Pergamon

Tetrahedron 55 (1999) 4377–4400

TETRAHEDRON

Non-Biaryl Atropisomers Derived from Carbohydrates. Part 1. Stereoselective Synthesis of 1-Aryl-5-hydroxyimidazolidine-2-thiones and Their Transformation into Imidazoline-2-thiones[1]

Martín Avalos, Reyes Babiano, Pedro Cintas, José L. Jiménez, Juan C. Palacios,* Guadalupe Silvero, and Concepción Valencia

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Extremadura, E-06071 Badajoz, Spain

Received 16 November 1998; revised 11 January 1999; accepted 28 January 1999

Abstract: A series of chiral 5-hydroxyimidazolidine-2-thiones bearing an *ortho*-substituted aromatic residue at N-1, which are readily accessible from D-glucosamine, have been synthesized as potential atropisomers. In general, these substances display a *trans* arrangement between H-4 and H-5, and hence the absolute configuration at C-5 was shown to be *R*. However, the first example of this type of structures having a *cis* configuration (*S* at C-5) is also described. Moreover, the mechanistic features associated with the conversion of 5-acetoxyimidazolidine-2-thiones into imidazoline-2-thiones have also been evaluated.

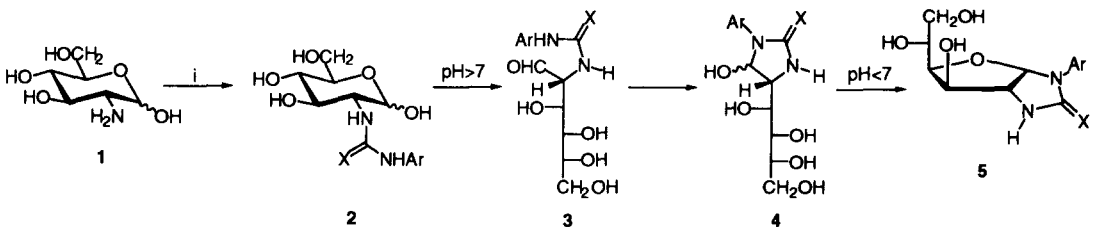
Keywords: Atropisomerism, carbohydrates, imidazolidine-2-thiones, imidazoline-2-thiones, NMR spectroscopy.

INTRODUCTION

In a series of recent papers we have worked out the mechanistic features of the condensation of 2-aminoaldoses with heterocumulenes,[2,3] a chemical transformation spanning a period of almost a century. In particular, the reaction of 2-amino-2-deoxy-D-glucopyranose (**1**) with isocyanates under neutral conditions produces 2-deoxy-2-ureido-D-glucopyranoses **2** (X=O), which cyclize to 5-hydroxyimidazolidine-2-ones **4** (X=O) at pH > 7, while imidazolidine-2-ones **5** (X=O) are obtained at pH < 7 (Scheme 1).[2]

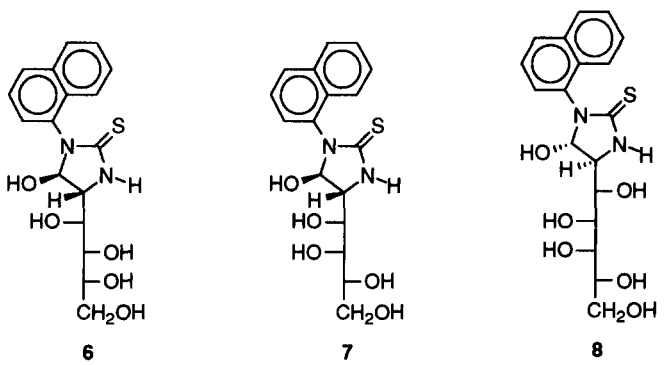
Isothiocyanates behave analogously.[2a,3] It was Scott,[4] in 1970, who attributed a structure of 5-hydroxyimidazolidine-2-thiones **4** (X=S) to the products isolated by reaction of arylisothiocyanates with 2-amino-2-deoxyaldoses; this hypothesis was later corroborated.[2a,3,5] In general, the intermediate thioureido derivative **2** (X=S) cannot be isolated and cyclizes spontaneously to yield **4** (X=S).[3]

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00109-X



Scheme 1. Reagents: i) Ar-NCX (X = O, S).

Structures such as **4** and **5** and their *O*-protected derivatives, generated as optically pure compounds, may be useful as chiral auxiliaries and, eventually as ligands for asymmetric catalysis if the C=X groups are good donor atoms for metals. The fact that NMR spectra of the corresponding 1-naphthyl derivatives **6-8** show two signal sets, suggests that the duplicated resonances might be attributed to the existence of rotational isomers.[3,6] The resolution of these non-biaryl atropisomers could also be particularly attractive owing to their inherent chirality provided by carbohydrate side chains of different configurations.



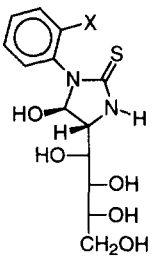
These observations prompted us to elucidate the structural requirements for the existence of atropisomerism in structures of imidazolidine-2-ones and 2-thiones. Thus, we have studied the influence of: a) substituents at the *ortho* position in the aromatic ring, b) the length of the C=O *versus* the C=S bond, and c) the presence of substituents at C-5 in the heterocyclic moiety.

In this work we have prepared some 1-aryl-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thiones and their transformation into diversely functionalized derivatives. Also, this research gains insight into the mechanistic pathways of such conversions. As we shall see, some substances bearing a naphthyl group have been obtained as a mixture of rotamers (see experimental section). In the accompanying paper (Part 2) the barriers to rotation in these and other compounds will be reported

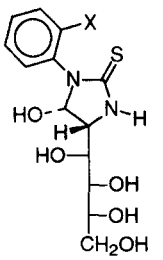
RESULTS

Synthesis of 1-aryl-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thiones. The reactions of 2-amino-2-deoxy-D-glucopyranose (**1**) with 2-fluoro-, 2-chloro-, and 2-bromo-phenyl

isothiocyanates in ethanol-water at ~45 °C for 30 min produced the corresponding (4*R*,5*R*)-1-aryl-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thiones (**9-11**) in high yields. Nevertheless, the analogous reaction with 2-methoxyphenyl isothiocyanate gave rise to (4*R*,5*S*)-5-hydroxy-1-(2-methoxyphenyl)-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (**16**), and not its (4*R*,5*R*) isomer, **12**.



9 X = F
10 X = Cl
11 X = Br
12 X = OMe



13 X = F
14 X = Cl
15 X = Br
16 X = OMe

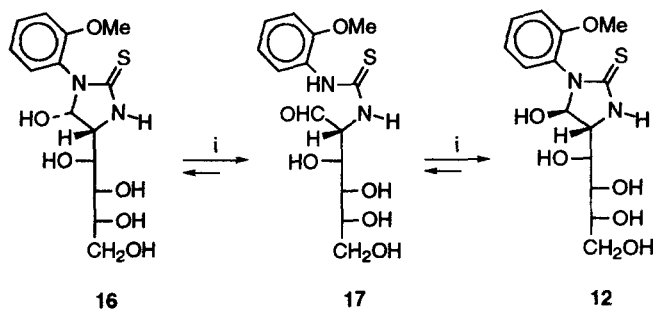
The monocyclic structures attributed to **9-11** and **16** are supported by their spectroscopic data, elemental analyses, syntheses and characterization of their per-*O*-acetyl derivatives, and based on previous citations on these reactions.[2-5] Although the interpretation of their ^{1}H NMR spectra is not obvious, some resonances can easily be identified, such as a signal at δ 8.51 characteristic of the NH proton, those for the aromatic protons, H-5 at δ 5.30, and four doublets for the OH protons, with the exception of the terminal OH at C-4' which appears as a triplet. Moreover, the number of OH resonances is consistent with an acyclic structure and not with a system of glycofurano[2,1-*d*]imidazolidine-2-thione.

The ^{13}C NMR spectrum shows a signal for C-5 at δ 87.3, but this resonance is close to that of C-1 of a 2-deoxy-2-thioureido-D-glucopyranose and, it cannot therefore be considered as evidence of an acyclic carbohydrate. However, C-1', C-2', and C-3' have almost the same apparent chemical shifts, which is potentially consistent with the presence of an acyclic polyhydroxyalkyl chain.[7] Furthermore, the signal for the C=S bond at δ 180.9 rules out the alternative isomeric structures of 2-iminothiazolidine or 2-aminothiazoline.

The configuration at C-5 could be assigned on the basis of the coupling constant $J_{4,5}$. The small dihedral angle[8] ($\theta < 25°$) between H-4 and H-5, which results from a *cis* disposition, corresponds to a typical coupling constant of 5-6 Hz,[9,10] whereas a *trans* arrangement is consistent with a dihedral angle of about 90° with $J_{4,5}$ ~0 Hz.[9] The ^{1}H NMR spectra of compounds **9-11**, upon addition of D_2O, show small values of $J_{4,5}$ (2.2 Hz), thereby evidencing a *trans* disposition between H-4 and H-5 and hence the absolute configuration at C-5 should be *R*.

In contrast, compound **16** shows a coupling constant $J_{4,5}$ of 7.4 Hz. Large values of $J_{4,5}$ (~5-6 Hz) reveal a *cis* disposition, which has been found in similar structures,[2,3,10] thereby demonstrating that the configuration at C-5 is *S*. It is noteworthy that this is the first imidazolidine-2-thione derivative of this type of substances with a *cis* stereochemical arrangement.

However, this isomer is less stable than its *5R* counterpart (**12**). The epimerization was also examined by ^{1}H NMR spectroscopy in DMSO-d_6 at room temperature, which occurs presumably through the acyclic intermediate **17** (Scheme 2). Figure 1 depicts the NMR monitoring, although no intermediate species could be detected.



Scheme 2. Reagents: i) DMSO-d_6, 23 °C.

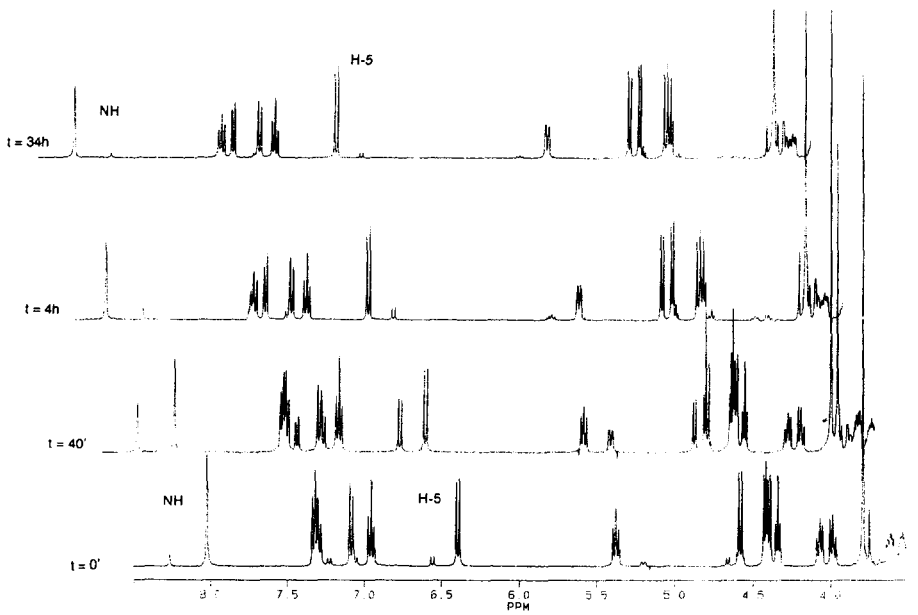
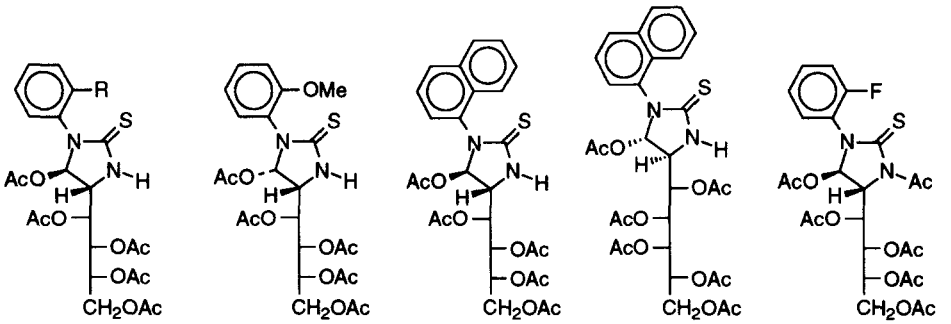


Figure 1. Interconversion of compound **16** into its epimer **12**.

