Synthesis of Seven-Membered Ring Glycals via *Endo*-Selective Alkynol Cycloisomerization

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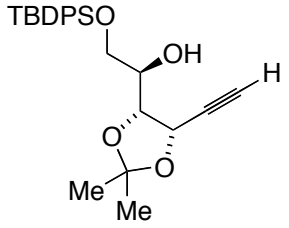
SUPPORTING INFORMATION

Contents:

General: ^{1}H NMR spectra were recorded at either 300 MHz on a Varian Mercury-300, at 400 MHz on an Inova-400 spectrometer, or at 600 MHz on an INOVA-600 spectrometer. ^{13}C NMR spectra were recorded at 75 MHz, 100 MHz, or 150 MHz on the same instruments. NMR spectra were recorded in deuterated chloroform ($CDCl_3$) solutions, with residual chloroform (δ 7.26 ppm for ^{1}H NMR and δ 77.00 ppm for ^{13}C NMR) taken as the internal standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer as neat films. Elemental analyses were performed by Atlantic Microlab Inc, P. O. Box 2288, Norcross, Georgia. Analytical Thin Layer Chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel 60 F_{254}; 0.25mm thickness). Flash column chromatography was conducted with silica gel 60 (230-400 mesh ASTM) from EM Science. Optical rotations were recorded with Perkin-Elmer model 241 or 341 polarimeters.

All reactions were carried out with anhydrous solvents in oven-dried or flame-dried and argon-charged glassware. All anhydrous solvents except as mentioned were freshly distilled. All solvents used in workup, extraction procedures and chromatography were used as received from commercial suppliers without prior purification. During reaction workup, the reaction mixture was usually diluted to three times the original volume, and washed with equal volume of water and/or aqueous solutions as needed. All reagents were purchased from the Aldrich Chemical Company.

(2*R*,3*R*,4*S*)-1-(*tert*-butyldiphenylsilyloxy)-3,4-(isopropylidenedioxy)-hex-5-yne-1,2-diol (4).

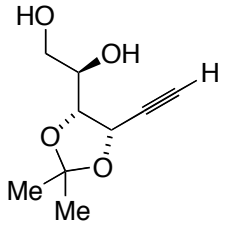


4

To a solution of $ClCH_2PPh_3Cl$ (3.24 g, 9.32 mmol) in THF (10 mL) was added dropwise BuLi (1.6 M in hexanes, 6.8 ml, 9.32 mmol), followed by TMEDA (1.4 ml, 9.32 mmol) and a solution of the 5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-D-ribofuranose (**3**, 1.0 g, 2.33 mmol) in 10 mL of THF. The reaction was stirred at room temperature for 1.5 hours and quenched with a saturated solution of NH_4Cl (130 mL). The solution was extracted with CH_2Cl_2, dried with $MgSO_4$ and evaporated. After a quick purification of the alkene this was dissolved in THF (5 mL), cooled at -78°C and treated dropwise with *n*-BuLi (1.6 M in hexanes, 5.7 mL, 9.10 mmol). After agitation during one hour the reaction was quenched with a saturated solution of NH_4Cl and extracted with CH_2Cl_2. After purification 596 mg (62%) of the alkynyl alcohol **4** was recovered.

m.p.: 82-83 °C; $[\alpha]^{23}_D$ = -18.88 ($CHCl_3$, c = 1.29); IR (neat): 3468, 3308, 3071, 3050, 2933, 2859, 2116, 1589, 1464, 1428, 1372, 1226, 1113, 1076, 967, 901, 865, 823, 740, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75-7.65 (m, 4H), 7.45-7.35 (m, 6H), 4.95 (dd, *J* = 5.8, 2.2 Hz, 1H), 4.17 (dd, *J* = 8.8, 5.6 Hz, 1H), 4.08 (m, 1H), 3.95 (dd, *J* = 10.6, 3.0 Hz, 1H), 3.90 (dd, *J* = 10.4, 4.4 Hz, 1H), 2.72 (d, *J* = 6.4 Hz, 1H), 2.57 (d, *J* = 2.0 Hz, 1H), 1.51 (s, 3H), 1.36 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz) δ 135.5, 135.5, 134.8, 133.0, 132.8, 129.8, 127.7, 127.6, 110.8, 80.2, 75.8, 72.7, 71.1, 68.6, 65.0, 27.5, 26.9, 26.0, 19.3.

(2*R*,3*R*,4*S*)-3,4-isopropylidenedioxy-hex-5-yne-1,2-diol (5).[1]



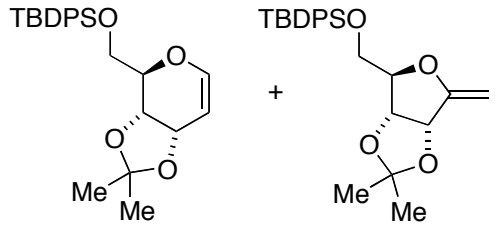
5

A solution of 5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-D-ribofuranose (**3**, 1.00 g, 2.33 mmol) and K_2CO_3 (966 mg, 6.99 mmol) in methanol (6 mL) at reflux was treated with a solution of dimethyl(diazo-2-oxopropyl)phosphonate (1.34 g, 6.99 mmol) in methanol (5 mL) dropwise over 8 hours. The reaction mixture was cooled and the precipitate filtered. Then the solution was neutralized with 1N HCl and evaporated at reduced pressure. Extractive work-up (EtOAc / H_2O) and silica gel chromatography (hexanes : EtOAc 4:1 to 1:1) gave the alkynyl diol **5** (218 mg, 50%).

m.p.: 71-72 °C; $[\alpha]^{23}_D$ = -16.91 ($CHCl_3$, c = 1.55); IR (neat): 3419, 3216, 2966, 2920, 2875, 2116, 1424, 1388, 1324, 1269, 1211, 1155, 1126, 1090, 1040, 1001, 923, 898, 834, 747, 724 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.66 (dd, *J* = 6.0, 1.8 Hz, 1H), 4.08 (t, *J* = 6.3 Hz, 1H), 3.81 (m, 1H), 3.74 (dt, *J* = 12.0, 3.6 Hz, 1H), 3.63 (dd, *J* = 11.4, 6.6 Hz, 1H), 3.11 (bs, 1H), 2.74 (bs, 1H), 2.56 (d, *J* = 1.8 Hz, 1H), 1.46 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (150 MHz) δ 110.8, 81.6, 81.5, 74.7, 71.7, 66.7, 63.1, 26.7, 25.8; Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.90; H, 7.59.

