Synthesis of a New C(1 → 2)-Linked Iminodisaccharide Starting from Levoglucosenone

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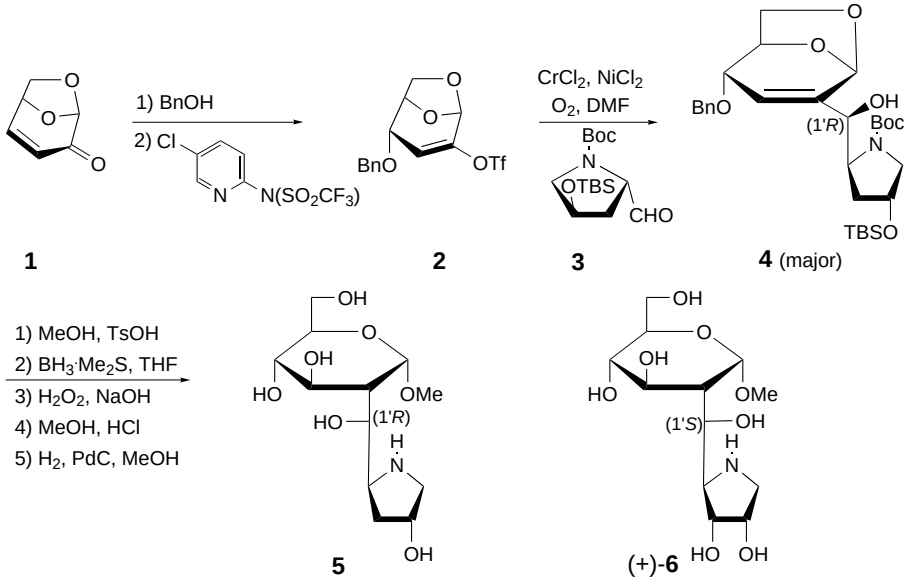
Methyl 2-deoxy-2-[(1*S*)-2,5-dideoxy-2,5-imino-L-ribitol-1-*C*-yl)-α-D-glucopyranoside ((+)-**6**) was obtained from the product of *Nozaki-Kishi* coupling of 2,5-{[(*tert*-butoxy)carbonyl]imino}-2,5-dideoxy-3,4-*O*-isopropylidene-L-ribose ((−)-**9**) and 4-*O*-benzyl-6-*O*-[(benzyloxy)methyl]-3-deoxy-2-*O*-[(trifluoromethyl)sulfonyl]-α-D-*erythro*-hex-2-enopyranoside ((+)-**12**). The alkenyl triflate (+)-**12** was derived from levoglucosenone (**1**).

Introduction. – Carbohydrate mimics are potentially useful molecular tools for biology [1] and may become leads for drug discovery [2]. In particular, C-linked disaccharides and oligosaccharides containing them offer the advantage of being resistant to acidic and enzymatic hydrolysis [3]. They are potential inhibitors of glycosidases and glycosyltransferases [4][5] and potential antibacterial, antiviral, antimetastatic, antidiabetes, antihyperglycemic, antiadhesive, and immunostimulatory agents [6][7]. A new class of selective glycosidase inhibitors has emerged, namely C-linked iminodisaccharides (aza-*C*-disaccharides) [8][9], which contain not only the steric and charge information of the glycosyl moiety liberated during the enzyme-catalyzed hydrolysis, but also that of the aglycon. The first example of a C-linked iminodisaccharide (1,5-dideoxy-1,5-imino-D-mannitol linked at C(6) of D-galactose through a CH_2 unit) was prepared by *Johnson et al.* [10]. Other examples of 'linear' C-linked iminodisaccharides were obtained by the groups of *Martin et al.* [11] and *van Boom* and co-workers [12]. We have prepared the first examples of 'branched' disaccharides [8][13]. Further examples were reported by *Johnson et al.* [9] and by our group [14][15]. *Brandi* and co-workers [16] have obtained the first examples of (1 → 2)-linked pseudo imino-*C*-disaccharides in which pyrrolidine-2,3-diol or a pyrrolidin-2-ol is linked at C(2) of D-glucose *via* a C−C bond.

In a preliminary report [17], our group had shown that (1 → 2)-C-linked disaccharides can be obtained applying the *Nozaki-Kishi* coupling reaction to triflate **2** (derived in two steps from levoglucosenone **1** [18]) and aldehyde **3** (derived from (4*R*)-4-hydroxy-L-proline). This generated allylic alcohol **4** (48%) that was converted (*Scheme 1*) to the imino-*C*-disaccharide **5**. We have now applied this method to the preparation of the new C-linked iminodisaccharide (+)-**6** in which a pyrrolidine-3,4-diol moiety is attached at C(2) of methyl α-D-glucopyranoside through a hydroxymethylene linker. As we shall see, the *Nozaki-Kishi* coupling was more difficult in this case and required a monocyclic alkenyl triflate rather than the bicyclic triflate **2** for a reasonable yield of condensation. Futhermore, the diastereoselectivity of the coupling was opposite to that reported with **2** + **3** → **4** [17].

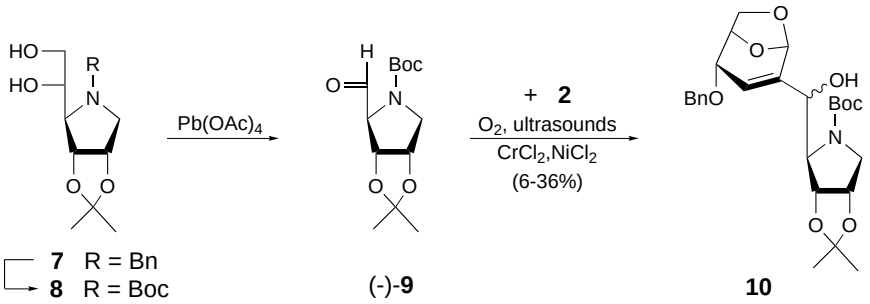
Scheme 1



Tf = CF_3SO_2; Bn = $PhCH_2$; TBS = (*t*-Bu)Me_2Si; Boc = (*t*-Bu)OCO

Results and Discussion. – The starting aldehyde (−)-**9** was derived from the known 1,4-(benzylimino)-1,4-dideoxy-2,3-*O*-isopropylidene-D-allitol (**7**) [19]. Hydrogenolysis (H_2,$Pd(OH)_2$/C) in MeOH containing an excess of (*t*-BuOCO)$_2$O ((Boc)$_2$O) provided **8** (86%) [19] that was oxidized with $Pb(OAc)_4$/$NaHCO_3$ (CH_2Cl_2, −78°) to aldehyde (−)-**9** in 80% yield (*Scheme 2*). After a large number of unsuccessful *Nozaki-Kishi* coupling [20] attempts with triflate **2** and aldehyde (−)-**9**, we found that a 2:1 diastereoisomer mixture **10** of allylic alcohols was formed in mediocre yield (6–36%) in the presence of *ca.* 5 mol-% of O_2 and under activation with ultrasound. This suggested that the *Nozaki-Kishi* coupling is highly sensitive to steric factors: aldehyde (−)-**9** is more hindered and less flexible than aldehyde **3**.

