JOC*Note*

# Synthesis of a *C*-Glycoside Analogue of *β*-D-Galactosylthreonine

Tomas Gustafsson, Maria Saxin, and Jan Kihlberg*

*Organic Chemistry, Department of Chemistry, Umeå University, SE-901 87 Umeå, Sweden*

*jan.kihlberg@chem.umu.se*

*Received November 24, 2002*

**Abstract:** A *C*-linked analogue of *β*-D-galactosylthreonine has been prepared from 2,3,4,6-tetra-*O*-benzyl-D-galactopyranolactone (**1**) in 14 steps. Three stereogenic centers were created during the synthesis, with the anomeric center of the *C*-glycoside being generated first by addition of a Grignard reagent to **1** and subsequent reduction of the intermediate hemiacetal with triethylsilane. The two stereogenic centers in the threonine moiety were both established by alkylation of Evans' chiral *N*-acyloxazolidinone enolates.

Most proteins are post-translationally modified by glycosylation, with *O*-glycosylation being found on serine, threonine, hydroxylysine, and tyrosine while *N*-glycosylation occurs on asparagine.[1,2] Glycosylation influences properties of proteins such as solubility, stability toward proteases, as well as conformation and folding. It can also affect the biological functions of proteins in events of molecular recognition, e.g., cell-to-cell communication and adhesion of bacteria or viruses to cell-surface proteins. In recent years, there has been an increasing interest in the synthesis of carbon-linked analogues of glycosylated amino acids, in which a methylene group has replaced the *O*- or *N*-glycosidic linkage.[3] Such *C*-glycosides mimic the native glycosides in many ways such as conformation and size, but differ in other aspects such as electrostatic and chemical properties.[4] In contrast to *O*-glycosides, *C*-glycosides are not degraded under acidic conditions or by glycosidases, nor do they undergo base-catalyzed *β*-elimination, which constitutes a problem for glycosides of serine and threonine. This makes *C*-glycosides interesting in efforts to modulate biological properties of glycopeptides and glycoproteins and suggests applications in drug discovery.

Several syntheses of *C*-linked analogues of glycosylated amino acids found in Nature have been reported, including different *C*-glycosides of serine[3,5−8] and asparagine.[3,9−11] Previous studies have thus focused on naturally occurring glycosylated amino acids where the amino acid moiety contains only one stereogenic center.[12] However, glycoproteins also carry a variety of saccharides linked to amino acids which have two stereogenic centers. For instance, in mucins which are found on epithelial cells, threonine carries α-D-*N*-acetylgalactosamine residues to which larger saccharide structures are often attached.[13] Nuclear pore proteins, transcriptional factors, and cytoskeletal proteins have *β*-D-*N*-acetylglucosamine moieties attached to threonine.[14] Hydroxylysine, found in the collagens, is often glycosylated with *β*-D-galactosyl moieties.[15] As part of a project directed toward *C*-glycosidic analogues of these two amino acids we now report the synthesis of a *C*-linked analogue of *β*-D-galactosylated threonine (cf. **13**, Scheme 2). Galactosylated threonine residues are found in the cuticle collagen of the deep-sea hydrothermal vent worm *Riftia pachyptila*, and were recently demonstrated to contribute to the relatively high thermal stability of this protein.[16]

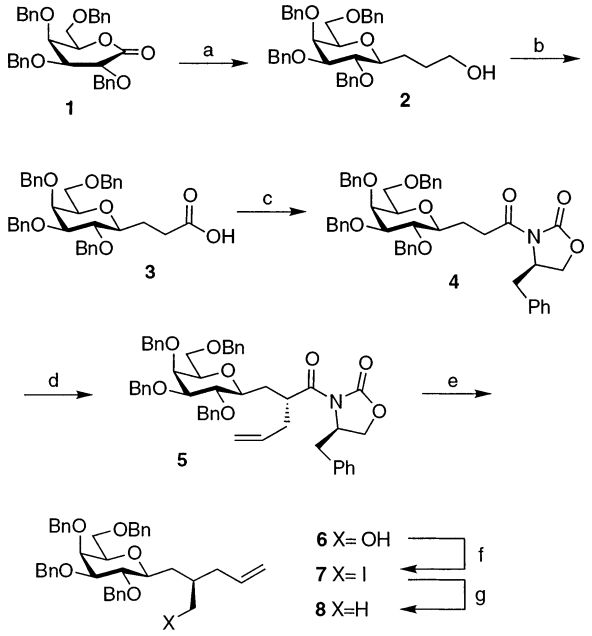
Synthesis of a *C*-linked analogue of *β*-D-galactosylated threonine requires stereocontrol at three centers, namely, the anomeric carbon of the *C*-glycoside and the two stereogenic centers of the threonine moiety. In the present work the configuration at the anomeric center was established first by synthesis of the *β*-linked *C*-glycoside **2** (Scheme 1). De novo synthesis of the threonine part was then carried out by building on the propanol moiety of **2**. The two key steps, in which the threonine stereogenic centers were established, both relied on alkylation of enolates derived from *N*-acyloxazolidinones, as developed by Evans.[17]

