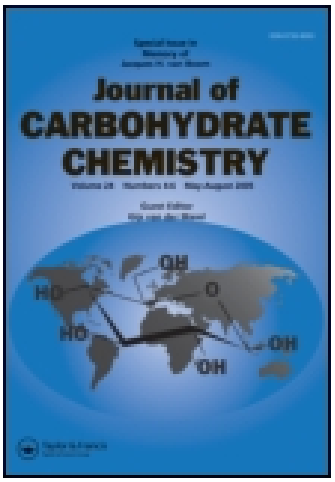

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Palladium-Mediated Cyclization on Carbohydrate Templates. 3. Extension of The Cyclization to the Threo Series.

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PALLADIUM-MEDIATED CYCLIZATION ON CARBOHYDRATE TEMPLATES. 3. EXTENSION OF THE CYCLIZATION TO THE THREO SERIES.

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ABSTRACT

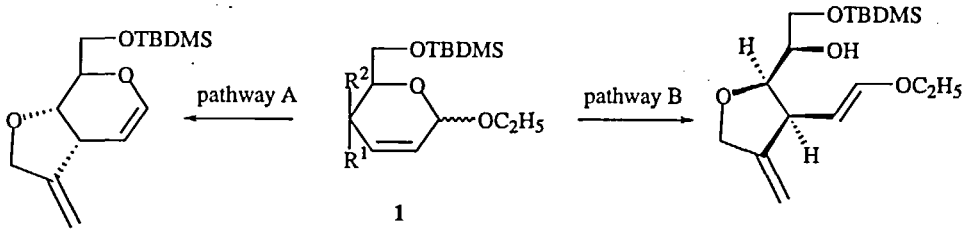
The palladium(0)-catalyzed Heck-type cyclization-β-alkoxy elimination reaction leading to enantiopure bicyclic compounds in the case of *erythro* 2,3-unsaturated glycosides has been successfully extended to the *threo* stereoisomer by only changing the aglycon moiety from an ethoxy group to an aryloxy moiety.

INTRODUCTION

One of the main tasks in modern synthetic chemistry is the synthesis of enantiomerically pure molecules. There are two different methodologies to achieve this goal. One way is the enantioselective transformation of prochiral substrates, the second one is the chemical transformation of enantiopure compounds from the chiral pool. In this latter case, carbohydrates are readily available and renewable enantiopure materials with a variety of functional and stereochemical features. Thus they are very useful intermediates for the synthesis of polycyclic enantiopure compounds such as furo- and pyrano-[2,3-*b*]pyrans.

Free-radical cyclization has been extensively studied in carbohydrate chemistry[1-3] and is an extremely efficient methodology for the preparation of such enantiopure bicyclic structures. Organometallic-induced cyclizations in carbohydrate chemistrry have been less studied,[4-8] although these reactions also generally occur with a high degree of stereoselectivity.

We recently described the use of an intramolecular palladium-catalyzed Heck reaction in carbohydrate chemistry leading to bicyclic glucals *via* an unusual dealkoxy-palladation pathway (Scheme 1, pathway A).[9] However, bicyclic structures could be obtained only in the *erythro* series, since in the *threo* series only the formation of a monocyclic structure was observed (Scheme 1, pathway B). In the present paper, we describe the extension of this methodology to the *threo* series by a proper choice of the aglycon moiety. Moreover, these results give more insight into the mechanism of this cyclization reaction.



2 1 3

pathway A: $R^1 = OCH_2CHBr{=}CH_2$; $R^2 = H$
pathway B: $R^1 = H$; $R^2 = OCH_2CHBr{=}CH_2$

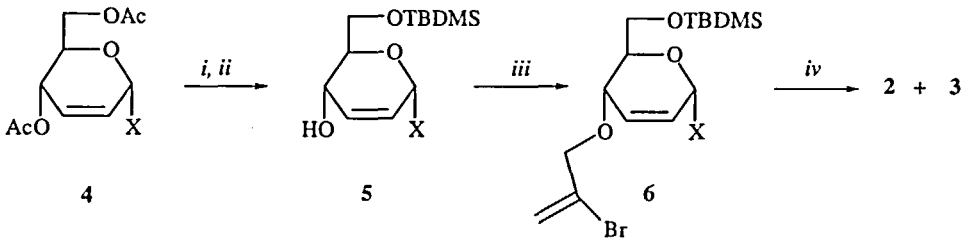
Scheme 1

RESULTS AND DISCUSSION

In our research to obtain bicyclic glucals even in the *threo* series, we first modified the experimental conditions previously used in our standard procedure[9] and then the nature of the aglycon moiety.

