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Note

Convenient conversion of wheat hemicelluloses pentoses (D-xylose and L-arabinose) into a common intermediate

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Abstract—The transformation of D-xylose and L-arabinose, the two major components of wheat straw and bran, into a unique multifunctional, optically pure, five-carbon synthon has been achieved. The synthetic sequence requires three steps: suitable protection of the hydroxyl groups of the pentoses, introduction of an iodide at the C-5 position and zinc-mediated opening of the furanose ring leading to the formation of a common substituted pent-4-enal.

Keywords: Hemicelluloses; Pentoses; D-Xylose; L-Arabinose; Iodination; Bernet–Vasella reaction

Hemicelluloses are the second most abundant plant material after cellulose. These carbohydrate polymers represent a complex group of structurally different polysaccharides that exist in the cell walls closely associated with cellulose. In spite of their abundance, hemicelluloses have not been as effectively utilized as starch or cellulose. Hemicelluloses from wheat straw and bran represent about 25% of the dry matter and are mainly composed of two pentoses: D-xylose, the major one, and L-arabinose. As a part of a research programme devoted to the valorization of hemicelluloses, from fractionation to fine chemistry, we were interested in the chemical transformation of these two pentoses to higher added-value products.

D-Xylose and L-arabinose are carbohydrates diastereoisomers at C-4. The approach targets the removal of the chirality on C-4 position to afford a common optically pure synthon susceptible of various applications in organic chemistry. Ideally, such a transformation could be applied directly to a mixture of the two pentoses. The chosen method was the zinc-mediated ring opening of halogenated carbohydrates at the primary position introduced by Bernet and Vasella.[1] From 5-iodo-D-xylofuranosides and L-arabinofuranosides with different protecting groups at C-2 and C-3 positions, this reaction should lead, as previously observed for various halogenated pentofuranosides,[2–6] to the same γ,δ-unsaturated aldehyde whatever the starting pentose (Chart 1).

In this paper, we report the chemical transformations of the two pentoses into the suitably protected 5-deoxy-5-iodo carbohydrates from D-xylose and L-arabinose separately and, as a model, from an equimolar mixture, and their conversion into the corresponding pent-4-enal derivatives via a Vasella-type reaction.

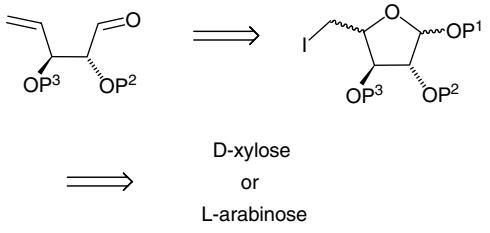

Chart 1. Retrosynthetic scheme for the formation of the common intermediate.

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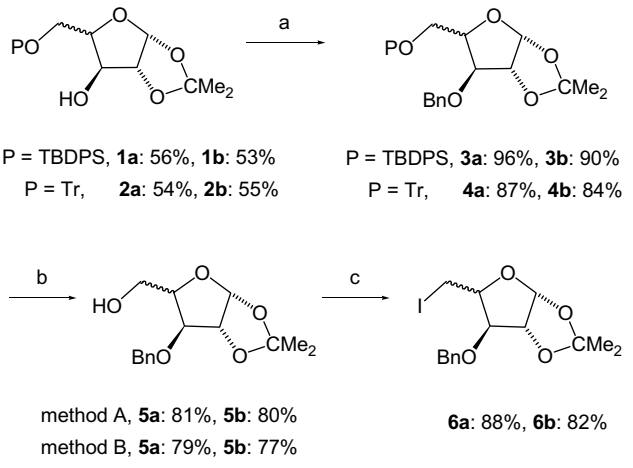
Our approach requires the formation of a similar intermediate from D-xylose and L-arabinose. Moreover, introduction of different protecting groups on the hydroxyl groups at C-2 and C-3 could allow further selective reactions on these two positions. We chose to carry out the following reaction sequence: selective protection of the primary hydroxyl groups by a bulky group to obtain pentofuranose derivatives and formation of the acetal in the 1,2-position in a second step.