Scheme 2



We then decided to convert the bicyclic triflate **2** into monocyclic derivative (+)-**12** (*Scheme 3*). Acidic methanolysis (MeOH/$FB_3 \cdot Et_2O$) of the anhydrohexose **2** provided (+)-**11** in 67% yield. Protection of the primary-alcohol moiety of (+)-**11** as a (benzyloxy)methyl (BOM) ether under standard conditions [21] provided (+)-**12** (68%). Its *Nozaki-Kishi* coupling with aldehyde (−)-**9** furnished as a single diastereoisomer the allylic alcohol (+)-**13**, isolated in 48% yield. In contrast to the coupling **2** + **3** → **4** (*Scheme 1*) for which the (1′*R*)-alcohol was obtained as major product, the reaction (−)-**9** + (+)-**12** → (+)-**13** generated a (1′*S*)-alcohol (for configuration assignment, see below). This implies that the *Re* face of aldehyde **3** is preferred for the addition of the alkenylchromium reagent derived from **2**, whereas the *Si* face of aldehyde (−)-**9** is preferred for the addition of the alkenylchromium reagent derived from (+)-**12** (see *Fig. 1*). The reason for this change in diastereoselectivity is unknown to us at the moment.

Scheme 3

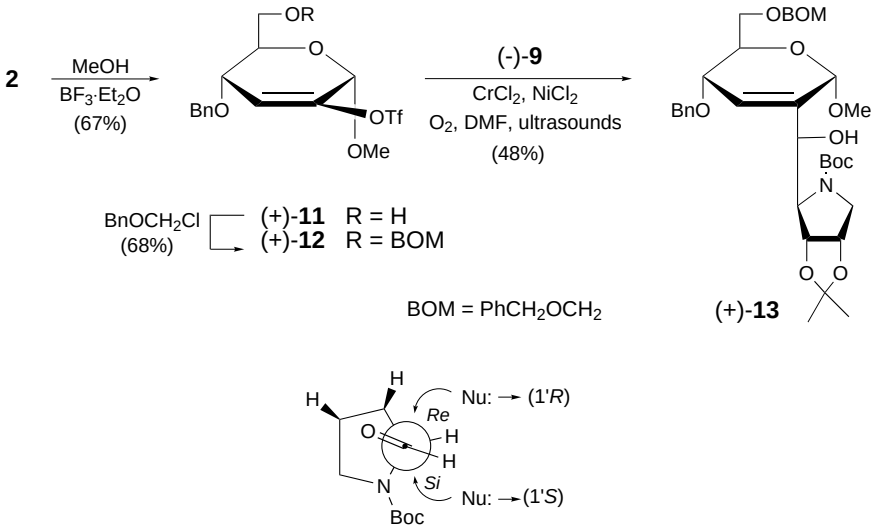
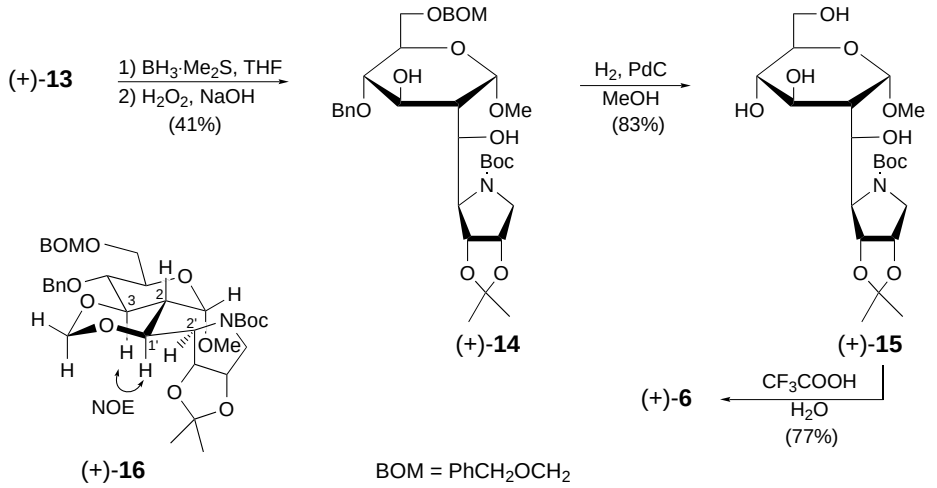


Fig. 1. *Possible nucleophilic additions to aldehydes* **3** *and (+)-*12 (*Felkin-Anh* model [22])

Hydroboration of the alkene moiety of (+)-**13** with $BH_3 \cdot Me_2S$ in THF, followed by oxidative workup (35% H_2O_2/NaOH) gave alcohol (+)-**14** in modest yield (41%) (*Scheme 4*). Attempts to hydroborate (+)-**13** with SmI_3/catecholborane [23], catecholborane/[$RhCl(PPh_3)$] [24] and dicyclohexylborane [25] were not met with success. As (+)-**13** was hydroborated very slowly, competitive decomposition occurred. Debenzylation of (+)-**14** (H_2, 10% Pd/C, MeOH) provided (+)-**15** (83%) that was further deprotected to give the methyl α-D-glucopyranoside (+)-**6** (77%) upon acidic treatment (CF_3COOH/H_2O 4:1).