The synthetic route started by addition of homoallylmagnesium bromide to lactone **1**,[18] followed by reduction of the intermediate hemiacetal with triethylsilane and boron trifluoride etherate (Scheme 1). Ozonolyzis of the resulting alkene and decomposition of the ozonide with $NaBH_4$ gave the *β*-linked *C*-glycoside **2**[19] (88% from **1**), which provided carboxylic acid **3** in excellent yield (99%) upon Jones oxidation of the propanol moiety. Carboximide **4** was then prepared (70% yield) by conversion of **3** into a mixed pivaloyl anhydride, which was immediately reacted with Evans chiral auxiliary, (*R*)-4-benzyloxazolidinone. Alkylation of **4** established the stereochemistry

(1) Lis, H.; Sharon, N. *Eur. J. Biochem.* **1993**, *218*, 1−27.
(2) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683−720.
(3) Dondoni, A.; Marra, A. *Chem. Rev.* **2000**, *100*, 4395−4421.
(4) Levy, D. E.; Tang, C. *The chemistry of C-glycosides*; Elsevier Science Ltd: Oxford, 1995; Vol. 13.
(5) Bertozzi, C. R.; Cook, D. G.; Kobertz, W. R.; Gonzalez-Scarano, F.; Bednarski, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 10639−10641.
(6) Lay, L.; Meldal, M.; Nicotra, F.; Panza, L.; Russo, G. *Chem. Commun.* **1997**, 1469−1470.
(7) Urban, D.; Skrydstrup, T.; Beau, J.-M. *Chem. Commun.* **1998**, 955−956.
(8) Dondoni, A.; Mariotti, G.; Marra, A.; Massi, A. *Synthesis* **2001**, 2129−2137.
(9) Campbell, A. D.; Paterson, D. E.; Raynham, T. M.; Taylor, R. J. K. *Chem. Commun.* **1999**, 1599−1600.
(10) Dondoni, A.; Marra, A.; Massi, A. *J. Org. Chem.* **1999**, *64*, 933−944.
(11) Dondoni, A.; Mariotti, G.; Marra, A. *Tetrahedron Lett.* **2000**, *41*, 3483−3487.
(12) *C*-Linked analogues of glycosylated amino acids, where the amino acid part contains two stereogenic centers, but which are not found in nature have been prepared. Cf. Westermann, B.; Walter, A.; Flörke, U.; Altenbach, H.-J. *Org. Lett.* **2001**, *3*, 1375−1378.
(13) Carraway, K. L.; Hull, S. R. *Glycobiol.* **1991**, *1*, 131−138.
(14) Zachara, N. E.; Hart, G. W. *Chem. Rev.* **2002**, *102*, 431−438.
(15) Kivirikko, K. I.; Myllylä, R. In *Collagen in health and disease*; Weiss, J. B., Jayson, M. I. V., Eds.; Churchill Livingstone: Edinburgh, 1982; pp 101−120.
(16) Bann, J. G.; Peyton, D. H.; Bächinger, H. P. *FEBS Lett.* **2000**, *473*, 237−240.
(17) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737−1739.
(18) Dondoni, A.; Scherrmann, M.-C. *J. Org. Chem.* **1994**, *59*, 6404−6412.
(19) Wellner, E.; Gustafsson, T.; Bäcklund, J.; Holmdahl, R.; Kihlberg, J. *ChemBioChem* **2000**, *1*, 272−280.

