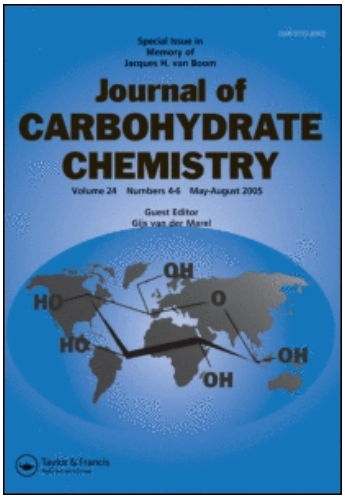

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SYNTHESIS AND MASS SPECTRA OF SUGAR THIOIMIDAZOLE DERIVATIVES

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ABSTRACT

The reaction of 1-halogenophenylglucofuranoimidazolidine-2-thiones (**1**, **2**) with benzyl chloride gives bicyclic *S*-benzylthioimidazolines (**3**, **4**) or tetrahydroxybutyl *S*-benzylthioimidazoles (**7**, **8**) depending on the presence or absence of sodium hydrogencarbonate. In the latter case a partial desulphuration takes place. The electron impact mass spectra of compounds **1-4**, **7**, **8**, and of the acetyl derivatives **5**, **6**, **9**, and **10** are examined. The primary fragmentations and two fragmentation pathways were observed, the importance of which depends on the cyclic character of the molecule and of the nature of the substituent (OH or OAc).

INTRODUCTION

The reaction of aminosugars with aryl (alkyl) isocyanates[2] and isothiocyanates[3-5] to obtain glycofuranoimidazolidine-2-thiones and several types of nucleoside imidazole derivatives has been widely studied. We have recently prepared *N*-nucleosides of chiral imidazolidines[6] through this reaction using sugar isothiocyanates instead of more simple heterocumulenes. A related reaction starting from D-fructose and potassium thiocyanate has also been described.[7]

The glycofuranoimidazolidine-2-thiones are versatile synthetic intermediates in the preparation of acyclic and cyclic *C*-nucleosides of both imidazoles and imidazoline-2-thiones[3,5] and in addition have been used in the synthesis of imidazole carboxaldehydes.[8] In several steps of these syntheses the protection of the sulphur atom is necessary to prevent undesirable oxidation reactions. At the same time polyhydroxyalkyl imidazoles are attractive synthetic targets[9,10] because of their biological activities such as glycoprocessing inhibitors[9] and therapeutic agents.[11,12] Although there are some mass spectral data on imidazole carboxaldehydes[13,14] and formyl imidazoline-2-thiones,[15] those on polyhydroxyalkylimidazoline-2-thiones[16] are very scarce, and there are none on glycofuranoimidazolidine-2-thiones and cyclic or acyclic *S*-alkylthioimidazole derivatives.

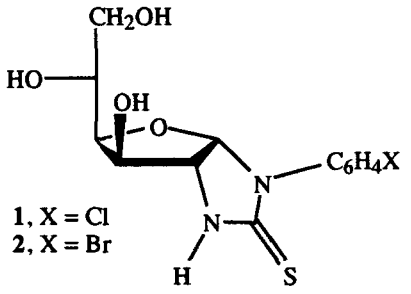
In this paper we report on the syntheses and mass spectra of the bicyclic *S*-benzylthioimidazolines **3-6**, and the acyclic *C*-nucleosides of the imidazoles **7-10**. All compounds **3-10** possess a halogen atom (Cl or Br), which facilitates the study of their fragmentation pathways in electron impact mass spectrometry. The mass spectra of the starting compounds **1** and **2** are also studied.

RESULTS AND DISCUSSION

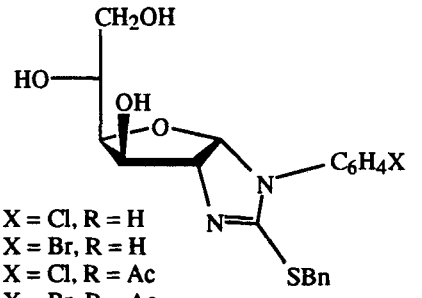
Synthesis. The *S*-benzylation[17] of the 1-halogenophenyl glucofuranoimidazoline-2-thiones[18] (**1, 2**) with benzyl chloride and an equivalent amount of sodium hydrogencarbonate gave the corresponding 2-benzylthio-1-halogenophenyl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]-2-imidazolines[19] (**3, 4**). When the same reaction was performed in the absence of sodium hydrogencarbonate, isomerization of the glycosyl moiety took place and the acyclic *C*-nucleosides of the imidazole **7, 8** were obtained. In these cases TLC showed the presence of **3** or **4** respectively prior to the occurrence of the isomerization reaction. When the compound **8** was prepared the bicyclic imidazolidine-2-one **11** was isolated as by-product indicating a partial desulphuration of **2**.

The structures of **3, 4, 7, 8,** and **11** were based on analytical and IR, ^{1}H (Tables 1, 2), and ^{13}C (Table 3) NMR and MS data (see below) and the corresponding data from the acetyl derivatives **5** , **6** , **9, 10,** and **12**. The latter were prepared by conventional acetylation of the respective polyhydroxy compound (**3, 4, 7, 8,** and **11**). Thus compounds **3-6** showed signals for the resonance of the *S*-CH_2 group at 4.27-4.34 ppm (δ H) and 35.1-36.2 ppm (δ C), δ C-2 of the imidazoline ring was 159.8-162.5 ppm instead of the value described[5] (≈182 ppm) for the C=S group of the imidazolidine-2-

