Regiocontrol in the palladium(II)-catalysed oxycarbonylation of unsaturated polyols

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Dedicated to Professor Lubor Fišera on his 60th birthday

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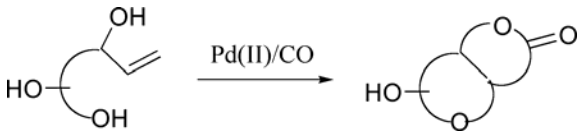
Abstract

The regiocontrol of palladium(II)-catalysed oxycarbonylation of pentenetriols was studied for its potential exploitation in the carbonylation methodology for construction of tetrahydrofuran derivatives with defined stereochemistry. Synthesis of model substrates, the partially protected pentenetriols with diverse protecting groups was carried out starting from D-mannitol. The availability of the protecting group for carbonylation was tested, from the chemo-, regio-, and stereoselectivity point of view. It was found that course as well as stereochemistry of the process may be controlled by β-OH with silyl protected *O*-function in the α-position.

Keywords: Palladium(II)-catalysis, regioselective oxycarbonylation, tetrahydrofurans

Introduction

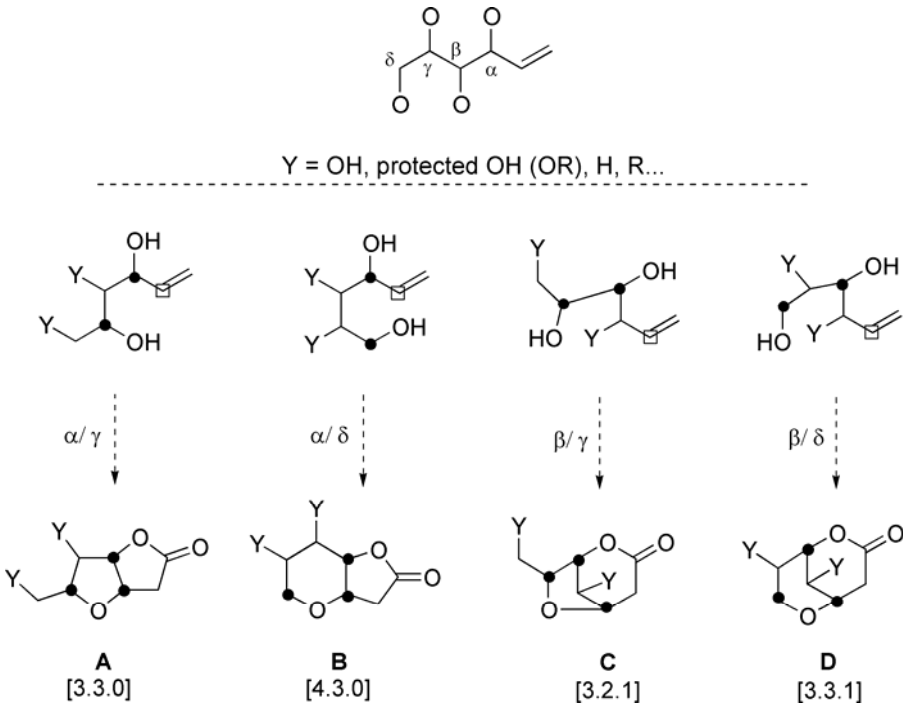
Cyclocarbonylation chemistry is widely used in organic synthesis and represents a useful method for preparation of a variety of cyclic compounds.[1] Transition metals and their complexes functioning as catalysts for carbonylation reactions usually promote the introduction of a carbonyl moiety into an organic molecule. Among the most interesting and synthetically useful carbonylation reactions is the cyclisation of unsaturated alcohols, amines and other suitable substrates accompanied by the insertion of carbon monoxide.[2] These reactions provide a convenient and effective one-step access to lactams and lactones.[3] In this account, we will discuss the regiocontrol in the Pd(II)-catalysed oxycarbonylation of unsaturated polyols (Scheme 1).



Scheme 1. Pd(II)-Catalysed oxycarbonylation of unsaturated polyols.

Results and Discussion

This type of Wacker reaction involves an intramolecular nucleophilic attack of hydroxyl group on C=C double bond coordinated to an electrophilic palladium(II) catalyst and followed by carbon monoxide insertion into the σ–type C-Pd bond in σ-alkylpalladium(II) intermediate.[4] In substrates with several free hydroxyl groups, each one can participate in both important steps of the process (Pd(II)-OH coordination, O-cyclization) and thus offer more possible courses of bicyclisation leading to various bicyclic products (**A**-**D**, Scheme 2).



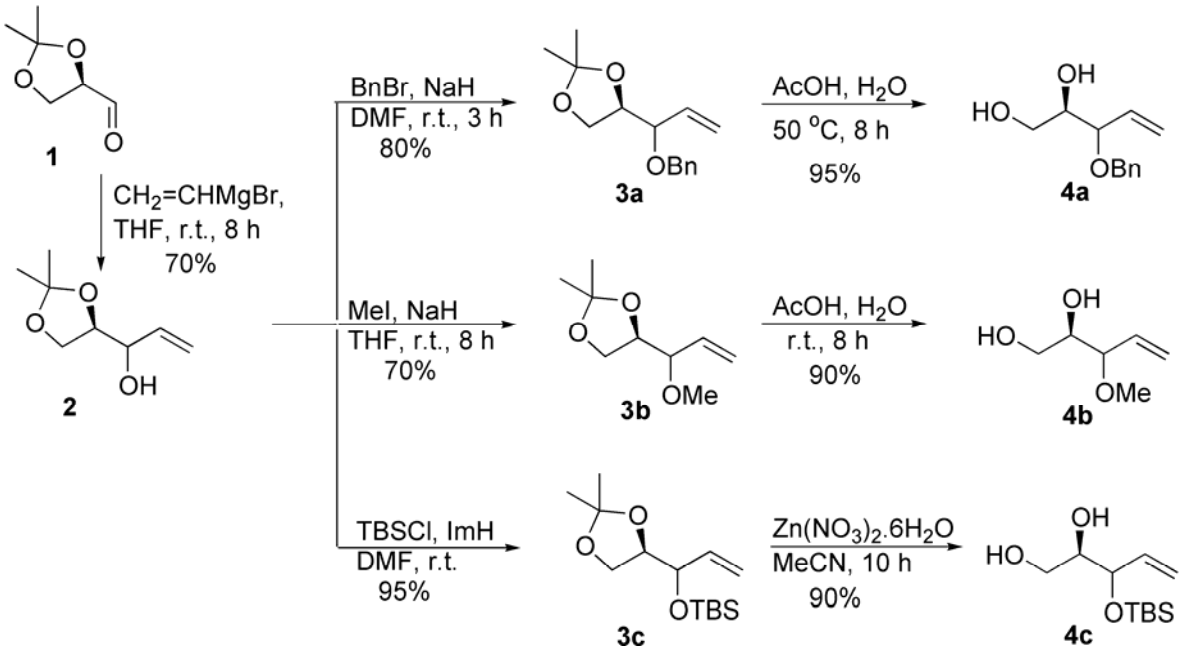
Scheme 2. Carbonylation of alkene polyols. Cyclisation modes.

