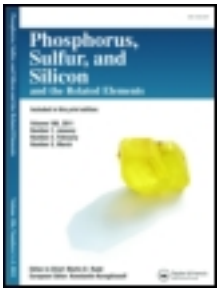


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

# SULFUR GLYCOSYLATION REACTIONS INVOLVING 3-ALLYL-2-THIOHYDANTOIN NUCLEOSIDE BASES AS POTENTIAL ANTIVIRAL AND ANTITUMOR AGENTS

Ahmed I. Khodair [a c] & Jean-Pierre Gesson [b]

[a] Chemistry Department, Faculty of Education, Tanta University (Kafr El-Sheikh Branch), Tanta, Egypt

[b] Laboratoire de Chimie XII, Université de Poitiers et CNRS, 40 Avenue du Recteur Pineau, 86022, Poitiers, France

[c] Laboratoire de Chimie XII, Université de Poitiers et CNRS, 40 Avenue du Recteur Pineau, 86022, Poitiers, France Fax: E-mail:

Published online: 24 Sep 2006.

*Phosphorus, Sulfur and Silicon*, 1998, Vol. 142, pp. 167-190
Reprints available directly from the publisher
Photocopying permitted by license only





# SULFUR GLYCOSYLATION REACTIONS INVOLVING 3-ALLYL-2-THIOHYDANTOIN NUCLEOSIDE BASES AS POTENTIAL ANTIVIRAL AND ANTITUMOR AGENTS

AHMED I. KHODAIR[a*†] and JEAN-PIERRE GESSON[b]

[a]*Chemistry Department, Faculty of Education, Tanta University (Kafr El-Sheikh Branch), Tanta, Egypt and* [b]*Laboratoire de Chimie XII, Université de Poitiers et CNRS, 40 Avenue du Recteur Pineau, 86022 Poitiers, France*

*(Received 25 June, 1998; In final form 18 August, 1998)*

3-Allyl-5-(Z)-arylidene-2-thiohydantoins **8a-f** were synthesized from the direct condensation of the aromatic aldehydes **7a-f** with 3-allyl-2-thiohydantoin **(6),** which in turn was prepared from the reaction of glycine and allyl isothiocyanate. The alkylation of **8a-f** with alkyl bromides **9a,b** gave 3allyl-5-(Z)-arylidene-2-(alkylmercapto)hydantoins **1a-l.** *S*-Glycosylation and *S*-ribosylation took place on the reaction of **8a-f** with pyranosyl bromides **11a,b** and furanosyl bromide **(15)** under anhydrous alkaline conditions. The *S*-nucleoside structure, and not that of the *N*-nucleoside isomer, has been selected for the products. This structure has been confirmed from a model study of the coupling of **8a** with α-D-glucose pentaacetate **(13)** and α-D-ribose tetrabenzoate **(16)** under Lewis acid conditions. The compounds do not display any antiviral and antitumoral activity.

*Keywords:* Pyranosyl bromides; 3-allyl-2-thiohydantoin; S-glycosylation; antiviral and antitumor

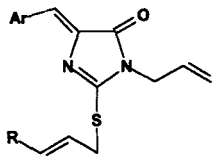
## INTRODUCTION

Several 5-arylidene-3-aryl-2-thiohydantoins and their nucleosides show potent activity against the herpes simplex virus (HSV),[1] the human immunodeficiency virus (HIV),[2] and the leukemia subpanel.[3] Moreover, a certain series of hydantoin derivatives showed interesting activities,

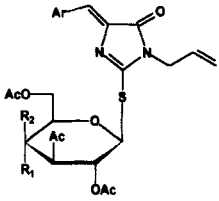
* Present address: Laboratoire de Chimie XII, Université de Poitiers et CNRS, 40 Avenue du Recteur Pineau, 86022 Poitiers, France. Fax: (00) 33 (05) 49 45 35 01, E-mail: ahmed.khodair@mailexcite.com
† Corresponding author

including antiviral,[4] antiinflammatory,[5–7] anticonvulsant,[8] antidepressant,[9] and platelet inhibitory activities[10] and have structural features like those of several inhibitors of aldose reductase.[11,12] 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.[1–3,13,14] In this respect, the linking of the latter to an unsaturated hydrocarbon moiety and sugar moiety were considered.

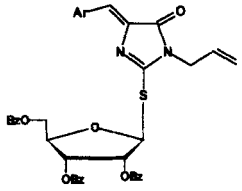
Structures such as **1a-l, 2a-l** and **3a,b** were selected and their synthesis planned with the anticipated coupling of these two moieties by a thiol unit. We report in this paper the synthesis of a new series of 3-allyl-2-thiohydantoins and their corresponding *S*-alkylated, *S*-glycosylated, and *S*-ribosylated derivatives *via* anhydrous alkaline and Lewis acid conditions.




**1a-l**




**2a-l**




**3a,b**

## RESULTS AND DISCUSSION

3-Allyl-2-thiohydantoin **(6)** was prepared in an overall yield of 65 % in two steps from the reaction of glycine **(4)** and allyl isothiocyanate **(5).** The appropirate aromatic aldehydes **7a-f** were condensed with **6** by refluxing in a solution of anhydrous sodium acetate and glacial acetic acid to give 3-allyl-5-*(Z)*-arylidene- 2-thiohydantoins **8a-f** (Scheme 1). The structures of compounds **8a-f** were established on the basis of spectral data (IR, $^1$H-NMR, $^{13}$C-NMR, and MS). The IR absorption spectra of compound **8a** was characterized by the presence of signals for NH and C=O groups at 3309 cm$^{-1}$ and 1728 cm$^{-1}$. The $^1$H-NMR (DMSO-$d_6$) spectrum of compound **8e** showed a singlet at δ 6.78, 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 (DMSO-$d_6$) spectra of 5-*(E)*- and 5-*(Z)*arylidene-3-methylhydantoins whose vinyl protons, respectively,

appear at δ 6.10-6.35 and 6.40-6.75[15]. The $^{13}$C-NMR (DMSO-$d_6$) spectrum of compound **8e** showed the presence of a signal at 105.67 was assigned to the vinilic carbon, indicating the presence of a *Z*-configuration for the exocyclic double bond, in agreement with the $^{13}$C-NMR (DMSO-$d_6$) spectra of 5-*(Z)*- and 5-*(E)*-arylidenehydantoin derivatives, respectively, give signals at δ 105-112 and 113-120[15–17]. This result was confirmed by the study of the energy calculations of **8a** at AM1 level[18] in order to determine the relative energies of the possible tautomeric forms. These also allow determination of the relative energies of the *E* and *Z* isomers of 5-arylidene-2-thiohydantoin derivatives. It was found that the *Z*-isomer is more stable by 2.50-3.60 kcal/mol for **8a** and thus no double bond isomerisation is anticipated. For compound **8a,** the 4 tautomeric forms α, β, γ, and δ were considered. This result confirms that the exocyclic double bond must be *Z*. Those results show that **8a** must be present as α form and can be applied to compounds **8a-f** (Figure 1).

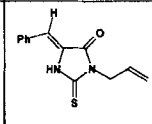
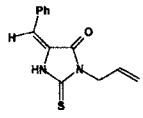
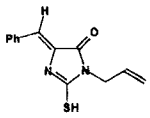
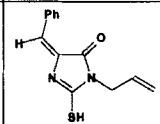
| Form (ΔE kcal/mol) | α (–9.40) | β (–5.80) | γ (–2.50) | δ (0) |
|---|---|---|---|---|
| |  |  |  |  |

FIGURE 1 Relative energies (kcal/mol) of toutomers (α – δ) for compound **8a**

Compounds **8a-f** were reacted with unsaturated alkyl bromides **9a,b** in the presence of aqueous sodium hydroxide to afford 3-allyl-5-*(Z)*-arylidene-2-(alkyl- mercapto)hydantoins **1a-l** (Scheme 1). The structures of **1a-l** were confirmed on the basis of elemental analyses and spectral data (IR, $^1$H-NMR, $^{13}$C-NMR, and MS). The IR absorption spectra of compound **1a** was characterized by the absence of signals for NH and C=S groups at 3309 cm$^{-1}$ and 1465 cm$^{-1}$ and the presence of a signal at 1707 cm$^{-1}$ due to the carbonyl group. The $^1$H-NMR ($CDCl_3$) spectrum of compound **1a** showed a singlet at δ 6.97 assigned to the vinylic proton, indicating the presence of a *Z*-configuration for the exocyclic double bond, in agreement with the $^1$H-NMR (DMSO-$d_6$) spectrum of its oxygen analogue **(10a).** The latter was prepared from the reaction of **1a** with 12 *N* hydro-

chloric acid in refluxing ethanol, who vinyl proton appears at δ 6.75 and the $^1$H-NMR (DMSO$d_6$) spectra of 5-*(E)*- and 5-*(Z)*-arylidene-3-methylhydantoins whose vinyl protons, respectively, appear at δ 6.10-6.35 and 6.40-6.75[15]. The $^{13}$C-NMR (DMSO-$d_6$) spectrum of compound **10b** showed the presence of a signal at 110.29 was assigned to the vinilic carbon, indicating the presence of a Z-configuration for the exocyclic double bond, in agreement with the $^{13}$C-NMR (DMSO-$d_6$) spectra of 5-*(Z)*- and 5-*(E)*-arylidenehydantoin derivatives, respectively, give signals at δ 105-112 and 113-120[15-17]. It was found that the $^{13}$C-NMR ($CDCl_3$) spectrum of compound **1a** showed the presence of a signal at 124.06 was assigned to the vinilic carbon, indicating the presence of a *E*-configuration for the exocyclic double bond. At this stage, energy calculations of **1a** at the AM1 level[18] were considered in order to determine the relative energies of the possible tautomeric forms. It was found that the *Z*-isomer is more stable by 2.36 kcal/mol for **1a** and thus no double bond isomerisation is anticipated. For compounds **1a** the 2 tautomeric forms α and β were considered. This result confirms that the exocyclic double bond must be Z. Those results show that **1a** must be present as α forms and can be applied to compounds **1a-l, 2a-l** and **3a,b** (Figure 2).