Preparation of 5-acetoxy-4-(polyacetoxyalkyl)-1-arylimidazolidine-2-thiones. Given the partial spectroscopic interpretation of the aforementioned compounds, our next target was the preparation of their per-*O*-acetyl derivatives. Likewise, this strategy has allowed us to evaluate the effect of a bulkier substituent at C-5. The acetylation was conducted in a mixture of acetic anhydride and pyridine at –15 °C for 24 h, whereby all the OH groups were protected but not the heterocyclic NH group, and both the initial structure and stereochemistry remained unaffected. Thus, acetylation of compounds **9**-**11** and **16** gave the corresponding

per-*O*-acetyl derivatives **18-21** in high yields. Compound **22**, epimer of **21** at C-5, was also obtained when a solution of **16** in DMSO was left at room temperature for 30 h which achieved its conversion into **12**, and the latter was then treated with acetic anhydride-pyridine. Analogously, the protected derivatives **23**[3] and **24** were obtained from **6**[4] and **8**[3] respectively. When the acetylation was run at 80 °C the *N*-acyl derivatives were obtained and thus, under such reaction conditions, **18** was transformed into **25**.



18 R = F
19 R = Cl
20 R = Br
22 R = MeO

21 **23** **24** **25**

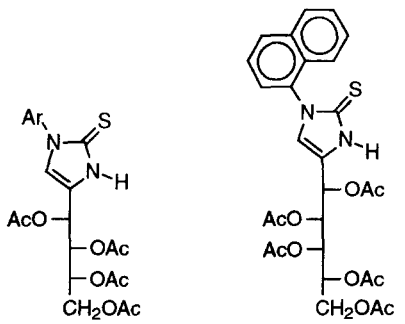
Again, the structures assigned to **18-24** are supported by their spectral data and elemental analyses. The IR spectra show the NH stretching vibration at ~3300 cm^{-1} and the ^1H NMR spectra show the most deshielded signals for the NH protons (δ ~7.5-8.5), thereby indicating the absence of *N*-acetylation. In contrast, the IR spectrum of **25** shows no NH absorption band, but a very informative amide band at 1700 cm^{-1}. The *N*-acetyl group in **25** induces a remarkable downfield shift of H-5 (Δδ = 0.94 ppm) and upfield shifts of C-4 and C=S (Δδ ~-4 ppm) when compared with those of **18**. An unusual deshielding for the methyl resonance of the acetamido group (Δδ ~0.7 ppm) is also observed in **25**, caused by its proximity to the heterocyclic C=S in the more stable *s-trans*-conformation. In this disposition the dipole-dipole repulsion between C=O and C=S groups is minimized. It is also noteworthy the change in the optical rotation with the presence of *N*-acyl groups. Thus, the $[\alpha]_D$ value of **18** is 46° greater than that of **25**.

Likewise, the stereochemistry of these substances at C-5 was confirmed by the vicinal coupling constant between H-4 and H-5. The value of $J_{4,5}$ ~0 Hz points to a *trans* arrangement and hence the absolute configuration of C-5 in the heterocyclic moiety should always be *R*. These configurations are the same as in **6**, **8**, **9-12** and **16**, which shows that both the structure and stereocenters are not altered during the acetylation reaction.

The ^{13}C NMR spectra show a signal at δ ~181 assigned to the thiocarbonyl group, a fact that rules out isomeric structures derived from 2-iminothiazolidine or 2-aminothiazoline nuclei.[3] The chemical shift of C-5 lies in the range of δ 84-89, analogous to those of the unprotected compounds **6**, **8**, **9-12** and **16**, although they are somewhat different from those of glycofuranoimidazolidine-2-thiones (δ 93-97). Despite these differences, the resonance of C-5 cannot be utilized unequivocally to characterize the structure of aminosugar-isothiocyanate

adducts. Furthermore, the almost identical chemical shifts for C-1', C-2' and C-3' agree with the existence of an acyclic polyhydroxyalkylated sugar chain.[7]

Synthesis of 4-(polyacetoxyalkyl)-1-arylimidazoline-2-thiones. In the course of this research, we have observed that, when the per-*O*-acetylated imidazolidine-2-thiones **18-20** and **22-24** are heated in DMSO-d_6, they undergo a rapid elimination of acetate at the heterocyclic ring to yield the corresponding 4-(polyacetoxyalkyl)-1-arylimidazoline-2-thiones **26-31**.



26 Ar = 2-FC_6H_4
27 Ar = 2-ClC_6H_4
28 Ar = 2-BrC_6H_4
29 Ar = 2-$MeOC_6H_4$
30 Ar = 1-$C_{10}H_7$

31

The transformation is quantitative as indicated by ^1H NMR monitoring and depicted in Figure 2 in the particular case of the conversion of **23** into **30**. It should be pointed out that compound **30** shows two signal sets at room temperature, which correspond to the existence of both atropisomers.

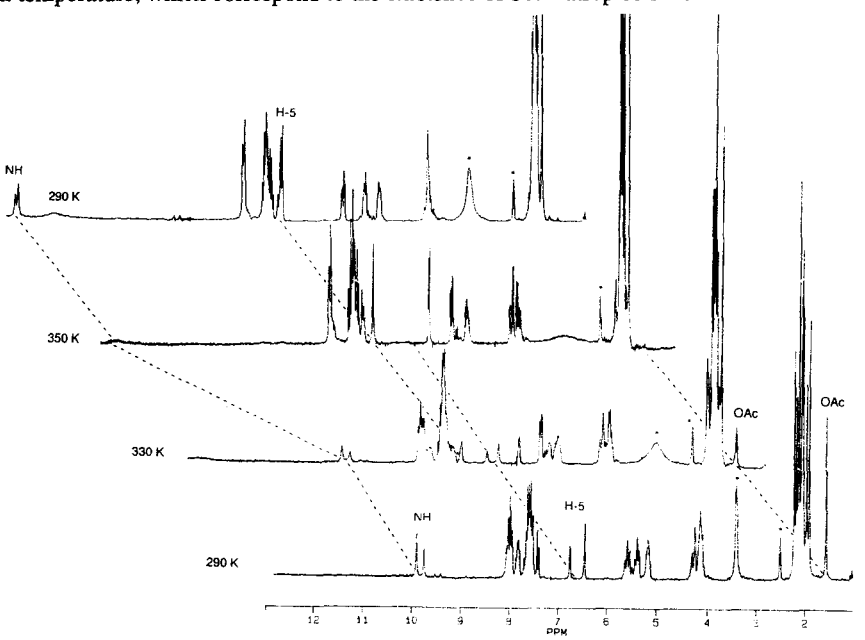


Figure 2. Thermal transformation of **23** into **30**.

The ^{1}H NMR spectrum reveals the lack of H-4 and a significant downfield shift for H-1' ($\Delta\delta$ ~0.5 ppm) due to its allylic nature. Moreover, the structures attributed to **26-31** are in agreement with the resonances for C-4 and C-5, which are observed at δ ~124 and δ ~118 respectively, as well as with a prominent upfield shift for the C=S group (δ ~163) when compared with the corresponding signal for **18-20** and **22-24**.

DISCUSSION

Formation of heterocyclic derivatives. The reaction of 2-amino-2-deoxyaldoses with *ortho*-substituted aryl isothiocyanates is analogous to the condensation with other isothiocyanates, and such a substitution does not cause steric hindrance to the formation of the corresponding polyhydroxyalkyl imidazolidine-2-thiones. So far, the products of these reactions have shown a *trans* relationship between the substituents at the heterocyclic moiety, whith the sole exception of **16**, which exhibits a *cis* configuration, although the latter was easily converted into **12** in DMSO-d_6 (Scheme 2, *vide supra*). The disappearance as a function of time was shown in Figure 1 and the sets of integration data were fit to a reversible first-order rate law, since no additional intermediates were observed. The kinetic data and data analysis are provided in the Experimental section, which enable the determination of the rate constant for isomerization at 23 °C (k_S = 1.92 x 10^{-4} s^{-1}, k_R = 1.95 x 10^{-5} s^{-1}). The ^{1}H NMR spectra of compounds **9-11**, like **12**, showed the presence of *cis* isomers **13-15** at very low concentrations; *e.g.* for **13** and **9** a mixture of two isomers in 1:12 ratio, which corresponds to a preponderance of the *trans* isomers in ~93%. The relatively easy epimerization of *cis* isomers and the greater stability of the *trans* derivatives together account for why the latter isomers are preferentially isolated.

Acetylation under mild conditions (–15 °C) modifies neither the structure nor the relative stereochemistries of the starting materials, and allows the incorporation of substituents other than hydrogen at C-5. Notably, acetic acid elimination to yield the corresponding imidazoline-2-thione alleviates the steric size. Differences in the molecular size of substituents may provide a useful information of their effects on the existence of atropisomerism.

In relation with the elimination reaction, and from a mechanistic viewpoint, the resulting *trans* configuration of the per-*O*-acetylated monocycles would favor a facile pyrolytic *syn*-elimination of acetic acid (cyclo-$D_HD_NA_n$)[11] through a pericyclic six-membered transition state **33** (Scheme 3).

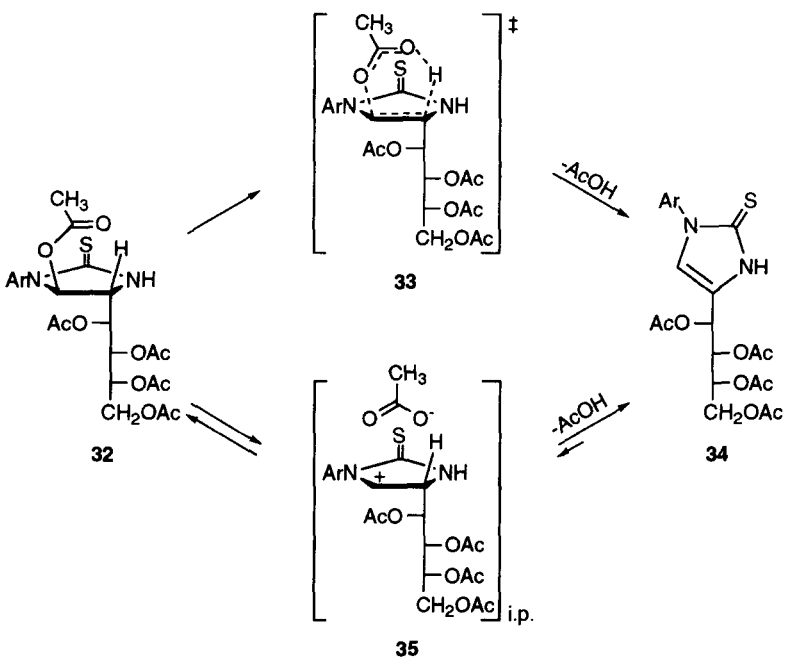
It was our hope that, in addition to furnishing a novel synthesis of imidazoline-2-thiones, the study of reaction conditions might afford further information on the elimination pathway. No elimination reactions were observed at room temperature in benzene, CH_2Cl_2, or $CHCl_3$. When reactions were conducted at reflux, it was seen that elimination occurred and yields were dependent on the nature of the substituent at the aromatic ring. Table 1 shows a series of experimental results obtained in refluxed benzene or $CHCl_3$ for 20 and 30 h, respectively, followed by solvent evaporation and analysis of crude mixtures by ^{1}H NMR.

Table 1. Transformation of **32** into **34** (%).

		Substituent X (Ar = 2-XC_6H_4)			
Solvent	Product	F	Cl	MeO	Br
Cl_3CH[a]	**34**	0	26	52	73
	32	100	74	48	27
C_6H_6[b]	**34**	0	53	c	71
	32	100	47	c	29

[a] Reflux, 30 h; [b] Reflux, 20 h; [c] Not determined.

Data clearly indicate that decreasing the electronegativity and/or increasing the size of the *ortho* substituent, progressively increased the reaction yield. The 2-fluoroderivative **18** did not react, although a quantitative transformation was observed, as also for other compounds, in polar solvents such as DMSO or in an acetic anhydride-acetic acid mixture. In these solvents, the elimination reactions were faster on heating at ~80 °C, but appreciable reaction rates were also observed at room temperature. However, *N*-acetylation occurred in a solvent mixture of acetic anhydride-pyridine affording **25**.



