Synthesis of α- and *β*-Glycosyl Asparagine Ethylene Isosteres (*C*-Glycosyl Asparagines) via Sugar Acetylenes and Garner Aldehyde Coupling†

Alessandro Dondoni,* Giandomenico Mariotti, and Alberto Marra

Dipartimento di Chimica, Laboratorio di Chimica Organica, Università di Ferrara, Via Borsari 46, 44100 Ferrara, Italy

adn@dns.unife.it

Received January 24, 2002

A convergent approach has been developed for the synthesis of *C*-glycosyl amino acids in which the glycinyl moiety $CH(NH_2)CO_2H$ is connected to the anomeric center of the sugar residue by a three carbon atom tether. Essentially, these compounds are isosteres of *N*-glycosyl asparagines in which the amide group has been replaced by an ethylene bridge. Following the coupling of α- or *β*-D-linked lithium *C*-glycoside acetylides with *N*-Boc D-serinal acetonide (Garner aldehyde), the resulting adducts were transformed into the final *N*-Boc-*C*-glycosyl-α-aminopentanoic acids via reduction of the triple bond, deoxygenation, and oxidative cleavage of the oxazolidine ring. By this protocol, 12 *C*-glycosyl asparagines, six pairs of α- and *β*-anomers, have been prepared incorporating the gluco, galacto, manno, and the corresponding 2-acetamido-2-deoxy residues.

Introduction

Protein glycosylation is one of the most common co- and post-translational modifications of proteins, in which most sugar chains are linked to asparagine or serine/threonine residues by an *N*- or *O*-glycosidic linkage to form the *N*- and *O*-linked glycoproteins, respectively.[1] Indeed, protein glycosylation appears to be implicated in affecting protein structure,[2] improving proteolytical stability, and mediating various biological functions such as in cellular differentiation, and in cell−cell communication.[3] To explore and better understanding these key properties, there is a pressing need for methods that will not only allow the preparation of pure glycosylated proteins but will also provide the access to nonnatural variants. For instance, the incorporation of *C*-glycosyl amino acids in glycopeptide may serve in preparing chemically and metabolically resistant analogues that display inhibitor activity toward *N*- and *O*-glycosidases.[4] The final goal of these synthetic efforts is the development of glycopeptide-based drugs with improved pharmacokinetic properties. Hence, the reasons for the current interest for the synthesis of *C*-glycosyl amino acids, especially carbon isosteres of *N*-glycosylasparagine and *O*-glycosylserine/threonine in which the essential modification is the replacement of the anomeric *N*- or *O*-linkage with a more robust carbon−carbon bond, become apparent (Figure 1). Various synthetic approaches to

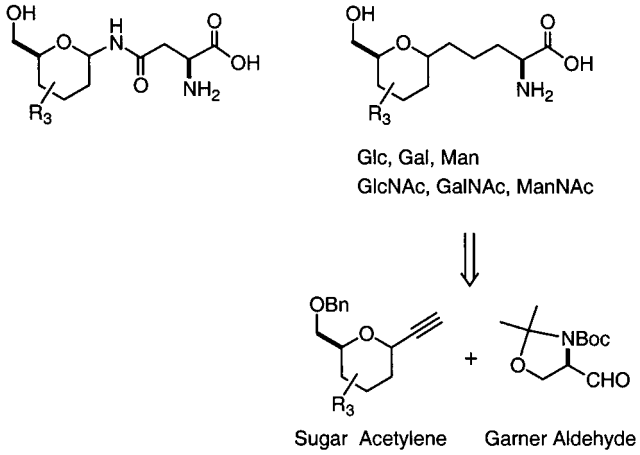


Figure 1. Natural glycosyl asparagines (R_3 = OH and NHAc) (left) and the α- and *β*-linked ethylene isosteres (right) prepared from sugar acetylenes and the Garner aldehyde.

C-glycosyl amino acids have been developed in relatively recent times.[5] Preference has been given to the discovery of new methods, while their scope was not established. By contrast, we report here on a new method for the synthesis of ethylene isosteres of *N*-glycosyl asparagines[6] that is centered on the coupling of metalated sugar acetylenes with the Garner aldehyde (Figure 1). The general scope of the method is corroborated by the synthesis of six pairs of these products incorporating the gluco, galacto, manno, and the corresponding 2-acetamido residues as both α and *β*-anomers.

† Dedicated to Professor Lutz F. Tietze on the occasion of his 60th birthday.

(1) (a) Varki, A. *Glycobiology* **1993**, *3*, 97−130. (b) Lee, Y. C.; Lee, R. T. *Acc. Chem. Res.* **1995**, *28*, 321−327. (c) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683−720.

(2) (a) Imperiali, B.; Shannon, K. L.; Rickert, K. W. *J. Am. Chem. Soc.* **1992**, *114*, 7942−7944. (b) Imperiali, B. *Acc. Chem. Res.* **1997**, *30*, 452−459.

(3) For a recent review, see: Seitz, O. *ChemBioChem* **2000**, *1*, 214−246.

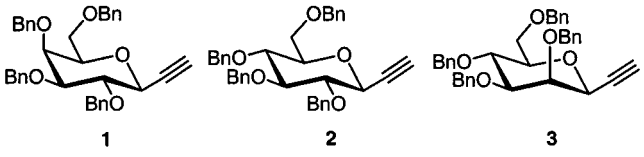
(4) Marcaurelle, L. A.; Bertozzi, C. R. *Chem. Eur. J.* **1999**, *5*, 1384−1390.

(5) Recent reviews: (a) Dondoni, A.; Marra, A. *Chem. Rev.* **2000**, *100*, 4395−4421. (b) Gruner, S. A. W.; Locardi, E.; Lohof, E.; Kessler, H. *Chem. Rev.* **2002**, *102*, 491−514. (c) Schweizer, F. *Angew. Chem., Int. Ed.* **2002**, *41*, 230−253.

(6) For a preliminary communication, see: Dondoni, A.; Mariotti, G.; Marra, A. *Tetrahedron Lett.* **2000**, *41*, 3483−3487.

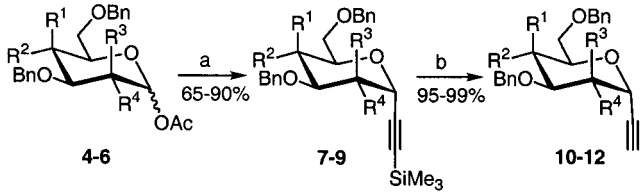
10.1021/jo020054m CCC: $22.00
Published on Web 05/24/2002

Chart 1



1 **2** **3**

Scheme 1[a]



4-6 **7-9** **10-12**

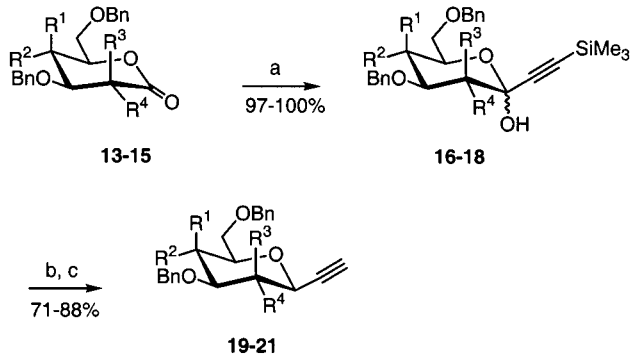
Product		R^1	R^2	R^3	R^4
Galacto	**4, 7, 10**	OBn	H	H	OBn
Gluco	**5, 8, 11**	H	OBn	H	OBn
Manno	**6, 9, 12**	H	OBn	OBn	H

[a] Reagents and conditions: (a) $Bu_3SnC{\equiv}CSiMe_3$, TMSOTf, rt; (b) 1 M NaOH, rt.

Results and Discussion

Synthesis of *C*-glycosyl Acetylenes. Known perbenzylated ethynyl β-*C*-glycosides **1**−**3** (Chart 1) were readily prepared as described by Meldal and Vasella and their co-workers[7] via addition of cerium TMS-acetylide to 1,5-galactonolactone, 1,5-gluconolactone, and 1,5-mannonolactone, respectively, followed by deoxygenation with triethylsilane and boron trifluoride etherate (Et_3SiH−$BF_3{\cdot}Et_2O$) and TMS cleavage with sodium hydroxide. On the other hand, guided by the recent work of Isobe and co-workers,[8] the α-linked derivatives **10**−**12** were obtained by *C*-glycosidation (ethynylation) of the corresponding sugar acetates **4**−**6** using tributylstannyl(trimethylsilyl)acetylene[9] (n-$Bu_3SnC{\equiv}CSiMe_3$) in the presence of trimethylsilyl triflate (TMSOTf) followed by desilylation of the initial adducts **7**−**9** (Scheme 1). Because many natural glycopeptides contain 2-acetamido-2-deoxyglycosyl residues,[1c] we decided to prepare suitable sugar acetylenes that would provide an entry to *C*-GlcNAc, *C*-GalNAc, and *C*-ManAc asparagines. Toward this goal, we focused on the synthesis of α- and β-linked ethynyl 2-azido-2-deoxy-*C*-glycosides since the azido functionality is a well-known precursor to the acetamido group. In Scheme 2 is reported the synthesis of the β-linked derivatives **19**−**21** starting from the corresponding sugar lactones[10] **13**−**15**. As for the preparation of the perbenzylated derivatives **1**−**3**, the reaction sequence involved the addition of cerium TMS-acetylide to the lactone followed by deoxygenation with Et_3SiH and alkaline desilylation. In all cases, the yields of each step were around 90% or higher and only the deoxygenation of the manno derivative **18** produced a mixture of α and β anomers (1:17) that were easily separated to give the pure β-linked isomer **21** in good yield.

Scheme 2[a]

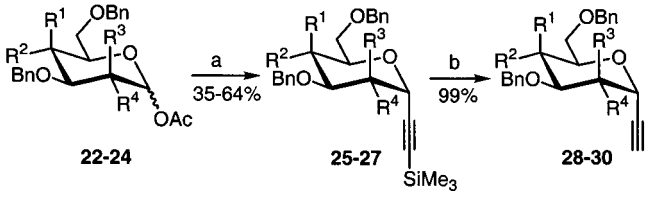


13-15 **16-18** **19-21**

Product		R^1	R^2	R^3	R^4
Galacto	**13, 16, 19**	OBn	H	H	N_3
Gluco	**14, 17, 20**	H	OBn	H	N_3
Manno	**15, 18, 21**	H	OBn	N_3	H

[a] Reagents and conditions: (a) $LiC{\equiv}CSiMe_3$, $CeCl_3$, -78 °C; (b) Et_3SiH, $BF_3{\cdot}Et_2O$, −10 °C; (c) 1 M NaOH, rt.

Scheme 3[a]



22-24 **25-27** **28-30**

Product		R^1	R^2	R^3	R^4
Galacto	**22, 25, 28**	OBn	H	H	N_3
Gluco	**23, 26, 29**	H	OBn	H	N_3
Manno	**24, 27, 30**	H	OBn	N_3	H

[a] Reagents and conditions: (a) $Bu_3SnC{\equiv}CSiMe_3$, TMSOTf, rt; (b) 1 M NaOH, rt.

In Scheme 3 is reported the synthesis of the α-linked derivatives **28**−**30**. Also in this case, the reaction sequence was similar to that of the perbenzylated derivatives although not devoid of some problems. Succinctly, the glycosidation reaction of sugar acetates **22**−**24** with excess n-$Bu_3SnC{\equiv}CSiMe_3$/TMSOTf in a minimum amount of CH_2Cl_2 afforded the corresponding α-linked *C*-glycosides **25**−**27** from which upon TMS cleavage by sodium hydroxide the target ethynyl derivatives **28**−**30** were obtained in variable overall yields. In fact, while the *C*-alkynylation reaction of the galacto derivative **22** proceeded cleanly enough to give the corresponding glycoside **25** in satisfactory yield (63%), the reaction with the gluco and manno derivatives **23** and **24** afforded the desired α-linked *C*-glycosides **26** and **27** in 43 and 35% yield, respectively, together with a comparable amount of the 1,6-anhydro sugars **32** and **33** (Chart 2). Evidently, in the latter cases the intermediate oxycarbenium ion generated by the TMSOTf activation of the substrate

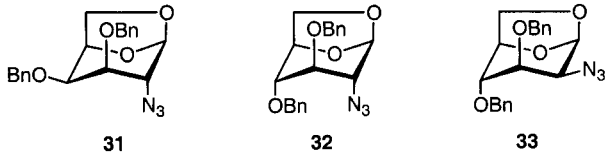
(7) (a) Alzeer, J.; Vasella, A. *Helv. Chim. Acta* **1995**, *78*, 177−193. (b) Lowary, T.; Meldal, M.; Helmboldt, A.; Vasella, A.; Bock, K. *J. Org. Chem.* **1998**, *63*, 9657−9668.

