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Carbohydrate Research 306 (1998) 567–573

CARBOHYDRATE RESEARCH

Note

Synthesis of arylidenehydrazono- and glycopyranosylhydrazino-sulfonylbenzylidene-2,4-imidazolidinediones as potential antiviral and antitumoral agents

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Received 30 September 1997; accepted 9 January 1998

Abstract

A series of 5-[(*Z*)-(4-(2-(*E*)-arylidene)hydrazonosulfonylbenzylidene)]-2,4-imidazolidinediones **6a**–**h** and 5-[(*Z*)-(4-(2-β-D-glycopyranosyl)hydrazinosulfonylbenzylidene)]-2,4-imidazolidinediones **10a**–**j** were synthesized via two different routes. The compounds did not display any antiviral and antitumoral activity.

Keywords: 2,4-Imidazolidinediones; Hydrazones; Glycopyranosylhydrazines; Antiviral; Antitumor agents

There has been a considerable interest in the synthesis and properties of derivatives of 2,4-imidazolidinedione which are useful synthetic intermediates and have also found applications as therapeutics [1–4], and as fungicides and herbicides [5] as well. Furthermore, several sulfonyl derivatives of 2,4-imidazolidinedione have been shown to possess antifungal activity [6–8] and inhibition properties of aldose reductase from rat and bovine lenses [9,10]. As a part of our program directed towards new, simple and efficient procedures for the synthesis of antiviral and antitumor agents [11–16], the linking of 5-substituted-2,4-imidazolidinediones to an hydrophilic moiety such as a glycose was considered.

Structures such as **10a**–**j** were selected and their synthesis planned by coupling of the two moieties by an sulfonyl unit. In a first approach, the preparation of simpler analogs such as **6a**–**h** was first studied in order to test two synthetic pathways and the possible tautomeric equilibrium of such structures.

The present report describes the synthesis and biological evaluation of a series of 5-[(*Z*)-(4-(2(*E*) arylidene)hydrazonosulfonylbenzylidene)]-2,4-imidazolidinediones **6a**–**h** and 5-[(*Z*)-(4-(2-β-D-glycopyranosyl)hydrazinosulfonylbenzylidene)]-2,4-imidazolidinediones **10a**–**j**.

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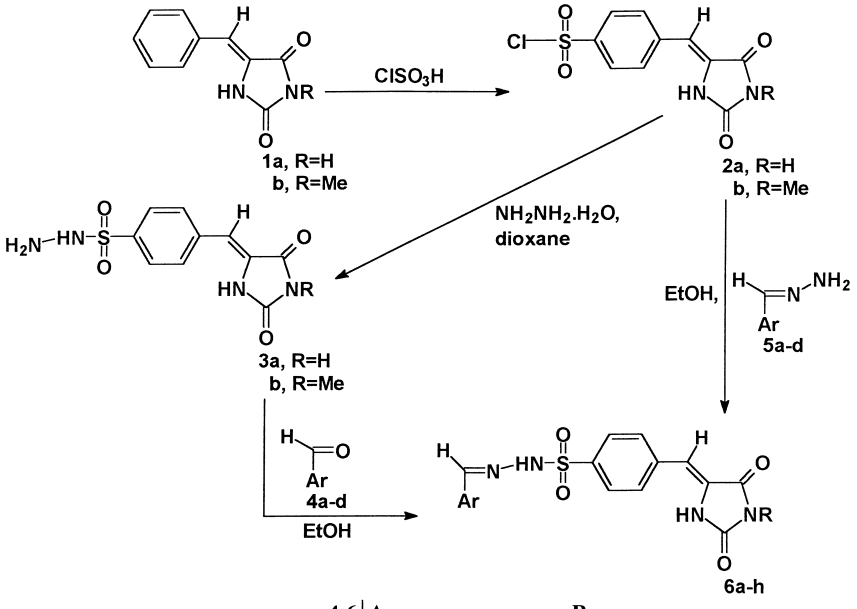
0008-6215/98/$19.00
PII S0008-6215(98)00024-X

