Stereoselective Synthesis of Differentially Protected Derivatives of the Higher Amino Sugars Destomic Acid and Lincosamine from Serine and Threonine

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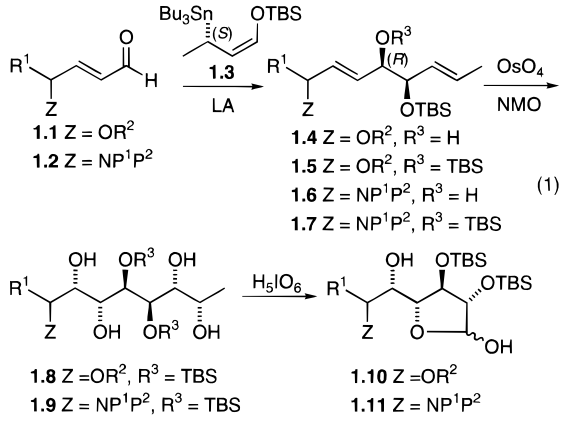
The aminoheptose destomic acid (**3.5**) and the aminooctose lincosamine (**6.8**) were synthesized in protected form by parallel sequences starting from the oxazolidine derivatives **2.4** and **5.1** of N-CBz serinal and N-BOC threoninal. The parallel sequences feature BF_3-promoted addition of the *(R)*-γ-OTBS allylic stannane **2.8** to the homologated enals **2.7** and **5.4**, respectively, followed by stereoselective bis-dihydroxylation of the derived bis-OTBS ethers **2.10** and **5.6**. Regioselective oxidative cleavage of the less hindered vicinal diol moieties of these intermediates led to the γ-lactols **3.2** and **5.8**, respectively. In the former case, treatment with TBAF and subsequent hydrolysis removed the OTBS and acetonide protecting groups affording the destomic acid precursor, pyranose **3.4**. Lactol **5.8** was converted to the pyranoside **6.3** by silyl ether cleavage, acidic hydrolysis, and bis-acetonide formation. Inversion of the C7 hydroxyl grouping was effected by the Mitsunobu methodology with *p*-$NO_2C_6H_4CO_2H$. Subsequent hydrolysis, cleavage of the BOC grouping, and N-acetylation afforded the lincosamine derivative **6.7**.

We recently described a sequence for the conversion of conjugated enals **1.1** to *syn,anti, syn,anti,syn* polyol derivatives **1.8** and their subsequent oxidative cleavage to carbohydrate γ-lactols **1.10** (eq 1).[1] The key elements of this approach are (1) highly *syn* selective addition of the enantioenriched γ-silyloxy allylic stannane **1.3** to the aforementioned enals **1.1**, (2) highly *anti* selective bis-dihydroxylation of the bis-TBS ethers **1.5** of these adducts, and (3) regioselective oxidative cleavage of the derived tetrols **1.8** at the more accessible 1,2-diol terminus, attended by *in situ* internal protection of the surviving, less reactive, 1,2-diol function through lactol formation.



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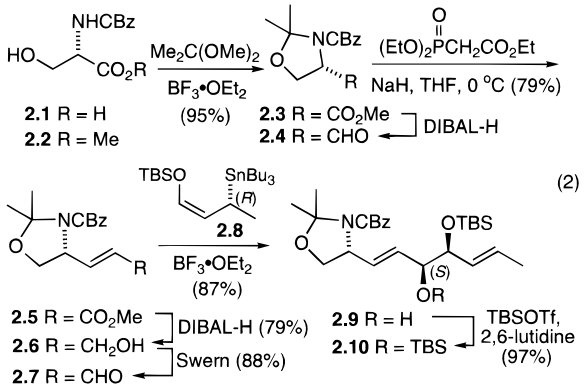
These preliminary studies were conducted with enals prepared from protected D-erythrose and D-arabinose leading, in the former case, to "D-α,α-galaoctonic lactone", a galactose homologue, first prepared by Fischer in 1895,[2] and in the latter case, an 11-carbon polyol intermediate employed by Schreiber and Ikemoto in their synthesis of the antibiotic hikizimycin.[3] Our current studies were undertaken to test the applicability of this methodology to the synthesis of higher amino sugars **1.11** (P^1, P^2 = protecting groups) from readily available α-amino acids.[4] It was of particular interest to assess the effect of a protected allylic amine function on the diastereoselectivity of the hydroxylation step **1.7** → **1.9** and the regioselectivity of the subsequent oxidative cleavage **1.9** → **1.11**.

As the first synthetic target of these studies we chose destomic acid (**3.5**), an aminohepturonic acid component of the destomycin and hygromycin antibiotics.[5] Our starting material for this project was the Cbz analogue **2.4** of the so-called Garner aldehyde, derived from N-Cbz L-serine (**2.1**) by esterification, oxazolidine formation, and reduction.[6] Horner−Emmons condensation with triethyl phosphonoacetate led to the *(E)*-conjugated ester **2.5** which was subjected to the usual sequential reduction−oxidation sequence to yield enal **2.7**. BF_3-promoted addition of the (*R*)-OTBS allylic stannane **2.8** afforded the *syn* adduct **2.9** in high yield as a single diastereoisomer. Conversion to the bis-TBS ether **2.10** was effected in near-quantitative yield with TBSOTf and 2,6-lutidine.



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[⊗] Abstract published in *Advance ACS Abstracts,* January 1, 1996.

(1) (a) Marshall, J. A.; Beaudoin, S. *J. Org. Chem.* **1994**, *59*, 6614. (b) Marshall, J. A.; Beaudoin, S. *J. Org. Chem.* **1994**, *59*, 7833.

(2) Fischer, E. *Liebigs Ann. Chem.* **1895**, *288*, 150.

(3) Ikemoto, N.; Schreiber, S. *J. Am. Chem. Soc.* **1992**, *114*, 2524.

(4) *Cf.* Jurczak, J.; Golebiowski, A. *Chem. Rev.* **1989**, *89*, 149. Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1531. Dondoni, A.; Perrone, D. *J. Org. Chem.* **1995**, *60*, 4794.

(5) (a) For a previous synthesis from D-galactose, see Hashimoto, H.; Asano, K.; Fujii, F.; Yoshimura, J. *Carbohydr. Res.* **1982**, *104*, 87. (b) For a recent approach see Golebiowski, A.; Kozak, J.; Jurczak, J. *J. Org. Chem.* **1991**, *56*, 7344. (c) Dondoni, A.; Franco, S.; Merchan, F.; Merino, P.; Tejero, T. *Synlett* **1993**, 78.

(6) (a) Garner, P.; Park, J.-M. *J. Org. Chem.* **1987**, *52*, 2361. (b) Garner, P.; Park, J.-M. *Org. Synth.* **1991**, *70*, 18. (c) McKillop, A.; Taylor, R. J. K.; Watson, R. J.; Lewis, N. *Synthesis* **1994**, 31.

