Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 1, pp. 203-218, 1996

0957-4166/96 $15.00 + 0.00

0957-4166(95)00437-8

Stereoselective Synthesis of Nucleoside Analogues of Chiral Imidazolidines from Sugar Isothiocyanates

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Abstract: The syntheses of the disaccharide **5** and the trisaccharide **6** glycosyl isothiocyanates starting from di- or monosaccharide *N*-dialkoxycarbonylvinylglycosylamines **1** and **2** are described. Compounds **5**, **6**, α-(D-ribopyranosyl) and β-(D-glucopyranosyl, D-ribopyranosyl) isothiocyanates and 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isothiocyanato-β-D-glucopyranose are used in the diastereoselective synthesis of the nucleoside analogues of (5*R*)- and (5*S*)-5-hydroxyimidazolidine-2-thiones **7**, **11**, **14**, **16**, **17**, **18a**, and **18b**. The 5*R*:5*S* ratio depends on the anomeric configuration (configuration of C-2' for **18a**, **18b**) of the sugar isothiocyanate. β-Glycosyl isothiocyanates give mostly the (5*R*)-epimer, whereas when a α-glycosyl isothiocyanate is used, there is practically no stereoselectivity.

INTRODUCTION

The preparation of chiral auxiliaires and chiral inductors for use in asymmetric synthesis and for the resolution of enantiomeric mixtures is nowadays an important topic in chemical research. The main source for such enantiomerically pure chiral agents is the chemical modification of natural chiral compounds[1]. Among these compounds the carbohydrates have many interesting advantages for asymmetric syntheses. They are inexpensive, widespread natural compounds, have numerous stereogenic centers and can be used in highly stereoselective reactions as a consequence of their conformational properties[2]. The number of different functional groups in natural carbohydrates is limited, but many synthetic sugar derivatives are easy to prepare.

The 2-oxo and thioxo-1,3-*N*-heterocycles are interesting compounds from both chemical and pharmaceutical points of view. They can be transformed into many fused heterocycles that also are pharmaceutically useful[3-6]. Particularly the antibiotics SF-1993[7] and CV-1[8] have structure of 2-oxoimidazolidines. At the same time the nucleosides have well known pharmaceutical properties[9,10]; for example they are used as antibiotics and the 2-deoxy-nucleosides in AIDS treatment[9,11], and much effort[12] is being directed to the syntheses of this type of molecule.

The reaction of 2-amino-2-deoxyaldoses with alkyl and aryl isothiocyanates to give glycofuranoimidazolidine-2-thiones has been widely studied[13,14]. The mechanism of this reaction was understood in 1991 when a 2-(3-alkyl, arylthioureido)-2-deoxy-D-glucopyranose which evolved to a chiral 5-hydroxyimidazolidine-2-thione was described as the intermediate product[6]. Recently this mechanism has been confirmed[15]. The intermediate 5-hydroxyimidazolidine-2-thione was obtained in high yield (75-85%) when the reaction was performed at temperatures lower than 70 °C in a neutral or basic medium. The ratio of 5*R*:5*S* stereoisomers in solutions (NMR data) was between 9:1 and 3:2 depending on the solvent and N-1 substituent, but in some cases the (5*R*)-isomer could be crystallised or chromatographically isolated. No mutarotation was

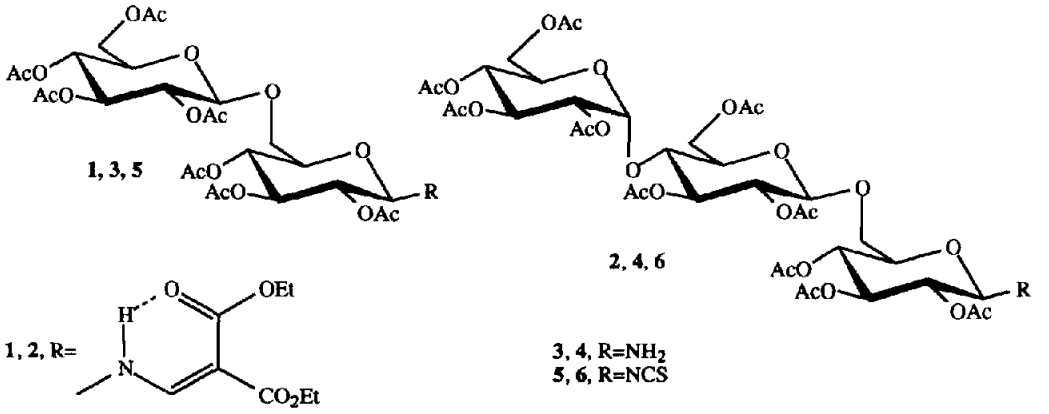
observed. The 5-hydroxyimidazolidine-2-thiones were transformed[6,15] into glycofuranoimidazolidine-2-thiones which can be converted[13, 16] into a variety of acyclic and cyclic C-nucleosides[13, 15].

The isothiocyanates are important reagents in heterocyclic chemistry[17]. In the last few years sugar isothiocyanates have been the focus of considerable attention[18], and recently have been used as chiral templates in the stereocontrolled syntheses of pseudo-C-nucleosides[19], bicyclic 1,3-*O*, *N*-heterocycles[20], several types of sugar thioureas[21, 22] and macrocycles[23]. Among the sugar isothiocyanates the most versatile as synthetic reagents are the glycosyl isothiocyanates which have been used in the syntheses of glycopyranothiazolines[24], glycosylthioureas[12], *N*-nucleosides[12, 18], *N*-glycopeptides[25-27], and other types of glycoconjugate[18, 28], and also they have been employed as enzymatic inhibitors[29]. The bibliographic data on glycosyl isothiocyanates are mainly on monosaccharide isothiocyanates and in spite of their interest there are few data on disaccharide[22, 30] and oligosaccharide[27] glycosyl isothiocyanates.

In this paper we report on the synthesis of the di- and trisaccharide glycosylisothiocyanates **5** and **6** and on the use of different types of sugar isothiocyanate in the synthesis of chiral (C-4, C-5) 1-glycosyl(and glucopyranos-2-yl)-5-hydroxy-4-(D-*arabino*tetritol-1-yl)imidazolidine-2-thiones **7**, **11**, **14**, and **18** observing the influence of the anomeric configuration of the sugar on C-5 (imidazolidine ring) configuration. The tetrahydroxy or tetraacetoxy compounds[7-17] have simultaneously structure of *N*-nucleoside and acyclic *C*-nucleoside.

RESULTS AND DISCUSSION

Preparation of oligosaccharide glycosyl isothiocyanates. The glycosyl isothiocyanates **5** and **6** were obtained in two steps from the *N*-diethoxycarbonylvinylgentiobiosylamine[31] **1** and from the trisaccharide glycosylenamine **2** respectively. Compound **2** was prepared through a glycosylation reaction using 2,3,4-tri-*O*-acetyl-*N*-(2,2-diethoxycarbonylvinyl)-6-*O*-trityl-β-D-glucopyranosylamine[31] as glycosyl acceptor, acetobromomaltose as glycosyl donor and silver perchlorate as promotor.



The structure of **2** was assigned on the bases of analytical, IR, ^{1}H-NMR (Table 1), and ^{13}C-NMR (Table 2) data. Thus, **2** had no IR or NMR signals for the trityl group and the signals for the enamino group were similar to those described for related compounds[31]. The δ values for NH (9.14 ppm), a CO_2Et group (167.6 ppm, C=O chelated), and the IR absorption at 1667 cm^{-1} (C=O chelated)[32,33] were indicative of the hydrogen bond shown in the structure. The $J_{1',2'}$ value (7.9 Hz) is in the range for antiperiplanar protons and

indicates that the new glycosidic bond is β. This configuration is confirmed by the chemical shift of the C-1' resonance (100.5 ppm)[34]. The $J_{1,NH}$ coupling constant (9.7 Hz) indicates that the corresponding protons are in *anti* relationship. The $^4C_1$ conformation for each sugar ring was evident from the $^3J_{H,H}$ values (Table 1).

Treatment of **1** and **2** with chlorine in chloroform[18] removed the *N*-protecting group and gave the corresponding di- or trisaccharide glycopyranosylamine (**3** and **4**), whose spectroscopic data (IR, NMR, and FABMS for **3** and FABMS for **4**) were consistent with the structures proposed.

The oligosaccharide glycopyranosyl isothiocyanates **5** and **6** were obtained by reaction of **3** and **4**, respectively, with thiophosgene in the presence of calcium carbonate. Compounds **5** and **6** had $\nu_{C=S}$ at 2025-2056 cm^{-1} and ^{13}C resonances at $\delta \approx 144$ ppm as is characteristic of the isothiocyanato group[18,30]. A ^1H doublet (Table 1) at 4.98-5.00 ppm ($J_{1,2}$ = 8.7-9.2 Hz, H-1) and a ^{13}C resonance at 83.2 ppm also agreed with the β-D-glucopyranosylisothiocyanate structure[30]. The coupling constant values (Table 1) supported the $^4C_1$(D) conformation for all glycosyl residues.

Table 1. ^1H-NMR data (500 MHz, $CDCl_3$) for the sugar rings of compounds **2**, **3**, **5**, and **6**.