Our previous work showed that unsaturated polyols (enitols) underwent Pd(II)-catalysed intramolecular oxycarbonylation with high chemo-, regio-, and diastereoselectivity.[4] In reactions starting from a variety of carbohydrate-derived substrates with up to five free OH groups bicycles of the [3.3.0] type (**A**) prevail. With partially protected or missing OH functions, formation of lactones with [4.3.0] (**B**) is preferred. The process is characterised by excellent

threo-selectivity concerning the newly formed stereogenic centre with respect to the configuration at the allylic centre. Thus, the stereochemistry of products (**A**, **B**) is controlled by configuration at α-position with hydroxyl group participating in the σ-acylpalladium(II)-complex. Setting aside of this group from the reaction, by protection, opens the door for the other types of bicyclisation (products **C**, **D**) with stereocontrol by OH in β-position.

With regard to our long-standing interest in application of Pd(II)-carbonylation in the total synthesis of natural products,[5] it seemed promising to explore regio-, and stereocontrol of this transformation. The present paper reports on regiocontrolled oxycarbonylation of partially protected pentenetriols.

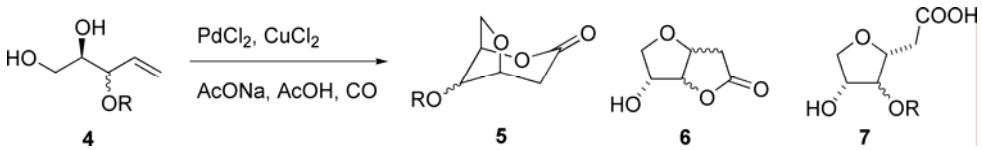
The first, easily accessible pentenetriols were chosen as model substrates for finding the suitable protecting group. Diastereomeric mixtures of 3-*O*-protected pent-4-ene-1,2,3-triols **4a**[8]**-c** with *erythro*- and *threo*-configuration were prepared from D-mannitol adopting known routes[6,7] to the olefinic intermediates **3a**[8]**-c**, see Scheme 3. Hydrolysis in these cases was effected either with aqueous acetic acid, to afford the triols **4a,b**, or with $Zn(NO_3)_2$ hydrate in acetonitrile[9] to give silylated triol **4c**, respectively.



Scheme 3. Synthetic sequence towards α-*O*-protected triols **4a**-**c**.

Model substrates **4a-c** with α-*O*-protected hydroxyl were exposed to the conditions of Pd(II)-catalysed oxycarbonylation. The reaction was carried out under standard conditions[3-5] with palladium(II)-chloride as catalyst (0.1 equiv) copper (II)-chloride as oxidant (3 equiv), sodium acetate (3 equiv) in acetic acid as buffer under carbon monoxide atmosphere (balloon) at room temperature. The results are summarised in Table 1.

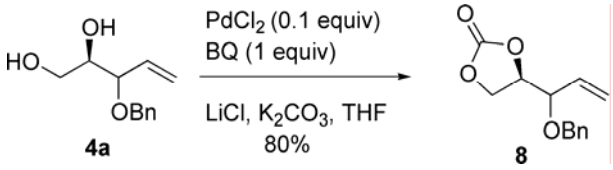
Table 1. Pd(II)-Catalysed oxycarbonylation of 3-*O*-R-pent-4-ene-1,2,3-triols **4**



4 5 6 7

Entry	Triol	R	Configuration	Yield (%)		
				5	**6**	**7**
1	**4a**	Bn	*erythro*/*threo* 1:1	19	22	33
2	*erythro*-**4a**	Bn	*erythro*	17	15	38
3	**4b**	Me	*erythro*/*threo* 1:1	26	0	30
4	**4c**	TBS	*erythro*/*threo* 1:1	80	0	0

Carbonylation of benzylated triol **4a** (Table 1: entries 1 and 2) led to formation of the desired bicyclic [3.2.1]lactone **5a** (product of β/γ-bicyclisation,) along with two side-products, lactone of the [3.3.0]-type **6** and the tetrahydrofuran derivative **7**. Lactone **6** possibly arises by α/γ-bicyclisation (product **A**, Scheme 2), which is the dominating process with unprotected polyols[4] after preliminary debenzylation of **4a** under the above reaction conditions. In order to suppress the assumed follow-up hydrolysis of six membered lactone ring in **5** leading to the acid **7**, the reaction was carried out with exclusion of water in dry THF using benzoquinone as reoxidant (Scheme 4). The transformation proceeded with low conversion of the educt and gave only the unexpected carbonate **8** in poor yield (25%). A simple addition of stronger base (K_2CO_3) increased the conversion of **4a** to carbonate **8**, which now proceeded in 80% yield. To the best of our knowledge, only one precedence have been reported for Pd(II)-catalysed carbonylation of the 1-phenylethane-1,2-diol in the literature[10] yet; we expect it to be a highly interesting alternative for protection of vicinal diols.



4a **8**

Scheme 4. Pd-Catalysed carbonylation of **4a**.