1. Results and discussion

5-(*Z*)-Benzylidene-2,4-imidazolidinediones **1a**,**b** (Scheme 1) were prepared following the method of Tan et al. [17] via the condensation of benzaldehyde with 2,4-imidazolidinedione and its 3-methyl derivative in glacial acetic acid in the presence of anhydrous sodium acetate. Compounds **1a**,**b** were treated with a large excess of chlorosulfonic acid at room temperature to give 5-[(*Z*)-(4-(chlorosulfonylbenzylidene)]-2,4-imidazolidinedione **2a** [8] and 5-[(*Z*)-(4-(chlorosulfonylbenzylidene)]-3-methyl-2,4-imidazolidinedione **2b**, respectively. 2-(*E*)-Arylidene hydrazones **5a–d** [18] were reacted with the sulfonyl chlorides **2a**,**b** to give 5-[(*Z*)-(4-(2-(*E*)-arylidene)hydrazonosulfonylbenzylidene)]-2,4-imidazolidinediones **6a–h**. Compounds **6a–h** were independently synthesized through the condensation of aromatic aldehydes **4a–d** with 5-[(*Z*)-(4-hydrazinosulfonylbenzylidene)]-2,4-imidazolidinedione **3a** [8] and its 3-methyl derivative **3b**, which in turn were prepared by the condensation of the sulfonyl chlorides **2a**,**b** with hydrazine hydrate in dioxane. The structures of **6a–h** were established and confirmed by their elemental analyses and spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS). Typically, the ^{1}H NMR spectrum of compound **6b** showed a singlet at δ 6.56 ppm assigned to a 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-(*E*)-arylidene-2,4-imidazolidinediones whose vinyl protons respectively appear at δ 6.10–6.35 and 6.40–6.75 ppm [14–17]. The singlet at δ 7.95 ppm was assigned to the vinyl proton at the other exocyclic double bond, indicating the presence of a *E*-configuration for this bond, in agreement with the ^{1}H NMR spectra and the conformational analysis of 5-(*Z*)-arylidene-2-[(2-(*E*)-benzylidene)-hydrazono]-4-imidazolidinediones whose vinyl protons appear at 7.75–8.25 ppm [16,19] (Table 1). The ^{13}C NMR spectrum of compound **6b** was characterized by a signal at δ 106.99 ppm assigned to a vinyl carbon atom, supporting the *Z*-configuration of the exocyclic double bond, in agreement with the ^{13}C NMR spectra of 5-(*E*)- and 5-(*Z*)-arylidene-2,4-imidazolidinediones whose vinyl carbon atoms give signal respectively at δ 105–112 ppm and 113–120 ppm [14–17]. The signal at 147.61 ppm was assigned to the other vinyl carbon atom (Table 2).



4-6	Ar	R
a	C_6H_5	H
b	4-$CH_3OC_6H_4$	H
c	4-$CH_3C_6H_4$	H
d	4-ClC_6H_4	H
e	C_6H_5	CH_3
f	4-$CH_3OC_6H_4$	CH_3
g	4-$CH_3C_6H_4$	CH_3
h	4-ClC_6H_4	CH_3

Scheme 1.

