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Stereocontrolled synthesis of thiohydantoin spironucleosides from sugar spiroacetals

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Dedicated to Professor J. Plumet on the occasion of his 60th birthday

Abstract—5-Epithiohydantocidin, *N*-alkyl and *N*-glycosylthiohydantoin spironucleosides are prepared from glycosylaminoesters and from furanoid and pyranoid methyl isothiocyanatoulosonates. The aminoesters and the isothiocyanates are obtained, in a stereocontrolled manner, from sugar spiroacetals through a high-yielding sequence involving ring opening with trimethyl azide, formation of an ester group, reduction of the azide, and, in the case of isothiocyanates, reaction with thiophosgene.

1. Introduction

The chemistry of spironucleosides, a type of nucleoside in which the anomeric carbon belongs simultaneously to the sugar ring and to the nitrogenated heterocyclic moiety,[1] has received considerable development in the last decade. This interest is due to the isolation from culture broths of *Streptomices hygroscopicus* of (+)-hydantocidin (**1**), the first natural spironucleoside.[2] The (+)-hydantocidin shows low toxicity for mammals and has herbicidal and plant growth-regulatory activities, which have been related to its inhibitory activity of adenylsuccinate synthase.[3] Other spiro-anulated compounds[4] also have biological interest due to their activity as inhibitors of glycogen phosphorilase and α-amylase.[5] Syntheses of (+)-hydantocidin have been reported,[6] and starting from 1993 many syntheses of hydantocidin analogues and related carbocyclic derivatives have been described.[1b,7]

Recently, we reported our preliminary results on the preparation of pyranoid and furanoid isothiocyanatoulosonates, a new type of sugar isothiocyanate which is used for the stereocontrolled preparation of thiohydantoin spironucleosides.[8] Some data on related ulosononitriles[9] and furanoid ulosonoisothiocyanates[10] have been reported later.

In this paper, we report the full data on a synthetic procedure to prepare furanoid and pyranoid spirothiohydantoins using methyl isothiocyanatoulosonates (**11**, **18**) and methyl aminoulosonates (**9**, **10**, and **17**) as key intermediates. We have previously shown[7f] that ketofuranosyl isothiocyanates are transient intermediates in the preparation of spironucleosides of 1,3-*O*,*N* five member heterocycles.

2. Results and discussion

The starting materials to prepare the pyranoid and furanoid 2-isothiocyanatoulosonic esters **11** and **18** (Scheme 1) were the β-azido-1-trimethyl ethers **3** and **13**, respectively, which we have previously reported,[7f] and were obtained by reaction of trimethylsilyl azide with the corresponding spiroacetal[11] **2** or **12** in freshly distilled acetonitrile, under stringently anhydrous conditions. Desilylation of **3** with a catalytic amount of TBAF (tetrabutyl ammonium fluoride). $3H_2O$ produced **4** in high yield. Swern[12] oxidation of **4** afforded the azido aldehyde **5**, whose NMR data showed the signals for **5** and additional signals corresponding to a hydrate as is described for related aldehydes.[13] Further oxidation ($NaClO_2$) of **5** followed by treatment with diazomethane gave the 3-*O*-benzylazido ester **7**. Treatment of **4** with ruthenium chloride-sodium metaperiodate produced simultaneous oxidation of the formyl and benzyl groups with formation of the 3-*O*-benzoyl ulosonic acid derivative **6**, which was not isolated, and in situ converted (reaction with CH_2N_2) into the methyl 3-*O*-benzoyl azido

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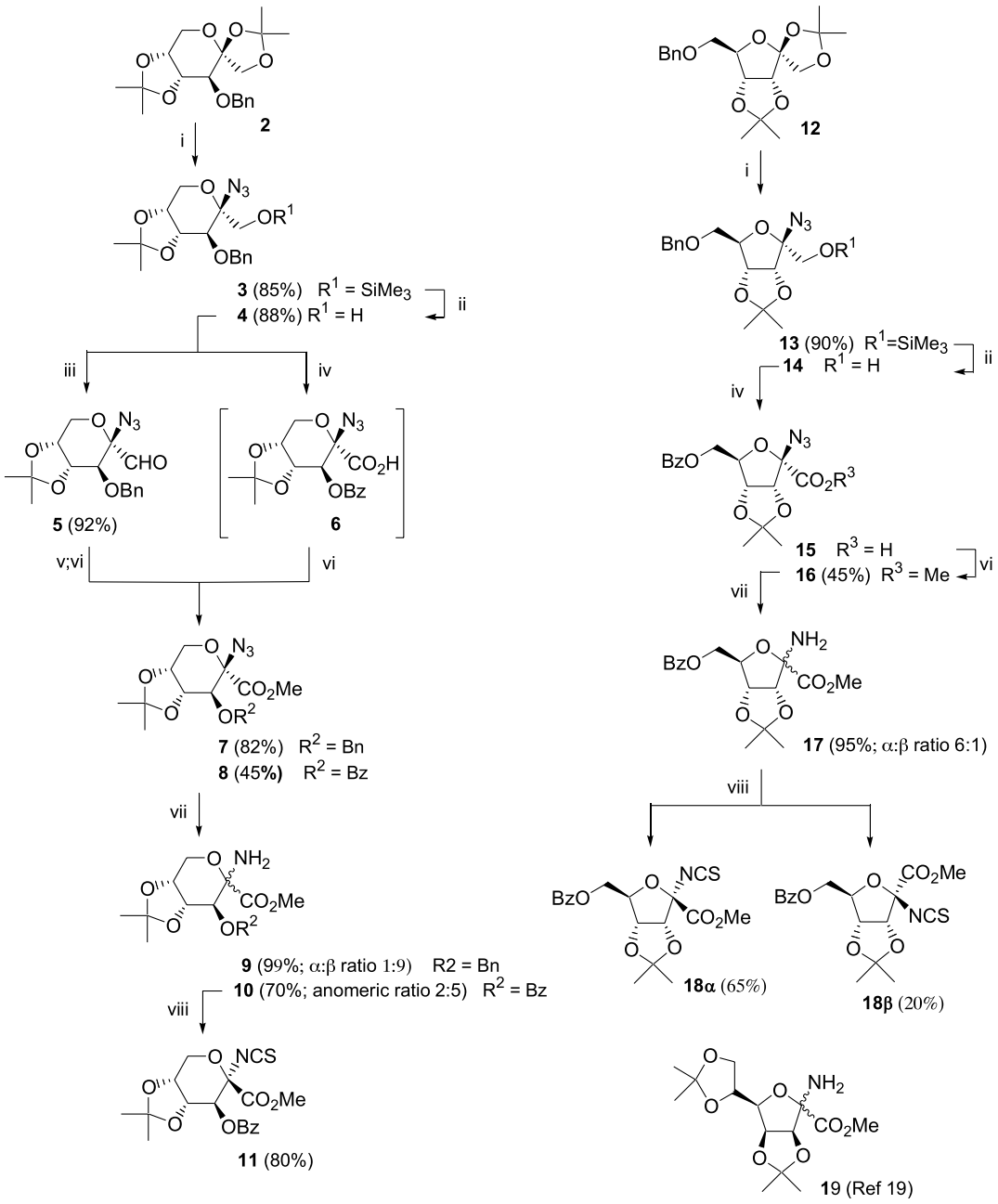
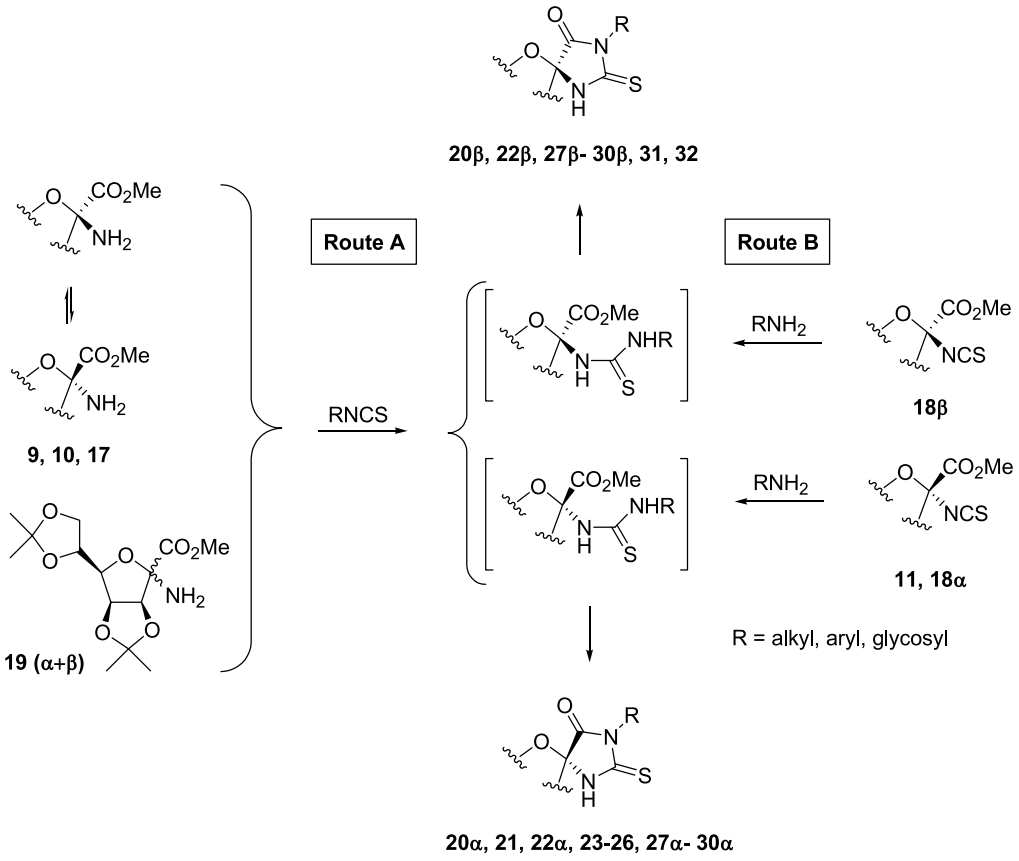


Scheme 1. Preparation of new glycosyl aminoulosonates and glycosyl isothiocyanatoulosonates from sugar spiroacetals. Reagents and conditions: (i) $TMSN_3$, TMSOTf, CH_3CN, 0 °C; (ii) TBFA.$3H_2O$, THF, rt; (iii) DMSO, CH_2Cl_2, −70 °C; (iv) $RuCl_3 \cdot H_2O$, $NaIO_4$, CH_3CN, H_2O, CCl_4, rt; (v) $NaClO_2$, $(CH_3)_2C{=}CH{-}CH_3$, $NaH_2PO_4 \cdot 2H_2O$, ^{t}BuOH, H_2O, 0 °C; (vi) CH_2N_2, Et_2O, MeOH, 0 °C; (vii) H_2/C–Pd, MeOH, rt; (viii) $CSCl_2$, $CHCl_3$, H_2O, $CaCO_3$, rt.

ester **8**. Catalytic hydrogenation of **7** and **8** gave the glycosylaminoester anomeric mixtures **9** and **10**, respectively, in good yields. The anomeric ratio for **9** was 1:9 (α:β, $CDCl_3$, rt, equilibrium), whereas in the case of **10** the ratio of the two anomers was 2:5 (same conditions), although the anomeric (C-2) configuration of each anomer for **10** was not determined. The anomeric mixture **9** was used only in route A (Scheme 2) for the synthesis of spirothiohydantoins. Compound **10** was also transformed, by reaction with thiophosgene in basic medium, into an anomeric mixture (α:β 16:1) of glycosyl isothiocyanates, from which only the α anomer **11** was isolated. This compound was used in route B of spirothiohydantoins (Scheme 2).

In a similar way, the reaction of **13** with TBAF· $3H_2O$ gave the known[6b] 1-*O*-unprotected furanosyl azide **14**, which by oxidation with ruthenium chloride–sodium metaperiodate (→**15**), followed by estherification with CH_2N_2, produced the methyl ulosonate **16**. Catalytic hydrogenation of **16** yielded the anomeric mixture (α:β ratio 6:1) of aminoesters **17** in virtually quantitative yield. Reaction of **17** with thiophosgene in the presence of $CaCO_3$ gave, after column chromatography, the α (65%) and β (20%) isothiocyanato ulosonates **18α** and **18β** as isolated products.

Table 1 shows selected spectroscopic data for the structural assignments of compounds **4**–**5**, **7**–**11**, and **16**–**18**. Thus the



Scheme 2. Preparation of 5-*epi*thiohydantocidin, *N*-alkyl and *N*-glycosylthiohydantoin spironucleosides from glycosylaminoesters (route A) and from methyl isothiocyanatoulosonates (route B).

IR spectra of the azido derivatives **4**–**5**, **7**, **8**, and **16** had absorption for the N_3 group at 2116–2128 cm^{-1}. The NMR spectra of **4** showed no signals for a $SiMe_3$ group, and the OH was evident from the IR absorption at 3497 cm^{-1} and from the interchangeable (D_2O) double doublet at 2.12 ppm in the ^1H NMR spectrum. The hydrated form of **5** appeared in the ^1H NMR spectrum in a 1:4 ratio with respect to the free aldehyde, the chemical shift for the resonance of H-1 of the hydrate being 5.22 ppm. The carbonyl groups of the β-azido ulosonic esters **7**, **8** and **16**, resonated at 165.4–166.7 ppm (Table 1) as is reported[14] for related azido esters. The signal for the resonance of the anomeric carbon in **4**, **5**, **7**, and **8** was close to 91 ppm, as is described for glycopyranosyl azides;[15] the same carbon for the furanoid derivative **16** resonated at 100.5 ppm. The β configuration for the major compound in the anomeric mixture **9** is proposed according to the order of formation, and the anomeric ratio is given in the equilibrium (NMR measurements). In the 6:1 anomeric mixture **17** the major compound was the α anomer. The anomeric configuration being supported on the order of formation, and on the differences of chemical shifts of H-3 and C-3 for the two anomers (H-3 is relatively deshielded in the α anomer whereas C-3 is relatively shielded in the same anomer), which is in agreement with reported data for related compounds.[16] The isothiocyanato group of **11**, **18α** and **18β** was evident from the corresponding IR absorptions

Table 1. Selected spectroscopic data (ν cm^{-1}, δ ppm, J Hz) for compound **3**–**5**, **7**–**11**, and **16**–**18**[a]

Compound	ν_{N3}[b]/ν_{NCS}[b]	δ C-1	δ C-2	δ C-3	δ NCS
4	2118	64.9	91.7	76.2	—
5	2122	192.5	90.9	74.6	—
7	2126	166.7	91.1	76.7	—
8	2128	165.8	90.3	70.8	—
9[c]	—	171.4	86.1	77.2	—
10[c]	—	170.9	85.4	72.2	—
11	2002	165.0	87.7	72.9	145.1
16	2116	165.4	100.5	86.9	—
17[c]	—	169.9	93.6	81.7	—
18α	2018	166.0	95.1	84.4	144.9
18β	2016	164.9	97.7	88.8	145.1

[a] NMR data are obtained in $CDCl_3$.
[b] KBr discs.
[c] Data for the major anomer.