The *gluco* configuration of (+)-**14**, (+)-(**15**), and (+)-**6** was given by their ^{1}H-NMR (1D, 2D-NOESY, and COSY) data (see *Exper. Part*). The (1′*S*) configuration at the hydroxymethylene linker was determined by the ^{1}H-NMR and 2D-NOESY data of the dioxane derivative (+)-**16** obtained by treatment of diol (+)-**14** with CH_2Br_2 under

Scheme 4



basic conditions (50% NaOH solution, Bu_4NBr, 60°) [26]. Typical $^3J(2,3) = 12.0$ Hz and $^3J(1',2) = 9.8$ Hz were measured. Futhermore, a strong NOE was observed for the signal pair at δ 4.36 and 4.40 assigned to H–C(1′) and H–C(3), respectively.

Conformational Analysis. – The 600-MHz ^{1}H-NMR spectra of (+)-**6** confirmed the chair conformation of the methyl α-D-glucopyranoside moiety (see *Exper. Part*). It showed a large vicinal coupling constant between protons H–C(2′) and H–C(3′) ($^3J =$ 12.8 Hz) of the pyrrolidine ring, suggesting the envelope configuration shown in *Fig. 2*.

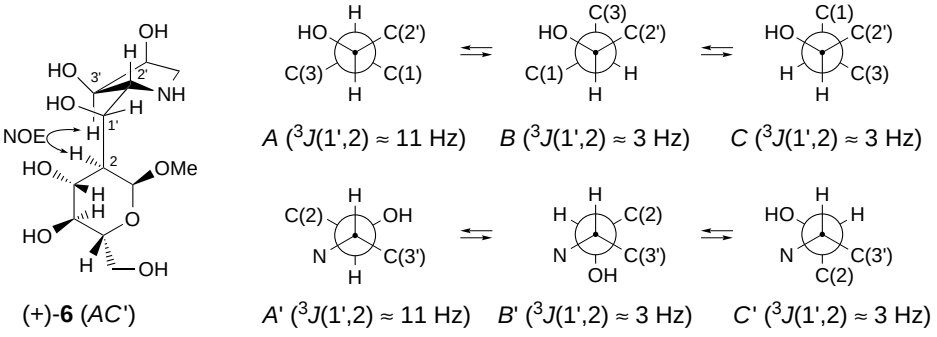


Fig. 2. *Possible conformations for (+)-***6**

The ^{1}H-NMR spectra of (+)-**6** measured in (D_5)pyridine at 25° showed similar vicinal coupling constants $^3J(1',2) = {}^3J(1',2') = 6.8$ Hz for the proton at δ 4.60 assigned to the hydroxymethylene linker. In D_2O, the coupling constant could be measured for $^3J(1',2)$ only and was somewhat smaller (5.2 Hz) than in (D_5)pyridine. These data are consistent with equilibria of rotamers about the bond σ(C(1′),C(2)) (rotamers *A*, *B*,

and *C*) and the bond σ(C(1′),C(2′)) (rotamers *A*′, *B*′, and *C*′). Conformers *A* and *A*′ (for which vicinal coupling constants $^3J(1',2)$ and $^3J(1',2')$ of *ca.* 11 Hz are expected [15]) must be populated at 40 to 50%. The 2D-NOESY ^{1}H-NMR spectra of (+)-**6** showed a intense cross-peak for proton pair H−C(3′) (δ 4.70) and H−C(2) (δ 2.75), as expected for the conformer *AC*′ represented in *Fig. 2*.

Preliminary enzymatic assays with (+)-**6** showed weak inhibitory activity toward α-mannosidases from jack bean (39% at 1 mM concentration) and from almond (26% at 1 mM concentration) [27]. Further enzymatic assays will be undertaken and will be reported in due course together with the synthesis of other C-linked iminodisaccharides.

Conclusion. – The *Nozaki-Kishi* coupling of sugar-derived alkenyl triflate with iminosugar-derived aldehydes was used to generate new C-linked iminodisaccharides. The yield and the diastereoselectivity of the coupling strongly depends on the nature of the alkenyl triflates and aldehydes. This method [17] allowed us to prepare for the first time a disaccharide mimetic in which a (2*R*,3*R*,4*S*)-3,4-dihydroxypyrrolidin-2-yl moiety (imitates α-mannosides) is attached at C(2) of methyl α-D-glucopyranoside through a hydroxymethylene linker.

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Experimental Part

General. Anh. solvents and reagents were freshly distilled under N_2 prior to use: Et_2O and THF from sodium and benzophenone; MeOH from magnesium; CH_2Cl_2, $(Me_3Si)_2NH$, iPr_2NEt, pyridine, and Et_3N from CaH_2. TLC: *Merck* silica gel *60* F_{254} plates. Flash column chromatography (FC): silica gel *60* (*Merck*, 230–400 mesh). Optical rotations: *JASCO DIP-370* digital polarimeter; at 25°; *c* in g/100 ml. UV Spectra: *Kontron-Uvikon 810 CW* spectrophotometer; λ_{max} in nm,ε inM^{-1} cm^{-1}. IR Spectra: *Perkin-Elmer Parangon-1000 FT-IR* spectrometer; in cm^{-1}. NMR Spectra: *Bruker DPX-400 FT* and *Bruker ARX-400 FT*, ^{13}C at 100.6 MHz; chemical shift δ in ppm, *J* in Hz; ^{1}H-assignment confirmed by 2D-COSY or/and NOESY when necessary. Mass spectra: *Nermag R-10-10C* mass spectrometer; chemical ionization (CI) mode; in *m*/*z* (rel. %).