The 2,3-unsaturated glycoside **6c** was prepared from the readily accessible derivative of tri-*O*-acetyl-D-glucal. Deacetylation of 4-nitrophenyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[10] (**4c**) in methanol followed by selective monoprotection of the primary hydroxyl function with TBDMSCl, NEt_3 and imidazole gave the unsaturated compound **5c** in 65% yield (Scheme 2). Treatment of **5c** with NaH and 2,3-dibromopropene in THF at 60 °C led to the *O*-alkylated compound **6c** in 33% yield.

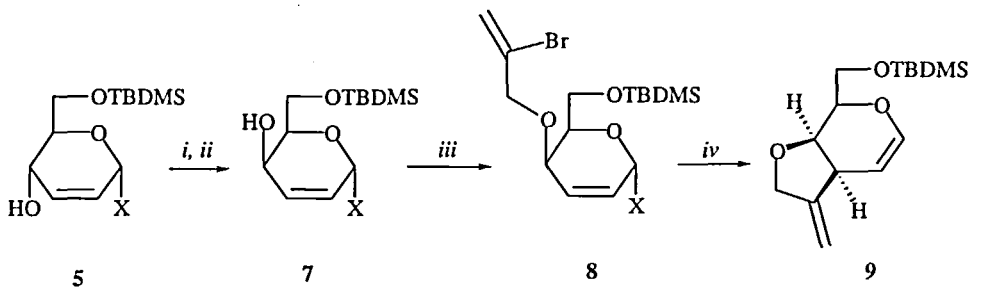
Compounds **7c** and **7d**, having the *threo* configuration, were synthesized from unsaturated *erythro* substrates **5c**[9] and **5d**,[9] respectively, in 65% and 36% yield, by inversion of configuration at C-4 *via* a Mitsunobu reaction (Scheme 3).[11] Alkylation of alcohols **7b**,[9] **7c**, and **7d** with 2,3-dibromopropene, as previously described, gave the unsaturated bromo compounds **8b**, **8c**, and **8d** in 76%, 60%, and 62% yield, respectively.



a: X = OC_2H_5; b: X = OC_6H_4-4-*t*-Bu; c: X = OC_6H_4-4-NO_2

Reagents and conditions: *(i)* cat. MeONa, MeOH; *(ii)* TBDMSCl, NEt_3, imidazole, CH_2Cl_2, rt, 24 h;*(iii)* NaH, $BrCH_2CBr{=}CH_2$, THF, 60 °C, 24 h; *(iv)* $Pd(OAc)_2$, PPh_3, NEt_3, Bu_4NHSO_4, CH_3CN/H_2O, 80 °C, 24 h

Scheme 2



a: X = OC_2H_5; b: X = OC_6H_4-4-*t*-Bu; c: X = OC_6H_4-4-NO_2; d: X = H

Reagents and conditions: *(i)* PPh_3, $ClCH_2CO_2H$, toluene, 0 °C, 15 min, then DEAD, 0 °C, 30 min, rt, 24 h; *(ii)* cat. MeONa, MeOH, rt, 24 h; *(iii)* NaH, $BrCH_2CBr{=}CH_2$, THF, 60 °C, 24 h;*(iv)* $Pd(OAc)_2$, PPh_3, NEt_3, Bu_4NHSO_4, CH_3CN/H_2O, 80 °C, 24 h

Scheme 3

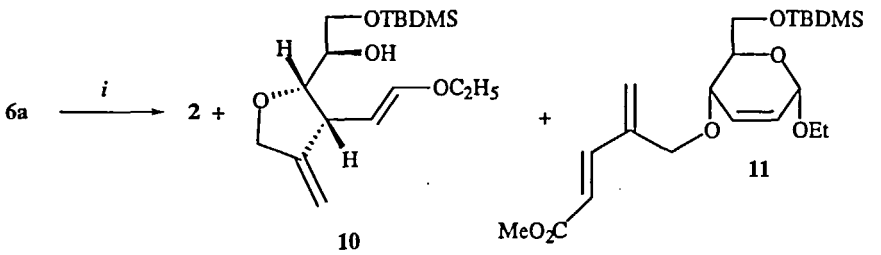
When the cyclization reaction was performed in CH_3CN on substrate **6a** in the absence of water, only a trace of bicyclic product **2** was obtained, together with recovered starting material and degradation products (Table 1, entry 2). This experiment clearly shows the importance of water in this cyclization (compared with Table 1, entry 1).