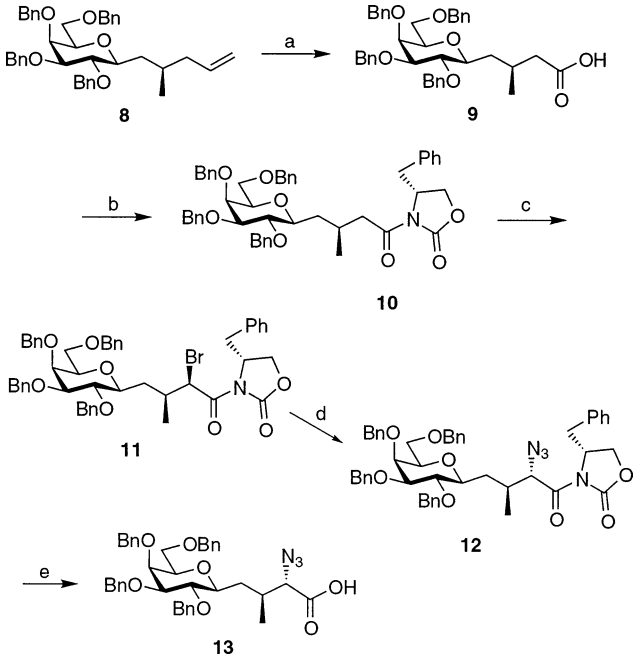
10.1021/jo026758d CCC: $25.00 
Published on Web 02/25/2003

**SCHEME 1**[a]



[a] Reagents and conditions: (a) three steps, see ref 19 (88%); (b) $CrO_3/H_2SO_4$, acetone, rt (99%); (c) (i) $Et_3N$, $Me_3CCOCl$, THF, −78 °C; (ii) (*R*)-4-benzyloxazolidin-2-one, BuLi, THF, −78 °C (70%); (d) LDA, allyl iodide, THF, −40 to −20 °C (60%); (e) $LiEt_3BH$, THF, rt (94%); (f) $I_2$, $PPh_3$, imidazole, toluene, rt (90%); (g) $LiEt_3BH$, THF, rt (96%).

**SCHEME 2**[a]



[a] Reagents and conditions: (a) (i) $O_3$, $CH_2Cl_2$/MeOH, −78 °C, (ii) $NaBH_4$, $CH_2Cl_2$/MeOH, −78 °C to rt, (iii) $CrO_3/H_2SO_4$, acetone, rt (93%); (b) (i) $Et_3N$, $Me_3CCOCl$, THF, −78 °C, (ii) (*R*)-4-benzyloxazolidin-2-one, BuLi, THF, −78 °C (79%); (c) (i) DIPEA, $Bu_2BOTf$, $CH_2Cl_2$, -78 °C to rt, (ii) NBS, $CH_2Cl_2$, −78 °C (57%); (d) tetramethylguanidinium azide, $CH_2Cl_2$, rt (97%); (e) LiOH, THF/$H_2O$, rt (97%).

at the $\beta$-carbon of the threonine moiety, and was accomplished by treatment with LDA and either of allyl bromide or allyl iodide. This gave **5** in 60% yield and excellent diastereoselectivety (>99:1), both of which were unaffected by the choice of electrophile. However, the alkylation proceeded considerably faster with the more reactive allyl iodide. The modest yield in this step is most likely explained by the observation that carboximide **4** decomposed during alkylation, even at −78 °C. Attempted reduction of oxazolidinone **5** with $LiAlH_4$ was surprisingly sluggish and gave, apart from **6**, the intermediate aldehyde which was almost inert, even to an excess of $LiAlH_4$. This was unexpected since the allylated product obtained from the (*S*)-benzyloxazolidinone analogue of **4** was easily reduced with $LiAlH_4$. Reduction of **5** was instead performed with $LiEt_3BH$, which provided a clean reduction to give alcohol **6** (94%). Deoxygenation of this alcohol, and the corresponding iodide **7**, was attempted with several methods. Tosylation of **6** and reduction with either $LiAlH_4$ or $LiEt_3BH$[20] was unsuccessful, as was reduction of iodide **7** using radical conditions ($Bu_3SnH$, AIBN) or hydrides ($LiAlH_4$, or $NaBH_4$ under phase-transfer conditions[21]). However, $LiEt_3BH$ was successfully employed to convert iodide **7** to the methyl analogue **8** in near quantitative yield.