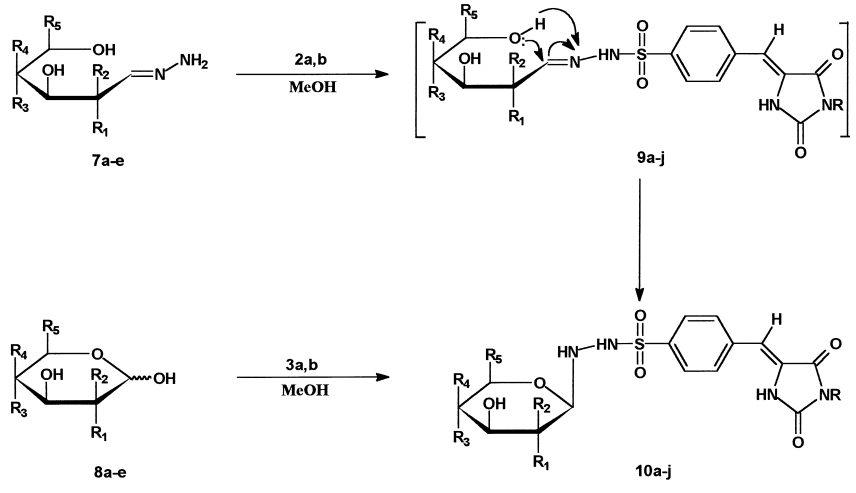
Table 1
IR and ^{1}H NMR data for 2–10

Compound	IR (KBr)(cm^{-1})	^{1}H NMR (Me_2SO)/δ
2a	—	—
2b	3450–3200 (NH), 1780, 1725 (C=O), 1370, 1168(SO_2)	11.15 (s, 1 H, N-lH), 8.10–7.60 (m, 4 H, Ar-H), 6.46 (s, 1 H, =CH), 2.95 (s, 3 H, Me)
3a	—	11.00 (s, l H, N-3H), 10.25 (s, 1 H, N-lH), 8 50 (s, l H, $NHSO_2$), 7.80 (m, 4 H, Ar-H), 6.50 (s, 1 H, =CH), 3.42 (s, 2 H, NH_2)
3b	3450–3200 (NH), 1780, 1720 (C=O), 1372, 1165 (SO_2)	11.40 (s, l H, N-lH), 8.48 (s, 1 H, $NHSO_2$), 7.80 (m, 4 H, Ar-H), 6.57 (s, 1 H, =CH), 3.40 (s, 2 H, NH_2), 2.96 (s, 3 H, Me)
6a	3450–3200 NH, 1770, 1725 (C=O), 1370, 1160 (SO_2)	11.60 (s, 1 H, N-3H), 11.40 (s, l H, $NHSO_2$), 10.75 (s, l H, N-lH), 7.94 (s, 1 H, N=CH), 7.83–7.40 (m, 9 H, Ar-H), 6.42 (s, 1 H, =CH)
6b	3450–3200 (NH), 1780, 1715 (C=O), 1378, 1172 (SO_2)	11.50 (s, 2 H, $NHSO_2$, N-3H), 10.86 (s, l H, N-lH), 7.99 (s, l H, N=CH), 7.94–7.07 (m, 8 H, Ar-H), 6.52 (s, 1 H, =CH), 3.86 (s, 3 H, O Me)
6c	3450–3200 NH, 1770, 1725 (C=O), 1374, 1170 (SO_2)	11.52 (s, 2 H, $NHSO_2$, N-3H), 10.84 (s, 1 H, N-lH), 8.02 (s, 1 H, N=CH), 7.90–7.15 (m, 8 H, Ar-H), 6.50 (s, 1 H, =CH), 2.32 (s, 3 H, Ar-Me)
6d	3450–3200 NH, 1780, 1720 (C=O), 1370, 1160 (SO_2)	11.55 (s, 2 H, $NHSO_2$, N-3H), 10.85 (s, 1 H, N-lH), 8.1 (s, 1 H, N=CH), 7.90–7.25 (m, 8 H, Ar-H), 6.56 (s, 1 H, =CH)
6e	3450–3200 (NH), 1780, 1720 (C=O), 1375, 1168 (SO_2)	11.62 (s, 2 H, $NHSO_2$, N-3H), 10.94 (s, 1 H, N-lH), 7.95 (s, 1 H, N=CH), 7.88–7.37 (m, 9 H, Ar-H), 6.53 (s, 1 H, =CH), 2.93 (s, 3 H, N-3Me)
6f	3450–3200 (NH), 1775, 1718 (C=O), 1373, 1165 (SO_2)	11.48 (s, l H, $NHS0_2$), 10.80 (s, l H, N-lH), 7.98 (s, 1 H, N=CH), 7.92–7.10 (m, 8 H, Ar-H), 6.55 (s, 1 H, =CH), 3.85 (s, 3 H, OMe), 2.90 (s, 3 H, N-3Me)
6g	3450–3200 (NH), 1778, 1728 (C=O), 1370, 1166 (SO_2)	11.50 (s, 1 H, $NHS0_2$), 10.80 (s, 1 H, N-lH), 8.05 (s, 1 H, N=CH), 7.96–7.20 (m, 8 H, Ar-H), 6.50 (s, 1 H, =CH), 2.92 (s, 3 H, N-3Me), 2.34 (s, 3 H, Ar-Me)