Table 2. Synthesis of thiohydantoin spironucleosides

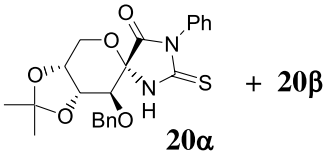
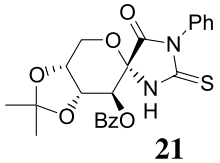
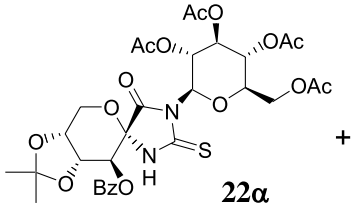
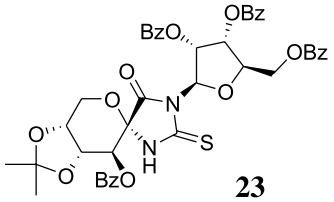
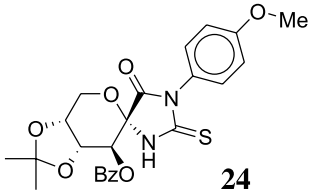
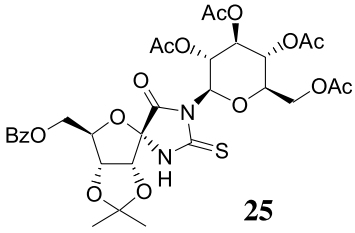
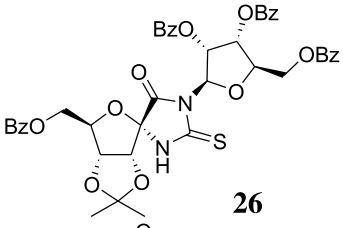
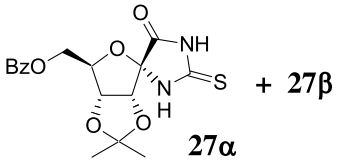
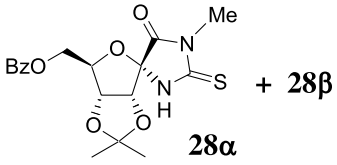
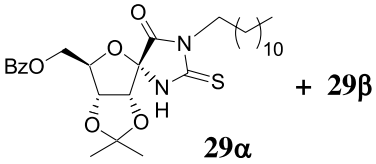
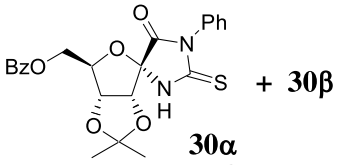
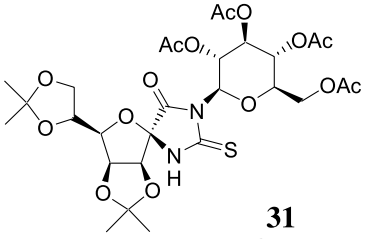
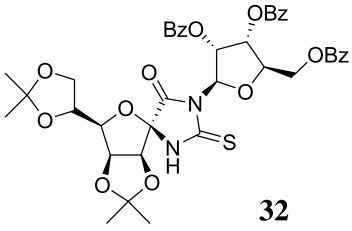
Entry	Starting aminoester or isothiocyanatoulosonate (anomeric ratio)	Route	Product (s)	Yield (%)
1	**9** (α:β 1:9)	A	 **20α** + **20β**	65 (**20α**) 31 (**20β**)
2	**10** (5:2)	A	 **21**	70
3	**10** (5:2)	A	 **22α** + **22β**	76 (**22α**) 9 (**22β**)
4	**10** (5:2)	A	 **23**	81
5	**11** (only α anomer)	B	 **24**	72
6	**17** (α:β 6:1)	A	 **25**	79
7	**17** (α:β 6:1)	A	 **26**	83
8	**18** (α:β 13:4)	B	 **27α** + **27β**	74 (**27α**) 20 (**27β**)
9	**18** (α:β 13:4)	B	 **28α** + **28β**	64 (**28α**) 21 (**28β**)

Table 2 (*continued*)

Entry	Starting aminoester or isothiocyanatoulosonate (anomeric ratio)	Route	Product (s)	Yield (%)
10	**18** (α:β 13:4)	B	 **29α** + **29β**	60 (**29α**) 17 (**29β**)
11	**18** (α:β 13:4)	B	 **30α** + **30β**	73 (**30α**) 21 (**30β**)
12	**19** (1:5)	A	 **31**	94
13	**19** (1:5)	A	 **32**	94

at 2000–2018 cm^{-1}, and from the ^{13}C resonances at roughly 145 ppm, characteristic of glycosyl isothiocyanates.[17] The vicinal coupling constants between the protons of the pyranoid ring of **11** were indicative of $^5C_2$ conformation, slightly distorted by the dioxolane ring (the value of $J_{5,6'}$, for example, was 6.9 Hz). The anomeric configuration (the NCS group is in α position) of this compound was deduced from its transformation into the spiranic compound **24** and from the NMR data of **24** (see below). The $^3J_{HH}$ values for the protons of the furanoid ring of **18β** were very close to that for the β-D-psicofuranosyl azide.[6b] The anomeric carbon in **18α** resonated at higher field (95.1 ppm) than the same carbon in **18β** (97.7 ppm), as in related pairs of anomers.[14b,16a,18] This assignment of the anomeric configurations were confirmed by the NMR data of **27–30** (see below).

The glycosylamines **9**, **10** and **17**, together with described[19] methyl 2-aminohept-2-ulofuranosonate **19** were used in the route A to prepare spirothiohydantoins (Scheme 2). Both anomers of **19** had been reported as isolated products. In our first attempt to prepare spirothiohydantoins from **19**, pure α and β anomers were used; but, due to the anomeric equilibrium under the reaction conditions, in both cases the same spirothiohydantoin was obtained, consequently, the anomeric mixture **19 α+β** was used in subsequent reactions. A related cyclization using phenylisocyanate as sole heterocumulene has been reported.[16a]

Treatment of the anomeric mixture of aminoesters **9** with phenyl isothiocyanate in DMF at 85 °C for 23 h resulted in 96% yield the resoluble mixture of spirothiohydantoins **20** (Scheme 2, route A and Table 2, entry 1). This reaction was low-yielding under milder conditions, probably due to the stabilization by hydrogen bondings between the amino group and the oxygen atoms on C-1 and C-3 in the starting aminoester. The reaction involves the formation of an intermediate thiourea which spontaneously cyclates to the thiohydantoin.[20]

The IR spectra of **20α** and **20β** had the signal for the carbonyl group ($\nu_{C=O}$) at 1765 cm^{-1}, and the C═S and C═O groups resonated (Table 3) at roughly 184 and 169.5 ppm, respectively, in accord with that described for related spirohydantoins.[21] The $^3J_{HH}$ values between protons of the pyranose ring were indicative of the $_4C^1$ conformation. The anomeric configuration is based on the value of the $^3J_{CH}$ between C-4 and H-10 (Fig. 1), which was in the range[18,21] for antiperiplanar nuclei in **20α** (6.8 Hz) and in the range for *gauche* nuclei in **20β** (2.6 Hz). Additionally, the resonance for H-1 (NH) of **20β** was at lower field than that for **20α**, as in spirohydantoins of other pyranoid sugars.[21]

The α configuration of **21** was deduced from the value (5.9 Hz) of the coupling constant between H-10 and C-4, indicative of *anti* relationship between the corresponding nuclei.

Similarly, the reaction of **10** with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate[22] and with 2,3,5-tri-*O*-

benzoyl-β-D-ribofuranosyl isothiocyanate[23] gave the *N*-glycosyl spirothiohydantoins **22α**, **22β** (entry 3) and **23** (entry 4).

The treatment of the ulofuranosonic aminoester **17** with the same glycosyl isothiocyanates gave, in high yield, the furanoid spirothiohydantoins **25** and **26** only as α anomers (Table 2, entries 6 and 7). Selected structural data, including representative diaxial $^{3}J_{H,H}$ values of pyranoids derivatives, of **22**, **23**, **25** and **26** are shown in Table 3. The anomeric configurations were supported on HMBC[24] and carbon-proton coupled experiments in a similar way to that above commented for **20**.

The last spirothiohydantoins prepared through route A were **31** and **32**, which were obtained, in almost quantitative yield, by reaction of the sugar aminoester anomeric mixture[19] **19** (see above) with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate[22] and with 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl isothiocyanate[23] respectively, under mild conditions (Table 2, entries 12 and 13). As the configuration of C-4 and C-3 in **31** and **32** are the contrary to those for **25**–**28**, and the spectroscopic data for the hydration

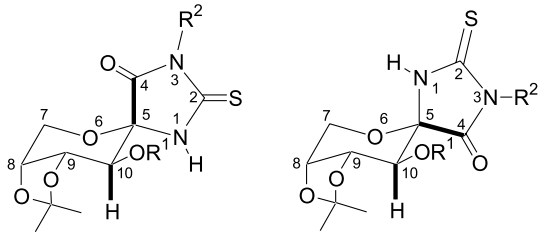


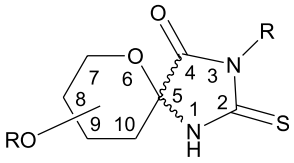
Figure 1. Relationship between H-10 and C-4 in C-5 epimers of pyranoid spirothiohydantoins.

moiety and C-4 of **31**–**32** practically coincide with those for the α anomers **25**, **26**, **27α**, **28α**, **29α**, and **30α**, we propose that in both cases the same spatial relationship exists, that is, **31** and **32** have β anomeric configuration.

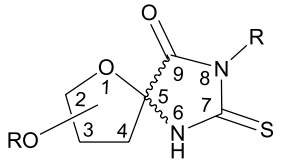
Compounds **22**–**26**, **31** and **32** had a glycosyl radical on N-8, consequently their structures are simultaneously those of *N*- and spiro-nucleoside.

The route B (Scheme 2) to prepare thiohydantoin spironucleosides is the reaction of methyl isothiocyanatoulosonates with ammonia, alkyl, and aryl amines.

Table 3. Selected NMR data (δ ppm, *J* Hz) for spironucleosides **20**–**35** at 500 MHz in $CDCl_3$



Compound[a]	δ H-1 (NH)	δ H-10	$J_{9,10}$	δ C-2 (C=S)	δ C-4 (C=O)	δ C-5	δ C-10
20α	7.06	3.70	7.1	183.6	169.4	86.6	77.7
20β	9.09	4.10	7.9	184.9	169.5	87.1	77.0
21(α)	8.04–7.18	5.67	7.4	182.8	168.7	85.6	71.2
22α	7.65	5.52	7.8	182.1	167.1	84.4	71.1
22β	8.24	5.79	6.9	183.5	166.7	84.5	68.4
23(α)	8.13–7.26	5.52	7.8	181.2	168.2	84.8	71.2
24(α)	7.52	5.65	7.4	183.2	168.9	85.5	71.1
33(α)	8.72	5.75	9.7	182.1	166.7	84.5	71.5
34(α)[b]	—	3.95	10.1	185.6	172.0	88.0	70.3



Compound[a]	δ H-6	δ H-4	$J_{3,4}$	δ C-7	δ C-9	δ C-5	δ C-4
25(α)	7.38	4.88	6.0	181.6	170.5	91.5	80.2
26(α)	8.13–7.34	4.63	6.0	181.2	169.9	92.1	80.6
27α	8.09–7.43	4.88	6.1	181.2	171.2	94.7	80.7
27β	7.49	4.93	6.4	180.8	168.1	95.8	86.2
28α	7.41	4.83	6.0	183.5	170.9	92.8	80.7
28β	7.43	4.92–4.87	—	183.3	168.0	93.8	86.1
29α	7.27	4.82	6.0	183.2	171.0	92.4	80.6
29β	7.32	4.92–4.85	—	183.1	168.2	93.6	86.1
30α	8.09–7.31	4.99	6.1	182.8	170.4	93.0	80.9
30β	7.76	5.00	6.1	182.7	167.5	94.1	86.3
31β	7.34	4.84	5.9	181.6	170.5	89.7	80.0
32β	7.31	4.89	5.9	181.4	170.6	90.2	80.1
35α	—	4.32	4.8	185.0	167.8	95.5	74.6

In MeOH-d_4.
[a] In the second part of the table (furanoid derivatives) the numbering of formulas changes, but homologous nuclei are in the same column as in the first part.
[b] In D_2O.

Thus, the treatment of the pyranoid isothiocyanate **11** with 4-methoxyaniline, in DMF at 85 °C, produced (Table 2, entry 5) the spirothiohydantoin **24**, whose spectroscopic data (Table 3) supported the indicated structure. The coupling constant (5.8 Hz) between C-4 and H-10 confirmed[18] the α configuration not only for **24**, but also for the starting isothiocyanate **11**.

Reactions of a mixture of the anomers **18α** and **18β** with ammonia, methylamine, dodecylamine, and aniline, gave the corresponding thioureido derivative, which spontaneously cyclates, in the reaction medium, and under mild conditions, to afford the corresponding spironucleosides (**27**–**30**) in high yields (Table 2, entries 8–11). In all cases, mixtures of spiroanomers were obtained, which could be resolved. Table 3 shows selected spectroscopic data for these compounds. The most significant differences between the NMR data for the α and the β anomers are the chemical shifts of H-2, C-4, and C-5, which resonated at lower field in the minor β anomers, than in the major α anomers. The difference in the chemical shift of H-2 has been previously reported,[16b] and has been used to define the anomeric configuration of thiohydantocidin.[16c] The δ values for C-2 and C-3 are virtually identical in all the α anomers, and differ by 2 ppm in the β anomers. The coupling constants between H-2 and CH_2OBz are higher in the α anomers than in the β anomers. These data further confirmed the anomeric configurations of **18α** and **18β**.