Comp	Ring[a]	Chemical shift (δ, ppm)						
		H-1	H-2	H-3	H-4	H-5	H-6a	H-6b
2	A	4.53 t	5.02 t	5.24 t	4.93 t	3.73 ddd	3.89 dd	3.52 dd
	B	4.50 d	4.78 dd	5.22 t	3.96 t	3.64 ddd	4.49 dd	4.20-4.14 m
	C	5.37 d	4.83 dd	5.32 dd	5.01 t	3.94 ddd	4.26-4.20m	4.02 dd
3	A	4.16 d	4.78 t	5.22 t	4.91 t	3.66 m	3.89 dd	3.56 dd
	B	4.58 d	4.98 dd	5.20 t	5.08 t	3.75-3.69 m	4.25 dd	4.14 dd
5	A	4.98 d	5.01 t	5.19 t	4.94 t	3.75-3.68 m	3.91 dd	3.58 dd
	B	4.56 d	4.99 t	5.21 t	5.08 t	3.75-3.68 m	4.28 dd	4.13 dd
6	A	5.00 d	5.08 dd	5.20 t	4.96 dd	3.73 ddd	3.89 dd	3.59 dd
	B	4.57 d	4.83 dd	5.27 t	4.01 t	3.69 ddd	4.53 dd	4.23 dd
	C	5.43 d	4.87 dd	5.37 t	5.07 t	3.97 m	4.27 dd	4.06 dd

Comp	Ring[a]	Coupling constants (*J*, Hz)							
		$J_{1,NH}$	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
2	A	9.7	9.7	9.7	9.7	9.7	2.3	6.0	11.1
	B	-	7.9	9.3	9.3	9.3	2.7	4.2	12.2
	C	-	4.0	10.5	9.5	9.5	3.8	2.3	12.4
3	A	-	9.4	9.4	9.4	9.4	2.1	6.1	11.0
	B	-	7.8	9.4	9.4	9.4	4.9	2.4	12.3
5	A	-	9.2	9.2	9.2	9.2	2.0	7.0	11.2
	B	-	9.0	9.0	9.0	9.0	4.6	2.2	12.4
6	A	-	8.7	9.5	9.5	10.0	2.1	6.7	11.8
	B	-	7.9	9.3	9.3	9.3	2.6	4.2	12.3
	C	-	4.0	10.4	10.4	10.4	3.8	2.3	12.5

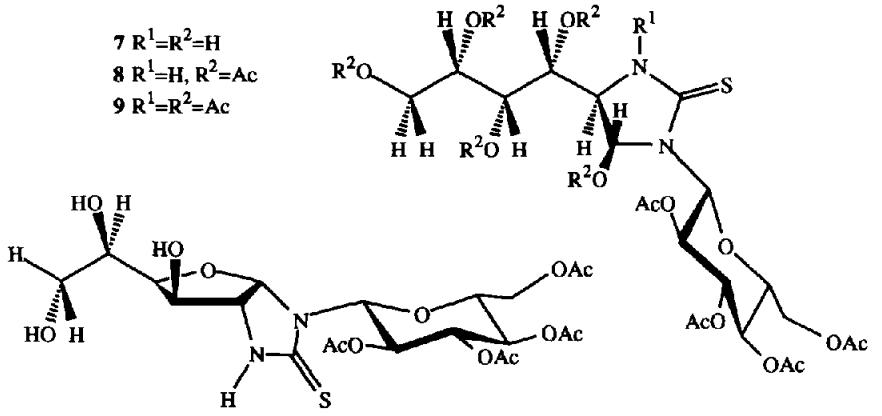
[a]Ring A refers to 1-*N*-functionalised D-gluco residue. For **2** and **6** ring B(') is the central D-gluco ring, and ring C(") the α-D-gluco residue. In the case of **3** and **5** ring B(') is the glucosyloxy residue.

Table 2. Sugar rings of compounds **2**, **3**, **5**, and **6**: ^{13}C-NMR (125.7 MHz) chemical shifts (δ ppm, $CDCl_3$)

Comp	Ring[a]	C-1	C-2	C-3	C-4	C-5	C-6
2	A	87.0	70.5	72.6	68.6	74.8	68.4
	B	100.5	71.7	75.1	68.5	72.4	62.4
	C	95.5	69.9	69.3	67.9	72.5	61.4
3	A	84.8	72.0	73.1	69.2	73.8	68.0
	B	100.6	70.9	72.6	68.2	71.8	61.8
5	A	83.2	71.7	71.8	68.0	75.1	68.2
	B	100.8	70.8	72.3	67.9	72.5	61.5
6	A	83.2	71.7	72.3	68.1	75.0	68.0
	B	100.3	71.6	75.0	72.2	72.3	62.3
	C	95.3	69.8	69.1	67.8	68.3	61.3

[a]See footnote [a] of Table 1.

Reaction of D-glucosamine with sugar isothiocyanates. Synthesis of nucleoside analogues. We have studied the reaction of D-glucosamine with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate[35], 2,3,4-tri-*O*-benzoyl-α- and β-D-ribopyranosyl isothiocyanates[36], **5**, **6**, and 1,2,4,6-tetra-*O*-acetyl-2-deoxy-2-isothiocyanato-β-D-glucopyranose[37]. The reactions were carried out at 20-50 °C in water:acetone except in the case of the 2-isothiocyanato sugar in which DMF was employed.



When 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate was used the ^{1}H- and ^{13}C-NMR spectra of the reaction product showed the presence of two compounds in the ratio 9:1 (digital integration of the non overlapped ^{1}H signals). Taking into account the bibliographic data on related reactions[6,15] and the $J_{4,5}$ values (2.3 and 6.6 Hz) we think that these compounds were respectively the 5*R N*-nucleoside **7** and its 5*S* epimer. This hypothesis is also supported by the results of the reactions starting from other sugar isothiocyanates (see below). After further chromatography (EtOAc:ether:acetone as eluant) compound **7** could be characterized but the 5*S* epimer was not isolated. During this purification a minor new product with structure **10** was formed.

The structure **7** was based on analytical and IR, ^{1}H and ^{13}C-NMR (Table 3), and MS data, and the corresponding data from the acetyl derivatives **9** and **10**. Thus a ^{13}C resonance at 184.2 ppm (183.2 and 181.6 in **9** and **10** respectively), attributable to the C=S group, rules out an isomeric structure of 2-iminothiazolidine. The presence of the imidazolidine ring was also confirmed by the chemical shifts of H-4 and H-5 close to that described for the same protons in related compounds[6]. However the resonance of C-5 appears shifted upfield (≈4 ppm) when it is compared with the same signal for N-1 aryl substituted imidazolidines. This can be due to the different influence of the neighbouring substituent (aryl or glycosyl). The C-5 configuration is in accord whith the small $J_{4,5}$ value (2.3 Hz) indicative[6,15] of a *trans* relationship between the corresponding protons. Solutions of compound **7** did not present mutarotation and their NMR spectra did not change with time, which is indicative of that **7** is a stable compound and anomeric mixtures (C-5 epimers) are not easy to reach. At the same time the NMR spectra did not undergo appreciable changes on increasing temperatures, which suggests that the atropoisomers originated by restricted rotation around the N1-C1' bond, suggested for imidazolidines having a bulky naphthyl substituent on N-1[15], are not formed in our case and probably the N1-C1' bond has free rotation at room temperature.

Conventional acetylation of **7** yielded after chromatography **8** (major) and **9** (minor) whose structures were confirmed by analytical and spectroscopic data (Table 3). Both compounds showed the close resemblance in the chemical shifts of C-1", C-2", and C-3" (polyacetoxy chain) described for related acyclic *C*-nucleosides[15]. The vicinal coupling constant values corresponding to the protons of the D-*arabino*tetraacetoxybutyl chain and H-4 showed that both compounds exist in chloroform solutions in the $_4G^-$ conformation indicated in the formulae. The chain end flexibility described for other D-*arabino* compounds[6,38] is possible.

Table 3. Selected NMR data (^{1}H 500 MHz, ^{13}C 125.7 MHz) for compounds **7** (δ ppm, *J* Hz).

Comp	C-5 conf.	δ_{H-4}	δ_{H-5}	$J_{4,5}$	$\delta_{H-1'}$	δ_{C-2}	δ_{C-4}	δ_{C-5}	$\delta_{C-1'}$
7[a]	*R*	3.74	5.33	2.3	5.96	184.2	67.1	84.6	84.2
8[b]	*R*	3.57	6.81	1.3	5.87	183.2	59.5	79.2	83.5
9[b]	*R*	4.70	6.72	0.0	6.08	181.6	59.9	77.5	83.2
11[a]	*R*	3.80	5.53	2.3	6.68	184.0	66.9	84.2	82.7
12[b]	*R*	3.80	7.10	0.0	6.52	183.7	60.0	80.0	81.7
13[b]	*R*	4.83	6.97	0.0	6.63	182.0	60.5	77.6	81.3
14[a]	*R*	3.83	5.54	2.2	6.10	184.2	65.3	86.0	82.1
15[a]	*S*	4.08	5.61	6.6	6.11	184.2	60.3	85.6	82.3
16[a]	*R*	3.81-3.60	5.37	2.3	5.95	184.1	67.2	84.3	83.5
17[a]	*R*	3.83	5.36	2.4	6.08	183.1	67.1	85.7	80.2
18a[a]	*R*	3.77	5.35	2.5	6.22	182.3	64.9	89.2	93.5
18b[a]	*S*	4.25	5.75	6.2	6.21	183.6	60.6	85.6	94.3