Starting from the known compounds **1a**–**2a**[7] and **1b**[8]–**2b**,[9] the remaining free hydroxyl group was then benzylated, using classical conditions,[10] to afford the fully protected pentofuranoses **3a**–**4a**[7] with 87–96% yields in the D-*xylo* series and **3b**[11]–**4b** with 84–90% yields in the L-*arabino* series (Scheme 1). For this benzylation step, D-*xylo* derivatives proved to react faster than the L-*arabino* ones, as observed for the selective protection of the primary hydroxyl group. Deprotection of the silylated ethers was classically achieved using an excess of trihydrated *n*-Bu_4NF in THF while deprotection of the triphenylmethyl ethers was performed in mild acidic conditions (60% aqueous HOAc) at 50 °C. Finally, iodination of compounds **5a**[7] and **5b**[11] was easily carried out[12] giving the target 5-iodo compounds **6a**[13] and **6b** with 82–88% yields (Scheme 1).

Overall yields for these five-step reaction sequence were 38% (Method A) and 32% (Method B) for D-xylose and 31% (Method A) and 29% (Method B) for L-arabinose.

The feasibility of our concept was checked by applying this procedure to a mixture of pentoses. From an equimolar mixture of D-xylose and L-arabinose considered as a model, the mixture of the iodo epimers **6a** and **6b** was obtained with a 28% overall yield (5 steps) via the 5-*O*-silyl protected derivatives. According to the lower reactivity of the L-arabino derivatives, a 65/35 ratio was obtained for **6a** (D-xylose)/**6b** (L-arabinose) as determined by ^1H NMR.



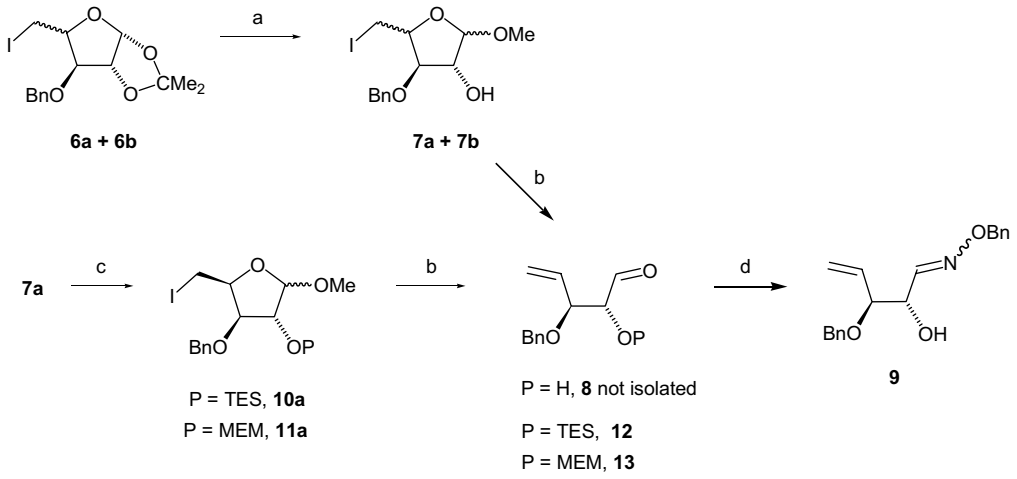
Scheme 1. Reagents and conditions: (a) NaH, 10% TBAI, BnBr, THF; (b) method A: TBAF·$3H_2O$, THF, rt; method B: HOAc–H_2O 3:2, 50 °C, 6 d; (c) I_2, PPh_3, imidazole, toluene, 70 °C.

As carefully detailed by Fürstner, the zinc-induced ring-opening reactions of 6-deoxy-6-halopyranose or 5-deoxy-5-halofuranose derivatives with metal–graphite reagents depends on various parameters such as steric and configurational effects.[14] For 5-deoxy-5-iodopentofuranoses, the reaction rate as well as the structure of the product formed strongly depends on the configuration (D-*xylo* vs D-*ribo*) and substitution pattern of the parent sugar.

