Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 435–452

TETRAHEDRON: *ASYMMETRY*

Chiral thioxohydroimidazoles with two sugar moieties. *N*-, *C*-, and spiro-nucleosides

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Received 29 October 1999; accepted 30 November 1999

Abstract

2-Amino (alkyl and arylamino)-2-deoxy-D-fructose and different sugar isothiocyanates are used in the diastereoselective synthesis of chiral imidazolidine-2-thione *N*-nucleosides **12**–**23**. Water β-elimination of these compounds produces imidazoline-2-thione *N*-nucleosides **27**–**31**, whereas cyclodehydration of the same products gives, with high stereoselectivity, chiral spironucleosides with an *N*-glycosyl radical **34**–**37**. Conformational aspects of some of the prepared compounds are discussed.

1. Introduction

Of the different types of nucleosides, *N*- and *C*-glycosyl derivatives of heterocycles are the most studied compounds,[1] and have in many cases interesting biological properties.[2] In 1991 the isolation of (+)-hydantocidin,[3] the first natural spironucleoside,[4] and the finding of its potent herbicidal activity was without toxicity for mammals, [5] has provoked a great interest in the chemistry of spironucleosides. Thus, much effort is being directed to the synthesis of hydantocidin,[6] carbocyclic analogues,[7] related pyranoid and furanoid compounds with different configurations and spironucleosides of various heterocycles.[8] Little attention has been given to the syntheses of sulfur-containing analogues.[9] At the same time, sugar isothiocyanates are suitable starting materials for the synthesis of different glycoconjugates.[10] Recently we have used the reaction of 2-amino-2-deoxy-D-glucopyranose with glycosyl isothiocyanates and with a 2-deoxy-2-isothiocyanato glucoside[11] for the preparation of imidazole *N*-nucleosides or 2-pseudonucleosides, respectively.

The reaction of 1-(alkyl, aryl)amino-1-deoxy-ketoses with simple alkyl and aryl isothiocyanates gives polyhydroxyalkylimidazoline-2-thiones.[12] In only one case were two low-yielding spiro imidazolidines isolated in addition to the imidazoline derivative.[13] Although an intermediate hydroxyimidazolidine has

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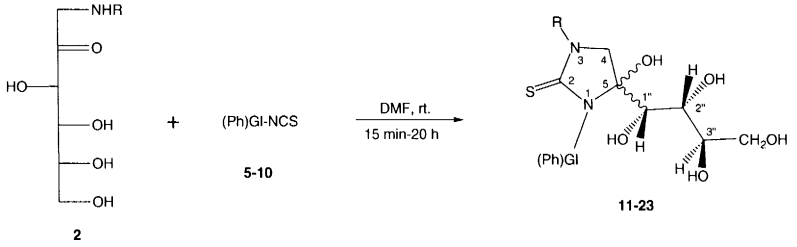
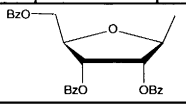
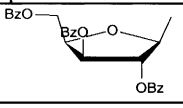
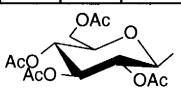
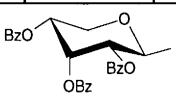
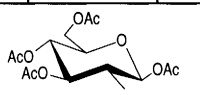
0957-4166/00/$ - see front matter
PII: S0957-4166(99)00550-9

been proposed[14] in this reaction, never have such hydroxyimidazolidines been isolated or experimentally detected.

In this paper, we describe the reaction of D-fructosamines **1**–**4** with different sugar isothiocyanates **6**–**10** to obtain chiral imidazolidine-2-thione *N*-nucleosides **12**–**21** or pseudonucleosides **22**, **23** (Scheme 1). Water β-elimination and cyclodehydration of the prepared hydroxyimidazolidines are competitive reactions. In the first case, compounds having simultaneously the structure of an *N*-nucleoside and of an acyclic *C*-nucleoside of imidazoline-2-thiones **25**, **30** are formed, whereas in the second case, spironucleosides having an *N*-glycosyl radical **33**–**36** are obtained.



	1	2	3	4	5	11	6	12	13	14	15	7	16
R	H	Me	*p*-MeC$_6$H$_4$	*p*-EtOC$_6$H$_4$	-	H	-	H	Me	*p*-MeC$_6$H$_4$	*p*-EtOC$_6$H$_4$	-	*p*-MeC$_6$H$_4$
Gl/Ph	-	-	-	-	Ph	Ph							

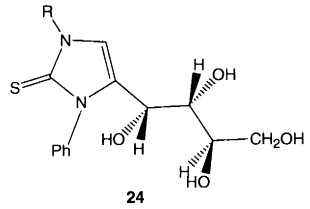
	8	17	18	19	9	20	21	10	22	23
R	-	H	Me	*p*-MeC$_6$H$_4$	-	H	*p*-MeC$_6$H$_4$	-	H	*p*-MeC$_6$H$_4$
Gl										

Scheme 1.

2. Results and discussion

The reaction of D-fructosamine acetate **1** with phenyl isothiocyanate in refluxing ethanol has been studied previously[15] and produced the imidazoline-2-thione **24** in 52% yield. Before studying the reaction of the same aminosugar with sugar isothiocyanates, and with the aim of having a hydroxyimidazolidine as a model compound and establishing the experimental conditions to prepare *N*-nucleosides of imidazolidine-2-thiones, we have carried out the reaction of **1** with phenyl isothiocyanate **5** under different conditions. When the reaction was performed at room temperature in DMF, the 5-hydroxy-1-phenylimidazolidine-2-thione **11** was obtained, as a pair of C-5 diastereomers, in practically quantitative yield. The spectroscopic data (see Table 1 and the Experimental) of the mixture of diastereomer **11** confirmed the proposed structure. Thus, the H-4a and H-4b protons of the imidazolidine ring resonated as an AB system at 4.35–4.38 ppm, and the signal for C-2 appeared at 183.0 ppm as is described for related imidazolidine-2-thiones[11] and other thioureas.[16] When the reaction of **1** and **5** was carried out

at temperatures over 50°C, the described[15] 1-phenyl-5-(D-*arabino*-tetritol-1-yl)imidazoline-2-thione **24** was the main product. The unreported ^{1}H and ^{13}C NMR data of **24** are included in Table 1 and the Experimental.



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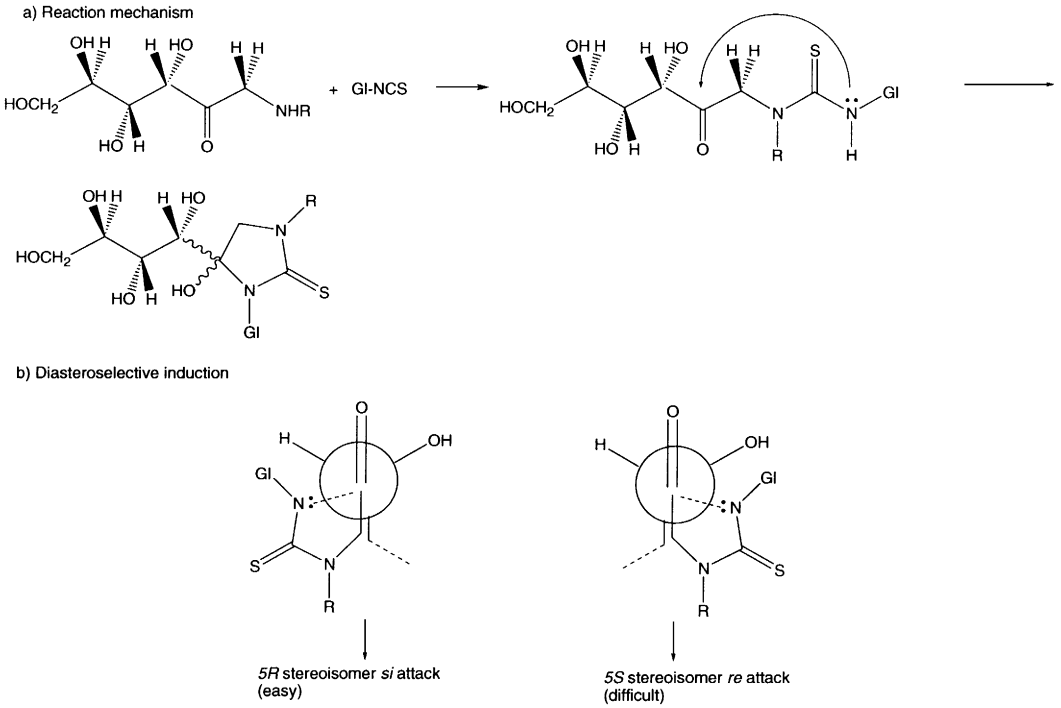
The treatment of 1-amino-1-deoxy-D-fructose **1**, and of its *N*-methyl-**2**, *N*-*p*-tolyl-**3**, and *N*-*p*-ethoxyphenyl-**4** derivatives with glycosyl (2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl **6**, 2,3,5-tri-*O*-benzoyl-β-D-xylofuranosyl **7**, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl **8**, and 2,3,4-tri-*O*-benzoyl-β-D-ribopyranosyl **9**) isothiocyanates gives the *N*-nucleosides of imidazolidine-2-thiones **12**–**21**. The same reaction starting from the aminofructoses **1** and **3**, and from the 2-deoxy-2-isothiocyanato-D-glucopyranose **10**, produces the pseudo *N*-nucleosides **22** and **23**, respectively. Compounds **12**–**23** were obtained as pairs of diastereomers (C-5 imidazolidine ring) in almost quantitative yield. The reactions were performed under the conditions established for **11**. When the aminosugar was **1** or **2**, the corresponding ammonium acetate was used and neutralisation was necessary, and the reaction times were shorter (15–20 min) than in the cases of *N*-aryl derivatives **3** and **4**, where free bases were used and the reaction times were 8–24 h. The spectroscopic data (Table 1 and the Experimental) of pairs of diastereomers **12**–**17** and **19**–**23** confirmed the proposed structures, whereas in the case of **18** acetylation to give **25** was necessary before the structural study (see below). The signals for the protons H-4a and H-4b of **12**–**17** and **19**–**23** appeared at 3.40–4.86 ppm, and when the corresponding coupling constant ($^{2}J_{H,H}$) could be measured, the value was 11.0–11.9 Hz; C-2 of the imidazolidine ring resonated in the interval 180.4–186.3 ppm in accord with reported data[11,16] for non-strained cyclic and acyclic thioureas. The pseudoanomeric carbon C-5 resonated at 93.0–99.0 ppm, showing a deshielding effect when this resonance is compared with the corresponding data for isomeric adjacent hydroxy-polyhydroxyalkyl imidazolidines.[11] The mechanism of the reaction of aminosugars with isothiocyanates involves the formation of an intermediate thiourea[14,17] which cyclises to the hydroxyimidazolidine with formation of a chiral centre (Scheme 2). The NMR data of **12**–**24** did not permit the assignment of the configuration of C-5, but assuming that, as in the case of thioureido derivatives of D-glucosamine,[16] Cram′s rule for the steric control of the asymmetric induction is fulfilled, the major stereoisomer is 5*R*. The nucleophilic attack of the NH on the *si* face of the carbonyl group to give the 5*R* stereoisomer involves lower steric hindrance than the attack on the *re* face, due to the interaction between the OH on C-3 of the D-fructosamine and the *N*-glycosyl radical. The same assignment is reached if the attack of the NH follows a Burgi–Dunitz trajectory.[18] The *R*:*S* ratio in compounds **11**–**23** is between 4:1 and 5:4, indicating a second asymmetric induction due to the *N*-sugar radical. This induction is higher for the glycosyl radicals **11**–**21** than for the glucopyranos-2-yl radicals **22**, **23**. No changes in the specific rotations or in the NMR spectra, of these pairs of diastereomers were observed when solutions in ethanol and acetone were left for 24 h at 27°C.

