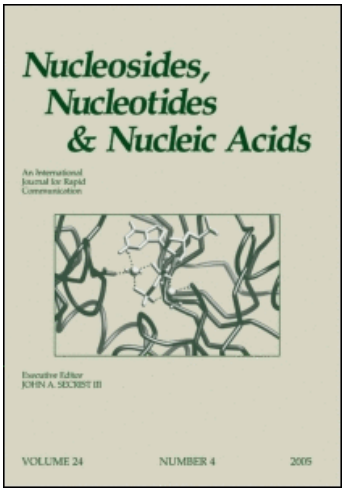

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SYNTHESIS OF 2-THIOHYDANTOINS AND THEIR *S*-GLUCOSYLATED DERIVATIVES AS POTENTIAL ANTIVIRAL AND ANTITUMOR AGENTS

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ABSTRACT

A series of 3-alkyl-5-((*Z*))-arylidene-2-thiohydantoins **4a-l** were synthesized from the direct condensation of the aromatic aldehydes with 3-alkyl-2-thiohydantoins **3a-c**, which in turn were prepared from the reaction of glycine (**1**) and alkyl isothiocyanates **2a-c**. The alkylation of **4a-l** with methylthioethyl chloride gave 5-((*Z*))-arylidene-3-alkyl-*S*-(2-methylthioethyl)-2-thiohydantoins **5a-e**. *S*-Glucosylation took place on the reaction of **4a-l** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide under anhydrous alkaline conditions. These structures have been confirmed from a model study of the coupling of **4a** with methylthioethyl chloride and α-D-glucose pentaacetate, respectively under Lewis acid conditions.

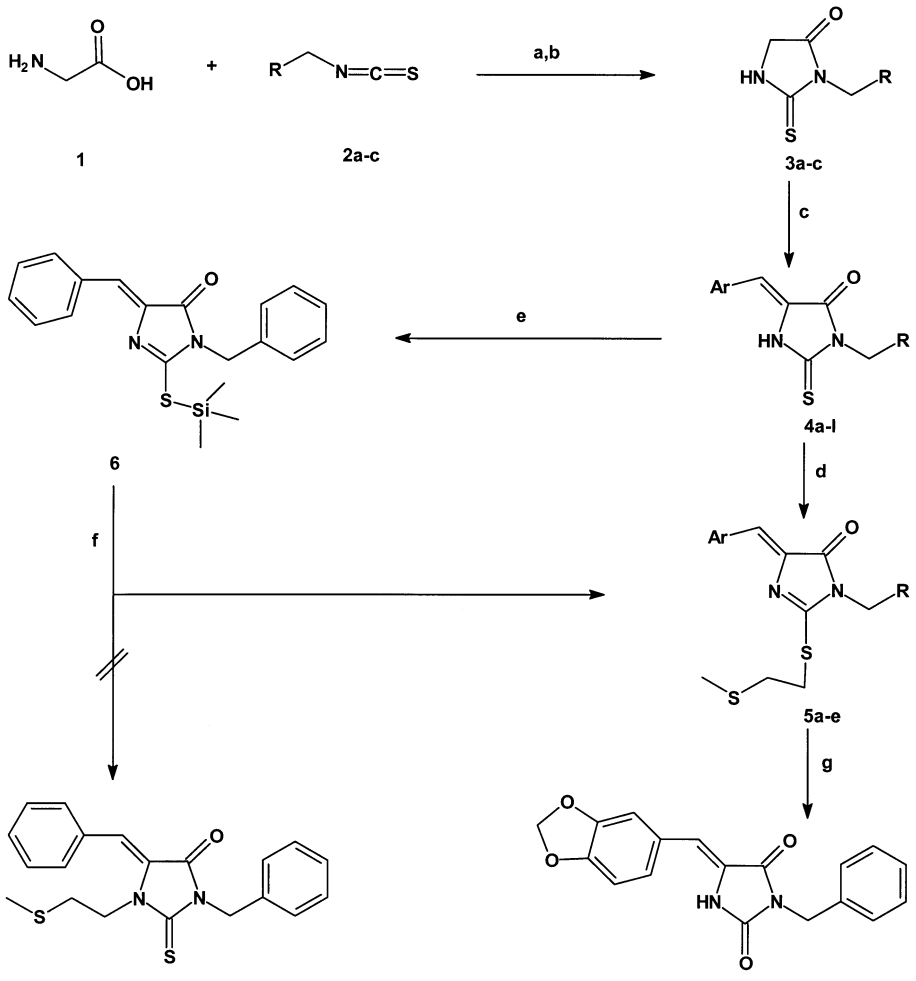
INTRODUCTION

The biological activity of hydantoin and 2-thiohydantoin derivatives has been known for a long time. The hydantoin nucleus containing an urea moiety is responsible for a variety of biological activities such as anti-arrhthmic[1], antihypertensive[2], antiviral[3] antispasmodic[4], anticonvulsant[5],

antiinflammatory[6] and antimicrobial activities[7]. Hydantoins are a conspicuous structural feature of several inhibitors of aldose reductase[8]. In addition, several 5-arylidene-3-aryl-2-thiohydantoins and their nucleosides show potent activity against the herpes simplex virus (HSV)[9], the human immunodeficiency virus (HIV)[10] and the leukemia subpanel[11]. In the course of identifying new chemical structures which may serve as leads for designing novel antitumor and antiviral agents, we were particularly interested in *S*-glycosylated of 2-thiohydantoins[9–15]. In this respect, the linking of the latter to a saturated hydrocarbon and sugar moieties were considered. The present work describes the synthesis of unreported series of 3-alkyl-5-((*Z*))-arylidene)-2-thiohydantoins (**4a-l**), 3-alkyl-5-((*Z*))-arylidene)-*S*-(2-methylthioethyl)-2-thiohydantoins (**5a-e**) and 3-alkyl-5-((*Z*))-arylidene)-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thiohydantoins (**9a-l**) as potential antiviral and antitumor activities.

RESULTS AND DISCUSSION

Glycine (**1**) was reacted with alkyl isothiocyanates **2a-c** in aqueous pyridine at 40 °C at pH = 9 to afford the corresponding thioureido derivatives as intermediates, which were cyclized by heating in 1N HCl at reflux to give the corresponding 3-alkyl-2-thiohydantoins **3a-c**. Compounds **3a-c** were condensed with the appropriate aromatic aldehydes by heating in a solution of anhydrous sodium acetate and glacial acetic acid at reflux to afford the corresponding 3-alkyl-5-((*Z*))-arylidene)-2-thiohydantoins **4a-l**. The structures of **4a-l** were confirmed on the bases of elemental analysis and spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and MS). The IR absorption spectra of compound **4c** was characterized by the presence of signals for NH and C=O groups at 3198 and 1750 cm^{-1}, respectively. The ^{1}H-NMR spectrum of compound **4c** showed a singlet at 6.71 ppm assigned to the vinyl proton, indicating the presence of a *Z*-configuration for the exocyclic double bond, in agreement with the ^{1}H-NMR spectra of 5-(*E*)- and 5-((*Z*))-arylidene)-3-methylhydantoins whose vinyl protons respectively appear at 6.10–6.35 and 6.40–6.75 ppm[16]. The ^{13}C-NMR spectrum of compound **4c** showed a singlet at 113.51 ppm assigned to the vinyl carbon, indicating the presence of a *Z*-configuration for the exocyclic double bond, in agreement with the ^{13}C-NMR spectra of 5-(*E*)- and 5-((*Z*))-arylidene)-3-methylhydantoins whose vinyl carbons respectively appear at δ 105–115 and 115–125 ppm[16] (Scheme 1). Compounds **4b,e,g,h,k** were reacted with methylthioethyl chloride in the presence of aqueous ethanolic potassium hydroxide to give 3-alkyl-5-((*Z*))-arylidene)-*S*-(2-methylthioethyl)-2-thiohydantoins (**5a-e**). Compound **5b** was also independently synthesized through another pathway via condensation of 5-((*Z*)-benzylidene)-3-phenymethyl-*S*-(trimethylsilyl)-2-thiohydantoin **6**, which in turn was prepared from the reaction of **4b** with



