Synthesis of Highly Functionalised Carbohydrate-Derived Spiroacetals by Ring-Closing Metathesis and Pauson–Khand Reaction of Ketoglycosidic Enynes

Michiel A. Leeuwenburgh,[a] Chantal C. M. Appeldoorn,[a] Peter A. V. van Hooft,[a] Herman S. Overkleeft,[a] Gijsbert A. van der Marel,[a] and Jacques H. van Boom*[a]

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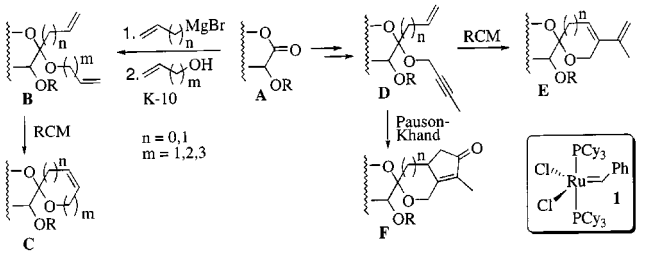
The synthesis of the ketoglycosidic enynes **5**, **7** and **8** starting from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranolactone (**2**) is described. These enynes are subjected to ruthenium-mediated ring-closing metathesis and Pauson–Khand cyclisation to afford the highly functionalised carbohydrate spiroacetals **9** and **11–14**.

Introduction

Over the past few years, the utility of carbohydrates as building blocks in organic synthesis[1] has been considerably enhanced by advances in transition metal chemistry.[2] For example, a recent contribution from this laboratory revealed[3] that carbohydrates are useful starting compounds for the addition of 2-*O*-allyl-1-vinyl and 2-*O*-propargyl-1-vinyl groups which, after ring-closing metathesis (RCM) under the influence of the Grubbs catalyst (**1**)[4] led to functionalised fused oxacycles. Furthermore, spiroacetals of type **C** (see Scheme 1), which are structural elements in many natural products,[5] have proved to be readily accessible[6] from 1-*O*-alkenyl-substituted ketoglycosides (type **B**). In turn, these dienes were prepared starting from the fully protected glucopyranolactone **A** by Grignard addition and subsequent K-10 mediated coupling[7] with a number of unsaturated alcohols.



Scheme 1. Synthesis of highly functionalised spiroacetals with the ring-closing metathesis and Pauson–Khand reactions

As an extension of the latter studies, we report here that by replacing the diene moieties in **B** by enynes (type **D**), a variety of other transition metal mediated transformations, such as enyne metathesis[8] and Pauson–Khand cycloaddition,[9] can be performed. The enyne metathesis reaction gives access to spiroacetals with a 1,3-diene moiety (e.g. type **E**). On the other hand, the Pauson–Khand reaction, a useful method for the preparation of various annulated carbohydrate derivatives,[10,11] is utilised to convert the aforementioned enynes to spiroacetals containing fused cyclopentenone moieties (type **F**).

Results and Discussion

Initial efforts were directed towards the synthesis of enynes **5** and **7** as depicted in Scheme 2. Compound **5** was synthesised from the known[12] precursor **3**, obtained by reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranolactone (**2**)[13] with allylmagnesium bromide, by the following two procedures. Trimethylsilylation of **3** with *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) and $BF_3{\cdot}OEt_2$-promoted coupling[14] of **4** with 2-butyn-1-ol gave the desired ketoglycosidic enyne **5** in 56% yield over the two steps. Alternatively, direct coupling of **3** with 2-butyn-1-ol under the influence of the heterogeneous environmentally benign solid acid montmorillonite K-10[6,7] in the presence of molecular sieves (4 Å) gave **5** in 72% yield. According to the latter procedure, K-10-mediated glycosidation of the known[15] ketose **6** with 2-butyn-1-ol yielded 1-*O*-2-butynyl-1-vinyl-glucose derivative **7** in 87%.

With the aim to create more diversity in the set of enynes, regioisomeric **8**, having a β-orientated alkynyl and an α-orientated alkenyl moiety, was synthesised. However, reaction of **2** with propynyllithium,[16] followed by K-10 mediated coupling with allyl alcohol led to the isolation of **8** along with the corresponding β-isomer in low yield. Fortunately, it was found that low-temperature quenching of the propynylation reaction of **2** with allyl bromide in the presence of HMPA as a cosolvent led to the formation of the 1-*O*-allyl-1-propynyl-substituted **8** as the major compound in good yield (80%, along with 5% of the β anomer).

