Chemistry of 4,6-*O*-Benzylidene-D-glycopyranosyl Triflates: Contrasting Behavior between the Gluco and Manno Series

David Crich* and Weiling Cai

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061

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Activation of either anomer of *S*-phenyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thia-D-glucopyranoside with triflic anhydride in dichloromethane at −78 °C in the presence of 2,6-di-*tert*-butyl-4-methylpyridine affords a highly active glycosylating species which, on addition of alcohols, provides α-glucosides with high selectivity. This selectivity stands in stark contrast to the analogous mannopyranoside series, which affords the *β*-mannosides with excellent selectivity under the same conditions. Low-temperature NMR experiments support the notion that a glucosyl triflate is formed in the initial activation step. Possible reasons for the diverging stereoselectivity in the gluco and manno series are discussed.

Introduction

We have recently developed a direct method for the formation of *β*-mannopyranosides. The protocol consists of activation of 4,6-*O*-benzylidene-D-mannopyranosyl sulfoxides, protected with nonparticipating groups at the 2- and 3-positions, at low temperature in dichloromethane solution with triflic anhydride in the presence of the non-nucleophilic base 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP), followed by addition of the glycosyl acceptor.[1−4] In this extension of Kahne's sulfoxide method[5−7] the key intermediate is an α-mannosyl triflate which is displaced S_N2-wise by the nucleophile to give the *β*-mannoside.[8] In subsequent work we also showed that 4,6-benzylidene protected mannosyl thioglycosides could be rapidly transformed into α-mannosyl triflates by treatment with benzenesulfenyl triflate in dichloromethane at low temperature and that very high ratios of *β*- to α-mannosides are then obtained on addition of the acceptor alcohol.[1,2] The success of both methods depends critically on the presence of the 4,6-benzylidene group which, we believe,[8] serves to torsionally disarm[9] the mannosyl triflate with respect to formation of the α-selective oxacarbenium ion. We reasoned that extension of this chemistry to the 4,6-benzylidene glucopyranose series should permit the formation of *β*-glucosides without the need for stereodirecting, participating protecting groups at the 2-position. Here, we report that, contrary to our expectations, the use of 2,3-di-*O*-benzyl-4,6-benzylidene protected glucopyranosyl sulfoxides leads with excellent selectivity to the formation of α-glucosides.

In a classical glycosyl strategy, involving coupling of electrophilic and nucleophilic partners, the formation of *β*-glucopyranosides is typically achieved through the use of glucosyl donors protected by esters at the O-2 position, which are capable of neighboring group participation.[10] This requirement, which obviously does not apply to nonclassical strategies such as the alkylation of anomeric alkoxides[11] and the opening of 1,2-anhydropyranoses as in Danishefsky's glycal assembly method,[12,13] holds true for all types of glycosyl donor. Indeed, in their initial publication on the sulfoxide method, Kahne and co-workers reported that the tetra-*O*-pivaloyl protected sulfoxide **1** gave excellent *β*-selectivity whereas its tetrabenzyl counterpart **2** was moderately α-selective.[5] In the course of our work on *β*-mannosylation we noted the importance of the 4,6-benzylidene protecting group. Thus, donors **3** and **4** gave excellent yields of *β*-mannosides under the typical conditions whereas **5** was much less selective. We explained this disparity in terms of the 4,6-benzylidene group stabilizing the intermediate α-triflate **6** with respect to formation of the oxacarbenium ion **7** whose sofa conformation imposes torsional strain on the second ring.[8,9] In reality, on the NMR time scale in CD_2Cl_2 solution at −78 °C, the oxacarbenium ions have no observable lifetime and the effect is more one of shifting the triflate/ion pair equilibrium so far toward the covalent triflate that Curtin−Hammett type kinetic schemes[14] going via the ion pair are not viable.[8] On this basis it seemed logical that an α-glucosyl triflate **8**, with its 4,6-benzylidene protecting group, would likewise be stabilized with respect to oxacarbenium ion (**9**) formation and so would permit highly selective *β*-glucoside formation without the requirement for a participating ester protecting group.

