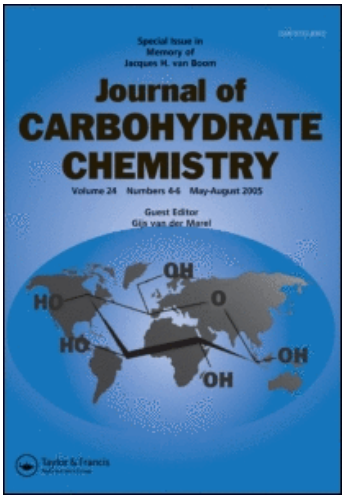

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Synthesis of *C*-Glycosyl Isoxazoles and Branched-Chain Enuloses From 2,3-*O*-Isopropylidene-D-Glyceraldehyde

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SYNTHESIS OF *C*-GLYCOSYL ISOXAZOLES AND BRANCHED-CHAIN ENULOSES FROM 2,3-*O*-ISOPROPYLIDENE-D-GLYCERALDEHYDE

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ABSTRACT

The synthesis of 5-glycosyl isoxazoles with 3-alkyl-, 3-aryl, 3,4-dialkyl, 3-aryl-4-alkyl or 3-alkyl-4-bromo substituents is reported. Deoxyenuloses were obtained from reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde and several phosphorus ylides, which contain a carbonyl group, by a Wittig reaction. *C*-glycosyl α,β-unsaturated ketones were obtained, with the polyhydroxylate chain lengthened by two or three carbon atoms. In the second phase the ketones were transformed into the corresponding *C*-glycosyl α,β-unsaturated ketoximes, leading to the *C*-glycosyl isoxazoles, which were converted into the title compounds via removal of the isopropylidene group of suitably protected carbohydrates. The solubility of the synthetized *C*-glycosyl isoxazoles were modified by free hydroxyl groups in such a way that their behaviour against certain viruses and their potential antiviral activity could be studied.

INTRODUCTION

For a long time, isoxazoles and their derivatives have been common substructures in medicinal and natural product chemistry.[1-3] Moreover, they are precursors of several functional groups by ring modification and cleavage.[4,5] They are generally prepared via dehydrative cyclization of the intermediate monoxime. In the case of unsymmetrical 1,3-diketones, however, this reaction leads to the formation of a mixture of isomers.[6] Another

route to the formation of isoxazoles is the 1,3-dipolar cycloaddition of nitrile oxides to acetylenes.[7] However, with non-symmetrical starting materials, neither of these methods is completely unequivocal with respect to site control and regioselectivity.[8] Only a few methods, such as treatment of acylketene dithioacetalketones with hydroxylamine-hydrochloride in the presence of alkali,[9] via *O*-tributylstannyl aldoximes,[10] cyclization of functionalized propargyloximes,[11] gold (III) catalyzed cycloaddition of nitric acid with alkyne,[12] condensation of carboxylic acid derivatives[13,14] or nitriles[15] with 1,4-dilithium oxime salts[16] lead to 3,5-disubstituted isoxazoles in a regioselective fashion.

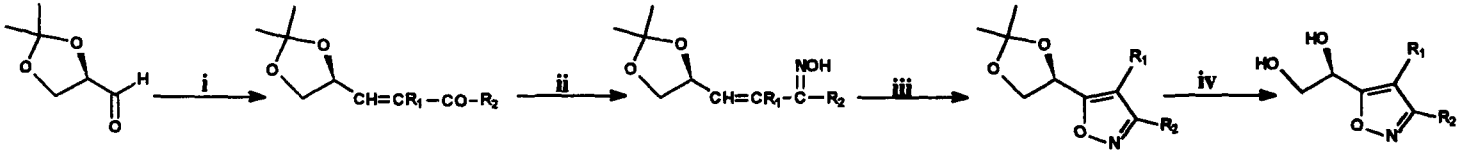
RESULTS AND DISCUSSION

In this paper, we describe the preparation of several *C*-glycosyl isoxazole derivatives from 2,3-*O*-isopropylidene-D-glyceraldehyde, **1**, and different phosphorous ylides in order to continue the research on the synthesis of *C*-glycosyl heterocycles.[17]

Scheme 1 shows the different stages in this process. First, different α,β-unsaturated ketones are formed via the Wittig reaction. Second, these ketones react with hydroxylamine hydrochloride to give the corresponding α,β-unsaturated *C*-glycosyl-oximes. Different *C*-glycosyl isoxazoles are obtained via oxidative cyclization of the monooxime with I_2/KI. Finally, the hydroxyl protecting groups of the *C*-glycosyl isoxazoles are removed. Compound **1** was synthesized through oxidation of 1,2:5,6-di-*O*-isopropylidene-D-mannitol with sodium periodate, in the presence of sodium monohydrogen carbonate.[18] Phosphorus ylides, **2**, **3** and **5**, were synthesized via a traditional route,[19] and **4**, **6** and **7** were synthesized via a two-stage alternative method from monosubstituted phosphorus ylides (see the experimental).

These reactions and the reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) with several phosphoranes have been extensively studied[20] and reported.[21] Reactions of phosphorus ylides with 2,3-*O*-isopropylidene-D-glyceraldehyde were carried out under the conditions of Wittig's reaction,[22] with the polyhydroxylate chain lengthened by two or three carbon atoms leading to the formation of enuloses and branched-chain enuloses.

In the reaction of **1** with acetylmethylenetriphenylphosphorane (**2**), two geometric isomers were obtained. Higher yields were obtained for the *Z*-isomer than for the *E*-isomer



1 **2-7** **8-13** **14-18** **19-22** **22-25**

2 R_1=H, R_2=CH_3	**8,9** R_1=H, R_2=CH_3	**14** R_1=H, R_2=CH_3	**19** R_1=H, R_2=CH_3	**23** R_1=H, R_2=CH_3
3 R_1=R_2=CH_3	**10,11** R_1=R_2=CH_3	**15,15a** R_1=H, R_2=CH_3	**20** R_1=R_2=CH_3	**24** R_1=R_2=CH_3
4 R_1=Br, R_2=CH_3	**12** R_1=Br, R_2=CH_3	**16** R_1=R_2=CH_3	**21** R_1=Br, R_2=CH_3	**25** R_1=Br, R_2=CH_3
5 R_1=CH_3, R_2=C_6H_5	**13** R_1=CH_3, R_2=C_6H_5	**17** R_1=Br, R_2=CH_3	**22** R_1=CH_3, R_2=C_6H_5	
6 R_1=CO_2Et, R_2=CH_3		**18** R_1=CH_3, R_2=C_6H_5		
7 R_1=C_6H_5, R_2=C_6H_5				

Scheme 1. Reagents and conditions: **i**, Ph_3P=CR_1-COR_2, CH_2Cl_2, rt or reflux; **ii**, $HONH_2$·ClH, Pyridine, MeOH, rt or reflux; **iii**, I_2/KI, $NaHCO_3$, THF, reflux; **iv**, AcOH (9:1), 50-90 °C.

(55% and 40% respectively). The explanation may rest with the fact that the phosphorus ylide is more reactive because it is less stabilized by resonance and is less sterically hindered than the rest of the ylides used. Of the two possible betains,[23] the *erythro* stereoisomer predominates and kinetic control might prevail over thermodynamic control as this phosphorus ylide shows the highest reactivity and the steric hindrance is small.[24] In the two isomers **10** and **11**, we found only traces of the *Z*-form isomer, but higher quantities of the *E*-configured isomer (yield 74%). The introduction of a methyl group to the methylene unit, increases the stereoselectivity of the reaction and the amount of *E*-isomer formed.[25,26] When a bromine atom was introduced at this position, only the *E*-configured isomer was isolated (yield 66%).

