Palladium-Mediated Cyclization on Carbohydrate Templates Synthesis of Enantiopure Annelated Tricyclic Compounds

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Various bromo unsaturated carbohydrates **2**–**4** have been prepared from ethyl and aryl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside by deacetylation, followed firstly by monosilylation with TBDMSCl and then by alkylation with 2-bromobenzyl bromide or 1-bromo-bromomethylcycloalkene. The *N*-, *C*-, and *O*-analogues **6**–**8** were prepared by palladium-mediated alkylation of the carbonate **5** with $TsNHCH_2$–C_6H_4-*o*-Br, $(CO_2Me)_2CH$–C_6H_4-*o*-Br, and HOC_6H_4-*o*-I, respectively. The *threo* analogue **10** was obtained using the same methodology as for **2**, after inversion of configuration at C-4 by means of a Mitsunobu reaction. Treatment of the unsaturated carbohydrates **2**–**4**, **6**–**8**, and **10** with a catalytic amount of $Pd(OAc)_2/PPh_3$ in DMF in the presence of Bu_4NHSO_4 and NEt_3 afforded the annelated tricyclic compounds **11**–**13** and **15**–**18** in good yields when the anomeric substituent was the *p*-*tert*-butylphenyl group, via an intramolecular Heck reaction followed by a β-alkoxy-palladium elimination

Introduction

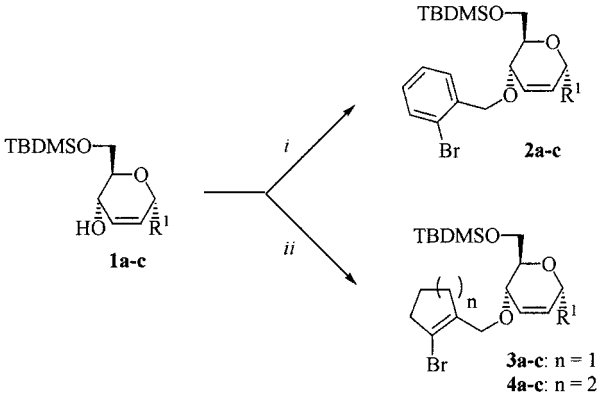
One of the main challenges in modern synthetic chemistry is the synthesis of enantiomerically pure molecules. To achieve this goal, there exist two different methodologies. One way is the enantioselective transformation of prochiral substrates; the second is the chemical transformation of enantiopure compounds from the chiral pool. In this latter case, carbohydrates represent readily available and renewable enantiopure materials with a variety of functional and stereochemical features; so they can be modified to give versatile synthons. Thus, they are very useful intermediates for the synthesis of polycyclic enantiopure compounds such as furo- and pyrano-[2,3-*b*]pyrans, closely related to the structural framework of many natural products.

In this field, the free radical cyclization process 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 chemistry have been less studied,[4−8] although these reactions also generally occur with a high degree of stereoselectivity. Effectively, this methodology, generally based on an intramolecular Heck reaction followed by a cascade reaction, makes possible the stereospecific and sometimes enantioselective formation of carbocyclic and heterocyclic systems. More recently, ruthenium-mediated ring-closing metathesis has also been extended by different groups for the construction of highly functionalized carbohydrate-based polycyclic structures.[9−11] We recently described a new stereospecific access to unsaturated enantiopure bicyclo[4.3.0]nonane and tricyclo[7.3.0.$2^{2,6}$]dodecane systems from carbohydrates by, in the former case, an unexpected palladium-catalyzed Heck-type cyclization followed by an unusual palladium-β-alkoxy elimination.[12] We also communicated preliminary results concerning the extension of this methodology to the preparation of unsaturated enantiopure bicyclo[4.4.0]decane systems.[13] In this paper, we describe a full account on our investigations concerning this cyclization reaction.

Results and Discussion

Preparation of the Unsaturated Starting carbohydrates

Treatment of 1,5-anhydro-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-erythro-hex-2-enitol (**1a**)[12c] with NaH and 2-bromobenzyl bromide, 1-bromo-5-bromomethyl-cyclopentene,[14] or 1-bromo-6-bromomethyl-cyclohexene,[14] in tetrahydrofuran at 60 °C, resulted in the formation of the 4-*O*-alkylated carbohydrates **2**−**4a**, in 86%, 86%, and 80% yield, respectively (Scheme 1). The same procedure, when



a: $R^1 = H$; **b**: $R^1 = OC_2H_5$; **c**: $R^1 = OC_6H_4$-*p*-*t*-Bu

Scheme 1. Synthesis of compounds **2**−**4**; reagents: (*i*) NaH, $BrCH_2C_6H_4$-*o*-Br, THF, 60 °C, 24 h; (*ii*) NaH, 1-$BrCH_2$-2-Br-cyclopent-1-ene or 1-$BrCH_2$-2-Br-cyclohex-1-ene, THF, 60 °C, 24 h

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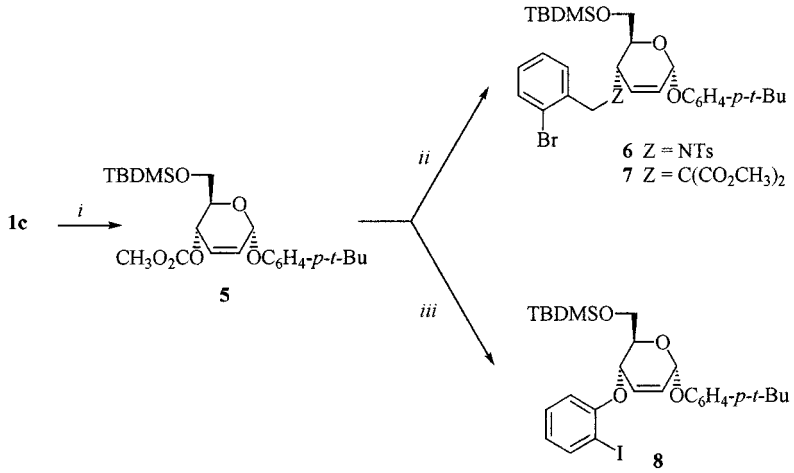
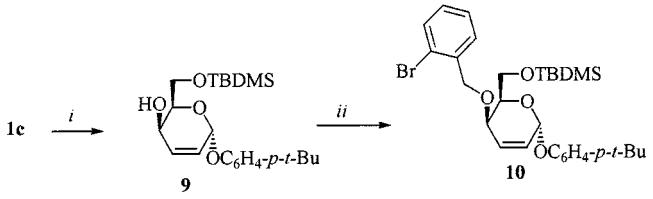


Scheme 2. Synthesis of compounds **6**−**8**; reagents: (*i*) pyridine, DMAP, $ClCO_2Me$, CH_2Cl_2, room temp., 24 h, 85% 24 h; (*ii*) for compound **6**, $TsNHCH_2C_6H_4$-*o*-Br, Pd_2dba_3, dppb, THF, 60 °C, 24 h, 73%; for compound **7**, $(MeO_2C)_2CHC_6H_4$-*o*-Br, Pd_2dba_3, dppb, THF, 60 °C, 24 h, 85%; (*iii*) HO−C_6H_4-*o*-I, Pd_2dba_3, dppb, THF, 60 °C, 24 h, 70%

applied to ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1b**) and *p*-*tert*-butylphenyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1c**), gave the corresponding 4-*O*-alkylated sugars **3b**−**c** and **4b**−**c** in 53−88% yield.