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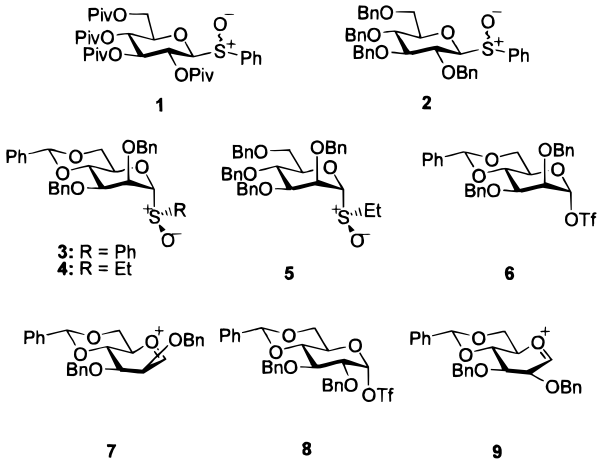
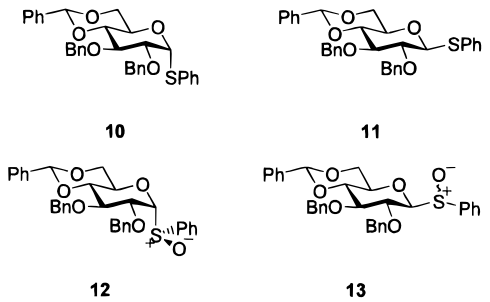


Results and Discussion

We began with the preparation of the α- and *β*-thioglucosides **10** and **11** according to literature protocols. These were oxidized in high yields to the corresponding sulfoxides **12** and **13**. As expected on the basis of



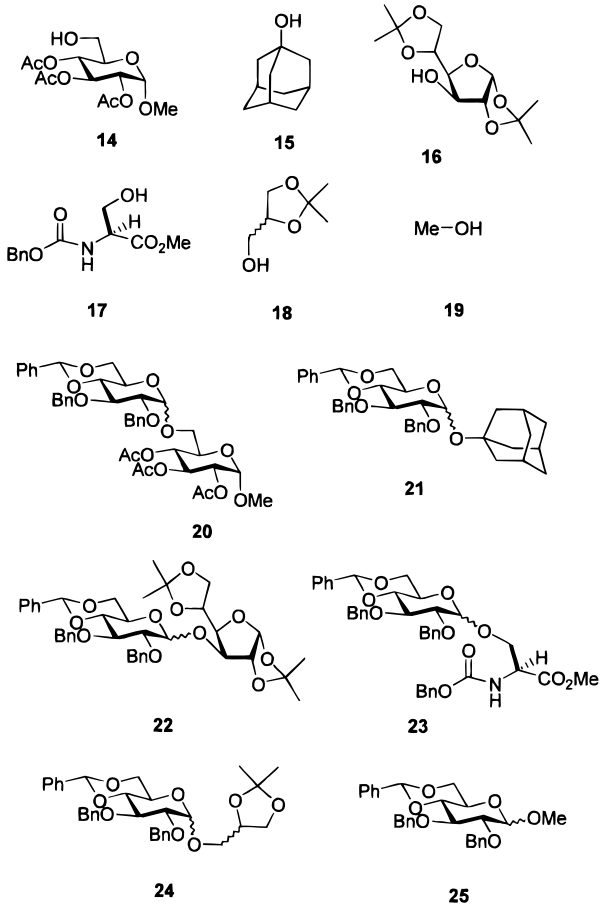
precedent, the *β*-anomer gave a mixture of sulfoxides whereas the α-anomer gave a single diastereomer, which we assign, by analogy to the crystallographically established mannoside series,[15] as the S_R epimer. This selectivity arises because of the conformation imposed on the aglyconic bond by the exo-anomeric effect and which sterically differentiates the prochiral faces of the thioglycoside to a much greater extent in the axial series.[15]

A series of coupling reactions were carried out with the results set out in Table 1. Contrary to our expectations, with the exception of the use of methanol as acceptor, these reactions were extremely α-selective. This was the case irrespective of whether the couplings were conducted with prior low-temperature activation of a thioglycosyl donor **10** or **11** with PhSOTf, or with a sulfoxide donor **12** or **13**, using activation by triflic anhydride. Similarly, excellent α-selectivity was obtained independent of the anomeric stereochemistry of the donor employed. A further example, involving the coupling of sulfoxide **13** to the residual hydroxyl group of allyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside, appeared recently in the literature and was reported to be completely α-selective.[16] As noted, the exception to the rule involved the use of methanol as glycosyl acceptor when moderate *β*-selectivity was repeatedly obtained.

