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Synthesis and Biological Evaluation of Sugars Containing α,β-Unsaturated γ-Lactones

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The stereocontrolled synthesis of new sugar derivatives carrying the α,β-unsaturated δ-lactone (butenolide) moiety is described. Sugar-fused or sugar-linked butenolides can be constructed by an efficient reaction sequence involving Wittig olefination of 3- or 5-keto sugars and intramolecular cyclization of the intermediate γ-hydroxy α,β-unsaturated esters. The antimicrobial activities of the products and that of a known sugar-derived pyranoid α,β-unsaturated δ-lactone were investigated against six pathogenic bacteria and six fungi. The pyranoid α,β-unsaturated δ-lactone **29** proved to be the most active compound in this series towards the plant pathogenic fungi *Colletotrichum coffeanum* (coffee berry disease) and *Pyricularia oryzae* (rice blast disease).

Introduction

α,β-Unsaturated γ-lactones are abundant in both naturally occurring and synthetic products and are known to show a variety of antimicrobial[1] or cytotoxic[2] properties. Some of these compounds were reported to be potential antitumor agents,[3] cyclooxygenase or phospholipase A2 inhibitors,[4] or antibiotics.[5]

In particular sugars bearing this moiety have become important molecular targets with respect to their significant biological profile and their functionalized nature, which make them suitable intermediates of distinct synthetic versatility.[6]

The practice of incorporating unsaturated lactones into carbohydrates has been achieved with success in our laboratory. Some of these compounds (exocyclic unsaturated γ-lactones, compounds of type **A**, Figure 1) show significant antifungal activity and are particularly effective against *Puccinia recondita* (wheat), *Botrytis cinerea* (pepper) and *Plasmopara viticola* (gravepine). They are considered potential wheat-, pepper-, or wine-protective agents.[7] Moreover, sugar-linked butenolides (endocyclic unsaturated γ-lactones, compounds of type **B**, Figure 1) have demonstrated their efficacy as potent and selective insecticides aginst *Drosophila melanogaster* Meig (fruitfly), and proved to be much more active than imidacloprid, the insecticide that is already commercially used.[8] The fungicidal lactones were synthesized via Reformatsky-type reaction with a dialdofuranose as starting material.[7,9] The approach described for the synthesis of the insecticidal compounds relies on the reaction of sugar epoxides with the dianion of phenylselenoacetic and -propionic acids, or their thioanalogues, followed by oxidation and elimination.[7,10] Various routes leading to sugar-*C*-linked butenolides have also been reported, including Wittig and iodo-lactonization reactions starting from a dialdofuranose and recently, ring-closing metathesis via sugar-derived Baylis–Hillman adducts.[11,12] With respect to sugar-fused α,β-unsaturated γ-lactones, some literature reports describe their use for the preparation of bioactive natural products and branched-chain sugars.[13,14]

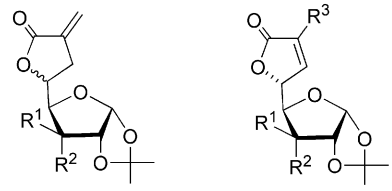

Figure 1. Structure of sugar-linked α,β-unsturated-γ-lactones possessing fungicidal (**A**) and insecticidal (**B**) properties.

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We have recently demonstrated an effective route to access various butenolides fused to pento- and hexopyranoses.[15] The strategy is based on the Wittig olefination of furanos-3-uloses containing acid-labile 5-*O*- or 5,6-di-*O*-protecting groups, followed by acid hydrolysis. According to our previous findings and as part of our ongoing search for strategies to insert these structural motifs into carbohydrate templates for the design of new potentially biologically active substances, we have planned the synthesis of analogues of the described insecticidal butenolides (compounds type **B**, Figure 1).

The developed methodology makes use of the Wittig reaction of 5-keto sugars with a resonance-stabilized ylide to give α,β-unsaturated esters. The latter are spontaneously converted into the corresponding lactones in the presence of a γ-hydroxy group, by controlling the stereochemistry of the Wittig products. Derivatives which differ in the steric bulk of the substituent at C-3 or in the C-3 configuration were synthesized in order to investigate the influence of these structural factors on the stereoselectivity. Moreover, to broaden the structural diversity of these sugar derivatives, we explored our recently reported methodology for the synthesis of new butenolides fused to pento- and hexopyranoses. One of the prospective applications of these bicyclolactones is the synthesis of fused-disaccharides by diol addition.

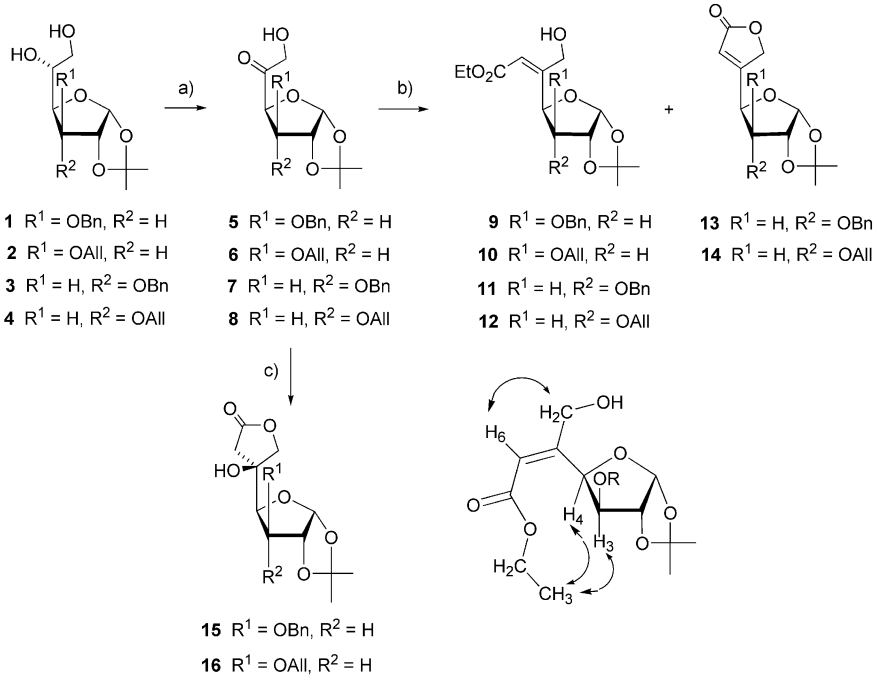
The results of the antimicrobial activity evaluation performed on the newly synthesized C–C-linked sugar-butenolides as well as on the previously reported bicyclic fused derivatives are presented here. To extend the range of the sugar-based unsaturated lactones tested, a pyranoid α,β-unsaturated γ-lactone[16] was included in our set of compounds. In addition, we compared these results with related data for known antifungal α-methylene γ-butyrolactones in order to rationalize, in terms of structure, the influence of the lactone system on the observed bioactivities. For this purpose we especially want to emphasize a possible relationship between the Michael-accepting ability of the tested compounds and their biological activities.

Results and Discussion

1. Chemistry

1.1. C–C-Linked Sugar-Butenolides

The synthesis of 5-keto sugars **5**–**8** (Scheme 1) was achieved by regioselective oxidation of the secondary hydroxy group of the 5,6-diol precursors **1**–**4** with the system Bu_2SnO/NBS[17] in 90, 78, 60 and 61% yield, respectively. The ^1H NMR spectra of the α-hydroxy ketone products show AB-system patterns for 6a-H, 6b-H, with geminal coupling constants from 20.2 to 20.5 Hz. The carbonyl groups of **5**–**8** give rise to characteristic signals in the ^{13}C-NMR spectra (δ = 208.2, 208.2, 207.1, and 207.3, respectively) and show IR band absorptions at 1725 and 1730 cm^{-1}. The lower yield obtained for the *ribo* derivatives may result from dimerization of the α-hydroxy ketones, which must depend on the stereochemistry at C-3, as suggested in the literature.[17] Hence dimerization occurs to a larger extent in *ribo* than in *xylo* compounds in which the orientation of the C-3 substituent results on increased steric hindrance to the formation of dimers. The 5-keto substrates were subjected to Wittig reaction with [(ethoxycarbonyl)-

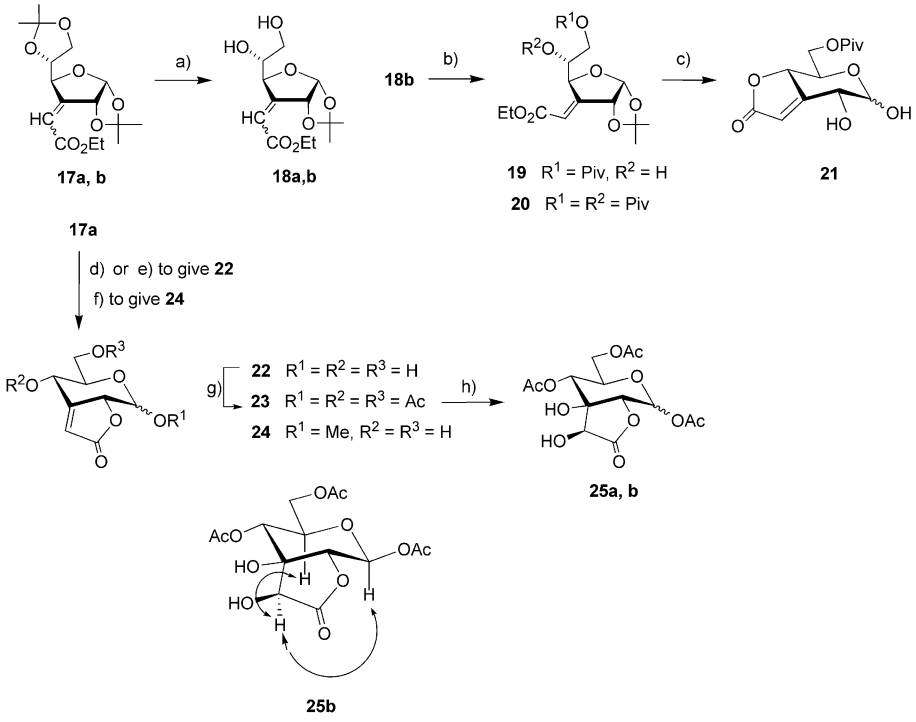


Scheme 1. Reactions and conditions: a) Bu_2SnO, toluene, reflux overnight, then NBS, CH_2Cl_2, 5 min; b) $Ph_3P{=}CHCO_2Et$, $CHCl_3$, reflux; c) $BrCH_2CO_2Et$, Zn, THF, 50 °C.

