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Stereoselective Synthesis of β-Oxy- and α-Methylene-γ-Butyrolactones on Pyranose Templates

Yousef Al-Abed, Taleb H. Al-Tel and Wolfgang Voelter*

Abteilung für Physikalische Biochemie des Physiologisch-chemischenInstituts der Universtät Tübingen, Hoppe-Seyler-Straße 4, D-7400 Tübingen, Germany

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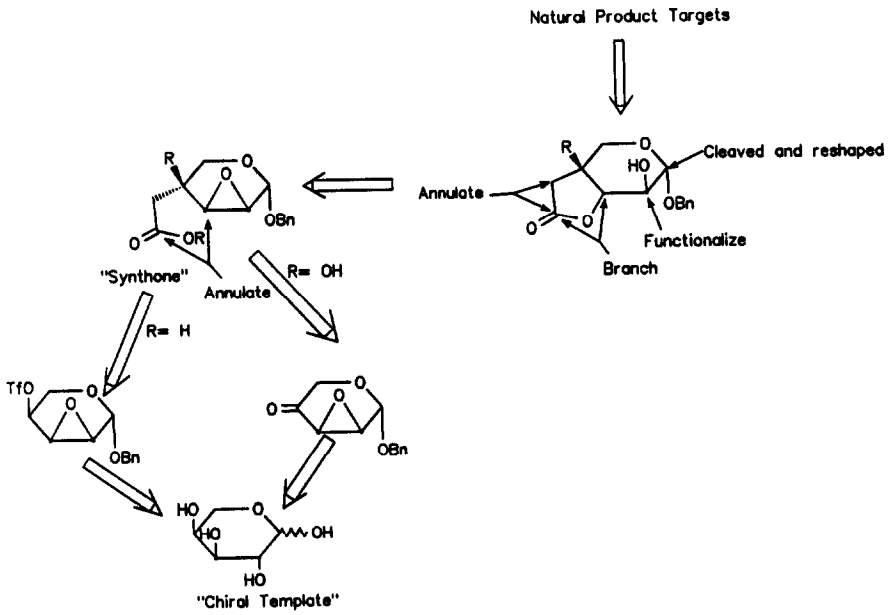
***Abstract**: Reaction of sugar derived epoxy triflates 1 and 2 or epoxy ketoses 11 and 12 with ester or acid enolates followed by acid-catalyzed ring closure affords poly-substituted chiral butenolides in excellent yields.*

Carbohydrates are ideally suited as synthons for natural products as the combination of the natural chirality and inherent topology of a cyclic sugar derivative provides a high degree of regio- and stereocontrol for the systematic functionalization of predetermined sites in the molecule. Such carbohydrate-derived " chiral templates" can then be further modified and eventually integrated into the structural framework of the synthetic target[1].

Butenolides and saturated γ-lactones are ubiquitious structural subunits found in a wide range of natural products[2], including flavour components, insect phermones or antileukaemic lignans[3,4]. The α-methylene-γ-butyrolactone moiety exists as a substructural unit in several biologically active natural products like e.g. vernolepin, a novel sesquiterpene tumor inhibitor, avenaciolide, alantolactone, elephantopin or euparotin and many others[5-7]. Therefore, the synthesis of such optically active building blocks are currently receiving considerable attention[2b,8].

In connection with our efforts to the total syntheses of biologically active natural products, starting from anhydro pentoses, we have developed new synthetic routes for butenolides and γ-butyrolactones bearing chemically differentiable substituents capable of being further elaborated. The retrosynthetic analysis of our approach is seen from Scheme 1: Two of the "on-template" sites (C-2, C-3) of the readily available benzyl pentopyranosides are stereochemically fixed via an oxirane ring, and C-4 is modified in such a way to be ready for chemical transformations. The regioselectivity of our annulation reaction is based on the tremendous difference in the reactivity of a suitably disposed oxirane ring and a trifluoromethanesulfonyl (triflyl) or keto group towards nucleophilic attacks yielding intermediates which in a further step are transformed to the desired cyclic compounds.

Dedicated to Professor Carl Djerassi on the occasion of his 70th birthday



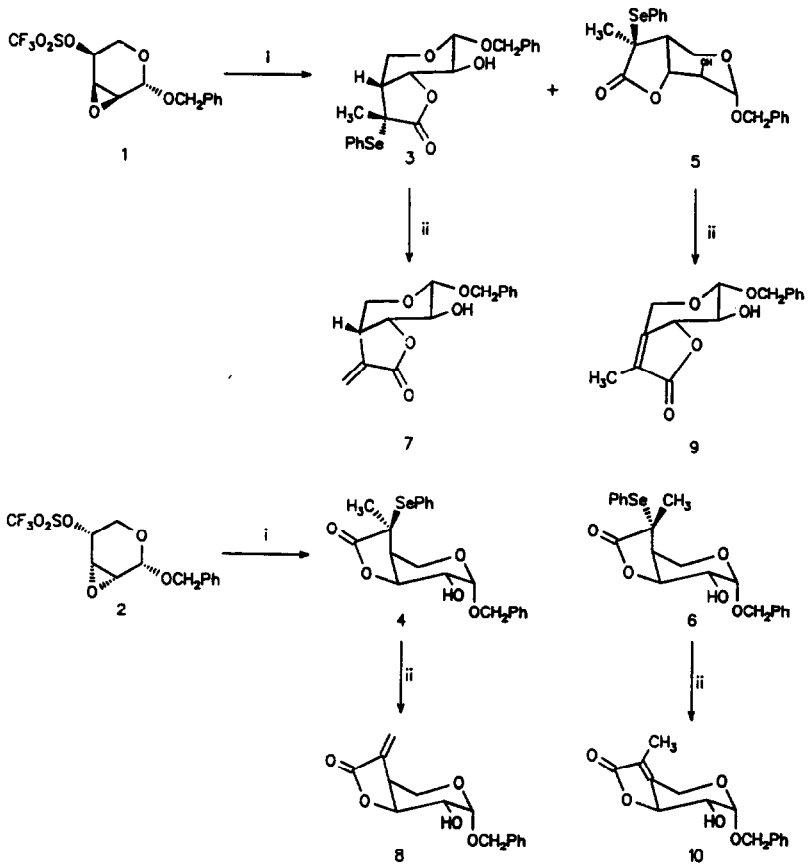
Scheme 1. Retrosynthetic analysis of our annulation strategy.