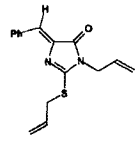
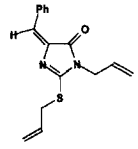
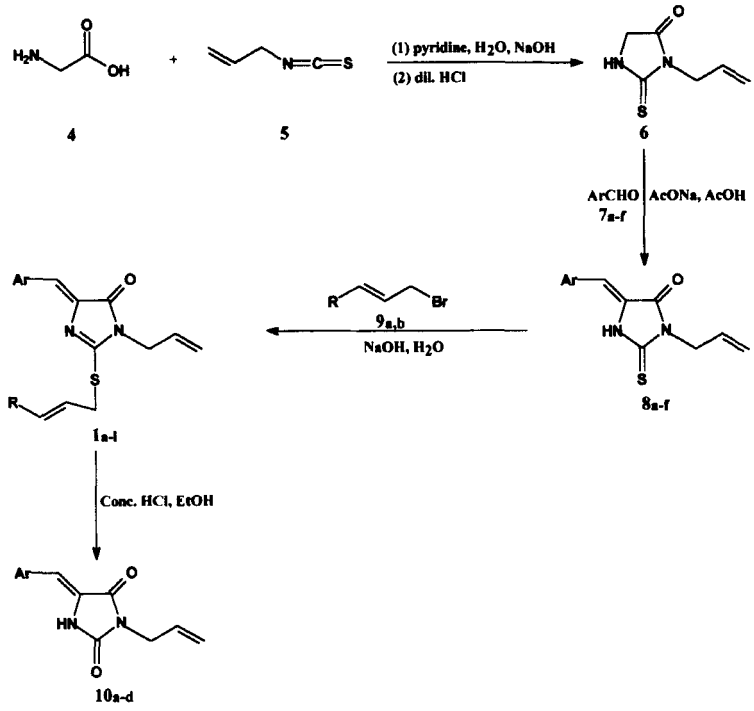
| Form (ΔE kcal/mol) | 1aα (–2.36) | 1aβ (0) |
|---|---|---|
| |  |  |

FIGURE 2 Relative energies (kcal/mol) of toutomers (α and β) for compound **1a**

Compounds **8a-f** were reacted with 1.1 equivalents of NaH in anhydrous acetonitrile followed by 1.1 equivalents of the 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromides[19] **11a,b** to give 3-allyl-5-(Z)-arylidene-2-(2′,3′,4′,6′-tetra- *O*-acetyl-β-D-glycopyranosylmercapto)hydantoins **2a-l**. Compound **2a** was also independently synthesized through another pathway *via* condensation of **3** allyl-5-(Z)-benzylidene-2-(trimethylsilylmercapto)hydantoin **(12)**, which in turn was prepared from the reaction of **8a**



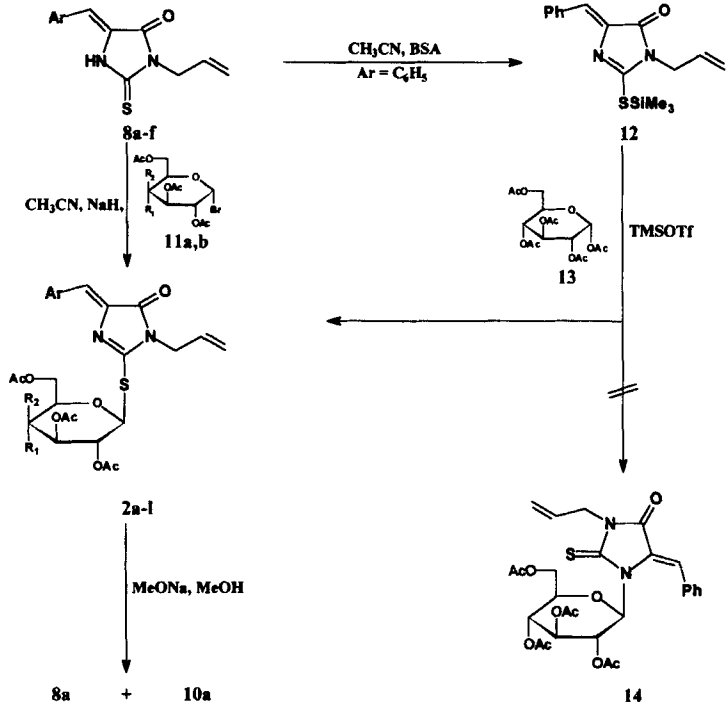

| 1,7,8,10 | Ar | R |
|---|---|---|
| a | $C_6H_5$ | H |
| b | 4-$MeOC_6H_4$ | H |
| c | 4-$MeC_6H_4$ | H |
| d | 4-$ClC_6H_4$ | H |
| e | 2-thienyl | H |
| f | 2-furyl | H |

| 1,7,8,10 | Ar | R |
|---|---|---|
| g | $C_6H_5$ | Me |
| h | 4-$MeOC_6H_4$ | Me |
| i | 4-$MeC_6H_4$ | Me |
| j | 4-$ClC_6H_4$ | Me |
| k | 2-thienyl | Me |
| l | 2-furyl | Me |

SCHEME 1

with bis(trimethylsilyl)acetamide (BSA) in acetonitrile with α-D-glucose pentaacetate **(13)** in the presence of trimethylsilyltrifluoromethane sulfonate (TMSOTf) at room temperature for 2 h. The nucleoside **2a** was isolated by silica gel column chromatograph (60%), and no other nucleoside was detected in the reaction mixture (TLC). The structure of compounds **2a-l** were established on the basis of spectral data (IR, $^1$H-NMR, $^{13}$C-NMR, and MS). The IR absorption spectra of compound **2a** was characterized by the absence of signal for NH group at 3309 $cm^{-1}$ and the presence of acetoxy groups of sugar moiety at 1751 $cm^{-1}$ in addition to the

signal of the carbonyl group at 1728 $cm^{-1}$. The $^1$H-NMR spectrum of compound **2a** showed a doublet at δ 5.80 with a spin-spin coupling constant of 10.38 Hz which corresponded to the diaxial orientation of 1′-H and 2′-H protons in agreement with a β-configuration.[1] The singlet at δ 6.99, which was assigned to the vinylic proton, confirmed the presence of a *Z*-configuration for the exocyclic double bond (Scheme 2). To on protecting acetyl groups from the glycon-moiety, **2a** was treated with sodium methoxide in methanol at 0 °C and only **8a** (50 %) and **10a** (38 %) were isolated. This type of cleavage explains the lack of success in the preparation of the corresponding deprotected nucleosides of **2a-1** and **3a,b.**

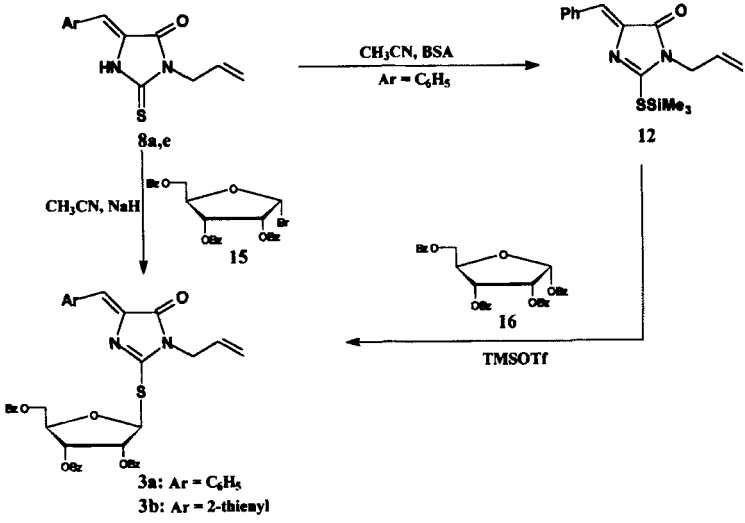



| 2a-f | Ar | $R_1$ | $R_2$ |
|---|---|---|---|
| a | $C_6H_5$ | Ac | H |
| b | 4-$MeOC_6H_4$ | Ac | H |
| c | 4-$MeC_6H_4$ | Ac | H |
| d | 4-$ClC_6H_4$ | Ac | H |
| e | 2-thienyl | Ac | H |
| f | 2-furyl | Ac | H |

| 2g-l | Ar | $R_1$ | $R_2$ |
|---|---|---|---|
| g | $C_6H_5$ | H | Ac |
| h | 4-$MeOC_6H_4$ | H | Ac |
| i | 4-$MeC_6H_4$ | H | Ac |
| j | 4-$ClC_6H_4$ | H | Ac |
| k | 2-thienyl | H | Ac |
| l | 2-furyl | H | Ac |

SCHEME 2

For the synthesis of 3-allyl-5-(Z)-arylidene-2-(2′,3′,5′-tri-*O*-benzoyl-β -D-ribofuranosylmercapto)hydantoins **3a,b,** compounds **8a,e** were likewise treated with 1 equivalent of the 2,3,5-tri-*O*-benzoyl-α-D-ribofuranosyl bromide[20] **(15).** When compound **8a** was subjected to a reaction with 1,2,3,5 -tetra-*O*-benzoyl-α-D-ribofuranoside[20] **(16)** in the presence of TMSOTf in anhydrous acetonitrile, the corresponding 4-imidazolidinone-2-thione riboside **3a** was obtained. This compound was shown to be the same as that obtained from the reaction of 4-imidazolidinone-2-thione **(8a)** with bromide **15.** The structure of compounds **3a,b** are in agreement with their spectral data (IR, $^1$H-NMR, $^{13}$C-NMR, and MS). The IR absorption spectra of compound **3a** was characterized by the absence of signal for NH group at 3309 cm$^{-1}$ and the presence of the carbonyl groups at 1727 cm$^{-1}$. The $^1$H-NMR spectrum of compound **3a** showed a doublet at δ 6.76 with a spin-spin coupling constant of 6.64 Hz which corresponded to the diaxial orientation of 1′-H and 2′-H protons, proving the presence of a β-configuration.[1] The singlet at δ 7.06 which was assigned to the vinylic proton, indicated the presence of a *Z*-configuration for the exocyclic double bond (Scheme 3).




