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This work reports the synthesis of isoxazoles linked to sugar derivatives in different positions of furanosidic rings, by intramolecular oxidative cyclization of α,β-unsaturated oximes with iodine, potassium iodide and sodium hydrogen carbonate. These oximes were obtained from aldehyde-sugar derivatives.

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Introduction.

Nitrogen and oxygen heterocyclic compounds have exhibited considerable biological applications, namely in medicine and agriculture. Heterocyclic compounds having an isoxazole ring have been used in the treatment of some different health problems, like epilepsy, arteriosclerosis [1], and more recently tested as potential anticonvulsant agents and membrane muscle relaxants [2,3].

Isoxazole compounds have a five membered π-excessive heterocycle ring with oxygen (furan-type) and nitrogen (pyridine-type) atoms and the partially reduced form of isoxazoles (dihydroisoxazoles or isoxazolines) exists in three isomeric forms, depending on the position of the double bond. The isoxazole ring is considered to be an aromatic heterocycle as it exhibits electrophilic substitution reactions and the NMR chemical shifts for ring protons are consistent with an aromatic system. The ring heteroatoms, however, modify appreciably the aromatic character of isoxazole [8].

Several methods are available for the synthesis of isoxazole compounds. The most widely used method consists of 1,3-dipolar cycloaddition reactions of nitrile oxides to activated acetylenes [9,10]. Isoxazoles can also be obtained by thermolysis of (*Z*)-β-azido-α,β-unsaturated ketones and esters [11,12,13]. In this communication we used the oxidative cyclization of α,β-unsaturated oxime with iodine, potassium iodide and sodium hydrogen carbonate, in water [8,9]. An aldehyde derivative was treated with acetonylidenetriphenylphosphorane in chloroform at room temperature to give the corresponding α,β-unsaturated ketone, which was converted into a ketoxime and then treated with iodine to give the expected isoxazole derivative.

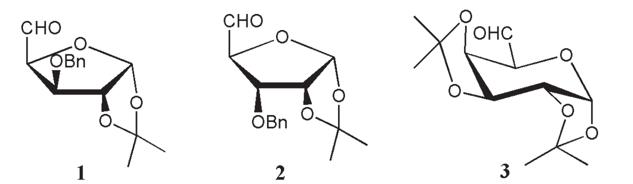
The search for new drugs with biological activity, high selectivity, and lower toxicity is an important area in carbohydrate research [2]. Significant changes in plasma membrane and function associated with malignant transformations are evident from studies on the properties and composition of the cell surfaces of normal and malignant cells. Many of those differences are associated with the carbohydrate portion/nature of the cell surface, which are implicated in antigenicity, and the degree of differentiation and behaviour of cells. The carbohydrate derivatives may became incorporated as components into cell-surface glycoconjugates, or interfere as metabolites with its cellular biosynthesis [14-17].

Taking into consideration the important biological applications of isoxazoles and some sugar derivatives, and our interest on the preparation and molecular structure of several types of nitrogen heterocyclic compounds [4-7], prompted us to devote our attention to another type of these compounds. In this work were synthesised new isoxazoles derivatives linked to sugar moieties, which can be regarded as pseudo-*C*-nucleosides and homopseudo-*C*-nucleosides.

Results and Discussion.

The synthesis of isoxazoles bearing sugar moieties started from formylfuranosidic derivatives **1-3**. These formyl-compounds were prepared in several steps from D-glucose, D-allose and D-galactose. Compounds **1** and **2** were obtained by oxidative cleavage of the corresponding diol derivatives with $NaIO_4$ [18,19]. The synthesis of compound **3** has been reported by several methods [20,21], but in this sequence the 6-OH oxidation of the commercially available 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose was performed with PCC and molecular sieves, in 73% yield. In this way **3** was obtained in a smaller reaction time, easy isolation process and better yield than that reported in literature. The presence of the formyl group was confirmed by ^{1}H and ^{13}C nmr spectra. In the ^{1}H nmr spectrum the resonance corresponding to the formyl proton was observed at δ 9.91 as doublet (J = 1.7 Hz), while in ^{13}C nmr the resonance of the formyl group appears at δ 199.4 as tertiary carbon. The structure can also be confirmed by the absence of hydroxyl group signals of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose.

The synthesis of formyl derivative **6** (Scheme 1) started from the ketofuranoside **4**, which was prepared



