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Synthesis of Aryl, Glycosyl, and Azido Septanosides through Ring Expansion of 1,2-Cyclopropanated Sugars

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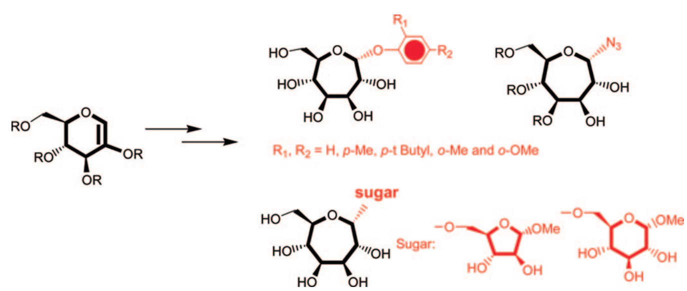

A ring-expansion methodology for the preparation of aryl septanosides, arabinofuranosyl and glucopyranosyl septanoside disaccharides, and azido septanosides is reported. A cyclopropanated adduct of the oxyglycal upon reaction with phenols, sugars, and azide led to the formation of ring-expanded septanoside derivatives. The ring expansion was found to be stereoselective with sugars, whereas phenols and the azide afforded an anomeric mixture of the ring expanded product. It was observed further that the conversion of the intermediate diketones to the diols, using $NaBH_4$, occurred with high diastereoselectivities for the α-anomers of the septanosides. This report consolidates further the generality of the oxyglycal ring-expansion method to prepare septanosides, possessing different substituents at their reducing ends.

Introduction

Septanoses, the higher homologues of commonly occurring furanoses and pyranoses, are unnatural sugars.[1] These ring-expanded sugars adopt flexible conformations. Few synthetic methods have been known previously to prepare septanoses and septanosides[2−6] and are studied further for their conformations.[7−9] Recent biological studies[10−12] such as protein binding studies provide evidence for the ability of the septanoside derivatives to bind proteins.

We have reported recently that the ring expansion of cyclopropanated pyranosides is a useful method to prepare septanosides from pyranosides.[13] The method involves primarily a ring-opening reaction of a *gem*-dihalocyclopropane adduct of oxyglycals in the presence of a methoxide, so as to lead to the formation of seven-membered oxepines. The ring-opening reaction was found to be stereoselective, and an exclusive formation of the α-anomer of oxepines was observed with methoxide. The α-anomer of the oxepine intermediates, having keto-functionalities, readily underwent $NaBH_4$-mediated conversion to alcohols, marked with higher diastereoselectivities at the newly generated C-2 and C-3 centers of the septanoside.

(1) Pakulski, Z. *Pol. J. Chem.* **2006**, *80*, 1293–1326.
(2) (a) Stevens, J. D. *Chem. Commun.* **1969**, 1140–1141. (b) Stevens, J. D. *Carbohydr. Res.* **1972**, *21*, 490–492. (c) Ng, C. J.; Stevens, J. D. *Carbohydr. Res.* **1996**, *284*, 241–248. (d) Driver, G. E.; Stevens, J. D. *Carbohydr. Res.* **2001**, *334*, 81–89.
(3) (a) Butcher, M. E.; Ireson, J. C.; Lee, J. B.; Tyler, M. J. *Tetrahedron* **1977**, *33*, 1501–1507. (b) Ovaa, H.; Leeuwenburgh, M. A.; Overkleeft, H. S.; van der Marel, G. A.; van Boom, J. H. *Tetrahedron Lett.* **1998**, *39*, 3025–3028. (c) Contour, M. O.; Fayet, C.; Gelas, J. *Carbohydr. Res.* **1990**, *201*, 150–152.
(4) Castro, S.; Fyvie, S.; Hatcher, S. A.; Peczuh, M. W. *Org. Lett.* **2005**, *21*, 4709–4712.
(5) Köver, A.; Matheu, M. I.; Díaz, Y.; Castillón, S. *ARKIVOC* **2007**, *iv*, 364–379.
(6) Schmidt, B.; Biernat, A. *Chem. Eur. J.* **2008**, *14*, 6135–6141.
(7) (a) Jackobs, J. J.; Reno, M. A.; Sundaralingam, M. *Carbohydr. Res.* **1973**, *28*, 75–85. (b) Molina, J. M.; Olea, D. P.; Baer, H. H. *Carbohydr. Res.* **1995**, *273*, 1–10. (c) Ng, C. J.; Craig, D. C.; Stevens, J. D. *Carbohydr. Res.* **1996**, *284*, 249–263. (d) Bailey, C. J.; Craig, D. C.; Grainger, C. T.; James, V. J.; Stevens, J. D. *Carbohydr. Res.* **1996**, *284*, 265–275.
(8) Danilova, V. A.; Krivdin, L. B. *Russ. J. Org. Chem.* **2004**, *40*, 57–62.
(9) (a) DeMatteo, M. P.; Snyder, N. L.; Morton, M.; Hadad, C. M.; Peczuh, M. W. *J. Org. Chem.* **2005**, *70*, 24–38. (b) DeMatteo, M. P.; Mei, S.; Fenton, R.; Morton, M.; Hadad, C. M.; Peczuh, M. W. *Carbohydr. Res.* **2006**, *341*, 2927–2945. (c) Markad, S. D.; Xia, S.; Snyder, N. L.; Surana, B.; Morton, M. D.; Hadad, C. M.; Peczuh, M. W. *J. Org. Chem.* **2008**, *73*, 6341–6354.
(10) Bozó, É.; Gáti, T.; Demeter, A.; Kuszmann, J. *Carbohydr. Res.* **2002**, *337*, 1351–1365.
(11) Castro, S.; Duff, M.; Snyder, N. L.; Morton, M.; Kumar, C. V.; Peczuh, M. W. *Org. Biomol. Chem.* **2005**, *3*, 3869–3872.
(12) Tauss, A.; Steiner, A. J.; Stütz, A. E.; Tarling, C. A.; Withers, S. G.; Wrodnigg, T. M. *Tetrahedron: Asymmetry* **2006**, *17*, 234–239.
(13) Ganesh, N. V.; Jayaraman, N. *J. Org. Chem.* **2007**, *72*, 5500–5504.

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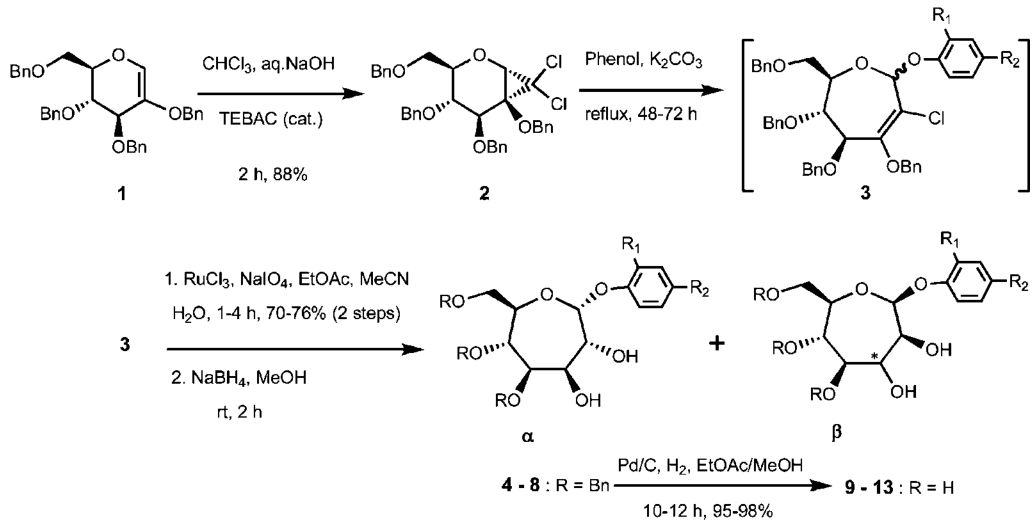
SCHEME 1



Continuing our efforts to extend the method, as well as to demonstrate the preparation of a variety of septanosides, the ring-expansion reaction of the cyclopropanated adduct with phenoxides, sugars, and azide was undertaken. In the event, it was found that whereas the ring opening with sugars was highly stereoselective, leading to an exclusive formation of the α-anomer of sugar oxepines, the phenoxides and azide led to a mixture of anomers of the corresponding oxepines in a ~1:1 ratio. Further, the α-anomer of the oxepine derived intermediates, having keto-functionalities, underwent $NaBH_4$-mediated conversion to alcohols with higher diastereoselectivities at the newly generated stereocenters, whereas the β-anomers did not retain the diastereoselectivities, in the case of aryl septanosides. The details of the synthesis of aryl septanosides, septanoside disaccharides presenting a furanoside and pyranoside units, and azido septanoside derivatives are described herein.

Results and Discussion

Synthesis of Aryl Septanosides. The ring expansion of a pyranoside to a septanoside is initiated with the cyclopropanation of an oxyglycal. Oxyglycals,[14−16] containing an oxygen functionality at C-2, are prepared through a dehydrohalogenation of an appropriately protected pyranosyl bromide. Cyclopropanation and its ring-expansion reactions in the case of glycals, without an oxygen functionality at C-2, have been studied previously.[17−20] Cyclopropanation of the oxyglucal **1**[13] was performed using dichlorocarbene. The carbene addition was found to be effective, and the 1,2-*C*-(dichloromethylene)-α-D-*glycero*-hexitol **2** was obtained as a single diastereomer in good yields (Scheme 1). In the present study, the dichloroadduct **2** served as the starting material for the ring-expansion reactions.

