Synthesis of Triazole-Linked Manno- and Glucopyranosyl Amino Acids

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Received 15 May 2007

Abstract: The synthesis of two types of triazole-linked glycosyl amino acids, at C-4 and at the anomeric position for mannopyranose and glucopyranose derivatives, respectively, via a copper-catalyzed [3+2] cycloaddition of acetylenic amino acid derivatives and azide-containing glycoside is described.

Key words: [3+2] cycloaddition, acetylenic amino acid, azidocarbohydrate, triazole, glycosyl amino acids

Glycopeptides constitute an important class of natural compounds which are widely found in living organisms and play crucial roles in various cellular recognition processes.[1] The synthesis of such glycopeptides, as well as the synthesis of models that mimic these natural glycopeptides, are attractive goals. The most commonly encountered members of this family, or their models, are N- and O-linked glycopeptides.[2] More recently, several efforts have been focused on the synthesis of C-linked glycopeptides,[2b,3] which are more stable towards chemical and enzymatic cleavages.

During the last few years, there has been an increasing interest in the use of the Huisgen's 1,3-dipolar cycloaddition reaction of organic azides with terminal acetylenes,[4] and particularly after the optimization of the reaction conditions via a copper(I)-catalyzed condensation.[5] In carbohydrate chemistry, this copper-catalyzed cycloaddition or 'click chemistry' has been used to construct well-defined glycoconjugates,[6] oligosaccharide mimics,[7] and macrocyclic systems such as glycodendrimers[8] or cyclodextrines.[9] The synthesis and in situ attachment of saccharides to the microtiter plate[10] as well as the synthesis of multiple labelled-carbohydrate oligonucleotides on solid support via 1,2,3-triazole formation have also been described.[11]

Surprisingly, despite the importance of glycosyl amino acids, the use of this methodology for the construction of triazole-linked glycosyl amino acids is scarce. One possibility is the combination of azidosugars with acetylenic amino acid derivatives,[6e–h,12a–e] anomeric azides as well as carbohydrates bearing a spacer between the sugar moiety and the azido function being used. The other approach is the combination of azidoamino acids and acetylenic sugars.[6h,12a,c,f,g]

In a research program involving the synthesis and biological evaluation of a series of new aminosugars,[13] we published a very convenient access to unsaturated 4-azidocarbohydrates via a palladium-catalyzed substitution of allylic sugar acetates or carbonates using NaN_3 or Me_3SiN_3 as the azide source.[14] These 4-azidocarbohydrates were used in the copper-coupling with various terminal alkynes, allowing an efficient access to some 1,2,3-triazole-linked glycoconjugates.[15] Herein we report the application of this methodology for the synthesis of some triazole-linked glycosyl amino acids derived from α-D-mannopyranose and the extension of this procedure to glycosyl amino acids derived from α- and β-D-glucopyranose, starting from azidosugars and various protected amino acids containing a terminal acetylenic function.

In order to perform the [2+3] cycloaddition, we have to introduce a terminal alkyne moiety in the amino acid. For this purpose, we prepared three different types of protected amino acids **1a–c** bearing the alkyne group on the acidic function as an amide group, on the amino function as an amide group, and also on the aromatic ring of the amino acid (Figure 1).

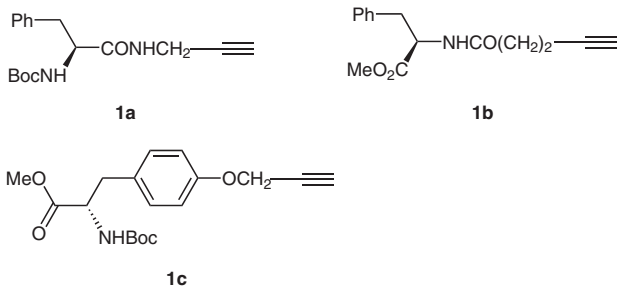


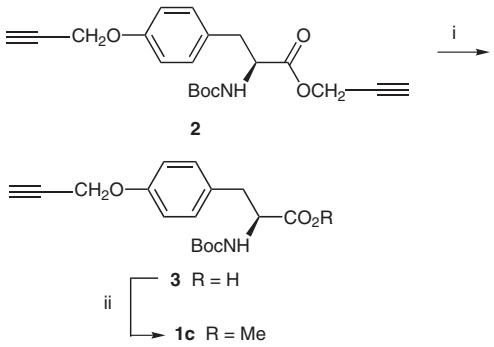
Figure 1 Acetylenic amino acids

Compounds **1a**[16] and **1b**[16a,17] were prepared according to the literature procedures. The synthesis of acetylenic amino acid **1c** was completed in two steps starting from compound **2** obtained from commercially available *N*-Boc-L-tyrosine according to the literature[18] (Scheme 1). Saponification of the propargylic ester of compound **2** in a methanolic solution of sodium hydroxide followed by reaction

SYNTHESIS 2007, No. 17, pp 2647–2652
Advanced online publication: 24.07.2007
DOI: 10.1055/s-2007-983813; Art ID: Z12007SS

with diazomethane gave acetylenic amino acid **1c** in an overall yield of 45%.

The starting ethyl 4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (**4**) was prepared according to the method described previously.[14]

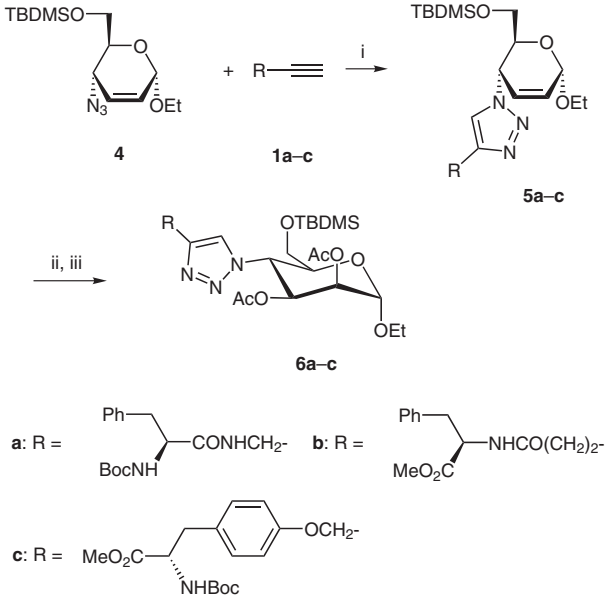


Scheme 1 *Reagents and conditions*: (i) NaOH 2.5%, MeOH, r.t., 55%; (ii) CH_2N_2, THF, r.t., 83%.

