A Convenient Route to Higher Sugars by Two-Carbon Chain Elongation Using Wittig/Dihydroxylation Reactions

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The combination of a Wittig olefination and a dihydroxylation reaction constitutes a facile synthetic protocol for the transformation of unprotected carbohydrates into higher sugars. The Wittig reaction is carried out with *tert*-butyl or diphenylmethyl ester stabilized phosphoranes to give (*E*)-configured α,*β*-unsaturated esters as the only products in most cases. These are dihydroxylated in a diastereoselective fashion using OsO_4/NMO. The stereochemical outcome in the dihydroxylation follows Kishi's empirical rule and gives high diastereoselectivity (5:1−8:1) when starting from sugars with the 2,3-threo configuration. When starting from sugars with the 2,3-erythro configuration, the diastereoselectivity in the dihydroxylation is low (2:1−2.5:1). As a result, the Wittig/dihydroxylation protocol is most effective for producing higher sugars with the galacto configuration at the reducing end. The two steps can either be carried out individually or, more efficiently, as a one-pot procedure.

Introduction

Higher carbon sugars are carbohydrates containing seven or more consecutive carbon atoms. They have been identified as subunits in a number of natural products of biological significance[1] and have found important use as chiral synthons.[2] However, the synthesis of higher sugars has been a challenge in carbohydrate chemistry for more than a century.[3] The addition of more carbon atoms to unprotected pentoses and hexoses is often plagued by low yield, poor diastereoselectivity, and troublesome isolation of the products. The classical methods for one carbon chain extension of aldoses are the Kiliani and the Sowden reactions using addition of cyanide and nitromethane, respectively.[3,4] More recently, a number of different methods have been developed for elongation of partially protected sugars.[3,5]

In 1965, Kochetkov and Dmitriev demonstrated that higher sugars could be obtained by Wittig reaction of unprotected aldoses followed by OsO_4-catalyzed dihydroxylation of the resulting α,*β*-unsaturated esters.[6] However, with the employed phosphorane, $Ph_3P{=}CHCO_2Et$, the yield in the Wittig reaction was moderate (30−60%) due to a concomitant intramolecular Michael addition in the products. In addition, the dihydroxylation of the unsaturated ester proceeded with only about 3:1 diastereoselectivity. The Michael addition side reaction is a well-known problem in Wittig reactions on unprotected aldoses with methyl or ethyl ester stabilized phosphoranes.[3] Addition of cupric acetate has been reported to diminish this side reaction to some extent.[7] However, in 1996, Railton and Clive reported that the Michael addition could be virtually completely suppressed by employing bulky *tert*-butyl and diphenylmethyl ester stabilized phosphoranes.[8] In addition, the bulky ester groups, particularly the diphenylmethyl group, also gave very high (*E*)-selectivity in the Wittig reactions. We speculated that the use of bulky ester groups would not only improve the selectivity and yield in the Wittig reaction but also might enhance the diastereoselectivity in the subsequent dihydroxylation reaction. Herein, we report an improved strategy for synthesis of higher sugars by Wittig/dihydroxylation of unprotected aldoses.

Results and Discussion

We first decided to probe the strategy by studying the chain elongation of D-galactose. Railton and Clive have already described the Wittig reactions on D-galactose with phosphoranes **1a** and **1b**[8] (Scheme 1). The liberated triphenylphosphine oxide is conveniently removed from the products by partitioning between dichloromethane and water. Unsaturated *tert*-butyl ester **2a** stays in the aqueous layer from which it can be isolated by crystallization, while the diphenylmethyl ester **2b** crystallizes directly at the interface of the organic and the aqueous

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(3) Györgydeák, Z.; Pelyvás, I. F. *Monosaccharide Sugars − Chemical Synthesis by Chain Elongation, Degradation and Epimerization*; Academic Press: San Diego, 1998.

(4) For some recent examples, see: Dromowicz, M.; Köll, P. *Carbohydr. Res.* **1998**, *308*, 169. Bell, A. A.; Nash, R. J.; Fleet, G. W. J. *Tetrahedron*: *Asymmetry* **1996**, *7*, 595. Lundt, I.; Madsen, R. *Synthesis* **1995**, 787. Sato, K.-i.; Miyata, T.; Tanai, I.; Yonezawa, Y. *Chem. Lett.* **1994**, 129.

(5) Dondoni, A.; Marra, A. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1997; p 173. Casiraghi, G.; Rassu, G. In *Studies in Natural Product Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1992; p 429.

(6) Kochetkov, N. K.; Dmitriev, B. A. *Tetrahedron* **1965**, *21*, 803.

