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Efficient synthesis of α,β-unsaturated γ-lactones linked to sugars†

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Abstract—A series of structurally diverse unsaturated sugar-derived lactones has been prepared. α,β-Butenolides were introduced to the sugar moiety starting from epoxides, while α-methylene-γ-lactones were constructed from a carbonyl precursor, either an aldehyde, a ketone or a lactone. In the last case, an unprecedented Reformatsky-type reaction has been developed. © 2001 Published by Elsevier Science Ltd.

1. Introduction

α,β-Unsaturated γ-lactones occur widely in nature and appear throughout the plant kingdom from the simple metabolites of lichens and fungi[1] to the sesquiterpenes[2] and the steroidal glycosides.[3] They have also been described in animal species such as sponges,[4] butterflies[5] and insects,[6] playing an important role as chemical defence weapons. Many of these compounds exhibit a variety of properties such as antifungal, insecticidal, antibacterial, phytotoxic, or anti-inflammatory activities, and some are antibiotics, potential anti-cancer agents and cyclooxygenase or phospholipase A_2 inhibitors.[7]

Due to their biological importance, many synthetic methods have been developed for the preparation of both exocyclic and endocyclic α,β-unsaturated γ-lactones. For the endocyclic class (α,β-butenolides), well established synthetic approaches described in the literature include the mercuration–carbonylation of propargylic alcohols,[8] condensation of 2,5-bis(trimethylsiloxy)furans with carbonyl compounds promoted by titanium tetrachloride,[9] and various transformations of C3 synthons, glycidaldehyde among others.[10] Distinct approaches have also been used, as in two recently reported examples dealing with the synthesis of some insect anti-feedant α,β-butenolide derivatives[11] and the preparation of γ-alkylidene-α,β-butenolides.[12] A general synthetic approach to the exocyclic class, α-methylene-γ-butyrolactones, through an indium promoted reaction of 2-(bromomethyl)acrylic acid with carbonyl compounds has been described, giving the products in 7–96% yields, depending on their structure.[13]

We have already reported the introduction of α,β-unsaturated γ-lactones in sugar derivatives by two different methodologies outlined in Scheme 1.[14,15] In one of them (path A), the sugar butenolide **2** was prepared through condensation of the sugar epoxide **1** with the dianion of phenylselenoacetic acid, followed by hydrolysis and subsequent oxidation of the intermediate phenylselenolactone.[16,17] Since the nucleophilic opening of the oxirane is stereospecific, the configuration of the stereogenic centre in the final lactone is determined by that of the starting epoxide. The second approach (path B) makes use of a Reformatsky-type reaction of a ketosugar or a dialdofuranose derivative with ethyl bromomethylacrylate and zinc in THF under reflux. Ethyl bromomethylacrylate and zinc–silver/graphite at −78°C have been successfully applied to the synthesis of hydroxyesters from cyclic ketones,[18] ketosugars and a

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† This article is dedicated to Professor Pierre Sinaÿ on the occasion of his 62nd birthday.

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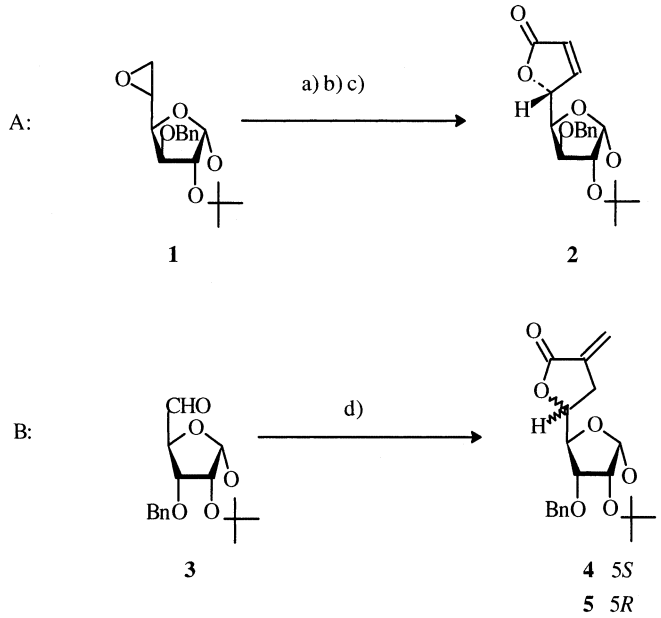


Scheme 1. (a) $PhSeCH_2CO_2H$/LDA; (b) H^+, Δ; (c) H_2O_2, H^+; (d) $BrCH_2C(=CH_2)CO_2Et$, Zn, THF, Δ.

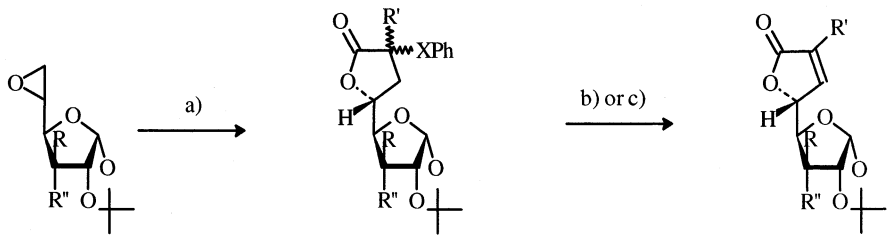
2,3-*O*-isopropylidene-D-erythronolactone,[19] and to the synthesis of α,β-unsaturated γ-lactones from some keto-sugars.[18] Synthesis of 3-ulosonic acids via a samarium iodide Reformatsky reaction on aldonolactones has also been reported.[20]

The fungicidal efficacy of some of the compounds previously synthesised[14,15] encouraged us to prepare new related derivatives. We also undertook the development of new synthetic methodologies to broaden the structural diversity of these α,β-unsaturated lactone sugars. Derivatives which differ only in hydroxyl protective groups or stereochemistry have been synthesised in order to investigate the influence of these structural factors on the bioactivity. The results of the synthetic work are reported herein.

2. Results and discussion

2.1. Synthesis of the α,β-butenolide sugar derivatives

The epoxides **1**,[15] **6**[21] and **7** (Scheme 2) were prepared through a Mitsunobu reaction from the corresponding diol precursors in 72, 73 and 76% yield, respectively. Deoxygenation at position 3 for the synthesis of **7** was accomplished via iodination of 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose with the system Ph_3P/I_2/imida-



1 R = OBn, R'' = H
6 R = H, R'' = OBn
7 R = R'' = H

8a,b R = OBn, R' = R'' = H, X = S
9a,b R = R' = H, R'' = OBn, X = S
10a,b R = R' = R'' = H, X = S
11a,b R = OBn, R' = R'' = H, X = Se
12a,b R = R' = H, , R'' = OBn, X = Se
13a,b R = OBn, R' = Me, R'' =H, X = Se
14a,b R = H, R' = Me, R'' =OBn, X = Se
15a,b R = R'' = H, R' = Me, X = Se

16 R = OBn, R' = R'' = H
17 R = R' = H, R'' = OBn
18 R = R' = R'' = H

19 R = OBn, R' = Me, R'' =H
20 R = H, R' = Me, R'' =OBn
21 R = R''= H, R' = Me

Scheme 2. (a) PhXCHR′COOH, LDA, THF, 0°C; (b) MCPBA for **8** and **9**; $NaIO_4$ for **10**; toluene, Δ; (c) H_2O_2, H^+ for **11**–**15**.

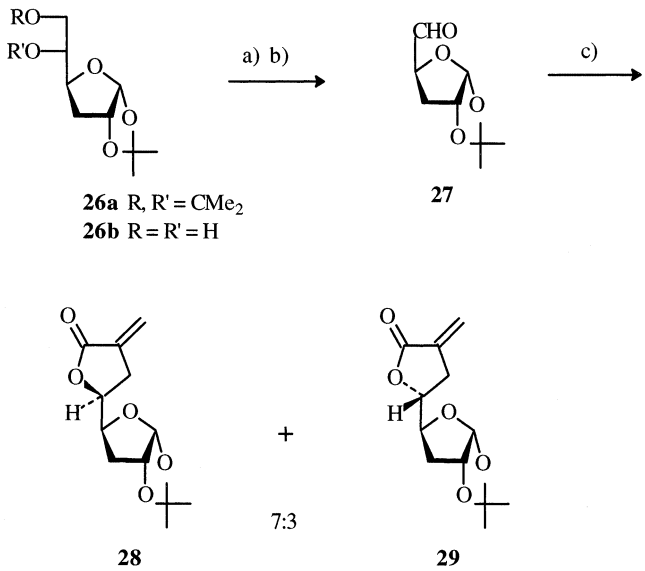
zole,[22] followed by reduction with $LiAlH_4$. Treatment of the epoxides **1**, **6** and **7** with the dianion of phenylthioacetic acid, gave, after cyclisation under acidic conditions, the corresponding phenylthiolactones **8** in 53% yield, **9** in 55% yield and 10 in 64% yield, as an inseparable diastereomeric mixture in 3:2, 5:3 and 2:1 ratios, respectively. These ratios were determined by the integration curves of the corresponding ^{1}H NMR C(1)H signals. Oxidation of these lactones with *m*-chloroperbenzoic acid[23] in the case of **8** and **9**, or with sodium metaperiodate in the case of **10**, afforded the corresponding sulfoxides, which were directly subjected to pyrolysis in refluxing toluene, giving the butenolides **16–18** in 43, 30 and 14% yields, respectively. In the ^{1}H NMR spectra of the new compounds **17** and **18**, the signals of the α and β olefinic protons appear respectively at δ 6.08 and δ 7.42 for **17** and at δ 6.19 and δ 7.59 for **18**, as expected for the conjugated double bond. When the epoxides **1** and **6** were condensed with the dianion of phenylselenoacetic acid (instead of phenylthioacetic acid), the phenylselenolactones **11** (51%) and **12** (80%) were isolated, both with a diastereomeric ratio of 1:1, as determined by the integration curve of the corresponding ^{1}H NMR signal of C(1)H; their acid catalysed oxidation with H_2O_2 then afforded the butenolides **16** and **17** in 75 and 91% yield, respectively. Therefore, with this last procedure the yield of the overall transformation is improved (32 versus 23% from **1** to **16**, and 73 versus 25% from **6** to **17**).

The epoxides **1**, **6** and **7** were also treated with the dianion of α-phenylselenopropionic acid to produce the lactones **13** (79%), **14** (47%) and **15** (58%), as inseparable mixtures of two diastereomers in the ratios 1:2, 3:2, and 7:3, respectively, calculated from the integration curve of the corresponding C(1)H signals in ^{1}H NMR. After oxidation–pyrolysis, compounds **13–15** gave the corresponding α-methyl-α,β-butenolides **19** (64%), **20** (73%) and **21** (93%). Diagnostic signals for the structural assignment of these molecules are the β-carbonyl olefinic proton at $\delta \sim 7.2$ and the singlet of the allylic methyl group at $\delta \sim 1.9$.

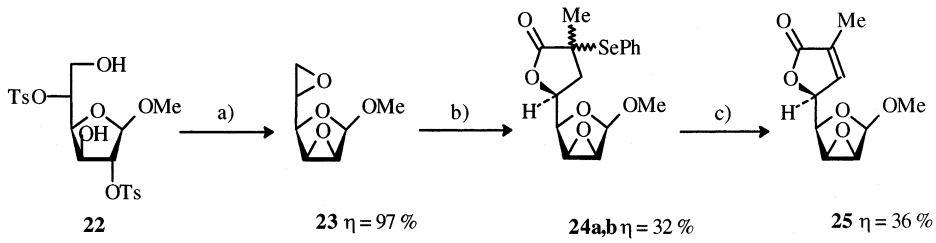
Reduction of methyl 2,5-di-*O*-tosyl-β-D-glucofuranosidurono-6,3-lactone[24] with lithium borohydride gave **22**, which was treated with potassium hydroxide, affording the bisepoxide **23** in 97% overall yield (Scheme 3). Condensation of **23** with α-phenylselenopropionic acid was regioselective furnishing a mixture of the lactones **24a** and **24b** (32%), with a diastereomeric ratio of 3:1. This reaction type was previously described using a 3-*C*-epoxyethyl sugar derivative as the starting material.[25] Acid catalysed oxidation of the lactones **24a** and **24b** with H_2O_2 yielded the butenolide **25** (36%). The ^{1}H NMR spectrum of **25** contained signals at δ 7.30 and δ 1.96, as expected for the olefinic proton and the methyl group, respectively, and at δ 3.71 and δ 3.61 with a coupling constant of 3 Hz, indicative of the epoxide.

2.2. Synthesis of the α-methylenebutyrolactone sugar derivatives

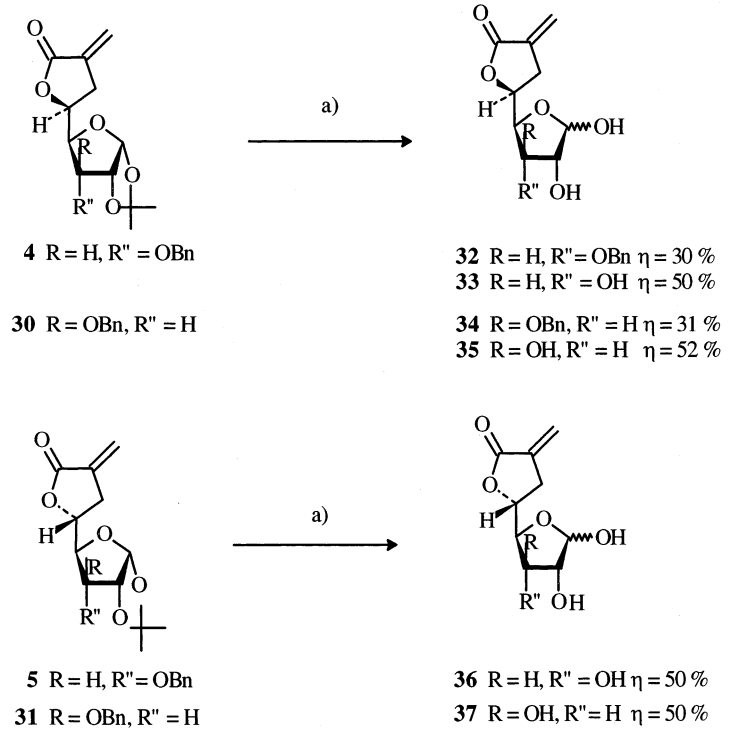
2.2.1. From aldehydes. Preparation of the dialdofuranose **27** (Scheme 4) was accomplished by partial hydrolysis of 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose **26a**[26] with acetic acid,[27] followed by sodium periodate oxidation in 52% overall yield, according to the procedure previously described for related compounds.[28] Reformatsky-type reaction of **27** with ethyl bromomethylacrylate and activated zinc[14,15] gave a diastereoisomeric mixture of **28** and **29** (ratio 7:3), determined by the ratio of the integration of the ^{1}H NMR C(1)H signals of the lactones **28** and **29**, isolated in 86% total yield. The related derivatives **4**, **30** and **31** (Scheme 5) have been previously shown to have fungicidal efficacy against *Puccinia recondita*, *Plasmopara*



Scheme 4. (a) 80% AcOH, Δ, 1 h; (b) $NaIO_4$, H_2O/EtOH; (c) $BrCH_2C(=CH_2)CO_2Et$, Zn, THF, Δ.



