Pergamon

Tetrahedron Vol. 51, No. 22, pp. 6349-6362, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00289-8

Stereoselective 1,3-Dipolar Cycloadditions of Nitrile Oxides to Sugar Olefins. Synthesis of Acyclic-Sugar Isoxazoline *C*-Nucleoside Analogs

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Abstract: The cycloaddition 1,3-dipolar of nitrile oxides to sugar nitro olefins and α,β-unsaturated carbonyl olefins has been investigated. The reaction is less regioselective that the cycloaddition of diazoalkanes to the same olefins and while nitrile oxides with bulky substituents afford the sterically less hindered cycloadducts, other nitrile oxides yield a mixture of the two possible regioisomers. However, the reactions seem to be highly stereoselective and single diastereomers were obtained in all the cases studied.

INTRODUCTION

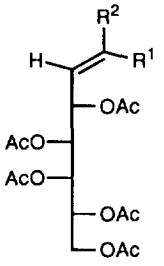
The biological importance of several naturally occurring *C*-nucleosides has generated a considerable interest over the years in the chemistry and biochemistry of this unusual class of nucleosides[1] , several of which exhibit anticancer[2] and broad-spectrum antiviral activity[3] in addition to their antibiotic properties[4]. This group of compounds contains a C-C linkage between the sugar and the heterocyclic moiety (*C*-glycosyl heterocycles) that is mostly responsible[5] for their biochemical and medicinal potential. So, the preparation of *C*-glycosyl compounds has become a very active area and new synthetic methods have been developed for the appendage of aliphatic and aromatic groups onto carbohydrates and for the novo synthesis of *C*-glycosyl compounds[6]. Our most recent contributions to this area have been centred around the stereoselective 1,3-dipolar cycloaddition reactions of diazoalkanes to sugar olefins to give acyclic-sugar pyrazoline *C*-nucleoside analogs[7]. In this communication we report on the 1,3-dipolar cycloaddition reaction of nitrile oxides to sugar nitro- and carbonyl-olefins. Although the antecedents on the cycloaddition of nitrile oxides to unsaturated sugars are very scarce, there are some papers describing the use of allylic ethers derived from sugars as dipolarophiles[8,9].

RESULTS AND DISCUSSION

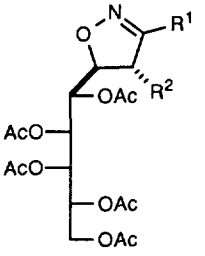
We have investigated the addition of benzonitrile oxide, 2,4,6-trimethylbenzonitrile (mesitonitrile) oxide, bromoformonitrile oxide and acetonitrile oxide to sugar nitroolefins (**1**, **5**) and α,β-unsaturated carbonyl sugar derivatives (**2**, **3**, **4**). In order to minimize the formation of furazan *N*-oxide (furoxan) dimers, the nitrile oxides

were generated *in situ* from the corresponding oxime. Only the stable mesitonitrile oxide was used as such.

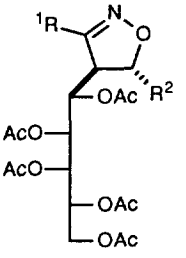
Benzonitrile oxide, generated at room temperature by slow addition of triethylamine to a solution of benzohydroximoyl chloride, was reacted with (*E*)-3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-*C*-nitro-D-*galacto*-hept-1-enitol (**1**)[10], in dichloromethane, to yield a mixture of the two possible regioisomers **6** and **17** in the 3:1 ratio, as was determined by NMR. The major product (**6**) could be separated by fractional crystallization and



1 R^1 = H, R^2 = NO_2
2 R^1 = H, R^2 = COMe
3 R^1 = H, R^2 = CO_2Me
4 R^1 = H, R^2 = CO_2Et
5 R^1 = Me, R^2 = NO_2



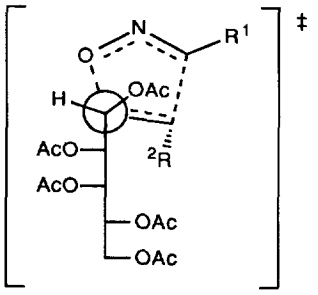
6 R^1 = Ph, R^2 = NO_2
7 R^1 = Mes, R^2 = NO_2
8 R^1 = Ph, R^2 = COMe
9 R^1 = Mes, R^2 = COMe
10 R^1 = Ph, R^2 = CO_2Me
11 R^1 = Mes, R^2 = CO_2Me
12 R^1 = Ph, R^2 = CO_2Et
13 R^1 = Mes, R^2 = CO_2Et
14 R^1 = Br, R^2 = CO_2Et
15 R^1 = Me, R^2 = CO_2Me
16 R^1 = Me, R^2 = CO_2Et



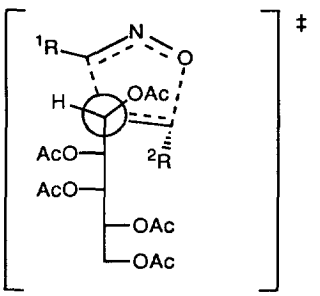
17 R^1 = Ph, R^2 = NO_2
18 R^1 = Br, R^2 = COMe
19 R^1 = Me, R^2 = COMe
20 R^1 = Br, R^2 = CO_2Me
21 R^1 = Br, R^2 = CO_2Et

Mes: 2,4,6-$(CH_3)_3C_6H_2$

its structure assigned from their analytical and spectroscopic properties. Thus, the signal for H-4 appeared as a doublet ($J_{4,5}$ 3.8 Hz) at 6.27 ppm, and H-5 gave a double doublet ($J_{5,1'}$ 6.5 Hz) at 5.16 ppm. Although the minor isomer (**17**) could not be separated by chromatography, it was possible to assign individual peaks in the NMR spectra. Mesitonitrile oxide reacted with the nitro olefin **1** to afford the isoxazoline **7** in high yield (94%) without detection of the other possible regioisomer. The NMR spectral data obtained for **7** were correlated with those obtained for **6**. Although the absolute stereochemistry on C-4 and C-5 has not been determined, the configuration of the isoxazoline must be *trans*, like in the parent nitro olefin. The $J_{4,5}$ values are correlated[11] with dihedral angles of about 130° for these protons, in agreement with a flattened E_5 conformation of the isoxazoline rings. Furthermore, the NMR spectra of **6** and **7** showed that only one diastereomer was obtained in each case, which could be the 4*S*,5*S*, in agreement with the *inside alkoxy effect* that is useful for predicting the stereoselectivity of nitrile oxide cycloadditions to chiral allylic ethers and other chiral allylic derivatives[12,13]. *Ab initio* and molecular mechanic calculations predict that in the lowest-energy transition state the allylic substituent adopts the inside position and the voluminous alkyl chain the sterically less-crowded *anti* conformation[12a]. In our case, the TS_1 must be the most stable transition state leading to compounds **6-16**, whereas TS_2 lead to **17-21**. This hypothesis was confirmed by the preparation of the bicyclic lactones **29-31** in the deacetylation reaction of **10**, **11**,**13**, and **20**, as we describe later. This diastereofacial selectivity is just the



TS_1



TS_2

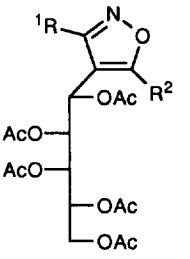
contrary of that observed in our preceding results on the cycloaddition of diazoalkanes to sugar olefins[7], where the structures of the adducts were demonstrated by X-ray diffraction[7d,14].

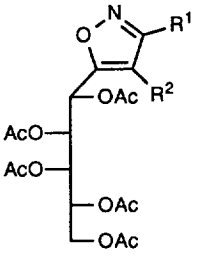
In a similar way, the reactions of (*E*)-5,6,7,8,9-penta-*O*-acetyl-1,3,4-trideoxy-D-*galacto*-non-3-enulose (**2**)[7a] or methyl[7b] and ethyl[15] (*E*)-4,5,6,7,8-penta-*O*-acetyl-2,3,-dideoxy-D-*galacto*-oct-2-enonate (**3** and **4**) with benzonitrile or mesitonitrile oxides afforded the 5-pentaacetoxypentyl-2-isoxazolines **8-13**, as single stereoisomers, with yields between 60-90%. As in the preceding cases, the $J_{4,5}$ values are correlated[11] with dihedral angles between 120° and 140° that indicate flattened or slightly flattened E_5 conformations.