Treatment of the carbonate **5**, obtained from treatment of the unsaturated carbohydrate **1c** with methyl chloroformate, with $TsNH-CH_2-C_6H_4$-*o*-Br or $(CH_3O_2C)_2CH-CH_2-C_6H_4$-*o*-Br in tetrahydrofuran in the presence of tris(benzylideneacetone)dipalladium and 1,4-bis(diphenylphosphanyl)butane (dppb) gave the corresponding 4-*N*-alkylated carbohydrate **6** and 4-*C*-alkylated carbohydrate **7** in 73% and 85% yield, respectively (Scheme 2). Following the same methodology and using 2-iodophenol as the nucleophile, the 4-*O*-alkylated carbohydrate **8** was obtained in 70% yield.

Compound **10** was synthesized from the unsaturated carbohydrate **1c** in a two-step sequence, involving inversion of configuration at C-4 of **1c** by means of a Mitsunobu reaction,[15] followed by alkylation of the resulting alcohol with 2-bromobenzyl bromide as previously described (Scheme 3).



Scheme 3. Synthesis of compound **10**; reagents: (*i*) ref [10]; (*ii*) NaH, $BrCH_2C_6H_4$-*o*-Br, THF, 60 °C, 24 h, 84%

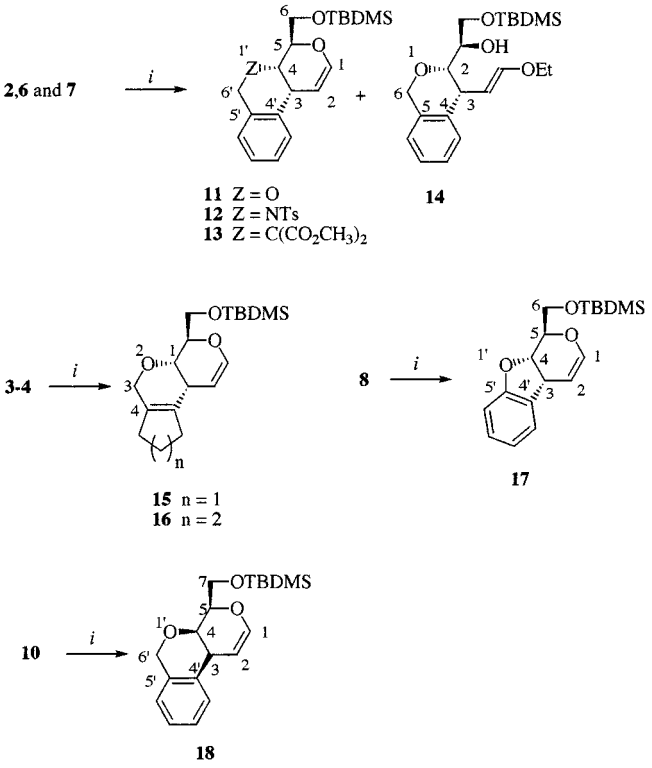
Palladium-Mediated Cyclization

The cyclization of compound **2b** was attempted under the previously described conditions[12] in the presence of $Pd(OAc)_2$, PPh_3, Bu_4NHSO_4, and NEt_3 at 80 °C in CH_3CN/H_2O (1:1) as the solvent. However, we never noticed formation of the cyclized product **11** under these conditions, only formation of ethyl 4-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside in 50% yield and of some by-products was observed. The palladium reduction of the bromo derivative **2b** is probably due to the presence of water.[16] Fortunately, the use of DMF as the solvent at 80 °C gave the expected bicyclic compound **11** in 15% yield, by an intramolecular Heck reaction followed by a β-palladium-alkoxy elimination, together with the ring-opened product **14** in 13% yield (Scheme 4). Compound **11** shows characteristic chemical shifts: at δ = 6.30, 4.65, 4.28, and 4.10 for the protons 1-H, 2-H, 5-H, and 4-H, respectively, with coupling constants $J_{1,2}$ = 6.3 Hz, $J_{1,3}$ = 2.6 Hz, and $J_{2,3}$ = 2.2 Hz. In the ^{13}C NMR spectrum, the chemical shifts for C-1, C-2, and C-3, are found, as expected, at δ = 140.6, 102.3, and 30.6, respectively.

The ^1H NMR spectrum of compound **14** showed a doublet of doublets at δ = 6.30 and a doublet of doublets at δ = 4.92 for the hydrogen atoms $CH{=}CH{-}OC_2H_5$. The coupling constant J = 12.9 Hz is typical of an *E* configuration about the double bond.[17]

From our previous study,[12] we anticipated that the presence at the anomeric position of a better leaving group than the ethoxy moiety would favor the formation of the bicyclic compound **11**. Indeed, under these conditions, unsaturated *p*-*tert*-butylphenyl hex-2-enopyranoside **2c** gave the cyclized product **11** as the sole product in 40% yield after purification by column chromatography. As expected, the unsaturated compound **2a** also gave the cyclized product **11** in 70% yield, by an usual intramolecular heck reaction. However it is to be noted that the use of absolutely dry DMF gave no reaction at all.

A similar reaction was performed with the *N*-tosyl, and *C*-substituted unsaturated carbohydrates **6** and **7** (Scheme 4). Compound **6** gave the cyclic aza-compound **12** in 55% yield; the cyclized compound **13** was obtained in 30% yield when starting from **7**. The ^1H NMR spectrum of compound **12** showed signals at δ = 6.96 and 4.96 for the vinylic hydrogens 1-H (dd) and 2-H (dd), respectively; si-



Scheme 4. Cyclization of compounds **2**−**4**, **6**−**8**, and **10**; reagents: (*i*) NEt_3, Bu_4NHSO_4, $Pd(OAc)_2$, PPh_3, DMF, 60 °C, 24 h

gnals corresponding to the same hydrogens were observed for compound **13** at δ = 6.56 and 5.20.

The cyclization process was extended to cyclopentenyl and cyclohexenyl derivatives **3** and **4**. The dihydropyrans **3a** and **4a** under the standard cyclization conditions gave the annelated dioxatricyclic compounds **15** and **16**, in 75 and 68% yield, respectively. The ^{1}H NMR spectra of these compounds again exhibited characteristic chemical shifts for the ethylenic protons: double doublets at δ = 6.28 and 6.29, respectively, for the proton α to the oxygen, and ddd signals at δ = 4.62 and 4.64, respectively, for the proton β to the oxygen. For compound **16**, the relative stereochemistry was confirmed by NOE experiments. Irradiation of the 10-H signal at δ = 2.41 gave enhancements of the signals corresponding to 11-H and 1-H of 7 and 10%, respectively, in agreement with the *cis* arrangement of 1-H and 10-H. The ethyl hex-2-enopyranosides **3b** and **4b** gave the cyclized products **15** and **16** in low yields (16 and 10%, respectively), together with degradation products. However, substitution of the ethyl aglycon by the *p*-*tert*-butylphenyl group resulted in these cyclized products **15** and **16** as the sole products, in 47 and 44% yield, respectively.

A similar reaction performed with *p*-*tert*-butylphenyl 4-*O*-(2-bromobenzyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**10**) resulted in the formation of the *cis*-fused bicyclic compound **18** in 55% yield. The ^{1}H NMR spectra of this compound exhibited characteristic chemical shifts for 1-H (d, δ = 6.37), and 2-H (d, δ = 4.68). The relative stereochemistry was again confirmed by NOE experiments. Irradiation of the 3-H signal at δ = 3.48 gave enhancements of the signals corresponding to 2-H, 4-H and 5-H of 7, 9 and 4%, respectively; this shows without doubt that these three hydrogens are on the same side of the dihydropyran ring.

