Supporting Information

A new ruthenium based protocol for cleavage of terminal olefins to primary alcohols – improved synthesis of a bicyclic nucleoside.

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List of contents:

General remarks. S2

All experimental procedures that are not covered in the main text,
i.e. for the products in Table 1 (except **5**) as well as the compounds **9-11** and **1** S2 - S7

NMR-spectra of the products in Table 1 including compound **5** as well as the
compounds **9-11** and **1** S8 – S24

General remarks. $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$ (40.6% Ru) was obtained from ChemPure, Germany. Reactions were performed under an atmosphere of nitrogen when anhydrous solvents were used. Column chromatography was carried out on glass columns using silica gel 60 (0.040 – 0.063 mm). Chemical shifts are reported in ppm relative to tetramethylsilane as internal standard for ^1H NMR (200, 300, or 500 MHz) and ^{13}C NMR (50, 75 or 125 MHz). Assignments of NMR spectra of new compounds when given are based on 2D spectra and follow standard carbohydrate and nucleoside style; i.e., the carbon atom next to a nucleobase is assigned C-1', etc. In nucleosides, C-1'' designates the carbon atom in the 3'-C branch; otherwise, C-1' designates the carbon atom in the 3-C branch. Compound names given in this section for the bicyclic compounds are given according to the von Baeyer nomenclature. HR-MALDI and EI mass spectra were recorded in positive-ion mode. Microanalyses were performed at The Microanalytical Laboratory, Department of Chemistry, University of Copenhagen.

4-C-Benzyloxymethyl-3,5-di-O-benzyl-1,2-di-O-isopropylidene-3-C-(2-hydroxyethyl)- α -D-ribofuranose. Prepared from 3-C-allyl-4-C-benzyloxymethyl-3,5-di-O-benzyl-1,2-di-O-isopropylidene- α -D-ribofuranose¹ (223 mg, 0.42 mmol) as starting material using the general procedure. Column chromatography (eluent: gradient of methanol (0 – 0.5%) in dichloromethane). Yield (167 mg, 75%) as a colourless oil. R_f 0.35 (19:1 dichloromethane / methanol). ^1H NMR (500 MHz, CDCl_3) δ 7.31–7.22 (m, 15H, Bn), 5.80 (d, 1H, $J_{\text{H1-H2}} = 4.0$ Hz, H-1), 4.75–4.46 (m, 7H), 4.08 (d, 1H, $J = 10.0$ Hz), 3.88 (d, 1H, $J = 10.0$ Hz), 3.83–3.77 (m, 3H), 4.47 (d, 1H, $J = 10.5$ Hz), 2.28 (m, 1H, H-1'), 2.01 (m, 1H, H-1'), 1.87 (br s, 1H, OH), 1.48 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 139.0, 138.4, 138.0, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.2, 126.9, 113.5, 103.6, 89.6, 85.6, 85.3, 73.8, 73.8, 69.7, 69.3, 66.4, 58.3, 34.2, 26.6, 26.6; HR-MALDI MS: m/z 557.2527 ($[\text{M} + \text{Na}]^+$, $\text{C}_{32}\text{H}_{38}\text{O}_7\text{Na}^+$ calc. 557.2509).

¹ Freitag, M.; Thomasen, H.; Christensen, N. K.; Petersen, M.; Nielsen, P. *Tetrahedron*, **2004**, 60, 3775-3786.

