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Non-Biaryl Atropisomers Derived from Carbohydrates. Part 2. Atropisomeric Behavior of Monocyclic and Bicyclic Imidazolidine-2-ones and 2-thiones[1,2]

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Abstract: High-yielding syntheses of bicyclic imidazolidine-2-ones and 2-thiones bearing an *ortho*-substituted aromatic ring have been described. Their atropisomeric behavior has been studied in depth taking into account the effects of substituents in the *ortho* position, the length of the exocyclic C=X bond, and the presence of substituents at C-5 in the heterocyclic ring. The barriers to rotation were independently estimated by dynamic NMR spectroscopy and molecular mechanics.

Keywords: Atropisomerism, carbohydrates, imidazolidines, molecular mechanics, rotational isomers.

INTRODUCTION

The 2-oxo and 2-thioxo-1,3-*N*-heterocycles derived from carbohydrates[3] are not only optically active substances that can easily be prepared from naturally-occurring or commercially available sugars, but may also have potential applications. Besides their immediate use as removable chiral auxiliaries or a source of chiral pool to perform stereoselective syntheses, certain compounds are also biologically active. Thus, the antibiotic CV-1[4] presents a structure of 2-oxoimidazolidine. Furthermore, some structures described in this work are in fact acyclic nucleosides, while the substituted 5,5-fused ring systems can be considered, at least formally, as 2,2'-*anhydro*-nucleoside analogs. Since nucleosides are being extensively evaluated as antitumor agents[5] or for AIDS therapy,[6] the preparation of these substances and their derivatives represents an area of additional interest.

From a structural viewpoint, we have shown[1,2,7] that 1-naphthylimidazolidine-2-thiones **1-3** derived

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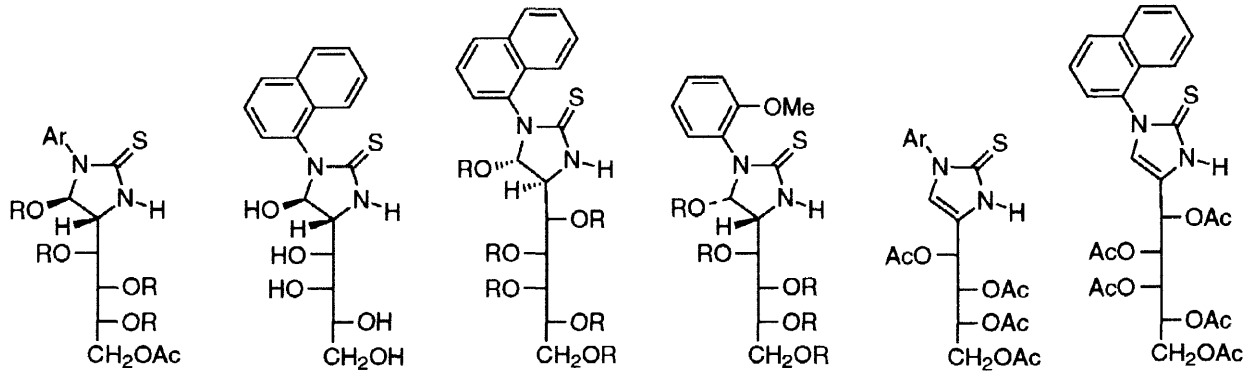
from 2-amino-2-deoxy-D-glucopyranose, 2-amino-2-deoxy-D-galactopyranose and 2-amino-2-deoxy-D-*glycero*-L-*gluco*-heptopyranose respectively, exhibit atropisomerism as a result of hindered rotation about the C-N single bond between the naphthyl substituent and the heterocyclic moiety.[8] These carbohydrates with restricted rotation around single bonds could be harnessed as potential chemical machines[9] or molecular gears,[10] topics of much interest in nanotechnology. Accordingly, we have prepared[1,2] the series of compounds **4-21** in order to investigate the structural requirements for atropisomerism to occur.



1 Ar = 1-$C_{10}H_7$, R = H
4 Ar = 2-FC_6H_4, R = H
5 Ar = 2-ClC_6H_4, R = H
6 Ar = 2-BrC_6H_4, R = H
8 Ar = 2-$MeOC_6H_4$, R = H
9 Ar = 2-FC_6H_4, R = Ac
10 Ar = 2-ClC_6H_4, R = Ac
11 Ar = 2-BrC_6H_4, R = Ac
12 Ar = 2-$MeOC_6H_4$, R = Ac
14 Ar = 1-$C_{10}H_7$, R = Ac

2

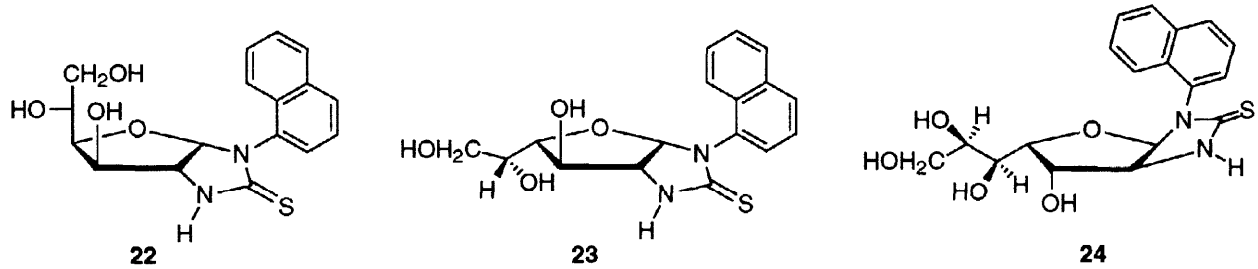
3 R = H
15 R = Ac

7 R = H
13 R = Ac

16 Ar = 1-$C_{10}H_7$
18 Ar = 2-FC_6H_4
19 Ar = 2-ClC_6H_4
20 Ar = 2-BrC_6H_4
21 Ar = 2-$MeOC_6H_4$

17

Nonbiaryl atropisomers are also **22-24**, which arise from **1-3** by acid-catalyzed cyclization.[7] These naphthyl thioamides could certainly be conveyors of chirality and, it is hoped that a day will soon come when asymmetric syntheses will involve the use of nonbiaryl atropisomerically pure ligands.[11] In this paper we describe the synthesis and atropisomeric behavior of a series of novel glycofuranoimidazolidine-2-ones and 2-thiones as well as compounds **1-24** which have been previously described.[1,2,7]



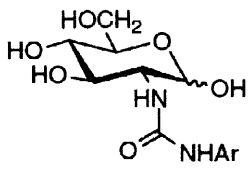
22 **23** **24**

RESULTS

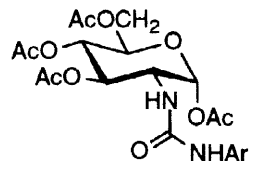
Synthesis of 1-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-ones. The direct condensation of 2-amino-2-deoxy-α-D-glucopyranose with *ortho*-monosubstituted aryl isocyanates proceeds

rapidly at room temperature in an aqueous solution of sodium bicarbonate-dioxane to afford the corresponding 2-(3-arylureido)-2-deoxy-D-glucopyranoses **25-29**, which can be utilized in the next step without further purification. The naphthylurea **29** was prepared as early as 1910 by Neuberg and Hirschberg[12] who assigned it the structure **33**, although at that time the hemiacetal structure of carbohydrates had not yet been elucidated.

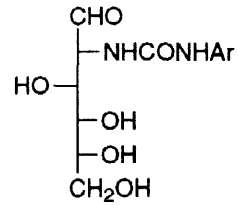
The structure of such ureido derivatives is consistent with their spectroscopic data. Their ^{13}C-NMR spectra in DMSO-d_6 are similar to those of other sugar ureas,[3] thereby showing that these compounds are obtained as a mixture of α and β anomers in which the former is prevalent. This fact could further be confirmed by preparing some per-*O*-acetyl derivatives in high yields (80-90%) as anomeric mixtures again. Fractional crystallization provides the α-anomers **30-32**. Their structures are also supported by their spectroscopic and polarimetric data and their elemental analyses. The NMR spectra are analogous to those of other per-*O*-acetylated sugar ureas described previously,[3] and the α-anomeric configuration is based on the small value of $J_{1,2'}$ (~ 3.6 Hz) and the high values of optical rotation $[\alpha]_D$.



25 Ar = 2-ClC_6H_4
26 Ar = 2-$MeOC_6H_4$
27 Ar = 2-MeC_6H_4
28 Ar = 2-$NO_2C_6H_4$
29 Ar = 1-$C_{10}H_7$



30 Ar = 2-$MeOC_6H_4$
31 Ar = 2-MeC_6H_4
32 Ar = 1-$C_{10}H_7$



33 Ar = 1-$C_{10}H_7$

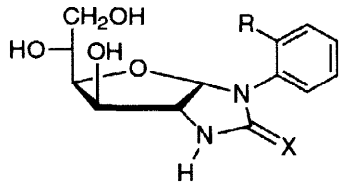
The chemical shift for H-2 is similar to that in *Z*-isomers of sugar formamides[13] and the high values of $J_{2,NH}$ (~ 9 Hz) suggest an *antiperiplanar* disposition between such protons in solution. Accordingly, the only conformer observed by NMR should present a *Z,Z-anti* configuration, sterically less hindered than a *Z,E-anti* one.[14]

The treatment of 2-(3-arylureido)-2-deoxy-D-glucopyranoses **25-29** with hot aqueous acetic acid provided a high-yielding preparation of the corresponding 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-ones **34-38**. These compounds could be characterized when their acetylated derivatives **39-43** were prepared by reaction with acetic anhydride and pyridine at –15 °C. Under these conditions only *O*-acetylation was observed. However, the treatment of **38** with acetic anhydride plus zinc chloride gave rise to *N*-acetylation[15] as well leading to **44**.

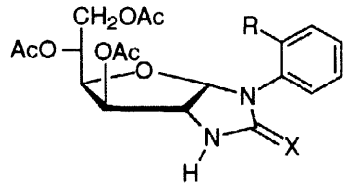
The structures attributed to **34-44** are also supported by their spectroscopic data, physical properties and elemental analyses. The small value of $J_{2,3}$ (~ 0 Hz) rules out a pyranose structure,[3] and confirms that **34-44** are glycofuranoses in which H-2 and H-3 display a *trans* arrangement. On the contrary, intermediate values of 5-7 Hz for $J_{2,3}$ would otherwise be consistent with a *cis* disposition as observed between H-1 and H-2. Thus, the experimental values of $J_{1,2}$ (6-7.5 Hz) confirm the existence of *cis*-fused rings.

The ^{13}C-NMR spectra of these substances show that C-4 (and not C-5) is the most deshielded signal, a fact also accounting for the furanoid character of the sugar moiety. The IR spectra of **39-43** show the

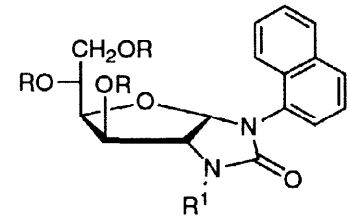
diagnostic absorption at ~3300 cm^{-1} (NH), which is of course absent in compound **44**, although the latter exhibits the amide band at 1685 cm^{-1}. A comparison between the optical rotations of compounds **43** and **44** indicates that the *N*-acetylation causes a decrease of ~60°.



34 R = Cl, X = O
35 R = MeO, X = O
36 R = Me, X = O
37 R = NO_2, X = O
45 R = F, X = S
46 R = Cl, X = S
47 R = Br, X = S
48 R = MeO, X = S
49 R = Me, X = S

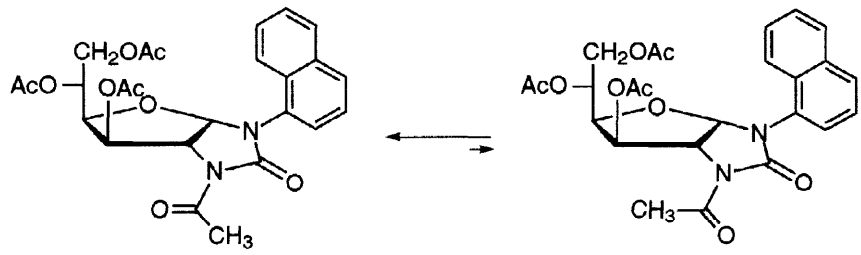


39 R = Cl, X = O
40 R = MeO, X = O
41 R = Me, X = O
42 R = NO_2, X = O
50 R = F, X = S
51 R = Cl, X = S
52 R = Br, X = S
53 R = MeO, X = S
54 R = Me, X = S



38 R = R^1 = H
43 R = Ac, R^1 = H
44 R = R^1 = Ac

The unusual chemical shift of the *N*-Ac methyl group (~2.6 ppm) of compound **44** is caused by its close proximity to the heterocyclic C=O bond in the most stable conformation (**44*E***), in which the methyl group is located in the deshielding zone of the carbonyl double bond. The alternative conformation (**44*Z***) is disfavored owing to dipole-dipole repulsion of carbonyl groups.[16-18]



44*E* **44*Z***

The unequivocal structure of **42** has been elucidated by single-crystal X-ray diffractometry as shown in Figure 1 with the crystallographic numbering.[19] This analysis reveals that the *P* atropisomer[20] exists exclusively in the solid state. In the crystal lattice, the dihedral angles between the mean planes phenyl ring-nitro group, phenyl ring-imidazolidine ring, and furanoid ring-imidazolidine ring are 40.5°, 40.7°, and 72.0°, respectively. Table 1 also shows the most representative torsion angles for the solid-state structure of **42**. The imidazolidine ring is only slightly puckered and shows a conformation close to an envelope, the C(1) atom being 0.102 Å out of the plane C(2)-N(1)-C(7)-N(2) [maximum mean-plane deviation for C(1) and C(2) = 0.003 Å]. This geometry is supported by the puckering parameters q_2 = 0.061 Å and ϕ_2 = 102.4°, calculated according to Cremer and Pople,[21] assuming that values of ϕ_2 = 108±n36° correspond to envelope conformations, while ϕ_2 = 90±n36° give half-chair conformations.