In a recent paper, we reported that reaction of the D-*xylose* derived compound **6a** with activated zinc[3–5] was unsuccessful whatever the reaction conditions.[15] Compound **6a** proved to be inert; even the simple reduction of the carbon–iodine bond, which was previously observed using the Zn/Ag–graphite complex,[14] did not occur. Surprisingly, the same reaction carried out on the epimeric L-*arabinose* derivative **6b** with activated zinc under sonication at 40 °C in a 4:1 THF–water mixture afforded the target pent-4-enal. The difference in the reactivity of these two iodo pentofuranoses in the reductive elimination reaction with activated zinc was studied in full details.[15]

Therefore, the mixture of the 1,2-*O*-isopropylidene derivatives **6a**,**b** was transformed in a mixture of the methyl D-xylofuranosides and methyl L-arabinofuranosides **7a**,**b** (α/β 40:60) by acidic methanolysis. The reductive elimination being compatible with unprotected hydroxyl group, the reaction was performed from this mixture to afford the unique pent-4-enal **8** isolated as its oxime ether **9** (4:1 isomeric mixture) with a 88% overall yield (Scheme 2). The remaining free hydroxyl group of the iodo D-*xylo* derivative **7a** (prepared separately) was protected either by a triethylsilyl group (TES) or a methoxyethoxymethyl group (MEM) to give the corresponding pentofuranosides **10a** and **11a** with 61% and 72% yield, respectively. Finally, reaction of these two compounds with zinc in the above described conditions resulted in the formation of the expected γ-enals **12** and **13**, which were purified and isolated with 91% and 78% yield, respectively (Scheme 2). These reactions were monitored by ESIMS, no product resulting from a reduction of the carbon–iodine bond was detected and the two anomers exhibited a similar reactivity.

In conclusion, a five-step reaction sequence has been achieved for the transformation of the two major components of wheat hemicelluloses, D-xylose and L-arabinose into a unique enantiopure five-carbon synthon. The synthesized substituted pent-4-enals represent versatile polyfunctionalized building-blocks with two well-defined stereogenic centres bearing differentiated hydroxyl groups. The transformation of these synthons to higher added-value compounds is currently under investigation and will be reported in due course.



Scheme 2. Reagents and conditions: (a) MeOH, AcCl cat., 100%; (b) activated Zn (10 equiv), THF–H_2O 4:1, 40 °C,))), **12**: 91%, **13**: 78%; (c) TES-Cl or MEM-Cl, pyridine, rt, **10a**: 61%, **11a**: 72%; (d) $BnONH_2$·HCl, 4 Å mol. sieves, anhyd THF, **9**: 88% (2 steps).

1. Experimental

1.1. General methods

All air- and moisture-sensitive reactions were carried out under an argon atmosphere. Tetrahydrofuran (THF) was distilled over Na/benzophenone before use. Optical rotations were recorded using a Perkin–Elmer 241 polarimeter with a thermally jacketed 10 cm cell in the specified solvents. Elementary analyses were taken on a Perkin–Elmer CHN 2400 elementary analysis instrument. Low-resolution mass spectra (ESIMS) were recorded on a ThermoFinnigan Trace MS spectrometer. High resolution mass spectra (HRESIMS) were performed on a Q-TOF Micro micromass positive ESI (CV = +30 V). All reported NMR spectra were recorded with a Bruker AC 250 at 250 MHz (^{1}H) and 62.5 MHz (^{13}C) in $CDCl_3$ as the solvent. Chemical shifts are reported as δ values relative to $CHCl_3$, peak defined at $\delta = 7.27$ ppm (^{1}H NMR) or $\delta = 77.00$ ppm (^{13}C NMR). Analytical thin-layer chromatography was performed using commercially prepared silica gel precoated plates and visualization was effected with short wavelength UV light or by spraying with an alcoholic solution of phosphomolybdic acid followed by heating. Preparative flash silica gel chromatography was performed using E. Merck Kieselgel 60 (40–63 μm).