SCHEME 3

In conclusion, we have described the successful synthesis of 3-allyl-2-thiohydantoins and their corresponding *S*-alkylated, *S*-glyco-

sylated and *S*-ribosylated derivatives *via* two different routes. Compounds **1a-l, 2a-l** and **3a,b** have been examined for antiviral properties. They did not inhibit HIV-1 even at 100 μg/ml.[21] For antitumor properties, compound **2e** was tested against L1210 leukemia preminary tests *in vivo* and was found to be inactive.[22]

## EXPERIMENTAL

### General Method

$^1$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). Melting points are uncorrected. 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. Elemental analysis were obtained from the Microanalytical Center Servace (CNRS, Lyon). Column chromatography was performed with silica gel 60 mesh ASTM (Merck). 2,3,4,6-Tetra-*O*-acetyl-α-D- glycopyranosyl bromides **11a,b** were prepared according to the published method of Lemieux,[19] while 2,3,5-tri-*O*-benzoyl-α-D-ribofuranosyl bromide **(15)** was prepared similar to the method used for the preparation of 2,3,5,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide.[20]

### 3-Allyl-2-thiohydantoin (6)

Glycine (**4**, 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. Allyl isothiocyanate (**5,** 1.95 ml, 20 mmol) was added with vigorous stirring. Small portions of 1 *N* NaOH were added to keep the pH at about 9. The reaction was completed when the alkali consumption ceased (calcd. 60 min). Pyridine and excess allyl isothiocyanate were then removed by repeated extractions with equal volumes of benzene. Subsequently an amount of conc. HCl (3 ml) was added and the mixture was refluxed for 2 h. The reaction mixture was concentrated to half its volume under vaccum,

and cooled to room temperature. The pale yellow solid was collected by filtration and recrystallized from methanol to give **6,** 1.01 g (65%). mp 104-106 °C. MS; *m/z:* 156 ($M^+$). Calculated for $C_6H_8N_2OS$ (156.20): C, 46.14; H, 5.16; N, 17.93. Found: C, 46.25; H, 5.18; N, 17.97. IR (KBr) : ν 3221 (NH), 1751 (C=O), 1525 (C=S) $cm^{-1}$. $^1$H-NMR ($CDCl_3$): δ 4.13 (2 H, S, 5-H), 4.44 (2 H, m, 3-$H_{allyl}$), 5.25 (2 H, m, 1-$H_{allyl}$), 5.88 (1 H, m, 2-$H_{allyl}$), 8.15 (1 H, s, NH). $^{13}$C-NMR ($CDCl_3$) : δ 43.18 (C-$3_{allyl}$), 48.58 (C-5), 118.55 (C-$1_{allyl}$), 130.40 (C-$2_{allyl}$), 171.36 (C-4), 184.53 (C-2).

### 3-Allyl-5-(*Z*)-arylidene-2-thiohydantoins 8a-f

To a mixture of 3-allyl-2-thiohydantoin (**6**, 1.56 g, 10 mmol), anhydrous sodium acetate, and glacial acetic acid (15 ml) was added the appropriate aromatic aldehyde **7a-f** (11 mmol). The mixture was heated under reflux for 3 h, cooled to room temperature, and then poured into cold water. The yellow solid was collected by filtration and recrystallized from acetic acid to give **8a-f.**

### 3-Allyl-5-(*Z*)-benzylidene-2-thiohydantoin (8a)

Yield 2.34 g (96%), mp 154-156 °C. MS; m/z: 244 ($M^+$). Calculated for $C_{13}H_{12}N_2OS$ (244.31): C, 63.91; H, 4.95; N, 11.47. Found: C, 63.80; H, 4.78; N, 11.22. IR (KBr) : ν 3309 (NH), 1709 (C=O), 1465 (C=S) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 4.64 (2 H, d, *J*= 3.06 Hz, 3-$H_{allyl}$), 5.24 (2 H, m, 1-$H_{allyl}$), 5.72 (1 H, m, 2-$H_{allyl}$), 6.75 (1 H, s, =CH), 7.40 (5 H, m, $H_{arom}$), 9.39 (1 H, s, NH). $^{13}$C-NMR ($CDCl_3$) : δ 43.33 (C-$3_{allyl}$), 113.92 (=CH), 118.60 (C$1_{allyl}$), 126.26 (C-$2_{allyl}$), 129.28, 129.39, 129.76, 130.37, 132.61 (C-5, Carom), 163.43 (C-4), 177.86 (C-2).

### 3-Allyl-5-(*Z*)-(4-methoxybenzylidene )-2-thiohydantoin (8b)

Yield 2.68 g (98%), mp 142-144 °C. MS; m/z: 274 ($M^+$). Calculated for $C_{14}H_{14}N_2O_2S$ (274.34): C, 61.29; H, 5.14; N, 10.21. Found: C, 61.51; H, 5.12; N, 10.03. IR (KBr) : ν 3226 (NH), 1724 (C=O), 1464(C=S) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 3.85 (3 H, s, $OCH_3$), 4.51 (2 H, d, *J*= 3.18 Hz, 3-$H_{allyl}$), 5.24 (2 H, m, 1-$H_{allyl}$), 5.88 (1 H, m, 2-$H_{allyl}$), 6.72 (1 H, s, =CH), 6.97, 7.45 (4 H, 2d, *J* = 9.20 Hz, $H_{arom}$), 9.33 (1 H, s, NH). $^{13}$C-NMR ($CDCl_3$) : δ 43.33 (C-$3_{allyl}$), 56.46 ($OCH_3$), 115.95 (=CH), 119.47

($C\text{-}1_{allyl}$), 125.53 ($C\text{-}2_{allyl}$), 126.14, 126.85, 131.50, 132.24, 161.88 (C-5, $C_{arom}$), 164.57 (C-4), 178.44 (C-2).

### 3-Allyl-5 -(*Z*)-(4-methylbenzylidene )-2-thiohydantoin (8c)

Yield 2.42 g (92%), mp 152-154 °C. MS; m/z: 258 ($M^+$). Calculated for $C_{14}H_{14}N_2OS$ (258.34): C, 65.09; H, 5.46; N, 10.84. Found: C, 65.21; H, 5.48; N, 10.88. IR (KBr) : ν 3249 (NH), 1731 (C=O), 1469(C=S) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 2.38 (3 H, s, $CH_3$), 4.52 (2 H, d, *J*= 3.18 Hz, $3\text{-}H_{allyl}$), 5.24 (2 H, m, $1\text{-}H_{allyl}$), 5.88 (1 H, m, $2\text{-}H_{allyl}$), 6.72 (1 H, s, =CH), 6.97, 7.45 (4 H, 2d, J = 9.20 Hz, $H_{arom}$), 9.33 (1 H, s, NH). $^{13}$C-NMR ($CDCl_3$) : δ 43.33 ($C\text{-}3_{allyl}$), 56.46 ($CH_3$), 115.95 (=CH), 119.47 ($C\text{-}1_{allyl}$), 125.53 ($C\text{-}2_{allyl}$), 126.14, 126.85, 131.50, 132.24, 161.88 (C-5, $C_{arom}$), 164.57 (C-4), 178.44 (C-2).

### 3-Allyl-5-(*Z*)-(4-chlorobenzylidene)-2-thiohydantoin (8d)

Yield 2.70 g (97%), mp 185-187 °C. MS; m/z: 278 ($M^+$). Calculated for $C_{13}H_{11}ClN_2OS$ (278.76): C, 56.01; H, 3.98; N, 10.05. Found: C, 56.07; H, 4.03; N, 10.15. IR (KBr) : ν 3242 (NH), 1729 (C=O), 1461(C=S) $cm^{-1}$. $^1$H-NMR ($CD_3COCD_3$) : δ 4.50 (2 H, d, *J*= 2.72 Hz, $3\text{-}H_{allyl}$), 5.20 (2 H, m, $1\text{-}H_{allyl}$), 5.90 (1 H, m, $2\text{-}H_{allyl}$), 6.65 (1 H, s, =CH), 7.49, 7.75 (4 H, 2d, *J* = 8.30 Hz, $H_{arom}$), 11.08 (1 H, s, NH). $^{13}$C-NMR ($CD_3COCD_3$) : δ 43.62 ($C\text{-}3_{allyl}$), 111.47 (=CH), 117.80 ($C\text{-}1_{allyl}$), 126.71 ($C\text{-}2_{allyl}$), 127.93, 129.86, 132.04, 132.57, 135.30 (C-5, $C_{arom}$), 164.25 (C-4), 179.24 (C-2).

### 3-Allyl-5-(*Z*)-(2-thienylidene)-2-thiohydantoin (8e)

Yield 2.30 g (92%), mp 146-148 °C. MS; m/z: 250 ($M^+$). Calculated for $C_{11}H_{10}N_2OS_2$(250.34): C, 52.78; H, 4.03; N, 11.19. Found: C, 52.93; H, 4.06; N, 11.27. IR (KBr) : ν 3365 (NH), 1717 (C=O), 1458(C=S) $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) : δ 4.42 (2 H, d, *J* = 4.76 Hz, $3\text{-}H_{allyl}$), 5.13 (2 H, m, $1\text{-}H_{allyl}$), 5.86 (1 H, m, $2\text{-}H_{allyl}$), 6.78 (1 H, s, =CH), 7.22, 7.82, 7.90 (3 H, 3d, J = 4.20 Hz, H-4, 3, $5_{thiophen}$), 12.25 (1 H, s, NH). $^{13}$C-NMR (DMSO-$d_6$) : δ 42.47 ($C\text{-}3_{allyl}$), 105.67 (=CH), 116.86 ($C\text{-}1_{allyl}$), 123.96 ($C\text{-}2_{allyl}$), 129.13, 130.70, 130.98, 131.39, 135.26 (C-5, C-3, 4, 5, $2_{thiophen}$), 163.33 (C-4), 177.62 (C-2).

**3-Allyl-5-(Z)-(2-furylidene )-2-thiohydantoin (8f)**

Yield 2.01 g (86%), mp 144-146 °C. MS; m/z: 234 ($M^+$). Calculated for $C_{11}H_{10}N_2O_2S$ (234.27): C, 56.40; H, 4.30; N, 11.96. Found: C, 56.50; H, 4.34; N, 12.01. IR (KBr) : ν 3239 (NH), 1731 (C=O), 1453 (C=S) $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) : δ 4.42 (2 H, d, $J$ = 3.58 Hz, 3-$H_{allyl}$), 5.14 (2 H, m, 1-$H_{allyl}$), 5.86 (1 H, m, 2-$H_{allyl}$), 6.57 (1 H, s, =CH), 6.69, 7.19, 7.88 (3 H, 3m, H-3, 4, $5_{furan}$), 12.10 (1 H, s, NH). $^{13}$C-NMR (DMSO-$d_6$) : δ 42.44 (C-$3_{allyl}$), 100.28 (C-$3_{furan}$), 113.18 (=CH), 116.05 (C-$1_{allyl}$), 116.86 (C-$4_{furan}$), 123.63 (C-$2_{allyl}$), 131.46 (C-5), 146.00 (C-$2_{furan}$), 148.77 (C-$5_{furan}$), 163.33 (C-4), 177.62 (C-2).