3-*O*-Benzyl-1,2;5,6-bis-*O*-isopropylidene-3-*C*-hydroxymethyl- α -D-allofuranose. Prepared from 3-*O*-Benzyl-1,2;5,6-bis-*O*-isopropylidene-3-*C*-vinyl- α -D-allofuranose² (376 mg, 1.0 mmol) as starting material using the general procedure. Column chromatography (eluent: gradient of methanol (0 – 1.5%) in dichloromethane). Yield (281 mg, 74%) as a colourless oil. R_f 0.50 (19:1 dichloromethane / methanol). ^1H NMR (300 MHz, CDCl_3) δ 7.41–7.24 (m, 5H, Bn), 5.76 (d, 1H, $J_{\text{H1-H2}} = 3.9$ Hz, H-1), 4.74 (s, 2H, CH_2Ph), 4.49 (d, 1H, $J_{\text{H2-H1}} = 3.9$ Hz, H-2), 4.37 (m, 1H, H-5), 4.18 (d, 1H, $J_{\text{H4-H5}} = 6.9$ Hz, H-4), 4.17–4.02 (m, 2H, $2 \times \text{H-6}$), 3.90 (dd, 1H, $J_{\text{H1'a-H1'b}} = 12.0$ Hz, $J_{\text{H1'a-OH}} = 6.0$ Hz, H-1'a), 3.80 (dd, 1H, $J_{\text{H1'a-H1'b}} = 12.0$ Hz, $J_{\text{H1'b-OH}} = 6.3$ Hz, H-1'b), 3.07 (dd, 1H, $J_{\text{H1'a-OH}} = 6.0$ Hz, $J_{\text{H1'b-OH}} = 6.3$ Hz, OH), 1.59 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 138.7 (atom ipso), 128.3, 127.6, 127.6 (Bn), 112.9 ($\text{C}(\text{CH}_3)_2$), 109.9 ($\text{C}(\text{CH}_3)_2$), 104.1 (C-1), 84.7, 82.0, 80.2, 73.8, 67.2, 66.8, 61.4 (C-2, C-3, C-4, C-5, C-6, C-1', 3'- OCH_2Ph), 27.0 (CH_3), 26.8 (CH_3), 26.4 (CH_3), 24.9 (CH_3); HR-MALDI MS: m/z 403.1720 ($[\text{M} + \text{Na}]^+$, $\text{C}_{20}\text{H}_{28}\text{O}_7\text{Na}^+$ calc. 403.1727).

1-Nonanol. A colourless oil prepared from 1-decene using the general procedure. ^1H NMR (200 MHz, CDCl_3) and ^{13}C NMR (125 MHz, CDCl_3) in accordance with the literature data³; EI-MS: m/z 126 $[\text{M} - \text{H}_2\text{O}]^+$.

² Ravn, J., Nielsen, P. *J. Chem. Soc., Perkin Trans. 1*, **2001**, 985-993.

³ SDBS database (<http://www.aist.go.jp/RIODB/SDBS/menu-e.html>) SDBS No. 3385CDS-03-098.

Benzyl alcohol. A colourless oil prepared from styrene using the general procedure. ^1H NMR (500 MHz, CDCl_3) and ^{13}C NMR (75 MHz, CDCl_3) in accordance with the literature data⁴; EI-MS: m/z 108 $[\text{M}]^+$.

1-(2-*O*-Acetyl-3-*C*-benzoyloxymethyl-3,5-di-*O*-benzyl- β -D-ribofuranosyl)thymine (9). To a stirred solution of **5** (615 mg, 1.54 mmol) in anhydrous pyridine (6 mL) at 0 °C was added benzoyl chloride (0.446 mL, 3.84 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was concentrated to dryness under reduced pressure and coevaporated with toluene (3 $\times$ 5 mL) in vacuo. The residue was partitioned between ethyl acetate (5 mL) and water (3 mL). The separated organic phase was washed with a saturated aqueous solution of sodium hydrogencarbonate (3 $\times$ 5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was dissolved in 80% aqueous acetic acid (6 mL) and the solution was stirred at 90 °C for 24 h. The solvents were removed, and the residue was coevaporated with 99% ethanol (3 $\times$ 5 mL), toluene (3 $\times$ 5 mL) and anhydrous pyridine (2 $\times$ 5 mL), and redissolved in anhydrous pyridine (3 mL). Acetic anhydride (2.5 mL) was added, and the solution was stirred at room temperature for 20 h. The reaction was quenched with ice-cold water (10 mL) and extracted with dichloromethane (2 $\times$ 10 mL). The combined extracts were washed with saturated aqueous sodium hydrogencarbonate (3 $\times$ 10 mL) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. To a stirred solution of the residue and thymine (346 mg, 2.75 mmol) in anhydrous acetonitrile (15 mL) was added *N,O*-bis(trimethylsilyl)acetamide (1.7 mL, 6.87 mmol). The reaction

