Articles

Asymmetric Pauson−Khand Reaction. Cobalt-Mediated Cycloisomerization of 1,6-Enynes in Carbohydrate Templates: Synthesis of Bis-Heteroannulated Pyranosides†

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The Pauson−Khand reaction on the carbohydrate derived precursors **1**−**6** is reported. We have described for the first time the cobalt-mediated cyclization of some *O*-branched chain 1,6-enynes in carbohydrate templates. The resulting bis-heteroannulated pyranosides **17**−**22** have been obtained in diastereomerically pure form, in moderate to good yield, and in one, simple synthetic operation. These enantiomerically pure, densely functionalized carbocycles are attractive advanced intermediates for the synthesis of complex natural products.

Introduction

Cobalt-mediated inter- and intramolecular annulations (Pauson−Khand reaction) are among the most potent methods for cyclopentenone synthesis.[1] In recent years, several modifications have improved the utility of the reaction; particularly useful has been the dry-state adsorption technique,[2] the inclusion of additives (DMSO, CH_3CN),[3] and the discovery that tertiary amine *N*-oxides accelerate the rate of cyclopentenone formation.[4]

Obviously, an asymmetric version of the Pauson−Khand reaction is highly desirable, but until 1990 no efficient approach had been described.[5] In that year Greene at al. reported the first auxiliary-directed asymmetric Pauson−Khand bicyclization;[6] in this and the following papers these authors extensively analyzed this approach in the intra-[7a] or intermolecular version.[7b] The use of chiral ligands[5] has been recently reinvestigated.[8] Chiral tertiary amine *N*-oxides have also been applied with limited success.[9] During these years homochiral enynes have also been submitted to the Pauson−Khand reaction, giving enantiomerically pure, differentially substituted cyclopentenones.[10] This is perhaps the most versatile and practical approach for the asymmetric synthesis of natural products.

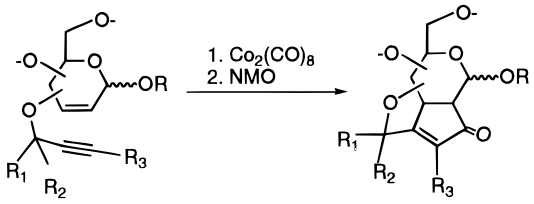

Figure 1. Pauson−Khand reaction on pyranoside templates.

In this context, in 1994, the first successful cobalt-mediated cyclization of a 1,6-enyne functionality embodied in a pyranoside substrate was reported (Figure 1).[11,12] Although sugars have been used as starting materials to prepare homochiral enynes for this annulation,[10e] in our approach, the pyranoside, without disturbing the anomeric center, was used as a chiral template for the cyclization process. A rich and highly functionalized bis-heteroannulated pyranoside should result from a simple one-pot reaction. These materials are enantiomerically pure, useful intermediates for further synthetic transformations (Ferrier carbocyclization reaction,[13a] free radical cyclization[13b]) directed to the preparation of prostanoids,[14] polyquinanes,[15] or iridoids.[16] It was also expected that the particular stereodirecting properties

† This paper is dedicated to the memory of Professor Wolfgang von Oppolzer.

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(12) Lindsell, W. E.; Preston, P. N.; Rettie, A. B. *Carbohydr. Res.* **1994**, *254*, 311 (in this paper the first synthesis and characterization of a hexacarbonyldicobalt complexes derived from 2-*O*-propynyl and 3-*O*-butynyl 4,6-dideoxy-α-D-*erythro*-hex-2-enopyranosides have been described; unfortunately, these authors were unable to transform them into the annulated cyclopentenones).

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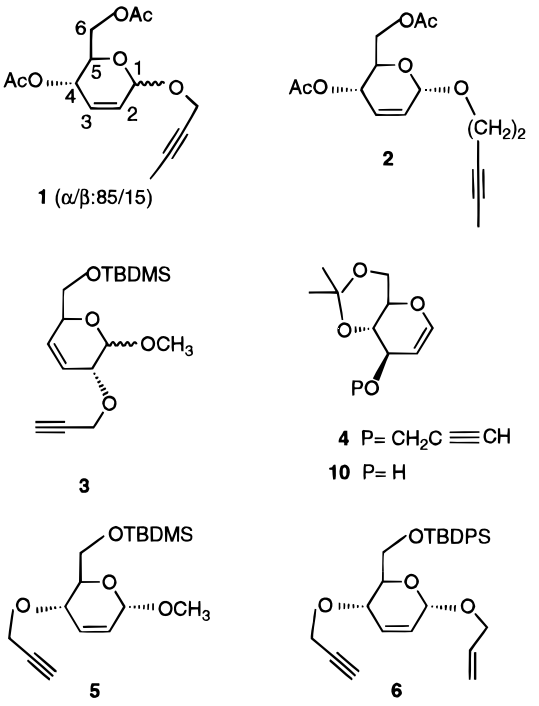
and conformational bias of these sugar derivatives offer potentially high degrees of stereochemical control in the formation of the new stereocenters. After our initial report[11] other authors, using our strategy, have described interesting results on this subject.[17]