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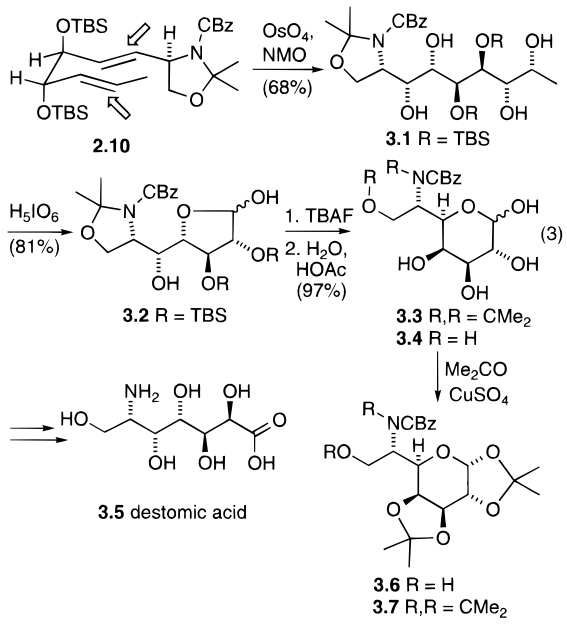
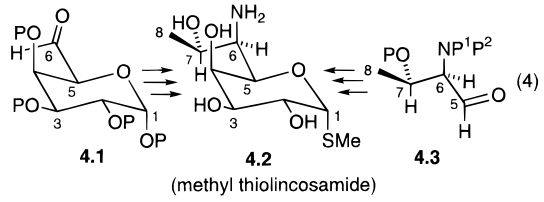
We were now in a position to evaluate the effect of the terminal oxazoline ring on the diastereoselectivity of the hydroxylation reaction. If the bis-OTBS diene **2.10** adopts the Saito conformation, as depicted in eq 3, we would expect addition to occur mainly *anti* to the OTBS substituents.[7] In fact, when diene **2.10** was treated with an excess of NMO in the presence of catalytic OsO_4,[8] a major tetrol product, presumably **3.1**, was isolated in 68% yield after separation from minor diastereomeric impurities. Allylic ethers tend to give *anti* dihydroxylation products, whereas allylic amine amides show modest to negligible directing effects on double bond additions.[9,10] Thus, it is not surprising that direction by the OTBS grouping is the dominant factor in the present case.



The selective oxidative cleavage of tetrol **3.1** proceeded smoothly to afford lactol **3.2** in 81% yield. Desilylation followed by acetonide hydrolysis afforded the pyranose derivative **3.4**, an intermediate in Hashimoto's synthesis of destomic acid from galactose.[5a] For the purpose of characterization, pyranose **3.4**, a mixture of α- and *β*-anomers, was converted to the known bis-acetonide **3.6**.[5] A small amount of the oxazolidine **3.7** was also formed in this reaction. The ^{1}H NMR spectrum and optical rotation of **3.6** were in excellent accord with the reported values.[5]

The second synthetic target of interest, lincosamine (**6.8**), is an amino octose component of lincomycin, a Gram-positive glycopeptide antibiotic which was structurally elucidated by workers at Upjohn in the 1960s.[11] Crucial to this elucidation was the finding that, upon hydrazinolysis, lincomycin is converted to methyl thiolincosaminide (**4.2**) and *trans*-1-methyl-4-propyl-L-proline. In subsequent years numerous synthetic routes to the thioglycoside and the parent pyranose have been reported. These fall into two main groups. The earliest approaches start from a galactose derived aldehyde **4.1** and introduce the additional two carbons.[12] Although conceptually simple these routes suffer from excessive protecting group manipulations and lack of stereocontrol. A recent synthesis along these lines by Knapp and Kukkola is an exception.[12h] Danishefsky, employing his diene/aldehyde cyclocondensation strategy, prepared racemic peracetyl *β*-methylincosaminide.[13a–c] Of special interest in this pioneering work, and the later studies of Knapp, is the stereocontrolled introduction of the C6/C7 amino alcohol array through functionalization of a C5 propenylated pyranoside.

In recent years several groups have described routes to lincosamine and analogues starting from a protected C5–C8 amino alcohol segment **4.3** (P, P^1, P^2 = protecting groups) derived from D-allothreonine.[13d–f] Clearly this approach is well suited to the studies at hand. However we chose the epimeric aldehyde **5.1**,[6] available from D-threonine, as a starting material over the seemingly more appropriate allothreonine counterpart **4.3**. We felt that the lower cost and greater stability of aldehyde **5.1** outweighed the possible disadvantage of the requisite later stage inversion at C7 (see **4.2**).



Horner–Emmons homologation[14] of aldehyde **5.1** proceeded smoothly, and the resulting *(E)* conjugated ester was transformed by successive reduction–oxidation to the enal **5.4**. BF_3-promoted addition of the *(R)*-silyloxy allylic stannane **2.8** gave the *syn* adduct **5.5** as the sole product.[1a] The derived bis-TBS ether **5.6** was bis-dihydroxylated with NMO and catalytic OsO_4[8] to the tetrol **5.7** as the major product. With diene **5.6**, the allylic amide function may reinforce the OTBS groupings in directing the dihydroxylation step but the effect is modest, at best.

Selective oxidative cleavage of the more accessible vicinal diol of **5.7** was effected in high yield. However, subsequent conversion of the resulting lactol **5.8** to pyranoside **6.2** proceeded in less than 30% yield under a variety of conditions . A considerable improvement was realized by performing this reaction on the deprotected lactol **6.1**. In this way, a 55:45 mixture of acetonides **6.2** and **6.3** was realized in 56% yield. The former was

(7) *Cf.* (a) Saito, S.; Narahara, O.; Ishikawa, T.; Asahara, M.; Moriwake, T.; Gawronski, J.; Kazimiercyzk, F. *J. Org. Chem.* **1993**, *58*, 6292. (b) Gung, B. W.; Melnick, J. P.; Wolf, M. A.; Marshall, J. A. Beaudoin, S. *J. Org. Chem.* **1994**, *59*, 5609.

(8) VanRheenen, V.; Kelly, R. C.; Chas, D. Y. *Tetrahedron Lett.* **1976**, 1973.

(9) *Cf.* (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3947. (b) Stork, G.; Kahn, M. *Tetrahedron Lett.* **1983**, *24*, 3951.

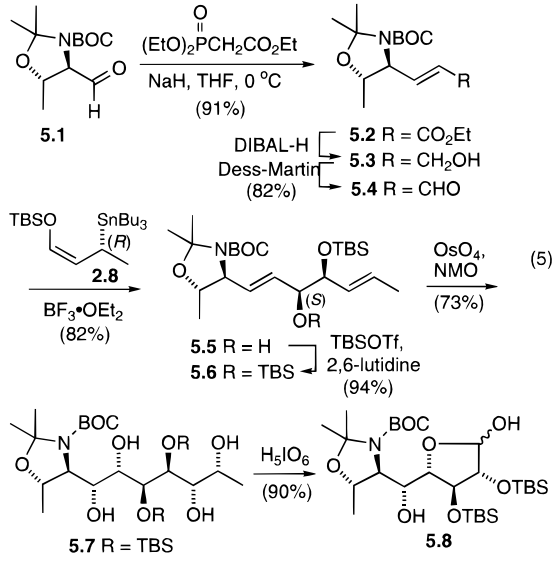
(10) (a) *Cf.* Krysan, D. J.; Rockway, T. W.; Haight, A. R. *Tetrahedron Asymmetry* **1994**, *5*, 625 and references therein. (b) For a recent review, see Cha, J. K.; Kim, N.-S. *Chem. Rev.* **1995**, *95*, 1761.