[1] Thiéry, J.-C.; Fréchou, C.; Demailly, G. *Tetrahedron Lett.* **2000**, *41*, 6337.

(2*R*,3*R*,4*S*)-2-*(tert*-butyldiphenylsilyloxymethyl)-3,4-isopropylidenedioxy-3,4-dihydro-2H-pyran (6) and (3*S*,4*R*,5*R*)-5-*(tert*-butyldiphenylsilyloxymethyl)-2-methylene-3,4-isopropylidenedioxy-tetrahydrofuran (7).



6 **7**

A flame-dried Schlenk flask fitted with a reflux condenser and a stir bar, under argon atmosphere, was charged with tungsten hexacarbonyl (68 mg, 0.19 mmol, dried under vacuum), alkynyl alcohol **4** (320 mg, 0.76 mmol, azeotropically dried from toluene), and DABCO (sublimed, 224 mg, 1.95 mmol), and this mixture was dissolved in toluene (3.6 mL). The solution was deoxygenated and then irradiated under an inert atmosphere for 5 h at 350 nm (Rayonet photoreactor) without cooling, to reach approximately 70°C. Volatile components were removed under reduced pressure and the product was purified by silica gel chromatography (hexanes : EtOAc 4:1 to 1:1 plus 0.1% Et_3N) to provide the 6-*endo* glycal **6** (256 mg, 80% yield) contaminated by ca. 5% of the 5-*exo* glycal **7**.

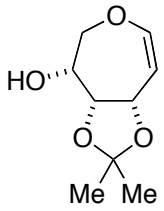
6-membered ring glycal (6):

$[\alpha]^{23}_D$ = +84.44 ($CHCl_3$, c = 0.81); IR (neat): 2931, 2856, 1642, 1428, 1371, 1230, 1216, 1150, 1113, 1064,986, 867, 823, 789, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73-7.70 (m, 4H), 7.45-7.35 (m, 6H), 6.66 (d, *J* = 6.0 Hz, 1H), 5.10 (dd, *J* = 5.8, 4.6 Hz, 1H), 4.64 (t, *J* = 5.0 Hz, 1H), 4.11 (dd, *J* = 9.8, 5.4 Hz, 1H), 4.03 (dd, *J* = 11.4, 2.2 Hz, 1H), 3.93 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.49 (ddd, *J* = 9.6, 5.2, 2.4 Hz, 1H), 1.40 (s, 3H), 1.38 (s, 3H), 1.07 (s, 9H); ^{13}C NMR (100 MHz) δ 148.3, 135.7, 135.6, 133.5, 133.5, 133.4, 129.6, 127.6, 108.3, 98.6, 76.3, 70.1, 67.6, 67.5, 62.8, 28.6, 26.8, 25.8, 19.3; Anal. Calcd for $C_{25}H_{32}O_4Si$: C, 70.72; H, 7.60. Found: C, 70.78; H, 7.63.

5-membered ring glycal (7):

$[\alpha]^{23}_D$ = -25.84 ($CHCl_3$, c = 0.37); IR (neat): 2931, 2858, 1674, 1427, 1380, 1252, 1223, 1155, 1113, 1083, 974, 870, 822, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68-7.65 (m, 4H), 7.45-7.35 (m, 6H), 5.12 (d, *J* = 6.0 Hz, 1H), 4.78 (d, *J* = 6.0 Hz, 1H), 4.49 (s, 1H), 4.41 (s, 1H), 4.22 (s, 1H), 3.79 (dd, *J* = 11.0, 3.0 Hz, 1H), 3.71 (dd, *J* = 11.4, 2.6 Hz, 1H), 1.52 (s, 3H), 1.40 (s, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz) δ 163.3, 135.6, 135.5, 132.9, 132.6, 129.9, 129.8, 127.8, 127.7, 112.6, 85.9, 84.0, 80.8, 80.3, 64.8, 27.1, 26.7, 25.9, 19.0.

(3*R*,4*R*,5*S*)-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine-3-ol (8).



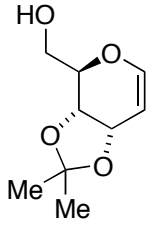
8

A flame-dried Schlenk flask fitted with a reflux condenser and a stir bar, under argon atmosphere, was charged with tungsten hexacarbonyl (58 mg, 0.16 mmol, dried under vacuum) and alkynyl diol **5** (200 mg, 1.07 mmol, azeotropically dried from toluene). This mixture was dissolved in freshly distilled dry THF (5.4 mL) and triethylamine (1.35 mL). The solution was deoxygenated and then irradiated under an inert atmosphere for 5 h at 350 nm (Rayonet photoreactor) without cooling, so that the solvent reflux point was reached. Volatile components were removed under reduced pressure and the product was purified by silica gel chromatography (hexanes : EtOAc 4:1 to 1:1 plus 0.1% Et_3N) gave the seven-membered glycal **8** (136 mg, 68%) separated from approximately 2% of the six-membered glycal byproduct.

7-membered ring glycal (8):

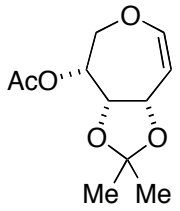
$[\alpha]^{23}_D$ = -66.47 ($CHCl_3$, c=0.73); IR (neat): 3472, 2985, 2926, 2855, 1640, 1459, 1372, 1332, 1238, 1168, 1121, 1083, 1020, 979, 910, 863, 788, 734, 679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (dd, *J* = 6.4, 2.0 Hz, 1H), 5.16 (dd, *J* = 6.4, 2.0 Hz, 1H), 4.87 (dt, *J* = 10.0, 2.0 Hz, 1H), 4.39 (dt, *J* = 8.4, 4.3 Hz, 1H), 4.22 (dd, *J* = 12.4, 5.2 Hz, 1H), 3.85 (dd, *J* = 9.6, 4.0 Hz, 1H), 3.75 (dd, *J* = 12.4, 8.0 Hz, 1H), 2.63 (bs, 1H), 1.46 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz) δ 148.6, 109.5, 108.8, 80.1, 72.7, 71.9, 65.9, 27.2, 26.5.