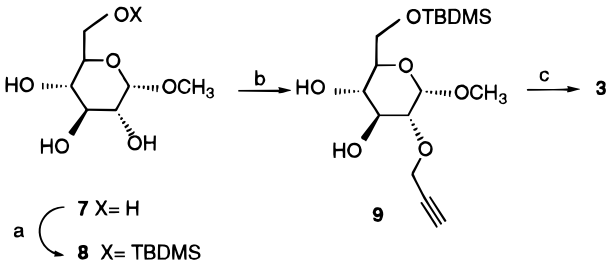
Results and Discussion

In this report, the results that have been obtained using some selected and representative 1,6-enynes in the D-glucopyranoside series are described in full. These substrates have been designed to determine general structure−reactivity trends and explore the different possibilities for the location on the functional groups on the 1,6-enyne moiety. A pyranoid nucleus allows the ideas to be examined. We have synthesized the carbohydrate-derived precursors **1**−**6**.



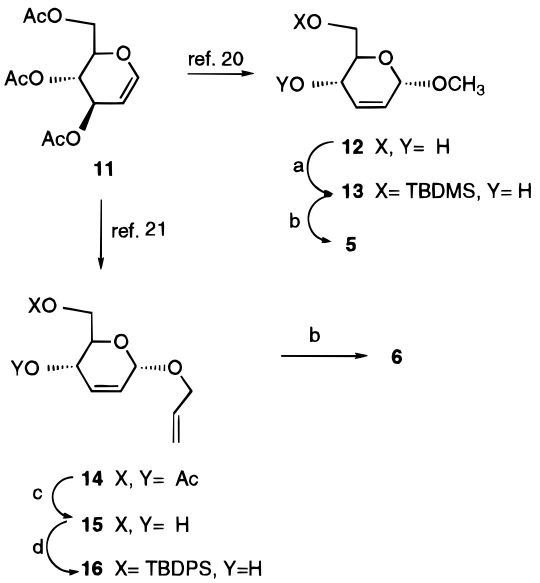
Synthesis of Enynes for the Pauson−Khand Reaction. Compounds **1** and **2**[12] are known and have been prepared by the described protocols. In these products, the *endo*-double bond is in positions C-2/C-3 and the *O*-propargyl or *O*-butynyl function has been located at C-1; the Ferrier glycosylation reaction[18] with tri-*O*-acetyl-D-glucal and the corresponding alcohol allowed preparation of an inseparable mixture of the anomers at C-1, the major isomer being the α-glycoside. Compound **3** has been obtained as shown in Scheme 1 by routine manipulations from commercial methyl α-D-glucopyranoside (**7**). In methyl glycoside **3** the *O*-propargyl branch is α orientated in C-2 and the *endo*-double bond is in positions C-3 and C-4. Product **4** has been prepared from 6,4-*O*-isopropylidene-3-*O*-propargyl-D-glucal (**10**)[19] by simple

Scheme 1[a]



[a] Reagents: (a) ClSi-*t*-BuMe$_2$, imidazole, DMF (49%); (b) (Bu$_3$Sn)$_2$O, propargyl bromide (52%); (c) Ph$_3$P, I$_2$ (48%).

Scheme 2[a]



[a] Reagents: (a) ClSi-*t*-BuMe$_2$, imidazole, DMF; (b) NaH, propargyl bromide (57% from **12**; 96% from **16**); (c) NaMeO, MeOH (90%); (d) ClSi-*t*-BuPh$_2$, imidazole, DMF (66%).

O-propargylation (77% yield). Compound **4** is a glucal with the double bond at C-1 and C-2; the *O*-propargyl arm is *β*-orientated in C-3. Finally, structures **5** and **6** have been obtained following similar synthetic sequences starting from tri-*O*-acetyl-D-glucal **11** (Scheme 2), using as intermediates the already known sugars **12**[20] or **14**.[21] In glycosides **5** and **6** the *O*-propargyl branch is α orientated in C-4, and the double bond is now at C-2 and C-3.