(11) Slomp, G.; MacKellar, F. A. *J. Am. Chem. Soc.* **1967**, *89*, 2454.

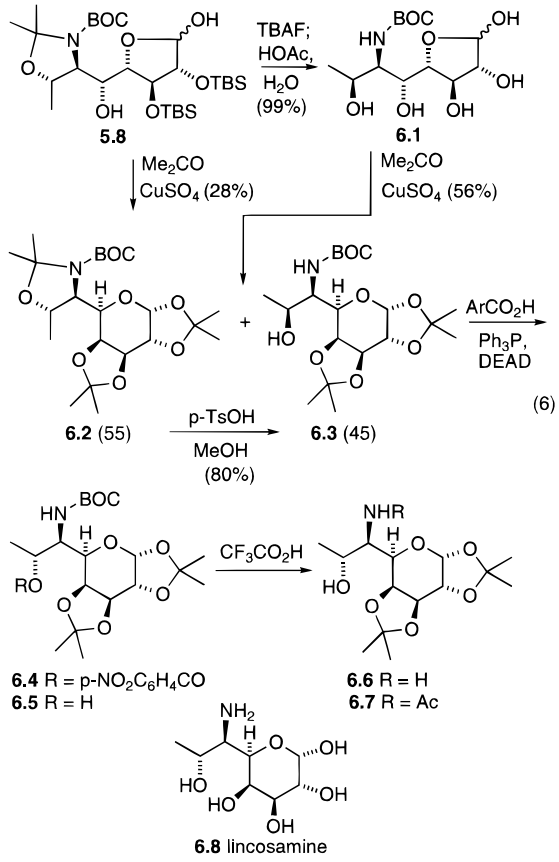
(12) (a) Magerlein, B. J. *Tetrahedron Lett.* **1970**, 33. (b) Howarth, G. B.; Szarek, W. A.; Jones, J. K. N. *J. Chem. Soc. (C)* **1970**, 2218. (c) Saeki, S.; Ohki, E. *Chem. Pharm. Bull.* **1970**, *18*, 789. (d) Fukumaru, T.; Atsumi, T.; Ogawa, T.; Matsui, M. *Agr. Biol. Chem.* **1973**, *37*, 2617. (e) Woolard, G. R.; Rathbone, E. B.; Szarek, W. A.; Jones, J. K. N. *J. Chem. Soc. Perkin Trans. 1* **1976**, 950. (f) Gateau-Olesker, A.; Sepulchre, A. M.; Vass, G.; Gíro, S. D. *Tetrahedron* **1977**, *33*, 393. (g) Hoppe, I.; Schöllkopf, U. *Liebigs Ann. Chem.* **1980**, 1474. (h) Knapp, S.; Kukkola, P. J. *J. Org. Chem.* **1990**, *55* 1632.

(13) (a) Larson, E. R.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 6715. (b) Danishefsky, S.; Larson, E.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1274. (c) Danishefsky, S.; DeNinno, M. P.; Schulte, G. *J. Org. Chem.* **1987**, *52*, 3173. (d) Golebiowski, A.; Jurczak, J.; Krajewski, J. W.; Galilskii, N. M.; Vernich, A. J. *Bull. Polish Acad. Sci.* **1989**, *37*, 307. (e) Golebiowski, A.; Jurczak, J. *Tetrahedron* **1991**, *47*, 1045. (f) Szechner, B.; Achmatowicz, O. J. *Carbohydrate Chem.* **1992**, *11*, 401.

(14) Wadsworth, W. S., Jr. *Org. React.* **1977**, *25*, 73.



smoothly converted to the latter by exposure to acidic methanol. These findings suggest that the oxazolidine function of lactol **5.8** in some way interferes with pyranoside formation. Unfortunately we were not able to isolate descrete intermediates that could shed light on the sequence of events leading to pyranoside **6.2**.



Inversion of the C7 carbinyl center was effected by the methodology of Mitsunobu. For this conversion, *p*-nitrobenzoic acid[15] proved superior to benzoic acid in both purity of the derived ester **6.4** and ease of its subsequent cleavage with methanolic KCN. The inverted alcohol **6.5** was treated with trifluoroacetic acid to remove the BOC protecting group. Acetylation of the resulting amine **6.6** afforded the known acetamide **6.7**. The ^{1}H NMR spectrum and optical rotation of this material closely matched the reported values.

It is clear from the foregoing results that protected α-amino aldehydes are suitable substrates for our previously described carbohydrate homologation sequence.[1] In the current studies we have employed methodology that favors *syn* adducts of the enal intermediates **2.7** and **5.4**. Recent findings that indium analogues of the enantioenriched stannane **2.8**, prepared *in situ*, afford *anti* adducts with enals extends the potential scope of this methodology.[16]

Experimental Section[17]

***N*-(Benzyloxycarbonyl)-L-Serine, Methyl Ester (2.2)**. To a solution of acid **2.1** (4.91 g, 20.5 mmol) in MeOH (40 mL) at 0 °C was added 2.3 mL (31.5 mmol) of $SOCl_2$ (*caution heat and HCl are evolved!*). After being stirred at rt for 24 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in Et_2O, washed with saturated $NaHCO_3$, and dried over Na_2SO_4 to give the ester **2.1** (4.93 g, 95%) as a yellow oil: $[\alpha]_D$ +8.5 (*c* 1.19, $CHCl_3$); IR 3404, 1714; ^{1}H NMR (400 MHz) δ 2.25 (1 H, bs), 3.76 (3 H, s), 3.94 (2 H, bd, J = 19.2 Hz), 4.43 (1 H, bs), 5.11 (2 H, s), 5.70 (1 H, bs), 7.28−7.35 (5 H, m). Anal. Calcd for $C_{12}H_{15}NO_5$: C; 56.91, H; 5.97, N; 5.53. Found: C; 56.65, H; 5.91, N; 5.46.