The benzyl protecting group having failed, *O*-methyl protection was tested (Table 1: entry 3). However, although the methyl group was stable for deprotection, another side product **7b** was observed. This was most probably due to competitive coordination of alkylated *O*-function in α-position in σ-acylpalladium(II)-complex **E**, which is an intermediate of the acid **7** (Figure 1). The σ-acyl intermediate **F** with γ-hydroxyl coordination led to the required product of bicyclisation **5** by reductive elimination of Pd(0).

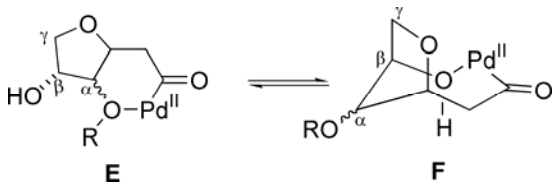


Figure 1. σ-Acylpalladium(II)-intermediates **E** and **F**.

The best result was achieved with *tert*-butyldimethylsilyloxy group in α-position, a group known for its unwillingness to coordinate with transition metals. In the fact, the carbonylation of the silylated triol **4c** worked well to afford the desired diastereomeric mixture of lactone **5c** as the sole product in good yield (80%, Table 1: entry 4), i.e. product of β/γ-bicyclisation. The structure of lactones **5a**,**b** was established by comparison of NMR data of the pure diastereomers of D-*arabino*-**5a**, D-*lyxo*-**5a** with the literature data of 3,6-anhydro-2-deoxy-L-*arabino*- and/or L-*lyxo*-1,5-hexonolactones.[4] The final confirmation of the absolute stereochemistry came from the single X-ray analysis of D-*arabino*-**5a**[11] (Figure 2) and D-*arabino*-**5b**[12] (Figure 3).

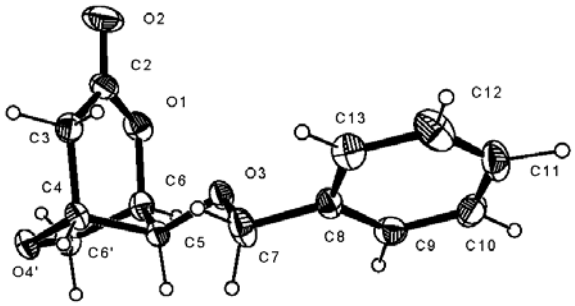


Figure 2. *ORTEP* of D-*arabino*-**5a**.

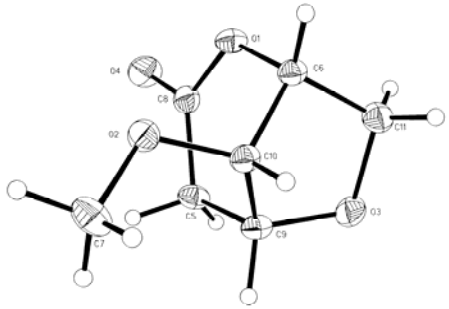
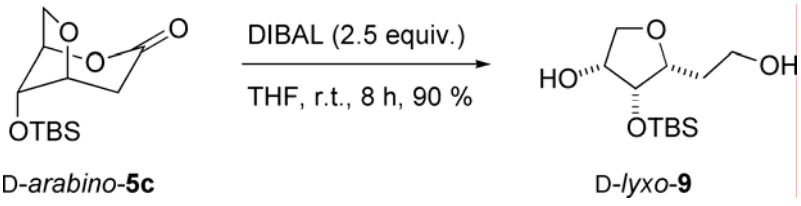


Figure 3. *ORTEP* of D-*arabino*-**5b**.

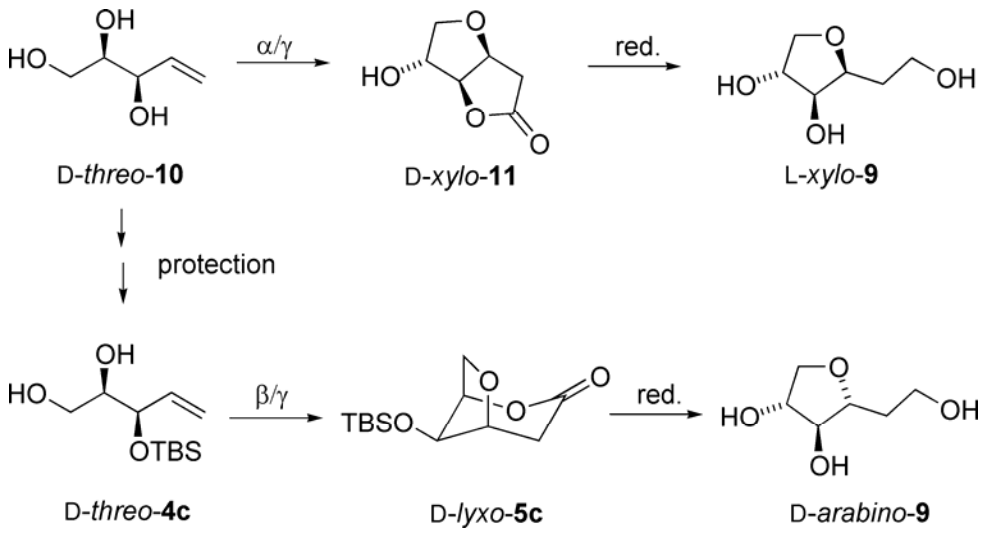
The configurations of the silylated lactones **5c** were assigned using DQ-COSY experiment showing the W-interaction of H-2A and H-4 protons (J=0.8 Hz) in D-*arabino*-**5c**, which confirmed the *cis* relationship of the newly formed stereogenic centre with respect to the β-OH group in Pd(II)-β/γ-bicyclisation. To test the methodology for the construction of tetrahydrofuran ring D-*arabino*-**5c** was reduced with DIBAL in THF to furnish very clearly an all *cis* trisubstituted tetrahydrofuran D-*lyxo*-**9** in good yield (Scheme 5).



Scheme 5. Reduction of D-*arabino*-**5c**.