While the reactions that we have just described are highly regioselective and all the studied olefins lead exclusively or preferentially to the sterically less hindered 5-pentaacetoxypentyl-2-isoxazolines, the behaviour of the same olefins in their reactions with bromoformonitrile and acetonitrile oxides is not so regular. So, the reaction of the nitro olefin **1** with bromoformonitrile oxide, generated *in situ* by treatment of dibromoformaldoxime with potassium hydrogen carbonate, occurred slowly to give a complex mixture of products, column chromathography of which afforded the 4-pentaacetoxypentyl-isoxazole **22**, in a 47% yield, probably formed by aromatization of the corresponding 4-pentaacetoxypentyl-2-isoxazoline. In the same way, the reaction of **1** with acetonitrile oxide, generated from acetaldoxime by reaction with *N*-chlorosuccinimide and triethylamine, also led to the 4-pentaacetoxypentyl-isoxazole (**23**). Both compounds showed the aromatic isoxazole protons at 8.27 and 7.26 ppm, respectively. The aromatic C-5 appeared at 158.1 and 155.7 ppm.

The reaction of the carbonyl olefin **2** with bromoformonitrile and acetonitrile oxides also afforded the 4-pentaacetoxypentyl-2-isoxazolines (**18** and **19**). These structures were confirmed because the H-5 protons, adjacents to the acetyl group, appeared as doublets at lower fields (5.09 and 4.98 ppm) than the expected for the corresponding regioisomers. Compound **19** was isolated impurified by the isoxazol **23**, probably formed by aromatization of **19** by losing the acetyl group. Although **19** and **23** were not separable by chromatography they were readily distinguished in the NMR spectra of the mixture by comparison of the spectral parameters with those of previously obtained for pure **23** prepared from **1** as described above.

The reaction of bromoformonitrile oxide with **3**, at room temperature, gave a 75% yield of the cycloadduct **20**, whereas the reaction with **4** afforded a 1:2 mixture (NMR) of the regioisomeric isoxazolines **14** and **21** in a combined yield of 80%. However, the cycloaddition of acetonitrile oxide to **3** and **4** yielded preferentially the 5-pentaacetoxypentyl-2-isoxazolines. From the reaction of **3**, after flash chromatography, the isoxazoline **15** was isolated (62% yield) as a crystalline product, and **4** gave **16** (65% yield) also as a crystalline white solid.





22 R^1 = Br, R^2 = H
23 R^1 = Me, R^2 = H
24 R^1 = Mes, R^2 = Me

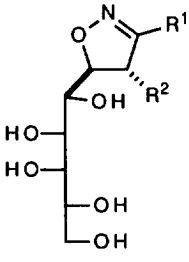
25 R^1 = Mes, R^2 = Me

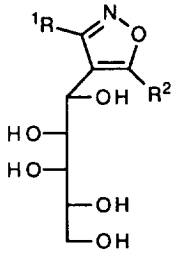
Mes: 2,4,6-$(CH_3)_3C_6H_2$

The NMR data of both compounds are in agreement with the assigned regiochemistry. These data also indicate that single stereoisomers are obtained in all the cases.

The regioselectivity of these reactions is lower than that shown by the addition of diazoalkanes to the same olefins[7]. These results can be interpreted on the basis of two competitive effects; the orbital effects that favor the formation of the 4-pentaacetoxypentyl-2-isoxazolines, and the steric factors that seem to be favorable to the formation of the 5-pentaacetoxypentyl-2-isoxazolines, specially if R^1 is a bulky substituent as phenyl or mesityl groups. On the other hand, trisubstituted sugar olefins seem to be less reactive with nitrile oxides than with diazoalkanes. So, (*E*)-4,5,6,7,8-penta-*O*-acetyl-1,2,3-trideoxy-2-*C*-nitro-D-*galacto*-oct-2-enitol (**5**) reacts with diazoalkanes, at low temperature, to give high yields of pyrazolines[7a], but failed in the reaction with nitrile oxides. The reaction of **5** with benzonitrile or mesitonitrile oxides did not yield the expected 2-isoxazolines, and a complex mixture of unreacted olefin, furoxans, and other unidentified products were detected chromatographically. However, when **5** was heated under reflux of dichloromethane with an excess of mesitonitrile oxide yielded a mixture of the isoxazoles **24** and **25**, which could be isolated in low yield by flash column chromatography.

Deacetylation reactions.- The treatement of the 2-isoxazolines **7** and **9** with sodium methoxide followed by neutralization with Amberlita IR-120 (H^+) leads to the corresponding pentahydroxypentyl isoxazolines (**26** and **27**). In the same way, deacetylation of **22** yields the pentahydroxypentyl isoxazole **28**. These compounds can be considered acyclic-sugar *C*-nucleoside analogs, structurally related with other natural and synthetic



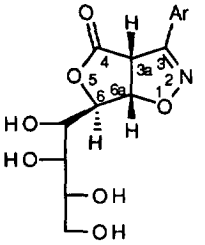


26 R^1 = Mes, R^2 = NO_2
27 R^1 = Mes, R^2 = COMe

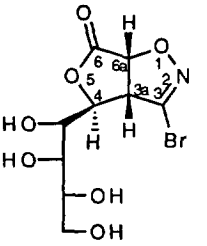
28 R^1 = Br, R^2 = H

C-nucleosides.

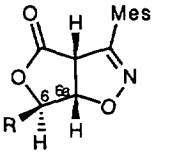
When this reaction was applied to the isoxazolines **11** or **13**, we obtained the bicyclic lactone **29** (quantitative yield), whose structure was determined on the basis of its elemental analysis and spectroscopic properties. The IR spectrum showed a band at 1760 cm^{-1} characteristic of a saturated five membered lactone. The ^{1}H- and ^{13}C-NMR spectra were completely assigned by deuterium exchange and homo- and heteronuclear COSY, and they are also indicative of a five membered lactone and discard a possible δ-lactone structure. So, in the proton spectrum, registered in DMSO-d_6, H-3a and H-6a appeared as a doublet (4.63 ppm, $J_{3a,6a}$ 9.2 Hz) and a double doublet (5.53 ppm, $J_{6,6a}$ 1.2 Hz), respectively. H-6 gave a narrow quartet at 5.05 ppm ($J_{6,1'}$ 0.5 Hz). The protons of the tetrahydroxybutyl chain, including the hydroxylic protons,



29 Ar = Mes
30 Ar = Ph



31



32 R = CHO
33 R = H

appeared between 3.41 and 5.40 ppm with their previewed multiplicities. The structure of **29** was confirmed by the preparation of the aldehyde **32** whose spectral data (IR and NMR) were very similar to that of **33**, previously described[16] by cycloaddition reaction of mesitonitrile oxide to $\Delta^{\alpha,\beta}$-butenolide. The $J_{6,6a}$ values of **29** and **32** (1.2 Hz) are also indicative of a *trans* arrangement for these protons[17-21], which demonstrates the *S* configuration of C-6a, in agreement with the assigned stereochemistry of the parent isoxazoline.

Analogously, the deacetylation reaction of the isoxazolines **10** and **20** gave the bicyclic lactones **30** and **31**, respectively, whose structures were also proved by elemental analysis and IR and NMR spectroscopy. In the formation of these lactones, the cyclization must be preceded by the epimerization of the isoxazoline carbon contiguous to the carboxylate group which must adopt a *cis* arrangement with the polyhydoxyl side chain. These epimerizations can take place easily in the basic medium of the deacetylation reaction through the corresponding carbanions on C-3a (**29**, **30**) or C-6a (**31**).

EXPERIMENTAL

General.- Chemicals were all used as purchased from Aldrich Chemical Co. Solvents were dried and purified when necessary, by appropriate standard procedures. Melting points were determined with a Gallenkamp apparatus and are uncorrected. Optical rotations were measured at 20 ± 5 °C with a Bellingham & Standley Inc., P20 polarimeter (5-cm cell). TLC was performed on silica gel 60 F_{254} (Merck) with detection by UV light or charring with sulphuric acid. Flash column chromatography: Merck silica gel 60 (230-400 mesh). FT IR spectra (films or KBr discs) were recorded with a Michelson 100 spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded with Bruker 200 AC-P and AMX 500 spectrometers.