Table 1. Representative torsion angles for the solid-state structure of **4 2**.

Torsion angle	Degrees
C(8)-C(9)-N(3)-O(3)	40.1
C(8)-C(9)-N(3)-O(4)	-143.8
C(1)-N(2)-C(7)-O(2)	-174.4
C(8)-N(2)-C(7)-O(2)	2.5
C(13)-C(8)-N(2)-C(7)	-135.7
C(2)-C(1)-N(2)-C(7)	-6.7
N(2)-C(1)-C(2)-N(1)	5.7
O(1)-C(1)-C(2)-C(3)	6.1

The furanose ring is more puckered. The puckering parameters (q_2 = 0.389 Å and ϕ_2 = 151.2°) describe an intermediate form between half-chair and envelope conformations, but closer to the latter, with C(4) and O(1) deviating 0.462 and 0.145 Å above and below, respectively, the C(1)-C(2)-C(3) plane.

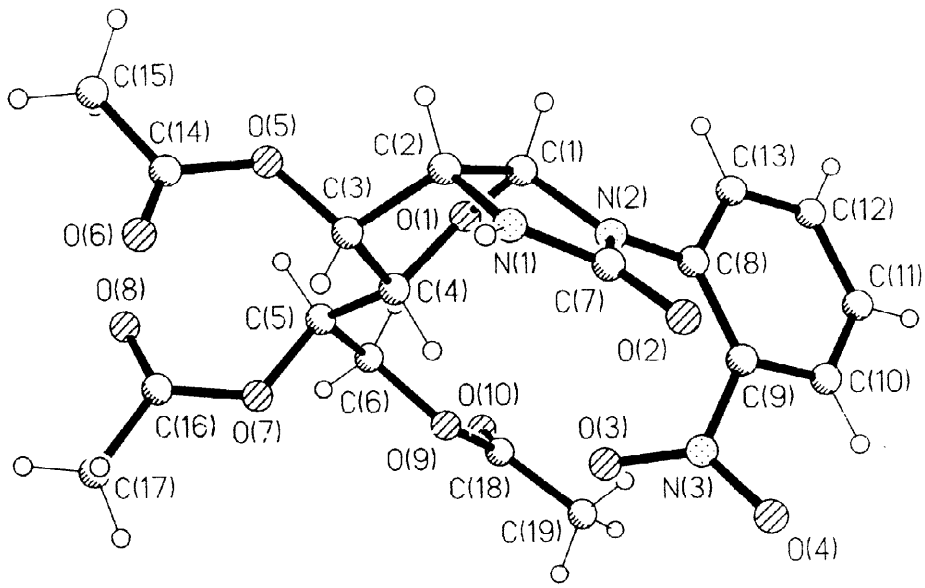


Figure 1. X-ray diffraction analysis of compound **4 2**.

There are also two intermolecular hydrogen bonds involving different acceptor atoms, which are collected in Table 2.

Table 2. Intermolecular hydrogen bonds for compound **4 2**.

Bond A···H–D	Position of atom D	A···D(Å)	A···H–D(°)
O(4)....H(1B)-N(1)	-0.5+x, 2.5-y, 2-z	3.191(5)	152.3(1)
O(2)....H(1B)-N(1)	-0.5+x, 2.5-y, 2-z	3.151(5)	124.8(1)

Synthesis of 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thiones. The treatment of compounds **4-7**[1,2] with hot 30% aqueous acetic acid for 30 min produced their conversion into **45-48** in high yields. Direct syntheses of **45-49** were also accomplished by condensation of 2-amino-2-deoxy-D-glucose with aryl isothiocyanates in the presence of acetic acid and heating the reaction mixture at 100 °C. When that temperature was kept for 30 min, in a similar manner for the preparation of other bicycles,[7,22] mixtures of imidazolidine-2-thiones were obtained which could be separated by fractional crystallization. The incomplete transformation is presumably due to steric interactions caused by substituents in the *ortho* position, thereby slowing down the process. Prolonged reaction times along with an increase in the amount of acetic acid yields **45-49** as the sole products. Further treatment with acetic anhydride and pyridine at –15 °C gave the per-*O*-acetyl derivatives **50-54** in high yields.

Again, the structures of **45-54** are consistent with their spectral data and elemental analyses. The zero value of $J_{2,3}$ accounts for the furanoid character of these bicycles, while the magnitude of $J_{1,2}$ (~6-7 Hz) demonstrates a *cis* fusion between both rings. The IR spectra of **50-52** display a signal at ~3300 cm^{-1} for the NH which confirms the selective protection of hydroxyl groups. Compounds **53** and **54** also exhibit absorption bands beyond 3400 cm^{-1} and a weak one peaking at ~1620 cm^{-1}, which can be attributed to water[23] as these substances crystallize as hydrates. The ^1H- and ^{13}C-NMR spectra are analogous to those of their oxygenated counterparts **39-43**,with the exception of the thiocarbonyl resonance at ~183 ppm.

Experimental determination of the barrier to rotation. Like compounds **1-24** described previously,[1,2,7] the atropisomerism of **34-54** is dependent on several factors and we have therefore undertaken an experimental and theoretical study on hindered rotation about a single bond. Structural variations herein considered include: a) lengths of bond types, C=O *versus* C=S; b) type of substituents at C-5 (OH in compounds **1-8**, OAc in **9-15**, H in **16-21**, and ring fusion through the oxygen bridge of the furanoid moiety in **22-24** and **34-54**; and c) nature of groups in the *ortho* positions, namely F, Cl, Br, Me, OMe, NO_2, and 1-naphthyl substituents.

The barrier to rotation has been determined by NMR experiments at different temperatures, since as the temperature is increased the lines coalesce at T_c because the interconversion of both atropisomers. At T_c the rate constant (k) between two equally populated equilibrium states is given by equation (1):[24]

$$k = \frac{\pi \Delta \nu}{\sqrt{2}} \qquad (1)$$

where $\Delta\nu$ represents the difference in frequency units (Hz) between two identical signals of the atropisomers when their interconversion is prevented or greatly slowed. The above expression, however, cannot strictly be applied when the states are unequally populated, but we may use the equation (1) to obtain an estimate of the barrier to rotation. The corresponding free energies of activation $\Delta G^{\ddagger}$ were calculated by substituting the coalescence temperature T_c and the chemical shift difference ($\Delta\nu$, in Hz) near the coalescence point into the equation (2), which results from the combination of (1) with the Eyring equation:[25]

$$\Delta G^{\ddagger}(\text{cal mol}^{-1}) = 1.987\ T_c(22.62 + \ln T_c/\Delta\nu) \qquad (2)$$

Experimental data together with the values of free energy of activation are given in Table 3.

Table 3. Barriers to rotation (kcal mol^{-1})[a] determined by dynamic NMR.[b]

Comp.	Δν (Hz)	T_c (K)	$\Delta G^{\ddagger}$	ΔG°
1	33.79	340	16.84	d
2	38.03	355	17.77	0.74
3	43.89	345	16.92	d
16	7.92	330	17.28	d
17	23.06	345	17.36	1.02
23	17.26	330	16.77	d
24	30.04	330	16.63	0.53
24c	31.54	330	16.60	d
24c	25.06	330	16.75	d
43	55.76	250	12.02	0.12
44	49.30	264	12.75	0.12
51	34.55	280	13.75	
54	10.03	298	15.40	

$\Delta G^{\circ} = |\Delta G^{\circ}_M - \Delta G^{\circ}_P|$; [a]1 kcal = 4.18 kJ. [b]Determined from ^{1}H-NMR spectra, unless otherwise specified, [c]Determined from ^{13}C NMR on different carbon signals. [d]Not determined.

Determination of the barrier to rotation by molecular mechanics. Free rotation about a single bond converts the *M* isomer into its *P* counterpart and vice versa.[20] In some cases, the substituents may be large enough to slow rotation greatly but not to prevent it completely. Such an interconversion takes place by rotation about the N-C(aryl) single bond and the corresponding transition states are the peaks of highest potential energy through a 360° rotation. The energy gradually increases until both the aromatic ring and the heterocycle are nearly coplanar. Figure 2 displays the particular situation of a monocyclic imidazolidine-2-thione derivative bearing a substituent at the *ortho* position. There are two, unequally populated, isomeric transition states **55** and **56** in which the cause of the barriers can be viewed. Thus, in structure **55** the barrier is caused by repulsion between overlapping orbitals of the *ortho* substituent and the exocyclic sulfur atom, whereas in **56** the barrier is due to repulsion between the hydrogen atom in the *ortho* position and the exocyclic sulfur atom. As we shall see later, such interactions mainly determine the rotation barrier heights.

At this moment, we also need a free-energy profile *versus* the reaction coordinate which corresponds to the angle of torsion about the N-C(aryl) bond, and the potential energy can easily be determined by means of molecular mechanics (MM2)[26] calculations. Starting from the *P* isomer, which is a conformation of low potential energy, rotation of the dihedral angle ϑ [$C_{(sp^3)}$-$N_{(sp^2)}$-$C_{(sp^2)}$-$C_{(sp^2)}$] at 30° intervals gives rise to a conformational energy diagram for the interconversion of atropisomers. A further refinement was also accomplished to determine the conformations when the energy is at a maximum, simply by rotation of the angle of torsion every 5° within the interval between −30° to +30° around the maxima found previously. These results are collected in Table 4.

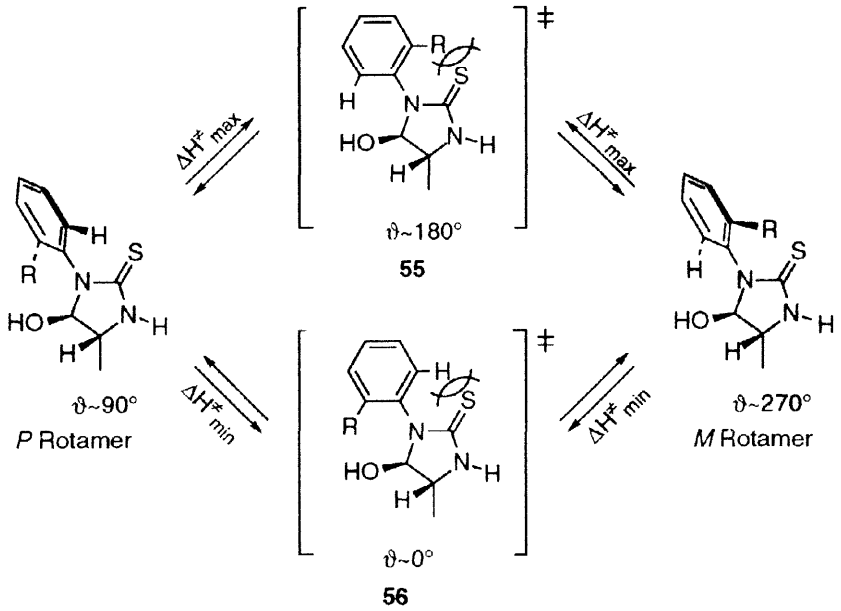


Figure 2. Transition states for the interconversion of *M* and *P* rotamers.

Table 4. Barriers to rotation (kcal mol^{-1})[a] determined by MM2.