6-membered ring glycal:



^1H NMR (400 MHz, $CDCl_3$) δ 6.64 (d, *J* = 6.0 Hz, 1H), 5.16 (t, *J* = 5.2 Hz, 1H), 4.45 (t, *J* = 5.0 Hz, 1H), 4.03 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.96 (m, 1H), 3.83 (dd, *J* = 11.8, 5.0 Hz, 1H), 3.45 (ddd, *J* = 10.0, 5.6, 2.8 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (100 MHz) δ 148.2, 108.8, 99.6, 76.0, 70.5, 67.8, 62.2, 29.9, 28.7.

(3*R*,4*R*,5*S*)-3-acetoxy-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine (9).

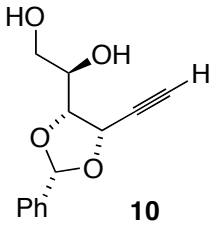


9

The same procedure for the synthesis of **8** was followed using alkynyl diol **5** (1.40 g, 7.53 mmol), $W(CO)_6$ (272 mg, 0.753 mmol) and Et_3N (18.75 mL) in THF (75 mL). In this case after the cycloisomerization reaction the crude was acetylated with Ac_2O (1.9 g, 18.6 mmol), Et_3N (1.8 mL), DMAP (20 mg) in CH_2Cl_2 (75 mL), affording after silica chromatography (Hexanes : EtOAc 4:1 plus 0.1% Et_3N) the desired ester **9** (1.33 g, 82%).

$[\alpha]^{23}_D$ = -77.89 ($CHCl_3$, c = 1.62); IR (neat): 3058, 2986, 2936, 2887, 1747, 1641, 1456, 1372, 1235, 1171, 1098, 1066, 1050, 1026, 990, 942, 897, 867, 805, 748, 715, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (dd, *J* = 6.0, 2.4 Hz, 1H), 5.48 (dt, *J* = 6.4, 3.6 Hz, 1H), 5.29 (dd, *J* = 6.2, 2.2 Hz, 1H), 4.89 (dt, *J* = 9.4, 2.2 Hz, 1H), 4.03 (dd, *J* = 12.8, 4.0 Hz, 1H), 3.89 (dd, *J* = 12.8, 6.2 Hz, 1H), 3.82 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.10 (s, 3H), 1.41 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz) δ 169.9, 148.0, 109.5, 111.8, 109.6, 78.4, 72.1, 70.3, 67.5, 27.0, 26.2, 20.8; Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.85; H, 7.03.

(2*R*,3*R*,4*S*)-3,4-benzylidene-dioxy-hex-5-yne-1,2-diol (10)



10

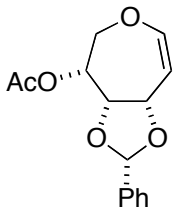
A solution of 2,3-*O*-(*R*)-benzylidene-D-ribofuranose[2] (1.0663 g, 4.4778 mmol) and K_2CO_3 (1.8527 g, 13.400 mmol) in methanol (11.5 mL) was heated to reflux. To this mixture was added a solution of dimethyl(diazo-2-oxopropyl)phosphonate (2.5795 g, 13.434 mmol) in methanol (9.5 mL) dropwise over 8 hours. The reaction mixture was cooled and neutralized with 1 M HCl and evaporated at reduced pressure. Extractive work-up (EtOAc / H_2O) and silica gel

[2] Chan, L.; Just, G. *Tetrahedron*, **1990**, *46*, 151.

chromatography (1:1 pentane/ethyl ether) gave the alkynyl diol **10** (0.3160 g, 30%) as a white solid.

m.p.: 126-127 ºC; $[\alpha]^{23}_{D}$ = -20.9 (MeOH, c = 0.88); IR(neat): 3291, 3172, 2926, 2119, 1732, 1466, 1406, 1314, 1270, 1221, 1088, 1069, 967, 759 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (mult, 2H); 7.41 (mult, 3H); 6.03 (s, 1H); 4.98 (dd, *J* = 4.8, 2.0 Hz, 1H); 4.26 (t, *J* = 5.6 Hz, 1H); 3.92 (app dt, *J* = 5.6, 3.9 Hz, 1H); 3.85 (dd, *J* = 11.5, 3.6 Hz, 1H); 3.76 (dd, *J* = 11.8, 5.6 Hz, 1H); 2.64 (d, *J* = 2.2 Hz, 1H); 2.49 (br s, 1H); 1.86 (br s, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 137.9, 130.8, 128.2, 105.1, 84.6, 82.7, 76.6, 73.8, 69.3, 64.4; Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.43; H, 6.20.

(3*R*,4*R*,5*S*)-3-acetoxy-4,5-benzylidene-dioxy-2,3,4,5-tetrahydrooxepine (11)