*2,5-[[(*tert*-Butoxy)carbonyl]imino}-2,5-dideoxy-3,4-*O*-isopropylidene-*L*-ribose* ((−)-**9**). $NaHCO_3$ (0.55 g, 6.54 mmol) and $Pb(OAc)_4$ (2.45 g, 5.53 mmol) were added to a soln. of diol **8** [19] (1 g, 3.30 mmol) in CH_2Cl_2 (25 ml) at −78°. After 50 min at −78°, the mixture was treated with a sat. aq. $NaHCO_3$ soln. (50 ml) and extracted with CH_2Cl_2 (3 × 50 ml). The combined org. extracts were washed with brine, dried (Na_2SO_4), and evaporated. FC (light petroleum ether/AcOEt 3:7) gave 1.4 g (80%) of (−)-**9**. Colorless oil. $[\alpha]_{589}^{25} = -96$, $[\alpha]_{577}^{25} = -106$, $[\alpha]_{546}^{25} = -116$, $[\alpha]_{435}^{25} = -222$, $[\alpha]_{405}^{25} = -291$ ($c = 1.0$, $CHCl_3$). UV (MeCN): 198 (2340). IR (KBr): 2980, 2935, 1735, 1695, 1400, 1170, 1120, 1055, 855, 770. ^{1}H-NMR (400 MHz, C_6D_6): 9.32 (*s*, H−C(1)); 4.47 (*m*, H−C(2)); 4.42 (*m*, H−C(3)); 4.10 (*m*, H−C(4)); 3.89 (*d*, $^2J = 12.8$, H_a−C(5)); 3.18 (*dd*, $^2J = 12.8$, $^3J(4,5_b) = 4.8$, H_b−C(5)); 1.47 (*s*, Me_3C)); 1.41, 1.16 (2*s*, Me_2C). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 197.9 (*s*, CO); 154.7 (*s*, NCOO); 112.4 (*s*, Me_2C); 80.7 (*s*, Me_3C); 79.6 (*d*, $J = 145$, C(3)); 78.6 (*d*, $J = 144$, C(4)); 71.8 (*d*, $J = 144$, C(2)); 52.1 (*t*, $J = 145$, C(5)); 28.1 (*q*, $J = 143$, Me_3C); 26.7, 24.7 (2*q*, $J = 143$, Me_2C). CI-MS (NH_3): 84 (29), 142 (91), 172 (63), 186 (44), 216 (100), 233 (68), 272 (78, $[M+1]^+$). Anal. calc. for $C_{13}H_{21}NO_5$ (271.31): C 57.55, H 7.80, N 5.16; found: C 57.62, H 7.83, N 5.10.

*1,6-Anhydro-4-*O*-benzyl-2-{(1*R *and 1*S*)-2,5-[[(*tert*-butoxy)carbonyl]imino}-2,5-dideoxy-3,4-*O*-isopropylidene-*L*-ribitol-1-*C*-yl}-2,3-dideoxy-β-*D*-*erythro*-hex-2-enopyranose* (**10**). A soln. of **2** [17] (0.45 g, 1.22 mmol) and (−)-**9** (0.25 g, 0.92 mmol) in anh. DMF (2 ml) was added to a mixture of $CrCl_2$ (0.66 g, 5.37 mmol) and $NiCl_2$ (3 mg, 0.023 mmol) under N_2. After injection of O_2 (5 ml, 0.22 mmol), the flask was sealed and sonicated at 20° for 1 h. The mixture was diluted with light petroleum ether/AcOEt 1:1. After the addition of 1M sodium serinate, the mixture was stirred vigorously at 20° for 2 h and extracted with CH_2Cl_2 (3 × 50 ml). The combined

org. phases were washed with brine, dried (Na_2SO_4), and evaporated. FC (light petroleum ether/AcOEt 3:2) gave 0.16 g (36%) of **10**, 2:1 diastereoisomer mixture. Colorless oil. UV (MeCN): 248 (1530), 233 (1200). IR (film): 3340, 2985, 1695, 1415, 1165, 1125, 1050, 985, 905. ^{1}H-NMR (400 MHz, $CDCl_3$; major isomer): 7.37 (*m*, Ph); 5.82 (*m*, H–C(3)); 5.64 (*s*, H–C(1)); 4.69 (*m*, PhCH_2, H–C(5), H–C(1′)); 4.20–3.64 (*m*, H–C(3′), H–C(4′), H–C(2′), H_{exo}–C(6), H–C(4), H_a–C(5′)); 3.49 (*dd*, ^2J = 12.4, ^3J(4′,5′b) = 5.2, H_b–C(5′)); 3.38 (*m*, H_{endo}–C(6)); 1.49 (*s*, Me_3C); 1.30 (*s*, Me_2C). ^{13}C-NMR (100.6 MHz, $CDCl_3$; major isomer): 154.9 (*s*, NCOO); 143.7 (*s*, C(2)); 138.1 (*s*, arom. C); 128.3, 127.5 (3*d*, ^1J(C,H) = 140, arom. C); 118.9 (*d*, *J* = 68, C(3)); 111.3 (*s*, Me_2C); 95.8 (*d*, *J* = 167, C(1)); 80.1 (*s*, Me_3C); 79.4 (*d*, *J* = 145, C(3′)); 78.9 (*d*, *J* = 144, C(4′)); 74.4 (*d*, *J* = 144, C(2′)); 72.4 (*d*, *J* = 145, C(1′)); 70.2 (*t*, *J* = 144, C(6)); 67.5 (*d*, *J* = 145, C(4)); 67.3 (*d*, *J* = 145, C(5)); 53.8 (*d*, *J* = 144, C(5′)); 28.3 (*q*, *J* = 144, *Me*$_3$C); 26.9, 24.8 (2*q*, *J* = 144, *Me*$_2$C). CI-MS (NH_3): 91 (39), 142 (89), 172 (32), 233 (100), 272 (55), 326 (17), 490 (78, $[M+1]^+$). Anal. calc. for $C_{26}H_{35}NO_8$ (489.57): C 63.79, H 7.21, N 2.86; found: C 63.90, H 7.15, N 2.91.