**3-Allyl-5-(Z)-arylidene-2-(alkylmercapto)hydantoins 1a-l**

3-Allyl-5-(Z)-arylidene–2-thiohydantoins **8a-f** (1 mmol) were dissolved in aqueous NaOH (1%, 5 ml) at room temperature. To this solution was added allyl or crotyl bromides **11a,b** (1 mmol), and the reaction mixture was stirred for 4 h at room temperature. The precipitated solid was collected by filteration and crystallized from methanol to give the products **1a-l.**

**3-Allyl-5-(Z)-benzylidene –2-(allylmercapto)hydantoin (1a)**

Yield 0.25 g (90%), mp 78-80 °C. MS; m/z: 284 ($M^+$). Calculated for $C_{16}H_{16}N_2OS$ (284.38): C, 67.58; H, 5.67; N, 9.85. Found: C, 67.66; H, 5.69; N, 9.87. IR ($CCl_4$) : ν 1707 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ 4.00, 4.21 (4 H, 2dd, $J$ =0.75, 7.12 Hz, 3-$H_{allyl}$), 5.19–5.27 (4 H, m, 1-$H_{allyl}$), 5.48, 6.09 (2 H, 2m, 2-$H_{allyl}$), 6.97 (1 H, s, =CH), 7.38–8.16 (5 H, m, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 33.44, 42.75 (C-$3_{allyl}$), 118.08, 119.50 (C-$2_{allyl}$), 124.06 (=CH), 128.66, 129.80, 131.20, 131.84, 132.00, 134.40, 138.14 (C-$1_{allyl}$, C-5, $C_{arom}$), 163.86 (C-2), 169.40 (C-4).

**3-Allyl-5 -(Z)-(4-methoxybenzylidene)-2-(allylmercapto)hydantoin (1b)**

Yield 0.30 g (94%), mp 89-91 °C. MS; m/z: 314 ($M^+$). Calculated for $C_{17}H_{18}N_2O_2S$ (314.40): C, 64.94; H, 5.77; N, 8.91. Found C 65.02; H, 5.81; N, 8.88. IR ($CCl_4$) : ν 1704 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ 3.85 (3 H, s, $CH_3$), 4.01, 4.21 (4 H, 2dd, $J$=0.74, 7.00 Hz, 3-$H_{allyl}$), 5.18–5.44 (4 H, m, 1-$H_{allyl}$), 5.80, 6.04 (2 H, m, 2-$H_{allyl}$), 6.84–6.94 (3 H, m, =CH, $H_{arom}$), 8.14 (2 H, d, $J$= 8.66 Hz, $H_{arom}$).

**3-Allyl-5 -(*Z*)-(4-methylbenzylidene )-2-(allylmercapto)hydantoin (1c)**

Yield 0.28 g (93%), mp 58-60 °C. MS; m/z: 298 ($M^+$). Calculated for $C_{17}H_{18}N_2OS$ (298.40): C, 68.43; H, 6.08; N, 9.39. Found: C, 68.14; H, 5.98; N, 9.52. IR ($CCl_4$) : ν 1714 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : 6 2.38 (3 H, s, $CH_3$), 4.01, 4.22 (4 H, 2dd, J= 0.72, 7.04 Hz, 3-$H_{allyl}$), 5.19–5.44 (4 H, m, 1-$H_{allyl}$), 5.80, 6.04 (2 H, 2m, 2-$H_{allyl}$), 6.95 (1 H, s, =CH), 7.23, 8.05 (4 H, 2d, *J*= 7.80 Hz, $H_{arom}$).

**3-Allyl-5-(*Z*)-(4-chlorobenzylidene)-2-(allylmercapto)hydantoin (1d)**

Yield 0.29 g (91%), mp 80-82 °C. MS; m/z: 318 ($M^+$). Calculated for $C_{16}H_{15}ClN_2OS$ (318.82): C, 60.28; H, 4.74; N, 8.79. Found: C, 60.31; H, 4.77; N, 8.86. IR ($CCl_4$) : ν 1722 $cm^{-1}$ (C=O). $^1$H-NMR ($CD_3COCD_3$) : δ 4.01, 4.22 (4 H, 2m, 3-$H_{allyl}$), 5.21–5.45 (4 H, m, 1-$H_{allyl}$), 5.75–6.09 (2 H, 2m, 2-$H_{allyl}$), 6.90 (1 H, s, =CH), 7.37, 8.10 (4 H, 2dd, J= 1.80, 8.50 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 33.84, 43.05 (C-$3_{allyl}$), 118.10, 118.38 (C-$2_{allyl}$), 119.65 (=CH), 127.61, 131.53, 132.47, 133.11, 133.65, 136.45, 138.43 (C-$1_{allyl}$, C-5, $C_{arom}$), 162.76 (C-2), 168.83 (C-4).

**3-Allyl-5-(*Z*)-(2-thienylidene)-2-(allylmercapto)hydantoin (1e)**

Yield 0.24 g (82%), mp 68-70 °C. MS; m/z: 290 ($M^+$). Calculated for $C_{14}H_{14}N_2OS_2$(290.40): C, 57.90; H, 4.86; N, 9.65. Found C, 57.95; H, 4.88; N, 9.67. IR ($CCl_4$) : ν 1707 $cm^{-1}$ (C=O). $^1$H-NMR (DMSO-$d_6$) : δ 4.03, 4.21 (4 H, 2dd, *J*= 0.75, 7.10 Hz, 3-$H_{allyl}$), 5.19–5.48 (4 H, m, 1-$H_{allyl}$), 5.74, 6.08 (2 H, 2m, 2-$H_{allyl}$), 7.09 (1 H, dd, *J*= 3.76, 5.06 Hz, H-$4_{thiophen}$), 7.26 (1 H, s, =CH), 7.47 (1H, d, *J*= 3.60, Hz, H-$3_{thiophen}$), 7.58 (1 H, d, *J*= 5.10 Hz, H-$5_{thiophen}$). $^{13}$C-NMR ($CDCl_3$) : δ 33.35, 42.67 (C-$3_{allyl}$), 118.10, 119.41 (C$2_{allyl}$), 122.24 (=CH), 128.73, 131.03, 131.80, 132.81, 132.83, 135.46, 138.34 (C-$1_{allyl}$, C-5, $C_{arom}$), 164.34 (C-4), 169.07 (C-2).

**3-Allyl-5-(*Z*)-(2-furylidene)-2-(allylmercapto)hydantoin (1f)**

Yield 0.20 g (86%), mp 55-57 °C. MS; m/z: 234 ($M^+$). Calculated for $C_{14}H_{14}N_2O_2S$ (274.34): C, 61.29; H, 5.14; N, 10.29. Found: C, 61.35; H, 5.17; N, 10.26. IR ($CCl_4$) : ν 1705 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ

4.01, 4.20 (4 H, 2d, $J$= 6.05 Hz, 3-$H_{allyl}$), 5.18–5.44 (4 H, m, 1-$H_{allyl}$), 5.79, 6.05 (2 H, m, 2-$H_{allyl}$), 6.58 (1 H, s, =CH), 6.92, 7.38, 7.57 (3 H, 3m, H-3, 4, 5$_{furan}$). $^{13}$C-NMR ($CDCl_3$) : δ 33.27, 42.44 (C-3$_{allyl}$), 111.53 (C-3$_{furan}$), 113.09 (C-4$_{furan}$), 117.22, 117.99 (C-1$_{allyl}$), 119.35 (=CH), 131.12, 131.84 (C-2$_{allyl}$), 135.70 (C-5), 144.89 (C-2$_{furan}$), 151.05 (C-5$_{furan}$), 163.09 (C-2), 168.59 (C-4).

### 3-Allyl-5-(*Z*)-benzylidene-2-(crotylmercapto)hydantoin (1g)

Yield 0.26 g (86%), mp 71-83 °C. MS; m/z: 298 ($M^+$). Calculated for $C_{17}H_{18}N_2OS$ (298.40): C, 68.43; H, 6.08; N, 9.39 Found: C, 68.50; H, 6.10; N, 9.43. IR ($CCl_4$) : ν 1711 $cm^{-1}$ (C=O). $^1$H -NMR ($CDCl_3$) : δ 1.73 (3 H, d, $J$= 6.30 Hz, 1-$H_{crotyl}$), 3.96 (2 H, d, $J$ = 7.28 Hz, 4-$H_{crotyl}$), 4.18 (2 H, d, $J$ = 5.42 Hz, 3-$H_{allyl}$), 5.18–5.23 (2 H, m, 1-$H_{allyl}$), 5.65–5.89 (3 H, m, 2-$H_{allyl}$, 2-$H_{crotyl}$, 3-$H_{crotyl}$), 6.95 (1 H, s, =CH), 7.34–7.42 (3 H, m, $H_{arom}$), 8.14 (2 H, d, $J$ = 6.87 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 17.73 (C-1$_{crotyl}$), 33.01 (C-4$_{crotyl}$), 42.63 (C-3$_{allyl}$), 117.97 (C-2$_{allyl}$), 123.75 (C-2$_{crotyl}$), 124.41 (=CH), 128.48, 129.60, 131.18, 131.75, 134.37, 138.17 (C-1$_{allyl}$, C-3$_{crotyl}$, C-5, $C_{arom}$), 164.17 (C-2), 169.35 (C-4).