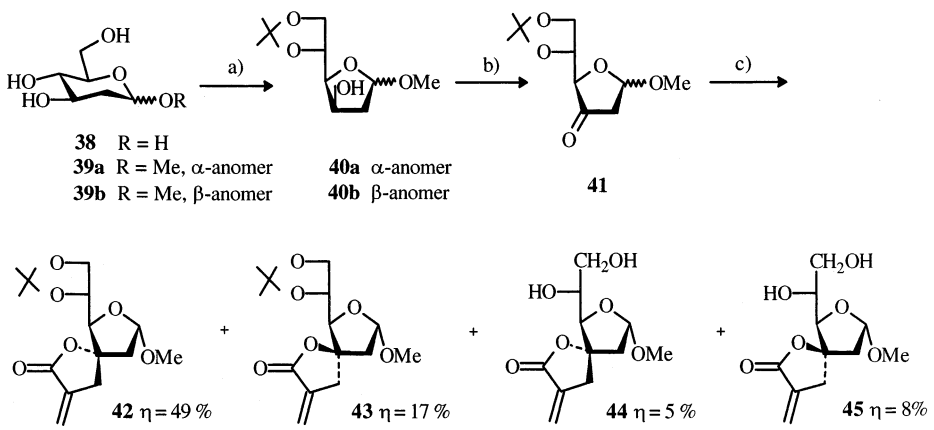
Scheme 3. (a) KOH/H_2O, rt; (b) PhSeCHMeCOOH, LDA, THF, 0°C; H_3O^+, Δ; (c) H_2O_2, H^+.



Scheme 5. (a) Me_2BBr, $ClCH_2CH_2Cl$, −78°C, 24 h.

viticola and *Botrytis cinerea*.[15] In order to determine the contribution of the protective groups to the biological activity, selective deprotection was attempted. Treatment of the (5*S*) diastereoisomers **4** and **30** with dimethylboron bromide in 1,2-dichloroethane at −78°C[29] gave the *O*-benzyl derivatives **32** (30%) and **34** (31%), along with the fully deprotected compounds **33** (50%) and **35** (52%), in the respective product mixtures. When the (5*R*) diastereoisomers **5** and **31** were subjected to the same treatment, only the fully deprotected compounds **36** and **37** were isolated in 50% yields.

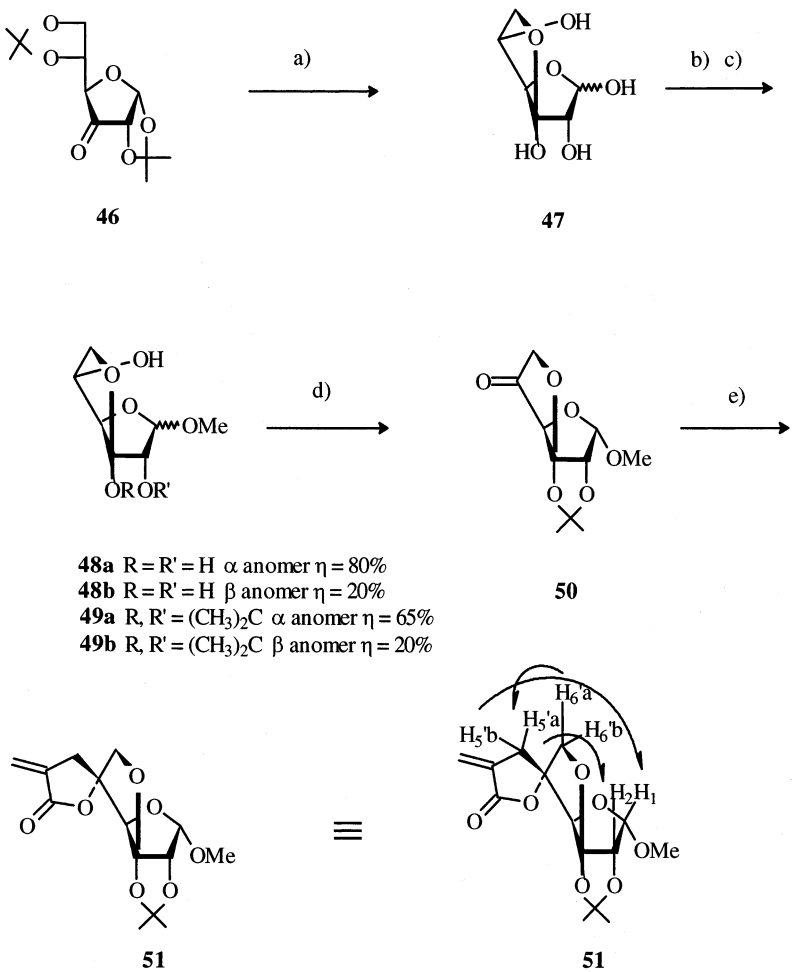
2.2.2. Spirolactones from ketosugars. Spirolactones at positions 2 and 3 of a furanoside ring have been reported previously[14,15] and it was shown that one of the diastereoisomers of the α,β-unsaturated spirolactone in position 3 was biologically active.[15] In order to introduce this unit into position 3 of a 2-deoxyfuranosidic system by a Reformatsky-type reaction, the precursor ketosugar **41** was prepared (Scheme 6), starting from 2-deoxy-D-glucose **38** in three steps. Reaction of **38** with MeOH/AcCl at room temperature over 3 h gave the α- and β-methyl glycosides **39a** and **39b** in 65 and 33% yield, respectively. Treatment of a mixture of



Scheme 6. (a) Me_2CO, H^+, $ZnCl_2$, rt, 40 h; **40a** $\eta = 65\%$, **40b** $\eta = 20\%$; (b) PCC/3 Å molecular sieves powder, CH_2Cl_2, 40°C, 2 h, $\eta = 85\%$; (c) $BrCH_2C(=CH_2)CO_2Et$, Zn, THF, Δ.

39a and **39b** with acetone/H^+ in the presence of zinc chloride and powdered 3 Å molecular sieves afforded the isopropylidene furanosidic anomers α **40a** and β **40b** in 65 and 20% yield, respectively. Oxidation of **40a** with PCC/powdered molecular sieves in CH_2Cl_2 at 40°C over 2 h gave the ketosugar **41** in 85% yield. The reaction of **41** with ethyl bromomethylacrylate and zinc in THF under reflux afforded a mixture of four compounds, the expected diastereoisomeric spirolactones **42** (49%) and **43** (17%) and the corresponding deprotected diols **44** (5%) and **45** (8%), presumably formed by hydrolysis of the 5,6-*O*-isopropylidene group during the acidic work up of the reaction mixture. The ^1H NMR spectra of compounds **42–45** contain two signals for the olefinic protons (at around δ 6.2 and δ 5.6) and two signals for the allylic protons (at around δ 3.4 and δ 2.9). The configuration of the new stereogenic centre was assigned by NOESY experiments, in which a correlation was detected between the allylic methylene group and C(4)H for compounds **43** and **45**, the isopropylidene group for C(6a)H in **42** and C(6b)H for compound **44**.

A second, more complex ketosugar substrate **50** was prepared as indicated in Scheme 7. Treatment of 1,2;5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranosid-3-ulose **46**[14] with 75% formic acid at 50°C gave **47** in 60% yield. Reaction of **47** with methanol/acetyl chloride at room temperature afforded the α/β methyl glycosides **48a** and **48b** which could be separated by column chromatography and isolated in 80 and 20% yield, respectively. Treatment of the glycoside mixture **48a** and **48b** with acetone/H^+ in the presence of $ZnCl_2$ led to the synthesis of the α-anomer **49a** in 65% yield and the β-anomer **49b** in 20% yield. Oxidation of **49a** with the PCC/powdered 4 Å molecular sieves system at 40°C afforded **50** in 90% yield. The Reformatsky-type reaction of **50** furnished the spirolactone **51** in 73% yield as a single diastereoisomer. The (*R*) configuration of the new stereogenic centre was elucidated by an NOESY NMR experiment, which showed a correlation of the allylic methylene group (δ 3.14 and δ 2.97) with C(1)H and C(2)H. The highest diastereofacial selectivity in the addition of the zinc reagent observed for the ketosugar



46 **47**

48a R = R' = H α anomer η = 80%
48b R = R' = H β anomer η = 20%
49a R, R' = $(CH_3)_2C$ α anomer η = 65%
49b R, R' = $(CH_3)_2C$ β anomer η = 20%

50

51 ≡ **51**

Scheme 7. (a) HCOOH (75%), 50°C, 1 h, $\eta = 60\%$ (α/β 2:1); (b) MeOH, AcCl, rt, 4 h; (c) Me_2CO, H^+, $ZnCl_2$, rt, 38 h; (d) PCC/4 Å molecular sieves powder, CH_2Cl_2, 40°C, 2 h, $\eta = 90\%$; (e) $BrCH_2C(=CH_2)CO_2Et$, Zn, THF, Δ, $\eta = 73\%$.

50 compared to **41** is probably due to the high steric hindrance impeding the approach of the Reformatsky-type reagent to the *endo* face of the carbonyl group of **50**.

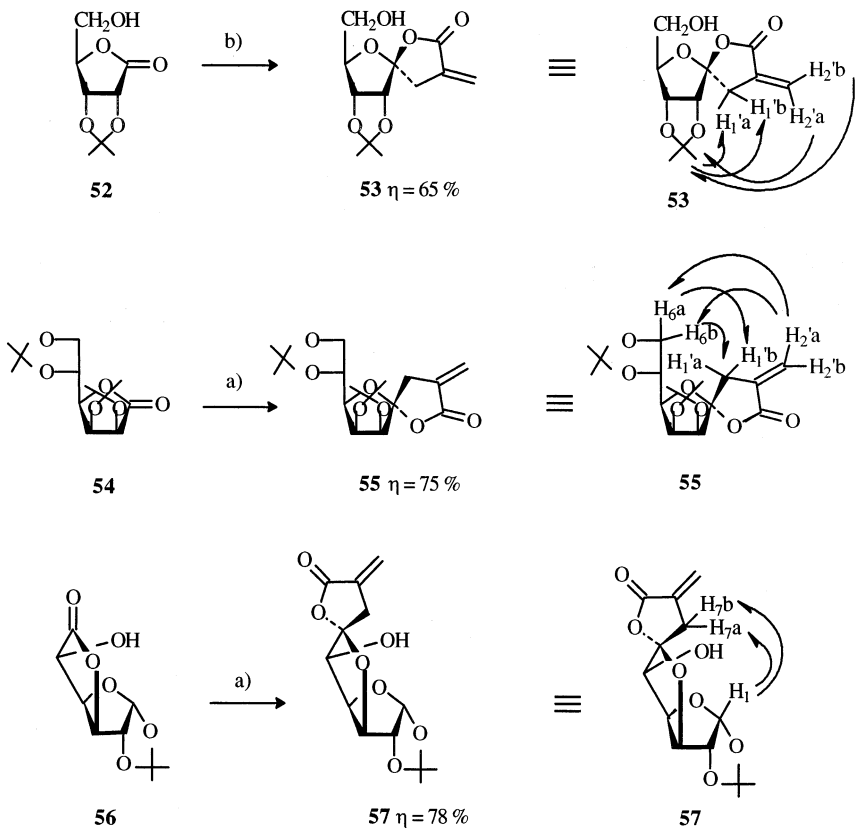
2.2.3. Spirolactones from sugar lactones. Although it is known from the literature that allylzinc bromide does not react with lactones,[30] during the course of these investigations, we realised that the Reformatsky-type reagent prepared from ethyl bromomethylacrylate and activated zinc was also reactive towards the carbonyl group of a lactone functionality. This new reaction brought about the possibility of synthesising new spirolactone sugar derivatives, broadening their structural diversity. Commercially available 2,3-*O*-isopropylidene-D-ribonic-γ-lactone **52** and 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone **56** were used as substrates for this reaction, along with the sugar lactone **54**[31] (Scheme 8), which was prepared from 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranose in 85% yield by PCC/molecular sieves oxidation. Starting from these substrates, the spirolactones **53**, **55** and **57** were obtained in 65, 75 and 78% yield, respectively, each as a single diastereoisomer. The configuration of these compounds was established by NOESY NMR as above, considering the interaction between the allylic methylene group of the new lactone ring and the isopropylidene group for **53**, the protons at C-(6) for **55** and the anomeric proton for **57**. For substrates **52** and **54**, in which the reacting lactone belongs to the furanose ring, the high diastereoselectivity may be due to a favourable interaction between the zinc reagent and an oxygen of the isopropylidene group in the transition state. In the case of **56**, most probably steric effects are again decisive.

In summary, a series of structurally diverse unsaturated lactone sugar derivatives have been prepared. α,β-Butenolides have been introduced to the sugar residue starting from epoxides, while α-methylene-γ-lactones have been constructed from a carbonyl group precursor, either of an aldehyde, a ketone or a lactone. In the last case, a novel Reformatsky-type reaction of lactones has been developed. The biological activity of these new sugar lactones is under study.

3. Experimental

3.1. General methods

Melting points were determined with a melting point apparatus (Tottoli) and are uncorrected. Optical rotations were measured with an Atago Polax-D polarimeter and IR spectra were recorded with a Biorad FTS 25 PC spectrophotometer. ^{1}H NMR spectra were carried out using a Varian Unity 300 MHz spectrometer (compounds **1**–**25**) or a Bruker ACC-250 P spectrometer (compounds **26**–**58**) and the NOE experiments were



Scheme 8. (a) $BrCH_2C(=CH_2)CO_2Et$, Zn, THF, Δ; (b) $BrCH_2C(=CH_2)CO_2Et$, Zn, dioxane, Δ.

with a Bruker AM-400 WB spectrometer. Chemical shifts are expressed in parts per million downfield from TMS. Homonuclear $^1H\{^1H\}$ experiments were performed at 400 MHz in acetone-d_6 or chloroform-*d*, using a low decoupler setting (typically 40 L, 5 mW approximately) with a total presaturation time of 6 s. The FiDs were acquired using 16 K points and a sweep width of 5000 Hz in alternate groups of eight, irradiation on/off resonance. A 90° pulse was used during acquisition. The ^{13}C NMR spectra were recorded with a Bruker AC-250 P spectrometer at 62.90 MHz. The progress of all reactions was monitored by thin-layer chromatography (TLC) using aluminium sheets precoated with silica gel $60F_{254}$ to a thickness of 0.2 mm (Merck). Preparative TLC was performed with aluminium plates coated with silica gel $60F_{254}$ to a thickness of 0.5 mm (Merck). Compounds were detected with UV light (254 nm) and/or by spraying the sheets with a 3% vanillin–sulfuric acid solution. Column chromatography (CC) was conducted under low pressure by elution of columns with silica gel (0.040–0.063 mm, Merck).

