

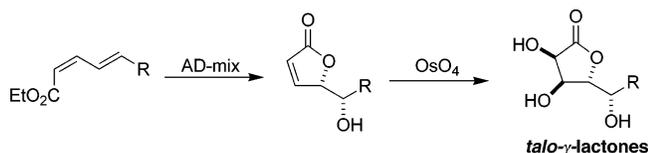
De Novo Asymmetric Syntheses of D- and L-Talose via an Iterative Dihydroxylation of Dienoates

Md. Moinuddin Ahmed and George A. O'Doherty\*

Department of Chemistry, West Virginia University,  
Morgantown, West Virginia 26506

george.odoherty@mail.wvu.edu

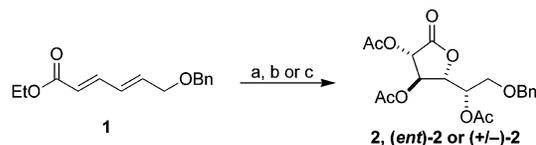
Received July 16, 2005



A short and highly efficient route to D- and L-talo- $\gamma$ -lactones has been developed. The key transformation was the sequential osmium-catalyzed bis-dihydroxylation reaction of substituted 2,4-dienoates. When the first dihydroxylation reaction is performed on (2*Z*,4*E*)-dienoates with use of the Sharpless AD-mix procedure, a regio- and enantioselective dihydroxylation resulted along with an in situ lactonization. A subsequent dihydroxylation, using OsO<sub>4</sub>/NMO in MeOH conditions, resulted in an exceedingly diastereo- and enantioselective synthesis of talo- $\gamma$ -lactone.

In response to the growing importance carbohydrate structures play in biology,<sup>1</sup> considerable efforts have been made to develop new synthetic routes to monosaccharides. This need in particular is driven by medicinal chemist's desire for unnatural sugar analogues for structure activity relationship studies. For the unnatural sugars in particular, there has been a growing interest in preparing these carbohydrates from achiral starting material, using enantioselective catalysis to set the asymmetry (de novo synthesis). This interest in de novo approach to the hexoses goes back to the seminal work of Sharpless and Masamune.<sup>2</sup> More recently this challenge has been taken up by MacMillan (iterative aldol strategy)<sup>3</sup> and us (both an Achmatowicz<sup>4</sup> and an iterative

SCHEME 1. 1- to 3-Step Stereoselective Synthesis of galacto- $\gamma$ -Lactone



- a: 1) 2% OsO<sub>4</sub>/4% (DHQD)<sub>2</sub>PHAL, K<sub>3</sub>Fe(CN)<sub>6</sub>/MeSO<sub>2</sub>NH<sub>2</sub>; 2) 10% OsO<sub>4</sub>/12% (DHQD)<sub>2</sub>PHAL, K<sub>3</sub>Fe(CN)<sub>6</sub>/MeSO<sub>2</sub>NH<sub>2</sub>; 3) Py•TsOH; 4) Ac<sub>2</sub>O/Py; 50% of **2**.  
 b: 1) 2% OsO<sub>4</sub>/4% (DHQD)<sub>2</sub>PHAL, K<sub>3</sub>Fe(CN)<sub>6</sub>/MeSO<sub>2</sub>NH<sub>2</sub>; 2) 10% OsO<sub>4</sub>/12% (DHQD)<sub>2</sub>PHAL, K<sub>3</sub>Fe(CN)<sub>6</sub>/MeSO<sub>2</sub>NH<sub>2</sub>; 3) Py•TsOH; 4) Ac<sub>2</sub>O/Py; 61% of (*ent*)-**2**.  
 c: 1) 2% OsO<sub>4</sub>/NMO; 2) Ac<sub>2</sub>O/Py; 71% of (+/-)-**2**.