2-4	R	Ar		R	Ar
a	CH_3	C_6H_5	**j**	CH_3	4-$Me_2NC_6H_4$
b	C_6H_5	C_6H_5	**k**	C_6H_5	4-$Me_2NC_6H_4$
c	$C_6H_5CH_2$	C_6H_5	**l**	$C_6H_5CH_2$	3,4,5-trimethoxyphenyl
d	CH_3	2-thienyl	**5**	C_6H_5	C_6H_5
e	C_6H_5	2-thienyl	**a**	C_6H_5	2-thienyl
f	$C_6H_5CH_2$	2-thienyl	**b**	CH_3	3,4-methylenedioxyphenyl
g	CH_3	3,4-methylenedioxyphenyl	**c**	C_6H_5	3,4-methylenedioxyphenyl
h	C_6H_5	3,4-methylenedioxyphenyl	**d**	C_6H_5	4-$Me_2NC_6H_4$
i	$C_6H_5CH_2$	3,4-methylenedioxyphenyl	**e**		

Scheme 1. Reagents and conditions: (a) Pyridine, H_2O, NaOH, 40 °C; (b) 1N HCl, reflux; (c) ArCHO, AcONa, AcOH, reflux; (d) $H_3CSCH_2CH_2Cl$, aq. KOH, EtOH, r.t.; (e) CH_3CN, BSA, r. t; (f), $H_3CSCH_2CH_2Cl$, r. t.; (g) Conc HCl, EtOH, reflux.

bis(trimethylsilyl)acetamide (BSA) in acetonitrile, with α-D-glucose pentaacetate in the presence of trimethylsily**l**trifluoromethane sulfonate (TMSO**T**f) at room temperature. The *S*-alkylated derivative **5b** was isolated by silica gel column chromatography in 68% yield and no *N*-alkylated derivative **7** was detected in the reaction mixture (TLC). The structures of **5a-e** were confirmed on the bases of elemental analysis and spectral data (IR, ^{1}H-NMR and MS). The IR absorption spectra of compound **5d** was characterized by the absence of signal for NH at 3190 cm^{-1} and the presence of a signal at 1708 cm^{-1} due to the carbonyl group. The ^{1}H-NMR spectrum of compound **5d** showed a singlet at 6.81 ppm assigned to the vinyl proton, indicating the presence of a *Z*-configuration for the exocyclic double bond in agreement with the ^{1}H-NMR spectrum of its oxygen analogue. The latter, prepared from the reaction of **5d** with 12N hydrochloric acid in refluxing ethanol, shows a vinyl proton at 6.65 ppm (Scheme 1).

Compounds **4a-l** were reacted with 1.1 equivalent of NaH in anhydrous acetonitrile followed by 1.1 equivalent of the 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide to give 3-alkyl-5-((*Z*)-arylidene)-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thiohydantoins **9a-l**. Compound **9a** was also independently synthesized through another pathway via condensation of 5-((*Z*)-benzylidene)-3-ethyl-*S*-(trimethylsilyl)-2-thiohydantoin **6**. The nucleoside **9a** was isolated by silica gel column chromatography in 62% yield and no *N*-glucosilated derivative **10** was detected in the reaction mixture (TLC). The structures of **9a-l** were confirmed on the bases of elemental analysis and spectral data (IR, ^{1}H-NMR and MS). The IR absorption spectra of compound **9c** was characterized by the absence of the signal for NH group at 3198 cm^{-1} and the presence of acetoxy groups of the sugar moiety at 1750 cm^{-1} in addition to the signal of the carbonyl group at 1727 cm^{-1}. The ^{1}H-NMR spectrum of compound **9c** showed a doublet at 5.83 ppm with spin-spin coupling constant equal to 10.50 Hz which corresponds to the diaxial orientation of 1′-H and 2′-H protons., in agreement with a β-configuration[9]. The singlet at 7.02 ppm which was assigned to the vinylic proton, confirmed the presence of a *Z*-configuration for the exocyclic double bond, in agreement with the ^{1}H-NMR spectrum of its oxygen analogue. The latter, prepared from the reaction of **9c** with sodium methoxide in methanol at room temperature, shows vinyl proton at 6.50 ppm. The ^{13}C-NMR spectrum of compound **11c** showed a singlet at 109.60 ppm assigned to the vinyl carbon, indicating the presence of a *Z*-configuration for the exocyclic double bond. This type of cleavage explains why we were not successful in the preparation of the corresponding deprotected nucleosides of **9a-l** (Scheme 2).

In conclusion, we have described the successful synthesis of 3-alkyl-2-thiohydantoins and their corresponding *S*-alkylated and *S*-glucosylated derivatives via simple and efficient methods. The antiviral and the antitumor activities of the new prepared compounds are under biological evaluation studies.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H-NMR (300.13 MHz) and ^{13}C-NMR (75.47 MHz) were measured on a Bruker Advance DPX 300 machine using tetramethylsilane as external reference. Mass spectra were recorded on a Finnigan MAT-INCOS 500 spectrometer with ionization by electron impact (70 ev). Elemental analysis were obtained from the Microanalytical Center at 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. IR spectra were measured on a Nicolet Magna 750. Column chromatography was performed with silica gel 60 mesh ASTM (Merck).