Finally, the cyclization reaction under the above conditions was extended to the unsaturated carbohydrate **8**. Formation of the bicyclic compound **17**, with a five-membered ring, occurred in 43% yield. The ^{1}H NMR spectrum of this compound exhibited the characteristic signals for H-1 and H-2 at δ = 6.55 (dd) and 5.14 (dd), respectively; more importantly, the hydrogen atom H-4 appeared as a doublet of doublets at δ = 4.90 with $J_{3,4}$ = 8.4 Hz and $J_{4,5}$ = 8.4 Hz, the former value being typical of a *cis* stereochemistry in such bicyclic structures.[12c]

Conclusion

We have shown that various alkyl and aryl 4-*O*-(*o*-bromobenzyl)- or (*o*-bromocycloalkenyl)-α-Δ^2-glycopyranosides and their *N*- and *C*-analogues, possessing the *erythro* configuration, underwent a palladium-mediated Heck-type cyclization followed by a β-palladium-alkoxy or -aryloxy elimination to afford the corresponding bi- or tricyclic enantiopure derivatives, when the reaction was performed in DMF in the presence of $Pd(OAc)_2$, PPh_3, NEt_3, and Bu_4NHSO_4. The cyclization was extended to compounds of *threo* configuration, and also to aryl 4-*O*-(*o*-iodophenyl)-α-Δ^2-glycopyranoside. Thus, we have extended the field of this previously described type of cyclization in carbohydrate chemistry, in particular to the synthesis of enantiopure annelated dioxatricyclic compounds.

Experimental Section

General Remarks: ^{1}H NMR (200 or 300 MHz) and ^{13}C NMR (50 or 75 MHz) spectra were obtained using a Bruker AM 200 or AM 300 spectrometer. − Optical rotations were determined using a Perkin−Elmer 241 polarimeter. − All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (60 F-254, Merck). Compounds were exposed 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). − Reactions involving palladium complexes were carried out in a Schlenk tube under a nitrogen atmosphere.

6-*O*-(*tert*-Butyldimethylsilyl)-1,5-anhydro-2,3-dideoxy-D-*erythro*-hex-2-enitol (**1a**),[12c] ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1b**),[12c] *p*-*tert*-butylphenyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1c**),[12c] *p*-*tert*-butylphenyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**9**),[15] (2-bromocyclopent-1-enyl)methyl bromide[14] and (2-bromocyclohex-1-enyl)methyl bromide[14] were prepared by known procedures.

Standard Procedure for *O*-Alkylation: To the 4-hydroxyl compound **1a**−**c** (8.3 mmol) in 50 mL of dry THF was added NaH (60%, 383 mg, 9.6 mmol). The solution was stirred for 1 h at room temperature, and the bromo compound (16.3 mmol) in THF (10 mL) 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 × 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.

1,5-Anhydro-4-*O*-(2-bromobenzyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-*erythro*-hex-2-enitol (2a): 86% yield; R_f = 0.58 (eluent: petroleum ether/ethyl acetate, 15:1); $[\alpha]_D^{20}$ = +59.8 (*c* = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, CMe_3), 3.50 (ddd, *J* = 7.9, 5.1, 2.6 Hz, 1 H, 5-H), 3.81 (dd, *J* = 11.3, 5.1 Hz, 1 H, 6-H), 3.92 (dd, *J* = 11.3, 2.6 Hz, 1 H, 6-H), 4.08 (dm, *J* = 7.9 Hz, 1 H, 4-H), 4.13−4.19 (m, 2 H, 1-H), 4.60 (d, *J* = 12.6 Hz, 1 H, OCH_2), 4.74 (d, *J* = 12.6 Hz, 1 H, OCH_2), 5.88 (dddd, *J* = 10.4, 2.0, 1.7, 1.7 Hz, 1 H, 3-H), 6.13 (dddd, *J* = 10.4, 1.9, 1.8, 1.8 Hz, 1 H, 2-H), 7.10−7.55 (m, 4 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.2 (Me_2Si), 18.4 (Me_3C), 25.7 (Me_3C), 63.4 (C-6), 65.3 (C-1), 70.1 (OCH_2), 70.6 (C-4), 77.7 (C-5), 122.7, 125.4, 127.3, 128.5, 129.3, 132.4, and 137.6 (C-2, C-3, C_{arom}). − $C_{19}H_{31}BrO_3Si$ (415.44): calcd. C 54.93, H 7.52; found C 55.20, H 7.07.

Ethyl 4-*O*-(2-Bromobenzyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (2b): 86% yield; R_f = 0.50 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = +66.9 (*c* = 0.8, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, CMe_3), 1.24 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 3.54 (dq, *J* = 9.6, 7.0 Hz, 1 H, CH_2CH_3), 3.79−3.93 (m, 4 H, 5-H, 6-H, CH_2CH_3), 4.10 (dm, *J* = 9.0 Hz, 1 H, 4-H), 4.59 (d, *J* = 12.7 Hz, 1 H, OCH_2), 4.73 (d, *J* = 12.7 Hz, 1 H, OCH_2), 5.01 (br. s, 1 H, 1-H), 5.81 (ddd, *J* = 10.1, 2.9, 2.6 Hz, 1 H, 3-H), 6.13 (bd, *J* = 10.1 Hz, 1 H, 2-H), 7.10−7.60 (m, 4 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.3 (MeSi), −5.2 (MeSi), 15.3 (CH_3), 18.4 (Me_3C), 25.9 (Me_3C), 63.2 and 63.9 (C-6, CH_2CH_3), 68.1 (OCH_2), 70.8 and 71.1 (C-4, C-5), 94.3 (C-1), 122.5, 127.0, 127.3, 128.9, 129.2, 130.2, 132.4 and 137.6 (C-2, C-3, C_{arom}). − $C_{21}H_{33}BrO_4Si$ (457.48): calcd. C 55.14, H 7.27; found C 54.88, H 7.45.

***p*-*tert*-Butylphenyl 4-*O*-(2-Bromobenzyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (2c):** 80% yield; R_f = 0.43 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = +123.4 (*c* = 1.1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, $SiCMe_3$), 1.31 (s, 9 H, CMe_3), 3.83−3.90 (m, 2 H, 6-H), 3.98 (ddd, *J* = 9.2, 2.9, 2.9 Hz, 1 H, 5-H), 4.24 (dm, *J* = 9.2 Hz, 1 H, 4-H), 4.65 (d, *J* = 12.5 Hz, 1 H, OCH_2), 4.77 (d, *J* = 12.5 Hz, 1 H, OCH_2), 5.64 (br. s, 1 H, 1-H), 5.92 (ddd, *J* = 10.3, 2.9, 2.2 Hz, 1 H, 3-H), 6.26 (bd, *J* = 10.3 Hz, 1 H, 2-H), 7.02−7.57 (m, 8 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.3 (MeSi), −5.2 (MeSi), 18.3 (Me_3CSi), 25.9 (Me_3CSi), 31.5 (Me_3C), 34.1 (Me_3C), 62.5 (C-6), 70.5 (OCH_2), 70.3 and 71.4 (C-4, C-5), 93.1 (C-1), 116.4, 122.6, 126.0, 126.1, 127.3, 129.0, 129.3, 131.4, 132.4, 137.5, 144.5 and 155.2 (C-2, C-3, C_{arom}). − $C_{29}H_{41}BrO_4Si$ (561.64): calcd. C 62.02, H 7.36; found C 61.46, H 7.28.