Reaction of phenols with **2** in PhMe, in the presence of K_2CO_3 and 18-C-6, for 48−72 h afforded chloro-oxepine **3**. The ^{1}H NMR spectrum of **3** (R_1, R_2 = H) showed resonances at 5.68 and 5.99 ppm, corresponding to the H-1 nucleus of the α- and β-anomers, in a ratio of 1:1, respectively. Similarly, ^{13}C NMR spectrum showed peaks at 98.7 and 101.5 ppm, corresponding to the anomeric carbon of the α- and β-anomers, respectively. The signals at ~121 and ~153 ppm confirmed the presence of chlorovinyl ether moiety in the product. HR-MS analysis further confirmed the composition of **3** (R_1, R_2 = H).

The chloro-oxepines were not stable, and thus the subsequent oxidation was conducted immediately after their preparation. Oxidation of **3** was performed using in situ generated RuO_4,[21] which led to the formation of the diketone derivative in 70−76% yield (2 steps). As a result of difficulty in separating the anomers of the diketones, their subsequent reduction to the diols was performed, using $NaBH_4$ in MeOH. The diols were obtained in good yields, as mixtures of anomers and epimers (Table 1). The isomeric diols **4**−**8** were separated through column chromatography and the α- and β-anomers were isolated in an approximately 1:1 ratio. It is pertinent to note that the β-anomers are epimeric, whereas the α-anomers are diastereomerically pure.

It was found that the α-anomers of the aryl-substituted diketones underwent $NaBH_4$ reduction in a highly diastereoselective manner. On the other hand, the β-anomers yielded a mixture of isomers. The anomeric proton of the α-anomers in **4α**−**8α** resonated in the range of 5.4−5.7 ppm, as a doublet, with J_{H1-H2} of ~4 Hz. The corresponding C-1 nucleus was observed at ~97 ppm, with the exception of *o*-methoxy derivative **8α**, which resonated at 101.2 ppm. The α-configuration was confirmed further with the observed $^1J_{C1-H1}$ of 170.2 Hz for **4α**. The resonances of the newly generated H-2 and H-3

(14) (a) Rao, D. R.; Lerner, L. M. *Carbohydr. Res.* **1972**, *22*, 345–350. (b) Varela, O.; de Fina, G. M.; de Lederkremer, R. M. *Carbohydr. Res.* **1987**, *167*, 187–196. (c) Ratcliffe, A.; Fraser-Reid, B. *J. Chem. Soc., Perkin. Trans. 1* **1990**, 747–750. (d) Jones, G. S.; Scott, W. J. *J. Am. Chem. Soc.* **1992**, *114*, 1491–1492.

(15) (a) Boettcher, A.; Lichtenthaler, F. W. *Tetrahedron: Asymmetry* **2004**, *15*, 2693–2701. (b) Lichtenthaler, F. W.; Weimer, T.; Immel, S. *Tetrahedron: Asymmetry* **2004**, *15*, 2703–2709.

(16) (a) Storkey, C. M.; Win, A. L.; Hoberg, J. O. *Carbohydr. Res.* **2004**, *339*, 897–899. (b) Chambers, D. J.; Evans, G. R.; Fairbanks, A. J. *Tetrahedron* **2004**, *60*, 8411–8419. (c) Moreno, B.; Quehen, C.; Rose-Hélène, M.; Leclerc, E.; Quirion, J. C. *Org. Lett.* **2007**, *9*, 2477–2480.

(17) Duchaussoy, P.; Cesare, P. D.; Gross, B. *Synthesis* **1979**, 198–200.

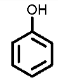
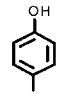
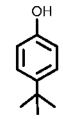
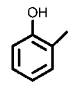
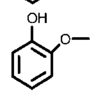
(18) (a) Hoberg, J. O.; Bozell, J. J. *Tetrahedron Lett.* **1995**, *36*, 6831–6834. (b) Hoberg, J. O. *J. Org. Chem.* **1997**, *62*, 6615–6618. (c) Cousins, G. S.; Hoberg, J. O. *Chem. Soc. Rev.* **2000**, *29*, 165–174. (d) Batchelor, R.; Hoberg, J. O. *Tetrahedron Lett.* **2003**, *44*, 9043–9045.

(19) Ramana, C. V.; Murali, R.; Nagarajan, M. *J. Org. Chem.* **1997**, *62*, 7694–7703.

(20) Kirsch, V.; Wolff, C.; Näther, C.; Tochtermann, W. *Eur. J. Org. Chem.* **2000**, 1741–1744.

(21) (a) Khan, F. A.; Prabhudas, B.; Dash, J.; Sahu, N. *J. Am. Chem. Soc.* **2000**, *122*, 9558–9559. (b) Chou, T. C.; Liao, K. C.; Lin, J. J. *Org. Lett.* **2005**, *7*, 4843–4846. (c) de Oliveira, L. F.; Costa, V. E. U. *Tetrahedron Lett.* **2006**, *47*, 3565–3567. (d) Frunzke, J.; Loschen, C.; Frenking, G. *J. Am. Chem. Soc.* **2004**, *126*, 3642–3652.

TABLE 1. Synthesis of Various Aryl Septanosides 4−8

Phenol	Product	R_1	R_2	Yield[a] (%)	C-3 Epimeric ratio[b]
	**4**	–H	–H	78	1.3 : 1.0
	**5**	–H	$-CH_3$	83	1.5 : 1.0
	**6**	–H	$-C(CH_3)_3$	85	1.7 : 1.0
	**7**	$-CH_3$	–H	81	3.3 : 1.0
	**8**	$-OCH_3$	–H	76	Only one epimer

[a] α/β anomeric ratio is ~1:1. [b] In the case of the β-anomers the ratio was determined by ^{1}H NMR spectroscopy.

of the α-anomers **4α−8α** merged with the benzylic protons, thereby precluding their assignments in the presence of the protecting groups.

Characterization of the β-anomers **4β−8β** showed that the anomeric proton resonated at ~5.5 ppm (app.s) and at ~5.35 ppm (app.s). The resonances of H-1 had varied ratios for each septanoside because of the epimeric mixture, and the ratios are given in Table 1. The ^{13}C NMR spectra of **4β−8β** also exhibited a set of resonance for C-1, in the range of 98.6−99.9 ppm. The $^1J_{C1-H1}$ values for **4β** at 160.0 and 157.4 Hz confirmed that the β-anomer was an epimeric mixture. This epimeric mixture was inferred to arise at the C-3 configuration, on the basis that the observed J_{H1-H2} values of ~1 Hz corresponding to a *cis*-orientation of the C-1 and C-2 substituents.

Subsequent hydrogenolysis was performed on **4−8**, in both the anomeric forms, to secure the free-hydroxyl group containing D-*glycero*-D-*galacto*-septanosides **9α−13α** and D-*glycero*-D-*ido/talo*-septanosides **9β−13β** (Figure 1). In the ^{1}H NMR spectrum, the anomeric proton in **9α−13α** resonated as a doublet at 5.5−5.6 ppm (J_{H1-H2} = ~3.3 Hz). The H-2 and H-3 appeared as a set of double doublets at 4.17−4.25 ppm (J_{H1-H2} = ~3.3 Hz, J_{H2-H3} = ~7.6 Hz) and 4.13−4.22 ppm (J_{H2-H3} = ~7.6 Hz, J_{H3-H4} = ~2.0 Hz), respectively. From these observed J values, the configurations at C-1, C-2, and C-3 were assigned, as given in Figure 1. In the ^{13}C NMR spectrum, the C-1 of the α-anomers **9α−13α** was observed in the range of 96−99 ppm.

The anomeric proton of **9β−13β** appeared as an apparent singlet at ~5.3 ppm and was seen with consistent upfield shift, when compared to the α-anomers **9α−13α**. The absence of coupling of H-1 with H-2 indicated a *cis*-orientation of these protons. On the other hand, the β-anomers **9β−12β** showed resonances at ~101.5 and 102.5 ppm for the C-1 nucleus in the ^{13}C NMR spectrum, thereby confirming the epimeric nature of the β-anomers. The *o*-methoxy derivative **13β** showed the C-1 resonance at 103.1 ppm.

Disaccharides Containing Septanosides. An appropriately protected sugar was chosen as the acceptor component in the ring-opening reaction, so as to afford disaccharides containing the septanose unit. The partially protected furanoside **14** and pyranoside **17** were synthesized by (i) tritylation; (ii) benzylation, and (iii) detritylation reactions.[22] The ring-opening reaction of **2** was conducted with **14** and **17** (2 molar equiv), under reflux conditions, in the presence of K_2CO_3 (10 molar equiv), in PhMe. The resulting chlorooxepine disaccharide derivatives **15** and **18** were obtained in moderate yields. Unlike the phenols, the ring opening with **14** and **17** occurred in a highly stereoselective manner, and only the α-anomers were obtained (Scheme 2).

^{1}H NMR spectra of **15** and **18** showed resonances at ~5.5 ppm for the anomeric proton; the corresponding ^{13}C NMR spectra showed a signal at ~99.6 ppm for the anomeric carbon. HR-MS analysis further confirmed the composition of **15** and **18**. The RuO_4-mediated oxidation of the double bond, followed by $NaBH_4$ reduction of diketones, afforded the corresponding disaccharides **16** and **19**, containing two free hydroxyl groups. The reactions were observed to occur with high diastereoselectivities and led to the formation of a single diastereomer, in good yields.