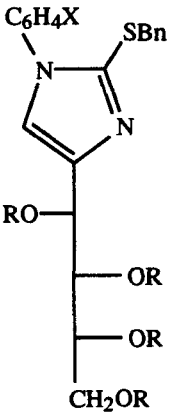
thiones, the $J_{2,3}$ value was zero as is reported[5] for related bicyclic systems with *trans* relationship between the corresponding protons, and δ H-4 (**5**, **6**) was ≈3.85 ppm confirming the furanoid structure. The specific optical rotations of **7**-**10** (see experimental) showed strong changes when they were compared with that for the corresponding compound **3**-**6**. The resonances for the *S*-CH_2 group of **3**-**6** appeared at 4.21-4.28 ppm (δ H) and 38.0-39.0 ppm (δ C), the chemical shift for H-5 of the imidazole ring was in the range 7.06-7.36 as corresponding to an aromatic structure and **9** and **10** showed the close resemblance in the chemical shifts of C-1', C-2', and C-3' (polyacetoxy chain) described for related acyclic *C*-nucleosides[5,6] Compounds **11** and **12** had negative sulphur analysis; their specific optical rotation values were close to those for glucofuranoimidazolidine-2-ones[2] and -2-thiones,[5] they showed an IR absorption at 1665-1680 cm^{-1} corresponding to the CO of the urea group[2] and no NMR signals for the benzyl group. Additionally the $J_{2,3}$ values were zero as in **3**-**6**.



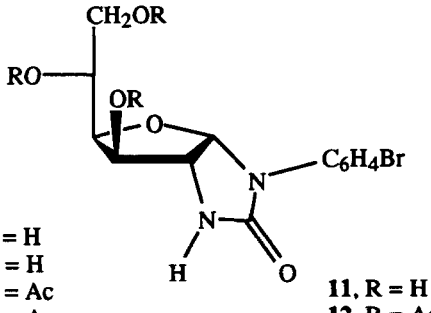
1, X = Cl
2, X = Br



3, X = Cl, R = H
4, X = Br, R = H
5, X = Cl, R = Ac
6, X = Br, R = Ac



7, X = Cl, R = H
8, X = Br, R = H
9, X = Cl, R = Ac
10, X = Br, R = Ac



11, R = H
12, R = Ac

The conformation of the tetrahydrofuran ring of **3**-**6**, **11**, and **12** has been studied by comparing the experimental J values, obtained from the ^1H NMR spectra, with sets of

Table 1. Selected ^{1}H NMR data (δ ppm, J Hz) at 500 MHz for **3-6**, **11**, and **12**.

Comp.	**3**[a]	**4**[a]	**5**[b]	**6**[a,c]	**11**[a,d]	**12**[b,d]
H-1	5.83d	5.83d	5.79d	6.04d	5.97d	5.99d
H-2	4.42d	4.42d	4.59d	4.62d	3.98d	4.20dd
H-3	4.23d	4.22d	5.55d	5.29d	4.05d	5.28d
H-4	3.44dd	3.44dd	3.89dd	3.82dd	3.67dd	4.39dd
H-5	3.73-3.70m	3.74-3.70m	5.23ddd	5.11ddd	3.71m	5.31m
H-6a	3.59-3.56m	3.57dd	4.51dd	4.36dd	3.55dd	4.55dd
H-6b	3.36dd	3.37-3.34m	4.16dd	4.07dd	3.33dd	4.16dd
CH_2(Bzl)	4.31d	4.30d	4.34d	4.32s	-	-
	4.28d	4.27d	4.30d			
$J_{1,2}$	5.8	5.8	5.7	5.8	6.2	6.2
$J_{2,3}$	0.0	0.0	0.0	0.0	0.0	3.0
$J_{3,4}$	2.4	2.4	2.7	2.7	2.0	2.9
$J_{4,5}$	8.5	8.5	9.4	9.1	8.5	9.1
$J_{5,6a}$	-	2.8	2.3	2.3	1.6	2.3
$J_{5,6b}$	6.2	-	5.5	6.3	5.3	4.8
$J_{6a,6b}$	11.2	11.2	12.3	12.3	11.2	12.3
$^2J_{CH_2}$	13.1	13.0	19.5	-	-	-

a. In Me_2SO-d_6; b. In $CDCl_3$; c. At 300 MHz; d. At 200 MHz.

Table 2. Selected ^{1}H NMR data (δ ppm, J Hz) at 500 MHz for compounds **7-10**[a]

Comp.	**7**[b]	**8**[c, d]	**9**[c]	**10**[c]
H-5	7.23s	7.36-7.16m	7.07s	7.06s
H-1'	4.80dd	4.79s	6.12d	6.11d
H-2'	3.67-3.61m	3.64-3.27m	5.79dd	5.77dd
H-3'	3.59-3.54m	3.64-3.27m	5.33td	5.32td
H-4'a	3.67-3.61m	3.64-3.27m	4.31dd	4.30dd
H-4'b	3.43dd	3.64-3.27m	4.18dd	4.17dd
CH_2(Bzl)	4.24d	4.23s	4.28d	4.27d
	4.21d		4.23d	4.22d
$J_{1',2'}$	7.0	-	5.5	5.5
$J_{2',3'}$	-	-	6.4	6.5
$J_{3',4'a}$	-	-	2.9	2.9
$J_{3',4'b}$	6.0	-	6.4	6.5
$J_{4'a,4'b}$	10.9	-	12.3	12.3
$^2J_{CH_2}$	12.7	-	12.8	12.8

a. H-5 belongs to the imidazole ring. The protons of the tetrahydroxy(acetoxy) chain are numbered as H-1', 2', etc; b. In Me_2SO-d_6; c. In $CDCl_3$; d. At 300 MHz.

calculated[20] J values for the dihedral angles shown by the protons of the conformations presented by these systems, measured using molecular models.[21] The conformations used are the maximally puckered extremes which contain at least one dihedral angle of 60°. It can thus be assumed that the most favoured conformation is close to ^3E and $^3T_4$.