3.2. General procedure for the synthesis of the epoxides 6 and 7

Triphenylphosphine (2.6 equiv.) was added to a solution of the diol (1 mmol) in benzene (17.5 mL) and the mixture was stirred at rt for 15 min. After addition of activated powdered molecular sieves (3 Å, 800 mg), DEAD (2.6 equiv.) was added dropwise to the mixture, which was stirred at 80°C for 48 h. After filtration and solvent evaporation under reduced pressure, the residue was subjected to CC.

3.2.1. 5,6-Anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose 6. 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-allofuranose[28] (2.40 g, 8.2 mmol) gave **6** (1.75 g, $\eta = 73\%$) as a syrup after purification by CC with EtOAc/*n*-hexane (1:3); $R_f = 0.41$ (EtOAc/*n*-hexane 1:3); $[\alpha]_D^{20} = +62$ (*c* 1.0, $CHCl_3$); IR (neat): 1262 (C–O, epoxide), 1380 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.39–7.29 (m, 5H, Ph), 5.74 (d, 1H, H-1, $J_{1,2} = 3.6$ Hz), 4.76, 4.72 (part A of AB system, OCH_2Ph, $J_{AB} = 11.7$ Hz), 4.59–4.55 (m, 2H, H-2, OCH_2Ph, part B of AB system), 3.66 (dd, 1H, H-3, $J_{2,3} = 4.2$ Hz, $J_{3,4} = 8.7$ Hz), 3.19–3.16 (m, 1H, H-5), 4.20 (dd, 1H, H-4, $J_{4,5} = 3.0$ Hz), 2.79–2.73 (m, 2H, H-6a, H-6b), 1.53 (s, 3H, Me), 1.37 (s, 3H, Me); ^{13}C NMR ($CDCl_3$): δ 137.1 (Cq, Ph), 128.5, 128.3, 127.9 (Ph), 112.8 (Cq, isop.), 103.8 (C-1), 71.8 (OCH_2Ph), 77.5 (C-2), 77.0 (C-3), 76.5 (C-4), 50.4 (C-5), 44.2 (C-6), 26.6 (Me), 26.4 (Me). Anal. calcd for $C_{16}H_{20}O_5$ (292.3): C, 65.74; H, 6.88. Found: C, 65.40; H, 6.88%.

3.2.2. 5,6-Anhydro-3-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose 7. Starting from 3-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose **26b** (730 mg, 3.57 mmol), this procedure gave **7** (500 mg, $\eta = 76\%$) after CC purification with EtOAc/*n*-hexane (1:3); $R_f = 0.34$ (EtOAc/*n*-hexane 1:3); $[\alpha]_D^{20} = -18$ (*c* 1.0, $CHCl_3$); IR (neat): 1380 (C–O, isop.), 1262 (C–O, epoxide) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.73 (d, 1H, H-1, $J_{1,2} = 3.8$ Hz), 4.76 (t, 1H, H-2, $J_{2,3a} = 4.4$ Hz), 4.05–4.12 (m, 1H, H-4), 3.04 (m, 1H, H-5), 2.70 (t, 1H, H-6a, $J_{6a,6b} = 5.1$ Hz, $J_{5,6a} = 4.47$ Hz), 2.49 (dd, 1H, H-6b, $J_{5,6b} = 3.0$ Hz), 1.95 (dd, 1H, H-3b, $J_{4,3b} = 4.4$ Hz, $J_{3a,3b} = 13.75$ Hz), 1.61 (ddd, 1H, H-3a, $J_{2,3a} = 4.4$ Hz, $J_{3a,4} = 4.7$ Hz), 1.50 (s, 3H, Me), 1.32 (s, 3H, Me); ^{13}C NMR ($CDCl_3$): δ 110.2 (Cq, isop.), 105.2 (C-1), 79.9 (C-2), 77.4 (C-4), 51.2 (C-5), 44.5 (C-6), 33.8 (C-3), 25.7 (Me), 26.3 (Me). Anal. calcd for $C_9H_{14}O_4$ (186.19): C, 58.05; H, 7.58. Found: C, 57.73; H, 7.34%.

3.3. General procedure for the preparation of the lactones 8–15

A solution of *n*-butyllithium (1.6 M in *n*-hexane, 2.75 mL, 4.4 mmol) was added dropwise to a solution of diisopropylamine (0.62 mL, 4.4 mmol) in anhydrous THF (8 mL) under argon at 0°C, and the mixture was stirred at 0°C for 25 min. A solution of either phenylselenoacetic, α-phenylselenopropionic or phenylthioacetic acid (2 mmol) in anhydrous THF (2 mL) was added dropwise at 0°C and the reaction mixture was stirred for 1 h at 0°C. A solution of the epoxide (2 mmol) in anhydrous THF (3 mL/g epoxide) was then added dropwise and, after stirring for 1 h at 0°C, the reaction mixture was stirred for 16 h at rt. The reaction mixture was treated with 50% acetic acid (5 mL) under reflux for 6 h, and cooled to rt. After neutralisation with a saturated $NaHCO_3$ solution, the mixture was extracted with diethyl ether (3×10 mL) and the organic phases were washed with water and dried over sodium sulfate. The lactones were isolated after solvent evaporation and purification by CC.

3.3.1. (7*R*)- and (7*S*)-3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-phenylsulfanyl-α-D-*gluco*-octofuranurono-8,5-lactone 8a and 8b. Starting from **1** (350 mg, 1.20 mmol), this procedure gave **8a** and **8b** (280 mg, $\eta = 53\%$, ratio **8a**/**8b** = 3:2); CC eluent: EtOAc/*n*-hexane (1:6); $R_f = 0.45$ (EtOAc/*n*-hexane 1:3); IR (neat): 1782 (C=O), 1382 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.57–7.54 (m, 4H, Ph), 7.38–7.29 (m, 16H, Ph), 5.91 (d, 1H, H-1**a**, $J_{1,2} = 3.6$ Hz), 5.88 (d, 1H, H-1**b**, $J_{1,2} = 3.6$ Hz), 4.73–4.55 (m, 6H, H-2, OCH_2Ph), 4.23 (d, 1H, H-3**a**, $J_{2,3} = 3.6$ Hz), 4.20 (d, 1H, H-3**b**, $J_{2,3} = 3.3$ Hz), 4.14–3.95 (m, 6H, H-5, H-4, H-7), 2.86–2.76 (m, 2H, H-6a), 2.43–2.33 (m, 2H, H-6b), 1.48 (s, 6H, Me), 1.31 (s, 6H, Me); ^{13}C NMR ($CDCl_3$): δ 174.5 (C=O), 137.1, 137.0 (Cq, Ph), 133.4, 133.3, 129.2, 128.6, 128.5, 128.1, 128.0, 127.7 (Ph), 112.2, 112.1 (Cq, isop.), 105.2, 105.0 (C-1), 82.3, 82.2, 81.6, 81.3, 81.0 (C-2, C-3, C-4), 75.2, 73.8 (C-5), 72.5, 72.3 (OCH_2Ph), 45.2, 44.5 (C-7), 33.0, 32.4 (C-6), 26.8, 26.7, 26.2, 26.1 (Me). Anal. calcd for $C_{24}H_{26}O_6S$ (442.50): C, 65.14; H, 5.92; S, 7.24. Found: C, 64.90; H, 5.92; S, 7.07%.

3.3.2. (7*R*)- and (7*S*)-3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-phenylsulfanyl-α-D-*allo*-octofuranurono-8,5-lactone 9a and 9b. Starting from **6** (280 mg, 0.96 mmol), this experiment gave **9** (232.6 mg, $\eta = 55\%$, ratio **9a**/**9b** = 5:3); CC eluent: EtOAc/*n*-hexane (1:3); $R_f = 0.21$ (EtOAc/*n*-hexane 1:3); IR (neat): 1786 (C=O), 1384 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.53–7.30 (m,

20H, Ph), 5.73 (d, 1H, H-1**a**, $J_{1,2}=3.6$ Hz), 5.69 (d, 1H, H-1**b**, $J_{1,2}=3.6$ Hz), 4.81–4.45 (m, 8H, OCH_2Ph, H-2, H-5), 4.26–4.22 (m, 2H, H-4), 3.95 (dd, 1H, H-7**b**), 3.82 (dd, 1H, H-7**a**), 3.70 (dd, 1H, H-3**b**, $J_{2,3}=4.2$ Hz, $J_{3,4}=8.7$ Hz), 3.63 (dd, 1H, H-3**a**, $J_{2,3}=4.5$ Hz, $J_{3,4}=9.3$ Hz), 2.54 (ddd, 1H, H-6a**a**, $J_{5,6a}=6.6$ Hz, $J_{6a,7}=9.0$ Hz), 2.42–2.32 (m, 2H, H-6a**b**, H-6b**b**, $J_{6a,7}=11.1$ Hz, $J_{6b,7}=9.3$ Hz), 2.04 (ddd, 1H, H-6b**a**, $J_{6b,7}=5.4$ Hz, $J_{6a,6b}=13.2$ Hz, $J_{5,6b}=7.8$ Hz), 1.59 (s, 6H, Me), 1.37 (s, 6H, Me); ^{13}C NMR ($CDCl_3$): δ 174.2 (C=O), 173.8 (C=O), 136.8 (Cq, Ph), 133.4, 133.1, 129.2, 128.7, 128.4, 128.2 (Ph), 113.4 (Cq, isop.), 104.0 (C-1), 78.2 (C-4), 77.7, 76.7 (C-2, C-5), 76.6 (C-3), 72.1 (OCH_2Ph), 45.8 (C-7**b**), 44.3 (C-7**a**), 30.4 (C-6**b**), 29.6 (C-6**a**), 26.8 (Me), 26.5 (Me). Anal. calcd for $C_{24}H_{26}O_6S$ (442.50): C, 65.14; H, 5.92; S, 7.24. Found: C, 65.15; H, 6.01; S, 7.06%.

3.3.3. (7*R*)- and (7*S*)-3,6,7-Trideoxy-1,2-*O*-isopropylidene-7-phenylsulfanyl-α-D-*ribo*-octofuranurono-8,5-lactone 10a and 10b. Starting from **7** (250 mg, 1.34 mmol), this experiment gave **10a** and **10b** (290 mg, $\eta=64\%$, ratio **10a**/**10b** = 2:1); CC eluent: EtOAc/*n*-hexane (1:3); $R_f=0.22$ (EtOAc/*n*-hexane 1:3); IR (KBr): 1774 (C=O), 1384 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$) of **10a**: δ 7.72–7.69 (m, 2H, Ph), 7.57–7.53 (m, 3H, Ph), 5.80 (d, 1H, H-1, $J_{1,2}=3.3$ Hz), 4.76–4.73 (m, 1H, H-5 or H-7), 4.74 (t, 1H, H-2, $J_{2,3b}=4.5$ Hz), 4.40–4.36 (m, 1H, H-7 or H-5), 3.95 (dd, 1H, H-4, $J_{4,3b}=9$ Hz, $J_{4,3a}=5.4$ Hz), 2.55–2.49 (m, 1H, H-6b), 2.35–2.33 (m, 1H, H-6a), 2.17 (m, 1H, H-3a), 1.67 (m, 1H, H-3b), 1.49 (s, 3H, Me), 1.31 (s, 3H, Me); ^{13}C NMR ($CDCl_3$) of **10a**: δ 174.2 (C=O), 133.5 (Cq, Ph), 131.6, 129.2, 128.7 (Ph), 111.6 (Cq, isop.), 105.6 (C-1), 80.3, 78.4, 78.4 (C-5, C-4, C-2), 44.5 (C-7), 34.9 (C-6), 31.5 (C-3), 26.7 (Me), 26.0 (Me). Anal. calcd for $C_{17}H_{20}O_5S$ (336.38): C, 60.70; H, 5.98; S, 9.53. Found: C, 60.80; H, 6.13; S, 9.46%.

3.3.4. (7*R*)- and (7*S*)-3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-phenylselenyl-α-D-*gluco*-octofuranurono-8,5-lactone 11a and 11b. Starting with the epoxide **1** (170 mg, 0.58 mmol), this procedure gave **11** (145 mg, $\eta=51\%$, ratio **11a**/**11b** = 1:1). CC eluent: EtOAc/toluene (1:5); $R_f=0.58$ (EOAc/toluene 1:5); IR (neat): 1772 (C=O), 1376 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$) of **11a**: δ 7.62–7.59 (m, 2H, Ph), 7.24–7.19 (m, 8H, Ph), 5.79 (s, 1H, H-1), 4.68–4.52 (m, 4H, H-3, H-5, OCH_2Ph), 4.06–3.95 (m, 3H, H-2, H-3, H-7), 2.75 (dd, 1H, H-6a, $J_{6a,6b}=13.4$ Hz), 2.30 (dd, 1H, H-6b), 1.40 (s, 3H, Me), 1.24 (s, 3H, Me); ^{13}C NMR ($CDCl_3$) of **11a**: δ 175.4 (C=O), 135.5 (Cq, Ph), 129.3, 128.8, 128.0, 127.6 (Ph), 112.2 (Cq, isop.), 105.2 (C-1), 82.6 (C-2), 81.5 (C-3), 81.5 (C-4), 74.5 (C-5), 72.7 (OCH_2Ph), 53.3 (C-7), 36.3 (C-6), 27.0 (Me), 26.4 (Me). Anal. calcd for $C_{24}H_{26}O_6Se$ (489.37): C, 58.90; H, 5.35. Found: C, 59.00; H, 5.38%.