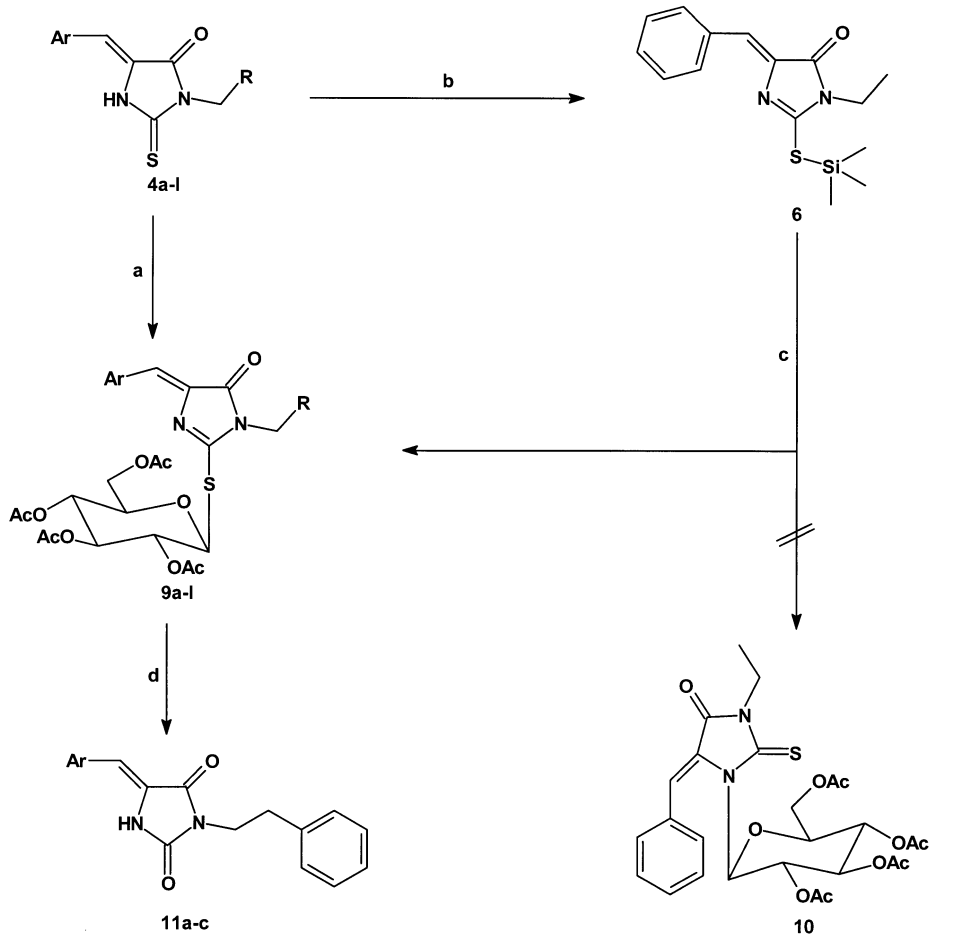
3-Alkyl-2-thiohydantoin **(3a-c)**

Glycine **(1)** (0.75 g, 10 mmol) was dissolved in a mixture of water (25 ml) and pyridine (25 ml). The pH of the solution was adjusted to about 9 as shown by an indicator paper by the addition of 1 N NaOH. The solution was heated to 40 °C and kept at that temperature during the reaction. Alkyl isothiocyanates **2a-c** (20 mmol) was added with vigorous stirring. Small portions of 1 N NaOH was added to keep the pH at about 9. The reaction was completed when the alkali consumption ceased (approx. 60 min). pyridine and excess alkyl isothiocyanates were then removed by repeated extraction with equal volumes of benzene. Subsequently, an amount of conc. HCl (3 ml) was added and the mixture was heated at reflux for 2 h. The reaction mixture was concentrated to half its volume under vacuum, and cooled to room temperature. The pale yellow solid precipitate was collected by filtration and recrystallized from methanol to give the products **3a-c**.

3-Ethyl-2-thiohydantoin (3a). Yield 0.86 g (60%), m. p. 136–138 °C. MS; *m/z*: 144 (M^+). Calculated for $C_5H_8N_2OS$ (144.18): C, 41.65; H, 5.59; N, 19.43. Found: C, 41.54; H, 5.78; N, 19.30. IR (KBr): ν 3198 (NH), 1750 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.25 (3H, t, J = 7.20 Hz, CH_3), 3.88 (2H, q, J = 7.20 Hz, CH_2), 4.07 (2H, s, 5-H), 7.44 (1H, s, N_1-H).

3-Phenylmethyl-2-thiohydantoin (3b). Yield 1.32 g (64%), m. p. 154–156 °C. MS; *m/z*: 206 (M^+). Calculated for $C_{10}H_{10}N_2OS$ (206.26): C, 58.23; H, 4.90; N, 13.60. Found: C, 58.05; H, 5.16; N, 13.58. IR (KBr): ν 3196 (NH), 1752 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 4.06 (2H, s, 5-H), 5.00 (2H, s, CH_2), 7.02 (1H, s, N_1-H), 7.25–7.50 (5H, m, Ar-H).

3-(2-Phenylethyl)-2-thiohydantoin (3c). Yield 1.50 g (68%), m. p. 158–160 °C. MS; *m/z*: 220 (M^+). Calculated for $C_{11}H_{12}N_2OS$ (220.29): C, 60.00; H, 5.49; N, 12.71. Found: C, 59.87; H, 5.76; N, 12.54. IR (KBr): ν 3198



	R	Ar		R	Ar
9a	CH_3	C_6H_5	**i**	$C_6H_5CH_2$	3,4-methylenedioxyphenyl
b	C_6H_5	C_6H_5	**j**	CH_3	4-$Me_2NC_6H_4$
c	$C_6H_5CH_2$	C_6H_5	**k**	C_6H_5	4-$Me_2NC_6H_4$
d	CH_3	2-thienyl	**l**	$C_6H_5CH_2$	3,4,5-trimethoxyphenyl
e	C_6H_5	2-thienyl	**11a**		C_6H_5
f	$C_6H_5CH_2$	2-thienyl	**b**		2-thienyl
g	CH_3	3,4-methylenedioxyphenyl	**c**		3,4-methylenedioxyphenyl
h	C_6H_5	3,4-methylenedioxyphenyl			

Scheme 2. Reagents and conditions: (a) 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide, NaH, CH_3CN, r. t.; (b) CH_3CN, BSA, r. t.; (c) 1,2,3,4,6-Penta-*O*-acetyl-α-D-glucopyranoside, reflux; (d) CH_3ONa, CH_3OH, r. t.

(NH), 1751 (C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.90 (2H, t, J = 7.11 Hz, 2′-H), 3.88 (2H, t, J = 7.11 Hz, 1′-H), 4.03 (2H, s, 5-H), 7.26 (5H, m, Ar-H), 10.11 (1H, s, N_1-H). ^{13}C-NMR (DMSO-d_6): δ 33.28 (C-′2), 41.42 (C-1′), 48.34 (C-5), 126.31, 128.30, 128.57, 138.02 (C-Ar), 171.97 (C-4), 183.47 (C-2).

3-Alkyl-5-((Z)-arylidene)-2-thiohydantoins **(4a-l)**

To a mixture of 3-alkyl-2-thiohydantoins **(3a-c)** (10 mmol), anhydrous sodium acetate (2.32 g, 28.29 mmol) and glacial acetic acid (15 ml) was added the appropriate aromatic aldehyde (11 mmol). The mixture was heated under reflux for 4 h, cooled to room temperature and then poured into cold water. The yellow solid precipitate was collected by filtration and recrystallized from acetic acid to give the products **4a-l**.

5-((Z)-Benzylidene)-3-ethyl-2-thiohydantoin (4a). Yield 2.25 g (97%), m. p. 152–154 °C. MS; *m/z*: 232 (M^+). Calculated for $C_{12}H_{12}N_2OS$ (232.30): C, 62.04; H, 5.21; N, 12.06. Found: C, 62.15; H, 5.36; N, 12.00. IR (KBr): ν 3199 (NH), 1756 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.30 (3H, t, J = 7.20 Hz, CH_3), 3.98 (2H, q, J = 7.20 Hz, CH_2), 6.74 (1H, s, =CH), 7.40–7.50 (5H, m, Ar-H), 8.68 (1H, s, N_1-H).