(8) (a) Isobe, M. *J. Synth. Org. Chem., Jpn.* **1994**, *52*, 968−979. (b) Isobe, M.; Nishizawa, R.; Hosokawa, S.; Nishikawa, T. *Chem. Commun.* **1998**, 2665−2676. (c) Nishika, T.; Ishikawa, M.; Isobe, M. *Synlett* **1999**, 123−125.

(9) We have found that a diethylaluminum derivative can be equally used as an efficient ethynylating agent in this reaction. Details on the scope of this environmentally friendly alkynylation reaction will be published elsewhere.

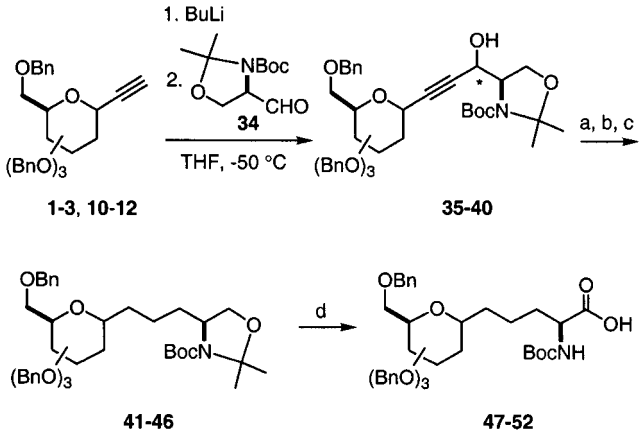
(10) These lactones were obtained in almost quantitative yield by oxidation with pyridinium chlorochromate of the corresponding 2-azido-2-deoxyaldopyranoses.

Chart 2



31 **32** **33**

Scheme 4[a]



[a] Reagents and conditions: (a) $TsNHNH_2$, AcONa, 85 °C; (b) $Im_2C{=}S$, DMAP, 70 °C; (c) Bu_3SnH, AIBN, 85 °C; (d) 1 M Jones reagent, acetone, 0 °C to rt.

undergoes substantial ring closure by intramolecular displacement of the benzyl cation from the C-6 *O*-benzyl group. Despite several attempts by changing the reaction conditions, this side reaction could not be suppressed. In any event, before closing this section it has to be pointed out that the β- and α-linkages of two ethynyl 2-azido-2-deoxy-*C*-glycosides triads **19**−**21** and **28**−**30** were unequivocally assigned by NMR analysis. The anomeric proton (H-3) of compounds **19** and **20** showed a $J_{3,4}$ value of 10.0 Hz, as expected for transdiaxial hydrogen atoms of pyranose units adopting a $^4C_1$ conformation (β-D configuration). On the other hand, the $J_{3,4}$ value of ∼6 Hz observed in the ^{1}H NMR spectra of the corresponding α-D isomers **28** and **29** proved the axial−equatorial relationship between H-3 and H-4 of these molecules. The anomeric configuration of the *C*-mannopyranosides **21** and **30** was established by NOE difference experiments. Upon irradiation of H-3 of both isomers, strong 1,3-diaxial NOE interactions with H-5 and H-7 were observed only for the β-D anomer **21**.

Reaction of Sugar Acetylenes with the Garner Aldehyde. We have developed a convergent approach to Boc *C*-glycosyl α-aminopentanoic acids that is constituted by the coupling of α- or β-D-linked lithium *C*-glycoside acetylides with *N*-Boc D-serinal acetonide (**34**, Garner aldehyde)[11] as a carbon−carbon bond-forming process. The final products are obtained by elaboration of the resulting adducts via reduction of the triple bond, deoxygenation, and oxidative cleavage of the oxazolidine ring (Scheme 4). This convergent approach employing a configurationally stable glycinyl group equivalent and nonanomerizable *C*-glycoside acetylenes avoids the problems encountered in other methods[5] in which the control of the stereochemistry at the anomeric carbon of the sugar residue and/or at the carbon atom of the amino acid group was established in the course of the synthetic sequence. The results of our synthetic efforts are shown below by the preparation of 12 significant examples of α- and β-D-*C*-glycosyl asparagines. In Table 1 are reported the results regarding the transformation of the perbenzylated α- and β-linked ethynyl galactoside, glucoside, and mannoside **1**−**3** and **10**−**12** into the corresponding *C*-glycosyl α-aminopentanoic acids **47**−**52**. In Table 1 are also shown the key intermediates **35**−**40** and **41**−**46** of the reaction sequence whose relevant yields give an estimate on the efficiency of the method. As shown in Scheme 4, the initial coupling was carried out between the in situ generated (BuLi in THF at −50 °C) organolithium derived from the sugar acetylene **1**−**3** and **10**−**12** with **34** to give the functionalized *C*-alkynyl glycosides **35**−**40** as mixtures of diastereomers.[12] These mixtures were first treated with diimide (from tosylhydrazine and sodium acetate)[13] to reduce the triple bond and then subjected to the classical Barton−McCombie deoxygenation protocol[14] to remove the hydroxy group. Each individual pure stereoisomer **41**−**46** was finally transformed into the target amino acid by oxidative cleavage of the oxazolidine ring with Jones reagent (CrO_3, H_2SO_4, H_2O).

While the conservation of the α- or β-configuration as in the original sugar acetylene was easily established by NMR analysis of the intermediates and final products, it appeared worth demonstrating that also the original configuration of the serine embodied in the *N*-Boc oxazolidine ring was maintained throughout the various synthetic manipulations, particularly the final cleavage with Jones reagent.[15] To this aim it was ascertained that the methyl ester of the glucopyranosyl α-amino acid **47** (compound **47a**) prepared from **41** via oxidation with Jones reagent (Table 1) was identical to the product obtained through the amino alcohol **53** and oxidation of the latter with TEMPO−BAIB[16,17] (Scheme 5). An additional proof on the structural integrity of **47a** was provided by an independent synthesis of its epimer **56a**

(11) For an improved synthesis of the Garner aldehyde from serine avoiding partial racemization, see: (a) Dondoni, A.; Perrone, D. *Synthesis* **1997**, 527−529. (b) Dondoni, A.; Perrone, D. *Org. Synth.* **1999**, *77*, 64−77.

(12) The ratio of diastereomeric alcohols as determined in some cases by NMR ranged between 3:1 and 4:1. On the basis of previous examples regarding the addition of nucleophiles to the Garner aldehyde, it may be suggested that the main product is the *anti* adduct (*S*-configured alcohol); see: (a) Dondoni, A.; Perrone, D. *Org. Synth.* **1999**, *77*, 78−90. (b) Liang, X.; Andersch, J.; Bols, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2136−2157.

(13) (a) Dewey, R. S.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1961**, *83*, 3729. (b) Hart, D. J.; Hong, W.-P.; Hsu, L.-Y. *J. Org. Chem.* **1987**, *52*, 4665−4673.

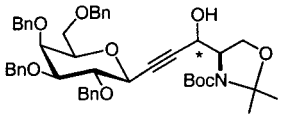
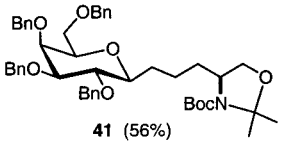
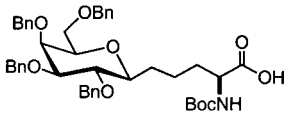
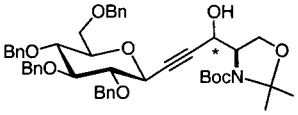
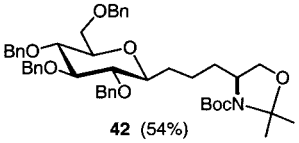
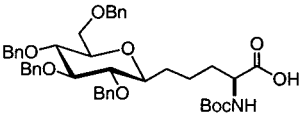
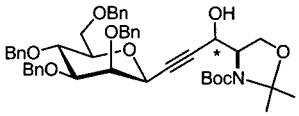
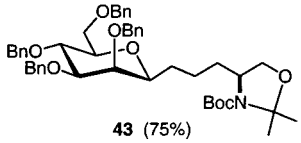
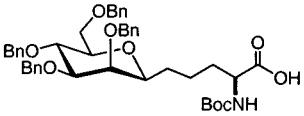
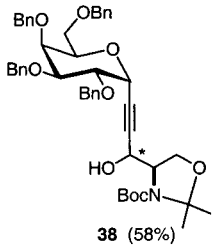
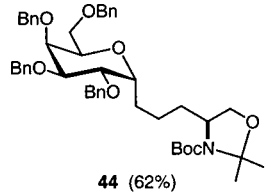
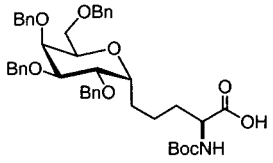
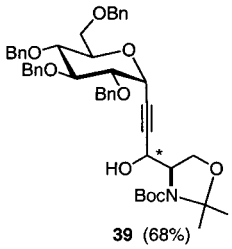
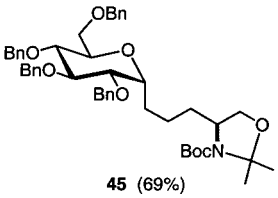
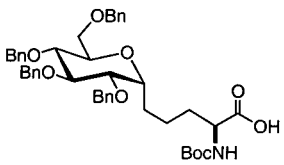
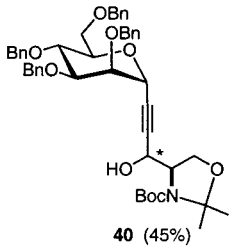
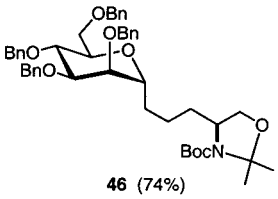
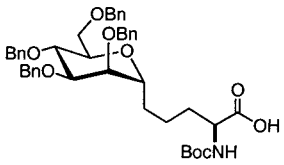
(14) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574−1585.

(15) The use of the *N*-Boc oxazolidine ring as a configurationally stable masked glycinyl moiety via the oxidative cleavage with Jones reagent has been demonstrated in several instances from work carried out in our laboratory. See: (a) Dondoni, A.; Marra, A.; Massi, A. *Tetrahedron* **1998**, *54*, 2827−2832. (b) Dondoni, A.; Marra, A.; Massi, A. *Chem. Commun.* **1998**, 1741−1742. (c) Dondoni, A.; Massi, A.; Marra, A. *Tetrahedron Lett.* **1998**, *39*, 6601−6604. (d) Dondoni, A.; Marra, A.; Massi, A. *J. Org. Chem.* **1999**, *64*, 933−944. (e) Dondoni, A.; Giovannini, P. P.; Marra, A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2380−2388. (f) Dondoni, A.; Mariotti, G.; Marra, A.; Massi, A. *Synthesis* **2001**, 2129−2137.

(16) Epp, J. B.; Widlanski, T. S. *J. Org. Chem.* **1999**, *64*, 293−295.

(17) This two-step oxidative procedure of the oxazolidine ring using TEMPO−BAIB has been recommended by Merino and co-workers when they realized that the use of the Swern reaction to give an open-chain amino aldehyde and treatment with $NaClO_2$ gave complete epimerization (Merino, P.; Franco, S.; Merchan, F. L.; Tejero, T. *J. Org. Chem.* **2000**, *65*, 5575−5589).