Briefly, these substrates have been designed in order to have the *O*-propargyl arm at C-1, C-2, C-3, and C-4 and the necessary double bond at different suitable positions for the preparation of the annulated bicyclo[3.3.0]cyclopentenones. As a consequence, the resulting Pauson−Khand molecules are annulated branched-chain sugars (or *C*-glycosides for compound **4**) at different positions in the pyranoside ring.

The Pauson−Khand Reaction. In the standard conditions for the Pauson−Khand reaction (see Experimental Section), after cobalt complex formation and *in situ* decomposition with NMO, the 1,6-enynes **1**−**6** gave the cyclopentenones **17**−**22**, in moderate to good yield, in one synthetic operation (see Figure 2). The moderate overall yield in the Pauson−Khand reaction is compen-

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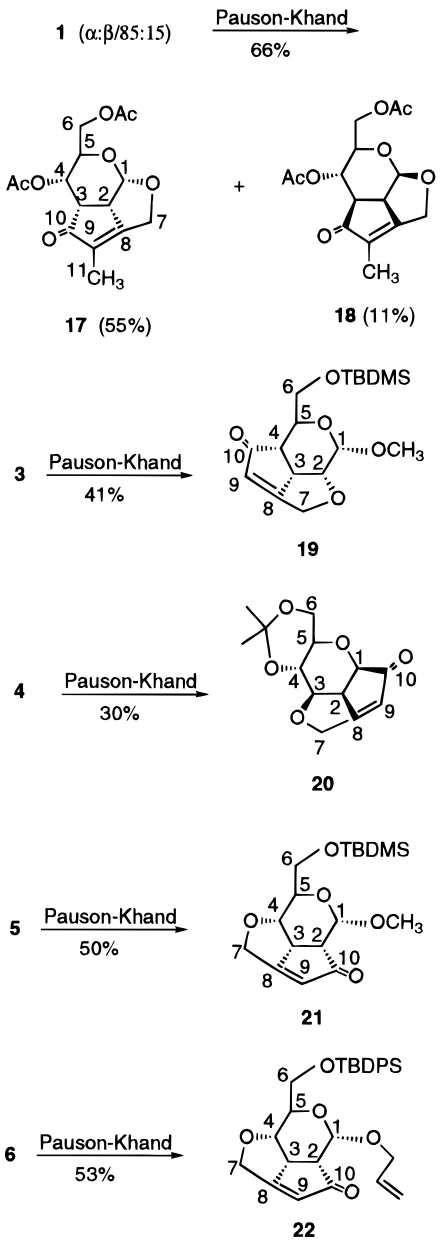

Figure 2. Pauson−Khand annulation of enynes **1** and **3**−**6**.

sated for by the efficiency of the one-pot process and the highly functionalized final products obtained, which are difficult to synthesize by other methodologies. Compounds **17**−**20** have been obtained using dry NMO, but in the case of enynes **5** and **6** we used NMO·H_2O; from the observed chemical yields it appears that each form of the reagent gives good results. Substrate **1** was submitted to cyclization as an inseparable mixture of α and β anomers; after annulation we could separate the corresponding Pauson−Khand reaction products (**17** and **18**) derived from each anomer; major isomer **17** comes from the α-glycoside. Enyne **2** afforded the hexacarbonyldicobalt complex, but after the usual treatment, only decomposition was observed and no annulated compound could be detected; this observation means that the use of *O*-butynyl side chains in order to prepare the annulated bicyclo[4.3.0] systems in these substrates are less favored than the formation of the analogous bicyclo-[3.3.0] structures, easily obtained from the *O*-propargyl derivatives. All the new Pauson−Khand reaction compounds showed the expected IR bands and the typical signal pattern in the NMR spectra (see Experimental Section). Compounds **17**−**22** were diastereomerically pure as we observed by ^{1}H NMR analysis. In fact, the observed vicinal coupling constants in the ^{1}H NMR spectra of products **17**−**22** (**17**: $J_{1,2} = 6.2$ Hz, $J_{2,3} = 6.7$ Hz; **18**: $J_{1,2} = 4.2$ Hz, $J_{2,3} = J_{3,4} = 6.0$ Hz; **19**: $J_{1,2} = 5.2$ Hz, $J_{2,3} = 9.1$ Hz, $J_{3,4} = 6.6$ Hz; **20** $J_{1,2} = 5.1$ Hz, $J_{2,3} = J_{3,4} = 8.4$ Hz; **21**: $J_{1,2} = 7.7$ Hz, $J_{2,3} = 7.5$ Hz, $J_{3,4} = 8.7$ Hz; **22**: $J_{1,2} = 7.6$ Hz, $J_{2,3} = 7.1$ Hz) suggested that the absolute configurations at the carbons where the fused-cyclopentenones are anchored are determined by the stereochemistry of the carbon linked to the *O*-propargyl branch. The carbonylative acetylenic insertion always takes place from the same side where the propargyl moiety is located. The cyclization of precursor **4** is particularly interesting because it gives a stereocontrolled *C*-glycosyl derivative in a one-pot reaction and complements another reported free radical based strategy for a similar transformation.[22]