Conclusions

In conclusion, the present study shows that the course of bicyclisation in palladium(II)-catalysed oxycarbonylation of unsaturated polyols can be controlled by protection of *O*-function, preferably with silyl protecting group. The α-*O*-silyl protected enitol provides a single regioisomer - bicyclic lactone of the [3.2.1] type, product of β/γ-bicyclisation (**C**, Scheme 2). The stereochemistry of the product is controlled by hydroxyl in β-position with *cis* arrangement according to newly formed stereogenic centre. The regiocontrol of Pd(II)-bicyclisation enhances the significance of carbonylation methodology for construction of tetrahydrofurans with defined stereochemistry. Thus, starting from D-*threo*-pentenetriol **10** with free OH groups, *via* D-*xylo* bicyclic lactone of [3.3.0] type (**11**, α/γ-transformation, Scheme 6), the tetrahydrofuran **9** of L-*xylo* configuration is produced;[4] starting from α-*O*-protected D-*threo*-pentenetriol **4c**, *via* bicycle D-*lyxo*-**5c** (product of β/γ-transformation), D-*arabino*-**9** diastereomer is expected; D-*erythro* triol convert to L-*lyxo*[4] and L-*arabino,* respectively etc.



Scheme 6. α/γ- *vs.* β/γ-Pd(II)-Catalysed oxycarbonylation of D-*threo*-pentenetriols **4c**, **10**.

Experimental Section

General Procedures. Commercial reagents were used without further purification. All solvents were distilled before use. Hexanes refer to the fraction boiling at 60-65°C. Flash column liquid chromatography (FLC) was performed on silica gel Kieselgel 60 (40-63 μm, 230-400 mesh) and analytical thin-layer chromatography (TLC) was performed on aluminium plates pre-coated with either 0.2 mm (DC-Alufolien, Merck) or 0.25 mm silica gel 60 F_{254} (ALUGRAM® SIL G/UV_{254}, Macherey-Nagel). The compounds were visualised by UV fluorescence and by dipping the plates in an aqueous H_2SO_4 solution of cerium sulphate/ammonium molybdate followed by charring

with a heat-gun. Melting points were obtained using the Boecius apparatus and are uncorrected. Optical rotations were measured with the POLAR L-μP polarimeter (IBZ Messtechnik) with a water-jacketed 10.000 cm cell at the wavelength of sodium line D (λ=589 nm). Specific rotations are given in units of 10^{-1} deg·cm^2·g^{-1} and concentrations are given in g/100 mL. Elemental analyses were run on FISONS EA1108 instrument. Infrared spectra were recorded either on a Philips Analytical PU9800 FTIR spectrometer or a Perkin-Elmer 1750 FTIR spectrophotometer as KBr discs (KBr) or as thin films on KBr plates (film). NMR spectra were recorded on a Varian VXR-300 spectrometer. Chemical shifts (δ) are quoted in ppm and are referenced to the tetramethylsilane (TMS) as internal standard. Compounds are numbered according to carbohydrate naming scheme.

4,5-*O*-Isopropylidene-D-*erythro* and D-*threo*-1-pentenitol (2).[7,8] Varying the described procedure,[7] the freshly distilled 2,3-*O*-isopropylidene-D-glyceraldehyde[6] **1** (1.5g, 11.5 mmol) was dissolved in dry THF (15 mL) and poured to a dry reaction flask kept under Ar, and immersed in water cooling bath (20°C). Vinylmagnesium bromide (14 mL, 14 mmol, 1.2 equiv, 1M in THF) was added dropwise during 25 min. The reaction mixture was stirred for additional 3 h, quenched with sat. NH_4Cl (20 mL), and extracted with AcOEt. Organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. Analytically pure product **2** as the mixture of diastereomers (*erythro*/*threo*, 52:48 by ^{13}C NMR) was obtained by FLC (8% AcOEt in hexanes) as colourless aromatic oil (1.25g, 70%). Anal. calcd. for $C_8H_{14}O_3$ (158.19): C 60.74, H 8.92; found: C 65.81, H 8.79. Spectral data were in full accordance with lit.[8]

4,5-*O*-Isopropylidene-3-*O*-benzyl-D-*erythro* and D-*threo*-1-pentenitol (3a).[8] Under Ar atmosphere, NaH (358 mg, 1.2 equiv, 60% dispersion in mineral oil) was washed with hexane (2x10 mL) and ether (10 mL). Dry DMF (5 mL) was added, and the flask was cooled to -20°C. The mixture of pentenitols **2** (1.18 g, 74.7 mmol) in DMF (10 mL) was added dropwise within 5 min, and the mixture stirred for additional 30 min. Benzyl bromide (1.532 g, 1.05 mL, 1.2 equiv) was added in several portions in order to keep the temperature below 10°C. After 3 h of stirring the excess of hydride was decomposed with MeOH (10 mL) and some water (25 mL) and Et_2O (25 mL) was added. Organic phase was separated and the water phase extracted with Et_2O. Combined organic extracts were dried over Na_2SO_4 and concentrated. Residual crude oil was purified by flash LC (10% AcOEt in hexanes). Yield 1.5g (80%) colourless oil. The product consisted of a 1:1 *erythro*/*threo* diastereomers **3a** (determined by ^{13}C-NMR). Pure diastereomers were isolated by additional chromatographic separation (50 g of silica gel for 1 g of mixture, 3% AcOEt in hexanes).