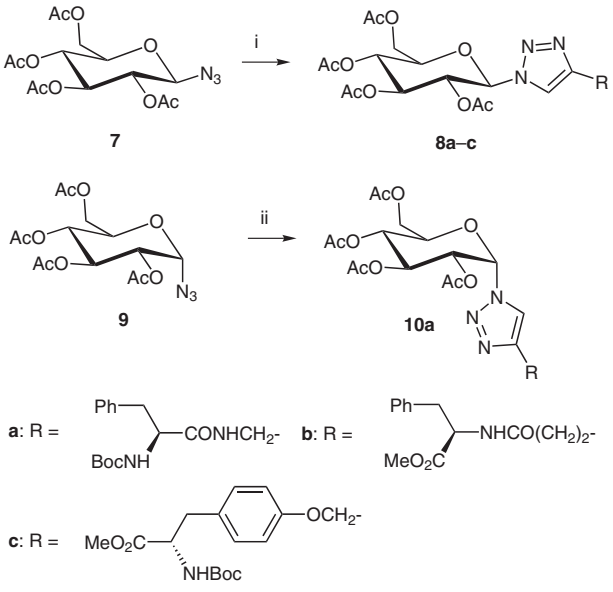
The reaction of unsaturated carbohydrate **4** with acetylenic amino acid **1a** in the presence of a catalytic amount of $Cu(OAc)_2$ and sodium ascorbate in a 1:1 mixture of *tert*-butyl alcohol and water at room temperature under nitrogen overnight afforded the 1*H*-1,2,3-triazole derivative **5a** as the exclusive product in 73% yield after column chromatography (Scheme 2). The regioselectivity of the 1,3-dipolar cycloaddition reaction was assigned according to the previous results using this methodology and based on the mechanism proposed by Sharpless et al.[5a] Under the same conditions the reaction of carbohydrate **4** with acetylenic amino acids **1b** and **1c** afforded 1*H*-1,2,3-triazole derivatives **5b** and **5c** in 70 and 60% yield, respectively.

These unsaturated triazole-linked glycosyl amino acids **5a–c** were subjected to the dihydroxylation reaction in the presence of a catalytic amount of OsO_4 and *N*-methylmorpholine oxide followed by acetylation of the crude mixture (Scheme 2). As expected, the corresponding triazole-linked α-D-mannopyranosid-4-yl amino acids **6a–c** were obtained as the sole products in 63, 50, and 61% yield, respectively. Compounds **6a–c** were formed by the dihydroxylation of the double bond from the less hindered side, in agreement with the previous findings for similar compounds.[19] The assigned configurations for compounds **6a–c** are mainly based on the coupling constant ($J_{4,5}$ = 10.7, 10.3, and 10.9 Hz, and $J_{3,4}$ = 10.7, 11.1, and 10 Hz, respectively), characteristic of an axial–axial disposition for H-3, H-4, and H-5.

The reaction of these protected acetylenic amino acids **1a–c** was also extended to glucopyranosyl azides **7** and **9**. However, we used the modified protocol recently published for similar condensations,[20] since it gave higher chemical yields in shorter reaction times. We performed the cycloaddition in the presence of CH_2Cl_2 as the co-solvent, instead of *t*-BuOH. Under these conditions, the β-glucopyranosyl azide **7** reacted in an efficient manner with the acetylenic amino acids **1a–c** to give the corresponding triazole-linked β-glycosyl amino acids in good yields after column chromatography (84, 65, and 73% yield for **8a**, **8b**, and **8c**, respectively), with retention of configuration at the anomeric center (Scheme 3). Likewise, the α-glucopyranosyl azide **9** reacted with the acetylenic amino acid **1a** to give the corresponding triazole-linked α-glycosyl amino acid **10** in 40% yield. This is a complementary methodology to that described by Rutjes's group,[12a] who used only the N-protected propargylglycine ester as the acetylenic amino acid, for the synthesis of various triazole-linked glycosyl amino acids.



Scheme 2 *Reagents and conditions*: (i) *t*-BuOH–H_2O (1:1), $Cu(OAc)_2$ (20 mol%), sodium ascorbate (40 mol%), r.t.; (ii) OsO_4 (2 mol%), NMO, acetone–H_2O, r.t.; (iii) Ac_2O, C_5H_5N, r.t.



Scheme 3 *Reagents and conditions*: (i) **1a–c**, CH_2Cl_2/H_2O (1:1), $Cu(OAc)_2$ (5 mol%), sodium ascorbate (15 mol%), r.t.; (ii) **1a**, CH_2Cl_2/H_2O (1:1), $Cu(OAc)_2$ (5 mol%), sodium ascorbate (15 mol%), r.t.

In conclusion, we have described a methodology for the synthesis of ethyl mannopyranoside bearing a triazole ring at C-4 linked to a protected amino acid moiety via the acidic or the amino function, or via the aromatic ring. The same amino acid moieties could be introduced very easily at the anomeric position of glucopyranose starting from azidoglucopyranoside.

Solvents were dried and distilled by standard methods before use. All commercially available reagents were used as received. All reactions were monitored by TLC analysis (TLC plates GF_{254} Merck). Column chromatography was performed on silica gel 60 (230–240 mesh, Merck). Melting points were determined on a Büchi apparatus and are uncorrected. Optical rotations were recorded using a PerkinElmer 241 polarimeter. NMR spectra were recorded with a Bruker AMX 300 spectrometer and referenced as following: ^{1}H (300 MHz), internal $SiMe_4$ at δ = 0.00, ^{13}C (75 MHz), internal standard at δ = 77.23. Exact mass measurements of the molecular ions were obtained on a Finnigan Mat 95 XL spectrometer.