Table 3. Selected ^{13}C NMR chemical shifts (ppm) for compouds **3-10**.

Comp.	**3**[a,b]	**4**[a,b]	**5**[c,d]	**6**[a,d]	**7**[a,b]	**8**[a,b]	**9**[b,c]	**10**[b,c]
C-1	96.1	96.1	96.6	96.3	-	-	-	-
C-2[e]	77.7	77.7	75.8	75.2	-	-	-	-
C-3	74.3	74.2	75.4	75.1	-	-	-	-
C-4[e]	79.8	79.8	76.3	75.9	135.8	135.8	135.1	135.6
C-5[e]	68.6	68.5	67.4	67.1	120.1	119.9	121.1	121.0
C-6	64.0	63.8	63.5	63.1	-	-	-	-
=C-S	159.8	159.7	162.5	161.2	145.5	145.4	142.2	142.1
CH_2-S	35.1	35.1	36.2	35.2	38.0	38.3	39.0	39.0
C-1'	-	-	-	-	67.1	67.3	67.5	67.5
C-2'	-	-	-	-	73.6	73.5	71.0	71.0
C-3'	-	-	-	-	71.2	71.2	69.0	69.0
C-4'	-	-	-	-	63.5	63.4	61.8	61.8

a. In Me_2SO-d_6; b. At 125.7 MHz;c. In $CDCl_3$; d. At 75.4 MHz; e. Of the imidazole ring for **7-10**.

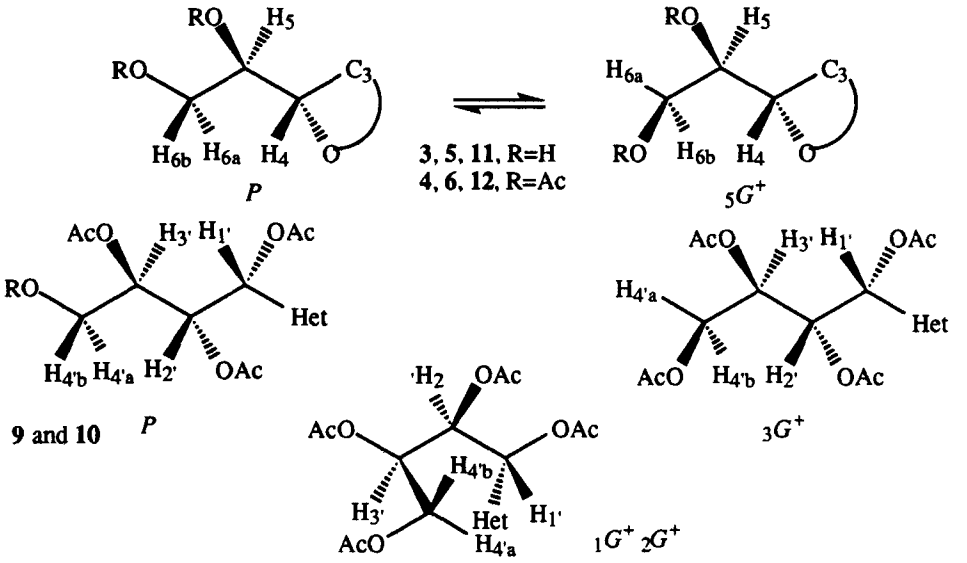
The $^3J_{H,H}$ values ($J_{4,5} \approx 9.0$, $J_{5,6a} \approx 2.3$, $J_{5,6b} \approx 6.0$ Hz) and the antecedents[6,22] on conformations of polyhydroxyalkyl and polyacetoxyalkyl chains, indicated that the exocyclic sugar backbone of **3-6**, **11**, and **12** are in a conformational equilibrium between the conformations *P* and $_5G^+$ (Scheme 1).

For compounds **9** and **10** the vicinal coupling constant observed between H-3' and H-4'a is of small magnitude (2.9 Hz), indicating gauche-disposed protons. The $^3J_{H,H}$ between H-1', H-2', H-3', and H-4'b are of intermediate value (5.5-6.5 Hz) establishing that the molecules exist in the conformational equilibrium *P*, $_3G^+$, $_1G^+$, $_2G^+$ (Scheme 1), which is different from that described for other D-*arabino*-tetraacetoxy acyclic-sugar derivatives[6,23] but with the same chain-end flexibility.[6,22]

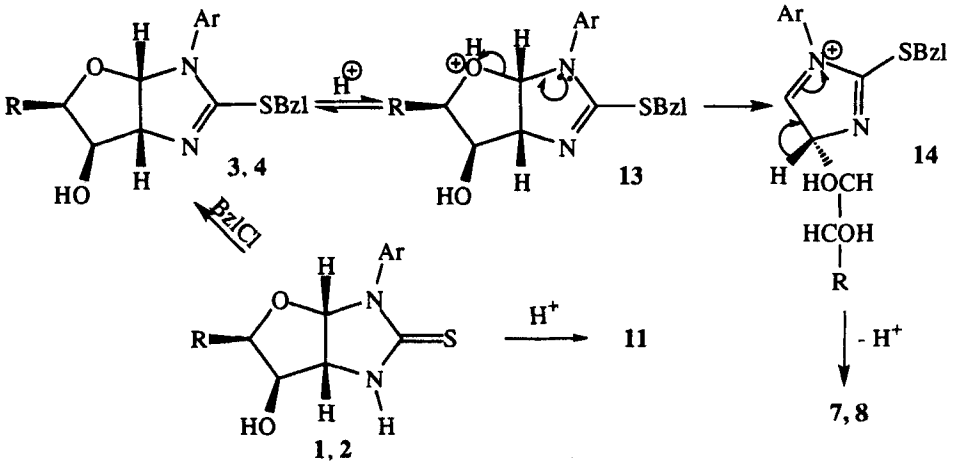
Scheme 2 shows possible mechanisms for the formation of **7**, **8**, and **11**. The *S*-benzylation of **1** or **2** through the thioenolic structure gives **3** or **4** (chromatographically detected). In the absence of sodium hydrogencarbonate the hydrochloric acid produces the oxonium ion **13**, which by opening of the tetrahydrofuran ring evolves to **14**, which converts to **7** or **8**. In an extension of the mechanism, **2** is protonated on the sulphur atom, then nucleophilic attack of water, and loss of hydrogen sulphide yields the oxocompound **11**.