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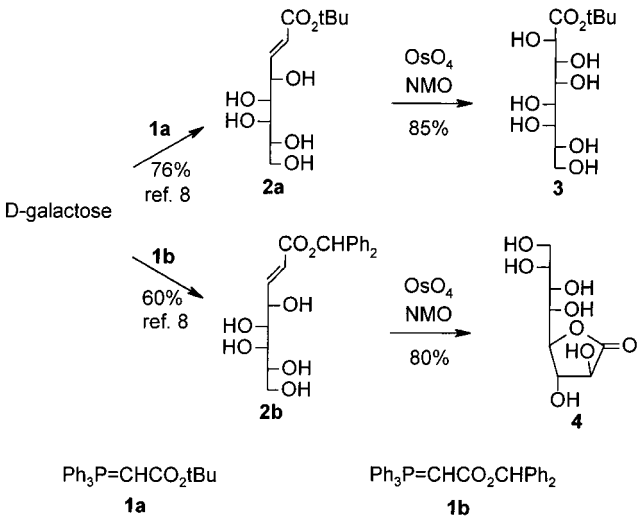
Scheme 1



layer.[8] This turns out to be general for many Wittig reactions on unprotected aldoses with bulky phosphoranes **1a** and **1b**.

The OsO_4-catalyzed dihydroxylation of **2a** and **2b** proceeded smoothly in an acetone−water mixture with NMO as reoxidant.[9] A 8:1 diastereomeric ratio between the two possible octonic acid esters was obtained in both cases as determined by means of ^{13}C NMR spectroscopy. For the *tert*-butyl ester, the major diastereomer **3** crystallized directly from the reaction mixture in 85% yield. For the more labile diphenylmethyl ester, the octonolactone **4** was isolated by crystallization after workup with acidic ion-exchange resin. Octonolactone **4** has previously been prepared by the Kiliani reaction.[10] It could also be obtained from *tert*-butyl ester **3** after reflux in dilute hydrochloric acid. The high diastereomeric ratio is a significant improvement over the 3:1 ratio obtained previously on the corresponding unsaturated ethyl ester or free acid.[6] The observed diastereoselectivity obeys Kishi's empirical rule.[11] This predicts that for dihydroxylation of acyclic allylic alcohols the relative stereochemistry between the preexisting hydroxy group and the adjacent newly introduced hydroxy group in the major product is erythro. Kishi's rule has previously been shown to apply in dihydroxylation of a variety of carbohydrate allylic systems and has also been exploited for the synthesis of complex natural products.[12]

Following the successful chain elongation of D-galactose, we now decided to explore the strategy on a wide assortment of substrates. Railton and Clive have also reacted D-glucose and D-mannose with phosphoranes **1a** and **1b** to give unsaturated esters **5** and **6**[8] (Chart 1). In addition, D-ribose and D-arabinose have been reacted with *tert*-butyl ester phosphorane **1a** to give **7a** and **8a**, respectively.[8] Notably, the reactions between D-mannose and D-ribose with **1a** give in both cases a mixture of (*E*)- and (*Z*)-olefins.[8] When we treated D-ribose with diphenylmethyl ester phosphorane **1b**, we obtained **7b**

Chart 1

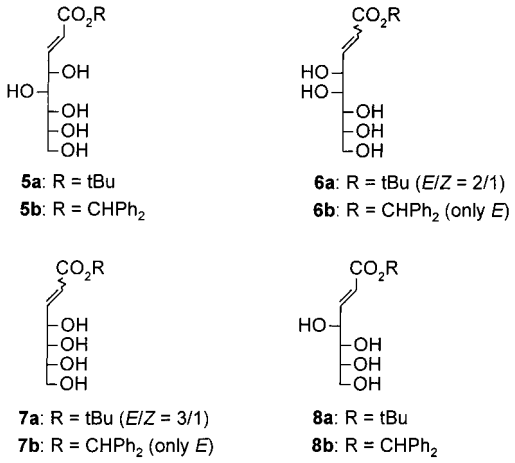
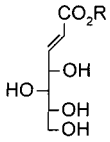
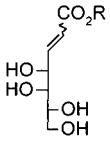
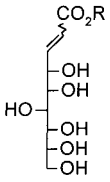
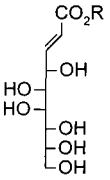


