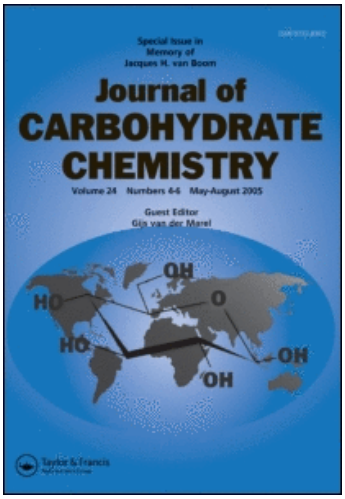

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Synthesis of the Aliphatic Subunit of the Macrolide LL-Z 1640-2 via Vasella Ring Opening of a 6-Iodo-4-deoxy-D-mannose

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Synthesis of the Aliphatic Subunit of the Macrolide LL-Z 1640-2 via Vasella Ring Opening of a 6-Iodo-4-deoxy-D-mannose

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The synthesis of the aliphatic subunit **9** of the macrolide LL-Z1640-2 (**I**), starting from a 4-deoxy-D-mannose derivative **2a**, is described. The procedure includes the first successful application of a Vasella ring opening reaction for a 4-deoxypyranoside. Nucleophilic addition of an alkynyllithium reagent to the aldehyde **4** led to the propargylic alcohol **7**, which was converted to the advanced building block **9** in two further steps.

Keywords 4-Deoxy-D-mannose, Vasella ring opening, Macrolide LL-Z1640-2, Activated zinc, Chiral pool synthesis

INTRODUCTION

In connection with a program for using carbohydrate templates as building blocks for complex targets such as macrolides,[1–3] we investigated the Vasella reaction.[4] This chemical transformation allows conversion of halosugars into building blocks possessing a carbonyl group tethered to an olefinic bond, such as hex-5-enals or pent-l-enals. The synthetic value of the ω-olefinic aldehydes is well documented in several total syntheses and the Vasella ring opening was, for instance, successfully employed as a key step in a sugar-based synthesis of pentenomycin,[5] ossamycin,[6] FK-506,[7] and various other natural products.[8–11] Our own interest in the Vasella reaction was connected with the synthesis of the highly biologically active macrolide

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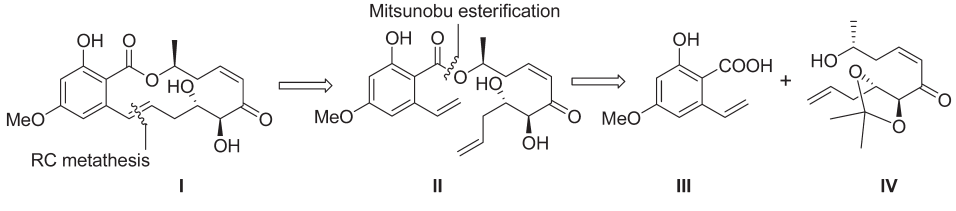
LL-Z1640-2 (**I**).[12–15] The interesting activity and structural challenge has initiated several syntheses of this macrolide antibiotic.[16–18]

In the present study, we wanted to investigate the use of mannose as a starting material that can provide two of the required stereocenters of the natural product **I**. In order to use the elegant Vasella method for ring opening of halo sugars to ω-unsaturated aldehydes, we prepared two new 6-deoxy-6-iodomannose derivatives, easily accessible from α-methyl mannopyranoside or glucose as described earlier.[3] These iodosugars were submitted to the Vasella ring opening reaction to obtain the required δ,ε-hexenals, precursors of building block **IV**, which may serve as advanced intermediates for a "chiral pool" synthesis of macrolide **I** as shown in the retrosynthetic Scheme 1. Retrosynthetic analysis for LL-Z1640–2 (**I**) further led to the fragment **II**, in turn traced back to the benzoic acid **III** and the aliphatic subunit **IV**.