### 3-Allyl-5-(*Z*)-(4-methoxybenzylidene )-2-(crotylmercapto )hydantoin (1h)

Yield 0.27 g (82%), mp 117-119 °C. MS; m/z: 328 ($M^+$). Calculated for $C_{18}H_{20}N_2O_2S$ (328.43): C, 65.83; H, 6.14; N, 8.53. Found: C, 65.88; H, 6.17; N, 8.57. IR($CCl_4$) : ν 1702 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ 1.71 (3 H, d, $J$= 6.42 Hz, 1-$H_{crotyl}$), 3.84 (3 H, s, $OCH_3$), 3.97 (2H, d, $J$= 7.21 Hz, 4-$H_{crotyl}$), 4.20 (2 H, d, $J$=4.44 Hz, 3-$H_{allyl}$), 5.18–5.23 (2 H, m, 1-$H_{allyl}$), 5.69–5.87 (3 H, m, 2-$H_{allyl}$, 2-$H_{crotyl}$, 3-$H_{crotyl}$, 6.93 (1 H, s, =CH), 6.95 (2 H, d, $J$= 8.73 Hz, $H_{arom}$), 8.13 (2 H, d, $J$= 8.73 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ, 18.16 (C-1$_{crotyl}$), 33.39 (C-4$_{crotyl}$), 43.03 (C-3$_{allyl}$), 55.65 ($CH_3$), 118.28 (C-1$_{allyl}$), 124.40 (C2$_{crotyl}$), 124.96 (=CH), 114.51, 127.75, 131.39, 131.76, 134.06, 136.95, 161.29 (C-2$_{allyl}$, C-3$_{crotyl}$, C-5, $C_{arom}$), 163.01(C-2), 169.85 (C-4).

### 3-Allyl-5-(*Z*)-(4-methylbenzylidene )-2-(crotylmercapto)hydantoin (1i)

Yield 0.26 g (83%), mp 67-69 °C. MS; m/z: 312 ($M^+$). Calculated for $C_{18}H_{20}N_2OS$ (312.43): C, 69.20; H, 6.45; N, 8.97. Found: C, 69.29; H,

6.47; N, 9.01. IR ($CCl_4$) : ν 1707 $cm^{-1}$ (C=O). 'H-NMR ($CDCl_3$) : δ 1.72 (3 H, d, $J$ = 6.27 Hz, 1-$H_{crotyl}$), 2.37 (3 H, S, $CH_3$), 3.95 (2 H, d, $J$ = 7.11 Hz, 4-$H_{crotyl}$), 4.20 (2 H, d, $J$ =5.31 Hz, 3-$H_{allyl}$), 5.20 (2 H, m, 1-$H_{allyl}$), 5.62–5.89 (3 H, m, 2-$H_{allyl}$, 2-$H_{crotyl}$, 3-$H_{crotyl}$), 6.94 (1 H, s, =CH), 7.22 (2 H, d, $J$ = 8.01 Hz, $H_{arom}$), 8.05 (2 H, d, $J$ = 8.05 Hz, Harom). $^{13}$C-NMR ($CDCl_3$) : δ 18.18 (C-$1_{crotyl}$), 21.98 ($CH_3$), 33.43 (C-$4_{crotyl}$), 43.07 (C-$3_{allyl}$), 118.36 (C-$1_{allyl}$), 124.52 (C-$2_{crotyl}$), 124.96 (=CH), 129.75, 131.44, 131.71, 132.12, 132.24, 137.99, 140.58 (C-$2_{allyl}$, C-$3_{crotyl}$, C-5, $C_{arom}$), 163.82(C-2), 169.87 (C-4).

### 3-Allyl-5-(Z)-(4-chlorobenzylidene)-2-(crotylmercapto)hydantoin (1j)

Yield 0.29 g (88%), mp 86-88 °C. MS; m/z: 332 ($M^+$). Calculated for $C_{17}H_{17}ClN_2OS$ (332.85): C, 61.34; H, 5.15; N, 8.42. Found: C, 61.50; H, 5.19; N, 8.47. IR ($CCl_4$) : ν 1708 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ 1.72 (3 H, d, $J$ = 6.34 Hz, 1-$H_{crotyl}$), 3.94 (2 H, d, $J$ = 7.07 Hz, 4-$H_{crotyl}$), 4.18 (2 H, d, $J$ = 5.23 Hz, 3-$H_{allyl}$), 5.18–5.29 (2 H, m, 1-$H_{allyl}$), 5.60–5.91 (3 H, m, 2-$H_{allyl}$, 2-$H_{crotyl}$, 3-$H_{crotyl}$), 6.86 (1 H, s, =CH), 7.35 (2 H, d, $J$= 8.35 Hz, $H_{arom}$), 8.06 (2H, d, $J$= 8.37 Hz, Harom). $^{13}$C-NMR ($CDCl_3$) : δ 18.29 (C-$1_{crotyl}$), 33.60 (C-$4_{crotyl}$), 43.23 (C-$3_{allyl}$), 118.65 (C-$1_{allyl}$), 122.55 (C-$2_{crotyl}$), 124.85 (=CH), 129.28, 131.64, 131.73, 133.36, 133.48, 135.96, 139.02 (C-$2_{allyl}$, C-$3_{crotyl}$, C-5, $C_{arom}$), 165.29 (C-2), 169.68 (C-4).

### 3-Allyl-5-(Z)-(2-thienylidene )-2-(crotylmercapto)hydantoin (1k)

Yield 0.24 g (78%), mp 63-65°C. MS; m/z: 304 ($M^+$). Calculated for $C_{15}H_{16}N_2OS_2$ (304.43): C, 59.18; H, 5.30; N, 9.20. Found: C, 59.29; H, 5.33; N, 9.25. IR ($CCl_4$) : ν 1710 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ 1.71 (3 H, d, J = 6.14 Hz, 1-$H_{crotyl}$), 3.98 (2 H, d, $J$= 6.92 Hz, 4-$H_{crotyl}$), 4.18 (2 H, d, $J$ =4.12 Hz, 3-$H_{allyl}$), 5.18–5.23 (2 H, m, 1-$H_{allyl}$), 5.67–5.93 (3 H, m, 2-$H_{allyl}$, 2-$H_{crotyl}$, 3-$H_{crotyl}$), 7.09 (1 H, d, $J$ = 3.61 Hz, H-$4_{thiophen}$), 7.22 (1 H, s, =CH), 7.45 (1 H, d, $J$ = 4.64, Hz, H-$3_{thiophen}$), 7.57 (1 H, d, $J$ = 4.64 Hz, H-$5_{thiophen}$). $^{13}$C-NMR ($CDCl_3$) : δ 17.84 (C-$1_{crotyl}$), 33.22 (C-$4_{crotyl}$), 42.74 (C-$3_{allyl}$), 117.58, 118.05, 124.64, 127.29, 131.07, 131.26, 132.74, 133.25, 136.24, 138.20 (C-$1_{allyl}$, C-$2_{crotyl}$, =CH, C-5, C-$2_{allyl}$, C-$3_{crotyl}$, $C_{arom}$), 162.85 (C-2), 168.59 (C-4).

**3-Allyl-5-(Z)-(2-furylidene )-2-(crotylmercapto)hydantoin (1l)**

Yield 0.20 g (70%), mp 48-50 °C. MS; m/z: 288 ($M^+$). Calculated for $C_{15}H_{16}N_2O_2S$ (288.37): C, 62.48; H, 5.59; N, 9.71. Found: C, 62.54; H, 5.67; N, 9.75. IR ($CCl_4$) : ν 1708 $cm^{-1}$ (C=O). $^1$H-NMR ($CDCl_3$) : δ 1.71 (3 H, d, *J*= 6.14 Hz, 1-$H_{crotyl}$), 3.98 (2 H, d, *J*= 6.93 Hz, 4-$H_{crotyl}$), 4.18 (2 H, d, *J*= 4.12 Hz, 3-$H_{allyl}$), 5.18–5.23 (2 H, m, 1-$H_{allyl}$), 5.67–5.92 (3 H, m, 2-$H_{allyl}$, 2-$H_{crotyl}$, 3-$H_{crotyl}$), 6.55 (1 H, s, =CH), 6.69 (1 H, d, *J* =3.61 Hz, H-$3_{furan}$), 7.25 (1 H, d, *J*= 3.55 Hz, H-$4_{furan}$), 7.57 (1 H, d, *J*= 4.64 Hz, H-$5_{furan}$). $^{13}$C-NMR ($CDCl_3$): δ 18.20 (C-$1_{crotyl}$), 33.43 (C-$4_{crotyl}$), 43.13 (C-$3_{allyl}$), 111.83, 113.54, 117.62, 118.43, 124.76, 131.62, 136.28, 145.31, 151.59 (C-$1_{allyl}$, C-$2_{crotyl}$, =CH, C-5, C-$2_{allyl}$, C-$3_{crotyl}$, $C_{arom}$), 163.98 (C-2), 169.14 (C-4).

**3-allyl-5-(Z)-arylidenehydantoins 10a-d**

To solution of 3-allyl-5-*(Z)*-arylidene-2-(alkylmercapto) hydantoins **1a-d** (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 products **10a-d.**

**3-allyl-5-(Z)-benzylidenhydantoin (10a)**

Yield 0.22 g (96%), mp 68-70 °C. MS; m/z: 228 ($M^+$). Calculated for $C_{13}H_{12}N_2O_2$ (228.25): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.52; H, 5.32; N, 12.34. IR (KBr) : ν 3192 (NH), 1758, 1709 (2 C=O) $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) : δ 4.11 (2 H, m, 3-$H_{allyl}$), 5.15 (2 H, m, 1-$H_{allyl}$), 5.85 (1 H, m, 2-$H_{allyl}$), 6.57 (1 H, s, =CH), 7.35–7.65 (5 H, m, $H_{arom}$), 10.86 (1 H, s, NH).

**3-Allyl-5-(Z)-(4-methoxybenzylidene)hydantoin (10b)**

Yield 0.25 g (98%), mp 143-145 °C. MS; m/z: 258 ($M^+$). Calculated for $C_{14}H_{14}N_2O_3$ (258.28): C, 65.11; H, 5.46; N, 10.85. Found: C, 65.17; H, 5.48; N, 10.93. IR (KBr) : ν 3206 (NH), 1756, 1720 (2 C=O) $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) : δ 3.80 (3 H, s, $CH_3$), 4.04 (2 H, m, 3-$H_{allyl}$), 5.14 (2 H, m, 1-$H_{allyl}$), 5.84 (1 H, m, 2-$H_{allyl}$), 6.54 (1H, s, =CH), 6.96, 7.64 (4

H, 2d, $J$= 8.78 Hz, $H_{arom}$), 10.73 (1 H, s, NH). $^{13}$C-NMR (DMSO-$d_6$) : δ 40.63 (C-$3_{allyl}$), 55.48 ($CH_3$), 110.29 (=CH), 116.64 (C-$1_{allyl}$), 124.78 (C-$2_{allyl}$), 114.53, 125.46, 131.50, 132.42, 154.95 (C-5& $C_{arom}$), 159.84 (C-2), 164.03 (C-4).