Table 1. Palladium-mediated cyclization of unsaturated carbohydrates[a]

Entry	Starting material	Solvent	T °C	Time (h)	Compounds (Yield)[b]
1	**6a**	CH_3CN-H_2O (5-1)	80	10	**2** (72%)[c]
2	**6a**	CH_3CN	80	24	**2** (trace)
3	**6a**	DMF	80	24	**2** (50%) + **10** (20%)
4	**6a**	DMF[d]	80	24	**2** (35%) + **10** (20%) + **11** (10%)
5	**6a**	Dry DMF	80	24	**2** (trace)
6	**6b**	CH_3CN-H_2O (5-1)	50	30	**2** (32%)
7	**6b**	DMF	80	24	**2** (70%)
8	**6c**	CH_3CN-H_2O (5-1)	50	27	**2** (23%)
9	**8a**	CH_3CN-H_2O (5-1)	80	10	**3** (57%)[c]
10	**8b**	CH_3CN-H_2O (5-1)	50	53	**9** (32%)
11	**8c**	CH_3CN-H_2O (5-1)	40	29	**9** (30%)
12	**8d**	CH_3CN-H_2O (5-1)	50	17	**9** (51%)

a. [Substrate]:[NEt_3]:[Bu_4NHSO_4]:[$Pd(OAc)_2$]:[PPh_3] = 10:25:10:1:2. b. Isolated yields after column chromatography on silica gel. c. Ref. 9. d. 3 equiv of methyl acrylate was added.

The cyclization reaction was also successfully performed in commercial DMF as the solvent (Table 1, entry 3); the bicyclic product **2** was obtained in 50% yield, together with compound **10** (20% yield) (Scheme 4). When methyl acrylate was present, compound **11** was also formed in 10 % yield (Table 1, entry 4) (Scheme 4) *via* a Heck reaction between methyl acrylate and the first σ-vinyl-palladium complex obtained by oxidative addition of bromide **6a** to palladium(0). However, it is noteworthy that dry DMF gave no reaction at all (Table 1, entry 5).



Reagents and conditions: *(i)* $Pd(OAc)_2$, PPh_3, NEt_3, Bu_4NHSO_4, DMF, CH_2=CH-CO_2Me

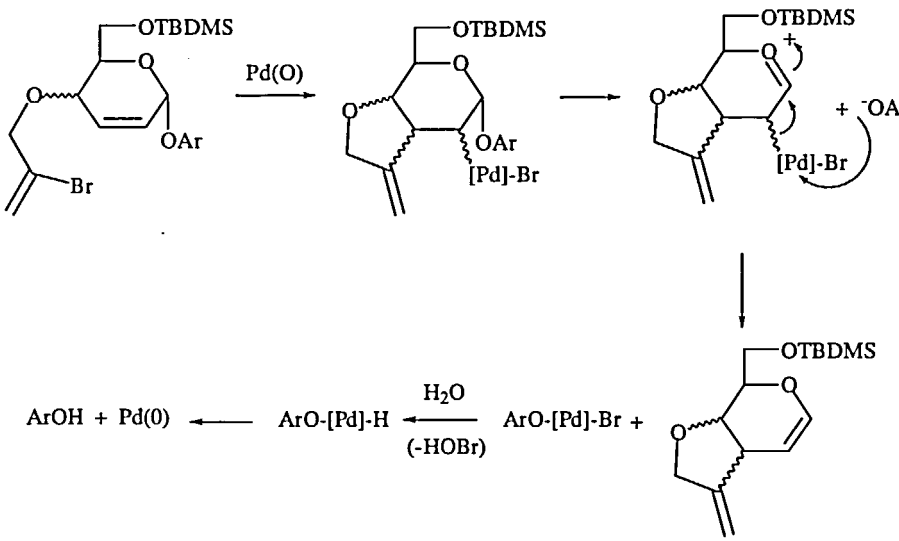
Scheme 4

We then turned our attention to the influence of the nature of the aglycon moiety on the cyclization. In our proposed mechanism of β-dealkoxypalladation,[9] we postulated an ionic and nonconcerted mechanism for this last step in agreement with the stereoselectivity observed. If this is true, the dissociation of the aglycon moiety will be favored over the cleavage of the carbohydrate moiety in the case of unsaturated aryl glycosides.

