Notes

Lipo α-Amino-*β*-hydroxy Acids and O-Linked Glycosides: Building Blocks for Ceramyl and Glycosphingoyl Peptides

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Received June 17, 2001

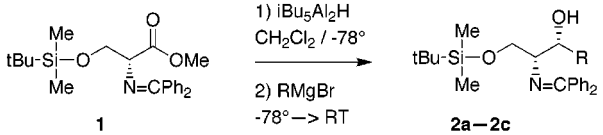
Introduction

β-hydroxy α-amino acids, including threonine, serine, and other unusual amino acids, are an important class of chiral, bioactive molecules.[1] In addition to being constituents of bioactive peptides such as cyclosporin,[2] they are also components of various natural products such as vancomycin and bouvardin. *β*-Hydroxy α-amino acids are also synthetic intermediates for complex products,[3] such as *β*-lactams,[4] *β*-fluoro amino acids,[5] and aziridines.[6]

The presence of *β*-hydroxy amino acids within a peptide allows for additional functionality, e.g., glycosylation.[7] Glycosides are critical for a number of biological processes, including molecular recognition,[8] stability to enzymatic degradation,[9] and enhanced transport and biodistribution.[10] In addition, compounds of this type constitute ceramide and glycosylceramide analogues and could provide biologically interesting peptide−glycosphingolipid chimeras.

A number of lipo-amino acid syntheses exist,[11] but few possess a side chain capable of glycosylation. The glycosides[12] of differentially protected amino diols[13] were assembled via three different routes and can be used to create several amphiphilic motifs, including novel glycosphingopeptides. The synthesis represents the first of its type, possessing an O-linked glycoside (as in endogenous glycoproteins) and a C-linked lipid chain to the amino acid, to provide a higher level of enzymatic stability in vivo.

Scheme 1



R	Yield	*threo* Selectivity	Product
CH_3−	60%	> 20:1	**2a**
$CH_3(CH_2)_5$−	60%	> 20:1	**2b**
$CH_3(CH_2)_9$−	72%	> 20:1	**2c**
$CH_3(CH_2)_{14}$−	62%	>20:1	**2d**

Results and Discussion

In all experiments, D-serine Schiff base **1** was used as the starting material. Reductive alkylation of the methyl ester[14] with $^{i}Bu_5Al_2H$[15] and alkyl Grignard reagents led to protected amino diols **2a**−**d** in enantiomerically pure form and in good yield[16] (Scheme 1). Regardless of chain length, all reductive alkylations proceeded in good yield (60−72%) with excellent diastereoselectivity for the threo product. The products of these reactions were then converted to their respective *β*-hydroxy amino acids.

In three cases, the reductive alkylation products **2a**−**c** were hydrogenated and reprotected as the Fmoc carbamates without purification (Scheme 2). This proceeded in 75−82% yield over two steps. The Fmoc-protected silyl amino diols **3a**−**c** were desilylated with $BF_3{\cdot}Et_2O$ (78−92%) and subjected to selective oxidation of the primary alcohol in the presence of the unprotected secondary alcohol. This was accomplished using the TEMPO oxidation procedure[17] as refined by a group at Merck[18] for substrates containing a single hydroxyl group. We ob-

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(14) In the hexyl and decyl case, the ethyl ester was also used, and produced no increase in yield, compared to the methyl ester.

(15) Alkylaluminum species aggregate into fluxional trimers in hydrocarbon solution or dimers in more coordinating solvents. NMR studies suggest that the Schiff base esters used in this study react with the $[^{i}Bu_3Al]_3$ and $[^{i}Bu_2AlH]_3$ trimers to promote the formation of a dimeric [$^{i}Bu_3Al{\cdot}{}^{i}Bu_2AlH$ or $^{i}Bu_5Al_2H$] complex prior to reductive alkylation. (a) Eisch, J. J.; Rhee, S. G. *J. Organomet. Chem.* **1974**, *42*, C73. (b) Polt, R.; Peterson, M. A.; DeYoung, L. *J. Org. Chem.* **1992**, *57*, 5469−5480.

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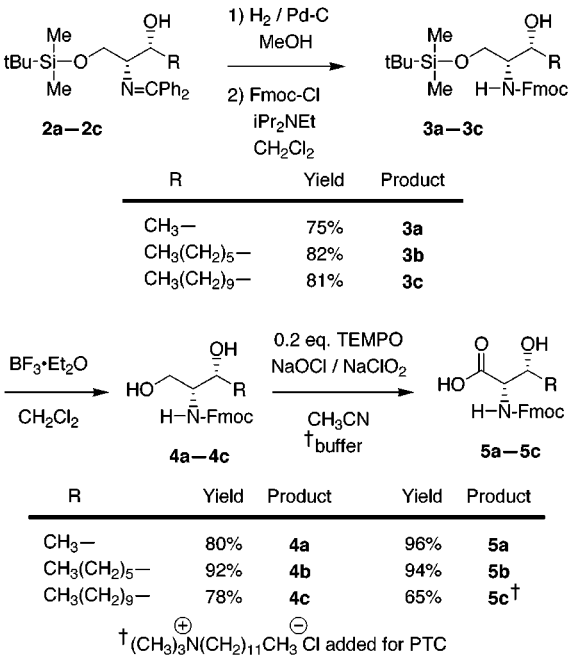
10.1021/jo015844v CCC: $20.00
Published on Web 09/21/2001

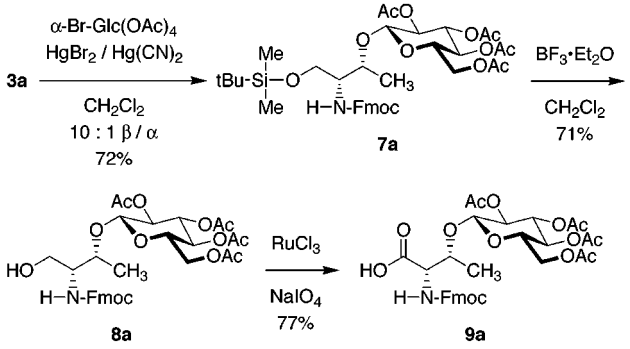
Scheme 2



R	Yield	Product	Yield	Product
CH_3—	80%	**4a**	96%	**5a**
$CH_3(CH_2)_5$—	92%	**4b**	94%	**5b**
$CH_3(CH_2)_9$—	78%	**4c**	65%	**5c**†

†$(CH_3)_3\overset{\oplus}{N}(CH_2)_{11}CH_3\ \overset{\ominus}{Cl}$ added for PTC

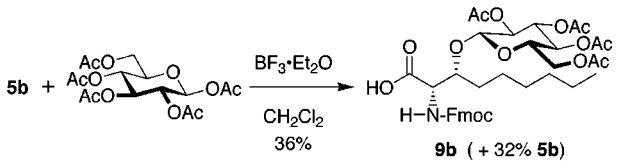
Scheme 3



served no over-oxidized (diketo) products in the reaction mixtures. With increasing alkyl chain length, it was observed that the oxidation rate slowed, probably due to steric interactions and/or micelle formation. The final step of this sequence proceeded in 65−96% yield. In the decyl case, phase-transfer conditions were required as a result of the high lipophilicity. This provided the protected C_4, C_9, and C_{13} β-hydroxy lipo amino acids in respectable overall yields, in five steps from the crystalline serine derivative **1**.