3.3.5. (7*R*)- and (7*S*)-3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-phenylselenyl-α-D-*allo*-octofuranurono-8,5-lactone 12a and 12b. Starting from **6** (300 mg, 1.03 mmol), this procedure gave **12a** and **12b** (240 mg, $\eta=80\%$, ratio **12a**/**12b** = 1:1); CC eluent: EtOAc/*n*-hexane (1:3); $R_f=0.34$ (EtOAc/*n*-hexane 1:3); IR (neat): 1774 (C=O), 1384 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.65–7.27 (m, 20H, Ph), 5.71–5.67 (m, 2H, H-1), 4.74–4.43 (m, 8H, H-2, OCH_2Ph, H-5), 4.21–4.17 (m, 2H, H-4), 4.00 (t, 1H, H-7**b**, $J_{6a,7}=J_{6b,7}=9.6$ Hz), 3.83 (dd, 1H, H-7**a**, $J_{6a,7}=9.3$ Hz, $J_{6b,7}=4.5$ Hz), 3.72–3.67 (m, 2H, H-3), 2.61 (ddd, 1H, H-6a**a**, $J_{5,6a}=8.4$ Hz), 2.42–2.35 (m, 2H, H-6a**b**, H-6b**b**), 2.04 (ddd, 1H, H-6b**a**, $J_{6a,6b}=14.1$ Hz, $J_{5,6b}=7.2$ Hz), 1.57 (s, 6H, Me), 1.33 (s, 6H, Me); ^{13}C NMR ($CDCl_3$): δ 175.1 (C=O), 136.8 (Cq, Ph), 135.7, 135.2, 129.4, 129.3, 129.1, 128.5, 128.3, 128.1 (Ph), 113.3 (Cq, isop.), 103.9 (C-1), 77.9, 77.8 (C-4), 77.4 (C-2), 77.3, 77.1 (C-5), 77.0, 76.0 (C-3), 72.0 (OCH_2Ph), 37.0, 36.0 (C-7), 30.8, 30.3 (C-6), 26.7 (Me), 26.5 (Me). Anal. calcd for $C_{24}H_{26}O_6Se$ (489.37): C, 58.90; H, 5.35. Found: C, 59.17; H, 5.41%.

3.3.6. (7*R*)- and (7*S*)-3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-methyl-7-phenylselenyl-α-D-*gluco*-octofuranurono-8,5-lactone 13a and 13b. Starting from **1** (430 mg, 1.47 mmol), the same experiment gave **13a** and **13b** (590 mg, $\eta=79\%$, ratio **13a**/**13b** = 1:2); CC eluent: EtOAc/*n*-hexane (1:6); $R_f=0.49$ (EtOAc/*n*-hexane 1:6); IR (neat): 1773 (C=O), 1382 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.67–7.63 (m, 4H, Ph), 7.41–7.26 (m, 16H, Ph), 5.95 (d, 1H, H-1**a**, $J_{1,2}=3.6$ Hz), 5.90 (d, 1H, H-1**b**, $J_{1,2}=3.6$ Hz), 4.83–4.17 (m, 7H, OCH_2Ph, H-2, H-5**a**), 4.18 (dd, 1H, H-4**a**, $J_{3,4}=10.2$ Hz, $J_{4,5}=3.3$ Hz), 4.09–4.05 (m, 2H, H-3), 3.78–3.75 (dd, 1H, H-4**b**, $J_{3,4}=7.2$ Hz, $J_{4,5}=3.3$ Hz), 3.16 (d, 1H, H-5**b**, $J_{5,6}=3.9$ Hz), 2.94 (dd, 1H, H-6a**b**, $J_{5,6a}=3.9$ Hz, $J_{6a,6b}=5.1$ Hz), 2.79 (dd, 1H, H-6b**b**, $J_{5,6b}=2.4$ Hz), 2.59 (dd, 1H, H-6a**a**, $J_{5,6a}=5.7$ Hz, $J_{6a,6b}=14.4$ Hz), 2.38 (dd, 1H, H-6b**a**, $J_{5,6b}=9.9$ Hz), 1.63 (s, 6H, Me-7), 1.51 (s, 6H, Me, isop.), 1.31 (s, 6H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 176.7 (C=O), 137.6 (CqPh), 129.8, 129.0, 128.5, 128.1, 127.8, 127.6 (Ph), 112.1 (Cq, isop.), 105.2 (C-1), 82.6 (C-2), 82.5, 82.0 (C-3), 81.7, 81.5 (C-4), 73.1 (C-5**a**), 72.6 (OCH_2Ph), 48.2 (C-5**b**), 46.9 (CH_2-6**a**), 45.0, 44.2 (C-7), 41.3 (CH_2-6**b**), 26.8 (Me, isop.), 26.2 (Me, isop.), 24.0 (Me-7). Anal. calcd for $C_{25}H_{28}O_6Se$ (503.42): C, 59.65; H, 5.60. Found: C, 60.00; H, 5.93%.

3.3.7. (7*R*)- and (7*S*)-3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-methyl-7-phenylselenyl-α-D-*allo*-octofuranurono-8,5-lactone 14a and 14b. Starting from **6** (360 mg, 1.23 mmol), this procedure gave **14a** and **14b** (290 mg, $\eta=47\%$, ratio **14a**/**14b** = 3:2); CC eluent: EtOAc/*n*-hexane (1:3); $R_f=0.40$ (EtOAc/*n*-hexane 1:3); IR (neat): 1774 (C=O), 1380 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$) of **14a** and **14b**: δ 7.67–7.62 (m, 4H, Ph), 7.42–7.26 (m, 16H, Ph), 5.72 (d, 1H, H-1**a**, $J_{1,2}=3.6$ Hz), 5.65 (d, 1H, H-1**b**, $J_{1,2}=3.6$ Hz), 4.78–4.72 (part A of AB system, 2H, OCH_2Ph, $J_{AB}=12$ Hz), 4.65–4.47 (m, 6H, part B of AB system, OCH_2Ph, H-2, H-5), 4.28 (dd, 1H, H-4**b**, $J_{2,3}=3.3$ Hz, $J_{3,4}=9.3$ Hz), 4.22 (dd, 1H, H-4**a**, $J_{2,3}=2.7$ Hz, $J_{3,4}=7.5$ Hz), 3.75–3.67 (m, 2H, H-3), 2.61 (dd, 1H, H-6a**b**, $J_{5,6a}=8.4$ Hz, $J_{6a,6b}=13.5$ Hz), 2.35 (dd, 1H, H-6a**a**, $J_{5,6a}=10.5$ Hz, $J_{6a,6b}=14$ Hz), 2.13–1.99 (m, 2H, H-6b), 1.59 (s, 6H, Me), 1.54 (s, 6H, Me), 1.36 (s, 6H, Me); ^{13}C NMR ($CDCl_3$) of **14a** and **14b**: δ 176.21 (C=O), 137.7, 137.6 (Cq, Ph), 129.9, 129.4, 129.1, 129.0, 128.6, 128.5, 128.3, 128.2, 128.1 (Ph), 113.3 (Cq, isop.), 103.9 (C-1), 77.8, 77.6 (C-3, C-4), 75.9 (C-5), 75.2 (C-2),

72.1, 71.9 (OCH_2Ph), 44.7, 44.0 (C-7), 37.5, 37.3 (C-6), 26.8, 26.7, 26.6, 26.5 (Me), 23.9, 23.6 (Me-7). Anal. calcd for $C_{25}H_{28}O_6Se$ (503.42): C, 59.65; H, 5.60. Found: C, 59.84; H, 5.80%.

3.3.8. (7*R*)- and (7*S*)-3,6,7-Trideoxy-1,2-*O*-isopropylidene-7-methyl-7-phenylselenyl-α-D-*ribo*-octofuranurono-8,5-lactone 15a and 15b. Starting from **7** (380 mg, 2.04 mmol), this experiment gave **15a** and **15b** (470 mg, $\eta = 58\%$, ratio **15a**/**15b** = 7:3); CC eluent: EtOAc/*n*-hexane (1:3); $R_f = 0.27$ (EtOAc/*n*-hexane 1:3); IR (KBr): 1754 (C=O), 1378 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$) of **15a**: δ 7.74–7.67 (m, 2H, Ph), 7.49–7.29 (m, 3H, Ph), 5.84 (d, 1H, H-1, $J_{1,2} = 3.3$ Hz), 4.78 (t, 1H, H-2, $J_{2,3b} = 3.9$ Hz), 4.48–4.41 (ddd, 1H, H-5, $J_{4,5} = 5.1$ Hz, $J_{5,6b} = 10.1$ Hz), 4.31–4.24 (ddd, 1H, H-4), 2.52 (dd, 1H, H-6a, $J_{5,6a} = 5.5$ Hz, $J_{6a,6b} = 14.1$ Hz), 2.27–2.14 (m, 2H, H-6b, H-3a), 1.73–1.66 (m, 4H, H-3b, Me), 1.53 (s, 3H, Me), 1.35 (s, 3H, Me); ^{13}C NMR ($CDCl_3$) of **15a**: δ 176.4 (C=O), 137.8 (Cq, Ph), 129.9, 129.1 (Ph), 111.6 (Cq, isop.), 105.6 (C-1), 80.2 (C-2), 78.6 (C-4), 76.9 (C-5), 44.7 (C-7), 40.5 (C-6), 35.1 (C-3), 26.7 (Me), 26.1 (Me), 24.0 (Me). Anal. calcd for $C_{18}H_{22}O_5Se$ (397.30): C, 54.41; H, 5.57. Found: C, 54.79; H, 5.72%.

3.4. General procedure for the preparation of the butenolides 16 and 17 (method A)

A solution of *m*-CPBA (43 mg, 0.25 mmol) in CH_2Cl_2 (0.5 mL) was added under an argon atmosphere to a solution of the phenylsulfanyllactone (0.2 mmol) in CH_2Cl_2 (0.8 mL), previously cooled to 0°C. The reaction mixture was stirred at 0°C for 1 h, washed with aqueous $NaHCO_3$ solution (10%) and extracted with CH_2Cl_2 (3×5 mL). The organic phase was dried with sodium sulfate and evaporated. The residue was solved in toluene (10 mL/mmol) and heated for 3 h under reflux. Solvent evaporation in vacuo gave a residue which was purified by CC with EtOAc/*n*-hexane (1:4).

3.4.1. 3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*gluco*-oct-6-enofuranurono-8,5-lactone 16. Method A: Starting from **8** (146 mg, 0.33 mmol), this method gave **16** (33 mg, $\eta = 43\%$). The physical and spectroscopic data were in full agreement with those given in the literature.[15]

3.5. General procedure for the synthesis of the butenolides 17, 19–21 and 25, starting from the corresponding phenylselenyllactones (method B)

Glacial acetic acid (1–2 drops) was added to a solution of the phenylselenyllactone (1 mmol) in THF (1 mL) at 0°C. H_2O_2 (6.7 equiv.) was added dropwise and the mixture was stirred at 0°C for 45 min. Treatment with saturated $NaHCO_3$ solution was followed by extraction with CH_2Cl_2 (3×5 mL). The organic phase was dried with sodium sulfate and evaporated in vacuo. The residue was purified by CC to give the butenolides.

3.5.1. 3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*allo*-oct-6-enofuranurono-8,5-lactone 17. Method A: Starting from **9** (90 mg, 0.2 mmol), this procedure gave **17** (20 mg, $\eta = 30\%$). Method B: Starting from **12** (130 mg, 0.3 mmol), this experiment gave **17** (100 mg, $\eta = 91\%$); $R_f = 0.60$ (EtOAc/*n*-hexane 1:1); $[\alpha]_D^{20} = +47$ (*c* 0.5, CH_2Cl_2); IR (KBr): 1774 (C=O), 1382 (C–O, isop.), 1662 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.42 (d, H-6, $J_{6,7} = 6$ Hz), 7.36–7.29 (m, 5H, Ph), 6.08 (dd, H-7, $J_{5,7} = 2.1$ Hz), 5.7 (d, H-1, $J_{1,2} = 3.6$ Hz), 5.28 (br s, H-5), 4.65, 4.61, 4.47 and 4.43 (AB system OCH_2Ph, $J_{AB} = 12$ Hz), 4.51 (dd, H-2, $J_{2,3} = 4.2$ Hz), 4.33 (dd, H-4, $J_{4,5} = 3.3$ Hz, $J_{3,4} = 9$ Hz), 3.62 (dd, H-3), 1.59 (s, 3H, Me, isop.), 1.35 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 173.8 (C=O), 152.9 (C-6), 136.4 (Cq, Ph), 128.6, 128.3 (Ph), 121.9 (C-7), 112.0 (Cq, isop.), 104.3 (C-1), 86.8 (C-5), 81.5 (C-4), 78.5 (C-2), 72.2 (OCH_2Ph), 68.0 (C-3), 26.5 (Me, isop.), 26.3 (Me, isop.). Anal. calcd for $C_{18}H_{20}O_6$ (332.33): C, 65.06; H, 6.06. Found: C, 65.05; H, 6.29%.

3.5.2. 3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-methyl-α-D-*gluco*-oct-6-enofuranurono-8,5-lactone 19. Method B: Starting from **13** (130 mg, 0.26 mmol), this procedure gave **19** (45 mg, $\eta = 64\%$); unreacted **13** was recovered (26 mg, $\eta = 20\%$); $R_f = 0.40$ (EtOAc/*n*-hexane 1:4); $[\alpha]_D^{20} = -22$ (*c* 1.0, $CHCl_3$); IR (neat): 1770 (C=O), 1378 (C–O, isop.), 1662 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.35–7.30 (m, 6H, H-6, Ph), 5.93 (d, 1H, H-1, $J_{1,2} = 3.6$ Hz), 5.17 (dd, 1H, H-5, $J_{4,5} = 8.6$ Hz, $J_{5,6} = 1.5$ Hz), 4.69 (s, 2H, OCH_2Ph), 4.63 (d, 1H, H-2), 4.14 (d, 1H, H-3, $J_{3,4} = 3.0$ Hz), 3.91 (dd, 1H, H-4), 1.93 (s, 3H, Me-7), 1.48 (s, 3H, Me, isop.), 1.25 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 174.0 (C=O), 148.7 (C-6), 137.1 (Cq, Ph), 130.2 (C-7), 128.5, 128.1, 127.8 (Ph), 112.3 (Cq, isop.), 105.3 (C-1), 82.3 (C-2), 81.8 (C-3), 81.5 (C-4), 76.8 (C-5), 72.8 (OCH_2Ph), 10.7 (Me-7), 26.73 (Me, isop.), 26.11 (Me, isop.). Anal. calcd for $C_{19}H_{22}O_6$ (346.35): C, 65.89; H, 6.39. Found: C, 65.57; H, 6.45%.