Chemical shifts are reported as parts per million downfield from tetramethylsilane. Elemental analyses were determined in the Microanalysis Laboratories at the Universidad de Sevilla and the Universidad Complutense de Madrid.

(4S,5S)-5-(Penta-O-acetyl-D-galacto-pentitol-1-yl)-4-nitro-3-phenyl-2-isoxazoline (6) and (4R,5S)-4-(penta-O-acetyl-D-galacto-pentitol-1-yl)-5-nitro-3-phenyl-2-isoxazoline (17).- A solution of triethylamine (0.30 ml, 2.28 mmol) in dichloromethane (10 ml) was slowly added to a solution of **1** (1.00 g, 2.31 mmol) and benzohydroximoyl chloride (0.36 g, 2.31 mmol) in dichloromethane (10 ml), and the mixture was stirred at room temperature for 24 h. The solution was then evaporated and the solid residue was washed with cold methanol to remove the triethylamine hydrochloride. Fractional crystallization from ethanol gave pure **6** (0.55 g, 43 %); m.p. 150-152 °C; $[\alpha]_D$ +117° (*c* 1, dichloromethane); R_f 0.59 (3:1 ether-hexane); υ_{max} 1752 (CO), 1557 and 1377 cm^{-1} (NO_2); NMR data: ^1H, δ 2.03-2.20 (5s, 15H, 5OAc), 3.81 (dd, 1H, $J_{4',5'}$ 7.2, $J_{5',5''}$ -11.6 Hz, H-5''), 4.28 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 5.16 (dd, 1H, $J_{4,5}$ 3.8, $J_{5,1'}$ 6.5 Hz, H-5), 5.20-5.35 (m, 2H, $J_{3',4'}$ 1.9 Hz, H-3'/4'), 5.37 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-1'), 5.64 (dd, 1H, $J_{2',3'}$ 9.8 Hz, H-2'), 6.27 (d, 1H, H-4), 7.44-7.71 (m, 5H, Ph). ^{13}C, δ 20.1-21.0 (Me), 62.0 (C-5'), 66.1-70.3 (C-1'/4'), 85.1 (C-5), 91.8 (C-4), 125.9-141.3 (Ph), 151.7 (C-3), 169.1-170.3 (OAc). Anal. Calcd for $C_{24}H_{28}N_2O_{13}$: C, 52.18; H, 5.11; N, 5.07. Found: C, 52.52; H, 5.51; N, 4.91.

Because of small proportion of **6**, the regioisomer **17** could not be obtained as an analytically pure sample. R_f 0.54 (3:1 ether-hexane); NMR data: ^1H, δ 2.03-2.20 (5s, 15H, 5OAc), 3.81 (dd, 1H, $J_{4',5'}$ 7.2, $J_{5',5''}$ -11.6 Hz, H-5''), 4.28 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 4.34 (dd, 1H, $J_{4,5}$ 1.5, $J_{4,1'}$ 1.0 Hz, H-4), 5.20-5.37 (m, 2H, $J_{3',4'}$ 1.9 Hz, H-3'/4'), 5.35 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-1'), 5.64 (dd, 1H, $J_{2',3'}$ 9.8 Hz, H-2'), 6.43 (d, 1H, H-5), 7.44-7.71 (m, 5H, Ph). ^{13}C, δ 20.1-21.0 (Me), 58.3 (C-4), 62.0 (C-5'), 66.1-70.3 (C-1'/4'), 105.9 (C-5), 126.0-141.3 (Ph), 158.1 (C-3), 169.1-170.3 (OAc).

(4S,5S)-5-(Penta-O-acetyl-D-galacto-pentitol-1-yl)-3-(2,4,6-trimethylphenyl)-4-nitro-2-isoxazoline (7).- A dichloromethane solution (5 ml) of mesitonitrile oxide (0.80 g, 4.97 mmol) was added to another solution of **1** (2.16 g, 4.99 mmol) in dichloromethane (10 ml). After 15 h at room temperature, the solvent was evaporated and the solid residue was crystallized from ethanol to afford **7** (2.78 g, 94 %); m.p. 156-158 °C; $[\alpha]_D$ +187° (*c* 1, dichloromethane); R_f 0.84 (1:4 ethyl acetate-dichloromethane); υ_{max} 1752 (CO), 1567 and 1371 cm^{-1} (NO_2); NMR data: ^1H, δ 2.04, 2.12 (2s, 9H, Me-Ar), 2.12-2.25 (5s, 15H, 5OAc), 3.81 (dd, 1H, $J_{4',5'}$ 7.3, $J_{5',5''}$ -11.7 Hz, H-5''), 4.30 (dd, 1H, $J_{4',5'}$ 4.9 Hz, H-5'), 5.22 (dq, 1H, $J_{3',4'}$ 2.1 Hz, H-4'), 5.29 (dd, 1H, $J_{2',3'}$ 9.9 Hz, H-3'), 5.29 (dd, 1H, $J_{4,5}$ 4.8, $J_{5,1'}$ 6.6 Hz, H-5), 5.48 (dd, 1H, $J_{1',2'}$ 2.1 Hz, H-1'), 5.66 (dd, 1H, H-2'), 6.17 (d, 1H, H-4), 6.91 (s, 2H, Mes ring). ^{13}C, δ 19.7-21.0 (Me), 62.1 (C-5'), 67.3 (C-4'), 67.4, 67.5 (C-2'/C-3'), 67.7 (C-1'), 83.3 (C-5), 94.3 (C-4), 121.1-140.3 (Mes ring), 151.2 (C-3), 169.3-170.6 (OAc). Anal. Calcd for $C_{27}H_{34}N_2O_{13}$: C, 54.54; H, 5.76; N, 4.71. Found: C, 54.57; H, 6.07; N, 4.56.

(4S,5S)-4-Acetyl-5-(penta-O-acetyl-D-galacto-pentitol-1-yl)-3-phenyl-2-isoxazoline (8).- A dichloromethane solution (20 ml) of **2** (2.80 g, 6.51 mmol) and benzohydroximoyl chloride (1.00 g, 6.45 mmol) was reacted with triethylamine (0.90 ml, 6.53 mmol), as described in the preparation of **6**.

Recrystallization from ethanol gave **8** (2.30 g, 64 %); m.p. 173-175 °C; $[\alpha]_D$ +120° (*c* 1, dichloromethane); R_f 0.54 (3:1 ether-hexane); υ_{max} 1748 cm^{-1} (CO); NMR data: ^1H, δ 2.02-2.12 (5s, 15H, 5OAc), 2.19 (s, 3H, Me-CO), 3.81 (dd, 1H, $J_{4',5''}$ 7.3, $J_{5',5''}$ -11.7 Hz, H-5''), 4.29 (dd, 1H, $J_{4',5'}$ 4.7 Hz, H-5'), 4.38 (d, 1H, H-4), 4.88 (dd, 1H, $J_{4,5}$ 4.1, $J_{5,1'}$ 5.6 Hz, H-5), 5.24 (m, 1H, $J_{3',4'}$ 1.9 Hz, H-4'), 5.26 (dd, 1H, $J_{2',3'}$ 10.1 Hz, H-3'), 5.38 (dd, 1H, $J_{1',2'}$ 2.0 Hz, H-1'), 5.58 (dd, 1H, H-2'), 7.44-7.63 (m, 5H, Ph). ^{13}C, δ 20.4-21.5 (Me), 26.4 (MeCO), 62.2 (C-5'), 63.9 (C-4), 67.8-69.9 (C-1'/4'), 83.1 (C-5), 127.0-130.0 (Ph), 155.1 (C-3), 169.6-170.2 (OAc), 202.0 (CO). Anal. Calcd for $C_{26}H_{31}NO_{12}$: C, 56.83; H, 5.69; N, 2.55. Found: C, 56.56; H, 5.67; N, 2.29.