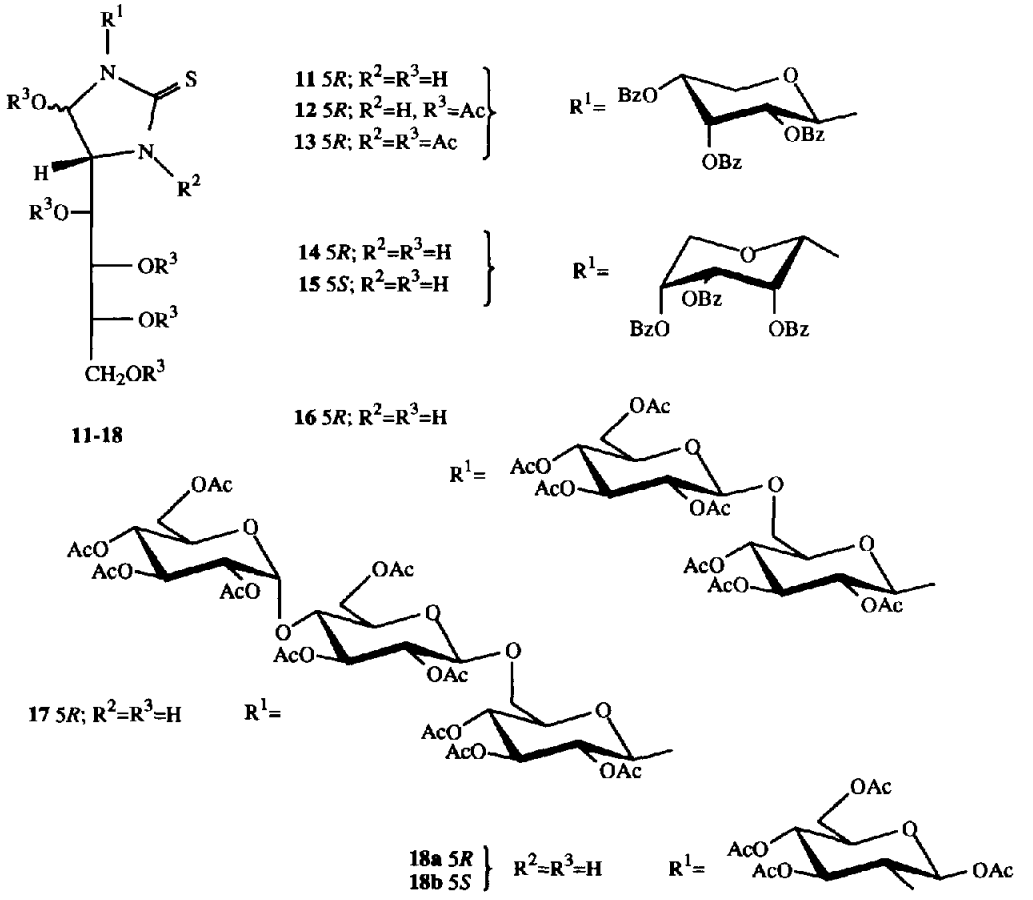
[a] In MeOH-d4. [b] In $CDCl_3$.

The $^3J_{H,H}$ values that could be measured in **7** and the antecedents[6] indicate the $_4G^-$ is also the main conformation although the $J_{4,1'}$ value (6.1 Hz) shows a participation of the *P* conformation.

The mass spectrum and the analytical data of the minor product **10**, formed during the purification of **7**, showed a loss of one molecule of AcOH with respect to **7**. At the same time significant NMR differences between the two compounds were observed. Thus the chemical shifts for the resonances of H-2' and C-2' in

10 underwent a shielding of 1.4 ppm and a deshielding of 2.1 ppm respectively when they were compared with the signals for the corresponding nucleus in **7**. Additionally the resonance of C-3' in **7** had the characteristic β-effect on acetylation compared with the same resonance in **10**. These data are indicative of deacetylation in position 2', probably due to the acidity of the chromatographic eluant. On the other hand the chemical shifts (^1H and ^{13}C) and coupling constants of the heterocyclic moiety of **10** (see experimental) coincides those described for glucofuranoimidazolidine-2-thiones[6]; for example the δ value of C-4 in **10** is 80.3 ppm, whereas the same carbon in **7** (C-2" using the numbering of **7**) resonated at 71.3 ppm and in glucofuranoimidazolidine-2-thiones at 77.0-80.0 ppm[6,14]. Consequently we propose that **10** has the *N*-nucleosidic structure of a bicyclic heterocycle indicated in the formula. The reaction is interpreted as a cyclodehydration from **7**, catalysed by the acidic medium during the chromatography.

According to the reported data[6,14] for glucofuranoimidazolidine-2-thiones the *J* values for the furan ring of **10** indicate the E_4 conformation; nevertheless the dihydroxyethyl chain has the conformation shown and does not present ($J_{5,6a} = J_{5,6b} = 2.8$ Hz) in solution in methanol the usual chain end flexibility.



Starting from 2,3,6-tri-*O*-benzoyl-β-D-ribopyranosyl isothiocyanate[36] the reaction took place in a similar way to the case of D-*gluco* derivative and compound **11** was isolated in high yield. The (5*S*)-epimer was

detected in low concentration (<7%) in the ^{1}H-NMR of the crude reaction product and could not be isolated. The structural analysis of **11** was based on the preparation of the acetyl derivatives **12** and **13** and on the analytical and spectroscopic data (Table 3 and experimental) of **11-13**. The ribopyranosyl ring is in the $_4C^1$ conformation and the chain conformation is the same as **7-9**. Neither debenzoylation nor formation of glucofuranoimidazolidine was observed during the purification of **11**.

In the case of the 2,3,6-tri-*O*-benzoyl-α-D-ribopyranosyl isothiocyanate there was practically no stereoselectivity and the (5*R*)-**14** and (5*S*)-**15** epimers were obtained in a ≈ 1:1 ratio. Compounds **14** and **15** had slightly different R_F (dichloromethane:methanol 9:1) and $[\alpha]_D$ values and identical FAB mass spectra. The main differences in the NMR spectra of the C-5 epimers of 5-hydroxy imidazolidine-2-thiones are the $J_{4,5}$ (2.3-2.9 Hz for 5*R*, and ≈ 6.8 Hz for 5*S*) and δ C-4 (65.3-65.9 for 5*R* and 60.5-61.0 for 5*S*) values[6]. Compound **14** had $J_{4,5}$ = 2.2 Hz and δC-4 65.3 ppm (Table 3) whereas **15** had $J_{4,5}$ = 6.6 Hz and δ C-4 60.3 ppm, indicative of 5*R* and 5*S* configurations respectively. The $^3J_{H,H}$ values between the protons of the ribopyranosyl ring showed the $^1C_4$ conformation for this ring, which is in agreement with reported data[36] for other α-D-ribopyranosyl derivatives bearing a bulky substituent on C-1.

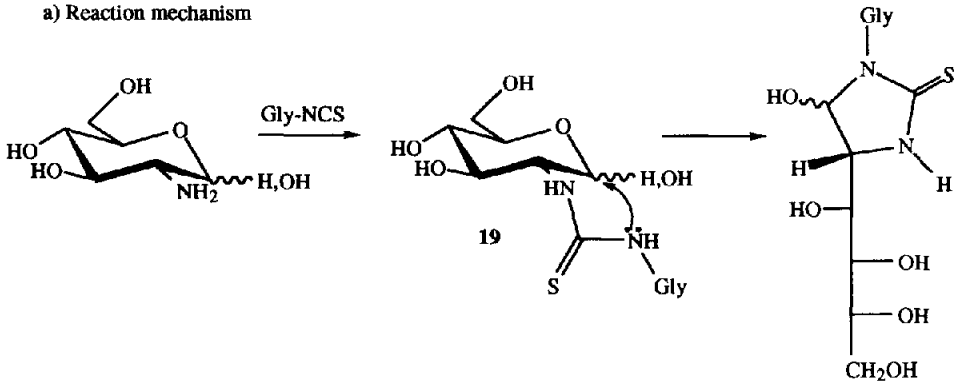
When the reaction was performed starting from the oligosaccharide β-glycosyl isothiocyanates **5** and **6** the (5*R*)-imidazolidines **16** and **17** respectively were obtained. In both cases the corresponding (5*S*)-stereoisomers were detected in very low concentration and were not isolated. During the chromatographic purification of **16** and **17** formation of products with loss of an acetic acid molecule (FAB mass spectrometry), and probably structure similar to **10**, was observed, but these products were not characterised. Compounds **16** and **17** had a $J_{4,5}$ value of 2.3-2.4 Hz and δ C-4 67.1-67.2 ppm (Table 3) confirming the 5*R* configuration. The coupling constants that could be measured showed the $^4C_1$ conformation for every D-glucopyranosyl ring.

The reaction has also been carried out using a sugar isothiocyanate with the isothiocyanato group in a non glycosidic position; specifically the 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isothiocyanato-β-D-glucopyranose[37] was used. In this case DMF was used instead of acetone and a 3:1 mixture of (5*R*)-**18a** and (5*S*)-**18b** chiral imidazolidine-2-thiones was obtained. The stereoselectivity was lower than in the cases of β-glycosylisothiocyanates but higher than in the case of α-D-ribopyranosyl isothiocyanate. The mixture of **18a** and **18b** could not be resolved, but the analytical and ^{1}H- and ^{13}C-NMR data (Table 3 and experimental) allowed the structural assignments of both compounds. Thus the *R* epimer **18a** had $J_{4,5}$ = 2.5 Hz and δ C-4 54.9 ppm whereas the *S* epimer **18b** had 6.2 Hz and 60.6 ppm respectively, in accord with the reported data for related compounds[6]. The glucopyranosyl ring of **18a** and **18b** is in the $^4C_1$ conformation with the imidazolidine-2-thione ring in an *equatorial* position.