1,5-Anhydro-4-*O*-[(2-bromocyclopent-1-enyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-*erythro*-hex-2-enitol (3a): 74% yield; R_f = 0.65 (eluent: petroleum ether/ethyl acetate, 5:1); $[\alpha]_D^{20}$ = +25.9 (*c* = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.92 (s, 9 H, CMe_3), 1.97 (m, 2 H, CH_2), 2.37−2.50 (m, 2 H, CH_2C=), 2.60−2.70 (m, 2 H, CH_2C=), 3.41 (ddd, *J* = 8.0, 5.1, 2.7 Hz, 1 H, 5-H), 3.79 (dd, *J* = 11.2, 5.1 Hz, 1 H, 6-H), 3.88 (m, 1 H, 4-H), 3.90 (dd, *J* = 11.2, 2.7 Hz, 1 H, 6-H), 4.07−4.27 (m, 4 H, 1-H, OCH_2), 5.87 (bd, *J* = 10.4 Hz, 1 H, 3-H), 5.97 (bd, *J* = 10.4 Hz, 1 H, 2-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.2 (Me_2Si), 18.5 (Me_3C), 21.7 (CH_2), 26.0 (Me_3C), 32.8 (CH_2C=), 40.2 (CH_2C=), 63.3 (C-6), 65.3 and 65.8 (C-1, OCH_2), 70.0 (C-4), 77.8 (C-5), 119.4 (=CHBr), 125.3 and 128.4 (C-2, C-3), 137.9 (=C<). − MS (CI, NH_3); *m*/*z*: 403 and 405 [M + H^+], 420 and 422 [M + NH_4^+].

Ethyl 4-*O*-[(2-Bromocyclopent-1-enyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (3b): 61% yield; R_f = 0.52 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = +33.3 (*c* = 0.8, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.92 (s, 9 H, CMe_3), 1.24 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.89−2.05 (m, 2 H, CH_2), 2.36−2.48 (m, 2 H, CH_2C=), 2.60−2.74 (m, 2 H, CH_2C=), 3.54 (dq, *J* = 9.6, 7.0 Hz, 1 H, CH_2CH_3), 3.75−3.95 (m, 5 H, 4-H, 5-H, 6-H, CH_2CH_3), 4.13 (d, *J* = 12.3 Hz, 1 H, OCH_2), 4.21 (d, *J* = 12.3 Hz, 1 H, OCH_2), 4.99 (bd, *J* = 2.6 Hz, 1 H, 1-H), 5.79 (ddd, *J* = 10.3, 2.6, 1.8 Hz, 1 H, 2-H), 6.10 (ddd, *J* = 10.3, 1.0, 1.0 Hz, 1 H, 3-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.2 (MeSi), −5.2 (MeSi), 15.4 (CH_3), 18.4 (Me_3C), 21.8 (CH_2), 26.0 (Me_3C), 32.9 (CH_2C=), 40.3 (CH_2C=), 63.0, 63.7 and 65.8 (C-6, OCH_2, CH_2CH_3), 70.2 and 70.6 (C-4, C-5), 94.1 (C-1), 119.4 (=CHBr), 127.0 and 130.4 (C-2, C-3), 137.8 (=C<). − MS (CI, NH_3); *m*/*z*: 446 and 448 [M + H^+], 464 and 466 [M + NH_4^+].

***p*-*tert*-Butylphenyl 4-*O*-[(2-Bromocyclopent-1-enyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (3c):** 63% yield; R_f = 0.63 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = +74.6 (*c* = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, $SiCH_3$), 0.89 (s, 9 H, $SiCMe_3$), 1.31 (s, 9 H, CMe_3), 1.90−2.05 (m, 2 H, CH_2), 2.40−2.50 (m, 2 H, CH_2C=), 2.60−2.75 (m, 2 H, CH_2C=), 3.80−3.92 (m, 3 H, 5-H, 6-H), 4.06 (m, 1 H, 4-H), 4.20 (bd, *J* = 12.2 Hz, 1 H, OCH_2), 4.27 (bd, *J* = 12.2 Hz, 1 H, OCH_2), 5.62 (bd, *J* = 2.6 Hz, 1 H, 1-H), 5.90 (ddd, *J* = 10.2, 2.6, 2.0 Hz, 1 H, 2-H), 6.26 (bd, *J* = 10.2 Hz, 1 H, 3-H), 7.05 (d, *J* = 8.6 Hz, 2 H, H_{arom}), 7.30 (d, *J* = 8.6 Hz, 2 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.3 (MeSi), −5.2 (MeSi), 18.4 (Me_3CSi), 21.7 (CH_2), 25.8 (Me_3CSi), 31.5 (Me_3C), 32.5 (CH_2C=), 32.7 (Me_3C), 36.2 (CH_2C=), 62.4 (C-6), 65.9 (OCH_2), 69.4 and 71.3 (C-4, C-5), 93.2 (C-1), 116.4, 119.6, 126.1, 126.4, 131.4, 137.6, 144.6 and 155.2 (C_{arom}, =CHBr, =C<, C-2, C-3). − MS (CI, NH_3); *m*/*z*: 401 and 403 [M + H^+ − *tert*Bu-C_6H_4OH].

1,5-Anhydro-4-*O*-[(2-bromocyclohex-1-enyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-*erythro*-hex-2-enitol (4a): 68% yield; R_f = 0.53 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = +39.6 (*c* = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, CMe_3), 1.68−1.70 (m, 4 H, CH_2), 2.20−2.25 (m, 2 H, CH_2C=), 2.50−2.55 (m, 2 H, CH_2C=), 3.41 (ddd, *J* = 7.8, 5.5, 2.2 Hz, 1 H, 5-H), 3.79 (dd, *J* = 11.0, 5.1 Hz, 1 H, 6-H), 3.88 (dd, *J* = 11.0, 2.2 Hz, 1 H, 6-H), 3.89 (bd, *J* = 7.8 Hz, 1 H, 4-H), 4.10−4.27 (m, 4 H, 1-H, OCH_2), 5.85 (bd, *J* = 10.3 Hz, 1 H, 3-H), 5.95 (bd, *J* = 10.3 Hz, 1 H, 2-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.2 (Me_2Si), 18.5 (Me_3C), 22.2 (CH_2), 24.6 (CH_2), 26.0 (Me_3C), 29.2 (CH_2C=), 36.7 (CH_2C=), 63.4 (C-6), 65.3 (OCH_2), 69.9 (C-4), 71.7 (C-1), 77.8 (C-5), 122.2 (=CHBr), 125.5 and 128.3 (C-2, C-3), 133.1 (=C<). − MS (CI, NH_3); *m*/*z*: 417 and 419 [M^+], 418 and 420 [M + H^+].

Ethyl 4-*O*-[(2-Bromocyclohex-1-enyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (4b): 83% yield; R_f = 0.57 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = +17.7 (*c* = 0.8, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, CMe_3), 1.22 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.67−1.69 (m, 4 H, CH_2), 2.15−2.25 (m, 2 H, CH_2C=), 2.45−2.55 (m, 2 H, CH_2C=), 3.53 (dq, *J* = 9.6 Hz, 7.0 Hz, 1 H, CH_2CH_3), 3.78−3.90 (m, 5 H, 4-H, 5-H, 6-H, CH_2CH_3), 4.15 (d,

J = 11.4 Hz, 1 H, OCH_2), 4.21 (d, J = 11.4 Hz, 1 H, OCH_2), 4.97 (br. s, 1 H, 1-H), 5.84 (bd, J = 9.2 Hz, 1 H, 2-H), 6.11 (bd, J = 9.2 Hz, 1 H, 3-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.1 (MeSi), −5.2 (MeSi), 15.2 (CH_3), 18.3 (Me_3C), 21.1 (CH_2), 24.6 (CH_2), 25.6 (CH_2C=), 25.9 (Me_3C), 29.0 (CH_2C=), 63.1 (C-6), 63.5 (OCH_2), 70.1 and 70.6 (C-4, C-5), 71.5 (CH_2CH_3), 94.0 (C-1), 122.1 (=CHBr), 126.7 and 130.4 (C-2, C-3), 133.0 (=C<). − MS (CI, NH_3); *m/z*: 478 and 480 [M + NH_4^+].