***(4S,5S)-4-Acetyl-5-(penta*-O-*acetyl-D*-galacto-*pentitol-1-yl)-3-(2,4,6-trimethylphenyl)-2-isoxazoline (9)*.-** It was prepared from **2** (2.00 g, 4.64 mmol) and mesitonitrile oxide (0.74 g, 4.60 mmol) as described for **7**. Crystallization from ethanol gave pure **9** (2.43 g, 88 %); m.p. 166-168 °C; $[\alpha]_D$ +183° (*c* 1, dichloromethane); R_f 0.86 (1:4 ethyl acetate-dichloromethane); υ_{max} 1750 cm^{-1} (CO); NMR data: ^1H, δ 1.82, 1.90 (2s, 9H, Me-Ar), 2.10-2.23 (5s, 15H, 5OAc), 2.30 (s, 3H, MeCO), 3.86 (dd, 1H, $J_{4',5''}$ 7.1, $J_{5',5''}$ -11.7 Hz, H-5''), 4.32 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 4.62 (d, 1H, H-4), 5.17 (t, 1H, $J_{4,5} = J_{5,1'} = 7.3$ Hz, H-5), 5.24 (dd, 1H, $J_{3',4'}$ 1.9 Hz, H-4'), 5.28 (dd, 1H, $J_{2',3'}$ 9.6 Hz, H-3'), 5.36 (dd, 1H, $J_{1',2'}$ 2.5 Hz, H-1'), 5.60 (dd, 1H, H-2'), 6.91 (s, 2H, Mes ring). ^{13}C, δ 19.8-21.0 (Me), 29.6 (MeCO), 62.1 (C-5'), 66.2 (C-4), 67.6-70.2 (C-1'/4'), 80.6 (C-5), 124.4-139.6 (Mes ring), 153.0 (C-3), 169.0-170.1 (OAc), 199.8 (CO). Anal. Calcd for $C_{29}H_{37}NO_{12}$: C, 58.88; H, 6.30; N, 2.37. Found: C, 58.92; H, 6.27; N, 2.24.

***(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-4-methoxycarbonyl-3-phenyl-2-isoxazoline (10)*.-** Treatment of **3** (2.80 g, 6.28 mmol), with benzohydroximoyl chloride (0.97 g, 6.26 mmol) and triethylamine (0.80 ml, 6.24 mmol), as described for **6** gave **10**. Recrystallized from ethanol (2.20 g, 62%), m.p. 180-182 °C; $[\alpha]_D$ +54° (*c* 1, dichloromethane); R_f 0.47 (3:1 ether-hexane); υ_{max} 1747 cm^{-1} (CO); NMR data: ^1H, δ 2.04-2.19 (5s, 15H, 5OAc), 3.71 (s, 3H, OMe), 3.82 (dd, 1H, $J_{4',5''}$ 7.5, $J_{5',5''}$ -11.7 Hz, H-5''), 4.31 (dd, 1H, $J_{4',5'}$ 4.6 Hz, H-5'), 4.50 (d, 1H, H-4), 4.98 (t, 1H, $J_{4,5}$ 5.6, $J_{5,1'}$ 5.8 Hz, H-5), 5.23 (m, 1H, $J_{3',4'}$ 2.0 Hz, H-4'), 5.27 (dd, 1H, $J_{2',3'}$ 9.9 Hz, H-3'), 5.40 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-1'), 5.62 (dd, 1H, H-2'), 7.38-7.82 (m, 5H, Ph). ^{13}C, δ 20.5-20.6 (Me), 53.0 (OMe), 55.5 (C-4), 62.3 (C-5'), 67.9-69.8 (C-1'/4'), 84.0 (C-5), 127.0-130.6 (Ph), 154.0 (C-3), 169.0-170.3 (OAc/CO_2Me). Anal. Calcd for $C_{26}H_{31}NO_{13}$: C, 55.22; H, 5.53; N, 2.48. Found: C, 54.88; H, 5.44; N, 2.14.

***(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-4-methoxycarbonyl-3-(2,4,6-trimethylphenyl)-2-isoxazoline (11)*.-** Treatment of **3** (1.00 g, 2.24 mmol) with mesitonitrile oxide (0.36 g, 2.24 mmol) as described in the preparation of **7** gave **11**. Recrystallized from ethanol (0.93 g, 68%), m.p. 183-185 °C; $[\alpha]_D$ +136° (*c* 1, dichloromethane); R_f 0.70 (1:4 ethyl acetate-dichloromethane); υ_{max} 1752 cm^{-1} (CO); NMR data: ^1H, δ 2.04, 2.08 (2s, 9H, Me-Ar), 2.11-2.28 (5s, 15H, 5OAc), 3.56 (s, 3H, OMe), 3.83 (dd, 1H, $J_{4',5''}$ 7.4, $J_{5',5''}$ -11.7 Hz, H-5''), 4.32 (dd, 1H, $J_{4',5'}$ 4.7 Hz, H-5'), 4.44 (d, 1H, H-4), 5.09 (dd, 1H, $J_{4,5}$ 7.1, $J_{5,1'}$ 6.5 Hz, H-5), 5.24 (m, 1H, $J_{3',4'}$ 1,8 Hz, H-4'), 5.26 (dd, 1H, $J_{2',3'}$ 9.7 Hz, H-3'), 5.48 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-1'), 5.63 (dd, 1H, H-2'), 6.87 (s, 2H, Mes ring). ^{13}C, δ 19.7-20.9 (Me), 52.6 (OMe), 58.5 (C-4), 62.2 (C-5'), 67.8-69.4

(C-1'/4'), 82.4 (C-5), 123.9-139.1 (Mes ring), 153.8 (C-3), 168.0-170.2 (OAc/CO_2Me). Anal. Calcd for $C_{29}H_{37}NO_{13}$: C, 57.33; H, 6.14; N, 2.31. Found: C, 57.26; H, 6.25; N, 2.14.

(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-4-ethoxycarbonyl-3-phenyl-2-isoxazoline (12).- It was prepared from **4** (0.46 g, 1.00 mmol) and benzohydroximoyl chloride (0.15 g, 1.00 mmol) as described in the preparation of **6**. Recrystallized from ethanol (0.33 g, 57%), m.p. 174-176 °C; $[\alpha]_D$ +49° (*c* 1, dichloromethane); R_f 0.56 (3:1 ether-hexane); υ_{max} 1747 cm^{-1} (CO); NMR data: ^{1}H, δ 0.97 (t, 3H, Et), 2.05-2.24 (5s, 15H, 5OAc), 3.84 (dd, 1H, $J_{4',5'}$ 7.5, $J_{5',5''}$ -11.7 Hz, H-5''), 4.13 (q, 2H, Et), 4.33 (dd, 1H, $J_{4',5'}$ 4.7 Hz, H-5'), 4.46 (d, 1H, H-4), 5.10 (t, 1H, $J_{4,5} = J_{5,1'}$ = 5.7 Hz, H-5), 5.31 (m, 1H, $J_{3',4'}$ 1.9 Hz, H-4'), 5.42 (dd, 1H, $J_{2',3'}$ 9.9 Hz, H-3'), 5.50 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-1'), 5.65 (dd, 1H, H-2'), 7.30-7.70 (m, 5H, Ph). ^{13}C, δ 13.8 (Et), 20.4-20.5 (Me), 55.9 (C-4), 62.1 (Et), 62.3 (C-5'), 68.0-70.0 (C-1'/4'), 84.0 (C-5), 127.1-130.4 (Ph), 154.0 (C-3), 169.3-170.1 (OAc/CO_2Et). Anal. Calcd for $C_{27}H_{33}NO_{13}$: C, 55.96; H, 5.74; N, 2.42. Found: C, 56.15; H, 5.71; N, 2.27.

(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-4-ethoxycarbonyl-3-(2,4,6-trimethylphenyl)-2-isoxazoline (13).- It was prepared from **4** (1.70 g, 3.69 mmol) and mesitonitrile oxide (0.59 g, 3.66 mmol) as described in the preparation of **7**. Recrystallized from ethanol (1.68 g, 73%), m.p. 176-178 °C; $[\alpha]_D$ +138° (*c* 1, dichloromethane); R_f 0.80 (1:4 ethyl acetate-dichloromethane); υ_{max} 1748 cm^{-1} (CO); NMR data: ^{1}H, δ 1.16 (t, 3H, Et), 2.04, 2.08 (2s, 9H, Me-Ar), 2.10-2.19 (5s, 15H, 5OAc), 3.82 (dd, 1H, $J_{4',5'}$ 7.4, $J_{5',5''}$ -11.6 Hz, H-5''), 4.15 (q, 2H, Et), 4.31 (dd, 1H, $J_{4',5'}$ 4.7 Hz, H-5'), 4.48 (d, 1H, H-4), 4.97 (dd, 1H, $J_{4,5}$ 6.3, $J_{5,1'}$ 7.1 Hz, H-5), 5.25 (m, 1H, $J_{3',4'}$ 1.9 Hz, H-4'), 5.27 (dd, 1H, $J_{2',3'}$ 9.7 Hz, H-3'), 5.41 (dd, 1H, $J_{1',2'}$ 2.1 Hz, H-1'), 5.63 (dd, 1H, H-2'), 6.87 (s, 2H, Mes ring). ^{13}C, δ 13.5 (Et), 19.6-20.9 (Me), 58.6 (C-4), 61.8 (Et), 62.2 (C-5'), 67.9-69.6 (C-1'/4'), 82.3 (C-5), 123.4-139.1 (Mes ring), 154.0 (C-3), 166.9-170.5 (OAc/CO_2Et). Anal. Calcd. for $C_{30}H_{39}NO_{13}$: C, 57.96; H, 6.32; N, 2.25. Found: C, 57.60; H, 6.60; N, 2.58.