1.2. General method for the preparation of compounds 3a,b and 4a,b

Compounds **1a**,**b** or **2a**,**b** (0.160 g, 0.37 mmol) were dissolved in dry THF (2 mL, 5 mL/mmol), and sodium hydride (60% in mineral oil, 0.75 mmol, 30 mg), *n*-tetrabutylammonium iodide (0.04 mmol, 15 mg) and benzyl bromide (0.55 mmol, 96 mg, 61 μL) were added. The mixture was stirred under argon, at room temperature. After 12 h for D-*xylo* derivatives and 24 h for L-*arabino* derivatives (1:9 EtOAc–petroleum ether), MeOH was added to the reaction mixture to decompose excess benzyl bromide. The reaction mixture was evaporated under diminished pressure at 40 °C to remove the solvents. The resulting oil was diluted with ethyl acetate, washed with water, dried over Na_2SO_4 and concentrated to dryness. Compounds **3a**,[7]**b**[11] and **4a**,[7]**b** were purified on a silica gel column (1:9 EtOAc–petroleum ether) to give pale yellow oils.

1.2.1. 3-*O*-Benzyl-1,2-*O*-isopropylidene-5-*O*-triphenylmethyl-β-L-arabinofuranose (4b). (0.122 g, 84%); $[\alpha]_D^{22}$ −55.2 (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.67–7.52 (m, 6H, $H_{arom.}$), 7.41–7.18 (m, 14H, $H_{arom.}$), 5.94 (d, 1H, $J_{1,2}$ 3.7 Hz, 1-H), 4.62–4.45 (m, 4H, 2 × H_{benzyl}, H-2, H-3), 4.12 (br s, 1H, H-4), 3.65–3.48 (m, 2H, H-5a, H-5b), 1.59 (s, 3H, $CH_{3\ isopropylidene}$), 1.49 (s, 3H, $CH_{3\ isopropylidene}$); ^{13}C NMR ($CDCl_3$): δ 143.9, 137.4 and 137.3 ($C_{q.arom.}$), 129.1, 128.9, 128.5, 128.3, 127.9, 127.6, 127.5 and 126.9 ($CH_{arom.}$), 112.2 ($C_{q\ isopropylidene}$), 105.8 (C-1), 87.1 (CPh_3), 84.4 (C-2), 80.5 (C-3), 79.8 (C-4), 72.9 (CH_2Ph), 62.8 (C-5), 27.4 and 26.1 (2 × $CH_{3\ isopropylidene}$); HRESIMS *m*/*z*: [$(M+Na)^+$] calcd for $C_{34}H_{34}O_5Na$, 545.2304; found, 545.2297.

1.3. General method for the preparation of compounds 6a and 6b

To a mixture of compounds **5a**[7] (5.5 g, 19.6 mmol) or **5b**[11] (0.5 g, 1.9 mmol) in toluene (20 mL/ mmol), triphenylphosphine (1.5 equiv) and imidazole (3.5 equiv) were slowly added and, after 10 min, iodine (1.5 equiv) by small portions. The soln was stirred at 70 °C until starting material disappeared (3:7 EtOAc–petroleum ether). The soln was then poured into a satd aq $NaHCO_3$ soln (20 mL/mmol) and stirred during 5 min. The excess

iodine was removed by addition of a satd aq $Na_2S_2O_4$ soln until the organic layer became clear. Then, the organic layer was separated and the aqueous soln was extracted with toluene. Organic layers were dried over Na_2SO_4 and solvents were removed. The triphenylphosphine oxide was crystallized in a 1:9 Et_2O–petroleum ether mixture and filtrated. Solvents were removed and the residue was purified on a silica gel column (3:7 EtOAc–petroleum ether) to give compounds **6a**[13] and **6b**.