Methyl 4-O-*Benzyl-3-deoxy-2*-O-*[(trifluoromethyl)sulfonyl]-α*-D-erythro-*hex-2-enopyranoside* ((+)-**11**). $BF_3 \cdot Et_2O$ (0.7 ml, 5.4 mmol) was added to a soln. of **2** [17] (0.5 g, 1.4 mmol) in MeOH (4 ml) at 0°. The mixture was left at 20° overnight. Evaporation and FC (light petroleum ether/AcOEt 1:1) gave 0.36 g (67%) of (+)-**11**. White solid. M.p. 85–86°. $[\alpha]_{589}^{25} = +102$, $[\alpha]_{577}^{25} = +130$, $[\alpha]_{546}^{25} = +142$, $[\alpha]_{435}^{25} = +152$, $[\alpha]_{405}^{25} = +163$ (*c* = 0.1, $CHCl_3$). UV (MeCN): 218 (19480), 206 (5380). IR (KBr): 3855, 3445, 3005, 1715, 1635, 1495, 1390, 1140, 910, 700. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39 (*m*, arom. C); 6.07 (*d*, ^3J(4,3) = 2.0, H–C(3)); 4.91 (*s*, H–C(1)); 4.62 (*AB*, ^2J = 11.6, PhCH_2); 4.35 (*dd*, ^3J(5,4) = 9.6, ^3J(3,4) = 2.0, H–C(4)); 3.92 (*ddd*, ^3J(4,5) = 9.6, ^3J(6b,5) = 3.6, ^3J(6a,5) = 1.6, H–C(5)); 3.38 (*dd*, ^2J = 11.6, ^3J(5,6a) = 1.6, H_a–C(6)); 3.37 (*dd*, ^2J = 11.6, ^3J(5,6b) = 3.6, H_b–C(6)); 3.48 (*s*, MeO). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 145.0 (*s*, CF_3); 137.1 (*s*, C(2)); 137.2 (*s*, arom. C); 128.6, 128.3, 127.9 (3*d*, *J* = 161, arom. C); 119.5 (*d*, *J* = 168, C(3)); 94.6 (*d*, *J* = 167, C(1)); 71.5 (*d*, *J* = 145, C(5)); 70.1 (*t*, *J* = 143, PhCH_2); 69.9 (*d*, *J* = 144, C(4)); 61.3 (*t*, *J* = 144, C(6)); 56.5 (*q*, *J* = 144, MeO). ^{19}F-NMR (376 MHz, $CDCl_3$): –77.6 (*s*, CF_3). CI-MS (NH_3): 91 (64), 108 (25), 338 (9), 384 (22), 415 (76, $[M+NH_3]^+$). Anal. calc. for $C_{15}H_{17}F_3O_7S$ (398.01): C 45.23, H 4.30, S 8.05; found: C 45.33, H 4.40, S 7.98.

Methyl 4-O-*Benzyl-6*-O-*[(benzyloxy)methyl]-3-deoxy-2*-O-*[(trifluoromethyl)sulfonyl]-α*-D-erythro-*hex-2-enopyranoside* ((+)-**12**). At 0°, (+)-**11** (0.36 g, 0.91 mmol) and ^{i}Pr$_2$NH (0.2 ml, 1.2 mmol) were mixed with benzyl chloromethyl ether (0.2 ml, 1.2 mmol). The mixture was allowed to stand at 20° overnight. Then 1N aq. HCl (1 ml) was added, the org. phase separated, dried, (Na_2SO_4) and evaporated. FC (light petroleum ether/AcOEt 4:1) gave 0.32 g (68%) of (+)-**12**. Colorless oil. $[\alpha]_{589}^{25} = +36$, $[\alpha]_{577}^{25} = +48$, $[\alpha]_{546}^{25} = +52$, $[\alpha]_{435}^{25} = +123$, $[\alpha]_{405}^{25} = +175$ (*c* = 0.1, $CHCl_3$). UV (MeCN): 218 (18000), 209 (4300). IR (film): 3440, 3005, 1715, 1635, 1485, 1490, 1380, 1140, 900, 700. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35 (*m*, arom. H); 6.09 (*d*, ^3J(4,3) = 2.4, H–C(3)); 4.95 (*s*, H–C(1)); 4.79 (*AB*, ^2J = 11.6, PhCH_2); 4.64 (*m*, CH_2); 4.41 (*dd*, ^3J(4,5) = 9.6, ^3J(3,4) = 2.0, H–C(4)); 4.04 (*ddd*, ^3J(4,5) = 9.6, ^3J(6b,5) = 3.6, ^3J(6a,5) = 1.6, H–C(5)); 3.81 (*m*, H–C(6)); 3.48 (*s*, MeO). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 145.0 (*s*, CF_3); 138.3 (*s*, C(2)); 137.1 (*s*, arom. C); 129.4, 129.5, 129.0, 128.7, 127.8, 127.4 (5*d*, *J* = 161, arom. C); 119.5 (*d*, *J* = 168, C(3)); 94.6 (*d*, *J* = 167, C(1)); 94.5 (*t*, *J* = 167, OCH_2O); 70.1 (*t*, *J* = 143, PhCH_2); 69.9 (*d*, *J* = 144, C(4)); 68.3 (*d*, *J* = 145, C(5)); 65.4 (*t*, *J* = 143, CH_2); 61.3 (*t*, *J* = 144, C(6)); 56.5 (*q*, *J* = 144, MeO). ^{19}F-NMR (376 MHz, $CDCl_3$): –77.6 (*s*, CF_3). CI-MS (NH_3): 91 (62), 108 (25), 217 (14), 535 (100, $[M+NH_3]^+$). Anal. calc. for $C_{23}H_{25}F_3O_8S$ (518.03): C 53.25, H 4.82, S 6.17; found: C 53.26, H 4.89, S 6.13.