With the goal of having *O*-unprotected spirothiohydantoins, the deprotections of **22α** and **27α** have been carried out (Scheme 3).

The isopropylidene group of **22α** was removed with DDQ[25] in acetonitrile:water 9:1 at 45 °C, obtaining **33**, which was *O*-debenzoylated by treatment with sodium methoxide in methanol. No measurable anomerization[14a] was observed, and the *O*-unprotected *N*- and spironucleoside **34** was obtained in 85% yield after preparative HPLC.

In the case of **27α** the acetal group was removed (→**35**) in 91% yield, by treatment with TFA:H_2O 2:3 as reported for its C-7 oxo analogue.[16b] The *O*-debenzoylation with sodium methoxide of **35** produced the 5-*epi*thiohydantocidin **36α**, together with its β anomer **36β** (α:β anomeric ratio 6:1, global yield 85%). Related spiroepimerizations have been reported.[7f,26] The spectroscopic data of **36α** and **36β** coincide with those previously reported[16c] for the same compounds prepared through an iminophosphorane intermediate.

3. Conclusion

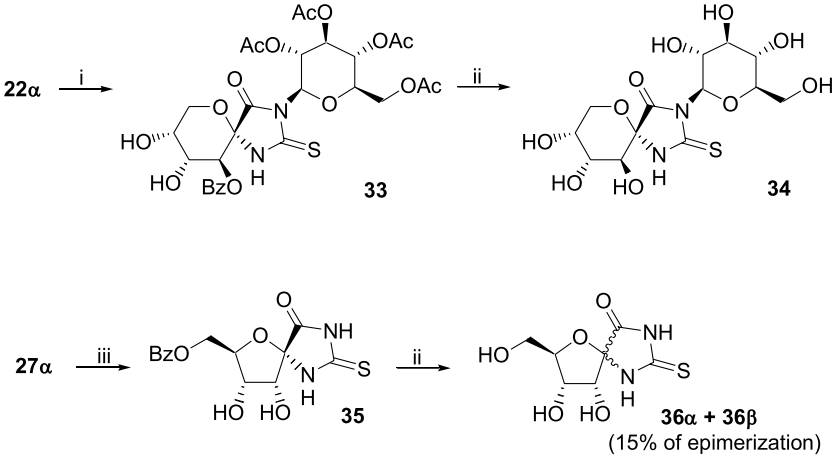
Glycosylaminoesters and 2-deoxy-2-isothiocyanato-hex-2-ulofura(pyra)nosonates —a new class of glycosyl isothiocyanate- are easily and stereoselectively prepared from sugar spiroacetals. Both types of compound can be transformed under mild conditions and in high yields, into glycosylspirothiohydantoins, including 5-*epi*thiohydantocidin. The target compounds are spironucleosides, and in the case of *N*-glycosyl derivatives are simultaneously *N*-nucleosides.

4. Experimental

4.1. General methods

Unless otherwise noted, starting materials were obtained for commercial suppliers and used without purification. All manipulations of air-sensitive compounds were carried out in an inert atmosphere under recirculation of nitrogen or argon. The following reaction solvents were distilled under nitrogen immediately before use: THF and Et_2O from Na/benzophenone; CH_2Cl_2 from CaH_2; toluene from Na; and MeOH from Mg. Et_2O and petroleum ether for column chromatography were also distilled under nitrogen from Na/benzophenone before use. TLC were performed on silica gel HF_{254}, with visualization by UV light or charring with 10% H_2SO_4 (EtOH) or 1% $Ce(SO_4)_2$. $4H_2O$-5% ammonium molybdate-6% H_2SO_4. Silica gel 60 (Merck, 70–230 or 230–400 mesh) was used for preparative chromatography.

A Perkin-Elmer model 141 MC polarimeter, tubes of 1 cm, and solutions in CH_2Cl_2, unless other stated, at 589 nm, were used for measurements of specific rotations. IR were



Scheme 3. Total deprotection of spirohydantoins **22α** and **27α**. Reagents and conditions: (i) DDQ, CH_3CN:H_2O 9:1, 45 °C, 36 h, 83%; (ii) NaOMe 1M, MeOH, 91% (**36α**+**36β**), 85% (**34**); (iii) TFA:H_2O 2:3, rt., 1 h, 91%.

recorded for KBr discs or films on a Bomen Michelson MB 120 FTIR spectrophotometer.

Mass spectra (EI, CI and FAB) were recorded with a Kratos MS-80RFA or a Micromass AutoSpecQ instrument with a resolution of 1000 or 60000 (10% valley resolution). For the FAB spectra ions were produced by a beam of xenon atoms (6–7 keV), using 3-nitrobenzyl alcohol or thioglycerol as matrix and NaI as salt.

A Waters 2690 instrument, with a PDA 996 detector, and a μBondpack C18 column (7,8×300 mm) was used for HPLC.

NMR experiments were recorded on a Bruker AMX 500 (500.13 MHz for ^{1}H and 125.75 MHz for ^{13}C) or on a Bruker AMX300 (300.5 MHz for ^{1}H and 75.50 MHz for ^{13}C). Sample concentrations were typically in the range 10–15 mg per 0.5 mL of $CDCl_3$. Chemical shifts are given in parts per million, and tetramethylsilane was the internal standard. 2D COSY, HMQC, TOCSY, HMBC and 1D NOESY experiments were carried out to assist in NMR signal assignments.

Compounds **2**[11], **12**[11] and **19**[19] were prepared according to the described literature procedures. Compounds **3** and **13** were prepared as we described in a previous work.[7f]

4.2. 2-Azido-3-*O*-benzyl-2-deoxy-4,5-*O*-isopropylidene-β-D-fructopyranose (4) and 2-azido-6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-β-D-psicofuranose (14)

To a solution of **3** (for **4**) or **13** (for **14**) (100 mg, 0.25 mmol) a catalytic amount of TBAF·$3H_2O$ in THF (3 mL) was added. The mixture was stirred at room temperature for 2 h, evaporated, and purified by column chromatography (Et_2O/petroleum ether 1:5).

Data for **4**. Yield: 0.072 g, 88% (syrup). $[\alpha]_D^{27}$ −158 (*c* 1.0). IR: ν_{max} 3497, 3032, 2986, 2934, 2880, 2118 (N_3), 1458, 1375, 1248, 1221, 1115, 1078 and 1022 cm^{-1}. ^{1}H RMN (500 MHz, CDCl3, δ ppm, *J* Hz): δ 7.38–7.26 (m, 5H, Ar), 4.92 (d, 1H, $^{2}J_{H,H}$=11.7 Hz, CHHPh), 4.68 (d, 1H, CHHPh), 4.38 (dd, 1H, $J_{4,5}$=5.89 Hz, $J_{3,4}$=7.2 Hz, H-4), 4.28 (dt, 1H, $J_{5,6a}$=$J_{5,6b}$=1.9 Hz, H-5), 4.14 (m, 2H, H-6a, H-6b), 3.88 (dd, 1H, $J_{1a,1b}$=11.7 Hz, $J_{1a,OH}$=6.3 Hz, H-1a), 3.81 (dd, 1H, $J_{1b,OH}$=7.9 Hz, H-1b), 3.65 (d, 1H, H-3), 2.12 (dd, OH), 1.50, 1.39 (each s, each 3H, 2CH3). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 128.6–127.4 (Ar), 109.1 (CCH_3), 91.7 (C-2), 76.5 (C-4), 76.2 (C-3), 73.2 (C-5), 73.0 (CH_2Bn), 64.9 (C-1), 61.6 (C-6), 27.8, 26.0 ($2CH_3$). HREIMS *m/z* calcd for C16H21O5N3 ([M]+): 335.1481, found: 335.1483.

Data for **14**. Yield: 0.088 g (92%). The spectroscopic data for **14** were coincident with those reported[6b] for the same compound prepared in a different way.

4.3. 2-Azido-3-*O*-benzyl-1-dehydro-2-deoxy-4,5-*O*-isopropylidene-β-D-fructopyranose (5)

To a cold solution (−70 °C) of oxalyl chloride (0.1 mL, 1.2 mmol) in CH_2Cl_2 (1 mL), under argon, a solution of DMSO (0.17 mL, 2.4 mmol) in CH_2Cl_2 (2 mL) was added. The mixture was stirred for 5 min, and a solution of **4** (100 mg, 0.3 mmol) in CH_2Cl_2 (1.5 mL) was then added dropwise. After 30 min, Et_3N (0.42 mL, 3 mmol) was added. The mixture was stirred at −70 °C for another 5 min, and then raised to room temperature slowly. A solution of saturated $NaHCO_3$ (2 mL) was added and the mixture was extracted with AcOEt (3×4 mL), dried ($MgSO_4$), evaporated, and purified by column chromatography (Et_2O/petroleum ether 1:2). Yield: 0.091 g, 92% (amorphous solid). IR: ν_{max} 2984, 2122 (N3), 1576, 1417, 1117 and 1101 cm^{-1}. ^{1}H NMR (500 MHz, CDCl3, δ ppm, *J* Hz): δ 9.28 (s, 1H, H-1), 7.36–7.30 (m, 5H, Ar), 4.77 (s, 2H, CH2Ph), 4.40 (dd, 1H, $J_{4,5}$=6.5 Hz, H-4), 4.31 (ddd, 1H, H-5), 4.24 (dd, 1H, $J_{5,6a}$=2.5 Hz, $J_{6a,6b}$=13.1 Hz, H-6a), 4.12 (dd, 1H, $J_{5,6}$=1.1 Hz, H-6b), 3.91 (d, 1H, $J_{3,4}$=5.7 Hz, H-3), 1.48, 1.35 (each s, each 3H, 2CH3). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 192.5 (C-1), 137.5–127.7 (Ar), 109.9 (CCH_3), 90.9 (C-2), 74.6 (C-3), 73.9 (C-4, CH_2Ph), 72.4 (C-5), 62.4 (C-6), 27.0, 25.3 ($2CH_3$). HRFABMS *m/z* calcd. for $C_{16}H_{21}N_3O_6Na$ ([M+H_2O+Na]$^+$): 374.1328, found: 374.1331.

^{1}H NMR data for the hydrate of **5**. (500 MHz, $CDCl_3$, δ ppm, *J* Hz) δ 7.35–7.30 (m, 5H, Ar), 5.22 (s, 1H, H-1), 4.93 (d, 1H, $^{2}J_{H,H}$=11.5 Hz, C*H*HPh), 4.67 (d, 1H, CH*H*Ph), 4.40 (dd, 1H, $J_{4,5}$=5.8 Hz, H-4), 4.30 (m, 1H, H-5), 4.20 (dd, 1H, $J_{5,6a}$=1.5 Hz, $J_{6a,6b}$=13.4 Hz, H-6a), 4.13 (dd, 1H, $J_{5,6b}$=3.0 Hz, H-6b), 3.92 (d, 1H, $J_{3,4}$=7.3 Hz, H-3), 1.52, 1.38 ($2CH_3$).

4.4. Methyl (3-*O*-benzyl-2-deoxy-4,5-*O*-isopropylidene-β-D-*arabino*-hex-2-ulopyranosyl)onate azide (7)

To a solution of **5** (100 mg, 0.3 mmol) and 2-methylbut-2-ene (0.32 mL, 3 mmol) in 2-methylpropan-2-ol (2 mL) at 0 °C, another solution of $NaClO_2$ (81 mg, 0.9 mmol) and $NaH_2PO_4.2H_2O$ (140 mg, 0.9 mmol) in H_2O (1 mL) was added. The mixture was stirred at room temperature for 2 h, evaporated to half, extracted with Et_2O (3×8 mL), washed with HCl (2%, 20 mL) and then with brine, dried ($MgSO_4$), and evaporated to dryness. The residue was dissolved in Et_2O:MeOH (5 mL) and stirred at 0 °C with a solution of CH_2N_2 in Et_2O (5 mL) for 20 min, then evaporated and purified by column chromatography (Et_2O/petroleum ether 2:1). Yield: 0.089 g, 82% (amorphous solid). $[\alpha]_D^{24}$ −106 (*c* 2.0). IR: ν_{max}. 2988, 2953, 2126(N_3), 1755, 1381, 1244, 1121 and 1074 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 7.33–7.27 (m, 5H, Ar), 4.84 (d, 1H, $^{2}J_{H,H}$=11.8 Hz, C*H*HPh), 4.69 (d, 1H, CH*H*Ph), 4.37 (dd, 1H, H-4), 4.30 (ddd, 1H, $J_{4,5}$=6.0 Hz, $J_{5,6a}$=2.5 Hz, $J_{5,6b}$=1.8 Hz, H-5), 4.16 (m, 2H, H-6a, H-6b), 4.01 (d, 1H, $J_{3,4}$=6.8 Hz, H-3), 3.75 (s, 3H, OCH_3), 1.52, 1.37 (each s, each 3H, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): δ 166.7 (C-1), 137.3–127.7 (Ar), 109.4 (CCH_3), 91.1 (C-2), 76.7 (C-3), 75.8 (C-4), 73.5 (CH_2Ph), 72.6 (C-5), 63.0 (C-6), 53.2 (OCH_3), 27.5, 25.8 ($2CH_3$). HRFABMS *m/z* calcd for $C_{17}H_{21}O_6N_3Na$ ([M+Na]$^+$): 386.1, found 386.1331. Anal. Calcd for $C_{17}H_{21}O_6N_3$: C, 56.19; H, 5.83; N, 11.56. Found: C, 56.29; H, 5.88; N, 11.65.