dihydroxylation strategy<sup>5,6</sup>). In contrast to the diastereoselective aldol approach to hexoses of MacMillan and others, we investigated the possibility of using a diastereoselective osmium-catalyzed dihydroxylation approach to the hexoses (Scheme 1). These efforts resulted in our recently reported synthesis of galacto-sugars from simple achiral precursors with complete stereocontrol.<sup>5</sup> Our optimized procedure affords either D-galacto- $\gamma$ -lactone (conditions a, Scheme 1) or L-galacto- $\gamma$ -lactone (conditions b, Scheme 1) in three steps.<sup>7,8</sup> Alternatively, racemic galacto- $\gamma$ -lactone (conditions c, Scheme 1) can be prepared in only one step. Key to the success of these transformations is the in situ lactonization of the initially formed tetraol products. The in situ lactonization along with peracylation significantly aid in isolation of the galacto-lactones **2**.

Herein, we present the expansion this iterative dihydroxylation strategy to the talo- $\gamma$ -lactones using the Sharpless dihydroxylation for enantiocontrol.<sup>9</sup> These studies resulted in a three-step synthesis of talo- $\gamma$ -lactones, which are amenable to various C-6 substituents.

Conceptually a bis-dihydroxylation reaction, which installs a hydroxyl group at every carbon atom, appears to be an ideal method for an efficient carbohydrate synthesis. In practice, however, there were issues associated with regioselectivity (which double bond reacts first), enantioselectivity (the facial selectivity of the first dihydroxylation) and double diastereoselectivity (a balance between substrate and catalyst stereocontrol).<sup>10,11</sup> The solution to these problems emerged from our continuing study of the Sharpless dihydroxylation of di- and

(1) (a) Ernst, B.; Hart, G. W.; Sinay, P., Eds. *Carbohydrates in Chemistry and Biology*; Wiley-VCH: New York, 2000. (b) Wong, P. G.; Bertozzi, C. P., Eds. *Glycochemistry. Principles, Synthesis and Applications*; Marcel Dekker Inc.: New York, 2001. (c) Vogel, P. In *Glycoscience*; Fraser-Reid, B. O., Tatsuta, K., Thiem, J., Eds.; Springer: Berlin, Germany, 2001; Vol. 2, pp 1023–1174.

(2) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A.; Sharpless, K. B. *Science* **1983**, *220*, 949–951.

(3) Northrup, A. B.; MacMillan, D. W. C. *Science* **2004**, *305*, 1752–1755.

(4) An Achmatowicz reaction is the oxidative rearrangement of furfuryl alcohols to 2-substituted 6-hydroxy-2H-pyran-3(6H)-ones. For examples of its use in de novo carbohydrate synthesis see: (a) Harris, J. M.; Keranen, M. D.; O'Doherty, G. A. *J. Org. Chem.* **1999**, *64*, 2982–2983. (b) Harris, J. M.; Keranen, M. D.; Nguyen, H.; Young, V. G.; O'Doherty, G. A. *Carbohydr. Res.* **2000**, *328*, 17–36. (c) Babu, R. S.; O'Doherty, G. A. *J. Am. Chem. Soc.* **2003**, *125*, 12406–12407. For its use in oligosaccharide synthesis see: (d) Babu, R. S.; Zhou, M.; O'Doherty, G. A. *J. Am. Chem. Soc.* **2004**, *126*, 3428–3429.

(5) (a) Ahmed, Md. M.; O'Doherty, G. A. *Tetrahedron Lett.* **2005**, *46*, 3015–3019. (b) Ahmed, Md. M.; Berry, B. P.; Hunter, T. J.; Tomcik, D. J.; O'Doherty, G. A. *Org. Lett.* **2005**, *7*, 745–748.

(6) For its application in synthesis, see: (a) Ahmed, Md. M.; O'Doherty, G. A. *Tetrahedron Lett.* **2005**, *46*, 4151–4155. (b) Gao, D.; O'Doherty, G. A. *Org. Lett.* **2005**, *7*, 1069–1072.

