Synthesis and Reactions of 1,4-Anhydrogalactopyranose and 1,4-Anhydroarabinose – Steric and Electronic Limitations

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Scope and limitations of 1,4-anhydro sugars as precursors of glycofuranosyl building blocks are described. The experiments revealed that the choice of the substituents is very important for an efficient preparation as well as a successful ring-opening reaction of 1,4-anhydro sugars. DFT Calculations suggest that selective protonation of 1,4-anhydro sugars is the key to the selective ring opening in order to afford only furanosides.

Introduction. – Various types of anhydro sugars have been investigated as monomer units to create synthetic polysaccharides, as building blocks for oligosaccharide synthesis, and as precursors *en route* to building blocks [1]. 1,2-Anhydro sugars are the basis of oligosaccharide synthesis by the glycal assembly approach [2]. Moreover, 1,2-anhydro sugars are useful not only as building blocks for oligosaccharide synthesis, but also as precursors of common oligosaccharide building blocks including thioglycosides, pent-4-enyl glycosides, and glycosyl phosphates [3].

Due to their high reactivity 1,2-anhydro sugars are usually generated *in situ* and used without isolation (*Fig. 1*). By contrast, 1,4-anhydro sugars and 1,6-anhydro sugars are stable enough to be isolated. Thus, the ring-opening reactions of these anhydro sugars have been extensively investigated. In the case of 1,6-anhydro sugars, the 1,6-ether bond is cleaved selectively, and pyranosides are obtained by hydrolysis, acetolysis, and alcoholysis. 1,4-Anhydro sugars, on the other hand, are known to give furanosides by acid-mediated reaction with nucleophiles and under ring-opening conditions polymerization [4].

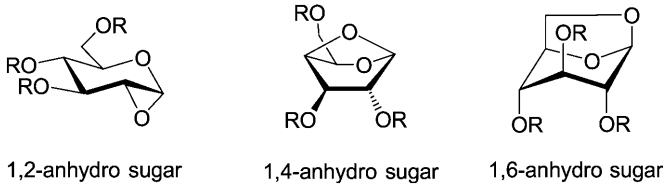


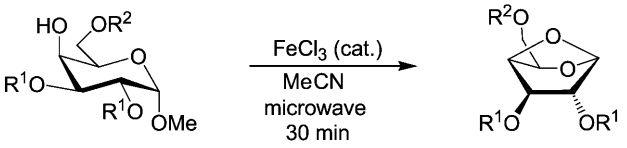
Fig. 1. *Representative structures of anhydro sugars*

We set out to explore whether 1,4-anhydro sugars are useful precursors of glycofuranoside building blocks for oligofuranoside synthesis. Oligofuranosides are of particular interest as they constitute a major part of mycolyl-arabinogalactan (AG), a compo-

nent of the mycobacterial cell wall [5]. Here, we discuss substituent effects on the formation and ring opening of 1,4-anhydro galactoses and 1,4-anhydro arabinoses.

Results and Discussion. – To investigate the suitability of 1,4-anhydro sugars as building blocks for oligosaccharide synthesis, we prepared 1,4-anhydrogalactopyranoses **2a**–**2c** from galactopyranosides **1a**–**1c** (*Scheme 1*) [6]. The $FeCl_3$-catalyzed reaction to form 1,4-anhydrogalactose was accelerated significantly by microwave irradiation, although the yields did not improve over conventional heating. The starting galactopyranoside was consumed within 30 min by microwave irradiation, while the same reaction takes several days with conventional heating. Anhydro sugars bearing a benzoyl (Bz) group instead of a benzyl (Bn) group were synthesized to test whether neighboring group participation of the 2-*O*-Bz group allows for control of the configuration at the anomeric position. Unfortunately, the electron-withdrawing nature of the Bz group suppressed the formation of 1,4-anhydro sugars **2b** dramatically. The nucleophilicity of the OH group at C(4) is decreased as well as the capability of MeO to act as a leaving group. Bulky protecting groups such as the (*t*-Bu)Me_2Si (TBS) group also resulted in a significant reduction of the yield as observed for anhydro sugar **2c**.