Comp.	E_M	E_P	$\Delta H^{\ddagger}_{min}$	$\Delta H^{\ddagger}_{max}$	$\Delta\Delta H^{\ddagger}$	ΔH°
1	13.97	13.80	15.70	38.60	22.90	0.17
2	14.81	14.42	17.01	38.09	21.08	0.39
22	18.81	18.99	16.05	42.37	26.32	0.18
23	19.47	17.31	18.35	45.20	26.85	2.16
24	18.62	18.95	15.29	44.88	29.59	0.33
34	24.79	24.76	13.80	16.78	2.98	0.03
35	29.42	29.55	11.81	14.32	2.51	0.13
36	23.91	23.82	12.33	16.68	4.35	0.49
43	34.19	33.75	11.10	16.94	5.84	0.44
44*E*	31.88	30.94	11.88	17.33	5.45	0.94
44*Z*	34.10	33.26	11.75	17.05	5.30	0.84
46	25.21	25.24	15.07	20.69	5.62	0.03
48	29.84	29.20	16.99	18.02	1.03	0.64
49	24.36	24.27	14.83	20.71	5.88	0.09
57	7.30	7.13	24.77	45.43	20.66	0.17
58	6.80	6.64	12.36	18.39	6.03	0.16
68	24.26	24.17	15.68	21.76	6.08	0.09

[a]1 kcal = 4.18 kJ. E_M or E_P denotes the potential energy of *M* or *P* conformers; $E^{\ddagger}_{min}$ ($E^{\ddagger}_{max}$) is the potential energy of the transition structure of the lowest (highest) energy; $\Delta H^{\circ} = |E_M - E_P|$; $\Delta H^{\ddagger}_{min}$ ($\Delta H^{\ddagger}_{max}$) = $E^{\ddagger}_{min}$ ($E^{\ddagger}_{max}$) - E_P; $\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}_{max} - \Delta H^{\ddagger}_{min}$.

The conformations of lower potential energy correspond to dihedral angles of ~90° (E_P) and ~270° (E_M). The difference in energy between both atropisomers, $\Delta H^{\circ} = |E_P - E_M|$, is in general too low, close to 0 kcal mol^{-1}. The points of higher potential energy are observed at ~0° ($E^{\neq}_{min}$) and ~180° ($E^{\neq}_{max}$), the latter being the conformation of highest potential energy, thereby indicating that the repulsion between the *ortho*-substituent and

the sulfur atom ($\Delta H^{\neq}_{max} = E^{\neq}_{max} - E_P$) is greater than the interaction between the *ortho* hydrogen and the sulfur atom ($\Delta H^{\neq}_{min} = E^{\neq}_{min} - E_P$), (see Fig. 2).

Molecular mechanics calculations permit the determination of $\Delta H^{\ddagger}$, whose values can be compared with those of $\Delta G^{\ddagger}$ which are estimated by dynamic NMR spectroscopy, if we make the assumption that for these reactions the entropy change can be neglected: $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} \approx \Delta H^{\ddagger}$.

DISCUSSION

The preparation of compounds **25-54** described in the present work has been carried out according to the synthetic protocols developed previously.[3,7]

Atropisomerism of 1-aryl-5-imidazolidine-2-thiones and imidazoline-2-thiones. Variable-temperature NMR experiments evidence that the experimental barriers to rotation for compounds **1-3** are ~17-18 kcal mol^{-1} (Table 3). A plot of potential energy *versus* the angle of torsion for compound **1** is also depicted in Figure 3. There are two extremes corresponding to transition structures: the one with a potential energy of ~38 kcal mol^{-1} and the other with a lower energy of ~16-17 kcal mol^{-1}. Either molecular mechanics or dynamic NMR provide similar values of the barrier to rotation.

The aromatic ring freely rotates at ambient temperature to enable the separation of both diastereoisomers, since the magnitude of the barrier should be greater than 23 kcal mol^{-1} in order for rotation to be prevented.[27,28] In such cases, single atropisomers can be prepared which are stable enough at room temperature. Nevertheless, the appearance of two signal sets in proton and carbon NMR spectra suggest a slow interconversion on the NMR time scale.

Calculations on the simplified models **57** and **58** demonstrate that the size of the acyclic side chain has no effect on the barriers to rotation (see Table 4).

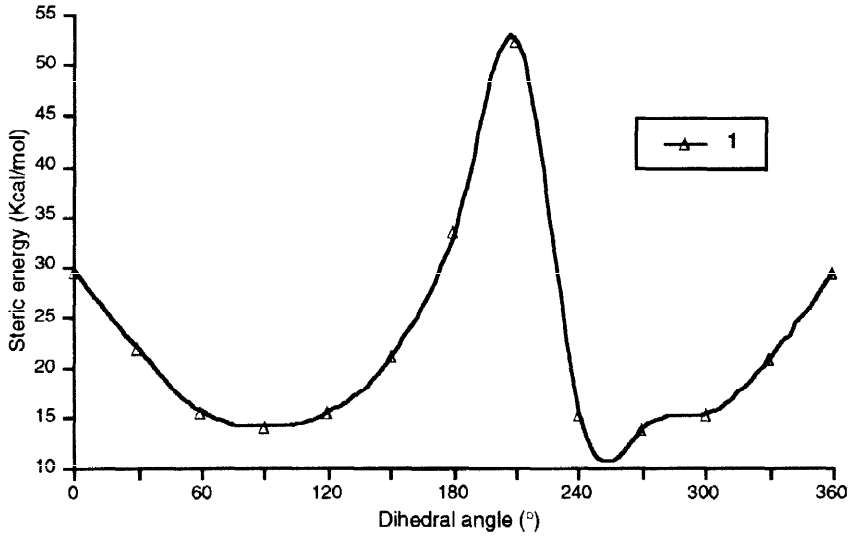


Figure 3. Conformational energy diagram (MM2) for compound **1**.

The energy difference between the transition structures ($\Delta\Delta H^{\ddagger} = \Delta H^{\ddagger}_{max} - \Delta H^{\ddagger}_{min}$), greater than 21 kcal mol^{-1}, secures that the interconversion mechanism follows a fan movement from +90° to –90° through 0°, but not through 180° (Figure 4).

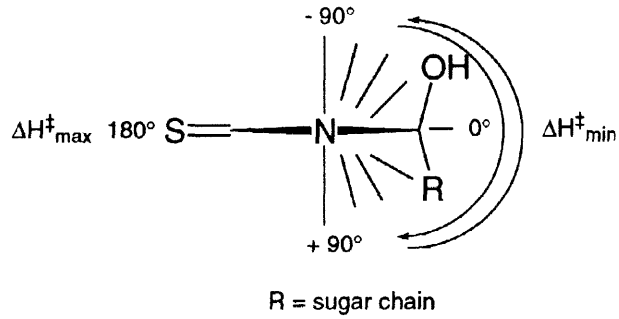
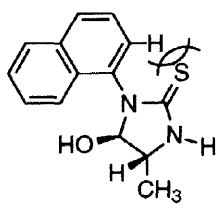


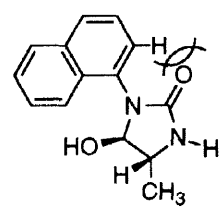
Figure 4.

The rest of 1-aryl-5-hydroxyimidazolidine-2-thiones monosubstituted in the *ortho* position such as **4-8** were also considered in the present study, but only compounds **5** and **6** showed duplicated signals in their NMR spectra. By looking at the per-*O*-acetylated compounds, the naphthyl derivatives **14** and **15** exhibit atropisomerism at ambient temperature, although their barriers to rotation could not be determined by dynamic NMR spectroscopy, because they converted rapidly into **16** and **17**, respectively.

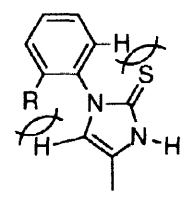
The presence of either a hydroxyl or acetate group in the heterocyclic moiety is not a requirement for atropisomerism to occur. This is confirmed by the fact that imidazoline-2-thiones **16** and **17** show two signal sets in their NMR spectra at room temperature, but coalescence occurs if higher temperatures are used to supply the energy necessary to force the groups past each other. The barrier to rotation for compounds **16** and **17** (~17 kcal mol^{-1}) remains practically unaffected with respect to that of **1** and **3** (Table 3). Presumably, a decrease in volume of the nonplanar substituent at C-5 (compounds **1**, **3**, **14**, and **15**), is compensated for the interaction with the hydrogen at C-5 which is now coplanar with the aromatic ring (compounds **16** and **17**). A schematic diagram of this situation is depicted below as structure **59**.



57



58



59

Atropisomerism of bicyclic 1-arylimidazolidine-2-ones monosubstituted in the *ortho* position. Our next target was to investigate the influence of a C=S bond on the barrier heights. In order to achieve this, the oxygenated bicycles **34-38** as well as their corresponding per-*O*-acetyl derivatives **39-44** were prepared. None of them showed atropisomerism at room temperature; however, on lowering the temperature a decoalescence of signal for atropisomers of **43** and **44** ocurred at –23 °C and –10 °C,

respectively. These oxygenated bicycles show a much lower barrier to rotation of about 11 kcal mol^{-1} than their thioanalogs, and the experimental values are almost coincidental with those of MM2 calculations (Table 4). Accordingly, free rotation takes place rapidly at room temperature for compounds **43** and **44** and neither proton nor carbon duplicities are observed in their NMR spectra. The smaller difference in the barrier height ($\Delta\Delta H^{\ddagger}$ ~5-6 kcal mol^{-1}), compared with the values obtained for imidazolidine-2-thiones **1** and **2** ($\Delta\Delta H^{\ddagger}$ >21 kcal mol^{-1}), can be attributed to the fact that a sulfur atom is larger (r_{vw} 1.85 Å) than an oxygen (r_{vw} 1.4 Å) as well as the increase in the length of the C=S bond (1.71 Å)[29] with respect to C=O (1.22 Å).

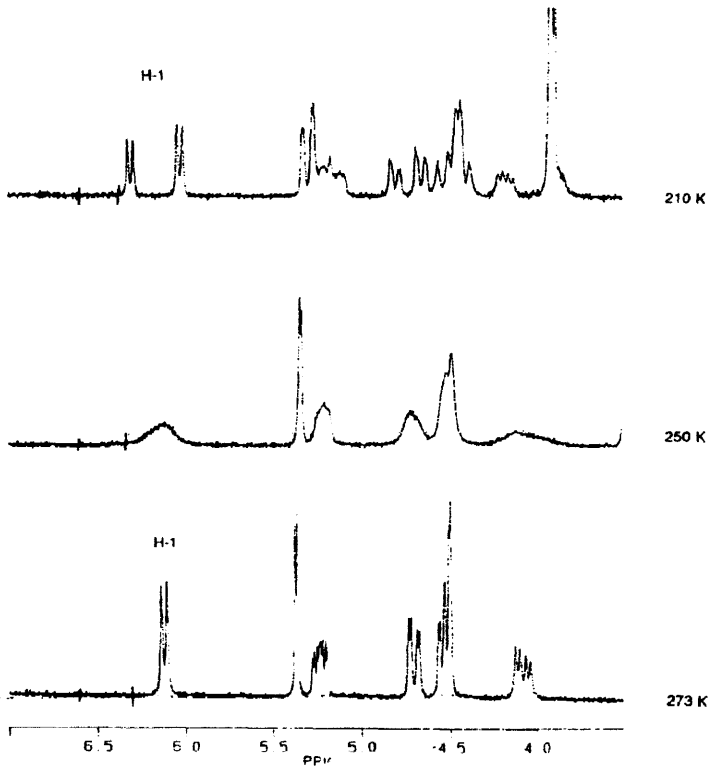
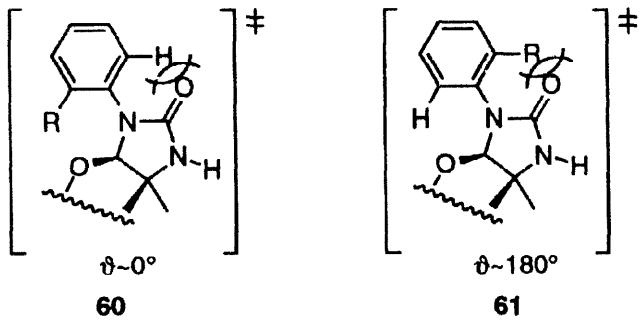


Figure 5. Variable-temperature ^{1}H-NMR experiments for compound **43** in CD_3COCD_3 showing the splittings due to slow C-N rotation.

When MM2 calculations are applied to compounds **34-36** (Table 4), that is bicyclic systems that do not carry naphthyl groups, the barriers to rotation corresponding to the transition structures **60** and **61** are close in energy ($\Delta\Delta H^{\ddagger}$<5 kcal mol^{-1}), and the lowest energy conformer is analogous to that of naphthyl derivatives discussed above, because in both cases an oxygen atom and a hydrogen are close to each other (see structures **60** and **62** for comparative purposes).