The results of the ruthenium-mediated conversion of ketoglycosidic enynes **5**, **7** and **8** into spiroacetals are summarised in Scheme 3. After treatment of the 1-allyl-1-*O*-butynyl derivative **5** with catalyst **1** (5 mol-%) at 60 °C in toluene for 12 h, the spiroacetal **9** was isolated in 82% yield. In contrast, cyclisation of 1-*O*-butynyl-1-vinyl-substituted **7** did not proceed at all under the same conditions. Prolonging the reaction time (up to 3 days) and addition of

[a] Leiden Institute of Chemistry,
P. O. Box 9502, 2300 RA Leiden, The Netherlands

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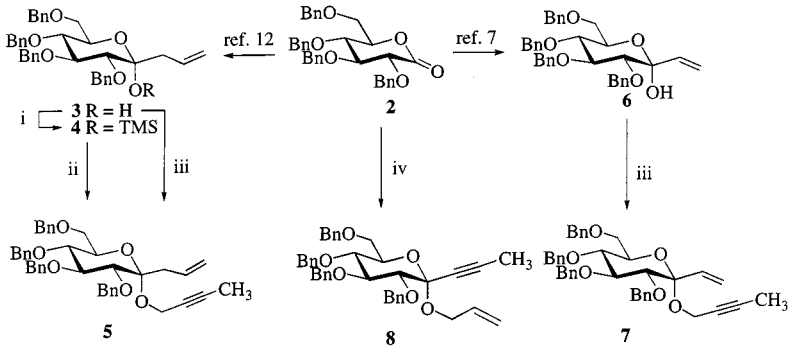
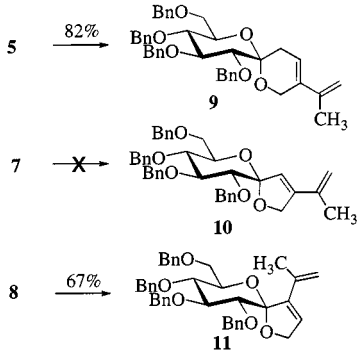
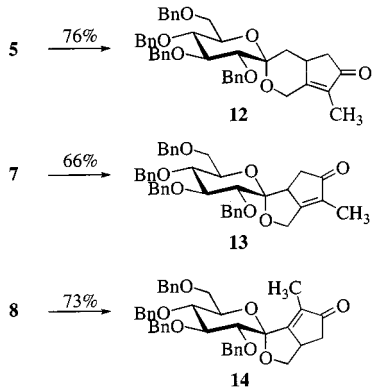


Scheme 2. Synthesis of ketoglycosidic enynes **5**, **7** and **8**; reagents and conditions: (i) BSTFA, DMF, 60 °C (80%); (ii) 2-butyn-1-ol, $BF_3{\cdot}OEt_2$, CH_2Cl_2 (70%); (iii) 2-butyn-1-ol, K-10, molecular sieves (4A), CH_2Cl_2 (72% **5**, 87% **7**); (iv) a. $BrHC{=}CHCH_3$, *n*BuLi, THF, –78 °C; b. allyl bromide, HMPA, –78 °C to room temp. (80%)



Scheme 3. Enyne metathesis reactions; reagents and conditions: Ru-catalyst **1** (5–7 mol-%), toluene, 60 °C



Scheme 4. Pauson–Khand cyclisations; reagents and conditions: $Co_2(CO)_8$ (1.1 equiv.), CH_2Cl_2, then NMO (6.3 equiv.), room temperature

more catalyst (up to 15 mol-% of **1**) only led to the formation of a complex mixture of products. This remarkable finding is all the more surprising since **5** and **7** are homologues differing only in one methylene group. Furthermore, enyne **8**, which is an isomer of **7**, did react under the conditions applied for the conversion of **5**→**9**, albeit in somewhat lower yield, to give the [5,4]spiroacetal derivative **11**. Attempts to promote the cyclisation of **7** by performing the reaction under an ethylene atmosphere[17] failed. The reluctance of this particular compound to undergo RCM was corroborated by an NMR experiment in which enyne **7** was incubated with 0.5 equivalent of catalyst **1**. It was found that the catalyst did not react either with the alkene or with the alkyne part of the molecule, even with reaction times in excess of one day. In this respect, it is of interest to note that the diene analogue (1-*O*-allyl-1-vinyl) of **7** underwent RCM very smoothly.[6] The latter observation may be explained by initial reaction of the catalyst with the less hindered *O*-allyl part of the molecule. In the case of **7**, interaction of the catalyst with the alkene part of the molecule may be impeded by steric hindrance of the *O*-butynyl substituent.[18] This assumption is consistent with the successful cyclisations of enynes **5** and **8**, which have less hindered alkene moieties.