Glycosylation was achieved directly for protected amino diol **3a** (Scheme 3), using Helferich[19] conditions ($HgBr_2$), to give the glycoside in 72% yield with greater than 20:1 selectivity for the β-product. Using $BF_3{\cdot}Et_2O$, the silyl ether was removed in 71% yield and the primary alcohol oxidized to the acid. However, the TEMPO oxidation was much slower than the simpler cases, proceeding to an unoptimized yield of 43%. Since there is no secondary alcohol in this case, another less selective method of oxidation was employed. Oxidation with $RuCl_3/NaIO_4$ provided the Fmoc methyl β-glycosyl amino acid in a 77% yield.

Scheme 4



Glycosylation of **3b** and **3c** failed using these same conditions. Similar electrophilic reactions also failed, including the Koenigs−Knorr, $Glc(OAc)_5$ with $BF_3{\cdot}OEt_2$ or TMSOTf, Schmidt's trichloroacetimidate method, as well as *tert*-butylation, acylation, and benzylation. A priori, these transformations appear to be facile, but from our experience with these compounds the secondary hydroxyl is much more hindered than expected, and its nucleophilicity is reduced due to unfavorable hydrogen bonding with the carbamate NH.[20]

Therefore, a different route to the other two glycosides was required. The unprotected hexyl β-hydroxy lipo amino acid (**5b**) was directly glycosylated with β-glucose penta-acetate[21] (Scheme 4). While yields in this reaction were very modest, they were comparable to those seen in similar cases and provided a direct route to the desired glycoside without any further protection or deprotection.

A slightly longer route was devised for synthesis of the C_{13} β-hydroxy amino acid glycoside (decyl adduct), which involved a protecting group switch to alleviate some steric hindrance at the secondary hydroxyl (Scheme 5). The reductive alkylation product **2c** was subjected to 2 M HCl in THF, resulting in simultaneous cleavage of the Schiff base and the silyl ether to provide the amino diol. This was protected with Fmoc-Cl without purification to yield **4c**. This diol was then regioselectively protected at the primary alcohol with benzyl chloroformate to provide **6c**. We hoped this compound would be less hindered than silyl-protected **3c** and the benzyl carbonate would compete for the carbamoyl N−H hydrogen bond. When the Fmoc alcohol **6c** was treated with the trichloroacetimidate and TMSOTf, this glycosylation proceeded in good yield and selectivity for the desired β glycoside **7c**. The benzyl ether was then cleaved by hydrogenolysis and oxidized in two steps via the aldehyde to give the final product (**9c**) in good yield.

This note describes the stereoselective synthesis of novel lipo-amino acids and three different routes to their glycosides. This approach appears to be the method of choice for the synthesis of these lipid-like glycosyl amino alcohols and acids, and allows for the preparation of lipophilic glycopeptides and peptides, prepared by solid-phase methods.[22] The resulting amphipathic glycopeptides may possess interesting drug transport activities.[23]

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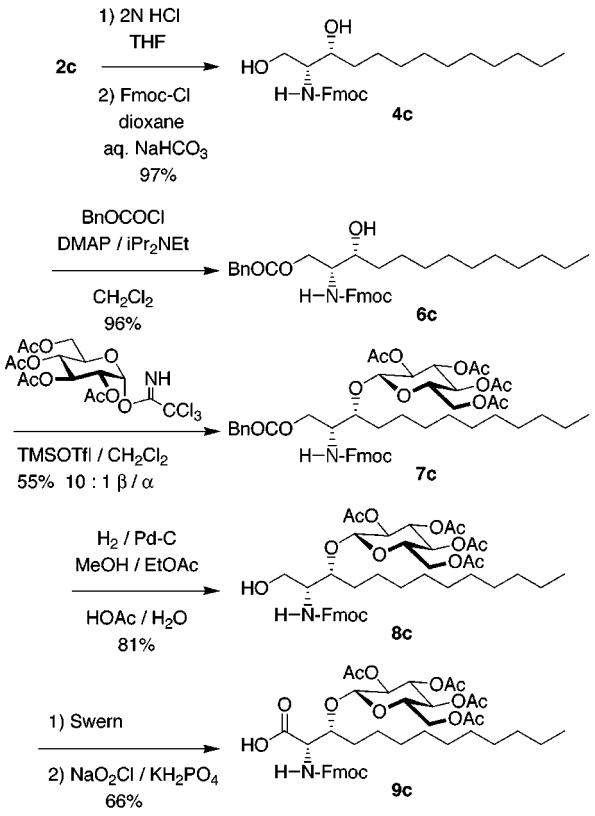
Scheme 5



Experimental Section

Procedure A. Reductive Alkylation with Grignards (2a−d). Compound **1** was dried overnight in vacuo over P_2O_5. A solution of **1** (1 equiv in 30−60 mL of CH_2Cl_2) was chilled to −78 °C under argon for 30 min. A solution of $^iBu_5Al_2H$ (1.0 equiv, 0.5 M of each in hexanes) was added dropwise via syringe to a stirring solution of **1** over 45 min at −78 °C. Immediately after the $^iBu_5Al_2H$ addition was complete, the alkylmagnesium bromide (3 equiv in Et_2O) was added dropwise via syringe to the stirring solution over 45 min at −78 °C. The solution was allowed to warm to rt and stir overnight. The resulting yellow solution was chilled to 0 °C, carefully quenched with 5 mL of saturated $NaHCO_3$, and then diluted with 100 mL of CH_2Cl_2 and washed 3× with saturated $NaHCO_3$ and 1× with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo.

Procedure B. Schiff Base Cleavage and Fmoc Reprotection (3a−c). Compound **2a−c** was dissolved in 100 mL of MeOH before 10% Pd−C (500 mg, regardless of amount of **2**) was added in one portion under Ar. The reaction was vigorously stirred under 1 atm of hydrogen (balloon) at rt. After 2 h, all of the starting material had been consumed, as judged by TLC. The reaction was quenched with 50 mL of CH_2Cl_2, filtered through Celite, and concentrated in vacuo. The crude mixture was then dissolved in dry CH_2Cl_2, and 3 equiv of $^iPr_2NEt$ was added in one portion, before Fmoc-Cl (1.0 equiv in 5 mL of CH_2Cl_2) was added dropwise over 30 min. The reaction was stirred at rt overnight, diluted with 100 mL of CH_2Cl_2, and washed 1× with aqueous HOAc (pH ∼3), 3× with saturated $NaHCO_3$, and 1× with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo.