Mass spectrometry. Mass spectra were obtained using electron impact ionisation; the composition of discussed ions was confirmed by accurate mass measurements at high resolving power and metastable spectra (daughter ions and loss of water) were run (resolution 1500) to confirm the fragmentation pathways.

The peaks containing Cl or Br are given with the mass corresponding to the isotope of lower mass. All compounds **1-10** presented molecular ions which in some



Scheme 1. Conformational equilibria of the exocyclic sugar backbone of **3-6**, **11**, and **12**, and of the polyacetoxyalkyl chain of **9** and **10**.



R= CHOH-CH_2OH, Ar= *p*-halogenophenyl

Scheme 2. Isomerization and desulphuration reactions.

cases (**5**, **6**) were the base peak. The spectra of the bicyclic polyhydroxy compounds **1**, **2**, **3**, and **4** had three main groups of signals, namely:

a) The primary fragmentations.

b) The route A coming from [$M^{+\cdot}$-H_2O].

c) The route B, corresponding mainly to the imidazole moiety which starts from [$M^{+\cdot}$-polyhydroxylic chain].

The spectra of the acyclic *C*-nucleosides **7**, **8** showed the primary fragmentations and the route A and those of the acetyl derivatives **5**, **6**, **9**, and **10** only the primary fragmentations. Table 4 shows the *m/z* values and the relative abundance for significant ions of compounds **1-4**, **7**, and **8**.

Probable structures of ions corresponding to routes A and B of compounds **1**, **2** are indicated in Scheme 3. In both cases the main fragmentation was the loss of the sugar moiety (route B) with formation of the peak B (scheme 3). Additionally **1** and **2** presented the peak B+30 described[16] for polyhydroxyalkylimidazoline-2-thiones and signals at *m/z* 111 (2, 28 %) and 155 (3, 27 %) corresponding to the aryl group. The peaks 251 (in **1**) and 295 (in **2**), besides that indicate in scheme 3, come from 219 or 313, respectively, by loss of water.

In compounds **3** and **4** route B (Scheme 3) was more important than route A. In both cases the base peak was the tropylium ion (*m/z* 91), and the peak B+30 was almost insignificant. The peak 300 (344 for **4**) is formulated in Scheme 3 with the Bzl group on the nitrogen atom because it presents an important loss of 143 (187 for **4**) corresponding to the XC_6H_4S group to give the ion 157 (47 and 12 %, respectively). This implies the rearrangement of the aryl group to the sulphur atom and consequently the Bzl group moving to the N-3 atom. The peaks XC_6H_4S (143 and 187, respectively) were also detected.

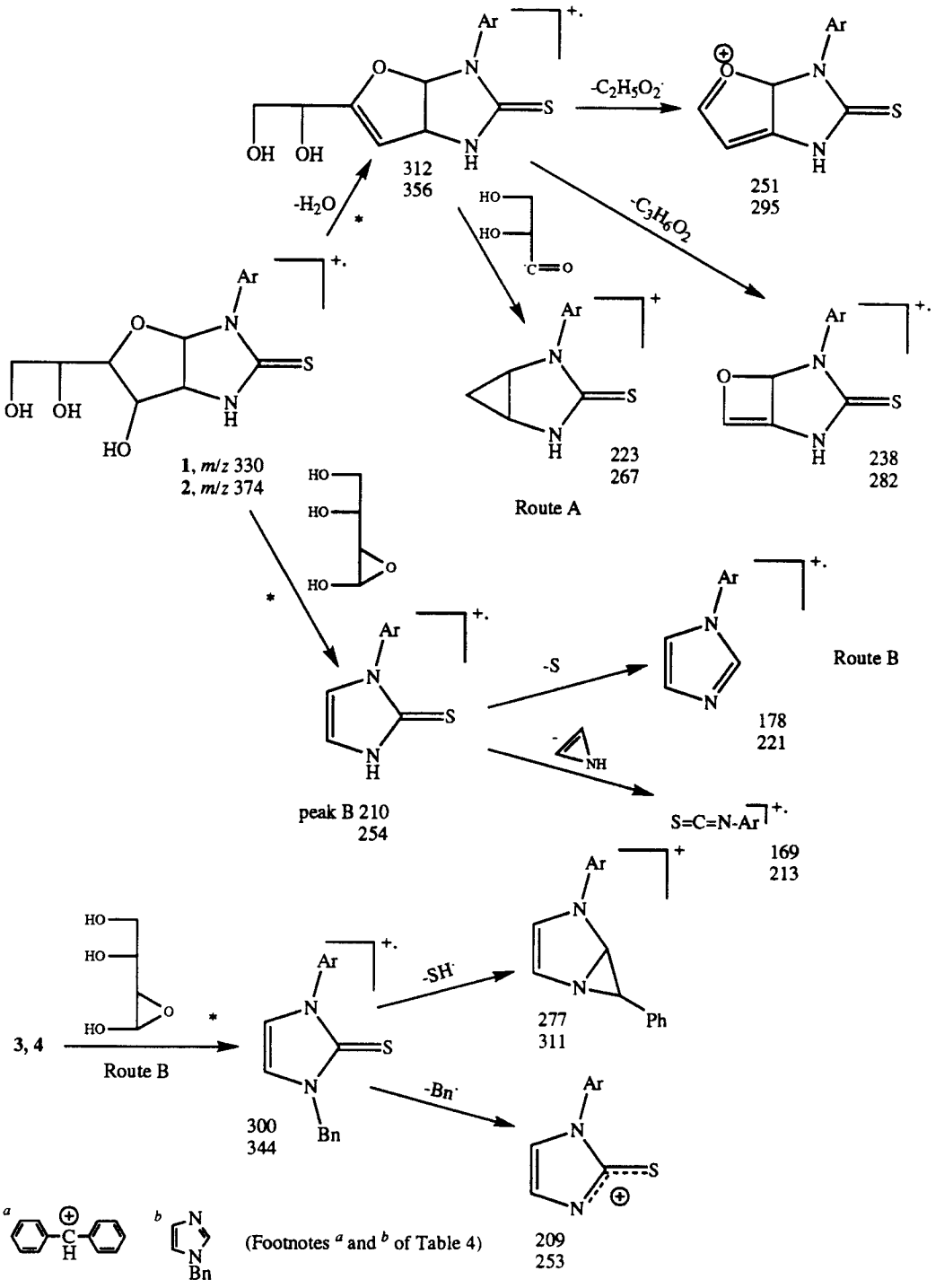
In compounds **7** and **8** there were molecular peaks, the base peak was 91 (Bzl^+), the primary loss of the tetrahydroxybutyl chain was insignificant and the majority of the peaks belong to route A, containing the heterocyclic ring and a sugar fragment (Table 4). Additionally prominent signals appear at *m/z* 199 [PhSCHPh]$^+$ and 185 [C6H4SPh]$^+$ indicative of rearrangement of the XC_6H_4 group to the sulphur atom.