The synthetic potential of the ketoglycosidic enynes **5**, **7** and **8** is further demonstrated by the Pauson–Khand reactions, the results of which are shown in Scheme 4. Of the several available methods for effecting this cyclisation reaction, the *N*-oxide-promoted reaction[10,19] of dicobalthexacarbonyl-complexed alkynes proved most convenient. Thus, after reaction of enyne **5** with dicobaltoctacarbonyl in CH_2Cl_2 at room temperature, cycloaddition was effected by adding an excess of *N*-methylmorpholine *N*-oxide (NMO). In this way, the cyclopentenone spiroacetal **12** was isolated in 76% yield as a single diastereoisomer. Similarly, **7** and **8** could be transformed into the corresponding cyclopentenones **13** and **14** (diastereomeric ratios were 7:1 and 5:1, respectively).

In summary, we have demonstrated the facile synthesis of ketoglycosidic enynes **5**, **7** and **8**, which are amenable to transition-metal-mediated cyclisation reactions. Ruthenium-mediated ring closing metathesis of these enynes (with the exception of **7**) provided spiroacetals with 1,3-diene functionalities, which could function as substrates in, for example, Diels–Alder reactions. Furthermore, Pauson–Khand cyclisations of the enynes **5**, **7** and **8** proceeded smoothly to generate the novel spiroacetals **12**, **13** and **14**, repectively, which, in turn, are valuable intermediates in the synthesis of more complex spiroacetals.

Experimental Section

^1H and ^{13}C NMR spectra were recorded with a Jeol JNM-FX-200 (200/50.1 MHz), a Bruker WM-300 (300/75.1 MHz) or a Bruker DMX 600 (600 MHz) spectrometer. Chemical shifts are given in

ppm (δ) relative to tetramethylsilane as internal standard. Coupling constants are given in Hz. Numbering of carbon and hydrogen atoms refers to the original sugar core. – Mass spectra were recorded with PE Sciex API 165 with ion spray interface. – Elemental analysis was performed on a Perkin–Elmer CHNS Analyzer 2400. Toluene was boiled under reflux with CaH_2 for 3 h, distilled and stored over molecular sieves (4 Å). 1,2-Dichloroethane (DCE, Biosolve, HPLC-grade), tetrahydrofuran (THF, Baker, HPLC grade), *N,N*-dimethylformamide (DMF, Baker, p.a.), dichloromethane (DCM, Baker, p.a.) and hexamethylphosphoramide (HMPA, Aldrich) were stored over molecular sieves (4 Å). *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA, Acros), 2-butyn-1-ol (Acros), *Z*/*E*-1-bromo-propene, montmorillonite K-10, *N*-methylmorpholine *N*-oxide (Aldrich) and dicobaltoctacarbonyl (Fluka) were used as received. – Column chromatography was performed either on Baker silica gel (0.063–0.200 mm) or Merck silica gel 60 (0.040–0.063 mm). – TLC-analysis was conducted on DC-Fertigfolien (Schleicher Schuell, F1500, LS254) or HPTLC aluminium sheets (Merck, silica gel 60, F254) with detection by UV absorption (254 nm) and charring with 20% H_2SO_4 in ethanol. Drying of organic extracts was effected with $MgSO_4$. Prior to reaction, residual water was removed from the starting compounds by coevaporation with either dry toluene or DCE. Reactions were run at ambient temperature, unless stated otherwise.

Trimethylsilyl 5,6,7,9-Tetra-*O*-benzyl-1,2,3-trideoxy-α-D-*gluco*-non-1-en-4-ulopyranoside (4): Keto sugar **3**[12] (0.55 g, 0.95 mmol) was dissolved in DMF (0.5 mL) and treated with BSTFA (1.0 equiv., 0.20 mL). The solution was heated (60 °C) for 2 h, then concentrated in vacuo. Column chromatography (10 to 25% EtOAc/light petroleum) afforded pure **4** (0.50 g, 0.76 mmol, 80%) as a colourless oil. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.35–7.23 (m, 20 H, H_{arom}), 5.85 (m, 1 H, =C*H*), 5.13–4.50 (m, 10 H, =CH_2, 4 × CH_2 Bn), 4.00–3.64 (m, 5 H, H3, H4, H5, 2 × H6), 3.42 (d, *J* = 9.3 Hz, 1 H, H2), 2.75–2.48 (m, 2 H, CH_2CH=), 0.18 (s, 9 H, CH_3 TMS). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 138.6, 138.2 (4 × C_{quat} Bn), 133.6 (=*C*H), 128.2–127.3 (*C*H_{arom}), 118.0 (=*C*H_2), 100.6 (C1), 83.5, 81.4, 78.5 (C2, C3, C4), 75.2, 74.9, 74.7, 73.1 (4 × *C*H_2 Bn), 71.6 (C5), 68.8 (C6), 42.7 (*C*H_2CH=), 2.0 (*C*H_3 TMS). – $C_{40}H_{48}OSi$: calcd. 652.3; MS (ESI): found *m*/*z* 675 (M + Na).