5-((Z)-Benzylidene)-3-phenymethyl-2-thiohydantoin (4b). Yield 2.60 g (88%), m. p. 215–217 °C. MS; *m/z*: 294 (M^+). Calculated for $C_{17}H_{14}N_2OS$ (294.37): C, 69.13; H, 4.79; N, 9.51. Found: C, 69.02; H, 5.00; N, 9.34. IR (KBr): ν 3190 (NH), 1752 (C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.00 (2H, s, CH_2), 6.54 (1H, s, =CH), 7.15–7.60 (10H, m, Ar-H), 11.98 (1H, s, N_1-H).

5-((Z)-Benzylidene)-3-(2-phenyethyl)-2-thiohydantoin (4c). Yield 2.90 g (94%), m. p. 169–171 °C. MS; *m/z*: 308 (M^+). Calculated for $C_{18}H_{16}N_2OS$ (308.40): C, 71.10; H, 5.23; N, 9.08. Found: C, 71.22; H, 5.30; N, 8.84. IR (KBr): ν 3198 (NH), 1750 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.02 (2H, t, J = 7.20 Hz, 2′-H), 4.13 (2H, t, J = 7.20 Hz, 1′-H), 6.71 (1H, s, =CH), 7.23–7.46 (10H, m, Ar-H), 9.35 (1H, s, N_1-H). ^{13}C-NMR ($CDCl_3$): δ 33.71 (C-′2), 42.60 (C-1′), 113.51 (=CH), 125.89 (C-5), 126.36, 126.72, 128.57, 128.96, 129.23, 129.27, 129.43, 129.51, 129.74, 132.82, 137.73 (C-Ar), 163.61 (C-4), 178.19 (C-2).

3-Ethyl-5-(Z)-2-thienylidene)-2-thiohydantoin (4d). Yield 2.00 g (84%), m. p. 166–168 °C. MS; *m/z*: 238 (M^+). Calculated for $C_{10}H_{10}N_2OS_2$ (238.32): C, 50.40; H, 4.23; N, 11.75. Found: C, 50.24; H, 4.38; N, 11.86. IR (KBr): ν 3198 (NH), 1754 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.30 (3H, t, J = 7.20 Hz, CH_3), 4.00 (2H, q, J = 7.20 Hz, CH_2), 6.92 (1H, s, =CH), 7.15 (1H, t, J = 4.20 Hz, H-4′), 7.50 (1H, d, J = 5.20 Hz, H-3′), 7.60 (1H, d, J = 3.00 Hz, H-5′), 8.58 (1H, s, N_1-H).

3-Phenymethyl-5-(Z)-2-thienylidene)-2-thiohydantoin (4e). Yield 2.60 g (86%), m. p. 207–209 °C. MS; *m/z*: 300 (M^+). Calculated for $C_{15}H_{12}N_2OS_2$ (300.41): C, 60.97; H, 4.03; N, 9.32. Found: C, 60.76; H, 4.27; N, 9.38. IR (KBr): ν 3190 (NH), 1750 (C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.4.98 (2H, s, CH_2), 6.67 (1H, s, =CH), 7.03–7.65 (10H, m, Ar-H), 11.36 (1H, s, N_1-H).

3-(2-Phenyethyl)-5-(Z)-2-thienylidene)-2-thiohydantoin (4f). Yield 2.76 g (88%), m. p. 156–158 °C. MS; *m/z*: 314 (M^+). Calculated for $C_{16}H_{14}N_2OS_2$ (314.43): C, 61.20; H, 4.49; N, 8.91. Found: C, 61.26; H, 4.32; N, 8.80. IR (KBr): ν 3197 (NH), 1752 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.02 (2H, t, J = 7.96 Hz, 2′-H), 4.13 (2H, t, J = 7.85 Hz, 1′-H), 6.91 (1H, s, =CH), 7.14–7.57 (8H, m, Ar-H), 8.66 (1H, s, N_1-H). ^{13}C-NMR ($CDCl_3$): δ 33.67 (C-′2), 42.69 (C-1′), 106.40 (=CH), 124.04 (C-5), 125.86, 126.71, 128.57, 128.72, 128.94, 129.57, 131.93, 136.05, 137.68 (C-Ar), 163.29 (C-4), 177.11 (C-2).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-ethyl-2-thiohydantoin (4g). Yield 2.25 g (97%), m. p. 131–133 °C. MS; *m/z*: 276 (M^+). Calculated for $C_{13}H_{12}N_2O_3S$ (276.31): C, 56.51; H, 4.38; N, 10.14. Found: C, 56.42; H, 4.56; N, 10.00. IR (KBr): ν 3196 (NH), 1754 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.28 (3H, t, J = 7.50 Hz, CH_3), 3.98 (2H, q, J = 7.20 Hz, CH_2), 6.04 (2H, s, CH_2), 6.64 (1H, s, =CH), 6.86–7.25 (5H, m, Ar-H), 8.67 (1H, s, N_1-H).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-phenymethyl-2-thiohydantoin (4h). Yield 2.70 g (80%), m. p. 207–209 °C. MS; *m/z*: 338 (M^+). Calculated for $C_{18}H_{14}N_2O_3S$ (338.38): C, 63.89; H, 4.17; N, 8.29. Found: C, 63.64; H, 4.08; N, 8.34. IR (KBr): ν 3190 (NH), 1750 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.09 (2H, s, CH_2), 6.03 (1H, s, OCH_2O), 6.64 (1H, s, =CH), 6.85–7.50 (8H, m, Ar-H), 8.69 (1H, s, N_1-H).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-(2-phenyethyl)-2-thiohydantoin (4i). Yield 2.98 g (85%), m. p. 193–195 °C. MS; *m/z*: 352 (M^+). Calculated for $C_{19}H_{16}N_2O_3S$ (352.46): C, 64.75; H, 4.57; N, 7.95. Found: C, 64.58; H, 4.70; N, 7.76. IR (KBr): ν 3197 (NH), 1751 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.01 (2H, t, J = 7.98 Hz, 2′-H), 4.12 (2H, t, J = 7.98 Hz, 1′-H), 6.00 (2H, s, CH_2), 6.65 (1H, s, =CH), 6.85–7.33 (8H, m, Ar-H), 9.24 (1H, s, N_1-H). ^{13}C-NMR ($CDCl_3$): δ 33.68 (C-′2), 42.59 (C-1′), 114.10 (=CH), 125.89 (C-5), 101.85, 108.61, 109.32, 124.95, 126.69, 126.79, 128.55, 128.93, 137.76, 148.68, 149.15 (C-Ar), 163.21 (C-4), 177.69 (C-2).

5-((Z)-4-Dimethylaminobenzylidene)-3-ethyl-2-thiohydantoin (4j). Yield 2.20 g (80%), m. p. 161–163 °C. MS; *m/z*: 275 (M^+). Calculated for $C_{14}H_{17}N_3OS$ (275.37): C, 61.07; H, 6.22; N, 15.26. Found: C, 60.85; H, 6.38; N, 15.06. IR (KBr): ν 3198 (NH), 1752 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.30

(3H, t, J = 7.20 Hz, CH_3), 3.08 (6H, s, Nme_2), 3.98 (2H, q, J = 7.20 Hz, CH_2), 6.69 (1H, s, =CH), 6.76, 7.32 (4H, 2d, J = 8.70, Hz, Ar-H), 8.67 (1H, s, N_1-H).