ACCESS TO α-METHYLENE-γ-BUTYROLACTONES

Grieco and Miyashita [9] have described a general procedure for α-methylenation of fused lactones via α-phenylseleno lactones. The success of this procedure depends on the proper stereochemical relationship between the α-phenylseleno substituent and the proton located in ß position to the carbonyl function. Accordingly, the first task in gaining access to compounds **7** to **10** centered on the nucleophilic attack of the dilithium enolate of α-phenylselenopropionic acid on the cis-oriented anhydro sugar triflates **1** and **2** (Scheme 2) to afford the *trans*- or antiperiplanar-oriented branched intermediates which cyclize in *situ* to the desired substituted γ-lactones **3** to **6**. From the pure samples **3** to **6**, the seleno function in each individual isomer was oxidatively eleminated using H_2O_2/ AcOH at 0 °C to arrive at **7** to **10**. The assignments of the configurations around C-6 are carried out by the chemical transformation of **3** and **4** to the α-methylene-γ-butyrolactones **7** and **8** which proves that the phenylseleno moiety is *trans*-oriented to H-4. However, compounds **5** and **6** yielded the endocyclic γ-butyrolactones **9** and **10** indicating a *cis*-relationship between H-4 and the phenylseleno residue.

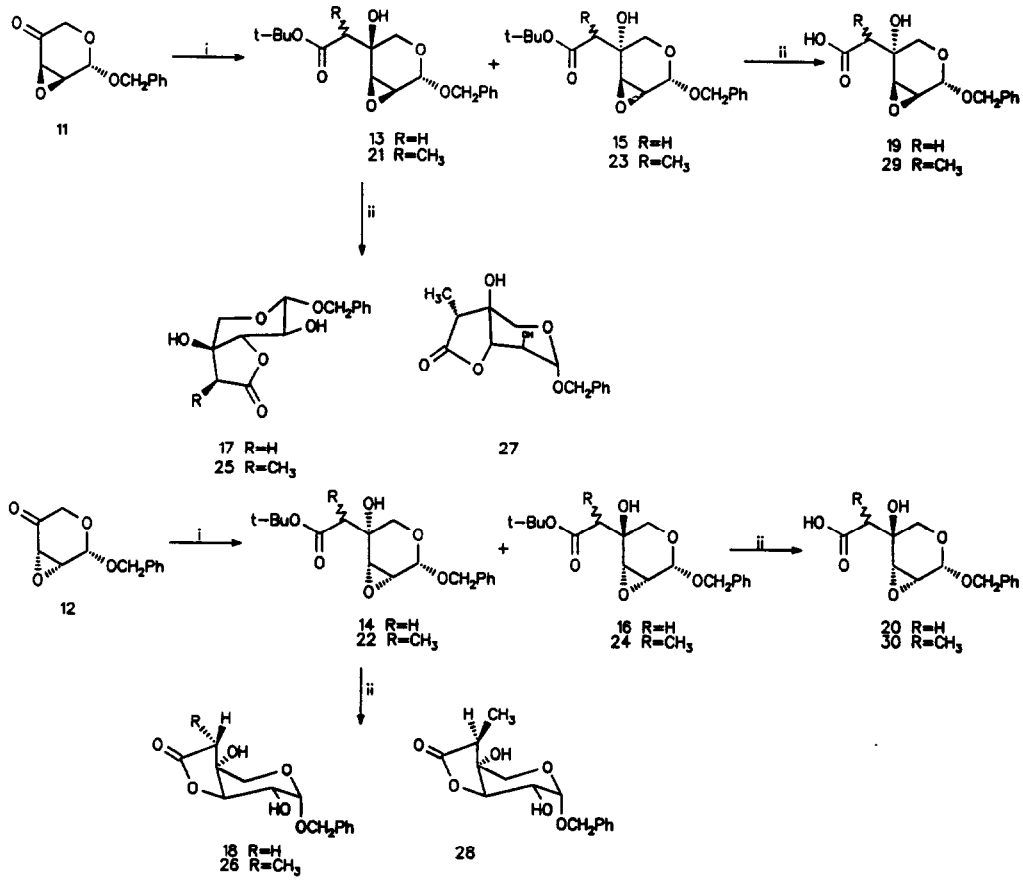
ACCESS TO ß-OXY-γ-BUTYROLACTONES

As ß-oxy-γ-butyrolactones exist also as substructural units in biologically interesting natural products[10], we were attracted to approach these targets by nucleophlic addition of the enolates of tert-butyl acetate or propionoate on epoxy pentuloses. The lithium enolate of tert-butyl acetate is reacted with the epoxy ketoses **11** and **12** (Scheme 3) in a mixture of THF/ HMPA (3:1) to afford **13**, **15** and **4**, **16**, respectively. The incapability of the tertiary alcohols **15** and **16** to undergo cyclization is due to the *cis*-orientation of the propionate residue with respect to the epoxide function. However, compounds **13** and **14** are quantitatively converted to the desired lactones **17** and **18** on treatment with TFA in CH_2Cl_2 at room temperature for 30 min. This general method, established for the synthesis of the ß-oxy-γ-butyrolactones, could be conveniently adapted for the simultaneous introduction of a chiral center on the "off-template".



Scheme 2. Reagents: i) $LiCCH_3(SePh)CO_2Li$/ THF/ HMPA/ -78 °C; ii) H_2O_2/ AcOH/ THF/ 0 °C.

The lithio tert-butyl propionate adduct reacted at -78°C in a mixture of THF/HMPA (3:1) or THF with the epoxy ketoses **11** and **12** (Scheme 3) to yield the carbinols **21**, **23** and **22**, **24**, respectively. The ^1H and ^{13}C NMR spectra of these isomers showed that each carbinol is a mixture of diastereomers (C-6), and the ratios are determined from the ^1H NMR data. Treatment of **21** and **22** with TFA in CH_2Cl_2 at room temperature quantitatively afforded a mixture of **25**, **27** and **26**, **28**, respectively. The non-stereoselective addition of enolates on the pentuloses was found to be in contrast to the results of Corey *et al*[11]. In our case, the effect of the solvent component was only noticeable in the reaction of **11** with the enolate of tert-butyl acetate: In THF the formation of **15** dominates, and in a mixture of THF/HMPA **13** and **15** are obtained in a ratio of 1:1. The assignments of the configurations around C-6 in **25** to **28** are carried out by NOE measurements. Irradiation of the C_4-OH respectively CH_3 protons in these compounds showed reciprocation NOE enhancements only in **25** and **26**, which proves that these functions are close in space.

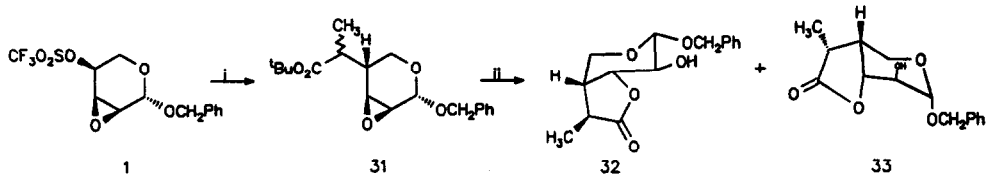


Scheme 3. Reagents: i) $LiCH_2CO_2Bu^t$ or $LiCH(CH_3)CO_2Bu^t$/ THF/ HMPA/ -78 °C ; ii) TFA/ CH_2Cl_2.