Treatment of 2,3-unsaturated carbohydrate **6b** in a CH_3CN-H_2O (5/1) mixture at 50 °C under the standard conditions [$Pd(OAc)_2$, PPh_3, Bu_4NHSO_4, NEt_3] for 20 h gave the bicyclic compound **2** in 32% yield (Table 1, entry 6); increasing the temperature in this case to 80 °C led to the formation of isomerized product and by-products. Compound **6c** also gave the expected bicyclic structure **2** in 23% yield (Table 1, entry 7). It is noteworthy that performing the cyclization of **6b** in DMF gave **2** with yields of up to 70% (Table 1, entry 6). So the cyclization could be performed at a lower temperature by changing the aglycon moiety from ethoxy to aryloxy; although the chemical yields were not optimized.

We then turned our investigation to the cyclization in the *threo* series. As expected, when the cyclization was performed on dihydropyran **8d** in CH_3CN-H_2O at 50 °C, the bicyclic derivative **9** was obtained in 51% yield (Table 1, entry 12) *via* a classical Heck-type cyclization reaction. It was previously shown that ethyl 4-*O*-(2'-bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**8a**) led under the same conditions, except at 80 °C, to the formation of compound **3** in 57% yield (Table 1, entry 9).[9] However, and as expected, when unsaturated aryl compounds **8b** and **8c** were subjected to the cyclization reaction at low temperature, only formation of the bicyclic compound **9** was observed in 32 and 30% yield, respectively, together with some degradation products (Table 1, entries 10 and 11). The formation of **9** is in agreement with the previously proposed Heck-type cyclization-β-alkoxy elimination mechanism; the scission of the aglycon moiety is favored *versus* the cleavage of the carbohydrate moiety in

these cases, and this is due to the better leaving group ability of an aryloxy group versus an alkyloxy group (Scheme 5). Compound **9** showed characteristic chemical shifts and coupling constants, particularly at δ 6.39 and 4.54 ppm for the olefinic protons H-1 and H-2, with coupling constants $J_{1,2}$ = 5.9 Hz and $J_{1,3}$ = 1.6 Hz. The hydrogen atom H-4 appeared as a doublet of doublets at δ 4.26 ppm with $J_{3,4}$ = 7.1 Hz and $J_{4,5}$ = 1.5 Hz, the former value being in agreement with a *cis*-fused structure. Additional characteristics are the ^{13}C chemical shifts of C-1, C-2, C-3, and C-4 at δ 143.2, 102.5, 40.6, and 75.0 ppm, respectively.



Scheme 5

CONCLUSION

In conclusion, we have extended our previously reported Heck-type cyclisation-β-alkoxy elimination used in the *erythro* series to the *threo* series by only modifying the nature of the aglycon moiety of the unsaturated carbohydrate. Moreover, these results agree well with our preceeding proposal of an ionic mechanism and not a concerted one for the β-dealkoxy-palladation.

EXPERIMENTAL

General methods. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (60 F-254, Merck). Compounds were visualized

under UV light (254 nm) or by spraying with an H_2SO_4 solution and heating. Column chromatography was performed on silica gel 60 (40-63 mesh, Merck). NMR spectra were obtained in $CDCl_3$, and chemical shifts are given in ppm on the δ scale from internal tetramethylsilane. Reactions involving palladium complexes were carried out in a Schlenk tube under a nitrogen atmosphere.

Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**4a**),[12] 4-*tert*-butylphenyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**4b**),[10] 4-nitrophenyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**4c**),[10] 4,6-di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-D-*erythro*-hex-2-enitol (**4d**),[13] ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**5a**),[9] 4-*tert*-butylphenyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**5b**),[9] 6-*O*-(*tert*-butyldimethylsilyl)-1,5-anhydro-2,3-dideoxy-D-*erythro*-hex-2-enitol (**5d**),[9] ethyl 4-*O*-(2'-bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**6a**),[9] 4-*tert*-butylphenyl 4-*O*-(2'-bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**6b**),[9] ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**7a**),[9] 4-*tert*-butylphenyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**7b**),[9] and ethyl 4-*O*-(2'-bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**8a**)[9] were prepared by known procedures. 1,2,3,4-Tetradeoxy-2',3',4',5'-tetrahydro-6-*O*-(*tert*-butyldimethylsilyl)-4'-methylene-D-*ribo*-hex-1-enopyranoso-[4,3-*b*] furan (**2**), and *(2R, 3S, 1'R)*-2-[1'-hydroxy-2'-[(*tert*-butyldimethylsilyl)-oxy]ethyl]-3-*(E)*-(2'-ethoxyethenyl)-4-methylenetetrahydrofuran (**3**) have been previously described.[9]