Procedure C. Silyl Ether Cleavage (4a−c). Compound **3a−c** was dissolved in 50 mL of dry CH_2Cl_2. Freshly distilled $BF_3{\cdot}OEt_2$ (6 equiv) was added to the solution in one portion and stirred at rt. After 2 h, all of the starting material had been consumed, as judged by TLC. The reaction was then chilled to 0 °C and quenched with 5 mL of saturated $NaHCO_3$. The solution was diluted with 100 mL of CH_2Cl_2 and washed 3× with saturated $NaHCO_3$ and 1× with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo.

Procedure D. TEMPO Oxidation (5a−c). Compound **4a−c** was dissolved in 3 mL of aqueous buffer (0.67 M KH_2PO_4/Na_2HPO_4 buffer) and 3 mL of MeCN and heated to 60 °C in an oil bath. To the rapidly stirring solution was added TEMPO (0.20 equiv) in one portion. Sodium hypochlorite, NaOCl (0.20 equiv, 5.25% commercial bleach dissolved in 0.5 mL of H_2O), and sodium chlorite, $NaClO_2$ (80%, 2.0 equiv dissolved in 0.5 mL of H_2O), were then added simultaneously over 1 h to the mixture, which was heated at 45 °C for the amount of time specified. The reaction was then acidified to pH 3 with dilute HCl and extracted 3× with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo.

(2*R*,3*R*)-2-(Benzhydrylideneamino)-1-(*tert*-butyldimethylsilanyloxy)butan-3-ol, 2a. Procedure A. The crude reductive alkylation product was chromatographed (4.5% EtOAc/hexanes/0.1% Et_3N, $R_f = 0.40$). Yield: 60% as a yellow oil. IR (cm^{-1}): 3302.2, 3061.4, 2925.5, 2332.7, 1659.6, 1449.7, 1252.1, 1091.6. ^1H NMR ($CDCl_3$) δ: 7.62 (d, 2H, $J = 7.5$ Hz), 7.46 (d, 2H, $J = 7.5$ Hz), 7.23 (m, 6H), 4.01 (m, 1H), 3.70 (ddd, 2H, $J =$ 4.5, 4.5, 10.5, 32.0 Hz), 2.97 (bs, 1H), 2.86 (m, 1H), 1.22 (d, 3H, $J = 6.0$ Hz), 0.81 (s, 9H), 0.00, 0.00 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 145.7, 145.4, 128.0, 127.8, 127.3, 127.1, 126.5, 125.9, 75.8, 66.5, 61.2, 25.7, 19.4, 18.1, −5.9. HRMS: calcd for $C_{23}H_{34}NO_2Si$ 384.2359, found 384.2358 (diff = 0.3 ppm).

(2*R*,3*R*)-2-(Benzhydrylideneamino)-1-(*tert*-butyldimethylsilanyloxy)nonan-3-ol, 2b. Procedure A. Crude **2b** was chromatographed (2.5% EtOAc/hexanes/0.1% Et_3N, $R_f = 0.40$). Yield: 60% as a yellow oil. IR (cm^{-1}): 3506.0, 3061.4, 2956.4, 2925.5, 2851.46, 2357.46, 1449.7, 1252.14, 1091.6. ^1H NMR δ: 7.70 (d, 2H, $J = 7.5$ Hz), 7.54 (d, 2H, $J = 7.5$ Hz), 7.30 (m, 2H), 7.24 (m, 2H), 3.95 (m, 1H), 3.77 (dd, 1H, $J = 5.0$, 10.5 Hz), 3.72 (dd, 1H, $J = 3.0$, 10.5 Hz), 3.00 (m, 1H), 1.58 (m, 1 H), 1.47 (m, 3H), 1.33 (m, 4 H), 1.01 (t, 2H, $J = 6.5$ Hz), 0.92 (t, 3H, $J = 7.5$ Hz), 0.89 (s, 9H), 0.07, 0.05 (s, 6H). ^{13}C NMR δ: 145.5, 145.2, 127.9, 127.7, 127.0, 126.4, 125.9, 79.7, 65.2, 61.7, 43.7, 34.6, 31.6, 29.2, 26.4, 25.8, 22.5, 18.4, 14.0, 0.9, −5.6. HRMS: calcd for $C_{28}H_{44}NO_2Si$ 454.3141, found 454.3154 (diff = 2.7 ppm).

(2*R*,3*R*)-2-(Benzhydrylideneamino)-1-(*tert*-butyldimethylsilanyloxy)tridecan-3-ol. Procedure A. Crude **2c** was chromatographed (2.5% EtOAc/hexanes, with 0.1% Et_3N, $R_f =$ 0.40). Yield: 72% as a yellow oil. IR (cm^{-1}): 3320.7, 3055.2, 2925.5, 2851.4, 2357.4, 1449.7, 1252.1, 1091.6. ^1H NMR ($CDCl_3$) δ: 7.69 (d, 2H, $J = 7.0$ Hz), 7.53 (d, 2H, $J = 7.5$ Hz), 7.31 (m, 6H), 3.95 (m, 1H), 3.77 (dd, 1H, $J = 4.5$, 10.3 Hz), 3.71 (dd,1H, $J = 3.0$, 10.5 Hz) 2.99 (m, 1H), 1.57, 1.47, 1.31 (m, 18H), 0.93 (t, 3H, $J = 6.5$ Hz), 0.88 (s, 9H), 0.07, 0.05 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 145.6, 145.4, 127.9, 127.2, 127.0, 126.4, 125.9, 98.7, 79.7, 65.2, 61.7, 34.6, 31.4, 29.6, 29.5, 29.5, 29.5, 29.3, 26.5, 25.7, 22.6, 14.0, −6.2. HRMS: calcd for $C_{32}H_{52}NO_2Si$ 510.3767, found 510.3678 (diff = 0.2 ppm).