To probe the nature of the reactive intermediate in the above glucosylation reactions, a CD_2Cl_2 solution of sulfoxide **12** and DTBMP was cooled to −78 °C and its ^{1}H NMR spectrum recorded before addition of cold (−78 °C) Tf_2O. The ^{1}H NMR spectrum, recorded within minutes of adding the anhydride, showed complete consumption of the sulfoxide and formation of one very major new glucoside. This species was most easily characterized at −78 °C by its very distinct anomeric proton resonance: a doublet at δ 6.3 with ^3J = 3.5 Hz. In the ^{13}C NMR spectrum the anomeric carbon was located at δ 100.6. By analogy with our work in the mannose series,[8] and from consideration of the coupling constant, we assign this intermediate as the α-glucosyl triflate **8**. In a continuation of this NMR experiment, the probe was gradually warmed, with acquisition of an ^{1}H NMR spectrum every 10 °C until decomposition of **8** occurred. This took place between +7 and +17 °C and led to the relatively clean formation of a new species, identified as the glycal **26**, which was subsequently isolated in 88% yield. Exactly analogous results were obtained for the anomeric sulfoxide **13**.

Table 1. Coupling Reactions with 4,6-Benzylidene Protected Glucosyl Donors

donor	acceptor	coupling reagent	product	% yield	α:*β* ratio
10	**14**	PhSOTf	**20**	98	>95:5
10	**15**	PhSOTf	**21**	87	>95:5
10	**16**	PhSOTf	**22**	70	>95:5
10	**17**	PhSOTf	**23**	85	>95:5
11	**16**	PhSOTf	**22**	80	>95:5
12	**18**	Tf_2O	**24**	89	>95:5
12	**19**	Tf_2O	**25**	72	1:7.5
13	**15**	Tf_2O	**24**	63	>95:5
13	**19**	Tf_2O	**25**	65	1:6



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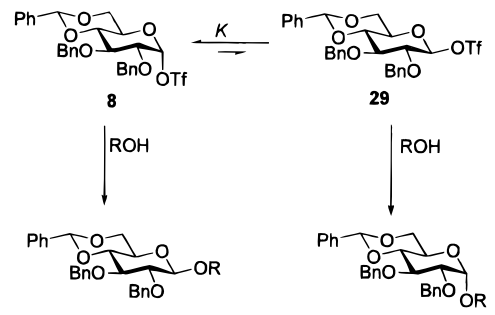
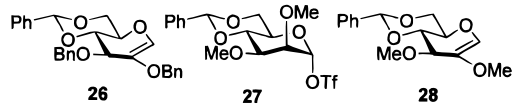
Scheme 1



This mode of decomposition mimics that of the α-mannosyl triflate **27**, generated from the sulfoxide, which decomposed to glycal **28**, with the exception that the