Table 1. Wittig Reactions on Unprotected Aldoses with Phosphoranes 1a and 1b

Entry	Aldose	Phosphorane	Product	R	#	Yield (*E*/*Z*)
1	D-xylose	**1a**		tBu	**9a**	94% (only *E*)
2	D-xylose	**1b**		$CHPh_2$	**9b**	81% (only *E*)
3	D-lyxose	**1a**		tBu	**10a**	75% (3/1)
4	D-lyxose	**1b**		$CHPh_2$	**10b**	51% (only *E*)
5	D-*glycero*-D-*gulo*-heptose	**1a**		tBu	**11a**	81% (3/1)
6	D-*glycero*-D-*galacto*-heptose	**1a**		tBu	**12a**	52% (only *E*)

in 62% yield as the pure (*E*)-conjugated ester (Chart 1). Under the same conditions, D-arabinose gave (*E*)-configured ester **8b** in 75% yield. In a similar way, we have treated D-xylose and D-lyxose with phosphoranes **1a** and **1b** to obtain the corresponding Wittig adducts (Table 1, entries 1−4). In addition, the heptoses D-*glycero*-D-*gulo*-heptose and D-*glycero*-D-*galacto*-heptose have also been homologated, but only with phosphorane **1a** (Table 1, entries 5 and 6).

These reactions were all carried out in dioxane or dioxane−DMF mixtures at 50−90 °C, and the Wittig products were separated from triphenylphosphine oxide after partitioning between dichloromethane and water. Finally, the products were purified by crystallization or flash chromatography. In all cases, good yields of the desired Wittig products were obtained. Byproducts arising from the intramolecular Michael addition were either not observed at all or only in minor amounts. The diphenylmethyl phosphorane **1b** always gave the (*E*)-

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(10) Maclay, W. D.; Hann, R. M.; Hudson, C. S. *J. Am. Chem. Soc.* **1938**, *60*, 1035.
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Chart 2

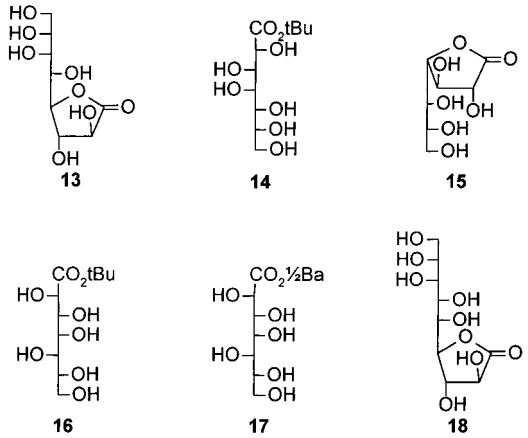

Table 2. Dihydroxylation of Unsaturated Aldonic Acid Esters

entry	original aldose	(*E*)-unsat. ester	diastereomeric ratio	major product isolated	yield (%)
1	D-glucose	**5a**	5:1	**13**	76
2	D-glucose	**5b**	5:1	**13**	60
3	D-mannose	**6a**	2.5:1		
4	D-mannose	**6b**	2.5:1		
5	D-ribose	**7a**	2.5:1		
6	D-ribose	**7b**	2.5:1		
7	D-arabinose	**8a**	7:1	**14**	69
8	D-arabinose	**8b**	7:1	**15**	74
9	D-xylose	**9a**	6:1	**16**	53
10	D-xylose	**9b**	6:1	**17**	51
11	D-lyxose	**10a**	2.0:1		
12	D-lyxose	**10b**	2.0:1		
13	D-*glycero*-D-*gulo*-heptose	**11a**	2.5:1		
14	D-*glycero*-D-*galacto*-heptose	**12a**	5:1	**18**	54

configurated olefin. The *tert*-butyl phosphorane **1a**, on the other hand, only gave (*E*)-olefins with sugars having the 2- and 3-hydroxy group in the threo configuration. Sugars with these two hydroxy groups in the erythro configuration all gave mixtures of (*E*)- and (*Z*)-olefins with phosphorane **1a**, although these *E*/*Z* mixtures could be separated by crystallization or flash chromatography.

Having prepared a variety of unsaturated aldonic acid esters we were now ready to carry out a more systematic study on the dihydroxylation of these (Chart 2, Table 2). The reactions were again performed in an acetone−water mixture with 0.5% OsO_4 and 1.2 equiv of NMO.

For both unsaturated (*E*)-esters derived from a given carbohydrate, we observed the same diastereoselectivity (Table 2, entries 1−12). All the substrates having the two hydroxy groups adjacent to the α,*β*-unsaturated ester in a relative threo configuration gave rise to high diastereoselectivities (ranging from 5:1 to 8:1). The diastereoselectivities were found to be in accordance with Kishi's rule in all cases.[11] In these cases, the dihydroxylation products could be isolated in good yields either as esters, lactones, or metal salts of the carboxylic acid. The structures of these products were verified by comparing the melting points and optical rotations with literature data.[13−16] As opposed to this, all (*E*)-ester substrates featuring erythro-configured hydroxy groups adjacent to the alkene moiety provided significantly poorer diastereoselectivities in the dihydroxylation reaction (ranging from 2:1 to 2.5:1). In these cases, no attempt has been made to isolate or identify the major products. The last entry in Table 2 is noteworthy. The starting material for the elongation, D-*glycero*-D-*galacto*-heptose, is prepared by reduction of lactone **15**,[17] which itself is available by the two step elongation of D-arabinose in entry 8. This shows that the Wittig/dihydroxylation method can be used in an iterative process to form higher sugars in a repetitive fashion.