(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-bromo-4-ethoxycarbonyl-2-isoxazoline (14) and (4R,5S)-4-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-bromo-5-ethoxycarbonyl-2-isoxazoline (21).- A solution of **4** (0.92 g, 2.00 mmol) in ethyl acetate (15 ml) was added to an excess of bromoformonitrile [prepared from dibromoformaldoxime (1.22 g, 6 mmol) and an excess of potassium hydrogen carbonate] and the mixture was stirred at room temperature for 24 h. The salts were filtered off, and the filtrate was evaporated under diminished pressure to a solid that was crystallized from ethanol. This solid consisted in a 1:2 mixture of **14** and **21** that could not be resolved (0.93 g, 80%). NMR data: major product **14**, ^{1}H, δ 1.30 (t, 3H, Et), 2.02-2.16 (5s, 15H, 5OAc), 3.80 (dd, 1H, $J_{4',5'}$ 7.3, $J_{5',5''}$ -11.7 Hz, H-5''), 4.22 (q, 2H, Et), 4.25 (d, 1H, $J_{4,5}$ 3.4 Hz, H-4), 4.28 (dd, 1H, $J_{4',5'}$ 5.1 Hz, H-5'), 4.95 (dd, 1H, $J_{5,1'}$ 6.7 Hz, H-5), 5.20 (m, 1H, $J_{3',4'}$ 1.8 Hz, H-4'), 5.25 (dd, 1H, $J_{2',3'}$ 9.8 Hz, H-3'), 5.45 (dd, 1H, $J_{1',2'}$ 2.5 Hz, H-2'), 5.58 (dd, 1H, H-1'). ^{13}C, δ 14.0 (Et), 20.2-20.9 (Me), 59.8 (C-4), 62.0 (Et), 62.2 (C-5'), 67.3 (C-2'), 67.5 (C-3'), 67.7 (C-4'), 69.7 (C-1'), 83.9 (C-5), 123.4 (C-3), 168.4-170.4 (OAc/CO_2Et); minor product **21**, ^{1}H, δ 1.31 (t, 3H, Et), 2.02-2.16 (5s, 15H, 5OAc), 3.72 (dd, 1H, $J_{4,5}$ 3.9, $J_{4,1'}$ 1.0 Hz, H-4), 3.80 (dd, 1H, $J_{4',5'}$ 7.3, $J_{5',5''}$ -11.7 Hz, H-5''), 4.22

(q, 2H, Et), 4.28 (dd, 1H, $J_{4',5'}$ 5.1 Hz, H-5'), 5.15 (d, 1H, H-5), 5.20 (m, 1H, $J_{3',4'}$ 1.8 Hz, H-4'), 5.25 (dd, 1H, $J_{2',3'}$ 9.8 Hz, H-3'), 5.45 (dd, 1H, $J_{1',2'}$ 2.5 Hz, H-2'), 5.58 (dd, 1H, H-1'). ^{13}C, δ 14.0 (Et), 20.2-20.9 (Me), 59.0 (C-4), 62.0 (Et), 62.2 (C-5'), 67.3 (C-2'), 67.5 (C-3'), 67.7 (C-4'), 69.7 (C-1'), 78.8 (C-5), 138.8 (C-3), 168.4-170.4 (OAc/CO_2Et). Anal. Calcd for $C_{21}H_{28}NO_{13}Br$: C, 43.31; H, 4.85; N, 2.41. Found: C, 43.62; H, 4.88 ; N, 2.41.

(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-4-methoxycarbonyl-3-methyl-2-isoxazoline (15).- A solution of acetaldoxime (0.23 g, 3.90 mmol) in pyridine (0.05 ml) was added to a suspension of *N*-chlorosuccinimide (NCS, 0.52 g, 3.90 mmol) in dichloromethane (3 ml) and the mixture was stirred at room temperature until the NCS was dissolved. Then a solution of **3** (0.35 g, 0.78 mmol) in toluene (25 ml) was added, followed by a slow addition (2 h) of another solution of triethylamine (0.80 ml, 5.50 mmol) in toluene (5 ml). The mixture was stirred at room temperature for 48 h, then concentrated. Column chromatography (3:1 ether-hexane) of the residue gave crystalline**15**. Recrystallized from ethanol (0.25 g, 62 %), m.p. 150-152 °C; $[\alpha]_D$ +188° (*c* 1, dichloromethane); R_f 0.46 (1:1 ethyl acetate-carbon tetrachloride); υ_{max} 1749 cm^{-1} (CO); NMR data: ^{1}H, δ 2.02 (s, 3H, MeC=N), 2.05-2.11 (5s, 15H, 5OAc), 3.77 (s, 3H, OMe), 3.80 (dd, 1H, $J_{4',5'}$ 7.2, $J_{5',5''}$ -11.6 Hz, H-5''), 3.95 (da, 1H, $J_{Me,4} < 0.5$, $J_{4,5}$ 6.5 Hz, H-4), 4.30 (dd, 1H, $J_{4',5'}$ 4.9 Hz, H-5'), 4.83 (t,1H, $J_{5,1'}$ 6.5 Hz, H-5), 5.10-5.20 (m,2H,H-3'/4'), 5.25 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-1'), 5.55 (dd, 1H, $J_{2',3'}$ 9.7 Hz, H-2'). ^{13}C, δ 12.0 (MeC=N), 20.5-20.6 (Me), 52.9 (OMe), 58.1 (C-4), 62.1 (C-5'), 67.2 (C-2'), 67.3 (C-4'), 67.5 (C-3'), 69.2 (C-1'), 81.4 (C-5), 152.3 (C-3), 168.1-170.3 (OAc/CO_2Me). Anal. Calcd. for $C_{21}H_{29}NO_{13}Br$: C, 50.10; H, 5.81; N, 2.78. Found: C, 50.45; H, 5.88; N, 2.58.

(4S,5S)-5-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-4-ethoxycarbonyl-3-methyl-2-isoxazoline (16).- The procedure described above in the preparation of **15** was used from **4** (0.36 g, 0.78 mmol) to give **16** (0.26 g, 65 %); m.p. 126-128 °C; $[\alpha]_D$+165° (*c* 1, dichloromethane); R_f 0.61 (1:1 ethyl acetate-carbon tetrachloride); υ_{max} 1748 cm^{-1} (CO); NMR data: ^{1}H, δ 1.25 (t, 3H, Et), 1.95 (s, 3H, MeC=N), 2.05-2.10 (5s, 15H, 5OAc), 3.80 (dd, 1H, $J_{4',5'}$ 7.4, $J_{5',5''}$ -11.7 Hz, H-5''), 3.93 (dq, 1H, $J_{4,5}$ 6.6 $J_{Me,4}$ 1.0 Hz, H-4), 4.22 (q, 2H, Et), 4.27 (dd, 1H, $J_{4',5'}$ 4.9 Hz, H-5'), 4.82 (t, 1H, $J_{5,1'}$ 6.6 Hz, H-5), 5.19 (m, 1H, $J_{3',4'}$ 2.0 Hz, H-4'), 5.23 (dd, 1H, $J_{2',3'}$ 9.9 Hz, H-3'), 5.25 (dd, 1H, H-1'), 5.50 (dd, 1H, $J_{1',2'}$ 2.0 Hz, H-2'),. ^{13}C, δ 12.1 (MeC=N), 14.0 (Et), 20.6-20.7 (Me), 58.4 (C-4), 62.0 (Et), 62.2 (C-5'), 67.2/69.3 (C-1'/4'), 81.4 (C-5), 152.4 (C-3), 167.6-170.4 (OAc/CO_2Et). Anal. Calcd for $C_{22}H_{31}NO_{13}$: C, 51.06; H, 6.04; N, 2.71. Found: C, 51.55 ; H, 6.15 ; N, 2.55.