Conclusions

The results reported here give a new insight in the cobalt-mediated cycloisomerization of chiral 1,6-enynes. The versatility of these pyranoside templates open many synthetic possibilities in the preparation of different types of 1,6-enyne precursors: carbon−carbon-branched chain sugars, azapropargyl chains, etc. In addition, other different transition metals (Pd,[23] Cr,[24] Zr,[25] etc.) could be applied with success to these substrates, giving rise to new types of useful synthetic intermediates. These endeavors are being pursued and will be reported in due course.

In summary, we have described for the first time the successful cobalt-mediated cyclization of some 1,6-enynes embodied in *O*-branched-chain D-glucopyranosides. The reaction conditions are very mild, the yields are modest,[26] and no special experimental conditions have to be observed. Finally, the Pauson−Khand compounds are valuable and advanced intermediates in the synthesis of some natural products.

Experimental Section

General Methods. See ref 11b.

General Procedure for *O*-Silylation. To a solution of the alcohol in anhydrous DMF (0.4 M), were added imidazole (2.2 equiv) and *tert*-butyldimethylsilyl chloride or *tert*-butyldiphenylsilyl chloride (1.1 equiv). The mixture was stirred at room temperature overnight. When the reaction was complete (TLC analysis), the mixture was diluted with methylene chloride, washed with saturated aqueous ammonium chloride solution, and extracted again with methylene chloride. The combined organic layers were back-washed with water, dried over sodium sulfate, and concentrated *in vacuo*.

General Procedure for *O*-Propargylation. To a solution of the alcohol in freshly distilled THF (0.12 M) was added sodium hydride (1.5 equiv, 60% oil suspension) in portions; gas evolution was observed. The mixture was stirred at room temperature for 3 h, and then propargyl bromide (2 equiv, 80% in toluene) was added at 0 °C. The mixture was stirred at room temperature overnight. The resulting suspension was quenched with saturated ammonium chloride and extracted

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(26) The rest of the mass was polar, unidentified material.

with diethyl ether. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*.

General Procedure for the Pauson−Khand Reaction. The substrate was placed in a round-bottomed flask that was then flushed with argon for 5−10 min. Methylene chloride was added, and $Co_2(CO)_8$ (1.1 equiv) was tipped inside. The resulting solution was stirred for 2−3 h at room temperature and cooled at 0 °C, and NMO·H_2O or dry NMO (6 equiv) was added. The cooling bath was removed and the mixture stirred at room temperature for the indicated time. The solvent was evaporated and the residue processed as indicated in each experiment.

Methyl 6-*O*-(*tert*-Butyldimethylsilyl)-α-D-glucopyranoside (8). Methyl α-D-glucopyranoside (**7**, 1.95 g, 10 mmol), submitted to the general procedure, after flash chromatography (4:6 hexanes−ethyl acetate) gave the silylated compound **8** (1.2 g, 49% yield) as a solid: mp 88−90 °C; $[\alpha]^{25}_D$ +85 (*c* 0.75, $CHCl_3$); IR (film) ν_{max} 3400 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.71 (d, J = 3 Hz, 1 H), 3.31−4.00 (m, 9 H), 3.40 (s, 3 H), 0.91 (s, 9 H), 0.12 (s, 6 H). Anal. Calcd for $C_{13}H_{28}O_6Si$: C, 50.62; H, 9.15. Found: C, 50.73; H, 9.11.

