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Concise and Practical Synthesis of *C*-Glycosyl Ketones from Sugar Benzothiazoles and Their Transformation into Chiral Tertiary Alcohols

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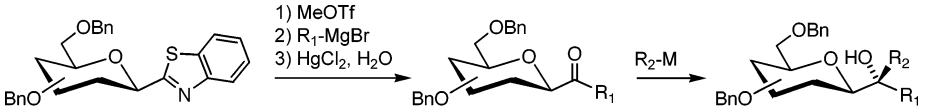
Received July 4, 2005



A collection of 13 unsymmetrical ketones, each one featuring a sugar (D-glucosyl, D-galactosyl, D-mannosyl, and L-fucosyl) and an aglycone moiety (phenyl, 2-thiazolyl, TMS-ethynyl, allyl, and 1-propenyl) was prepared by a uniform route based on the use of benzothiazole as a carbonyl group equivalent. Succinctly, *C*-glycosylbenzothiazoles readily prepared by addition of 2-lithiobenzothiazole to sugar lactones and deoxygenation, were subjected to a one-pot reaction sequence involving *N*-methylation of the heterocyclic ring by MeOTf, treatment of the *N*-methylbenzothiazolium salt with a Grignard reagent, and $HgCl_2$-promoted hydrolysis of the benzothiazoline thus formed. The resulting ketones were isolated in yields varying from 35 to 80%. Treatment of the sugar ketones with various organometals containing the phenyl, 2-thiazolyl, TMS-ethynyl, or ethynyl group as a substituent afforded chiral tertiary alcohols. These addition reactions were highly stereoselective as observed by crude NMR analysis and isolation of a single epimer in high yield in each case examined. However, because of the complexity of the reagents involved, the stereochemical outcome of these reactions appears to be difficult to rationalize by simple classical steric models, thus, ab initio studies taking into account the role of the sugar fragment are advisable. An interesting synthetic elaboration of a propargylic alcohol containing the thiazole ring into a propargylic alcohol bearing the formyl and carboxylate groups is reported.

Introduction

Asymmetric nucleophilic additions on prochiral ketones that display a high amount of neighboring functionality to afford tertiary alcohols in almost complete enantiomeric purity are key processes in a multitude of complex natural and designed product syntheses. This is notoriously a challenging task because, in addition to difficulties inherent to the construction of the quaternary carbon center through a highly congested transition state,[1,2] there is the need to control the relative positions of the four different substituents so that a carbon stereocenter with the desired configuration is formed. A variety of methods have been developed to attain the latter goal, which rely on internal stereoselection by stereocenters resident in either of the reactants[3] or external stereoselection by chiral organic molecules either in a free form or as ligands in metal complexes.[4] Recently, in connection with our ongoing research on *C*-glycoside synthesis,[5] we became particularly interested in accessing the (*R*)- and (*S*)-configured tertiary alcohols **4a** and **5a** bearing fucosyl, phenyl, and thiazolyl groups[6] (Scheme 1). The synthesis of each stereoisomer was performed starting from the β-L-*C*-fucosyl aldehyde **1** and use of metalated phenyl and thiazolyl derivatives in a reversed order. Specifically, the (*R*)-epimer **4a** was obtained by reaction

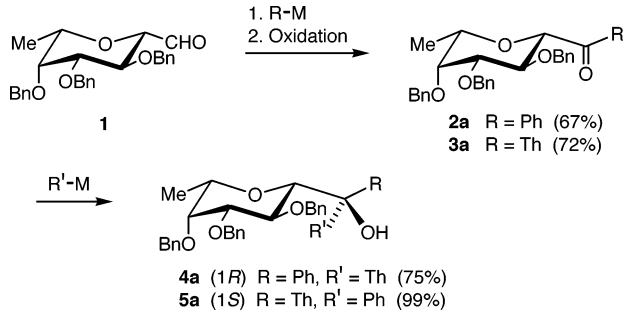
(1) For reviews concerning the asymmetric construction of quaternary carbon centers, see: (a) Martin, S. F. *Tetrahedron* **1980**, *36*, 419. (b) Romo, D.; Meyers, A. I. *Tetrahedron* **1991**, *47*, 9503. (c) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037. (d) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 388. (e) Christoffers, J.; Mann, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4591. (f) Christoffers, J.; Baro, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1688. (g) A. Denissova, I.; Barriault, L. *Tetrahedron* **2003**, *59*, 10105.

(2) For recent papers with leading references to earlier publications, see: (a) Burke, E. D.; Gleason, J. L. *Org. Lett.* **2004**, *6*, 405. (b) Jiang, B.; Xu, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2543. (c) Keränen, M. D.; Eilbracht, P. *Org. Biomol. Chem.* **2004**, *2*, 1688. (d) Kennedy, J. W. J.; Hall, D. G. *J. Org. Chem.* **2004**, *69*, 4412.

(3) (a) Huryn, D. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 1, p 49.

10.1021/jo051377w CCC: $30.25
Published on Web 10/18/2005

SCHEME 1. Synthesis of the Tertiary Alcohols 4a and 5a (Th = 2-thiazolyl)



of **1** with phenylmagnesium bromide (PhMgBr), oxidation of the resulting alcohol to ketone **2a**, and addition of 2-lithiothiazole (2-ThLi) to the latter. The (*S*)-epimer **5a** was instead formed by first adding 2-trimethylsilylthiazole (2-TST) to **1**, oxidizing the alcohol to ketone **3a**, and then reacting the latter with PhMgBr. This synthesis of ketones **2a** and **3a** can be viewed as a thiazole-based route because the progenitors of the aldehyde **1** were a protected fuconolactone derivative and 2-ThLi, the latter serving as a masked formylating agent.[7] In light of the key role of ketones **2a** and **3a** as ultimate precursors to the chiral tertiary alcohols **4a** and **5a**, we envisaged a more concise and direct entry to these compounds from fuconolactone, avoiding the intermediacy of aldehyde **1**. The new method is based on a seemingly trivial change such as the use of benzothiazole in place of thiazole as a masked carbonyl functionality. The resulting improved route was successfully validated by the synthesis of other ketones containing sugar residues of the D-*gluco*, D-*galacto*, and D-*manno* series. Hence, in the present report, we describe a benzothiazole-based route to *C*-glycosylated ketones and their stereoselective transformation into tertiary alcohols. One aim of this research was to provide a general synthesis of *C*-glycosyl ketones that avoids the chemical and stereochemical problems associated with the introduction of an acyl group at the anomeric center of a sugar residue. Earlier methods[8] via coupling of C-1-metalated derivatives with electrophilic acylating agents lacked generality and afforded ketones as α- and β-anomers in low overall yields. A second reason that led us to embark on this new piece of work stemmed from the potential use of *C*-glycosylated tertiary alcohols in synthetic approaches to complex glycoconjugates such as the family of natural antitumor antibiotics altromycins[9] and flavonoids hydroxyaloins.[10] Recent works by Pasetto and Frank[11a] and by Koo and McDonald[11b] served to focus some attention on these *C*-glycoconjugates while showing the need for expeditious syntheses.

Results and Discussion

Synthesis of *C*-Glycosyl Ketones. In 1988, Chikashita et al. reported on a new synthesis of ketones involving 2-substituted *N*-methylbenzothiazolium salts as key intermediates.[12] The method followed an earlier report by Corey[13] focusing on the use of benzothiazole (BTh) as a masked carbonyl equivalent. In fact, the Japanese group's synthesis relied on the easy carbon−carbon bond formation at C-2 of BTh by organometallic chemistry, followed by nitrogen methylation, then nucleophilic addition of an organometallic reagent to the benzothiazolium fragment, and finally carbonyl unmasking by hydrolysis of the benzothiazoline ring. By this method, a collection of six ketones was prepared, all bearing an achiral hydroxyalkyl group. Apparently, the Chikashita synthesis of unsymmetrical ketones did not attract a great deal of attention over the years,[14] very likely because of a plethora of other popular methods.[15] However, after our many-year involvement with thiazole as a synthetic auxiliary,[7] we set for ourselves a program to develop the synthesis of *C*-glycosyl ketones by the Chikashita reaction as shown in Scheme 2. This decision was made after several unsuccessful attempts to establish an effective thiazole-based version of the Chikashita route because of the lack of satisfactory addition of organometallic reagents to *N*-methylthiazolium salts.[16]

We first examined the synthesis of the L-fucosyl ketones **2a** and **3a** because this constituted a test of the efficiency of the new method compared to that shown in Scheme 1. The benzothiazolyl β-L-*C*-fucoside **10a**, the starting material according to the synthetic plan in

(4) For selected recent papers, see: (a) Dosa, P. I.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 445. (b) Tietze, L. F.; Völkel, L.; Wulff, C.; Weigand, B.; Bittner, C.; McGrath, P.; Johnson, K.; Schäfer, M. *Chem. Eur. J.* **2001**, *7*, 1304. (c) Tian, S.-K.; Deng, L. *J. Am. Chem. Soc.* **2001**, *123*, 6195. (d) Waltz, K. M. Gavenonis, J.; Walsh, P. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3697. (e) García, C.; LaRochelle, L. K.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 10970. (f) Jeon, S.-J.; Walsh, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 9544. (g) Tian, S.-K.; Hong, R.; Deng, L. *J. Am. Chem. Soc.* **2003**, *125*, 9900. (h) Wada, R.; Oisaki, K.; Kanai, M., Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910. (i) Li, H.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 6538. (j) Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 284

(5) For reviews and recent papers, see: (a) Dondoni, A.; Marra, A. *Chem. Commun.* **1999**, 2133. (b) Dondoni, A. *Pure Appl. Chem.* **2000**, *72*, 1577. (c) Dondoni, A.; Marra, A. *Chem. Rev.* **2000**, *100*, 4395. (d) Dondoni, A.; Massi, A. *Mol. Diversity* **2003**, *6*, 261. (e) Dondoni, A., Giovannini, P. P., Marra, A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2380. (f) Dondoni, A.; Marra, A.; Mizuno, M.; Giovannini, P. P. *J. Org.* Chem. **2002**, *67*, 4186. (g) Dondoni, A.; Mariotti, G.; Marra, A. *J. Org. Chem.* **2002**, *67*, 4475. (h) Dondoni, A.; Massi, S.; Sabbatini, S.; Bertolasi, V. *J. Org. Chem.* **2002**, *67*, 6979. (i) Dondoni, A.; Massi, A.; Minghini, E., Bertolasi, V. *Helv. Chim. Acta* **2002**, *85*, 3331. (j) Dondoni, A.; Massi, A.; Sabbatini, S.; Bertolasi, V. *Tetrahedron Lett.* **2004**, *45*, 2381. (k) Dondoni, A.; Giovannini, P. P.; Massi, A. *Org. Lett.* **2004**, *6*, 2929.

(6) Dondoni, A.; Catozzi, N.; Marra, A. *J. Org. Chem.* **2004**, *69*, 5023.

(7) For the use of thiazole as a synthetic auxiliary, see: (a) Dondoni, A. *Synthesis* **1998**, 1681. (b) Dondoni, A.; Marra, A. *Chem. Rev.* **2004**, *104*, 2557.

(8) (a) Frey, O.; Hoffmann, M.; Wittmann, V.; Kessler, H.; Vasella, A. *Helv. Chim. Acta* **1994**, *77*, 2060. (b) Belosludtsev, Y. Y.; Bhatt, R. K.; Falck, J. R. *Tetrahedron Lett.* **1995**, *36*, 5881. (c) DeShong, P.; Soli, E. D.; Slough, G. A.; Sidler, D. R.; Elango, V.; Rybczynski, P. J.; Vosejpka, L. J. S.; Lesse, T. A.; Le, T. X.; Anderson, G. B.; von Philipsborn, W.; Vöhler, M.; Rentsch, D.; Zerbe, O. *J. Organomet. Chem.* **2000**, *593*, 49.

(9) Brill, G. M.; Jackson, M.; Whittern, D. N.; Buko, A. M.; Hill, P.; Chen, R. H.; McAlpine, J. B. *J. Antibiot.* **1994**, *47*, 1160.

(10) Dagne, E.; Bisrat, D.; Van Wyk, B.-E.; Viljoen, A. *J. Nat. Prod.* **1998**, *61*, 256.

(11) (a) Pasetto, P.; Franck, R. W. *J. Org. Chem.* **2003**, *68*, 8042. (b) Koo, B.; McDonald, F. E. *Org. Lett.* **2005**, *7*, 3621.

(12) Chikashita, H.; Ishibaba, M.; Ori, K.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3637.

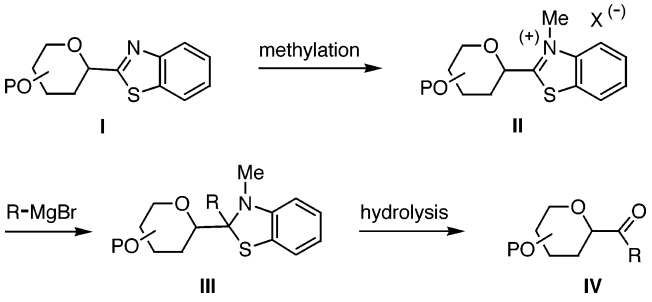
(13) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 5.

(14) From the date of publication to the present, the Chikashita paper has received only 26 citations by other authors.