⁴ SDBS database (<http://www.aist.go.jp/RIODB/SDBS/menu-e.html>) SDBS No. 685HSP-41-136

mixture was stirred at reflux for 30 min. After cooling to 0 °C, trimethylsilyl triflate (0.42 mL, 2.34 mmol) was added dropwise, and the solution was stirred for 24 h at room temperature. The reaction was quenched with cold saturated aqueous sodium hydrogencarbonate (10 mL), and the resulting mixture was extracted with dichloromethane (3 × 5 mL). The combined extracts were washed with saturated aqueous solution of sodium hydrogencarbonate (2 × 5 mL) and brine (2 × 5 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: gradient of methanol (0 – 3%) in dichloromethane) to give nucleoside **9** as a white foam (654 mg, 69%): ¹H NMR (300 MHz, CDCl₃) δ 8.48 (br s, 1H, NH), 7.95–7.92 (m, 2H, atom ortho Bz), 7.68 (d, 1H, *J* = 1.2 Hz, H-6), 7.62–7.23 (m, 13 H, Bn, Bz), 6.50 (d, 1H, *J*_{H1'-H2'} = 8.1 Hz, H-1'), 5.69 (d, 1H, *J*_{H1'-H2'} = 8.1 Hz, H-2'), 4.97–4.89 (m, 2H), 4.77–4.51 (m, 5H), 3.90 (dd, 1H, *J*_{H5'a-H5'b} = 11.1 Hz, *J*_{H5'a-H4'} = 2.7 Hz, H-5'a), 3.72 (dd, 1H, *J*_{H5'a-H5'b} = 11.1 Hz, *J*_{H5'b-H4'} = 1.5 Hz, H-5'b), 2.07 (s, 3H, COCH₃), 1.54 (d, 3H, *J* = 1.2 Hz, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 170.2 (COCH₃), 165.9 (COPh), 163.6 (C-4), 150.9 (C-2), 138.0 (atom ipso), 136.5 (C-6), 135.8 (atom ipso), 133.7 (atom para Bz), 129.8, 129.4, 128.9, 128.7, 128.6, 128.5, 127.9, 127.8, 127.4 (Bn, Bz), 111.7 (C-5), 84.8, 83.4, 82.6, 76.2, 74.0, 69.3, 67.0, 62.7 (C-1', C-2', C-3', C-4', C-5', C-1'', 2×OCH₂Ph), 20.8 (COCH₃), 12.2 (CH₃); HR-MALDI MS: *m/z* 637.2125 ([M + Na]⁺, C₃₄H₃₄N₂O₉Na⁺ calc. 637.2156). Anal. Calcd for C₃₄H₃₄N₂O₉ + ½H₂O: C, 65.48; H, 5.65; N, 4.49. Found: C, 65.61; H, 5.60; N, 4.04.

1-(3,5-Di-*O*-benzyl-2-*O*-methanesulfonyl-3-*C*-methanesulfonyloxymethyl-β-D-

ribofuranosyl)thymine (10). To a stirred solution of nucleoside **9** (643 mg, 1.05 mmol) in anhydrous methanol (5 mL) was added sodium methoxide (230 mg, 4.20 mmol). The mixture was stirred overnight at room temperature and then neutralized with dilute aqueous hydrochloric acid. The mixture was extracted with dichloromethane (2 × 15 mL), and the combined extract was washed with a saturated aqueous solution of sodium hydrogencarbonate (3 × 10 mL) and dried (Na₂SO₄). The solvent was removed under reduced pressure to give a residue as a white foam (498 mg, quantitative) which was dissolved in anhydrous pyridine (7 mL) and cooled to 0 °C.