Table 1. Synthesis of *C*-Glycosyl Asparagines from Sugar Acetylenes

Sugar Acetylene	Adduct	Sugar Oxazolidine	Product
1	 **35** (56%)	 **41** (56%)	 **47** (93%)
2	 **36** (68%)	 **42** (54%)	 **48** (95%)
3	 **37** (55%)	 **43** (75%)	 **49** (95%)
10	 **38** (58%)	 **44** (62%)	 **50** (93%)
11	 **39** (68%)	 **45** (69%)	 **51** (95%)
12	 **40** (45%)	 **46** (74%)	 **52** (95%)

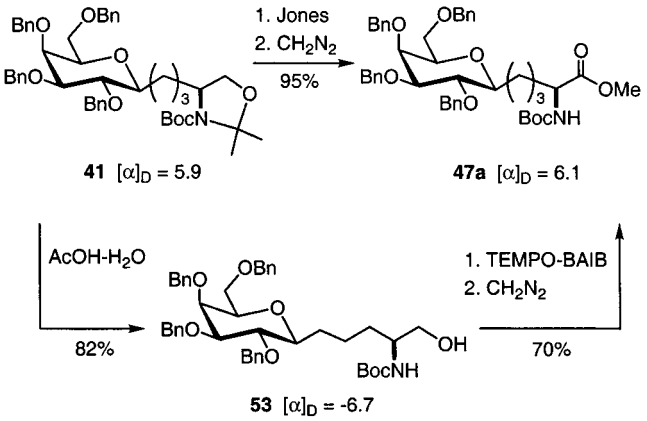
starting from the sugar (*R*)-oxazolidine[18] **54** via both Jones oxidation protocol and the TEMPO−BAIB route of the amino alcohol **55** (Scheme 6). The comparison of the ^{1}H NMR spectra of the two amino esters showed that none of the two products **47a** and **56a** was contaminated by the other epimer (see the Supporting Information). Hence, it may be concluded that the Jones oxidative cleavage of the *N*-Boc oxazolidine ring is a highly reliable protocol for the unmasking of the glycinyl group and there is no need to follow the stepwise and more troublesome processes via either the Swern−$NaClO_2$ or the TEMPO−BAIB route.[17]

As an expanded scope of the methodology we considered of great interest also the synthesis of the 2-acetamido-2-deoxy derivatives of the above *C*-glycosyl asparagines because in the high percentages of naturally occurring *N*-glycopeptides of cell surfaces, asparagine residues are α- or *β*-D-*N*-linked to *N*-acetylgalactosamine (GalNAc), *N*-acetylglucosamine (GlcNAc), and *N*-acetylmannosamine (ManNAc).[1c,19] Glycosidation reactions of

(18) This was prepared by coupling the lithium derivative of the sugar acetylene **1** with the *N*-Boc L-serinal acetonide followed by the usual reduction and deoxygenation steps (see the Experimental Section).

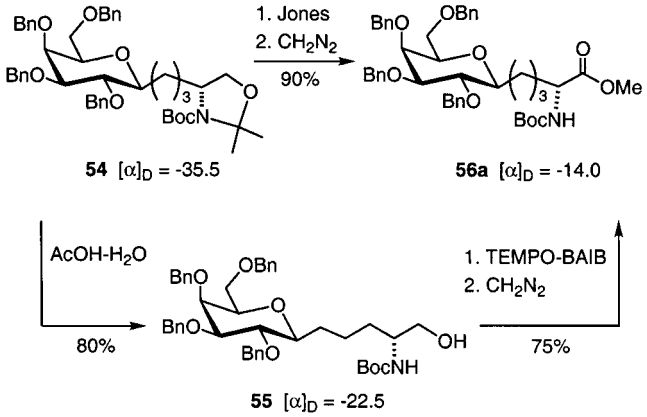
(19) (a) Danishefsky, S. J.; Hu, S.; Cirillo, P. F.; Eckhardt, M.; Seeberger, P. H. *Chem. Eur. J.* **1997**, *3*, 1617−1628. (b) Mizuno, M.; Haneda, K.; Iguchi, R.; Muramoto, I.; Kawakami, T.; Aimoto, S.; Yamamoto, K.; Inazu, T. *J. Am. Chem. Soc.* **1999**, *121*, 284−290.

Scheme 5[a]



[a] Key: $[\alpha]_D$ values measured in $CHCl_3$ with $c = 0.7-1.5$.

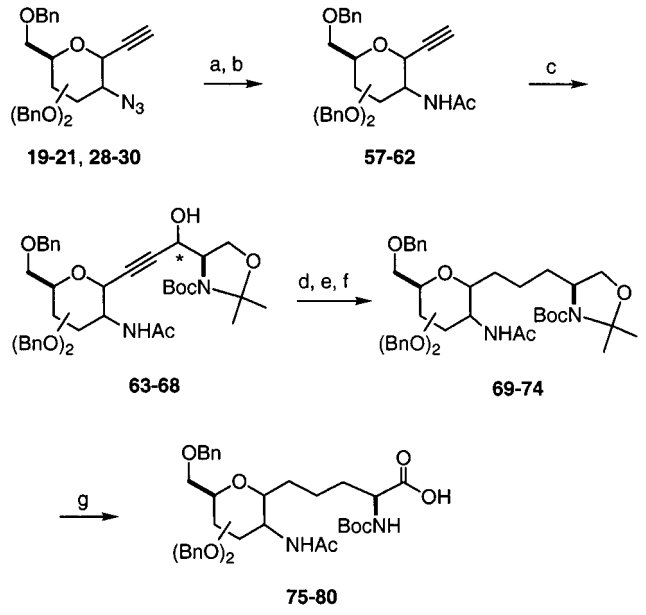
Scheme 6[a]



[a] Key: $[\alpha]_D$ values measured in $CHCl_3$ with $c = 0.4-1.7$.

2-azido-2-deoxy sugar derivatives bearing an unsaturated carbon−carbon bond linked to the anomeric carbon atom are well-known to be complicated by intramolecular 1,3-dipolar cycloaddition reactions of the azido group to the adjacent unsaturated center.[20] This problem became apparent in the reactions between most of the ethynyl 2-azido-2-deoxy-glycosides with the aldehyde **34** which in fact afforded in the majority of the cases an unstable product, very likely a cycloadduct, instead of the desired *C*-glycoside. Therefore, we decided to transform the 2-azido group into the 2-acetamido group in all the azido sugars **19**−**21** (β-linked ethynyl derivatives) and **28**−**30** (α-linked ethynyl derivatives). This reaction was carried out by the classical Staudinger method using triphenylphosphine followed by the hydrolysis of the iminophosphorane intermediate[21] (Scheme 7). The resulting amine was acetylated in situ with acetic anhydride to give the target 2-acetamido derivatives **57**−**62**. After considerable experimentation with different bases (NaH, BuLi, MeLi, LDA, KHMDS) we found that the dianion of the ethynyl 2-acetamido-2-deoxy-*C*-glycosides **57**−**62** was conveniently generated in one step by the use LiHMDS in THF at −20 °C while the addition to the Garner aldehyde **34** was carried out at lower temperature

Scheme 7[a]



[a] Reagents and conditions: (a) PPh_3, H_2O, rt; (b) Ac_2O, rt; (c)LiHMDS, −20 °C, then **34**, −45 °C; (d) $TsNHNH_2$, AcONa, 85 °C; (e) $Im_2C{=}S$, DMAP, 70 °C; (f) Bu_3SnH, AIBN, 85 °C; (g) 1 M Jones reagent, acetone, 0 °C to rt.

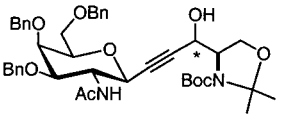
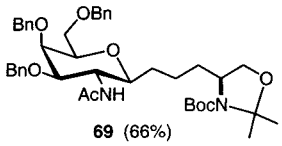
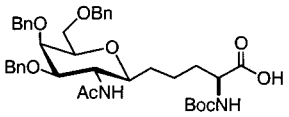
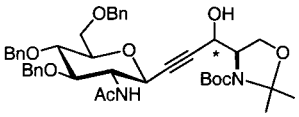
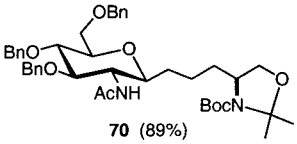
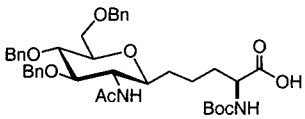
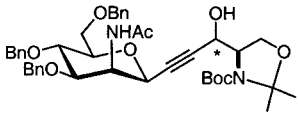
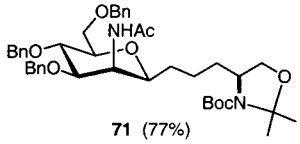
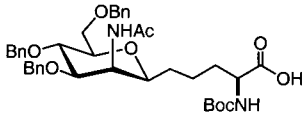
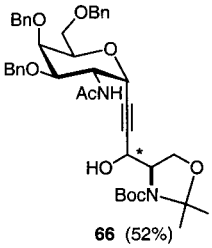
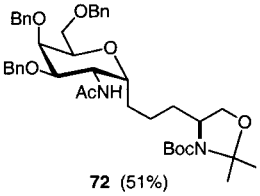
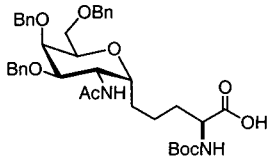
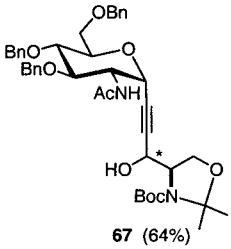
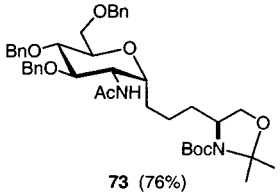
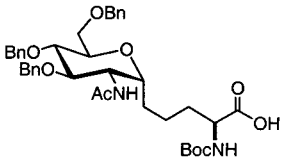
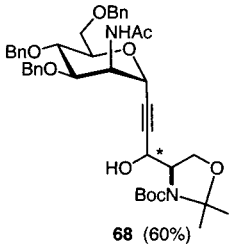
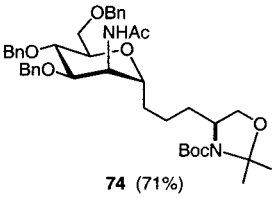
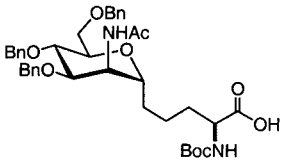
(−45 °C) to avoid racemization of this reagent. Also in these cases the resulting propargylic alcohols **63**−**68** that were obtained as mixtures of diastereomers[12] were suitably elaborated into the sugar alkyl oxazolidine **69**−**74** via reduction of the triple bond using diimide[13] and deoxygenation via the Barton−McCombie protocol.[14] Finally, the cleavage of the *N*-Boc oxazolidine residue by the usual Jones reagent afforded in one step the target 2-acetamido-3,4,5-tri-*O*-benzyl-2-deoxyglycosyl *N*-Boc α-amino acids **75**−**80**. The yields of each of these transformations are collected in Table 2, where it appears that although the values are relatively lower than in Table 1 they remain at satisfactory levels. It is worth mentioning that the sugar oxazolidines **69**−**74** can be also elaborated into peracetylated *N*-Boc and *N*-Fmoc glycosyl amino acids suitable for peptide synthesis by different techniques (see the Supporting Information).

A brief recapitulation and a few comments before closing this section may help to better evaluate the above results. For the first time, a significant number of *C*-glycosyl amino acid isosteres of *N*-glycosyl asparagines have been prepared by a single general reaction scheme whose key operation is the coupling between a stereochemically stable sugar acetylene derivative and a serine derived aldehyde. Hence, the method highlights the use of ethynyl *C*-glycosides as readily accessible and configurationally stable synthetic equivalents of α- and β-ethyl glycoside carbanions and therefore may serve to introduce these reagents as building blocks of great synthetic utility. Some of the amino acids presented in Tables 1 and 2 have been the targets of disparate synthetic approaches that appear plagued of much less generality.[5] For example, our earlier synthesis of the β-linked perbenzylated triad **47**−**49** by a Mukaiyama-type condensation reaction of sugar aldehydes and silyl enol ether[15d] can be hardly extended to the α-linked triad because of the difficult access and instability of formyl α-*C*-glycosides. A single example exists of a previous synthesis of a 2-acetamido-2-deoxy derivative despite the great bio-

(20) (a) Bertozzi, C. R.; Bednarski, M. D. *Tetrahedron Lett.* **1992**, *33*, 3109−3112. (b) Dondoni, A.; Scherrmann, M.-C.; Marra, A.; Delépine, J.-L. *J. Org. Chem.* **1994**, *59*, 7517−7520.

(21) A similar procedure on a sugar derivative has been described; see: Leteux, C.; Veyrières, A. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2647−2655.