The acetylation of **18** with acetic anhydride and pyridine gave, after chromatography, the 5-hydroxy-tetraacetoxybutyl derivative **25** and the elimination product **26**. Compound **25** presented an IR absorption at 3410 cm^{-1} (OH group), and the δ values for the resonances of the protons of the butylic chain confirmed the introduction of four acetyl groups. The configuration of C-5 could not be determined, but is probably *R*, as in **18** the major stereoisomer is 5*R*. Compound **26** showed no signals for OH, and showed resonances at 6.80 (*H*C=) and 164.2 ppm (*C*=S), in agreement with reported data[19] for

Table 1
Selected NMR data (δ ppm, J Hz) for compounds **11**–**37**[a,b]

Comp.	δH4a	δH4b	J4a,4b	δH-1'	δH-1"	δC-2	δC-4	δC-5	δC-1'	δC-1"
11[c]	4.48	4.35	12.3	-	3.70	183.0	52.6	96.9	-	73.1
12[c]	←4.65-4.56→		-	6.49	3.59	184.5	50.8	98.9	87.2	69.8
13[d]	←4.77-4.68→		-	5.93	4.30	180.7	58.0	92.6	89.1	70.4
14[d]	4.76	3.83	11.9	5.89	4.31	180.2	59.1	92.8	89.2	70.6
15[d]	4.80	3.85	11.9	6.02	4.41	180.1	59.2	92.5	88.9	70.4
16[d] *4 R*	4.22	3.77	11.8	6.28	4.54	185.1	63.1	97.3	93.2	74.3
16[d] *4 S*	4.86	3.77	11.2	6.93	4.70	186.3	64.3	98.3	94.7	77.1
17[d]	4.18	3.46-3.40	-	5.87	3.57	185.3	51.0	98.5	84.6	71.5
19	←4.10-4.00→		-	6.45	3.64	182.8	56.5	98.2	84.6	72.3
20[e]	←3.82-3.40→		-	6.21	3.82-3.40	183.7	55.9	96.9	79.7	74.8
21[e]	4.67	3.41-3.44	11.3	7.04	3.52-3.47	180.4	58.4	92.8	82.0	72.8
22[c]	←3.68-3.52→		-	5.75	3.55	184.5	62.1	99.1	94.0	69.8
23[c]	3.66	3.60	11.0	6.46	4.34	180.9	58.4	93.7	84.6	72.0
24[c]	7.08		-	-	4.57	162.7	115.2	137.5	-	65.1
25	4.25	3.17	12.3	6.25	5.86	180.3	59.3	91.6	85.0	72.4
26	6.80	-	-	6.45	6.62	164.2	119.5	134.3	84.4	62.8
27[d]	7.12	-	-	7.05	5.29	170.0	123.1	138.5-133.3	94.9	68.4
28[d]	7.24	-	-	7.12	5.31	166.8	118.9	138.8-129.2	90.7	63.9
29[d]	7.22	-	-	7.18	5.37	166.7	119.0	138.8-115.3	90.9	64.3
30[d]	7.30	-	-	7.31	5.69	170.6	123.6	142.9-130.9	94.9	68.2
31[d]	7.14	-	-	6.68	5.42	165.2	119.8	138.9-126.7	85.1	64.2
32[d]	7.37	-	-	7.12	6.32	166.6	120.7	139.2-125.9	90.5	65.7
33[d]	7.28	-	-	6.63	6.74	166.9	121.2	139.3-126.2	85.2	64.2
	H-9a	H-9b	J9a,9b	H-1'	H-4	C-7	C-5	C-9	C-1'	C-4
34[d]	3.54	4.59	11.8	5.74	4.44	180.7	98.9	56.7	89.1	78.8
35[d]	3.95	4.51	11.4	5.87	4.55	179.8	98.9	57.7	89.4	79.2
36[d]	4.11	4.33	11.7	5.87	4.34	181.2	100.0	62.2	91.6	82.0
37[d]	3.93	4.49	11.4	5.86	4.54	180.0	98.2	58.1	89.3	79.1

[a] The *N*-glycosyl ring is numbered with ', the tetritol-1-yl chain is numbered with ". [b] The data for the chiral imidazolidines **11**-**15** and **17**-**23** correspond to the major *4 R* stereoisomer. [c] In MeOH-d_4. [d] In Me_2CO-d_6. [e] In Me_2SO-d_6.



Scheme 2.

imidazoline-2-thiones and with the corresponding values obtained for **24**. The vicinal coupling constant values of the protons of the D-*arabino*-tetraacetoxybutyl chain showed that, in compounds **25** and **26**, the main conformation of this chain in solutions in chloroform is the planar *P* conformation depicted in the formulas. It is noteworthy that compounds **12**–**23**, **25**, and **26**, in addition to being *N*-nucleosides, are acyclic-*C*-nucleosides (Fig. 1).

The acid-catalysed dehydration of imidazolidines **13**–**16** leads to *N*-nucleosides of imidazoline-2-thione (**27**–**31**) or to resoluble mixtures of the imidazoline-2-thiones **27**–**29** and the spironucleoside **34**–**37** (Scheme 3). *N*-Nucleosides **27**–**31** are formed by β-elimination of H_2O, and the yields are high at room temperature. However, when the competitive formation of imidazoline-2-thiones **27**–**29** and spiroimidazolidines **34**–**37** is studied, the formation of **27**–**29** increases with temperature. Conventional acetylation of **28** and **31** with acetic anhydride and pyridine afforded the corresponding tetra-*O*-acetyl derivatives **32** and **33**. The structure of compounds **27**–**31** was supported by their spectroscopic (IR, ^{1}H and ^{13}C NMR, and MS) data and those for the acetyl derivatives **32** and **33**. The resonances of H-4 and C-2 of the imidazoline ring of **27**–**33** had chemical shift values similar to those for **24** and **26**, and very close to reported data for 4-imidazoline-2-thiones.[19,20] The vicinal coupling constant values corresponding to the protons of the D-*arabino*-tetraacetoxybutyl chain showed that this chain was, in acetone solutions, an equilibrium of the planar *P* conformation (see formulas) and the $_3G^+$ conformation associated with the chain-end flexibility described for other D-*arabino* compounds.[21] In the case of the polyhydroxylic nucleosides **27**–**31**, the coupling constant values that could be measured are compatible with the same conformational assignment.

The spironucleosides **34**–**37**, also having structure of *N*-nucleoside, are formed from compounds **13**–**15** by cyclodehydration between the hydroxyl group on C-5 of the imidazolidine ring and the HO-3 of the polyhydroxyalkyl chain. In all the cases, a mixture of the two epimers in C-5 was formed; from these mixtures it was possible to isolate, as pure compounds, the major stereoisomers **34**, **35**, and **37**, and in

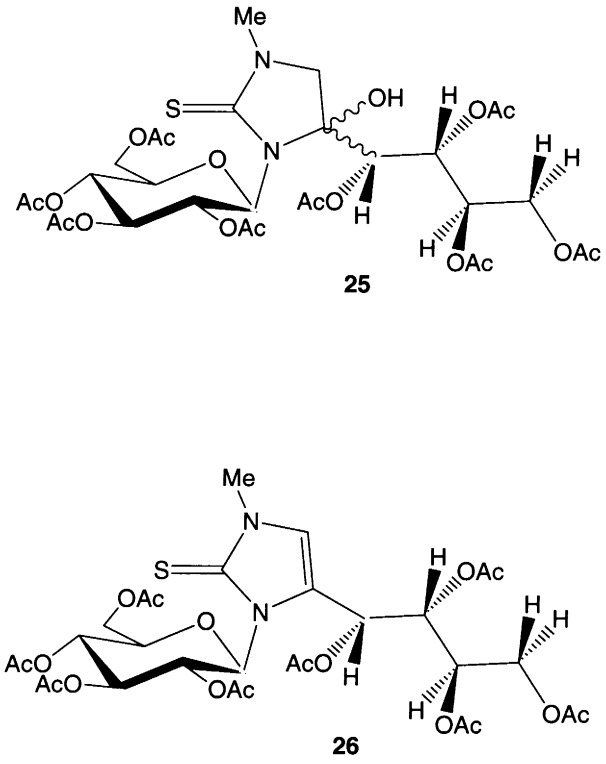
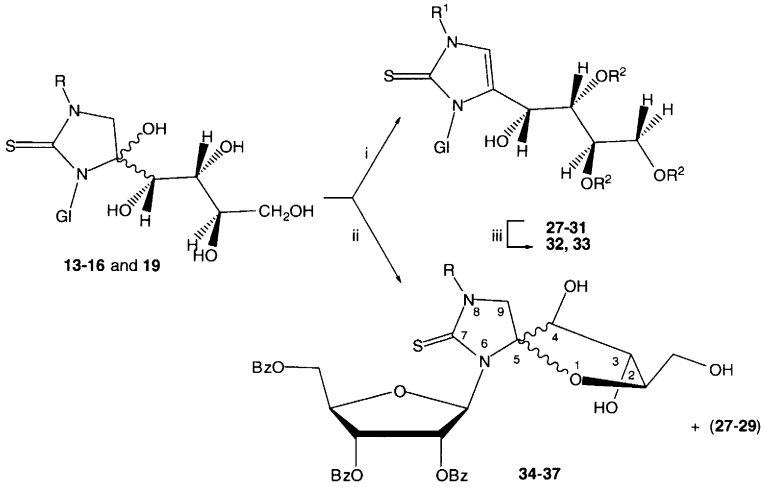
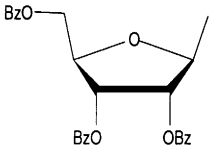
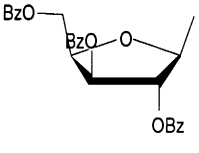
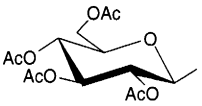


Fig. 1.

the case of the *p*-tolyl derivative, the minor stereoisomer **36**, with 66% diastereoisomeric excess, was also isolated. The spectroscopic data of **34**–**37** supported the proposed structures. The protons H-9a and H-9b resonated as doublets (J=11.4–11.8 Hz) at δ values close to those for the corresponding protons of the imidazolidines **11**–**23** and **25** (Table 1), and the resonances of C-7 appeared at 98.2–100.0 ppm, also confirming the presence of the imidazolidine-2-thione ring. Spiro pyranoid isomeric structures were ruled out because the ^{1}H NMR spectra showed signals for a CH_2OH group, where the OH resonated as a double doublet or triplet. The configuration of C-5 was determined by NOE experiments. Thus, in compounds **34** and **35** (Fig. 2a) the signal for H-9a had an increase of 2% on irradiation of H-4 and of 1% on irradiation of CH_2OH; an increase of 5% in the signal of H-1′ (ribofuranose ring) on irradiation of H-4 was also observed. These results confirmed the 5*S* configuration for the major reaction products. The main spectroscopic differences between the 5*S* isomers (**34**, **35** and **37**) and the 5*R* isomer that could be isolated (**36**) are: (a) the difference, $\Delta\delta$, between the δ values for H-9a and H-9b (>0.56 for *S* isomers and 0.22 for the *R* isomer) and (b) the chemical shifts for the resonances of the carbon C-5, whose configuration changes, of the adjacent carbons C-4 and C-9, and also of C-7 and C-1′ (ribofuranose ring) (Table 1). Different conditions were studied for the dehydration reactions of **12**–**23**, and β-elimination and cyclodehydration were observed as competitive reactions; the formation of byproducts was also observed; the results in the case of **14** are summarised in Table 2. In all the cases, an acidic catalyst was necessary, which supports a unimolecular mechanism through the stabilised cation indicated in Fig. 2b. This cation is formed by protonation of the OH group on C-5, and loss of H_2O. The abstraction of one proton of C-4 produces the elimination product **31**, which is the more stable compound. Attack of the hydroxyl group (C-3 of polyhydroxyalkyl chain) produces the cyclodehydration products **35** and **36** (paths a and b, respectively). The 5*S* spironucleoside **35** predominates on **36**, as it comes from the



Reagents and conditions. (i) 10 % TFA, EtOH, rt; (ii) Dowex®50W-X8, EtOH, molecular sieve 4 A°, 45 °C, 4 h; (iii) Ac_2O/Py

	27	28	29	32	30	31	33
R^1	Me	*p*-MeC_6H_4	*p*-$EtOC_6H_4$	*p*-MeC_6H_4	*p*-MeC_6H_4	*p*-MeC_6H_4	*p*-MeC_6H_4
R^2	H	H	H	Ac	H	H	Ac
Gl							

	34	35	36	37
R	Me	*p*-MeC_6H_4	*p*-MeC_6H_4	*p*-$EtOC_6H_4$
C-5 conf.	*S*	*S*	*R*	*S*

Scheme 3.

attack on the opposite face to the $-OH_2^+$ leaving group in the major stereoisomer of **14**. The best conditions to obtain the *N*-nucleoside **31** are shown in Table 2, entries 2 and 3. The best conditions for the spironucleosides **5** and **6** are shown in entry 7. Increasing temperature favours the formation of **31** (entries 8, 10, 12, and 13).

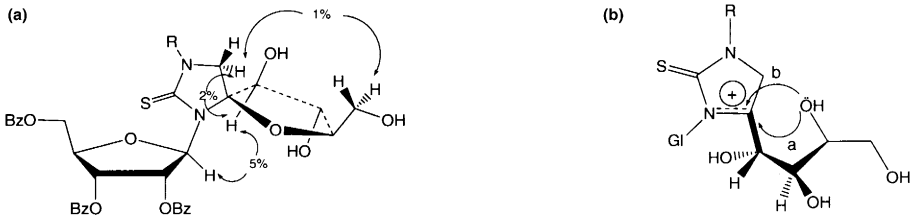


Fig. 2. (a) NOE experiments on **34**, **35**; (b) intermediate cation for the β-elimination and cyclodehydration

Table 2
Reaction conditions to obtain **35**, **36**

Entry	Catalyst	Solvent	Temp.(°C)	Time	Ratio (a) **14**:**35**+**36**:byproducts
1	F_3CCO_2H	F_3CCO_2H	rt	2 h	61:0:49
2	F_3CCO_2H (10 %)	EtOH	rt	8 h	90:7:3
3	F_3CCO_2H (10 %)	EtOH	4	4 days	88:7:5
4	F_3CCO_2H (65 %)	H_2O	rt	2 h	45:20:35
5	F_3CCO_2H (65 %)	EtOH	- 30	6 h	49:30:21
6	Dowex 50W-X8	EtOH	rt	-	no reaction
7	Dowex 50W-X8	EtOH	45	4 h	58:42:0
8	Dowex 50W-X8	EtOH	65	30 min	62:27:11
9	Dowex 50W-X8	EtOH:H_2O 3:1	45	40 min	64:21:15
10	Dowex 50W-X8	DMF	45	30 h	75:6:19
11	AcOH (30 %)	EtOH	rt	(b)	(b)
12	AcOH (20 %)	EtOH	45	20 h	65:32:3
13	AcOH (20 %)	EtOH	65	15 h	71:23:6

(a) Measured by digital integration of ^{1}H-NMR signals. (b) The starting material does not disappear after 14 days.