Scheme 1. *Synthesis of 1,4-Anhydrogalactoses* **2a**–**2c**

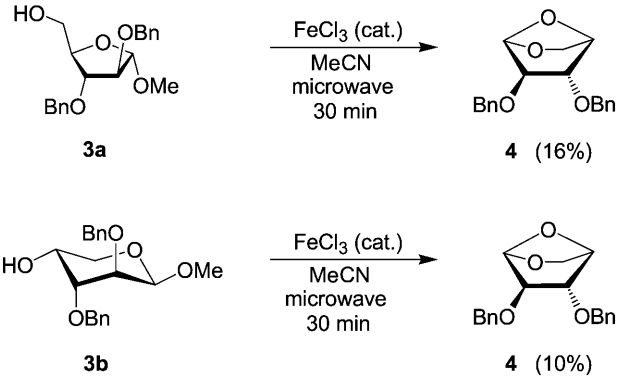


1a	(R^1 = Bn, R^2 = Bn)	**2a** (51%)
1b	(R^1 = Bz, R^2 = Bn)	**2b** (12%)
1c	(R^1 = Bn, R^2 = TBS)	**2c** (25%)

1,4-Anhydro-D-arabinopyranose **4** was prepared according to the method developed for 1,4-anhydro-D-galactopyranose **2**, starting from arabinofuranoside **3a** and arabinopyranoside **3b** (*Scheme 2*). In both cases, the monomers were obtained in poor yield (16 and 10%, resp.), while a series of oligoarabinosides was obtained as major products. The oligoarabinosides were less than five-units-long as determined by mass-spectrometric analysis. All attempts to identify conditions that would suppress the undesired formation of oligoarabinosides failed. The *Lewis* acid $FeCl_3$ favors not only the formation of anhydro sugars, but also initiates the ring opening of the bicyclic system to create oligomeric structures.

Reaction of 1,4-anhydrogalactopyranose **2a** with alcohols in the presence of trifluoromethanesulfonic acid (TfOH) or camphorsulfonic acid (CSA) was examined (*Table*). Various alcohols afforded the corresponding galactofuranose products that are useful as building blocks for oligosaccharide synthesis. When the reaction was performed in the presence of MeOH, methyl galactofuranoside **5a** was obtained as a 1:2 mixture of α- and β-isomers (*Entry 1*). Reaction with allylic alcohol and subsequent allylation gave allyl galactofuranoside **5b** with better stereoselectivity (*Entry 2*). Galactofuranoside **5b** is useful for the synthesis of galactofuranosyl galactofuranose units as

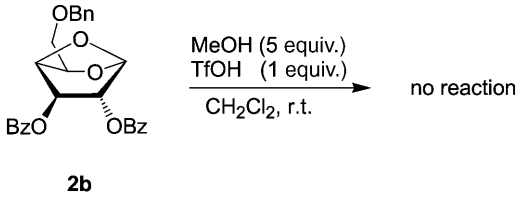
Scheme 2. *Synthesis of 1,4-Anhydroarabinose*



reported by *Ogawa* and co-workers [7]. Pentenyl galactofuranoside **5c** was prepared, when pent-4-en-1-ol was employed (*Entry 3*). Octan-1-ol gave octyl galactofuranoside **5d** in the presence of CSA (*Entry 4*). CSA proved to be superior in this reaction to TfOH that afforded a highly complex mixture. When octyl 2,3,5-tri-*O*-benzyl-β-D-galactofuranoside was used as an acceptor, (1 $\rightarrow$ 6)-linked galactofuranosyl disaccharide **5e** was obtained as a difficult-to-separate mixture of α- and β-isomers in the presence of CSA instead of TfOH (*Entry 5*). Disaccharide **5e** is one of the repeating units in the *Mycobacterium tuberculosis* galactan [8]. These results suggest that TfOH is a strong-enough acid to degrade the octyl galactofuranoside.

Next, we introduced a benzoate group at the 2-*O* position in order to control the configuration at the anomeric position. Unfortunately, the reaction of 1,4-anhydro-2,3-di-*O*-benzoylgalactofuranose **2b** did not afford any furanoside, and starting material was recovered without degradation (*Scheme 3*). This result indicates that the electron-withdrawing nature of benzoate protecting groups decreases the electron density of the 4-O-atom significantly. Thus, selective protonation of the 4-O atom did not occur.

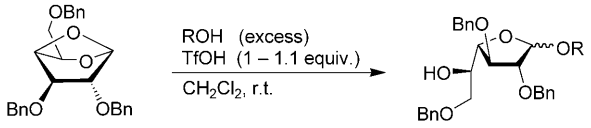
Scheme 3. *The Ring Opening of 1,4-Anhydrogalactose Bearing Benzoyl Groups*