(*S*)-Methyl 3-(Benzyloxycarbonyl)-2,2-dimethyloxazolidine-4-carboxylate (2.3). To a solution of ester **2.2** (4.80 g, 19.0 mmol) in acetone (68 mL) and 2,2-dimethoxypropane (20 mL) was added 0.13 mL (1.06 mmol) of BF_3·OEt_2. After 25 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with 1:1 saturated $NaHCO_3$-H_2O and brine, and dried over Na_2SO_4. Purification by flash chromatography on silica gel (1:1, hexanes−Et_2O) gave oxazolidine **2.3** (5.28 g, 95%): $[\alpha]_D$ −51.9 (*c* 1.06, $CHCl_3$); IR 1758, 1716; ^{1}H NMR δ (C_6D_6, 70 °C): 1.54 (3 H, s), 1.85 (3 H, s), 3.25 (3 H, s), 3.69 (1 H, dd, J = 7.0, 9.0 Hz), 3.82 (1 H, dd, J = 2.8, 9.0 Hz), 4.26 and 4.45 (1 H, bs), 4.98 and 5.12 (2 H, ABq, J = 12.5 Hz), 7.03−7.20 (5 H, m). Anal. Calcd for $C_{15}H_{19}NO_5$: C; 61.42, H; 6.53, N; 4.78. Found: C; 61.48, H; 6.55, N; 4.78.

(*S*)-3-(Benzyloxycarbonyl)-4-formyl-2,2-dimethyloxazolidine (2.4). To a solution of ester **2.3** (5.08 g, 17.3 mmol) in $PhCH_3$ (35 mL) at −78 °C was added 20 mL (30.0 mmol) of 1.5 M DIBAL-H in $PhCH_3$. After 2 h, an additional 7 mL (10.5 mmol) of 1.5 M DIBAL-H in $PhCH_3$ was added and after 1 h, another 7 mL (10.5 mmol) portion was added. Stirring was continued for 1 h, and the reaction mixture was quenched with MeOH (11.6 mL) followed by aqueous potassium sodium tartrate and allowed to warm to rt. After being stirred for 3 h, the aqueous phase was extracted with Et_2O, and the combined organic extracts were dried over Na_2SO_4. Purification by flash chromatography on silica gel (4:6, hexanes−Et_2O) gave aldehyde **2.4** (3.42 g, 75%): $[\alpha]_D$ −63.7 (*c* 1.23, $CHCl_3$); IR 2886, 2819, 1713; ^{1}H NMR (C_6D_6, 70 °C): δ 1.42 (3 H, s), 1.60 (3 H, s), 3.45 (1 H, dd, J = 7.2, 9.3 Hz), 3.64 (1 H, dd, J = 2.0, 9.3 Hz), 3.86 (1 H, bs), 5.00 (2 H, s), 7.04−7.16 (5 H, m), 9.24 (1 H, bs). Anal. Calcd for $C_{14}H_{17}NO_4$: C; 63.87, H; 6.51, N; 5.32. Found: C; 63.76, H; 6.48, N; 5.27.

(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-[(*E*)-2-carbomethoxyvinyl]oxazolidine (2.5). To a suspension of NaH (338 mg, 14.1 mmol) in THF (25 mL) at 0 °C was added 2.9 mL (14.6 mmol) of triethyl phosphonoacetate. After 30 min, aldehyde **2.4** (3.13 g, 11.9 mmol) in THF (25 mL) was added dropwise. After being stirred for 1 h, the reaction mixture was quenched with H_2O, diluted with Et_2O, washed with brine,

(15) Martin, S. F.; Dodge, J. A. *Tetrahedron Lett.* **1991,** *32*, 3107. Dodge, J. A.; Trujillo, J. I.; Presnell, M. *J. Org. Chem.* **1994**, *59*, 234.

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(17) Unless otherwise indicated ^{1}HNMR spectra were recorded at 300 MHz in $CDCl_3$. Infrared spectra were determined as thin films and are reported in cm^{-1}. For a summary of experimental protocols, see Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 960.

and dried over Na_2SO_4. Purification by flash chromatography on silica gel (7:3, hexanes−Et_2O) gave ester **2.5** (3.11 g, 79%): $[\alpha]_D$ −62.5 (*c* 1.34, $CHCl_3$); IR 1708, 1662; ^1H NMR (C_6D_6, 70 °C) δ 1.00 (3 H, t, J = 7.1 Hz), 1.45 (3 H, s), 1.59 (3 H, s), 3.33 (AB, 1 H, dd, J = 2.5, 9.1Hz) , 3.53 (AB, 1 H, dd, J = 6.4, 9.1Hz), 4.02 (2 H, q, J = 7.1 Hz), 4.12 and 4.34 (1 H, bs and d, J = 5.1 Hz), 4.96 and 5.04 (2 H, AB, J =12.3 Hz), 5.95 (1 H, bd, J = 15.6 Hz), 6.90 (1 H, dd, J =7.0, 15.6 Hz), 7.05−7.20 (5 H, m). Anal. Calcd for $C_{18}H_{23}NO_5$: C; 64.85, H; 6.95, N; 4.20. Found: C; 64.88, H; 6.96, N; 4.10.

(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-[(*E*)-3-hydroxy-1-propenyl]oxazolidine (2.6). To a solution of ester **2.5** (2.93 g, 8.79 mmol) in THF (26 mL) at −78 °C was added 32 mL (32.0 mmol) of 1.0 M DIBAL-H in hexanes. After 2 h, the reaction mixture was quenched with saturated Rochelle's salt and warmed to rt. After being stirred for 3 h, the aqueous phase was extracted with Et_2O, and the combined organic extracts were dried over $MgSO_4$. Purification by flash chromatography on silica gel (3:1 Et_2O−hexanes) gave alcohol **2.6** (2.03 g, 79%) as a colorless oil: $[\alpha]_D$ −13.2 (*c* 1.16, $CHCl_3$); IR 3457, 1698; ^1H NMR (DMSO-d_6, 85 °C): δ 1.47 (3 H, s), 1.54 (3 H, s), 3.10 (1 H, bs), 3.72 (1 H, dd, J = 2.3, 8.9 Hz), 3.93 (2 H, d, J =2.9 Hz), 4.05 (1 H, dd, J = 6.1, 8.9 Hz), 4.43 (1 H, bs), 5.05 and 5.11 (2 H, ABq, J = 12.7 Hz), 5.63−5.67 (2 H, m), 7.32−7.38 (5 H, m). Anal. Calcd for $C_{16}H_{21}NO_4$: C; 65.96, H; 7.27, N; 4.81. Found: C; 65.71, H; 7.32, N; 4.78.

(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-[(*E*)-2-formylvinyl]oxazolidine (2.7). To a solution of oxalyl chloride (0.67 mL, 7.68 mmol) in CH_2Cl_2 (20 mL) at −78 °C was added 1.1 mL (20.8 mmol) of DMSO. After 5 min, alcohol **2.6** (1.94 g, 6.6 mmol) in CH_2Cl_2 (20 mL) was added dropwise. After 15 min, Et_3N (4.6 mL, 33.0 mmol) was added. After being stirred at 0 °C for 30 min, the reaction mixture was washed with H_2O, 10% HCl, saturated $NaHCO_3$, H_2O, and brine, and dried over $MgSO_4$. Purification by flash chromatography on silica gel (2:1, Et_2O−hexanes) gave aldehyde **2.7** (1.73 g, 90%): $[\alpha]_D$ −62.8 (*c* 1.09, $CHCl_3$); IR 2821, 2725, 1694; ^1H NMR (DMSO-d_6, 85 °C) δ 1.51 (3 H, s), 1.57 (3 H, s), 3.88 (1 H, dd, J = 2.4, 9.3 Hz), 4.17 (1 H, dd, J = 6.6, 9.3 Hz), 4.70−4.75 (1 H, m), 5.07 and 5.14 (2 H, ABq, J = 12.5 Hz), 6.07 (1 H, dd, J = 7.6, 15.6 Hz), 6.94 (1 H, dd, J = 6.3, 15.6 Hz), 7.30−7.35 (5 H, m), 9.55 (1 H, d, J = 7.6 Hz). Anal. Calcd for $C_{16}H_{19}NO_4$: C; 66.42, H; 6.62 N; 4.79. Found: C; 66.16, H; 6.56, N; 4.79.