3. Conclusion

The reaction of D-fructosamine with glycosyl isothiocyanates and with a 2-deoxy-2-isothiocyanato sugar is a convenient way to the stereoselective preparation of *N*-nucleosides **11**–**21** or pseudonucleosides **22**, **23** of chiral imidazolidine-2-thiones. Acid-catalysed dehydration reactions of these imidazolidine-2-thiones are an inexpensive method for the stereocontrolled preparation of imidazolidine-2-thione spironucleosides having an *N*-glycosyl subtituent **34**–**37** and of imidazoline-2-thione *N*-nucleosides **27**–**31**. Either spironucleosides or *N*-nucleosides were obtained depending on the catalyst, solvent and temperature of reaction.

4. Experimental

4.1. General methods

Melting points are uncorrected. Optical rotations were measured for solutions in dichloromethane. FT-IR spectra were recorded for KBr discs or thin film. ^{1}H NMR spectra (500 MHz) were obtained for solutions in $CDCl_3$, DMSO-d_6, MeOH-d_4 or $(CD_3)_2CO$. Assignments were confirmed by homonuclear 2D COSY correlated and NOE experiments. ^{13}C NMR spectra were recorded at 125.7 MHz. Heteronuclear 2D correlated spectra were obtained in order to assist in carbon resonance assignments. Mass spectra (EI and FAB) were recorded with Kratos MS-80RFA and Micromass AutoSpecQ instruments with a resolution of 1 000 or 10 000 (10% valley definition). For the FAB spectra, ions were produced by a beam of xenon atoms (6–7 KeV), using 3-nitrobenzyl alcohol and thioglycerol as matrix and NaI as salt. TLC was performed on silica gel HF_{254}, with detection by UV light or charring with H_2SO_4. Silica gel 60 (Merck, 70–230 and 230–400 mesh) was used for preparative chromatography.

4.2. Preparation of *11*–*25*

*Method a (for compounds **11**–**13**, **17**, **18**, **20** and **22**)*: A solution of the corresponding amino fructose acetate[22] **1** for **11**, **12**, **17**, **20** and **22**; **2** for **13** and **18** (0.257 mmol) and 22 mg (0.257 mmol) $NaHCO_3$ in

water (2.6 mL) at rt was gradually added to a stirred solution of 0.257 mmol of phenyl isothiocyanate **5** for **11**, 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl isothiocyanate **6**[23] for **12** and **13**, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **8**[24] for **17** and **18**, 2,3,4-tri-*O*-benzoyl-β-D-ribopyranosyl isothiocyanate **9**[25] for **20**, and 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isothiocyanato-β-D-glucopyranose **10**[26] for **22** in DMF (2.6 mL). The solution was stirred at rt for *t* min and then concentrated. The residues were purified by column chromatography to yield the products as amorphous solids.

*Method b (for compounds **14–16**, **19**, **21** and **23**)*: A solution of 1-*p*-tolylamino-1-deoxy-D-fructose[27] **3** for **14**, **16**, **19**, **21** and **23**; 1-*p*-ethoxyphenylamino-L-deoxy-D-fructose[27] **4** for **15** (0.257 mmol) in DMF (2.6 mL) at rt, was gradually added to a stirred solution of 0.257 mmol of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl isothiocyanate **6**[23] for **14** and **15**, 2,3,5-tri-*O*-benzoyl-β-D-xylofuranosyl isothiocyanate **7**[23] for **16**, 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **8**[24] for **19**, 2,3,4-tri-*O*-benzoyl-β-D-ribopyranosyl isothiocyanate **9**[24] for **21**, and 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isothiocyanato-β-D-glucopyranose **10**[26] for **23** in DMF (2.6 mL). The solution was stirred at rt for *t* hours and then concentrated. The residues were purified by column chromatography to yield the products as amorphous solids.

*4.2.1. (5*R,S*)-5-Hydroxy-1-phenyl-5-(*D-arabino-*tetritol-1-yl)imidazolidine-2-thione **11***

R:*S* (3:1); *t*=15 min; chromatography eluent dichloromethane:methanol (15:1); yield 0.080 g (99%); IR ν_{max} 3295, 2930, 1591, 1545, 1499, 1400, 1084 and 1034 cm^{-1}; ^1H NMR (MeOH-d_4) δ 7.41–7.19 (m, 5H, Ph), 4.48 (d, 1H, $J_{4a,4b}$=12.3, H-4a), 4.35 (d, 1H, H-4b), 4.01 (dd, 1H, $J_{3',4'}$=0, $J_{4'a,4b'}$=12.4, H-4′a), 3.86 (m, 1H, H-3′), 3.81 (dd, 2H, $J_{2',3'}$=3.4, H-2′), 3.70 (d, 1H, $J_{1',2'}$=9.7, H-1′) and 3.62 (m, 1H, H-4′b) ppm; ^{13}C NMR (MeOH-d_4) δ 183.0 (C-2), 132.4–129.3 (6C, Ph), 96.9 (C-5), 73.1 (C-1′), 71.6 (C-3′), 69.8 (C-2′), 64.8 (C-4′), 52.6 (C-4); FABMS *m/z* 337 $[M+Na]^+$; HRFABMS calcd for $C_{13}H_{18}N_2O_5SNa$: 337.0834; found: 337.0846.

*4.2.2. 5(*R,S*)-5-Hydroxy-5-(*D-arabino-*tetritol-1-yl)-1-(2′,3′,4′-tri-*O-*benzoyl-β-*D-*ribofuranosyl)imidazolidine-2-thione **12***

R:*S* (4:1); *t*=15 min; chromatography eluent dichloromethane:methanol (15:1); yield 0.161 g (92%); IR ν_{max} 3339, 3065, 2928, 1723, 1560, 1510, 1451, 1316, 1269, 1105 and 1026 cm^{-1}; ^1H NMR (MeOH-d_4) δ 8.09–7.37 (m, 15 H, 3 Ar), 6.49 (bs, 1 H, H-1′), 5.80 (t, 1H, $J_{2',3'}=J_{3',4'}$=5.0, H-3′), 5.60 (bs, 1H, H-2′), 4.65–4.56 (m, 3H, H-4′, H-5′a, H-5′b), 4.19 (d, 1H, $J_{4a,4b}$=13.7, H-4a), 3.98 (dd, 1H, $J_{3'',4''a}$=1.0, $J_{4''a,4''b}$=11.3, H-4′′a), 3.81 (ddd, 1H $J_{2'',3''}$=3.4, $J_{3'',4''b}$=1.7, H-3′′), 3.76 (dd, 1H, $J_{1'',2''}$=9.9, H-2′′), 3.60 (dd, 1H, H-4′′b) and 3.45 (d, 1H, H-4b) ppm; ^{13}C NMR (MeOH-d_4) δ 185.7 (C-2), 167.7, 166.8, 166.7 (3C, 3*C*OPh), 134.7–129.6 (18C, 3 Ph), 98.9 (C-5), 87.7 (C-1′), 79.9 (C-4′), 75.5 (C-2′), 73.0 (C-3′), 71.2 (C-2′′), 70.9 (C-3′′), 70.3 (C-1′′), 65.6 (C-5′), 664.1 (C-4′′) and 51.4 (C-4) ppm; FABMS *m/z* 683 $[M+H]^+$, 705 $[M+Na]^+$; HRFABMS calcd for $C_{33}H_{35}N_2O_{12}S$: 683.1911; found: 683.1963. Anal. calcd for $C_{33}H_{34}N_2O_{12}S$: C, 58.06; H, 5.02; N, 4.10; S, 4.70. Found: C, 58.33; H, 5.14; N, 4.04; S, 4.38.

*4.2.3. 5(*R,S*)-5-Hydroxy-3-methyl-5-(*D-arabino-*tetritol-1-yl)-1-(2′,3′,4′-tri-*O-*benzoyl-β-*D-*ribofuranosyl)imidazolidine-2-thione **13***[28]

R:*S* (4:1); *t*=15 min; chromatography eluent dichloromethane:methanol (20:1); yield 0.150 g (84%); IR ν_{max} 3292, 2928, 1717, 1526, 1273, 1115 and 1020 cm^{-1}; ^1H NMR (Me_2CO-d_6) δ 8.06–7.30 (m, 15H, Ar), 6.91 (dd, 1H, $J_{1',2'}$=3.7, $J_{2',3'}$=6.9, H-2′), 6.41 (t, 1H, $J_{3',4'}$=6.9, H-3′), 5.93 (d, 1H, H-1′), 4.77–4.68 (m, 2H, H-5′a, H-5′b), 4.60 (dt, 1H, $J_{4',5'a}=J_{4',5'b}$=5.0, H-4′), 4.39 (d, 1H, $J_{4a,4b}$ =12.0, H-4a), 4.30 (dd, 1H, $J_{1'',2''}$=1.2, $J_{1'',HO}$=5.7, H-1′′), 3.95 (td, 1H, $J_{2'',3''}=J_{2'',HO}$=8.0, H-2′′), 3.77 (m, 1H, H-3′′), 3.73–3.58 (m, 2H, H-4′′a, H-4′′b), 3.49 (d, 1H, H-4b) and 2.81 (s, 3H, CH_3) ppm; ^{13}C

NMR (Me_2CO-d_6) δ 180.7 (C-2), 166.7, 165.9, 165.5 (3C, 3*C*OPh), 130.5–129.2 (18C, 3 Ar), 92.6 (C-5), 89.1 (C-1′), 78.9 (C-4′), 73.4 (C-2′), 72.7 (C-3′′), 71.8 (C-2′′), 71.6 (C-3′), 70.4 (C-1′′), 64.8 (C-5′), 64.7 (C-4′′), 58.0 (C-4) and 33.9 (CH_3) ppm; FABMS *m/z* 719 $[M+Na]^+$; HRFABMS calcd for $C_{34}H_{36}N_2O_{12}SNa$: 719.1887; found: 719.1920. Anal. calcd for $C_{34}H_{36}N_2O_{12}S$: C, 58.61; H, 5.20; N, 4.02. Found: C, 58.81; H, 5.21; N, 4.01.

*4.2.4. 5(*R,S*)-5-Hydroxy-5-(*D-arabino*tetritol-1-yl)-3-*p-*tolyl-1-(2′,3′,4′-tri-*O-*benzoyl-β-*D-*ribofuranosyl)imidazolidine-2-thione* **14**[28]

R:*S* (4:1); *t*=6 h; chromatography eluent dichloromethane:methanol (30:1); yield 0.184 g (93%); IR ν_{max} 3340, 2928, 1724, 1659, 1273, 1105 and 1026 cm^{-1}; ^1H NMR (Me_2CO-d_6+D_2O) δ 8.02–7.15 (m, 19H, Ar), 6.94 (dd, 1H, $J_{1',2'}$=3.3, $J_{2',3'}$=7.2, H-2′), 6.41 (t, 1H, $J_{3',4'}$=7.2, H-3′), 4.76 (d, 1H, $J_{4a,4b}$=11.9, H-4a), 4.74 (dd, 1H, $J_{4',5'a}$=4.7, $J_{5'a,5'b}$=13.3, H-5′a), 4.68 (dd, 1H, $J_{4',5'b}$=5.0, H-5′b), 4.63 (m, 1H, H-4′), 4.31 (d, 1H, $J_{1'',2''}$=1.2, H-1′′), 3.93 (dd, 1H, $J_{2'',3''}$=8.5, H-2′′), 3.83 (d, 1H, H-4b), 3.78 (dd, 1H, $J_{3'',4''a}$=3.6, $J_{4''a,4''b}$=11.0, H-4′′a), 3.75 (m, 1H, H-3′′), 3.62 (dd, 1H, $J_{3'',4''b}$=5.4, H-4′′b), 2.27 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 180.2 (C-2), 166.8, 165.9, 165.5 (3 C, 3*C*OPh), 138.0–126.6 (24C, 4 Ar), 92.7 (C-5), 89.2 (C-1′), 79.0 (C-4′), 73.5 (C-2′), 72.6 (C-3′′), 71.8*, 71.5* (2C, C-3′, C-2′′), 70. 6 (C-1′′), 64.7 (C-4′′), 64.6 (C-5′), 59.1 (C-4) and 21.0 ($ArCH_3$) ppm; FABMS *m/z* 773 $[M+H]^+$; HRFABMS calcd for $C_{40}H_{41}N_2O_{12}S$: 773.2380; found: 773.2355. Anal. calcd for $C_{40}H_{40}N_2O_{12}S$: C, 62.17; H, 5.22; N, 3.63. Found: C, 62.62; H, 5.66; N, 3.48.