***p*-*tert*-Butylphenyl 4-*O*-[(2-Bromocyclohex-1-enyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (4c):** 53% yield; R_f = 0.44 (eluent: petroleum ether/ethyl acetate, 25:1); $[\alpha]_D^{20}$ = +67.8 (c = 0.8, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.87 (s, 9 H, $SiCMe_3$), 1.26 (s, 9 H, CMe_3), 1.60−1.80 (m, 4 H, CH_2), 2.30−2.40 (m, 2 H, CH_2C=), 2.50−2.60 (m, 2 H, CH_2C=), 3.83−3.90 (m, 3 H, 5-H, 6-H), 4.06 (bd, J = 9.2 Hz, 1 H, 4-H), 4.21 (bd, J = 11.8 Hz, 1 H, OCH_2), 4.26 (bd, J = 11.9 Hz, 1 H, OCH_2), 5.62 (br. s, 1 H, 1-H), 5.89 (ddd, J = 10.3, 2.2, 2.2 Hz, 1 H, 2-H), 6.24 (bd, J = 10.3 Hz, 1 H, 3-H), 7.04 (d, J = 8.5 Hz, 2 H, H_{arom}), 7.29 (d, J = 8.5 Hz, 2 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.3 (MeSi), −5.2 (MeSi), 18.4 (Me_3CSi), 22.1 (CH_2), 24.6 (CH_2), 25.9 (Me_3CSi), 29.1 (CH_2C=), 31.5 (Me_3C), 34.1 (Me_3C), 36.7 (CH_2C=), 62.5 (C-6), 69.4 and 71.3 (C-4, C-5), 71.8 (OCH_2,), 93.2 (C-1), 114.7, 125.8, 126.1, 131.6, 132.9, 144.6 and 155.2 (C_{arom}, = CHBr, =C<, C-2, C-3). − MS (CI, NH_3); *m/z*: 565 and 567 [M + H^+], 581 and 583 [M + NH_4^+].

***p*-*tert*-Butylphenyl 4-*O*-(2-Bromobenzyl)-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (10):** 84% yield; R_f = 0.60 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = −64.3 (c = 1.1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 6 H, $SiCH_3$), 0.84 (s, 9 H, $SiCMe_3$), 1.31 (s, 9 H, CMe_3), 3.82 (dd, J = 10.1, 6.4 Hz, 1 H, 6-H), 3.92 (dd, J = 5.2, 2.5 Hz, 1 H, 4-H), 3.96 (dd, J = 10.1, 7.1 Hz, 1 H, 6-H), 4.25 (ddd, J = 7.1, 6.4, 2.5 Hz, 5-H), 4.69 (d, J = 13.0 Hz, 1 H, OCH_2), 4.79 (d, J = 13.0 Hz, 1 H, OCH_2), 5.76 (d, J = 2.8 Hz, 1 H, 1-H), 6.15 (dd, J = 10.0, 2.8 Hz, 1 H, 2-H), 6.37 (dd, J = 10.0, 5.2 Hz, 1 H, 3-H), 7.08−7.54 (m, 8 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.3 (MeSi), 18.3 (Me_3CSi), 26.0 (Me_3CSi), 31.6 (Me_3C), 34.2 (Me_3C), 62.0 (C-6), 67.7 (C-5), 70.8 (OCH_2), 72.1 (C-4), 93.3 (C-1), 116.7, 122.6, 126.4, 127.4, 127.8, 129.0, 129.4, 132.5, 138.0, 144.5 and 155.3 (C-2, C-3, C_{arom}). − $C_{29}H_{41}O_4BrSi$ (561.64): calcd. C 62.02, H 7.36; found C 62.43, H 7.45.

***p*-*tert*-Butylphenyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-4-*O*-(methoxycarbonyl)-α-D-*erythro*-hex-2-enopyranoside (5):** To a solution of **1c** (1.5 g, 3.8 mmol) in CH_2Cl_2 (20 mL) at room temperature was added DMAP (46 mg, 0.38 mmol), pyridine (3.1 mL, 38.2 mmol), and methyl chloroformate (2.95 mL, 38.2 mmol). The mixture was stirred for 24 h at room temperature. After addition of 60 mL of an aqueous solution of $CuSO_4 \cdot 5H_2O$, the solution was extracted with 4 × 50 mL of Et_2O. The organic layer was dried, the solvent was removed under reduced pressure, and the product was purified by column chromatography on silica gel with petroleum ether/ethyl acetate 5:1 as the eluent to give 1.46 g (85%) of the carbonate **5** as an oil: R_f = 0.60; $[\alpha]_D^{20}$ = 152.3 (c = 1.2, CH_2Cl_2). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.04 (s, 6 H, $SiCH_3$), 0.86 (s, 9 H, $SiCMe_3$), 1.31 (s, 9 H, CMe_3), 3.80 (d, J = 3.4 Hz, 2 H, 6-H), 3.83 (s, 3 H, CH_3), 4.06 (dt, J = 9.5, 3.4 Hz, 1 H, 5-H), 5.31 (ddd, J = 9.5, 1.5, 1.4 Hz, 1 H, 4-H), 5.70 (br. s, 1 H, 1-H), 5.98 (ddd, J = 10.1, 2.7, 1.9 Hz, 1 H, 2-H), 6.12 (bd, J = 10.1 Hz, 1 H, 3-H), 7.03 (d, J = 8.9 Hz, 2 H, H_{arom}), 7.30 (d, J = 10.1 Hz, 2 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.1 (MeSi), 18.4 (Me_3CSi), 25.9 (Me_3CSi), 31.6 (Me_3C), 34.2 (Me_3C), 55.0 (CH_3O), 62.4 (C-6), 68.7 and 69.9 (C-4, C-5), 93.1 (C-1), 116.5, 126.3, 127.5, 129.8, 145.0 and 155.1 (C-2, C-3, C_{arom}), 155.2 (CO). − $C_{24}H_{38}O_6Si$ (450.65): calcd. C 63.97, H 8.50; found C 64.19, H 8.41.

General Procedure for *N*-, *C*- and *O*-Alkylation: To a solution of the carbonate **5** (500 mg, 1.1 mmol) in dry THF (10 mL) was added either $TsNHCH_2C_6H_4$-*o*-Br (574 mg, 1.5 mmol), or $(MeO_2C)_2CHCH_2C_6H_4$-*o*-Br (451 mg, 1.5 mmol), or *o*-iodophenol (330 mg, 1.5 mmol), together with the catalytic system obtained by treating $Pd_2(dba)_3$ (25.2 mg, 0.027 mmol) with dppb (23.5 mg, 0.055 mmol) in 5 mL of THF. The mixture was stirred at 60 °C for 24 h and quenched with 10 mL of H_2O. After extraction with 3 × 15 mL of Et_2O, the organic layer was dried. The solvent was removed under reduced pressure to give an oil that was purified by column chromatography on silica gel, using petroleum ether/ethyl acetate as the eluent.