In compound **8**, the desired stereochemistry has been established for the *C*-glycosidic linkage, and for the methyl group which corresponds to the $\beta$-carbon of the threonine moiety. To complete the synthesis of the target *C*-linked analogue of $\beta$-D-galactosyl threonine it remains to convert the alkene part of **8** into an L-amino acid moiety. This was accomplished by first performing an oxidative cleavage of the alkene moiety using ozone, followed by reduction with $NaBH_4$ and Jones oxidation of the resulting alcohol, to provide carboxylic acid **9** in 93% yield (Scheme 2). Compound **9** was then transformed into oxazolidinone **10** (79%) using the same condidtions as for **4**. Direct azidation of **10** to give **12** (enolization by KHMDS, then treatment with trisyl azide and acetic acid) proved to be difficult and a two-step procedure was therefore used instead. First a boron enolate was prepared from **10** and employed in an electrophilic bromination with *N*-bromosuccinimide to give **11**. Then nucleophilic displacement of the bromine atom in **11** with tetramethylguanidinium azide[22] gave azido oxazolidinone **12** in 54% yield over these two steps. The stereoselectivity in the bromination step was somewhat disappointing since a 93:7 mixture of the two diastereomers was formed. However, the minor diastereomer could easily be removed by silica gel flash chromatography, either at the bromo (**11**) or the azido stage (**12**). Surprisingly, both **11** and **12** decomposed somewhat on the column during purification (silica gel or alumina), but a higher yield was obtained if **11** was purified before conversion into **12**. Finally, the synthesis was completed by hydrolysis of oxazolidinone **12** using aqueous LiOH which provided azido acid **13** in 97% yield. Building block **13** is ready for use in solid-phase synthesis since it is known that α-azido acids can be activated and coupled to peptides in excellent yields without racemization.[23] The azido

(20) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1976**, *41*, 3064−3066.

(21) Rolla, F. *J. Org. Chem.* **1981**, *46*, 3909−3911.

(22) Papa, A. J. *J. Org. Chem.* **1966**, *31*, 1426−1430.

group can then be reduced on the solid support,[23,24] followed by further elongation of the peptide chain and deprotection of the benzyl ethers during or after cleavage of the *C*-linked glycopeptide from the solid phase.

Epimerization could potentially have occurred at C-α of the threonine moiety, either during nucleophilic substitution of **11** or during base-catalyzed hydrolysis of **12** to give **13**. To investigate the stereochemical purity of **13** a mixture of **13** and *epi*-**13** (i.e., **13** that had been epimerized at the C-α position) was synthesized. This was done by treatment of bromide **11** with tetrabutylammonium bromide in refluxing THF to form a ∼1:1 mixture of **11** and *epi*-**11**, as determined by $^1$H NMR spectroscopy. This mixture was treated with tetramethylguanidinium azide, and hydrolysis of the oxazolidinone, as described for **12**, then provided a ∼1:1 mixture of **13** and *epi*-**13**. Analytical reversed-phase HPLC displayed two peaks for this mixture, one of which had the same retention time as that of **13**. In addition $^1$H NMR spectroscopy revealed two sets of signals for the mixture, one of which matched the spectrum of **13**. By using HPLC and $^1$H NMR spectroscopy it could thus be conclusively determined that epimerization had not occurred during the azide displacement of **11**, or in the hydrolysis to give **13**.

In conclusion, a synthesis of the *C*-linked analogue of *β*-D-galactosyl threonine, **13**, has been accomplished from **1** in 12% total yield over fourteen steps. The synthesis involved creation of three stereogenic centers, with the anomeric center of the *C*-glycoside being generated first. The configuration of the two stereogenic centers in the threonine moiety of **13** was established in key steps relying on alkylation of enolates derived from *N*-acyloxazolidinones. We anticipate that building blocks such as **13** will be useful in studies of the unexpectedly high thermal stability of cuticle collagen from the deep-sea hydrothermal vent worm *Riftia pachyptila*.