N-(*tert*-Butoxycarbonyl)-*N*-prop-2-yn-1-yl-L-phenylalaninamide (**1a**),[16a] methyl *N*-pent-4-ynoyl-L-phenylalaninate (**1b**),[16a,17] prop-2-yn-1-yl *N*-(*tert*-butoxycarbonyl)-*O*-prop-2-yn-1-yl-L-tyrosinate (**2**),[18] ethyl 4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (**4**),[14] 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**7**),[21] and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl azide (**9**)[22] were prepared according to reported procedures. Hexanes used had bp 40–65 °C.

N-(*tert*-Butoxycarbonyl)-*O*-prop-2-yn-1-yl-L-tyrosine (3)

A mixture of propargyl *N*-(*tert*-butoxycarbonyl)-*O*-prop-2-yn-1-yl-L-tyrosinate (**2**) (1.12 g, 3.14 mmol) in a methanolic solution of 2.5% NaOH (40 mL) was stirred at r.t. for 3 h. The pH was then adjusted to 6.0 by adding a 30% aq solution of HCl, and the mixture was extracted with EtOAc (3 × 50 mL). Evaporation of the solvent under reduced pressure followed by purification on silica gel chromatography using EtOAc as the eluent afforded acid **3** (550 mg, 55%) as a yellow oil; R_f = 0.54 (EtOAc); $[\alpha]_D^{20}$ +26 (*c* = 0.5, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, *t*-C_4H_9), 2.52 (t, *J* = 2.4 Hz, 1 H, C≡CH), 3.03 (dd, *J* = 14.0, 6.1 Hz, 1 H, C*H*$_2$Ph), 3.14 (dd, *J* = 14.0, 5.1 Hz, 1 H, C*H*$_2$Ph), 4.57 (m, 1 H, CHN), 4.67 (d, *J* = 2.4 Hz, 2 H, CH_2C≡C), 4.95 (d, *J* = 7.7 Hz, 1 H, NH), 6.92 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.12 (d, *J* = 8.5 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.7, 37.4, 54.7, 56.2, 76.0, 79.0, 115.4, 130.9, 157.0, 157.1, 176.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{21}NO_5$ + Na: 342.1317; found: 342.1319.

Methyl *N*-(*tert*-Butoxycarbonyl)-*O*-prop-2-yn-1-yl-L-tyrosinate (1c)

To a solution of **3** (0.2 g, 0.63 mmol) in THF (5 mL) was added at r.t. an ethereal solution of diazomethane obtained by reacting *N*-methyl-*N*-nitrosotoluene-*p*-sulfonamide (320 mg, 1.5 mmol) with ethanolic KOH (34 mg in 0.9 mL). After total consumption of the starting amino acid, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using EtOAc as the eluent to afford the methyl ester **1c** (174 mg, 83%) as a colorless solid; mp 78–80 °C; R_f = 0.7 (EtOAc); $[\alpha]_D^{20}$ +35.7 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, *t*-C_4H_9), 2.52 (t, *J* = 2.5 Hz, 1 H, C≡CH), 2.99 (dd, *J* = 14.0, 6.0 Hz, 1 H, C*H*$_2$Ph), 3.06 (dd, *J* = 14.0, 5.9 Hz, 1 H, C*H*$_2$Ph), 3.71 (s, 3 H, OCH_3), 4.54 (ddd, *J* = 7.9, 6.0, 5.9 Hz, 1 H, CHN), 4.66 (d, *J* = 2.5 Hz, 2 H, CH_2C≡C), 4.97 (d, *J* = 7.9 Hz, 1 H, NH), 6.90 (d, *J* = 8.6 Hz, 2 H_{arom}), 7.06 (d, *J* = 8.6 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.7, 37.9, 52.6, 54.9, 56.2, 75.9, 79.0, 80.3, 115.3, 129.4, 130.7, 155.5, 157.0, 172.8.

Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 7.21. Found: C, 64.52; H, 7.21.

Unsaturated Triazole Derivatives 5a–c; General Procedure

4-Azidosugar **4** (313 mg, 1 mmol) and the appropriate acetylenic amino acid derivative **1** (3 mmol) were suspended in 1:1 mixture of *t*-BuOH and H_2O (4 mL), and THF (2 mL). To this solution was added a mixture of $Cu(OAc)_2$ (36 mg, 0.2 mmol) and sodium ascorbate (79 mg, 0.4 mmol) in *t*-BuOH–H_2O (1 mL). The reaction was stirred under N_2 at r.t. until TLC analysis indicated complete consumption of the product. H_2O (3 mL) was added, and the organic product was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel using the indicated eluent to give the corresponding compound **5**.

N-(*tert*-Butoxycarbonyl)-*N*-{[1-(ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-L-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}-L-phenylalaninamide (5a)

Prepared from **4** and **1a**; colorless solid; yield: 449 mg (73%); mp 54 °C; R_f = 0.53 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{20}$ +59.2 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, $SiCH_3$), 0.01 (s, 3 H, $SiCH_3$), 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.26 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.39 (s, 9 H, *t*-C_4H_9), 3.06 (d, *J* = 6.8 Hz, 2 H, CH_2), 3.53–3.63 (m, 2 H, H-6, CH_2CH_3), 4.07 (ddd, *J* = 9.4, 3.0, 2.1 Hz, 1 H, H-5), 4.33 (d, *J* = 7.2 Hz, 1 H, NH), 4.43 (dd, *J* = 15.2, 5.6 Hz, 1 H, C*H*$_2$Ph), 4.50 (dd, *J* = 15.2, 5.6 Hz, 1 H, C*H*$_2$Ph), 4.95 (br s, 1 H, NH), 5.13 (br s, 1 H, H-1), 5.32 (br d, *J* = 9.4 Hz, 1 H, H-4), 5.89 (br d, *J* = 10.4 Hz, 1 H, H-2), 6.05 (ddd, *J* = 10.2, 2.8, 2.4 Hz, 1 H, H-3), 6.36 (t, *J* = 6.8 Hz, 1 H, CHN), 7.16 (d, *J* = 7.5 Hz, 2 H_{arom}), 7.24–7.30 (m, 3 H_{arom}), 7.46 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 26.2, 28.6, 35.3, 39.0, 55.2, 62.7, 64.5, 71.2, 94.2, 121.5, 127.3, 127.9, 128.9, 129.6, 129.7, 137.0, 145.2, 155.7, 171.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{49}N_5O_6Si$ + Na: 638.3349; found: 638.3348.