Table 2. Synthesis of 2-Acetamido-2-deoxy-*C*-glycosyl Asparagines from Sugar Acetylenes

Sugar Acetylene	Adduct	Sugar Oxazolidine	Product
57	 **63** (75%)	 **69** (66%)	 **75** (90%)
58	 **64** (88%)	 **70** (89%)	 **76** (94%)
59	 **65** (88%)	 **71** (77%)	 **77** (92%)
60	 **66** (52%)	 **72** (51%)	 **78** (87%)
61	 **67** (64%)	 **73** (76%)	 **79** (94%)
62	 **68** (60%)	 **74** (71%)	 **80** (75%)

logical relevance of these compounds. In fact, the β-linked gluco derivative **76** was prepared by Kessler via amino aldehyde coupling with dilithio *N*-acetylglucosamine.[22] However, this method does not appear to be extensible to the synthesis of α-linked derivatives or to any type of polyhydroxylated products as discussed in a recent account.[5] In conclusion, the examples reported in Tables 1 and 2 and the satisfactory yields of each step support the generality and efficiency of this new synthetic protocol leading to ethylene isosteres of *N*-glycosyl asparagines and indicate the potential of the method for the preparation of glycosyl α-amino pentanoic acids with great molecular diversity in the glycoside residue.

Experimental Section

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Anhydrous solvents were dried over standard drying agents[23] and freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (5 μm average particle size) were used without further activation. Reactions were monitored by TLC

(22) Burkhart, F.; Hoffmann, M.; Kessler, H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1191−1192.

(23) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth-Heinemann: Oxford, 1996.

on silica gel 60 F_{254} with detection by charring with sulfuric acid and/or ninhydrin. Flash column chromatography[24] was performed on silica gel 60 (230−400 mesh). Melting points were determined with a capillary apparatus. Optical rotations were measured at 20 ± 2 °C in the stated solvent; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H (300 MHz) NMR spectra were recorded for $CDCl_3$ solutions at rt unless otherwise specified; chemical shifts are in ppm (δ) from $SiMe_4$ (TMS) as internal standard; assignments were aided by homo- and heteronuclear two-dimensional experiments. MALDI-TOF mass spectra were acquired using α-cyano-4-hydroxycinnamic acid as the matrix. Tributylstannyl(trimethylsilyl)acetylene[25] and Garner aldehyde[11] **34** were prepared on a multigram scale as described. Ethynyl β-D-glycosides **1**−**3** were synthesized according to the experimental procedure reported in the literature.[7b] Galactoside **1**: mp 79−80 °C (pentane); $[\alpha]_D$ = +9.9 (*c* 0.9, $CHCl_3$) (lit.[7b] $[\alpha]_D$ = +5.9 (*c* 0.8, $CHCl_3$)). Glucoside **2**: mp 66−67 °C (pentane); $[\alpha]_D$ = +17.3 (*c* 2.0, $CHCl_3$) (lit.[7a] mp 58 °C, $[\alpha]_D$ = +17.4 (*c* 1.6, $CHCl_3$)). Mannoside **3**: mp 94−96 °C (pentane); $[\alpha]_D$ = −31.8 (*c* 1.1, $CHCl_3$) (lit.[7b] $[\alpha]_D$ = −29.1 (*c* 0.5, $CHCl_3$)). Known tetra-*O*-benzylpyranose acetates **4**,[26] **5**,[26] and **6**[27] and 2-azido-tri-*O*-benzylpyranose acetates **22**,[28] **23**,[28] and **24**[29] were obtained as a mixture of anomers by acetylation (Ac_2O, Py) of the corresponding 1-OH derivatives. Sugar lactones **13**,[30] **14**,[31] and **15**[32] were prepared by oxidation of the corresponding hemiacetal with pyridinium chlorochromate.[33]

3,7-Anhydro-4,5,6,8-tetra-*O*-benzyl-1,2-dideoxy-D-*glycero*-L-*gluco*-oct-1-ynitol (10). A mixture of acetate **4** (1.00 g, 1.71 mmol), tributylstannyl(trimethylsilyl)acetylene (1.32 g, 3.42 mmol), activated 4-Å powdered molecular sieves (1.0 g), and anhydrous CH_2Cl_2 (7 mL) was stirred at rt for 15 min, and then trimethylsilyl triflate (0.61 mL, 3.42 mmol) was added dropwise. The dark brown mixture was stirred at rt for an additional 1.5 h, diluted with Et_3N (1 mL) and CH_2Cl_2 (30 mL), filtered through a pad of Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 20:1 to 10:1) to afford syrupy **7** (917 mg, 87%) slightly contaminated by tin-containing byproducts. ^{1}H NMR: δ 7.42−7.23 (m, 20 H, 4 Ph), 4.96 and 4.60 (2 d, 2 H, *J* = 11.3 Hz, PhC*H*$_2$), 4.87 (d, 1 H, $J_{3,4}$ = 5.9 Hz, H-3), 4.83 and 4.75 (2 d, 2 H, *J* = 11.9 Hz, PhC*H*$_2$), 4.79 and 4.72 (2 d, 2 H, *J* = 11.8 Hz, PhC*H*$_2$), 4.51 and 4.43 (2 d, 2 H, *J* = 12.0 Hz, PhC*H*$_2$), 4.15 (ddd, 1 H, $J_{6,7}$ = 0.5 Hz, $J_{7,8a}$ = 5.9 Hz, $J_{7,8b}$ = 7.0 Hz, H-7), 4.10 (dd, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 3.97 (dd, 1 H, $J_{5,6}$ = 3.0 Hz, H-6), 3.88 (dd, 1 H, H-5), 3.58 (dd, 1 H, $J_{8a,8b}$= 10.0 Hz, H-8a), 3.55 (dd, 1 H, H-8b), 0.21 (s, 9 H, $SiMe_3$). MALDI-TOF MS: 644.4 (M^+ + Na), 660.6 (M^+ + K).

A solution of **7** (1.00 g, 1.60 mmol) in 5:1 CH_3OH−CH_2Cl_2 (56 mL) was treated at rt for 1 h with 1 N NaOH (2.8 mL), neutralized with 1 N HCl, and concentrated to remove the organic solvent. The residue was diluted with AcOEt (100 mL), washed with H_2O, dried (Na_2SO_4), concentrated, and filtered through a short column of silica gel (3 × 8 cm, d × h) with 10:1 cyclohexane−AcOEt to afford **10** (0.88 g, 100%) as a syrup. $[\alpha]_D$ = +31.1 (*c* 1.7, $CHCl_3$). ^{1}H NMR: δ 7.43−7.24 (m, 20 H, 4 Ph), 4.96 and 4.59 (2 d, 2 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.88 and 4.74 (2 d, 2 H, *J* = 12.0 Hz, PhC*H*$_2$), 4.83 and 4.78 (2 d, 2 H, *J* = 11.9 Hz, PhC*H*$_2$), 4.82 (dd, 1 H, $J_{1,3}$ = 2.5 Hz, $J_{3,4}$ = 6.0 Hz, H-3), 4.51 and 4.42 (2 d, 2 H, *J* = 12.0 Hz, PhC*H*$_2$), 4.15 (ddd, 1 H, $J_{6,7}$ = 0.5 Hz, $J_{7,8a}$ = $J_{7,8b}$ = 6.0 Hz, H-7), 4.12 (dd, 1 H, $J_{4,5}$ = 9.8 Hz, H-4), 4.00 (dd, 1 H, $J_{5,6}$ = 3.0 Hz, H-6), 3.57 (dd, 1 H, $J_{8a,8b}$ = 9.5 Hz, H-8a), 3.53 (dd, 1 H, H-8b), 3.91 (dd, 1 H, H-5), 2.54 (d, 1 H, H-1). MALDI-TOF MS: 572.1 (M^+ + Na), 588.3 (M^+ + K). Anal. Calcd for $C_{36}H_{36}O_5$: C, 78.80; H, 6.61. Found: C, 78.70; H, 6.55.

4-Azido-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-1-*C*-(trimethylsilyl)-D-*galacto*-oct-1-yn-3-ulopyranose (16). Commercially available $CeCl_3$·$7H_2O$ (2.98 g, 7.87) was heated in a reaction flask at 120 °C/0.1 mbar for 1 h and 140 °C/0.1 mbar for 1 h, cooled to 0 °C in an argon atmosphere, diluted with anhydrous THF (31 mL), stirred at rt for 2 h, and then cooled to −78 °C. To a cooled (−78 °C), stirred solution of commercially available trimethylsilylacetylene (1.50 mL, 10.93 mmol) in anhydrous THF (12 mL) was slowly added butyllithium (6.8 mL, 10.9 mmol, of a 1.6 M solution in hexane). The solution was stirred at −78 °C for 45 min, transferred via cannula into the stirred suspension of $CeCl_3$ in THF, prepared immediately before the use. The resulting yellow mixture was stirred at −78 °C for 30 min, and then a solution of sugar lactone **13** (2.07 g, 4.37 mmol) in anhydrous THF (31 mL) was added dropwise. The mixture was stirred at −78 °C for an additional 2 h, diluted with 0.1 M HCl (50 mL), allowed to reach rt, and extracted with Et_2O (3 × 60 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give syrupy **16** (2.41 g, 98%) as a 1:1 mixture of anomers ∼95% pure by ^{1}H NMR analysis. This product was used for the following step without further purification. ^{1}H NMR selected data: δ 7.45−7.23 (m, 15 H, 3 Ph), 4.97 and 4.59 (2 d, 1 H, *J* = 11.0 Hz, PhC*H*$_2$), 4.96 and 4.59 (2 d, 1 H, *J* = 11.9 Hz, PhC*H*$_2$), 4.76 and 4.72 (2 d, 1 H, *J* = 11.7 Hz, PhC*H*$_2$), 3.08 (m, 0.5 H, *J* = 1.2 Hz, OH), 0.22 and 0.21 (2 s, 9 H, $SiMe_3$).

3,7-Anhydro-4-azido-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-D-*glycero*-L-*manno*-oct-1-ynitol (19). To a cooled (−10 °C), stirred solution of **16** (2.41 g, 4.20 mmol) and triethylsilane (2.67 mL, 16.80 mmol) in anhydrous CH_3CN (56 mL) and CH_2Cl_2 (28 mL) was added dropwise freshly distilled BF_3·Et_2O (2.1 mL, 16.80 mmol). Stirring was continued at −10 °C for an additional 1 h, and then the mixture was diluted with Et_3N (2 mL) and concentrated. A solution of the residue in CH_2Cl_2 (200 mL) was washed with H_2O, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 10:1 cyclohexane−AcOEt to afford 3,7-anhydro-4-azido-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-1-*C*-(trimethylsilyl)-D-*glycero*-L-*manno*-oct-1-ynitol as a syrup (1.76 g). ^{1}H NMR selected data: δ 7.42−7.24 (m, 15 H, 3 Ph), 4.91 and 4.60 (2 d, 2 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.72 (s, 2 H, PhC*H*$_2$), 4.48 and 4.42 (2 d, 2 H, *J* = 11.5 Hz, PhC*H*$_2$), 3.97 (dd, 1 H, $J_{3,4}$ = 10.0, $J_{4,5}$ = 9.5 Hz, H-4), 3.93 (dd, 1 H, $J_{5,6}$ = 3.0, $J_{6,7}$ = 0.5 Hz, H-6), 3.87 (d, 1 H, H-3), 3.27 (dd, 1 H, H-5), 0.20 (s, 9 H, $SiMe_3$). This compound was desilylated as described for the preparation of **10** to give, after column chromatography on silica gel (9:1 cyclohexane−AcOEt), **19** (1.48 g, 73%) as a white solid. Mp: 80−82 °C (cyclohexane). $[\alpha]_D$ = +0.1 (*c* 1.5, $CHCl_3$). ^{1}H NMR: δ 7.48−7.25 (m, 15 H, 3 Ph), 4.92 and 4.59 (2 d, 2 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.76 and 4.70 (2 d, 2 H, *J* = 12.0 Hz, PhC*H*$_2$), 4.49 and 4.42 (2 d, 2 H, *J* = 12.0 Hz, PhC*H*$_2$), 4.00 (dd, 1 H, $J_{3,4}$ = 10.0 Hz, $J_{4,5}$ = 9.5 Hz, H-4), 3.96 (dd, 1 H, $J_{5,6}$ = 2.5 Hz, $J_{6,7}$ = 0.5 Hz, H-6), 3.85 (dd, 1 H, $J_{1,3}$ = 2.0 Hz, H-3), 3.62−3.50 (m, 3 H), 3.36 (dd, 1 H, H-5), 2.57 (d, 1 H, H-1). Anal. Calcd for $C_{29}H_{29}N_3O_4$: C, 72.02; H, 6.06; N, 8.69. Found: C, 72.20; H, 6.14; N, 8.60.