But-2-ynyl 5,6,7,9-Tetra-*O*-benzyl-1,2,3-trideoxy-α-D-*gluco*-non-1-en-4-ulopyranoside (5). – Method A: TMS-glycoside **4** (0.50 g, 0.76 mmol) and 2-butyn-1-ol (1.5 equiv., 85 µL) were dissolved in dry CH_2Cl_2 (4 mL) and placed under a nitrogen atmosphere. The solution was treated with $BF_3{\cdot}OEt_2$ (0.2 equiv., 19 µL) and stirred for 15 min after which time the reaction was quenched with triethylamine. The mixture was extracted with EtOAc, the organic layer washed with water and brine, dried and concentrated. Silica gel chromatography (10 to 25% EtOAc/light petroleum) gave enyne **5** (0.34 g, 0.53 mmol, 70%) as a colourless oil.

Method B: A solution of **3** (0.93 g, 1.6 mmol) and 2-butyn-1-ol (6 equiv., 0.71 mL) in CH_2Cl_2 (2 mL) was added to a slurry of previously flame-dried montmorillonite K-10[7] (1.0 g) and molecular sieves (4 Å, 1.7 g) in CH_2Cl_2 (5 mL). After stirring for 30 min, TLC analysis (25% EtOAc/light petroleum) showed complete consumption of the donor. Methanol/pyridine (1:1, 5 mL) was added and the resulting slurry was stirred for a further 5 min, then the solids were filtered off and rinsed thoroughly with EtOAc. The filtrate was concentrated in vacuo and the residue subjected to column chromatography as described for method A, giving pure **5** (0.73 g, 1.16 mmol, 72%). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.36–7.17 (m, 20 H, H_{arom}), 5.80 (m, 1 H, =C*H*), 5.07–4.51 (m, 10 H, =CH_2, 4 × CH_2 Bn), 4.18 (q, *J* = 2.3 Hz, 2 H, OCH_2C≡), 3.82–3.57 (m, 5 H, H3, H4, H5, 2× H6), 3.51 (d, *J* = 9.5 Hz, 1 H, H2), 2.64 (bd, *J* = 6.9 Hz, 2 H, CH_2CH=), 1.81 (t, 3 H, CH_3). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 138.5, 138.3, 138.2, 137.9 (4 × C_{quat} Bn), 133.1 (=*C*H), 128.2–127.3 (*C*H_{arom}), 118.0 (=*C*H_2), 102.0 (C1), 83.2 (C2/3/4), 81.5 (*C*≡C), 80.7, 78.3 (2 × C2/3/4), 75.5 (C≡*C*), 75.2, 74.8, 74.7, 73.0 (4 × *C*H_2 Bn), 71.9 (C5), 68.4 (C6), 49.1 (O*C*H_2CH=), 37.8 (*C*H_2CH=), 3.5 (*C*H_3). – MS (ESI); calcd. $C_{41}H_{44}O_6$: 632.3; found *m*/*z* 655 [M + Na], 661 [M + K]. – HRMS (FAB); calcd. $C_{41}H_{44}O_6Na$: 655.3035; found 655.3042