4-Nitrophenyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (5c). Diacetate **4c** (3.04 g, 8.66 mmol) was treated with a catalytic amount of sodium methoxide in methanol (100 mL) at room temperature. After evaporation of the solvent, the free hydroxyl unsaturated glycoside was obtained in quantitative yield and used without further purification. This diol was treated with 1.25 equiv of TBDMSCl (1.62 g, 10.77 mmol), 1.3 equiv of NEt_3 (1.6 mL, 11.2 mmol), and 0.05 equiv of imidazole (30 mg, 0.43 mmol) in CH_2Cl_2 (30 mL) at room temperature for ca. 24 h. After addition of 25 mL of water and extraction with 3 x 30 mL of CH_2Cl_2, the organic layer was dried. After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography using petroleum ether/ethyl acetate as the eluent to give compound **5c** (215 mg, 65 %): R_f 0.43 (petroleum ether/ethyl acetate 3/1); $[\alpha]^{20}_D$ +148.7 (*c* 1.4, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.10 (s, 6H, Me_2Si), 0.89 (s, 9H, Me_3CSi), 2.97 (d, 1H, *J* = 3.5 Hz, OH), 3.79-3.83 (m, 3H, H-5, H-6, H-6'), 4.33 (m, 1H, H-4), 5.77 (s, 1H, H-1), 5.91 (ddd, 1H, *J* = 10.1, 2.6 and 2.2 Hz, H-2), 6.18 (bdd, 1H, *J* = 10.1 and 1.3 Hz, H-3), 7.17 (d, 2H, *J* = 8.8 Hz, H-arom), 8.22 (d, 2H, *J* = 8.8 Hz, H-arom); ^{13}C ($CDCl_3$) δ -5.5 (Me_2Si), 18.2 (Me_3CSi), 25.8 (Me_3CSi), 64.7 (C-6),

66.1 (C-4), 71.6 (C-5), 92.5 (C-1), 116.5 and 125.7 (C-2 and C-3), 123.9, 134.8, 142.3 and 161.2 (C-arom).

Anal. Calcd for $C_{18}H_{27}O_6NSi$ (381.50): C, 56.67; H, 7.13. Found: C, 56.41; H, 6.82.

General Procedure for Inversion of Configuration at C-4. To the 4-hydroxyl *erythro* compound **5c-d** (6.1 mmol) in 60 mL of toluene was added 3.19 g (12.2 mmol) of PPh_3 and 1.16 g (12.2 mmol) of $ClCH_2CO_2H$. The solution was stirred for 30 min at 0 °C, and 1.9 mL (12.2 mmol) of DEAD was slowly injected. After the solution was stirred for 30 min at 0 °C and 24 h at room temperature, $OPPh_3$ was separated and the resulting solution was concentrated under vacuum. The resulting ester was directly treated with a catalytic amount of sodium methoxide in methanol (100 mL). After evaporation of the solvent and addition of 50 mL of CH_2Cl_2, the organic layer was washed with 0.1 M aqueous NH_4Cl and saturated aqueous NaCl. After drying, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate as eluent to afford the corresponding 4-hydroxyl *threo* compound **7c-d**.

4-Nitrophenyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (7c): yield 65%; oil; R_f 0.18 (petroleum ether/ethyl acetate 3/1); $[\alpha]^{20}_D$ +46.8 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 6H, Me_2Si), 0.84 (s, 9H, Me_3CSi), 2.40 (d, 1H, *J* = 6.9 Hz, OH), 3.84 (dd, 1H, *J* = 10.7 and 6.1 Hz, H-6), 3.91 (dd, 1H, *J* = 10.7 and 5.6 Hz, H-6'), 4.05-4.13 (m, 2H, H-4, H-H-5), 5.86 (dd, 1H, *J* = 3.1 and 0.6 Hz, H-1), 6.07 (dd, 1H, *J* = 9.9 and 3.1 Hz, H-2), 6.38 (ddd, 1H, *J* = 9.9, 6.1 and 0.6 Hz, H-3), 7.18 (dd, 2H, *J* = 9.3 and 2.2 Hz, H-arom), 8.20 (dd, 2H, *J* = 9.3 and 2.2 Hz, H-arom); ^{13}C ($CDCl_3$) δ -5.5 (Me_2Si), 18.1 (Me_3CSi), 25.7 (Me_3CSi), 61.6 (C-4), 62.7 (C-6), 71.8 (C-5), 92.9 (C-1), 116.6 and 125.7 (C-2 and C-3), 126.5, 131.1, 142.3 and 162.2 (C-arom).