Methyl 6-*O*-(*tert*-Butyldimethylsilyl)-3-*O*-propargyl-α-D-glucopyranoside (9). Compound **8** (476 mg, 1.5 mmol) was dissolved in toluene (15 mL), and dibutyltin oxide (400 mg, 1.65 mmol) was added. The suspension was stirred and warmed at reflux for 3 h. Then, the solution was cooled, and propargyl bromide (0.48 mL, 3.3 mmol, 80% toluene solution) and tetrabutylammonium iodide (590 mg, 1.6 mmol) were added, and the reaction was stirred at room temperature overnight. The solvent was removed and the residue submitted to chromatography (1:1 hexanes−ethyl acetate) to give compound **9** (275 mg, 52% yield) as an oil: $[\alpha]^{25}_D$ +62 (*c* 1.6, $CHCl_3$); IR (film) ν_{max} 3400, 3300, 2120 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.91 (d, J = 3.4 Hz, 1 H), 4.36 (d, J = 2.2 Hz, 2 H), 3.50−4.00 (m, 5 H), 3.41 (s, 3 H), 3.16 (br s, 1 H), 2.79 (br s, 1 H), 2.48 (t, J = 2.2 Hz, 1 H), 1.75 (br s, 1 H), 0.91 (s, 9 H), 0.12 (s, 6 H). Anal. Calcd for $C_{16}H_{30}O_6Si$: C, 55.46; H, 8.72. Found: C, 55.30; H, 8.61.

Methyl 6-*O*-(*tert*-Butyldimethylsilyl)-3-*O*-propargyl-3,4-dideoxy-α-D-*erythro*-hex-2-enopyranoside (3). Diol **9** (275 mg, 0.79 mmol) was dissolved in toluene (10 mL) and treated with triphenylphosphine (602 mg, 2.3 mmol), imidazole (210 mg, 3.1 mmol), and iodine (584 mg, 2.3 mmol) at reflux for 40 min. The mixture was diluted with ethyl acetate and washed with 10% aqueous sodium thiosulfate and brine. The organic layers were washed with water, dried with sodium sulfate, filtered, and evaporated. Flash chromatoghraphy (4:1 hexanes−ethyl acetate) gave compound **3** (121 mg, 48% yield) as an oil: $[\alpha]^{25}_D$ +5 (*c* 1.5, $CHCl_3$); IR (film) ν_{max} 3300, 2120 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.85 (dt, J = 1.5, 1.8 Hz, 1 H), 5.78 (dq, J = 10.7, 1.5 Hz, 1 H), 4.99 (d, J = 3.9 Hz, 1 H), 4.32 (m, 1 H), 4.28 (d, J = 2.4 Hz, 2 H), 4.15 (m, 1 H), 3.71 (dd, J = 5.6 Hz, J = 10.3 Hz, 1 H), 3.60 (dd, J = 10.3 Hz, J = 6.0 Hz, 1 H), 3.51 (s, 3 H), 2.44 (t, J = 2.4 Hz, 1 H), 0.91 (s, 9 H), 0.12 (s, 6 H). Anal. Calcd for $C_{16}H_{28}O_4Si$: C, 61.49; H, 9.03. Found: C, 61.35; H, 8.97.

6,4-*O*-Isopropylidene-3-*O*-propargyl-D-glucal (4). Starting from 6,4-*O*-isopropylidene-3-*O*-propargyl-D-glucal (**10**)[19] (66 mg, 0.35 mmol) and following the general procedure, after flash chromatoghraphy (85:15 hexanes−ethyl acetate) we obtained compound **4** (61 mg, 77% yield) as an oil: $[\alpha]^{25}_D$ +8 (*c* 2.7, $CHCl_3$); IR (film) ν_{max} 3300, 2120, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.32 (dd, J = 16.1 Hz, J = 1.4 Hz, 1 H), 4.78 (dd, J = 16.1, 2.0 Hz, 1 H), 4.37 (dd, J = 15.6, 2.5 Hz, 1 H), 4.29 (dd, J = 15.6, 2.5 Hz, 1 H), 4.25 (ddd, J = 7.3, 2.0, 1.4 Hz, 1 H), 3.65−4.05 (m, 4 H), 2.44 (t, J = 2.5 Hz, 1 H), 1.53 (s, 3 H), 1.42 (s, 3 H). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.44; H, 7.39.