4.5. General procedure for the oxidation of 4 and 14 with RuO_4. Preparation of compounds 8 and 16

To a stirred solution of **4** (for **8**) or **14** (for **16**) (335 mg, 1.0 mmol), CH_3CN (5.4 mL), CCl_4 (5.4 mL), H_2O (8 mL) and $NaIO_4$ (1.12 g, 5.2 mmol) $RuCl_3$. H_2O (0.12 g, 0.52 mmol) was added. The mixture was stirred vigorously for 15 min at room temperature, diluted with buffer AcOH/AcO^- (1 M; pH=4), filtered over Celite, extracted with CH_2Cl_2 (20 mL), dried ($MgSO_4$), and evaporated to dryness. The residue was dissolved in Et_2O:MeOH 1:1 (15 mL) and stirred at 0 °C with a solution of CH_2N_2 in Et_2O for 20 min, evaporated, and purified by column chromatography (Et_2O/petroleum ether 1:6).

4.5.1. Methyl (3-*O*-benzoyl-2-deoxy-4,5-*O*-isopropylidene-β-D-*arabino*-hex-2-ulopyranosyl)onate azide (8). Yield: 0.170 g, 45% (syrup). $[\alpha]_D^{25}$ −95 (*c* 0.9). IR: ν_{max} 2988, 2948, 2128(N_3), 1755, 1732, 1385, 1223, 1076 and 1101 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.06–7.42 (m, 5H, Ar), 5.69 (d, 1H, $J_{3,4}$=7.3 Hz, H-3), 4.44 (dd, 1H, $J_{4,5}$=5.6 Hz, H-4), 4.35 (m, 2H, H-5, H-6a), 4.24 (dd, 1H, $J_{5,6b}$=2.8 Hz, $J_{6a,6b}$=13.5 Hz, H-6b), 3.79 (s, 3H, OCH_3), 1.61, 1.39 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 165.8, 164.9 (C-1, C=O), 133.5–127.8 (Ar), 110.2 (*C*CH_3), 90.3 (C-2), 73.5 (C-4), 72.7 (C-5), 70.8 (C-3), 62.9 (C-6), 53.6 (OCH_3), 27.3, 26.0 ($2CH_3$). HRCIMS *m/z* calcd for $C_{17}H_{20}O_7N_3$ ($[M+H]^+$): 378.1301, found: 378.1304.

4.5.2. Methyl (6-*O*-benzoyl-2-deoxy-3,4-*O*-isopropylidene-β-D-*ribo*-hex-2-ulofuranosyl)onate azide (16). Yield: 0.170 g, 45% (syrup). $[\alpha]_D^{25}$ −104 (*c* 0.85). IR: ν_{max} 2990, 2116(N_3), 1763, 1724, 1453, 1375, 1273, 1107 and 1070 cm^{-1}. ^{1}H NMR: (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.09–7.43 (m, 5H, Ar), 4.89 (dd, 1H, $J_{4,5}$=1.5 Hz, H-4), 4.82 (dt, 1H, H-5), 4.70 (d, 1H, $J_{3,4}$=5.8 Hz, H-3), 4.55 (dd, 1H, $J_{5,6a}$=6.0 Hz, $J_{6a,6b}$=11.8 Hz, H-6a), 4.48 (dd, 1H, $J_{5,6b}$=6.1 Hz, H-6b), 3.89 (s, 3H, OCH_3), 1.48, 1.32 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 166.0, 165.4 (C-1, C=O), 133.2–128.1 (Ar), 114.3 (*C*CH_3), 100.5 (C-2), 86.9 (C-3), 85.7 (C-5), 81.9 (C-4), 63.9 (C-6), 53.1 (OCH_3), 26.0, 25.1 ($2CH_3$). HRFABMS *m/z* calcd for $C_{17}H_{19}O_7N_3Na$ ($[M+Na]^+$): 400.1121, found: 400.1124. Anal. Calcd for $C_{17}H_{19}O_7N_3$: C, 54.11; H, 5.08; N, 11.14. Found: C, 54.32; H, 5.09; N, 11.14.

4.6. General procedure for the reduction of azides 7, 8 and 16. Preparation of amines 9, 10 and 17

A solution of the corresponding azide **7** (for **9**), **8** (for **10**) or **16** (for **17**) (*x* mg, 0.3 mmol) in MeOH (10 mL) was stirred at room temperature in the presence of Pd-C 10% (20 mg) and hydrogen (balloon pressure) for 1 h. The mixture was filtered over Celite, evaporated, and purified by column chromatography.

4.6.1. Methyl (3-*O*-benzyl-2-deoxy-4,5-*O*-isopropylidene-α,β-D-*arabino*-hex-2-ulopyranosyl)onate amine (9). *x*=0.109 g. Relationship of diastereoisomers in C-2 ratio (α:β) 1:9. Column chromatography: Et_2O/petroleum ether 1:6. Yield: 0.10 g, 99% (syrup). IR: ν_{max}. 3395, 3335, 2984, 1743, 1433, 1381, 1249, 1167 and 1068 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm *J* Hz): δ 7.33–7.27 (m, 5H, Ar), 4.85 (d, 1H, $^2J_{H,H}$=11.7 Hz, C*H*HPh), 4.65 (d, 1H, CH*H*Ph), 4.39 (dd, 1H, $J_{5,6a}$=2.9 Hz, $J_{6a,6b}$=13.1 Hz, H-6a), 4.30 (t, 1H, H-4), 4.23 (dd, 1H, $J_{4,5}$=6.4 Hz, H-5), 3.98 (d, 1H, $J_{3,4}$=7.1 Hz, H-3), 3.97 (d, 1H, H-6b), 3.70 (s, 3H, OCH_3), 2.17 (bs, 2H, NH_2), 1.54, 1.38 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 171.4 (C-1), 137.8–127.7 (Ar), 108.9 (*C*CH_3), 86.1 (C-2), 77.2 (C-3), 77.0 (C-4), 73.4 (C-5), 72.9 (CH_2Ph), 59.8 (C-6), 52.8 (OCH_3), 27.9, 26.2 ($2CH_3$). HRFABMS *m/z* calcd for $C_{17}H_{23}O_6NNa$ ($[M+Na]^+$): 360.1423, found: 360.1423.

4.6.2. Methyl (3-*O*-benzoyl-2-deoxy-4,5-*O*-isopropylidene-α,β-D-*arabino*-hex-2-ulopyranosyl)onate amine (10). *x*=0.113 g. Diastereoisomers in C-2 ratio 5:2 (configuration not determinated). Column chromatography: Et_2O/petroleum ether 2:3. Yield: 0.074 g, 70% (syrup). HRCIMS: *m/z* calcd for ($[M+H]^+$): 352.1396, found: 352.1399. IR: $\nu_{max.}$ 3412, 3309, 2986, 1743, 1734, 1437, 1249, 1119 and 1099 cm^{-1}.

NMR data for the major anomer. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.03–7.41 (m, 5H, Ar), 5.66 (d, 1H, $J_{3,4}$=7.7 Hz, H-3), 4.42 (dd, 1H, $J_{5,6a}$=2.9 Hz, H-6a), 4.39 (dd, 1H, $J_{4,5}$=5.5 Hz, H-4), 4.30 (dd, 1H, H-5), 4.13 (d, 1H, $J_{6a,6b}$=13.2 Hz, H-6b), 3.74 (s, 3H, OCH_3), 2.11 (bs, 2H, NH_2), 1.65, 1.37 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (170.9 (C-1), 164.7 (COPh), 133.3–128.3 (Ar), 109.6 (*C*CH_3), 85.4 (C-2), 74.3 (C-4), 73.3 (C-5), 72.2 (C-3), 59.9 (C-6), 53.26 (OCH_3), 27.6, 26.2 ($2CH_3$).

NMR data for the minor anomer. ^{1}H NMR (500 MHz, $CDCl_3$, (ppm, *J* Hz): (8.03–7.40 (m, 5H, Ar), 5.37 (d, 1H, $J_{3,4}$=7.1 Hz, H-3), 4.84 (t, 1H, $J_{4,5}$=6.1 Hz, H-4), 4.33 (dd, 1H, H-5), 4.20 (dd, 1H, $J_{5,6a}$=2.0 Hz, $J_{6a,6b}$=13.7 Hz, H-6a), 3.88 (dd, 1H, $J_{5,6b}$=3.1 Hz, H-6b), 3.78 (s, 3H, OCH_3), 2.38 Method, 2H, NH_2), 1.62, 1.57 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (167.6 (C-1), 165.2 (COPh), 133.3–128.3 (Ar), 109.3 (*C*CH_3), 87.6 (C-2), 74.7 (C-4), 73.5 (C-3), 72.8 (C-5), 63.1 (C-6), 52.4 (OCH_3), 27.7, 26.0 ($2CH_3$).

4.6.3. Methyl (6-*O*-benzoyl-2-deoxy-3,4-*O*-isopropylidene-α,β-D-*ribo*-hex-2-ulofuranosyl)onate amine (17). *x*=0.113 g. Diastereoisomers in C-2 ratio (α:β) 6:1. Column chromatography: Et_2O/petroleum ether 1:2. Yield: 0.10 g, 95% (syrup). IR: ν_{max} 3422, 3343, 2988, 1734, 1720, 1655, 1383, 1273 and 1097 cm^{-1}. HRCIMS *m/z* calcd for $C_{17}H_{22}O_7N_1$($[M+H]^+$): 352.1396, found: 352.1398. Anal. Calcd for $C_{17}H_{21}O_7N$: C, 58.11; H, 6.02; N, 3.99, found C, 57.94; H, 6.06; N, 3.82.

NMR data for the α anomer. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.05–7.46 (m, 5H, Ar), 5.02 (d, 1H, $J_{3,4}$= 6.1 Hz, H-3), 4.85 (dd, 1H, $J_{4,5}$=3.4 Hz, H-4), 4.45 (td, 1H, $J_{5,6a}$=$J_{5,6b}$=5.7 Hz, H-5), 4.34 (m, 2H, H-6a, H-6b), 3.73 (s, 3H, OCH_3), 2.56 (bs, 2H, NH_2), 1.59, 1.38 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 169.9 (C-1), 166.1 (COPh), 133.1–128.3 (Ar), 113.8 (*C*CH_3), 93.6 (C-2), 82.4 (C-4), 81.8 (C-5), 81.7 (C-3), 64.2 (C-6), 52.7 (OCH_3), 26.8, 25.2 ($2CH_3$).

NMR data for the β anomer. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.05–7.42 (m, 5H, Ar), 4.89 (dd, 1H, $J_{4,5}$= 1.9 Hz, H-4), 4.71 (td, 1H, $J_{5,6a}=J_{5,6b}=6.4$ Hz, H-5), 4.61 (d, 1H, $J_{3,4}=6.1$ Hz, H-3), 4.56 (ddd, 2H, $J_{6a,6b}=11.4$ Hz, H-6a, H-6b), 3.83 (s, 3H, OCH_3), 1.48, 1.32 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 170.9 (C-1), 166.1 (COPh), 133.0–128.0 (Ar), 113.9 (CCH_3), 96.2 (C-2), 88.4 (C-3), 84.7 (C-5), 82.7 (C-4), 65.3 (C-6), 52.6 (OCH_3), 26.2, 25.1 ($2CH_3$).

4.7. General procedure for the preparation of the isothiocyanatoulosonates 11, 18α, and 18β

To a mixture of a solution of the glycosylaminoester **10** (for **11**) or **17** (for **18α** and **18β**) (150 mg, 0.43 mmol) in CH_2Cl_2 (3 mL), and $CaCO_3$ (300 mg, 3.0 mmol) in H_2O (0.75 mL), was added $CSCl_2$ (120 μl, 1.5 mmol). The mixture was stirred vigorously at room temperature for 3 days, diluted with CH_2Cl_2 (30 mL), washed with water and then brine, dried ($MgSO_4$), and evaporated to dryness. The residue was purified by column chromatography.

4.7.1. Methyl (2-deoxy-3-*O*-benzoyl-4,5-*O*-isopropylidene-α-D-*arabino*-hex-2-ulopyranosyl)onate isothiocyanate (11). The residue was a 16:1 mixture of anomers. Column chromatography: Et_2O/petroleum ether 1:6.Yield: 0.135 g, 80% (syrup). $[\alpha]_D^{26}$ +79 (*c* 1.0). IR: $\nu_{max.}$ 2986, 2002 (NCS), 1740, 1736, 1314, 1261, 1103 and 1070 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 7.98–7.43 (m, 5H, Ar), 5.70 (d, 1H, $J_{3,4}=4.4$ Hz, H-3), 4.50 (dd, 1H, $J_{4,5}=6.1$ Hz, H-4), 4.43 (dd, 1H, H-5), 4.15 (d, 1H, $J_{5,6a}$= 5.4 Hz, H-6a), 4.04 (dd, 1H, $J_{6a,6b}=12.6$ Hz, $J_{5,6b}=6.9$ Hz, H-6b), 377 (s, 3H, OCH_3), 1.61, 1.37 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (165.0 (C-1), 164 (C=O), 145.1 (NCS), 133.8–127.6 (Ar), 110.7 (CCH_3), 87.7 (C-2), 72.9 (C-4), 71.3 (C-3), 69.3 (C-5), 63.6 (C-6), 53.6 (OCH_3), 27.3, 25.6 ($2CH_3$). HRFABM *m/z* calcd for ($[M+Na]^+$): 416.0780, found: 416.0772. Anal. Calcd for $C_{18}H_{19}O_7NS$: C, 54.95; H, 4.87; N, 3.56. Found: C, 54.91; H, 4.89; N, 3.59.

4.7.2. Methyl (2-deoxy-6-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-*ribo*-hex-2-ulofuranosyl)onate isothiocyanate (18α). Column chromatography: Et_2O/petroleum ether 1:9. Yield: 0.110 g, 65% (syrup). $[\alpha]_D^{28}$ −62 (*c* 0.86). IR: ν_{max}. 2986, 2018 (NCS), 1757, 1724, 1601, 1271 and 1099 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.05–7.45 (m, 5H, Ar), 5.07 (d, 1H, $J_{3,4}=6.8$ Hz, H-3), 4.84 (dd, 1H, $J_{4,5}=3.1$ Hz, H-4), 4.68 (dd, 1H, H-5), 4.58 (dd, 1H, $J_{5,6a}=3.8$ Hz, $J_{6a,6b}=12.2$ Hz, H-6a), 4.49 (dd, 1H, $J_{5,6b}=4.2$ Hz, H-6b), 3.80 (s, 3H, OCH_3), 1.71, 1.40 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 166.0 (C-1), 165.9 (C=O), 144.9 (NCS), 133.5–128.1 (Ar), 117.3 (CCH_3), 95.1 (C-2), 84.4 (C-3), 82.6 (C-5), 80.9 (C-4), 63.5 (C-6), 53.8 (OCH_3), 26.1, 25.3 ($2CH_3$). HRCIMS *m/z* calcd for $C_{18}H_{20}O_7NS$ ($[M+H]^+$): 394.0961, found: 394.0959. Anal. Calcd for $C_{18}H_{19}O_7NS$: C, 54.95; H, 4.87; N, 3.56. Found: C, 55.10; H, 4.76; N, 3.60.