Anal. Calcd for $C_{18}H_{27}O_6NSi$ (381.50): C, 56.67; H, 7.13. Found: C, 57.15; H, 7.27.

6-*O*-(*tert*-Butyldimethylsilyl)-1,5-anhydro-2,3-dideoxy-D-*threo*-hex-2-enitol (7d): yield 36%; oil; R_f 0.46 (petroleum ether/ethyl acetate 4/1); $[\alpha]^{20}_D$ -146.7 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 6H, Me_2Si), 0.91 (s, 9H, Me_3CSi), 1.96 (d, 1H, *J* = 8.7 Hz, OH), 3.55 (ddd, 1H, *J* = 6.5, 6.0 and 1.9 Hz, H-5), 3.81 (dd, 1H, *J* = 10.5 and 6.0 Hz, H-6), 3.91 (dd, 1H, *J* = 10.5 and 6.5 Hz, H-6'), 3.91 (m, 1H, H-4), 4.09-4.23 (m, 2H, H-1, H-1'), 5.96 (ddd, 1H, *J* = 10.1, 3.1 and 1.6 Hz, H-2), 6.07 (H-3); ^{13}C ($CDCl_3$) δ -5.4 (Me_2Si), -5.3 (Me_2Si), 18.3 (Me_3CSi), 25.9 (Me_3CSi), 62.6 (C-4), 62.9 (C-1), 66.2 (C-6), 78.2 (C-5), 126.7 and 130.3 (C-2 and C-3).

Anal. Calcd for $C_{12}H_{24}O_3Si$ (244.40): C, 58.97; H, 9.90. Found: C, 58.70; H, 9.83.

General Procedure for *O*-Alkylation. To the 4-hydroxyl compound **5** or **7** (7.75 mmol) in 40 mL of dry THF was added 620 mg (15.5 mmol) of NaH (60%). The solution was stirred for 2 h at room temperature, and 1.6 mL (15.5 mmol) of 2,3-dibromopropene was added. After being stirred at 60 °C for 24 h, the solution was cooled and the reaction quenched with 35 mL of H_2O and extracted with 3 x 40 mL of Et_2O. After drying, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel with petroleum ether/ethyl acetate as the eluent to afford the *O*-alkylated compound.

4-Nitrophenyl 4-*O*-(2'-Bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (6c): yield 33%; oil; R_f 0.58 (petroleum ether/ethyl acetate 3/1); $[\alpha]^{20}_D$ +131.2 (*c* 1.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 6H, Me_2Si), 0.84 (s, 9H, Me_3CSi), 3.82 (m, 3H, H-5, H-6, H-6'), 4.14-4.22 (m, 3H, H-4, OCH_2), 5.62 (bs, 1H, $=CH_2$), 5.75 (bs, 1H, H-1), 5.87-5.93 (m, 2H, $=CH_2$, H-2), 6.26 (d, 1H, J = 10.2 Hz, H-3), 7.15 (d, 2H, J = 7.5 Hz, H-arom), 8.18 (d, 2H, J = 7.5 Hz, H-arom); ^{13}C ($CDCl_3$) δ -5.3 (Me_2Si), -5.2 (Me_2Si), 18.3 (Me_3CSi), 25.9 (Me_3CSi), 62.2 (C-6), 69.8 (C-4), 72.0 (C-5), 73.7 (OCH_2), 92.9 (C-1), 116.6, 118.5, 124.9, 125.7, 125.7, 129.2, 132.7, 142.3 and 162.3 (C-2, C-3, $=CH_2$, $>C=CH_2$, C-arom).

Anal. Calcd for $C_{21}H_{30}O_6NSiBr$ (500.46): C, 50.40; H, 6.04. Found: C, 50.95; H, 6.10.