5-((Z)-4-Dimethylaminobenzylidene)-3-phenymethyl-2-thiohydantoin (4k). Yield 2.53 g (75%), m. p. 208–210 °C. MS; *m/z*: 337 (M^+). Calculated for $C_{19}H_{19}N_3OS$ (337.44): C, 67.63; H, 5.67; N, 12.45. Found: C, 67.74; H, 5.82; N, 12.30. IR (KBr): ν 3190 (NH), 1750 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.06 (6H, s, Nme_2), 5.10 (2H, s, CH_2), 6.69 (1H, s, =CH), 6.79–7.52 (9H, m, Ar-H), 8.66 (1H, s, N_1-H).

5-((Z)-3,4,5-Trimethoxybenzylidene)-3-(2-phenyethyl)-2-thiohydantoin (4l). Yield 3.10 g (78%), m. p. 86–88 °C. MS; *m/z*: 398 (M^+). Calculated for $C_{21}H_{22}N_2O_4S$ (398.48): C, 63.30; H, 5.56; N, 7.03. Found: C, 63.45; H, 5.60; N, 6.82. IR (KBr): ν 3198 (NH), 1752 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.02 (2H, t, J = 8.00 Hz, 2′-H), 3.88 (9H, s, $30M_e$), 4.12 (2H, t, J = 8.00 Hz, 1′-H), 6.62–7.44 (7H, m, =CH, Ar-H), 9.65 (1H, s, N_1-H). ^{13}C-NMR ($CDCl_3$): δ 33.71 (C-′2), 42.60 (C-1′), 114.05 (=CH), 125.89 (C-5), 106.60, 126.13, 126.71, 128.32, 128.52, 128.57, 128.63, 128.94, 128.97, 129.02, 137.72, 139.50, 153.72 (C-Ar), 163.66 (C-4), 178.17 (C-2).

3-Alkyl-5-((Z)-arylidene)-S-(2-methylthioethyl)-2-thiohydantoins **(5a-e)**

Method A: (Z)-5-arylidene-3-Alkyl-2-thiohydantoins **(4b,e,g,h,k)** (2 mmol) were dissolved in aqueous KOH (6%, 2 ml) and EtOH (8 ml) at room temperature. To this solution methylthioethyl chloride (143 mg, 2.20 mmol) was added, and the reaction mixture was stirred for 12 h at room temperature. The yellow precipitated solid was collected by filtration and recrystallized from methanol to give the products **5a-e**.

Method B: Compound **4b** (0.29 g, 1 mmol) suspended in anhydrous acetonitrile (5 ml) and BSA (0.25 ml, 1 mmol) was added, and the reaction mixture was stirred at room temperature for 30 min. The methylthioethyl chloride (0.11 g, 1 mmol) dissolved in anhydrous acetonitrile (5 ml) was added to the reaction mixture *via* a canula. Finally TMSOTf (0.2 ml, 1 mmol) was added, and the reaction mixture was stirred at room temperature for 6 h saturated $NaHCO_3$ was added to quench the reaction and the resulting mixture extracted with CH_2Cl_2. The combined organic fractions were washed with saturated NaCl solution, dried over $MgSO_4$, filtered, and evaporated to dryness. The solid obtained was purified by flash chromatography (eluent 50%, diethyl ether/petroleum ether, 40–60 °C) to give 68% of **5b**.

5-((Z)-Benzylidene)-3-phenymethyl-S-(2-methylthioethyl)-2-thiohydantoin (5a). Yield 0.70 g (95%), m. p. 88–90 °C. MS; *m/z*: 368 (M^+). Calculated for $C_{20}H_{20}N_2OS_2$ (368.52): C, 65.18; H, 5.47; N, 7.60. Found: C, 65.00; H,

5.48; N, 7.32. IR (KBr): ν 1708 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.23 (3H, s, SCH_3), 2.95 (2H, d, J = 7.50 Hz, 2″-H), 3.53 (2H, d, J = 7.50 Hz, 1″-H), 4.78 (2H, s, 1′-H), 7.00 (1H, s, =CH), 7.30–8.14 (10H, m, Ar-H).

3-Phenymethyl-5-((Z)-2-thienylidene)-S-(2-methylthioethyl)-2-thiohydantoin (5b). Yield 0.60 g (80%), m. p. 75–77 °C. MS; *m/z*: 374 (M^+). Calculated for $C_{18}H_{18}N_2OS_3$ (374.54): C, 57.72; H, 4.84; N, 7.48. Found: C, 57.92; H, 5.00; N, 7.30. IR (KBr): ν 1707 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.21 (3H, s, SCH_3), 2.98 (2H, d, J = 7.50 Hz, 2″-H), 3.54 (2H, d, J = 7.50 Hz, 1″-H), 4.77 (2H, s, 1′-H), 7.07-7.57 (8H, m, =CH, Ar-H).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-ethyl-S-(2-methylthioethyl)-2-thiohydantoin (5c). Yield 0.60 g (86%), m.p. 94–96 °C. MS; *m/z*: 350 (M^+). Calculated for $C_{16}H_{18}N_2O_3S_2$ (350.46): C, 54.84; H, 5.78; N, 7.99. Found: C, 54.68; H, 5.80; N, 7.78. IR (KBr): ν 1710 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$): δ 1.25 (2H, t, J = 7.50 Hz, 2′-H), 2.26 (3H, s, SCH_3), 2.98 (2H, d, J = 7.50 Hz, 2″-H), 3.56 (2H, d, J = 7.50 Hz, 1″-H), 3.67 (2H, q, J = 7.50 Hz, 1′-H), 6.01 (2H, s, OCH_2O), 6.80 (2H, d, J = 8.10 Hz, Ar-H), 6.87 (1H, s, =CH), 7.38 (2H, d, J = 8.10 Hz, Ar-H), 8.00 (1H, s, Ar-H).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-phenymethyl-S-(2-methylthioethyl)-2-thiohydantoin (5d). Yield 0.80 g (97%), m.p. 130–132 °C. MS; *m/z*: 412 (M^+). Calculated for $C_{21}H_{20}N_2O_3S_2$ (412.53): C, 61.14; H, 4.89; N, 6.79. Found: C, 60.78; H, 5.15; N, 6.56. IR (KBr): ν 1708 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$): δ 2.23 (3H, s, SCH_3), 2.95 (2H, d, J = 7.50 Hz, 2″-H), 3.50 (2H, d, J = 7.50 Hz, 1″-H), 4.77 (2H, q, J = 7.50 Hz, 1′-H), 6.01 (2H, s, OCH_2O), 6.81–8.00 (9H, s, =CH, Ar-H).

5-((Z)-4-Dimethylaminobenzylidene)-3-phenymethyl-S-(2-methylthioethyl)-2-thiohydantoin (5e). Yield 0.80 g (97%), m.p. 114–116 °C. MS; *m/z*: 411 (M^+). Calculated for $C_{22}H_{25}N_3OS_2$ (411.60): C, 64.20; H, 6.12; N, 10.21. Found: C, 64.00; H, 6.16; N, 10.05. IR (KBr): ν 1707 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$): δ 2.23 (3H, SCH_3), 2.95 (2H, d, J = 7.50 Hz, 2″-H), 3.05 (6H, s, NMe_2), 3.50 (2H, d, J = 7.50 Hz, 1″-H), 4.78 (2H, q, J = 7.50 Hz, 1′-H), 6.70–8.07 (10H, s, =CH, Ar-H).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-phenylmethylhydantoin **(8)**.