In the ^{1}H NMR spectra, H-1 of the septanoside moiety in disaccharides **16** and **19** appeared as a doublet at ~5.02 ppm (J = ~4.3 Hz). The signal corresponding to H-2 of **16** appeared as a broadband at 4.0 ppm. A selective irradiation of H-1 in **16** resulted in a clear doublet for H-2, and J_{H2-H3} was found to be 9.3 Hz. Thus, the configurations of the newly formed stereocenters were assigned as shown in Scheme 2. The anomeric carbon corresponding to the septanoside unit in **16** and **19** appeared at 99.8 and 98.7 ppm, respectively.

The *O*-benzyl groups in the disaccharides **16** and **19** were deprotected (Pd/C, H_2) to afford the free hydroxyl groups containing D-*glycero*-D-*galacto*-septanoside disaccharides **20** and **21**, quantitatively (Figure 2). The composition of the disaccharides **20** and **21** were confirmed by NMR spectroscopic and HR-MS techniques.

It is emphasized that the present method providing the disaccharides is different from the existing methods. Hindsgaul and co-workers[23] reported disaccharide-containing septanoses that were formed through glycosylation of preformed saccharides. Recently Peczuh and co-workers[4,24] reported the synthesis of disaccharides containing septanosides, including septanose disaccharides linked through a 1,7-linkage. The disaccharides were prepared through epoxide ring opening of preformed septanose glycal epoxides, as well as by glycosylation of a thiophenyl septanoside donor. In the method presented herein, the ring-opening reaction with sugars occurs in conjunction with the formation of the septanoside.

Synthesis of Azido Septanosides. The use of an azide[25] in the ring opening of a cyclopropanated pyranoside was anticipated to afford azido septanosides. Although a ring-opening reaction with NaN_3[26] in PhMe and under reflux conditions did not proceed well, it was possible to secure the ring-expanded 1-azido chloro oxepine product **22** in a quantitative yield when DMF was used as the solvent (Scheme 3).

(22) (a) Bernotas, R. C.; Pezzone, M. A.; Ganem, B. *Carbohydr. Res.* **1987**, *167*, 305–311. (b) Tennant-Eyles, R. J.; Davis, B. G.; Fairbanks, A. J. *Tetrahedron: Asymmetry* **2000**, *11*, 231–243.

(23) Mc Auliffe, J. C.; Hindsgaul, O. *Synlett* **1998**, 307–309.

(24) (a) Peczuh, M. W.; Snyder, N. L.; Fyvie, W. S. *Carbohydr. Res.* **2004**, *339*, 1163–1171. (b) Fyvie, W. S.; Morton, M.; Peczuh, M. W. *Carbohydr. Res.* **2004**, *339*, 2363–2370.

(25) The ring-opening reaction of **2** with amines such as benzyl amine, *n*-octyl amine, and morpholine was attempted initially. However, the reactions were not successful even after modifying the temperature, reaction duration, and concentrations. In most cases, decomposition of the starting material was observed.

(26) The use of $TMSN_3$ as an azide source resulted no product formation.

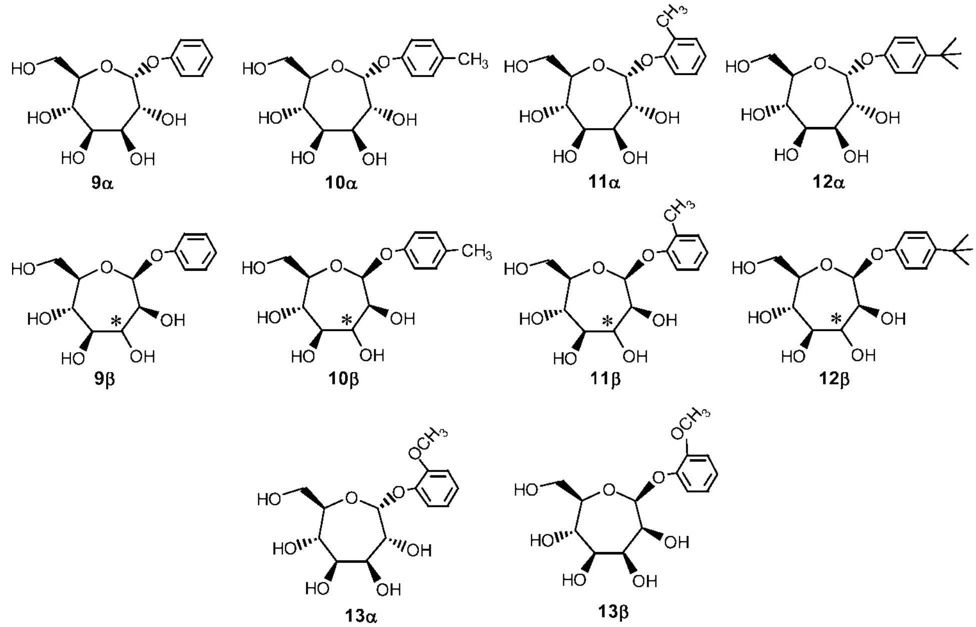
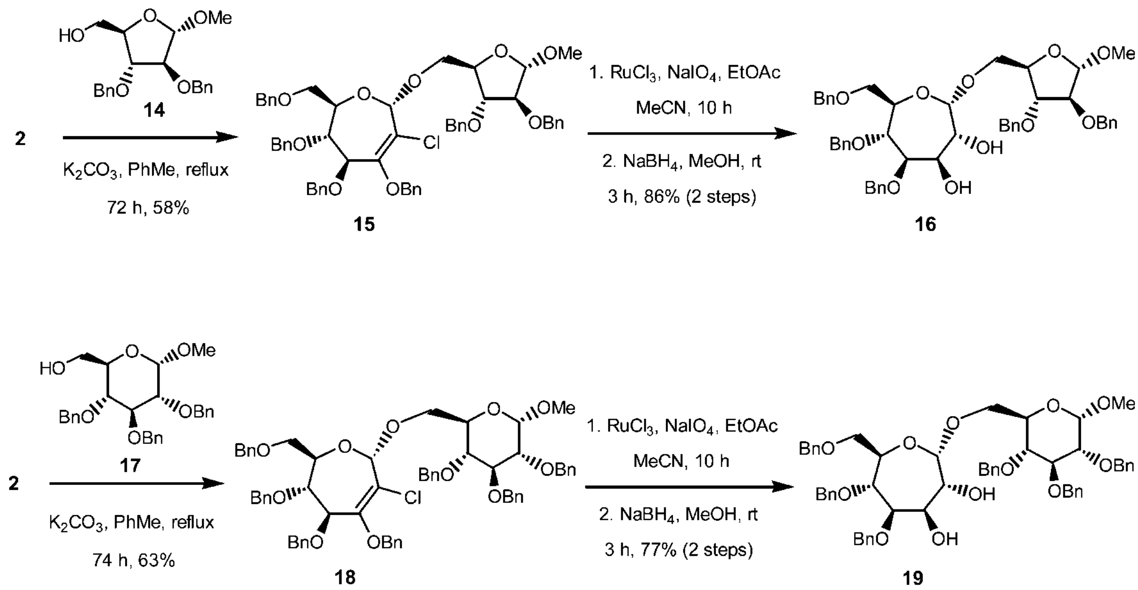


FIGURE 1. Molecular structures of the aryl septanosides **9**−**13**.

SCHEME 2



The presence of the newly introduced azide functionality was identified from IR spectra (ν 2109 cm^{-1}). The ^{1}H NMR spectrum of **22** showed signals at 5.09 and 5.90 ppm, in a ratio of 2:1, corresponding to an α- and β-mixture. Similarly, ^{13}C NMR spectrum showed peaks at 91.7 and 91.2 ppm, corresponding to the anomeric carbon of the anomers. The signals at ~119 and ~153 ppm confirmed the presence of chlorovinyl ether moiety in the product. HR-MS analysis further confirmed the composition of **22**.

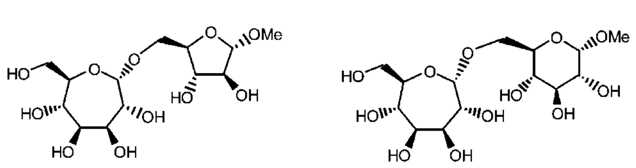
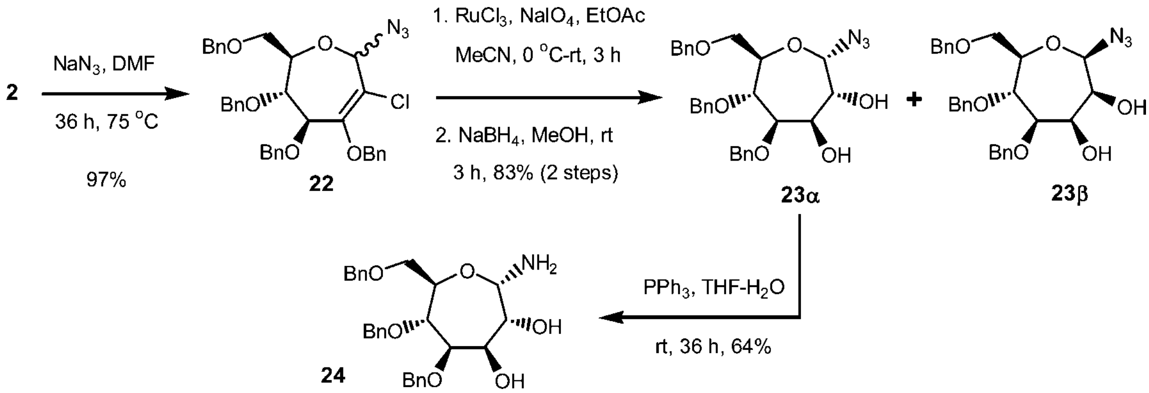


FIGURE 2. Molecular structures of the disaccharides containing septanosides **20** and **21**.