Methyl 4-O-*Benzyl-6*-O-*[(benzyloxy)methyl]-2-[(1S)-2,5-[[*(tert-*butoxy)carbonyl]imino]-2,5-dideoxy-3,4*-O-*isopropylidene*-L-*ribitol-1*-C-*yl]-3-deoxy-α*-D-erythro-*hex-2-enopyranoside* ((+)-**13**). As described for **10**, with (+)-**12** (0.27 g, 0.52 mmol), (–)-**9** (0.1 g, 0.37 mmol), DMF (2 ml), $CrCl_2$ (0.33 g, 2.68 mmol), $NiCl_2$ (2.6 mg, 0.012 mmol), and O_2 (3 ml, 0.14 mmol). FC (light petroleum ether/AcOEt 1:1) gave 0.11 g (48%) of (+)-**13**. Colorless oil. $[\alpha]_{589}^{25} = +229$, $[\alpha]_{577}^{25} = +234$, $[\alpha]_{546}^{25} = +248$, $[\alpha]_{435}^{25} = +312$, $[\alpha]_{405}^{25} = +456$ (*c* = 0.8, $CHCl_3$). UV (MeCN): 218 (16600), 260 (2212). IR (film): 3370, 2985, 1710, 1655, 1435, 1550, 1105, 1015, 970, 855, 775, 705. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34–7.28 (*m*, arom. H); 6.01 (*m*, H–C(3)); 5.12 (*s*, H–C(1)); 4.81, 4.78 (*AB*, ^2J = 16.4, PhCH_2); 4.69 (*m*, H–C(4), H–C(5), H_a–C(6)); 4.63 (*s*, CH_2O); 4.42 (*dd*, ^2J = 11.2, ^3J(5,6b) = 3.6, H_b–C(6)); 4.04 (*m*, H–C(1′)); 4.14 (*m*, H–C(2′)); 3.48 (*s*, MeO); 3.95 (*d*, ^2J = 12.0, H_a–C(5′)); 3.86 (*m*, H–C(3′)); 3.81 (*dd*, ^3J(3′,4′) = ^3J(5′b,4′) = 4.8, H–C(4′)); 3.42 (*dd*, ^2J = 12.0, ^3J(4′,5′b) = 4.8, H_b–C(5′)); 1.48 (*s*, Me_3C); 1.46, 1.33 (2*s*, Me_2C). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 154.1 (*s*, NCOO); 138.3 (*s*, C(2)); 136.5 (*s*, arom. C); 129.4, 129.5, 129.0, 128.7, 127.8, 127.4 (6*d*, *J* = 161, arom. C); 124.1 (*d*, *J* = 168, C(3)); 111.5 (*s*, Me_2C); 95.8 (*d*, *J* = 167, C(1)); 94.5 (*t*, *J* = 144, OCH_2O), 82.5 (*s*, *Me*$_3$C); 80.1 (*d*, *J* = 145, C(3′)); 79.0 (*d*, *J* = 144, C(4′)); 72.4 (*d*, *J* = 144, C(2′)); 71.4 (*d*, *J* = 145, C(1′)); 70.8 (*d*, *J* = 143, CH_2O); 69.1 (*t*, *J* = 144, C(6)); 68.9 (*d*, *J* = 144, C(4)); 67.2 (*d*, *J* = 145, C(5)); 66.3 (*d*, *J* = 143, CH_2O); 55.7 (*q*, *J* = 144, MeO); 53.1 (*d*, *J* = 144, C(5′)); 28.9, 28.5, 28.1 (3*q*, *J* = 144, *Me*$_3$C); 27.3, 25.0 (2*q*, *J* = 144, *Me*$_2$C). CI-MS (NH_3): 91 (40), 142 (31), 172

(31), 186 (16), 233 (100), 273 (12), 611 (63). Anal. calc. for $C_{35}H_{47}NO_{10}$ (641.04): C 65.49, H 7.33, N 2.18; found: C 65.42, H 7.45, N 2.27.

Methyl 4-O-*Benzyl-6*-O-*[(benzyloxy)methyl]-2-{(1*S*)-2,5-[[(*tert-*butoxy)carbonyl]imino}-2,5-dideoxy-3,4*-O-*isopropylidene*-L-*ribitol-1-C-yl}-2-deoxy-α*-D-*glucopyranoside* ((+)-**14**). A 10M $BH_3 \cdot SMe_2$ soln. (0.15 ml, 1.5 mmol) was added dropwise to a stirred soln. of (+)-**13** (0.1 g, 0.15 mmol) in THF (3 ml) under N_2 cooled to 0°. The mixture was heated under reflux for 1 h. After cooling to 0°, 3M NaOH (4 ml), then 35% H_2O_2 soln. (4 ml) were added. The mixture was stirred vigorously at 20° for 1 h. Then, 1M potassium tartrate (6 ml) was added, and the mixture was extracted with CH_2Cl_2 (4 × 10 ml). The combined org. phases were dried (Na_2SO_4) and evaporated. FC (AcOEt/light petroleum ether 3:2) gave 41 mg (41%) of (+)-**14**. Colorless oil. $[\alpha]_{589}^{25} = +2$, $[\alpha]_{577}^{25} = +4$, $[\alpha]_{546}^{25} = +7$, $[\alpha]_{435}^{25} = +13$, $[\alpha]_{405}^{25} = +14$ ($c = 0.8$, $CHCl_3$). UV (MeCN): 206 (10500). IR (film): 3375, 2985, 1675, 1405, 1550, 1210, 1165, 870, 755. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34–7.28 (*m*, arom. H); 5.26 (*d*, $^3J(2,1) = 3.5$, H–C(1)); 4.90 (*dd*, $^3J(5,4) = 5.9$, $^3J(3,4) = 3.2$, H–C(4)); 4.83, 4.79 (*AB*, $^2J = 16.4$, PhCH_2); 4.67 (*m*, H–C(5), H_a–C(6)); 4.61 (*s*, CH_2O); 4.57 (*m*, H_b–C(6)); 4.01 (*m*, H–C(1′)); 3.86 (*m*, H_a–C(5′)); 3.74 (*m*, H–C(3), H–C(3′)); 3.66 (*dd*, $^3J(3',4') = {}^3J(5'b,4') = 5.4$, H–C(4′)); 3.47 (*dd*, $^3J(3',2') = 9.1$, $^3J(1',2') = 4.0$, H–C(2′)); 3.38 (*s*, MeO); 3.22 (*dd*, $^2J = 12.0$, $^3J(4',5'b) = 4.8$, H_b–C(5′)); 1.95 (*ddd*, $^3J(3,2) = 11.4$, $^3J(1',2) = 7.5$, $^3J(1,2) = 3.5$, H–C(2)); 1.45 (*s*, Me_3C); 1.32, 1.29 (2*s*, Me_2C). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 155.4 (*s*, NCOO); 137.7 (*s*, arom. C); 129.4, 129.5, 129.0, 128.7, 127.8, 127.4 (6*d*, $J = 161$, arom. C); 111.3 (*s*, Me_2C); 97.7 (*d*, $J = 167$, C(1)); 94.9 (*t*, $J = 144$, OCH_2O); 80.2 (*s*, Me_3C); 80.1 (*d*, $J = 145$, C(3′)); 78.9 (*d*, $J = 144$, C(4′)); 72.4 (*d*, $J = 144$, C(2′)); 70.8 (*d*, $J = 145$, C(1′)); 70.1 (*d*, $J = 143$, CH_2O); 69.3 (*t*, $J = 144$, C(6)); 67.5 (*d*, $J = 144$, C(4)); 66.7 (*d*, $J = 145$, C(5)); 65.2 (*t*, $J = 143$, CH_2O); 63.5 (*d*, $J = 145$, C(3)); 54.2 (*d*, $J = 144$, C(5′)); 52.6 (*q*, $J = 144$, MeO); 40.2 (*d*, $J = 145$, C(2)); 28.3 (*q*, $J = 144$, Me_3C); 27.3, 25.0 (2*q*, $J = 144$, Me_2C). CI-MS (NH_3): 91 (13), 142 (50), 174 (28), 186 (16), 202 (13), 218 (99), 219 (52), 235 (28), 275 (57), 661 (16). Anal. calc. for $C_{35}H_{49}NO_{11}$ (659.13): C 63.73, H 7.44, N 2.13; found: C 63.68, H 7.56, N 2.18.

