Synthesis of Medium and Large Rings, XLVII[+]
Synthesis of Heptano Bridged Pyranoside Derivatives

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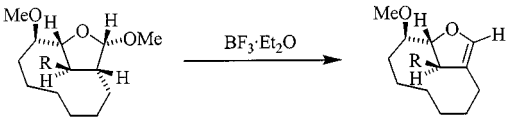
Addition of dichlorocarbene to the glycal (±)-**2** followed by cyclopropyl-allyl rearrangement leads to the chloro-2*H*-pyran (±)-**4**. Oxidation of (±)-**4** and reduction of the obtained hydroxypyranone (±)-**5** gave the methyl pyranoside (±)-**6**. The relative configuration of (±)-**6** was established by X-ray structural analysis of the corresponding acetate (±)-**7**. The synthesis of the optically active starting materials (+)-**2** and (–)-**2** is also reported.

Introduction

Unnatural and modified carbohydrate derivatives are interesting target structures for many reasons.[1] In previous publications[2–4] of this series we have reported on the synthesis of racemic and optically active heptano-bridged methyl furanoside and furanose derivatives. We now report on an approach to the corresponding heptano-bridged pyranosides by ring enlargement.

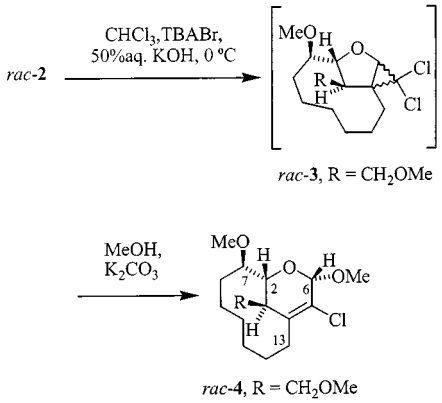
Treatment of the acetal *rac*-**1** with boron trifluoride–diethyl ether in dichloromethane, followed by the usual workup and purification by column chromatography, furnished the corresponding glycal *rac*-**2**[5] in 95% yield (Scheme 1). Glycals are versatile starting materials for many syntheses in carbohydrate chemistry.[6]



rac-**1**, R = CH_2OMe *rac*-**2**, R = CH_2OMe

Scheme 1

The addition of a dihalocarbene to unsaturated sugar derivatives followed by solvolytic rearrangement of the generated cyclopropane is a useful ring enlargement procedure.[7] Glycal *rac*-**2** was dissolved in chloroform and treated with 50% aq. potassium hydroxide in the presence of catalytic amounts of tetrabutylammonium bromide for 22 h at 0 °C to afford a highly sensitive colourless oil (Scheme 2). After workup at room temp. and purification, the mass spectrum of an analytical sample indicated the presence of an intermediate dichloro derivative *rac*-**3** (see Experimental Section). Refluxing the crude reaction product in anhydrous methanol with a large excess of potassium carbonate, followed by the usual workup and column chromatography, led to the chloro-2*H*-pyran *rac*-**4** in 60% isolated yield over two steps.



Scheme 2

Homoallylic coupling constants of J = 0.6 Hz and J = 1.4 Hz between the acetal hydrogen atom 6-H and the protons on C-13 indicate the presence of a double bond. The relative configuration at C-6 was derived by comparison with its oxidation product *rac*-**5**.

After several unsuccessful attempts,[8] the chlorovinyl structure in *rac*-**4** was finally oxidized by means of ruthenium(VIII) oxide[9] according to the protocol of Overman et al.[10] The hydroxypyranone *rac*-**5** was obtained in 67% yield (Scheme 3). The relative configuration at C-6 of *rac*-**5** was determined by NOESY experiments, showing distinctive NOE enhancements between 2-H and 6-H. The *cis* arrangement of the bridge was confirmed by a similar NOE between 7-H and one proton at C-13.