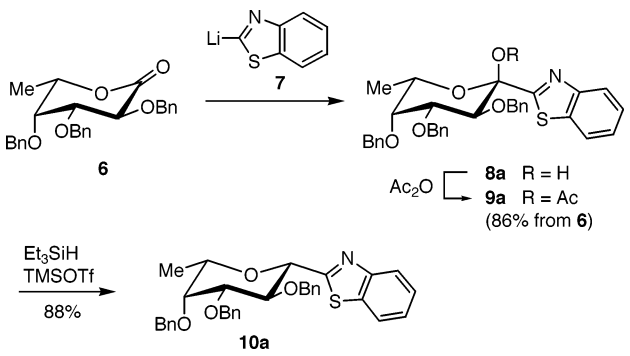
(15) (a) Waring, A. J. In *Comprehensive Organic Chemistry*; Barton, D., Ollis, W. D., Eds.; Pergamon Press: Oxford, U.K., 1979; Vol. 1, p 1017. (b) Larock, R. C. *Comprehensive Organic Transformations*; VCH: New York, 1989.

(16) The addition at low temperature (−30 to −15 °C) of PhMgBr to the *N*-methylthiazolium salt derived from 2-(2,3,4,6-tetra-*O*-benzyl-β-d-glucopyranosyl)thiazole followed by Ag-assisted hydrolysis led to a complex mixture of products from which the corresponding *C*-glycosyl ketone **2b** was isolated in ca. 10% yield.

SCHEME 2. Synthesis of *C*-Glycosyl Ketones through Benzothiazolium Salts



SCHEME 3



Scheme 2, was prepared by the standard method developed in our laboratory that allows the introduction of the thiazole or benzothiazole ring at the anomeric carbon of carbohydrates.[5a−c] This involved the addition of 2-lithiobenzothiazole (2-BThLi, **7**) to 2,3,4-*O*-benzyl-L-fuconolactone **6**, followed by reductive dehydroxylation of **8a** through the *O*-acetate **9a** (Scheme 3).

Then, the one-pot reaction sequence outlined in Scheme 2 was performed. This involved *N*-methylation of **10a** with methyl triflate (MeOTf), addition of the organomagnesium reagent RMgBr to the crude benzothiazolium salt, and finally $HgCl_2$-promoted hydrolysis of the C-2-disubstituted benzothiazoline. The use of PhMgBr (Table 1, entry 1) in the second step of this sequence afforded the ketone **2a**, whereas the use of 2-ThMgBr furnished the ketone **3a** (entry 2). The overall yield of each ketone from the lactone **6** (51 and 53%) was similar to that (50 and 54%) obtained in the thiazole route via the aldehyde **1** shown in Scheme 1. Hence, from the standpoint of chemical efficiency, there is no difference to carrying on the synthesis of ketones **2a** and **3a** by either the thiazole or benzothiazole route. However, in general, the latter route should be preferred because it requires a small number of steps and avoids the intermediacy of sugar aldehydes whose stability and manipulability can be much lower than those of **1**. Finally, the benzothiazole route appears to be more economical owing to the lower price of commercially available reagents compared to the thiazole counterparts.[17] It has to be pointed out that different reagents and conditions were employed compared to those in the Chikashita procedure. First, the key for a successful synthesis was the use of the Grignard reagents PhMgBr and 2-ThMgBr, as very poor results were obtained with PhLi and 2-ThLi. In this respect, the improved preparation of a simple yet useful organometallic reagent such as 2-ThMgBr was crucial in this program.[18] Moreover, the use of 1.5 equiv of MeOTf instead of a large excess of MeI allowed the *N*-methylation of the benzothiazole ring to be performed in a few minutes and almost quantitatively. Finally, $AgNO_3$ was replaced by the more thiophilic salt $HgCl_2$ in the carbonyl unmasking step.[19] However, the addition of 1.0 equiv of Et_3N was needed to keep the reaction mixture under neutral conditions and allow the hydrolysis of the heterocycle to proceed rapidly to completion.

Encouraged by the above results, the improved ketone synthesis was applied to benzothiazoles bearing three common sugar residues, namely, the β-D-*C*-glucosyl **10b**, *C*-galactosyl **10c**, and *C*-mannosyl **10d** derivatives (Table 1, entries 3−13). The preparation of **10b** and **10c** from 1,5-glucono- and galactonolactone, respectively, and 2-BThLi **7** was recently reported by us.[5f,20] In a similar way, **10d** was prepared from 2,3,4,6-tetra-*O*-benzyl-D-mannonolactone (see Experimental Section).[21]

Starting from *C*-glycosyl benzothiazoles **10b**, **10c**, and **10d**, the corresponding pairs of nonsymmetrical *C*-glycosyl ketones **2b** and **3b** (entries 3 and 4), **2c** and **3c** (entries 6 and 7), and **2d** and **3d** (entries 9 and 10) bearing the phenyl or 2-thiazolyl group were prepared by the standard reaction sequence involving methylation, Grignard addition, and hydrolysis (Table 1).[21] The yields of all isolated products were close to the average value of ca. 70%. It is worth noting that the ketones **2c** and **3b** were formed in as low a yield as only ca. 35% when prepared via the thiazole route. Furthermore, as a validation of the methodology, the addition of TMS-ethynylmagnesium bromide to each of the individual *C*-glycosylbenzothiazoles **10b**−**10d** was carried out to afford the corresponding alkynyl ketones **11b**−**11d**, although in lower yields (35−55%). Finally, the addition of allylmagnesium bromide to the *C*-mannosylbenzothiazole **10d** was performed as well. In this case, the reaction product varied depending on the conditions under which the $HgCl_2$-mediated hydrolysis was carried out. Specifically, hydrolysis in the presence of Et_3N afforded the allyl ketone **12d** (entry 12), whereas in the absence of the amine, acid-catalyzed isomerization of the latter product occurred to give the thermodynamically more stable 1-propenyl isomer **13d** (entry 13). In summary, the collection of *C*-glycosyl ketones prepared appears to

(17) This preference for benzothiazole over thiazole as a carbonyl group equivalent should not be taken as a general rule because, in some syntheses, the use of the latter is highly preferred if not crucial. For comments on this issue, see footnote 144 in ref 7b above and footnote 16 in ref 5f above.

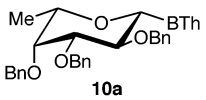
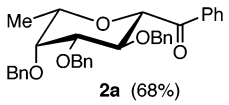
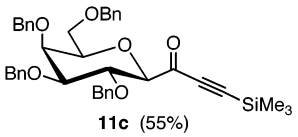
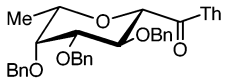
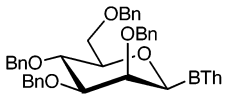
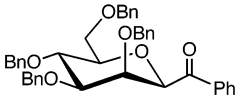
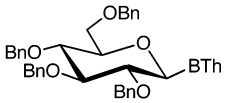
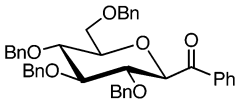
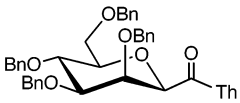
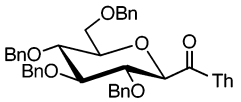
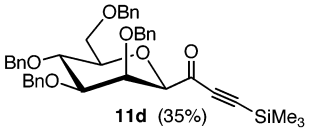
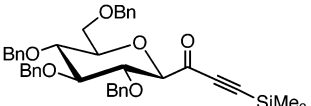
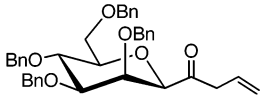
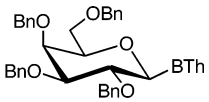
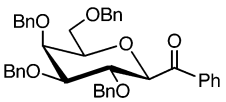
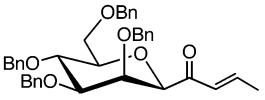
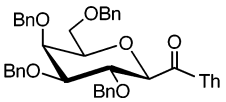
(18) The preparation of this reagent (see Experimental Section) required adjustments of older (Metzger, J.; Koether, B. *Bull. Soc. Chim.* **1953**, 702) and more recent (Abarbri, M.; Thibonnet, J.; Bérillon, L.; Dehmel, F.; Rottländer, M.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 4618) methods, which, in fact, in our hands, produced a material that failed to react with *C*-glycosyl benzothiazolium salts.

(19) Various salts with different metal cations (silver, copper, mercury) have been employed in the hydrolysis of the thiazolidine and benzothiazoline rings (Dondoni, A.; Marra, A.; Perrone, D. *J. Org. Chem.* **1993**, *58*, 275). However, although $AgNO_3$ and $CuCl_2$/CuO are quite effective in the thiazole route, $HgCl_2$ gave the best results in the benzothiazole route. Unfortunately, the latter salt is quite toxic.

(20) Dondoni, A.; Marra, A. *Tetrahedron Lett.* **2003**, *44*, 13.

(21) For the *C*-mannopyranoside derivatives **2d**−**5d** and **10d**−**13d**, the β-D configuration was established by nOe experiments showing substantial enhancements between the anomeric proton and the other axial hydrogen atoms of the pyranose ring. The β-D anomeric configuration of the ketones **2b**,**c**, **3b**,**c**, and **11b**,**c** and the alcohols **4b**,**c**, **5b**,**c**, and **14b**−**20b** was assigned on the basis of the large vicinal coupling constants (ca. 9 Hz) between the anomeric hydrogen atom (H-2) and H-3.

TABLE 1. ***C*-Glycosyl Ketones Prepared by the Reaction Sequence Shown in Scheme 2 (BTh = 2-benzothiazolyl; Th = 2-thiazolyl)**

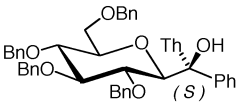
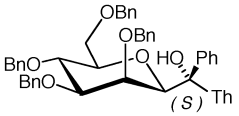
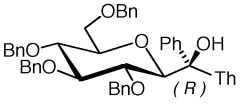
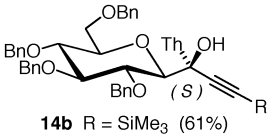
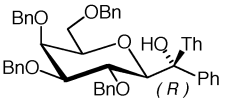
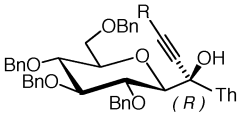
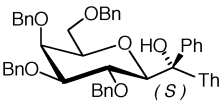
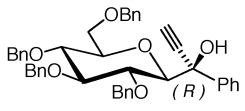
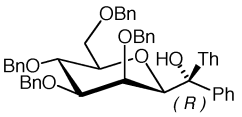
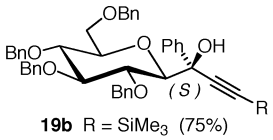
Entry	Benzothiazolyl *C*-glycoside	Ketone[a]	Entry	Benzothiazolyl *C*-glycoside	Ketone[a]
1	 **10a**	 **2a** (68%)	8	**10c**	 **11c** (55%)
2	**10a**	 **3a** (70%)	9	 **10d**	 **2d** (64%)
3	 **10b**	 **2b** (70%)	10	**10d**	 **3d** (73%)
4	**10b**	 **3b** (64%)	11	**10d**	 **11d** (35%)
5	**10b**	 **11b** (55%)	12	**10d**	 **12d** (71%)[b]
6	 **10c**	 **2c** (75%)	13	**10d**	 **13d** (80%)
7	**10c**	 **3c** (65%)			

[a] Isolated yields in parentheses. [b] Also, the isomer **13d** was isolated in 10% yield.

demonstrate that the benzothiazole-based entry to this class of nonsymmetrical ketones bears a good degree of generality and therefore should be extensible to the preparation of a larger library of these compounds.

Synthesis of *C*-Glycosyl Tertiary Alcohols. Whereas the highly stereoselective addition of 2-ThLi to the *C*-fucosyl ketone **2a** and the addition of PhMgBr to **3a** to give the epimer tertiary alcohols **4a** and **5a**, respectively (Scheme 1), were described in our earlier paper,[6] we were delighted to observe that similarly effective addition reactions occurred with other *C*-glycosyl ketones reported in Table 1. Hence, the glucosyl derivatives **2b** and **3b** were transformed into the pair of (*S*)- and (*R*)-epimers **4b** and **5b**, the galactosyl derivatives **2c** and **3c** into the pair **4c** and **5c**, and the mannosyl derivatives **2d** and **3d** into the pair **4d** and **5d** (Table 2).[21] Apparently, these reactions occurred with high stereoselectivity as judged by crude ^{1}H NMR analysis and isolation in each case of a single stereoisomer in remarkably high yield of up to the 99% value for the alcohol **5d**. The lower yields of the two alcohols **4c** and **4d** (73 and 70%) with respect to the other isomers can be ascribed to the partial consumption of the respective ketones **2c** and **2d** as shown by their presence (5−16%) in the crude reaction mixtures. The scarce reactivity of these ketones, the low temperature (−75 to −65 °C), and impurities in the solution of 2-ThLi might be responsible for this result. Experimentation with the ketone **2c** showed that the use of 2-ThMgBr at higher temperature (from −80 to 20 °C, 3 h) solved the problem, as the recorded yield was fairly high (95%), but introduced another drawback in that the two epimers were formed in 3:1 ratio. Given the importance of optically active propargylic alcohols as synthetic intermediates in asymmetric syntheses,[4j,22] the construction of the tertiary propargylic alcohol moiety as a carbon-linked side chain of glucose was considered. Hence, the pair of diastereomeric (*S*)- and (*R*)-alcohols **14b** and **16b** featuring the sugar residue and the 2-thiazolyl ring as

TABLE 2. Chiral Tertiary Alcohols Prepared by Addition of Organometal Reagents to *C*-Glycosyl Ketones (Th = 2-thiazolyl)