3,7-Anhydro-4-azido-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-1-*C*-(trimethylsilyl)-D-*glycero*-L-*gluco*-oct-1-ynitol (25). A mixture of acetate **22** (2.00 g, 3.86 mmol), tributylstannyl-(trimethylsilyl)acetylene (4.47 g, 11.58 mmol), activated 4-Å powdered molecular sieves (2.0 g), and anhydrous CH_2Cl_2 (19 mL) was stirred at rt for 15 min, and then trimethylsilyl triflate (1.7 mL, 7.72 mmol) was added dropwise. The dark brown mixture was stirred at rt for an additional 2.5 h, diluted with Et_3N (2 mL) and CH_2Cl_2 (60 mL), filtered through a pad of Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 20:1 to 10:1) to afford first syrupy **25** (1.37 g, 64%) slightly contaminated by tin-containing byproducts. ^{1}H NMR: δ 7.45−7.23 (m, 15

(24) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.
(25) Logue, M. W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549−2553.
(26) Austin, P. W.; Hardy, F. E.; Buchanan, J. G.; Boddiley, J. *J. Chem. Soc.* **1964**, 2128−2137.
(27) Meuwly, R.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 25−34.
(28) Bovin, N. V.; Zurabyan, S. E.; Khorlin, A. Y. *Carbohydr. Res.* **1981**, *98*, 25−36.
(29) Paulsen, H.; Larentzen, J. P.; Kutschker, W. *Carbohydr. Res.* **1985**, *136*, 153−176.
(30) Dondoni, A.; Scherrmann, M.-C. *J. Org. Chem.* **1994**, *59*, 6404−6412.
(31) Ayadi, E.; Czernecki, S.; Xie, J. *J. Carbohydr. Chem.* **1996**, *15*, 191−200.
(32) Dupradeau, F.-Y.; Hakomori, S.; Toyokuni, T. *J. Chem. Soc., Chem. Commun.* **1995**, 221−222.
(33) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647−2650.

H, 3 Ph), 4.92 and 4.59 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.80 (d, 1 H, $J_{3,4}$ = 5.5 Hz, H-3), 4.79 and 4.70 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.57 and 4.46 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.14 (ddd, 1 H, $J_{6,7}$ = 1.0 Hz, $J_{7,8a}$ = 7.0 Hz, $J_{7,8b}$ = 6.0 Hz, H-7), 4.07 (dd, 1 H, $J_{5,6}$ = 2.5 Hz, H-6), 4.03 (dd, 1 H, $J_{4,5}$ = 10.5 Hz, H-4), 3.91 (dd, 1 H, H-5), 3.62 (dd, 1 H, $J_{8a,8b}$ = 11.0 Hz, H-8a), 3.59 (dd, 1 H, H-8b), 0.20 (s, 9 H, $SiMe_3$). Eluted second was the anhydro sugar **31** (142 mg, 10%) as a syrup. $[\alpha]_D$ = +31.3 (*c* 0.6, $CHCl_3$) (lit.[35] $[\alpha]_D$ = +32.8 (*c* 1.0, $CHCl_3$)). ^{1}H NMR: δ 7.41−7.30 (m, 10 H, 2 Ph), 5.45 (dd, 1 H, $J_{1,2}$ = $J_{1,3}$ = 1.5 Hz, H-1), 4.70 (s, 2 H, PhCH_2), 4.64 and 4.55 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.62−4.50 (m, 2 H), 3.89 (dddd, 1 H, $J_{2,3}$ = 1.4 Hz, $J_{3,4}$ = 5.0 Hz, $J_{3,5}$ = 1.5 Hz, H-3), 3.84 (ddd, 1 H, $J_{4,5}$ = 3.5 Hz, $J_{4,6b}$ = 1.0 Hz, H-4), 3.71 (ddd, 1 H, $J_{5,6b}$ = 5.5 Hz, $J_{6a,6b}$ = 7.0 Hz, H-6b), 3.58 (dd, 1 H, H-2). MALDI-TOF MS: 391.5 (M^+ + Na), 407.8 (M^+ + K). Anal. Calcd for $C_{20}H_{21}N_3O_4$: C, 65.38; H, 5.76; N, 11.44. Found: C, 65.40; H, 5.70; N, 11.54.

3,7-Anhydro-4-azido-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-1-*C*-(trimethylsilyl)-D-*glycero*-D-*ido*-oct-1-ynitol (26). A mixture of acetate **23** (1.16 g, 2.25 mmol), tributylstannyl-(trimethylsilyl)acetylene (4.34 g, 11.25 mmol), and activated 4-Å powdered molecular sieves (1.0 g) was stirred at rt for 15 min, and then a solution of trimethylsilyl triflate (0.81 mL, 4.50 mmol) in anhydrous CH_2Cl_2 (9 mL) was added over a 10 min period. The dark brown mixture was stirred at rt for an additional 3 h, diluted with Et_3N (1 mL) and CH_2Cl_2 (50 mL), filtered through a pad of Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane-AcOEt (from 50:1 to 20:1) to afford first syrupy **26** (537 mg, 43%) slightly contaminated by tin-containing byproducts. ^{1}H NMR: δ 7.42−7.18 (m, 15 H, 3 Ph), 4.95 and 4.90 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.83 (d, 1 H, $J_{3,4}$ = 5.7 Hz, H-3), 4.82 and 4.56 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.65 and 4.53 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.01 (ddd, 1 H, $J_{6,7}$ = 9.5 Hz, $J_{7,8a}$ = 3.5 Hz, $J_{7,8b}$ = 2.0 Hz, H-7), 3.93 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, $J_{5,6}$ = 9.0 Hz, H-5), 3.82 (dd, 1 H, $J_{8a,8b}$ = 11.0 Hz, H-8a), 3.74 (dd, 1 H, H-6), 3.70 (dd, 1 H, H-8b), 3.56 (dd, 1 H, H-4), 0.23 (s, 9 H, $SiMe_3$). Eluted second was the anhydro sugar **32** (336 mg, 40%) as a syrup. $[\alpha]_D$ = + 36.7 (*c* 0.6, $CHCl_3$) (lit.[36] $[\alpha]_D$ = +37 (*c* 1, $CHCl_3$); lit.[37] $[\alpha]_D$ = +37.8 (*c* 0.34, $CHCl_3$)). ^{1}H NMR: δ 7.43−7.22 (m, 10 H, 2 Ph), 5.49 (dd, 1 H, J = 0.5 Hz), 4.72 and 4.51 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.58 (dd, 1 H, J = 0.5, 6.0 Hz), 4.52 and 4.46 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.28 (d, 1 H, J = 7.6 Hz), 3.89 (dd, 1 H, J = 1.5, 5.8 Hz), 3.79 (dd, 1 H, J = 6.0, 6.3 Hz), 3.48 (d, 1 H, J = 1.0 Hz), 3.16 (dd, 1 H, J = 1.0, 5.0 Hz). MALDI-TOF MS: 391.4 (M^+ + Na), 407.7 (M^+ + K). Anal. Calcd for $C_{20}H_{21}N_3O_4$: C, 65.38; H, 5.76; N, 11.44. Found: C, 65.32; H, 5.76; N, 11.46.

3,7-Anhydro-4-azido-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-1-*C*-(trimethylsilyl)-D-*glycero*-D-*talo*-oct-1-ynitol (27). A mixture of acetate **24** (710 mg, 1.36 mmol), tributylstannyl-(trimethylsilyl)acetylene (2.62 g, 6.80 mmol), activated 4-Å powdered molecular sieves (0.6 g), and anhydrous CH_2Cl_2 (2.7 mL) was stirred at rt for 15 min, and then trimethylsilyl triflate (245 mL, 1.36 mmol) was added over a 10 min period. The dark brown mixture was stirred at rt for an additional 2 h, diluted with Et_3N (0.5 mL) and CH_2Cl_2 (50 mL), filtered through a pad of Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 10:1 to 5:1) to afford first **27** (264 mg, 35%) as a syrup. $[\alpha]_D$ = +57.2 (*c* 0.9, $CHCl_3$). ^{1}H NMR: δ 7.42−7.21 (m, 15 H, 3 Ph), 4.86 and 4.54 (2 d, 2 H, J = 10.7 Hz, PhCH_2), 4.78 (s, 2 H, PhCH_2), 4.73 (d, 1 H, $J_{3,4}$ = 2.0 Hz, H-3), 4.68 and 4.54 (2 d, 2 H, J = 12.3 Hz, PhCH_2), 4.14 (ddd, 1 H, $J_{6,7}$ = 9.1 Hz, $J_{7,8a}$ = 3.7 Hz, $J_{7,8b}$ = 1.9 Hz, H-7), 3.94−3.88 (m, 3 H), 3.78 (dd, 1 H, $J_{8a,8b}$ = 11.0 Hz, H-8a), 3.68 (dd, 1 H, H-6b), 0.19 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{32}H_{37}N_3O_4Si$: C, 69.15; H, 6.72; N, 7.56. Found: C, 69.20; H, 6.78; N, 7.47. Eluted second was the anhydro sugar **33** (174 mg, 35%) slightly contaminated by uncharacterized byproducts. ^{1}H NMR selected data: δ 7.42−7.25 (m, 10 H, 2 Ph), 5.58 (bs, 1 H, H-1), 4.70 and 4.50 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.52 and 4.45 (2 d, 2 H, J = 12.2 Hz, PhCH_2), 4.28 (dd, 1 H, J = 0.8, 7.4 Hz), 3.78 (dd, 1 H, J = 6.1, 7.4 Hz), 3.16 (dd, 1 H, J = 1.0, 5.5 Hz). MALDI-TOF MS: 391.3 (M^+ + Na), 407.6 (M^+ + K).

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,4,5-trideoxy-1,2-*N*,*O*-isopropylidene-2-(*tert*-butoxycarbonylamino)-D-*lyxo*-D-*manno*- and -D-*altro*-undec-4-ynitol (35). To a cooled (−50 °C), stirred solution of **1** (0.83 g, 1.50 mmol) in anhydrous THF (7 mL) was slowly added butyllithium (1.03 mL, 1.65 mmol, of a 1.6 M solution in hexane). Stirring was continued for 30 min, and then a solution of **34** (0.86 g, 3.75 mmol) in anhydrous THF (1.5 mL) was added dropwise. The reaction mixture was stirred at −50 °C for an additional 1.5 h, diluted with 1 M phosphate buffer at pH = 7 (8 mL), and allowed to reach rt. The suspension was diluted with Et_2O (40 mL), and the phases were separated. The aqueous layer was extracted twice with Et_2O (40 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 4:1 to 3:1) to afford first unreacted **1** (0.17 g, 20%). Eluted second was syrupy **35** as a ∼4:1 mixture of diastereomers (0.65 g, 56%). ^{1}H NMR (DMSO-d_6, 120 °C) selected data of the main isomer: δ 7.40−7.20 (m, 20 H, 4 Ph), 5.20 (d, 1 H, J = 7.0 Hz, OH), 4.99 and 4.61 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.98 and 4.65 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.79 and 4.72 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.52 and 4.45 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 3.51 (d, 1 H, $J_{6,7}$ = 9.0 Hz, H-6), 1.56 and 1.45 (2 s, 6 H, 2 Me), 1.42 (s, 9 H, *t*-Bu). MALDI-TOF MS: 802.2 (M^+ + Na), 818.2 (M^+ + K). Anal. Calcd for $C_{47}H_{55}NO_9$: C, 72.56; H, 7.13; N, 1.80. Found: C, 72.43; H, 7.31; N, 1.86.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-1,2-*N*,*O*-isopropylidene-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*galacto*-undecitol (41). To a warmed (85 °C), stirred solution of **35** (600 mg, 0.77 mmol) and freshly recrystallized *p*-toluenesulfonhydrazide (859 mg, 4.62 mmol) in dimethoxyethane (5 mL) was added 1 M aqueous sodium acetate (4.6 mL) in six portions during 3 h. After an additional 2.5 h at 85 °C, the mixture was diluted with H_2O (4 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The organic phase was dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane-AcOEt to give a mixture of syrupy **3-hydroxy-41** (481 mg, 80%) as a ∼4:1 mixture of diastereomers. ^{1}H NMR (DMSO-d_6, 60 °C) selected data of the main isomer: δ 7.42−7.25 (m, 20 H, 4 Ph), 5.82 (dd, 1 H, OH), 4.98 and 4.64 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.96 and 4.69 (2 d, 2 H, J = 10.3 Hz, PhCH_2), 4.79 and 4.71 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.51 and 4.45 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 3.98 (dd, 1 H, $J_{8,9}$ = 2.6 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.91 (dd, 1 H $J_{7,8}$ = 9.0 Hz, H-8), 3.71 (dd, 1 H, $J_{6,7}$ = 9.0 Hz, H-7), 3.30 (ddd, 1 H, $J_{5a,6}$ = 9.0 Hz, $J_{5b,6}$ = 2.6 Hz, H-6), 1.58 and 1.48 (2 s, 6 H, 2 Me), 1.46 (s, 9 H, *t*-Bu).