(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-[(1*E*,5*E*,3*S*,4*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-3-hydroxy-1,5-heptadienyl]oxazolidine (2.9). To a solution of aldehyde **2.7** (1.06 g, 3.66 mmol) and (*R*)-stannane **2.8** (2.26 g, 4.75 mmol) in CH_2Cl_2 (25 mL) was added 0.6 mL (4.9 mmol) of $BF_3{\cdot}OEt_2$. After 2 h, the reaction mixture was quenched with saturated $NaHCO_3$, allowed to warm to rt, diluted with Et_2O, washed with H_2O and brine, and dried over $MgSO_4$. Purification by flash chromatography on silica gel (1:1, hexanes−Et_2O) gave alcohol **2.9** (1.51 g, 87%): $[\alpha]_D$ −20.6 (*c* 1.43, $CHCl_3$); IR 3490, 1708; ^1H NMR (DMSO-d_6, 85 °C) δ 0.02 (3 H, s), 0.04 (3 H, s), 0.87 (9 H, s), 1.46 (3 H, s), 1.54 (3 H, s), 1.60 (3 H, d, J = 6.3 Hz), 3.68 (1 H, dd, J = 2.1, 8.8 Hz), 3.87−3.91 (1 H, m), 3.96−4.00 (1 H, m), 4.05 (1 H, dd, J = 6.1, 8.8 Hz), 4.43−4.45 (1 H, m), 5.03, 5.11 (ABq, J = 12.7 Hz), 5.38 (1 H, ddq, J = 1.4, 6.3, 15.4 Hz), 5.48−5.70 (3 H, m), 7.30−7.35 (5 H, m). Anal. Calcd for $C_{26}H_{41}NO_5Si$: C; 65.65, H; 8.69, N; 2.94. Found: C; 65.47, H; 8.65, N; 2.93.

(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-[(1*E*,5*E*,3*S*,4*S*)-3,4-bis[(*tert*-butyldimethylsilyl)oxy]-1,5-heptadienyl]oxazolidine (2.10). To a solution of alcohol **2.9** (1.41 g, 2.95 mmol) in CH_2Cl_2 (35 mL) at 0 °C was added 0.76 mL (6.52 mmol) of 2,6-lutidine followed by 1.2 mL (5.2 mmol) of TBSOTf. After 30 min, the reaction mixture was diluted with Et_2O, washed with H_2O, 10% HCl, saturated $NaHCO_3$, H_2O, and brine, and dried over $MgSO_4$. Purification by flash chromatography on silica gel (4:1, hexanes−Et_2O) gave disilyl ether **2.10** (1.68 g, 97%) as a colorless oil: $[\alpha]_D$ −54.0 (*c* 1.07, $CHCl_3$); IR 1710; ^1H NMR (DMSO-d_6, 67 °C) δ 0.08 (3 H, s), 0.10 (3 H, s), 0.11 (3 H, s), 0.13 (3 H, s), 0.99 (9 H, s), 1.00 (9 H, s), 1.53 (3 H, s), 1.59 (3 H, d, J = 4.5 Hz), 1.76 (3 H, s), 3.60 (1 H, dd, J = 1.9, 8.7 Hz), 3.72 (1 H, dd, J = 5.9, 8.7 Hz), 4.15−4.35 (3 H, m), 5.07 (1 H, d, J = 12.4 Hz), 5.15−5.20 (1 H, m), 5.60−5.90 (4 H, m), 7.30−7.35 (5 H, m). Anal. Calcd for $C_{32}H_{55}NO_5Si_2$: C; 65.15, H; 9.40, N; 2.37. Found: C; 65.25, H; 9.36, N; 2.39.

(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-[(1*R*,2*S*,3*S*,4*S*,5*S*,6*R*)-3,4-bis-[(*tert*-butyldimethylsilyl)-oxy]-1,2,5,6-tetrahydroxyl]oxazolidine (3.1). To a solution of diene **2.10** (1.57 g, 2.66 mmol) in Me_2CO (27 mL) and H_2O (7 mL) was added 1.56 g (13.2 mmol) of NMO followed by 2.6 mL (0.24 mmol) of 2.5% OsO_4 in *t*-BuOH. After 22 h, saturated $NaHSO_3$ was added. After being stirred for 30 min, the reaction mixture was concentrated under reduced pressure. The aqueous phase was extracted with CH_2Cl_2 and dried over $MgSO_4$. Purification by flash chromatography on silica gel (2:1, Et_2O−hexanes) gave tetrol **3.1** (1.18 g, 68%) as a waxy solid and a faster eluting inseparable mixture of isomers (165 mg, 9%). **3.1**: $[\alpha]_D$ −46.7 (*c* 0.66, $CHCl_3$); IR 3466, 1710; ^1H NMR (DMSO-d_6, 74 °C) δ 0.10 (3 H, s), 0.11 (3 H, s), 0.12 (3 H, s), 0.13 (3 H, s), 0.88 (9 H, s), 0.89 (9 H, s), 1.09 (3 H, d, J = 6.2 Hz), 1.13 (3 H, s), 1.16 (3 H, s), 3.29 (1 H, t, J = 8.5 Hz), 3.49−4.06 (11 H, m), 4.23 (1 H, dd, J = 5.0, 8.6 Hz), 5.08 (1 H, d, J = 12.6 Hz), 5.16 (1 H, d, J = 12.6 Hz), 7.31−7.40 (5 H, m). Anal. Calcd for $C_{32}H_{59}NO_9Si_2$: C; 58.41, H; 9.04, N; 2.13. Found: C; 58.46, H; 9.03, N; 2.12.

Silylated Lactol 3.2. To a solution of tetrol **3.1** (1.02 g, 1.55 mmol) in THF (15 mL) at 0 °C was added 396 mg (1.74 mmol) of H_5IO_6. After 30 min, the reaction mixture was diluted with Et_2O, washed with saturated $NaHCO_3$, H_2O, and brine, and dried over $MgSO_4$. Purification by flash chromatography on silica gel (1:1, Et_2O−hexanes) gave lactol **3.2** (766 mg, 81%) as a glassy solid: $[\alpha]_D$ −17.3 (*c* 1.31, $CHCl_3$). Anal. Calcd for $C_{30}H_{53}NO_8Si_2$: C; 58.86, H; 8.34, N; 2.15. Found: C; 58.63, H; 8.46, N; 2.26.