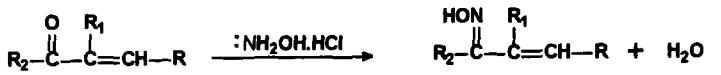
The reaction of **1** with phosphorus ylides **6** and **7** at several temperatures, using different solvents (CH_2Cl_2, $CHCl_3$, THF, C_6H_6) and varying reaction times, did not lead to the formation of the corresponding α,β-unsaturated ketones. The high stability of these ylides might explain their low reactivity, in accordance with data reported in the literature.[24]

In the ^1H NMR spectra of compounds **8**, **9**, **10** and **11**, the chemical shifts of all the protons appeared at lower fields for the *E*-configuration enones than for the *Z* forms, with the exception of one of the diastereotopic hydrogens (CH_2) of the sugar in compounds **8** and **9**, at 4.43 ppm in compound **8** and at 4.21 ppm in its *E* isomer. With respect to the chemical shift of the H-C5 (vicinal to the double bond), for these same compounds moved to lower fields for the *Z*-isomer, 5.34 ppm, than for the **9** isomer, 4.65 ppm. The shift of the olefinic hydrogen in **12** is also higher than for the rest of the ketones due to the presence of a bromine group bonded at C3. This proton appears as a doublet with a small coupling constant J=6.4 Hz.

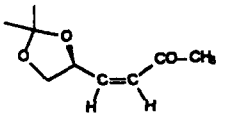
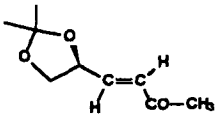
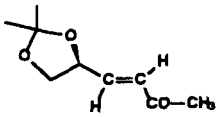
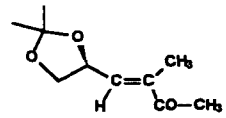
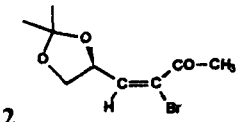
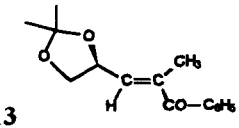
Table 1 shows the ketoximes, **14-18**, obtained from α,β-unsaturated ketones with hydroxylamine hydrochloride, using pyridine as the base.

Only one oxime, **14**, was isolated from **8**, a compound of *Z*-configuration. Its structure was established from ^1H NMR data which showed the coupling constant between the olefinic protons as $J_{3,4}$ = 11.7 Hz with the signals appearing as two double doublets. In the reaction with the *E*-configured isomer **9**, two fractions were separated by chromatography: the one eluting first containing compound **15**, showed that the coupling

TABLE 1. Synthesis of *C*-glycosyl α,β-unsaturated ketoximes from enuloses



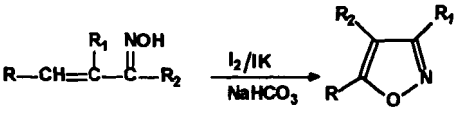
8-13 14-18

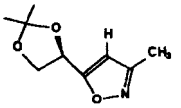
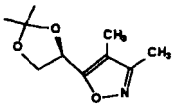
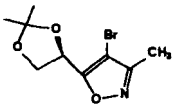
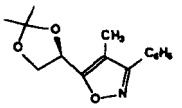
Enuloses	Ketoximes	Yield (%)	$[\alpha]^{25}_D$ ($CHCl_3$)	mp (°C)
 8	14	40	+36.5°, *c* 0.52	syrup
 9	15 (syn)	49	+31.8°, *c* 1.38	syrup
 9	15a (anti)	-	only mixture with 15	-
 11	16	83	+25.5°, *c* 1.09	54.5-56
 12	17	45	+37.8°, *c* 1.07	68-69
 13	18a,18b	60	-	syrup

constant between the two olefinic protons was at $J_{3,4}$=16 Hz. The second fraction was a mixture of two isomers, compound **15** and its corresponding *anti* isomer **15a**.

Only one oxime, **16 or 17**, was isolated from the *E*-configuration enones, **11** and **12**, respectively. The chemical shifts of all the signals from compound **17**, were at lower fields due to the presence of a bromine atom bonded to C-3. A 1:1 mixture (as judged by measuring 4-H, δ 5.50 and 5.41 ppm, respectively) was obtained in the preparation of *syn/anti* oximes **18a** and **18b**.

TABLE 2. Synthesis of *C*-glycosyl isoxazole derivatives by oxidative cyclization



Ketoximes	Isoxazoles (19-22)	Yield (%)[a]	$[\alpha]^{25}_D$ ($CHCl_3$)	Mp (°C)
14 and 15		**70**	**+30.2°, *c* 1.29**	**syrup**
16		**65**	**+9.9°, *c* 1.20**	**syrup**
17		**30**	**-18.8°, *c* 0.80**	**71.5-72**
18		**50**	**-2.1° , *c* 0.95**	**syrup**

a. Isolated product

The ^{1}H NMR spectra showed important differences in the chemical shifts of the two olefinic hydrogens, indicating 6.01 and 6.38 ppm for the first isomer and 6.09 and 7.12 ppm for the same protons of the **15a** isomer, respectively. The elucidation of the spectroscopic differences of these oximes is in progress.

C-glycosyl isoxazoles derivatives **19-22** (Table 2) were formed by oxidative cyclization[27] of the monooximes **14-18**. The protected hydroxyl groups of the *C*-glycosyl isoxazoles obtained were deprotected in a 9:1 mixture of acetic acid and water.[28] The compounds were obtained as solids, easy to recrystallize, in nearly quantitative yields, except the compound **25** (85 %).

Finally, the activity potential of compounds **23** and **24** was tested for six viral strains: *herpes simplex* type I, *herpes simplex* type II, adenovirus, enterovirus (ECHO 4),

cytomegalovirus and respiratory syncytial virus. No antiviral activity was observed for these isoxazoles.

EXPERIMENTAL

General methods. Tetrahydrofuran (THF), benzene and diethyl ether were distilled from sodium using benzophenone radical as an indicator, and stored under argon before use. Other solvents and reagents were purified and dried according to standard procedures. Extracts were dried over anhydrous $MgSO_4$ and solvents evaporated under reduced pressure at 40-50 °C. Reaction progress and product mixtures were routinely monitored by thin-layer chromatography (TLC) on glass plates coated with silica gel G (Merck), spots being visualised with iodine vapours or by charring with sulfuric acid in ethanol (10%). Column chromatography was performed using Silica Gel Merck 60 (70-230 mesh, ASTM). Melting points were obtained in open capillary tubes with a Gallenkamp MFB-595 and are uncorrected. Optical rotations were measured with a 141 Perkin-Elmer. $[\alpha]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}.^{1}H NMR spectra were measured using Bruker AC-80 and AC-300 spectrometers. Chemical shift values are expressed in ppm (δ), relative to Me_4Si as the internal reference. J-values are given in Hz. The ^{13}C NMR spectra were recorded with Bruker AC-80 and AC-300 spectrometers. IR spectra were measured using a Nicolet FTIR-20-SX spectrometer. Mass spectra were recorded by the direct-insertion technique, using an HP-588-A spectrometer at 70 eV with a temperature source of 200 °C. Elemental analyses were determined with a Carlo Erba Elemental Analyzer 1106.