**3-Allyl-5-(*Z*)-(4-methylbenzylidene)hydantoin (10c)**

Yield 0.22 g (92%), mp 174-176 °C. MS; m/z: 242 ($M^+$). Calculated for $C_{14}H_{14}N_2O_2$ (242.28): C, 69.41; H, 5.82; N, 11.56. Found: C, 69.46; H, 5.84; N, 11.64. IR (KBr) : ν 3203 (NH), 1758, 1725 (2 C=O) $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) : δ 2.34 (3 H, s, $CH_3$), 4.11 (2 H, m, 3-$H_{allyl}$), 5.16 (2 H, m, 1-$H_{allyl}$), 5.86 (1 H, m, 2-$H_{allyl}$), 6.53 (1 H, s, =CH), 7.24, 7.56 (4 H, 2d, J = 8.10 Hz, $H_{arom}$), 10.77 (1 H, s, NH).

**3-Allyl-5-(*Z*)-(4-chlorobenzylidene)hydantoin (10d)**

Yield 0.25 g (97%), mp 205-207 °C. MS; m/z: 262 ($M^+$). Calculated for $C_{13}H_{11}ClN_2O_2$ (262.70): C, 59.44; H, 4.22; N, 10.66. Found: C, 59.35; H, 4.26; N, 10.76. IR (KBr) : ν 3222 (NH), 1754, 1724 (C=O) $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) : δ 4.09 (2 H, m, 3-$H_{allyl}$), 5.15 (2 H, m, 1-$H_{allyl}$), 5.83 (1 H, m, 2-$H_{allyl}$), 6.55 (1 H, s, =CH), 7.45, 7.66 (4 H, 2d, $J$= 8.20 Hz, $H_{arom}$), 10.89 (1 H, s, NH).

**3-Allyl-5-(*Z*)-arylidene-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosylmercapto)hydantoins 2a-l**

***General Precedures***

*Method A:* 3-allyl-5-(*Z*)-arylidene-2-thiohydantoins **8a-f** (1 mmol) was suspended in anhydrous MeCN (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 **(11a)** or D-galactopyranosyl bromide **(11b)** (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 chromatogra-

phy (eluent 50%, diethyl ether/petroleum ether, 40–60 °C) to give the products **2a-l.**

*Method B:* Compound 8a (0.23 g, 1 mmol) suspended in anhydrous acetonitrile (5 ml), and BSA (0.25 ml, 1 mmol) was added. The reaction mixture was stirred at room temperature for 30 min. The 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranoside (**13**, 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 stirred at room temperature for 2 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 56 % of **2a.**



### 3-Allyl-5-(*Z*)-benzylidene-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosylmercapto)hydantoin (2a)

Yield 0.43 g (75%), mp 149-151 °C. MS; m/z: 574 ($M^+$). Calculated for $C_{27}H_{30}N_2O_{10}S$ (574.60): C, 56.44; H, 5.26; N, 4.88. Found: C, 56.39; H, 5.24; N, 4.78. IR ($CCl_4$) : ν 1751, 1728 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.82, 2.05, 2.08 (12 H, 3 s, 4 Ac), 3.93–4.25 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.12–5.45 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.73 (1 H, m, 2-$H_{allyl}$), 5.86 (1 H, d, $J$=10.38 Hz, 1′-H), 7.07 (1 H, s, =CH), 7.45 (3 H, m, $H_{arom}$), 8.15 (2 H, m, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.33, 20.45, 20.48 (4 Ac), 42.75 (C-$3_{allyl}$), 61.73 (C-6′), 68.01 (C-2′), 68.94 (C-3′), 73.62 (C-4′), 76.87 (C-5′), 81.28 (C-1′), 118.44 (C-$1_{allyl}$), 125.58 (=CH), 128.60, 130.15, 130.85, 131.92, 134.04, 137.66 (C-$2_{allyl}$, C-5, $C_{arom}$), 161.04 (C-2), 168.86, 169.30, 169.35, 169.94, 170.46 (4 C=O, C-4).

### 3-Allyl-5-(*Z*)-(4-methoxybenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosylmercapto)hydantoin (2b)

Yield 0.47 g (78%), mp 155-157 °C. MS; m/z: 604 ($M^+$). Calculated for $C_{28}H_{32}N_2O_{11}S$ (604.63): C, 55.62; H, 5.33; N, 4.63. Found: C, 55.67; H, 5.36; N, 4.42. IR ($CCl_4$) : ν 1752, 1719 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.81, 2.04, 2.05 (12 H, 3 s, 4 Ac), 3.86 (3 H, s, $OCH_3$), 4.12–4.22 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.12–5.20 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.70

(1 H, m, 2-$H_{allyl}$), 5.80 (1 H, d, $J$= 10.35 Hz, 1′-H), 6.95 (2 H, d, $J$=8.91 Hz, $H_{arom}$), 6.99 (1 H, s, =CH), 8.09 (2 H, d, $J$ = 8.85 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : 6 20.49, 20.55, 20.59, 20.71 (4 Ac), 42.79 (C-$3_{allyl}$), 55.42 ($OCH_3$), 61.78 (C-6′), 68.07 (C-2′), 68.97 (C-3′), 73.68 (C-4′), 76.86 (C-5′), 81.39 (C-1′), 118.38 (C-$1_{allyl}$), 114.29, 126.02, 126.98, 131.02, 133.89, 135.99, 159.28 (=CH, C-$2_{allyl}$, C-5, $C_{arom}$), 161.39 (C-2), 169.07, 169.41, 169.47, 170.13, 170.62 (4 C=O, C-4).

### 3-Allyl-5-(Z)-(4-methylbenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosylmercapto)hydantoin (2c)

Yield 0.42 g (71%), mp 172-174 °C. MS; m/z: 588 ($M^+$). Calculated for $C_{28}H_{32}N_2O_{10}S$ (588.63): C, 57.13; H, 5.48; N, 4.76. Found: C, 56.99; H, 5.62; N, 4.67. IR ($CCl_4$) : ν 1752, 1720 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.84, 2.05, 2.09 (12 H, 3 s, 4 Ac), 2.36 (3 H, s, $CH_3$), 3.93–4.27 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.13–5.45 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.76 (1 H, m, 2-$H_{allyl}$), 5.85 (1 H, d, $J$= 10.35 Hz, 1′-H), 7.03 (1 H, s, =CH), 7.25, 8.04 (4 H, 2d, $J$= 7.53 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.45, 20.52, 20.57, 21.64 (4 Ac, $CH_3$), 42.77 (C-$3_{allyl}$), 61.71 (C6′), 67.977 (C-2′), 68.95 (C-3′), 73.65 (C-4′), 76.88 (C-5′), 81.34 (C-1′), 118.43 (C-$1_{allyl}$), 125.99 (=CH), 129.46, 130.94, 131.36, 132.01, 137.02, 140.86 (C-$2_{allyl}$, C-5, $C_{arom}$), 160.23 (C-2), 168.99, 169.37, 169.44, 170.04,170.59 (4 C=O, C-4).

### 3-Allyl-5-(Z)-(4-chlorobenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosylmercapto)hydantoin (2d)

Yield 0.46 g (76%), mp 160-162 °C. MS; m/z: 608 ($M^+$). Calculated for $C_{27}H_{29}ClN_2O_{10}S$ (609.05): C, 53.25; H, 4.80; N, 4.60. Found: C, 53.62; H, 4.77; N, 4.62. IR ($CCl_4$) : ν 1752, 1722 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.87, 2.06, 2.11 (12 H, 3 s, 4 Ac), 3.92–4.31 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.13–5.45 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.75 (1 H, m, 2-$H_{allyl}$), 5.82 (1 H, d, $J$= 10.40 Hz, 1′-H), 7.28(1 H, s, =CH), 7.44, 8.10 (4 H, 2d, $J$= 8.12 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.48, 20.61, 20.63, 20.79 (4 Ac), 42.91 (C-$3_{allyl}$), 61.64 (C-6′), 68.02 (C-2′), 68.97 (C3′), 73.67 (C-4′), 76.90 (C-5′), 81.57 (C-1′), 118.59 (C-$1_{allyl}$), 119.46 (=CH), 127.49, 130.94, 133.72, 134.23, 135.68, 137.81, (C-$2_{allyl}$, C-5, $C_{arom}$), 159.56(C-2), 168.23, 169.45, 169.45, 170.16,170.68 (4 C=O, C-4).

**3-Allyl-5-(*Z*)-(2-thienylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosylmercapto)hydantoin (2e)**

Yield 0.42 g (73%), mp 150-152 °C. MS; m/z: 580 ($M^+$). Calculated for $C_{25}H_{28}N_2O_{10}S_2$(580.62): C, 51.72; H, 4.86; N, 4.82. Found: C, 51.78; H, 4.91; N, 4.92. IR ($CCl_4$) : ν 1745, 1719 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.87, 2.05, 2.10, 2.17 (12 H, 4 s, 4 Ac), 4.01–4.27 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.15-5.42 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.70 (1 H, m, 2-$H_{allyl}$), 5.90 (1 H, d, *J*=10.41 Hz, 1′-H), 7.13 (1 H, dd, *J*= 3.78, 5.04 Hz, H-$4_{thiophen}$), 7.32 (1 H, s, =CH), 7.46 (1 H, d, *J*=3.60, Hz, H-$3_{thiophen}$), 7.68 (1 H, d, *J* = 5.07 Hz, H-$5_{thiophen}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.46, 20.53, 20.59, 20.63 (4 Ac), 42.94 (C-$3_{allyl}$), 61.89 (C-6′), 68.07 (C-2′), 69.05 (C-3′), 73.70 (C-4′), 76.95 (C5′), 81.38 (C-1′), 118.71 (C-$1_{allyl}$), 124.13 (=CH), 129.02, 130.81, 132.68, 133.09, 136.20, 138.02 (C-$2_{allyl}$, C-5, $C_{thiophen}$), 161.73 (C-2), 168.86, 169.45, 169.49, 170.10, 170.57 (4 C=O, C-4).

