = 5.2 Hz, H-5 thienyl). Calculated for $C_{23}H_{26}N_2O_{10}S_2$ (554.59): C, 49.81; H, 4.73; N, 5.05. Found: C, 50.18; H, 4.53; N, 5.25.

***5-(2-Furylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-methyl-2-thiohydantoin* 10j**

Yield 4.43 g (88%); m.p. 183–185 °C. IR (KBr): ν 1752 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.78, 1.97, 2.00, 2.04 (12H, 4s, 4Ac), 3.05 (1H, s, Me), 4.00–4.16 (2H, m, H-6', 6''), 4.50 (1H, t, J = 6.2 Hz, H-5'), 5.15 (1H, t, J = 10.0 Hz, H-4'), 5.35 (1H, d, J = 3.4 Hz, H-2'), 5.55 (1H, dd, J = 3.6, 9.7 Hz, H-3'), 6.00 (1H, d, J = 10.4 Hz, H-1'), 6.48 (1H, s,=CH), 6.70 (1H, s, H-4 furyl), 7.22 (1H, d, J = 3.4 Hz, H-3 furyl), 7.88 (1H, s, H-5 furyl). Calculated for $C_{23}H_{26}N_2O_{11}S$ (538.53): C, 51.30; H, 4.87; N, 5.20. Found: C, 51.00; H 5.17; N 5.45.

***5-(3-Indolylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-methyl-2-thiohydantoin* 10k**

Yield 5.15 g (87%); m.p. 198–200 °C. IR (KBr): ν 1752 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.68, 1.90, 2.04, 2.08 (12H, 4s, 4Ac), 3.12 (1H, s, Me), 4.00–4.16 (2H, m, H-6', 6''), 4.52 (1H, t, J = 6.8 Hz, H-5'), 5.20 (1H, t, J = 10.0 Hz, H-4'), 5.41 (1H, d, J = 3.4 Hz, H-2'), 5.65 (1H, dd, J = 3.6, 9.8 Hz, H-3'), 6.00 (1H, d, J = 10.2 Hz, H-1'), 7.20–8.70 (11H, m,=CH Ar-H). Calculated for $C_{27}H_{29}N_3O_{10}S$ (587.60): C, 55.14; H, 4.97; N, 7.15. Found: C, 55.40; H 5.02; N, 7.48.

***5-(2-Pyridylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-methyl-2-thiohydantoin* 10l**

Yield 4.50 g (82%); m.p. 191–193 °C. IR (KBr): ν 1752 cm^{-1} (CO). Calculated for $C_{24}H_{27}N_3O_{10}S$ (549.55): C, 52.45; H, 4.95; N, 7.65. Found: C, 52.78; H 5.15; N 7.80.

***5-(2-Thienylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-phenyl-2-thiohydantoin* 10m**

Yield 4.50 g (84%); m.p. 201–203 °C. IR (KBr): ν 1756 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.71, 1.98, 2.04, 2.12 (12H 4s, 4Ac), 4.00–4.15 (2H, m, H-6', 6''), 4.42 (1H, t, J = 6.0 Hz, H-5'), 5.24 (1H, t, J = 9.80 Hz, H-4'), 5.38 (1H, d, J

= 3.4 Hz, H-2'), 5.47 (1H, dd, J = 3.6, 9.8 Hz, H-3'), 6.02 (1H, d, J = 10.5 Hz, H-1'), 7.16–7.86 (8H, m, Ar-H). Calculated for $C_{28}H_{28}N_2O_{10}S_2$ (616.66): C, 54.54; H, 4.58; N, 4.54. Found: C, 54.76; H, 4.45; N, 4.82.

5-(2-Furylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-phenyl-2-thiohydantoin **10n**

Yield 5.30 g (86%); m.p. 186–198 °C. IR (KBr): ν 1758 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.84, 1.96, 2.05, 2.10 (12H, 4s, 4Ac), 4.00–4.24 (2H, m, H-6', 6''), 4.46 (1H, t, J = 6.1 Hz, H-5'), 5.18 (1H, t, J = 10.2 Hz, H-4'), 5.41 (1H, d, J = 3.5 Hz, H-2'), 5.55 (1H, dd, J = 3.6, 9.7 Hz, H-3'), 6.05 (1H, d, J = 10.4 Hz, H-1'), 6.46 (1H, s,=CH), 6.72–8.02 (8H, m, Ar-H). Calculated for $C_{28}H_{28}N_2O_{11}S$ (600.60): C, 56.00; H, 4.70; N, 4.66. Found: C, 56.32; H 4.86; N 4.53.

5-(3-Indolylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-phenyl-2-thiohydantoin **10o**

Yield 5.38 g (83%); m.p. 199–221 °C. IR (KBr): ν 1752 cm^{-1} (CO). ^{1}H-NMR (DMSO-d_6): δ 1.68, 1.98, 2.04, 2.08 (12H, 4s, 4Ac), 4.02–4.20 (2H, m, H-6', 6''), 4.44 (1H, t, J = 6.6 Hz, H-5'), 5.15 (1H, t, J = 9.9 Hz, H-4'), 5.41 (1H, d, J = 3.4 Hz, H-2'), 5.70 (1H, dd, J = 3.6, 9.6 Hz, H-3'), 6.18 (1H, d, J = 10.4 Hz, H-1'), 7.20–8.80 (11H, m,=CH Ar-H). Calculated for $C_{32}H_{31}N_3O_{10}S$ (649.67): C, 59.16; H, 4.81; N, 6.47. Found: C, 59.40; H, 5.01; N, 6.75.