On the basis of these findings, some general rules can be established for preparation of higher sugars with this two-step methodology. With diphenylmethyl phosphorane **1b**, the Wittig reaction always gives the (*E*)-olefin. For the *tert*-butyl phosphorane **1a**, pure (*E*)-olefins are only obtained with 2,3-threo sugars while 2,3-erythro sugars give mixtures of (*E*)- and (*Z*)-olefins. In the dihydroxylation, however, the same selectivity is obtained for both bulky ester groups. Instead, the diastereoselectivity is controlled by the two hydroxy groups adjacent to the olefin. When these have the threo configuration the dihydroxylation occurs with high diasteroselectivity. On the contrary, when these hydroxy groups have the erythro configuration the selectivity in the dihydroxylation is poor. Hence, the dihydroxylation becomes an efficient protocol for preparing higher sugars with the galacto configuration at these four stereogenic centers. Attempts at improving or reversing the diastereomeric ratio by the use of Sharpless' chiral hydroquini(di)ne phthalazine and pyrimidine ligands were unsuccessful.[18] With NMO as reoxidant, the same diastereomeric ratio and rate were observed as in the absence of the ligands. With potassium ferricyanide as reoxidant it proved impossible to remove the iron salts from the products.

Furthermore, we speculated whether it would be possible to develop a one-pot procedure to allow a more rapid access to higher carbohydrates. Although the intermediate α,*β*-unsaturated esters are generally crystalline, their isolation from triphenylphosphine oxide can still in some cases be a little tedious. We decided to concentrate on the *tert*-butyl phosphorane **1a** for these one-pot studies because some of the corresponding dihydroxylation products crystallize directly during the oxidation reaction. First, D-galactose was treated with **1a** in dioxane according to the procedure of Railton and Clive.[8] However, instead of isolating the generated ester **2a**, the mixture was cooled to room temperature followed by addition of OsO_4 (0.5%) and NMO (1.5 equiv). This mixture was then stirred at room temperature for 6 h during which time the dihydroxylation product **3** crystallized out directly. Simple filtration gave 77% yield of **3** based on D-galactose (Table 3, entry 1). This has to be compared with the 65% yield for the two-step sequence as shown in Scheme 1. Encouraged by this result, we also treated D-glucose, D-arabinose, and D-xylose with phosphorane **1a** followed by direct dihydroxylation. With D-glucose, the octonolactone **13** was isolated after workup to separate triphenylphosphine oxide, while with D-

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(14) Montgomery, E. M.; Hudson, C. S. *J. Am. Chem. Soc.* **1942**, *64*, 247.
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(16) Fischer, E.; Passmore, F. *Chem. Ber.* **1890**, *23*, 2226. Karabinos, J. V.; Hann, R. M.; Hudson, C. S. *J. Am. Chem. Soc.* **1953**, *75*, 4320.
(17) de Lederkremer, R. M.; Deferrari, J. O. *J. Org. Chem.* **1962**, *27*, 2561.
(18) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

Table 3. One-Pot Wittig/Dihydroxylation Using Phosphorane 1a

entry	original aldose	isolated product	yield (%)
1	D-galactose	**3**	77
2	D-glucose	**13**	68
3	D-arabinose	**14**	73
4	D-xylose	**16**	63

arabinose and D-xylose the heptonic acid esters **14** and **16** were isolated by direct crystallization from the reaction mixture (Table 3, entries 2−4). In all cases, the yields for these one-pot procedures were higher than for the two-step sequence. In this way, two carbon atoms and two new stereogenic centers have been added to unprotected sugars in a one-pot procedure with excellent diastereocontrol and good overall chemical yield. This clearly demonstrates that the one-pot protocol is a superior method for this two-carbon chain elongation procedure.

In conclusion, we have further developed an efficient and facile route from unprotected aldoses to higher sugars using Wittig and dihydroxylation reactions. The two reactions can be carried out independently or as a one-pot transformation. The outcome of the overall transformation is predictable, and the protocol is particularly effective for the construction of higher sugars featuring the galacto configuration at the reducing end.

Experimental Section

General Procedures. Thin-layer chromatography was performed on aluminum plates precoated with silica gel (Merck 1.05554). Compounds were visualized by charring after dipping in a solution of ammonium molybdate (6.25 g) and cerium(IV) sulfate (2.5 g) in 10% aqueous H_2SO_4 (250 mL). Flash chromatography was performed using silica gel 60 (Amicon 85040). Microanalyses were conducted by the Department of Chemistry at the University of Copenhagen.