4.7.3. Methyl (2-deoxy-6-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-*ribo*-hex-2-ulofuranosyl)onate isothiocyanate (18β). Column chromatography: Et_2O/Hex 1:9. Yield: 0.034 g, 20%. $[\alpha]_D^{25}$ −115 (*c* 0.5). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.09–7.45 (m, 5H, Ar), 4.98 (d, 1H, $J_{3,4}=5.8$ Hz, H-3), 4.94 (dd, 1H, $J_{4,5}=1.3$ Hz, H-4), 4.81 (td, 1H, H-5), 4.55 (dd, 1H, $J_{5,6a}=6.1$ Hz, H-6a), 4.50 (dd, 1H, $J_{5,6b}=5.6$ Hz, $J_{6a,6b}=12.0$ Hz, H-6b), 3.92 (s, 3H, OCH_3), 1.47, 1.33 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 165.9 (C=O), 164.9 (C-1), 145.1 (NCS), 133.2–128.4 (Ar), 114.6 (CCH_3), 97.7 (C-2), 88.8 (C-3), 85.8 (C-5), 81.8 (C-4), 63.5 (C-6), 53.4 (OCH_3), 25.8, 25.0 ($2CH_3$). HRCIMS *m/z* calcd for $C_{18}H_{20}O_7NS$ ($[M+H]^+$): 394.0961, found: 394.0971.

4.8. General procedures for the reactions of the glycosylaminoesters 9, 10, 17, and 19 (α+β) with alkyl or aryl isothiocyanates (Route A). Preparation of the hydantocidin-related spironucleosides 20α, 20β, 21, 22α, 22β, 23, 25, 26, 31, and 32[†]

Method I (used for the preparation of compounds **20α** and **20β**). A solution of **9** (100 mg, 0.3 mmol) in DMF was stirred with phenylisothiocyanate (53 μL, 0.45 mmol) at 85 °C for 23 h. The solvent was evaporated and the residue was purified by column chromathography.

Method II (used for the preparation of compounds **21**, **22α**, **22β**, **23**, **25**, **26**, **31**, and **32**). A solution of the aminoester **10** (for **21**, **22α**, **22β** and **23**), **17** (for **25** and **26**), or **19**(α+β) (for **31** and **32**) (0.3 mmol) in THF (2 mL) was stirred at 40 °C with phenylisothiocyanate (for **21**), 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylisothiocyanate (for **22α**, **22β**, **25**, and **31**) or 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosylisothiocyanate (for **23**, **26**, and **32**) (0.33 mmol). After *t* days, the solvent was evaporated and the residue was purified by column chromatography.

4.8.1. (5*R*,8*R*,9*R*,10*S*)-10-Benzyloxy-8,9-dimethylmethylenedioxy-4-oxo-3-phenyl-2-thioxo-6-oxa-1,3-diazaspiro-[4.5]decane (20α). *Method I*. Column chromatography: Et_2O/petroleum ether 1:4. Yield: 0.086 g, 65% (amorphous solid). $[\alpha]_D^{22}$ −84 (*c* 0.5). IR: ν_{max} 2986, 2916, 1765, 1726, 1402, 1159 and 1030 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, α ppm, *J* Hz): (7.47–7.22 (m, 10H, Ar), 7.06 (bs, 1H, NH), 4.91 (d, 1H, $^2J_{H,H}=11.8$ Hz, C*H*HPh), 4.73 (d, 1H, CH*H*Ph), 4.72 (t, 1H, H-9), 4.59 (dd, 1H, $J_{7a,8}=3.2$ Hz, $J_{7a,7b}=13.5$ Hz, H-7a), 4.39 (ddd, 1H, $J_{8,9}=5.6$ Hz, H-8), 4.16 (dd, 1H, $J_{7b,8}=2.2$ Hz, H-7b), 3.70 (d, 1H, $J_{9,10}$= 7.1 Hz, H-10), 1.54, 1.41 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (183.6 (C-2), 169.4 (C-4), 136.9–128.2 (Ar), 109.7 (CCH_3), 86.6 (C-5), 77.7 (C-10), 76.8 (C-9), 73.3 (CH_2Ph), 72.9 (C-8), 63.0 (C-7), 27.9, 25.9 ($2CH_3$). HRFABMS *m/z* calcd for $C_{23}H_{24}O_5N_2SNa$ ($[M+Na]^+$): 463.1304, found: 463.1293.

4.8.2. (5*S*,8*R*,9*R*,10*S*)-10-Benzyloxy-8,9-dimethylmethylenedioxy-4-oxo-3-phenyl-2-thioxo-6-oxa-1,3-diazaspiro-[4.5]decane (20β). *Method I*. Column chromatography: Et_2O/petroleum ether 1:4. Yield: 0.041 g, 31% (amorphous

[†] For nomenclature of the spironucleosides we have followed the IUPAC rules for spiro compounds (see rule B-10.1 in IUPAC Nomenclature of organic Chemistry, Edition of 1979, Pergamon Press). Alternatively, the second part of the rule 2-Carb-35.3 of Nomenclature of Carbohydrates, recomendations 1996 (*Carbohydr. Res. 1997*, **297**,1) would be used.

solid). $[\alpha]_D^{26}$ −110 (*c* 1.1). IR: $\nu_{max.}$ 2986, 1768, 1591, 1406, 1107 and 1022 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 9.09 (bs, 1H, NH), 7.47–7.15 (m, 10H, Ar), 4.93 (d, 1H, C*H*HPh), 4.60 (d, 1H, $^2J_{H,H}$=10.0 Hz, CH*H*Ph), 4.43 (dd, 1H, $J_{9,10}$=7.9 Hz, $J_{8,9}$=5.5 Hz, H-9), 4.30 (dd, 1H, $J_{7a,8}$=1.6 Hz, H-7a), 4.28 (m, 1H, H-8), 4.13 (dd, 1H, $J_{7a,7b}$=10.9 Hz, $J_{7b,8}$=3.2 Hz, H-7b), 4.10 (d, 1H, $J_{9,10}$=7.9 Hz, H-10), 1.54, 1.38 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (184.9 (C-2), 169.5 (C-4), 137.1–127.6 (Ar), 109.9 (CCH_3), 87.1 (C-5), 77.0 (C-10), 76.0 (C-9), 73.5 (CH_2Ph), 72.5 (C-8), 63.2 (C-7), 27.8, 25.9 ($2CH_3$). HRFABMS *m/z* calcd for $C_{23}H_{24}O_5N_2SNa$ ([M+Na]$^+$): 463.1304, found 463.1292.

4.8.3. (5*R*,8*R*,9*R*,10*S*)-10-Benzoyloxy-8,9-dimethylmethylenedioxy-4-oxo-3-phenyl-2-thioxo-6-oxa-1,3-diazaspiro[4.5]decane (21). *Method II*. *t*=3 days. Column chromatography: Et_2O/Hex 1:5. Yield: 0.095 g, 70% (amorphous solid). $[\alpha]_D^{20}$ −77 (*c* 1.1). IR: $\nu_{max.}$ 3291, 2986, 1755, 1732, 1593, 1491, 1252 and 1103 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.04–7.18 (m, 11H, Ar, NH), 5.67 (d, 1H, $J_{9,10}$=7.4 Hz, H-10), 4.88 (dd, 1H, $J_{8,9}$=5.9 Hz, H-9), 4.65 (dd, 1H, $J_{7a,8}$=2.9 Hz, H-7a), 4.50 (m, 1H, H-8), 4.34 (d, 1H, $J_{7a,7b}$=13.6 Hz, H-7b), 1.67, 142 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, CDCl3, δ ppm): δ 182.8 (C-2), 168.7 (C-4), 165.5 (C=O), 133.8–128.1 (Ar), 110.3 (CCH_3), 85.6 (C-5), 73.7 (C-9), 72.9 (C-8), 71.2 (C-10), 63.4 (C-7), 27.6, 25.9 ($2CH_3$). HRCIMS *m/z* calcd for $C_{23}H_{22}O_6N_2S$ ([M+H]$^+$): 455.1277, found: 455.1264.

4.8.4. (5*R*,8*R*,9*R*,10*S*)-10-Benzoyloxy-8,9-dimethylmethylenedioxy-4-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thioxo-6-oxa-1,3-diazaspiro[4.5]decane (22α). *Method II*. *t*=4 days. Column chromatography: Et_2O/petroleum ether 1:1. Yield: 0.161 g, 76% (amorphous solid). $[\alpha]_D^{24}$ −46 (*c* 0.9). IR: ν_{max} 2986, 2942, 1957, 1953, 1499, 1375, 1223 and 1099 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 7.97–7.37 (m, 5H, Ar), 7.65 (bs, 1H, NH), 5.97 (t, 1H, $J_{2',3'}$=9.4 Hz, H-2′), 5.77 (d, 1H, $J_{1',2'}$=9.6 Hz, H-1′), 5.52 (d, 1H, $J_{9,10}$=7.8 Hz, H-10), 5.33 (t, 1H, $J_{3',4'}$=9.3 Hz, H-3′), 5.24 (t, 1H, $J_{4',5'}$=9.6 Hz, H-4′), 4.88 (dd, 1H, $J_{8,9}$=5.5 Hz, H-9), 4.56 (dd, 1H, $J_{7a,8}$=2.9 Hz, H-7a), 4.42 (m, 1H, H-8), 4.31 (d, 1H, $J_{7a,7b}$=13.7 Hz, H-7b), 4.20 (m, 2H, H-6′a, H-6′b), 3.76 (dt, 1H, $J_{5',6'a}$=$J_{5',6'b}$=3.3 Hz, H-5′), 2.04, 2.03, 2.02, 1.97, 1.61, 1.38 (each s, each 3H, $6CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 182.1 (C-2), 170.5, 169.9, 169.4, 169.3, 165.6 (5C=O), 167.1 (C-4), 133.7–128.4 (Ar), 110.1 (*C*CH_3), 84.4 (C-5), 81.0 (C-1′), 74.4 (C-5′), 74.1 (C-9), 73.2 (C8, C3′), 71.1 (C-10), 68.0 (C-4′), 67.1 (C-2′), 63.0 (C-7), 61.7 (C-6′), 27.8, 26.0, 20.5, 20.4, 20.3 ($6CH_3$). HRCIMS *m/z* calcd for $C_{31}H_{37}O_{15}N_2S$ ([M+H]$^+$): 709.1915, found: 709.1916. Anal. Calcd for $C_{31}H_{36}O_{15}N_2S$: C, 52.54; H, 5.12; N, 3.95. Found: C, 52.62; H, 5.23; N, 4.00.

4.8.5. (5*S*,8*R*,9*R*,10*S*)-10-Benzoyloxy-8,9-dimethylmethylenedioxy-4-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thioxo-6-oxa-1,3-diazaspiro[4.5]decane (22β). *Method II*. *t*=4 days. Column chromatography: Et_2O/petroleum ether 1:1. Yield: 0.019 g, 9% (amorphous solid). $[\alpha]_D^{22}$ −83 (*c* 0.6). IR: ν_{max} 2986, 2942, 1957, 1953, 1499, 1375, 1223 and 1099 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.24 (bs, 1H, NH), 8.05–7.40 (m, 5H, Ar), 5.94 (t, 1H, H-2′), 5.80 (d, 1H, $J_{2',3'}$=9.3 Hz, H-1′), 5.79 (d, 1H, $J_{9,10}$=6.9 Hz, H-10), 5.23 (t, 1H, $J_{2',3'}$=9.3 Hz, H-3′), 5.16 (t, 1H, $J_{3',4'}$=9.8 Hz, H-4′), 4.39 (m, 2H, H-8, H-9), 4.33 (dd, 1H, $J_{7a,8}$=2.1 Hz, $J_{7a,7b}$=13.8 Hz, H-7a), 4.21 (d, 1H, $J_{6'a,6'b}$=12.3 Hz, H-6′a), 4.16 (dd, 1H, $J_{5',6'b}$=3.0 Hz, H-6′b), 4.07 (dd, 1H, $J_{7b,8}$=3.2 Hz, H-7b), 3.77 (m, 1H, H-5′), 2.08, 2.01, 1.95, 1.67, 1.38 and 1.27 (each s, each 3H, $6CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 183.5 (C-2), 170.8, 170.1, 169.2, 168.9, 166.7, 164.0 (6C=O), 133.4–128.4 (Ar), 111.1 (CCH_3), 84.5 (C-5), 81.2 (C-1′), 74.4*, 74.2* (C-9, C5′), 73.4 (C-3′), 71.9 (C-8), 68.4 (C-10), 67.7 (C-4′), 67.4 (C-2′), 62.9 (C-7), 61.5 (C-6′), 27.2, 25.9, 20.7, 20.5 (2C), 19.2 ($6CH_3$). HRCIMS *m/z* calcd for $C_{31}H_{37}O_{15}N_2S$ ([M+H]$^+$): 709.1915, found: 709.1910.