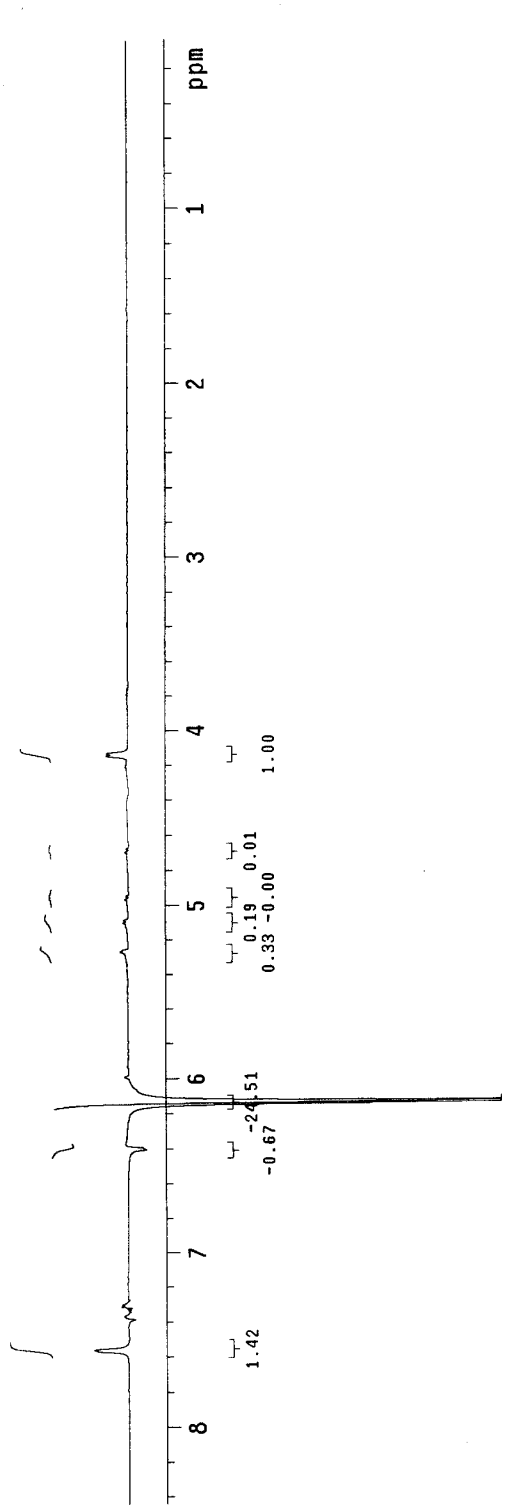


11

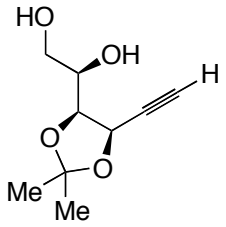
A flame-dried Schlenk flask, reflux condenser, and stir bar was charged with alkynyl diol **10** (0.1142 g, 0.4878 mmol, azeotropically dried from toluene), tungsten hexacarbonyl (0.0246 g, 0.0699 mmol) and, freshly sublimed DABCO (0.1099 g, 0.9797 mmol). The mixture was dissolved in toluene (2.5 mL) and irradiated at 350 nm for 6 h at 70 ºC. Upon completion, volatile components were removed under reduced pressure. To the crude mixture was added CH_2Cl_2 (2.0 mL), followed by acetic anhydride (70 μL, 0.742 mmol), and DMAP (0.1197g, 0.9798 mmol). After 1 h, volatiles were removed and the product was purified by silica gel chromatography (9:1 pentane/ethyl ether plus 1% triethylamine) to give the seven-membered glycal **11** (0.1102 g, 82%) as a clear oil.

$[\alpha]^{23}_{D}$ = -9.9 ($CHCl_3$, c = 0.74); IR(neat): 3635, 3474, 3061, 3034, 2918, 2892, 1744, 1638, 1494, 1458, 1371, 1324, 1233, 1104, 1069, 969 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (mult, 2H); 7.38 (mult, 3H); 6.43 (dd, *J* = 6.2, 2.4 Hz, 1H); 6.16 (s, 1H); 5.69 (app dt, *J* = 6.2, 3.8 Hz, 1H); 5.42 (dd, *J* = 6.2, 2.4 Hz, 1H); 4.97 (dt, *J* = 10.0, 2.4, 1.9 Hz, 1H); 4.15 (dd, *J* = 12.9, 3.8 Hz, 1H); 4.06 (dd, *J* = 9.5, 3.3 Hz, 1H); 3.95 (dd, 12.9, 6.7 Hz, 1H); 2.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3, 148.5, 139.3, 129.3, 128.5, 126.3, 111.8, 104.4, 80.3, 72.2, 70.7, 67.6, 21.1; Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.42; H, 5.99.

nOe spectrum of **11** (600 MHz, $CDCl_3$):



(2*R*,3*S*,4*R*)-3,4-isopropylidenedioxy-hex-5-yne-1,2-diol (12).[1]

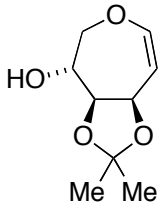


12

The procedure for the synthesis of **5** was followed, using 2,3-*O*-isopropylidene-D-lyxofuranose (583 mg, 3.07 mmol), K_2CO_3 (1.27 g, 9.21 mmol) in methanol (8 mL), and the solution of dimethyl(diazo-2-oxopropyl)phosphonate (1.90 g, 9.21 mmol) in methanol (6.7 mL). After chromatographic purification, the alkynyl diol **12** (284 mg, 49% yield) was obtained.

$[\alpha]^{23}_D$ = -21.64 ($CHCl_3$, c = 1.65); IR (neat): 3401, 3291, 2989, 2937, 2896, 2122, 1382, 1242, 1214, 1162, 1130, 1064, 879, 808, 641 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.61 (dd, *J* = 7.5, 2.1 Hz, 1H), 4.07 (dd, *J* = 8.1, 2.7 Hz, 1H), 3.73 (m, 3H), 3.07 (d, *J* = 6.6 Hz, 1H), 2.89 (bs, 1H), 2.55 (d, *J* = 1.8 Hz, 1H), 1.46 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (150 MHz) δ 111.0, 82.2, 80.2, 75.1, 69.7, 66.7, 64.3, 26.5, 26.0.

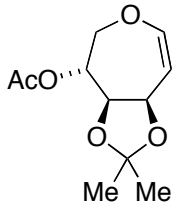
(3*R*,4*S*,5*R*)-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine-3-ol (13-OH).