Diphenylmethyl 2-(Triphenylphosphonium)acetate Bromide (1b·HBr). Benzhydrol (26.0 g, 141 mmol) was dissolved in a mixture of redistilled dimethyl aniline (20 mL) and Et_2O (50 mL) at 0 °C. Bromoacetyl bromide (28.5 g, 141 mmol) was added dropwise to the vigorously stirred solution during 10 min (after 5 min a white solid precipitated). The stirring was continued for 1.5 h and the mixture allowed to warm to room temperature. TLC (hexane/EtOAc = 5:1) showed consumption of most of the benzhydrol. The mixture was washed with water (50 mL). The organic phase was washed further with 10% aqueous H_2SO_4 (25 mL) and dried ($MgSO_4$). A solution of PPh_3 (37.5 g, 141 mmol) in Et_2O (200 mL) was then added. The cloudy solution was allowed to stand overnight at room temperature to precipitate **1b**·HBr. After filtration and washing with Et_2O, the phosphonium salt **1b**·HBr was obtained as a white solid (66.3 g, 117 mmol, 83%) with NMR data in accordance with literature values.[8]

General Procedure for Wittig Reactions. Following a slightly modified version of Railton and Clive's method,[8] the phosphonium salt **1a**·HBr (5.64 g, 12 mmol) or **1b**·HBr (6.83 g, 12 mmol) was dissolved in $CHCl_3$ (25 mL) and shaken gently with 2 M aqueous NaOH (25 mL) in a separatory funnel for 5 min. The organic phase was dried ($MgSO_4$) and concentrated. The aldose (10 mmol) was added to the residue. Finally, dioxane (25 mL) or dioxane/DMF (1:1, 25 mL) was added. The resulting solution was stirred for 6 h at 90 or 70 °C and then at 50 °C overnight. During workup, the solution was concentrated and the residue partitioned between water and CH_2Cl_2. The products from the **a**-series were crystallized from MeOH/$CHCl_3$ after concentration of the aqueous layer. Generally, the products from the **b**-series crystallized directly at the phase boundary in the separatory funnel and were recrystallized from MeOH/$CHCl_3$. In a few cases, the products had to be purified by flash chromatography.

General Procedure for Dihydroxylations. The substrate (2.00 g) was dissolved in acetone/water (3 mL/1 mL), and NMO (1.2 equiv as a 50% aqueous solution) was added. Finally, OsO_4 (0.5% as a 5% aqueous solution) was added and the reaction stirred at room temperature for 5−6 h. During workup, the mixture was concentrated. The residue was dissolved in water (5 mL, **a**-series) or water/Et_2O (1:1, 10 mL, **b**-series) and treated with acidic ion-exchange resin (5 mL, Amberlite IR-120-H^+) for 2 h. The resin was filtered off and the aqueous phase concentrated. The products were isolated by crystallization.

General Procedure for One-Pot Wittig/Dihydroxylations. The olefination was performed with phosphorane **1a** as described above with only dioxane as the solvent. After the solution was cooled to room temperature, 0.5% OsO_4 and NMO·H_2O (1.5 equiv) were added. The mixture was then stirred at room temperature for 5−6 h. The higher sugars crystallized directly during the reaction as the *tert*-butyl esters, except when starting from D-glucose where octonolactone **13** was isolated after partitioning between water and CH_2Cl_2 and treatment of the aqueous layer with acid.

***tert*-Butyl D-*threo*-L-*galacto*-Octonate (3).** R_f = 0.30 ($CHCl_3$/MeOH = 3:1). Mp: 167−169 °C (H_2O). $[\alpha]_D$: +10.1 (*c* 2, H_2O). ^{1}H NMR (D_2O, 300 MHz): δ 4.55 (d, J = 1.7 Hz, 1H), 4.13 (dd, J = 9.7, 1.6 Hz, 1H), 4.07 (ddd, J = 7.5, 6.8, 1.5 Hz, 1H), 3.98 (m, 2H), 3.77 (m, 3H), 1.57 (s, 9H). ^{13}C NMR (D_2O, 75 MHz): δ 174.2, 84.0, 71.4, 71.3, 70.6, 69.7, 68.5, 68.3, 63.6, 27.5 (3C). Anal. Calcd for $C_{12}H_{24}O_9$: C, 45.89; H, 7.54. Found: C, 46.15; H, 7.75.