3.5.3. 3-*O*-Benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-methyl-α-D-*allo*-oct-6-enofuranurono-8,5-lactone 20. Method B: Starting from **14** (100 mg, 0.2 mmol), this method gave **20** (40 mg, $\eta = 73\%$, based upon reacted starting material), recovered **14** (20 mg, $\eta = 20\%$); $R_f = 0.23$ (EtOAc/*n*-hexane 1:3); $[\alpha]_D^{20} = +122$ (*c* 1.0, $CHCl_3$); IR (neat): 1786 (C=O), 1384 (C–O, isop.), 1662 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.41–7.30 (m, 5H, Ph), 7.25 (s, 1H, H-6), 5.77 (d, 1H, H-1, $J_{1,2} = 3.6$ Hz), 5.16 (br s, 1H, H-5), 4.68, 4.64 (part A of AB system, OCH_2Ph, $J_{AB} = 12$ Hz), 4.56 (t, 1H, H-2, $J_{2,3} = 4.4$ Hz), 4.49, 4.45 (part B of AB system), 4.32 (dd, 1H, H-4, $J_{3,4} = 8.7$ Hz, $J_{4,5} = 3.0$ Hz), 3.65 (dd, 1H, H-3), 1.93 (s, 3H, Me-7), 1.55 (s, 3H, Me, isop.), 1.39 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 173.8 (C=O), 145.3 (C-6), 136.9 (Cq, Ph), 130.4 (C-7), 128.5, 128.2, 128.0 (Ph), 113.3 (Cq, isop.), 104.1 (C-1), 79.3 (C-5), 78.6 (C-4), 72.1 (OCH_2Ph), 76.6 (C-2), 75.5 (C-3), 26.8 (Me, isop.), 26.5 (Me, isop.), 10.7 (Me-7). Anal. calcd for $C_{19}H_{22}O_6$ (346.35): C, 65.89; H, 6.39. Found: C, 65.63; H, 6.48%.

3.5.4. 3,6,7-Trideoxy-1,2-*O*-isopropylidene-7-methyl-α-D-*ribo*-oct-6-enofuranurono-8,5-lactone 21. Method B: Starting from **15** (100 mg, 0.25 mmol), this method gave **21** (50 mg, $\eta = 93\%$, based upon reacted starting material), recovered **15** (10 mg, $\eta = 10\%$); $R_f = 0.27$

(EtOAc/*n*-hexane 1:3); $[\alpha]_D^{20}=+40$ (*c* 1.0, CH_2Cl_2); IR (neat): 1766 (C=O), 1380 (C–O, isop.), 1662 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.18 (br s, 1H, H-6), 5.84 (d, 1H, H-1, $J_{1,2}=3.6$ Hz), 4.87 (br d, 1H, H-5, $J_{4,5}=4.5$ Hz), 4.77 (t, 1H, H-2, $J_{2,3b}=3.9$ Hz), 4.19 (ddd, 1H, H-4, $J_{3a,4}=4.5$ Hz, $J_{3b,4}=10.5$ Hz), 2.19 (dd, 1H, H-3a, $J_{3a,3b}=13.5$ Hz), 1.74 (ddd, 1H, H-3b), 1.94 (s, 3H, Me-7), 1.49 (s, 3H, Me, isop.), 1.32 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 173.7 (C=O), 146.4 (C-6), 130.9 (C-7), 111.7 (Cq, isop.), 105.6 (C-1), 81.2 (C-5), 80.2 (C-2), 78.3 (C-4), 35.2 (C-3), 26.8 (Me, isop.), 26.7 (Me, isop.), 10.7 (Me-7). Anal. calcd for $C_{12}H_{16}O_5$ (240.24): C, 60.00; H, 6.71. Found: C, 59.83; H, 6.80%.

3.5.5. Methyl 2,3-anhydro-6,7-dideoxy-7-methyl-β-D-*manno*-oct-6-enofuranurono-8,5-lactone 25. Method B: Starting from **24a** and **24b** (145 mg, 0.25 mmol), this experiment gave **25** (30 mg, $\eta=36\%$); $R_f=0.13$ (EtOAc/*n*-hexane 1:1); $[\alpha]_D^{20}=-116$ (*c* 1.5, CH_2Cl_2); IR (KBr): 1762 (C=O), 1662 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30 (d, 1H, H-6), 5.10 (d, 1H, H-5, $J_{4,5}=3.9$ Hz, $J_{5,6}=3.3$ Hz), 5.07 (s, 1H, H-1), 4.12 (dd, 1H, H-4, $J_{3,4}=5.7$ Hz), 3.71 (d, 1H, H-2, $J_{2,3}=3$ Hz), 3.61 (d, 1H, H-3), 3.55 (s, 3H, OMe), 1.96 (s, 3H, Me); ^{13}C NMR ($CDCl_3$): δ 174.0 (C=O), 146.2 (C-6), 130.0 (C-7), 102.5 (C-1), 79.5 (C-5), 77.9 (C-4), 57.2 (OMe), 55.2 (C-2), 53.3 (C-3), 10.8 (Me). Anal. calcd for $C_{10}H_{12}O_5$ (212.2): C, 56.60; H, 5.69. Found: C, 56.17; H, 5.94%.

3.6. 3,6,7-Trideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-oct-6-enofuranurono-8,5-lactone 18

A solution of $NaIO_4$ (143 mg, 0.67 mmol) in H_2O (1.7 mL) was added dropwise to a solution of **10** (190 mg, 0.56 mmol) in MeOH (1.7 mL), previously cooled to 0°C. After 1 h at 0°C, the reaction mixture was stirred at rt for 17 h. The solids were separated by filtration and the filtrate was extracted with CH_2Cl_2 (3×5 mL). The organic phase was washed with water, and dried with sodium sulfate; solvent evaporation in vacuo afforded a residue which was purified by CC with EtOAc/*n*-hexane (1:1) giving the intermediate sulfoxide (60 mg, 0.17 mmol), which was dissolved in toluene (2 mL) and heated under reflux for 3 h to give, after evaporation, **18** (17 mg, $\eta=14\%$); $R_f=0.35$ (EtOAc/*n*-hexane 1:1); $[\alpha]_D^{20}=+6$ (*c* 1.0, CH_2Cl_2); IR (neat): 1792 (C=O), 1382 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.59 (d, 1H, H-6), 6.19 (dd, 1H, H-7, $J_{5,7}=1.5$ Hz, $J_{6,7}=6.0$ Hz), 5.85 (d, 1H, H-1, $J_{1,2}=3.0$ Hz), 5.00 (dd, 1H, H-5, $J_{4,5}=6.0$ Hz), 4.78 (t, 1H, H-2, $J_{2,3a}=3$ Hz), 4.22 (ddd, 1H, H-4, $J_{3a,4}=9.0$ Hz, $J_{3b,4}=3.0$ Hz), 2.22 (dd, 1H, H-3b, $J_{3a,3b}=12.0$ Hz), 1.77 (ddd, 1H, H-3a), 1.50 (s, 3H, Me, isop.), 1.33 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 172.5 (C=O), 154.1 (C-6), 122.5 (C-7), 111.9 (Cq, isop.), 105.7 (C-1), 83.6 (C-5), 80.82 (C-2), 78.0 (C-4), 35.4 (C-3), 27.1 (Me, isop.), 26.8 (Me, isop.). Anal. calcd for $C_{11}H_{14}O_5$ (226.21): C, 58.40; H, 6.23. Found: C, 57.92; H, 6.44%.

3.7. Methyl (7*R*)- and (7*S*)-2,3-anhydro-6,7-dideoxy-7-methyl-7-phenylselenyl-β-D-*manno*-octofuranurono-8,5-lactone 24a and 24b

Starting from **23** (624 mg, 3.95 mmol), this procedure gave **24a** and **24b** (460 mg, $\eta=32\%$, ratio **24a**/**24b** = 3:1); $R_f=0.23$ (EtOAc/*n*-hexane 1:1); IR (neat): 1784 (C=O), 1286 (C–O, epoxide) cm^{-1}; ^1H NMR ($CDCl_3$) of **24a**: δ 7.68–7.65 (m, 2H, Ph), 7.48–7.36 (m, 3H, Ph), 5.08 (s, 1H, H-1), 4.77 (ddd, 1H, H-5, $J_{4,5}=6.9$ Hz, $J_{5,6a}=5.7$ Hz, $J_{5,6b}=10.5$ Hz), 4.02 (d, 1H, H-4, $J_{3,4}=6.6$ Hz), 3.74 (d, 1H, H-3, $J_{2,3}=2.7$ Hz), 3.68 (d, 1H, H-2), 3.55 (s, 3H, OCH_3), 2.52 (dd, 1H, H-6a, $J_{6a,6b}=14.1$ Hz), 2.32 (dd, 1H, H-6b), 1.66 (s, 3H, Me); ^{13}C NMR ($CDCl_3$) of **24a**: δ 176.0 (C-8), 137.7 (Cq, Ph), 129.7, 128.9 (Ph), 102.2 (C-1), 77.0 (C-4), 75.7 (C-5), 56.8 (OMe), 54.7 (C-2), 53.4 (C-3), 44.5 (C-7), 39.0 (C-6), 23.9 (Me). Anal. calcd for $C_{16}H_{18}O_5Se$ (369.25): C, 52.04; H, 4.90. Found: C, 51.78; H, 4.95%.

3.8. Methyl 2,5-di-*O*-tosyl-β-D-glucofuranoside 22

A solution of methyl 2,5-di-*O*-tosyl-β-D-glucofuranurono-6,3-lactone[24] (500 mg, 1 mmol) in THF (10 mL) was added dropwise over 1 h to a suspension of $LiBH_4$ (42 mg, 1.93 mmol) in THF (5 mL), previously cooled to −10°C. The suspension was then stirred at +14°C for 16 h. Neutralisation with acetic acid (50% in H_2O), filtration and concentration under reduced pressure gave a syrup which was treated with MeOH (3×5 mL) and concentrated in vacuo. The residue was solved in EtOAc and extracted with H_2O. The organic phase was dried with sodium sulfate and evaporated under reduced pressure. The residue was purified by CC with EtOAc/toluene (1:3) to give **22** (472 mg, $\eta=94\%$); $R_f=0.25$ (EtOAc/toluene 1:3); $[\alpha]_D^{20}=+44$ (*c* 1, $CHCl_3$); IR (KBr): 3500 (OH) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.85–7.82 (m, 4H, Ph), 7.41–7.37 (m, 4H, Ph), 4.92–4.88 (m, 2H, H-1, H-5), 4.70 (s, 1H, H-2), 4.35 (t, 1H, H-3, $J_{3,OH}=8.1$ Hz), 4.32 (dd, 1H, H-4, $J_{4,5}=3.9$ Hz, $J_{3,4}=8.4$ Hz), 3.90–3.82 (m, 2H, H-6a, H-6b), 3.31 (s, 3H, OCH_3), 2.46 (s, 3H, CH_2Ph), 2.45 (s, 3H, CH_2Ph); ^{13}C NMR ($CDCl_3$): δ 145.0, 145.1 (Cq, Ph), 130.0, 129.8, 128.8, 127.9 (CH, Ph), 100.8 (C-1), 83.3 (C-2), 79.2 (C-5), 76.7 (C-4), 73.5 (C-3), 61.7 (C-6), 56.0 (OMe), 21.7 (CH_3, Ts). Anal. calcd for $C_{21}H_{26}O_{10}S_2$ (502.54): C, 50.21; H, 5.21; S, 12.76. Found: C, 50.23; H, 5.30; S, 12.65%.

3.9. Methyl 2,3;5,6-dianhydro-β-D-mannofuranoside 23

A solution of KOH (56 mg, 1.0 mmol) in water (1 mL) was cooled to 10°C and added to a solution of methyl 2,5-ditosyl-β-D-glucofuranoside **22** (202 mg, 0.4 mmol) in water (4.0 mL) and THF (1.0 mL), previously cooled to 10°C. The reaction mixture was stirred at rt and followed by TLC until the reaction was complete. After extraction with $CHCl_3$ (10×10 mL), the organic phases were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by CC with EtOAc/toluene (1:3) to give **23** (61 mg, $\eta=97\%$); $R_f=0.5$ (EtOAc/*n*-hexane 1:1); $[\alpha]_D^{20}=+66$ (*c* 0.5, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 5.01 (s, 1H, H-1), 3.78 (d, 1H, H-4, $J_{4,5}=6.0$ Hz), 3.68–3.65 (m, 2H, H-2, H-3), 3.43 (s, 3H, OCH_3), 3.19 (ddd, 1H, H-5), 2.87 (dd, 1H, H-6a, $J_{5,6a}=4.2$ Hz), 2.75 (dd, 1H, H-6b, $J_{5,6b}=3$ Hz, $J_{6a,6b}=6$ Hz); ^{13}C NMR ($CDCl_3$): δ 102.4 (C-1), 76.7 (C-4), 55.7

(OMe), 55.6 (C-2), 53.7 (C-3), 50.4 (C-5), 44.0 (C-6). Anal. calcd for $C_7H_{10}O_4$ (158.14): C, 53.16; H, 6.36. Found: C, 53.13; H, 6.35%.

3.10. 3-Deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-pentodialdo-1,4-furanose 27

A mixture of 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose **26a**[26] (1.0 g, 4.1 mmol) and 80% acetic acid (29 mL) was stirred at 60°C for 1 h. After cooling to rt, the reaction mixture was concentrated in vacuo and toluene (3×21 mL) was added and evaporated under reduced pressure. The residue was purified by CC with the eluent EtOAc/toluene 1:4 to give 3-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose **26b** as a syrup (0.67 g, $\eta=80\%$); $R_f=0.39$ (EtOAc/toluene 2:1); $[\alpha]_D^{22}=+20$ (*c* 1.4, $CHCl_3$); IR (neat): 3580 (OH), 1385 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.79 (d, 1H, H-1, $J_{1,2}=3.1$ Hz), 4.74 (t, 1H, H-2, $J_{2,3}=3.6$ Hz), 4.35 (br s, 1H, OH-6), 4.20–4.13 (m, 1H, H-4), 3.81–3.80 (m, 1H, H-5), 3.72–3.64 (m, 1H, H-6a), 3.53–3.50 (m, 1H, H-6b), 2.05 (dd, 1H, H-3a, $J_{3,4}=3.5$, $J_{3a,3b}=13.3$), 1.87–1.78 (m, 1H, H-3b), 1.49 (s, 3H, Me, isop.), 1.31 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 111.0 (Cq, isop.), 105.0 (C-1), 80.3 (C-2), 78.2 (C-4), 72.2 (C-5), 63.4 (C-6), 33.5 (C-3), 26.5 (Me), 25.9 (Me). A solution of sodium metaperiodate (1.7 g, 8 mmol) in water (30 mL) was added to the solution of **26b** (0.67 g, 3.3 mmol) in ethanol (7 mL). After 20 min stirring at rt in the dark, ethanol (250 mL) was added and the mixture was filtered and concentrated. The residue was extracted with dichloromethane (3×20 mL), and the dichloromethane solution was dried with sodium sulfate and concentrated to give **27** as a syrup (0.67 g, $\eta=65\%$); $R_f=0.59$ (EtOAc/toluene 2:1); $[\alpha]_D^{22}=+32$ (*c* 1.4, $CHCl_3$); IR (neat): 1775 (C=O), 1380 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.60 (s, 1H, H-5), 5.77 (d, 1H, H-1, $J_{1,2}=2.9$ Hz), 4.69 (t, 1H, H-2, $J_{2,3}=3.5$ Hz), 4.18–4.15 (m, 1H, H-4), 3.82–3.72 (m, 2H, H-5, H-6a), 3.48–3.43 (m, 1H, H-6b), 2.09–2.01 (m, 1H, H-3a), 1.87–1.78 (m, 1H, H-3b), 1.42 (s, 3H, Me, isop.), 1.24 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 199.8 (C-5), 111.1 (Cq, isop.), 105.5 (C-1), 95.9 (C-2), 80.3 (C-4), 34.1 (C-3), 26.5 (Me), 25.9 (Me).