Ketone	R-M (equiv.)	Alcohol[a]	Ketone	R-M (equiv.)	Alcohol[a]
Glc-C(O)-Ph **2b**	2-ThLi (2)	 **4b** (88%)	Man-C(O)-Th **3d**	PhMgBr (3)	 **5d** (99%)
Glc-C(O)-Th **3b**	PhMgBr (3)	 **5b** (87%)	Glc-C(O)-C≡CSiMe$_3$ **11b**	2-ThLi (2)	 **14b** R = SiMe$_3$ (61%) **15b** R = H (98%)
Gal-C(O)-Ph **2c**	2-ThLi (2)	 **4c** (73%)	Glc-C(O)-Th **3b**	Me$_3$SiC≡CCeCl$_2$ (2.5)	 **16b** R = SiMe$_3$ (82%) **17b** R = H (98%)
Gal-C(O)-Th **3c**	PhMgBr (3)	 **5c** (81%)	Glc-C(O)-Ph **2b**	CH≡CMgBr (3)	 **18b** (91%)
Man-C(O)-Ph **2d**	2-ThLi (2)	 **4d** (70%)	Glc-C(O)-C≡CSiMe$_3$ **11b**	PhMgBr (3)	 **19b** R = SiMe$_3$ (75%) **20b** R = H (98%)

[a] Isolated yields in parentheses.

the other two substituents at the quaternary carbon atom were obtained by addition of 2-ThLi to *C*-glucosyl TMS-ethynyl ketone **11b** and by addition of the cerium TMS-acetylide reagent[5g] to the *C*-glucosyl thiazolyl ketone **3b**, respectively. Also, these reactions occurred with excellent selectivity, as demonstrated by the formation of a single diastereoisomer in both cases. Optimized yields should be considered those reported in Table 2 by the use of the reagents employed because 2-ThMgBr gave only 35% yield of **14b** and other ethynyl organometals (TMS−C≡CMgBr, HC≡MgBr, TMS−C≡CLi) produced **16b** in 20% yield or even lower values. The second pair of tertiary (*R*)- and (*S*)-propargylic alcohols **18b** and **19b** in which the phenyl ring was the fourth substituent at the quaternary carbon atom were obtained by addition of ethynyl and phenyl Grignard reagents to the suitable sugar ketones **2b** and **11b**, respectively.[21] Also in these cases, the yields were quite satisfactory, and the diasteroselectivity was practically complete. It is worth noting that the TMS group was easily removed from the substituted propargylic alcohols **14b**, **16b**, and **19b** upon treatment with KOH in MeOH−CH_2Cl_2, thus affording the desilylated products **15b**, **17b**, and **20b** in almost quantitative yields.

The absolute configurations of the C-1 quaternary carbon atom of alcohols **4b**−**d** and **5b**−**d**, all featuring a $^5C_2$ conformation, were assigned by mono- and bidimensional nuclear Overhauser effect (nOe) experiments. The (1*S*)-configured alcohols **4b** and **5d** appeared to adopt a preferential conformation where the 2-thiazolyl ring was anti to H-2 and the OH group anti to the C-2−O-6 bond (Figure 1). This arrangement was mainly deduced by the strong nOe between OH-1 and both H-2 and H-3, in the case of **4b**, and both H-3 and the benzylic protons of the BnO group at C-3, in the case of **5d**. Moreover, the NMR spectra of these alcohols showed a significant nOe between the H_{ortho} of the phenyl ring at C-1 and H-2. The absence of nOe between the latter aromatic protons and H-3 or the benzylic protons of the BnO group at C-3 supported the conformation proposed for **4b** and **5d**. The nOe observed between OH-1 and H-3 and between the H_{ortho} of the phenyl ring at C-1 and H-2 of compounds **4c**

(22) For recent papers with leading references, see: (a) Frantz, D. E.; Fässler, R., Tomooka, C. S.; Carreira, E. M. *Acc. Chem. Res.* **2000**, *33*, 373. (b) Marshall, J. A.; Bourbeau, M. P. *Org. Lett.* **2003**, *5*, 3197. (c) Li, M.; Zhu, X. Z.; Yuan, K.; Cao, B. X.; Hou, X. L. *Tetrahedron: Asymm.* **2004**, *15*, 219. (d) Xu, Z. Q.; Chen, C.; Xu, J. K.; Miao, M. B.; Yan, W. J.; Wang, R. *Org. Lett.* **2004**, *6*, 1193. (e) Dahmen, S. *Org. Lett.* **2004**, *6*, 2113. (f) Denmark, S. E.; Yang, S.-M. *J. Am. Chem. Soc.* **2004**, *126*, 12432. (g) Nicewicz, D. A.; Johnson, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 6170. (h) Raminelli, C.; da Silva, N. C.; Dos Santos, A. A.; Porto, A. L. M.; Andrade, L. H.; Comasseto, J. V. *Tetrahedron* **2005**, *61*, 409. (i) Han, Z. J.; Wang, R.; Zhou, Y. F.; Liu, L. *Eur. J. Org. Chem.* **2005**, 934.

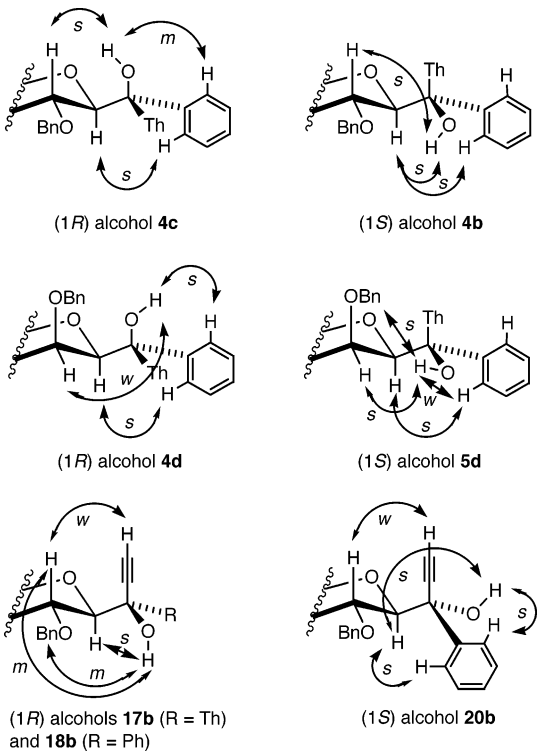


FIGURE 1. Nuclear Overhauser effects observed for the tertiary alcohols shown in Table 2.

and **4d** indicated a (1*R*)-configuration for these alcohols adopting the conformation depicted in Figure 1. Unfortunately, the nOe experiments indicated a free rotation about the *C*-glycosidic bond of the alcohols **5b** and **5c**, so their configurations were indirectly assigned as those of the epimers of **4b** and **4c**, respectively.

Similar NMR experiments allowed the tentative attribution of the absolute configuration at C-1 of the propargylic alcohols **17b**, **18b**, and **20b** (Figure 1), whereas that of **15b** could only be deduced as being the opposite of **17b**. In particular, the presence of a weak nOe between the acetylenic hydrogen atom and H-3, as well as the concomitant lack of nOe between the former atom and the anomeric proton H-2, indicated that the acetylene moiety was anti to H-2 in all three cases. Moreover, the spectra of **17b** and **18b** showed a strong nOe between OH-1 and H-2, as well as medium nOes between the former atom and both H-3 and the benzylic protons of the BnO group at C-3. These effects suggested that OH-1 was anti to the C-2−O-6 bond and therefore that the configuration of these alcohols was 1*R* (Figure 1). On the other hand, OH-1 of **20b** showed a substantial nOe only with H-2 and the H_{ortho} of the phenyl ring at C-1. This finding, together with the strong nOe observed between the latter aromatic protons and H-2, indicated that the phenyl ring at C-1 was anti to the C-2−O-6 bond. The conformation deduced by the NMR data (Figure 1) led us to assign the (1*S*)-configuration to the alcohol **20b**.

Each pair of *C*-glycosyl ketones bearing the same sugar fragment appears to undergo the addition of various organometallic reagents to the same carbonyl diastereoface. However, the sense of diastereofacial selectivity varied with the type of sugar residue. For example, the pair of the L-fucosyl ketones **2a** and **3a** reacted with 2-ThLi and PhMgBr, respectively, to give to the alcohols (*R*)-**4a** and (*S*)-**5a**, whereas the *C*-glucosyl pair **2b** and **3b** reacted with the same organometallic reagents to give to the alcohols (*S*)-**4b** and (*R*)-**5b**. Moreover, it can be observed that ketones **2b**−**d** and **3b**−**d** featuring the pyranose ring in the same $^4C_1$ conformation and displaying the same absolute configuration (*β*-D) at the carbon atom adjacent to the carbonyl function, did not produce identically configured tertiary alcohols **4b**−**d** and **5b**−**d**, respectively (Table 2). Also quite intriguing is the observation that the L-fucosyl ketones **2a** and **3a**, i.e., 7-deoxy enantiomers of the D-galactosyl ketones **2c** and **3c**, did not show opposite stereochemical outcome in reactions with the same organometals 2-ThLi and PhMgBr, as both pairs of ketones led to alcohols with the same (*R*)- and (*S*)-configuration, i.e., (*R*)-**4a** and (*S*)-**5a** from the former pair and (*R*)-**4c** and (*S*)-**5c** from the latter. Hence, from these observations, it appears that the sugar residue plays an important and rather complex role in the stereochemical outcome of the addition of organometallic reagents to *C*-glycosyl ketones. Because of the complexity of the substrates as well as the different natures of the organometallic reagents employed, the stereochemical outcome of the reactions is hard to rationalize by simple classical steric models.[23] In line with the modern trend focusing on ab initio studies,[24] we plan to provide some insight into the transition states occurring in the above nucleophilic additions to *C*-glycosyl ketones by an ab initio approach that is underway in our laboratory.

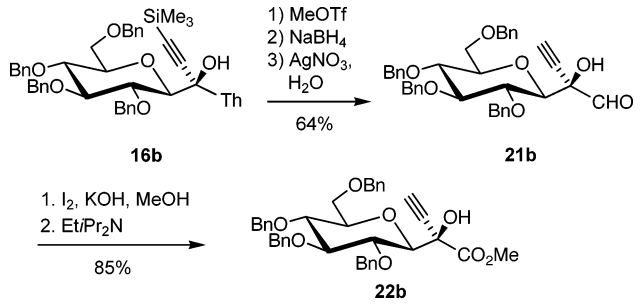
Conclusions

Although the development of a new and effective synthesis of important *C*-glycoconjugates such as C-glycosyl ketones based on benzothiazole chemistry was a key issue in this program, the use of these ketones as substrates leading to *C*-glycosylated tertiary alcohols appeared to be the most attractive result from this work. Quite noteworthy is the high level of diastereofacial selectivity occurring in the addition of organometal reagents to the above ketones and through which chiral tertiary alcohol fragments carbon linked to the anomeric center of various sugars were assembled. The nonsugar residues that were present in these alcohols were precious tools for convenient synthetic elaborations. For instance, the presence of the thiazole ring was not fortuitous, as this heterocycle was deliberately introduced with the aim of exploiting its potential as a formyl group equivalent.[7] A demonstration of the useful service of this heterocycle was reported in our recent paper[6] showing the transformation of **4a** and **5a** (see Scheme 1) into the corresponding L-fucosyl phenylhydroxy acetates. The reaction sequence shown in Scheme 4 is also centered on the use of the thiazole ring as a formyl group

(23) (a) Cram models: Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. (b) Cornforth dipolar model: Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112. (c) Karabatsos model: Karabatsos, G. J. *J. Am. Chem. Soc.* **1967**, *89*, 1367. (d) Felkin model: Chérest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. For a review, see: Mengel, A.; Reiser, O. *Chem. Rev.* **1999**, *99*, 1191.

(24) (a) Yamazaki, S.; Yamabe, S. *J. Org. Chem.* **2002**, *67*, 9346. (b) Takahashi, O.; Saito, K.; Kohno, Y.; Suezawa, H.; Ishihara, S.; Nishio, M. *New J. Chem.* **2004**, *28*, 355.

SCHEME 4



equivalent. The TMS-protected propargylic alcohol **16b** containing the thiazole ring as one of the substituents was transformed into the TMS-free chiral aldehyde **21b**, which, in turn, was oxidized to the ester **22b** in good yield. This reaction sequence provides an entry to a special and new class of propargylic alcohols featuring a *C*-glycosyl residue and a carboxylate group. The asymmetric synthesis of structurally related but nonglycosylated propargylic alcohols of this type has been recently reported as an important achievement by Jiang and coworkers[25] via chiral amino alcohol-catalyzed nucleophilic addition of terminal alkynes to α-ketoesters.

Experimental Section

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Anhydrous solvents were dried over standard drying agents[26] 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 on silica gel 60 F_{254} with detection by charring with sulfuric acid. Flash column chromatography[27] 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 deg·mL·g^{-1}·dm^{-1}. ^{1}H NMR spectra (300 and 400 MHz) were recorded for $CDCl_3$ solutions at room temperature unless otherwise specified; chemical shifts are in ppm (δ) from $SiMe_4$ (TMS) as internal standard; peak assignments were performed by ^{1}H−^{1}H COSY experiments. MALDI-TOF mass spectra were acquired using 2,6-dihydroxy-benzoic acid as the matrix. L-Fuconolactone **6**[28] and 2,3,4,6-tetra-*O*-benzyl-D-mannonolactone[29] were prepared by oxidation of the corresponding hemiacetals[30,31] with pyridinium chlorochromate.[32] Known[33] trimethylsilylethynylmagnesium bromide was prepared by a slightly modified procedure. Phenylmagnesium bromide, allylmagnesium bromide, ethynylmagnesium bromide, benzothiazole, and 2-bromothiazole were commercially available.