decomposition of **27** began at the considerably lower temperature of −10 °C. If, as we have previously suggested,[8] the relative decomposition temperatures of two anomeric triflates can be taken as a measure of the differing covalent triflate/oxacarbenium ion equilibrium constants, then we conclude that in the glucose series the equilibrium favors the covalent triflate even more than in the mannose series. Clearly, this is not in accord with any hypothesis in which the formation of the α-glucosides observed preparatively takes place by a Curtin−Hammett kinetic scheme with the oxacarbenium ion **9** as the true reactive species. We therefore are led to the conclusion that we are observing a dynamic system in which the α-triflate (**8**) is in equilibrium with its less stable but more reactive *β*-anomer (**29**) and that the rate and equilibrium constants are such as to provide preferentially the α-glucoside (Scheme 1). This type of system, which derives its α-selectivity from the higher reactivity of the less stable *β*-triflate, is by no means new. The preferential formation of tetra-*O*-acetyl α-glucosides from α-acetobromoglucose in the presence of added bromide ion was first described by Lemieux and attributed to the enhanced reactivity of the higher energy *β*-bromide.[17,18] Why then is such a situation not seen in the mannose series? We suggest that the difference lies in the α-triflate/*β*-triflate equilibrium constants, i.e., in the magnitude of the anomeric effect. In effect, the anomeric effect is larger in mannose than in glucose: thus it was noted many years ago that whereas the equilibration of methyl tetramethyl α- and *β*-glucosides in 5% methanolic HCl gives a 3:1 α:*β* mixture, the corresponding experiment in the mannose series provides the α-methyl mannoside almost quantitatively.[19] Mannose itself mutarotates to an approximately 69:31 α:*β* mixture whereas glucose reaches equilibrium at a 37:63 α:*β* mixture;[17] pentaacetyl α-mannopyranose is favored over its *β*-anomer by 1.69 kcal.mol^{-1} whereas in the glucose series the equilibrium only favors the α-anomer by 1.10 kcal.mol^{-1}.[17] Thus it seems perfectly reasonable that the more significant preference for the α-triflate in the mannose series shuts off any Curtin−Hammett kinetic scheme leading to the α-glycoside via the minor *β*-triflate, whereas the reduced anomeric effect in the glucose series permits such a scheme to operate. In this respect we note that although the low-temperature experiment described above indicates the preferential formation of only one triflate, the combination of relatively poor signal-to-noise ratio and resolution is such that 5% of a second anomer would likely not be seen.

A final problem concerns the inverted selectivity observed on the use of methanol as glycosyl acceptor. Here, with this much smaller, less hindered nucleophile, we can only suggest that the direct displacement of the α-triflate is so rapid as to override any indirect *β*-glucosidation according to Scheme 1.[20] We note that Schuerch and co-workers had previously made a related observation wherein a series of 4,6-di-*O*-(*N*-phenylcarbamoyl)-2,3-di-*O*-benzylgalactopyranosyl-1α-sulfonates (especially the triflate) gave considerably higher *β*-selectivity with methanol than on coupling to other alcohols.[21,22]

Experimental Section[23]

***S*-Phenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thia-α-D-glucopyranoside (10) and *S*-Phenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thia-*β*-D-glucopyranoside (11).** α-D-Glucose pentaacetate (20.0 g, 51 mmol) was dissolved in dichloromethane (100 mL) followed by the addition of PhSH (4.5.0 mL, 60 mmol) and $SnCl_4$ (4.2 mL, 35 mmol). The reaction mixture was heated to reflux under Ar overnight before it was quenched by addition of saturated aqueous $NaHCO_3$ (250 mL). The aqueous layer was extracted by EtOAc (3 × 75 mL), and the combined organic layers were washed with brine and dried over Na_2SO_4. The crude product obtained on removal of the solvent was treated with NaOH (5% aq, 50 mL) to remove the excess PhSH. A white crystalline solid (15.4 g, 68%, a 1/2 α/*β* mixture) was obtained by recrystallization of the residue from EtOAc/hexane (1/10). This white crystalline solid (15.0 g, 34.0 mmol) was dissolved in MeOH (120 mL) and treated at room temperature with a catalytic amount of Na. After completion (2 h, TLC), the reaction mixture was neutralized by DOWEX H⊕ and concentrated to give the tetrahydroxyl intermediate (9.2 g, 100%), which was further protected by treatment with $PhCH(OMe)_2$ (9.3 mL, 62 mmol) refluxing in THF (100 mL) for 4 h in the presence of CSA (0.35 g, 1.0 mmol). The reaction was quenched by addition of saturated aqueous $NaHCO_3$ (150 mL), and the aqueous layer was extracted by EtOAc (3 × 70 mL). The combined organic layers were washed with brine and dried over Na_2SO_4, then concentrated. The residue obtained was recrystallized in EtOAc/Hexane (1/10) to give *S*-phenyl 4,6-*O*-benzylidene-1-deoxy-1-thiaglucopyranoside (6.6 g, 66%). This substance (3.6 g, 10 mmol) was further treated with NaH (2.9 g, 59.0 mmol) and benzyl bromide (4.6 mL, 39 mmol) in THF (75 mL) at reflux for 4 h under Ar. After addition of saturated aqueous $NaHCO_3$, the aqueous phase was extracted by EtOAc (3 × 30 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by chromatography on silica gel, eluting with EtOAc/Hexane (1/8), to give compounds **10** (1.6 g, 28%) and **11** (3.0 g, 56%). **10:** $[\alpha]_D = -20.0$ ($c = 1.4$, $CHCl_3$); ^{1}H NMR, δ: 7.44 (m, 20H), 5.61 (d, $J = 5.2$ Hz, 1H), 5.58 (s, 1H), 4.94 and 4.87 (2d, $J = 11.1$ Hz, 2H), 4.82 and 4.76 (2d, $J = 12.0$ Hz, 2H), 4.40 (m,