But-2-ynyl 1,2-Dideoxy-4,5,6,8-tetra-*O*-benzyl-α-D-*gluco*-oct-1-en-3-ulopyranoside (7): Keto sugar **6**[6,15] (0.44 g, 0.71 mmol) was converted into enyne **7** (0.38 g, 0.62 mmol, 87%) as described for **5** (method B). – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.34–7.18 (m, 20 H, H_{arom}), 5.89 (dd, J_1 = 10.8 Hz, J_2 = 17.4 Hz, 1 H, =C*H*), 5.57 (dd, J_1 = 1.5 Hz, 1 H, =C*H*H), 5.28 (dd, 1 H, =CH*H*), 4.97–4.52 (m, 8 H, 4 × CH_2 Bn), 4.16 (t, *J* = 9.4 Hz, 1 H, H3/4), 4.02 (m, 2 H, OCH_2C≡), 3.94–3.65 (m, 4 H, H3/4, H5, 2 × H6), 3.35 (d, *J* = 9.6 Hz, 1 H, H2), 1.79 (t, *J* = 1.9 Hz, 3 H, CH_3). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 138.6, 138.0, 137.8 (4 × C_{quat} Bn), 134.6 (=*C*H), 128.2–126.6 (*C*H_{arom}), 119.0 (=*C*H_2), 100.0 (C1), 83.8, 82.8 (C2/3/4), 80.8 (*C*≡C), 78.2 (C2/3/4), 75.7, 75.4, 74.9 (3 × *C*H_2 Bn), 74.8 (C≡*C*), 73.2 (*C*H_2 Bn), 71.8 (C5), 68.4 (C6), 50.4 (O*C*H_2C≡), 3.5 (*C*H_3). – MS (ESI); calcd. $C_{40}H_{42}O_6$: 618.3; found *m*/*z* 619 (M + H), 641 (M + Na).

Allyl 5,6,7,9-Tetra-*O*-benzyl-1,2,3-trideoxy-α-D-*gluco*-non-2-yn-4-ulopyranoside (8): To a solution of *Z*/*E*-bromopropene (0.39 mL, 4.5 mmol) in THF (5 mL) under N_2 at –78 °C was added *n*BuLi (4.14 mL, 1.6 M in hexanes, 6.6 mmol). Stirring was continued at –78 °C for 2 h, after which a solution of lactone **2** (1.61 g, 3.0 mmol) in THF (5 mL) was added dropwise. After 30 min, TLC analysis (25% EtOAc/light petroleum) indicated complete consumption of the lactone. Next, the mixture was treated with allyl bromide (0.51 mL, 6.0 mmol) and HMPA (5 mL) and the solution was allowed to warm to room temperature over 2 h. After stirring for an additional period of 1 h at room temperature, the mixture was poured into saturated NH_4Cl and extracted with EtOAc. The organic layer was washed with water and brine, dried and concentrated. Silica gel chromatography (10 to 25% EtOAc/light petroleum) yielded **8** (1.48 g, 2.40 mmol, 80%) as a colourless oil. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.38–7.10 (m, 20 H, H_{arom}), 5.93 (m, 1 H, =C*H*), 5.34–5.12 (m, 2 H, =CH_2), 5.02–4.47 (m, 8 H, 4 × CH_2 Bn), 4.35 (m, 1 H, H3/4), 4.18–4.06 (m, 4 H, H3/4, H5, 2 × H6), 3.98 (d, *J* = 9.5 Hz, 1 H, H2), 3.70 (m, 2 H, OCH_2CH=), 1.83 (s, 3 H, CH_3). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 138.9, 138.6, 138.3 (4 × C_{quat} Bn), 134.4 (=*C*H), 128.4–127.6 (*C*H_{arom}), 117.0 (=*C*H_2), 96.1 (C1), 84.6 (C2/3/4), 82.8 (*C*≡C), 82.6, 78.2 (C2/3/4), 76.2 (C≡*C*), 75.7, 75.1, 73.4 (4 × *C*H_2 Bn), 71.8 (C5), 68.7 (C6), 65.0 (O*C*H_2CH=), 3.7 (*C*H_3). – MS (ESI); calcd. $C_{40}H_{42}O_6$: 618.3; found *m*/*z* 619 [M + H], 641 [M + Na].

2,3,4,6-Tetra-*O*-benzyl-(1*S*)-2′,3′-dihydro-5′-(2-propenyl)spiro[1,5-anhydro-D-glucitol-1,2′-pyran] (9): A solution of enyne **5** (0.21 g, 0.33 mmol) in dry toluene (3 mL), was degassed by bubbling through with nitrogen for 20 min. Catalyst **1** (5 mol-%, 14 mg) was added and degassing was continued for 20 min, after which the solution was heated to 60 °C. After 4 h, HPTLC analysis (10% EtOAc/light petroleum) showed complete consumption of the starting compound. The solvent was removed and the residue purified by column chromatography (10 to 20% EtOAc/light petroleum) to give a greyish-green solid which was crystallised from EtOAc/light petroleum to remove residual catalyst waste, affording **9** as colourless crystals (0.17 g, 0.27 mmol, 82%). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.17 (m, 20 H, H_{arom}), 5.74 (br. s, 1 H, =C*H*),