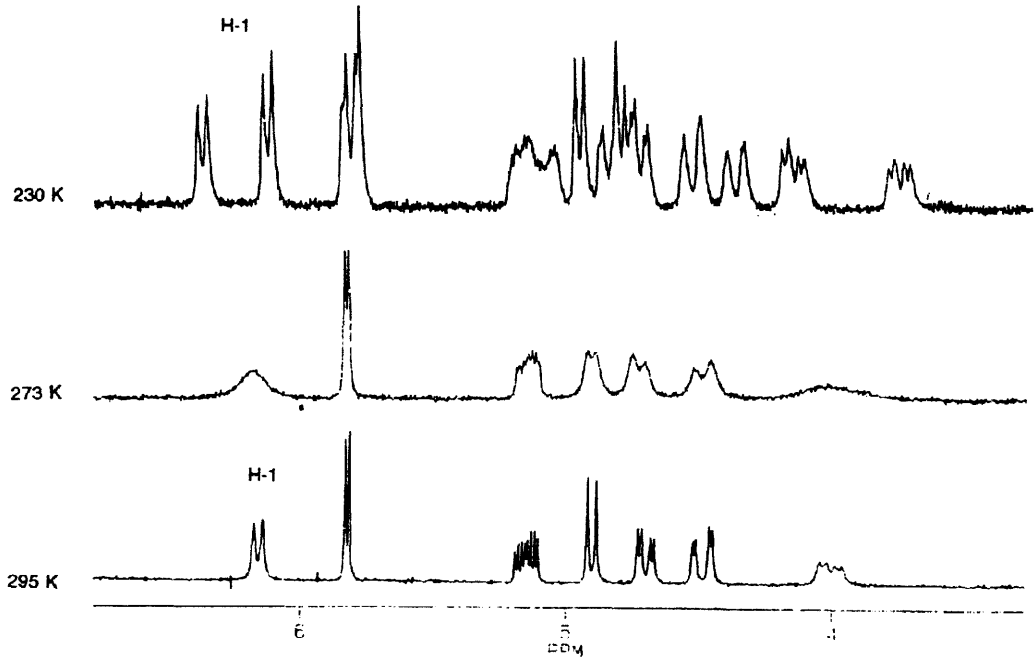
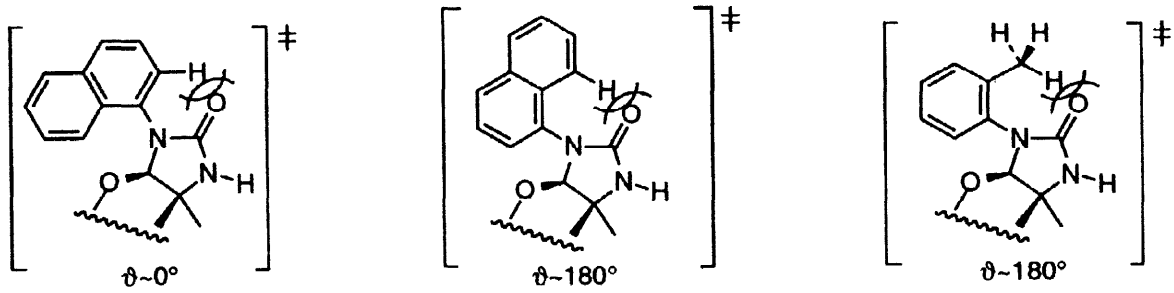


Figure 6. Variable-temperature ^{1}H-NMR experiments for compound **44**.

The relatively low barrier to rotation observed in **61**, which is the maximum of potential energy, suggests that the interaction between the R substituent (OMe, Me, Cl, F, NO_2) and the oxygen is smaller than in the case of naphthyl derivatives bearing an additional phenyl group (see transition state **63**). The NMR spectra of compounds **34-37** and **39-42** display only one signal set. In the case of the nitroderivative **37** the signals did not decoalesce even at –25 °C (248 K).



In the case of the *N*-acetylated derivative **44** we have also calculated the conformational energies of its *E* and *Z* rotamers, namely the conformers in which carbonyl groups show an *anti* or *syn* arrangement, respectively (Figure 7). The former minimizes the dipolar interactions at the transition state because polar carbonyl-to-carbonyl bonds are in an antiparallel arrangement, thereby decreasing the barrier height. The difference in energy between both rotamers is of about 2.2 kcal mol^{-1}, which corresponds to a percentage of ~98% of **44*E*** at ambient temperature.

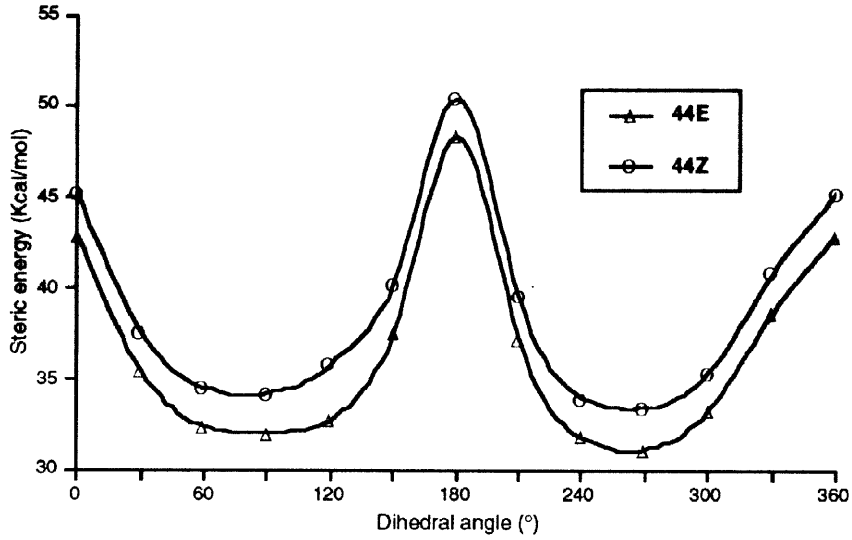


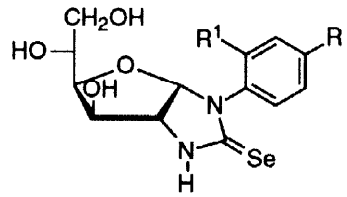
Figure 7. Plot of potential energy *versus* the angle of torsion for **44*E*** and **44*Z*** rotamers (MM2 calculations).

Atropisomerism of bicyclic 1-arylimidazolidine-2-thiones monosubstituted in the *ortho* position. Besides the naphthyl derivatives **22-24**, we have also investigated the atropisomeric behavior of other 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thiones (**45-49**) and their per-*O*-acetylated derivatives **50-54**, which carry different substituents in the *ortho* position.

For compounds **22-24** some signals in their NMR spectra at room temperature were split into two, as expected, in agreement with the magnitudes of their barriers to rotation which were determined by dynamic NMR spectroscopy and further confirmed by MM2 calculations (Tables 3 and 4). Likewise, most signals were duplicated at room temperature in NMR spectra of a series of bicycles with different substituents at the *ortho* position: Cl (**46**), Br (**47**) and Me (**49**). In relation with the acetylated derivatives, however, only **51** and **54** showed some duplicated resonances at room temperature, but all signals were split into two at a lower temperature (0 °C, 273 K). As expected, compounds **46**, **48** and **49** have a higher barrier to rotation than their oxygenated counterparts (Table 4), but the height is similar to that of **22-24**. This is the consequence to suppose that the bulkier the substituent (including C=S instead of C=O bonds) the higher the barrier.

Noteworthy is the enormous decrease of the higher barrier to rotation on comparing derivatives that carry a naphthyl group with respect to those bearing a substituent at the *ortho* position. For instance, the *ortho*-tolyl derivative **49** shows the value $\Delta H^{\ddagger}_{max}$= 20.71 kcal mol^{-1} whereas for compound **22** the barrier to rotation was estimated to be $\Delta H^{\ddagger}_{max}$= 42.37 kcal mol^{-1}. The naphthyl group could be considered a methyl group in which the conformation of one of the hydrogens is fixed without changing its bulkiness (**63** and **64**). Such conformation locking raises the barrier by ~22 kcal mol^{-1} and evidences the greater conformational flexibility of the methyl group at the transition state. This flexible motion can avoid severe steric interactions with the thiocarbonyl sulfur, for example, by a gear-like rotation of the methyl group or bending the C-C bond. These mechanisms are considerably restricted in naphthyl derivatives.

An interesting possibility consists in evaluating the atropisomerism of *ortho*-substituted 1-arylimidazolidine-2-selones[30] (such as **65-67**) in which the sulfur atom is replaced for selenium. Due to the long C=Se bond length ($d_{C=Se}$ 1.84 Å)[29] it would be expected a higher barrier to rotation. Nevertheless, MM2 calculations for **68** (Table 4) do predict a small increase of the barrier height.



65 R = R^1 = H
66 R = Br, R^1 = H
67 R = Me, R^1 = H
68 R = H, R^1 = Me

EXPERIMENTAL

General Methods. General methods have been described in a previous paper.[2]

General procedure for the preparation of 2-(3-arylureido)-2-deoxy-D-glucopyranoses. To a solution of 2-amino-2-deoxy-α-D-glucopyranose hydrochloride (6.48 g, 30.0 mmol) in water (33.0 mL), were added successively and with vigorous stirring, sodium hydrogencarbonate (2.52 g, 30.0 mmol) and a solution of aryl isocyanate (36.0 mmol) in dioxane (7.5 mL). The resulting suspension was stirred for 30 min, then it was filtered and the solid washed with cold water, acetone-ethanol, and diethyl ether. The following compounds were prepared according to this protocol.

2-[3-(2-Chlorophenyl)ureido]-2-deoxy-D-glucopyranose (25). Obtained from 2-chlorophenyl isocyanate in 80% yield, m.p. 191-192 °C, $[\alpha]_D$ +49° (*c* 1.0, DMF) [lit.[31] m.p. 189-192 °C, $[\alpha]_D$ +56° (*c* 1.0 DMF)]; ν_{max} 3600-3100 (OH, NH), 1635 (C=O), 1585 (NH), 860 cm^{-1} (aromatic); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ **25**α: 155.0 (C=O), 137.0, 129.2, 127.5, 122.4, 121.1, 120.8 (aromatic), 91.2 (C-1), 72.2 (C-5), 71.3 (C-3, C-4), 61.2 (C-6), 54.6 (C-2); **25**β: 155.7 (C=O), 136.9, 129.5, 127.6, 122.7, 121.1 (aromatic), 96.1 (C-1), 77.0 (C-5), 74.7 (C-3), 71.0 (C-4), 61.2 (C-6), 58.1 (C-2).

2-Deoxy-2-[3-(2-methoxyphenyl)ureido]-D-glucopyranose (26). From 2-methoxyphenyl isocyanate: 67% yield, m.p. 173-175 °C, $[\alpha]_D$ +53° (*c* 1.0, DMF); ν_{max} 3500-3100 (OH, NH), 1645 (C=O), 1567 (NH), 1259 (OCH_3), 1606, 1490, 741 cm^{-1} (aromatic); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ **26**α: 155.5 (C=O), 147.6, 129.7, 121.1, 120.6, 118.3, 110.8 (aromatic), 91.4 (C-1), 72.2 (C-5), 71.4 (C-4), 71.0 (C-3), 61.3 (C-6), 54.6 (C-2); Anal. Calcd for $C_{14}H_{20}N_2O_7$: C, 51.22; H, 6.14; N, 8.53. Found: C, 50.93; H, 6.22; N, 8.39.

2-Deoxy-2-[3-(2-tolyl)ureido]-D-glucopyranose (27). From 2-tolyl isocyanate: 85% yield, m.p. 192-194 °C (EtOH-H_2O), $[\alpha]_D$ +41° (*c* 1.0, DMF); ν_{max} 3500-3200 (OH, NH), 1637 (C=O), 1583 (NH),

1459, 749 cm^{-1} (aromatic); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ **27α**: 155.6 (C=O), 138.4, 130.2, 126.2, 121.6, 120.0 (aromatic), 91.6 (C-1), 72.4 (C-5), 71.9 (C-4), 71.5 (C-3), 61.5 (C-6), 54.8 (C-2), 18.1 (CH_3); **27β**: 157.0 (C=O), 138.2, 130.2, 126.7, 122.0, 120.5 (aromatic), 96.6 (C-1), 76.9 (C-5), 75.0 (C-3), 71.2 (C-4), 62.3 (C-6), 58.4 (C-2), 18.3 (CH_3). Anal. Calcd for $C_{14}H_{20}N_2O_6$: C, 53.84; H, 6.45; N, 8.97. Found: C, 53.67; H, 6.32; N, 8.88.