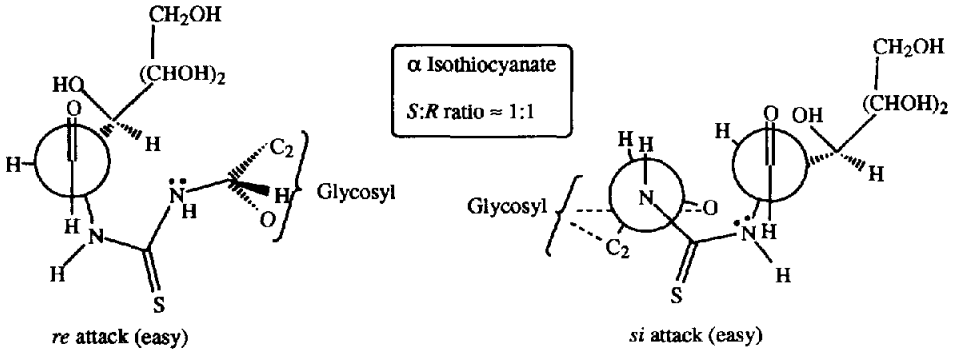
From a stereochemical point of view the process can be summarized as that the reaction between D-glucosamine and glycosyl isothiocyanates takes place with a high degree of diastereoselectivity when β-glycosyl isothiocyanates are used and there is practically no stereoselectivity when an α-isothiocyanate is used. A possible explanation of this fact is shown in figure 1. The part a) represents the mechanism described[6,15] for the reaction of D-glucosamine with alkyl and aryl isothiocyanates. The part b) shows the open chain form of the 2-deoxy-2-(3-glycosylthioureido)-D-glucose **19** intermediate whose cyclization produces the chiral imidazolidine-2-thione *N*-nucleoside analogues, assuming that the Cram rule of the steric control of the asymmetric induction is fulfilled. In the case of the α-D-ribopyranosyl isothiocyanate the attacks of the NH on the *re* (to give 5*S*) and *si* (to give 5*R*) faces of the carbonyl group are equally probable as in both cases the

ribose ring is far from the bulky polyhydroxyalkyl chain. For the β-glycosyl isothiocyanates the attack on the *si* face is more difficult than the attack on the *re* face because in the former the glycosyl ring and the polyhydroxyalkyl chain are close to each other. That is the configuration of the anomeric centre modifies the asymmetric induction of C-2 of the D-glucosamine derivative **19**.

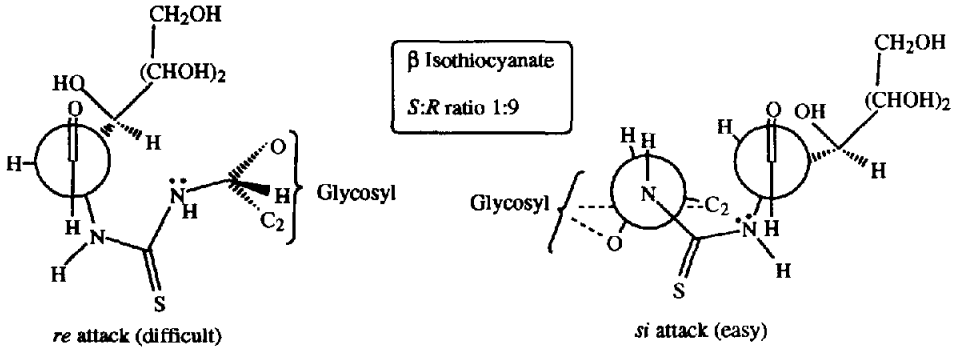
a) Reaction mechanism



b) Chiral imidazolidine formation from the open chain form of **19**



re attack (easy) *si* attack (easy)



re attack (difficult) *si* attack (easy)

Fig. 1.- Diastereoselective induction of the anomeric centre on C-5 configuration.

The case of the 2-deoxy-2-isothiocyanato-D-glucose to give **18** is similar to that for β-glycosyl isothiocyanates, because in this particular case the spatial arrangement around C-2 of the D-*gluco* ring is similar to that for β-D-glucosyl radicals.

EXPERIMENTAL

General. Melting points are uncorrected. Optical rotations were measured at 19-26 °C for solutions in dichloromethane. FTIR spectra were recorded for KBr discs or thin film. ^{1}H NMR spectra (500 MHz) were obtained for solutions in $CDCl_3$ or MeOH-d_4. Assignments were confirmed by homonuclear 2D COSY correlated 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. FAB-mass spectra were recorded with a Kratos MS-80RFA instrument with a resolution of 1000 or 10000 (10% valley definition). Ions were produced by a beam of xenon atoms (6-7 KeV) using a matrix consisting of thioglycerol or 3-nitrobenzyl alcohol 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.

*2,3,4-Tri-*O*-acetyl-*N*-(2,2-diethoxycarbonylvinyl)-6-*O*-[2',3',6'-tri-*O*-acetyl-4'-*O*-(2'',3'',4'',6''-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranosyl]-β-D-glucopyranosylamine 2.* To a solution of silver perchlorate (0.56 g, 2.72 mmol) in freshly distilled nitromethane (4.5 mL) drierite was added (0.28 g, 2.09 mmol) and the mixture was kept at 0 °C under nitrogen for 5 min. Then 2,3,4-tri-*O*-acetyl-*N*-(2,2-diethoxycarbonylvinyl)-6-*O*-trityl-β-D-glucopyranosylamine[31] (1.50 g, 2.09 mmol) and acetobromomaltose (1.46g, 2.09 mmol) were added. The mixture was stirred for 4 h at r.t. under nitrogen. The organic layer was diluted with dichloromethane (15 mL), then filtered through Celite, the insoluble material was washed with dichloromethane (15 mL), and the combined filtrate and washing were washed with water at 0 °C (15 mL), saturated aqueous sodium hydrogencarbonate (15 mL), and water (4×15 mL), dried ($MgSO_4$) and the solvent evaporated. The residue was purified by column chromatography (dichloromethane:methanol 25:1), giving a white solid (2.30 g, 27%) which crystallised from methanol had mp 194-195 °C; $[\alpha]^{22}_D$ +3 (*c* 1.0, chloroform); IR ν_{max} 3499, 2961, 2920, 1753, 1667, 1377, 1233, and 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$): Table 1 and δ 9.14 (dd, 1 H, $J_{NH,=CH}$ = 13.2, NH), 7.90 (d, 1 H, =CH), 4.26-4.14 (m, 4 H, 2 C*H*$_2$CH$_3$), 2.13, 2.12, 2.07, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96 (each s, each 3 H, 10 Ac), 1.30, and 1.27 ppm (each t, each 3 H, $^3J_{H,H}$ = 7.1, CH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$): Table 2 and δ 170.5 (2 *C*OCH$_3$), 170.4, 170.1, 170,0, 169.9, 169.7, 169.5, 169.4, 169.3 (8 *C*OCH$_3$), 167.6 (C=O chelated), 165.4 (C=O free), 157.2 (=CH), 94.6 (=C), 60.3, 60.1 (2 *C*H$_2$CH$_3$), 20.8 (2 C, 2 CO*C*H3), 20.6 (CO*C*H$_3$), 20.5 (3 C, 3 CO*C*H$_3$), 20.4 (4 C, 4 CO*C*H$_3$), 14.3, and 14.2 ppm (2 CH$_2$*C*H$_3$); FABMS *m/z* 1117 (100, [M+Na]$^{+\cdot}$). Anal. calcd for $C_{46}H_{63}O_{29}N$: C, 50.50; H, 5.80; N, 1.28. Found: C, 50.59; H; 5.94; N; 1.40.

General procedure for the preparation of 3 and 4. A solution of **1** or **2** (0.91 mmol) in chloroform saturated of chlorine (8 mL) was stirred at r.t. for 15 min. The reaction was controlled by TLC (dichloromethane:methanol 20:1) until total consumption of the starting material. The solvent was evaporated and the residue was treated with dry ether (5 mL) until a solid product was obtained. This product filtered and washed with dry ether (3×5 mL) was a white and amorphous solid. The following compounds were prepared in this manner.

*2,3,4-Tri-*O*-acetyl-6-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranosylamine 3.* A small portion was purified by TLC (dichloromethane:EtOAc:methanol 10:5:0.75) for study; $[\alpha]^{25}_D$ +34 (*c* 1.0); IR ν_{max} 3327, 2940, 2865, 1755, 1589, 1441, 1371, 1223, and 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$): Table 1 and δ 2.09, 2.07, 2.06 (each s, each 3 H, 3 Ac), 2.02 (s, 6 H, 2 Ac), 2.01, and 1.99 ppm (each s, each 3 H, 2 Ac); ^{13}C NMR ($CDCl_3$): Table 2 and δ 170.5 (*C*OCH$_3$), 170.1 (3 C, 3 *C*OCH$_3$) 169.5 (*C*OCH$_3$), 169.3 (2 C, 2 *C*OCH$_3$), 20.7 (CO*C*H$_3$), 20.6 (2 C, 2 CO*C*H$_3$), 20.5 (3 C, 3 CO*C*H$_3$), and 20.4 ppm (CO*C*H$_3$); FABMS *m/z* 659 (100, [M+Na]$^{+\cdot}$).