*4.2.5. 5(*R,S*)-3-*p-*Ethoxyphenyl-5-hydroxy-5-(*D-arabino*tetritol-1-yl)-1-(2′,3′,4′-tri-*O-*benzoyl-β-*D-*ribofuranosyl)imidazolidine-2-thione* **15**[28]

R:*S* (7:3); *t*=3 h; chromatography eluent dichloromethane:methanol (30:1); yield 0.187 g (91%); IR ν_{max} 3314, 2928, 1732, 1651, 1514, 1273, 1103 and 1028 cm^{-1}; ^1H NMR (Me_2CO-d_6+D_2O) δ 8.06–6.91 (m, 19H, Ar), 6.97 (dd, 1H, $J_{1',2'}$=3.6, $J_{2',3'}$=7.0, H-2′), 6.45 (t, 1H, $J_{3',4'}$=7.0, H-3′), 4.80 (d, 1H, $J_{4a,4b}$=11.9 H-4a), 4.79 (dd, 1H, $J_{4',5'a}$=4.3, $J_{5'a,5'b}$=11.7, H-5′a), 4.72 (dd, 1H, $J_{4',5'b}$=5.5, H-5′b), 4.65 (m, 1H, H-4′), 4.41 (d, 1H, $J_{1'',2''}$<1, H-1′′), 4.05 (q, 2H, $^3J_{H,H}$=7.0, CH_2CH$_3$), 4.02–3.64 (m, 3H, H-3′′, H-4′′a, H-4′′b), 3.85 (d, 1H, H-4b) and 1.35 ppm (t, 3H, CH_2CH_3); ^{13}C NMR (Me_2CO-d_6+D_2O) δ 180.1 (C-2), 166.5, 165.7, 165.2 (3C, 3*C*OPh), 163.5–114.8 (24C, 4 Ar), 92.5 (C-5), 88.9 (C-1′), 78.7 (C-4′), 73.2 (C-2′), 72.4*, 71.6*, 71.3* (3C, C-3′, C-2′′, C-3′′), 70.4 (C-1′′), 64.8 (C-5′), 64.5 (C-4′′), 64.0 (*C*H$_2$CH$_3$), 59.2 (C-4) and 14.8 (CH_2CH_3) ppm; FABMS *m/z* 825 $[M+Na]^+$; HRFABMS calcd for $C_{41}H_{42}N_2O_{13}SNa$: 825.2305; found: 825.2276. Anal. calcd for $C_{41}H_{42}N_2O_{13}S$: C, 61.34; H, 5.27; N, 3.49; S, 3.99. Found: C, 61.24; H, 5.36; N, 3.54; S, 4.47.

*4.2.6. 5(*R,S*)-5-Hydroxy-5-(*D-arabino*tetritol-1-yl)-3-*p-*tolyl-1-(2′,3′,5′-tri-*O-*benzoyl-β-*D-*xylofuranosyl)imidazolidine-2-thione* **16**[28]

R:*S* (7:3); *t*=10 h; chromatography eluent dichloromethane:methanol (25:1); yield 0.176 g (89%); IR ν_{max} 3357, 2924, 1716, 1653, 1539, 1456, 1105 and 1066 cm^{-1}; ^1H NMR of *R* isomer (Me_2CO-d_6+D_2O) δ 8.13–7.44 (m, 19H, 4 Ar), 7.12 (dd, 1H, $J_{1',2'}$=6.3, $J_{2',3''}$=2.5, H-2′), 6.28 (d, 1H, H-1′), 6.02 (dd, 1H, $J_{3',4''}$=5.9, H-3′), 4.90 (ddd, 1H, $J_{4',5'a}$=6.4, $J_{4',5'b}$=5.6, H-4′), 4.80 (dd, 1H, $J_{5'a,5'b}$=11.6), 4.72 (d, 1H, $J_{4a,4b}$=11.8, H-4a), 4.70 (dd, 1H, H-5′b), 4.54 (d, 1H, $J_{1'',2''}$=1.2, H-1′′), 4.05 (dd, 1H, $J_{2'',3''}$=8.1, H-2′′), 3.80 (dd, 1H, $J_{3'',4''a}$=4.0, $J_{4''a,4''b}$=10.7, H-4′′a), 3.77 (d, 1H, H-4b), 3.73 (m, 1H, H-3′′), 3.68 (dd, 1H, $J_{3'',4''b}$5.2, H-4′′b) and 2.28 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 185.1 (C-2), 171.1, 170.6, 170.5 (3C, 3 *C*OPh), 143.2–130.9 (24C, 4 Ar), 97.3 (C-5), 93.3 (C-1′), 83.7 (C-3′), 83.1 (C-2′), 81.0 (C-4′), 77.0 (C-3′′), 75.5 (C-2′′), 74.3 (C-1′′), 68.6 (C-4′′), 67.5 (C-5′), 63.1 (C-4) and 25.2 ($ArCH_3$) ppm; FABMS *m/z* 795 $[M+Na]^+$; HRFABMS calcd for $C_{40}H_{40}N_2O_{12}SNa$: 795.2200; found:

795.2218. Anal. calcd for $C_{40}H_{40}N_2O_{12}S$: C, 62.17; H, 5.22; N, 3.63. Found: C, 62.22; H, 5.01; N, 3.48. ^{1}H NMR data of *S* isomer (Me_2CO-d_6+D_2O) δ 8.13–7.44 (m, 19H, 4 Ar), 6.93 (d, 1H, $J_{1',2'}$=5.9, H-1′), 6.74 (dd, 1H, $J_{2',3''}$=2.3, H-2′), 5.91 (dd, 1H, $J_{3',4''}$=4.9, H-3′), 4.86 (d, 1H, $J_{4a,4b}$=11.2, H-4a), 4.79 (m, 1H, H-4′), 4.75 (dd, 1H, $J_{4',5'a}$=5.8, $J_{5'a,5'b}$=10.9, H-5′a), 4.70 (m, 1 H, H-5′b), 4.70 (bs, 1H, H-1′′), 4.02 (dd, 1H, $J_{1'',2''}$=0.6, $J_{2'',3''}$=6.7, H-2′′), 3.78–3.73 (m, 2H, H-3′′, H-4′′a), 3.77 (d, 1H, H-4b), 3.64 (m, 1H, H-4′′b) and 2.28 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 186.3 (C-2), 171.0, 170.5, 170.4 (3C, 3 *C*OPh), 143.2–130.9 (24C, 4 Ar), 98.3 (C-5), 94.7 (C-1′), 83.8 (C-2′), 82.1 (C-3′), 80.8 (C-4′), 77.7 (C-3′′), 77.1 (C-1′′), 75.4 (C-2′′), 68.3 (C-4′′), 67.2 (C-5′), 64.3 (C-4) and 25.2 ($ArCH_3$) ppm.

*4.2.7. (5*R,S*)-5-Hydroxy-1-(2′,3′,4′,6′-tetra*-O-*acetyl-β*-D-*glucopyranosyl)-5-(*D-arabino*tetritol-1-yl)-imidazolidine-2-thione* ***17***

R:*S* (3:1); *t*=15 min; chromatography eluent dichloromethane:methanol (6:1); yield 0.139 g (95%); IR ν_{max} 3356, 2959, 1750, 1543, 1454, 1427, 1371, 1233 and 1038 cm^{-1}; ^{1}H NMR (Me_2CO-d_6+D_2O) δ 5.87 (bs, 1H, H-1′), 5.34 (t, 1H, $J_{2',3'}$=$J_{3',4'}$=9.8, H-3′), 5.02 (t, 1H, $J_{4,5}$=9.8, H-4′), 4.96 (t, 1H, $J_{1',2'}$=9.8, H-2′), 4.24 (dd, 1H, $J_{5',6'a}$=4.7, $J_{6'a,6'b}$=12.4, H-6′a), 4.18 (bd, 1H, H-4a), 4.07 (dd, 1H, $J_{5',6'b}$=2,4, H-6′b), 3.99 (ddd, 1H, H-5′), 3.94 (dd, 1H, $J_{3'',4''a}$=1.4, $J_{4''a,4''b}$=12.4, H-4′′a), 3.84 (m, 1H, H-3′′), 3.79 (dd, 1H, $J_{1'',2''}$=9.7, $J_{2'',3''}$=3.4, H-2′′), 3.61–3.55 (m, 2H, H-1′′, 4′′b), 3.46–3.40 (m, 1H, H-4b), 2.03, 2.02, 2.01 and 1.97 (each s, each 3H, 4 Ac) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 185.3 (C-2), 171.1, 171.0, 170.5, 170.3 (each 1C, 4 *C*OCH_3), 98.5 (C-5), 84.6 (C-1′), 74.0* (C-3′), 73.8* (C-5′), 71.5 (C-1′′), 70.5 (C-2′′), 70.0 (C-3′′), 69.6 (C-2′), 69.2 (C-4′), 64.0 (C-4′′), 62.7 (C-6′), 51.0 (C-4) and 20.6–20.5 (4C, 4 CO*C*H_3) ppm; FABMS *m/z* 337 [M+Na]$^+$. Anal. calcd for $C_{21}H_{32}N_2O_{14}S$: C, 44.36; H, 5.67; N, 4.93. Found: C 43.98; H, 5.44; N, 4.66.

*4.2.8. (5*R,S*)-5-Hydroxy-3-methyl-1-(2′,3′,4′,6′-tetra*-O-*acetyl-β*-D-*glucopyranosyl)-5-(*D-arabino-*tetritol-1-yl)imidazolidine-2-thione* ***18***[28]

t=10 min; chromatography eluent (dichloromethane:methanol 20:1); yield 0.141 g (94%); FABMS *m/z* 605 [M+Na]$^+$; HRFABMS calcd for $C_{22}H_{34}O_{14}N_2SNa$: 605.1628; found: 605.1654. This compound was characterised as the tetra-*O*-acetyl derivative **25**.

*4.2.9. (5*R,S*)-5-Hydroxy-1-(2′,3′,4′,6′-tetra*-O-*acetyl-β*-D-*glucopyranosyl)-5-(*D-arabino*tetritol-1-yl)-3-*p-*tolylimidazolidine-2-thione* ***19***

R:*S* (4:1); *t*=3 days; chromatography eluent dichloromethane:methanol (20:1); yield 0.163 g (96%); IR ν_{max} 3474, 3032, 2936, 1751, 1431, 1375, 1229, 1090 and 1036 cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 7.35–7.18 (m, 4H, Ar), 6.45 (d, 1H, $J_{1',2'}$=9.6, H-1′), 5.77 (t, 1H, $J_{2',3'}$=9.6, H-2′), 5.25 (t, 1H, $J_{3',4'}$=9.6, H-3′), 5.12 (t, 1H, $J_{4',5'}$=9.6, H-4′), 4.40 (m, 1H, H-6′a), 4.40–4.10 (m, 1H, H-4a, H-4b), 4.16 (m, 1H, H-6′b), 3.96–3.88 (m, 1H, H-5′), 3.91 (dd, 1H, $J_{1'',2''}$=8.7*, $J_{2'',3''}$=1.0*, H-2′′), 3.82–3.76 (m, 1H, H-3′′, 4′′a), 3.68–3.60 (m, 2H, H-1′′, 4′′b), 2.34 (s, 3H, $ArCH_3$), 2.04, 2.02, 1.99 and 1.97 (each s, each 3H, 4 Ac) ppm; ^{13}C NMR (MeOH-d_4) δ 182.8 (C-2), 172.5, 171.8, 171.3, 171.2 (each 1C, 4 *C*OCH_3), 139.0–127.4 (6C, Ar), 98.2 (C-5), 85.9 (C-1′), 76.2 (C-3′), 75.9 (C-5′), 72.4 (C-2′), 72.3 (C-1′′), 71.6 (C-3′′), 71.3 (C-2′′), 69.0 (C-4′), 64.8 (C-4′′), 63.0 (C-6′), 56.5 (C-4) and 21.1–20.5 (4C, 4 CO*C*H_3) ppm; FABMS *m/z* 681 [M+Na]$^+$. Anal. calcd for $C_{28}H_{38}N_2O_{14}S$: C, 51.06; H, 5.82; N, 4.25. Found: C, 51.33; H, 5.74; N, 3.89.