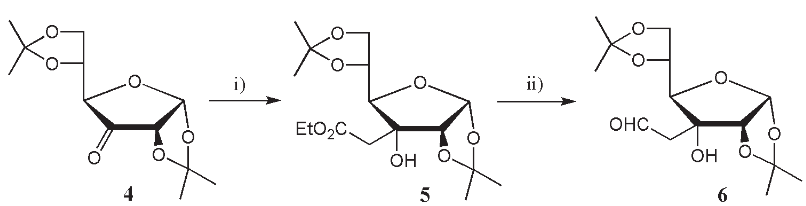
1 2 3

Figure 1

by 3-OH oxidation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, with PCC and molecular sieves [21]. The carbon chain elongation in position 3 of keto-compound **4** was carried out by the Reformatsky reaction with ethyl bromoacetate, to afford ester **5** in 67% yield. The presence of the 3-*C*-ethoxycarbonylmethylene group of **5** was assigned in their ^{1}H and ^{13}C nmr spectra. In ^{1}H nmr spectrum the resonances of the methylenic protons (CH$_2$-1') appeared as an AB spin system at δ 2.85 and 2.44 (J = 14.9 Hz) and the ethyl group appeared at δ 4.22-4.05 (multiplet) and δ 1.26 (triplet). The ^{13}C nmr spectrum showed the resonances of the carbonyl group at δ 170.6, the C-3 (quaternary) at δ 78.2, the ethyl group at δ 61.0 and 14.1 and also the methylene group (CH$_2$-1') at δ 37.1 ppm. Reduction of compound **5** with LiAlH$_4$ leads to **6** in 67% yield (Scheme 1). The ^{1}H and ^{13}C nmr spectra of **6** showed the presence of the formyl group by the resonances at δ 9.93 and 201.4, respectively.

α,β-Unsaturated ketones **7-10** [22] were obtained by Wittig reactions of the aldehydo-sugar derivatives **1-3** and **6** with the semi-stabilized ylide acetonylidenetriphenylphosphorane (Scheme 2). The relative stability of this phosphorane is due to the presence of the carbonyl group [14]. A mixture of the acetonylidenetriphenylphosphorane and the appropriate carbonyl derivative **1-3** or **6** in chloroform, at room temperature, during five hours, gave the corresponding α,β-unsaturated ketones **7-10** [23-28] (Scheme 2). Compounds **1** and **3** lead to the formation of diastereomeric mixtures of ketones **7** and **9**, which were separated by flash chromatography. The *E*-isomers **7a** and **9a** were obtained in 72% and 82% yield, respectively and the *Z* forms **7b** and **9b** were obtained in 8%, and 18% yield, respectively. Compounds **8**, and **10** were obtained in *E*-form in 80% and 78% yield, respectively. The pure *E* stereochemistry was confirmed by analysis of their ^{1}H nmr spectra, since the coupling constant of their vinylic protons was $^3J_{H\alpha\text{-}H\beta}$ ~ 16 Hz.

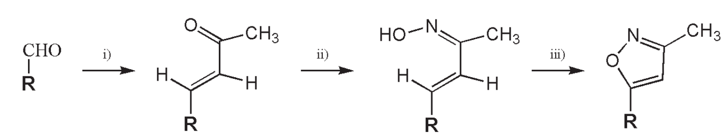
Scheme 1



4 5 6

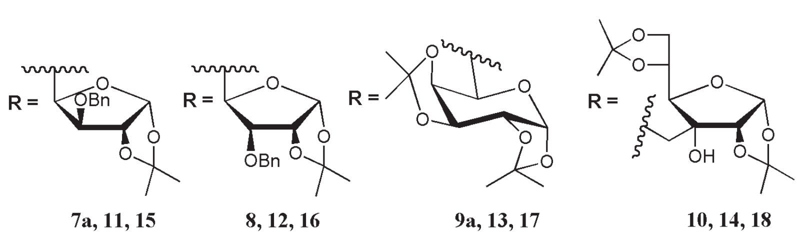
i) BrCH$_2$CO$_2$Et, Zn, THF, N$_2$, 50°C, 2 hours
ii) LiAlH$_4$, THF, room temperature, 30 minutes

Scheme 2



1-3, 6 7a, 8, 9a, 10 11-14 15-18

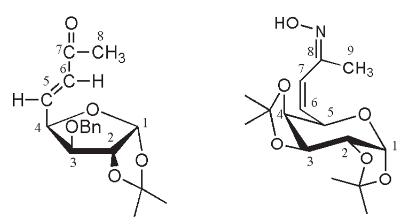
i) Ph$_3$PCHCOCH$_3$, CHCl$_3$, r. t., 5 hours
ii) NH$_2$OH.HCl, py/MeOH, r. t., 2 hours
iii) KI, I$_2$, NaHCO$_3$, H$_2$O, 100ûC, 4 hours



7a, 11, 15 8, 12, 16 9a, 13, 17 10, 14, 18 α,β-Unsaturated ketones (*E*-isomer) **7a**, **8**, **9a** and **10** were converted into the α,β-unsaturated ketoxime derivatives **11-14** [22] by reaction with hydroxylamine hydrochloride in a mixture of pyridine and methanol, at room temperature, during 2 hours, in 93-98% yield (Scheme 2). This method constitutes an improvement to that reported in literature [9], since we used less excess of hydroxylamine hydrochloride, smaller reaction times, and compounds **11-14** were obtained in better yields. In our case the reaction gave a single spot by tlc and their ^{1}H and ^{13}C nmr spectra showed the presence of only one compound. The analysis of ^{1}H and ^{13}C nmr spectra of **7a, 8**, **9a** and **10** and **11-14** supported the transformation of the keto group **7a, 8**, **9a** and **10** into the oximes **11-14**, since the β-proton and carbon atoms of these functional groups were shielded in the later compounds.