3.11. General procedure for the synthesis of compounds 28, 29, 42–45, 51, 53, 55 and 57 by Reformatsky-type reaction

A solution of ethyl bromomethylacrylate[32] (5 mmol) in anhydrous THF (2.5 mL) was added at rt under nitrogen to the mixture of activated[33] granulated zinc 20 mesh and a solution of the carbonyl compound (3 mmol) in anhydrous THF (1.2 mL). The reaction mixture was heated at 45°C for 1 h under nitrogen. After cooling to rt, a 10% hydrochloric acid solution (25 mL), previously cooled to 0°C, was added. After extraction with dichloromethane (3×15 mL), the organic phase was neutralised with aqueous sodium hydrogen carbonate solution (2.5% 25 mL) and then dried with sodium sulfate. Evaporation of the solvent afforded a residue which was purified by CC.

3.11.1. 3,6,7-Trideoxy-1,2-*O*-isopropylidene-7-*C*-methylene-β-L-*lyxo*-octofuranurono-8,5-lactone 28 and 3,6,7-trideoxy-1,2-*O*-isopropylidene-7-*C*-methylene-α-D-*ribo*-octofuranurono-8,5-lactone 29

Starting from **27** (0.5 g, 2.9 mmol), this method gave a mixture of **28** and **29** (0.60 g, $\eta=86\%$, ratio **28**/**29** = 7:3); IR (neat): 1767 (C=O), 1668 (C=C), 1370 (C–O, isop.) cm^{-1}. Physical and spectroscopic data for **28**: $R_f=0.59$ (EtOAc/toluene 2:1); ^1H NMR ($CDCl_3$): δ 6.15 (t, 1H, H-7′a, $J_{7'a,6a}=J_{7'a,6b}=2.9$ Hz), 5.70 (d, 1H, H-1, $J_{1,2}=3.5$ Hz), 5.56 (t, 1H, H-7′b, $J_{7'b,6a}=J_{7'b,6b}=2.5$ Hz), 4.68 (dd, 1H, H-2, $J_{2,3a}=7.5$ Hz, $J_{2,3b'}=5.5$ Hz), 4.53–4.47 (m, 1H, H-5), 4.29–4.25 (m, 1H, H-4), 2.99–2.95 (m, 2H, H-6a, H-6b), 2.03–1.87 (m, 2H, H-3a, H-3b), 1.44 (s, 3H, Me, isop.), 1.25 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 170.0 (C-8), 133.7 (C-7), 121.9 (C-7′), 111.5 (Cq, isop.), 105.5 (C-1), 80.4 (C-2), 78.9 (C-4), 75.4 (C-5), 33.8 (C-3), 30.0 (C-6), 26.8 (Me, isop.), 26.0 (Me, isop.). Anal. calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.22; H, 6.67%.

3.11.2. (3*S*) - 2,3 - Dideoxy - 5,6 - *O* - isopropylidene - 1-*O*-methyl-3′-methylene-2′-oxospiro[α-D-*erythro*-hexofuranose-3,5′-tetrahydrofuran] 42

Starting from **41** (1 g, 4.63 mmol), this method gave **42** (0.64 g, $\eta=49\%$); $R_f=0.78$ (EtOAc/toluene 10:1); $[\alpha]_D^{22}=+18$ (*c* 1.9, $CHCl_3$); IR ($CHCl_3$): 1775 (C=O), 1669 (C=C), 1375 (CO, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.18 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.8$ Hz), 5.61 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.5$ Hz), 5.13 (dd, 1H, H-1, $J_{1,2a}=3.4$ Hz, $J_{1,2b}=5.6$ Hz), 4.23–4.19 (m, 1H, H-5), 4.12 (dd, 1H, H-6a, $J_{5,6a}=4.9$ Hz, $J_{6a,6'b}=8.4$ Hz), 3.96 (dd, 1H, H-6b, $J_{5,6b}=6.2$ Hz), 3.82 (d, 1H, H-4, $J_{4,5}=8.1$ Hz), 3.36 (s, 3H, OMe), 3.27 (dt, 1H, H-4′a, $J_{4'a,4'b}=17.5$ Hz), 3.02 (dt, 1H, H-4′b), 2.65 (dd, 1H, H-2), 2.12 (dd, 1H, H-2b, $J_{2a,2b}=14.7$ Hz), 1.37 (s, 3H, Me, isop.), 1.27 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 168.9 (C=O), 134.3 (H_2C=$\underline{C}$), 121.0 ($H_2\underline{C}$=), 109.1 (Cq, isop.), 103.5 (C-1), 87.8 (C-3), 83.1 (C-4), 72.7 (C-5), 67.2 (C-6), 55.0 (OMe), 47.7 (C-2), 35.2 (C-4′), 26.2 (Me, isop.), 24.7 (Me, isop.). Anal. calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.11; H, 7.14%.

3.11.3. (3*R*) - 2,3 - Dideoxy - 5,6 - *O* - isopropylidene - 1-*O*-methyl-3′-methylene-2′-oxospiro[α-D-*erythro*-hexofuranose-3,5′-tetrahydrofuran] 43

Starting from **41** (1 g, 4.63 mmol), this method gave **43** (0.22 g, $\eta=17\%$); $R_f=0.76$ (EtOAc/toluene 10:1); $[\alpha]_D^{22}=+8.3$ (*c* 2.4, $CHCl_3$); IR ($CHCl_3$): 1767 (C=O), 1660 (C=C), 1375 (CO, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.19 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.8$ Hz), 5.61 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.5$ Hz), 5.01 (dd, 1H, H-1, $J_{1,2a}=5.5$ Hz, $J_{1,2b}=2.2$ Hz), 4.16–3.93 (m, 4H, H-4, H-5, H-6a, H-6b), 3.37 (s, 3H, OMe), 3.53 (dt, 1H, H-4′a, $J_{4'a,4'b}=17.2$ Hz), 2.75 (dt, 1H, H-4′b), 2.45 (dd, 1H, H-2b, $J_{2a,2b}=14.3$ Hz), 2.25 (dd, 1H, H-2a), 1.34 (s, 3H, Me, isop.), 1.28 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 168.9 (C=O), 134.8 (H_2C=$\underline{C}$), 120.9 ($H_2\underline{C}$=), 110.1 (Cq, isop.), 103.1 (C-1), 87.6 (C-3), 82.7 (C-4), 74.2 (C-5), 68.1 (C-6), 55.2 (OMe), 46.8 (C-2), 34.9 (C-4′), 26.5 (Me, isop.), 25.5 (Me, isop.). Anal. calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.23; H, 7.14%.

3.11.4. (3*S*)-2,3-Dideoxy-1-*O*-methyl-3′-methylene-2′-oxospiro[α-D-*erythro*-hexofuranose-3,5′-tetrahydrofuran] 44. Starting from **41** (1 g, 4.63 mmol), this method gave **44** (0.04 g, $\eta=5\%$); $R_f=0.21$ (EtOAc/toluene 10:1); $[\alpha]_D^{22}=+45.0$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3447 (OH), 1759 (C=O), 1636 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.19 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.8$ Hz), 5.61 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.5$ Hz), 5.13 (dd, 1H, H-1, $J_{1,2a}=5.5$ Hz, $J_{1,2b}=3.2$ Hz), 4.19–3.65 (m, 4H, H-4, H-5, H-6a, H-6b), 3.37 (s, 3H, OMe), 3.40 (dt, 1H, H-4′a, $J_{4'a,4'b}=17.2$ Hz), 3.01 (dt, 1H, H-4′b), 2.64 (dd, 1H, H-2a, $J_{2a,2b}=14.6$ Hz), 2.12 (dd, 1H, H-2b); ^{13}C NMR ($CDCl_3$): δ 170.0 (C=O), 134.6 (H_2C=C), 121.8 (H_2C=), 103.6 (C-1), 88.7 (C-3), 74.3 (C-4),), 69.8 (C-5), 62.3 (C-6), 55.4 (OMe), 48.0 (C-2), 35.9 (C-4′). Anal. calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 53.98; H, 6.65%.

3.11.5. (3*R*)-2,3-Dideoxy-1-*O*-methyl-3′-methylene-2′-oxospiro[α-D-*erythro*-hexofuranose-3,5′-tetrahydrofuran] 45. Starting from **41** (1 g, 4.63 mmol), this method gave **45** (0.08 g, $\eta=8\%$); $R_f=0.13$ (EtOAc/toluene 10:1); $[\alpha]_D^{22}=-5.3$ (*c* 1.9, $CHCl_3$); IR ($CHCl_3$): 3448 (OH), 1763 (C=O), 1645 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.21 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.8$ Hz), 5.65 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.5$ Hz), 4.47 (dd, 1H, H-1, $J_{1,2a}=5.4$ Hz, $J_{1,2b}=2.1$ Hz), 3.92–3.55 (m, 4H, H-4, H-5, H-6a, H-6b), 3.50 (s, 3H, OMe), 3.33 (dt, 1H, H-4′a, $J_{4'a,4'b}=17.2$ Hz), 2.93 (dt, 1H, H-4′b), 2.14 (dd, 1H, H-2a, $J_{2a,2b}=14.1$ Hz), 1.79 (dd, 1H, H-2b); ^{13}C NMR ($CDCl_3$): δ 170.0 (C=O), 134.4 (H_2C=C), 122.2 (H_2C=), 99.5 (C-1), 88.1 (C-3), 74.0 (C-4), 70.6 (C-5), 62.3 (C-6), 55.1 (OMe), 42.4 (C-2), 36.3 (C-4′). Anal. calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.06; H, 6.64%.

3.11.6. (5*R*)-3,6-Anhydro-2,3-*O*-isopropylidene-1-*O*-methyl-3′-methylene-2′-oxospiro[α-D-*ribo*-hexofuran-3-uloside-5,5′-tetrahydrofuran] 51. Starting from **50** (1 g, 4.35 mmol), this method gave **51** (0.95 g, $\eta=73\%$); mp = 155.0–155.5°C; $R_f=0.5$ (EtOAc/toluene 1:2); $[\alpha]_D^{22}=+88$ (*c* 1.6, $CHCl_3$); IR ($CHCl_3$): 1783 (C=O), 1628 (C=C), 1385 (CO, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.26 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.7$ Hz), 5.98 (d, 1H, H-1, $J_{1,2}=2.5$ Hz), 5.71 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.4$ Hz), 4.55 (d, 1H, H-2), 4.26 (s, 1H, H-4), 4.22 (part A of AB system, 1H, H-6a, $J_{AB}=10.0$ Hz), 3.99 (part B of AB system, 1H, H-6b), 3.42 (s, 3H, OMe), 3.14 (td, 1H, H-4′a, $J_{4'a,4'b}=17.4$ Hz), 2.97 (td, 1H, H-4′b), 1.55 (s, 3H, Me, isop.), 1.38 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 168.2 (C=O), 132.8 (H_2C=C), 128.8 (C-5), 123.2 (H_2C=), 114.9 (C-3), 114.0 (Cq, isop.), 107.2 (C-1), 87.6 (C-4), 80.1 (C-2), 75.2 (C-6), 51.8 (OMe), 36.0 (C-4′), 27.4 (Me, isop.), 26.9 (Me, isop.). Anal. calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.25; H, 6.03%.

3.11.7. (1*S*)-1-Deoxy-2,3-*O*-isopropylidene-3′-methylene-2′-oxospiro[D-ribofuranose-1,5′-tetrahydrofuran] 53. Starting from **52** (0.5 g, 2.66 mmol), and using dioxane (3 mL) as solvent, this method gave **53** (0.44 g, $\eta=65\%$); $R_f=0.43$ (EtOAc/toluene 1:1); $[\alpha]_D^{22}=+81$ (*c* 1.6, $CHCl_3$); IR (neat): 3488 (OH), 1783 (C=O), 1669 (C=C), 1383 (CO, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.28 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.9$ Hz), 5.73 (t, 1H, H-3″b, $J_{3'b,4'a}=J_{3''b,4'b}=2.5$ Hz), 4.89 (d, 1H, H-3, $J_{2,3}=5.8$ Hz), 4.72 (d, 1H, H-2), 4.38 (t, 1H, H-4, $J_{4,5a}=5.2$ Hz, $J_{4,5b}=4.9$ Hz), 4.14–3.72 (m, 2H, H-5a, H-5b), 3.44 (dt, 1H, H-4′a, $J_{4'a,4'b}=18.2$ Hz), 2.95 (dt, 1H, H-4′b), 1.50 (s, 3H, Me, isop.), 1.35 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 167.8 (C=O), 133.1 (H_2C=C), 123.2 (H_2C=), 114.1 (Cq, isop.), 112.1 (C-1), 87.9 (C-4), 85.1 (C-2), 81.5 (C-3), 63.1 (C-5), 34.2 (C-4′), 26.2 (Me, isop.), 24.9 (Me, isop.). Anal. calcd for $C_{12}H_{16}O_6$: C, 56.25; H, 6.29. Found: C, 56.22; H, 6.33%.

3.11.8. (1*R*)-1-Deoxy-2,3;5,6-di-*O*-isopropylidene-3′-methylene-2′-oxospiro[D-mannofuranose-1,5′-tetrahydrofuran] 55. Starting from **54** (0.5 g, 1.94 mmol), this method gave **55** (0.47 g, $\eta=75\%$); $R_f=0.65$ (EtOAc/toluene 1:2); $[\alpha]_D^{22}=+120$ (*c* 2.0, $CHCl_3$); IR (neat): 1768 (C=O), 1665 (C=C), 1385 (C-O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.28 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.2$ Hz), 5.73 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.5$ Hz), 4.93 (dd, 1H, H-3, $J_{3,4}=3.6$ Hz), 4.70 (d, 1H, H-2, $J_{2,3}=5.7$ Hz), 4.40–4.33 (m, 1H, H-5), 4.10–3.95 (m, 3H, H-4, H-6a, H-6b), 3.33 (dt, 1H, H-4′a, $J_{4'a,4'b}=18.3$ Hz), 2.89 (dt, 1H, H-4′b), 1.48 (s, 3H, Me, isop.), 1.44 (s, 3H, Me, isop.), 1.37 (s, 3H, Me, isop.), 1.34 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 167.8 (C=O), 132.8 (H_2C=C), 123.0 (H_2C=), 113.1 (Cq, isop.), 111.9 (C-1), 109.2 (Cq, isop.), 84.3 (C-2), 80.8 (C-4),), 79.4 (C-3), 72.4 (C-5), 66.5 (C-6), 32.9 (C-4′), 26.7 (Me, isop.), 25.7 (Me, isop.), 25.0 (Me, isop.), 24.5 (Me, isop.). Anal. calcd for $C_{16}H_{22}O_7$: C, 58.89; H, 6.79. Found: C, 58.85; H, 6.69%.