The azido chlorooxepine **22** was subjected to RuO_4 oxidation, followed by $NaBH_4$ reduction, so as to afford the azido septanose derivatives **23**, in a good yield. The reduction led to the formation of azido diols **23** in a 2:1 ratio of α/β mixture (Scheme 3). The diols **23α** and **23*β*** were separated through column chromatography.

In the ^{1}H NMR spectrum of **23α**, the anomeric proton resonated as a doublet, at 5.57 ppm with J = ~3 Hz. The anomeric carbon of **23α** resonated at 87.7 ppm. On the other hand, the resonances corresponding to H-2 and H-3 were found to be complex. Irradiation of H-1 led the signal for H-2 to appear as a doublet with J = 6.6 Hz. This observation indicated a *cis* and *trans* relationship between H-1−H-2 and H-2−H-3, respectively. Similarly, the anomeric proton of β-azide diol (**23*β***) appeared as an apparent singlet, at 5.03 ppm, and the signal for H-2 was observed as a broad peak at 3.96 ppm. The configuration at C-2 and C-3 in **23*β*** was resolved through irradiation

SCHEME 3



experiments. The H-2 signal appeared as a sharp doublet (J = 3.1 Hz) upon irradiation of H-1, which confirmed that H-1, H-2, and H-3 were oriented *cis* to each other.

Having the azide diol **23α**, a one-step azide reduction and benzyl group deprotection was performed by hydrogenolysis (Pd/C, H_2). However, the reaction was not successful, leading to the formation of a complex mixture. The selective reduction of the anomeric azide to amine was thus attempted using PPh_3/THF.[27] Treatment of **23α** (1 molar equiv) with PPh_3 (4 molar equiv), in THF/H_2O (4:1), for 36 h, afforded amino septanose **24** in a moderate yield. In the ^{1}H NMR spectrum of anomeric amine **24**, resonances of the septanose ring protons appeared as sets of multiplets at 4.84−4.35, 4.13−3.81, and 3.69−3.54 ppm. The ^{13}C NMR spectrum showed peaks at 78.4, 74.4, 70.1, and 69.9 ppm, corresponding to the ring carbons of the amino septanose **24**. HR-MS analysis confirmed the presence of the anticipated anomeric amine **24**, in addition to a peak that could be attributed to a disaccharide, formed through condensation of two septanosides, with the loss of an ammonia molecule.

In conclusion, the ring-opening reaction of cyclopropanated pyranosides, in the presence of phenols, sugars, and azides was examined. Important observations are the following: (i) The ring-opening reactions with phenols, sugars, and azides are found to be effective and provided the chlorooxepines in good yields. (ii) The stereoselectivity of the product formed during the ring-opening reaction was affected with phenolates and azide, whereas the presence of sugars did not have an effect and highly stereoselective products formed. This observation leads us to presume that the π-orbitals in the phenolate and azide may have a role in the product formation, wherein the addition of these nucleophiles occur via a S_N1-type mechanism, involving the oxocarbenium ion of the septanose. On the other hand, the sugars might experience a kinetic anomeric effect upon addition to the oxocarbenium ion of the septanose, thereby resulting in the α-anomeric product, similar to the previously studied NaOMe as the nucleophile. (iii) The $NaBH_4$-mediated reduction of diketone intermediates of the α-anomers was diastereoselective, whereas the β-anomers led to an epimeric mixture of diols in case of aryl septanosides. The diketone intermediate of the β-anomer of azido septanoside afforded a diastereoselective product upon reduction. The previously established ring-expansion reaction of the pyranosides to septanosides proved to be a reiterative method to synthesize aryl septanosides, disaccharides, and azido septanosides.

(27) (a) Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635–646. (b) Vaultier, M.; Knouzi, N.; Carrié, R. *Tetrahedron Lett.* **1983**, *24*, 763–764.

Experimental Section

1,5-Anhydro-2,3,4,6-tetra-*O*-benzyl-1,2-C-(dichloromethylene)-α-D-*glycero*-D-*galacto*-hexitol (2). To a solution of **1** (1.3 g, 2.5 mmol) and benzyltriethylammonium chloride (TEBAC) (cat.) in $CHCl_3$ (8 mL), aqueous NaOH (50%, 7 mL) was added. The mixture was stirred for 2 h, then diluted with brine solution (50 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The resulting residue was purified (hexane/EtOAc = 9:1) to afford **2** (1.32 g, 88%), as a colorless oil. R_f 0.70 (hexane/EtOAc = 9:1); $[\alpha]^{24}_D$ +34.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.20 (m, 20H), 4.95−4.85 (m, 3H), 4.68−4.59 (m, 3H), 4.45 (d, J = 12.0 Hz, 1H), 4.32 (d, J = 12.0 Hz, 1H), 4.14 (d, J = 10.0 Hz, 1H), 4.05 (dd, J = 10.2 Hz, 10.0 Hz,1H), 3.97 (s, 1H), 3.89−3.86 (m, 1H), 3.60 (dd, J = 10.4, 2.9 Hz, 1H), 3.47 (dd, J = 10.4, 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 137.8, 137.6, 137.4, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 80.7, 77.2, 74.5, 73.9, 73.5, 72.8, 71.3, 70.5, 66.9, 65.4, 63.7; HRMS *m/z* $C_{35}H_{34}Cl_2O_5Na$ calcd 627.1681, found 627.1680.

General Procedure for the Synthesis of Chloro-oxepine (3). To a stirred solution of **2** (1 mmol), K_2CO_3 (20 mmol), and 18-C-6 (cat.) in PhMe (20 mL) was added phenol (5 mmol), and the mixture was refluxed for 48−72 h. The reaction mixture was filtered through basic alumina using hexane/EtOAc (1:1), and solvents were removed in vacuo to afford an anomeric mixture of the chloro-oxepine derivatives **3**. The crude chloro-oxepine was subjected immediately to the next reaction without further purification.

Phenyl 2-Chloro-2-deoxy-3,4,5,7-tetra-*O*-benzyl-α/*β*-D-*arabino*-hept-2-enoseptanoside 3. (R_1, R_2 = H) Isolated as a mixture of isomers. Colorless oil; R_f 0.47 (hexane/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.12 (m, 50H), 5.99 (s, 1H), 5.68 (s, 1H), 4.82−4.61 (m, 6H), 4.55−4.45 (m, 5H), 4.42−4.23 (m, 9H), 3.91 (dd, J = 8.1, 2.4 Hz, 1H), 3.82−3.73 (m, 1H), 3.65 (dd, J = 8.1, 2.1 Hz, 1H), 3.60−3.51 (m, 2H), 3.42 (dd, J = 10.5, 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 157.4, 153.6, 153.2, 138.1, 138.0, 137.7, 137.3, 136.9, 136.8, 129.7, 129.4, 129.3, 128.9, 128.4, 127.9, 127.3, 122.5, 121.3, 121.1, 120.6, 117.0, 115.3, 101.5, 98.7, 80.0, 79.9, 78.2, 73.4, 73.1, 72.5, 72.3, 72.2, 71.4, 71.2, 71.1, 70.8, 70.2; HRMS *m/z* $C_{41}H_{39}ClO_6Na$ calcd 685.2333, found 685.2330.

General Procedure for Synthesis of Aryl 4,5,7-Tri-*O*-benzyl-α/*β*-D-*glycero*-D-*galacto*/*ido*/*talo*-septanoside (4−8). To a stirred solution of chloro-oxepine (**3**) (1 mmol) in MeCN/EtOAc (25 mL, 1:1) a solution of $RuCl_3 \cdot 3H_2O$ (0.07 mmol) and $NaIO_4$ (1.3 mmol) in water (5 mL) dropwise at 0 °C. After stirring (1−4 h) at room temperature, the reaction mixture was diluted with EtOAc (20 mL) and CH_2Cl_2 (20 mL), filtered through a pad of silica gel, washed with EtOAc (2 × 30 mL), and the solvents were removed in vacuo. The resulting residue was purified (hexane/EtOAc = 3:2) to afford 2,3-diketo derivative as an anomeric mixture. Overall yield: 70−76% (2 steps).

To a solution of the 2,3-diketo derivative (1 mmol) in MeOH (6 mL) was added $NaBH_4$ (5 mmol) was added at 0 °C, stirred for 2 h. Solvents were removed in vacuo, the resulting residue was dissolved in EtOAc (30 mL), washed with brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo, and the crude product was purified (hexane/EtOAc = 3:2) to afford the diols **4**-**8**.

Phenyl 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanoside (4α). Isolated as a single isomer. Colorless oil; R_f 0.44 (hexane/EtOAc = 7:3); $[\alpha]^{24}_D$ +56.6 (*c* 0.7, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.01 (m, 20H), 5.73 (d, *J* = 4.3 Hz, 1H), 4.83−4.75 (m, 2H), 4.46−4.39 (m, 2H), 4.38−4.36 (m, 1H), 4.30−4.19 (m, 3H), 4.12−4.08 (m, 2H), 3.78 (dd, *J* = 9.5, 9.4 Hz, 1H), 3.49 (dd, *J* = 10.5, 4.1 Hz, 1H), 3.32 (dd, *J* = 10.5, 2.3 Hz, 1H), 2.81 (br s, 1H), 2.47 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 138.4, 138.1, 137.7, 129.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 122.7, 116.5, 96.6, 80.5, 77.7, 73.5, 73.0, 72.8, 71.1, 70.5, 70.2, 70.1; HRMS *m/z* $C_{34}H_{36}O_7Na$ calcd 579.2359, found 579.2370.