methylene]triphenylphosphorane in refluxing chloroform to give compounds **9**–**12**. Starting from 3-*O*-benzyl- and 3-*O*-allyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**5**, **6**), the (*Z*)-α,β-unsaturated esters **9**, **10** were obtained in 74% and 60% yield, respectively, and no cyclization was observed. In the ^{1}H NMR spectra, the signals of the olefinic protons appear at δ = 6.02 and 6.08, respectively, as broad singlets. Diagnostic signals for the configuration assignment of these molecules are the 4-H protons, which are relatively downfield shifted (δ = 5.83 and 5.84 ppm), thus reflecting the orientation of the ethoxycarbonyl group. Furthermore, the (*Z*)-configuration around the double bond could be confirmed by NOESY experiments, due to the correlations of 3-H and 4-H with CH_3 (Et) protons and those of 6-H with 5′a-H, 5′b-H. However, when the *ribo*-hexofuranos-5-ulose derivatives **7**–**8** were used as starting materials, the corresponding Wittig reaction provided mainly the formation of the (*E*) adducts, the spontaneous cyclization of which gave the α,β-unsaturated-γ-lactones **13**, **14** in 47% and 49% yield, respectively. The carbonyl groups of the butenolide moeties were confirmed by the signals at δ = 173.3 in their ^{13}C NMR spectra. In the ^{1}H NMR spectra, olefinic protons give rise to signals at δ = 6.06 and 6.12, respectively, and as a consequence of lactonization, chemical shifts values for 4-H around δ = 4.85 are much smaller than those observed for their acyclic (*Z*)-aducts **11** and **12**, which were isolated in only 12 and 11% yield, respectively. These results suggest that the stereoselectivity of the Wittig reaction to the formation of the (*E*)-isomers and consequently, to their spontaneous lactonization, depends on the orientation of the C-3 substituent. A possible steric hindrance due to C-3 configuration in *xylo*-hexofuranose derivatives with a bulky benzyloxy group or with allyl ether protection at position 3 may be envisaged. The 5-keto sugars **5**, **6** were also used as precursors for a Reformatsky reaction with ethyl bromoacetate to afford the sugar-linked β-hydroxy lactones **15**, **16**, formed in low yield (16 and 19%, respectively), together wih a complex mixture of degradation products. A salient feature of the ^{1}H NMR spectra of **15** and **16** is the two separate sets of AB systems for the five-membered ring lactone unit, assigned for 5′a-H, 5′b-H, and 6a-H, 6b-H, the latter shifted upfield. The presence of the signals at 174.8 and 175.1 for the carbonyl groups of **15** and **16**, respectively, in their ^{13}C NMR spectra confirmed the lactone skeleton. Our proposed configuration for the stereogenic centre (C-5) of the formed lactone is based on the assumption that the nucleophilic attack of the Reformatsky reagent to **5**–**6** should occur from the less hindered face of the carbonyl group.

1.2. Sugar-Fused Butenolides

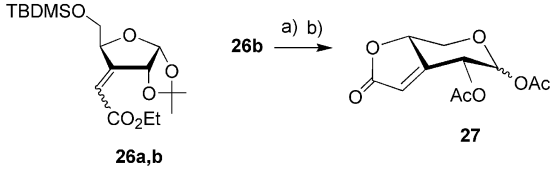
The synthesis of sugar-fused butenolides was accomplished following the approach previously reported by us, starting from readily available furanos-3-uloses.[15] Thus, Wittig reaction of 1,2;5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranosid-3-ulose[9] with [(ethoxycarbonyl)methylene]-triphenylphosphorane in refluxing chloroform afforded the known (*E*)- and (*Z*)-α,β-unsaturated esters **17a**,**b**[18] (Scheme 2) in 12% yield and 68% yield, respectively. The (*E*) adduct **17b** was partially hydrolysed at the primary ace-



Scheme 2. Reactions and conditions: a) AcOH 60% aq., room temp.; b) PivCl, CH_2Cl_2/py, 0 °C; c) AcOH 70% aq., reflux; d) Amberlite IR-120 H^+, MeOH, reflux overnight; e) DOWEX 50W H^+, MeOH, reflux, 2 h; f) DOWEX 50W H^+, MeOH, reflux, overnight; g) Ac_2O, py, room temp., 5 min; OsO_4, py, room temp.

tonide with aq. acetic acid (60%) to the corresponding diol **18b** which was subsequently treated with pivaloyl chloride in pyridine/dichloromethane at 0 °C. The mono-pivaloyl derivative **19**, selectively obtained in 81% yield, was submitted to hydrolysis with aqueous acetic acid (70%) under reflux to provide the hexopyranose-fused butenolide **21** as a mixture of α,β-anomers in 58% yield. Noteworthy in this step, in which cleavage of the acetal, isomerization to the pyranose form, and accompanying intramolecular lactonization occur, is that the pivaloyl group unexpectedly remains in the final product and no migration was observed. This feature could indeed be confirmed by the observed HMBC correlation between 6a,b-H and the carbonyl carbon of the pivaloyl group. On the other hand, conversion of the (*Z*)-α,β-unsaturated ester **17a** to the butenolide **22** in one single step was initially performed by treatment with IR-120 H^+ resin in refluxing methanol overnight in 90% yield. Manipulation of the reaction conditions using an ion-exchange resin with stronger acidic properties, Dowex-50W, the reaction time was reduced to 2 h, whereas the corresponding methyl glycoside **24** was formed in 57% yield after overnight stirring. Dihydroxylation of the triacetate-derived butenolide **23** with osmium tetroxide gave the α/β-*cis*-diols **25a**,**b** which could be separated by column chromatography and isolated in 33 and 23% yield, respectively. The (*S*)-configuration of the new stereocenter could be assigned by 2D-NOESY analysis of the β-anomer, with the detection of NOEs between 3′-H-5-H and 3′-H-1-H (Scheme 2). These compounds constitute non-natural fused disaccharides which comprise a butyrolactone and a pyranose system.

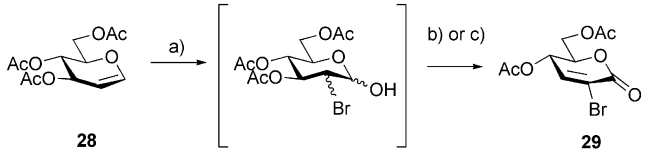
Similarly to the hexofuranose derivatives, the (*E*)-α,β-unsaturated ester **26b**, a minor stereoisomer, prepared by Wittig olefination of 1,2-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-α-D-*erythro*-furan-3-ulose,[15] was subjected to an analogous acid hydrolysis, which was followed by acetylation (Scheme 3). The bicyclolactone **27**, the structure of which comprises the butenolide moiety fused to a pentopyranose unit at positions 3 and 4, was obtained in 74% overall yield.



Scheme 3. Reactions and conditions: a) AcOH 70%, reflux; b) Ac_2O, py, room temp., 5 min.

1.3. Synthesis of a Sugar Pyranoid α,β-Unsaturated δ-Lactone

The hex-2-enono-1,5-lactone **29** was synthesized by reaction of 1,5-anhydro-3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hex-1-enitol (**28**) (non-preferred trivial name: 3,4,6-tri-*O*-acetyl-D-glucal) with *N*-bromosuccinimide (NBS) and water followed by oxidation of the 2-bromolactol formed, according to the approach previously reported (Scheme 4).[16] Two different chromium-based reagents were used at the oxidation step: pyridinium chlorochromate (PCC) as in the original procedure and pyridinium dichromate (PDC). In both cases, after reaction completion, the mixture was filtered through a short Florisil plug, which efficiently retained the green Cr^{III} species, facilitating the purification of the enonolactone **29** by column chromatography. However the first oxidizing methodology provided the best result in this one-pot, two-step procedure, forming the target compound in 43% overall yield, when compared to 31% yield using PDC.



Scheme 4. Reactions and conditions: a) NBS, H_2O/THF; b) PCC, molecular sieves (3 Å), CH_2Cl_2, room temp.; c) PDC, Ac_2O, CH_2Cl_2, room temp.