The same procedure for the synthesis of **8** was followed using alkynyl diol **12** (211 mg, 1.14 mmol), $W(CO)_6$ (52 mg, 0.114 mmol) and Et_3N (3.5 mL) in THF (14.2 mL). After silica chromatography (Hexanes : EtOAc 4:1 to 1:1 plus 0.1% Et_3N) the 7-*endo* glycal (157 mg, 75% yield) was obtained.

m.p.: 129-130 °C; $[\alpha]^{23}_D$ = -10.65 ($CHCl_3$, c = 1.11); IR (neat): 3431, 2978, 2928, 2874, 1642, 1448, 1422, 1374, 1295, 1268, 1252, 1233, 1168, 1143, 1100, 1083, 1058, 1030, 998, 983, 915, 863, 835, 793, 746, 705, 650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.37 (dd, *J* = 6.6, 1.8 Hz, 1H), 5.08 (dd, *J* = 6.6, 1.4 Hz, 1H), 4.54 (d, *J* = 9.6 Hz, 1H), 4.06 (m, 2H), 3.99 (d, *J* = 13.6, 3.6 Hz, 1H), 3.92 (dd, *J* = 9.6, 7.2 Hz, 1H), 2.62 (bs, 1H), 1.46 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz) δ 149.0, 109.8, 107.0, 83.8, 75.1, 73.4, 73.3, 27.0, 27.0; Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.97; H, 7.35.

(3*R*,4*S*,5*R*)-3-acetoxy-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine (13).

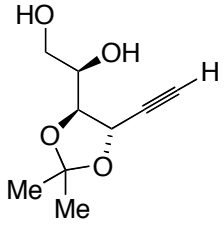


13

Following the same sequence as with **8**, alkynyl diol **12** (211 mg, 1.14 mmol), $W(CO)_6$ (52 mg, 0.114 mmol) and Et_3N (3.5 mL) in THF (14.2 mL) were irradiated. After 3 hours the crude was acetylated with Ac_2O (176 mg, 1.72 mmol) and DMAP (401 mg, 3.42 mmol). After purification the desired acetate **13** (199 mg, 81% yield) was obtained.

$[\alpha]^{23}_D$ = -65.65 ($CHCl_3$, c = 0.63); IR (neat): 2987, 2932, 2851, 1743, 1643, 1452, 1372, 1230, 1172, 1133, 1085, 1062, 1019, 988, 933, 867, 842, 803, 742, 705, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.38 (dd, *J* = 6.2, 1.8 Hz, 1H), 5.15 (dd, *J* = 7.7, 2.0 Hz, 1H), 5.05 (dd, *J* = 6.2, 1.4 Hz, 1H), 4.64 (dt, *J* = 9.6, 1.6 Hz, 1H), 4.23 (dd, *J* = 14.0, 1.2 Hz, 1H), 4.18 (dd, *J* = 10.0, 7.6 Hz, 1H), 4.01 (dd, *J* = 14.0, 2.8 Hz, 1H), 2.15 (s, 3H), 1.45 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz) δ 170.6, 149.1, 119.8, 109.9, 80.2, 75.6, 73.5, 68.7, 27.0, 26.9, 20.7; Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.82; H, 7.12.

(2*R*,3*S*,4*S*)-3,4-isopropylidenedioxy-hex-5-yne-1,2-diol (14).[1]



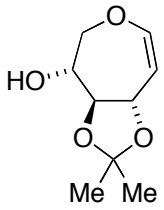
14

The same procedure for the synthesis of **5** was followed using 1-*O*-benzoate-2,3-*O*-isopropylidene-D-xylopyranose (798 mg, 2.71 mmol), K_2CO_3 (1.12 g, 8.13 mmol) in methanol (6.8 mL), and the solution of dimethyl(diazo-2-oxopropyl)phosphonate (1.55 g, 8.13 mmol) in methanol (5.8 mL). After chromatographic purification, the alkynyl diol **14** (276 mg, 55% yield) was obtained.

$[\alpha]^{23}_D$ = -20.27 ($CHCl_3$, c = 1.18); IR (neat): 3429, 3291, 2989, 2936, 2896, 2115, 1710, 1640, 1456. 1382, 1243, 1215, 1162, 1129, 1060, 879, 809, 658 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ

4.62 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.09 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.74 (m, 3H), 2.86 (bs, 2H), 2.55 (d, *J* = 1.8 Hz, 1H), 1.47 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (150 MHz) δ 111.0, 82.3, 80.2, 75.1, 69.6, 66.7, 64.4, 26.5, 26.0.

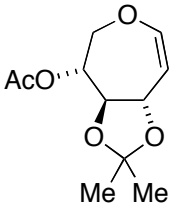
(3*R*,4*S*,5*S*)-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine-3-ol (15-OH).



The same procedure for the synthesis of **8** was followed using alkynyl diol **14** (207 mg, 1.11 mmol), $W(CO)_6$ (63 mg, 0.16 mmol) and Et_3N (2.6 mL) in THF (5.3 mL). After silica chromatography (Hexanes : EtOAc 4:1 to 1:1 plus 0.1% Et_3N), the 7-*endo* glycal (92 mg, 45% yield) was isolated.

$[\alpha]^{23}_D$ = -8.67 ($CHCl_3$, c = 0.98); IR (neat): 3434, 2980, 2946, 2876, 1644, 1449, 1422, 1376, 1296, 1268, 1253, 1235, 1169, 1144, 1100, 1059, 1031, 984, 916, 863, 836, 795, 747, 706 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (dd, *J* = 6.4, 2.0 Hz, 1H), 5.05 (dd, *J* = 6.4, 1.6 Hz, 1H), 4.52 (dt, *J* = 9.8, 1.8 Hz, 1H), 3.98 (m, 3H), 3.90 (dd, *J* = 9.8, 7.4 Hz, 1H), 3.13 (bs, 1H), 1.41 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz) δ 149.0, 109.7, 106.8, 83.7, 75.2, 73.3, 73.0, 26.9, 26.9; Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.97; H, 7.57.

(3*R*,4*S*,5*S*)-3-acetoxy-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine (15).

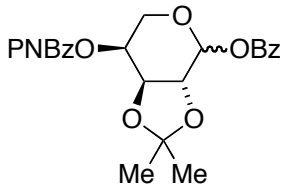


15

Following the same sequence as with **9**, alkynyl diol **14** (253 mg, 1.36 mmol), $W(CO)_6$ (49 mg, 0.136 mmol) and Et_3N (3.4 mL) in THF (13.6 mL) were irradiated. After 3 hours the crude was acetylated with Ac_2O (211 mg, 2.06 mmol) and DMAP (481 mg, 4.08 mmol). After purification the desired acetate **15** (179 mg, 61%) was obtained.