1-*O*-Acetyl-2,3,4-tri-*O*-benzyl-1-*C*-(2-benzothiazolyl)-α-L-fucopyranose (9a). To a cooled (−70 °C), stirred solution of ^{n}BuLi (1.7 mL of a 1.6 M solution in hexane, 2.70 mmol) in anhydrous Et_2O (6 mL) was added dropwise a solution of freshly distilled benzothiazole (0.30 mL, 2.70 mmol) in anhydrous Et_2O (3 mL) over a 15-min period. The yellow solution was stirred at −70 °C for 30 min, and then a solution of fuconolactone **6** (842 mg, 1.95 mmol) in anhydrous Et_2O (6 mL) was added slowly (15 min). After an additional 1 h at −70 °C, the mixture was allowed to warm to −50 °C in 1 h and then poured into 30 mL of a 1 M phosphate buffer at pH 7. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give crude **8a** (1.23 g) as a yellow-green syrup. ^{1}H NMR (300 MHz): δ 8.10−8.07 and 7.89−7.86 (2m, 2H, BTh), 7.54−7.30 and 7.12−6.88 (2m, 17H, BTh, Ar), 5.10 and 4.79 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.82 (s, 2H, PhCH_2), 4.81 (bs, 1H, OH), 4.72 and 4.43 (2d, 2H, J = 11.0 Hz, PhCH_2), 4.52 (d, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 4.31 (dq, 1H, $J_{4,5}$ = 0.8 Hz, $J_{5,6}$ = 6.4 Hz, H-5), 4.10 (dd, 1H, $J_{3,4}$ = 2.6 Hz, H-3), 3.80 (dd, 1H, H-4), 1.28 (d, 3H, 3H-6).

To a solution of crude **8a** (1.23 g) in anhydrous CH_2Cl_2 (10 mL) were added at room temperature triethylamine (2.9 mL) and acetic anhydride (2.1 mL). The solution was kept at room temperature for 48 h and then concentrated. The residue was eluted from a column of silica gel with cyclohexane/AcOEt (from 2:1 to 1:2) to give **9a** (1.02 g, 86% from **6**) as a white solid. Mp 147−148 °C (Et_2O); $[\alpha]_D$ = −35.3 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz): δ 8.06−8.03 and 7.83−7.80 (2m, 2H, BTh), 7.47−7.28 (m, 12H, BTh, Ar), 7.15−7.12 (m, 2H, Ar), 7.09−7.05 (m, 1H, Ar), 6.99−6.94 (m, 2H, Ar), 5.04 and 4.73 (2d, 2H, J = 11.9 Hz, PhCH_2), 4.86 and 4.79 (2d, 2H, J = 11.8 Hz, PhCH_2), 4.56 and 4.38 (2d, 2H, J = 11.0 Hz, PhCH_2), 4.16 (app d, 2H, J = 0.8 Hz, H-2, H-3), 3.97 (dq, 1H, $J_{4,5}$ = 1.3 Hz, $J_{5,6}$ = 6.4 Hz, H-5), 3.78 (app q, 1H, H-4), 2.21 (s, 3H, Ac), 1.31 (d, 3H, 3H-6). Anal. Calcd for $C_{36}H_{35}NO_6S$: C, 70.91; H, 5.79; N, 2.30. Found: C, 71.08; H, 5.82; N 2.18. The anomeric configuration of this ketose was assigned on the basis of the nOe between the protons of the acetyl group and H-5.

2-(2,3,4-Tri-*O*-benzyl-β-L-fucopyranosyl)benzothiazole (10a). To a stirred mixture of **9a** (880 mg, 1.44 mmol), activated 4-Å powdered molecular sieves (1.4 g), and triethylsilane (2.33 mL, 14.44 mmol) in anhydrous CH_2Cl_2 (24 mL) was added TMSOTf (392 μL, 2.17 mmol). The mixture was stirred at room temperature for 1 h, then diluted with triethylamine (1.3 mL) and CH_2Cl_2 (25 mL), filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane/AcOEt (from 5:1 to 3:1) to give **10a** (700 mg, 88%) as a syrup. $[\alpha]_D$ = +38.8 (*c* 1.5, $CHCl_3$). ^{1}H NMR (300 MHz, C_6D_6): δ 8.08−8.05 (m, 1H, BTh), 7.43−7.39 (m, 2H, Ar), 7.37−7.32 (m, 3H, Ar), 7.24−7.06 and 7.03−6.92 (2m, 13H, BTh, Ar), 5.00 and 4.62 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.84 (d, 1H, $J_{1,2}$ = 9.3 Hz, H-1), 4.62 and 4.54 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.58 and 4.41 (2d, 2H, J = 10.7 Hz, PhCH_2), 4.42 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 3.45 (dd, 1H, $J_{3,4}$ = 2.8 Hz, H-3), 3.26 (dd, 1H, $J_{4,5}$ = 0.8 Hz, H-4), 3.12 (dq, 1H, $J_{5,6}$ = 6.3 Hz, H-5), 1.16 (d, 3H, 3H-6). Anal. Calcd for $C_{34}H_{33}NO_4S$: C, 74.02; H, 6.03; N, 2.54. Found: C, 74.20; H, 6.24; N, 2.60.

2-(2,3,4,6-Tetra-*O*-benzyl-β-D-mannopyranosyl)benzothiazole (10d). 2,3,4,6-Tetra-*O*-benzyl-D-mannonolactone (5.80 g, 10.77 mmol) was allowed to react with 2-lithiobenzothiazole as described for the preparation of **8a** to give crude 2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-benzothiazolyl)-D-mannopyranose. The crude ketose derivative was acetylated as described for the preparation of **9a** to give, after column chromatography on silica gel (3:1 cyclohexane/AcOEt), 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-benzothiazolyl)-α-D-mannopyranose (6.50 g, 84% from the perbezylated D-mannonolactone) as a white solid. Mp 133−134 °C (cyclohexane); $[\alpha]_D$ = +0.7 (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.02−7.98 and 7.92−7.88 (2m, 2H, BTh), 7.50−7.25 (m, 17H, Ar), 7.12−7.05 (m, 1H, Ar), 7.00−6.94 (m, 2H, Ar), 6.82−6.76 (m, 2H, Ar), 4.97 and 4.70 (2d, 2H, J = 10.7 Hz, PhCH_2), 4.95 and 4.73 (2d, 2H, J = 11.6 Hz, PhCH_2), 4.85

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and 4.79 (2d, 2H, $J = 11.5$ Hz, PhCH_2), 4.63 and 4.18 (2d, 2H, $J = 11.0$ Hz, PhCH_2), 4.59 (d, 1H, $J_{2,3} = 2.7$ Hz, H-2), 4.35 (dd, 1H, $J_{3,4} = 9.5$ Hz, $J_{4,5} = 9.7$ Hz, H-4), 4.25 (dd, 1H, H-3), 4.06 (dd, 1H, $J_{5,6a} = 4.0$ Hz, $J_{6a,6b} = 12.3$ Hz, H-6a), 3.95 (dd, 2H, $J_{5,6b} = 1.6$ Hz, H-6b), 3.92 (ddd, 1H, H-5), 2.11 (s, 3H, Ac). Anal. Calcd for $C_{43}H_{41}NO_7S$: C, 72.15; H, 5.77; N, 1.96. Found: C, 72.23; H, 5.83; N, 1.82. The anomeric configuration of this ketose was assigned on the basis of the nOes between the protons of the acetyl group and both H-3 and H-5.

The ketose acetate (1.16 g, 1.62 mmol) was deoxygenated as described for the preparation of **10a** to give, after column chromatography on silica gel (from 7:1:1 to 3:1:1 cyclohexane/AcOEt/CH_2Cl_2), **10d** (0.88 g, 83%) as a white solid. Mp 129−130 °C (cyclohexane/pentane); $[\alpha]_D = +18.4$ (c 1.2, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.96−7.92 (m, 2H, BTh), 7.54−7.48 (m, 1H, Ar), 7.45−7.24 (m, 21H, Ar), 4.97 and 4.66 (2d, 2H, $J = 10.8$ Hz, PhCH_2), 4.93 (d, 1H, $J_{1,2} = 1.3$ Hz, H-1), 4.83 and 4.72 (2d, 2H, $J = 12.0$ Hz, PhCH_2), 4.82 and 4.70 (2d, 2H, $J = 11.7$ Hz, PhCH_2), 4.68 and 4.40 (2d, 2H, $J = 11.5$ Hz, PhCH_2), 4.56 (dd, 1H, $J_{2,3} = 2.6$ Hz, H-2), 4.13 (dd, 1H, $J_{3,4} = 9.3$ Hz, $J_{4,5} = 9.7$ Hz, H-4), 3.91 (d, 2H, $J_{5,6} = 3.5$ Hz, 2 H-6), 3.87 (dd, 1H, H-3), 3.75 (dt, 1H, H-5). Anal. Calcd for $C_{41}H_{39}NO_5S$: C, 74.86; H, 5.98; N, 2.13. Found: C, 74.98; H, 6.07; N, 2.01.

Preparation of the Thiazolylmagnesium Bromide Solution (ca. 0.5 M). To a cooled (0 °C), stirred solution of ethylmagnesium bromide (3.34 mL of a 3 M solution in Et_2O, 10.0 mmol) in anhydrous THF (16 mL) was added dropwise freshly distilled 2-bromothiazole (900 μL, 10.00 mmol) over a 5-min period. The pale yellow solution was stirred for 30 min at 0 °C and then allowed to warm to 20 °C in 30 min and stirred for an additional 1 h. The resulting deep red solution was stored at 25 °C and used within 8 h. Upon prolonged storage at room temperature, the solution turned to a black suspension.

Preparation of the Trimethylsilylethynylmagnesium Bromide Solution (ca. 1 M). To a cooled (0 °C), stirred solution of commercially available trimethylsilylacetylene (565 μL, 4.00 mmol) in anhydrous THF (2.7 mL) was added dropwise ethylmagnesium bromide (1.33 mL of a 3 M solution in Et_2O, 4.00 mmol) over a 15-min period. The colorless solution was stirred at 0 °C for 30 min and then allowed to warm to 25 °C in 30 min and used within 3 h.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-deoxy-1-*C*-phenyl-*aldehydo*-L-*glycero*-D-*manno*-heptose (2a). A mixture of **10a** (110 mg, 0.20 mmol), activated 4-Å powdered molecular sieves (0.20 g), and anhydrous CH_3CN (2 mL) was stirred at room temperature for 10 min, and then methyl triflate (34 μL, 0.30 mmol) was added. The suspension was stirred at room temperature for 15 min, concentrated to dryness, diluted with CH_2Cl_2, filtered through a pad of Celite, and concentrated to give the *N*-methylbenzothiazolium salt as a white foam (150 mg).

To a cooled (−10 °C), stirred solution of phenylmagnesium bromide (200 μL of a 3 M solution in Et_2O, 0.60 mmol) in THF (2.5 mL) was added a solution of the crude *N*-methylbenzothiazolium salt (150 mg) in anhydrous THF (1.5 mL). The solution was stirred for an additional 2 h at −10 °C, then diluted with 1 M phosphate buffer at pH 7 (20 mL), and extracted with AcOEt (2 × 50 mL). The combined organic phases were washed with brine (2 × 20 mL), dried (Na_2SO_4), and concentrated to give the corresponding benzothiazolines as a yellow syrup (115 mg).