*4.2.10. 5(*R,S*)-5-Hydroxy-5-(*D-arabino*tetritol-1-yl)-1-(2′,3′,4′-tri*-O-*benzoyl-a*-D-*ribopyranosyl)-imidazolidine-2-thione* **20**

R:*S* (3:1); *t*=30 min; chromatography eluent dichloromethane:methanol (15:1); yield 0.174 g (99%); IR ν_{max} 3391, 3065, 2924, 1726, 1443, 1346, 1275, 1103 and 1024 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.68 (bs, 1H, NH), 8.00–7.40 (m, 15H, 3 Ph), 6.21 (bs, 1H, H-1′), 6.10 (m, 1H, H-3′), 5.49 (m, 1H, H-4′), 5.33 (m, 1H, H-2′), 4.14 (dd, 1H, $J_{4',5'a}$=4.7, $J_{5'a,5'b}$=11.4, H-5′a), 4.07 (m, 1H, H-5′b), 3.82–3.40 (m, 7H, H-4a, 4b, 1′′, 2′′, 3′′, 4′′a, 4′′b) ppm; ^{13}C NMR (DMSO-d_6) δ 185.7 (C-2), 165.0 (1 C, *C*OPh), 164.5 (2C, 2 *C*OPh), 133.8–128.6 (18C, 3 Ph), 96.9 (C-5), 79.7 (C-1′), 74.8 (C-1′′), 69.8 (C-4′), 69.3 (2C, C-3′, 3′′), 68.5 (C-2′), 68.3 (C-2′′), 63.0 (C-5′), 62.0 (C-4′′) and 55.9 (C-4) ppm; FABMS *m/z* 705 $[M+Na]^+$; HRFABMS calcd for $C_{33}H_{34}N_2O_{12}SNa$: 705.1730; found: 705.1792.

*4.2.11. 5(*R,S*)-5-Hydroxy-5-(*D-arabino*tetritol-1-yl)-3-*p*-tolyl-1-(2′,3′,4′-tri*-O-*benzoyl-β*-D-*ribopyranosyl)imidazolidine-2-thione* **21**[28]

R:*S* (3:1); *t*=32 h; chromatography eluent dichloromethane:methanol (15:1); yield 0.196 g (99%); IR ν_{max} 3391, 3065, 2924, 1726, 1605, 1443, 1373, 1275, 1103 and 1024 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.06–7.17 (m, 15H, 3 Ph), 7.04 (m, 1H, H-1′), 6.21 (m, 1H, H-3′), 5.48–5.42 (m, 1H, H-2′, 4′), 4.67 (d, 1H, $J_{4a,4b}$=11.3, H-4a), 4.33–4.28 (m, 1H, H-3′′), 4.22 (dd, 1H, $J_{4',5'a}$=6.6, $J_{5'a,5'b}$=13.2, H-5′a), 4.10 (m, 1H, H-5′b), 3.80 (t, 1H, $J_{1'',2''}=J_{2'',3''}$=8.3, H-2′′*), 3.74 (t, 1H, $J_{1'',2''}=J_{2'',3''}$=7.3, H-2′′*), 3.62–3.56 (m, 1H, H-4′′a), 3.52–3.47 (m, 1H, H-1′′), 3.44–3.41 (m, 1H, H-4′′b) and 2.29 (s, 1H, $ArCH_3$) ppm; ^{13}C NMR (DMSO-d_6) δ 180.4 (C-2), 165.2, 165.1, 164.4, 164.3 (each 1C, 4*C*OPh), 164.5 (2C, 2 *C*OPh), 138.1–125.6 (18C, 3 Ph), 92.8 (C-5), 82.0 (C-1′), 72.8 (C-1′′), 71.2 (C-3′′), 69.8 (C-2′), 69.1 (C-3′), 67.0 (C-4′′), 66.9 (C-2′′), 63.3 (C-4′′), 62.9 (C-5′), 58.4 (C-4) and 20.6 (Ar*C*H_3) ppm; FABMS *m/z* 795 $[M+Na]^+$; HRFABMS calcd for $C_{40}H_{40}N_2O_{12}SNa$: 795.2200; found: 795.2194.

*4.2.12. (5*R,S*)-5-Hydroxy-1-(1′,3′,4′,6′-tetra*-O-*acetyl-2-deoxy-β*-D-*glucopyranos-2-yl)-5-(*D-arabino-*tetritol-1-yl)imidazolidine-2-thione* **22**

R:*S* (5:4); *t*=40 min; chromatography eluent dichloromethane:methanol (6:1); yield 0.142 g (97%); IR ν_{max} 3352, 2936, 1559, 1429, 1375, 1227, 1080 and 1040 cm^{-1}; ^1H NMR (MeOH-d_4) δ 5.75 (bs, 1H, H-1′), 5.25 (bs, 1H, H-2′), 5.07* (t, 1H, $J_{2',3'}=J_{3',4'}$=9.9, H-3′), 5.06 (t, 1H, $J_{4,5}$=9.9, H-4′), 4.28 (dd, 1H, $J_{5',6'a}$=4.4, $J_{6'a,6'b}$=12.5, H-6′a), 4.11 (dd, 1H, $J_{5',6'b}$=4,4, H-6′b), 3.97 (m, 1H, H-4′′a), 3.93 (ddd, 1H, H-5′), 3.83 (m, 1H, H-3′′), 3.79 (dd, 1H, $J_{1'',2''}$=9.7, $J_{2'',3''}$=3.4, H-2′′), 3.55 (d, 1H, H-1′′), 3.68–3.52 (m, 3H, H-4′′b, H-4a, H-4b), 2.15, 2.11, 2.10, 2.08, 2.05, 2.01, 2.00 and 1.99 (each s, each 3 H, 8 Ac) ppm; ^{13}C NMR (MeOH-d_4) δ 184.5 (C-2), 172.3, 172.2, 171.2, 171.1, 171.0 (each 1C, C-2 and 4 *C*OCH_3), 99.1 (C-5), 94.0 (C-1′), 74.4 (C-2′), 73.7 (C-5′), 71.0* (C-3′′), 70.8* (C-2′′), 69.6 (3 C, C-3′, 4′, 1′′), 64.7 (C-4′′), 63.0 (2 C, C-4, C-6′), and 20.9, 20.7, 20.6 and 20.5 (4C, 4 CO*C*H_3) ppm; FABMS *m/z* 591 $[M+Na]^+$; HRFABMS calcd for $C_{21}H_{32}N_2O_{14}SNa$: 591.1472; found: 591.1491.

*4.2.13. (5*R,S*)-5-Hydroxy-1-(1′,3′,4′,6′-tetra*-O-*acetyl-2-deoxy-β*-D-*glucopyranos-2-yl)-3-*p*-*tolyl-5-(*D-arabino*tetritol-1-yl)imidazolidine-2-thione* **23**

R:*S* (5:4); *t*=4 days; chromatography eluent dichloromethane:methanol (6:1); yield 0.142 g (97%); IR ν_{max} 3352, 2936, 1559, 1429, 1375, 1227, 1080 and 1040 cm^{-1}; ^1H NMR (MeOH-d_4) δ 7.37–7.09 (m, 4H, Ar), 6.46 (d, 1H, $J_{1',2'}$=9.5, H-1′), 5.77 (t, 1H, $J_{2',3'}$=9.5, H-2′), 5.25 (t, 1H, $J_{3',4'}$=9.5, H-3′), 5.12 (t, 1H, $J_{4',5'}$=9.5, H-4′), 4.41 (dd, 1H, $J_{5',6'a}$=4.0, $J_{6'a,6'b}$=12.3, H-6′a), 4.34 (bs, 1H, H-1′′), 4.25 (dd, 1H, $J_{3'',4''a}$=4.7, $J_{4''a,4''b}$=12.4, H-4′′a), 4.15 (dd, 1H, $J_{5',6'b}$=2.2, H-6′b), 4.04 (dd, 1H, $J_{3'',4''b}$=2.2, H-4′′b), 3.92–3.86 (m, 1H, H-5′, 3′′), 3.92–3.79 (m, 1H, H-2′′), 3.66, (d, 1H, $J_{4a,4b}$=7.0, H-4a), 3.60 (d, 1H, H-4b), 2.37, 2.34 (each s, each 3H, 2 $ArCH_3$), 2.05, 2.04, 2.02, 2.01, 1.99, 1.98, 1.97 and 1.94 (each s, each

3H, 4 Ac) ppm; ^{13}C NMR (MeOH-d_4) δ 180.9 (C-2), 172.5, 171.8, 171.3, 171.2 (each, 1C, 4 *C*OCH$_3$), 138.7–126.2 (6C, Ar), 93.7 (C-5), 84.6 (C-1′), 73.0 (C-3′), 63.4 (C-5′), 71.3 (C-2′), 72.0 (C-1′′), 70.9 (C-3′′), 70.6 (C-2′′), 68.3 (C-4′), 63.0 (C-4′′), 62.6 (C-6′), 58.2 (C-4) and 21.6–21.1 (5C, ArCH$_3$, 4 CO*C*H$_3$) ppm; FABMS *m/z* 681 [M+Na]$^+$; HRFABMS calcd for $C_{28}H_{38}N_2O_{14}SNa$: 681.19415; found: 681.19781.

4.3. (5R,S)-5-Hydroxy-3-methyl-1-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-5-(1′′,2′′,3′′,4′′-tetra-O-acetyl-D-arabinotetritol-1-yl)imidazolidine-2-thione **25**[28] and 3-methyl-1-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-5-(1′′,2′′,3′′,4′′-tetra-O-acetyl-D-arabinotetritol-1-yl)-4-imidazoline-2-thione **26**

Compound **18** (0.257 mmol) was dissolved in dry pyridine (1.2 mL) at 0°C, acetic anhydride (0.95 mL) was added and the solution was left at rt for 8 days; column chromatography (dichloromethane:methanol 60:1) of the residue gave **25** (0.050 g, 26%) and **26** (0.138 g, 73%) as amorphous solids.

Compound **25** had IR ν_{max} 3410, 2958, 1753, 1441, 1371, 1223, 1099 and 1044 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.25 (d, 1H, $J_{1',2'}$=9.4, H-1′), 5.86 (d, 1H, $J_{1'',2''}$=2.2, H-1′′), 5.68 (dd, 1H, $J_{2'',3''}$=7.7, H-2′′), 5.46 (t, 1H, $J_{2',3'}$=9.4, H-2′), 5.38 (t, 1H, $J_{3',4'}$=9.4, H-3′), 5.17 (t, 1H, $J_{4',5'}$=9.4, H-4′), 5.13 (td, 1H, $J_{3'',4''a}$=2.8, $J_{3'',4''b}$=7.7, H-3′′), 4.40 (dd, 1H, $J_{5',6'a}$=4.5, $J_{6'a,6'b}$=12.5, H-6′a), 4.29 (dd, 1H, $J_{5',6'b}$=2.4, H-6′b), 4.25, (d, 1H, $J_{4a,4b}$=12.0, H-4a), 4.17 (dd, 1H, $J_{4''a,4''b}$=12.3, H-4′′a), 3.97 (ddd, 1H, H-4′), 3.94 (dd, 1H, H-4′′b), 3.17 (d, 1H, H-4b), 2.15, 2.13, 2.09, 2.06, 2.04, 2.02, 2.01 and 2.00 (each s, each 3H, 8 Ac) ppm; ^{13}C NMR (CDCl$_3$) δ 180.3 (C-2), 170.8, 170.4, 170.0, 169.4, 168.2 (each 1C, 5 *C*OCH$_3$), 169.6 (3C, 3 *C*OCH$_3$), 91.6 (C-5), 85.0 (C-1′), 75.1 (C-5′), 73.9 (C-2′), 72.6 (C-3′), 72.4 (C-1′′), 68.7 (2, C, C-4′, 2′′), 67.8 (C-3′′), 62.3 (C-4′′), 61.7 (C-6′), 59.3 (C-4), 29.6 (N-*C*H$_3$) and 20.8–20.3 (8C, 8 CO*C*H$_3$) ppm; FABMS *m/z* 773 ([M+Na]$^+$); HRFABMS calcd for $C_{30}H_{42}N_2O_{18}SNa$: 773.2051; found: 773.2058.

Compound **26** had $[\alpha]_D^{19}$ +35 (*c* 0.8); IR ν_{max} 2953, 1750, 1439, 1373, 1217, 1098 and 1040 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.80 (s, 1H, H-4), 6.62 (d, 1H, $J_{1'',2''}$=4.7, H-1′′), 6.45 (d, 1H, $J_{1',2'}$=9.2, H-1′), 5.53–5.43 (m, 3H, H-2′, 3′, 2′′), 5.20–5.13 (m, 2H, H-4′, 3′′), 4.45 (dd, 1H, $J_{5',6'a}$=6.3, $J_{6'a,6'b}$=12.5, H-6′a), 4.21 (dd, 1H, $J_{5',6'b}$=2.5, H-6′b), 4.16 (m, 1H, H-4′′a), 3.98–3.92 (m, 1H, H-4′′b), 3.54 (s, 3H, N-CH$_3$), 2.17, 2.15, 2.13, 2.12, 2.07, 2.03, 2.01 and 1.93 (each s, each 3H, 8 Ac) ppm; ^{13}C NMR (CDCl$_3$) δ 170.4, 170.3, 170.0, 169.6, 169.5, 169.3, 169.1, 168.7 (each 1C, 8 *C*OCH$_3$), 164.2 (C-2), 124.3 (C-5), 119.6 (C-4), 84.4 (C-1′), 75.2 (C-5′), 72.0 (C-3′), 70.9 (C-2′′), 70.1 (C-2′), 68.8 (C-4′), 68.1 (C-3′′), 62.8 (C-1′′), 61.8 (C-6′), 61.7 (C-4′′), 35.2 (N-*C*H$_3$) and 20.7–20.4 (8C, 8 CO*C*H$_3$) ppm; FABMS *m/z* 755 ([M+Na]$^+$; HRFABMS calcd for $C_{30}H_{40}N_2O_{17}SNa$: 755.1945; found: 755.1975.