Scheme 3

Given the results obtained, the elimination rate appears to be largely dependent on the solvent polarity, which is inconsistent with a pericyclic process.[12] An E1cb mechanism ($A_{xh}D_H+D_N$)[11] is also unlikely because of the lack of acidity of H-4. Nevertheless, an unimolecular elimination ($D_N+A_{xh}D_H$) is plausible since it would proceed *via* the initial formation of an encounter pair (**35**) and this species could revert to the starting material,

or the acetate counterion, held in close proximity for some time by the surrounding solvent molecules, could promote elimination to produce the imidazoline-2-thione **34** (Scheme 3).

The ion-pair mechanism involving **35** may be operative because of the stabilizing effect of the lone pair on the adjacent nitrogen (N-1), which is increased either by a decrease in electronegativity of the *ortho* substituent at the aromatic ring, or by an increase in size of the *ortho* substituent, that causes inhibition of resonance because the aromatic ring and the heterocyclic moiety are sterically forced out of planarity. On the other hand, the two unshared electrons of the unsubstituted nitrogen (N-3) would contribute to delocalize the C=S bond by a resonance effect. Only if this donation is reduced or prevented, there will be a competitive effect between the stabilization of the carbonium ion and delocalization of the C=S bond by the lone pair on N-1.

Accordingly, factors inhibiting the stabilization of the carbonium ion will prevent or retard the elimination pathway. This fact was evident when the elimination of **25** was attempted under more drastic conditions than those described for **26-31**. Thus, no elimination of acetic acid was observed in DMSO-d_6 at 152 °C and **25** was recovered unaffected. In this case, the lone-pair orbital on N-1 is likely involved in delocalizing the thiocarbonyl group, which results in a diminished stabilization of the carbonium ion.

An alternative mechanism would also be possible if H-4 at the heterocyclic moiety and the acetate group bear an *anti* disposition. Thus, the elimination was studied in the case of **21**, an isomer of **22**, with a relative *cis* stereochemistry, which was converted quantitatively into **29** in DMSO-d_6 and ^{1}H NMR spectra did not provide evidence for the formation of intermediates (Figure 3).

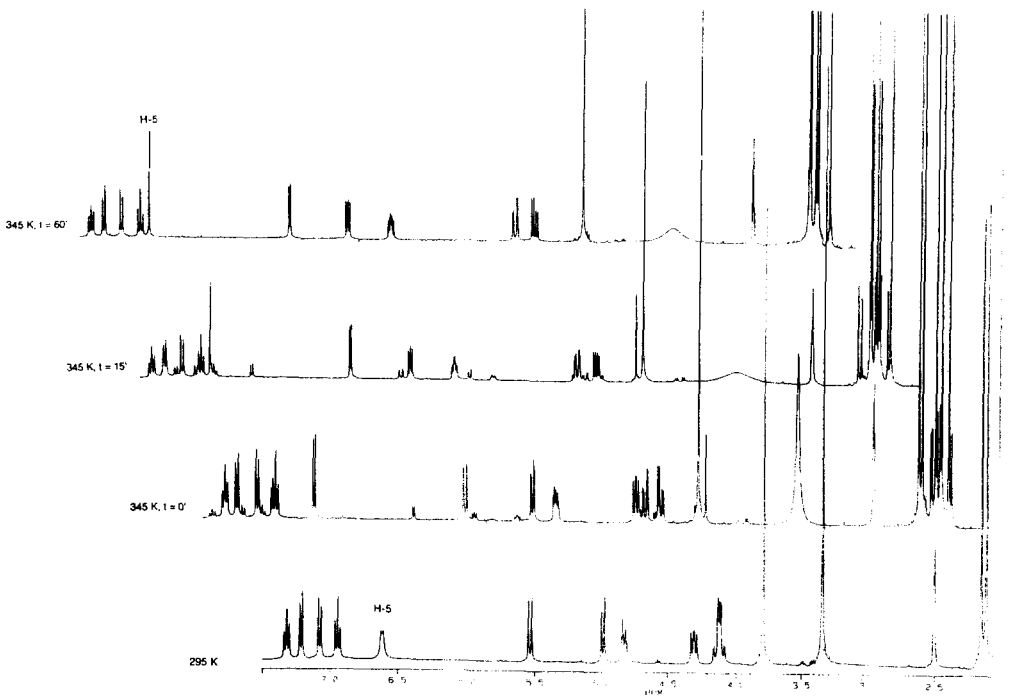
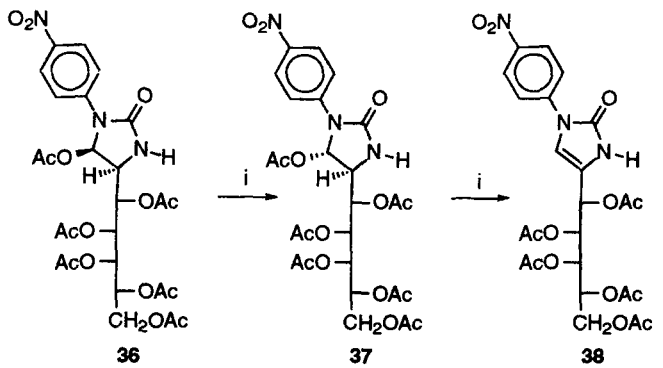


Figure 3. Thermal transformation of **21** into **29**.

This type of elimination reaction had already been observed[2] in the synthesis of per-*O*-acetylated monocyclic structures derived from imidazolidine-2-ones, the oxoanalogs of **32**. Since the mechanistic pathway should presumably be the same, we decided to investigate the elimination of **36** in which the substituents at the heterocyclic moiety adopt a *cis* relationship as well. Variable-temperature ^{1}H NMR experiments run in DMSO-d_6 (Figure 4) revealed the conversion of **36** ($\delta_{H\text{-}5}$ 7.01, $J_{4,5}$ 5.8 Hz) into its *trans* isomer **37** ($\delta_{H\text{-}5}$ 6.71, $J_{4,5}$ 0.0 Hz), which underwent elimination to produce **38** ($\delta_{H\text{-}5}$ 7.19, $J_{4,5}$ 0.0 Hz)[2b] in quantitative yield (Scheme 4).



Scheme 4. *Reagents:* i) DMSO-d_6, Δ.

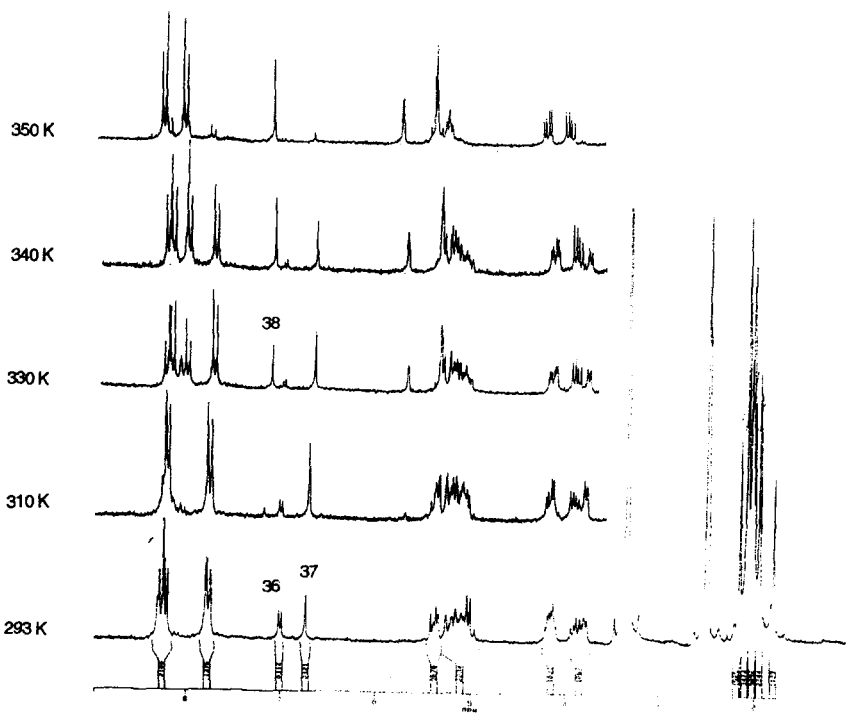
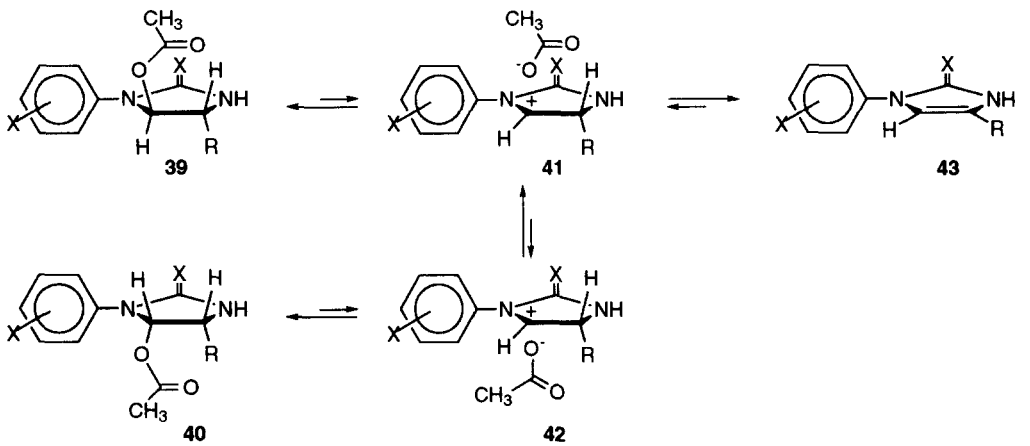


Figure 4. Elimination reaction of **36**.

A concerted E2 process ($A_{xh}D_HD_N$)[11] cannot take place since the stereoelectronic requisite of an *antiperiplanar* arrangement cannot be reached owing to the almost rigid planarity of the imidazolidine-2-one ring, and it does not explain the formation of **37** either. The above-mentioned results are consistent with the E1 mechanism (D_N+$A_{xh}D_H$)[11] outlined in Scheme 5. Either with a relative *trans* (**39**) or *cis* (**40**) stereochemistry at the heterocyclic moiety, the first step is the formation of an encounter ion or ion pairing (**41** or **42**). The *cis* pair **42** isomerizes to the *trans* pair **41**, and the latter releases acetic acid to afford **43** or goes back to **39**.



Scheme 5

With these premises a similar rationale may be invoked to account for the formation of other unsaturated structures derived from carbohydrates.[13-15] It has been mentioned that the elimination reactions occur quantitatively in DMSO or in a solvent mixture consisting of acetic anhydride plus acetic acid, but from a synthetic viewpoint such solvents are unpractical. The elimination proceeds equally well either in benzene or $CHCl_3$ at reflux in the presence of solid $KHCO_3$. Probably, the added base removes acetic acid, thereby avoiding the formation of an equilibrium. The protocol is quite simple and compounds **26-28** were obtained in moderate, but not optimized, yields (30-50%).

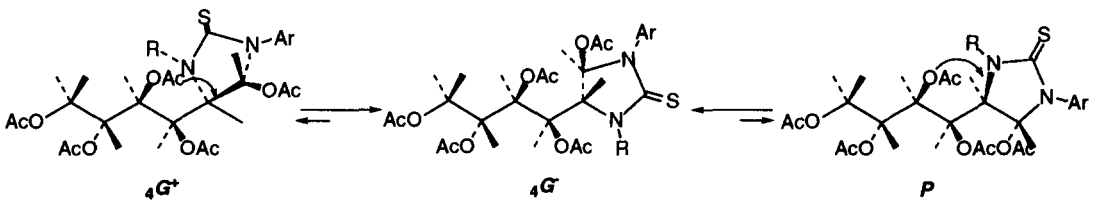
These results constitute a novel route for the preparation of polyacetoxylalkyl imidazoline-2-thiones (**34**), which are versatile raw materials in the synthesis of acyclic *C*-nucleosides *via* mesoionic heterocycles.[16] Derivatives **34** have so far been obtained by isomerization of bicyclic imidazolidine-2-thiones **5** (X=S) in strong acid media,[17-20] or by reaction of 1-arylamino-1-deoxy-D-fructoses with thiocyanate[21-23] followed by acetylation.

Conformational analysis of 4-(polyacetoxyalkyl)-1-arylimidazolidine-2-thiones, -1-arylimidazoline-2-thiones, and their oxoanalogs. When dealing with carbohydrate skeleta, the conformational mobility should also be evaluated since the stereochemical outcome of reactions is often a consequence of the conformation. Herein we report a conformational analysis of these open chain derivatives in

solution.