6h	3450–3200 (NH), 1778, 1720 (C=O), 1370, 1168 (SO_2)	11.50 (s, 1 H, $NHS0_2$), 10.86 (s, l H, N-lH), 8.12 (s, l H, N=CH), 7.9–7.25 (m, 8 H, Ar-H), 6.55 (s, 1 H, =CH), 2.93 (s, 3 H, N-3 Me)
10a	3450–3200 (OH, NH), 1780, 1720 (C=O), 1370, 1160 (SO_2)	11.41 (s, 1 H, N-3 H), 10.78 (s, l H, N-lH), 9.01 (s, 1 H, $NHSO_2$), 8.47 (s, 1 H, NH), 8.47–7.80 (m, 4 H, Ar-H), 6.45 (s, 1 H, =CH), 5.52 (d, $J_{1',2'}$ = 7.89 Hz, l H, H-1′), 4.98 ((m, 1 H, HO-2′), 4.91 (d, J = 4.30 Hz, 1 H, HO-3′), 4.51 (d, J = 4.05 Hz, 1 H, HO-4′), 4.36 (d, J = 4.11 Hz, 1 H, H O-6′), 3.45–3.60 (m, 4 H, H-5′, H-6′, H-2′), 3.02 (m, 1 H, H-3′), 2.91 (m, 1 H, H-4′)
10b	3450–3200 (OH, NH, 1776, 1723 (C=O), 1372, 1166 (SO_2)	11.50 (s, l H, N-3H), 10.87 (s, l H, N-lH), 9.12 (s, l H, $NHS0_2$), 8.30 (s, 1 H, NH), 8.23–7.89 (m, 4 H, Ar-H), 6.55 (s, 1 H, =CH), 5.46 (d, $J_{1',2'}$ = 7.80 Hz, l H, H-1′), 4.90 ((s, l H, HO-2′), 4.60 (s, 1 H, H O-3′), 4.40 (m, 1 H, HO-4′), 4.21 (m, 1 H, H O-6′), 3.68–3.32 (m, 6 H, H-4′, H-3′, H-5′, H-6′, H-2′)
10c	3450–3200 (OH, NH), 1780, 1728 (C=O), 1370, 1162 (SO_2)	11.50 (s, l H, N-3H), 10.84 (s, l H, N-lH), 9.10 (s, 1 H, $NHS0_2$), 8.15–7.89 (m, 4 H, A-H), 8.30 (s, 1 H, NH), 6.50 (s, 1 H, =CH), 5.52 (d, $J_{1',2'}$ = 7.68 Hz, l H, H-1′), 4.90 ((s, l H, HO-2′), 4.60 (s, 1 H, HO-3′), 4.40 (m, 1 H, HO-4′), 4.20 (m, 1 H, HO-6′), 3.70–3.30 (m 6 H H-4′, H-3′, H-5′, H-6′, H-2′)
10d	3450–3200 (OH, NH), 1776, 1725 (C=O), 1370, 1164 (SO_2)	11.41 (s, l H, N-3H), 10.98 (s, l H, N-lH), 9.04 (s, 1 H, $NHS0_2$), 8.46 (s, 1 H, NH), 8.23–7.90 (m, 4 H, Ar-H), 6.56 (s, 1 H, =CH), 5.51 (d, $J_{1',2'}$ = 7.75 Hz, l H, H-1′), 4.89 (s, 1 H, HO-2′), 4.53 (m, l H, HO-3′), 4.32 (s, l H, HO-4′), 3.72–2.98 (m, 5 H, H-4′, H-3′, H-5′, H-2′)
120e	3450–3200 (OH, NH), 1778, 1722 (C=O), 1369, 1160 (SO_2)	11.51 (s, l H, N-3H), 10.88 (s, l H, N-lH), 9.17 (s, 1 H, $NHSO_2$), 8.46 (s, 1 H, NH), 8.20–7.91 (m, 4 H, Ar-H), 6.56 (s, 1 H, =CH), 5.52 (d, $J_{1',2'}$ = 8.05 Hz, l H, H-1′), 5.11 (s, 1 H, HO-2′), 4.32 (s, 1 H, HO-3′), 3.72–3.26 (m, 6 H, H-4′, H-3′, H-5′, H-2′, HO-4′)