4.4. General procedure for the preparation of **27–31**

A solution of the corresponding imidazolidine **13**–**16** and **19** (0.200 mmol) in trifluoracetic acid–ethanol (1:9) was kept at rt for *t* hours. The acid was eliminated by repeated evaporations with ethanol and the residue was purified by column chromatography.

4.4.1. 3-Methyl-5-(D-arabinotetritol-1-yl)-1-(2′,3′,5′-tri-O-benzoyl-β-D-ribofuranosyl)-4-imidazoline-2-thione **27**[28] from **13**

t=0.5 h; chromatography eluent dichloromethane:methanol (35:1); yield 0.087 g (65%); $[\alpha]_D^{25}$ −27 (*c* 0.8); IR ν_{max} 3366, 2928, 1724, 1680, 1273, 1113, 1072 and 1030 cm^{-1}; ^{1}H NMR (Me$_2$CO-d_6) δ 8.06–7.36 (m, 15H, 3 Ar), 7.12 (s, 1H, H-4), 7.05 (d, 1H, $J_{1',2'}$=5.2, H-1′), 6.56 (dd, 1H, $J_{2',3'}$=7.0,

H-2′), 6.14 (t, 1H, $J_{3',4'}$=7.0, H-3′), 5.29 (d, 1H, $J_{1'',HO}$=8.2, H-1′′), 4.85 (d, 2H, $J_{4',5'a}=J_{4',5'b}$=5.5, H-4′a, 5′b), 4.74 (m, 1H, H-4′), 3.87 (t, 1H, $J_{3'',HO}=J_{2'',3''}$=7.0, H-2′′), 3.77 (m, 2H, H-3′′, H-4′′a), 3.67 (m, 1H, H-4′′b) and 2.82 (s, 3H, CH_3) ppm; ^{13}C NMR (Me_2CO-d_6) δ 170.9 (C-2), 170.0 (2C 2 COBz, 169.9, (1C, COBz), 138.5–133.3 (19C, 3 Ar and C-5), 123.1 (C-4), 94.9 (C-1′), 84.3 (C-4′), 78.4* (C-2′), 78.3* (C-2′′), 76.4 (C-3′′), 75.8 (C-3′), 69.3 (C-5′), 69.1 (C-4′′), 68.4 (C-1′′) and 39.1 (CH_3); FABMS *m/z* 701 ($[M+Na]^+$; HRFABMS calcd for $C_{34}H_{34}N_2O_{11}SNa$: 701.1781; found: 701.1771. Anal. calcd for $C_{34}H_{34}N_2O_{11}S$: C, 60.17; H, 5.05; N, 4.13. Found: C, 59.90; H, 5.17; N, 4.03.

*4.4.2. 5-(*D-arabino*tetritol-1-yl)-1-3*-p-*Tolyl-(2′,3′,5′-tri*-O-*benzoyl-β*-D-*ribofuranosyl)-4-imidazoline-2-thione* ***28****[28] from* ***14***

t=8 h; chromatography eluent (dichloromethane:methanol 30:1); yield 0.116 g (77%); $[\alpha]_D^{25}$ −32 (*c* 0.7); IR ν_{max} 3393, 3061, 2924, 1724, 1653, 1547, 1406, 1354, 1111, 1069 and 1030 cm^{-1}; ^{1}H NMR (Me_2CO-d_6+D_2O) δ 8.02–7.27 (m, 19H, 4 Ar), 7.24 (s, 1H, H-4), 7.12 (d, 1H, $J_{1',2'}$=5.1, H-1′), 6.60 (dd, 1H, *J*2′,3′0=7.3, H-2′), 6.14 (t, 1H, $J_{3',4'}$=7.3, H-3′), 5.31 (bs, 1H, H-1′′), 4.85 (d, 2H, $J_{4',5'a}=J_{4',5'b}$=5.6, H-4′a, 5′b), 4.76 (m, 1H, H-4′), 3.89 (dd, 1H, $J_{1'',2''}$=1.4, $J_{2'',3''}$=8.0, H-2′′), 3.76 (m, 1H, H-3′′), 3.76 (dd, 1H, $J_{3'',4''a}$=3.5, $J_{4''a,4''b}$=12.5, H-4′′a), 3.64 (dd, 1H, $J_{3'',4''b}$=6.7, H-4′′b) and 2.34 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 166.8 (C-2), 165.9, 165.7, 165.5 (each 1C, 3 *C*OBz), 138.8–129.2 (25C, 4 Ar and C-5), 118.9 (C-4), 90.7 (C-1′), 79.8 (C-4′), 73.9 (C-2′), 73.3 (C-2′′), 71.8 (C-3′′), 71.5 (C-3′), 65.0 (C-5′), 64.4 (C-4′′), 63.9 (C-1′′) and 21.0 ($ArCH_3$); FABMS *m/z* 755 ($[M+H]^+$) HRFABMS calcd for $C_{40}H_{39}N_2O_{11}S$: 755.2275; found: 755.2276.

4.4.3. 3-p-*Ethoxyphenyl-5-(*D-arabino*tetritol-1-yl)-1-(2′,3′,5′-tri*-O-*benzoyl-β*-D-*ribofuranosyl)-4-imidazoline-2-thione* ***29****[28] from* ***15***

t=0.5 h; chromatography eluent dichloromethane:methanol (70:1); yield 0.109 g (70%); $[\alpha]_D^{25}$ −28 (*c* 0.9); IR ν_{max} 3314, 2924, 1724, 1680, 1545, 1273, 1103, 1072 and 1030 cm^{-1}; ^{1}H NMR (Me_2CO-d_6) δ 7.99–6.98 (m, 19H, 4 Ar), 7.22 (s, 1H, H-4), 7.18 (d, 1H, $J_{1',2'}$=5.1, H-1′), 6.59 (dd, 1H, $J_{2',3'}$=7.1, H-2′), 6.15 (t, 1H, $J_{3',4'}$=7.1, H-3′), 5.37 (d, 1H, $J_{1'',HO}$=8.5, H-1′′), 4.87 (d, 2H, $J_{4',5'a}=J_{4',5'b}$=5.7, H-4′a, 5′b), 4.80 (m, 1H, H-4′), 4.09 (q, 2H, $^3J_{H,H}$=7.0, CH_2CH$_3$), 3.95 (dd, 1H, $J_{3'',HO}=J_{2'',3''}$=6.9, H-2′′), 3.80–3.75 (m, 2H, H-3′′, H-4′′a), 3.68 (m, 1H, H-4′′b) and 1.37 (t, 1H, CH$_2$CH_3) ppm; ^{13}C NMR (Me_2CO-d_6) δ 166.7 (C-2), 166.3, 165.9, 165.7 (each 1C, 3 *C*OBz), 138.8–115.3 (25C, 4 Ar and C-5), 119.0 (C-4), 90.9 (C-1′), 80.1 (C-4′), 74.2 (C-2′), 73.8 (C-2′′), 72.0 (C-3′′), 71.5 (C-3′), 65.1 (C-5′), 64.9 (C-4′′), 64.4 (*C*H$_2$CH$_3$), 64.3 (C-1′′) and 15.0 (4 (CH$_2$*C*H$_3$); FABMS *m/z* 807 ($[M+Na]^+$); HRFABMS calcd for $C_{41}H_{40}N_2O_{12}SNa$: 807.2200; found: 807.2249. Anal. calcd for $C_{41}H_{40}N_2O_{12}S$: C, 62.75; H, 5.14; N, 3.57; S, 4.08. Found: C, 62.87; H, 5.33; N, 3.55; S, 4.57.

*4.4.4. 5-(*D-arabino*tetritol-1-yl)-3*-p-*Tolyl-1-(2′,3′,5′-tri*-O-*benzoyl-β*-D-*xylofuranosyl)-4-imidazoline-2-thione* ***30****[28] from* ***16***

t=15 h; chromatography eluent dichloromethane:methanol (40:1); yield 0.105 g (70%); $[\alpha]_D^{25}$ +35 (*c* 0.7); IR ν_{max} 3315, 2936, 1722, 1514, 1454, 1366, 1269, 1072 and 1028 cm^{-1}; ^{1}H NMR (Me_2CO-d_6+D_2O) δ 8.31–7.25 (m, 19H, 4 Ar), 7.31 (d, 1H, $J_{1',2'}$=6.1, H-1′), 7.30 (s, 1H, H-4), 6.46 (dd, 1H, $J_{2',3'}$=1.7, H-2′), 6.10 (dd, 1H, $J_{3',4'}$=5.2, H-3′), 5.69 (bs, 1H, H-1′′), 5.07 (ddd, 1H, $J_{4',5'a}$=7.5, $J_{4',5'b}$=4.4, H-4′), 4.97 (dd, 1H, $J_{5'a,5'b}$=11.7, H-4′a), 4.83 (dd, 1H, H-4′b), 3.99 (dd, 1H, $J_{1'',2''}$=1.5, $J_{2'',3''}$=8.2, H-2′′), 3.90–3.85 (m, 2H, H-3′′, H-4′′a), 3.76 (dd, 1H, $J_{3'',4''b}$=5.1, $J_{4''a,4''b}$=10.7, H-4′′b) and 2.36 (s, 3H, $ArCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 170.7, 170.6, 170.4, 170.1 (each 1C, 3 *C*OBz, C-2), 142.9–130.9 (25C, 4 Ar and C-5), 123.6 (C-4), 94.9 (C-1′), 86.5 (C-2′), 83.1 (C-3′), 82.4

(C-4′), 78.7 (C-2′′), 76.3 (C-3′′), 69.2 (C-4′′), 68.2 (C-1′′), 67.3 (C-5′) and 25.3 ($ArCH_3$); FABMS *m/z* 755 $[M+H]^+$; HRFABMS calcd for $C_{40}H_{39}N_2O_{11}S$: 755.2275; found: 755.2249.

4.4.5. 1-(2′,3′,4′,6′-Tetra-O-*acetyl-β*-D-*glucopyranosyl)-5-(*D-arabino*tetritol-1-yl)-3*-p-*tolyl-4-imidazoline-2-thione **31** from **19***

t=24 h; chromatography eluent dichloromethane:methanol (30:1); yield 0.087 g (68%); $[\alpha]_D^{25}$+12 (*c* 1.0); IR ν_{max} 3447, 2930, 1748, 1514, 1418, 1370, 1229, 1109 and 1042 cm^{-1}; ^1H NMR (Me_2CO-d_6+D_2O) δ 7.38–7.25 (m, 4H, Ar), 7.14 (s, 1H, H-4), 6.68 (d, 1H, $J_{1',2'}$=9.3, H-1′), 5.80 (t, 1H, $J_{2',3'}$=9.3, H-2′), 5.50 (t, 1H, $J_{3',4'}$=9.3, H-3′), 5.42 (bs, 1H, H-1′′), 5.18 (t, 1H, $J_{4',5'}$=9.3, H-4′), 4.40 (dd, 1H, $J_{5',6'a}$=5.7, $J_{6'a,6'b}$=12.3, H-6′a), 4.23 (ddd, 1H, $J_{5',6'b}$=1.9, H-4′), 4.18 (dd, 1H, H-6′b), 3.81–3.69 (m, 3H, H-2′′, 3′′, 4′′a), 3.63 (dd, 1H, $J_{3'',4''b}$=5.8, $J_{4''a,4''b}$=10.2, H-4′′b), 2.33 (s, 3H, $ArCH_3$), 2.03, 2.02, 1.96 and 1.89 (each s, each 3H, 4 $COCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6+D_2O) δ 171.7, 170.7, 170.6, 170.5 (each 1C, 4 *C*OCH_3), 165.2 (C-2), 138.9–126.7 (7C, 1 Ar and C-5), 119.8 (C-4), 85.1 (C-1′), 75.6 (C-5′), 73.4 (C-3′), 73.3 (C-2′′), 72.2 (C-2′), 71.9 (C-3′′), 68.9 (C-4′), 64.4 (C-4′′), 64.2 (C-1′′), 63.0 (C-6′), 20.9 ($ArCH_3$), 20.7, 20.6, 20.5 and 20.4 (4 $COCH_3$); FABMS *m/z* 641 $[M+H]^+$; HRFABMS calcd for $C_{28}H_{37}N_2O_{13}S$: 641.2016; found: 641.2021.