3.11.9. (6*S*)-3,6-Anhydro-1,2-*O*-isopropylidene-3′-methylene-2′-oxospiro[α-D-glucofuranose-6,5′-tetrahydrofuran] 57. Starting from **56** (0.5 mg, 2.50 mmol), this method gave **57** (0.55 g, $\eta=78\%$); mp = 145–146°C; $R_f=0.65$ (EtOAc/toluene 1:5); $[\alpha]_D^{22}=+86$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 1786 (C=O), 1626 (C=C), 1380 (C-O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.22 (t, 1H, H-3″a, $J_{3''a,4'a}=J_{3''a,4'b}=2.7$ Hz), 6.14 (d, 1H, H-1, $J_{1,2}=3.4$ Hz), 5.63 (t, 1H, H-3″b, $J_{3''b,4'a}=J_{3''b,4'b}=2.4$ Hz), 4.84 (t, 1H, H-4, $J_{3,4}=J_{4,5}=4.9$ Hz), 4.70 (d, 1H, H-3), 4.64 (d, 1H, H-2), 4.18 (br d, 1H, H-5), 3.86 (br s, 1H, OH-5), 3.14 (td, 1H, H-4′a, $J_{4'a,4'b}=17.6$ Hz), 2.90 (td, 1H, H-4′b), 2.42 (s, 3H, Me, isop.), 1.29 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 168.1 (C=O), 132.7 (H_2C=C), 123.1 (H_2C=), 113.4 (Cq, isop.), 109.2 (C-6), 107.3 (C-1), 86.0 (C-2), 85.0 (C-3), 79.4 (C-4), 76.5 (C-5), 35.3 (C-4′), 27.5 (Me, isop.), 27.0 (Me, isop.). Anal. calcd for $C_{13}H_{16}O_7$: C, 54.93; H, 5.67. Found: C, 54.91; H, 5.69%.

3.12. General procedure for the synthesis of compounds 32–37

A solution of dimethylboron bromide (7.5 mL, 10.8 equiv.) in 1,2-dichloroethane (25 mL) was added at −78°C under argon to a solution of the protected lactone (2.9 mmol) in dichloromethane (24 mL). After stirring for 2 h at −78°C, the temperature was raised to 0°C and triethylamine (0.082 mL) was added. The

mixture was stirred at 18°C for 1 h and cooled to 0°C. Addition of THF (30 mL) was followed by addition of a saturated solution of sodium hydrogen carbonate (12 mL), dichloromethane (14 mL) and finally diethyl ether (14 mL). The organic phase was washed with a saturated solution of sodium chloride (2×9 mL), dried with sodium sulfate, and evaporated in vacuo.

3.12.1. 3-*O*-Benzyl-6,7-dideoxy-7-*C*-methylene-L-*talo*-octofuranurono-8,5-lactone 32. Starting from **4** (1 g, 2.89 mmol), this method gave **32** (0.27 g, $\eta = 30\%$); mp = 139–141°C; $R_f = 0.30$ (EtOAc/toluene 1:1); $[\alpha]_D^{22} = +86.5$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3446 (OH), 1770 (C=O), 1665 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.32–7.20 (m, 5H, Ph), 6.17 (t, 1H, H-7′a, $J_{7'a,6a} = J_{7'a,6b} = 2.6$ Hz), 5.82 (d, 1H, H-1, $J_{1,2} = 4.3$ Hz), 5.58 (t, 1H, H-7′b, $J_{7'b,6a} = J_{7'b,6b} = 2.5$ Hz), 4.79, 4.75 (part A of AB system, 1H, OCH_2Ph, $J_{AB} = 11.2$ Hz), 4.67–4.64 (m, 2H, H-2, H-5), 4.56, 4.52 (part B of AB system), 4.03 (dd, 1H, H-3, $J_{2,3} = 5.5$ Hz, $J_{3,4} = 8.8$ Hz), 3.82 (d, 1H, H-4), 2.99–2.88 (m, 2H, H-6a, H-6b); ^{13}C NMR ($CDCl_3$): δ 169.6 (C=O), 136.9 (Cq, Ph), 133.3 ($H_2C=\underline{C}$), 127.9, 127.9, 127.8 (Ph), 121.7 ($H_2\underline{C}=$), 104.3 (C-1), 78.7 (C-4), 77.2 (C-2), 76.8 (C-3), 72.9 (C-5), 72.0 (OCH_2Ph), 29.3 (C-6). Anal. calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.71; H, 5.89%.

3.12.2. 6,7-Dideoxy-7-*C*-methylene-L-*talo*-octofuranurono-8,5-lactone 33. Starting from **4** (1 g, 2.89 mmol), this method gave **33** (0.31 g, $\eta = 50\%$); mp = 150–151°C; $R_f = 0.15$ (EtOAc/toluene 1:1); $[\alpha]_D^{22} = +142$ (*c* 1.1, $CHCl_3$); IR ($CHCl_3$): 3452 (OH), 1771 (C=O), 1660 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.28 (t, 1H, H-7′a, $J_{7'a,6a} = J_{7'a,6b} = 2.7$ Hz), 6.07 (d, 1H, H-1, $J_{1,2} = 4.2$ Hz), 5.72 (t, 1H, H-7′b, $J_{7'b,6a} = J_{7'b,6b} = 2.3$ Hz), 4.87–4.82 (ddd, 1H, H-5), 4.69 (dd, 1H, H-2, $J_{2,3} = 2.6$ Hz), 4.38–4.36 (d, 1H, H-4, $J_{3,4} = 2.3$ Hz), 3.86 (dd, 1H, H-3, $J_{2,3} = 8.0$ Hz), 3.15–3.06 (m, 2H, H-6a, H-6b); ^{13}C NMR ($CDCl_3$): δ 170.2 (C=O), 133.3 ($H_2C=\underline{C}$), 123.7 ($H_2\underline{C}=$), 104.9 (C-1), 86.3 (C-4), 80.6 (C-2), 74.3 (C-3), 73.1 (C-5), 30.7 (C-6). Anal. calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 50.04; H, 5.57%.

3.12.3. 3-*O*-Benzyl-6,7-dideoxy-7-*C*-methylene-L-*ido*-octofuranurono-8,5-lactone 34. Starting from **30** (1 g, 2.89 mmol), this method gave **34** (0.28 g, $\eta = 31\%$); mp = 135–136°C; $R_f = 0.30$ (EtOAc/toluene 1:1); $[\alpha]_D^{22} = +99.5$ (*c* 2.0, $CHCl_3$); IR ($CHCl_3$): 3509 (OH), 1769 (C=O), 1667 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.38–7.33 (m, 5H, Ph), 6.27 (t, 1H, H-7′a, $J_{7'a,6a} = J_{7'a,6b} = 2.9$ Hz), 6.04 (d, 1H, H-1, $J_{1,2} = 4.4$ Hz), 5.69 (t, 1H, H-7′b, $J_{7'b,6a} = J_{7'b,6b} = 2.5$ Hz), 4.88–4.67 (m, 4H, H-5, H-2, OCH_2Ph), 4.09 (d, 1H, H-3, $J_{3,4} = 3.2$ Hz), 3.94 (dd, 1H, H-4, $J_{4,5} = 7.5$ Hz), 3.08–3.05 (m, 2H, H-6a, H-6b), 1.93 (s, 1H, OH), 1.73 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): δ 169.8 (C=O), 136.9 (Cq, Ph), 133.4 ($H_2C=\underline{C}$), 128.4, 128.0, 127.7 (Ph), 123.0 ($H_2\underline{C}=$), 104.8 (C-1), 83.1 (C-2), 81.6 (C-3), 80.0 (C-4), 72.9 (C-5), 72.4 (OCH_2Ph), 30.2 (C-6). Anal. calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.77; H, 5.88%.

3.12.4. 6,7-Dideoxy-7-*C*-methylene-L-*ido*-octofuranurono-8,5-lactone 35. Starting from **30** (1 g, 2.89 mmol), this method gave **35** (0.32 g, $\eta = 52\%$); mp = 153–154°C; $R_f = 0.16$ (EtOAc/toluene 1:1); $[\alpha]_D^{22} = +122$ (*c* 1.5, $CHCl_3$); IR ($CHCl_3$): 3452 (OH), 1771 (C=O), 1660 (C=C) cm^{-1}; ^1H NMR (C_3D_6O): δ 6.09–6.05 (m, 2H, H-7′a, H-1), 5.70 (t, 1H, H-7′b, $J_{7'b,6a} = J_{7'b,6b} = 2.3$ Hz), 4.93–4.86 (m, 2H, H-5, OH-3), 4.68 (d, 1H, H-2, $J_{1,2} = 4.3$ Hz), 4.25 (d, 1H, H-3, $J_{3,4} = 2.7$ Hz), 4.03 (dd, 1H, H-4, $J_{4,5} = 5.9$ Hz), 3.12–3.07 (m, 2H, H-6a, H-6b), 1.23 (br s, 1H, OH), 0.90 (br s, 1H, OH); ^{13}C NMR (C_3D_6O): δ 170.3 (C=O), 133.9 ($H_2C=\underline{C}$), 121.6 ($H_2\underline{C}=$), 105.7 (C-1), 87.4 (C-2), 81.0 (C-4), 75.2 (C-3), 74.4 (C-5), 29.8 (C-6). Anal. calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 50.05; H, 5.56%.

3.12.5. 6,7-Dideoxy-7-*C*-methylene-D-*allo*-octofuranurono-8,5-lactone 36. Starting from **5** (1 g, 2.89 mmol), this method gave **36** (0.31 g, $\eta = 50\%$); mp = 145–146°C; $R_f = 0.12$ (EtOAc/toluene 1:1); $[\alpha]_D^{22} = +88$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3450 (OH), 1775 (C=O), 1669 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.28 (t, 1H, H-7′a, $J_{7'a,6a} = J_{7'a,6b} =$ 2.8 Hz), 5.81 (d, 1H, H-1, $J_{1,2} = 4.1$ Hz), 5.60 (t, 1H, H-7′b, $J_{7'b,6a} = J_{7'b,6b} = 2.5$ Hz), 4.81–4.78 (m, 1H, H-5), 4.66 (t, 1H, H-2, $J_{2,3} = 4.1$ Hz), 4.25 (dd, 1H, H-4, $J_{3,4} = 2.3$ Hz, $J_{4,5} = 8.6$ Hz), 3.70 (dd, 1H, H-3), 3.11–3.05 (m, 1H, H-6a), 2.95–2.83 (m, 1H, H-6b); ^{13}C NMR ($CDCl_3$): δ 169.7 (C=O), 133.5 ($H_2C=\underline{C}$), 121.5 ($H_2\underline{C}=$), 104.9 (C-1), 84.0 (C-4), 79.5 (C-2), 75.4 (C-3), 73.5 (C-5), 30.8 (C-6). Anal. calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.96; H, 5.63%.

3.12.6. 6,7-Dideoxy-7-*C*-methylene-D-*gluco*-octofuranurono-8,5-lactone 37. Starting from **31** (1 g, 2.89 mmol), this method gave **37** (0.31 g, $\eta = 50\%$); mp = 140–141°C; $R_f = 0.12$ (EtOAc/toluene 1:1); $[\alpha]_D^{22} = +85$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3451 (OH), 1776 (C=O), 1670 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.18 (t, 1H, H-7′a, $J_{7'a,6a} = J_{7'a,6b} =$ 2.8 Hz), 5.99 (d, 1H, H-1, $J_{1,2} = 3.6$ Hz), 5.54 (t, 1H, H-7′b, $J_{7'b,6a} = J_{7'b,6b} = 2.5$ Hz), 4.78–4.74 (m, 1H, H-5), 4.60 (d, 1H, H-2), 4.24–4.21 (m, 1H, H-4), 3.99–3.96 (m, 1H, H-3), 2.90–2.84 (m, 1H, H-6a), 2.59–2.45 (m, 1H, H-6b); ^{13}C NMR ($CDCl_3$): δ 171.1 (C=O), 134.0 ($H_2C=\underline{C}$), 122.5 ($H_2\underline{C}=$), 106.0 (C-1), 82.2 (C-4), 77.8 (C-2), 78.8 (C-3), 72.0 (C-5), 29.6 (C-6). Anal. calcd for $C_9H_{12}O_6$: C, 50.00; H, 5.59. Found: C, 49.96; H, 5.63%.

3.13. Methyl 2-deoxy-α,-β-D-arabinopyranoside 39a and 39b

2-Deoxyglucose (1.0 g, 6.1 mmol) was added to a solution of acetyl chloride in methanol, previously dried over 3 Å molecular sieves. After stirring for 3 h at rt, the reaction mixture was neutralised with potassium carbonate, filtered over Celite and concentrated, affording a mixture of **39a**, **39b** (1.04 g, $\eta = 98\%$, ratio **39a**/**39b** = 2:1). Spectroscopic data of **39a**: ^1H NMR (C_3D_6O): δ 4.75 (br d, 1H, H-1, $J_{1,2b} = 2.9$ Hz), 4.14 (br s, 3H, OH-3, OH-4, OH-6), 3.87–3.67 (m, 3H, H-5, H-6a, H-6b), 3.45–3.23 (m, 5H, H-3, H-4, OMe), 2.07–1.98 (m, 1H, H-2b), 1.60 (td, 1H, H-2a, $J_{2a,2b} = J_{2a,3} = 9.4$ Hz, $J_{1,2a} = 1.3$ Hz); ^{13}C NMR (C_3D_6O): δ 97.4 (C-1), 71.5 (C-4), 71.3 (C-3), 67.7 (C-5), 60.8 (C-6), 52.9 (OMe), 36.5 (C-2). Spectroscopic data of **39b**: ^1H NMR (C_3D_6O): δ 4.45 (dd, 1H, H-1, $J_{1,2a} = 7.5$ Hz, $J_{1,2b} = 1.8$ Hz), 4.14 (br s, 3H, OH-3, OH-4, OH-6), 3.87–3.67 (m, 3H, H-5, H-6a, H-6b), 3.45–3.23

(m, 5H, H-3, H-4, OMe), 2.07–1.98 (m, 1H, H-2b), 1.41 (q, 1H, H-2a, $J_{1,2a}=J_{1,2b}=J_{2a,2b}=9.4$ Hz); ^{13}C NMR (C_3D_6O): δ 99.9 (C-1), 79.5 (C-4), 75.5 (C-3), 70.2 (C-5), 61.0 (C-6), 54.7 (OMe), 38.0 (C-2).