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1H), 4.20 (dd, J = 4.9, 10.3 Hz, 1H), 3.99 (t, J = 9.1 Hz, 1H), 3.92 (m, 1H), 3.69 (m, 2H); ^{13}C NMR, δ: 138.8, 137.8, 137.5, 132.2, 129.2, 129.1, 128.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.6, 126.2, 101.5, 88.0, 81.9, 79.4, 79.0, 75.5, 73.2, 68.9, 63.6. Anal. Calcd for $C_{33}H_{32}O_5S$: C, 73.31; H, 5.97; Found: C, 73.11; H, 5.96. **11:**[16] ^{1}H NMR, δ: 7.45 (m, 20H), 5.60 (s, 1H), 4.94 (d, J = 11.1 Hz, 1H), 4.85 (m, 4H), 4.41 (dd, J = 5.0, 12.6 Hz, 1H), 3.85 (m, 2H), 3.74 (t, J = 9.2 Hz, 1H), 3.54 (m, 2H).

General Procedure for Oxidation of Thioglycosides to Sulfoxides. An aqueous solution (20 mL) of Oxone (0.62 g, 1 mmol) was added to a stirred solution of **10** or **11** (1.08 g, 2 mmol) in THF (20 mL) at 0 °C. After stirring for 3−5 h, when TLC indicated complete consumption of the substrate, the reaction mixture was diluted with EtOAc (30 mL), and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were evaporated and the residue was purified by chromatography on silica gel eluting with EtOAc /hexane (1:3).

***S*-Phenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thia-α-D-glucopyranoside Sulfoxide (12).** $[\alpha]_D$ = −64 (c = 2.1, $CHCl_3$); ^{1}H NMR, δ: 7.45 (m, 20H), 5.50 (s, 1H), 4.81 and 4.68 (2d, J = 10.8 Hz, 2H), 4.74 (s, 2H), 4.63 (d, J = 3.8 Hz, 1H), 4.29 (t, J = 4.0 Hz, 1H), 4.09 (m, 3H), 3.71 (dd, J = 7.2, 9.7 Hz, 1H), 3.47 (t, J = 9.6 Hz, 1H); ^{13}C NMR, δ: 142.1, 137.3, 137.1, 131.6, 129.2, 129.1, 128.6, 128.5, 128.4, 128.3, 128.1, 126.2, 125.8, 101.4, 95.0, 81.6, 78.1, 77.2, 73.7, 73.5, 69.0, 66.3. Anal. Calcd for $C_{33}H_{32}O_6S$: C, 70.06; H, 5.87. Found: C, 69.53; H, 5.55.