Synthesis of phosphorus ylides:

Acetylmethylenetriphenylphosphorane and **(1-Acetylethylidene)triphenylphosphorane (2)** and **(3)**, were prepared as described in the literature.[19]

Acetylbromomethylenetriphenylphosphorane (4). Acetylmethylenetriphenylphosphorane (4.48 g, 14.09 mmol) in dichloromethane (107 mL) was cooled to -70 °C. Then bromine (0.8 mL), dissolved in carbon tetrachloride (27 mL), was slowly added. The phosphonium salt was shaken vigorously with aqueous sodium hydroxide (5%, 300 mL). Crystallization from acetone-hexane yielded compound **4** (4.1 g, 61%) as a white solid: mp

163-164 °C; R_f 0.3 (diethyl ether); IR (KBr) 3045 (PC), 2953 (CH_3), 1638 (C=O); 1433 (Ar), 1103 (P-Ar), 748 and 692 (Ar), ^{1}H NMR ($CDCl_3$) δ 2.10 (s, 3H, CH_3) and 7.46-7.60 (m, 15H, ArH); ^{13}C NMR ($CDCl_3$) δ 28.57 (CH_3), 103.39 (C-CO) 128.44-134.56 (CHAr and CAr) and 196.62 (C=O); *m/z* 397 (21%, M^+), 317 (26, M^+-Br), 303 (100, M^+-Br-CH_3), 262 (16, $P(C_6H_5)_3^+$), 183 (47), 165 (22), 107 (10) and 77 (20, $C_6H_5^+$).

Anal. Calcd for $C_{21}H_{18}OPBr$: C, 63.49; H, 4.57; Br, 20.11. Found: C, 63.51; H, 4.53.

1-Benzoylethylidenetriphenylphosphorane (5). α-Bromopropiophenone (2 mL, 13.4 mmol) was dissolved in benzene (10 mL) and added to a stirred solution of triphenylphosphine (5.26 g, 20.06 mmol) in benzene (36 mL) under reflux for 24 h to give a yellow solid. After washing with diethyl ether, 1-benzoylethylidenephosphonium bromide (5.4 g, 85%), mp 233-235 °C was obtained. The phosphonium salt (4 g, 8.42 mmol) was vigorously shaken for 9 h with aqueous sodium hydroxide (5%, 200 mL). The resulting precipitate was purified by column chromatography (ethyl acetate-chloroform 10:1) affording compound **5** (2.79 g, 80%) as a yellow solid: mp 170-172 °C; IR (KBr) 3050 (PC), 2975 (C-H), 1660 (C=O), 1475 (Ar), 1010 (P-Ar), 710 and 690 (Ar); ^{1}H NMR ($CDCl_3$) δ 1.73 (d, 3H, J_{vic} =16.3, $PCCH_3$), 7.33-7.70 (m, 20H, ArH); ^{13}C NMR ($CDCl_3$) δ 15.38 (CH_3), 118.95 (C-2), 128.16 -134.64 (CHAr and CAr), 197.79 (CO).

Anal. Calcd for $C_{27}H_{23}OP$: C, 82.21; H, 5.87. Found : C, 82.02; H, 5.94.

Ethoxycarbonylacetylmethylenetriphenylphosphorane (6). To a solution of freshly distilled acetyl chloride (0.5 mL, 7.03 mmol) in benzene (7.5 mL) was slowly added ethoxycarbonylmethylenetriphenylphosphorane[29] (5.22 g, 15 mmol) in benzene (37.5 mL) and the mixture was stirred for 3 h at room temperature. The solvent was evaporated and the residue was chromatographed (ethyl acetate-chloroform 10:1). Compound **6** (4.27 g, 73%) was obtained as a white solid: mp 169-170 °C; R_f 0.7 (EtOAc-$CHCl_3$ 10:1); IR (KBr) 3055 (PC), 2974-2922 (C-H), 1652 (C=O), 1485 (Ar), 1370-1252 (C-O), 1105 (P-Ar), 752 and 690 (Ar); ^{1}H NMR ($CDCl_3$) δ 0.58 (t, 3H, J_{vic} = 7.1, CH_3-CH_2), 2.32 (s, 3H, CH_3-CO), 3.60 (q, 2H, J_{vic} = 7.1, CH_2-CH_3) and 7.47-7.66 (m, 15H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.70 (CH_3-CH_2), 29.24 (CH_3-CO), 58.35 (CH_2-CH_3), 127.45 (C=P), 128.39, 131.54 (CHAr) and 133.02 (CAr), 163.14 (CO_2Et) and 195.49 (C=O); *m/z* 390 (32%, M^+), 375 (85, M^+-15), 347 (17, M^+- $C_2H_3O^+$), 303 (100), 279 (19), 228 (5), 183 (84), 165 (50), 115 (7), 77 (26, $C_6H_5^+$) and 43 (26, $C_2H_3O^+$).

Anal. Calcd for $C_{24}H_{23}O_3P$: C, 73.84; H, 5.93. Found: C, 73.45; H, 5.98.

Benzoylphenylmethylenetriphenylphosphorane (7). Triphenylphosphine (6.2 g, 23.65 mmol) was dissolved in freshly distilled benzyl chloride (2.73 mL, 23.62 mmol). The resulting mixture was stirred and a white solid appeared in five minutes. After filtration, the solid, triphenylbenzylphosphonium chloride (2.75 g, 5.54 mmol) was poured into diethyl ether (100 mL) and *n*-BuLi (5 mL, 7.91 mmol) was added. The reaction mixture was stirred for 35 min and freshly distilled benzoyl chloride (5.8 mL, 50.03 mmol) dissolved in diethyl ether (25 mL) was added. Compound **7** (1.13g, 45%), was isolated as a white solid: mp 191-192 °C; IR (KBr) 3053 (P-C), 1614 (C=O), 1437 (Ar), 1119 (P-Ar), 721 and 696 (Ar); ^{1}H NMR ($CDCl_3$) δ 7.43-7.58 (m, 15H, ArH), 7.64-7.72 (m, 10H, ArH); ^{13}C NMR ($CDCl_3$) δ 128.39-134.05 (CHAr and CAr), 197.03 (CO).

Anal. Calcd for $C_{32}H_{25}OP$: C, 84.19; H, 5.52. Found : C, 84.32; H, 5.50.

Reactions of Wittig reagents with 2,3-*O*-isopropylidene-D-glyceraldehyde. General procedure. To a solution of 2,3-*O*-isopropylidene-D-glyceraldehyde **1** (11 mmol), prepared as in the literature,[18] in CH_2Cl_2 (30 mL), the phosphorane (15 mmol) in CH_2Cl_2 was slowly added. The mixture was stirred at room temperature (5 h-12 h), the solvent evaporated and the residue chromatographed.

(*Z* and *E*)-1,3,4-Trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose (8 and 9). A stirred solution of **1** (2.25 g, 17 mmol) in dichloromethane (23 mL) at room temperature was treated with acetylmethylenetriphenylphosphorane **2** (10.5 g, 34 mmol) in the same solvent (23 mL). The mixture was stirred at room temperature for 5 h and then chromatographed (hexane-ether, 5:1) to yield **8** and **9** :

a) (*Z*)-1,3,4-Trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose (8) (1.6 g, 55%) as a colourless mobile oil: R_f 0.8 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 194.8° (*c* 1.19, chloroform); IR (KBr) 3000 (C=C), 2900-2800 (C-H), 1695 (C=O), 1620 (C=C), 1380-1370 ($C(CH_3)_2$), 1265-1060 (C-O-C-O-C), 760 (C=C, Z); ^{1}H NMR ($CDCl_3$) δ 1.39 and 1.45 (2s, 6H, $C(CH_3)_2$), 2.24 (s, 3H, CH_3-CO), 3.57 (dd, 1H, $J_{6,6'}$ = 8.3, $J_{6,5}$ = 6.7, 6-H), 4.43 (dd, 1H, $J_{6',6}$ = 8.3, $J_{6',5}$ = 7.1, 6'-H), 5.34 (ddd, 1H, $J_{5,6}$ = 6.7, $J_{5,6'}$ = 7.1, $J_{5,4}$ = 0.6, 5-H), 6.24 (d, 1H, $J_{4,5}$ = 0.6, 3-H), 6.25 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$) δ 25.31 and 26.54 ($C(CH_3)_2$), 31.04 ($\underline{C}H_3$-CO), 69.43 (C-6), 74.18 (C-5), 109.63 ($\underline{C}(CH_3)_2$), 127.19 (C-3), 147.74 (C-4), 198.36