Anal. Calcd for $C_{31}H_{49}N_5O_6Si$: C, 60.46; H, 8.02. Found: C, 59.74; H, 7.84.

Methyl *N*-{3-[1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazol-4-yl]propanoyl}-L-phenylalaninate (5b)

Prepared from **4** and **1b**; colorless oil; yield: 401 mg (70%); R_f = 0.63 (hexanes–EtOAc, 2:1); $[\alpha]_D^{20}$ +94.7 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, $SiCH_3$), 0.02 (3 s, 3 H, $SiCH_3$), 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.25 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 2.61 (t, *J* = 7.0 Hz, 1 H, CH_2), 3.02 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.07 (m, 1 H, C*H*$_2$Ph), 3.11 (dd, *J* = 14.1, 6.0 Hz, 1 H, C*H*$_2$Ph), 3.53–3.61 (m, 2 H, CH_2CH_3, H-6), 3.65 (dd, *J* = 11.7, 2.1 Hz, 1 H, H-6), 3.71 (s, 3 H, OCH_3), 3.87 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_2CH_3), 4.06 (ddd, *J* = 9.8, 4.9, 2.1 Hz, 1 H, H-5), 4.85 (ddd, *J* = 7.5, 6.0, 5.9 Hz, 1 H, CHN), 5.11(br s, 1 H, H-1), 5.29 (ddd, *J* = 9.8, 1.9, 1.7 Hz, 1 H, H-4), 5.90 (br d, *J* = 10.0 Hz, 1 H, H-2), 6.00 (ddd, *J* = 10.0, 2.6, 2.6 Hz, 1 H, H-3), 6.16 (br d, *J* = 7.5 Hz, 1 H, NH), 7.04 (dd, *J* = 7.6, 1.6 Hz, 2 H_{arom}), 7.20–7.31 (m, 3 H_{arom}), 7.39 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 21.7, 26.2, 38.7, 38.2, 52.6, 53.6, 55.1, 62.7, 64.5, 71.3, 94.2, 120.7, 127.4, 128.2, 128.9, 129.4, 129.5, 136.2, 147.0, 171.9, 172.3.

Anal. Calcd for $C_{29}H_{44}N_4O_6Si$: C, 60.81; H, 7.74. Found: C, 60.68; H, 7.80.

Methyl *N*-(*tert*-Butoxycarbonyl)-*O*-{[1-(ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazol-4-yl)]methyl}-L-tyrosinate (5c)

Prepared from **4** and **1c**; colorless oil; yield: 388 mg (60%); R_f = 0.58 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{20}$ +81.9 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$), 0.88 [s, 9 H, $SiC(CH_3)_3$], 1.27 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.43 (s, 9 H, *t*-C_4H_9), 3.01 (dd, *J* = 14.5, 6.2 Hz, 1 H, CH_2Ph), 3.07 (dd, *J* = 14.1, 6.0 Hz, 1 H, CH_2Ph), 3.56–3.72 (m, 3 H, CH_2CH_3, H-6), 3.72 (s, 3 H, OCH_3), 3.89 (dq, *J* = 9.5, 7.1 Hz, 1 H, CH_2CH_3), 4.12 (m, 1 H, H-5), 4.55 (m, 1 H, CHN), 4.98 (br d, *J* = 7.9 Hz, 1 H, NH), 5.15 (br s, 1 H, H-1), 5.18 (s, 2 H, OCH_2), 5.38 (br d, *J* = 9.8 Hz, 1 H, H-4), 5.98 (br d, *J* = 10.0 Hz, 1 H, H-2), 6.05 (ddd, *J* = 10.0, 2.5, 2.5 Hz, 1 H, H-3), 6.92 (d, *J* = 8.6 Hz, 2 H_{arom}), 7.05 (d, *J* = 8.6 Hz, 2 H_{arom}), 7.70 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 26.2, 28.7, 52.6, 53.8, 55.3, 62.5, 62.7, 64.6, 71.4, 94.2, 115.1, 122.0, 128.0, 129.0, 129.7, 130.7, 144.9, 155.5, 157.7, 172.7.

Anal. Calcd for $C_{32}H_{50}N_4O_8Si$: C, 59.42; H, 7.79. Found: C, 58.81; H, 7.73.

Dihydroxylation of Unsaturated Triazole Derivatives 6a–c; General Procedure

To a solution of unsaturated 4-triazolyl glycopeptide **5** (0.5 mmol) in a 4:1 mixture of acetone–H_2O (2 mL), was added OsO_4 (0.125 mg, 0.5 μmol, 2 mol%) and *N*-methylmorpholine-*N*-oxide (233 mg, 2 mmol) at 0 °C. The mixture was stirred overnight at r.t., then $NaHSO_3$ (250 mg) was added, and the contents were stirred for 30 min at r.t. The mixture was diluted with H_2O (3 mL), and extracted with EtOAc (2 × 5 mL). The organic phase was separated, dried (Na_2SO_4), and the solvent was evaporated to give the corresponding diol. The crude residue was directly acetylated using Ac_2O (153 mg, 1.5 mmol) in pyridine (2 mL) for 1 d. After removing the solvent under reduced pressure, the residue was purified by column chromatography on silica gel using the corresponding eluent to afford the 4-triazolyl carbohydrate **6**.