Methanesulfonyl chloride (0.31 mL, 4.02 mmol) was added dropwise, and the mixture was stirred at 0 °C for 2 h and then at room temperature for 1 h. The reaction mixture was cooled to 0 °C and water (10 mL) was added followed by a saturated aqueous solution of sodium hydrogencarbonate (10 mL). The resulting mixture was extracted with dichloromethane (3 × 20 mL) and the organic phase was dried (Na₂SO₄). The solvent was evaporated under reduced pressure to give nucleoside **10** as a yellowish foam (658 mg, quantitative): ¹H NMR (300 MHz, CDCl₃) δ 9.58 (br s, 1H, NH), 7.57 (d, 1H, *J* = 1.2 Hz, H-6), 7.40–7.25 (m, 10 H, Bn), 6.45 (d, 1H, *J*_{H1'-H2'} = 7.8 Hz, H-1'), 5.36 (d, 1H, *J*_{H1'-H2'} = 7.8 Hz, H-2'), 4.91 (d, 1H, *J* = 11.1 Hz), 4.80–4.70 (m, 4H), 4.59 (d, 1H, *J* = 11.1 Hz), 4.47 (m, 1H, H-4'), 3.89 (dd, 1H, *J*_{H5'a-H5'b} = 11.1 Hz, *J*_{H5'a-H4'} = 2.7 Hz, H-5'a), 3.80 (dd, 1H, *J*_{H5'a-H5'b} = 11.1 Hz, *J*_{H5'b-H4'} = 1.8 Hz, H-5'b), 3.01 (s, 3H, SO₂CH₃), 2.90 (s, 3H, SO₂CH₃), 1.55 (d, 3H, *J* = 1.2 Hz, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.7 (C-4), 151.1 (C-2), 137.5 (atom ipso), 136.4 (C-6), 135.2 (atom ipso), 129.0, 128.6, 128.6, 128.0, 127.8, 127.4 (Bn), 112.3 (C-5), 84.7, 82.7, 81.4, 79.2, 73.9, 68.7, 67.3, 66.6 (C-1', C-2', C-3', C-4', C-5', C-1'', 2×OCH₂Ph), 38.7 (SO₂CH₃), 37.3 (SO₂CH₃), 12.1 (CH₃); HR-MALDI MS: *m/z* 647.1357 ([M + Na]⁺, C₂₇H₃₂N₂O₁₁S₂Na⁺ calc. 647.1339).

(1*R*,2*R*,4*R*,5*S*)-1-Benzyloxy-2-benzyloxymethyl-4-(thymine-1-yl)-3,6-dioxabicyclo[3.2.0]heptane (11). To a stirred solution of nucleoside **10** (658 mg crude) in a mixture of EtOH and H₂O (28 mL, 1:1 (v/v)) was added an aqueous solution of NaOH (2 M, 2.5 mL). The mixture was heated under reflux for 2 h and, after cooling to room temperature, extracted with dichloromethane (3 × 10 mL). The combined organic phase was washed with a saturated aqueous solution of sodium hydrogencarbonate (3 × 5 mL), dried (Na₂SO₄), and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: gradient of methanol (0 – 2.3%) in dichloromethane) affording nucleoside **11** (249 mg, 53% from **9**) as a white foam after evaporation of the solvents. ¹H NMR (300 MHz, CDCl₃) and ¹³C NMR (75 MHz, CDCl₃) in

accordance with published data¹; HRMALDI MS: m/z 473.1660 ($[M + Na]^+$, $C_{25}H_{26}N_2O_6Na^+$ calc. 473.1683).

(1*R*,2*R*,4*R*,5*S*)-1-Hydroxy-2-hydroxymethyl-4-(thymine-1-yl)-3,6-dioxabicyclo[3.2.0]heptane

(1). To a stirred solution of nucleoside **11** (76 mg, 0.17 mmol) in ethanol (1.5 mL) was added 20% palladium hydroxide over carbon (38 mg). The mixture was degassed several times with argon and placed under a hydrogen atmosphere. The reaction mixture was stirred at room temperature for 6 h and then filtered through Celite. The filtrate was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (eluent: gradient of methanol (0 – 4%) in dichloromethane) to give nucleoside **1** as a white foamy material (45 mg, 98%): All spectra data in accordance with the published data¹; HR-MALDI MS: m/z 293.0755 ($[M + Na]^+$, $C_{11}H_{14}N_2O_6Na^+$ calc. 293.0744).