From the values of the coupling constants, it is possible to estimate the conformational mobility of imidazolidines **18-25** and imidazolines **26-31** and **38**. The magnitudes of coupling constants exhibited by the protons in acyclic chains with D-*arabino* and D-*galacto* configurations agree with a preferential *P* conformation[24] in solution[25-29] as in imidazolines **26-31** and **38**[2b], which are not disfavored by 1,3-diaxial interactions.

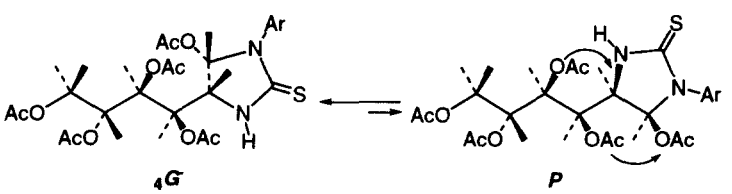
Scheme 6 displays the possible conformations of compounds **18-20**, **22** and **23**. The *P* conformation,[24] one planar zigzag including both the acyclic chain and the heterocyclic moiety, suffers from a serious 1,3-diaxial interaction between the C4–N bond and the acetate group at C-2'. This steric interaction disappears by a rotation through 120° around the C4-C1' bond. In the resulting conformation $_4G$- the atoms H-4 and H-1' as well as H-2' and H-3' are *antiperiplanar*, which is reflected in their relatively large coupling constants ($J_{4,1'}$ and $J_{2',3'} \geq 6$ Hz), whereas the *gauche* disposition between H-1' and H-2' leads to a small value $J_{1',2'}$ (~3 Hz).



Scheme 6

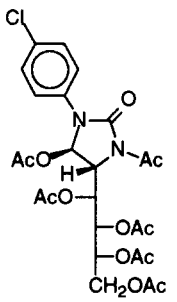
The opposite rotation around the C4-C1' bond would lead to a sterically hindered $_4G$+ conformation. Several structural variations do alter these equilibria. Thus, for compounds **18-20** the $_4G$- conformation is prevalent on increasing the size of the halogen atom ($J_{4,1'}$ 5.2, 8.9 and 9.1 Hz, respectively), but it is disfavored in the absence of *ortho* substituents at the aromatic rings or by the presence of *N*-acetyl groups at the heterocyclic moiety. The $_4G$+ conformation is prevalent for homomorphous compounds **24** and **36**.

The *cis* isomer **21** shows an additional 1,3-diaxial interaction between the acetate groups at C-5 and C-1' in a *P* conformation, and the equilibrium is then shifted to the $_4G$- conformer as evidenced by the larger coupling constant $J_{4,1'}$ (10 Hz) (Scheme 7). Like **21**, the large coupling $J_{4,1'}$ (~10 Hz) for the homomorphous *cis* isomer **36** arises from a $_4G$+ conformation.

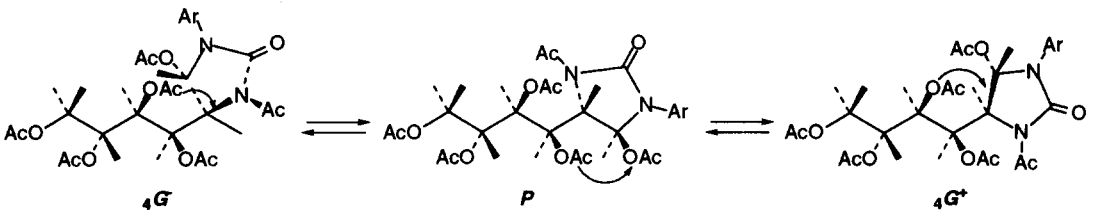


Scheme 7

In contrast, the configurational change at C-4 (*e.g.* **44** *versus* its thioanalog **21**) causes a complex conformational equilibrium (Scheme 8). The three conformations $_4G$-, *P* and $_4G$+ exhibit 1,3-diaxial interactions and there is no preponderance of a particular conformer. This fact explains the extremely small value of $J_{4,1'}$ (1 Hz).



44



Scheme 8

EXPERIMENTAL

General Methods. All solvents were purchased from commercial sources and used as received unless otherwise stated. The reactions and the purities of compounds were monitored by TLC performed on precoated silica gel plates (benzene-acetone, 3:1; cloroform-methanol, 3:1, benzene-methanol, 3:1) with a fluorescent indicator (Merck 60 GF_{254}), and detection with UV light or iodine vapor. Melting points were determined on Gallenkamp and Electrothermal apparatus and are uncorrected. Optical rotations were measured at 20 ± 2 °C on a Perkin-Elmer 241 polarimeter at 589 nm (D-line). IR spectra were recorded in the range 4000-600 cm^{-1} on Perkin-Elmer 399 and FT-IR MIDAC spectrophotometers. Solid samples were recorded on KBr (Merck) pellets. ^1H- (400 and 200 MHz) and ^{13}C-NMR (100 and 50.3 MHz) spectra were recorded on Bruker AC 200-E and Bruker 400 AC/PC spectrometers in different solvent systems. Assignments were confirmed by homo- and heteronuclear double-resonance, DEPT (distortionless enhancement by polarization transfer), and variable temperature experiments. TMS was used as the internal standard (δ = 0.00 ppm) and all *J* values are given in Hz. Microanalyses were determined by the *Servei de Microanàlisi del CSIC*, at Barcelona (C,H,N,S) and *Universidad de Sevilla* (C,H,N). High resolution mass spectra (chemical ionisation) were recorded on a VG Autospec spectrometer by the *Servicio de Espectrometría de Masas de la Universidad de Córdoba.* Compounds **6** and **8** were obtained by methods previously described.[3,4]

General procedure for the preparation of 1-aryl-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thiones. To a solution of 2-amino-2-deoxy-α-D-glucopyranose hydrochloride **1** (10.8 g, 50.0 mmol) in water (60.0 mL) were added sodium hydrogencarbonate (4.6 g, 55.0 mmol) and the corresponding aryl isothiocyanate (50.0 mmol) under vigorous stirring. The reaction mixture was diluted with ethanol (90.0 mL) until a homogeneous solution and heated at ~45 °C (external bath) for 30 min. In general, white solids were obtained on cooling, which were filtered and washed with cold ethanol and diethyl ether, unless otherwise specified.

(4*R*, 5*R*)-1-(2-Fluorophenyl)-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (9). This compound was obtained from 2-fluorophenyl isothiocyanate in 73% yield by spontaneous crystallization on cooling the reaction mixture: m.p. 183-184 °C (96% aq. EtOH), $[\alpha]_D$ –8.8° (*c* 1.0, DMF), ν_{max} 3450-3000 (OH, NH), 1450 (NH), 1490, 740, 710 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.51 (s, 1H, NH), 7.40-7.21 (m, 4H, Ar), 6.81 (d, $J_{5,OH}$ = 8.3 Hz, 1H, C5-OH), 5.30 (dd, $J_{4,5}$ = 2.2 Hz, $J_{5,OH}$ = 8.2 Hz, 1H, H-5), 4.84 (d, $J_{1',OH}$ = 6.1 Hz, 1H, C1'-OH), 4.60 (d, $J_{2',OH}$ = 5.8 Hz, 1H, C2'-OH), 4.54 (d, $J_{3',OH}$ = 8.0 Hz, 1H, C3'-OH), 4.46 (t, $J_{4',OH}$ = $J_{4'',OH}$ = 5.5 Hz, 1H, C4'-OH), 3.75-3.35 (m, 6H, H-4, H-1', H-2', H-3', H-4', H-4''); ^{13}C-NMR (50.33 MHz, DMSO-d_6) δ 180.9 (C=S), 158.6 (d, $J_{C2,F}$ = 249.1Hz), 132.1(C6ar), 129.6 (d, $J_{C4,F}$ = 7.3 Hz), 126.3 (d, $J_{C1,F}$ = 12.0 Hz), 124.4 (C5ar), 116.2 (d, $J_{C3,F}$ = 17.9 Hz) (aromatics), 87.3 (C-5), 71.4 (C-1'), 70.4 (C-2'), 69.4 (C-3'), 65.7 (C-4), 63.5 (C-4'). Anal. Calcd for $C_{13}H_{17}FN_2O_5S$: C, 46.98; H, 5.16; N, 8.43; S, 9.65. Found: C, 46.82; H, 5.18; N, 8.29; S, 9.44.

(4*R*, 5*R*)-1-(2-Chlorophenyl)-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (10). This compound was prepared from 2-chlorophenyl isothiocyanate in 76% yield by spontaneous crystallization on cooling the reaction mixture: m.p. 177-179 °C (EtOH), $[\alpha]_D$ –24.0° (*c* 1.0, DMF), ν_{max} 3480-3000 (OH, NH), 1460 (NH), 1490, 750, 710 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 8.59 (bs, 1H, NH), 7.56-7.36 (m, 4H, Ar), 6.81 (d, $J_{5,OH}$ = 8.0 Hz, 1H, C5-OH), 5.21 (bs, 1H, H-5), 4.78 (s, 1H, C1'-OH), 4.60 (d, $J_{2',OH}$ = 5.4 Hz, 1H, C2'-OH), 4.53 (d, $J_{3',OH}$ = 7.9 Hz, 1H, C3'-OH), 4.45 (t, $J_{4',OH}$ = $J_{4'',OH}$ = 5.6 Hz, 1H, C4'-OH), 3.79-3.32 (m, 6H, H-4, H-1', H-2', H-3', H-4', H-4''); ^{13}C-NMR (50.33 MHz, DMSO-d_6) δ 180.7 (C=S), 135.5, 134.1, 132.7, 129.7, 129.6, 127.4 (aromatics), 86.1 (C-5), 71.2 (C-1'), 70.2 (C-2'), 69.6 (C-3'), 65.6 (C-4), 63.5 (C-4'). Anal. Calcd for $C_{13}H_{17}ClN_2O_5S$: C, 44.77; H, 4.91; N, 8.03; S, 9.19. Found: C, 44.59; H, 4.92; N, 7.87; S, 8.96.

(4*R*, 5*R*)-1-(2-Bromophenyl)-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (11). This compound was prepared from 2-bromophenyl isothiocyanate in 65% yield by spontaneous crystallization on cooling the reaction mixture: m.p. 178-181 °C (EtOH), $[\alpha]_D$ –21.0° (*c* 1.0, DMF), ν_{max} 3500-3000 (OH, NH), 1490, 750, 720 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.62 (s, 1H, NH), 7.73-7.29 (m, 4H, Ar), 6.83 (d, $J_{5,OH}$ = 8.4 Hz, 1H, C5-OH), 5.18 (d, $J_{5,OH}$ = 7.7 Hz 1H, H-5), 4.73 (d, $J_{1',OH}$ = 6.5 Hz, 1H, C1'-OH), 4.59 (d, $J_{2',OH}$ = 5.7 Hz, 1H, C2'-OH), 4.52 (d, $J_{3',OH}$ = 8.0 Hz, 1H, C3'-OH), 4.42 (t, $J_{4',OH}$ = $J_{4'',OH}$ = 5.5 Hz, 1H, C4'-OH), 3.85-3.35 (m, 6H, H-4, H-1', H-2', H-3', H-4', H-4''); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 180.6 (C=S), 136.7, 134.5, 132.7, 129.9, 127.9, 123.4 (aromatics), 85.9 (C-5), 71.1 (C-1'), 70.0 (C-2'), 69.7 (C-3'), 65.5 (C-4), 63.5 (C-4'). Anal. Calcd for $C_{13}H_{17}BrN_2O_5S$: C,

39.71; H, 4.36; N, 7.12; S, 8.15. Found: C, 39.85; H, 4.38; N, 6.96; S, 7.99.

(4*R*,5*S*)-5-Hydroxy-1-(2-methoxyphenyl)-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (16). This compound was obtained from 2-methoxyphenyl isothiocyanate in 68% yield after concentration of the reaction mixture: m.p. 196-198 °C (dec., aq. EtOH), $[\alpha]_D$ +12.5° (t = 10 min), $[\alpha]_D$ −28.5° (final value) (*c* 0.3, DMSO), ν_{max} 3450-3000 (OH, NH), 1450 (NH), 1490, 750 y 720 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.03 (s, 1H, NH), 7.33-6.94 (m, 4H, Ar), 6.40 (d, $J_{5,OH}$ = 8.2 Hz, 1H, C5-OH), 5.37 (t, $J_{4,5}$ =7.4 Hz, 1H, H-5), 4.60 (d, $J_{1',OH}$ = 7.5 Hz, 1H, C1'-OH), 4.44 (d, $J_{2',OH}$ = 5.8 Hz, 1H, C2'-OH), 4.41 (d, $J_{3',OH}$ = 6.0 Hz, 1H, C3'-OH), 4.36 (t, $J_{4',OH}$ = $J_{4'',OH}$ = 5.6 Hz, 1H, C4'-OH), 3.78 (s, 3H, OCH_3), 3.68-3.33 (m, 6H, H-4, H-1', H-2', H-3', H-4', H-4''). Anal. Calcd for $C_{14}H_{20}N_2O_6S$: C, 48.83; H, 5.85; N, 8.13; S, 9.31. Found: C, 48.68; H, 5.81; N, 8.07; S, 9.18.