1.3.1. 3-*O*-Benzyl-5-deoxy-5-iodo-1,2-*O*-isopropylidene-β-L-arabinofuranose (6b). (pale yellow solid, 0.57 g, 82%); mp 85–86 °C; $[\alpha]_D^{20}$ +13.5 (*c* 0.26, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.30–7.23 (m, 5H, $H_{arom.}$), 5.90 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 4.58 (d, 1H, $J_{A,B}$ 11.7 Hz, H_{benzyl}), 4.58 (d, 1H, $J_{2,1}$ 3.7 Hz, H-2), 4.55 (d, 1H, $J_{A,B}$ 11.7 Hz, H_{benzyl}), 4.30 (br t, 1H, $J_{4,5a} = J_{4,5b}$ 7.5 Hz, H-4), 4.07 (s, 1H, H-3), 3.36–3.30 (m, 2H, H-5a, H-5b), 1.46 (s, 3H, $CH_{3\ isopropylidene}$), 1.24 (s, 3H, $CH_{3\ isopropylidene}$); ^{13}C NMR ($CDCl_3$): δ 137.0 ($C_{q.arom.}$), 128.5, 128.0 and 127.9 ($CH_{arom.}$), 112.7 ($C_{q\ isopropylidene}$), 106.5 (C-1), 85.6 (C-3), 84.6 (C-2), 83.8 (C-4), 71.6 (CH_2Ph), 27.0 and 25.9 ($2\times CH_{3\ isopropylidene}$), 6.2 (C-5); HRESIMS *m/z*: [$(M+Na)^+$] calcd for $C_{15}H_{19}O_4INa$, 413.0226; found, 413.0216; Anal. Calcd for $C_{15}H_{19}O_4I$: C, 46.15; H, 4.87. Found: C, 46.18; H, 4.91.

1.4. General method for the preparation of compounds 7a and 7b

Compound **6a** (1.5 g, 3.85 mmol) or a mixture **6a** + **6b** was dissolved in MeOH (50 mL, 13 mL/mmol). Acetyl chloride (2 mL, 0.028 mmol) was slowly added at 0 °C. The mixture was warmed to room temperature and stirred for 8 h. A saturated aqueous $NaHCO_3$ soln was added until pH 7. The solvents were evaporated and the residue was dissolved in CH_2Cl_2 (100 mL), washed twice with water (2×30 mL) and dried over Na_2SO_4. The solvent was removed to give **7a** or a mixture of **7a** + **7b** without any purification as a yellow oil.

1.4.1. Methyl 3-*O*-benzyl-5-deoxy-5-iodo-α,β-D-xylofuranoside (7a). (1.34 g, 96%, α/β ratio: 42:58 determined by GC); ^1H NMR ($CDCl_3$): δ 7.40–7.20 (m, 5H, $H_{arom.}$), 5.06 (d, 0.4H, $J_{1\alpha,2}$ 4.3 Hz, H-1 α-anomer), 5.05 (br s, 0.6H, H-1 β-anomer), 4.84–4.41 (m, 3H, H-2, $2\times H_{benzyl}$), 4.49 (ddd, 1H, $J_{4,3}$ 2.7, $J_{4,5a}$ 5.9, $J_{4,5b}$ 9.3 Hz, H-4), 4.27 (br s, 1H, H-3), 3.55–3.22 (m, 5H, H-5a, H-5b, OCH_3); ^{13}C NMR ($CDCl_3$): δ 137.9 and 137.8 ($C_{q.arom.}$), 128.9, 128.8, 128.4, 128.3 and 128.2 ($CH_{arom.}$), 113.0 ($C_{q\ isopropylidene}$), 110.1 (C-1β), 102.6 (C-1α), 83.9 and 83.8 (C-3), 82.3 and 79.9 (C-2), 79.5 and 76.7 (C-4), 73.1 and 72.6 (CH_2Ph), 56.5 and 56.4 (OCH_3), 5.0 and 2.1 (C-5); HRESIMS *m/z*: [$(M+Na)^+$] calcd for $C_{13}H_{17}O_4INa$, 387.0069; found, 387.0062; Anal. Calcd for $C_{13}H_{17}O_4I$: C, 42.86; H, 4.67. Found: C, 42.97; H, 4.63.