Methyl 2,3-Dideoxy-4-*O*-propargyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hex-2-enopyranoside (5). Starting from methyl 2,3-dideoxy-4,6-dihydroxy-α-D-*erythro*-hex-2-enopyranoside (**12**)[20] (1.89 g, 11.81 mmol) and following the general procedure, we obtained the silylated compound **13**, as a crude that was pure enough for further transformation. Using the general procedure, after flash chromatography (4:1 hexanes−ethyl acetate) we finally obtained the propargylated product **5** (2.1 g, 57% overall yield from **12**) as an oil: IR (film) ν_{max} 3300, 2120 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.03 (br d, J = 10.3 Hz, 1 H), 5.71 (ddd, J = 2.0, 2.7 Hz, 1 H), 4.81 (m, 1 H), 4.19 (d, J = 2.4 Hz, 2 H), 4.07 (ddd, J = 9.1, 3.3, 1.6 Hz, 1 H), 3.69−3.88 (m, 3 H), 3.38 (s, 3 H), 2.38 (t, J = 2.4 Hz, 1 H), 0.91 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 130.1, 126.6, 95.0, 76.1, 74.2, 70.2, 69.9, 62.5, 56.1, 55.3, 25.7, 18.1, −5.3; MS (70 eV) *m*/*z* 295 (M^+ − 1, 3), 281 (M^+ − 15, 100). Anal. Calcd for $C_{16}H_{28}O_4Si$: C, 61.49; H, 9.03. Found: C, 61.25; H, 8.87.

Allyl 2,3-Dideoxy-4,6-dihydroxy-α-D-*erythro*-hex-2-enopyranoside (15). Allyl 4,6-di-*O*-acetyl-α-D-*erythro*-hex-2-enopyranoside (**14**)[21] (837 mg, 3.1 mmol) was treated with sodium methoxide (cat.) in methanol (15 mL) at room temperature (2 h). The solvent was removed, and the residue was submitted to flash chromatography (1:4 hexanes−ethyl acetate) to give compound **15** (660 mg, 90%) as an oil: $[\alpha]^{25}_D$ +69 (*c* 1.1, $CHCl_3$); IR (film) ν_{max} 3600−3100, 3080, 3060, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.75−6.00 (m, 3 H), 5.19−5.35 (m, 2 H), 5.02 (s, 1 H), 3.80−4.40 (m, 6 H), 2.32 (d, J = 6.9 Hz, 1 H), 1.74 (br s, 1 H). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.90; H, 7.81.

Allyl 2,3-Dideoxy-6-*O*-(*tert*-butyldiphenylsilyl)-4-hydroxy-α-D-*erythro*-hex-2-enopyranoside (16). Starting from compound **15** (660 mg, 3.5 mmol) and following the general procedure the silylated product **16** (1.07 g, 66% yield) was obtained as an oil: $[\alpha]^{25}_D$ +12 (*c* 1.3, $CHCl_3$); IR (film) ν_{max} 3600−3100, 3080, 3060, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35−7.50 and 7.65−7.72 (m, 10 H), 5.94 (br d, J = 1.1 Hz, 1 H), 5.82 (m, 1 H), 5.75 (ddd, J = 10.3, 2.1, 2.6 Hz, 1 H), 5.24 (dq, J = 9.1, 1.7 Hz, 1 H), 5.14 (dq, J = 17.2, 1.7 Hz, 1 H), 4.97 (dd, J = 2.6, 1.1 Hz, 1 H), 3.70−4.30 (m, 6 H), 2.56 (d, J = 4.6 Hz, 1 H), 0.89 (s, 9H). Anal. Calcd for $C_{25}H_{32}O_4Si$: C, 70.72; H, 7.59. Found: C, 70.59; H, 7.77.

Allyl 2,3-Dideoxy-6-*O*-(*tert*-butyldiphenylsilyl)-4-*O*-propargyl-α-D-*erythro*-hex-2-enopyranoside (6). Starting from compound **16** (1.07 g, 2.5 mmol) and following the general procedure the propargylated product **6** (1.09 g, 96% yield) was obtained as a solid: mp 41−43 °C; $[\alpha]^{25}_D$ +31(*c* 1.2, $CHCl_3$); IR (film) ν_{max} 3300, 3080, 3060 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35−7.50 and 7.65−7.72 (m, 10 H), 6.08 (br d, J = 1.1 Hz, 1 H), 5.92 (m, 1 H), 5.80 (ddd, J = 10.3, 2.1, 2.6 Hz, 1 H), 5.24 (dq, J = 9.1, 1.7 Hz, 1 H), 5.14 (dq, J = 17.2, 1.7 Hz, 1 H), 5.07 (dd, J = 2.6, 1.1 Hz, 1 H), 3.70−4.30 (m, 8 H), 2.34 (t, J = 2.4 Hz, 1 H), 0.89 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 135.8, 135.6, 134.5, 133.8, 133.5, 130.4, 129.5, 127.6, 127.5, 126.9, 117.1, 93.3, 79.8, 74.4, 70.5, 70.2, 68.7, 63.4, 56.4, 26.8, 19.3. Anal. Calcd for $C_{28}H_{34}O_4Si$: C, 72.68; H, 7.40. Found: C, 72.49; H, 7.27.