To a vigorously stirred solution of the crude benzothiazolines in a CH_3CN (2 mL) and CH_2Cl_2 (0.2 mL) mixture was added dropwise H_2O (0.2 mL) and then $HgCl_2$ in one portion (109 mg, 0.40 mmol). The mixture was stirred at room temperature for 15 min and then diluted with Et_3N (ca. 28 μL, 0.20 mmol) to reach pH 7. After an additional 30 min of stirring, the mixture was diluted with 1 M phosphate buffer at pH 7 (20 mL) and partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C). The suspension was extracted with CH_2Cl_2 (2 × 40 mL), and the combined organic phases were washed with 20% aqueous KI, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 8:1 toluene/AcOEt to give **2a** (71 mg, 68%) as a white solid. The physical and spectroscopic data of **2a** were identical to those of the product prepared by another route.[6]

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-*aldehydo*-D-*glycero*-D-*gulo*-heptose (2b). Compound **10b** (500 mg, 0.76 mmol) was treated as described for the preparation of **2a** to give, after column chromatography on silica gel (6:1 cyclohexane/AcOEt), **2b** (334 mg, 70%) as a white solid. Mp 99−100 °C (MeOH); $[\alpha]_D = +16.1$ (c 0.7, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.12−8.08 (m, 2H, Ar), 7.63−7.58 (m, 1H, Ar), 7.50−7.44 (m, 2H, Ar), 7.38−7.18 (m, 18H, Ar), 7.06−7.00 (m, 2H, Ar), 4.96 (s, 2H, PhCH_2), 4.88 and 4.63 (2d, 2H, $J = 10.8$ Hz, PhCH_2), 4.74 and 4.62 (2d, 2H, $J = 10.5$ Hz, PhCH_2), 4.67 (d, 1H, $J_{2,3} = 9.5$ Hz, H-2), 4.58 and 4.52 (2d, 2H, $J = 11.8$ Hz, PhCH_2), 4.07 (dd, 1H, $J_{3,4} = 9.0$ Hz, H-3), 3.92−3.85 (m, 1H), 3.82−3.67 (m, 4H). Anal. Calcd for $C_{41}H_{40}O_6$: C, 78.32; H, 6.41. Found: C, 78.18; H, 6.35.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-*aldehydo*-D-*glycero*-L-*manno*-heptose (2c). Compound **10c** (487 mg, 0.74 mmol) was treated as described for the preparation of **2a** to give, after column chromatography on silica gel (5:1 cyclohexane/AcOEt), **2c** (350 mg, 75%) as a white solid. Mp 103−105 °C (cyclohexane); $[\alpha]_D = +7.5$ (c 0.8 $CHCl_3$). ^{1}H NMR (400 MHz): δ 8.12−8.07 (m, 2H, Ar), 7.56−7.51 (m, 1H, Ar), 7.41−7.24 (m, 17H, Ar), 7.19−7.15 (m, 3H, Ar), 7.04−7.00 (m, 2H, Ar), 5.04 and 4.64 (2d, 2H, $J = 11.5$ Hz, PhCH_2), 4.81 and 4.75 (2d, 2H, $J = 11.7$ Hz, PhCH_2), 4.75 and 4.52 (2d, 2H, $J = 10.5$ Hz, PhCH_2), 4.55 (d, 1H, $J_{2,3} = 9.6$ Hz, H-2), 4.47 (dd, 1H, $J_{3,4} = 9.5$ Hz, H-3), 4.47 and 4.41 (2d, 2H, $J = 11.7$ Hz, PhCH_2), 4.06 (dd, 1H, $J_{4,5} = 2.6$ Hz, $J_{5,6} = 0.6$ Hz, H-5), 3.75 (dd, 1H, H-4), 3.74 (ddd, 1H, $J_{6,7a} = 5.7$ Hz, $J_{6,7b} = 7.0$ Hz, H-6), 3.65 (dd, 1H, $J_{7a,7b} = 9.5$ Hz, H-7a), 3.62 (dd, 1H, H-7b). Anal. Calcd for $C_{41}H_{40}O_6$: C, 78.32; H, 6.41. Found: C, 78.22; H, 6.30.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-*aldehydo*-D-*glycero*-D-*galacto*-heptose (2d). Compound **10d** (600 mg, 0.91 mmol) was treated as described for the preparation of **2a** to give, after column chromatography on silica gel (6:1 cyclohexane/AcOEt), **2d** (366 mg, 64%) as a syrup. $[\alpha]_D = -1.8$ (c 1.5, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.12−8.08 (m, 2H, Ar), 7.57−7.51 (m, 1H, Ar), 7.42−7.12 (m, 22H, Ar), 4.96 and 4.66 (2d, 2H, $J = 10.9$ Hz, PhCH_2), 4.82 and 4.53 (2d, 2H, $J = 11.2$ Hz, PhCH_2), 4.80 and 4.73 (2d, 2H, $J = 11.7$ Hz, PhCH_2), 4.64 and 4.57 (2d, 2H, $J = 12.2$ Hz, PhCH_2), 4.47 (dd, 1H, $J_{2,3} = 1.3$ Hz, $J_{3,4} = 3.0$ Hz, H-3), 4.45 (d, 1H, H-2), 4.08 (dd, 1H, $J_{4,5} = 9.3$ Hz, $J_{5,6} = 9.7$ Hz, H-5), 3.83 (dd, 1H, $J_{6,7a} = 3.0$ Hz, $J_{7a,7b} = 11.0$ Hz, H-7a), 3.79 (dd, 1H, $J_{6,7b} = 4.5$ Hz, H-7b), 3.78 (dd, 1H, H-4), 3.59 (ddd, 1H, H-6). Anal. Calcd for $C_{41}H_{40}O_6$: C, 78.32; H, 6.41. Found: C, 78.11; H, 6.55.

2,6-Anhydro-3,4,5-tri-*O*-benzyl-7-deoxy-1-*C*-(2-thiazolyl)-*aldehydo*-L-*glycero*-D-*manno*-heptose (3a). A mixture of **10a** (110 mg, 0.20 mmol), activated 4-Å powdered molecular sieves (0.20 g), and anhydrous CH_3CN (0.20 mL) was stirred at room temperature for 10 min, and then methyl triflate (34 μL, 0.30 mmol) was added. The suspension was stirred at room temperature for 15 min, concentrated to dryness, diluted with CH_2Cl_2, filtered through a pad of Celite, and concentrated to give *N*-methylbenzothiazolium salt as a white foam (150 mg).

To a cooled (0 °C), stirred solution of thiazolylmagnesium bromide in Et_2O/THF (1.20 mL of a ca. 0.5 M solution prepared as described above, 0.60 mmol) was added a solution of crude *N*-methylbenzothiazolium salt in anhydrous THF (1.5 mL). The mixture was allowed to warm to room temperature in 30 min, then diluted with 1 M phosphate buffer at pH 7 (20 mL), and extracted with AcOEt (2 × 50 mL). The combined organic phases were washed with brine (2 × 20 mL), dried (Na_2SO_4), and concentrated to afford the corresponding benzothiazolines as a yellow syrup (125 mg).

To a vigorously stirred solution of the crude benzothiazolines in a CH_3CN (2 mL) and CH_2Cl_2 (0.2 mL) mixture was added dropwise H_2O (0.20 mL) and then $HgCl_2$ in one portion (109 mg, 0.40 mmol). The mixture was stirred at room temperature

for 1 h and then diluted with Et_3N (ca. 28 μL, 0.20 mmol) to reach pH 7. After an additional 2 h of stirring, the mixture was diluted with 1 M phosphate buffer at pH 7 (20 mL) and partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C). The suspension was extracted with CH_2Cl_2 (2 × 40 mL), and the combined organic phases were washed with 20% aqueous KI, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 5:1 cyclohexane/AcOEt to give **3a** (74 mg, 70%) as a white solid. The physical and spectroscopic data of **3a** were identical to those of the product prepared by another route.[6]

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-*aldehydo*-D-*glycero*-D-*gulo*-heptose (3b). Compound **10b** (170 mg, 0.26 mmol) was treated as described for the preparation of **3a** to give, after column chromatography on silica gel (4:1 cyclohexane/AcOEt), **3b** (105 mg, 64%) as a solid. Mp 86−87 °C (MeOH); $[\alpha]_D = -8.6$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, C6D6): δ 7.43 and 6.46 (2d, 2H, J = 3.0 Hz, Th), 7.30−6.94 (m, 20H, Ar), 5.46 (d, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 4.81 (s, 2H, PhCH_2), 4.80 and 4.63 (2d, 2H, J = 11.2 Hz, PhCH_2), 4.79 and 4.57 (2d, 2H, J = 11.3 Hz, PhCH_2), 4.40 and 4.28 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.34 (dd, 1H, $J_{3,4}$ = 8.8 Hz, H-3), 3.84 (dd, 1H, $J_{4,5}$ = 8.8 Hz, $J_{5,6}$ = 9.2 Hz, H-5), 3.79 (dd, 1H, H-4), 3.64 (dd, 1H, $J_{6,7a}$ = 4.1 Hz, $J_{7a,7b}$ = 11.2 Hz, H-7a), 3.58 (dd, 1H, $J_{6,7b}$ = 1.8 Hz, H-7b), 3.56 (ddd, 1H, H-6). Anal. Calcd for $C_{38}H_{37}NO_6S$: C, 71.79; H, 5.87; N, 2.20. Found: C, 71.58; H, 5.75; N, 2.11.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-*aldehydo*-D-*glycero*-L-*manno*-heptose (3c). Compound **10c** (1.60 g, 2.43 mmol) was treated as described for the preparation of **3a** to give, after column chromatography on silica gel (4:1 cyclohexane/AcOEt), **3c** (1.00 g, 65%) as a syrup. $[\alpha]_D = -5.5$ (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz): δ 8.05 and 7.71 (2d, 2H, J = 3.0 Hz, Th), 7.41−7.24 (m, 15H, Ar), 7.20−7.14 (m, 3H, Ar), 6.98−6.94 (m, 2H, Ar), 5.18 (d, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 5.01 and 4.68 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.86 and 4.54 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.80 and 4.74 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.46 and 4.40 (2d, 2H, J = 11.7 Hz, PhCH_2), 4.43 (dd, 1H, $J_{3,4}$ = 9.5 Hz, H-3), 4.07 (dd, 1H, $J_{4,5}$ = 2.8 Hz, $J_{5,6}$ = 0.7 Hz, H-5), 3.84 (dd, 1H, H-4), 3.82 (dt, 1H, $J_{6,7}$ = 6.4 Hz, H-6), 3.62 (d, 2H, 2H-7). Anal. Calcd for $C_{38}H_{37}NO_6S$: C, 71.79; H, 5.87; N, 2.20. Found: C, 71.61; H, 5.96; N, 2.03.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-*aldehydo*-D-*glycero*-D-*galacto*-heptose (3d). Compound **10d** (600 mg, 0.91 mmol) was treated as described for the preparation of **3a** to give, after column chromatography on silica gel (6:1 cyclohexane/AcOEt), **3d** (423 mg, 73%) as a syrup. $[\alpha]_D = +20.0$ (*c* 2.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 and 7.62 (2d, 2H, J = 3.0 Hz, Th), 7.42−7.25 (m, 13H, Ar), 7.20−7.16 (m, 2H, Ar), 7.09−7.02 (m, 5H, Ar), 5.00 (d, 1H, $J_{2,3}$ = 1.3 Hz, H-2), 4.90 and 4.59 (2d, 2H, J = 10.7 Hz, PhCH_2), 4.82 and 4.76 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.74 (dd, 1H, $J_{3,4}$ = 2.7 Hz, H-3), 4.73 and 4.50 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.66 (s, 2H, PhCH_2), 3.99 (dd, 1H, $J_{4,5} = J_{5,6}$ = 9.5 Hz, H-5), 3.88 (dd, 1H, H-4), 3.85 (dd, 1H, $J_{6,7a}$ = 2.2 Hz, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.81 (dd, 1H, $J_{6,7b}$ = 5.7 Hz, H-7b), 3.63 (ddd, 1H, H-6). Anal. Calcd for $C_{38}H_{37}NO_6S$: C, 71.79; H, 5.87; N, 2.20. Found: C, 71.58; H, 5.80; N, 2.08.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-trimethylsilylethynyl-*aldehydo*-D-*glycero*-D-*gulo*-heptose (11b). A mixture of **10b** (520 mg, 0.79 mmol), activated 4-Å powdered molecular sieves (0.80 g), and anhydrous CH_3CN (4 mL) was stirred at room temperature for 10 min, and then methyl triflate (135 μL, 1.18 mmol) was added. The suspension was stirred at room temperature for 15 min, concentrated to dryness, diluted with CH_2Cl_2, filtered through a pad of Celite, and concentrated to give the *N*-methylbenzothiazolium as a white foam.

To a cooled (0 °C), stirred solution of trimethylsilylethynylmagnesium bromide in THF (2.37 mL of a ca. 1 M solution prepared as described above, 2.37 mmol) was added a solution of crude *N*-methylbenzothiazolium salt in anhydrous THF (1.5 mL) over a 15-min period. The mixture was allowed to warm to room temperature in 30 min and then diluted with 1 M phosphate buffer at pH 7 (20 mL) and extracted with AcOEt (100 mL). The organic phase was washed with brine (2 × 20 mL), dried (Na_2SO_4), and concentrated to give the corresponding benzothiazolines as a yellow syrup (640 mg).