(2*R*,3*R*)-2-(Benzhydrylideneamino)-1-(*tert*-butyldimethylsilanyloxy)octadecan-3-ol, 2d. Procedure A. Crude **1d** was chromatographed (35% DCM/hex with 0.1% Et_3N, $R_f = 0.24$). Yield: 65.6% as a yellow oil. IR (cm^{-1}): 3320.3, 3055.6, 2924.9, 2852.1, 2357.0, 1449.2, 1252.0, 1089.1. ^1H NMR ($CDCl_3$): 7.69 (d, $J = 7.5$ Hz, 2H), 7.54 (d, $J = 7.0$ Hz, 2H), 7.24 (m, 4H), 3.95 (dt, 1H), 3.73 (ddd, $J = 15.0$, 5.0, 3.5 Hz, 2H), 2.99 (m, 1H), 1.28 (m, 28H), 0.93 (t, $J = 8.0$ Hz, 3H), 0.90 (s, 9H), 0.06 (s, 3H), 0.04(s, 3H). $^{13}C(CDCl_3)$:145.8,145.6, 128.0, 127.9, 126.5, 126.0, 79.8, 65.3, 61.8, 34.7, 32.0, 29.7, 29.6, 29.4, 26.6, 25.8, 22.7, 14.1, −5.4. HRMS: (*m*/*z*) obsd = 580.4559, calcd = 580.4557 (diff = 1.9 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-1-*O*-(*tert*-butyldimethylsilyl)butane-1,3-diol, 3a. Procedure B. Crude **3a** was chromatographed (20% EtOAc/hexanes $R_f = 0.35$). Yield: 82% as a yellow oil. IR (cm^{-1}): 3438.0, 3061.4, 2925.5, 1702.9, 1511.4, 1252.1, 1103.9. ^1H NMR ($CDCl_3$) δ: 7.69 (d, 2H, $J = 7.5$ Hz), 7.53 (t, 2H, $J = 7.0$ Hz), 7.32 (t, 2H, $J = 7.5$ Hz) 7.23 (t, 2H, $J = 7.5$ Hz), 5.38 (d, $J = 8.5$ Hz), 4.33 (m, 2H), 4.15 (t, 1H, $J = 7.0$ Hz), 4.12 (m, 1H), 3.78 (ddd, 2H, $J = 2.0$, 3.5, 10.5, 30.0), 3.48 (m, 1H), 3.20 (bs, 1H), 1.12 (d, 3H, $J = 7.0$ Hz), 0.83 (s, 9H), 0.00, 0.00 (s, 6H). ^{13}C NMR δ: 156.5, 143.9, 141.2, 127.6, 126.9, 125.0, 119.9, 69.0, 66.7, 66.1, 55.2, 47.2, 25.7, 19.8, 17.0, −5.9. HRMS: calcd for $C_{25}H_{36}NO_4Si$ 442.2414, found 442.2435 (diff = 4.9 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-1-*O*-(*tert*-butyldimethylsilyl)nonane-1,3-diol, 3b. Procedure B. Crude **3b** was chromatographed (20% EtOAc/hexanes, $R_f =$ 0.40). Yield: 82% as a yellow oil. IR (cm^{-1}): 3431.9, 2950.26,

2925.5, 2857.63, 1696.7, 1503.32, 1449.7, 1252.1, 1103.95. ^{1}H NMR δ: 7.77 (d, 2H, J = 7.5 Hz), 7.63 (t, 2H, J = 6.5 Hz), 7.40 (t, 2H, J = 7.5 Hz) 7.31 (t, 2H, J = 7.5 Hz), 5.46 (d, J = 8.5 Hz), 4.41 (m, 2H), 4.24 (t, 1H, J = 7.5 Hz), 4.00 (m, 1H), 3.92, 3.85 (dd, 2H, J = 2.0, 10.5 Hz), 3.63 (d, 1H J = 8.0 Hz), 3.28 (bs, 1H), 1.56, 1.45 1.30 (m, 10H), 0.92 (s, 9H), 0.90 (d, 3H, J = 6.5 Hz), 0.00, 0.00 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 156.3, 143.9, 141.2, 127.5, 126.9, 125.0, 119.8, 73.1, 66.7, 66.4, 53.8, 47.2, 33.8, 31.6, 29.1, 25.6, 25.4, 18.0, 14.0, −5.2. HRMS: calcd for $C_{30}H_{46}NO_4Si$ 512.3196, found 512.3181 (diff = −2.9 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-1-*O*-(*tert*-butyldimethylsilyl)tridecane-1,3-diol, 3c. Procedure B. Crude **3c** was chromatographed (17% EtOAc/hexanes, R_f = 0.40). Yield: 81% as a yellow oil. IR (cm^{-1}): 3438.0, 3073.7, 2925.5, 2851.4, 1696.7, 1505.3, 1449.7, 1252.1, 1103.9. ^{1}H NMR ($CDCl_3$) δ: 7.77 (d, 2H, J = 7.5 Hz), 7.61 (t, 2H, J = 7.5 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.31 (t, 2H, J = 7.5 Hz), 5.46 (d, J = 9.0 Hz), 4.39 (m, 2H), 4.24 (t, 1H, J = 7.5 Hz), 3.99 (t, 1H, J = 5.0 Hz), 3.92 (dd, 1H, J = 3.0, 10.5 Hz), 3.84 (dd, 1H, J = 2.0, 10.5 Hz), 1.55 (m, 2H), 1.28−1.20 (m, 16H), 0.91 (s, 9H), 0.87 (t, 3H, J = 7.5 Hz), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 156.3, 143.9, 141.2, 127.5, 126.9, 125.0, 119.9, 73.2, 66.7, 66.5, 53.8, 47.3, 33.8, 31.8, 29.5, 29.5, 29.2, 25.7, 25.5, 22.6, 18.0, 14.0, −5.6. HRMS: calcd for $C_{34}H_{54}NO_4Si$ 568.3822, found 568.3839 (diff = 2.9 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)butane-1,3-diol, 4a. Procedure C. Crude **4a** was chromatographed (50% EtOAc/hexanes, R_f = 0.35). Yield: 80% as a white solid. ^{1}H NMR ($CDCl_3$/MeOH) δ: 7.75 (d, 2H, J = 8.0 Hz), 7.62 (d, 2H, J = 7.5 Hz), 7.39 (t, 2H, J = 7.5 Hz), 7.31 (t, 2H, J = 8.0 Hz), 5.96 (d, 1H, J = 9.0 Hz), 4.44 (dd, 1H, J = 7.0, 10.5 Hz), 4.37 (dd, 1H, J = 7.0, 10.5 Hz), 4.21 (t, 1H, J = 7.0 Hz), 4.06 (m, 1H), 3.75 (bs, 1H), 3.65 (d, 2H, J = 5.5 Hz), 3.52 (m, 1H), 1.17 (d, 3H, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$/CD_3OD) δ: 157.2, 143.5, 141.0, 127.4, 126.7, 124.7, 119.6, 66.4, 66.3, 62.5, 56.6, 48.4, 46.9, 19.3. HRMS: calcd for $C_{19}H_{22}NO_4$ 328.1549, found 328.1552 (diff = 1.0 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-nonane-1,3-diol, 4b. Procedure C. Crude **4b** was chromatographed (50% EtOAc/hexanes, R_f = 0.35). Yield: 92% as a light yellow oil. IR (cm^{-1}): 3438.0, 2931.7, 1641.17, 1233.1, 1036.0. ^{1}H NMR ($CDCl_3$) δ: 7.77 (d, 2H, J = 7.5 Hz), 7.60 (d, 2H, J = 7.5 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.31 (t, 2H, J = 7.5 Hz), 5.48 (d, 1H, J = 8.0 Hz), 4.43 (m, 2H), 4.22 (t, 1H, J = 7.0 Hz), 3.93 (t, 1H, J = 6.5 Hz), 3.81 (m, 2H), 3.64 (t, 1H, J = 6.5 Hz), 1.48 (m, 2H), 1.28−1.20 (m, 8H), 0.92 (dd, 1H, J = 7.0, 9.5 Hz), 0.87 (t, 3H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 156.2, 143.8, 141.3, 127.6, 127.0, 124.9, 119.9, 72.5, 66.7, 64.9, 54.8, 47.2, 34.1, 31.7, 29.1, 25.5, 22.5, 22.1, 13.9. HRMS: calcd for $C_{24}H_{32}NO_4$ 398.2331, found 398.2325 (diff = 1.6 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)tridecane-1,3-diol, 4c. Procedure C. Crude **4c** was chromatographed (50% EtOAc/hexanes, R_f = 0.40). Yield: 78% as a white solid. IR (cm^{-1}): 3345.4, 3061.4, 2919.3, 2845.2, 1690.5, 1536.1, 1449.7, 1252.1, 1079.2. ^{1}H NMR ($CDCl_3$) δ: 7.76 (d, 2H, J = 8.0 Hz), 7.60 (d, 2H, J = 7.0 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.31 (t, 2H, J = 7.5 Hz), 5.50 (d, 1H, J = 8.0 Hz), 4.43 (dd, 2H, J = 7.0, 15.0 Hz), 4.22 (t, 1H, J = 7.0 Hz), 3.92 (t, 1H, J = 6.5 Hz), 3.81 (bs, 2H), 3.64 (bs, 1H), 1.48 (m, 2H), 1.28−1.20 (m, 16H), 0.88 (t, 3H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 156.8, 143.8, 141.3, 127.6, 127.0, 125.0, 119.9, 72.8, 66.7, 65.2, 54.6, 47.2, 34.1, 31.8, 29.5, 29.5, 29.5, 29.5, 29.3, 25.5, 22.6, 14.0. HRMS: calcd for $C_{28}H_{40}NO_4$ 454.2957, found 454.2957 (diff = 0.1 ppm).