10f	3450–3200 (OH, NH), 1778, 1720 (C=O), 1370, 1162 (SO_2)	10.99 (s, l H, N-lH), 9.00 (s, 1 H, $NHSO_2$), 7.84–7.76 (m, 5 H, Ar-H, NH), 6.56 (s, 1 H, =CH), 5.50 (d, $J_{1',2'}$ = 8.16 Hz, 1 H, H-1′), 4.95 (m, 1 H, HO-2′), 4.88 (d, J = 4.33 Hz, 1 H, HO-3′), 4.45 (dd, J = 4.10, 7.90 Hz, 1 H, HO-4′), 4.32 (d, J = 4.11 Hz, 1 H, HO-6′), 3.63 (t, J = 10.98 Hz, H-2′), 3.46–3.37 (m, 3 H, H-5′, H-6′), 3.04 (m, 1 H, H-3′), 2.97 (s, 3 H, N-3 Me), 2.93 (m, 1 H, H-4′)
10g	3450–3200 (OH, NH), 1772, 1718 (C=O), 1370, 1165 (SO_2)	10.87 (s, l H, N-lH), 9.12 (s, 1 H, $NHSO_2$), 7.89 (m, 5 H, Ar-H, NH), 6.55 (s, 1 H, =CH), 5.50 (d, $J_{1',2'}$ = 7.59 Hz, 1 H, H-l′), 4.98 (s, 1 H, HO-2′), 4.62 (s, 1 H, HO-3′), 4.43 (m, 1 H, HO-4′), 4.20 (m, 1 H, HO-6′), 3.30–3.70 (m, 6 H, H-4′, H-3′, H-5′, H-6′, H-2′), 2.95 (s, 3H, N-3 Me)
10h	3450–3200 (OH, NH), 1780, 1720 (C=O), 1370, 1160 (SO_2)	10.97 (s, l H, N-lH), 8.99 (s, 1 H, $NHSO_2$), 7.81 (m, 5 H, Ar-H, NH), 6.57 (s, 1 H, =CH), 5.50 (d, $J_{1',2'}$ = 7.86 Hz, 1 H, H-l′), 4.93 (s, 1 H, HO-2′), 4.88 (s, 1 H, HO-3′), 4.45 (s, 1 H, HO-4′), 4.31 (s, 1 H, HO-6′), 3.63 (t, J = 9.24 Hz, 1 H, H-2′), 3.35–3.46 (m, 3 H, H-5′, H-6′), 3.01–2.92 (m, 5 H, H-4′, N-3 Me, H-3′)
10i	3450–200 (OH, NH), 1775, 1720 (C=O), 1370, 1160 (SO_2)	10.85 (s, l H, N-lH), 9.01 (s, 1 H, $NHSO_2$), 7.91 (m, 5 H, Ar-H, NH), 6.60 (s, 1 H, =CH), 5.50 (d, $J_{1',2'}$ = 7.89 Hz, 1 H, H-l′), 5.12 (s, 1 H, HO-2′), 4.55 (s, 1 H, HO-3′), 4.32 (s, 1 H, HO-4′). 2.98–3.70 (m, 5 H, H-4′, H-3′, H-5′, H-2′), 2.94 (s, 3 H, N-3 Me)
10j	3450–3200 (OH, NH), 1780, 1720 (C=O), 1366, 1160 (SO_2)	10.97 (s, l H, N-lH), 9.03 (s, 1 H, $NHSO_2$), 7.95 (m, 5 H, Ar-H, NH), 6.50 (s, 1 H, =CH), 5.36 (d, $J_{1',2'}$ = 8.17 Hz, 1 H, H-l′), 5.12 (s, 1 H, HO-2′), 4.35 (s, 1 H, HO-3′), 3.26–3.70 (m, 6 H, H-4′, H-3′, H-5′, H-2, HO-4′), 2.96 (s, 3 H, N-3 Me)