***S*-Phenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-1-thia-β-D-glucopyranoside Sulfoxide (13).**[16] $[\alpha]_D$ = −130 (c = 1.3, $CHCl_3$); ^{1}H NMR, δ: 7.42 (m, 20H), 5.52 (s, 1H), 5.04 and 4.95 (2d, J = 10.6 Hz, 2H), 4.98 and 4.82 (2d, J = 10.5 Hz, 2H), 4.15 (t, J = 9.2 Hz, 1H), 4.02 (dd, J = 4.8, 11.6 Hz, 1H), 4.01 (d, J = 9.8 Hz, 1H), 3.91 (t, J = 9.2 Hz, 1H), 3.74 (t, J = 9.7 Hz, 1H), 3.28 (m, 1H); ^{13}C NMR, δ: 139.6, 138.4, 137.7, 137.2, 131.3, 129.2, 129.1, 128.7, 128.6, 128.4, 128.3, 127.9, 126.1, 125.6, 125.3, 101.4, 93.8, 82.8, 81.3, 76.3(2), 75.1, 71.1, 68.2.

General Protocol for Coupling with Sulfoxides 12 or 13. Sulfoxide **12** or **13** (56 mg, 0.1 mmol) and DTBMP (41 mg, 0.2 mmol) were dissolved in dry dichloromethane (3 mL) under Ar and cooled to −78 °C, followed by the rapid addition of Tf_2O (18 μL, 0.12 mmol). After 5−10 min the acceptor (0.2 mmol) in dichloromethane (2 mL) was then added dropwise. After stirring for a further 2−3 h, the reaction was quenched at −78 °C by adding saturated aqueous $NaHCO_3$ (0.5 mL). The resulting mixture was diluted with EtOAc (20 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography eluting with EtOAc/hexane (1/5) or by preparative TLC.

General Protocol for Coupling with Thioglucosides 10 or 11. PhSCl (42 mg, 0.3 mmol) in dichloromethane (1 mL) was added slowly to AgOTf (91 mg, 0.4 mmol) in dichloromethane (2 mL) containing pulverized 3A MS (20 mg) at −78 °C, followed by stirring for 5 min before a solution of **10** or **11** (56 mg, 0.01 mmol) and DTBMP (41 mg, 0.2 mmol) in dichloromethane (1 mL) was added dropwise. After stirring for 15 min, the acceptor (0.2 mmol) in dichloromethane (1 mL) was added. After stirring for 2−3 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ (1 mL) before it was warmed to room temperature. The reaction mixture then was diluted with EtOAc (20 mL) and was filtered over Na_2SO_4. The residue obtained on removal of the solvent was purified by chromatography column eluting with EtOAc/hexane (1/5).

Methyl 2,3,4-Tri-*O*-acetyl-6-*O*-[2,3-di-*O*-benzyl-4,6-benzylidene-α-D-glucopyranosyl]-α-D-glucopyranoside (20). $[\alpha]_D$ = +60.8 (c = 2.3, $CHCl_3$); ^{1}H NMR, δ: 7.37 (m, 15H), 5.53 (s, 1H), 5.48 (t, J = 9.9 Hz, 1H), 4.97 (m, 4H), 4.87 (d, J = 3.3 Hz, 1H), 4.73 (d, J = 3.6 Hz, 1H), 4.22 (dd, J = 3.9, 10.2 Hz, 1H), 3.95, (m, 3H), 3.68 (m, 7H), 3.37 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H); ^{13}C NMR, δ: 170.2, 169.9, 138.8, 138.4, 137.6, 128.6, 128.4, 128.1, 127.7, 126.2, 101.4, 98.3, 96.7, 82.3, 79.2, 76.0, 75.3, 73.5, 71.1, 70.5, 69.5, 69.0, 68.3, 67.8, 62.7, 56.5, 20.8(3). Anal. Calcd for $C_{40}H_{46}O_{14}\cdot H_2O$: C, 62.49; H, 6.29. Found: C, 62.65; H, 6.24.