Isoxazole derivatives **15-18** were prepared by treatment α,β-unsaturated oximes **11-14** with potassium iodide, iodine and sodium hydrogen carbonate, at 100 ºC, during 4 hours. Intramolecular oxidative cyclization of **11-14** gave the corresponding isoxazoles **15-18** in good yields (66-69%) (Scheme 2). The obtained residue was purified by flash chromatography using silica gel and a mixture of ethyl acetate:toluene as eluent. This method constitutes an improvement to the Moffatt method (oxidative cyclization of unsaturated oxime) [9], since we have only used water as solvent and smaller reaction times. This heterocycle derivative was obtained as a single compound confirmed by tlc, ^{1}H and ^{13}C nmr spectra.

In the ^{1}H nmr spectra of **15-18** the isoxazole proton resonance appears as a singlet near δ 6, while the ^{13}C nmr spectra showed the resonances of O-*C*=C (C-5) at δ 168.3-167.4 and the C=N at δ 160.3-159.6 ppm as quaternary carbons. The resonance of C-4 appears at δ 105.1-103.8 as CH.



Conclusions.

In this work the synthesis of the new pseudo-*C*-nucleosides 5-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-furanos-4-yl)-3-methyl-isoxazole (**15**), 5-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-furanos-4-yl)-3-methyl-isoxazole (**16**) and 5-(1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-pyranos-5-yl)-3-methyl-isoxazole (**17**) and the new homopseudo-*C*-nucleoside 5-[(1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanos-3-yl)methyl]-3-methyl-isoxazole (**18**) was reported. It involves an intramolecular oxidative cyclization of the appropriate α,β-unsaturated ketoxime derivative and was carried out using water as solvent.

EXPERIMENTAL

General Methods.

NMR spectra were recorded on Bruker AC-P 250 spectrometer (250 MHz for ^{1}H and 62.9 MHz for ^{13}C), with $CDCl_3$ as solvent with TMS as internal standard. Chemical shifts (δ) are reported in ppm values and coupling constants (J) in Hertz. High-resolution mass spectra (hrms) were performed on an APEX III FT-ICR MS (Bruker Daltonics, Billerica, MA), equipped with a 7T actively shielded magnet. Ions were generated using an Apollo API electrospray ionization (ESI) source. Ionization was achieved by an electrospray ionization source (Bruker Daltonics, Billerica, MA), with a voltage of between 1800 and 2200 V (to optimize ionization efficiency) applied to the needle, and counter voltage of 450 V applied to capillary. Samples were prepared by adding a spray solution of 50:49.5:0.5 (v/v/v) water/methanol/formic acid to the sample at a v/v ratio of 1 to 5% to give best signal-to-noise ratio. Data acquisition and data processing were performed using the XMASS software version 6.1.2 (Bruker Daltonics). Infrared (ir) spectra were obtained in a FT-IR Mattson Genesis II spectrophotometer. Optical rotations were determined on a Bellingham+Stanley Ltd ADP 220. Melting point was determined on a Leitz-Biomed with platinum plate apparatus and is uncorrected. Thin-layer chromatography (tlc) was carried out on silica gel F-254 plates and the column chromatography in silica gel 60 (230-400 mesh).

3-*C*-Ethoxycarbonylmethylene-1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanose (**5**).

A solution of ethyl bromoacetate (0.4 ml, 2.8 mmol) in dry THF (1 ml) was added drop by drop with stirring, under nitrogen atmosphere at room temperature, to a mixture of granulated zinc 20 mesh (0.095 g, 1.48 mmol) and **4** (0.258 g, 1 mmol) in dry THF (0.5 ml). The mixture was stirred for 1 hour at 45 ºC, and then cooled to room temperature. A cold aqueous solution of HCl (5%) (2 ml) was added, followed by extraction with dichloromethane (3x15 ml). The organic layer was washed with an aqueous solution of sodium bicarbonate (2.5%) (15 ml), dried and the solvent evaporated. The obtained residue was purified by column chromatography with ethyl acetate:toluene (1:5 v/v) and **5** was obtained as syrup in 67% yield (0.232 g). R_f = 0.69 (ethyl acetate:toluene 2:1). ^{1}H nmr: δ 5.70 (d, 1H, H-1, J = 3.6 Hz), 4.76 (d, 1H, H-2, J = 3.6 Hz), 4.29-4.05 (m, 4H, H-4, H-5, CH_2-6), 3.88-3.76 (m, 2H, OCH_2CH_3); 2.85 and 2.44 (AB system, 2H, CH_2-1', J = 14.9 Hz), 1.57, 1.43, 1.34 (3s, 4 x 3H, $4CH_3$ isopropylidene), 1.26 ppm (t, 3H, OCH_2CH_3, J = 6.3 Hz). ^{13}C nmr: δ 170.6 (Cq, CO_2Et), 112.6, 109.8 (Cq, isopropylidene), 103.3 (CH, C-1), 81.5 (2 x CH, C-2 and C-4), 78.3 (Cq, C-3), 73.2 (CH, C-5), 67.9 (CH_2, C-6), 61.0 (CH_2, OCH_2CH_3), 37.1 (CH_2, C-1'), 26.6, 26.5, 26.4, 25.2 ($4CH_3$, isopropylidene), 14.1 ppm (CH_3, OCH_2CH_3).

3-*C*-Formylmethylene-1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanose (**6**).