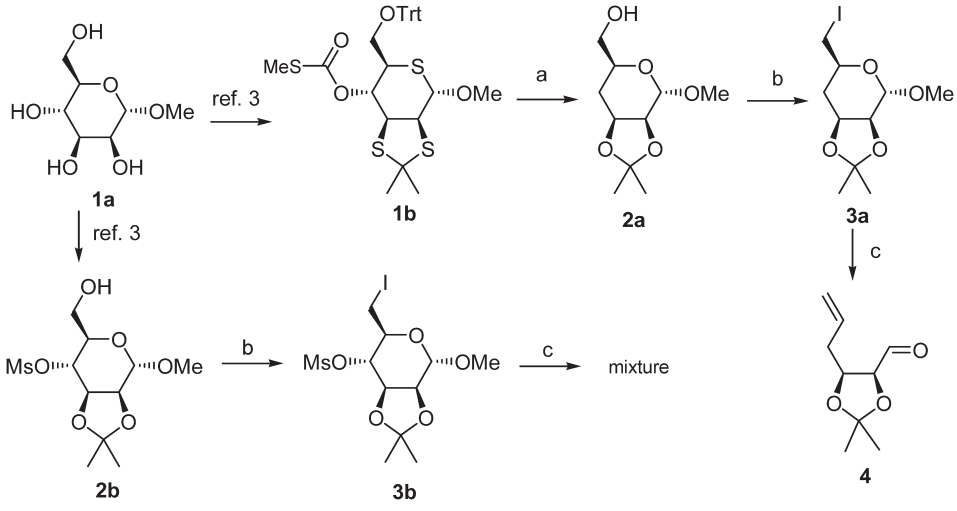
RESULTS AND DISCUSSION

The synthesis of mannose derivatives **2a** and **2b** started from methyl-α-D-mannopyranoside (**1a**) via **1b** as previously reported (Sch. 2).[3] The alcohols **2a** and **2b** were subjected to reaction with iodine and triphenylphosphine,[19] producing the 6-iodo sugars **3a** and **3b** in excellent yields. The 6-iodomannopyranosides **3a** and **3b** were then treated with activated zinc to probe the Vasella ring-opening reaction. The reaction of the mesylate **3b** afforded a complex mixture of products, probably due to concurrent interaction of zinc with the mesylate group. However, zinc treatment of the deoxysugar **3a** afforded the targeted aldehyde **4** in 60% yield under sonication conditions.[20] To the best of our knowledge, this is the first successful application of the Vasella reaction to 6-halo-4-deoxypyranosides.

According to the retrosynthetic analysis (Sch. 1), aldehyde **4** should be coupled with vinyl iodide **6** or, alternatively, with the easily accessible acetylene **5**,[21] followed by catalytic reduction of the triple bond to the *Z*-olefin.[22] The *Z*-vinyl iodide **6**[17] could be obtained from racemic alkyne **5** in a two-step sequence by iodination followed by stereoselective diimide reduction in 50% overall yield.

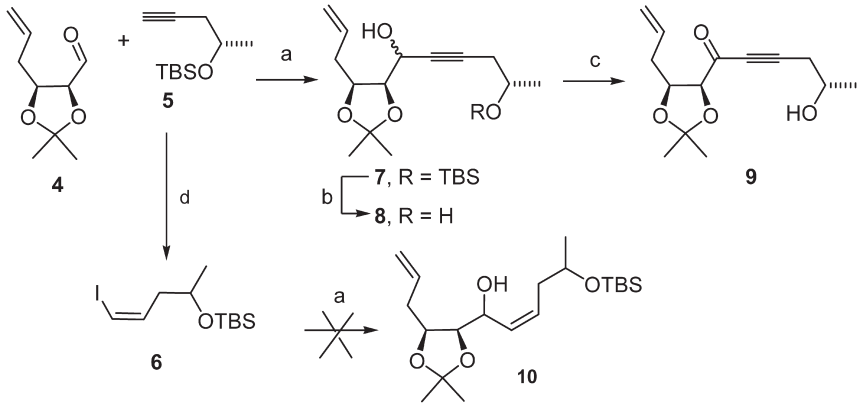


Scheme 1: Retrosynthetic analysis for the synthesis of macrolide LL-Z1640–2 (**I**).



Scheme 2: Reagents and conditions: a) 1. H_3PO_2/AIBN, Et_3 N, dioxane, reflux, 90%; 2. p-TsOH, acetone, 90%; b) Ph_3P, I_2, r.t., 90%; c) activated Zn, *i*-PrOH, sonication, 50°C, 60%.