Alternate Procedure for (2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)tridecane-1,3-diol, 4c. Compound **2c** (161 mg, 0.3163 mmol) was dissolved in 2 M HCl (3 mL) and THF (3 mL) and stirred at rt for 2 h. Upon completion, as judged by TLC, the crude reaction mixture was made basic (pH ≈ 8.5) with solid $NaHCO_3$. Fmoc-Cl (108 mg, 0.4174 mmol, 1.3 equiv in 1 mL dioxane) was then added via syringe to the stirring mixture over 30 min at rt and allowed to react overnight. The mixture was diluted with 50 mL of EtOAc and washed 3× with saturated $NaHCO_3$ and 1× with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. Crude **4c** was chromatographed (50% EtOAc/hexanes, R_f = 0.40). Yield: 110.1 mg (77% over three transformations, as a light yellow oil).

(2*S*,3*R*)-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-hydroxybutanoic Acid, 5a. Procedure D. Total reaction time was 12 h. Crude **5a** was chromatographed (gradient: 100% EtOAc, followed by EtOAc with 0.5% HOAc, R_f = 0.60). Yield: 96% as a white solid. IR (cm^{-1}): 3376.3, 2944.0, 1752.3, 1517.6, 1369.4, 1221.2, 1042.2. ^{1}H NMR δ: 7.77 (d, 2H, J = 7.0 Hz), 7.61 (dd, 2H, J = 7.5, 11.5 Hz), 7.33 (t, 2H, J = 7.5), 7.26 (t, 2H, J = 7.5 Hz), 4.32 (1H, d, J = 7.5 Hz), 4.30 (2H, m), 4.17 (1H, m), 4.15 (1H, t, J = 7.5 Hz), 1.19 (3H, d, J = 6.5 Hz). ^{13}C NMR (MeOH) δ: 174.5, 158.8, 145.0, 142.4, 128.7, 128.0, 126.1, 120.8, 68.5, 68.0, 61.0, 48.2, 20.3. HRMS: calcd for $C_{19}H_{20}NO_5$ 342.1341, found 342.1352 (diff = 3.1 ppm).

(2*S*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-hydroxynonanoic acid, 5b. Procedure D. Total reaction time 24 h. Crude **5b** was chromatographed (gradient: 100% EtOAc, followed by EtOAc with 0.5% HOAc, R_f = 0.65). Yield: 94% as a yellow oil. IR (cm^{-1}): 3444.2, 2931.7, 2061.0, 1690.5, 1641.1, 1517.6, 1227.4, 1054.5. ^{1}H NMR ($CDCl_3$) δ: 7.73 (d, 2H, J = 7.5 Hz), 7.58 (t, 2H, J = 8.5 Hz), 7.37 (m, 2H), 7.27 (t, 2H, J = 7.5 Hz), 5.95 (1H, d, J = 8.5 Hz), 4.42 (1H, d, J = 8.5 Hz), 4.36 (2H, d, J = 7.5 Hz), 4.23 (1H, t, J = 6.5 Hz), 4.19 (1H, t, J = 7.5 Hz), 1.52 (2H, m), 1.26 (10H, m), 0.85 (3H, t, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 175.0, 157.8, 143.6, 141.2, 128.2, 127.5, 125.0, 120.2, 71.7, 67.4, 57.8, 46.9, 33.2, 31.5, 29.0, 25.4, 22.3, 13.9. HRMS: calcd for $C_{24}H_{30}NO_5$ 412.2124, found 412.2127 (diff = 0.8 ppm).

(2*S*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-hydroxytridecanoic Acid, 5c. Procedure D. Total reaction time was 24 h. Crude **5c** was chromatographed (gradient: 100% EtOAc, followed by EtOAc with 0.5% HOAc, R_f = 0.70). Yield: 66% as a yellow oil. IR (cm^{-1}): 3357.8, 3607.5, 2925.5, 2851.4, 1721.4, 1530.0, 1449.7, 1252.1, 1085.4. ^{1}H NMR ($CDCl_3$/MeOH) δ: 7.75 (d, 2H, J = 8.0 Hz), 7.63 (t, 2H, J = 8.5 Hz), 7.36 (t, 2H, J = 7.5 Hz), 7.28 (t, 2H, J = 7.5 Hz), 6.53 (d, 1H, J = 9.5 Hz), 4.39 (dd, 1H, J = 7.5, 11.0 Hz), 4.34 (dd, 1H, J = 7.0, 11.0 Hz), 4.27 (bs, 1H), 4.22 (t, 1H, J = 7.0 Hz), 4.11 (t, 1H, J = 6.5), 1.49 (t 2H, J = 8.0), 1.28−1.20 (m 16H), 0.85 (t, 3H, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$/MeOH) δ: 173.5, 157.3, 143.2, 140.5, 127.0, 126.2, 124.2, 119.2, 70.6, 66.6, 57.7, 47.2, 33.2, 31.1, 28.7, 28.7, 28.7, 28.7, 24.8, 21.8, 12.8. HRMS: calcd for $C_{28}H_{38}NO_5$ 468.2750, found 468.2745 (error = −1.0 ppm).