CONFORMATIONAL ANALYSIS OF THE FUSED BUTYROLACTOPYRANOSIDES

In accordance with the Fürst-Plattner rule[12], nucleophilic opening of conformationally rigid 2,3-anhydrohexopyranosides predominantly yields *trans*-diaxial products which undergo ring inversion to give the more stable 2,3-diequatorial conformations.In a preliminary report[13] we have described the synthesis of substituted γ-butyrolactones leading to products which were in full agreement with the Fürst-Plattner rule. However, the introduction of substituted branched moieties yields after intramolecular cyclization the anti-Fürst-Plattner products **5** and **27**. It is noteworthy that compounds **3** and **5** or **25** and **27** have totally different conformations as concluded from their ^1H and ^{13}C NMR spectra. For example, the coupling constant of H-1/H-2 in **3**, **5**, **25** and **27** is equal to 7.8, 2.5, 8.1 and 4.4 Hz, respectively. Further salient features of the ^1H NMR spectra are the H-2/ H-3 coupling constants in **3**, **5**, **25** and **27** equal to 8.2, 5.0, 8.1 and 5.1 Hz, respectively. From these spectral data and compared with those of the literature[14], compounds **3** and **25** adopt the $^1C_4$ while **5** and **27** have the $^4C_1$ conformation.The formation of **5** and **27** in which the $^4C_1$ conformation is dominat can be explained only by the influence of the configuration of the residues around C-6. These results could be confirmed by the reaction of **1** with the enolate of tert-butyl propionoate which afforded quantitatively **31** (Scheme 4). The ^1H and ^{13}C NMR data show that **31** is a

mixture of diastereomers in a ratio of 44:56. Compound **31** is smoothly converted to **32** and **33** in a mixture of TFA/ CH_2Cl_2 at room temperature demonstrating that the chiral center at C-6 forces the pyranose moieties to the energetically more favourable $^4C_1$ respectively $^1C_4$ conformations which is also noticeable from Dreiding models. The conformation as well as the configuration around C-6 follows from the ^1H NMR data: H-1 in **32** resonates at δ 4.22 (J=7.8 Hz) and in **33** at δ 4.64 (J=2.3 Hz). Besides, H-4 in **32** shows a coupling of 12.3 Hz proving a *trans*-diaxial orientation to H-6, and consequently the methyl group occuppies the *exo*-face. The much smaller axial-equatorial coupling (7.1 Hz) between H-4 and $H\text{-}6_{exo}$ in **33** proves that its methyl group is *endo*-oriented (trans). These interpretations are in full agreement with the ^1H NMR data recorded for methyl 4,6-O-bezylidine-3-deoxy-3-(prop-2-yloxycarbonyl)-2,3-butyrolactone-α-D-allopyranoside[1e].



1 31 32 33

Scheme 4. Reagents: i) $LiCH(CH_3)CO_2But$/ THF/ HMPA/ -78 °C; ii) TFA/CH_2Cl_2.

As is demonstrated, the sugar derived epoxy triflates **1** and **2** and epoxy ketoses **11** and **12** are suitable starting materials for the synthesis of optically pure α-methylene- and ß-oxy-γ-butyrolactones on pyranose templates which may serve as intermediates for a wide range of natural products. Though ring opening of anhydropentopyranosides with external nucleophiles usually is accompanied by ring inversion leading to the more stable diequatorial compounds, the investigations show that epoxy ring opening by intramolecular cyclization may yield *trans*-diaxial products caused by bulky substituents neighbouring the lactone function.

EXPERIMENTAL

General Methods and Materials. NMR spectra were obtained with the indicated solvents on Bruker AC 250 or Bruker WM 400 instruments and chemical shifts are given in ppm on the δ scale from internal tetramethylsilane. Mass spectra were recorded on a Varian MAT 711 spectrometer. Elemental analyses were performed on a Perkin-Elmer elemental analyser, model 240. Optical rotations were measured using a Zeiss Digital Polarimeter, model LEP AZ. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (60 F-254, E. Merck, Darmstadt, Germany). Plates were visualized under UV light (where appropriate), sprayed with an orcinol/ H_2SO_4 solution and heated to develop. Preparative thin-layer chromatography was performed on 0.5x20x20 silica gel plates (60 F-254, E. Merck). THF was distilled from sodium benzophenone ketyl under nitrogen and diisopropylamine and HMPA were distilled from CaH_2. All other reagents were used as recieved. The α-phenylseleno propionic acid is prepared in 85% yield according to reference 15. ^1H and ^{13}C NMR data are given for the major isomers of **21-24**, **29** and **30**. For the NMR interpretations the following numbering (Figure 1) is adopted.

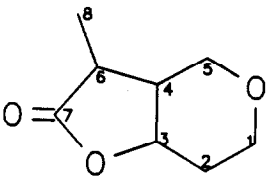


Figure 1

Workup Procedure: The reaction was quenched with a saturated ammonium chloride solution at -30 °C., the mixture distibuted between diethyl ether and H_2O, the organic layer washed with brine, dried over sodium sulfate, filtered and concentrated to give an oily residue. Separation or purification was done by column chromatography on silica gel (10-15 g, 8 cm) using CH_2Cl_2 enriched with ethyl acetate as an eluent to afford almost pure compounds. Further purification was performed on preparative thin-layer chromatography using acetone-dichloromethane-hexane-toluene (1:1:1:1) as an eluent.

General Procedure for the Syntheses of 3-6: Lithium diisopropylamide (6.5 mmol) was prepared from diisopropylamine and n-butyllithium (1.6M, hexane) in THF (0 °C, 15 min, nitrogen atmosphere), the solution was cooled to -78 °C and α-phenylseleno propionic acid (687 mg, 3 mmol) added in THF (3ml). After stirring for 1h at -78 °C, the epoxides **1** respectively **2** were added in 2 ml THF/HMPA (3:1) . After stirring for 1 h at -78 °C, the reaction is warmed to -30 °C followed by the workup procedure.

General Procedure for the Syntheses of 13-16, 21-24 and 31: *tert*-Butyl acetate or propionoate was added as neat to a 3.5 eq. LDA solution, prepared as described above, at -78 °C. After stirring for 1 h at -78 °C, solutions of **11** or **12** (110 mg, 0.5 mmol) in 2 ml THF-HMPA (3:1) were added. After stirring for 1 h at -78 °C the reaction mixture were warmed to -30 °C followed by the workup procedure.