To a warmed (70 °C), stirred solution of **3-hydroxy-41** (150 mg, 0.19 mmol) in anhydrous THF (1.5 mL) were added 1,1-thiocarbonyldiimidazole (339 mg, 1.90 mmol) and 4-*N*,*N*-(dimethylamino)pyridine (348 mg, 2.85 mmol). The mixture was stirred at 70 °C for an additional 5 h and then concentrated. The residue was eluted from a short column of silica gel (1 × 10 cm, d × h) with 3:1 cyclohexane−AcOEt to give the corresponding thiocarbonylimidazolides (146 mg) slightly contaminated by uncharacterized byproducts. To a warmed (85 °C), stirred solution of the thiocarbonylimidazolides in anhydrous toluene (1.5 mL) were added Bu_3SnH (0.43 mL, 1.60 mmol) and AIBN (26 mg, 0.16 mmol). The solution was stirred at 85 °C for an additional 2 h and then concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 10:1 to 4:1) to give **41** (104 mg, 70%) as a syrup; $[\alpha]_D$ = +6.0 (*c* 0.9, $CHCl_3$) (lit.[15d] $[\alpha]_D$ = +5.9 (*c* 0.7, $CHCl_3$)). The ^{1}H NMR spectrum of compound **41** was identical to that of the product prepared by another route.[15d]

(34) Goekjian, P. G.; Wu, T.-S.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6422−6434.
(35) Paulsen, H.; Kolár, C.; Stenzel, W. *Chem. Ber.* **1978**, *111*, 2358−2369.
(36) Paulsen, H.; Stenzel, W. *Ber.* **1978**, *111*, 2334−2347.
(37) Hori, H.; Nishida, Y.; Ohrui, H.; Meguro, H. *J. Org. Chem.* **1989**, *54*, 1347−1353.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*galacto*-undeconic Acid (47). To a cooled (0 °C), stirred solution of **41** (67 mg, 0.09 mmol) in acetone (1.5 mL) was added freshly prepared 1 M Jones reagent (0.26 mL, 0.26 mmol). The mixture was allowed to warm to room temperture over 30 min, stirred at rt for an additional 3 h, and then diluted with 2-propanol (~0.1 mL). The suspension was neutralized with saturated aqueous $NaHCO_3$, diluted with Et_2O (30 mL), and washed with brine (2 × 5 mL). The organic phase was dried (Na_2SO_4) and concentrated to afford **47** (62 mg, 93%) as a syrup ~95% pure by ^{1}H NMR analysis. The ^{1}H NMR spectrum of compound **47** was identical to that of the product prepared by another route.[15d]

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*galacto*-undeconate (47a). Route a. Treatment of a solution of crude acid **47** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (5:1 cyclohexane−AcOEt), **47a** as a syrup. $[\alpha]_D = +6.3$ (*c* 0.8, $CHCl_3$) (lit.[15d] $[\alpha]_D = +6.4$ (*c* 0.5, $CHCl_3$)). The ^{1}H NMR spectrum of compound **47a** was identical to that of the product prepared by another route.[15d]

Route b. A mixture of **53** (107 mg, 0.15 mmol), [bis(acetoxy)-iodo]benzenze (BAIB, 104 mg, 0.32 mmol), 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO, 4.7 mg, 0.03 mmol), CH_3CN (0.5 mL), and H_2O (0.5 mL) was stirred at rt for 4 h, filtered through a pad of Celite, and concentrated. Treatment of a solution of the residue in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column cromatography on silica gel (5:1 cyclohexane−AcOEt), **47a** (79 mg, 70%) as a syrup. $[\alpha]_D = +6.1$ (*c* 1.0, $CHCl_3$).

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*galacto*-undeconic Acid (48). Compound **42** (200 mg, 0.26 mmol) was treated with Jones reagent as described for the preparation of **47** to give **48** (180 mg, 95%) as a syrup ~95% pure by ^{1}H NMR analysis. The ^{1}H NMR spectrum of **48** was identical to that of the product prepared by another route.[15d]

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*galacto*-undeconate (48a). Treatment of a solution of crude acid **48** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (5:1 cyclohexane−AcOEt), **48a** as a syrup. $[\alpha]_D = +6.2$ (*c* 0.8, $CHCl_3$) (lit.[15d] $[\alpha]_D = +6.2$ (*c* 0.7, $CHCl_3$)). The ^{1}H NMR spectrum of compound **48a** was identical to that of the product prepared by another route.[15d]

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gluco*-undeconic Acid (49). Compound **43** (110 mg, 0.14 mmol) was treated with Jones reagent as described for the preparation of **47** to give **49** (98 mg, 95%) as a syrup ~95% pure by ^{1}H NMR analysis. The ^{1}H NMR spectrum of **49** was identical to that of the product prepared by another route.[15d]

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonyl-amino)-D-*erythro*-L-*gluco*-undeconate (49a). Treatment of a solution of crude acid **49** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (5:1 cyclohexane−AcOEt), **49a** as a syrup. $[\alpha]_D = +5.2$ (*c* 0.4, $CHCl_3$) (lit.[15d] $[\alpha]_D = +5.5$ (*c* 0.6, $CHCl_3$)). The ^{1}H NMR spectrum of compound **49a** was identical to that of the product prepared by another route.[15d]

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*gulo*-undeconic Acid (50). Compound **44** (100 mg, 0.13 mmol) was treated with Jones reagent as described for the preparation of **47** to give **50** (89 mg, 93%) as a syrup ~90% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.22 (m, 20 H, 4 Ph), 5.01 (d, 1 H, $J_{2,NH} = 8.0$ Hz, NH), 4.75 and 4.64 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.72 and 4.58 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.65 and 4.56 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.56 and 4.46 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 1.43 (s, 9 H, *t*-Bu).

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*gulo*-undeconate (50a). Treatment of a solution of crude acid **50** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (3:1 cyclohexane−AcOEt), **50a** as a syrup. $[\alpha]_D = +26.5$ (*c* 0.6, $CHCl_3$). ^{1}H NMR: δ 7.40−7.22 (m, 20 H, 4 Ph), 5.00 (d, 1 H, $J_{2,NH} = 8.2$ Hz, NH), 4.76 and 4.64 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.73 and 4.59 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.64 and 4.52 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 4.54 and 4.48 (2 d, 2 H, $J = 12.5$ Hz, PhCH_2), 4.31−4.26 (m, 1 H, H-2), 3.99 (dd, 1 H, $J_{8,9} = 2.5$ Hz, $J_{9,10} = 0.5$ Hz, H-9), 3.98−3.88 (m, 3 H), 3.81−3.76 (m, 1 H), 3.71 (s, 3 H, OMe), 3.70−3.63 (m, 1 H), 3.64 (dd, 1 H, $J_{10,11a} = 4.5$ Hz, $J_{11a,11b} = 10.0$ Hz, H-11a), 1.79−1.64 (m, 6 H), 1.44 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{45}H_{55}NO_9$: C, 71.69; H, 7.35; N, 1.86. Found: C, 71.59; H, 7.40; N, 1.90.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gulo*-undeconic Acid (51). Compound **45** (258 mg, 0.34 mmol) was treated with Jones reagent as described for the preparation of **47** to give **51** (234 mg, 95%) as a syrup ~95% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.10 (m, 20 H, 4 Ph), 5.10 (d, 1 H, $J_{2,NH} = 7.5$ Hz, NH), 4.37−4.22 (m, 1 H, H-2), 3.86−3.55 (m, 7 H), 1.90−1.10 (m, 6 H), 1.40 (s, 9 H, *t*-Bu).

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gulo*-undeconate (51a). Treatment of a solution of crude acid **51** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (5:1 cyclohexane−AcOEt), **51a** as a white solid. Mp: 79−81 °C (cyclohexane). $[\alpha]_D = +36.3$ (*c* 1.4, $CHCl_3$). ^{1}H NMR selected data: δ 7.40−7.12 (m, 20 H, 4 Ph), 5.04 (d, 1 H, $J_{2,NH} = 8.0$ Hz, NH), 4.96 and 4.82 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.84 and 4.48 (2 d, 2 H, $J = 11.0$ Hz, PhCH_2), 4.71 and 4.64 (2 d, 2 H, $J = 11.8$ Hz, PhCH_2), 4.65 and 4.52 (2 d, 2 H, $J = 12.0$ Hz, PhCH_2), 3.73 (s, 3 H, OMe), 1.46 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{45}H_{55}NO_9$: C, 71.69; H, 7.35; N, 1.86. Found: C, 71.65; H, 7.38; N, 1.91.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*allo*-undeconic Acid (52). Compound **46** (70 mg, 0.09 mmol) was treated with Jones reagent as described for the preparation of **47** to give **52** (64 mg, 95%) as a syrup ~95% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.20 (m, 20 H, 4 Ph), 1.45 (s, 9 H, *t*-Bu).

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*allo*-undeconate (52a). Treatment of a solution of crude acid **52** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (4:1 cyclohexane−AcOEt), **52a** as a syrup. $[\alpha]_D = +22.6$ (*c* 0.8, $CHCl_3$). ^{1}H NMR selected data: δ 7.40−7.20 (m, 20 H, 4 Ph), 5.01 (d, 1 H, $J_{2,NH} = 8.5$ Hz, NH), 3.72 (s, 3 H, OMe), 1.46 (s, 9 H, *t*-Bu). MALDI-TOF MS: 777.6 (M^+ + Na), 793.7 (M^+ + K). Anal. Calcd for $C_{45}H_{55}NO_9$: C, 71.69; H, 7.35; N, 1.86. Found: C, 71.60; H, 7.42; N, 1.78.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*galacto*-undecitol (53). A solution of **41** (155 mg, 0.20 mmol) in acetic acid (1.0 mL) and H_2O (0.2 mL) was kept at rt for 26 h and then concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane−AcOEt to give **53** (120 mg, 82%) as a syrup. $[\alpha]_D = -6.7$ (*c* 1.5, $CHCl_3$). ^{1}H NMR: δ 7.41−7.29 (m, 20 H, 4 Ph), 4.96 and 4.65 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.95 and 4.65 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 4.77 and 4.69 (2 d, 2 H, $J = 12.5$ Hz, PhCH_2), 4.65−4.60 (m, 1 H, H-2), 4.51 and 4.43 (2 d, 2 H, $J = 11.5$ Hz, PhCH_2), 3.98 (dd, 1 H, $J_{8,9} = 3.0$ Hz, $J_{9,10} = 0.5$ Hz, H-9), 3.67 (dd, 1 H, $J_{6,7} = 9.0$ Hz, $J_{7,8} = 8.5$ Hz, H-7), 3.62−3.48 (m, 7 H), 3.21 (ddd, 1 H, $J_{5a,6} = 8.5$ Hz, $J_{5b,6} = 2.0$ Hz, H-6), 2.50−2.41 (m, 1 H, OH), 1.82−1.76 (m, 6 H), 1.43 (s, 9 H, *t*-Bu). MALDI-TOF MS: 749.6 (M^+ + Na), 765.8 (M^+ + K). Anal. Calcd for $C_{44}H_{55}NO_8$: C, 72.80; H, 7.64; N, 1.93. Found: C, 72.82; H, 7.58; N, 1.89.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-1,2-*N*,*O*-isopropylidene-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*talo*-undecitol (54). The *C*-galactoside **1** (200 mg, 0.36 mmol) was treated with the *N*-Boc L-serinale acetonide *ent*-**34** (0.25 g, 1.09 mmol) as described for the preparation of **35**. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 5:1 to 3:1) to afford first unreacted **1** (60 mg, 30%). Eluted second was 6,10-anhydro-7,8,9,11-tetra-*O*-benzyl-2,4,5-trideoxy-1,2-*N*,*O*-isopropylidene-2-(*tert*-butoxycarbonylamino)-D-*lyxo*-D-*allo*- and -D-*gluco*-undec-4-ynitol as a ∼3:1 mixture of diastereomers (145 mg, 52%). ^{1}H NMR (DMSO-d_6, 100 °C) of the main isomer: δ 7.43−7.25 (m, 20 H, 4 Ph), 5.22−5.18 (m, 1 H, OH), 4.98 and 4.61 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.89 and 4.61 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.74 (s, 2 H, PhCH_2), 4.84 and 4.41 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.06−3.91(m, 5 H), 3.58−3.48 (m, 4 H), 1.54 and 1.52 (2 s, 6 H, 2 Me), 1.48 (s, 9 H, *t*-Bu). MALDI-TOF MS: 802.3 (M^+ + Na), 818.5 (M^+ + K). Anal. Calcd for $C_{47}H_{55}NO_9$: C, 72.56; H, 7.13; N, 1.80. Found: C, 72.45; H, 7.26; N, 1.84.