To a solution of **5** (0.346 mg, 1.0 mmol) in dry THF (20 ml) at 0 ºC was added $LiAlH_4$ (0.038 mg, 1 mmol) in small portions. The reaction mixture was stirred at room temperature for 30 minutes. The excess of $LiAlH_4$ was eliminated by addition of a solution THF/water (70%, 20ml). The mixture was filtrated through celite and concentrated. The obtained residue was purified by column chromatography with ethyl acetate:toluene (1:2 v/v). 3-*C*-formylmethylene-1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanose (**6**) was obtained in 67% yield (0.230 g). R_f = 0.58 (ethyl acetate:toluene 2:1); ^{1}H nmr: δ 9.93 (t, 1H, C*H*O, J = 1.7 Hz), 5.69 (d, 1H, H-1, J = 3.8 Hz), 4.37 (d, 1H, H-2, J = 3.8 Hz), 3.71-4.05 (m, 4H, H-4, H-5 and CH_2-6); 2.99-2.92 and 2.39-2.31 (2m, 2H, CH_2-1'), 1.55, 1.42, 1.32, 1.31 ppm (4s, 4x3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 201.4 (CH, CHO), 113.1, 110.2 (Cq, isopropylidene), 103.7 (CH, C-1), 82.0 (2 x CH, C-2 and C-4), 78.7 (Cq, C-3), 73.4 (CH, C-5), 68.2 (CH_2, C-6), 61.9 (CH_2, O*C*H_2CH_3), 45.3 (CH_2, C-1'), 26.8, 26.6, 26.5, 25.3 ($4CH_3$, isopropylidene), 14.1 ppm (CH_3, OCH_2*C*H_3).

General Procedure for the Preparation of α,β-Unsaturated Ketones 7-10.

Acetonylidenetriphenylphosphorane (0.35 g, 1.1 mmol) was added to a solution of the appropriate formyl derivatives **1-3** or **6** (1.0 mmol) in chloroform (20 ml). The reaction mixture was stirred at room temperature during 5 hours, then evaporated to dryness and the obtained residue was purified by column chromatography using ethyl acetate:toluene (1:10 v/v).

3-*O*-Benzyl-5,6,8-trideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-oct-5-(*E*)-enfuranos-7-ulose (**7a**).

This compound was obtained as syrup in 72% yield (0.229 g). R_f = 0.38 (ethyl acetate:*n*-hexane 1:3); ir 1722 (C=O), 1638 (C=C) cm^{-1}; ^{1}H nmr: δ 7.39-7.16 (m, 5H, Ph of benzyl), 6.78 (dd, 1H, H-5, J = 5.3, 16.1 Hz), 6.38 (d, 1H, H-6, J = 16.1 Hz), 6.02 (d, 1H, H-1, J = 3.7 Hz), 4.84-4.80 (m, 1H, H-4), 4.69 (d, 1H, H-2, J = 3.7 Hz), 4.58 and 4.49 (AB system, 2H, CH_2 of benzyl, J = 12.1Hz), 4.02 (d, 1H, H-3, J = 3.2 Hz), 2.26 (s, 3H, CH_3-8), 1.51, 1.35 ppm (2s, 2 x 3H, $2CH_3$, isopropylidene); ^{13}C NMR δ: 197.5 (Cq, C=O, C-7), 140.2 (CH, C-6), 136.9 (Cq, Ph of benzyl), 131.5 (CH, C-5), 128.8, 127.9, 127.5 (CH, Ph of benzyl), 111.7 (Cq, isopropylidene), 104.8 (CH, C-1), 82.9 (CH, C-3), 82.4 (CH, C-2), 79.4 (CH, C-4), 72.2 (CH_2, benzyl), 27.2 (CH_3-8), 26.6, 27.0 ppm ($2CH_3$, isopropylidene).

3-*O*-Benzyl-5,6,8-trideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-oct-5-(*Z*)-enfuranos-7-ulose (**7b**).

This compound was obtained as syrup in 8% yield (0.028 g). R_f = 0.25 (ethyl acetate:*n*-hexane 1:3); ^{1}H nmr: δ 7.43-7.18 (m, 5H, Ph of benzyl), 6.33-6.23 (m, 2H, H-5, H-6), 6.00 (d, 1H, H-1, J = 3.8 Hz), 5.48 (m, 1H, H-4), 4.63 (d, 1H, H-2, J = 3.8 Hz), 4.57 and 4.43 (AB system, 2H, CH_2 of benzyl, J = 12.0 Hz), 4.36 (d, 1H, H-3, J = 3.2 Hz), 2.19 (s, 3H, CH_3-8), 1.57, 1.32 ppm (2s, 2 x 3H, $2CH_3$, isopropylidene); ^{13}C nmr: δ 198.4 (Cq, C-7), 143.5 (CH, C-6), 137.6 (Cq, Ph of benzyl), 128.4, 127.8, 127.7 (CH, Ph of benzyl), 127.6 (CH, C-5), 111.8 (Cq, isopropylidene), 105.2 (CH, C-1), 84.3 (CH, C-3), 83.3 (CH, C-2), 78.8 (CH, C-4), 72.3 (CH_2, benzyl), 31.2 (CH_3-8), 26.93, 26.45 ppm ($2CH_3$, isopropylidene).