**3-Allyl-5-(*Z*)-(2-furylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosylmercapto)hydantoin (2f)**

Yield 0.38 g (68%), mp 144-146 °C. MS; m/z: 564 ($M^+$). Calculated for $C_{25}H_{28}N_2O_{11}S$ (564.57): C, 53.19; H, 5.00; N, 4.96. Found: C, 52.85; H, 4.99; N, 5.04. IR ($CCl_4$) : ν 1747, 1719 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.79, 2.05, 2.08 (12 H, 3 s, 4 Ac), 3.91–4.22 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.11–5.43 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.76 (1 H, m, 2-$H_{allyl}$), 5.86 (1 H, d, *J*=10.33 Hz, 1′-H), 6.99 (1 H, S, =CH), 6.64, 7.34, 7.63 (3 H, 3m, H-3, 4, $5_{furan}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.11, 20.20, 20.32, 20.48 (4 Ac), 42.80 (C-$3_{allyl}$), 61.76 (C-6′), 68.04 (C-2′), 68.99 (C-3′), 73.60 (C-4′), 76.71 (C-5′), 81.25 (C-1′), 112.96 (C-$3_{furan}$), 113.35 (C-$4_{furan}$), 117.85 (C-$1_{allyl}$), 118.46 (=CH), 130.85 (C-5), 135.21 (C-$2_{allyl}$), 145.52 (C-$2_{furan}$), 150.86(C-$5_{furan}$), 160.18 (C-2), 169.32, 169.39, 169.98, 170.00, 170.52 (4 C=O, C-4).

**3-Allyl-5 -(*Z*)-benzylidene-2-(2′,3′,4 ′,6′-tetra-*O*-acetyl-β-D-galactopyranosylmercapto)hydantoin 2g)**

Yield 0.45 g (78%), mp 148-150 °C. MS; m/z: 574 ($M^+$). Calculated for $C_{27}H_{30}N_2O_{10}S$ (574.61): C, 56.44; H, 5.26; N, 4.88. Found: C, 56.56; H,

5.28; N, 4.92. IR ($CCl_4$) : ν 1749, 1718 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.80, 2.05, 2.10, 2.20 (12 H, 4 s, 4 Ac), 4.18-4.29 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.22–5.35 (3 H, m, 4′-H, 1-$H_{allyl}$), 5.48 (1 H, d, *J*= 10.26 Hz, 2′-H), 5.60 (1 H, d, *J*= 3.25 Hz, 3′-H),5.75 (1 H, m, 2-$H_{allyl}$), 5.94 (1 H, d, *J*= 10.45 Hz, 1′-H), 7.08 (1 H, s, =CH), 7.48 (3 H, m, $H_{arom}$), 8.19 (3 H, d, J= 7.93 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.23, 20.28, 20.40, 20.50 (4 Ac), 42.56 (C-$3_{allyl}$), 61.60 (C-6′), 66.26 (C-2′), 67.30 (C-3′), 71.65 (C-4′), 76.80 (C-5′), 81.77 (C1′), 118.32 (C-$1_{allyl}$), 125.80 (=CH), 129.40, 130.92, 131.92, 132.10, 134.50, 138.15 (C-$2_{allyl}$, C-5, $C_{arom}$), 161.76 (C-2), 168.76, 169.31, 169.34, 169.87, 170.46 (4 C=O, C-4).

**3-Allyl-5-(*Z*)-(4-methoxybenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosylmercapto)hydantoin (2h)**

Yield 0.46 g (76%), mp 140-142 °C. MS; m/z: 604 ($M^+$). Calculated for $C_{28}H_{32}N_2O_{11}S$ (604.63): C, 55.62; H, 5.33; N 4.63. Found: C, 55.62; H, 5.39; N 4.45. IR ($CCl_4$) : ν 1752, 1722 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.81, 2.03, 2.06, 2.18 (12 H, 4 s, 4 Ac), 3.89 (3 H, s, $OCH_3$), 4.16 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.24 (3 H, m, 4′-H, 1-$H_{allyl}$), 5.42 (1 H, t, *J*= 10.24 Hz, 2′-H), 5.58 (1 H, d, *J*= 3.30 Hz, 3′-H),5.70 (1 H, m, 2-$H_{allyl}$), 5.84 (1 H, d, *J*= 10.42 Hz, 1′-H), 7.02 (2 H, d, *J* = 8.85 Hz, $H_{arom}$), 7.26 (1 H, s, =CH), 8.09 (2 H, d, *J* = 8.86 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.67, 20.75, 20.83, 20.90 (4 Ac), 43.08 (C-$3_{allyl}$), 55.70 ($OCH_3$), 61.90 (C-6′), 67.58 (C-2′), 68.30 (C-3′), 72.07 (C-4′), 76.82 (C-5′), 82.24 (C-1′), 118.67 (C-$1_{allyl}$), 114.62, 126.11, 127.28, 131.36, 134.11, 136.33, 159.58 (=CH, C-$2_{allyl}$, C-5, $C_{arom}$), 161.75 (C-2), 169.38, 169.98, 170.20, 170.39, 170.64 (4 C=O, C-4).

**3-Allyl-5-(*Z*)-(4-methylbenzylidene)-2-(2′.3′.4′.6′-tetra-*O*-acetyl-β-D-galactopyranosylmercapto)hydantoin (2i)**

Yield 0.43 g (73%), mp 125-127 °C. MS; m/z: 588 ($M^+$). Calculated for $C_{28}H_{32}N_2O_{10}S$ (588.63): C, 57.13; H, 5.48; N, 4.76. Found: C, 57.29; H, 5.49; N 4.81. IR ($CCl_4$) : ν 1753, 1720 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.80, 2.06, 2.09, 2.18 (12 H, 4 s, 4 Ac), 2.42 (3 H, s, $CH_3$), 4.18 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.23 (3 H, m, 4′-H, 1-$H_{allyl}$), 5.46 (1 H, t, *J*= 10.25 Hz, 2′-H), 5.55 (1 H, d, *J*= 3.38 Hz, 3′-H), 5.75 (1 H, m, 2-$H_{allyl}$), 5.90 (1 H, d, *J* = 10.50 Hz, 1′-H), 7.03 (1 H, s, =CH), 7.28, 8.04 (4 H, 2d,

J = 8.08 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.24, 20.29, 20.41, 20.48 (4 Ac), 21.51 ($CH_3$), 42.68 (C-$3_{allyl}$), 61.64 (C-6′), 66.35 (C-2′), 67.27 (C-3′), 71.65 (C4′), 75.62 (C-5′), 81.76 (C-1′), 118.30 (C-$1_{allyl}$), 125.75 (=CH), 129.40, 130.92, 131.29, 131.93, 136.98, 140.76 (C-$2_{allyl}$, C-5, $C_{arom}$), 160.37 (C-2), 168.94, 169.59, 169.75, 170.00,170.25 (4 C=O, C-4).

### 3-Allyl-5-(*Z*)-(4-chlorobenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosylmercapto)hydantoin (2j)

Yield 0.45 g (75%), mp 156–158 °C. MS; m/z: 608 ($M^+$). Calculated for $C_{27}H_{29}ClN_2O_{10}S$ (609.05): C, 53.25; H, 4.80; N, 4.60. Found: C, 53.19; H, 4.86; N 4.59. IR ($CCl_4$) : v 1750, 1718 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.81, 2.03, 2.07, 2.19 (12 H, 4s, 4 Ac), 4.10–4.25 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.19–5.33 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.46 (1 H, t, *J*=10.30 Hz, 2′-H), 5.57 (1 H, d, *J*= 3.34 Hz, 3′-H), 5.75 (1 H, m, 2-$H_{allyl}$), 5.90 (1 H, d, *J*= 10.44 Hz, 1′-H), 6.97 (1 H, s, =CH), 7.42, 8.10 (4 H, 2d, *J* = 8.63 Hz, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 19.89, 20.13, 20.20, 20.24 (4 Ac), 42.49 (C-$3_{allyl}$), 61.53 (C-6′), 66.15 (C-2′), 66.17 (C-3′), 71.50 (C-4′), 75.31 (C5′), 81.43 (C-1′), 118.12 C-$1_{allyl}$), 123.41 =CH), 128.52, 130.59, 132.54, 132.72, 135.57, 137.76 (C-$2_{allyl}$, C-5, $C_{arom}$), 161.71 (C-2), 168.32, 169.23, 169.27, 169.71, 169.90 (4 C=O, C-4).

### 3-Allyl-5-(*Z*)-(2-thienylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosylmercapto)hydantoin (2k)

Yield 0.40 g (70%), mp 155-157 °C. MS; m/z: 580 ($M^+$). Calculated for $C_{25}H_{28}N_2O_{10}S_2$(580.62): C, 51.72; H, 4.86; N, 4.82. Found: C, 51.87; H, 5.89; N, 4.90. IR ($CCl_4$) : v 1742, 1718 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.87, 2.02, 2.07, 2.18 (12 H, 4 s, 4 Ac), 4.15-4.26 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.16–5.28 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.46 (1 H, t, *J*= 10.33 Hz, 2′-H), 5.55 (1 H, d, *J*= 3.36 Hz, 3′-H), 5.75 (1 H, m, 2-$H_{allyl}$), 5.90 (1 H, d, *J*= 10.40 Hz, 1′-H), 7.10 (1 H, dd, *J*= 3.78, 5.04 Hz, H-$4_{thiophen}$), 7.34 (1 H, s, =CH), 7.45 (1 H, d, *J*= 3.60, Hz, H-$3_{thiophen}$), 7.67 (1 H, d, *J* = 5.07 Hz, H-$5_{thiophen}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.42, 20.50, 20.56, 20.60 (4 Ac), 42.94 (C-$3_{allyl}$), 61.65 (C-6′), 66.50 (C-2′), 67.30 (C-3′), 71.82 (C-4′), 76.42 (C-5′), 81.86 (C-1′), 118.72 (C-$1_{allyl}$), 124.20 (=CH), 129.12, 130.80, 132.78, 133.29, 136.25, 138.32 (C-$2_{allyl}$, C-5, $C_{thiophen}$), 161.13 (C2), 168.84, 169.55, 169.58, 170.12, 170.54 (4 C=O, C-4).