The reaction of **2a**,**b** with 2-(*E*)-polyhydroxyalkylidene hydrazones **7a**–**e** [19,20] (Scheme 2) was not as straightforward as with **5a**–**d**. Heating of **2a**,**b** with **7a**–**e** in methanol for 2 h gave 5-[(*Z*)-(4-(2-*β*-D-glycopyranosyl)hydrazinosulfonylbenzylidene)]-2,4-imidazolidinediones **10a**–**j**. The formation of **9** from **2** and **7** is assumed to proceed by a sequence initiated by an exchange reaction between the chlorosulfonyl group of **2** and the amino group of **7** to give 5-[(*Z*)-(4-(2-polyhydroxyalkylidene) hydrazonosulfonylbenzylidene)]-2,4-imidazolidinediones **9a**–**j** as intermediate. This intermediate then cyclizes via intramolecular nucleophilic attack by the oxygen atom at 5′-position of the sugar moiety to give **10a**–**j**. Compounds **10a**–**j** were also prepared by the condensation of **3a**,**b** with monosaccharides **8a**–**e** under the same conditions. The structures of **10a**–**j** were established on the basis of their elemental analyses and spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS). Analytical data for **10a**

Table 2
^{13}C NMR data for some selected compounds listed in Table 1

Compound	^{13}C NMR (Me_2SO)/δ
6e	164.26 (C-4), 155.60 (C-2), 147.61 (HC=N), 138.17, 137.71, 133.79, 130.40, 130.04, 129.20, 129.03, 127.68, 127.03, (C-Arom, C-5), 106.99 (=CH), 24.57 (N-3 Me)
10a	165.62 (C), 155.98 (C-2), 138.70, 137.38, 130.40, 130.04, 129.76, 128.16, (C-Arom, C-5), 106.54 (=CH), 90.29 (C-1′), 78.22 (C-3′), 77.23 (C-5′), 70.84 (C-2′), 70.73 (C-4′), 61.48 (C-6′)
10b	165.68 (C-4), 156.07 (C-2), 138.69, 137.40, 130.40, 130.09,129.86, 128.11 (C-Arom, C-5), 107.31 (=CH), 91.13 (C-1′), 76.78 (C-3′), 73.97 (C-5′), 68.64 (C-2′), 68.23 (C-4′), 61.06 (C-6′)
10d	165.69 (C-4), 156.10 (C-2), 138.33,137.40,129.72,128.28,127.73 (C-Arom, C-5), 106.62 (=CH), w 90.95 (C-1′), 74.39 (C-3′), 71.07 (C-5′), 70.26 (C-2′), 63.60 (C-4′)
10f	164.26 (C-4), 155.55 (C-2), 138.82,137.13,129.72,128.81,127.95 (C-Arom, C-5), 107.31 (=CH), 90.19 (C-1′), 78.10 (C-3′), 77.15 (C-5′), 70.89 (C-2′), 70.66 (C-4′), 62.08 (C-6′), 24.52 (N-3 Me)
10h	165.45 (C-4), 156.58 (C-2), 138.52, 138.16, 130.63, 129.49, 128.97 (C-Arom, C-5), 108.84 (=CH), 90.73 (C-1′), 78.48 (C-3′), 77.41 (C-5′), 71.48 (C-2′), 71.01 (C-4′), 62.40 (C-6′), 25.42 (N-3 Me)



7-10	R	R^1	R^2	R^3	R^4	R^5
a	H	OH	H	OH	H	CH_2OH
b	H	OH	H	H	OH	CH_2OH
c	H	H	OH	OH	H	CH_2OH
d	H	OH	H	H	OH	H
e	H	OH	H	OH	H	H
f	Me	OH	H	OH	H	CH_2OH
g	Me	OH	H	H	OH	CH_2OH
h	Me	H	OH	OH	H	CH_2OH
i	Me	OH	H	H	OH	H
j	Me	OH	H	OH	H	H

Scheme 2.

revealed a molecular formula $C_{16}H_{20}N_4O_9S$ (*m*/*z* 444). The ^1H and ^{13}C NMR spectra were used to confirm this structure for the product. Thus, the ^1H NMR spectrum of **10a** showed a doublet at δ 5.52 ppm which was assigned to the anomeric proton of the glucose moiety with $J_{1',2'}$ coupling constant of 7.89 Hz in agreement with a diaxial orientation for the corresponding protons, and then a β-configuration of the glucopyranosyl hydrazine **10a** which excludes the possibility of a glucose hydrazone **9a**. The singlet at δ 6.45 ppm is due to the vinyl proton, indicating the presence of a *Z*-configuration for the exocyclic double bond. The four NH groups appeared as four singlets at δ 8.47, 9.01, 10.78 and 11.41 ppm (exchangeable with deuterium oxide). The ^1H NMR spectrum of **10h** (methanol-d_4) was characterized by the presence of a doublet at δ 5.46 ppm due to the anomeric proton of the mannose moiety with spin-spin coupling constant of 8.09 Hz which corresponds to a diaxial orientation for H-1′ and H-2′ protons, in agreement with a β-configuration of the mannopyranosyl hydrazine **10h** which excludes the possibility of the mannose hydrazone **9h**. The singlet at δ 6.59 ppm was assigned to the vinyl proton, indicating the presence of a *Z*-configuration for the exocyclic double bond (Table 1). The ^{13}C NMR spectrum of compound **10b** showed a signal at 90.20 ppm which was assigned to C-1′ in the β-configuration. Five signals appeared at δ 78.14, 77.15, 70.89, 70.66 and 62.08 ppm corresponding respectively to C-3′, C-5′, C-2′, C-4′ and C-6′ of the galactose moiety, in support of the exclusive β-configuration of the galactopyranosyl hydrazine **10b** which excludes the possibility of the galactose hydrazone **9b**. In the literature, the D-ribose *E*-thiosemicarbazone and 4-(β-D-ribopyranosyl)-thiosemicarbazide anomeric protons are described respectively at δ 146.79 and 87.10 ppm [21]. The signal at δ 107.31 ppm is due to the vinyl carbon atom, indicating the presence of a *Z*-configuration of the exocyclic double bond (Table 2).