D-*threo*-L-*galacto*-Octono-1,4-lactone (4). R_f = 0.09 ($CHCl_3$/MeOH = 5:1). Mp: 218−220 °C (H_2O). $[\alpha]_D$: +51.0 (*c* 2, H_2O) (lit.[10] mp 219−220 °C (H_2O); $[\alpha]_D$ +64.8 (*c* 0.8, H_2O)). ^{1}H NMR (D_2O, 300 MHz): δ 4.47 (d, J = 9.1 Hz, 1H), 4.38 (dd, J = 8.4, 5.1 Hz, 1H), 4.22 (dd, J = 8.7, 8.6 Hz, 1H), 3.96 (m, 1H), 3.80−3.56 (m, 4H). ^{13}C NMR (D_2O, 75 MHz): δ 176.3, 79.8, 74.1, 72.8, 70.2, 69.5, 66.7, 63.3.

Diphenylmethyl (*E*)-2,3-Dideoxy-D-*ribo*-hept-2-enoate (7b). R_f = 0.47 ($CHCl_3$/MeOH = 5:1). Syrup purified by flash chromatography ($CHCl_3$ → $CHCl_3$/MeOH = 9:1). $[\alpha]_D$: +8.47 (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 7.41−7.20 (m, 10H), 7.11 (dd, J = 15.7, 4.8 Hz, 1H), 6.81 (s, 1H), 6.08 (dd, J = 15.7, 1.7 Hz, 1H), 4.34 (dt, J = 4.7, 1.7 Hz, 1H), 3.50−3.25 (m, 4H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 164.6, 150.7, 140.5, 128.4, 127.6, 126.4, 119.8, 76.0, 74.9, 72.4, 70.9, 63.1. Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19. Found: C, 66.74; H, 6.01.

Diphenylmethyl (*E*)-2,3-Dideoxy-D-*arabino*-hept-2-enoate (8b). R_f = 0.67 ($CHCl_3$/MeOH = 5:1). Isolated directly as a solid at the phase boundary between water and CH_2Cl_2. Mp: 175−177 °C (MeOH/$CHCl_3$). $[\alpha]_D$: −11.2 (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 7.42−7.23 (m, 10H), 7.10 (dd, J = 15.8, 4.2 Hz, 1H), 6.80 (s, 1H), 6.12 (dd, J = 15.7, 2.0 Hz, 1H), 4.46 (ddd, J = 4.2, 2.0, 1.9 Hz, 1H), 3.50 (dd, J = 9.1, 1.9 Hz, 1H), 3.46 (dd, J = 9.2, 1.1 Hz, 1H), 3.40 (bs, 1H), 3.37 (bd, J = 1.5 Hz, 1H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 164.6, 152.4, 140.5, 128.4, 127.6, 126.4, 119.4, 76.0, 73.0, 71.4, 70.0, 63.3. Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19. Found: C, 66.80; H, 6.17.

***tert*-Butyl (*E*)-2,3-Dideoxy-D-*xylo*-hept-2-enoate (9a).** R_f = 0.67 ($CHCl_3$/MeOH = 3:1). Isolated as a syrup after flash chromatography ($CHCl_3$/MeOH = 9:1 → 5:1). The syrup crystallized from Et_2O on standing. Mp: 133−135 °C (MeOH/$CHCl_3$). $[\alpha]_D$: −9.3 (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 6.80 (dd, J = 15.5, 4.9 Hz, 1H), 5.84 (dd, J = 15.5, 1.7 Hz, 1H), 4.18 (ddd, J = 5.2, 4.9, 1.7 Hz, 1H), 3.45−3.25 (m, 4H), 1.39 (s, 9H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 165.9, 149.3, 122.3, 80.3, 73.7, 72.1, 71.9, 63.1, 28.5 (3C). Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.33; H, 8.12. Found: C, 53.22; H, 8.08.

Diphenylmethyl (*E*)-2,3-Dideoxy-D-*xylo*-hept-2-enoate (9b). R_f = 0.56 ($CHCl_3$/MeOH = 5:1). Isolated as a crystalline product after flash chromatography ($CHCl_3$/MeOH = 9:1 → 5:1). Mp: 114−118 °C (EtOAc/hexane). $[\alpha]_D$: −9.43 (*c* 2, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 7.50−7.25 (m, 10H), 7.17 (dd, J = 15.8, 4.5 Hz, 1H), 6.83 (s, 1H),

6.10 (dd, J = 15.8, 1.7 Hz, 1H), 4.31 (ddd, J = 4.5, 3.0, 1.7 Hz, 1H), 3.55−3.30 (m, 4H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 164.7, 151.1, 140.6, 128.5, 127.7, 126.5, 119.3, 76.1, 73.1, 71.5, 71.5, 62.6. Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19. Found: C, 67.06; H, 6.10.