1.4.2. Methyl 3-*O*-benzyl-5-deoxy-5-iodo-2-*O*-triethylsilyl-α,β-D-xylofuranoside (10a). To a soln of compound **7a** (0.206 g, 0.57 mmol) in dry pyridine (4 mL), at 0 °C, under argon, was added slowly triethylchlorosilane (0.86 mmol, 0.129 g, 145 μL). The reaction was then stirred at room temperature until starting material disappeared (1:4 EtOAc–petroleum ether). Pyridine was evaporated and the residue was dissolved in CH_2Cl_2 (20 mL) and washed with water (2×10 mL). The organic layer was dried over Na_2SO_4 and solvents were evaporated. The residue was purified on a silica gel column (15:85 EtOAc–petroleum ether) to give **10a** as a yellow oil.

(0.176 g, 65%, α/β ratio: 44:56 determined by GC); ^1H NMR ($CDCl_3$): δ 7.32–7.25 (m, 5H, $H_{arom.}$), 4.87 (d, 0.4H, $J_{1\alpha,2}$ 4.1 Hz, H-1 α-anomer), 4.83 (br s, 0.6H, H-1 β-anomer), 4.80–4.42 (m, 3H, H-4, $2\times H_{benzyl}$), 4.27 (m, 1H, H-2), 4.09 (dd, 0.4H, $J_{3,4}$ 5.1, $J_{3,2}$ 6.2 Hz, H-3), 3.85 (dd, 0.6H, $J_{3,4}$ 2.2, $J_{3,2}$ 5.2 Hz, H-3), 3.48–3.23 (m, 5H, H-5a, H-5b, OCH_3), 0.94 (t, 5H, *J* 7.6 Hz, CH_3), 0.92 (t, 4H, *J* 7.6 Hz, CH_3), 0.63–0.57 (m, 6H, $3\times CH_2$); ^{13}C NMR ($CDCl_3$): δ 138.4 and 138.2 ($C_{q.arom.}$), 129.0, 128.5, 128.4 and 128.2 ($CH_{arom.}$), 111.4 (C-1β), 102.9 (C-1α), 84.4 and 84.1 (C-3), 82.7 and 80.2 (C-4), 78.2 (C-2), 73.5 and 73.4 (CH_2Ph), 56.6 and 56.2 (OCH_3), 7.4 (CH_2CH_3), 5.3 and 5.2 (CH_2CH_3), 4.5 and 4.2 (C-5); HRESIMS *m/z*: [$(M+Na)^+$] calcd for $C_{19}H_{31}O_4ISiNa$, 501.0934; found, 501.0933; Anal. Calcd for $C_{19}H_{31}O_4ISi$: C, 47.70; H, 6.48. Found: C, 47.47; H, 6.55.

1.4.3. Methyl 3-*O*-benzyl-5-deoxy-5-iodo-2-*O*-methoxyethoxymethyl-α,β-D-xylofuranoside (11a). To a soln of compound **7a** (0.196 g, 0.54 mmol) in dry pyridine (4 mL), at 0 °C, under argon, was slowly added methoxyethoxymethyl chloride (0.81 mmol, 0.101 g, 93 μL). The reaction was stirred at room temperature until starting material disappeared (3:7 EtOAc–petroleum ether). Pyridine was evaporated, the residue was dissolved in CH_2Cl_2 (20 mL) and washed with water (2×5 mL). The organic layer was dried over Na_2SO_4 and solvents were evaporated. The residue was purified on a silica gel column (25:75 EtOAc–petroleum ether) to give **11a** as a colourless oil.