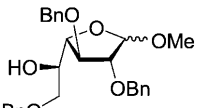
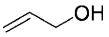
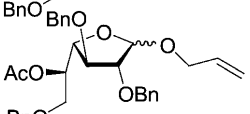
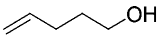
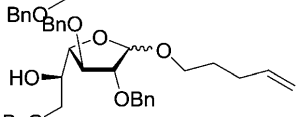
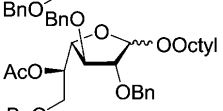
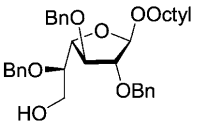
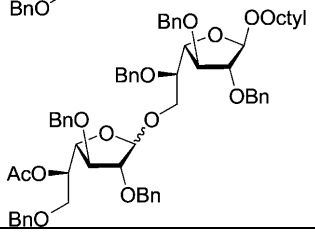
1,4-Anhydroarabinose **4** gave only arabinofuranoside in good yield when MeOH was used as a nucleophile in the presence of TfOH (*Scheme 4*) [9]. Although the high reactivity of 1,4-anhydroarabinose **4** makes its preparation very difficult as mentioned before, 1,4-anhydroarabinose is a potentially promising precursor for arabinofuranoside building blocks.

Our experiments revealed only furanose products in the acid-initiated ring-opening reactions of our 1,4-anhydro sugars. In principal, two different reaction pathways can be envisioned (*Fig. 2*, *A* and *B*). To achieve a better understanding of this system,

Table. *The Ring Opening of 1,4-Anhydrogalactose with Alcoholic Nucleophiles*



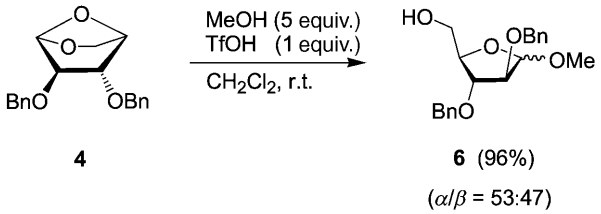
2a **5a – 5e**

Entry	Nucleophile	Product		Yield [%]	Selectivity α/β
1	MeOH		**5a**	74	32:68
2			**5b**	78	20:80
3			**5c**	81	45:55
4[a])	$C_8H_{17}OH$		**5d**	44	47:53
5[a])			**5e**	59	26:74

[a]) CSA (3 equiv.)

model calculations on a simple unsubstituted bicyclic compound were performed. For this purpose, we selected 2,7-dioxabicyclo[2.2.1]heptane as the core structure of 1,4-anhydro sugars [10]. Geometry optimization was carried out using density functional theory (DFT; B3LYP/6-311G(d)) [11][12] and the Gaussian03 program package [13]. Frequency calculations ensured the stationarity of the optimized structures (NImag = 0). A natural bond orbital (NBO) analysis elucidated the relative contributions of s and p orbitals of the different lone pairs. No significant differences in s and p character were encountered. However, the NBO analysis revealed a significant overlap of one O-atom lone pair (n_O) with a low-lying σ^*(C–O) orbital that are collinear with each other (see *Fig. 2*, *bottom*). As a result, the energy of this lone pair as well as its basicity decreases. By the same token, the bond length *a* increases. For the lone pairs of the other O-atom, no such favorable arrangement of n_O and σ^*(C–O) exists.

Scheme 4. *The Ring Opening of 1,4-Anhydroarabinose*



4 **6** (96%)

(α/β = 53:47)

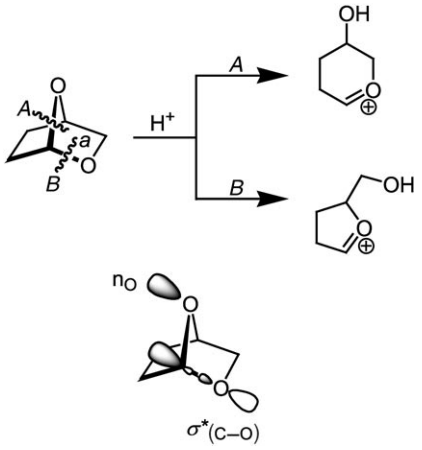


Fig. 2. *Two possibilities,* A *and* B*, for the ring opening of 1,4-Anhydro sugars*

Therefore, the pathway *B*, the protonation of the lower O-atom (5-O) and the ring opening to afford the five-membered ring is favored.

Other studies involving model compounds with OR substituents were also in line with this view. To corroborate the results of the NBO considerations, four different protonated isomers of the parent compound were elucidated. An immediate ring opening subsequent to the attack of the proton was set to be forbidden. *Fig. 3* shows the different protonated isomers and their *Hartree-Fock* (*HF*) energies, as well as their relative energies that are easily understood by the different basicity as discussed before. The protonation of 5-O-atom is the most favorable to afford the furanose as ring-opened product. Taking these significant energetic differences into a *Boltzmann* distribution at 300 K and assuming similar reactivity (similar activation barriers), only *ca.* 10% of the starting material should be converted to the pyranose. The substitution pattern does not influence this result significantly as selected model studies have shown. This simple theoretical view may explain why only furanoses were encountered as ring-opened products of 1,4-anhydro sugars.