***N*-(*tert*-Butoxycarbonyl)-*N*-{[1-(ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-acetyl-4-deoxy-α-D- mannopyranosid-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}-L-phenylalaninamide (6a)**

Prepared from **5a**; colorless solid; yield: 231 mg (63%); mp 66 °C; R_f = 0.75 (CH_2Cl_2–EtOAc, 1:1); $[\alpha]_D^{20}$ +39.4 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$), 0.92 [s, 9 H, $SiC(CH_3)_3$], 1.29 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.39 (s, 9 H, *t*-C_4H_9), 1.83 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3), 3.05 (d, *J* = 6.8 Hz, 2 H, CH_2), 3.34 (dd, *J* = 11.9, 3.0 Hz, 1 H, H-6), 3.56 (dq, *J* = 9.8, 7.2 Hz, 1 H, CH_2CH_3), 3.63 (br d, *J* = 11.9 Hz, 1 H, H-6), 3.80 (dq, *J* = 9.8, 7.2 Hz, 1 H, CH_2CH_3), 4.38–4.35 (m, 2 H, H-5, NH), 4.41 (dd, *J* = 15.2, 5.6 Hz, 1 H, CH_2Ph), 4.52 (dd, *J* = 15.2, 5.8 Hz, 1 H, CH_2Ph), 4.91 (br s, 1 H, H-1), 4.94 (br s, 1 H, NH), 4.98 (dd, *J* = 10.7, 10.7 Hz, 1 H, H-4), 5.33 (dd, *J* = 2.8, 1.7 Hz, 1 H, H-2), 5.83 (dd, *J* = 10.7, 3.2 Hz, 1 H, H-3), 6.48 (dd, *J* = 5.8, 5.6 Hz, 1 H, CHN), 7.14 (d, *J* = 7.4 Hz, 2 H_{arom}), 7.22–7.32 (m, 3 H_{arom}), 7.48 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –6.5, –6.3, 13.9, 17.2, 19.4, 19.8, 24.8, 27.2, 33.9, 55.1, 60.5, 62.9, 67.9, 68.0, 70.0, 96.4, 122.3, 126.0, 127.7, 128.3, 135.5, 168.0, 168.9, 170.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{55}N_5O_{10}Si$ + Na: 756.3616; found : 756.3610.

Methyl *N*-{3-[1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazol-4-yl]propanoyl}-L-phenylalaninate (6b)

Prepared from **5b** colorless oil; yield: 173 mg (50%); R_f = 0.66 (CH_2Cl_2–EtOAc, 1:1); $[\alpha]_D^{20}$ +52.8 (*c* = 0.6, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$), 0.92 [s, 9 H, $SiC(CH_3)_3$], 1.28 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.83 (s, 3 H, CH_3), 2.17 (s, 3 H, CH_3), 2.62 (t, *J* = 7.3 Hz, 2 H, CH_2), 3.03 (t, *J* = 7.8 Hz, 2 H, CH_2), 3.10 (dd, *J* = 13.6, 7.8 Hz, 1 H, CH_2Ph), 3.15 (dd, *J* = 13.6, 5.8 Hz, 1 H, CH_2Ph), 3.35 (dd, *J* = 11.9, 3.4 Hz, 1 H, H-6), 3.63–3.49 (m, 2 H, CH_2CH_3, H-6), 3.74 (s, 3 H, OCH_3), 3.81 (dq, *J* = 9.8, 7.1 Hz, 1 H, CH_2CH_3), 4.33 (br d, *J* = 10.3 Hz, 1 H, H-5), 4.87 (ddd, *J* = 7.8, 6.0, 5.8 Hz, 1 H, CHN), 4.91(d, *J* = 1.5 Hz, 1 H, H-1), 4.97 (dd, *J* = 11.1, 10.3 Hz, 1 H, H-4), 5.33 (dd, *J* = 3.2, 1.7 Hz, 1 H, H-2), 5.85 (dd, *J* = 11.1, 3.4 Hz, 1 H, H-3), 6.14 (d, *J* = 7.5 Hz, 1 H, NH), 7.09 (dd, *J* = 6.2, 1.7 Hz, 2 H_{arom}), 7.26–7.34 (m, 3 H_{arom}), 7.40 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.1, –4.9, 15.3, 18.7, 20.8, 21.2, 21.6, 26.2, 35.7, 38.2, 52.7, 53.5, 56.4, 62.0, 64.3, 69.2, 69.5, 71.6, 97.7, 122.5, 127.6, 129.0, 129.6, 136.2, 169.5, 170.3, 171.7, 172.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{50}N_4O_{10}Si$ + Na: 713.3194; found: 713.3190.

Methyl *N*-(*tert*-Butoxycarbonyl)-*N*-{[1-(ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3-di-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazol-4-yl]methyl}-L-tyrosinate (6c)

Prepared from **5c**; colorless solid; yield: 233 mg (61%); mp 63 °C; R_f = 0.81 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{20}$ +62.3 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.06 (s, 3 H, $SiCH_3$), 0.00 (s, 3 H, $SiCH_3$), 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.23 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.38 (s, 9 H, *t*-C_4H_9), 1.75 (s, 3 H, $OCOCH_3$), 2.10 (s, 3 H, $OCOCH_3$), 2.95 (dd, *J* = 14.0, 6.2 Hz, 1 H, CH_2Ph), 3.01 (dd, *J* = 14.0, 5.8 Hz, 1 H, CH_2Ph), 3.28 (dd, *J* = 11.8, 3.2 Hz, 1 H, H-6), 3.51 (dq, *J* = 9.8, 7.1 Hz, 1 H, CH_2CH_3), 3.59 (br d, *J* = 12.0 Hz, 1 H, H-6), 3.67 (s, 3 H, OCH_3), 3.74 (dq, *J* = 9.8, 7.1 Hz, 1 H, CH_2CH_3), 4.32 (br d, *J* = 10.0 Hz, 1 H, H-5), 4.49 (m, 1 H, CHN), 4.86 (d, *J* = 1.3 Hz, 1 H, H-1), 4.93 (br d, *J* = 8.0 Hz, 1 H, NH), 4.97 (dd, *J* = 10.9, 10.9 Hz, 1 H, H-4), 5.14 (s, 2 H, OCH_2), 5.28 (dd, *J* = 2.8, 2.1 Hz, 1 H, H-2), 5.85 (dd, *J* = 11.2, 3.3 Hz, 1 H, H-3), 6.84 (d, *J* = 8.5 Hz, 2 H_{arom}), 6.99 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.59 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.2, –4.9, 15.3, 18.6, 20.8, 21.2, 26.2, 28.7, 37.8, 52.6, 54.9, 56.6, 61.9, 62.5, 64.3, 69.2, 69.5, 71.6, 97.8, 115.2, 124.1, 129.0, 130.7, 144.3, 157.7, 169.4, 170.3, 172.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{36}H_{57}N_4O_{12}Si$: 765.3742; found: 765.3733.