6-[*N*-(Carbobenzyloxy)amino]-6-deoxy-L-*glycero*-α-D-*galacto*-heptopyranose (3.4). To a solution of lactol **3.2** (600 mg. 0.98 mmol) in THF (6 mL) was added 2.5 mL (2.5 mmol) of 1.0 M TBAF in THF followed by 0.15 mL (2.62 mmol) of acetic acid. After 24 h, the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography on silica gel (95:5, EtOAc−MeOH) gave furanose **3.3** (323 mg, 86%) as a glassy solid. A solution of this oxazolidine furanose (254 mg, 0.66 mmol) in 9:1 AcOH−H_2O (1 mL) was heated at 50 °C for 1.5 h and concentrated under reduced pressure. Residual HOAc was removed by codistillation with $PhCH_3$ affording pyranose **3.4** (221 mg, 97%) as a white solid: mp 164−166 °C after recrystallization from MeOH [lit.[5b] 170−173 °C (dec)]; $[\alpha]_D$ +32.8 (*c* 0.91, H_2O), [lit.[5b] +52.9 (*c* 1.0, H_2O)]; ^1H NMR (D_2O) δ 3.45−4.05 (7 H, m), 4.50 (0.6 H, d, J = 7.8 Hz), 5.12 (2 H, s), 5.20 (0.4 H, bs), 7.42 (5 H, s).

1,2:3,4-Di-*O*-isopropylidene-6-[*N*-(carbobenzyloxy)amino]-6-deoxy-L-*glycero*-α-D-*galacto*-heptopyranose (3.6). To a solution of pyranose **3.4** (40 mg, 0.12 mmol) in anhydrous Me_2CO (0.5 mL) was added 47 mg (0.29 mmol) of $CuSO_4$ followed by 2 μL (0.13 mmol) of concd H_2SO_4. After being stirred for 16 h, the reaction mixture was filtered. The filtrate was neutralized with $Ca(OH)_2$ (23 mg, 0.31 mmol) and filtered through Celite and then concentrated under reduced pressure. Purification by flash chromatography on silica gel (1:1 then 3:1 Et_2O−hexanes) gave the pyranoside diacetonide **3.6** (23 mg, 46%) as a glassy solid and oxazolidine **3.7** (14 mg, 26%).

3.6: $[\alpha]_D$ −47.1 (*c* 0.72, $CHCl_3$), [lit. −47.3 (*c* 0.2, $CHCl_3$),[5a] −48.8 (*c* 2, $CHCl_3$)[5b]]; ^1H NMR δ 1.32 (6 H, s), 1.42 (3 H, s), 1.51 (3 H, s), 3.22 (1 H, bs), 3.70−3.90 (3 H, m), 4.10 (1 H, bd, J = 5.8 Hz), 4.30 (1 H, dd, J = 1.5, 8.0 Hz), 4.35 (1 H, dd, J = 1.5, 8.0 Hz), 4.62 (1 H, dd, J = 2.3, 8.0 Hz), 5.11 (2 H, s), 5.40−5.50 (1 H, m), 5.52 (1 H, d, J = 5.0 Hz), 7.26−7.36 (5 H, m).

3.7: IR 1703; ^1H NMR (DMSO-d_6, 85 °C) 1.27 (9 H, s), 1.40 (3 H, s), 1.46 (3 H, s), 1.54 (3 H, s), 3.73 (1 H, bd, J = 9.3 Hz), 3.83 (1 H, dd, J = 5.4, 9.2 Hz), 3.95 (1 H, d, J = 9.1 Hz), 4.25−4.35 (3 H, m), 4.52 (1 H, d, J = 7.7 Hz), 4.98, 5.01 (2 H, ABq, J = 11.6 Hz), 5.39 (1 H, d, J = 5.2 Hz), 7.20−7.30 (5 H, m).

(4*S*,5*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(*E*)-carbomethoxyvinyl]-5-methyloxazolidine (5.2). The procedure described above for ester **2.5** was employed with 7.18 g (29.5 mmol) of aldehyde **5.1**, 847 mg (35.3 mmol) of NaH, and 7.0 mL (35.3 mmol) of triethyl phosphonoacetate affording

ester **5.2** (8.46 g, 91%) as a colorless oil: $[\alpha]_D$ +31.2 (1.30, $CHCl_3$), IR 1703, 1660; ^1H NMR (DMSO-d_6, 85 °C) 1.22 (3 H, d, J = 2.9 Hz), 1.23 (3 H, t, J = 7.0 Hz), 1.38 (9 H, s), 1.49 (3 H, s). 1.53 (3 H, s), 3.80−4.00 (2 H, m), 4.17 (2 H, q, J = 7.0 Hz), 5.95 (1 H, d, J = 15.7 Hz), 6.69 (1 H, dd, J = 7.6, 15.7 Hz). Anal. Calcd for $C_{16}H_{27}NO_5$: C; 61.32, H; 8.68, N; 4.47. Found: C; 61.03, H; 8.58, N; 4.44.

(4*S*,5*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(*E*)-3-hydroxy-1-propenyl]-5-methyloxazolidine (5.3). The procedure described above for alcohol **2.6** was employed with 8.03 g (25.6 mmol) of ester **5.2** and 57.0 mL (57.0 mmol) of 1.0 M DIBAL-H in hexanes affording alcohol **5.3** (8.46 g, 91%) as a colorless oil: $[\alpha]_D$ −6.6 (*c* 1.23, $CHCl_3$); IR 3441, 1699; ^1H NMR (DMSO-d_6, 85 °C): 1.20 (3 H, d, J = 6.0 Hz), 1.39 (9 H, s), 1.45 (3 H, s), 1.51 (3 H, s), 3.70 (1 H, t, J = 7.7 Hz), 3.78−3.86 (1 H, m), 3.97 (2 H, td, J = 1.2, 5.1 Hz), 4.45 (1 H, td, J = 1.1, 5.4 Hz), 5.49 (1 H, tdd, J = 1.6, 7.7, 15.4 Hz), 5.68 (1 H, tdd, J = 0.6, 4.9, 15.4 Hz). Anal. Calcd for $C_{14}H_{25}NO_4$: C; 61.97, H; 9.29, N; 5.16. Found: C; 61.88, H; 9.30, N; 5.09.

(4*S*,5*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(*E*)-2-formylvinyl]-5-methyl oxazolidine (5.4). The procedure described above for aldehyde **2.7** was employed with 2.79 g (10.3 mmol) of alcohol **5.3**, 1.0 mL (11.5 mmol) of oxalyl chloride, 1.6 mL (22.8 mmol) of DMSO, and 7.1 mL (50.9 mmol) of Et_3N affording aldehyde **5.4** (8.46 g, 91%) as a colorless oil: $[\alpha]_D$ +21.0 (*c* 1.03, $CHCl_3$); IR 1694; ^1H NMR (DMSO-d_6, 85 °C): 1.25 (3 H, d, J = 6.0 Hz), 1.35 (9 H, s), 1.50 (3 H, s), 1.55 (3 H, s), 3.80−4.06 (2 H, m), 6.16 (1 H, ddd, J = 0.8, 7.7, 15.6 Hz), 6.88 (1 H, dd, J = 7.5, 15.6 Hz), 9.59 (1 H, d, J = 7.5 Hz). Anal. Calcd for $C_{14}H_{23}NO_4$: C; 62.43, H; 8.61, N; 5.20. Found: C; 62.29, H; 8.67, N; 5.10.