(2*R*,3*R*)-Carbonic Acid Benzyl Ester 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-hydroxytridecyl Ester, 6c. Diol **4c** (930.0 mg, 2.052 mmol) and DMAP (36.1 mg, 14.4 mol %) were placed in a flame-dried flask. CH_2Cl_2 (25 mL) was added, and the resulting suspension was chilled to −78 °C. ^{i}Pr$_2$NEt (700 μL, 1.96 equiv) and benzylchloroformate (300 μL, 1.02 equiv) were then added sequentially to the stirring suspension. The mixture was slowly allowed to warm to rt and reacted for a total of 48 h. The product was diluted with 50 mL of CH_2Cl_2 and washed 1× with dilute HCl (pH ∼3), 3× with saturated $NaHCO_3$, and 1× with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. Crude **4c** was chromatographed (30% EtOAc/hexanes, R_f = 0.45). Yield: 1.09 g, 96% as a white solid. IR (cm^{-1}): 3376.3, 2944.0, 1752.3, 1517.6, 1369.4, 1221.2, 1042.2. ^{1}H NMR ($CDCl_3$) δ: 7.75 (d, 2H, J = 7.5 Hz), 7.57 (d, 2H, J = 7.5, 11.5 Hz), 7.35 (m, 6H), 7.29 (t, 2H, J = 7.5 Hz), 5.19 (d, 1H, J = 9.0 Hz), 5.15 (s, 2H), 4.40 (2H, d, J = 6.0 Hz), 4.29 (1H, dd, J = 11.5, 7.0 Hz), 4.21 (1H, dd, J = 11.5, 7.0 Hz), 4.20 (1H, t, J = 7.5 Hz), 3.87 (1H, d, J = 6.5 Hz), 3.74 (1H, bs), 1.42 (4H, m), 1.24 (14H, m), 0.87 (3H, t, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 156.4, 155.3, 143.8, 141.3, 134.9, 128.6, 128.3, 127.6, 127.0, 125.0, 119.9, 70.0, 69.8, 67.1, 66.8, 53.1, 47.2, 33.7, 31.8, 29.5, 29.5, 29.4, 29.3, 25.6, 22.6, 14.0.

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-1-*O*-(*tert*-butyldimethylsilyl)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)butane-1,3-diol, 7a. In a flame-dried flask, the Fmoc acceptor **3a** (80.1 mg, 0.1813 mmol), acetobromoglucose (120.0 mg, 0.2919 mmol, 1.61 equiv), and powdered 3 Å molecular sieves (200 mg) were dissolved in CH_2Cl_2 and the mixture chilled to 0 °C. A mixture of $Hg(CN)_2$ (60.0 mg, 0.2375 mmol, 1.30 equiv) and $HgBr_2$ (81.1 mg, 0.2250 mmol, 1.24 equiv) was added portionwise over 45 min by solid-addition funnel to the stirring suspension. The suspension was then allowed to warm to rt and stirred for a total of 40 h. After being quenched with Et_3N (0.2 mL), the solution was diluted with 50 mL of CH_2Cl_2 and filtered through Celite. The mixture was then washed 1× with saturated aqueous Na_2SO_4, 1× with saturated aqueous $NaHCO_3$, and 1×

with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Crude **7a** was chromatographed (35% EtOAc/hexanes, R_f = 0.40). Yield: 101 mg, 72%, as a yellow oil. IR (cm^{-1}): 3067.5, 2950.2, 1752.3, 1511.4, 1369.4, 1221.2, 1042.2. ^1H NMR ($CDCl_3$) δ: 7.73 (d, 2H, J = 8.0 Hz), 7.60 (dd, 2H, J = 7.5, 4.5 Hz), 7.37 (t, 2H, J = 7.5 Hz), 7.29 (m, 2H), 5.21 (t, 1H, J = 9.5 Hz), 5.06 (t, 1H, J = 9.5 Hz), 5.03 (d, 2H, J = 8.0 Hz), 4.94 (t, 1H, J = 8.5 Hz), 4.52 (d, 1H, J = 8.0 Hz), 4.35 (t, 1H, J = 6.5 Hz), 4.20 (m, 1H), 4.13 (dd, 1H, J = 2.0, 6.0 Hz), 4.07 (dd, 1H, J = 2.0, 12.5 Hz), 3.64 (m, 2H), 3.63 (t, 1H, J = 8.0 Hz), 3.57 (dd, 1H, J = 4.0, 9.0 Hz), 2.02, 2.00, 2.00, 1.99 (s, 12H), 1.14 (d, 3H, J = 6.5 Hz), 0.85 (s, 9H), 0.03, 0.02 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 170.1, 170.0, 169.4, 169.3, 156.4, 143.9, 141.2, 127.6, 127.0, 125.1, 119.9, 98.3, 72.4, 72.0, 71.8, 71.4, 68.3, 66.6, 61.8, 56.2, 47.2, 25.7, 20.6, 20.6, 20.5, 20.5, 18.1, 16.3, −5.9. HRMS: calcd for $C_{39}H_{54}NO_{13}$-Si 772.3364, found 772.3370 (error = 0.7 ppm).