*Methyl 2-{(1*S*)-2,5-[[(*tert-*Butoxy)carbonyl]imino}-2,5-dideoxy-3,4*-O-*isopropylidene*-L-*ribitol-1*-C-*yl}-2-deoxy-α*-D-*glucopyranoside* ((+)-**15**). A degassed vac. line mixture of (+)-**14** (35 mg, 0.053 mmol), 10% Pd/C (12 mg, 0.01 mmol), and MeOH (3 ml) was stirred under H_2 at 20° overnight. The catalyst was filtered off and the solvent evaporated: 20 mg (83%) of (+)-**15**. White solid. M.p. 135–136°. $[\alpha]_{589}^{25} = +123$, $[\alpha]_{577}^{25} = +133$, $[\alpha]_{546}^{25} = +135$, $[\alpha]_{435}^{25} = +190$, $[\alpha]_{405}^{25} = +417$ ($c = 0.6$, H_2O). UV (MeCN): 199 (7680). IR (KBr): 3855, 3365, 2975, 2365, 1670, 1575, 1365, 1210, 870, 775. ^{1}H-NMR (400 MHz, D_2O): 4.98 (*d*, $^3J(2,1) = 4.9$, H–C(1)); 4.81 (*m*, H–C(4), H–C(5), H_a–C(6), H_b–C(6)); 3.96 (*dd*, $^2J = 10.0$, $^3J(4',5'b) = 4.8$, H–C(5′)); 3.37 (*m*, H–C(3′)); 3.71 (*m*, H–C(4′)); 3.66 (*m*, H–C(1′), H–C(2′)); 3.55 (*dd*, $^2J = 10.0$, $^3J(4',5'a) = 4.4$, H_a–C(5′)); 3.38 (*dd*, $^3J(2,3) = 12.7$, $^3J(4,3) = 4.8$, H–C(3)); 3.29 (*s*, MeO); 1.82 (*ddd*, $^3J(3,2) = 12.7$, $^3J(1',2) = 7.5$, $^3J(1,2) = 4.9$, H–C(2)); 1.37 (*s*, Me_3C); 1.35, 1.25 (2*s*, Me_2C). ^{13}C-NMR (100.6 MHz, D_2O): 156.4 (*s*, NCOO); 111.9 (*s*, Me_2C); 98.7 (*d*, $J = 167$, C(1)); 82.1 (*d*, $J = 145$, C(3′)); 81.1 (*s*, Me_3C); 78.7 (*d*, $J = 144$, C(4′)); 71.4 (*d*, $J = 144$, C(2′)); 71.1 (*d*, $J = 145$, C(1′)); 69.4 (*d*, $J = 144$, C(4)); 66.9 (*d*, $J = 145$, C(5)); 69.3 (*t*, $J = 144$, C(6)); 60.7 (*d*, $J = 145$, C(3)); 54.6 (*d*, $J = 144$, C(5′)); 51.3 (*q*, $J = 144$, MeO); 43.2 (*d*, $J = 145$, C(2)); 27.6 (*q*, $J = 144$, Me_3C); 25.6 (*q*, $J = 144$, Me_2C). CI-MS (NH_3): 85 (25), 142 (55), 186 (30), 242 (19), 284 (7), 344 (3), 450 (3, $[M+1]^+$). Anal. calc. for $C_{20}H_{35}NO_{10}$ (449.23): C 53.43, H 7.85, N 3.12; found: C 53.35, H 7.90, N 3.83.

*Methyl 2-Deoxy-2-[(1*S*)-2,5-dideoxy-2,5-imino*-L-*ribitol-1*-C-*yl]-α*-D-*glucopyranoside* ((+)-**6**). A mixture of (+)-**15** (37 mg, 0.082 mmol) and 80% aq. CF_3COOH soln. (4 ml) was stirred at 20° for 2 h. The soln. was poured onto a column (1 × 5 cm) of *Dowex 50WX8* (100–200 mesh) and the column eluted sequentially with MeOH (20 ml), H_2O (5 ml), and 25% aq. NH_3 soln. (40 ml). The product fractions afforded 20 mg (77%) of (+)-**6**. White solid. M.p. 160° (dec.). $[\alpha]_{589}^{25} = +53$, $[\alpha]_{577}^{25} = +54$, $[\alpha]_{546}^{25} = +63$, $[\alpha]_{435}^{25} = +105$, $[\alpha]_{405}^{25} = +161$ ($c = 0.4$, H_2O). UV (MeCN): 208 (4700). IR (KBr): 3885, 2535, 1495, 1440, 1210, 1135, 1025, 835, 800, 725. ^{1}H-NMR (600 MHz, (D_5) pyridine): 5.55 (*d*, $^3J(2,1) = 4.0$, H–C(1)); 4.70 (*dd*, $^3J(2',3') = 12.8$, $^3J(4',3') = 5.6$, H–C(3′)); 4.60 (*t*, $^3J(2,1') = {}^3J(2',1') = 6.8$, H–C(1′)); 4.54 (*dd*, $^3J(2,3) = 10.8$, $^3J(4,3) = 7.6$, H–C(3)); 4.45 (*m*, H–C(4′), H_a–C(5′), H_a–C(6)); 4.31 (*dd*, $^2J = 12.4$, $^3J(5,6b) = 5.6$, H_b–C(6)); 4.21 (*m*, H–C(5)); 4.13 (*dd*, $^3J(5,4) = 9.6$, $^3J(3,4) = 7.6$, H–C(4)); 4.08 (*dd*, $^3J(3',2') = 12.8$, $^3J(1',2') = 6.8$, H–C(2′)); 3.31 (*m*, H_b–C(5′)); 3.35 (*s*, MeO); 2.75 (*ddd*, $^3J(3,2) = 10.8$, $^3J(1',2) = 6.8$, $^3J(1,2) = 4.0$, H–C(2)). ^{13}C-NMR (100.6 MHz, (D_5)pyridine): 100.4 (*d*, $J = 167$, C(1)); 74.5 (*d*, $J = 145$, C(3′)); 73.9 (*d*, $J = 144$, C(4′)); 73.2 (*d*, $J = 144$, C(2′)); 72.7 (*d*, $J = 145$, C(1′)); 71.3 (*d*, $J = 144$, C(4)); 70.8 (*d*, $J = 145$, C(5)); 66.5 (*t*, $J = 144$, C(6)); 62.8 (*d*, $J = 145$, C(3)); 54.3 (*d*, $J = 144$, C(5′)); 52.2 (*q*, $J = 144$, MeO); 48.9 (*d*, $J = 145$, C(2)). CI-MS (NH_3): 102 (65), 134 (83), 180 (10), 229 (13), 256 (36), 278 (29), 310 (66, $[M+1]^+$). Anal. calc. for $C_{12}H_{23}NO_8$ (309.32): C 46.60, H 7.49, N 4.53; found: C 46.55, H 7.36, N 4.45.