The stereoselective reduction of *rac*-**5** with lithium tri-*tert*-butoxyhydridoaluminate,[11] followed by the usual workup and purification by flash chromatography, provided the methyl pyranoside *rac*-**6** in 71% yield. The relative configuration of *rac*-**6** and of its precursors was finally established by an X-ray structural analysis (Figure 1) of the

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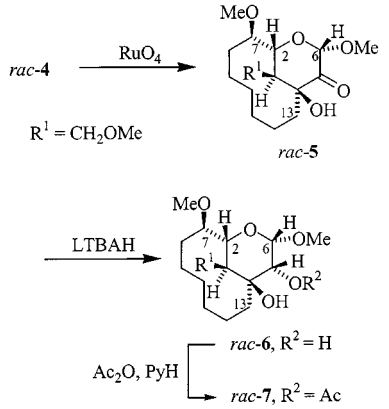


Scheme 3

monoacetate *rac*-**7** obtained from *rac*-**6** and acetic anhydride/pyridine in 90% yield.

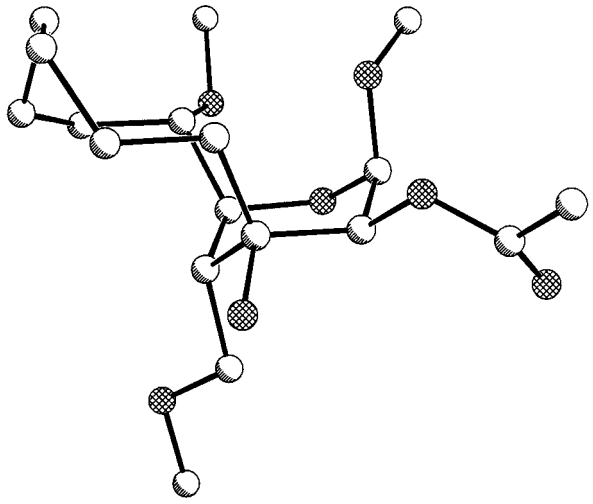
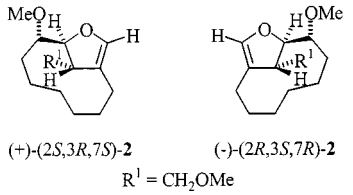


Figure 1. A molecule of *rac*-**7** in the crystal[15]

Figure 1 shows that *rac*-**7** adopts a conformation with an axial methoxy group. A comparison of the hydrogen distances in the crystal and those calculated from the NOESY experiments[12] reveals that *rac*-**7** adopts a similar conformation in $CDCl_3$ solution, too. This compound can be considered as a methyl *rac*-β-2-acetoxy-4-deoxy-4-(methoxymethyl)-6-*O*-methyl-3,6-hexanoidopyranoside derivative that adopts a $_4C^1$ conformation.[13] However, we cannot decide whether the anomeric effect or the steric requirements of our system are responsible for the preferential formation of the stereoisomer *rac*-**4**. Another diastereomer was not detected. The outcome of the reduction step *rac*-**5** → *rac*-**6** to give an equatorial hydroxy group is as expected.[14]

The new racemic compounds described here can also be obtained in an optically active form because (+)-**2** and (–)-**2** are available from (+)-**1** and (–)-**1**, applying our recently reported resolution procedure via dicamphanoates (Scheme 4).[4]



Scheme 4

Experimental Section

General Remarks: IR: Perkin–Elmer 1600 FTIR. – ^{1}H NMR (TMS int.): Bruker DRX 500, the positions of the multiplets of the alkano bridge hydrogen atoms were determined by HSQC and other 2D spectra. – ^{13}C NMR (TMS int.): Bruker ARX 300, DRX 500, multiplicity determined by DEPT 135° or gated ^{13}C NMR spectra. – MS: Finnigan-MAT 8230; direct inlet (EI: 70 eV; CI: isobutane). – CC: Macherey–Nagel Silica gel MN 60 (0.04–0.063 mm). – Flash chromatography: Macherey–Nagel Silica gel MN 60 (0.04–0.063 mm), excess pressure (1–2 bar) generated by nitrogen. – TLC: Macherey–Nagel Silica gel SIL G/UV_{254}. – Melting points (uncorrected): Büchi 510. – Optical rotations: Perkin–Elmer polarimeter 241. – Reactions were monitored by GC or TLC analyses of hydrolyzed aliquots. – Elemental analyses were performed by the Mikroanalytisches Laboratorium Ilse Beetz, Kronach, Germany.