Conclusions. – Here, we have shown the scope and limitations of 1,4-anhydro sugars as glycofuranosyl building blocks. Our experiments revealed that the choice of the substituents is very important for efficient synthesis as well as a successful ring opening of

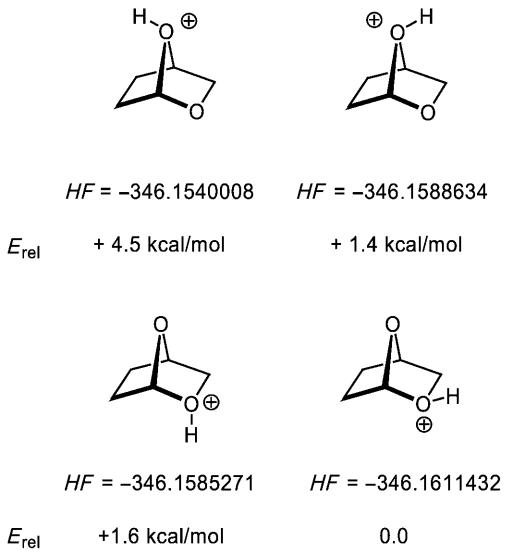


Fig. 3. *Different possibilities for the protonation of 1,4-anhydro sugars and their* HF *energies* [hartree] *and relative energies* [kcal/mol]

1,4-anhydro sugars. The use of microwaves as an alternative energy source decreased the reaction times for the $FeCl_3$-catalyzed formation of the 1,4-anhydrogalactose sugars significantly. In general, the use of electron-withdrawing and sterically demanding protecting groups such as (*t*-Bu)Me_2Si resulted in a significant decrease in yield. In contrast, Bn-substituted 1,4-anhydroarabinose proved to be extremely reactive in the ring-opening reaction. Little stereoselectivity was obtained in all cases. DFT Calculations suggest that different basicities of the corresponding O-atom lone pairs play a major role in selective protonation of 1,4-anhydro sugars. This behavior was assumed to be the key to the selective ring opening affording only furanoside structures.

We are grateful to ETH-Zürich, the *Alexander von Humboldt Foundation* (*Feodor Lynen Research Fellowship* to *D. B. W.*), and to the *Deutsche Forschungsgemeinschaft* (*Emmy Noether Fellowship* to *D. B. W.*) for generous support of this research. We would like to thank *CEM Corporation* for support of our microwave chemistry program.

Experimental Part

General. All chemicals used were reagent-grade and used as supplied except where noted. CH_2Cl_2 was purchased from *JT Baker* and purified by a *Cycle-Tainer Solvent Delivery System*. Pyridine and MeCN were refluxed over CaH_2 and distilled prior to use. Anal. TLC was performed on *E. Merck* silica-gel *60* F_{254} plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulfate ammonium molybdate soln., followed by heating. Liquid chromatography (LC) was performed using forced flow of the indicated solvent on *Sigma H*-type silica (10–40 mm). ^{1}H-NMR Spectra were obtained on *Varian VXR-300* (300 MHz) and *Varian Mercuryplus-400* (400 MHz) spectrometers, and are reported in ppm (δ) relative to $CHCl_3$ (7.26 ppm). Coupling constants (*J*) are reported in Hertz. ^{13}C-NMR Spectra were obtained on *Varian VXR-300* (75 MHz) and *Varian Mercuryplus-400* (100 MHz) spectrometers, and are reported in δ relative to $CDCl_3$ (77.0 ppm) as an internal reference. Microwave irradiations were performed by means of a monopod reactor (*Discover* from *CEM Corporation*) with focused microwaves.

General Procedure for the Preparation of 1,4-Anhydro Sugars by Microwave Chemistry. Galactopyranoside *i.e.*, (**1a**–**1c**) (0.1–0.4 mmol) and $FeCl_3$ (10–30%) were dissolved in MeCN (5 ml). Microwave heating was performed in a sealed tube for 30 min at 90°. The maximum power of microwave was set to 150 W, and the power was controlled during the heating to keep 90°. After microwave irradiation and cooling, the mixture was filtered over a short silica gel pad and concentrated. The crude product was purified by flash silica-gel column chromatography (FC) with mixtures of AcOEt and hexane as eluent.