(0.182 g, 75%, α/β ratio: 41:59 determined by GC); ^1H NMR ($CDCl_3$): δ 7.35–7.26 (m, 5H, $H_{arom.}$), 5.02–4.46 (m, 4H, H-1, H-4, $2\times H_{benzyl}$), 4.24 (br s, 1H, H-2), 3.76–3.33 (m, 15H, H-3, H-5a, H-5b, $3\times CH_2$, $2\times OCH_3$); ^{13}C NMR ($CDCl_3$): δ 138.0 ($C_{q.arom.}$), 127.8, 127.4, 127.3, 127.2 and 127.0 ($CH_{arom.}$), 109.4 (C-1β), 101.5 (C-1α), 95.0 (OCH_2O), 83.0 and 82.4 (C-3), 81.5 and 81.4 (C-4), 78.6 and 77.8 (C-2), 72.0 and 71.4 (CH_2Ph), 71.1 and 66.1 (OCH_2), 58.3 and 55.3

(OCH_3), 3.9 and 1.0 (C-5); HRESIMS *m/z*: [$(M+Na)^+$] calcd for $C_{17}H_{25}O_6INa$, 475.0594; found, 475.0605.

1.5. General method for the Bernet–Vasella reaction

1.5.1. Zinc activation. Zinc dust was stirred in a 3 N aqueous HCl soln (0.5 mL/mmol of zinc) during 5 min, then filtered and washed with water (0.5 mL/mmol), EtOH (0.5 mL/mmol) and ether (0.5 mL/mmol). Finally, the material was dried under high vacuum with a heatgun until the powder became pale grey.

1.5.2. Reaction with activated zinc, preparation of compound 9. To a soln of 5-iodo pentofuranosides **7a** + **7b** in a 4:1 THF–water mixture (5 mL/mmol) was added activated zinc dust (10 equiv). The reaction was sonicated at 40 °C until starting material disappeared. The mixture was filtered through cotton to eliminate zinc and solvents were evaporated. The residue was immediately dissolved in dry THF (9 mL, 16 mL/mmol) with 4 Å molecular sieves (0.19 g). The mixture was flushed with argon and benzylhydroxylamine hydrochloride was added (1.14 mmol, 182 mg). After 8 h, molecular sieves were filtered and the solvent evaporated. The residue was dissolved in CH_2Cl_2 (10 mL), washed twice with water (2 × 5 mL), dried over Na_2SO_4 and concentrated. The residue was purified on a silica gel column (3:7 EtOAc–petroleum ether) to afford **9** as a yellow oil.

1.5.3. (2*R*,3*S*)-3-Benzyloxy-2-hydroxypent-4-enal *O*-benzyloxime 9. (0.146 g, 88%, 80:20 mixture of isomers determined by GC); IR (film); *ν* 3440, 3083, 3063, 3031, 2920, 2848, 1026, 928, 734 and 697 cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 7.47 (d, 0.8H, $J_{1,2}$ 5.5 Hz, H-1 major isomer), 7.38–7.32 (m, 10H, $H_{arom.}$), 6.82 (d, 0.2H, $J_{1,2}$ 5.5 Hz, H-1 minor isomer), 5.82–5.76 (m, 1H, H-4), 5.40–5.29 (m, 2H, H-5), 5.10 (s, 0.8H, H_{benzyl} oxime), 5.07 (s, 0.2H, H_{benzyl} oxime), 4.66 (d, 1H, $J_{A,B}$ 11.7 Hz, H_{benzyl}), 4.38 (d, 1H, $J_{A,B}$ 11.7 Hz, H_{benzyl}), 4.32–4.29 (m, 1H, H-2), 3.98 (t, 0.2H, $J_{3,4}$ 7.5, $J_{3,2}$ 7.5 Hz, H-3 minor isomer), 3.90 (t, 0.8H, $J_{3,2}$ 7.5, $J_{3,4}$ 7.5 Hz, H-3 major isomer), 2.88 (s, 1H, OH); ^{13}C NMR ($CDCl_3$): 149.8 (C-1), 138.3, 138.0 and 137.9 ($C_{q.arom.}$), 134.8 and 134.5 (C-4), 129.1, 129.0, 128.9, 128.7, 128.6 and 128.5 ($CH_{arom.}$), 121.4 and 120.5 (C-5), 82.4 and 81.6 (C-3), 78.6 and 76.9 (CH_2Ph oxime), 72.2 (C-2), 72.1 (CH_2Ph); HRESIMS *m/z*: [$(M+Na)^+$] calcd for $C_{19}H_{21}O_3NNa$, 334.1419; found, 334.1411.