2,3,4-Tri-O-acetyl-6-O-[2',3',6'-tri-O-acetyl-4'-O-(2",3",4",6"-tetra-O-acetyl-α-D-glucopyranosyl)-β-D-glucopyranosyl]-β-D-glucopyranosylamine **4** FABMS of the crude reaction product *m/z* 946 (100, $[M+Na]^{+\cdot}$).

General procedure for the preparation of 5 and 6. To an heterogeneous mixture of **3** or **4** (0.91 mmol) in chloroform (11.4 mL) and calcium carbonate (0.23 g, 2.30 mmol) in water (11.4 mL) thiophosgene (0.13 mL, 1.39 mmol) was added. The mixture was stirred vigorously (2 h for **3**, and 12 h for **6**) and then filtered; the organic layer was separated, washed with water (2×10 mL), dried ($MgSO_4$), and concentrated to dryness, and the residue was purified as indicated.

2,3,4-Tri-O-acetyl-6-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-glucopyranosyl isothiocyanate **5**. Column chromatography (chloroform) of the residue gave an amorphous solid (0.23 g, 38% from **1**) which crystallised from chloroform-hexane, had mp 173-174 °C; $[\alpha]^{24}_D$ +3 (*c* 1.0); IR ν_{max} 2967, 2099, 2056, 1751, 1435, 1377, 1256, and 1030 cm^{-1}; ^1H NMR ($CDCl_3$): Table 1 and δ 2.10 (6 H, 2 Ac), 2.09, 2.03 (each s, each 3 H, 2 Ac), and 2.01 ppm (s, 9 H, 3 Ac); ^{13}C NMR ($CDCl_3$): Table 2 and δ 170.5, 170.0, 169.9, 169.4 (4 $COCH_3$), 169.3 (2 C, 2 $COCH_3$), 168.9 ($COCH_3$), 144.1 (NCS), 20.6 , 20.5 (2 $COCH_3$), and 20.4 ppm (5 C, 5 $COCH_3$); FABMS *m/z* 700 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{27}H_{35}O_{17}NS$: C, 47.86; H, 5.21; N, 2.07; S, 4.73. Found: C, 47.55; H, 5.25; N, 1.71; S, 4.84.

2,3,4-Tri-O-acetyl-6-O-[2',3',6'-tri-O-acetyl-4'-O-(2",3",4",6"-tetra-O-acetyl-α-D-glucopyranosyl)-β-D-glucopyranosyl]-β-D-glucopyranosyl isothiocyanate **6**. Column chromatography (chloroform:methanol 20:1) of the residue gave an amorphous solid (0.65 g, 65% from **2**); $[\alpha]^{25}_D$ +62 (*c* 0.17); IR ν_{max} 2924, 2114, 2025, 1759, 1433, 1371, 1258, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$): Table 1 and δ 2.17, 2.12, 2.11, 2.07, 2.06, 2.05, 2.04, 2.03 (each s, each 3 H, 8 Ac), and 2.02 ppm (s, 6 H, 2 Ac); ^{13}C NMR ($CDCl_3$): Table 2 and δ 170.3 (2 C, 2 $COCH_3$), 170.2, 170.0, 169.9, 169.7, 169.6, 169.2, 169.1, 168.9 (8 C, 8 $COCH_3$), 144.0 (NCS), 20.7 (2 C, 2 $COCH_3$), 20.5 ($COCH_3$), 20.4 (4 C, 4 $COCH_3$), and 20.3 ppm (3 C, 3 $COCH_3$); FABMS *m/z* 988 (100, $[M+Na]^{+\cdot}$). Anal. calcd for $C_{39}H_{51}O_{25}NS$: C, 48.50; H, 5.32; N, 1.45; S, 3.32. Found: C, 48.25; H, 5.70; N, 1.28; S, 3.15.

*(4R,5R)-5-Hydroxy-1-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-(D-*arabino*tetritol-1-yl)-imidazolidine-2-thione* **7**. A solution of 2-amino-2-deoxy-D-glucose (0.29 mmol) in water (3 mL) was gradually added to a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate[35] (0.29 mmol) in acetone (3 mL) under nitrogen. The resulting solution was stirred at r.t. for 2h, the solvent was evaporated under diminished pressure and the residue was purified by column chromatography (dichloromethane:methanol 6:1) to give 0.12 g (74 %) of a 9:1 mixture of **7** (major) and another product (minor, probably 5*S* epimer of **7**). A new column chromatography of this mixture using EtOAc:ether:acetone 1:2:1 as eluant yielded **7** (83 %) and **10** (17 %). Compound **7** was an amorphous solid which had $[\alpha]^{19}_D$ +68 (*c* 0.64); IR ν_{max} 3349, 2963, 1750, 1495, 1442, 1375, 1235, and 1040 cm^{-1}; ^1H NMR (MeOH-d_4) δ 8.52 (s, 1 H, H-3), 5.96 (d, 1 H, $J_{1',2'}$ = 9.5, H-1'), 5.45 (t, 1 H, $J_{2',3'}$ = 9.5, H- 2'), 5.35 (t, 1 H, $J_{3',4'}$ =9.5, H-3'), 5.33 (d, 1 H, $J_{4,5}$ = 2.3, H-5), 5.10 (t, 1 H, $J_{4',5'}$ = 9.5, H-4'), 4.25 (dd, 1 H, $J_{6'a,6'b}$ = 12.3, H-6'a), 4.15 (dd, 1 H, H-6'b), 3.89 (ddd, 1 H, $J_{5',6'a}$ = 5.1, $J_{5',6'b}$ = 2.5, H-5'), 3.79-3.73 (m, 1 H, H-3"), 3.74 (dd, 1 H, $J_{4'1"}$ = 6.1, H-4), 3.65-3.61 (m, 3 H, H-1", 2", 4"a), 3.49 (dd, 1 H, $J_{4"a,4"b}$ = 7.7, $J_{3",4"b}$ = 1.9, H-4"b), 2.02, 1.98, 1.97, and 1.93 ppm (each s, each 3 H, 4 Ac); ^{13}C NMR (MeOH-d_4) δ 184.2 (C=S), 172.6, 172.0, 171.6, 171.4 (4 $COCH_3$), 84.6 (C-5), 84.2 (C-1'), 75.6 (C-3'), 75.2 (C-5'), 72.8 (C-3"),

72.7 (C-1"), 71.3 (C-2"), 69.8 (C-4'), 69.1 (C-2'), 67.1 (C-4), 64.7 (C-4"), 63.5 (C-6'), 20.8, 20.7, 20.6, and 20.5 ppm (4 $COCH_3$); FABMS *m/z* 591 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{21}H_{32}O_{14}N_2S$: C, 44.36; H, 5.67; N, 4.93; S, 5.64. Found: C, 44.55; H, 5.90; N, 4.92; S, 5.72.

1-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-d] imidazolidine-2-thione ***10*** was an amophous solid which had $[\alpha]^{19}_D$ +43 (*c* 0.6); IR ν_{max} 3345, 2963, 1755, 1501, 1435, 1377, 1235, and 1036 cm^{-1}; ^1H NMR δ 8.50 (s, 1 H, NH), 6.10 (d, 1 H, $J_{1,2}$ = 6.9, H-1), 5.72 (d, 1 H, $J_{1',2'}$ = 9.6, H- 1'), 5.14 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 9.6, H-3'), 4.97 (dd, 1 H, $J_{4',5'}$ = 10.0, H-4'), 4.25 (dd, 1 H, $J_{5',6'a}$ = 4.7, $J_{6'a,6'b}$ = 12.5, H-6'a), 4.18 (d, 1 H, $J_{2,3}$ = 0, H-2), 4.17 (d, 1 H, $J_{3,4}$ = 2.5, H-3), 4.10 (dd, 1 H, $J_{5',6'b}$ = 2.3, H-6'b), 4.05 (t, 1 H, H-2'), 3.93 (dt, 1 H, $J_{4,5}$ = 8.8, $J_{5,6a} = J_{5,6b}$ = 2.8, H-5), 3.88 (ddd, 1 H, H-5'), 3.81 (dd, 1 H, H-4), 3.74 (dd, 1 H, $J_{6a,6b}$ = 11.3, H-6a), 3.71 (dd, 1 H, H-6b), 2.03 (s, 3 H, Ac), and 2.01 ppm (s, 6 H, 2 Ac); ^{13}C NMR δ 185.4 (C=S), 172.4, 172.0, 171.5 (3 $COCH_3$), 90.4 (C-1), 85.9 (C-1'), 80.3 (C-4), 77.0 (C-3'), 75.7 (C-3), 75.2 (C-5'), 71.2 (C-2'), 70.0 (C-4'), 69.0 (C-5), 67.2 (C-2), 65.5 (C-6), 63.4 (C-6'), 20.8 ($COCH_3$), and 20.6 ppm (2 C, 2 $COCH_3$); FABMS *m/z* 531 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{19}H_{28}O_{12}N_2S$: C, 44.88; H, 5.55; N, 5.51; S, 6.31. Found: C, 45.00; H, 5.66; N, 5.38; S, 5.97.