A. Syntheses with Racemic Compounds

(±)-(2*R,3*S**,6*R**)-6-Methoxy-3-methoxymethyl-2,3-dihydro-2,4-heptanofuran (*rac*-2):** Boron trifluoride–diethyl ether (6.5 mL, 36.5 mmol) was added at 0 °C to a solution of (±)-**1** (5.26 g, 19.3 mmol) in anhydrous CH_2Cl_2 (250 mL). The solution was stirred under nitrogen at room temp. for 1.5 h until no starting material was detected anymore (GC). After stirring with satd. aq. $NaHCO_3$ (100 mL), the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by CC (Et_2O/*n*-pentane, 1:1) to provide 4.55 g (95%) of (±)-**2** (R_f = 0.55, Et_2O/*n*-pentane, 1:1) as a colourless oil. – IR (film): $\tilde{\nu}$ = 1655 ($\nu_{C=C}$). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.16 (m, 1 H, 11-*H*), 1.23 (m, 1 H, 10-*H*), 1.29 (m, 1 H, 9-*H*), 1.33 (m, 1 H, 9-*H*), 1.37 (m, 1 H, 8-*H*), 1.50 (m, 1 H, 8-*H*), 1.57 (m, 1 H, 10-*H*), 1.61 (m, 1 H, 7-*H*), 1.66 (m, 1 H, 11-*H*), 1.75 (ddddd, J = 1.0 Hz, J = 7.4 Hz, J = 10.2 Hz, J = 10.2 Hz, J = 15.4 Hz, 1 H, 7-*H*), 1.87 (ddd, J = 4.2 Hz, ^2J = 13.7 Hz, J = 13.7 Hz, 1 H, 12-*H*), 2.15 (dddd, $^4J_{12,5}$ = 1.7 Hz, J = 3.5 Hz, J = 3.5 Hz, ^2J = 13.7 Hz, 1 H, 12-*H*), 3.19 (dd, J = 5.4 Hz, $^3J_{1',3}$ = 8.4 Hz, 1 H, 1′-*H*), 3.20 (dd, $^3J_{3,2}$ = 1.2 Hz, $^3J_{3,1'}$ = 8.4 Hz, 1 H, 3-*H*), 3.33 (dd, J = 4.4 Hz, J = 9.4 Hz, 1 H, 1′-*H*), 3.35 (s, 3-H, CH_2OCH_3 on C-3), 3.39 (s, 3 H, OCH_3 on C-6), 3.43 (ddd, J = 0.7 Hz, $^3J_{6,2}$ = 4.7 Hz, J = 7.4 Hz, 1 H, 6-*H*), 4.60 (ddd, $^4J_{2,5}$ = 0.7 Hz, $^3J_{2,3}$ = 1.2 Hz, $^3J_{2,6}$ = 4.7 Hz, 1 H, 2-*H*), 6.11 (dd, $^4J_{5,2}$ = 0.7 Hz, $^4J_{5,12}$ = 1.7 Hz, 1 H, 5-*H*). – ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 17.6 (t, C-8), 20.7 (t, C-10), 21.9 (t, C-11), 22.5 (t, C-7), 25.0 (t, C-12), 27.2 (t, C-9), 42.5 (d, C-3), 56.9 (q, OCH_3 on C-6), 58.8 (q, CH_2OCH_3 on C-3), 74.7 (t, CH_2OCH_3 on C-3), 78.2 (d, C-6), 84.5 (d, C-2), 114.7 (s, C-4), 142.9 (s, C-5). – MS (EI); *m*/*z* (%): 240 (30) [M^+], 195 (84) [$M^+ - CH_2OMe$]. – HRMS ($C_{14}H_{24}O_3$): calcd. 240.1725; found 240.1723; $C_{13}{}^{13}CH_{24}O_3$: calcd. 241.1759, found 241.1757. – $C_{14}H_{24}O_3$ (240.3): calcd. C 69.96, H 10.06; found C 69.30, H 9.87.