$[\alpha]^{23}_{D}$ = -65.25 ($CHCl_3$, c = 0.36); IR (neat): 2986, 2935, 2850, 1741, 1643, 1450, 1372, 1230, 1172, 1132, 1085, 1061, 1018, 988, 932, 867, 842, 802, 789, 741, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.38 (dd, *J* = 6.4, 2.0 Hz, 1H), 5.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 5.05 (dd, *J* = 6.6, 1.40 Hz, 1H), 4.65 (dt, *J* = 10.0, 1.6 Hz, 1H), 4.23 (dd, *J* = 14.0, 1.2 Hz, 1H), 4.18 (dd, *J* = 9.6, 7.6 Hz, 1H), 4.01 (dd, *J* = 14.4, 2.8 Hz, 1H), 2.16 (s, 3H), 1.45 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz) δ 171.2, 149.2, 109.8, 105.8, 80.3, 75.6, 73.5, 73.2, 27.0, 26.9, 21.2; Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.91; H, 7.17.

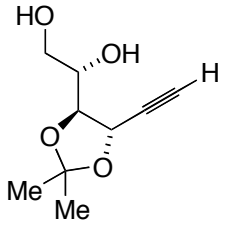
2,3-*O*-isopropylidene-4-*O*-*p*-nitrobenzoate-α,β-L-*arabino*-benzoate-pyranoside (A).



A flame dried flask was charged with 1-*O*-benzoate-2,3-*O*-isopropylidene-D-xylopyranose (1.0 g, 3.40 mmol), PPh_3 (1.77 g, 6.80 mmol), *p*-nitrobenzoic acid (1.14 g, 6.80 mmol) and anhydrous ether (160 mL). This mixture was cooled at 0°C and then DEAD (40% in toluene, 3.1 mL, 6.80 mmol) was added dropwise. After removal of the cooling bath the reaction was stirred overnight. Once the reaction was done the solvent was evaporated and the residue was chromatographed (Hexanes : EtOAc 4:1) providing the *p*-nitrobenzoate L-arabinose product **A** (1.18 g, 78 %).

^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (m, 2H), 8.25 (m, 2H), 8.12 (m, 2H), 7.59 (m, 1H), 7.45 (m, 2H), 6.09 (d, *J* = 8.0 Hz, 1H), 5.68 (d, *J* = 2.4 Hz, 1H), 4.30 (d, *J* = 12.8 Hz, 1H), 4.18 (dd, *J* = 9.6, 8.4 Hz, 1H), 3.99 (dd, *J* = 13.6, 2.0 Hz, 1H), 3.92 (dd, *J* = 9.8, 3.0 Hz, 1H), 1.49 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (150 MHz) δ 164.8, 163.9, 150.8, 134.8, 133.8, 130.9, 130.2, 128.7, 128.4, 123.7, 111.7, 94.5, 76.5, 72.7, 69.5, 66.8, 26.5, 26.4.

(2*S*,3*S*,4*S*)-3,4-isopropylidenedioxy-hex-5-yne-1,2-diol (16).

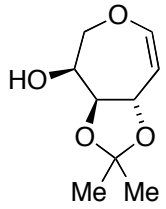


16

The procedure for the synthesis of **5** was followed, using protected L-arabinose derivative **A** (prepared above, 1.41 g, 3.17 mmol), K_2CO_3 (1.96 g, 14.26 mmol) in methanol (8 mL), and the solution of dimethyl(diazo-2-oxopropyl)phosphonate (2.71 g, 14.26 mmol) in methanol (6.7 mL). After chromatography purification the alkynyl diol **16** (64.8 mg, 11%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 (dd, *J* = 6.6, 1.8 Hz, 1H), 4.11 (dd, *J* = 6.6, 5.4 Hz, 1H), 3.85 (m, 1H), 3.74 (m, 1H), 3.66 (dd, *J* = 11.4, 6.2 Hz, 1H), 3.06 (bs, 1H), 2.69 (bs, 1H), 2.55 (d, *J* = 2.0 Hz, 1H), 1.48 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (150 MHz) δ 110.8, 81.8, 81.5, 74.7, 71.5, 66.5, 63.1, 26.8, 25.8.

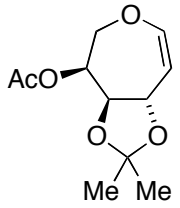
(3*S*,4*S*,5*S*)-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine-3-ol (17-OH).



The same procedure for the synthesis of **8** was followed using alkynyl diol **16** (64.8 mg, 0.35 mmol), $W(CO)_6$ (19 mg, 0.05 mmol) and Et_3N (425 μL) in THF (1.7 mL). In the crude NMR the product was observed, but could not be isolated as the free alcohol after silica chromatography (Hexanes : EtOAc 4:1 to 1:1 plus 0.1% Et_3N).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (dd, *J* = 6.2, 2.2 Hz, 1H), 5.16 (dd, *J* = 6.2, 1.8 Hz, 1H), 4.87 (app. d, *J* = 9.6 Hz, 1H), 4.38 (dt, *J* = 8.3, 4.2 Hz, 1H), 4.20 (dd, *J* = 12.4, 5.2 Hz, 1H), 3.84 (dd, *J* = 9.6, 4.0 Hz, 1H), 3.75 (m, 1H), 3.01 (bs, 1H), 1.45 (s, 3H), 1.43 (s, 3H).

(3*S*,4*S*,5*S*)-3-acetoxy-4,5-isopropylidenedioxy-2,3,4,5-tetrahydrooxepine (17).

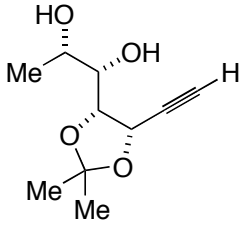


17

Following the same sequence as with **9**, alkynyl diol **16** (38.4 mg, 0.21 mmol), $W(CO)_6$ (11 mg, 0.03 mmol) and Et_3N (500 μL) in THF (2.0 mL) were irradiated. After 4 hours the crude was acetylated with Ac_2O (32 mg, 0.31 mmol) and DMAP (73 mg, 0.63 mmol). After purification the desired acetate **17** (22.5 mg, 63% yield) was obtained.