Epimerization of (4*R*,5*S*)-5-hydroxy-1-(2-methoxyphenyl)-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (16). A solution of **16** (0.03 g) in DMSO-d_6 (0.5 mL) was monitorized by ^{1}H-NMR, which detected the complete conversion into (4*R*,5*R*)-5-hydroxy-1-(2-methoxyphenyl)-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (**12**). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.27 (s, 1H, NH), 7.31-6.93 (m, 4H, Ar), 6.56 (d, $J_{5,OH}$ = 8.5 Hz, 1H, C5-OH), 5.18 (dd, $J_{4,5}$ =2.5 Hz, $J_{5,OH}$ =8.4 Hz, 1H, H-5), 4.66 (d, $J_{1',OH}$ = 6.8 Hz, 1H, C1'-OH), 4.60 (d, $J_{2',OH}$ = 5.6 Hz, 1H, C2'-OH), 4.43 (d, $J_{3',OH}$ = 8.4 Hz, 1H, C3'-OH), 4.40 (t, $J_{4',OH}$ = $J_{4'',OH}$ = 5.4 Hz, 1H, C4-OH), 3.73 (s, 3H, OCH_3), 3.77-3.29 (m, 6H, H-4, H-1', H-2', H-3', H-4', H-4''); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 181.2 (C=S), 155.6, 132.6, 129.0, 126.9, 120.1, 112.3 (aromatics), 86.3 (C-5), 71.3 (C-1'), 70.2 (C-2'), 69.6 (C-3'), 65.3 (C-4), 63.7 (C-4'), 55.8 (OCH_3).

Rate constants for the epimerization of (4*R*,5*S*)-5-hydroxy-1-(2-methoxyphenyl)-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (16). A solution of **16** (0.030 g) in DMSO-d_6 (0.5 mL) was monitorized by ^{1}H-NMR, which detected the complete conversion into (4*R*,5*R*)-5-hydroxy-1-(2-methoxyphenyl-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (**12**). Since no intermediates were detected, the transformation of **16** into **12** can be considered as a *first-order* reversible process:

$$16 \underset{k_R}{\overset{k_S}{\rightleftharpoons}} 12 \qquad \ln [\, x_e/(x_e-x)\,] = (k_S + k_R)t \quad (1)$$

$$K_e = k_S / k_R = x_e / (a-x_e) \quad (2)$$

The rate constants were determined according to equations (1) and (2) where *a* = initial concentration of **16**, x_e and (a-x_e) are the concentrations in the equilibrium of **12** and **16**, respectively, and *x* is the concentration of **12** with time *t*. Resolution of such equations at a temperature of 23 °C gives the following values:

t (min)	16(%)	12(%)
0	100.0	0.0
5	89.0	11.0
20	84.1	15.9
40	71.6	28.4
120	28.9	71.1
240	9.2	90.8
2040	10.8	89.2

$k_S + k_R = 0.0127$ $(r > 0.99)$
$K_e = k_S / k_R = 9.846$

$k_S = 1.92 \times 10^{-4}\ s^{-1}$
$k_R = 1.95 \times 10^{-5}\ s^{-1}$

General procedure for the preparation of 5-acetoxy-4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazolidine-2-thiones. To a solution of the corresponding 1-aryl-5-hydroxy-4-(D-alditol-1-yl)imidazolidine-2-thione (2.4 mmol) in pyridine (10.0 mL), cooled at –20 °C for 15 min, was added acetic anhydride (6.0 mL) and the reaction mixture was kept at that temperature for 24 h. Then, it was poured into ice-water and the resulting solid was filtered and washed with cold water. Analytical samples were crystallized from 96% aqueous ethanol, unless otherwise specified.

(4*R*, 5*R*)-5-Acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-fluorophenyl)-imidazolidine-2-thione (18). This compound was obtained according to the general procedure from **9** in 98% yield: m.p. 154-155 °C, $[\alpha]_D$ +40.5° (*c* 1.0, $CHCl_3$), ν_{max} 3300 (NH), 1740, 1720 (C=O, ester), 1240, 1220, 1200 (C-O-C, ester), 1500, 760, 720 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H, NH), 7.42-7.15 (m, 4H, Ar), 6.45 (s, 1H, H-5), 5.52 (dd, $J_{4,1'}$ = 5.3 Hz, $J_{1',2'}$ = 3.5 Hz, 1H, H-1'), 5.38 (dd, $J_{1',2'}$ = 3.4 Hz, $J_{2',3'}$ = 7.8 Hz, 1H, H-2'), 5.11 (m, 1H, H-3'), 4.28 (dd, $J_{3',4'}$ = 2.9 Hz, $J_{4',4''}$ = 12.6 Hz, 1H, H-4'), 4.16 (dd, $J_{3',4''}$ = 4.4 Hz, $J_{4',4''}$ = 12.4 Hz, 1H, H-4''), 4.02 (d, $J_{4,1'}$ = 5.2 Hz, 1H, H-4), 2.15 (s, 6H, OAc), 2.10 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C-NMR (50.33 MHz, $CDCl_3$) δ 183.8 (C=S), 170.5 (CH_3-*C*O), 170.0 (CH_3-*C*O), 169.9 (CH_3-*C*O), 169.6 (2C, CH_3-*C*O), 158.4 (d, $J_{C2,F}$ = 251.1 Hz), 131.3 (C6ar), 130.5 (d, $J_{C4,F}$ = 8.1 Hz), 124.3, 124.0, 116.4 (d, $J_{C3,F}$ = 19.8 Hz) (aromatic), 86.8 (C-5), 68.9 (C-2'), 68.7 (C-1'), 68.4 (C-3'), 61.5 (C-4), 61.1 (C-4'), 20.5 (5C, *C*H_3-CO). Anal. Calcd for $C_{23}H_{27}FN_2O_{10}S$: C, 50.92; H, 5.02; N, 5.16; S, 5.91. Found: C, 50.92; H, 5.04; N, 5.03; S, 5.69.

(4*R*, 5*R*)-5-Acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-chlorophenyl)imidazolidine-2-thione (19). This compound was prepared from **10** in 75% yield: m.p. 174-176 °C, $[\alpha]_D$ +47.0° (*c* 1.0, $CHCl_3$), ν_{max} 3300 (NH), 1730, 1710 (C=O, ester), 1235, 1220, 1195 (C-O-C, ester), 1490, 710 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 8.70 (s, 1H, NH), 7.58-7.32 (m, 4H, Ar), 6.63 (s, 1H, H-5), 5.63 (dd, $J_{4,1'}$ = 8.9 Hz, $J_{1',2'}$ = 2.3 Hz, 1H, H-1'), 5.45 (dd, $J_{1',2'}$ = 2.3 Hz, $J_{2',3'}$ = 8.4 Hz, 1H, H-2'), 5.11 (m, 1H, H-3'), 4.30 (dd, $J_{3',4'}$ = 3.1 Hz, $J_{4',4''}$ = 12.5 Hz, 1H, H-4'), 4.18 (dd, $J_{3',4''}$ = 4.6 Hz, $J_{4',4''}$ = 12.5 Hz, 1H, H-4''), 4.14 (d, $J_{4,1'}$ = 8.9 Hz, 1H, H-4), 2.16 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.03 (s, 6H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 183.1 (C=S), 170.5 (CH_3-*C*O), 169.9 (CH_3-*C*O), 169.7 (2C, CH_3-*C*O), 169.3 (CH_3-*C*O), 133.8, 133.4, 131.9, 130.3, 130.2, 127.5 (aromatics), 84.7 (C-5), 68.4 (C-2'), 68.1 (C-1'), 67.7 (C-3'), 61.0 (C-4'), 60.9 (C-4), 20.7 (2C, *C*H_3-CO), 20.5 (3C, *C*H_3-CO). Anal. Calcd for $C_{23}H_{27}ClN_2O_{10}S$: C, 49.42; H, 4.87; N, 5.01; S, 5.74. Found: C, 49.46; H, 4.96; N, 4.93; S, 5.75.

(4*R*, 5*R*)-5-Acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-bromophenyl)imidazolidine-2-thione (20). This compound was obtained from **11** in 70% yield: m.p. 177-179 °C, $[\alpha]_D$ +50.0° (*c* 1.0, $CHCl_3$), ν_{max} 3300 (NH), 1740, 1720 (C=O, ester), 1230, 1210, 1190 (C-O-C, ester) 1490, 720 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H, NH), 7.70-7.28 (m, 4H, Ar), 6.58 (s, 1H, H-5), 5.63 (d, $J_{4,1'}$ = 9.1 Hz, 1H, H-1'), 5.34 (d, $J_{2',3'}$ = 8.8 Hz, 1H, H-2'), 5.03 (m, 1H, H-3'), 4.22 (m, 2H, H-4', H-4''), 3.88 (d, $J_{4,1'}$ = 9.1 Hz, 1H, H-4), 2.18 (s, 3H, OAc), 2.12 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 6H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 183.0 (C=S), 170.6 (2C, CH_3-*C*O), 169.9 (CH_3-*C*O), 169.7 (CH_3-*C*O), 169.2 (CH_3-*C*O), 135.1, 133.4, 132.3, 130.6, 128.2, 123.7 (aromatics), 84.2 (C-5), 68.4 (C-2'), 68.1 (C-1'), 67.3 (C-3'), 61.1 (C-4'), 60.7 (C-4), 20.8 (2C, *C*H_3-CO), 20.6 (3C, *C*H_3-CO). Anal. Calcd for $C_{23}H_{27}BrN_2O_{10}S$: C, 45.78; H, 4.51; N, 4.64; S, 5.31. Found: C, 45.66; H, 4.43; N, 4.52 ; S, 5.10.

(4*R*, 5*S*)-5-Acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-methoxyphenyl)imidazolidine-2-thione (21). This substance was obtained from **16** in 81% yield: m.p. 131-133 °C, $[\alpha]_D$ +11° (*c* 1.0, $CHCl_3$), ν_{max} 3640-3200 (H_2O, NH), 2930 (OCH_3) 1750 (C=O, ester), 1610 (H_2O),[30] 1170-1250 (C-O-C, ester), 1590, 1500 y 730 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H, NH), 7.36-6.94 (m, 4H, Ar), 6.93 (d, $J_{4,5}$ = 6.7 Hz, 1H, H-5), 5.65 (dd, $J_{4,1'}$ = 10.2 Hz, $J_{1',2'}$ = 1.0 Hz, 1H, H-1'), 5.10 (dd, $J_{1',2'}$ = 0.7 Hz, $J_{2',3'}$ = 9.2 Hz, 1H, H-2'), 4.88 (m, 1H, H-3'), 4.22 (m, 3H, H-4, H-4', H-4''), 3.88 (s,3H, OCH_3), 2.18 (s, 3H, OAc), 2.15 (s, 3H, OAc), 2.12 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.99 (s,3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.3 (C=S), 170.4 (CH_3-*C*O), 170.1 (CH_3-*C*O) 169.8 (CH_3-*C*O), 169.5 (CH_3-*C*O), 168.7 (CH_3-*C*O), 155.2, 130.7, 130.0, 124.6, 120.2, 111.9 (aromatics), 82.4 (C-5), 68.2 (C-2'), 68.0 (C-1'), 67.4 (C-3'), 60.8 (C-4'), 57.2 (C-4), 55.7 (OCH_3), 20.9 (*C*H_3-CO), 20.8 (*C*H_3-CO), 20.5 (*C*H_3-CO), 20.3 (*C*H_3-CO), 20.2 (*C*H_3-CO). Anal. Calcd for $C_{24}H_{30}N_2O_{11}S.H_2O$: C, 50.34; H, 5.63; N, 4.89; S, 5.60. Found: C, 50.71; H, 5.43; N, 5.15 ; S, 5.49.