(4R,5S)-5-Acetyl-4-(penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-bromo-2-isoxazoline (18) .- Treatment of **2** (0.86 g, 2.00 mmol) with an excess of bromoformonitrile oxide (3:1) for 18 h, as described in the preparation of **14**, and crystallization of the product from ethanol gave **18** (0.81 g, 73 %); m.p. 158-160 °C; $[\alpha]_D$+164° (*c* 1, dichloromethane); R_f 0.60 (3:1 ether-hexane); υ_{max} 1750 cm^{-1} (CO); NMR data: ^{1}H, δ 2.01-2.12 (5s, 15H, 5OAc), 2.31 (s, 3H, MeCO), 3.69 (dd, 1H, $J_{4,5}$ 3.9, $J_{4,1'}$ 1.0 Hz, H-4), 3.81 (dd, 1H, $J_{4',5'}$ 7.2, $J_{5',5''}$ -11.6 Hz, H-5''), 4.27 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 5.09 (d, 1H, H-5), 5.17 (m, 1H, $J_{3',4'}$ 1.9 Hz, H-4'),

5.32 (dd, 1H, $J_{2',3'}$ 9.8 Hz, H-3'), 5.45 (dd, 1H, $J_{1',2'}$ 2.6 Hz, H-2'), 5.53 (dd, 1H, H-1'). ^{13}C, δ 20.2-20.6 (Me), 26.3 (MeCO), 56.9 (C-4), 61.8 (C-5'), 65.8 (C-4'), 67.2 (C-3'), 67.9 (C-2'), 69.1 (C-1'), 85.0 (C-5), 139.0 (C-3), 169.3-170.3 (OAc), 205.8 (CO). Anal. Calcd for $C_{20}H_{26}NO_{12}Br$: C, 43.49; H, 4.74; N, 2.54. Found: C, 43.41; H, 4.89; N, 2.41.

(4R,5S)-5-Acetyl-4-(penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-methyl-2-isoxazoline (19) .- A solution of **2** (0.33g, 0.78 mmol) in toluene (25 ml) was treated with acetaldoxime (0.23 g, 3.90 mmol) for 36 h as described in the preparation of **15**. Evaporation of the solvents and column chromatography (2:1 ether-hexane) of the residue afforded **19** (0.23 g) as a syrup contaminated by a small proportion of the isoxazole **23**. NMR data: **19**, ^{1}H, δ 1.98 (s, 3H, MeC=N), 2.03-2.26 (5s, 15H, 5OAc), 2.48 (s, 3H, MeCO), 3.45 (da, 1H, $J_{4,5}$ 3.6, $J_{4,1'}$ < 1.0 Hz, H-4), 3.81 (dd, 1H, $J_{4',5''}$ 7.2, $J_{5',5''}$ -11.6 Hz, H-5''), 4.30 (dd, 1H, $J_{4',5'}$ 5.2 Hz, H-5'), 4.98 (d, 1H, H-5), 5.15 (m, 1H, $J_{3',4'}$ 1.8 Hz, H-4'), 5.35 (dd, 1H, $J_{2',3'}$ 9.9 Hz, H-3'), 5.50 (dd, 1H, $J_{1',2'}$ 1.9 Hz, H-2'), 5.60 (d, 1H, H-1'). ^{13}C, δ 12.5 (MeC=N), 20.4-20.8 (Me), 30.4 (MeCO), 55.1 (C-4), 61.9 (C-5'), 65.9-68.2 (C-1'/4'), 84.1 (C-5), 155.7 (C-3), 169.7-171.2 (OAc), 192.1 (CO).

***(4R,5S)-4-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-bromo-5-methoxycarbonyl-2-isoxazoline (20)*.-** A solution of **3** (0.89 g, 2.00 mmol), in ethyl acetate (15 ml) was treated with bromoformonitrile oxide for 24 h as described in the preparation of **14**. Evaporation of the solvents and crystallization from ethanol gave **20** (0.85 g, 75 %); m.p. 143-145 °C; $[\alpha]_D$ +124° (*c* 1, dichloromethane); R_f 0.36 (3:1 ether-hexane); υ_{max} 1750 cm^{-1} (CO); NMR data: ^{1}H, δ 2.02-2.12 (5s, 15H, 5OAc), 3.69 (dd, 1H, $J_{4,5}$ 3.9, $J_{4,1'}$ 1.1 Hz, H-4), 3.78 (s, 3H, OMe), 3.80 (dd, 1H, $J_{4',5''}$ 7.3, $J_{5',5''}$ -11.7 Hz, H-5''), 4.27 (dd, 1H, $J_{4',5'}$ 4.9 Hz, H-5'), 5.20 (m, 1H, $J_{3',4'}$ 1.8 Hz, H-4'), 5.23 (d, 1H, H-5), 5.31 (dd, 1H, $J_{2',3'}$ 9.8 Hz, H-3'), 5.50 (dd, 1H, $J_{1',2'}$ 2.6 Hz, H-2'), 5.55 (dd, 1H, H-1'). ^{13}C, δ 20.2-20.9 (Me), 53.1 (OMe), 59.1 (C-4), 61.9 (C-5'), 65.3 (C-4'), 67.2 (C-3'), 67.6 (C-2'), 69.7 (C-1'), 78.5 (C-5), 138.3 (C-3), 169.9-170.3 (OAc/CO_2Me). Anal. Calcd for $C_{20}H_{26}NO_{13}Br$: C, 42.27; H, 4.61; N, 2.46. Found: C, 42.52; H, 4.72; N, 2.32.

***4-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-bromoisoxazole (22)*.-** A solution of **1** (0.87 g, 2.00 mmol) in ethyl acetate was treated with bromoformonitrile oxide for 4 days, as described in the preparation of **14**. Evaporation of the solvents and column chromatography (2:1 ether-hexane) of the syrupy residue gave crystalline **22** (0.48 g, 47 %). Recrystallized from ethanol, m.p. 157-159 °C; $[\alpha]_D$ +28° (*c* 1, dichloromethane); R_f 0.41 (3:1 ether-hexane); λ_{max} 220 nm (ε_{mM} 3.52); υ_{max} 1749 cm^{-1} (CO); NMR data: ^{1}H, δ 1.99-2.14 (5s, 15H, 5OAc), 3.85 (dd, 1H, $J_{4',5''}$ 7.3, $J_{5',5''}$ -11.6 Hz, H-5''), 4.30 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 5.20-5.50 (m, 3H, H-2'/4'), 5.89 (d, 1H, $J_{1',2'}$ 1.8 Hz, H-1'), 8.27 (s, 1H, H-5). ^{13}C, δ 20.5-20.7 (Me), 62.0 (C-5'), 64.5 (C-4'), 68.0 (C-3'), 68.1 (C-2'), 68.6 (C-1'), 117.7 (C-4), 139.4 (C-3), 158.1 (C-5), 168.9-170.2 (OAc). Anal. Calcd for $C_{18}H_{22}NO_{11}Br$: C, 42.53; H, 4.36; N, 2.67. Found: C, 42.68;H, 4.29; N, 2.63.