Phenyl 4,5,7-Tri-*O*-benzyl-*β*-D-*glycero*-D-*ido*/*talo*-septanoside (4*β*). Isolated as a mixture of isomers. Amorphous solid; R_f 0.35 (hexane/EtOAc = 7:3); ^1H NMR (400 MHz, $CDCl_3$) (C-3 epimeric ratio, 1.3:1.0) δ 7.36−7.19 (m, 41.4H), 7.05−6.98 (m, 4.6H), 5.53 (app.s, 1.3H), 5.39 (s, 1H), 4.64−4.36 (m, 13.5H), 4.20−4.07 (m, 8.5H), 3.96−3.92 (m, 2.5H), 3.85 (dd, *J* = 5.6, 2.4 Hz, 1.3H), 3.68 (d, *J* = 4.8 Hz, 1H), 3.64−3.54 (m, 4.6H), 3.46 (dd, *J* = 7.8, 7.2 Hz, 1.3H), 3.29 (d, *J* = 8.7 Hz, 1H), 3.17 (d, *J* = 10.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 156.7, 137.9, 137.8, 137.3, 137.1, 136.8, 129.5, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 122.6, 122.4, 117.1, 116.9, 98.9, 98.6, 84.6, 81.2, 80.7, 80.3, 79.2, 76.8, 76.0, 75.4, 74.8, 74.2, 73.6, 73.4, 73.3, 72.1, 71.2, 70.9, 70.7, 67.5; HRMS *m/z* $C_{34}H_{36}O_7Na$ calcd 579.2359, found 579.2360.

***p*-Tolyl 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanoside (5α).** Isolated as a single isomer. Colorless oil; R_f 0.47 (hexane/EtOAc = 7:3); $[\alpha]^{24}_D$ −3.9 (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−6.96 (m, 19H), 5.68 (d, *J* = 4.5 Hz, 1H), 4.83−4.74 (m, 2H), 4.47−4.40 (m, 2H), 4.37−4.32 (m, 1H), 4.31−4.16 (m, 3H), 4.12−4.08 (m, 2H), 3.77 (dd, *J* = 9.6, 9.5 Hz, 1H), 3.49 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.33 (dd, *J* = 10.6, 2.1 Hz, 1H), 2.80 (br s, 1H), 2.48 (br s, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 138.4, 138.2, 137.9, 132.1, 130.0, 128.4, 128.2, 127.8, 127.5, 117.0, 116.4, 96.9, 80.6, 77.8, 73.6, 73.1, 72.9, 71.2, 70.5, 70.2, 20.6; HRMS *m/z* $C_{35}H_{38}O_7Na$ calcd 593.2515, found 593.2515.

***p*-Tolyl 4,5,7-Tri-*O*-benzyl-*β*-D-*glycero*-D-*ido*/*talo*-septanoside (5*β*).** Isolated as a mixture of isomers. White foam; R_f 0.35 (hexane/EtOAc = 7:3); ^1H NMR (400 MHz, $CDCl_3$) (C-3 epimeric ratio, 1.5:1.0) δ 7.32−7.07 (m, 38H), 7.04−6.89 (m, 10H), 5.47 (s, 1.5H), 5.38 (s, 1H), 4.59−4.35 (m, 13.5H), 4.19−4.06 (m, 9H), 3.96−3.93 (m, 3H), 3.83 (dd, *J* = 5.4, 2.4 Hz, 1H), 3.70 (d, *J* = 3.6 Hz, 1.5H), 3.65−3.53 (m, 5H), 3.45 (dd, *J* = 7.5, 7.2 Hz, 1.5H), 3.29 (d, *J* = 7.5 Hz, 1H), 3.19−3.17 (m, 1H), 2.28 (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 154.6, 137.9, 137.8, 137.3, 137.1, 136.8, 131.9, 131.8, 129.9, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 117.1, 116.9, 99.3, 98.9, 84.5, 81.1, 80.7, 80.3, 79.2, 76.8, 75.9, 75.5, 74.8, 74.2, 73.6, 73.4, 73.3, 72.0, 71.3, 71.0, 70.7, 67.5, 20.6, 20.5; HRMS *m/z* $C_{35}H_{38}O_7Na$ calcd 593.2515, found 593.2515.

***p*-*tert*-Butyl Phenyl 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanoside (6α).** Isolated as a single isomer. Colorless oil; R_f 0.61 (hexane/EtOAc = 7:3); $[\alpha]^{24}_D$ +46.1 (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.01 (m, 19H), 5.68 (d, *J* = 3.9 Hz, 1H), 4.84−4.74 (m, 2H), 4.45−4.32 (m, 3H), 4.28−4.18 (m, 3H), 4.13−4.07 (m, 2H), 3.77 (dd, *J* = 9.6, 9.3 Hz, 1H), 3.50 (dd, *J* = 10.2, 3.9 Hz, 1H), 3.35 (dd, *J* = 10.5, 2.1 Hz, 1H), 2.83 (br s, 1H), 2.46 (br s, 1H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 145.5, 138.4, 138.2, 137.8, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.4, 126.3, 116.0, 96.9, 80.4, 77.7, 73.5, 73.0, 72.8, 71.1, 70.4, 70.3, 70.1, 34.2, 31.4; HRMS *m/z* $C_{38}H_{44}O_7Na$ calcd 635.2985, found 635.2972.

***p*-*tert*-Butyl Phenyl 4,5,7-Tri-*O*-benzyl-*β*-D-*glycero*-D-*ido*/*talo*-septanoside (6*β*).** Isolated as a mixture of isomers. Amorphous solid; R_f 0.53 (hexane/EtOAc = 7:3); ^1H NMR (400 MHz, $CDCl_3$) (C-3 epimeric ratio, 1.7:1.0) δ 7.33−7.20 (m, 46H), 6.99−6.92 (m, 5.4H), 5.48 (s, 1.7H), 5.35 (s, 1H), 4.62−4.37 (m, 17.3H), 4.19−4.07 (m, 9.2H), 3.94 (br s, 2H), 3.85−3.82 (m, 1.6H), 3.67−3.44 (m, 7.5H), 3.31−3.19 (m, 3H), 1.28 (s, 24.3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 145.2, 137.9, 137.2, 137.0, 129.8, 128.6, 128.4, 128.1, 127.9, 126.3, 125.2, 116.6, 116.4, 99.2, 99.0, 84.6, 81.1, 80.4, 79.1, 75.9, 75.6, 74.8, 74.3, 73.7, 73.5, 72.1, 71.4, 71.2, 70.9, 67.7, 65.6, 34.2, 31.5; HRMS *m/z* $C_{38}H_{44}O_7Na$ calcd 635.2985, found 635.3000.

o-Tolyl 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanoside (7α). Isolated as a single isomer. Colorless oil; R_f 0.43 (hexane/EtOAc = 7:3); $[\alpha]^{24}_D$ +36.0 (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−6.89 (m, 19H), 5.72 (d, *J* = 3.9 Hz, 1H), 4.84−4.74 (m, 2H), 4.49−4.25 (m, 6H), 4.09−4.04 (m, 2H), 3.82 (dd, *J* = 9.6, 9.3 Hz, 1H), 3.49 (dd, *J* = 10.5, 3.9 Hz, 1H), 3.32 (dd, *J* = 10.5, 2.4 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 138.4, 138.1, 137.9, 130.8, 128.3, 128.2, 128.1, 127.9, 127.7, 127.1, 126.8, 122.3, 114.4, 96.5, 80.8, 73.5, 73.1, 73.0, 71.3, 70.8, 70.3, 16.3; HRMS *m/z* $C_{35}H_{38}O_7Na$ calcd 593.2515, found 593.2527.

***o*-Tolyl 4,5,7-Tri-*O*-benzyl-*β*-D-*glycero*-D-*ido*/*talo*-septanoside (7*β*).** Isolated as a mixture of isomers. Colorless oil; R_f 0.30 (hexane/EtOAc = 7:3); ^1H NMR (300 MHz, $CDCl_3$) (C-3 epimeric ratio, 3.3:1.0) δ 7.31−6.92 (m, 82H), 5.45 (s, 3.3H), 5.31 (s, 1H), 4.62−4.36 (m, 30H), 4.16−4.03 (m, 11.1H), 3.97−3.84 (m, 8.5H), 3.69−3.54 (m, 7.5H), 3.49−3.44 (m, 1H), 3.32 (br s, 2.5H), 3.18 (d, *J* = 10.2 Hz, 3.5H), 2.27 (s, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 137.9, 137.8, 137.3, 137.2, 136.9, 130.9, 130.7, 128.6, 128.5, 128.4, 127.9, 127.8, 127.6, 127.2, 126.9, 126.8, 122.7, 122.6, 115.9, 115.8, 99.9, 99.6, 81.1, 80.3, 79.1, 76.0, 74.4, 74.3, 73.7, 73.6, 73.5, 73.4, 73.3, 71.5, 71.3, 70.7, 70.6, 16.4; HRMS *m/z* $C_{35}H_{38}O_7Na$ calcd 593.2515, found 593.2513.