Glucopyranosyl-Linked Triazole Derivatives 8a–c and 10a; General Procedure

Azidosugar **7** or **9** (1 mmol) and the appropriate acetylenic amino acid (1.1 mmol) were suspended in 1:1 mixture of CH_2Cl_2 and H_2O (4 mL). To this solution was added a mixture of $Cu(OAc)_2$ (36 mg, 0.2 mmol) and sodium ascorbate (79 mg, 0.4 mmol). The resulting mixture was stirred under N_2 at r.t. until TLC analysis indicated complete consumption of the azidosugar. The mixture was diluted with CH_2Cl_2 (5 mL) and H_2O (5 mL). The organic layer was separated, and the aqueous phase was extracted again with CH_2Cl_2 (5 mL). The combined organic layers were dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica using the indicated eluent to give the corresponding 1,2,3-triazoles **8a–c** or **10a**.

***N*-(*tert*-Butoxycarbonyl)-*N*-({1-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl]-1*H*-1,2,3-triazol-4-yl}methyl)-L-phenylalaninamide (8a)**

Prepared from **7** and **1a**; colorless solid; yield: 439 mg (65%); mp 135 °C; R_f = 0.71 (EtOAc); $[\alpha]_D^{20}$ –19.7 (*c* = 1.0, CH_2Cl_2).

1H NMR (300 MHz, DMSO-d_6): δ = 1.31 (s, 9 H, *t*-C_4H_9), 1.79 (s, 3 H, $OCOCH_3$), 1.97 (s, 3 H, $OCOCH_3$), 1.99 (s, 3 H, $OCOCH_3$), 2.03 (s, 3 H, $OCOCH_3$), 2.74 (dd, *J* = 13.6, 10.0 Hz, 1 H, CH_2Ph), 2.94 (dd, *J* = 13.6, 4.3 Hz, 1 H, CH_2Ph), 4.05–4.18 (m, 3 H, H-6, CHN), 4.33 (d, *J* = 5.5 Hz, 2 H, CH_2N), 4.37–4.40 (m, 1 H, H-5), 5.17 (dd, *J* = 9.4, 9.2 Hz, 1 H, H-4), 5.55 (dd, *J* = 9.4, 9.2 Hz, 1 H, H-3), 5.61 (dd, *J* = 9.4, 8.5 Hz, 1 H, H-2), 6.33 (d, *J* = 8.7 Hz, 1 H, H-1), 6.95 (d, *J* = 8.5 Hz, 1 H_{arom}), 7.18–7.24 (m, 5 H, 4 H_{arom}, NH), 8.06 (s, 1 H, NCH=), 8.50 (br t, *J* = 5.0 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 20.9, 20.9, 21.0, 28.6, 35.2, 40.0, 61.9, 68.0, 70.7, 73.1, 75.4, 86.0, 127.2, 129.0, 129.7, 137.0, 169.2, 169.7, 170.3, 170.9, 171.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{42}N_5O_{12}$: 676.2830; found: 676.2857.

Methyl *N*-(3-{1-[2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl]-1*H*-1,2,3-triazol-4-yl}propanoyl)-L-phenylalaninate (8b)

Prepared from **7** and **1b**; colorless solid; yield: 531 mg (84%); mp 155 °C; R_f = 0.38 (EtOAc); $[\alpha]_D^{20}$ +10.0 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.78 (s, 3 H, $OCOCH_3$), 1.96 (s, 3 H, $OCOCH_3$), 1.99 (s, 3 H, $OCOCH_3$), 2.03 (s, 3 H, $OCOCH_3$), 2.41 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.74 (t, *J* = 7.3 Hz, 2 H, CH_2), 2.87 (dd, *J* = 13.6, 9.2 Hz, 1 H, CH_2Ph), 3.02 (dd, *J* = 13.6, 5.6 Hz, 1 H, CH_2Ph), 3.60 (s, 3 H, OCH_3), 4.04 (dd, *J* = 12.4, 2.3 Hz, 1 H, H-6), 4.14 (dd, *J* = 12.4, 5.3 Hz, 1 H, H-6), 4.37 (ddd, *J* = 9.8, 5.3, 2.3 Hz, 1 H, H-5), 4.47 (ddd, *J* = 11.1, 5.6, 3.4 Hz, 1 H, CHN), 5.15 (dd, *J* = 9.6, 9.6 Hz, 1 H, H-4), 5.55 (dd, *J* = 9.2, 9.0 Hz, 1 H, H-3), 5.59 (dd, *J* = 9.0, 8.9 Hz, 1 H, H-2), 6.29 (d, *J* = 8.9 Hz, 1 H, H-1), 7.19–7.31 (m, 5 H_{arom}), 8.06 (s, 1 H, NCH=), 8.43 (d, *J* = 7.7 Hz, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 20.9, 20.9, 21.0, 21.6, 35.5, 38.1, 52.7, 53.5, 61.9, 68.1, 70.6, 73.1, 75.3, 85.9, 120.3, 127.5, 128.9, 129.6, 136.3, 147.6, 169.2, 169.8, 170.3, 170.9, 171.6, 172.4.

Anal. Calcd for $C_{29}H_{36}N_4O_{12}$: C, 55.06; H, 5.74. Found: C, 54.77; H, 5.82.