(±)-(2*R,3*S**,6*R**,7*R**)-5-Chloro-7-methoxy-3-methoxymethyl-3,6-dihydro-2*H*-2,4-heptanopyran (*rac*-4):** (±)-**2** (3.07 g, 12.8 mmol) was

dissolved in $CHCl_3$ (80 mL) and cooled to 0 °C. Tetrabutylammonium bromide (390 mg, 1.21 mmol) and 50% aq. KOH (80 mL) were then added. The solution was stirred at 0 °C for 22 h. The mixture was poured into iced water (200 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated at room temp. in vacuo. An analytical amount was purified by CC (Et_2O/*n*-pentane, 1:5) to yield a colourless oil. A mass spectrum confirmed the presence of the dichloro derivative (±)-**3**: $C_{15}H_{24}Cl_2O_3$ (323.3). – MS (CI); *m*/*z* (%): 327 (10) [M^+(^{37}Cl, ^{37}Cl)], 326 (9) [M^+(^{37}Cl, ^{35}Cl) + 1], 325 (56) [M^+(^{37}Cl, ^{35}Cl)], 324 (14) [M^+(^{35}Cl, ^{35}Cl) + 1], 323 (85) [M^+(^{35}Cl, ^{35}Cl)].

Crude (±)-**3** and potassium carbonate (15.0 g) were suspended in anhydrous MeOH (140 mL) and refluxed for 7 h. The mixture was diluted with CH_2Cl_2 (100 mL) and H_2O (50 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification by CC (Et_2O/*n*-pentane, 1:5) provided 2.45 g (60%, over two steps) of (±)-**4** (R_f = 0.17, Et_2O/*n*-pentane, 3:1) as colourless solid, m.p. 56–57 °C (Et_2O/*n*-pentane). The first fraction contained only unidentified less polar by-products (TLC). – IR (KBr): $\tilde{\nu}$ = 1666 ($\nu_{C=C}$). – ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 1.31 (m, 1 H, 10-*H*), 1.32 (m, 1 H, 11-*H*), 1.46 (m, 1 H, 9-*H*), 1.47 (m, 1 H, 10-*H*), 1.48 (m, 1 H, 9-*H*), 1.49 (m, 1 H, 11-*H*), 1.51 (m, 1 H, 8-*H*), 1.66 (m, 1 H, 12-*H*), 1.68 (m, 1 H, 8-*H*), 1.72 (m, 1 H, 12-*H*), 1.99 (dddd, $^5J_{13,6}$ = 1.4 Hz, *J* = 5.0 Hz, *J* = 5.0 Hz, ^2J = 13.5 Hz, 1 H, 13-*H*), 2.69 (dddd, $^5J_{13,6}$ = 0.6 Hz, *J* = 5.5 Hz, *J* = 9.9 Hz, ^2J = 13.5 Hz, 1 H, 13-*H*), 2.78 (ddd, $^3J_{3,2}$ = 0.6 Hz, ^3J = 4.4 Hz, ^3J = 9.1 Hz, 1 H, 3-*H*), 3.31 (dd, ^3J = 4.4 Hz, ^2J = 9.1 Hz, 1 H, CH_2OCH$_3$ on C-3), 3.31 (s, 3 H, CH$_2$OCH_3 on C-3), 3.33 (s, 3 H, OCH_3 on C-7), 3.35 (dd, ^3J = 9.1 Hz, ^2J = 9.1 Hz, 1 H, CH_2OCH$_3$ on C-3), 3.50 (s, 3 H, OCH_3 on C-6), 3.86 (dd, $^3J_{2,3}$ = 0.6 Hz, $^3J_{2,7}$ = 8.5 Hz, 1 H, 2-*H*), 3.91 (ddd, ^3J = 2.2 Hz, ^3J = 5.5 Hz, $^3J_{7,2}$ = 8.5 Hz, 1 H, 7-*H*), 4.73 (dd, $^5J_{6,13}$ = 1.4 Hz, $^5J_{6,13}$ = 0.6 Hz, 1 H, 6-*H*). – ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 24.3 (t, C-10). 24.4 (t, C-12), 25.9 (t, C-9), 26.2 (t, C-11), 28.3 (t, C-8), 31.6 (t, C-13), 42.0 (d, C-3), 55.6 (q, OCH$_3$ on C-6), 56.3 (q, OCH$_3$ on C-7), 58.6 (q, CH$_2$O*C*H$_3$ on C-3), 72.2 (t, *C*H$_2$OCH$_3$ on C-3), 75.8 (d, C-2), 80.5 (d, C-7), 96.5 (d, C-6), 125.8 (s, C-5), 135.4 (s, C-4). – MS (CI); *m*/*z* (%): 289 (33) [M^+(^{37}Cl) – OCH$_3$], 287 (100) [M^+(^{35}Cl) – OCH$_3$]. – HRMS ($C_{16}H_{27}{}^{37}ClO_4$): calcd. 320.1568; found 320.1567. – $C_{16}H_{27}ClO_4$ (318.8): calcd. C 60.27, H 8.84; found C 60.23, H 8.56.