5-(2-Pyridylidene)-2-(2',3',4',6'-tetra-O-acetyl-β-D-galactopyranosyl)-3-phenyl-2-thiohydantoin **10p**

Yield 4.88 g (80%); m.p. 195–197°C. IR (KBr): ν 1754 cm^{-1} (CO). Calculated for $C_{29}H_{29}N_3O_{10}S$ (611.62): C, 56.95; H, 4.78; N, 6.87. Found: C, 57.27; H, 5.10; N, 6.63.

5-Arylidene-3-substitutedhydantoins **12a–h**

A mixture of the protected nucleosides **10a–p** (2.5 mmol) and concentrated hydrochloric acid (5 ml) in ethanol (20 ml) was heated under reflux for 2 h until the starting material was consumed (TLC with $CHCl_3$/MeOH; 9.8:0.2). The solid, which separated, was collected and recrystallized from glacial acetic acid to give the products **12a–h**.

5-(2-Thienylidene)-3-methylhydantoin **12a**

Yield 0.82 g (79%); m.p. 213–215 °C. IR (KBr): ν 3290 cm^{-1} (NH), 1757, 1718 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.15 (3H, s, Me), 6.75 (1H, s,=CH), 7.20 (1H, dd, J = 3.8, 4.9 Hz, H-4 thienyl), 7.65 (1H, d, J = 3.8 Hz, H-3 thienyl), 7.80 (1H, d, J = 4.8 Hz, H-5 thienyl), 10.78 (1H, s, N_1-H). Calculated for $C_9H_8N_2O_2S$ (208.23): C, 51.91; H, 3.87; N, 13.45. Found: C, 51.76; H, 4.05; N 13.18.

5-(2-Furylidene)-3-methylhydantoin **12b**

Yield 0.70 g (73%); m.p. 203–205°C. IR (KBr): ν 3292 cm^{-1} (NH), 1760, 1725 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.05 (3H, s, Me), 6.38 (1H, s,=CH), 7.06 (1H, dd, J = 1.8, 3.2 Hz, H-4 furyl), 7.35 (1H, d, J = 3.1 Hz, H-3 furyl), 7.75 (1H, d, J = 1.7 Hz, H-5 furyl), 11.10 (1H, s, N_1-H). Calculated for $C_9H_8N_2O_3$ (192.17): C, 56.25; H, 4.20; N, 14.58. Found: C, 55.98; H, 4.15; N, 14.77.

5-(3-Indolylidene)-3-methylhydantoin **12c**

Yield 1.00 g (83%); m.p. 235–237°C. IR (KBr): ν 3280 cm^{-1} (NH), 1755, 1717 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.18 (3H, s, Me), 6.70 (1H s,=CH), 7.10–7.25 (3H, m, H-4, H-5, H-6 indole), 8.10 (1H, d, H-7 indole), 8.35 (1H, d, H-2 indole), 10.60 (1H, s, N_1-H). Calculated for $C_{13}H_{11}N_3O_2$ (241.25): C, 64.72; H, 4.60; N, 17.42. Found: C, 64.55; H 4.82; N 17.18.

5-(3-Pyridylidene)-3-methylhydantoin **12d**

Yield 0.68 g (67%); m.p. 210–212°C. IR (KBr): ν 3298 cm^{-1} (NH), 1765, 1719 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 3.12 (3H, s, Me), 6.55 (1H, s,=CH), 7.58–8.67 (3H, m, Ar-H), 10.45 (1H, s, N_1-H). Calculated for $C_{10}H_9N_3O_2$ (203.20): C, 59.11; H, 4.46; N, 20.68. Found: C, 58.84; H, 4.87; N 20.45.

5-(2-Thienylidene)-3-phenylhydantoin **12e**

Yield 1.05 g (78%); m.p. 232–234°C. IR (KBr): ν 3296 cm^{-1} (NH), 1766, 1723 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 6.85 (1H, s,=CH), 7.10–7.80 (8H, m, Ar-H), 10.65 (1H, s, N_1-H). Calculated for $C_{14}H_{10}N_2O_2S$ (270.31): C, 62.21; H, 3.73; N, 10.36. Found: C, 62.06; H, 3.60; N 10.15.

5-(2-Furylidene)-3-phenylhydantoin 12f

Yield 1.00 g (78%); m.p. 266–268°C. IR (KBr): ν 3287 cm^{-1} (NH), 1760, 1719 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 6.40 (1H, s,=CH), 6.60–8.30 (8H, m, Ar-H), 11.10 (1H, s, N_1-H). Calculated for $C_{14}H_{10}N_2O_3$ (254.25): C, 66.14; H, 3.96; N, 11.02. Found: C, 66.40; H 3.92; N, 11.30.

5-(3-Indolylidene)-3-phenylhydantoin 12g

Yield 1.20 g (71%); m.p. 284–286 °C. IR (KBr): ν 3280 cm^{-1} (NH), 1759, 1722 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 6.76 (1H, s,=CH), 7.10–8.40 (10H, m, Ar-H), 10.50 (1H, s, N_1-H), 11.78 (1H, s, NH indole). Calculated for $C_{18}H_{13}N_3O_2$ (303.32): C, 71.28; H, 4.32; N, 13.85. Found: C, 71.56; H, 4.15; N, 13.72.

5-(3-Pyridylidene)-3-phenylhydantoin 12h

Yield 0.90 g (68%); m.p. 250–252 °C. IR (KBr): ν 3292 cm^{-1} (NH), 1764, 1725 cm^{-1} (2CO). ^{1}H-NMR (DMSO-d_6): δ 6.60 (1H, s,=CH), 7.20–8.70 (9H, m, Ar-H), 10.50 (1H, s, N_1-H). Calculated for $C_{15}H_{11}N_3O_2$ (265.27): C, 67.92; H, 4.18; N, 15.84. Found: C, 67.68; H, 4.50; N, 15.71.

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