1.5.4. Reaction with activated zinc, preparation of compounds 12 and 13. To a soln of 5-iodo-pentofuranosides **10a** or **11a** in a 4:1 THF–water mixture (5 mL/mmol) was added activated zinc dust (10 equiv). The reaction was sonicated at 40 °C until starting material disappeared. The mixture was filtered through cotton to eliminate zinc and solvents were evaporated. The residue was purified on a neutralized silica gel column (1:4 EtOAc–petroleum ether) to give **12** or **13** as a colourless oil.

1.5.5. (2*R*,3*S*)-3-Benzyloxy-2-triethylsilyloxypent-4-enal (12). (0.189 g, 91%); $[\alpha]_D^{23}$ +26.3 (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): *δ* 9.66 (s, 1H, H-1), 7.37–7.26 (m, 5H, $H_{arom.}$), 5.91 (ddd, 1H, $J_{4,3}$ 6.8, $J_{4,5cis}$ 10.7, $J_{4,5trans}$ 17.4 Hz, H-4), 5.38–5.30 (m, 2H, H-5a, H-5b), 4.66 (d, 1H, $J_{A,B}$ 12.1 Hz, H_{benzyl}), 4.37 (d, 1H, $J_{A,B}$ 12.1 Hz, H_{benzyl}), 4.10–4.04 (m, 2H, H-2, H-3), 0.91 (t, 9H, *J* 7.7 Hz, CH_3), 0.63 (q, 6H, *J* 7.7 Hz, CH_2); ^{13}C NMR ($CDCl_3$): *δ* 203.5 (C-1), 138.3 ($C_{q.arom.}$), 134.6 (C-4), 129.0, 128.5 and 128.3 ($CH_{arom.}$), 120.3 (C-5), 81.5 (C-3), 80.4 (C-2), 71.1 (CH_2Ph), 7.3 (CH_2CH_3), 5.3 (CH_2CH_3); HRESIMS *m/z*: [$(M+Na)^+$] calcd for $C_{18}H_{28}O_3SiNa$, 343.1705; found, 343.1716.

1.5.6. (2*R*,3*S*)-3-Benzyloxy-2-methoxyethoxymethyloxypent-4-enal (13). (0.111 g, 78%); ^1H NMR ($CDCl_3$): *δ* 9.68 (1H, s, 1-H), 7.36–7.26 (m, 5H, $H_{arom.}$), 5.95–5.86 (m, 1H, H-4), 5.38–5.30 (m, 2H, H-5a, H-5b), 4.93–4.76 (m, 2H, OCH_2O), 4.63 (d, 1H, $J_{A,B}$ 12.0 Hz, H_{benzyl}), 4.35 (1H, d, $J_{A,B}$ 12.0 Hz, H_{benzyl}), 4.11–4.06 (m, 2H, H-2, H-3), 3.36 (s, 3H, OCH_3), 3.79–3.72 (m, 2H, OCH_2), 3.76–3.33 (m, 2H, OCH_2); ^{13}C NMR ($CDCl_3$): *δ* 202.1 (C-1), 137.8 ($C_{q.arom.}$), 134.1 (C-4), 128.9, 128.6, 128.0 and 127.4 ($CH_{arom.}$), 120.5 (C-5), 96.5 (OCH_2O), 84.1 (C-3), 80.0 (C-2), 71.9 (OCH_2), 71.1 (CH_2Ph), 60.8 (OCH_2), 59.4 (OCH_3).

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