## Experimental Section

**General Procedures**. All reactions were carried out under an inert atmosphere with dry solvents under anhydrous conditions, unless otherwise stated. $CH_2Cl_2$ was distilled from calcium hydride, whereas THF and toluene were distilled from potassium benzophenone and sodium, respectively. Methanol was dried over 3 Å molecular sieves. TLC was performed on silica gel 60 $F_{254}$ (Merck) with detection by UV light and staining with a solution of ethanolic phosphomolybdic acid. Flash column chromatography (eluents given in brackets) was performed on silica gel (Matrex, 60 Å, 35−70 μm, Grace Amicon). $^1$H and $^{13}$C NMR spectra were recorded at 400 and 100 MHz, respectively, for solutions in $CDCl_3$ [residual $CHCl_3$ ($\delta_H$ 7.26 ppm) or $CDCl_3$ ($\delta_C$ 77.0 ppm), as internal standard] at 298 K. First-order chemical shifts and coupling constants were obtained from one-dimensional spectra; carbon and proton resonances were assigned from COSY and HETCOR experiments. Resonances for aromatic hydrogen and carbon atoms are not reported.

**3-(2,3,4,6-Tetra-*O*-benzyl-*β*-D-galactopyranosyl)propionic Acid (3).** Jones' reagent (aq 1 M $CrO_3$, 4.4 M $H_2SO_4$) was added to a solution of alcohol **2** (1.42 g, 2.44 mmol) dissolved in acetone (50 mL) at 0 °C. The mixture was allowed to attain rt and was then stirred for an additional 90 min. *i*-PrOH (4 mL) was added, and the solution was brought to pH 4 with $NaHCO_3$ (aq, satd). It was extracted twice with diethyl ether, and the combined organic phases were dried over $Na_2SO_4$, filtered, and concentrated. Purification by flash column chromatography (heptane/ethyl acetate 1:1) gave **3** (1.43 g, 99%) as a colorless oil: $[\alpha]_D = -6.3$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{37}H_{40}NaO_7$ 619.2672 $[M + Na]^+$, found 619.2680.

**(*R*)-4-Benzyl-3-[3-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosyl)propionyl]oxazolidin-2-one (4)**. Triethylamine (1.26 mL, 9.05 mmol) was added to a solution of carboxylic acid **3** (4.91 g, 8.23 mmol) in THF (80 mL) cooled to −78 °C. The solution was stirred for 5 min, and pivaloyl chloride (1.11 mL, 9.05 mmol) was added. After 15 min, a mixture of (*R*)-4-benzyloxazolidin-2-one (1.60 g, 9.05 mmol) and BuLi (3.62 mL, 2.5 M in hexanes, 9.05 mmol) in THF (30 mL) was transferred to this solution via cannula. The mixture was stirred for 30 min at −78 °C, and then the reaction was quenched by addition of $NH_4Cl$ (aq, satd). After extraction twice with $CH_2Cl_2$, the combined organic phases were dried over $Na_2SO_4$, filtered and concentrated. Purification by flash column chromatography (heptane/ethyl acetate 3:1) gave **4** (4.37 g, 70%) as a colorless oil: $[\alpha]_D = -27.8$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{47}H_{49}NNaO_8$ 778.3356 $[M + Na]^+$, found 778.3354.

**(*R*)-4-Benzyl-3-[2-(*R*)(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)pent-4-enoyl]oxazolidin-2-one (5)**. LDA (6.18 mL, 1.0 M in hexanes, 6.18 mmol) was added to a solution of oxazolidinone **4** (4.25 g, 5.62 mmol) in THF (50 mL) cooled to −78 °C. After 30 min, allyl iodide (1.80 mL, 19.7 mmol) was added, and the temperature was raised to −20 °C during 2 h. The solution was poured into $NH_4Cl$ (aq, satd), the phases were separated, and the organic phase was washed twice with brine. The combined aqueous phases were extracted twice with $CH_2Cl_2$, after which the combined organic phases were dried over $Na_2SO_4$, filtered, and concentrated. Purification by flash column chromatography (heptane/ethyl acetate 3:1) gave **5** (5.44 g, 62%) as an amorphous solid: $[\alpha]_D = -27.3$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{50}H_{53}NNaO_8$ 818.3669 $[M + Na]^+$, found 818.3676.