4.8.6. (5*R*,8*R*,9*R*,10*S*)-10-Benzoyloxy-8,9-dimethylmethylenedioxy-4-oxo-2-thioxo-3-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-oxa-1,3-diazaspiro[4.5]decane (23). *Method II*. *t*=5 days. Column chromatography: Et_2O/petroleum ether 1:3. Yield: 0.20 g, 81% (amorphous solid). $[\alpha]_D^{27}$ −31 (*c* 0.9). IR: ν_{max} 2991, 1730, 1599, 1489, 1379, 1265, 1105 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.13–7.26 (m, 21H, Ar, NH), 6.41 (d, 1H, $J_{1',2'}$=2.4 Hz, H-1′), 6.26 (dd, 1H, $J_{2',3'}$=6.3 Hz, H-2′), 6.22 (t, 1H, $J_{3',4'}$=6.6 Hz, H-3′), 5.52 (d, 1H, $J_{9,10}$=7.8 Hz, H-10), 4.88 (dd, 1H, $J_{4',5'a}$=3.0 Hz, $J_{5'a,5'b}$=11.8 Hz, H-5′a), 4.64 (dd, 1H, H-4′), 4.63 (dd, 1H, $J_{7b,8}$=2.7 Hz, H-7b), 4.61 (dd, 1H, $J_{4',5'b}$=3.8 Hz, H-5′b), 4.60 (dd, 1H, $J_{8,9}$=5.8 Hz, H-9), 4.38 (m, 1H, H-8), 4.31 (d, 1H, $J_{7a,7b}$=13.6 Hz, H-7a), 1.62, 1.40 (each s, each 3H, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): δ 181.2 (C-2), 168.2, 166.1, 165.6, 165.1, 165.0 (5C=O), 133.6–128.0 (Ar), 110.1 (*C*CH_3), 86.2 (C-1′), 84.8 (C-5), 78.9 (C-4′), 73.7 (C-9), 72.9 (C-8), 72.5 (C-2′), 71.2 (C-10), 70.3 (C-3′), 63.2 (C-7), 62.6 (C-5′), 27.6, 25.9 ($2CH_3$). Anal. Calcd for $C_{43}H_{38}N_2O_{13}S$: C, 62.77; H, 4.65; N, 3.40. Found: C, 62.74; H, 4.82; N, 3.21.

4.8.7. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-9-oxo-8-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (25). *Method II*. *t*=5 days. Column chromatography: Et_2O/petroleum ether 2:3. Yield: 0.168 g, 79% (amorphous solid). $[\alpha]_D^{25}$ −36 (*c* 1.2). IR: ν_{max} 2988, 2936, 1755, 1491, 1273, 1215 and 1097 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.09–7.42 (m, 5H, Ar), 7,38 (bs, 1H, NH), 5.92 (t, 1H, $J_{2',3'}$=9.5 Hz, H-2′), 5.82 (d, 1H, $J_{1',2'}$=9.5 Hz, H-1′), 5.30 (t, 1H, H-3′), 5.19 (t, 1H, $J_{3',4'}$=9.8 Hz, H-4′), 4.94 (dd, 1H, $J_{2,3}$=1.6 Hz, H-3), 4.88 (d, 1H, $J_{3,4}$=6.0 Hz, H-4), 4.56 (m, 2H, H-2, C*H*HOBz), 4.48 (dd, 1H, $^2J_{H,H}$=13.3 Hz, $J_{2,H}$=8.6 Hz, CH*H*OBz), 4.19 (m, 2H, H-6′a, H-6′b), 3.83 (ddd, 1H, $J_{5',6'a}$=2.8 Hz, $J_{5',6'b}$=4.4 Hz, H-5′), 2.09, 2.04, 2.01, 1.90, 1.60, 1.40 (each s, each 3H, $6CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): δ 181.6 (C-7), 170.5, 170.0, 169.2, 169.1, 168.7, 165.9 (6C=O), 133.1–128.3 (Ar), 114.5 (*C*CH_3), 91.5 (C-5), 82.8 (C-2), 82.6 (C-3), 80.9 (C-1′), 80.2 (C-4), 74.6 (C-5′), 73.2 (C-3′), 67.7 (C-4′), 66.9 (C-2′), 64.1 (CH_2OBz), 61.5 (C-6′), 26.5, 24.7, 20.6, 20.4 (for 2C), 20.1

($6CH_3$). Anal. Calcd for $C_{31}H_{36}O_{15}N_2S$ C, 52.54; H, 5.12; N, 3.95. Found: C, 52.38; H, 5.44; N, 3.99.

4.8.8. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-9-oxo-7-thioxo-8-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-1-oxa-6,8-diazaspiro[4.4]nonane (26). *Method II*. $t=5$ days. Column chromatography: Et_2O/petroleum ether 1:3. Yield: 0.205 g, 83% (amorphous solid). $[\alpha]_D^{27}$ −47 (*c* 1.0). IR: ν_{max} 2996, 1773, 1724, 1601, 1269 and 1099 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, *(* ppm, *J* Hz): 8.13–7.34 (m, 21H, Ar, NH), 6.48 (d, 1H, $J_{1',2'}=3.0$ Hz, H-1′), 6.28 (dd, 1H, $J_{2',3'}=6.2$ Hz, H-2′), 6.20 (t, 1H, $J_{3',4'}=6.5$ Hz, H-3′), 4.89 (dd, 1H, $J_{4',5'a}=3.6$ Hz, $J_{5'a,5'b}=12.2$ Hz, H-5′a), 4.75 (dd, 1H, $J_{2,3}=2.4$ Hz, H-3), 4.65 (ddd, 1H, $J_{4',5'b}=4.7$ Hz, H-4′), 4.63 (d, 1H, $J_{3,4}=6.0$ Hz, H-4), 4.57 (td, 1H, $J_{2,CH2}=6.0$ Hz, H-2), 4.53 (dd, 1H, H-5′b), 4.53 (m, 2H, CH_2OBz), 1.58, 1.33 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (181.2 (C-7), 169.9 (C-9), 166.1, 166.0, 165.0 (4C=O), 133.5–128.3 (Ar), 114.6 (CCH_3), 92.1 (C-5), 86.4 (C-1′), 83.1 (C-2), 82.2 (C-3), 80.6 (C-4), 79.6 (C-4′), 72.6 (C-2′), 70.6 (C-3′), 64.1 (CH_2OBz), 62.9 (C-5′), 26.6, 24.8 ($2CH_3$). HRCIMS *m/z* calcd for $C_{43}H_{39}O_{13}N_2S$ ($[M+H]^+$): 823.217, found: 823.2173. Anal. Calcd for $C_{43}H_{38}O_{13}N_2S$: C, 62.77; H, 4.65; N, 3.40. Found: C, 62.52; H, 4.64; N, 3.94.

4.8.9. (2*R*,3*S*,4*S*,5*S*,4″*R*)-2-(2″,2″-Dimethyl-1″,3″-dioxolan-4″-yl)-3,4-dimethylmethylenedioxy-9-oxo-8-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-7-thioxo-1-oxa-6,8-dizaspiro[4.4]nonane (31). *Method II*. $t=5$ days. Column chromatography: Et_2O/petroleum ether 1:6 $[\alpha]_D^{25}$ +31 (*c* 1.0). Yield: 0.190 g, 94% (amorphous solid). IR: $\nu_{max.}$ 2985, 2942,1757, 1753, 1491, 1377,1227, 1223, 1098 and 1068 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, *(* ppm, *J* Hz): 7.34 (bs, 1H, NH), 5.82 (d, 1H, $J_{1',2'}=9.2$ Hz, H-1′), 5.71 (t, 1H, $J_{2',3'}=9.2$ Hz, H-2′), 5.34 (t, 1H, $J_{3',4'}=9.4$ Hz, H-3′), 5.16 (t, 1H, $J_{4',5'}=9.8$ Hz, H-4′), 4.99 (m, 1H, H-3), 4.84 (d, 1H, $J_{3,4}=5.9$ Hz, H-4), 4.33 (m, 2H, H-2, H-4″), 4.22 (m, 2H, H-6′a, H-6′b), 4.05 (m, 2H, H-5″a, H-5″b), 3.82 (dt, 1H, $J_{5',6'a}=J_{5',6'b}=3.6$ Hz, H-5′), 2.10, 2.04, 2.02, 1.97, 1.54, 1.44, 1.39, 1.36 (each s, each 3H, $8CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$, (ppm): (181.6 (C-7),170.5, 170.1, 169.8, 169.5, 169.3 (5C=O), 113.9, 109.5 ($2CCH_3$), 89.7 (C-5), 81.2 (C-1′), 80.0 (C-3+C-4), 79.0 (C-2), 74.6 (C-5′), 72.7*, 72.6* (C-3′, C-4″), 68.1 (C-2′), 67.8 (C-4′), 66.6 (C-5″), 61.6 (C-6′), 26.8, 25.8, 25.0, 24.3, 20.6, 20.5, 20.4 ($8CH_3$). Anal. Calcd for $C_{28}H_{38}O_{15}N_2S_1$: C, 49.85; H, 5.68; N, 4.15, found: C, 49.28; H, 5.63; N, 4.18.

4.8.10. (2*R*,3*S*,4*S*,5*S*,4″*R*)-2-(2″,2″-Dimethyl-1″,3″-dioxolan-4″-yl)-3,4-dimethylmethylenedioxy-9-oxo-7-thioxo-8-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)-1-oxa-6,8-diazaspiro[4.4]nonane (32). *Method II*. $t=4$ days. Column chromatography: Et_2O/petroleum ether 1:3. Yield: 0.177 g, 75% (amorphous solid). $[\alpha]_D^{26}$ +18 (*c* 1.1). IR: ν_{max} 2988, 2930, 1730, 1719, 1489, 1269, 1099 and 1068 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, *(* ppm, *J* Hz): *(* 8.08–7.31 (m, 15H, Ar), 7.31 (s, 1H, NH), 6.43 (d, 1H, $J_{1',2'}=4.0$ Hz, H-1′), 6.32 (dd, 1H, $J_{2',3'}=6.3$ Hz, H-2′), 6.02 (t, 1H, $J_{3',4'}=6.3$ Hz, H-3′), 5.02 (dd, 1H, $J_{2,3}=3.3$ Hz, $J_{3,4}=5.9$ Hz, H-3), 4.89 (d, 1H, H-4), 4.76 (dd, 1H, $J_{4',5'a}=3.8$, $J_{5'a,5'b}=11.3$ Hz, H-5′a), 4.67 (ddd, 1H, H-4′), 4.64 (dd, 1H, $J_{4',5'b}=5.4$ Hz, H-5′b), 4.34 (m, 2H, H-2, H-4″), 4.08 (m, 1H, H-5″a), 3.96 (m, 1H, H-5″b), 1.56, 1.46, 1.40, 1.38 (each s, each 3H, $4CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): 181.4 (C-7), 170.6 (C-9), 166.1, 165.2, 165.1 (3C=O), 133.5–128.3 (Ar), 114.1, 109.5 ($2CCH_3$), 90.2 (C-5), 86.2 (C-1′), 80.1 (C-3+C-4), 79.4 (C-2), 79.2 (C-4′), 72.7 (C-4″), 71.8 (C-2′), 71.2 (C-3′), 66.9 (C-5″), 63.4 (C-5′), 26.8, 25.8, 25.1, 24.2 ($4CH_3$). HRCIMS *m/z* calcd for $C_{40}H_{41}O_{13}N_2S$ ($[M+H]^+$): 789.2329, found: 789.2329. Anal. Calcd for $C_{40}H_{40}O_{13}N_2S$: C, 60.90; H, 5.11; N, 3.55. Found: C, 60.84; H, 4.98; N, 3.47.

4.9. General procedures for the reactions of the isothiocyanatoulosonates 11, 18α, and 18β with ammonia, alkyl, aryl, and glycosyl amines (Route B). Preparation of the hydantocidin-related spironucleosides 24, 27α, 27β, 29α, 28α, 28β, 29α, 29β, 30α, and 30β

Method III (starting from free amines; used for the preparation of compounds **24**, **27α**, **27β**, **29α**, **29β**, **30α**, and **30β**). A solution of the isothiocyanatoulosonate **11** (for **24**) or a mixture 6.5:2 of **18α** and **18β** (for **27α**, **27β**, **29α**, **29β**, **30α**, and **30β**) (90 mg, 0.23 mmol) in THF (3 mL) was stirred with NH_3 (for **27α** and **27β**), dodecylamine (for **29α** and **29β**) or aniline (for **30α** and **30β**) (*x* mmol) at *T* °C for *t* min. The solvent was evaporated and the residue was purified by column chromatography.

Method IV (starting from amines as ammonium salts; used for the preparation of compounds **28α and 28β**). To a solution of a mixture 6.5:2 of the isothiocyanatoulosonates **18α** and **18β** (90 mg, 0.23 mmol), a solution of CH_3NH_2. HCl (17 mg, 0.25 mmol) and $NaHCO_3$ (21 mg, 0.25 mmol) in H_2O (0.2 mL) was added. The mixtue was stirred for 10 min at room temperature, concentrated to half, diluted with CH_2Cl_2 (15 mL), washed with brine, dried ($MgSO_4$), and evaporated to dryness. The residue was purified by column chromatography.

4.9.1. (5*R*,8*R*,9*R*,10*S*)-10-Benzoyloxy-8,9-dimethylmethylenedioxy-3-*p*-methoxyphenyl-4-oxo-2-thioxo-6-oxa-1,3-diazaspiro[4.5]decane (24). *Method III*. $x=$ 31 mg, 0.25 mmol. $T=40$ °C. $t=2$ h. Column chromatography: Et_2O/petroleum ether 1:4. Yield: 0.08 g, 72%. $[\alpha]_D^{22}$ −88 (*c* 1.3). IR: ν_{max} 3291, 2984, 1755, 1732, 1599, 1489, 1379, 1252 and 1105 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.04–6.93 (m, 9H, Ar), 7.52 (bs, 1H, NH), 5.65 (d, 1H, $J_{9,10}=7.4$ Hz, H-10), 4.88 (dd, 1H, $J_{8,9}=5.8$ Hz, H-9), 4.65 (dd, 1H, $J_{7a,7b}=13.6$ Hz, $J_{7a,8}=2.9$ Hz, H-7a), 4.49 (m, 1H, H-8), 4.33 (dd, 1H, $J_{7b,8}<1$, H-7b), 3.82 (s, 3H, OCH_3), 1.66, 1.42 (each s, each 3H, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): δ 183.2 (C-2), 168.9 (C-4), 165.4 (C=O), 160.0–114.3 (Ar), 110.3 (CCH_3), 85.5 (C-5), 73.7 (C-9), 72.8 (C-8), 71.1 (C-10), 63.3 (C-7), 55.3 (OCH_3), 27.5, 25.8 ($2CH_3$). HRCIMS *m/z* calcd for $C_{24}H_{24}O_7N_2S$ ($[M+H]^+$): 485.1383, found: 485.1377.