Hydrogenation of this alkynol (320 mg, 0.40 mmol) as described for the preparation of **3-hydroxy-41** gave, after column cromatography on silica gel (3:1 cyclohexane-AcOEt), syrupy **3-hydroxy-54** (269 mg, 85%) as a ∼3:1 mixture of diastereomers. ^{1}H NMR (DMSO-d_6, 60 °C) selected data of the main isomer: δ 7.42−7.25 (m, 20 H, 4 Ph), 4.96 and 4.64 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.95 and 4.68 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.77 and 4.69 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.48 and 4.41 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.00 (dd, 1 H, $J_{8,9}$ = 2.7 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.71 (dd, 1 H, $J_{6,7}$ = 9.0 Hz, $J_{7,8}$ = 9.0 Hz, H-7), 3.60 (dd, 1 H, H-8), 3.22 (ddd, 1 H, $J_{5a,6}$ = 8.0 Hz, $J_{5b,6}$ = 2.0 Hz, H-6), 1.42 and 1.41 (2 s, 6 H, 2 Me), 1.38 (s, 9 H, *t*-Bu). MALDI-TOF MS: 806.3 (M^+ + Na), 821.8 (M^+ + K). Anal. Calcd for $C_{47}H_{59}NO_9$: C, 72.19; H, 7.61; N, 1.79. Found: C, 72.10; H, 7.78; N, 1.72.

The alcohol **3-hydroxy-54** (72 mg, 0.09 mmol) was deoxygenated as described for the preparation of **41** to give, after column chromatography on silica gel (from 10:1 to 1.5:1 cyclohexane−AcOEt), **54** (49 mg, 69%) as a syrup. $[\alpha]_D$ = −35.5 (*c* 0.4, $CHCl_3$). ^{1}H NMR (DMSO-d_6, 120 °C): δ 7.42−7.24 (m, 20 H, 4 Ph), 4.84 and 4.56 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.83 and 4.61 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.79 and 4.66 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.53 and 4.47 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.05 (dd, 1 H, $J_{8,9}$ = 3.0 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.85 (dd, 1 H, $J_{1a,1b}$ = 8.5 Hz, $J_{1a,2}$ = 6.0 Hz, H-1a), 3.76−3.72 (m, 1 H, H-2), 3.69 (dd, 1 H, $J_{7,8}$ = 9.5 Hz, H-8), 3.64−3.49 (m, 5 H), 3.21 (ddd, 1 H, $J_{5a,6}$ = 3.0 Hz, $J_{5b,6}$ = 8.0 Hz, $J_{6,7}$ = 9.0 Hz, H-6), 1.78−1.53 (m, 6 H), 1.49 and 1.43 (2 s, 6 H, 2 Me), 1.41 (s, 9 H, *t*-Bu). MALDI-TOF MS: 789.9 (M^+ + Na), 805.8 (M^+ + K). Anal. Calcd for $C_{47}H_{59}NO_8$: C, 73.70; H, 7.76; N, 1.83. Found: C, 73.83; H, 7.65; N, 1.65.

6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*talo*-undecitol (55). A solution of **54** (75 mg, 0.10 mmol) in acetic acid (0.5 mL) and H_2O (0.1 mL) was kept at rt for 26 h and then concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane−AcOEt to give **55** (58 mg, 80%) as a syrup. $[\alpha]_D$ = −22.5 (*c* 1.7, $CHCl_3$). ^{1}H NMR: δ 7.40−7.22 (m, 20 H, 4 Ph), 4.96 and 4.64 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.95 and 4.64 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.78 and 4.69 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.64−4.59 (m, 1 H, H-2), 4.49 and 4.41 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 3.98 (dd, 1 H, $J_{8,9}$ = 2.8 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.67 (dd, 1 H, $J_{6,7}$ = 9.0 Hz, $J_{7,8}$ = 9.5 Hz, H-7), 3.65−3.30 (m, 7 H), 3.19 (dd, 1 H, $J_{5a,6}$ = 2.0 Hz, $J_{5b,6}$ = 8.5 Hz, H-6), 2.46−2.39 (m, 1 H, OH), 1.81−1.52 (m, 6 H), 1.43 (s, 9 H, *t*-Bu). MALDI-TOF MS: 749.7 (M^+ + Na), 765.6 (M^+ + K). Anal. Calcd for $C_{44}H_{55}NO_8$: C, 72.80; H, 7.64; N, 1.93. Found: C, 72.90; H, 7.72; N, 2.01.

Methyl 6,10-Anhydro-7,8,9,11-tetra-*O*-benzyl-2,3,4,5-tetradeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*talo*-undeconate (56a). Route a. The alcohol **55** (73 mg, 0.10 mmol) was treated with Jones reagent as described for the preparation of **47** to give **56** (69 mg, 90%) as a syrup ∼95% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.39−7.23 (m, 20 H, 4 Ph), 5.02 (m, 1 H, NH), 4.96 and 4.64 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.95 and 4.63 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.77 and 4.68 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.48 and 4.42 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 3.22−3.19 (m, 1 H, H-6), 1.98−1.52 (m, 6 H), 1.42 (s, 9 H, *t*-Bu).

Treatment of a solution of crude acid **56** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column cromatography on silica gel (5:1 cyclohexane−AcOEt), **56a** as a syrup. $[\alpha]_D$ = −13.9 (*c* 0.7, $CHCl_3$). ^{1}H NMR selected data: δ 7.40−7.12 (m, 20 H, 4 Ph), 5.00 (d, 1 H, $J_{2,NH}$ = 7.7 Hz, NH), 4.95 and 4.64 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.94 and 4.65 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.77 and 4.68 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.49 and 4.42 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.28 (m, 1 H, H-2), 4.00 (dd, 1 H, $J_{8,9}$ = 2.5 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.71 (s, 3 H, OMe), 3.69 (dd, 1 H, $J_{6,7}$ = 9.0 Hz, $J_{7,8}$ = 9.5 Hz, H-7), 3.59 (dd, 1 H, H-8), 3.58−3.48 (m, 3 H), 3.19 (ddd, 1 H, $J_{5a,6}$ = 8.5 Hz, $J_{5b,6}$ = 2.0 Hz, H-6), 1.89−1.62 (m, 6 H), 1.42 (s, 9 H, *t*-Bu). MALDI-TOF MS: 779.7 (M^+ + Na), 795.9 (M^+ + K). Anal. Calcd for $C_{45}H_{55}NO_9$: C, 71.69; H, 7.35; N, 1.86. Found: C, 71.60; H, 7.25; N, 1.96.

Route b. A mixture of **55** (50 mg, 0.07 mmol), [bis(acetoxy)-iodo]benzene (BAIB, 48 mg, 0.15 mmol), 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO, 2 mg, 0.01 mmol), CH_3CN (0.25 mL), and H_2O (0.25 mL) was stirred at rt for 3 h, filtered through a pad of Celite, and concentrated. Treatment of a solution of the crude acid in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (5:1 cyclohexane−AcOEt), **56a** (39.6 mg, 75%) as a syrup. $[\alpha]_D$ = −14.0 (*c* 1.0, $CHCl_3$).

4-Acetamido-3,7-anhydro-5,6,8-tri-*O*-benzyl-1,2,4-trideoxy-D-*glycero*-L-*manno*-oct-1-ynitol (57). A solution of **19** (300 mg, 0.62 mmol), triphenylphosphine (179 mg, 0.68 mmol), and anhydrous THF (3.2 mL) was kept at rt for 3 h, diluted with H_2O (40 μL 2.48 mmol), kept at rt for an additional 10 h, and concentrated. A solution of crude product in acetic anhydride (1 mL) and pyridine (1 mL) was kept at rt for 3 h and then concentrated. The residue was eluted from a column of silica gel with 1:1 cyclohexane−AcOEt to give **57** (288 mg, 93%) as a white solid. Mp 174−176 °C (cyclohexane−AcOEt). $[\alpha]_D$ = +36.1 (*c* 0.9, $CHCl_3$). ^{1}H NMR: δ 7.40−7.20 (m, 15 H, 3 Ph), 5.55 (d, 1 H, $J_{4,NH}$ = 7.5 Hz, NH), 4.91 and 4.61 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.72 (dd, 1 H, $J_{1,3}$ = 2.0 Hz, $J_{3,4}$ = 10.5 Hz, H-3), 4.68 and 4.49 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.50 and 4.43 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.25 (dd, 1 H, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 10.5 Hz, H-5), 4.03 (dd, 1 H, $J_{6,7}$ = 0.5 Hz, H-6), 3.82 (ddd, 1 H, H-4), 3.68 (ddd, 1 H, $J_{7,8a}$ = 5.5 Hz, $J_{7,8b}$ = 7.5 Hz, H-7), 3.64−3.58 (m, 2 H, 2 H-8), 2.45 (d, 1 H, H-1), 1.95 (s, 3 H, Ac). MALDI-TOF MS: 523.4 (M^+ + Na), 539.6 (M^+ + K). Anal. Calcd for $C_{31}H_{33}NO_5$: C, 74.51; H, 6.67; N, 2.80. Found: C, 74.30; H, 6.60; N, 2.78.

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,4,5,7-tetradeoxy-1,2-*N*,*O*-isopropylidene-2-(*tert*-butoxycarbonylamino)-D-*lyxo*-D-*manno*- and -D-*altro*-undec-4-ynitol (63). To a cooled (−20 °C), stirred solution of **57** (500 mg, 1.00 mmol) in anhydrous THF (4 mL) was slowly added lithium bis(trimethylsilyl)amide (2.50 mL, 2.50 mmol, of a 1 M solution in hexane). The solution was stirred at −20 °C for 45 min, cooled to −45 °C, and then a solution of **34** (687 mg, 3.00 mmol) in anhydrous THF (2 mL) was added dropwise. The reaction mixture was stirred at −45 °C for an additional 3 h, diluted with 1 M phosphate buffer at pH = 7 (10 mL), and allowed to reach rt. The suspension was diluted with Et_2O (50 mL), and the phases were separated. The aqueous layer was extracted twice with Et_2O (50 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane−AcOEt (from 3:1 to 1:1) to afford first unreacted **57** (100 mg, 20%). Eluted second was syrupy **63** as a ∼8:1 mixture of diastereomers (546 mg, 75%). ^{1}H NMR (DMSO-d_6, 120 °C) of the main isomer: δ 7.40−7.20 (m, 15 H, 3 Ph), 5.08 (d, 1 H, $J_{7,NH}$ = 6.0 Hz, NH), 4.81 and 4.53 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.71 and 4.59 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.66−4.60 (m, 1 H, H-3), 4.53 and 4.47 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.21 (dd, 1 H, $J_{3,6}$ = 0.5 Hz, $J_{6,7}$ = 10.0 Hz, H-6), 4.06 (ddd, 1 H, $J_{7,8}$ = 9.0 Hz, H-7), 4.04 (dd, 1 H, $J_{1a,1b}$ = 9.0 Hz, $J_{1a,2}$ = 3.5 Hz, H-1a), 3.99 (dd, 1 H, $J_{8,9}$ = 3.0 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.94 (dd, 1 H, $J_{1b,2}$ =

3.0 Hz, H-1b), 3.88−3.82 (m, 1 H, H-2), 3.75 (dd, 1 H, H-8), 3.66−3.54 (m, 4 H), 1.99 (s, 3 H, Ac), 1.49 and 1.44 (2 s, 6 H, 2 Me), 1.44 (s, 9 H, *t*-Bu). MALDI-TOF MS: 752.2 ($M^+ + Na$), 768.3 ($M^+ + K$). Anal. Calcd for $C_{42}H_{52}N_2O_9$: C, 69.21; H, 7.19; N, 3.84. Found: C, 69.20; H, 7.02; N, 3.95.