General Method for the Synthesis of 7-10: Following the literature procedure[9], solutions of the compounds **3-6** (0.2 mmol) in THF (1 ml), containing acetic acid (0.03 ml), were treated with 30% H_2O_2 (0.14 ml) at 0 °C for 45 min, then poured into a cold saturated $NaHCO_3$ solution (1.5 ml) and extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, then the solvent was evaporated. The crude product was purified by chromatography on silica gel using EtOAc-CH_2Cl_2 (1:9) as an eluent.

General Method for the Hydrolysis of the *tert*-Butyl Derivatives 13-16, 21-24 and 31: CH_2Cl_2 solutions of the above mentioned compounds were treated with 40% TFA in CH_2Cl_2. The mixtures were stirred at 0 °C for 10 min, then at room temperature for 30 min followed by evaporation of the solvents and reagents. The crude products were purfied or separated by chromatography on silica gel using EtOAc-CH_2Cl_2 (1:1) as an eluent.

***cis*-α-Methyl-α-phenylseleno-γ-lactone (3)**: (48%) amorphous; ^1H NMR ($CDCl_3$) δ: 1.40 (s, 3H, CH_3); 2.64 (dd, 1H, J=8.6, 3.9 Hz, H-4); 3.76 (dd, 1H, J=13.1, 4.6 Hz, H-5); 4.20 (d, 1H, J=7.8 Hz, H-1); 4.27 (d, J= 13.1 Hz, H-5'); 4.30 (dd, 1H, J= 8.2 Hz, H-2); 4.43 (dd, 1H, J= 8.2 Hz, H-3); 4.56 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.89 (d, 1H, J= 11.8 Hz, OC*H*HPh); 7.20-7.61 (m, 10H, aromatic protons). ^{13}C NMR ($CDCl_3$) δ: 24.1 (CH_3); 44.0 (C-6); 46.9 (C-4); 61.5 (C-5); 70.8 (OCH_2Ph); 72.3 (C-2); 78.9 (C-3); 101.7 (C-1); 125.9-138.5 (aromatic carbons); 176.5 (C-7). FDMS m/z 434 (M^++1).

***cis*-α-Methyl-α-phenylseleno-γ-lactone (4)**: (46%) amorphous; ^1H NMR ($CDCl_3$) δ: 1.42 (s, 3H, CH_3); 2.70 (dd, 1H, J=8.6, 4.6 Hz, H-4); 3.89 (d, 1H, J=12.8 Hz, H-5); 4.00 (dd, 1H, J=12.8, 4.8 H-5'); 4.43 (dd, 1H, J=8.4, 3.9 Hz, H-2); 4.50 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.55 (d, 1H, J=8.5 Hz, H-3);

4.70 (d, 1H, J=8.8 Hz,OC*H*HPh); 4.98 (d, 1H, J=3.9 Hz, H-1); 7.17-7.58 (m, 10H, aromatic protons). ^{13}C NMR ($CDCl_3$) δ: 24.4 (CH_3); 44.3 (C-6); 46.4 (C-4); 56.1 (C-5); 69.7 (C-2); 70.2 (OCH_2Ph); 77.9 (C-3); 97.4 (C-1); 125.5-138.5 (aromatic carbons); 176.6 (C-7)). FDMS m/z 434 (M^++1).

***cis*-α-Methyl-α-phenylseleno-γ-lactone (5)**: (46%) oil; ^{1}H NMR ($CDCl_3$) δ: 1.42 (s, 3H, CH_3); 2.66 (ddd, 1H, J=10.2, 6.0, 5.5 Hz, H-4); 3.52 (dd, 1H, J=12.2, 6.4 Hz, H-5); 3.65 (dd, 1H, J=12.2, 10.1 Hz, H-5`); 3.86 (m, 1H, H-2); 4.43 (d, 1H, J=12.3 Hz, OC*H*HPh); 4.66 (d, 1H, J=2.5 Hz, H-1); 4.68 (d, 1H, J=12.3 Hz, OC*H*HPh); 4.70 (dd, 1H, J=5.0 Hz, H-3); 7.20-7.60 (m, 10H, aromatic protons). ^{13}C NMR ($CDCl_3$) δ: 18.8 (CH_3); 40.7 (C-4); 56.2 (C-5); 66.5 (C-2); 69.4 (OCH_2Ph); 76.1 (C-3); 98.2 (C-1); 127.7-138.1 (aromatic carbons). FDMS m/z 434 (M^++1).

***cis*-α-Methyl-α-phenylseleno-γ-lactone (6)**: (42%) oil.^{1}H NMR ($CDCl_3$) δ: 1.47 (s, 3H, CH_3); 2.63 (dd, 1H, J=8.6, 4.6 Hz, H-4); 3.49 (dd, 1H, J=12.4, 6.4 Hz, H-5); 3.99 (m, 2H, H-2 and H-5`); 4.52 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.66(d, 1H, J=3.0 Hz, H-1); 4.78 (m, 1H, H-3); 4.78 (d, 1H, J=11.7 Hz, OC*H*HPh); 7.23-7.57 (m, 10H, aromatic protons). ^{13}C NMR ($CDCl_3$) δ: 18.9 (CH_3); 42.0 (C-4); 60.0 (C-5); 65.8 (C-2); 70.0 (OCH_2Ph); 75.8 (C-3); 95.7 (C-1); 127.9-138.0 (aromatic carbons). FDMS m/z 434 (M^++1).

Benzyl 4-deoxy-4-C-(carboxymethylenemethyl)-3,4-γ-butyrolacto-α-D-arabinopyranoside (7): (100%) amorphous. ^{1}H NMR ($CDCl_3$) δ: 3.31 (m, 1H, H-4); 3.53 (dd, 1H, J=7.4, 6.6 Hz, H-2); 3.80 (dd, 1H, J=12.4, 5.9 Hz, H-5); 3.94 (dd, 1H, J=12.4, 5.9 Hz, H-5`); 4.46 (d, 1H, J=6.4 Hz, H-1); 4.49 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.60 (dd, 1H, J=7.9 Hz, H-3); 4.75 (d, 1H, J=11.8 Hz, OC*H*HPh); 5.55 (d, 1H, J=2.8 Hz, H-8); 6.25 (d, 1H, J=3.2 Hz, H-8`); 7.22-7.30 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 38.9 (C-4); 60.7 (C-5); 70.2 (OCH_2Ph); 72.2 (C-2); 78.5 (C-3); 100.3 (C-1); 122.5 (C-8); 128.0-137.0 (*Ph*); 134.7 (C-6); 170.0 (C-7). FDMS m/z 277 (M^++1). $[\alpha]_D$ -67° (c=1.48 ,$CHCl_3$). Anal.Calcd. for $C_{15}H_{16}O_5$: C 65.21; H 5.84. Found: C 65.33; H 5.93.