D-*erythro*-**3a**: R_f = 0.44 (20% AcOEt in hexanes); $[\alpha]^D_{25}$ = +40 (c 0.18, MeOH) (Lit[8] +30.4 (c 0.68, $CHCl_3$)); spectral data were in full accordance with lit.[8]

D-*threo*-**3a**: R_f = 0.40 (20% AcOEt in hexanes); $[\alpha]^D_{25}$ = -19 (c 0.21, MeOH (Lit[8] -18.7 (c 0.72, $CHCl_3$)); spectral data were in full accord with lit.[8]

4,5-*O*-Isopropylidene-3-*O*-methyl-D-*erythro* and D-*threo*-1-pentenitol (3b). To a suspension of NaH (200 mg, 60% dispersion in mineral oil, 1.5 equiv, washed as above) in THF (5 mL) a

solution of **2** (526 mg, 3.3 mmol) in dry THF (5 mL) was added at 0°C within 5 min, and the mixture was stirred for additional 90 min. Colourless suspension had turned to a clear, pale yellow solution. MeI (0.42 mL, 0.96 g, 1.1 equiv) was added in one portion and the mixture was stirred at r.t. for 100 min. Then Et_2O (15 mL) and water (7 mL) was added, phases were separated and the water phase was extracted several times with Et_2O; collected organic phases were dried over Na_2SO_4 and concentrated. Pale yellow oily residue (411mg, 73%) was used in subsequent reaction without any purification. Title compound **3b** was prepared and characterised as the mixture of diastereomers (1:1). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.35, 1.37, 1.47, 1.48 (all s, 12H, Me), 3.31, 3.34 (all s, 6H, OMe), 3.45-3.70 (m, 2H), 3.83-3.96 (m, 2H), 4.02-4.17 (m, 4H, H-3, H-4, H-5), 5.27-5.40 (m, 4H, $J_{1Z,2}$ = 10.5 Hz, $J_{1E,2}$ = 18.3 Hz, H-1), 5.57-5.81 (m, 2H, $J_{1Z,2}$ = 10.5 Hz, $J_{1E,2}$ = 18.3 Hz, H-2); ^{13}C-NMR ($CDCl_3$, 75 MHz,) δ 25.2, 25.4, 26.4, 26.4 (all q, Me,), 56.5, 56.7 (all q, OMe), 65.9, 66.4 (all t, C-5), 77.4 (d, C-4), 83.5, 84.4 (all d, C-3), 109.5, 109.8 (all s, $\underline{C}HMe_2$), 119.6, 120.2 (all t, C-2), 134.0, 134.8 (all d, C-1).

4,5-*O*-Isopropylidene-3-*O*-*t*-butyldimethylsilyl-D-*erythro* and D-*threo*-1-pentenitol (3c). A mixture of **2** (2.55 g, 16 mmol), *tert*-butyldimethylsilyl chloride (2.677 g, 17.7 mmol), imidazole (3.02 g, 44.4 mmol) in DMF (20 mL) was stirred at r.t. for 10 h. Reaction was quenched with water (20 mL) and extracted with isohexane (6x25 mL). Combined organic extracts were washed with 3% HCl (20 mL), dried over Na_2SO_4 and concentrated. Title compound **3c** was isolated as colourless mobile oil with characteristic odour (4.3 g, 97%, diastereomeric mixture 1:1). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.01, 0.04, 0.05, 0.08 (all s, 12H, TBDMS), 0.89 (s, 18H, TBDMS), 1.33, 1.34, 1.40, 1.41 (all s, 12H, Me), 3.78 (dd, 1H, 1H, $J_{5A,5B}$ = 8.4 Hz, $J_{4,5}$ = 6.3 Hz, H-5), 3.88 (dd, *J* = 3.5 Hz, *J* = 4.4 Hz), 3.90-4.00 (m, 4H), 4.03 (dd, 1H, *J* = 5.8 Hz, *J* = 6.4 Hz), 4.12 (dddd, 1H, *J* = 6.2 Hz, *J* = 5.3 Hz, *J* = *J* = 1.3 Hz), 4.23 (dddd, 1H, *J* = *J* = 5.4 Hz, *J* = *J* = 1.5 Hz, H-3, H-4, H-5), 5.18 (ddd, 1H, $J_{1Z,2}$ = 10.3 Hz, $J_{1E,1Z}$ = 1.9 Hz, $J_{1,3}$ = 1.2 Hz, H-1Z), 5.19 (ddd, 1H, $J_{1Z,2}$ = 10.8 Hz, $J_{1E,1Z}$ = 1.9 Hz, $J_{1,3}$ = 1.2 Hz, H-1Z), 5.28 (ddd, 1H, $J_{1E,2}$ = 17.1 Hz, $J_{1E,1Z}$ = 1.9 Hz, $J_{1,3}$ = 1.2 Hz, H-1E), 5.31 (ddd, 1H, $J_{1E,2}$ = 17.1 Hz, $J_{1E,1Z}$ = 1.9 Hz, $J_{1,3}$ = 1.2 Hz, H-1E), 5.85 (m, 2H, $J_{1E,2}$ = 17.1 Hz, $J_{1Z,2}$ = 10.5 Hz, $J_{2,3}$ = 7.2 Hz, H-2); ^{13}C-NMR ($CDCl_3$, 75MHz) δ -4.9, -4.8, -4.7, -4.2 (all q, TBDMS), 25.2, 25.5, 25.7, 25.8, 26.4, 26.7 (all q, Me, TBDMS), 65.3, 66.1 (all t, C-5), 74.0, 74.2 (all d, C-3), 78.6, 79.0 (all d, C-4), 109.4 (s, $\underline{C}HMe_2$), 116.4, 116.5 (all t, C-1), 136.5, 138.3 (all d, C-2).

3-*O*-Benzyl-D-*erythro* and D-*threo*-1-pentenitol (4a). Alkenitol **3a** (580 mg, 2.3 mmol) was dissolved in 60% AcOH (10mL) and left to stay overnight. Solvents were removed *in vacuo* and the oily residue (480 mg, 99%) was used for subsequent reaction in the state of isolation. The compound mixture can be void of eventual minorities by FLC purification (30% AcOEt in hexanes).

D-*erythro*-**4a**: $[\alpha]^D_{25}$ = +37 (c 0.23, MeOH) (Lit[8] +44.6 (c 0.81, $CHCl_3$)); spectral data were in full accordance with lit.[8]; Anal. calcd. for $C_{12}H_{16}O_3$ (208.25): C 69.21, H 7.74; found: C 68.81, H 7.99.