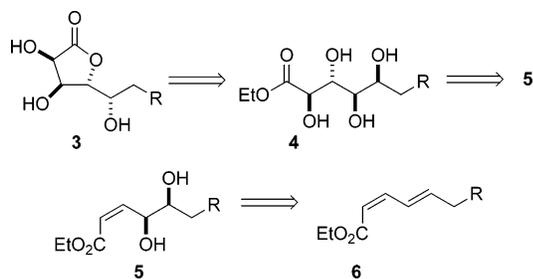
(7) Although it is a rare sugar, L-galacto- $\gamma$ -lactone is a naturally occurring metabolite produced in plants as an intermediate in the biosynthesis of vitamin C, see: Smirnov, N. *Nat. Biotechnol.* **2003**, *21*, 134–136.

(8) It has been suggested that the level of the important antioxidant ascorbic acid can be increased by treatment with L-galacto- $\gamma$ -lactone, see: Smirnov, N. *Philos. Trans. R. Soc. London* **2001**, *335*, 1455–1464.

(9) (a) Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570–7571. (b) Heinrich, B.; Marcos, S. A.; Sharpless, K. B. *Tetrahedron* **1995**, *51*, 1345–76.

(10) Masamune, S.; Choy, W.; Petersen, J.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1–76.

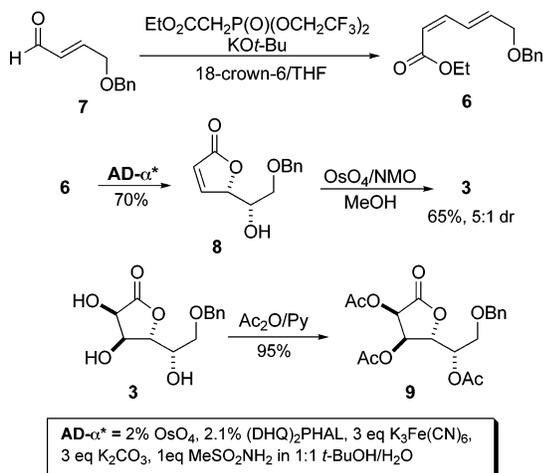
(11) Morikawa, K.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 5575–5578.

SCHEME 2. Retrosynthesis of *talo*- $\gamma$ -Lactones

trienoates.<sup>12,13</sup> As with the *galacto*-lactones, we planned to establish the C-2 to C-5 tetrol stereochemistry of the *talo*-lactones from (*Z,E*)-dienoates (i.e., **3** from **6**, Scheme 2).<sup>14</sup> These (*Z,E*)-dienoates were easily prepared by a Still–Gennari olefination of 4-substituted crotyl aldehydes.<sup>15</sup> Once again we targeted the  $\gamma$ -lactone **3**, for ease of isolation (Scheme 2).<sup>5</sup>

Encouraged by our success with the de novo synthesis of *galacto*-lactones **2**, we decided to next examine the possibility of an iterative dihydroxylation on a double bond isomer for the preparation of sugar stereoisomers. Because the Sharpless dihydroxylation occurs with greater selectivity for trans double bonds, we selected (*2Z,4E*)-dienoate **6** to study.<sup>14</sup> To our surprise, when diennoate **6** was dihydroxylated neither diol **5** nor tetrol **4** was detected, instead a concomitant lactonization reaction also occurred.

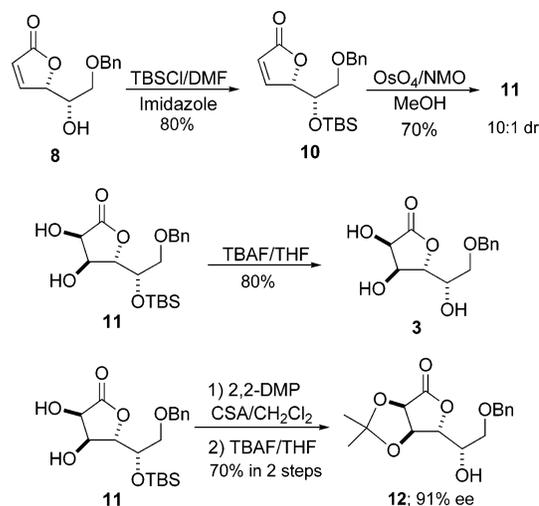
In practice, the diennoate **6** was prepared by treating a THF solution of crotyl aldehyde **7** with both EtO<sub>2</sub>CCH<sub>2</sub>P(O)(OCH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub> and KO*t*-Bu in the presence of excess 18-crown-6 (Scheme 3). This procedure reliably prepared diennoate **6** in both excellent yield (95%) and double bond stereoselectivity (12:1 *Z/E*-ratio). Exposing