4.97 (d, J = 11.4 Hz, 1 H, C*H*H Bn), 4.93 (s, 2 H, CH_2 Bn), 4.85 (d, J = 10.7 Hz, 1 H, C*H*H Bn), 4.83 (br. s, 1 H, OC*H*HC=), 4.71 (br. s, 1 H, OCH*H*C=), 4.69 (d, 1 H, C*H*H Bn), 4.60–4.46 (m, 3 H, CH_2 Bn, C*H*H Bn), 4.42 (bd, J = 14.8 Hz, 1 H, =C*H*H), 4.24 (m, 1 H, =CH*H*), 4.19 (t, J = 9.2 Hz, 1 H, H3), 3.82 (dt, J_1 = 10.0 Hz, J_2 = 3.1 Hz, 1 H, H5), 3.70 (d, J = 2.8 Hz, 2 H, H6), 3.67 (t, J = 9.9 Hz, 1 H, H4), 3.39 (d, J = 9.5 Hz, 1 H, H2), 2.63 (bd, J = 16.8 Hz, 1 H, C*H*HC=), 1.92 (m, 1 H, C*H*HC=), 1.87 (s, 3 H, CH_3). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 139.5 (=C_{quat}), 138.5, 138.0, 137.6 (4 × C_{quat} Bn), 132.9 (=*C*H), 128.4–127.5 (*C*H$_{arom}$), 118.6 (=*C*H), 109.6 (=*C*H$_2$), 96.7 (C1), 83.3, 81.6, 78.5 (C2, C3, C4), 75.6, 75.4, 74.7, 73.2 (4 × *C*H$_2$ Bn), 71.6 (C5), 68.5 (C6), 59.9 (O*C*H$_2$CH=), 30.3 (*C*H$_2$CH=), 20.0 (*C*H$_3$). – MS (ESI); calcd. $C_{41}H_{44}O_6$: 632.3; found m/z 633 [M + H], 655 [M + Na]. – HRMS (FAB); calcd. $C_{41}H_{44}O_6Na$: 655.3036; found 655.3029.

2,3,4,6-Tetra-*O*-benzyl-(1*S*)-2′,5′-dihydro-3′-(2-propenyl)spiro[1,5-anhydro-D-glucitol-1,2′-furan] (11): Prepared as described for **9** with 7 mol-% of catalyst **1** and stirring for 48 h. Yield 0.14 g (0.23 mmol) based on 0.21 g (0.34 mmol) of **8** (67%). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.18 (m, 20 H, H$_{arom}$), 6.17 (bt, J = 1.7 Hz, 1 H, =C*H*), 5.57 (br. s, 1 H, =C*H*H), 5.12 (br. s, 1 H, =CH*H*), 4.92–4.82 (m, 3 H, CH_2 Bn, C*H*H Bn), 4.76 (bd, J = 1.4 Hz, 2 H, OCH_2CH=), 4.65–4.55 (m, 3 H, CH_2 Bn, CH*H* Bn), 4.48–4.43 (m, 2 H, CH_2 Bn), 4.11–4.00 (m, 3 H, H2, H3/4, H5), 3.88–3.82 (m, 2 H, H3/4, H6$_A$), 3.70 (dd, J_1 = 1.9 Hz, J_2 = 10.9 Hz, 1 H, H6$_B$), 1.95 (s, 3 H, CH_3). – ^{13}C NMR (75.1 MHz, $CDCl_3$): δ = 138.8, 138.7, 138.5 (4 × C_{quat} Bn), 134.7 (=C_{quat}), 128.5–127.3 (*C*H$_{arom}$, =C_{quat}, =*C*H), 115.8 (=*C*H$_2$), 111.9 (C1), 83.6 (C2), 80.9, 77.9 (C3, C4), 75.7, 74.9, 74.6, (3 × *C*H$_2$ Bn), 74.1 (O*C*H$_2$CH=), 73.1 (*C*H$_2$ Bn), 72.0 (C5), 68.8 (C6), 22.3 (*C*H$_3$). – MS (ESI); calcd. $C_{40}H_{42}O_6$: 618.3; found m/z 619 [M + H], 641 [M + Na]. – HRMS (FAB); calcd. $C_{40}H_{42}O_6Na$: 641.2879; found 641.2884.