*General Procedure for Ring Opening of 1,4-Anhydro Sugars: Pentenyl 2,3,6-Tri-*O*-benzyl-*D*-galactofuranoside* (**5c**). 1,4-Anhydrogalactose **2a** (135 mg, 0.31 mmol) and pent-4-en-1-ol (134 mg, 1.6 mmol) were dissolved in CH_2Cl_2 (3 ml) and cooled to 0°. After 10 min, TfOH (30 µl, 51 mg, 0.34 mmol) was added, then the soln. was allowed to warm slowly to r.t. The completion of the reaction was checked by TLC, then the mixture was neutralized with Et_3N and concentrated *in vacuo*. The residue was purified by FC (silica gel; AcOEt/hexane 2:5) to yield **5c** (130 mg, 81%) as a colorless syrup.

*Methyl 2,3-Di-*O*-benzoyl-6-*O*-benzyl-α-*D*-galactopyranoside* (**1b**). The selective ring-opening reaction of 4,6-O-benzylidene acetal was performed according to the method mentioned above. The ring opening of methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactopyranose (1.0 g, 2.0 mmol) afforded 0.73 g (72%) of **1b**. TLC (AcOEt/hexane 2:5): R_f 0.35. $[\alpha]_D = +109.0$ ($c = 2.4$, $CHCl_3$). IR ($CHCl_3$) 3008, 1721, 1452, 1281, 1107. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.01–7.97 (*m*, 4 H); 7.52–7.47 (*m*, 2 H); 7.38–7.32 (*m*, 9 H); 5.74–5.66 (*m*, 2 H); 5.22 (*d*, $J = 2.7$, 1 H); 4.64 (*d*, $J = 12.0$, 1 H); 4.59 (*d*, $J = 11.7$, 1 H); 4.45 (*s*, 1 H); 4.15 (*t*, $J = 4.5$, 1 H); 3.88–3.79 (*m*, 2 H); 3.43 (*s*, 3 H); 3.17–3.13 (*s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 166.3; 166.1; 137.7; 133.5; 133.4; 130.1; 129.7; 129.7; 128.8; 128.6; 128.6; 128.1; 128.0; 97.9; 74.1; 71.3; 70.3; 69.5; 69.3; 68.5, 55.8. HR-MALDI-MS: 515.1684 ($[M+Na]^+$, $C_{28}H_{28}NaO_8^+$, calc. 515.1682).

*1,4-Anhydro-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-*D*-galactopyranose* (**2b**). Compound **1b** (200 mg, 0.40 mmol) afforded 23 mg (12%) of **2b**. TLC (AcOEt/hexane 2:5): R_f 0.65. $[\alpha]_D = +159.0$ ($c = 1.8$, $CHCl_3$). IR ($CHCl_3$) 3032, 1722, 1271, 1113. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.10–8.05 (*m*, 4 H); 7.64–7.56 (*m*, 2 H); 7.49–7.43 (*m*, 4 H); 7.36–7.28 (*m*, 5 H); 5.95 (*d*, $J = 2.4$, 1 H); 5.17 (*d*, $J = 1.5$, 1 H); 5.12 (*m*, 1 H); 4.82 (*d*, $J = 1.5$, 1 H); 4.58 (*d*, $J = 12.0$, 1 H); 4.54 (*d*, $J = 12.0$, 1 H); 4.09 (*dd*, $J = 7.2$, 6.0, 1 H); 3.48 (*dd*, $J = 9.6$, 5.7, 1 H); 3.42 (*dd*, $J = 9.6$, 7.2, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 165.8; 165.7; 137.5; 133.4; 133.4; 129.8; 129.7; 129.0; 128.4; 128.3; 127.7; 127.7; 98.4; 81.6; 81.3; 77.2; 74.4; 73.6; 69.6. HR-MALDI-MS: 483.1420 ($[M+Na]^+$, $C_{27}H_{24}NaO_7^+$; calc. 483.1420).

*1,4-Anhydro-2,3-di-*O*-benzyl-6-*O*-[(*tert*-butyl)dimethylsilyl]-β-*D*-galactopyranose* (**2c**). *Methyl 2,3-di-*O*-benzyl-6-*O*-[(*tert*-butyl)dimethylsilyl]-α-*D*-galactopyranoside* (**1c**) (170 mg, 0.35 mmol) afforded 40 mg (25%) of **2c**. TLC (AcOEt/hexane 2:5): R_f 0.80. $[\alpha]_D = +42.8$ ($c = 1.2$, $CHCl_3$). IR ($CHCl_3$) 2930, 1454, 1256, 1109, 1007. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.40–7.31 (*m*, 10 H); 5.36 (*d*, $J = 4.2$, 1 H); 4.69 (*d*, $J = 11.4$, 1 H); 4.56 (*d*, $J = 11.7$, 1 H); 4.54 (*d*, $J = 11.7$, 1 H); 4.49 (*d*, $J = 12.0$, 1 H); 4.16–4.14 (*m*, 1 H); 4.09–4.02 (*m*, 1 H); 3.92 (*ddd*, $J = 10.8$, 6.0, 1.5, 1 H); 3.72 (*t*, $J = 10.8$, 1 H); 0.90 (*s*, 9 H); 0.12 (*s*, 3 H); 0.09 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 137.7; 137.5; 128.4; 128.4; 128.1; 128.0; 127.8; 127.7; 97.0; 85.5; 82.0; 81.0; 72.5; 71.3; 66.2; 63.4; 25.7; 17.9; −4.6; −4.6. HR-MALDI-MS: 479.2232 ($[M+Na]^+$, $C_{26}H_{36}NaO_5Si^+$; calc. 479.2230).