(4R, 5R)-5-Acetoxy-1-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-(1",2",3",4"-tetra-O-acetyl-D-arabinotetritol-1-yl) imidazolidine-2-thione ***8*** *and (4R, 5R)-5-acetoxy-3-acetyl-1-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-(1",2",3",4"-tetra-O-acetyl-D-arabinotetritol-1-yl) imidazolidine-2-thione* ***9***. To a stirred solution of **7** (0.28 mmol) in pyridine (0.5 mL) at 0 °C, acetic anhydride (0.4 mL, 4.26 mmol) was added. The resulting solution was kept at r.t. with stirring for 24h and then poured into ice-water. TLC (ether:hexane 6:1) of the resulting solid yielded **8** (0.18 g, 84 %, lower R_F value) and **9** (0.02 g, 9 %, higher R_F value) as amorphous solids.

Compound **8** had $[\alpha]^{25}_D$ +312 (*c* 0.33); IR ν_{max} 3302, 2963, 1751, 1507, 1439, 1373, 1223, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93 (s, 1 H, H-3), 6.81 (d, 1 H, $J_{4,5}$ = 1.3, H-5), 5.87 (d, 1 H, $J_{1',2'}$ = 9.5, H-1'), 5.50 (t, 1 H, $J_{2',3'}$ = 9.5, H-2'), 5.31 (t, 1 H, $J_{3',4'}$ = 9.5, H-3'), 5.30 (dd, 1 H, $J_{1",2"}$ = 1.4, $J_{2",3"}$ = 9.2, H-2"), 5.17 (dd, 1 H, $J_{4,1"}$ = 10.5, H-1"), 5.08-5.04 (m, 1 H, H-3"), 4.94, (t, 1 H, $J_{4',5'}$ = 9.5, H-4'), 4.34 (dd, 1 H, $J_{6'a,6'b}$ = 12.6, $J_{5',6'a}$ = 4.5, H-6'a), 4.15 (dd, 1 H, $J_{3",4"a}$ = 2.7, $J_{4"a,4"b}$ = 12.5, H-4"a), 4.10 (dd, 1 H, $J_{3",4"b}$ = 4.6, H-4"b), 3.87 (dd, 1 H, $J_{5',6'b}$ = 1.8, H-6'b), 3.71 (ddd, 1 H, H-5'), 3.57 (dd, 1 H, H-4), 2.07 (s, 6 H, 2 Ac), 2.04, 2.02, 2.01, 2.00, 1.97, 1.96, and 1.95 (each s, each 3 H, 7 Ac); ^{13}C NMR ($CDCl_3$) δ 183.2 (C=S), 170.7, 170.6, 170.4 (3 $COCH_3$), 169.9 (2 C, 2 $COCH_3$), 169.4, 169.3, 169.1, 169.0 (4 $COCH_3$), 83.5 (C-1'), 79.2 (C-5), 74.2 (C-5'), 72.7 (C-3'), 68.4 (C-2'), 67.8 (C-1"), 67.7 (C-3"), 67.4 (C-4'), 67.1 (C-2"), 61.5 (2 C, C-6',4"), 59.5 (C-4), 20.8, 20.7 (2 $COCH_3$), 20.6 (3 C, 3 $COCH_3$), 20.5 (2 C, 2 $COCH_3$), 20.4, and 20.3 (2 $COCH_3$); FABMS *m/z* 801 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{31}H_{42}O_{19}N_2S$: C, 47.81; H, 5.44; N, 3.60. Found: C, 47.42; H, 5.34; N, 3.41.

Compound **9** had IR ν_{max} 3308, 2959, 2866, 1746, 1425, 1373, 1223, and 1044 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.72 (s, 1 H, H-5), 6.08 (d, 1 H, $J_{1',2'}$ = 9.5, H-1'), 5.71 (t, 1 H, $J_{2',3'}$ = 9.5, H-2'), 5.41 (dd, 1 H, $J_{1",2"}$ = 2.0, $J_{2",3"}$ = 8.5, H-2"), 5.36 (t, 1 H, $J_{3',4'}$ = 9.5, H-3'), 5.25 (ddd, 1 H, $J_{3",4"a}$ = 2.4, $J_{3",4"b}$ = 4.8, H-3"), 5.02 (t, 1 H, $J_{4',5'}$ = 9.5, H-4'), 5.01 (dd, 1 H, $J_{4,1"}$ = 9.7, H-1"), 4.70 (d, 1 H, $J_{4,5}$ = 0.0, H-4), 4.42 (dd, 1 H, $J_{5',6'a}$ = 4.4, $J_{6'a,6'b}$ = 12.6, H-6'a), 4.26 (dd, 1 H, $J_{4"a,4"b}$ = 12.4, H-4"a), 4.18 (dd, 1

H, H-4"b), 3.93 (dd, 1 H, $J_{5',6'b}$ = 2.0, H-6'b), 3.77 (ddd, 1 H, H-5'), 2.21, 2.08 (each s, each 3 H, 2 Ac), 2.07 (s, 6 H, 2 Ac), 2.06, 2.04 (each s, each 3 H, 2 Ac), 2.03 (s, 6 H, 2 Ac), 2.01, and 2.00 (each s, each 3H, 2 Ac); ^{13}C NMR ($CDCl_3$) δ 181.6 (C=S), 170.7 (2 C, 2 $COCH_3$), 170.6, 170.3, 170.2, 169.9, 169.8, 169.6, 169.2, 169.0 (8 $COCH_3$), 83.2 (C-1'), 77.5 (C-5), 74.2 (C-5'), 73.3 (C-3'), 68.2 (C-2'), 68.0 (C-1"), 67.9 (C-3"), 67.3 (C-4'), 67.2 (C-2"), 61.9 (C-4"), 61.3 (C-6'), 59.9 (C-4), 20.8 (2 C, 2 $COCH_3$), 20.7 ($COCH_3$), 20.6, 20.5 (each 3 C, 6 $COCH_3$), and 20.1 ($COCH_3$); FABMS *m/z* 843 (100, $[M+Na]^{+\cdot}$).

Procedure for the preparation of* N-*nucleosides of imidazolidine-2-thiones 11, and 14-17. These compounds were prepared in a similar way that **7**, starting from 2-amino-2-deoxy-D-glucose (0.29 mmol) and the glycosyl isothiocyanate (0.29 mmol) indicated in each case. The temperatures were T °C and the time of stirring t hours. Every residue was purified as indicated.

*(4*R*,5*R*)-5-Hydroxy-4-(D-*arabino*tetritol-1-yl)-1-(2',3',4'-tri-*O*-benzoyl-β-D-ribopyranosyl) imidazolidine-2-thione 11.* From 2,3,4-tri-O-benzoyl-β-D-ribopyranosyl isothiocyanate[36]; T= 50 °C; t= 3h; The residue purified by column chromatography (dichloromethane:methanol 9:1) yielded 0.15 g (74 %) of a white amorphous solid which had $[\alpha]^{22}_D$ +6 (*c* 1.0); IR ν_{max} 3358, 3067, 2928, 1730, 1601, 1499, 1452, 1397, 1267, 1101, 1072, and 1026 cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 8.13-7.25 (m, 15 H, 3 Ph), 6.68 (d, 1 H, $J_{1',2'}$ = 10.8, H-1'), 6.33 (m, 1 H, H-3'), 5.82 (dd, 1 H, $J_{2',3'}$ = 3.2, H-2'), 5.56-5.47 (m, 1 H, H-4'), 5.53 (d, 1 H, $J_{4,5}$ = 2.3, H-5), 4.28-4.16 (m, 2 H, H-5'a, 5'b), 3.80 (dd, 1 H, $J_{4,1"}$ = 6.4, H-4), 3.66-3.62 (m, 1 H, H-3"), 3.56 (dd, 1 H, $J_{1",2"}$ = 1.3, $J_{2",3"}$ = 7.8, H-2"), and 3.52-3.44 ppm (m, 3 H, H-1", 4"a, 4"b); ^{13}C NMR (MeOH-d_4) δ 184.0 (C=S), 167.1, 166.5, 166.4 (3 C, 3 *C*OPh), 131.0-129.2 (18 C, 3 Ph), 84.2 (C-5), 82.7 (C-1'), 72.8 (C-3"), 72.3 (C-1"), 70.9 (C-2"), 70.7 (C-3'), 68.5 (C-4'), 67.8 (C-2'), 66.9 (C-4), 64.7 (C-4"), and 64.6 ppm (C-5'); FABMS *m/z* 705 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{33}H_{34}O_{12}N_2S$: C, 58.06; H, 5.02; N, 4.10; S, 4.70. Found: C, 58.02; H, 5.16; N, 4.12; S, 4.95.

*[(4*R*,5*R*)-14 and (5*S*)-15]-5-Hydroxy-4-(D-*arabino*tetritol-1-yl)-1-(2',3',4',-tri-*O*-benzoyl-α-D-ribopyranosyl) imidazolidine-2-thiones.* From 2,3,4-tri-*O*-benzoyl-α-D-ribopyranosyl isothiocyanate[36]; T= 50 °C; t= 3h; TLC (dichloromethane:methanol 9:1) of the residue yielded **14** (93 mg, 47 %, lower R_F value) and **15** (89 mg, 45 %, higher R_F value) as white amorphous solids.