The aldehyde **4** was reacted with the lithium reagents, prepared in situ by treatment of alkyne **5**[23] or vinyl iodide **6** with *n*-BuLi (Sch. 3). However, in the reaction of aldehyde **4** with the vinyllithium reagent, the formation of a complex mixture of products was observed and the desired allylic alcohol could not be isolated in pure form. In contrast, the coupling of aldehyde **4** with the lithiated alkyne **5** provided a mixture of expected diastereomeric propargyl alcohols **7** in a 1:2.3 ratio, according to ^{1}H NMR analysis. The terminal TBS protecting group in **7** was easily cleaved by treatment with hydrofluoric acid in pyridine to afford the diol **8**.[24] Selective oxidation of the hydroxyl



Scheme 3: Reagents and conditions: a) *n*-BuLi, THF, −78°C, 50%; b) Py*HF, THF, r.t., 73%; c) MnO_2, benzene, r.t., 80%; d) **1**. *n*-BuLi, I_2, 2. $N_2(CO_2K)_2$, (50%).

group with manganese dioxide led to propargylic ketone **9**. The building block **9** is ideally suited for esterification of the secondary alcohol group with acid **III**, followed by *Z*-selective reduction of the acetylene and RC metathesis to form **I** as outlined in Scheme 1.

In conclusion, the 6-iodo-4-deoxymannose derivative **3a** was subjected to the Vasella ring-opening reaction to yield the δ,ε-hexenal **4**. Coupling of **4** with the acetylene **5** afforded the propargylic ketone **9** in only two further steps. This advanced building block may serve as a late intermediate in the enantioselective synthesis of the macrolide antibiotic LL-Z 1640–2 (**I**).

EXPERIMENTAL

General

Thin-layer chromatography was performed on precoated TLC plates (silica gel, Merck). Melting points were measured with a Gallenkamp apparatus and are not corrected. NMR spectra were recorded on Bruker Avance 500 at the following frequencies: 500.13 MHz (1H) and 125.76 MHz. (13C). Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in ppm downfield from TMS as an internal standard. Elemental analyses were performed with a Perkin-Elmer Elemental Analyzer 2400. Optical rotations were measured at 25°C on a Perkin- Elmer Polarimeter 241. Mass spectra were recorded using a Finnigan MAT 8430 spectrometer in the electron-impact mode at 70 eV and chemical ionization is given as m/z values and relative abundances. The infrared spectra were recorded using a FT-IR Spectrometer Nicolet 510.

*Methyl 4,6-Dideoxy-6-iodo-2,3-O-isopropylidene-α-D-mannopyranoside (**3a**)*

A solution of iodine (1.2 g, 4.7 mmol) in toluene (40 mL) was added dropwise with vigorous stirring to the solution of alcohol **2a**[3] (0.9 g, 4.1 mmol), triphenylphosphine (1.2 g, 4.6 mmol), and imidazole (0.6 g, 8.8 mmol) in dry toluene (160 mL). The reaction mixture was stirred for 1 h at 20°C and monitored by TLC (CH_2Cl_2). The solution was decanted and the solid residue was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with $Na_2S_2O_3$ solution, dried over $MgSO_4$, filtered, and concentrated at reduced pressure. Purification of the residue by silica gel column chromatography (CH_2Cl_2/petroleum ether 1:1) gave the iodide **3a** (1.22 g, 90%) as a colorless oil. $[\alpha]_D^{20} = +66.1$ (c = 1.1, $CHCl_3$). IR (film): ν = 1383, 1371, 1221, 1138, 1092, 1084, 1057, 1024, 862. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.35 (s, 3H, CCH_3), 1.53 (s, 3H, CCH_3), 1.55–1.60 (m, 1H, 4a-H), 2.07 (ddd, 1H, $J_{4b,5}$ = 2.7 Hz, $J_{4b,3}$ = 6.4 Hz, $J_{4b,4a}$ = 13.2 Hz, 4b-H), 3.25–3.26 (m, 2H, 6-H), 3.5 (s, 3H, OCH_3), 3.74–3.8 (m, 1H, 5-H), 3.93 (d, $J_{2,3}$ = 5.7 Hz, 1H, 2-H), 4.36 (ddd, $J_{3,2}$ = 5.7 Hz, $J_{3,4b}$ = 6.4 Hz,

$J_{3,4b} = 9.0$ Hz, 1H, 3-H), 4.95 (s, 1H, 1-H). ^{13}C NMR (125 Hz, $CDCl_3$): $\delta = 8.40$ (C-6), 26.1 (CCH_3), 28.1 (CCH_3), 33.8 (C-4), 55.5 (OCH_3), 66.5 (C-2), 70.6 (C-5), 72.3 (C-3), 99.2 (C-1), 109.1 (CMe$_2$). MS (CI, isobutane) m/z (%): 329 (17) $[M + 1]^+$, 297 (2) $[M - CH_3O]^+$. Anal. Calc. for $C_{10}H_{17}IO_4$ (328.14) C 36.6; H 5.22. Found. C, 37.2; H 5.27.