2. Antibacterial and Antifungal Screening

The antimicrobial activities of sugar-linked butenolides **13**, **14**, sugar-fused butenolides **22**, **23**, **30**[15] and **31**[15] (Figure 2) and pyranoid α,β-unsaturated δ-lactone **29** were investigated using the paper disk diffusion method.[19,20] These compounds were evaluated for their in vitro antibacterial activity against pathogens such as *Bacillus cereus*, *Bacillus subtilis*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Their antifungal activity was studied on a panel of plant pathogenic fungi which may also cause human allergies including *Botrytis* spp., *Colletotrichum coffeanum*, *Fusarium culmorum*, *Pyricularia oryzae*, and *Rhizopus* spp., and the human fungal pathogen *Candida albicans*. The results are presented in Table 1. The sugar-linked butenolide **14** exhibited weak effects toward *Bacillus subtilis* and *Candida albicans* while the 3-*O*-benzyl counterpart **13**, showed virtually no activity at all. Regarding these results and in contrast with those of the analogues possessing an α-methylene-γ-lactone moiety (compounds type **B**, Figure 1), particularly against *Botrytis* spp., *Fusarium culmorum* and *Pyricularia oryzae*, it is clear that the exocylic double bond in the lactone enhances the antifungal activity of these compounds. Given their structure, the exocyclic α,β-unsaturated γ-lactones have greater ability than the endocyclic derivatives to act as Michael acceptors, which is commonly related to the bioactivity of α,β-unsaturated carbonyl compounds.[21] Hence, the pres-

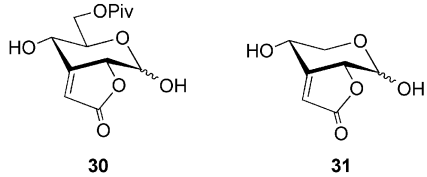


Figure 2. Structure of sugar-fused butenolides **30**, **31** submitted to bioactivity tests.

Table 1. Antimicrobial activities of compounds **13**, **14**, **22**, **23**, **29**, **30** and **31**.[a]

Microbes and bacteria	**13**	**14**	**22**	**23**	**29**	**30**	**31**	Control[b] I	II
Bacillus cereus	<6.4	<6.4	<6.4	<6.4	11	<6.4	<6.4	24	38
Bacillus subtilis	<6.4	9	10	16	<6.4	10	<6.4	30	46
Enterococcus faecalis	<6.4	<6.4	<6.4	<6.4	9	<6.4	<6.4	26	40
Escherichia coli	<6.4	<6.4	<6.4	<6.4	9	<6.4	<6.4	28	42
Pseudomonas aeruginosa	<6.4	<6.4	<6.4	<6.4	9	<6.4	<6.4	<6.4	22
Staphylococcus aureus	<6.4	<6.4	<6.4	<6.4	9	<6.4	<6.4	27	40
Fungi									
Botrytis spp.	<6.4	<6.4	8	8	11	<6.4	<6.4	<6.4	20
Candida albicans	<6.4	9	8	8	10	8	8	<6.4	16
Colletotrichum coffeanum	<6.4	<6.4	<6.4	<6.4	16	<6.4	<6.4	16	24
Fusarium culmorum	<6.4	<6.4	<6.4	<6.4	<6.4	<6.4	<6.4	12	18
Pyricularia oryzae	<6.4	<6.4	<6.4	<6.4	15	<6.4	<6.4	39	63
Rhizopus spp.	<6.4	<6.4	<6.4	<6.4	<6.4	<6.4	<6.4	11	18

[a] Compound solutions tested [300 μg compound in DMSO (15 μL)]. [b] Chloramphenicol was used for all bacteria and for *C. albicans*, whereas actidione was used for the filamentous fungi; a solution of the control (I: 30 μg, II: 300 μg) in DMSO (15 μL) was used.

ence of the quaternary hindered β-carbon in the lactone system of **13** and **14**, considerably reduces their propensity to a nucleophilic attack, especially by sulfhydryl groups of enzymes.

Sugar-fused butenolides **22**, **23** and **30** display selective antibacterial activity against *Bacillus subtilis*; the highest activity was observed for the triacetate derivative **23** with moderate effect. The antibacterial effect of compound **31** is practically negligible. With respect to the antifungal activity assays, all the butenolide derivatives show similar and weak activities toward *Candida albicans*. Compounds **22** and **23** exhibit weak activities against *Botrytis* spp., although butenolides **30** and **31** are inactive against these pathogens. The results of the antimicrobial evaluation made on this series may be also related to the presence of the hindered double bond in the lactone conjugated system, which is now fused to a six-membered ring, making the system less susceptible to Michael addition. The pyranoid α,β-unsaturated δ-lactone **29** proved to be the most active compound of this set; **29** is active against all the bacteria tested, except for *Bacillus subtilis*, for which no effect was detected. Regarding the tested fungi, lactone **29** shows weak activities against *Botrytis* spp. and *Candida albicans* and moderate activity against *Colletotrichum coffeanum* (coffee berry disease) and *Pyricularia oryzae* (rice blast disease). The greater Michael-accepting ability of **29** when compared to that of the previous lactones, due to the electron-withdrawing influence of the bromine atom and absence of steric hindrance in the reactive double bond, may indeed contribute to the biological results obtained.

Conclusions

A series of novel sugar-containing butenolides was synthesized. C–C-Linked sugar-butenolides were prepared by Wittig olefination of hexofuranos-5-uloses followed by intramolecular lactonization of the intermediate γ-hydroxy α,β-unsaturated esters. The configuration at C-3 seems to be an important structural factor to control the cyclization step. Hence, butenolides were prepared from *ribo*-furanos-5-ulose derivatives, while olefination of *xylo*-5-uloses did not afford the appropriate stereoisomer for spontaneous cyclization. The synthesis of sugar-fused butenolides was accomplished starting from pento- and hexofuranos-3-uloses, using our previously reported Wittig olefination–acid hydrolysis approach.[15] The biological evaluation performed on some of the new targets suggests that the presence of a non-hindered double bond in the conjugated system is essential for the biological activity. The low molecular flexibility of the new sugar-linked and sugar-fused butenolides possessing a quaternary Cβ does not allow their expression as Michael acceptors and probably explains the weak antimicrobial effect observed for these compounds. The pyranoid α,β-unsaturated δ-lactone **29**, which is undoubtedly more susceptible to Michael addition, displays activity against most of the bacteria studied and moderate antifungal effect toward *Colletotrichum coffeanum* and *Pyricularia oryzae*, confirming therefore the above disclosed assumptions.

Experimental Section

General Methods: Melting points were determined with a Stuart Scientific SMP 3 apparatus or a Leitz apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 343 polarimeter at 20 °C. IR spectra were acquired using a Hitachi 270–50 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 or a Bruker AMX-400 spectrometer, both operating at 400.13 MHz for ^{1}H or 100.62 MHz for ^{13}C. Chemical shifts are expressed in parts per million and are referenced either to TMS as internal standard for ^{1}H or to the solvent signal (^{13}C NMR: δ = 77.16 for $CDCl_3$). Assignments were made, when needed, with the help of DEPT, COSY, HMQC, NOESY and HMBC experiments. HRMS spectra were acquired in an Apex Ultra FTICR Mass Spectrometer equipped with an Apollo II Dual ESI/MALDI ion source, from Bruker Daltonics, and a 7T actively shielded magnet from Magnex Scientific.

All reactions were followed by TLC on Merck 60 F_{254} silica gel aluminum plates. UV at 254 nm and a solution of 10% H_2SO_4 in

EtOH were used for detection. Column chromatography was carried out on silica gel 60 G (0.040–0.063 mm, from Merck).

General Procedure for the Synthesis of Hexofuranos-5-uloses 5–8: Dibutyltin oxide (0.221 g, 0.89 mmol) was added to a solution of 5,6-diol (0.81 mmol) in toluene (5.4 mL). The mixture was stirred under reflux with a Dean–Stark apparatus. The solvent was evaporated and the residue was dried in vacuum for 30 min. The crude was then taken up in dry $CHCl_3$ (5.4 mL) and *N*-bromosuccinimide (NBS, 0.158 g, 0.89 mmol) was added. The resulting solution was stirred for 5 min. The solvent was removed in vacuum, and the residue was purified by column chromatography (CC) on silica gel.

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (5): 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[22] (0.250 g, 0.81 mmol) gave **5** (0.220 g, 90%) as a white solid, after purification by CC (EtOAc/ petroleum ether, 3:7). NMR spectroscopic data was in full agreement with those reported in the literature.[17]

3-*O*-Allyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (6): 3-*O*-Allyl-1,2-*O*-isopropylidene-α-D-glucofuranose[23] (0.374 g, 1.44 mmol) gave **6** (0.291 g, 78%) as a colorless oil, after purification by CC (EtOAc/cyclohexane, 3:7). R_f = 0.28 (EtOAc/petroleum ether, 1:9). $[\alpha]_D^{20}$ = –70 (*c* = 1, in CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1725 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.05 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.80–5.71 (m, 1 H, C*H* allylic), 5.25–5.17 (m, 2 H, =CH_2 allylic), 4.80 (d, $^3J_{3,4}$ = 3.5 Hz, 1 H, 4-H), 4.58 (d, 1 H, 2-H), 4.57, 4.56, 4.52, 4.51 (part AX of ABX system, $^2J_{6a,6b}$ = 20.2, $J_{OH,H\text{-}6b}$ = 4.3 Hz, 6a-H), 4.49, 4.48, 4.44, 4.43 (part BX of ABX system, $^3J_{OH,H\text{-}6b}$ = 4.0 Hz, 6b-H), 4.25 (d, 1 H, 3-H), 4.07, 4.06, 4.05, 4.03 (part AX of ABX system, $^2J_{a,b}$ = 12.6, $^3J_{a,H\text{-}all}$ = 5.3 Hz, a-H, OCH_2 allylic), 3.95, 3.94, 3.92, 3.91 (part BX of ABX system, $^3J_{b,H\text{-}all}$ = 5.8 Hz, b-H, OCH_2 allylic), 2.93 (t, 1 H, OH), 1.48 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.2 (CO), 133.3 (*C*H allylic), 118.2 (=*C*H_2 allylic), 112.7 (Cq, isopr.), 106.0 (C-1), 84.6 (C-4), 83.2 (C-3), 81.9 (C-2), 71.5 (O*C*H_2 allylic) 68.3 (C-6), 27.0 (Me), 26.3 (Me) ppm. HRMS: calcd. for $C_{12}H_{18}O_6$ [*M* + H]$^+$ 259.1176, found 259.1177; calcd. for [*M* + Na]$^+$ 281.0996, found 281.0996; calcd. for [*M* + K]$^+$ 297.0735, found 297.0735.