SCHEME 3. Two-Step Highly Enantio- and Diastereoselective Synthesis of *talo*- $\gamma$ -Lactone

(12) Zhang, Y.; O'Doherty, G. A. *Tetrahedron* **2005**, *61*, 6337–6351.  
 (13) (a) Smith, C. M.; O'Doherty, G. A. *Org. Lett.* **2003**, *5*, 1959–1962. (b) Hunter, T. J.; O'Doherty, G. A. *Org. Lett.* **2002**, *4*, 4447–4450.

(14) Thus the order of double bond reactivity in diennoate **6** is controlled by taking advantage of the differing electronic nature of the two double bonds, along with the preference for the AD-mix reagent system to react with trans olefins, see ref 9.

(15) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408.

SCHEME 4. Four-Step Synthesis of *talo*- $\gamma$ -Lactone

(*2Z,4E*)-dienoate **6** to the typical Sharpless AD-mix procedure (2% OsO<sub>4</sub>/2.1% (DHQ)<sub>2</sub>PHAL, 3 equiv of K<sub>3</sub>Fe(CN)<sub>6</sub>/K<sub>2</sub>CO<sub>3</sub>, 1 equiv of MeSO<sub>2</sub>NH<sub>2</sub>)<sup>9</sup> afforded lactone **8** in good yield (70%) and enantiomeric excess (90% ee). When the lactone **8** was further dihydroxylated under ligandless conditions (OsO<sub>4</sub>/NMO in MeOH), the *talo*- $\gamma$ -lactone **3** was produced in good yield (65%, 5:1 dr). As with the *galacto*-lactones (cf. Scheme 1), the triol **3** was per-acetylated giving **9** in an excellent yield (95%).

We next looked to improve the diastereoselectivity of the second dihydroxylation in the sequence by making the alcohol of **8** more sterically hindered (Scheme 4). To these ends, we protected the alcohol with TBSCl, affording **10** in good yield (80%). When the TBS-protected alcohol **10** was exposed to the same dihydroxylation conditions improved diastereoselectivity was observed (10:1 instead of 5:1). The *talo*-lactone **11** was isolated in good yield (70%). To prove the stereochemistry the lactone **11** was deprotected with TBAF to afford the identical *talo*- $\gamma$ -lactone **3** in good yield (80%).

To perform a Mosher ester analysis, the diol **11** was protected as the acetonide and the TBS group was deprotected to give the alcohol **12** in good yield (70% for 2 steps). Conversion of **12** to the corresponding Mosher esters followed by NMR analysis indicated that **12** was formed in 91% ee. The *talo*-stereochemistry of **12** was assigned by a series of nOe experiments (see the Supporting Information). Finally, this procedure was also used to produce the enantiomer of **3** (*D-talo*- $\gamma$ -lactone) in similar overall yield and enantiopurity (43% and 93% ee), by simply switching to the (DHQD)<sub>2</sub>PHAL ligand system in the initial dihydroxylation.

In conclusion, our strategy for the synthesis of either enantiomer of *talo*-sugars provides rapid and practical access to important sugars, which should be of further use for oligosaccharide synthesis. In contrast to the recently reported enantioselective aldol approach<sup>3</sup> to hexoses, which uses a change in aldol mechanism to prepare stereoisomers, this approach can be used to prepare either *galacto*- or *talo*-sugars by simply changing the diennoate double bond geometry. Thus, by simply changing one of the double bond geometries, optically pure **3** was prepared in two steps from (*2Z,4E*)-dienoate **8** (45% overall yield).