(2*R*,3*R*)-Carbonic Acid Benzyl Ester 2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)tridecyl Ester, 7c. To a flame-dried flask were added acceptor **6c** (31.3 mg, 0.0576 mmol) and tetra-*O*-acetyl-glucose α-trichloroacetimidate (69.1 mg, 2.44 equiv), and the mixture was azeotroped 2× with $PhCH_3$. Molecular sieves (4 Å, ∼100 mg) were added to the mixture before it was dissolved in CH_2-Cl_2 (6 mL) and chilled to 0 °C. TMSOTf (23 μL, 2.20 equiv) was then added to the stirring solution dropwise over 10 min. The mixture was stirred and allowed to warm to rt overnight. The reaction was filtered through Celite, washed three times with saturated aqueous $NaHCO_3$, dried with $MgSO_4$, filtered again, and concentrated in vacuo. The crude was chromatographed (25% EtOAc/hexanes, R_f = 0.35). Yield: 27.7 mg (55%, as brittle white foam). ^1H NMR ($CDCl_3$/CD_3OD) δ: 7.77 (d, 2H, J = 7.5 Hz), 7.62 (t, 2H, J = 6.0 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.33 (m, 8H), 5.97 (d, 1H, J = 9.0 Hz), 5.23 (t, 1H, J = 9.5 Hz), 5.13 (d, 2H, J = 8.0 Hz), 5.06 (t, 1H, J = 10.0 Hz), 4.97 (t, 1H, J = 9.5 Hz), 4.56 (d, 1H, J = 8.0 Hz), 4.37 (t, 2H, J = 6.0 Hz), 4.29 (dd, 1H, J = 7.0, 10.0 Hz), 4.22 (t, 1H, J = 7.0 Hz), 4.16 (dd, 1H, J = 7.0, 12.0 Hz), 4.16 (m, 1H), 4.10 (dd, 1H, J = 2.5, 12.0 Hz), 4.05 (m, 1H,), 3.78 (m, 1H,), 3.72 (m, 1H), 2.08, 2.05, 2.04, 2.03 (s, 12H), 1.57 (m, 2H), 1.25 (m, 16H, J = 6.4 Hz), 0.87 (t, 3H, J = 7.5 Hz), ^{13}C NMR ($CDCl_3$/CD_3OD) δ: 171.5, 170.8, 170.2, 170.1, 157.2, 144.1, 141.5, 128.8, 127.9, 125.3, 120.1, 100.5, 78.8, 73.2, 73.0, 72.0, 71.8, 70.2, 70.0, 68.7, 62.1, 47.4, 32.1, 32.0, 29.5, 29.3, 29.1, 25.8, 23.5, 20.4, 20.4, 14.9.

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)butane-1,3-diol, **8a**. To a stirring solution of (1.56 g, 2.021 mmol, in 20 mL of CH_2Cl_2) was added by syringe freshly distilled BF_3·OEt_2 (1.53 mL, 12.129 mmol, 6.0 equiv) in one portion and the mixture stirred at rt for 2 h. The reaction was then chilled to 0 °C before 3 mL of saturated aqueous $NaHCO_3$ was added to quench the reaction. The mixture was then washed three times with saturated aqueous $NaHCO_3$, dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude was chromatographed (66% EtOAc/hexanes, R_f = 0.35). Yield: 870 mg (66%, as brittle white foam). IR (cm^{-1}): 3342.2, 2950.2, 1752.3, 1511.4, 1375.6, 1221.2, 1036.0. ^1H NMR ($CDCl_3$) δ: 7.71 (d, 2H, J = 7.5 Hz), 7.56 (d, 2H, J = 7.0 Hz), 7.35 (t, 2H, J = 7.5 Hz), 7.27 (m, 2H), 5.19 (t, 1H, J = 9.5 Hz), 5.08 (d, 2, J = 9.0 Hz), 4.99 (t, 1H, J = 9.5 Hz), 4.91 (t, 1H, J = 9.0 Hz), 4.48 (d, 1H, J = 8.0 Hz), 4.38 (t, 1H, J = 8.5 Hz), 4.32 (t 1H, J = 7.0 Hz), 4.22 (d, 1H, J = 11.5 Hz), 4.18 (t, 1H, J = 7.0 Hz), 4.07 (m, 1H), 3.67 (m, 2H), 3.59 (t, 1H, J = 5.7 Hz), 2.03, 1.99, 1.99, 1.97 (s, 12H), 1.12 (d, J = 6.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 170.6, 170.1, 169.3, 169.3, 156.6, 143.8, 141.2, 127.6, 127.0, 125.1, 119.9, 99.3, 77.3, 74.2, 72.4, 71.9, 71.1, 68.5, 66.7, 62.1, 61.8, 55.7, 47.2, 20.5, 20.5, 20.5, 20.5, 16.7. HRMS: calcd for $C_{33}H_{40}NO_{13}$ 658.2500, found 658.2502 (error = 0.4 ppm).

(2*R*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)tridecane-1,3-diol, **8c.** Benzyl carbonate **7c** (22.4 mg, 0.0256 mmol) was placed in a round-bottom flask. To this were added MeOH (5 mL), EtOAc (5 mL), aqueous HOAc (0.5 mL, pH ∼3.5), and Pt−C (24.0 mg). The reaction was purged with H_2 four times and stirred under 1 atm of H_2 until judged complete by TLC (2 h). The reaction was quenched with 20 mL of CH_2Cl_2, filtered through Celite, and washed three times with saturated aqueous $NaHCO_3$, dried with $MgSO_4$, filtered again, and concentrated in vacuo. The crude was chromatographed (54% EtOAc/hexanes, R_f = 0.45). Yield: 16.2 mg (80.6%, as a colorless oil). ^1H NMR ($CDCl_3$) δ: 7.76 (d, 2H, J = 7.5 Hz), 7.60 (m, 2H,), 7.38 (t, 2H, J = 8.0 Hz), 7.32 (q, 2H, J = 7.5 Hz), 5.23 (t, 1H, J = 9.5 Hz), 5.02 (t, 1H, J = 9.0 Hz), 4.99 (t, 1H, J = 9.0 Hz), 4.56 (d, 1H, J = 8.0 Hz), 4.38 (t, 2H, J = 7.0 Hz), 4.29 (dd, 1H, J = 7.0, 10.0 Hz), 4.23 (t, 1H, J = 7.0 Hz), 4.16 (dd, 1H, J = 7.0, 12.0 Hz), 4.05 (m, 1H,), 3.78 (d, 1H, J = 8.0 Hz), 3.73 (m, 1H, J = 9.5 Hz), 2.09, 2.05, 2.05, 2.02 (s, 12H), 1.57 (m, 2H), 1.25 (m, 16H, J = 6.5 Hz), 0.87 (t, 3H, J = 7.0 Hz). HRMS: calcd for $C_{42}H_{58}NO_{13}$ 784.3908, found 784.3912 (error = 0.5 ppm).