To solution of (*Z*)-5-(3,4-methylenedioxybenzylidene)-3-phenylmethyl-2-(2-methylthioethyl)-2-thiohydantoin **(5d)** (0.41 g, 1 mmol) in ethanol (10 ml) was added 12 N HCl (1 ml). The reaction mixture was refluxed for 2 h until the starting material was consumed (TLC), cool to room temperature, the separated solid was filtered off and recrystallized from acetic acid to give

the product **8**: Yield 0.27 g (83%), m.p. 206–208 °C. MS; *m/z*: 322 (M^+). Calculated for $C_{18}H_{14}N_2O_4$ (322.32): C, 67.07; H, 4.38; N, 8.69. Found: C, 66.82; H, 4.50; N, 8.38. IR (KBr): ν 3190 (NH), 1758, 1707 (2 C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.10 (2H, s, CH_2), 6.03 (2H, s, OCH_2O), 6.65 (1H, s, =CH), 6.86–7.50 (8H, m, H-Ar), 8.60 (1H, s, NH).

3-Alkyl-5-((Z)-arylidene)-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoins **(9a-l)**

Method A: (*Z*)-5-arylidene-3-alkyl-2-thiohydantoins **(4a-l)** (1 mmol) were suspended in anhydrous acetonitrile (5 ml) at room temperature. To this suspension was added NaH (60%, 45 mg, 1 mmol), and the mixture was stirred at room temperature for 30 min. The mixture became clear after 15 min., 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0.41 g, 1 mmol) was added, and the mixture was stirred at room temperature for 6 h until the starting material was consumed (TLC) and then filtered. The residue from the evaporation of the filtrate under reduced pressure was purified by flash chromatography (eluent 50%, diethyl ether/petroleum ether, 40–60 °C) to give the products **9a-l**.

Method B: Compound **4a** (0.23 g, 1 mmol) suspended in anhydrous acetonitrile (5 ml) and BSA (0.25 ml, 1 mmol) was added, and the reaction mixture was stirred at room temperature for 30 min. The 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranoside (0.39 g, 1 mmol) dissolved in anhydrous acetonitrile (5 ml) was added to the reaction mixture *via* a canula. Finally TMSOTf (0.2 ml, 1 mmol) was added, and the reaction mixture was heated under reflux 1 h saturated $NaHCO_3$ was added to quench the reaction and the resulting mixture extracted with CH_2Cl_2. The combined organic fractions were washed with, saturated NaCl solution, dried over $MgSO_4$, filtered, and evaporated to dryness. The solid obtained was purified by flash chromatography (eluent 50%, diethyl ether/petroleum ether, 40–60 °C) to give 62% of **9a**.

5-((Z)-Benzylidene)-3-ethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9a). Yield 0.47 g (84%), m.p. 170–172 °C. MS; *m/z*: 562 (M^+). Calculated for $C_{26}H_{30}N_2O_{10}S$ (562.59): C, 55.51; H, 5.37; N, 4.98. Found: C, 55.32; H, 5.44; N, 4.76. IR (KBr): ν 1750, 1730 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.26 (3H, t, J = 7.20 Hz, CH_3), 2.03, 2.06, 2.10 (12H, 3s, 4Ac), 3.62 (2H, q, J = 7.20 Hz, CH_2), 3.91–4.26 (3H, m, 6′-H, 5′-H), 5.11–5.44 (5H, m, 4′-H, 2′-H, 3′-H), 5.86 (1H, d, J = 10.50 Hz, 1′H), 7.01 (1H, s, =CH), 7.39–8.13 (5H, m, Ar-H).

5-((Z)-Benzylidene)-3-phenylmethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9b). Yield 0.55 g (88%), m.p. 202–204 °C. MS; *m/z*: 624 (M^+). Calculated for $C_{31}H_{32}N_2O_{10}S$ (624.62): C, 59.61; H, 5.16; N, 4.48. Found: C, 59.50; H, 5.36; N, 4.24. IR (KBr): ν 1751, 1728 (2C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ 1.82, 1.91, 2.00, 2.05 (12H, 4s, 4Ac), 3.87−4.27 (3H, m, 6′-H, 5′-H), 4.60, 4.90 (2H, 2d, J = 15.90 Hz, CH_2), 5.12 (1H, t, J = 9.90 Hz, 4′-H), 5.25 (1H, t, J = 9.90 Hz, 2′-H), 5.36 (1H, t, J = 9.90 Hz, 3′-H), 5.78 (1H, d, J = 10.50 Hz, 1′-H), 7.07 (1H, s, =CH), 7.27−8.14 (10H, m, Ar-H).

5-((Z)-Benzylidene)-3-(2-phenylethyl)-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9c). Yield 0.50 g (78%), m.p. 118−120 °C. MS; *m/z*: 638 (M^+). Calculated for $C_{32}H_{34}N_2O_{10}S$ (638.69): C, 60.18; H, 5.36; N, 4.38. Found: C, 60.26; H, 5.38; N, 4.22. IR (KBr): ν 1750, 1727 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.81, 2.05, 2.06, 2.08 (12H, 4s, 4Ac), 2.93 (2H, t, J = 7.44 Hz, CH_2), 3.74−.94 (3H, m, 6′-H, 5′-H), 4.21 (2H, m, CH_2), 5.15 (1H, t, J = 9.90 Hz, 4′-H), 5.29 (1H, t, J = 9.90 Hz, 2′-H), 5.40 (1H, t, J = 9.90 Hz, 3′-H), 5.83 (1H, d, J = 10.50 Hz, 1′-H), 7.02 (1H, s, =CH), 7.18−8.14 (10H, m, Ar-H). ^{13}C-NMR ($CDCl_3$): δ = 20.46, 20.62, 20.65 (4 Ac), 35.03 (CH_2), 42.64 (CH_2), 61.83 (C-6′), 68.11 (C-2′), 69.07 (C-3′), 73.80 (C-4′), 77.23 (C-5′), 81.37 (C-1′), 125.58, 126.89, 128.74, 128.92, 130.27, 132.02, 134.18, 137.25, 137.90 (=CH, C-5, C-Ar), 161.02 (C-2), 169.32, 169.46, 170.13, 170.64 (4C=O, C-4).

3-Ethyl-5-((Z)-2-thienylidene)-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9d). Yield 0.45 g (79%), m.p. 146−148 °C. MS; *m/z*: 568 (M^+). Calculated for $C_{24}H_{28}N_2O_{10}S_2$ (568.62): C, 50.70; H, 4.96; N, 4.93. Found: C, 50.54; H, 4.86; N, 4.72. IR (KBr): ν 1750, 1728 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.24 (3H, t, J = 7.50 Hz, CH_3), 1.87, 2.04, 2.07, 2.10 (12H, 4s, 4Ac), 3.61 (2H, q, J = 7.50 Hz, CH_2), 4.01−4.25 (3H, m, 6′-H, 5′-H), 5.20 (1H, t, J = 9.60 Hz, 4′-H), 5.32 (1H, t, J = 9.75 Hz, 2′-H), 5.43 (1H, t, J = 9.30 Hz, 3′-H), 5.83 (1H, d, J = 10.50 Hz, 1′-H), 7.12 (1H, t, J = 4.35 Hz, H-4″), 7.28 (1H, s, =CH), 7.45 (1H, d, J = 5.70 Hz, H-3″), 7.65 (1H, d, J = 3.60 Hz, H-5″).