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (7): 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-allofuranose[24] (1.00 g, 3.22 mmol) gave **7** (0.595 g, 60%) as a colorless syrup after after purification by CC (EtOAc/petroleum ether, 2:3). R_f = 0.36 (EtOAc/petroleum ether, 2:3). $[\alpha]_D^{20}$ = +24 (*c* = 0.4, in CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1730 cm^{-1} (C=O). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5 H, Ph), 5.81 (d, $^3J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 4.76, 4.73 (part A of AB system, $^2J_{a,b}$ = 11.9 Hz, a-H, OCH_2Ph), 4.64–4.59 (m, 2 H, b-H, 4-H), 4.57 (br. t, 1 H, 2-H), 4.45, 4.40, (part A of AB system, $^2J_{6a,6b}$ = 20.2 Hz, 6a-H), 4.38, 4.33, (part B of AB system, 6b-H), 3.81 (dd, $^3J_{2,3}$ = 4.4, $^3J_{3,4}$ = 9.3 Hz, 1 H, 3-H), 1.59 (s, 3 H, Me), 1.36 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.1 (CO), 136.7 (Cq, Ph), 128.6, 128.3, 128.1, (*C*H, Ph), 113.8 (Cq, isopr.), 104.6 (C-1), 80.4 (C-4), 79.4 (C-3), 77.6 (C-2), 72.5 (O*C*H_2Ph), 66.5 (C-6), 26.9 (Me), 26.5 (Me) ppm. HRMS: calcd. for $C_{16}H_{20}O_6$ [*M* + H]$^+$ 309.1333, found 309.1335; calcd. for [*M* + Na]$^+$ 331.1152, found 331.1159; calcd. for [*M* + K]$^+$ 347.0891, found 347.0884.

3-*O*-Allyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (8): 3-*O*-Allyl-1,2-*O*-isopropylidene-α-D-allofuranose[25] (0.473 g, 1.82 mmol) gave **8** (0.289 g, 61%) as a colorless oil after purification by CC (EtOAc/cyclohexane, 3:7). R_f = 0.23 (EtOAc/cyclohexane, 2:3). $[\alpha]_D^{20}$ = +56 (*c* = 0.7, in CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1725 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.00–5.87 (m, 1 H, CH allylic), 5.87 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.37–5.24 (m, 2 H, =CH_2 allylic), 4.67 (br. t, 1 H, 2-H), 4.60 (d, $^3J_{3,4}$ = 9.1 Hz, 1 H, 4-H), 4.51, 4.46 (part A of AB system, $^2J_{6a,6b}$ = 20.5 Hz, 6a-H), 4.46, 4.41 (part B of AB system, 6b-H), 4.23, 4.22, 4.20, 4.19 (part AX of ABX system, $^2J_{a,b}$ = 12.6, $^3J_{a,H\text{-}all}$ = 5.8 Hz, a-H, OCH_2 allylic), 4.14, 4.13, 4.11, 4.10 (part BX of ABX system, $^3J_{b,H\text{-}all}$ = 5.8 Hz, b-H, OCH_2 allylic), 3.83 (dd, $^3J_{2,3}$ = 4.0 Hz, 1 H, 3-H), 3.09 (br. s, 1 H, OH), 1.59 (s, 3 H, Me), 1.38 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.3 (CO), 133.8 (CH allylic), 119.1 (=CH_2 allylic), 113.9 (Cq, isopr.), 104.6 (C-1), 80.3 (C-4), 79.8 (C-3), 77.8 (C-2), 72.0 (O*C*H_2 allylic), 66.7 (C-6), 26.9 (Me), 26.6 (Me) ppm. HRMS: calcd. for [*M* + Na]$^+$ 281.0996, found 281.0996.

General Procedure for the Preparation of the α,β-Unsaturated Esters 9–12 and Butenolides 13–14: [(Ethoxycarbonyl)methylene]triphenylphosphorane (0.153 g, 0.44 mmol) was added to a solution of hexofuranos-5-ulose (0.26 mmol) in dry $CHCl_3$ (2.1 mL). The mixture was stirred under reflux until complete conversion, as indicated by TLC. The solvent was removed and the residue was purified by column chromatography (CC) on silica gel.

Ethyl (5*Z*)-3-*O*-Benzyl-5,6-dideoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-D-*xylo*-5-enoheptofuranuronate (9): Wittig olefination of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (0.080 g, 0.26 mmol) was completed within 4 h to give **9** (0.073 g, 75%) as a colorless syrup after purification by CC (EtOAc/petroleum ether, 1:4). R_f = 0.47 (EtOAc/petroleum ether, 1:4). $[\alpha]_D^{20}$ = –91 (*c* = 0.6, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.21 (m, 5 H, Ph), 6.02 (s, 1 H, 6-H), 6.00 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 5.83 (s, 1 H, 4-H), 4.65–4.59 (m, $^2J_{a,b}$ = 11.6 Hz, 2 H, a-H, OCH_2Ph, 2-H), 4.45–4.40 (m, 2 H, b-H, OCH_2Ph, 3-H), 4.35 (br. s, 2 H, 5′a-H, 5′b-H), 4.08 (q, ^3J = 7.2 Hz, 2 H, CH_2CH$_3$), 1.52 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.25 (t, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0 (CO), 156 (C-5), 137.1 (Cq, Ph), 128.4, 128.0, 127.9, (*C*H, Ph), 117.0 (C-6), 112.1 (Cq, isopr.), 104.9 (C-1), 83.2 (C-3), 82.5 (C-2), 80.0 (C-4), 72.4 (O*C*H_2Ph), 64.5 (C-5′), 60.2 (*C*H_2CH$_3$), 26.9 (Me), 26.4 (Me), 14.2 (CH$_2$*C*H_3) ppm. HRMS: calcd. for $C_{20}H_{26}O_7$ [*M* + H]$^+$ 379.1751, found 379.1754; calcd. for [*M* + Na]$^+$ 401.1571, found 401.1574; calcd. for [*M* + K]$^+$ 417.1310, found 417.1314.

Ethyl (5*Z*)-3-*O*-Allyl-5,6-dideoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-D-*xylo*-5-enoheptofuranuronate (10): Wittig olefination of 3-*O*-allyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (0.184 g, 0.71 mmol) was completed within 4 h and gave **10** (0.139 g, 60%) as a colorless syrup, after purification by CC (EtOAc/cyclohexane, 1:4). R_f = 0.28 (EtOAc/petroleum ether, 1:4). $[\alpha]_D^{20}$ = –31 (*c* = 0.4, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.08 (br. s, 1 H, 6-H), 5.99 (d, $^3J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.84 (s, 1 H, 4-H), 5.82–5.72 (m, 1 H, C*H* allylic), 5.26–5.13 (m, 2 H, =CH_2 allylic), 4.57 (d, 1 H, 2-H), 4.38 (d, $^3J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 4.34 (br. d, 2 H, 5′a-H, 5′b-H), 4.19 (q, ^3J = 7.1 Hz, 2 H, CH_2CH$_3$), 4.08, 4.06, 4.05, 4.03 (part AX of ABX system, $^2J_{a,b}$ = 12.9, $^3J_{a,H\text{-}all}$ = 5.3 Hz, a-H, OCH_2 allylic), 3.95, 3.94, 3.92, 3.91 (part BX of ABX system, $^3J_{b,H\text{-}all}$ = 5.8 Hz, OCH$_2$ allylic), 2.54 (t, *J* = 5.8 Hz, 1 H, OH), 1.53 (s, 3 H, Me), 1.34 (s, 3 H, Me), 1.29 (t, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9 (CO), 156.3 (C-5), 133.8 (*C*H allylic), 117.9 (=*C*H_2 allylic), 117.1 (C-6), 112.1 (Cq, isopr.), 105.0 (C-1), 83.6 (C-3), 82.9 (C-2), 79.9 (C-4), 71.5 (O*C*H_2 allylic) 64.5 (C-5′), 60.4 (*C*H_2CH$_3$), 27.0 (Me), 26.5 (Me), 14.4 (CH$_2$*C*H_3) ppm. HRMS: calcd. for $C_{16}H_{24}O_7$ [*M* + H]$^+$ 329.1595, found 329.1593; calcd. for [*M* + Na]$^+$ 351.1414, found 351.1410; calcd. for [*M* + K]$^+$ 367.1154, found 367.1152.