3.14. Methyl 2-deoxy-5,6-*O*-isopropylidene-α,-β-D-*arabino*-hexofuranoside 40a and 40b

Methyl 2-deoxy-α,-β-D-arabinopyranoside **39a** and **39b** (1.0 g, 5.62 mmol) was added to acetone, previously dried over 3 Å molecular sieves, containing powdered anhydrous zinc chloride (0.13 g), orthophosphoric acid (0.03 mL) and powdered 3 Å molecular sieves. The mixture was stirred at rt for 40 h, filtered, neutralised with basic ion-exchange resin and concentrated. After extraction of the residue with chloroform (3×25 mL), the solution was dried with sodium sulfate and evaporated. CC with EtOAc/toluene 1:5 gave **40a** (0.8 g, $\eta=65\%$) and **40b** (0.25 g, $\eta=20\%$).

Data for **40a**: $R_f=0.6$ (EtOAc); $[\alpha]_D^{20}=+48.6$ (*c* 1.3, $CHCl_3$); IR (neat): 3441 (OH), 1370 (C–O isop.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.08 (t, 1H, H-1, $J_{1,2a}=J_{1,2b}=4.3$ Hz), 4.43–4.38 (dd, 1H, H-4, $J_{3,4}=8.4$ Hz, $J_{4,5}=3.5$ Hz), 4.26–4.24 (m, 1H, H-3), 4.09 (t, 1H, H-6a, $J_{5,6a}=J_{6a,6b}=8.5$ Hz), 3.93–3.73 (m, 2H, H-5, H-6b), 3.27 (s, 3H, OMe), 2.11–2.07 (m, 2H, H-2a, H-2b), 1.36 (s, 3H, Me, isop.), 1.20 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 109.7 (Cq, isop.), 105.2 (C-1), 81.9 (C-4), 73.8 (C-3), 71.8 (C-5), 68.0 (C-6), 55.5 (OMe), 42.5 (C-2), 27.1 (Me, isop.), 25.6 (Me, isop.). Anal. calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.29; H, 8.10%.

Data for **40b**: $R_f=0.5$ (EtOAc); $[\alpha]_D^{20}=+2.8$ (*c* 1.0, $CHCl_3$); IR (neat): 3440 (OH), 1373 (C–O, isop.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.05 (d, 1H, H-1, $J_{1,2b}=5.6$ Hz), 4.42 (t, 1H, H-4, $J_{3,4}=J_{4,5}=3.9$ Hz), 4.13–4.07 (m, 1H, H-3), 3.89 (dd, 1H, H-6a, $J_{5,6a}=2.5$ Hz, $J_{6a,6b}=11.2$ Hz), 3.79–3.66 (m, 2H, H-5, H-6b), 3.36 (s, 3H, OMe), 2.20–2.16 (m, 2H, H-2a, H-2b), 1.36 (s, 3H, Me, isop.), 1.27 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 106.0 (Cq, isop.), 101.0 (C-1), 79.4 (C-4), 74.6 (C-3), 70.4 (C-5), 63.5 (C-6), 55.2 (OMe), 39.2 (C-2), 29.4 (Me, isop.), 25.6 (Me, isop.). Anal. calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.37; H, 8.09%.

3.15. General procedure for the preparation of compounds 41, 50 and 54 by oxidation with pyridinium chlorochromate/powdered molecular sieves

The starting material (4.39 mmol) was added to a suspension of molecular sieves powder (4 Å, 4.39 g) and pyridinium chlorochromate (3.8 g, 13.6 mmol) in anhydrous dichloromethane (22 mL). After stirring for 2 h at 40°C, the reaction mixture was cooled to rt and added to diethyl ether (260 mL) under stirring. The suspension was filtered and filtered again over florisil (21 g). The colourless solution was evaporated to dryness.

3.15.1. Methyl 2-deoxy-5,6-*O*-isopropylidene-α-D-*erythro*-hexofuranosid-3-ulose 41. Starting from methyl 2-deoxy-5,6-*O*-isopropylidene-α-D-*arabino*-hexofuranoside **40a** (1.0 g, 4.39 mmol), this method gave **41** as a syrup (0.82 g, $\eta=85\%$); $R_f=0.7$ (EtOAc/toluene 10:1); $[\alpha]_D^{20}=+65$ (*c* 1.6, $CHCl_3$); IR ($CHCl_3$): 1775 (C=O), 1375 (C–O, isop.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.36 (d, 1H, H-1, $J_{1,2a}=5.3$ Hz), 4.40–3.98 (m, 4H, H-4, H-5, H-6a, H-6b), 3.44 (s, 3H, OMe), 2.64 (dd, 1H, H-2a, $J_{2a,2b}=14.3$), 2.47 (d, 1H, H-2b), 1.47 (s, 3H, Me, isop.), 1.36 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 210.8 (C-3), 110.0 (Cq, isop.), 101.1 (C-1), 78.8, 75.1 (C-4, C-5), 66.1 (C-6), 55.9 (OMe), 44.2 (C-2), 25.8 (Me, isop.), 25.3 (Me, isop.). Anal. calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.25; H, 7.66%.

3.15.2. Methyl (3*R*)-3,6-anhydro-2,3-*O*-isopropylidene-α-D-*ribo*-hexo-3,5-diulofuranoside 50. Starting from **49a** (1.15 g, 5 mmol), this method gave **50** (1.04 g, $\eta=90\%$); mp = 139–141°C; $R_f=0.7$ (EtOAc/toluene 1:1); $[\alpha]_D^{22}=+60$ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 1765 (C=O), 1380 (CO, isop.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.99 (d, 1H, H-1, $J_{1,2}=3.7$ Hz), 4.63 (d, 1H, H-2), 4.37, 4.32 (part A of AB system, 1H, H-6a, $J_{AB}=10.8$ Hz), 4.30–4.21 (m, 2H, part B of AB system, H-6b, H-4), 3.49 (s, 3H, OMe), 1.57 (s, 3H, Me, isop.), 1.39 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 206.2 (C-5), 114.4 (C-3), 113.6 (Cq, isop.), 108.1 (C-1), 79.8 (C-4), 79.7 (C-2), 70.0 (C-6), 51.7 (OMe), 27.3 (Me, isop.), 27.0 (Me, isop.). Anal. calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.20; H, 6.29%.

3.15.3. 2,3;5,6-Di-*O*-isopropylidene-D-mannono-1,4-lactone 54[31]. Starting from 2,3;5,6-di-*O*-isopropylidene-D-mannofuranose (1.0 g, 3.85 mmol), this method gave **54** (0.84 g, $\eta=85\%$); $R_f=0.56$ (EtOAc/toluene 1:2); IR (neat): 1797 (C=O), 1389 (C–O, isop.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.91–4.84 (m, 2H, H-2, H-3), 4.48–4.36 (m, 2H, H-4, H-5), 4.19–4.05 (m, 2H, H-6a, H-6b), 1.49 (s, 3H, Me, isop.), 1.47 (s, 3H, Me, isop.), 1.43 (s, 3H, Me, isop.), 1.40 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 173.5 (C-1), 114.4 (Cq, isop.), 109.9 (Cq, isop.), 78.0 (C-4), 75.8 (C-2), 75.8 (C-3), 72.5 (C-5), 66.4 (C-6), 26.9 (Me, isop.), 26.7 (Me, isop.), 25.9 (Me, isop.), 25.0 (Me, isop.). Anal. calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.76; H, 7.08%.

3.16. 3,6-Anhydro-D-*ribo*-hex-3-ulofuranose 47

A solution of **46**[16] (1.0 g, 3.9 mmol) in 75% formic acid (36 mL) was heated at 50°C for 1 h. The reaction mixture was concentrated under vacuum and, after adding toluene (20 mL) to the residue, the solution was concentrated. This procedure was repeated three times and the final residue was purified by CC with EtOAc/toluene 1:1 to give **47** (0.42 g, $\eta=60\%$); IR (neat): 3580 (OH) cm^{-1}; ^{1}H NMR (C_3D_6O): δ 5.31 (d, 1H, H-1, $J_{1,2}=3.2$ Hz), 4.36–4.29 (m, 2H, H-4, H-5), 3.98–3.94 (d, 1H, H-2), 3.70–3.65 (m, 2H, H-6a, H-6b); ^{13}C NMR (C_3D_6O): 114.3 (C-3), 96.7 (C-1), 76.5 (C-4), 73.7 (C-2), 73.5 (C-6), 68.2 (C-5). Anal. calcd for $C_6H_{10}O_6$: C, 40.45; H, 5.66. Found: C, 40.55; H, 5.60%.

3.17. Methyl 3,6-anhydro-α,-β-D-*ribo*-hex-3-ulofuranoside 48a and 48b

Acetyl chloride (0.17 mL) was added to a solution of **47a** and **47b** (1 g, 5.6 mmol, ratio 2:1) in dry methanol

(17 mL). After stirring for 4 h at rt, the reaction mixture was neutralised with potassium carbonate, filtered over Celite (8.0 g) and evaporated to dryness. The residue was purified by CC with EtOAc/toluene 1:5 and gave **48a** (0.86 g, 80%) and **48b** (0.22 g, 20%).

Data for compound **48a**: $R_f = 0.53$ (EtOAc/toluene 1:2); $[\alpha]_D^{20} = +60$ (*c* 1.0, $CHCl_3$); IR (neat): 3589 (OH) cm^{-1}; ^1H NMR (C_3D_6O): δ 5.31 (d, 1H, H-1, $J_{1,2} = 3.2$ Hz), 4.26–4.19 (m, 2H, H-4, H-5), 3.91–3.86 (m, 2H, H-2, H-6a), 3.70–3.65 (m, 1H, H-6b), 3.31 (s, 3H, OMe); ^{13}C NMR ($CDCl_3$): δ 114.3 (C-3), 99.9 (C-1), 81.5 (C-4), 76.4 (C-2), 73.3 (C-6), 70.3 (C-5), 50.3 (OMe). Anal. calcd for $C_7H_{12}O_6$: C, 43.75; H, 6.29. Found: C, 43.70; H, 6.20%.

Data for compound **48b**: $R_f = 0.4$ (EtOAc/toluene 1:2); $[\alpha]_D^{20} = +2.0$ (*c* 1.4, $CHCl_3$); IR (neat): 3600 (OH) cm^{-1}; ^1H NMR (C_3D_6O): δ 5.30 (s, 1H, H-1), 4.37 (br s, 1H, H-4), 4.26–4.20 (m, 1H, H-5), 4.01–3.90 (m, 3H, H-2, H-6a, H-6b), 3.29 (s, 3H, OMe); ^{13}C NMR ($CDCl_3$): δ 115.7 (C-3), 106.1 (C-1), 85.7 (C-4), 75.00 (C-6), 71.4 (C-2), 71.0 (C-5), 50.5 (OMe). Anal. calcd for $C_7H_{12}O_6$: C, 43.75; H, 6.29. Found: C, 43.98; H, 6.01%.

3.18. Methyl 3,6-anhydro-2,3-*O*-isopropylidene-α,-β-D-*ribo*-hex-3-ulofuranoside 49a and 49b

Methyl 3,6-anhydro-α,-β-D-*ribo*-hex-3-ulofuranoside **48a** and **48b** in a 4:1 ratio (1.0 g, 5.2 mmol) was added to the suspension of powdered anhydrous zinc chloride (0.11 g) and 3 Å molecular sieves powder (1.45 g) in dry acetone (7 mL), to which 85% phosphoric acid (0.028 mL) was previously dropped. After stirring during 38 h at rt, the reaction mixture was filtered, neutralised with Amberlite IRA-400 ion-exchange resin and concentrated. The residue was extracted with chloroform (3× 25 mL), dried over sodium sulfate, evaporated to dryness and purified by CC with EtOAc/toluene 1:5 giving **49a** (0.79 g, $\eta = 65\%$) and **49b** (0.24 g, $\eta = 20\%$).

Data for compound **49a**: $R_f = 0.53$ (EtOAc/toluene 1:2); $[\alpha]_D^{20} = +48.8$ (*c* 1.8, $CHCl_3$); IR (neat): 3468 (OH), 1380 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.91 (d, 1H, H-1, $J_{1,2} = 3.5$ Hz), 4.55 (d, 1H, H-2), 4.46 (br s, 2H, H-4, H-5), 4.16 (dd, 1H, H-6a, $J_{5,6a} = 6.3$ Hz, $J_{6a,6b} = 9.3$ Hz), 3.80 (dd, 1H, H-6b, $J_{5,6b} = 4.5$ Hz), 3.40 (s, 3H, OMe), 2.90 (br s, 1H, OH-5), 1.60 (s, 3H, Me, isop.), 1.40 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 114.4, 114.3 (C-3, Cq, isop.), 107.1 (C-1), 83.2 (C-4), 80.4 (C-2), 74.5 (C-6), 71.4 (C-5), 51.5 (OMe), 27.5 (Me, isop.), 27.0 (Me, isop.). Anal. calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 51.75; H, 6.90%.

Data for compound **49b**: $R_f = 0.58$ (EtOAc/toluene 1:2); $[\alpha]_D^{20} = +3.5$ (*c* 1.3, $CHCl_3$); IR (neat): 3480 (OH), 1386 (C–O, isop.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.40 (s, 1H, H-1), 4.58 (s, 1H, H-2), 4.45 (br s, 2H, H-4, H-5), 4.18 (dd, 1H, H-6a, $J_{5,6a} = 6.4$ Hz, $J_{6a,6b} = 9.4$ Hz), 3.82 (dd, 1H, H-6b, $J_{5,6b} = 4.4$ Hz), 3.36 (s, 3H, OMe), 2.93 (br s, 1H, OH-5), 1.62 (s, 3H, Me, isop.), 1.42 (s, 3H, Me, isop.); ^{13}C NMR ($CDCl_3$): δ 115.0, 114.9 (C-3, Cq, isop.), 111.8 (C-1), 85.8 (C-4), 82.3 (C-2), 74.1 (C-6), 72.2 (C-5), 50.5 (OMe), 28.0 (Me, isop.), 26.8 (Me, isop.). Anal. calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 51.98; H, 6.57%.

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