(±)-(2*R,3*S**,4*S**,6*S**,7*R**)-4-Hydroxy-7-methoxy-3-methoxymethyl-2,4-heptanotetrahydropyran-5-one (*rac*-5):** (±)-**4** (1.57 g, 4.95 mmol), sodium metaperiodate (7.19 g, 33.6 mmol) and ruthenium(III) chloride hydrate (15 mg, 0.07 mmol) were dissolved in a mixture of CCl_4 (40 mL), CH_3CN (40 mL) and H_2O (20 mL) and stirred at room temp. for 11 h. The mixture was diluted with CH_2Cl_2 (100 mL) and the organic layer was separated and washed with satd. aq. $Na_2S_2O_3$. The combined aqueous layers were extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification by CC (Et_2O/*n*-pentane, 3:1) provided 1.05 g (67%) of (±)-**5** (R_f = 0.43, Et_2O/*n*-pentane, 3:1) as colourless crystals, m.p. 117–119 °C (Et_2O/*n*-pentane). – IR (KBr): $\tilde{\nu}$ = 3453 (OH), 1743 (C=O). – ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 1.41 (m, 1 H, 11-*H*), 1.43 (ddd, *J* = 9.0 Hz, *J* = 9.0 Hz, ^2J = 15.0 Hz, 1 H, 13-*H*), 1.57 (m, 1 H, 10-*H*), 1.63 (m, 1 H, 10-*H*), 1.67 (m, 1 H, 9-*H*), 1.67 (m, 1 H, 12-*H*), 1.74 (m, 1 H, 9-*H*), 1.77 (m, 1 H, 11-*H*), 1.86 (dddd, *J* = 3.7 Hz, *J* = 6.3 Hz, *J* = 7.6 Hz, *J* = 15.5 Hz, 1 H, 8-*H*), 1.89 (tdd, *J* = 7.5 Hz, *J* = 7.5 Hz, *J* = 15.0 Hz, 1 H, 8-*H*), 2.37 (ddd, *J* = 3.6 Hz, *J* = 8.0 Hz, ^2J = 15.0 Hz, 1 H, 13-*H*), 3.00 (ddd, ^3J = 2.6 Hz, ^3J = 4.0 Hz, $^3J_{3,2}$ = 4.2 Hz, 1 H, 3-*H*), 3.19 (s, 1 H, O*H*), 3.22 (s, 3 H, CH$_2$OCH_3), 3.30 (ddd, *J* = 0.6 Hz, ^3J = 2.6 Hz, ^2J = 8.9 Hz, 1 H, CH_2OCH$_3$), 3.43 (s, 3 H, OCH_3 on C-7), 3.57 (s, 3 H, OCH_3 on C-6), 3.61 (dd, ^3J = 4.0 Hz, ^2J = 8.9 Hz, 1 H, CH_2OCH$_3$), 3.79 (ddd, ^3J = 3.8 Hz, $^3J_{7,2}$ = 5.1 Hz, ^3J = 7.5 Hz, 1 H, 7-*H*), 4.21 (dd, $^3J_{3,2}$ = 4.2 Hz, $^3J_{2,7}$ = 5.1 Hz, 1 H, 2-*H*), 4.85 (s, 1 H, 6-*H*). – ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 19.5 (t, C-12), 19.8 (t, C-9), 25.4 (t, C-11), 26.1 (t, C-10), 28.6 (t, C-8), 34.9 (t, C-13), 39.7 (d, C-3), 57.2 (q, OCH$_3$ on C-7), 57.4 (q, OCH$_3$ on C-6), 58.9 (q, CH$_2$O*C*H$_3$ on C-3), 72.2 (t, *C*H$_2$OCH$_3$ on C-3), 75.6 (d, C-2), 77.0 (s, C-4), 80.7 (d, C-7), 101.1 (d, C-6), 208.4 (s, C-5). – MS (CI); *m*/*z* (%): 317 (13) [M^+ + 1], 299 (18) [M^+ – OH], 285 (89) [M^+ – OCH$_3$], 268 (60) [M^+ – OH – OCH$_3$], 253 (100) [M^+ – H_2O – CH$_2$OCH$_3$]. – $C_{16}H_{28}O_6$ (316.4): calcd. C 60.74, H 8.92; found C 60.68, H 9.02.