The spectra of the acetyl derivatives **5**, **6**, **9**, and **10** had molecular ions and the main signals are due to primary fragmentations (see experimental), with important losses of Ac$^\cdot$, AcO$^\cdot$, AcOH, Ac_2O, 2 AcOH, 3 AcOH, and Ac_2O-AcOH as described for related acetyl derivatives.[16] Compounds **5** and **6** showed a simultaneous loss of the exocyclic chain and AcOH with formation of the ion *m/z* 341 (385 for **6**) with similar structure to the ion 251 of **1** (see scheme 3). The daughter ions scans in compounds **9** and

Table 4. *m/z* Values and relative abundance (% of the base peak) of important signals in the EIMS of compounds **1-4**, **7**, and **8**.

Comp	$M^{+\cdot}$	Primary fragmentation [$M^{+\cdot}$-R]									Route A (loss of R)			Route B (loss of R)				
		R									R			R				
		HO	H_2O	SH_2	$C_2H_5O_2$	$C_4H_8O_4$	SH	Ph	Bn	XC_6H_4	$C_2H_5O_2$	$C_3H_6O_2$	$C_3H_5O_3$	H	S	C_2H_3N		
1	330	313	312	296	269	210	-	-	-	111	251	238	223	209	178	169		
	(93)	(1)	(1)	(4)	(3)	(100)				(30)	(8)	(4)	(15)	(96)	(5)	(5)		
2	374	357	356	240	313	254	-	-	-	155	295	282	267	253	222	213		
	(65)	(16)	(7)	(11)	(10)	(100)				(22)	(8)	(9)	(23)	(95)	(10)	(25)		
											SH	Bn	$C_4H_5O_3$	SH	XC	Bn	*a*	*b*
3	420	-	402	-	-	300	387	343	329	111	369	311	301	267	253	209	201	157
	(2)		(2)			(12)	(1)	(1)	(1)	(11)	(1)	(1)	(4)	(8)	(2)	(7)	(29)	(47)
4	464	-	446	-	-	344	431	387	373	155	413	355	345	311	253	253	245	157
	(16)		(19)			(10)	(4)	(1)	(7)	(7)	(1)	(1)	(3)	(2)	(19)	(19)	(9)	(12)
											Route A							
				$3\,H_2O$	XC_6H_4S	*a*					SH	Bn	OH	C_2H_4O	C_3H_7O	$C_3H_5O_2$	XC_6H_4S	$PhCHC_6H_4X$
7	420	-	402	366	277	201			329	111	369	311	385	358	343	329	259	201
	(7)		(9)	(9)	(1)	(12)			(11)	(8)	(3)	(1)	(2)	(5)	(1)	(11)	(1)	(12)
8	464	-	446	410	277	245			373	145	413	355	429	402	387	373	259	245
	(6)		(35)	(23)	(1)	(17)			(13)	(91)	(16)	(1)	(9)	(4)	(6)	(13)	(3)	(17)

a. Peak daughter of $M^{+\cdot}$ and [$M^{+\cdot}$-120]. For probable structure see Scheme 3. b. For probable structure see Scheme 3.



Scheme 3. Proposed structure corresponding to ions of routes A (1, 2) and B (1-4).

10 indicate that the peak *m/z* 427 (471 for **10**) came from the molecular ion and also from 486 (530 for **10**) by loss of an acetoxy group.