Ethyl (5*Z*)-3-*O*-Benzyl-5,6-dideoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-D-*ribo*-5-enoheptofuranuronate (11) and 3-*O*-Benzyl-

5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-5-enoheptofuranurono-7,5′-lactone (13): Wittig olefination of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (0.187 g, 0.61 mmol) was completed within 1 h 30 min and gave **11** (0.027 g, 12%) as a colorless syrup and **13** (0.096 g, 47%) as a white solid, after purification by CC (EtOAc/petroleum ether, 1:4). Data for **11**: R_f = 0.45 (EtOAc/petroleum ether, 2:3). $[\alpha]_D^{20}$ = +6 (*c* = 0.9, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.27 (m, 5 H, Ph), 6.06 (s, 1 H, 6-H), 5.85 (d, $^3J_{3,4}$ = 9.9 Hz, 1 H, 4-H), 5.74 (d, $^3J_{1,2}$ = 3.3 Hz, 1 H, 1-H), 4.70, 4.66 (part A of AB system, $^2J_{a,b}$ = 11.9 Hz, a-H, OC*H*$_2$Ph), 4.58 (t, 1 H, 2-H), 4.56, 4.53 (part B of AB system, b-H, OC*H*$_2$Ph), 4.28–4.09 (m, 3 H, 5′a-H, C*H*$_2$CH$_3$), 4.03, 4.01, 3.99, 3.97 (part BX of AB system, $^2J_{5a,5b}$ = 14.9, $^3J_{5b,OH}$ = 7.1 Hz, 5′b-H), 3.81 (dd, $^3J_{2,3}$ = 3.8 Hz, 1 H, 3-H), 1.65 (s, 3 H, Me), 1.37 (s, 3 H, Me), 1.26 (t, 3 H, CH$_2$C*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.9 (CO), 152.2 (C-5), 137.6 (Cq, Ph), 128.5, 128.1, 128.0 (*C*H, Ph), 120.0 (C-6), 113.6 (Cq, isopr.), 104.2 (C-1), 81.0 (C-3), 77.8 (C-2), 75.0 (C-4), 72.3 (O*C*H$_2$Ph), 62.5 (C-5′), 60.4 (*C*H$_2$CH$_3$), 27.0 (Me), 26.9 (Me), 14.3 (CH$_2$*C*H$_3$) ppm. HRMS: calcd. for $C_{20}H_{26}O_7$ [*M* + H]$^+$ 379.1751, found 379.1757; calcd. for [*M* + Na]$^+$ 401.1571, found 401.1577; calcd. for [*M* + K]$^+$ 417.1310, found 417.1319. Data for **13**: R_f = 0.21 (EtOAc/petroleum ether, 1:3); m.p. 158–159 °C. $[\alpha]_D^{20}$ = +35 (*c* = 0.4, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 5 H, Ph), 6.06 (br. d, 1 H, 6-H), 5.83 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.87 (d, $^3J_{3,4}$ = 9.2 Hz, 1 H, 4-H), 4.84, 4.80 (part AX of ABX system, $^2J_{5'a,5'b}$ = 18.2, $^3J_{5'a,6}$ = 1.6 Hz, 5′a-H), 4.81, 4.78 (part A of AB system, $^2J_{a,b}$ = 11.6 Hz, a-H, OC*H*$_2$Ph), 4.72, 4.68 (part BX of ABX system, 5′b-H), 4.66 (t, 1 H, 2-H), 4.56, 4.53 (part B of AB system, b-H, OC*H*$_2$Ph), 3.65 (dd, $^3J_{2,3}$ = 4.1 Hz, 1 H, 3-H), 1.62 (s, 3 H, Me), 1.39 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3 (C-7), 166.2 (C-5), 136.5 (Cq, Ph), 128.9, 128.7, 128.4 (*C*H, Ph), 116.1 (C-6), 113.8 (Cq, isopr.), 104.5 (C-1), 81.5 (C-3), 76.9 (C-2), 74.6 (C-4), 72.6 (O*C*H$_2$Ph), 70.9 (C-5′), 26.8 (Me), 26.5 (Me) ppm. HRMS: calcd. for $C_{18}H_{20}O_6$ [*M* + H]$^+$ 333.1333, found 333.1333.

Ethyl (5*Z*)-3-*O*-Allyl-5,6-dideoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-D-*ribo*-5-enoheptofuranuronate (12) and 3-*O*-Allyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-5-enoheptofuranurono-7,5′-lactone (14): Wittig olefination of 3-*O*-allyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranos-5-ulose (0.163 g, 0.63 mmol) was completed within 2 h and gave **12** (0.023 g, 11%) as a colorless syrup and **14** (0.087 g, 49%) as a white solid, after purification by CC (EtOAc/cyclohexane, 1:4). Data for **12**: R_f = 0.34 (EtOAc/petroleum ether, 2:3). $[\alpha]_D^{20}$ = +3 (*c* = 0.3, in CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ = 6.10 (s, 1 H, 6-H), 5.92–5.81 (m, 1 H, C*H* allylic), 5.80–5.74 (m, 2 H, 1-H, 4-H), 5.30–5.17 (m, 2 H, =C*H*$_2$ allylic), 4.64 (t, $^3J_{1,2}$ = $^3J_{2,3}$ = 4.80 Hz, 1 H, 2-H), 4.35, 4.34, 4.31, 4.30 (part AX of ABX system, $^2J_{5'a,5'b}$ = 15.2, $^3J_{5'a,OH}$ = 3.8 Hz, 5′a-H), 4.22–4.10 (m, ^3J = 7.1 Hz, 3 H, 5′b-H, C*H*$_2$CH$_3$), 4.16, 4.14, 4.12, 4.11 (part AX of ABX system, $^2J_{a,b}$ = 13.4, $^3J_{a,H\text{-}all}$ = 6.1, a-H, OC*H*$_2$ allylic), 4.06, 4.04, 4.02, 4.01 (part BX of ABX system, $^3J_{b,H\text{-}all}$ = 5.6, b-H, OC*H*$_2$ allylic), 3.81 (dd, $^3J_{3,4}$ = 9.1, 1 H, 3-H), 3.36 (t, 1 H, OH), 1.64 (s, 3 H, Me), 1.37 (s, 3 H, Me), 1.29 (t, 3 H, CH$_2$C*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.9 (CO), 151.4 (C-5), 134.4 (*C*H allylic), 120.3 (C-6), 118.1 (=*C*H$_2$ allylic), 113.7 (Cq, isopr.), 104.1 (C-1), 81.4 (C-3), 77.9 (C-2), 75.2 (C-4), 71.8 (O*C*H$_2$ allylic), 63.1 (C-5′), 60.5 (*C*H$_2$CH$_3$), 27.0 (Me), 26.8 (Me), 14.3 (CH$_2$*C*H$_3$) ppm. HRMS: calcd. for $C_{16}H_{24}O_7$ [*M* + H]$^+$ 329.1595, found 329.1610; calcd. for [*M* + Na]$^+$ 351.1414, found 351.1403. Data for **14**: R_f = 0.18 (EtOAc/petroleum ether, 1:3); m.p. 64–66 °C. $[\alpha]_D^{20}$ = +65 (*c* = 1.2, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.12 (br. s, 1 H, 6-H), 5.98–5.86 (m, 1 H, C*H* allylic), 5.85 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.37–5.25 (m, 2 H, =C*H*$_2$ allylic), 4.94, 4.89 (part AX of ABX system, $^2J_{5'a,5'b}$ = 18.2 Hz, 5′a-H), 4.87–4.79 (m, 2 H, 4-H, 5′b-H), 4.70 (t, 1 H, 2-H), 4.27, 4.26, 4.24, 4.22 (part AX of ABX system, $^2J_{a,b}$ = 12.4, $^3J_{a,H\text{-}all}$ = 5.6 Hz, a-H, OC*H*$_2$ allylic), 4.09, 4.07, 4.06, 4.04 (part BX of ABX system, $^3J_{b,H\text{-}all}$ = 6.3 Hz, b-H, OC*H*$_2$ allylic), 3.66 (dd, $^3J_{2,3}$ = 4.1, $^3J_{3,4}$ = 9.4 Hz, 1 H, 3-H), 1.61 (s, 3 H, Me), 1.39 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3 (C-7), 166.4 (C-5), 133.6 (*C*H allylic), 119.3 (=*C*H$_2$ allylic), 115.8 (C-6), 113.8 (Cq, isopr.), 104.5 (C-1), 82.0 (C-3), 77.0 (C-2), 74.5 (C-4), 71.9 (O*C*H$_2$ allylic), 71.0 (C-5′), 26.8 (Me), 26.5 (Me) ppm. HRMS: calcd. for $C_{14}H_{18}O_6$ [*M* + H]$^+$ 283.1176, found 283.1181.

General Procedure for the Synthesis of β-Hydroxy Lactones 15–16: To a mixture of previously activated granulated zinc 20 mesh (78 mg, 1.2 mmol) and hexofuranos-5-ulose (0. 8 mmol) in anhydrous THF (0.6 mL) was added a solution of ethyl bromoacetate (0.13 mL, 1.1 mmol) in THF (0.7 mL) under argon. The mixture was stirred at 50 °C for 1 h 30 min. After cooling to room temp., a 10% HCl solution (8 mL, cooled to 0 °C) was added. The mixture was extracted with CH_2Cl_2 (3 × 4 mL), the organic phase was neutralized with a diluted $NaHCO_3$ solution, washed with water and dried with anhydrous $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (CC) on silica gel.