(CO); *m/z* 170 (11%, M^+), 155 (1, M^+-15), 127 (32, $C_7H_{11}O_2^+$), 109 (3), 95 (2), 85 (4), 69 (95, $C_4H_5O^+$), 59 (10, $C_3H_7O^+$) and 43 (100, $C_2H_3O^+$).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.57; H, 8.32.

b) (*E*)-1,3,4-Trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose[30] (9) (1.2 g, 40%) as a colourless mobile oil: R_f 0.6 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 65.1° (*c* 1.12, chloroform); IR (KBr) 3000 (C=C), 2900-2800 (CH), 1685 (C=O), 1635 (C=C), 1380-1370 ($C(CH_3)_2$), 1265-1050 (C-O-C-O-C), 970 (C=C, *E*); ^{1}H NMR ($CDCl_3$) δ 1.42 and 1.46 (2s, 6H, $C(CH_3)_2$), 2.29 (s, 3H, CH_3-CO), 3.70 (dd, 1H, $J_{6,6'}$ = 8.3, $J_{6,5}$ = 7.2, 6-H), 4.21 (dd, 1H, $J_{6',6}$ = 8.3, $J_{6',5}$ = 6.6, 6'-H), 4.65 (ddd, 1H, $J_{5,6}$ = 7.2, $J_{5,6'}$ = 6.6, $J_{5,4}$ = 5.8, 5-H), 6.32 (dd, 1H, $J_{4,3}$ = 16.0, $J_{4,5}$ = 5.8, 3-H), 6.71 (dd, 1H, $J_{3,4}$ = 16.0, J_{vic} =1.3, 4-H); ^{13}C NMR ($CDCl_3$) δ 25.68 and 26.48 ($C(CH_3)_2$), 27.42 ($\underline{C}H_3$-CO), 68.84 (C-6), 75.09 (C-5), 110.24 ($\underline{C}(CH_3)_2$), 131.08 (C-3), 143.29 (C-4), 198.02 (CO); *m/z* 170 (0.1%, M^+), 155 (36, M^+-15), 140 (5, M^+-30), 127 (0.3, $C_7H_{11}O_2^+$), 113 (32, M^+-C_3H_5O), 97 (7), 82 (29), 72 (15), 54 (6, $C_3H_2O^+$) and 43 (100, $C_2H_3O^+$).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.53; H, 8.24.

(*Z* and *E*)-1,3,4-Trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*glycero*-hex-3-eno-2-ulose (10 and 11). This experiment was carried out following the aforementioned procedure but using 2,3-*O*-isopropylidene-D-glyceraldehyde **1** (1.4 g, 0.011 mol) and (1-acetylethylidene)triphenylphosphorane **3** (3.37 g, 0.011 mol). The residue was chromatographed (hexane:diethyl ether 5:1), to give:

a) (*Z*)-1,3,4-Trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*glycero*-hex-3-eno-2-ulose (10), traces, as a colourless mobile oil: R_f 0.65 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 56.4° (*c* 0.75, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.37 and 1.43 (2s, 6H, 2s, $C(CH_3)_2$), 1.89 (d, 3H, J= 1.4, CH_3-C3), 1.98 (s, 3H, CH_3-CO), 3.56 (t, 1H, $J_{6,6'}$ = 8.2, 6-H), 4.10 (dd, 1H, $J_{6',6}$ = 8.2, $J_{6',5}$ = 6.2, 6'-H), 4.76 (ddd, 1H, $J_{5,6}$ = 7.1, $J_{5,6'}$ = 6.2, $J_{5,4}$ = 8.5, 5-H), 5.44 (dd, 1H, $J_{4,5}$ = 8.5, J = 1.4, 4-H).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.32; H, 8.69.

b) (*E*)-1,3,4-Trideoxy-5,6-*O*-isopropylidene-3-*C*-methyl-D-*glycero*-hex-3-eno-2-ulose (11), (1.39 g, 74%) as a colourless mobile oil: R_f 0.6 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 66.3° (*c* 1.13, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.42 and 1.47 (2s, 6H, $C(CH_3)_2$), 1.81 (d, 3H, J=1.4, CH_3-C3), 2.34 (s, 3H, CH_3-CO), 3.63 (dd, 1H, $J_{6,6'}$ = 8.2, $J_{6,5}$ = 7.3, 6-H), 4.21 (dd, 1H,

$J_{6',6}$ = 8.2, $J_{6',5}$ = 6.4, 6'-H), 4.93 (ddd, 1H, $J_{5,6'}$ = 6.4, $J_{5,6}$ = 7.3, $J_{5,4}$ = 7.3, 5-H), 6.53 (dd, 1H, $J_{4,5}$ = 7.3, J = 1.4, 4-H); ^{13}C NMR ($CDCl_3$) δ 11.53 (CH_3-C3), 25.25 and 25.49 ($C(CH_3)_2$), 26.44 ($\underline{C}H_3$-CO), 68.57 (C-6), 72.93 (C-5), 109.66 ($\underline{C}(CH_3)_2$), 139.26 (C-4), 198.89 (CO); *m/z* 169 (9%, M^+-15), 154 (1, M^+-30), 127 (15), 109 (12), 72 (24), 53 (9) and 43 (100, $C_2H_3O^+$).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.25; H, 8.71.

(*E*)-3-*C*-Bromo-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose, (12). As before, 2,3-*O*-isopropylidene-D-glyceraldehyde **1** (1.54 g, 0.012 mol) was reacted with acetylbromomethylenetriphenylphosphorane **4** (4.4 g, 0.012 mol). The residue was chromatographed (hexane: diethyl ether 7:1) to give two compounds. Only traces of the first compound, as a mobile oil. R_f 0.7 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 32.4° (*c* 0.88, chloroform), were isolated.

The second compound was a colourless mobile oil (1.95 g, 66%), identified as (*E*)-3-*C*-bromo-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose, **12**. R_f 0.5 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 43.3° (*c* 1.02, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.42, 1.48 (2s, 6H, $C(CH_3)_2$), 2.48 (s, 3H, CH_3-CO), 3.74 (dd, 1H, $J_{6,6'}$ = 8.3, $J_{6,5}$ = 6.5, 6-H), 4.37 (dd, 1H, $J_{6',6}$ = 8.3, $J_{6',5}$ = 6.5, 6'-H), 5.01 (ddd, 1H, $J_{5,6}$ = 6.5, $J_{5,6'}$ = 6.5, $J_{5,4}$ = 6.4, 5-H), 7.23 (d, 1H, $J_{4,5}$ = 6.4, 4-H); ^{13}C NMR ($CDCl_3$) δ 25.36 and 26.39 ($C(CH_3)_2$), 26.10 ($\underline{C}H_3$-CO), 68.19 (C-6), 75.83 (C-5), 110.42 ($\underline{C}(CH_3)_2$), 127.02 (C-3), 143.97 (C-4), 190.93 (CO); *m/z* 307 (16%, M^++58), 279 (83, M^++30), 249 (26, M^+), 221 (18), 191 (72), 169 (19, M^+-Br), 127 (25), 113 (100, $C_6H_9O_2^+$), 101 (23, $C_5H_9O_2^+$).

Anal. Calcd for $C_9H_{13}O_3Br$: C, 43.39; H, 5.24; Br, 32.08. Found: C, 43.52; H, 5.20.