(4*R*, 5*R*)-5-Acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(1-methoxyphenyl)imidazolidine-2-thione (22). A solution of (4*R*,5*S*)-5-hydroxy-1-(2-methoxyphenyl)-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (**16**) (0.25 g, 0.73 mmol) in DMSO (3.0 mL) was kept at room temperature for 30 h, which produced its complete transformation into the (4*R*,5*R*) epimer. Pyridine (3.0 mL) and acetic anhydride (1.8 mL) were then added and the reaction mixture was kept at –20 °C for 40 h. The mixture was poured into ice-water and the resulting solid was filtered and washed with cold water (0.22 g, 55%), m.p. 68-71 °C. An analytical sample was obtained after crystallization from ether; m.p. 99-102 °C, $[\alpha]_D$ +13° (*c* 0.5, $CHCl_3$), ν_{max} 3300 (NH), 2930 (OCH_3) 1750 (C=O, ester), 1150-1300 (C-O-C, ester), 1590, 1500 y 750 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36-6.93 (m, 4H, Ar), 6.81 (s, 1H, NH), 6.53 (s 1H, H-5), 5.59 (dd, $J_{4,1'}$ = 5.5 Hz, $J_{1',2'}$ = 2.9 Hz, 1H, H-1'), 5.41 (dd, $J_{1',2'}$ = 2.8 Hz, $J_{2',3'}$ = 8.2 Hz, 1H, H-2'), 5.10 (m, 1H, H-3'), 4.26 (dd, $J_{3',4'}$ = 2.7 Hz, $J_{4',4''}$ = 12.5 Hz, 1H, H-4'), 4.17 (dd, $J_{3',4''}$ = 4.5 Hz, $J_{4',4''}$ = 12.4 Hz, 1H, H-4''), 3.92 (d, $J_{4,1'}$ = 5.4 Hz, 1H, H-4), 3.87 (s, 3H, OCH_3), 3.48 (c, CH_2, ether of crystallization), 2.18 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.06 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.21 (t, CH_3, ether of crystallization); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.5 (C=S), 170.6 (CH_3-*C*O),

169.9 (CH_3-*C*O), 169.8 (2C, CH_3-*C*O), 169.6 (CH_3-*C*O), 169.4 (CH_3-*C*O), 155.1, 131.2, 130.0, 125.5, 120.5, 112.0 (aromatic), 86.3 (C-5), 69.2 (C-2'), 68.8 (C-1'), 68.4 (C-3'), 61.4 (C-4), 61.3 (C-4'), 55.6 (OCH_3), 20.8 (*C*H_3-CO), 20.7 (*C*H_3-CO), 20.6 (*C*H_3-CO), 20.4 (2C, *C*H_3-CO). HRMS: m/z 555.1682. Calcd for M+H^+ of $C_{24}H_{30}N_2O_{11}S$: 555.1649. Anal. Calcd for $C_{24}H_{30}N_2O_{11}S.1/2\,C_4H_{10}O$: C, 52.78; H, 5.96; N, 4.73; S, 5.42. Found: C, 52.60; H, 5.79; N, 4.76; S, 5.40.

(4*R*, 5*R*)-5-Acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(1-naphthyl)imidazolidine-2-thione (23).[31] This compound was obtained from **6**[3,4] in 94% yield: m.p. 151-152 °C, $[\alpha]_D$ +43.5° (*c* 1.0, $CHCl_3$), ν_{max} 3180 (NH), 1750 (C=O, ester), 1425 (NH), 1240 (C=S), 1210 (C-O-C, ester), 1595, 1505, 770 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 8.04 (s, 1H, NH, **a**), 7.97-7.41 (m, 14H, Ar, **a** and **b**), 7.29 (s, 1H, NH, **b**), 6.62 (s, 1H, H-5, **b**), 6.42 (s, 1H, H-5, **a**), 5.63 (dd, $J_{4,1'}$ = 7.4, $J_{1',2'}$ = 3.2, 1H, H-1', **a**), 5.55 (dd, $J_{4,1'}$ = 4,4, $J_{1',2'}$ = 2.9, 1H, H-1', **b**), 5.43 (dd, $J_{1',2'}$ = 2.9 Hz, $J_{2',3'}$ = 8.4 Hz, 1H, H-2', **b**), 5.34 (dd, $J_{1',2'}$ = 3.2 Hz, $J_{2',3'}$ = 7.9 Hz, 1H, H-2', **a**), 5.17 (m, 1H, H-3', **b**), 5.09 (m, 1H, H-3', **a**), 4.26 (dd, $J_{3',4'}$ = 2.9, $J_{4',4''}$ = 12.6 Hz, 1H, H-4', **a**), 4.16 (dd, $J_{3',4''}$ = 4.2, $J_{4',4''}$ = 12.6, 1H, H-4'', **a**), 4.14 (dd, $J_{3',4''}$ = 4.1, $J_{4',4''}$ = 12.7 Hz, 1H, H-4'', **b**), 4.08 (m, 1H, H-4, **b**), 4.06 (d, 1H, H-4, **a**), 2.23 (s, 3H, OAc), 2.22 (s, 3H, OAc), 2.17 (s, 3H, OAc), 2.12 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.08 (s, 6H, 2 OAc), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.76 (s, 3H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 184.3 (C=S, **b**), 184.1 (C=S, **a**), 170.5 (2C, CH_3-*C*O), 170.4 (2C, CH_3-*C*O), 170.2 (2C, CH_3-*C*O), 169.7 (2C, CH_3-*C*O), 169.2 (2C, CH_3-*C*O), 134.4, 134.1, 133.8, 132.5, 131.5, 130.3, 129.6 (2C), 129.2, 128.7, 128.1, 128.0, 127.0, 126.4, 126.2, 125.9, 125.6, 125.2, 123.8, 121.9 (aromatics), 89.4 (C-5, **b**), 86.0 (C-5, **a**), 69.4 (C-2', **a**), 69.0 (C-2', **b**), 68.3 (2C, C-1', **a** and **b**), 68.1 (C-3', **b**), 67.9 (C-3', **a**), 61.5 (C-4, **b**), 61.2 (C-4', **b**), 60.9 (C-4', **a**), 60.8 (C-4, **a**), 20.7 (2C, *C*H_3-CO), 20.6 (2C,*C*H_3-CO), 20.5 (2C,*C*H_3-CO), 20.4 (2C,*C*H_3-CO), 20.3 (2C,*C*H_3-CO). Anal. Calcd for $C_{27}H_{30}N_2O_{10}S$: C, 56.44; H, 5.26; N, 4.87. Found: C, 56.65; H, 5.52; N, 4.87.

(4*S*, 5*S*)-5-Acetoxy-4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-5-acetoxy-1-(1-naphthyl)imidazolidine-2-thione (24).[31] This compound was obtained from **8** in 87% yield: m.p. 120-122 °C, $[\alpha]_D$ –17.4° (*c* 0.5, $CHCl_3$), ν_{max} 3180 (NH), 1750 (C=O, ester), 1425 (NH), 1240 (C=S), 1210 (C-O-C, ester), 1595, 1505, 770 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H, NH, **a**), 7.94-7.43 (m, 14H, Ar, **a** and **b**), 7.10 (s, 1H, NH, **b**), 6.63 (d, $J_{4,5}$ = 0.9, 1H, H-5, **b**), 6.49 (s, 1H, H-5, **a**), 5.48 (dd, $J_{4,1'}$ = 8.8, $J_{1',2'}$ = 1.2, 1H, H-1', **a**), 5.43 (dd, $J_{4,1'}$ = 2.7, $J_{1',2'}$ = 3.4, 1H, H-1', **b**), 5.40 (m, 2H, H-3',**a** and **b**), 5.29-5.24 (m, 3H, H-2', **a**, H-4', **a** and **b**), 5.21 (dd, $J_{2',3'}$ = 9.9 Hz, 1H, H-2', **b**), 4.28 (dd, $J_{4',5'}$ = 2.6, $J_{5',5''}$ = 11.8, 1H, H-5', **a**), 4.27 (dd, $J_{4',5'}$ = 3.3, $J_{5',5''}$ = 11.8, 1H, H-5', **b**), 3.98 (d, $J_{4,1'}$ = 2.7, 1H, H-4, **b**), 3.87 (d, 1H, H-4, **a**), 3.85 (dd, $J_{4',5''}$ = 7.5, $J_{5',5''}$ = 11.6 Hz, 1H, H-5'', **b**), 3.79 (dd, $J_{4',5''}$ = 7.5, $J_{5',5''}$ = 11.7 Hz, 1H, H-5'', **a**), 2.23 (s, 3H, OAc), 2.22 (s, 3H, OAc), 2.17 (s, 3H, OAc), 2.16 (s, 3H, OAc), 2.15 (s, 3H, OAc), 2.09 (s, 6H, 2 OAc), 2.07 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.76 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.9 (C=S, **b**), 184.3 (C=S, **a**), 170.5 (CH_3-*C*O), 170.4 (2C, CH_3-*C*O), 170.2 (4C, CH_3-*C*O), 170.0 (CH_3-*C*O),169.6 (2C, CH_3-*C*O), 169.2 (2C, CH_3-*C*O), 134.6, 134.3, 133.8, 132.6, 131.5, 130.4, 129.8 (3C), 128.8, 128.2, 127.9, 127.2, 126.5,

126.4, 125.7 (2C), 125.3, 123.9, 122.0 (aromatics), 90.6 (C-5, **b**), 86.0 (C-5, **a**), 69.3 (C-2', **a**), 69.0 (C-2', **b**), 67.9 (C-1', **a**), 67.7 (C-1', **b**), 67.5 (C-3', **b**), 67.4 (C-3', **a**), 67.3 (2C, C-4', **a** and **b**), 62.2 (C-5', **a**), 62.1 (C-4, **a**), 61.9 (C-5', **b**), 60.9 (C-4, **b**), 20.8, 20.6, 20.5, 20.4 (12C,CH_3-CO). Anal. Calcd for $C_{30}H_{34}N_2O_{12}S$: C, 55.72; H, 5.30; N, 4.33; S, 4.96. Found: C, 55.16; H, 5.29; N, 4.44; S, 4.82.

(4*R*,5*R*)-4-Acetoxy-1-acetyl-5-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(2-fluorophenyl)imidazolidine-2-thione (25). A solution of (4*R*,5*R*)-5-acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-fluorophenyl)imidazolidine-2-thione (**18**) (0.13 mg, 0.23 mmol) in a mixture of pyridine-acetic anhidride (1:1, 2.0 mL) is heated at 75-85 °C for 10 hours. The reaction was controlled by TLC (benzene-acetone 3:1). The mixture was poured into ice-water and the resulting solid was filtered and washed with cold water (0.09 g, 67%). Recrystallization from ethanol gave a material having m.p. 58-61 °C, $[\alpha]_D$ –4.6° (*c* 0.5, $CHCl_3$), ν_{max} 3500 (ethanol of crystallization), 1740 (C=O, ester), 1700 (C=O, amide), 1220 (C-O-C, ester), 1500, 770, 740 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.45-7.20 (m, 4H, Ar), 6.38 (s, 1H, H-4), 5.60 (dd, $J_{5,1'}$ = 7.3, $J_{1',2'}$ = 3.4 Hz, 1H, H-1'), 5.41 (dd, $J_{1',2'}$ = 3.4, $J_{2',3'}$ = 7.7 Hz, 1H, H-2'), 5.33 (m, 1H, H-3'), 4.96 (d, $J_{5,1'}$ = 7.3 Hz, 1H, H-5), 4.31 (dd, $J_{3',4'}$ = 2.7, $J_{4',4''}$ = 12.4 Hz, 1H, H-4'), 4.17 (dd, $J_{3',4''}$ = 5.1, $J_{4',4''}$ = 12.5 Hz, 1H, H-4''), 3.72 (m, CH_2, ethanol of crystallization), 2.84 (s, 3H, N-COCH_3), 2.17 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.24 (t, CH_3, ethanol of crystallization); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 180.2 (C=S), 171.4 (N-$COCH_3$), 170.6 (CH_3-CO), 170.1 (CH_3-CO), 169.8 (CH_3-CO), 169.7 (CH_3-CO), 169.4 (CH_3-CO), 158.4 (d, $J_{C2,F}$ = 251.6 Hz), 131.2 (d, $J_{C4,F}$ = 9.0 Hz), 130.7 (C6 ar), 124.8 (C5 ar), 124.5 (d, $J_{C1,F}$ = 11.5 Hz), 116.9 (d, $J_{C3,F}$ = 20.2 Hz) (aromatic), 82.7 (C-4), 68.6 (C-2'), 68.3 (2C, C-1', C-3'), 61.7 (C-4'), 61.3 (C-5), 58.4 (CH_2, ethanol of crystallization), 26.5 (N-$COCH_3$), 20.7 (2C, CH_3-CO), 20.6 (CH_3-CO), 20.5 (CH_3-CO), 20.3 (CH_3-CO), 18.4 (CH_3, ethanol of crystallization). Anal. Calcd for $C_{25}H_{29}FN_2O_{11}S$. 1/2 CH_3CH_2OH: C, 51.40; H, 5.31; N, 4.61. Found: C, 51.09; H, 5.31; N, 4.60.