***o*-Methoxy Phenyl 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanoside (8α).** Isolated as a single isomer. White foam; R_f 0.50 (hexane/EtOAc = 3:2); $[\alpha]^{24}_D$ +23.4 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44−6.69 (m, 19H), 5.42 (d, *J* = 4 Hz, 1H), 4.88−4.75 (m, 2H), 4.52−4.39 (m, 3H), 4.37−4.32 (m, 1H), 4.29−4.21 (m, 2H), 4.18−4.09 (m, 2H), 3.83 (s, 3H), 3.63−3.49 (m, 4H), 3.07 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 146.8, 138.5, 138.1, 137.7, 128.6, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 124.2, 121.3, 120.1, 111.5, 101.2, 79.7, 78.3, 73.6, 73.1, 72.3, 71.1, 70.4, 70.0, 55.6; HRMS *m/z* $C_{35}H_{38}O_8Na$ calcd 609.2464, found 609.2455.

***o*-Methoxy Phenyl 4,5,7-Tri-*O*-benzyl-*β*-D-*glycero*-D-*talo*-septanoside (8*β*).** Isolated as a single isomer. White solid; mp 101 °C; R_f 0.26 (hexane/EtOAc = 3:2); $[\alpha]^{24}_D$ −41.3 (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−6.78 (m, 19H), 5.38 (s, 1H), 4.56−4.25 (m, 7H), 4.13 (br s, 1H), 4.05−4.00 (m, 2H), 3.89−3.74 (m, 4H), 3.61−3.52 (m, 2H), 3.42 (dd, *J* = 7.5, 7.2 Hz, 1H), 3.19 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9, 145.7, 137.9, 137.5, 137.3, 128.6, 128.5, 128.4, 128.1, 127.9, 127.8, 120.8, 112.4, 99.9, 84.6, 81.2, 75.7, 74.8, 73.2, 72.0, 70.9, 67.9, 55.9; HRMS *m/z* $C_{35}H_{38}O_8Na$ calcd 609.2464, found 609.2460.

General Procedure for the Synthesis of Aryl α/*β*-D-*glycero*-D-*galacto*/ido/*talo*-septanosides (9−13). To a solution of the diols **4**−**8** (0.17 mmol) in EtOAc/MeOH (1:1, 25 mL) Pd/C (10%, 0.030 g) was added, and the mixture was stirred under a positive pressure of hydrogen gas for 15 h. The reaction mixture was filtered over a celite pad and washed with MeOH (3 × 20 mL), and solvents were removed in vacuo to afford aryl septanosides **9**−**13**. Yield: 93−98%.

Phenyl α-D-*Glycero*-D-*galacto*-septanoside (9α). Colorless oil; R_f 0.67 ($CH_3OH/CHCl_3$ = 1:1); $[\alpha]^{24}_D$ +35.3 (*c* 1.00, MeOH); ^1H NMR (400 MHz, D_2O) δ 7.32−7.25 (m, 2H), 7.04−6.96 (m, 3H), 5.55 (d, *J* = 3.6 Hz, 1H), 4.17 (dd, *J* = 7.6, 3.6 Hz, 1H), 4.13 (dd, *J* = 7.6, 2 Hz, 1H), 3.89−3.85 (m, 2H), 3.56 (dd, *J* = 7.4, 7.3 Hz, 1H), 3.44−3.43 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 156.0, 129.8, 122.9, 117.0, 95.9, 74.1, 73.1, 71.1, 70.5, 70.4, 62.1; HRMS *m/z* $C_{13}H_{18}O_7Na$ calcd 309.0950, found 309.0948.

Phenyl β-D-*Glycero*-D-*ido*/*talo*-septanoside (9β). Isolated as a mixture of isomers. White foam; R_f 0.47 ($CH_3OH/CHCl_3$ = 2:3); ^{1}H NMR (400 MHz, D_2O) (C-3 epimeric ratio, 1.3:1.0) δ 7.27−7.22 (m, 4.6H), 7.00−6.92 (m, 7H), 5.32 (d, *J* = 1.8 Hz, 2.3H), 4.15 (br s, 1.3H), 4.01 (br s, 1H), 3.89−3.78 (m, 3.2H), 3.68−3.62 (m, 3.1H), 3.58−3.45 (m, 6.2H), 3.23−3.28 (m, 1.3H); ^{13}C NMR (100 MHz, D_2O) δ 155.9, 131.2, 124.5, 124.4, 118.5, 118.3, 102.0, 101.2, 82.9, 81.9, 79.1, 75.6, 75.1, 74.6, 73.4, 72.2, 70.9, 64.2, 63.5; HRMS *m/z* $C_{13}H_{18}O_7Na$ calcd 309.0950, found 309.0943.

***p*-Tolyl α-D-*Glycero*-D-*galacto*-septanoside (10α).** White foam; R_f 0.32 ($CH_3OH/CHCl_3$ = 1:4); $[\alpha]^{24}_D$ +64.1 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.17 (d, *J* = 8 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 5.61 (d, *J* = 2.4 Hz, 1H), 4.25 (dd, *J* = 7.6, 3.2 Hz, 1H), 4.22 (dd, *J* = 7.6, 2 Hz, 1H), 3.99−3.96 (m, 2H), 3.67 (dd, *J* = 7.6, 7.2 Hz, 1H), 3.55−3.54 (m, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, D_2O) δ 156.4, 135.4, 132.7, 119.6, 98.7, 76.7, 75.7, 73.7, 73.0, 64.7, 22.1; HRMS *m/z* $C_{14}H_{20}O_7Na$ calcd 323.1107, found 323.1107.

***p*-Tolyl β-D-*Glycero*-D-*ido*/*talo*-septanoside (10β).** Isolated as a mixture of isomers. Colorless oil; R_f 0.31 ($CH_3OH/CHCl_3$ = 1:4); ^{1}H NMR (400 MHz, D_2O) (C-3 epimeric ratio, 1.5:1.0) δ 7.18−7.16 (d, *J* = 8 Hz, 5H), 6.96 (t, *J* = 8 Hz, 5H), 5.36 (app.s, 2.5H), 4.25 (s, 1.5H), 4.12 (s, 1H), 3.95−3.90 (m, 3.5H), 3.81−3.73 (m, 3.7H), 3.66−3.59 (m, 5.5H), 3.45−3.40 (m, 2.3H), 2.24 (s, 7.5H); ^{13}C NMR (100 MHz, D_2O) δ 155.6, 134.4, 131.4, 118.5, 118.2, 102.3, 101.5, 82.8, 81.8, 78.9, 75.6, 75.0, 74.3, 73.3, 72.0, 70.7, 64.1, 63.3, 20.8; HRMS *m/z* $C_{14}H_{20}O_7Na$ calcd 323.1107, found 323.1107.

o-Tolyl α-D-*Glycero*-D-*galacto*-septanoside (11α). White foam; R_f 0.43 ($CH_3OH/CHCl_3$ = 1:4); $[\alpha]^{24}_D$ +29.8 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.19−7.06 (m, 3H), 6.96−6.89 (m, 1H), 5.56 (d, *J* = 2.8 Hz, 1H), 4.21 (dd, *J* = 7.2, 3.2 Hz, 1H), 4.17 (dd, *J* = 7.2, 1.6 Hz, 1H), 3.93−3.91 (m, 2H), 3.59 (dd, *J* = 8.1, 8.0 Hz, 1H), 3.45−3.41 (m, 2H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, D_2O) δ 155.2, 132.5, 129.9, 128.3, 124.2, 116.9, 96.9, 75.1, 74.9, 72.5, 72.2, 71.4, 63.3, 16.7; HRMS *m/z* $C_{14}H_{20}O_7Na$ calcd 323.1107, found 323.1103.

o-Tolyl β-D-*Glycero*-D-*ido*/*talo*-septanoside (11β). Isolated as a mixture of isomers. Amorphous solid; R_f 0.40 ($CH_3OH/CHCl_3$ = 1:4); ^{1}H NMR (400 MHz, D_2O) (C-3 epimeric ratio, 3.3:1.0) δ 7.18−7.12 (m, 8.6H), 7.00−6.94 (m, 8.6H), 5.31 (app.s, 3.3H), 5.26 (s, 1H), 4.22 (br s, 1.5H), 4.03 (br s, 1H), 3.95−3.85 (m, 4.5H), 3.72−3.67 (m, 7.6H), 3.58−3.48 (m, 12H), 3.40−3.37 (m, 3.5H), 2.15(s, 12.9H); ^{13}C NMR (100 MHz, D_2O) δ 155.6, 155.4, 132.4, 130.4, 128.3, 124.6, 120.7, 117.7, 102.9, 101.9, 83.2, 82.0, 78.9, 75.8, 75.4, 75.2, 74.5, 73.2, 72.1, 70.7, 64.2, 63.4, 16.7; HRMS *m/z* $C_{14}H_{20}O_7Na$ calcd 323.1107, found 323.1102.

***p*-*tert*-Butyl Phenyl α-D-*Glycero*-D-*galacto*-septanoside (12α).** Colorless oil; R_f 0.65 ($CH_3OH/CHCl_3$ = 3:7); $[\alpha]^{24}_D$ +81.7 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.42 (d, *J* = 8.7 Hz, 2H), 7.08 (d, *J* = 8.7 Hz, 2H), 5.51 (d, *J* = 3.3 Hz, 1H), 4.25 (dd, *J* = 7.6, 3.2 Hz, 1H), 4.21 (dd, *J* = 7.6, 1.6 Hz, 1H), 3.99−3.95 (m, 2H), 3.66 (dd, *J* = 7.6, 7.2 Hz, 1H), 3.55−3.54 (m, 2H), 1.25 (s, 9H);^{13}C NMR (100 MHz, D_2O) δ 156.4, 148.9, 129.2, 119.3, 98.7, 76.7, 75.6, 73.6, 73.0, 64.7, 36.1, 33.2; HRMS *m/z* $C_{17}H_{26}O_7Na$ calcd 365.1576, found 365.1576.