EXPERIMENTAL

General methods. Melting points are uncorrected. Optical rotations were measured at 20 °C for solutions in pyridine. IR spectra were recorded for KBr discs or thin film, and the UV spectra using a Perkin-Elmer 554 spectrophotometer, with absolute ethanol as solvent, concentrations between 10^{-4} and 10^{-5} M, and path length 1 cm. ^{1}H NMR spectra (200, 300, and 500 MHz) were obtained for solutions in $CDCl_3$ or DMSO-d_6. Assignments were confirmed by homonuclear 2D COSY correlated experiments. ^{13}C NMR spectra were recorded at 75.4 and 125.7 MHz. Heteronuclear 2D correlated spectra were obtained in order to assist in carbon resonance assignments. EIMS spectra (70 eV) were measured with a Kratos MS-80RFA spectrometer with an ionising current of 100 μA, an accelerating voltage of 4 kV, a resolution of 1500 (10% valley definition), and a scan rate of 3 sec/decade. Metastable peaks in the free region were obtained at a 10 sec/decade scan rate. TLC was performed on Silica Gel HF_{254}, with detection by UV light or charring with H_2SO_4. Silica Gel 60 (Merck, 70-230 and 230-400 mesh) was used for preparative chromatography.

1 - (*p*-chlorophenyl) - (1,2-dideoxy-α-D-glucofurano) [2,1-*d*]imidazolidine-2-thione (1). Yield 66%; mp 243-244 °C (Literature[18] yield 71%, mp 250-251 °C); EIMS Table 4.

1 - (*p*-bromophenyl) - (1,2-dideoxy-α-D-glucofurano) [2,1-*d*]imidazolidine-2-thione (2). Yield 65%; mp 243-244 °C (Literature[18] yield 73%, mp 250-252 °C); EIMS Table 4.

General procedure for the preparation of 3 and 4 . To a suspension of **1** (for **3**) or **2** (for **4**) (4 mmol) in 90% ethanol (50 mL), sodium hydrogencarbonate (0.35 g, 4 mmol) and benzyl chloride (0.53 mL, 4 mmol) were added. The mixture was heated under reflux for 2 h and then its volume reduced to half. From the remaining solution the corresponding compound (**3** or **4**) crystallized. The solids were purified by recrystallization from ethanol.

2- Benzylthio -1- (*p*-chlorophenyl) - (1,2-dideoxy-α-D-glucofurano) [2,1-*d*]-2-imidazoline (3). Yield (1.16 g, 69%), mp 133-136 °C; $[\alpha]_D$ +110° (*c* 1.0); λ_{max} 255 nm; IR ν_{max} 3500-3200, 3050, 3020, 2935, 2870, 1590, 1490, 830, and 745 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): Table 1 and δ 7.43-7.36 (m, 4 H, C_6H_4Cl), 7.31-7.25 (m, 5 H,

Ph), 5.22 (d, 1 H, $J_{3,OH}$= 4.6, O*H*-3), 4.67 (d, 1 H, $J_{5,OH}$= 5.8, O*H*-5), 4.46 (t, 1 H, $J_{6a,OH}$= $J_{6b,OH}$= 5.6, O*H*-6); ^{13}C NMR (125.7 MHz, DMSO-d_6): Table 3 and δ 137.3-126.5 (12 C, Ar); EIMS Table 4 and 91 (100, tropylium ion).

Anal. Calcd for $C_{20}H_{21}ClN_2O_4S$: C, 57.07; H, 5.03; N, 6.66; S,.7.62 Found: C, 56.80; H, 5.04; N, 6.52; S, 7.58..

2-Benzylthio -1- (*p*-bromophenyl) - (1,2-dideoxy-α-D-glucofurano) [2,1-*d*]-2-imidazoline (4). Yield (1.25 g, 67%), mp 135-137 °C; $[\alpha]_D$ +97° (*c* 1.0); λ_{max} 258 nm;IR ν_{max} 3500-3200, 3050, 3020, 2940, 2865, 1595, 1485, 820, and 730 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): Table 1 and δ 7.58-7.46 (m, 4 H, C_6H_4Br), 7.37-7.20 (m, 5 H, Ph), 5.22 (d, 1 H, $J_{3,OH}$= 4.7, O*H*-3), 4.68 (d, 1 H, $J_{5,OH}$= 5.8, O*H*-5), 4.46 (t, 1 H, $J_{6a,OH}$= $J_{6b,OH}$= 5.6, O*H*-6); ^{13}C NMR (125.7 MHz, DMSO-d_6): Table 3 and δ 137.5-118.6 (12 C, Ar); EIMS Table 4 and 91 (100, tropylium ion).

Anal. Calcd for $C_{20}H_{21}BrN_2O_4S$: C, 51.62; H, 4.55; N, 6.02; Found: C, 51.73; H, 4.36; N, 5.89.

2-Benzylthio-1-(*p*-chlorophenyl)-4-(D-*arabino*-tetritol-1-yl)imidazole (7). To a solution of **1** (1.00 g, 3 mmol) in 90 % ethanol (40 mL), benzyl chloride (0.4 mL, 3 mmol) was added and the resulting mixture heated for 2 h 30 min under reflux. Then its volume was reduced to a 20 % and the residue diluted with water (25 mL), giving a white solid consisting mostly of **1**. The solid was filtered off and the solution extracted with ethyl ether (3x25 mL) crystallizing **7** (0.52g; 41%), which purified by recrystallization from 90 % ethanol has mp 159-160 °C; $[\alpha]_D$ -25° (*c* 1.0); λ_{max} 267 nm; IR ν_{max} 3450-3200, 3050, 3010, 2925, 2900, 1590, 1490, 835, and 735 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): Table 2 and δ 7.51-7.49 (m, 4 H, C_6H_4Cl), 7.25-7.17 (m, 5 H, Ph); ^{13}C NMR (125.7 MHz, DMSO-d_6): Table 3 and δ 139.1-127.1 (12 C, Ar); EIMS Table 4 and 91 (100, tropylium ion).