*1,4-Anhydro-2,3-di-*O*-benzyl-α-*D*-arabinopyranose* (**4**). *Methyl 2,3-di-*O*-benzyl-α-*D*-arabinopyranose* (**3a**; 112 mg, 0.32 mmol) afforded 16 mg (16%) of **4**. TLC (AcOEt/hexane 2:5): R_f 0.30. $[\alpha]_D = -65.1$ ($c = 1.6$, $CHCl_3$). IR ($CHCl_3$) 2900, 1725, 1454, 1115. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.38–7.31 (*m*, 10 H); 5.53 (*d*, $J = 2.4$, 1 H); 4.71 (*dd*, $J = 4.5$, 1.5, 1 H); 4.61 (*d*, $J = 11.7$, 1 H); 4.53 (*d*, $J = 11.7$, 1 H); 4.52 (*s*, 2 H); 3.86–3.84 (*m*, 1 H); 3.63 (*dd*, $J = 7.2$, 3.9, 1 H); 3.58 (*d*, $J = 7.2$, 1 H); 3.55 (*d*, $J = 1.5$, 1 H). ^{13}C-NMR (75 MHz, $CHCl_3$): 137.3; 128.4; 128.0; 127.9; 127.8; 127.8; 98.5; 87.4; 82.9; 80.0; 72.4; 71.0; 65.5. HR-MALDI-MS: 335.1261 ($[M+Na]^+$, $C_{19}H_{20}NaO_4^+$; calc. 335.1259).

*Methyl 2,3,6-Tri-*O*-benzyl-α-*D*-galactofuranoside* (**5aα**). The ring opening with MeOH (45 mg, 1.4 mmol) afforded 15 mg (24%) of **5aα** and 33 mg (50%) of **5aβ** (α/β 32:68). TLC (AcOEt/hexane 2:5): R_f 0.30 (**5aα**), 0.20 (**5aβ**). $[\alpha]_D = +22.4$ ($c = 2.0$, $CHCl_3$). IR ($CHCl_3$) 2928, 1453, 1364, 1108. ^{1}H-NMR (300 MHz, $CHCl_3$): 7.37–7.26 (*m*, 15 H); 4.72 (*d*, $J = 11.4$, 1 H); 4.70 (*d*, $J = 4.2$, 1 H); 4.62 (*s*, 2 H); 4.57 (*d*, $J = 11.4$, 1 H); 4.55 (*d*, $J = 12.3$, 1 H); 4.50 (*d*, $J = 12.0$, 1 H); 4.34 (*dd*, $J = 7.2$, 6.3, 2 H); 4.11–4.05 (*m*, 2 H); 3.81–3.75 (*m*, 1 H); 3.48 (*d*, $J = 6.0$, 1 H); 3.40 (*s*, 3 H); 2.79 (*d*, $J = 6.9$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 137.9; 137.8; 137.3; 128.4; 128.3; 128.2; 128.1; 128.0; 127.7; 127.7; 127.5; 101.8; 84.3; 81.5; 81.1; 73.3; 72.7; 72.5; 70.9; 55.9. HR-MALDI-MS: 487.2098 ($[M+Na]^+$; $C_{30}H_{34}NaO_7^+$; calc. 487.2097).

*Methyl 2,3,6-Tri-*O*-benzyl-β-*D*-galactofuranoside* (**5aβ**). $[\alpha]_D = -51.0$ ($c = 1.9$, $CHCl_3$). IR ($CHCl_3$) 2923, 1454, 1362, 1101, 1042. ^{1}H-NMR (300 MHz, $CHCl_3$): 7.36–7.26 (*m*, 15 H); 4.95 (*s*, 1 H); 4.60–4.46 (*m*, 6 H); 4.13 (*dd*, $J = 5.7$, 3.3, 2 H); 4.05 (*dd*, $J = 6.6$, 2.1, 1 H); 3.98 (*dd*, $J = 2.4$, 0.9, 1 H); 3.91 (*td*, $J = 6.0$, 3.6, 1 H);

3.55 (*d*, *J* = 5.7, 2 H); 3.37 (*s*, 3 H); 2.46 (*d*, *J* = 6.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 137.9; 137.5; 137.1; 128.3; 128.3; 128.3; 127.8; 127.7; 127.6; 107.2; 87.2; 83.1; 81.7; 73.4; 72.3; 71.8; 71.5; 70.1; 54.9. HR-MALDI-MS: 487.2091 ($[M+Na]^+$, $C_{30}H_{34}NaO_7^+$; calc. 487.2097).