Benzyl 4-deoxy-4-(carboxymethylenemethyl)-3,4-γ-butyrolacto-ß-L-arabinopyranoside (8): (95%) oil. ^{1}H NMR ($CDCl_3$) δ: 3.08 (bs, 1H, OH); 3.19 (m, 1H, H-4); 3.67 (m, 1H, H-2); 3.72 (dd, 1H, J=12.2, 2.8Hz, H-5); 4.09(dd, 1H, J=12.2, 4.7Hz, H-5`); 4.52 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.68 (dd, 1H, J=7.8, 6.5 Hz, H-3); 4.75 (d, 1H, J=11.8, OC*H*HPh); 4.82 (d, 1H, J=3.5 Hz, H-1); 5.64 (d, 1H, J=2.6 Hz, H-8); 6.30 (d, 1H, J=3.0 Hz, H-8`); 7.20-7.35(m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 38.7 (C-4); 59.6 (C-5); 69.3 (C-2); 69.9 (OCH_2Ph); 77.4 (C-3); 96.3 (C-1); 122.2 (C-8); 128.1-137.0 (*Ph*). FDMS m/z 277 (M^++1). $[\alpha]_D$ +140° (c=0.79 ,$CHCl_3$). Anal. calcd for $C_{15}H_{16}O_5$: C 65.21; H 5.84. Found: C 64.6; H 6.08.

Endocyclic Isomer (9): (85%) amorphous.^{1}H NMR ($CDCl_3$) δ: 1.8 (bs, 3H, CH_3); 3.08 (bs, 1H, OH); 3.38 (dd, 1H, J=8.8, 6.8 Hz, H-2); 4.17 (d, 1H, J=14.1 Hz, H-5); 4.51 (d, 1H, J=6.8 Hz, H-1); 4.56 (d, 1H, J=11.6 Hz, OC*H*HPh); 4.64 (d, 1H, J=14.1 Hz, H-5`); 4.68 (d, 1H, J=8.8 Hz, H-3); 4.82 (d, 1H, J=11.6, OC*H*HPh); 7.20-7.33 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 8.7 (CH_3); 59.3 (C-5); 71.3 (OCH_2Ph), 76.8 (C-2); 81.7 (C-3); 101.5 (C-1); 123.4 (C-6); 128.2-136.6 (*Ph*); 152.3 (C-4). FDMS m/z 277 (M^++1). $[\alpha]_D$ +109° (c=0.47 ,$CHCl_3$). Anal. calcd for $C_{15}H_{16}O_5$: C 65.21; H 5.84. Found: C 65.41; H 6.02.

Endocyclic Isomer (10): (89%) oil. ^{1}H NMR ($CDCl_3$) δ: 1.81 (bs, 3H, CH_3); 2.62 (bs, 1H, OH); 3.43 (dd, 1H, J=9.1; 3.5 Hz, H-2); 4.30 (d, 1H, J=13.1 Hz, H-5); 4.38 (d, 1H, J=13.1 Hz, H-5`); 4.57 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.76 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.89 (d,1H, J=9.1 Hz, H-3); 4.99 (d,

1H, J=3.5 Hz, H-1); 7.25-7.35(m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 8.8 (CH_3); 56.0 (C-5); 70.5 (OCH_2Ph); 75.6 (C-2); 81.2 (C-3); 97.9 (C-1); 122.0 (C-6); 128.1-137.0 (*Ph*); 151.9 (C-4). FDMS m/z 277 (M+1). $[\alpha]_D$ +147° (c=0.26 ,CHCl3). Anal. calcd for $C_{15}H_{16}O_5$: C 65.21; H 5.84. Found: C 65.15; H 5.86.

Benzyl 2,3-anhydro-4-C-(*tert*-butyloxycarbonylmethyl)-ß-L-ribopyranoside (13): (48%). ^{1}H NMR ($CDCl_3$) δ: 2.45 (d, 1H, J=15.2 Hz, H-6); 2.53 (d, 1H, J=15.2 Hz, H-6`); 3.17# (d, 1H, J=3.8 Hz, H-3); 3.30 (dd, 1H, J=12.0, 1.0 Hz, H-5); 3.43# (d, 1H, J=3.8 Hz, H-2); 3.65 (d, 1H, J=12.0, H-5`); 4.51 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.73 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.96 (bs, 1H, H-1); 7.20-7.35(m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 28.0 ((CH_3)$_3$C); 42.1 (C-6); 52.3# (C-2); 56.0# (C-3); 64.7 (C-5); 70.1 (OCH_2Ph); 93.8 (C-1); 128.0-137.7 (*Ph*).

Benzyl 2,3-anhydro-4-C-(*tert*-butyloxycarbonylmethyl)-α-D-ribopyranoside (14): (46%). ^{1}H NMR ($CDCl_3$) δ: 2.34 (d, 1H, J=16.1 Hz, H-6); 2.55 (d, 1H, J=16.1 Hz, H-6`); 3.25 (d, 1H, J=3.9 Hz, H-3); 3.30 (d, 1H, J=11.9 Hz, H-5); 3.32 (dd, 1H, J=3.9, 3.0 Hz, H-2); 3.65 (d, 1H, J=11.9 Hz, H-5`); 4.55 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.74 (d, 1H, J=12.2 Hz, OC*H*HPh); 5.00 (d, 1H, J=3.0 Hz, H-1); 7.20-7.30(m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 28.0 ((CH_3)$_3$C); 40.1 (C-6); 53.0# (C-2); 54.9# (C-3); 64.5 (C-5); 69.0 (OCH_2Ph); 68.0 ((CH_3)$_3$C); 91.6 (C-1); 127.5-137.0 (*Ph*); 171.0 (C-7).

Benzyl 2,3-anhydro-4-C-(*tert*-butyloxycarbonylmethyl)-α-D-lyxopyranoside (15): (90)% oil. ^{1}H NMR ($CDCl_3$) δ: 2.35 (d, 1H, J=16.7 Hz, H-6); 2.73 (d, 1H, J=16.7 Hz, H-6`); 3.02 (d, 1H, J=3.7 Hz, H-2); 3.22 (d, 1H, J=3.7 Hz, H-3); 3.14 (dd, 1H, J=11.4, 1.2 Hz, H-5); 3.51 (d, 1H, J=11.4 Hz, H-5`); 4.43 (d, 1H, J=11.7 Hz, OCHHPh); 4.67 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.85 (bs, 1H, H-1); 7.22-7.30 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 28.1 ((CH_3)$_3$C); 40.4 (C-6); 50.6 (C-2); 57.0 (C-3); 63.5 (C-5); 65.2 ((CH_3)$_3$C); 69.9 (OCH_2Ph); 82.2 (C-4); 94.2 (C-1); 128.0-137.0 (*Ph*); 172.5 (C-7).