Pauson−Khand Products 17 and 18. Starting from compound **1** (87 mg, 0.3 mmol; as a mixture of anomers α:*β*/85:15) and following the general procedure (2 h 30 min for the formation of the complex and 5 h 30 min for the NMO treatment), after flash chromatography (2:3 hexanes−ethyl acetate) compounds **17** (49 mg, 55% yield) and **18** (10 mg, 11% yield) were obtained. **17**: oil; $[\alpha]^{25}_D$ −17 (*c* 2.3, $CHCl_3$); IR (film) ν_{max} 1760−1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59 (d, J = 6.2 Hz, 1 H), 4.97 (dd, J = 8.9, 10.3 Hz, 1 H), 4.84 (d, J = 14.6 Hz, 1 H), 4.59 (d, J = 14.6 Hz, 1 H), 4.17 dd, J = 11.7, 4.1 Hz, 1 H), 4.10 (dd, J = 11.7, 2.7 Hz, 1 H), 3.70 (ddd, J = 2.7, 4.1, 10.3 Hz, 1 H), 3.50 (d, J = 6.2, 6.7 Hz, 1 H), 3.35 (m, 1 H), 2.08, 2.05 (s, s, 3 H, 3 H), 1.82 (br s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 172.3, 170.5, 169.8, 134.6, 96.2, 66.6, 66.1, 65.1, 62.7, 45.4, 44.9, 20.6, 9.1. Anal. Calcd for $C_{15}H_{18}O_7$: C, 58.06; H, 5.85. Found: 57.85; H, 6.10. **18**: oil; $[\alpha]^{25}_D$ +6 (*c* 0.69, $CHCl_3$); IR (film) ν_{max} 1760−1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.43 (d, J = 4.2 Hz, 1 H), 4.83−4.68 (m, 3 H), 4.11 (dd, J = 12.0 Hz, J = 5.7 Hz, 1 H), 4.00 (dd, J = 12.0 Hz, J = 3.0 Hz, 1 H), 3.70 (ddd, J = 5.7, 3.0, 2.8 Hz, 1 H), 3.28 (m, 1 H), 3.02 (t, J = 6.0 Hz, 1 H), 2.11, 2.04 (s, s, 3 H, 3 H), 1.82 (br s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 170.4, 169.4, 169.3, 133.3, 98.4, 74.1, 66.2, 65.8, 63.1, 50.6, 46.3, 20.7, 20.55, 9.2. Anal. Calcd for $C_{15}H_{18}O_7$: C, 58.06; H, 5.85. Found: 57.95; H, 6.08.

Pauson−Khand Product 19. Starting from compound **3**

(121 mg, 0.38 mmol) and following the general procedure (2 h 30 min for the formation of the complex and 2 h for the NMO treatment), after flash chromatography (2:3 hexanes−ethyl acetate) compound **19** (51 mg, 41% yield) was obtained: oil; $[\alpha]^{25}_D$ −57 (*c* 1.9, $CHCl_3$); IR (film) ν_{max} 1760−1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.95 (br s, 1 H), 4.78 (d, J = 5.2 Hz, 1 H), 4.76 (d, J = 15.8 Hz, 1 H), 4.71 (d, J = 15.8 Hz, 1 H), 4.33 (dd, J = 5.2, 9.1 Hz, 1 H), 3.91 (dd, J = 11.2, 2.2 Hz, 1 H), 3.74 (dd, J = 11.2, 6.7 Hz, 1 H), 3.48 (ddd, J = 2.2, 6.7 Hz, 10.5 Hz, 1 H), 3.41 (m, 1 H), 3.29 (s, 3 H), 2.79 (dd, J = 10.5, 6.6 Hz, 1 H), 0.89, 0.087 (s, s, 9 H, 6 H); ^{13}C NMR (75 MHz $CDCl_3$) δ 209.1, 182.6, 121.5, 98.3, 71.7, 65.4, 67.4, 64.5, 55.4, 47.5, 44.9, 25.8, 18.3, −5.4. Anal. Calcd for $C_{17}H_{28}O_5Si$: C, 59.96; H, 8.28. Found: C, 59.77; H, 8.47.