3-*O*-Benzyl-6-deoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-L-*ido*-heptofuranurono-7,5′-lactone (15): 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (0.25 g, 0. 8 mmol) gave **15** (0.041 g, 15%) as a colorless oil, after purification by CC (EtOAc/petroleum, 3:7). R_f = 0.44 (EtOAc/petroleum ether, 2:3). $[\alpha]_D^{20}$ = –51 (*c* = 0.9, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.31 (m, 5 H, Ph), 6.01 (s, $^3J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.76, 4.73 (part A of AB system, $^2J_{a,b}$ = 11.7 Hz, a-H, OC*H*$_2$Ph), 4.67 (d, 1 H, 2-H), 4.49, 4.46 (part B of AB system, b-H, OC*H*$_2$Ph), 4.42, 4.39 (part A of AB system, $J_{5'a,5'b}$ = 10.4 Hz, 5′a-H, C*H*$_2$OCO), 4.25, 4.22 (part B of AB system, 5′b-H, C*H*$_2$OCO), 4.21 (d, 1 H, 3-H), 4.14 (d, $^3J_{3,4}$ = 3.8 Hz, 1 H, 4-H), 2.68, 2.64 (part A of AB system, $^3J_{6a,6b}$ = 17.5 Hz, 6a-H), 2.46, 2.42 (part B of AB system, 6b-H), 1.49 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8 (CO), 135.8 (Cq, Ph), 129.1, 128.9, 128.5 (*C*H, Ph), 112.2 (Cq, isopr.), 105.2 (C-1), 82.3 (C-3), 81.8 (C-2), 81.0 (C-4), 76.9 (C-5′), 76.6 (C-5), 72.2 (OCH$_2$Ph), 40.6 (C-6), 26.8 (Me), 26.2 (Me) ppm. HRMS: calcd. for $C_{18}H_{22}O_7$ [*M* + H]$^+$ 351.1438, found 351.1439.

3-*O*-Allyl-6-deoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-L-*ido*-heptofuranurono-7,5′-lactone (16): 3-*O*-Allyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (0.22 g, 0.86 mmol) gave **16** (0.048 g, 19%) as a colorless oil, after purification by CC (EtOAc/cyclohexane, 1:4). R_f = 0.22 (EtOAc/petroleum ether, 1:4). $[\alpha]_D^{20}$ = –21 (*c* = 1.1, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (s, $^3J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 5.94–5.82 (m, 1 H, C*H* allylic), 5.38–5.28 (m, 2 H, =C*H*$_2$ allylic), 4.60 (d, 1 H, 2-H), 4.48, 4.46 (part A of AB system, $J_{5'a,5'b}$ = 10.4 Hz, 5′a-H, C*H*$_2$OCO), 4.32, 4.29 (part B of AB system, 5′b-H, C*H*$_2$OCO), 4.26 (d, $^3J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 4.24, 4.22, 4.21, 4.19 (part AX of ABX system, $^2J_{a,b}$ = 12.6, $^3J_{a,H\text{-}all}$ = 5.3 Hz, a-H, OC*H*$_2$ allylic), 4.11 (d, 1 H, 4-H), 4.03, 4.01, 4.00, 3.98 (part BX of ABX system, $^3J_{b,H\text{-}all}$ = 6.6 Hz, b-H, OC*H*$_2$ allylic), 2.85, 2.81 (part A of AB system, $^2J_{6a,6b}$ = 17.4 Hz, 6a-H), 2.61, 2.57 (part B of AB system, 6b-H), 1.50 (s, 3 H, Me), 1.34 (s, 3 H, Me) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1 (CO), 132.7 (*C*H allylic), 119.8 (=*C*H$_2$ allylic), 112.3 (Cq, isopr.), 105.2 (C-1), 82.7 (C-4), 81.9 (C-2), 81.2 (C-3), 77.2 (C-5′), 76.8 (C-5), 71.2 (O*C*H$_2$ allylic), 40.8 (C-6), 26.9 (Me), 26.3 (Me) ppm. HRMS: calcd. for $C_{14}H_{20}O_7$ [*M* + H]$^+$ 301.1282, found 301.1287.

3-Deoxy-3-*C*-[(*E*)-(ethoxycarbonyl)methylene]-1,2-*O*-isopropylidene-5,6-di-*O*-pivaloyl-α-D-*ribo*-hexofuranose (19a) and 3-Deoxy-3-*C*-

[(*E*)-(ethoxycarbonyl)methylene]-1,2-*O*-isopropylidene-6-*O*-pivaloyl-α-D-*ribo*-hexofuranose (19b): To a solution of 3-deoxy-3-*C*-[(*E*)-(ethoxycarbonyl)methylene]-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (66 mg, 0.23 mmol) in dry pyridine (1 mL) at 0 °C was added a solution of pivaloyl chloride (0.25 mmol, 0.03 mL) in dry CH_2Cl_2 (0.4 mL), under N_2. The whole solution was kept whilst stirring at 0 °C for 1 h. The solvent was then removed under vacuum. The residue was poured into water (10 mL) and extracted with CH_2Cl_2 (3 × 5 mL). Combined organic layers were washed with a sat. aq. $NaHCO_3$ solution, water and brine, and dried with $MgSO_4$. After filtration and evaporation of the solvent, the residue was purified by column chromatography (EtOAc/petroleum ether, 1:4) to afford the mono-*O*-pivaloyl derivative **19** (69 mg, 81%) and the di-*O*-pivaloyl derivative **20** (6.5 mg, 6.8%) derivatives as colorless oils. Data for **19**: R_f = 0.16 (EtOAc/petroleum ether, 1:4). $[\alpha]_D^{20}$ = +189 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.25 (t, $J_{2,3'} \approx J_{3',4} \approx$ 1.9, 1 H, 3′-H), 5.91 (d, $^3J_{1,2}$ = 4.8, 1-H), 5.66 (dt, $^4J_{2,4} \approx {}^4J_{3',4}$, $^3J_{4,5}$ = 5.9, 1 H, 4-H), 5.16 (dt, 1 H, 2-H), 4.27–4.16 (m, $^3J_{5,6a}$ = 3.6, $^2J_{6a,6b}$ = 11.7, 3 H, 6a-H, CH_2CH$_3$), 4.06 (dd, $^3J_{5,6b}$ = 6.1, 1 H, 6b-H), 3.89 (dddd, 1 H, 5-H), 1.43 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.31 (t, ^3J = 7.1, 3 H, CH$_2$CH_3), 1.22 (br. s, 9 H, Me, piv.). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 178.8 (CO, piv.), 166.6 (CO), 158.0 (C-3), 118.9 (C-3′), 113.9 (Cq, isopr.), 103.7 (C-1), 81.8 (C-2), 80.7 (C-4), 73.0 (C-5), 65.3 (C-6), 61.3 (CH_2CH$_3$), 39.0 (Cq, piv.), 28.0 (Me, isopr.), 27.9 (Me, isopr.), 27.3 (Me, piv.), 14.2 (CH$_2$CH_3) ppm. HRMS: calcd. for $C_{18}H_{28}O_8$ [*M* + Na]$^+$ 395.1677, found 395.1687. Data for **20**: R_f = 0.61 (EtOAc/petroleum ether, 2:3). $[\alpha]_D^{20}$ = +18 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.19 (t, $^4J_{2,3'} \approx {}^4J_{3',4} \approx$ 1.9, 1 H, 3′-H), 5.89 (d, $^3J_{1,2}$ = 4.7, 1-H), 5.79 (dt, $^4J_{2,4} \approx {}^4J_{3',4}$, $^3J_{4,5}$ = 4.1, 1 H, 4-H) 5.25 (ddd, 5-H), 5.12 (dt, 1 H, 2-H), 4.29–4.17 (m, $^3J_{5,6a}$ = 3.8, $^2J_{6a,6b}$ = 11.7, 3 H, 6a-H, CH_2CH$_3$), 4.10, 4.08, 4.07, 4.05 (part BX of ABX system, $^3J_{5,6b}$ = 7.6, 1 H, 6b-H), 1.42 (s, 3 H, Me), 1.38 (s, 3 H, Me), 1.29 (t, 3 H, ^3J = 7.1, CH$_2$CH_3), 1.24 (br. s, 9 H, Me, piv.), 1.18 (br. s, 9 H, Me, piv.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.6 (CO, piv.), 165.0 (CO), 156.4 (C-3), 119.3 (C-3′), 113.8 (Cq, isopr.), 103.9 (C-1), 81.6 (C-2), 79.5 (C-4), 72.9 (C-5), 62.8 (C-6), 61.0 (CH_2CH$_3$), 38.9 (Cq, piv.), 38.6 (Cq, piv.), 28.0 (Me, isopr.), 27.9 (Me, isopr.), 27.3 (Me, piv.), 27.2 (Me, piv.), 14.2 (CH$_2$CH_3) ppm. HRMS: calcd. for $C_{23}H_{36}O_9$ [*M* + H]$^+$ 457.2432, found 457.2446; calcd. for [*M* + Na]$^+$ 479.2252, found 479.2267.

3-*C*-(Carboxymethylene)-3-deoxy-6-*O*-pivaloyl-α-D-*ribo*-hexopyranose-3′,4-lactone (21): A solution of 3-deoxy-3-*C*-[(*E*)-(ethoxycarbonyl)methylene]-1,2-*O*-isopropylidene-6-*O*-Piv-α-D-*ribo*-hexofuranose (62 mg, 0.17 mmol) in 70% aq. AcOH (1.46 mL) was stirred under reflux for 1 h 45 min. The solvent was coevaporated with toluene (3×) and the crude was purified by column chromatography on silica gel (EtOAc/petroleum ether, 3:2) to afford **21** (28 mg, 58%) as a colorless oil. R_f = 0.21 (EtOAc/petroleum ether, 4:1). $[\alpha]_D^{20}$ = –5 (*c* = 0.8, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$, α anomer) δ = 6.15 (br. s, 3′-H), 5.50 (d, $^3J_{1,2}$ = 3.8, 1-H), 4.76 (d, $J_{4,5}$ = 9.2, 4-H), 4.59 (br. d, 2-H), 4.54, 4.53, 4.51, 4.50 (part AX of ABX system, $^3J_{5,6a}$ = 2.5, $^2J_{6a,6b}$ = 12.2, 6a-H), 4.30, 4.29, 4.27, 4.26 (part BX of ABX system, $^3J_{5,6b}$ = 4.6, 6b-H), 3.93 (ddd, 5-H), 1.22 (s, Me, piv.). ^{13}C NMR (100 MHz, $CDCl_3$, α anomer) δ = 178.7 (CO, piv.), 172.4 (CO, lact.), 168.8 (C-3), 114.8 (C-3′), 92.9 (C-1), 76.9 (C-4), 71.4 (C-5), 69.1 (C-2), 62.9 (C-4β), (C-6), 39.2 (Cq, piv.), 27.3 (Me, piv.) ppm. HRMS: calcd. for $C_{13}H_{18}O_7$ [*M* + H]$^+$ 287.1125, found 287.1134; calcd. for [*M* + Na]$^+$ 309.0945, found 309.0953.