Benzyl 2,3-anhydro-4-C-(*tert*-butyloxycarbonylmethyl)-ß-L-lyxopyranoside (16): (44%) oil. ^{1}H NMR (DMSO-d_6) δ: 2.52 (d, 1H, J=15.8 Hz, H-6); 2.60 (d, 1H, J=15.8 Hz, H-6`); 3.22 (d, 1H, J=11.2 Hz, H-5); 3.26 (d, 1H, J=3.9 Hz, H-3); 3.36 (dd, 1H, J=3.9, 2.8 Hz, H-2); 3.68 (bs, 1H, OH); 3.71 (d, 1H, J=11.4 Hz, H-5`); 4.52 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.74 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.86 (d, 1H, J=2.7 Hz, H-1); 7.20-7.30 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 28.0 ((CH_3)$_3$C); 40.1 (C-6); 54.4# (C-2); 55.4# (C-3); 63.4 (C-5); 68.5 ((CH_3)$_3$C); 69.3 (OCH_2Ph); 82.5 (C-4); 91.7 (C-1); 127.8-137.0 (*Ph*).

Benzyl 4-C-(carboxymethyl)-3,4-γ-butyrolacto-α-D-xylopyranoside (17): (100%) oil. ^{1}H NMR (DMSO-d_6) δ: 2.26 (d, 1H, J=17.3 Hz, H-6); 2.92 (d, 1H, J=17.3 Hz, H-6`); 3.33 (ddd, 1H, J=8.0, 7.7, 5.6 Hz, H-2); 3.45 (d, 1H, J=12.2 Hz, H-5); 3.86 (d, 1H, J=12.2 Hz, H-5`); 4.10 (d, 1H, J=8.2 Hz, H-3); 4.37 (d, 1H, J=7.7 Hz, H-1); 4.60 (d, 1H, J=12.2 Hz; OC*H*HPh); 4.79 (d, 1H, J=12.2 Hz, OC*H*HPh); 5.71 (s, 1H, OH); 5.80 (d, 1H, J=5.6 Hz, OH); 7.23-7.30 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 40.0 (C-6); 66.50 (C-5); 69.6 (OCH_2Ph); 74.0 (C-4); 88.9 (C-3); 101.8 (C-1); 127.5-137.6 (*Ph*); 175.4 (C-7). FDMS m/z 280 (M^+). Anal. calcd for $C_{14}H_{16}O_6$: C 60.00; H 5.75. Found: C 59.94; H 6.00.

Benzyl 4-C-(carboxymethyl)-3,4-γ-butyrolacto-α-D-xylopyranoside (18): 100% oil. ^{1}H NMR (DMSO-d_6) δ: 2.23 (d, 1H, J=17.1 Hz, H-6); 2.92 (d, 1H, J=17.1 Hz, H-6`); 3.49 (dd, 1H, J=8.7, 3.7 Hz,

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assignments may be reversed.

H-2); 3.56 (d, 1H, J=11.7 Hz, H-5); 3.64 (d, 1H, J=11.7 Hz, H-5`); 4.24 (d, 1H, J=8.7 Hz, H-3); 4.50 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.71 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.78 (d, 1H, J=3.7 Hz, H-1); 5.76 (bs, 2H, OH); 7.20-7.30 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 40.0 (C-6); 61.2 (C-5); 68.7 (OCH_2Ph); 70.9 (C-2); 73.2 (C-4); 87.0 (C-3); 97.6 (C-1); 127.6-138.0 (*Ph*); 175.6 (C-7). FDMS m/z 280 (M^+). Anal. calcd for $C_{14}H_{16}O_6$: C 60.00; H 5.75. Found: C 60.09; H 5.81.

Benzyl 2,3-anhydro-4-C-(carboxymethyl)-α-D-lyxopyranoside (19):. 100% oil. ^{1}H NMR (DMSO-d6) δ: 2.35 (d, 1H, J=15.2 Hz), H-6); 2.62 (d, 1H, J=15.2 Hz, H-6`); 3.15# (d, 1H, J=3.8 Hz, H-2); 3.30# (d, 1H, J=3.8 Hz, H-3); 3.33 (d, 1H, J=11.3 Hz, H-5); 3.41 (d, 1H, J=11.3 Hz, H-5`); 4.55 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.70 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.98 (bs, 1H, H-1). ^{13}C NMR (DMSO-d_6) δ: 40.7 (C-6); 50.3 (C-2)#; 57.0 (C-3)#; 63.4 (C-5); 64.3 (C-4); 69.2 (OCH_2Ph); 94.2 (C-1); 127.7-137.6 (*Ph*); 171.9 (C-7).

Benzyl 2,3-anhydro-4-C-(carboxymethyl)-ß-L-lyxopyranoside (20): 100% oil. ^{1}H NMR (DMSO-d_6) δ: 2.27 (d, 1H, J=14.1 Hz, H-6); 2.42 (d, 1H, J=14.1 Hz, H-6`); 3.29 (m, 1H, H-3 and H-5); 3.44 (bdd, 1H, J=3.6, 3.3 Hz, H-2); 3.56 (d, 1H, J=11.9 Hz, H-5`); 4.52 (d, 1H, J=11.8 Hz, OC*H*HPh); 4.68 (d, 1H, J=11.8 Hz, OC*H*HPh); 5.08 (d, 1H, J=3.0 Hz, H-1); 7.23-7.30 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 41.2 (C-6); 52.2# (C-2); 53.8# (C-3); 64.4 (C-5); 67.0 (C-4); 68.8 (OCH_2Ph); 92.6 (C-1); 127.6-138.0 (*Ph*); 171.2 (C-7).

Benzyl 2,3-anhydro-4-C-(prop-2yl-*tert*-butyloxycarbonyl)-ß-L-ribopyranoside (21): (35%) oil. ^{1}H NMR ($CDCl_3$) δ: 1.22 (d, 3H, J=7.2 Hz, CH_3); 1.35 (s, 9H, (CH_3)$_3$C); 2.54 (q, 1H, J=14.4, 7.1 Hz, H-6); 3.24 (d, 1H, J=12.0 Hz, H-5); 3.14-3.60 (m, 2H, H-2,3); 3.71 (d, 1H, J=12.0 Hz, H-5`); 4.50 (d, 1H, J=11.7Hz, OC*H*HPh); 4.71 (d, 1H, J=11.7, OC*H*HPh); 4.96 (s, 1H, H-1); 7.25-7.31 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 11.3 (CH_3); 27.9 ((CH_3)$_3$C); 45.8 (C-6); 51.9# (C-2); 54.4# (C-3); 63.9 (C-5); 66.6 ((CH_3)$_3$C)); 70.0 (OCH_2Ph); 81.5 (C-4); 93.6 (C-1); 128.0-137.6 (*Ph*).