Anal. Calcd for $C_{20}H_{21}ClN_2O_4S$: C, 57.17; H, 5.06; N, 6.55. Found: C, 57.07; H, 4.99; N, 6.65.

2-Benzylthio-1-(*p*-bromophenyl)-4-(D-*arabino*-tetritol-1-yl)imidazole (8) and 1-(*p*-bromophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*] imidazoline-2-one (11). To a solution of **2** (1.13 g, 3 mmol) in 90 % ethanol (50 mL) benzyl chloride (0.4 mL, 3 mmol) was added and the resulting mixture heated for 3.5 h under reflux. Then its volume was reduced to around 20 % and the residue diluted with water (25 mL), giving a white solid "A", consisting of two compounds with Rf 0.46 and 0.36, respectively, (dichloromethane-methanol 6:1), the latter corresponding to **2**. Fractional crystallization of "A" from absolute ethanol gave **8** (more soluble) and **2** (less soluble). The filtrate from which "A" was extracted with ethyl ether (3x25 mL) to remove the remaining benzyl chloride. On cooling the aqueous solution the solid "B" crystallised as a mixture of **8** and

a compound with Rf 0.34. Recrystallization from ethanol gave **8**. TLC (dichloromethane:methanol 6:1) of the mother liquor gave **11**.

2-Benzylthio-1-(*p*-bromophenyl)-4-(D-*arabino*-tetritol-1-yl) imidazole (**8**). Total yield 0.32g (24%), mp 141-144 °C; $[\alpha]_D$ -17° (*c* 1.0); λ_{max} 266 nm; IR ν_{max} 3450-3200, 3050, 3010, 2925, 2905, 1600, 1490, 835, and 740 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): Table 2 and δ 7.66-7.63 (m, 4 H, C_6H_4Br), 7.36-7.16 (m, 5 H, Ph); ^{13}C NMR (125.7 MHz, DMSO-d_6): Table 3 and δ 139.0-126.8 (12 C, Ar); EIMS Table 4 and 91 (100, tropylium ion).

Anal. Calcd for $C_{20}H_{21}BrN_2O_4S$: C, 51.62; H, 4.55; N, 6.02. Found: C, 51.26; H, 4.37; N, 5.76.

1-(*p*-bromophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*] imidazoline-2-one (**11**). A syrup (0.069g, 6.4%) which has $[\alpha]_D$ +99° (*c* 1.0); λ_{max} 202, 243, 270 nm; IR ν_{max} 3500-3200, 3090, 3070, 2940, 1665 (CO of urea), 1590, 1490, 820, and 710 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): Table 1 and δ 7.64 (s, 1 H, NH), 7.61-7.47 (m, 4 H, Ar), 5.55, 4.99, and 4.50 (each s, each 1 H, 3 OH). This compound was analyzed as the acetyl derivative **12**.

General procedure for the preparation of 5, 6, 9 , 10 and 12. To a solution of the corresponding compound (**3**, **4** , **7**, **8** , 2 mmol) and **11** (0.04 mmol) in pyridine (8.0 mL), acetic anhydride (5.5 mL, 59 mmol for **5** and **6**, and 4.3 mL, 46 mmol for **9** and **10**, and 0.11 mL, 1.2 mmol for **11**) was added with stirring. The mixture was kept for 24 h at 5 °C, and then poured into ice-water (130 mL). The white solids were filtered off, washed with cold water and crystallized from absolute ethanol.

2 - Benzylthio - 1 - (*p*-chlorophenyl) - (3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]-2-imidazoline (5). Yield 0.79 g (72%), mp 118-119 °C; $[\alpha]_D$ +99° (*c* 1.0); λ_{max} 255 nm; IR ν_{max} 3080, 3050, 3020, 2960, 2930, 2895, 1740 1590, 1550, 1490, 1450, 1370, 1240, 830, and 745 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): Table 1 and δ 7.38-7.21 (m, 9 H, Ar), 2.10, 2.06, 2.05 (each s, each 3 H, 3 Ac); ^{13}C NMR (75.4 MHz, $CDCl_3$): Table 3 and δ 170.5, 169.7, 169.5 (3 $COCH_3$), 136.3-126.0 (12 C, Ar), 20.7 (2 $COCH_3$), 20.6 ($COCH_3$); EIMS *m/z* 546.1227 (100, M^+), 513 (13, M^+-SH), 503 (1, M^+-Ac), 487 (3, M^+-OAc), 469 (1, M^+-Ph), 455 (11, M^+-Bzl), 421 (3, M^+-C_6H_4NCl), 403 (2, M^+-C_6H_4NClS), 341 (5, M^+-205), 301 (9, M^+-245), 201 (25, Ph_2CHCl^+), 111 (5, $PhCl^+$), 91 (75, Bzl^+), and 43 (55, Ac^+).

Anal. Calcd for $C_{26}H_{27}ClN_2O_7S$: C, 57.09; H, 4.98; N, 5.12. Found: C, 56.70; H, 4.97; N, 5.05.

2 - Benzylthio - 1 - (*p*-bromophenyl) - (3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]-2-imidazoline (6). Yield 0.91 g (77%), mp 107-110 °C; $[\alpha]_D$ +97° (*c* 1.0); λ_{max} 256 nm; IR ν_{max} 3080, 3050, 3020, 2960, 2930, 2895, 1740, 1550, 1485,

1450, 1370, 1240, 820, and 730 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): Table 1 and δ 7.60-7.56 (m, 4 H, C_6H_4Br), 7.40-7.22 (m, 5 H, Ph), 2.02, 2.00, 1.96 (each s, each 3 H, 3 Ac); ^{13}C NMR (75.4 MHz, DMSO-d_6): Table 3 and δ 170.1, 169.4, 169.3 (3 $COCH_3$), 137.1-119.2 (12 C, Ar), 20.8, 20.6, 20.5 (3 $COCH_3$); EIMS *m/z* 590.0723 (100, $M^{+\cdot}$), 557 (7, M^+-SH), 547 (2, M^+-Ac), 531 (2, M^+-OAc), 513 (3, M^+-Ph), 499 (9, M^+-Bzl), 421 (5, M^+-C_6H_4NBr), 403 (2, M^+-C_6H_4NBr), 385 (4, M^+-205), 345 (7, M^+-245), 245 (20, Ph_2CHBr^+), 155 (4, $PhBr^+$), 91 (47, Bzl^+), and 43 (27 Ac^+).