2. Experimental

General method.—Melting points are uncorrected. Precoated aluminum sheets of Silica Gel 60 F_{254} (E. Merck) were used for TLC. Detection was effected by viewing under a short-wavelength UV lamp. IR spectra were obtained (KBr disc) on a Pye Unicam Spectra-1000 equipment. ^1H and ^{13}C NMR spectra were measured on a Bruker Advance DPX 300 MHz spectrometer for solns in $(CD_3)_2SO$, using Me_4Si as internal standard. Chemical shifts are given in δ and *J* values in Hz. 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. 5-[(*Z*)-(4-Chlorosulfonylbenzylidene)]-2,4-imidazolidinedione **2a** and 5-[(*Z*)-(4-hydrazinosulfonylbenzylidene)]-2,4-imidazolidinedione **3a** were prepared according to the method of Cremlyn et al. [8]. 2-(*E*)-Arylidene hydrazones **5a–d** and 2-(*E*)-polyhydroxyalkylidene hydrazones **7a–e** were prepared according to published methods [18–20].

Biological evaluation.—Compounds **6a–h** and **10a–j** have been examined for antiviral and antitumoral properties. Both, even at 100 μg mL^{-1} did not inhibit HIV-1 [22]. No antiviral activity against herpes and influenza virus was found. No antitumoral activity in the NCI in vitro disease-oriented human cells screening panel assay was found [23,24].

5-[(Z)-(4-Chlorosulfonylbenzylidene)]-3-methyl-2,4-imidazolidinedione **2b**. *General procedure.*—5-(*Z*)-Benzylidene-3-methyl-2,4-imidazolidinedione **1b** [17] (2.02 g, 0.01 mol) was added portionwise to chlorosulfonic acid (10 mL) at 0 °C with stirring. The solution was stirred for 6 h at room temperature and poured into ice (50 g). The precipitate was filtered off, washed with water, dried under reduced pressure and crystallized from EtOH to give **2b** (Table 3).

5-[(Z)-(4-Hydrazinosulfonylbenzylidene)]-3-methyl-2,4-imidazolidinedione **3b**. *General procedure.*—A mixture of the sulfonyl chloride **2b** (3.00 g, 0.01 mol) and hydrazine hydrate (1.00 g, 0.02 mol) in dioxane (50 mL) was initially stirred at 0 °C and then left at room temperature for 4 h. Addition of ice gave a precipitate which was filtered off, washed with water, dried under reduced pressure and crystallized from EtOH to afford **3b** (Table 3).

5-[(Z)-(4(2-(E)-Arylidene)hydrazonosulfonylbenzylidene)]-2,4-imidazolidinediones **6a–h**. *General procedures.—Method A:* A mixture of 5-[(*Z*)-(4-chlorosulfonylbenzylidene)]-2,4-imidazolidinediones **2a**,**b** (0.05 mol) and 2-(*E*)-arylidene hydrazones **5a**,**b** [18] (0.05 mol) in anhyd EtOH (30 mL) was heated under reflux for 2 h. After cooling, the separated solid was collected and recrystallized from EtOH to give **6a–h** (Table 3).