Pauson−Khand Product 20. Starting from compound **4** (31 mg, 0.13 mmol) and following the general procedure (3 h for the formation of the complex and 3 h for the NMO treatment), after flash chromatography (1:1 hexanes−ethyl acetate) compound **20** (10 mg, 30% yield) was obtained as a solid: mp 145−148 °C; $[\alpha]^{25}_D$ −190 (*c* 0.13, $CHCl_3$); IR (film) ν_{max} 1760−1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07 (br s, 1 H), 4.76 (br s, 2 H), 4.40 (d, J = 5.1 Hz, 1 H), 4.36 (d, J = 8.4 Hz, 1 H), 3.91 (dd, J = 11.1, 6.0 Hz, 1 H), 3.62 (dd, J = 11.1, 9.9 Hz, 1 H), 3.49−3.43 (m, 2 H), 3.27 (ddd, J = 6.0, 9.9, 5.7 Hz, 1 H), 1.42, 1.47 (s, s, 3 H, 3 H); ^{13}C NMR (75 MHz $CDCl_3$) δ 203.5, 179.0, 121.8, 99.6, 77.1, 76.5, 71.7, 68.9, 65.4, 61.6, 47.9, 28.9, 18.3. Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 61.57; H, 6.11.

Pauson−Khand Product 21. Starting from compound **5** (302 mg, 0.97 mmol) and following the general procedure (3 h for the formation of the complex and overnight for the NMO treatment), after flash chromatography (4:1 hexanes−ethyl acetate) compound **21** (204 mg, 62% yield) was obtained: oil; $[\alpha]^{25}_D$ +160 (*c* 1.16, EtOH); IR (film) ν_{max} 1760−1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.70 (br s, 1 H), 4.79 (d, J = 7.7 Hz, 1 H), 3.99 (s, 2 H), 3.90−3.86 (m, 2 H), 3.66 (dd, J = 11.1, 6.5 Hz, 1 H), 3.41 (m, 1 H), 3.09 (s, 3 H), 2.87 (dd, J = 7.7, 7.5 Hz, 1 H), 2.67 (m, 1 H), 0.89, 0.087 (s, s, 9 H, 6 H); ^{13}C NMR (75 MHz $CDCl_3$) δ 206.9, 178.6, 125.1, 96.5, 70.6, 66.6, 65.2, 63.0, 55.2, 51.7, 45.4, 25.8, 18.3, −5.4. Anal. Calcd for $C_{17}H_{28}O_5Si$: C, 59.96; H, 8.28. Found: C, 59.75; H, 8.02.

Pauson−Khand Product 22. Starting from compound **6** (289 mg, 0.62 mmol) and following the general procedure (1 h for the formation of the complex and 4 h for the NMO treatment), after flash chromatography (4:1 hexanes−ethyl acetate) compound **22** (166 mg, 53% yield) was obtained: oil; $[\alpha]^{25}_D$ +136 (*c* 1.08, $CHCl_3$); IR (film) ν_{max} 1760−1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70−7.30 (m, 10 H), 5.90 (br s, 1 H), 5.76 (m, 1H), 5.06 (d, J = 7.6 Hz, 1 H), 5.15−5.00 (m, 2 H), 4.59 (d, J = 15.8 Hz, 1 H), 4.50 (d, J = 15.8 Hz, 1 H), 4.42 (ddd, J = 15.7, 1.5, 1.5 Hz, 1 H), 4.38 (ddd, J = 15.7 Hz, J = 1.5, 1.5 Hz, 1 H), 3.98 (m, 1 H), 3.76 (dd, J = 11.3, 6.5 Hz, 1 H), 3.62 (dd, J = 11.3, 2.2 Hz, 1 H), 3.40 (ddd, J = 6.5, 2.2, 9.1 Hz, 1 H), 3.26 (m, 1 H), 3.16 (dd, J = 7.6, 7.1 Hz, 1 H), 0.89 (s, 9H); ^{13}C NMR (75 MHz $CDCl_3$) δ 206.7, 178.3, 133.5, 135.6, 133.4, 129.6, 127.6, 125.1, 116.4, 94.3, 70.7, 66.8, 67.8, 65.2, 63.9, 51.6, 45.5, 26.7, 19.1. Anal. Calcd for $C_{29}H_{34}O_5Si$: C, 70.98; H, 6.98. Found: C, 70.65; H, 6.77.

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