*Methyl 6-Deoxy-6-iodo-2,3-O-isopropylidene-4-O-mesyl-α-D-mannopyranoside (**3b**)*

A solution of iodine (0.12 g, 0.47 mmol) in toluene (5 mL) was added slowly with vigorous stirring to the solution of alcohol **2b**[3] (130 mg, 0.42 mmol), triphenylphosphine (120 mg, 0.46 mmol), and imidazole (60 mg, 0.88 mmol) in dry toluene (10 mL). Workup was done as described for **3a** to yield the iodide **3b** (150 mg, 90%) as a colorless oil. $[\alpha]_D^{20} = +20.3$ (c = 1.3, $CHCl_3$). IR (film): $\nu = 2987$ (CH), 2935 (CH), 2922, 1373, 1352 (SO_2O), 1248 (C-O), 1223, 1201, 1171, 1134, 1092, 1030, 1011, 978, 964, 852. ^{1}H NMR (500 Hz, $CDCl_3$): $\delta = 1.38$ (s, 3H, CCH_3), 1.59 (s, 3H, CCH_3), 3.22 (s, 3H, SO_2CH_3), 3.21 (dd, $J_{6a,5} = 10.0$ Hz, $J_{6a,6b} = 11.0$ Hz, 1H, 6a-H), 3.56 (s, 3H, OCH_3), 3.60 (dd, 1H, $J_{6b,5} = 2.2$ Hz, $J_{6b,6a} = 11.0$ Hz, 6b-H), 3.75–3.80 (ddd, $J_{5,6b} = 2.2$ Hz, $J_{5,6a} = 10.0$ Hz, $J_{5,4} = 10.1$ Hz, 1H, 5-H), 4.15 (d, $J_{2,3} = 5.4$ Hz, 1H, 2-H), 4.29 (m, $J_{3,4} = 7.4$ Hz, $J_{3,2} = 5.4$ Hz, 1H, 3-H), 4.41 (dd, $J_{4,3} = 7.4$ Hz, $J_{4,5} = 10.1$ Hz, 4-H), 4.99 (s, 1H, 1-H). ^{13}C NMR (125 Hz, $CDCl_3$): $\delta = 3.49$ (CH_2I), 26.2 (C(CH_3)$_2$), 27.8 (C(CH_3)$_2$), 39.1 (SO_2CH_3), 56.0 (OCH_3), 67.7 (C-5), 77.2 (C-3), 75.6 (C-2), 82.6 (C-4), 98.0 (C-1), 110.5 (CMe$_2$). MS (70 eV) m/z (%): 422 (2) $[M]^+$, 407 (19) $[M - CH_3]^+$, 268 (8) $[M - CH_4SO_3 - C_3H_6O]^+$, 235 (100) $[M - CH_4SO_3 - C_3H_6O - CH_4O]^+$, 69 (8) $[C_3H_6O]^+$.

*(4S,5S)-5-Allyl-2,2-dimethyl-[1,3]dioxolane-4-carbaldehyde (**4**)*

Zinc dust (0.6 g, 9.2 mmol) was stirred for 5 min with 1 N HCl (50 mL). The activated zinc was then washed with distilled water (2 × 20 mL) and ethanol (2 × 20 mL) and added to a solution of iodide **3a** (0.65 g, 2.0 mmol) in 2-propanol (10 mL). The resulting suspension was sonicated at 40°C for 3 h until TLC analysis showed complete conversion. The reaction mixture was filtered through celite and concentrated at reduced pressure. Diethyl ether (100 mL) and water (10 mL) were added, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated at reduced pressure. Purification by silica gel column chromatography (CH_2Cl_2) gave the aldehyde **4** (0.20 g, 60%) as a colorless oil. $[\alpha]_D^{20} = -18.5$ (c = 0.3, $CHCl_3$). IR (KBr): $\nu = 3459$, 2986 (CH), 2937 (CH), 1732 (C=O), 1642, 1382, 1371, 1219, 1164, 1068, 917. ^{1}H NMR (500 Hz, $CDCl_3$): $\delta = 2.37–2.43$ (m, 2H, CH_2), 4.33 (dd, $J = 3.2$ Hz, $J = 7.1$ Hz, 1H, CH-CHO), 4.45 (m, 1H, CH_2-CH), 5.15–5.20 (m, 2H, =CH_2), 5.86–5.90 (m, 1H, =CH), 9.71 (d, $J = 3.2$ Hz, 1H, CHO). ^{13}C NMR (125 Hz, $CDCl_3$): $\delta = 25.3$ (CH_3), 27.5 (CH_3), 34.1 (CH_2), 78.0 (CH-allyl), 81.9 (CH-CHO), 118.2 (CH_2=), 133.3 (CH=), 201.8 (CHO). MS