2,3,4,6-Tetra-*O*-benzyl-(1*S*)-2′-methyl-8′-oxaspiro[1,5-anhydro-D-glucitol-1,7′-bicyclo[4.3.0]non-1′-en-3′-one] (12): Enyne **5** (0.40 g, 0.64 mmol) was dissolved in CH_2Cl_2 (5 mL) and $Co_2(CO)_8$ (0.24 g, 0.70 mmol) was added under a stream of nitrogen. The mixture was stirred for 1.5 h, after which TLC analysis (25% EtOAc/light petroleum) showed complete conversion of the starting compound into a high-running red spot. NMO (0.54 g, 4.0 mmol) was then added and stirring was continued for 1.5 h. TLC showed complete consumption of the cobalt complex and formation of a low-running spot. The solvent was removed and the residue subjected to column chromatography (20 to 40% EtOAc/light petroleum) giving pure **12** (0.32 g, 0.48 mmol, 76%) as a solid. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.20 (m, 20 H, H$_{arom}$), 4.94–4.85 (m, 4 H, 2 × CH_2 Bn), 4.63–4.53 (m, 5 H, 2 × CH_2 Bn, OC*H*HC=), 4.26 (d, J = 13.4 Hz, 1 H, OCH*H*C=), 4.11 (t, J = 9.3 Hz, 1 H, H3), 3.78–3.66 (m, 4 H, H4, H5, 2× H6), 3.33 (d, J = 9.5 Hz, 1 H, H2), 3.10 (m, 1 H, CH$_2$C*H*CH$_2$), 2.51 (dd, J_1 = 6.3 Hz, J_2 = 18.6 Hz, 1 H, C*H*HCO), 1.78 (d, 1 H, CH*H*CO), 1.73–1.64 (m, 4 H, CH_3, C*H*HC1), 1.53 (t, J = 12.9 Hz, 1 H, CH*H*C1). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 207.5 (C=O), 165.2 (*C*=C–CO), 138.2, 137.7, 137.1 (4 × C_{quat} Bn), 134.2 (=*C*–*C*O), 128.7–127.3 (*C*H$_{arom}$), 98.3 (C1), 83.0, 81.6, 78.1 (C2, C3, C4), 75.6, 75.4, 74.7, 73.1 (4 × *C*H$_2$ Bn), 71.5 (C5), 68.4 (C6), 58.4 (O*C*H$_2$C=), 40.3 (*C*H$_2$CO), 38.2 (*C*H$_2$C1), 32.1 (CH$_2$*C*HCH$_2$), 7.4 (*C*H$_3$). – MS (ESI); calcd. $C_{42}H_{44}O_7$: 660.3; found m/z 661 (M + H). – $C_{42}H_{44}O_7$: C 76.34, H 6.71; found C 76.71, H 6.89.

2,3,4,6-Tetra-*O*-benzyl-(1*S*,5′*RIS*)-2′-methyl-7′-oxaspiro[1,5-anhydro-D-glucitol-1,6′-bicyclo[3.3.0]oct-1′-en-3′-one] (13): Enyne **7** (0.22 g, 0.35 mmol) was treated as described for the conversion of **5** into **12**, yielding **13** (0.15 g, 0.23 mmol, 66%) as an inseparable 7:1 mixture of diastereoisomers. **Main isomer:** ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46–7.25 (m, 20 H, H$_{arom}$), 4.99–4.94 (m, 3 H, CH_2 Bn, C*H*H Bn), 4.85 (d, 1 H, CH*H* Bn), 4.71 (bd, J = 14.5 Hz, 1 H, OC*H*HC=), 4.69 (d, 1 H, CH*H* Bn), 4.61 (d, 1 H, C*H*H Bn), 4.46 (bd, 1 H, OCH*H*C=), 4.43 (AB, 2 H, CH_2 Bn), 4.12 (t, J = 9.4 Hz, 1 H, H3), 3.80 (ddd, J = 10.4 Hz, 1 H, H5), 3.65–3.60 (m, 2 H, H4, H6$_A$), 3.52–3.50 (m, 2 H, H2, H6$_B$), 3.10 (m, 1 H, C*H*CH$_2$CO), 2.13 (dd, J_1 = 3.4 Hz, J_2 = 17.6 Hz, 1 H, C*H*HCO), 1.68–1.64 (m, 4 H, CH*H*CO, CH_3). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 209.5 (C=O), 173.0 (*C*=C–CO), 138.4, 138.0, 137.0 (4 × C_{quat} Bn), 132.2 (=*C*–*C*O), 129.2–127.2 (*C*H$_{arom}$), 103.6 (C1), 83.9, 78.2, 76.8 (C2, C3, C4), 75.5, 75.1, 74.8, 72.8 (4 × *C*H$_2$ Bn), 71.9 (C5), 68.1 (C6), 64.5 (O*C*H$_2$C=), 46.7 (*C*HCH$_2$CO), 35.1 (*C*H$_2$CO), 8.7 (*C*H$_3$). – MS (ESI); calcd. $C_{41}H_{42}O_7$: 646.3; found m/z 647 [M + H]. – $C_{41}H_{42}O_7$: C 76.14, H 6.55; found C 75.76, H 6.92.