*4.5. Acetylation of compounds **28** and **31***

The imidazolines **28** and **31** (0.100 mmol) were dissolved in dry pyridine (0.5 mL) at 0°C and acetic anhydride was then added. The solution was kept at 4°C for 24 h, worked up by the conventional method, and purified by column chromatography to give the corresponding derivatives **32** and **33**, respectively, in quantitative yield.

4.5.1. 5-(1′′,2′′,3′′,4′′-Tetra-O-*acetyl*-D-arabino*tetritol-1-yl)-3*-p-*tolyl-1-(2′,3′,5′-tri*-O-*benzoyl-β*-D-*ribofuranosyl)-4-imidazoline-2-thione **32**[28]*

Chromatography eluent ether: hexane (3:2); $[\alpha]_D^{25}$ −43 (*c* 1.0); IR ν_{max} 3061, 2924, 1740, 1651, 1516, 1406, 1369, 1103, 1068 and 1030 cm^{-1}; ^1H NMR (Me_2CO-d_6) δ 8.06–7.29 (m, 19H, 4 Ar), 7.37 (s, 1H, H-4), 7.12 (d, 1H, $J_{1',2'}$=5.5, H-1′), 6.40 (dd, 1H, *J*2′,3′=7.4, H-2′), 6.32 (d, 1H, $J_{1'',2''}$=4.1, H-1′′), 6.14 (t, 1H, $J_{3',4'}$=7.4, H-3′), 5.73 (dd, 1H, $J_{2'',3''}$=7.9, H-2′′), 5.31 (ddd, 1H, $J_{3'',4''a}$=2.7, $J_{3'',4''b}$=5.8, H-3′′), 5.00 (dd, 1H, $J_{4',5'a}$=4.4, $J_{5'a,5'b}$=11.8, H-4′a), 4.93 (dd, 1H, $J_{4',5'b}$=6.4, H-4′b), 4.86 (ddd, 1H, H-4′), 4.27 (dd, 1H, $J_{4''a,4''b}$=12.4, H-4′′a), 4.12 (dd, 1H, H-4′′b), 2.37, (s, 3H, $ArCH_3$), 2.11, 2.08, 2.06 and 1.88 (each s, each 3H, 4 $COCH_3$) ppm; ^{13}C NMR (Me_2CO-d_6) δ 170.6 (2C, 2 *C*OCH_3), 170.3, 169.9 (each 1C, 2 $COCH_3$), 166.6 (C-2), 166.5, 165.7, 165.6 (each 1C, 3 *C*OBz), 139.2–125.9 (25C, 4 Ar and C-5), 120.7 (C-4), 90.5 (C-1′), 80.2 (C-4′), 73.9 (C-2′), 71.2 (C-3′), 70.5 (C-2′′), 70.1 (C-3′′), 65.7 (C-1′′), 64.9 (C-5′), 62.7 (C-4′′), 21.1, 20.9, 20.7, 20.6 and 20.5 (5C, 4 CO*C*H_3, $ArCH_3$); FABMS *m/z* 923 $[M+H]^+$, 945 $[M+Na]^+$; HRFABMS calcd for $C_{48}H_{46}N_2O_{15}SNa$: 945.2516; found: 945.2524.

4.5.2. 5-(1′′,2′′,3′′,4′′-Tetra-O-*acetyl*-D-arabino*tetritol-1-yl)-1-(2′,3′,4′,6′-tetra*-O-*acetyl-β*-D-*glucopyranosyl)-3*-p-*tolyl-4-imidazoline-2-thione **33***

Chromatography eluent dichloromethane:methanol (100:1); $[\alpha]_D^{25}$ +1 (*c* 0.7); IR ν_{max} 2953, 1734, 1653, 1541, 1456, 1103 and 1061 cm^{-1}; ^1H NMR (Me_2CO-d_6) δ 7.31 (m, 4H, Ar), 7.28 (s, 1H, H-4), 6.74 (d, 1H, $J_{1'',2''}$=4.0, H-1′′), 6.63 (d, 1H, $J_{1',2'}$=9.3, H-1′), 5.66 (t, 1H, $J_{2',3'}$=, $J_{3',4'}$=9.3, H-3′), 5.53 (dd, 1H, $J_{2'',3''}$=8.9, H-2′′), 5.23 (ddd, 1H, $J_{3'',4'a'}$=2.6, $J_{3'',4''b}$=6.2, H-3′′), 5.22 (t, 1H, $J_{4',5'}$=9.3, H-4′), 4.50 (dd, 1H, $J_{5',6'a}$=6.4, $J_{6'a,6'b}$=12.2, H-6′a), 4.43 (ddd, 1H, $J_{5',6'b}$=2.5, H-4′), 4.26 (dd, 1H, H-6′b), 4.25 (dd, 1H, $J_{4''a,4''b}$=12.4, H-4′′a), 4.16 (dd, 1H, H-4′′b), 2.37 (s, 1H, $ArCH_3$), 2.13, 2.11, 2.08,

2.07, 2.06, 2.00, 1.95 and 1.87 (each s, each 3H, 8 Ac) ppm; ^{13}C NMR (Me_2CO-d_6) δ 170.8, 170.7, 170.4, 170.3, 170.2, 170.1, 169.8, 169.7 (each 1C, 8 *C*OCH$_3$), 166.9 (C-2), 139.3–126.2 (7C, Ar, C-5), 121.2 (C-4), 85.2 (C-1′), 75.9 (C-5′), 72.6 (C-3′), 72.4 (C-2′), 71.1 (C-2′′), 69.5 (2C, C-4′, C-3′′), 64.2 (C-1′′), 63.2 (C-6′), 62.9 (C-4′′) and 21.2–20.5 (8C, 8 CO*C*H$_3$, ArCH$_3$) ppm; FABMS *m/z* 809 [M+H]$^+$, 831 [M+Na]$^+$; HRFABMS calcd for $C_{36}H_{45}N_2O_{17}SNa$: 809.2439; found: 809.2447.

*4.6. General procedure for the preparation of **34**–**37***

The corresponding imidazolidine **13**–**15** (0.200 mmol) was dissolved in dry ethanol (0.5 mL), and Dowex® 50 W-X8 (1.0 m equiv.) resin and molecular sieves were added. The mixture was heated at 45°C for *t* hours. The resin was filtered off and the solution was concentrated. The residue was purified by column chromatography.

*4.6.1. (2*R*,3*S*,4*S*,5*S*)-3,4-Dihydroxy-2-hydroxymethyl-8-methyl-7-thioxo-6-(2′,3′,5′-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-1-oxa-6,8-diazaspiro[4,4]nonane **34** from **13***

t=2 h; chromatography eluent dichloromethane:methanol (30:1); yield 0.023 g (17%); $[\alpha]_D^{25}$ −33 (*c* 0.5); IR ν_{max} 3564, 2924, 1716, 1645, 1516, 1454, 1315, 1105, 1062 and 1028 cm^{-1}; ^{1}H NMR (500 MHz, Me_2CO-d_6) δ 8.07–7.27 (m, 15H, Ar), 6.90 (dd, 1H, $J_{1',2'}$=3.9, $J_{2',3'}$=7.1, H-2′), 6.34 (dd, 1H, $J_{3',4'}$=7.4, H-3′), 5.74 (d, 1H, H-1′), 5.35 (d, 1H, $J_{4,OH}$=5.1, HO-4), 4.74 (dd, 1H, $J_{4',5'a}$=4.4, $J_{5'a,5'b}$=11.8, H-5′a), 4.71 (d, 1H, $J_{3,OH}$=4.8, *H*O-3), 4.67 (dd, 1H, $J_{4',5'b}$=5.4, H-5′b), 4.59 (ddd, 1H, H-4′), 4.59 (d, 1H, $J_{9a,9b}$=11.8, H-9a), 4.44 (dd, 1H, $J_{3,4}$=8.2, H-4), 4.07 (td, 1H, $J_{2,3}$=8.0, H-3), 3.89 (td, 1H, $J_{2,CH2OH}$=2.8, H-2), 3.54 (d, 1H, H-9b), 3.83 (t, 1H, J_{CH_2OH}=6.0, CH_2O*H*), 3.44 (m, 2H, C*H*$_2$OH) and 3.10 ppm (s, 3H, Me); ^{13}C NMR (125.7 MHz, Me_2CO-d_6) δ 180.7 (C-7), 166.6, 165.6, 165.5 (3 CO), 134.1–129.2 (18C, Ar), 98.9 (C-5), 89.1 (C-1′), 82.6 (C-2), 78.8 (C-4, 4′), 73.8 (C-3), 72.8 (C-2′), 71.5 (C-3′), 64.8 (C-5′), 60.9 (CH_2OH), 56.7 (C-9) and 33.8 ppm (Me). FABMS *m/z* 701 [M+Na]$^+$; HRFABMS calcd for $C_{34}H_{34}N_2O_{11}SNa$: 701.1781; found: 701.1744. Anal. calcd for $C_{34}H_{34}N_2O_{11}S$: C, 60.17; H, 5.05; N, 4.13; S, 4.72. Found: C, 60.29; H, 5.33; N, 4.03; S, 5.49.

*4.6.2. (2*R*,3*S*,4*S*,5*S*)-3,4-Dihydroxy-2-hydroxymethyl-7-thioxo-8-(*p*-tolyl)-6-(2′,3′,5′-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-1-oxa-6,8-diazaspiro[4,4]nonane **35** and (2*R*,3*S*,4*S*,5*R*)-3,4-dihydroxy-2-hydroxymethyl-7-thioxo-8-(*p*-tolyl)-6-(2′,3′,5′-tri-*O*-benzoyl-β-*D*-ribofuranosyl)-1-oxa-6,8-diazaspiro[4,4]nonane **36** from **14***

t=4 h; column chromatography (dichloromethane:methanol 40:1) of the residue gave **35** (0.060 g, 40%, d.e. 100%) and **36** (0.009 g, 7%, d.e. 66%). Compound **35** had $[\alpha]_D^{25}$ −62 (*c* 0.7); IR ν_{max} 3649, 2924, 1717, 1653, 1541, 1489, 1103 and 1067 cm^{-1}; ^{1}H NMR (Me_2CO-d_6) δ 8.07–7.20 (m, 19H, Ar), 6.91 (dd, 1H, $J_{1',2'}$=3.8, $J_{2',3'}$=7.2, H-2′), 6.34 (t, 1H, $J_{3',4'}$=7.2, H-3′), 5.87 (d, 1H, H-1′), 5.49 (d, 1H, $J_{4,OH}$=5.2, HO-4), 4.77 (dd, 1H, $J_{4',5'a}$=4.2, $J_{5'a,5'b}$=11.8, H-5′a), 4.74 (d, 1H, $J_{3,OH}$=5.0, HO-3), 4.70 (dd, 1H, $J_{4',5'b}$=5.3, H-5′b), 4.65 (ddd, 1H, H-4′), 4.55 (dd, 1H, $J_{3,4}$=8.2, H-4), 4.51 (d, 1H, $J_{9a,9b}$=11.4, H-9a), 4.12 (td, 1H, $J_{2,3}$=8.2, H-3), 3.95 (d, 1H, H-9b), 3.94 (td, 1H, J_{2,CH_2OH}=2.8, H-2), 3.86 (dd, 1H, $J_{CH_2,OH}$=6.7 and 5.4, CH_2O*H*), 3.48 (m, 2H, C*H*$_2$OH) and 2.32 ppm (s, 3H, Me); ^{13}C NMR (Me_2CO-d_6) δ 179.8 (C-7), 166.6, 165.6, 165.5 (3 CO), 138.4–126.4 (24C, Ar), 98.9 (C-5), 89.4 (C-1′), 82.8 (C-2), 79.2 (C-4), 78.9 (C-4′), 73.8 (C-3), 72.7 (C-2′), 71.4 (C-3′), 64.8 (C-5′), 60.9 (CH_2OH), 57.7 (C-9) and 21.0 ppm (Me); FABMS *m/z* 755 ([M+H]$^+$), 777 [M+Na]$^+$; HRFABMS calcd for $C_{40}H_{38}N_2O_{11}SNa$: 777.2094; found: 777.2099. Compound **36** had^{1}H NMR (Me_2CO-d_6) δ 8.07–7.21 (m, 19H, Ar), 7.00 (dd, 1H, $J_{1',2'}$=3.3, $J_{2',3'}$=7.3, H-2′), 6.44 (t, 1H, $J_{3',4'}$=7.3, H-3′), 5.87 (bs, 1H, H-1′), 5.08 (d, 1H, $J_{4,OH}$=5.1, HO-4), 4.81 (d, 1H, $J_{3,OH}$=4.6, HO-3), 4.76 (dd, 1H, $J_{4',5'a}$=3.8, $J_{5'a,5'b}$=11.7, H-5′a), 4.65

(dd, 1H, $J_{4',5'b}$=6.4, H-5′b), 4.56 (ddd, 1H, H-4′), 4.34 (dd, 1H, $J_{3,4}$=6.5, H-4), 4.43 (m, 1H, H-3), 4.33 (d, 1H, $J_{9a,9b}$=11.7, H-9[a]), 4.11 (d, 1H, H-9b), 3.93 (dd, 1H, $J_{CH_2,OH}$=9.1 and 2.4, CH_2OH), 3.85 (m, 2H, H-2), 3.73 (m, 1H, CH*H*OH) and 2.33 ppm (s, 3H, Me); ^{13}C NMR (125.7 MHz, Me_2CO-d_6) δ 181.2 (C-7), 166.6, 165.7, 165.5 (3 CO), 137.2–126.4 (24C, Ar), 100.0 (C-5), 91.6 (C-1′), 82.7 (C-2), 82.0 (C-4), 78.7 (C-4′), 75.5 (C-3), 73.5 (C-2′), 71.0 (C-3′), 65.0 (C-5′), 62.2 (C-9), 61.2 (CH_2OH) and 21.0 ppm (Me); FABMS *m/z* 755 $[M+H]^+$, 777 $[M+Na]^+$.