(±)-(2*R,3*S**,4*S**,5*R**,6*S**,7*R**)-4,5-Dihydroxy-7-methoxy-3-methoxymethyl-2,4-heptanotetrahydropyran (*rac*-6):** Lithium tri-*tert*-butoxyhydridoaluminate (823 mg, 3.24 mmol) was suspended in anhydrous THF (8 mL) under argon. At 0 °C a solution of (±)-**5** (410 mg, 1.30 mmol) in anhydrous THF (5 mL) was added. After 45 min, the ice bath was removed and the mixture was stirred at room temp. for 4 h. After cooling to 0 °C, the mixture was slowly hydrolyzed with iced water (10 mL) and stirred for 30 min. The solution was extracted with ethyl acetate (4 × 25 mL) and the combined organic layers were washed with brine (twice) and dried (Na_2SO_4). After concentrating in vacuo the remaining residue was purified by flash chromatography (Et_2O/ethyl acetate , 1:1) to provide 295 mg (71%) of (±)-**6** (R_f = 0.15, Et_2O/ethyl acetate, 1:1) as colorless crystals, m.p. 122–123 °C (CH_2Cl_2/*n*-pentane). – IR (KBr): $\tilde{\nu}$ = 3396 (OH). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.53 (m, 1 H, 11-*H*), 1.56 (m, 1 H, 10-*H*), 1.56 (m, 1 H, 12-*H*), 1.58 (m, 1 H, 8-*H*), 1.60 (m, 1 H, 12-*H*), 1.62 (m, 1 H, 11-*H*), 1.66 (m, 1 H, 9-*H*), 1.67 (m, 1 H, 10-*H*), 1.73 (ddd, *J* = 9.1 Hz, ^2J = 8.6 Hz, *J* = 15.4 Hz, 1 H, 13-*H*), 1.78 (m, 1 H, 9-*H*), 1.83 (m, 1 H, 8-*H*), 1.89 (ddd, *J* = 2.6 Hz, 5.7 Hz, ^2J = 8.6 Hz, 1 H, 13-*H*), 2.31 (d, $^3J_{5\text{-}OH,5}$ = 9.1 Hz, 1 H, O*H* on C-5), 2.68 (ddd, $^3J_{3,2}$ = 1.1 Hz, ^3J = 5.7 Hz, ^3J = 8.0 Hz, 1 H, 3-*H*), 2.97 (s, 1 H, broad, O*H* on C-4), 3.35 (s, 3 H, CH$_2$OCH_3 on C-3), 3.45 (s, 3 H, OCH_3 on C-7), 3.53 (dd, ^3J = 8.0 Hz, ^2J = 9.1 Hz, 1 H, CH_2OCH$_3$ on C-3), 3.57 (s, 3 H, OCH_3 on C-6), 3.80 (dd, $^3J_{5,6}$ = 5.0 Hz, $^3J_{5,5\text{-}OH}$ = 9.1 Hz, 1 H, 5-*H*), 3.83 (dd, $^3J_{2,3}$ = 1.1 Hz, $^3J_{2,7}$ = 9.8 Hz, 1 H, 2-*H*), 3.93 (dd, ^3J = 5.7 Hz, ^2J = 9.1 Hz, 1 H, CH_2OCH$_3$ on C-3), 4.14 (ddd, *J* = 2.4 Hz, *J* = 5.3 Hz, $^3J_{7,2}$ = 9.8 Hz, 1 H, 7-*H*), 4.87 (d, $^3J_{6,5}$ = 5.0 Hz, 1 H, 6-*H*). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.7 (t, C-12), 21.3 (t, C-10), 26.7 (t, C-11), 26.9 (t, C-9), 27.8 (t, C-13), 29.6 (t, C-8), 41.2 (d, C-3), 56.6 (q, OCH$_3$ on C-6), 56.7 (q, OCH$_3$ on C-7), 58.9 (q, CH$_2$O*C*H$_3$ on C-3), 72.6 (t, *C*H$_2$OCH$_3$ on C-3), 73.0 (d, C-5), 73.4 (s, C-4), 79.6 (d, C-2), 80.0 (d, C-7), 101.6 (d, C-6). – MS (EI); *m*/*z* (%): 318 (7) [M^+], 268 (13) [M^+ – H_2O – MeOH]. – $C_{16}H_{30}O_6$ (318.4): calcd. C 60.36, H 9.50; found C 60.22, H 9.00.