2-Deoxy-2-[3-(2-nitrophenyl)ureido]-D-glucopyranose (28). From 2-nitrophenyl isocyanate: 60% yield, m.p. 190-192 °C, $[\alpha]_D$ +59° (*c* 1.0, DMF); ν_{max} 3500-3000 (OH, NH), 1640 (C=O), 1580 (NH), 1530, 1330 (NO_2), 1600, 1490, 860, 840 cm^{-1} (aromatic); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ **28α**: 154.5 (C=O), 137.1, 135.8, 134.9, 125.4, 122.4, 121.5 (aromatic), 91.1 (C-1), 72.3 (C-5), 71.3 (C-3), 71.1 (C-4), 61.2 (C-6), 55.0 (C-2). Anal. Calcd for $C_{13}H_{17}N_3O_8.\sqrt{}\ H_2O$: C, 44.32; H, 5.14; N, 11.92. Found: C, 44.14; H, 4.91; N, 11.98.

2-Deoxy-2-[3-(1-naphthyl)ureido]-D-glucopyranose (29). From 1-naphthyl isocyanate: 90% yield, m.p. 235-237 °C (EtOH-H_2O), $[\alpha]_D$ +36° (*c* 0.5, DMF) [lit.[12] m.p. 234-236 °C]; ν_{max} 3500-3200 (OH, NH), 1640 (C=O), 1570 (NH), 1610, 1500, 790, 770 cm^{-1} (aromatic); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ **29α**: 155.8 (C=O), 135.4, 133.9, 128.6, 126.1, 125.9, 125.5, 125.2, 121.9, 121.4, 115.9 (aromatic), 91.4 (C-1), 72.4 (C-5), 71.7 (C-4), 71.3 (C-3), 61.3 (C-6), 54.7 (C-2); **29β**: 156.9 (C=O), 135.4, 133.9, 128.6, 126.1, 125.9, 125.5, 125.2, 121.9, 121.4, 115.9 (aromatic), 96.4 (C-1), 76.9 (C-5), 74.9 (C-3), 71.1 (C-4), 61.3 (C-6), 58.5 (C-2).

General procedure for the preparation of per-*O*-acetyl-2-(3-arylureido)-2-deoxy-D-glucopyranoses. To a solution of the corresponding 2-(3-arylureido)-2-deoxy-D-glucopyranose (20.0 mmol) in pyridine (18.0 mL) was added acetic anhydride (30.0 mL). After 24 h at room temperature, the reaction mixture was poured into ice-water to give a mixture of α and β anomers that was filtered and washed with cold water. Purification by crystallization affords, in general, pure α anomers.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(2-methoxyphenyl)ureido]-α-D-glucopyranose (30). The anomeric mixture (70%) was obtained from **26**. The α anomer (**30**, 56%) was isolated by crystallization from 96% aqueous EtOH, m.p. 183-185 °C, $[\alpha]_D$ +91° (*c* 1.0, $CHCl_3$); ν_{max} 3390 y 1540 (NH), 1760, 1230 (ester), 1718 (C=O urea), 1610, 1495, 770 cm^{-1} (aromatic); ^1H-NMR (200 MHz, $CDCl_3$) δ 8.01 (m, 1H, Ar), 7.20 (s, 1H, Ar-NH), 6.98-6.73 (m, 3H, Ar), 6.24 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 5.72 (d, $J_{2,NH}$ = 9.4 Hz, 1H, sugar NH), 5.37-5.22 (m, 2H, H-3, H-4), 4.51 (ddd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 9.5, $J_{2,NH}$ = 9.4, 1H, H-2), 4.26 (dd, $J_{5,6}$ = 4.1, $J_{6,6'}$ = 12.4 Hz, 1H, H-6), 4.09 (m, 2H, H-5, H-6'), 3.68 (s, 3H, OCH_3), 2.12 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.02 (s, 3H, OAc), 2.01 (s, 3H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 171.5 (CH_3-*C*=O), 170.7 (CH_3-*C*=O), 169.0 (CH_3-*C*=O), 168.6 (CH_3-*C*=O), 154.4 (NH-*C*O-NH), 147.8, 127.8, 122.7, 120.9, 119.3, 109.9 (aromatic), 91.1 (C-1), 70.9 (C-3), 69.5 (C-5), 67.6 (C-4), 61.6 (C-6), 55.3 (OCH_3), 51.3 (C-2), 20.6 (*C*H_3-CO), 20.5 (2C, *C*H_3-CO), 20.3 (*C*H_3-CO). Anal. Calcd for $C_{22}H_{28}N_2O_{11}$: C, 53.22; H, 5.68; N, 5.64. Found: C, 53.19; H, 5.75; N, 5.57.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(2-tolyl)ureido]-α-D-glucopyranose (31). Compound **27** afforded the anomeric mixture (81%). The α anomer (**31**, 49%) was isolated by crystallization from 96%

aqueous EtOH, m.p. 154-156 °C, $[\alpha]_D$ +82° (*c* 0.5, $CHCl_3$); ν_{max} 3320, 1560 (NH), 1745, 1240 (ester), 1660 (C=O urea), 1590, 1490, 750 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.39-7.10 (m, 4H, Ar), 7.03 (s, 1H, Ar-NH), 6.25 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 5.29 (bs, 1H, sugar NH), 5.24-5.14 (m, 2H, H-3, H-4), 4.44 (ddd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 9.5, $J_{2,NH}$ = 9.5, 1H, H-2), 4.27 (dd, $J_{5,6}$ = 3.9, $J_{6,6'}$ = 12.4 Hz, 1H, H-6), 4.10-4.00 (m, 2H, H-5, H-6'), 2.22 (s, 3H, CH_3), 2.11 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.05 (s, 3H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 171.1 (CH_3-*C*=O), 170.7 (CH_3-*C*=O), 169.0 (CH_3-*C*=O), 168.6 (CH_3-*C*=O), 155.7 (NH-*C*O-NH), 135.3, 132.4, 130.8, 126.8, 126.1, 125.2 (aromatic), 91.0 (C-1), 70.7 (C-3), 69.6 (C-5), 67.4 (C-4), 61.5 (C-6), 51.4 (C-2), 20.6 (3C, *C*H_3-CO), 20.4 (*C*H_3-CO), 17.5 (CH_3). Anal. Calcd for $C_{22}H_{28}N_2O_{10}$: C, 55.00; H, 5.87; N, 5.83. Found: C, 54.99; H, 5.90; N, 5.96.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(1-naphthyl)ureido]-α-D-glucopyranose (32). Compound **29** produced the anomeric mixture (61%). The α anomer (**32**, 38%) was isolated by crystallization from EtOH-H_2O, m.p. 128-130 °C, $[\alpha]_D$ +115° (*c* 1.0, $CHCl_3$); ν_{max} 3440, 3300 (NH), 1740, 1220 (ester), 1650 (C=O urea), 1550 (NH), 790, 760 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.92-7.40 (m, 7H, Ar), 7.55 (s, 1H, Ar-NH), 6.20 (d, $J_{1,2}$ = 3.7 Hz, 1H, H-1), 5.21 (d, $J_{2,NH}$ = 9.1, 1H, sugar NH), 5.16 (t, $J_{2,3}$ = $J_{3,4}$ = 9.7 Hz, 1H, H-3), 5.07 (t, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, 1H, H-4), 4.41 (ddd, $J_{1,2}$ = 3.7, $J_{2,3}$ = 9.7, $J_{2,NH}$ = 9.1, 1H, H-2), 4.20 (dd, $J_{5,6}$ = 4.4, $J_{6,6'}$ = 12.5 Hz, 1H, H-6), 4.01 (dd, $J_{5,6'}$ = 2.0, $J_{6,6'}$ = 12.5 Hz, 1H, H-6'), 3.90 (m, 1H, H-5), 2.06 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.85 (s, 3H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 171.1 (CH_3-*C*=O), 170.7 (CH_3-*C*=O), 169.0 (CH_3-*C*=O), 168.5 (CH_3-*C*=O), 156.3 (NH-*C*O-NH), 134.3, 132.4, 129.1, 128.4, 126.9, 126.6, 126.3, 125.6, 123.2, 121.6 (aromatic), 90.9 (C-1), 70.6 (C-3), 69.6 (C-5), 67.4 (C-4), 61.5 (C-6), 51.6 (C-2), 20.6 (*C*H_3-CO), 20.5 (2C, *C*H_3-CO), 20.4 (*C*H_3-CO). Anal. Calcd for $C_{25}H_{28}N_2O_{10}$: C, 58.14; H, 5.46; N, 5,42. Found: C, 57.75; H, 5.60; N, 5.34.

General procedure for the preparation of 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-ones. To a suspension of the corresponding 2-arylureido-2-deoxy-D-glucopyranose (10.7 mmol) in water (12.0 mL) was added acetic acid (3.5 mL) [plus ethanol (7.0 mL) for compound **34** and **37**], and the mixture was heated at ~100 °C (external bath) for 30-60 min. The hot solution was filtered and title compounds crystallized on cooling.

1-(2-Chlorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (34). The title compound was obtained from **25** in 25% yield, m.p. 246-248 °C, $[\alpha]_D$+89° (*c* 1.0, DMF) [lit.[31] m.p. 260-261 °C, $[\alpha]_D$+87° (*c* 1.0, DMF)]; ν_{max} 3560-3100 (OH, NH), 1670 (C=O), 1460 (NH), 1590, 1490, 770, 730 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 7.56-7.33 (m, 5H, Ar, NH), 5.79 (d, $J_{1,2}$ = 6.2 Hz, 1H, H-1), 5.25 (d, $J_{3,OH}$ = 4.9 Hz, 1H, C3-OH), 4.78 (d, $J_{5,OH}$ = 5.4 Hz, 1H, C5-OH), 4.51 (t, $J_{6,OH}$ = $J_{6',OH}$ = 5.3 Hz, 1H, C6-OH), 4.06 (m, 2H, H-2, H-3), 3.86 (dd, $J_{3,4}$ = 1.8 Hz, $J_{4,5}$ = 8.8 Hz, 1H, H-4), 3.76 (m, 1H, H-5), 3.56 (m, 1H, H-6), 3.37 (m, 1H, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 157.6 (C=O), 134.9, 133.1, 131.6, 129.9, 129.2, 127.9 (aromatic), 90.3 (C-1), 79.2 (C-4), 74.6 (C-3), 68.5 (C-5), 64.1 (C-6), 61.8 (C-2).

1-(2-Methoxyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (35). This substance was obtained from **26** in 60% yield, m.p. 228-230 °C, $[\alpha]_D$+ 95.5° (*c* 1.0, DMF); ν_{max} 3500-3000 (OH, NH), 2920, 2860, 2820, 1240 (OCH_3), 1675 (C=O), 1460 (NH), 1590, 1505, 750 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 7.31-6.89 (m, 4H, Ar), 7.19 (s, 1H, NH), 5.76 (d, $J_{1,2}$ = 6.2 Hz, 1H, H-1), 5.20 (d, $J_{3,OH}$ = 5.0 Hz, 1H, C3-OH), 4.76 (d, $J_{5,OH}$ = 5.1 Hz, 1H, C5-OH), 4.48 (t, $J_{6,OH}$ = $J_{6',OH}$ = 5.5 Hz, 1H, C6-OH), 4.03-3.97 (m, 2H, H-2, H-3), 3.75 (m, 5H, H-4, H-5, OCH_3), 3.51 (m, 1H, H-6), 3.33 (m, 1H, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 158.3 (C=O), 155.6, 130.5, 128.4, 125.7, 120.3, 112.1 (aromatic), 89.9 (C-1), 78.9 (C-4), 74.8 (C-3), 68.7 (C-5), 64.2 (C-6), 61.5 (C-2), 55.6 (OCH_3). Anal. Calcd for $C_{14}H_{18}N_2O_6$: C, 54.19 H, 5.85; N, 9.03. Found: C, ; H, ; N, .

1-(2-Tolyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (36). This compound was obtained from **27** in 66% yield, m.p. 232-234 °C, $[\alpha]_D$ +78.5° (*c* 1.0, DMF); ν_{max} 3600-3100 (OH, NH), 1670 (C=O), 1470 (NH), 1600, 1500, 760 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 7.21 (m, 5H, Ar, NH), 5.76 (d, $J_{1,2}$ = 6.2 Hz, 1H, H-1), 5.22 (d, $J_{3,OH}$ = 4.7 Hz, 1H, C3-OH), 4.75 (d, $J_{5,OH}$ = 3.8 Hz, 1H, C5-OH), 4.50 (m, 1H, C6-OH), 4.04 (m, 2H, H-2, H-3), 3.84 (dd, $J_{3,4}$ = 2.0 Hz, $J_{4,5}$ = 8.6 Hz, 1H, H-4), 3.75 (m, 1H, H-5), 3.57 (m, 1H, H-6), 3.38 (m, 1H, H-6'), 2.17 (s, 3H, CH_3); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 158.0 (C=O), 137.3, 136.6, 130.5, 128.8, 127.5, 126.5 (aromáticos), 91.3 (C-1), 79.0 (C-4), 74.5 (C-3), 68.5 (C-5), 64.0 (C-6), 61.7 (C-2). Anal. Calcd for $C_{14}H_{18}N_2O_5.\sqrt{}$ H_2O: C, 55.44; H, 6.31; N, 9.24. Found: C, 55.12; H, 6.11; N, 9.09.