(*E*)-1-*C*-Phenyl-2,3-trideoxy-4,5-*O*-isopropylidene-D-*glycero*-pent-2-eno-1-ulose (13). Compound **1** (1.5 g, 0.012 mol), dissolved in CH_2Cl_2 (90 mL), was treated with 1-benzoylethylidenetriphenylphosphorane, **5** (4.84 g, 12 mmol), following the procedure previously described, the reaction mixture being stirred under reflux for 12 h. Compound **13**, (1.42 g, 60%), was obtained as a yellow syrup; R_f 0.6 (hexane-diethyl ether 1:1); $[\alpha]_D$ +31.8° (*c* 2.73, $CHCl_3$); IR (KBr) 3000 (C=C), 2900-2800 (CH), 1655 (C=O), 1600 (C=C), 1380-1370 ($C(CH_3)_2$), 1260-1010 (C-O-C-O-C), 790-710 (Ar); ^{1}H NMR ($CDCl_3$) δ 1.40 and 1.42 (6H, 2s, $C(CH_3)_2$), 2.03 (3H, d, J = 1.3, CH_3-C2), 3.60 (1H, dd, $J_{5,5'}$ = 8.1, $J_{5,4}$ = 7.5, 5-H), 4.21 (1H, dd, $J_{5',5}$ = 8.1, $J_{5',4}$ = 6.3, 5'-H), 5.00 (1H, ddd, $J_{4,5}$ = $J_{4,3}$ = 7.5, $J_{4,5'}$ = 6.3, 4-H), 6.21

(1H, dd, $J_{3,4}$ = 7.5, J = 1.3, 3-H), 7.41-7.54 (3H, m, ArH), 7.68-7.70 (2H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 13.27 (CH_3-C2), 25.76 and 26.56 ($C(CH_3)_2$), 68.70 (C-5), 72.98 (C-4), 109.83 ($\underline{C}(CH_3)_2$), 128.25, 129.45 and 133.03 (CHAr), 137.48 (CAr), 138.45 (C-2), 140.91 (C-3), 198.08 (CO); *m/z* 246 (0.6%, M^+), 216 (4, M^+-30), 188 (44), 171 (93, $(M+1)^+$-C_6H_5), 158 (76), 129 (28), 105 (59, $C_7H_5O^+$), 91 (10), 77 (100, $C_6H_5^+$), 43 (75, $C_2H_3O^+$).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15, H, 7.30. Found: C, 73.28; H, 7.30.

α,β-Unsaturated oximes. General procedure. A solution of hydroxylamine hydrochloride (0.71g, 10.2 mmol) and methanol (85 mL) was added to a stirred solution of α,β-unsaturated *C*-glycosyl ketones (4 mmol) in pyridine (25 mL). The solution was stirred at room temperature for two h, the solvent was then evaporated and the residue chromatographed.

Oxime of (*Z*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose, (14). A mixture of compound **8** (1.03 g, 6.04 mmol), hydroxylamine hydrochloride (1.04 g, 14.9 mmol), pyridine (37 mL) and methanol (124 mL) was stirred at room temperature for 2 h. The residue was then chromatographed (hexane-diethyl ether 2:1) to give compound **14** (0.45 g, 40%) as a colourless syrup; R_f 0.5 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 36.5° (*c* 0.52, $CHCl_3$); IR (KBr) 3352 (N-OH), 2984-2878 (C-H), 1625 (C=N), 1616 (C=C), 1380-1370 ($C(CH_3)_2$), 1217-1153 (C-O-C-O-C), 970 (N-O); ^{1}H NMR ($CDCl_3$) δ 1.40 and 1.45 (6H, 2s, $C(CH_3)_2$), 1.97 (3H, s, CH_3-C=N), 3.59 (1H, t, $J_{6,6'}$ = 7.8, 6-H), 4.21 (1H, dd, $J_{6',6}$ = 7.8, $J_{6',5}$ = 6.5, 6'-H), 5.09 (1H, ddd, J_{vic} = 6.4, $J_{5,6'}$ = 6.5, $J_{5,4}$ = 7.4, 5-H), 5.78 (1H, dd, $J_{4,3}$ = 11.7, $J_{4,5}$ = 7.4, 3-H), 5.91 (1H, t, $J_{3,4}$ = 11.7, 4-H), 7.78 (1H, broad, NOH); ^{13}C NMR ($CDCl_3$) δ 14.61 (CH_3-C2), 25.77 and 26.68 ($C(CH_3)_2$); 69.66 (C-6); 73.68 (C-5); 109.54 ($\underline{C}(CH_3)_2$); 127.32 (C-3); 134.60 (C-4); 154.28 (C-2); *m/z* 170 (26%, M^+-15), 155 (2, M^+-30), 138 (39), 128 (51, $(M+1)^+$-CHNO), 110 (44), 97 (48), 82 (39), 72 (90), 55 (19) and 43 (100, $CHNO^+$).

Anal. Calcd for $C_9H_{15}O_3N$: C, 58.36, H, 8.16, N, 7.5. Found: C, 58.42, H, 8.09, N, 7.54.

Oximes of (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose, (15, 15a). A similar procedure to that above was followed using compound **9** (0.91 g, 5.35 mmol), hydroxylamine hydrochloride (0.92 g, 13.24 mmol) and freshly distilled pyridine (33 mL). The first compound isolated by chromatography (hexane-diethyl ether 2:1) as a colourless syrup, was the oxime **15** (0.48 g, 49%); R_f 0.4 (hexane-diethyl ether 1:1); $[\alpha]_D$ +

31.8° (*c* 1.38, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.41 and 1.46 (6H, 2s, $C(CH_3)_2$), 2.02 (3H, s, CH_3-C=N), 3.65 (1H, t, $J_{6,6'}$ = 8.0, 6-H), 4.15 (1H, dd, $J_{6',6}$ = 8.0, $J_{6',5}$ = 6.3, 6'-H), 4.64 (1H, ddd, $J_{5,6'}$ = 6.3, J_{vic} = 0.9, $J_{5,4}$ = 7.4, 5-H), 6.01 (1H, dd, $J_{4,3}$ = 16.0, $J_{4,5}$ = 7.4, 3-H), 6.38 (1H, dd, $J_{3,4}$ = 16.0, J_{vic} = 0.9, 4-H), 9.45 (1H, broad, NOH); ^{13}C NMR ($CDCl_3$) δ 9.73 (CH_3-C2), 25.80 and 26.64 ($C(CH_3)_2$), 69.34 (C-6), 76.53 (C-5), 109.78 ($\underline{C}(CH_3)_2$), 130.36 (C-3), 132.01 (C-4), 155.65 (C-2); *m/z* 185 (0.5%, M^+), 170 (66, M^+-15), 138 (76), 128 (100, $(M+1)^+$-C_2H_4NO), 110 (88), 97 (74), 72 (71), 69 (22) and 43 (96, $CHNO^+$).

Anal. Calcd for $C_9H_{15}O_3N$: C, 58.36, H, 8.16, N, 7.56. Found: C, 58.39, H, 8.22, N 7.53.

Next isolated was a colourless syrup (0.19 g, 1.01 mmol); R_f 0.4 (hexane:diethyl ether, 1:1). It was identified as a mixture of *syn* and *anti* oximes of (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose, **15** and **15a**.