(±)-(2*R,3*S**,4*S**,5*R**,6*S**,7*R**)-5-Acetoxy-4-hydroxy-6,7-dimethoxy-3-methoxymethyl-2,4-heptanotetrahydropyran (*rac*-7):** A solution of (±)-**6** (69 mg, 0.22 mmol) in anhydrous pyridine (2 mL) and acetic anhydride was stirred for 18 h at room temperature. The mixture was hydrolyzed with water (30 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed twice with 2 N HCl, dried (Na_2SO_4) and the solvent was removed in vacuo. The resulting colourless residue was purified by flash chromatography (Et_2O) to afford 71 mg (90%) of (±)-**7** (R_f = 0.27, Et_2O) as colourless crystals, m.p. 103–104 °C (CH_2Cl_2/*n*-pentane). – IR (KBr): $\tilde{\nu}$ = 3645 cm^{-1} (OH), 1743 (ester C=O). – ^{1}H NMR

(500 MHz, $CDCl_3$): δ = 1.56 (m, 1 H, 11-*H*), 1.57 (m, 1 H, 10 *H*), 1.58 (m, 1 H, 8-*H*), 1.59 (m, 2 H, 12-*H*), 1.60 (m, 1 H, 11-*H*), 1.60 (m, 1 H, 8-*H*), 1.65 (m, 1 H, 9-*H*), 1.76 (m, 1 H, 10-*H*), 1.79 (m, 1 H, 9-*H*), 1.89 (dd, J = 8.9 Hz, ^2J = 15.7 Hz, 1 H, 13-*H*), 2.07 (ddd, J = 3.2 Hz, J = 7.8 Hz, ^2J = 15.7 Hz, 1 H, 13-*H*), 2.17 (s, 3 H, OCOC*H*$_3$), 2.79 (ddd, $^3J_{3,2}$ = 1.1 Hz, ^3J = 6.9 Hz, ^3J = 7.2 Hz, 1 H, 3-*H*), 3.38 (s, 3 H, CH_2OCH_3 on C-3), 3.45 (s, 3 H, OCH_3 on C-7), 3.47 (d, J = 0.9 Hz, 1 H, O*H* on C-4), 3.52 (s, 3 H, OCH_3 on C-6), 3.60 (dd, ^3J = 6.9 Hz, ^2J = 9.3 Hz, 1 H, CH_2OCH_3 on C-3), 3.74 (dd, $^3J_{2,3}$ = 1.1 Hz, $^3J_{2,7}$ = 9.8 Hz, 1 H, 2-H), 4.03 (dd, ^3J = 7.2 Hz, ^2J = 9.3 Hz, 1 H, CH_2OCH_3 on C-3), 4.24 (ddd, J = 2.5 Hz, J = 5.3 Hz, $^3J_{7,2}$ = 9.8 Hz, 1 H, 7-H), 5.00 (d, $^3J_{6,5}$ = 4.9 Hz, 1 H, 6-H), 5.04 (d, $J_{5,6}$ = 4.9 Hz, 1 H, 5-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.8 (t, C-12), 21.1 (q, OCO*C*H$_3$), 21.3 (t, C-10), 26.6 (t, C-11), 26.8 (t, C-9), 28.6 (t, C-13), 29.7 (t, C-8), 41.5 (d, C-3), 56.6 (q, OCH_3 on C-6), 56.7 (q, OCH_3 on C-7), 59.1 (q, CH_2OCH_3 on C-3), 72.6 (s, C-4), 73.9 (t, CH_2OCH_3 on C-3), 74.5 (d, C-5), 79.7 (d, C-7), 79.9 (d, C-2), 99.73 (d, C-6), 171.1 (s, O*C*-OCH_3). – MS (CI); *m*/*z* (%): 361 (1) [M^+ + H], 343 (3) [M^+ – OH], 311 (100) [M^+ – MeOH – OH]. – $C_{18}H_{32}O_7$ (360.4): calcd. C 59.98, H 8.95; found C 59.99, H 8.97.