1-(2-Nitrophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (37). This compound was obtained from **28** in 69% yield, m.p. 235-237 °C, $[\alpha]_D$ +61° (*c* 1.0, DMF); ν_{max} 3500-3000 (OH, NH), 1690 (C=O), 1530, 1360 (NO_2), 1450 (NH), 1600, 1490, 790, 780, 710 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 7.96-7.43 (m, 5H, Ar, NH), 6.08 (d, $J_{1,2}$ = 6.2 Hz, 1H, H-1), 5.36 (d, $J_{3,OH}$ = 4.8 Hz, 1H, C3-OH), 4.84 (d, $J_{5,OH}$ = 5.4 Hz, 1H, C5-OH), 4.58 (t, $J_{6,OH}$ =$J_{6',OH}$ = 5.5 Hz, 1H, C6-OH), 4.11 (m, 2H, H-2, H-3), 3.91 (dd, $J_{3,4}$ = 1.7 Hz, $J_{4,5}$ = 8.5 Hz, 1H, H-4), 3.84 (m, 1H, H-5), 3.65 (m, 1H, H-6), 3.47 (m, 1H, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 156.8 (C=O), 145.5, 134.0, 131.1, 127.4, 126.9, 125.1 (aromatic), 90.3 (C-1), 79.6 (C-4), 74.3 (C-3), 68.6 (C-5), 64.2 (C-6), 62.0 (C-2). Anal. Calcd for $C_{13}H_{15}N_3O_7$: C, 48.00; H, 4.65; N, 12.92. Found: C, 47.85; H, 4.64; N, 12.75.

1-Naphthyl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (38). A suspension of **29** (1.7 g, 5.0 mmol) in 30% aqueous acetic acid (35.0 mL) and ethanol (8.0 mL) was heated at ~100 °C for 30 min. The insoluble *N*,*N'*-bis(1-naphthyl)urea (0.163 g) was filtered and the title compound (0.96 g, 60%) crystallized from the filtrate on cooling, m.p. 264-266 °C (96% aq. EtOH), $[\alpha]_D$ +85° (c, 0.5 C_5H_5N); ν_{max} 3500-3100 (OH, NH), 1660 (C=O), 1590, 1500, 770 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 7.99-7.41 (m, 8H, Ar, NH), 5.82 (d, $J_{1,2}$ = 6.1 Hz, 1H, H-1), 5.26 (d, $J_{3,OH}$ = 4.8 Hz, 1H, C3-OH), 4.79 (d, $J_{5,OH}$ = 5.8 Hz, 1H, C5-OH), 4.52 (t, $J_{6,OH}$ = $J_{6',OH}$ = 5.3 Hz, 1H, C6-OH), 4.20 (d, $J_{1,2}$ = 6.4 Hz, 1H, H-2), 4.13 (m, 1H, H-3), 4.00 (dd, $J_{3,4}$ = 1.8 Hz, $J_{4,5}$ = 8.7 Hz, 1H, H-4), 3.76 (m, 1H, H-5), 3.55 (m, 1H, H-6), 3.42 (m, 1H, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 158.7 (C=O), 134.4, 133.9, 131.3, 128.0, 127.8, 126.8 (2C), 126.3, 125.8, 123.7 (aromatic), 91.5 (C-1), 79.1 (C-4), 74.5 (C-3), 68.4 (C-5),

64.0 (C-6), 61.8 (C-2). Anal. Calcd for $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.47; H, 5.62; N, 8.63.

General procedure for the preparation of 1-aryl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one. To a solution of the corresponding 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (3.0 mmoles) in pyridine (10.0 mL), cooled at −15 °C, 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 obtained by crystallization from 96% aqueous EtOH.

1-(2-Chlorophenyl)-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (39). This compound was obtained from **34** in 71% yield, m.p. 204-206 °C, $[\alpha]_D$ +95° (*c* 1.0, $CHCl_3$); ν_{max} 3420 (NH), 1750, 1730 (C=O, ester), 1225 (C-O-C, ester), 1585, 1485, 770, 735, 710 (aromatic), 1065, 1030 (C-O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.51-7.28 (m, 4H, Ar), 6.86 (d, $J_{2,NH}$ = 1.7 Hz, 1H, N-H), 5.95 (d, $J_{1,2}$ = 6.3 Hz, 1H, H-1), 5.33 (d, $J_{3,4}$ = 2.7 Hz, 1H, H-3), 5.21 (m, 1H, H-5), 4.54 (m, 2H, H-4, H-6), 4.26 (dd, $J_{2,NH}$ = 1.9 Hz, $J_{1,2}$ = 6.3 Hz, 1H, H-2), 4.08 (dd, $J_{5,6'}$ = 4.8 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6), 2.10 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.5 (CH_3-*C*O), 169.6 (CH_3-*C*O), 169.5 (CH_3-*C*O), 158.5 (C=O), 133.4, 133.3, 130.9, 130.3, 129.6, 127.6 (aromatic), 91.0 (C-1), 75.6 (C-3), 75.4 (C-4), 67.2 (C-5), 63.0 (C-6), 60.4 (C-2), 20.7 (2C, *C*H_3-CO), 20.5 (*C*H_3-CO). Anal. Calcd for $C_{19}H_{21}N_2O_8Cl$: C, 51.77; H, 4.80; N, 6.35. Found: C, 51.63; H, 4.87; N, 6.22.

1-(2-Methoxyphenyl)-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (40). This compound was obtained from **35** in 60% yield, m.p. 157-159 °C, $[\alpha]_D$ +102.5° (*c* 1.0, $CHCl_3$); ν_{max}3350 (NH), 2835 (OCH_3), 1740, 1720, 1710 (C=O, ester), 1260, 1230, 1210 (C-O-C, ester), 1590, 1500, 750 (aromatic), 1060, 1040, 1030, 1015, 1000 (C-O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33-6.96 (m, 4H, Ar), 6.85 (d, $J_{2,NH}$ = 1.9 Hz, 1H, N-H), 5.99 (d, $J_{1,2}$ = 6.4 Hz, 1H, H-1), 5.30 (d, $J_{3,4}$ = 2.7 Hz, 1H, H-3), 5.20 (m, 1H, H-5), 4.50 (dd, $J_{5,6}$ = 2.3 Hz, $J_{6,6'}$ = 12.3 Hz, 1H, H-6), 4.44 (dd, $J_{3,4}$ = 2.7 Hz, $J_{4,5}$ = 9.4 Hz, 1H, H-4), 4.19 (dd, $J_{2,NH}$ = 2.1 Hz, $J_{1,2}$ = 6.4 Hz, 1H, H-2), 4.05 (dd, $J_{5,6'}$ = 5.2 Hz, $J_{6,6'}$ = 12.3 Hz, 1H, H-6'), 3.85 (s, 3H, OCH_3), 2.07 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.4 (CH_3-*C*O), 169.6 (CH_3-*C*O), 169.5 (CH_3-*C*O), 159.3 (C=O), 155.3, 130.2, 129.2, 124.1, 120.7, 111.7 (aromatic), 90.7 (C-1), 75.7 (C-3), 75.3 (C-4), 67.2 (C-5), 63.2 (C-6), 60.2 (C-2), 55.4 (OCH_3), 20.6 (*C*H_3-CO), 20.5 (2C, *C*H_3-CO). Anal. Calcd for $C_{20}H_{24}N_2O_9$: C, 55.04; H, 5.54; N, 6.42. Found: C, 54.93; H, 5.59; N, 6.43.

1-(2-Tolyl)-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (41). The title compound was prepared from **36** in 77% yield, m.p. 165-167 °C, $[\alpha]_D$ +97.5° (*c* 1.0, $CHCl_3$); ν_{max} 3390 (NH), 2820 (CH_3), 1740, 1720, (C=O, ester), 1235, 1215, (C-O-C, ester), 1595, 1490, 750, 740 (aromatic), 1060, 1025 (C-O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29-7.14 (m, 4H, Ar), 6.96 (s, 1H, NH), 5.83 (d, $J_{1,2}$ = 6.3 Hz, 1H, H-1), 5.32 (d, $J_{3,4}$ = 2.5 Hz, 1H, H-3), 5.19 (m, 1H, H-5), 4.58 (dd, $J_{5,6}$ = 1.7 Hz, $J_{6,6'}$ = 12.3 Hz, 1H, H-6), 4.53 (dd, $J_{3,4}$ = 2.5 Hz, $J_{4,5}$ = 9.4 Hz, 1H, H-4), 4.19 (d, $J_{1,2}$ = 6.3 Hz, 1H,

H-2), 4.08 (dd, $J_{5,6'}$ = 4.4 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6'), 2.29 (s, 3H, CH_3), 2.10 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.02 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.4 (CH_3-*C*O), 169.5 (CH_3-*C*O), 169.4 (CH_3-*C*O), 158.9 (C=O), 137.0, 134.7, 130.9, 128.5, 128.3, 126.7 (aromatic), 91.9 (C-1), 75.3 (2C, C-3, C-4), 67.2 (C-5), 62.8 (C-6), 60.3 (C-2), 20.6 (2C, *C*H_3-CO), 20.5 (*C*H_3-CO), 17.8 (CH_3). Anal. Calcd for $C_{20}H_{24}N_2O_8$: C, 57.14; H, 5.75; N, 6.66. Found: C, 57.01; H, 5.77; N, 6.67.

1-(2-Nitrophenyl)-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (42). This compound was obtained from **37** in 91% yield, m.p. 178-179 °C, $[\alpha]_D$ +47.5° (*c* 0.5, $CHCl_3$); ν_{max}3420 (NH), 1740, 1700, (C=O, ester), 1230 (C-O-C, ester), 1520, 1370 (NO_2),1600, 1580, 1490, 745 (aromatic), 1060, 1045, 1020 (C-O) cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.98-7.47 (m, 4H, Ar), 6.65 (bs, 1H, N-H), 6.02 (d, $J_{1,2}$ = 6.3 Hz, 1H, H-1), 5.34 (d, $J_{3,4}$ = 2.8 Hz, 1H, H-3), 5.27 (m, 1H, H-5), 4.56 (dd, $J_{3,4}$ = 2.8 Hz, $J_{4,5}$ = 9.4 Hz, 1H, H-4), 4.53 (dd, $J_{5,6}$ = 2.5 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6), 4.34 (dd, $J_{2,NH}$ = 1.8 Hz, $J_{1,2}$ = 6.3 Hz, 1H, H-2), 4.18 (dd, $J_{5,6'}$ = 5.0 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6'), 2.07 (s, 6H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.8 (CH_3-*C*O), 169.8 (CH_3-*C*O), 169.7 (CH_3-*C*O), 157.8 (C=O), 146.3, 133.8, 130.4, 129.0, 128.0, 125.5 (aromatic), 91.5 (C-1), 76.2 (C-3), 75.4 (C-4), 67.5 (C-5), 63.2 (C-6), 60.7 (C-2), 20.7 (3C,*C*H_3-CO). Anal. Calcd for $C_{19}H_{21}N_3O_{10}$: C, 50.56; H, 4.69; N, 9.31. Found: C, 50.50; H, 4.78; N, 9.25.