Table 3
Yields, melting points and analytical data for 2–10

Compound	mp (°C)	Yield (%)	Mol formula	Found/Calcd (%)			M^+ (*m*/*z*)
				C	H	N	
2a	270	87	$C_{10}H_7ClN_2O_4S$ (286)	[Ref. 3]			
2b	298	80	$C_{11}H_9ClN_4O_4S$ (300)	43.65/43.92	2.90/3.01	9.37/9.31	300
3a	219	78	$C_{10}H_{10}N_4O_4S$ (282)	[Ref. 3]			
3b	209	76	$C_{11}H_{12}N_4O_4S$ (296)	44.86/44.59	4.11/4.08	18.79/18.91	296
6a	245	70[a] 83[b]	$C_{17}H_{14}N_4O_4S$ (370)	54.90/55.13	3.79/3.81	15.06/15.12	370
6b	240	75[a] 87[b]	$C_{18}H_{16}N_4O_5S$ (400)	54.43/53.99	3.99/4.03	13.86/13.99	400
6c	258	78[a] 85[b]	$C_{18}H_{16}N_4O_4S$ (384)	56.53/56.24	4.00/4.19	14.42/14.57	384
6d	252	77 90	$C_{17}H_{13}ClN_4O_4S$ (404)	50.21/50.43	3.32/3.23	13.78/13.83	404
6e	237	71[a] 82[b]	$C_{18}H_{16}N_4O_4S$ (384)	56.61/56.24	4.16/4.19	14.48/14.57	384
6f	209	72[a] 84[b]	$C_{19}H_{18}N_4O_5S$ (414)	54.73/55.06	4.35/4.38	13.44/13.52	414
6g	227	70[a] 80[b]	$C_{19}H_{18}N_4O_5S$ (398)	57.52/57.27	4.57/4.55	14.12/14.06	398
6h	238	79[a] 92[b]	$C_{18}H_{15}ClN_4O_4S$ (418)	51.35/51.62	3.59/3.61	13.20/13.37	418
10a	227	69[a] 80[b]	$C_{16}H_{20}N_4O_9S$ (444)	43.06/43.24	4.35/4.53	12.47/12.60	444
10b	194	72[a] 83[b]	$C_{16}H_{20}N_4O_9S$ (444)	42.98/43.24	4.48/4.53	12.52/12.60	444
10c	192	74[a] 82[b]	$C_{16}H_{20}N_4O_9S$ (444)	43.02/43.24	4.28/4.53	12.46/12.60	444
10d	184	74[a] 79[b]	$C_{15}H_{18}N_4O_8S$ (414)	43.16/43.47	4.24/4.38	13.32/13.52	414
10e	206	68[a] 76[b]	$C_{15}H_{18}N_4O_8S$ (414)	43.28/43.47	4.19/4.38	13.45/13.52	414
10f	202	76[a] 85[b]	$C_{17}H_{22}N_4O_9S$ (458)	44.25/44.54	4.69/4.83	12.16/12.22	458
10g	160	78[a] 82[b]	$C_{17}H_{22}N_4O_9S$ (458)	44.27/44.54	4.55/4.83	12.08/12.22	458
10h	188	70[a] 83[b]	$C_{17}H_{22}N_4O_9S$ (458)	44.40/44.54	4.42/4.83	12.05/12.22	458
10i	172	72[a] 80[b]	$C_{16}H_{20}N_4O_8S$ (428)	44.49/44.85	4.66/4.70	12.97/13.08	428
10j	173	63[a] 78[b]	$C_{16}H_{20}N_4O_8S$ (428)	44.44/44.85	4.60/4.70	12.86/13.08	428

[a] Method A.
[b] Method B.

Method B:—A suspension of 5-[(*Z*)-(4-hydrazinosulfonylbenzylidene)]-2,4-imidazolidinediones **3a**,**b** (0.05 mole) in anhyd EtOH (30 mL) and the appropriate aldehyde **4a**–**d** (0.05 mole) was heated under reflux for 2 h. During the reaction period, the hydrazine dissolved with the formation of hydrazone. It was filtered and recrystallized from EtoH to give **6a**–**h** in quantitative yield (Table 3).

5-[(Z)-(4-(2-β-D-Glycopyranosyl)hydrazinosulfonylbenzylidene)]-2,4-imidazolidinediones **10a**–**j**. *General procedures. Method A:* A mixture of 5-[(*Z*)-(4-chlorosulfonylbenzylidene)]-2,4- imidazolidinediones **2a**,**b** (0.05 mol) and 2-(*E*)-polyhydroxyalkylidene hydrazones **7a**–**e** [19,20] (0.05 mole) in MeOH (50 mL) was heated under reflux until the reaction was found complete by TLC (4 h, 95:5 $CHCl_3$–MeOH). Cooling to room temperature resulted in a precipitate which was collected by filtration and recrystallized from MeOH to give **10a**–**j** (Table 3).

Method B:—A suspension of 5-[(*Z*)-(4-hydrazinosulfonylbenzylidene)]-2,4-imidazolidinediones **3a**,**b** (0.05 mol) in MeOH (50 mL) and the appropriate monosaccharide **8a**–**d** (D-glucose, D-galactose, D-mannose, L-arabinose or D-xylose) (0.05 mol) was heated under reflux until the reaction was judged complete by TLC (6 h, 95:5 $CHCl_3$-MeOH). Cooling to room temperature, resulted in a precipitate which was collected by filtration and recrystallized from MeOH to give **10a**–**j** in quantitative yield (Table 3).

Acknowledgements

The author expresses gratitude and thanks to Professor Nils G. Johansson, Medicinal Chemistry, Medivir AB, Huddinge, Sweden, for carrying out the antiviral testing, Professor John P. Bader, Antiviral Evaluation Branch and Professor V. L. Narayanan, Drug Synthesis and Chemistry Branch, National Cancer Institute, Bethesda, USA for carrying out the antitumor screening.

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