**(*R*)-2-(2,3,4,6-Tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)pent-4-en-1-ol (6).** $LiEt_3BH$ (712 μL, 1 M in THF, 0.712 mmol) was added to a solution of oxazolidinone **5** (189 mg, 0.237 mmol) in THF (1.5 mL) previously cooled to 0 °C. After 20 min, EtOH (1 mL), $H_2O$ (0.5 mL), NaOH (0.5 mL, 5 M), and $H_2O_2$ (0.3 mL, 30% aq) was added, and stirring was continued for 5 min. The mixture was poured onto NaCl (aq, satd) and was extracted three times with $CH_2Cl_2$. The combined organic phases were dried over $Na_2SO_4$, filtered, and concentrated. Purification by flash column chromatography (heptane/ethyl acetate 3:1) gave **6** (139 mg, 94%) as an amorphous solid: $[\alpha]_D = -1.7$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{40}H_{46}NaO_6$ 645.3192 $[M + Na]^+$, found 645.3200.

**(*R*)-4-(2,3,4,6-Tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)-5-iodopent-1-ene (7).** $I_2$ (1.64 g, 6.47 mmol), triphenylphosphine (2.14 g, 8.17 mmol), and imidazole (0.62 g, 9.19 mmol) were added to a solution of alcohol **6** (2.12 g, 3.40 mmol) in toluene (70 mL). After 20 min, $H_2O_2$ (1 mL, 30% aq) was added, and stirring was continued for 1 min. The resulting mixture was poured into $NaHSO_3$ (10% aq) and extracted twice with toluene. The combined organic phases were washed with $NaHCO_3$ (aq, satd.) and brine, then dried over $Na_2SO_4$, filtered, and concentrated. Flash column chromatography (heptane/ethyl acetate 4:1) gave iodide **7** (2.25 g, 90%) as a slightly yellow oil: $[\alpha]_D = -8.6$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{40}H_{45}INaO_5$ 755.2209 $[M + Na]^+$, found 755.2208.

**(*R*)-4-(2,3,4,6-Tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)pent-1-ene (8).** $LiEt_3BH$ (8.35 mL, 1 M in THF, 8.35 mmol) was added to a solution of **6** (2.04 g, 2.78 mmol) in THF (65 mL) and stirred for 20 min. Then EtOH (15 mL, 95%), $H_2O$ (7 mL), NaOH (5 mL, 5 M aq), and $H_2O_2$ (3 mL, 30% aq) were added. After being stirred for 10 min, the mixture was poured into brine and extracted twice with ethyl acetate. The combined organic phases were dried over $Na_2SO_4$, filtered, and concentrated to afford **8** (1.63 g, 96%) as a colorless oil. Alkene **6** was sufficiently pure to be used directly in the next step. A small amount of **8** was purified by flash column chromatography (heptane/ethyl

(23) Tornoe, C. W.; Davis, P.; Porreca, F.; Meldal, M. *J. Peptide Sci.* **2000**, *6*, 594−602.

(24) Brickmann, K.; Yuan, Z.; Sethson, I.; Somfai, P.; Kihlberg, J. *Chem. Eur. J.* **1999**, *5*, 2241−2253.

acetate 2:1): $[\alpha]_D = -19.2$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{39}H_{44}NaO_7$ 629.3243 $[M + Na]^+$, found 629.3241.

**(*S*)-3-(2,3,4,6-Tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)butyric Acid (9).** Alkene **8** (1.60 g, 2.64 mmol) was dissolved in $CH_2Cl_2$ (35 mL) and MeOH (30 mL), and the solution was cooled to −78 °C. $O_3$ (g) was bubbled through the solution until it turned slightly blue, and then $O_2$ (g) was passed through until the solution became colorless. $NaBH_4$ (0.30 g, 7.91 mmol) was added, and the mixture was allowed to attain rt and then stirred for an additional 30 min. The reaction was quenched by addition of HCl (5% aq), after which the mixture was poured into brine and extracted twice with $CH_2Cl_2$. The combined organic phases were dried over $Na_2SO_4$, filtered and concentrated. The residue was dissolved in acetone (40 mL), Jones' reagent (aq 1 M $CrO_3$, 4.4 M $H_2SO_4$) was added at 0 °C, and the mixture was stirred at rt for 5 min. *i*-PrOH (4 mL) was added, and the solution was brought to pH 4 with $NaHCO_3$ (aq, satd). It was then extracted three times with diethyl ether. The combined organic phases were dried over $Na_2SO_4$, filtered, and concentrated, after which the crude product was purified by flash column chromatography (heptane/ethyl acetate 2:1) to afford **9** (1.52 g, 93%) as a colorless oil: $[\alpha]_D = -5.8$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{39}H_{44}NaO_7$ 647.2985 $[M + Na]^+$, found 647.2985.