***p*-*tert*-Butylphenyl 4-[*N*-(2-Bromobenzyl)-*N*-tosylamino]-6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (6):** 73% yield; R_f = 0.65 (eluent: petroleum ether/ethyl acetate, 5:1); $[\alpha]_D^{20}$ = 112.1 (c = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, $SiCH_3$), 0.80 (s, 9 H, $SiCMe_3$), 1.26 (s, 9 H, CMe_3), 2.47 (s, 3 H, CH_3), 3.58−3.80 (m, 3 H, 6-H, 5-H), 4.38 (bd, J = 16.9 Hz, 1 H, CH_2N), 4.57−4.67 (m, 2 H, 4-H, CH_2N), 5.27 (bd, J = 10.3 Hz, 1 H, 2-H), 5.52 (br. s, 1 H, 1-H), 5.94 (bd, J = 10.3 Hz, 1 H, 3-H), 7.07−7.50 (m, 8 H, H_{arom}), 7.68 (d, J = 7.7 Hz, 2 H, H_{arom}), 7.77 (d, J = 8.1 Hz, 2 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.3 (MeSi), 18.3 (Me_3CSi), 21.7 (CH_3), 25.9 (Me_3CSi), 31.5 (Me_3C), 34.1 (Me_3C), 48.9 (CH_2N), 53.4 (C-4), 62.6 (C-6), 69.6 (C-5), 92.2 (C-1), 116.6, 122.5, 126.1, 127.5, 127.6, 128.9, 129.3, 130.1, 132.7, 137.0, 144.1, 144.8 and 155.0 (C-2, C-3, C_{arom}). − $C_{36}H_{49}O_5BrNSSi$ (715.84): calcd. C 60.40, H 6.90; found C 60.31, H 6.83.

***p*-*tert*-Butylphenyl 4-[1-(2-Bromobenzyl)-1,1-bis(methoxycarbonyl)methyl]-6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (7):** 85% yield; R_f = 0.8 (eluent: petroleum ether/ethyl acetate, 5:1); $[\alpha]_D^{20}$ = 11.5 (c = 0.4, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.12 (s, 6 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.94 (s, 9 H, $SiCMe_3$), 1.30 (s, 9 H, CMe_3), 2.96 (m, 1 H, 4-H), 3.57 (s, 3 H, OCH_3), 3.60−3.65 (m, 2 H, CH_2), 3.69 (s, 3 H, OCH_3), 3.84 (dd, J = 11.4, 7.0 Hz, 1 H, 6-H), 3.90 (dd, J = 11.4, 4.1 Hz, 1 H, 6-H), 4.35 (m, 1 H, 5-H), 5.74 (br. s, 1 H, 1-H), 6.03 (bd, J = 10.3 Hz, 1 H, 2-H), 6.11 (dd, J = 10.3, 3.3 Hz, 1 H, 3-H), 7.07−7.12 (m, 3 H, H_{arom}), 7.19−7.55 (m, 2 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.3 (MeSi), −5.1 (MeSi), 18.4 (Me_3CSi), 26.0 (Me_3CSi), 31.6 (Me_3C), 34.2 (Me_3C), 37.4 (CH_2), 39.3 (C-4), 52.6 (OCH_3), 52.7 (OCH_3), 61.5 (CCO_2Me), 64.1 (C-6), 73.1 (C-5), 91.6 (C-1), 116.0, 126.1, 127.3, 128.3, 128.4, 128.6, 132.0, 132.5, 144.4 and 155.4 (C-2, C-3, C_{arom}), 170.1 and 170.5 (CO). − $C_{34}H_{47}BrO_7Si$ (675.74): calcd. C 60.43, H 7.01; found C 60.74, H 7.03.

***p*-*tert*-Butylphenyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-4-*O*-(*o*-iodophenyl)-α-D-*erythro*-hex-2-enopyranoside (8):** 70% yield; R_f = 0.52 (eluent: petroleum ether/ethyl acetate, 9:1); $[\alpha]_D^{20}$ = 38.5 (c = 0.5, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, $SiCH_3$), 0.80 (s, 9 H, $SiCMe_3$), 1.26 (s, 3 H, $CH_3-C_6H_4$), 3.88 (dd, J = 11.8, 3.7 Hz, 1 H, 6-H), 3.94 (dd, J = 11.8, 1.8 Hz, 1 H, 6-H), 4.23 (ddd, J = 9.1, 3.7, 1.8 Hz, 1 H, 5-H), 5.04 (bd, J = 9.1 Hz, 1 H, 4-H), 5.72 (br. s, 1 H, 1-H), 5.98 (ddd, J = 10.3, 2.5, 2.2 Hz, 1 H, 2-H), 6.23 (bd, J = 10.3 Hz, 1 H, 3-H), 6.73 (dd, J = 7.7, 1.5 Hz, 1 H, H_{arom}), 6.93 (d, J = 7.7 Hz, 1 H, H_{arom}), 7.68 (d, J = 7.7 Hz, 2 H, H_{arom}), 7.06−7.15 (m, 2 H, H_{arom}), 7.26−7.34 (m, 2

H, H_{arom}), 7.78 (dd, J = 7.7, 1.5 Hz, 1 H, H_{arom}). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.2 (MeSi), 18.4 (Me_3CSi), 26.0 (Me_3CSi), 31.6 (Me_3C), 34.2 (Me_3C), 37.4 (CH_2), 62.1 (C-6), 69.6, 71.0 (C-4, C-5), 87.5 (C_{arom}), 93.5 (C-1), 113.4, 116.4, 123.1, 126.3, 127.0, 129.5, 130.3, 139.9, 144.9 and 155.2 (C-2, C-3, C_{arom}). − $C_{28}H_{39}IO_4Si$ (594.61): calcd. C 56.56, H 6.61; found C 56.15, H 6.54.

Ethyl 4-*O*-Benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside: A solution of compound **2b** (561 mg, 1.0 mmol) in CH_3CN (15 mL) and H_2O (3 mL) was heated in the presence of $Pd(OAc)_2$ (11 mg, 0.05 mmol), PPh_3 (26.5 mg, 0.10 mmol), Bu_4NHSO_4 (1.0 mmol), and NEt_3 (700 μL, 2.5 mmol) at 80 °C for 24 h. The reaction was quenched with 10 mL of water, and the mixture was extracted with 3 × 30 mL of Et_2O. Evaporation of the solvent under reduced pressure gave an oil that was purified by column chromatography on silica gel, with petroleum ether/ethyl acetate 10:1 as the eluent, to give 190 mg (50%) of ethyl 4-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside as an oil: R_f = 0.4 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = 120.3 (c = 1.2, CH_2Cl_2). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.05 (s, 6 H, $SiCH_3$), 0.08 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, $SiCMe_3$), 1.21 (t, J = 7.1 Hz, 1 H, CH_3), 3.57 (dq, J = 9.6, 7.1 Hz, 1 H, CH_2CH_3), 3.25−3.78 (m, 4 H, 5-H, 6-H, CH_2CH_3), 4.04 (dd, J = 9.2, 1.3 Hz, 1 H, 4-H), 4.54 (d, J = 11.6 Hz, 1 H, OCH_2), 4.64 (d, J = 11.6 Hz, 1 H, OCH_2), 5.00 (dd, J = 2.8, 1.1 Hz, 1 H, 1-H), 5.80 (ddd, J = 10.2, 2.7, 2.7 Hz, 1 H, 2-H), 6.08 (bd, J = 10.2 Hz, 1 H, 3-H), 7.24−7.43 (m, 5 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.1 (MeSi), −5.0 (MeSi), 15.4 (CH_2CH_3), 18.5 (Me_3CSi), 26.1 (Me_3CSi), 63.1 and 63.7 (C-8, OCH_2CH_3), 70.6 and 70.7 (C-4, C-5), 70.8 (C-6), 94.2 (C-1), 127.8 and 130.7 (C-2, C-3), 127.1, 127.8, 128.5 and 140.0 (C_{arom}). − $C_{21}H_{34}O_4Si$ (378.59): calcd. C 66.62, H 9.05; found C 65.98, H 9.39.