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*galacto*-undeconic Acid (75). Compound **69** (50 mg, 0.07 mmol) was treated with Jones reagent as described for the preparation of **47** to give **75** (43 mg, 90%) as a syrup ∼90% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.20 (m, 15 H, 3 Ph), 5.31 (d, 1 H, J = 7.0 Hz, NH), 4.90 and 4.58 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.72 and 4.40 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.70 (d, 1 H, J = 8.0 Hz, NH), 4.52 and 4.40 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 1.94 (s, 3 H, Ac), 1.41 (s, 9 H, *t*-Bu).

Methyl 7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*galacto*-undeconate (75a). Treatment of a solution of crude acid **75** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (2:1 cyclohexane−AcOEt), **75a** as a syrup. $[\alpha]_D$ = +27.0 (*c* 0.6, $CHCl_3$). ^{1}H NMR: δ 7.40−7.24 (m, 15 H, 3 Ph), 5.26 (d, 1 H, $J_{7,NH}$ = 7.0 Hz, NH), 5.02 (d, 1 H, $J_{2,NH}$ = 8.5 Hz, NH), 4.92 and 4.63 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.70 and 4.42 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.51 and 4.45 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.26 (ddd, 1 H, $J_{2,3a}$ = 5.5 Hz, $J_{2,3b}$ = 6.0 Hz, H-2), 4.03 (d, 1 H, $J_{8,9}$ = 1.5 Hz, $J_{9,10}$ = 0.5 Hz, H-9), 3.79 (ddd, 1 H, $J_{6,7}$ = 9.3 Hz, $J_{7,8}$ = 9.5 Hz, H-7), 3.70 (s, 3 H, OMe), 3.68−3.52 (m, 5 H), 1.92 (s, 3 H, Ac), 1.42 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{40}H_{52}N_2O_9$: C, 68.16; H, 7.44; N, 3.97. Found: C, 68.20; H, 7.50; N, 4.00.

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*galacto*-undeconic Acid (76). Compound **70** (277 mg, 0.39 mmol) was treated with Jones reagent as described for the preparation of **47** to give **76** (252 mg, 94%) as a syrup ∼95% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 8.11 (d, 1 H, $J_{7,NH}$ = 7.5 Hz, NH), 7.40−7.18 (m, 15 H, 3 Ph), 4.87 and 4.65 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.82 and 4.56 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.62 (s, 2 H, PhCH_2), 3.78−3.30 (m, 8 H), 1.83 (s, 3 H, Ac), 1.80−1.50 (m, 6 H), 1.45 (s, 9 H, *t*-Bu).

Methyl 7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*galacto*-undeconate (76a). Treatment of a solution of crude acid **76** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (2:1 cyclohexane−AcOEt), **76a** as a syrup. $[\alpha]_D$ = +32.2 (*c* 0.8, $CHCl_3$). MALDI-TOF MS: 728.2 ($M^+ + Na$), 744.3 ($M^+ + K$). Anal. Calcd for $C_{40}H_{52}N_2O_9$: C, 68.16; H, 7.44; N, 3.97. Found: C, 68.00; H, 7.55; N, 4.03. The ^{1}H NMR spectrum of **76a** was identical to that of the product prepared by another route.[22]

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gluco*-undeconic Acid (77). Compound **71** (64 mg, 0.09 mmol) was treated with Jones reagent as described for the preparation of **47** to give **77** (57 mg, 92%) as a syrup ∼90% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.41−7.17 (m, 15 H, 3 Ph), 6.00 and 5.27 (2 bs, 2 NH), 4.85 and 4.42 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.82 and 4.44 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.62 and 4.44 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 3.76−3.62 (m, 5 H), 3.43−3.37 (m, 2 H), 2.10 (s, 3 H, Ac), 1.73−1.65 (m, 6 H), 1.40 (s, 9 H, *t*-Bu).

Methyl 7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gluco*-undeconate (77a). Treatment of a solution of crude acid **77** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (1:1 cyclohexane−AcOEt), **77a** as a syrup. $[\alpha]_D$ = −9.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ 7.41−7.18 (m, 15 H, 3 Ph), 5.71 (d, 1 H, $J_{7,NH}$ = 10.0 Hz, NH), 5.09 (d, 1 H, $J_{2,NH}$ = 9.0 Hz, NH), 4.91 and 4.46 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.86 and 4.49 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.67 (ddd, 1 H, $J_{6,7}$ = 4.0 Hz, $J_{7,8}$ = 4.5 Hz, H-7), 4.64 and 4.50 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.32 (ddd, 1 H, $J_{5a,6}$ = 7.0 Hz, $J_{5b,6}$ = 8.0 Hz, H-6), 3.76 (s, 3 H, OMe), 3.74−3.68 (m, 3 H), 3.64 (dd, 1 H, $J_{8,9}$ = $J_{9,10}$ = 9.0 Hz, H-9), 3.41−3.36 (m, 2 H), 2.19 (s, 3 H, Ac), 1.85−1.55 (m, 6 H), 1.43 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{40}H_{52}N_2O_9$: C, 68.16; H, 7.44; N, 3.97. Found: C, 68.73; H, 7.44; N, 3.76.

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*gulo*-undeconic Acid (78). Compound **72** (34 mg, 0.04 mmol) was treated with Jones reagent as described for the preparation of **47** to give **78** (30 mg, 87%) as a syrup ∼95% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.20 (m, 15 H, 3 Ph), 5.30 (d, 1 H, J = 8.0 Hz, NH), 4.70 and 4.61 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.64 and 4.62 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.63 and 4.58 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 1.81 (s, 3 H, Ac), 1.43 (s, 9 H, *t*-Bu).

Methyl 7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*threo*-L-*gulo*-undeconate (78a). Treatment of a solution of crude acid **78** in 1:1 Et_2O-MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (2:1 AcOEt−cyclohexane), **78a** as a syrup. $[\alpha]_D$ = +23.3 (*c* 1.2, $CHCl_3$). ^{1}H NMR: δ 7.40−7.22 (m, 15 H, 3 Ph), 5.58 (d, 1 H, J = 8.0 Hz, NH), 5.04 (d, 1 H, J = 8.0 Hz, NH), 4.74 and 4.63 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.59 and 4.54 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.56 and 4.47 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 3.71 (s, 3 H, OMe), 1.96 (s, 3 H, Ac), 1.44 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{40}H_{52}N_2O_9$: C, 68.16; H, 7.44; N, 3.97. Found: C, 68.10; H, 7.48; N, 3.89.

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gulo*-undeconic Acid (79). Compound **73** (60 mg, 0.08 mmol) was treated with Jones reagent as described for the preparation of **47** to give **79** (51 mg, 94%) as a syrup ∼95% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.24 (m, 15 H, 3 Ph), 6.63 (d, 1 H, J = 9.0 Hz, NH), 5.21−5.14 (m, 1 H, NH), 4.63−4.38 (m, 6 H), 4.35−4.17 (m, 3 H), 3.91−3.50 (m, 5 H), 1.92 (s, 3 H, Ac), 1.65−1.43 (m, 6 H), 1.41 (s, 9 H, *t*-Bu).

Methyl 7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*gulo*-undeconate (79a). Treatment of a solution of crude acid **79** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (from 20:1 to 8:1 CH_2Cl_2−acetone), **79a** as a white solid. Mp: 103 °C (cyclohexane−AcOEt). $[\alpha]_D$ = +8.0 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.40−7.22 (m, 15 H, 3 Ph), 6.50 (d, 1 H, $J_{2,NH}$ = 9.5 Hz, NH), 5.04 (d, 1 H, $J_{7,NH}$ = 8.0 Hz, NH), 4.62 and 4.51 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.60 and 4.45 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.53 (s, 2 H, PhCH_2), 4.30−4.24 (m, 1 H, H-2), 4.22−4.17 (m, 1 H), 4.16 (ddd, 1 H, $J_{6,7}$ = 6.5 Hz, $J_{7,8}$ = 9.0 Hz, H-7), 3.88−3.74 (m, 3 H), 3.72 (s, 3 H, OMe), 3.69 (ddd, 1 H, $J_{5a,6}$ = 1.0 Hz, $J_{5b,6}$ = 3.5 Hz, H-6), 3.63−3.56 (m, 1 H), 1.85 (s, 3 H, Ac), 1.60−1.47 (m, 6 H), 1.45 (s, 9 H, *t*-Bu). Anal. Calcd for $C_{40}H_{52}N_2O_9$: C, 68.16; H, 7.44; N, 3.97. Found: C, 68.10; H, 7.48; N, 3.89.

7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*allo*-undeconic Acid (80). Compound **74** (50 mg, 0.07 mmol) was treated with Jones reagent as described for the preparation of **47** to give **80** (36 mg, 75%) as a syrup ∼90% pure by ^{1}H NMR analysis. ^{1}H NMR selected data: δ 7.40−7.24 (m, 15 H, 3 Ph), 6.01 (d, 1 H, J = 9.0 Hz, NH), 5.16 (d, 1 H, J = 7.0 Hz, NH), 4.64−4.39 (m, 6 H), 3.87−3.64 (m, 6 H), 1.98 (s, 3 H, Ac), 1.82−1.43 (m, 6 H), 1.45 (s, 9 H, *t*-Bu).

Methyl 7-Acetamido-6,10-anhydro-8,9,11-tri-*O*-benzyl-2,3,4,5,7-pentadeoxy-2-(*tert*-butoxycarbonylamino)-D-*erythro*-L-*allo*-undeconate (80a). Treatment of a solution of crude acid **80** in 1:1 Et_2O−MeOH with ethereal diazomethane at 0 °C for 5 min gave, after column chromatography on silica gel (from 8:1 to 6:1 CH_2Cl_2−acetone), **80a** as a syrup. $[\alpha]_D$ = +21.1 (*c* 0.8, $CHCl_3$). ^{1}H NMR: δ 7.40−7.21 (m, 15 H, 3 Ph), 5.94 (d, 1 H, J = 9.0 Hz, NH), 5.05 (d, 1 H, J = 8.5 Hz, NH), 4.78 and 4.50 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.61 and 4.49 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.61 and 4.48 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.46−4.40 (m, 1 H), 4.28 (ddd, 1 H, $J_{5a,6}$ = 2.5 Hz, $J_{5b,6}$ = 8.5 Hz, $J_{6,7}$ = 2.5 Hz, H-6), 3.82−3.62 (m, 7

H), 3.73 (s, 3 H, OMe), 1.98 (s, 3 H, Ac), 1.92−1.43 (m, 6 H), 1.43 (s, 9 H, *t*-Bu). MALDI-TOF MS: 728.3 (M^+ + Na), 744.5 (M^+ + K). Anal. Calcd for $C_{40}H_{52}N_2O_9$: C, 68.16; H, 7.44; N, 3.97. Found: C, 68.20; H, 7.40; N, 3.90.

Acknowledgment. We thank Mr. P. Formaglio (University of Ferrara, Italy) for NMR measurements. This research was financially supported by MURST, COFIN-2000 (Italy). We are grateful to Ajinomoto Co., Inc. (Tokyo, Japan) for an unrestricted grant.

Supporting Information Available: Experimental procedures and physical data of compounds **11**, **12**, **17**, **18**, **20**, **21**, **28**−**30**, **36**−**40**, **42**−**46**, **58**−**62**, and **64**−**74**. Syntheses of the peracetylated *N*-Fmoc and *N*-Boc analogues of *C*-glycosylasparagine derivatives **76** and **77**, respectively. ^{1}H NMR spectra of epimeric *C*-galactosylasparagine derivatives **47a** and **56a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO020054M