Benzyl 2,3-anhydro-4-C-(prop-2-yl-*tert*-butyloxycarbonyl)-α-D-ribopyranoside (22): (73%) oil. ^{1}H NMR ($CDCl_3$) δ: 1.13 (d, 3H, J=7.3 Hz, CH_3); 1.41 (s, 9H, (CH_3)$_3$C); 2.62 (q, 1H, J=14.6, 7.3 Hz, H-6); 3.12-3.30 (m, 2H, H-2 and H-3); 3.35 (d, 1H, J=11.8 Hz, H-5); 3.66 (d, 1H J=11.8 Hz, H-5`); 3.82 (bs, 1H, OH); 4.54 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.73 (d, 1H, J=12.2 Hz, OC*H*HPh); 5.00 (d, 1H, J=3.0 Hz, H-1); 7.20-7.35 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 11.0 (CH_3); 28.0 ((CH_3)$_3$C); 44.0 (C-6); 52.2# (C-2); 54.4# (C-3); 62.5 (C-5); 64.4 ((CH_3)$_3$C); 69.4 (OCH_2Ph); 82.5 (C-4); 92.0 (C-1); 127.9-137.0 (*Ph*).

Benzyl 2,3-anhydro-4-C-(prop-2-yl-*tert*-butoxycarbonyl)-α-D-lyxopyranoside (23): (57%) oil. ^{1}H NMR ($CDCl_3$) δ: 1.62 (d, 3H, J=7.3 Hz, CH_3); 2.64 (q, 1H, J=14.8, 7.5 Hz, H-6); 3.15-3.42 (m, 4H, H-2,3,5 and H-5`); 4.55 (d, 1H, J=11.7, OC*H*HPh); 4.71 (d, 1H, J=11.74 Hz, OC*H*HPh); 4.96 (s, 1H, H-1); 5.15 (bs, 1H, OH). ^{13}C NMR (DMSO-d_6) δ: 10.9 (CH_3); 27.7 ((CH_3)$_3$C); 43.5 (C-6); 50.0# (C-2); 57.6# (C-3); 61.1 (C-5); 65.9 ((CH_3)$_3$C) ; 69.2 (OCH_2Ph); 79.5 (C-4); 94.4 (C-1); 126.4-137.6 (*Ph*), 173.1 (C-7).

Benzyl 2,3-anhydro-4-C-(prop-2-yl-*tert*-butyloxycarbonyl)-ß-L-lyxopyranoside (24): (18%) oil. ^{1}H NMR ($CDCl_3$) δ: 1.22 (d, 3H, J=7.2 Hz, CH_3); 1.40 (s, 9H, (CH_3)$_3$C); 2.58(q, 1H, J=14.4, 7.2 Hz, H-6); 3.25-3.45 (m, 4H, H-2,3,5 and OH); 3.63 (d, 1H, J=11.6 Hz, H-5`); 4.52 (d, 1H, J=12.3 Hz, OC*H*HPh); 4.74 (d, 1H, J=12.3 Hz, OC*H*HPh); 4.82 (bd, 1H, J=2.6 Hz, H-1); 7.20-7.30 (m, 5H, *Ph*).

^{13}C NMR ($CDCl_3$) δ: 11.8 (CH_3); 27.9 (($CH_3)_3C$); 43.6 (C-6); 54.6# (C-2); 55.2# (C-3); 61.9 (C-5); 64.4 (($CH_3)_3C$); 69.3 (OCH_2Ph); 82.6 (C-4); 92.0 (C-1); 127.8-137.0 (*Ph*).

Benzyl 4-C-(prop-2yloxycarbonyl)-3,4-γ-butyrolacto-α-D-xylopyranoside (25): (65%) amorphous. ^1H NMR (DMSO-d_6) δ: 1.00 (d, 3H, J=7.1 Hz, CH_3); 2.82 (q, 1H, J=14.1, 7.0 Hz, H-6); 3.35 (ddd, 1H, J=8.1, 8.1, 5.5 Hz, H-2); 3.41 (d, 1H, J=12.3 Hz, H-5); 3.83 (d, 1H, J=12.3 Hz, H-5); 4.1 (d, 1H, J=8.1 Hz, H-3); 4.34 (d, 1H, J=8.1 Hz, H-1); 4.62 (d, 1H, J=12.2 Hz, OC*H*HPh); 4.81 (d, 1H, J=12.2 Hz, OC*H*HPh); 5.60 (bs, 1H, OH); 5.82 (d, 1H, J=5.5 Hz, OH); 7.30-7.45 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 6.3 (C-7); 40.2 (C-6); 65.3 (C-5); 69.8 (OCH_2Ph); 72.3 (C-2); 75.1 (C-4); 87.9 (C-3); 102.1 (C-1); 127.6-137.6 (*Ph*); 177.9 (C-7). FDMS m/z 294 (M^++1). $[\alpha]_D$ +37.7° (c=0.27 ,CH_3OH). Anal. calcd for $C_{15}H_{18}O_6$: C 61.22; H 6.16. Found: C 61.45; H 6.19.

Benzyl 4-C-(prop-2-yloxycarbonyl)-3,4-γ-butyrolacto-α-D-xylopyranoside (26): (60%) oil. ^1H NMR (DMSO-d_6) δ: 1.01 (d, 3H, J=7.0Hz, CH_3); 2.81 (q, 1H, J=14.0, 7.0Hz, H-6); 3.39 (m, 1H, H-2); 3.52 (d, 1H, J=11.9Hz, H-5); 3.61 (d, 1H, J=11.9, H-5`); 4.24 (d, 1H, J=8.6Hz, H-3); 4.51 (d, 1H, J=12.4Hz, OC*H*HPh); 4.72 (d, 1H, J=12.4Hz, OC*H*HPh); 4.79 (d, 1H, J=3.7Hz, H-1); 5.50 (d, 1H, J=6.5Hz, OH); 5.67 (bs, 1H); 7.25-7.35 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 6.3 (C-8); 40.0 (C-6); 59.9 (C-5); 68.8 (OCH_2Ph); 70.4 (C-2); 74.2 (C-4); 85.9 (C-3); 97.8 (C-1); 127.6-137.5 (*Ph*); 178.0 (C-7). FDMS m/z 294 (M+1). $[\alpha]_D$ +118° (c=0.36, CH3OH). Anal. calcd for $C_{15}H_{18}O_6$: C 61.22; H 6.16. Found: C 61.45; H 6.19.