Compound **14** had $[\alpha]^{24}_D$ -49 (*c* 0.55); IR ν_{max} 3308, 3067, 2963, 2926, 1724, 1597, 1507, 1449, 1284, 1262, 1086, 1024, and cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 9.20 (s, 1 H, H-3), 8.10-7.20 (m, 15 H, 3 Ph), 6.10 (d, 1 H, $J_{1',2'}$ = 3.1, H-1'), 5.95 (m, 1 H, H-4'), 5.81 (t, 1 H, $J_{2',3'}$ = 3.1, H-2'), 5.62 (dd, 1 H, $J_{3',4'}$ = 2.6, H-3'), 5.54 (d, 1 H, $J_{4,5}$ = 2.2, H-5), 4.43 (dd, 1 H, $J_{4',5'a}$ = 2.2, $J_{5'a,5'b}$ = 12.0, H-5'a), 4.22 (dd, 1 H, $J_{4',5'b}$ = 1.8, H-5'b), 3.83 (dd, 1 H, $J_{4,1"}$ = 6.3, H-4), 3.83 (dd, 1 H, $J_{1",2"}$ = 1.9, H-1"), 3.81 (dd, 1 H, $J_{3",4"a}$ = 3.0, $J_{4"a,4"b}$ = 11.9, H-4"a), 3.74 (dd, 1 H, $J_{3",4"b}$ = 5.6, H-4"b), and 3.73-3.60 ppm (m, 2 H, H-2", 3"); ^{13}C NMR (MeOH-d_4) δ 184.2 (C=S), 167.6, 167.4, 166.1 (3 C, 3 *C*OPh), 134.6-129.0 (18 C, 3 Ph), 86.0 (C-5), 82.1 (C-1'), 72.0 (C-3"), 70.6, 70.1 (C-1", 2"), 69.6 (C-2'), 69.3 (C-3'), 66.0 (C-4'), 65.3 (C-4), 64.6 (C-5'), and 63.6 ppm (C-4"); FABMS *m/z* 705 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{33}H_{34}O_{12}N_2S$: C, 58.06; H, 5.02; N, 4.10; S, 4.70. Found: C, 58.13; H, 5.23; N, 4.15; S, 5.00.

Compound **15** had $[\alpha]^{24}_D$ -54 (*c* 0.7); IR ν_{max} 3318, 3069, 2959, 1724, 1597, 1516, 1451, 1368, 1283, 1262, 1082, and 1026 cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 8.10-7.20 (m, 15 H, 3 Ph), 6.11 (d, 1 H, $J_{1',2'}$ = 2.7, H-1'), 5.81 (t, 1 H, $J_{2',3'}$ = 2.7, H-2'), 5.75 (m, 1 H, H-4'), 5.61 (d, 1 H, $J_{4,5}$ = 6.6, H-5), 5.56 (t, 1

H, $J_{3',4'}$ = 2.7, H-3'), 4.33 (dd, 1 H, $J_{4',5'a}$ = 2.0, $J_{5'a,5'b}$ = 12.9, H-5'a), 4.22 (dd, 1 H, $J_{4',5'b}$ = 1.7, H-5'b), 4.08 (dd, 1 H, $J_{4,1''}$ = 9.0, H-4), 3.86 (dd, 1 H, $J_{1'',2''}$ = 1.7, H-1''), and 3.81-3.70 (m, 4 H, H-2'', 3'', 4''a, 4''b); ^{13}C NMR (MeOH-d_4) δ 184.2 (C=S), 167.6, 167.4, 166.1 (3 C, 3 *C*OPh), 134.3-129.1 (18 C, 3 Ph), 85.6 (C-5), 82.3 (C-1'), 71.2 (C-2''), 70.2 (C-3''), 70.1 (2 C, C-2', 3'), 69.1 (C-1''), 65.4 (C-4'), 64.5 (C-5'), 62.8 (C-4''), and 60.3 ppm (C-4); FABMS *m/z* 705 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{33}H_{34}O_{12}N_2S$: C, 58.06; H, 5.02; N, 4.10; S, 4.70. Found: C, 57.77; H, 5.19; N, 4.20; S, 4.81.

*(4*R*,5*R*)-5-Hydroxy-1-[2',3',4'-tri*-O-*acetyl-6-*O*-*(2''',3''',4''',6'''-tetra*-O-*acetyl-β-*D*-glucopyranosyl)-β-*D*-glucopyranosyl]-4-(*D*-*arabino*tetritol-1-yl) imidazolidine-2-thione* **16**. From **5**; T= r.t.; t= 3h; the residue purified by column chromatography (dichloromethane:methanol 9:1 and afterwards EtOAc:ether:acetone 1:2:1) yielded 0.16 g (66 %) of a white amorphous solid which had $[\alpha]^{26}_D$ +19 (*c* 1.0); IR ν_{max} 3354, 2951, 2899, 1753, 1499, 1442, 1371, 1227, 1072, and 1038 cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 5.95 (d, 1 H, $J_{1',2'}$ = 9.0, H-1'), 5.37 (d, 1 H, $J_{4,5}$ = 2.3, H-5), 5.33 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 9.4, H-3'), 5.11-4.96 (m, 5 H, H-2', 4', 2''', 3''', 4'''), 4.79 (d, 1 H, $J_{1''',2'''}$ = 8.0, H-1'''), 4.28-4.26 (m, 1 H, H-6'''a), 4.14-4.11 (m, 1 H, H-6'''b), 3.84 (ddd, 1 H, $J_{4',5'}$ = 10.0, $J_{5',6'a}$ = 4.7, $J_{5',6'b}$ = 2.5, H-5'), 3.81-3.60 (m, 9 H, H-4, 6'a, 6'b, 1'', 2'', 3'', 4''a, 4''b, 5'''), and 2.08-1.95 ppm (m, 21 H, 7 Ac); ^{13}C NMR (MeOH-d_4) δ 184.1 (C=S), 172.4, 172.3, 171.9, 171.8, 171.6, 171.3, 171.2 (7 *C*OCH$_3$), 101.3 (C-1'''), 84.3 (C-5), 83.5 (C-1'), 76.4 (C-5'), 75.7 (C-3'), 74.3 (C-2''), 72.8 (3 C, C-1'', 3'', 5'''), 72.6 (C-3'''), 70.1 (C-2'''), 69.8 (2 C, C-2', 4'), 68.1 (C-4'''), 67.2 (C-4), 64.7 (C-6'), 63.1 (2 C, C-4'', 6'''), and 20.9-20.5 ppm (7 C, 7 CO*C*H$_3$); FABMS *m/z* 879 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{33}H_{48}O_{22}N_2S$: C, 46.26; H, 5.65; N, 3.27; S, 3.74. Found: C, 46.20; H, 5.69; N, 3.25; S, 4.01.

*(4*R*,5*R*)-5-Hydroxy-1-[2,3,4-tri*-O-*acetyl-6-*O*-*(2,3,6-tri*-O-*acetyl-4-*O*-*(2,3,4,6-tetra*-O-*acetyl-α-*D*-glucopyranosyl)-β-*D*-glucopyranosyl)-β-*D*-glucopyranosyl)]-4-(*D*-*arabino*tetritol-1-yl) imidazolidine-2-thione* **17**. From **6**; T= r.t.; t= 2h; TLC (EtOAc:ether:acetone 1:1:1) yielded **17** (106 mg, 32%) and other compound resulting of the loss of an AcOH molecule from **17** (85 mg, 26 %). Compound **17** had $[\alpha]^{25}_D$ +158 (*c* 0.24); ^{1}H NMR (MeOH-d_4) δ 6.08 (d, 1 H, $J_{1',2'}$ = 9.0, H-1'), 5.36 (d, 1 H, $J_{4,5}$ = 2.4, H-5), 5.36-4.95 (m, 9 H, H of acetylated positions of D-glucopyranosyl rings and H-1α), 4.62-3.90 and 3.74-3.56 (16 H, H-4, 5, 6 of D-glucopyranosyl rings, H-1 and H-4 of the central glucopyranosyl ring, H-1'', 2'', 3'', 4''a and 4''b), 3.83 (dd, 1 H, $J_{4,1''}$ = 8.8, H-4), and 2.12-1.89 ppm (m, 30 H, 10 Ac); ^{13}C NMR (MeOH-d_4) δ 183.0 (C=S), 172.5-171.1 (10 C, 10 *C*OCH$_3$), 101.7, 97.1, 80.2 (C-1 of sugar rings), 85.7 (C-5), 79.0-69.0 (15 C, C-2, 3, 4, 5 of sugar rings, C-1'', 2'', 3''), 67.1 (C-4), 65.3 (C-4''), 64.4, 64.2, 63.1 (C-6 of sugar rings), and 21.2-20.5 ppm (10 C, 10 CO*C*H$_3$); HRFABMS: $[M+Na]^{+\cdot}$ Calculated for $C_{45}H_{64}O_{30}N_2SNa$ 1167.3162. Found: 1167.3170.