4.9.2. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro-[4.4]nonane (27α). *Method III*. $x=5$ min bubbling NH_3. $T=$ room temperature. $t=15$ min. Column chromatography: Et_2O/petroleum ether 1:2. Yield: 0.064 g, 74% (amorphous solid). $[\alpha]_D^{25}$ −68 (*c* 1.2). IR $\nu_{max.}$ 3288, 2992, 2944, 1771, 1717, 1507, 1385, 1275 and 1099 cm^{-1}. ^1H

NMR (500 MHz, $CDCl_3$, δ ppm, J Hz): δ 8.76 (bs, 1H, NH), 8.09–7.43 (m, 6H, Ar+NH), 4.92 (dd, 1H, $J_{2,3}=2.5$ Hz, H-3), 4.88 (d, 1H, $J_{3,4}=6.1$ Hz, H-4), 4.60 (td, 1H, H-2), 4.55 (dd, 1H, $J_{2,CH2a}=5.6$ Hz, CH_2a), 4.50 (dd, 1H, $^2J_{H,H}=11.7$ Hz, $J_{2,CH2b}=6.5$ Hz, CH_2b), 1.61, 1.38 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 181.2 (C-7), 171.2 (C-9), 166.1 (C=O), 133.4–127.6 (Ar), 114.9 (*C*CH_3), 94.7 (C-5), 82.8 (C-2), 82.2 (C-3), 80.7 (C-4), 64.3 (CH_2OBz), 26.6, 24.8 ($2CH_3$). Anal. Calcd for $C_{17}H_{18}N_2O_6S$: C, 53.96; H, 4.79; N, 7.40. Found: C, 53.67; H, 5.19; N, 7.01.

4.9.3. (2*R*,3*R*,4*R*,5*S*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (27β). *Method III*. $x=5$ min bubbling NH_3. $T=$ room temperature. $t=15$ min. Column chromatography: Et_2O/petroleum ether 1:2. Yield: 0.017 g, 20% (amorphous solid). $[\alpha]_D^{25}$ −160 (*c* 0.6). IR: $\nu_{max.}$ 3229, 2928, 1777, 1717, 1593, 1379, 1265, 1103 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, (ppm, *J* Hz): (8.42 (bs, 1H, NH), 8.03–7.49 (m, 5H, Ar), 7.48 Method, 1H, NH), 4.93 (d, 1H, $J_{3,4}=6.4$ Hz, H-4), 4.90 (dd, 1H, $J_{2,3}=2.0$ Hz, H-3), 4.88 (m, 1H, H-2), 4.63 (dd, 1H, $^2J_{H,H}=12.4$ Hz, $J_{2,CH2a}=4.3$ Hz, CH_2a), 4.47 (dd,1H, $J_{2,CH2b}=3.3$ Hz, CH_2b), 1.62, 1.35 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (180.8 (C-7), 168.1 (C-9), 166.0 (C=O), 133.8–128.4 (Ar), 116.5 (*C*CH_3), 95.8 (C-5), 86.2 (C-4), 83.4 (C-2), 81.3 (C-3), 64.7 (CH_2OBz), 25.0, 24.9 ($2CH_3$). HREIMS *m*/*z* calcd for $C_{17}H_{18}O_6N_2S$ ($[M]^+$): 378.0886, found: 378.0889.

4.9.4. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-8-methyl-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (28α). *Method IV*. Column chromatography: Et_2O/petroleum ether 1:9. Yield: 0.057 g, 64%. $[\alpha]_D^{26}$ −82 (*c* 1.1). IR: ν_{max}. 2988, 2942, 1757, 1717, 1489, 1375, 1275 and 1099 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, (ppm, *J* Hz): (8.09–7.43 (m, 5H, Ar), 7.41 (sb, 1H, NH), 4.92 (dd, 1H, $J_{2,3}=1.8$ Hz, H-3), 4.83 (d, 1H, $J_{3,4}=6.0$ Hz, H-4), 4.60–4.48 (m, 3H, H-2, CH_2OBz), 3.23 (s, 3H, NCH_3), 1.68, 1.37 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (183.5 (C-7), 170.9 (C-9), 166.0 (C=O), 133.1–128.3 (Ar), 114.7 (*C*CH_3), 92.8 (C-5), 82.5 (C-2), 82.2 (C-3), 80.7 (C-4), 64.3 (CH_2OBz), 27.3, 26.5, 24.7 ($3CH_3$). HRCIMS *m*/*z* calcd for $C_{18}H_{21}O_6N_2S$ ($[M+H]^+$): 393.1120, found: 393.1114.

4.9.5. (2*R*,3*R*,4R,5*S*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-8-methyl-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (28β). *Method IV*. Column chromatography: Et_2O/petroleum ether 1:9.Yield: 0.019 g, 21% (amorphous solid). $[\alpha]_D^{24}$ −132 (*c* 1.1). IR: ν_{max} 3308, 2982, 2941, 1763, 1724, 1489, 1275 and 1097 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$, *(* ppm, *J* Hz): *(* 8.05–7.49 (m, 5H, Ar), 7.43 (bs, 1H, NH), 4.92–4.87 (m, 3H, H-2, H-3, H-4), 4.63 (dd, 1H, $J_{2,H}=4.3$ Hz, C*H*HOBz), 4.46 (dd, 1H, $^2J_{H,H}=12.4$ Hz, $J_{2,H}=3.2$ Hz, CH*H*OBz), 3.23 (s, 3H, NCH_3), 1.64, 1.34 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (183.3 (C-7), 168.0 (C-9), 165.9 (C=O), 133.7–128.3 (Ar), 116.4 (*C*CH_3), 93.8 (C-5), 86.1 (C-4), 83.1*, 81.3* (C-2, C-3), 64.7 (CH_2OBz), 27.4, 25.1, 24.9 ($3CH_3$). HRCIMS *m*/*z* calcd for $C_{18}H_{21}O_6N_2S$ ($[M+H]^+$): 393.1120, found: 393.1122.

4.9.6. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-8-dodecyl-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (29α). *Method III*. $x=0.047$ mg, 10.25 mmol. $T=$ room temperature. $t=30$ min. Column chromatography: Et_2O/petroleum ether 1:9–1:5 gradient. Yield: 0.075 g, 60% (syrup). $[\alpha]_D^{25}$ −64 (*c* 0.9). IR: ν_{max} 2924, 2853, 1751, 1724, 1474, 1273 and 1101 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, (ppm, *J* Hz): (8.09–7.42 (m, 5H, Ar), 7.27 Method, 1H, NH), 4.92 (dd, 1H, $J_{2,3}=2.0$ Hz, H-3), 4.82 (d, 1H, $J_{3,4}=6.0$ Hz, H-4), 4.60–4.48 (m, 3H, H-2, CH_2OBz), 3.76 (t, 2H, $^3J_{H,H}=7.5$ Hz, NCH_2), 1.65–1.25 (m, 26H, $(CH_2)_{10}$, $2CH_3$), 0.87 (t, 3H, $^3J_{H,H}=6.3$ Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, (ppm): (183.2 (C-7), 171.0 (C-9), 165.9 (C=O), 133.1–128.3 (Ar), 114.6 (*C*CH_3), 92.4 (C-5), 82.4 (C-2), 82.3 (C-3), 80.6 (C-4), 64.2 (CH_2OBz), 41.2 (NCH_2), 31.7, 29.4 (for 2C), 29.3, 29.23, 29.1, 28.9, 27.4, 26.5 (for 2C), 24.7, 22.5 ($(CH_2)_{10}$, $2CH_3$), 13.9 (CH_3). Anal. Calcd for $C_{29}H_{42}O_6N_2S$: C, 63.71; H, 7.74; N, 5.12, found C, 63.68; H, 7.84; N, 5.14.

4.9.7. (2*R*,3*R*,4*R*,5*S*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-8-dodecyl-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (29β). *Method III*. $x=0.047$ mg, 10.25 mmol. $T=$ room temperature. $t=30$ min. Column chromatography: Et_2O/petroleum ether 1:9–1:5 gradient. Yield: 0.021 g, 17% (syrup). $[\alpha]_D^{26}$ −102 (*c* 1.0). IR: $\nu_{max.}$ 3295, 2926, 2855, 1763, 1723, 1599, 1489, 1273 and 1101 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, *(* ppm, *J* Hz): 8.07–7.48 (m, 5H, Ar), 7.32 (bs, 1H, NH), 4.92–4.85 (m, 3H, H-2, H-3, H-4), 4.62 (dd, 1H, $J_{2,H}=3.9$ Hz, C*H*HOBz), 4.48 (dd, 1H, $J_{2,H}=3.1$ Hz, $^2J_{H,H}=12.3$ Hz, CH*H*OBz), 3.77 (m, 2H, NCH_2), 1.63–0.85 (m, 26H, $(CH_2)_{10}$, $2CH_3$), 0.88 (t, 3H, $^3J_{H,H}=6.5$ Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$, (ppm): (183.1 (C-7), 168.2 (C-9), 165.9 (C=O), 133.7–128.3 (Ar), 116.5 (*C*CH_3), 93.6 (C-5), 86.1 (C-4), 83.0*, 81.3* (C-2, C-3), 64.7 (CH_2OBz), 41.3 (NCH_2), 31.8, 29.5 (for 2C), 29.4, 29.37, 29.2, 29.1, 27.5, 26.5, 25.1, 24.9, 22.6 ($(CH_2)_{10}$, $2CH_3$), 14.0 (t, 3H, CH_3). HRCIMS *m*/*z* Calcd for $C_{29}H_{43}N_2O_6S$ ($[M+H]^+$): 547.2842, found: 547.2835.

4.9.8. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-9-oxo-8-phenyl-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (30α). *Method III*. $x=23$ μl, 0.25 mmol. $T=40$ °C. $t=3$ h. Column chromatography: toluene/AcOEt 100:1–50:1 gradient. Yield: 0.076 g, 73% (amorphous solid). $[\alpha]_D^{24}$ −73 (*c* 1.0). IR: ν_{max}. 2987, 1763, 1719, 1497, 1452, 1230 and 1071 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.09–7.31 (m, 11H, Ar, NH), 4.99 (d, 1H, $J_{3,4}=6.1$ Hz, H-4), 4.97 (dd, 1H, $J_{2,3}=2.3$ Hz, H-3), 4.65 (td, 1H, H-2), 4.58 (dd, 1H, $J_{2,H}=5.7$ Hz, C*H*HOBz), 4.54 (dd, 1H, $J_{2,H}=6.5$ Hz, $^2J_{H,H}=11.8$ Hz, CH*H*OBz), 1.65, 1.42 (each s, each 3H, $2CH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$, δ ppm): δ 182.8 (C-7), 170.4 (C-9), 166.0 (C=O), 133.2–127.9 (Ar), 114.9 (*C*CH_3), 93.0 (C-5), 82.8 (C-2), 82.4 (C-3), 80.9 (C-4), 64.3 (CH_2OBz), 26.6, 24.8 ($2CH_3$). Anal. Calcd for $C_{23}H_{22}O_6N_2S$: C, 60.78; H, 4.88; N, 6.16. Found: C, 60.85; H, 5.01; N, 6.11.

4.9.9. (2*R*,3*R*,4*R*,5*S*)-2-Benzoyloxymethyl-3,4-dimethylmethylenedioxy-9-oxo-8-phenyl-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (30β). *Method III*. $x=23$ μl, 0.25 mmol. $T=40$ °C. $t=3$ h. Column chromatography:

Toluene: AcOEt 100:1–50:1 gradient. Yield: 0.022 g, 21% (amorphous solid). $[\alpha]_D^{24}$ −138 (*c* 0.9). IR: $\nu_{max.}$ 3291, 2936, 1775, 1593, 1489, 1271 and 1103 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, (ppm, *J* Hz): (8.06–7.30 (m, 10H, Ar), 7.76 (bs, 1H, NH), 5.00 (d, 1H, $J_{3,4}=6.1$ Hz, H-4), 4.93 (m, 2H, H-2, H-3), 4.66 (dd, 1H, $J_{2,H}=3.9$ Hz, $^2J_{H,H}=12.3$ Hz, C*H*HOBz), 4.51 (dd, 1H, $J_{2,H}=2.9$ Hz, CH*H*OBz), 1.61, 1.36 (each s, each 3H, $2CH_3$). ^{13}C NMR: (125.7 MHz, $CDCl_3$, (ppm): (182.7 (C-7), 167.5 (C-9), 166.0 (C=O), 133.7–128.2 (Ar), 116.7 (*C*CH_3), 94.1 (C-5), 86.3 (C-4), 83.1*, 81.2* (C-2, C-3), 64.6 (CH_2OBz), 25.1, 25.0 ($2CH_3$). HRCIMS *m/z* calcd for $C_{23}H_{23}O_6N_2S$ ($[M+H]^+$): 455.1277, found: 455.1272.

4.10. (5*R*,8*R*,9*R*,10*S*)-10-Benzoyloxy-8,9-dihydroxy-4-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thioxo-6-oxa-1,3-diazaspiro[4.5]decane (33)

To a solution of 22α (100 mg, 0.14 mmol) in CH_3CN: H_2O 9:1 (3 mL), DDQ (7.5 mg, 0.033 mmol) was added. The mixture was stirred at 45 °C for 36 h. The solution was concentrated to dryness and the residue was purified by column chromatography (Et_2O). Yield: 0.078 g, 83% (amorphous solid). $[\alpha]_D^{25}$ −29 (*c* 0.1). IR: ν_{max} 2945, 1755, 1732, 1599, 1489, 1377, 1240 and 1103 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ ppm, *J* Hz): δ 8.72 (bs, 1H, NH), 7.89–7.32 (m, 5H, Ar), 5.98 (t, 1H, $J_{2',3'}=9.3$ Hz, H-2′), 5.80 (d, 1H, $J_{1',2'}=9.5$ Hz, H-1′), 5.75 (d, 1H, $J_{9,10}=9.7$ Hz, H-10), 5.31 (t, 1H, $J_{3',4'}=9.5$ Hz, H-3′), 5.26 (t, 1H, H-4′), 4.71 (dd, 1H, $J_{8,9}=2.9$ Hz, H-9), 4.54 (d, 1H, $J_{7a,7b}=12.7$ Hz, H-7a), 4.35 (dd, 1H, $J_{5',6'a}=4.2$ Hz, H-6′a), 4.24 (m, 1H, H-8), 4.18 (dd, 1H, $J_{5',6'b}=2.3$ Hz, $J_{6'a,6'b}=12.5$ Hz, H-6′b), 4.14 (d, 1H, H-7b), 3.78 (dt, 1H, $J_{4',5'}=9.6$ Hz, H-5′), 2.05, 2.04, 2.03, 1.94 (each s, each 3H, $4CH_3$), 1.68 (bs, 2H, 2OH). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): δ 182.1 (C-2), 170.6, 169.9, 169.4, 169.3, 167.4, 166.7 (6C=O), 134.0–127.8 (Ar), 84.5 (C-5), 80.9 (C-1′), 74.3 (C-5′), 73.0 (C-3′), 71.5 (C-10), 68.9*, 68.8* (C-8, C-9), 67.8 (C-4′), 67.2 (C-2′), 65.8 (C-7), 61.7 (C-6′), 20.5, 20.4 (parta 2C), 20.1 ($4CH_3$). HRCIMS *m/z* calcd for $C_{28}H_{33}O_{15}N_2S$ ($[M+H]^+$): 669.1602, found: 669.1594.