***p*-*tert*-Butyl Phenyl β-D-*Glycero*-D-*ido*/*talo*-septanoside (12β).** Isolated as a mixture of isomers. White foam; R_f 0.44 ($CH_3OH/CHCl_3$ = 3:7); ^{1}H NMR (400 MHz, D_2O) (C-3 epimeric ratio, 1.7:1.0) δ 7.47−7.45 (d, *J* = 7.6 Hz, 5.4H), 7.05 (m, 5.4H), 5.43 (app.s, 2.7H), 4.30 (br s, 1H), 4.16 (br s, 1.7H), 3.99−3.94 (m, 2.8H), 3.82−3.65 (band, 11.7H), 3.48−3.43 (m, 1.7H), 1.29 (s, 24.3H); ^{13}C NMR (100 MHz, D_2O) δ 156.0, 148.8, 127.9, 118.3, 118.0, 102.2, 101.5, 82.8, 81.8, 79.0, 75.6, 75.0, 74.4, 73.3, 72.0, 70.8, 64.1, 63.3, 35.8, 31.9; HRMS *m/z* $C_{17}H_{26}O_7Na$ calcd 365.1576, found 365.1570.

***o*-Methoxy Phenyl α-D-*Glycero*-D-*galacto*-septanoside (13α).** Amorphous solid; R_f 0.43 (CH_3OH/ $CHCl_3$ = 1:4); $[\alpha]^{24}_D$ +36.5 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.15 (d, *J* = 8.8 Hz, 1H), 7.04−7.00 (m, 2H), 6.92−6.89 (m, 1H), 5.50 (d, *J* = 3.2 Hz, 1H), 4.23 (dd, *J* = 7.2, 3.2 Hz, 1H), 4.17 (dd, *J* = 7.2, 2.4 Hz, 1H), 3.96−3.90 (m, 2H), 3.76 (s, 3H), 3.59 (dd, *J* = 8.0, 7.6 Hz, 1H), 3.48−3.47 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 151.1, 146.2, 126.7, 124.0, 121.1, 115.7, 99.4, 76.3, 75.9, 73.9, 73.3, 72.5, 64.5, 58.3; HRMS *m/z* $C_{14}H_{20}O_8Na$ calcd 339.1056, found 339.1051.

***o*-Methoxy Phenyl β-D-*Glycero*-D-*talo*-septanoside (13β).** White foam; R_f 0.40 ($CH_3OH/CHCl_3$ = 1:4); $[\alpha]^{24}_D$ +8.4 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 7.07−6.93 (m, 4H), 5.29 (app.s, 1H), 4.28 (br s, 1H), 4.09 (br s, 1H), 3.96−3.86 (m, 1H), 3.79−3.50 (band, 6H), 3.39 (br s, 1H); ^{13}C NMR (100 MHz, D_2O) δ 150.8, 146.3, 125.6, 122.7, 119.7, 114.5, 103.1, 83.6, 79.0, 75.2, 72.1, 70.4, 64.2, 57.2; HRMS *m/z* $C_{14}H_{20}O_8Na$ calcd 339.1056, found 339.1051.

General Procedure for the Synthesis of Chloro-oxepine 15 and 18. To a stirred solution of **2** (1 mmol), K_2CO_3 (10 mmol), and 18-C-6 (cat.) in PhMe (20 mL) was added sugar alcohol **14**/**17** (2 mmol). Then the reaction mixture was refluxed for 72−74 h, and solvents were removed in vacuo. The resulting residue was purified (hexane/EtOAc = 9:1) to afford chloro oxepine derivatives **15** (58%)/**18** (63%).

Methyl-*O*-(2-chloro-2-deoxy-3,4,5,7-tetra-*O*-benzyl-α-D-*arabino*-hept-2-eno septanosyl)-(1→5)-2,3-di-*O*-benzyl-α-D-*arabino*-furanoside (15). Isolated as a single isomer. Colorless oil; R_f 0.38 (hexane/EtOAc = 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.05 (m, 30H), 5.42 (s, 1H), 4.92 (s, 1H), 4.71 (dd, *J* = 12.5, 11.5 Hz, 2H), 4.59−4.41 (m, 9H), 4.31−4.18 (m, 4H), 4.04−3.93 (m, 3H), 3.77−3.70 (m, 2H), 3.59−3.48 (m, 2H), 3.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 138.2, 138.0, 137.8, 137.6, 137.3, 136.8, 128.3, 128.2, 127.9, 127.8, 127.6, 127.5, 122.2, 107.2, 99.7, 88.3, 83.7, 80.6, 80.4, 72.9, 72.4, 72.3, 72.0, 71.8, 71.4, 71.2, 70.6, 67.8, 54.9; HRMS *m/z* $C_{55}H_{57}ClO_{10}Na$ calcd 935.3538, found 935.3529.

Methyl-*O*-(2-chloro-2-deoxy-3,4,5,7-tetra-*O*-benzyl-α-D-*arabino*-hept-2-eno septanosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-*gluco*-pyranoside (18). Isolated as a single isomer. Colorless oil; R_f 0.30 (hexane/EtOAc = 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.04 (m, 35H), 5.52 (s, 1H), 4.95 (d, *J* = 10.8 Hz, 1H), 4.86−4.74 (m, 2H), 4.69 (d, *J* = 5.1 Hz, 6H), 4.64−4.52 (m, 4H), 4.43 (dd, *J* = 12.6, 12.0 Hz, 2H), 4.29 (d, *J* = 11.7 Hz, 1H), 4.18 (d, *J* = 11.6 Hz, 2H), 4.00−3.93 (m, 1H), 3.89−3.86 (m, 1H), 3.74−3.65 (m, 3H), 3.57−3.47 (m, 3H), 3.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5, 140.8, 138.9, 138.3, 138.2, 137.8, 137.3, 136.8, 128.5, 128.4, 128.3, 128.2, 128.0, 127.7, 127.6, 127.5, 126.9, 122.6, 99.6, 97.9, 81.9, 80.6, 80.2, 77.9, 77.2, 75.7, 74.9, 73.4, 72.9, 72.3, 72.1, 71.1, 70.9, 70.7, 66.0, 65.4, 55.1; HRMS *m/z* $C_{63}H_{65}ClO_{11}Na$ calcd 1055.4113, found 1055.4108.

General Procedure for the Synthesis of 16 and 19. To a stirred solution of chloro-oxepine **15**/**18** (1 mmol) in MeCN/EtOAc (25 mL, 1:1) at 0 °C was added a solution of $RuCl_3 \cdot 3H_2O$ (0.07 mmol) and $NaIO_4$ (1.3 mmol) in water (5 mL) dropwise. After 10 h of stirring at room temperature, the reaction mixture was diluted with EtOAc (20 mL) and CH_2Cl_2 (20 mL), filtered through a pad of silica gel, and washed with EtOAc (2 × 30 mL), and the solvents were removed in vacuo. To the crude 2,3-diketo derivative in MeOH (6 mL) at 0 °C was added $NaBH_4$ (2 mmol), the mixture was stirred for 3 h, and solvents were removed in vacuo. The resulting residue was dissolved in EtOAc (30 mL), washed with brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo, and the crude product was purified (hexane/EtOAc = 3:2) to afford diol **16** (86%)/**19** (77%).

Methyl-*O*-(4,5,7-tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanosyl)-(1→5)-2,3-di-*O*-benzyl-α-D-*arabino*-furanoside (16). Isolated as a single isomer. Colorless oil; R_f 0.33 (hexane/EtOAc = 6:4); $[\alpha]^{24}_D$ +58.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.10 (m, 25H), 5.01 (d, *J* = 4.5 Hz, 1H), 4.95 (s, 1H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.69 (d, *J* = 12.1 Hz, 1H), 4.54−4.40 (m, 6H), 4.35 (d, *J* = 11.0 Hz, 1H), 4.11−4.08 (m, 2H), 4.01−3.92 (m, 6H), 3.84 (d, *J* = 9.7 Hz, 1H), 3.67 (dd, *J* = 12.4, 2.2 Hz, 1H), 3.49−3.43 (m, 3H), 3.35 (s, 3H), 3.17 (br s, 1H), 2.56 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 138.3, 137.7, 137.5, 136.9, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.6, 127.5, 107.2, 99.8, 87.2, 83.1, 82.2, 79.7, 78.7, 73.5, 73.4, 73.3, 72.2, 72.1, 71.5, 70.9, 70.0, 69.6, 68.2, 54.7; HRMS *m/z* $C_{48}H_{54}O_{11}Na$ calcd 829.3564, found 829.3597.

Methyl-*O*-(4,5,7-tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-*gluco*-pyranoside (19). Isolated as a single isomer. Colorless oil; R_f 0.38 (hexane/EtOAc = 6:4); $[\alpha]^{24}_D$ +55.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.05 (m, 30H), 5.04 (d, *J* = 4.2 Hz, 1H), 4.96 (d, *J* = 11 Hz, 1H), 4.84−4.73 (m, 6H), 4.68 (d, *J* = 6.6 Hz, 1H), 4.63−4.52 (m, 2H), 4.47−4.29 (m, 3H), 4.15−3.94 (m, 7H), 3.74−3.67(m, 2H), 3.55−3.41(m, 4H), 3.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 138.5, 138.2, 138.1, 137.8, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.4, 98.7, 97.9, 81.9, 80.1, 80.0, 78.0, 77.2, 75.7, 74.9, 73.5, 73.3, 73.1, 72.6, 71.2, 71.1, 70.3, 70.2, 69.6, 67.5, 55.3; HRMS *m/z* $C_{56}H_{62}O_{12}Na$ calcd 949.4139, found 949.4130.