Standard Palladium(0)-Mediated Cyclization Procedure: A solution of the unsaturated glycoside (0.36 mmol) in DMF (9 mL) was heated in the presence of $Pd(OAc)_2$ (8 mg, 0.036 mmol), PPh_3 (18.7 mg, 0.07 mmol), Bu_4NHSO_4 (120 mg, 0.36 mmol), and NEt_3 (0.13 mL, 0.89 mmol) at 80 °C for 48 h. Water (10 mL) was added at room temperature, and the solution was treated with 3 × 15 mL of 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.

D-*ribo*-Hex-1-enopyranoso[4,3-*b*]benzopyran (11) R_f = 0.5 (eluent: petroleum ether/ethyl acetate, 16:1); $[\alpha]_D^{20}$ = 128.6 (c = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$, primed assignments refer to the benzopyran moiety): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, $SiCMe_3$), 3.37 (m, 1 H, 3-H), 3.77 (dd, J = 10.6, 7.4 Hz, 1 H, 6-H), 3.85 (dd, J = 10.6, 5.7 Hz, 1 H, 6-H), 4.10 (m, 1 H, 4-H), 4.28 (ddd, J = 7.4, 5.7, 2.2 Hz, 1 H, 5-H), 4.65 (ddd, J = 6.3, 2.2, 1.8 Hz, 1 H, 2-H), 4.89 (d, J = 15.1 Hz, 1 H, 6′-H), 4.92 (d, J = 15.1 Hz, 1 H, 6′-H), 6.30 (dd, J = 6.3, 2.6 Hz, 1 H, 1-H), 7.02−7.29 (m, 4 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.3 (MeSi), 18.3 (Me_3CSi), 25.9 (Me_3CSi), 30.6 (C-3), 61.9 (C-6), 67.8 (C-6′), 69.4 (C-4), 76.6 (C-5), 102.3 (C-2), 124.3, 126.4, 127.2, 128.6, 134.2, 135.7 (C_{arom}), 140.6 (C-1). − $C_{19}H_{28}O_3Si$ (332.52): calcd. C 68.43, H 8.49; found C 69.19, H 8.75.

D-*ribo*-Hex-1-enopyranoso[4,3-*b*]isoquinoline (12): 55% yield; R_f = 0.5 (eluent: petroleum ether/dichloromethane, 1:1); $[\alpha]_D^{20}$ = 85.7 (c = 1.1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$, primed assignments refer to the isoquinoline moiety): δ = 0.06 (s, 6 H, $SiCH_3$), 0.92 (s, 9 H, $SiCMe_3$), 2.34 (CH_3), 3.23 (bdd, J = 5.5, 5.1 Hz, 1 H, 3-H), 3.79 (ddd, J = 9.2, 3.7, 3.2 Hz, 1 H, 5-H), 3.91 (dd, J = 14.0, 3.3 Hz, 1 H, 6-H), 3.97 (dd, J = 14.0, 3.7 Hz, 1 H, 6-H), 4.31 (dd, J = 9.2, 5.1 Hz, 1 H, 4-H), 4.40 (d, J = 17.3 Hz, 1 H, 6′-H), 4.74 (d, J = 17.3 Hz, 1 H, 6′-H), 4.96 (dd, J = 5.9, 5.5 Hz, 1 H, 2-H), 6.96 (dd, J = 5.9, 1.5 Hz, 1 H, 1-H), 7.01 (d, J = 6.6 Hz, 1 H, H_{arom}), 7.10−7.15 (m, 1 H, H_{arom}), 7.60 (d, J = 8.1 Hz, 1 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.3 (MeSi), −5.2 (MeSi), 18.5 (Me_3CSi), 21.5 (C-3), 26.0 (Me_3CSi), 34.9 (CH_3), 43.9 (C-6′), 50.8 (C-4), 63.6 (C-6), 75.1 (C-5), 101.1 (C-2), 126.0, 126.3, 127.1, 127.4, 128.2, 129.6, 130.1, 136.4 and 137.0 (C_{arom}), 143.4 (C-1). − $C_{26}H_{35}O_4NSSi$ (485.72): calcd. C 64.29, H 7.26; found C 64.47, H 8.09.

D-*ribo*-Hex-1-enopyranoso[4,3-*b*]naphthalene (13) 30% yield; R_f = 0.4 (eluent: petroleum ether/dichloromethane, 1:2); $[\alpha]_D^{20}$ = 52.6 (c = 0.7, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$, primed assignments refer to the naphthaline moiety): δ = 0.09 (s, 6 H, $SiCH_3$), 0.91 (s, 9 H, $SiCMe_3$), 2.34 (dd, J = 9.6, 1.2 Hz, 1 H, 4-H), 3.36 (d, J = 16.2 Hz, 1 H, 6′-H), 3.47 (d, J = 16.2 Hz, 1 H, 6′-H), 3.74 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.68−3.83 (m, 2 H, 6-H, 3-H), 3.87 (dd, J = 11.6, 2.2 Hz, 1 H, 6-H), 4.37 (ddd, J = 9.6, 8.5, 2.2 Hz, 1 H, 5-H), 5.20 (dd, J = 5.9, 1.8 Hz, 1 H, 2-H), 6.56 (dd, J = 5.9, 2.6 Hz, 1 H, 1-H), 7.10−7.30 (m, 4 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.1 (MeSi), −5.0 (MeSi), 18.6 (Me_3CSi), 26.1 (Me_3CSi), 36.0 (C-4), 38.7 (C-6′), 43.1 (C-3), 52.7 (OCH_3), 52.9 (OCH_3), 56.6 (C-1′), 64.4 (C-6), 80.7 (C-5), 101.8 (C-2), 124.8, 126.5, 126.7, 128.0, 132.8, 137.0 (C_{arom}), 144.2 (C-1), 170.4 (CO_2), 172.5 (CO_2). − CI-HRMS (NH_3) (measured on M + H^+ peak). − $C_{24}H_{34}O_6Si$: calcd. 447.22029, found 447.22065.

***(2S,3R,1′R)*-2-[-2′-(*tert*-Butyldimethylsilyloxy)-1′-hydroxyethyl]-3-[*(E)*-2′-ethoxyethenyl]-2,3-dihydro-*6H*-benzopyran (14):** 13% yield; R_f = 0.4 (eluent: petroleum ether/ethyl acetate, 16:1); $[\alpha]_D^{20}$ = −87.3 (c = 1, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiCH_3$), 0.90 (s, 9 H, $SiCMe_3$), 1.23 (t, J = 7.0 Hz, 1 H, CH_2CH_3), 2.45 (s, 1 H, OH), 3.47 (dd, J = 9.6, 2.4 Hz, 1 H, 3-H), 3.52 (dd, J = 9.2, 2.4 Hz, 1 H, 2-H), 3.65−3.76 (m, 3 H, CHO-H,OCH_2CH_3), 3.81 (dd, J = 9.9, 4.4 Hz, 1 H, CH_2OTBDMS), 3.87 (dd, J = 9.9, 4.4 Hz, 1 H, CH_2OTBDMS), 4.77 (d, J = 15.1 Hz, 1 H, 6-H), 4.87 (d, J = 15.1 Hz, 1 H, 6-H), 4.92 (dd, J = 12.6, 9.6 Hz, 1 H, −CH=), 6.30 (d, J = 12.9 Hz, 1 H, =CH−O), 6.96−7.00 (m, 1 H, H_{arom}), 7.14−7.19 (m, 3 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 5.4 (MeSi), 14.7 (CH_3), 18.3 (Me_3CSi), 25.9 (Me_3CSi), 38.6 (C-3), 63.8 (OCH_2CH_3), 64.3 (CH_2OTBDMS), 68.6 (C-6), 70.6 (CHOH), 76.8 (C-2), 103.4 (−CH=), 123.8, 126.1, 126.5, 130.0, 133.7, 137.4 (C_{arom}), 147.4 (=CH−O). − $C_{21}H_{34}O_4Si$ (358.59): calcd. C 66.62, H 9.05; found C 67.22, H 9.09.