To a vigorously stirred solution of the crude benzothiazolines in a CH_3CN (4 mL) and CH_2Cl_2 (2 mL) mixture was added dropwise H_2O (0.5 mL) and then $HgCl_2$ in one portion (320 mg, 1.18 mmol). The mixture was stirred at room temperature for 15 min and then diluted with Et_3N (ca. 0.11 mL, 0.79 mmol) to reach pH 7. After an additional 15 min of stirring, the mixture was diluted with 1 M phosphate buffer at pH 7 (20 mL) and partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C). The suspension was extracted with CH_2Cl_2 (2 × 60 mL), and the combined organic phases were washed with 20% aqueous KI, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 7:1 cyclohexane/AcOEt to give **11b** (281 mg, 55%) as a syrup. $[\alpha]_D = +14.6$ (*c* 1.5, $CHCl_3$). ^{1}H NMR (400 MHz): δ 7.39−7.28 (m, 18H, Ar), 7.24−7.20 (m, 2H, Ar), 4.89 (s, 2H, PhCH_2), 4.84 and 4.62 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.77 and 4.65 (2d, 2H, J = 10.6 Hz, PhCH_2), 4.65 and 4.58 (2d, 2H, J = 12.1 Hz, PhCH_2), 3.94 (d, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 3.83 (dd, 1H, $J_{3,4}$ = 8.6 Hz, H-3), 3.76 (dd, 1H, $J_{4,5}$ = 8.8 Hz, H-4), 3.74 (d, 2H, $J_{6,7}$ = 3.1 Hz, 2H-7), 3.68 (dd, 1H, $J_{5,6}$ = 9.6 Hz, H-5), 3.53 (dt, 1H, H-6), 0.18 (s, 9H, 3Me). Anal. Calcd for $C_{40}H_{44}O_6Si$: C, 74.04; H, 6.83. Found: C, 73.81; H, 6.96.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-trimethylsilylethynyl-*aldehydo*-D-*glycero*-L-*manno*-heptose (11c). Compound **10c** (743 mg, 1.13 mmol) was treated as described for the preparation of **11b** to give, after column chromatography on silica gel (6:1:1 cyclohexane/AcOEt/CH_2Cl_2), **11c** (403 mg, 55%) as a syrup. $[\alpha]_D = +2.8$ (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz): δ 7.41−7.25 (m, 20H, Ar), 5.00 and 4.63 (2d, 2H, J = 11.8 Hz, PhCH_2), 4.88 and 4.70 (2d, 2H, J = 10.5 Hz, PhCH_2), 4.79 and 4.73 (2d, 2H, J = 11.7 Hz, PhCH_2), 4.52 and 4.45 (2d, 2H, J = 11.8 Hz, PhCH_2), 4.26 (dd, 1H, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 9.4 Hz, H-3), 4.02 (dd, 1H, $J_{4,5}$ = 2.8 Hz, $J_{5,6}$ = 0.5 Hz, H-5), 3.91 (d, 1H, H-2), 3.68 (dd, 1H, H-4), 3.67−3.62 (m, 3H, H-6, 2H-7), 0.20 (s, 9H, 3Me). Anal. Calcd for $C_{40}H_{44}O_6Si$: C, 74.04; H, 6.83. Found: C, 73.88; H, 6.92.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-trimethylsilylethynyl-*aldehydo*-D-*glycero*-D-*galacto*-heptose (11d). Compound **10d** (269 mg, 0.41 mmol) was treated as described for the preparation of **11b** to give, after column chromatography on silica gel (5:1:1 cyclohexane/AcOEt/toluene), **11d** (94 mg, 35%) as a syrup. $[\alpha]_D = +5.7$ (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.42−7.20 (m, 20H, Ar), 4.94 and 4.64 (2d, 2H, J = 11.2 Hz, PhCH_2), 4.90 and 4.63 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.80 and 4.74 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.78 and 4.58 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.46 (dd, 1H, $J_{2,3}$ = 1.3 Hz, $J_{3,4}$ = 2.9 Hz, H-3), 4.04 (dd, 1H, $J_{4,5}$ = 9.3 Hz, $J_{5,6}$ = 10.0 Hz, H-5), 3.97 (d, 1H, H-2), 3.88 (d, 2H, $J_{6,7}$ = 3.5 Hz, 2H-7), 3.70 (dd, 1H, H-4), 3.54 (dt, 1H, H-6), 0.20 (s, 9H, 3Me). Anal. Calcd for $C_{40}H_{44}O_6Si$: C, 74.04; H, 6.83. Found: C, 73.80; H, 6.89.

1-*C*-Allyl-2,6-anhydro-3,4,5,7-tetra-*O*-benzyl-*aldehydo*-D-*glycero*-D-*galacto*-heptose (12d). A mixture of **10d** (1.00 g, 1.52 mmol), activated 4-Å powdered molecular sieves (1.52 g), and anhydrous CH_3CN (10 mL) was stirred at room temperature for 10 min, and then methyl triflate (260 μL, 2.28 mmol) was added. The suspension was stirred at room temperature for 15 min, concentrated to dryness, diluted with CH_2Cl_2, filtered through a pad of Celite, and concentrated to give the *N*-methylbenzothiazolium salt as a white foam.

To a cooled (−30 °C), stirred solution of allylmagnesium bromide in anhydrous THF (4.6 mL of a 1 M solution in Et_2O, 4.60 mmol) was added a solution of the crude *N*-methylbenzothiazolium salt in anhydrous THF (3 mL) over a 15-min period. The mixture was stirred for an additional 1 h at −30 °C and then diluted with 1 M phosphate buffer at pH 7 (20 mL) and extracted with AcOEt (2 × 100 mL). The combined

organic phase were washed with brine (2 × 50 mL), dried (Na_2SO_4), and concentrated to afford the corresponding benzothiazolines as a yellow syrup.

To a vigorously stirred solution of the crude benzothiazolines and Et_3N (0.2 mL,1.52 mmol) in CH_3CN (15 mL) and CH_2Cl_2 (5 mL) was added dropwise H_2O (1.5 mL) and then $HgCl_2$ in one portion (618 mg, 2.28 mmol). The mixture was stirred at room temperature for 15 min and then diluted with 1 M phosphate buffer at pH 7 (50 mL) and partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C). The suspension was extracted with CH_2Cl_2 (150 + 50 mL), and the combined organic phases were washed with 20% aqueous KI, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 5:1 cyclohexane/AcOEt to give first **12d** (640 mg, 71%) as a syrup. $[a]_D = +1.9$ (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz): δ 7.38−7.20 (m, 20H, Ar), 5.95 (dddd, 1H, J = 6.8, 7.0, 10.3, and 17.0 Hz, CH_2=C*H*), 5.16 (dddd, 1H, J = 1.0, 1.0, 1.0, and 10.3 Hz, CH_2=CH), 5.04 (dddd, 1H, J = 1.0, 1.0, 1.0, and 17.0 Hz, CH_2=CH), 4.90 and 4.48 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.89 and 4.59 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.79 and 4.68 (2d, 2H, J = 11.7 Hz, PhCH_2), 4.67 and 4.59 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.34 (dd, 1H, $J_{2,3}$ = 1.2 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 3.93 (dd, 1H, $J_{4,5} = J_{5,6}$ = 9.5 Hz, H-5), 3.85 (d, 1H, H-2), 3.81 (dd, 1H, $J_{6,7a}$ = 2.0 Hz, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.76 (dd, 1H, $J_{6,7b}$ = 5.0 Hz, H-7b), 3.64 (dd, 1H, H-4), 3.53 (dddd, 1H, J = 1.0, 1.0, 6.8, and 19.4 Hz, CH_2=CHCH_2), 3.50 (ddd, 1H, H-6), 3.40 (dddd, 1H, J = 1.0, 1.0, 7.0, and 19.4 Hz, CH_2=CHCH_2). Anal. Calcd for $C_{38}H_{40}O_6$: C, 77.00; H, 6.80. Found: C, 77.18; H, 6.87. Eluted second was **13d** (90 mg, 10%) as a syrup.

2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-(1-propenyl)-*aldehydo*-D-*glycero*-D-*galacto*-heptose (13d) A mixture of **10d** (100 mg, 0.15 mmol), activated 4-Å powdered molecular sieves (0.15 g), and anhydrous CH_3CN (1 mL) was stirred at room temperature for 10 min, and then methyl triflate (26 μL, 0.23 mmol) was added. The suspension was stirred at room temperature for 15 min, concentrated to dryness, diluted with CH_2Cl_2, filtered through a pad of Celite, and concentrated to give the *N*-methylbenzothiazolium salt as a white foam.

To a cooled (−30 °C), stirred solution of allylmagnesium bromide in anhydrous THF (150 μL of a 1 M solution in Et_2O, 0.15 mmol) was added a solution of the crude *N*-methylbenzothiazolium salt in anhydrous THF (0.5 mL) over a 15-min period. The mixture was stirred for an additional 1 h at −30 °C and then diluted with 1 M phosphate buffer at pH 7 (5 mL) and extracted with AcOEt (2 × 50 mL). The combined organic phase were washed with brine (2 × 50 mL), dried (Na_2SO_4), and concentrated to afford the corresponding benzothiazolines as a yellow syrup.

To a vigorously stirred solution of the crude benzothiazolines in a CH_3CN (2 mL) and CH_2Cl_2 (0.2 mL) mixture was added dropwise H_2O (0.2 mL) and then $HgCl_2$ in one portion (62 mg, 0.23 mmol). The mixture was stirred at room temperature for 1 h and then diluted with 1 M phosphate buffer at pH 7 (10 mL) and partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C). The suspension was extracted with CH_2Cl_2 (2 × 30 mL), and the combined organic phases were washed with 20% aqueous KI, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 5:1 cyclohexane/AcOEt to give **13d** (72 mg, 80%) as a syrup. $[\alpha]_D = +3.9$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz): δ 7.42−7.20 (m, 20H, Ar), 7.04 (dq, 1H, J = 6.8 and 15.5 Hz, CH_3C*H*), 6.81 (dq, 1H, J = 1.5 and 15.5 Hz, C(O)C*H*=CH), 4.93 and 4.60 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.83 and 4.56 (2d, 2H, J = 11.3 Hz, PhCH_2), 4.77 and 4.67 (2d, 2H, J = 11.7 Hz, PhCH_2), 4.70 and 4.63 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.39 (dd, 1H, $J_{2,3}$ = 1.4 Hz, $J_{3,4}$ = 2.8 Hz, H-3), 3.94 (dd, 1H, $J_{4,5}$ = 9.3 Hz, $J_{5,6}$ = 9.7 Hz, H-5), 3.91 (d, 1H, H-2), 3.84 (dd, 1H, $J_{6,7a}$ = 2.3 Hz, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.79 (dd, 1H, $J_{6,7b}$ = 5.5 Hz, H-7b), 3.68 (dd, 1H, H-4), 3.55 (ddd, 1H, H-6), 1.90 (dd, 3H, J = 1.5 and 6.8 Hz, CH_3CH). Anal. Calcd for $C_{38}H_{40}O_6$: C, 77.00; H, 6.80. Found: C, 77.24; H, 6.93.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-(2-thiazolyl)-D-*glycero*-D-*gulo*-heptitol (4b). To a cooled (−78 °C), stirred solution of ^{n}BuLi (250 μL of a 1.6 M solution in hexane, 0.40 mmol) in anhydrous Et_2O (1 mL) was added dropwise a solution of freshly distilled 2-bromothiazole (36 μL, 0.40 mmol) in anhydrous Et_2O (0.5 mL) over a 15-min period. The yellow solution was stirred at −75 °C for 30 min, and then a solution of ketone **2b** (130 mg, 0.20 mmol) in anhydrous Et_2O (2 mL) was added slowly (15 min). After an additional 30 min at −75 °C, the mixture was allowed to warm to −65 °C in 40 min and then poured into 20 mL of a 1 M phosphate buffer at pH 7 and extracted with AcOEt (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane/AcOEt (3:1) to give **4b** (130 mg, 88%) as a syrup. $[\alpha]_D = +33.2$ (*c* 0.6, $CHCl_3$). ^1H NMR (400 MHz): δ 7.87−7.82 (m, 2H, H_{ortho} of Ph), 7.78 (d, 1H, J = 3.2 Hz, Th), 7.36−7.16 (m, 22H, Th, Ar), 6.90−6.85 (m, 2H, Ar), 5.09 (s, 1H, OH), 4.74 and 4.69 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.68 and 4.54 (2d, 2H, J = 11.1 Hz, PhCH_2), 4.50 (d, 1H, $J_{2,3}$ = 7.5 Hz, H-2), 4.44 and 3.95 (2d, 2H, J = 10.9 Hz, PhCH_2), 4.42 and 4.33 (2d, 2H, J = 12.4 Hz, PhCH_2), 3.84 (dd, 1H, $J_{3,4}$ = 7.5 Hz, H-3), 3.77 (dd, 1H, $J_{4,5}$ = 7.0 Hz, H-4), 3.68−3.61 (m, 1H, H-5), 3.60−3.53 (m, 3H, H-6, 2H-7). Anal. Calcd for $C_{44}H_{43}NO_6S$: C, 74.03; H, 6.07; N, 1.96. Found: C, 74.20; H, 6.15; N, 1.78.

(1*R*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-(2-thiazolyl)-D-*glycero*-L-*manno*-heptitol (4c). (a) Compound **2c** (280 mg, 0.44 mmol) was treated as described for the preparation of **4b** to give, after column chromatography on silica gel (4:1 cyclohexane/AcOEt), **4c** (232 mg, 73%) as a syrup. $[\alpha]_D = +44.2$ (*c* 1.8, $CHCl_3$). ^1H NMR (400 MHz): δ 7.87−7.82 (m, 2H, H_{ortho} of Ph), 7.74 (d, 1H, J = 3.3 Hz, Th), 7.39−7.10 (m, 22H, Th, Ar), 6.82−6.77 (m, 2H, Ar), 4.94 and 4.55 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.79 (s, 1H, OH), 4.74 (d, 1H, $J_{2,3}$ = 8.9 Hz, H-2), 4.68 and 4.54 (2d, 2H, J = 11.6 Hz, PhCH_2), 4.53 and 3.58 (2d, 2H, J = 10.7 Hz, PhCH_2), 4.27 and 4.23 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.14 (dd, 1H, $J_{3,4}$ = 8.9 Hz, H-3), 3.96 (dd, 1H, $J_{4,5}$ = 2.8 Hz, $J_{5,6}$ = 1.0 Hz, H-5), 3.78 (ddd, 1H, $J_{6,7a}$ = 6.8 Hz, $J_{6,7b}$ = 5.8 Hz, H-6), 3.74 (dd, 1H, H-4), 3.52 (dd, 1H, $J_{7a,7b}$ = 9.7 Hz, H-7a), 3.40 (dd, 1H, H-7b). Anal. Calcd for $C_{44}H_{43}NO_6S$: C, 74.03; H, 6.07; N, 1.96. Found: C, 74.15; H, 6.10; N, 1.88.

(b) To a cooled (−80 °C), stirred solution of ketone **2c** (40 mg, 0.06 mmol) in anhydrous THF (1.0 mL) was added dropwise a solution of thiazolylmagnesium bromide (380 μL of a 0.5 M solution prepared as described above, 0.19 mmol) over a 5-min period. The solution was allowed to warm to 20 °C in 3 h, then poured into 10 mL of a 1 M phosphate buffer at pH 7, and extracted with AcOEt (2 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 4:1 cyclohexane/AcOEt to give first **4c** (33 mg, 73%). Eluted second was **5c** (10 mg, 22%).