D-*threo*-**4a**: physical data were in full accordance with lit.[8]

3-*O*-Methyl-D-*erythro* and D-*threo*-1-pentenitol (4b). Diastereomeric mixture of acetonides **3b** (600 mg, 3.5 mmol) was dissolved in 60% AcOH (10 mL) and left at r.t. for 10 h. The solvents were removed *in vacuo* and the crude product was purified by FLC (50% AcOEt in hexanes); yield 415 mg (90%); colourless viscose oil. During FLC separation the ratio of isomers had changed from original 50:50 to 60:40. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.94 (bs, 4H, OH), 3.32, 3.33 (all s, 6H, OMe), 3.40-3.80 (m, 8H, H-3, H-4, H-5), 5.30-5.44 (m, 4H, H-1E, H-1Z), 5.62-5.84 (m, 2H, H-2); ^{13}C-NMR ($CDCl_3$, 75 MHz); *major diastereomer*: δ 56.8 (q, OMe), 63.2 (t, C-5), 73.2 (d, C-3), 84.6 (d, C-4), 120.0 (t, C-1), 134.7 (d, C-2); *minor diastereomer*: 56.5 (q, OMe), 62.0 (t, C-5), 73.9 (d, C-3), 83.8 (d, C-4), 120.5 (t, C-1), 134.4 (d, C-2).

3-*O*-*t*-Butyldimethylsilyl-D-*erythro* and D-*threo*-1-pentenitol (4c). According to procedure described by Vijayasarandhi *et al.* (lit. [9]), a mixture of **3c** (4.3 g, 15.8 mmol) and $Zn(NO_3)_2.6H_2O$ (23.4 g, 79 mmol) in acetonitrile (10 mL) was stirred at r.t. for 15 h, then diluted with water (50 mL), and extracted with AcOEt. The extracts were dried over Na_2SO_4 and concentrated. Resulting colourless oil (2.88 g, 78%) was satisfactory pure for the consecutive reaction. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 6H, TBDMS), 0.08, 0.09 (all s, 6H, TBDMS), 0.89 (s, 18H, TBDMS), 2.43 (bs, 4H, OH), 3.48-3.59 (m, 3H), 3.62-3.77 (m, 3H, H-5, H-4), 4.14 (dd, $J_{3,4}$ = 5.9 Hz, $J_{2,3}$ = 6.8 Hz, H-3), 4.23 (dd, $J_{3,4}$ = 4.7Hz, $J_{2,3}$ = 6.0 Hz, H-3), 5.20 (d, 1H, $J_{1Z,2}$ = 10.3 Hz, H-1Z), 5.22 (d, 1H, $J_{1Z,2}$ = 10.7Hz, H-1Z), 5.27 (d, 2H, $J_{1E,2}$ = 17.1 Hz, H-1E), 5.75-5.89 (m, 2H, $J_{2,3}$ = 6.8Hz, $J_{1Z,2}$ = 10.5 Hz, $J_{1E,2}$ = 17.1 Hz, H-2); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ -5.0, -4.9, -4.5, -4.1 (all q, TBDMS), 18.1 (s, TBDMS), 25.8 (q, TBDMS), 63.0 (all t, C-5), 73.8 (d, C-3), 74.6 (d, C-3, C-4), 76.4 (d, C-4), 117.0, 117.3 (all t, C-1), 137.5, 137.6 (all d, C-2).

General procedure for oxycarbonylation of pentenitols 4. A 25 mL-flask with stopcock equipped side inlet was charged with $PdCl_2$ (0.1 equiv), $CuCl_2$ (3 equiv) and AcONa (3 equiv). Alkenol **3** in AcOH (5 mL) was added and the flask was purged with CO from balloon (residual air was removed through side inlet with water aspirator). The mixture was vigorously stirred at r.t. until colour of the mixture changed from green to pale brown (approx. 21 h). Inorganic material was removed on Cellite® pad and the filtrate was concentrated *in vacuo*. Crude product mixture was separated on silica gel column (35% AcOEt in hexanes).

3,6-Anhydro-4-*O*-benzyl-2-deoxy-D-*arabino* and D-*lyxo*-1,5-hexonolactone (5a). The typical procedure was followed: pentenitol **4a** (133 mg, 0.64 mmol), $PdCl_2$ (11 mg, 0.06 mmol), $CuCl_2$ (253 mg, 1.92 mmol), AcONa (157 mg, 1.92 mmol).

Hexonolactones **5a**: yield 28 mg (19%); colourless oil (1:1 mixture of diastereomers, D-*arabino*-**5a** can eventually crystallise);

D-*arabino*-**5a**: a single diastereomer for X-ray analysis was obtained by recrystallisation from ethylacetate-hexane; m.p. 92-93°C; $[\alpha]_D^{20}$ = -49 (c 0.15, $CHCl_3$); R_f = 0.57 (50% AcOEt in hexanes); IR (film, cm^{-1}) 2932, 2887, 1784, 1745, 1454, 1372, 1365, 1344, 1313, 1290, 1203, 1157, 1078, 1012, 937, 742, 700; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.65 (dd, 1H, $J_{2A,2B}$ = 18.4 Hz, $J_{2A,3}$ = 2.1 Hz, H-2A), 2.90 (dd, 1H, $J_{2A,2B}$ = 18.4 Hz, $J_{2B,3}$ = 2.7 Hz, H-2B), 4.13 (s, 1H, H-5), 4.22 (s, 2H, H-6), 4.46 (bs, 1H, H-4), 4.64, 4.71 (all d, 2H, J_{AB} = 11.5 Hz, Bn), 4.76 (bs, 1H, H-

3), 7.32-7.43 (m, 5H, Bn); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 39.1 (t, C-2), 71.6 (t, Bn), 72.7 (t, C-6), 73.7 (d, C-3), 78.9, 79.1 (all d, C-4, C-5), 127.9, 128.4, 128.7 (all d, Bn), 136.5 (s, Bn), 168.9 (s, C-1). Anal. calcd. for $C_{13}H_{14}O_4$ (234.25): C 66.66, H 6.02; found: C 66.31, H 6.19.