Transformation of 5-acetoxy-4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazolidine-2-thione into 4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazoline-2-thione. A solution of 5-acetoxy-4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazolidine-2-thione (0.23 mmol) in the appropiate solvent (5 mL) was heated at reflux for t h. Then, the reaction mixture was evaporated to dryness and the crude was analyzed by NMR spectroscopy, in order to determine the extent of the transformation into the corresponding 4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazoline-2-thione: a) Solvent: $CHCl_3$, t = 30 h. b) Solvent: benzene, t = 20 h. c) Solvent: $CHCl_3$ with potassium hydrogencarbonate (0.05 g), t = 9 h. d) Solvent: benzene with potassium hydrogencarbonate (0.05 g), t = 9 h. e) Solvent: acetic anhydride-glacial acetic acid (1:1), t = 30 h.

f) A solution of 5-acetoxy-4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazolidine-2-thione (0.08 g) in DMSO-d_6 (0.5 mL) was heated at 80 °C and the transformation was monitored by ^{1}H-NMR. The resulting 4-(per-*O*-acetyl-D-alditol-1-yl)-1-arylimidazoline-2-thione was characterized by NMR spectroscopy.

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-fluorophenyl)imidazoline-2-thione (26). This substance was formed from **18**: a) 0%, b) 0%, c) 100%, d) 100%, e) 100%, f) 100%. ^{1}H-NMR (400 MHz, DMSO-d_6, at 353 K) δ 7.53-7.30 (m, 4H, Ar), 7.14 (s, 1H, H-5), 5.92 (d, $J_{1',2'}$ = 4.3 Hz, 1H, H-

1'), 5.48 (dd, $J_{1',2'}$ = 4.5, $J_{2',3'}$ = 7.3, 1H, H-2'), 5.18 (m, 1H, H-3'), 4.27 (dd, $J_{3',4'}$ = 3.1, $J_{4',4''}$ = 12.3, 1H, H-4'), 4.13 (dd, $J_{3',4''}$ = 5.8, $J_{4',4''}$ = 12.3, 1H, H-4''), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.91 (s, 3H, OAc); ^{13}C-NMR (50.33 MHz, DMSO-d_6, at 298 K) δ 170.1 (CH_3-*C*O), 169.4 (CH_3-*C*O), 169.3 (CH_3-*C*O), 169.1 (CH_3-*C*O), 163.6 (C=S), 156.6 (d, $J_{2ar,\ F}$ = 251.7), 130.9, (d, $J_{6ar,\ F}$ = 7.9), 130.0, 125.3, 124.9 (d, $J_{ar,\ F}$ = 9.4), 116.6 (d, $J_{2ar,\ F}$ = 18.8) (aromatics), 124.0 (C-4), 118.4 (C-5), 69.4 (C-2'), 68.1 (C-3'), 64.9 (C-1'), 61.6 (C-4'), 20.5 (3C, *C*H_3-CO), 20.3 (*C*H_3-CO).

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-chlorophenyl)imidazoline-2-thione (27). This compound was formed from **19**: a) 26%, b) 53%, d) 100%, f) 100%. ^{1}H-NMR (400 MHz, DMSO-d_6, at 298 K) δ12.67 (s, 1H, NH) 7.65-7.43 (m, 4H, Ar), 7.18 (s, 1H, H-5), 5.89 (d, $J_{1',2'}$ = 3.6 Hz, 1H, H-1'), 5.47 (dd, $J_{1',2'}$ = 3.8, $J_{2',3'}$ = 7.8, 1H, H-2'), 5.15 (m, 1H, H-3'), 4.19 (d, $J_{3',4'}$ = 2.5, 1H, H-4'), 4.14 (d, $J_{3',4''}$ = 5.4, 1H, H-4''), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.90 (s, 3H, OAc); ^{13}C-NMR (100 MHz, DMSO-d_6, at 298 K) δ 170.3 (CH_3-*C*O), 169.6 (CH_3-*C*O), 169.5 (CH_3-*C*O), 169.3 (CH_3-*C*O), 163.7 (C=S), 135.4, 131.5, 131.0, 130.9, 130.3, 128.2, (aromatics), 124.1 (C-4), 118.3 (C-5), 69.6 (C-2'), 68.3 (C-3'), 65.1 (C-1'), 61.8 (C-4'), 20.8 (2C, *C*H_3-CO), 20.7 (*C*H_3-CO), 20.6 (*C*H_3-CO).

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-bromophenyl)imidazoline-2-thione (28). This substance was formed from **20**: a) 73%, b) 71%, d) 100%, f) 100%. ^{1}H-NMR (400 MHz, DMSO-d_6, at 298 K) δ 12.64 (s, 1H, NH), 7.79-7.38 (m, 4H, Ar), 7.15 (s, 1H, H-5), 5.90 (s, 1H, H-1'), 5.48 (dd, $J_{1',2'}$ = 3.8, $J_{2',3'}$ = 7.8 Hz, 1H, H-2'), 5.15 (m, 1H, H-3'), 4.22 (dd, $J_{3',4'}$ = 1.8, $J_{4',4''}$ = 12.4 Hz, 1H, H-4'), 4.13 (dd, $J_{3',4''}$ = 5.5, $J_{4',4''}$ = 12.4 Hz, 1H, H-4''), 2.06 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.01 (s, 3H, OAc); ^{13}C-NMR (100 MHz, DMSO-d_6, at 298 K) δ 170.3 (2C, CH_3-*C*O), 169.5 (CH_3-*C*O), 169.3 (CH_3-*C*O), 163.6 (C=S), 137.0, 133.4, 131.2, 130.9, 128.8, 121.8, (aromatics), 124.0 (C-4), 118.1 (C-5), 69.7 (C-2'), 68.3 (C-3'), 65.1 (C-1'), 61.8 (C-4'), 20.8 (2C, *C*H_3-CO), 20.7 (*C*H_3-CO), 20.6 (*C*H_3-CO).

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-methoxyphenyl)imidazoline-2-thione (29). This compound was formed from **21** or **22**: a) 52%, f) 100%. ^{1}H-NMR (400 MHz, DMSO-d_6, at 298 K) δ 12.05 (s, 1H, NH), 7.43-7.00 (m, 4H, Ar), 7.05 (s, 1H, H-5), 5.88 (d, $J_{1',2'}$ = 4.3, 1H, H-1'), 5.47 (dd, $J_{1',2'}$ = 4.4, $J_{2',3'}$ = 7.9 Hz, 1H, H-2'), 5.14 (m, 1H, H-3'), 4.21 (dd, $J_{3',4'}$ = 2.8, $J_{4',4''}$ = 12.4 Hz, 1H, H-4'), 4.12 (dd, $J_{3',4''}$ = 5.5, $J_{4',4''}$ = 12.4 Hz, 1H, H-4''), 3.74 (s, 3H, OCH_3), 2.07 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C-NMR (50.33 MHz, DMSO-d_6, at 298 K) δ 170.2 (CH_3-*C*O), 169.5 (CH_3-*C*O), 169.4 (CH_3-*C*O), 169.3 (CH_3-*C*O), 163.4 (C=S), 154.4, 130.3, 129.6, 126.2, 120.4, 113.0, (aromatics), 123.1 (C-4), 119.2 (C-5), 69.6 (C-2'), 68.4 (C-3'), 65.1 (C-1'), 61.7 (C-4'), 56.0 (OCH_3), 20.7 (3C, *C*H_3-CO), 20.5 (*C*H_3-CO).

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(1-naphthyl)imidazoline-2-thione (30).[31] This compound was formed from **23**:[3] f) 100%. ^{1}H-NMR (200 MHz, DMSO-d_6, at 350 K) δ 10.20 (s, 1H, NH), 8.07-7.35 (m, 7H, Ar), 7.16 (s, 1H, H-5), 6.02 (d, $J_{1',2'}$ = 4.1, 1H, H-1'), 5.56 (dd, $J_{1',2'}$ = 4.1, $J_{2',3'}$ = 7.2 Hz, 1H, H-2'), 5.25 (m, 1H, H-3'), 4.34 (dd, $J_{3',4'}$ = 3.1, $J_{4',4''}$ = 12.3 Hz, 1H, H-4'), 4.19

(dd, $J_{3',4''}$ = 5.6, $J_{4',4''}$ = 12.3 Hz, 1H, H-4''), 2.10 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.92 (s, 3H, OAc); ^{13}C-NMR (50.3 MHz, DMSO-d_6, at 298 K) δ 170.2 (3C, CH_3-*C*O), 169.5 (3C, CH_3-*C*O), 169.4 (2C, CH_3-*C*O), 163.8 (C=S, **a**), 164.1 (C=S, **b**), 134.3 (2C), 134.2 (2C), 134.0 (2C), 129.6, 129.4 (2C), 128.4 (2C), 127.1 (2C), 126.7, 126.4, 125.6 (2C), 122.9, 122.5, (aromatics), 124.4 (C-4, **a**), 124.1 (C-4, **b**) 119.2 (C-5, **b**), 119.0 (C-5, **a**), 70.1 (C-2', **b**), 69.5 (C-2', **a**), 68.2 (C-3', **b**), 68.0 (C-3', **a**) 65.0 (2C, C-1' **a** and **b**), 61.7 (2C, C-4' **a** and **b**), 21.2 (*C*H_3-CO), 21.1 (*C*H_3-CO), 21.0 (2C, *C*H_3-CO), 20.6 (2C,*C*H_3-CO), 20.5 (*C*H_3-CO), 20.4 (*C*H_3-CO).

4-(1,2,3,4,5-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(1-naphthyl)imidazoline-2-thione (31).[31] This compound was prepared from **24**: f) 100%. ^{1}H-NMR (400 MHz, DMSO-d_6, at 375 K) δ 12.34 (s, 1H, NH), 8.04-7.32 (m, 7H, Ar), 7.05 (s, 1H, H-5), 5.89 (d, $J_{1',2'}$ = 2.3, 1H, H-1'), 5.46 (dd, $J_{2',3'}$ = 8.8, $J_{3',4'}$ = 2.9 Hz, 1H, H-3'), 5.39 (dd, 1H, H-2'), 5.26 (ddd, $J_{4',5'}$ = 4.7, $J_{4',5''}$ = 6.9 Hz,1H, H-4'), 4.23 (dd, $J_{5',5''}$ = 11.7 Hz, 1H, H-5'), 4.00 (dd, 1H, H-5''), 2.11 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.91 (s, 3H, OAc); ^{13}C-NMR (100 MHz, DMSO-d_6, at 295 K) δ 170.2 (3C, CH_3-*C*O, **a**), 169.9 (2C, CH_3-*C*O, **b**), 169.7 (2C, CH_3-*C*O, **a**), 169.4 (2C, CH_3-*C*O, **b**), 169.3 (C, CH_3-*C*O, **b**), 163.9 (C=S, **b**), 163.6 (C=S, **a**), 134.4 (2C, **b**), 134.1 (2C, **a**), 129.7 (2C, **b**), 129.5 (2C, **a**), 128.5 (**a**), 128.4 (**b**), 127.2 (2C, **a**), 126.9 (2C, **b**), 126.7 (**a**), 126.5 (**b**), 125.8 (2C, **a** and **b**), 123.1 (**b**), 122.6 (**a**) (aromatics), 124.7 (C-4, **a**), 124.4 (C-4, **b**) 119.0 (C-5, **b**), 118.9 (C-5, **a**), 69.2 (C-2', **b**), 68.7 (C-2', **a**), 67.7 (4C, C-3', **a** and **b**, C-1', **a** and **b**), 64.9 (C-4', **b**) 64.8 (C-4', **a**), 62.1 (2C, C-5' **a** and **b**), 20.8 (4C,*C*H_3-CO), 20.7 (4C, *C*H_3-CO), 20.6 (2C, *C*H_3-CO).

General procedure for the preparation of 4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-arylimidazoline-2-thiones. To a solution of 5-acetoxy-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-arylimidazolidine-2-thione (0.23 mmol) in benzene (5.0 mL) was added solid potassium hydrogencarbonate (0.05 g) and the reaction mixture was refluxed for 9 h. The progress of the reaction was controlled by TLC (benzene-acetone 3:1). Then, the inorganic salt was filtered and the solution washed twice with water, dried (anhydrous $MgSO_4$), and evaporated to dryness to afford the title compound as a chromatographically pure amorphous solid.