3-Phenylmethyl-5-((Z)-2-thienylidene)-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9e). Yield 0.51 g (81%), m.p. 217−219 °C. MS; *m/z*: 630 (M^+). Calculated for $C_{29}H_{30}N_2O_{10}S_2$ (630.68): C, 55.23; H, 4.79; N, 4.44. Found: C, 55.36; H, 4.82; N, 4.12. IR (KBr): ν 1752, 1727 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.87, 1.91, 2.02, 2.07 (12H, 4s, 4Ac), 3.98−4.24 (3H, m, 6′-H, 5′-H), 4.60, 4.90 (2H, 2d, J = 15.90 Hz, CH_2), 5.16 (2H, t, J = 9.75 Hz, 4′-H), 5.26 (1H, t, J = 9.60 Hz, 2′-H), 5.43 (1H, t, J = 9.15 Hz, 3′-H), 5.84 (1H, d, J = 10.20 Hz, 1′-H), 7.12 (1H, t, J = 4.35 Hz, H-4″), 7.26−7.33 (6H, s, =CH, H-Ar), 7.46 (1H, d, J = 5.70 Hz, H-3″), 7.66 (1H, d, J = 3.90 Hz, H-5″).

3-(2-Phenylethyl)-5-((Z)-2-thienylidene)-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9f). Yield 0.50 g (78%), m.p. 166−168 °C. MS; *m/z*: 644 (M^+). Calculated for $C_{30}H_{32}N_2O_{10}S_2$ (644.71): C, 55.89; H, 5.00; N, 4.34. Found: C, 55.68; H, 4.80; N, 4.25. IR (KBr): ν 1751, 1727 (2C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): δ 1.86, 2.05, 2.06, 2.08 (12H, 4s, 4Ac), 2.92 (2H, t, J = 7.40 Hz, CH_2), 3.69−4.27 (5H, m, 6′-H, 5′-H, CH_2), 5.18 (1H, t, J = 9.67 Hz, 4′-H), 5.30 (1H, t, J = 9.72 Hz, 2′-H), 5.42 (1H, t, J = 9.16 Hz, 3′-H), 5.84 (1H, d, J = 10.44 Hz, 1′-H), 7.11−7.68 (9H, m, =CH, H-Ar). ^{13}C-NMR ($CDCl_3$): δ = 20.45, 20.62, 20.67 (4 Ac), 35.07 (CH_2), 42.64 (CH_2), 61.63 (C-6′), 68.01 (C-2′), 68.97 (C-3′), 73.90 (C-4′), 77.24 (C-5′), 81.51 (C-1′), 119.19 (=CH), 125.89, 126.86, 127.47, 128.73, 128.90, 133.62, 134.13, 135.84, 137.26, 137.84 (C-5, C-Ar), 159.44 (C-2), 168.45, 169.45, 170.15, 170.65 (4C=O, C-4).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-ethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydanto-in (9g). Yield 0.45 g (74%), m. p. 166−168 °C. MS; *m/z*: 606 (M^+). Calculated for $C_{27}H_{30}N_2O_{12}S$ (606.60): C, 53.46; H, 4.98; N, 4.62. Found: C, 53.28; H, 5.12; N, 4.46. IR (KBr): ν 1750, 1728 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.23 (3H, t, J = 7.05 Hz, CH_3), 1.89, 2.01, 2.06 (12H, 4s, 4Ac), 3.62 (2H, q, J = 7.20 Hz, CH_2), 3.93−4.32 (3H, m, 6′-H, 5′-H), 5.17 (1H, t, J = 9.60 Hz, 4′-H), 5.28 (1H, t, J = 9.60 Hz, 2′-H), 5.43 (1H, t, J = 9.15 Hz, 3′-H), 5.82 (1H, d, J = 10.50 Hz, 1′-H), 6.04 (2H, s, OCH_2O), 6.86 (1H, d, J = 8.10 Hz, H-Ar), 6.94 (1H, s, =CH), 7.35 (1H, dd, J = 1.20, 8.10 Hz, H-Ar), 8.02 (1H, d, J = 1.20 Hz, H-Ar).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-phenylmethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9h). Yield 0.50 g (75%), m. p. 201−203 °C. MS; *m/z*: 668 (M^+). Calculated for $C_{32}H_{32}N_2O_{12}S$ (668.67): C, 57.48; H, 4.82; N, 4.19. Found: C, 57.32; H, 5.10; N, 4.22. IR (KBr): ν 1752, 1727 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.90, 1.91, 2.02, 2.05 (12H, 4s, 4Ac), 3.90−4.32 (3H, m, 6′-H, 5′-H), 4.60, 4.85 (2H, 2d, J = 15.90 Hz, CH_2), 5.14 (1H, t, J = 9.60 Hz, 4′-H), 5.24 (1H, t, J = 9.60 Hz, 2′-H), 5.34 (1H, t, J = 9.15 Hz, 3′-H), 5.74 (1H, d, J = 10.50 Hz, 1′-H), 6.04 (2H, s, OCH_2O), 6.84−8.05 (9H, m, =CH, H-Ar).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-(2-phenylethyl)-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9i). Yield 0.520 g (76%), m. p. 143−145 °C. MS; *m/z*: 682 (M^+). Calculated for $C_{33}H_{34}N_2O_{12}S$ (682.70): C, 58.06; H, 5.03; N, 4.10. Found: C, 57.82; H, 5.18; N, 4.32. IR (KBr): ν 1750, 1727 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): β 1.89, 2.05, 2.06, 2.08 (12H, 4s, 4Ac), 2.92 (2H, t, J = 7.40 Hz, CH_2), 3.69−4.27 (5H, m, 6′-H, 5′-H, CH_2), 5.18 (1H, t, J = 9.67 Hz, 4′-H), 5.30 (1H, t, J = 9.72 Hz, 2′-H), 5.43 (1H, t, J = 9.16 Hz, 3′-H), 5.82 (1H, d, J = 10.44 Hz, 1′-H), 6.05 (2H, s, OCH_2O), 6.85−8.04 (9H, m, =CH, H-Ar). ^{13}C-NMR ($CDCl_3$): δ = 20.51, 20.61, 20.63, 20.67 (4 Ac), 35.03 (CH_2), 42.59 (CH_2), 61.68 (C-6′), 67.92 (C-2′), 69.09 (C-3′), 73.81 (C-4′), 76.86 (C-5′), 81.54 (C-1′), 101.63, 108.51, 110.83, 125.75, 126.85, 128.55, 128.71, 128.89, 136.45, 137.27, 137.79, 148.04, 148.62, 149.60 (=CH, C-5, C-Ar), 159.60 (C-2), 169.22, 169.48, 170.14, 170.68 (4C=O, C-4).