1-Adamantanyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (21). $[\alpha]_D$ = +2.6 (c = 1.7, $CHCl_3$); ^{1}H NMR, δ: 7.45 (m, 15H), 5.56 (s, 1H), 5.23 (d, J = 3.6 Hz, 1H), 4.92 (d, J = 11.2, 1H), 4.84 (d, J = 11.2, 1H), 4.77 (d, J = 12.0 Hz, 1H), 4.70 (d, J = 12.0 Hz, 1H), 4.23 (dd, J = 9.1, 10.2 Hz, 1H), 4.10 (m, 2H), 3.67 (t, J = 10.2 Hz, 1H), 3.59 (t, J = 9.3 Hz, 1H), 3.52 (dd, J = 3.6, 9.3 Hz, 1H), 1.95 (m, 15H); ^{13}C NMR, δ: 139.2, 138.8, 138.7, 138.6, 137.8, 137.7, 132.5, 129.3, 128.9, 128.5, 128.4, 128.2, 128.0, 127.9, 127.6, 126.7, 126.2, 101.3, 91.2, 82.9, 79.6, 78.8, 75.4, 75.0, 73.4, 69.4, 62.2, 42.7, 36.4, 30.8. Anal. Calcd for $C_{37}H_{42}O_6\cdot H_2O$: C, 73.97; H, 7.38. Found: C, 73.56; H, 7.21.

3-*O*-(2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (22). $[\alpha]_D$ = +5.8 (c = 0.8, $CHCl_3$); ^{1}H NMR, δ: 7.38 (m, 15H), 5.92 (d, J = 3.6 Hz, 1H), 5.59 (s, 1H), 5.25, (d, J = 3.6 Hz, 1H), 4.94 (d, J = 11.4 Hz, 1H), 4.83 (d, J = 11.4 Hz, 1H), 4.79 (s, 2H), 4.59 (d, J = 3.6 Hz, 1H), 4.50 (m, 1H), 4.34 (dd, J = 3.6, 9.8 Hz, 1H), 4.25 (d, J = 2.4 Hz, 1H), 4.02 (m, 4H), 3.85 (dd, J = 4.5, 9.6 Hz, 1H), 3.78 (m, 2H), 3.59 (dd, J = 4, 9.3 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.32 (s, 3H), 1.26 (s, 3H); ^{13}C NMR, δ: 137, 136, 134, 129, 128, 127.8, 127.6, 125.8, 114, 108.5, 105.1, 101.0, 98.7, 84.0, 82.1, 81.1, 80.2, 79.3, 78.0, 75.1, 73.6, 72.0, 68.8, 67.0, 63.3, 27.0, 26.8, 26.3, 25.4. Anal. Calcd for $C_{39}H_{46}O_{11}$: C, 67.81; H, 6.71. Found: C, 67.86; H, 6.71.

***N*-Benzyloxycarbonyl-*O*-[2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl]-L-serine Methyl Ester (23).** $[\alpha]_D$ = +8.3 (c = 1.2, $CHCl_3$); ^{1}H NMR, δ: 7.35 (m, 20H), 5.83 (d, J = 8.4 Hz, 1H), 5.56 (s, 1H), 5.14 (s, 2H), 4.85 (m, 5H), 4.79 (d, J = 4.5 Hz, 1H), 4.55 (m, 1H), 4.28 (dd, J = 4.5, 9.9 Hz, 1H), 3.98 (m, 3H), 3.72 (m, 3H), 3.54 (dd, J = 4.0, 9.3 Hz, 1H); ^{13}C NMR, δ: 170.6, 138.9, 138.3, 137.5, 136.2, 129.0, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 126.2, 101.4, 99.2 ($^1J_{CH}$ = 168.9 Hz), 82.1, 79.3, 78.4, 75.4, 73.5, 69.5, 68.9, 67.3, 63.1, 54.5, 52.8. Anal. Calcd for $C_{39}H_{41}NO_{10}$: C, 68.51; H, 6.04; N, 2.05. Found: C, 68.68; H, 6.40; N, 1.87.