3-*O*-Benzyl-5,6,8-trideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-oct-5-(*E*)-enfuranos-7-ulose (**8**).

This compound was obtained as syrup in 80% yield (0.254 g). R_f = 0.25 (ethyl acetate:*n*-hexane 1:3); ir: 1721 (C=O), 1641 (C=C) cm^{-1}; ^{1}H nmr: δ 7.42-7.27 (m, 5H, Ph of benzyl), 6.68 (dd, 1H, H-5, J = 4.9, 16.1 Hz), 6.35 (d, 1H, H-6, J = 16.1 Hz), 5.78 (d, 1H, H-1, J = 3.6 Hz), 4.77, 4.56 (AB system, CH_2 benzyl, 2H, J = 12.1 Hz), 4.67-4.60 (m, 2H, H-2 and H-4), 3.54 (q, 1H, H-3, J = 3.6, 9.2 Hz), 2.22 (s, 3H, CH_3-8), 1.62, 1.34 ppm (2s, 2 x 3H, $2CH_3$, isopropylidene); ^{13}C nmr: δ 197.9 (Cq, C-7), 142.1 (CH, C-6), 137.0 (Cq, Ph of benzyl), 130.9 (CH, C-5), 128.5, 128.2, 128.1 (CH, Ph of benzyl), 113.2 (Cq, isopropylidene), 104.0 (CH, C-1), 81.8 (CH, C-3), 77.3 (CH, C-2), 76.9 (CH, C-4), 72.4 (CH_2, benzyl), 27.4 (CH_3-8), 26.7, 26.4 ppm ($2CH_3$, isopropylidene).

6,7,9-Trideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-non-6-(*E*)-enpyranos-8-ulose (**9a**).

This compound was obtained as pellets (120-121 ºC) in 82% yield (0.820 g). R_f = 0.48 (ethyl acetate:*n*-hexane 1:3); ir: 1722 (C=O), 1635 (C=C) cm^{-1}; ^{1}H nmr: δ 6.76 (dd, 1H, H-6, J = 16.0, 4.8 Hz), 6.37 (d, 1H, H-7, J = 16.0 Hz), 5.69 (d, 1H, H-1, J = 5.0 Hz), 4.66 (dd, 1H, H-3, J = 7.7, 2.2 Hz), 4.49-4.47 (m, 1H, H-5), 4.37 (dd, 1H, H-2, J = 2.2, 5.0 Hz), 4.30 (dd, 1H, H-4, J = 7.7, 2.4 Hz), 2.30 (s, 3H, CH_3-9), 1.59, 1.45, 1.36, 1.34 ppm (4s, 4 x 3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 198.6 (Cq, C-8), 142.0 (CH, C-7), 131.3 (CH, C-6), 109.8, 108.9 (Cq, isopropylidene), 96.4 (CH, C-1), 72.8 (CH, C-4), 70.5 (CH, C-3), 69.2 (CH, C-5), 67.8 (CH, C-2), 27.4 (CH_3-9); 25.0, 24.9, 24.4, 24.2 ppm ($4CH_3$, isopropylidene).

6,7,9-Trideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-non-6-(*Z*)-enpyranos-8-ulose (**9b**).

This compound was obtained as syrup in 18% yield (0.021 g). R_f = 0.38 (ethyl acetate:*n*-hexane 1:3); ^{1}H nmr: δ 6.31 (d, 1H, H-6, J = 11.5 Hz), 6.16 (dd, 1H, H-7, J = 11.5, 6.9 Hz), 5.55 (d, 1H, H-1, J = 5.1 Hz), 5.35 (d, 1H, H-5, J = 6.9 Hz), 4.66 (dd, 1H, H-3, J = 2.5, 7.8 Hz), 4.51 (dd, 1H, H-4, J = 2.5, 7.8 Hz), 4.35 (t, 1H, H-2, J = 2.5, 5.1 Hz), 2.02 (s, 3H, CH_3-9), 1.56, 1.48, 1.34, 1.32 ppm (4s, 4 x 3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 198.6 (Cq, C-8), 144.5 (CH, C-7), 126.6 (CH, C-6), 109.3, 109.0 (Cq, isopropylidene), 96.5 (CH, C-1), 73.2 (CH, C-4), 71.1 (CH, C-3), 70.2 (CH, C-5), 65.9 (CH, C-2), 31.5 (CH_3-9); 26.0, 25.1, 24.4 ppm ($4CH_3$, isopropylidene).

3-*C*-[4-Oxopent-2-(*E*)-enyl]-1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanose (**10**).