D-*lyxo*-**5a**: R_f = 0.53 (50% AcOEt in hexanes); IR (film, cm^{-1}) 2926, 2880, 1745, 1454, 1371, 1068, 1026, 986; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.70 (dd, 1H, $J_{2A,2B}$ = 18.4 Hz, $J_{2A,3}$ = 1.7 Hz, H-2A), 2.91 (dd, 1H, $J_{2A,2B}$ = 18.4 Hz, $J_{2B,3}$ = 3.0 Hz, H-2B), 4.08 (dd, 1H, $J_{6A,6B}$ = 11.1 Hz, $J_{5,6A}$ = 3.0 Hz, H-6A), 4.16 (dd, 1H, $J_{5,6A}$ = 3.0 Hz, $J_{4,5}$ = 5.6 Hz, H-5), 4.23 (d, 1H, $J_{6A,6B}$ = 11.1 Hz, H-6B), 4.32 (m, 1H, H-4), 4.61, 4.76 (all d, 1H, J_{AB} = 11.5 Hz, Bn), 4.81 (ddd, 1H, $J_{2A,3}$ = 1.7 Hz, $J_{2B,3}$ = $J_{3,4}$ = 3.0 Hz, H-3), 7.32-7.41 (m, 5H, Bn); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 36.4 (t, C-3), 71.4 (d, C-3), 72.4 (t, C-6, Bn), 75.0 (d, C-5), 76.0 (d, C-4), 127.7, 128.3, 128.7 (all d, Bn), 136.7 (s, Bn), 167.9 (s, C-1).

3,6-Anhydro-4-*O*-benzyl-2-deoxy-D-*arabino*- and D-*xylo*-1,4-hexonolactone (6a). yield 20mg (22%, diastereomeric mixture, 1:1) white crystals, captured physical data were in full agreement with the published ones for L-enantiomers.[4]

(3-Benzyloxy-4-hydroxy-tetrahydrofuran-2-yl)-acetic acid (7a). yield 50 mg (33%, an intricate mixture of three acids), pale brown oil. Chemical structure of acid's mixture was proven as follows: the mixture of acids **7a** (55mg, 0.22 mmol) and *p*-toluenesulphonic acid (10 mg) was dissolved in toluene (15 mL), the flask was covered with small Dean-Stark receiver and the solution was refluxed for 30 h. The colourless oil (15 mg, 29%) obtained after concentration and purification on silica gel column (25% AcOEt in hexanes) was identified by NMR as the mixture of lactones **4a** in companion with unreacted acids (13 mg).

3,6-Anhydro-2-deoxy-4-*O*-methyl-D-*arabino*-1,5-hexonolactone (D-*arabino*-5b). Triol **4b** (132 mg, 1 mmol) was converted according the general procedure to give a complex mixture of compounds with close R_f, therefore only one of the lactone products, D-*arabino* isomer **5b** was isolated. Yield 36 mg (23%), colourless crystals recrystallised from ethylacetate-hexane, m.p. 94-96°C, $[\alpha]_D^{25}$ = -79 (c 0.27, $CHCl_3$); R_f = 0.45 (50% AcOEt in hexanes). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.7 (dd, 1H, $J_{2A,3}$ = 1.8 Hz, $J_{2A,2B}$ = 18.6 Hz, H-2A), 2.86 (dd, 1H, $J_{2B,3}$ = 3.0 Hz, $J_{2A,2B}$ = 18.6 Hz, H-2B), 3.51 (s, 3H, Me), 4.02 (dd, 1H, $J_{4,5}$ = 3.0 Hz, $J_{3,4}$ = 5.4Hz, H-4), 4.12 (dd, 1H, $J_{5,6A}$ = 2.7 Hz, $J_{6A,6B}$ = 10.8 Hz, H-6A), 4.25 (d, 1H, $J_{6A,6B}$ = 11.0 Hz, H-6B), 4.36 (ddd, 1H, $J_{2A,3}$ = 2.0 Hz, $J_{2B,3}$ = 3.0 Hz, $J_{3,4}$ = 5.4 Hz, H-3), 4.87 (dd, 1H, $J_{4,5}$ = $J_{5,6A}$ = 3.0 Hz, H-5); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 36.4 (t, C-2), 57.8 (q, OMe), 71.3 (d, C-3), 72.5 (t, C-6), 75.7, 77.3 (all d, C-4, C-5), 168.9 (s, C-1). Anal. calcd. for $C_7H_{10}O_4$ (158.15): C 53.16, H 6.37; found: C 53.31, H 6.29.

3,6-Anhydro-2-deoxy-4-*O*-t-butydimethylsilyl-D-*arabino*- and D-*lyxo*-1,5-hexonolactone (5c). In accord with the typical procedure pentenitol **4c** (200 mg, 0.77 mmol) was converted to give **5c** by stirring at r.t. for 50 h. Chromatography separation of the crude mixture afforded colourless oil fraction, identified as pure D-*arabino*-**5c** (47 mg, 23%), intermediate fraction (70 mg, 36%, ~ 1:1 mixture of D-*arabino*-**5c**/D-*lyxo*-**5c**) and a fraction, identified as a mixture of D-*arabino*-**5c**/D-*lyxo*-**5c** in 1:3 ratio (44 mg, 21%).

D-*arabino*-**5c**: R_f = 0.76 (50% AcOEt in hexanes); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.13 (s, 6H, TBDMS), 0.89 (s, 9H, TBDMS), 2.65 (dd, 1H, $J_{2A,3}$ = 2.6 Hz, $J_{2A,2B}$ = 18.4 Hz, H-2A), 2.86 (dd, 1H, $J_{2B,3}$ = 3.0 Hz, $J_{2A,2B}$ = 18.4 Hz, H-2B), 4.18 (d, 2H, $J_{5,6}$ = 1.5 Hz, H-6), 4.19 (ddd, 1H, $J_{3,5}$ = $J_{5,6}$ = 1.5 Hz, $J_{4,5}$ = 1.8 Hz, H-5), 4.30 (d, 1H, $J_{2,4}$ = 0.8 Hz, $J_{4,5}$ = 1.8 Hz, H-4), 4.55 (ddd, 1H, $J_{3,5}$ = 1.5 Hz, $J_{2A,3}$ = $J_{2B,3}$ = 3.0 Hz, H-3); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ -4.9 (q, TBDMS), 17.9 (s, TBDMS), 25.5 (q, TBDMS), 39.1 (t, C-2), 72.5 (t, C-6), 73.8 (d, C-4), 76.5 (d, C-5), 81.0 (d, C-3), 167.8 (s, C-1);