Experimental Section<sup>16</sup>

**(2Z,4E)-Ethyl 6-(Benzyloxy)hexa-2,4-dienoate (6).** A solution of  $(\text{CF}_3\text{CH}_2\text{O})_2\text{P}(\text{O})\text{CH}_2\text{CO}_2\text{CH}_2\text{CH}_3$  (3 g, 9.0 mmol) and 18-crown-6 (7.1 g, 27.0 mmol) in THF (60 mL) was cooled to  $-78^\circ\text{C}$  and treated with *t*-BuOK (1.2 g, 10.8 mmol). After the mixture was stirred for 15 min, a solution of the aldehyde **7** (1.6 g, 9.1 mmol) in THF (10 mL, plus 5 mL of rinse) was added by cannula. The resulting mixture was stirred at  $-78^\circ\text{C}$  for 2.5 h, the reaction mixture was quenched by the addition of saturated aqueous  $\text{NH}_4\text{Cl}$ , and the bulk of THF was removed under reduced pressure. The residue was extracted with ether ( $3 \times 30$  mL) and the organic extracts were washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and concentrated. The crude product was purified by flash chromatography on silica gel (25:1 (v/v) hexane/EtOAc) to yield (2Z,4E)-ethyl 6-(benzyloxy)hexa-2,4-dienoate **6** (2.1 g, 12:1 *Z/E* ratio, 95% yield) as a viscous oil. Major isomer **6**:  $R_f$  (30% EtOAc/hexanes) 0.6; IR (thin film,  $\text{cm}^{-1}$ ) 2983, 2928, 2872, 1766, 1650, 1620, 1496, 1454, 1436, 1362, 1268, 1141, 1073, 1029, 953;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.58 (dddd,  $J = 15.6, 11.4, 1.2, 1.2$  Hz, 1H), 7.33 (m, 5H), 6.59 (dd,  $J = 11.4, 11.4$  Hz, 1H), 6.12 (ddd,  $J = 15.6, 6, 6$  Hz, 1H), 5.68 (d,  $J = 11.4$  Hz, 1H), 4.54 (br s, 2H), 4.20 (q,  $J = 7.2$  Hz, 2H), 4.17 (d,  $J = 6$  Hz, 1H), 4.16 (d,  $J = 6$  Hz, 1H), 1.30 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  166.2, 143.6, 139.3, 137.9, 128.4 (2C), 128.1, 127.7 (2C), 127.6, 118.1, 72.5, 70.0, 60.0, 14.2; CIHRMS calcd for  $[\text{C}_{15}\text{H}_{18}\text{O}_3 + \text{Na}]^+$  269.2914, found 269.2917.