This compound was obtained as syrup in 78% yield (0.267 g). R_f = 0.47 (ethyl acetate); ir: 1724 (C=O), 1633 (C=C), cm^{-1}; ^{1}H nmr: δ 7.05-6.93 (m, 1H, H-2'), 6.14 (d, 1H, H-3', J = 15.6 Hz), 5.68 (d, 1H, H-1, J = 3.8 Hz), 4.22 (d, 1H, H-2, J = 3.8 Hz), 4.16-4.06 (m, 2H, CH_2-6), 4.04-4.00 (m, 1H, H-5), 3.95-3.77 (m, 1H, H-4), 2.97 (brs, 1H, OH-3), 2.75 (dd, 1H, H-1', J = 6.1, 13.1 Hz), 2.23 (dd, 1H, H-1', J = 6.1, 13.1 Hz), 1.99 (s, 3H, CH_3-5'), 1.56, 1.43, 1.34, 1.28 ppm (4s, 4 x 3H, $4CH_3$, isopropylidene); ^{13}C-nmr: δ 197.9 (Cq, C-4'), 143.4 (CH, C-3'), 125.3 (CH, C-2'), 112.6 (Cq, isopropylidene), 109.7 (Cq, isopropylidene), 104.7 (CH, C-1), 85.5 (CH, C-4), 83.1 (CH, C-5), 81.5 (Cq, C-3), 73.1 (CH, C-2), 67.8 (CH_2, C-6), 36.0 (CH_2, C-1'), 27.6 (CH_3-5'), 27.1, 26.7, 26.5, 25.2 ppm ($4CH_3$, isopropylidene).

General Procedure to Prepare α,β-Unsaturated Oximes **11-14**.

A solution of α,β-unsaturated ketone **7a, 8, 9a** or **10** (*E* isomers) (1.0 mmol) and hydroxylamine hydrochloride (0.167 g, 2.4 mmol) in a mixture of pyridine (10 ml) and methanol (30 ml) was stirred at room temperature for 2 hours and then evaporated to dryness. The residue was co-evaporated twice with toluene and purified by column chromatography using ethyl acetate:toluene 1:5 (v/v) to give the oxime derivatives **11-14** as pure compounds.

3-*O*-Benzyl-5,6,8-trideoxy-7-hydroxyimino-1,2-*O*-isopropylidene-α-D-*xylo*-oct-5-(*E*)-enfuranose (**11**).

This compound was obtained as syrup in 93% yield (0.310 g); R_f = 0,3 (ethyl acetate:toluene 1:3); ir: 3485 (OH), 1634 (C=C) cm^{-1}; ^{1}H nmr: δ 9.45 (br s, 1H, NOH), 7.37-7.12 (m, 5H, Ph of benzyl), 6.43 (d, 1H, H-6, J =16.1 Hz), 6.22, (dd, 1H, H-5, J =8.2, 16.1 Hz), 5.99 (d, 1H, H-1, J = 3.7 Hz), 4.78-4.64 (m, 3H, 1H of CH_2 of benzyl, H-2, H-4), 4.50 (part B from AB system, 1H, CH_2 of benzyl, J = 12.2 Hz), 3.92 (d, 1H, H-3 J =2.9 Hz), 2.35 (s, 3H, CH_3-8), 1.51, 1.26 ppm (s, 3H, $2CH_3$, isopropylidene); ^{13}C nmr: δ 155.8 (Cq, C-7), 137.4 (Cq, Ph of benzyl), 131.1 (CH, C-6), 129.0, 128.6, 128.1 (CH, Ph of benzyl), 127.7 (CH, C-5), 111.9 (Cq, isopropylidene), 105.1 (CH, C-1), 83.9 (CH, C-2), 83.7 (CH, C-4), 81.0 (CH, C-3), 72.3 (CH_2, benzyl), 26.9, 26.3 ($2CH_3$, isopropylidene), 9.8 ppm (CH_3-8).

3-*O*-Benzyl-5,6,8-trideoxy-7-hydroxyimino-1,2-*O*-isopropylidene-α-D-*ribo*-oct-5-(*E*)-enfuranose (**12**).

This compound was obtained as syrup in 98% yield (0.326 g); R_f = 0,5 (ethyl acetate:toluene 1:2); ir: 3500 (OH), 1630 (C=C) cm^{-1}; ^{1}H nmr: δ 7.40-7.15 (m, 5H, Ph of benzyl), 6.48 (d, 1H, H-6, J =16.1 Hz), 5.92 (dd, 1H, H-5, J =8.2, 16.1 Hz), 5.76 (d, 1H, H-1, J =3.4 Hz), 4.76 (part A from AB system, 1H, CH_2 of benzyl J =12.4 Hz), 4,68-4,48 (m, 3H, 1H of CH_2 of benzyl, H-2, H-4), 3.53 (dd, 1H, H-3 and J = 9.1, 4.3 Hz), 1.96 (s, 3H, CH_3-8), 1.63, 1.37 ppm (s, 3H, $2CH_3$, isopropylidene); ^{13}C nmr: δ 155.3 (Cq, C-7), 137.1 (Cq, Ph of benzyl), 130.8 (CH, C-6), 130.3 (CH, C-5), 128.3, 128.1, 127.9 (CH, Ph of benzyl), 112.9 (Cq, isopropylidene), 103.6 (CH, C-1), 81.7 (CH, C-2), 78.1 (CH,C-4), 77.3 (CH, C-3), 72.1 (CH_2, of benzyl), 26.6, 26.3 ($2CH_3$, isopropylidene), 9.5 ppm (CH_3-8).

6,7,9-Trideoxy-8-hydroxyimino-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-non-6-(*E*)-enpyranose (**13**).