General Procedure for the Synthesis of Disaccharides 20 and 21. To a solution of the diols **16/19** (0.062 mmol) in MeOH (15 mL) was added Pd/C (10%, 0.020 g), and the mixture was stirred under a positive pressure of hydrogen gas for 20 h. The reaction mixture was filtered over a celite pad and washed with MeOH (3 × 20 mL), and solvents were removed in vacuo to afford disaccharides **20** (96%) and **21** (98%).

Methyl-*O*-(α-D-*glycero*-D-*galacto*-septanosyl)-(1→5)-α-D-*arabino*-furanoside (20). White foam; R_f 0.50 (MeOH/$CHCl_3$ = 1:1); $[\alpha]^{24}_D$ +116.1 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 4.75 (d, *J* = 3.0 Hz, 1H), 4.73 (s, 1H), 4.00−3.96 (m, 1H), 3.92 (d, *J* = 6.9 Hz, 1H), 3.88−3.82 (m, 4H), 3.74−3.67 (m, 2H), 3.64−3.59 (m, 2H), 3.54 (dd, *J* = 6.8, 6.4 Hz, 1H), 3.45 (t, *J* = 8.4 Hz, 1H), 3.19 (s, 3H); ^{13}C NMR (75 MHz, D_2O) δ 109.4, 97.9, 83.7, 81.4, 77.4, 74.5, 74.1, 72.2, 71.7, 70.7, 68.1, 62.9, 55.8; HRMS *m/z* $C_{13}H_{24}O_{11}Na$ calcd 379.1216, found 379.1201.

Methyl-*O*-(α-D-*glycero*-D-*galacto*-septanosyl)-(1→6)-α-D-*gluco*-pyranoside (21). White foam; R_f 0.30 (MeOH/$CHCl_3$ = 1:1); $[\alpha]^{24}_D$ +117.3 (*c* 1.00, MeOH); ^{1}H NMR (400 MHz, D_2O) δ 4.73 (d, *J* = 2.8 Hz, 1H), 3.90−3.80 (m, 3H), 3.73 (d, *J* = 8.0 Hz, 1H), 3.70−3.61 (m, 4H), 3.58−3.51 (m, 2H), 3.48−3.41 (m, 2H), 3.36−3.30 (m, 2H), 3.19 (s, 3H); ^{13}C NMR (75 MHz, D_2O) δ 100.6, 97.8, 75.3, 74.2, 72.6, 72.4, 72.3, 71.3, 70.6, 67.4, 63.2, 56.4; HRMS *m/z* $C_{14}H_{26}O_{12}Na$ calcd 409.1322, found 409.1315.

Synthesis of Azido 2-Chloro-2-deoxy-3,4,5,7-tetra-*O*-benzyl-α/β-D-*arabino*-hept-2-enoseptanoside (22). To a stirred solution of **2** (0.102 g, 0.168 mmol) in DMF (2 mL) was added NaN_3 (0.044 g, 0.674 mmol). Then the reaction mixture was heated to 75 °C for 36 h, and solvents were removed in vacuo. The resulting residue was purified (hexane/EtOAc = 9:1) to afford **22** (0.095 g, 97%) as a colorless oil. Isolated as a mixture of isomers. R_f 0.50 (hexane/EtOAc = 9:1); IR (neat) 3061, 3029, 2864, 2109, 1640, 1452, 1097, 1073, 736, 696; ^{1}H NMR (400 MHz, $CDCl_3$) (α:β ratio, 2:1) δ 7.35−7.04 (m, 60H), 5.90 (s, 1H), 5.09 (s, 2H), 4.76−4.41 (m, 20H), 4.30−4.14 (m, 10H), 3.77 (dd, *J* = 8.2, 2.1 Hz, 1H), 3.68−3.60 (m, 3H), 3.56−3.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.5, 138.0, 137.9, 137.5, 137.3, 136.9, 136.7, 136.4, 136.3, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 119.8, 119.5, 91.7, 91.2, 79.5, 78.3, 78.1, 76.2, 74.1, 73.4, 73.2, 72.5, 72.3, 72.2, 71.2, 70.8, 70.4, 70.1; HRMS *m/z* $C_{35}H_{34}ClN_3O_5Na$ calcd 634.2085, found 634.2085.

Synthesis of Azido 4,5,7-Tri-*O*-benzyl-α/β-D-*glycero*-D-*galacto*/*talo*-septanoside (23). To a stirred solution of azido chloro-oxepine (**22**) (0.140 g, 0.229 mmol) in MeCN/EtOAc (4 mL, 1:1) at 0 °C was added a solution of $RuCl_3 \cdot 3H_2O$ (cat.) and $NaIO_4$ (0.064 g, 0.297 mmol) in water (1 mL) dropwise. After 3 h of stirring at room temperature, the reaction mixture was diluted with EtOAc (10 mL) and CH_2Cl_2 (10 mL), filtered through a pad of silica gel, and washed with EtOAc (2 × 20 mL), and the solvents were removed in vacuo. To the crude 2,3-diketo derivative in MeOH (3 mL) at 0 °C was added $NaBH_4$ (0.017 g, 0.455 mmol), the mixture was stirred for 3 h, and solvents were removed in vacuo. The resulting residue was dissolved in EtOAc (2 × 20 mL), washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo, and the crude product was purified (hexane/EtOAc = 3:2) to afford **23α** (0.064 g, 55%) and **23β** (0.032 g, 28%).

Azido 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanoside (23α). Isolated as a single isomer. Colorless oil; R_f 0.44 (hexane/EtOAc = 7:3); $[\alpha]^{24}_D$ +59.5 (*c* 1.00, $CHCl_3$); IR (neat) 3443, 3032, 2916, 2115, 1722, 1454, 1260, 1080, 737, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.12 (m, 15H), 5.57 (d, *J* = 3 Hz, 1H), 4.78−4.56 (m, 4H), 4.47−4.41 (m, 2H), 4.34 (d, *J* = 10.8 Hz, 1H), 4.10 (dd, *J* = 6.6, 1.5 Hz, 1H), 4.05−4.02 (m, 1H), 3.96 (dd, *J* = 6.6, 3 Hz, 1H), 3.95−3.86 (m, 1H), 3.65 (d, *J* = 3.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 137.8, 137.7, 128.7, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.6, 87.7, 80.9, 76.1, 74.2, 74.1, 73.7, 73.3, 71.1, 70.9, 70.6; HRMS *m/z* $C_{28}H_{31}N_3O_6Na$ calcd 528.2111, found 528.2120.

Azido 4,5,7-Tri-*O*-benzyl-β-D-*glycero*-D-*talo*-septanoside (23β). Isolated as a single isomer. Colorless oil; R_f 0.38 (hexane/EtOAc = 7:3); $[\alpha]^{24}_D$ +22.7 (*c* 1.00, $CHCl_3$); IR (neat) 3447, 3033, 2917, 2115, 1722, 1455, 1260, 1079, 737, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.12 (m, 15H), 5.03 (app.s, 1H), 4.62−4.42 (m, 6H), 4.22−4.18 (m, 1H), 4.16−4.14 (m, 1H), 4.05−3.99 (m, 2H), 3.96 (br s, 1H), 3.69 (dd, *J* = 9.6, 6.5 Hz, 1H), 3.52 (dd, *J* = 9.5, 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 136.6, 136.3, 128.6, 128.5, 128.4, 128.2, 128.0, 127.8, 127.7, 87.8, 81.6, 79.9, 79.2, 77.7, 73.6, 73.5, 72.9, 70.9, 70.5; HRMS *m/z* $C_{28}H_{31}N_3O_6Na$ calcd 528.2111, found 528.2123.

Synthesis of Amino 4,5,7-Tri-*O*-benzyl-α-D-*glycero*-D-*galacto*-septanose (24). To a stirred solution of **23α** (0.040 g, 0.079 mmol) in THF/H_2O (4 mL, 4:1) at room temperature was added PPh_3 (0.083 g, 0.316 mmol). Then the mixture was stirred for 36 h, and solvents were removed in vacuo. The resulting residue was purified ($CHCl_3$/MeOH = 4:1) to afford **24** (0.024 g, 64%) as a colorless oil; $[\alpha]^{24}_D$ +18.1 (*c* 1.00, $CHCl_3$); IR (neat) 3361, 3059, 2919, 1725, 1445, 1162, 1119, 722, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54−7.26 (m, 15H), 4.84−4.35 (m, 8H), 4.13−3.81 (m, 4H), 3.69−3.54 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 138.1, 137.8, 133.6, 133.2, 132.1, 128.7, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 78.4, 78.1, 74.4, 74.2, 74.1, 73.4, 71.3, 71.2, 70.1, 69.9; HRMS *m/z* $C_{28}H_{33}NO_6Na$ + H calcd 503.2284, found 503.2262; *m/z* $C_{56}H_{63}NO_{12}Na$ + H calcd 965.4326, found 965.4371.

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Supporting Information Available: General experimental procedure, ^{1}H and ^{13}C NMR data and spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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