3-*C*-(Carboxymethylene)-3-deoxy-D-*ribo*-hexopyranose-3′,2-lactone (22). Method A: To a solution of 3-deoxy-3-*C*-[(*Z*)-(ethoxycarbonyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose[18] (0.11 g, 0.33 mmol) in MeOH (1.8 mL) was added Amberlite IR-120 H$^+$ resin (35 mg). The mixture was moderately stirred under reflux overnight. After filtration of the resin and evaporation of the solvent, the crude was purified by CC on silica gel using AcOEt as eluent to afford **22** (60 mg, 90%) as a white solid.

Method B: Alternatively, an analogous procedure using Dowex-50W (H$^+$ form) resin led the reaction to completion within 2 h. After filtration of the resin and evaporation of the solvent, compound **22** was crystallized from AcOEt (yield 57%), R_f = 0.22 (EtOAc), m.p. 168–174 °C. $[\alpha]_D^{20}$ = +192 (*c* = 0.9, MeOH). ^{1}H NMR (400 MHz, [D$_6$]DMSO) δ = 7.56 (d, ^3J = 5.6, 1β-OH), 7.04 (d, ^3J = 4.6, 1α-OH), 6.00 (d, ^3J = 5.8, 4β-OH), 5.95–5.87 (m, 3′α-H, 3′β-H, 4α-OH), 5.47 (t, 1α-H), 4.96 (d, $^3J_{1,2(\alpha)}$ = 4.1, 2α-H), 4.89 (t, 6β-OH), 4.79 (t, 6α-OH), 4.65 (d, $^3J_{1,2(\beta)}$ = 7.1, 2β-H), 4.37–4.30 (m, 1β-H, 4α-H, 4β-H), 3.79–3.52 (m, $^3J_{5,6a(\beta)}$ = 5.3, $^2J_{6a,6b(\beta)}$ = 12.1, $^3J_{5,6a(\alpha)}$ = 5.3, $^2J_{6a,6b(\alpha)}$ = 11.6, 6aα-H, 6aβ-H, 6bα-H, 6bβ-H, 5α-H), 3.12 (ddd, 5β-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO) δ = 172.9 (CO), 171.1 (C-3α), 111.7 (C-3′α, C-3′β), 98.7 (C-1β), 90.4 (C-1α), 82.0 (C-2β), 80.2 (C-5β), 78.6 (C-2α), 74.4 (C-5α), 66.1 (C-4β), 65.7 (C-4α), 60.1 (C-6a, C-6β) ppm. HRMS: calcd. for $C_8H_{10}O_6$ [*M* + H]$^+$ 203.0550, found 203.0550; calcd. for [*M* + Na]$^+$ 225.0370, found 225.0369; calcd. for [*M* + K]$^+$ 241.0109, found 241.0109. $C_8H_{10}O_6$ (202.16): C 47.53, H 4.99; found C 47.60, H 4.90.

1,4,6-Tri-*O*-acetyl-3-*C*-(carboxymethylene)-3-deoxy-α,β-D-*ribo*-hexopyranose-3′,2-lactone (23): To a solution of 3-*C*-(carboxymethylene)-3-deoxy-D-*ribo*-hexopyranose-3′,2-lactone (68 mg, 0.34 mmol) in pyridine (2 mL), was added acetic anhydride (1 mL) and the mixture was stirred at room temp. for 5 min. After coevaporation with toluene (3×), the crude was purified by column chromatography on silica gel (EtOAc/petroleum ether, 1:1) to afford **23** (94 mg, 85%) as a colorless oil. R_f = 0.32 (EtOAc/petroleum ether, 1:1). $[\alpha]_D^{20}$ = +178 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR (400 MHz,$CDCl_3$) δ = 6.60 (d, H-1α, $^3J_{1,2}$ = 4.6), 6.02–5.96 (m, 3′α-H, 3′β-H), 5.71 (dd, $^3J_{3',4(\alpha)}$ = 1.52, $^3J_{4,5(\alpha)}$ = 9.6, 4α-H), 5.66 (dd, $^3J_{3',4(\beta)}$ = 1.52, $^3J_{4,5(\beta)}$ = 9.6, 4α-H), 5.40 (d, $^3J_{1,2(\beta)}$ = 7.6, 1β-H), 5.10 (dd, $^3J_{2,3'(\alpha)}$ = 1.5, 2α-H), 4.90 (dd, $^3J_{2,3'(\beta)}$ = 1.5, 2β-H), 4.40–4.32 (m, 6aα-H, 6aβ-H) 4.24 (t, 6bα-H, 6bβ-H), 4.00 (ddd, 5α-H), 3.77 (ddd, 5β-H), 2.22 (s, Me, Ac, α, Me, Ac, β), 2.21 (s, Me, Ac, β), 2.11 (s, Me, Ac, α, Me, Ac, β), 2.09 (s, Me, Ac, α) ppm.^{13}C NMR (100 MHz $CDCl_3$) δ = 171.0 (CO, Ac, α), 170.6 (CO, Ac, β, CO, lact., α, CO, lact., β), 169.1 (CO, Ac, β), 169.1 (CO, Ac, α), 168.7 (CO, Ac, β), 168.2 (CO, Ac, α), 163.2 (C-3β), 161.6 (C-3α), 115.3 (C-3′α), 114.7 (C-3′β), 95.4 (C-1β), 88.8 (C-1α), 78.9 (C-2β), 76.4 (C-2α), 76.2 (C-5β), 71.9 (C-5α), 66.4 (C-4β), 66.0 (C-4α), 61.4 (C-6α), 61.3 (C-6β), 20.8, 20.7, 20.7, 20.5 (Me, Ac) ppm. HRMS: calcd. for $C_{14}H_{16}O_9$ [*M* + H]$^+$ 329.0867, found 329.0864; calcd. for [*M* + Na]$^+$ 351.0687, found 351.0690; calcd. for [*M* + K]$^+$ 367.0426, found 367.0417.

Methyl 3-*C*-(Carboxymethylene)-3-deoxy-α,β-D-*ribo*-hexopyranoside-3′,2-lactone (24): To a solution of 3-deoxy-3-*C*-[(*Z*)-(ethoxycarbonyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose[18] (0.14 g, 0.43 mmol) in MeOH (2 mL) was added Dowex-50W (H$^+$ form) resin (42 mg). The mixture was stirred under reflux overnight. After filtration of the resin and evaporation of the solvent, the crude was purified by CC on silica gel (EtOAc/petroleum ether, 7:3) to afford **24** (52 mg, 57%) as a colorless oil. R_f = 0.15 (EtOAc/petroleum ether, 7:3). $[\alpha]_D^{20}$ = +14 (*c* = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, [D$_6$]acetone) δ = 5.98 (t, 1 H, 3′β-H), 5.92 (t, ^4J = 1.5, 1 H, 3′α-H), 5.24 (d, ^3J = 6.3, 1 H, 4β-OH), 5.18–5.12 (m, 1α-H, 4α-OH), 4.97 (dd, $^3J_{1,2(\alpha)}$ = 4.5, 1 H, 2α-H), 4.66–4.57 (m, $^3J_{1,2(\beta)}$ = 7.3, 4α-H, 4β-H, 2β-H), 4.24 (d, 1β-H), 3.96–3.77 (m, 6aα-

H, 6aβ-H, 6bα-H, 6bβ-H), 3.54–3.48 (m, Meβ, 5α-H), 3.41 (s, Meα), 3.29 (ddd, 5β-H). ^{13}C NMR ([D$_6$]acetone, 100.62 MHz): δ = 173.1 (COα), 172.6 (COβ), 171.9 (C-3β), 170.3 (C-3α), 113.3 (C-3′β), 112.8 (C-3′α), 106.3 (C-1β), 98.5 (C-1α), 81.5 (C-2β), 79.0 (C-2α), 75.8 (C-5α), 67.6 (C-4β), 67.0 (C-4α), 61.9 (C-6β), 61.8 (C-6α). 56.9 (Meβ), 55.3 (Meα) ppm. HRMS: calcd. for $C_9H_{12}O_6$ [M + H]$^+$ 217.0707, found 217.0700; calcd. for [M + Na]$^+$ 239.0526, found 239.0518.