This compound was obtained as syrup in 97% yield (0.304 g); R_f = 0,45 (ethyl acetate:toluene 1:2); ir: 3490 (OH), 1632 (C=C) cm^{-1}; ^{1}H nmr: δ 9.46 (br s, 1H, NOH), 6.39 (d, 1H, H-7, J = 16.1 Hz), 6.12 (dd, 1H, H-6, J = 16.1, 8.2 Hz), 5.59 (d, 1H, H-1, J = 4.9 Hz), 4.64 (dd, 1H, H-4, J = 7.8, 6.5 Hz), 4.41 (d, 1H, H-5, J = 8.2, 6.5 Hz), 4.34 (q, 1H, H-2, J = 4.9, 2.3 Hz), 4.24 (dd, 1H, H-3, J = 7.8, 2.3 Hz), 2.02 (s, 3H, CH_3-9), 1.55, 1.48, 1.35 ppm (s, 3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 155.3 (Cq, C-8), 130.2 (CH, C-7), 130.1 (CH, C-6), 109.4, 108.7 (Cq, isopropylidene), 96.4 (CH, C-1), 73.3 (CH, C-4), 70.8 (CH, C-3), 70.3 (CH, C-5), 68.8 (CH, C-2), 26.1, 25.9, 24.9, 24.3 ($4CH_3$, isopropylidene), 9.7 ppm (CH_3-9).

3-*C*-[4-Hydroxyiminopent-2-(*E*)-enyl]-1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanose (**14**).

This compound was obtained as syrup in 96% yield (0.343 g); R_f = 0,47 (ethyl acetate); ir: 3490 (OH), 1631 (C=C) cm^{-1}; ^{1}H nmr: δ 6.27-6.15 (m, 2H, H-3',H-2'), 5.67 (d, 1H, H-1, J = 3.4 Hz), 4.28 (d, 1H, H-2, J = 3.4 Hz), 4.14-4,09 (m, 2H, CH_2-6), 3,92-3,89 (m, 1H, H-5), 3.82 (d, 1H, H-4, J = 7.5 Hz), 2.82-2.74 (m, 2H, H-1', OH-3), 2.25 (dd, 1H, H-1', J = 7.3, 8.3 Hz), 2.01 (s, 3H, CH_3, C-5'), 1.56, 1.43, 1.34, 1.28 ppm (s, 3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 155.9 (Cq, C-4'), 131.0 (CH, C-2'), 130.0 (CH, C-3'), 112.6, 109.7 (Cq, isopropylidene), 103.4 (CH, C-1), 81.8 (CH, C-2), 81.3 (CH, C-4), 78.9 (Cq, C-3), 73.1 (CH, C-5), 67.9 (CH_2, C-6), 35.5 (CH_2, C-1'), 27.1, 26.5, 26.3, 25.2 (CH_3, $4CH_3$, isopropylidene), 9.6 ppm (CH_3, C-5').

General Procedure for the Preparation of Isoxazoles **15-18**.

A solution of potassium iodide (0.581 g, 3.5 mmol) and iodine (0.279 g, 1.1 mmol) in water (5 ml) was added in the dark to a stirred solution of the appropriate oxime derivative **11-14** (1 mmol) and sodium bicarbonate (0.336 g, 4 mmol) in water (5 ml). The mixture was heated under reflux for 4 hours, cooled, diluted with saturated aqueous sodium thiosulfate (3 ml), and extracted with dichloromethane (3 x 20 ml). The organic phase was dried and evaporated to dryness and the obtained residue was purified by column chromatography with ethyl acetate:toluene (1:4 v:v) to give the isoxazoles **15-18**.

5-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-furanos-4-yl)-3-methylisoxazole (**15**).

This compound was obtained as syrup in 66% yield (0.218 g); R_f=0,71 (ethyl acetate:*n*-hexane 2:1); α_D^{20}= -23.33º (c 2.0, $CHCl_3$); ir: 1618 (C=C) cm^{-1}; hrms: $(M+Na)^+$, found 354.1375, $C_{18}H_{21}NO_5Na$, requires, 354.1318, $(M+H)^+$ found 332.1502, $C_{18}H_{22}NO_5$, requires 332.1498; ^{1}H nmr: δ 7.38-7.18 (m, 5H, Ph of benzyl), 6.23 (s, 1H, H-4), 6.02 (d, 1H, H-1', J = 3.6 Hz), 5.33 (d, 1H, H-4', J = 3.1 Hz), 4.68 (d, 1H, H-2' J = 3.6 Hz), 4.57, 4.49 (AB system CH_2 of benzyl, J = 11.9 Hz), 4.02 (d, 1H, H-3' J = 3.1 Hz), 2.29 (s, 3H, CH_3-3), 1.52, 1.33 ppm (2s, 2x3H, $2CH_3$, isopropylidene); ^{13}C nmr: δ: 167.4 (Cq, C-5), 159.8 (Cq, C-3), 136.9 (Cq, Ph of benzyl), 128.5, 128.0, 127.7 (CH, Ph of benzyl), 111.9 (Cq, isopropylidene), 105.0 (CH, C-4), 104.4 (CH, C-1'), 83.0 (CH, C-2'), 82.3 (CH,C-4'), 75.9 (CH, C-3'), 72.6 (CH_2, benzyl), 26.9, 26.2 ($2CH_3$, isopropylidene), 11.4 ppm (CH_3-3).