Methyl *N*-(*tert*-Butoxycarbonyl)-*O*-{[1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazol-4-yl]methyl}-L-tyrosinate (8c)

Prepared from **7** and **1c**; colorless solid; yield: 515 mg (73%); mp 158 °C; R_f = 0.83 (EtOAc); $[\alpha]_D^{20}$ –1.3 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 9 H, *t*-C_4H_9), 1.77 (s, 3 H, $OCOCH_3$), 1.97 (s, 3 H, $OCOCH_3$), 2.00 (s, 3 H, $OCOCH_3$), 2.03 (s, 3 H, $OCOCH_3$), 2.78 (dd, *J* = 13.4, 10.0 Hz, 1 H, CH_2Ph), 2.91 (dd, *J* = 13.4, 4.9 Hz, 1 H, CH_2Ph), 3.60 (s, 3 H, OCH_3), 4.04–4.16 (m, 3 H, H-6, CHN), 4.37 (ddd, *J* = 10.0, 5.1, 2.6, 1 H, H-5), 5.11 (s, 2 H, OCH_2), 5.18 (dd, *J* = 9.8, 9.6 Hz, 1 H, H-4), 5.56 (dd, *J* = 9.4, 9.4 Hz, 1 H, H-3), 5.68 (dd, *J* = 9.4, 9.1 Hz, 1 H, H-2), 6.38 (d, *J* = 9.0 Hz, 1 H, H-1), 6.94 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.16 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.27 (d, *J* = 8.1 Hz, 1 H, NH), 8.54 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 20.8, 20.9, 21.1, 28.7, 37.9, 52.6, 61.9, 62.3, 68.0, 70.6, 73.0, 75.5, 86.1, 115.3, 121.5, 126.2, 129.2, 130.8, 145.4, 157.6, 169.3, 169.7, 170.3, 170.9, 172.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{43}N_4O_{14}$: 707.2776; found: 707.2763.

***N*-(*tert*-Butoxycarbonyl)-*N*-({1-[2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl]-1*H*-1,2,3-triazol-4-yl}methyl)-L-phenylalaninamide (10a)**

Prepared from **9** and **1a**; colorless solid; yield: 270 mg (40%); mp 82 °C; R_f = 0.65 (EtOAc); $[\alpha]_D^{20}$ +62.0 (*c* = 0.5, CH_2Cl_2).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.40 (s, 9 H, *t*-C_4H_9), 1.88 (s, 3 H, $OCOCH_3$), 2.03 (s, 3 H, $OCOCH_3$), 2.06 (s, 3 H, $OCOCH_3$), 2.07 (s, 3 H, $OCOCH_3$), 3.06 (d, *J* = 7.0 Hz, 2 H, CH_2Ph), 4.01 (dd, *J* = 12.4, 1.9 Hz, 1 H, H-6), 4.26 (dd, *J* = 12.4, 3.9 Hz, 1 H, H-6), 4.30–4.35 (m, 2 H, H-5, CHN), 4.47 (dd, *J* = 15.8, 5.6 Hz, 1 H, CH_2N), 4.52 (dd, *J* = 15.8, 5.8 Hz, 1 H, CH_2N), 4.95 (br s, 1 H, N*H*-Boc), 5.26 (dd, *J* = 9.8, 9.4 Hz, 1 H, H-4), 5.32 (dd, *J* = 10.0, 6.0 Hz, 1 H, H-2), 6.25 (d, *J* = 6.0 Hz, 1 H, H-1), 6.26 (dd, *J* = 10.0, 9.4 Hz, 1 H, H-3), 6.43 (dd, *J* = 5.8, 5.6 Hz, 1 H, NH), 7.15 (dd, *J* = 7.7, 2.1 Hz, 2 H_{arom}), 7.25–7.32 (m, 3 H_{arom}), 7.44 (s, 1 H, NCH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5, 18.7, 18.8, 26.4, 28.6, 32.9, 54.9, 66.2, 67.9, 68.5, 69.3, 79.6, 122.7, 125.2, 126.9, 127.5, 134.6, 167.8, 168.2, 168.7, 1169.5, 169.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{41}N_5O_{12}$ + Na: 698.2649; found: 698.2649.

Acknowledgment

We are indebted to the CAPES/COFECUB program no. 334/01 for financial support, and CNPq-Brazil for providing a fellowship (J.A.).

References

(1) (a) Varski, A. *Glycobiology* **1993**, *3*, 97. (b) *Glycopeptides and Related Compounds, Synthesis, Analysis and Applications*; Large, D. G.; Warren, C. D., Eds.; Marcel Dekker: New York, **1997**. (c) Dwek, R.-A. *Chem. Rev.* **1996**, *96*, 683.

(2) (a) Seitz, O. *ChemBioChem* **2000**, *1*, 214. (b) Schweizer, F. *Angew. Chem. Int. Ed.* **2002**, *41*, 230. (c) Spiro, R. G. *Glycobiology* **2002**, *12*, 43R.

(3) (a) Postema, M. H. D. *C-Glycoside Synthesis*; CRC Press: Boca Raton, **1995**. (b) Dondoni, A.; Marra, A. *Chem. Rev.* **2000**, *100*, 4395. (c) Beau, J.-M.; Gallagher, T. *Top. Curr. Chem.* **1997**, *187*, 1. (d) Yuan, X.; Linhardt, R. J. *Curr. Top. Med. Chem.* **2005**, *5*, 1393.

(4) Huisgen, R.; Knorr, R.; Moebius, L.; Szeimies, G. *Chem. Ber.* **1965**, *98*, 4014.

(5) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596. (b) Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057. (c) Wang, Q.; Chittaboina, S.; Barnhill, H. N. *Lett. Org. Chem.* **2005**, *2*, 293. (d) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51. (e) Lutz, J.-F. *Angew. Chem. Int. Ed.* **2007**, *46*, 1018. (f) Wu, P.; Fokin, V. V. *Aldrichimica Acta* **2007**, *40*, 7.