(CI, isobutane) m/z (%): 171 (18) $[M+1]^+$, 141 (20) [M - CHO]$^+$, 113 (21) [M - C_3H_5O]$^+$.

*(Z)-tert-Butyl(5-iodopent-4-en-2-yloxy)dimethylsilane (**6**)*[15]

To a solution of the crude 4-*tert*butyl- dimethylsilanyloxy-1-iodopent-1-yne[17] (2.0 g, 6.2 mmol) in methanol (40 mL) was added 20.0 g (100 mmol) of dipotassium azodicarboxylate. A solution of glacial acetic acid (5.9 mL) in 40 mL of methanol was added slowly (2h, rt) and stirring was continued overnight. When no starting material could be detected by GLC analysis of aliquots, 100 mL of water was added. The reaction mixture was extracted with petroleum ether (3 × 125 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated at reduced pressure. *n*-Propylamine (10 mL) was added to the crude product and the reaction mixture was stirred for 1 h. The reaction mixture was diluted with petroleum ether (200 mL) and washed with water (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated at reduced pressure. Iodoalkene **6** (1.2 g, 60%) was isolated as a colorless liquid after distillation at reduced pressure. ^{1}H NMR (500 Hz, $CDCl_3$): $\delta = 0.10$ (s, 6H, Si(CH_3)$_2$), 0.95 (s, 9H, C(CH_3)$_3$), 1.01–1.02 (d, $J_{1,2} = 6.1$ Hz, 3H, 1-H), 2.16–2.27 (m, 2H, 3-H), 3.71–3.77 (m, 1H, 2-H), 5.97–6.00 (m, 1H, 5-H and 4-H). ^{13}C NMR (125 MHz, C_6D_6): −4.9 (SiCH$_3$), −4.6 (SiCH$_3$), −3.0 (Si-C(CH$_3$)$_3$), 24.0 (C-1), 26.3 (C(CH$_3$)$_3$), 44.6 (C-3), 67.3 (C-2), 83.7 (C-5), 138.1 (C-4).

*(5S)-1-((4R,5S)-5-Allyl-2,2-dimethyl-1,3-dioxolan-4-yl)-5-(tert-butyldimethylsilyloxy)hex-2-yn-1-ol (**7**)*

n-Buthyllithium (1.6 M in hexane, 0.45 mL, 0.5 mmol) was added slowly at −60°C to the solution of (*S*)-isopropyldimethyl(pent-4-yn-2-yloxy)silane (**5**)[23] (90 mg, 0.5 mmol) in dry THF (20 mL). The reaction mixture was stirred for 15 min at −60°C. Then the aldehyde **4** (30 mg, 0.16 mmol) in dry THF was slowly added at −78°C under nitrogen. The reaction mixture was stirred for 1 h at −78°C and was then allowed to warm to 0°C. The mixture was stirred for 30 min at 20°C until TLC analysis showed complete conversion. The reaction was quenched by addition of NH_4Cl solution, the aqueous phase was extracted with Et_2O, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated at reduced pressure. Purification by silica gel column chromatography (CH_2Cl_2/methanol 98:2) gave the propargyl alcohol **7** (30 mg, 50%) as a colorless oil. IR (film): $\nu = 2985$ (OH), 1421, 1265 (C-O), 897 (C═C-H). ^{1}H NMR (500 Hz, $CDCl_3$): $\delta = 0.07$ (s, 6H, Si-CH$_3$), 0.88 (s, 9H, Si-C(CH$_3$)$_3$), 1.21 (d, $J = 6.0$ Hz, 3H, 1-H), 1.38 (s, 3H, 14-H), 1.49 (s, 3H, 13-H), 2.23–2.43 (m, 2H, 3-H), 2.33–2.53 (m, 2H, 9-H), 3.90–3.99 (m, 1H, 2-H), 4.09–4.21 (m, 1H, 7-H), 4,23– 4.30 (m, 1H, 8-H), 4.33–4.36 (m, 1H, 6-H), 5.08–5.18 (m, 2H, 11-H), 5.84–5.92 (m, 1H, 10-H). ^{13}C NMR (125 Hz, $CDCl_3$): $\delta = -4.8$ (Si-CH$_3$), −4.7 (Si-CH$_3$), 18.1 (SiCMe$_3$), 23.3 (C-1),