Anal. Calcd for $C_{26}H_{27}BrN_2O_7S$:: C, 52.79; H, 4.60; N, 4.73. Found: C, 52.57; H, 4.64; N, 4.64.

2 - Benzylthio - 1 - (*p*-chlorophenyl) - 4 - (tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazole (9). Yield 0.96 g (82%), mp 44-46 °C; $[\alpha]_D$ -39° (*c* 1.0); λ_{max} 258 nm; IR ν_{max} 3045, 3015, 2955, 2920, 1740 1590, 1490, 1445, 1365, 1250, 830, and 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): Table 2 and δ 7.35-7.32 (m, 4 H, C_6H_4Cl), 7.18-7.16 (m, 5 H, Ph), 2.13, 2.11, 2.09, 2.07 (each s, each 3 H, 4 Ac); ^{13}C NMR (125.7 MHz, $CDCl_3$): Table 3 and δ 170.5, 169.9, 169.8, 169.5 (4 $COCH_3$), 137.9-126.8 (12 C, Ar), 20.9, 20.8, 20.7, 20.6 (4 $COCH_3$); EIMS *m/z* 588.1333 (20, $M^{+\cdot}$), 545 (3, M^+-Ac), 529(8, M^+-OAc), 486 (7, M^+-Ac_2O), 468 (2, M^+-2AcOH), 427 (21, M^+-Ac_2O-AcO), 445 (11, M^+-ClC_6H_4S), 408 (2, M^+-3AcOH), 385(11, M^+-168-Cl), 369 (5, M^+-Ph_2CHCl^+), 91 (63, Bzl^+), 60 (100, $AcOH^+$), and 43 (59, Ac^+).

Anal. Calcd for $C_{28}H_{29}ClN_2O_8S$: C, 57.09; H, 4.96; N, 4.76. Found: C, 56.92; H, 5.04; N, 4.44.

2 - Benzylthio - 1 - (*p*-bromophenyl) - 4 - (tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazole (10). Yield 0.90 g (71%), mp 42-44 °C; $[\alpha]_D$ -20° (*c* 1.0); λ_{max} 266 nm; IR ν_{max} 3045, 3020, 2950, 2905, 1740, 1485, 1450, 1365 1250, 830, and 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): Table 2 and δ 7.52-7.46 (m, 4 H, C_6H_4Br), 7.26-7.16 (m, 5 H, Ph), 2.12, 2.10, 2.07, 2.05 (each s, each 3 H, 4 Ac); ^{13}C NMR (125.7 MHz, $CDCl_3$): Table 3 and δ 170.5, 170.0, 169.8, 169.4 (4 $COCH_3$), 139.9.1-120.2 (12 C, Ar), 20.8, 20.7 (2 $COCH_3$), 20.6 (2 $COCH_3$); EIMS *m/z* 632.0312 (15, $M^{+\cdot}$), 589 (1, M^+-Ac), 573 (3, M^+-OAc), 530 (12 M^+-Ac_2O), 512 (1, M^+-2AcOH), 471 (10, M^+-Ac_2O-AcO), 445 (7, M^+-BrC_6H_4S), 452 (1, M^+-3AcOH), 413 (24, M^+-Ph_2CHBr^+), 385(4, M^+-168-Br), 91 (100, Bzl^+), 60 (20, $AcOH^+$), and 43 (59, Ac^+).

Anal. Calcd for $C_{28}H_{29}BrN_2O_8S$: C, 53.08; H, 4.61; N, 4.42. Found: C, 52.86; H, 4.92; N, 4.68.

1-(*p*-bromophenyl)-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano) [2,1-*d*]-imidazolidine-2-one (12). Yield 17 mg (86%), mp 65-67 °C; $[\alpha]_D$ +93° (*c* 1.0); λ_{max} 202, 243, and 268 nm; IR ν_{max} 3400-3200, 3050, 3005, 2940, 2905, 1740, (CO, ester), 1680 (CO urea), 1585, 1490, 1460, 1240, 820, and 720 cm^{-1}; ^1H NMR (200 MHz,

$CDCl_3$): Table 2, and δ 7.57-7.44 (m, 4 H, Ar), 5.63 (d, 1 H, NH), 2.11, 2.03, and 1.99 (each s, each 3 H, 3 Ac).

Anal. Calcd for $C_{19}H_{21}BrN_2O_8$: C, 47.02; H, 4.36; N, 5.76. Found: C, 46.91; H, 4.46; N, 5.80.

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19. To point up the carbohydrate structure of compounds **3-6**, **11**, and **12** the nomenclature employed in recent papers (see refs. 1, 3-5) on related bicyclic compounds is used. As an alternative the I.U.P.A.C. rules for fused heterocyclic

systems can be used. Thus compounds **3** and **4**, for example, would be [5*S*(1*R**), 6*R*, 3a*S*, 6a*S*] 2-benzylthio-3-(4-halogenophenyl)-3a,6a,5,6-tetrahydro-6-hydroxy-5-(1,2-dihydroxyethyl)furo[2,3-*d*]imidazoles.

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