4-*tert*-Butylphenyl 4-*O*-(2'-Bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (8b): yield 76%; oil; R_f 0.66 (petroleum ether/ethyl acetate 3/1); $[\alpha]^{20}_D$ +23.4 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.05 (s, 6H, Me_2Si), 0.90 (s, 9H, Me_3CSi), 1.30 (s, 3H, Me_3C), 3.77-3.96 (m, 3H, H-5, H-6, H-6'), 4.17-4.19 (m, 3H, H-4, OCH_2), 5.63 (bs, 1H, H-1), 5.73 (bd, 1H, J = 2.1 Hz, $=CH_2$), 5.97 (bd, 1H, J = 2.1 Hz, $=CH_2$), 6.13 (dd, 1H, J = 10.8 and 1.5 Hz, H-2), 6.32 (dd, 1H, J = 10.8 and 5.2 Hz, H-3), 7.05 (d, 2H, J = 11.4 Hz, H-arom), 7.29 (d, 2H, J = 11.4 Hz, H-arom); ^{13}C ($CDCl_3$) δ -5.4 (Me_2Si), -5.3 (Me_2Si), 18.2 (Me_3CSi), 25.9 (Me_3CSi), 31.6 (Me_3C), 34.2 (Me_3C), 61.8 (C-6), 67.4 (C-4), 71.9 (C-5), 73.6 (OCH_2), 93.1 (C-1), 116.6, 117.6, 126.3, 127.5, 129.4, 129.8, 144.9 and 155.2 (C-2, C-3, $=CH_2$, $>C=CH_2$, C-arom).

4-Nitrophenyl 4-*O*-(2'-Bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (8c): yield 60%; oil; R_f 0.39 (petroleum ether/ethyl acetate 3/1); $[\alpha]^{20}_D$ +13.5 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 6H, Me_2Si), 0.81 (s, 9H, Me_3CSi), 3.70-4.25 (m, 2H, OCH_2), 3.75 (dd, 1H, J = 10.4 and 6.5 Hz, H-6), 3.94 (dd, 1H, J = 10.4 and 8.3 Hz, H-6'), 4.13 (m, 1H, H-5), 4.25 (m, 1H, H-4), 5.64 (bd, 1H, J = 1.0 Hz, $=CH_2$), 5.88 (bd, 1H, J = 2.6 Hz, H-1), 5.97 (bd, 1H, J = 1.5 Hz, $=CH_2$), 6.15 (dd, 1H, J = 10.0 and 2.6 Hz, H-2), 6.40 (ddd,

1H, J = 10.0, 5.1 and 1.0 Hz, H-3), 7.19 (d, 2H, J = 7.5 Hz, H-arom), 8.20 (d, 2H, J = 7.5 Hz, H-arom); ^{13}C ($CDCl_3$) δ -5.5 (Me_2Si), -5.4 (Me_2Si), 18.1 (Me_3CSi), 25.7 (Me_3CSi), 61.7 (C-6), 67.1 (C-4), 72.6 (C-5), 73.7 (OCH_2), 92.7 (C-1), 116.7, 118.0, 125.7, 128.0, 128.5, 129.5, 142.4 and 162.2 (C-2, C-3, $=CH_2$, $>C=CH_2$, C-arom).

Anal. Calcd for $C_{21}H_{30}O_6NSiBr$ (500.46): C, 50.40; H, 6.04. Found: C, 50.44; H, 6.47.

4-*O*-(2'-Bromoprop-2'-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-1,5-anhydro-2,3-dideoxy-D-*threo*-hex-2-enitol (8d): yield 62%; oil; R_f 0.3 (petroleum ether/ethyl acetate 9/1); $[\alpha]^{20}_D$ -14.7 (*c* 1.1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.09 (s, 6H, Me_2Si), 0.91 (s, 9H, Me_3CSi), 3.58 (ddd, 1H, J = 6.9, 6.5 and 2.0 Hz, H-5), 3.80-3.95 (m, 3H, H-4, H-6, H-6'), 4.10-4.35 (m, 4H, H-1, H-1', OCH_2), 5.59 (s, 1H, $=CH_2$), 5.96-6.05 (m, 3H, H-2, H-3, $=CH_2$); ^{13}C ($CDCl_3$) δ -5.2 (Me_2Si), -5.1 (Me_2Si), 18.4 (Me_3CSi), 26.1 (Me_3CSi), 62.4 (C-1), 66.1 (C-6), 68.8 (C-4), 73.2 (OCH_2), 78.5 (C-5), 117.4 ($=CH_2$), 123.6 and 132.0 (C-2 and C-3), 130.1 ($>C=CH_2$).

Anal. Cald for $C_{15}H_{27}O_3SiBr$ (363.37): C, 49.58; H, 7.49. Found: C, 49.55; H, 7.38.