25.4 (C-14), 25.8 (Si*C*Me$_3$), 27.9 (C-13), 29.7 (C-3), 34.0 (C-9), 61.3 (C-6), 67.4 (C-2), 76.7 (C-8), 79.3 (C-4), 84.7 (C-7), 80.4 (C-5), 108.7 (C-12), 117.1 (C-11), 134.7 (C-10). MS (CI, isobutane): m/z (%) = 369 (11) $[M + 1]^+$, 341 (1), 323 (5), 311 (5) $[M - C_4H_9]^+$, 243 (5), 159(5).

*(5S)-1-((4R,5S)-5-Allyl-2,2-dimethyl-1,3-dioxolan-4-yl)hex-2-yne-1,5-diol (**8**)*

Hydrofluoric acid in pyridine (0.05 mL, 0.8 mmol, 15 equiv.) was slowly added to a solution of silyl ether **8** (20 mg, 0.054 mmol) in abs. THF (1 mL) in a polyethylene flask. The reaction mixture was stirred for 15 min at 20°C until TLC analysis showed complete conversion. The reaction was quenched with $NaHCO_3$ solution (1 mL). The aqueous phase was extracted with Et_2O (3 × 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated at reduced pressure. Purification by silica gel column chromatography (CH_2Cl_2/methanol 98:2) gave the (5*S*)-1-((4*R*,5*S*)-5-allyl-2,2-dimethyl-1,3-dioxolan-4-yl)hex-2-yne-1,5-diol (**8**) (10 mg, 0.039 mmol, 73%) as a colorless oil. ^{1}H NMR (500 Hz, $CDCl_3$): $\delta = 1.25$ (d, $J = 6{,}3$ Hz, 3H, 1-H), 1.38 (s, 3H, 14-H), 1.50 (s, 3H, 13-H), 1.62 (br s, 1H, OH), 2.13 (br s, 1H, OH), 2.29–2.46 (m, 2H, 3-H), 2.39–2.55 (m, 2H, 9-H), 3.93–4.00 (m, 1H, 2-H), 4.10–4.14 (m, 1H, 7-H), 4.25–4.29 (m, 1H, 8-H), 4.35–4.41 (m, 1H, 6-H), 5.09–5.19 (m, 2H, 11-H), 5.83–5.93 (m, 1H, 10-H). ^{13}C NMR (125 Hz, $CDCl_3$): $\delta = 22.4$ (C-1), 25.3 (C-14), 27.8 (C-13), 29.4 (C-3), 33.9 (C-9), 61.3 (C-6), 66.2 (C-2), 76.7 (C-8), 80.2 (C-7), 80.6 (C-4), 83.8 (C-5), 108.7 (C-12), 117.2 (C-11), 134.6 (C-10). MS (EI, 70 eV): m/z (%) = 253 (3) $[M - 1]^+$, 239 (36) $[M - CH^3]^+$, 213 (6), 155 (8), 141 (100) $[C_8H_{13}O_2]^+$, 83 (64) $[C_5H_7O]^+$.

*(S)-1-((4S,5S)-5-Allyl-2,2-dimethyl-1,3-dioxolan-4-yl)-5-hydroxyhex-2-yn-1-one (**9**)*