Oxime of (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-3-*C*-methylhex-3-eno-2-ulose (16). To a stirred solution of (*E*)-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-3-*C*-methylhex-3-eno-2-ulose, **11**, (0.84 g, 4.59 mmol) and freshly distilled pyridine (28 mL), was added a solution of hydroxylamine hydrochloride (0.79 g, 11 mmol) in methanol (95 mL). The mixture was stirred for an additional 2 h at rt. The residue was chromatographed (hexane-diethyl ether 1:1), to give compound **16** (0.84 g, 83%), as a white solid; mp 54.5-56 °C; R_f 0.5 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 25.5° (*c* 1.09, $CHCl_3$); IR (KBr) 3364 (N-OH), 2984-2874 (C-H), 1630 (C=N), 1625 (C=C), 1380-1371 ($C(CH_3)_2$), 1155-1057 (C-O-C-O-C), 970 (N-O); ^1H NMR ($CDCl_3$) δ 1.43 and 1.46 (6H, 2s, $C(CH_3)_2$), 1.91 (3H, d, J_{vic} = 1.2, CH_3-C3), 2.06 (3H, s, CH_3-C=N), 3.58 (1H, t, $J_{6,6'}$ = 8.0, 6-H), 4.16 (1H, dd, $J_{6',6}$ = 8.0, $J_{6',5}$ = 6.1, 6'-H), 4.98 (1H, ddd, $J_{5,6'}$ = 6.1, J_{vic} = 2.3, $J_{5,4}$ = 7.8, 5-H), 5.89 (1H, dd, $J_{4,5}$ = 7.8, J_{vic} = 1.2, 4-H), 9.38 (1H, broad, NOH); ^{13}C NMR ($CDCl_3$) δ 10.03 (CH_3-C3), 13.24 (CH_3-C2), 25.85 and 26.73 ($C(CH_3)_2$), 69.20 (C-6), 72.99 (C-5), 109.41 ($\underline{C}(CH_3)_2$), 129.41 (C-3), 136.36 (C-4), 157.02 (C-2); *m/z* 199 (0.5%, M^+), 184 (4, M^+-15), 169 (2, M^+-30), 141 (42, M^+-C_2H_4NO), 124 (86), 111 (78), 96 (35), 72 (100) and 43 (83, $CHNO^+$).

Anal. Calcd for $C_{10}H_{17}O_3N$: C, 60.28, H, 8.60, N, 7.03. Found: C, 60.03, H, 8.65, N 6.97.

Oxime of (*E*)-3-*C*-bromo-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose (17). A solution of **12** (1.03 g, 4.14 mmol) and hydroxylamine hydrochloride

(0.71 g, 10.22 mmol) in a mixture of pyridine (25 mL) and methanol (85 mL) was stirred at room temperature for 3 h and then concentrated to dryness. The residue was coevaporated twice with toluene and chromatographed on a silica gel column using hexane-diethyl ether, 2:1, to give two components. The second component was not identified because it was completely modified in the column. The first component eluted, **17**, was isolated as a white solid (0.44 g, 45%); mp 68-69 °C; R_f 0.5 (hexane-diethyl ether 2:1); $[\alpha]_D$ + 37.8° (*c* 1.07, $CHCl_3$); IR (KBr) 3339 (N-OH), 2984-2874 (CH), 1640 (C=N), 1618 (C=C), 1370 ($C(CH_3)_2$), 1153-1050 (C-O-C-O-C), 1012 (N-O); ^{1}H NMR ($CDCl_3$) δ 1.42 and 1.47 (6H, 2s, $C(CH_3)_2$), 2.15 (3H, s, CH_3-C=N), 3.69 (1H, dd, $J_{6,6'}$ = 8.3, $J_{6,5}$ = 6.6, 6-H), 4.33 (1H, dd, $J_{6',6}$ = 8.3, $J_{6',5}$ = 6.7, 6'-H), 5.10 (1H, dd, $J_{5,6}$ = 6.6, $J_{5,6'}$ = 6.7, 5-H), 6.53 (1H, d, $J_{4,5}$ = 6.6, 4-H), 10.00 (1H, s, NOH); ^{13}C NMR ($CDCl_3$) δ 11.65 (CH_3-C2), 25.51 and 26.50 ($2C(CH_3)_2$), 68.58 (C-6); 75.99 (C-5), 109.97 ($\underline{C}(CH_3)_2$), 123.18 (C-3), 134.53 (C-4), 152.46 (C-2); *m/z* 264 (4%, M^+), 233 (5, $(M+1)^+$-15), 216 (8, M^+-CHON), 190 (19), 188 (20), 160 (5), 126 (8, $C_7H_{10}O_2^+$), 109 (8), 80 (11, Br^+), 65 (8) and 43 (100, $C_2H_3O^+$).

Anal. Calcd for $C_9H_{14}O_3NBr$: C, 40.93, H 5.34, N 5.30, Br 30.25.

Oximes of (*E*)-1-*C*-phenyl-2,3-dideoxy-2-*C*-methyl-4,5-*O*-isopropylidene-D-*glycero*-pent-2-eno-1-ulose (18a and 18b). To a solution of compound **13** (3.2 g, 13 mmol) in methanol (270 mL), hydroxylamine hydrochloride (2.3 g, 33.1 mmol) and pyridine (81 mL) were added. The mixture was heated under reflux for 2 h, then concentrated under reduced pressure. The residue was purified using hexane-diethyl ether 2:1 as eluent, to give a mixture of *syn* and *anti* isomeric oximes, **18a** and **18b** (2.03 g, 60%) in a 1:1 ratio (from H-3, δ value). This mixture was identified from ^{1}H NMR and ^{13}C NMR spectra. R_f 0.6 (hexane-diethyl ether 1:1); ^{1}H NMR ($CDCl_3$) δ 1.32, 1.37, 1.41 and 1.44 (12H, 4s, $2(C(CH_3)_2)$, (a) and (b)), 2.00 (3H, s, CH_3-C2, (a)), 2.02 (3H, s, CH_3-C2, (b)), 3.45 (1H, dd, $J_{5,5'}$ = 7.9, $J_{5,4}$ = 4.8, 5-H, (a)), 3.65 (1H, t, $J_{5,4}$ = 8.0, 5-H, (b)), 4.09 (1H, dd, $J_{5',5}$ = 7.9, $J_{5',4}$ = 6.1, 5'-H, (a)), 4.21 (1H, dd, $J_{5',5}$ = 8.0, $J_{5',4}$ = 6.1, 5'-H, (b)), 4.97 (2H, ddd, $J_{4,3}$ = 7.9, $J_{4,5'}$ = 6.1, $J_{4,5}$ = 4.8, 4-H, (a) and (b)), 5.41 (1H, dd, $J_{3,4}$ = 7.9, J_{vic} = 1.3, 3-H, (a)), 5.50 (1H, dd, $J_{3,4}$ = 8.1, J_{vic} = 1.1, 3-H, (b)), 7.20-7.60 (10H, m, ArH), 8.94 (2H, s, NOH); ^{13}C NMR ($CDC1_3$) δ 13.52 (CH_3-C=N, (a)), 15.84 (CH_3-C=N, (b)), 25.80 and 26.59 ($C(CH_3)_2$, (a)), 25.93 and 26.69 ($C(CH_3)_2$, (b)), 69.02 and 69.08 (2 C-5, (a) and (b)), 72.33 and 72.93 (2 C-4, (a) and (b)), 109.37 and 109.41

($2\underline{C}(CH_3)_2$, (a) and (b)), 128.22-130.14 (CHAr and CAr), 133.64 and 133.72 (2 C-2,(a) and (b)), 134.35 (C-3, (a)), 136.75 (C-3, (b)), 159.35 (C-1, (b)), 160.12 (C-1, (a)).[31]

Synthesis of isoxazoles derivatives by cyclization of α, β-unsaturated ketoximes. To a solution of α,β-unsaturated ketoxime in methanol and tetrahydrofuran, was added a solution of sodium bicarbonate with iodine and potassium iodide. The reaction was carried out in darkness and maintained at reflux (5 h-15 h). A saturated solution of sodium bisulfite was added to eliminate excess iodine. Once the organic phase separated, the aqueous phase was extracted several times with diethyl ether. The organic extracts were dried with anhydrous sodium sulfate, and the solvent evaporated at reduced pressure, to give a syrup later purified by column chromatography.