(1*R*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-(2-thiazolyl)-D-*glycero*-D-*galacto*-heptitol (4d). Compound **2d** (140 mg, 0.22 mmol) was treated as described for the preparation of **4b** to give, after column chromatography on silica gel (5:1 cyclohexane/AcOEt), **4d** (111 mg, 70%) as a syrup. $[\alpha]_D = -16.7$ (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz): δ 7.85−7.80 (m, 2H, H_{ortho} of Ph), 7.65 and 7.12 (2d, 2H, J = 2.5 Hz, Th), 7.50−7.20 (m, 23H, Ar), 5.65 (bs, 1H, OH), 5.00 and 4.10 (2d, 2H, J = 10.3 Hz, PhCH_2), 4.84 and 4.63 (2d, 2H, J = 11.0 Hz, PhCH_2), 4.70 and 4.63 (2d, 2H, J = 11.7 Hz, PhCH_2), 4.52 (d, 1H, $J_{2,3}$ = 0.7 Hz, H-2), 4.45 and 4.30 (2d, 2H, J = 11.8 Hz, PhCH_2), 3.98 (dd, 1H, $J_{4,5} = J_{5,6}$ = 9.5 Hz, H-5), 3.77 (dd, 1H, $J_{3,4}$ = 2.5 Hz, H-3), 3.71 (dd, 1H, $J_{6,7a}$ = 2.5 Hz, $J_{7a,7b}$ = 11.3 Hz, H-7a), 3.68 (dd, 1H, $J_{6,7b}$ = 4.0 Hz, H-7b), 3.62 (dd, 1H, H-4), 3.57 (ddd, 1H, H-6). Anal. Calcd for $C_{44}H_{43}NO_6S$: C, 74.03; H, 6.07; N, 1.96. Found: C, 74.22; H, 6.20; N, 1.81.

(1*R*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-(2-thiazolyl)-D-*glycero*-D-*gulo*-heptitol (5b). To a cooled (−80 °C), stirred solution of ketone **3b** (160 mg, 0.25 mmol) in

anhydrous THF (2.5 mL) was added dropwise a solution of commercially available phenylmagnesium bromide (250 μL of a 3.0 M solution in Et_2O, 0.75 mmol) over a 15 min period. The solution was allowed to warm to −35 °C in 2 h, then poured into 20 mL of a 1 M phosphate buffer at pH 7, and extracted with AcOEt (2 × 50 mL). The combined organic layers were washed with brine (2 × 30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 3:1 cyclohexane/AcOEt to give **5b** (156 mg, 87%) as a white solid. Mp 133−134 °C (cyclohexane); $[\alpha]_D = +46.1$ (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz): δ 7.91−7.86 (m, 2H, H_{ortho} of Ph), 7.70 and 7.17 (2d, 2H, *J* = 3.3 Hz, Th), 7.40−7.21 (m, 21H, Ar), 7.13−7.08 (m, 2H, Ar), 5.09 (s, 1H, OH), 4.86 and 4.76 (2d, 2H, *J* = 11.0 Hz, PhCH_2), 4.76 and 4.58 (2d, 2H, *J* = 10.8 Hz, PhCH_2), 4.74 and 4.17 (2d, 2H, *J* = 10.8 Hz, PhCH_2), 4.43 and 4.38 (2d, 2H, *J* = 12.3 Hz, PhCH_2), 4.32 (d, 1H, $J_{2,3}$ = 8.6 Hz, H-2), 3.84 (dd, 1H, $J_{3,4}$ = 8.5 Hz, $J_{4,5}$ = 8.3 Hz, H-4), 3.68 (dd, 1H, H-3), 3.62 (dd, 1H, $J_{5,6}$ = 9.5 Hz, H-5), 3.62 (d, 2H, $J_{6,7}$ = 2.6 Hz, 2H-7), 3.52 (dt, 1H, H-6). Anal. Calcd for $C_{44}H_{43}NO_6S$: C, 74.03; H, 6.07; N, 1.96. Found: C, 73.95; H, 6.01; N, 1.90.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-(2-thiazolyl)-D-*glycero*-L-*manno*-heptitol (5c). Compound **3c** (200 mg, 0.31 mmol) was treated as described for the preparation of **5b** to give, after column chromatography on silica gel (8:2:1 cyclohexane/AcOEt/CH_2Cl_2), **5c** (182 mg, 81%) as white solid. Mp 113−115 °C (cyclohexane); $[\alpha]_D = +63.5$ (*c* 0.5, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.97−7.92 (m, 2H, H_{ortho} of Ph), 7.66 and 7.13 (2d, 2H, *J* = 3.3 Hz, Th), 7.41−7.25 (m, 19H, Ar), 7.23−7.19 and 7.14−7.10 (2m, 4H, Ar), 5.12 (s, 1H, OH), 4.98 and 4.54 (2d, 2H, *J* = 11.6 Hz, PhCH_2), 4.85 and 4.06 (2d, 2H, *J* = 10.6 Hz, PhCH_2), 4.77 and 4.63 (2d, 2H, *J* = 11.6 Hz, PhCH_2), 4.32 and 4.27 (2d, 2H, *J* = 11.7 Hz, PhCH_2), 4.22 (d, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 4.14 (dd, 1H, $J_{3,4}$ = 9.0 Hz, H-3), 4.03 (dd, 1H, $J_{4,5}$ = 2.6 Hz, $J_{5,6}$ = 0.5 Hz, H-5), 3.80 (dd, 1H, H-4), 3.67−3.60 (m, 2H, H-6, H-7a), 3.50−3.42 (m, 1H, H-7b). Anal. Calcd for $C_{44}H_{43}NO_6S$: C, 74.03; H, 6.07; N, 1.96. Found: C, 73.90; H, 5.98; N, 1.87.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-(2-thiazolyl)-D-*glycero*-D-*galacto*-heptitol (5d). Compound **3d** (230 mg, 0.36 mmol) was treated as described for the preparation of **5b** to give, after column chromatography on silica gel (4:1 cyclohexane/AcOEt), **5d** (256 mg, 99%) as a syrup. $[\alpha]_D = -28.4$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz): δ 7.83 (d, 1H, *J* = 3.4 Hz, Th), 7.76−7.72 (m, 2H, H_{ortho} of Ph), 7.34−7.10 (m, 24H, Th, Ar), 6.38 (s, 1H, OH), 5.04 and 4.17 (2d, 2H, *J* = 10.0 Hz, PhCH_2), 4.85 and 4.63 (2d, 2H, *J* = 10.8 Hz, PhCH_2), 4.78 and 4.73 (2d, 2H, *J* = 11.5 Hz, PhCH_2), 4.49 (d, 1H, $J_{2,3}$ = 0.5 Hz, H-2), 4.40 and 4.23 (2d, 2H, *J* = 11.8 Hz, PhCH_2), 4.18 (dd, 1H, $J_{3,4}$ = 2.5 Hz, H-3), 3.98 (dd, 1H, $J_{4,5}$ = $J_{5,6}$ = 9.5 Hz, H-5), 3.79 (dd, 1H, H-4), 3.67 (dd, 1H, $J_{6,7a}$ = 2.3 Hz, $J_{7a,7b}$ = 12.0 Hz, H-7a), 3.63 (dd, 1H, $J_{6,7b}$ = 4.8 Hz, H-7b), 3.44 (ddd, 1H, H-6). Anal. Calcd for $C_{44}H_{43}NO_6S$: C, 74.03; H, 6.07; N, 1.96. Found: C, 74.28; H, 6.16; N, 1.81.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-1-*C*-trimethylsilylethynyl-D-*glycero*-D-*gulo*-heptitol (14b). To a cooled (−78 °C), stirred solution of ^{n}BuLi (288 μL of a 1.6 M solution in hexane, 0.46 mmol) in anhydrous Et_2O (2 mL) was added dropwise a solution of freshly distilled 2-bromothiazole (40 μL, 0.46 mmol) in anhydrous Et_2O (0.2 mL) over a 15-min period. The yellow solution was stirred at −75 °C for 30 min, and then a solution of ketone **11b** (100 mg, 0.15 mmol) in anhydrous Et_2O (2 mL) was added slowly (15 min). After an additional 2 h at −75 °C, the mixture was allowed to warm to −65 °C in 40 min, then poured into 20 mL of a 1 M phosphate buffer at pH 7, and extracted with AcOEt (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with cyclohexane/AcOEt (3:1) to give **14b** (69 mg, 61%) as a syrup. $[\alpha]_D = +4.8$ (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.78 and 7.16 (2d, 2H, *J* = 3.2 Hz, Th), 7.38−7.18 (m, 18H, Ar), 7.02−6.97 (m, 2H, Ar), 4.87 and 4.79 (2d, 2H, *J* = 11.3 Hz, PhCH_2), 4.84 and 4.75 (2d, 2H, *J* = 10.8 Hz, PhCH_2), 4.83 and 4.64 (2d, 2H, *J* = 11.0 Hz, PhCH_2), 4.70 (s, 1H, OH), 4.60 and 4.53 (2d, 2H, *J* = 12.2 Hz, PhCH_2), 4.24 (d, 1H, $J_{2,3}$ = 8.5 Hz, H-2), 3.92 (dd, 1H, $J_{3,4}$ = 8.7 Hz, H-3), 3.84 (dd, 1H, $J_{4,5}$ = 7.6 Hz, H-4), 3.78 (dd, 1H, $J_{6,7a}$ = 3.9 Hz, $J_{7a,7b}$ = 11.5 Hz, H-7a), 3.73 (dd, 1H, $J_{6,7b}$ = 1.8 Hz, H-7b), 3.70 (dd, 1H, $J_{5,6}$ = 9.5 Hz, H-5), 3.64 (ddd, 1H, H-6), 0.23 (s, 9H, 3Me). Anal. Calcd for $C_{43}H_{47}NO_6SSi$: C, 70.36; H, 6.45; N, 1.91. Found: C, 70.54; H, 6.43; N, 1.74.

(1*R*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-1-*C*-trimethylsilylethynyl-D-*glycero*-D-*gulo*-heptitol (16b). Commercially available $CeCl_3 \cdot 7H_2O$ (158 mg, 0.42 mmol) was heated in a reaction flask at 120 °C/0.1 mbar for 1 h and 140 °C/0.1 mbar for 1 h and then cooled to 0 °C in a nitrogen atmosphere, diluted with anhydrous THF (1.7 mL), stirred at room temperature for 30 min, and then cooled to −78 °C. To a cooled (−78 °C), stirred solution of commercially available trimethylsilylacetylene (82 μL, 0.59 mmol) in anhydrous THF (0.6 mL) was slowly added ^{n}BuLi (368 μL of a 1.6 M solution in hexane, 0.59 mmol). The solution was stirred at −78 °C for 45 min and then 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 ketone **3b** (107 mg, 0.17 mmol) in anhydrous THF (1 mL) was added dropwise. The mixture was stirred at −78 °C for an additional 15 min and then allowed to reach room temperature in 3 h. The reaction mixture was diluted with 0.1 M HCl (10 mL) and extracted with AcOEt (2 × 30 mL). The combined organic layers were washed with 1 M phosphate buffer at pH 7 (2 × 10 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 4:1 cyclohexane/AcOEt to give **16b** (102 mg, 82%) as a syrup. $[\alpha]_D = -6.9$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.80 (d, 1H, *J* = 3.2 Hz, Th), 7.39−7.25 (m, 21H, Th, Ar), 5.27 (bs, 1H, OH), 5.13 and 4.95 (2d, 2H, *J* = 10.5 Hz, PhCH_2), 5.00 and 4.92 (2d, 2H, *J* = 10.9 Hz, PhCH_2), 4.88 and 4.71 (2d, 2H, *J* = 11.8 Hz, PhCH_2), 4.53 and 4.38 (2d, 2H, *J* = 12.1 Hz, PhCH_2), 4.19 (dd, 1H, $J_{2,3}$ = 9.3 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 3.90 (dd, 1H, $J_{4,5}$ = 9.2 Hz, H-4), 3.87 (d, 1H, H-2), 3.76 (dd, 1H, $J_{5,6}$ = 9.7 Hz, H-5), 3.67 (dd, 1H, $J_{6,7a}$ = 4.3 Hz, $J_{7a,7b}$ = 12.0 Hz, H-7a), 3.55 (dd, 1H, $J_{6,7b}$ = 1.3 Hz, H-7b), 3.44 (ddd, 1H, H-6), 0.26 (s, 9H, 3Me). Anal. Calcd for $C_{43}H_{47}NO_6SSi$: C, 70.36; H, 6.45; N, 1.91. Found: C, 70.60; H, 6.57; N, 1.83.