4.11. (2*R*,3*R*,4*R*,5*R*)-2-Benzoyloxymethyl-3,4-dihydroxy-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (35)

A solution of **27α** (55 mg, 0.145 mmol) in TFA:H_2O 2:3 (5 mL) was stirred at room temperature for 1 h. The solution was concentrated to dryness and the residual amount of acid was eliminated by repeated evaporations with toluene. The residue was purified by column chromatography (EtOAc/petroleum ether 1:2). Yield: 0.045 g, 91%. $[\alpha]_D^{20}$ −14 (*c* 1.0, MeOH). IR: ν_{max}. 3237, 2926, 1765, 1717, 1599, 1505, 1379, 1279 and 1103 cm^{-1}. ^1H NMR (500 MHz, MeOD, δ ppm, *J* Hz): δ 8.11–7.45 (m, 5H, Ar), 4.49 (dd, 1H, $^2J_{H,H}=13.4$ Hz, $J_{2,H}=5.0$ Hz, C*H*HOBz), 4.40 (m, 2H, H-2, CH*H*OBz), 4.34 (dd, 1H, $J_{2,3}=3.8$ Hz, H-3), 4.32 (d, 1H, $J_{3,4}=4.8$ Hz, H-4). ^{13}C NMR (125.7 MHz, MeOD, δ ppm): δ 185.0 (C-7), 174.9, 167.8 (2C=O), 134.4–129.6 (Ar), 95.5 (C-5), 83.7 (C-2), 74.6*, 73.2* (C-3, C-4), 65.4 (CH_2OBz). HRFABMS *m/z* calcd for $C_{14}H_{14}N_2O_6SNa$ ($[M+Na]^+$): 361.0470, found: 361.0478.

4.12. Preparation of 34 and 36(α+β)

To a solution of **33** (for **34**) ó **35** [for **36**(α+β)] (*x* mg, 0.15 mmol) in MeOH (1 mL), another solution of NaMeO 1 M in MeOH (1 mL) was added. The solution was stirred for 1 h at room temperature, neutralized with Dowex®, filtered, and concentrated to dryness. The residue was purified by HPLC (reversed-phase).

4.12.1. (5*R*,8*R*,9*R*,10*S*)-4-Oxo-8,9,10-trihydroxy-3-(β-D-glucopyranosyl)-2-thioxo-6-oxa-1,3-diazaspiro[4.5]-decane (34).

x=100 mg. HPLC: MeOH/H_2O 70: 1. Yield 0.037 g, 85%. $[\alpha]_D^{22}$ −32 (c 0.5, MeOH). IR: ν_{max}. 3308, 2893, 1763, 1491, 1379, 1103, 1071 cm^{-1}. ^1H NMR 500 MHz, D_2O, δ ppm, *J* Hz): δ 5.66 (d, 1H, $J_{1',2'}=9.6$ Hz, H-1′), 4.39 (dd, 1H, $^2J_{H,H}=13.0$ Hz, $J_{7a,8}<1$, H-7a), 4.34 (t, 1H, $J_{2',3'}=9.4$ Hz, H-2′), 4.28 (dd, 1H, $J_{8,9}=3.3$ Hz, H-9), 4.05 (m, 1H, H-8), 3.95 (d, 1H, $J_{9,10}=10.1$ Hz, H-10), 3.87 (dd, 1H, $J_{7b,8}=2.0$ Hz, H-7b), 3.83 (dd, 1H, $J_{5',6'a}=1.7$ Hz, H-6a), 3.69 (dd, $^2J_{H,H}=12.5$ Hz, $J_{5',6'b}=4.4$ Hz, H-6′b), 3.49 (m, 3H, H-3′, H-4′, H-5′). ^{13}C NMR (125.7 MHz, D_2O, δ ppm): δ 185.6 (C-7), 172.0 (C-9), 88.0 (C-5), 84.2 (C-1′), 79.8, 77.8, 70.5, 70.3 (C-3′, C-4′, C-5′, C-10), 69.3, 69.2 (C-8, C-2′), 67.7 (C-7), 61.6 (C-6′). HRFABMS calcd for $C_{13}H_{21}N_2O_{10}S$: 397.0917, found: 397.0891.

4.12.2. (2*R*,3*R*,4*R*,5*R* and *S*)-2-Hydroxymethyl-3,4-dihydroxy-9-oxo-7-thioxo-1-oxa-6,8-diazaspiro[4.4]nonane (36 α+β).

x=50 mg. HPLC: AcOEt/MeOH 10:1. Diastereoisomers in C-5 ratio (*R*:*S*): 6:1. Yield: 29 mg, 87%. The spectroscopic data were coincident with those reported[16c] in the literature.

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References and notes

1. (a) Fernández-Bolaños, J.; Blasco López, A.; Fuentes Mota, J. *Carbohydr. Res.* **1990**, *199*, 239–242. (b) Gimisis, T.; Castellari, C.; Chatgilialoglu, Ch. *Chem Comun.* **1997**, *21*, 2089–2090. (c) Renard, A.; Lhomme, J.; Kotera, M. *J. Org. Chem.* **2002**, *67*, 1302–1307.
2. Haruyama, H.; Takayanna, T.; Kinosita, T.; Kondo, M.; Nakajima, M.; Haneishi, T. *J. Chem. Soc. Perkin Trans. 1* **1991**, 1637–1640.
3. See as examples: (a) Poland, B. W.; Lee, S. F.; Subramanian, M. V.; Siehl, D. L.; Andersen, R. J.; Fromm, H. J.; Honzatko, R. B. *Biochemistry* **1996**, *35*, 15753–15759. (b) Fonne-Pfister, R.; Chemia, P.; Ward, E.; Girarded, M.; Krenz, K. E.;

Hanzatko, R. B.; From, H. J.; Schar, H-P. ; Grütter, M. G.; Cowan-Jacob, S. W. *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 9431–9436. (c) Walters, E. W.; Lee, S. F.; Niderman, T.; Bernasconi, P.; Subramanian, M. V.; Siehl, D. L. *Plant Physiol.* **1997**, *62*, 125–134.

4. (a) Somsák, L.; Nagy, V.; Hadady, Z.; Docsa, T.; Gergely, P. *Curr. Pharm. Des.* **2003**, *9*, 1177–1189. (b) Somsák, L.; Kovács, L.; Tóth, M.; Szilágyi, L.; Györgydeák, Z.; Dinya, Z.; Docsa, T.; Tóth, B.; Gergely, P. *J. Med. Chem.* **2001**, *44*, 2843–2848. (c) Bichard, C. J. F.; Mitchel, E. P.; Wormald, M. R.; Watson, K. A.; Johnson, L. N.; Zographos, S. E.; Koutra, D. D.; Oikonomakos, N. G.; Fleet, G. W. J. *Tetrahedron Lett.* **1995**, *36*, 2145–2148.
5. Gyémánt, G.; Kandra, L.; Nagy, V.; Somsák, L. *Biochem. Biophys. Res. Commun.* **2003**, *313*, 334–339.
6. (a) Mio, S.; Ichinose, R.; Goto, K.; Sugai, S.; Sato, S. *Tetrahedron* **1991**, *47*, 2111–2120. (b) Mio, S.; Kumagawa, Y.; Sugai, S. *Tetrahedron* **1991**, *47*, 2133–2144. (c) Matsumoto, M.; Kirihara, M.; Yoshino, T.; Katoh, T.; Terashima, S. *Tetrahedron Lett.* **1993**, *34*, 6289. (d) Chemla, P. *Tetrahedron Lett.* **1993**, *34*, 7391–7394. (e) Harrington, P.; Jung, M. *Tetrahedron Lett.* **1994**, *35*, 5145–5148. (f) Nakajima, N.; Matsumoto, M.; Kirihara, M.; Hashimoto, M.; Katoh, T.; Terashima, S. *Tetrahedron* **1996**, *52*, 1177–1194.
7. (a) For recent reviews see: Dondoni, A; Marra, A. *Chem. Rev.* **2000**, *100*, 4395–4421; (b) Schweizer, F. *Angew. Chem. Int. Ed.* **2002**, *41*, 230–253. For recent references on the preparation of furanoid hydantoin spironucleosides see: (c) Long, D. D.; Smith, M. D.; Martin, A.; Wheatley, J. R.; Watkin, D. G.; Mueller, M.; Fleet, G. W. J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1982–1998; pyranoid spiro-thiohydantoines see: (d) Somsák, L.; Nagy, V.; Docsa, T.; Tóth, B.; Gergely, P. *Tetrahedron: Asymmetry* **2000**, *11*, 405–408. Carbocyclic derivatives of hydantocidin see: (e) Sano, H.; Sugai, S. *Tetrahedron: Asymmetry* **1995**, *6*, 1143–1150. For the preparation of different spironucleosides and spiro-C-glycosides during the last ten years see: (f) Gasch, C.; Pradera, M. A.; Salameh, B. A. B.; Molina, J. L.; Fuentes, J. *Tetrahedron: Asymmetry* **2001**, *12*, 1267–1277 and references cited therein. See also: (g) Freire, R.; Martín, A.; Pérez-Martín, I.; Suárez, E. *Tetrahedron Lett.* **2002**, *43*, 5113—5116. (h) Andersch, J.; Hennig, L.; Wilde, H. *Carbohydr. Res.* **2000**, 329, 693–697.
8. Gasch, C.; Salameh, B. A. B.; Pradera, M. A.; Fuentes, J. *Tetrahedron Lett.* **2001**, *42*, 8615–8617.
9. Somsák, L.; Czifrák, K.; Deim, T.; Szilágyi, L.; Bényei, A. *Tetrahedron: Asimmetry* **2001**, *12*, 731–736.
10. (a) Shiozaki, M. *Carbohydr. Res.* **2002**, *337*, 2077–2088. (b) *Carbohydr. Res.* **2001**, *335*, 147–150.
11. Prisbe, E. J.; Smejkal, J.; Verheyden, J. P.; Moffatt, J. G. *J. Org. Chem.* **1976**, *41*, 1836–1846.
12. Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.
13. Dondoni, A.; Scherrmann, M. C.; Marra, A.; Delépine, J. L. *J. Org. Chem.* **1994**, *59*, 7517–7520.
14. (a) Brandstetter, T. W.; Wormald, M. R.; Dwek, R. A.; Butters, T. D.; Platt, F. M.; Tsitsanou, K. E.; Zographos, S. E.; Oikonomakos, N. G.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **1996**, *7*, 157–170. (b) Brandstetter, T. W.; delaFuente, C.; Kim, Y.-h.; Cooper, R. I.; Watkin, D. J.; Oikonomakos, N. G.; Jonson, L. N.; Fleet, G. W. J. *Tetrahedron* **1996**, *52*, 10711–10720. (c) See also 7d.
15. (a) Praly, J. P.; Bonnevie, C.; Haug, P.; Descotes, G. *Tetrahedron* **1996**, *52*, 9057–9068. (b) Gyorgydeák, Z.; Szilágyi, L.; Paulsen, H. *J. Carbohydr. Chem.* **1993**, *13*, 139–163.
16. (a) Brandstetter, T. W.; de la Fuente, C.; Kim, Y-h. ; Johnson, L. N.; Crook, S.; Lilley, P. M. Q.; Watkin, D. J.; Tsisanou, K. E.; Zographos, S. E.; Chrysina, E. D.; Oikonomakos, N. G.; Fleet, G. W. J. *Tetrahedron* **1996**, *52*, 10721–10736. (b) Fairbanks, A. J.; Fleet, G. W. J. *Tetrahedron* **1995**, *51*, 3881–3894. (c) Sano, H.; Mio, S.; Kitagawa, J.; Shindou, M.; Honma, T.; Sugai, S. *Tetrahedron* **1995**, *51*, 12563–12572.
17. (a) Fuentes, J.; Molina, J. L.; Olano, D.; Pradera, M. A. *Tetrahedron: Asymmetry* **1996**, *7*, 203–218. (b) Marino, C.; Varela, O.; Lederkremer, R. M. *Carbohydr. Res.* **1997**, *304*, 257–260.
18. Pretsch, E.; Bühlmann, P.; Affolter, C.; Herrera, A.; Marínez, R. *Determinación Estructural de Compuestos Orgánicos*; Springer: Barcelona, 2001; pp. 79–81.
19. Dondoni, A.; Schermann, M. C. *J. Org. Chem.* **1994**, *59*, 6404–6412.
20. Castro, E. *Chem. Rev.* **1999**, *99*, 3505–3524.
21. (a) Osz, E.; Sós, E.; Somsák, L.; Szilágyi, L.; Dinya, Z. *Tetrahedron* **1997**, *53*, 5813–5824. (b) Somsák, L.; Nagy, V. *Tetrahedron: Asymmetry* **2000**, *11*, 1719–1727.
22. Babiano Caballero, R.; Fuentes Mota, J.; Galbis Pérez, J. A. *Carbohydr. Res.* **1986**, *154*, 280–288.
23. Marino, C.; Varela, O.; Lederkremer, R. M. *Tetrahedron* **1997**, *53*, 16009–16016.
24. Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093–2094.
25. García Fernandez, J. M.; Ortiz Mellet, C.; Moreno Marín, A.; Fuentes, J. *Carbohydr. Res* **1995**, *274*, 263–268.
26. Merchán, F. L.; Merino, P.; Tejero, T. *Glycoconjugate J.* **1997**, 497–499.