(2*S*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)butanoic Acid, **9a.** Protected glycoside **7a** (61.6 mg, 0.0936 mmol) was dissolved in aqueous MeCN (6 mL, 50%) before $NaIO_4$ (200 mg, 0.9350 mmol, 9.98 equiv) and $RuCl_3$·H_2O (3.0 mg, 0.0144 mmol, 15 mol %) were added in one portion. The resulting mixture was stirred at rt for 4 h. Once all of the starting material had been consumed, the reaction was quenched with ^{i}PrOH (20 mL) and stirred for an additional 2 h. The mixture was then filtered through Celite, washed twice with saturated aqueous sodium sulfate, washed one time with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude was chromatographed (gradient: 100% EtOAc, followed by 100% EtOAc with 0.5% HOAc, R_f = 0.65). Yield: 48.9 mg (77%, as a white solid). IR (cm^{-1}): 3376.3, 2944.0, 1752.3, 1517.6, 1369.4, 1221.27, 1042.2. ^1H NMR δ: 7.76 (d, 2H, J = 8.0 Hz), 7.63 (t, 2H, J = 8.0 Hz), 7.39 (t, 2H, J = 7.5 Hz), 7.32 (m, 2H), 5.66 (d, 1H, J = 9.0 Hz), 5.19 (t, 1H, J = 9.5 Hz), 5.09 (t, 1H, J = 9.5 Hz), 4.95 (t, 1H, J = 8.0 Hz), 4.54 (d, 1H, J = 8.0 Hz), 4.43 (d, 1H, J = 8.0 Hz), 4.39 (m, 2H), 4.39 (m, 1H), 4.38 (dd, 1H, J = 2.0, 6.0 Hz), 4.25 (t, 1H, J = 7.5 Hz), 4.09 (dd, 1H, J = 3.5, 12.5 Hz), 3.65 (d, 1H, J = 9.5 Hz), 2.10, 2.04, 2.03, 2.01 (s, 12H), 1.23 (d, 3H, J = 6.5 Hz). ^{13}C NMR δ: 172.4, 171.7, 170.2, 169.3, 169.2, 156.7, 143.7, 141.1, 127.6, 127.0, 125.1, 119.8, 99.4, 75.8, 72.5, 71.5, 71.0, 68.3, 67.2, 61.5, 58.0, 47.0, 29.5, 20.7, 20.5, 20.5, 20.3, 17.5. HRMS: calcd for $C_{33}H_{38}NO_{14}$ 672.2292, found 672.2288 (error = −0.7 ppm).

(2*S*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)nonanoic acid, **9b.** Threonine analogue **5b** (63.3 mg, 0.1540 mmol) and β-glucose penta-acetate (71.0 mg, 0.1820 mmol, 1.18 equiv) were placed in a 50 mL round-bottom flask and azeotroped 2× with toluene. The mixture was dissolved in CH_2Cl_2 and treated with BF_3·OEt_2 (60 μL, 0.4739 mmol, 3.07 equiv). The solution was then stirred at rt for 36 h. After being judged complete by TLC, the reaction mixture was diluted with 15 mL of CH_2Cl_2 and quenched with 1 mL of sat. $NaHCO_3$. The mixture was then washed 1× with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude was chromatographed (5% MeOH/95% CH_2Cl_2 with 0.4% HOAc, R_f = 0.35). Yield: 40.2 mg (36%, as a yellow oil). ^1H NMR ($CDCl_3$/CD_3OD/toluene-d_8) δ: 7.75 (d, 2H, J = 7.5 Hz), 7.62 (t, 2H, J = 8.0 Hz), 7.39 (t, 2H, J = 7.5 Hz), 7.31 (t, 2H, J = 7.5 Hz), 5.60 (d, 1H, J = 9.0 Hz), 5.18 (t, 1H, J = 9.5 Hz) 5.10 (t, 1H, J = 10.0 Hz), 4.99 (t, 1H, J = 9.0 Hz), 4.56 (d, 1H, J = 8.0 Hz), 4.47 (m, 1H,), 4.38 (m, 2H), 4.25 (m, 1H), 4.20 (m, 1H), 4.09 (m, 2H), 3.62 (d, 1H, J = 10.5 Hz), 2.10, 2.03, 2.02, 2.00 (s, 12H), 1.58, 1.50 (m, 2H), 1.25 (m, 8H), 0.87 (t, 3H, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$/MeOH/$PhCH_3$) δ: 172.0, 171.8, 170.2, 169.3, 169.1, 156.7, 143.3, 141.2, 128.8, 128.1, 125.2, 119.9, 100.9, 80.7, 72.7, 71.7, 71.2, 68.3, 67.6, 67.4, 61.4, 56.8, 47.2, 29.6, 25.3, 22.5, 21.4, 20.9, 13.9. HRMS: calcd for $C_{38}H_{47}NO_{14}Na$ 764.2889, found 764.2909 (error = 2.6 ppm).

(2*S*,3*R*)-2-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-3-*O*-(2,3,4,6-tetra-*O*-acetylglucosyl)tridecanoic Acid, **9c.** Glycoside **8a** (17.2 mg, 0.02193 mmol) was azeotroped with toluene ×2. One milliliter of CH_2Cl_2 was added to a round-bottom flask and chilled to −40 °C. Oxayl chloride (15 μL, 0.1713 mmol, 7.8 equiv) and DMSO (15 μL, 0.2111 mmol, 9.6 equiv) were sequentially added in an inert atmosphere, and the mixture was stirred for 2 min. Compound **8a** was then dissolved in 1 mL of CH_2Cl_2 and added via syringe. The mixture was stirred at −40 °C for 30 min prior to the addition of Et_3N (51 μL, 0.3635 mmol, 16.5 equiv). The reaction was allowed to warm to rt and stirred for 1 h until judged complete by TLC. The completed reaction was then diluted with 10 mL of CH_2Cl_2, washed with saturated aqueous NH_4Cl ×4, and concentrated in vacuo. The residue was redissolved in ^{t}BuOH (5 mL) and EtOAc (5 mL), charged with $NaClO_2$ (46 mg, 0.3376 mmol, 15.0 equiv) and KH_2PO_4 (55.2 mg,

0.4029 mmol, 18.3 equiv), and stirred for 30 min at rt. The crude was chromatographed (5% MeOH/ 95% CH_2Cl_2 with 0.2% HOAc, $R_f = 0.35$). Yield: 11.3 mg (65%, as a yellow oil). ^1H NMR ($CDCl_3$/MeOH) δ: 7.74 (d, 2H, $J = 8.0$ Hz), 7.62 (t, 2H, $J = 6.5$ Hz), 7.37 (t, 2H, $J = 7.5$ Hz), 7.29 (t, 2H, $J = 7.5$ Hz), 5.88 (d, 1H, $J = 9.5$ Hz), 5.16 (t, 1H, $J = 9.5$ Hz), 5.09 (t, 1H, $J = 10.0$ Hz), 4.97 (t, 1H, $J = 8.5$ Hz), 4.56 (d, 1H, $J = 8.0$ Hz), 4.37 (t, 1H, $J = 7.5$ Hz,), 4.32 (d, 1H, $J = 4.5$ Hz), 4.26 (m, 1H), 4.24 (m, 1H), 4.20 (m, 2H), 3.64 (d, 1H, $J = 9.5$ Hz), 2.05, 2.03, 2.00, 1.99 (s, 12H), 1.58, (m, 2H), 1.25 (m, 16H, $J = 6.5$ Hz), 0.85 (t, 3H, $J = 8.0$ Hz), HRMS: calcd for $C_{42}H_{55}NO_{14}Na$ 820.3515, found 820.3478 (error = 4.5 ppm).

Acknowledgment. We thank the A.R.C.S. Foundation (Phoenix Chapter − Spetzler Fellowship), the U.S. Army (DAMD17-99-1-9539), the National Science Foundation (CHE-9526909 and CHE-920112), and NIDA (DA-06284) for partial funding.

Supporting Information Available: NMR spectra for obtained compunds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO015844V