3-Methyl-5(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole (19). A solution of potassium iodide (8.28 g, 49.9 mmol) and iodine (3.99 g, 15.7 mmol) in water (85 mL) was added in darkness to a stirred solution of **15** (2.64 g, 14.26 mmol) and sodium bicarbonate (4.79 g, 57 mmol) in a mixture of tetrahydrofuran (57 mL) in water (43 mL). The mixture was heated under reflux for 8 h, cooled, diluted with saturated aqueous sodium bisulfite (145 mL), and extracted four times with diethyl ether (4 x 25 mL). The collected organic phases were concentrated and the residue chromatographed on a silica gel column using chloroform-ethyl acetate (100:1) as eluent, to give a single compound **19** (1.82, 70%) as a yellow syrup: R_f 0.5 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 30.2° (*c* 1.29, chloroform); IR (KBr) 3000 (=CH, isoxazole), 2950-2850 (C-H), 1625 (C=N, isoxazole), 1460 (C=C, isoxazole), 1380-1370 (CMe_2), 1250-1060 (C-O-C-O-C); ^{1}H NMR ($CDCl_3$) δ 1.45 and 1.50 (2s, 6H, $C(CH_3)_2$), 2.29 (s, 3H, CH_3-C3), 4.07 (dd, 1H, $J_{2',2''}$ = 8.5, $J_{2',1'}$ = 6.3, 2'-H), 4.33 (dd, 1H, $J_{2'',2'}$ = 8.5, $J_{2'',1'}$ = 6.6, 2''-H), 5.17 (dd, 1H, $J_{1',2'}$ = 6.3, $J_{1',2''}$ = 6.6, 1'-H), 6.11 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$) δ 11.13 (CH_3-C3), 25.37 and 26.09 ($2C(CH_3)_2$), 68.27 (C-2'); 70.15 (C-1'), 102.36 (C-4), 110.49 ($\underline{C}(CH_3)_2$), 159.39 (C-3), 170.58 (C-5); *m/z* 183 (0.03%, M^+), 168 (64, (M^+-15), 153 (1, M^+-30), 126 (100), 112 (1), 84 (5, $C_4H_6ON^+$), 72 (15), 56 (7) and 43 (72, $C_2H_3O^+$).

Anal. Calcd for $C_9H_{13}O_3N$: C, 59.00; H, 7.16; N, 7.64. Found: C, 58.87; H, 7.09; N, 7.72.

3,4-Dimethyl-5-(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole (20). Compound **16** (0.73 g, 3.64 mmol), sodium bicarbonate (1.24 g, 15 mmol),

tetrahydrofuran (15 mL) and water (11 mL) was treated with a solution of potassium iodide (2.14 g, 13 mmol) and iodine (1.03 g, 4 mmol) in water (22 mL) following the procedure previously described for the preparation of compound **19**. After purification by column chromatography (chloroform-ethyl acetate 50:1), compound **20** (0.47 g, 65%) was obtained as a yellow liquid: R_f 0.5 (hexane-diethyl ether 1:1); $[\alpha]_D$ + 9.9° (*c* 1.2, $CHCl_3$); IR (KBr) 3000 (C=N), 2931-2888 (CH), 1642 (C=N, isoxazole), 1455 (C=C, isoxazole), 1377 (CMe_2), 1256-1060 (C-O-C-O-C); ^{1}H NMR ($CDCl_3$) δ 1.46 and 1.51 (2s, 6H, $C(CH_3)_2$), 2.00 (s, 3H, CH_3-C4), 2.21 (s, 3H, CH_3-C3), 4.22 (2dd, 2H, $J_{2',1'}$ = 6.8, J_{vic} = 7.2, J_{vic} = 3.2, 2'-H), 5.16 (dd, 1H, $J_{1',2'}$ = 6.8, $J_{1',2'}$ = 7.2, 1'-H); ^{13}C NMR ($CDCl_3$) δ 6.60 (CH_3-C4), 9.95 (CH_3-C3), 25.68 and 25.94 ($C(CH_3)_2$), 67.59 (C-2'), 69.42 (C-1'), 110.52 ($\underline{C}(CH_3)_2$), 111.90 (C-4), 160.47 (C-3), 162.99 (C-5); *m/z* 197 (0.7%, M^+), 182 (73, M^+-15), 167 (1, M^+-30), 140 (100), 138 (8), 110 (10), 96 (8, $C_5H_6ON^+$), 82 (5), 72 (24, $C_3H_6ON^+$), and 43 (72, $C_2H_3O^+$).

Anal. Calcd for $C_{10}H_{15}O_3N$: C, 60.89; H, 7.66; N, 7.11. Found: C, 60.86; H, 7.64; N, 6.99.

3-Methyl-4-bromo-5-(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole (21). Oxime of (*E*)-3-*C*-bromo-1,3,4-trideoxy-5,6-*O*-isopropylidene-D-*glycero*-hex-3-eno-2-ulose, **17** (1.5 g, 5.7 mmol), sodium bicarbonate (1.9 g, 23 mmol), tetrahydrofuran (25 mL) and water (32 mL) was treated with a solution of potassium iodide (3.3 g, 19.9 mmol) and iodine (1.6 g, 6.3 mmol) in water (35 mL) at reflux for 15 h as in the general procedure. The residue was chromatographed (chloroform-ethyl acetate 30:1), to give compound **21** (0.45 g, 30%) as a solid: mp 71.5-72 °C; R_f 0.65 (chloroform-ethyl acetate 20:1); $[\alpha]_D$ -18.8° (*c* 0.8, $CHCl_3$); IR (KBr) 2993 (C=N), 2933-2890 (C-H), 1616 (C=N, isoxazole), 1451 (C=C, isoxazole), 1380-1375 (CMe_2), 1260-1059 (C-O-C-O-C); ^{1}H NMR ($CDCl_3$) δ 1.47 and 1.56 (2s, 6H, $C(CH_3)_2$), 2.29 (s, 3H, CH_3-C3), 4.20 (dd, 1H, $J_{2',2''}$ = 8.5, $J_{2',1'}$ = 6.8, 2'-H), 4.31 (dd, 1H, $J_{2'',2'}$ = 8.5, $J_{2'',1'}$ = 6.6, 2''-H), 5.21 (dd, 1H, $J_{1',2'}$ = 6.8, $J_{1',2''}$ = 6.6, 1'-H); ^{13}C NMR ($CDCl_3$) δ 12.00 (CH_3-C3), 25.68 and 25.87 ($C(CH_3)_2$), 67.53 (C-2'), 69.85 (C-1'), 103.98 (C-4), 111.23 ($\underline{C}(CH_3)_2$), 161.97 (C-3), 168.11 (C-5); *m/z* 262 (0.3%, M^+), 246 (30), 233 (1, $(M+1)^+$-30), 204 (39), 162 (7, $C_4H_4ONBr^+$), 134 (6, $C_3H_4NBr^+$), 97 (3), 72 (16), 43 (100, $C_2H_3O^+$).

Anal. Calcd for $C_9H_{12}O_3NBr$: C, 60.89; H, 7.66; N, 7.11. Found: C, 60.86; H, 7.64; N, 6.99.