(3,3-Dimethyl-2,4-dioxolanyl)methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (24). A ∼1:1 diastereomeric mixture at the aglycone. ^{1}H NMR, δ: 7.45 (m, 15H), 5.60 (d, J = 4.1 Hz, 1H), 4.85 (m, 4H), 4.69 (dd, J = 5.5, 12.0 Hz, 1H × 1/2,), 4.55 (t, J = 6.7 Hz, 1H × 1/2), 4.32 (m, 2H), 4.05 (m, 2H), 3.75 (m, 7H), 3.48 (m, 2H), 1.42 (d, J = 3.3, 3H), 1.35 (s, 3H); ^{13}C NMR, δ: 138.6, 138.1, 137.3, 128.8, 128.3, 128.1, 127.9, 125.9, 109.4, 104.2, 101.1, 98.3, 81.9, 81.3, 79.2, 78.3, 75.2, 75.0, 74.3, 73.4, 71.3, 70.7, 66.8, 65.9, 62.5, 26.8, 25.2. Anal. Calcd for $C_{33}H_{38}O_8$: C, 70.44; H, 6.80. Found: C, 69.97, H, 6.86.

Methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (25α).[24] ^{1}H NMR, δ: 7.34 (m, 15H), 5.55 (s, 1H), 4.91 and 4.69 (2d, J = 12.0 Hz, 2H), 4.86 and 4.82 (2d, J = 6.9 Hz, 2H), 4.60 (d, J = 3.6 Hz, 1H), 4.26 (dd, J = 4.5, 10. 1 Hz, 1H), 4.05 (t, J = 9.3 Hz, 1H), 3.81 (dd, J = 4.7, 9.9 Hz, 1H), 3.71 (t, J = 10.2 Hz, 1H), 3.60 (t, J = 9.3 Hz, 1H), 3.55 (dd, J = 3.9, 9.2 Hz, 1H), 3.40 (s, 3H).

Methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (25β).[25] ^{1}H NMR, δ: 7.36 (m, 15H), 5.58 (s, 1H), 4.86 (m, 4H), 4.43 (d, J = 7.7 Hz, 1H), 4.37 (dd, J = 5.1, 10.5 Hz, 1H), 3.73 (m, 3H), 3.59 (s, 3H), 3.45 (m, 2H).

Monitoring of the Formation and Decomposition of Triflate 8 by Variable Temperature NMR Spectroscopy. Isolation of 1,5-Anhydro-4,6-*O*-benzylidene-2,3-di-*O*-benzyl-D-arabino-hex-1-enitol (26). The sulfoxide **12** or **13** (5.6 mg, 0.01 mmol) was mixed with DTBMP (4.5 mg, 0.02 mmol) and dissolved in dichloromethane-d_2 (0.5 mL) in an NMR tube under Ar, and the ^{1}H NMR spectrum was recorded at −78 °C. Precooled Tf_2O (2 μL, 0.012 mmol) was then injected at −78 °C and the tube shaken before it was reinserted into the cold (−78 °C) probe. A ^{1}H NMR spectrum, taken immediately, at the same temperature showed the sulfoxide to have been consumed in favor of one very major new substance characterized by a new anomeric doublet at δ 6.3 (d, J = 3.5 Hz). In the

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^{13}C NMR spectrum the anomeric carbon resonated at δ 100.6. Subsequently the temperature of the probe was raised in 10 °C steps with monitoring by ^{1}H NMR. Decomposition of the triflate occurred between 280 and 290 K giving one very major species, which was identified as the hexenitol **26**. $[\alpha]_D = +9.3$ ($c = 1.5$, $CHCl_3$); ^{1}H NMR, δ: 7.37 (m, 15H), 6.29 (s, 1H), 5.65 (s, 1H), 4.87 (s, 2H), 4.73 (s, 2H), 4.49 (dd, $J = 0.9$, 7.5 Hz), 4.36 (m, 2H), 4.08 (dd, $J = 7.3$, 9.9 Hz, 1H), 3.76 (m, 2H); ^{13}C NMR, δ: 139.7, 138.7, 137.4, 137.1, 136.8, 129.5, 129.1, 128.6, 128.4, 128.2, 127.7, 126.2, 102.6, 101.2, 80.0, 74.9, 73.6, 71.6, 69.2, 68.5, 52.4. Anal. Calcd for $C_{27}H_{26}O_5 \cdot 0.33H_2O$: C, 74.30; H, 6.10. Found: C, 74.27; H, 6.26.

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