D-*lyxo*-**5c**: R_f = 0.71 (50% AcOEt in hexanes); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ -0.01(s, 6H, TBDMS), 0.9 (s, 9H, TBDMS), 2.71 (dd, 1H, $J_{2A,3}$ = 2.6 Hz, $J_{2A,2B}$ = 18.4 Hz, H-2A), 2.88 (dd, 1H, $J_{2B,3}$ = 2.6 Hz, $J_{2A,2B}$ = 18.4 Hz, H-2B), 4.24 (bd, 2H, $J_{5,6}$ = 4.0 Hz, H-6), 4.34 (m, 1H, H-5), 4.41 (d, 1H, $J_{3,4}$ = 1.8 Hz, H-4), 4.72 (m, 1H, H-3); ^{13}C-NMR ($CDCl_3$, 75 MHz,) δ -4.8 (q, TBDMS), 17.9 (s, TBDMS), 25.7 (q, TBDMS), 38.7 (t, C-2), 72.3 (t, C-6), 73.0 (d, C-4), 76.4 (d, C-5), 80.6 (d, C-3), 168.1 (s, C-1).

3-*O*-benzyl-D-*erythro* and D-*threo*-1-pentenitol-4,5-carbonate (8). A 25 mL-flask with stopcock equipped side inlet was charged with $PdCl_2$ (19 mg, 0.11 mmol, 0.1 equiv), *p*-benzoquinone (118 mg, 2.18 mmol, 2 equiv), LiCl (91 mg, 2.18 mmol, 2 equiv) and K_2CO_3 (677 mg, 4.61 mmol, 4.5 equiv). A mixture of pentenitols **4a** (227 mg, 1.09 mmol) in abs. THF (15 mL) was added and the flask was purged with CO from balloon (residual air was removed through side inlet with water aspirator). The mixture was vigorously stirred at 50°C for 24 h. Inorganic material was removed on Cellite pad and the filtrate was concentrated *in vacuo*. Crude product mixture was separated on silica gel column (22% AcOEt in hexanes) to provide the carbonate **8** (208 mg, 80%) and a small portion of starting alkenol **4a** (10 mg). Requisite diastereomeric mixture of **8** was isolated as colourless viscose oil. R_f = 0.68 (50% AcOEt in hexanes); ^{1}H-NMR ($CDCl_3$, 300MHz) δ 3.95 (dddd, 1H, $J_{3,4}$ = 4.5 Hz, $J_{2,3}$ = 7.7 Hz, $J_{1E,3}$ = $J_{1Z,3}$ = 0.9 Hz, H-3), 4.12 (dddd, 1H, $J_{3,4}$ = 4.3 Hz, $J_{2,3}$ = 6.4 Hz, $J_{1E,3}$ = $J_{1Z,3}$ = 1.0 Hz, H-3), 4.29-4.49 (m, 6H, H-5, H-6), 4.60-4.74 (m, 4H, H-4, Bn), 5.46 (d, 1H, $J_{1Z,2}$ = 10.3 Hz, H-1Z), 5.47 (d, 1H, $J_{1E,2}$ = 17.1 Hz, H-1E), 5.49 (d, 2H, $J_{1E,2}$ = 18.1 Hz, H-1E), 5.50 (d, 1H, $J_{1Z,2}$ = 9.8 Hz, H-1Z), 5.63-5.88 (m, 2H, $J_{2,3}$ = 6.2 Hz, $J_{2,3}$ = 7.6 Hz, $J_{1Z,2}$ = 10.5 Hz, $J_{1E,2}$ = 17.1 Hz, $J_{1E,2}$ = 18.1 Hz, H-2); ^{13}C-NMR ($CDCl_3$, 75MHz) δ 65.2, 65.7 (all t, C-5), 70.4, 71.1 (all t, Bn), 76.8, 76.9 (all d, C-4), 78.4, 78.7 (all d, C-3), 121.3, 122.4 (all t, C-1), 127.8, 128.0, 128.5 (all d, Bn), 131.7, 131.8 (all d, C-2), 137.1, 137.2 (all s, Bn), 154.8, 154.9 (all s, C=O).

1,4-Anhydro-3-*O*-t-butyldimethylsilyl-5-deoxy-D-*lyxo*-hexitol (D-*lyxo*-9). A flame-dried 25mL-flask with side outlet under Ar was charged with solution of D-*arabino*-**5c** (50 mg, 0.2 mmol) in dry THF (5 mL). Diisobutylaluminium hydride (0.5 mL, 0.5 mmol, 2.5 equiv, 1M in THF) was added by syringe under vigorous stirring. The solution was stirred at r.t. for 8 h and quenched by addition of 1M HCl (5 mL). The water phase was separated, and extracted with AcOEt (3x10 mL). The extracts were washed with sat. NaCl, dried over Na_2SO_4 and concentrated. Flash chromatography of the crude oil (33% AcOEt in hexanes) afforded requisite hexenitol D-*lyxo*-**9** as colourless oil (45 mg, 86%). R_f = 0.25 (50% AcOEt in hexanes); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.09, 0.11 (all s, 6H, TBDMS), 0.89 (s, 9H, TBDMS), 1.92 (ddd, 2H, $J_{5,6A}$

= $J_{5,6B}$= $J_{4,5}$ = 5.0 Hz, H-5), 2.36 (bs, 2H, OH), 3.76-3.87 (m, 4H, H-2, H-3, H-6), 3.93 (dd, 2H, $J_{1A,1B}$ = 10.0 Hz, $J_{1,2}$ = 3.6 Hz, H-1), 4.06 (m, 1H, H-4); ^{13}C-NMR ($CDCl_3$, 75 MHz,) δ 25.7 (s, TBDMS), 34.9 (t, C-5), 60.9 (t, C-6), 73.9 (t, C-1), 78.9, 82.9, 86.0 (all d, C-2, C-3, C-4), 214.0, 214.2 (s and q, mirrored TBDMS signals).

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