***tert*-Butyl (*E*)-2,3-Dideoxy-D-*lyxo*-hept-2-enoate (10a).** R_f = 0.53 ($CHCl_3$/MeOH = 3:1). The product was isolated by flash chromatography (hexane → EtOAc). Yield 75% as a 3:1 (*E*)/(*Z*) mixture. Further purification by flash chromatography gave pure (*E*)-isomer with the following data. $[\alpha]_D$: +24.8 (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 6.99 (dd, J = 15.8, 4.6 Hz, 1H), 5.83 (dd, J = 15.6, 1.7 Hz, 1H), 4.11 (ddd, J = 8.1, 4.5, 1.7 Hz, 1H), 3.65 (dt, J = 6.6, 2.0 Hz, 1H), 3.42−3.30 (m, 2H), 3.24 (dd, J = 8.2, 1.9 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 165.9, 150.6, 121.8, 80.2, 73.1, 70.3, 70.2, 62.9, 28.2 (3C). Anal. Calcd for $C_{11}H_{20}O_6$: C, 53.33; H, 8.12. Found: C, 53.31; H, 8.38.

Diphenylmethyl (*E*)-2,3-Dideoxy-D-*lyxo*-hept-2-enoate (10b). R_f = 0.63 ($CHCl_3$/MeOH = 5:1). Mp: 98−100 °C (MeOH/$CHCl_3$). $[\alpha]_D$: −7.5 (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 7.43−7.20 (m, 11H), 6.80 (s, 1H), 6.17 (dd, J = 15.7, 0.1 Hz, 1H), 4.20 (m, 1H), 3.67 (m, 1H), 3.45−3.22 (m, 3H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 165.5, 153.2, 141.0, 129.2, 128.4, 126.9, 119.7, 76.9, 73.1, 70.4, 70.3, 63.1. Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19. Found: C, 66.71; H, 5.97.

***tert*-Butyl (*E*)-2,3-Dideoxy-D-*glycero*-D-*gulo*-non-2-enoate (11a).** R_f = 0.23 ($CHCl_3$/MeOH = 3:1). The product was isolated as a 3:1 mixture of (*E*)- and (*Z*)-isomers. Further purification by flash chromatography gave pure (*E*)-isomer. $[\alpha]_D$: −12.4 (*c* 2, H_2O). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 6.86 (dd, J = 15.7, 4.3 Hz, 1H), 5.82 (dd, J = 15.7, 1.6 Hz, 1H), 4.38 (m, 1H), 3.70−3.20 (m, 6H), 1.38 (s, 9H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 165.7, 150.8, 121.8, 80.1, 71.8, 71.5, 70.1, 69.6, 69.0, 64.0, 28.1 (3C). Anal. Calcd for $C_{13}H_{24}O_8$: C, 50.64; H, 7.85. Found: C, 50.68; H, 7.75.

***tert*-Butyl (*E*)-2,3-Dideoxy-D-*glycero*-D-*galacto*-non-2-enoate (12a).** R_f = 0.26 ($CHCl_3$/MeOH = 3:1). Isolated as a crystalline 7:1 mixture of the (*E*)-olefin and the corresponding Michael product. Recrystallization from MeOH/$CHCl_3$ afforded the desired product in 52% yield. Mp: 175−177 °C (H_2O). $[\alpha]_D$: −7.86 (*c* 1, MeOH). ^{1}H NMR (D_2O, 300 MHz): δ 6.93 (dd, J = 15.7, 4.3 Hz, 1H), 6.02 (dd, J = 15.7, 1.8 Hz, 1H), 4.59 (ddd, J = 4.3, 2.5, 1.8 Hz, 1H), 3.87 (d, J = 9.2 Hz, 1H), 3.79 (dd, J = 11.5, 2.3 Hz, 1H), 3.77−3.64 (m, 3H), 3.60 (dd, J = 11.5, 5.6 Hz, 1H), 1.43 (s, 9H). ^{13}C NMR (CD_3OD, 75 MHz): δ 167.7, 150.2, 123.6, 81.5, 73.4, 73.2, 71.7, 71.2, 70.7, 65.2, 28.4 (3C). Anal. Calcd for $C_{13}H_{24}O_8 \cdot {}^1/_2H_2O$: C, 49.20; H, 7.74. Found: C, 49.56; H, 7.65.