Benzyl 4-C-(prop-2-yloxycarbonyl)-3,4-γ-butyrolacto-ß-L-xylopyranoside (27): (35%) amorphous ^1H NMR (DMSO-d_6) δ: 1.08 (d, 3H, J=7.7 Hz, CH_3); 2.65 (q, 1H, J=15.3, 7.6 Hz, H-6); 3.46(d, 1H, J=12.6Hz, H-5`); 3.52 (m, 1H, H-2); 3.83 (d, 1H, J=12.6 Hz, H-5); 4.17 (d,1H, J=5.1 Hz, H-3); 4.51 (d, 1H, J=12.3 Hz, OC*H*HPh); 4.57 (d, 1H, J=4.4 Hz, H-1); 4.71 (d, 1H, J=12.3 Hz, OC*H*HPh); 5.65 (bd, 1H, J=6.0 Hz, OH); 5.66 (bs, 1H,OH); 7.25-7.35 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6) δ: 9.0 (C-8); 45.5 (C-6); 62.6 (C-5); 68.5 (C-2); 68.8 (OCH_2Ph); 72.7 (C-4); 84.5 (C-3); 99.8 (C-1); 127.5-137.6 (*Ph*); 177.4 (C-7). FDMS m/z 294 (M^++1). $[\alpha]_D$ +79° (c=0.28, CH_3OH). Anal. calcd for $C_{15}H_{18}O_6$: C 61.22; H 6.16. Found: C 61.20; H 6.06.

Benzyl C-(prop-2-yloxycarbonyl)-3,4-γ-butyrolacto-α-D-xylopyranoside (28): (40%). ^1H NMR (DMSO-d_6) δ: 1.20 (d, 3H, J=8.0Hz, CH_3); 3.54 (dd, 1H, J=8.1, 3.6Hz, H-2); 3.69 (d, 1H, J=12.2Hz, H-5); 3.76 (d, 1H, J=12.2Hz, H-5`); 4.35 (d, 1H, J=8.1Hz, H-3); 4.51 (d, 1H, J=12.3Hz, OC*H*HPh); 4.72 (d, 1H, J=12.3Hz, OC*H*HPh); 4.76 (d, 1H, J=3.6Hz, H-1); 5.53 (bs, 1H, OH); 5.74 (bs, 1H, OH); 7.25-7.35 (m, 5H, *Ph*). ^{13}C NMR (DMSO-d_6)) δ: 11.0 (C-8); 45.8 (C-7); 61.8 (C-5); 68.9 (OCH_2Ph); 70.2 (C-2); 73.6 (C-4); 86.8 (C-3); 97.3 (C-1); 127.5-137.5 (*Ph*); 179.0(C-7). FDMS m/z 294 (M^++1). $[\alpha]_D$ +64° (c=0.36, CH_3OH). Anal. calcd for $C_{15}H_{18}O_6$: C 61.22; H 6.16. Found: C 61.45; H 6.19.

Benzyl 2,3-anhydro-4-C-(prop-2-yl-carboxy)-α-D-lyxopyranoside (29): (100%) oil. ^1H NMR (DMSO-d_6) δ: 1.09 (d, 3H, J=7.3 Hz, CH_3); 2.64 (q, 1H, J=14.6, 7.3 Hz, H-6); 3.13-3.57 (m, 4H, H-2, H-3, H-5,5`); 4.55 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.71 (d, 1H, J=11.7 Hz, OC*H*HPh); 4.95 (s, 1H, H-1). ^{13}C NMR (DMSO-d_6) δ: 11.0 (C-8); 42.3 (C-6); 50.3 (C-2); 57.6 (C-3); 60.9 (C-5); 65.8 (C-4); 69.2 (OCH_2Ph); 94.4 (C-1); 127.7-137.6 (*Ph*); 176.2 (C-7).

Benzyl 2,3-anhydro-4-C-(prop-2-yl-carboxy)-ß-L-lyxopyranoside (30): (100%) oil. ^1H NMR (DMSO-d_6) δ: 1.02 (d, 3H, J=7.2 Hz, CH_3); 2.44 (q, 1H, J=14.4, 7.2 Hz, H-6); 3.12-3.70 (m, 4H, H-2, H-3,

H-5,5`); 4.51 (d, 1H, J=11.9 Hz, OC*H*HPh); 4.67 (d, 1H, J=11.9 Hz, OC*H*HPh); 5.05 (d, 1H, J=3.0Hz, H-1).

Benzyl 4-deoxy-4-(prop-2-yloxycarbonyl)-3,4-γ-butyrolacto-α-D-arabinoopyranoside (32): (56%) amorphous. ^{1}H NMR ($CDCl_3$) δ: 1.16 (d, 3H, J=6.9 Hz, CH_3); 2.21 (m, 1H, H-4); 2.55 (ddd, 1H, J=13.8, 12.3, 6.9 Hz, H-6); 3.21 (bs, 1H, OH); 3.47 (dd, 1H, J=7.8 Hz, H-2); 3.64 (dd, 1H, J=12.9, 3.6 Hz, H-5); 3.90 (dd, 1H, J=12.9, 1.5 Hz, H-5`); 4.22 (d, 1H, J=7.8 Hz, H-1); 4.36 (dd, 1H, J=7.8 Hz, H-3); 4.53 (d, 1H, J=11.6 Hz, OC*H*HPh); 4.83 (d, 1H, J=11.6 Hz, OC*H*HPh); 7.25-7.35 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 13.2 (C-8); 35.9 (C-4); 43.9 (C-6); 61.7 (C-5); 71.0 (OCH_2Ph); 72.8 (C-2); 79.5 (C-3); 101.6 (C-1); 128.2-136.8 (*Ph*); 178.4 (C-7). $[\alpha]_D$ -234° (c=0.6, $CHCl_3$)

Benzyl 4-deoxy-4-(prop-2-yloxycarbonyl)-3,4-γ-butyrolacto-α-D-ribopyranoside (33): (44%) oil· ^{1}H NMR ($CDCl_3$) δ: 1.09 (d, 3H, J=7.1 Hz, CH_3); 2.61-2.78 (m, 2H, H-4,6); 3.18(bs, 1H, OH); 3.52 (dd, 1H, J=12.1, 6.0 Hz, H-5); 3.64 (dd, 1H, J=12.1, 10.0 Hz, H-5`); 3.84 (m, 1H, H-2); 4.36 (dd, 1H, J=4.1 Hz, H-3); 4.42 (d, 1H, J=12.3 Hz, OC*H*HPh); 4.64 (d, 1H, J=2.3 Hz, H-1); 4.69 (d, 1H, J=12.3 Hz, OC*H*HPh); 7.20-7.3 (m, 5H, *Ph*). ^{13}C NMR ($CDCl_3$) δ: 9.6 (C-8); 34.3 (C-4); 38.3 (C-6); 56.1 (C-5); 66.0 (C-2); 69.2 (OCH_2Ph); 77.1 (C-3); 98.2 (C-1); 127.7-137.1 (*Ph*); 178.3 (C-7). $[\alpha]_D$ +61° (c=0.5, $CHCl_3$)

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