**(S)-5-((S)-2'-(Benzyloxy)-1'-hydroxyethyl)furan-2(5H)-one (8).** Into a 100-mL round-bottom flask was added 20 mL of *t*-BuOH, 20 mL of water,  $\text{K}_3\text{Fe}(\text{CN})_6$  (9.6 g, 29 mmol),  $\text{K}_2\text{CO}_3$  (4.03 g, 29 mmol),  $\text{MeSO}_2\text{NH}_2$  (0.93 g, 9.7 mmol),  $(\text{DHQ})_2\text{PHAL}$  (158 mg, 0.2 mmol, 2.1 mol %), and  $\text{OsO}_4$  (49 mg, 0.19 mmol, 2 mol %). The mixture was stirred at room temperature for about 15 min and then cooled to  $0^\circ\text{C}$ . To this solution was added (2Z,4E)-ethyl 6-(benzyloxy)hexa-2,4-dienoate (**6**) (2.4 g, 9.7 mmol) and the reaction was stirred vigorously at  $0^\circ\text{C}$  overnight. The reaction was quenched with solid sodium sulfite (100 mg) at room temperature. Ethyl acetate (30 mL) was added to the reaction mixture, and after separation of the layers, the aqueous phase was further extracted with the organic solvent ( $2 \times 20$  mL). The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. After removal of the solvents in vacuo, flash chromatography on silica gel (7:3 (v/v) hexanes/EtOAc) afforded 1.6 g (70% yield) of (S)-5-((S)-2'-(benzyloxy)-1'-hydroxyethyl)furan-2(5H)-one (**8**) as a white solid: mp  $74\text{--}75^\circ\text{C}$ ;  $R_f$  (50% EtOAc/hexanes) 0.16;  $[\alpha]_D^{25} -52.33$  (c 1.2,  $\text{CH}_2\text{Cl}_2$ ); IR (thin film,  $\text{cm}^{-1}$ ) 3424, 2927, 2899, 1745, 1602, 1500, 1475, 1454, 1399, 1365, 1340, 1266, 1217, 1167, 1096, 1072, 993, 913  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.47 (dd,  $J = 6, 1.2$  Hz, 1H), 7.33 (m, 5H), 6.14 (dd,  $J = 6, 1.8$  Hz, 1H), 5.16 (ddd,  $J = 4.2, 1.8, 1.8$  Hz, 1H), 4.58 (d,  $J = 12$  Hz, 1H), 4.54 (d,  $J = 12$  Hz, 1H), 4.01 (dddd,  $J = 6, 5.4, 4.8, 4.2$  Hz, 1H), 3.64 (dd,  $J = 9.6, 5.4$  Hz, 1H), 3.58 (dd,  $J = 9.6, 5.4$  Hz, 1H), 2.42 (d,  $J = 6$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  172.9, 153.8, 137.2, 128.5 (2C), 128.0, 127.8 (2C), 122.2, 83.7, 73.6, 70.2, 70.0; CIHRMS calcd for  $[\text{C}_{13}\text{H}_{14}\text{O}_4 + \text{Na}]^+$  257.0784, found 257.0782; the COSY spectral analysis confirmed the formation of  $\gamma$ -lactone.

**(3R,4S,5R)-5-((S)-2'-(Benzyloxy)-1'-hydroxyethyl)-3,4-dihydroxydihydrofuran-2(3H)-one (3).** Into a 25-mL round-

bottom flask was added (S)-5-((S)-2'-(benzyloxy)-1'-hydroxyethyl)furan-2(5H)-one (**8**) (100 mg, 0.42 mmol) and 1 mL of MeOH and then the mixture was cooled to  $0^\circ\text{C}$ . To this solution were added 0.3 mL of 50% NMO in  $\text{H}_2\text{O}$  (1.28 mmol) and  $\text{OsO}_4$  (2.1 mg,  $8 \mu\text{mol}$ , 2 mol %) and the reaction was stirred vigorously at  $0^\circ\text{C}$  overnight. The reaction was quenched with solid sodium sulfite (150 mg) at room temperature. Then the reaction mixture was filtered through a pad of Celite/florisil and eluted with 20 mL of 50% ethyl acetate/MeOH. The combined organic layers were dried over anhydrous sodium sulfate. Removal of the solvents in vacuo and flash chromatography on silica gel (1:9 (v/v) MeOH/EtOAc) afforded (3R,4S,5R)-5-((S)-2'-(benzyloxy)-1'-hydroxyethyl)-3,4-dihydroxydihydrofuran-2(3H)-one (**3**) (74 mg, 5:1 dr, 65% yield) as a viscous oil.  $R_f$  (2% MeOH/EtOAc) 0.14;  $[\alpha]_D^{25} 41.2$  (c 1.1, MeOH); IR (thin film,  $\text{cm}^{-1}$ ) 3396, 2928, 2874, 1779, 1455, 1366, 1316, 1215, 1179, 1092, 1027, 978, 905;  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ , 600 MHz)  $\delta$  7.37 (m, 5H), 4.67 (d,  $J = 6$  Hz, 1H), 4.61 (s, 2H), 4.52 (d,  $J = 1.8$  Hz, 1H), 4.38 (dd,  $J = 6, 0.6$  Hz, 1H), 4.02 (ddd,  $J = 7.2, 6.6, 1.8$  Hz, 1H), 3.60 (dd,  $J = 9, 7.2$  Hz, 1H), 3.56 (dd,  $J = 9, 6.6$  Hz, 1H), 3.76 (br s, 3H);  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ , 150 MHz)  $\delta$  178.9, 139.6, 129.5 (2C), 129.0, 128.9 (2C), 86.9, 74.5, 72.0, 71.7, 70.3, 70.2; CIHRMS calcd for  $[\text{C}_{13}\text{H}_{16}\text{O}_6 + \text{Na}]^+$  291.0839, found 291.0830.