1-Naphthyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (43). A solution of **38** (0.16 g, 0.5 mmol) in pyridine (3.0 mL) and acetic anhydride (1.5 mL) was kept at room temperature for 12 h. Then it was poured into ice-water affording **43** as a white solid, which was filtered and washed with cold water (0.2 g, 90%). An analytical sample was recrystallized from 96% aqueous EtOH and had m.p. 192-193 °C, $[\alpha]_D$+115° (*c* 0.5, $CHCl_3$); ν_{max} 3380 (NH), 1750, 1740, 1260, 1250, 1230, 1220 (C=O ester), 1720 (C=O), 1600, 1500, 790, 780, 760, 750 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.93-7.39 (m, 7H, Ar), 6.75 (d, $J_{2,NH}$ = 1.8 Hz, 1H, NH), 5.89 (d, $J_{1,2}$ = 6.3 Hz, 1H, H-1), 5.37 (d, $J_{3,4}$ = 2.8 Hz, 1H, H-3), 5.20 (m, 1H, H-5), 4.64 (dd, $J_{3,4}$ = 2.7 Hz, $J_{4,5}$ = 9.8 Hz, 1H, H-4), 4.59 (dd, $J_{5,6}$ = 2.3 Hz, $J_{6,6'}$ = 12.7 Hz, 1H, H-6), 4.29 (dd, $J_{2,NH}$ = 2.0 Hz, $J_{1,2}$ = 6.3 Hz, 1H, H-2), 4.09 (dd, $J_{5,6'}$ = 4.5 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6'), 2.14 (s, 3H, OAc), 2.04 (s, 6H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 170.6 (CH_3-*C*O), 169.7 (CH_3-*C*O), 169.6 (CH_3-*C*O), 159.6 (C=O), 134.6, 132.4, 130.9, 129.1, 128.6, 127.0, 126.8, 126.4, 125.5, 122.5 (aromatic), 92.0 (C-1), 75.7 (C-3), 75.6 (C-4), 67.4 (C-5), 63.0 (C-6), 60.6 (C-2), 20.8 (2C, *C*H_3-CO), 20.6 (*C*H_3-CO); HRMS: Calcd for M^+($C_{23}H_{24}N_2O_8$): 456.1532. Found: 456.1521. Anal. Calcd for $C_{23}H_{24}N_2O_8$: C, 60.52; H, 5.30; N, 6.14. Found: C, 60.49; H, 5.32; N, 5.98.

1-Acetyl-3-(1-naphthyl)-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-one (44). Compound **38** (0.24 g, 0.75 mmol) was treated with acetic anhydride (3.0 mL) and freshly melted zinc(II) chloride (0.1 g). After 12 h at room temperature, the mixture was poured into ice-water to afford **44**, that was filtered and washed with cold water (0.4 g, 99%). An analytical sample was recrystallized from 96% aqueous EtOH and had m.p. 230-232 °C, $[\alpha]_D$ +51.4° (*c* 1.0, $CHCl_3$); ν_{max} 1745, 1260, 1250, 1230, 1210 (C=O ester), 1685 (C=O), 1590, 780, 760 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.96-7.38 (m, 7H, Ar), 5.95 (d, $J_{1,2}$ = 6.5 Hz, 1H, H-1), 5.83 (d, $J_{3,4}$ = 2.9 Hz, 1H, H-3), 5.19

(m, 1H, H-5), 4.84 (d, $J_{1,2}$ = 6.5 Hz, 1H, H-2), 4.56 (dd, $J_{5,6}$ = 2.2 Hz, $J_{6,6'}$ = 12.3 Hz, 1H, H-6), 4.49 (dd, $J_{3,4}$ = 2.8 Hz, $J_{4,5}$ = 9.6 Hz, 1H, H-4), 4.06 (dd, $J_{5,6'}$ = 4.0 Hz, $J_{6,6'}$ = 12.3 Hz, 1H, H-6'), 2.61 (s, 3H, NAc), 2.11 (s, 6H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (50.3 MHz, $CDCl_3$) δ 170.3 (2C, CH_3-*C*O), 169.7 (CH_3-*C*O), 168.5 (N-*C*O), 152.9 (C=O), 134.4, 131.1, 130.1, 129.7, 128.7, 127.1, 126.5, 125.4, 121.7 (aromatic), 87.8 (C-1), 75.6 (C-4), 73.4 (C-3), 66.8 (C-5), 62.8 (C-6), 62.3 (C-2), 23.9 (*C*H_3-CO-N), 20.7 (2C, *C*H_3-CO), 20.6 (*C*H_3-CO). Anal. Calcd for $C_{25}H_{26}N_2O_9$: C, 60.24; H, 5.26; N, 5.62. Found: C, 60.40; H, 5.40; N, 5.65.

General procedure for the preparation of 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thiones. Procedure A: To a solution of 2-amino-2-deoxy-α-D-glucopyranose hydrochloride (10.8 g., 50.0 mmol) in water (60.0 mL) was added sodium hydrogencarbonate (4. 62 g., 55.0 mmoles) and then aryl isothiocyanate (50.0 mmol) under stirring, and the reaction mixture was diluted with ethanol (100 mL). The reaction mixture was heated at ~60 °C (external bath) for 30 min and then it was treated with acetic acid (20.0 mL) and heating at ~70 °C was continued for 80 min. The solution was partially evaporated and 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione crystallized on cooling. Solid was filtered and washed with cold water, ethanol, and diethyl ether. A second crop could be obtained by concentration of the mother liquors.

Procedure B: As described above in procedure A, but using less acetic acid (13 mL) and a shorter heating time (20 min).

Procedure C: A suspension of 1-aryl-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidine-2-thione (10.0 mmol) in 30% aqueous acetic acid (100 mL) was heated at ~100 °C (external bath) for 30 min.

1-(2-Fluorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (45). Procedure A: Compound **45** was obtained in 69% yield from 2-fluorophenyl isothiocyanate, m.p. 210-212 °C, $[\alpha]_D$ +106.5° (*c* 1.0 DMF); ν_{max} 3480-2980 (OH, NH), 1460 (NH), 1590, 1490, 750, 720 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 9.27 (s, 1H, NH), 7.43-7.20 (m, 4H, Ar), 5.94 (d, $J_{1,2}$ = 6.4 Hz, 1H, H-1), 5.42 (d, $J_{3,OH}$ = 5.0 Hz, 1H, C3-OH), 4.84 (d, $J_{5,OH}$ = 5.3 Hz, 1H, C5-OH), 4.57 (t, $J_{6,OH}$ = $J_{6',OH}$ = 5.3 Hz, 1H, C6-OH), 4.26 (d, $J_{1,2}$ = 6.4 Hz, 1H, H-2), 4.14 (d, $J_{3,4}$ = 4.8 Hz, 1H, H-3), 3.72-3.37 (m, 4H, H-4, H-5, H-6, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 181.9 (C=S), 158.7, 131.6, 130.1, 125.9, 124.7, 116.2 (aromatic), 94.1 (d, $J_{C1,F}$ = 19.8 Hz, C-1), 79.6 (d, $J_{C4,F}$ = 7.8 Hz, C-4), 74.1 (d, $J_{C3,F}$ = 12.2 Hz, C-3), 68.3 (C-5), 65.9 (d, $J_{C2,F}$ = 249.5 Hz, C-2), 64.0 (C-6). Anal. Calcd for $C_{13}H_{15}N_2O_4SF$: C, 49.67; H, 4.81; N, 8.91; S, 10.20. Found: C, 49.64; H, 4.82; N, 8.82; S, 10.17.

Procedure C: Compound **45** was obtained in 93% yield from **4**.[2] The resulting hot solution was filtered and evaporated until the appearance of crystals, which were filtered and washed with cold EtOH.

1-(2-Chlorophenyl)-(1,2-dideoxy-α-D-glucofurano)-[2,1-*d*]imidazolidine-2-thione (46). Procedure A: Compound **46** was obtained in 67% yield from 2-chlorophenyl isothiocyanate, m.p. 216-218 °C (96% aq. EtOH), $[\alpha]_D$ +117° (*c* 1.0, DMF) [lit.[31] m.p. 215-216 °C (H_2O), $[\alpha]_D$ +119.7° (*c* 1.0 DMF)], ν_{max} 3400-3000 (OH, NH), 1475 (NH), 1500, 760, 720 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 9.24 (s, 1H, NH), 7.55-7.39 (m, 4H, Ar), 5.91 (sa, 1H, H-1), 5.40 (d, $J_{3,OH}$ = 4.4 Hz, 1H, C3-OH), 4.83 (d,

$J_{5,OH}$ = 4.0 Hz, 1H, C5-OH), 4.57 (sa, 1H, C6-OH), 4.28 (d, $J_{1,2}$ = 6.1 Hz, 1H, H-2), 4.16 (d, $J_{3,4}$ = 4.2 Hz, 1H, H-3), 3.79 (m, 2H, H-4, H-5), 3.56 (m, 1H, H-6), 3.44 (m, 1H, H-6'); ^{13}C-RMN (50.3 MHz, DMSO-d_6) δ 181.7 (C=S), 135.5, 133.3, 129.9 (2C), 129.8, 127.9 (aromatic), 93.1 (C-1), 79.5 (C-4), 74.2 (C-3), 68.3 (C-5), 66.1 (C-2), 64.0 (C-6).

Procedure B: Crystallization afforded **5**[2] in 41% yield. Further crystallization from the mother liquors provided **46** (21%).

Procedure C: Compound **46** was obtained in 76% yield from **5**.[2] The reaction mixture was evaporated to dryness and the resulting white solid crystallized from 96% aqueous EtOH.

1-(2-Bromophenyl)-(1,2-dideoxy-α-D-glucofurano)-[2,1-*d*]imidazolidine-2-thione (47). Procedure A: Compound **47** was obtained in 46% yield from 2-bromophenyl isothiocyanate, m.p. 210-212 °C (96% aq. EtOH), $[\alpha]_D$ +102° (*c* 1.0, DMF) [lit.[31] m.p. 215-216 °C (H_2O), $[\alpha]_D$ +119.7° (*c* 1.0 DMF)], ν_{max} 3560-3000 (OH, NH), 1480 (NH), 1070, 1030 (C-O), 1480, 1445, 760, 725, 710 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 9.24 (s, 1H, NH), 7.74-7.32 (m, 4H, Ar), 5.84 (d, $J_{1,2}$ = 5.7 Hz, 1H, H-1), 5.38 (m, 1H, C3-OH), 4.80 (sa, 1H, C5-OH), 4.58 (m, 1H, C6-OH), 4.27 (d, $J_{1,2}$ = 5.4 Hz, 1H, H-2), 4.13 (d, $J_{3,4}$ = 4.7 Hz, 1H, H-3), 3.74 (m, 2H, H-4, H-5), 3.56 (m, 1H, H-6), 3.42 (m, 1H, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 181.7 (C=S), 136.7, 133.6, 132.8, 130.2, 128.3, 123.4 (aromatic), 92.8 (C-1), 79.1 (C-4), 74.0 (C-3), 67.9 (C-5), 66.0 (C-2), 63.7 (C-6). Anal. Calcd for $C_{13}H_{15}N_2O_4BrS$: C, 41.61; H, 4.03; N, 7.47; S, 8.54. Found: C, 41.75; H, 4.04; N, 7.39; S, 8.31.

Procedure B: Crystallization afforded **6**[2] in 39% yield. Further crystallization from the mother liquors provided **47** (7%).

Procedure C: Compound **47** was obtained in 74% yield from **6**.[2] The reaction mixture was evaporated to dryness to give a white solid that was crystallized from 96% aqueous EtOH.

1-(2-Methoxyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (48). Procedure B: Crystallization afforded **48** in 45% yield from 2-methoxyphenyl isothiocyanate, m.p. 210-213 °C (EtOH), $[\alpha]_D$ +137° (*c* 1.0, DMF), ν_{max} 3500-3000 (OH, NH), 2930, 2860, 1240 (OCH_3), 1460 (NH), 1590, 1500, 780, 735 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz, DMSO-d_6) δ 9.02 (s, 1H, NH), 7.37-6.92 (m, 4H, Ar), 5.87 (d, $J_{1,2}$ = 6.5 Hz, 1H, H-1), 5.33 (d, $J_{3,OH}$ = 5.1 Hz, 1H, C3-OH), 4.79 (d, $J_{5,OH}$ = 5.2 Hz, 1H, C5-OH), 4.50 (t, $J_{6,OH}$ = $J_{6'-OH}$ = 5.5 Hz, 1H, C6-OH), 4.19 (d, $J_{1,2}$ = 6.6 Hz, 1H, H-2), 4.10 (bd, $J_{3,OH}$ = 4.7 Hz, 1H, H-3), 3.76 (s, 3H, OCH_3), 3.69 (m, 2H, H-4, H-5), 3.51 (m, 1H, H-6), 3.35 (m, 1H, H-6'); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 182.1 (C=S), 155.7, 131.6, 129.3, 126.3, 120.2, 112.2 (aromatic), 93.4 (C-1), 79.3 (C-4), 74.3 (C-3), 68.3 (C-5), 65.5 (C-2), 64.0 (C-6), 55.7 (OCH_3). Anal. Calcd for $C_{14}H_{18}N_2O_5S$: C, 51.52; H, 5.56; N, 8.58; S, 9.82. Found: C, 51.66; H, 5.60; N, 8.54; S, 9.70.

Procedure C: Compound **48** was obtained in 78% yield from **7**.[2] The reaction mixture was evaporated to dryness to give a white solid that was crystallized from 96% aqueous EtOH.