1,4,6-Tri-*O*-acetyl-3-C-[(*R*)-(carboxy)hydroxymethyl]-α-D-glucopyranose-3′,2-lactone (25a) and 1,4,6-Tri-*O*-acetyl-3-C-[(*R*)-(carboxy)hydroxymethyl]-β-D-glucopyranose-3′,2-lactone (25b): To a solution of 1,4,6-tri-*O*-acetyl-3-*C*-(carboxymethylene)-3-deoxy-α,β-D-*ribo*-hexopyranose-3′,2-lactone (94 mg, 0.29 mmol) in pyridine (2.3 mL), was added osmium tetroxide (97 mg, 0.38 mmol) and the mixture was stirred at room temp. for 15 min. Saturated $NaHSO_3$ solution (9 mL) and pyridine (3 mL) were added and the whole mixture was kept on stirring within 5 min to cleave the osmium complex. After extraction with $CHCl_3$ (3 × 15 mL), the combined organic layers were washed with water and dried with Na_2SO_4. After filtration and evaporation of the solvent, the residue was purified by column chromatography (EtOAc/, petroleum ether, 2:3) to afford the α-anomer **25a** (33 mg, 33%) and the β-anomer **25b** (23 mg, 23%) as white solids. Data for **25a**: R_f = 0.27 (EtOAc/petroleum ether, 2:3); m.p. 181.1–183.2 °C. $[\alpha]_D^{20}$ = +87 (c = 2.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.43 (d, $^3J_{1,2}$ = 5.3, 1 H, 1-H), 5.03 (d, $^3J_{4,5}$ = 10.4, 1 H, 4-H), 4.69 (s, 1 H, OH), 4.67–4.63 (m, 2 H, 2-H, 3′-H), 4.37, 4.36, 4.35, 4.33 (part AX of ABX system, $^3J_{5,6a}$ = 4.1, $^2J_{6a,6b}$ = 12.5, 1 H, 6a-H), 4.24, 4.24, 4.22, 4.21 (part BX of ABX system, $^3J_{5,6b}$ = 2.3, 1 H, 6b-H), 4.07 (ddd, 1 H, 5-H), 2.72–2.67 (m, 1 H, OH), 2.17 (s, 3 H, Ac), 2.14 (s, 3 H, Ac), 2.11 (s, 3 H, Ac),^{13}C NMR (100 MHz, $CDCl_3$) δ = 87.5 (C-1), 77.7 (C-2), 72.6 (C-4), 69.6 (C-3′), 67.0 (C-5), 61.9 (C-6), 20.9, 20.8, 20.7 (3 × CH_3, Ac) ppm. HRMS: calcd. for $C_{14}H_{18}O_{11}$ [M + Na]$^+$ 385.0741, found 385.0753. Data for **25b**: R_f = 0.33 (EtOAc/petroleum ether, 2:3); m.p. 139–140.7 °C. $[\alpha]_D^{20}$ = +35 (c = 1.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.54 (d, $^3J_{1,2}$ = 8.4, 1 H, 1-H), 5.00 (d, $^3J_{4,5}$ = 10.4, 1 H, 4-H), 4.63 (s, 1 H, OH), 4.52 (d, 1 H, 3′-H), 4.46 (d, 1 H, 2-H), 4.36, 4.35, 4.34, 4.33 (part AX of ABX system, $^3J_{5,6a}$ = 4.8, $^2J_{6a,6b}$ = 12.5, 1 H, 6a-H), 4.27, 4.25 (part BX of ABX system, $^3J_{5,6b}$ = 2.3, 1 H, 6b-H), 3.90 (ddd, 1 H, 5-H), 2.81–2.76 (m, 1 H, OH), 2.18 (s, 3 H, Ac), 2.16 (s, 3 H, Ac), 2.11 (s, 3 H, Ac) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ = 92.6 (C-1), 81.0 (C-2), 73.1 (C-4), 72.7, (C-5), 69.4 (C-3′), 62.0 (C-6), 20.9, 20.8, 20.7 (3×CH_3, Ac) ppm. HRMS: calcd. for $C_{14}H_{18}O_{11}$ [M + Na]$^+$ 385.0741, found 385.0740.

1,2-Di-*O*-Acetyl-3-*C*-(carboxymethylene)-3-deoxy-α,β-D-*erythro*-pentopyranose-3′,2-lactone (27): A solution of 5-*O*-TBDMS-3-deoxy-3-C-[(*E*)-(ethoxycarbonyl)methylene]-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranose[15] (51 mg, 0.14 mmol) in 70% aq. AcOH (1.1 mL) was stirred under reflux for 1h 30 min. The solvent was then removed under vacuum. Acetic anhydride (0.4 mL) and pyridine (0.8 mL) were added to the residue and the mixture was stirred for 5 min. After coevaporation with toluene, the crude was purified by column chromatography on silica gel (EtOAc/petroleum ether, 1:3) to afford the title compound (26.3 mg, 74%) as a colorless oil. R_f = 0.23 (EtOAc/petroleum ether, 1:3). $[\alpha]_D^{20}$ = –12 (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.47 (d, $^3J_{1,2(\alpha)}$ = 4.5, 1α-H), 6.05 (t, $^4J_{2,3'(\alpha)} \approx {}^4J_{3',4(\alpha)} \approx 2$, 3′α-H), 5.97 (t, $^4J_{2,3'(\beta)} \approx {}^4J_{3',4(\beta)} \approx 2.0$, 3′β-H), 5.78 (ddd, $^4J_{2,3'(\alpha)}$ = 2.0, $^4J_{2,4(\alpha)}$ = 0.5, 2α-H), 5.69 (ddd, $^3J_{1,2(\beta)}$ = 7.6, $^4J_{2,3'(\beta)}$ = 2.0, $^3J_{2,4(\beta)}$ = 0.5, 2β-H), 5.49 (d, 1β-H), 5.02–4.96 (m, 4α-H, 4β-H), 4.57 (dd, $^3J_{4,5a(\beta)}$ = 6.8, $^2J_{5a,5b(\beta)}$ = 10.8, 5aβ-H), 4.36 (dd, $^3J_{4,5a(\alpha)}$ = 6.8, $^2J_{5a,5b(\alpha)}$ = 10.8, 5aα-H), 3.56 (t, $^3J_{4,5b(\alpha)} \approx {}^2J_{5a,5b(\alpha)}$ = 10.5, 5bα-H), 3.28 (dd, $^3J_{4,5b(\beta)}$ = 10.0, 5bβ-H) 2.20, 2.16, 2.16, 2.12 (4s, Me, Ac, α,β) ppm. ^{13}C NMR ($CDCl_3$, 100.62 MHz): δ = 114.9 (C-3′β), 114.8 (C-3′α), 94.7 (C-1β), 89.3 (C-1α), 76.0 (C-4β), 75.6 (C-4α), 69.7 (C-2β), 68.5 (C-5β), 68.3 (C-2α), 65.4 (C-5α), 20.9, 20.8, 20.6, 20.5 (Me, Ac) ppm. HRMS: calcd. for $C_{11}H_{12}O_7$ [M + Na]$^+$ 279.0475, found 279.0469.

4,6-Di-*O*-acetyl-2-bromo-2,3-dideoxy-D-erythro-hex-2-enono-1,5-lactone (29)

Method A: The protocol described in ref.[16] was used, except the number of equivalents of PCC, which was reduced to 2.5, and slight modifications concerning the work-up procedure. After total consumption of **28**, as indicated by TLC, the solvent was evaporated under reduced pressure. Ethyl ether was added to the residue, in order to precipitating the Cr^{III} species and the resulting mixture was filtered through a short Florisil pad. The filtrate was concentrated in vacuo and the crude was purified by column chromatography on silica gel (EtOAc/petroleum ether, 3:7) to afford **29** in 43% yield (0.24 g, starting from 0.5 g of **28**) as a colorless oil. ^{1}H NMR spectroscopic data was in fully agreement with that reported.[16]

Method B: The oxidation step was carried out as follows. To the residue obtained from the first step in dichloromethane (6 mL), was added a mixture of pyridinium dichromate (1.38 g, 3.66 mmol) and acetic anhydride (1.4 mL, 14.8 mmol) in dichloromethane (15 mL) at room temp. under argon. The whole mixture was stirred at room temp. for 30 h. After a similar work up than that described above and purification by column chromatography, compound **29** was obtained in 31% yield (345 mg starting from 1 g of **28**).

Biological Assays

The susceptibility of microorganisms to the unsaturated lactones **13**, **14**, **22**, **23**, **29**, **30** and **31** was evaluated by the disk diffusion method according to the standard procedure CLSI (Clinical Laboratory Standards Institute/National Committee for Clinical Laboratory Standards).[19,20] The microorganisms used in the tests belong to the American Type Culture Collection (ATCC) and Centraalbureau voor Schimmelcultures (CBS) collections, from United States and The Netherlands, respectively. Additional fungi kept in our lab were also used. The group of bacteria chosen for the study consisted of Gram-negative strains such as *Escherichia coli* (ATCC 8739) and *Pseudomonas aeruginosa* (ATCC 27853) and the following Gram-positive bacteria: *Bacillus cereus* (ATCC 11778), *Bacillus subtilis* (ATCC 6633), *Enterococcus faecalis* (ATCC 29212) and *Staphylococcus aureus* (ATCC 25923). For the antifungal bioassays, six fungi were tested: *Botrytis* spp., *Candida albicans* (ATCC 10231), *Colletotrichum coffeanum* (CBS 396.67), *Fusarium culmorum* (CBS 129.73), *Pyricularia oryzae* (CBS 433.70), and *Rhizopus* spp. The culture medium and incubation temperature used for fungal growth was Potato Dextrose Agar and 25 °C, whereas for bacteria, Nutrient Agar incubated at 37 °C was used. Paper disks of 6.4 mm were placed on the agar and the solution of each substance (300 μg) in DMSO (15 μL) was applied on each disk. Chloramphenicol was used as control for all bacteria tested and *C. albicans*, whereas actidione was used for the filamentous fungi. After incubation, the nearest diameter of the inhibition zone was measured. Zones less than 15 mm in diameter and uniform growth in the dish were considered indicative of weak antimicrobial activity; 15–20, moderate activity. Each sample was tested in three equivalent experiments.

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