Methyl 4-O-*Benzyl-6*-O-*[(benzyloxy)methyl]-2-{(1′*S*)-2,5-[[(*tert-*butoxy)carbonyl]imino}-2′,5′-dideoxy-3′,4′*-O-*isopropylidene*-L-*ribitol-1′*-C-*yl]-2-deoxy-1′,3*-O-*methylene-α*-D-*glucopyranoside* (=*(6*S*)-6-{(1*R*)-1,4-*

*{[(*tert-*Butoxy)carbonyl]imino}-1,4-dideoxy-2,3-*O-*isopropylidene-*L-*erythritol-1-*C-*yl}-5,6-dihydro(methyl 4-*O-*benzyl-6-*O-*[(benzyloxy)methyl]-2,3-dideoxy-α-*D-*glucopyranosido)[2,3-*d*]-4*H-*1,3-dioxin*; (+)-**16**). A mixture of (+)-**14** (32 mg, 0.048 mmol), 50% aq. NaOH soln. (0.7 ml, 0.87 mmol), Bu_4NBr (2 mg, 0.006 mmol), and CH_2Br_2 (0.19 ml, 1.1 mmol) was vigorously stirred at 55° for 2 h. Then, the mixture was extracted with CH_2Cl_2 (4 × 10 ml) and the combined org. phase dried (Na_2SO_4) and evaporated. FC (AcOEt/light petroleum ether 1:1) gave 16 mg (46%) of (+)-**16**. Colorless oil. $[\alpha]_{589}^{25} = +12$, $[\alpha]_{577}^{25} = +13$, $[\alpha]_{546}^{25} = +14$, $[\alpha]_{435}^{25} = +23$, $[\alpha]_{405}^{25} = +35$ ($c = 0.4$, $CHCl_3$). UV (MeCN): 194 (2530). IR (film): 2995, 2935, 1675, 1380, 1210, 1165, 870, 505. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.30–7.27 (*m*, arom. H); 5.07 (*m*, H–C(4)); 4.94 (*d*, $^3J(2,1) = 2.5$, H–C(1)); 4.92 (*m*, CH_2O); 4.83, 4.77 (*AB*, $^2J = 16.4$, PhCH_2); 4.66 (*m*, H–C(5), H_a–C(6), H_b–C(6)); 4.59 (*s*, OCH_2O); 4.40 (*dd*, $^3J(2,3) = 12.0$, $^3J(4,3) = 3.7$, H–C(3)); 4.36 (*dd*, $^3J(2,1') = 9.8$, $^3J(2',1') = 3.4$, H–C(1′)); 3.85 (*dd*, $^3J(3',2') = 9.3$, $^3J(1',2') = 3.4$, H–C(2′)); 3.65 (*m*, H_a–C(5′)); 3.63 (*m*, H–C(4′), H–C(3′), H_b–C(5′)); 3.35 (*s*, MeO); 2.57 (*ddd*, $^3J(3,2) = 12.0$, $^3J(1',2) = 9.8$, $^3J(1,2) = 2.5$, H–C(2)); 1.42 (*s*, Me_3C); 1.25 (*s*, Me_2C). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 155.4 (*s*, NCOO); 137.7 (*s*, arom. C); 129.4, 129.5, 129.0, 128.7, 127.8, 127.4 (6*d*, $J = 161$, arom. C); 110.6 (*s*, Me_2C); 97.7 (*d*, $J = 167$, C(1)); 94.9 (*t*, $J = 144$, OCH_2O); 89.3 (*t*, $J = 144$, OCH_2O); 81.8 (*s*, Me_3C); 79.8 (*d*, $J = 145$, C(3′)); 79.7 (*d*, $J = 144$, C(4′)); 74.6 (*d*, $J = 144$, C(2′)); 74.5 (*d*, $J = 145$, C(1′)); 72.2 (*d*, $J = 145$, C(3)); 70.3 (*d*, $J = 143$, CH_2O); 69.3 (*t*, $J = 144$, C(6)); 66.6 (*d*, $J = 144$, C(4)); 65.8 (*d*, $J = 145$, C(5)); 55.1 (*t*, $J = 143$, CH_2O); 53.9 (*t*, $J = 144$, C(5′)); 43.5 (*q*, $J = 144$, MeO); 34.1 (*d*, $J = 145$, C(2)); 28.5 (*q*, $J = 144$, Me_3C); 26.8, 24.5 (2*q*, $J = 144$, Me_2C). ES-MS (NH_3): 434 (10), 459 (25), 540 (100), 559 (60), 640 (10), 672 (12), 720 (5, M^+). Anal. calc. for $C_{39}H_{61}NO_{11}$ (719.92): C 65.07, H 8.54, N 1.95; found: C 64.97, H 8.15, N 1.94.

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