(6) (a) Pérez-Balderas, F.; Ortega-Muñoz, M.; Morales-Sanfrutos, J.; Hernández-Mateo, F.; Calvo-Flores, F. G.; Calvo-Asín, J. A.; Isac-García, J.; Santoyo-González, F. *Org. Lett.* **2003**, *5*, 1951. (b) Casas-Solvas, J. M.; Vargas-Berenguel, A.; Capitán-Vallvey, L. F.; Santoyo-González, F. *Org. Lett.* **2004**, *6*, 3687. (c) Zhu, X.; Schmidt, R. R. *J. Org. Chem.* **2004**, *69*, 1081. (d) Périon, R.; Ferrières, V.; Garcia-Moreno, M. I.; Mellet, C. O.; Duval, R.; Fernàndez, J. M. G.; Plusquellec, D. *Tetrahedron* **2005**, *61*, 9118. (e) Chittaboina, S.; Xie, F.; Wang, Q. *Tetrahedron Lett.* **2005**, *46*, 2331. (f) Temelkoff, D. P.; Zeller, M.; Norris, P. *Carbohydr. Res.* **2006**, *341*, 1081. (g) Wilkinson, B. L.; Bornaghi, L. F.; Poulsen, S.-A.; Houston, T. A. *Tetrahedron*

2006, *62*, 8115. (h) Hotha, S.; Kashyap, S. *J. Org. Chem.* **2006**, *71*, 364.
(7) (a) Marmuse, L.; Nepogodiev, S. A.; Field, R. A. *Org. Biomol. Chem.* **2005**, *3*, 2225. (b) Cheshev, P.; Marra, A.; Dondoni, A. *Org. Biomol. Chem.* **2006**, *4*, 3225. (c) Hasegawa, T.; Umeda, M.; Numata, M.; Li, C.; Bae, A.-H.; Fujisawa, T.; Haraguchi, S.; Sakurai, K.; Shinkai, S. *Carbohydr. Res.* **2006**, *341*, 35.
(8) (a) Joosten, J. A. F.; Tholen, N. T. H.; El Maate, F. A.; Brouwer, A. J.; van Esse, G. W.; Rijkers, D. T. S.; Liskamp, R. M. J.; Pieters, R. J. *Eur. J. Org. Chem.* **2005**, 3182. (b) Fernandez-Megia, E.; Correa, J.; Rodríguez-Meizoso, I.; Riguera, R. *Macromolecules* **2006**, *39*, 2113.
(9) (a) Calvo-Flores, F. G.; Isac-García, J.; Hernández-Mateo, F.; Pérez-Balderas, F.; Calvo-Asín, J. J. A.; Sanchéz-Vaquero, E.; Santoyo-González, F. *Org. Lett.* **2000**, *2*, 2499. (b) Bodine, K. D.; Gin, D. Y.; Gin, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 1638. (c) Dörner, S.; Westermann, B. *Chem. Commun.* **2005**, 2852.
(10) Fazio, F.; Bryan, M. C.; Blixt, O.; Paulson, J. C.; Wong, C.-H. *J. Am. Chem. Soc.* **2002**, *124*, 14397.
(11) Bouillon, C.; Meyer, A.; Vidal, S.; Jochum, A.; Chevolot, Y.; Cloarec, J.-P.; Praly, J.-P.; Vasseur, J.-J.; Morvan, F. *J. Org. Chem.* **2006**, *71*, 4700.
(12) (a) Kuijpers, B. H. M.; G roothuys, S.; Keereweer, A. R.; Quaedflieg, P. J. L. M.; Blaauw, R. H.; van Delft, F. L.; Rutjes, F. P. J. T. *Org. Lett.* **2004**, *6*, 3123. (b) Kuijpers, B. H. M.; Dijkmans, G. C. T.; Groothuys, S.; Quaedflieg, P. J. L. M.; Blaauw, R. H.; van Delft, F. L.; Rutjes, F. P. J. T. *Synlett* **2005**, 3059. (c) Groothuys, S.; Kuijpers, B. H. M.; Quaedflieg, P. J. L. M.; Roelen, H. C. P. F.; Wiertz, R. W.; Blaauw, R. H.; van Delft, F. L.; Rutjes, F. P. J. T. *Synthesis* **2006**, 3146. (d) Billing, J. F.; Nilsson, U. J. *J. Org. Chem.* **2005**, *70*, 4847. (e) Tejler, J.; Tullberg, E.; Frejd, T.; Leffler, H.; Nilsson, U. J. *Carbohydr. Res.* **2006**, *341*, 1353. (f) Dondoni, A.; Giovannini, P. P.; Massi, A. *Org. Lett.* **2004**, *6*, 2929. (g) Arosio, D.; Bertoli, M.; Manzoni, L.; Scolastico, C. *Tetrahedron Lett.* **2006**, *47*, 3697.
(13) (a) de Brito, T. M. B.; da Silva, L. P.; Siqueira, V. L.; Srivastava, R. M. *J. Carbohydr. Chem.* **1999**, *18*, 609. (b) de Freitas Filho, J. R.; Srivastava, R. M.; da Silva, W. J. P.; Cottier, L. D.; Sinou, D. *Carbohydr. Res.* **2003**, *338*, 673. (c) de Freitas Filho, J. R.; Cottier, L.; Srivastava, R. M.; Sinou, D. *Synlett* **2003**, 1358.
(14) de Oliveira, R. N.; Cottier, L.; Sinou, D.; Srivastava, R. M. *Tetrahedron* **2005**, *61*, 8271.
(15) de Oliveira, R. N.; Sinou, D.; Srivastava, R. M. *J. Carbohydr. Chem.* **2006**, *25*, 407.
(16) (a) Curran, T. P.; Grant, A. L.; Lucht, R. A.; Carter, J. C.; Affonso, J. *Org. Lett.* **2002**, *4*, 2917. (b) Löser, R.; Schilling, K.; Dimmig, E.; Gütschow, M. *J. Med. Chem.* **2005**, *48*, 7688.
(17) Lai, L. M.; Lam, J. W. Y.; Tang, B. Z. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 6190.
(18) Deiters, A.; Cropp, T. A.; Mukherji, M.; Chin, J. A.; Anderson, J. C.; Schultz, P. G. *J. Am. Chem. Soc.* **2003**, *125*, 11782.
(19) (a) Stevens, C. L.; Filippi, J. B.; Taylor, K. G. *J. Org. Chem.* **1966**, *31*, 1292. (b) Donohoe, T. J.; Garg, R.; Moore, P. R. *Tetrahedron Lett.* **1996**, *37*, 3407.
(20) Lee, B.-Y.; Park, S. R.; Jeon, H. B.; Kim, K. S. *Tetrahedron Lett.* **2006**, *47*, 5105.
(21) Györgydeák, Z.; Szitagyi, L.; Paulsen, H. *J. Carbohydr. Chem.* **1993**, *12*, 139.
(22) Soli, E. D.; Manoso, A. S.; Patterson, M. C.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 3171.