Standard Palladium(0)-Mediated Cyclization Procedure. A solution of 1.2 mmol of the unsaturated glycoside in CH_3CN (20 mL) and H_2O (4 mL) was heated in the presence of $Pd(OAc)_2$ (29 mg, 0.13 mmol), PPh_3 (35.3 mg, 0.13 mmol), Bu_4NHSO_4 (379 mg, 1.17 mmol), and NEt_3 (0.41 mL, 2.9 mmol) at 50 °C. The progress of the reaction was monitored by TLC. When the starting material was no longer present, the solvent was evaporated under reduced pressure, and the mixture was extracted with 3 x 30 mL Et_2O. Evaporation of the solvent under reduced pressure gave an oil that was purified by column chromatography on silica gel to give the pure product.

1,2,3,4-Tetradeoxy-2',3',4',5'-tetrahydro-6-*O*-(*tert*-butyldimethylsilyl)-4'-methylene-D-*lyxo*-hex-1-enopyranoso-[4,3-*b*]furan (9): yield 32%; oil; R_f 0.14 (petroleum ether/ethyl acetate 30/1); $[\alpha]^{20}_D$ -137.6 (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.09 (s, 6H, Me_2Si), 0.91 (s, 9H, Me_3CSi), 3.23 (m, 1H, H-3), 3.80-3.91 (m, 3H, H-5, H-6, H-6'), 4.26 (dd, 1H, J = 7.1 and 1.5 Hz, H-4), 4.26 (ddd, 1H, J = 13.0, 2.4 and 2.0 Hz, H-5'), 4.56 (ddd, 1H, J = 13.0, 2.4 and 2.0 Hz, H-5'), 4.51-4.59 (m, 1H, H-2), 4.92 (ddd, 1H, J = 5.7, 2.0 and 2.0 Hz, $=CH_2$), 5.05 (ddd, 1H, J = 5.7, 2.4 and 2.4 Hz, $=CH_2$), 6.39 (dd, 1H, J = 5.9 and 1.6 Hz, H-1); ^{13}C ($CDCl_3$) δ -6.0 (Me_2Si), -5.7 (Me_2Si), 18.5 (Me_3CSi), 26.0 (Me_3CSi), 40.6 (C-3), 62.8 (C-6), 70.7 (C-5'), 75.0 and 76.2 (C-4, C-5), 102.5 (C-2), 105.0 ($=CH_2$), 143.2 (C-1), 150.8 (C-4').

Anal. Calcd for $C_{15}H_{26}O_3Si$ (282.45): C, 63.79; H, 9.28. Found: C, 63.46; H, 9.39.

Ethyl 4-*O*-(2'-methylene-4'methylcarbonylbut-3-enyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (11): yield 10%; oil; R_f 0.17 (petroleum ether/ethyl acetate 3/1); $[\alpha]^{20}_D$ +21.9 (*c* 0.6, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.07 (s, 6H, Me_2Si), 0.90 (s, 9H, Me_3CSi), 1.22 (t, 1H, *J* = 7.1 Hz, CH_2CH_3), 3.53 (dq, 1H, *J* = 9.6 and 7.1 Hz, CH_2CH_3), 3.76 (s, 3H, CH_3), 3.76-4.00 (m, 5H, H-4, H-5, H-6, CH_2CH3), 4.10 (bd, 1H, *J* = 12.6 Hz, OCH_2), 4.31 (bd, 1H, *J* = 12.6 Hz, OCH_2), 4.38 (bs, 1H, H-1), 5.40 (bs, 1H, $=CH_2$), 5.60 (bs, 1H, $=CH_2$), 5.78 (ddd, 1H, *J* = 10.1, 2.5 and 1.9 Hz, H-2), 6.01 (d, 1H, *J* = 16.1 Hz, =CH-), 6.08 (bd, 1H, *J* = 10.1, H-3), 7.35 (d, 1H, *J* = 16.1 Hz, =CH-); ^{13}C ($CDCl_3$) δ -5.5 (Me_2Si), -5.4 (Me_2Si), 15.3 (CH_2CH_3), 18.4 (Me_3CSi), 25.9 (Me_3CSi), 51.6 (CH_3CO), 62.9 (C-6), 63.7 (CH_2CH_3), 68.1 (CH_2O), 70.5 (C-4 and C-5), 94.1 (C-1), 118.8 ($=CH_2$), 124.9 (=CH-), 127.2 and 130.1 (C-2 and C-3), 141.0 ($>C=CH_2$), 144.0 (=CH-), 172.6 (CO_2).

Anal. Calcd for $C_{21}H_{36}O_6Si$ (412.60): C, 61.13; H, 8.79. Found: C, 60.94; H, 8.79.

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