(4*S*,5*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(1*E*,5*E*,3*S*,4*S*)-4-[*tert*-butyldimethylsilyl)oxy]-3-hydroxy-1,5-heptadienyl]-5-methyloxazolidine (5.5). The procedure described above for alcohol **2.9** was employed with 557 mg (2.07 mmol) of aldehyde **5.4**, 1.28 g (2.69 mmol) of (*R*)-stannane **2.8**, and 0.33 mL (2.68 mmol) of $BF_3{\cdot}OEt_2$ affording alcohol **5.5** (772 mg, 82%) as a colorless oil: $[\alpha]_D$ −0.3 (*c* 1.18, $CHCl_3$); IR 3459, 1700; ^1H NMR (400 MHz), δ 0.01 (3 H, s), 0.04 (3 H, s), 0.87 (9 H, s), 1.22 (3 H, d, J = 5.8 Hz), 1.41 (9 H, s), 1.48 (3 H, s), 1.57 (3 H, s), 1.66 (3 H, dd, J = 1.4, 6.5 Hz), 2.69 (1 H, bs), 3.65−3.85 (4 H, m), 5.30−5.70 (4 H, m). Anal. Calcd for $C_{24}H_{45}NO_5Si$: C; 63.26, H; 9.95, N; 3.07. Found: C; 63.18, H; 10.03, N; 2.99.

(4*S*,5*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(1*E*,5*E*,3*S*,4*S*)-3,4-bis-[(*tert*-butyldimethylsilyl)oxy]-1,5-heptadienyl]-5-methyloxazolidine (5.6). The procedure described above for disilyl ether **2.10** was employed with 780 mg (1.71 mmol) of alcohol **5.5**, 0.44 mL (3.78 mmol) of 2,6-lutidine, and 0.69 mL (3.00 mmol) of TBSOTf affording disilyl ether **5.6** (911 mg, 94%) as a colorless oil: $[\alpha]_D$ −8.9 (*c* 1.05, $CHCl_3$); IR 1704; ^1H NMR (400 MHz) δ −0.01 (3 H, s), 0.01 (3 H, s), 0.02 (3 H, s), 0.04 (3 H, s), 0.86 (9 H, s), 0.87 (9 H, s), 1.24 (3 H, d, J = 5.8 Hz), 1.41 (12 H, s), 1.46 (3 H, s), 1.64 (3 H, d J = 6.2 Hz), 3.75−3.79 (2 H, m), 3.95−4.05 (2 H, bs), 5.41−5.60 (4 H, m). Anal. Calcd for $C_{30}H_{59}NO_5Si_2$: C; 63.22, H; 10.43, N; 2.46. Found: C; 63.27, H; 10.49, N; 2.39.

(4*S*,5*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(1*R*,2*S*,3*S*,4*S*,5*S*,6*R*)-3,4-bis-[(*tert*-butyldimethylsilyl)-oxy]-1,2,5,6-tetrahydroxylheptyl]-5-methyloxazolidine (5.7). The procedure described above for tetrol **3.1** was employed with 570 mg (0.96 mmol) of diene **5.6**, 565 mg (4.80 mmol) of NMO, and 2.0 mL (0.20 mmol) of 0.1 M OsO_4 in H_2O affording tetrol **5.7** (446 mg, 73%) as a white glassy solid after chromatography along with a mixture of isomers (104 mg, 17%): mp 54−56 °C; $[\alpha]_D$ −6.02 (*c* 1.03, $CHCl_3$); IR 3452, 1663; ^1H NMR (400 MHz) δ 0.13 (3 H, s), 0.15 (3 H, s), 0.16 (6 H, s), 0.88 (18 H, s), 1.22 (3 H, d, J = 6.5 Hz), 1.32 (3H, d, J = 6.4 Hz), 1.44 (3 H, s), 1.47 (9 H, s), 1.61 (3 H, s), 2.12 (1 H, bd, J = 9.8 Hz), 3.56 (1 H, bs), 3.64 (1 H, t, J = 8.5 Hz), 3.71 (1 H, d, J = 8.2 Hz), 3.76 (1 H, dd, J = 2.6, 6.8 Hz), 3.79−3.98 (4 H, m), 4.10 (1 H, bs), 4.27 (1 H, bs), 4.37 (1 H, bd, J = 5.4 Hz). Anal. Calcd for $C_{30}H_{63}NO_9Si_2$: C; 56.42, H; 9.95, N; 2.20. Found: C; 56.46, H; 9.98, N; 2.22.

Silylated Lactol 5.8. The procedure described above for lactol **3.2** was employed with 606 mg (0.95 mmol) of tetrol **5.7** and 242 mg (1.06 mmol) of H_5IO_6 affording lactol **5.8** (504 mg, 90%) as a solid foam: mp 55−61 °C, $[\alpha]_D$ +48.9 (*c* 0.97, $CHCl_3$); IR 3445, 1673. Anal. Calcd for $C_{28}H_{57}NO_8Si$: C; 56.82, H; 9.75, N; 2.37. Found: C; 56.85, H; 9.75, N; 2.43.

6-[(*tert*-Butoxycarbonyl)amino]-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-D-*threo*-α-D-*galacto*-octopyranose (6.3). The procedure described above for pyranose **3.4** was employed with 1.10 g (1.86 mmol) of lactol **5.8**, 4.7 mL (4.7 mmol) of 1.0M TBAF in THF and 0.28 mL (4.90 mmol) of HOAc affording pyranoside **5.9** (670 mg, 99%) of a solid foam: mp 95−100 °C. A 388-mg sample of this material was heated with 4.0 mL of 9:1 HOAc-H_2O as described above affording 388 mg of crude lactol **6.1** which was treated as described above for diacetonide **3.6** with 5.0 mL of acetone, 480 mg of $CuSO_4$, and 0.02 mL of H_2SO_4 affording diacetonide **6.3** (126 mg, 26%) and oxazolidine **6.2** (161 mg, 30%) as a white solid.

6.2: mp 127−129 °C; $[\alpha]_D$ +4.0 (*c* 1.08, $CHCl_3$); IR (CCl_4) 1694; ^1H NMR δ 1.30 (6 H, s), 1.31 (3 H, d, J = 6.3 Hz), 1.42 (3 H, s), 1.47 (12 H, s), 1.53 (3 H, s), 1.59 (3 H, s), 3.86 (1 H, bs), 4.10−4.30 (2 H, m), 4.27 (1 H, dd, J = 2.2, 4.9 Hz), 4.58 (1 H, dd, J = 2.1, 3.9 Hz), 4.65 (1 H, dq, J = 2.3, 6.3 Hz), 5.58 (1 H, d, J = 5.0 Hz). Anal. Calcd for $C_{22}H_{37}NO_8$: C; 59.58, H; 8.41, N; 3.16. Found: C; 59.66, H; 8.37, N; 3.10.