Prop-2-enyl 5-O-*Acetyl-2,3,6-tri*-O-*benzyl-β*-D-*galactofuranoside* (**5b**). The ring opening with allylic alcohol (58 mg, 1.0 mmol) and the sequential protection at 5-*O* afforded 45 mg (78%) of **5b*α*** and **5b*β*** (*α*/*β* 20 : 80). TLC (AcOEt/texane 2 : 5): R_f 0.45 (**5b*α***), 0.50, (**5b*β***). Selected data for **5b*β***: ^{1}H-NMR (300 MHz, $CDCl_3$): 7.36–7.26 (*m*, 15 H); 5.97–5.84 (*m*, 1 H); 5.36 (*td*, *J* = 6.3, 3.6, 1 H); 5.29 (*ddd*, *J* = 17.4, 3.0, 1.5, 1 H); 5.18 (*ddd*, *J* = 10.8, 3.0, 1.2, 1 H); 5.09 (*s*, 1 H); 4.58–4.44 (*m*, 6 H); 4.24 (*dd*, *J* = 7.2, 3.6, 1 H); 4.18 (*ddt*, *J* = 12.9, 5.1, 1.5, 1 H); 4.03 (*dd*, *J* = 3.0, 1.8, 1 H); 3.96 (*ddt*, *J* = 12.6, 6.0, 1.5, 1 H); 3.84 (*dd*, *J* = 7.2, 3.0, 1 H); 3.64 (*d*, *J* = 6.0, 1 H); 2.02 (*s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.4; 137.9; 137.5; 137.4; 134.1; 128.4; 128.3; 128.0; 127.9; 127.8; 127.6; 127.5; 117.3; 105.1; 88.1; 83.0; 79.4; 73.0; 72.3; 72.1; 70.4; 68.7; 68.1; 20.9. HR-MALDI-MS: 555.2365 ($[M+Na]^+$, $C_{32}H_{36}NaO_7^+$; calc. 555.2359).

Pent-4-enyl 2,3,6-Tri-O-*benzyl-β*-D-*galactofuranoside* (**5c**). The ring opening with pent-4-en-1-ol (134 mg, 1.6 mmol) afforded 130 mg (81%) of **5c*α*** and **5c*β*** (*α*/*β* 45 : 55). TLC (AcOEt/hexane 2 : 5): R_f 0.45. Selected data for **5c*β***: $[\alpha]_D = -20.6$ (*c* = 2.2, $CHCl_3$). IR ($CHCl_3$) 2921, 1747, 1263, 1102. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.78 (*d*, *J* = 7.2, 2 H); 7.65 (*d*, *J* = 7.5, 2 H); 7.43–7.27 (*m*, 19 H); 5.91–5.75 (*m*, 1 H); 5.25 (*dt*, *J* = 6.9, 4.5, 1 H); 5.08–4.97 (*m*, 3 H); 4.62–4.48 (*m*, 6 H); 4.42–4.39 (*m*, 2 H); 4.29–4.24 (*m*, 2 H); 4.05 (*dd*, *J* = 3.6, 1.5, 1 H); 3.97 (*dd*, *J* = 7.2, 3.3, 1 H); 3.78–3.67 (*m*, 3 H); 3.43 (*dt*, *J* = 9.9, 6.6, 1 H); 2.17–2.10 (*m*, 2 H); 1.75–1.66 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.8; 143.3; 143.2; 141.1; 138.0; 137.7; 137.4; 137.3; 128.3; 128.2; 127.9; 127.8; 127.7; 127.5; 127.4; 127.0; 125.2; 119.9; 114.8; 105.9; 88.2; 83.0; 79.0; 75.1; 73.1; 72.3; 72.1; 70.0; 68.7; 67.0; 46.7; 30.3; 28.8. HR-MALDI-MS: 763.3260 ($[M+Na]^+$, $C_{47}H_{48}NaO_8^+$; calc. 763.3247).