**(3R,4S,5R)-5-((S)-2'-(Benzyloxy)-1'-acetoxyethyl)-3,4-diacetoxydihydrofuran-2(3H)-one (9).** To a solution of (3R,4S,5R)-5-((S)-2'-(benzyloxy)-1'-hydroxyethyl)dihydro-3,4-dihydroxyfuran-2(3H)-one (**3**) (50 mg, 0.18 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) was added excess  $\text{Ac}_2\text{O}$  (80  $\mu\text{L}$ , 0.74 mmol), pyridine (120  $\mu\text{L}$ , 1.5 mmol), and a catalytic amount of DMAP (1.1 mg, 5 mol %). The reaction was stirred for 6 h, after which 5 mL of ether and 5 mL of  $\text{NH}_4\text{Cl}$  were added to remove excess base. The organic layer was washed with 5 mL of  $\text{CuSO}_4$  solution and 5 mL of brine and the aqueous layer was further extracted with ether ( $3 \times 5$  mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (7:3 (v/v) hexane/EtOAc) to yield (3R,4S,5R)-5-((S)-2'-(benzyloxy)-1'-acetoxyethyl)-3,4-diacetoxydihydrofuran-2(3H)-one (**9**) (70 mg, 95% yield) as a viscous oil.  $R_f$  (40% EtOAc/hexanes) 0.3;  $[\alpha]_D^{25} 8.6$  (c 1.0,  $\text{CH}_2\text{Cl}_2$ ); IR (thin film,  $\text{cm}^{-1}$ ) 2953, 2922, 2876, 2863, 1808, 1749, 1373, 1234, 1179, 1100, 1069, 1044;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.33 (m, 5H), 5.69 (d,  $J = 6$  Hz, 1H), 5.39 (d,  $J = 6$  Hz, 1H), 5.27 (ddd,  $J = 7.8, 5.4, 3$  Hz, 1H), 4.86 (d,  $J = 3$  Hz, 1H), 4.57 (d,  $J = 12$  Hz, 1H), 4.54 (d,  $J = 12$  Hz, 1H), 3.65 (dd,  $J = 9.6, 5.4$  Hz, 1H), 3.60 (dd,  $J = 9.6, 7.8$  Hz, 1H), 2.14 (s, 3H), 2.13 (s, 3H), 2.11 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  170.2, 169.5, 169.3, 169.1, 137.2, 128.5 (2C), 128.0, 127.8 (2C), 80.7, 73.6, 70.3, 69.8, 66.4, 66.1, 20.8, 20.4, 20.1; CIHRMS calcd for  $[\text{C}_{19}\text{H}_{22}\text{O}_9 + \text{Na}]^+$  417.1156, found 417.1158.

**Acknowledgment.** We would like to thank Dirk Friedrich for his helpful discussions regarding the NMR assignment of the stereochemistry of **12**. We are grateful to NIH (GM63150) and NSF (CHE-0415469) for support of our research program and NSF-EPSCoR (0314742) for the 600-MHz NMR at WVU.

**Supporting Information Available:** Complete experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO051476+

(16) Only the procedures for our initial preparation of *talo*-sugar **9** are presented in the Experimental Section (Scheme 3). Complete experimental procedures and spectral data for all new compounds (Schemes 3 and 4) are presented in the Supporting Information.