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-fluorophenyl)imidazoline-2-thione (26). This substance was prepared from **18** (51%), m. p. 88-90 °C, $[\alpha]_D$ –31.8° (*c* 0.5, $CHCl_3$), ν_{max} 3000 (NH), 1750 (C=O, ester), 1260, 1200 (C-O-C, ester), 1510 760 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60-7.22 (m, 4H, Ar), 6.82 (s, 1H, H-5), 6.04 (d $J_{1',2'}$ = 3.6 Hz, 1H, H-1'), 5.53 (dd, $J_{1',2'}$ = 3.9 $J_{2',3'}$ = 8.3 Hz, 1H, H-2'), 5.21 (m, 1H, H-3'), 4.26 (dd, $J_{3',4'}$ = 2.7, $J_{4',4''}$ = 12.4 Hz, 1H, H-4'), 4.13 (dd, $J_{3',4''}$ = 4.9, $J_{4',4''}$ = 12.7 Hz, 1H, H-4''), 2.16 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (50.33 MHz, $CDCl_3$) δ 170.5 (2C, CH_3-*C*O), 169.7 (CH_3-*C*O), 169.4 (CH_3-*C*O), 164.1 (C=S), 156.7 (d, $J_{2ar,F}$ = 253.2 Hz), 130.9 (d, $J_{6ar,F}$ = 7.6 Hz), 129.5, 124.6 (d, $J_{ar,F}$ = 19.4 Hz), 124.5, 116.8 (d, $J_{ar,F}$ = 19.6 Hz), (aromatics), 124.1 (C-4), 117.7 (C-5), 70.2 (C-2'), 68.4 (C-3'), 64.4 (C-1'), 61.5 (C-4'), 20.6 (4C, *C*H_3-CO). HRMS: m/z 482.1185. Calcd for M^+ of $C_{21}H_{23}FN_2O_8S$: 482.1159.

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-chlorophenyl)imidazoline-2-thione (27). This compound was prepared from **19** (40%), m. p. 99-101 °C, $[\alpha]_D$ −19.8° (*c* 0.5, $CHCl_3$), ν_{max} 3000 (NH), 1740 (C=O, ester), 1200 (C-O-C, ester), 1040 (C-O), 760, 720 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1H, NH), 7.55-7.27 (m, 4H, Ar), 6.76 (s, 1H, H-5), 6.04 (s, 1H, H-1'), 5.52 (d, $J_{1',2'}$ = 4.4 Hz, 1H, H-2'), 5.21 (m, 1H, H-3'), 4.25 (dd, $J_{3',4'}$ = 2.8, $J_{4',4''}$ = 12.6 Hz, 1H, H-4'), 4.12 (dd, $J_{3',4''}$ = 4.8, $J_{4',4''}$ = 12.5 Hz, 1H, H-4''), 2.20 (s, 3H, OAc), 2.15 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.5 (CH_3-*C*O), 169.8 (CH_3-*C*O), 169.7 (CH_3-*C*O), 169.4 (CH_3-*C*O), 163.9 (C=S), 134.6, 131.9, 130.7, 130.3, 128.2, 127.6, (aromatics), 124.0 (C-4), 117.3 (C-5), 70.3 (C-2'), 68.3 (C-3'), 64.4 (C-1'), 61.5 (C-4'), 20.7 (2C, *C*H_3-CO), 20.6 (2C, *C*H_3-CO). HRMS: m/z 498.0888. Calcd for M^+ of $C_{21}H_{23}ClN_2O_8S$: 498.0864 (^{35}Cl). m/z 501.0963 and 499.0927. Calcd for M+H$^+$ of $C_{21}H_{23}ClN_2O_8S$: 501.0912 (^{37}Cl) and 499.0942 (^{35}Cl).

4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(2-bromophenyl)imidazoline-2-thione (28). This substance was obtained from **20** (30 %), m. p. 90-92 °C, $[\alpha]_D$ −32° (*c* 0.5, $CHCl_3$), ν_{max} 3000 (NH), 1740 (C=O, ester), 1220 (C-O-C, ester), 1030 (C-O), 760, 710 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.8 (s, 1H, NH), 7.73-7.27 (m, 4H, Ar), 6.74 (s, 1H, H-5), 6.03 (d, $J_{1',2'}$ = 3.0 Hz, 1H, H-1'), 5.52 (dd, $J_{1',2'}$ = 2.8, $J_{2',3'}$ = 7.8 Hz, 1H, H-2'), 5.20 (m, 1H, H-3'), 4.25 (dd, $J_{3',4'}$ = 2.7, $J_{4',4''}$ = 12.5 Hz, 1H, H-4'), 4.12 (dd, $J_{3',4''}$ = 4.9, $J_{4',4''}$ = 12.5 Hz, 1H, H-4''), 2.17 (s, 3H, OAc), 2.13 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.5 (CH_3-*C*O), 169.9 (CH_3-*C*O), 169.7 (CH_3-*C*O), 169.4 (CH_3-*C*O), 163.9 (C=S), 136.3, 133.7, 131.0, 130.2, 128.3, 121.9, (aromatics), 124.0 (C-4), 117.2 (C-5), 70.3 (C-2'), 68.4 (C-3'), 64.4 (C-1'), 61.5 (C-4'), 20.8 (2C, *C*H_3-CO), 20.7 (2C, *C*H_3-CO). HRMS: m/z 542.0399. Calcd for M^+ of $C_{21}H_{23}BrN_2O_8S$: 542.0358 (^{79}Br). m/z 545.0434 and 543.0438. Calcd for M+H$^+$ of $C_{21}H_{23}BrN_2O_8S$: 545.0416 (^{81}Br) and 543.0437 (^{79}Br).

Transformation of (4*S*,5*R*)-5-acetoxy-4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(4-nitrophenyl)imidazolidine-2-one (36) into 4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(4-nitrophenyl)imidazoline-2-one (38). A solution of **36**[2b] (0.08 g) in DMSO-d_6 (0.5 mL) was heated at 80 °C and its transformation was monitorized by ^{1}H-NMR spectroscopy. The formation of the epimeric (4*S*,5*S*)-5-acetoxy-4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(4-nitrophenyl)-imidazolidine-2-one (**37**) was initially observed, and then its complete conversion into 4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(4-nitrophenyl)imidazoline-2-one (**38**), which was characterized spectroscopically by comparison with an authentical sample.[2b]

Acknowledgement. This work was made possible by the financial support of DGICYT (PB95-0259-C02-01) and Junta de Extremadura-Fondo Social Europeo (PRI97-C175). Special thanks to Mr. I. López for his valuable help in NMR studies. G. Silvero would like to thank Junta de Extremadura for a fellowship.

REFERENCES AND NOTES

1. Preliminary studies have been presented at the 2nd International Meeting of the Portuguese Carbohydrate Chemistry Group, Porto, Portugal, 21-25 September 1997, Book of Abstracts, p 61.
2. (a) Valencia, C., M.A. Thesis, University of Extremadura, Badajoz, **1990**. (b) Avalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Palacios, J. C.; Valencia, C. *Tetrahedron* **1993**, *49*, 2655, 2676.
3. Avalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Palacios, J. C.; Valencia, C. *Tetrahedron* **1994**, *50*, 3273 and references cited therein.
4. Scott, J. E. *Carbohydr. Res.* **1970**, *14*, 389.
5. Fernández-Bolaños, J.; García, S.; Fernández-Bolaños, J.; Díanez, M. J.; López-Castro, A. *Carbohydr. Res.* **1991**, *210*, 125.
6. For some examples of atropisomerism in heterocycles with naphthyl or *ortho*-substituted phenyl groups, see: (a) Bock, L. H.; Adams, R. *J. Am. Chem. Soc.* **1931**, *53*, 374, and 3519. (b) Jochims, J. C.; Voithenberg, H.; Wegner, G. *Chem. Ber.* **1978**, *111*, 2745. (c) Fujiwara, H.; Bose, A. K.; Manhas, M. S.; van der Veen, J. M. *J. Chem. Soc., Perkin Trans. 2* **1979**, 653. (d) Kashima, C.; Katoh, A. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1599. (e) Roussel, C.; Adjimi, M.; Chemlal, A.; Djafri, A. *J. Org. Chem.* **1988**, *53*, 5076. (f) Rubiralta, M.; Jaime, C.; Feliz, M.; Giralt, E. *J. Org. Chem.* **1990**, *55*, 2307. (g) Saito, K.; Yamamoto, M.; Yamada, K. *Tetrahedron* **1993**, *49*, 4549.
7. Bock, K.; Pedersen, C. *Adv. Carbohydr. Chem. Biochem.* **1983**, *41*, 54.
8. Kondo, H.; Horiguchi, D.; Ikeda, S.; Sunamoto, J.; Tsujii, K. *J. Org. Chem.* **1979**, *44*, 4430.
9. Coxon, B. *Methods Carbohydr. Chem.* **1972**, *6*, 513.
10. Jochims, J. C. *Angew. Chem. Int. Ed. Engl.* **1975**, *108*, 2320.
11. (a) IUPAC Commission on Physical Organic Chemistry, *Pure Appl. Chem.* **1989**, *61*, 23. (b) *ibidem*, **1989**, *61*, 57. (c) Guthrie, R. D.; Jencks, W. P. *Acc. Chem. Res.* **1989**, *22*, 343.
12. Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry, 2nd Ed.;* VCH: Weinheim, 1990; pp 160-170.
13. Dalton, L. K. *Austr. J. Chem.* **1966**, *19*, 445.
14. Jochims, J. C. *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 964.
15. Fernández-Bolaños, J.; Blasco, A.; Fuentes, J. *An. Quím.* **1990**, *86*, 675.
16. Areces, P.; Avalos, M.; Babiano, R.; González, L.; Jiménez, J. L.; Palacios, J. C.; Pilo, M. D. *Carbohydr. Res.* **1991**, *222*, 99.
17. Kruger, F.; Rudy, H. *Justus Liebigs Ann. Chem.* **1963**, *669*, 146.
18. Fuentes, J.; Fernández, J. I.; Areces, P.; Rebolledo, F.; Galbis, J. A. *Nucleosides & Nucleotides* **1988**, *7*, 457.
19. García, F.; Menéndez, M.; Ariza, F.; Alvarez, C. *An. Real. Soc. Esp. Fís. Quím.* **1968**, *64B*, 407.

20. Pradera, M. A.; Yruela, M.; Fuentes, J.; Fernández-Bolaños, J. *An. Quím.* **1978**, *74*, 945.
21. Huber, G.; Schier, O.; Druey, J. *Helv. Chim. Acta* **1960**, *43*, 713, 1787.
22. Fernández-Bolaños, J.; García González, F.; Gasch Gómez, J.; Menéndez, M. *Tetrahedron* **1963**, *19*, 1883.
23. (a) García, F.; Fernández-Bolaños, J.; Fuentes, J.; *Carbohydr. Res.* **1972**, *22*, 436. (b) García, F.; Fernández-Bolaños, J.; Fuentes, J.; Pradera, M. A. *Carbohydr. Res.* **1973**, *26*, 427. (c) Fernández-Bolaños, J.; Trujillo, J. M.; Fuentes, J.; Viguera, F. J.; Cert, A. *An. Quím.* **1985**, *81C*, 147.
24. Horton, D.; Wander, J. D. *J. Org. Chem.* **1974**, *39*, 1859.
25. Lee, J. B.; Scanlon, B. F. *Tetrahedron* **1965**, *25*, 3413.
26. Seldes, A. M.; Gross, E. G.; Thiel, I. M. E.; Deferrari, J. O. *Carbohydr. Res.* **1975**, *39*, 11.
27. Sweeting, L. M.; Coxon, B.; Varma, R. *Carbohydr. Res.* **1979**, *72*, 43.
28. Blanc-Muesser, M.; Defaye, J.; Horton, D. *Carbohydr. Res.* **1980**, *87*, 71.
29. Avalos, M.; Jiménez, J. L.; Palacios, J. C.; Galbis, J. A. *Carbohydr. Res.* **1986**, *158*, 53.
30. (a) Nakanishi, K.; Solomon, P. H. *Infrared Absorption Spectroscopy, 2nd ed.*; Holden-Day: San Francisco, 1977; p 25. (b) Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds, 3rd ed.*; Wiley: New York, 1978; p 227.
31. The compound was obtained as a mixture of rotamers, these are indicated by adding letters **a** (major) and **b** (minor).