$[\alpha]^{23}_D$ = +52.86 ($CHCl_3$, c = 0.69); IR (neat): 2986, 2930, 2857, 1747, 1640, 1456, 1371, 1233, 1171, 1098, 1066, 1050, 1027, 990, 979, 942, 890, 866, 804, 747, 714 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.39 (dd, *J* = 6.4, 2.4 Hz, 1H), 5.51 (dt, *J* = 6.4, 3.6 Hz, 1H), 5.32 (dd, *J* = 6.0, 2.0 Hz, 1H), 4.92 (dt, *J* = 9.6, 2.2 Hz, 1H), 4.06 (dd, *J* = 13.0, 4.2 Hz, 1H), 3.93 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.85 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.13 (s, 3H), 1.44 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz) δ 170.0, 148.1, 111.9, 109.8, 78.5, 72.2, 70.4, 67.6, 27.0, 26.3, 20.9.

(3*S*,4*R*,5*S*,6*S*)-3,4-isopropylidenedioxy-hept-1-yne-5,6-diol (18)



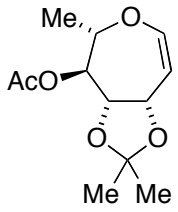
18

A solution of 2,3-*O*-isopropylidene-L-rhamnose (0.5395 g, 2.642 mmol) and K_2CO_3 (1.0960 g, 7.9271 mmol) in methanol (6.7 mL) was heated to reflux. To this solution was added a solution of dimethyl(diazo-2-oxopropyl)phosphonate (1.5222 g, 7.9273 mmol) in methanol (5.6 mL) dropwise over 8 hours. The reaction mixture was cooled and neutralized with 1 M HCl and evaporated at reduced pressure. Extractive work-up (EtOAc / H_2O) and silica gel chromatography (1:1 pentane/ethyl ether) gave the alkynyl diol **18** (0.2094 g, 40%) as a clear oil.

$[\alpha]^{23}_D$ = +33.0 ($CHCl_3$, c = 2.10); IR(neat): 3435, 3294, 2988, 2934, 2122, 1726, 1636, 1456, 1380, 1243, 1216, 1164, 1052, 879 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.71 (dd, *J* = 7.8, 2.0 Hz, 1H), 4.27 (dd, *J* = 7.6, 2.5 Hz, 1H), 3.89 (mult, 1H), 3.51 (dd, *J* = 5.4, 2.5 Hz, 1H), 2.55 (d, *J*

= 1.9 Hz, 1H), 2.32 (br s, 2H), 1.50 (s, 3H), 1.44 (s, 3H), 1.32 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.1, 81.1, 80.5, 75.3, 71.8, 69.7, 67.1, 26.8, 26,4, 19.8; Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 60.09; H, 8.11.

(2*S*,3*S*,4*S*,5*S*)-3-acetoxy-4,5-isopropylidenedioxy-2-methyl-2,3,4,5-tetrahydrooxepine (19)



19

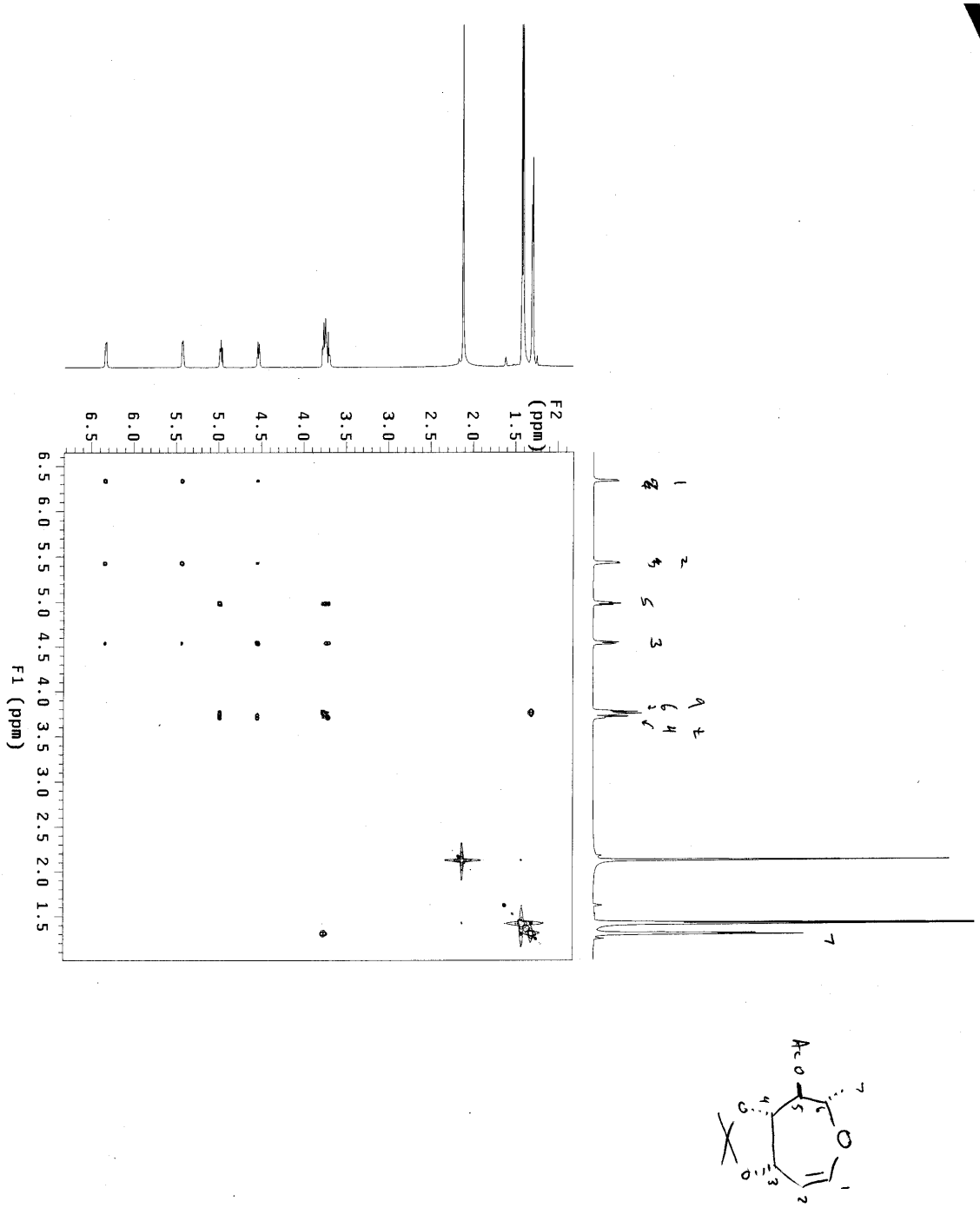
Method A (with Et_3N as base and THF as solvent): A flame-dried Schlenk flask, reflux condenser, and stir bar was charged with alkynyl diol **18** (130.1 mg, 0.6499 mmol, azeotropically dried from toluene) and tungsten hexacarbonyl (34.5 mg, 0.0980 mmol). Anhydrous THF (6.0 mL) and Et_3N (1.5 mL) were added and the reaction was irradiated at 350 nm for 6 h at 65 ºC under argon atmosphere. Upon completion, volatile components were removed under reduced pressure. To the crude mixture was added CH_2Cl_2 (2.6 mL), acetic anhydride (74 μL, 0.78 mmol), Et_3N (0.12 mL, 0.86 mmol), and DMAP (8.6 mg, 0.070 mmol). After 3 h, volatiles were removed and the product was purified by silica gel chromatography (99:1 pentane/ethyl ether plus 1% triethylamine) to give the seven-membered glycal **19** (71.1 mg, 45%) as a clear oil.