X-ray Structural Analysis of (±)-7:[15] $C_{18}H_{32}O_7 \cdot 1/2CH_2Cl_2$, colourless plate, 0.6 mm × 0.6 mm × 0.2 mm, a = 24.503(3) Å, b = 11.496(1) Å, c = 15.181(2) Å, β = 106.79(1)°, V = 4039.9(8) Å^3 (T = 200 K), monoclinic, space group $C2/c$, Z = 8, $\rho_{calcd.}$ = 1.307 g·cm^{-3}, μ = 0.2 mm^{-1}. Intensity data were collected using a CAD4 4-circle diffractometer with graphite-monochromated Mo-K_α radiation (0.71073 Å). The structure was solved with direct methods using SHELXS-86. Refinement (full-matrix least squares) was performed against F^2 using SHELXL-93. All nonhydrogen atoms were refined with anisotropic displacement factors. All methyl, methylene and methine hydrogen atoms were positioned with idealized geometry and refined with isotropic displacement factors using the riding model. The hydroxy hydrogen atoms were refined with varying coordinates and varying isotropic displacement factor. 4317 measured reflections in the range of 3° ≤ 2φ ≤ 50°, 3772 unique reflections and 2796 with $F_o > 4\sigma(F_o)$. $R1$ [$F_o > 4\sigma(F_o)$] = 0.0477, $wR2$ for all data = 0.1288, GoF = 1.044, residual electron density: 0.42/–0.47e/Å^3.

B. Syntheses with Optically Active Compounds

(+)-(2*S*,3*R*,6*S*)-6-Methoxy-3-methoxymethyl-2,3-dihydro-2,4-heptanofuran [(+)-2]: Compound (+)-**2** was obtained from (+)-**1**[4] in 54% yield by the same procedure as described for (±)-**2**. – $[\alpha]_D^{22}$ = +50.0 (c = 1.14, $CHCl_3$). – The spectral data are identical to those of *rac*-**2**.

(–)-(2*R*,3*S*,6*R*)-6-Methoxy-3-methoxymethyl-2,3-dihydro-2,4-heptanofuran [(–)-2]: Compound (–)-**2** was obtained from (–)-**1**[4] in 39% yield by the same procedure as described for (±)-**2**. – $[\alpha]_D^{22}$ = –50.0 (c = 1.17, $CHCl_3$). – The spectral data are identical to those of *rac*-**2**.

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