D-*erythro*-L-*galacto*-Octono-1,4-lactone (13). R_f = 0.30 ($CHCl_3$/MeOH = 3:1). Mp: 142−144 °C (EtOH). $[\alpha]_D$: +51.3 (*c* 2, H_2O) (lit.[13] mp 151−152 °C (EtOH); $[\alpha]_D$ +53.7 (*c* 1.65, H_2O)). ^{1}H NMR (D_2O, 300 MHz): δ 4.55 (d, J = 9.1 Hz, 1H), 4.36 (dd, J = 8.5, 5.1 Hz, 1H), 4.22 (t, J = 8.8 Hz, 1H), 3.97 (dd, J = 5.1, 1.4 Hz, 1H), 3.75 (m, 1H), 3.73−3.62 (m, 2H), 3.60 (m, 1H). ^{13}C NMR (D_2O, 75 MHz): δ 176.2, 81.9, 74.0, 73.9, 70.1, 70.1, 69.3, 63.0.

***tert*-Butyl D-*glycero*-D-*galacto*-Heptonate (14).** R_f = 0.43 ($CHCl_3$/MeOH = 3:1). The product precipitated directly during the dihydroxylation reaction when using acetone as the solvent. Mp: 175−177 °C (H_2O). $[\alpha]_D$: −7.91 (*c* 1, MeOH). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 4.21 (bs, 1H), 3.83−3.38 (m, 6H), 1.37 (s, 9H). ^{13}C NMR (DMSO-d_6 + 1% D_2O, 75 MHz): δ 174.5, 83.6, 72.3, 72.1, 71.9, 70.0, 69.2, 64.5, 28.8 (3C). Anal. Calcd for $C_{11}H_{22}O_8$: C, 46.80; H, 7.86. Found: C, 46.48; H, 7.74.

D-*glycero*-D-*galacto*-Heptono-1,4-lactone (15). R_f = 0.33 ($CHCl_3$/MeOH = 3:1). Mp: 145−147 °C (EtOH). $[\alpha]_D$: −72.3 (*c* 2, H_2O) (lit.[14] mp 149−151 °C (EtOH); $[\alpha]_D$ −74.2 (*c* 2, H_2O)). ^{1}H NMR (D_2O, 300 MHz): δ 4.57 (d, J = 9.2 Hz, 1H), 4.48 (d, J = 8.6 Hz, 1H), 4.33 (dd, J = 9.2, 8.6 Hz, 1H), 3.79 (bd, J = 10.9 Hz, 1H), 3.73−3.58 (m, 3H). ^{13}C NMR (D_2O, 75 MHz): δ 176.2, 79.6, 74.0, 72.7, 70.9, 67.6, 63.1.

***tert*-Butyl D-*glycero*-L-*galacto*-Heptonate (16).** R_f = 0.42 ($CHCl_3$/MeOH = 3:1). Mp: 130−132 °C (EtOH). $[\alpha]_D$: +2.5 (*c* 1, H_2O). ^{1}H NMR (DMSO-d_6 + 1% D_2O, 300 MHz): δ 4.15 (d, J = 1.7 Hz, 1H), 3.72 (dd, J = 9.5, 1.6 Hz, 1H), 3.54 (dd, J = 10.5, 5.0 Hz, 1H), 3.52−3.38 (m, 3H), 3.34 (dd, J = 11.0, 5.9 Hz, 1H), 1.39 (s, 9H). Anal. Calcd for $C_{11}H_{22}O_8$: C, 46.80; H, 7.86. Found: C, 46.35; H, 7.71.

Barium D-*glycero*-L-*galacto*-Heptonate (17). R_f = 0.02 ($CHCl_3$/MeOH = 3:1). $[\alpha]_D$: +1.4 (*c* 1, H_2O) (lit.[15] $[\alpha]^{20}_D$ +1.5 (*c* 3, H_2O)). ^{1}H NMR (D_2O, 300 MHz): δ 4.32 (d, J = 1.7 Hz, 1H), 4.01 (dd, J = 9.2, 1.6 Hz, 1H), 3.92−3.87 (m, 2H), 3.81−3.74 (m, 2H), 3.66 (m, 1H). ^{13}C NMR (D_2O, 75 MHz): δ 180.2, 73.5, 72.1, 72.1, 71.1, 69.9, 62.8.

D-*arabino*-L-*galacto*-Nonono-1,4-lactone (18). R_f = 0.04 ($CHCl_3$/MeOH = 2:1). Mp: 174−176 °C (EtOH/H_2O). $[\alpha]_D$: −37.5 (c 0.5, H_2O) (lit.[16] mp 175−177 °C (EtOH). $[\alpha]^{20}_D$: −41.0 (*c* 10, H_2O)). ^{1}H NMR (D_2O, 300 MHz): δ 4.55 (d, J = 11.5 Hz, 1H), 4.20 (dd, J = 7.0, 14.2 Hz, 1H), 4.02 (d, J = 10.0 Hz, 1H), 3.96−3.52 (m, 6H). ^{13}C NMR (D_2O, 75 MHz): δ 175.3, 79.9, 71.5, 71.3, 71.2, 69.6, 68.6, 68.2, 63.5.

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