Octyl 5-O-*Acetyl-2,3,6-tri*-O-*benzyl-β*-D-*galactofuranoside* (**5d**). The ring opening with octan-1-ol (326 mg, 2.5 mmol) and the protection at 5-*O* afforded 119 mg (44%) of **5d*α*** and **5d*β*** (*α*/*β* 47 : 53). TLC (AcOEt/hexane 1 : 5): R_f 0.30. Selected data for **5d*β***: $[\alpha]_D = -10.7$ (*c* = 0.6, $CHCl_3$). IR (neat): 2926, 1744, 1455, 1237. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37–7.26 (*m*, 15 H); 5.36 (*td*, *J* = 6.0, 3.2, 1 H); 4.58–4.45 (*m*, 6 H); 4.20 (*dd*, *J* = 7.2, 3.2, 1 H); 3.99 (*dd*, *J* = 3.2, 1.6, 1 H); 3.82 (*dd*, *J* = 7.2, 3.2, 1 H); 3.69–3.63 (*m*, 3 H); 3.38 (*dt*, *J* = 6.4, 6.4, 1 H); 2.03 (*s*, 3 H); 1.57 (br. *s*, 2 H); 1.28 (br. *s*, 10 H); 0.89 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR (100 MHz, $CHCl_3$): 170.2; 137.9; 137.5; 137.4; 128.3; 128.2; 128.2; 128.2; 127.8; 127.8; 127.6; 127.5; 127.4; 105.9; 88.3; 83.0; 79.1; 73.1; 72.4; 72.1; 70.5; 68.8; 67.8; 32.0; 29.7; 29.5; 29.4; 26.3; 22.8; 21.1; 14.2. HR-FAB-MS: 605.3477 ($[M+H]^+$, $C_{37}H_{47}O_7^+$; calc. 605.3478).

Octyl 5-O-*Acetyl-2,3,6-tri*-O-*benzyl-β*-D-*galactofuranosyl-(1 → 6)-2,3,5-tri*-O-*benzyl-β*-D-*galactofuranoside* (**5e**). The ring opening of **2a** with octyl 2,3,5-tri-*O*-benzyl-*β*-D-galactofuranoside (112 mg, 0.20 mmol) and the sequential protection of 5-*O* with Ac_2O and pyridine afforded 63 mg (59%) of **5e*α*** and **5e*β*** (*α*/*β* 26 : 74). TLC (AcOEt/hexane 1 : 5): R_f 0.25. Selected data for **5e*β***: $[\alpha]_D = -47.8$ (*c* = 1.0, $CHCl_3$). IR (neat): 2926, 1744, 1454, 1237. ^{1}H-NMR (400 MHz, $CHCl_3$): 7.35–7.21 (*m*, 30 H); 5.08 (*s*, 1 H); 5.04 (*s*, 1 H); 4.73 (*d*, *J* = 11.4, 1 H); 4.62–4.40 (*m*, 10 H); 4.29 (*d*, *J* = 11.7, 1 H); 4.12 (*dd*, *J* = 6.3, 3.3, 1 H); 4.08–4.02 (*m*, 1 H); 4.01–3.98 (*m*, 3 H); 3.88 (*dd*, *J* = 9.9, 3.0, 1 H); 3.78 (*dt*, *J* = 7.8, 3.0, 1 H); 3.72–3.62 (*m*, 3 H); 3.53–3.51 (*m*, 2 H); 3.35 (*dt*, *J* = 9.6, 6.9, 1 H); 2.39 (*d*, *J* = 6.0, 1 H); 1.52 (br. *s*, 2 H); 1.26 (br. *s*, 10 H); 0.87 (br. *t*, *J* = 6.9, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 170.2; 138.3; 137.8; 137.7; 137.6; 137.5; 137.2; 128.3; 128.24; 128.22; 128.20; 128.16; 128.1; 128.0; 127.9; 127.8; 127.7; 127.62; 127.55; 127.45; 127.39; 106.5; 105.8; 88.5; 88.1; 83.2; 82.9; 80.6; 79.5; 72.1; 72.0; 71.9; 70.5; 69.1; 68.8; 67.7; 31.9; 29.6; 29.5; 26.3; 22.8; 21.1; 14.2. HR-FAB-MS: 1037.5439 ($[M+H]^+$, $C_{64}H_{78}O_{12}^+$; calc. 1037.5415).

Computational Details. The geometries of the model compounds were fully optimized with GAUSSIAN03 [13] at the density functional level of theory (B3LYP) [11] by use of the split-valence 6-311G(d) basis set [12] for C, H, and O. Frequency calculations were carried out to characterize the nature of the stationary points. The electronic structures were analyzed by Natural Bond Orbital (NBO) analysis.

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Received July 22, 2005