(1*R*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-ethynyl-1-*C*-phenyl-D-*glycero*-D-*gulo*-heptitol (18b). To a cooled (0 °C), stirred solution of ketone **2b** (200 mg, 0.32 mmol) in anhydrous THF (2 mL) was added dropwise a solution of commercially available ethynylmagnesium bromide (1.92 mL of a 0.5 M solution in THF, 0.96 mmol) over a 15-min period. The solution was allowed to warm to room temperature in 30 min, stirred an additional 2 h at room temperature, then poured into 20 mL of a 1 M phosphate buffer at pH 7, and extracted with AcOEt (2 × 50 mL). The combined organic layers were washed with brine (2 × 30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 8:1 cyclohexane/AcOEt to give **18b** (190 mg, 91%) as a syrup. $[\alpha]_D = +5.6$ (*c* 2.4, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.73−7.68 (m, 2H, H_{ortho} of Ph), 7.41−7.22 (m, 23H, Ar), 5.34 (s, 1H, OH), 5.16 and 4.97 (2d, 2H, *J* = 10.5 Hz, PhCH_2), 5.04 and 4.94 (2d, 2H, *J* = 11.0 Hz, PhCH_2), 4.84 and 4.68 (2d, 2H, *J* = 11.0 Hz, PhCH_2), 4.47 and 4.33 (2d, 2H, *J* = 11.8 Hz, PhCH_2), 4.28 (dd, 1H, $J_{2,3}$ = 9.1 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 3.88 (dd, 1H, $J_{4,5}$ = 9.0 Hz, H-4), 3.74 (dd, 1H, $J_{5,6}$ = 9.7 Hz, H-5), 3.62 (dd, 1H, $J_{6,7a}$ = 4.1 Hz, $J_{7a,7b}$ = 11.6 Hz, H-7a), 3.50 (dd, 1H, $J_{6,7b}$ = 1.4 Hz, H-7b), 3.38 (d, 1H, H-2), 3.26 (ddd, 1H, H-6), 2.82 (s, 1H, C≡CH). Anal. Calcd for $C_{43}H_{42}O_6$: C, 78.87; H, 6.46. Found: C, 78.70; H, 6.39.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-phenyl-1-*C*-trimethylsilylethynyl-D-*glycero*-D-*gulo*-heptitol (19b). To a cooled (−20 °C), stirred solution of ketone **11b** (162 mg, 0.25 mmol) in anhydrous THF (3 mL) was added dropwise a

solution of commercially available phenylmagnesium bromide (250 μL of a 3.0 M solution in Et_2O, 0.75 mmol) over a 15-min period. The solution was allowed to warm to room temperature in 1 h, then poured into 20 mL of a 1 M phosphate buffer at pH 7, and extracted with AcOEt (2 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 6:1 cyclohexane/AcOEt to give **19b** (136 mg, 75%) as a syrup. $[\alpha]_D = +1.1$ (*c* 0.7, $CHCl_3$). ^{1}H NMR (300 MHz): δ 7.75−7.70 (m, 2H, H_{ortho} of Ph), 7.44−7.16 (m, 21H, Ar), 6.78−6.73 (m, 2H, Ar), 4.84 and 4.70 (2d, 2H, J = 11.0 Hz, PhCH_2), 4.83 and 4.67 (2d, 2H, J = 10.9 Hz, PhCH_2), 4.74 and 4.46 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.68 and 4.62 (2d, 2H, J = 12.2 Hz, PhCH_2), 4.41 (s, 1H, OH), 3.86−3.67 (m, 6H), 3.60 (ddd, 1H, $J_{5,6}$ = 9.2 Hz, $J_{6,7a}$ = 2.0 Hz, $J_{6,7b}$ = 3.8 Hz, H-6), 0.22 (s, 9H, 3Me). Anal. Calcd for $C_{46}H_{50}O_6Si$: C, 76.00; H, 6.93. Found: C, 76.18; H, 7.01.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-ethynyl-1-*C*-(2-thiazolyl)-D-*glycero*-D-*gulo*-heptitol (15b). A solution of **14b** (150 mg, 0.20 mmol) in 5:1 CH_3OH/CH_2Cl_2 (6 mL) was treated at room temperature for 30 min with 1 N KOH (0.4 mL), then neutralized with 1 N HCl, and concentrated to remove the organic solvent. The residue was diluted with AcOEt (50 mL), washed with brine, dried (Na_2SO_4), concentrated, and filtered through a short column of silica gel (1.5 × 5 cm, $d \times h$) with 4:1 cyclohexane/AcOEt to afford **15b** (127 mg, 98%) as a syrup. $[\alpha]_D = +13.8$ (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, C_6D_6): δ 7.43 and 6.48 (2d, 2H, J = 3.2 Hz, Th), 7.26−7.00 (m, 20H, Ar), 5.05 (s, 1H, OH), 4.99 and 4.93 (2d, 2H, J = 11.3 Hz, PhCH_2), 4.72 and 4.67 (2d, 2H, J = 11.3 Hz, PhCH_2), 4.68 and 4.46 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.35 and 4.28 (2d, 2H, J = 12.2 Hz, PhCH_2), 4.31 (d, 1H, $J_{2,3}$ = 8.7 Hz, H-2), 4.10 (dd, 1H, $J_{3,4}$ = 8.2 Hz, H-3), 3.67 (dd, 1H, $J_{4,5}$ = 8.3 Hz, H-4), 3.61 (dd, 1H, $J_{5,6}$ = 9.5 Hz, H-5), 3.50 (dd, 1H, $J_{6,7a}$ = 4.1 Hz, $J_{7a,7b}$ = 11.6 Hz, H-7a), 3.46 (dd, 1H, $J_{6,7b}$ = 2.2 Hz, H-7b), 3.36 (ddd, 1H, H-6), 2.17 (s, 1H, C≡CH). Anal. Calcd for $C_{40}H_{39}NO_6S$: C, 72.59; H, 5.94; N, 2.12. Found: C, 72.41; H, 5.82; N, 2.00.

(1*R*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-ethynyl-1-*C*-(2-thiazolyl)-D-*glycero*-D-*gulo*-heptitol (17b). Compound **16b** (25 mg, 0.03 mmol) was desilylated as described for the preparation of **15b** and filtered through a short column of silica gel (1 × 2 cm, $d \times h$) with CH_2Cl_2 and then 10:1 CH_2Cl_2/AcOEt to give **17b** (22 mg, 98%) as a syrup. $[\alpha]_D = +4.6$ (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz): δ 7.67 (d, 1H, J = 3.1 Hz, Th), 7.26−7.10 (m, 21H, Th, Ar), 5.23 (s, 1H, OH), 4.98 and 4.83 (2d, 2H, J = 10.5 Hz, PhCH_2), 4.89 and 4.80 (2d, 2H, J = 11.0 Hz, PhCH_2), 4.73 and 4.56 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.39 and 4.26 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.12 (dd, 1H, $J_{2,3}$ = 9.3 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 3.78 (dd, 1H, $J_{4,5}$ = 8.9 Hz, H-4), 3.71 (d, 1H, H-2), 3.59 (dd, 1H, $J_{5,6}$ = 9.8 Hz, H-5), 3.55 (dd, 1H, $J_{6,7a}$ = 4.5 Hz, $J_{7a,7b}$ = 11.7 Hz, H-7a), 3.49 (dd, 1H, $J_{6,7b}$ = 1.7 Hz, H-7b), 3.34 (ddd, 1H, H-6), 2.72 (s, 1H, C≡CH). Anal. Calcd for $C_{40}H_{39}NO_6S$: C, 72.59; H, 5.94; N, 2.12. Found: C, 72.71; H, 6.02; N, 1.94.

(1*S*)-2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-*C*-ethynyl-1-*C*-phenyl-D-*glycero*-D-*gulo*-heptitol (20b). Compound **19b** (38 mg, 0.05 mmol) was desilylated as described for the preparation of **15b** and filtered through a short column of silica gel (1 × 3 cm, $d \times h$) with 3:1 cyclohexane/AcOEt to give **20b** (33 mg, 98%) as a syrup. $[\alpha]_D = +8.7$ (*c* 1.2, $CHCl_3$). ^{1}H NMR (400 MHz): δ 7.74−7.70 (m, 2H, H_{ortho} of Ph), 7.39−7.16 (m, 21H, Ar), 6.81−6.78 (m, 2H, Ar), 4.86 and 4.71 (2d, 2H, J = 11.5 Hz, PhCH_2), 4.79 and 4.63 (2d, 2H, J = 11.0 Hz, PhCH_2), 4.74 and 4.40 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.64 and 4.60 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.44 (s, 1H, OH), 3.86 (d, 1H, $J_{2,3}$ = 9.0 Hz, H-2), 3.81−3.77 (m, 2H, 2H-7), 3.77 (dd, 1H, $J_{3,4}$ = 8.6 Hz, $J_{4,5}$ = 8.5 Hz, H-4), 3.69 (dd, 1H, H-3), 3.64 (dd, 1H, $J_{5,6}$ = 9.7 Hz, H-5), 3.59 (ddd, 1H, $J_{6,7a} = J_{6,7b}$ = 2.9 Hz, H-6), 2.72 (s, 1H, C≡CH). Anal. Calcd for $C_{43}H_{42}O_6$: C, 78.87; H, 6.46. Found: C, 79.02; H, 6.53.

3,7-Anhydro-4,5,6,8-tetra-*O*-benzyl-2-*C*-ethynyl-*aldehydo*-D-*erythro*-L-*talo*-octose (21b). A solution of **16b** (72 mg, 0.10 mmol) and methyl triflate (17 μL, 0.15 mmol) in anhydrous CH_2Cl_2 (0.5 mL) and CH_3CN (0.5 mL) was kept at room temperature for 15 min and then concentrated. To a solution of the crude *N*-methylthiazolium salt in EtOH (1 mL) was added $NaBH_4$ (9 mg, 0.30 mmol). The mixture was stirred at room temperature for an additional 15 min, then diluted with acetone, and concentrated. A solution of the residue in CH_2Cl_2 (50 mL) was washed with 1 M phosphate buffer at pH 7 (2 × 10 mL), dried (Na_2SO_4), and concentrated. To a vigorously stirred solution of the thiazolidines in CH_2Cl_2 (0.5 mL) and CH_3CN (1.8 mL) was added dropwise H_2O (0.2 mL) and then $AgNO_3$ in one portion (50 mg, 0.30 mmol). The mixture was stirred at room temperature for 15 min, then diluted with 1 M phosphate buffer at pH 7 (20 mL), partially concentrated to remove CH_3CN (bath temperature not exceeding 40 °C), and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic phases were dried (Na_2SO_4) and concentrated to give syrupy **21b** (37 mg, 64%) at least 95% pure by ^{1}H NMR analysis. ^{1}H NMR (300 MHz): δ 9.41 (s, 1H, H-1), 7.40−7.18 (m, 20H, Ar), 4.99 and 4.86 (2d, 2H, J = 11.2 Hz, PhCH_2), 4.86 and 4.44 (2d, 2H, J = 10.4 Hz, PhCH_2), 4.82 and 4.64 (2d, 2H, J = 10.8 Hz, PhCH_2), 4.67 (s, 2H, PhCH_2), 4.04 (bs, 1H, OH), 3.84 (dd, 1H, $J_{7,8a}$ = 1.8 Hz, $J_{8a,8b}$ = 11.6 Hz, H-8a), 3.81−3.64 (m, 5H), 3.58 (ddd, 1H, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 4.5 Hz, H-7), 2.68 (s, 1H, C≡CH).

Methyl 3,7-Anhydro-4,5,6,8-tetra-*O*-benzyl-2-*C*-ethynyl-*aldehydo*-D-*erythro*-L-*talo*-octonate (22b). To a vigorously stirred solution of crude **21b** (37 mg, 0.06 mmol) in CCl_4 (0.5 mL) and CH_3OH (2.5 mL) was added solid KOH (33 mg, 0.60 mmol) and, after 15 min, iodine (152 mg, 0.60 mmol). Stirring was continued for an additional 45 min, and then the reaction mixture was treated with solid NH_4Cl until pH 8 and concentrated. A suspension of the residue in AcOEt (100 mL) was washed with saturated aqueous NH_4Cl (30 mL) and then 20% aqueous $Na_2S_2O_3$ (2 × 30 mL), dried (Na_2SO_4), and concentrated to give **22b** (40 mg, white solid) as an adduct with HI (MS analysis). A solution of this product and Et^iPr_2N (10 μL) in toluene (1 mL) was stirred at 80 °C for 3 h and then concentrated. The residue was eluted from a column of silica gel with 3:1 cyclohexane/AcOEt to give pure **22b** (32 mg, 85%) as an amorphous solid. $[\alpha]_D = +33.8$ (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, C_6D_6): δ 7.39−7.36 (m, 2H, Ar), 7.25−7.22 (m, 2H, Ar), 7.20−6.97 (m, 16H, Ar), 4.94 and 4.47 (2d, 2H, J = 10.6 Hz, PhCH_2), 4.84 and 4.72 (2d, 2H, J = 11.2 Hz, PhCH_2), 4.71 and 4.52 (2d, 2H, J = 11.4 Hz, PhCH_2), 4.58 and 4.54 (2d, 2H, J = 12.0 Hz, PhCH_2), 4.02 (d, 1H, $J_{3,4}$ = 9.5 Hz, H-3), 4.01 (s, 1H, OH), 3.97−3.92 (m, 1H, H-4), 3.76 (dd, 1H, $J_{7,8a}$ = 1.7 Hz, $J_{8a,8b}$ = 11.6 Hz, H-8a), 3.68−3.61 (m, 3H, H-5, H-6, H-8b), 3.48−3.43 (m, 1H, H-7), 3.08 (s, 3H, OMe), 2.05 (s, 1H, C≡CH). Anal. Calcd for $C_{39}H_{40}O_8$: C, 73.56; H, 6.33. Found: C, 73.35; H, 6.24.

Acknowledgment. We thank Mr. P. Formaglio (University of Ferrara) for assistance in the NMR measurements and the University of Ferrara for financial support (research project 2004).

JO051377W