3-Phenyl-4-methyl-5-(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole (22). A solution of *syn/anti* mixture **(18a** and **18b)** (0.9 g, 3.3 mmol), sodium bicarbonate (1.1 g, 3.5 mmol), tetrahydrofuran (13 mL) and water (10 mL) was treated with a solution of potassium iodide (2 g, 11.8 mmol) iodine (0.9 g, 3.8 mmol) in water (20 mL) at reflux for 12 h following the procedure previously described for the preparation of isoxazole **19**. After purification by column chromatography (chloroform-ethyl acetate 75:1), compound **22** (0.45 g, 50%) was obtained as a yellow syrup: R_f 0.7 (chloroform-ethyl acetate 20:1); $[\alpha]_D$ -2.1° (*c* 0.95, chloroform); IR (KBr) 3063 (C=N), 2984-2898 (CH), 1634 (C=N, isoxazole), 1454 (C=C, isoxazole), 1371 (CMe_2), 1257-1058 (C-O-C-O-C), 773-700 (Ar); ^{1}H NMR ($CDCl_3$) δ 1.49 and 1.56 (2s, 6H, $C(CH_3)_2$), 2.19 (s, 3H, CH_3-C4), 4.31 (2dd, 2H, $J_{2',1'}$ = 7.0, $J_{2',2''}$ = 8.5, $J_{2',1'}$ = 6.6, 2'-H), 5.25 (dd, 1H, $J_{1',2'}$ = 7.0, $J_{1',2'}$ = 6.6, 1'-H), 7.46-7.49 (m, 3H, ArH), 7.61-7.64 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$) δ 7.80 (CH_3-C4), 25.68 and 25.92 ($C(CH_3)_2$), 67.54 (C-2'), 69.27 (C-1'), 110.68 ($\underline{C}(CH_3)_2$), 111.40 (C-4), 128.14, 128.72 and 129.49 (CHAr and CAr), 163.50 (C-3), 164.31 (C-5); *m/z* 259 (0.9%, M^+), 244 (16, (M^+-15), 229 (1, M^+-30), 202 (19), 158 (10, $C_{10}H_8ON^+$), 130 (8), 115 (4), 104 (9, $C_7H_6N^+$), 77 (47, $C_6H_5^+$) and 43 (100, $C_2H_3O^+$).

Anal. Calcd for $C_{15}H_{17}O_3N$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.55; H, 6.56; N, 5.38.

3-Methyl-5(1',2'-dihydroxyethyl-D-*glycero*)isoxazole (23). A solution of 3-methyl-5(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole **19** (1.1 g, 6 mmol) and 90% acetic acid (10 mL) was stirred at 90 °C for 45 min. The mixture was then coevaporated several times with benzene, the residue was crystallized from hexane-ethyl acetate 10:1, to give the title compound **23** (0.81 g, 94%) as a white solid: mp 60-61 °C; R_f 0.3 (diethyl ether); $[\alpha]_D$ +34.1° (*c* 0.59, chloroform); IR (KBr) 3360 (C-OH), 2930-2879 (C-H), 1604 (C=N, isoxazole), 1455 (C=C, isoxazole), 1417 (O-H), 1234-1058 (C-O); ^{1}H NMR (DMSO) δ 2.20 (s, 3H, CH_3-C3), 3.57 (dt, 2H, $J_{2',HO2'}$ = 5.7, $J_{2',1'}$ = 5.8, 2',2''-H), 4.61 (dd, 1H, $J_{1',HO1'}$ = 5.9, $J_{1',2'}$ 5.8, H-1'), 4.94 (t, 1H, $J_{HO1',1'}$ = 5.9, HO-1', disappears with D_2O), 5.74 (d, 1H, $J_{HO2',2'}$ = 5.7, HO-2', disappears with D_2O), 6.21 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$) δ 11.34 (CH_3-C3), 64.69 (C-2'), 67.74 (C-1'), 102.65 (C-4), 159.95 (C-3), 171.52 (C-5); *m/z* 143 (2%, M^+), 125 (2), 114 (2), 112 (37), 96 (11), 84 (100), 82 (13, $C_4H_4ON^+$), 68 (7, $C_3H_2ON^+$).), 56 (24), 42 (36, $C_2H_4N^+$).

Anal. Calcd for $C_6H_9O_3N$: C, 50.35; H, 6.34; N, 9.78. Found: C, 49.96; H, 6.15; N, 9.81.

3,4-Dimethyl-5(1',2'-dihydroxyethyl-D-*glycero*)isoxazole (24). 3,4-Dimethyl-5(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole **20** (0.7 g, 3.5 mmol) in 90% acetic acid (5 mL) was stirred at 90 °C for 50 min, giving compound **24** (0.52 g, 93%) as white solid: mp (from hexane-EtOAc) 82.5-83 °C; R_f 0.3 (diethyl ether); $[\alpha]_D$ +15° (*c* 0.72, chloroform); IR (KBr) 3319 (C-OH), 2955-2866 (C-H), 1640 (C=N, isoxazole), 1449 (C=C, isoxazole), 1404 (O-H), 1090 (C-H, isoxazole), 1190-1052 (C-O); ^{1}H NMR (DMSO) δ 1,91 (s, 3H, CH_3-C4), 2.13 (s, 3H, CH_3-C3), 3.50-3.65 (m, 2H, 2',2''-H), 4.63 (dt, 1H, $J_{1',HO1'}$ = 6.3, $J_{1',2'}$ = 5.4, H-1'), 4.88 (dd, 2H, $J_{HO1',1'}$ = 6.3, $J_{HO1',2'}$ = 5.8, HO-1', disappears with D_2O), 5.60 (d, 1H, $J_{HO2',2'}$ = 5.4, HO-2', disappears with D_2O); ^{13}C NMR ($CDCl_3$) δ 6.57 (CH_3-C4), 9.90 (CH_3-C3), 64.64 (C-2'), 67.13 (C-1'), 111.25 (C-4), 160.57 (C-3), 164.77 (C-5); *m/z* 157 (2%, M^+), 126 (20), 110 (3), 98 (45, $C_5H_8ON^+$), 82 (3, $C_4H_4ON^+$), 70 (23, 68 (7, $C_4H_8N^+$), 55 (15), 42 (100, $C_2H_4N^+$).

Anal. Calcd for $C_7H_{11}O_3N$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.45; H, 7.05; N, 8.91.

3-Methyl-4-bromo-5(1',2'-dihydroxyethyl-D-*glycero*)isoxazole (25). A solution of 3-methyl-4-bromo-5-(1',2'-*O*-isopropylidene-1',2'-dihydroxyethyl-D-*glycero*)isoxazole **22** (0.28 g, 1.1 mmol) in 90% acetic acid (3 mL) was stirred at 50 °C for 2 h. The mixture was then coevaporated several times with benzene, and the residue was chromatographed (hexane-diethyl ether 2:1) to give compound **25** (0.20 g, 85%) as a white syrup: R_f 0.2 (hexane-diethyl ether 1:2); $[\alpha]_D$ +17° (*c* 0.45, chloroform); IR (KBr) 3310 and 3230 (C-OH), 2957-2883 (C-H), 1687 (C=N, isoxazole), 1452 (C=C, isoxazole), 1406 (O-H), 1190-1055 (C-O); ^{1}H NMR (DMSO) δ 2.27 (s, 3H, CH_3-C3), 3.77-3.93 (m, 2H, 2',2''-H), 4.04 (dd, 1H, $J_{HO1',1'}$ = 5.4, J_{vic} = 7.1, HO-1', disappears with D_2O), 4.92 (dd, 1H, $J_{1',HO1'}$ = 5.4, $J_{1',HO2'}$ = 7.8, H-1'), 5.12 (dd, 1H, $J_{HO2',1'}$ = 7.8, J_{vic} = 5.6, HO-2', disappears with D_2O); ^{13}C NMR (DMSO) δ 11.97 (CH_3-C3), 64.51 (C-2'), 68.06 (C-1'), 107.58 (C-4), 161.59 (C-3), 170.80 (C-5); *m/z* 222 (23%, M^+), 207 (100, M^+-15), 161 (6, $C_4H_3ONBr^+$), 141 (9, $(M+1)^+$- C_4H_4ON), 133 (2, $C_3H_3NBr^+$), 80 (4, Br^+), 82 (42, $C_4H_4ON^+$), 57 (3, $C_2H_3ON^+$), 42 (23).

Anal. Calcd for $C_6H_8O_3NBr$: C, 32.46; H, 3.63; N, 6.31; Br; 35.99. Found: C, 32.41; H, 3.64; N, 6.31.

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