**(*R*)-4-Benzyl-3-[3-(*S*)-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)butyryl]oxazolidin-2-one (10).** Carboxylic acid **9** (1.45 g, 2.32 mmol) was reacted with (*R*)-4-benzyloxazolidin-2-one (452 mg, 2.55 mmol) as described in the preparation of **4**. After workup, purification by flash column chromatography (heptane/ethyl acetate 3:1) gave **10** (1.43 g, 79%) as an amorphous solid: $[\alpha]_D = -22.0$ (*c* 4.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{49}H_{53}NNaO_8$ 806.3669 $[M + Na]^+$, found 806.3664.

**(*R*)-4-Benzyl-3-[(2*R*,3*S*)-bromo-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)butyryl]oxazolidin-2-one (11).** Diisopropylethylamine (64 *μ*L, 0.367 mmol) and dibutylboron-triflate (337 *μ*L, 1 M in $CH_2Cl_2$, 0.337 mmol) were added to a solution of carboximide **10** (240 mg, 0.306 mmol) in $CH_2Cl_2$ (1 mL) cooled to −78 °C. After 15 min, the solution was warmed to 0 °C and stirred for an additional 1 h. The solution was cooled to −78 °C and transferred to a suspension of NBS (109 mg, 0.612 mmol) in $CH_2Cl_2$ (1 mL), which was precooled to −78 °C. After 2 h, $NaHSO_3$ (5% aq) was added, and the solution was extracted three times with ethyl acetate. The combined organic phases were washed with $NaHSO_3$ (5% aq) and brine, dried over $Na_2SO_4$, filtered, and concentrated. Purification by flash column chromatography (heptane/ethyl acetate 3:1) gave **11** (151 mg, 57%) as a slightly yellow oil: $[\alpha]_D = -29.2$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{49}H_{52}BrNNaO_8$ 884.2774 $[M + Na]^+$, found 884.2790.

**(*R*)-4-Benzyl-3-[(2*S*,3*R*)-azido-3-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)butyryl]oxazolidin-2-one (12).** A solution of bromide **11** (38 mg, 0.044 mmol) and tetramethylguanidinium azide (21 mg, 0.132 mmol) in $CH_2Cl_2$ (0.5 mL) was stirred for 24 h. Concentration followed by purification by flash column chromatography (heptane/ethyl acetate 3:1) gave azide **12** (35 mg, 97%) as an amorphous solid: $[\alpha]_D = -12.2$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{49}H_{52}N_4NaO_8$ 847.3683 $[M + Na]^+$, found 847.3695.

**(2*S*,3*S*)-Azido-3-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosylmethyl)butyric Acid (13).** LiOH (606 *μ*L, 0.10 M aq, 61 *μ*mol) was added to a solution of carboximide **12** (25.1 mg, 30 *μ*mol) in THF (1.5 mL) cooled to 0 °C. After 5 min, the solution was neutralized with Amberlite IR120, filtered and concentrated. Flash column chromatography (heptane/ethyl acetate 3:1) gave carboxylic acid **13** (19.2 mg, 97%) as an amorphous solid: $[\alpha]_D = -14.2$ (*c* 1.0, $CHCl_3$); HR-MS (FAB) calcd for $C_{39}H_{43}N_3NaO_8$ 688.2999 $[M + Na]^+$, found 688.3017.

**Acknowledgment.** We thank Dr. Magnus Johansson at the Department of Environmental Chemistry at Umeå University for performing MS analysis. This work was funded by grants from the Swedish Research Council and the Göran Gustafsson Foundation for Research in Natural Sciences and Medicine.

**Supporting Information Available:** Copies of $^1H$ and $^{13}C$ NMR spectra for compounds **3**−**13**, as well as listed $^1H$ and $^{13}C$ NMR data for these compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026758D