Method B (with DABCO as base and toluene as solvent): A flame-dried Schlenk flask, reflux condenser, and stir bar was charged with alkynyl diol **18** (95.2 mg, 0.476 mmol, azeotropically dried from toluene), tungsten hexacarbonyl (25.1 mg, 0.0713 mmol) and, freshly sublimed DABCO (107.7 mg, 0.9601 mmol). The mixture was dissolved in toluene (2.4 mL) and irradiated at 350 nm for 6 h at 70 ºC under argon atmosphere. Upon completion, volatile components were removed under reduced pressure. To the crude mixture was added CH_2Cl_2 (1.9 mL), followed by acetic anhydride (67.9 μL, 0.0720 mmol), Et_3N (0.1143 mL, 0.8201 mmol), and catalytic DMAP (5.9 mg, 0.048 mmol). After 3 h, volatiles were removed and the product was purified by silica gel chromatography (99:1 pentane/ethyl ether plus 1% triethylamine) to give the seven-membered glycal **19** (79.7 mg, 69%) as a clear oil.

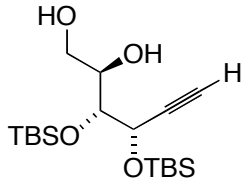
$[\alpha]^{23}_D$ = -11.1 ($CHCl_3$, c = 2.14); IR(neat): 2988, 2938, 1745, 1643, 1453, 1373, 1231, 1177, 1088, 1038, 867, 740 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.31 (dd, *J* = 5.9, 2.1 Hz, 1H); 5.40 (dd, *J* = 5.7, 2.4 Hz, 1H); 4.95 (dd, *J* = 9.1, 7.1 Hz, 1H); 4.51 (dt, *J* = 9.1, 2.4, 1.9 Hz, 1H); 3.73 (pentet, *J* = 6.7 Hz, 1H); 3.69 (t, *J* = 9.1 Hz, 1H); 2.10 (s, 3H); 1.40 (s, 3H); 1.39 (s, 3H); 1.27 (d,

J = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 146.2, 114.1, 109.9, 79.8, 77.9, 77.0, 73.9, 27.1, 26.9, 21.3, 18.3; Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.61; H, 7.67.

COSY (^{1}H-^{1}H) spectrum of **19** (600 MHz, $CDCl_3$):



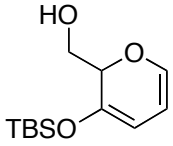
(2*R*,3*R*,4*S*)-3,4-bis-(*tert*-butyldimethylsiloxy)-hex-5-yne-1,2-diol (22)



22

IR (neat): 3447, 3312, 2955, 2930, 2888, 2859, 1472, 1362, 1255, 1098, 885, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.54 (dd, *J* = 4.8, 2.2 Hz, 1H); 4.09 (pentet, *J* = 3.7 Hz, 1H); 3.76-3.70 (mult, 3H); 2.47 (d, *J* = 2.2 Hz, 1H); 0.92 (s, 9H); 0.90 (s, 9H); 0.20 (s, 3H); 0.16 (s, 3H); 0.13 (s, 3H); 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.6, 75.2, 73.0, 71.9, 67.7, 63.4, 25.8, 18.2, 18.1, -4.6, -4.7, -5.2; Anal. Calcd for $C_{18}H_{38}O_4$: C, 57.70; H, 10.22. Found: C, 57.60; H, 10.33.

5-*tert*-butyldimethylsiloxy-6-hydroxymethyl-oxa-2,4-cyclohexadiene (24)



24

IR (neat): 3337, 2930, 2888, 2859, 1647, 1605, 1472, 1256, 1050, 984, 909, 839, 781 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.20 (dd, *J* = 17.2, 10.7 Hz, 1H); 5.42 (d, *J* = 17.5 Hz, 1H); 5.11 (d, *J* = 10.8 Hz, 1H); 5.06 (t, *J* = 7.2 Hz, 1H); 4.24 (d, *J* = 7.0 Hz, 2H); 1.01 (s, 9H); 0.13 (s, 6H).

COSY (^{1}H-^{1}H) spectrum of **24** (400 MHz, $CDCl_3$):