MnO_2 (20 mg, 0.23 mmol, 6 equiv.) was added to the solution of diol **8** (10 mg, 0.04 mmol) in dry CH_2Cl_2 (5 mL). The reaction mixture was stirred for 12 h at 20°C until TLC analysis showed full conversion. The resulting solution was filtered through celite and concentrated at reduced pressure. Purification by silica gel column chromatography (CH_2Cl_2/methanol 98:2) gave ketone **9** (8 mg) as a colorless oil (80%). ^{1}H NMR (500 Hz, $CDCl_3$): $\delta = 1.31$ (d, $J_{1,2} = 6{,}3$ Hz, 3H, 1-H), 1.40 (s, 3H, 14-H), 1.65 (s, 3H, 13-H), 2.01 (br s, 1H, OH), 2.25–2.45 (m, 2H, 3-H), 2.55–2.64 (m, 2H, 9-H), 4.04 – 4.10 (m, 1H, 2-H), 4.44 (ddd, $J_{8,6a} = 3.6$ Hz, $J_{7,8} = 7.3$ Hz, $J_{8,6b} = 9.2$ Hz, 1H, 8-H), 4.52 (d, $J_{7,8} = 7.3$ Hz, 1H, 7-H), 5.10–5.18 (m, 2H, 11-H), 5.80–5.89 (m, 1H, 10-H). ^{13}C NMR (125 Hz, $CDCl_3$): $\delta = 22.7$ (C-1), 25.2 (C-14), 27.0 (C-13), 29.7 (C-3), 34.5 (C-9), 65.8 (C-2), 77.9 (C-8), 83.0 (C-7), 77.2 (C-4), 82.2 (C-5), 110.8 (C-12), 117.8 (C-11), 133.8 (C-10), 186.49 (C-6). MS (EI, 70 eV): m/z (%) = 253 (4) $[M + 1]^+$, 237 (16) $[M - CH_3]^+$, 211 (10) $[M - C_3H_5]^+$, 167 (12), 149 (9), 83 (93) $[C_5H_7O]^+$.

REFERENCES

[1] Krohn, K.; Gehle, D.; Flörke, U. New derivatives of levoglucosan by tandem epoxide allylalcohol rearrangement-cuprate cross-coupling. Eur. J. Org. Chem. **2005**, 2841–2848.

[2] Krohn, K.; Gehle, D.; Flörke, U. New chiral building blocks and branched 1,6-anhydro sugars from regio- and stereoisomeric Cerný epoxides. Eur. J. Org. Chem. **2005**, 4557–4562.

[3] Krohn, K.; Shuklov, I. Two efficient syntheses of protected 4-deoxy-D-lyxo-hexose (4-desoxy-D-mannose). J. Carbohydr. Chem. **2006**, *25*, 331–343.

[4] Bernet, B.; Vasella, A. Carbocyclische Verbindungen aus Monosaccariden. I. Umsetzungen in der Glucosereihe. Helv. Chim. Acta **1979**, *62*, 1990–2016.

[5] Gallos, J.K.; Stathakis, C.I.; Kotoulas, S.S.; Koumbis, A.E. An improved approach to chiral cyclopentenone building blocks. Total synthesis of pentenomycin I and neplanocin A. J. Org. Chem. **2005**, *70*, 6884–6890.

[6] Kutsumura, N.; Nishiyama, S. Asymmetric synthesis of the polyol subunit (I) of the macrolide antibiotic, ossamycin (II). Tetrahedron Lett. **2005**, *46*, 5707–5709.

[7] Villalobos, A.; Danishefsky, S.J. Stereoselective routes to the Cl0-C19 fragment of FK-506. J. Org. Chem. **1990**, *55*, 2776–2786.

[8] Lopez-Herrera, F.J.; Sarabia-Garcia, F.; Pino-Gonzalez, M.S.; Garcia-Aranda, J.F. A new synthesis of 2-C-methyl-D-ribono-1,4-lactone and the C-9/C-13 fragment of methynolide. J. Carbohydr. Chem. **1994**, *13*, 767–775.

[9] Beau, J.-M.; Aburaki, S.; Pougny, J.-R.; Sinay, P. Total synthesis of (+)-methyl pseudomonate C from carbohydrates. J. Am. Chem. Soc. **1983**, *105*, 621–622.

[10] Hanessian, S.; Ugolini, A.; Therien, M. Stereocontrolled synthesis of the spiro ketal unit of avermectin B1a aglycon. J. Org. Chem. **1983**, *48*, 4427–4430.