***4-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl)-3-methylisoxazole (23)*.-** A solution of **1** (0.34g, 0.78 mmol) in toluene (25 ml) was treated with acetaldoxime (0.23 g, 3.90 mmol) for 5 days, as described in the preparation of **15**. Evaporation of the solvents and column chromatography (1:1 ether-hexane) gave **23** as a syrup (0.17 g, 46%); $[\alpha]_D$ +11° (*c* 1, dichloromethane); R_f 0.49 (3:1 ether-hexane); λ_{max} 259 (ε_{mM} 4.44) and

210 nm (ε_{mM} 6.98); υ_{max} 1743 cm^{-1} (CO); NMR data: ^1H, δ 2.00-2.22 (5s, 15H, 5OAc), 2.54 (s, 3H, MeC=N), 3.92 (dd, 1H, $J_{4',5''}$ 7.5, $J_{5',5''}$ -11.5 Hz, H-5''), 4.31 (dd, 1H, $J_{4',5'}$ 5.1 Hz, H-5'), 5.41 (m, 1H, $J_{3',4'}$ 2.0 Hz, H-4'), 5.52 (dd, 1H, $J_{1',2'}$ 1.6 Hz, H-2'), 5.62 (dd, 1H, $J_{2',3'}$ 10.0 Hz, H-3'), 6.36 (d, 1H, H-1'), 7.26 (s, 1H, H-5). ^{13}C, δ 11.3 (MeC=N), 20.1-20.6 (Me), 61.9 (C-5'), 66.1-67.5 (C-1'/4'), 113.9 (C-4), 129.8 (C-3), 155.7 (C-5), 167.9-170.4 (OAc). Anal. Calcd for $C_{19}H_{25}NO_{11}$: C, 51.47; H, 5.68; N, 3.16. Found: C, 51.95; H, 6.25; N, 3.02.

***4-(Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl*)-5-methyl-3-(2,4,6-trimethylphenyl)isoxazole (24) and 5-(*Penta*-O-*acetyl*-D-galacto-*pentitol-1-yl*)-4-methyl-3-(2,4,6-trimethylphenyl)isoxazole (25).**-To a solution of **5** (2.00 g, 4.47 mmol) in dichloromethane (15 ml) was added another solution of mesitonitrile oxide (1.44 g, 8.94 mmol) in dichloromethane (10 ml), and the mixture was heated under reflux for a long time (2 months). Evaporation of the solvent and column chromathography (1:1 ether-hexane) allowed the isolation of **24** (0.30 g, 12%) and **25** (0.35 g,14%) that were recrystallized from ethanol.Compound **24**, m.p. 140-142 °C; $[\alpha]_D$ +19° (*c* 1, dichloromethane); R_f 0.50 (3:1 ether-hexane); λ_{max} 209 nm (ε_{mM} 7.82); υ_{max} 1752 cm^{-1} (CO); NMR data: ^1H, δ 1.78, 1.99 (2s, 9H, Me-Ar), 2.02-2.13 (5s, 15H, 5OAc), 2.47 (s, 3H, Me-C_5), 3.71 (dd, 1H, $J_{4',5''}$ 7.4, $J_{5',5''}$ -11.6 Hz, H-5''), 4.16 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 4.99 (dd, 1H, $J_{2',3'}$ 9.7 Hz, H-2'), 5.13 (m, 1H, $J_{3',4'}$ 2.0 Hz, H-4'), 5.21 (dd, 1H, H-3'), 5.40 (d, 1H, $J_{1',2'}$ 1.7 Hz, H-1'), 6.93 (s, 2H, Mes ring). ^{13}C, δ 12.1 (Me-C_5), 19.7-21.0 (Me), 61.9 (C-5'), 64.4-70.0 (C-1'/4'), 110.9 (C-4), 123.9-138.9 (Mes ring), 161.0 (C-3), 167.6 (C-5), 168.8-170.4 (OAc). Anal. Calcd for $C_{28}H_{35}NO_{11}$: C, 59.88; H, 6.28; N, 2.49. Found: C, 60.28; H, 6.22; N, 2.28.

Compound **25**, 160-162 °C; $[\alpha]_D$ +45° (*c* 1, dichloromethane); R_f 0.60 (3:1 ether-hexane); λ_{max} 206 nm (ε_{mM} 6.92); υ_{max} 1749 cm^{-1} (CO); NMR data: ^1H, δ 1.78, 1.97 (2s, 9H, Me-Ar), 2.05-2.14 (5s, 15H, 5OAc), 2.30 (s, 3H, Me-C_4), 3.87 (dd, 1H, $J_{4',5''}$ 7.4, $J_{5',5''}$ -11.6 Hz, H-5''), 4.29 (dd, 1H, $J_{4',5'}$ 5.0 Hz, H-5'), 5.31-5.38 (m, 1H, $J_{3',4'}$ 1.7 Hz, H-4'), 5.49 (dd, 1H, $J_{1',2'}$ 2.0 Hz, H-2'), 5.56 (dd, 1H, $J_{2',3'}$ 9.7 Hz, H-3'), 6.08 (d, 1H, H-1'), 6.89 (s, 2H, Mes ring). ^{13}C, δ 6.6 (Me-C_4), 19.6-21.0 (Me), 62.0 (C-5'), 65.1 (C-1'), 67.6 (C-4'), 67.7 (C-3'), 68.5 (C-2'), 112.6 (C-4), 124.5-138.9 (Mes ring), 160.7 (C-3), 163.4 (C-5), 168.9-170.4 (OAc). Anal. Calcd for $C_{28}H_{35}NO_{11}$: C, 59.88; H, 6.28; N, 2.49. Found: C, 60.32; H, 6.09; N, 2.13.

***(4* S, *5*S)-*5-(D*-galacto-*pentitol-1-yl*)--*3-(2,4,6-trimethylphenyl)-4-nitro-2-isoxazoline*(26).**- A suspension of **7** (2.00 g, 3.37 mmol) in absolute methanol (75 ml) was treated with a 2N solution of sodium methoxide in methanol (0.1 ml). After 2 h at room temperature, the solution was neutralized with Amberlite IR 120 (H^+), the resin was filtered off and washed with methanol. The combined filtrate and washings were concentrated under diminished pressure to a solid residue that was crystallized from ethanol (1.15 g, 89 %); m.p. 162-164 °C; $[\alpha]_D$ +190° (*c* 1, pyridine); R_f 0.45 (7:1 dichloromethane-methanol); υ_{max} 3340 (OH), 1563 and1364 cm^{-1} (NO_2); NMR data: ^1H, δ 2.12, 2.22 (2s, 9H, Me-Ar), 3.36-3.57 (m, 5H, H-2'/5''), 3.60-5.00 (m, 5H, 5OH), 4.10 (dd, 1H, $J_{5,1'}$ 4.5, $J_{1',2'}$ 2.4 Hz, H-1'), 5.44 (t, 1H, $J_{4,5}$ 5.0 Hz, H-5), 6.52 (d, 1H, H-4), 6.93 (s, 2H, Mes ring),. ^{13}C, δ 19.4-21.0 (Me), 63.1 (C-5'), 68.0-70.5 (C-1'/4'), 87.6 (C-4), 95.1 (C-5), 122.6-139.9 (Mes ring), 151.3 (C-3). Anal. Calcd for $C_{17}H_{24}N_2O_8$: C, 53.12; H, 6.25; N, 7.29. Found: C, 52.94; H, 6.38; N, 7.00.

***(4S, 5S)-4-Acetyl-3-(2,4,6-trimethylphenyl)-5-(D-galacto-pentitol-1-yl)-2-isoxazoline* (27).-** Compound **9** (0.25 g, 0.42 mmol) was treated in the same way that we described above for **7**. The methanolic solution was evaporated and column chromatography of the residue (10:1 dichloromethane-methanol) gave **27**. Recrystallized from ethanol (0.12 g, 72 %); m.p. 159-161 °C ; $[\alpha]_D$ +135° (*c* 1, pyridine); R_f 0.49 (7:1 dichloromethane-methanol); υ_{max} 3348 (OH), 1719 cm^{-1} (CO); NMR data: ^1H, δ 1.78 (s, 3H, MeCO), 2.08, 2.26 (2s, 9H, Me-Ar), 3.37-3.46 (m, 5H, H-2'/5"), 3.50-3.70 (m, 5H, 5OH), 4.02 (d, 1H, $J_{5,1'} = J_{1',2'}$ = 1.3 Hz, H-1'), 4.95 (s, 2H, H-4/5), 6.93 (s, 2H, Mes ring). ^{13}C, δ 19.5-20.6 (Me), 30.7 (MeCO), 63.2 (C-5'), 64.0 (C-4), 67.0-70.2 (C-1'/4'), 85.8 (C-5), 125.5-138.6 (Mes ring), 153.7 (C-3), 203.1 (CO). Anal. Calcd for $C_{19}H_{27}NO_7$. H_2O: C, 57.08; H, 7.26; N, 3.50. Found: C, 57.48; H, 6.91; N, 3.11.