*4.6.3. (2*R,*3*S,*4*S,*5*S*)-8-(*p*-*Ethoxyphenyl)-3,4-dihydroxy-2-hydroxymethyl-7-thioxo-6-(2′,3′,5′-tri*-O-*benzoyl-β*-D-*ribofuranosyl)-1-oxa-6,8-diazaspiro[4,4]nonane **37** from **15***

t=3.5 h; chromatography eluent (dichloromethane:methanol 70:1); yield 0.025 g (16%); $[\alpha]_D^{25}$ −71 (*c* 0.5); IR ν_{max} 3649, 2924, 1740, 1645, 1514, 1456, 1103 and 1001 cm^{-1}; ^{1}H NMR (500 MHz, Me_2CO-d_6) δ 8.07–7.30 (m, 19H, Ar), 6.97 (dd, 1H, $J_{1',2'}$=3.9, $J_{2',3'}$=7.2, H-2′), 6.35 (t, 1H, $J_{3',4'}$=7.2, H-3′), 5.86 (d, 1H, H-1′), 5.51 (d, 1H, $J_{4,OH}$=5.0, HO-4), 4.76 (dd, 1H, $J_{4',5'a}$=4.2, $J_{5'a,5'b}$=11.7, H-5′a), 4.69 (dd, 1H, $J_{4',5'b}$=5.4, H-5′b), 4.65 (ddd, 1H, H-4′), 4.54 (dd, 1H, $J_{3,4}$=8.3, H-4), 4.49 (d, 1H, $J_{9a,9b}$=11.4, H-9a), 4.11 (m, 1H, H-3), 3.94 (td, 1H, $J_{2,3}$=8.0, J_{2,CH_2OH}=2.7, H-2), 4.06 (q, 2H, $^3J_{H,H}$=7.0, CH_2CH$_3$), 3.93 (d, 1H, H-9b), 3.88 (dd, 1H, J_{CH_2OH}=6.8 and 5.4, CH_2OH), 3.47 (m, 2H, CH_2OH) and 1.36 ppm (t, 3H, CH_2CH_3); ^{13}C NMR (125.7 MHz, Me_2CO-d_6) δ 180.0 (C-7), 166.6, 165.6, 165.5 (3 CO), 158.5–115.2 (24C, Ar), 98.2 (C-5), 89.3 (C-1′), 82.7 (C-2), 79.1 (C-4), 78.8 (C-4′), 73.6 (C-3), 72.7 (C-2′), 71.4 (C-3′), 64.8 (C-5′), 64.2 (CH_2CH$_3$), 60.9 (CH_2OH), 58.1 (C-9) and 15.1 ppm (CH_2CH_3); FABMS *m/z* 785 $[M+H]^+$, 807 $[M+Na]^+$; HRFABMS calcd for $C_{41}H_{40}N_2O_{12}SNa$: 807.2200; found 807.2155. Anal. calcd for $C_{41}H_{40}N_2O_{12}S$: C, 62.75; H, 5.14; N, 3.57. Found: C, 62.67; H, 5.31; N, 3.57.

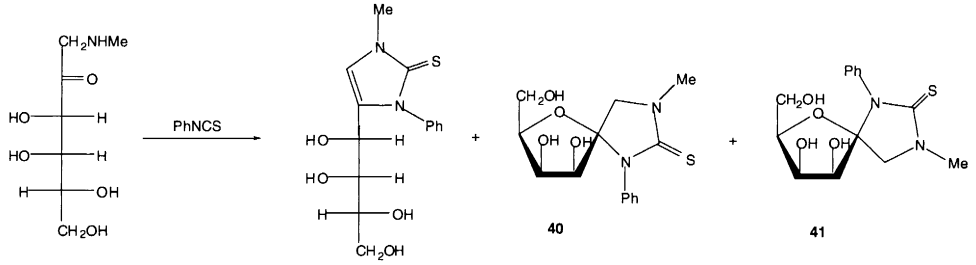
Acknowledgements

We thank the Dirección General de Investigación Científica y Técnica of Spain (grant number PB 97/0730) and the Junta de Andalucia (FQM 134) for financial support. We also thank the Ministerio de Asuntos Exteriores of Spain and the Fundación Cámara of the University of Seville for the award of grants to B.S. and J.L.M., respectively.

References

1. For a recent review on different aspects of nucleoside chemistry, see: *Carbohydrate Chemistry. Monosaccharides, Disaccharides, and Specific Oligosaccharides, No. 030*; Ferrier, R. J., Ed. Nucleosides. The Royal Society of Chemistry, 1998; pp. 268–315.
2. For example, a review on AIDS-driven nucleoside chemistry has been published by Hurin, D. N.; Ocabe, M. *Chem. Rev*. **1992**, *92*, 1745–1768.
3. Haruyama, H.; Takayanna, T.; Kinoshita, T.; Kondo, M.; Nakajima, M.; Haneishi, T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1637–1640**.**
4. The term spironucleoside was introduced into the bibliography in 1990 (see: Fernández-Bolaños, J.; Blasco López, A.; Fuentes Mota, J. *Carbohydr. Res.* **1990**, *199*, 239–242) to designate a class of sugar derivative with spiranic structure, in which the anomeric carbon simultaneously belonged to the sugar ring and to a heterocyclic base. This type of compound had been reported previously but, as far as we are aware, without the use of the term spironucleoside. Since then, this generic term has been widely used and applied to hydantocidin and related compounds. See as examples: (a) Gimisis, T.; Castellari, C.; Chatgilialoglu, C. *Chem. Commun.* **1997**, 2089–2090; (b) Sano, H.; Mio, S.; Kitagawa, J.; Shindou, M.; Honma, T.; Sugai, S. *Tetrahedron* **1995**, *46*, 12563–12572; (c) Tronchet, J. M. J.; Kovacs, I.; Barbalat-Rey, F.; Holm, M. V. *Nucleosides and Nucleotides* **1998**, *17*, 1115–1123; (d) See also Refs. 7a, 7b, 8h and 8g.

5. Nakajima, N.; Itoi, K.; Takamatsu, Y.; Okazaki, H.; Kinoshita, T.; Shindou, M.; Kawakubo, K.; Honna, T.; Toujigamori, M.; Haneishi, T. *J. Antibiot.* **1991**, *44*, 293–300.
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**, *44*, 2133–2144; (c) Nakajima, N.; Matsumoto, M.; Kirihara, M.; Hashimoto, M.; Katoh, T.; Terashima, S. *Tetrahedron* **1996**, *52*, 1177–1194.
7. (a) Sano, H.; Sugai, S. *Tetrahedron: Asymmetry* **1995**, *5*, 1143–1150; (b) *Ibidem Tetrahedron* **1995**, *51*, 4635–4646.
8. (a) Brandstetter, T. W.; Worlmad, 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.; de la Fuente, C.; Kim, Y.; Johnson, L.; Crook, S.; Lilley, P. M. de Q.; Watkin, D. J.; Tritsanou, K. E.; Zographos, S. E.; Chrysina, E. D.; Oikonomakos, N. G.; Fleet, G. W. J. *Tetrahedron* **1996**, *52*, 10721–10736; (c) Osz, E.; Sos, E.; Somsák, L.; Szilágyi, L.; Dinya, Z. *Tetrahedron* **1997**, *53*, 5813–5824; (d) Estevez, J. C.; Smith, M. D.; Worlmad, M. R.; Besra, G. S.; Brennan, P. J.; Nash, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **1996**, *7*, 391–394; (e) Estevez, J. C.; Smith, M. D.; Lane, A. L.; Crook, S.; Watkin, D. J.; Besra, G. S.; Brennan, P. J.; Nash, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **1996**, *7*, 387–390; (f) Sowa, C. E.; Stark, M.; Heildeberg, T. H.; Thiem, J. *Synlett* **1996**, 227–228; (g) Sano, H.; Mio, S.; Kitagawa, J.; Sugai, S. *Tetrahedron*: *Asymmetry* **1994**, *5*, 2233–2240; (h) Sano, H.; Mio, S.; Tsukaguchi, N.; Sugai, S. *Tetrahedron* **1995**, *51*, 1387–1394; (i) Paquette, L. A. Brand, S.; Behrens, C. *J. Org. Chem.* **1999**, *64*, 2010–2025.
9. For the synthesis of thioxo-analogues of hydantocidin see Refs. 4b and 8c. For the preparation of related spirothiazolidines, see: Osz, E.; Szilagyi, L.; Somsak, L.; Benyei, A. *Tetrahedron* **1999**, *55*, 2419–2430.
10. (a) For a review, see: García Fernández, J. M.; Ortiz Mellet, C. *Sulfur Reports* **1996**, *19*, 61–169; (b) see also Fuentes, J.; Molina, J. L.; Pradera, M. A. *Tetrahedron: Asymmetry* **1998**, *9*, 2517–2532.
11. (a) Fuentes, J.; Molina, J. L.; Olano, D.; Pradera, M. A. *Tetrahedron: Asymmetry* **1996**, *7*, 203–218; (b) Fernández-Bolaños, J. G.; Zafra, E.; Lopez, O.; Robina, I.; Fuentes, J. *Tetrahedron: Asymmetry* **1999**, *10*, 3011–3023.
12. Fernández-Bolaños, J.; Trujillo Pérez-Lanzac, M.; Fuentes Mota, J.; Viguera Rubio, F. J.; Cert Ventulá, A. *An. Quim.* **1985**, *81C*, 147–152 and references cited therein.
13. In the reaction of 1-deoxy-1-methylamino-D-lyxohexulose **38** with phenyl isothiocyanate, the imidazoline-2-thione derivative **39** (11%) and the two spiroimidazolidines **40** (7%) and **41** (1%) were isolated. See: Fernández-Bolaños, J.; Trujillo Pérez-Lanzac, M.; Fuentes Mota, J.; Cert Ventulá, A. *Carbohydr Res.* **1985**, *143*, 260–265.



38 39 40 41

14. Avalos, M.; Babiano, R.; Cintas, P.; Jimenez, J. L.; Palacios, J. C.; Valencia, C. *Tetrahedron* **1994**, 3273–3296.
15. García González, F.; Fernández-Bolaños, J.; Fuentes Mota, J. *Carbohydr. Res.* **1972**, *22*, 436–440.
16. Fuentes, J.; Cuevas, T.; Pradera, M. A. *Carbohydr. Res.* **1994**, *260*, 137–144.
17. Fernández-Bolaños Guzmán, J.; García Rodriguez, S.; Fernández-Bolaños, J.; Dianez, M. J.; López-Castro, A. *Carbohydr. Res.* **1991**, *210*, 125–143.
18. Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353–3361.
19. Fuentes, J.; Moreda, W.; Ortiz, C.; Robina, I.; Welsh, C. *Tetrahedron* **1992**, *48*, 6413–6424.
20. Katritzky, A. R. In *Handbook of Heterocyclic Chemistry*; Pergamon Press: Oxford, 1985; pp. 104–105.
21. Blanc-Muesser, M.; Defaye, J.; Horton, D. *Carbohydr. Res.* **1980**, *87*, 71–86.
22. Druey, J.; Huber, G. *Helv. Chim. Acta* **1957**, *40*, 342–349.
23. Marino, C.; Varela, O.; Lederkremer, R. M. *Carbohydr. Res.* **1997**, *304*, 257–260.
24. Babiano, R.; Fuentes, J. A.; Galbis, J. *Carbohydr. Res.* **1986**, *154*, 280–288.
25. Fuentes, J.; Pradera, M. A.; Ortiz, C.; García, J. M.; Babiano, R.; Galbis, J. A. *Carbohydr. Res.* **1988**, *173*, 1–16.
26. Jochims, J. C.; Seeliger, A. *Tetrahedron* **1965**, *21*, 2611–2616.
27. (a) Weygand, F. W. *Ber.* **1940**, *73*, 1259; (b) Huber, G.; Schier, O.; Druey, J. *Helv. Chim. Acta* **1960**, *43*, 713–717.
28. According to the IUPAC rules for the numbering of the imidazole nitrogen atoms, in compounds **13**–**16**, **18**, **21**, **25**, **27**–**30** and **32**, due to the alphabetical order of the substituents, N-1 and N-3 should be inverted; but to simplify the discussion all the compounds (**11**–**33**) have the same numbering.