[11] (a) Lau, C.K.; Crumpler, S.; Macfarlane, K.; Lee, F.; Berthelette, C. Synthesis of AB and CD spiroketal of spongistatin 1. Synlett. **2004**, 2281–2286; (b) Fuerstner, A.; Jumbam, D.; Teslic, J.; Weidmann, H. Metal-graphite reagents in carbohydrate chemistry. Part 8. The scope and limitations of the use of zinc/silver-graphite in the synthesis of carbohydrate-derived substituted hex-5-enals and Pent-4-enals. J. Org. Chem. **1991**, *56*, 2213–2217; (c) Poulsen, C.S.; Madsen, R. Carbohydrate carbocyclization by a zinc-mediated tandem reaction and ring-closing enyne metathesis. J. Org. Chem. **2002**, *67*, 4441–4449; (d) Tanaka, K.; Yamano, S.; Mitsunobu, O. Reductive ring opening of 6-deoxy-6-iodopyranosides and 5-deoxy-5-iodofuranosides by manganese. A convenient procedure for the preparation of chiral 5-hexenals and 4-pentenals. Synlett. **2001**, 1620–1622; (e) Kleban, M.; Kautz, U.; Greul, J.; Hilgers, P.; Kugler, R.; Dong, H.-Q.; Jaeger, V. Vitamin B12 catalysis of zinc-mediated 6-deoxy-6-iodopyranoside fragmentation: a mild and convenient preparation of w-unsaturated hexose derivatives (5-hexenoses). Synthesis. **2000**, 1027–1033.

[12] Ellestad, G.A.; Lovell, F.M.; Perkinson, N.A.; Hargreaves, R.T.; McGahren, W.J. New zearalenone related macrolides and isocoumarins from an unidentified fungus. J. Org. Chem. **1978**, *43*, 2339–2343.

[13] Giese, N.A.; Lokker, N. Cor Therapeutics, Inc., USA, WO, 9613259. Chem. Abstr. **1996**, *125*, 457801.

[14] Yoshimura, K.; Yamane, M.; Harada, S. Takeda Chemical Industries, Ltd., Japan, JP, 08040893. Chem. Abstr. **1996**, *124*, 307584.

[15] Ninomiya-Tsuji, J.; Kajino, T.; Ono, K.; Ohtomo, T.; Matsumoto, M.; Shiina, M.; Mihara, M.; Tsuchiya, M.; Matsumoto, K.A. Resorcylic acid lactone, 5Z-7-Oxozeaenol, prevents inflammation by inhibiting the catalytic activity of TAK1 MAPK kinase. J. Biol. Chem. **2003**, *278*, 18485–18490.

[16] Tatsuta, K.; Takano, S.; Sato, T.; Nakano, S. The first total synthesis of a macrocyclic antiprotozoan, LL-Z1640–2. Chem. Lett. **2001**, 172–173.

[17] Selles, P.; Lett, R. Convergent stereospecific synthesis of C292 (or LL-Z1640–2), and hypothemycin. Part 1. Tetrahedron Lett. **2002**, *43*, 4621–4625.

[18] Selles, P.; Lett, R. Convergent stereospecific synthesis of LL-Z1640–2 (or C292), hypothemycin and related macrolides. Part 2. Tetrahedron Lett. **2002**, *43*, 4627–4631.

[19] Skaanderup, P.R.; Poulson, C.S.; Hyldtoft, L.; Jörgensen, M.R.; Madsen, R. Regioselective conversion of primary alcohols into iodides in unprotected methyl furanosides and pyranosides. Synthesis. **2002**, 1721–1727.

[20] Skaanderup, P.R.; Hyldtoft, L.; Madsen, R. Zinc-mediated fragmentation of methyl 6-deoxy-6-iodo-hexopyranosides. Monatsh. Chem. **2002**, *133*, 467–472.

[21] Dimitriadis, C.; Gill, M.; Harte, M.F. The first stereospecific approach to both enantiomers of mellein. Tetrahedron Asymm. **1997**, *8*, 2153–2158.

[22] de Fatima, Â.; Kohn, L.K.; Antônio, M.A.; de Carvalho, J.E.; Pilli, R.A. Enantioselective syntheses of (R)- and (S)-argentilactone and their cytotoxic activities against cancer cell lines. Bioorg. Med. Chem. **2004**, 5437–5442.

[23] Paquette, L.A.; Hofferberth, J.E. Effect of 9,10-cyclic acetal stereochemistry on feasible operation of the α-ketol rearrangement in highly functionalized paclitaxel (taxol) precursors. J. Org. Chem. **2003**, *68*, 2266–2275.

[24] Nicolaou, K.C.; Webber, S.E. Stereocontrolled total synthesis of lipoxins B. Synthesis. **1986**, 453–461.