### 3-Allyl-5-(Z)-(2-furylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosylmercapto)hydantoin (21)

Yield 0.36 g (68%), mp 143-145 °C. MS; m/z: 564 ($M^+$). Calculated for $C_{25}H_{28}N_2O_{11}S$ (564.56): C, 53.19; H, 5.00; N, 4.96. Found: C, 53.30; H, 5.04; N, 5.01. IR ($CCl_4$) : v 1745, 1717 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 1.87, 2.02, 2.07, 2.18 (12 H, 4 s, 4 Ac), 4.12-4.23 (5 H, m, 6′-H, 5′-H, 3-$H_{allyl}$), 5.18–5.25 (5 H, m, 4′-H, 2′-H, 3′-H, 1-$H_{allyl}$), 5.45 (1 H, t, *J*= 10.30 Hz, 2′-H), 5.54 (1 H, d, J= 3.32 Hz, 3′-H), 5.75 (1 H, m, 2-$H_{allyl}$), 5.90 (1 H, d, *J* = 10.38 Hz, 1′-H), 7.00 (1 H, s, =CH), 6.66, 7.38, 7.64 (3 H, 3 d, *J* = 3.49 Hz, H-3, 4, $5_{furan}$). $^{13}$C-NMR ($CDCl_3$) : δ 20.36, 20.45, 20.52, 20.65 (4 Ac), 42.90 (C-$3_{allyl}$), 61.66 (C-6′), 66.51 (C-2′), 67.32 (C-3′), 71.83 (C-4′), 76.37 (C5′), 81.89 (C-1′), 113.13 (C-$3_{furan}$), 113.49 (C-$4_{furan}$), 118.09 (C-$1_{allyl}$), 118.55 (=CH), 130.97 (C-5), 135.32 (C-$2_{allyl}$), 145.65 (C-$2_{furan}$), 150.95 (C-$5_{furan}$), 160.48 (C-2), 168.46, 169.76, 169.96, 170.18, 170.46 (4 C=O, C-4).

### Reaction of 2a with sodium methoxide

A mixture of the protected nucleoside (**2a**, 0.57 g, 1 mmol) in 15 ml of anhydrous $CH_3OH$ and 5 ml of 1% $CH_3ONa$ was allowed to stirr at room temperature for 1 h until the starting material was consumed (TLC). The reaction mixture was subsequently cooled and neutralized with an acidic ion exchange resin (IR 50). After evaporation of the solvent, the residue was purified by flash chromatography (eluent 50%, diethyl ether/petroleum ether, 40–60 °C) to give 0.12 g (49%) of **8a** and 0.08 g (38%) of **10a**, respectively.

### 3-Allyl-5-(Z)-arylidene-2-(2′,3′ 5′-tri-*O*-benzoyl-β-D-ribofuranosylmercapto)hydantoins 3a,b

#### *General Precedures*

*Method A*: 3-allyl-5-*(Z)*-arylidene-2-thiohydantoins **8a,e** (1 mmol) was suspended in anhydrous MeCN (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. 2,3,5-Tri-*O*-benzoyl-α-D-ribofuranosyl bromide (**15,** 0.44 g, 1 mmol) was added, and the mixture was stirred at room temperature for 4 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 **3a,b.**

*Method B:* Compound **8a** (0.23 g, 1 mmol) suspended in anhydrous acetonitrile (5 ml) and BSA (0.25 ml, 1 mmol) was added. The reaction mixture was stirred at room temperature for 30 min. The 1,2,3,5-tetra-*O*-acetyl-α-D-ribofuranoside (**16,** 0.51 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 2 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 0.33 g (48%) of **3a.**



### 3-Allyl-5-(*Z*)-benzylidene-2-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosylmercapto)hydantoin (3a)

Yield 0.47 g (68%), Yellow foams. MS; m/z: 688 ($M^+$). Calculated for $C_{39}H_{32}N_2O_8S$ (688.75): C, 68.01; H, 4.68; N, 4.07. Found: C, 68.13; H, 4.73; N, 4.20. IR ($CCl_4$) : v 1727 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 4.20 (2 H, d, $J$= 5.12 Hz, 3-$H_{allyl}$), 4.40 (2 H, m, 5′-H), 5.15 (2 H, m, 1-$H_{allyl}$), 5.66 (1 H, m, 3′-H), 5.75 (1 H, m, 2-$H_{allyl}$), 5.84 (1 H, m, 2′-H), 6.15 (1 H, m, 4′-H), 6.76 (1 H, d, $J$ = 6.64 Hz, 1′-H), 7.06 (1 H, s, =CH), 7.10-8.02 (20 H, m, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 42.61 ($C3_{allyl}$), 60.13 (C-5′), 65.28 (C-2′), 66.83 (C-3′), 68.90 (C-4′), 81.39 (C-1′), 118.17 ($C\text{-}1_{allyl}$), 125.56 (=CH), 128.07, 128.23, 128.38, 128.45, 128.77, 129.51, 129.65, 129.83, 130.86, 131.88, 133.18, 133.35, 134.12, 137.58 ($C\text{-}2_{allyl}$, C-5, $C_{arom}$), 161.16 (C-2), 164.93, 164.98, 165.29 (3 C=O), 168.86 (C-4).

### 3-Allyl-5-(*Z*)-(2-thienylidene)-2-(2′,3′,5′-tri -*O*/-benzoyl-β-D-ribofuranosylmercapto )hydantoin (3b)

Yield 0.49 g (71%)), Yellow foams. MS; m/z: 694 ($M^+$). Calculated for $C_{37}H_{30}N_2O_8S_2$ (694.77): C 63.96, H 4.35, N 4.03. Found: C, 63.90; H, 4.37; N, 3.98. IR ($CCl_4$) : v 1725 (2C=O) $cm^{-1}$. $^1$H-NMR ($CDCl_3$) : δ 4.18

(2 H, d, $J$= 5.39 Hz, 3-$H_{allyl}$), 4.38 (2 H, d, $J$= 6.13 Hz, 5′-H), 5.17 (2 H, m, 1-$H_{allyl}$), 5.60 (1 H, m, 3′-H), 5.74 (1 H, m, 2-$H_{allyl}$), 5.77 (1 H, m, 2′-H), 6.17 (1 H, m, 4′H), 6.75 (1 H, d, $J$= 7.66 Hz, 1′-H), 7.00–8.13 (19 H, m, =CH, $H_{arom}$). $^{13}$C-NMR ($CDCl_3$) : δ 42.90 (C-$3_{allyl}$), 65.50 (C-5′), 65.86 (C-2′), 67.16 (C-3′), 68.96 (C-4′), 81.39 (C-1′), 118.56 (C-$1_{allyl}$), 119.41 (=CH), 127.37, 128.37, 128.41, 128.44, 128.47, 128.67, 129.76, 129.89, 129.95, 130.83, 133.34, 133.55, 133.58, 135.76, 138. (C-$2_{allyl}$, C-5, $C_{arom}$), 160.20 (C-2), 164.93, 164.98, 165.29 (3 C=O), 168.27 (C-4).

***Acknowledgements***

The authors would like to express their gratitude and thanks to Prof. John Nielsen, Department of Organic Chemistry, The Thechnical University of Denmark, for carrying out the antiviral testing of the prepared compounds.



***References***

[1] A. A. El-Barbary, A. I. Khodair, E. B. Pedersen, C. Nielsen, *J. Med. Chem.*, **37**, 73 (1994).

[2] A. I. Khodair, H. I. El-Subbagh, A. A. El-Emam, *Boll. Chim. Farmaceutica,* **136**, 561 (1997).

[3] A. M. Al-Obaid, H. I. EL-Subagh, A. I. Khodair, M. M. A. Elmazar, *Anti-Cancer Drugs,* **7**, 873 (1996).

[4] K. R. Bharucha, V. Pavilinis, D. Ajdukovic, H. M. Shrenk, *Ger. Offen.*, **2**, 329, 745 (1974); *Chem. Abstr.,* **80**, 95948d (1974).

[5] M. Blanc, M. Cussac, A. Boucherle, G. Leclere, *Eur. J. Med. Chem.,* **27**, 267 (1992).

[6] V. Chazeau, M. Cussac, A. Boucherle, *Eur. J. Med. Chem.,* **27**, 615 (1992).

[7] B. M. Nilsson, H. M. Vargas, U. Hacksell, *J. Med. Chem.,* **35**, 3270 (1992).

[8] N. Mehta, C.A. Risiger, F.E. Soroko, *J. Med. Chem.,* **24**, 465 (1981).

[9] F. L. Wessels, T. J. Schwan, S. F. Pong, *J. Pharm. Sci.,* **69**, 1102 (1980).

[10] A. G. Caldwell, C. J. Harris, R. Stepney, N. Wittaker, *J. Chem. Soc., Perkin Trans.* **I, 495** (1980).

[11] P. F. Kador, J. H. Kinoshita, N. E. Sharpless, *J. Med. Chem.,* **28**, 841 (1985).

[12] N. A. Meanwell, H. R. Roth, E. C. R. Smith, D. L. Smith, J. K. Wright, *J. Org. Chem.,* **56**, 6897 (1991).

[13] A. I. Khodair, *Phosphorus, sulfur, and Silicon,* **122**, 9 (1997).

[14] A. I. Khodair, E. I. Ibrahim, *Nucleosides & Nucleotides,* **15**, 1927 (1996).

[15] S. F. Tan, K. P. Ang, Y. F. Fong, *J. Chem. Soc.,Perkin Trans.,* **II**, 1941 (1986).

[16] A. A. El-Barbary, A. I. Khodair and E. B. Pedersen, *J. Org. Chem.,* **58**, 5994 (1993).

[17] A. I. Khodair and P. Bertrand, *Tetrahedron,* **54**, 4859 (1998).

[18] Calculations were carried out with the Hyperchem 4® software (Hypercube Inc.).

[19] R. U. Lemieux, *Methods Carbohydr. Chem.,* **2**, 221 (1963).

[20] B. S. Furniss, A. J. Hannaford, P. W. G. Smith, A. R. Tatchell, *Vogel's,* **5**, 646 (1989).

[21] O. W. Weislow, R. Kiser, D. Fine, J. Bader, R. H. Skoemaker, and M. R. Boyd, *J. Natl. Concer Inst.,* **81**, 577 (1989).

[22] M. R. Boyd and K. D. Poull, *Drug Dev. Res.,* **34**, 91 (1995).