***3-Bromo-4-(D-galacto-pentitol-1-yl)isoxazole* (28).-** It was prepared from **22** (0.20 g, 0.39 mmol) as described above for **27**. El isoxazole **28** was an oil (0.10 g, 87 %), $[\alpha]_D$ +10° (*c* 1, pyridine); R_f 0.34 (7:1 dichloromethane-methanol); λ_{max} 271 nm (ε_{mM} 0.71) and 217nm (ε_{mM} 5.01); υ_{max} 3453 cm^{-1} (OH); NMR data: ^{13}C, δ 63.2 (C-5'), 63.5-71.5 (C-1'/4'), 123.3 (C-4), 140.4 (C-3), 159.8 (C-5). Anal. Calcd for $C_8H_{12}NO_6Br$: C, 32.23; H, 4.06; N, 4.70. Found: C, 32.27; H, 4.43; N, 4.27.

***(3aR, 6S, 6aS)-4-Oxo-6-(D-lyxo-tetritol-1-yl)-3-(2,4,6-trimethylphenyl)tetrahydrofuro[3,4-d]2-isoxazoline* (29).-** It was obtained in quantitative yield from **11** (2.00 g, 3.29 mmol) or **13** (2.00 g, 3.22) as we described above for **7**. Recrystallized from ethanol m.p. 168-170 °C; $[\alpha]_D$ +6° (*c* 1, pyridine); R_f 0.53 (7:1 dichloromethane-methanol); υ_{max} 3382 (OH), 1760 cm^{-1} (CO); NMR data: ^1H, δ 2.12, 2.25 (2s, 9H, Me-Ar), 3.38-3.47 (m, 3H, H-2', H-4' y H-4"), 3.68 (m, 1H, $J_{3',OH}$ 6.7 Hz, H-3'), 3.82 (ddd, 1H, $J_{1',6}$ 0.5, $J_{1',2'}$ 9.5, $J_{1',OH}$ 6.5 Hz, H-1'), 4.28 (d, 1H, OH-3'), 4.50 (t, 1H, OH-4'), 4.58 (d, 1H, $J_{2',OH}$ 7.9Hz, OH-2'), 4.63 (d, 1H, $J_{3a,6a}$ 9.2 Hz, H-3a), 5.05 (q, 1H, $J_{6,6a}$ 1.2 Hz, H-6), 5.40 (d 1H, OH-1'), 5.53 (dd, 1H, H-6a), 6.94 (s, 2H, Mes ring). ^{13}C, δ 20.1-21.6 (Me), 58.7 (C-3a), 63.3 (C-4'), 69.7 (C-2'), 70.0 (C-3'), 70.3 (C-1'), 85.7 (C-6a), 86.7 (C-6), 124.1, 129.5, 137.9, 140.5 (Mes ring), 154.0 (C-3), 172.1 (CO). Anal. Calcd for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.30; N, 3.83. Found: C, 59.02; H, 6.36; N, 3.75.

***(3aR, 6S, 6aS)-4-Oxo-3-phenyl-6-(D-lyxo-tetritol-1-il)tetrahydrofuro[3,4-d]2-isoxazoline* (30).-** It was obtained from **10** (1.20 g, 2.12 mmol) as a syrup (0.63 g, 91 %) as we described above. $[\alpha]_D$ +20° (*c* 1, pyridine); R_f 0.51 (7:1 dichloromethane-methanol); υ_{max} 3357 (OH), 1765 cm^{-1} (CO); NMR data: ^1H, δ 4.95 (d, 1H, $J_{3a,6a}$ 9.0 Hz, H-3a), 5.09 (bs, 1H, $J_{6,6a} \sim J_{6,1'} \sim 0$ Hz, H-6), 5.47 (d, 1H, H-6a), 7.50-7.80 (m, 5H, Ph). ^{13}C, δ 54.1 (C-3a), 62.6 (C-4'), 68.7-69.3 (C-1'/C-3'), 84.8 (C-6a), 86.8 (C-6), 126.8, 127.7, 128.9, 130.9 (Ph), 153.5 (C-3), 171.6 (CO). Anal. Calcd for $C_{15}H_{17}NO_7$ .1/2 H_2O: C, 54.22; H, 5.42; N, 4.22. Found: C, 54.09; H, 5.67; N, 3.92.

***(3aR, 4S, 6aR)-3-Bromo-6-oxo-4-(D-lyxo-tetritol-1-yl)tetrahydrofuro[4,3-d]2-isoxazoline* (31).-** It was obtained from **10** (0.20 g, 0.35 mmol) as a syrup (0.10 g, 85 %) as we described above. $[\alpha]_D$ +28° (*c* 1, pyridine); R_f 0.45 (7:1 dichloromethane-methanol); υ_{max} 3372 (OH), 1750 cm^{-1} (CO); NMR data: ^1H, δ 3.75

(d, 1H, $J_{3a,6a}$ 8.0 Hz, H-3a), 4.18 (bs, 1H, $J_{4,3a} \sim J_{4,1'} \sim 0$ Hz, H-4), 5.29 (d, 1H, H-6a), 3.50-4.50 (m, 9H, side chain). ^{13}C, δ 60.7 (C-3a), 62.3 (C-4'), 68.9-72.6 (C-1'/ C-3'), 78.9 (C-6a), 79.8 (C-4), 141.9 (C-3), 169.2 (CO). Anal. Calcd for $C_9H_{12}NO_7$: C, 33.15; H, 3.71; N, 4.30. Found: C, 32.88; H, 3.47; N, 4.02.

(3aR, 6S, 6aS)-6-Formyl-4-oxo-3-(2,4,6-trimethylphenyl-tetrahydrofuro[3,4-d]Δ²-isoxazoline **(32).**- To a solution of **29** (0.20 g, 0.55 mmol) in 1:1 dioxane-water (25 ml), a water solution (10 ml) of sodium metaperyodate (0.47 g, 2.20 mmol) was added and the mixture was stirred at room temperature for 1 h. The inorganic salts were filtered off and the solution was extracted with ether (3 x 30 ml). The combined extracts were dried (sodium sulfate) and evaporated to give solid **32** that was crystallized from ethanol (0.15 g, 90 %); m.p. 136-138 °C; $[\alpha]_D$ +18° (*c* 1, dichloromethane); R_f 0.65 (10:1 dichloromethane-methanol); υ_{max} 3468 (OH), 1766 cm^{-1} (CO); NMR data (Acetone-d_6): ^1H, δ 2.10-2.30 (2s, 9H, Me-Ar), 4.56 (d, 1H, $J_{3a,6a}$ 9.3 Hz, H-3a), 4.67 (dd, 1H, $J_{6,1'}$ 2.7, $J_{6,6a}$ 1.1 Hz, H-6), 5.30 (d, 1H, H-1' hydrated form), 5.68 (dd, 1H, H-6a), 6.90 (s, 2H, Mes ring), 9.75 (s, 1H, H-1' carbonyl form). ^{13}C, δ 19.7-21.0 (Me), 58.4 (C-3a), 82.7 (C-6a), 87.6 (C-6), 89.1 (C-1' hydrated form), 124.6, 129.3, 137.9 , 139.9 (Mes ring), 153.3 (C-3), 171.3 (CO), 198.0 (C-1' carbonyl form). (DMSO-d_6; hydrated form only): ^1H, δ 2.10-2.30 (2s, 9H, Me-Ar), 4.59 (dd, 1H, $J_{6,1'}$ 3.1, $J_{6,6a}$ 1.2 Hz, H-6), 4.65 (d, 1H, $J_{3a,6a}$ 9.4 Hz, H-3a), 5.03 (td, 1H, $J_{1',OH'} = J_{1',OH''} = 5.5$ Hz, H-1'), 5.57 (dd, 1H, H-6a), 6.60 (d, 1H, OH'), 6.61 (d, 1H, OH''), 6.93 (s, 2H, Mes ring). Anal. Calcd for $C_{16}H_{17}NO_5 .1/2H_2O$: C, 61.53; H, 5.81; N, 4.48. Found: C, 61.41; H, 5.97; N, 4.70.

ACKNOWLEDGMENT

We thank the CICYT (Comisión Interministerial de Ciencia y Tecnología) for financial support (Grant MAT93-0555-C02).

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(*Received in UK* 15 *November* 1994; *revised* 10 *April* 1995; *accepted* 12 *April* 1995)