5-((Z)-4-Dimethylaminobenzylidene)-3-ethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohydantoin (9j). Yield 0.49 g (82%), m. p. 165–167 °C. MS; *m/z*: 605 (M^+). Calculated for $C_{28}H_{35}N_3O_{10}S$ (605.66): C, 55.53; H, 5.82; N, 6.94. Found: C, 55.35; H, 6.14; N, 6.76. IR (KBr): ν 1751, 1729 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.23 (3H, t, J = 7.05 Hz, CH_3), 1.86, 2.04, 2.06, 2.07 (12H, 4s, 4Ac), 3.09 (6H, s, NMe_2), 3.61 (2H, d, J = 7.80 Hz, CH_2), 3.91–4.24 (3H, m, 6′-H, 5′-H), 5.15 (1H, t, J = 9.75 Hz, 4′-H), 5.32 (1H, t, J = 9.75 Hz, 2′-H), 5.42 (1H, t, J = 9.15 Hz, 3′-H), 5.85 (1H, d, J = 10.20 Hz, 1′-H), 6.77 (2H, d, J = 8.10 Hz, H-Ar), 6.99 (1H, s, =CH), 7.28 (5H, m, H-Ar), 8.02 (1H, d, J = 9.00 Hz, H-Ar).

5-((Z)-4-Dimethylaminobenzylidene)-3-phenylmethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thio-hydantoin (9k). Yield 0.56 g (84%), m. p. 182–184 °C. MS; *m/z*: 667 (M^+). Calculated for $C_{33}H_{37}N_3O_{10}S$ (667.73): C, 59.36; H, 5.58; N, 6.29. Found: C, 59.62; H, 5.45; N, 6.20. IR (KBr): ν 1750, 1727 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.87, 1.90, 2.02, 2.06 (12H, 4s, 4Ac), 3.09 (6H, s, Nme_2), 3.87–4.22 (3H, m, 6′-H, 5′-H), 4.60, 4.90 (2H, 2d, J = 15.60, CH_2), 5.12 (1H, t, J = 9.60 Hz, 4′-H), 5.25 (1H, t, J = 9.75 Hz, 2′-H), 5.37 (1H, t, J = 9.00 Hz, 3′-H), 5.78 (1H, d, J = 10.50 Hz, 1′-H), 6.75 (2H, d, J = 8.70 Hz, H-Ar), 7.05 (1H, s, =CH), 7.28 (5H, m, H-Ar), 8.04 (1H, d, J = 8.70 Hz, H-Ar).

5-((Z)-3,4,5-Trimethoxybenzylidene)-3-phenylmethyl-S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2-thiohy-dantoin (9l). Yield 0.60 g (82%), m. p. 151–153 °C. MS; *m/z*: 728 (M^+). Calculated for $C_{35}H_{40}N_2O_{13}S$ (728.77): C, 57.68; H, 5.53; N, 3.84. Found: C, 57.52; H, 5.68; N, 3.80. IR (KBr): ν 1751, 1727 (2C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.96, 2.03, 2.04, 2.06 (12H, 4s, 4Ac), 2.94 (3H, t, J = 7.50 Hz, CH_2), 3.75–4.29 (14H, m, CH_2, $3OCH_3$, 6′-H, 5′-H), 5.13–5.25 (3H, m, 4′-H, 2′-H, 3′-H), 5.94 (1H, d, J = 9.50 Hz, 1′-H), 6.94 (1H, s, =CH), 7.18–7.45 (7H, m, H-Ar). ^{13}C-NMR ($CDCl_3$): δ = 20.53, 20.55, 20.57, 20.65 (4 Ac), 35.02 (CH_2), 42.57 (CH_2), 56.40, 61.05 ($3OCH_3$), 61.68 (C-6′), 67.83 (C-2′), 69.64 (C-3′), 73.72 (C-4′), 76.84 (C-5′), 81.41 (C-1′), 109.81, 125.61, 125.90, 126.92, 128.74, 128.92. 129.48, 137.07, 137.21, 153.19 (=CH, C-5, C-Ar), 160.68 (C-2), 169.24, 169.29, 169.33, 169.90, 170.48 (4C=O, C-4).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-(2-phenylethyl)hydantoins **(11a-c)**

A mixture of the protected nucleoside **9c,f,i** (1 mmol) in 15 ml of anhydrous CH_3OH and 5 ml of 1% CH_3ONa was stirred at room temperature for 12 h. The separated solid was filtered off and recrystallized from acetic acid to give the products **11a-c**.

(Z)-5-Benzylidene-3-(2-phenylethyl)hydantoin (11a). Yield 0.15 g (53%), m.p. 219–221 °C. MS; *m/z*: 292 (M^+). Calculated for $C_{18}H_{16}N_2O_2$ (292.34): C,

73.95; H, 5.52; N, 9.58. Found: C, 73.62; H, 5.70; N, 9.34. IR (KBr): ν 3192 (NH), 1758, 1710 (2 C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.93 (2H, t, J = 7.40, CH_2), 3.75 (2H, t, J = 7.44 Hz, CH_2), 6.50 (1H, s, =CH), 7.17−7.60 (10H, m, H-Ar), 10.69 (1H, s, NH). ^{13}C-NMR (DMSO-d_6): δ 33.51 (CH_2), 40.84 (CH_2), 109.60 (=CH), 125.51, 126.34, 128.32, 128.35, 128.54, 128.61, 128.67, 128.95, 129.41, 132.80, 137.93 (C-5, C-Ar), 154.92 (C-2), 163.87 (C-4).

3-(2-Phenylethyl)-5-((Z)-2-thienylidene)hydantoin (11b). Yield 0.14 g (46%), m.p. 198−200 °C. MS; *m/z*: 298 (M^+). Calculated for $C_{16}H_{14}N_2O_2S$ (298.36): C, 64.41; H, 4.73; N, 9.39. Found: C, 64.60; H, 5.00; N, 9.32. IR (KBr): ν 3190 (NH), 1757, 1709 (2 C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.96 (2H, t, J = 7.60, CH_2), 3.79 (2H, t, J = 7.60 Hz, CH_2), 6.68 (1H, s, =CH), 7.11−7.81 (8H, m, H-Ar), 10.32 (1H, s, NH). ^{135}Dept-NMR (DMSO-d_6): δ 33.11 (CH_2), 39.81 (CH_2), 103.27 (=CH), 126.62, 127.97, 128.37, 128.61, 129.06 (CH-Ar).

5-((Z)-3,4-Methylenedioxybenzylidene)-3-(2-phenylethyl)hydantoin (11c). Yield 0.16 g (47%), m.p. 223−225 °C. MS; *m/z*: 336 (M^+). Calculated for $C_{19}H_{16}N_2O_4$ (336.35): C, 67.85; H, 4.79; N, 8.33. Found: C, 67.58; H, 5.02; N, 8.15. IR (KBr): ν 3192 (NH), 1756, 1708 (2 C=O) cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.94 (2H, t, J = 7.60, CH_2), 3.75 (2H, t, J = 7.60 Hz, CH_2), 6.03 (2H, s, OCH_2O), 6.45 (1H, s, =CH), 6.83−7.30 (8H, m, H-Ar), 10.55 (1H, s, NH).

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