5-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-furanos-4-yl)-3-methylisoxazole (**16**).

This compound was obtained as syrup in 67% yield (0.222 g); R_f = 0,68 (ethyl acetate:*n*-hexane 1:1); α_D^{20}= +47.78º (c 1.5, $CHCl_3$); ir: 1614 (C=C) cm^{-1}; hrms: $(M+Na)^+$, found 354.1327, $C_{18}H_{21}NO_5Na$, requires, 354.1318, $(M+H)^+$ found 332.1506, $C_{18}H_{22}NO_5$, requires 332.1498; ^{1}H nmr: δ 7.36-7.19 (m, 5H, Ph of benzyl), 6.08 (s, 1H, H-4), 5.84 (d, 1H, H-1', J = 3.5 Hz), 5.09 (d, 1H, H-4', J = 9.1 Hz), 4.64-4.46 (m, 3H, CH_2 benzyl, H-2'), 4.05 (dd, 1H, H-3' J = 9.1, 4.0 Hz), 2.29 (s, 3H CH_3-3), 1.70, 1.38 ppm (2s, 2x3H, $2CH_3$, isopropylidene); ^{13}C nmr: δ 168.1 (Cq, C-5), 159.7 (Cq, C-3), 137.0 (Cq, Ph of benzyl), 128.5, 128.1, 128.0 (CH, Ph of benzyl), 113.4 (Cq, isopropylidene), 104.5 (CH, C-4), 104.1 (CH, C-1'), 80.8 (CH, C-2'), 77.6 (CH, C-4'), 72.6 (CH_2, benzyl), 72.3 (CH, C-3'), 26.9 26.4 ($2CH_3$, isopropylidene), 11.4 ppm (CH_3-3).

5-(1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-pyranos-5-yl)-3-methylisoxazole (**17**).

This compound was obtained as syrup in 64% yield (0.199 g); R_f = 0,62 (ethyl acetate:*n*-hexane 1:2); α_D^{20}= -109.52º (c 1.4, $CHCl_3$); ir: 1615 (C=C) cm^{-1}; hrms: $(M+Na)^+$, found 334.1276, $C_{15}H_{21}NO_6Na$, requires, 334.1267, $(M+H)^+$ found 312.1450, $C_{15}H_{22}NO_6$, requires 312.1447; ^{1}H nmr: δ 6.17 (s, 1H, H-4), 5.59 (d, 1H, H-1', J = 4.9 Hz), 4.96 (d, 1H, H-5', J =1.1 Hz), 4.69 (dd, 1H, H-2' J = 7.8, 4.9 Hz), 4.49 (dd, 1H, H-3', J = 7.8, 1.9 Hz), 4.36 (dd, 1H, H-4' J =1.9, 1.1 Hz), 2.25 (s, 3H CH_3-3), 1.52, 1.40, 1.32, 1.29 ppm (s, 4x3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 168.3 (Cq, C-5), 159.6 (Cq, C-3), 109.8, 109.0 (Cq, isopropylidene), 103.8 (CH, C-4), 96.5 (CH, C-1'), 71.6 (CH, C-2'), 70.6 (CH, C-3'), 70.5 (CH, C-5'), 64.5 (CH, C-4'), 26.1, 25.8, 24.8, 24.3 ($4CH_3$, isopropylidene), 11.4 ppm (CH_3-3).

5-[(1,2:5,6-Di-*O*-isopropylidene-α-D-*allo*-furanos-3-yl)methyl]-3-methylisoxazole (**18**).

This compound was obtained as syrup in 68% yield (0.245 g), R_f = 0,63 (ethyl acetate:*n*-hexane 1:1), α_D^{20}= +14.44º (c 2.0, $CHCl_3$); ir: 3418 (OH), 1608 (C=C) cm^{-1}; hrms: $(M+Na)^+$, found 378.1523, $C_{17}H_{25}NO_7Na$, requires, 378.1529; ^1H nmr: δ 6.17 (s, 1H, H-4), 5.76 (d, 1H, H-1', J = 3.8 Hz), 4.25 (d, 1H, H-2', J = 3.8 Hz), 4.21-4.15 (m, 2H, CH_2-6'), 3.98-3.85 (m, 1H, H-5'), 3.83 (d, 1H, H-4', J = 7.5 Hz), 3.28 (part A from AB system, 1 H of methylene, J = 15.3 Hz), 2.93-2.85 (m, 2 H, part B from AB system, 1H of methylene, OH-3') , 2.30 (s, 3H, CH_3-3), 1.58, 1.48, 1.38, 1.33 ppm (4s, 4x3H, $4CH_3$, isopropylidene); ^{13}C nmr: δ 167.9 (Cq, C-5), 160.3 (Cq, C-3), 112.8, 110.0 (Cq, isopropylidene), 105.1 (CH, C-4), 103.6 (CH, C-1'), 81.9 (CH, C-4'), 81.0 (CH, C-2'), 78.8 (Cq, C-3'), 73.2 (CH, C-5'), 68.2 (CH_2, C-6'), 29.6 (CH_2, methylene), 26.9, 26.7, 26.5, 25.3 ($4CH_3$, isopropylidene), 11.5 ppm (CH_3-3).

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