1-(2-Tolyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (49). Procedure B: Crystallization afforded **49** in 43% yield from 2-tolyl isothiocyanate, m.p. 208-210 °C (EtOH), $[\alpha]_D$ +105° (*c* 1.0, DMF), ν_{max} 3500-3000 (OH, NH), 1460 (NH), 1490, 720 cm^{-1} (aromatic); ^{1}H-NMR (200 MHz,

DMSO-d_6) δ 9.05 (s, 1H, NH), 7.26 (m, 4H, Ar), 5.89 (bs, 1H, H-1), 5.37 (d, $J_{3,OH}$ = 4.9 Hz, 1H, C3-OH), 4.80 (m, 1H, C5-OH), 4.55 (bs, 1H, C6-OH), 4.24 (d, $J_{1,2}$ = 6.6 Hz, 1H, H-2), 4.14 (d, $J_{3,4}$ = 4.6 Hz, 1H, H-3), 3.75 (m, 2H, H-4, H-5), 3.57 (m, 1H, H-6), 3.44 (m, 1H, H-6'), 2.22 (s, 3H, CH_3); ^{13}C-NMR (50.3 MHz, DMSO-d_6) δ 181.4 (C=S), 137.1, 130.5 (2C), 128.2 (2C), 126.5 (aromatic), 93.4 (C-1), 79.7 (C-4), 74.1 (C-3), 68.2 (C-5), 65.8 (C-2), 63.8 (C-6). Anal. Calcd for $C_{14}H_{18}N_2O_4S$: C, 54.18; H, 5.85; N, 9.03; S, 10.33. Found: C, 54.12; H, 6.08; N, 9.03; S, 10.29.

General procedure for the preparation of per-*O*-acetylated (1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thiones. To a solution of the corresponding imidazolidine-2-thione derivative (3.0 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 obtained by crystallization from 96% aqueous EtOH.

3,5,6-Tri-*O*-acetyl-1-(2-fluorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (50). The title compound was obtained from **45** in 91% yield, m.p. 100-102 °C, $[\alpha]_D$ +116° (*c* 0.5, $CHCl_3$), ν_{max} 3300 (NH), 1740, 1710 (C=O, ester), 1230 (C-O-C, ester), 1035 (C-O), 1500, 1450, 755, 725 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H NH),7.44-7.18 (m, 4H, Ar), 6.04 (d, $J_{1,2}$ = 6.5 Hz, 1H, H-1), 5.32 (d,$J_{3,4}$ = 2.9 Hz, 1H, H-3), 5.27 (m, 1H, H-5), 4.50 (dd, $J_{5,6}$ = 2.2 Hz, $J_{6,6'}$ = 12.5 Hz, 1H, H-6), 4.46 (dd, $J_{3,4}$ = 2.9 Hz, $J_{4,5}$ = 9.4 Hz, 1H, H-4), 4.42 (dd, $J_{1,2}$ = 6.5 Hz, $J_{2,NH}$ = 1.0 Hz, 1H, H-2), 4.09 (dd, $J_{5,6'}$ = 4.8 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6'), 2.11 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 183.5 (C=S), 170.7 (CH_3-*C*O), 169.9 (CH_3-*C*O), 169.7 (CH_3-*C*O), 158.9 (d, *J* = 250.9 Hz), 130.9, 130.7 (d, *J* = 8.2 Hz), 124.8 (2C), 116.8 (d, *J* = 19.2 Hz) (aromatic), 95.0 (C-1), 76.1 (C-3), 75.5 (C-4), 67.3 (C-5), 64.3 (C-2), 63.0 (C-6), 20.9 (*C*H_3-CO), 20.8 (*C*H_3-CO), 20.7 (*C*H_3-CO). Anal. Calcd for $C_{19}H_{21}N_2O_7FS$: C, 51.81; H, 4.81; N, 6.36; S, 7.28. Found: C, 51.71; H, 4.83; N, 6.38; S, 7.09.

3,5,6-Tri-*O*-acetyl-1-(2-chlorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (51). The title compound was obtained from **46** in 67% yield, m.p. 94-96 °C, $[\alpha]_D$ +123.0° (*c* 0.5, $CHCl_3$), ν_{max} 3350 (NH), 1750 (C=O, ester), 1230 (C-O-C, ester), 1035 (C-O), 1590, 1490, 760, 720 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54-7.26 (m, 4H, Ar), 7.03 (s, 1H, NH), 6.09 (d, $J_{1,2}$ = 6.5 Hz, 1H, H-1), 5.32 (d, $J_{3,4}$ = 2.9 Hz, 1H, H-3), 5.27 (m, 1H, H-5), 4.58 (dd, $J_{5,6}$ = 2.3 Hz, $J_{6,6'}$ = 12.4 Hz, 1H, H-6), 4.45 (m, 2H, H-2, H-4), 4.07 (m, 1H, H-6'), 2.11 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 183.4 (C=S), 170.6 (CH_3-*C*O), 170.0 (CH_3-*C*O), 169.7 (CH_3-*C*O), 134.6, 132.5, 130.5, 130.4 (2C), 127.8 (aromatic), 94.1 (C-1), 76.2 (C-3), 75.5 (C-4), 67.4 (C-5), 64.2 (C-2), 63.0 (C-6), 20.8 (2C, *C*H_3-CO), 20.7 (*C*H_3-CO). Anal. Calcd for $C_{19}H_{21}N_2O_7ClS$: C, 49.95; H, 4.63; N, 6.13; S, 7.02. Found: C, 49.82; H, 4.61; N, 6.10; S, 6.98.

3,5,6-Tri-*O*-acetyl-1-(2-bromophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (52). This substance was obtained from **47** in 69% yield, m.p. 98-100 °C, $[\alpha]_D$ +113.5° (*c* 0.5, $CHCl_3$), ν_{max}3340 (NH), 1745 (C=O, ester), 1230 (C-O-C, ester), 1030 (C-O), 1580, 1480,

760, 715 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72-7.25 (m, 4H, Ar), 7.14 (s, 1H, NH), 6.10 (d, $J_{1,2}$ = 6.3 Hz, 1H, H-1), 5.33 (d, $J_{3,4}$ = 2.8 Hz, 1H, H-3), 5.28 (m, 1H, H-5), 4.59 (d, $J_{6,6'}$ = 12.3 Hz, 1H, H-6), 4.48-4.43 (m, 2H, H-2, H-4), 4.09 (dd, $J_{5,6'}$ = 3.9 Hz, $J_{6,6'}$ = 12.2 Hz, 1H, H-6'), 2.14 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.04 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 183.5 (C=S), 170.5 (CH_3-*C*O), 169.9 (CH_3-*C*O), 169.6 (CH_3-*C*O), 133.6, 132.7, 130.7 (2C), 128.4, 123.4 (aromatic), 94.1 (C-1), 76.1 (C-3), 75.4 (C-4), 67.3 (C-5), 64.3 (C-2), 63.0 (C-6), 20.8 (*C*H_3-CO), 20.7 (*C*H_3-CO), 20.6 (*C*H_3-CO). Anal. Calcd for $C_{19}H_{21}N_2O_7BrS$: C, 45.52; H, 4.22; N, 5.59; S, 6.39. Found: C, 45.49; H, 4.12; N, 5.58; S, 6.22.

3,5,6-Tri-*O*-acetyl-1-(2-methoxyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (53). This substance was obtained from **48** in 99% yield, m.p. 140-142 °C, $[\alpha]_D$ +132° (*c* 1.0, $CHCl_3$), ν_{max} 3570, 3470, 1625 (H_2O),[23] 3300 (NH), 2840 (OCH_3), 1740, 1715 (C=O, ester), 1240 (C-O-C, ester), 1070, 1040, 1020 (C-O), 1595, 1505, 1465, 760, 740, 690 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H NH), 7.40-7.00 (m, 4H, Ar), 6.10 (d, $J_{1,2}$ = 6.6 Hz, 1H, H-1), 5.30 (d $J_{3,4}$ = 2.3 Hz, 1H, H-3), 5.26 (m, 1H, H-5), 4.52 (d, $J_{6,6'}$ = 11.3 Hz, 1H, H-6), 4.41-4.36 (m, 2H, H-2, H-4), 4.03 (dd, $J_{5,6'}$ = 5.2 Hz, $J_{6,6'}$ = 12.2 Hz, 1H, H-6'), 3.85 (s, 3H, OCH_3), 2.09 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 183.4 (C=S), 170.4 (CH_3-*C*O), 169.7 (CH_3-*C*O), 169.5 (CH_3-*C*O), 155.3, 131.0, 130.0, 125.1, 120.5, 111.9 (aromatic), 94.1 (C-1), 75.8 (C-3), 75.3 (C-4), 67.1 (C-5), 63.8 (C-2), 63.0 (C-6), 55.6 (OCH_3), 20.6 (*C*H_3-CO), 20.5 (2C, *C*H_3-CO). Anal. Calcd for $C_{20}H_{24}N_2O_8S.\sqrt{}H_2O$: C, 52.01; H, 5.42; N, 6.07. Found: C, 51.67; H, 5.28; N, 6.01.

3,5,6-Tri-*O*-acetyl-1-(2-tolyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-thione (54). This compound was obtained from **49** in 95% yield, m.p. 102-104 °C, $[\alpha]_D$ +122.5° (*c* 1.0, $CHCl_3$), ν_{max} 3530, 3450, 1610 (H_2O)[23], 3200 (NH), 1740, 1710 (C=O, ester), 1230 (C-O-C, ester), 1050, 1030 (C-O), 1490, 1450, 760, 750, 710 cm^{-1} (aromatic); ^{1}H-NMR (400 MHz, $CDCl_3$, 273 K: two rotamers) δ 7.58 (s, 1H NH), 7.57 (s, 1H NH), 7.35-7.10 (m, 8H, Ar), 6.06 (d, $J_{1,2}$ = 6.6 Hz, 1H, H-1), 5.99 (d, $J_{1,2}$ = 6.4 Hz, 1H, H-1), 5.36 (bs, 1H, H-3), 5.33 (bs, 1H, H-3), 5.26 (m, 1H, H-5), 5.21 (m, 1H, H-5), 4.61 (dd, $J_{5,6}$ = 4.4, $J_{6,6'}$ = 12.2 Hz, 2H, H-6), 4.56-4.42 (m, 4H, H-2, H-4), 4.10 (dd, $J_{5,6'}$ = 3.8, $J_{6,6'}$ = 12.4 Hz, 1H, H-6'), 3.99 (dd, $J_{5,6'}$ = 3.6, $J_{6,6'}$ = 12.5 Hz, 1H, H-6'), 2.32 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.12 (s, 3H, OAc), 2.08 (s, 6H, 2 OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.99 (s, 3H, OAc); ^{13}C-NMR (100 MHz, $CDCl_3$, 273K) δ 182.9 (C=S), 182.8 (C=S), 170.7 (CH_3-*C*O), 169.8 (CH_3-*C*O), 169.7 (CH_3-*C*O), 138.3, 136.7, 136.5, 135.3, 131.2, 131.1, 130.3, 129.3, 129.2, 127.6, 127.4, 126.8 (aromatic), 97.1 (C-1), 94.0 (C-1), 76.0 (C-3), 75.6 (C-3), 75.3 (C-4), 74.9 (C-4), 67.2 (C-5), 67.0 (C-5), 64.1 (C-2), 64.0 (C-2), 62.9 (C-6), 62.6 (C-6), 20.8 (6C, *C*H_3CO), 18.3 (CH_3), 17.8 (CH_3). Anal. Calcd for $C_{20}H_{24}N_2O_7S.H_2O$: C, 52.85; H, 5.77; N, 6.16. Found: C, 52.98; H, 5.72; N, 6.16.

Data for the X-Ray Structure Analysis of Compound 42.[19] The structure was determined with a Siemens P4 automatic diffractometer using MoKα graphite-monochromated radiation (λ = 0.71073 Å), and solved by direct methods and refined with the full-matrix, least-squares method. A greenish yellow, prismatic

crystal with the dimensions 0.42 x 0.25 x 0.18 mm was mounted on a glass capillary: $C_{19}H_{21}N_3O_{10}$ (451.4); crystal system: orthorhombic; space group: $P2_12_12_1$; a = 8.077(1), b = 8.322(1), c = 30.980(3) Å; Z = 4; V = 2082.4(7) Å^3; ρ(calcd) = 1.440 g cm^{-3}; T = 298 K; μ = 0.118 mm^{-1}; F(000) = 944; scan type: 2θ–θ with 2θ range from 2.0 to 60.0°; 3 standard reflections were measured every 97 reflections; of 4391 reflections collected, 4136 were independent (R_{int} = 0.0176) and 2095 observed ($F > 4.0\sigma(F)$); number of parameters refined: 289; R = 0.0472, wR = 0.0507 (for observed data); R = 0.101, wR = 0.197 (for all data); GOF = 1.30; data-to-parameter ratio = 7.2; largest and mean Δ/α = 0.001, 0.000.

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