*(4*R*,5*R*) and (5*S*)-5-Hydroxy-1-(1',3',4',6'-tetra*-O-*acetyl-2-deoxy-β-*D*-glucopyranos-2-yl)-4-(*D*-*arabino*tetritol-1-yl) imidazolidine-2-thione* **18a, 18b**. A solution of 2-amino-2-deoxy-β-D-glucopyranose (55 mg, 0.31 mmol) in water (0.5 mL) was added gradually to a solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-isothiocyanato-β-D-glucopyranose[37] (0.1 g, 0.26 mmol), in DMF (0.5 mL) under nitrogen. The resulting solution was stirred at r.t. for 10 min. The solvent was evaporated under diminished pressure and the residue was purified by column chromatography (dichloromethane:methanol 9:1). Yield 78 mg, (60 % of a 3:1 mixture

of **18a** and **18b**; $[\alpha]^{25}_D$ +35 (*c* 1.2); IR ν_{max} 3424, 2936, 1753, 1493, 1445, 1371, 1229, and 1040 cm^{-1}; ^1H NMR[40] (MeOH-d_4) δ 6.22 (d, 1 H, $J_{1',2'}$ = 8.0, H-1'*R*), 6.21 (d, 1 H, $J_{1',2'}$ = 8.0, H-1'*S*), 5.75 (d, 1 H, $J_{4,5}$ = 6.2, H-5*S*), 5.35 (d, 1 H, $J_{4,5}$ = 2.5, H-5*R*), 5.33 (t, 1 H, $J_{2',3'} = J_{3',4'}$ = 8.7, H-3'*R*), 5.31 (t, 1 H, $J_{4',5'}$ = 8.7, H-4'*R*), 5.13 (t, 1 H, $J_{3',4'} = J_{4',5'}$ = 8.7, H-4'*S*), 5.12 (t, 1 H, $J_{2',3'}$ = 8.7, H-3'*S*), 4.33, 4.31 (each dd, each 1 H, H-2'*R* and *S*), 4.29 (dd, 1 H, $J_{5',6'a}$ = 2.1, $J_{6'a,6'b}$ = 12.5, H-6'a*R*), 4.25 (dd, 1 H, $J_{4,1''}$ = 8.0, H-4*S*), 4.19 (dd, 1 H, $J_{5',6'a}$ = 2.1, $J_{6'a,6'b}$ = 12.5, H-6'a*S*), 4.13 (dd, 1 H, $J_{5',6'b}$ = 4.2, H-6'b*R*), 4.11 (dd, 1 H, $J_{5',6'b}$ = 4.2, H-6'b*S*), 3.99 (ddd, 1 H, H-5'*R*), 3.94 (ddd, 1 H, H-5'S), 3.84-3.60 (m, 8 H, H-1", 2", 3", 4"*R* and *S*), 3.77 (dd, 1 H, $J_{4,1''}$ = 9.8, H-4*R*), 3.49 (m, 2 H, H-4"b*R* and *S*), and 2.09-1.96 ppm (m, 24 H, 8 Ac); ^{13}C NMR[40] (MeOH-d_4) δ 183.6 (C=S*S*), 182.3 (C=S*R*), 172.5-170.9 (8 C, 8 *C*OCH$_3$), 94.3, 94.5 (C-1'*R* and *S*), 89.2 (C-5*R*), 85.6 (C-5*S*), 75.4, 75.2 (C-5'*R* and *S*), 73.8, 73.3 (C-3'*R* and *S*), 72.7-70.0 (6 C, C-1", 2", 3"*R* and *S*), 72.1, 71.4 (C-2'*R* and *S*), 67.3, 67.1 (C-4'*R* and *S*), 65.3, 65.2 (C-6'*R* and *S*), 64.9 (C-4*R*), 64.6, 64.3 (C-4"*R* and *S*), 60.6 (C-4*S*), and 21.1-20.6 ppm (8 C, 8 CO*C*H$_3$); FABMS *m/z* 531 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{19}H_{28}O_{12}N_2S$: C, 44.88; H, 5.55; N, 5.51; S, 6.31. Found: C, 44.60; H, 5.44; N, 5.29; S, 6.47.

*(4*R*,5*R*)-5-Acetoxy-4-(1",2",3",4"-tetra*-O*-acetyl-D*-arabino*tetritol-1-yl)-1-(2',3',4'-tri*-O*-benzoyl-β-D-ribopyranosyl) imidazolidine-2-thione* **12** and *(4*R*, 5*R*)-5-acetoxy-3-acetyl-4-(1",2",3",4"-tetra*-O*-acetyl-D*-arabino*tetritol-1-yl)-1-(2',3',4'-tri*-O*-benzoyl-β-D-ribopyranosyl) imidazolidine-2-thione* **13**. These compounds were prepared by acetylation of **11** in the same manner that **8** and **9** from **7**, but using a temperature of 4 °C. TLC of the residue (ether:hexane 6:1) yielded **12** (0.21 g, 84 %, lower R_F value) and **13** (0.02 g, 7 %, higher R_F value) as amorphous solids.

Compound **12** had $[\alpha]^{26}_D$ +59 (*c* 0.8); IR ν_{max} 3337, 3189, 3067 2963, 2861, 1753, 1599, 1499, 1445, 1371, 1262, 1208, 1070, and 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21–7.24 (m, 15 H, 3 Ph), 7.13 (s, 1 H, $J_{4,5}$ = 0.0, H-5), 6.82 (s, 1 H, H-3), 6.52 (d, 1 H, $J_{1',2'}$ = 9.6, H-1'), 6.25 (m, 1 H, H-3'), 6.07 (dd, 1 H, $J_{2',3'}$ = 3.1, H-2'), 5.50 (dd, 1 H, $J_{1'',2''}$ = 1.7, $J_{2'',3''}$ = 8.4, H-2"), 5.38 (td, 1 H, $J_{3',4'}$ = 2.5, $J_{4',5'a} = J_{4',5'b}$ = 8.2, H-4'), 5.19 (dd, 1 H, $J_{4,1''}$ = 9.7, H-1"), 5.07 (m, 1 H, H-3"), 4.24 (dd, 1 H, $J_{3'',4''a}$ = 2.7, $J_{4''a,4''b}$ = 12.5, H-4"a), 4.19 (dd, 1 H, $J_{3'',4''b}$ = 4.6, H-4"b), 4.13 (d, 2 H, H-5'a, 5'b), 3.80 (d, 1 H, H-4), 2.16, 2.12, 2.11, 1.92, and 1.83 ppm (each s, each 3 H, 5 Ac); ^{13}C NMR ($CDCl_3$) δ 183.7 (C=S), 170.6, 169.8, 169.6, 169.0, 168.8 (5 *C*OCH$_3$), 165.5, 165.3, 164.9 (3 *C*OPh), 133.4-128.1 (18 C, 3 Ph), 81.7 (C-1'), 80.0 (C-5), 69.5 (C-3'), 68.5 (C-1"), 68.1 (C-3"), 67.6 (C-2"), 66.8 (C-4'), 66.4 (C-2'), 63.2 (C-5'), 61.3 (C-4"), 60.0 (C-4), 20.9, 20.5, 20.4, 20.3, and 20.2 ppm (5 CO*C*H$_3$); FABMS *m/z* 915 (100, $[M+Na]^{+\cdot}$). Anal. Calcd for $C_{43}H_{44}O_{17}N_2S$: C, 57.84; H, 4.97; N, 3.14; S, 3.59. Found: C, 57.90; H, 5.00; N, 3.34; S, 3.89.

Compound **13** had $[\alpha]^{24}_D$ +50 (*c* 0.26); IR ν_{max} 3300, 3069, 2963, 1751, 1601, 1420, 1371, 1260, 1219, 1082, and 1022 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.18–7.25 (m, 15 H, 3 Ph), 6.97 (s, 1 H, $J_{4,5}$ = 0.0, H-5), 6.63 (d, 1 H, $J_{1',2'}$ = 9.8, H-1'), 6.30 (dd, 1 H, $J_{2',3'}$ = 3.2, H-2'), 6.25 (m, 1 H, H-3'), 5.51 (dd, 1 H, $J_{1'',2''}$ = 2.3, $J_{2'',3''}$ = 8.5, H-2"), 5.38 (ddd, 1 H, $J_{3',4'}$ = 2.6, $J_{4',5'a}$ = 9.8, $J_{4',5'b}$ = 6.6, H-4'), 5.12 (m, 1 H, H-3"), 4.97 (dd, 1 H, $J_{4,1''}$ = 10.1, H-1"), 4.83 (d, 1 H, H-4), 4.22 (dd, 1 H, $J_{3'',4''a}$ = 4.6, $J_{4''a,4''b}$ = 12.6, H-4"a), 4.17-4.14 (m, 2 H, H-5', 6'a), 4.13 (dd, 1 H, $J_{3'',4''b}$ = 2.7, H-4"b), 2.79, 2.17, 2.13, 2.10, 1.88, and 1.40 ppm (each s, each 3 H, 6 Ac); ^{13}C NMR ($CDCl_3$) δ 182.0 (C=S), 170.8, 170.5, 169.8, 169.6, 169.4, 169.3 (6 *C*OCH$_3$), 165.4, 165.2, 164.9 (3 *C*OPh), 133.5-128.2 (18 C, 3 Ph), 81.3 (C-1'),

77.6 (C-5), 69.6 (C-3'), 68.3 (C-3"), 67.9 (C-2"), 67.4 (C-1"), 66.7 (C-4'), 66.3 (C-2'), 63.4 (C-5'), 61.4 (C-4"), 60.5 (C-4), 26.8, 20.8 (2 $COCH_3$), 20.5 (2 C, 2 $COCH_3$), 19.9, and 19.8 ppm (2 $COCH_3$); FABMS *m/z* 957 (100, $[M+Na]^{+\cdot}$). HRFABMS: $[M+Cs]^{+\cdot}$ Calculated for $C_{45}H_{46}O_{18}N_2SCs$ 1067.1581. Found: 1067.1520.

ACKNOWLEDGMENTS

We thank the Dirección General de Investigación Científica y Técnica of Spain for the financial support (grant number PB 94/1440 C02-01).

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40. Assignments indicated with *R* and *S* correspond to **18a** and **18b** respectively.

(*Received in UK* 23 *October* 1995; *accepted* 4 *December* 1995)