***(1S,9R,13S)*-13-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-2,12-dioxatricyclo[7,4,0,$0^{4,8}$]trideca-4(8),10-diene (15):** R_f = 0.53 (eluent: petroleum ether/ethyl acetate, 8:1); $[\alpha]_D^{20}$ = 233.6 (c = 2.5, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 6 H, $SiCH_3$), 0.90 (s, 9 H, $SiCMe_3$), 1.86−1.98 (m, 2 H, CH_2), 2.25−2.29 (m, 3 H, CH_2), 2.50 (m, 1 H, CH_2), 2.70 (br. s, 1 H, 9-H), 3.74 (dd, J = 10.7, 6.6 Hz, 1 H, CH_2OTBDMS), 3.80 (dd, J = 10.7, 6.3 Hz, 1 H, CH_2OTBDMS), 3.84 (ddd, J = 9.2, 4.4, 1.5 Hz, 1 H, 1-H), 4.17 (ddd, J = 9.2, 6.6, 6.3 Hz, 1 H, 13-H), 4.18 (d, J = 15.4 Hz, 1 H, 3-H), 4.24 (d, J = 15.4 Hz, 1 H, 3-H), 4.62 (ddd, J = 6.3, 2.6, 1.5 Hz, 1 H, 10-H), 6.28 (dd, J = 6.3, 2.6 Hz, 1 H, 11-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.3 (MeSi), 18.3 (Me_3CSi), 21.9 (CH_2), 25.9 (Me_3CSi), 29.8 (C-9), 33.1 and 33.3 (CH_2CH=), 62.0 (CH_2OTBDMS), 65.9 (C-3), 76.1 and 77.4 (C-1, C-13), 99.2 (C-10), 132.9 and 133.8 (C-4, C-8), 140.8 (C-11). − CI-HRMS (NH_3) (measured on M + H^+ peak); $C_{18}H_{30}O_3Si$: calcd. 323.20425, found 323.20332.

***(1S,10R,14S)*-14-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-2,13-dioxatricyclo[8,4,0,0^{4,9}]tetradeca-4(9),11-diene (16):** R_f = 0.42 (eluent: petroleum ether/ethyl acetate, 10:1); $[\alpha]_D^{20}$ = 337.7 (*c* = 2.6, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 6 H, $SiCH_3$), 0.90 (s, 9 H, $SiCMe_3$), 1.44−1.72 (m, 8 H, CH_2), 2.41 (m, 1 H, 10-H), 3.70 (dd, *J* = 10.8, 6.1 Hz, 1 H, C*H*$_2$OTBDMS), 3.82 (dd, *J* = 10.8, 6.1 Hz, 1 H, C*H*$_2$OTBDMS), 3.93 (m, 1 H, 1-H), 4.01 (d, *J* = 16.2 Hz, 1 H, 3-H), 4.07 (d, *J* = 16.2 Hz, 1 H, 3-H), 4.21 (ddd, *J* = 9.7, 7.0, 6.1 Hz, 1 H, 14-H), 4.64 (ddd, *J* = 6.3, 2.1, 1.9 Hz, 1 H, 11-H), 6.29 (dd, *J* = 6.3, 2.5 Hz, 1 H, 12-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.5 (MeSi), −5.3 (MeSi), 18.3 (Me_3*C*Si), 22.3 and 22.7 (CH_2), 25.9 (*Me*$_3$CSi), 25.0 and 26.9 (*C*H$_2$CH=), 31.6 (C-10), 62.0 (*C*H$_2$OTBDMS), 68.4 (C-3), 69.1 and 76.6 (C-1, C-14), 99.4 (C-11), 126.9 and 127.5 (C-4, C-9), 140.5 (C-12). − CI-HRMS (NH_3) (measured on M + H^+ peak); $C_{19}H_{32}O_3Si$: calcd. 337.21990, found 337.21966.

D-*ribo*-Hex-1-enopyranoso[4,3-*b*]benzofuran (17): 43% yield; R_f = 0.5 (eluent: petroleum ether/ethyl acetate, 15:1); $[\alpha]_D^{20}$ = 69.5 (*c* = 1.3, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$, primed assignments refer to the benzopyran moiety): δ = 0.11 (s, 6 H, $SiCH_3$), 0.88 (s, 9 H, $SiCme_3$), 3.59 (ddd, *J* = 8.4, 4.0, 1.5 Hz, 1 H, 3-H), 3.94 (dd, *J* = 11.4, 4.4 Hz, 1 H, 6-H), 4.00 (dd, *J* = 11.4, 2.9 Hz, 1 H, 6-H), 4.01 (m, 1 H, 5-H), 4.90 (dd, *J* = 8.4, 8.4 Hz, 1 H, 4-H), 5.14 (dd, *J* = 5.9, 4.0 Hz, 1 H, 2-H), 6.55 (dd, *J* = 5.9, 1.5 Hz, 1 H, 1-H), 6.81 (dd, *J* = 7.6, 7.6 Hz, 1 H, H_{arom}), 6.89 (dd, *J* = 7.6, 7.6 Hz, 1 H, H_{arom}), 7.11 (bd, *J* = 7.6 Hz, 1 H, H_{arom}), 7.16 (bd, *J* = 7.6 Hz, 1 H, H_{arom}). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.2 (MeSi), 18.5 (Me_3*C*Si), 26.0 (*Me*$_3$CSi), 37.5 (C-3), 62.6 (C-6), 74.5 (C-5), 76.7 (C-4), 100.5 (C-2), 110.4, 121.1, 124.1, 128.3, 131.0 (C_{arom}), 144.4 (C-1). − EI-HRMS; $C_{18}H_{26}O_3Si$: calcd. 318.16512, found 318.16521.

D-*lyxo*-Hex-1-enopyranoso[4,3-*b*]benzopyran (18): 55% yield; R_f = 0.5 (eluent: petroleum ether/ethyl acetate, 15:1); $[\alpha]_D^{20}$ = −23.4 (*c* = 0.6, CH_2Cl_2). − ^{1}H NMR (300 MHz, $CDCl_3$, primed assignments refer to the benzopyran moiety): δ = 0.12 (s, 6 H, $SiCH_3$), 0.92 (s, 9 H, $SiCMe_3$), 3.48 (m, 1 H, 3-H), 3.86 (dd, *J* = 13.2, 10.3 Hz, 1 H, 6-H), 4.00 (dd, *J* = 13.2, 8.8 Hz, 1 H, 6-H), 4.07 (m, 1 H, 5-H), 4.09 (m, 1 H, 4-H), 4.68 (d, *J* = 5.9 Hz, 1 H, 2-H), 4.81 (d, *J* = 15.4 Hz, 1 H, 6′-H), 4.92 (d, *J* = 15.4 Hz, 1 H, 6′-H), 6.37 (d, *J* = 5.9 Hz, 1 H, 1-H), 7.02 (d, *J* = 5.9 Hz, 1 H, H_{arom}), 7.16−7.26 (m, 3 H, H_{arom}). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.4 (MeSi), −5.3 (MeSi), 18.4 (Me_3*C*Si), 26.0 (*Me*$_3$CSi), 34.1 (C-3), 61.3 (C-6), 68.3 (C-6′), 68.4 (C-4), 76.7 (C-5), 104.1 (C-2), 124.2, 126.4, 127.1, 128.8, 134.2, 135.9 (C_{arom}), 141.9 (C-1). − CI-HRMS (NH_3) (measured on the M + H^+ peak); $C_{19}H_{28}O_3Si$: calcd. 333.18860, found 333.18874.

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