6.3: $[\alpha]_D$ −28.8 (*c* 1.03, $CHCl_3$); IR (CCl_4) 3447, 1705; ^1H NMR δ 1.16 (3 H, d, J = 6.4 Hz), 1.31 (3 H, s), 1.33 (3 H, s), 1.43 (9 H, s), 1.45 (3 H, s), 1.49 (3 H, s), 2.60 (1 H, bs), 3.70−3.75 (1 H, m), 3.89 (1H, d, J = 5.4 Hz), 4.29 (1 H, dd, J = 2.2, 4.9 Hz), 4.32 (1 H, dd, J = 1.0, 8.1 Hz), 4.58 (1 H, dd, J = 1.8, 7.8 Hz), 5.16 (1 H, d, J = 9.2 Hz), 5.53 (1 H, d, J = 5.0 Hz).

A solution of the above oxazolidine **6.2** (154 mg, 0.35 mmol) and $TsOH{\cdot}H_2O$ (7 mg, 0.04 mmol) in MeOH (2 mL) was stirred for 8 h, neutralized with Et_3N, and then concentrated under reduced pressure. Purification by flash chromatography on silica gel (3:2 Et_2O−hexanes) gave additional diacetonide **6.3** (112 mg, 80%).

Ester 6.4. To a suspension of alcohol **6.2** (108 mg, 0.27 mmol), Ph_3P (105 mg, 0.40 mmol), and *p*-nitrobenzoic acid (68 mg, 0.40 mmol) in benzene (2 mL) was added 0.06 mL (0.04 mmol) of DEAD. After 48 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in Et_2O (0.3 mL) and after 30 min, 0.15 mL of hexanes was added. The resulting precipitate was filtered on Celite and washed with a 1:1 mixture of hexanes−Et_2O (1.4 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (first column: 1:1, hexanes−Et_2O, second column: 3:2, hexanes−EtOAc) affording 101 mg (74%) of a glassy solid: mp 86−88 °C; $[\alpha]_D$ −50.3 (*c* 0.93, $CHCl_3$); IR 3254, 3137, 1725, 1699, 1530, 1373; ^1H NMR δ 1.31 (3 H, s), 1.33 (3 H, s), 1.38−1.44 (15 H, m), 1.48 (3 H, s), 3.60−3.85 (2 H, m), 4.30−4.50 (3 H, m), 4.58 (1 H, dd, J = 2.3, 7.9 Hz), 5.26 (1 H, bd, J = 8.1 Hz), 5.44 (1 H, dq, J = 5.8, 6.0 Hz), 5.54 (1 H, d, J = 5.2 Hz), 8.18−8.25 (4 H, m). Anal. Calcd for $C_{26}H_{36}N_2O_{11}$: C; 56.56, H; 8.24, N; 3.47. Found: C; 56.32, H; 8.08, N; 3.47.

6-[(*tert*-Butoxycarbonyl)amino]-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-D-*erythro*-α-D-*galacto*-octopyranose (6.5). A solution of ester **6.4** (91 mg, 0.16 mmol) and KCN (6 mg, 0.08 mmol) in MeOH (1 mL) was stirred for 20 h and then concentrated under reduced pressure. Purification by flash chromatography on silica gel (3:2, hexanes−EtOAc) gave alcohol **6.5** (59 mg, 89%) as a white solid: mp 48−50 °C; $[\alpha]_D$ −41.0 (*c* 0.80, $CHCl_3$); IR 3431, 1703;^1H NMR δ 1.24 (3 H, d, J = 6.7 Hz), 1.32 (3 H, s), 1.34 (3 H, s), 1.43 (9 H, s), 1.48 (3 H, s), 1.52 (3 H, s), 2.82 (1 H, bs), 3.75−3.83 (1 H, m), 4.02 (2 H, bs), 4.29 (1 H, dd, J = 2.3, 5.0 Hz), 4.39 (1 H, dd, J = 1.2, 7.9 Hz), 4.60 (1 H, dd, J = 2.5, 8.0 Hz), 5.22 (1 H, bs), 5.53 (1 H, d, J = 5.0 Hz).

6-Acetamido-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-D-*erythro*-α-D-*galacto*-octopyranose (6.7). A solution of the N-BOC pyranoside **6.5** (11 mg, 0.03 mmol) in CH_2Cl_2−TFA (1:1, 0.4 mL) was stirred at rt for 10 min, diluted with CH_2Cl_2, and then made basic with 5% NaOH. The aqueous layer was extracted with CH_2Cl_2, and the combined extracts were dried over Na_2SO_4 to give the crude amine **6.6** (7 mg, 82%): ^1H NMR δ 1.15 (3 H, d, J = 6.6 Hz), 1.31 (3 H, s), 1.34 (3 H,

s), 1.44 (3 H, s), 1.51 (3 H, s), 1.88 (3 H, s), 3.10 (1 H, dd, J = 4.6, 9.2 Hz), 3.54 (1 H, dd, J = 1.7, 9.4 Hz), 4.00 (1 H, qd, J = 5.0, 6.2 Hz), 4.31 (1 H, dd, J = 2.5, 5.2 Hz), 4.61 (1 H, dd, J = 2.5, 7.9 Hz), 5.50 (1 H, d, J = 5.0 Hz).

This material in MeOH (0.5 mL) was stirred with 3 drops of Ac_2O. After 15 h, the reaction mixture was quenched with pyridine (4 drops) and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with 10% HCl and saturated $NaHCO_3$, and dried over Na_2SO_4. Purification by flash chromatography on silica gel (95:5 EtOAc−MeOH) gave acetamide **6.3** (7 mg, 94%) as a white solid: mp 164−165 °C ([lit. mp 165.5−166.5[12c]]; $[\alpha]_D$ −54.0 (*c* 0.70, $CHCl_3$) [lit. −53.8 (*c* 3.2, $CHCl_3$)[12c] mp 166−167 °C, $[\alpha]_D$ −53.0 (*c* 0.98, $CHCl_3$)[12e]] after recrystallization from EtOAc-hexanes; IR 3400−3100, 1657 ; ^{1}H NMR δ 1.24 (3 H, d, J = 6.3 Hz), 1.32 (3 H, s), 1.35 (3 H, s), 1.49 (3 H, s), 1.51 (3 H, s), 1.99 (3 H, s), 3.03 (1 H, bs), 3.98−4.16 (3 H, m), 4.30 (1 H, dd, J = 2.2, 5.0 Hz), 4.44 (1 H, d, J = 8.1 Hz), 4.61 (1 H, dd, J = 2.2, 7.9 Hz), 5.52 (1 H, d, J = 5.0 Hz), 6.48 (1 H, d, J = 6.6 Hz).

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Supporting Information Available: ^{1}H NMR spectra for all intermediates (28 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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