2,3,4,6-Tetra-*O*-benzyl-(1*S*,5′*RIS*)-2′-methyl-7′-oxaspiro[1,5-anhydro-D-glucitol-1,8′-bicyclo[3.3.0]oct-1′-en-3′-one] (14a/b): Enyne **8** (0.54 g, 0.87 mmol) was treated as described for the conversion of **5** into **12**, with the exception that stirring with NMO was continued for 4 h to give **14a** (0.34 g, 0.52 mmol, 60%) and **14b** (69 mg, 0.11 mmol, 12%). **14a:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.18 (m, 20 H, H$_{arom}$), 5.00–4.44 (m, 8 H, 4 × CH_2 Bn), 4.29 (t, J = 7.6 Hz, 1 H, OC*H*HCHCH$_2$), 4.07 (t, J = 9.3 Hz, 1 H, H3), 3.96 (ddd, J_1 = 10.0 Hz, J_2 = 3.4 Hz, J_3 = 1.8 Hz, 1 H, H5), 3.82 (t, J = 9.2 Hz, 1 H, H4), 3.80–3.76 (m, 2 H, H2, H6$_A$), 3.61 (dd, J_1 = 11.1 Hz, J_2 = 1.8 Hz, 1 H, H6$_B$), 3.44 (dd, J_1 = 11.0 Hz, J_2 = 7.8 Hz, 1 H, OCH*H*CHCH$_2$), 3.16 (m, 1 H, CH$_2$C*H*CH$_2$), 2.48 (dd, J_1 = 6.3 Hz, J_2 = 17.9 Hz, 1 H, C*H*HCO), 2.07 (dd, J = 3.4 Hz, 1 H, CH*H*CO), 1.59 (d, J = 2.5 Hz, 3 H, CH_3). – ^{13}C NMR (75.1 MHz, $CDCl_3$): δ = 209.6 (CO), 174.5 (*C*=C–CO), 138.4, 138.3, 138.1, 137.0 (4 × C_{quat} Bn), 135.2 (=*C*–*C*O), 128.7–126.9 (*C*H$_{arom}$), 102.7 (C1), 83.8 (C3), 79.8 (C2), 77.9 (C4), 75.7, 75.1, 75.0 (3 × *C*H$_2$ Bn), 73.1 (C5), 73.0 (*C*H$_2$ Bn), 71.1 (O*C*H$_2$CHCH$_2$), 68.5 (C6), 44.2 (CH$_2$*C*HCH$_2$), 38.6 (*C*H$_2$CO), 8.0 (*C*H$_3$). – MS (ESI); calcd. $C_{41}H_{42}O_7$: 646.3; found m/z 669 [M + Na]. – HRMS (FAB); calcd. $C_{41}H_{42}O_7Na$: 669.2828; found 669.2817.

14b: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.14 (m, 20 H, H$_{arom}$), 4.98–4.40 (m, 8 H, 4 × CH_2 Bn), 4.36 (t, J = 7.6 Hz, 1 H, OC*H*HCHCH$_2$), 4.13 (t, J = 9.3 Hz, 1 H, H3), 3.96 (ddd, J_1 = 10.0 Hz, J_2 = 3.4 Hz, J_3 = 1.8 Hz, 1 H, H5), 3.82 (t, J = 9.2 Hz, 1 H, H4), 3.76–3.69 (m, 2 H, H2, H6$_A$), 3.56 (dd, J_1 = 11.1 Hz, J_2 = 1.8 Hz, 1 H, H6$_B$), 3.38 (dd, J_1 = 11.0 Hz, J_2 = 7.8 Hz, 1 H, OCH*H*CHCH$_2$), 2.91 (m, 1 H, CH$_2$C*H*CH$_2$), 2.57 (dd, 1 H, C*H*HCO), 2.18 (dd, 1 H, CH*H*CO), 1.68 (d, 3 H, CH_3). – ^{13}C NMR (50.1 MHz, $CDCl_3$): δ = 209.1, 171.5, 138.4–136.9, 132.7, 128.5–126.8, 101.3, 84.2, 80.7, 77.9, 75.6–73.2, 72.5, 72.7, 68.5, 41.9, 39.0, 8.8. – MS (ESI); calcd. $C_{41}H_{42}O_7$: 646.3; found m/z 669 (M + Na).

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